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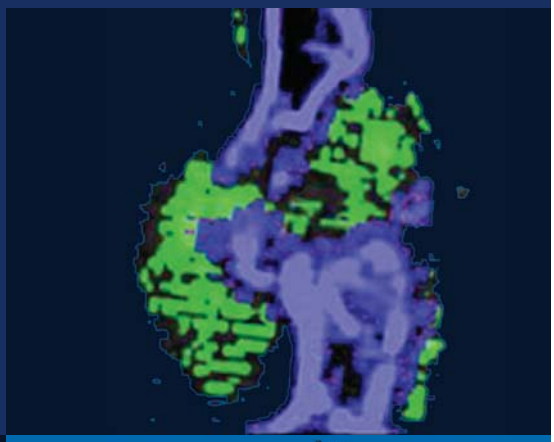

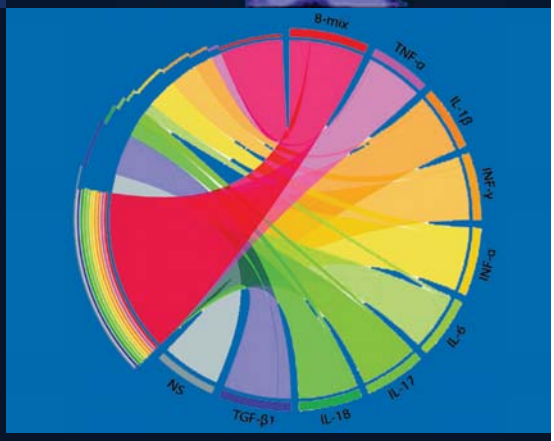

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Oral Presentations

Addressing the effect of Placebo, Nocebo and Contextual factors in RMDs

OP0001

"I WILL NEVER FORGET THE SHAME I FELT": A SURVEY TO PEOPLE WITH A RHEUMATIC DISEASE ABOUT INVALIDATION FROM HEALTH PROFESSIONALS AND OTHER PEOPLE

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Background: The term invalidation refers to the patients' perception that their medical condition is not recognised, either in denying, lecturing, not supporting or not acknowledging the condition. This may be the felt from health professionals themselves but also from family, friends, at work and in other social areas, imposing great suffering.[1] The European Alliance of Associations for Rheumatology (EULAR) has made efforts to raise awareness for the burden imposed by rheumatic and musculoskeletal conditions (RMDs) and promote the best quality of care, including recognition and psychosocial support. However, it is unclear how frequent and severe the problem remains nowadays.
Objectives: The aims of this national survey were: (i) to identify the levels of invalidation and lack of understanding felt by adults with RMDs from health professionals and other people, (ii) to investigate the relationship between invalidation, sociodemographic characteristics and disease; and (iii) to understand its impact on people's life and health outcomes.
Methods: An online survey was developed by the national health professionals in rheumatology and patients' organisations and opened between May and December of 2021. The questionnaire included demographic and disease information, the Illness Invalidation Inventory (3*I),[1] with additional questions in a Likert format and open questions for a detailed understanding of the phenomenon. The 3*I is composed of 8 items, measured from 1 (=never) to 5 (=very often), forming two factors: Discounting (mean of 5 items; lower scores indicating more discounting) and Lack of understanding (mean of 3 items; Higher scores representing higher lack of understanding).
Quantitative data were analysed using descriptive statistics. Associations were tested with a t-student and ANOVA one-way test (Bonferroni correction). Open responses were categorised using the content analysis technique, and themes were defined *a posteriori*.
Results: From the > 1500 responses obtained, 1410 responses were filled out completely (mean age of 46 years [SD=11], 95% females, 60% with FM, among which 59% were diagnosed in the last 5 years).
Invalidation was reported by 86% of the participants and 70% rated ≤5 on a scale from 0 (nothing) to 10 (totally) on feeling understood by other people. Invalidation was mostly felt from family (56%), health professionals (48%), friends (39%) and social environment (38%). The impact of this invalidation is mainly on the psychological well-being (58%), also reducing seeking health care (41%) and therapeutic adherence (17%), affecting work (41%), and to a less extent, (family) relations (31%).
Figure 1 shows the frequency of responses and means scores on the 3*I items and factors for participants with and without FM. The burden is greater for people with FM, which was statistically significant. People with higher education felt more discounting and more lack of understanding. No differences (p>0.05) were observed for gender or civil status.
Elucidative expressions of invalidation were shared, mostly by people with FM, encompassing their ability to work and need for social support, faking pain and treatment efficacy, and even intimacy aspects. These emotionally uncomfortable situations can be linked to lesser engagement with healthcare and disease management, and therefore, with worse health outcomes.
Conclusion: Invalidation remains a source of suffering, affecting well-being and health outcomes. Specific awareness and educational campaigns are needed to target this problem on different play-actors.

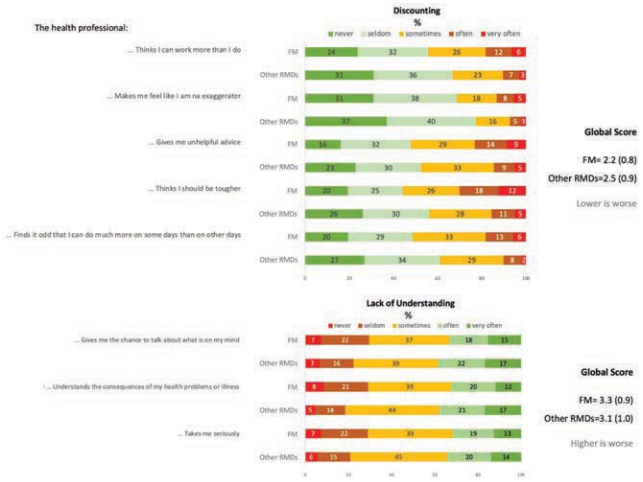

Figure 1. Percentages of responses per type of disease for the eight items of the Illness Invalidation Inventory.

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Bench to Bedside: The complement system in rheumatic diseases

OP0002

LOW COMPLEMENT LEVELS IN THE FIRST TRIMESTER PREDICT DISEASE FLARE IN SLE PREGNANCY: A NETWORK META-ANALYSIS ON 532 PATIENTS.

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Background: The complement system is a key-player in the pathogenesis of systemic lupus erythematosus (SLE); its decreases correlate with disease activity and precedes flare. Since synthesis of complement proteins increase during gestational course, it is debated whether complement levels exert a prognostic role in pregnant women with SLE.
Objectives: We performed a network meta-analysis to assess the prognostic role of complement in pregnant SLE women, to evaluate the possible role of complement fluctuations during pregnancies.
Methods: Data from available prospective studies (Jan 2002-Dec 2020) investigating pregnancies in at least 50 SLE patients, excluding miscarriages before 12 weeks, were pooled together. After a systematic literature search, corresponding authors of 19 retrieved studies meeting inclusion criteria were invited to contribute with additional data, including complement levels [6 months before pregnancy, at conception, 1st trimester (T1), 2nd trimester (T2), 3rd trimester (T3) and 3 months after delivery].
Results: A total of 532 SLE women from four eligible studies were included in the analysis [1-4]. Lupus Nephritis (LN) was diagnosed in 237 patients (44.5%) and Antiphospholipid Syndrome in 68 (12.8%). A total of 170 patients (32%) experienced a flare during pregnancy, defined as need of new Immunosuppressants or increase of prednisone > 9 mg/day.
Patients with LN had significantly lower mean levels of complement (C3 at conception; C3 at T1; C3 after 3 months of delivery; C4 at all timepoints except for C4 at T3). SLE patients who experienced flares during pregnancy had significantly lower mean levels of complement (all timepoints for both C3 and C4). Table 1 shows the mean C3 and C4 levels in different timepoints according to diagnosis and flare during pregnancy. The lowest levels of complement were observed in patients with a concomitant diagnosis of LN and presence of flare, particularly during the T1 (Figure 1). Nevertheless, both in LN and flare groups the lowest levels of C3 and C4 were documented at T1.

Table 1. Complement levels at the different timepoints according to diagnosis or presence of flare (bold results are statistically significant)

	Patients with LN (237)	Patients without LN (295)	Patients with Flare (170)	Patients without Flare (362)	Patients with LN and Flare (73)	Patients with LN and without Flare (164)
C3 6 months before pregnancy (mean ±SD)	90.7±18.6	94.1±25.2	**85.6±19.1**	**95.6±23.3**	**75 ±17.9**	**99.1±12.5**
C3 conception (mean ±SD)	**96.1±13.9**	**91.1±13**	**95.3±19.5**	**91.8±9.1**	97 ±21.6	95.6±7.1
C3 1st trimester (mean ±SD)	**84.6±32.2**	**98.4±14.1**	**78.3±22.8**	**100.5±20.7**	**56.8 ±19.9**	**97.2±28.7**
C3 2nd trimester (mean ±SD)	108.5±21	108.3±12.2	**94.16±13.4**	**115.7±12.3**	**87.5 ±10.9**	**118.6±16.8**
C3 3rd trimester (mean ±SD)	105.5±15.7	108.2±19.1	**98.97±18.6**	**111.4±16**	**98.1 ±12.6**	**109.1±15.8**
C3 3 months after delivery (mean ±SD)	**93.4±12**	**103.1±15.4**	**92.4±15.7**	**102.6±13.4**	**90.5 ±10.8**	**94.8±12.3**
C4 6 months before pregnancy (mean ±SD)	**15.7±5.5**	**14.1±2.8**	**11.8±3.9**	**16.5±3.3**	**10.5±3.4**	**18.4±4.2**
C4 conception (mean ±SD)	**15.4±4.1**	**13.9±2.8**	**13.3±3.2**	**15.7±3.4**	**11±1.3**	**17.8±3**
C4 1st trimester (mean ±SD)	**15±7.8**	**16.3±2.8**	**12.5±5.9**	**17.5±4.2**	**9.3±7.6**	**17.9±6.2**
C4 2nd trimester (mean ±SD)	**17.7±4.7**	**18.7±4.2**	**15.5±4.3**	**19.8±3.7**	**13.6±4.1**	**19.6±3.5**
C4 3rd trimester (mean ±SD)	17.8±4.4	17.5±5.1	**15.7±5.8**	**18.6±4**	**15.8±4.8**	**18.8±3.9**
C4 3 months after delivery (mean ±SD)	**16.2±4.3**	**19.8±6.9**	**14.9±3.9**	**20±6.4**	**13.3±3.1**	**17.6±4**

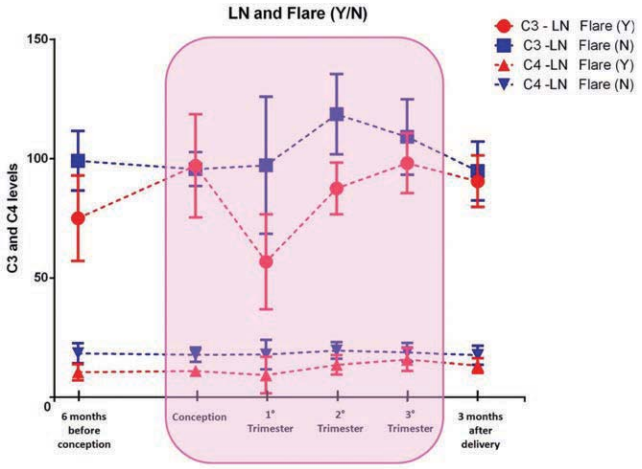

Figure 1. Complement Levels during time in patients with Lupus Nephritis and presence, or absence, of flare.

Conclusion: In this prospective large cohort of SLE patients low C3/C4 levels, particularly in T1, were associated with a higher frequency of flare. Lowering levels of complement, especially in T1, even within normal range might alert the treating clinicians in predicting disease course and consequently avoid flares, especially in LN.

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Breaking the barriers: gut, lung and skin in arthritis pathogenesis

OP0003

DOES IMMUNOSUPPRESSIVE THERAPY IMPROVE GASTROINTESTINAL SYMPTOMS IN PATIENTS WITH SYSTEMIC SCLEROSIS?

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Background: The gastrointestinal (GI) tract is frequently affected in systemic sclerosis (SSc), leading to considerable morbidity and even mortality. While important progress has been made in the last years regarding treatment of SSc, there is no disease-modifying treatment available for SSc-related GI involvement.

Objectives: We aimed to identify, in an observational cohort study of real-life patients with SSc, an association between immunosuppressive therapy and the severity of GI symptoms, measured by the University of California at Los Angeles / Scleroderma Clinical Trial Consortium Gastro-Intestinal Tract instrument 2.0 (UCLA GIT 2.0).

Methods: We selected patients from our EUSTAR centre who met the 2013 ACR/EULAR classification criteria for SSc and had at least two visits with completed UCLA GIT 2.0 questionnaires, with an interval of 12±3 months between visits. We defined the first visit with a completed UCLA GIT 2.0 questionnaire as baseline visit. Immunosuppressive therapy was defined as exposure for at least 6 months between the two visits to at least one of the following drugs, regardless of indication: mycophenolate mofetil (MMF), cyclophosphamide, methotrexate, azathioprine, leflunomide, glucocorticoids (>10mg/d prednisone-equivalent), rituximab, tocilizumab, and abatacept. The study outcome was the UCLA GIT 2.0 score at the follow-up visit. We performed multivariable linear regression with this outcome as dependent variable and immunosuppressive therapy during follow-up, immunosuppressive therapy before baseline, baseline UCLA GIT 2.0 score and several baseline parameters selected by clinical judgment as potentially influencing GI symptoms, as independent variables. Multiple imputation was implemented to handle missing values.

Results: We included 209 patients. Baseline characteristics were: 82.3% female, median (IQR) age 59.0 (48.6, 68.2) years, median disease duration 6.0 (2.7, 12.5) years, 40 (19.1%) diffuse cutaneous SSc, median baseline UCLA GIT 2.0 score 0.19 (0.06, 0.43). Of these, 71 patients were exposed to immunosuppressive therapy during the observation period: 27/71 methotrexate, 1/71 cyclophosphamide, 17/71 MMF, 3/71 leflunomide, 3/71 azathioprine, 6/71 glucocorticoids >10mg/d, 16/34 rituximab, 18/34 tocilizumab. Patients on immunosuppressive therapy during the observation period had, compared to patients without such treatment, overall more severe SSc, higher prevalence of treatment with proton pump inhibitors, similar UCLA GIT 2.0 scores at baseline and at follow up and tendentially less severe GI symptoms at baseline and follow-up by medical history. In multivariable linear regression, immunosuppressive therapy, lower body mass index, longer disease duration and lower baseline UCLA GIT 2.0 score were significantly associated with lower (better) UCLA GIT 2.0 scores at follow-up (Table 1).

Table 1.

Predictors of UCLA GIT 2.0 score at follow-up	*Estimates*	*95% CI*	*p*
Age	0.002	-0.001 – 0.006	0.136
Sex [male]	-0.056	-0.172 – 0.061	0.347
Disease duration	-0.005	-0.009 – -0.000	**0.030**
Body mass index	0.014	0.002 – 0.025	**0.017**
UCLA GIT 2.0 total score baseline	0.690	0.571 – 0.809	**<0.001**
Immunosuppressive therapy during observation period	**-0.119**	**-0.228 – -0.010**	**0.032**
Immunosuppressive therapy before baseline	0.080	-0.032 – 0.192	0.160
Modified Rodnan Skin Score	-0.001	-0.008 – 0.007	0.860
Forced vital capacity	-0.001	-0.004 – 0.001	0.302
Erythrocyte sedimentation rate	0.003	-0.001 – 0.006	0.116
Proton pump inhibitors	-0.034	-0.120 – 0.052	0.435
(Intercept)	-0.120	-0.531 – 0.291	0.566

Baseline factors associated with the total UCLA GIT 2.0 score at the end of the observation period. Multiple linear regression model with imputation for missing variables. N=209 patients

Conclusion: Immunosuppressive treatment was associated with lower UCLA GIT 2.0 scores, which suggests potential effects of immunosuppressants on GI manifestations in patients with SSc. These results need verification in additional studies and randomised controlled clinical trials.

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Does AI really help me diagnosing RMDs?

OP0004 AUTOMATED RECOGNITION AND MONITORING OF DORSAL SKIN FOLDS BY A CONVOLUTIONAL NEURAL NETWORK AS A POTENTIAL DIGITAL BIOMARKER FOR JOINT SWELLING IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: To monitor rheumatic diseases, digital biomarkers such as wearables are of increasing interest, but they lack disease specificity.
Objectives: In this study, we apply convolution neural networks (CNN) to real world hand photographs in order to automatically detect, extract and analyse dorsal finger folds lines as a correlate of proximal interphalangeal (PIP) joint swelling in patients with rheumatoid arthritis (RA).
Methods: Hand photographs from 190 RA patients were taken by a smartphone camera in a standardized manner. PIP joints were categorised as either swollen or not swollen based on clinical judgement and ultrasound. Images were automatically preprocessed by cropping PIP joints and extracting dorsal finger folds. Subsequently, metrical analysis of dorsal finger folds was performed and a CNN was trained to classify the dorsal finger lines into swollen versus non-swollen joints. Representative horizontal finger folds were also quantified in a subset of patients before and after resolution of PIP swelling and in patients with disease flares, respectively.
Results: In swollen joints, the number of automatically extracted double-contoured, deep skinfold imprints was significantly reduced compared to non-swollen joints (1.3, SD 0.8 vs. 3.3, SD 0.49). The joint diameter / deep skinfold ratio was significantly higher in swollen (4.1, SD 1.4) versus non-swollen joints (2.1 SD 0.6). The CNN model successfully differentiated swollen from non-swollen joints based on finger fold patterns with a validation accuracy of 0.84. A heatmap of the original images obtained by an extraction algorithm confirmed finger folds as the region of interest for correct classification. After significant response to DMARD +/- corticosteroid therapy, longitudinal metrical analysis of eight representative deep finger folds showed a decrease of the mean diameter/ finger fold length (finger fold index, FFI) from 3.03 (SD 0.68) to 2.08 (SD 0.57). Conversely, the FFI increased in patients with a flare of joint swelling.
Conclusion: Automated preprocessing and the application of CNN algorithms in combination with longitudinal metrical analysis of dorsal finger fold patterns extracted from real world hand photos might serve as a digital biomarker in RA.
Disclosure of Interests: Thomas Hügle Shareholder of: Atreon SA., Speakers bureau: Multiple. Not relevant for this work., Grant/research support from: Multiple. Not for this work., Leo Caratsch: None declared, Matteo Matteo Caorsi Employee of: MC is an employee of L2F., Jules Maglione: None declared, Diana Dan: None declared, Alexandre Dumusc Speakers bureau: Multiple. Not relevant for this work., Marc Blanchard Shareholder of: Atreon SA., Gabriel Kalweit: None declared, Maria Kalweit: None declared.
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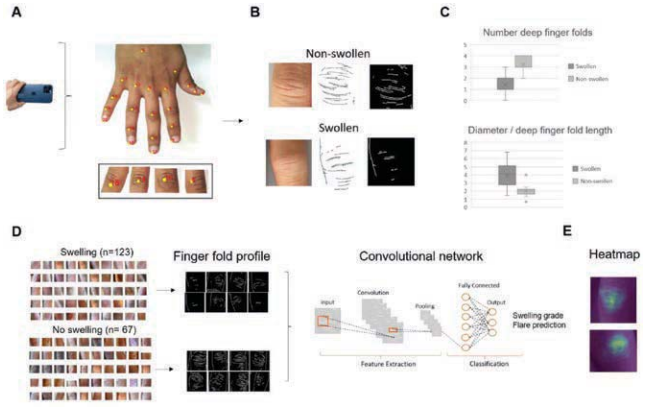

Figure 1. Automated finger fold recognition to monitor rheumatoid arthritis (RA). Hand photographs are taken by a smartphone (A). Hands, and subsequently proximal interphalangeal (PIP) joints, are automatically recognized and extracted. Finger fold lines are isolated from the images, measured and related to the joint diameter (B,C). A convolutional deep neural network was used to train a model for classification of extracted finger fold patterns into swollen vs. non swollen joints (D). On cropped PIP joint images, the heatmap of the same classification task confirms finger folds as the region of interest (E).

How to maintain your quality of life after an RMD diagnosis

OP0005-PARE DEVELOPMENT OF CONVERSATION AIDS: HOW TO GET THE MOST OUT OF YOUR RMD APPOINTMENT AND ADVANCE YOUR QUALITY OF LIFE

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Background: Having a Rheumatic and Musculoskeletal Disease (RMD) has a big impact on your daily life, work, relationships and quality of life. It can cause various complaints, problems and questions. Research shows that people with an RMD are often insufficiently aware that they can talk about these challenges with their RMD professional. They also don't realize that these challenges matter when making a fitting choice for treatment. It also appears that RMD professionals do not sufficiently take into account the priorities of their patient, when a treatment choice has to be made. This is unfortunate because research shows that people who decide together with their RMD professional make better informed treatment choices. They are also more likely to adhere to their treatment or medication use. A conversation aid can help people to become aware of the most important challenges or problems in their daily lives with an RMD. These uncovered challenges and problems can set the agenda for a good conversation in the RMD consultation room. Together with the RMD professional the conversation can focus on ways to deal with or treat these challenges or problems.
Objectives: To develop a conversation aid for people with an RMD that allows them to become aware of the most important challenges in their life with an RMD and that guides them in how to discuss these aspects with an RMD professional.
Methods: In the first step a review was made of all important aspects of a patient's life with an RMD. The outcome measures of ICHOM for inflammatory arthritis1 and hip- and knee osteoarthritis2 formed the starting point for this review. This was complemented with additional outcomes as measured in Dutch RMD apps and patient dashboards of Dutch hospitals. In the second step, the list of outcomes was assessed by means of a survey among Dutch patients with an RMD. The third step was to discuss the complete list with important outcomes with the Dutch rheumatology department of the Bravis Medical Centre. A first draft version of the conversation aids was made. This draft version was evaluated by patientpartners of the National Association ReumaZorg Nederland (RZN) and the Bravis Medical Centre.
Results: A total of 4 conversation aids (https://reumazorgnederland.nl/samen-beslissen-gesprekskaarten/) were made. Each aid addressing a main category of challenges with an RMD. Each main category was divided into 5 sub-categories. The 4 conversation aids are:

- **Disease**: Concerning the sub-categories: Disease activity, pain, fatigue, medication & side effects and knowledge about the disease.
- **Daily activity**: Concerning the sub-categories: Work/school, personal care, household & family, mobility, and spare time.

- **Lifestyle:** Concerning the sub-categories: Activity, food, stress & relaxing, smoking, and weight.
- **Relationships and well-being**: Concerning the sub-categories: Social contacts, intimate relationships & pregnancy & wish for children, incomprehension, loneliness, and gloom.

To advance Shared Decision Making (SDM), a separate conversation aid was made with tips and tricks for having a good conversation with your RMD professional:

- **A good conversation**: tips and tricks for preparing a conversation with your RMD professional. As well as tips and tricks that can be used during and after your conversation.

In Figure 1 the conversation aid with main category **lifestyle** is presented.

Figure 1. *Example of the conversation aid with main category Lifestyle.*

Conclusion: A consultation aid can advance a good conversation and therefore SDM, between people with an RMD and their RMD professional. A patient organisation can play an important role in developing a consultation aid.

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Is gender sufficiently studied in RMDs?

OP0006

CLEANING ACTIVITIES, DUSTY CLOTHES LAUNDRY AND TALCUM HANDLING ARE UNDERESTIMATED MAJOR SOURCES OF EXPOSURE TO CRYSTALLINE SILICA IN WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Inhalation of crystalline silica ($cSiO_2$) is associated with rheumatoid arthritis (RA). Research on $cSiO_2$ has historically focused on professional exposures and on male workers. However, $cSiO_2$ is ubiquitously present in the environment, substantial exposure can take place in both men and women, in other professional activities and even beyond occupational context.
Objectives: To identify the main sources of exposure to crystalline silica in a series of RA patients not selected based on their professional activity, and to assess the association between silica exposure and disease features.
Methods: The Dust Exposure Life-Course Questionnaire (DELCQ) is a novel tool that longitudinally quantifies both occupational and non-occupational lifetime exposure to crystalline silica. The DELCQ was previously validated in a representative sample of the general French population that serves as control source for studies in specific diseases. The DELCQ was administered to 97 consecutive patients with RA, exposure scores were compared between cases and age-, sex- and smoking status-matched controls (1:4). The main sources of silica exposure were identified in cases and controls and source-specific exposure levels compared. The association between DELCQ scores and disease variables in cases was tested at uni- and multivariable analysis.
Results: In women with RA, the main sources of crystalline silica exposure were: cleaning activities, dusty clothes laundry and talcum powder handling, with higher exposure levels from these sources vs. the general population ($p<0.005$). In the whole series of RA patients, high silica exposure was independently associated with interstitial lung disease (OR 6.5 (95% CI: 1.3 to 32.6)) and mediastinal lymphadenopathy (OR 6.3 (95% CI: 1.4 to 27.7).
Conclusion: Cleaning activities, dusty clothes laundry and talcum handling are underestimated sources of crystalline silica exposure that are overrepresented in women with RA compared to the general population and may contribute to the pathogenesis of the disease.

Table 1. Association between occupational silica exposure (by quartile) and HRCT lung abnormalities

HRCT abnormality	OES (Quartiles)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Mediastinal lymphadenopathy	Q1-Q3	(ref)	(ref)
	Q4	4.1 (1.2 to 13.9)	**6.3 (1.4 to 27.7)**
Interstitial lung disease	Q1-Q3	(ref)	(ref)
	Q4	6.3 (1.5 to 26.6)	**6.5 (1.3 to 32.6)**
Emphysema	Q1-Q3	(ref)	(ref)
	Q4	6.4 (1.6 to 24.7)	2.9 (0.6 to 13.7)

Abbreviations: OES occupational exposure score. Adjusted OR: adjusted on smoking, sex, disease duration, ACPA and RF status.

Disclosure of Interests: None declared.

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"Not another pill!" Integrative pain management approaches

OP0007-HPR

AN EPIDEMIOLOGICAL STUDY OF FOOT AND ANKLE PAIN AND HEALTH-RELATED JOB LOSS IN ADULTS OVER 50: CROSS-SECTIONAL FINDINGS FROM THE HEAF COHORT

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Background: Foot and ankle pain (FAP), particularly that of musculoskeletal origin, is increasingly prevalent in our aging populations[1]. Moreover, governments need people to work to older ages to reduce the costs of pensions and welfare benefits. It is not currently known however whether people with FAP are able to keep working or to what extent it pushes people out of work. We investigated this question in older working adults.
Objectives: To determine whether FAP is associated with HRJL amongst older working adults.
Methods: Health And Employment After Fifty[2] is a longitudinal population-based cohort incepted 2013 to investigate health and retirement. At follow-up two years later, people were asked to complete a full-body mannequin which included the ankles/feet. Mannequins were coded: foot/ankle pain (FAP) with pain at other sites; pain elsewhere but not FAP; and no pain. Two years later, participants were asked whether they had left paid work entirely or partly because of health (Health-related job loss (HRJL). A Cox proportional hazards model was used to explore associations between health-related job loss, FAP, and other potential risk factors (such as age, mental health, BMI, and finances). A sensitivity analysis was carried out to determine which occupational activities were significantly associated with health-related job loss due to FAP.
Results: At 2 years, 4050 participants completed a pain mannequin, amongst whom 3762 were in paid work. Over 2 further years of follow-up, there were 235 incident HRJLs. Amongst those with HRJL, 73 had no pain, 54 had pain involving FAP, 108 had pain not involving FAP. After adjusting for age and sex, people with FAP had 83% increased risk of HRJL compared to people with no pain (HR=1.83, 95% CI 1.29-2.61), whilst those with pain NOT involving FAP had 34% increased

risk (HR1.34, 95% CI 1.00 – 1.80). FAP remained a significant predictor of HRJL within a fully adjusted model (HR=1.65, 95% CI 1.15-2.36). Sensitivity analyses confirmed that doing jobs which involved climbing more than 30 flights of stairs was associated with increased risk of HRJL amongst people with FAP (HR=1.96, 95% CI 1.00-3.80).

Conclusion: FAP is a risk factor for HRJL amongst older working adults, particularly if their job involves stair climbing. Potentially, modification of duties to reduce stair climbing could mitigate job loss amongst people with FAP.

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Disclosure of Interests: None declared.

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Plenary Abstract Session

OP0008 A NOVEL SITE-SPECIFIC PEGYLATED IL-2 WITH POTENT AND TREG-SELECTIVE ACTIVITY IN VIVO

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Background: Decreased regulatory T cells (Tregs) and Treg dysfunction are hallmarks of a various autoimmune and inflammatory diseases. While low-dose IL-2 therapy induces Treg expansion *in vivo* and has clinical benefits in some diseases (e.g., SLE and chronic graft-versus-host disease [GvHD]), there are many concerns about adverse events due to low Treg-selectivity. Furthermore, frequent dosing is needed due to the short half-life.

Objectives: We discovered a novel site-specific PEGylated IL-2 variant, KKC80, with high Treg selectivity and a long half-life *in vivo*, which overcomes the issues of low-dose IL-2 therapy.

Methods: Based on the co-crystal structure of wild-type IL-2 and its heterotrimeric receptor (PBD ID: 2ERJ), amino acid residues that were to be PEGylation sites were substituted with oAzZLys, an azide-containing lysine derivative. The PEG molecule was site-specifically attached to oAzZLys-incorporated IL-2 by copper-free click chemistry. The binding property to the IL-2 receptors were measured by surface plasmon resonance (SPR). *In vitro*, Treg selectivity was evaluated by the IL-2-dependent proliferation activity of Tregs and NK cells from human peripheral blood mononuclear cells (PBMCs). *In vivo* pharmacological activity after the single subcutaneous administration in cynomolgus monkeys was measured by changes in Treg count and Treg activation status in peripheral blood by flow cytometry. Pharmacokinetic parameters were calculated according to serum PEGylated IL-2 concentration. Efficacy in mouse xenogeneic GvHD model using human PBMC-transplanted NOG mice and in monkey DTH model were evaluated.

Results: A novel PEGylated IL-2, KKC80 (human IL-2 desA1/C125S /I129oAzZLys_W-shaped 80 kDa PEG) was discovered by optimizing the PEGylation site and PEG structure based on Treg selectivity and PK. SPR analysis showed that the binding affinity of KKC80 to CD25 was moderately decreased from wild-type IL-2, while binding affinity of KKC80 to IL-2Rβγ was remarkably decreased due to a significant change of the association rate constant. *In vitro*, wild-type IL-2 activated both Tregs and NK cells in the same concentration range, whereas KKC80 selectively activated Tregs. The Treg selectivity of KKC80 was comparable to another IL-2 mutein, Fc.IL-2 V91K. KKC80, but not Fc.IL-2 V91K, retained its biological activity, even in the presence of a large amount of recombinant soluble CD25, which mimicked the endogenous decoy receptor for IL-2. In monkeys, KKC80 selectively increased peripheral blood Tregs in a dose-dependent manner; the average maximum rate of increase of Treg count in animals treated with 0.01, 0.03, 0.1, 0.3 and 1 mg/kg was 1.5, 3.5, 28, 50 and 154-fold, respectively. In contrast to Tregs, the rates of increase of conventional CD4+ T, CD8+ T and NK cells were low. The Treg increase peaked on day 8 or 11 and lasted for over day 29. KKC80 showed a more sustained upregulation of functional Treg markers (e.g., Foxp3 and CD25) in comparison to Fc.IL-2 V91K. The half-life of KKC80 was calculated as 83.5 to 150 h. At high doses, inflammation-related adverse effects, including increased CRP (≥0.3 mg/kg) and deterioration of general conditions (1 mg/kg) were observed. In the mouse xenogenic GvHD model, KKC80 ameliorated GvHD symptoms and suppressed multiple tissue inflammation markers. Decreased soluble CD25 and IFN-γ were also confirmed, suggesting Treg-mediated anti-inflammatory effect by KKC80 administration were exerted *in vivo.* In the monkey DTH model, KKC80 suppressed skin inflammation and antibody production.

Conclusion: Among next-generation IL-2 variants, KKC80 showed a best-in-class biological profile for Treg activation. A drastic and sustained increase of Tregs with high Treg-selectivity and anti-inflammatory effects were observed *in vivo*. These data suggest that in comparison to current IL-2 therapy, KKC80 provides superior therapeutic index and efficacy in patients with autoimmune and inflammatory diseases.

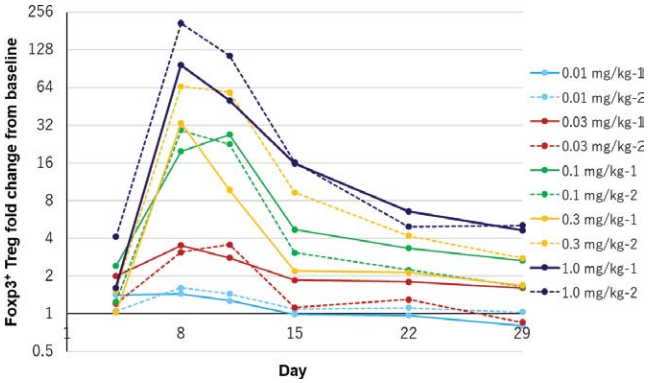

Figure 1.

Disclosure of Interests: Masahiro Ikeda Employee of: Kyowa Kirin Co., Ltd., Shinpei Yamaguchi Employee of: Kyowa Kirin Co., Ltd., Masumi Murakami Employee of: Kyowa Kirin Co., Ltd., Shigeki Takaoka Employee of: Kyowa Kirin Co., Ltd., Yasuko Sakaguchi Employee of: Kyowa Kirin Co., Ltd., Shunki Yasui Employee of: Kyowa Kirin Co., Ltd., Kousuke Iijima Employee of: Kyowa Kirin Co., Ltd., Kenichiro Nanya Employee of: Kyowa Kirin Co., Ltd., Hideyuki Onodera Employee of: Kyowa Kirin Co., Ltd., Toru Amano Employee of: Kyowa Kirin Co., Ltd.

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OP0009 MACHINE LEARNING IDENTIFIES A COMMON SIGNATURE FOR ANTI-SSA/RO60 ANTIBODY EXPRESSION ACROSS AUTOIMMUNE DISEASES

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Background: Anti-SSA/Ro autoantibodies are among the most frequently detected extractable nuclear antigen autoantibodies and have mainly been associated with primary Sjögren's syndrome (pSS), systemic lupus erythematosus (SLE) and undifferentiated connective tissue disease (UCTD).

Objectives: Is there a common signature to all patients expressing anti-Ro60 autoantibodies regardless of their disease phenotype?

Methods: Using high-throughput multi-omics data collected within the cross-sectional cohort from the PRECISESADS IMI project [1] (genetic, epigenomic, transcriptomic, combined with flow cytometric data, multiplexed cytokines, classical serology and clinical data), we assessed by machine learning the integrated molecular profiling of 520 anti-Ro60-positive (anti-Ro60$^+$) compared to 511 anti-Ro60-negative (anti-Ro60$^-$) patients with pSS, SLE and UCTD, and 279 healthy controls (HCs).

Results: The selected features for RNA-Seq, DNA methylation and GWAS data allowed a clear separation between anti-Ro60$^+$ and anti-Ro60$^-$ patients. These results demonstrate that the different features selected by machine learning from the anti-Ro60$^+$ patients constitute specific signatures when compared to anti-Ro60$^-$ patients and HCs. Remarkably, the gene transcript *z*-score of three genes (*ATP10A*, *MX1* and *PARP14*), presenting an overexpression associated with a hypomethylation and genetic variation, and independently identified by the Boruta algorithm, was clearly higher in anti-Ro60$^+$ patients compared to anti-Ro60$^-$ patients in all the diseases (Figure 1). Finally, we demonstrate that these signatures, enriched in interferon stimulated genes, were also found in anti-Ro60$^+$ patients with rheumatoid arthritis and systemic sclerosis.

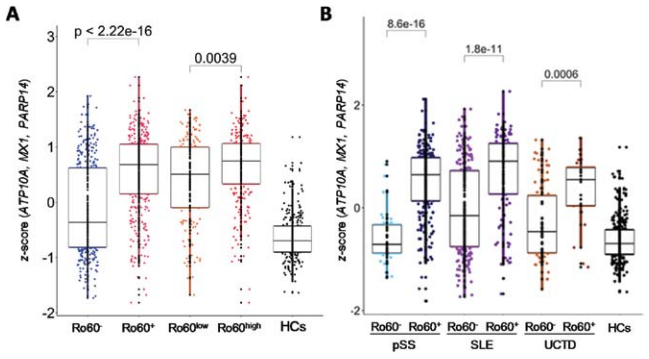

Figure 1. Three genes common to RNA-Seq, DNA methylation and GWAS analysis characterize anti-Ro60$^+$ patients. (A) *ATP10/MX1/PARP14 z*-score analyses were performed for 731 patients and 254 HCs according to anti-Ro60 expression. **(B)** *ATP10/MX1/PARP14 z*-score analyses were performed for 286 pSS, 351 SLE and 94 UCTD patients and 254 HCs. Two-tailed pairwise Wilcoxon-rank sum test results are shown. Plots show median, with error bars indicating ± interquartile range. (pSS: primary Sjögren's syndrome, SLE: systemic lupus erythematosus, UCTD: undifferentiated connective tissue disease, HCs: healthy controls).

Conclusion: Anti-Ro60$^+$ patients present a specific inflammatory signature regardless of their disease suggesting that a dual approach targeting both Ro-associated RNAs and anti-Ro60 autoantibodies should be considered.

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Acknowledgements: The study has been conducted thank to the contribution of the PRECISESADS clinical consortium and the PRECISESADS flow cytometry consortium.

Disclosure of Interests: None declared.

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OP0010 A MORE MATURE PLASMA CELL AND PLASMABLAST COMPARTMENT IS ASSOCIATED WITH DISEASE MANIFESTATION IN PRIMARY SJÖGREN'S SYNDROME

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Background: Sjögren's syndrome (pSS) is an autoimmune disorder often associated with fatigue, dry eyes and dry mouth symptoms and characterized by chronic inflammation of moisture-producing glands like salivary and lacrimal glands (1). Auto-antibodies, B cell infiltration of affected glands and lymphoma development are signs for B cell hyperactivity in pSS (1-3). The B cell effector branch, namely antibody-secreting cells (ASC) like plasmablasts and plasma cells, can sustain autoimmune pathogenicity over long time periods by secretion of auto-antibodies (4,5).

Objectives: Since B cell hyperactivity is an important pathogenic feature in pSS, antibody-secreting cells as B effector cells are studied to characterize their abundance, maturation stage and inflammatory properties and relate them to pSS manifestations.

Methods: Peripheral blood mononuclear cells (PBMC) from pSS patients and healthy individuals were subjected to spectral flow cytometry phenotyping. CD27+CD38++ ASCs were analyzed with a comprehensive tSNE approach as well as based on expression of ASC markers. This includes markers described for maturity like CD19, CD138, CD28, Blimp1 and HLA-DR and markers relevant for ASC survival like Mcl1 and BCMA. The pro-inflammatory status of the cells was assessed by CXCR3 and CXCR4 expression and their immune regulatory properties with markers like IL-10 and Lag-3. ASC properties like maturity state were correlated to characteristic pSS disease-associated features.

Results: Patients with pSS had higher frequencies and absolute numbers of ASCs then healthy controls. ASCs displayed a higher degree of maturation in pSS. ASC frequencies and their maturity state, for example reflected by CD19 down-regulation or increased CD28 expression (6), correlated with several pSS disease characteristics like ANA titers, focus scores and ocular scores indicating glandular impairment. Additionally, more mature ASCs that express low amounts of CD19 had increased Mcl1 levels indicating prolong survival of these cells. The maturation state of ASCs was associated with CXCR3+ ASC frequencies in pSS patients. Expression levels of anti-inflammatory IL-10 and pathogenic CXCR3 by ASCs in pSS patients was negatively correlated. tSNE related clusters enriched for ASCs from pSS patients were more mature but also had higher expression levels of CXCR3.

Conclusion: Circulating ASCs in pSS are more abundant and have a more mature phenotype compared to healthy individuals. Their frequencies and degree of maturation could be linked to pSS disease features. Prolonged survival and pro-inflammatory status might further increase the impact of circulating ASCs on disease manifestations. Together these findings underpin the role of B cell hyperactivity in pSS, that culminates in an altered ASC compartment.

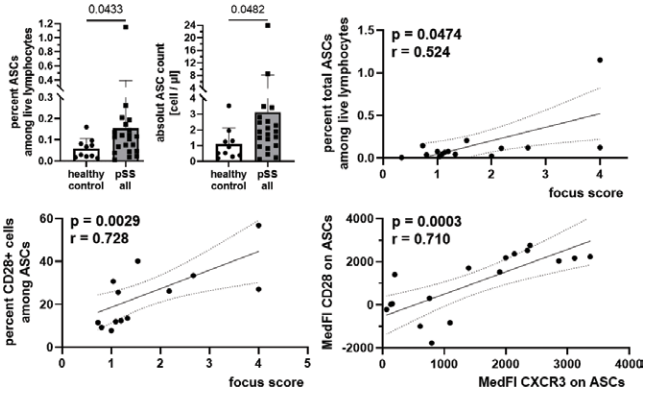

Figure 1. (A) Frequencies and absolute numbers of antibody-secreting cells (ASC) are increased in pSS patients and (B) correlate with salivary gland focus scores. (C) More mature CD28+ ASCs are associated with focus scores and (D) higher pro-inflammatory levels of CXCR3.

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OP0011 HIGHLY DIFFERENTIATED CD4 AND CD8 T EFFECTOR MEMORY CELLS RE-EXPRESSING CD45RA (TEMRA) ARE ASSOCIATED WITH ACTIVE DISEASE REFRACTORY TO ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS

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Background: Highly differentiated T cells have been reported to be enriched in rheumatoid arthritis (RA) compared to healthy individuals[1]. The role of terminally differentiated T effector memory re-expressing CD45RA (Temra) in RA pathogenesis and disease activity is still unclear, including whether they can be used as a marker of sustained disease activity in RA patients receiving anti-TNF therapy.

Objectives: To investigate whether the frequency of peripheral blood Temra can be used as a biomarker to identify disease refractory to anti-TNF therapy in RA, if they correlate with inflammation in anti-TNF treated patients, and whether they associate with a flare following tapering anti-TNF.

Methods: RA patients on anti-TNF therapy were recruited from rheumatology clinic (cross-sectional cohort). Clinical data and whole blood were collected.

Patients were stratified based on disease activity. Remission was defined as no recorded DAS28-CRP≥2.4, no swollen joints, no C-reactive protein (CRP) of >5mg/L, and on a stable DMARD dose and no reported disease flare/loss of remission in the 6 months prior. Non-remission was defined as any other disease activity which does not fulfil the remission definition. Patients on abatacept, or methotrexate monotherapy and healthy volunteers were recruited as comparison groups. A separate cohort of anti-TNF patients (longitudinal cohort) who have been in remission on a stable dose of anti-TNF for ≥6 months and no use of corticosteroids in the last 6 months, was also recruited. Whole blood was obtained prior to dose tapering (dose halving) and at the point of a flare. Whole blood was processed by gradient centrifugation to obtain peripheral blood mononuclear cells (PBMC). PBMC were stained with fluorochrome-conjugated antibodies for multi-parameter flow cytometry. Analysis was performed on live lymphocytes using FlowJo software version 10.8. Two-tailed Mann-Whitney U test or unpaired t-test were used to obtain unadjusted values, analysis of variance (ANOVA) of log-transformed data was used to obtain age-adjusted values, Spearman's rank correlation was used to compare correlation between Temra and CRP.

Results: RA patients (36 anti-TNF, 12 abatacept, 16 methotrexate monotherapy) and 14 healthy individuals were recruited. There was a higher proportion of CD4 (age-adjusted p = 0.004) and CD8 Temra (age-adjusted p = 0.0007) in RA patients on anti-TNF with persistent disease activity compared to those who had achieved remission. These differences were confirmed when analysing absolute numbers of CD4 and CD8 Temra. Unexpectedly, the difference in Temra frequency between remission and non-remission RA was not observed in patients treated with methotrexate or abatacept. The median CD4 and CD8 Temra frequencies in RA patients in remission with all treatments studied were similar to healthy individuals.

Temra were not observed to increase with age in the anti-TNF, abatacept, or methotrexate cohorts in contrast to previous reports in healthy individuals[2]. The frequency of CD4 and CD8 Temra correlated with CRP only in patients on anti-TNF (CD4 Temra Spearman r = 0.5185, p = 0.001, and CD8 Temra Spearman r = 0.5040, p = 0.005).

There was an increase in CD4 (p = 0.003) but not CD8 Temra at 3 months in patients who flared on tapering anti-TNF compared to those who remained in remission (Figure 1).

Conclusion: Increased CD4 and CD8 Temra frequency were associated with persistent disease activity in anti-TNF treated patients but not with other DMARD therapies (abatacept and methotrexate). CD4 Temra increased in those who flared on tapering anti-TNF. These results suggest that Temra may play a role in driving persistent disease activity refractory to anti-TNF therapy rather than merely a marker of inflammation.

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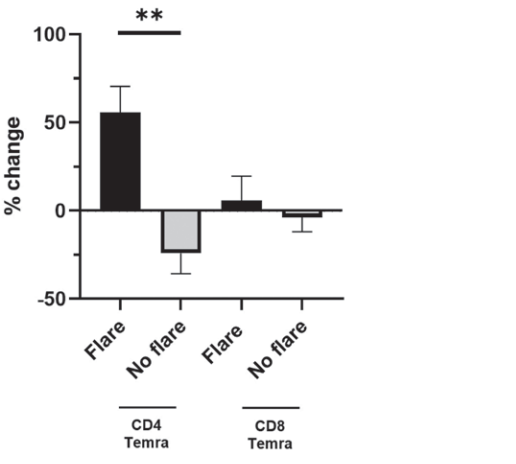

Figure 1. Percentage (%) change in CD4 and CD8 Temra between baseline (pre-taper) and 3 months after anti-tumour necrosis factor (TNF) tapering comparing patients who flared (n = 5), and those who remained in remission (n = 5). Data expressed as mean±SEM. **p=0.003 by unpaired t test. Temra = T effector memory re-expressing CD45RA.

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OP0012 INTERFERON-A MEDIATED THERAPEUTIC RESISTANCE IN EARLY RA IMPLICATES EPIGENETIC REPROGRAMMING

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Background: An interferon gene signature (IGS) is present in approximately 50% of early, treatment naive rheumatoid arthritis (eRA) patients. We previously demonstrated it negatively impacts on initial disease outcomes.

Objectives: To 1) reproduce previous findings demonstrating the harmful effects of the IGS on early RA clinical outcomes, 2) identify which IFN class is responsible for the IGS and 3) seek evidence that IFN-α exposure contributes to harmful epigenetic footprint at disease onset.

Methods: In a large multicentre inception cohort (n=190) of eRA patients (RA-MAP TACERA) whole blood transcriptome, IGS (*MxA, IFI44L, OAS1, ISG15, IFI6)* and circulating interferons (IFN)-α, -β, -γ and -λ was examined at baseline and 6 months in conjunction with disease activity and clinical characteristics. A separate eRA cohort of paired methylome and transcriptome from CD4 T and CD19 B cells (n=41 for each) was used to explore any epigenetic influence of the IGS.

Results: The baseline IGS reproducibly and significantly negatively impacts on 6-month clinical outcomes. In the high IGS cohort there was increased DAS-28 (p=0.025) and reduced probability of achieving a good EULAR response (p=0.034) at 6-months. In addition, the IGS in eRA is shown for the first time to predominantly reflect raised circulating IFN-α protein, not other classes of IFN and examination of whole blood upstream nucleic acid sensors expression suggest a RNA trigger. Both the IGS and IFN-α significantly fell in parallel at 6 months (p<0.0001), whereas other classes of IFN remained statistically static. There was a significant association with IFN-α and RF titre but not ACPA. Comparison of CD4 T and CD19 B cells between IGS high and low eRA patients demonstrated differentially methylated CPG sites and altered transcript expression of disease relevant genes e.g. *PARP9, STAT1, EPTSI1* which was similarly, and persistently, altered 6 months in the separate TACERA cohort. Differentially methylated CPGs implicated altered transcription factor binding in B cells (GATA3, ETSI, NFATC2, EZH2) and T cells (p300, HIF1α) which cumulatively suggested IFN-α induced epigenetic changes promoting increased, and sustained, lymphocyte activation, proliferation and loss of anergy in the IGS high cohort.

Conclusion: We validate that the IGS is a robust prognostic biomarker in eRA predicting poor therapeutic response. Its persistent harmful effects may be driven via epigenetic modifications. These data have relevance for other IFN-α states, such as COVID-19, but also provide a rationale for the initial therapeutic targeting of IFN-α signalling, such as with JAKi, at disease onset in stratified eRA subsets.

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OP0013 LOSS OF SYNOVIAL TISSUE MACROPHAGE HOMEOSTASIS PRECEDES RHEUMATOID ARTHRITIS CLINICAL ONSET

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Background: Synovial tissue macrophages significantly contribute to Rheumatoid Arthritis, yet the precise nature/function of macrophage subsets within the inflamed joint remains unexplored.
Objectives: To fully explore the spectrum of distinct macrophage activation states residing within the synovium of RA, at risk and healthy individuals.
Methods: Single-cell synovial tissue suspensions from RA (n=44), IAR (n=5), HC (n=11), PsA (n=11) and OA (n=4) were obtained, and synovial macrophage subsets examined by advanced multiparameter flow cytometric analysis, bulk RNA-sequencing, metabolic and functional assays.
Results: Multidimensional analysis identifies enrichment of CD206+CD163+ synovial-tissue macrophages co-expressing CD40 in the RA joint compared to healthy synovial-tissue, with frequency of CD206+CD163+CD40+ macrophages associated with increased disease activity and treatment response. In contrast, CX3CR1-expressing macrophages which form a protective barrier in healthy synovium are significantly depleted in RA. Importantly this signature of enriched CD40 expression coupled with depleted CX3CR1 expression is an early phenomenon, occurring prior to clinical manifestation of disease in individuals 'at-risk' of RA (IAR). RNAseq and metabolic profiling of sorted RA synovial-macrophages identified that this population is transcriptionally distinct, displaying unique inflammatory, phagocytic and tissue-resident gene signatures, paralleled by a bioenergetically stable profile as indicated by NAD(P)H emission. Functionally CD206+CD163+ RA macrophages are potent producers of pro-inflammatory mediators (reversed by CD40-signalling inhibition) and induce an invasive phenotype in healthy synovial-fibroblasts. These findings identify a distinct pathogenic population of synovial-tissue macrophage involved in shaping the immune response in RA. Crucially, this signature is present pre-disease representing a unique opportunity for early diagnosis and therapeutic intervention.
Conclusion: We have identified a novel population of tissue-resident macrophages in the RA synovium which are transcriptionally/metabolically distinct and capable of contributing to disease pathology. Uncovering the molecular patterns and cues that transform this immunoregulatory macrophage population into a dysfunctional inflammatory activation state may provide opportunities to reinstate joint homeostasis in RA patients.
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OP0014 CTLA4-IG INDUCES TOLEROGENIC PROPERTIES OF DENDRITIC CELLS BY ALTERING CELLULAR METABOLISM

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Background: Dendritic cells (DCs) are well-recognized for their dual role either for T cell activation (1) or for inducing T cells tolerance (2). Their ability to modulate T-cell responses has made them an interesting tool for the immunotherapy of autoimmune diseases (3). Cytotoxic T lymphocyte antigen 4 (CTLA4) is a negative co-stimulatory molecule, which binds to CD80/CD86 on DCs. CTLA4 induces its immunoregulatory function through trans-endocytosis resulting in impaired co-stimulation (4), or through the induction of indoleamine-pyrrole 2,3-dioxygenase (IDO) enzyme (5). Moreover, it has been demonstrated that CTLA4 impairs the autophagic machinery of DCs and therefore suppresses DC inflammatory function (6). Nevertheless, the molecular mechanisms underlying the CTLA4-mediated immunomodulatory phenotype, require a more comprehensive understanding.
Objectives: In this study we focused on tolerogenic DCs (tolDCs) and we applied CTLA4-Ig as a tool to induce them. We aim to assess the immunoregulatory potential of CTLA4-mediated tolDCs and to investigate thoroughly the intracellular pathways that are involved in the induction of tolerance.
Methods: Healthy human monocytes were isolated from peripheral blood and differentiated into monocyte-derived dendritic cells (DCs). After 6 days, immature DCs activated with LPS were treated with CTLA4-Ig or IgG control for 18 hours. The anti-inflammatory function of DCs was validated using RT-PCR and flow cytometry and DCs proceeded to RNA sequencing. The metabolic pathways were studied using a Seahorse bioanalyzer.
Results: CTLA4-Ig-treated DCs showed significantly decreased HLA-DR, CD80/CD86 expression as compared to IgG-treated cells (n=4, p=0,0294, n=5 p=0,0079). Moreover, IL6 and TNFα mRNA expression, hallmarks of inflammatory cytokines secreted by DCs, was reduced upon CTLA4-Ig (n=5, p=0,0079). To elucidate the pathways involved in DC reprogramming upon CTLA4-Ig treatment, we performed RNA sequencing and we concluded with 1270 differentially expressed genes (p-value <0.05 counts>10). Interestingly, transcriptomic analysis revealed that the majority of genes (n=900) participated in metabolic processes, specifically in OXPHOS pathway and mitochondrial function. To further support the above metabolic changes, we performed Seahorse assays and confirmed that tolDCs had lower basal OXPHOS and decreased ATP production compared with mature DCs. Furthermore, expression of phosphorylated mammalian target of rapamycin (mTOR) and AKT1, central regulators of metabolism, was increased in CTLA4-mediated tolDCs (n=3, p= 0,0308 and p=0,0347).
Conclusion: Herein we confirmed that CTLA4 restricts the pro-inflammatory properties of activated DCs. RNA-seq analysis revealed that this anti-inflammatory deviation of DCs is characterized by the modification of the expression of genes implicated in cellular metabolism. Metabolic experiments confirmed that CTLA4-mediated tolDCs have reduced OXPHOS and ATP production, whereas, mTOR signaling is upregulated. In future experiments, we will investigate the mechanism that CTLA4 may promote metabolic changes thus contributes to the immunoregulatory phenotype of DCs and could represent a therapeutic target.
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OP0015 PROINFLAMMATORY MONOCYTES AND MACROPHAGES IN SYNOVIAL FLUID AND BURSAL TISSUE OF PATIENTS WITH POLYMYALGIA RHEUMATICA: POTENT PRODUCERS OF IL-6 AND GM-CSF

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Background: Polymyalgia rheumatica (PMR) is a common, rheumatic inflammatory disease. Inflammation of bursae and tendon sheaths is a characteristic finding

in patients with PMR. Glucocorticoid treatment remains the mainstay treatment for PMR. A study published in 1996 reported that macrophages dominate the inflammatory infiltrates in the glenohumeral synovium of PMR patients[1], suggesting the importance of these cells in the immunopathology of PMR. However, the functional and phenotypical heterogeneity of the tissue-infiltrating macrophages in PMR remains obscure. Although treatment with anti-IL-6 receptor (tocilizumab) has shown promising results[2], it is unclear whether macrophages contribute to IL-6 production in PMR. Additionally, anti-GM-CSF receptor therapy (mavrilimumab), recently shown to be efficacious in the closely related disease giant cell arteritis[3], may also be useful for the treatment of PMR. Knowledge on the functional heterogeneity of monocytes/macrophages in PMR may aid in identifying novel therapeutic targets for this condition.

Objectives: To determine the phenotype of monocyte/macrophages in peripheral blood, bursal/tenosynovial fluid and bursal tissue of patients with PMR.

Methods: Paired peripheral blood (PB), bursal/tenosynovial fluid (SF) and bursal tissue biopsy samples from 11 PMR patients were included in our study. Bursal and tenosynovial samples were obtained from the shoulder. Distribution of the monocyte subsets (classical, intermediate and non-classical monocytes) was determined based on the level of CD14 and CD16 expression by flow cytometry. To study monocyte activation status, markers of 'M1' like (CD80 and CD64) and 'M2' like (CD206 and FRβ) macrophage polarization were included in the flow cytometry analysis. Immunohistochemistry of bursal tissue biopsies was focused on macrophage markers (CD68, CD86, CD64, CD206 and FRβ) andproinflammatory cytokines (IL-6 and GM-CSF), which were scored semi-quantitatively. Double immunofluorescence stainings were performed to determine the expression of IL-6 and GM-CSF by tissue-infiltrating macrophages in bursal tissue.

Results: Monocytes were detected in the SF of PMR patients. The proportion of classical monocytes was significantly lowered (p=0.001) in SF versus PB, while the proportion of intermediate monocytes was significantly elevated (p=0.001). The expression of CD206 was significantly elevated (p=0.001) but not FRβ in SF monocytes, suggesting GM-CSF skewed phenotype. In bursal tissue, macrophages displayed mixed 'M1'/'M2' traits with high expression of all macrophage polarization markers. Proinflammatory cytokines IL-6 and GM-CSF were highly expressed throughout the bursal tissue biopsies. Double immunofluorescence staining confirmed the expression of IL-6 and GM-CSF by the infiltrating macrophages.

Conclusion: SF monocytes and bursal tissue macrophages show a pro-inflammatory phenotype in PMR. Moreover, tissue-infiltrating macrophages show a prominent IL-6 and GM-CSF response in PMR. Our data add to the rationale of targeting IL-6 and GM-CSF as treatment options in PMR.

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AxSpA drug treatment: new and old drugs

OP0016

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL

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Background: Janus kinase (JAK) inhibitors have been recognized as a potential therapeutic option in ankylosing spondylitis (AS), also known as radiographic axial spondyloarthritis (r-axSpA).[1] Upadacitinib (UPA), a JAK inhibitor, has demonstrated efficacy and safety in the treatment of AS[2]; however, no JAK inhibitor studies have been conducted in non-radiographic axSpA (nr-axSpA) to date.

Objectives: To assess the efficacy and safety of UPA in patients (pts) with active nr-axSpA.

Methods: SELECT-AXIS 2 (NCT04169373) was conducted under a master protocol comprising two independent studies, one in an AS population with an inadequate response to biologic disease-modifying antirheumatic drugs and one in an nr-axSpA population. The nr-axSpA study is a randomized, double-blind, placebo(PBO)-controlled, phase 3 trial that enrolled adults ≥18 years with a clinical diagnosis of nr-axSpA (who also fulfilled 2009 ASAS classification criteria for axSpA but did not meet the radiologic criterion of modified New York criteria), who had objective signs of active inflammation consistent with axSpA on MRI of the sacroiliac (SI) joints and/or high sensitivity C-reactive protein (hs-CRP) >upper limit of normal (2.87 mg/L) at screening, and who had BASDAI and pt's assessment of total back pain scores ≥4 based on a 0 to 10 numeric rating scale at study entry. Pts were randomized 1:1 to receive oral UPA 15 mg once daily (QD) or PBO during a 52-week (wk) double-blind treatment period. The primary endpoint was ASAS40 response at wk 14. Multiplicity-controlled secondary endpoints assessed at wk 14 included BASDAI50, ASDAS ID (<1.3), ASDAS LDA (<2.1), ASDAS PR, and ASAS20, and the change from baseline (Δ) in ASDAS (CRP), SPARCC MRI SI joint inflammation score, total and nocturnal back pain, BASFI, ASQoL, ASAS HI, BASMI, and MASES. Treatment-emergent adverse events (TEAEs) are reported through wk 14 for pts who received ≥1 dose of study drug.

Results: Of 314 pts randomized at baseline, 313 received study drug (UPA 15 mg, n=156; PBO, n=157) and 295 (94%) received study drug through wk 14. Baseline demographic and disease characteristics were balanced across treatment groups and consistent with an active nr-axSpA population (58% female; mean age 42.1 years; mean BASDAI 6.9; mean hs-CRP 12.1 mg/L).

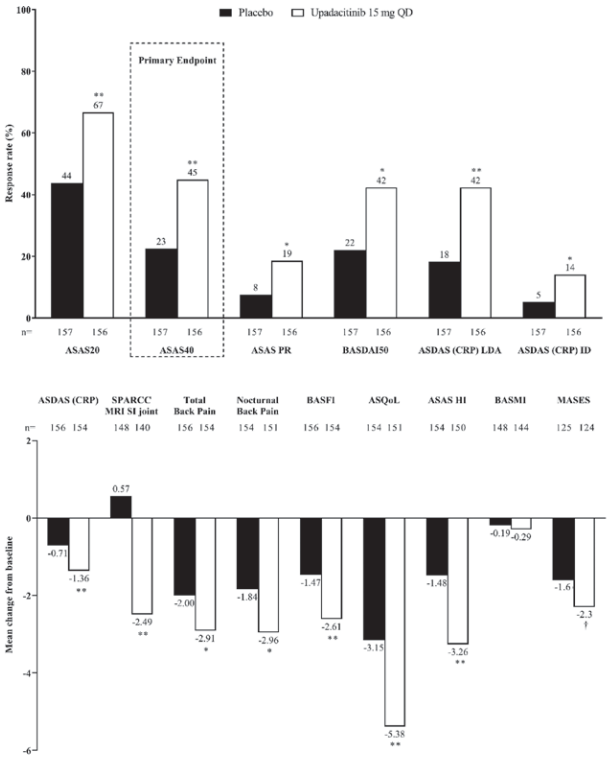

Figure. Analysis of Primary and Multiplicity-Controlled Secondary Endpoints at Wk 14

ASAS20=Assessment of SpondyloArthritis international Society 20 response; ASAS40=Assessment of SpondyloArthritis international Society 40 response; ASAS HI=Assessment of SpondyloArthritis international Society Health Index; ASAS PR=Assessment of SpondyloArthritis international Society partial remission; ASDAS (CRP)=Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS (CRP) ID=Ankylosing Spondylitis Disease Activity Score C-reactive protein inactive disease; ASDAS (CRP) LDA=Ankylosing Spondylitis Disease Activity Score C-reactive protein low disease activity; ASQoL=Ankylosing Spondylitis Quality of Life; BASDAI50=at least 50% improvement from baseline in Bath Ankylosing Spondylitis Disease Activity Index. BASFI=Bath Ankylosing Spondylitis Functional Index; BASMI=Bath Ankylosing Spondylitis Metrology Index; CMH=Cochran-Mantel-Haenszel; MASES=Maastricht Ankylosing Spondylitis Enthesitis Score; MMRM=mixed-effect model for repeated measurements; NRI-MI=non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; QD=once daily; SPARCC=Spondyloarthritis Research Consortium of Canada.
†Nominal P<0.05
**P<0.01; ***P<0.0001; Significant in multiplicity-adjusted analysis.
ASDAS LDA was defined as ASDAS (CRP) <2.1 and ASDAS ID as ASDAS (CRP) <1.3.
MASES was assessed in pts with baseline enthesitis.
Binary endpoints were analyzed using the CMH test, and NRI-MI was used to handle missing data. Continuous endpoints were analyzed using MMRM. N was the number of unique subjects contributing to MMRM model estimates.

A significantly higher ASAS40 response rate at wk 14 was achieved with UPA vs PBO (45% vs 23%; *P*<0.0001; Figure 1). Statistical significance was also achieved in the first 12 of the 14 multiplicity-controlled secondary endpoints (ie, all endpoints except BASMI and MASES) at wk 14 for UPA compared with PBO (*P*<0.01; Figure 1). The proportion of pts who experienced a TEAE was similar between treatment groups (UPA, 48%; PBO, 46%). Serious TEAEs and TEAEs leading to discontinuation were reported in 4 (2.6%) pts treated with UPA and 2 (1.3%) pts treated with PBO, respectively. Few pts had serious infection or herpes zoster (each 2 [1.3%] pts on UPA; each 1 [0.6%] pt on PBO, respectively). Uveitis was reported in 1 (0.6%) pt on UPA who had a history of uveitis and none on PBO. No malignancy other than non-melanoma skin cancer, major adverse cardiovascular events, venous thromboembolic events, inflammatory bowel disease (IBD), or death were reported in the study; 1 event of basal cell carcinoma occurred with PBO.

Conclusion: UPA 15 mg QD demonstrated significantly greater improvements in disease activity, pain, function, quality of life, and MRI-detected SI joint inflammation than PBO after 14 wks of treatment in pts with active nr-axSpA. The safety profile of UPA was consistent with what has been observed with other inflammatory musculoskeletal diseases,[3–5] and no new risks were identified. These results support the potential use of UPA in pts with active nr-axSpA.

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OP0017

RECAPTURE RATES WITH IXEKIZUMAB AFTER WITHDRAWAL OF THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS AT WEEK 104 FROM A RANDOMIZED PLACEBO-CONTROLLED WITHDRAWAL STUDY

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Background: COAST-Y is the first study to evaluate the effect of continuing vs withdrawing an IL-17A antagonist, Ixekizumab (IXE) on the maintenance of disease control in patients (pts) with ankylosing spondylitis and non-radiographic axial spondyloarthritis through 104 Weeks (wks).

Objectives: Here, we describe the final results of pts re-randomized to either placebo (PBO; IXE Withdrawal) or IXE, who experienced flare, and recaptured response before or after open label retreatment during COAST-Y.

Methods: COAST-Y (NCT03129100) is a Phase 3, long-term extension study that included a double-blind, PBO-controlled, randomized withdrawal-retreatment period (RWP). Eligible pts who completed an originating study (COAST-V, -W, or -X) entered a 24-Week (Wk) lead-in period and received 80 mg IXE every 2 (Q2W) or 4 wks (Q4W) (the treatment regimen at the end of the originating study); pts receiving PBO at the end of COAST-X were assigned to IXE Q4W in COAST-Y. Pts who achieved remission (Ankylosing Spondylitis Disease Activity Score (ASDAS) <1.3 (inactive disease; ID) at least once at Wk 16 or 20, and <2.1 (low disease activity; LDA) at both visits) were randomized 2:1 at Wk 24 to continue IXE (as per lead-in period) or withdrawn to PBO. Pts who subsequently experienced flare (ASDAS ≥2.1 at 2 consecutive visits or ASDAS >3.5 at any visit) were switched to open label IXE Q2W or Q4W at the next visit (same as lead-in period). Time to first flare was analyzed using the Kaplan-Meier method with treatment comparison performed using log-rank test. The observed proportion of pts who recaptured ASDAS LDA and ID were summarized for pts who experienced flare and were retreated with open label IXE.

Results: A total of 155 pts met the criteria for remission and entered the RWP (PBO [IXE withdrawal], N=53; IXE Q4W, N=48; IXE Q2W, N=54) and 138 completed Wk 104. At Wk 104, significantly more pts in the combined IXE group (75.5%, p<0.001, IXE Q4W: 75.0%, p<0.001; IXE Q2W: 75.9%, p<0.001) remained flare free through Wk 104 vs PBO (Figure 1). Notably, 35.8% of pts on PBO (IXE Withdrawal) never experienced flare. Of the PBO pts who experienced flare and were retreated during Wk 24-104 (N=28), 4 recaptured LDA before switching to open label IXE retreatment, while 23 recaptured LDA and 19 met ID after switching (Table 1). Of the continuously treated IXE pts (N=13), 7 recaptured LDA before switching to open label IXE retreatment, while 5 recaptured LDA and 4 met ID after.

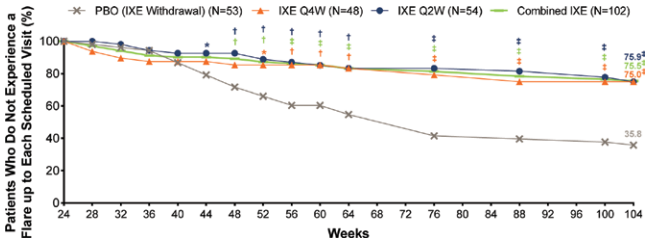

Figure 1. The proportion (%) of patients who remained flare free through 104 weeks. ‡p<0.001, †p<0.01, *p<0.05 vs PBO (IXE Withdrawal).

Table 1. Recapture of first treatment response before or after switching to open label IXE through 104 weeks among placebo (ixekizumab withdrawal)-treated patients who experienced a flare and retreated

Total patients who flared and were switched to open-label ixekizumab retreatment	Placebo (ixekizumab withdrawal) (N=28)	
ASDAS disease activity status	LDA	ID
Recaptured response before open label ixekizumab retreatment	4	1
Recaptured response with open label ixekizumab retreatment (≤16 weeks)	23	14
Recaptured response with open label ixekizumab retreatment (>16 weeks)	0	5
Total patients who recaptured response at week 104	27/28 (96%)	20/28 (71%)

Data are presented as n, (%) for the total row and n only for all other rows. In each column, the denominator is 28. ASDAS, Ankylosing Spondylitis Disease Activity Score; ID, inactive disease; LDA, low disease activity including ID; N, number of patients in the analysis population.

Conclusion: Pts continuously treated with IXE were less likely to experience flare vs pts on PBO (IXE withdrawal). The vast majority of pts withdrawn from IXE to PBO recaptured at least LDA and over half met ID with IXE retreatment. This may provide support for pts who require interruption in therapy.

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OP0018

COMPARISON OF THE EFFECT OF TREATMENT WITH NSAIDS ADDED TO ANTI-TNF THERAPY VERSUS ANTI-TNF THERAPY ALONE ON PROGRESSION OF STRUCTURAL DAMAGE IN THE SPINE OVER TWO YEARS IN PATIENTS WITH ANKYLOSING SPONDYLITIS (CONSUL) – AN OPEN-LABEL, RANDOMIZED CONTROLLED, MULTICENTER TRIAL

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Background: There is some evidence that NSAIDs, in particular celecoxib (CEL), might possess not only symptomatic efficacy but also disease-modifying properties in radiographic axial spondyloarthritis (r-axSpA) formerly known as ankylosing spondylitis, retarding progression of structural damage in the spine if taken continuously. For biological disease-modifying antirheumatic drugs (bDMARDs), retardation of structural damage progression has also been demonstrated, but at least 4 years of treatment seem to be necessary (at least for tumour necrosis factor inhibitors – TNFi) to see such an effect. Therefore, a combination of an NSAID with a TNFi might bring additional benefits in terms of retardation of structural damage progression especially in high-risk patients.

Objectives: The aim of this RCT was to evaluate the impact of treatment with the COX-II-selective NSAID (CEL) when added to a TNFi (golimumab - GOL) compared with TNFi (GOL) alone on progression of structural damage in the spine over 2 years in patients with r-axSpA.

Methods: Eligible patients had r-axSpA and high disease activity (BASDAI ≥4), NSAID failure and risk factors for radiographic spinal progression: C-reactive protein >5 mg/l and/or ≥1 syndesmophyte(s). The trial consisted of two phases: a 12-week run-in phase, in which all included patients received treatment with GOL 50 mg every 4 weeks sc, followed by a 96-week controlled treatment period, in which patients who achieved a BASDAI improvement of ≥2 points were randomly assigned to GOL + CEL 200 mg bid or GOL alone arms. The primary endpoint was radiographic spinal progression as assessed by the change in the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) after 108 weeks in the intent-to-treat population, read by 3 independent readers blinded for the treatment arm and the time-point.

Results: Of the 157 screened patients, 81.5% (n=128) were enrolled into the run-in phase. 109 patients fulfilled the BASDAI response criterion at w12 and were randomized 1:1 (54 vs. 55) to GOL+CEL or GOL alone; 97 (45 vs. 52) patients completed the study at w108. Clinical characteristics of the randomized patients are shown in Tab. 1. The mSASSS change after w108 was 1.1 (95%CI 0.2; 2.0) vs. 1.7 (95%CI 0.8; 2.6) in the GOL+CEL vs. GOL alone groups, respectively, p=0.79. Figure 1 shows the cumulative probability of the mSASSS change in both treatment arms. New syndesmophytes in the opinion of three readers occurred in 11% vs. 25% of the patients in the GOL+CEL vs. GOL alone groups, respectively, p=0.12. During the study, a total of 14 serious adverse events (SAE) were reported (7 in the GOL+CEL group, 5 in the GOL alone group and 2 during the run-in phase).

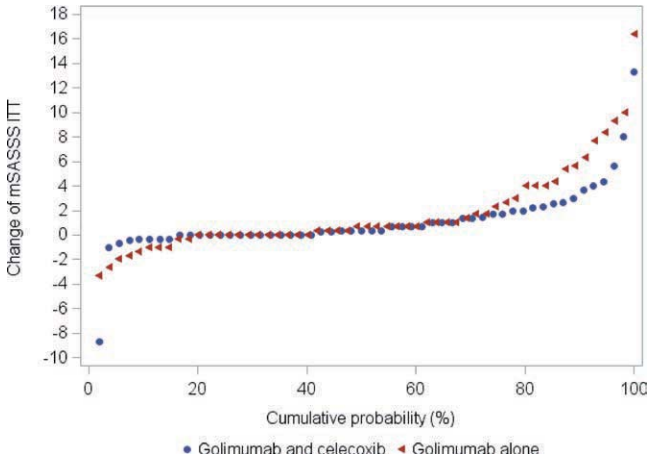

Figure 1. Cumulative probability plot of mSASSS progression over 108 weeks of treatment.

Conclusion: In this study, a combined therapy with GOL+CEL did not show significant superiority over GOL monotherapy in retarding radiographic spinal progression over two years in r-axSpA patients.

However, the observed numerical reduction in radiographic spinal progression associated with the combined treatment might be, however, clinically relevant for patients at high risk for progression.

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Table 1. Baseline characteristics of randomized patients

Parameters		GOL+CEL N=54		GOL alone N=55		All patients N=109	
		validn	value	validn	value	validn	value
Sex, male	n (%)	54	40 (74.1)	55	41 (74.5)	109	81 (74.3)
Age, years	Mean (SD)	54	39.9 (9.9)	55	37.5 (10.8)	109	38.7 (10.4)
Smoker	n (%)	53	19 (35.8)	55	22 (40)	108	41 (38)
HLA-B27 positivity	n (%)	54	45 (83.3)	51	47 (92.2)	105	92 (87.6)
BASDAI	Mean (SD)	54	6.2 (1)	55	6.1 (1.1)	109	6.1 (1.1)
BASMI	Mean (SD)	54	2.6 (1.9)	54	2.9 (1.4)	108	2.8 (1.6)
CRP > 5 mg/L	n (%)	54	38 (70.4)	55	38 (69.1)	109	76 (69.7)
ASDAS-CRP	Mean (SD)	54	3.6 (0.6)	55	3.7 (0.9)	109	3.7 (0.8)
Prior bDMARDs	n (%)	54	17 (31.5)	55	9 (16.4)	109	26 (23.9)
Presence of ≥ 1 syndesmophyte(s)	n (%)	54	27 (50)	55	28 (50.9)	109	55 (50.5)
mSASSS	Mean (SD)	54	13.5 (16.9)	55	10.3 (13.2)	109	11.9 (15.2)

OP0019

BIMEKIZUMAB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 24-WEEK EFFICACY & SAFETY FROM BE MOBILE 2, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED STUDY

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Background: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. In a phase 2b study, BKZ showed rapid and sustained efficacy and was well tolerated up to 156 weeks (wks) in patients (pts) with active ankylosing spondylitis (AS).[1,2]

Objectives: To assess efficacy and safety of BKZ vs placebo (PBO) in pts with active AS up to Wk 24 in the ongoing pivotal phase 3 study, BE MOBILE 2.

Methods: BE MOBILE 2 (NCT03928743) comprises a 16-wk double-blind, PBO-controlled period and 36-wk maintenance period. Pts were aged ≥18 yrs, met modified New York criteria and had active AS (BASDAI ≥4, spinal pain ≥4) at BL. Pts were randomised 2:1, BKZ 160 mg Q4W:PBO. From Wk 16, all pts received BKZ 160 mg Q4W. Primary and secondary efficacy endpoints were assessed at Wk 16.

Results: Of 332 randomised pts (BKZ: 221; PBO: 111), 322 (97.0%) completed Wk 16 and 313 (94.3%) Wk 24. BL characteristics were comparable between groups: mean age 40.4 yrs, symptom duration 13.5 yrs; 72.3% pts male, 85.5% HLA-B27+, 16.3% TNFi-experienced. At Wk 16, the primary (ASAS40: 44.8% BKZ vs 22.5% PBO; p<0.001) and all ranked secondary endpoints were met (Table 1). Responses with BKZ were rapid, including in PBO pts who switched to BKZ at Wk 16, and increased to Wk 24 (Figure 1; Table 1). Substantial reductions of hs-CRP by Wk 2 and MRI SIJ and spine inflammation by Wk 16 were achieved with BKZ vs PBO (Table 1). At Wk 24, ≥50% pts had achieved ASDAS <2.1 (Figure 1).

Over 16 wks, 120/221 (54.3%) BKZ pts had ≥1 TEAE vs 48/111 (43.2%) PBO; three most frequent on BKZ were nasopharyngitis (BKZ: 7.7%; PBO: 3.6%), headache (4.1%; 4.5%) and oral candidiasis (4.1%; 0%). No systemic candidiasis was observed. Up to 16 wks, incidence of SAEs was low (1.8%; 0.9%); no MACE or deaths were reported; 2 (0.9%) IBD cases occurred in pts on BKZ.

Conclusion: Dual inhibition of IL-17A and IL-17F with BKZ in pts with active AS resulted in rapid, clinically relevant improvements in efficacy outcomes vs PBO. No new safety signals were observed.[1,2]

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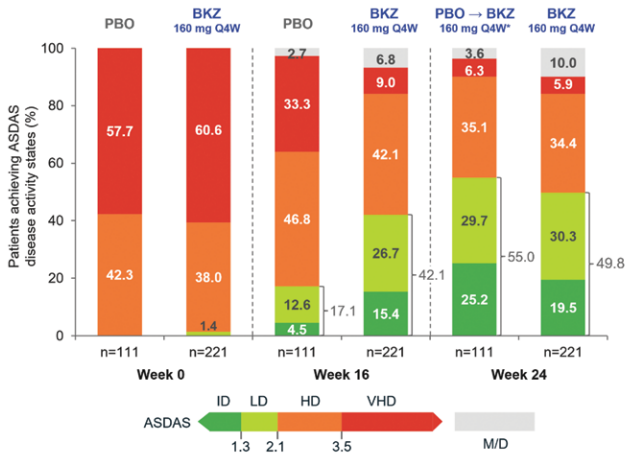
Table 1. Efficacy at Wks 16 and 24

		BL		Wk 16			Wk 24	
		PBO N=111	BKZ 160 mg Q4W N=221	PBO N=111	BKZ 160 mg Q4W N=221	p value	PBO→BKZ 160 mg Q4W N=111	BKZ 160 mg Q4W N=221
Ranked endpoints in hierarchical order	**ASAS40*** [NRI] n (%)	-	-	25 (22.5)	99 (44.8)	<0.001	63 (56.8)	119 (53.8)
	ASAS40 in TNFi-naïve† [NRI] n (%)	-	-	22 (23.4)[a]	84 (45.7)[b]	<0.001	56 (59.6)[a]	100 (54.3)[b]
	ASAS20† [NRI] n (%)	-	-	48 (43.2)	146 (66.1)	<0.001	85 (76.6)	159 (71.9)
	BASDAI CfB† [MI] mean (SE)	6.5 (0.1)	6.5 (0.1)	–1.9 (0.2)	–2.9 (0.1)	<0.001	–3.3 (0.2)	–3.3 (0.1)
	ASAS PR† [NRI] n (%)	-	-	8 (7.2)	53 (24.0)	<0.001	28 (25.2)	56 (25.3)
	ASDAS-MI† [NRI] n (%)	-	-	6 (5.4)	57 (25.8)	<0.001	43 (38.7)	67 (30.3)
	ASAS 5/6† [NRI] n (%)	-	-	16 (14.4)	94 (42.5)	<0.001	57 (51.4)	107 (48.4)
	BASFI CfB† [MI] mean (SE)	5.2 (0.2)	5.3 (0.2)	–1.1 (0.2)	–2.2 (0.1)	<0.001	–2.2 (0.2)	–2.4 (0.2)
	Nocturnal spinal pain CfB† [MI] mean (SE)	6.8 (0.2)	6.6 (0.1)	–1.9 (0.2)	–3.3 (0.2)	<0.001	–3.7 (0.3)	–3.8 (0.2)
	ASQoL CfB† [MI] mean (SE)	8.5 (0.4)	9.0 (0.3)	–3.2 (0.3)	–4.9 (0.3)	<0.001	–4.9 (0.4)	–5.4 (0.3)
	SF-36 PCS CfB† [MI] mean (SE)	34.6 (0.8)	34.4 (0.6)	5.9 (0.8)	9.3 (0.6)	<0.001	10.6 (0.8)	10.8 (0.6)
	BASMI CfB† [MI] mean (SE)	3.8 (0.2)	3.9 (0.1)	–0.2 (0.1)	–0.5 (0.1)	0.005	–0.5 (0.1)	–0.6 (0.1)
Other endpoints[n]	**Enthesitis-free state†c** [NRI] n (%)	-	-	22 (32.8)[d]	68 (51.5)[e]	-	33 (49.3)[d]	70 (53.0)[e]
	ASAS40 in TNFi-experienced [NRI] n (%)	-	-	3 (17.6)[f]	15 (40.5)[g]	-	-	-
	ASDAS-CRP CfB [MI] mean (SE)	3.7 (0.1)	3.7 (0.1)	–0.7 (0.1)	–1.4 (0.1)	-	–1.7 (0.1)	–1.6 (0.1)
	hs-CRP (mg/L) [MI] geometric mean (median)	6.7 (6.3)	6.5 (8.2)	6.0 (6.3)	2.4 (2.4)	-	1.9 (2.2)	2.1 (2.3)
	MRI spine Berlin CfB[h] [OC] mean (SD)	3.3 (4.9)[i]	3.8 (5.3)[j]	0.0 (1.4)[k]	–2.3 (3.9)[l]	-	-	-
	SPARCC MRI SIJ score CfB[h] [OC] mean (SD)	5.8 (7.7)[i]	7.4 (10.7)[m]	1.1 (6.9)[k]	–5.6 (9.9)[l]	-	-	-

Randomised set. *Primary endpoint; †Secondary endpoint; [a]n=94; [b]n=184; [c]MASES=0 in pts with BL MASES >0; [d]n=67; [e]n=132; [f]n=17; [g]n=37; [h]In pts in MRI sub-study; [i]n=45; [j]n=82; [k]n=43; [l]n=79; [m]n=83; [n]Nominal p values not shown.

Figure. ASDAS states over time



Randomised set. Data reported as observed case. *At Wk 16, pts on PBO switched to BKZ.

Abbreviations: AS: ankylosing spondylitis; ASAS20/40: Assessment of SpondyloArthritis international Society 20/40% response; ASAS PR: ASAS partial remission; ASDAS -CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS-MI: ASDAS major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; HD: high disease; HLA-B27: human leukocyte antigen B27; hs-CRP: high sensitivity-CRP; IBD: inflammatory bowel disease; ID: inactive disease; IL: interleukin; LD: low disease; MACE: Major Adverse Cardiovascular Event; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; M/D: missing data; MI: multiple imputation; MRI: magnetic resonance imaging; n: number; NRI: non-responder imputation; OC: observed case; PBO: placebo; Pts: patients; Q4W: every four weeks; SAEs: serious adverse events; SD: standard deviation; SE: standard error; SPARRC: Spondyloarthritis Research Consortium of Canada; SIJ: Sacroiliac Joints; SF-36 PCS: Short Form-36 Physical Component Summary; TNFi: tumour necrosis factor inhibitor; VHD: very high disease; Wks: weeks; yr: year.

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OP0020

SEX DIFFERENCES IN EFFECTIVENESS OF FIRST-LINE TUMOR NECROSIS FACTOR INHIBITORS IN AXIAL SPONDYLOARTHRITIS; RESULTS FROM FIFTEEN COUNTRIES IN THE EUROSPA RESEARCH COLLABORATION NETWORK

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Background: Evidence reveals sex differences in physiology, disease presentation and response to treatment in axial spondyloarthritis (axSpA). Pooled data from four randomized controlled trials demonstrated reduced treatment efficacy of a tumor necrosis factor inhibitor (TNFi) in females compared to males with ankylosing spondylitis[1]. However, real-life evidence confirming these data in large cohorts is scarce. We sought to validate prior studies using data from a large multinational cohort based on real-life clinical practice.

Objectives: To investigate sex differences in treatment response and drug retention rates in clinical practice among patients with axSpA, treated with their first TNFi.

Methods: Data from biologic-naïve axSpA patients initiating a TNFi in the EuroSpA registries were pooled. In the primary analysis, propensity-score weighting was applied to assess the causal effect of sex on clinically important improvement (CII) according to ASDAS-CRP at 6 months. A generalized linear regression model was used to estimate the causal risk difference (RD) and relative risk (RR) of sex on CII. Possible covariates influencing the outcome were determined a priori and selected based on availability in the database (<20% missing). The final covariates included in the model were country, age and TNFi start year. In the secondary analysis, drug retention was assessed over 24 months of follow-up by Kaplan-Meier curves and log-rank test.

Results: In total, 6,451 axSpA patients with available data on ASDAS-CRP at baseline and 6 months were assessed for treatment response. Baseline characteristics are shown in the Table 1. In the adjusted analysis, the probability for females to have CII was 15% (RR, 0.85; 95% confidence interval [CI], 0.82 to

0.89) lower compared to males and the difference in probability for having CII was 9.4 percentage points (RD, 0.094; 95% CI, 0.069 to 0.12). The survival analysis included 28,608 axSpA patients with available data on retention rates. The TNFi 6/12/24-month retention rates were significantly lower in females (81%/69%/58%) compared to males (89%/81%/72%), see Figure 1.

Table 1.

	Female	Male
	Mean (SD), Median [IQR] or percentages	Mean (SD), Median [IQR] or percentages
Age (years)	42.0 (12.1)	41.4 (12.3)
Fulfilment of mNYC	66%	80%
Disease duration (years)	2.0 [1.0, 7.0]	3.0 [1.0, 9.0]
TNFi start year		
Start 1999-2009	7.2%	9.8%
Start 2010-2013	26%	27%
Start 2014-2016	37%	36%
Start 2017-2020	30%	27%
BASDAI, mm	59 (20)	54 (21)
BASFI, mm	48 (25)	46 (24)
ASDAS, units	3.5 (0.9)	3.5 (1.0)
CRP (mg/L)	6.7 [2.5, 16.0]	11.9 [4.0, 25.0]
SJC (0-28)	0 [0, 0]	0 [0, 0]
TJC (0-28)	0 [0, 2]	0 [0, 1]
VAS pain, mm	63 (22)	59 (24)
VAS fatigue, mm	65 (25)	59 (26)

mNYC, modified New York criteria; TNFi, tumor necrosis factor inhibitor; BASDAI, Bath Ankylosing Spondylitis Disease Activity Indexf; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS, Ankylosing Spondylitis Disease Activity Score; CRP, C-reactive protein; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale.

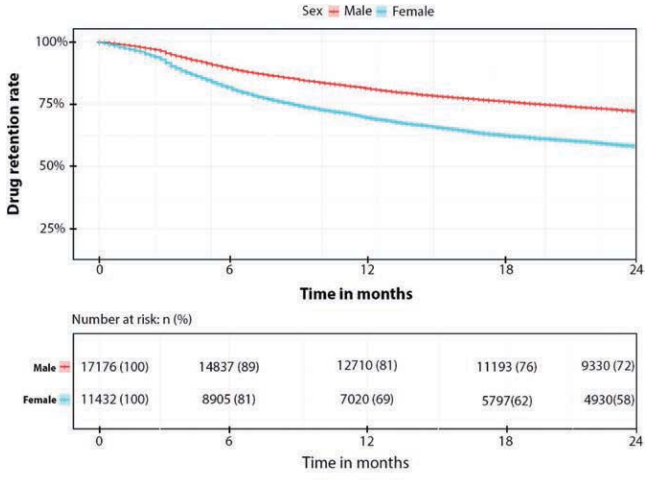

Figure. Sex differences in 24-month retention rates in first-line tumor necrosis factor inhibitors in patients with axial spondyloarthritis in EuroSpA (Kaplan-Meier, log-rank test; p<0.001).

Conclusion: Treatment efficacy and retention rates are lower among female patients with axSpA initiating their first TNFi. Females presented with lower C-reactive protein levels and higher scores on patient reported outcomes at baseline, reflecting differences in disease expression. Recognizing these sex differences is of relevance for customized patient care and may improve patient education.

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[1] van der Horst-Bruinsma et al. Ann Rheum Dis. 2013 Jul;72(7):1221-4.

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OP0021

TREATMENT WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IS ASSOCIATED WITH RETARDATION OF RADIOGRAPHIC SPINAL PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: 10-YEAR RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: There are conflicting data regarding effect of nonsteroidal anti-inflammatory drugs (NSAID) on radiographic spinal progression in axial spondyloarthritis (axSpA). The analysis of the first 2-year of the GErman SPondyloarthritis Inception Cohort (GESPIC) showed that higher NSAID intake may retard new bone formation in r-axSpA. It remained, however, unclear, whether cyclooxygenase-2 selective inhibitors (COX2i) might have a stronger effect than non-selective (NS) ones and if the effect could be observed also in nr-axSpA.

Objectives: To investigate the effect of NSAIDs (COX2i and NS) intake on radiographic spinal progression in patients with r-axSpA and nr-axSpA.

Methods: Based on availability of at least two sets of spinal radiographs during 10-year follow-up, 243 patients with early axSpA (130 and 113 nr- and r-axSpA, respectively) from GESPIC were included in this analysis. The patients contributed a total of 540 2-year radiographic intervals. Radiographs were scored by 3 trained and calibrated readers according to modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Final mSASSS was calculated as a mean of 3 readers, and progression was defined as absolute mSASSS change score over 2 years. NSAID type, daily dose, and frequency of intake were recorded at visits. The ASAS index of NSAID intake (0-100) counting both dose and duration of intake was calculated for intervals. The association between NSAID intake

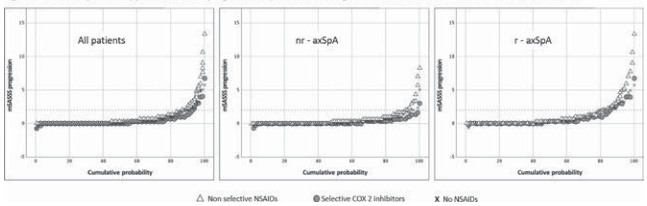
(NSAID type and NSAID score) and radiographic spinal progression over 2 years was analysed using longitudinal generalized estimated equations (GEE).
Results: At baseline, 161 (66.3%) patients were treated with NSAIDs. While 289 (53.5%) and 128 (23.7%) 2-year radiographic intervals were covered by NS and COX-2i respectively, 123 (22.8%) intervals were not covered by NSAID. The significant association between higher NSAID intake and retardation of radiographic spinal progression was found in adjusted multivariable longitudinal GEE analysis. This effect was mostly attributable to patients with r-axSpA (Table 1). mSASSS progression was numerically lower in patients taking COX2i (irrespectively of dose) as compared to patients treated with NS-NSAIDs; in stratified analysis, however, there was no clear dose-dependency (as reflected by NSAID index) in both groups (Figure 1, Table 1).

Table 1. The association between radiographic spinal progression (mSASSS change score) and NSAID intake in patients with axSpA in multivariable longitudinal GEE

	All axSpA β (95% CI)* (n=461)	nr-axSpA β (95% CI)* (n=244)	r-axSpA β (95% CI)* (n=217)
NSAID intake score, per 10 points	**-0.04 (-0.09, 0.00)**	-0.02 (-0.06, 0.02)	**-0.07 (-0.13, 0.00)**
NSAID type§			
NS inhibitors vs No NSAID	0.30(-0.07, 0.66)	0.25(-0.07, 0.57)	0.26(-0.40, 0.92)
COX2i vs No NSAID	0.17(-0.19, 0.54)	0.15(-0.15, 0.46)	0.18(-0.49, 0.85)
COX2i vs NS inhibitors	-0.12(-0.37, 0.12)	-0.10(-0.28, 0.09)	-0.08(-0.57, 0.40)
Analysis stratified according to NSAID type			
Non-selective NSAID intake score, per 10 points	-0.06(-0.12, 0.00)	-0.04(-0.09, 0.01)	-0.07(-0.17, 0.03)
COX2 selective NSAID intake score, per 10 points	-0.06(-0.13, 0.02)	-0.03(-0.07, 0.02)	-0.09(-0.18, 0.01)

axSpA: axial spondyloarthritis; COX2i, cyclooxygenase-2 selective inhibitors; n, number of current 2-year radiographic intervals in multivariable analyses; NS, non-selective COXi; NSAID, non-steroidal anti-inflammatory drugs. *All multivariable models were adjusted for sex, symptom duration at the beginning of the interval, time-averaged ASDAS the interval, classification as radiographic axSpA, smoking in the interval, mSASSS at the beginning of theinterval, and TNFi use in the interval. §NSAID intake score was added in this model.

Figure. Cumulative probability plots of mSASSS progression in patients receiving no NSAIDs, non-selective NSAIDs and selective COX2i.



Conclusion: Higher NSAID intake is associated with lower radiographic spinal progression, particularly in r-axSpA patients. COX2i might possess a stronger inhibitory effect on radiographic progression as compared to NS-NSAIDs.
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OP0022 DISEASE ACTIVITY-GUIDED TAPERING OF BIOLOGICS IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A RANDOMISED, OPEN-LABEL, EQUIVALENCE TRIAL

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Background: Traditionally, biologics are maintained lifelong at standard dose in patients with inflammatory arthritis (IA) when sustained low disease activity (LDA) is reached. However, evidence of possible tapering is emerging but data on the optimal approach is lacking.
Objectives: The primary outcomes at 18 months follow-up are:

- *Superiority:* The proportion of patients reduced to ≤50% of their baseline biologic dose.
- *Equivalence:* Disease activity (rheumatoid arthritis [RA] and psoriatic arthritis [PsA]: Disease Activity Score28-C-Reactive Protein [DAS28-CRP] and axial spondyloarthritis [axSpA]: Ankylosing Spondylitis Disease Activity Score [ASDAS]).

Methods: The BIODOPT trial was a randomised, open-label, equivalence trial (EudraCT 2017-001970-41). Eligible patients were adults with RA, PsA, or axSpA in LDA on stable biologic doses during ≥12 months. The randomisation ratio was 2:1 (tapering:continuation) stratified by diagnosis, centre, and repeated biologic failures. In the tapering group, the biologic dosing interval was prolonged by 25% every four months until flare or discontinuation. The continuation group was kept on their baseline biologic dosing interval; however, a small increase was allowed (as usual practise) if requested by the patient. The sample size calculation was based on a pre-defined equivalence margin of ±0.5 disease activity points (<half of the minimal important difference in DAS28-CRP [>1.2] or ASDAS [>1.1]) yielding a power of 87% for 180 enrolled patients. All analyses were based on the intention-to-treat population. Continuous outcomes were analysed with repeated-measures linear mixed-effects models with group, diagnosis, centre, repeated biologic failures, time point, and the interaction between group and time as fixed factors and the baseline value of the relevant variable as a covariate. Categorical outcomes were analysed using logistic regression with missing data imputed as trial failures.
Results: Between May, 2018, and March, 2020, 142 patients were enrolled of which 95 were randomised to tapering and 47 to continuation; inclusion was closed in April 2020 due to national implications of the coronavirus pandemic.
At 18 months, significantly more patients in the tapering group (35 patients [(37%]) achieved a significant reduction in their biologic dose (≥50%) compared to the continuation group (one patient [2%]), absolute risk difference (RD) 35%, 95%CI: 24% to 45%, p<0.0001, Table 1. Furthermore, disease activity at 18 months was within the equivalence margins of ±0.5, mean difference between groups 0.08, 95%CI: -0.12 to 0.29; Table 1 and Figure 1. Flares were more frequent in the tapering group (39 [41%] vs 10 [21%], RD 0.20, 95%CI: 0.04 to 0.35, p=0.011) but managed with rescue therapy (e.g. biologic dose escalation or glucocorticoids) as only one patient (1%) in the tapering group and three patients (6%) in the continuation group lost therapeutic response and were switched to another biological agent.

Table 1. Comparison at 18 months in the ITT population

Outcome	Tapering group N = 95	Continuation group N = 47	Group difference (95%CI)	p-value
Primary outcome:				
Biologics reduced to ≤50%, n (%)	35 (37%)	1 (2%)	0.35 (0.24 to 0.45)	<0.001
Disease activity, LSMeans (SE)	1.84 (0.15)	1.75 (0.16)	0.08 (-0.12 to 0.29)	0.428
Key secondary outcomes:				
Remission[1], n (%)	63 (66%)	33 (70%)	-0.04 (-0.20 to 0.12)	0.637
Low disease activity[2], n (%)	79 (83%)	41 (87%)	-0.04 (-0.16 to 0.08)	0.511
Flares[3], n (%)	39 (41%)	10 (21%)	0.20 (0.04 to 0.35)	0.011

N: number, CI: confidence interval, LSMeans: Least squares means, SE: Standard error. [1]: RA or PsA: DAS28-CRP <2.6. AxSpA: ASDAS <1.3. [2]: RA or PsA: DAS28-CRP <3.2. AxSpA: ASDAS <2.1. [3]: RA or PsA: ΔDAS28-CRP >1.2 or ΔDAS28-CRP >0.6 AND current DAS28-CRP ≥3.2. AxSpA: inflammatory back pain AND ΔASDAS ≥0.9 and/or ≥1 swollen joint.

Conclusion: Across IA conditions, a significant reduction of biologic dose is possible with disease activity-guided tapering while maintaining a similar disease activity state compared to continuation of biologic as usual care.
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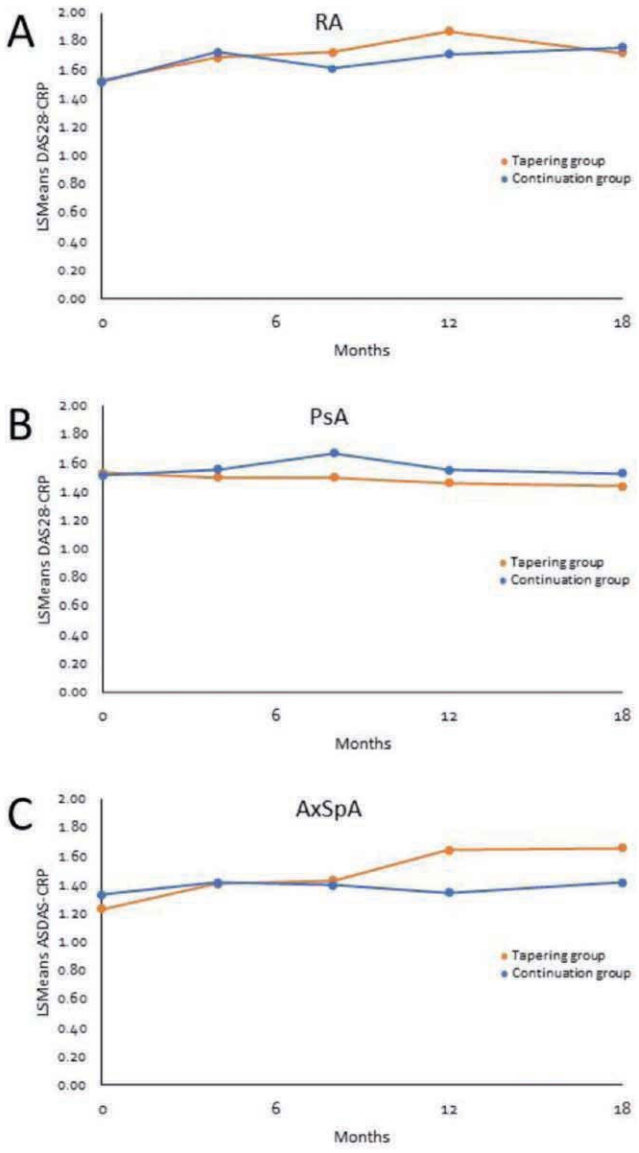
Figure 1: Disease activity during the study period by diagnosis



sequence, and CCH for data management. The Parker Institute, Bispebjerg and Frederiksberg Hospital is supported by a core grant from the Oak Foundation (OCAY-18-774-OFIL).

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OP0023

A RANDOMIZED, DOUBLE-BLIND TRIAL COMPARING SECUKINUMAB 300 MG AND 150 MG AT WEEK 52 IN PATIENTS WITH ANKYLOSING SPONDYLITIS WHO DID NOT ACHIEVE INACTIVE DISEASE DURING AN INITIAL 16 WEEKS OF OPEN-LABEL TREATMENT WITH SECUKINUMAB 150 MG

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Background: Ankylosing spondylitis (AS) is a chronic, systemic inflammatory condition characterized by inflammatory back pain and is associated with extra-musculoskeletal manifestations and systemic comorbidities. Secukinumab (SEC) doses of 150 mg and 300 mg are approved to treat AS, although no dose escalation studies are available in patients who have inadequate response to SEC 150 mg.

Objectives: The ASLeap study (NCT03350815) estimated the difference in clinical response to SEC 300 mg vs 150 mg at Week (Wk) 52 in patients with AS who failed to achieve Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease status on SEC 150 mg at Wk 16.

Methods: In this randomized, double-blind, parallel-group, multicenter, phase 4 study, 322 patients with AS were assigned to receive open-label SEC 150 mg administered per the label for 16 Wks (period 1). At Wk 16, patients who did not achieve inactive disease (ASDAS < 1.3) at Wks 12 and 16 were randomized 1:1 in a double-blind manner to SEC 150 mg or escalated to SEC 300 mg q4w to Wk 52 (period 2). The primary efficacy variable was achievement of ASDAS < 1.3 and the primary analysis time point was Wk 52. Secondary efficacy variables were achievement of ASDAS clinically important improvement ≥ 1.1, 50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50), Assessment of SpondyloArthritis international Society responses (ASAS20, ASAS40, and ASAS partial remission), and change from baseline in BASDAI, ASAS Health Index (ASAS-HI), and the Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-F). Safety was evaluated by incidence of treatment-emergent adverse events (TEAEs) through Wk 52. No statistical hypothesis tests for superiority or equivalence were planned in the protocol and none were performed.

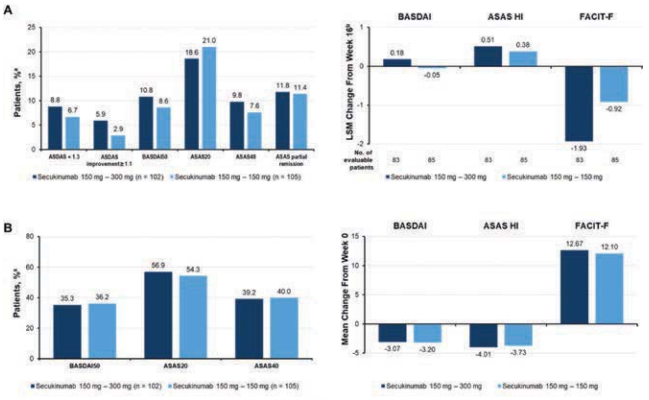
Results: Of 279 patients receiving SEC 150 mg who completed the 16-wk open-label period 1, 22 (7.9%) achieved ASDAS < 1.3 at Wks 12 or 16 and continued receiving SEC 150 mg; 207 patients did not attain ASDAS < 1.3 at Wk 12 and Wk 16 and initiated period 2. Demographics and baseline disease characteristics were balanced between patients randomized to SEC 150 mg and SEC 300 mg, including the proportion of patients who were TNFi naive (SEC 150 mg: 73 [72.3%]; SEC 300 mg: 73 [69.5%]) (Table 1). Approximately 60% of patients in either SEC group were HLA-B27 positive. After having an inadequate response to SEC 150 mg through Wk 16, patients receiving either dose of SEC experienced similar improvements at Wk 52 in disease activity as measured by achievement of ASDAS < 1.3, ASDAS clinically important improvement ≥ 1.1, BASDAI50, ASAS20, ASAS40, and ASAS partial remission; and mean changes in BASDAI, quality of life as measured by ASAS HI, and fatigue as measured by FACIT-F (Figure 1). The incidence of TEAEs through Wk 52 was similar between patients receiving SEC 300 mg (63.4%) and 150 mg (68.6%).

Table 1. Demographics and Baseline Disease Characteristics of Patients in Period 2 (safety set)

Characteristic	Secukinumab 150 mg → 300 mg N = 101	Secukinumab 150 mg → 150 mg N = 105
Age, mean (SD), years	48.5 (14.1)	47.0 (13.7)
Female, n (%)	43 (42.6)	52 (49.5)
BMI, mean (SD), kg/m^2	32.0 (8.0)	32.1 (7.7)
HLA-B27 positive, n (%)	60 (59.4)	65 (61.9)
Time since axial symptom onset, mean (SD), years	13.9 (11.7)	14.0 (12.5)
Time since diagnosis of AS, mean (SD), years	4.7 (8.6)	5.1 (9.7)
TNFi naive, n (%)	73 (72.3)	73 (69.5)
History of extra-axial involvement, n (%)		
Peripheral arthritis	34 (33.7)	30 (28.6)
Enthesitis	29 (28.7)	31 (29.5)
Uveitis	13 (12.9)	17 (16.2)
Psoriasis	14 (13.9)	14 (13.3)
Dactylitis	7 (6.9)	4 (3.8)
Inflammatory bowel disease	2 (2.0)	1 (1.0)

AS, ankylosing spondylitis; BMI, body mass index; TNFi, tumor necrosis factor inhibitor.

Figure 1. Improvements at Week 52 Among Patients Randomized at Week 16 Using **(A)** Week 16 as Baseline and **(B)** Week 0 as Baseline



ASAS, Assessment of SpondyloArthritis international Society; ASAS HI, Assessment of SpondyloArthritis international Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue Scale; LSM, least-squares mean.
[a] Analysis was conducted using nonresponder imputation for binary efficacy variables.
[b] LSMs are based on a mixed-effects model for repeated measures.

Conclusion: Patients with AS who did not achieve inactive disease by Wk 16 after receiving SEC 150 mg experienced similar clinical response and safety through Wk 52 regardless of dose escalation to SEC 300 mg or continuation on SEC 150 mg.

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Clinical aspects in Psoriatic Arthritis

OP0024

DIFFERENTIATION BETWEEN IL-6 AND IL-17 PATHWAY INHIBITION IN RELATIONSHIP WITH CLINICAL OUTCOMES IN NON-BIOLOGICAL DMARD-IR AND BIOLOGICAL DMARD-IR PSORIATIC ARTHRITIS PATIENTS TREATED WITH UPADACITINIB IN SELECT-PSA 1 AND SELECT-PSA 2 STUDIES

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Background: The differential contribution of IL-6 and IL-17 pathways to the pathogenesis of psoriatic arthritis (PsA) is not fully understood. Upadacitinib (UPA), an oral JAK inhibitor, was more effective than placebo (PBO) in improving key clinical manifestations of PsA in two global phase 3 trials, SELECT-PsA 1 (non-biological DMARD-IR, nbDMARD-IR) and SELECT-PsA 2 (biological DMARD-IR, bDMARD-IR).[1,2] Targeted proteomic analysis suggested that UPA modulates multiple biological pathways in innate and adaptive immune systems via direct and indirect inhibition of key regulators, including IL-6 and IL-17 pathways, with a possible shift from Th1 predominance in nbDMARD-IR PsA to a more Th17 bias in bDMARD-IR PsA.[3]

Objectives: We assessed the relationship between IL-6 and IL-17 pathway modulation and different clinical outcomes after UPA treatment in nbDMARD-IR and bDMARD-IR PsA patients.

Methods: A subset of patients was randomly selected from SELECT-PsA 1 (n=74 of UPA 15 mg QD, n=74 of PBO) and PsA 2 studies (n=90 of UPA 15 mg QD, n=81 of PBO). Serum levels of IL-6, IL-17A, IL-17F, and beta-defensin 2 (BD2) proteins were measured at baseline, week 2, and week 12 by validated immunoassays. The quantitative cytokine measurements were transformed as log10, and PASI score was transformed as $\log_{10}$ (x+1) prior to analysis. A Repeated Measure Mixed Linear Model was used to compare UPA versus PBO treatment effects in overall selected patients and between responders and non-responders defined by PASDAS score ≤ 3.6 (Minimal Disease Activity, MDA)[4] and PASI75 at week 12, respectively. The relationships between cytokines and clinical outcomes (PASI and DAS28-CRP) were assessed by Pearson's correlation at baseline and after treatment.

Results: In nbDMARD-IR PsA patients, baseline IL-17A, IL-17F, and BD2 levels correlated with each other and with PASI, while IL-6 appeared independent from the IL-17 pathway and correlated with DAS28-CRP. At week 12, UPA treatment significantly decreased IL-6 and BD2. The decrease of IL-6 was more pronounced in PASDAS MDA responders and correlated with DAS28-CRP improvement, but the decrease of BD2 was significant in PASI75 responders and correlated with PASI improvement. In contrast, IL-17A and IL-17F were not significantly changed after UPA treatment, neither correlated with clinical outcomes at week 12.

In bDMARD-IR PsA patients, baseline IL-17A level was significantly elevated compared to nbDMARD-IR patients but weakly correlated with other cytokines and show no correlation with PASI. At week 12, the reduction of IL-6 after UPA treatment was not different between responders and non-responders (PASDAS MDA or PASI75) and did not correlate with DAS28-CRP improvement, while the reduction of BD2 remained significant in PASI75 responders and correlated with PASI improvement. Further, UPA treatment significantly reduced IL-17A in PASDAS MDA responders and IL-17F in PASI75 responders compared to non-responders, respectively. The reduction of IL-17F correlated with PASI improvement at week 12.

Conclusion: IL-6 and IL-17 pathway inhibition after UPA treatment showed different profiles in relationship with clinical outcomes in nbDMARD-IR versus bDMARD-IR PsA patients. IL-6 decrease was more pronounced in nbDMARD-IR PsA patients and associated with joint manifestation improvement, while IL-17A and IL-17F decreases were only observed in bDMARD-IR PsA patients and associated with psoriasis improvement. BD2, a biomarker of Th17-associated skin pathology, significantly decreased after UPA treatment in both nbDMARD-IR and bDMARD-IR PsA studies, which likely contributed to UPA effects on psoriasis improvement in a broad range of PsA patients.

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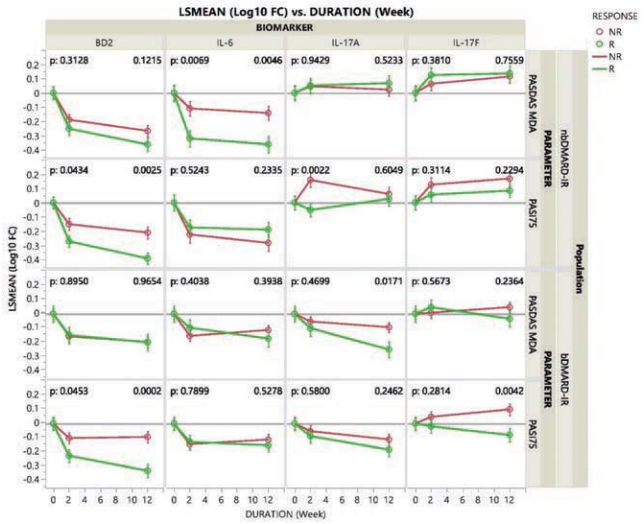
Figure: Biomarker inhibition effects in responders vs. non-responder subgroups differ between nbDMARD-IR and bDMARD-IR PsA patients treated with UPA (number annotations represent nominal p values of the comparison between subgroups at week 2 and week 12, respectively)



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OP0025

FACTORS ASSOCIATED WITH FATIGUE AND ITS IMPROVEMENT – A PRINCIPAL COMPONENT ANALYSIS OF PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS FROM GUSELKUMAB PHASE 3 TRIALS

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Background: Fatigue, one of the top 3 patient (pt)-reported symptoms of psoriatic arthritis (PsA) and a recent PsA outcome domain,[1] causes impaired health-related quality-of-life, diminished productivity, and disability.[1-3] Although the origins of fatigue are multifactorial, inflammation is hypothesized to play an important role.[4] In pts with active PsA, treatment with guselkumab (GUS) led to clinically meaningful and sustained improvements in fatigue through 1 year in DISCOVER-1 (D1) and DISCOVER-2 (D2).[5]

Objectives: To identify 1) factors associated with fatigue and 2) factors associated with change in fatigue among pts with PsA treated with GUS.

Methods: In the Phase 3 D1 (N=381, biologic-naïve and tumor necrosis factor inhibitor-experienced) and D2 (N=739, biologic-naïve) studies, pts with active PsA despite standard therapies and/or biologic disease-modifying antirheumatic drugs were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO) with crossover to GUS 100 mg Q4W at W24. The pt-reported Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale measured fatigue (scored 0-52). In these post-hoc analyses of D1 and D2 pts, a principal component analysis (PCA) was performed using W0 data to identify the underlying baseline factors associated with fatigue. Additionally, linear regression analyses were performed to identify covariates associated with change in fatigue from W0 to W24.

Results: In 1120 pts (mean age 47 yrs, mean disease duration 5.9 yrs, 48% female), mean FACIT-Fatigue scores at baseline ranged from 29.1 to 31.4 (vs 43.6 for the general US population).[5] PCA showed that 62% of the variability in fatigue could be explained by 3 components (Figure 1). The first component, explaining 34% of variability in fatigue, largely comprised systemic disease activity and function measures such as pain, pt global assessment of disease activity (PtGDA), physician's global assessment of disease activity, and Health Assessment Questionnaire-Disability Index (HAQ-DI). The second component, explaining 16% of variability, comprised joint manifestations including swollen joint count (SJC) and tender joint count (TJC). Skin involvement as assessed by Psoriasis Area and Severity Index (PASI) and systemic inflammation (C-reactive protein [CRP]) could explain 12% of the variability in fatigue (Figure 1 and Table 1). In a multivariate linear regression analysis, after adjusting for effects from other variables, improvement in CRP, physical function (HAQ-DI), PtGDA, and PASI score were significantly associated with fatigue improvement in GUS-treated pts at W24 (all p<0.001).

Table 1. PCA of Pts With Active PsA in D1+D2 (N=1120; Pooled W0 data): Factor Loading Estimates by Covariates

	Component1 Systemic Disease Activity and Function	Component 2 Joint Manifestations	Component 3 Skin Involvement and Inflammation
PsA disease duration, yr	0.10	0.14	0.25
PASI total score (0-72)	0.22	0.23	**0.74**
CRP, mg/dL	0.36	-0.13	**0.55**
HAQ-DI score (0-3)	**0.73**	-0.09	-0.19
Pain (0-10 VAS)	**0.83**	-0.35	-0.13
PtGDA (0-10 VAS)	**0.82**	-0.36	-0.16
Physician global assessment of disease activity (0-10 VAS)	**0.65**	-0.18	0.23
SJC (0-66)	0.50	**0.74**	-0.12
TJC (0-68)	0.54	**0.70**	-0.18

VAS=Visual Analog Scale.

Conclusion: Among pts with PsA, measures of systemic disease activity and function, followed by joint manifestations, and skin involvement/inflammation accounted for 62% of the variability in fatigue. The large residual effect (38%) that was unexplained by the current model suggests the need for further research to identify additional factors (eg, distinct molecular pathways) contributing to the fatigue reported by PsA pts.

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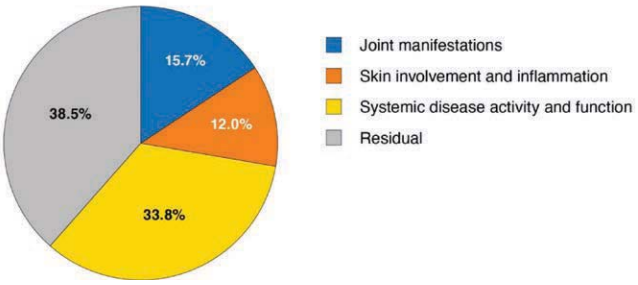
Figure. PCA of Pts With Active PsA in D1+D2 (N=1120; Pooled W0 data): Proportion of Fatigue Variability Explained by Identified Components



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OP0026

CLINICAL AND IMAGING-BASED CHARACTERIZATION OF A PROSPECTIVE COHORT OF PATIENTS WITH AXIAL PSORIATIC ARTHRITIS (AXIAL PSA). GESPIC-AXIAL PSA: RESULTS OF AN INTERIM ANALYSIS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease, which is subsumed together with axial spondyloarthritis (axial SpA) under the umbrella term spondyloarthritis, whose clinical presentations are very heterogeneous. Axial involvement (axial PsA) has been described to be present in 34% of PsA patients [1] and has been systematically investigated only retrospectively or in cross-sectional studies [2]. Although axial PsA seems to have similar characteristics to axial SpA, it is not clear whether axial PsA and axial SpA, are a spectrum of the same disease with different expression patterns or different diseases with great similarities.

Objectives: To prospectively investigate the clinical and imaging morphology patterns in a well-defined cohort of patients with axial PsA from the German SPondyloarthritis Inception Cohort (GESPIC).

Methods: Prospective, longitudinal, observational study of patients with an imaging confirmed diagnosis of axial PsA. In addition to clinical and laboratory characterization, conventional radiographs and magnetic resonance imaging (MRI) - scans of the entire spine and sacroiliac joints (SIJs) are performed at the baseline visit and patients are followed up every 6 months according to a predefined protocol. After 2 years, additional imaging (X-ray and MRI) is performed for follow-up. In this interim analysis baseline data are presented.

Results: Between August 2019 and December 2021, 85 axial PsA patients were included. The mean age was 45.2 ± 12.9 years with a proportion of 55.3% female patients. Peripheral involvement was present in 43 (50.6%) patients, HLA-B27 was positive in 39 (45.9%), and C-reactive protein was elevated (>5mg/l) in 27 (31.8%) patients. Inflammatory back pain (IBP) in the discretion of the treating rheumatologist was present in 64 (75.3%) patients (Table 1). The modified New York criteria were fulfilled in 44.9% (n=35). MRI of the SIJ showed active inflammatory changes in 44 (55%) and structural changes in 59 (73.8%) patients. MRI of the spine showed active inflammation in 60% (n=48). Exclusively active and/or structural changes of the spine without changes in the SIJ were seen in 18.8% (n=15) (Figure 1).

Table 1. Characteristics of patients with axial PsA

Parameters	Axial PsA (n=85)
Age in years (mean ± SD)	45.2 ± 12.9
Female sex, n (%)	47 (55.3%)
Inflammatory back pain (IBP) present, n (%)	64 (75.3%)
Peripheral Involvement, n (%)	43 (50.6%)
Nail Involvement, n (%)	39 (45.9%)
PASI-Score (mean ± SD)	3.3 ± 5.1
BASDAI (mean ± SD), 0-10	4.9 ± 2.0
BASFI (mean ± SD), 0-10	3.8 ± 2.5
ASDAS-CRP (mean ± SD)	2.8 ± 1.0
DAPSA (mean ± SD)	14.5 ± 9.2
HLA-B 27 positive, n (%)	39 (45.9%)
CRP >5mg/l, n (%)	27 (31.8%)

ASDAS-CRP =Ankylosing Spondylitis Disease Activity Score - CRP, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, BASFI =Bath Ankylosing Spondylitis Functional Index, CRP = C-reactive protein, DAPSA = Disease Activity in PSoriatic Arthritis-Score, PASI = Psoriasis Area Severity Index, PsA = Psoriatic arthritis*, SD = standard deviation.*

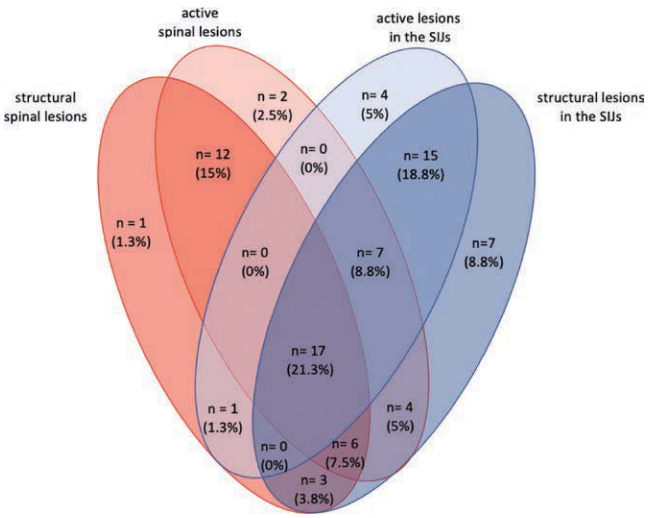

Figure 1. MRI-imaging patterns of axial PsA patients (n=80*)**.** MRI= magnetic resonance imaging, SIJs= sacroiliac joints. *Full imaging data available for 80 patients only due to variable reasons.

Conclusion: In the here presented interims analysis of the baseline data of our prospective cohort study of patients with an imaging-based diagnosis of axial PsA, it is shown that these patients are less frequently HLA-B27 positive and more frequently female when compared to previously described cohorts of "classical" axial SpA patients. Noteworthy, nearly 20% of the patients showed an isolated spinal involvement without active or structural changes in the SIJs.

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OP0027

ASSOCIATION BETWEEN BASELINE CARDIOVASCULAR RISK AND INCIDENCE RATES OF MAJOR ADVERSE CARDIOVASCULAR EVENTS AND MALIGNANCIES IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS RECEIVING TOFACITINIB

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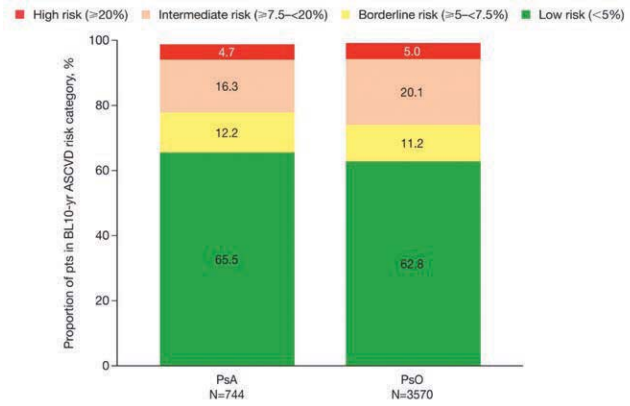
Background: Common comorbidities of psoriatic arthritis (PsA) and psoriasis (PsO) are cardiovascular (CV) disease and metabolic syndrome (MetS).[1,2] Risk of CV disease may be associated with increased risk of future malignancies.[3] Tofacitinib is a JAK inhibitor for treatment of PsA and has been investigated for treatment of PsO.
Objectives: To examine baseline (BL) CV risk and its association with incidence rates (IRs) of major adverse CV events (MACE) and malignancies in tofacitinib-treated patients (pts) with PsA and PsO.
Methods: Analysis included data from 3 (Phase [P]3/long-term extension [LTE]) trials of pts with PsA and 7 (P2/3/LTE) trials of pts with PsO receiving ≥1 dose of tofacitinib (5 or 10 mg twice daily). IRs (pts with events/100 pt-yrs) for MACE and malignancies (excluding non-melanoma skin cancer) were stratified by: history of coronary artery disease (HxCAD [≥1 of myocardial infarction, coronary heart disease, coronary artery procedure or stable angina pectoris]); BL 10-yr atherosclerotic CV disease (ASCVD) risk (ASCVD-pooled cohort equations calculator [only in pts without HxCAD]); and BL MetS (≥3 of hypertension, raised triglycerides, reduced high-density lipoprotein cholesterol, high waist circumference or high fasting glucose levels).
Results: Of 783 and 3663 pts with PsA and PsO, total tofacitinib exposure was 2038 and 8950 pt-yrs, and median duration of exposure was 3.0 and 2.4 yrs, respectively. In pts with PsA and PsO, 5.0% and 2.5% had HxCAD, respectively; in those without HxCAD, >20% had intermediate/high BL 10-yr ASCVD risk (Figure 1). At BL, 40.9% and 32.7% of pts with PsA and PsO had MetS, respectively. IRs of MACE were greatest in pts with PsA and PsO who had HxCAD/high BL 10-yr ASCVD risk (Table 1). In the PsA cohort, 5/6 pts with MACE had BL MetS. IRs of malignancies in pts with PsA were greatest in those with intermediate/high BL 10-yr ASCVD risk; 8/9 pts with malignancies in these risk categories had BL MetS (Table 1). In the PsO cohort, IR of malignancies was notably greater in those with high vs low/intermediate BL 10-yr ASCVD risk (Table 1).

Fig. BL 10-yr ASCVD risk in pts without HxCAD with PsA and PsO receiving tofacitinib



Data unavailable for 1.3% of pts with PsA and 1.0% of pts with PsO
PsA trials: NCT01877668; NCT01882439; NCT01976364. PsO trials: NCT01276639; NCT01309737; NCT01241591; NCT01186744; NCT00678210; NCT01710046; NCT01163253
N, total pts

Conclusion: In tofacitinib-treated pts with PsA and PsO, raised CV risk and MetS at BL were potentially associated with higher IRs of MACE and malignancies. Our findings support assessing CV risk in pts with PsA and PsO and enhanced monitoring for malignancies in those with raised CV risk.

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Table 1. IRs of MACE and malignancies in pts with PsA and PsO receiving tofacitinib, stratified by HxCAD, BL 10-yr ASCVD risk and BL MetS

	MACE				Malignancies			
	PsA		PsO		PsA		PsO	
	n/N[n1]	IR (95% CI)	n/N[n1]	IR (95% CI)	n/N[n1]	IR (95% CI)	n/N[n1]	IR (95% CI)
HxCAD								
Yes	1/39[0]	0.97 (0.02, 5.38)	3/93[0]	1.49 (0.31, 4.36)	0/39[0]	0.00 (0.00, 3.52)	0/93[0]	0.00 (0.00, 1.83)
No	5/744[5]	0.25 (0.08, 0.59)	20/3570[10]	0.22 (0.13, 0.34)	15/744[10]	0.75 (0.42, 1.24)	60/3570[26]	0.66 (0.51, 0.85)
BL 10-yr ASCVD risk category								
High risk (≥20%)	1/35[1]	1.26 (0.03, 7.01)	7/179[4]	1.67 (0.67, 3.43)	1/35[1]	1.26 (0.03, 7.03)	15/179[10]	3.57 (2.00, 5.89)
Intermediate risk(≥7.5–<20%)	2/121[2]	0.62 (0.07, 2.23)	9/716[6]	0.50 (0.23, 0.95)	8/121[7]	2.46 (1.06, 4.86)	23/716[9]	1.28 (0.81, 1.92)
Borderline risk(≥5–<7.5%)	1/91[1]	0.42 (0.01, 2.32)	2/400[0]	0.19 (0.02, 0.67)	2/91[1]	0.83 (0.10, 3.01)	5/400[1]	0.47 (0.15, 1.09)
Low risk (<5%)	1/487[1]	0.08 (0.00, 0.42)	2/2241[0]	0.03 (0.00, 0.13)	4/487[1]	0.30 (0.08, 0.77)	17/2241[6]	0.30 (0.17, 0.47)
BL MetS								
Yes	5/320	0.60 (0.20, 1.40)	10/1197	0.34 (0.16, 0.63)	10/320	1.20 (0.58, 2.21)	26/1197	0.89 (0.58, 1.31)
No	1/463	0.08 (0.00, 0.44)	13/2466	0.20 (0.11, 0.35)	5/463	0.40 (0.13, 0.92)	34/2466	0.54 (0.37, 0.75)

Follow-up time calculated up to the day of the first event and subject to risk period of 28 days beyond the last dose of study drug.
CI, confidence interval; N, total pts; n, pts with MACE/malignancies; n1, pts with MACE/malignancies and BL MetS.

OP0028

EARLY ACHIEVEMENT OF MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS IS ASSOCIATED WITH LONG-TERM IMPROVEMENTS IN QUALITY OF LIFE

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Background: Minimal disease activity (MDA) is a treatment target in psoriatic arthritis (PsA) that takes both clinical manifestations (joints, skin and enthesis) and the patient perspective into account (1). In a previous study we have shown that achieving MDA in the first year is associated with better quality of life (QoL) regardless whether this was achieved early or late in the first year (2). However, the impact of achieving MDA within the first year on the long-term is lacking.
Objectives: To compare quality of life at 1, 2 and 3 years between PsA patients who achieve MDA in the first year and those who do not.
Methods: Newly diagnosed, DMARD naïve PsA patients with oligo- or polyarthritis and at least 3 years of follow-up, participating in the Dutch southwest Early PsA cohoRt (DEPAR) were included. In short the DEPAR is an observational cohort of newly diagnosed PsA (3). Study visits took place at 3, 6, 9, 12, 18, 24 and 36 months after diagnosis. Patients were categorized in three groups by achievement of MDA in the first year:

- Sustained MDA, includes patients who were in MDA at both their 9- and 12-month visit;
- Non-sustained MDA, includes patients who achieved MDA in the first year but did not sustain it at both 9- and 12-months;
- No MDA, includes patients who did not achieve MDA in the first year.

To measure QoL at 1, 2 and 3 years the Short form-36 (SF-36) questionnaire was used. Descriptive statistics were used to compare QoL.
Results: We included 243 patients (51% male) of whom 113 (47%) were classified as sustained MDA, 64 (26%) as non-sustained MDA and 66 (27%) as no MDA. At baseline, patients had a mean age of 52.7 years and median symptom duration of 9.3 months. Patients in the no MDA group seemed to be older, were more often female and had a longer symptom duration (Table 1). QoL of sustained MDA patients was comparable to the general Dutch population (4) after 1, 2 and 3 years of follow-up. However, patients who did not achieve MDA in the first year had a lower QoL compared to the sustained MDA group and these differences persist in the years thereafter (Figure 1). The physical as well as the mental QoL domains were worse in the no MDA group compared to the other groups.

Table 1. Baseline characteristics of patients categorized by MDA group

	Sustained MDA (n=113)	Non-sustained MDA (n=64)	No MDA (n=66)
Demographics			
Age (years)	51.8 ± 13	51.8 ± 14	55.3 ± 13
Sex (male)	69 (61)	33 (52)	21 (32)
Symptom duration (months)	8.5 (4-24)	8.1 (3-28)	12.9 (5-51)
Disease activity			
Swollen joint count (66)	3 (2-5)	4 (1-6)	4 (2-8)
Tender joint count (68)	3 (1-6)	4 (2-8)	8 (4-13)
Psoriasis	95 (84)	58 (91)	56 (85)
BSA in case of psoriasis (%)	3 (2-4)	3.3 (1-6.5)	3 (1.5-6)
Enthesitis	29 (26)	28 (44)	38 (58)
LEI in case of enthesitis	1 (1-2)	2 (1-2)	2 (1-4)
HAQ	0.38 (0.13-0.75)	0.75 (0.5-1)	1 (0.75-1.38)
VAS global	31 (15-56)	46 (23-65)	59 (50-77)
VAS pain	28 (12-52)	50 (26-66)	69 (53-80)

Results are shown as mean ± standard deviation, n (%) or median (interquartile range). BSA: Body Surface Area; LEI: Leeds Enthesitis Index; HAQ: Health Assessment Questionnaire; VAS: visual analogue scale.

Over the years, treatment was intensified in all groups, with biologicals use after three years at 18%, 25% and 31% in the sustained MDA, non-sustained MDA and no MDA group, respectively.

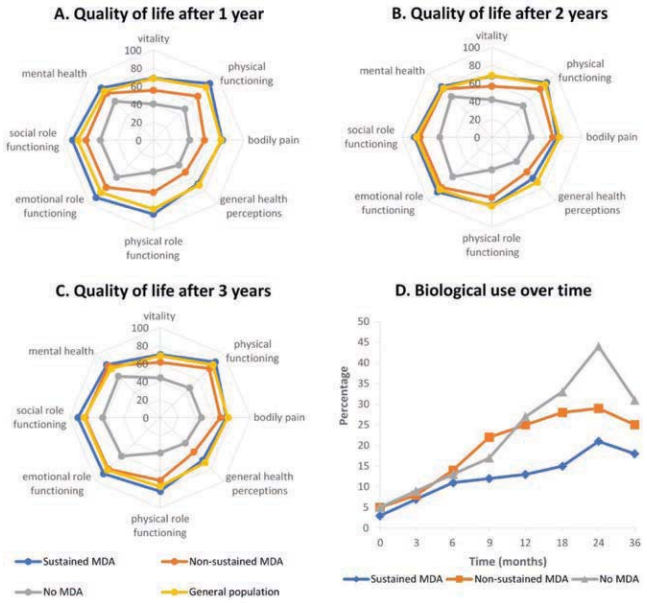

Figure 1. (A) 1 year, (B) 2 year and (C) 3 year quality of life scores, measured with the SF-36 domains, for MDA groups and compared with the general Dutch population norms (4), (D) percentage of patients who use biologicals over time per MDA group.

Conclusion: Failure to achieve MDA in the first year after PsA diagnosis is associated with worse quality of life outcomes that persist over the years despite more intensified treatment.

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OP0029

PROSPECTIVE, DOUBLE-BLIND STUDY ON THE VALUE OF HANDHELD MUSCULOSKELETAL ULTRASOUND PERFORMED BY DERMATOLOGISTS FOR DETECTION OF PSORIATIC ARTHRITIS - THE PSOSONE STUDY

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Background: The early diagnosis of psoriatic arthritis (PsA) requires a close interdisciplinary cooperation between rheumatology and dermatology. Recent publications underlined the key role of dermatologists in this process (1). Despite available screening tools like questionnaires, there is a need to increase

sensitivity and specificity of diagnostic screening tools for PsA. Musculoskeletal ultrasonography (MSUS) has been shown to be a reliable tool for diagnosing PsA, even in preclinical situations. However, the use of MSUS screening by dermatologists in the early detection of PsA has not been studied so far.

Objectives: The purpose of this study was to assess the accuracy of early PsA identification by dermatologists who have been previously trained in MSUS utilizing an innovative handheld-ultrasound device (Butterfly IQ).

Methods: Twelve dermatologists have been trained in MSUS (2) previously by a newly designed curriculum. Six working at the clinic for Dermatology and Allergology of the University Hospital Bonn, while the remaining six serve in private practices. The MSUS training curriculum focused mainly on detecting joint effusion and synovial hyperperfusion in all joints. After successful training, these colleagues were provided with handheld-ultrasound devices in order to screen 140 psoriasis patients presenting with arthralgia. Dermatologists were asked to determine whether or not the patient had PsA based on the medical history, clinical examination, and GEPARD questionnaire. Subsequently a MSUS exam of up to three painful joints was conducted by the dermatologists using the provided handheld-ultrasound devices. The post MSUS decision was also recorded. All prescreened patients were then referred to blinded board-certified rheumatologists with MSUS certification (EFSUMB level II and III), which repeated medical history, clinical examination and MSUS. We investigated the impact of MSUS on the sensitivity and specificity of early PsA diagnosis by comparing dermatologists' pre- and post-ultrasound PsA suspicion with the final diagnosis determined by the rheumatologist.

Results: In total, 140 patients were enrolled. PsA was detected in 24 cases. The sensitivity of dermatologists' pre-MSUS PsA suspicion was 81.0 %, while the specificity was 54.5 %. After conducting MSUS the sensitivity and specificity changed to 61.9% and 90.9%, respectively. The MSUS findings lead the dermatologists to change their presumed PsA diagnosis in 46 cases, with PsA being ruled out in 45 of them.

Conclusion: We were able to demonstrate that targeted MSUS performed by dermatologists increases specificity while decreasing sensitivity, perhaps leading to fewer referrals to rheumatologists and an earlier diagnosis of PsA.

Figure 1: Accuracy of the pre- and post-ultrasound PsA suspicion by dermatologists compared to the final diagnosis determined by the rheumatologists

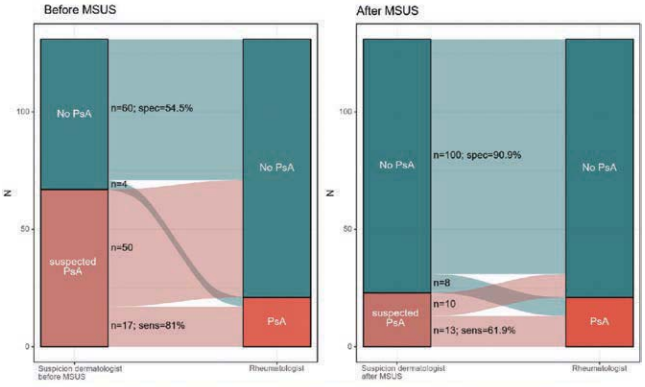

Figure 1: the change of PsA suspicion between pre-and post-ultrasound PsA screening performed by the dermatologists alongside the resulting sensitivity and specificity is shown compared to the final diagnosis set by board-certified rheumatologists. Due to inconsistent dermatological screening results in nine cases, only 131 out of 140 patients have been included in the final statistical analysis.

Abbreviations: PsA: psoriatic arthritis, n: absolute number of probands, MSUS: musculoskeletal ultrasound, sens: sensitivity, spec: specificity

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OP0030 ASSOCIATION OF TRADITIONAL AND DISEASE-RELATED RISK FACTORS WITH CARDIOVASCULAR EVENTS IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS

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Background: Patients with psoriatic arthritis and psoriasis, collectively termed psoriatic disease (PsD), have an increased risk for cardiovascular (CV) disease.

Objectives: We aimed to identify traditional CV risk factors and PsD-related risk factors associated with CV events.

Methods: Patients from a longitudinal PsD cohort without a prior history of CV events were included. Detailed information on demographics, comorbidities including traditional cardiovascular risk factors, medications and disease activity is collected according to a standard protocol. The study outcome included any of the following CV events occurring within the first 10 years of patients' initial clinic visit: angina, myocardial infarction, congestive heart failure, transient ischemic attack, cerebrovascular accident, revascularization procedures and CV death. A total of 10 traditional CV risk factors and 15 PsD-related risk factors were assessed. The association of each risk factor with incident CVEs were analyzed separately using Cox proportional hazards regression models with time-dependent covariates, adjusted for age and sex.

Results: A total of 1,376 patients with PsD, followed between 1978 and 2020, were analyzed (mean age 48.3 ± 12.9 years, 46.8% female). During the follow-up period, 102 (7.4%) patients developed incident CV events. In Cox regression models adjusted for age and sex, age (Hazard Ratio (HR) 1.08, 95% Confidence Interval (CI) 1.06, 1.10), diabetes (HR 1.88, 95% CI 1.17, 3.02), systolic blood pressure (HR 1.02, 95% CI 1.01, 1.03), body mass index (BMI) (HR 1.04, 95% CI 1.01, 1.08), triglycerides (HR 1.24, 95% CI 1.07, 1.43), treatment for hypertension (HR 1.70, 95% CI 1.13, 2.56), and use of lipid-lowering medications (HR 1.70, 95% CI 1.13, 2.56) were among the traditional CV risk factors associated with increased CV risk. Among the PsD-related risk factors, psoriasis area and severity index (PASI) (HR 1.05, 95% CI 1.02, 1.08), erythrocyte sedimentation rate (ESR) (HR 1.02, 95% CI 1.01, 1.02), number of tender joints (HR 1.03, 95% CI 1.01, 1.05), number of swollen joints (HR 1.06, 95% CI 1.01, 1.12), health assessment questionnaire (HAQ) score (HR 1.63, 95% CI 1.23, 2.17), and daily use of non-steroidal anti-inflammatory drugs (NSAIDs) (HR 1.72, 95% CI 1.16, 2.55) were associated with increased CV risk. Use of biologic medications (HR 0.63, 95% CI 0.40, 1.00) was not found to be significantly protective against CV events.

Conclusion: In patients with PsD, we identified six PsD-related risk factors that were significantly associated with incident CV events. These risk factors may be useful for the development of a PsD-specific CV risk prediction score that uses routine clinical assessments in combination with PsD-related biomarkers.

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Disclosure of Interests: None declared.

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OP0031

SEROLOGICAL COLLAGEN BIOMARKERS CAN DIFFERENTIATE PATIENTS WITH PSORIASIS FROM PSORIATIC ARTHRITIS

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Background: Psoriasis is a common chronic immune-mediated skin disease. About 25% of psoriasis patients have psoriatic arthritis (PsA) which is a chronic inflammatory disease affecting the joints, enthesis, and axial skeleton. Delayed diagnosis of PsA is associated with joint damage and disability. Therefore, optimized screening methods including identifying predictors of arthritis in patients with psoriasis have become a medical priority. Collagens are major proteins in all tissues, including skin, bone, cartilage, and connective tissues, which are affected by inflammatory processes present in both psoriasis and PsA. Throughout degradation and remodelling of the extracellular matrix (ECM), proteases cleave collagens leading to protein breakdown products which are released into the circulation. These collagen fragments can be quantified in serum as biomarkers of tissue remodelling and may be helpful in screening patients with psoriasis that have or will develop PsA.

Objectives: Our aim is to identify serum biomarkers that can differentiate patients with psoriasis without PsA (PsC) from PsA

Methods: Patients with PsC (n=87, mean ±SD age 42.01 ±12.20, 44% female; underwent a full rheumatologic assessment to exclude PsA) and patients with PsA (n=99, mean ±SD age 45.94 ±12.47, 49% female) were recruited at the Toronto Western Hospital, Canada, after appropriate ethics approval. ECM remodelling was estimated using as indices serological anabolic biomarkers quantifying formation of type III, IV, and VI collagen (PRO-C3, PRO-C4, and PRO-C6 respectively), and catabolic biomarkers measuring degradation of type I, III, IV and VI collagen (C1M, C3M, C4M, C6M respectively). Data are presented as mean ± standard deviation (SD). Statistically significant difference between the two groups was calculated by Mann-Whitney U test and a p-value below 0.05 was considered significant. Area under the receiver operating characteristic (ROC) curve (AUC) analysis was performed to describe the discrimination accuracy of each biomarker between the two patient groups.

Results: Patients with PsA presented higher levels of C1M, C3M, C6M, and PRO-C6 compared to PsC (p<0.0460-p<0.0009, Figure 1 A, B, D, G), while biomarkers levels of C4M, PRO-C3, and PRO-C4 were not significantly different between PsC and PsA patients (Figure 1 C, E, F). Moreover, C1M and C6M were able to separate between PsC and PsA patients with an AUROC=0.6277 (p=0.0027) and AUROC=0.6446 (p=0.0010), respectively, indicating that these biomarkers may be markers of joint involvement (Figure 1 H, I).

Conclusion: This work provides evidence that serum degradation biomarkers of type I and VI collagen were able to differentiate patients with PsA from PsC and may be potential biomarkers of inflammatory systemic musculoskeletal involvement. These findings suggest that serological biomarkers may be used to identify the 25% of psoriasis patients that have PsA.

Disclosure of Interests: Solveig Skovlund Groen: None declared, Signe Holm Nielsen Employee of: Signe Holm Nielsen is employed by Nordic Bioscience, Anne-Christine Bay-Jensen Shareholder of: Anne C. Bay-Jensen holds stock in Nordic Bioscience, Employee of: Anne C. Bay-Jensen is employed by Nordic Bioscience, Mozhgan Rasti: None declared, Darshini Ganatra: None declared, Katerina Oikonomopoulou: None declared, Vinod Chandran: None declared.
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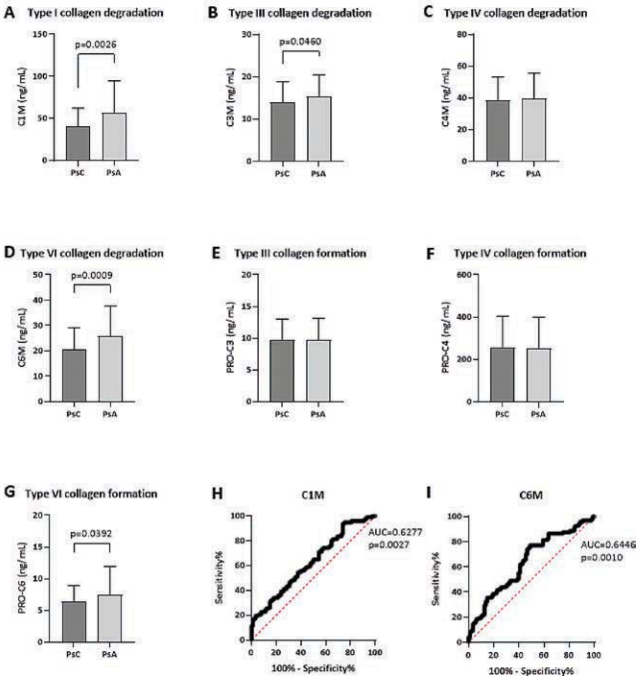
Fig. 1



From risk assesment to societal outcomes

OP0032

AN ECONOMIC WINDOW OF OPPORTUNITY FOR PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: 5-YEAR COST-EFFECTIVENESS ANALYSIS OF THE CARERA TRIAL

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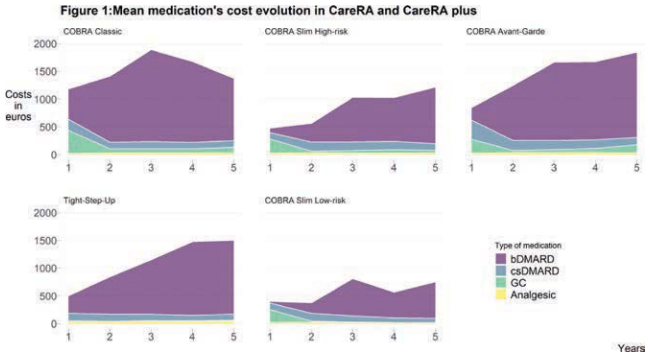
Background: The CareRA trial showed that remission induction with methotrexate (MTX) and glucocorticoid (GC) bridging in a treat-to-target setting is cost-effective up to 2 years in early Rheumatoid Arthritis (eRA) patients.

Objectives: To evaluate the long-term cost-effectiveness of treat-to-target treatments among recently diagnosed (<1 year), DMARD naïve patients with eRA using MTX and a step-down GC scheme (COBRA-Slim) compared to (a) the same combination with either sulphasalazine (COBRA-Classic) or leflunomide (COBRA-Avant-Garde) in high-risk patients and (b) MTX without GCs (Tight-Step-Up: TSU) in low-risk patients up to 5 years.

Methods: We used data from the 2-year RCT CareRA trial and its 3-year observational follow-up, CareRA plus. Patients completing the 2-year visit of CareRA were eligible for participation in CareRA plus, in which patients were evaluated every 6 months till year 5. Healthcare costs considered in this piggyback economic analysis were rheumatology visits, RA-related medication (synthetic and biological DMARDs, GCs, and all recorded analgesics including paracetamol, non-steroidals, tramadol and opioids), hospital admissions, laboratory tests and radiographs occurring during the 5-year trial. All pricing is based on December 2021 rates. Total costs per resource were calculated by multiplying the number of resources by the cost unit price extracted from Belgian national websites. Total costs per patient were obtained by summing costs of all resources. Effectiveness was measured with DAS28-CRP and compared between the originally allocated treatment arms. An incremental cost-effectiveness ratio (ICER) was calculated by dividing the cost difference by the DAS28-CRP<2.6 remission difference per pair of treatment schemes. Multiple imputation was used to handle missing data and non-parametric bootstrapping with 25000 iterations of random sampling with replacement to calculate confidence intervals (95% CIs).

Results: Of 322 eligible patients, 252 were included in CareRA plus, of which 203 completed the trial. Rates of disease control (DAS28-CRP<2.6) at year 5 in high-risk patients were 68%, 72% and 64% in the Classic, Slim and Avant-Garde group respectively (p=0.63) and related total costs were €11 358.39 (CI 7 776.84-14 939.93), €8 463.12 (CI 6 789.44-10 136.80), €11 752.47 (CI 7 705.11-15 799.82) respectively. In the low-risk population, 80% of patients in Slim and the TSU arm reached remission (DAS28-CRP<2.6) at year 5. While the costs were €6 332.55 (CI 3 607.63-9 057.48) for Slim, and €10 398.19 (CI 4165.95-16630.43) for TSU. In the high-risk group, Classic (ICER -€723.82) and Avant-Garde (ICER -€411.17) were more expensive and less effective compared to Slim. In the low-risk group, Slim was less expensive (Δ -€4 065.64) and equally effective as TSU. Figure 1 depicts how the different medication costs evolved during the 5-year follow-up. 22% of all patients were ever on bDMARDs. More specifically in 23% (16/69) of Classic, 21% (16/75) of Slim high-risk, 25% (15/59) of Avant-Garde, 17% (4/23) of Slim low-risk, and in 15% (4/26) of TSU patients. On average a first bDMARD was started later in the Slim arms, more specifically at week 69 for Classic, week 106 for Slim high-risk, week 97 for Avant-Garde, week 102 for Slim low-risk and week 76 for TSU.

Conclusion: The combination of MTX with a GC bridging scheme (COBRA Slim) was more cost-effective (less expensive with comparable disease control) than more intensive step-down combination strategies or a conventional step-up approach 5 years after initial treatment. Over 5 years, around one-fifth of all patients, were in need of starting biological treatment and the transition to a bDMARD was later in COBRA Slim. These results point out the possibility of an early "economic" window of opportunity for diminishing costs long-term while still maintaining optimal disease control.



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OP0033

EFFECTIVENESS OF NON-PHARMACOLOGICAL INTERVENTIONS TO PROMOTE WORK PARTICIPATION IN PEOPLE WITH RMDS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Work participation among people with rheumatic and musculoskeletal diseases (RMDs) remains reduced when compared to the general population. A EULAR taskforce was established to agree on Points to Consider (PtC) to support people with RMD in healthy and sustainable work participation. Non-pharmacological interventions (NPI) could have an important role in improving work participation in RMDs. However, a comprehensive evidence synthesis of the effectiveness of NPIs in people with RMDs is lacking.
Objectives: To summarise the literature on effectiveness of NPIs on work participation in people with RMDs.
Methods: A search in four databases (MEDLINE, EMBASE, CENTRAL and CINAHL) was performed. Randomised Controlled Trials (RCTs) and Longitudinal Observational Studies (LOS) assessing non-pharmacological/non-surgical interventions until August 2020 were screened. Studies including people with any RMD (except low back pain or work-related RMDs) and assessing a work participation outcome domain (sick leave, work status, presenteeism) were considered eligible. For qualitative evidence synthesis, RCTs and LOS were considered. For quantitative evidence synthesis, only RCTs were considered. For each randomized comparison, standardised mean differences (SMDs) were calculated for the three outcome domains and used as effect size in the meta-analyses; i.e. a negative SMD favouring the NPI over control. Next, Mixed Effects Meta-Regression Analyses were performed, with random effects for randomised comparisons, and a fixed effect factor for the stratified subgroups of clinical interest. Subgroups within diseases (musculoskeletal pain disorders vs. other types of RMDs), risk status for sick leave at baseline (on sick leave or at risk for sick leave; not at risk for sick leave; a combination; or not specified) and single vs. multiple component NPIs were pre-defined. Risk of Bias (RoB) of RCTs was assessed using the Cochrain tool.

Results: Out of 8,864 records, 64 studies (71 treatment comparisons) were included. Studies usually included a mixed population of several RMDs (42%). Most NPIs were conducted in a clinical setting (n=44, 62%) and NPIs usually had multiple components (n=57, 80%), such as vocational support combined with physical training (n=18, 25%). Sick leave was the most frequently reported outcome domain (n=56, 88%). In the qualitative syntheses, 30%/50%/29% of interventions were considered plausible in improving sick leave, work status and presenteeism, respectively.
In the quantitative synthesis, NPIs (37 RCTs, 42 comparisons with mostly moderate to high RoB) showed small to moderate effect sizes, favouring NPIs over comparators for sick leave (SMD=-0.23, 95%CI -0.33 to -0.13), work status (SMD=-0.38, 95%CI -0.63 to -0.12) and presenteeism (SMD=-0.25, 95%CI -0.39 to -0.12). The forest plot for sick leave is shown (Figure 1).
Subgroup analyses for sick leave revealed that, compared to control, NPIs were not effective in musculoskeletal pain disorders, in contrast to the other types of RMDs. For both other subgroup analyses (baseline risk for sick leave; single vs. multicomponent NPI), NPIs improved sick leave similarly in subgroups compared to the control. Subgroup analyses for work status and presenteeism had generally similar effects in subgroups, but the interpretation requires caution in view of the small number of comparisons. Of note, clinical and methodological heterogeneity between studies was substantial, with some concerns about methodological quality related blinding and completeness of follow up.

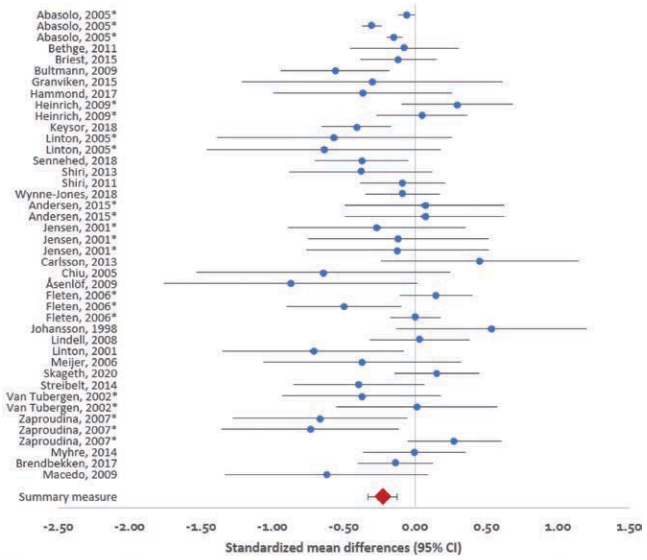

Figure. Forest plot of 42 treatment comparisons (sick leave) [<0.00 favours non-pharmacological intervention; >0.00 favours control]. An asterisk (*) indicated if a study has multiple treatment comparisons, which was taken into account in the analysis, and were therefore included multiple times in the forest plot.

Conclusion: Overall, NPIs seem to have significant, but on the average population level only small to moderate effects on sick leave, work status and presenteeism in RMDs. However, effects on sick leave varied substantially between subgroups. This synthesis suggests that tailoring NPIs to individuals' needs and context could be clinically valuable.
Disclosure of Interests: None declared.
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OP0034

IXEKIZUMAB IMPROVES SIGNS, SYMPTOMS, AND QUALITY OF LIFE IN PATIENTS WITH AXIAL SPA IRRESPECTIVE OF DISEASE DURATION: RESULTS FROM THE COAST-V, COAST-W AND COAST-X TRIALS

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Background: Ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A,[1] has demonstrated superior efficacy to placebo (PBO) in the treatment of patients (pts) with radiographic axial spondyloarthritis

(r-axSpA) (COAST-V [NCT02696785]; -W [NCT02696798]), and non-radiographic axial spondyloarthritis (nr-axSpA) (COAST-X [NCT02757352]).
Objectives: Assess treatment response to IXE categorised by disease duration since symptom onset (<5 years (yrs), ≥5yrs) in pts with r-axSpA and nr-axSpA up to 52 Weeks (Wks).
Methods: Pts fulfilled ASAS classification criteria for r-axSpA or nr-axSpA and were randomised to receive 80mg subcutaneous IXE every 2Wks or 4Wks, or PBO (16Wks COAST-V/W; 52Wks COAST-X). Data were summarized by disease duration and treatment in eligible intent-to-treat (ITT) pts. Wk16 treatment comparisons were conducted using Cochran-Haenszel-Mantel test and ANCOVA. Missing data were handled using non-responder imputation and modified baseline observation carried forward, for categorical and continuous endpoints, respectively.
Results: Table 1 presents pt demographics and baseline characteristics. Data is from pooled IXE pts. In pts with r-axSpA and <5yrs symptom duration, ASAS40 response was achieved by 51.5% at Wk16 and 60.6% at Wk52, compared to 36.9% at Wk16, significantly different to PBO (p<0.001), and 40.5% at Wk52, in pts with ≥5yrs symptom duration. In pts with nr-axSpA and <5yrs symptom duration, ASAS40 response was achieved by 42.5% at Wk16, significantly different to PBO (p=0.012), and 54.8% at Wk52, compared to 36.0% at Wk16 and 41.4% at Wk52 in pts with ≥5yrs symptom duration (Figure 1). In pts with r-axSpA and <5yrs symptom duration, ASDAS LDA <2.1 response was achieved by 39.4% at Wk16 and 48.5% at Wk52, compared to 27.5% at Wk16, significantly different to PBO (p<0.001), and 35.6% at Wk52 in pts with ≥5yrs symptom duration. In pts with nr-axSpA and <5yrs symptom duration, ASDAS LDA <2.1 response was achieved by 32.9% at Wk16, significantly different to PBO (p=0.003), and 49.3% at Wk52, compared to 23.9% at Wk16 and 36.9% at Wk52 in pts with ≥5yrs symptom duration. At Wk16, in pts with r-axSpA pts and <5yrs symptom duration, the Change from Baseline (CFB) in SF-36 Physical Component Summary (PCS) Score (LSM±SE) was 7.91 (±1.52), compared to 6.81 (±0.40) in pts with ≥5yrs symptom duration. In pts with nr-axSpA and <5yrs symptom duration, this score was 8.95 (±0.95) compared to 7.07 (±0.73) in pts with ≥5yrs symptom duration; both were significantly different to PBO (r-axSpA: p<0.001; nr-axSpA: p=0.037).

Table 1. Patient demographics and Baseline Characteristics

	Pts with r-axSpA		Pts with nr-axSpA	
	<5yrs (Ns=33)	≥5yrs (Ns=306)	<5yrs (Ns=73)	≥5yrs (Ns=111)
Age (years)	33.1 (8.15)	45.1 (12.12)	31.9 (10.07)	46.4 (11.86)
Male, n (%)	26 (78.8)	245 (80.1)	40 (54.8)	53 (47.7)
Female, n (%)	7 (21.2)	61 (19.9)	33 (45.2)	58 (52.3)
Age at axSpA onset (years)	30.4 (8.29)	27.0 (9.06)	29.9 (10.22)	29.5 (8.76)
ASDAS score, mean (SD)	3.87 (0.79)	4.03 (0.82)	3.79 (0.80)	3.85 (0.78)
BASDAI score, mean (SD)	7.16 (1.64)	7.25 (1.35)	7.00 (1.33)	7.30 (1.26)
SF-36 PCS, mean (SD)	34.02 (7.73)	32.86 (7.63)	32.84 (7.86)	32.57 (6.97)

Abbreviations: IXE=ixekizumab, n=number of pts in specified category, Ns=number of pts in each subgroup, SD=standard deviation.

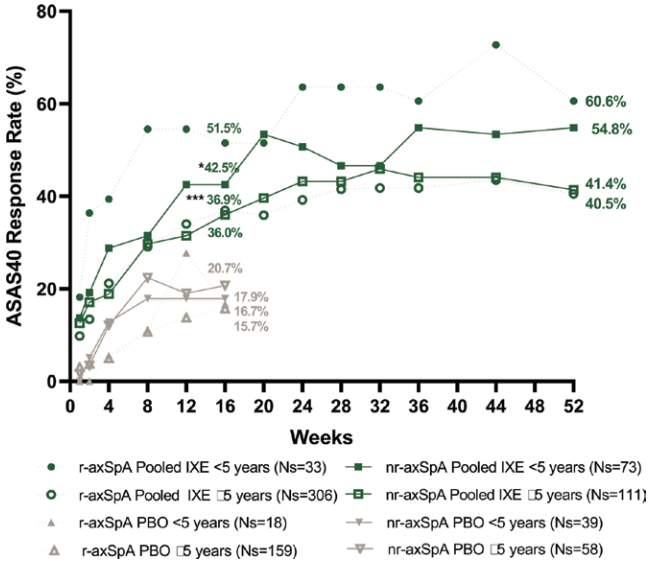

Figure 1. ASAS40 Response Rates for patients with r-axSpA (COAST-V/W) and nr-axSpA (COAST-X) Symptom Duration <5 and ≥5 years up to Week 52, ITT, NRI: Significantly greater response of IXE versus PBO at Week 16 denotated by * (p≤0.05), *** (p≤0.001). Abbreviations: PBO, placebo; IXE, Ixekizumab; NRI, nonresponder imputation; ITT, Intent-to-Treat (population), ASAS, Assessment of Spondyloarthritis International Society.

Conclusion: Efficacy response to the therapy with IXE was observed in both subgroups based on disease duration (<5 and ≥5yrs) with more robust responses in the <5 years subgroup.
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Novartis: Research grant 2021 (Payment to institution), John D Reveille Speakers bureau: Eli Lilly and Company and UCB Pharma, Consultant of: UCB Pharma, Grant/research support from: Eli Lilly and Company, Proton Rahman Speakers bureau: Abbott, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, and Company Janssen, Novartis, and Pfizer., Paid instructor for: Advisory Board: Abbott, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, Novartis, and Pfizer., Grant/research support from: Janssen and Novartis, José Maldonado-Cocco Speakers bureau: Pfizer, Merck Sharp Dohme, Wyeth, Sanofi Aventis, Novartis, Bristol Myers Squibb, Roche, Shering-Plough, Abbvie, UCB, Gilead., Consultant of: Pfizer, Merck Sharp Dohme, Wyeth, Sanofi Aventis, Novartis, Bristol Myers Squibb, Roche, Shering-Plough, Abbvie, UCB, Gilead., Grant/research support from: Pfizer, Merck Sharp Dohme, Wyeth, Sanofi Aventis, Novartis, Bristol Myers Squibb, Roche, Shering-Plough, Abbvie, UCB, Gilead., Marina Magrey Speakers bureau: Novartis, Abbvie, Eli Lilly and Company., Consultant of: Novartis, Eli Lilly and Comapny, Pfizer, Janssen, UCB Pharma, Abbvie, BMS., Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, So Young Park Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Andris Kronbergs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Martin Rudwaleit Speakers bureau: Abbvie, BMS, Boehringer Ingelheim, Chugai, Eli Lilly and Company, Novartis, Pfizer, UCB., Paid instructor for: Abbvie, Eli Lilly, Novartis, UCB., Consultant of: UCB, Grant/research support from: Galapagos, UCB, Novartis.
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OP0035 WHAT EXPLAINS THE WORLDWIDE GRADIENT OF AGE AT ONSET OF RHEUMATOID ARTHRITIS ALONG LATITUDE? A MULTILEVEL ANALYSIS IN THE METEOR REGISTRY

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Background: It has been suggested that rheumatoid arthritis (RA) starts at a younger age in cities with a lower latitude (closer to both sides of the equator). This consistent finding still remains to be explained. It has been hypothesized that latitude is a proxy for presence of genetic (eg. ACPA) and environmental risk factors (eg. smoking) for RA onset.
Objectives: To study how age at RA onset varies with latitude worldwide and to what extent patient and country level factors explain this variability.
Methods: RA patients from the worldwide METEOR registry were included. Age at diagnosis as a proxy for age at RA onset, measured at the patient level, was the main outcome. The explanatory variable was the absolute value of latitude, measured as the latitude of the hospital (hospital level). Patient factors considered potentially relevant were gender, RF and ACPA positivity, smoking status, symptom duration (months), year of first visit and BMI (all patient level). Country level factors were socioeconomic indicators (physician density, health expenditure, life expectancy, GDP per capita and gross enrolment in secondary school), derived from country statistics. We hypothesized that both patient and country level factors explain (ie. mediate) a relationship between latitude and age at diagnosis (Figure 1).
We applied Bayesian multilevel linear structural equations models, which not only quantify effects at multiple levels but also disentangle at which level the effects take place. For example, they can differentiate whether hospital or country latitude affects age at diagnosis.

We examined: 1. the total effect of latitude on age at diagnosis at hospital and country level (Main model); 2. the amount of the total effect that is mediated by patient factors at the patient and hospital level (Model A); and 3. the amount of the total effect that is mediated by country factors at the country level (Model B). In each model we disentangle the effect in different measurement levels. For example, a patient level variable can vary at the patient, hospital and country level.

Results: We included 39 782 patients nested in 94 hospitals nested in 17 countries. The mean age at diagnosis per country ranged from 39 to 55 years. The study spanned a range of latitude between 9.9 and 55.8 degrees (ie. from Nigeria to the United Kingdom). In the main model, we confirmed the association between latitude and age at diagnosis and found that it only occurred at the country level (not at the hospital level). Per degree increase in country latitude, the average age at diagnosis per country increased by 0.23 years (95% credibility interval 0.07; 0.40). At the hospital level however, this effect was negligible: β= 0.040 (-0.16; 0.31). Associations between latitude and several patient factors were found at the country level, but these patient factors only associated with age at diagnosis at the patient level, not at the country (or hospital) level (Model A). This means patient-factors did not explain the association between latitude and age at diagnosis at the country level (main effect changed from 0.23 before to 0.37 after inclusion of patient factors). In model B latitude associated with most country factors (except GDP per capita). Even though none of these variables separately were significantly associated with age at diagnosis, inclusion of the set of country level factors reduced the country level effect of latitude on age at diagnosis from 0.23 to almost zero: β=-0.033 (-0.51; 0.37). Sensitivity analyses with age at symptom onset as outcome provided similar results.

Conclusion: Patients living close at the equator indeed get RA far earlier than those living closer to the poles. We here suggest that, rather than due to variation in patients' characteristics, this latitude gradient is a country level phenomenon explained by indicators of countries' socioeconomic status, and not by patient specific genetic or environmental factors. This big data analysis in a worldwide prevalence cohort provides a direct link between countries' levels of welfare and the onset of RA.

Disclosure of Interests: Sytske Anne Bergstra Grant/research support from: Pfizer, Alexandre Sepriano Speakers bureau: Novartis, Consultant of: UCB, Arvind Chopra: None declared, Lai-Ling Winchow: None declared, David Vega-Morales: None declared, Karen Solomon-Escoto: None declared, Xanthe Matthijssen: None declared, Robert B.M. Landewé Shareholder of: Director of Rheumatology Consultancy BV, Consultant of: Honoraria from AbbVie, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Eli-Lilly, Novartis, Pfizer, UCB Pharma.

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OP0036 CLINICALLY SUSPECT ARTHRALGIA PATIENTS WITH A LOW LEVEL OF EDUCATIONAL ATTAINMENT HAVE AN INCREASED RISK TO DEVELOP INFLAMMATORY ARTHRITIS

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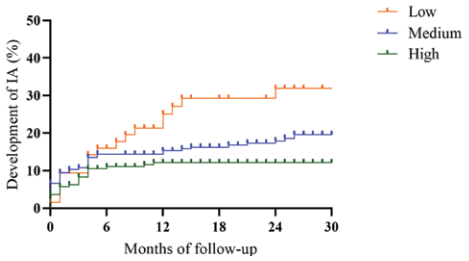
Background: Cross-sectional studies on educational levels have shown that inflammatory arthritis (IA) and rheumatoid arthritis (RA) are more prevalent among people with a lower educational attainment. Studies on educational attainment in individuals at risk for RA could shed light on the influence of socioeconomic factors on RA development, which is divided in an asymptomatic and symptomatic pre-RA stage. To our knowledge, longitudinal studies on educational attainment and IA-development in symptomatic individuals at risk of RA are lacking.

Objectives: To determine the association between educational attainment and progression from clinically suspect arthralgia to IA and to perform mediation analysis to elucidate pathways.

Methods: 600 consecutive patients presenting with clinically suspect arthralgia were followed for the development of IA, identified at joint examination by rheumatologists during median follow-up of 25 months. Educational attainment was defined as low (lower general secondary education), medium, or high (college or university education). Contrast enhanced 1.5T MRI of hand and foot were made at baseline and were evaluated for synovitis/tenosynovitis/osteitis, according to the method of rheumatoid arthritis MRI scoring system (RAMRIS) and Havaardsholm. Association between educational attainment and IA-development was studied with cox-regression analysis. To evaluate if subclinical joint inflammation is intermediary in the path of educational attainment and IA-development, a three-step mediation analysis was performed, before and after correction for age.

Results: Patients with a low level of educational attainment were older, had a higher BMI, and smoked more often compared to patients with a high educational level. Low educational attainment was associated with increased IA-development (HR=2.5, 95%CI=1.4-4.7. p=0.003; see Figure 1), also after correction for age, BMI and smoking-status (HR=2.1, 95%CI=1.03-4.4, p=0.041). Moreover, patients with a lower educational level had higher levels of subclinical inflammation at presentation, which associated with a higher risk of progression to IA. Mediation analyses revealed that the association between low educational attainment and IA-development reduced when adding the level of subclinical inflammation (HR=1.8, 95%CI=0.9-3.5, p=0.073), suggesting that the association between educational attainment and IA-development is partly mediated by higher levels of subclinical inflammation. Mediation analysis with age correction provided similar results.

Figure. Progression from clinically suspect arthralgia to inflammatory arthritis (IA), according to educational attainment



Conclusion: This is the first evidence that lower educational attainment of patients with arthralgia is associated with a higher risk of developing arthritis. This is partly caused by more severe subclinical joint inflammation. Further research into the role of socioeconomic factors on the development of RA is warranted.

Disclosure of Interests: None declared.

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OP0037 USE OF PRIMARY HEALTHCARE AND RADIOLOGICAL IMAGING PRECEDING A DIAGNOSIS OF RHEUMATOID ARTHRITIS: A DANISH NATIONWIDE COHORT STUDY

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Background: Focus on early diagnosis and treatment initiation is key in rheumatoid arthritis (RA) to prevent permanent joint damage and systemic manifestations. Increased use of healthcare services before an RA diagnosis can be seen as a proxy for symptom presentation and the actions taken by healthcare professionals, and thus indicate an opportunity for earlier diagnosis. However, little is known about where and when people use healthcare services before an RA diagnosis.

Objectives: To explore the pattern in use of healthcare services during the 12 months preceding a diagnosis of RA in Denmark.

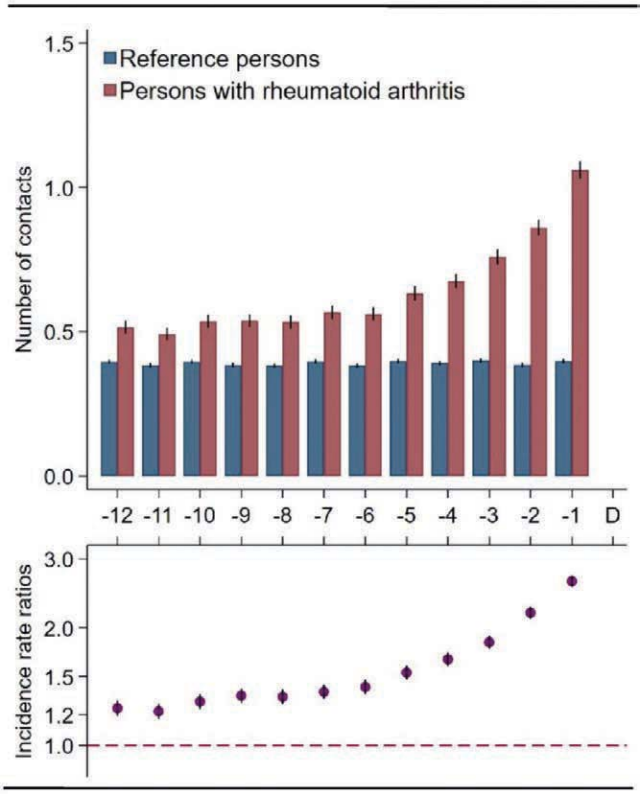
Methods: We conducted a population-based cohort study using data from Danish national registries. For every patient diagnosed with RA in 2014-2018 we matched ten reference persons from the Danish general population without RA, listed in the same general practice and with same age and sex. Healthcare use was defined as: daytime face to face contacts to general practice, contacts to private practicing physiotherapists. We estimated the monthly healthcare use for patients with RA and reference persons in the 12 months preceding the diagnosis, and we compared their healthcare use by incidence rate ratios (IRR) for each month, adjusted for socio-demographic characteristics and comorbidity.

Results: 7,427 patients with RA and 74,270 reference persons were included in the study. The median age was 62 years (interquartile interval (IQI): 51-71), and 65% were women. Patients with RA had an average of 0.5 contacts per month in general practice from 12 months until six months prior to the diagnosis (Figure 1); this number increased from six months before the diagnosis to an average of one contact in the last month before the diagnosis. Reference persons had an average of 0.4 contacts per months throughout the entire study period. Compared to their references, patients with RA had statistically significantly more contacts during all 12 months before the diagnosis date; IRR increased from 1.25 (95% CI: 1.19-1.30) to 2.63 (2.55-2.71) during the study period. Patients with RA also had statstistically significantly more contacts to physiotherapists compared to their references throughout the entire study period, and increasing contact rates from eight months before the diagnosis. This was primarily driven by more contacts in women with RA compared to their references.

Conclusion: Patients with RA had more contacts to general practice and physiotherapists in all 12 months preceding the RA diagnosis compared to references and these contact rates increased further the last six to eight months in patients with RA. This indicates symptom presentation for several months before the RA

is diagnosed, and it indicates that a window of opportunity exists to expedite referral to specialist care and the diagnosis of RA.

Figure 1: Contacts with a general practitioner in the 12 months preceding the date of a rheumatoid arthritis diagnosis and a corresponding index date assigned to references persons without rheumatoid arthritis.



Upper part: unadjusted rates. Lower part: incidence rate rations adjusted for age, civil status, ethnicity, educational level, household income and comorbidity.
Black lines represent 95% confidence intervals.

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OP0038

VITAMIN D AND MARINE N-3 FATTY ACID SUPPLEMENTATION FOR PREVENTION OF AUTOIMMUNE DISEASE IN THE VITAL RANDOMIZED CONTROLLED TRIAL: OUTCOMES OVER 7 YEARS

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Background: Strong biologic rationale supports both vitamin D and marine omega-3 (n-3) fatty acids for prevention of autoimmune disease (AD). Within the randomized, double-blind, placebo-controlled **VIT**amin D and Omeg**A**-3 Tria**L** (**VITAL**), we tested the effects of these supplements on AD incidence. We previously reported results after 5.3 years of randomized follow-up showing overall protective effects for vitamin D on AD incidence (HR 0.78, 95% CI 0.61-0.99) and suggestive results for n-3 fatty acids (HR 0.85, 95%CI 0.67-1.08)[1].
Objectives: We aimed to test effects of these supplements with two more years of post-intervention follow-up in VITAL.
Methods: VITAL enrolled and randomized men and women (age ≥50 and ≥55 years, respectively) in a 2-by-2 factorial design to vitamin D_3 (2000 IU/d) and/or n-3 fatty acids (1000 mg/d) or placebo and followed for median 5.3 years. Here, we followed participants for another 2 years of observation to assess for sustained effects. Incident AD diagnoses were reported by participants annually and confirmed by medical record review by expert physicians using existing classification criteria. The primary endpoint was total incident AD, including rheumatoid arthritis (RA), polymyalgia rheumatica (PMR), autoimmune thyroid disease (AITD), psoriasis, and all others. Pre-specified secondary endpoints included individual common AD; and probable AD. Cox models calcuated hazard ratios (HR) for incident ADs.
Results: Of 25,871 participants randomized, 71% self-reported non-Hispanic Whites, 20% Black, 9% other racial/ethnic groups, 51% women, mean age was 67.1 years. During 7.5 years median follow-up, confirmed AD was diagnosed in 156 participants in vitamin D arm vs 198 in vitamin D placebo arm, HR 0.79 (0.64-0.97). Incident AD was confirmed in 167 participants in n-3 fatty acid arm and 187 in n-3 fatty acid placebo arm, HR 0.89 (0.72-1.10). For vitamin D, HRs trended toward reduction for RA 0.67 (0.37- 1.21), PMR 0.69 (0.46-1.03) and psoriasis 0.57 (0.33-0.99). For n-3 fatty acids, HRs trended toward reduction for RA 0.55 (0.30-1.10) and AITD 0.61 (0.33-1.12). Vitamin D's effect on AD incidence was stronger in those with body mass index (BMI) < 25 (HR 0.65, 0.44-0.96) than ≥ 25 kg/m^2 (p interaction 0.01).
Conclusion: Supplementation for 5.3 years with 2000 IU/day vitamin D (compared to placebo), followed by 2 years of observational follow-up, significantly reduced overall incident AD by 21% in older adults. HRs for RA, PMR and psoriasis trended toward reduction with vitamin D, with stronger effect in those with normal BMI. Supplementation with 1000 mg/day n-3 fatty acids did not significantly reduce total AD.

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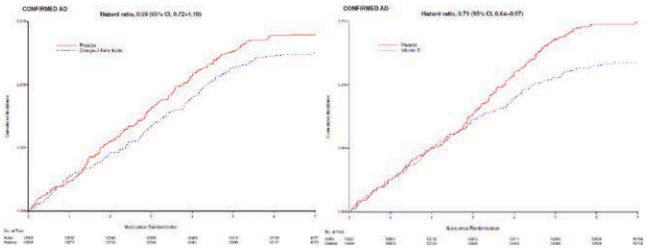

Figure 1.

Table 1. Hazard Ratios for Primary and Secondary Endpoints, by Randomized Assignment to Vitamin D/Placebo (Left), N-3 Fatty Acids/Placebo (Right)[a]

Endpoint	Vitamin D_3 (N=12,927)	Placebo (N=12,944)	Hazard Ratio (95% CI)	p	N-3 Fatty Acids (N=12,933)	Placebo (N=12,938)	Hazard Ratio (95% CI)	p
Primary: Confirmed AD	156	198	**0.79 (0.64-0.97)**	**0.03**	167	187	0.89 (0.72-1.10)	0.27
Secondary:								
Confirmed + probable AD	265	321	**0.83 (0.70-0.97)**	**0.02**	271	315	0.86 (0.73-1.01)	0.06
Excluding subjects with any pre-randomization AD								
Confirmed AD	127	162	**0. 79 (0.62-0.99)**	**0.04**	141	148	0.95 (0.75-1.20)	0.66
Confirmed + probable AD	211	270	**0. 78 (0.65-0.94)**	**0.007**	232	249	0.93 (0.78-1.11)	0.41
Excluding first 2 years follow-up								
Confirmed AD	86	130	**0.66 (0.50-0.87)**	**0.003**	104	112	0.92 (0.71-1.21)	0.56
Confirmed + probable AD	147	205	**0.72 (0.58-0.89)**	**0.002**	172	180	0.95 (0.77-1.17)	0.63
Individual AD[b]								
RA	18	27	0.67 (0.37-1.21)	0.18	16	29	0.55 (0.30-1.01)	0.06
PMR	39	57	0.69 (0.46-1.03)	0.07	46	50	0.92 (0.61-1.37)	0.67
AITD	27	18	1.50 (0.82-2.71)	0.19	17	28	0.61 (0.33-1.12)	0.11
Psoriasis	20	35	**0.57 (0.33-0.99)**	**0.05**	34	21	1.62 (0.94-2.79)	0.08

[a]Analyses from Cox regression models controlled for age, sex, race, and other (n-3 fatty acid or vitamin D) randomization group [b]Confirmed AD.

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OP0039

RISK OF ARRHYTHMIA AMONG NEW USERS OF HYDROXYCHLOROQUINE: A LONGITUDINAL POPULATION-BASED COHORT STUDY ON NEWLY DIAGNOSED RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Previous findings on hydroxychloroquine (HCQ) use and the risk of arrhythmia are contradictory and low-level evidence-based results. Additional research is required to evaluate the safety profile of HCQ to arrhythmia in managing rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).
Objectives: To assess the association between HCQ initiation and risk of incident arrhythmia among newly diagnosed RA and SLE patients.
Methods: All patients with incident RA or SLE and no arrhythmic events or anti-arrhythmic medications and no HCQ use prior to disease index date in British Columbia, Canada, between January 1997 and March 2015 were identified using administrative databases. HCQ initiator and HCQ non-initiator groups were identified and matched 1:1 by propensity scores using baseline confounders on demographics including presence of RA or SLE disease and duration of disease prior to the index date of HCQ initiators or non-initiators, comorbidities, other medications, and healthcare utilization. Matching was done within the same calendar year to account for a potential secular trend in HCQ use and risk of arrhythmia. Outcomes were any new arrhythmias, atrial fibrillation, abnormal electrocardiogram including prolonged QT syndrome and conduction disorder, and other unspecified arrhythmias during follow-up. We used Cox proportional hazard models with death as a competing event to assess the association of HCQ initiation and the outcomes.
Results: We identified 11,518 HCQ initiators (10,655 RA and 863 SLE patients, mean ± SD age 55.9 ± 15.1 years, 76.1% female) and 11,518 HCQ non-initiators (10,639 RA and 879 SLE patients, mean ± SD age 56.0 ± 16.2 years, 76.4% female) after 1:1 propensity score matching. Over the mean follow-up of eight years, there were 1,610 and 1,646 incident arrhythmias in the HCQ initiator and non-initiator groups, respectively. The crude incidence rates of arrhythmia were 17.5, and 18.1 per 1,000 person-years, respectively. Cumulative risk of incident arrhythmia remained similar for both groups. (Figure 1). Adjusted hazard ratio (aHR) of incident arrhythmia from the Cox proportional hazard model for HCQ initiators was 0.99 (95% CI: 0.92-1.06) compared to non-initiators (Table 1). The corresponding aHRs for HCQ initiators in subtypes of arrhythmia – atrial fibrillation, abnormal electrocardiogram, and other unspecified arrhythmias were 0.95 (95% CI: 0.84-1.06), 1.04 (95% CI: 0.87-1.26), and 0.96 (95% CI: 0.86-1.08), respectively.

Table 1. Incident arrhythmias of any type among RA and SLE patients initiating HCQ prescription compared with HCQ non-initiators

	HCQ initiator	HCQ non-initiator
Participants (number)	11,518	11,518
Mean follow-up (years)	8.00	7.89
Events (number)	1,610	1,646
Crude incidence rate per 1000 person-years	17.48	18.12
Unadjusted HR (95% CI)	0.98 (0.91-1.05)	1.00 (reference)
Adjusted# HR (95% CI)	0.99 (0.92-1.06)	1.00 (reference)

Abbreviations: **HCQ**, hydroxychloroquine; **HR**, hazard ratio.#The multivariable Cox proportional hazard model was adjusted for baseline confounders on demographics, comorbidities, medications, and healthcare utilization.

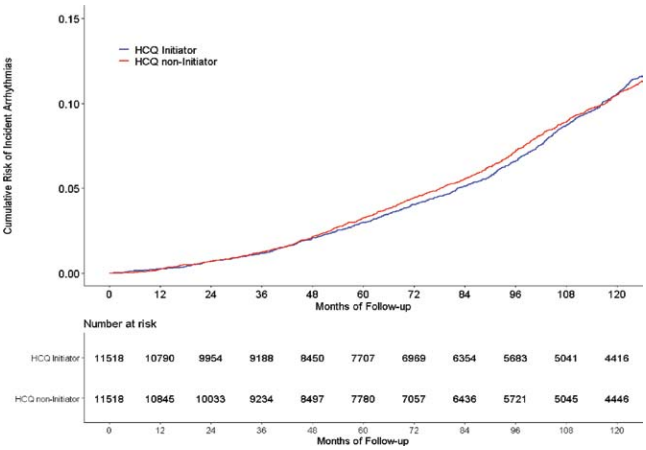

Figure 1. Cumulative risk of incident arrhythmias for HCQ initiators and non-initiators over the follow-up time.

Conclusion: There is no increased risk of any type of arrhythmia among new users of HCQ in RA and SLE patients. We believe the results of this large cohort study will add to the confidence with which HCQ can be used in RA and SLE management.
Disclosure of Interests: None declared.
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In dialogue with the expert: axSpA and Sjögren's syndrome

OP0040-PARE

THE WEBINAR SERIES FOR THE PATIENTS "PREGNANCY AFTER DIAGNOSING ANKYLOSIS SPONDYLITIS"

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Background: Having been diagnosed with ankylosis spondylitis (AS), 68,2% of females in Russia reconsider their plans for pregnancy, with 13% giving up motherhood altogether out of fear for their own and their child's potential health problems. However, most females allow pregnancy while experiencing emotional discomfort and anxiety[1].
Objectives: To shed more light on the mutual influence of AS and pregnancy, AS pregnancy outcomes, clinical course of AS as well as medication options during AS and lactation.
Methods: From 03/2021 to 12/2021 an on-line series of eight webinars was conducted together with the patients' Russian ankylosing spondylitis association. Each webinar included lectures of one or two rheumatologists and an obstetrician; furthermore, the series included the presentations of a physical therapy instructor (with the demonstration of exercises) and of a breast-feeding specialist. After the lecture each speaker answered the audience's questions. Topics of rheumatologists' lectures were "AS and pregnancy: problem introduction", "What do we know about AS genetics", "Features of pregnancy planning" (included therapy issues for men with AS who are planning to father a child), "Rheumatologist prenatal and postnatal care" (included the analysis of AS clinical manifestations such as potential changes in back pain type);"-Contemporary approaches to AS pregnancy treatment". A brochure for the patients with the main provisions of the lectures had been developed in support of the series.

Results: Webinars scored 703±192 views (by 29.01.2022). According to the questionnaire survey of the audience, 43,8% first knew that it was necessary to plan AS pregnancy minimum 3-6 months before conception; 25% – that conception is optimal during remission or low AS activity; 31,3% – that medical therapy can be continued during pregnancy; 18,8% – that it is necessary to inform the obstetrician about AS diagnosis and therapy received. 80% of the participants are fully satisfied with the information provided by the web series; 13,3% – reported not to had received enough information.
Conclusion: The interest in webinars shows that the choice of the form and the information provided was successful. The content of the series can be used to develop FAQ-section on the patient's website "Ankylosing Spondylitis Association». In 2022, lectures will continue taking into account patients' feedback.
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Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2022-eular.3180

OP0041-PARE SJÖGREN EUROPE: REVIEW OF ITS FIRST THREE YEARS OF ACTIVITY

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Background: Sjögren Europe was founded on 23 February 2019 by several European patient organisations representing Sjögren's patient to help to address the lack of visibility, attention, and solutions for Sjögren's.
Objectives: To show the first achievements and contributions of the federation.
Methods: Sjögren Europe's purpose is to promote the advancement of knowledge, research, information, treatment, and care, to foster patient involvement and participation in research and any other relevant area, to increase awareness, identify the different unmet needs and articulate patient voices throughout Europe.
Results: Finding one's bearings and the right rhythm during the first years of an organisation's life is a challenge in itself. The Covid-19 pandemic has made this process even more difficult. Our first goal was to organise a first face-to-face European patient conference. This meeting had to be postponed. However, we were able to adapt and develop a range of activities.
We organised a series of informative webinars on different topics by leading European experts for patients and others interested in the subject. We have organised various awareness campaigns such as a campaign for Sjögren Awareness Month in 2021 for which we have created 2 awareness videos and published several testimonials. We also created a 3-axis campaign about fatigue for World Sjögren's Day 2021 which won the Best Practice Award at the 2021 PARE Conference, and during which we shared the patients' perspective on fatigue in publications in 13 languages on social media. We published a booklet about fatigue developed by a specialist and produced 3 informative leaflets for patients. We also subtitled 2 videos made by one of our members in 10 European languages to disseminate quality information that many patients miss. We have been involved in various research projects, working groups and patient panels and have been able to bring the patient perspective to various stakeholders on many occasions.
Conclusion: Despite the limited contacts, we were able to create strong links and rich discussions that stimulated our creativity. Sjögren Europe has become a privileged partner, recognised, and appreciated by the various stakeholders. Patients with Sjögren's are better represented at the supranational level. It is our members, the national patient organisations, who by their trust give us our legitimacy. In return, Sjögren Europe has been able to inject a new energy and dynamism that can be felt at the different national levels and that opens up many perspectives and opportunities. We have been able to strengthen our presence and visibility with patients on social networks, where our audience is constantly growing, as well as in the rheumatology field with researchers, clinicians, industry, and associations such as EULAR. The resumption of face-to-face contacts is eagerly awaited to consolidate the links already created and to feed the richness, relevance, originality and diversity of our discussions and activities.
Disclosure of Interests: None declared.
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Infection-related and other orphan rheumatic disorders

OP0042 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF) - INTERIM ANALYSIS OF THE RELIANCE REGISTRY

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Background: Familial Mediterranean Fever (FMF) is a chronic disease characterized by recurrent attacks of fever as well as serositis and bears the risk of serious complications (e. g. amyloidosis). Treatment of FMF according to EULAR aims to control acute attacks and subclinical inflammation as well as to improve patient´s quality of life[1]. Clinical data indicate that the inhibition of interleukin-1β with canakinumab (CAN) is effective in controlling and preventing flares in FMF patients[2].
Objectives: The present study explores the long-term efficacy and safety of canakinumab in routine clinical practice conditions in pediatric (age ≥2 years) and adult FMF patients.
Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up period. Patients with clinically confirmed FMF diagnosis who routinely receive canakinumab are enrolled in order to evaluate effectiveness and safety of canakinumab. Disease activity and remission by physicians´ assessment, disease activity, fatigue and impact on social life by patients' assessment, inflammatory markers and AIDAI (Auto-Inflammatory Diseases Activity Index) score were recorded at baseline and assessed at 6-monthly intervals within the 3-year observation period of the study.
Results: This interim analysis of FMF patients (N=74) enrolled by December 2021 includes baseline as well as 6- to 24-month data. Mean age in this cohort was 25 years (2–61 years) and the proportion of female patients was 51 % (N=38). At baseline, median duration of prior CAN treatment was 1.0 years (0–6 years).
At month 24, physician ratings report around 63% of patients in disease remission and patient-reported disease activity (mean PPA) decreased from moderate (3.0) to low (2.6) during the observation period. Other disease activity parameters also decreased (Table 1). A total of 18 serious adverse events were reported, of which 2 (1 case of tonsillectomy and 1 case of tachycardia) were classified as drug - related.

Table 1. Baseline characteristics and 4th interim analysis data of patients with FMF

	Baseline	12 months	24 months
Number of patients, N	74	46	24
Number (%) of patients with days absent from work/school during last 6 months	6 (8)	11 (24)	9 (38)
Number (%) of patients in disease remission (physician assessment)	22 (45)	23 (72)	12 (63)
Patient's assessment of current disease activity; 0–10, median (min; max)	2.0 (0; 10)	2.0 (0; 7)	2.0 (0; 10)
Patient's assessment of current fatigue; 0–10, median (min; max)	5.0 (0; 10)	2.0 (0; 10)	4.0 (0; 10)
Number (%) of patients without impairment of social life by the disease	27 (50)	28 (80)	8 (67)
CRP (mg/dl) I SAA (mg/dl) I ESR (mm/h); median	0.2 I 0.7 I 8.0	0.2 I 0.5 I 4.0	0.2 I 0.7 I 6.0
Number (%) of patients with disease-related symptoms	prior to inclusion into the study I at baseline	12 months	24 months
Fever	68 (93) I 14 (29)	8 (25)	3 (16)
Abdominal pain	67 (92) I 20 (41)	10 (31)	4 (21)
Thoracic pain	45 (62) I 5 (10)	3 (9)	1 (5)
Headache	34 (47) I 11 (22)	7 (22)	5 (26)
Myalgia	23 (32) I 6 (12)	4 (13)	2 (11)
Arthralgia/arthritis	39 (54) I 16 (33)	9 (28)	5 (26)
Dermal symptoms (urticarial, maculopapulose)	15 (21) I 5 (10)	3 (9)	0 (0)
SAE	**Number of events**	**Incidence rate# per 100 patient years**	
All types of SAE	18	14.03	
SADR	2	1.56	

Incidence rate = number of events * 36,525 / sum of observation days (=46,848).CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; n. a., not annotated; SAA, serum amyloid A; SADR, serious adverse drug reaction; SAE, serious adverse events.

Conclusion: Interim data of FMF patients from the RELIANCE study, the longest running real-life canakinumab registry confirm efficacy and safety of long-term canakinumab treatment.

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OP0043

TOCILIZUMAB SIGNIFICANTLY REDUCES SERUM AMYLOID A IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER – DATA FROM THE PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND TOFFIFE STUDY

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Background: Uncontrolled inflammation in patients with familial Mediterranean fever (FMF) can lead to severe organ failure due to amyloidosis. Colchicine is still the standard treatment and the only therapy that has been proven to reduce the risk for amyloidosis. Besides colchicine the Interleukin (IL)1-antagonists Anakinra and Canakinumab are approved, but new treatment options are still needed. The IL-6 antagonist Tocilizumab (TCZ) effectively reduces inflammation and is approved in several other rheumatic indication. Here we present data from our phase II study TCZ for the treatment of FMF – TOFFIFE.

Objectives: To explore the efficacy and safety of tocilizumab in FMF.

Methods: The TOFFIFE study was a placebo-controlled, double-blinded, randomized trial to investigate the efficacy and safety of TCZ in patients with colchicine resistant (cr)FMF. The physician's global assessment of disease activity (PGA) based on a 5 point-scale for 6 symptoms (range 0-24) was used as a clinical score and had to be >2 at screening. Patients were randomized 1:1 to either receive monthly TCZ intravenously with 8 mg/kg bodyweight or placebo over a period of 24 weeks. Patients with inadequate response after week 12 had the opportunity to receive open label TCZ at week 16. The primary endpoint was the number of patients achieving an adequate response to treatment at week 16, defined as a PGA ≤ 2 + normalized ESR or CRP (the item that led to inclusion had to be normalized) + normalized SAA. Secondary endpoints included normalization of SAA during treatment and safety of TCZ in FMF patients.

Results: 25 patients were randomized with a median age of 31 years (range 18 - 53y), of which 14 (56%) were female. At week 16, which was the timepoint for the primary end point, 2 (15.4%) patients in the TCZ arm reached the primary end point with a PGA ≤ 2 and normalization of SAA and CRP and/or ESR but none of the patients in the placebo arm. Therefore, the superiority of TCZ compared to placebo could be shown concerning the pre-specified significance level of α=0.2 (p=0.089). SAA levels normalized with TCZ but not with PBO. This difference between TCZ und PBO was highly significant; SAA p < 0.015. At week 28 with 17 remaining patients and after having had the opportunity for a rescue treatment at week 16, the responder rates (PGA ≤ 2 + normalization of SAA, ESR and/or CRP) were 25% (n=1) in those patients who changed from placebo to TCZ (n=4) and 20% (n=2) in those patients who continued with TCZ (n=10). Of note, all 3 patients remaining on PBO were non-responders (p= 0.642). In 75% of patients (n=3) CRP and in 50% SAA (n=2) normalized after changing to TCZ. No new safety aspects occurred.

Conclusion: In this first randomized, placebo-controlled study in patients with active crFMF TCZ significantly reduced and normalized SAA levels. The trial met the primary endpoint to demonstrate the superiority of TCZ over PBO although only a small numerical difference was found. Nevertheless, the proportion of patients with a successful TCZ-therapy was lower than expected due to very strict response criteria; patients had to achieve a complete remission with a PGA ≤2 (on a 0-24 scale) and normalization of the inflammatory parameters (CRP/ESR and SAA). This required no or only mildest symptoms during the last 4 weeks. A larger multicenter study is therefore justifiable and needs to clarify the benefit of TCZ treatment in FMF.

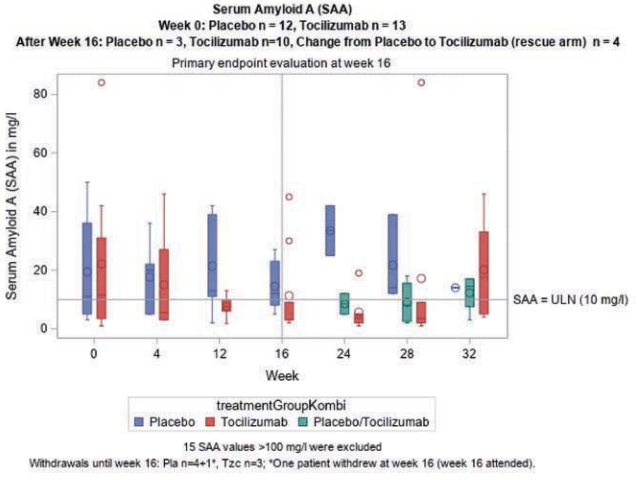

Figure 1. Secondary endpoint: Serum Amyloid A over time, showing a clear reduction in the TCZ but not in the PBO arm and rerise of SAA after discontinuation after week 28. Normal SAA value = < 10mg/l. Outliers > 100mg/l were excluded in this graph.

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OP0044 CYTOKINE PROFILE, HYPERFERRITINEMIA, AND MULTI-VISCERAL INVOLVEMENT CHARACTERISE MACROPHAGE ACTIVATION SYNDROME COMPLICATING ADULT ONSET STILL'S DISEASE. RESULTS FROM A MULTIDIMENSIONAL EVALUATION

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Background: Adult-onset Still's disease (AOSD) is a rare multigenic autoinflammatory disease of unknown aetiology burdened by life-threatening, such as macrophage activation syndrome (MAS) [1]. Considering the poor outcome of MAS patients, previous works tried to assess predictive factors of its occurrence during AOSD [2-4]. However, an integrated evaluation of clinical features with biomolecules, more reflecting the pathogenic mechanisms of the disease and its complications, is still missing.
Objectives: To multidimensionally characterise MAS complicating AOSD considering cytokine profile, inflammatory markers, and multi-visceral involvement of the disease. To perform a high-dimensional phenotypic analysis of circulating immune cells in AOSD patients with and without MAS. To assess interferon (IFN)-related pathways in AOSD synovial tissues by a bulky RNA sequencing.
Methods: The present evaluation was designed to multidimensionally compare AOSD patients with or without MAS, considering cytokine profile, inflammatory markers, and multi-visceral involvement of the disease. Clinical and biologic data were collected and compared in AOSD patients with and without MAS. Sera biomolecules were analysed by Luminex multiplexing technology. Mass cytometry (CyTOF) was used to characterise circulating immune cells. A bulky RNA sequencing was performed in AOSD synovial tissues.
Results: In this study, 40 consecutive AOSD patients (47.7±15.0 years, 50.0% male gender) were assessed at the time of diagnosis before the administration of any immunosuppressive therapy. Out of those, 14 (35%) patients were complicated by MAS. Paralleling with increases of systemic score and ferritin, MAS patients were characterised by an increased concentration of IL-1α, IL-1β, IL-1Ra, IL-2Ra, IL-6, IL-10, IL-17A, IFN-γ, G-CSF, MCP-1, MIP-1α, SCF. Among these biomolecules, IL-1Ra, IFN-γ, MCP-1, and SCF were correlated with MAS. Combining the discriminatory ability of these data in identifying MAS, the best model was composed by systemic score, ferritin, IFN-γ, and IL-10. This model was characterised by AUC=0.99 (Standard error: 0.008; 95%CI: 0.976–1.000), sensitivity=100%, specificity=95.45%. By CyTOF analysis, AOSD patients, who were complicated or not with MAS were characterised by a significant increase of circulating "classical monocytes" (CD14+CD38+). MAS patients were characterised by a significant reduction of NK cells (CD45RA+CD56dim) than AOSD patients. Finally, the transcriptomic profile, by RNA-sequencing analysis, showed that 3477 among type I, II, and III IFN-related genes (IRGs) were significantly different in AOSD synovial tissues.
Conclusion: A multidimensional characterisation of AOSD patients was provided suggesting that IFN-γ, IL-10, ferritin, and systemic score discriminated MAS, thus identifying the occurrence of the cytokine storm syndrome. The inflammatory *milieu* of AOSD and MAS may be associated with a signature of circulating immune cells. Finally, our results about IRGs reinforced the role of IFN-γ in these patients.
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OP0045 TREATMENT OF IDIOPATHIC RECURRENT PERICARDITIS WITH GOFLIKICEPT - FIRST DATA FROM THE INTERIM ANALYSIS OF PHASE 2/3 ONGOING STUDY

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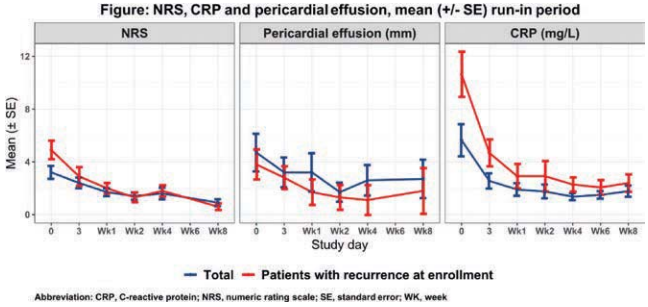
Background: Idiopathic recurrent pericarditis (IRP) is a rare autoinflammatory disease [1,2] that has similar pathogenesis with adult-onset Still's disease and monogenic autoinflammatory diseases [3,4]. IL-1α and IL-1β are the pivotal cytokines in the pathophysiology of acute pericarditis and its recurrence [5]. This report presents the interim analysis of clinical trial with goflkicept (original, fusion protein, heterodimer, binding IL-1α and IL-1β) in patients with IRP. Trial registration: ClinicalTrials.gov, NCT04692766.
Objectives: To evaluate the efficacy and safety of goflikicept treatment in patients with IRP.
Methods: Subjects with recurrence (n=9) or in inter-recurrence period (n=13) were enrolled in the run-in period of 12 weeks for treatment with NSAIDs and/or colchicine or 24 weeks for treatment with corticosteroids (CS).
Dose finding approach was applied, where subjects from the first cohort (n=10) received subcutaneous goflikicept 80 mg every 2 weeks, subjects from the second cohort (n=12) - 240 mg load within the first week, 80 mg within the second week, thereafter 80 mg every 2 weeks on top of background NSAIDs, colchicine and/or CS. Treatment response is considered as an achievement or maintenance of the following criteria: chest pain NRS≤3, CRP≤5 mg/L, absent or mild (<10 mm) pericardial effusion on Day 14. In responders NSAIDs/colchicine were stopped immediately, CS therapy was reduced and terminated within 12 weeks and for the next 12 weeks patients were on goflikicept monotherapy. At the end of the run-in responders proceeded into the double-blind, placebo-controlled randomized-withdrawal (RW) period, where received goflikicept 80 mg every 2 weeks or placebo. Primary endpoint was the time to the first pericarditis recurrence. In case of recurrence, the patients were unblinded, patients from placebo group retreated with goflikicept. According to interim analysis plan efficacy/safety analysis included only unblinded data during the RW period.
Results: Treatment response was achieved in 8 of 9 patients, enrolled with recurrence and all patients enrolled without recurrence remained in remission at Day 4. There were no new recurrence events on goflikicept therapy, despite NSAIDs/colchicine/CS discontinuation during the run-in period. In the run-in period mean NRS, CRP and pericardial effusion decreased from baseline (Figure 1). Decrease of concentrations of IL-1RA, IL-6, calprotectin was reported during the run-in period, which confirms anti-inflammatory effect of goflikicept. A total of 20 patients were randomized. Recurrent pericarditis occurred in 8 of 10 patients in placebo group, there were no recurrence events in goflikicept group to the moment of this interim analysis. After retreatment with goflikicept and recurrence resolution there were no new recurrence events. Adverse events (AEs) occurred in 15 of 22 patients (68,2%) during the run in period. During the run- in period, 6 of 22 patients (27%) experienced infections, 4 (18,2%) cholesterol elevation, 3 (13,6%) lymphopenia, 2 (9,1%) lipase elevation, 2 (9,1%) injection site reactions. AEs occurred in 4 of 8 patients (50%) during placebo treatment in the RW period. AEs occurred in 6 of 8 patients (75%) after retreatment with goflikicept. There were no deaths, no new safety signals. Overall safety profile was similar to those described for other IL-1 blockers.

Figure: NRS, CRP and pericardial effusion, mean (+/- SE) run-in period



Abbreviation: CRP, C-reactive protein; NRS, numeric rating scale; SE, standard error; WK, week

Conclusion: The first data show ability to achieve and maintain IRP remission on goflikicept monotherapy with favorable risk-benefit ratio. Final data will be provided.

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OP0046 EVALUATION OF THE EFFICACY OF TOPICALLY APPLIED TACROLIMUS IN THE TREATMENT OF ORAL ULCERS IN BEHCET'S DISEASE: A DOUBLE BLIND PLACEBO CONTROLLED STUDY

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Background: Treatment of Behcet disease (BD) associating oral ulcers is still challenging despite the advances in the systemic treatment modalities.
Objectives: We aimed to evaluate the clinical efficacy of topical Tacrolimus for treatment of BD.
Methods: In this double blind placebo controlled trial, forty BD patients with persistent active oral ulceration were equally randomized into group I (20 patients received oral colchicine plus topically applied tacrolimus) and group II (20 patients received oral colchicine plus placebo oral gel). All participants were evaluated based on Behcet's Disease Current Activity Form (BDCAF), Ulcer Severity Score (USS) and visual analog scale (VAS) before treatment, and at four-time points post-treatment (15 days, 1st, 2nd, and 3rd months).
Results: VAS was significantly lower in group I after 2 weeks (p= 0.037) and 3 months (0.025) than in group II. USS was significantly lower in group I after 3 months of follow up regarding the number of ulcers (p=0.014), ulcer size (p=0.022), and duration (p=0.009). BDCAF showed significant improvement in 3 months follow up within each group (p<0.001 for both groups), while there was insignificant difference between both groups(p=0.347).
Conclusion: Topical Tacrolimus has been proven to be a safe and effective adjunctive therapy in the management of oral ulcerations in BD.

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OP0047 IMPAIRED JAK-STAT PATHWAY IN PATIENTS WITH PYODERMA GANGRENOSUM

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Background: Pyoderma gangrenosum (PG) is an inflammatory disease with an unknown etiology. Currently there is an unmet need in the of PG. In recent years, JAK/STAT pathway have been shown to have an important role in the etiology of inflammatory conditions particularly in the field of dermato-rheumatology. However, current data on JAK/STAT pathway in PG is significantly limited.
Objectives: Herein we aimed to investigate the JAK/STAT signaling pathway in the skin biopsies of PG patients and compared with psoriasis (PSO) and healthy subjects (HS).

Table 1. Summary of the findings

			Healthy Subjects (n=26)	Pyoderma Gangrenosum (n=31)	Psoriasis (n=35)
	Age, mean ± SD		**60,3 ± 18,3**	**58,1 ± 16,1**	**46,5 ± 18,4**
	Women/men (%)		**14/12**	**18/13**	**15/20**
Dermal staining	**JAK1**	Positive, n (%)	0	7 (22.6)*	3 (8.5)
	JAK3	Positive, n (%)	0	27 (87)*	31 (88.5)**
	TYK2	Positive, n (%)	0	31 (100)*	34 (97.2)**
	STAT1	Positive, n (%)	0	20 (64.5)*	27 (77.1)**
	STAT3	Positive, n (%)	0	29 (93.6)*	1 (2.8)
	STAT4	Positive, n (%)	0	7 (22.6)*	11 (31.4)**
	STAT5	Positive, n (%)	0	9 (29.3)	27 (77.1)**
	STAT6	Positive, n (%)	0	3 (9.7)	33 (94.3)**
cytoplasmic parts of epidermis	**JAK1**	Negative, n (%)	0	1	0
		Mildly positive, n (%)	0	0	0
		Moderately positive, n (%)	23 (88.4)	6 (19.4)	24 (68.5)
		Strongly positive, n (%)	3 (11.5)	24 (77.4)*	11 (31.5)**
	TYK2	Negative, n (%)	0 (0)	1 (3.2)	2 (5.7)
		Mildly positive, n (%)	0 (0)	4 (12.9)	1 (2.8)
		Moderately positive, n (%)	18 (69.2)	18 (58.1)	11 (31.4)
		Strongly positive, n (%)	8 (30.8)	8 (25.8)	21 (60)**
	STAT3	Negative, n (%)	0	1 (3.2)	0
		Mildly positive, n (%)	0	1 (3.2)	0
		Moderately positive, n (%)	12 (46.1)	1 (3.2)	1 (2.8)
		Strongly positive, n (%)	14 (53.9)	28 (90.4)*	34 (97.2)**
	STAT4	Negative, n (%)	0	1 (3.2)	0
		Mildly positive, n (%)	0	1 (3.2)	0
		Moderately positive, n (%)	12 (46.1)	3 (9.7)	6 (17.1)
		Strongly positive, n (%)	14 (53.9)	26 (83.9) *	29 (82.9) **
	STAT6	Negative, n (%)	18 (69,2%)	15 (48,4%)	1 (2,8%)
		Mildly positive, n (%)	8 (30,8%)	16 (51,6%)	0
		Moderately positive, n (%)	0	0	20 (57,2%)
		Strongly positive, n (%)	0	0	14 (40%)**
nuclear part of epidermis	**TYK2**	Negative, n (%)	22 (84,6%)	1 (3,2%)	2 (5,7%)
		Mildly positive, n (%)	4 (15,4%)	10 (32.2%)	6 (17,1%)
		Strongly positive, n (%)	0	20 (64,6%)*	27 (77,2%)**
	STAT3	Negative, n (%)	0	1 (3,2%)	0
		Mildly positive, n (%)	16 (61,5%)	2 (6,5%)	5 (14,3%)
		Strongly positive, n (%)	10 (38,5%)	28 (90,4%)*	30 (85,7%)**

Data were shown mean±SD and n (%), *= significant expression HS vs PG, **= significant expression HS vs PSO.

Methods: 31 patients with PG, 35 patients with PSO and 26 HS were included. Immunohistochemical methods were used to evaluate the expression of JAK1, JAK2, JAK3, Tyrosine Kinase 2 (TYK2), STAT1, STAT3, STAT4, STAT5, and STAT6. In the dermis the staining intensity was recorded as 'positive' or 'negative. The epidermal part is divided into cytoplasmatic and nuclear parts and staining intensity recorded by semi-quantitively as follows: negative, mildly positive, moderately positive and strongly positive.
Results: In total, there were 92 biopsies. Dermal staining was significant for all the JAK/STAT proteins for patients with PG and PSO when compared to HS. On the other hand, there were no differences in the staining patterns of PG and PSO. For the investigation of cytoplasmic parts of epidermis JAK1, STAT3, and STAT4 were highly expressed in the PG and PSO, STAT6, and TYK2 were only significantly overexpressed in psoriasis. JAK3 was overexpressed in healthy skin, PG and psoriasis. The assessment of the nuclear part of epidermis TYK2 and STAT3 were highly expressed in the PG and PSO. JAK1 was overexpressed in PG versus PSO in cytoplasmic parts of the epidermis ($p<0.001$). TYK2 and STAT6 were highly expressed in the PSO versus PG in cytoplasmic parts of the epidermis ($p = 0.024$, $p<0.001$). In the investigation of nuclear parts of epidermis STAT1, STAT6 were highly expressed in the PSO versus PG. The summary of the findings is given in Table 1.
Conclusion: In this study, the JAK/STAT inflammatory pathway is significantly activated in PG patients which is adding up new information to the current literature. Considering the unmet need in PG targeting of this pathway could be beneficial for the treatment of refractory PG.
Disclosure of Interests: None declared.
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OP0048

FIRST INTERIM ANALYSIS OF THE INTERNATIONAL X-LINKED HYPOPHOSPHATAEMIA (XLH) REGISTRY: ADULT POPULATION BASELINE CHARACTERISTICS

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Background: X-Linked Hypophosphataemia (XLH) is a rare, progressive, lifelong, hereditary phosphate wasting disorder characterised by a pathological increase in fibroblast growth factor 23 concentration/activity.[1] Despite XLH being increasingly recognised as a chronic progressive disease, there are few data documenting its natural history or the impact of treatment and other medical interventions on patient outcomes.[2] The multicentre, international, XLH patient registry was established to address this lack of information in XLH to help inform future clinical practice.
Objectives: To report data from the first interim analysis of the International XLH Registry (NCT03193476), focusing on baseline characteristics of adults (aged ≥18 years [y]).
Methods: The International XLH Registry was initiated August 2017 to collect information on the natural history of XLH and will run for 10 years, aiming to recruit 1,200 people with XLH. Subjects diagnosed with XLH were enrolled from 81 sites in 16 countries (Last Patient In: 30/11/2020; Database Lock: 29/03/2021). Parameters collected at baseline included demographics, medical/treatment history, and clinical presentation.
Results: In total, 217 adults were eligible for inclusion in this analysis (18–<30y, n=56; 30–<50y, n=96; ≥50y, n=65); and 150 (69.1%) were female. Mean (SD) age was 41.9y (15.5y); median 41.1y. Mean height was 155.8 cm (n=79); mean weight, 70.0 kg (n=96); mean BMI 26.5 kg/m^2 (n=48). Most subjects resided in the UK (50.7%, n=110) and in France (18.9%, n=41). Treatment data were available for 118 subjects: conventional therapy (phosphate salts and active vitamin D), 83.9% (99/118); burosumab, 11.0% (13/118); no treatment recorded 5.1% (6/118). Of 163 subjects with available data, a genetic test result was recorded for 68 (41.7%), of whom 62 (91.2%) had a confirmed *PHEX* mutation. Data on XLH family history were available for 187 subjects; 56/140 (40.0%) reported their biological mother was affected; and 22/141 (15.6%) reported their biological father was affected. The mean time to diagnosis from first symptoms was longer in older vs younger adults: 18–<30y, 25 months (mo) (n=21); 30–<50y, 21mo (n=21); ≥50y, 112mo (n=13).
Retrospective XLH clinical data were available at study entry for 110 adult subjects. Among these subjects, joint conditions were reported by 36.4% (40/110), with osteoarthritis of the knees (60%), hips (42.5%), and shoulders (22.5%) the most frequently affected. Skeletal abnormalities were noted for 71.8% (79/110) of subjects; most common conditions were *genu varum* 53.2% (42/79), *genu valgum* 26.6% (21/79), and enthesopathy 21.5% (17/79). Historical fracture data ("yes/no") were available for 111 subjects; 41 were reported to have had a fracture. Femur fracture was reported for 22 subjects, and hip fractures for 5 subjects. Details of historical orthopaedic surgery were reported for 99 adults; osteotomy was reported for 89 subjects, and hip replacements reported in 14 subjects.
Conclusion: The demographics and baseline characteristics of subjects in the International XLH Registry are as expected for adults with XLH. The shorter time to diagnosis in younger vs older adults may indicate improved recognition and diagnosis of XLH in recent years. The analysis of this young population treated with conventional therapy highlights the frequency of musculoskeletal involvement (osteoarthritis, enthesopathies, etc). The information collected within this rare-disease registry during these 10 years provides an exciting opportunity to integrate large-scale real-world evidence into clinical practice, with the aim of improving the care and quality of life of people living with this debilitating disease.
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OP0049

FURTHER CHARACTERIZATION OF CLINICAL AND LABORATORY FEATURES OCCURRING IN VEXAS SYNDROME IN A LARGE-SCALE ANALYSIS OF MULTICENTER CASE-SERIES OF 116 FRENCH PATIENTS

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Background: A new autoinflammatory syndrome related to somatic mutations of *UBA1* was recently described and called VEXAS syndrome.
Objectives: To describe clinical characteristics, laboratory findings and outcomes of VEXAS syndrome.
Methods: Case-series. Patients referred to a French multicenter registry between November 2020 and May 2021.
116 patients with VEXAS syndrome. Frequency and median of parameters and vital status, from diagnosis to the end of the follow-up.
Results: Main clinical features were skin lesions (83.5%), non-infectious fever (63.6%), weight loss (62%), lung involvement (49.6%), ocular symptoms (38.8%), relapsing chondritis (36.4%), venous thrombosis (34.7%), lymph nodes (33.9%), and arthralgia (27.3%). Hematological disease was present in 58 cases (50%), considered as myelodysplastic syndrome (MDS, n= 58) and monoclonal gammapathy of unknown significance (n=12).*UBA1* mutations included p.M41T (44.8%), p.M41V (30.2%), p.M41L (18.1%), and splice mutations (6.9%). After a median follow-up of 3.0 years, 18 patients died (15.5%), from infectious origin (n=9) and MDS progression (n=3). Unsupervised analysis identified 3 clusters: cluster 1 (47%) with mild-to-moderate disease; cluster 2 (16%) with underlying MDS and higher mortality rates; cluster 3 (37%) with constitutional manifestations, higher C-reactive protein levels and less frequent chondritis. Five-year probability of survival was 84.2% in cluster 1, 50.5 % in cluster 2, and 89.6% in cluster 3. *UBA1* p.Met41Leu mutation was associated with a better prognosis.
Conclusion: VEXAS syndrome displays a large spectrum of organ manifestations and shows different clinical and prognostic profiles. It also raises a potential impact of the identified *UBA1* mutation.
Disclosure of Interests: None declared.
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Managing chronic pain in RMDs

OP0050

INTRAARTICULAR MORPHINE IN CHRONIC KNEE-ARTHRITIS – RESULTS OF A RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Background: Patients with chronic inflammatory arthritis (e.g. rheumatoid arthritis; RA) or inflammatory exacerbations of chronic degenerative joint diseases (e.g. osteoarthritis; OA) suffer from recurrent pain, restricted function

and reduction of daily activities. The current standard of intraarticular (i.a.) therapy is the injection of steroids, which can increase risk of infection, cartilage degenerations, and other well-known systemic side effects. A novel approach without such complications could be the activation of peripheral opioid receptors, e.g. by i.a. application of small, systemically inactive doses of morphine.

Objectives: The aim of this randomized placebo-and active drug controlled double blind trial was to investigate reduction of pain in chronic knee arthritis patients following i.a. injections of morphine, a standard steroid (triamcinolone), or placebo. The primary hypothesis was that i.a. morphine results in significantly lower pain scores than placebo. The primary outcome parameter was reduction of the Visual Analogue Scale (VAS) pain at day 7.

Methods: Adult patients with chronic knee arthritis because of osteoarthritis (OA) or inflammatory arthritis (IA, rheumatoid arthritis, psoriatic arthritis, spondyloarthritis, oligoarthritis or monarthritis) and a high level of pain (VAS pain ≥ 4 out of 10) at baseline received a single dose of either morphine 3 mg i.a., or triamcinolone 40 mg i.a., or placebo (NaCl 0.9%) i.a., Patients were monitored closely throughout the entire study period with a total of 4 visits over weeks and documented pain in the morning and evening in a patient´s diary. Safety data was collected during the whole study period. P-values were calculated using two-sided T-tests.

Results: 114 patients were screened, 93 were treated and 89 (96%) completed day 7. Of these n= 61 (66%) were diagnosed with OA and n= 32 (34%) with IA 48 (52%) patients were female, mean age was 58.5 (SD 14 years) and mean disease duration 6.7 years (median 2 years, range <1 year – 42 yearss, IQR <1 – 10 years). The mean VAS pain improvement at day 7 for morphine, triamcinolone and placebo was -22.8, -37.7, and -19.8 respectively. The differences were not significant (p=0.69) for placebo vs. morphine, but significant for placebo vs. triamcinolone and for triamcinolone vs. morphine (p=0.013 and p=0.006). Mean improvements of the everyday pain documentation are shown in Figure 1. During the study period, there were no serious adverse events and 45 adverse events, most of them were mild.

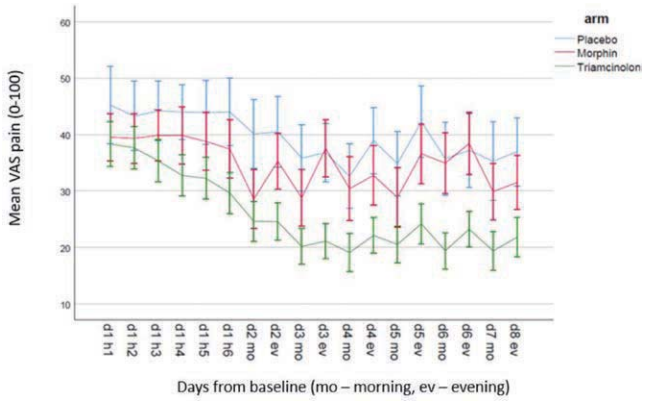

Figure 1. Mean VAS pain over one week in patients with chronic knee arthritis treated with morphine, triamcinolone or placebo as a single intraarticular injection.

Conclusion: In this randomized, placebo and active controlled double blind trial a single dose of 3 mg i.a. administered morphine did not lead to significant improvements in comparison to placebo and was inferior to triamcinolone at day 7. The same was true during the first 7 days as shown in the pain documentation in patient diaries. These data does not support the use of i.a. morphine for pain reduction in patients with chronic arthritis.

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OP0051

TRENDS FOR OPIOID PRESCRIPTIONS AMONG PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES BETWEEN 2006-2020

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Background: Opioid prescribing has contributed to a North American epidemic with increasing trends in several European countries[1]. Rheumatic and musculoskeletal diseases (RMDs) are one of the most common indications for prescribed opioids despite there being little evidence on opioid prescribing and the benefit of long-term use in RMDs.

Objectives: To investigate national UK opioid prescribing trends by studying the patterns of opioid prescribing in new users with the following six RMDs: rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (AxSpA), systemic lupus erythematosus (SLE), osteoarthritis (OA) and fibromyalgia.

Methods: Patients aged 18 years and older with a diagnosis of RA, PsA, AxSpA, SLE and OA with a new episode of opioid use without cancer in the Clinical Practice Research Datalink (CPRD) were included between 01/01/2006 and 31/12/2020. CPRD is a database of anonymised UK primary care electronic health records representative of the national population. New opioid users were defined as individuals with RMDs who had a new episode of opioid use in a 2-year time window up to 6 months before or after an RMD diagnosis. Rates of new opioid users were calculated by dividing the number of new opioid users with an RMD per year by the number of eligible patients registered in CPRD per year. Age- and gender-standardised rates for new opioid users were obtained using direct standardisation for each RMD. Rates of opioid prescriptions among new users for each RMD were calculated by dividing the number of opioid prescriptions among new users with an RMD in the year they had new opioid episodes by patient-years of the new users with an RMD. Trends for the rates in the study period were tested using negative binomial regression. Significant change points were identified by looking at the points where the derivative (i.e. rate of change) of the trends for the rates crossed zero. Recurrent opioid users were defined as patients who had at least 3 opioid prescriptions issued within 3 months after a new opioid episode.

Results: This study included 21,505 RA patients, 8,392 PsA patients, 4,491 AxSpA patients, 4,508 SLE patients, 944,078 OA patients, and 33,829 fibromyalgia patients, who had new opioid episodes between 2006-2020. Whilst the overall trend for RA (2.7* vs 3.9*), PsA (1.0* vs 1.8*) and fibromyalgia (3.7* vs 8.3*) has significantly increased over 15 years, from 2018 onwards, trends of new opioid users appeared to stabilise/decrease (Figure 1). The year 2018 was found to be a significant decreasing change point in the trends of new opioid users for RA, AxSpA, and SLE, whilst this was 2013 in OA and 2019 for fibromyalgia. Opioid prescription rates among new opioid users increased in SLE (4.3# vs 5.4#), OA (4.6# vs 4.9#) and fibromyalgia (5.6# vs 6.5#) but decreased in RA (5.7# vs 5.3#) from 2006 to 2020, despite fluctuations in the rates observed in this period. The highest proportions of recurrent opioid users among the 6 RMDs were patients with RA (32.6%) and fibromyalgia (31.9%).

* The number of new opioid users per 10000 persons

The number of opioid prescriptions in new users per patient years

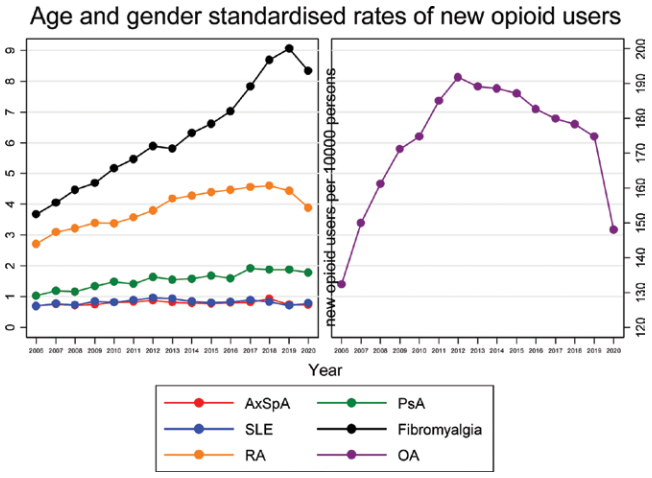

Figure 1. Trends of new opioid users by RMD, 2006-2020.

Conclusion: RA, PsA and fibromyalgia had an overall increase in new opioid users since 2006. The slight decrease in the trends of new opioid users among most of the RMDs after 2018 may reflect an increasing awareness of the opioid epidemic. The high proportions of recurrent opioid users in RA and fibromyalgia patients highlight the importance of exploring the safety of long-term opioid use and effective pain interventions for patients with RMDs.

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OP0052

THE EFFECT OF TOFACITINIB ON RESIDUAL PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS WITH COMPLETE CONTROL OF INFLAMMATION

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Background: Residual pain often remains in patients (pts) with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) who achieve low disease activity or remission.[1,2] Tofacitinib is an oral JAK inhibitor for the treatment of RA and PsA. A descriptive analysis showed that tofacitinib may have a beneficial effect on residual pain in pts with PsA with abrogated inflammation.[3]

Objectives: To assess efficacy of tofacitinib, adalimumab (ADA) and placebo (PBO) on residual pain in pts with RA and PsA with abrogated inflammation, using a network meta-analysis (NMA).

Methods: Data were pooled from 9 randomised clinical trials of pts with RA (NCT00960440/NCT00847613/NCT00814307/NCT00856544/NCT00853385/NCT01039688/NCT02187055) or PsA (NCT01877668/NCT01882439). This analysis included pts who received ≥1 dose of tofacitinib 5 mg twice daily (BID), ADA 40 mg once every 2 weeks or PBO with background therapy, and had abrogated inflammation (swollen joint count [SJC] = 0 and C-reactive protein [CRP] <6 mg/L) at Month (M)3. ADA was included in NCT00853385/NCT02187055/NCT01877668; NCT02187055 performed tofacitinib/ADA non-inferiority/superiority comparisons. Primary outcome was pt assessment of Pain (visual analogue scale [VAS] 0 [no pain] – 100 mm [most severe pain]) at M3; scores were summarised descriptively; treatment comparisons were assessed by Bayesian NMA on individual pt-level data, accounting for within-trial imbalances and treatment effect modifiers.

Results: Abrogated inflammation at M3 was achieved in 14.1% (328/2330), 14.9% (87/585) and 3.0% (20/673) of RA and 22.7% (54/238), 29.2% (31/106) and 12.7% (30/236) of PsA pts receiving tofacitinib, ADA and PBO, respectively. RA and PsA pts receiving tofacitinib/ADA had higher CRP vs pts receiving PBO. RA pts receiving tofacitinib/ADA had lower SJC and longer disease duration vs pts receiving PBO. PsA pts receiving tofacitinib had a longer disease duration and higher Pain VAS vs pts receiving ADA/PBO. In both groups, a lower % of female pts received tofacitinib/ADA vs PBO (Table 1). Observed median (Q1; Q3) values for Pain VAS at M3 were 17.0 (6.0; 31.0), 19.0 (7.0; 31.0) and 33.5 (7.0; 48.0) in RA and 24.0 (8.0; 44.0), 21.0 (9.0; 49.0) and 27.0 (8.0; 52.0) in PsA pts treated with tofacitinib, ADA or PBO, respectively. Differences between active treatments and PBO were less prominent in PsA vs RA pts, per posterior probability values (Fig).

Conclusion: In this NMA, pts with RA and PsA achieving abrogated inflammation with tofacitinib or ADA at M3 had greater residual pain reduction vs those receiving PBO. This may imply that tofacitinib/ADA have analgesic benefits beyond those related to inflammation reduction.

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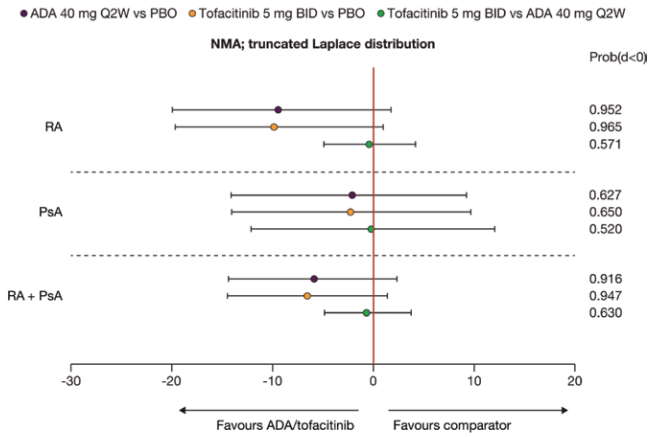
Fig. Bayesian NMA of pt assessment of arthritis pain outcome at M3



Data are mean ± 95% credible interval
Treatment effects were adjusted for baseline covariates (disease, disease duration, age, sex, Pain [VAS] and PASI) and for concomitant treatments at M3. Where RA and PsA were analysed separately, disease was excluded from the list of covariates
PASI defaulted to 0 for all pts with RA and also for those pts with PsA who had <3% of body surface area affected at baseline
ADA was included in NCT00853385/NCT02187055/NCT01877668; NCT02187055 performed tofacitinib/ADA non-inferiority/superiority comparisons
Prob(d<0): posterior probability of a superiority in pain reduction
PASI, Psoriasis Area and Severity Index

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Table 1. Demographics and baseline characteristics of pts with abrogated inflammation at M3

	RA			PSA		
	Tofacitinib 5 mg BID (N=328)	ADA[a] 40 mg Q2W (N=87)	PBO(N=20)	Tofacitinib 5 mg BID (N=54)	ADA[a] 40 mg Q2W (N=31)	PBO(N=30)
Age, yrs, mean (SD)	50.7(12.8)	49.2(13.9)	44.6(9.9)	51.1(11.7)	47.4(11.6)	49.7(11.6)
Female, %	79.0	77.0	90.0	44.4	35.5	70.0
Weight, kg, mean (SD)	68.9(16.9)	72.5(21.8)	71.4(25.0)	89.1(22.7)	83.2(19.0)	76.7(15.7)
Disease duration, yrs, median (Q1; Q3)	4.8(1.4; 9.5)	5.8(2.4; 11.1)	2.6(1.7; 8.5)	7.8(4.0; 14.3)	2.7(1.0; 6.0)	4.3(2.7; 10.0)
SJC, median(Q1; Q3)	9.0(7.0; 14.0)	8.0(6.0; 12.0)	10.5(9.0; 19.5)	6.0(4.0; 10.0)	5.0(4.0; 8.0)	5.0(4.0; 7.0)
CRP, mg/L, median (Q1; Q3)	8.0(3.6; 20.0)	8.6(3.6; 15.7)	3.9(1.4; 6.4)	3.7(1.1; 9.2)	3.6(1.2; 12.5)	2.2(1.2; 4.5)
Pain VAS, median (Q1; Q3)	57.0(39.0; 72.7)	52.5(35.0; 69.0)	62.0(38.5; 67.0)	58.0(51.0; 75.0)	48.0(36.0; 65.0)	48.5(21.0; 61.0)

[a]ADA was included in NCT00853385/NCT02187055/NCT01877668; NCT02187055 performed tofacitinib/ADA non-inferiority/superiority comparisons. N, number of pts; Q1, 1st quartile (25th percentile); Q2W, once every 2 weeks; Q3, 3rd quartile (75th percentile); SD, standard deviation.

OP0053

LUMBAR MECHANICALS TRACTIONS IN RADICULAR PAIN OF DISCUS ORIGIN: A PROSPECTIVE CONTROLLED RANDOMIZED TRIAL OF SUPERIORITY ON 428 PATIENTS IN REIMS HOSPITAL UNIVERSITY RHEUMATOLOGY SERVICE

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Background: Medical cares guidelines for lumbosciatics pains are well codified in several country: NSAIDs, analgesics and physical therapy associated, at physician's discretion, to lumbar epidural infiltrations.
Lumbar mechanical tractions have not a clear identified place in the lumbosciatic pain treatment. It is empirically realized in France's several medical centers.
However, no current literature studies have shown a significant efficacy of lumbar mechanicals tractions in this indication. Most of the time, studies presented a lack of power or methodological bias. (1,2)
Objectives: The aim of this study is to demonstrate the superiority of lumbar traction associated with standard treatment (epidural injections, analgesics, NSAID) compared to medical treatment alone in lombosciatics pains of discal origin.
Methods: We performed a monocentric interventional prospective superiority study from 2013 to 2021, randomized controlled in the rheumatology unit of Reims University Hospital. Patients included had to present a lumboradicular pain, with a concordant discal hernia on MRI or scanner, and to be naive of any lumbar surgery. We recorded demographical and clinical data at baseline and during the follow up. After their consent, patients were randomized between the traction group and the medical group. The medical group received the standard treatment (NSAIDs, analgesics) associated with at least 2 epidural infiltrations. The traction group received the standard treatment, infiltrations and at least 3 lumbar tractions. Treatment was considered as effective if there was a pain diminution at least 25 % between baseline and at 1 month. Patients were assessed on their pain at baseline, at 1 month and at 3 months of their treatment. Pain was assessed using a visual analog scale on lumbar and radicular localisation.
Superiority analysis has been performed by using the Chi-2 test.
Results: Four Hundred twenty-eight patients were included: 207 patients in the lumbar traction group, 210 patients in the medical treatment alone group and 11 patients with missing data. The male/female sex ratio was 1.39:1. The patients suffered from 49.52% (205 patients) right and 50.48% (209 patients) left lumboradiculalgia, mostly L5 (41% or 172 patients) and S1 (50% or 207 patients).
The pains evaluation at one month was recorded for 377 patients: 190 in traction group (50.3%) and 187 in medical group (49.7%). Two hundred twelve/377 (56.2%) patients had a pain reduction of at least 25 % at one month: 117/377 patients in tractions group (31%) and 95/377 in medical group (25%).
Twenty/377 patients (5%) were operated on before the one-month recall. Therefore, patients treated with lumbar traction had a significant reduction in pain (p=0.036) compared to patients with medical treatment alone.
Conclusion: This study is one of the first randomized controlled studies highlighting the superiority of lumbar traction in combination with standard treatment compared to medical treatment alone.

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OP0054

REDUCING THE BURDEN OF LOW BACK PAIN: RESULTS FROM A NEW MICROSIMULATION MODEL

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Background: Low back pain (LBP) has been the leading cause of disability worldwide for the past 30 years. In 2019, LBP was responsible for 64 million years lived with disability (YLDs) [1].
Objectives: The purpose of the present study was to project and compare the impact of three strategies for reducing the population health burden of LBP: weight loss, ergonomic interventions, and an exercise program.
Methods: We have developed a microsimulation model of LBP in Canada using a novel simulation platform, SimYouLate. The initial population was derived from Cycle 1 (2001) of the Canadian Community Health Survey (CCHS). We modeled an open population 20 years of age and older. Key variables included age, sex, education, body mass index (BMI), type of work, having a back problem, pain level in persons with back problems, and exercise. The effects of interventions on the risk of LBP were obtained from the CCHS for the effect of BMI, the Global Burden of Disease Study for occupational risks, and a published meta-analysis for the effect of exercise. All interventions lasted from 2021 to 2040. Strength of the interventions varied over a wide range. YLDs were defined as LBP prevalence multiplied by disability weight. The population health impact of the interventions was calculated as a difference in YLDs between the base-case scenario and each intervention scenario and expressed as YLDs averted per intervention unit and as % of total LBP-related YLDs.
Results: In the base-case scenario, LBP in 2020 was responsible for 424,900 YLDs in Canada and the amount increased to 460,312 YLDs in 2040. The effects of the interventions on YLDs were as follows: 27,993 (95% CI 23,373, 32,614) YLDs averted over 20 years per 0.1 unit change in log-transformed BMI (10.5% change in BMI) among overweight and obese individuals, 19,416 (16,275, 22,557) YLDs averted per 1% reduction in the proportion of workers exposed to occupational risks, and 26,058 (22,455, 29,661) YLDs averted per 1% increase in the proportion of eligible patients with back problems participating in the exercise program. Table 1 shows the intervention impact as % of total LBP-related YLDs and Figure 1 shows YLD-equivalence between the interventions. A one unit reduction in BMI per year among the overweight and obese individuals would be approximately equivalent in terms of disability reduction to an effective ergonomic intervention in 35% of at-risk workers and an exercise intervention in 27% of eligible patients with back problems over the same period (Figure 1).

Table 1. YLDs averted between 2021 and 2040 as % of total LBP-related YLDs, according to intervention type and level, in persons aged 20+ in Canada

Intervention	Effect (%)	95% LCL	95% UCL
Reduction in BMI per year			
0.1	1.4	-1.4	4.1
0.3	4.8	2.2	7.3
0.5	6.3	3.9	8.8
1.0	8.5	6.0	11.0
3.0	11.9	9.4	14.4
5.0	13.5	10.9	16.0
Reduction in occupational exposure			
20%	5.2	1.9	8.5
40%	9.5	6.4	12.7
60%	13.8	10.6	16.9
80%	18.1	14.8	21.4
100%	22.4	18.8	25.9
Increase in exercise participation			
20%	6.6	2.8	10.4
40%	12.4	8.7	16.0
60%	18.1	14.5	21.7
80%	23.9	20.1	27.6
100%	29.6	25.5	33.7

LCL: lower confidence limit. UCL: upper confidence limit.

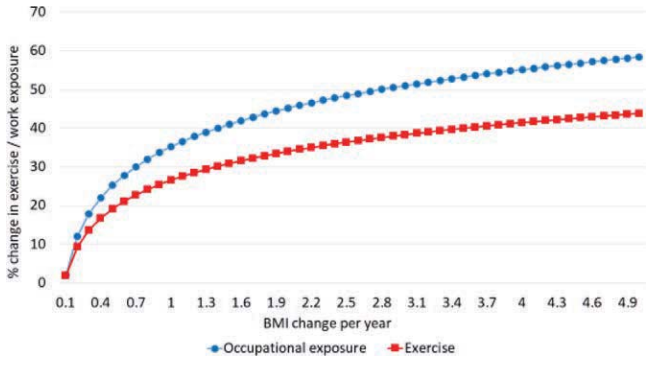

Figure 1. Equivalence between BMI, ergonomic and exercise interventions in terms of their impact on YLDs. Each point represents a specific number of YLDs averted. Values on the y-axis show reduction in % of workers at risk and increase in % exercising that are required to achieve the same reduction in YLDs as the corresponding reduction in BMI shown on the x-axis.

Conclusion: This is the first population-based microsimulation study to compare currently available preventive strategies in LBP in terms of YLDs averted and to provide measures of equivalence between these strategies.

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OP0055 THE COMPARISON OF EFFECTS OF TWO DIFFERENT EXERCISE PROGRAM ON FUNCTIONAL CAPASITY AND QUALITY OF LIFE IN PREGNANT WOMEN WITH LOW BACK PAIN

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Background: Low back pain is the most common musculoskeletal problem which negatively affects functional capasity and quality of life during pregnancy (1). So, from the beginning of pregnancy, pregnant women should be supported by appropriate exercise approaches recomended as first-line therapy to reduce the complaints about low back pain (2, 3). Although there are different opinions about the type, intensity and frequency of exercise in order to improve function in pregnant women with low back pain, there are no comparative studies on the diversity and length of the exercise program.

Objectives: The aim of this study was to compare the effects of supervised, long and multivarity an exercise program (LEP) and a short exercise program (SEP), planned based on core stabilization and in line with the needs of pregnant women, on functional capasity and quality of life.

Methods: A total of 27 pregnant women complained about low back pain, without obstetric and medical complications were included in this study. Detailed sociodemographic and obstetric characteristics were recorded. Back pain intensity, functional capacity and the quality of life were determined by the Vidual Analogue Scale (VAS), 6-minute walk test and Short Form-36 Quality of Life Questionnaire. All outcome measures were evaluated at baseline, at 24 and 32 weeks of pregnancy. Starting from the 16th week of pregnancy to the 32nd week, for 16 weeks, 2 days a week, under the supervision of a physiotherapist, a stabilization-based exercise program consisting of posture training, upper extremity, lower extremity, abdominal and pelvic floor strengthening and breathing exercises was applied to the pregnant women by progressing modified. During the warm-up, loading and cool-down, while LEP consists of a total 20 different exercises; SEP consists of 9 different exercises. Both groups were advised to walk as an aerobic modarate exercise for 30 minutes, 3 days a week. The Independent Groups t-test was used to compare variables between groups at baseline 16th, 24th and 32nd week of pregnancy. Statistical significance was set at $p<0.05$.

Results: 14 pregnant women (mean age: 30.50 ± 4.11 years, mean body mass index $(BMI)_{16th,\ 24th,\ 32nd\ week\ of\ pregnancy}$: 23.42±3.81, 25.02±3.71, 26.25±3.73 kg/m^2) in LEP, 13 pregnant women (mean age: 30.75±5.05 years, $BMI_{16th,\ 24th,\ 32nd\ week\ of\ pregnancy}$: 24.73±3.84, 26.28±3.85, 27.91±3.60 kg/m^2) in SEP completed this study. Baseline parameters were similar between the two groups ($p>0.05$). There was no superiority between groups in terms of back pain intensity at the 24th and 32nd week of pregnancy ($p>0.05$). While at the 24th week of pregnancy, 6-minute walking test distance, emotional role limitation and pain sub-dimension scores of health-related quality of life were found to be higher in LEP ($p<0.05$), at the 32nd week of pregnancy, only 6 minutes walking test distance were found to be higher in LEP ($p<0.05$).

Conclusion: LEP is more effective in terms of increasing functional capacity, emotinal role limitation and pain-related quality of life in the short term and is more effective in terms of increasing functional capacity in the long term than SEP during pregnancy. In this respect; our study will guide clinicians to create indiviually exercise programs for the neeeds of pregnancy.

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OP0056 "BECAUSE THAT'S THEIR JOB, ISN'T IT?": EXPLORING CHILDREN AND YOUNG PEOPLES' EXPERIENCES OF AND PERSPECTIVES ABOUT PAIN COMMUNICATION IN PAEDIATRIC RHEUMATOLOGY IN THE UK

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Background: Pain communication should be an integral part of every clinical consultation, particularly in paediatric rheumatology where children/young people often present complex long-term conditions in which chronic pain is a feature. Researchers investigating pain communication in paediatric healthcare encounters have been focused on healthcare professionals, yielding inconsistent findings about the occurrence and nature of pain discussions with children/young people. There has been limited research examining children/young peoples' own experiences and perspectives on this in the literature to date.

Objectives: The objective of this study was to investigate children/young peoples' experiences and perceptions of communicating about pain with paediatric rheumatology healthcare professionals in the UK.

Methods: Twenty-six children/young people were recruited from three UK paediatric rheumatology centres. Data were collected using semi-structured telephone interviews between April-October, 2021. A framework analysis approach was used to explore similarities and divergences in participants' narrative accounts.

Results: The mean age of children/young people was 14.0 years (SD=3.6 years, Range= 6-18 years, 58% female). Diagnoses included; Juvenile Idiopathic Arthritis, Chronic Regional Pain Syndrome, diffuse idiopathic chronic pain, localised idiopathic pain, hypermobility (including Ehlers Danlos Syndrome) and Raynaud's disease.

Findings are organised into four themes.

1) Nature and focus of appointments. Children/young people talked about pain with several professionals from the team. Participants reported that pain conversations predominantly occurred during physical examinations.
2) Co-ordination of pain communication. Children/young people identified how professionals mostly started pain conversations. They explained how they were often asked to verbally rate pain rather than use a written assessment tool. For some, questions about pain were directed to parents. Participants reported that this was problematic as parents "can't feel" pain.
3) Reflections on pain communication. There were expectations that pain should always be asked about as it was considered a main reason for a consultation. Participants discussed how these conversations gave them an opportunity to "get it off their chest" and made them feel "reassured" that professionals "care." Being asked about pain reminded them that they were different to peers and they were concerned it could highlight "something else is wrong." Children/young people talked about how it became easier to talk about pain with familiar professionals.
4) Moving forward after pain communication. Children/young people discussed how professionals could give mixed messages about how to manage pain at home following consultations, offering advice which was difficult to put into practice (e.g. "doing too much" vs "not doing enough"). Children/young people expressed their need to discuss the emotional as well as the physical effects of their pain.

Conclusion: These study findings highlight a range of effective and ineffective pain communication approaches from the experiences and perspectives of children/young people. These will be used to create recommendations for improving the communication of chronic pain in paediatric rheumatology in the future, in a way that is acceptable and valuable to children/young people.

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OP0057

RESPONSE TO INJECTION CAN PREDICT OUTCOMES OF FEMOROACETABULAR IMPINGEMENT

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Background: Femoroacetabular impingement syndrome (FAIS) is a highly prevalent painful disorder that is considered a risk factor for hip osteoarthritis. In order to relieve pain and improve cartilage preservation, surgery is often performed. However, many operated patients do not show satisfactory outcomes. Reliable diagnostic tests that can inform prognosis of surgery in patients with FAIS are needed for optimized indications and contraindications to surgery.
Objectives: This systematic review aimed to answer the following question: "Can the response to intra-articular anesthetic injections be used to predict surgical outcomes in patients with FAIS?".
Methods: This study was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement. Embase, CINAHL, LILACS, PubMed, SCOPUS, SPORTDiscuss, The Cochrane Library, and Web of Science databases were screened. All studies that assessed the capability of the response to intra-articular anesthetic injections in predicting surgical outcomes for patients with FAIS were considered eligible. Study selection and data collection were performed by three independent reviewers. Risk of bias of the included studies was assessed through the QUIPS tool.
Results: Seventeen articles were selected for full-text reading, of which 6 were considered eligible and included for analysis [1-6]. A summary of the studies' descriptive characteristics can be found in the Table 1. A high risk of bias due to study attrition and the presence of confounding factors was observed for all included studies. Five out of six studies [1-4,6] presented "high risk" of bias associated to the prognostic factor measurement. A high overall risk of bias was evidenced by QUIPS for all studies (Figure 1). From 6 included studies, 5 indicated that the response to intra-articular injections can be useful in the prediction of surgical outcomes [2-6].
Conclusion: Although there seems to be some evidence supporting the use of intra-articular anesthetic injections to predict surgical outcomes in patients with FAIS, it is not conclusive. Future studies taking into account the various possible sources of bias in prognostic studies are needed. Standardizing and optimizing injection protocols as well as post-injection pain assessment and outcomes measurements are also essential to fill this gap.

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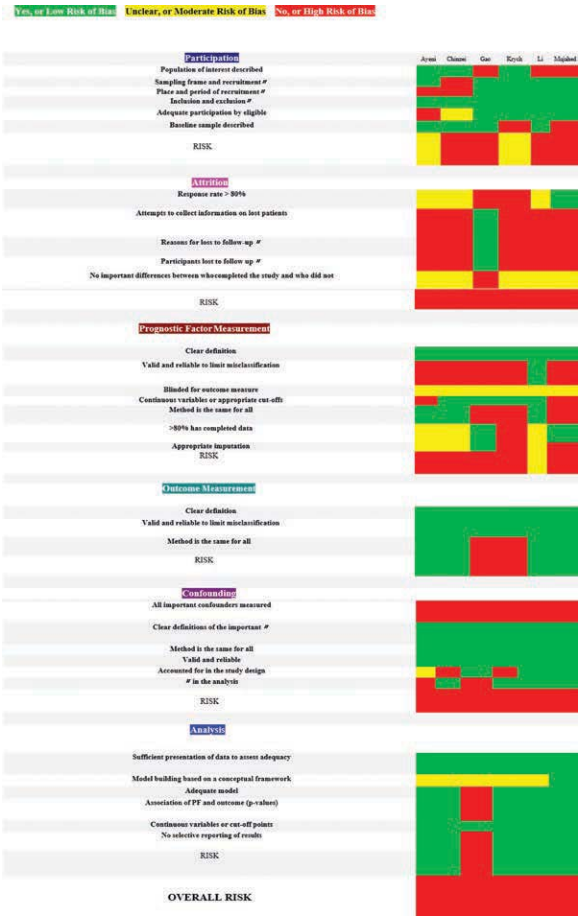

Figure 1.

Modern biological treatment in RA

OP0058

CERTOLIZUMAB-PEGOL, ABATACEPT, TOCILIZUMAB OR ACTIVE CONVENTIONAL THERAPY IN EARLY RHEUMATOID ARTHRITIS: CLINICAL AND RADIOGRAPHIC 48-WEEKS RESULTS OF THE INVESTIGATOR-INITIATED RANDOMIZED NORD-STAR TRIAL

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Table 1.

Author	Mean Age	N (Female)	Injection Content	Time for pain assessment after injection (Way)	Intervention group (Control)	Follow-up time after surgery (Score used)	Results
Ayeni	? (16-62)	52 (30)	Bupivacaine + prednisolone	Daily for 2 weeks (provocative activities)	42 with any pain relief (10)	6 months (mHHS)	Likelihood Ratio of reaching >70 points (LR) for responders was 1.15; LR for nonresponders was 0.57 (p>0.05)
Chinzei	36.7 ± 14.7	49 (27)	Lidocaine	2 weeks (?)	30 with >50% of pain relief (19)	12 months (mHHS)	Good responders showed better mHHS, pre- (p=0.048) and post-operatively (p=0.026)
Gao	36.5 (16-65)	78 (41)	Lidocaine + betamethasone	10 min and 1 week (routine tasks)	33 with >50% of pain relief (3)	22.8 ± 9.7 months (mHHS)	100% of good responders surpassed the MCID, while only 1/3 of poor responders achieved it
Krych	37.6 ± 14.0	319 (?)	Variable	2 weeks, reporting the relief of the first 24h (?)	70 with >50% of pain relief (26)	11–30 months (HOS and mHHS)	For Tönnis grade 1 patients, good responders had higher HOS-SS (p=0.03)
Li	38.6 ± 14.9	60 (33)	Lidocaine + ropivacaine	30 min (physical tests)	-	12 months (mHHS and iHOT-12)	Correlation between iHOT after injection and iHOT at 12 months after surgery (r=0.784; p<0.01)
Mujahed	? (16-65)	242 (?)	Lidocaine + betamethasone	? (?)	120 with any pain relief (88)	24 months (HOS and mHHS)	Responders had greater improvement (p<0.05) in all metrics, except for MCID at mHHS (p=0.24)

P. Bøyesen[5], I. Olsen[9], K. Lend[10], K. Hørslev-Petersen[11], T. Uhlig[5], T. Sokka-Isler[12], G. Gröndal[8], S. Krabbe[13], J. Lindqvist[14], I. Gjertsson[15], D. Glinatsi[1], M. C. Kapetanovic[16], A. B. Aga[5], F. Faustini[17], P. Parmanne[18], T. Lorenzen[19], G. Cagnotto[20], J. Back[21], O. Hendricks[22], D. Vedder[2], T. Rannio[23], E. Grenholm[24], H. M. Lindegaard[25], M. K. A. Ljosa[26], E. Brodin[27], A. Soderbergh[28], M. Rizk[29], E. Hermansson[30], L. Uhrenholt[31], P. Larsson[32], S. A. Just[33], G. Bakland[34], D. Stevens[35], T. B. Laurberg[36], E. A. Haavardsholm[5], J. Lampa[37], on behalf of NORD-STAR study group. *[1]Rigshospitalet, Glostrup, Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; *[2]Amsterdam University Medical Center, Amsterdam Rheumatology Center, Amsterdam, Netherlands*; *[3]Sahlgrenska University Hospital, Rheumatology Clinic, Gothenburg, Sweden*; *[4]Rigshospitalet, Glostrup, DANBIO and COPECARE, Centre for Rheumatology and Spine Diseases, Glostrup, Denmark*; *[5]Diakonhjemmet Hospital, Dept of Rheumatology, Oslo, Norway*; *[6]Helsinki University Hospital, Division of Internal Medicine and Rheumatology, Helsinki, Finland*; *[7]Amsterdam University Medical Center, Location VUmc, Amsterdam, Netherlands*; *[8]University of Iceland, Dept of Rheumatology, Reykjavik, Iceland*; *[9]Oslo University Hospital, Dept of Research Support for Clinical Trials, Oslo, Norway*; *[10]Amsterdam University Medical Center/Karolinska Institute, Dept of Rheumatology and Amsterdam Rheumatology Center/Center for Molecular Medicine, Amsterdam, Netherlands*; *[11]Kong Chr X's Hospital for Rheumatic Diseases, Dept of Rheumatology, Gråsten, Denmark*; *[12]University of Eastern Finland, Dept of Rheumatology, Jyväskylä, Finland*; *[13]Herlev University Hospital, Dept of Radiology, Herlev, Denmark*; *[14]Karolinska University Hospital, Dept of Medicine, Rheumatology Unit, Center of Molecular Medicine (CMM), Stockholm, Sweden*; *[15]Sahlgrenska University Hospital, Dept of Rheumatology, Gothenburg, Sweden*; *[16]Skåne University Hospital, Dept of Clinical Sciences, Lund, Sweden*; *[17]Karolinska University Hospital, Dept of Medicine, Rheumatology, Stockholm, Sweden*; *[18]Helsinki University Hospital, Division of Rheumatology, Helsinki, Finland*; *[19]Silkeborg University Hospital, Dept of Rheumatology, Silkeborg, Denmark*; *[20]Skåne University Hospital, Dept of Clinical Sciences, Malmö, Sweden*; *[21]Uppsala University Hospital, Dept of Medical Sciences, Uppsala, Sweden*; *[22]Danish Hospital for Rheumatic Diseases, Dept of Rheumatology, Sønderborg, Denmark*; *[23]Finland Central Hospital, Dept of Rheumatology, Jyväskylä, Finland*; *[24]Falun Hospital, Dept of Rheumatology, Falun, Sweden*; *[25]Oden se University Hospital, Rheumatology Research Unit, Odense, Denmark*; *[26]Ålesund Hospital, Dept of Rheumatology, Ålesund, Norway*; *[27]Haukeland University Hospital, Dept of Rheumatology, Haukeland, Norway*; *[28]Örebro University Hospital, Dept of Rheumatology, Örebro, Sweden*; *[29]Värmlands Hospital, Rheumatology Clinic, Västerås, Sweden*; *[30]Linköping University Hospital, Department of Rheumatology, Linköping, Sweden*; *[31]Ålborg University Hospital, Dept of Rheumatology, Ålborg, Denmark*; *[32]Academic specialist center. Stockholm, Center for Rheumatology, Stockholm, Sweden*; *[33]Odense Universitetshospital, Svendborg, Section of Rheumatology, Svendborg, Denmark*; *[34]University Hospital of North Norway, Dept of Rheumatology, North Norway, Norway*; *[35]University Hospital of Trondheim, Dept of Rheumatology, Trondheim, Norway*; *[36]Århus University Hospital, Dept of Rheumatology, Århus, Denmark*; *[37]Karolinska University Hospital, Dept of Rheumatology, Stockholm, Sweden*

Background: The optimal first-line treatment of patients with early rheumatoid arthritis (eRA) is not established.

Objectives: To compare clinical and radiographic outcomes of active conventional therapy (ACT) with each of three biological therapies with different modes of action.

Methods: In this investigator-initiated, randomized, open-label, blinded-assessor study (NCT01491815), patients with treatment-naïve eRA with DAS28>3.2 and RF+/ACPA+/CRP>10mg/L, were randomized 1:1:1:1 to methotrexate combined with: 1) oral prednisolone (tapered quickly; discontinued at w36); or: sulphasalazine, hydroxychloroquine and mandatory intra-articular (IA) glucocorticoid injections in swollen joints (ACT); 2) certolizumab-pegol (CZP); 3) abatacept (ABA) or 4) tocilizumab (TCZ). IA glucocorticoid was allowed in all arms except w20-24 and w44-48. Co-primary outcomes at w48 were CDAI remission (CDAI≤2.8) and change in total van der Heijde-modified Sharp Score from baseline ($\Delta vdHSS_{w0\text{-}w48}$). A combination of Bonferroni and Dunnet's procedure adjusted for multiple testing. The primary endpoints were estimated using logistic regression and analysis of covariance, adjusted for sex, anti-CCP status and country.

Results: 812 patients were randomized. Adjusted CDAI remission rates at w48 were: 59.3% (ABA), 52.3% (CZP), 51.9% (TCZ) and 39.2% (ACT). Compared to ACT, CDAI remission rates were superior for ABA (adjusted difference +20.1%; adjusted p<0.001) and CZP (+13.1%; p=0.021), but not TCZ (+12.7%; p=0.030) (Table 1). Key secondary clinical outcomes were consistently better in biological groups compared to ACT. Adjusted mean $\Delta vdHSS_{w0\text{-}w48}$ was low (Table 1), with no significant differences between drugs.

Table 1.

Baseline characteristics	ACT (n=200)	CZP+MTX (n=203)	ABA+MTX (n=204)	TCZ+MTX (n=188) §
Age (y)	55 (15)	55 (15)	55 (14)	52 (15)
Women, %	139 (70%)	139 (69%)	140 (69%)	129 (69%)
Time from diagnosis to baseline, days	13 (21)	12 (17)	16 (34)	16 (33)
Anti-CCP/RF positive, %	82% / 76%	82% / 73%	83% / 78%	82% / 72%
CDAI	28.7 (12.1)	27.9 (12.4)	28.6 (11.3)	26.6 (11.7)
Total vdHSS (0-448) [median; IQR)	6.3 (8.2) [4; 1 - 8.5]	5.9 (7.6) [3; 1 - 8]	5.8 (9.8) [3; 1 - 6]	4.2 (6.7) [2; 0.5 - 5]
Estimated adjusted outcome (ITT)[1], Primary CDAI remission, w48	39.2% (32.5 - 45.9)	52.3% (45.5 - 59.1)	59.3% (52.6 - 66)	51.9% (44.9 - 59.0)
Δ1.9% (44.9 -	0.45 (0.31 to 0.59)	0.47 (0.33 to 0.61)	0.62 (0.48 to 0.76)	0.5 (0.36 to 0.64)
Estimated adjusted treatment difference (ITT)[2], Primary CDAI remission, w48	Ref	**13.1% (3.5 to 22.6)***	**20.1% (10.6 to 29.5)***	12.7% (3 to 22.5)
Δ2.7% (3 to 2	Ref	0.02 (-0.17 to 0.22)	0.17 (-0.02 to 0.37)	0.05 (-0.15 to 0.25)
Key secondary				
ACR/EULAR Boolean remission, w48	Ref	14.7% (5.4 to 23.9)	19.4% (10.1 to 28.7)	13% (3.5 to 22.4)
DAS28 remission,w48	Ref	12.9% (3.5 to 22.2)	17.4% (8.2 to 26.6)	14.4% (5 to 23.9)
EULAR good response, w48	Ref	8.2% (-0.6 to 17.1)	11.3% (2.7 to 20)	2.9% (-6.3 to 12.2)
vdHSS progression ≤0.5, w0-w48	Ref	-3.3% (-11.1 to 4.6)	3.5% (-4.7 to 11.8)	-2.2% (-10.3 to 5.9)

Values are mean (SD), if not otherwise indicated. §Finnish patients randomised to TCZ+MTX, but not receiving it due to unavailability, are not included. [1]Values are estimated adjusted marginal means and estimated marginal differences against ACT with 95% CI. ITT: intention to treat population. *Superiority compared with ACT was demonstrated.

No new safety signals were reported. Total numbers of serious adverse events (% patients with ≥1 event) were for ABA 21 (8.3%), CZP 28 (12.4%), TCZ 20 (9.2%) and ACT 23 (10.7%).

Conclusion: Compared with active conventional therapy (csDMARD + glucocorticoids), superiority regarding CDAI remission rates was demonstrated for abatacept and certolizumab-pegol, and not for tocilizumab. Radiographic progression was low and similar between treatments.

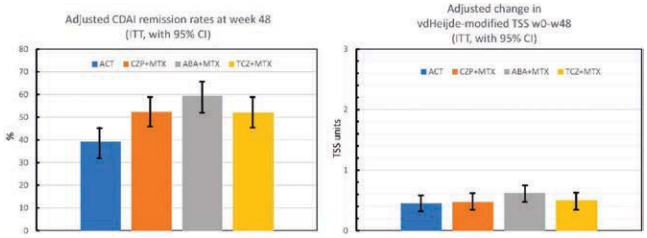

Figure 1.

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Disclosure of Interests: Mikkel Østergaard Speakers bureau: AbbVie, BMS, Boehringer-Ingelheim, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, Orion, Hospira, Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, Orion, Hospira, Grant/research support from: AbbVie, BMS, Merck, UCB, Celgene, Novartis, Ronald van Vollenhoven Speakers bureau: AbbVie, AstraZeneca, Biogen, Celgene, Galapagos, Gilead, Janssen, Pfizer, Servier, UCB, Consultant of: AbbVie, AstraZeneca, Biogen, Celgene, Galapagos, Gilead, Janssen, Pfizer, Servier, UCB, Grant/research support from: BMS, GSK, Eli Lilly, UCB, Pfizer, Roche, Anna Rudin Grant/research support from: AstraZeneca, Merete L. Hetland Speakers bureau: Merck, Biogen, Pfizer, Eli Lilly, Orion Pharma, CellTrion, Samsun Bioepsi, Janssen Biologics BV, MSD, Consultant of: Merck, Biogen, Pfizer, Eli Lilly, Orion Pharma, CellTrion, Samsun Bioepsi, Janssen Biologics BV, MSD, Grant/research support from: BMS, AbbVie, Roche, Novartis, Merck, Biogen, Pfizer, Marte Heiberg Speakers bureau: Eli Lilly, Consultant of: Eli Lilly, Dan Nordström Grant/research support from: UCB, BMS, AbbVie, Celgene, MSD, Novartis, Pfizer, Michael Nurmohamed Speakers bureau: Celltrion, Eli Lilly, Consultant of: Celltrion, Eli Lilly, Grant/research support from: BMS, AbbVie, MSD, Pfizer, Amgen, Björn Gudbjornsson Speakers bureau: Novartis, Consultant of: Novartis, Lykke Midtbøll Ørnbjerg Grant/research support from: Novartis, Pernille Bøyesen: None declared, Inge Olsen: None declared, Kristina Lend: None declared, Kim Hørslev-Petersen: None declared, Till Uhlig Speakers bureau: Grünenthal, Eli Lilly, Novartis, Pfizer, Consultant of: Grünenthal, Eli Lilly, Novartis, Pfizer, Grant/research support from: NORDFORSK, Tuulikki Sokka-Isler Speakers bureau: AbbVie, BMS, Celgene, Medac, Merck, Novartis Orion Pharma, Pfizer, Roche, Sandoz, UCB, Boehringer Ingelheim, Consultant of: AbbVie, BMS, Celgene, Medac, Merck, Novartis Orion Pharma, Pfizer, Roche, Sandoz, UCB, Boehringer Ingelheim, Gerdur Gröndal: None declared, Simon Krabbe Grant/research support from: AbbVie, MSD, Novartis, Joakim Lindqvist: None declared, Inger Gjertsson: None declared, Daniel Glinatsi Speakers bureau: AbbVie, Eli Lilly, Consultant of: AbbVie, Eli Lilly, Meliha C Kapetanovic: None declared, Anna-Birgitte Aga Speakers bureau: AbbVie, Eli Lilly, Novartis, Pfizer, Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer, Francesca Faustini: None declared, Pinja Parmanne Speakers bureau: Novartis, Consultant of: Novartis, Tove Lorenzen Speakers bureau: UCB, Consultant of: UCB, Giovanni Cagnotto: None declared, Johan Back: None declared, Oliver Hendricks Speakers bureau: AbbVie, Novartis, Consultant of: AbbVie, Novartis, Daisy Vedder: None declared, Tuomas Rannio: None declared, Emma Grenholm: None declared, Hanne Merete Lindegaard: None declared, Maud-Kristine A Ljosa: None declared, Eli Brodin: None declared, Annika Soderbergh: None declared, Milad Rizk: None declared, Elsa Hermansson: None declared, Line Uhrenholt Speakers bureau: AbbVie, Eli Lilly, Novartis, Consultant of: AbbVie, Eli Lilly, Novartis, Per Larsson: None declared, Søren Andreas Just: None declared, Gunnstein Bakland Speakers bureau: BMS, Consultant of: BMS, David Stevens Grant/research support from: KLINBEFORSK, Trine Bay Laurberg Speakers bureau: UCB, Consultant of: UCB, Espen A Haavardsholm Speakers bureau: Pfizer, AbbVie, Celgene, Novartis, Janssen, Gilead, Eli Lilly, UCB, Consultant of: Pfizer, AbbVie, Celgene, Novartis, Janssen, Gilead, Eli Lilly, UCB, Grant/research support from: NORDFORSK, Jon Lampa: None declared.
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OP0059

PROFOUND ANTICOAGULANT EFFECTS OF INITIAL ANTIRHEUMATIC TREATMENTS IN EARLY RHEUMATOID ARTHRITIS PATIENTS: A NORD-STAR SPIN-OFF STUDY

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Background: Patients with rheumatoid arthritis (RA) are at an increased risk of venous thromboembolism. Thus far, there have not been any comparative studies investigating the effects of initial antirheumatic treatments in (very) early RA patients.
Objectives: To assess the effects of different initial treatments on hemostatic parameters in patients with early RA.
Methods: NORD-STAR is an international, multicentre, open-label, assessor-blinded, phase 4 study where patients with newly diagnosed RA started methotrexate (MTX) and were randomised 1:1:1:1 to a) conventional treatment (either prednisolone tapered to 5mg/day, or sulfasalazine combined with hydroxychloroquine and intra-articular corticosteroids), b) certolizumab pegol, c) abatacept, d) tocilizumab[1]. This study is a spin-off from the main NORD-STAR study extensively investigating hemostatic system in 24 per protocol consecutive Dutch participants at baseline, 12 weeks and 24 weeks after the start of the treatment. Statistical analysis was done using paired samples t-test in SPSS version 28.
Results: The mean age of investigated patients was 51.8 (± 12.7) years and 58.3% were female. At baseline patients had an average DAS28 score of 4.6 (± 0.9) and had elevated levels of investigated coagulation biomarkers: Factor 1+2, fibrinogen, D-dimer and parameters of the two global hemostatic assays, i.e. endogenous thrombin potential (ETP) and overall hemostasis potential (OHP). These biomarkers decreased significantly at 12 and 24 weeks in patients in all groups (Table 1). Overall fibrinolytic potential (OFP) was decreased and clot lysis time (CLT) was prolonged at baseline, demonstrating impaired fibrinolytic activity in early RA. The reduction of coagulation parameters was significantly higher in biological treatment arms in comparison to the standard MTX treatment arm. In addition, tocilizumab was more effective compared to certolizumab and abatacept, (Figure 1), which was expected considering the direct inhibitory effect of this drug on the IL-6 synthesis and consequently the coagulation activation as well. After 24 weeks of treatment with methotrexate and tocilizumab, the average fibrinogen of patients was reduced by 63% vs 31% and 36% in the certolizumab and abatacept groups, respectively. The changes in DAS-28 and the changes in fibrinogen had a correlation of 0.385 which did not reach statistical significance.

Table 1. ***Measurements are marked with * if p<0.05, ** if p<0.01 and *** if p<0.001***

	Baseline	W12	W24
Factor 1+2 (pmol/L)	270.25 (149.4)	190.36 (108.6)**	179.52 (85.3)***
Fibrinogen (g/L)	4.64 (1.5)	3.61 (1.6)**	2.63 (1.2)***
D-dimer (mg/L)	2.17 (3.0)	0.33 (0.23)**	0.29 (0.2)**
OHP (Abs-sum)	157.38 (64.9)	120.62 (68.7)*	100.49 (53.8)***
OCP (Abs-sum)	369.52 (58.8)	305.04 (101.7)*	275.91 (83.1)***
OFP (%)	57.97 (13.1)	63.20 (12.7)*	65.25 (11.4)***
Lag time (s)	304.5 (71.1)	306.8 (71.8)	312.7 (65.4)
Slope	0.07 (0.02)	0.066 (0.03)	0.094 (0.12)
Max Abs	1.17 (0.3)	1.00 (0.4)*	0.91 (0.3)**
CLT (s)	1405 (356)	1317 (377)	1231 (320)**
ETP (nM*min)	1480 (471)	1395 (395)*	1337 (429)*
Peak (nM)	231 (78)	223 (68)	223 (74)
Lagtime (min)	4.06 (2.1)	3.28 (1.2)**	2.87 (1.0)***
ttPeak (min)	7.40 (2.2)	6.61 (1.5)*	6.13 (1.4)**

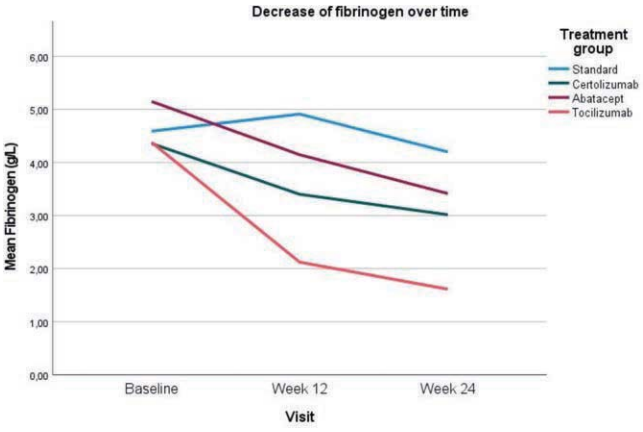

Figure 1.

Conclusion: Our results indicate an enhanced coagulation and fibrinolytic impairment in newly diagnosed RA patients. Effective antirheumatic treatments reduce this hemostatic imbalance, with significantly more pronounced effects of biologic drugs compared to conventional (MTX+glucocorticoids) treatment.

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[1] Hetland M et al. BMJ. 2020

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OP0060 EXPOSURE TO SPECIFIC TUMOR NECROSIS FACTOR INHIBITORS AND RISK OF DEMYELINATING AND INFLAMMATORY NEUROPATHY IN PATIENTS WITH INFLAMMATORY ARTHRITIS. A COLLABORATIVE OBSERVATIONAL STUDY ACROSS FIVE NORDIC RHEUMATOLOGY REGISTERS

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Background: Though rare, studies have reported increased risk of neurological events including demyelinating disease of CNS (DML), multiple sclerosis (MS), and inflammatory neuropathy (INP) in patients with inflammatory joint disease treated with tumor necrosis factor inhibitors (TNFi).[1,2] More in-depth investigations are required to elucidate the association between TNFi and neurological events in these patients, especially whether rates differ across type of TNFi mode of action.

Objectives: To estimate the incidence of neurological events in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA, including axial spondyloarthritis and psoriatic arthritis) starting treatment with TNFi across five Nordic countries. To compare the incidence of neurological events in etanercept (ETN)-treated patients to patients treated with other TNFi (oTNFi).

Methods: We defined treatment cohorts of patients initiating TNFi between 2001 through 2018 from clinical rheumatology registers in Denmark (DK), Finland (FI), Iceland (IS), Norway (NO), and Sweden (SE). One patient could contribute to more than one treatment episode. Demographic data (sex, age), co-medication (methotrexate) and clinical variables (CRP, disease duration (<1 year, 1 to 5 years, >5 years) were extracted and used as covariates. We estimated crude incidence rates (IR) for neurological events and subtypes (ICD-10 codes: MS: G35, DML: G35, G36.0, G36.8-9, G37.1, G37.3, G37.5, G37.8-9, H46, H48.1, G04.8-9, INP: G61.0, G61.8-9), all countries pooled. We compared risk of neurological events between patients treated with ETN and oTNFi using Cox regression with time since treatment start, adjusted for the above covariates, robust standard errors, and stratified by country.

Results: We included 52,682 treatment starts, in 33,885 RA patients (DK 8,259, FI 3,765, IS 723, NO 1353, SE 19,785; 75% women, mean age 56 years) and 46,549 treatment starts in 28,772 SpA patients (DK 7,000, FI 2,885, IS 962, NO 2,684, SE 15,241; 47% women, mean age 45 years).

Numbers of DML, MS, INP and all neurological events, person-years (pyrs), and IRs in RA and SpA patients, for the two treatment groups are displayed in Figure 1. IRs for these neurological events showed some variation by diagnosis (RA vs. SpA), with rates of DML (and MS) in SpA patients around two (and three, respectively) times higher than the corresponding rates in RA ($p<0.01$), but similar rates for INP in RA and SpA patients. Comparing oTNFi to ETN, all Cox regression hazard ratios (HR) were statistically non-significant and close to one, whatever the outcome and the group of patients (Figure 1), with the adjusted HR (95%CI) for developing any neurological event in oTNFi compared to ETN being 1.08 (0.91-1.28) in RA patients and 0.96 (0.78-1.19) in SpA patients.

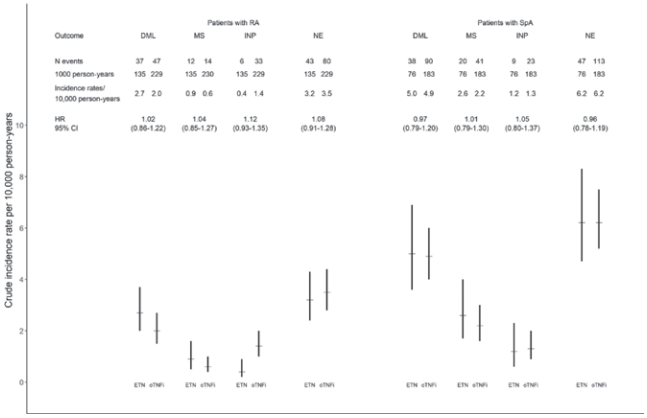

Figure 1. Number of events, pyrs and IRs of DML, MS, INP and all neurological events (NE) in RA and SpA patients, treated with ETN or oTNFi. HRs (95%CI) comparing oTNFi to ETN.

Conclusion: The incidences of DML and MS were lower in RA compared to SpA patients, while rates of INP were similar in both patients' groups. There was no evidence of differences in these rates between ETN and oTNFi. The findings are of importance from a safety perspective for patients starting TNFi.

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OP0061

TIGHT CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TARGETED THERAPIES ACROSS THE COVID-19 PANDEMIC ERA

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Background: The ongoing coronavirus disease 2019 (COVID-19) pandemic and subsequent waves still represent a healthcare issue. Their impact on the treat-to-target (T2T) strategy in rheumatoid arthritis (RA) patients has been seldom investigated. Difficult access to rheumatology outpatient clinic, laboratory and imaging investigations as well as nationwide containment measures could potentially affect disease activity and tight-control strategy. Recently, we reported how a telephone-based tight control strategy ensured satisfactory management of RA treated with targeted therapies during the first wave of the pandemic [1]. However, the performance of our different patterns of healthcare delivery across different pandemic waves has not been studied yet.

Objectives: To analyze the impact of different patterns of healthcare delivery on remission of RA patients treated with targeted therapies during the first wave (2020) and second/third waves (2021) of pandemic compared to the pre-pandemic period (2019).

Methods: In this observational real-life study, data of our cohort of RA patients treated with biologic or targeted synthetic drugs were extracted from a longitudinal registry. Clinical Disease Activity Index (CDAI) was analyzed in the same period from 22nd of February to 18th of May for three consecutive years: before the pandemic (2019), during the first wave (2020), and during the second/third waves (2021). During the first wave, patients could choose whether to receive home drug delivery or to maintain their face-to-face visits, in the other periods only in-person visits were delivered. A generalized linear model with the binomial error was fitted to evaluate the difference in the proportion of patients in CDAI remission. Quantile regression was used to compare the median of CDAI in difficult-to-treat (D2T) patients [2]. In both models, the correlation of different measurements on the same patient was considered.

Results: In the pre-pandemic period (2019), 407 RA patients were included in this study. During the first wave (2020) we analyzed 450 patients, of whom 359 patients chose in-person visits, while 91 patients home drug delivery and virtual visit. Finally, 540 patients were included in 2021 (second/third wave). The percentages of patients in CDAI remission were similar in the three periods (prevalence ratio 1.07, p-value 0.423 between 2020 and 2019, and 1.01, p-value 0.934 between 2021 and 2019). The CDAI remission rate was 40.55% (N=163), 43.18% (N=155) and 40.82% (N=220) in 2019, 2020 and 2021, respectively. The disease activity profile during the three periods is reported in detail in the Table 1 below. Among our cohort of D2T patients, the median value of CDAI before (2019), during the first wave (2020), and during the second/third wave (2021) changed significantly (p= 0.053 between 2020 and 2019 and p=0.006 between 2021 and 2019).

Table 1.

RA patients	CDAI	2019		2020		2021	
		No. missing	N (%)	No. missing	N (%)	No. missing	N (%)
	Remission	0	163 (40.55%)	89	155 (43.18%)	6	220 (40.82%)
	Low	0	151 (37.56%)	89	140 (39.00%)	6	227 (42.12%)
	Moderate/ high	0	88 (21.89%)	89	64 (17.83%)	6	92 (17.07%)

Conclusion: Although the pandemic has imposed changes in our healthcare delivery, these different strategies seem to be effective in ensuring satisfactory management of RA treated with targeted therapies. The approaches modulated in the context of the different periods have been a feasible compensation for ensuring disease control even in D2T patients.

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OP0062

EFFICACY AND SAFETY OF ADALIMUMAB WITH LOW AND HIGH DOSE-METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: THE RANDOMISED CONTROLLED MIRACLE STUDY

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that causes not only joint pain but also bone destruction resulting in impairment of quality of life. Tumor necrosis factor inhibitors have improved prognosis of patients with rheumatoid arthritis dramatically, especially in combination with methotrexate, however, the optimal dose of the concomitant methotrexate is unclear.

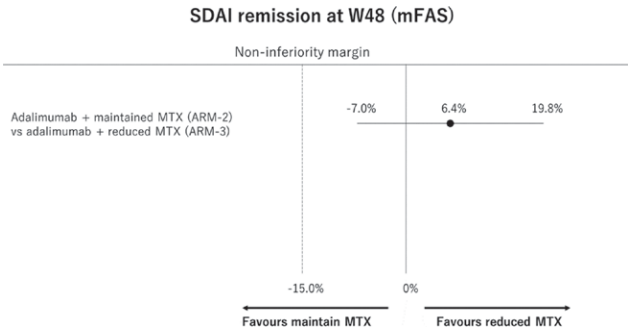
Objectives: To evaluate the efficacy and safety of adalimumab in combination with reduced dose of methotrexate in patients with early RA with inadequate response to methotrexate.

Methods: The MIRACLE study was a multinational, randomized, open-label study in patients with RA with inadequate response to methotrexate conducted in Asia. It compared low dose and high dose methotrexate upon starting adalimumab. Methotrexate-naive patients with RA with a disease duration of less than two years started methotrexate at 6 to 8 mg/week and increased it to the maximum tolerable dose by week 12. Patients who have not achieved remission according to simplified disease activity index (SDAI) despite methotrexate ≥ 10 mg/week at week 24 were randomised to the maximum tolerable dose of

methotrexate group (10 to 25 mg/week) or the reduced dose group (6 to 8 mg/week) and started to receive subcutaneous adalimumab 40 mg every other week. The primary endpoint was non-inferiority in the achievement of SDAI remission at week 48 in the reduced dose group compared with the maximum tolerable dose group with a non-inferiority margin of -15% based on two-sided 90% confidence interval. (NCT03505008)

Results: A total of 300 patients were enrolled in the study. Among them, 291 started methotrexate and were included in the analysis. The mean age was 57.7±15.2 years, female was 74.6%, and the mean disease duration from the diagnosis of RA was 21.1±56.2 days. Anti-CCP antibody was positive in 211 (73.0%) and the mean SDAI at study enrollment was 26.5±12.4. At week 24, with the mean dose of methotrexate of 12.6±2.9 mg/week, 108 patients (37.1%) achieved remission according to SDAI and continued MTX monotherapy. 134 patients (46.0%) were randomised and started adalimumab with 68 patients in the maximum tolerable dose group and 66 patients in the reduced dose group. At week 48, the remission achievement rates were 38.4 % and 44.8 %, respectively, with the adjusted risk difference of the reduced dose group to the maximum tolerable dose group of 6.4% (-7.0% to 19.8%, 90% CI), which met the criterion for noninferiority. No significant difference was found in health assessment questionnaire disability index ≤0.5 (59.1% vs 62.0%, respectively, p=0.72) and in radiological remission rates (Δmodified total Sharp score ≤0.5, 66.3% vs 62.0 %, respectively, p=0.59). Adverse drug reactions tended to be more frequent in the maximum tolerable dose group than in the reduced dose group (22.1% vs 9.1%, respectively, p=0.06).

Conclusion: The MIRACLE randomised study demonstrated that, in patients with inadequate response to methotrexate, the efficacy of adalimumab with reduced dose of concomitant methotrexate was not inferior to that with maximum tolerable dose of methotrexate with better safety profile.



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OP0063 OLOKIZUMAB IMPROVES PATIENT REPORTED OUTCOMES IN MODERATE TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS PATIENTS INADEQUATELY CONTROLLED BY METHOTREXATE (MTX-IR): RESULTS FROM THE PHASE 3 RANDOMIZED CONTROLLED TRIAL, CREDO 2

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Background: Olokizumab (OKZ) is an interleukin-6-inhibitor for treatment of Rheumatoid Arthritis (RA). In these analyses, we present patient reported outcomes (PROs) reported by MTX-IR patients with moderate to severely active RA treated with OKZ vs adalimumab (ADA) or placebo in a phase 3 randomized controlled trial (RCT) (ClinicalTrials.gov number, NCT02760407).

Objectives: To assess the effect of OKZ treatment compared with placebo and ADA in patient global assessment of disease activity (PtGA), pain, physical function (HAQ-DI), fatigue (FACIT-F) and health related quality of life (SF-36 physical (PCS) and mental (MCS) component summary and domain scores) and work participation (WPS-RA) at week 12.

Methods: 1648 patients receiving MTX were randomized to receive SQ injections: 1) OKZ 64 mg every 2 weeks (q2w, n=464), 2) OKZ 64 mg q4w (n=479), 3) ADA 40 mg q2w (n=462) and 4) placebo q2w (n=243). At week 14, non-responders: subjects without ≥ 20% improvements in both swollen and tender joint counts, added rescue medication (sulfasalazine and/or hydroxychloroquine) to study treatment. Between groups differences in least-squares mean (LSM) changes from baseline were analyzed.

Results: At week 12, treatment with both OKZ doses and ADA resulted in statistically greater LSM changes from baseline than placebo across all PROs, including 7 of 8 domains of SF-36 with exception of role emotional (Table 1 and Figure 1). Reported work and household work impairments, days productivities were reduced by half and missed household work days because of arthritis were all improved (p<0.01) with OKZ and ADA treatment. PROs further improved to week 24 in the active treatment arms. Post hoc analyses demonstrated that a higher proportion of patients receiving both doses of OKZ as well as ADA reported improvements ≥ minimum clinically important differences vs placebo (p<0.01) across all PROs, indicating clinically meaningful benefits on an individual patient basis. Estimates of numbers needed to treat indicated that between 5 and 10 patients would need to be treated to achieve these benefits. More patients in both OKZ groups reported scores ≥ normative values in PtGA, HAQ-DI and SF-36 PCS scores; with ADA in PtGA and HAQ-DI.

Table 1. Mean baseline PROs and LSM changes to week 12

	Baseline, mean (standard deviation)				12 weeks LSM changes (standard error)			
	OKZ q2w, N=464	OKZ q4w, N=479	ADA q2w, N=462	Placebo, N=243	OKZ q2w, N=464	OKZ q4w, N=479	ADA q2w, N=462	Placebo, N=243
PtGA-VAS	67.5(20.2)	66.8(20.9)	66.7(21.0)	67.4(20.0)	-29.7(1.1)#	-29.5(1.0)#	-31.6(1.1)#	-21.0(1.5)
Pain-VAS	68.4(20.6)	67.1(21.0)	66.8(21.5)	66.5(20.7)	-31.8(1.1)#	-31.7(1.1)#	-32.7(1.1)#	-21.3(1.6)
HAQ-DI*	1.7(0.58)	1.7(0.60)	1.7(0.57)	1.7(0.62)	-0.6(0.03)#	-0.6(0.03)#	-0.6(0.03)#	-0.4(0.04)
Comparison vs. ADA LSM difference [97.5% CI]					-0.03 [-0.12;0.05]	0.00 [-0.08;0.08]		
SF-36 PCS	31.8(7.0)	31.6(7.2)	31.4(7.4)	31.9(7.5)	8.1(0.4)#	7.8(0.4)#	8.1(0.4)#	4.9(0.5)
SF-36 MCS	42.9(11.4)	43.50(11.3)	44.1(11.4)	43.1(11.0)	5.1(0.4)†	4.9(0.4)†	5.0(0.4)†	3.1(0.6)
FACIT-F	26.7(10.7)	27.3(10.4)	27.4(11.3)	27.3(10.2)	8.4(0.4)#	8.1(0.4)ŧ	8.9(0.4)#	5.2(0.6)

Footnotes: LSM difference (SE) 97.5% CI by ANCOVA. NRS imputation.*, secondary endpoint; †p≤0.05, ŧp<0.01, #p<0.001 vs placebo; VAS (mm).

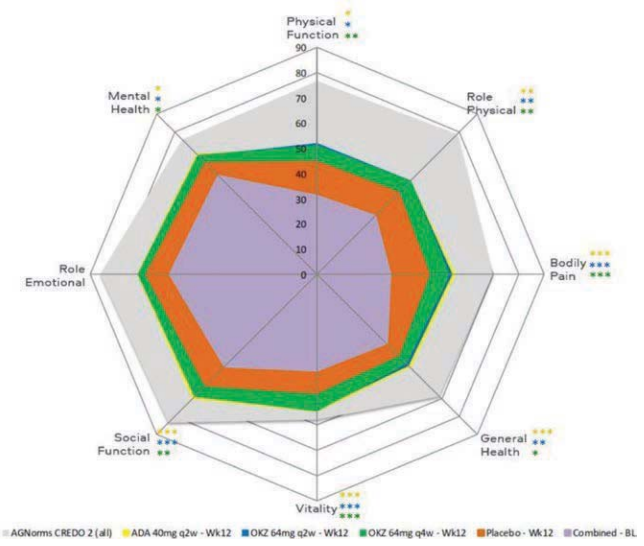

Figure 1. SF-36 domain changes from baseline to week 12. *p≤0.05, **p<0.01, ***p<0.001 ADA vs placebo; *p≤0.05, **p<0.01, ***p<0.001 OKZ q2w vs placebo; *p≤0.05, **p<0.01, ***p<0.001 OKZ q4w vs placebo. AGNorms, age- and gender-matched; BL, baseline.

Conclusion: Treatment with both doses of OKZ resulted in similar, statistically significant improvements across PROs vs placebo in MTX-IR patients with moderate to severely active RA, comparable to ADA, that were clinically meaningful.

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OP0064

FREQUENCY AND PREDICTORS OF MULTIPLE TREATMENT SWITCHING IN RHEUMATOID ARTHRITIS

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Background: Despite the significant improvements in the field of rheumatoid arthritis (RA) treatment, a significant and troubling minority of patients remain refractory to multiple disease modifying antirheumatic drugs (DMARDs). The consequence of this ''difficult-to-treat" state is irreversible damage, risk of co-morbid conditions, and substantial loss of quality of life. Early, precise, and actionable identification of this challenging group of RA patients is crucial for optimal prevention and management.

Objectives: To assess the frequency and to identify predictors of switching between multiple biological and targeted synthetic DMARDs (b/tsDMARDs) in RA patients in a large national register.

Methods: Observational cohort study including RA patients starting a first-ever b/tsDMARD 2009-2018, based on data from the Swedish Quality Rheumatology register. Comorbidities were identified through linkage to the national Patient Register. Baseline (time of RA diagnosis) characteristics of the population were described. Three groups were investigated: A) Patients starting ≥3 treatment courses; B) Patients starting ≥4 treatment courses; and C) Patients starting ≥5 treatment courses. Predictors of multi-switching were explored using univariate and multivariable logistic regression analyses.

Results: 23,908 RA patients were identified. Proportions of patients starting ≥3, ≥4 or ≥5 b/tsDMARDs treatment courses were 7%, 3.2% and 1.6%, during a mean (95% CI) of 3.6 (3.5-3.7), 4.3 (4.2-2.5) and 4.9 (4.7-5.2) years from RA diagnosis, respectively. In Table 1 baseline characteristics for each multi-switching group are summarized. For definition A, the following baseline univariate predictors were identified: female sex (OR=1.57, 95% CI=1.39-1.76), younger age (OR=0.96, 95% CI=0.95-0.96), positive RF (OR=1.36, 95% CI=1.22-1.53) and ACPA (OR=1.40,

Table 1. Baseline (time of RA diagnosis) characteristics

		Multi-switching definition		
	All patients	A: ≥3 b/tsDMARDs	B: ≥4 b/tsDMARDs	C: ≥5 b/tsDMARDs
N, %	23 908 (100)	1677 (7)	755 (3.2)	385 (1.6)
Age (years), mean (SD)	59.5 (15.2)	50.3 (14.5)	50.0 (14.6)	47.6 (14.7)
Sex (male) %	30.7%	22.5%	22.4%	21.6%
CRP, mg/L (median, IQR)	8.9 (4-22)	10 (4-24)	10 (4.2-25)	10 (4-29)
ESR (median, IQR)	23 (12-40)	23 (25-39)	23 (11-37.5)	22 (11.8-36.3)
Patient global, VAS 0-100 (mean, SD)	48.8 (26.8)	58.4 (25.3)	59.8 (24.5)	60.8 (24.0)
Patient pain, VAS 0-100 (mean, SD)	50.2 (26.8)	59.2 (25.4)	59.8 (25.2)	59.9 (25.2)
Fatigue, VAS 0-100 (mean, SD)	48.5 (28.8)	61.2 (26.5)	63.1 (25.9)	64.6 (23.6)
HAQ (mean, SD)	0.97 (0.66)	1.1 3(0.64)	1.15 (0.64)	1.13 (0.63)
Swollen joint count (median, IQR)	5 (2-9)	6 (3-10)	6 (3-10)	6 (3-10)
Tender joint count (median, IQR)	5 (2-9)	6 (3-12)	6 (3-12)	7 (3-11.25)
Concomitant csDMARD, %	52.5%	50.4%	51.7%	51.4%
Reumatoid factor positive, %	63.1%	69.6%	69.8%	67.8%
ACPA positive, %	67.0%	73.4%	74.3%	72.7%
DAS28-ESR (mean, SD)	4.62 (1.51)	5.00 (1.41)	5.10 (1.37)	5.12 (1.33)
VAS general health physician (mean, SD)	42.28 (23.02)	45.30 (22.19)	45.68 (20.69)	51.40 (25.83)

95% CI=1.24-1.58), higher DAS28 (OR=1.21, 95% CI=1.15-1.26), HAQ (OR=1.46, 95%=1.33-1.61), pain (OR=1.014, 95% CI=1.012-1.017) and fatigue (OR=1.017, 95% CI=1.014-1.021). In the multivariable logistic regression model, female sex, younger age, higher HAQ, pain and fatigue at baseline were independent predictors of multiple treatment switching. Similar results were found for all three multi-switch definitions. Several comorbidities (i.e. heart failure, ischemic heart disease, malignancy, renal failure) were associated with a lower risk for multiple treatment switching, suggestive of medical contraindications for b/tsDMARDs.

Conclusion: In this large national observational cohort, multiple treatment switching, indicative of difficult to treat RA, was observed in a significant proportion of patients, ranging between around 2 to 7% during the first 5 years from time of diagnosis. Risk factors include female gender, younger age, higher HAQ, pain and fatigue at the time of RA diagnosis, suggesting increased attention to this challenging group of patients.

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OP0065

INFLIXIMAB BIOSIMILAR-TO-BIOSIMILAR SWITCHING IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: CLINICAL OUTCOMES IN REAL-WORLD PATIENTS FROM THE DANBIO REGISTRY

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Background: In routine care, biosimilar-to-biosimilar infliximab switching may occur to save costs (=non-medical switching). Previous studies have investigated the efficacy and safety of switches from originator infliximab to a corresponding biosimilar in patients with inflammatory rheumatic diseases (1). However, the outcomes after switching from one infliximab biosimilar to a second infliximab biosimilar remain scarcely investigated. Denmark has recently conducted a nationwide mandatory infliximab biosimilar-to-biosimilar switch.

Objectives: To investigate the effectiveness of infliximab biosimilar-to-biosimilar switch (CTP-13 to GP1111) among patients with RA, PsA and AxSpA, including patients who had previously switched from originator (originator-experienced) to CT-P13 as well as patients who were originator-naïve.

Methods: Observational cohort study based on DANBIO registry (for clinical data upon switch =baseline) linked with national patient registries (to identify prior comorbidities). Patients with RA, PsA or AxSpA who performed a biosimilar-to-biosimilar switch from CT-P13 to GP1111 between April 1st 2019 and February 1st 2020 were included. Patient were divided into two groups: originator-naïve and originator-experienced. Main outcomes in the two groups were one-year GP1111 treatment retention (Kaplan Meier "drug survival curves") and changes in disease activity 4 months before versus 4 months after switch in individual patients. Also, factors associated with GP1111 treatment retention for both groups combined were explored with Cox proportional hazard regression analyses, stratified by diagnosis (univariate-, age-and gender adjusted and fully adjusted). Analyses were adjusted for relevant clinical factors (for details: see Table 1)

Results: In total, 1,605 patients underwent an infliximab biosimilar-to-biosimilar switch and were included; 1,171 were originator-naïve and 434 were originator-experienced, 685 RA/314 PsA/606 AxSpA, median disease duration was 9 years, 42% were in DAS28/ASDAS remission at the time of switch.

At one year, 83% (95% CI 81-85) of the originator-naive and 92% (95% CI 90-95) of the originator-experienced switchers maintained GP1111 treatment (Figure 1). Changes in disease activity 4 months pre- and post-switch were close to zero for all disease activity measures (e.g. DAS28, ASDAS, VAS pain, not shown).

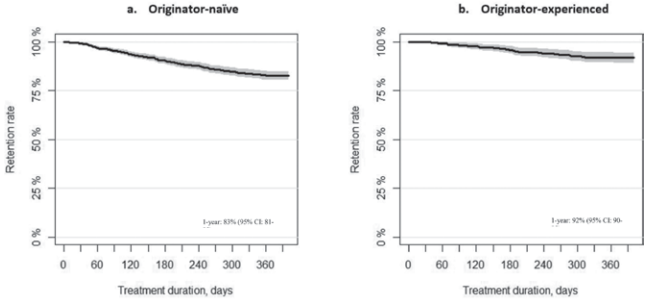

Figure 1. Kaplan-Meier plots of crude GP1111 treatment retention rates after an infliximab biosimilar-to-biosimilar switch among patients with inflammatory arthritis

The risk of GP1111 withdrawal was lower in originator-experienced compared to originator-naïve patients in patients with RA and PsA: HR 0.4 (95% CI 0.2-0.9, p-value 0.01) and HR 0.1 (0.1-0.6, p=0.01), but not significantly for AxSpA 0.56 (0.27-1.13, p=0.1). Across all indications, lower disease activity at baseline (DAS28/ASDAS remission) was associated with higher retention (Table 1).

Conclusion: Biosimilar-to-biosimilar infliximab switch was effective and well-tolerated in >1,500 real-world patients. Retention was higher in originator-experienced switchers and patients, who were in remission at the time of the switch, suggesting retention to be more affected by patient-related than drug-related factors.

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Table 1. Baseline variables associated with GP1111 withdrawal (RA shown below, similar findings for PsA and AxSpA)

	Univariate		Age- and gender adjusted		Multivariate	
	HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**	**HR (95%CI)**	**p-value**
RA						
Female gender	0.9 (0.6-1.3)	0.4	-		0.7 (0.5-1.2)	0.2
Age, years	1.0 (0.9-1.0)	0.9	-		1.0 (0.9-1.1)	0.6
Originator-experienced versus originator naïve to infliximab	**0.5 (0.3-0.8)**	**0.002**	**0.5 (0.3-0.8)**	**0.002**	**0.4 (0.2-0.9)**	**0.01**
Methotrexate use, yes	**0.5 (0.3-0.7)**	**<0.001**	**0.5 (0.3-0.7)**	**<0.001**	**0.6 (0.4-0.9)**	**0.01**
Comorbidities ≥1	1.1 (0.7-1.5)	0.8	1.1 (0.7-1.5)	0.8	0.9 (0.6-1.4)	0.7
In remission (yes)	**0.4 (0.3-0.6)**	**<0.001**	**0.4 (0.2-0.6)**	**<0.001**	**0.5 (0.3-0.7)**	**<0.001**
DAS28	**1.7 (1.4-1.9)**	**<0.001**	**1.7 (1.5-1.9)**	**<0.001**	-	-
Patient global VAS, mm	**1.0 (1.0-1.1)**	**<0.001**	**1.0 (1.0-1.1)**	**<0.001**	-	-

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

OP0066

IMPACT OF DIAGNOSIS AND TREATMENT OF TROPHERYMA WHIPPLEI INFECTION IN PATIENTS WITH PRE-EXISTING CHRONIC INFLAMMATORY RHEUMATIC DISEASES: DATA FROM THE NATIONAL TW-IRD REGISTRY

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Background: Tropheryma whipplei (Tw) infection is a rare condition, characterized by inflammatory joint symptoms in more than 75% of the cases, which can lead the physician to diagnose chronic inflammatory rheumatic diseases (IRD) and to initiate DMARDs. DMARDs are often ineffective and may reveal digestive signs, systemic manifestations or involvement of other organs. We hypothesized that treatment of Tw infection has a favorable impact on rheumatologic and extra-rheumatologic manifestations attributed to IRD.
Objectives: To validate this hypothesis, we initiated a registry with the objectives to describe the characteristics of IRD and their treatments, the diagnostic and therapeutic modalities of Tw infections and the impact of the treatment of Tw infection on the evolution of IRD and associated DMARDs.
Methods: We initiated a French National register including adult patients with pre-existing IRD, treated with DMARDs, later diagnosed with Tw infection. Cases were identified through a call for observation via the "Club Rhumatismes et inflammations" website. We collected clinical and biological data about the characteristics of IRD and their treatments, the diagnostic and therapeutic modalities of Tw infections, and the impact of the treatment of Tw infection on the evolution of IRD and associated DMARDs.
Results: Seventy-three IRD patients were included. Mean age at diagnosis was 49 years (SD +/- 10.9), with 78% of men, median IRD duration was 79 months (IQR 36; 140), including rheumatoid arthritis (31 cases), spondyloarthritis (14 cases), psoriatic arthritis (6 cases) and other IRDs (22 cases). All IRD patients were treated with DMARDs, with no therapeutic response in 51% of the cases, worsening of rheumatologic symptoms in 34% of the cases, and occurrence of extra-articular manifestations in 27% of the cases. Screening for Tw infection mainly involved saliva and stool PCR, while diagnostic modalities involved organ specific PCR and biopsies, in particular duodenal biopsies (PCR positive in 87% of cases and histology in only 38% of cases). At the time of Tw infection diagnosis, mean age was 58 years (SD +/- 10.1), all patients had joint involvement, 33% axial involvement, 11% entheseal involvement, 84% extra-articular manifestations, 93% elevated CRP, 86% hypoalbuminemia and 67% anemia. Tw infection treatment modalities (median follow-up of 22 months) mainly involved a combination of doxycycline (95%) and hydroxychloroquine (96%), with complete recovery in 79% of the cases and Tw-related deaths in 2 cases. At the same time, Tw infection treatment was associated with IRD remission in 93% of cases, with a median time to remission of 2 months (IQR 1; 4.25), leading to DMARD withdrawal in 94% of cases and corticosteroid therapy withdrawal in 65% of cases.
Conclusion: A Tw infection should be considered in IRD patients with peripheral joint involvement and inadequate response to DMARDs, particularly in the presence of extra-articular manifestations, elevated CRP and hypoalbuminemia. In such patients, positive results of screening and diagnostic tests for Tw infection may lead to the initiation of Tw infection treatment which is associated with complete recovery of Tw infection and rapid remission of the IRD, allowing DMARD and corticosteroid therapy withdrawal in most the cases.

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OP0067

MORE THAN SIX-FOLD INCREASED MORTALITY RISK IN PATIENTS WITH INCIDENT RHEUMATOID ARTHRITIS AND DEPRESSION IN A LARGE COHORT WITH 10-YEAR FOLLOW-UP

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Background: The occurrence of depression is increased in patients with rheumatoid arthritis (RA) compared with the background population. (1) Recently, we described that in RA the most frequent indication for filling antidepressant prescriptions is depression and the frequency of filling coincides with the occurrence of depression reported in the scientific literature. (2) In patients with stroke, depression defined as filling of antidepressants or a diagnosis with depression is associated with increased mortality risk and the risk is similar for both definitions of depression. (3)
Objectives: We used the first filling of antidepressants as proxy for depression with the objective to describe the mortality risk associated with depression in patients with incident RA.
Methods: We included patients diagnosed with incident RA (index date) from the nationwide DANBIO register (4) from January 1, 2008 to September 30, 2018. Participants were identified by unique personal registration numbers. Included patients were without a recorded filling of methotrexate (Anatomic Therapeutic Chemical code L01BA01) and antidepressants (N06A) in the Danish National Prescription Register or recorded hospital contacts with RA and depression (International Classification of Diseases (version 10) codes M05, M06, F32) in the Danish National Patient Register, three years prior to the index date. From the index date, we defined depression as first filling of antidepressants and collected death dates from the Danish Civil Registration System. The participants were followed until December 31, 2018 and all-cause mortality estimated in two dynamic risk periods: the period from the index date until first filling of antidepressants (if it occurred) and the period after filling of antidepressants. We calculated hazard rate ratios (HRR) by modelling filling of antidepressants as time-varying exposure for total follow-up and adjusted for potential confounders defined *a priori*: age, sex, comorbidity, cohabitation, employment status, highest attained education, and income. Cumulative mortality was described by Kaplan-Meier curves. Results were reported with 95% confidence intervals (CI).
Results: Among 11,071 RA patients followed for 56,993 person-years, 1,095 (10%) filled prescriptions for antidepressants. The median age at diagnosis was 61 years, 66% were female, and 64% diagnosed with seropositive RA. Adjusted HRR was highest in the age group <55 years but also increased between 55-70 years, >70 years, among females and males, and in patients diagnosed with seropositive and seronegative RA (Table 1). The cumulative mortality is seen in Figure 1.

Table 1.

Strata		HRR (95% CI)	
		Crude	Adjusted
Age, years	<55	8.40 (4.20-16.80)	6.66 (2.80-15.85)
	55-70	3.27 (2.35-4.54)	3.30 (2.27-4.80)
	>70	2.97 (2.36-3.75)	2.94 (2.26-3.83)
Sex	Female	3.72 (2.95-4.70)	2.91 (2.22-3.81)
	Male	3.10 (2.32-4.15)	3.70 (2.66-5.14)
RA diagnosis	Seropostive (M05)	3.73 (2.99-4.65)	3.45 (2.66-4.47)
	Seronegative (M06)	2.85 (2.07-3.91)	3.08 (2.17-4.37)

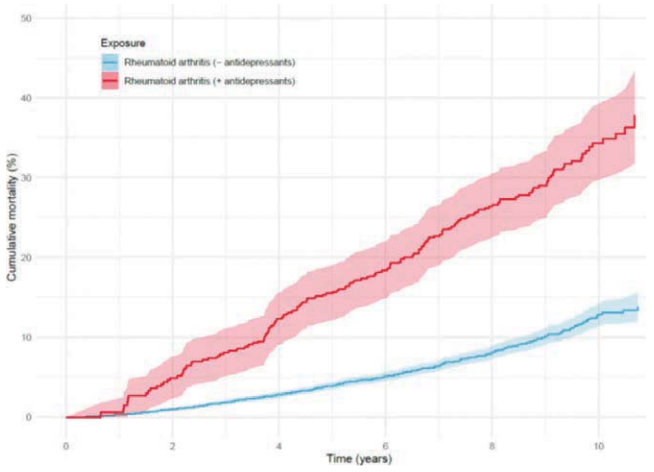

Figure 1.

Conclusion: Depression, defined as first filling of antidepressants, was associated with more than six-fold increased mortality risk in patients with incident RA.

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OP0068

DISTINCT STROMAL AND IMMUNE CELL INTERACTIONS SHAPE THE PATHOGENESIS OF RHEUMATOID AND PSORIATIC ARTHRITIS

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Background: Rheumatoid (RA) and psoriatic arthritis (PsA) are common autoimmune and autoinflammatory diseases of unknown aetiology characterised by complex synovial pathology with a detrimental effect on the patient's quality of life. Significant differences in pathophysiology may explain distinct clinical manifestations and account for differential responses to specific therapeutics. Recent implementation of single cell transcriptomic analysis of sorted synovial cells has revealed the diverse cellular landscape of the RA synovial stromal and immune cell compartments, however, a complete analysis of immune and stromal cells in tandem, for RA and PsA patient synovial tissue has not been performed.

Objectives: To combine novel scRNA transcriptomic approaches and *ex vivo* assays in order to: identify differences in the cellular landscape of RA and PsA synovial tissue inflammation and immune – stromal cell interactions that drive pathology in RA and PsA.

Methods: Single cell transcriptomic profiling of 178,000 synovial tissue cells from 5 PsA and 4 RA patients, importantly, without prior sorting of immune and stromal cells. This approach enabled the generation of a unique cell atlas of intact synovial tissue identifying immune and stromal cell interactions. State of the art data integration and annotation techniques identified and characterised 18 stromal and 14 immune cell clusters. Bioinformatic examination of cell-cell communication via construction of receptor-ligand interaction networks with further *in vitro* validation of stromal and immune cell crosstalk through flow cytometric analysis, multiplex ELISA and mitochondrial and single cell metabolic profiling by multiphoton and florescent lifetime imaging microscopy, seahorse.

Results: Following quality control and data integration the PsA and RA cellular landscape was generated and nine mega clusters indicative of fibroblasts, endothelial cells, pericytes, macrophages, dendritic cells (DC), B cells, plasma cells, T cells and NKT consisting of several sub clusters were identified. Distinct points of transcriptomic deviation and convergence between RA and PsA were identified for each of the major cell types of the joint. Specifically, cell cycle and trajectory analysis revealed that only a fraction of synovial T cells are actively proliferating. Additionally, the differential usage of immunoglobulin light chains by memory and plasma cells indicates that plasma cells are potentially not derived from the local memory B cell pool of the synovial tissue. Importantly, we report distinct fibroblast and endothelial cell transcriptomes indicating differentially abundant subpopulations in RA and PsA characterised by distinct transcription factor usage and signalling pathway enrichment. Specifically transcriptomic imputation analysis revealed abundance of invasive FAPα^{+}THY1^{+} regulated by transcription factor TEAD1 in RA compared to PsA synovial tissue. In order to identify potential cell-cell communication driving inflammation in RA and PsA, novel receptor–ligand interaction networks were generated and downstream of the receptor, target characterisation was performed. Herein we identify RA-specific synovial T cell-derived TGF-β and macrophage IL-1β synergy in driving the transcriptional profile of FAPα^{+}THY1^{+} invasive synovial-fibroblasts, expanded in RA compared to PsA synovial tissue biopsies (Figure 1). Ex vivo treatment of RA patient synovial fibroblasts identified TGF-b and IL-1b synergy are a major driver of IL-6 production, fibroblast activation and adhesion molecule expression. Interestingly, the aforementioned proinflammatory changes of RA patient synovial fibroblasts were coupled with significant alterations in mitochondrial eccentricity and size and a marked metabolic adaptation towards a strongly glycolytic profile (Figure 1).

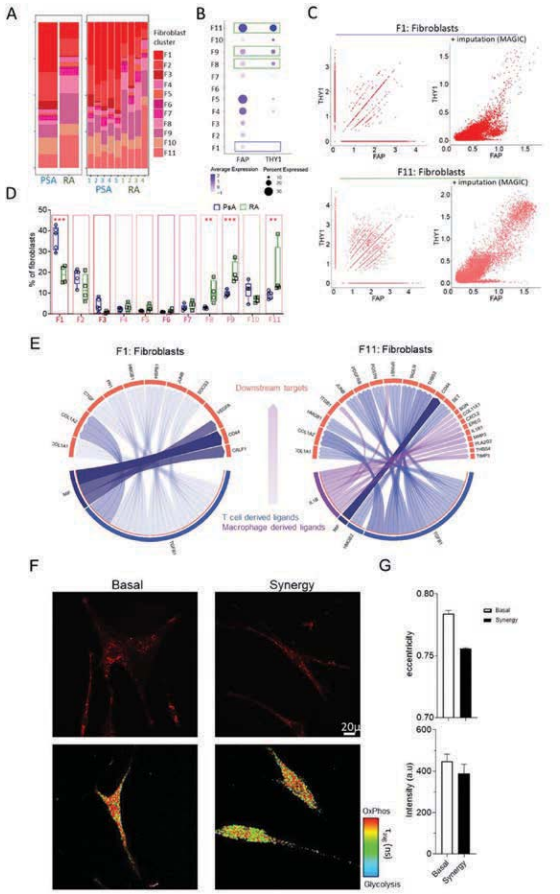

Figure: Immune-stromal cell crosstalk as a driver of synovial inflammation.
A. Abundance of fibroblast clusters in RA and PsA patient synovial biopsies. B. Expression and percentage of positive cells per fibroblast cluster for FAP and THY1. C. Scatterplots for showing the relation between THY1 and FAP expressing cells before and after data imputation for RA and PsA fibroblast cluster 1 and fibroblast cluster 11. Fibroblast clusters with significantly different abundances between RA and PsA are indicated by green (higher in RA) and blue (higher in PsA) boxes. D. Frequency of fibroblast clusters in PsA and RA patient synovial biopsies (n=4-5), data are presented as Box and whiskers plots (min to max), symbols represent individual samples. E. Circo plot depicting the top ligand and downstream target interaction for enriched in PsA synovial fibroblast cluster F1 and enriched in RA, invasive synovial fibroblast cluster F11. F. Representative images of RA patient synovial fibroblasts mitochondrial and metabolic analysis. G. Synovial fibroblast eccentricity and staining intensity under basal conditions or following treatment with TGF-b and IL-1B.

Figure 1.

Conclusion: Disrupting specific immune and stromal cell interactions offers novel opportunities for targeted therapeutic intervention in RA and PsA.
Disclosure of Interests: Achilleas Floudas: None declared, Conor Smith: None declared, Orla Tynan: None declared, Nuno Neto: None declared, Vinod Krishna Employee of: Janssen Pharmaceuticals, Sarah Wade: None declared, Megan Hanlon: None declared, Clare Cunningham: None declared, Viviana Marzaioli: None declared, Mary Canavan: None declared, Jean Fletcher: None declared, Suzanne Cole Employee of: Janssen Pharmaceuticals, Ling-Yang Hao Employee of: Janssen Pharmaceuticals, Sunil Nagpal Employee of: Janssen Pharmaceuticals, GSK, Michael Monaghan: None declared, Douglas Veale Consultant of: Janssen, Eli Lilly, Pfizer, Ursula Fearon Consultant of: Janssen, Eli Lilly, Pfizer.
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OP0069 INCLUSION OF PATIENT RESEARCH PARTNERS IN REMEDY – A RESEARCH CENTER FOR TREATMENT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Active collaboration between patients and researchers in development and implementation of scientific projects is important to ensure a good match between patient's preferences and the scientific focus in research, contribute to more patient-oriented health research agendas, enhance patient friendly design of research projects, and creating support for implementation (1). Such involvement is strongly advocated by EULAR and is often a prerequisite to receive funding for clinical research projects. At Diakonhjemmet Hospital in Norway, the division of rheumatology and research has for many years worked to involve patient research partners (PRPs) in research. A patient advisory board was established in 2007, led by a person (20% position) who herself has a rheumatic disease. In eight years from 2022, the division will receive funding from the Norwegian Research Council to establish and host a clinical research center for treatment of Rheumatic and Musculoskeletal diseases – the REMEDY center.
Objectives: To describe how involvement of PRPs are organised within the REMEDY center.
Methods: An organisation map was developed as part of the application for funding. The leader of the patient advisory board, together with three senior researchers, were involved in several rounds of discussions on how PRP involvement should be organised in the center, and also in meetings with the larger research group.
Results: The organisation of REMEDY is shown in Figure 1.

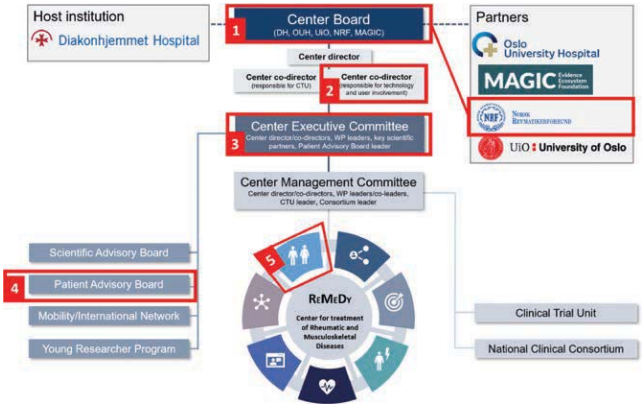

Figure 1. Organisation of REMEDY.

1.All partners, including **The Norwegian Rheumatism Association,** (the largest patient organisastion in the field), are represented at the Center Board. This ensures patient involvement at the strategic level, including setting research agendas and priorities.
2.The center is led by a centre director and two **co-directors**, of which one has a specific responsibility of PRP-involvement
3.The Centre Executive Committee (CEC) consist of the Center Director and co-directors, the WP leaders, **the leader of the patient advisory board**, the key senior scientific staff members of the partner institutions involved in the center and senior staff members deemed appropriate by the Centre Director.
4.**The patient advisory board**, consisting of 10-15 PRPs, is central within the center. Members of the board will be involved in all research projects, collaborating with researchers to improve design, methodology, research outcomes and implementation. The board provides a platform for the members for education, development, and exchange of knowledge and experience.
5.There are seven work packages (WPs) in REMEDY, each approaching the knowledge needs within rheumatic and musculoskeletal diseases (RMDs) treatment from different angles, and with international collaborators. WP7 (Empowering the individual) will provide **a platform for the Patient advisory board**, facilitating input from PRPs to all WPs. The chair of the EULAR study group for collaborative research is an international collaborator in WP7.
The leader of the Patient Advisory board has a 50% position. Additionally, there is funding for board activities, and for PRP involvement in initial project phases, whereas PRP activities are included in applications for external funding.
Conclusion: The REMEDY center is organised to ensure involvement of PRPs at all organisational levels, from individual research trials to the strategic and operational management of the center.
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OP0070 INTERVENTION WITH METHOTREXATE IN ARTHRALGIA AT RISK FOR RHEUMATOID ARTHRITIS TO REDUCE THE DEVELOPMENT OF PERSISTENT ARTHRITIS AND ITS DISEASE BURDEN (TREAT EARLIER): A DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED TRIAL

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Background: Rheumatoid arthritis (RA) is the most common autoimmune disease, and requires long-term treatment to suppress inflammation. Currently, methotrexate is initiated as first-line treatment when arthritis becomes clinically apparent with joint swelling. However, disease processes begin long before and become clinically recognizable when patients develop symptoms. We hypothesized that the 'at risk phase' of symptoms and subclinical joint-inflammation is a therapeutic window to permanently modify the disease course.
Objectives: We studied if intervention in the pre-arthritis phase of arthralgia and subclinical joint inflammation prevents the development of clinical arthritis or reduces the burden of disease.
Methods: In this randomised, double-blind, 2-year proof-of-concept trial, adults with arthralgia clinically suspected of progressing to RA and MRI-detected subclinical joint-inflammation, recruited from all rheumatology outpatient-clinics in the south-west-Netherlands, were randomly assigned (1:1) to a single intramuscular glucocorticoid injection (120 mg) and a one-year course of oral methotrexate (up to 25 mg/week), or placebo injection and placebo tablets. Subsequently, participants were followed for another year without study medication. The primary endpoint was the development of clinically detectable arthritis (fulfilling the 2010 RA-criteria or involving ≥2 joints) that persisted for at least 2 weeks. Patient reported physical functioning, along with symptoms and workability, were key secondary endpoints and measured 4-monthly. Additionally, the course of MRI-detected inflammation was studied (the sum of tenosynovitis, synovitis, osteitis, scored with the RA-MRI Scoring (RAMRIS) method). All participants entered the intention-to-treat analysis. We performed two prespecified subgroup analyses. Firstly, analyses were restricted in participants with high risk of clinical arthritis development (PPV ≥70%). Secondly, analyses were stratified for ACPA-status. The trial is registered with the Netherlands Trials Registry (NTR4853 trial NL4599).
Results: From April 16th, 2015 to September 11th, 2019, we randomly assigned 236 participants to treatment (n=119) or placebo (n=117). After 24 months, arthritis free survival was similar in both groups (80% versus 82%, HR 0.81 (95%CI 0.45, 1.48)). Physical functioning improved more in the treatment-group during the first months and remained better (mean between-group difference over two-years HAQ -0·1(-0·2,-0·03;p=0·004). Similarly, pain (-9 on scale 0-100: (95%CI -12,-4; p<0·001), morning stiffness (-12 (95%CI -16,-8;p<0·001), presenteeism (-8% (95%CI -13%,-3%;p=0·001) showed sustained improvement compared to placebo. MRI-detected joint-inflammation was also persistently improved (mean difference over 2 years -1·4 points (95%CI -2·0,-0.9;p<0·001). High-risk participants in the treatment group showed a delay in clinical arthritis development: they developed the endpoint less often during treatment, but frequencies became similar at 24 months (67% in both groups). A similar delaying effect was observed in ACPA-positive participants, where 48% and 52% had developed persistent clinical arthritis at 24 months. The number of serious adverse events was equal between the groups; adverse events were as expected from methotrexate.

Conclusion: Methotrexate, the cornerstone treatment of RA, initiated at the pre-arthritis stage of joint symptoms and subclinical inflammation, did not prevent the development of clinical arthritis, but modified the disease course as measured by sustained improvement in MRI-detected inflammation, related symptoms and impairments. These findings of sustained disease modification may open up a new treatment landscape in a pre-arthritis phase of RA, where limitations can be just as severe as at the onset of clinical arthritis.

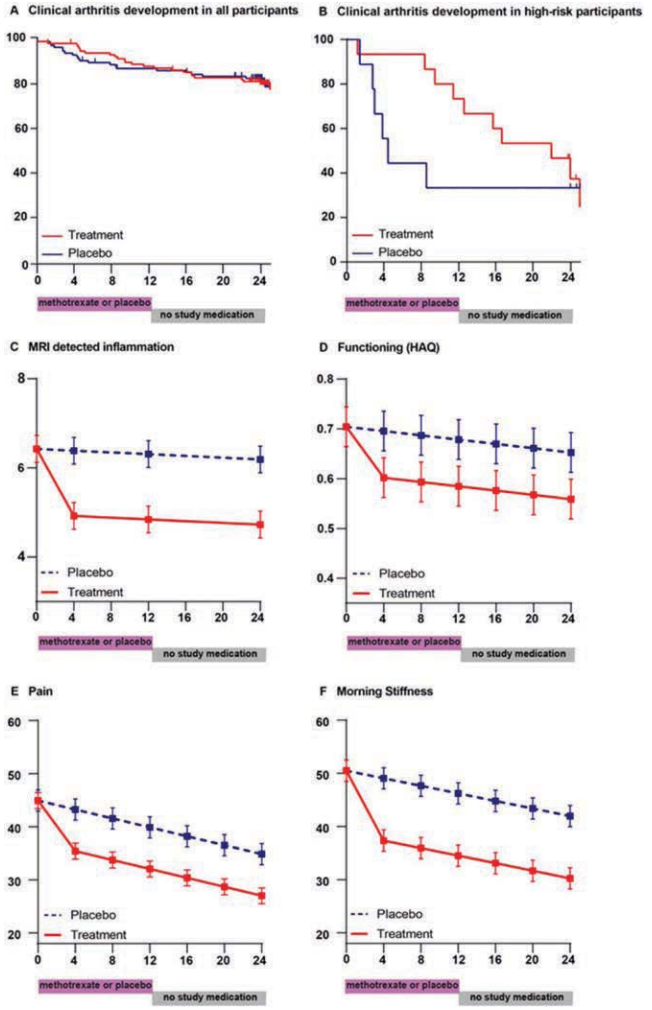

Figure 1.

Acknowledgements: We thank Prof. dr. R. ten Cate, prof. dr. S. le Cessie and dr. A.M.J. Langers for their role in the Data Safety and Monitoring Board. We thank all participants, and all rheumatologist of the following hospitals: Albert Schweitzer Hospital, Alrijne Hospital, Erasmus Medical Center, Haven-policlinic Rotterdam, IJselland Hospital, Ikazia Hospital, Franciscus Gasthuis & Vlietland Hospital, Groene Hart Hospital, Haaglanden Medical Center (all locations), Haga Hospital, Langeland Hospital, Meander Medical Center, Maasstad, Hospital, Reinier de Graaf Gasthuis, Reumazorg Zuid-West Nederland and Spaarne Gasthuis. We acknowledge the team of treating rheumatologists and research nurses of the LUMC, in particular Dr F.J. van der Giesen. Our gratitude also goes to the PhD students who scored MRIs for trial screening, in particular dr. H.W. van Steenbergen, dr. W. Nieuwenhuis, dr. R.M. ten Brink, dr. D.M. Boeters, dr. L. Mangnus, X.M.E. Matthijssen and F. Wouters. We thank dr. M. Reijnierse, prof. dr. S.C. Cannegieter and prof. dr. D. van der Heijde for their advice, and dr. J. Schoones for his help with the systematic literature search. We acknowledge the funder of the study: NWO ZonMW grant (program 'translationeel onderzoek', project number 95104004).
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OP0071

ASSOCIATION BETWEEN LONG-TERM EXPOSURE TO AIR POLLUTION AND IMMUNE-MEDIATED DISEASES: A POPULATION-BASED COHORT STUDY

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Background: Environmental air pollution has been associated with disruption of the immune system at a molecular level.
Objectives: The primary aim of the present study is to describe the association between long-term exposure to air pollution and risk of developing immune-mediated conditions.
Methods: We conducted a retrospective observational study on a nation-wide dataset of women and men. Diagnoses of various immune-mediated diseases were retrieved. Data on the monitoring of PM10 and PM2.5 concentrations were retrieved from the Italian institute of environment protection and research (ISPRA). The long-term average PMs concentrations were the exposure of interest. Every study subject was linked to a PMs exposure value, which resulted from the average concentration of urban, rural and near-traffic stations of the subject residency from January 2013 to November 2020. Patients were linked to the nearest air quality station through ZIP code centroids. Generalized linear models were employed to determine the relationship between autoimmune diseases prevalence and PM. The fully adjusted model included age, body mass index (BMI), menopause, glucocorticoid treatment, treatment with adjuvant hormone therapy for breast or prostate cancer, specialty of the physician that entered the data and macro-area of residency (stratified as a categorical variable: northern Italy, central Italy and southern Italy.
Results: 81,363 subjects were included in the study. We found a positive association between PM10 and the risk of autoimmune diseases (ρ +0.007, p 0.014). Every 10 µg/m3 increase in PM10 concentration was associated with an incremental 7% risk of having autoimmune disease. Exposure to PM10 above 30 µg/m3 and PM2.5 above 20 µg/m3 was associated with a 12% and 13% higher risk of autoimmune disease pooled together, respectively (aOR 1.12, 95% CI 1.05-1.20 and aOR 1.13, 95% CI 1.06-1.20). Exposure to PM10 was associated with an increased risk of rheumatoid arthritis (aOR 1.408, 95% CI 1.271-1.560) but no other autoimmune diseases, whereas exposure to high levels of PM2.5 were associated with an increased risk of rheumatoid arthritis (aOR 1.559, 95% CI 1.401-1.734), CTDs (aOR 1.147, 95% CI 1.024-1.286) and IBDs (1.206, 95% CI 1.028-1.415) but no other autoimmune diseases.
Conclusion: Long-term exposure to air pollution was associated with higher risk of developing autoimmune diseases, in particular rheumatoid arthritis, CTDs and IBD. Chronic exposure to levels above the threshold for human protection was associated with a 10% higher risk of developing immune-mediated diseases.

Figure 1. A. Prevalence of auto-immune diseases across Italy in the DeFRA database; B. Long-term exposure to particulate matter (PM) of less than 10 µm in Italy (2013-2019 average concentration µg/m3)

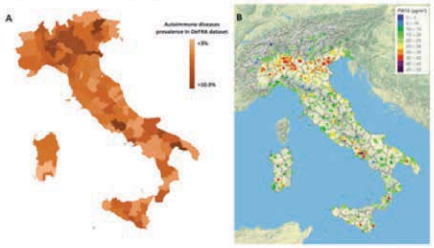


Figure 2. Risk of immune-mediated conditions at chronic exposure to PM10 ≥30 µg/m³

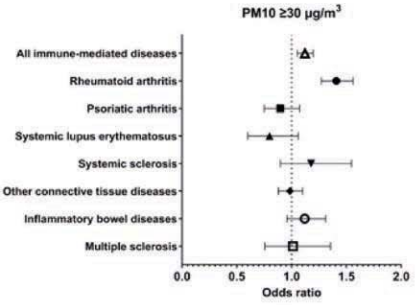
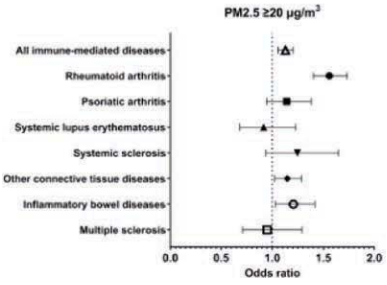


Figure 3. Risk of immune-mediated conditions at chronic exposure to PM2.5 ≥20 µg/m³



Disclosure of Interests: Giovanni Adami Shareholder of: Galapagos, Theramex, Marco Pontalti: None declared, Camilla Benini: None declared, Angelo Fassio: None declared, Eugenia Bertoldo: None declared, Davide Gatti: None

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OP0072 **SMILE-RA - SELF-MANAGEMENT INDIVIDUALISED LEARNING ENVIRONMENT IN RHEUMATOID ARTHRITIS**

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Background: An important but insufficient aspect of care in people with inflammatory arthritis (IA) is empowering them to acquire good understanding of their disease and build ability to deal effectively with the practical, physical and psychological impacts of it. This extends beyond drug therapy and emphasises the ability to self-manage, **with the right support**, as an **essential** component of care. Good self-efficacy and coping skills reduce health and financial burden to the individual as well as the health service, benefitting society overall. Provision of excellent supported self-management education is at the heart of what NRAS does and it was due to the difficulty of getting Commissioners to fund our face-to-face group self-management that led to our building an e-learning programme to expand on and replace our 6-week programme.
Objectives: To co-create an intuitive, easy to use, modular e-learning programme, free for all and which health professionals (HCPs) could refer their patients to. This makes supported self-management and evidence-based education accessible to all, wherever they live. SMILE enables HCPs to meet both NICE guideline and quality standards in RA against which rheumatology units in England and Wales are currently audited, as well as EULAR Recommendations for self-management strategies in inflammatory arthritis.
Methods: In 2019 with initial funding in place, we worked with our provider to help us realise our goal of developing a state-of-the art e-learning experience in a modular format for people with RA. The programme had to be 1) simple to use; 2) interactive; 3) innovative and engaging; 4) able to measure impact through achievement of learning objectives and use of a validated patient reported outcome measure. The programme also had to be integrable with our Salesforce database enabling us to collect data and target resources to individuals, driven by identified need.
Results: Delayed by COVID, we launched with 4 modules on 17/09/2021. The 4 modules comprise: Foundation Module covering the importance of self-management which has the RA Impact of Disease PROM embedded; Newly Diagnosed; Meet the Team and Managing Pain and Flares. A fifth module on Medicines in RA will be launched 1st quarter 2022 and 4 further modules will be uploaded in 2022. To date (26/01/22), 760 people have registered, of which 313 have completed a baseline RAID and this reveals that <50% are achieving minimal acceptable state of 3 or less. Over 78% of registrants are not NRAS members, and 634 modules have been completed. Early indications are that almost all are achieving learning objectives. More data will be available by June 2022.
Conclusion: Early indications demonstrate that people are successfully engaging with the programme and we have marketing activity lined up to raise further awareness of the value of SMILE with both potential users and rheumatology teams in 2022. Massive workforce issues together with significant backlogs of existing patients caused by the pandemic, have restricted the ability of Teams to provide education and self-management support for their patients. SMILE offers high quality, evidence-based learning opportunities for their patients and has been co-created with health professionals and people with RA at every step. With remote consultations here to stay, the importance of patients having access to evidence based online learning which they can tailor to their specific needs and improve their self-efficacy is even more critical.
Acknowledgements: I would like to acknowledge the support of our E-Learning Advisory Board and all health professionals and people with RA who have provided input to SMILE.
Disclosure of Interests: Ailsa Bosworth Grant/research support from: NRAS has received educational grants from a number of pharmaceutical companies. I have never received any personal payment from Industry.
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OP0073 **NEW PERSPECTIVES IN AXIAL SPONDYLOARTHRITIS - FIRST RESULTS OF GENDER-SPECIFIC ASSESSMENT OF MRI IMAGING CRITERIA**

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Background: Gender-specific differences in patients with axial spondyloarthritis (axSpA) are often seen in the clinical presentation and may differ in MRI findings[1]. Male axSpA patients tend to show structural changes earlier, whereas in female axSpA patients the peripheral joints are more often affected[2]. This can lead to a delay in axSpA diagnosis in women. For this reason, gender-specific data collection and establishment of gender-specific imaging criteria are of particular importance.
Objectives: To evaluate the diagnostic performance of different combinations of imaging markers to derive data-driven imaging criteria for MRI in axSpA, separately for men and women.
Methods: A total of 1194 patients were included in the study. Considering the exclusion criteria (available MRI image data sets, confirmed diagnoses), 684 patients (379 axSpA and 305 control group) were included for further statistical analysis. Two trained readers scored the MRI images separately for the presence of ankylosis, as well as erosion, sclerosis, fat metaplasia, and bone marrow edema differentiated for 3 regions (ventral/mid/dorsal) for sacral-sided and iliac-sided sacroiliac joint. Chi^2 test was applied to compare lesion frequencies per group. Contingency table analysis was performed to assess diagnostic performances. The diagnostic performances were compared using the diagnostic odd ratio (DOR).
Results: Overall, 136 female and 243 male axSpA patients were included. Higher prevalence for ankylosis (24.3 vs. 7.4%) and fat metaplasia (58.8 vs. 42.6%) was shown in male axSpA patients; in contrast, sclerosis was more common in female axSpA patients (75.0 vs. 57.6%). No sex differences in frequency were shown for bone marrow edema and erosion. In male axSpA patients, the most significant difference in individual parameters was shown for ankylosis (DOR 40.1) compared with females (DOR 4.7). The detection of erosion and fat metaplasia as markers was also better in male axSpA patients (DOR 17.6 vs. 11.1 and 18.6 vs. 6.3). Sclerosis and bone marrow edema were better suited in female axSpA patients (DOR 3.0 vs. 2.5 and 5.0 vs. 3.7). Overall, diagnostic accuracy was improved when only lesions in the middle and dorsal articular compartments were considered.
Conclusion: The diagnostic performance of established image markers on MRI is significantly lower in female axSpA patients. This is especially true for ankylosis, which provides the risk for false-positive findings in women. Based on these findings, future revisions of imaging criteria may include gender-specific recommendations to improve diagnostic accuracy for male and female axSpA patients.
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Disclosure of Interests: Sevtap Tugce Ulas: None declared, Fabian Proft Speakers bureau: Novartis, Lilly and UCB, as well as personal fees from AbbVie, AMGEN, BMS, Hexal, Janssen, MSD, Pfizer and Roche, Grant/research support from: Novartis, Eli Lilly and UCB., Torsten Diekhoff Speakers bureau: MSD, Novartis and Eli Lilly., Valeria Rios Rodriguez Speakers bureau: AbbVie and Falk e.V., Judith Rademacher Grant/research support from: Berlin Institute of Health (BIH) during the conduct of this study (Clinician Scientist Programme)., Mikhail Protopopov Grant/research support from: UCB, Sarah Ohrndorf: None declared, Denis Poddubnyy Speakers bureau: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, Bristol-Myers Squibb, Roche, UCB, Biocad, GlaxoSmithKline and Gilead, Grant/research support from: AbbVie, Eli Lilly, MSD, Novartis and Pfizer., Katharina Ziegeler Grant/research support from: Assessment of Spondyloarthritis international Society (ASAS) during the conduct of this study.
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Rheumatoid arthritis - aetiology, pathogenesis and animal models

OP0074 **DISTINCT CIRCULATING LYMPHOCYTE SUBSETS DISTINGUISH FLARE FROM DRUG-FREE REMISSION IN RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is characterised by relapsing joint and systemic inflammation, yet the immunopathological basis of these disease flares and their clinical prediction remain uncertain.
Objectives: Using mass cytometry and single cell RNA sequencing, we aimed to identify circulating lymphocyte subsets associated with RA flare, and identify potential cellular biomarkers to predict flare versus drug-free remission (DFR).
Methods: We analysed peripheral blood mononuclear cells (PBMCs) from patients recruited to the BioRRA study (Figure 1), a prospective clinical trial of conventional synthetic disease-modifying anti-rheumatic drug (csDMARD) cessation.[1] Patients with RA in clinical (DAS28-CRP < 2.4) and ultrasound (absence of power Doppler signal in 7 joints) remission stopped csDMARDs, with flare defined as DAS28-CRP ≥ 2.4 during 6 month follow-up. A 44-marker mass cytometry panel was used to profile PBMCs from 36 patients (20 flare, 16 DFR) at two time points each (baseline, and flare onset / month 6 DFR). In a subset of patients (n = 12: 8 flare, 4 DFR), fluorescence-activated cell sorting of T and B cells was followed by single cell sequencing (n = 81,923 cells) incorporating 320 immune genes, 34 oligo-tagged surface protein antibodies, and TCR/BCR CDR3 sequence. Clones were defined as ≥2 cells with identical CDR3 nucleotide sequence, and clonal expansion as a significant increase in proportion from baseline to final study visit. Statistical significance was assessed after Benjamini-Hochberg multiple test correction (adj p < 0.05).

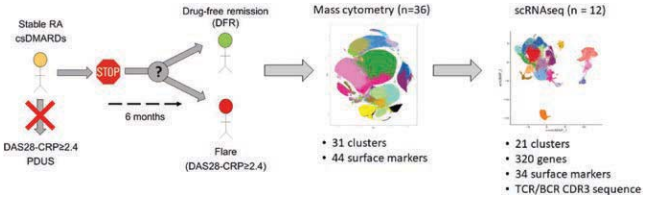

Figure 1.

Results: Mass cytometry revealed 31 distinct cell clusters: notably, greater proportions of memory (CD45RO+/PD1hi) CD4+ and CD8+ T cells, and memory (CD27+/CD21-) B cells, were observed at onset of flare versus baseline (Table 1).

Table 1.

Mass cytometry (n = 20 flare + 16 DFR)			
Contrast	Cluster	Median %	Adj. p (GLMM)
Flare onset vs baseline: Flare patients	CD4+/CD45RO+/PD1+ memory T cells	2.14 vs 0.24	<0.001
	CD8+/CD45RO+/PD1+ memory T cells	6.64 vs 0.07	<0.001
	CD19+/CD27+/CD21- memory B cells	2.39 vs 0.03	<0.001
Single cell RNAseq (n = 8 flare + 4 DFR)			
Contrast	Cluster	Median %	Adj. p (Wilcoxon)
Flare onset vs baseline: Flare patients	IgA+ plasma cells	0.37 vs 0.21	0.020
Flare vs DFR patients: Baseline	CD4+/CD25+/Foxp3+ Treg cells	0.55 vs 1.27	0.022

To better characterise these flare-associated subsets, single cell sequencing of CD45RO+/PD1hi CD4+ and CD8+ T cells, and CD19+ B cells, was performed and identified 21 distinct clusters. CDR3 sequencing revealed significant clonal expansion (Fisher exact, adj. p < 0.05) at flare onset within five unique CD8+ clones (4 patients), one CD4+ clone (1 patent), and no B clones. Overall, there was a significantly greater proportion of IgA+ plasma cells at flare onset versus baseline. In contrast, a significantly lower proportion of CD25+/FoxP3+ regulatory T cells were present at csDMARD cessation (baseline) in subsequent flare versus DFR patients (Table 1), suggesting biomarker potential.
To further assess the predictive performance of CD4+ Tregs as a biomarker for flare versus DFR, we analysed PBMCs from an independent cohort of 50 patients (25 flare, 25 DFR) stopping csDMARDs in the ongoing BIO-FLARE study.[2] By flow cytometry, we confirmed a lower proportion of CD4+/CD25hi Tregs at baseline in flare vs DFR (median 4.74 versus 6.37%, Wilcoxon p = 0.037; AUC: 0.67). In this cohort, stopping csDMARDs only in patients with elevated (> 6.11% total CD4) baseline Tregs would have prevented drug cessation in 18/25 (72%) of flare patients; 9/25 (36%) of DFR patients would have continued csDMARDs unnecessarily.
Conclusion: We present a detailed longitudinal characterisation of circulating lymphocyte surface phenotype, gene expression, and clonal expansion in RA flare vs DFR. Furthermore our data, across two independent cohorts, suggests a role for CD4+ Tregs in promoting drug-free remission meriting further investigation, with potential for future clinical biomarker development.
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Acknowledgements: This work was funded by research grants from Wellcome Trust [102595/Z/13/A to KFB], Newcastle NIHR Biomedical Research Centre [BH136167/PD0045 to KFB], British Society for Rheumatology [KFB], Academy of Medical Sciences [SGL022\1074 to KFB], Newcastle University Wellcome Trust Translational Partnership [KFB], Newcastle Hospitals Charity [8033 to KFB], and a National Institute for Health Research Clinical Lectureship [CL-2017-01-004 to KFB]. Our work is supported by the Research into Inflammatory Arthritis Centre Versus Arthritis (RACE) (grant number 20298), and Rheuma Tolerance for Cure (European Union Innovative Medicines Initiative 2, grant number 777357). AGP and JDI are named as inventors on a patent application by Newcastle University ("Prediction of Drug-Free Remission in Rheumatoid Arthritis"; International Patent Application Number PCT/GB2019/050902). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health and Social Care.
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OP0075 FIBROBLAST/MACROPHAGE CROSSTALK VIA LACTATE: NEW THERAPEUTIC TARGET IN RHEUMATOID ARTHRITIS

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Background: The synovial membrane is the principal site of inflammation in rheumatoid arthritis (RA) and distinct subsets of fibroblasts and macrophages, with different effector functions, have been described within it[1,2,3]. Inflammation renders the RA synovial microenvironment hypoxic and acidic, with increased levels of lactate, the end product of glycolysis. Lactate acts as an immunomodulatory molecule within the synovium[4], interacting with lactate transporters present on fibroblasts and macrophages to regulate their function, movement and metabolism.
Objectives: To test whether dysfunctional crosstalk between fibroblasts and macrophages, driven by lactate, promotes the persistence of synovial inflammation.
Methods: Synovial tissues (n = 8) from patients fulfilling the 2010 ACR/EULAR RA criteria were obtained by ultrasound-guided synovial biopsy. Osteoarthritis (OA) synovial tissues of subjects undergoing joint replacement were used as control group. Monocarboxylate transporter 1 (MCT)1 and MCT4 expression on fibroblasts and macrophages was assessed via confocal microscopy. We used RA synovial fibroblasts and monocyte-derived macrophages to test the effect of lactate in vitro. Migration was assessed in trans-well plates or via scratch test assays. Seahorse was used to evaluate metabolic pathways. IL6 production was measured by ELISA. Bioinformatic data were confirmed on publicly available scRNAseq datasets.
Results: We showed that: i) The expression of MCT1 and MCT4 which regulate lactate import and export respectively, is up-regulated upon inflammation. ii) Fibroblasts preferentially express MCT1, while MCT4 is more highly expressed by macrophages. iii) Lactate, at the concentration found in RA synovial fluid (10 mM), has divergent effects on the effector functions of these two cell types. In fibroblasts, lactate promotes IL6 production and cell motility; these effects are reduced by pre-treatment with a pan-lactate transporter inhibitor. In contrast macrophages respond to lactate by reducing migration, IL6 secretion and glycolysis.
Conclusion: The contrasting effects of lactate on macrophage and fibroblast migration, IL6 production and metabolism suggest that lactate represents a key

metabolite ensuring linked choreography between fibroblast and macrophage movement in the synovium which may become uncoupled in disease. We propose that dysfunctional crosstalk between these two cell types due to high lactate levels, promotes inflammation and the establishment of persistent disease in RA. Targeting lactate/MCTs pathway may provide a novel therapeutic strategy, to restore cellular crosstalk and to reduce inflammation in RA patients.

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Disclosure of Interests: Valentina Pucino: None declared, Meriam Nefla: None declared, Vincent Gauthier: None declared, Sally A Clayton: None declared, Andrew Filer Consultant of: Abbvie, Roche, Janssen, Grant/research support from: Roche, UCB, Nascient, Mestag, GSK, Janssen, Andy R Clark: None declared, Karim Raza: None declared, Christopher D Buckley Consultant of: GSK, Astra-Zenica, Roche, Pfizer, Lilly, Janssen Mestag, Grant/research support from: GSK, Roche, Pfizer, Janssen Mestag.
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OP0076 L-ARGININE REPROGRAMS OSTEOCLAST PURINE METABOLISM AMELIORATING BONE LOSS IN RHEUMATOID ARTHRITIS

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Background: Bone erosion is a clinical feature of rheumatoid arthritis related to disease severity and poor functional prognosis. Excessive osteoclast differentiation and insufficient osteoblast function are the main reasons for the erosive process in RA. Our previous investigation indicated that L-arginine supplementation not only diminished arthritic inflammation in the serum-induced arthritis (K/BxN) model but also decreased inflammatory joints osteoclast numbers (1).
Objectives: In the present study, we aim to investigate the metabolic action of L-arginine supplementation in RA, especially on periarticular bone erosion and systemic bone loss. We plan to depict the metabolic features of TNFα induced inflammatory osteoclasts after *in vitro* L-arginine supplementation.
Methods: Three murine arthritis models (serum-induced arthritis (K/BxN) model, collagen-induced arthritis model, and hTNFtg mice model) were analysed in this study. L-arginine was supplemented within the drinking water after the onset of arthritis. Bone parameters for axial skeleton (spine) and peripheral skeleton (tibia) from the respective group were quantified by µCT. HE and TRAP staining were performed to address further the erosion area and osteoclast numbers in periarticular sites. *In vitro* osteoclast differentiation was conducted with or without L-arginine treatment, in the presence or not of TNFα activation. Seahorse and SCENITH analyses were adopted to delineate the metabolic features. JC-1 staining and transmission electron microscopy (TEM) were used to depict the mitochondria metabolism. RNA-seq and mass spectrometry (MS) were performed to investigate the underlying molecular mechanism.
Results: Inflammation was diminished in all three arthritis models after L-arginine supplementation with a significant reduction in arthritic score. Moreover, an amelioration of periarticular bone erosion, systemic bone loss, and decreased osteoclast numbers in periarticular sites were observed in arthritic mice after L-arginine treatment. L-arginine also inhibited osteoclastogenesis *in vitro*, particularly under TNFα activation. Seahorse and SCENITH analyses indicated TNFα promoted glycolysis while blocking mitochondria-driven oxidative phosphorylations (OXPHOS) in pre-osteoclasts. Meanwhile, JC-1 staining and TEM images also showed that TNFα decreased mitochondria membrane potential and prompted damage of mitochondria. Surprisingly, L-arginine rescued the TNFα inhibition of OXPHOS while promoting ATP production. RNA-seq and MS data confirmed the boost of OXPHOS after L-arginine treatment under TNFα activation. To interfere with OXPHOS, L-arginine inhibited cJun thus altered arginase-1 and arginase-2 expression. Moreover, the increased ATP in L-arginine treated cells facilitated purine metabolism, especially the production of inosine and hypoxanthine, contributing to the inhibition of osteoclastogenesis. Increasing Adenosine deaminase (ADA) is essential for the production of inosine and hypoxanthine due to the decreased inhibitory regulation of the transcription factor c-Jun.
Conclusion: These data strongly demonstrated that L-arginine ameliorates bone erosion in RA through metabolic reprogramming and perturbation of purine metabolism in osteoclasts. L-arginine might therefore benefit RA therapy by reducing joint inflammation and also ameliorating bone destruction.

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OP0077 SYNOVIAL RNA-SEQ ANALYSIS OF THE R4RA TRIAL IDENTIFIES SIGNATURES OF TREATMENT RESISTANCE AND REFRACTORY STATE IN RHEUMATOID ARTHRITIS

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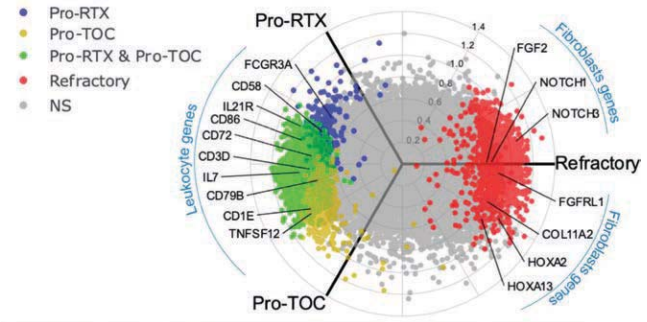
Background: Although up to 5-20% of rheumatoid arthritis (RA) patients do not respond to all current medications including biologic therapies, relatively little is known about the underlying pathogenic mechanisms driving non-response. In the first biopsy-driven randomized clinical trial in RA (R4RA)[1], patients, in whom synthetic-DMARDs and at least one anti-TNF drug were not effective, were randomised 1:1 to rituximab (RTX) or tocilizumab (TOC) with a balanced stratification based on their synovial B-cell rich/poor signature, and response was assessed at 16 weeks. Non-responders were subsequently allowed to switch to the alternative drug with 48-week follow-up.
Objectives: Investigate mechanisms of response and non-response to RTX and TOC through deep molecular (RNA-Sequencing) profiling of synovial tissue.
Methods: RNA-Seq from baseline synovial tissue biopsies of patients who received RTX (n=88) or TOC (n=94) at any point in the trial was analysed for differentially expressed genes and associated modules between responders and non-responders. Response was defined as 50% improvement in clinical disease activity index (CDAI) score. Patients who had received both drugs during the trial were subdivided into RTX only responders (pro-RTX, n=9), TOC only responders (pro-TOC, n=12) and refractory patients (no response to both RTX & TOC, n=32) and analysed for differential gene expression and performed gene module analysis.
Results: 6625 genes were significantly differentially expressed between RTX responders compared to non-responders, with a predominance of antigen presentation as well as T- and B-cell genes being associated with response, while non-response was linked to fibroblast associated genes. Comparison between TOC responders and non-responders identified fewer (85) differentially expressed genes, however lymphocyte and immunoglobulin genes were also high in the synovial tissue of TOC responders similar to RTX responders, while non-responder genes and modules also included a fibroblast signature. The cross-over study design enabled comparison of rituximab-specific responders (pro-RTX), tocilizumab-specific responders (pro-TOC) and refractory patients (non-responders to both RTX & TOC, n=32) in a 3-way analysis (see Figure 1). This identified 1980 genes upregulated both in pro-RTX and pro-TOC patients, 175 genes exclusive to the pro-RTX group and 306 to the pro-TOC group, while 1277 genes were exclusive to the refractory group. While leukocyte modules and genes dominated RTX & TOC response, the refractory state was strongly associated with fibroblast genes and modules. We confirmed the observed expansion of fibroblasts from the RNA-Seq data by immunohistochemistry showing the presence of DKK3+ sublining fibroblasts in refractory rather than responder patients.



Polar plot of 3-way differential gene expression analysis on baseline synovial biopsies.
Polar plot showing analysis of RNA-Seq TPM counts tested for differential expression by DESeq2, comparing patients who failed tocilizumab and responded to rituximab (pro-RTX, blue if False Discovery Rate <0.05), who failed rituximab but responded to tocilizumab (pro-TOC, yellow if FDR<0.05), or who failed both drugs (refractory, red if FDR<0.05).
Genes in green show significant genes overlapping in pro-RTX and pro-TOC patients and genes in grey are statistically non-significant.

Conclusion: We provide novel insights into the cellular and molecular pathways underpinning multi-biologic resistance that define a refractory RA phenotype, characterised by a stromal/fibroblast signature.

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OP0078 ALTERED IMMUNOLOGICAL CIRCADIAN RHYTHMS AND THE EFFECT OF TREATMENT WITH GLUCOCORTICOIDS ON CIRCADIAN RHYTHMS OF IMMUNE CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS: BRING BACK THE RHYTHM

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Background: In rheumatoid arthritis (RA), pain, joint swelling, and stiffness follow a clear circadian pattern. Most of these symptoms are most pronounced in the early morning and primarily attributed to elevated levels of the key proinflammatory cytokines IL-6 and TNFα, which usually peak before clinical symptoms worsen (1). Synthetic glucocorticoids (GCs) are among the most prescribed drugs in the management of patients with RA. GCs have effects on almost every immune cell. GCs suppress expression of various cytokines, including IL-1β, TNFα, IL-6, and GM-CSF. Moreover, circadian rhythms of immune cells are known to be influenced by GCs. For example, GCs govern in part the rhythm of circulating CD4+ and CD8+ T cells.
Objectives: To identify circadian patterns for optimization of diagnosis and treatment strategies, we conducted a clinical study comparing healthy donors (HD) and patients with RA in terms of circadian rhythms. We examined the effect of treatment with GCs on circadian immune rhythms in patients with RA.
Methods: We recruited 12 HD and 13 patients with active RA (DAS28≥4.0) who either were (n=8) or, for comparison, were not (n=5) under current treatment with GCs. Their biological clock was synchronized for a week before the study day by a scheduled sleep and mealtime regimen. On the study day, participants were provided with regular meals, allowed to eat snacks ad libitum and carry passive activities. We collected blood samples every two hours over a period of 24 hours. The absolute number of circulating immune cells, clock gene expression, and serum cytokine levels were measured with TruCount, qPCR, and multiplex suspension assay, respectively.
Results: Peripheral regulatory T cells are circadian in HD and RA, but the number was notably reduced in RA (Table 1). $CD8^+$ T cells, $CD14^+$ monocytes, and $CD19^+$ B cells lost their circadian rhythms in RA, but these rhythms were restored with GC treatment. Circulating NK and NK T cells, which are not diurnal in HD, exhibited circadian fluctuations in RA. GC treatment suppressed diurnal pathological circulation rhythms of NK and NK T cells by reducing the amplitude by half. In monocytes, *BMAL1*, *PER1*, *PER2*, and *REVERBA* are only circadian in HD. GC restored the rhythms of *PER2* and *REVERBA*. *CRY1* expression showed diurnal variation in RA, but not in HD. IL-6 exhibited a circadian pattern in both groups, and GC treatment showed no significant effects on IL-6. Serum IL-4, IL-5, and MIP3α showed circadian variation in HD only. The following cytokines were notably elevated in RA-patients: IFNγ, MIP1α, MIP1β, IL-1β, IL-2, IL-17A, and IL-21. GC reduced the expression of IL-10 significantly in RA.

Table 1. ***Circadian rhythms in the cellular, gene, and protein levels in HD, RA, and RA with ongoing GC treatment***

Comparison	Circadian / GC impact	Circulating immune cells	Clock genes in monocytes	Serum cytokines
HD *vs.* RA	Non-circadian in HD and RA	-	*CLOCK, CRY2, DBP, RORA*	Fractaline, IFNγ, CXCL11, GM-CSF, MIP1α, MIP1β, IL-1β, IL-2, IL-4, IL-7, IL-8, IL-10, IL-12, IL-13, IL-17A, IL-21, IL-23
	Circadian in HD and RA	$CD3^+$, $CD4^+$, regulatory T cells	*PER3*	IL-6
	Circadian in HD	$CD8^+$ T cells, $CD14^+$ monocytes, $CD19^+$ B cells	*BMAL1,PER1, PER2, REVERBA*	IL-4, IL-5, MIP3α
	Circadian in RA	NK cells, NK T cells	*CRY1*	-
RA *vs.* GCs-treated RA	Restorative effect by GC	$CD8^+$ T cells, $CD19^+$ B cells	*PER2, REVERBA*	-
	Enhancing effect by GC	regulatory T cells	*PER3, CRY1*	-
	Dampening effect by GC	NK T cells, NK cells	-	-

Conclusion: In patients with RA, we found a certain loss of circadian rhythms and the establishment of "inflammatory" rhythms. GC treatment in patients with RA resulted in three different types of effects on circadian rhythms at immune cell level: restoration, amplification, and attenuation. In conclusion, these findings provide new insights into the pathophysiology of circadian rhythms in RA that could be used to optimize diagnosis and treatment.

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OP0079 SYNOVIAL FIBROBLASTS – T CELL INTERACTIONS ARE MAJOR DRIVERS OF INFLAMMATION: A CLOSER LOOK INTO THE JOINT

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disease, which is characterized by synovial inflammation resulting in bone and cartilage destruction. Crosstalk between activated fibroblast-like synoviocytes (FLS) and immune cells, such as $CD4^+$ T cells, within the synovium might amplify synovial inflammation and joint destruction.
Objectives: To define the interaction profile of activated FLS and $CD4^+$ T cells within an inflammatory setting and to elucidate its consequence on synovial inflammation.
Methods: To screen for factors that activate FLS in RA, isolated FLS were treated with different inflammatory cytokines and transcriptomic changes were measured with RNA-seq. Fluorescence activated cell sorting (FACS) purified naïve $CD4^+$ T-cells from the same patients were co-cultured with the cytokine pre-treated FLS. Automated fluorescence microscopy and downstream bioinformatic image analysis allowed visualization and quantification of cell-cell interactions. After co-culture T-cells were isolated and T-cell activation, proliferation and differentiation was determined by flow cytometry.
Results: To model the *in vivo* situation, FLS were pre-stimulated with different pro- and anti-inflammatory cytokines. RNA-seq revealed cytokine specific activation patterns of FLS. Correspondingly, we observed distinct $CD4^+$ T cells – FLS interaction profiles depending on the cytokine used for FLS activation. In line with distinct interaction profiles, specific patterns in $CD4^+$ T cells activation, proliferation and differentiation of naïve T cells into $CD62L^{high}$ $CD45RO^{high}$ memory T cells could be detected. Signatures of cytokine-stimulated FLS could be identified in transcriptomic data from synovial tissue samples.
Conclusion: Within this study, we describe how cytokine induced $CD4^+$ T cells – FLS interactions impact on T-cell proliferation, activation and differentiation.

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OP0080 STAT3 DEGRADERS INHIBIT TH17 DEVELOPMENT AND CYTOKINE PRODUCTION RESULTING IN PROFOUND INHIBITION OF COLLAGEN-INDUCED AUTOIMMUNE MURINE ARTHRITIS

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Background: Signal transducer and activator of transcription 3 (STAT3) is a transcription factor that belongs to a class of targets devoid of catalytic function, thus deemed "undruggable" by standard modalities such as small molecule inhibitors or biologics. STAT3 can be activated by various receptor- and non-receptor tyrosine kinases, playing a critical role in activation pathways triggered by cytokines, hormones, and growth factors, making it an attractive target for the treatment of inflammatory diseases.
Objectives: Kymera has developed heterobifunctional molecules that selectively target STAT3 for degradation and elimination by the ubiquitin-proteasome pathway. We sought to evaluate the pharmacologic potential of these STAT3 degraders through in vitro and in vivo studies relevant to human autoimmune disease, including murine collagen-induced arthritis.
Methods: We evaluated the impact of STAT3 degraders on the activation of human monocytes, dermal fibroblasts, CD4+ T cells, and PBMC by LPS, IL-6/IL-6R, IL-21, IL-23, as well as anti-CD3/CD28 plus a cocktail of cytokines and antibodies. STAT3 degradation and pSTAT3 inhibition were determined in comparison to a JAK1/2 small molecule inhibitor. Inhibition of cytokines, chemokines, and collagen release, as well as Th17 (CD4+CD25-RORγt+CXCR6+) and Treg (CD4+CD25+CD127lowFOXP3+) expansion were used as in vitro efficacy assays. Finally, STAT3 degraders were tested in vivo, in a mechanistic (IL-6 challenge) as well as a disease model (murine CIA) relevant to rheumatology indications.
Results: STAT3 degraders showed broad and potent activity *in-vitro* against TLR receptor and cytokine-induced activation of immune and stromal cells, including soluble mediator release such as MCP-1/CCL2 and Collagen1a1. STAT3 degradation in CD4+ T cells robustly inhibited the development of Th17 cells, abrogating IL-17, IL-22, IL-8/CXCL8, and TNFα production, and increased Treg numbers in a manner superior to JAK1/2 inhibition. In mice injected with IL-6, plasma levels of serum amyloid A were dose-dependently suppressed by STAT3 degradation. In the murine collagen-induced arthritis model, STAT3 degradation resulted in robust, dose-dependent delay of disease onset and decreased disease incidence, clinical scores, local cytokine expression (paws) and histopathological scores, including the complete alleviation of periosteal bone growth.
Conclusion: These data demonstrate the broad activity of STAT3 degradation in alleviating autoimmune inflammation in models relevant to human disease. Targeted protein degradation of STAT3 thus represents a novel therapeutic approach to treating autoimmune/autoinflammatory diseases such as rheumatoid arthritis.
Disclosure of Interests: Cedric Hubeau Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Jeffrey Sullivan Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Crystal Brown Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Michele Mayo Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Vaishali Dixit Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Bradley Enerson Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Haojing Rong Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Bin Yang Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Chris De Savi Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Jared Gollob Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Nello Mainolfi Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics, Anthony Slavin Shareholder of: Kymera Therapeutics, Employee of: Kymera Therapeutics.
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OP0081 IL-13 REDUCES BONE EROSION IN RHEUMATOID ARTHRITIS BY UP-REGULATING OPG IN SYNOVIAL FIBROBLASTS

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Background: Bone erosion in rheumatoid arthritis (RA) is partly caused by excessive activation of osteoclasts[1]. Osteoclasts can be derived from RA synovium and their differentiation can be inhibited by OPG, a decoy receptor of the osteoclastogenesis promoting cytokine RANKL[2,3]. Fibroblast-like synoviocytes (FLSs) are a main type of stromal cells in the synovium that can secret OPG[4]. The OPG secretion by FLSs can be modulated by various cytokines[5]. Interleukin (IL)-13 is a cytokine rich in early RA synovial fluid and it decreases as RA progresses[6]. IL-13 was reported to alleviate bone erosion in RA mouse models[7]. However, how IL-13 reduces bone destruction remains unclear.
Objectives: To investigate if IL-13 can inhibit osteoclast differentiation by up-regulating OPG in FLSs of RA patients (RA-FLSs), thus reduces bone erosion in RA.
Methods: FLSs were isolated from the synovium tissue of RA patients with informed consent who underwent joint replacement surgery (Ethics No. 2021-544-01). OPG and RANKL expression by RA-FLSs were evaluated by qRT-PCR. OPG secretion was determined by ELISA. Western blot was performed to analyze OPG expression and the activation of STAT6 pathway. IL-13 and OPG siRNA pre-treated RA-FLSs conditioned medium were used in osteoclast induction to test if IL-13 can inhibit osteoclastogenesis by up-regulating OPG in RA-FLSs. Micro-CT scanning and immunofluorescence were done to determine if IL-13 can induce OPG expression and alleviate bone erosion in vivo.
Results: IL-13 can significantly upregulate OPG expression and secretion by RA-FLSs. Meanwhile, RANKL/OPG ratio was downregulated (Figure 1A). STAT6 phosphorylation and OPG upregulation of RA-FLSs by IL-13 can be significantly inhibited by a STAT6 inhibitor (inh.) (Figure 1B). IL-13 receptor α1 (IL-13Rα1) and IL-13 receptor α2 (IL-13Rα2) knockdown can inhibit OPG upregulation by IL-13 in RA-FLSs, indicating that IL-13 can induce OPG secretion in RA-FLSs through IL-13Rα1 and IL-13Rα2 via STAT6 pathway (Figure 1C). 20% conditioned medium of RA-FLSs pretreated by IL-13 can significantly inhibited osteoclast differentiation in vitro. OPG knockdown in RA-FLSs significantly reversed the inhibition, indicating that IL-13 inhibits osteoclastogenesis by upregulating OPG in RA-FLSs (Figure 1D). In collagen-induced arthritis mice, IL-13 injection can reduce bone destruction in the ankle joint. Meanwhile, OPG expression in vemintin positive FLSs was increased (Figure 1E and F).

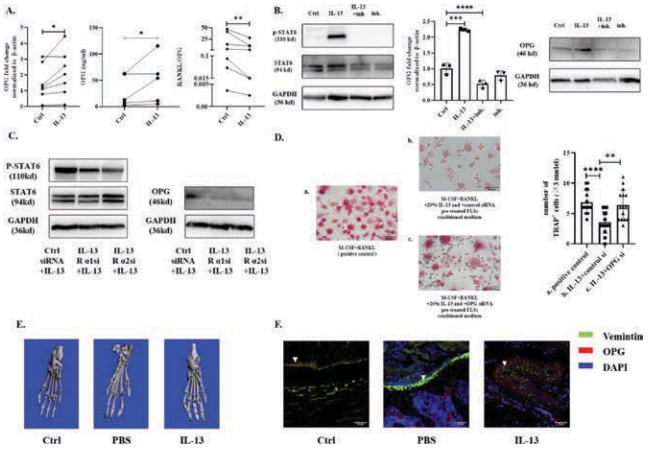

Figure 1.

Conclusion: IL-13 can inhibit osteoclastogenesis by up-regulating OPG in RA-FLSs through IL-13 receptors via STAT6 pathway, thus ameliorate bone erosion in RA.
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Rheumatoid arthritis - prognosis and prediction

OP0082 DISCORDANCE BETWEEN DAS28ESR AND PRESENCE OF ULTRASOUND POWER DOPPLER DURING EARLY TREATMENT IS ASSOCIATED WITH DISTINCT CLINICAL AND IMAGING PHENOTYPES AT PRESENTATION

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Background: Discordance between DAS28ESR and musculoskeletal ultrasound (MSUS) detected power Doppler synovitis (PDUS) is well-recognised and may lead to under/overtreatment. We hypothesize that clinical and imaging features at diagnosis associate with early discordance of DAS28-PDUS and change in DAS28-PDUS status following DMARD treatment.
Objectives: To identify pre-treatment clinical factors associated with discordance and change in DAS28-PDUS status during early treatment in an early RA trial cohort.
Methods: The 'VEDERA' trial[1] randomised 120 treatment-naïve, new-onset RA patients to either first-line etanercept + methotrexate (ETN+MTX) or methotrexate treat-to-target (MTX-TT) regime with escalation to ETN+MTX if not in DAS28ESR remission at week 24. Clinical and MSUS assessments were completed at baseline, weeks 12, 24 and 48. DAS28ESR ≤ 2.6 and DAS28ESR > 2.6 categorised remission and active disease respectively. PDUS presence was defined as total PDUS score ≥ 1. Active concordance (AC) was defined as active disease with PDUS while active discordance (AD) was defined as active disease without PDUS. Remission concordance (RC) was defined as DAS28ESR remission without PDUS while remission discordance (RD) was defined as DAS28ESR remission with PDUS. Bayesian multinomial logistic regression (posterior estimate and 95% credible intervals reported) was used to address the study objectives with AC as the comparator group.
Results: At baseline all patients had active disease (moderate or high DAS-28ESR) in line with trial eligibility - 68% (81/120) were AC and 32% (39/120) were AD. Compared to AD patients, AC patients were older (median age 53 vs 44), had higher DAS28ESR (5.90 vs 5.16) and CRP (11.6mg/L vs 3.6mg/L), as well as a higher presence of greyscale (GS - 100% vs 67%), power Doppler tenosynovitis (PDTS - 78% vs 49%) and erosions (20% vs 0) ($p < 0.01$). Figure 1 illustrates the pre-treatment proportions and change in group proportions at each timepoint, revealing an early shift of AC to AD (36% by week 12) or RC (22% by week 12) but persistence of those in AD from baseline at subsequent timepoints (64% at week 12). Baseline characteristics associated with each group compared to the comparator AC group (at weeks 12, 24 and 48) are reported in Table 1. For AD versus AC these were lower CRP at week 12 and female sex at week 24. For RC versus AC these were lower CRP and allocation to ETN+MTX at week 12, allocation to ETN+MTX and presence of PDTS at week 24 and younger age at week 48. For RD versus AC these were presence of PDTS at week 24 and male sex at week 48.

Table 1. Baseline characteristics associated with longitudinal discordance vs concordance. AC is the comparator group. Results in posterior estimate with 95% credible intervals

	Week 12	Week 24	Week 48
AD vs AC			
Female	0.53 (-0.44 to 1.48)	**1.52 (0.51 to 2.59)**	0.17(-0.91 to 1.25)
CRP	**-0.05 (-0.1 to -0.01)**	-0.01 (-0.04 to 0.05)	0.01(-0.02 to 0.02)
RC vs AC			
Age at diagnosis	-0.04(-0.09 to 0.01)	-0.02(-0.06 to 0.03)	**-0.08(-0.13 to -0.03)**
CRP	**-0.05 (-0.10 to -0.01)**	0.001(-0.04 to 0.03)	0.01(-0.02 to 0.04)
ETN+MTX	**1.57, (0.57 to 2.64)**	**1.26, (0.29 to 2.33)**	0.91(-0.02 to 1.85)
PDTS	0.58 (-0.5 to 1.68)	**1.23(0.2 to 2.29)**	0.8 (-0.2 to 1.83)
RD vs AC			
Female	0.23 (-1.26 to 1.72)	0.9 (-0.41 to 2.26)	**-1.59(-2.9 to -0.35)**
PDTS	1.00 (-0.55 to 2.69)	**1.79 (0.44 to 3.33)**	0.95(-0.29 to 2.27)

Conclusion: DAS28ESR and PDUS discordance and concordance have distinct clinical and imaging phenotypes at presentation. Baseline active concordance and discordance respond differently to treatment –a sizeable proportion of former transition into active discordance early on and the latter persist in the face of effective treatment. Understanding the basis for these phenotypes is essential to facilitate optimal aggressive treatment and/or alternative management strategies.

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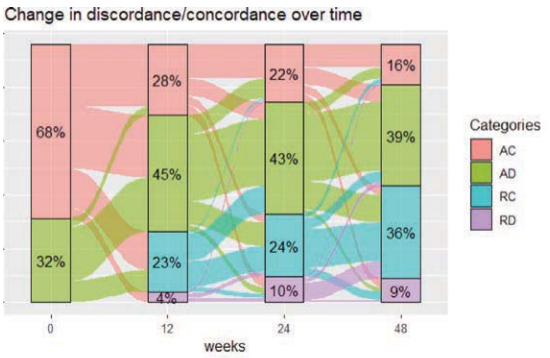

Figure 1: Proportion in different discordant/concordant groups from baseline to week 48. AC: active concordance, AD: active discordance, RC: remission concordance, RD: remission discordance.

Disclosure of Interests: None declared.
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OP0083 HAND AND FOOT MRI IN CONTEMPORARY UNDIFFERENTIATED ARTHRITIS: IN WHICH PATIENTS IS MRI VALUABLE TO DETECT RHEUMATOID ARTHRITIS EARLY? – A LARGE PROSPECTIVE STUDY

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Background: Identifying patients that will develop rheumatoid arthritis(RA) among those presenting with undifferentiated-arthritis(UA) remains a clinical dilemma. Although magnetic-resonance-imaging(MRI) is helpful according to EULAR-recommendations, this has only been determined in UA-patients not fulfilling 1987-RA-criteria, whilst part of these patients are currently considered as RA because they fulfill the 2010-criteria.
Objectives: We studied the predictive value of MRI for progression to RA in the current UA-population: i.e. not fulfilling RA-classification-criteria (neither 1987- or 2010-criteria), and not having an alternate diagnosis. Additionally, the value of MRI was studied in patients with a clinical diagnosis of UA, regardless of the classification-criteria.
Methods: Two UA-populations were studied: criteria-based-UA as described above(n=405) and expert-opinion-based-UA(n=564), i.e. UA indicated by treating rheumatologists. These patients were retrieved from a large cohort of consecutively included early arthritis patients that underwent contrast-enhanced MRI-scans of hand and foot at baseline. MRIs were scored for osteitis, synovitis and tenosynovitis. Patients were followed for RA-development during 1-year. Test-characteristics of MRI were determined separately for subgroups based on joint-involvement and autoantibody-status.
Results: Among criteria-based-UA-patients(n=405), 21% developed RA. MRI-detected synovitis and MRI-detected tenosynovitis were predictive. MRI-detected tenosynovitis was independently associated with RA-progression(OR 2.79; 95%CI 1.40-5.58), especially within ACPA-negative UA-patients(OR 2.91; 1.42-5.96). Prior risks of RA-development for UA-patients with mono-/oligo-/polyarthritis were 3%, 19%, 46%, respectively. MRI-results changed this risk most within the oligoarthritis-subgroup: PPV was 27% and NPV 93%. Similar results were found in expert-opinion-based-UA(n=564).
Conclusion: This large cohort-study showed that MRI is most valuable in ACPA-negative UA-patients with oligoarthritis; a negative MRI could aid in preventing overtreatment.

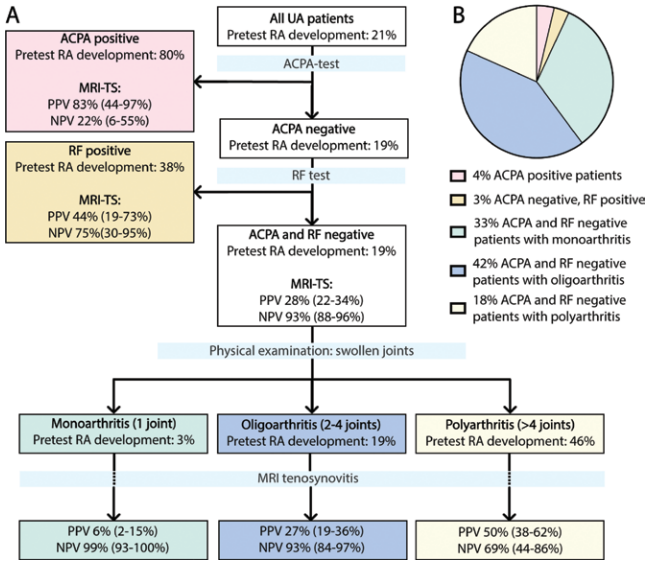

Figure 1. Flowchart for criteria-based UA-patients showing pre-test and post-test predictive-value for RA-development (A) and percentages of patients within these subgroups (B). 1A) Flowchart with NPV and PPV for MRI-detected tenosynovitis within the specified groups. Pretest-probability of developing RA is shown as a percentage of patients fulfilling 1987 and/or 2010 RA-criteria. 1B) A total of 404 patients were studied, 15 patients were ACPA-positive(4%), 13 patients were ACPA-negative and RF-positive(3%), 376 patients were ACPA- and RF-negative(93%), from which 133 patients had monoarthritis (1 swollen joint, 33%), 169 patients had oligoarthritis (2-4 swollen joints, 42%) and 74 patients had polyarthritis (more than 4 joints, 18%). 1 patient is missing in this analysis due to missing outcome for MRI-detected tenosynovitis, this patient belonged in the oligoarthritis group. *UA, Undifferentiated arthritis; RA, Rheumatoid Arthritis; ACPA, Anti-Citrullinated Peptide Antibodies (considered positive if ≥10U/mL); RF, Rheumatoid Factor (considered positive if ≥5.0IU/mL); MRI-TS, MRI detected tenosynovitis; NPV, negative predictive value; PPV, positive predictive value; Swollen joints, based on a 68-swollen joint count.*

Disclosure of Interests: None declared.

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OP0084 DIGITAL SPATIAL PROFILING REVEALS DISTINCT SYNOVIAL TISSUE MACROPHAGE TRANSCRIPTOMIC SIGNATURE OF SUSTAINED REMISSION IN RHEUMATOID ARTHRITIS PATIENTS AT RISK OF DISEASE FLARE AFTER TREATMENT CESSATION

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Background: Sustained remission is the treatment goal for Rheumatoid Arthritis (RA) and once achieved patients are eligible to treatment tapering or discontinuation. However, this exposes patients to the occurrence of unpredictable disease flare, and to date there are no definitive predictive biomarkers of flare for RA in remission that could be used in clinical practice.

Objectives: To assess the impact of clinical classification of remission on synovial tissue (ST) features of RA in sustained remission and to identify predictive biomarkers of disease flare.

Methods: 200 RA in sustained clinical (102 RA with DAS<1.6 and 98 RA fulfilling Boolean remission criteria for at least 9 months, respectively) and ultrasound (US) remission (PD negative) under Methotrexate with or without biological-Disease Modifying Anti-Rheumatic Drugs (bDMARDs) were enrolled and underwent to US guided ST biopsy. 373 naive RA were included as comparison. For each patient, synovitis degree was determined using a H&E-based semiquantitative score[1]. Some ST samples of remission RA were used for synovial tissue macrophage (STMs)(CD206/MerTK) FACS phenotyping and digital spatial profiling (GeoMx DSP, Nanostring) to quantitate transcript abundance of $CD68^{pos}$ cells in 138 spatially distinct ST regions of interest (ROI). After study entry, RA were randomly assigned to tapering/discontinuation (TAP/DISC) (tapering c- or b-DMARD treatment for 6 months and discontinuing c- or bDMARD afterwards) or maintaining the same therapeutic scheme (CONT). Each RA was followed every 3 months to assess flare rate after treatment modifications for 24 months.

Results: Regardless of either DAS- or Boolean-defined, remission patients had significantly lower KSS than naive RA (p<0.0001 for both). However, ST of RA in Boolean remission had lower KSS (p<0.0001) and was enriched in $CD206^{pos}MerTK^{pos}$ STMs (p=0.0012) as compared to DAS-defined remission RA. 73(36.5%) RA experienced a disease flare regardless of the treatment change during 24 months follow-up. Stratifying RA in remission based on remission definition and treatment group, DAS-defined remission RA who had a disease flare within at least 6 months follow-up had, at study entry, significantly higher KSS (p<0.0001) than RA who maintained a sustained remission, regardless of the treatment change (CONT:p=0.0027 and TAP/DISC:p=0.0011). Logistic regression analysis revealed that baseline KSS≥3 [AUC:0.748(95%CI:0.649-0.846)p<0.0001] was an independent predictive factor of disease flare [OR:6.9(95%CI:2.82-16.81)] within 24 months follow-up in DAS-defined remission RA. Conversely, RA in Boolean remission did not differ for KSS at study entry in both the CONT (p>0.05) and the TAP/DISC (p>0.05) group in relation to disease flare. However, considering STMs phenotype, RA in Boolean remission in the TAP/DISC group who had low levels of $CD206^{pos}MerTK^{pos}$ (<38.1%), experienced more likely a disease flare compared to RA in the CONT subgroup with $CD206^{pos}MerTK^{pos}$≥38.1% (p=0.0014). Logistic regression analysis confirmed that, before treatment change, STMs phenotype ($CD206^{pos}MerTK^{pos}$ <38.1%) in RA in remission is an independent predictor of disease flare [OR:6.25(95%CI:1.33-29.43)] within 24 months. Finally, DSP analysis using CD68 morphology marker, revealed that lining and sublining layer $CD68^{pos}$ spatial transcriptomics distinguished, at baseline, remission RA who flared after treatment modification from those who did not.

Conclusion: Disease flare is a common event in RA in sustained remission after treatment modification. KSS and STMs phenotype identified by flow cytometry or by tissue spatial transcriptomic can identify RA in remission at higher risk of flare after treatment modification. Thus, spatial transcriptomic with defined panel of markers on histological biopsy tissues could be a way forward in predicting disease flare.

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OP0085 CELL LINEAGE-SPECIFIC TRANSCRIPT DECONVOLUTION OF SYNOVIAL BIOPSIES FROM THE R4RA TRIAL IDENTIFIES CELL POPULATIONS ASSOCIATED WITH RESPONSE TO RITUXIMAB AND TOCILIZUMAB

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Background: The R4RA trial, the first biopsy-based randomised trial in TNF-i inadequate responder patients with Rheumatoid Arthritis, showed that molecular stratification of RA synovial tissue was associated with clinical response, demonstrating that, in patients with low/absent B-cell lineage signature in synovial-tissue, tocilizumab is superior to rituximab[1].

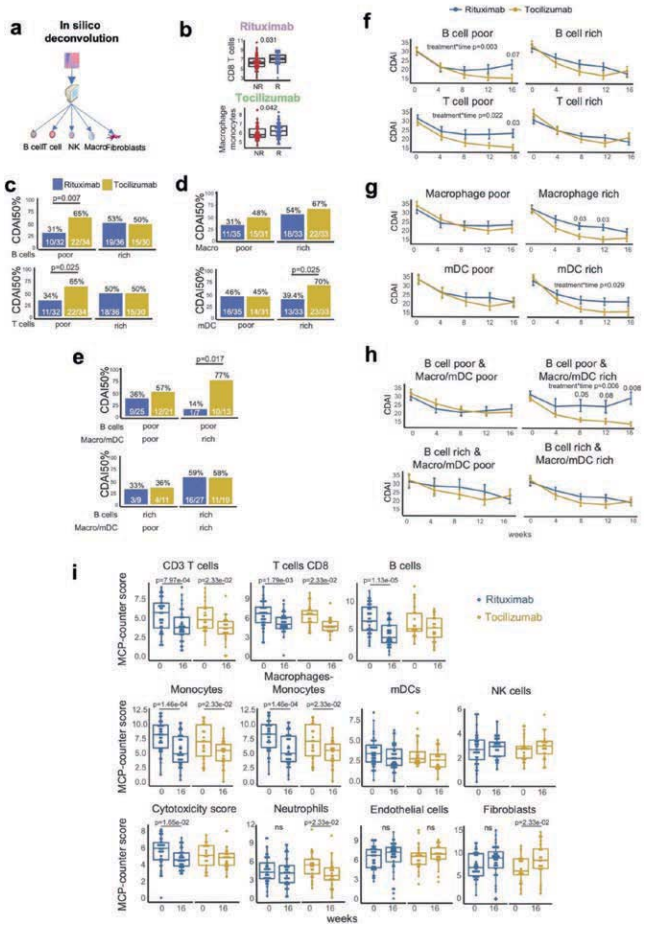
Objectives: Here, we aimed to perform cell-transcript deconvolution of pre-and post-treatment synovial biopsies from the R4RA trial.

Methods: A total of 164 patients underwent pre-treatment synovial biopsy (US-guided or arthroscopic) prior to randomization 1:1 to rituximab (83) or tocilizumab (81). 65 patients had a repeat biopsy at 16 weeks when clinical response was assessed using Clinical Disease Activity Index (CDAI) 50% improvement. RNA extracted from a minimum of 6 synovial samples/patient underwent RNA-sequencing and the abundance of tissue-infiltrating immune and stromal cell populations was estimated using the Microenvironment Cell Populations-counter (MCP-counter) method (Figure 1a).

Results: At baseline, while synovial semiquantitative immunohistochemistry scores did not differ between CDAI50% responders and non-responders,

both for rituximab and tocilizumab, MCP-counter analysis showed significantly higher CD8 T-cells in responders to rituximab and higher macrophage-monocytes and myeloid dendritic cells (mDC) in responders to tocilizumab (Figure 1b). Moreover, when patients were classified according to MCP-counter scores, B-cell poor patients (MCP-counter B cell score <median value) showed significantly higher response rates to tocilizumab, while no difference was found in B-cell rich patients (Figure 1c). In contrast, macrophage and myeloid dendritic cell (mDC) rich individuals showed higher responses to tocilizumab (Figure 1d). Combined scores for lymphoid and myeloid cells demonstrated that patients poor in B-cells but rich in macrophages/mDC had a significantly higher response to tocilizumab (77% responders to tocilizumab vs 14% responders to rituximab, p=0.017, OR 16.48, 95%CI 1.29-1000.5) (Figure 1e). By analysing disease activity over time from baseline to week 16, we found a statistically significant interaction effect between treatments and time in B-cell poor (p=0.003), T-cell poor (p=0.022), mDC rich (p=0.029) and B-cell poor/Macrophages-mDC rich patients (p=0.006) (Figure 1f-g-h). Finally, by applying MCP-counter on matched pre-and post-treatment biopsies, rituximab-treated patients showed a significant reduction of B-cells, T-cells and monocyte/macrophages, while tocilizumab-treated patients showed a significant reduction of monocyte/macrophages, T-cells, but also neutrophils, myeloid dendritic cells and, interestingly, an increase in fibroblast signature (Figure 1i).

Figure 1



Conclusion: In silico deconvolution of the synovial tissue identify pre-treatment lymphoid cell lineages associated with response to rituximab and myeloid cells for tocilizumab. The longitudinal analysis of matched pre- and post-treatment synovial biopsies indicated that both medications have an effect on synovial immune cells, but tocilizumab can also affect stromal cells.

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Disclosure of Interests: None declared.

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OP0086 ANTIBODIES AGAINST ADVANCED GLYCATION END-PRODUCTS (ANTI-AGE) DISTINGUISH PATIENTS WITH A MORE INFLAMMATORY PROFILE AND WORSE OUTCOME IN SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA) around two-thirds of patients are autoantibody-positive for rheumatoid factor, anti-citrullinated protein antibodies (ACPA) and/or anti-carbamylated protein antibodies (anti-CarP). The remaining seronegative subgroup of RA is clinically heterogeneous and thus far, biomarkers predicting the disease course in these patients are lacking. Therefore, we set out to investigate the value of a new/different autoantibody in rheumatoid arthritis directed against advanced glycation end-product (AGE) modified proteins (anti-AGE). AGEs are a marker of oxidative stress, and anti-AGE have been described in multiple diseases including diabetes, and hypertension.
Objectives: To investigate the prevalence of anti-AGE in RA and non-RA arthritis patients, as well as their association with clinical parameters and disease outcome in RA.
Methods: In 648 RA patients and 538 non-RA arthritis patients from the Leiden Early Arthritis Clinic anti-AGE IgG antibody levels were measured using an in-house fetal calf serum (FCS) ELISA based assay using native FCS as control. The cutoff for positivity was set as the mean optical density plus two times the standard deviation of 80 healthy controls. Radiological progression was measured with the with Sharp van der Heijde score (SHS) on yearly basis and the association with anti-AGE was assessed with a multivariate normal regression model.
Results: Anti-AGE was found in 299 (46%) of RA patients versus 163 (30%) of non-RA arthritis patients. Interestingly, 67 (34%) of completely seronegative (RF-, ACPA- and anti-CarP-negative) RA patients were positive for anti-AGE. Within RA, anti-AGE-positive patients had significantly higher ESR (median anti-AGE-positive: 38, anti-AGE-negative: 32, p<0.001) and CRP (median anti-AGE-positive: 19, anti-AGE-negative: 17, p<0.001), indicating an more inflammatory profile in these patients. Radiographic progression, was significantly higher in anti-AGE+ patients (Figure 1A, B=1.05, p<0.001). Since ACPA and anti-CarP (in ACPA-patients) are associated with radiological progression, the analysis was first stratified for ACPA-status. In the anti-AGE+ACPA- patients a significant association with SHS was found (Figure 1B: B=1.04, P<0.001), indicating that anti-AGE is associated with radiological progression in ACPA-negative patients. Next, the ACPA-negative stratum was also stratified for anti-CarP. Interestingly, SHS was significantly higher in all anti-AGE+ groups compared to the autoantibody-negative group.
Conclusion: Almost half of the RA patients are anti-AGE positive including a substantial part of otherwise completely seronegative RA patients. Anti-AGE antibodies are associated with inflammatory parameters and radiologic progression in seronegative RA patients. Therefore, although these autoantibodies are not specific for RA, anti-AGE could potentially identify patients with a more inflammatory phenotype and more severe disease outcome in "classic" autoantibody-negative RA patients.

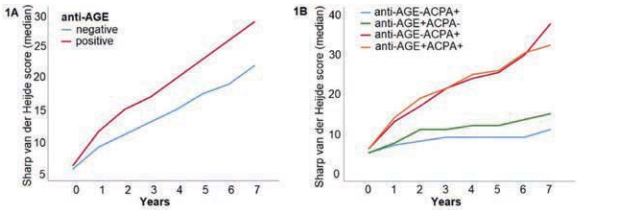

Figure 1. Erosion scores according to the presence of autoantibodies. Figure 1A: Median erosions scores assessed by Sharp van der Heijde method (SHS) during the disease course stratified for anti-advanced glycation end-products antibodies (anti-AGE). A significant difference was found between anti-AGE-negative patients and anti-AGE-positive patients (B=1.05, p<0.001). Figure 1B: Median erosions scores assessed by SHS during the disease course stratified for anti-AGE and anti-citrullinated protein antibodies (ACPA). SHS was significantly higher in all autoantibody-positive groups compared to the anti-AGE-ACPA- group.

Disclosure of Interests: None declared.

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OP0087 INTEGRATED SYSTEMS ANALYSIS OF THE GUT MICROBIOTA PHENOTYPES IN THE RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) displays extreme dysbiosis in microbiota. However, such dysbiosis is difficult to characterize owing to the high dimensional complexity of the gut microbiota[1,2].
Objectives: The aim of this study was to discover the enterotype characters of intestinal flora in RA.
Methods: Fecal samples from 145 RA patients were collected for bacterial 16S rRNA genes sequencing. Mathematical modeling using Dirichlet multinomial mixtures (DMM) was applied to describe the variability in the microbiome data and cluster samples into enterotypes. The alpha-diversity, beta-diversity and the microbial composition analysis of the gut microbiome were used to define the difference of gut microbiota profiles between different enterotypes. The nonredundant taxonomic biomarkers for each enterotype were selected by using LEfSe. Inflammatory biomarkers (ESR, CRP), auto-antibodies(ACPA, MCV), peripheral lymphocytes subsets and cytokines were analyzed in our cohort using the Kruskal-Wallis test.
Results: Laplace approximation of DMM indicated two significantly distinct bacterial microbiota structures (RAE1 and RA E2) existed in the dataset (Figure 1a). Principal co-ordinates analyses confirmed that these two microbiota states explained a reasonable proportion of observed variance in microbiota composition(ANOSIM R2 = 0.267, p = 0.001; Figure 1b), with distinct bacterial genus distribution of in each enterotype (Figure 1c). RA E1 were primarily dominated by Prevotella while RA E2 by Bacteroides. Interestingly, Chao1, ACE, Shannon and Simpson revealed a higher alpha diversity in Prevotella-enriched enterotype (p< 0.001, Figure 1d). Fourteen selected taxonomic biomarkers at different phylogenetic levels showed great discriminant ability, with Log10 LDA score > 4.0 (Figure 1e-g). Further, inflammatory biomarkers (ESR, CRP) and auto-antibodies(ACPA, MCV) as well as the number of T, B and CD4+T, Th1, Th2, Th17, and Treg were consistent in RA E1 and RA E2 (p > 0.05, Figure 2h). But CD8+T were significantly higher in RA E2 than in RA E2 (p < 0.05).

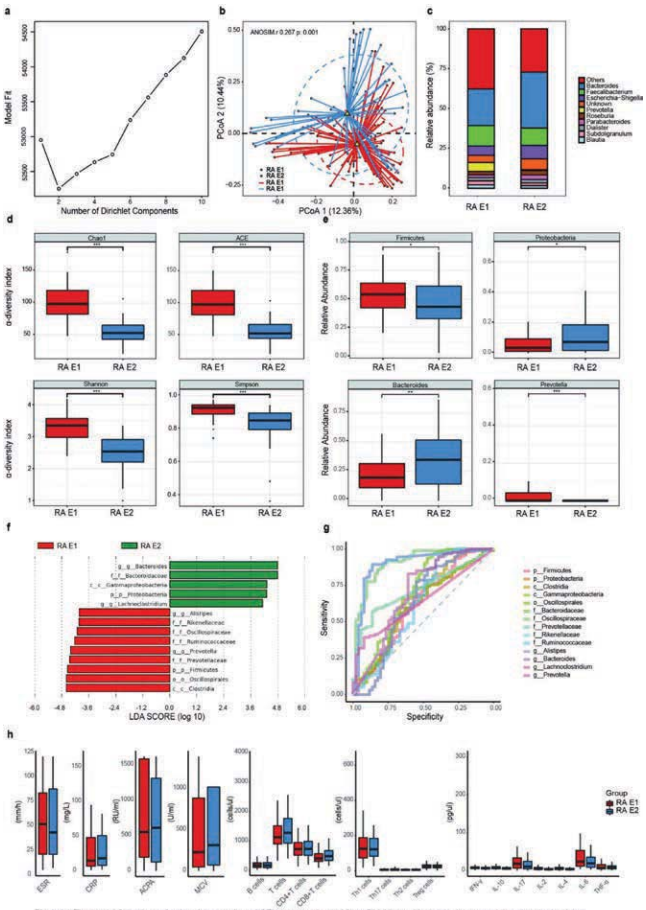

Fig 1. (a) The model fit is shown for the given number of OTU types estimated from Dirichlet multinomial mixture models using the Laplace approximation. **(b)** Principal component analysis (PCoA) plot generated from the Bray-Curtis distances. **(c)** Microbiota composition based on relative abundance at the genus levels. **(d)** Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson). Median estimates compared across cohorts. **(e)** Relative abundance of Bacteroides, Prevotella for individuals within each of the two enterotypes. **(f)** Bacterial taxa differences between RA patients and HCs using LEfSe analysis. **(g)** ROC was performed for all samples using the 14 individual taxonomic biomarkers. **(h)** Alterations in inflammatory biomarkers (ESR, CRP), auto-antibodies (ACPA, MCV), peripheral lymphocytes subsets and cytokines of RA patients and HCs. Bars in a-d represent median values with interquartile ranges. Statistics were calculated using the Kruskal-Wallis test. *P < 0.05; **P < 0.01; ***P < 0.001.

Conclusion: Despite RA gut microbiota being of different dysbiosis, two patterns of dysbiosis, designated as RA-enterotypes, were predominant among the RA patient cohort. RA E2 exhibited a loss of Prevotella but a growth of Bacteroides, while RA E1 presented the opposite results.

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OP0088 STRATIFIED MEDICINE: GENETIC PREDICTORS OF RADIOGRAPHIC OUTCOME IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) displays great heterogeneity between patients for susceptibility to developing erosions. Genetic variations within the HLA-DRB1 gene (the shared epitope (SE) and polymorphisms coding for Valine at position 11) have been consistently associated with both susceptibility and radiographic outcome in RA.(1) However, associations of non-HLA markers are much less conclusive. Most studies looking outside the HLA have been candidate gene studies and very few have been replicated in independent cohorts.
Objectives:
1. Identify all single nucleotide polymorphisms (SNPs) outside the HLA that have ever been associated with radiographic outcome in RA
2. To perform a replication study to determine which of these are associated with radiographic outcome in the Norfolk Arthritis Register (NOAR), the worldwide largest prospective cohort with genetic and radiographic outcome data.

Methods: A systematic literature search was conducted as shown in the Figure 1.

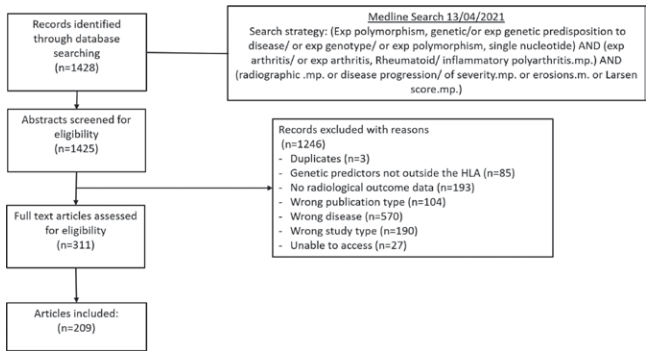

Figure 1. Flow chart for systematic review.

The Norfolk Arthritis register (NOAR) is a large primary care-based inception cohort of patients diagnosed with inflammatory polyarthritis. Patients were recruited at baseline from 1989 and followed up prospectively for up to 20 years with serial X-rays. Genome-wide genotyping was performed on the Illumina Human/Infinium Core Exome array and imputed with Minimac4 to the Haplotype Reference Consortium panel. Quality control resulted in 7.5 million SNPs available in each patient. SNPs identified from the literature were extracted and tested for an association with the presence of erosions (as a longitudinal binary

variable) using a generalized estimating equation (GEE) model in STATA/IC 14.0.in NOAR.

Results: A total of 2119 participants (2440 radiographs) were identified with both genetic and radiographic data available. 66.2% of these patients were female and 33.3% were anti-CCP positive. Median age of onset was 54.5 and 74.9% satisfied the American College of Rheumatology (ACR) 1987 criteria for rheumatoid arthritis.

A total of 113 different non-HLA SNPs associated with radiographic outcome in RA were identified from the literature. Of these, 102 were successfully identified within NOAR and 91 were deemed to be independent SNPs based on R^2 of 0.6. 14 SNPs were found to be significantly associated with the presence of erosions within NOAR (Table 1).

Table 1. SNPs found to be associated with radiographic severity within NOAR. *Significant results only; Dominant models used (Odds ratios displayed in relation to minor alleles)

Gene	Chromosome	SNP (single nucleotide polymorphism	Odds ratio (95% CI)	P value
IL2RB	2	rs743777	1.23 (1.01, 1.05)	0.0398
IL15	4	rs6821171	0.82 (0.67, 1.00)	0.0451
IL4	5	rs2243250	1.36 (1.08, 1.70)	0.0094
FOX03	6	rs12212067	0.75 (0.58, 0.97)	0.0278
OPG	8	rs2073618	0.79 (0.64, 0.98)	0.0295
TRAF1	9	rs10760130	1.33 (1.06, 1.65)	0.0118
TRAF1	9	rs10818488	1.32 (1.06, 1.64)	0.0141
TRAF1	9	rs2900180	1.32 (1.07, 1.61)	0.0079
IL4r	16	rs1805010	1.25 (1.01, 1.56)	0.0393
IL4r	16	rs1805011	1.31 (1.03, 1.66)	0.0260
LGALS9	17	rs3763959	1.28 (1.03, 1.59)	0.0260
SOST	17	rs4792909	1.34 (1.09, 1.65)	0.0052
LILRA3	19	rs103294	0.80 (0.65, 0.98)	0.0334
MMP9	20	rs11908352	0.70 (0.57, 0.85)	0.0005

Conclusion: 113 non-HLA SNPs have been previously reported to be associated with radiographic outcome in RA. Of these, only ~15% also showed an association in NOAR, the largest cohort with genetic and radiographic outcome data worldwide. Interestingly, rs2243250, a SNP located on chromosome 5 (IL4), previously found to be associated in a small Egyptian cohort, has been replicated in NOAR.(2) Current work consists of assessing the added clinical value of a genetic risk score based on HLA and non-HLA markers in predicting radiographic outcome when combined with clinical/serological/demographic markers.

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Disclosure of Interests: None declared.

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OP0089 RNASEQ PROFILING OF RHEUMATOID ARTHRITIS PATIENTS TO PREDICT RESPONSE TO TOFACITINIB

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Background: Rheumatoid arthritis (RA) is characterized by chronic inflammatory synovitis and progressive disability. Nowadays the natural history and the prognosis of the disease has deeply changed thanks to the availability of conventional and targeted disease modifying anti-rheumatic drugs (DMARDs). Nevertheless, clinical response to treatment is highly variable and a considerable proportion of patients do not - or only partially - respond to the treatment. The stratification of patients through the identification of biological predictors of good clinical response to treatment could allow the selection of the best therapeutic strategy for each patient. Recently, precision medicine in rheumatology could rely on the development of new transcriptomics techniques, such as RNA sequencing (RNAseq), that permit to explore complex cellular and molecular networks associated with pathophysiological aspects.

Objectives: To characterize the transcriptomic profiles (RNAseq) of whole-blood samples of moderate to severe RA patients to predict the clinical response to tofacitinib.

Methods: We selected patients with active RA, candidate to receive tofacitinib after failure of a previous therapy with conventional or biologic DMARDs. RNAseq profiling on whole-blood samples (PAX gene tubes) was performed at baseline and after 24 weeks of treatment with tofacitinib. Treatment response was evaluated at week 24 by CDAI EULAR response criteria as drug responder (major or moderate response) or non-responder (minor or no response). Differential expression of gene ontology (GO) biological processes (BP) pathways was analyzed to identify the response-associated pathways. Machine learning models were built by different data mining algorithm to predict response to tofacitinib.

Results: The study population included 33 patients, of whom 7 discontinued prematurely the treatment (5 because of adverse events and 2 because of inefficacy) and 2 were lost to follow-up. At week 24, 10 patients (38.5%) had major, 4 (15.4%) moderate, 6 (23.1%) minor, and 6 (23.1%) no clinical response to tofacitinib. No significant difference was observed between responders and non-responders in terms of baseline characteristics (age, sex, rheumatoid factor and anti–cyclic citrullinated peptide [ACPA] positivity, DMARDs and prednisone exposure, Table 1). Overall, 307 out of 2137 coding transcripts and 85 GO BP pathways were differentially expressed after treatment in responders vs non-responders (Figure 1). In detail, an up-regulation of JAK-dependent pathways, including cation transport, metabolism of membrane lipids, calcium-mediated signaling, and osteoblast proliferation was observed in responders. Conversely, in non-responders, processes related to B cell activation, proliferation, and signaling along with mRNA epigenetic modifications were increased. After extensive internal validation (50 runs of 80:20 hold-out sampling) with univariate selection of GO terms, the accuracy of Support vector Machine (SVM) learning models to predict the correct clinical response was equal to 88.3% (AUROC = 0.940).

Table 1. Demographic and baseline clinical characteristics of the study population*

	Non responders(n = 12)	Responders(n = 14)
Female, n (%)	11 (91.7%)	11 (78.6%)
Age, years (±SD)	52.6±11.2	54.3±10.5
Rheumatoid factor, n (%)	7 (58.3%)	7 (50%)
ACPA, n (%)	9 (75%)	8 (57.1%)
Concomitant csDMARDs, n (%)	5 (41.7%)	8 (57.1%)
bsDMARDs naïve, n (%)	12 (100%)	11 (78.6%)
Prednisone ≥ 5mg/day, n (%)	4 (33.3%)	6 (42.8%)

* There were no significant differences, determined by Fisher's exact test for categorical variables

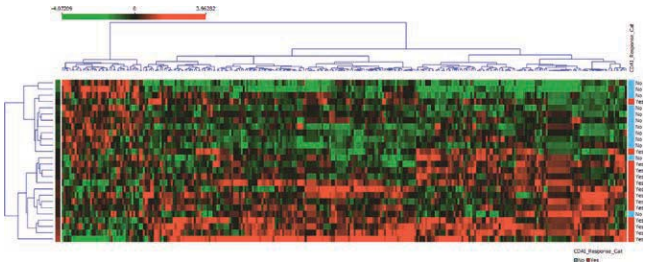

Figure 1. Heatmap representation of selected GO BP pathways in responders/non-responders.

Conclusion: Machine learning models based on transcriptomic functional pathways can accurately predict response to tofacitinib. Our study could contribute to improve the treatment customization and the optimization of RA treatment strategy toward a personalized approach. Furthermore, these findings may help to understand the mechanisms underlying the clinical response to JAK inhibitors.

Disclosure of Interests: None declared.

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The Yin and Yang of scleroderma and vasculitis

OP0090 **PRECLINICAL STUDIES OF A NOVEL CATHEPSIN C INHIBITOR IN MPO-ANCA-ASSOCIATED VASCULITIS MODEL**

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Background: MPO-ANCA-associated vasculitis (MPO-AAV) is a systemic small vessel vasculitis with the production of MPO-ANCA in the serum. This disease develops necrotizing and crescent glomerulonephritis (NCGN) and peritubular capillaritis-mediated interstitial damages in the kidneys, and pulmonary hemorrhage due to capillaritis in the lungs. Recent studies have revealed that neutrophil extracellular traps (NETs) induced by MPO-ANCA are critically involved in its pathogenesis,[1] and neutrophil elastase (NE) plays an essential role in the formation of NETs.[2] Cathepsin C (CatC) functions as a key enzyme in the activation process of several neutrophil serine proteases (NSPs) such as NE, proteinase 3 and cathepthin G by converting the inactive forms of the NSPs to the active forms by digesting dipeptides at the N-terminus of the enzymes.[3]

Objectives: Although glucocorticoids and immunosuppressive drugs used as the standard of cares can lead remission in MPO-AAV patients, there are remaining unmet medical needs such as severe side effects, resistance to the treatment and relapse. Therefore, development of new therapeutic strategies is awaited. The aim of this study is to demonstrate the efficacy of MOD06051, a novel CatC inhibitor, against MPO-AAV, using an MPO-AAV rat model established previously.[4]

Methods: In vitro studies: Cathpsins and NE inhibitory activity was measured using recombinant enzymes and fluorescent substrates. Cellular NE activity in the granulocytes differentiated from the primary human bone marrow-derived hematopietic stem cells under the presence or absence of MOD06051 was determined using fluorescent substrates.

In vivo studies: 4-week-old Wistar Kyoto (WKY) rats were immunized with human MPO according to Little's protocol.[4] The rats were divided into three groups (n=8 in each group), and vehicle (0.5% methylcellulose) or MOD06051 (0.3 or 3 mg/kg bid) was orally administered every day for 42 days. All rats were euthanized at the end of the study for serological and histological evaluations.

Results: In vitro studies: MOD06051 inhibited the enzymatic activity of human recombinant CatC with an IC50 value of 1.5 nM, and no other cathepsins nor NE inhibition was observed at 10 μM. The NE activity in primary human granulocytes was suppressed by MOD06051 with an IC50 value of 18 nM.

In vivo studies: MPO-ANCA was induced in all groups at the same level. The percentage of affected glomeruli including those with NCGN, NET-forming neutrophils in the peripheral blood and glomeruli, and glomerular neutrophil counts were significantly suppressed by MOD06051 treatment in a dose-dependent manner. Furthermore, hematuria score, urinary NGAL (Neutrophil Gelatinase-Associated Lipocalin), tubular erythrocyte cast counts, and pulmonary hemorrhage foci were significantly decreased in the 3 mg/kg of MOD06051 treated group with the similar trends in 0.3 mg/kg group.

Conclusion: MOD06051 showed sepcific inhibition of CatC activity. This compound suppressed the serine proteases activation in primary human neutrophils and NET formation in the MPO-AAV model rats, resulting in amelioration of MPO-ANCA-induced tissue destruction, including NCGN and tubular interstitial damages in the kidneys, and disorder of alveolar septal capillaries in the lungs. MOD06051 appears to be a promising agent for treatment of MPO-AAV patients.

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OP0091

EXPANSION OF MYELOPEROXIDASE (MPO)-SPECIFIC IGM B CELLS IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS

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Background: ANCA-associated vasculitides (AAV) are characterized by recurrent, chronic small vessel inflammation and deleterious organ damage. The main targets of ANCA are myeloperoxidase (MPO) and proteinase 3 (PR3). ANCA, B cells and the complement system are crucial to AAV pathogenesis, as evidenced by the clinical benefit of B cell depletion with rituximab and, more recently, the C5a receptor antagonist avacopan. While ANCA in serum have been studied extensively, phenotypic and functional characteristics of the underlying B cell responses remain largely unknown.

Objectives: To develop a flow cytometry-based technique for identifying MPO-specific B cells in the circulation of MPO-positive AAV patients in order to characterize this B cell response and its potential contribution to disease pathogenesis.

Methods: Human neutrophil-derived MPO was conjugated to two different fluorochromes and used to identify MPO-specific B cells by flow cytometry. An antigen-specific staining protocol was developed and validated using MPO- and PR3-specific hybridoma cells. MPO-specific B cells were phenotypically characterized and isolated from the peripheral blood of AAV patients by fluorescence activated cell sorting (FACS) and cultured as single cells. MPO-specificity was confirmed by ELISA on culture supernatants. B cell receptor (BCR) sequences were obtained from MPO-positive clones by full length ARTISAN-PCR and Sanger sequencing. MPO-specific IgG and IgM monoclonal antibodies (mAb) were produced to validate specificity and to examine their ability to activate complement. Finally, MPO-positive AAV patient plasma and plasma depleted of IgG or IgM was tested in in vitro complement assays.

Results: The newly developed, differential antigen labelling approach successfully identified MPO-specific but not PR3-specific hybridoma cells. Subsequently, we detected MPO-specific B cells in the circulation of MPO-positive AAV patients at a frequency of up to 1:1000 B cells. FACS sorting and single cell culture yielded an enrichment of MPO-specificity of ~80%. Notably, the majority of isolated, MPO-specific B cells (60-95%) displayed an IgM memory phenotype, which corresponded to the presence of anti-MPO IgM in plasma. The remainder of the MPO-specific cells were mainly IgG memory B cells and few naive cells. BCR sequencing revealed a polyclonal IgM response with diverse V-gene usage, consisting of both germline and highly mutated clones. Generation of mAb (n=5) confirmed MPO specificity by inhibition ELISA for both germline and somatically mutated clones. Interestingly, anti-MPO IgM mAb showed a high capacity for complement factor deposition upon MPO binding. MPO-specific complement assays with IgG- and IgM-depleted patient plasma showed that anti-MPO IgM activated complement much more efficiently than anti-MPO IgG.

Conclusion: We demonstrate the direct ex-vivo identification, isolation and characterization of MPO-specific B cells in human AAV. Intriguingly, we observed a remarkable expansion of MPO-specific, IgM-expressing memory B cells in patients. This so far unrecognized, active IgM-compartment may be clinically relevant, as both mAb and plasma-derived polyclonal MPO-specific IgM strongly activated complement, a pathway thought to play a central role in AAV. Next to these novel insights into autoreactive B cell biology in AAV, our findings now provide new opportunities for studying auto-reactive B cell responses in different clinical phases of AAV, amongst which active disease, remission and (imminent) flares.

Disclosure of Interests: None declared.

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OP0092

DECIPHERING THE SYNOVIAL TISSUE AND FIBROBLAST SUBSETS IN SYSTEMIC SCLEROSIS

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Background: Articular involvement is underestimated in systemic sclerosis (SSc), but represents a major cause of disability and is a marker of disease severity. There is no approved effective therapy for arthritis in SSc and immunosuppressive treatments are given to SSc patients by analogy with rheumatoid arthritis (RA), but with limited effect. The last few years have revolutionized the understanding of the pathogenesis of RA by deciphering the heterogeneity of synovium at both the cellular and molecular levels. Nevertheless, the pathogenesis of joint involvement in SSc remains largely unknown.

Objectives: To characterize the synovium in SSc at tissue and cellular levels and to compare it with RA synovium.

Methods: Nine consecutive patients fulfilling SSc classification criteria and having joint synovitis were included. Patients with overlap with other autoimmune rheumatic diseases were excluded. Synovial tissues (8 wrists, 1 knee) were obtained by ultrasound-guided biopsy and were compared to those obtained from five RF and CCP positive RA patients (3 wrists, 3 knees). Tolerance of the procedure was assessed after 3-5 days. Histological analysis of the synovium determined the Krenn synovitis score (0-9) and stratified the synovial tissue according to previously published histological features1. One biopsy, without synovial tissue, was not processed further. ScRNA-seq libraries were prepared with 10X Genomics technology and sequenced on NovaSeq 6000. Integrated bioinformatics analysis used Cell Ranger and Seurat software. Overexpressed genes were selected using log2 ratio (>0.25) and false discovery rate adjusted p value (< 0.05). For pathway enrichment analysis, Enrichr software was used.

Results: Of the nine SSc-patients, 6 were women, median age was 65 [IQR: 58-67] years, median disease duration was 2 [0.5-5] years and 2 had diffuse cutaneous subtype. The antibody status was as follows: anti-Scl70 (2), anti-centromere (2), anti-RNA polymerase III (3), anti-Ku (1) and isolated ANA (1). In the RA cohort, 4/5 were women, median age was 56 [54-59] years and median disease duration 6.5 [5-7.5] years. Synovial biopsy was well-tolerated by all the patients. Krenn synovitis score was lower in SSc as compared to RA across the three components of the synovitis score (lining layer, stroma and inflammatory infiltrate). In SSc, 7/8 (87.5%) biopsies were characterized by a pauci-immune pathotype, whereas in RA 3/6 (50%) were pauci-immune. Due to the low inflammatory pauci-immune pathotype in all but one SSc patients, we focused the scRNA sequencing analysis on synovial fibroblasts (SF) (number of SF studied: 4876 in SSc and 5885 in RA). We identified four clusters of SF with respective marker genes: SF1 (CXCL12, APOE, RARRES2, CCL2), SF2 (PRG4, MMP1, MMP3, CD55), SF3 (POSTN, ASPN, COMP, COL1A1) and SF4 (FN1, TIMP1, SERPIN2, PRELP). Comparison between SSc and RA SF subtypes showed differences in the proportion of the clusters between both diseases with higher enrichment of SF2 corresponding to the lining SF in SSc. 741 genes were differentially expressed between SSc and RA SF with 414 genes overexpressed in SSc SF. Pathway enrichment analysis of these 414 genes identified TGF-β (p.adj: 3.708e-18) and interferon (p.adj: 1.071e-8) signaling pathways. TGF-β signaling was enriched across all the clusters of SF, whereas interferon signaling mostly in sublining SF. The most overexpressed genes in SSc included PLCG2 (encoding the signaling enzyme PLCγ2, which plays a regulatory role in various immune pathways), PCOLCE2 (encoding a procollagen C-endopeptidase enhancer) and the transcription factor AHR (negative regulator of TGF-β).

Conclusion: Synovitis in SSc differs from RA synovitis both at histological and molecular levels. By highlighting the low inflammatory nature of the synovium and the enrichment in TGF-β and interferon signaling pathways in SSc SF, our study questions the use of the same immunosuppressive therapies in RA and SSc. These results are the basis for the development of specific targeted therapies for arthritis in SSc.

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OP0093

INCREASED RISK OF SEVERE INFECTIONS AND MORTALITY IN PATIENTS WITH NEWLY DIAGNOSED ANTINEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS: A POPULATION-BASED STUDY

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Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAVs) are a group of multisystem inflammatory diseases of the small blood vessels, characterized by leukocytoclastic inflammation of small blood vessels and triggered by production of ANCA autoantibodies [1]. Due to the multiorgan involvement and relapsing nature, AAV is among the systemic autoimmune rheumatic diseases with the highest morbidity and mortality [1, 2].
Objectives: To evaluate the risk of severe infection and infection-related mortality among patients with newly diagnosed AAV.
Methods: We conducted an age- and gender- matched cohort study of all patients with incident AAV between January 1, 1997 and March 31, 2015 using administrative health data from British Columbia, Canada. Primary outcome was the first severe infection after AAV onset necessitating hospitalization or occurring during hospitalization. Secondary outcomes were total number of severe infections and infection-related mortality.
Results: We identified 549 AAV patients and matched them with 5,490 non-AAV individuals from the general population, yielding 184 and 509 first severe infections during 2,539 and 33,342 person-years follow-up, respectively. The crude incidence rate ratios for first severe infection and infection-related mortality were 5.03 (95% CI, 4.25-5.96) and 3.72 (95% CI, 2.44-5.67), respectively. The corresponding adjusted hazard ratios were 3.77 (95% CI 2.94-4.85) and 3.84 (95% CI, 2.13-6.91). AAV patients had an increased risk of a greater total number of severe infections with crude rate ratio of 4.99 (95% CI, 4.42-5.62) and adjusted rate ratio of 3.20 (95% CI, 2.73-3.74).
Conclusion: AAV is independently associated with increased risks of first severe infection (3.8-fold), a greater total number of severe infections (3.2-fold) and infection-related mortality (3.8-fold).
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Table 1. Risk of severe infection in AAV relative to non-AAV during follow-up

Post-AAV diagnosis first severe infection

	AAV cohort	Non-AAV cohort
	N=549	N=5,490
No. of events	184	509
IR per 1,000 person-years	72.46	14.40
IRR (95% CI)	5.03 (4.25-5.96)	1
Age and gender adjusted HR (95% CI)	5.29 (4.43-6.31)	1
All but GC adjusted HR (95% CI)	3.32 (2.67-4.13)	1
Fully adjusted HR* (95% CI)	3.77 (2.94-4.85)	1
Post-AAV total number of severe infections		
Infection episodes	396	868
IR per 1,000 person-years	116.42	23.35
IRR (95% CI)	4.99 (4.42-5.62)	1
Age and gender adjusted rate ratio (95% CI)	5.27 (4.78-5.93)	1
All but GC adjusted rate ratio (95% CI)	3.13 (2.72-3.59)	1
Fully adjusted rate ratio* (95% CI)	3.20 (2.73-3.74)	1
Infection-related mortality		
No. of infection-related death events	29	85
IR per 1,000 person-years	8.53	2.29
IRR (95% CI)	3.72 (2.44-5.67)	1
Age and gender adjusted HR (95% CI)	4.43 (2.89-6.79)	1
All but GC adjusted HR (95% CI)	3.67 (2.14-6.31)	1
Fully adjusted HR* (95% CI)	3.84 (2.13-6.91)	1

Abbreviations: **AAV**, Antineutrophil cytoplasmic antibody-associated vasculitides; **IR**, incidence rate; **IRR**, incidence rate ratio; **HR**, hazard ratio; **CI**, confidence interval. *Adjusted for baseline covariates. All but GC HRs represent the total effect while fully adjusted HRs represent the direct effect of AAV.

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OP0094

IDENTIFICATION OF NEW AUTOANTIGENS IN PATIENTS WITH SYSTEMIC SCLEROSIS THROUGH IMMUNOPRECIPITATION COMBINED WITH LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY

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Background: In up to 20% of patients with systemic sclerosis (SSc) none of the established SSc-specific autoantibodies are present [1]. Notwithstanding, in many of these patients high-titer autoantibodies can be detected on the HEp-2 indirect immunofluorescence assay (HEp-2 IIFA) which suggests the presence of an autoantibody to an intracellular protein expressed by the HEp-2 cell line. Immunoprecipitation of unlabeled cell extract followed by gel-free liquid chromatography tandem mass-spectrometry analysis has the potential to identify new autoantigens in an unbiased manner.
Objectives: To identify new autoantigens through immunoprecipitation combined with liquid chromatography-tandem mass spectrometry (IP + LC-MS/MS) in HEp-2 IIFA-positive patients with SSc in whom none of the established SSc-specific autoantibody specificities are present.
Methods: Forty-nine patients from the University Hospitals Leuven that fulfilled the EULAR-ACR 2013 classification criteria for systemic sclerosis or LeRoy and Medsger's criteria for early systemic sclerosis and who were negative on the EliA CTD Screen (Thermo Fisher Scientific, United States), which includes centromere protein B, topoisomerase I, RNA polymerase III, fibrillarin, PM-Scl and U1 ribonucleoprotein, were identified. Immunoprecipitation was performed by incubation of sera of these patients (1/30 in 300 µl Tris-buffered saline) with Pierce A/G magnetic beads, subsequent cross-linking with bissulfosuccinimidyl suberate (BS3) followed by incubation with nuclear extract of HeLa cells (100-150 µg) overnight at 4°C. The eluted protein was analyzed through liquid chromatography with tandem mass spectrometry. Mass spectrometry data were matched against the Uniprot Homo Sapiens database with the Mascot search engine. Candidate autoantigens were confirmed through immunoprecipitation followed by western blot of the eluate with target-specific polyclonal rabbit antibodies or western blot of recombinant protein incubated with sera of the index patients.
Results: We identified multiple new autoantigens, including the THO complex subunit 1 (THOC1) and other subunits of the THO complex in 3 patients, nuclear valosin-containing protein like-2 (NVL) in 2 patients, nucleolar and coiled-body phosphoprotein 1 (NOLC1) and multiple interacting proteins in 1 patient, probable 28S rRNA (cytosine(4447)-C(5))-methyltransferase (NOP2) in 1 patient, telomeric repeat-binding factor 2 (TERF2) and TERF2-interacting protein (TERF2IP) in 1 patient and regulator of chromosome condensation 1 (RCC1) in 1 patient. The new targets were confirmed through immunoprecipitation-western blot or western blot of recombinant protein incubated with sera (Figure 1). Furthermore, in 10 patients known SSc-associated autoantigens were strongly immunoprecipitated including multiple Th/To subunits in 5 patients, RuvBL1/2 in 2 patients, multiple PM-Scl subunits in 2 patients (who both were negative on the EliA CTD Screen), and fibrillarin in 1 patient (who was also negative on the EliA CTD .).

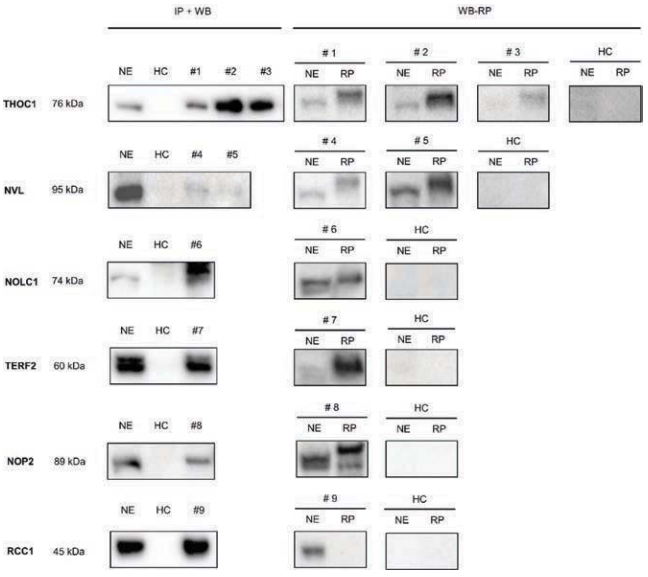

Figure 1.

Immunoprecipitation-western blot with target-specific rabbit polyclonal antibody (1/500-2000 dilution), numbers corresponding to order of description of patients, HC healthy control. NE nuclear extract. RP recombinant protein WB-RP western blot of recombinant protein incubated with patient's sera.

Conclusion: Multiple new autoantigens were identified and confirmed in patients with SSc without previously identified autoantibody specificity. Further evaluation of reactivity against the newly identified autoantigens in patients with SSc with known autoantibody specificities and other cohorts is required. IP + LC-MS/MS can identify new and established autoantigens in patients with SSc.

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OP0095 SINGLE-CELL RNA SEQUENCING REVEALS POTENT ANTI-INFLAMMATORY AND ANTIFIBROTIC ACTIVITIES OF DIMETHYL-ALPHA-KETOGLUTARATE ON EXPLANTED SKIN FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Activated fibroblasts are the main drivers of skin fibrosis in SSc. We have recently identified dimethyl alpha-ketoglutarate (dm-aKG) as a potential repressor of myofibroblast differentiation and profibrotic activity in cultured skin fibroblasts.

Objectives: To further analyse the clinical translation of our findings by investigating the antifibrotic capacity of dm-aKG on explanted skin biopsies from SSc patients.

Methods: We cultured forearm punch skin biopsies from SSc patients (n=10) for 24h *ex vivo* in the presence/absence of 6 mM dm-aKG. Thereafter, skin biopsies (n=4) were dissociated into single cells using a combined mechanical-enzymatic dissociation protocol, followed by single cell (sc)RNA-seq library preparation (10x Genomics) and sequencing (Illumina, NovaSeq6000, 50,000 reads/cell). We mapped the scRNA-seq reads to the reference genome GRCh38.p13 and analysed the data with R/Bioconductor tools. We deconvoluted cell types in bulk skin transcriptomes from SSc cohorts (GSE: 45485, 59785, 9285, 32413) using human skin scRNA-seq data[1]. The secretion of IL-6, procollagen-1, PRO-C1 (N-terminal type I collagen pro-peptide), C1M (MMP-degradation fragment of type I collagen), and fibronectin (FBN-C) from cultured skin (n=10) was measured in supernatants by ELISA. We analysed gene and protein expression in TGFβ-activated healthy and SSc dermal fibroblasts (DF, n=10) treated or not with dm-aKG using qPCR, Western blot and ELISA. Contractile properties of DF were assessed by gel contraction assay. Traction forces generated by DF were determined by reference-free traction force microscopy.

Results: Dissociated cultured SSc skin exhibited comparable cell yield and viability in the presence (20,203; 89%) and absence (25,280; 93%) of dm-aKG, respectively. scRNA-seq skin analysis included 20,869 high quality single cell profiles segregating into 10 distinct skin cell populations (Figure 1A). This analysis demonstrated decreased proportion of fibroblasts and increased proportion of keratinocytes in dm-aKG treated skin (p<0.05; Figure 1B). Among skin cell types, skin fibroblasts exhibited the largest amount of differentially expressed genes upon dm-aKG treatment (44%, n=779, x-fold>0.5, FDR<0.05), suggesting that these cells are key targets of dm-aKG therapy in SSc skin. We identified inflammatory/cytokine signalling (hub genes *IL6, STAT1*) and extracellular matrix (ECM) organization (hub genes *MMP1, ITGB3*) as top downregulated biological processes in fibroblasts in dm-aKG treated SSc skin (Figure 1C), coinciding with a decreased abundance of proinflammatory skin fibroblast subpopulation. Specifically, these cells were identified as the main source of *IL6* (Figure 1D) and were enriched in SSc skin as revealed by deconvolution analysis of skin transcriptomes. Furthermore, dm-aKG reduced the secretion of IL-6, procollagen-1 and C1M, but not pro-C1 and FBN-C, from cultured skin explants. In cultured DF, dm-aKG blocked the inflammatory (IL-6, pSTAT3), profibrotic (aSMA, Fibronectin, Procollagen-1, Pro-C1) and contractile activities, and significantly diminished traction forces exerted by DF on the matrix substrate.

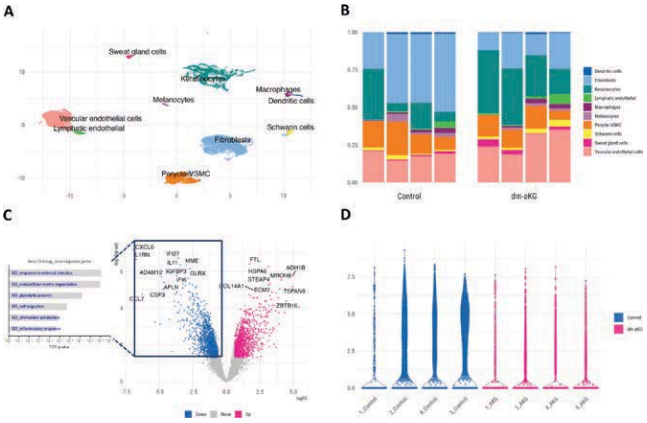

Figure 1. scRNA-seq – comparison of untreated and dm-aKG treated paired skin biopsies. (A) UMAP plot with annotated skin cells, (B) differential abundance of main skin cell types, (C) volcano plot of DE genes with top downregulated gene ontology (GO) pathways in dm-aKG treated skin fibroblasts, (D) *IL6* expression in untreated (blue) and treated (pink) skin fibroblasts.

Conclusion: Dm-aKG broadly interferes with inflammatory and ECM organizational activities of skin fibroblasts in culture and in explanted skin from SSc patients. These results confirm that dm-aKG might represent a potential new therapeutic approach for efficient targeting of skin inflammation and fibrosis in SSc.

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OP0096 CAN IMMUNOGLOBULINS G FROM SYSTEMIC SCLEROSIS PATIENTS INFLUENCE THE SECRETOME OF DERMAL FIBROBLASTS?

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Background: Autoantibodies (Aab) are frequent in systemic sclerosis (SSc) [1]. Recently, it has been showed that immunoglobulins G (IgG) from SSc promoted proinflammatory and profibrotic phenotype in monocyte secretome [2]. Fibroblasts (FB) are key effectors cells in SSc and data on FB proteins secretion in the presence of IgG from SSc patients are lacking. While recognized as potent biomarkers, the pathogenic role of Aab is much more debated.
Objectives: To explore the FB secretome in the presence of purified IgG from SSc patients
Methods: Normal dermal FB were cultured in the presence of purified IgG from patients with diffuse cutaneous SSc (dcSSc), limited cutaneous SSc (lcSSc) or healthy controls (HC). After 72 h of culture, the cell supernatants were collected, centrifuged and passed through a filter to remove the cells. After proteins digestion, secretome was explored using mass spectrometry coupled with liquid chromatography (LC-MS/MS). Analysis of variance (ANOVA) and hierarchical clustering were used to identify proteins responses patterns.
Results: Proteomic identified and quantified 1268 proteins, among them 377 were significant after ANOVA. SSc and HC secretome appeared distinct. Hierarchical clustering on significant proteins after ANOVA showed 3 distinct groups of patients secretome: a first group including mostly dcSSc anti-topoisomerase-I (ATA) positive (dcSSc ATA+) patients, a second group including mostly dcSSc ATA negative (dcSSc ATA-) patients, a third group more heterogeneous including the majority of HC, lcSSc anti-centromere positive (lcSSc ACA+) patients and dcSSc ATA- patients (Figure 1.**A**). The comparison of FB secretome in the presence of purified IgG from dcSSc ATA+ vs IgG HC revealed 203 differentially expressed proteins (DEP) (Figure 1.**B**). The enriched Gene Ontology (GO) terms upregulated in IgG dcSSc ATA+ were involved in endocytic vesicle lumen, vesicle lumen, extracellular matrix or glycosaminoglycan binding. The comparisons of IgG dcSSc ATA- vs IgG HC and IgG lcSSc ACA+ vs IgG HC revealed 85 and 15 DEP, respectively. Follistatin, amyloid beta A4 protein, myosin-9 and calreticulin were commonly overexpressed in the 3 subtypes of SSc. 40 proteins were exclusively overexpressed in the condition dcSSc ATA+. Among them, collagen alpha-1(VII) chain, galectin-3-binding protein, desintegrin and metalloproteinase domain-containing 10, low affinity immunoglobulin gamma Fc region receptor III-A, CD59 glycoprotein, growth arrest-arrest specific protein and clusterin were overexpressed in the condition dcSSc ATA+ (Figure 1.**C**).

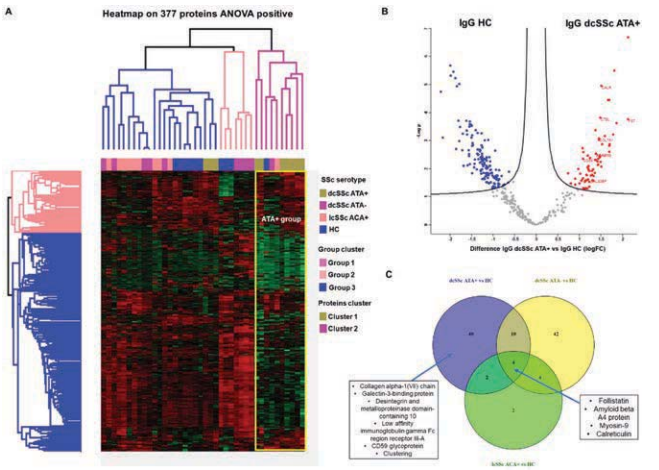

Figure 1. Heatmap representing the 377 differentially expressed proteins after ANOVA in all samples. Cluster analysis identified 3 group of patients and 2 different clusters of protein expression (A). Volcanoplot represented the comparison IgG dcSSc ATA+ vs IgG HC (B). Venn diagram representing the proteins in common and exclusive of the following comparison: IgG dcSSc ATA+ vs HC, IgG dcSSc ATA- vs IgG HC and IgG dcSSc ATA- vs IgG HC (C). *IgG HC: purified IgG from healthy controls; IgG dcSSc ATA+: purified IgG from diffuse systemic sclerosis anti-topoisomerase-I positive patients; IgG dcSSc ATA-: purified IgG from diffuse systemic sclerosis anti-topoisomerase-I negative patients; IgG lcSSc ACA+: purified IgG from limited systemic sclerosis anti-centromere positive patients. ANOVA: analysis of variance.*

Conclusion: Using sensitive proteomic approach, we identified that purified IgG from SSc patients modified FB secretome in a serotype dependent manner. The data support the pathogenic role of Aab in SSc.

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OP0097 PROOF-OF-CONCEPT OF FIBROBLAST-TARGETED PHOTODYNAMIC THERAPY IN HUMAN 3D SCLERODERMA SKIN MODEL AND BLEOMYCIN-INDUCED SKIN FIBROSIS IN MICE

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Background: Systemic sclerosis (SSc) is a rare, severe auto-immune disease characterized by inflammation, vasculopathy and fibrosis. Activated (myo)fibroblasts are crucial drivers of fibrosis. By exploiting their expression of fibroblast activation protein (FAP) to perform targeted photodynamic therapy (tPDT), we can locoregionally deplete these pathogenic cells.
Objectives: We explored the use of FAP-tPDT to selectively target primary skin fibroblasts from SSc patients, both in 2D and 3D cultures, as well as in biopsies from fibrotic skin lesions in the murine bleomycin-induced skin fibrosis model.
Methods: The FAP targeting monoclonal antibody (clone 28H1) was conjugated with the photosensitizer IRDye700DX. Primary skin fibroblasts were obtained from lesional skin biopsies of SSc patients via spontaneous out-growth and subsequently cultured on plastic or collagen type I. For 2D FAP-tPDT, cells were incubated in buffer with or without the antibody-photosensitizer (Ab-PS) construct, washed after 4 h and exposed to λ = 689 nm light (50 J/cm^2 at 280 mW/cm^2). Cell viability was measured using CellTiter Glo. For 3D FAP-tPDT, cells were seeded in collagen plugs and underwent the same treatment procedure. Contraction of the plugs was followed over time to determine myofibroblast activity. Skin fibrosis was induced in mice by 3x/week injections of 1.5 IU bleomycin intradermally on the back of the mouse. After 5 weeks the mice were sacrificed and biopsies were taken from affected and not affected skin. These were incubated with or without the FAP targeting Ab-PS construct or a control Ab-PS. After washing, the biopsies were exposed to light, incubated for 1h and subsequently formalin fixed and paraffin embedded. Sections were immuno stained for the presence of cleaved caspase-3.
Results: FAP-tPDT resulted in antibody-dose dependent cytotoxicity in primary skin fibroblasts upon light exposure. Cells not exposed to light or incubated with a control Ab-PS construct did not show this response. FAP-tPDT fully prevented contraction of collagen plugs seeded with primary SSc fibroblasts. Even incubation with a very low dose of antibody (0.4 nM) inhibited contraction in 2 out of 3 donors. In fibrotic skin biopsies from mice with bleomycin-induced skin fibrosis, an upregulation of apoptosis, as evidenced by increased caspase-3 staining (Figure 1), was observed in response to FAP-tPDT. The same treatment on biopsies of control skin did not increase caspase-3 staining, nor did incubation with a control Ab-PS construct or light alone.

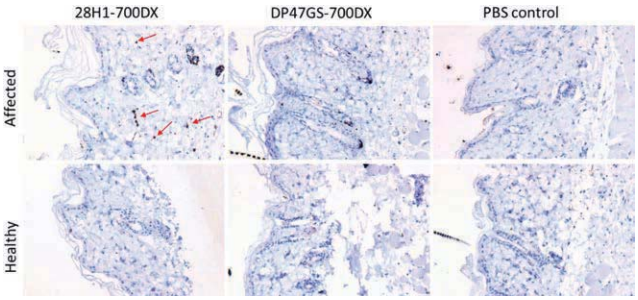

Figure 1. *Cleaved caspase-3 staining of biopsies from the skin of mice with bleomycin-induced dermal fibrosis upon treatment with FAP-tPDT. The red arrows indicate the presence of positive fibroblasts.*

Conclusion: Here we have shown, for the first time, the potential of FAP-tPDT for the selective targeting of pathogenic fibroblasts and treatment of fibrosis in SSc skin both in relevant patient-derived culture models as well as an *in vivo* model of fibrosis.
Disclosure of Interests: Daphne Dorst: None declared, Arjan van Caam: None declared, Elly Vitters: None declared, Birgitte Walgreen: None declared, Monique Helsen: None declared, Christian Klein Employee of: CK is an employee of Roche pharmaceutics, Shreya Gudi: None declared, Tirza Wubs: None declared, Jyoti

Kumari: None declared, Przemysław Błyszczuk: None declared, Madelon Vonk: None declared, Peter van der Kraan: None declared, Marije Koenders: None declared.
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Microbiome and SpA

OP0098

PREDICTING TREATMENT OUTCOME IN PATIENTS WITH SPONDYLOARTHRITIS USING MICROBIOTA ANALYSIS

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Background: Autoimmune-related rheumatic diseases such as rheumatoid arthritis (RA) and spondyloarthritis (SpA) are caused by an interplay of various factors including genetics, environmental factors and lifestyle. Among them, the intestinal microbiome has been suggested to influence disease initiation and progression. While the pathogenic connection between the microbiome and autoimmunity remains ambiguous, there is evidence that, for instance, microbiota-derived antigens cross-react with autoantibodies triggering an immune response and disease development[1]. However, other hypothesis such as the leaky gut model have been explored[2]. In addition to this potential involvement in disease initiation, microbial signatures have been identified to predict treatment outcome, i.e., as shown for the first-line medication Methotrexate (MTX) in RA patients[3].
Objectives: Our study aimed to longitudinally compare gut microbiota composition between treatment-naïve patients with different forms of rheumatic disorders from disease onset to remission/relapse to identify i) disease-specific signatures and ii) their impact on therapeutic responses.
Methods: Patients with new onset of rheumatic disorders as well as their household members were recruited in the Rheuma-VOR cohort. The patients presented without treatment with steroids or DMARDs. The diagnosis was made by experienced rheumatologists. Native and stabilized fecal samples were collected, and 16S rRNA amplicon sequencing was performed to determine microbiota composition. Patients with non-inflammatory rheumatic disorders served as controls, whereas treatment was initiated in patients with inflammatory rheumatic diseases. Clinical data of patients was recorded including monitoring of medication and treatment response.
Results: A total of 422 fecal samples were analyzed from patients diagnosed with different forms of immune-mediated rheumatic diseases, non-inflammatory rheumatic diseases as well as from household controls (Table 1). Using 16S rRNA amplicon sequencing, we did not detect any clustering of patient groups during disease onset based on the microbiota composition (Figure 1A). However, PsA patients responding to MTX (MTX-R) (=patients in DAPSA remission 3-6 months after MTX initiation or patients showing partial response) and patients not in remission (MTX-NR) differed in microbial diversity (Figure 1B) and specific bacteria were enriched in MTX responders.

Table 1. ***Overview of RheumaVOR samples analyzed in this study***

Diagnosis	total number of samples	MTX treatment	MTX response: remission	MTX response: no remission	MTX response: response data not available yet
Household controls	188				
Non-inflammatory rheumatic diseases (NRD)	110				
Rheumatoid arthritis (RA)	33	28	11	6	11
Psoriatic arthritis (PsA)	47	34	13	12	9
Axial spondyloarthritis (axSpA)	35				
Reactive arthritis (ReA)	9				
In total	422				

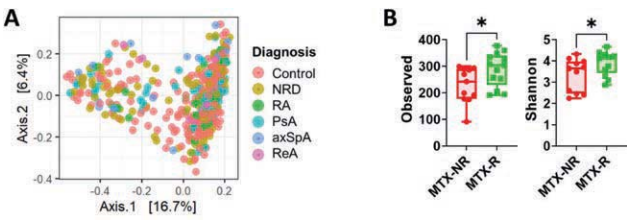

Figure 1. Microbiome analysis of RheumaVOR fecal samples. A: Analysis of beta diversity (PCoA) using Bray-Curtis distances. B: Alpha diversity of PsA patients receiving MTX as first-line medication. P values represent an unpaired nonparametric Mann–Whitney test, *p < 0.05.

Conclusion: While our study did not reveal global differences in the bacterial composition of the gut microbiota between patients diagnosed with RA and SpA as well as control groups, we identified changes in microbial diversity and the abundance of specific bacteria between MTX responders and non-responders in PsA patients. Further investigations are needed to clarify the complex interactions between the microbiome, disease onset in rheumatic disorders and DMARD treatment response to ameliorate disease progression and improve therapeutic outcome.

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The role of the synovial microenvironment during onset and progression of arthritis

OP0099

INCREASED FREQUENCY OF CD4+ AND CD8+ FOLLICULAR HELPER T CELLS IN HUMAN LYMPH NODE BIOPSIES DURING THE EARLIEST STAGES OF RHEUMATOID ARTHRITIS

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Background: Follicular T helper (Tfh) cells provide key help for B cell differentiation into plasma and memory B cells and are essential in germinal center formation and (auto) antibody generation (1).
Objectives: To gain more insights into the role of Tfh cells in RA development, we assessed whether Tfh cells have an altered frequency, phenotype and cytokine profile in peripheral blood, lymphoid and synovial tissues during the earliest stages of RA development.
Methods: Using flow cytometry, we analyzed the phenotpe, frequencies and cytokine profile of Tfh cells and B cells in peripheral blood and lymph node biopsies of healthy controls (HCs), autoantibody positive individuals at risk for developing RA (RA-risk individuals), and early RA patients. Using immunofluorescene we confirmed the presence of Tfh in B cell follicles of lymph nodes and synovial tissue biopsies of RA patients.
Results: In blood, the frequency of Tfh cells did not differ between study groups. In lymphoid and synovial tissue, Tfh cells were localized in B-cell areas, and their frequencies correlated strongly with the frequency of $CD19^+$ B cells. Compared to lymphoid tissue of healthy controls, that of RA patients and RA-risk individuals, showed more $CD19^+$ B cells and more $CD4^+CXCR5^+$ and $CD8^+CXCR5^+$ follicular T cells. Of note, compared to healthy controls, specifically lymph node Tfh cells of RA-risk and early RA patients produced less IL-21 upon ex-vivo stimulation.
Conclusion: Tfh cells are localised in B-cell rich areas in lymphoid and synovial tissues of early RA patients. The analysis of lymph node tissue in early RA patients showed increased frequencies of Tfh cells, where they clearly associate with B cells. Interestingly, IL-21 production is already aberrant in the very early at risk phase of the disease. Our data suggest that Tfh cells may present a novel rationale for therapeutic targeting during the preclinical stage of RA to prevent further disease progression.

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Disclosure of Interests: Dornatien Anang: None declared, Tamara H.Ramwadhdoebe: None declared, Janine Hahnlein: None declared, Bo van Kuijk: None declared, Smits Noortje: None declared, Krijn P. van Lienden: None declared, Mario Maas: None declared, Danielle Gerlag Employee of: Employee of UCB Pharma. UCB pharma was not involved in this study, Paul-Peter Tak Employee of: Employee of Candel therapeutics. Candel therapeutics was not involved in the study, Niek de Vries: None declared, Lisa van Baarsen: None declared.
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Exploring the origin of inflammation in spondyloarthritis

OP0100 IL-17A BLOCKADE MODULATES DISEASE SPECIFIC IMMUNE AND STROMAL PATHWAYS IN PERIPHERAL SPONDYLOARTHRITIS SYNOVITIS

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Background: The cellular and molecular mechanisms driving inflammation and structural remodelling in spondyloarthritis (SpA) remain largely unknown, though the IL-23/IL-17 pathway can contribute to synovial inflammation and radiographic progression.
Objectives: To investigate the molecular pathways affected by IL-17A blockade (IL-17Ai) with secukinumab in SpA synovitis, and assess if this response is tissue- and/or treatment-specific.
Methods: Synovial biopsies were obtained from peripheral SpA patients by needle arthroscopy before and after 12 weeks of IL-17Ai with secukinumab (n=12), and analyzed by RNA-sequencing and qPCR. We performed pathway enrichment analysis of the differentially expressed genes (DEGs) to identify pathways modulated after treatment. We compared the synovial tissue response in patients with psoriatic arthritis (PsA) in our cohort (n=7) with open source gene expression data of skin biopsies of psoriasis patients receiving secukinumab (n=22)[1] and of synovial biopsies of PsA patients receiving IL-12p40/IL-23p40 blockade (n=7)[2].
Results: IL-17Ai significantly modulated the expression of 1255 genes (549 up- and 706 down-regulated, FDR 0.1) in the synovium at week 12 compared to baseline (Figure 1). Genes downregulated upon IL-17Ai were significantly enriched in GO terms and KEGG pathways related to immune and inflammatory responses, including neutrophil and monocyte chemotaxis, TNF-mediated, NF-κB-, Wnt-, and JAK-STAT signalling pathways, and, importantly, bone-remodelling responses, such as osteoblast and osteoclast differentiation. Upregulated genes are enriched in JNK-, MAPK-, Wnt-, and PI3K-Akt signalling and negative regulation of osteoblast differentiation. We validated differential expression of selected genes from several pathways by qPCR, including: *IL1B*, p=0.027; *CXCL6*, p=0.020; *ADAMTS4*, p=0.002; *MMP3*, p=0.020; and *CHRDL2*, p= 0.039.

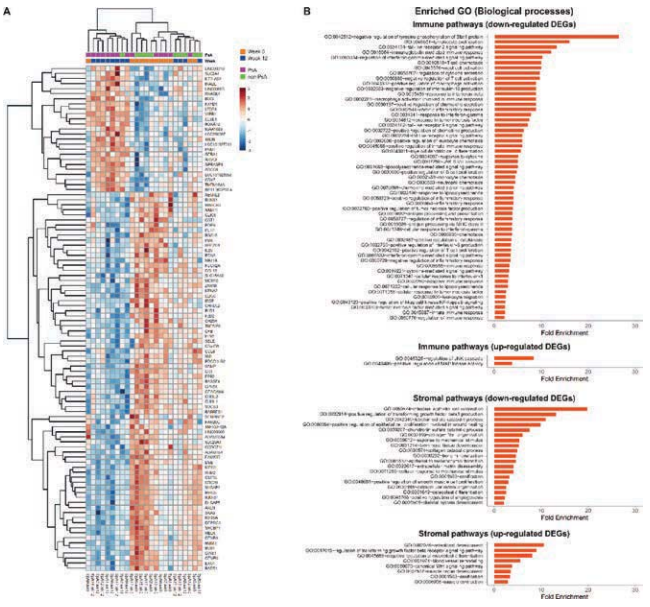

Figure 1. Heatmap of differentially expressed genes (DEGs) and pathway enrichment analyses of changes in peripheral SpA synovium 12 weeks after anti-IL-17A treatment (IL-17Ai). A. Hierarchical cluster analysis of the top 100 most significant DEGs (FDR < 0.1) modulated by IL-17Ai separates pre- and post-treated groups. Normalized and scaled log2 gene expression levels are shown. B. Pathway enrichment analysis through DAVID. Enriched (p < 0.05) gene ontology terms from IL-17Ai-induced up- and down-regulated DEGs in peripheral SpA synovium are shown.

To assess if this response is tissue- and/or treatment-specific, we compared changes in gene expression by IL-17Ai in PsA synovium versus psoriatic skin, and in the PsA synovium after IL-17Ai versus IL-12p40/IL-23p40 blockade. While many inflammation-related GO terms and KEGG pathways were over-represented in both tissues and treatments, NF-κB-, JAK-STAT-, and PI3K-Akt-signaling were enriched in DEGs in both skin and synovium after IL-17Ai, whereas JNK cascade, IL-17 signalling pathway and Th17 cell differentiation were over-represented in DEGs after IL-17Ai in the synovium specifically. Remarkably, IL-17Ai, but not IL-12p40/IL-23p40 blockade, modulated multiple bone-remodelling related pathways. Also, IL-17Ai modulated ossification and collagen catabolic process terms in PsA synovium and psoriatic skin in the opposite direction: these terms were over-represented in downregulated genes in synovium, but in upregulated genes in skin. Accordingly, genes upregulated after IL-17Ai were enriched in negative regulation of osteoblast differentiation in the synovium, but in positive regulation of osteoblast differentiation in the skin.
Conclusion: These first *in vivo* human data provide molecular confirmation of previously reported animal data[3] that demonstrated down-modulation of disease-relevant immune and stromal pathways in the synovium in response to IL-17Ai.
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Disclosure of Interests: Renée Fiechter: None declared, Leonieke van Mens: None declared, Ihsan Hammoura: None declared, Henriëtte de Jong: None declared, Desire Pots: None declared, Inka Fluri: None declared, Sander Tas: None declared, Dominique Baeten Employee of: Current employee of UCB Pharma, Marleen G.H. van de Sande Consultant of: Novartis and AbbVie, Grant/research support from: Janssen, Novartis and Eli Lilly, Nataliya Yeremenko: None declared.

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OP0101 MECHANICAL LOADING-INDUCED BHLHE40 PROMOTES INFLAMMATORY ARTHRITIS

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Background: Force induced microdamage to joint tissue is hypothesized to trigger inflammatory events in the joint leading to arthritis. Patients with inflammatory arthritis, such as rheumatoid arthritis (RA) and spondyloarthritis (SpA), are found to have inflammation in “mechanical hotspots” and mechanical loading in mouse models of these diseases is pro-arthritogenic[1,2]. To date, the molecular mechanism involved in converting force to a biological signal that promotes arthritis is not known.
Objectives: This study aims to identify stretch induced genes in synovial fibroblasts, and the effect of these “mechano-sensitive” genes on arthritis.
Methods: Human synovial fibroblasts were stretched in vitro for 4hrs using the FlexCell system and analysed by microarray. Top stretch induced genes were measured in RA, SpA and healthy synovial tissue by qPCR. Patient synovium was further analysed by immunohistochemistry. Bhlhe40 deficient mice were subjected to collagen induced arthritis (CIA) and KBxN serum transfer arthritis (STA). FACS was performed on ankle synovium. uCT was performed on whole ankles, with morphological changes scored by blinded readers, and calcaneus erosions by customs scripts in FIJI.
Results: 600 genes were found to be differentially expressed in stretched synovial fibroblasts (fold change > +/-1.5, adjusted p<0.05). 25% of these genes were found to be transcription factors, which included BHLHE40. BHLHE40 mRNA was elevated in the synovial tissue of RA/SpA vs healthy subjects (1.56 fold change), and BHLHE40 protein was widely detectable in synovial fibroblasts and macrophages (Figure 1). Bhlhe40 deficient mice were completely protected against CIA (incidence: 0% vs 40%, n=30 per group), but Bhlhe40 did not block the generation of anti-collagen antibodies. Bhlhe40 deficient mice were partially protected against STA (peak clinical score at day 7; 5.2 vs 6.8, n=15 per group), with reduced synovial macrophage (CD11b+Ly6G-F4/80+) and neutrophil (CD11b+Ly6G+) frequency observed in the arthritic Bhlhe40 deficient mice compared to wildtype controls. Bhlhe40 had no impact on bone erosions with STA.

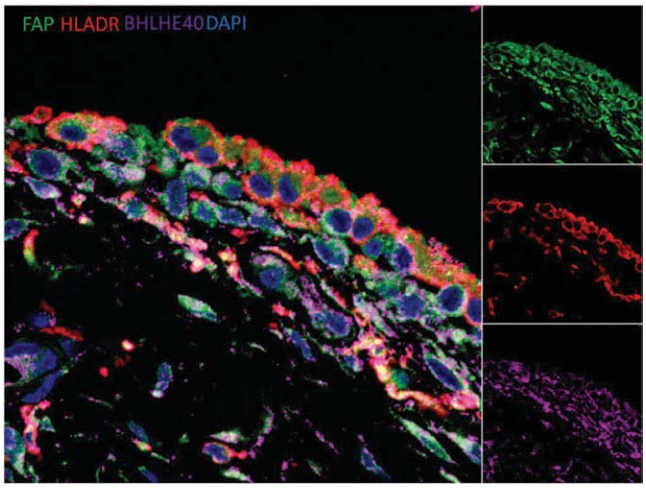

Figure 1. BHLHE40 is widely expressed in human synovium. Synovium obtained from total knee replacement. FFPE samples were stained for synovial macrophages (HLADR+) and fibroblasts (FAP+). Images acquired with the Zeiss LSM 780.

Conclusion: BHLHE40 was identified as a force-induced gene in synovial fibroblasts and was found to be upregulated in patients with inflammatory arthritis. Importantly, Bhlhe40 strongly promotes joint inflammation in murine models of arthritis and uncouples systemic autoimmunity from joint tissue inflammation. Thus, we have identified BHLHE40 as a novel regulator of mechanical loading-associated inflammation.

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Disclosure of Interests: None declared

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OP0102

THE SYNOVIUM IN CHRONIC INFLAMMATORY JOINT DISEASES: COMPARISON OF CLINICAL, HISTOLOGICAL AND SCRNA-SEQ DATA BETWEEN RA, PSA, SPA AND UA

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Background: The synovium is the primary location of inflammation in various rheumatic diseases. However, specific differences of joint inflammation have not been explored on a single-cell level so far.

Objectives: To characterize the synovium of rheumatoid arthritis (RA), psoriatic arthritis (PsA), spondyloarthritis (SpA) and undifferentiated arthritis (UA) based on clinical and histological characteristics and single-cell RNA sequencing (scRNA-seq).

Methods: We performed ultrasound (US) guided synovial biopsy in patients fulfilling classification criteria: 10 RA, 4 PsA, 4 SpA and 3 UA. 3 osteoarthritis (OA) samples were obtained from surgery. Clinical data were collected at time of biopsy. Histological analysis of the synovium included Krenn score [1], synovial pathotype [2], vascularization [3] and presence of lymphoid follicles. OA histology was not available. We prepared scRNA-seq libraries with 10X Genomics and sequenced on NovaSeq 6000. ScRNA-seq data was analysed with Cell Ranger, Seurat and Harmony R packages. We selected overexpressed genes using log2 ratio (>0.25) and FDR adjusted p value < 0.05.

Results: Patients showed typical disease characteristics. In RA, 6/10 were seropositive, 8/10 were female and median age was 59 years (IQR 12). Patients with PsA, SpA and UA were seronegative. 2/4 SpA and 1/4 PsA patients were HLA-B27 positive. Median age was 53 years in PsA (IQR 14.2), 52.5 in SpA (IQR 14.8) and 53 in UA (IQR 3.5). In PsA 3/4, SpA 2/4 and UA 1/3 patients were male. RA joints had significantly higher B-Mode US scores compared to PsA and SpA joints (mean B-Mode Score: RA 2.7; PsA 2; SpA 2). Correspondingly, RA patients reported a significantly higher amount of swelling in the biopsied joint compared to PsA and SpA (mean "Swelling-Score": RA 6.85; PsA 4.25; SpA 4).

Histology showed no clear differences in the cell composition; most joints showed a lympho-myeloid pathotype. Mean Krenn Score was highest in RA (4.78) and lowest in SpA (3.33). PD-Mode US score showed a significant positive association with histological vascularization. Lymphoid follicles were significantly more seen in RA compared to all other diseases.

Integration of scRNA-seq data revealed 16 cell clusters with respective marker gene: PRG4 synovial fibroblasts (SF), THY1 SF, ACTA2 smooth muscle cells, VWF endothelial cells, TPSB2 mastcells, IGHG plasma cells, CD79 B-cells, CD69 T-Cells, CCL5 natural killer cells, DMTN Treg-cells, CXC2 neutrophil granulocytes, TREM2 macrophages, CD48 macrophages, CLEC10A macrophages, CD4 dendritic cells, MKI67 proliferating cells. OA had the lowest and RA the highest number of inflammatory cells within the synovium. SpA synovium had the highest number of neutrophils. Re-Clustering of only SF revealed 4 subtypes: PRG4 SF (3578 cells), CXCL12 SF (4539 cells), POSTN SF (2387 cells) and MFAP5 SF (1734 cells). Top 5 marker genes are shown in the Table 1. Most differentially expressed genes in OA were found in PRG4 SF; the previously described OA specific gene CSN1S1 [3] was not only underexpressed in RA but also in other inflammatory joint diseases (Figure 1). PGF, a gene associated with pathological angiogenesis, was one of the top discriminator genes, highly expressed in PsA SF (mostly PRG4 SF). RA SF (mostly CXCL12 SF) showed a high expression of CHI3L1, which is a RA specific autoantigen. High expression of hemoglobin genes was found in SpA PRG4 SF; an unexplored but previously described finding [5, 6].

Table 1. Top 5 synovial fibroblast (SF) marker genes.

Cluster	Gene
PRG4 SF	PRG4
	CSN1S1
	MMP3
	CRTAC1
	HTRA1
CXCL12 SF	APOE
	CXCL12
	CCL2
	PTGDS
	CD74
POSTN SF	COMP
	COL1A1
	POSTN
	CILP
	PTN
MFAP5 SF	MFAP5
	SFRP2
	APOD
	CXCL14
	CFD

Conclusion: We were able to compare the synovium of the most common chronic inflammatory joint diseases on various levels for the first time. The findings set the path for future diagnostic, prognostic, and therapeutic approaches in inflammatory joint diseases.

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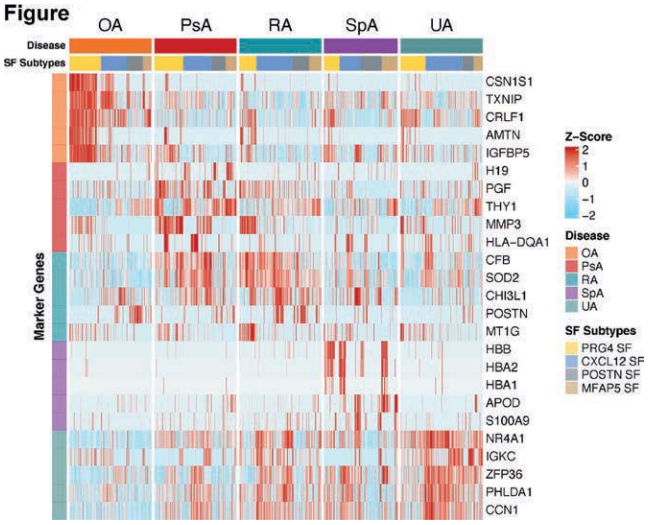
Figure



Disclosure of Interests: None declared

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OP0103

GENE EXPRESSION PROFILES RETRIEVED FROM SINGLE CELL RNA SEQUENCING REVEAL PHENOTYPIC TRAITS IN PATIENTS WITH PSORIATIC ARTHRITIS INITIATING TUMOUR NECROSIS FACTOR ALPHA INHIBITOR AND INTERLEUKIN-17 INHIBITOR

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Background: Patients with Psoriatic Arthritis (PsA) suffer from heterogenous debilitating symptoms caused by immune-mediated inflammation. However, great diversity in clinical response to available medical therapies targeting the immune response in PsA complicates treatment decision-making.
Objectives: The primary objective of the study was to evaluate gene expression profiles at baseline in responders versus non-responders of Tumour Necrosis Factors alpha inhibitor (TNFi) and Interleukin-17 inhibitor (IL-17i), respectively, to examine the foundation for future improved PsA patient stratification.
Methods: Single cell RNA sequencing (scRNAseq) was included to evaluate the transcriptome in responders versus non-responders of Tumour Necrosis Factor alpha inhibitor (TNFi) and Interleukin-17 inhibitor (IL-17i). Peripheral blood mononuclear cells (PBMCs) was isolated for scRNAseq and Disease Activity Score in PsA (DAPSA) retrieved in 40 PsA patients; 20 initiating TNFi and 20 initiating IL-17i. Responders and non-responders were stratified based on 50% improvement after 4-months (DAPSA50). The BD Rhapsody Whole Transcriptome Approach [1] was applied to prepare cDNA libraries sequenced to a depth of approximately 50.000 reads pr. cells on the Illumina NovaSeq 6000. The Seurat pipeline [2] was implemented for the analysis of gene expression on single cell level.
Results: A total of 273.515 cells were retrieved after initial quality control. Comparing patient demographics and characteristics at baseline revealed no difference between groups (Table 1). Dimensionality reduction with principal component analysis and additional clustering analysis indicated different phenotypic traits of responders and non-responders to TNFi and IL-17i (Figure 1). The results were limited by the DAPSA50 stratification only requiring 50% improvement at 4-month. Nevertheless, it is believed that scRNAseq can be included to improve PsA patient stratification.

Table 1. Patient characteristics

	All (n=40)	TNFi responders (n=12)	TNFi non-responders (n=8)	IL-17i responders (n=8)	IL-17i non-responders (n=12)	p-value
Sex, female	23 (57.5)	7 (58.3)	4 (50.0)	4 (50.0)	8 (66.7)	0.853
Age	51.9 ±12.1	48.4 ±10.9	54.7 ±11.6	49.6 (17.5)	52.7 ±9.9	0.766
Disease duration	8.1 ±7.4	6.7 ±6.8	10.1 ±10.1	10.4 ±7.9	13.7 ±6.4	0.903
DAPSA	36.5 ±18.5	34.4 ±23.2	34.1 ±13.8	50.5 ±17.3	38.5 ±17.9	0.176

Patient characteristics were presented as number with corresponding percentage or mean with corresponding standard deviations. P-value < 0.05 was considered statically significant. TNFi; Tumour Necrosis Factor alpha inhibitor, IL-17i; Interleukin-17 inhibitor, DAPSA; Disease Activity in Psoriatic Arthritis.

Conclusion: High-dimensional data, retrieved from scRNAseq combined with bioinformatical data modelling and clinical knowledge, is important and should possibly be implemented to explore PsA disease heterogeneity and for better stratification of PsA patients prior to initiating available medical therapies.
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Acknowledgements: We wish to acknowledge all patients participating in this study, our patient research partner Dorte Kongshøj Marcussen for valuable talks during the project and data manager Christian Cato Holm. Additionally, we wish to thank the parties providing funding to complete the study; Eli Lilly, The Danish Rheumatism Association, Elisabeth and Karl Ejnar Nis-Hanssens Mindelegat and Minister Erna Hamiltons Legat for Videnskab og Kunst.
Disclosure of Interests: Marie Skougaard Speakers bureau: has received speaking fees from Janssen, Grant/research support from: has received research funding from Eli Lilly, Pfizer, The Danish Rheumatism Association and the Danish Psoriasis Association., Clara Drachmann: None declared, Zara Rebecca Stisen: None declared, Sisse B. Ditlev: None declared, Leon Eyrich Jessen: None declared, Lars Erik Kristensen Speakers bureau: from Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Consultant of: from Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Grant/research support from: Novo, UCB, Eli Lilly; Novartis and Abbvie

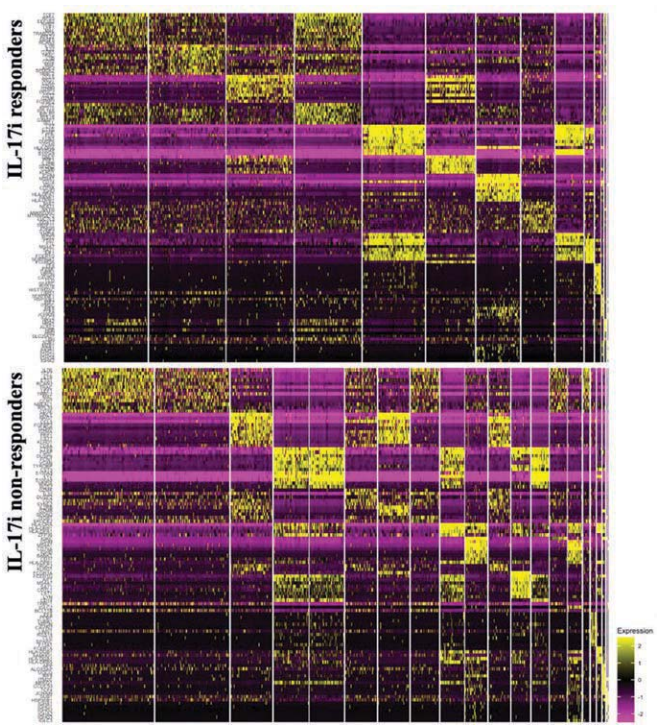

Figure 1. Gene expression profiles of DAPSA50 responders and non-responders to IL-17i Heat maps revealing differential gene expression of DAPSA50 responders and non-responders to IL-17i implying the possibility of improved stratification of PsA patients

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OP0104

EXPANDED CD8+ T CELL CLONES FROM HLA-B*27-POSITIVE PATIENTS WITH SPONDYLOARTHRITIS SHOW SIGNS OF ANTIGEN-EXPERIENCE

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Background: The pathogenesis of Spondyloarthritis (SpA) remains unknown but its strong association with some alleles of HLA-B*27 is peculiar. The arthritogenic antigen hypothesis assumes the existence of specific peptides presented by risk-conferring HLA-B*27 alleles to antigen-specific CD8+ T cells, which then initiate or sustain autoimmune reactions. Several studies analyzing T cell receptor (TCR) repertoire found preferred Variable TCR chains and motifs in the hypervariable complementary determining region (CDR) 3, but analyzed only TCR β-chains in bulk analyses[1,2].
Objectives: To analyze full sequence information of TCR including matching α- and β-chains from single CD8+ T cells and characterize the transcriptomes of expanded and non-expanded clonotypes in synovial fluid (SF) of SpA patients.
Methods: We included 17 patients with active gonarthritis: 10 patients with HLA-B27 positive (B27pos) SpA, 4 with HLA-B27 negative (B27neg) SpA and 3 rheumatoid arthritis (RA) patients. Antigen-experienced CD8+ T cells were sorted out of SF by flow cytometry. Single cell sequencing was performed for all patients to

analyze matching TCR α- and β-chains. For 7 patients (3 B27pos SpA, 2 B27neg SpA, 2 RA), additionally whole transcriptome analyses were performed.
Results: We found strong biases when analyzing α and β chains of TCR Variable regions and CDR1 and CDR2 sequences (Figure 1 a,b): AV21, AV12-2, and AV17 were highly enriched in B27pos SpA as compared to B27neg subjects. Amongst the highest expressed clones, we could confirm enrichment for previously described TRBV genes as BV19, BV5-1 and BV6-2. We examined TCR α/β combinations and focused on those detected in at least three different B27pos SpA but not in any of the B27neg patients (Figure 1 c-f). The combinations TRBV19/TRAV21 and TRBV6-2/TRAV21 were most likely specific for B27pos SpA and might reflect interaction of these TCR chains with HLA-B*27.

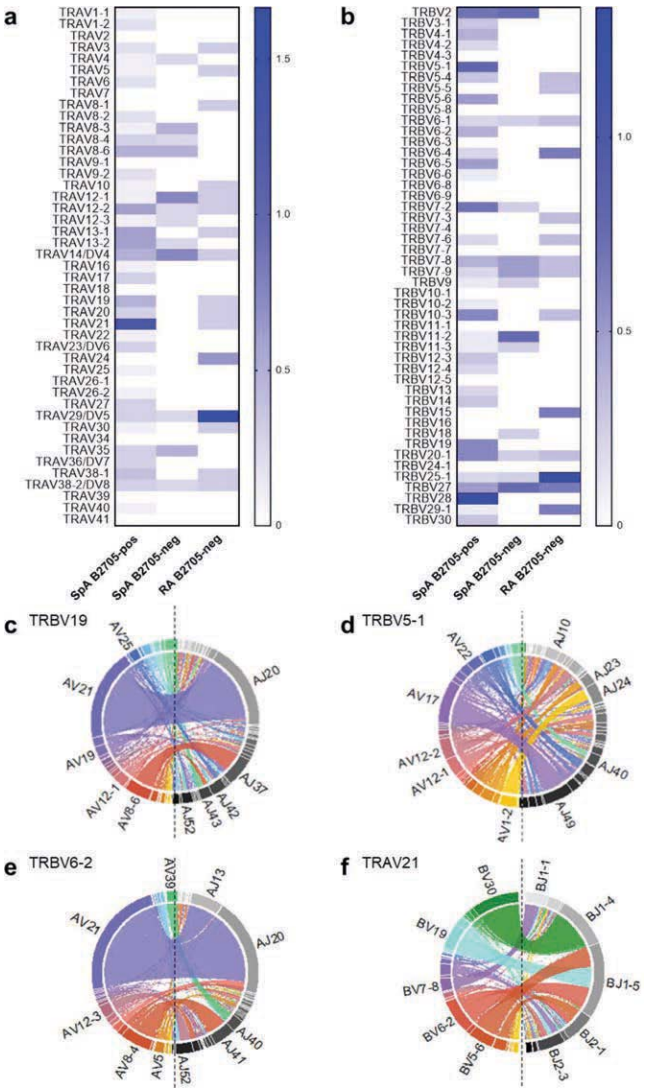

Figure 1. Distinct TCRαβ V chain usage in expanded clones from HLA-B27 positive SpA patients. A,B Mean number of all productive TRAV (A) and TRBV (B) genes used in expanded, antigen-experienced CD8 T cell clones (>1% of all cells) from SF of 10 B27pos SpA, 4 B27neg SpA and 3 B27neg RA patients. **C-F** TRAV chains paired with TRBV19 (C), TRBV5-1 (D), TRBV6-2 (E), or TRBV chains paired with TRAV21 (F) with corresponding TRAJ spanning partners in expanded cells (frequency ≥2) from all 10 B27pos SpA. Number of chains are 1250 (C), 886 (D), 1220 (E), and 4006 (F).

Sequences of CDR3 loops, which predominantly interact with HLA-bound antigenic peptides, revealed striking common structural motifs in α- and β-chains. Focusing on the most prominent TRAV21 chains pairing with TRBV19, 5-1 and 6-2 chains, revealed identical sequences in different patients and striking common structural motifs in α- and β-CDR3 sequences in other patients. Such marked similarities in the antigen-recognition loops of the β-chains associated with TRAV21 suggest common or highly similar antigens.
Gene expression levels provided evidence that expanded cell populations had tissue resident memory (TRM) phenotypes (elevated expression of activation, migration and tissue retention markers, downregulated genes characteristic for T cell egress), while this phenotype was not very pronounced in non-expanded cells. Furthermore, markers for T cell exhaustion and apoptosis were elevated in expanded cells of B27pos SpA patients.
Conclusion: Analysis of single antigen experienced CD8+ T cells from SF of B27pos SpA patients revealed significant clonal expansions and common motifs in the CDR loops. Two of the four CDR1 and CDR2 loops were highly homologous suggesting that these loops interact with α-helices of HLA-B*27. Common motifs in CDR3 loops of expanded clonotypes suggest recognition of a limited set of antigenic peptides presented by HLA-B*27. Many of the expanded clonotypes showed a TRM phenotype, were exhausted and on the way to become apoptotic, which suggests that these clones had sustained contact to specific antigens.
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Disclosure of Interests: None declared

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OP0105

MIRNOME PROFILE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: microRNAs (miRNAs) are small non-coding RNAs regulating up to 60 % of human mRNAs, including genes related to axial spondyloarthritis (axSpA) (1).
Objectives: This study aims to profile miRNome and to identify candidate miRNAs determining disease severity in patietns with non-radiographic (nr) and radiographic (r) axSpA.
Methods: The miRNome profiling experiment included peripheral blood mononuclear cells (PBMCs) of 96 subjects (38 patients with nr-axSpA, 38 patients with r-axSpA and 20 healthy controls). Firstly, massive parallel sequencing on NextSeq 500 (MPS, Illumina) was performed for miRNA screening. Selected candidate miRNAs were further validated using the qRT-PCR system (SmartChip) on the validation cohort of 141 subjects (47 patients with nr-axSpA, 44 patients with r-axSpA and 50 healthy controls). We employed the DESeq2 algorithm and generalized linear modelling with a negative binomial assumption (GLM-NB) to evaluate the association of candidate miRNAs to axSpA subtype and clinical disease activity (ASDAS and CRP).
Results: MPS revealed 432 unique miRNAs in all samples. We identified 13 differently expressed miRNAs in axSpA patients compared to healthy controls, and 14 differently expressed miRNAs in axSpA patients with high to very high ASDAS compared to patients with inactive disease. Data from validation cohort revealed that the expression level of miR-4286 was higher in patients with very high disease activity compared to patients with inactive disease. Simultaneously, miR-4286 positively correlated with ASDAS. miR-4286 has been recently associated with osteogenesis and angiogenesis (2). None of the validated miRNAs was associated with the levels of CRP.
Conclusion: In this study, we identified that miR-4286 is related to disease activity and could play a role in the pathogenesis of axSpA.
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Disclosure of Interests: None declared

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OP0106 **SOLUBLE PD-1 PROMOTES LOCAL IL-17A PRODUCTION IN THE INFLAMED MICROENVIRONMENT IN SPA**

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Background: Programmed death 1 (PD-1) is an immune checkpoint receptor expressed by activated T-cells. Activation of the PD-1 pathway reduces T cell activation and inflammation. Targeting PD-1 in cancer can result in autoimmune disease, which highlights the importance of this pathway in balancing inflammation. Both PD-1 and its ligands are present in soluble (s) forms, and we have previously showed that sPD-1 is associated to bone erosions in rheumatoid arthritis. Spondyloarthritis (SpA) is characterized by both bone erosions and bone formation. Current evidence suggests an important interaction between the PD-1 pathway and the proinflammatory cytokine IL-17A. IL-17A is central in promoting inflammation in SpA and direct osteoclast activation leading to bone erosion. We have previously demonstrated that the PD-1 ligand, PD-L2, reduces osteoclast formation under inflammatory conditions.
Objectives: We aimed at investigating the interplay between the PD-1 pathway and IL-17A in relation to inflammation and bone homeostasis in patients with SpA.
Methods: From early SpA patients, plasma was collected at baseline and after 1 year of treatment with Adalimumab. From chronic SpA patients, plasma, synovial fluid (SF), peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) were collected. Plasma and PBMCs were also collected from healthy controls (HC) for comparison. Disease activity was measured by ASDAS and progression by inflammation and new bone formation in the total spine.
Facet joint biopsies were collected from SpA patients during surgery for correction of rigid hyperkyphosis. Levels of sPD-1 and sPD-L2 were measured in plasma and SF. Surface expression of PD-1 and CCR6 was evaluated on PBMCs and SFMCs. Levels of IL-17A were measured in the supernatant from stimulated PBMC cultures with recombinant human (rh)PD-1. Facet joint biopsies were stained for the presence of PD-1, PD-L1, PD-L2 and CCR6.
Results: Plasma levels of sPD-1 and sPD-L2 were equally increased in both early and chronic SpA compared to HC. Plasma levels of sPD-1 and sPD-L2 did not change following one year of treatment. In chronic SpA patients, sPD-1 levels were higher in SF than in plasma. Levels of sPD-1 and sPD-L2 in plasma and SF did not correlate with any disease activity scores or progression. Expression of PD-1 on the cell surface of PBMCs from SpA patient was comparable to healthy controls. On SFMCs, PD-1 expression was increased, supporting continuous T-cell activation in the local microenvironment. After stimulation with anti CD3/CD28, SpA PBMCs produced more IL-17A when cultured with rhPD-1 compared to healthy control PBMCs.
PD-1 and CCR6 were highly present in facet joint biopsies, but PD-L2 and PD-L1 could not be detected. This supports the PD-1 pathway to play a role at the actual site of pathology.
Conclusion: Plasma levels of the PD-1 family is unaffected by addition of anti-TNFα antibody treatment in SpA. The early SpA cohort had a low degree of progression in structural changes in the observation period, which could explain the lack correlation with sPD-1 and sPD-L2 and disease progression. Soluble PD-1 is high in the inflamed microenvironment, where it may result in increased IL-17A production. Collectively, these data suggest that the PD-1 pathway could play a role in the pathogenesis of SpA, acting in the inflamed microenvironment.
Disclosure of Interests: None declared

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OP0107 **SERUM GRANULOCYTE-MONOCYTE COLONY STIMULATING FACTOR (GM-CSF) IS INCREASED IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS (AS) AND PERSISTS DESPITE ANTI-TNF TREATMENT**

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Background: There is increasing evidence of the pathogenetic role of monocytes and neutrophils in AS, while the neutrophil-to-lymphocyte ratio correlates with disease activity (1). Granulocyte-Monocyte Colony Stimulating Factor (GM-CSF) is a growth factor for both myeloid lineages and a potent pro-inflammatory cytokine activating myeloid cells, including pro-inflammatory M1 macrophage polarization, production of TNF and other cytokines, and promoting osteoclastogenesis (2). It signals through the JAK-STAT pathway.
Objectives: To measure serum GM-CSF together with markers of bone metabolism in patients with AS before and after anti-TNF treatment.
Methods: The study included patients with the clinical diagnosis of AS (also fulfilling the 1984 modified NY criteria) with increased disease activity despite treatment with NSAIDs, all being eligible for treatment with a biologic DMARD. Decision for treatment with a TNF-inhibitor was made by the treating rheumatologist. Healthy donors were sampled as controls. Serum was collected before (baseline, BL) and after 4-6 months (follow-up, FU) of anti-TNF treatment and the following molecules were measured using ELISA: GM-CSF, Sclerostin (SOST) and Dickkopf-1 (Dkk-1).
Results: Twelve patients with AS (7 males, 5 females, median age 37 years, range 22-52) with a median disease duration of 1 year (range 0.5-25) and 16 age- and sex-matched controls were included. At BL, patients had mean BASDAI 6.3±2 and ASDAS 3.2±0.7. At FU the mean BASDAI decreased to 4.1±1.7 and ASDAS decreased to 2.2±0.6. At BL, AS patients had significantly higher mean serum levels of GM-CSF (150 vs 62pg/ml, p=0.049), significantly lower Dkk-1 (1228 vs 3052pg/ml, p=0.001), but similar levels of SOST (369 vs 544pg/ml, p=0.144) compared to controls. Anti-TNF treatment did not significantly affect GM-CSF, Dkk-1 or SOST levels (p>0.05 for all comparisons at FU vs baseline). Spearman correlation analysis showed that GM-CSF correlated positively with ASDAS at baseline (r=0.61, p=0.039), negatively with age (r=-0.68, p=0.018), but not with disease duration (r=-0.27, p=0.400). No correlations were identified between bone markers (Dkk-1, SOST) and GM-CSF or disease activity indices.
Conclusion: GM-CSF is increased in patients with active AS, particularly in younger ages, and strongly correlates with disease activity, but not with disease duration. In contrast, TNF inhibition does not affect GM-SCF levels, despite improving disease activity. GM-CSF may represent an important pathway in AS that could be responsible for residual inflammation during TNF blockade, but also explain the efficacy pathway of treatment with JAK inhibitors.
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Disclosure of Interests: None declared
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From gene to function: genetic basis of rheumatic diseases

OP0108 **NEW INSIGHTS IN THE GENOMIC "GRAMMAR" OF RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is a complex disease, caused by a combination of genetic, epigenetic and environmental factors common to other related autoimmune diseases including Multiple Sclerosis (MS) and Systemic Lupus Erythematosus (SLE) [1]. Using state of the art Bioinformatics tools we are able to formulate an ensemble of associated components (genomic grammar) for each disease and distinguish important differences and common aspects in a specific group of disease such as ensembles of autoimmune diseases [2].
Objectives: To create, collect and evaluate the most credible and unique gene variants, epigenetic variants and single nucleotide polymorphisms (SNPs) causing the basis of an immune disease (the genomic grammar of the disease), which could potentially assist in the process of the RA disease prevention, diagnosis and treatment [3].
Methods: RA related publications from the PubMed have been analyzed using data mining and semantic techniques towards extracting the candidate causative SNPs. The extracted knowledge has been filtered, evaluated, annotated, and classified in a structured database which also includes GWAS information regarding SNPs. Additional clinical, genomic, structural, functional and biological information was also extracted from biological databases including dbSNP, LitVar, ClinVar and OMIM and cross-correlated with other available autoimmune disease related SNP databases, including the Demetra application, Epione application and Panacea application databases [3, 4].

Results: A holistic genetic map of the studied autoimmune diseases with more than 2000 related SNPs has been estimated and specific sub-clusters with crucial nodes have been identified across the RA, SLE and MS diseases. Based on these results, the three studied autoimmune diseases share a 10% common SNPs genetic background (Figure 1 and Table 1) [5]. The optimal genomic grammar of the RA contains 1682 SNPs, with 73% responding to non-coding regions and 27% responding to coding regions of more than 1.300 genes, pseudogenes, primers and promoters. RA also shares 464 common SNPs with SLE and 113 with MS.

Table 1. Common Related Genes based on the analyzed SNP targets in the studied disease.

A/A	Gene / Region	A/A	Gene / Region
1.	*ADAM33*	2.	*LOC285626*
3.	*ADIPOQ*	4.	*MIR3142HG*
5.	*CD40*	6.	*MIR499A*
7.	*CIITA*	8.	*MTHFR*
9.	*CTLA4*	10.	*MT-ND5*
11.	*FCRL3*	12.	*NCF1*
13.	*HLA-DPB1*	14.	*NLRP1*
15.	*HLA-DRA*	16.	*NOS3*
17.	*HLA-G*	18.	*NR3C1*
19.	*IL17A*	20.	*PADI4*
21.	*IL1RN*	22.	*PDCD1*
23.	*IL2*	24.	*PON1*
25.	*IL23R*	26.	*STAT4*
27.	*IL6*	28.	*TGFB1*
29.	*IL7R*	30.	*TLR9*
31.	*IRAK1*	32.	*TNF*
33.	*VDR*	34.	*TNFRSF1A*
35.	*IRF5*	36.	*TYK2*
37.	*KIF5A*	38.	*UCP2*
39.	*LEP*		

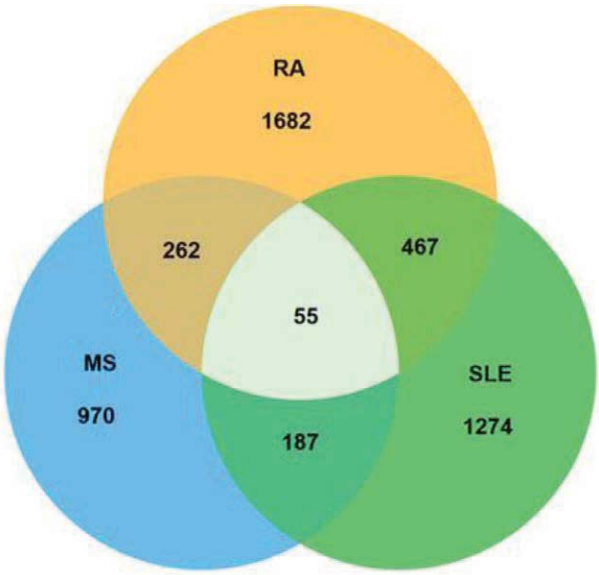

Figure 1. Three class Venn diagram of the genomic grammar between RA, MS and SLE.

Conclusion: The identification of the optimal genomic grammar in RA will help towards understanding the nature of the disease. Specific genetic targets via determined SNPs could act as biomarkers that aid in forming the right diagnosis [6].

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OP0109

EXPRESSION QUANTITATIVE TRAIT LOCI IN EARLY TREATMENT-NAÏVE RHEUMATOID ARTHRITIS

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Background: To date more than 100 genetic loci have been associated with rheumatoid arthritis (RA), particularly in the human leukocyte antigen (HLA) region. Our understanding of the functional consequences of genetic variation in RA causality, however, is limited and it has been shown that a substantial portion of complex disease risk alleles modify gene expression in a cell-specific manner [1]. The Pathobiology of Early Arthritis Cohort (PEAC) is a longitudinal study looking at treatment-naïve RA patients with genotyped data as well as both synovial and blood RNA-sequenced biopsies prior to treatment with disease modifying anti-rheumatic drugs (DMARDs).

Objectives: To explore expression quantitative trait loci (eQTL) in synovium and blood within PEAC and characterise the effects of genetic variation on gene expression measured by RNA-sequencing. A further goal was to investigate the role of these variants in RA disease severity and response variables.

Methods: Genotypes were generated by Illumina Human CoreExome-24 version 1-0 array in 118 RA patients. Single nucleotide polymorphisms (SNPs) in the HLA region were imputed using HLA-TAPAS. A candidate gene study was performed on variants within the HLA region using Plink v2.0. Synovial (n=85) and blood (n=51) RNA-sequenced samples then underwent *cis*-eQTL analysis (loci within $\pm 5x10^5$Mb of the variant) based on linear regression models with the matrixeQTL R package using PEER [2] and PCA eigenvectors as covariates. Differences in eQTL between tissues were determined using a linear interaction term.

Results: The candidate gene study determined several amino acids around *HLA-DRB1* acting as markers for seropositivity, which replicated findings by Raychaudhuri et. al. [3]. Using eQTL analysis, around 33,000 synovial SNPs were found with genome-wide significance ($p \leq 5x10^{-8}$) and around 29,000 in blood. This corresponded to 279 unique significant genes in synovium and 417 in blood (Figure 1). There were 100 genes common to both synovium and blood, including *PSORS1C3, HLA-DRB9* and *ERAP2,* which have known associations with autoimmune diseases and inflammatory arthritis. Notably, 92 genes showed significantly different patterns of QTL expression between synovial tissue and blood ($p \leq 5x10^{-8}$). eQTL data also confirmed the triad of genetic variants significantly driving tissue gene expression of *HLA-DPB2*, while both *HLA-DPB2* SNPs and *HLA-DPB2* RNA-sequencing synovial expression correlated highly with erythrocyte sedimentation rate (ESR).

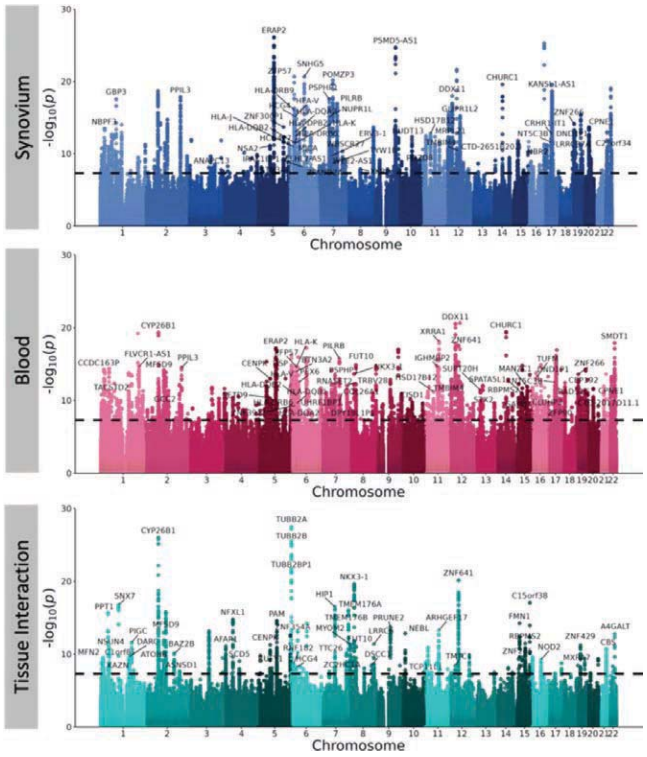

Figure 1. Manhattan plots for *cis*-expression quantitative trait loci (eQTL) analysis performed on 85 synovial samples (top) and 51 blood samples (middle). Tissue interaction eQTL (bottom) show significant differences between tissues ($p \leq 5x10^{-8}$).

Conclusion: The high significance of genes in the HLA region in both tissues is in-keeping with the strong association between HLA and susceptibility to RA, as well as other autoimmune diseases. Most notably variants linked to *HLA-DPB2* synovial expression were found to be a marker for disease severity through ESR association. Additionally, the significant differences between eQTL in blood and synovium highlight the need to explore functional consequences of genetic associations in the diseased tissue directly.

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OP0110 CELL-TYPE-SPECIFIC TRANSCRIPTOME ARCHITECTURE UNDERLYING THE ESTABLISHMENT AND EXACERBATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with unknown etiology involving multiple immune cells and has diverse clinical phenotypes. This heterogeneous nature has hampered a better understanding of SLE pathogenesis and the development of effective therapeutic agents. While recent single-cell RNA sequencing studies of SLE identified several important cell subpopulations, they were limited by sparse expression information at single-cell level and small sample sizes.

Objectives: This study aimed to elucidate the dysregulated gene expression pattern linked to multiple clinical statuses of SLE with a fine cellular resolution and higher sensitivity. We also attempted to resolve a complex interaction between risk variants and the transcriptome dysregulation seen in SLE patients.

Methods: We conducted a large-scale bulk transcriptome study of 6,386 RNA-sequencing data including 27 purified immune cell types in peripheral blood from 136 SLE and 89 healthy donors in the Immune Cell Gene Expression Atlas from the University of Tokyo (ImmuNexUT) cohort[1]. At enrollment, SLE patients had diverse clinical manifestations (disease activity, organ involvement and treatment profiles) and 22 patients were re-evaluated after belimumab treatment.

Results: We first profiled two distinct cell-type-specific transcriptomic signatures: disease-state and disease-activity signatures, reflecting disease establishment and exacerbation, respectively.

After confirming the high replicability of both signatures in independent cohorts, we identified candidates of biological processes unique to each signature: e.g., upregulated *E2F* transcriptional activity in Th1, CD8+ memory T-lineage and NK cells, and dynamic increase of *IL21* and *CXCL13* in Th1 cells in an active phase of SLE. Pathway analysis highlighted the importance of immunometabolic process for SLE (e.g., oxidative phosphorylation) in cell-type-specific resolution.

Moreover, we demonstrated cell-type-specific contributions to diverse organ involvement, e.g., Th1 for mucocutaneous, monocyte-lineage cells for musculoskeletal, neutrophil-lineage cells for renal activity, respectively.

We also observed the strong associations of disease-activity signatures with treatment effect: (i) belimumab suppressed activity signatures from B-lineage cells, especially in good responders and (ii) mycophenolate mofetil substantially suppressed activity signatures from plasmablast, Th1, and central memory CD8 cells.

However, through stratified LD score regression using large-scale SLE-GWASs, we revealed that disease-activity signatures were less enriched around SLE risk variants than disease-state signatures. Consistent with this result, the directions of SLE risk alleles' expression quantitative trait locus (eQTL) effects were significantly concordant with the directions of disease-state signatures, but not with those of activity signatures. These findings suggested that the current genetic case-control studies may not well capture clinically vital biology linked to drug target discovery for SLE. Meanwhile, we also detected some examples of activity signatures that might contribute to the disease risk by modulating risk allele's eQTL effects.

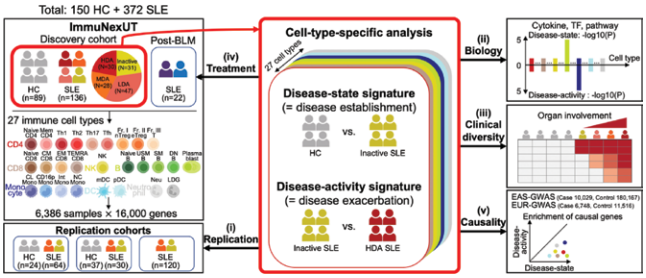

Figure 1.

Conclusion: We identified comprehensive gene signatures reflecting the establishment and exacerbation of SLE, which provide essential foundations for future genomic, genetic, and clinical studies.

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OP0111 INTEGRATION OF GWAS AND EPIGENETIC STUDIES IDENTIFIES NOVEL GENES THAT ALTER EXPRESSION IN THE MINOR SALIVARY GLAND IN SJÖGREN'S DISEASE

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Background: Sjogren's disease (SjD) is an autoimmune disease characterized by reduced function of exocrine glands (i.e., salivary and lacrimal glands). Epithelial cell damage resulting from lymphocytic infiltration has been implicated in SjD etiology [1]. How genetic and epigenetic changes influence epithelial-immune cell interactions in SjD pathogenesis remain understudied.

Objectives: Evaluate the role of SjD risk loci in salivary gland tissue to gain insights into the potential genes involved in salivary gland dysfunction.

Methods: SNPs from 16 regions with SNP-SjD associations (P<5x10-8) in our GWAS study (3232 SjD cases) and meta-analysis of ImmunoChip data (619 SjD cases) [2] were interrogated for eQTLs using Genotype-Tissue Expression (GTEx) minor salivary gland data. Subsequent analysis identified genes that were both eQTLs in the minor salivary gland and significantly expressed in RNA-seq and ATAC-seq data from the submaxillary salivary gland epithelial cell line, A253. Pathway enrichment analysis was performed using gProfiler on the genes where coalescence of eQTL, RNA-seq, and ATAC-seq data was observed. To further validate the results, we performed transcriptome-wide association study (TWAS) analysis using GWAS summary statistics and minor salivary gland eQTL GTEx data.

Results: In total, 5884 genome-wide significant SNPs from 16 SjD risk loci were identified as potential minor salivary gland eQTLs using two discovery thresholds: p(FDR)<0.05 provided by eQTL study (3566 SNPs) and p(FDR)>0.05 and p<0.05 in eQTL study (2318 SNPs). Further analysis revealed 10 SjD risk loci with SNPs that were minor salivary gland eQTLs for a total of 155 unique genes that had a coalescence of RNA- and ATAC-seq data in A253 cells. Many SNPs altered the expression of the nearest gene to the risk allele (i.e., index gene), such as *IRF5* and *TNPO3* on chromosome 7 at 128Mb; however, this locus had 12 additional genes that were eQTLs in minor salivary gland. In contrast, other loci had no reported eQTLs for the index gene, but several reported eQTLs for other genes, such *TYK2* on chromosome 19 at 10Mb that showed no change in *TYK2* expression but eQTLs for 8 distant genes, including *ICAM1*. Pathway enrichment analysis revealed an enrichment in Butyrophilin (BTN) family interactions (R-HSA-8851) (PAdj=1.564x10-5), including the *BTN2A1*, *BTN2A2*, *BTN3A1*, *BTN3A2* and *BTN3A3* gene cluster in the MHC region. In further support, TWAS of the minor salivary gland and the SjD GWAS summary statistics (after Bonferroni correction) showed association between SjD and *BTN3A2* (p=1.24x10-42), as well as many other loci in the MHC region. In addition, several long non-coding (lnc) RNAs on chromosome 17 were significant, peaking at *RP11-259G18.1* (p=4.43x10-10).

Conclusion: This study shows that SjD-associated risk alleles influence disease by altering gene expression in immune cells and minor salivary glands. Further, our analysis suggests that altered gene expression in the minor salivary gland expands beyond effects on the index gene to several genes on each locus. Interestingly, we observed minor salivary gland eQTLs for several BTN family genes, which act as cell-surface binding partners to regulate cell-cell interactions, including interactions between epithelial cells and activated T cells [3]. Future work will assess chromatin-chromatin-interactions within the 10 SjD risk loci in salivary gland cells and tissues to map local chromatin regulatory networks that regulate gene expression. Additional transcriptional studies of SjD minor salivary gland tissues will provide further insights into how altered gene expression in the salivary gland influences SjD pathology.

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OP0112

THE EVER-LARGEST ASIAN GWAS FOR SYSTEMIC SCLEROSIS AND TRANS-POPULATION META-ANALYSIS IDENTIFIED SEVEN NOVEL LOCI AND A CANDIDATE CAUSAL SNP IN A CIS-REGULATORY ELEMENT OF THE FCGR REGION

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Background: Genome-wide association studies (GWASs) have identified 29 disease-associated single nucleotide polymorphisms (SNPs) for systemic sclerosis (SSc) in non-human leukocyte antigen (HLA) regions (1-7). While these GWASs have clarified genetic architectures of SSc, study subjects were mainly Caucasians limiting application of the findings to Asians.

Objectives: The study was conducted to identify novel causal variants for SSc specific to Japanese subjects as well as those shared with European population. We also aimed to clarify mechanistic effects of the variants on pathogenesis of SSc.

Methods: A total of 114,108 subjects comprising 1,499 cases and 112,609 controls were enrolled in the two-staged study leading to the ever-largest Asian GWAS for SSc. After applying a strict quality control both for genotype and samples, imputation was conducted using the reference panel of the phase 3v5 1,000 genome project data combined with a high-depth whole-genome sequence data of 3,256 Japanese subjects. We conducted logistic regression analyses and also combined the Japanese GWAS results with those of Europeans (6) by an inverse-variance fixed-effect model. Polygenicity and enrichment of functional annotations were evaluated by linkage disequilibrium score regression (LDSC), Haploreg and IMPACT programs. We also constructed polygenic risk score (PRS) to predict SSc development.

Results: We identified three (*FCRLA-FCGR*, *TNFAIP3*, *PLD4*) and four (*EOMES*, *ESR1*, *SLC12A5*, *TPI1P2*) novel loci in Japanese GWAS and a trans-population meta-analysis, respectively. One of Japanese novel risk SNPs, rs6697139, located within *FCGR* gene clusters had a strong effect size (OR 2.05, $P=4.9\times10^{-11}$). We also found the complete LD variant, rs10917688, was positioned in cis-regulatory element and binding motif for an immunomodulatory transcription factor IRF8 in B cells, another genome-wide significant locus in our trans-ethnic meta-analysis and the previous European GWAS. Notably, the association of risk allele of rs10917688 was significant only in the presence of the risk allele of the *IRF8*. Intriguingly, rs10917688 was annotated as one enhancer-related histone marks, H3K4me1, in B cells, implying that *FCGR* gene(s) in B cells may play an important role in the pathogenesis of SSc. Furhtermore, significant heritability enrichment of active histone marks and a transcription factor C-Myc were found in B cells both in European and Japanese populations by LDSC and IMPACT, highlighting a possibility of a shared disease mechanism where abnormal B-cell activation may be one of the key drivers for the disease development. Finally, PRS using effects sizes of European GWAS moderately fit in the development of Japanese SSc (AUC 0.593), paving a path to personalized medicine for SSc.

Conclusion: Our study identified seven novel susceptibility loci in SSc. Downstream analyses highlighted a novel disease mechanism of SSc where an interactive role of *FCGR* gene(s) and IRF8 may accelerate the disease development and B cells may play a key role on the pathogenesis of SSc.

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OP0113

FUNCTIONAL GENOMICS IN PRIMARY T CELLS AND MONOCYTES IDENTIFIES MECHANISMS BY WHICH GENETIC SUSCEPTIBILITY LOCI INFLUENCE SYSTEMIC SCLEROSIS RISK

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Background: Systemic sclerosis (SSc) is a complex autoimmune disease with a strong genetic component. However, the underlying mechanism by which genetics increase disease risk is still unknown. The most recent GWAS studies have identified 27 independent signals associated to SSc [1]. However, the majority of these signals affect regulatory elements that can regulate genes often located hundreds of kilobases away.

The challenge in the post-GWAS era is to use functional genomics to translate genetic findings into patients' benefit, particularly in disease-relevant cell types.

Objectives: In this study we use chromatin conformation and gene expression analysis in patient derived primary cells and healthy individuals to assess potential mechanisms by which GWAS variants increase disease risk. We identify the potentially affected genes in a cell type specific manner and potential drug targets already in use or with potential for re-purposing.

Methods: Promoter capture Hi-C (pCHi-C) and RNA sequencing experiments were performed in a total of 15 CD4+ T cells and CD14+ monocytes samples each isolated from peripheral blood from SSc patients and healthy controls. We linked SSc-associated variants with their target genes and performed differential expression and differential interaction analyses between both cell types. Potential drug targets were identified using a protein-protein interaction model and queried against the OpenTargets database.

Results: We linked SSc-associated loci to 39 new potential target genes, confirming 7 previously assigned genes. We highlight novel causal genes, such as *CXCR5* as the most probable candidate gene for the *DDX6* locus (Figure 1). We confirm some previously linked SSc genes such as *IRF8*, *STAT4*, or *CD247* which interestingly showed cell type specific interactions. We also identified 15 potential drug targets already in use in other similar immune-mediated diseases that could be repurposed for SSc treatment. Furthermore, we observed that interactions are directly related with the expression of important genes implicated in cell type specific pathways.

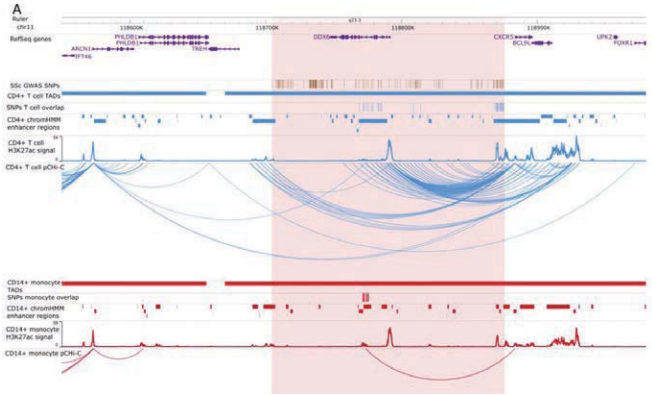

Figure 1. Promoter Capture Hi-C interactions linking the *DDX6* GWAS loci with the promoter of *CXCR5* in CD4+ T cells and CD14+ monocytes. CD4+ T cells show significantly stronger interactions as well as *CXCR5* gene expression.

Conclusion: Our study reveals potential causal genes for SSc-associated loci, some of them acting in a cell type specific manner, suggesting novel drug targets and biological mechanisms that may mediate SSc pathogenesis.

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OP0114 IDENTIFICATION AND FUNCTIONAL PREDICTION OF LONG NONCODING RNA RELATED TO CONNECTIVE TISSUE DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASES

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Background: Recently, the role of long noncoding RNA (lncRNA) in rheumatic immune diseases has attracted widespread attention[1]. However, knowledge of lncRNA in connective tissue disease-associated interstitial lung disease (CTD-ILD) is limited.

Objectives: To explore the expression profile of lncRNA in peripheral blood mononuclear cells (PBMCs) of CTD-ILD patients and the possible mechanisms of significantly differentially expressed lncRNA involved in CTD-ILD, especially systemic sclerosis (SSc)-ILD and rheumatoid arthritis (RA)-ILD.

Methods: LncRNA microarray analysis was used to identify the pattern of lncRNA dysregulation between CTD-ILD and connective tissue disease without associated interstitial lung disease (CTD-NILD). Differential genes were identified by bioinformatic analysis. Relative expression levels of five differentially expressed lncRNAs in 120 SSc and RA patients with or without ILD were detected by quantitative reverse-transcription PCR (qRT-PCR).

Results: The differential gene expression analysis revealed 46 lncRNAs were upregulated while 194 lncRNAs were downregulated in the CTD-ILD group compared to the CTD-NILD group (Figure 1). Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathway analyses identified several significant biological processes and signaling pathways, including NF-kappa B signaling pathway, IL-17 signaling pathway, Toll-like receptor signaling pathway, B cell receptor signaling pathway. QRT-PCR confirmed that the selected target genes were differentially expressed in different groups. In particular, the ENST00000604692 expression level was significantly higher in the ILD than the NILD group ($p<0.05$, Figure 1); T311354 and arginase-1were significantly higher in SSc than RA group; Furthermore, the area under receiver operating characteristic curve for ENST00000604692 in predicting ILD from NILD was 0.797 (Figure 1).

Conclusion: This research has demonstrated, for the first time, the specific profile of lncRNA in PBMCs of CTD-ILD patients and the potential signal pathways related to the pathogenesis of CTD-ILD. ENST00000604692 can effectively distinguish ILD group from NILD group,which may be a diagnostic indicator of CTD-ILD, especially SSc-ILD and RA-ILD.

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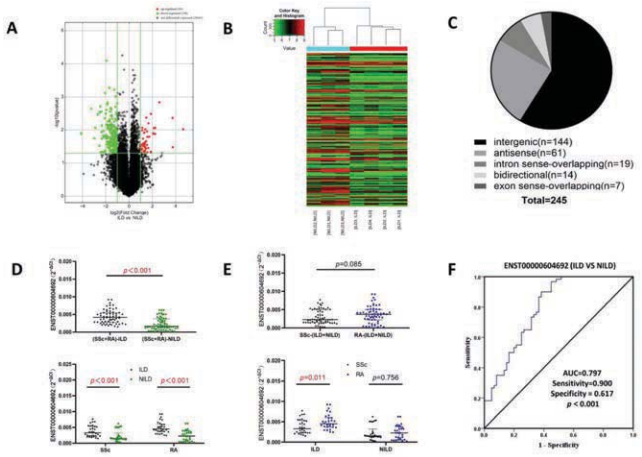

Figure 1 Expression of lncRNA in CTD-ILD and CTD-NILD. (A) Volcano plots visualizing differentially expressed lncRNAs between the two groups; (B) Clustered heatmap showing the comparison of all important lncRNAs between the two groups; (C) Differentially expressed lncRNA classification and subgroup analysis; (D) Relative expression (qRT-PCR) of the ENST00000604692 in ILD group and NILD group; (E) Relative expression (qRT-PCR) of the ENST00000604692 in SSc group and RA group; (F) ROC curve for analyzing the diagnostic value of ENST00000604692 for CTD-ILD.

Disclosure of Interests: None declared

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OP0115 MTDNA D-LOOP VARIANT M.16519C INCREASES THE RISK OF RAPID PROGRESSION OF KNEE OSTEOARTHRITIS. A META-ANALYSIS AND FUNCTIONAL STUDY

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Background: The development of a tool capable of identifying patients suffering the rapid progressive knee Osteoarthritis (RPOA) was established as a goal to implement prevention strategies and to include them in clinical trials. Previous studies showed that mitochondrial DNA (mtDNA) variation plays a role on the incidence and progression of OA, but their influence on the development of RPOA is unknown.

Objectives: To find new mtDNA variants related to RPOA in order to develop a predictive model based on genetic and clinical variables.

To find out the functional significance of these variants using transmitochondrial cybrids.

Methods: We used data from three independent prospective cohorts of patients: the Osteoarthritis Initiative (OAI) (N=1102) and the pooling of two European cohorts as replication cohort (N=706): the Cohort Hip and Cohort Knee (CHECK) and the Prospective Cohort of Osteoarthritis from A Coruña (PROCOAC). We classified the patients based on the following criteria:

- Rapid progressors (N Discovery=268, N Replication=107), subjects with baseline KL grade 0-1 and increase up to KL≥3 during 48-month follow-up; or baseline KL grade 2 and increase up to KL grade 4 during the follow-up.
- Non-rapid progressors (N Discovery=827, N Replication=592), subjects with the same baseline characteristics as rapid progressors, but with a slower or no evolution over time.

mtDNA variants were screened in the OAI by in-depth sequencing. Resulting variant was analyzed in the replication cohort by mini-sequencing techniques. Appropriate statistical approaches adjusting for confounding variables followed by a meta-analysis were applied.

We developed a functional study using two types of transmitochondrial cybrids carrying the most common haplogroup H: one harboring the mtDNA variant m.16519C and the other the wild type m.16519T. Cybrids were used to assess mitochondrial biosynthesis and mitochondrial fission/fusion by gene expression analyses, as well as cell viability to oxidative stress and mitochondrial reactive oxygen species (ROS) production.

Results: The in-depth sequencing of mtDNA showed the D-loop variant mt16519C significantly overrepresented in rapid-progressors (OR=1,558;95%CI=1,148-2,113;nominal p-value=0,004; Benjamini-Hochberg corrected p-value=0,044). The analysis of this variant in the replication cohort showed a similar significant trend (OR=1,647;95%CI=1,013-2,678; p=0,043).

The logistic regression model revealed that, regardless of the different clinical variables, the variant m.16519C was significantly associated with RPOA in the OAI cohort (OR=1,559;95%CI=1,125-2,161; p=0,008) (Table 1). The development of this model in the replication cohort showed a similar trend that borderlined the statistical significance (OR=1,506;95%CI=0,848-2,675;p=0,162) (Table 1). The subsequent meta-analysis for both ORs showed the variant m.16519C significantly associated with RPOA (OR=1,58;95% CI=1,22-2,05;p=0,0027) (Figure 1).

Table 1. Binary regression model including clinical variables and m.16519C in both cohorts.

Variable	A. Discovery				B. Replication			
	Sig.	O.R.	95% CI O.R.		Sig.	O.R.	95% CI O.R.	
			min	MAX			min	MAX
Age	<0,001*	1,054	1,036	1,072	0,138	0,972	0,937	1,009
BMI	<0,001*	1,073	1,037	1,110	0,727	1,010	0,957	1,066
Sex (Female)	0,142	1,258	0,926	1,710	0,190	1,582	0,796	3,144
Contralateral OA (Yes)	<0,001*	2,475	1,830	3,348	0,048*	2,056	1,005	4,208
WOMAC	<0,001*	1,122	1,065	1,183	0,060	1,062	0,997	1,130
mt.16519C	0,008*	1,559	1,125	2,161	0,162	1,506	0,848	2,675

BMI: Body Mass Index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; OR: Odds Ratio; CI: confidence interval; *: statistical significance declared at P < 0.05

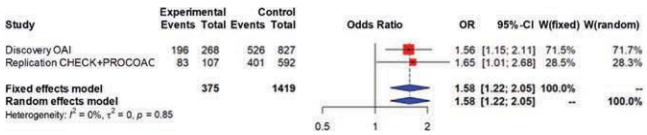

Figure 1. Forest plot of the meta-analysis of the ORs of the two predictive models

Cybrids harboring the mtDNA variant m.16519C showed lower levels of *PGC-1α* (p=0,0024) and *FIS1* (p=0,0519) than cybrids with the wild type. In addition, cybrids harboring the variant m.16519C showed lower average cell survival under oxidative stress conditions (23,42±8,88 vs 115,7±64,1;p=0,0043), as well as higher mitochondrial ROS production (4,21±1,29 vs 2,21±1,34;p=0,014).

Conclusion: D-loop variant m.16519C increases the risk of developing a rapid progression of knee OA. Among the effects caused by this variant both mitochondrial biogenesis and fission/fusion processes, as well as cell survival under oxidative stress conditions and mitochondrial ROS production seem to be affected

Disclosure of Interests: None declared
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HPR: From prevention to management

OP0116-HPR

PATIENTS' EXPERIENCES OF GROUP-BASED COGNITIVE BEHAVIOURAL THERAPY FOR INSOMNIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: A QUALITATIVE STUDY

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Background: Despite disease-modifying anti-rheumatic drugs, residual arthritis-related symptoms and burdens are still common in patients with rheumatoid arthritis (RA)[1]. In addition, insomnia – characterised by reduced sleep quantity and quality – is highly prevalent, occurring in up to 70% of patients with RA[2]. Insomnia is associated with increased pain, fatigue, and depressive symptoms. Cognitive behavioural therapy for insomnia (CBT-I) is recommended first-line treatment for chronic insomnia[3] but has not been evaluated in patients with RA until now.

Objectives: The objective of this study was to explore patients' experiences of CBT-I and how the components of CBT-I are incorporated in their sleep management.

Methods: Participants were patients with RA who had received CBT-I as experimental treatment for insomnia in a randomised controlled trial (RCT)[4]. Data were collected during an individual face-to-face interview using a semi-structured interview guide. The analysis was based on reflexive thematic method by Braun and Clarke[5].

Results: Eleven participants (10 women and one man) from the intervention group of the RCT were interviewed. Prior to inclusion in the RCT, they had insomnia complaints for 8 years (median; interquartile range: 3;20 years).

Five themes emerged: 1) *When knowledge contributes to an altered perception of sleep* referring to the reduced misperception and increased motivation that followed sleep education, 2) *Overcoming habits and perceptions to accelerate sleep onset* referring to barriers related to sleep behaviour and mindset and how stimulus control was enabling them to find meaningful behaviour and rhythm, 3) *The sleep window of challenges in learning how to sleep right* referring to that payoff from sleep restriction did not come easily or by magic, and commitment led to progress and gave them confidence to continue, 4) *Relaxation becomes a behavioural habit and goes beyond sleep* referring to a means to achieve a relaxed body and mind and how they thereby coped better with RA-related symptoms, and 5) *Break the cycle and regain control* referring to how awareness of a vicious cycle was central to their perception of sleep and how trust in one's own accomplishment was crucial to reducing worrying (See Figure 1).

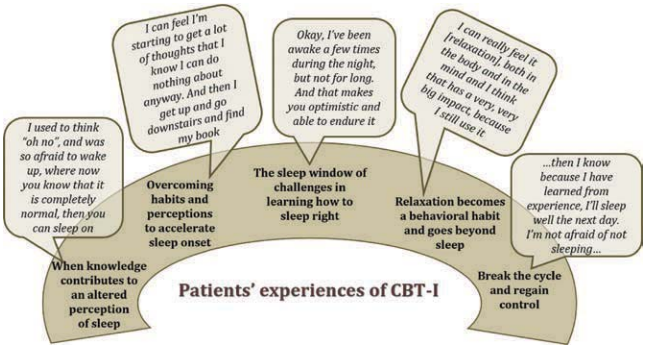

Figure 1. The five themes with quotes from participants

Overall, the participants experienced CBT-I as challenging and demanding but at the same time meaningful. The participants considered persistency, stringency, and inflexibility necessary to succeed. After the intervention, the participants had continued using those components that enabled them individually to further improve their sleep.

Conclusion: The process towards eliminating insomnia was a bodily experience and involved a changed mindset that altered behaviour and cognitions.

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[3] PMID: 28875581
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Disclosure of Interests: None declared

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OP0117-HPR FROM CURE TO COPING: EXPLORING TASK-SHIFTING BETWEEN NORWEGIAN RHEUMATOLOGISTS AND OCCUPATIONAL THERAPISTS IN THE CARE OF HAND OSTEOARTHRITIS

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Background: Task-shifting between physicians and other health professionals is increasingly used as a strategy to optimise health care services. However, there is a lack of evidence regarding task-shifting within the field of rheumatology, specifically hand osteoarthritis (HOA). HOA is a highly prevalent rheumatic joint disease, and the number of people living with debilitating HOA will continue to rise in the coming decades [1, 2]. HOA is diagnosed based on clinical examination and the first choice of treatment is non-pharmacological. Despite this, patients with HOA are increasingly referred to rheumatologists (RTs) in specialist care, contributing to long wait times and bottle-necks within the health care service. A possible solution to this challenge is task-shifting to occupational therapists (OTs).

Objectives: To explore the process of task-shifting in the care of patients with HOA between RTs and OTs in a Norwegian health care context.

Methods: This is a multi-centre qualitative study. Individual semi-structured interviews were conducted in-person or digitally with RTs and OTs between December 2020-June 2021.They were audio-recorded and transcribed verbatim. Reflexive Thematic Analysis was employed to analyse the data, and carried out in NVivo.

Results: In total, 17 participants were interviewed; 9 RTs and 8 OTs. Majority of respondents were female (n= 14), had an average of 20,5 years of experience and were 48,5 years old. Interviews lasted on average 90 minutes, (range: 45-120 minutes). The analysis resulted in 5 main themes

(1) Attitudes towards task-shifting of HOA care: Both RTs and OTs were overwhelmingly positive about task-shifting and reported OTs to be better suited caring for patients with HOA than RTs. There was agreement amongst RTs that generally, they had little to offer HOA patients besides information.

(*2) Desirability of caring for HOA*: RTs felt no occupational "ownership" of the HOA diagnosis due to the lack of curative medical treatment, and would prefer HOA patients to be seen by an OT. OTs on the other hand perceived themselves as a profession with tools, skills and competencies that would benefit patients with HOA.*3) Practical and theoretical knowledge:* OTs and RTs viewed different kinds of knowledge as central for task-shifting. Respondents emphasised that OTs must have good anatomical knowledge of the hand and confidence in identifying differential diagnoses that could potentially be more serious. Lack of knowledge lead to insecurity and hampered successful implementation of task-shifting. (*4) Communication between RTs and OTs:* RTs perceived OTs to be passive in communicating their willingness and competence in caring for this patient group. They expressed a wish for more "self-promotion" from OTs. OTs and RTs viewed communication between them as essential for task shifting. Good communication, understanding and inquisitive conversations acted as facilitators.

(5) *The importance of informal interpersonal relationships in the workplace:* Informal interpersonal relationships facilitated trust and subsequent task-shifting between RTs and OTs. Personal relations directly affected engagement in the task-shifting process.

Conclusion: The findings show a unanimous wish for HOA care to be shifted from RTs to OTs. Attitudes towards HOA as a diagnosis, interpersonal relationships between RTs and OTs, and knowledge are key facilitators and barriers affecting this process. The findings contribute to the growing body of knowledge on strategies used to optimise health care services and can be used in the design and implementation of new care pathways for patients with HOA.

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OP0118-HPR GAMING FOR ADHERENCE TO MEDICATION USING E-HEALTH IN RHEUMATOID ARTHRITIS (GAMER) STUDY – A RANDOMISED CLINICAL TRIAL

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Background: Effectiveness of pharmacological therapy in rheumatoid arthritis (RA) is limited by inadequate medication adherence. Medication adherence can be influenced by implicit attitudes of personal medication needs and concerns about adverse consequences. We targeted these implicit attitudes using a serious puzzle game.

Objectives: To assess the effectiveness of a serious game compared to usual care to improve adherence to disease modifying anti-rheumatic drugs (DMARDs) in patients with rheumatoid arthritis (RA).

Methods: A multicentre randomised clinical trial was performed with a 3 month follow-up period.[1] Inclusion criteria were adulthood, RA diagnosis, use of DMARDs and possession of a smartphone/tablet. All participants received usual care. In addition, intervention participants were invited to play the serious puzzle game at will. The game was designed to influence players' attitudes toward medication.[2] Collected data consisted of serious game play data, Compliance Questionnaire in Rheumatology (CQR), Beliefs about Medication Questionnaire (BMQ), Health Assessment Questionnaire (HAQ) and Rheumatoid Arthritis Disease Activity Index (RADAI).

Primary outcome was DMARD implementation adherence at three months assessed as the difference in proportion of non-adherent patients (<80% taking adherence) between intervention and control group using the discriminant function of the CQR using the Chi-squared test.

Two sample t-tests and Wilcoxon rank-sum test were performed to test for differences on secondary outcomes between study groups where appropriate.

Results: 229 participants were randomised and 186 participants completed the study. Of the 85 intervention participants, 70 (82%) played the serious game for at least one hour. The serious game was played a median of 36 sessions with an average playtime of 25 minutes leading to a median overall playtime of 9.7 hours. A total of 59 (69%) intervention participants showed at least 40 days of gaming activity. Control group adherence (54%) and intervention group adherence (63%) based on the dichotomised CQR-score did not differ at three months (p = 0.26) (see Table 1). Neither was there a significant difference in CQR continuous score (p = 0.20), beliefs about medication differential score (p = 0.43) or clinical outcomes (HAQ: p = 0.97; RADAI: p = 0.90) (see Table 1).

Table 1. Study outcomes at end-point (3 months)

	Control group (n=101)	*Intervention group (n=85)*	*p-value*
Primary outcome			
Adherent	55 (54)	52 (63)	0.26
*no. (%)**			
Secondary medication outcomes			
CQR continuous	75 ± 12	73 ± 11	0.20
mean ± SD			
BMQ-Specific NCD score	4.8 ± 4.2	5.3 ± 4.7	0.43
mean ± SD			
Secondary clinical outcomes			
RADAI score	2.5 [1.2 – 4.0]	2.5 [1.5 – 4.2]	0.90
median [IQR]			
HAQ score	0.8 [0.3 – 1.4]	0.6 [0.3 – 1.4]	0.97
median [IQR]			

Abbreviations: no. – number; SD – standard deviation; CQR – Compliance Questionnaire on Rheumatology; BMQ – Beliefs about Medication questionnaire; IQR – interquartile range* *Percentage of the total number of participants excluding missing data.*

Conclusion: This multicentre randomised clinical trial showed that a serious puzzle game aimed at reinforcing a positive attitude towards DMARDs was frequently played during three months. Playing the game did not improve medication adherence nor influenced beliefs about medication or clinical outcomes in RA patients.

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OP0119-HPR WHO ACCEPTS OR DECLINES AN INVITATION TO CARDIOVASCULAR SCREENING – A REGISTER STUDY ON PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: At the Danish Hospital for Rheumatic Diseases, patients with rheumatoid arthritis (RA) have been invited to systematic cardiovascular (CV) risk assessments since 2011, in accordance with the EULAR recommendations.(1). Patients who are assessed to have high or very high risk for CV death according to the modified Systematic Coronary Risk Evaluation (mSCORE) (SCORE multiplied by 1.5) (1, 2) or have known CV disease or diabetes mellitus, are invited to a follow-up screening consultation after one year. Information about who accepts vs. declines the CV screening invitation can help optimize the screening and tailor it to individual needs.

Objectives: I) to explore participation in the systematic CV risk assessment for patients with RA; II) explore differences between patients with high risk who accepted vs. declined a follow-up screening and III) explore differences in additional CV risk factors not included in the mSCORE between patients with low vs. high risk.

Methods: Data from all outpatients with RA connected to the Danish Hospital for Rheumatic Diseases in the period 2011-2021 were retrieved from the national rheumatology quality database, DANBIO. Differences between patients with a mSCORE (≥5%) who accepted vs. declined a follow-up consultation in terms of triglycerides, long-term blood sugar, lifestyle factors (alcohol consumption, physical activity level and waist circumference) and measures of disease impact (pain, fatigue, patient global assessment, HAQ and EQ-5D-5L) were analysed using Wilcoxon rank sum test and Fisher's exact test for groups. Crude and multiple regression analyses using the same explanatory variables, were performed to explore differences between patients with a low to moderate (<5%) vs. high to very high (≥5%) risk.

Results: Data were retrieved from 2.222 patients, of which 1.608 (72%) had been invited to screening consultations. 614 (28%) had not been invited and of these 139 (23%) were 75 years or older. 354 (22%) declined and 1.254 (78%) patients accepted the invitation. The patients who declined the invitation were older (mean 78.37 (SD 14.82) vs. mean 63.40 (SD 10.88) and had longer disease duration (mean 15.4 (SD 12.05) vs. mean 10.11 (SD 10.64)) compared to patients who had participated in a CV screening consultation. After excluding patients above 70 years of age, 888 patients remained, including patients with known CV disease or diabetes mellitus. Of these, 162 (18%) had a high or very high risk for CV death within ten years and 93 (57%) of these accepted a follow-up screening consultation. There were no significant differences between patients with a mSCORE ≥ 5% who accepted vs. declined a follow-up consultation in any of the studied variables. In the crude analyses, a significant difference was only found between patients with low to moderate vs. high or very high risk in triglycerides OR 1.70 (95% CI 1.20-2.28) and high waist circumference for women, OR 11.90 (95% CI 4.64-30.52). However, no significant differences were found between the two groups in the multivariate analysis.

Conclusion: Eight out of ten patients with RA accepted the first invitation to a CV screening consultation, and 2/3 of the patients with high or very risk for CV death adhered to a follow-up invitation. This study could not identify differences between patients with high risk SCORE who accepted vs. declined a follow-up CV screening. There is a need to explore barriers and facilitators for patients' adherence to CV screening.

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OP0120-HPR IMPACT OF DIFFERENT TYPES OF PHYSICAL ACTIVITY PROGRAMS ON ANKYLOSING SPONDYLITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease characterized by inflammation and ankylosis of the spine. Spinal ankylosis is responsible for significant morbidity and disability. Despite public health campaigns supporting the benefits of physical activity (PA) the average level of PA in patients with AS is low.

Objectives: This systematic review and meta-analysis of controlled studies aimed to assess the efficacy of different types of physical activity (PA) programs on ankylosing spondylitis (AS) activity, function and mobility.

Methods: We searched PubMed/Medline, Cochrane Library and Embase databases for reports of controlled trials of patients with AS with at least one activity or function outcome published up to August 2020. The studies were classified by intervention into categories defined by the 4 dimensions of PA established by the World Health Organization: aerobic, muscle strength, flexibility and neuromotor performance. We performed both overall (including any kind of PA) and subgroup analysis by type of PA program.

Results: Forty-three studies were included in qualitative synthesis and 27 in meta-analysis. The overall analysis showed a moderate effect of PA on BASDAI (-0.57, 95% CI -0.92,-0.21, p=0.002), BASFI (-0.63, 95% CI -0.85,-0.42, p<0.0001) and BASMI (-0.58, 95% CI -1.02,-0.14, p=0.01). The effect of "flexibility+muscle strength exercises" PA was large for BASMI (-1.03, 95% CI -1.64,-0.42, p=0.0009), moderate for BASDAI (-0.56, 95% CI -1.07,-0.05, p=0.03) and BASFI (-0.63, 95% CI -0.88,-0.39, p<0.005). Home-based unsupervised "flexibility+muscle strength exercises" programs improved the BASFI but not BASDAI. The effect of "flexibility+muscle strength+aerobic exercises" PA was large for BASFI (-1.26, 95% CI -1.70,-0.81, p<0.005), moderate for BASDAI (-0.77, 95% CI -1.40,-0.14, p=0.02).

Conclusion: PA has a moderate effect on AS activity and function. Programs including flexibility and muscle strength exercises may have a large effect, especially for spinal mobility. Programs including aerobic exercise showed significant efficacy for function.

Disclosure of Interests: None declared

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HPR: From prevention to management

OP0121-HPR THE SELF- AND SHARED-MANAGEMENT OF JIA: A NEW FRAMEWORK FOR RESEARCH, POLICY, AND PRACTICE

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Background: Juvenile idiopathic arthritis (JIA) is a complex long-term condition requiring lifelong management [1]. Children and young people (CYP) should be empowered to self-manage their health and wellbeing (H&W) from diagnosis [2], while families should be supported in their shared-management role [3]. Self- and shared-management (SSM) interventions can be used to develop SSM capacity [4]; however, few studies have explored SSM in this population.
Objectives: To develop a framework to promote JIA SSM, applicable to CYP, families, and professionals involved in their healthcare, wellbeing, and education.
Methods: Using a realist approach [5] and underpinned by the individual and family self-management theory [6], evidence syntheses and a qualitative study were undertaken to identify, test, and refine a series of theories promoting JIA SSM. The theories developed and tested were referred to as 'question theories', akin to programme or intervention theories, written at a middle level of abstraction to map theory for future research. Twenty stakeholders were interviewed using a teacher-learner cycle approach. Data were analysed using hybrid deductive-inductive thematic analysis and were integrated into a framework promoting JIA SSM at a higher level of abstraction.
Results: Six refined question theories outlining the mechanisms by which the SSM of JIA is likely to transpire, and the different contexts under which interventions achieve their desired outcomes, were developed, and assimilated into a new, JIA-SSM framework. Within the framework, four levels of context related to SSM were identified. These were at an individual and interpersonal level of CYP, families and professionals, and at institutional and infrastructural levels across health and social care, education, and voluntary sectors. Individual healthcare plans can also act as shared-management tools to facilitate communication between CYP, families, and professionals across healthcare, wellbeing, and education.
Conclusion: The JIA-SSM framework encourages a shift towards a multi- intervention, multi-disciplinary, multi-agency approach which works with CYP and families in equipping them with the knowledge, skills, and behaviours to competently manage their H&W. Further research is recommended to apply and validate this framework in practice, to aid future design, delivery, evaluation, and implementation of SSM interventions in JIA.
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OP0122-HPR DEVELOPMENT OF A SMARTPHONE APPLICATION FOR TREATMENT OF HAND OSTEOARTHRITIS – HAPPY HANDS

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Background: International recommendations state that all patients with hand osteoarthritis (HOA) should receive education and training in ergonomic principles, use of assistive devices and hand exercises as first-line treatment (1). However, research shows that the quality-of-care service in general is sub-optimal for this patient group, with few patients receiving recommended first-line treatment before being referred to specialist healthcare (2).
Objectives: To make recommended treatment available for patients with HOA by developing a user-friendly self-management application (H*APP*Y Hands).
Methods: The development process was conducted four phases: 1) information needs analysis and patient interviews; 2) app illustrations and prototype development; 3) heuristic evaluation; and 4) pilot-testing.
Two patient research partners were involved in developing the content of the app. Researchers, in collaboration with experienced clinicians, the patient research partners and professional film photographers and animators, developed short informational videos and animations. Illustrations and a prototype of the app was developed in five two-week iterations by the University Center for Information Technology at the University of Oslo (Figure 1). Digital meetings were conducted at the end of each two-week iteration, where illustrations and prototype were discussed with developers, researchers, and patient research partners, informing the next iteration. The H*APP*Y Hands app will be pilot tested in 70 participants with HOA, simultaneously assessing the feasibility and usability of the app.

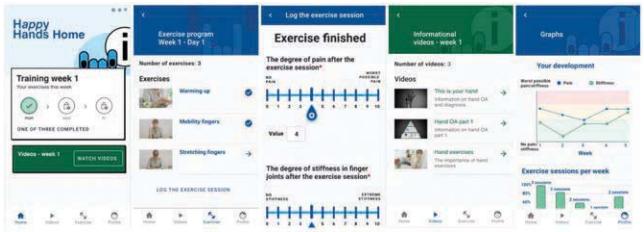

Figure 1. Illustrations of the Happy Hands smartphone application

Results: The prioritized content themes presented by the patient research partners were 1) information about hand OA; 2) goal setting, motivation, and self-efficacy; 3) assistive devices; 4) hand exercises; 5) orthoses; and 6) communication. The app was developed based on a combination of behavioural change techniques informed by Social cognitive theory and the EULAR recommendations on management of HOA. The 12-week intervention consists of 25 short informational videos addressing the prioritized themes. Additionally, the intervention includes a hand exercise program consisting of 8 videos providing instructions on warm up, exercises to improve mobility, strength and coordination, and a stretching exercise. The informational videos and exercise program are delivered in a progressive order over the 12 weeks. When downloading the app, participants are asked to specify when they plan to use the app (three days a week with time points). Thereafter, the patients get a notification on their smartphone with that week's informational videos and hand exercises at the specified days. After each exercise session the patients are asked to rate their pain and stiffness. Their answers are used to generate graphs that visualise their development over the 12-week intervention period. Each month, patients also answer questions about hand function, which they can use to self-monitor their development. Encouragement and motivational messages are provided each week to enhance continued adherence to the intervention. To date, 60 patients have been included in pilot testing of the app.
Conclusion: In this study we successfully implemented a user-centred and iterative approach to develop a e-self-management intervention for treatment of patients with hand OA. The 12-week follow-up in the pilot study will be finished medio May 2022.
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OP0123-HPR INVESTIGATION OF THE EFFECTS OF UPPER EXTREMITY HOME EXERCISES ON GRIP STRENGTH, RANGE OF MOTION, ACTIVITY PERFORMANCE AND FUNCTIONALITY IN INDIVIDUALS WITH SCLERODERMA

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Background: Scleroderma is an autoimmune disease that affects the skin and internal organs such as joints, muscles, and heart and lungs. Hand involvement in individuals with scleroderma leads to functional disability. Loss of grasping ability and impaired hand mobility may be one of the important factors affecting the daily living activities of patients with scleroderma. Although hand rehabilitation is not supported by strong levels of evidence, it has been the subject of studies, and a number of interventions have been described in patients with scleroderma, but no established guidelines for rehabilitation have been established. Passive and active stretching has been shown to help the patient maintain joint range of motion and lengthen tendons and muscles, especially when fibrotic retraction is present. Literature has been shown that self-administered home programs to be benefical. In addition, evidence-based rehabilitation interventions for the upper extremity in scleroderma are limited.
Objectives: The aim of the study is to examine the effects of upper extremity exercises on joint range of motion, grip strength, activity performance and functionality in patients with scleroderma.
Methods: 46 SSc patients (42 female, 4 male) with an average age of 55.52±11.54 were included in the study. Patients were randomized into intervention (group 1) and control (group 2) groups. Group 1 received upper extremity home exercise for 5 days a week for 8 weeks. Group 2 received principles of joint protection education program. Goniometric measurement was used to evaluate the upper extremity range of motion. Dinamometer and pinchmeter was used to evaluate the hand grip and pinch strength. Canadian Occupational Performance Measure (COPM) was used to evaluate the activity performance and satisfaction. Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH), Duruöz Hand Index (DHI), and Score for Assessment and Quantification of Chronic Rheumatic Affections of the Hands (SACRAH) was used to evaluate the upper extremity and hand functionality. All evaluations were performed at baseline and at the end of the 8th week.
Results: When the groups were compared before training, there was no significant difference ($p > 0.05$). In post-training comparisons, there was a significant difference in shoulder, elbow, forearm, wrist and fingers range of motion (p: 0.00-0.04); hand grip and pinch strength (p: 0.00-0.02); COPM performance-satisfaction (p: 0.00); SACRAH total and subparameters (p: 0.00), DASH and DHI (p: 0.00) in Group 1. There was a significant difference in shoulder, elbow and fingers range of motion (p: 0.00-0.04); pinch strength (p: 0.00); SACRAH total and subparameters (p: 0.00); DASH and DHI (p: 0.00) in Group 2. Comparing the groups for post-training, Group 1 was found to be superior in terms of shoulder flexion and rotations, elbow extention and deviations, fingers flexion, extention and abduction (p: 0.00-0.04); pinch strength (p: 0.00-0.04); SACRAH total and subparameters (p: 0.00-0.04).
Conclusion: As a result of our study, upper extremity home exercise program has a positive effect on ROM, hand grip and pinch strength, activity performance and functionality. In rehabilitation programs, upper extremity exercises -not only hand exercises- may be effective to increase ROM, grip strength, activity performance and functionality.
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Pregnancy outcomes in rheumatic diseases

OP0124

FETAL AND MATERNAL MORBIDITY IN PREGNANT SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS: A 10-YEAR U.S. NATIONAL STUDY

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disorder that affects women in their childbearing years. Previously, we demonstrated that fetal and maternal mortality has declined in SLE patients over the years, however little is known about morbidity (1).
Objectives: To determine the proportion of fetal and maternal *morbidity* in SLE deliveries compared to non-SLE deliveries in a US nationwide study over a decade.
Methods: We used retrospective data from the National Inpatient Sample database to identify all delivery related hospital admissions of patients with and without SLE from 2008 to 2017 using ICD-9 (710.0) and 10 (M32*) codes. Fetal morbidity indicators included preterm delivery and intrauterine growth restriction. 21 indicators of severe maternal morbidity were identified using the standard CDC definition: these are unexpected outcomes of labor and delivery that result in significant short- or long- term consequences to a woman's health (2). Descriptive statistics and their 95% confidence intervals were calculated using sample weights from the dataset.
Results: Among the 40 million delivery-related admissions, 51,161 patients (10,297 unweighted) were reported to have SLE. SLE patients were more likely to be older and have more comorbidities compared to non-SLE patients (Table 1). Patients with SLE had a higher risk of fetal morbidity, including intrauterine growth restriction (8.0% vs 2.7%) and preterm delivery (14.5% vs 7.3%) than patients without SLE. Amongst the CDC maternal morbidity indicators - SLE patients faced a greater risk of blood transfusion, puerperal cerebrovascular disorders, acute renal failure, eclampsia or DIC, cardiovascular and peripheral vascular disorders, and general medical issues than those without SLE (Figure 1).

Table 1. Characteristics for deliveries of patients with and without Systemic Lupus Erythematosus

	SLE deliveries		Non-SLE deliveries	
	Percent (%)	**(95 %CI)**	**Percent (%)**	**(95 %CI)**
N	51,161* (10,297 unweighted)	(49,419.14, 52,903.37)	40,000,000* (8,055,025 unweighted)	(39,200,000; 40,700,000)
Age (years)	30.05	(29.92, 30.18)	28.19	(28.14, 28.24)
Race				
White	46.15	(44.83, 47.47)	52.43	(51.74, 53.11)
African American	24.68	(23.55, 25.85)	15.01	(14.62, 15.42)
Hispanic	18.48	(17.40, 19.60)	21.45	(20.81, 22.10)
Other	10.69	(9.93, 11.50)	11.11	(10.76, 11.47)
Insurance				
Medicare	5.32	(4.83, 5.86)	0.7	(0.66, 0.75)
Medicaid	38.2	(37.00, 39.41)	43.79	(43.20, 44.39)
private insurance	51.84	(50.55, 53.13)	49.8	(49.15, 50.45)
self-pay	1.39	(1.13, 1.70)	2.74	(2.57, 2.92)
no charge	0.04	(0.02, 0.12)	0.13	(0.09, 0.18)
other	3.21	(2.84, 3.63)	2.84	(2.73, 2.95)
Elixhauser				
0	0	(*no obs)	80.56	(80.32, 80.80)
1 to 4	97.84	(97.50, 98.12)	19.4	(19.16, 19.64)
5+	2.16	(1.88, 2.50)	0.04	(0.03, 0.04)

*Population weighted values are listed.

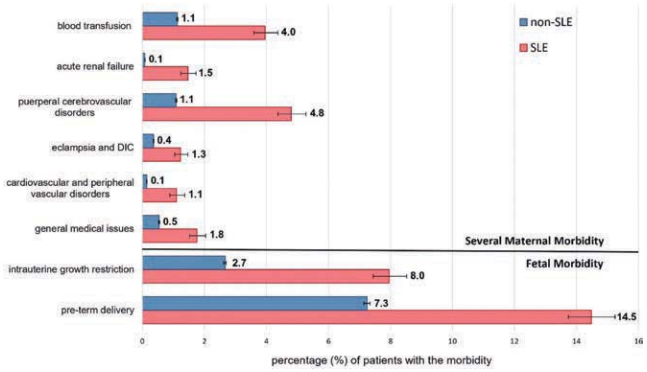

Figure 1. Fetal and severe maternal morbidity outcomes in Systemic Lupus Erythematosus (SLE) and non-SLE patients. Cardiovascular and peripheral vascular disorders include acute myocardial infarction, aneurysm, amniotic fluid embolism, cardiac arrest/ventricular fibrillation, heart failure, pulmonary edema/acute heart failure, sickle cell disease with crisis, air and thrombotic embolism, and conversion of cardiac rhythm. General medical issues include hysterectomy, shock, sepsis, adult respiratory distress syndrome, and severe anesthesia complications, temporary tracheostomy, and ventilation.

Conclusion: Our study demonstrates that fetal morbidity and severe maternal morbidity occur at a higher rate in patients with SLE compared to those without, even in this most recent decade. This work can help inform physicians to counsel and manage patients with SLE during pregnancy and its planning.
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OP0125 THE MANAGEMENT OF PREGNANCY IN AUTOIMMUNE RHEUMATIC DISEASES: ANALYSIS OF 758 PREGNANCIES FROM THE PROSPECTIVE NATIONWIDE P-RHEUM.IT STUDY (THE ITALIAN REGISTRY OF PREGNANCY IN THE RHEUMATIC DISEASES)

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Background: Pregnancy is a topic of fundamental importance for women living with autoimmune rheumatic diseases (ARD). Efforts at national and international levels have been put in the collection and harmonization of data in order to implement an evidence-based management of pregnant patients.

Objectives: The P-RHEUM.it study was designed as a nationwide, web-based longitudinal observational cohort study to collect data about pregnancy in ARD in 26 centers in Italy. The study started in May 2018 and has been supported by the Italian Society for Rheumatology.

Methods: Pregnant patients with a definite rheumatic disease according international criteria were enrolled up to gestational week (GW) 20. The course of maternal disease activity, the use of medications, fetal and maternal complications, and the quality of life (EuroQoL questionnaire) were collected for each trimester, as well as pregnancy outcome, mode of delivery, neonatal complications, and maternal and children's follow-up to 6 months after delivery, including the screening for post-partum depression by means of EPDS (Edinburgh Postnatal Depression Scale).

Results: As of December 2021, 758 pregnancies had been enrolled, 205 (27%) ongoing and 553 (73%) with outcome. Pregnancy loss occurred in 54 (9.8%) cases (40 spontaneous miscarriages; 6 voluntary terminations). Live births were 495 (89.5%), perinatal death occurred in 4 (0.7%) cases. Table 1 reports on the group of 495 live births, along with subgroups of Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE), the two most represented diseases. Regarding treatments, 166 (30%) pregnancies were exposed to corticosteroids, 239 (43%) to hydroxychloroquine, 59 (10.7%) to csDMARDs, 84 (15.2%) to TNF inhibitors, 1 (0.2%) to non-TNFi bDMARDs, 299 (54%) to low dose acetylsalicylic acid, and 126 (22.8%) to heparin.

Table 1.

PREGNANCIES WITH LIVE BIRTHS, EXCLUDING PERINATAL DEATHS	Total pregnancies (n=495)	RA pregnancies (n=69)	SLE pregnancies (n=93)
Age at conception (years)	34 (31 - 37)	34.5 (32 - 38)	34 (31 - 36)
Disease duration (years)	6.1 (2.2 - 11.1)	7.1 (4.3 - 11.6)	9.3 (5.9 - 15.9)
Caucasian	431 (87.8%)	53 (79.1%)	75 (80.6%)
Never smokers	358 (73.8%)	53 (80.3%)	66 (71.7%)
Body Mass Index >30	45 (9.5%)	7 (10.3%)	5 (5.6%)
Arterial Hypertension	6 (1.2%)	0 (0%)	2 (2.2%)
Time to pregnancy (months)	3 (1 - 6)	3 (1 - 6)	3 (0 - 10)
Physician-reported flares in the 12 months prior to conception	107 (23%)	22 (34.4%)	13 (14.8%)
Physician global assessment at enrolment (VAS 0-100)	5 (0 - 17)	5 (0 - 20)	4 (0 - 10)
Patient global health at enrolment (VAS 0-100)	18 (7 - 30)	10 (5 - 29)	10 (5 - 25)
EuroQoL at enrolment (-1.6 – 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)
Flares during pregnancy	35 (7.1%)	6 (8.7%)	7 (7.5%)
Hypertensive disturbances*	8 (1.7%)	1 (1.6%)	6 (6.6%)
Delivery at term (≥37 GW)	410 (85.1%)	53 (77.9%)	74 (80.4%)
Spontaneous vaginal delivery	173 (35.9%)	23 (33.8%)	23 (25.3%)
Congenital malformations	11 (2.4%)	2 (3.1%)	1 (1.1%)
Small for gestational age (SGA) neonate	24 (4.9%)	1 (1.4%)	9 (9.9%)
Breastfeeding in the first 4 weeks after delivery	341 (79.7%)	45 (77.6%)	59 (76.6%)
EPDS score at risk for post-partum depression	22 (14.1%)	0 (0%)	3 (10.3%)

Continuous variables are expressed as median (interquartile range); *gestational hypertension/preeclampsia/HELLP syndrome/eclampsia.

Conclusion: Multiple factors may have contributed to the high rate of live births, including good disease control before and during pregnancy thanks to the use of anti-rheumatic drugs and low frequency of general risk factors. SLE pregnancy was affected by a higher frequency of complications (hypertensive disturbances, SGA babies) as compared to RA pregnancy. Nearly 80% of patients breastfed in the first month after delivery. For the first time, data about the screening questionnaire for post-partum depression were collected, showing at least 1 out 10 patients can be at risk.

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OP0126 ARE WOMEN WITH SPONDYLOARTHRITIS AT INCREASED RISK OF ADVERSE MATERNAL AND INFANT OUTCOMES? – A SWEDISH COHORT STUDY

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Background: An increased risk of adverse pregnancy and neonatal outcomes has been reported for pregnancies in women with several rheumatic diseases including rheumatoid arthritis and psoriatic arthritis. In spondyloarthritis (SpA), findings have not been uniform, with some studies reporting increased risks of Cesarean delivery, preterm birth, infants born small-for-gestational-age (SGA), and gestational diabetes- and hypertension, while others have failed to identify any significant differences between women with SpA and general population control women. Most studies reporting no differences have either been small or lacked an appropriate comparison group [1].

Objectives: To assess the risk of adverse maternal and infant pregnancy outcomes in women with SpA compared to the general population.

Methods: In this nationwide register-based study, we included singleton births between April 2007 and December 2019 in women diagnosed with ankylosing spondylitis (AS; ICD-10 codes M45 or M08.1) or undifferentiated SpA (uSpA; ICD-10 codes M46.8 or M46.9). This was performed through linkage between the National Patient Register and the Medical Birth Register. Each birth was matched on birth year, maternal age, and parity to ten comparator births in women free from chronic inflammatory arthritis at time of birth. Relative risks (RR) of adverse outcomes were estimated by Poisson regression, adjusting for

maternal country of birth, BMI, smoking in early pregnancy, educational level, and disposable income in the year before pregnancy.

Results: Women with SpA (n=1394) were found to be at increased risk of several adverse outcomes compared to general population comparators (n=13932), as displayed in the Figure 1. Women with SpA had an increased risk of gestational diabetes (adjusted RR 1.88 [95% CI 1.10; 2.56]), elective and emergency Cesarean delivery (adjusted RR 1.54 [95% CI 1.32; 1.79] and 1.23 [95% CI 1.02; 1.48], respectively), and moderately preterm birth (adjusted RR 1.52 [95% CI 1.18; 1.97]). An association was seen with both spontaneous and medically indicated preterm birth, but the increase was only significant for spontaneous preterm birth. The risk estimate for preeclampsia was also increased, but failed to reach significance (adjusted RR 1.32 [95% CI 0.96; 1.81]). Infants to mothers with SpA were not more likely to be born SGA, but there was a slightly increased risk estimate of infection during their first year of life (adjusted RR 1.23 [95% CI 0.98; 1.53]).

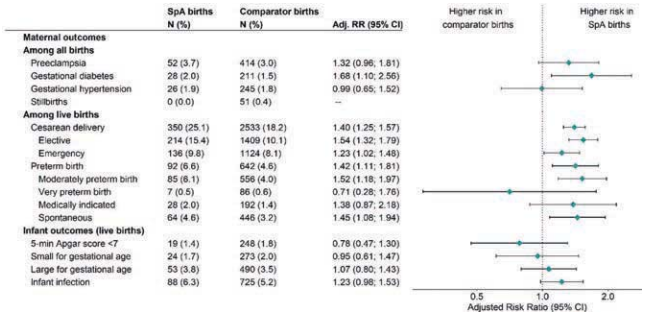

Figure 1. Number of events of adverse pregnancy outcomes among a nationwide cohort of births (n=1394) in Swedish women with SpA and comparator births (n=13932, matched 1:10 on birth year, maternal age, and parity). Relative risks from Poisson regression, adjusted for maternal country of birth, BMI, smoking in early pregnancy, educational level, and disposable income in the year before pregnancy.

Conclusion: While most pregnancies in women with SpA are uneventful, there is an increased risk for a number of adverse pregnancy outcomes. The increased risks for both emergency Cesarean delivery and spontaneous preterm birth suggest that these differences are not only driven by a different management of SpA pregnancies.

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OP0127

UNFAVORABLE PREGNANCY OUTCOME IS SIGNIFICANTLY ASSOCIATED WITH CORTICOSTEROID EXPOSURE DURING PREGNANCY IN WOMEN WITH RHEUMATOID ARTHRITIS: ANALYSIS OF THE PROSPECTIVE GR2 COHORT

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Background: Rheumatoid arthritis (RA) is one of the most common chronic inflammatory diseases and regularly affects women of childbearing age[1]. However, there is limited knowledge about the impact of the disease and its treatment on pregnancy.

Objectives: The aim of the study was to determine the factors associated with adverse pregnancy outcome in women with RA.

Methods: All RA patients (diagnosis according to the Rheumatologist) included in the national multicenter GR2 cohort from 2015 to June 2021 were included in the analysis. Patients could be included either with a pregnancy wish (i.e., preconceptional period) or because of a clinical pregnancy (<12 weeks of gestation). The main endpoint was favorable pregnancy outcome, a composite outcome defined as a live birth at term ≥ 37 gestation weeks of a healthy newborn with a weight greater than the 10th percentile. Disease activity was defined by a DAS28-CRP score > 3.2 at least once during pregnancy. We performed a multilevel logistic regression model, in which we considered patient and center random effects (patient random effect for some women included in the cohort two times). We used a multiple imputation procedure to address missing data among the explanatory variables. Results are presented as an odds ratio (OR) with confidence interval (CI).

Results: Among the 167 pregnancies in women with RA included in the GR2 cohort, 92 were retained for analysis of obstetrical outcome. Of these, 43 (46.2%), 8 (7.9%), 40 (43.5%) were exposed to corticosteroid, NSAID and biologics at least once during pregnancy, respectively. A moderate or severe disease activity at least once during pregnancy was found in 20 (21.8%) pregnancies. A live birth was found in 83 (90.2%) women, including 69 (83.1%) full-term births. Early miscarriages were observed in 9 (0.1%) women. A caesarean section was performed in 22 (23.9%) cases.

A favorable pregnancy outcome was found in 52 (56.5%) of the women. Unfavorable pregnancy outcome was mainly due to prematurity and small for gestational age, observed in 14 (16.9%) and 17 (20.5%), respectively. The multivariate model adjusted for age, BMI, nulliparity, active disease during pregnancy, smoking, and exposure to biologics and corticosteroids during pregnancy found an association between an unfavorable pregnancy outcome and nulliparity (OR 6.2 95% CI [2.1-17.8] p = 0.002), age (OR (per year) 1.1 95% CI [1.0-1.3] p = 0.02) and exposition to corticosteroids during pregnancy (OR 3.2 95% CI [1.1-9.6] p = 0.04).

Conclusion: This study provides original results on pregnancy in women with RA. It found a favorable pregnancy outcome in 56.5% of women. Unfavorable pregnancy outcome was associated with age, nulliparity and corticosteroids use during pregnancy, which argues for their careful use during pregnancy.

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Table 1. Multilevel logistic regression model: factors associated with unfavorable pregnancy outcome in women with RA.

	Univariate analyses		Multivariate analyses	
	Crude OR 95% CI	p	Adjusted OR 95% CI	p
Age	1.09 [1.01-1.19]	0.036	1.14 [1.02-1.28]	0.019
BMI	0.93 [0.83-1.04]	0.196	0.91 [0.77-1.08]	0.204
Nulliparity	4.18 [1.66-10.53]	0.003	6.16 [2.13-17.76]	0.002
Smoking	1.08 [0.29-3.36]	0.996	1.65 [0.37-7.22]	0.141
Disease activity*	1.06 [0.40-2.81]	0.911	0.98 [0.21-2.28]	0.753
Corticosteroids**	2.45 [1.05-5.68]	0.039	3.22 [1.09-9.57]	0.038
Biologics**	1.05 [0.11-3.54]	0.589	2.02 [0.70-4.12]	0.194

* Moderate or severe disease activity at least once during pregnancy. ** Use at least once during pregnancy

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OP0128

ADHERENCE TO MEDICATIONS DURING PREGNANCY IN SYSTEMIC AUTOIMMUNE DISEASE

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Background: Low medication adherence is a well known issue in the management of patients with systemic autoimmune diseases (SAD), little however is known on adherence to medication during pregnancy, especially in these patients with high risk pregnancies.

Objectives: This study is aimed at evaluating the level of adherence to medication in pregnant patients with SAD in comparison with non-pregnant patients with SAD, and at identifying determinants of low adherence.

Methods: Pregnant and non-pregnant patients with an established diagnosis of SAD were consecutively enrolled. Pregnant patients were included in a tight monitoring protocol for high risk pregnancies, and treatments were checked every month. The following data were collected at enrolment: epidemiological and demographic characteristics, disease duration and type of medications. Each patient completed the following anonymous questionnaires: the 8-item Morisky Medication Adherence Scale (MMAS-8) and Hospital Anxiety and Depression Scale (HADS) to assess the presence of anxiety and depression. With regard to MMAS-8, we assessed adherence to hydroxychloroquine (HCQ) and to other disease modifying antirheumatic drugs (DMARDs) separately. We considered a score ≥ 6 as indicator of good adherence. Vitamins and dietary supplements were not considered.
Results: A total of 80 pregnant women and 72 non-pregnant women were enrolled. Clinical data and results of the questionnaires are summarized in Table 1.

Table 1. Characteristics of the cohort

	Pregnant patients N=80	Non-pregnant patients N=72	P value
Age at study entry (years, mean ±SD)	35.8±4.3	40.1±12.2	**0.001**
Disease duration (years, mean ±SD)	8.5±6.6	8.6±9.1	n.s
Number of tablets/day (mean ±SD)	4.3±1.6	4.1±1.8	n.s
Number of assumption/day (mean ±SD)	1.4±0.6	1.6±0.8	n.s
Score MMAS for HCQ (mean ±SD)	6.99±0.2	6.38±0.2	**0.039**
Score MMAS for other DMARDs (mean ±SD)	6.99±0.3	6.39±0.2	**0.018**
Patients with good adherence to HCQ (%)	38/50 (76.0%)	34/59 (57.6%)	**0.044**
Patients with good adherence to medications (%)	53/71 (74.6%)	37/60 (61.7%)	n.s
Patients with low adherence to HCQ (%)	12/50 (24%)	25/59 (42.4%)	**0.044**
Patients with low adherence to medications (%)	18/71 (25.4%)	23/60 (38.3%)	n.s
Anxiety (%)	20 (25%)	30 (41.7%)	**0.029**
Depression (%)	11 (13.7%)	19 (26.4%)	0.051

MMAS-8 score was significantly higher in pregnant women both for HCQ (p=0.039) and other DMARDs (p=0.018), as well as the rate of patients with good medication adherence for HCQ (76.0% vs 57.6%, p=0.044). The rate of patients with good medication adherence for other DMARDs was higher in pregnant patients (74.6% vs 61.7%) but this different was not statistically different.
Demographic and clinical characteristics and the number of therapies received didn't seem to influence treatment adherence. Fifty patients (32.8%) suffered from anxiety, and this disorder was a significant determinant of low medication adherence in all groups. Conversely, depression didn't seem to have an impact on adherence on neither group.
Conclusion: Overall, pregnant patients with SAD had a good adherence to prescribed medication; nevertheless, 25% of patients didn't take therapies adequately despite being closely monitored in a dedicated clinic for high risk pregnancies and an adequate pregnancy counselling; anxiety seems to be one determinant of low medications adherence both in pregnant and non-pregnant women.
Disclosure of Interests: None declared
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OP0129 REPORTED CONGENITAL MALFORMATIONS AFTER EXPOSURE TO NON-TNF-A INHIBITORS: A RETROSPECTIVE COMPARATIVE STUDY IN EUDRAVIGILANCE DATABASE

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Background: Tumor necrosis factor-α inhibitors (TNFis) such as certolizumab pegol (CZP), are a subgroup of biologics, which have shown no increase in risk of congenital malformations (CMs) after use during pregnancy. (1) However, for the subgroup of non-TNFis, very scarce data is available.
Objectives: To evaluate the number and nature of reported CMs after intrauterine exposure to non-TNFis compared to CZP, in Eudravigilance database.
Methods: A retrospective comparative study in EudraVigilance database was conducted. Reports of all pregnancies exposed to non-TNFis and CZP, were extracted. Multiple versions of a unique case, pregnancies with unknown outcome, paternal exposures, CMs due to known genetic abnormalities, and cases exposed only via breast milk were excluded. Odd ratios for CMs were calculated for each non-TNFi, with CZP as reference group. Due to limitations of pharmacovigilance databases, such as possibility of under-reporting normal outcomes and information bias (2), in consultation with a clinical geneticist, CM patterns were compared between non-TNFi and CZP groups.
Results: In total 851 non-TNFi and 1179 CZP exposed pregnancy reports were included. Numerical differences for CMs after exposure to non-TNFis were not statistically significant except for belimumab and vedolizumab (Table 1).

Table 1. Reported number, crude and adjusted ORs [95%CIs] for major and minor CMs and TOPFAs after intrauterine exposure to non-TNFis compared to CZP

Medication	Reported CMs and TOPFAs, n/N (%)	Crude ORs [95%CIs],	Adjusted ORs (for maternal age) [95%CIs],	Stratified ORs (teratogen unexposed cases only) [95%CIs] *
Certolizumab pegol	**95/1179 (8.05)**	**Reference**	**Reference**	**Reference**
Abatacept	2/64 (3.12)	0.36 [0.08, 1.52]	0.35 [0.08, 1.47]	0.69 [0.16, 2,96]
Anakinra	3/20 (15.00)	2.01 [0.57, 6.99]	2.81 [0.77, 10.20]	3.39 [0.91, 12.63]
Belimumab	17/93 (18.27)	2.55 [1.44, 4.49]	2.63 [1.40, 4.93]	2.65 [1.35, 5.20]
Ixekizumab	1/29 (3.44)	0.40 (0.05, 3.02]	0.39 [0.05, 2.96]	0.42 [0.05, 3.16]
Rituximab	8/57 (14.03)	1.86 [0.85, 4.04]	2.47 [1.05, 5.80]	2.55 [0.94, 6.95]
Secukinumab	4/128 (3.12)	0.36 [0.13, 1.01]	0.34 [0.10, 1.11]	0.37 [0.11, 1.19]
Tocilizumab	10/124 (8.06)	1.00 [0.50, 1.97]	0.79 [0.37, 1.68]	0.62 [0.22, 1.76]
Ustekinumab	19/215 (8.83)	1.10 [0.66, 1.85]	0.92 [0.51, 1.66]	1.01 [0.56, 1.82]
Vedolizumab	23/113 (20.35)	2.91 [1.76, 4.82]	2.66 [1.53, 4.61]	2.27 [1.24, 4.15]

OR: odds ratio; CI: confidence interval; CM: congenital malformation; TOPFA: termination of pregnancy due to foetal anomaly anomaly. *After adjusting for maternal age, stratified ORs are presented for patients who had no reported teratogen exposure during pregnancy.

Pattern of CMs were reviewed by a clinical geneticist. Except for vedolizumab, no specific CM patterns were observed. For vedolizumab four cases of corpus callosum agenesis (CCA) were reported (versus null in CZP and other investigated non-TNFis). Three of the CCA cases were associated with other neurological CMs such as a neural tube defect, microcephaly and polymicrogyria. This indicates that the reported CCAs may have been related to undiagnosed genetic alterations or were associated with underlying maternal disease, although a definite relationship cannot be ruled out.
Conclusion: Except for vedolizumab, no special safety signal was identified regarding occurrence of CMs after exposure to non-TNFis. Based on available information, no firm conclusions can be made regarding observed CCA cases in vedolizumab group.
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OP0130 SERIOUS INFECTIONS IN OFFSPRING EXPOSED TO TUMOUR NECROSIS FACTOR INHIBITORS DURING PREGNANCY: COMPARISON OF AGENTS WITH LOW AND HIGH PLACENTAL TRANSFER

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Background: During pregnancy, maternal circulating antibodies cross the placenta. Offspring exposed in utero to tumour necrosis factor inhibitors (TNFi) may experience immunosuppression and subsequent infections in their first year of life due to TNFi entering the fetal bloodstream. TNFi subtypes have differential trans-placental passage capabilities. Most (i.e. adalimumab, infliximab, golimumab) are monoclonal antibodies, with adalimumab and infliximab having the highest transfer, reaching

higher fetal than maternal levels. Certolizumab (a pegylated Fab fragment) and etanercept (a fusion protein) display the lowest passage. Thus, depending on the TNFi subtype, the risk of immunosuppression may differ, and some offspring may be exposed to supra-therapeutic doses of TNFi. Therefore, the risk of serious infections in offspring by TNFi subtype needs to be clarified.
Objectives: We evaluated the risk of serious infections leading to hospitalization in offspring born to mothers with chronic inflammatory diseases who used TNFi during pregnancy depending on whether they had low or high placental transfer.
Methods: In this population cohort study, we identified offspring born in 2011-2019 to women with a prior diagnosis of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, and/or inflammatory bowel diseases in the IBM MarketScan commercial database using commercial claims only. Women were included if they had been continuously enrolled within MarketScan with medical and pharmacy coverage for ≥12 months prior to delivery and had a child linked to them. TNFi exposure was defined as ≥1 filled prescription and/or infusion procedure code during pregnancy. Exposure was further categorized into high (i.e. infliximab, adalimumab, golimumab) and low (i.e. certolizumab, etanercept) placental transfer ability. Serious infections were ascertained based on ≥1 hospitalization with infection as the primary diagnosis in the offspring's first year of life. We performed multivariable time-to-event analysis using a Cox proportional hazards model, adjusting for maternal age at delivery, chronic inflammatory disease diagnosis, maternal co-morbidities (pre-gestational diabetes, asthma), pregnancy complications (gestational diabetes, preterm birth), and other drug use (corticosteroids and non-biologic DMARDs).
Results: We identified 26,088 offspring, among whom 2,902 (11.1%) were exposed to TNFi during pregnancy. The majority of offspring (1,506; 51.9%) were born to mothers with inflammatory bowel diseases. Out of the 2,902 offspring with TNFi exposure, 797 (27.5%) and 2,105 (72.5%) were low and high placental transfer drugs, respectively. The frequency of serious infections was 1.3% and 1.8% in those offspring exposed to TNFi with low and high placental transfer, respectively. The incidence rate (IR) of serious infections in offspring exposed to TNFi with high vs. low placental transfer was, respectively, 2.27 (95% confidence interval, CI 1.61, 3.12) cases per 100 person-years at risk vs. IR 1.59 cases per 100 person-years at risk (95% CI 0.76, 2.92). In multivariable analyses, the adjusted hazard ratio for serious infections with the use of TNFi with high versus low placental transfer was 1.20 (95% CI 0.54, 2.64).
Conclusion: Although children exposed to high transfer TNFi may have a higher risk of serious infection, we saw no clear excess risk of serious infections in children exposed in utero to TNFi with high versus low placental transfer due to the wide confidence interval.
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Disclosure of Interests: None declared
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OP0131

WHAT IS THE EFFECT OF METHOTREXATE ON SEMEN PARAMETERS OF MEN DIAGNOSED WITH IMMUNE-MEDIATED DISEASES? RESULTS OF A PROSPECTIVE COHORT STUDY (IFAME-MTX).

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Background: Methotrexate (MTX) is one of the most frequently prescribed medications for the treatment of several immune-mediated diseases (IMD). MTX has well-established safety and efficacy profiles. Nonetheless, the available scientific evidence to support the decision whether men with an active desire to become a father should be treated with MTX is dubious (1). This knowledge gap is characterized by a lack of prospective studies evaluating the semen parameters before and after exposure to MTX (2).
Objectives: Our objective is to compare the semen parameters (sperm concentration, volume and progressive motility) between men diagnosed with IMD (pre and post exposure to MTX) and healthy controls.
Methods: This is a prospective cohort study. Men diagnosed with an IMD (RA, SpA, psoriasis) who were older than 18 years and received a medical indication to start therapy with MTX were invited to participate (naïve cases). These men were instructed to produce 2 semen samples (a pre-exposure sample before initiating MTX therapy and a post-exposure sample 12 weeks after initiating MTX therapy). Healthy men who were over 18 years old were invited to participate as healthy controls. Furthermore, to evaluate the semen parameters of men chronically exposed to MTX, men diagnosed with an IMD who had been exposed to MTX (≥15 mg/week) for at least 1 year were also invited to participate (chronic cases). These men produced one semen sample (post-exposure). All participants were proven fertile (fathered a child or their partner reported a positive pregnancy test). Continuous variables were compared using a paired t-test or a one-way analysis of variance.
Results: In total 18 naïve cases, 25 healthy controls and 5 chronic cases were included. Their demographic characteristics and the results of the conventional semen analysis are presented per group in Table 1. Compared to the semen parameters (sperm concentration, volume and progressive motility) from healthy controls, pre-exposure and post-exposure semen parameters from naïve cases were not statistically significant different (see Figure 1). The semen parameters of chronic cases were also not statistically significant different compared to pre-exposure samples from naïve cases and to healthy controls. Oligospermia (sperm concentration <15 10^6/mL) was identified in two samples from a naïve case (pre and post-exposure to MTX) and no cases of azoospermia were identified.

Table 1. Demographic, clinical characteristics and semen parameters

	MTX naïve		Controls	MTX chronic	p value
	Pre-exposure	Post-exposure			
Total, n	18		25	5	
Age, mean (95% CI)	36.52 (33.65-39.39)		34.56 (32.75-36.36)	36.80 (31.95 – 41.64)	
MTX dose mg/ week, mean (95% CI)	-	16.52 (14.54 – 18.49)	-	18.00 (14.59 – 21.40)	
Sperm concentration, mean × 10^6/ mL (95% CI)	84.27 (44.27-123.83)	64.31 (42.55 – 86.35)	92.56 (60.45 –124.66)	44.60 (25.11 – 64.08)	p=0.358* p=0.280**
Progressive motility*, % (95% CI)	63.20 (55.44-70.95)	60.11 (49.56-70.67)	56.95 (51.05-62.85)	50.40 (34.82 – 65.97)	p=0.562* p=0.456**
Semen volume, mean mL, (95% CI)	2.93 (2.09-3.76)	2.90 (2.08-3.71)	3.12 (2.51-3.73)	2.50 (1.55-3.44)	p=0.608* p=0.593**

*Comparisons between pre and post exposure samples were tested using a paired t-test,**Comparisons between pre, post exposure and healthy controls were tested using a one way analysis of variance.

Conclusion: This is the largest prospective study ever conducted to evaluate the impact of MTX on semen parameters in men diagnosed with IMDs. We demonstrated that exposure to MTX did not result in statistically significant different semen parameters. Based on semen parameters, our findings suggest that MTX therapy can be continued in men diagnosed with an IMD and a wish to become a father.
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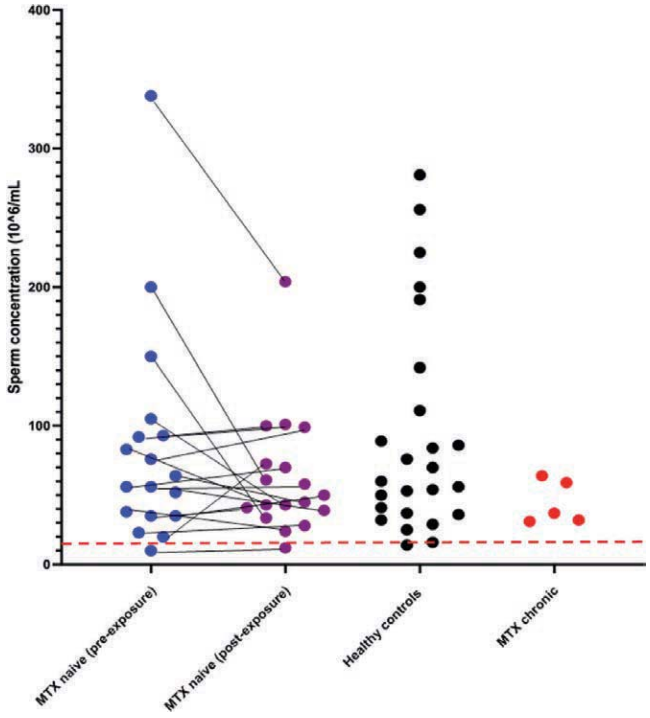

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RA: Clinical aspects and comorbidities - I

OP0132

PREVALENCE AND COMORBIDITIES OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE IN SPAIN: A RETROSPECTIVE ANALYSIS OF ELECTRONIC HEALTH RECORDS USING NATURAL LANGUAGE PROCESSING

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Background: Interstitial lung disease (ILD) is one of the most frequent extra-articular manifestations of rheumatoid arthritis (RA) and leads to a significantly increased risk for morbidity and mortality compared with RA alone [1]. The analysis of Electronic Health Records (ERHs) using machine learning (ML) and Natural Language Processing (NLP) holds great promise to better characterize the disease in real-world settings.

Objectives: This study aims to a) estimate the prevalence of RA in Spain, b) determine the frequency of RA-ILD among RA patients, and c) describe the demographic and clinical characteristics in RA/RA-ILD patients.

Methods: Observational, retrospective, and multicenter study based on the secondary use of unstructured clinical data in EHRs from 6 Spanish hospitals between January 1, 2014 and December 31, 2019. The free-text information from patients' records was captured with SAVANA's *EHRead*, a validated NLP technology which extracts clinical information from EHRs and standardizes it into a SNOMED-CT-based clinical terminology [2]. The study population comprised all adult patients ≥18 years with RA in the selected period and sites. Descriptive statistics were presented in summary tables. Prevalence was calculated dividing the total number of patients with RA over the total number of attended patients. This analysis was performed by age and sex.

Results: Among all attended patients in the participating hospitals within the study period, 11,163 patients with RA were identified; of these, 8.6% (n = 959) had RA-associated ILD (RA-ILD). The age-adjusted prevalence of RA is shown in Figure 1. The estimated prevalence (95% CI) in the overall population was 0.49 (0.37-0.60), being 0.26 (0.19-0.32) in males and 0.71 (0.54-0.87) in females. Most patients in the RA (73.9%; n = 8,250) and RA-ILD populations (63.3%, n = 607) were female (Table 1). The median age (Q1, Q3) was 60.8 (49, 74) and 67 (56, 77) years in the RA and RA-ILD groups, respectively. Regarding disease course, the time from RA to ILD diagnosis was 27.6 (3.7, 73.2) months. Most comorbidities presented higher rates in the RA-ILD population, as shown in Table 1. Among patients with available ILD subtype information (n = 618), the most common was usual interstitial pneumonia (29.8%; n = 184).

Table 1. Demographics and comorbidities in the RA and RA-ILD patient populations

	RA* N=11,163	RA-ILD N=959
Gender, n (%)		
Female	8,250 (73.9)	607 (63.3)
Male	2,913 (26.1)	352 (36.7)
Age at first mention of disease (years)[1]		
Median (Q1, Q3)	61 (49, 74)	67 (56, 77)
Comorbidities, n (%)		
Dyslipidaemia	4369 (39.1)	316 (33)
Hypertension	3851 (34.5)	320 (33.4)
Diabetes mellitus	2970 (26.6)	248 (25.9)
Infections	2129 (19.1)	328 (34.2)
Bone fracture	1875 (16.8)	210 (21.9)
Osteoporosis	1275 (11.4)	150 (15.6)
Malignancies	1004 (9)	169 (17.6)
Kidney failure	1006 (9)	156 (16.3)
Heart failure	993 (8.9)	184 (19.2)
Depression	825 (7.4)	99 (10.3)
Psoriasis	773 (6.9)	39 (4.1)
Obesity	732 (6.6)	90 (9.4)
Asthma	740 (6.6)	82 (8.6)
Atrial Fibrillation	729 (6.5)	102 (10.6)

*RA includes patients in the RA-ILD population. [1]Patients' age when either RA or ILD was first detected in the EHRs. RA = rheumatoid arthritis; ILD = interstitial lung disease

Conclusion: This pioneering study is the first to characterize RA-ILD using NLP methodology in a multicenter setting. By analyzing readily available real-world data in patients EHRs, we were able to estimate the prevalence of RA in the Spanish population and describe the demographic and clinical characteristics of patients with RA/RA-ILD.

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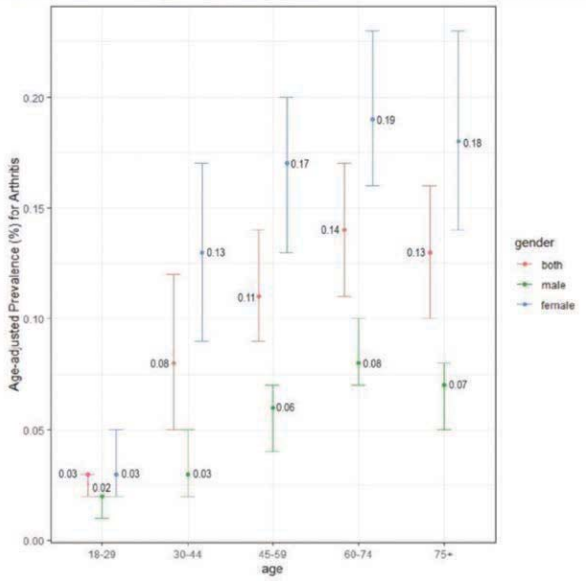
Figure 1. Estimated age-adjusted population prevalence for rheumatoid arthritis



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OP0133

THE DECREASE OF MUSCLE MASS BY THE BEHAVIORAL RESTRICTION OF COVID-19 PANDEMIC IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: We previously reported the prevalence of sarcopenia and body compositions at patients with rheumatoid arthritis (RA)[1]. The behavioral restriction of COVID-19 pandemic influenced for the lifestyle of people included patients with RA.
Objectives: The change of exercise and daily life activity of patients with RA were investigated and body composition and muscle function were compared pre- and post-behavioral restriction.
Methods: We used the date from prospective observational study (CHIKARA study: UMIN000023744). 70 from 100 patients with RA were followed-up and evaluated the change of exercise and daily life activity by visual analog scale. They were measured the muscle mass, fat mass, basal metabolic rate by body composition analyzer and grip strength as muscle function. The relationship between the change of exercise and daily life activity and body composition was investigated by univariate analysis.
Results: Mean age was 69.7 years (women n=57, men n=13). The rate of decrease of exercise by <25%, 26~50%, and 51%< were 70%, 21%, and 9%, respectively (mean:20% decrease). Whereas, the rate of decrease of daily life activities by <25%, 26~50%, and 51%< were 37%, 27%, and 36%, respectively (mean:44% decrease). Muscle mass at post-behavioral restriction decrease significantly compared that at pre-behavioral restriction activities (34.0kg vs 34.7kg, P<0.001). Fat mass at post-behavioral restriction increase significantly compared that at pre-behavioral restriction (16.2kg vs 15.5kg, P=0.014). Grip strength at post-behavioral restriction decrease significantly compared that at pre-behavioral restriction (16.2kg vs 17.2kg, P=0.026). The change of exercise was significantly positively correlated with the change of muscle mass and basal metabolic rate (R=0.273, P=0.021 and R=0.256, P=0.033, relatively) at Table 1. Whereas, the change of daily living activities was not significantly correlated with the change of muscle mass and muscle function.

Table 1. Univariate analysis of the changes in daily living activities or exercise and those in body composition or muscle function

	Change of daily living activities		Change of exercise	
	R value	P value	R value	P value
Δ Weight (kg)	-0.123	0.311	-0.131	0.279
Δ BMI (kg/m^2)	-0.108	0.397	-0.113	0.345
Δ Muscle mass (kg)	0.140	0.311	0.273	0.021
Δ Fat mass (kg)	-0.061	0.614	-0.075	0.539
Δ Fat percentage (%)	-0.003	0.982	-0.018	0.884
Δ Basal metabolic rate (kcal)	0.201	0.095	0.256	0.033
Δ Grip strength (kg)	0.117	0.336	0.037	0.762
Δ Walk speed (m/s)	0.169	0.161	0.139	0.250

Δ, change from pre- to post-behavioral restriction; BMI, body mass indexAnalyzed by Spearman's rank correlation coefficient

Conclusion: Muscle mass and grip strength decrease and fat mass increase in patients with RA by the behavioral restriction of COVID-19 pandemic. Muscle mass and basal metabolic rate decrease in patients without exercise habits. Maintenance of muscle mass might be important during the COVID-19 pandemic.
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OP0134 ACTIVE RHEUMATOID ARTHRITIS AND ASSOCIATED COMORBIDITIES INCREASE RISK OF DEMENTIA: A POPULATION-BASED COHORT STUDY

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Background: Growing evidence from observational studies indicates that patients with rheumatoid arthritis (RA) have a higher risk of developing dementia. However, the incidence of dementia among RA patients has declined in recent years [1]. It is unknown if this reflects broader trends of dementia incidence over time, changes in the prevalence or treatment of associated comorbidities, advances yielding better control of inflammation in RA, or other factors (e.g., environmental risk factors). Longitudinal population-based studies assessing risk factors for dementia among RA patients are scarce [2].
Objectives: We aimed to identify risk factors for incident dementia in a large inception cohort of patients with RA.
Methods: This retrospective population-based cohort study included residents of Olmsted County, MN, who were ≥50 years when they met 1987 ACR criteria for incident RA in 1980-2014. All individuals were followed until death/migration or 12/31/2019. Patients with dementia before RA incidence were excluded (n=12). Incident dementia was defined as two relevant ICD-9/10 codes at least 30 days apart. Risk factors including socio-demographics, RA disease characteristics and medications, cardiovascular/cerebrovascular disease (CVD) risk factors and other comorbidities were abstracted from medical records. Any CVD was defined as coronary heart disease (i.e., angina pectoris, coronary artery disease, myocardial infarction, coronary revascularization procedures, cerebral stroke or heart failure (HF). Association of individual risk factors with incident dementia was examined using Cox proportional hazard models. Three models were utilized: Model 1, adjusting for age, sex, and calendar year of RA incidence; Model 2, adding smoking, obesity, hypertension, diabetes mellitus, and hyperlipidemia to the first; and Model 3, adding 'any CVD' to the second. Time-dependent covariates were used to represent factors that developed during follow-up.
Results: The study included 886 patients with RA (mean age 65 years, 65% females). During the follow-up period (median=8.5 years), 103 patients developed dementia. Mean age at the diagnosis of dementia was 82.3 (7.2) years. The cumulative incidence of dementia increased by 2-3% every 5 years after the diagnosis of RA. Older age at RA incidence (Hazard Ratio (HR) 1.14 per 1 year increase, confidence interval (CI): 1.12-1.17) was consistently associated with risk of dementia. Presence of rheumatoid nodules (HR 1.76, CI: 1.05-2.95), large joint swelling (HR 2.11, CI: 1.33-3.34), hypertension (HR 1.84, CI: 1.19-2.85), HF (HR 2.72, CI: 1.29-5.74), and depression (HR 2.23, CI: 1.36-3.67) at baseline or during the first year after RA incidence were significantly associated with risk of dementia. Large joint swelling (HR 2.03, CI: 1.14-3.60), any CVD (HR 2.25, CI: 1.38-3.66), anxiety (HR 1.86, CI: 1.16-2.97), and depression (HR 2.63, CI: 1.76-3.93) at any time during the disease increased the risk of dementia. Among CVD conditions, stroke (HR 3.16, CI: 1.84-5.43) and HF (HR 1.82, CI: 1.10-3.00) significantly increased risk of dementia. After adjusting for CVD risk factors (Model 2), or CVD risk factors plus any CVD (Model 3), all the covariates listed above were still significantly associated with the risk of dementia.
Conclusion: Apart from age, CVD (particularly hypertension), depression and anxiety, which are universally recognized risk factors for dementia, we observed that clinically active RA was associated with an elevated risk of dementia incidence among RA patients. Studies are ongoing to further evaluate the role of systemic inflammation and its interactions with other risk factors in dementia overall and by dementia subtype in patients with RA.
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OP0135 RISK OF CARDIOVASCULAR EVENTS UNDER JANUS KINASE INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: OBSERVATIONAL DATA FROM THE GERMAN RABBIT REGISTER

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Background: In 2021, the European and US-American regulatory agencies EMA and FDA issued warnings about the cardiovascular (CV) safety of the Janus kinase inhibitor (JAKi) tofacitinib and required changes in labelling. These actions were based on results of the post-authorisation safety trial Oral Surveillance[(1)].
Objectives: To analyse major cardiovascular events (MACE) under treatment with JAKi, tumor necrosis factor inhibitors (TNFi) or conventional synthetic

Table 1. Patient characteristics at the start of a JAKi, TNFi or csDMARD.

	ALL PATIENTS			HIGH RISK PATIENTS*		
	JAKi	**TNFi**	**csDMARD**	**JAKi**	**TNFi**	**csDMARD**
# treatment starts	2030	2338	871	1215	1254	508
Age	59.9 ± 11.6	57.6 ± 13.0	59.5 ± 12.7	64.3 ± 8.9	63.5 ± 8.9	64.4 ± 9.2
Women	1573 (77.5)	1707 (73.0)	627 (72.0)	907 (74.7)	864 (68.9)	355 (69.9)
Disease duration	12.6 ± 9.6	8.9 ± 8.5	5.7 ± 6.6	13.3 ± 9.9	9.7 ± 9.1	6.0 ± 7.0
Rheumatoid factor/ ACPA positive	1531 (79.2)	1672 (74.2)	548 (66.3)	917 (79.7)	890 (73.7)	321 (66.5)
# previous bDMARDs	2.0 ± 1.8	0.7 ± 1.2	0	2.0 ± 1.8	0.7 ± 1.2	0
DAS28-ESR	4.2 ± 1.4	4.5 ± 1.4	4.2 ± 1.3	4.4 ± 1.5	4.7 ± 1.3	4.3 ± 1.3
Percentage of full physical function	63.3 ± 24.1	68.6 ± 22.4	72.3 ± 21.9	60.3 ± 24.2	64.4 ± 23.3	69.6 ± 22.7
Glucocorticoids ≥10 mg/d	170 (17.5)	239 (21.5)	49 (12.4)	112 (18.6)	142 (22.3)	23 (10.0)
BMI >30 kg/m^2	565 (28.2)	631 (27.4)	271 (31.7)	383 (31.8)	413 (33.3)	180 (36.0)
Sum of comorbidities	2.9 ± 2.5	2.6 ± 2.4	2.2 ± 2.2	3.7 ± 2.6	3.5 ± 2.5	3.1 ± 2.3
Current smokers	461 (26.3)	617 (28.5)	274 (33.5)	355 (33.5)	466 (39.5)	202 (42.3)
Previous smokers	551 (31.4)	692 (31.9)	230 (28.1)	300 (28.3)	338 (28.6)	114 (23.9)

Values are given as mean ± standard deviation or number (percentage). *Age ≥50 years and ≥ 1 CV risk factor (hypertension, coronary heart disease, diabetes, hyperlipoproteinaemia, current smoking)

disease-modifying anti-rheumatic drugs (csDMARDs - bionaive) in patients with rheumatoid arthritis (RA) observed in daily rheumatological care.

Methods: Data from patients enrolled in the biologics register RABBIT with treatment episodes from 01/2017 - 04/2021 were included. Incidence rates (IR) of MACE per 100 patient-years (PY) with 95% confidence intervals (CI) and adjusted risk ratios (RR) were calculated for all and for high-risk patients (age ≥ 50 years and ≥ 1 CV risk factor). Poisson regression analysis was adjusted for age, sex, smoking, disease activity, prior therapies, glucocorticoids and comorbidities.

Results: Starting from 2017, 2030 JAKi, 2338 TNFi and 871 csDMARD initiations were documented. Patients with a JAKi start were slightly older, more often women and had a longer RA disease duration (Table 1). The proportion with positive autoantibodies was higher than in the TNFi and csDMARD group, the physical function was lower, and they had received more previous biologic treatments. Characteristics of high-risk patients are also given in the Table 1.

In total, 28 incident MACE were reported. Patients under treatment with JAKi, TNFi and csDMARD showed comparable IR for MACE between 0.26 and 0.41 events per 100 PY (Figure 1). High-risk patients showed higher IRs. The median time under treatment was 10 months on JAKi and TNFi, and 12 months on csDMARDs. The majority of events were reported in the first year after treatment start. In the adjusted analyses, JAKi (RR 0.94 [95% CI 0.39; 2.28]) and csDMARDs (RR 0.85 [0.25; 2.88]) did not show a significantly increased risk for MACE compared with TNFi in unselected patients, and also not in high-risk patients (JAKi: RR 0.90 [0.37; 2.17]; csDMARDs: RR 0.61 [0.16; 2.28]).

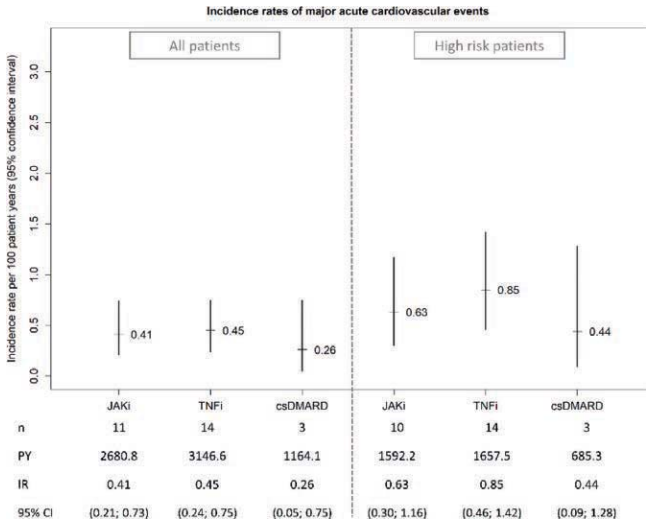

Figure 1. Incidence rates of MACE per 100 patient years by treatment group.

Conclusion: IR of MACE in patients receiving JAKi in a real-world setting was lower than the IR reported for tofacitinib in the Oral Surveillance study. We found no evidence of an increased risk of MACE with JAKi compared to TNFi, although patients in the JAKi group were older and had longer disease duration.

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OP0136

SERUM CHOLESTEROL LOADING CAPACITY ON MACROPHAGES AND INTERACTIONS WITH TREATMENTS ON CORONARY ATHEROSCLEROSIS BURDEN AND EVENT RISK IN RHEUMATOID ARTHRITIS

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Background: Cholesterol loading capacity (CLC) describes the ability of serum to deliver cholesterol to cells. It is linked to foam cell formation, a pivotal step in atherosclerotic plaque development. Rheumatoid arthritis (RA) serum promoted foam cell formation significantly more than control serum. Likewise, RA patients display greater plaque burden and higher-risk features than non-RA controls. bDMARDs and statins lower cardiovascular risk by reducing new coronary plaque formation, promoting regression, altering the composition and stabilizing prevalent atherosclerotic lesions.

Objectives: To evaluate the associations between CLC, coronary plaque burden and cardiovascular event risk in patients with RA. We further explored the conditioning effects of RA treatments on these relationships.

Methods: 140 patients underwent coronary CT angiography for atherosclerosis evaluation and were prospectively followed for cardiovascular events over 6.0±2.4 years. Coronary artery calcium score (CAC), number of segments with plaque (segment involvement score [SIS]) and plaque composition were assessed. CLC was the macrophage cholesterol content, measured by fluorometric assay, after a 24-hour incubation with whole serum. Robust linear regression examined the effects of CLC and the interaction between CLC and bDMARD use on SIS and CAC. Negative binomial regression evaluated CLC and CLC × bDMARD interaction effects on number of high-risk (low-attenuation) plaques. With data discretized into 1-month intervals, weighted pooled logistic regression models with robust variance estimation evaluated CLC and time-varying bDMARD use as predictors of event risk, and the effect of CLC × time-varying bDMARD use on risk. Stabilized inverse probability of treatment and censoring weights were estimated as a function of ASCVD risk, SIS, RA duration, and baseline and time-varying CRP and statin use.

Results: Mean (SD) CLC was 12.67 (2.83) μg/mg protein. In analyses adjusting for ASCVD score, HDL, prednisone and statin use, CLC (per 1-SD unit) was not related to SIS (β -0.05 [95%CI -1.19,0.09]), number of high-risk plaques (rate ratio [RR] 1.20 [95%CI 0.80-1.80]) or ln-transformed CAC (β 0.017 [95%CI -0.133,0.147]). However, in analyses stratified by baseline bDMARD use, CLC

(per 1-SD unit) was positively related to number of high-risk plaques (RR 2.14 [95%CI 1.04-4.40]) and ln-transformed CAC (β 0.21 [95%CI 0.01-0.41]) among bDMARD-naïve individuals (Figure 1). In addition, CLC inversely associated with SIS (per SD increment; β -0.16 [95%CI -0.32, -0.01]) only in bDMARD-treated patients. Baseline statin use did not significantly modify the effect of CLC on coronary plaque (not shown). CLC associated with cardiovascular event risk (per SD increment; adjusted odds ratio 2.02 [95%CI 1.27-3.50], p=0.011) covarying for ASCVD score and time-varying bDMARD use. The CLC × time-varying bDMARD use interaction also predicted event risk (p =0.010); current bDMARD use associated with lower event risk at higher (1 SD above the mean) CLC levels (p=0.037) but not average or lower (1 SD below the mean) CLC levels (p=0.064 and 0.756, respectively).

Conclusion: CLC associated with greater CAC score and high-risk plaque burden in bDMARD-naïve RA patients and lower total plaque burden in bDMARD-treated patients at baseline. CLC also predicted long-term cardiovascular risk and its effect was mitigated by bDMARD use.

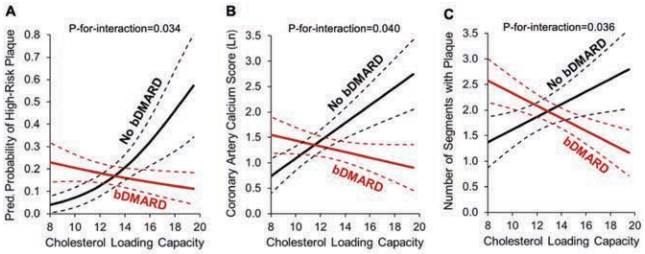

Figure 1 Impact of CLC on coronary atherosclerosis burden in RA and mitigation by bDMARDs

Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi-Genzyme-Regeneron, Janssen, Bristol-Meyer-Squibb, Consultant of: Sanofi-Genzyme-Regeneron, Janssen, Bristol-Meyer-Squibb, Grant/research support from: Pfizer, Bianca Papotti: None declared, Sarah Ormseth: None declared, Marcella Palumbo: None declared, Elizabeth Hernandez: None declared, Cinzia Marchi: None declared, Francesca Zimetti: None declared, Matthew Budoff Consultant of: Pfizer, Nicoletta Ronda: None declared

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OP0137

ABDOMINAL OBESITY MAY CONFOUND THE ACCURACY OF CARDIOVASCULAR RISK PREDICTION IN RHEUMATOID ARTHRITIS; CAN CORONARY ATHEROSCLEROSIS IMAGING AND BIOMARKERS HELP?

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Background: Accurate cardiovascular risk stratification is essential in rheumatoid arthritis (RA) care. RA patients who are underweight incur greater total and cardiovascular mortality compared to those who are overweight or obese.

Objectives: We explored whether abdominal obesity impaired the accuracy of risk prediction estimates in RA patients without known cardiovascular disease (CVD). We further interrogated the potential utility of coronary atherosclerosis assessment and serum levels of related cardiac damage biomarkers to optimize risk prediction in obese RA patients.

Methods: In a single center observational study, 150 participants with coronary CT angiography for atherosclerosis evaluation and prospective follow-up for cardiovascular events over 6.0±2.4 years were assessed. Framingham cardiovascular risk score was computed at baseline. Obesity was defined as waist circumference >88 cm in females and >102 cm in males. Segment involvement score (SIS) described the number of coronary segments with plaque. Serum highly-sensitive cardiac troponin I (hscTnI)-related both to coronary plaque burden and event risk in RA- was measured with Erenna immunoassay. Serum leptin, which is closely related to obesity, was measured with radioimmunoassay. CVD risk estimates were contrasted in non-obese vs. obese patients and those with low vs. high leptin correspondingly using area under the curve (AUC) comparisons. Improvements in risk estimate accuracy in obese patients were explored by sequentially adding hscTnI information and coronary plaque burden estimates to a baseline model of Framingham score and evaluating sequential change in AUC, net reclassification index (NRI) and integrated discrimination improvement (IDI).

Results: A significant interaction between Framingham cardiovascular risk score and obesity was observed (p=0.032). Lower estimates were seen in obese [AUC 0.660, 95%CI 0.487-0.832] vs. non-obese RA patients [AUC 0.952, 95%CI 0.897-1.007, p=0.002, Figure 1A]. Likewise, risk estimates were lower in patients with higher (>22.1 ng/ml) vs. lower (<22.1 ng/ml) leptin [AUC 0.618, 95%CI 0.393-0.842 vs. 0.874, 95%CI 0.772-0.976 respectively, p=0.042, Figure 1B]. In obese patients, sequential addition of the highest hscTnI tertile values and extensive atherosclerotic plaque presence (SIS>5) to a base model including Framingham risk score, significantly improved risk prediction estimates based on changes in NRI [1.093 95%CI 0.517-1.574], IDI [0.188, 95%CI 0.060-0.526], as well as AUC [0.179, 95%CI 0.058-0.378, p=0.02]. The final, combined model accurately predicted 83.9% of incident cardiovascular events (Figure 1C).

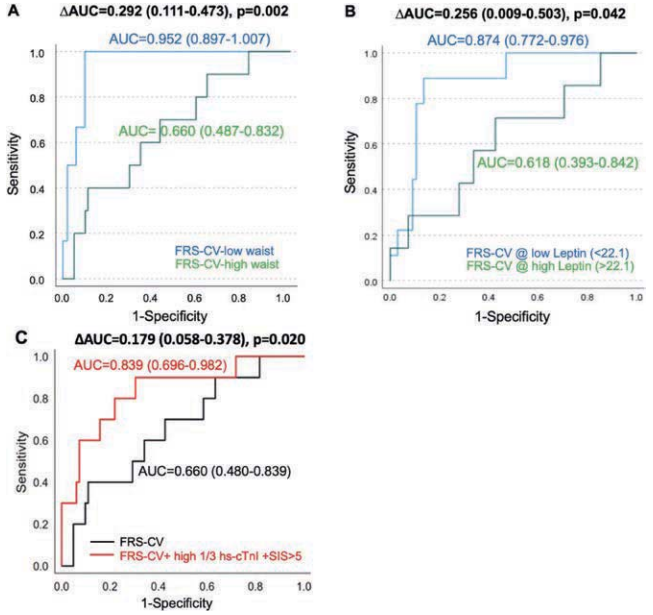

Figure 1. **A** and **B.** Obesity attenuates accuracy of clinical cardiovascular risk estimates in RA. **C.** Addition of information from hs-cTnI measurements and coronary atherosclerosis assessment significantly improve risk prediction

Conclusion: Obesity significantly reduced cardiovascular risk estimate accuracy in patients with RA. The optimization of cardiac risk stratification with the help of non-invasive assessment of coronary atherosclerosis burden and related cardiac damage biomarkers in the serum may warrant further study.

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

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OP0138

RISK OF CANCER AFTER BIOLOGIC AND TARGETED SYNTHETIC DMARDS INITIATION IN PATIENTS WITH RHEUMATIC DISEASES AND A HISTORY OF PRIOR MALIGNANCY: DATA FROM THE BIOBADASER REGISTRY

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Background: Patients with a history of cancer are routinely excluded from randomized controlled trials. As consequence, data on the safety of biologic disease modifying antirheumatic drugs (bDMARDS) and targeted synthetic (ts) DMARDs are limited. Although real world data from various national registries have not provided evidence of increased cancer recurrence, additional data from real-world registries may help to confirm safety of non-TNFi bDMARDs and tsDMARDs regarding cancer recurrence to guide treatment decisions.

Objectives: To compare the risk of incident malignancy with exposure to different bDMARDs and tsDMARDs in patients with rheumatic diseases and a prior malignancy.

Table 1. Baseline characteristics and rate of incident cancer.

	Anti-TNF (n = 185)	JAKi (n = 61)	Anti-CD20 (n= 61)	Anti-IL6 (n= 68)	Anti-CTLA-4 (n= 47)	Anti-IL17 (n= 39)	Total (n=352)
Female, n (%)	129 (69.7)	49 (80.3)	43 (70.5)	54 (79.4)	34 (72.3)	21 (53.9)	247 (70.2)
Age, mean (SD)	64.4 (13.1)	66.7 (13.1)	67.8 (10.0)	70.5 (11.6)	71.8 (10.4)	59.5 (14.6)	65.3 (13.0)
Start treatment age, mean (SD)	60.0 (12.9)	64.8 (12.8)	65.7 (9.6)	67.3 (11.3)	62.8 (12.7)	56.9 (14.5)	61.6 (12.8)
Disease duration, median (IQR)	6.7 (3.0-13.1)	12.3 (7.4-19.6)	10.8 (6.3-19.4)	8.5 (4.0-16.8)	8.2 (4.1-16.6)	8.4 (4.7-16.1)	7.0 (2.9-15.5)
Time of follow-up months, mean (SD)	23.1 (25.3)	15.9 (13.3)	11.5 (2.5)	16.8 (17.6)	23.7 (22.6)	18.4 (15.5)	17.5 (18.2)
Charlson comorbidity index	4.9 (2.0)	5.2 (2.2)	5.1 (2.0)	5.5 (2.1)	6.1 (2.6)	6.9 (2.6)	5.2 (2.1)
Prior malignancy							
Non-lymphoproliferative (solid or melanoma), n (%)	174 (94.5)	58 (95.1)	54 (88.5)	65 (95.6)	46 (97.9)	36 (92.3)	331 (94.0)
Lymphoproliferative, n (%)	9 (4.9)	3 (4.9)	13 (21.3)	4 (5.9)	4 (8.5)	5 (12.8)	29 (8.2)
Metastatic cancer, n (%)	2 (1.1)	2 (3.3)	2 (3.3)	1 (1.5)	3 (6.4)	0 (0.0)	7 (2.0)
Incident cancer							
New cancer diagnosis, n (%)	18	2	2	5	5	0	32
Time of exposure, sum (years)	470,1	91,6	163	104,9	96,8	63,8	1178,6
Rate of incident cancer (per 1,000 PY)	38.3 (24.1-60.8)	21.8 (5.5-87.3)	12.3 (3.1-49.1)	47.7 (19.8-114.5)	51.7 (21.5-124.1)	0 (0-0)	27.1 (18.6-38.3)
Rate ratio of incident cancer (vs anti-TNF)	-	0.6 (0.1-2.5)	0.3 (0.1-1.4)	1.2 (0.5-3.4)	1.3 (0.5-3.6)	-	-

Methods: The study population comprised patients with a prior malignancy from the BIOBADASER 3.0 up to 2021. BIOBADASER is a large national drug safety registry of patients with rheumatic diseases starting treatment with any bDMARD or tsDMARD and followed thereafter at the time an adverse event or a change in biological therapy occurs. Incident cancer was defined as any cancer (new primaries, local recurrence or metastases) during the exposure classified according to Meddra dictionary. Incidence rate ratios of cancer per 1000 patients-year (PY) and 95% CI were estimated. Rates of incident cancer in tsDMARDs and other bDMARDs versus anti-TNF treated patients were compared.

Results: A total of 9,129 patients treated with bDMARDs and tsDMARDs are included in BIOBADASER 3.0 at the time of the study. Of them, 352 with a prior history of malignancy at time of enrollment were selected for analysis (Figure 1). Overall, there were 32 incident malignancies (17 solid cancer, 14 non-melanoma skin cancer and 1 melanoma). The overall rate of incident malignancy was 27.1 (95% CI 18.6-38.3) events/1,000 PY, ranging between none events/1000 PY in the anti-IL17 group to 51.7 events/1000 PY in the anti-CTLA-4 group (Table 1). The overall rate of incident cancer did not differ significantly in patients exposed to JAKi [0.6 (95% CI 0.1-2.5)], anti-CD20 [0.3 (95% CI 0.1-1.4)], anti-IL6 [1.2 (95% CI 0.5-3.4)] or anti-CTLA-4 [1.3 (95% CI 0.5-3.6) versus anti-TNF therapy. The rate of different types of cancer (melanoma, non-melanoma skin cancer or solid tumors) did not differ between the different treatment groups when compared to anti-TNF therapy (Table 1).

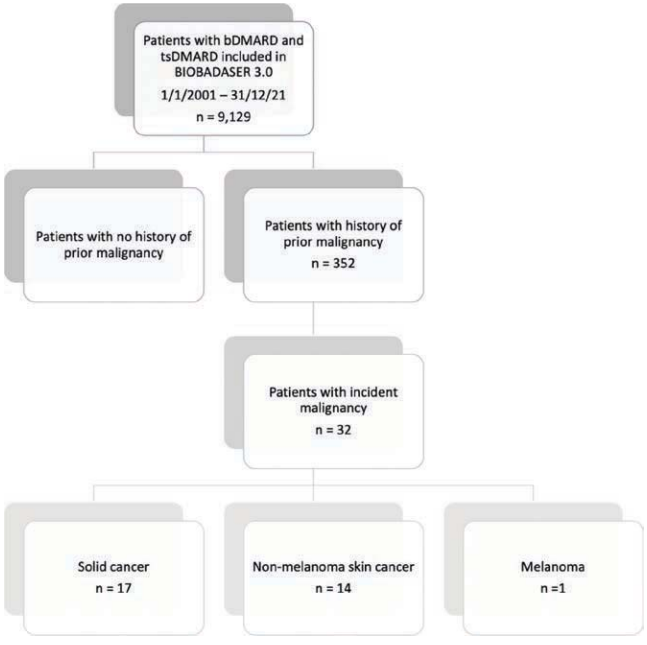

Figure 1. Flowchart of patients included.

Conclusion: The risk of incident cancer in patients with rheumatic diseases and a prior malignancy does not differ according to the type of bDMARD and tsDMARD exposure.

Disclosure of Interests: None declared

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OP0139

IMPACT OF CHRONIC JOINT DISEASES ON THE SEXUAL SPHERE WITH REGARDS TO A HEALTHY POPULATION: A MULTICENTER STUDY.

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Background: Chronic joint diseases impair the quality of life. This occurs not only by the deformity generated, but also by the pain and disability produced by them [1, 2]. There are a limited number of studies on joint diseases and sexuality [3, 4]. Besides, many lack a control group and do not explore the different areas of sexuality[1-4].

Objectives: To describe the prevalence of sexual dysfunction (SD) in patients with rheumatoid arthritis (RA) and psoriatic arthritis (PA). To compare the results obtained between the two diseases and a healthy population. To analyse the factors associated with SD in the 3 populations.

Methods: Cross-sectional observation study. Patients diagnosed of PA (CASPAR criteria) and RA (EULAR/ACR 2010 criteria), followed in outpatient Rheumatology offices of two different university hospitals of the same geographical area, were consecutively included. The following variables were collected: (age, gender, year of diagnoses, perceived health, marital status, level of education, employment situation and the annual level of income), as well as (history of depression and active treatment of mental health disease). The results were compared against healthy individuals, acting as a control group. Only adult patients, of any sexual orientation, were included. The CSFQ-14 questionnaire, which evaluates changes in sexual function due to the disease or its medication, was applied. This questionnaire studies 4 different domains in both genders (pleasure, desire, arousal, orgasm and pain during orgasm) and in addition, it evaluates orgasm completion in women and erection in men. A regression model was created to estimate the influence of the collected variables on the obtained results.

Results: 188 patients were included (52.7% women and 47.3% men); 72 of them were diagnosed of PA and 27 of RA. Moreover, 30.43% of the patients with PA, 48.15% of the patients with RA and 5.88% of the control group had scores on the CSFQ-14 test in the SD range.

SD was found related to being diagnosed of PA and RA ($p < 0.001$), age ($p < 0.001$), employment status ($p < 0.001$) and the annual level of income ($p = 0.002$). On the CSFQ-14 test, men had a mean score 7.5 points higher than women, although this score decreased to 6.15 points in men with PA. Furthermore, patients with PA and RA had a mean score 8.2 points lower than the control goup. All of the domains of the CSFQ-14 questionnaire were negatively affected by having PA or RA ($p < 0.001$). The estimated odds ratio of having SD was 8.7 times higher in patients diagnosed of PA and 10 times higher in patients diagnosed of RA.

Conclusion: Patients with RA or PA have a deteriorated sexual life when compared to a healthy population. This detriment affects all of the domains of the sexual sphere (pleasure, desire, arousal and orgasm). As shown in previous studies, age, gender, perceived health, employment situation and economic status, are related to the risk of suffering from SD. Therefore, these factors must be considered when attending this area of our patient's health. The CSFQ-14 questionnaire provides a complete approach to sexual health and can be a tool for the management of chronic joint diseases.

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Remission, flares and predictive factors in SLE, Sjogren and anti-phospholipid syndrome

OP0140 IMPACT OF TIME TO REMISSION, FLARES AND TIME ON IMMUNOSUPPRESSIVES ON THE ESTIMATED GLOMERULAR FILTRATION RATE IN LUPUS NEPHRITIS

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Background: Time to complete remission, subsequent flares and time on immunosuppressives after complete remission are major determinants of the progression to advanced chronic kidney disease in lupus nephritis (LN). However, the impact of these factors on the rate of glomerular filtration rate (GFR) deterioration is not known.
Objectives: To determine the impact of time to remission, flares and time on immunosuppressives after remission on the estimated GFR in LN.
Methods: Patients with LN based on biopsy or abnormal proteinuria (>0.5g/day) with or without hematuria or pyuria or casts for two consecutive visits were retrieved from the Toronto Lupus Clinic long-term longitudinal database. Individuals with advanced chronic kidney disease at baseline (eGFR≤29ml/min/1.73m^2) were excluded. All patients were followed for at least 5 years. The primary outcome was any decrease of the estimated GFR on an annual basis (slope). Remission was defined as proteinuria<0.5g/24h, inactive urinary sediment and serum creatinine ≤120% of the baseline value. Flare was defined as any abnormal proteinuria (>0.5g/day) or increase in serum creatinine (SCR) from normal to abnormal or >120% of the baseline value after remission. Slopes of eGFR changes (standard error) were calculated using Ordinary Least Square method in each complete remission/flare group. Linear Mixed model was performed to account for factors associated with deterioration of eGFR.
Results: Out of 418 eligible patients, 209 (50%) achieved remission within the first year from LN diagnosis, 102 (24.4%) within the 2nd and 3rd years, 70 (16.7%) after 3 years and 37 (8.9%) never achieved remission. Regarding flares, 82 patients (19.6%) never flared, 75 (18%) had one flare and 261 (62.4%) had two or more flares. The trajectory and annual slope of eGFR according to time to remission and number of flares is shown in the Figure 1.

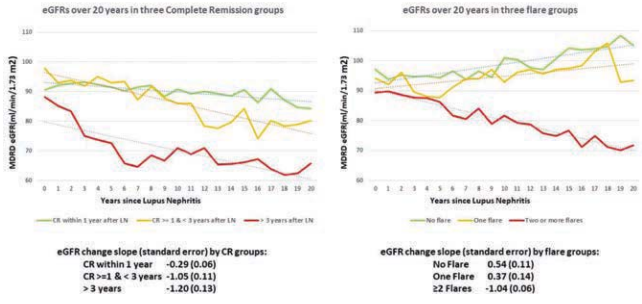

Figure 1.

Regression analysis (linear mixed model) for the outcome of eGFR was performed to adjust for other variables that impact eGFR (Table 1).

Predictors	Estimate	Standard Error	p value
Each one later decade of LN onset	4.45	0.93	<0.0001
Years on immunosuppressives since remission	0.71	0.19	<0.0001
Age at LN onset	-0.76	0.11	<0.0001
Hypertension at LN	-7.73	2.75	0.005
CR < 1 year after LN	0 (Ref.)		
CR between 1-3 years comparing to < 1 year after LN	-1.60	2.90	0.581
No CR or CR later than 3 years comparing to < 1 year after LN	-12.31	2.90	<0.0001
No Flare	0 (Ref.)		
One flare any time after LN vs. no flare	-3.48	3.79	0.358
Two or more flares any time after LN vs. no flare	-14.79	3.01	<0.0001

Conclusion: Complete remission after 3 years or no remission is associated with a significant decrease in eGFR, while remission during the 2nd and 3rd year from LN diagnosis is not associated with significant decrease of renal function over time. Patients with one flare did not have significant impact on their renal function. Patients with 2 or more flares had a significant decrease of eGFR over 20 years, even after adjustment for other covariates. Time on immunosuppressives after complete remission is protective against eGFR decline. Our findings emphasize the importance of rapid remission and flare prevention by prolonged maintenance treatment with immunosuppressives to optimize renal outcomes.
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OP0141 TREAT TO TARGET IN SYSTEMIC LUPUS ERYTHEMATOSUS FROM THE PATIENTS' PERSPECTIVE – RESULTS FROM AN INTERNATIONAL PATIENT SURVEY

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Background: Treat-to-target (T2T) is a generally accepted treatment concept in rheumatology care. It is assumed that T2T could significantly improve systemic lupus erythematosus (SLE) care and the patients' outcomes. However, T2T has not yet been studied systematically and clinical trials are currently in preparation [1]. Furthermore, the patients' opinion on T2T has barely been taken into account.
Objectives: As the success of T2T is largely determined by the involvement of patients, it was our aim to investigate the attitude towards, need, and willingness of SLE patients to participate in a T2T study and to identify possible obstacles.
Methods: A questionnaire on T2T, its acceptance, the need and willingness to participate in a T2T trial and possible obstacles for T2T was designed by the authors in cooperation with patient research partner and performed in the Netherlands (NL), Austria (AU), Germany (GE) and Bulgaria (BG). The web-based survey consisted of 13 questions with single and multiple answers and/or free text. After back-and-forth translation from German to Dutch and Bulgarian, it was distributed among members of the patient organizations of NL, GE, AU, BG via newsletter (GE, AU, BG), personal invitation (NL) and a closed Facebook group (BG). Castor Electronic Data Capture (NL) and SoSci-Survey (GE, AU, BG) were used as platforms.
Results: A total of 863 patients (n=316 NL, n=271 GE, n=232 BG, n=44 AU) with self-declared diagnosis of SLE completed the questionnaire. 93.3% were female, 52.2% were 41-60 years old. The disease duration was longer than 10 years in 54.8%, 12.4% had a disease duration of 0-2 years. Regarding the satisfaction with the current health status, 56.2% were somewhat to all the way satisfied, 29.3% were not at all or hardly satisfied. 65.5% were satisfied with their current therapeutic treatment, 14.8% where not at all or hardly satisfied.

48.4% declared being currently in remission, 13% did not know if they were in remission. As most important treatment goal, normalization of quality of life was chosen most frequently (37.4%) followed by prevention of organ damage (24.6%) and the absence of disease activity (22.6 %).
Regarding shared decision making, the majority reported to be somewhat to all the way involved in treatment decisions (62.1%) while 20,7% where hardly or not at all involved.
As most difficult decisions in T2T and shared decision making, respondents named the start of new SLE medication (37.9%) and to change medication while feeling good (39.4%). An increase in the dose of glucocorticoids to reach remission was difficult for 22.7%.
The majority of patients considered research of T2T in SLE useful (55,4% all the way, 29.8% somewhat useful) and 67% would probably or definitely participate in such scientific research. The perceived advantages and disadvantages of T2T are depicted in Figure 1.

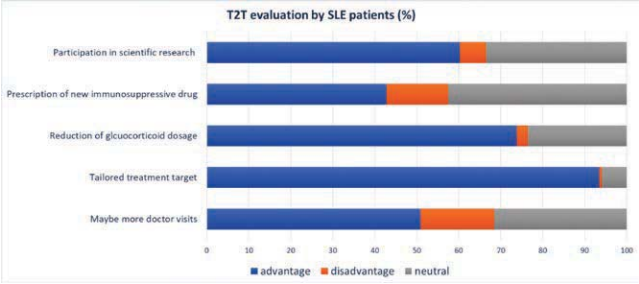

Figure 1. Consequences of T2T rated as advantage or disadvantage by SLE patients. *SLE systemic lupus erythematosus, T2T treat-to-target.*

Conclusion: Despite many SLE patients being satisfied with their treatment and health status, T2T is considered an important subject to be studied in clinical trials. Advantages did overweigh possible disadvantages of T2T with the possibility of more doctors' visits and the prescription of a new drug as biggest disadvantage. Quality of life named as most important treatment goal emphasizes its importance as outcome parameter. Most patients would be willing to participate in a trial about T2T.

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OP0142

COMPARISON OF ATTAINMENT AND PROTECTIVE EFFECTS OF THE LUPUS LOW DISEASE ACTIVITY STATE IN PATIENTS WITH NEWLY DIAGNOSED VERSUS ESTABLISHED SLE - A MULTICENTRE PROSPECTIVE STUDY

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Background: Lupus low disease activity state (LLDAS) attainment has been reported to be associated with reduced damage accrual, flare, and mortality, as well as improved quality of life, in cohorts of SLE patients with established disease. Whether these associations are present in recent-onset disease is less well known.
Objectives: To evaluate the associations of LLDAS attainment with outcomes in patients with recent onset SLE.
Methods: Data from a 13-country longitudinal SLE cohort (ACR/SLICC criteria) were collected prospectively between 2013 and 2020 using standard templates. Organ damage and flare were captured using SLICC Damage Index and SELENA-SLEDAI Flare Index, respectively. LLDAS was defined as Golder *et al.*, 2019 [1]. An inception cohort was defined based on duration since SLE diagnosis<1 year at enrolment. Patient characteristics between inception and non-inception cohorts were compared using Wilcoxon rank-sum (continuous variables) or Pearson's Chi-squared tests (categorical variables). Survival analyses were performed to examine the association between LLDAS attainment and damage accrual and flare.
Results: The study cohort included 4,106 patients of whom 680 (16%) were recruited within 1 year of SLE diagnosis (inception cohort). Compared to the non-inception cohort, inception cohort patients were significantly younger, had higher disease activity (SLEDAI-2K and physician global assessment), used more glucocorticoids and immunosuppressants but had less organ damage at enrolment and only 88 (13.6%) patients accrued damage during a median 2.2 years follow-up (Table 1).

Table 1.

	Non-inception cohort	Inception cohort	p-value
	n=3426	n=680	
Age at enrolment (years), *median [IQR]*	40 [31, 51]	33 [25, 44]	<0.001
Age at diagnosis (years), *median [IQR]*	28 [21, 38]	33 [25, 43]	<0.001
SLE duration at enrolment (years), *median [IQR]*	10 [5, 16]	1 [0, 1]	<0.001
Study duration (years), *median [IQR]*	2.5 [1.0, 5.4]	2.2 [0.9, 3.7]	<0.001
Females, *n (%)*	3155 (92.1%)	623 (91.6%)	0.68
Asian ethnicity, *n (%)*	3037 (89.1%)	595 (88.1%)	0.49
Prednisolone (PNL) use - ever, *n (%)*	2865 (83.6%)	620 (91.2%)	<0.001
Time adjusted mean (TAM)-PNL, *median [IQR]*	5.0 [2.2, 8.6]	6.2 [3.2, 10.3]	<0.001
Cumulative PNL (g), *median [IQR]*	3.4 [0.5, 9.7]	3.8 [1.1, 8.5]	0.26
Anti-Malarial use - ever, *n (%)*	2669 (77.9%)	569 (83.7%)	<0.001
Immunosupressant use -ever, *n (%)*	2367 (69.1%)	521 (76.6%)	<0.001
AMS (TAM-SLEDAI-2K), *median [IQR]*	2.8 [1.2, 4.6]	3.1 [1.6, 5.0]	0.002
TAM-PGA, *median [IQR]*	0.4 [0.2, 0.7]	0.4 [0.3, 0.8]	<0.001
Mild/moderate/severe flare ever, *n (%)*	1789 (52.2%)	391 (57.5%)	0.012
Organ damage accrual, *n (%)*	629 (20.8%)	88 (13.6%)	<0.001
LLDAS at baseline, *n (%)*	1730 (50.5%)	195 (28.7%)	<0.001
LLDAS-ever (at least once), *n (%)*	2637 (78.2%)	492 (73.9%)	0.014
≥50% time in LLDAS (LLDAS-5), *n (%)*	1612 (50.6%)	256 (41.1%)	<0.001

Significantly fewer inception cohort patients were in LLDAS at enrolment than the non-inception cohort (29% vs. 51%, p<0.001). However, 74% of inception and 78% of non-inception cohort patients achieved LLDAS at least once during follow-up. Limiting analysis only to patients not in LLDAS at enrolment, time to first LLDAS attainment was assessed: inception cohort patients were 60% more likely to attain their first LLDAS (HR = 1.60 (95%CI: 1.40, 1.82), p<0.001) than non-inception cohort patients. LLDAS attainment was significantly protective against flare in the inception (HR, 95% CI) and non-inception (HR, 95% CI) cohorts. Trends towards protection against damage accrual in association with LLDAS in the inception cohort were not significant.

Conclusion: LLDAS attainment is protective from flare in recent onset SLE. Significant protection from damage accrual was not observed, due to low rates of damage accrual in the first years after SLE diagnosis.

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Janssen Pharmaceuticals – advisory board, Grant/research support from: Novartis, Employee of: Eli Lilly, Kristine Ng Speakers bureau: speaker fees and advisory board (Abbvie, Novartis, Janssen), Annie Law: None declared, Nicola Tugnet: None declared, Sunil Kumar: None declared, Cherica Tee: None declared, Michael Tee: None declared, Yoshiya Tanaka Speakers bureau: Daiichi-Sankyo, Eli Lilly, Novartis, YL Biologics, Bristol-Myers, Eisai, Chugai, Abbvie, Astellas, Pfizer, Sanofi, Asahi-kasei, GSK, Mitsubishi-Tanabe, Gilead, Janssen, Grant/research support from: Daiichi-Sankyo, Eli Lilly, Novartis, YL Biologics, Bristol-Myers, Eisai, Chugai, Abbvie, Astellas, Pfizer, Sanofi, Asahi-kasei, GSK, Mitsubishi-Tanabe, Gilead, Janssen, C.S. Lau Shareholder of: Pfizer, Sanofi and Janssen, Mandana Nikpour Speakers bureau: Actelion, GSK, Janssen, Pfizer, UCB, Paid instructor for: UCB, Consultant of: Actelion, Boehringer Ingelheim, Certa Therapeutics, Eli Lilly, GSK, Janssen, Pfizer, UCB, Grant/research support from: Actelion, Astra Zeneca, BMS, GSK, Janssen, UCB, Alberta Hoi Consultant of: AH is on the advisory board for Abbvie and GSK, Grant/research support from: AH has received research support from AstraZeneca, GSK, BMS, Janssen, and Merck Serono, Eric F. Morand Speakers bureau: AstraZeneca, Paid instructor for: Eli Lilly, Consultant of: AstraZeneca, Amgen, Biogen, BristolMyersSquibb, Eli Lilly, EMD Serono, Genentech, Janssen, Grant/research support from: AstraZeneca, BristolMyersSquibb, Eli Lilly, EMD Serono, Janssen

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OP0143 INTERCURRENT INFECTION AS A RISK FACTOR FOR DISEASE FLARES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Intercurrent infections are presumed potential triggers of systemic lupus erythematosus (SLE) disease flares.[1] However, most of the evidence is obtained from a limited number of observational studies, and the results of these studies are conflicting.[2,3]

Objectives: To determine whether intercurrent infections are a risk factor for disease flares in SLE.

Methods: Demographic and clinical characteristics of 203 SLE patients from the Amsterdam SLE cohort were collected at baseline, and at the start of an intercurrent infection that either was or was not followed by a flare within three months. Relevant data regarding infections and flares were collected systematically by chart review. Major and minor infections were defined as, respectively: infections for which hospital admission or intravenous antibiotic therapy was required, and infections (proven or not proven, but highly likely based on clinical symptoms and/or response to therapy) for which hospital admission was not warranted. SLE flares were defined as an increase in disease activity requiring intensification of immunosuppressive therapy. Flares were categorized as major or minor depending on fulfillment of a predefined set of criteria.[4] Incidence rates for infections, flares, and infections followed by a flare within three months were calculated using Poisson regression. Descriptive analyses were performed where appropriate. Proportional hazard models with recurrent events and time-varying covariates were used to estimate the hazard ratio of SLE flares.

Results: Table 1 shows the demographic and clinical characteristics of all 203 SLE patients. Fifty-six major infections occurred in 1060 patient years, and 670 minor infections occurred in 1048 patient years. The incidence rates of major and minor infections were 5.3 per 100 patient years (95% CI: 4.1 – 6.9) and 63.9 per 100 patient years (95% CI: 59.3 – 69.0), respectively. In total, 198 flares occurred within 1060 patient years. The incidence rate of flares is 18.7 per 100 patient years (95% CI: 16.3 – 21.5), 3.6 per 100 patient years (95% CI: 2.6 – 4.9) for major flares and 15.1 per 100 patient years (95% CI: 12.9 – 17.6) for minor flares. The incidence rates of, respectively, major and minor infections followed by a flare within three months were 0.7 per 100 patient years (95% CI: 0.3 – 1.4) and 2.3 per 100 patient years (95% CI: 1.5 – 3.4). Intercurrent infections (major and minor) were associated with the occurrence of SLE flares (major and minor; HR 1.9, 95% CI:1.3 – 2.9) (Figure 1). The hazard ratio for a major SLE flare following a major infection was 7.4 (95% CI 2.2 – 24.6). Major infections were not associated with the occurrence of minor flares.

Table 1. Baseline demographic and clinical characteristics

Variables	SLE patients (n = 203)
Sex, Female, n (%)	184 (91)
Age, years (median (IQR))	40.0 (32.0 – 47.0)
Caucasian ethnicity, n (%)	137 (68)
SLICC/ACR damage index (median (IQR))	1 (0 – 2)
SELENA-SLEDAI2k (median (IQR))	4 (2 – 6)
Disease duration, years (median (IQR))	6 (1 – 11)
History of:	
Biopsy proven lupus nephritis, n (%)	38 (19)
Renal insufficiency (eGFR < 45), n (%)	6 (3)
Diabetes mellitus, n (%)	7 (3)
Malignancy, n (%)	5 (3)
Stroke, n (%)	12 (6)
Asplenia, n (%)	5 (3)
Treatment variables:	
Glucocorticoids, n (%)	106 (52)
Antimalarials, n (%)	151 (74)
Immunosuppressants, n (%)	75 (37)
NSAIDs, n (%)	67 (33)

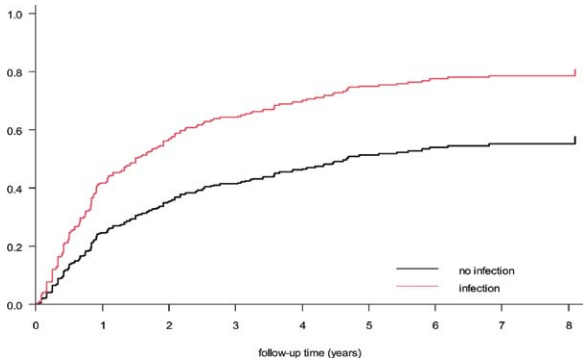

Figure 1. Estimated cumulative incidence of SLE flares (major and minor) following an intercurrent infection within three months

Conclusion: The results of the present study confirm a high frequency of infections in SLE patients and suggest that intercurrent infection is a risk factor for SLE flares. These findings underline the importance of prevention and treatment of infections in SLE patients and create awareness of infections as potential triggers of SLE flares.

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OP0144 SLE-T2T – A DIGITAL TREAT-TO-TARGET CLINICAL DECISION SUPPORT SYSTEM FOR THE MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: DEVELOPMENT AND USABILITY EVALUATION

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Background: Treating-to-target (T2T), a treatment approach focussed on achieving a specific goal by stepwise changes in treatment, is a well-established strategy in various diseases and has been proposed for systemic lupus erythematosus (SLE)[1]. However, the implementation of such strategies has been shown to be difficult in practice with low clinician adherence[2]. Clinical decision support systems (CDSS) are designed to assist health care professionals in their decision-making process[3]. SLE-T2T is an online CDSS tool designed to help rheumatologists to apply a T2T strategy in the management of SLE patients.

Objectives: We aimed to design and develop a first prototype of SLE-T2T, and test its usability for the implementation of a treat-to-target strategy in the management of patients with SLE.

Methods: The creation process was composed of three phases: first, SLE-T2T was conceived as a web-based application with a specific task - to generate appropriate treatment advice based on entered patients' data. A general sketch of the program was made, and general consensus was achieved with regards to the desired functionalities. In the development phase, a beta version of SLE-T2T was conceived using a free integrated development environment, and based on Javascript, HTML and CSS. After, the system was hosted temporarily on the website of the Amsterdam Rheumatology & Immunology Center[4], to be accessible for the participants in evaluation phase. Finally, a System Usability Score survey (SUS)[5,6] was chosen as the usability test tool, given its simplicity and advantages; coupled with unstructured feedback about areas of improvement, collected from the participants using the "think aloud" method to determine whether the CDSS was user-friendly, comprehensible, easy-to-deliver, and workflow-oriented.

Results: The SLE-T2T web-based system was developed, consisting of: (1) an input scheme with the set of indexes and scores existing for the measurement of SLE disease activity (cSLEDAI-2K, SLEDAI-2K, PGA score) as well as the patients' medication; (2) a rule-based interface that collects and processes patients' data, and (3) an output dashboard with the generated set of recommendations tailored for the patients clinical state and aiming to reach a pre-stablished target of treatment (Figure 1). In the interim usability and acceptance evaluation, 7 participants completed the SUS survey. The mean usage time for SLE-T2T was 8 minutes. On a scale of 0 (worst) to 100 (best), the median SUS score of SLE-T2T was 79, categorizing the application as 'good' and indicating the need for minor improvements to the design necessary to reach a final version for later implementation in a treat-to-target pilot study.

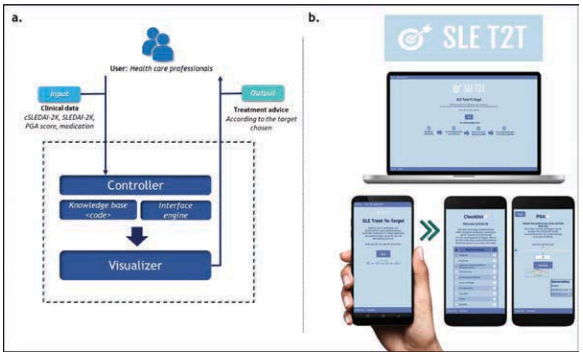

Figure 1. ***Overview of SLE-T2T CDSS tool.*** a. Architecture of the SLE-T2T app. b. Desktop and mobile example views.

Conclusion: To the best of our knowledge, SLE-T2T is the first eHealth tool to be designed for the management of SLE patients in a treat-to-target context. The SUS score and unstructured feedback showed high acceptance of this digital instrument.

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OP0145 VALIDATION OF 3 PREDICTION MODELS FOR THROMBOSIS IN ANTIPHOSPHOLIPID SYNDROME PATIENTS BASED ON A PROSPECTIVE COHORT

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Background: Antiphospholipid syndrome (APS) is a rare and complicated acquired autoimmune thrombophilia characterized by arterial/venous thrombosis and/or recurrent pregnancy loss. Thrombosis is the first cause of death of APS patients. However, there has been no generally acknowledged model to predict thrombosis. Only adjusted global APS score (aGAPSS) was developed for prediction but based on a cross-sectional study[1]. Additionally, the predictive ability of Padua score and Caprini score has not been validated in APS patients.

Objectives: Aim to validate the ability of aGAPSS, Padua score and Caprini score to predict thrombosis in APS patients basing on a prospective cohort.

Methods: Consecutive APS patients who fulfilled the 2006 Sydney Revised Classification Criteria for APS, referred to Peking Union Medical College Hospital were included. Clinical data, aGAPSS, Padua score, and Caprini score at the time of diagnosis were collected. Patients with less than 1-year follow-up were excluded. Harrell c-index and calibration curve were used to validate the prediction models.

Results: A total of 302 patients were enrolled in this study. The mean age was 32±12 years old, and 202 (66.9%) were female (Table 1). Patients were followed up for a median of 36 months. During the follow-up period, there were 62 thrombotic events, with 40 (13.25%) venous and 22 (7.28%) arterial thrombosis. The 1-, 3-, and 5-year thrombosis risks were 8.9%, 16.9%, and 21.3% respectively (Figure 1A). The Harrell c-indexes for predicting thrombosis of aGAPSS, Padua score, and Caprini score were 0.56 (95% confidence interval [CI], 0.52-0.60), 0.58 (95% CI, 0.54-0.62), and 0.61 (95%CI, 0.57-0.65) respectively. The model predicting venous thrombosis with the best discrimination was Padua score whose Harrell c-index was 0.64 (95% CI, 0.60-0.68), and the model predicting arterial thrombosis with the best discrimination was Caprini score whose Harrell c-index was 0.62 (95%CI, 0.56-0.68). The calibration curves illustrated that the calibration for predicting thrombosis within 3 years after diagnosis of all the 3 models was poor (Figure 1B-D).

Table 1. Demographic characteristics and clinical manifestations at baseline

	N=302		N=302
Age, mean±SD	32±12	**Clinical manifestations**	
Female, n (%)	202 (66.9)	Venous thrombosis, n (%)	156 (51.7)
Disease duration (months), median (Q1, Q3)	11.50 (3.00, 44.00)	Deep venous thrombosis, n (%)	112 (37.1)
Secondary to SLE, n (%)	73 (24.2)	Pulmonary embolism, n (%)	70 (23.2)
Smoking history, n (%)	63 (20.9)	Visceral venous thrombosis, n (%)	12 (4.0)
Hypertension, n (%)	59 (19.5)	Cranial venous sinus thrombosis, n (%)	13 (4.3)
Hyperlipidemia, n (%)	151 (50.0)	Arterial thrombosis, n (%)	113 (37.4)
BMI, mean±SD	23.96±3.89	Stroke/TIA, n (%)	62 (20.5)
LA positive, n (%)	241 (79.8)	Myocardial infarction, n (%)	14 (4.6)
aCL positive, n (%)	208 (68.9)	Arterial thrombosis of lower extremities, n (%)	22 (7.3)
aβ2GPI positive, n (%)	242 (80.1)	Visceral arterial thrombosis, n (%)	18 (6.0)
Triple aPL positive, n (%)	165 (54.6)	Thrombocytopenia, n (%)	118 (39.1)
Obstetric manifestations, n (%)	**N=202**	Valvular lesions, n (%)	24 (7.9)
Pregnancy morbidity	103 (51.0)		
Early miscarriages (<10 weeks)	13 (6.4)		
Fetal death (>= 10 weeks)	68 (33.7)		
Preeclampsia, eclampsia and placental dysfunction	36 (17.8)		

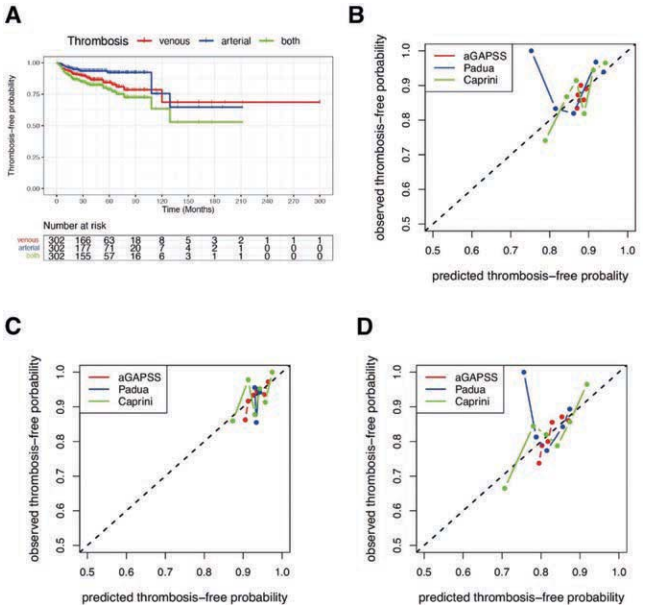

Figure 1. The Kaplan-Meier curve and the calibration curve of 3 prediction models within 3 years after diagnosis. A: The Kaplan-Meier curve of venous, arterial and both venous and arterial thrombosis. B: The calibration curves for venous thrombosis. C: The calibration curves for arterial thrombosis. D: The calibration curves for both venous and arterial thrombosis.

Conclusion: The ability of aGAPSS, Padua score and Caprini score to predict thrombosis in APS patients is relatively poor. Construction of a new prediction model specifically for APS patients is required to help with early prevention and treatment.

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OP0146

ISOLATED ANTI-RO52 ANTIBODIES IN SJÖGREN'S SYNDROME: A MILDER INFLAMMATORY PHENOTYPE AT HIGHER RISK FOR FIBROTIC ORGAN INVOLVEMENT

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Background: Autoimmune response against the Ro antigen (Ro52 and/or Ro60 subunits) represents a distinctive serological hallmark in primary Sjögren Syndrome (pSS). The double positivity for anti-Ro60 and anti-Ro52 has been associated with a higher glandular inflammation and B-cell hyperactivity. By contrast, the clinical significance of isolated anti-Ro52 antibodies in pSS remains controversial.

Objectives: To investigate the association between isolated anti-Ro52 antibodies and glandular and extra-glandular pSS features in order to explore whether anti-Ro52 antibodies may help to identify a specific subset of pSS.

Methods: In this retrospective study we included unselected pSS patients prospectively followed at our Unit between 2012 to 2021. Of them, anti-Ro/SSA positive patients were identified and stratified by the presence of anti-Ro52 isolated, anti-Ro60 isolated and both anti-Ro60 and anti-Ro52. Demographics, clinical, biological and histological data were compared between the three groups. Data were presented as mean±SD, or percent frequency as appropriate. Intergroup comparisons were made using the t-test/Mann–Whitney test for continuous variables and Fisher's exact test for categorical variables.

Results: Out of a study cohort of 432 pSS patients, we included 300 anti-Ro/SSA positive patients (21 M: 279 F, mean age 57±14 yrs) followed for a mean follow-up of 6.5±6.7 years. Of them, 59/300 (19.7%) presented isolated Ro52 antibodies, 214/300 (71.3 %) both anti-Ro60 and anti-Ro52 and 27/300 (9%) had isolated Ro60 antibodies. At diagnosis, patients with anti-Ro52 alone were older than those with double positivity (57.4±13.2 vs 48.8±13.8, p=0.0001) and presented a lower focus score (FS) in their minor salivary gland biopsies (MSGBs) (p=0.9±1.0 vs 1.6±0.9, p=0.02). No differences in demographic and glandular infiltrate were detected between anti-Ro52 alone and anti-Ro60 alone patients. Similarly, the three subgroups did not differ in oral and ocular function tests as well as in the patient reported outcomes (ESSPRI, OHIP and OSDI). Salivary gland ultrasonography showed a decreasing trend of the OMERACT scoring system with the highest grade detected more commonly in anti-Ro60 and anti-Ro52 patients and the lowest grade in anti-Ro60 alone. Regarding extraglandular manifestations significant differences were observed among the three subgroups as shown in the heat map (Figure 1). Patients with anti-Ro52 alone presented the highest frequency of interstitial lung disease (ILD) and primary biliary cirrhosis (PBC) and the lowest prevalence of lymphadenopathy, anti-La/SSB and hyper-IgG (p<0.05). By contrast, patients presenting anti-Ro52 in association with anti-Ro60 had a prominent B cell hyperactivity with higher levels of serum IgG, anti-La SSB antibodies and Rheumatoid factor positivity (p<0.05). Finally, patients with isolated anti-Ro60 presented a milder disease activity and an ESSDAI (3.4±4.5 vs 6.3±4.8 vs 5.2±5.1, p=0.009) significantly lower than the other two subgroups.

Conclusion: Patients with isolated anti-Ro52 seems to represent a specific subset of pSS with milder tissue focal inflammation but at higher risk for systemic fibrotic changes, particularly in the lungs. The identification of molecular pathogenetic processes, common to both isolated anti-Ro52 pSS and other anti-Ro52 positive connective tissue diseases may offer new insights into our understanding of disease etiology, and facilitate the development of targeted therapeutic approaches.

	Ro52	Ro52/Ro60	Ro60	p-value
Salivary Gland Enlargement	20	26	19	ns
arthralgias	34	49	41	ns
arthritis	5	10	19	ns
purpura	2	8	0	ns
lymphadenopathy	12	32	22	0.007
kidney	2	6	7	ns
lymphopenia	10	16	7	ns
neutropenia	7	17	0	0.014
Interstitial lung disease	15	6	0	0.036
peripheral nervous system	3	3	0	ns
central nervous system	2	3	4	ns
myositis	2	1	4	ns
non-Hodgkin's lymphoma	3	7	7	ns
C3	22	26	19	ns
C4	15	17	11	ns
Hyper-IgG	17	60	30	0.0001
anti-La/SSB	0	59	11	0.0001
Rheumatoid factor	22	52	22	0.0001
Primary Biliary Cholangitis	9	2	0	0.04

Fig 1. The Heat map color scale (green to red) shows the frequency of pSS features in patients stratified by the presence of anti-Ro52 isolated, anti-Ro60 isolated and both anti-Ro60 and anti-Ro52.

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OP0147

THE SLE-DAS REMISSION AND LOW DISEASE ACTIVITY STATES DISCRIMINATE DRUG FROM PLACEBO AND BETTER HEALTH-RELATED QUALITY OF LIFE: POST-HOC ANALYSIS OF THE BLISS-52 AND BLISS-76 PHASE III TRIALS.

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Background: Accurate and practical outcome measures for clinical trials in systemic lupus erythematosus (SLE) are lacking. The SLE Disease Activity Score (SLE-DAS) is a recently validated 17-item instrument, with high accuracy and sensitivity to changes in SLE disease activity. The SLE-DAS definitions of remission and low disease activity (LDA) were newly validated in the clinical setting[1,2]. These definitions may constitute accurate and easy to apply endpoints for SLE trials.
Objectives: (1) To evaluate the ability of SLE-DAS remission and LDA definitions to discriminate drug from placebo in SLE phase 3 trials; (2) To determine if attainment of these SLE-DAS targets are associated with better health-related quality of life (HR-QoL).
Methods: Post-hoc analysis of the merged study population in the BLISS-52 and -76 trials (NCT00424476; NCT00410384) of intravenous belimumab versus placebo for moderate to severe SLE disease activity. We analyzed the British Isles Lupus Assessment Group (BILAG), Physician Global Assessment (PGA), Functional Assessment of Chronic Illness Therapy (FACIT) and 36-Item Short Form Survey (SF-36) trial data. The fulfillment of SLE-DAS remission and LDA definitions were retrospectively assessed from the individual participants' data. Proportion of patients attaining SLE-DAS Boolean remission (defined as absence of all SLE-DAS clinical items and prednisone ≤5mg/day) and LDA (defined as SLE-DAS≤2.48 and prednisone ≤7.5mg/day), at week 52, was compared between belimumab and placebo arms, using likelihood ratio chi-square test. We further compared the SF-36 physical component summary (PCS) and mental component summary (MCS) and domain scores and the FACIT score between patients attaining SLE-DAS remission *vs* non-remission and SLE-DAS LDA *vs* non-LDA, using t-test and Mann-Whitney test.
Results: A total of 1684 SLE patients were included: 562 on placebo, 559 on belimumab 1mg/Kg and 563 on belimumab 10mg/Kg. At week 52, significantly more patients attained SLE-DAS LDA on belimumab 1mg/Kg and 10mg/Kg as compared with placebo (13.0% *vs* 17.9%, OR=1.459, p=0.023, and 13.0% *vs* 21.7%, OR=1.853, p<0.001, respectively). Likewise, more patients attained SLE-DAS remission on belimumab 10mg/Kg as compared with placebo (10.1% *vs* 14.7%, OR= 1.532, p=0.019) (Table 1). Importantly, none of the patients achieving SLE-DAS remission or LDA presented a new BILAG A or more than 1 new B domain score, neither a worsening in PGA≥0.3.
At week 52, patients attaining SLE-DAS remission and SLE-DAS LDA presented higher SF-36 domain and summary scores (all p<0.001) (Figure 1). Additionally, FACIT scores were higher in patients attaining SLE-DAS remission than non-remission patients (mean±SD: 38.24±10.65 *vs* 33.45±12.13, p<0.001), and in patients attaining SLE-DAS LDA than non-LDA (mean±SD: 37.22±11.00 *vs* 33.37±12.17, p<0.001), at week 52.

Table 1. Attainment of SLE-DAS Boolean remission and LDA at week 52 in BLISS-52 and BLISS-76 trials, according to the treatment groups (n =1684).

	Placebo	Belimumab 1mg/Kg	Belimumab 10mg/Kg
SLE-DAS remission (n=211)	10.1%	12.7%, OR=1.289 (0.89-1.866), p=0.178	14.7%, OR 1.532 (1.069-2.195), p=0.019
SLE-DAS LDA (n=295)	13.0%	17.9%, OR=1.459 (1.052-2.025), p=0.023	21.7%, OR 1.853 (1.349-2.545), p<0.001

LDA: Low disease activity; SLE-DAS Boolean remission: absence of all SLE-DAS clinical items and prednisone ≤5mg/day; SLE-DAS LDA: SLE-DAS≤2.48 and prednisone ≤7.5mg/day.

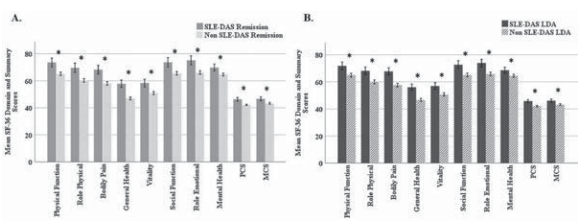

Figure 1. Mean SF-36 domain and summary scores at week 52; *p<0.001; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Medical Outcomes Survey Short Form.

Conclusion: The SLE-DAS remission and LDA showed discriminant validity for identifying patients receiving active drug in clinical trials. These treatment targets are associated with better HR-QoL and lower fatigue.

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Spondyloarthritis in practice: imaging, outcome assessment and comorbidities

OP0148

THE ASAS CORE MEASUREMENT SET FOR AXIAL SPONDYLOARTHRITIS

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Background: Recently, the core domains of the 20-years old core outcome set for ankylosing spondylitis were updated.[1] The next step is to define the measurement core set, which includes at least one instrument for each domain.
Objectives: To define the instruments for the ASAS-OMERACT core outcome set for axial spondyloarthritis (axSpA).
Methods: The scientific committee invited an international working group representing all key stakeholders (patients, rheumatologists, health professionals and pharmaceutical industry). The instrument selection process is presented in Figure 1.

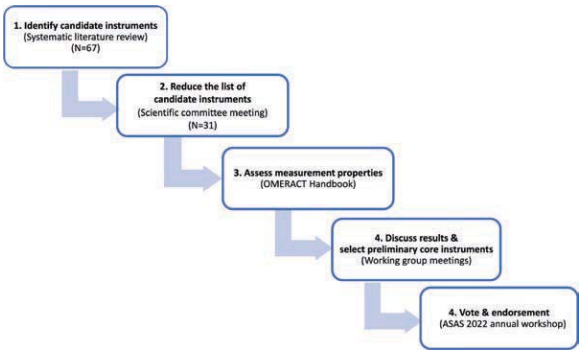

Figure 1. Development process to determine the core measurement set

Results: The updated core measurement set for axSpA is shown in Table 1. This includes seven instruments for six domains that are mandatory for all trials: ASDAS and NRS patient global assessment for disease activity, NRS total back pain for pain, composite index for morning stiffness, NRS fatigue for fatigue, BASFI for physical function, and ASAS Health Index for overall functioning and health. There are 9 additional instruments for disease modifying drugs (DMARDs): two MRI activity scores (SPARCC SIJ and SPARCC spine) for disease activity, the three extra-musculoskeletal manifestations uveitis, IBD and psoriasis assessed as recommended by ASAS[2], the three peripheral manifestations (44 swollen joint count, MASES and Dactylitis count[2]) and mSASSS for structural damage. The imaging outcomes are mandatory to be included at least in one trial for a drug that is considered to be a DMARD. The other instruments specific for DMARDs should be included in every trial. This core set is applicable to patients with radiographic and non-radiographic axSpA. Furthermore, 11 other instruments were also endorsed by ASAS and can additionally be used in axSpA trials: BASDAI, CRP, Berlin MRI-SIJ and MRI-spine activity scores for disease activity, NRS back pain at night for pain, severity (BASDAI Q5) and duration (BASDAI Q6) for morning stiffness, SF-36 for overall functioning and health, 66 swollen joint count and SPARCC enthesitis for peripheral manifestations and MRI-SIJ erosions scores (SPARCC SSS) for structural damage.

Table 1. Updated core measurement set for axial spondyloarthritis.

Instruments mandatory for all trials	
Domain	**Instrument**
Disease activity	ASDAS
	Patient global assessment of disease activity (NRS)
Pain	NRS total back pain (BASDAI Q2)
Morning stiffness	Severity and duration (BASDAI (Q5+Q6)/2))
Fatigue	NRS fatigue (BASDAI Q1)
Physical function	BASFI
Overall functioning & health	ASAS Health Index
Additional instruments mandatory for disease modifying drugs trials	
Disease activity	SPARCC MRI-SIJ*
	SPARCC MRI-spine*
Extra-musculoskeletal manifestations	uveitis (ASAS CRF)[2]
	psoriasis (ASAS CRF)[2]
	inflammatory bowel disease (ASAS CRF)[2]
Peripheral manifestations	44 Swollen joint count
	MASES
	Dactylitis count (ASAS CRF)[2]
Structural damage	mSASSS*

*Needs to be assessed at least once in a disease modifying drug programme; [2]Dougados M, et al. Ann Rheum Dis 2012;71(6):1103-04. ASDAS: Ankylosing Spondylitis Disease Activity Score; NRS: Numerical Rate Scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; Q: question; BASFI: Bath Ankylosing Spondylitis Functional Index; SPARCC: SpondyloArthritis Research Consortium of Canada Scoring System; MRI: Magnetic Resonance Imaging; SIJ: Sacroiliac Joint; CRF: Case Report Form; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score.

Conclusion: The previous core measurement set has been updated and endorsed by ASAS for the use in all axSpA trials.

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OP0149

RADIOGRAPHIC PROGRESSION FROM NON-RADIOGRAPHIC TO RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM A 5-YEAR MULTICOUNTRY PROSPECTIVE OBSERVATIONAL STUDY

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Background: Patients (pts) with axial spondyloarthritis (axSpA) are classified into radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA) based on the presence or absence of radiographic sacroiliitis. Approximately 20% to 80% of newly diagnosed axSpA pts have nr-axSpA and 8% to 40% progress to r-axSpA over the next 2 to 10 years.

Objectives: To evaluate progression from nr-axSpA to r-axSpA over 5 years in a prospective multicentre cohort.

Methods: PROOF was a global, real-world, prospective, observational study conducted in rheumatology clinical practices in 29 countries across 6 different geographic regions.[1] The study enrolled adults with chronic back pain for ≥3 months and onset before 45 years of age. This analysis included pts diagnosed with axSpA who also fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA. Study visits occurred at baseline (BL) and yearly thereafter. Baseline and follow-up radiographs of sacroiliac joints (SIJ) were evaluated for pts with initial nr-axSpA diagnosis independently by 2 central readers according to the modified New York criteria. In the case of disagreement on the classification (nr- or r-axSpA), images were adjudicated by a third reader. Radiographic progression from nr-axSpA to r-axSpA over 5 years was evaluated by Kaplan-Meier analysis. Cox proportional hazards regression analyses for time to radiographic progression from nr-axSpA to r-axSpA were conducted. For model 1, 'imaging arm vs clinical arm' was used as an independent variable, and for model 2, 'active inflammation on magnetic resonance imaging highly suggestive of sacroiliitis associated with SpA' was used. Further, potential predictive factors included in the models were age, gender, back pain duration, number of SpA parameters, smoking status, CRP, good response to NSAIDs, HLA-B27 status, and current use of NSAIDs and TNF inhibitors.

Results: Among 2633 enrolled pts, 2165 (82%) were diagnosed with axSpA and fulfilled the ASAS classification criteria. Among these, 1612 (74%) were classified as having r-axSpA (1050 [65%]) or nr-axSpA (562 [35%]) by central reading. The majority of nr-axSpA pts (77%) fulfilled the ASAS classification criteria due to positive findings on imaging (plus ≥1 SpA feature) and 23% were classified according to the clinical arm. A total of 246 nr-axSpA pts who had ≥1 follow-up SIJ radiograph were included in this analysis. Among these 246 pts, progression from initial nr-axSpA to r-axSpA at any of the follow-up visits was observed in 40 pts (16%) over 5 years. Mean time to radiographic progression was 2.4 years (ranging from 0.9 to 5.1 years) in descriptive analysis (Kaplan-Meier curve shown in Figure 1). In model 1 of the Cox regression analysis, male gender (hazard ratio [HR]: 3.16 [95% CI: 1.22–8.17]; P=0.0174), fulfilment of the imaging arm (HR: 6.64 [1.37–32.25]; P=0.0188), and good response to NSAIDs, (HR: 4.66 [1.23–17.71]; P=0.0237), were significantly associated with progression to r-axSpA (Figure 1). In model 2, HLA-B27 positivity showed a significant association with progression (HR: 3.99 [1.10–14.49]; P=0.0353; Figure 1).

Conclusion: In this study, 16% of nr-axSpA pts progressed to r-axSpA within 5 years. The mean time to disease progression was 2.4 years. Predictors of radiographic progression were male gender, good response to NSAIDs, and fulfilment of the imaging arm as well as HLA-B27 positivity.

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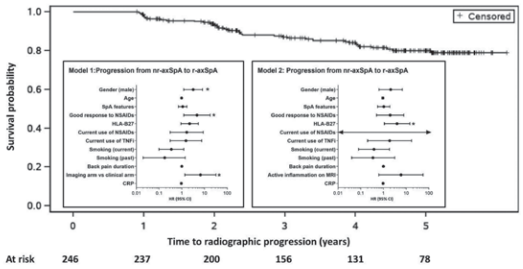
Figure. Time to Radiographic Progression and Cox Regression Analysis for Progression from nr-axSpA to r-axSpA (inset)



Cox proportional hazards regression analyses were conducted for patients with initial nr-axSpA classification. The target variable was Time to radiographic progression from nr-axSpA to AS. In model 1, "imaging arm vs clinical arm" was included as an independent variable. In model 2, "active inflammation on MRI highly suggestive of sacroiliitis associated with SpA" was included as an independent variable. *Statistically significant $P<0.05$. HLA-B27, human leukocyte antigen B27; nr-axSpA, non-radiographic axial SpA; NSAIDs, nonsteroidal anti-inflammatory drugs; r-axSpA, radiographic axial SpA; SpA, spondyloarthritis; TNFi, tumor necrosis factor inhibitor.

Disclosure of Interests: Denis Poddubnyy Speakers bureau: AbbVie, Bristol Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Biocad, Eli Lilly, Gilead, GlaxoSmithKline, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, Eli Lilly, MSD, Novartis, and Pfizer, Joachim Sieper Speakers bureau: AbbVie, Janssen, Merck, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Servet Akar Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Roche, Janssen, and UCB, Consultant of: AbbVie, Lilly, MSD, Novartis, Pfizer, Roche, Janssen, and UCB, Grant/research support from: AbbVie, Lilly, MSD, Novartis, Pfizer, Roche, Janssen, and UCB, Santiago Muñoz-Fernández Speakers bureau: AbbVie, BMS, Galapagos, Janssen, MSD, Novartis, Pfizer, Roche, and UCB., Consultant of: AbbVie, BMS, Galapagos, Janssen, MSD, Novartis, Pfizer, Roche, and UCB., Grant/research support from: AbbVie, BMS, Galapagos, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Hildrun Haibel Speakers bureau: AbbVie, Janssen, MSD, Pfizer, Sobi, Novartis, and Roche, Consultant of: Boehringer, Janssen, MSD, Novartis, and Roche, Torsten Diekhoff Paid instructor for: Novartis, MSD, Canon MS, Consultant of: Eli Lilly, Mikhail Protopopov: None declared, Elisabeth Altmaier Consultant of: AbbVie, Fabiana Ganz Shareholder of: Owns AbbVie stock or stock options., Employee of: AbbVie, Robert Inman Consultant of: AbbVie, Amgen, Janssen, Lilly, Novartis, Pfizer, and Sandoz, Grant/research support from: AbbVie, Amgen, and Janssen
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OP0150

ASAS RECOMMENDATIONS FOR REQUESTING AND REPORTING IMAGING EXAMINATIONS IN PATIENTS WITH SUSPECTED AXIAL SPONDYLOARTHRITIS

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Background: Clinicians face uncertainties in their daily practice when requesting imaging examinations for patients with suspected axial spondyloarthritis (axSpA) or when producing an imaging report because the requirements and desired information of radiologists and rheumatologists / orthopedics alike are sometimes not completely known or understood.
Objectives: This project aimed to develop practical consensus recommendations for the standardized communication around imaging of sacroiliac joints and spine for diagnostic purposes in patients with suspected axSpA or their management in clinical practice.
Methods: An international task force was established combining radiologists (n=7) and rheumatologists (n=13) from the Assessment of SpondyloArthritis international Society (ASAS), two members of Young ASAS and a patient representative. The task force defined the project's aims and developed a project statement. Then, considering published literature and the work of other groups, two survey rounds were designed, and all ASAS members invited to respond: first, to identify items for further consideration, second, to consider the detail of information to be communicated. Finally, ASAS members discussed the recommendations proposed by the task force during the ASAS annual workshop in January 2022 and voted regarding endorsement of the recommendations.
Results: The final set of recommendations is presented in Figure 1. Six recommendations deal with imaging requests in patients with axSpA. The first three recommendations entail clinical features, patients' symptoms and risk factors. Recommendation 4 concerns previous imaging and reports and recommendation 5 refers to contraindications to imaging or contrast media. Recommendation 6 is about the suspected diagnosis and possible clinical differential diagnoses and the reason for the examination. Eleven additional recommendations refer to the radiology report. The first point addresses clinical information included in the report. Recommendations 2 to 4 advise on information about the technical conduct of the exam, the use of contrast media and image quality. Imaging findings that should be mentioned in the report if present are listed in recommendations 5 to 7. Finally, recommendations 8 to 11 combine advice for the conclusion, and for suggesting additional imaging or referral to a rheumatology expert if a different physician requested the imaging. The recommendations were endorsed by ASAS with approval from 73% of voting members (43 agreed, 10 rejected, 6 abstained).

	Imaging request
1	The referring physician should communicate important clinical information when requesting imaging exams. This clinical information should include the patient's age, sex and HLA-B27 status.
2	Requests for imaging should include current or past history of back pain, its duration, localization, and inflammatory features, whether present or not. For follow-up exams, a change in clinical symptoms should be indicated.
3	Radiologists should be informed if the patient undertakes physically demanding activities or has history of childbirth (number of children and date of most recent childbirth).
4	Radiologists should have access to previous exam images for comparison or to the respective reports if those are not available.
5	The referral should include possible contraindications to certain types of imaging or contrast medium.
6	The referring physician should indicate the suspected clinical diagnosis and possible alternative explanations for the symptoms, whether SpA was previously diagnosed, and if the exam is requested for primary diagnosis, to assess disease activity or treatment response.

	Imaging report
	Clinical data
1	The report should start by summarising essential clinical information, including the patient's age, sex, a summary of symptoms, the suspected diagnosis, whether the exam was requested for primary diagnosis or follow-up, and what imaging was available for comparison.
	Technical data
2a	Radiography: The report should include the number of images, types of projections, and the patient's positioning.
2b	MRI: The report should include the applied field strength and sequences with slice orientation and thickness, if fat suppression was applied, and whether and what type of contrast medium was administered.
2c	CT: The report should include the patient's position, reconstructions' orientation and slice thickness, and a general indicator for the radiation dose (e.g., dose length product).
3	The anatomical coverage of the exam should be indicated.
4	The report should include a general statement about image quality and complications from imaging, particularly if the exam or its interpretation is affected.
	Report
5a	SIJ: Bone marrow oedema/osteitis, erosions and fat lesions are significant findings that the report should list semi-quantitatively with their localization specified. Their absence should be stated clearly.
5b	SIJ: The report should include if other active or structural lesions are present. Structural lesions should be reported per individual bone. The radiologists can summarize the absence of those active or structural lesions in the report.
6a	Spine: The report should semi-quantitatively list bone marrow oedema/osteitis at vertebral corners. All other active and structural lesions should be mentioned if present.
6b	Spine: The location of the findings mentioned above is essential for clinical correlation, and it should be stated at the level of the individual vertebra or discovertebral unit.
7	Findings unrelated to SpA but of potential clinical importance should be mentioned when present. These include for example gas inside the joint ("vacuum phenomenon"), osteophytes, transitional vertebrae, anatomical variations, and spinal malposition.
	Conclusion
8	The radiologist should state clearly if findings are compatible with SpA, based on the images and clinical information available. The conclusion should provide whether there is active inflammation or structural changes with the most prominent lesions, and give an indication of the confidence in interpretation of the findings.
9	Based on the exam findings, differential diagnoses and their probability should be mentioned, especially if more likely than SpA.
10	If the exam findings are inconclusive, radiologists should suggest further imaging according to their expertise.
11	If the exam is indicative of SpA and a rheumatologist did not request the imaging investigation, the report should recommend referral to a rheumatologist for further assessment.

Figure 1. ASAS recommendations for requesting and reporting imaging in patients with suspected axial Spondyloarthritis.

Conclusion: These ASAS recommendations provide guidance for requesting and reporting imaging examinations in the context of axSpA and for standardizing and enhancing communication between rheumatologists and radiologists to improve diagnosis and patient care.
Disclosure of Interests: Torsten Diekhoff Paid instructor for: Novarits, Eli Lilly, MSD, Canon MS, Consultant of: Eli Lilly, Iris Eshed: None declared, Chiara Giraudo: None declared, Kay-Geert Hermann: None declared, Manouk de Hooge: None declared, Lennart Jans: None declared, Anne Grethe Jurik: None declared, Robert G Lambert: None declared, Pedro M Machado: None declared, Walter P Maksymowych: None declared, Michael Mallinson: None declared, Helena Marzo-Ortega: None declared, Victoria Navarro-Compán: None declared, Susanne Juhl Pedersen: None declared, Mikkel Østergaard: None declared, Monique Reijnierse: None declared, Martin Rudwaleit: None declared, Fernando Sommerfleck: None declared, Ulrich Weber: None declared, Xenofon Baraliakos: None declared, Denis Poddubnyy: None declared
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OP0151

PREDICTION OF RADIOGRAPHIC PROGRESSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: USING GROUP-BASED TRAJECTORY MODELING AND DECISION TREE ANALYSIS

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Background: Ankylosing spondylitis (AS) tends to develop at a relatively young age and is characterized by long-term disease progression (1). During that time, various radiographic changes occur in the spine, which eventually lead to disability in the patient's lifetime (2). Although the duration of the disease, aging, and passage of time are predicted to be highly associated with spinal progression of AS, it is difficult to predict its progression in the spine of patients.

Objectives: We aimed to find ways to predict spinal progression over time in patients with AS and analyze its associated clinical factors.

Methods: Data from the medical records from a single center were extracted between 2001 and 2018. We analyzed the data on patients who fulfilled the modified New York Criteria for AS and had two or more sets of radiographs taken during the observation period. The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) was estimated by two independent radiologists. Group-based trajectory modeling (GBTM) was used to classify patients into distinct subgroups of longitudinal mSASSS. And when these trajectories and statistically associated factors acted on a patient, which group the patient was most likely to belong to was predicted using a decision tree analysis.

Results: Data on 1,125 patients were analyzed, and the trajectories were evaluated by dividing them into three groups based on duration of the disease. We confirmed that sex, age at diagnosis, ocular involvement and peripheral joint involvement were associated with the classified spinal progression trajectories. AS onset in older age and ocular involvement were associated with worse radiographic progression, while female sex and peripheral joint involvement were associated with slower radiographic progression (Figure 1 and Table 1).

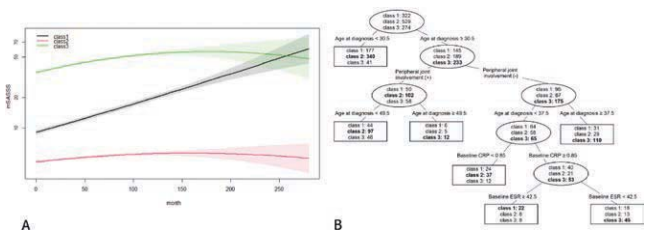

Figure 1. Longitudinal mSASSS trajectory groups for disease duration (A) and decision tree for three trajectory classes (B). (A) Time in month is shown along the x-axis, and logarithmic transformed total mSASSS is shown along the y-axis. The solid line represents the estimated mean in the same-colored area representing the 95% confidence interval. (B) In each terminal node, the class written in bold text is the class representing that node.

Conclusion: We identified three patterns of radiographic progression according to duration of the disease. The progression trend of patients with AS identified in this study is expected to be helpful in the treatment and management of patients in actual clinical settings.

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Table 1. Multivariate logistic regression analysis for predictors of mSASSS progression according to disease duration (class 2 and other classes)

	Univariate				Multivariable			
		OR 95% CI				OR 95% CI		
Variables	OR	Lower	Upper	*p*-value	OR	Lower	Upper	*p*-value
Sex	2.02	1.39	2.94	<0.001	**2.41**	**1.38**	**4.21**	**0.002**
Age at diagnosis (10y)	0.50	0.43	0.58	<0.001	**0.51**	**0.42**	**0.61**	**<0.001**
Ocular involvement	0.61	0.47	0.80	<0.001	**0.61**	**0.44**	**0.84**	**0.003**
Peripheral involvement	2.14	1.65	2.79	<0.001	**2.56**	**1.86**	**3.52**	**<0.001**
HLA B27 positivity	0.61	0.32	1.16	0.133				
Smoking*				<0.001				0.444
Ex-smoker	0.48	0.34	0.62	<0.001	0.78	0.52	1.16	0.218
Smoker	0.56	0.41	0.73	<0.001	0.84	0.57	1.23	0.364
Baseline BASDAI	1.00	0.92	1.09	0.950				
Baseline ESR	1.00	1.00	1.00	0.013				
Log baseline ESR	0.77	0.70	0.85	<0.001	**0.78**	**0.69**	**0.88**	**<0.001**
Baseline CRP	0.98	0.94	1.03	0.476				
Log baseline CRP	0.78	0.66	0.91	0.002	¶	¶	¶	¶

Note: Bold text means statistically significant values. *Analysis with non-smoker as a reference.¶It was excluded when performing multivariate analysis due to multicollinearity.

OP0152

A DEEP LEARNING FRAMEWORK FOR MRI DETECTION OF ACTIVE INFLAMMATORY AND STRUCTURAL CHANGES IN THE SACROILIAC JOINT CONSISTENT WITH AXIAL SPONDYLOARTHRITIS: AN INTERNATIONAL COLLABORATIVE STUDY

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Background: Magnetic resonance tomography (MRI) plays a key role in the early diagnosis of axial spondyloarthritis (axSpA). However, the detection of changes indicative of axSpA requires specific expertise, which poses a challenge to non-specialized centers. Deep learning (an advanced machine learning method) based on training an artificial neural network may facilitate and support diagnostics in clinical practice.

Objectives: To create a reliable deep learning tool for the detection of active inflammatory and structural changes indicative of axSpA on MRI of sacroiliac joints.

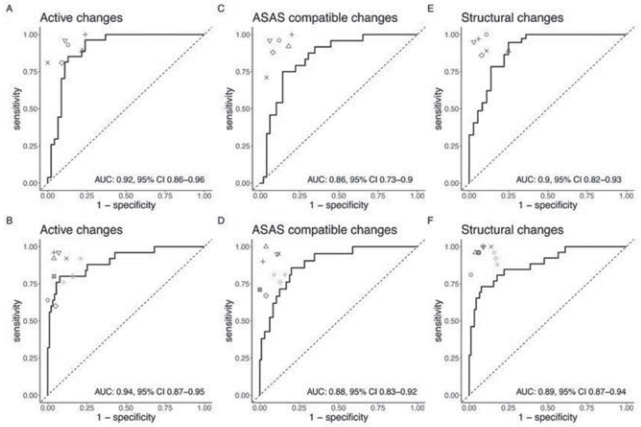
Methods: In this study, MRIs of sacroiliac joints from 477 patients from four cohorts (GESPIC-AS, GESPIC-Crohn, GESPIC-Uveitis and OptiRef comprising 266 patients with and 211 without axSpA) were used to develop a deep learning framework (randomly divided into training, n=404, and validation, n=73, datasets). MRIs from the ASAS cohort (n=116) were used for independent testing (test dataset). Each examination in the training/validation dataset was evaluated for the presence of active inflammatory and structural changes indicative of SpA by six experienced, trained and calibrated readers and by seven expert readers in the test dataset. The presence of the changes was defined as the majority vote amongst readers. Discordant cases in the training/validation dataset underwent consensus reading. In addition, the test dataset was evaluated by three radiologists not specifically trained in SpA. Diagnostic performance was evaluated using the area under the receiver operating characteristic curve (AUC), accuracy, sensitivity and specificity.

Results: The prevalence of positive imaging findings for active inflammatory/structural changes indicative of axSpA was 41%/51% in the training/validation dataset and 22%/22% in the test dataset. The model for the detection of active inflammatory changes showed an AUC of 0.91 (0.83 – 0.97) – Figure 1 – and an accuracy of 84% on the validation dataset; the corresponding sensitivity and specificity were 96% and 76%, respectively. Despite a substantially lower prevalence of active inflammatory changes in the test dataset, the model showed good generalization with an AUC of 0.91 (0.84–0.97) and an accuracy of 75%; the sensitivity and specificity were 88% and 71%, respectively. The model demonstrated

a similar performance on the validation and test datasets for the detection of active inflammatory changes fulfilling the ASAS definition. The model for the detection of structural changes indicative of axSpA showed good performance on the validation dataset with an AUC of 0.90 (0.82-0.96) for the detection of structural changes and an overall accuracy of 85%. The associated sensitivity and specificity were 95% and 75%, respectively. The model showed reasonable generalization to new data with an AUC of 0.89 (0.81–0.96) and an accuracy of 79%; the sensitivity and specificity were 85% and 78%, respectively. Overall, the model performed close to the individual human experts - Figure 1.

Conclusion: The developed framework allowed the detection of active inflammatory and structural changes indicative of axSpA on MRI. This approach may be used as an assistant tool in the diagnostic workflow.

Figure 1. ROC curves and associated AUCs for model performance compared to the individual human experts.



A, C and E represent the ROC curves for diagnostic performance on the validation dataset, while the ROC curves for the test dataset are given in B, D and F. The model performance did not exceed that of the trained experts (black symbols) but came close, especially for the detection of active inflammatory changes. The performance of three board-certified radiologists who did not undergo specific training for axSpA imaging is indicated by the orange symbols in B, D and F.

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OP0153

PRECONCEPTIONAL NSAID TREATMENT IS ASSOCIATED WITH LONGER TIME-TO-CONCEPTION IN WOMEN WITH SPONDYLOARTHRITIS: ANALYSIS OF THE PROSPECTIVE GR2 COHORT

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Background: Spondyloarthritis (SpA) is one of the most common chronic inflammatory diseases and regularly affects women of childbearing age[1]. However, there is limited knowledge about the impact of the disease and its treatment on fertility[2].
Objectives: The aim of the study was to determine factors associated with time-to-conception in women with SpA.
Methods: We performed an analysis of SpA patients (diagnosis according to the rheumatologist) included in the national multicenter cohort GR2 from 2015 to June 2021. Patients could be included either with a pregnancy wish (i.e., preconceptional period) or because of a clinical pregnancy (<12 weeks of gestation): for this analysis, only patients included preconceptionally were included. The main endpoint was time-to-conception, and the secondary endpoints were the number of subfertile patients (i.e., time-to-conception >12 months or non-achievement of pregnancy), as well as the number exposed to csDMARDs and biologics in the preconception period. We performed survival analyses, using a Cox model including a random effect for the center to account for heterogeneity of practices among participating centers. We used a multiple imputation to address missing data among the explanatory variables. Results are presented as a hazard ratio (HR) with confidence interval (CI) to assess associations between the factors studied and time-to-conception.
Results: Among the 207 patients with SpA included in the GR2 cohort, 88 were selected for analysis of time-to-conception (i.e., include preconceptionally). Of these, 56 (63.6%) had a clinical pregnancy during follow-up. Subfertility was observed in 40 (45.4%) women and the median time-to-conception was 16.1 months. The mean preconceptional BASDAI score was 2.9 (+/- 2.1). Patients were treated with NSAIDs, corticosteroids, csDMARDs and biotherapy in 23 (26.1%), 8 (9.1%), 12 (13.6%), and 61 (69.3%) cases, respectively. The multivariate model adjusted for age, BMI, nulligestity, BASDAI, disease duration, smoking, form of spondyloarthritis (axial, peripheral, or both), and exposure to NSAIDs, csDMARDs, and biotherapy in the preconception period found an association between longer time-to-conception and age (HR 1. 22 95% CI [1.08-1.40] p < 0.001), as well as the use of NSAIDs during preconception (HR 3.01 95% CI [2.15-3.85] p = 0.01).
Conclusion: This study provides original results on fertility in women with SpA. The factors associated with a longer time-to-conception were age and the NSAIDs use during the preconception period, which argues for their cautious use in case of pregnancy wish in patients needing continuous NSAID intake for the management of their disease.
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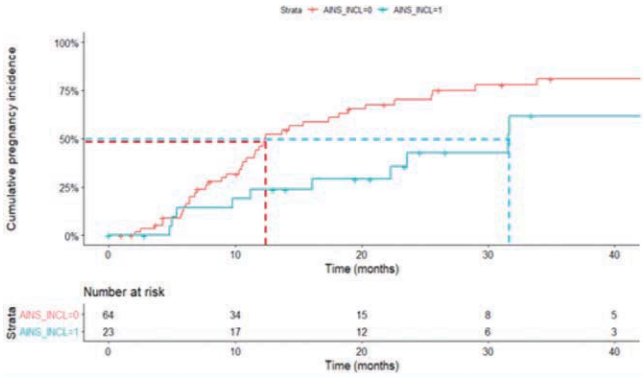

Figure 1. *Cumulative incidence curves for pregnancies in women with SpA according to NSAIDs use in preconception period.*

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OP0154

COMORBIDITY CLUSTERS IN ANKYLOSING SPONDYLITIS AND THEIR ASSOCIATION WITH DISEASE ACTIVITY AND FUNCTIONAL IMPAIRMENT: DATA FROM THE PSOAS COHORT

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Background: Comorbidities in ankylosing spondylitis (AS) occur more frequently than in the general population and are associated with higher morbidity and mortality. Some comorbidities may occur together, making one more likely in the presence of another, and different combinations of comorbidities may have differential considerations for AS management and outcomes.

Objectives: To examine the association of baseline comorbidities with disease activity and functional status in AS.

Methods: We used baseline data from the Prospective Study Of Ankylosing Spondylitis (PSOAS) cohort, a multicenter, prospective cohort from five centers (4 in the US, 1 in Australia). AS patients ≥ 18 years fulfilling mNY criteria for AS (2002-20) were included. Patient-reported AS comorbidities (N=28) and extra-musculoskeletal manifestations (EMMs, N=2) within 3 years of enrollment (prespecified on the baseline case-report form) and only those occurring in ≥1% were included. Undocumented comorbidities were assumed to be absent if missing in <15% of patients, and those missing in >50% of patients were excluded. Comorbidity clusters were identified using K-median clustering. The optimal number of clusters was determined using scree plot of the sum of squared errors and "elbow" on the graph line. Baseline characteristics of the clusters were compared, and associations of with disease activity and functional status measures (primary outcomes: ASDAS-CRP and BASFI) were examined using linear regression adjusted for age and sex.

Results: There were 1,270 AS patients included with a mean age of 44.6 ±14.3 years, 74.4% males, and 81.2% whites. Mean AS symptom duration was 20.6±5.6 years, 81.6% HLA-B27 positive, and CRP elevated in 27.5% of patients at baseline. Depression was the most prevalent comorbidity (31.4%) followed by hypertension (26.1%); uveitis was the most common EMM (30.4%). The five clusters identified included depression (27%), no comorbidities (22%), hypertension (21%), uveitis (20%), and asthma/low bone mass (10%) (Figure 1). The cluster with no comorbidities was significantly younger, with lower symptom duration (p<0.001). Females had higher odds of being in the depression (OR=2.00, 95% CI 1.38- 2.90) and uveitis (OR=2.09, 95% CI 1.41-3.11) clusters compared to the cluster with no comorbidities. The number of comorbidities and clusters with depression and hypertension were significantly associated with worse disease activity and functional status (Table 1).

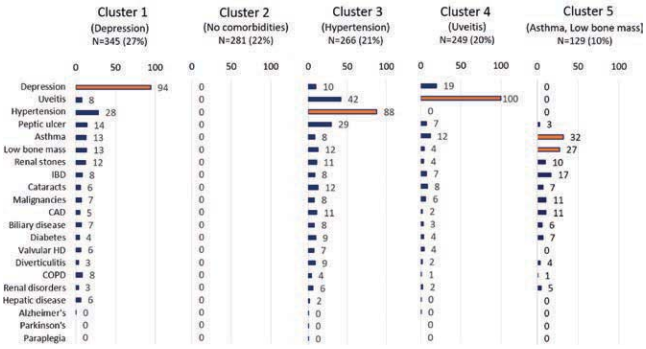

Figure 1. Comorbidity clusters in PSOAS cohort at baseline

Conclusion: Distinct comorbidity clusters were identified in AS patients in the PSOAS cohort. In addition to the number of comorbidities, the type of comorbidity seems to be important. Depression and hypertension clusters seem to be associated with worse disease activity and function.

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OP0155

DO FATTY LESIONS EXPLAIN THE ASSOCIATION BETWEEN INFLAMMATION AND NEW SYNDESMOPHYTES IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS?

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Table 1. Age and sex adjusted associations between comorbidity clusters, compared to cluster 3, and baseline disease activity/ functional status measures in ankylosing spondylitis based on Linear regression models.

	Cluster 1 (depression)	Cluster 3 (hypertension)	Cluster 4 (uveitis)	Cluster 5 (asthma, low bone mass)
Outcomes	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
ASDAS-CRP	0.98 (0.78-1.18)	0.43 (0.18-0.68)	0.04 (-0.19-0.27)	0.16 (-0.12-0.44)
BASFI (0-10)	1.92 (1.51-2.34)	1.00 (0.53-1.48)	-0.03 (-0.49-0.42)	0.64 (0.076-1.20)
Enthesitis count	1.17 (0.73-1.61)	0.73 (0.19-1.26)	0.18 (-0.32-0.68)	0.48 (-0.13-1.08)
Swollen joint count (0-44)	0.27 (-0.08-0.62)	0.43 (-0.01-0.86)	0.31 (-0.09-0.71)	-0.95 (-0.58-0.39)
Tender joint count (0-46)	1.24 (0.59-1.88)	0.44 (-0.34-1.23)	0.56 (-0.18-1.29)	0.34 (-0.55-1.23)
BASDAI (0-10)	2.30 (1.88-2.71)	0.88 (0.36-1.40)	0.30 (-0.17-0.78)	0.61 (0.03-1.19)
Patient Global (0-10)	2.25 (1.82-2.68)	0.76 (0.21-1.30)	-0.22 (-0.71-0.27)	0.29 (-0.31-0.89)
Patient Pain (0-10)	2.45 (1.95-2.94)	1.00 (0.37-1.62)	0.19 (-0.38-0.75)	0.16 (-0.54-0.85)
Spinal pain (0-10)	2.40 (1.89-2.91)	1.05 (0.41-1.70)	0.43 (-0.16-1.01)	0.76 (0.04-1.47)

Background: Presence of vertebral corner inflammation (VCI) increases the likelihood of a new syndesmophyte in the same vertebral corner (VC) in patients with r-axSpA. It was suggested that subsequent vertebral corner fat deposition (VCFD) partially explains this effect. However, this has not been formally tested.
Objectives: To determine how much of the effect of VCI on the development of new syndesmophytes is explained by new VCFD.
Methods: Two datasets (SIAS cohort, ASSERT clinical trial) were analyzed. Patients with r-axSpA were assessed at baseline (T0), an intermediate visit (T1) (SIAS: 1 year; ASSERT: 24 weeks) and the end of follow-up (T2) (SIAS: 2 years; ASSERT: 102 weeks). Syndesmophytes were assessed on whole spine low dose CT (SIAS) or spinal radiographs (ASSERT) at T0 and T2 and considered present if seen by 2 of 2 readers. VCI (T0) and VCFD (T0 and T1) on spinal MRI were present if seen by ≥2 of 3 readers (SIAS) or 2 of 2 readers (ASSERT). VCs with VCFD or a syndesmophyte at baseline were excluded. We used the counterfactual approach[1] to decompose the total effect of VCI at T0 (binary exposure) on the formation of a new syndesmophyte in the same VC at T2 (binary outcome) into the effect that is explained (natural indirect effect, NIE) and the effect that is not explained (natural direct effect, NDE) by new VCFD (binary mediator) at T1. Because there was no interaction between the exposure and mediator (p=0.88 for SIAS; p=0.82 for ASSERT), the average NIE (aNIE) and average NDE (aNDE) are reported. The aNIE, aNDE and total effect, expressed as absolute increase in risk, were estimated in R using the 'mediation' package, which takes into account the 2-level structure of the data (VCs nested within patients).
Results: In total, 49 patients (2,667 corners) in SIAS and 168 patients (2,918 corners) in ASSERT were included. A new syndesmophyte occurred at T2 in 124/2,667 (5%) corners in SIAS and 91/2,918 (3%) corners in ASSERT (Table 1). New VCFD at T1 was also uncommon (SIAS: 4%; ASSERT: 2%), but occurred more often in corners with (SIAS: 12%; ASSERT: 18%) than without VCI at T0 (SIAS: 3%; ASSERT: 1%). Applying the mediation formula, in SIAS, the presence of VCI at T0 increased the probability of a new syndesmophyte in the same VC at T2 by 9.3% [total effect (95% CI)=9.3% (4.5; 15.0)]. There was only a 0.2% increase in this probability that was mediated by the formation of new VCFDs at T1 [aNIE=0.2% (-0.4; 1.0)]. In contrast, 9.1% of the increase in probability remained unexplained [aNDE=9.1 (4.3; 15.0)]. This means that only 2% (0.2/9.3) of the total effect of VCI on the formation of new syndesmophytes was explained by new VCFD [% mediated=2.0% (-4.1; 13)]. In ASSERT, the total effect was somewhat lower than in SIAS [total effect=7.3% (2.0; 16.0)], and again the aNIE was small [aNIE=0.8% (-0.2; 3.0)], and the aNDE composed most of the total effect [aNDE=6.5% (1.3; 14.0)]. The proportion of the total effect explained by VCFD (0.8/7.3=10% (-3.1;44)) was larger than in SIAS but still non-significant.
Conclusion: In these two datasets we see that VCI only infrequently leads to syndesmophyte formation via visible VCFD.

Table 1. Marginal and conditional probabilities

SIAS

VCI T0	New VCFD T1	New SYND T2	n	P (SYND|VCI, VCFD)	P(VCFD|VCI)
0	0	0	2302	P (SYNDI0,0)	P(VCFDI0)
0	0	1	90	=90/2392= 0.038	= 74/2466=0.030
0	1	0	70	P (SYNDI0,1)	
0	1	1	4	=4/74 = 0.054	
1	0	0	152	P (SYNDI1,0)	P(VCFDI1)
1	0	1	25	= 25/177 = 0.141	= 24/201 =0.119
1	1	0	19	P (SYNDI1,1)	
1	1	1	5	= 5/24 = 0.208	

ASSERT

VCI T0	New VCFD T1	New SYND T2	n	P (SYND|VCI, VCFD)	P(VCFD|VCI)
0	0	0	2660	P (SYNDI0,0)	P(VCFDI0)
0	0	1	76	= 76/2736= 0.028	= 35/2771 =0.013
0	1	0	34	P (SYNDI0,1)	
0	1	1	1	=1/35= 0.029	
1	0	0	112	P (SYNDI1,0)	P(VCFDI1)
1	0	1	9	= 9/121= 0.074	= 26/147 =0.177
1	1	0	21	P (SYNDI1,1)	
1	1	1	5	= 5/26 = 0.192	

VCI, vertebral corner inflammation; VCFD, vertebral corner fat deposition; Synd, syndesmophytes; T0, baseline; T1, intermediate visit; T2, end of follow-up; n, number of vertebral corners; P, probability

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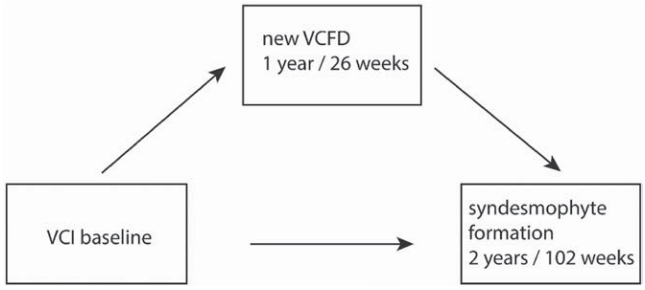

Figure 1. The pathways under study. VCI, vertebral corner inflammation; VCFD, vertebral corner fat deposition

Disclosure of Interests: Rosalinde Stal: None declared, Alexandre Sepriano Speakers bureau: Novartis, Consultant of: UCB, Sofia Ramiro Speakers bureau: Eli Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB, Sanofi, Grant/research support from: AbbVi, Galapagos, MSD, Novartis, Pfizer, UCB, Floris A. van Gaalen Consultant of: Novartis, MSD, AbbVie, Bristol Myers Squibb, Eli Lilly, Grant/research support from: Stichting vrienden van Sole Mio, Stichting ASAS, Jacobus Stichting, Novartis, UCB, Pedro Machado Consultant of: Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, Xenofon Baraliakos: None declared, Rosaline van den Berg: None declared, Monique Reijnierse Grant/research support from: reader for ASAS CLASSIC study, Juergen Braun: None declared, Robert B.M. Landewé Consultant of: AbbVie, Amgen, BMS, GSK, Janssen, Eli Lilly, Novartis, Pfizer, UCB, Désirée van der Heijde Consultant of: AbbVie, Gilead, Glaxo-Smith-Kline, Lilly, Novartis, UCB Pharma, Grant/research support from: Dutch Rheumatism Association
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The treatment and outcome of scleroderma

OP0156 **TOCILIZUMAB USE IN SYSTEMIC SCLEROSIS: SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Systemic sclerosis (SSc) is a low-prevalent autoimmune disease with a heterogeneous presentation. Skin involvement is the most frequent symptom and its treatment is orphan, only attending at Raynaud's phenomenon and classic immunosuppressive therapy for fibrosis. Lung implication is still remaining as the first cause of death. Interstitial lung disease (ILD) is the most frequent presentation and treatments most used includes cyclophosphamide and mycophenolate.[1] In 2021, the Food and Drug Administration (FDA) approved the first biologic therapy for ILD-SSc, tocilizumab (TCZ), based on 2 clinical trials.[2,3]
Objectives: To assess TCZ efficacy in SSc, either in ILD or skin involvement.
Methods: A systematic literature review was made using Medline, Embase, Cochrane Library and the Web of Science databases. Search strategy focused in synonyms of SSc and TCZ, also including MeSH terms. A random-effects model meta-analysis was performed to evaluate TCZ efficacy, when comparable measures were found. Clinical trials, observational studies and case-series were eligible.
Results: Search strategy identified 1036 articles, finally 13 studies were eligible for the review. Regarding the effect of TCZ in SSc skin involvement, measured by the modified Rodnan Skin Score (mRSS), a non-significant 40% improvement in mRSS and change in mean mRSS was reported (OR 1.22 [0.74-2.01], p=0.43 and SMD -0.69 [-1,48-0.10], p=0.09, respectively). About ILD-SSc, a significant non-worsening 10% Forced Vital Capacity (FVC) was reported in patients treated with TCZ (OR 0.45 [0.23-0.86), p=0.02) (Figure 1). As well, a non-significant Diffusing capacity for carbon monoxide (DLCO) was observed in patients treated with TCZ (SMD -0.66 [-1.48- -0.17], p=0.12).

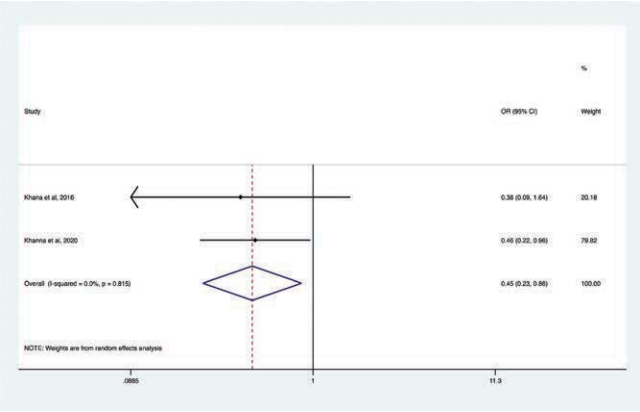

Figure 1.

Conclusion: Our study is the first review and meta-analysis of SSc patients treated with TCZ. This results show that TCZ could delay the worsening of ILD-SSc, being one therapeutic alternative to classical immunosuppressive therapy. Further studies are needed for better disease understanding and TCZ implications in other organ impairment.

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Disclosure of Interests: None declared

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OP0157

EFFECT OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) AND RISK FACTORS FOR RAPID DECLINE IN FORCED VITAL CAPACITY: FURTHER ANALYSES OF THE SENSCIS TRIAL

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Background: In the SENSCIS trial conducted in a population of subjects with SSc-ILD with a mean time since first non-Raynaud symptom of 3.5 years and 52% with diffuse cutaneous SSc (dcSSc), nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 44% versus placebo. Risk factors for a rapid decline in FVC in patients with SSc include early SSc, elevated inflammatory markers, significant skin involvement, and dcSSc. Patients with SSc with these risk factors for rapid progression of ILD are typically given immunosuppressants but not nintedanib.

Objectives: To analyse the rate of decline in FVC and the effect of nintedanib on FVC decline in subjects with risk factors for a rapid decline in FVC in the SENSCIS trial.

Methods: In post-hoc analyses of data from the SENSCIS trial, we analysed the rate of decline in FVC (mL/year) over 52 weeks in all subjects and in those with early SSc (<18 months since first non-Raynaud symptom), elevated inflammatory markers (C-reactive protein ≥6 mg/L and/or platelets ≥330 x 10^9/L), or significant skin fibrosis using two approaches (modified Rodnan skin score [mRSS] 15-40 or mRSS >18) at baseline. We also analysed the rate of decline in FVC over 52 weeks in subjects with one of these risk factors and dcSSc.

Results: Of 575 subjects analysed, 79 (13.7%) had <18 months since first non-Raynaud symptom, 210 (36.5%) had elevated inflammatory markers, 172 (29.9%) had mRSS 15-40 and 118 (20.5%) had mRSS >18. Of 299 subjects with dcSSc, 29 (9.7%) had <18 months since onset of first non-Raynaud symptom, 129 (43.1%) had elevated inflammatory markers, 162 (54.2%) had mRSS 15-40 and 118 (39.5%) had mRSS >18. In the placebo group, the rate of decline in FVC over 52 weeks was numerically greater in subjects with these risk factors for rapid decline in FVC compared with all subjects (Figure 1). Across the subgroups, the rate of decline in FVC was numerically lower in subjects treated with nintedanib than placebo (Figure 1).

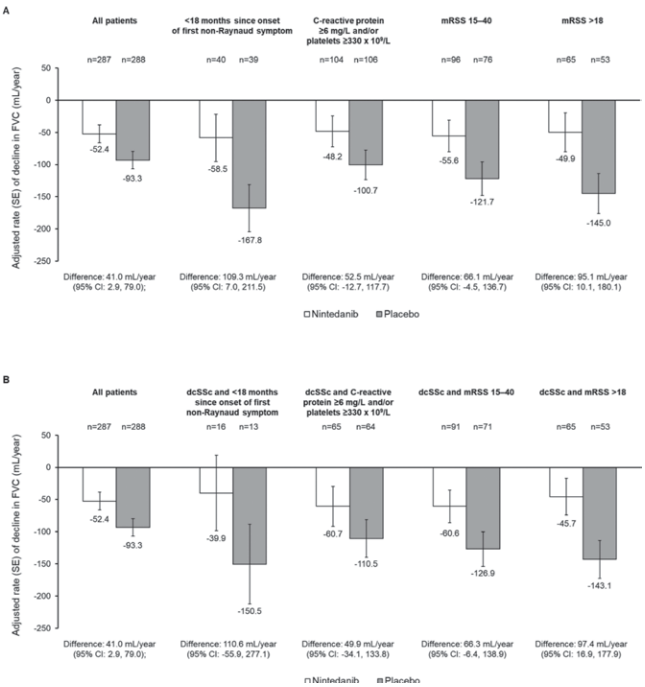

Figure 1. Rate of decline in FVC (mL/year) over 52 weeks in (A) all patients and in patients with risk factors for rapid decline in FVC at baseline and (B) all patients and in patients with dcSSc and risk factors for rapid decline in FVC at baseline in the SENSCIS trial.

Conclusion: The SENSCIS trial included a broad range of subjects with a fibrotic ILD complicating SSc, including those with risk factors for a rapid decline in FVC. In the placebo group, subjects with these risk factors had a more rapid decline in FVC over 52 weeks compared with the overall trial population. By targeting fibrosis with nintedanib, the rate of decline in FVC in patients with risk factors for FVC decline was reduced in patients treated with nintedanib compared with placebo.

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OP0158

COHORT ENRICHMENT STRATEGIES FOR PROGRESSIVE INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS FROM EUSTAR

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Background: Enrichment strategies from clinical trials for progressive systemic sclerosis-associated interstitial lung disease (SSc-ILD) have been partly successful but have not been tested in a real life cohort.

Objectives: Analyse the efficacy, representativeness and feasibility of enrichment strategies in SSc-ILD patients from the EUSTAR cohort.

Methods: We applied the inclusion criteria of major recent SSc-ILD trials (focuSSced, SLS II and SENSCIS) in SSc-ILD patients and assessed progressive ILD, defined as absolute change in forced vital capacity (FVC) and as significant progression (FVC decline >10%) over time. Data were compared to all patients and patients not fulfilling any inclusion criteria.

Results: In total, 2258 SSc-ILD patients were included, with 31.2% meeting SENSCIS, 5.8% SLS II, 1.6% focuSSced criteria and 1529 (67.7%) not meeting any criteria (Table 1). In the first 12+/-3 months, a slow FVC% decline of –0.1% was seen in the total, unselected cohort and in patients fulfilling SENSCIS criteria. Patients fulfilling criteria from focuSSced showed a strong FVC decline of –3.7%. Notably, patients enriched for SLS II criteria showed FVC improvement of +2.3% (Figure 1). Similarly, compared to the total unselected cohort, the number of significant progressive events was numerically higher in patients fulfilling focuSSced criteria, the same for SENSCIS criteria and even slightly lower for patients fulfilling the SLS2 criteria.

Table 1. Demographics and baseline clinical characteristics of EUSTAR patients

	Not fulfilling any criteria (n=1529)	focuSSced (n=36)	SLS II (n=132)	SENSCIS (n=704)
Age, years (SD)	58.4 (2.9)	51.5 (12.2)†	51.2 (12.7)†	54.2 (13.8)†
Male, n (%)	231 (15.1)	7 (19)	35 (27)**	156 (21)*
Disease duration, months (SD)	156.3 (99.4)	16.1 (13.9)†	40.7 (25.2)†	39.4 (23.9)†
DcSSc, n (%)	597 (43.8)	36 (100)†	85 (65)†	35 (52)†
ATA, n (%)	735 (51.1)	24 (67)*	85 (69)†	370 (56)
mRSS, mean (SD)	9.5 (8.3)	21 (6.5)*	13 (9.6)*	11 (9.2)
GERD, n (%)	1002 (65.9)	25 (69)	92 (70)	430 (62)
ESR, mean (SD)	27 (20.5)	43.1 (23)†	29.6 (19.6)†	24.7 (20.7)
MMF, n (%)	75 (16.5)	0 (0)†	0 (0)†	52 (22)†
MTX, n (%)	42 (9.2)	0 (0)†	2 (5)	20 (9)
FVC % predicted, mean (SD)	85.7 (22.5)	88 (13.6)*	66 (9.1)†	88 (19.8)
DL_{CO} % predicted, mean (SD)	58.9 (21.5)	61 (12.7)	49(14.6)†	59 (14.2)
NYHA class, n (%)				
3	261 (17.8)	6 (19)	28 (21)	72 (10)*
4	40 (2.7)	0 (0)	3 (2)	4 (1)*

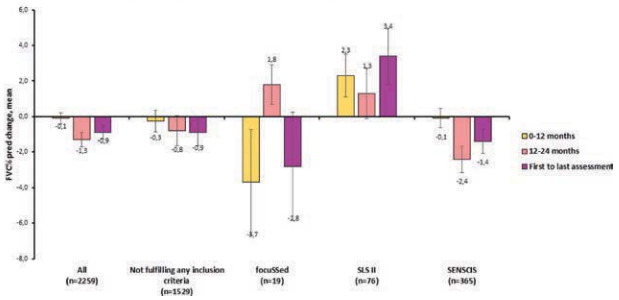
*P-value: 0.001–0.05; †P<0.001, between focuSSced, SENSCIS or SLS compared with not fulfilling any study criteria.

In the second 12 months period, SENSCIS enriched patients had a further absolute FVC% decline as described for the total cohort. In contrast, patients fulfilling the focuSSced and SLS II inclusion criteria showed numerical improvement of lung function in the second period (Figure 1). There were no significant associations of enrichment criteria and ILD progression in the second period.

Over the mean observation period of 2.3 years, patients not fulfilling any inclusion criteria showed the same FVC decline of –0.9 (12.1) as observed for the total cohort (–0.9% (12.6)). There were numerical differences in FVC changes in the enriched patient cohorts, varying from –2.8% FVC decline in patients fulfilling the focuSSced criteria to +3.4% FVC improvement with SLS II criteria.

Conclusion: Application of enrichment criteria from previous clinical trials showed enrichment for progression with variable success but led to selected patient populations reducing feasibility of recruitment. These findings are important for future clinical trial design and interpretation of the results of published trials.

Figure: Mean FVC% pred change from 0-12 months, 12-24 months and from first to last assessment



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OP0159

INCREASE RISK FOR CORONARY ARTERY DISEASE AND MYOCARDIAL INFARCTION IN SCLERODERMA-A NATIONAL INPATIENT SAMPLE ANALYSIS

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Background: Several rheumatologic diseases such as SLE and Rheumatoid arthritis are well known to increase cardiovascular risk. Scleroderma is well known to cause microvascular dysfunction, which can cause microvascular Coronary artery disease (CAD). However, Scleroderma is not classically associated with macrovascular CAD.

Objectives: We wanted to study the association of both microvascular and macrovascular CAD and Myocardial infarction (MI) in Scleroderma patients using the NIS (National inpatient sample) of the United States (US).

Methods: We included adult patients admitted to teaching hospitals with a primary or secondary diagnosis of Scleroderma from the National inpatient sample (NIS) of 2016, 2017, and 2018. The NIS is the largest publicly available all-payer inpatient care database in the United States, containing data on more than seven million hospital stays. After coding for the relevant variables based on the ICD-10 coding system, we performed univariate and multivariate logistic regression analysis to determine if Scleroderma was associated with CAD and MI. As there was no ICD-10 code for macrovascular CAD, we used Percutaneous intervention (PCI) and Coronary artery bypass grafting (CABG) to indicate the presence of macrovascular CAD. Four separate models with outcomes as CAD, MI, PCI, and CABG were created.

Results: A total of weighted 57,739 (95% CI 55,787-59,692) hospitalizations with Scleroderma were included. Only 0.1% of CAD and MI patients had a history of Scleroderma. On univariate logistic regression, Scleroderma was not associated with an increased risk of CAD (OR 0.82, 95% CI 0.79-0.86, P<0.01). After adjusting for age, sex, race, family history of CAD, dyslipidemia, diabetes, hypertension, and smoking, Scleroderma was associated with CAD (OR 1.40, 95% CI 1.34-1.47, P<0.01) (Table 1) and MI (OR 1.13, 95% CI 1.02-1.25, P=0.01) but not with PCI (OR 0.86, 95% CI 0.73-1.01, P=0.07) or CABG (OR 0.79, 95% CI 0.61-1.03, P=0.09).

Conclusion: CAD in Scleroderma is due to the combined effect of Scleroderma itself and co-existing cardiovascular risk factors. In our large epidemiological study, Scleroderma was associated with CAD and MI despite adjusting for the traditional risk factors for CAD, which is consistent with our current understanding of Scleroderma. Scleroderma is suspected of causing recurrent coronary microvascular inflammation and ischemia, which leads to ischemic necrosis and myocardial fibrosis (1). Other mechanisms include coronary Raynaud phenomenon and myocarditis. The lack of association of PCI and CABG with Scleroderma likely suggests that CAD in Scleroderma is mostly microvascular. Potential limitations of our study are its retrospective nature and the lack of catheterization data. Cardiovascular diseases account for 12% of mortality, and CAD accounts for 5% mortality in Scleroderma patients (2). Therefore, care for Scleroderma patients should involve aggressive management of Scleroderma and the risk factors for CAD.

Table 1. Multivariate logistic regression model for CAD

Variable	OR (95% CI)	P-value
Age	1.03 (1.03-1.03)	0.000
Female	0.50 (0.50-0.51)	0.000
Race		
Whites	Reference	
African American	0.82(0.81-0.83)	0.000
Hispanic	0.79(9.78-0.81)	0.000
Asian/pacific islander	0.75(0.73-0.76)	0.000
Native American	0.98(0.93-1.04)	0.718
Others	0.91(0.87-0.95)	0.000
Family history of MI	1.72(1.69-1.75)	0.000
Dyslipidemia	2.18(2.17-2.20)	0.000
Diabetes	1.70(1.69-1.71)	0.000
Hypertension	2.08(2.07-2.10)	0.000
Nicotine dependence	1.34(1.33-1.35)	0.000
Scleroderma	1.40(1.34-1.34-1.47)	0.000

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OP0160

HLA-DRB1 ASSOCIATIONS WITH AUTOANTIBODY-DEFINED SUBGROUPS IN IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM)

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Background: There is a gap between how IIM patients are classified in practice and current validated classification criteria[1]. Also, different associations with genetic variations in *HLA* can inform about different T-cell mechanisms involved in disease pathogenesis.

Objectives: We aimed to systematically study associations between *HLA-DRB1* alleles, clinical manifestations, and autoantibody-defined IIM subgroups.

Methods: We included 1348 IIM patients from five European countries. An unsupervised cluster analysis was performed using 14 autoantibodies: anti-Jo1, -PL7, -PL12, -EJ, -OJ, -SRP, -U1RNP, -Ro52, -Mi2, -TIF1γ, -MDA5, -PMScl, -SAE1, and -NXP2 to identify patients' subgroups. Logistic regressions were used to estimate the associations between *HLA-DRB1* alleles, clinical manifestations and the identified subgroups.

Table 1. Autoantibody-defined subgroups using an unsupervised cluster analysis.

	Subgroups/ Medoids								
Variables	**1 Ro52**	**2 U1RNP**	**3 PMScl**	**4 Mi2**	**5 Jo1**	**6 Jo1/Ro52**	**7 TIF1**	**8 None***	**All**
n (%)	137 (10)	183 (14)	107 (8)	65 (5)	119 (9)	140 (10)	78 (6)	519 (39)	1348 (100)
Female (%)	93 (68)	116 (63)	79 (74)	45 (69)	76 (64)	96 (69)	64 (82)	313 (60)	882 (65)
Age at diagnosis, median (IQR)	56 (16)	51.5 (23)	51 (25)	57 (22.5)	47.5 (23.25)	52 (19.5)	53.5 (21.75)	58 (22)	55 (23)
Autoantibodies									
Anti-Jo1	0	6 (3)	0	1 (2)	119 (100)	140 (100)	0	0	266 (20)
Anti-PL7	7 (5)	13 (7)	0	0	0	0	0	0	20 (1.5)
Anti-PL12	5 (4)	3 (2)	1 (1)	0	1 (1)	0	0	0	10 (0.7)
Anti-EJ	2 (2)	0	0	0	0	0	0	0	2 (0.1)
Anti-OJ	0	7 (4)	0	0	0	0	0	0	7 (0.5)
Anti-TIF1	10 (7)	2 (1)	2 (2)	0	0	0	78 (100)	0	92 (7)
Anti-Mi2	1 (1)	1 (1)	1 (1)	65 (100)	0	2 (1)	0	0	70 (5)
Anti-SAE1	8 (6)	23 (13)	0	0	0	0	0	0	31 (2)
Anti-NXP2	1 (1)	23 (13)	1 (1)	0	0	0	0	0	25 (2)
Anti-MDA5	9 (7)	10 (6)	1 (1)	1 (2)	0	1 (1)	0	0	22 (2)
Anti-SRP	8 (6)	32 (18)	0	0	0	0	0	0	40 (3)
Anti-Ro52	137 (100)	16 (9)	0	0	0	140 (100)	0	0	293 (22)
Anti-PMScl	11 (8)	1 (1)	107 (100)	0	0	0	0	0	119 (9)
Anti-U1RNP	0	79 (43)	0	0	0	3 (2)	0	0	82 (6)

*IIM patients negative for the tested autoantibodies.

Results: Eight subgroups were defined by the autoantibody status (Table 1). Three of the subgroups (1, 2 and 6) have overlapping autoantibodies, while four are almost monospecific (3,4,5 and 7), and one (8) has patients negative for tested autoantibodies. Figure 1 represents the significant associations between *HLA-DRB1* alleles and the eight subgroups. Heliotrope rash and Gottron's sign were significantly more frequent in subgroups 3 (OR:2.2 95%CI:[1.1-4.8], OR:2.6 95%CI:[1.3-5.9], respectively), 4 (OR:12 95%CI:[3.6-75], OR:7.8 95%CI:[2.8-33], respectively) and 7 (OR:22 95%CI:[4.5-385], OR:10 95%CI:[3.1-65], respectively), and Raynaud's phenomenon was significantly more frequent in subgroup 6 (OR:3.3 95%CI:[1.2-11]).

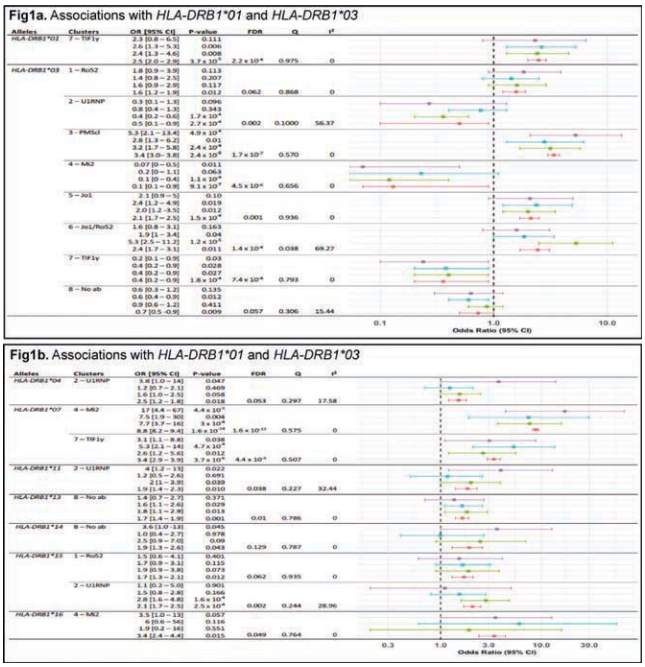

Figure 1. Forest plot of significant associations of *HLA. *DRB1* alleles with autoantibody-defined subgroups. Scandinavia includes patients from Denmark, Norway, and Sweden.

Conclusion: Our study reveals that certain subgroups of IIM patients are characterized by overlap of myositis -specific and -associated autoantibodies, which in turn are associated with different *HLA-DRB1* alleles including potential novel associations. These results point to different disease mechanisms in the subgroups, as well as suggest that IIM classification could be improved by integrating broader serological and genetic data.

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OP0161

TREATMENT PATTERNS OF IDIOPATHIC INFLAMMATORY MYOPATHIES: RESULTS FROM AN INTERNATIONAL COHORT OF OVER 1,400 PATIENTS

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Background: Idiopathic inflammatory myopathies (IIM) are a group of heterogeneous autoimmune disorders with limited standardization of treatment protocols.
Objectives: To evaluate frequency and patterns of various treatments used for IIM based on disease subtype, world region, and organ involvement.
Methods: Cross-sectional data from the international CoVAD self-report e-survey[1] was extracted on Sep 14th, 2021. Patient details included demographics, IIM subtypes (dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM), antisynthetase syndrome (ASSD), necrotizing myositis (NM) and overlap myositis (OM)), clinical symptoms, disease duration and activity, and current treatments. Treatments were categorized in corticosteroids (CS), antimalarials, immunosuppressants (IS), intravenous immunoglobulins (IVIG), biologics, and others. Typical clinical symptoms (dyspnea, dysphagia) were used as surrogate for organ involvement. Factors associated with IS were analyzed using multivariable logistic regression, adjusting for IIM subtype, demographics, world region, disease activity, and prevalent clinical symptoms (>10%).
Results: In 1418 patients with IIM, median age was 61 years [IQR 49-70], 62.5% were females, median disease duration was 6 years [IQR 3-11], most common subset was DM (32.4%).
The most used treatments were IS (49.4%, including Methotrexate 19.6%, Mycophenolate Mofetil 18.2%, Azathioprine 8.8%, Cyclosporine 2.7%, Tacrolimus 2%, Leflunomide 1.6%, Sulfasalazine 1%, and Cyclophosphamide 0.6%), followed by CS (40.8%), antimalarials (13.8%) and IVIG (9.4%). Biologics were used in 4.3% of patients.
Treatment patterns differed significantly by IIM subtypes with a higher frequency of IS (77.7%) and CS (63.4%) use in ASSD; antimalarials (28.6%) and biologics (9.8%) use in OM and IVIG use in NM (24.6%) (Table 1). Also, treatment patterns were different in regions of the world (Figure 1), with a higher frequency of CS use in Europe (60.5%) and IS use in South America (77.2%). Antimalarials were most used in Asia (19.4%), while IVIG use was most common in Oceania (16.9%). Dyspnea was associated with higher use of IS (69.9%) and CS (65.8%) (p<0.001), whereas dysphagia was negatively associated with IS (39.7%) and CS (32.7%) likely due to a higher proportion in IBM patients reporting dysphagia.
Multivariable logistic regression analysis showed an association of IS with the IIM subtype (least used in IBM (OR 0.07 [95%CI 0.04-0.13] compared to DM), world region (most used in South America (OR 2.35 [1.12-4.91] compared to North America), active and worsening disease activity (OR 3.49 [1.76-6.91] compared to remission), and some clinical features (dyspnea, fatigue, and muscle weakness).
Conclusion: IIM treatment patterns differ significantly by disease subtypes, world regions and organ involvement, highlighting the need for unified international consensus-driven guidelines.

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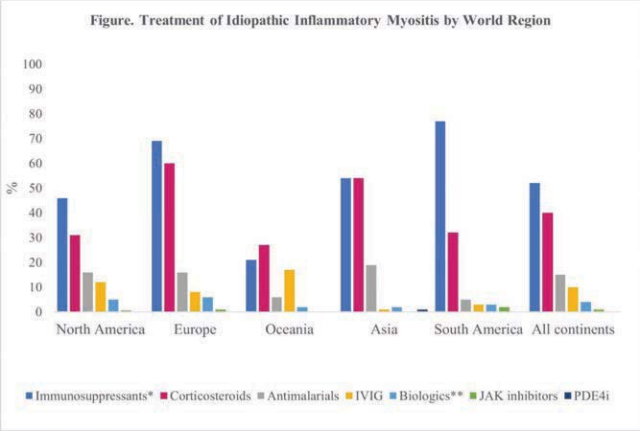

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OP0162

EFFICACY AND SAFETY OF LENABASUM IN THE PHASE 3 DETERMINE TRIAL IN DERMATOMYOSITIS

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Background: Safe and effective treatments are of significant unmet need in DM. Lenabasum, a CB2 agonist that activates resolution of inflammation, improved skin disease, patient-reported outcomes, and biomarkers in a Phase 2 study of DM patients with active skin disease.
Objectives: To evaluate the efficacy and safety of lenabasum in a Phase 3 double-blind study in DM.
Methods: DM patients ≥ 18 years old with active skin with or without muscle involvement were enrolled in 55 sites in North America, Europe, and Asia-Pacific. Stable doses of background immunosuppressants were allowed. Subjects were randomized 2:1:2 to lenabasum 20 mg BID, lenabasum 5 mg BID, or placebo BID for 52 weeks, with visits ≤ 8 weeks apart. The study was stopped after all subjects completed Week 28. Some subjects had completed Week 52 by then. The primary efficacy endpoint was Total Improvement Score (TIS) at Week 28 and a secondary efficacy endpoint was TIS at Week 52, for lenabasum 20 mg BID vs placebo.
Results: 175 subjects (69 lenabasum 20 mg BID, 35 lenabasum 5 mg BID, 71 placebo BID) received study drug; 167 completed Week 28, and 103 completed Week 52. The most common reasons for study discontinuation were study stopped by Sponsor (34.3%), withdrawal of consent (4.5%), and adverse events (AEs, 3.9%), with similar rates among groups. Baseline demographics and disease measurements were similar among groups and in total subjects were (mean or %): age 52.0 years; 81.1% female, 75.4% White; MMT-8 133.3; CDASI activity score 23.4; HAQ-DI 0.84, MDGA 5.55, EMGA 5.23; and PtGA

Table 1. Current Treatments for IIM, Stratified by Disease Subtypes

	Dermatomyositis	Polymyositis	Inclusion Body Myositis	Anti-synthetase syndrome	Necrotizing myositis	Overlap syndrome	All IIM	p-value
Number of patients	**459**	**182**	**348**	**148**	**57**	**224**	**1418**	
Immunosuppressants*	269 (58.6)	107 (58.8)	39 (11.2)	115 (77.7)	40 (70.2)	130 (58.0)	700 (49.4)	<0.001
Corticosteroids	208 (48.0)	81 (46.8)	32 (9.7)	90 (63.4)	32 (59.3)	103 (50.0)	546 (40.8)	<0.001
Antimalarials	99 (21.6)	7 (3.8)	0 (0.0)	25 (16.9)	1 (1.8)	64 (28.6)	196 (13.8)	<0.001
Intravenous Immunoglobulins	54 (11.8)	16 (8.8)	19 (5.5)	10 (6.8)	14 (24.6)	20 (8.9)	133 (9.4)	<0.001
Biologics**	17 (3.7)	7 (3.8)	0 (0.0)	13 (8.8)	2 (3.5)	22 (9.8)	61 (4.3)	<0.001
Others***	6 (1.3)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	5 (2,2)	12 (0.8)	0.098

**Methotrexate (278), Mycophenolate Mofetil (258), Azathioprine (125), Cyclosporine (38), Tacrolimus (28), Leflunomide (23), Sulfasalazine (14), Cyclophosphamide (9). **Rituximab (44), Abatacept (5), TNF inhibitors (4), Tocilizumab (3), Belimumab (3), Secukinumab (1). ***JAK(10) and PDE4 inhibitors (2)*

5.12. Corticosteroids were used by 48.1% and 38.0%, immunoglobulins by 5.8% and 7.0%, and other immunosuppressives by 51.0% and 54.9%, and monoclonal antibodies by 8.7% and 7.0% of lenabasum and placebo groups at baseline, respectively. The primary efficacy endpoint was not met - mean (SD) TIS score was 28.3 (19.75) vs 27.2 (19.23) at Week 28 for lenabasum 20 mg BID vs placebo, p = 0.3311, MMRM. Week 52 values were 40.6 (16.88) vs 34.8 (19.94), p = 0.2290. When analyses were restricted to subjects with muscle weakness at baseline (MMT8 < 142), TIS scores and treatment differences were greater and reached nominal statistical significance at Week 40, p = 0.0172. Mean (SD) improvements in CDASI activity score were numerically greater but not statistically different between lenabasum 20 mg BID group vs placebo at Week 28 [-7.1 (7.76) vs -5.8 (8.88) points, p = 0.2775] and Week 52 [-10.0 (9.45) vs -6.2 (12.8) points, p = 0.0932]. When restricting analysis of participants without muscle weakness (MMT-8 = 150), improvement in CDASI activity score was greater in the lenabasum 20 mg BID group vs placebo at Week 28, p = 0.0461, and Week 52 p = 0.0059.

Treatment-emergent AEs (TEAEs) occurred in 87.0%, 85.7%, and 87.3% of lenabasum 20 mg BID, lenabasum 5 mg BID, and placebo groups, with no deaths. Related TEAEs leading to withdrawal of study product were infrequent, occurring in 1.4%, 0%, and 2.0% of subjects in the same groups. Serious TEAEs occurred in 11.6%, 8.6%, and 4.2% of subjects in the lenabasum 20 mg BID, lenabasum 5 mg BID, and placebo groups. No serious TEAE preferred term occurred in more than 1 subject in any group. TEAE occurring in ≥ 10% of lenabasum 20 mg BID subjects were (% lenabasum vs % placebo): dermatomyositis (flare) 27.5% vs 40.8%; diarrhea 14.5% vs 8.5%; dizziness 13.0% vs 4.2%; nausea 11.6% vs 4.2%; headache 10.1% vs 14.1%; and arthralgia 10.1% vs 2.8%.

Conclusion: Although, primary or secondary endpoints were not met in the study, subgroup analysis of patients with muscle weakness and without muscle weakness, showed improvement in muscle strength and rash, respectively in lenabasum 20 mg BID group vs placebo. Lenabasum was administered safely and was well-tolerated in this study.

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OP0163

A MATRIX PREDICTION MODEL FOR THE SIX-MONTH MORTALITY RISK IN PATIENTS WITH ANTI-MELANOMA DIFFERENTIATION-ASSOCIATED PROTEIN-5 POSITIVE DERMATOMYOSITIS

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Background: Recently, the autoantibody recognizing melanoma differentiation-associated gene 5 (anti-MDA5) is of the greatest concern as a specific autoantibody of dermatomyositis (DM), since it delineates a unique clinical phenotype of DM with a high risk of life-threatening lung complications. Considering routine clinical characteristics at baseline are still desired candidates for

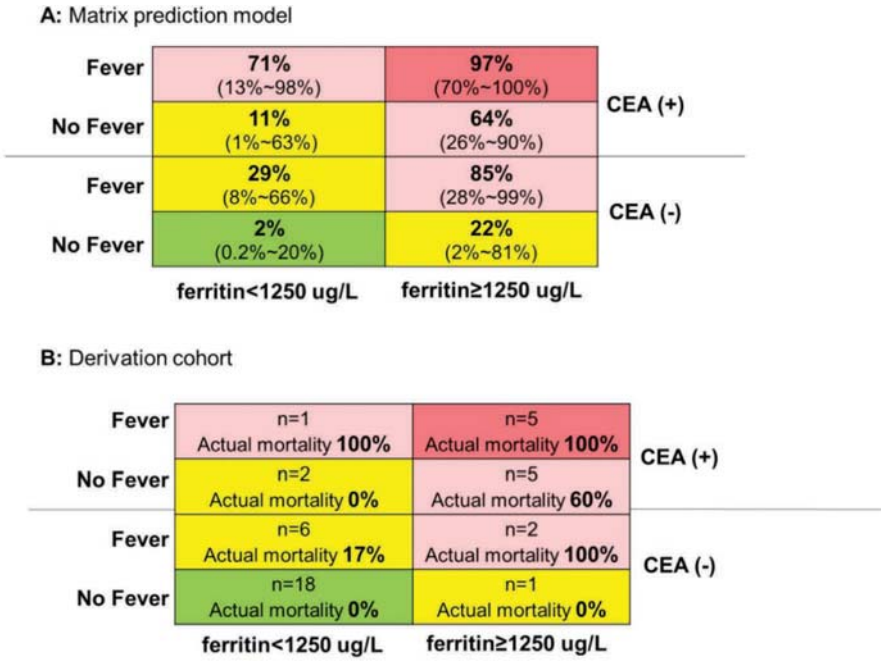

Figure 1 Matrix prediction model for 6-month all-cause mortality in anti-MDA5-positive DM patients.

A: Fever yes or no, CEA positive or negative, and ferritin<1250 ug/L or ≥1250 ug/L were combined to generate a matrix and then the relative mortality risk probability of death within six months in each grid was calculated. The 95% confidence intervals of the probabilities were shown in the parentheses. The anti-MDA5-positive IIM patients could be stratified into three subpopulations: high-risk (in red, the predicted mortality >50%; dark red indicated extremely high-risk), moderate risk (in yellow, the predicted mortality between 49%~10%), and low-risk (in green, the predicted mortality <10%). CEA, carcinoembryonic antigen. B: The actual mortality in each grid.

screening potential mortality predictors, in order to as early as possible stratify the mortality risk in anti-MDA5 positive DM patients before making therapeutic strategies.

Objectives: To investigate the baseline independent risk factors for predicting 6-month mortality of anti-MDA5-positive DM patients and develop a matrix prediction model formed by these risk factors.

Methods: This was a real-world prospective observational study. The hospitalized patients with DM were included if they fulfilled the criteria including: aged over 18 years old; diagnosed as having DM according to the criteria proposed by Bohan and Peter or the modified Sontheimer definitions; and positive anti-MDA5 which was determined by both line immunoassay testing and enzyme-linked immunosorbent testing. The primary outcome was all-cause 6-month mortality after enrolment. A matrix prediction model was built with the mortality risk probability.

Results: There were 82 DM patients enrolled (mean age of onset 50±11 years and 63% female), with 40 (49%) showing positive anti-MDA5. Gottron sign/papules (OR: 5.135, 95%CI: 1.489~17.708), arthritis (OR: 5.184, 95%CI: 1.455~18.467), interstitial lung disease (ILD, OR: 7.034, 95%CI: 1.157~42.785), and higher level of C4 (OR: 1.010, 95%CI: 1.002~1.017) were independent associators with positive anti-MDA5 in DM patients. Anti-MDA5-positive DM patients had significant higher 6-month all-cause mortality than those with anti-MDA5-negative (30% vs. 0%). Among anti-MDA5-positive DM patients, compared to the survivors, non-survivors had significantly advanced age of onset (59±6 years vs. 46±9 years), higher rates of fever (75% vs. 18%), positive carcinoma embryonic antigen (CEA, 75% vs. 14%), higher level of ferritin (median 2858 ug/L vs. 619 ug/L, all p<0.05). Multivariate COX regression showed ferritin≥1250 μg/L (HR: 10.4, 95%CI: 1.8~59.9), fever (HR: 11.2, 95%CI: 2.5~49.9), and positive CEA (HR: 5.2, 95%CI: 1.0~25.7) were independent risk factors of 6-month mortality.

According to the matrix prediction model, anti-MDA5-positive DM patients could be stratified into three subgroups based on various probabilities of predicted mortality: (i) High-risk: eight patients with two of the above three features (including fever, serum ferritin≥1250 μg/L, and positive CEA) had high predicted mortality probability with 64%~85% (three red grids in Figure 1A), and the actual mortality was 75% (n=6) with 60%, 100%, and 100% respectively in three red grids (Figure 1B). Five patients with all of three features had extremely high predicted mortality probability with 97% (95%CI: 70%~100%, the dark red grid of Figure 1A), and the actual mortality was 100% in Figure 1B; (ii) Moderate-risk: nine patients with one of the above three features had moderate predicted mortality probability with 11%~29% (three yellow grids in Figure 1A), and the actual mortality was 11% (n=1) with 0%, 0%, and 17% respectively in three yellow grids (Figure 1B); (iii) Low-risk: eighteen patients with none of the above three features had low predicted mortality probability with 2% (95%CI: 0.2%~20%, the green grid in Figure 1A), and the actual mortality was 0% in the green grid (Figure 1B).

Conclusion: Baseline characteristics of fever, positive CEA, and ferritin≥1250 μg/L are risk factors for 6-month all-cause mortality in anti-MDA5-positive DM patients. A novel matrix prediction model composed of these three clinical indicators is firstly proposed to provide a chance for exploration of individual treatment strategies in anti-MDA5-positive DM subgroups with various probabilities of mortality risk.

Disclosure of Interests: None declared

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Translational and Clinical Research in Crystal Arthritis

OP0164

A POPULATION-BASED, PROSPECTIVE METABOLOMICS STUDY IN THE UK BIOBANK IDENTIFIES GLYCOPROTEIN ACETYLS AS A NOVEL BIOMARKER OF INCIDENT GOUT

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Background: Serum urate (SU) level is the strongest known causal predictor of clinical gout, but only ~20% with prolonged hyperuricemia develop gout, motivating the need for additional biomarkers for risk prediction and stratification. The metabolome represents a compelling intermediate trait between genome and phenome to elucidate disease mechanisms. Multiple cross-sectional studies of *prevalent* gout from men in Asia have been conducted, but *no prospective data for incident gout* (prediagnostic metabolome) are available.

Objectives: Our objectives were to (1) conduct a discovery-based metabolome-wide study to *identify novel* biomarkers of incident gout; and (2) replicate novel metabolomic biomarkers of gout in independent samples.

Methods: We conducted a prospective cohort analysis of 105,703 UK Biobank (UKB) participants (46% males, mean age 57.2 years) with targeted NMR metabolomic profiling (N=168 metabolites, including routine lipids and amino acids) available from baseline samples (2006-10), and no prior diagnosis of gout or urate lowering therapy use. Incident cases of gout were documented from linked medical records until gout diagnosis, death, or end of study period (Dec 31/19). We used Cox proportional hazard models to obtain hazard ratios (HR) and 95% confidence intervals (CIs) per standard deviation (SD) increase in each of the 168 metabolites to determine associations with incident gout.

To replicate our findings, we assessed association of metabolome-wide significant metabolites in a replication set, restricted to 4,804 **non-overlapping** participants who provided blood in the repeat assessment visit (2012-13).

Results: During a median 10.4 years follow-up, we documented 1,367 cases of incident gout in the discovery set. After correction for multiple comparisons, glycoprotein acetyls (GlycA) were positively associated with risk of incident gout (multivariable HR per 1SD increase = 1.34 (1.27 to 1.41), P = 9.04×10^{-28}) after adjusting for age, sex, and lifestyle and clinical covariates (Table 1). This association persisted even after SU adjustment (HR 1.07, P = 0.0091). In the replication set, among 4,804 participants followed for a median of 6.8 years, we documented 22 cases. In this dataset, we replicated GlycA association with incident gout (multivariable HR per 1SD increase =1.56 (1.08 to 2.25), P = 0.017).

Conclusion: In this large-scale, prospective metabolomics study, we identified and independently replicated our findings that plasma levels of GlycA are associated with incident gout in UKB participants. GlycA is novel for gout, though this pro-inflammatory biomarker has predicted risk of other cardiometabolic-inflammatory phenotypes, independent of CRP.[1] These findings may provide insight into the metabolic-inflammatory pathogenesis of gout, with implications for risk prediction, even beyond SU, but call for further investigation with more extensive metabolome profiling and external replication.

Table 1. Association of glycoprotein acetyls (GlycA) with risk of incident gout in the UK Biobank

Model	Univariable HR, (95% CI)	*P*	Multivariable HR, (95% CI)	*P*
Discovery (N= 105,703)				
Per Standard deviation:				
GlycA, per SD	1.48 (1.41 to 1.60)	3.7×10^{-59}	1.34 (1.27 to 1.41)	9.04×10^{-28}
Categorized as quintiles:				
GlycA, **Q1**	1.0 Ref		1.0 Ref	
GlycA, **Q2**	1.43 (1.13 – 1.80)	0.002	1.30 (1.03 – 1.64)	0.0252
GlycA, **Q3**	2.06 (1.66 – 2.56)	4.88×10^{-11}	1.73 (139 – 2.15)	7.64×10^{-07}
GlycA, **Q4**	2.53 (2.05 – 3.12)	4.15×10^{-18}	1.98 (1.60 – 2.45)	3.96×10^{-10}
GlycA, **Q5**	3.70 (3.02 – 4.52)	3.21×10^{-37}	2.63 (2.12 – 3.23)	2.01×10^{-19}
Replication (N= 4804)				
Per Standard deviation:				
GlycA, per SD	1.65 (1.19 to 2.29)	0.0027	1.56 (1.08 to 2.25)	0.0172

[1] Hazard ratios (HR) and 95% confidence intervals (CIs) obtained after adjusting for the first 4 genomic principal components (controlling for population stratification), age, sex, fasting (<4 hrs, 4-8 hrs and ≥8 hrs), smoking (never, former, current), freq of alcohol, BMI, diabetes (yes/no) and hypertension at baseline (yes/ no).

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OP0165

JAK3-STAT5 SIGNALING PATHWAY IS INVOLVED IN THE PATHOGENESIS OF GOUTY INFLAMMATION

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Background: Studies have confirmed that JAKs-STATs signaling pathway is involved in the pathogenesis of a variety of autoinflammatory diseases, and has been transformed into the treatment of rheumatic diseases. So far, the research of JAKs-STATs in the mechanism of gout is very limited.
Objectives: To determine whether JAKs-STATs pathway is involved in the pathogenesis of gouty inflammation.
Methods: 1.The transcription and protein phosphorylation levels of 4 JAKs (JAK1, JAK2, JAK3 and Tyk2) and 7 STATs (STAT1, stat2, STAT3, STAT4, STAT5a/5b and STAT6) in PBMCs of 100 gout patients (concluding acute gout (AG) and intermittent gout (IG) patients 50 cases, respectively) and 50 healthy subjects (HC) were measured; 2.To detect the changes of JAK3-STAT5 signal pathway in synovium of rat ankle model of gouty inflammation;3.To explore the changes of JAK3-STAT5 signal pathway in synovium of gouty inflammation model after colchicine treatment.
Results: 1.The phosphorylation levels of JAK3 and STAT5 in PBMCs,the plasma IL-2 level in the AG group were all significantly higher than those in the HC group (P<0.05, respectively; Figure 1G,H), while there were no differences with respect to the other JAKs and STATs molecules between the two groups (P>0.05, respectively); 2.JAK3 and STAT5 phosphorylation levels in synovial tissue of rat ankle, cytokine IL-1β and IL-2 productions in synovial fluid of rat ankle from gout model were all significantly increased (P<0.05, respectively;Figure 1A-F);3.Phosphorylation levels of JAK3 and STAT5,IL-1β and IL-2 levels were significantly reduced after colchicine treatment (P<0.05, respectively;Figure 1A-F)

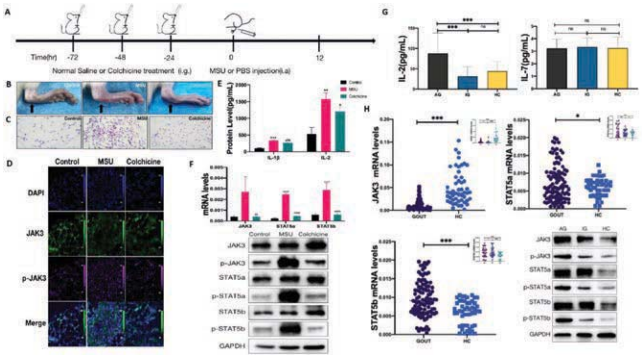

Figure 1. JAK3-STAT5 participates in the pathogenesis of gouty inflammation. In vivo experimental protocol (A-F): A. Male Wistar rats were used. The model Colchicine group was intragastrically administered with 0.104 mg/kg/d colchicine solution, and the Control group was intragastrically administered with the same amount of saline. After 3 days of continuous intragastric administration, the right ankle joint was injected with MSU (8 mg/100μl) or PBS (100 μl) to establish a gout arthritis model(MSU group) or Control group. B. Representative photographs of ankles 12 hr after MSU or PBS injection. C. Representative microscopic photos of ankle tissue sections from Control, MSU and Colchicine groups. D. Representative confocal laser scanning images showed JAK3 protein and its phosphorylated protein staining in ankle tissues in the three groups. Areas staining positive for JAK3 protein are shown in green. Regions staining positive for p-JAK3 protein are shown in red. E. IL-1β and IL-2 production in ankle flushing was detected by ELISA.*P <.05,**P<.01,***P<.001, significantly different from Control group; #P<.05,##P<.01, ###P< .001,significantly different from MSU group. F. At 12 h after MSU injection, JAK3 and STAT5 mRNA, protein in ankle tissues were determined by qRT-PCR and Western blotting, respectively. The panel displays the representative images of JAK3, STAT5, p-JAK3, p-STAT5a and GAPDH protein expression from the three groups.*P <.05,**P<.01,***P<.001, significantly different from Control group; #P<.05,##P<.01, ###P< .001, significantly different from MSU group. G.IL-2 and IL-7 levels in plasma of acute gout(AG), intermittent gout(IG) patients and healthy individuals (HC) were detected using ELISA. *P<.05, **P<.01, ***P < .001. H. JAK3 and STAT5 mRNA, protein levels in PBMCs of AG, IG, and HC groups were measured by qRT-PCR and Western blotting, respectively. *P<.05, **P<.01, ***P < .001.

Conclusion: IL-2-JAK3-STAT5 signaling pathway is involved in the regulation of gouty inflammation. Colchicine could treat gouty inflammation through inhibiting IL-2-JAK3-STAT5 pathway; JAK3 is expected to be a therapeutic target for acute gouty inflammation.
Disclosure of Interests: None declared
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OP0166

CHRONIC KIDNEY DISEASE AND AMPLIFICATION OF SERUM URATE IMPACT ON GOUT RISK: POPULATION-BASED STUDY OF > 450,000 UK BIOBANK PARTICIPANTS

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Background: Serum urate (SU) is a necessary causal factor for development of gout, while chronic kidney disease (CKD) is associated with increased inflammatory biomarkers, cytokines, and reduced AMPK activity levels. Furthermore, CKD has been found to be associated with an increased risk of incident gout, even beyond (i.e., independent of) SU levels. As such, the impact of SU may be enhanced by presence of CKD, but this hypothesis has not been evaluated.
Objectives: To prospectively examine whether CKD modifies the relation between SU levels and risk of incident gout.
Methods: We conducted a prospective cohort analysis of UK Biobank participants with urate and creatinine levels available from baseline blood samples (2006-2010), and no prior diagnosis of gout or urate lowering therapy use. CKD Stage ≥ 3 status (eGFR <60 mL/min) was determined from latest CKD-Epi equations (*NEJM* 2021; *JASN* 2021).[1,2] Incident cases of gout were ascertained from linked hospitalisation, primary care, and death records. Participants were

Table 1. Cumulative incidence and hazard ratio (HR) of incident gout according to baseline serum urate levels and CKD status

CKD Stage ≥ 3								**Hyperuricemia (Dichotomous)**	
Serum urate, mg/dL	**<5**	**5.0 to < 6.0**	**6.0 to < 7.0**	**7.0 to < 8.0**	**8.0 to < 9.0**	**9.0 to < 10.0**	**≥10**	**<7.0**	**≥7.0**
N cases	6	15	28	95	150	104	87	49	436
10-Year Cumulative Incidence	0.6%	1.1%	1.7%	7.6%	19.1%	28.0%	42.0%	1.2%	16.6%
Incidence Rate Ratio	1.0 (Ref)	1.7	2.7	12.3	33.8	56.1	107.7	1.0 (Ref)	15.2
No CKD									
Serum urate, mg/dL	**<5**	**5.0 to < 6.0**	**6.0 to < 7.0**	**7.0 to < 8.0**	**8.0 to < 9.0**	**9.0 to < 10.0**	**≥10**	**<7.0**	**≥7.0**
N cases	393	446	1056	1769	1251	363	84	1,895	3,467
10-Year Cumulative Incidence,	0.2%	0.4%	1.4%	6.0%	15.6%	23.5%	27.5%	0.5%	8.8%
Incidence Rate Ratio	1.0 (Ref)	2.1	8.0	34.6	96.9	155.9	198.8	1.0 (Ref)	20.2
Joint Effect of Serum Urate and CKD									
Serum urate, mg/dL	**<5**	**5.0 to < 6.0**	**6.0 to < 7.0**	**7.0 to < 8.0**	**8.0 to < 9.0**	**9.0 to < 10.0**	**≥10**	**<7.0**	**≥7.0**
Age-, Sex-, and Race- Adjusted HR									
No CKD	1.0 (Ref)	1.9	7.0	29.8	83.0	133.3	170.3	1.0 (Ref)	15.7
CKD	3.2	5.1	7.8	34.1	93.3	155.9	302.3	2.5	30.5
Fully adjusted HR*									
No CKD	1.0 (Ref)	1.8	6.4	25.8	69.4	108.7	132.9	1.0 (Ref)	12.5
CKD	3.1	4.7	6.8	28.9	75.2	121.1	241.8	2.3	22.4

*Adjusted for age, sex, race, body mass index, hypertension, diuretic use, smoking, and consumption of alcohol, coffee, meat, fish, poultry, and milk.

followed from baseline up to 10 years or until gout diagnosis, death, or end of study period (Dec 31/19).
We calculated 10-year cumulative incidence of gout according to baseline SU category and CKD status and evaluated their individual and joint impact on gout risk using multivariable Cox proportional hazards models.
We further assessed for additive and multiplicative interactions[3] between levels of SU and inverted eGFR, on a standardized continuous scale per SD.
Results: We included 458,244 individuals (45% male, mean age 56.5 years), of whom 6,559 had CKD at baseline, and documented 5,847 cases of incident gout over 4,442,866 person-years.
10-year cumulative incidence of gout ranged from 0.2% (baseline SU < 5 mg/dL) to 33% (baseline SU ≥ 10 mg/dL), and in each category incidence was higher for those with CKD than without (Table 1; Figure 1**-left**), Multivariable hazard ratio (HR) for the joint effect of CKD and highest SU level (≥ 10 mg/dL), compared to non-CKD and lowest SU (<5mg/dL), was 242 (95% CI: 189 to 309) (Figure 1**-right**).
There was a significant additive interaction between continuous SU and eGFR (relative excess risk due to interaction=0.16 [0.09 to 0.24], p < 0.001), with HRs of 3.7 (3.6 to 3.8) per SD increase of SU, 1.2 (1.2 to 1.3) per SD increase of inverted eGFR, and 4.1 (3.9 to 4.2) for their joint effect. Their multiplicative interaction was also significant (p < 0.001).
Conclusion: These large prospective cohort data suggest CKD presence enhances the effect of elevated SU levels on risk of incident gout. They support roles of CKD-associated factors beyond SU in developing gout, such as reduced AMPK activity levels and altered inflammatory factors in CKD, which warrant further investigation.
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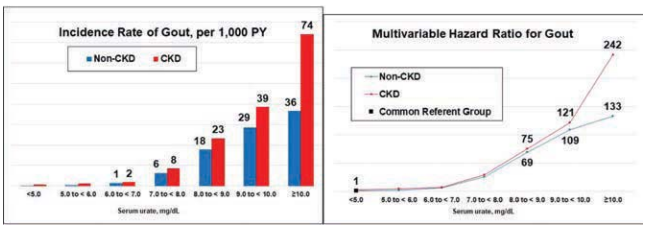
[3] *ARD* (2021) PMID 34857519

Figure: 10-year incidence rate (left) and multivariable hazard ratio (right) for incident gout, according to serum urate level and CKD status.



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OP0167 ULTRASONOGRAPHY IN THE PREDICTION OF GOUT FLARES: A 12-MONTH PROSPECTIVE OBSERVATIONAL STUDY

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Background: Gout flares are a distinctive feature of gout. Although imaging techniques, such as ultrasonography (US), can visualise monosodium urate (MSU) crystals and synovial inflammation and estimate their burden, the role of imaging in predicting gout flares has not been fully investigated.
Objectives: To evaluate whether US findings indicative of MSU deposits and subclinical inflammation predict gout flares over 12 months.
Methods: Participants with gout on urate-lowering therapy (ULT) for at least the preceding six months were enrolled consecutively in this 12-month prospective, observational, single-centre study.
A nested case-control analysis was performed. Cases were participants with at least one gout flare in the follow-up period while controls did not self-report any gout flares. Clinical assessment was scheduled at 6-month intervals. In addition, at baseline, each patient underwent an US examination using a standardised scanning protocol including the following sites: knees, ankles, 1st metatarsophalangeal joints, elbows, wrists and 2nd metacarpophalangeal joints. The US findings indicating MSU deposits [i.e., aggregates, double contour (DC) sign and tophi] and inflammation [i.e., Power Doppler (PD) signal] were identified according to the 2015 Outcome Measure in Rheumatology definitions (Figure 1).

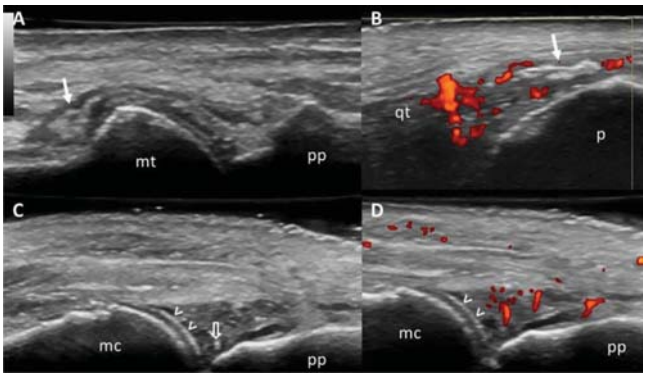

Figure 1.

Summated scores were calculated for each US finding.
During follow-up visits, patients were asked to report any gout flares using an internationally-validated definition [1].
Multivariate logistic regression analysis was used to measure the association between baseline US findings and the occurrence of gout flares over 12 months. US scores were tested separately, including the following covariates: age, gender, disease duration, presence of subcutaneous tophi, current serum urate>360 µmol/l, increasing dose of ULT during the study period and ongoing flare prophylaxis. In addition, multivariate zero-inflated Poisson regression analysis was used to investigate the association between US findings and the number of flares over 12 months.
Results: Eighty-one gout participants were enrolled, and 71 completed the study. Thirty (42.3%) of 71 participants experienced at least one flare over 12 months, with a median of 2.0 flares. There was no difference among baseline clinical and laboratory characteristics of patients with and without flares except for the presence of subcutaneous tophi (23.3% vs 4.9%; p=0.02) and higher current SU levels (360.8 vs 301.4 µmol/l mol/L, p=0.01).
Participants with flares had a greater baseline US burden of MSU deposits (2.0±1.8 vs 0.5±0.9, p=0.01 for DC sign; 2.1±2.3 vs 0.8±1.0, p=0.01 for tophi; 2.6±2.0 vs 1.6±1.6, p=0.03 for aggregates) and of subclinical inflammation (3.73±3.53 vs 0.82±1.44, p<0.01).
The baseline extent of MSU deposits and subclinical inflammation estimated by US was significantly associated with gout flares over 12 months in multivariate logistic regression analyses. DC sign score (aOR: 2.20, 95%CI: 1.22-4.34; p=0.01), tophi score (aOR: 2.16, 95%CI: 1.12-4.18; p=0.02) and PD score (aOR: 1.63, 95%CI: 1.12-2.40; p=0.01) predicted gout flares, whereas aggregates score (aOR: 1.40, 95%CI: 0.94-2.10; p=0.10) did not reach the statistical significance. Similar results were obtained in multivariate Poisson regression models (aIRR for DC score: 1.39, 95%CI: 1.18-1.64, p<0.01, aIRR for tophi score: 1.30, 95%CI: 1.17-1.45, p<0.01, aIRR for PD score: 1.29, 95%CI: 1.19-1.40, p<0.01, aIRR for aggregates score: 1.13, 95%CI: 1.00-1.29, p=0.05).
Conclusion: Baseline US findings indicating MSU deposits and subclinical inflammation are independent predictors of gout flares over 12 months.
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Disclosure of Interests: None declared
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OP0168 DEVELOPMENT OF AN ULTRASOUND SCORING SYSTEM FOR CPPD EXTENT: RESULTS FROM A DELPHI PROCESS AND WEB-RELIABILITY EXERCISE BY THE OMERACT US WORKING GROUP

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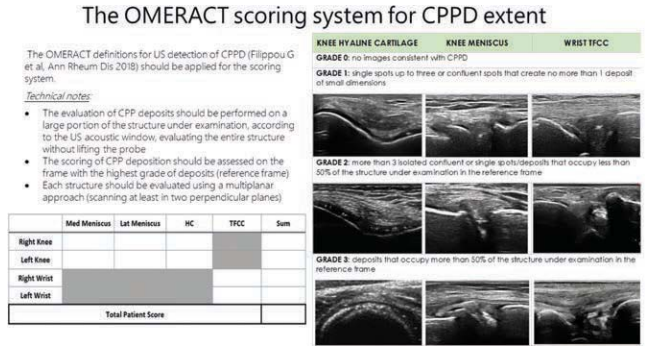
Background: Ultrasound (US) has proven to be an excellent imaging technique for detecting calcium pyrophosphate (CPP) deposition disease (CPPD); it is also widely available and inexpensive and can be performed during the clinic visit making it the preferred imaging modality for many rheumatologists. However, no validated grading systems have yet been developed allowing for a quantification of the extent of crystal deposition in CPPD.
Objectives: The aim of this study was to develop a scoring system for the quantification of CPP deposition at a patient level according to the OMERACT framework.
Methods: As part of the OMERACT methodology, we performed a systematic literature review (SLR) and meta-analysis aimed to estimate the prevalence of CPP deposition in peripheral joints by imaging, in order to identify relevant joints for CPPD monitoring. A preliminary survey was also circulated among the members of the OMERACT US – CPPD working group to collect their own suggestions according to their personal experience. Subsequently, a Delphi survey was prepared and circulated between members of the group, including statements that reflected both the results of the SLR and of the preliminary survey. In total, 32 statements were generated regarding the type of scoring for single structures, the sites to be included, the final scoring at patient level, and the scanning technique. Participants were asked to reply on a 5-point Likert scale (1, strongly disagree to 5, strongly agree) and agreement was achieved when 4 and 5 grades reached 75% or more of concordance. In case of disagreement, new statements were proposed according to the members' suggestions and circulated for voting in a subsequent round. After agreement of a scoring system, the validation process began. Two rounds of a web-based exercise on static images were conducted on 120 images representing equally all sites under investigation and all degrees of crystal deposition, to assess the intra- and inter-reader reliability of the new scoring system. Representative images of the scoring system were visible throughout the entire exercise in order to facilitate the scoring of the lesions.
Results: Three Delphi rounds were needed to reach agreement on all items. 32/41 members of the OMERACT US-CPPD working group replied in the first round, 26/32 in the second, and 25/26 in the third round. Twenty statements were approved in the first round, 3 in the second, and 3 in the third round. Only the knees (menisci and hyaline cartilage) and the triangular fibrocartilage of the wrist were included in the final score, using a four-grade system (0-3). It was decided that each anatomical structure should be scored separately and then also summed in order to define the joint score. The sum of the assessed joints was the total score at patient level. The final scoring system with the definitions and the relative technical notes is represented in Figure 1. 33/41 members participated to the reliability exercise. The inter-reader reliability of the scoring was substantial (kappa of 0.72), and the intra-reader reliability was almost perfect (kappa of 0.82).
Conclusion: This is the first study for developing a scoring system for the extent of CPP crystal deposition in patients with CPPD. The scoring system demonstrated to be reliable in static images. The next step of the validation process is to assess the reliability of the scoring system in a patient-based exercise. This study represents a fundamental step in the OMERACT process of validating US as an outcome measure instrument, and above proposed scoring system will hopefully provide a useful tool for clinical practice and research.



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OP0169 **INPATIENT DISCONTINUATION OF ALLOPURINOL – A QUALITATIVE IMPROVEMENT (QI) INITIATIVE**

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Background: Gout is a chronic inflammatory arthritis induced by hyperuricemia and manifested by recurrent acute flares of debilitating joint pain, when left untreated. Allopurinol is often used as long-term urate lowering therapy. Discontinuation of allopurinol leads to worsening flares, disability, poor quality of life, and frequent use of acute care facilities. Recent data revealed that 56% of hospitalized patients had allopurinol discontinued during an episode of acute gout flare, suggesting an unmet need for ongoing provider education (1). Gout flares are 14 times more likely to develop in patients who have allopurinol discontinued upon admission to the hospital (2).
Objectives: We performed a qualitative analysis of the current rate of discontinuation of allopurinol during hospitalizations at an academic hospital in order to develop a continuous improvement model.
Methods: We leveraged our electronic health records (EHR) to obtain data on gout patients admitted to the university hospital from 2019-2020, with IRB approval. Patients on allopurinol as an active home medication that was discontinued during hospitalization and/or after hospital discharge were included to calculate the rate of discontinuation. Lean thinking methodology with A3 process mapping for root cause analysis (RCA) was utilized. We first identified stakeholders involved in medication reconciliation – nurses and various providers, including trainees, and invited them to participate in an anonymous survey to understand the rationale behind allopurinol discontinuation during hospitalization. Next, we created countermeasures and actionable recommendations that could be implemented at an institutional level.
Results: A total of 2138 patients who were hospitalized had allopurinol listed as an active home medication. Of these, 364 (17%) did not receive allopurinol during hospitalization. Based on the survey data, providers chose to discontinue allopurinol due to the following factors – acute gout flare, renal impairment, gastrointestinal issues, cytopenia, drug interactions, NPO status, and always discontinued the medication. The RCA revealed layers of reasoning at various levels of the medication reconciliation process which impacted the decision-making algorithm. This in turn led to discontinuation during the admission and subsequent omission of allopurinol on the discharge medication list. Several actionable and high-impact recommendations emerged as countermeasures, including – a) pharmacy involvement at admission medication reconciliation, b) creation of a clinical practice guideline, and c) automated routing by EHR to standardized guidelines when allopurinol was discontinued on admission (Figure 1).

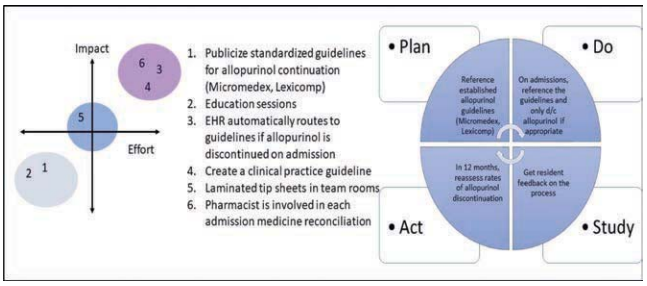

Figure 1. Countermeasures and Implementation Plan

Conclusion: There is evidence of inappropriate discontinuation of allopurinol that leads to gout flares in the outpatient setting and unnecessary resource utilization. We developed an implementation plan to mitigate this systematically at an institutional level. Testing these recommendations next to devise a standardized protocol as a continuous improvement strategy may help improve gout care and patient outcomes.

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OP0170

PHASE 2A, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF THE EFFICACY AND SAFETY OF A TRANSDERMAL ALKALINIZING AND PAIN-RELIEVING TREATMENT FOR REDUCING PAIN ASSOCIATED WITH AN ACUTE GOUT FLARE

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Background: Monosodium urate (MSU) deposition is pathognomonic for gouty arthropathy. MSU crystal formation and dissolution is affected by pH and theoretically, alkalinizing agents (eg, sodium bicarbonate, $NaHCO_3$) that raise the joint microenvironment pH, could facilitate MSU crystal dissolution[1] and decrease the pain of an acute gout flare. However, oral $NaHCO_3$ use is fraught with intolerable gastrointestinal side effects.

Objectives: To determine if $NaHCO_3$ in a patented transdermal formulation could effectively and safely reduce the pain of an acute gout flare.

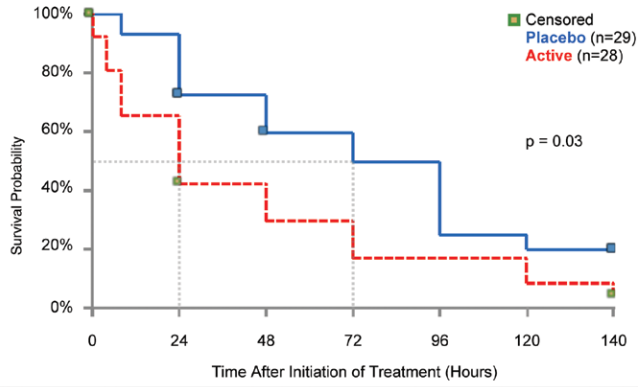
Methods: A Phase 2a prospective, double-blind, randomized, placebo-controlled study enrolled 418 subjects across 20 US sites. Patients with a diagnosis of gout using ACR/EULAR criteria (Score ≥ 8), ages 18-75, history of ≥ 2 gout flares in 12 months prior to randomization and on stable doses of urate lowering therapy were included. Exclusion criteria were BMI > 40kg/m^2, > 12 gout flares in the year prior to randomization, history of rheumatoid arthritis, psoriatic arthritis, evidence of septic arthritis, acute polyarticular gout (≥ 4 joints), and arthritis of any other cause. Patients were randomized to receive placebo lotion or transdermal $NaHCO_3$. Upon flare they initiated colchicine (1.2 mg followed by 0.6 mg 1 hour later) and applied study product to the limb of the affected joint. Outcome measures included pain-numeric rating scale (NRS, 0-10), time to resolution of pain (50% reduction), rescue medication use, joint tenderness, and physical function (PROMIS PF-20). Data were collected in patient diaries for the pain and PROMIS measures at several time points from baseline through Day 7, as were adverse events. Statistical analyses utilized ANCOVA (baseline pain as a covariate), Kaplan-Meier curves for homogeneity, and two-proportion z-test, all with α=0.05.

Results: 98 patients had a gout flare during the 14-month study period. Those in the active arm (ITT, N=48) had an overall responder rate of 94.5% vs. 79.3% (p=0.01) in the placebo arm (ITT, N=50) over the 7-day follow up. Rescue medication use was lower in the active arm vs. placebo (6.3% vs. 20.0%, p=0.02); and PROMIS PF-20 showed greater improvements over 7 days (22.2 vs. 16.7 points, p=0.05). The most common adverse event was hypertension (14.2%) with no significant difference between arms. Per protocol analyses were conducted to adjust for adherence on Day 1 for time to resolution of pain (Figure 1) and additional 24hr endpoints (Table 1).

Table 1. Key 24hr Endpoints (Per Protocol, n = 57)

	Active (n = 28)	Placebo (n = 29)	P value
Median time to resolution, hrs[1]	24	72	0.03
Change in 24hr PROMIS PF-20 score[2]	16.7	9.4	0.01
Physician-assessed moderate-to-severe joint tenderness 24hr[3]	28.0%	57.1%	0.02

[1]≥ 50% reduction in pain; K-M Est.; Subjects using rescue medication, discontinuing study drug, or missing pain scores censored [2]Consists of 20, 0-5-point questions; higher scores indicate better function [3]LIKERT: 0 (no pain), 1 (pain), 2 (wincing), 3 (wincing and withdrawal)



[1] Resolution is defined as at least a 50% reduction in pain; Kaplan-Meier Estimates; Subjects who use rescue pain medication, discontinue use of study drug, or otherwise have missing pain score data were censored at the date of the latest valid NRS pain score; Log-rank test for homogeneity between treatment K-M curves.

Figure 1. Time to resolution of pain[1] (per protocol population, n = 57)

Conclusion: Transdermal $NaHCO_3$ reduced the pain intensity and duration of an acute gout flare with higher overall response rates, faster time to resolution, improvements in physical function and a reduction in rescue medication use. The lack of adverse events makes this topical a promising therapeutic choice; especially during debilitating acute gout flares in patients with concomitant comorbidities.

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OP0171

A RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, MULTICENTER, STUDY OF METHOTREXATE COMBINED WITH PEGLOTICASE IN PATIENTS WITH UNCONTROLLED GOUT

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Background: Patients (pts) with gout refractory to oral urate-lowering therapy (ULT) have few treatment options. Pegloticase (pegylated uricase) lowers serum uric acid (sUA) in these pts,[1] but response rates are limited by anti-drug antibodies (ADAs), which decrease urate-lowering efficacy and increase infusion reaction (IR) risk.[2] Because methotrexate (MTX) is commonly used in RA

and prevents ADA development against biologics, co-administering MTX with pegloticase in uncontrolled gout pts is of interest. A small open-label study of pegloticase+oral MTX suggested an increased efficacy rate,[3] so a randomized controlled trial (RCT) was conducted to compare pegloticase with/without MTX immunomodulation.

Objectives: To determine safety/efficacy of oral MTX as co-therapy with pegloticase for sustained urate-lowering response in a randomized placebo (PBO) controlled trial.

Methods: Pegloticase+MTX and pegloticase+PBO co-therapy were compared in uncontrolled gout pts (sUA≥7 mg/dL, ULT failure/intolerance, and ≥1 of the following: ≥1 tophus, ≥2 flares in past yr, chronic gouty arthritis). Primary endpoint was the proportion of Month 6 treatment responders (sUA<6 mg/dL for ≥80% of the time during Wks 20-24). Key exclusion criteria included MTX contraindication, immunosuppressant use, G6PD deficiency, and renal impairment (eGFR<40 ml/min/1.73 m^2). Pts were randomized 2:1 to oral MTX (15 mg/wk) or PBO. Following a 4 wk MTX/PBO run-in, pegloticase was initiated (Day 1). Both pegloticase (biweekly 8 mg infusions) and MTX/PBO were administered over 52-wks (treatment period). Efficacy was examined in the intent-to-treat population (ITT, all randomized pts); safety (AEs, laboratory values) in the safety population (all pts receiving ≥1 dose blinded MTX/PBO). Treatment was discontinued if pre-infusion sUA >6 mg/dL for 2 consecutive visits Wk 2 or later.

Results: 152 pts (88.8% male) were randomized at 42 sites; 100 to pegloticase+MTX, 52 to pegloticase+PBO. 4 MTX, 3 PBO pts discontinued before first pegloticase dose; 26 MTX, 30 PBO pts who received pegloticase discontinued treatment at or before Wk 24. The primary endpoint was met with a 6-month response rate of 71.0% (71/100) vs 38.5% (20/52) in the MTX vs PBO co-therapy groups (p<0.0001; modified ITT [all pts receiving ≥1 pegloticase dose]: 74.0% [71/96] vs 40.8% [20/49], p<0.0001). In the first 24 wks of therapy, 81.3% vs 95.9% experienced ≥1 AE (Table 1), with gout flare in 66.7% (64/96) vs 69.4% (34/49) of MTX vs PBO pts. Infusion reactions (IRs) were more frequent in the PBO group (30.6%) than in the MTX group (3.1% plus anaphylaxis [NIAID/FAAN criteria] in 1 MTX pt). A single cardiovascular event of cardiac arrest occurred in 1 MTX pt >2 wks after pegloticase infusion 3 (deemed unrelated to study drug by site investigator). MTX-associated AEs[4] did not occur more frequently in the MTX group (Table 1).

Table 1. Key efficacy and safety findings through Month 6 of treatment.

	Pegloticase+MTX	Pegloticase+PBO
ITT population	N=100	N=52
Age, yrs, mean±SD	55.6±12.7	53.0±12.1
Tophi at baseline, %	74.0%	78.8%
sUA at baseline, mg/dL, mean±SD	8.7±1.6	9.1±1.7
6-mo treatment responders (primary endpoint), %	71.0%	38.5%
Safety population	N=96	N=49
≥1 Serious AE, %	8.3%	10.2%
≥1 treatment-emergent AE, %	81.3%	95.9%
Gout flare*	66.7%	69.4%
IR*, anaphylaxis*	3.1%, 1.0%	30.6%, 0%
Cardiac event*	1.0%	0%
Infection/infestation†	10.4%	16.3%
Gastrointestinal†	9.4%	16.3%
Skin†	7.3%	12.2%
Respiratory/thoracic†	5.2%	4.1%
Blood/lymphatic†	2.1%	2.0%
Renal/urinary†, hepatobiliary†	2.1%, 0%	2.0%, 2.0%

*AE of special interest, †known MTX AE

Conclusion: This RCT demonstrated significantly higher rate of sustained urate-lowering response over 6 months in pts co-treated with pegloticase+MTX vs pegloticase+PBO. No new safety concerns were seen through Month 6 and IR incidence was markedly lower in patients co-administered MTX vs PBO.

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Vaccination against SARS-CoV-2

OP0172

THE IMPACT OF IMMUNOMODULATING TREATMENT ON THE IMMUNOGENICITY OF COVID-19 VACCINES IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY RHEUMATIC DISEASES COMPARED TO HEALTHY CONTROLS. A SWEDISH NATIONWIDE STUDY (COVID19-REUMA)

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Background: Initial studies on the immunogenicity of COVID-19 vaccines in patients with immune-mediated inflammatory rheumatic diseases (IRD) reported diminished antibody response in general, and particularly when treated with rituximab or abatacept (1). Additional data are needed, especially for patients with IRD and immunomodulatory treatments.

Objectives: To elucidate the antibody response after two doses of COVID-19 vaccine in patients with IRD treated with biologic or targeted synthetic disease modifying anti-rheumatic drugs (b/ts DMARDs) as monotherapy or combined with conventional synthetic DMARDS (csDMARDs).

Methods: Antibodies against two antigens representing Spike full length protein and Spike S1 and a Nucleocapsid C-terminal fragment (used to confirm previously COVID-19 infection) were measured in serum obtained before and after the second vaccination using a multiplex bead-based serology assay (2). Patients with IRD receiving immunomodulating treatment, followed at a rheumatology department and healthy individuals (controls) were recruited from five Swedish regions. Antibody positivity was classified as the signal passing an antigen specific cutoff based on the mean intensity signal of 12 selected negative pre-pandemic controls plus 6SD for Spike/S1 and 12SD for Nucleocapsid-C. Good vaccine response was defined as having antibodies over cut-off level for both spike antigens. Percentage of responders in each treatment group was compared to controls (Chi2 test). Predictors of antibody response were determined using logistic regression analysis.

Results: In total, 414 patients (320 RA/JIA/psoriatic arthritis/axial spondylarthritis, 60 systemic vasculitis and 32 other IRD) and 61 controls participated. Patients receiving rituximab (n=145; 65% female; mean age 65years), abatacept (n=21; 77% female; mean age 66 years), IL6 inhibitors (n=77; 74% female; mean age 64years), JAK-inhibitors (n=58; 75% female, mean age 53years), TNF-inhibitors (n=68; 66% female; mean age 44years;), IL17 inhibitors (n=42; 54% female; mean age 44years) and controls (n=61; 74% female, mean age 49years) were studied. Patients receiving IL6 inhibitor (81.0%), abatacept (43.8%) or rituximab (33.8%) had a significantly lower antibody response rate compared to controls (98.4%), further pronounced if combined with csDMARD (p<0.001) (Figure 1). In the adjusted logistic regression analysis, higher age, rituximab, abatacept, concomitant csDMARD but not IL6 inhibitors, concomitant prednisolone, or a vasculitis diagnosis, remained significant predictors of antibody response (Table 1). All vaccines were well tolerated. 14 (3.4%) patients reported an increased activity in their IRD following vaccination.

Conclusion: In this nationwide study including IRD patients receiving b/ts DMARDs a decreased immunogenicity of COVID-19 vaccines was observed in patients receiving rituximab, abatacept and to some extent IL-6 inhibitors. Concomitant csDMARD gave further attenuation. Patients on rituximab and abatacept should be prioritized for booster doses of COVID19 vaccine.

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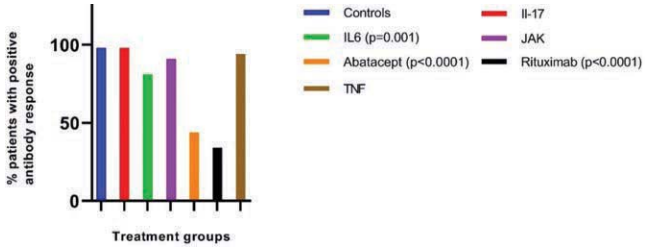
Table 1. Predictors of antibody response to COVID-19 vaccine

Rituximab	-1.799	<0.001	0.17	0.07-0.42
Abatacept	-1.971	0.001	0.14	0.04-0.45
IL6 inhibitor	0.023	0.965	1.02	0.36-2.94
Age (years)	-0.081	0.000	0.92	0.89-0.96
csDMARD	-1.127	0.002	0.32	0.16-0.66
Prednisolone (mg/day)	-0.064	0.206	0.94	0.85-1.04

Frequency (%) of individuals with good antibody response to COVID-19 vaccine



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OP0173

INCIDENCE OF COVID-19 INFECTION AND HOSPITALISATION ACCORDING TO VACCINATION STATUS AND DMARD TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE MATCHED COHORT STUDY FROM DENMARK

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Background: Patients with rheumatoid arthritis (RA) may have impaired immunogenicity to COVID-19 vaccines.

Objectives: To investigate the incidence of COVID-19 infection and hospitalisation in unvaccinated and vaccinated patients with RA compared with matched individuals; and secondarily in patients with RA according to DMARD treatment.

Methods: Danish nationwide matched cohort study from January to October 2021. Patients with RA were identified in DANBIO and matched 1:20 with individuals from the general population on age, sex, and vaccination status (month and exact type of vaccination). Primary and secondary outcomes were COVID-19 hospitalisation (Danish National Patient Register) and positive SARS-CoV2 PCR test (Danish COVID-19 Surveillance Register), respectively. Stratified by vaccination status, incidence rates (IRs) per 1000 person years (PY) and comorbidity-adjusted hazard ratios (aHRs) in cause-specific Cox models were calculated with 95% confidence intervals. Using the Aalen-Johansen estimator, the cumulative incidence of COVID-19 hospitalisations was visualised according to RA and vaccine exposure status.

Results: Regardless of vaccination status, patients with RA had increased incidence of COVID-19 hospitalisation compared to matched individuals (Table 1). However, the absolute risk was 0.20% for unvaccinated patients at 60 days and 0.08% for comparators, whereas it remained below 0.05% at 180 days of follow-up in both groups when fully vaccinated (Figure 1). Increased SARS-CoV2 infection rates were seen only among unvaccinated patients with RA (Table 1). Unadjusted analyses showed increased incidence of COVID-19 hospitalisation among rituximab-treated compared with conventional DMARD treated: unvaccinated HR 4.71 (1.98 to 11.18) and vaccinated HR 11.69 (2.07 to 66.06). However, the proportions of patients with previous cancer and treated with prednisolone were higher among the rituximab treated.

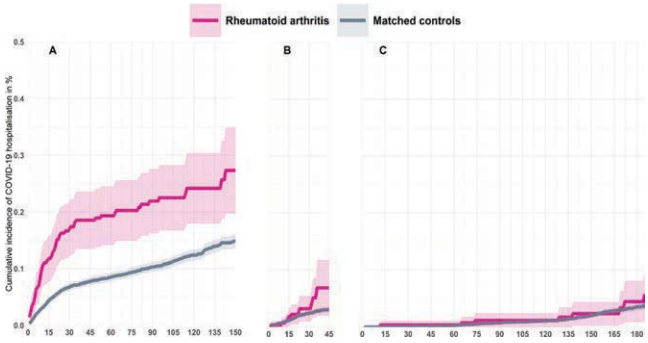

Figure 1. Cumulative incidence of COVID-19 hospitalisation (%) as a function of follow-up time (days) for (A) unvaccinated, (B) partially vaccinated and (C) fully vaccinated patients and comparators.

Conclusion: The incidence of COVID-19 hospitalisation was increased for both unvaccinated and vaccinated patients with RA compared with controls. Importantly, the parallel decreasing risk for patients with RA suggests a comparable

Table 1.

	Unvaccinated		Partially vaccinated		Fully vaccinated	
	RA	**Controls**	**RA**	**Controls**	**RA**	**Controls**
N	28 447	568 940	27 154	542 610	26 217	523 826
Women, %	71.3	71.3	71.2	71.2	71.0	71.0
Age in years, median [IQR]	67.7 [34.2 to 88.3]	67.8 [34.2 to 88.4]	68.4 [36.4 to 88.6]	68.4 (36.5 to 88.6)	68.9 [40.9 to 88.7]	68.9 (41.0 to 88.7)
Methotrexate /	55.5 /	0.5 /	55.4 /	1.2 /	55.7 /	1.3 /
Sulfasalazine /	14.2 /	0.1 /	13.7 /	0.3 /	13.5 /	0.3 /
Hydroxychloroquine /	10.4 /	0.1 /	10.3 /	0.0 /	10.3 /	0.0 /
Other csDMARD,	11.0 /	0.2 /	10.7 /	0.3 /	10.6 /	0.3 /
Prednisolone,all in %	12.5	2.0	12.2	0.5	12.2	0.5
TNFi /	16.9 /	0.1 /	17.2 /	2.9 /	17.1 /	3.1 /
abatacept /	1.5 /	0.0 /	1.5 /	0.5 /	1.5 /	0.5 /
tocilizumab /	3.0 /	0.0 /	3.0 /	0.0 /	2.9 /	0.0 /
rituximab, all in %	2.2	0.1	2.1	0.1	2.1	0.1
COVID-19 hospitalisation						
N	65	727	11	95	11	131
Median [IQR] days of follow-up	102 [62 to 137]	115 [88 to 146]	28 [22 to 35]	30 (21 to 39)	150 [111 to 189]	150 (111 to 189)
Rate per 1000 PY	10.4 (8.0 to 13.4)	4.7 (4.3 to 5.1)	5.5 (3.0 to 10.0)	2.2 (1.8 to 2.7)	0.9 (0.5 to 1.6)	0.5 (0.4 to 0.6)
Adjusted HR [a]	1.88 (1.44 to 2.46)	1 (Ref.)	2.47 (1.25 to 4.89)	1 (Ref.)	1.94 (1.03 to 3.66)	1 (Ref.)
SARS-CoV2 infection						
Rate per 1000 PY	37.8 (33.6 to 42.6)	33.9 (33.1 to 34.8)	27 (20.7 to 35.1)	28.5 (27 to 30.2)	11.3 (9.2 to 13.9)	10.4 (9.9 to 10.9)
Adjusted HR [a]	1.22 (1.09 to 1.57)	1 (Ref.)	0.87 (0.95 to 1.74)	1 (Ref.)	1.09 (0.92 to 1.14)	1 (Ref.)

IQR, Interquartile range. [a] Adjusted for cancer history, cardiovascular disease, diabetes mellitus, chronic kidney disease, and chronic lung disease.

relative benefit of vaccination. Less favourable outcomes among rituximab-treated warrant that this drug should be considered with extra care.

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OP0174 T-CELL RESPONSE AFTER COVID-19 VACCINE IS NOT IMPAIRED BY EARLY RITUXIMAB TREATMENT OR BELIMUMAB IN SYSTEMIC AUTOIMMUNE DISORDERS

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Background: Patients with autoimmune systemic diseases have an increased risk to contract infections and develop severe complications; infections in turn can reactivated and worsen the disease itself in a vicious circle. Thus, vaccination is the main weapon to prevent infectious diseases and represents an important and safe instrument of care for rheumatic patients that needs to be further promoted. However, the immunosuppressive drugs used to treat rheumatic diseases may impair response to vaccines, in particular those targeting B or T cells directly (1).

Objectives: The aim of this study is to evaluate the B and T-cell mediated immune response to mRNA vaccination in patients with systemic autoimmune diseases, such as vasculitis or systemic connective tissue diseases, early or continuously treated with B-cell targeting therapies, rituximab (RTX) or belimumab (BEL), by comparing with controls and each other. Secondary we evaluated the in vitro effective neutralizing capacity in belimumab-exposed patients.

Methods: Twenty-eight consecutive patients under treatment with rituximab (RTX, n=11) or belimumab (BEL, n=17) and 13 age/sex matched controls (non-rheumatic healthcare personnel) were enrolled in the study. Nobody presented anti-SARS-CoV2 antibodies related to previous viral contact and all were always negative at the molecular swab monthly control. All patients and controls received mRNA vaccines and were tested three to four weeks after complete vaccination. All RTX patients started vaccination within 5 months from the last infusion, and all but one of them were B-cell depleted. Anti-SARS-CoV-2 RBD total antibodies were analysed by a diagnostic assay (Elecsys, Roche) while T-cell response was evaluated using the IGRA test (Euroimmun). A subgroup of BEL-patients was tested with pseudovirus neutralization assay.

Results: Detectable anti-SARS-CoV2 RBD antibodies were documented in 1/11 RTX patients versus 16/17 BEL patients ($p<0.0001$). The median concentration was significantly lower than that observed in controls (39.6 AU/ml vs 1133 AU/ml, $p<0.0001$). A very low titer of anti-RBD antibodies were documented only in 1 out of 11 patients in the RTX subgroup (0.93 U/ml, positive if >0,79 U/ml) and the patient was the only one who showed an initial B-cell recovery (CD19+ B-cell 5 cells/microL). Anti-RBD antibodies were documented in 16 out 17 of patients in the BEL subgroup. The median anti-RBD antibody titer in patients receiving BEL was 243 [77.55-744.0] U/ml, and it was significantly lower compared to the controls ($p=0.002$).

The IGRA test was positive in 8/11 (72.7%) RTX patients vs 16/17 (94.1%) BEL patients ($p=0.7$), with interferon release comparable to control subjects ($p=0.2$).

Six patients with BEL were also stratified according to total antibodies (IgG+IgA+IgM) against-RBD into high responders (>800 AU/mL, n=3) and low responders (≤45 AU/mL, n=3) and tested with pseudovirus neutralization assay. Two thirds of low titer group of patients neutralized the Wuhan-Hu1 strain at medium-low titer (IC50 ≈102) but were almost ineffective in inhibiting the B.1.1.7 entry into target cells (IC50 =10). Regarding high responders, while two patients were able to inhibit both the strains at medium-high titer (approximately IC50 ≈103 for Wuhan-Hu1 and B.1.1.7), one patient neutralized only the WT strain.

Conclusion: B-cell targeting therapies do not preclude SARS-CoV-2 vaccination since a cellular immunity can raise even in the absence of circulating B cells. Most importantly, the immunogenicity of COVID-19 vaccination in SLE patients treated with belimumab is supported. However, patients showing the lowest humoral response to vaccine could remain at higher risk of infections, due to low neutralizing capacity.

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OP0175 TYPE OF MRNA COVID-19 VACCINE AND TREATMENT INFLUENCE ANTIBODY KINETICS IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: Patients on immunomodulatory treatments mount an attenuated immune response following mRNA COVID-19 vaccination, yet long-term studies of vaccine-induced anti-SARS-CoV-2 antibody (Ab) kinetics are missing.

Objectives: In this prospective observational study, we mapped the humoral antibody response to mRNA COVID-19 vaccines up to 24 weeks post full vaccination in patients with inflammatory rheumatic diseases (IRDs). We aimed to assess differences due to treatment, age, past SARS-CoV-2 infection, and vaccine (BNT162b2 vs. mRNA-1273).

Methods: Adult patients from the SCQM cohort who assented to an mRNA COVID-19 vaccine were recruited between 3/21 – 9/21. Participants answered questionnaires via an app and received kits for the self-collection of capillary blood samples at baseline, 4, 12, and 24 weeks post full vaccination. Samples were tested for IgG Ab against the S1 domain of the SARS-CoV-2 spike protein (anti-S1-IgG) using the EUROIMMUN ELISA. To examine differences in Ab titres arising from the defined parameters, while accounting for inter-assay variability, mixed effects continuous outcome logistic regression models were applied at each timepoint.

Results: Samples were obtained from 570 patients: 67% female, mean age 53 y (SD 12 y) with 37% RA, 36% axSpA, 21% PsA, and 6% UA (undifferentiated arthritis), on no medication (no DMARDs & no glucocorticoids; 15%), csDMARDs (10%), TNFi (48%), IL-1/6/17/23i (14%), JAKi (6%), rituximab (RTX; 4%), or abatacept (ABA; 2%) in mono/combination therapy at the first vaccination. 10% of patients had a past SARS-CoV-2 infection, 54% received BNT162b2, 46% mRNA-1273.

For any Ab threshold, the odds of having a higher Ab titre at 4, 12, and 24 weeks post full vaccination were 3.3 – 4 times higher with mRNA-1273 compared to BNT162b2 (Table 1, Figure 1). TNFi, JAKi, RTX, and ABA as monotherapy resulted in significantly lower Ab levels compared to no medication at almost all timepoints. In combination therapy, TNFi, IL-1/6/17/23i, RTX, and csDMARDs led to consistently lower Ab titres at all timepoints compared to respective monotherapy.

Table 1. The OR of being above a given Ab threshold, regardless of the threshold. Ref. levels: mean age, no medication, no past SARS-CoV-2 inf., BNT162b2. Included in model but not shown: diagnosis, infrequently used medication (all non-signif.)

	Weeks post full vacc.	4		12		24	
		OR (95% CI); p					
	Age	**0.96** (0.94 – 0.97)	****	**0.98** (0.96 – 0.996)	*	0.98 (0.97 – 1.00)	
	mRNA-1273 (vs BNT162b2)	**3.28** (2.34 – 4.61)	****	**3.96** (2.83 – 5.54)	****	**3.94** (2.93 – 5.50)	****
	Past COVID inf. (vs none)	**7.56** (4.32 – 13.2)	****	**8.14** (4.78 – 13.86)	****	**11.65** (6.62 – 20.50)	****
	csDMARD†	1.27 (0.67 – 2.41)		1.78 (0.94 – 3.35)		1.70 (0.86 – 3.36)	
	TNFi†	**0.46** (0.28 – 0.71)	****	**0.30** (0.19 – 0.48)	****	**0.13** (0.081 – 0.22)	****
	IL-1/6/17/23i†	0.97 (0.54 – 1.75)		1.04 (0.57 – 1.89)		0.89 (0.49 – 1.64)	
	JAKi†	**0.38** (0.16 – 0.91)	*	**0.38** (0.16 – 0.91)	*	0.53 (0.22 – 1.28)	
	RTX†	**0.078** (0.013 – 0.46)	**	**0.078** (0.015 – 0.42)	**	**0.16** (0.037 – 0.71)	*
	ABA†	**0.14** (0.039 – 0.51)	**	**0.087** (0.022 – 0.35)	***	**0.068** (0.017 – 0.27)	***
Interactions§	Age:vaccine‡	**1.04** (1.02 – 1.07)	**	1.02 (0.99 – 1.05)		**1.03** (1.0008 – 1.058)	*
	csDMARD:combi	**0.12** (0.02 – 0.70)	*	**0.17** (0.029 – 0.95)	*	**0.11** (0.023 – 0.56)	**
	TNFi:combi	**0.34** (0.20 – 0.59)	***	**0.37** (0.22 – 0.61)	***	**0.36** (0.21 – 0.62)	***
	IL-1/6/17/23i:combi	**0.26** (0.09 – 0.78)	*	**0.25** (0.085 – 0.70)	**	**0.20** (0.071 – 0.58)	**
	JAKi:combi	1.76 (0.33 – 9.44)		1.23 (0.32 – 4.70)		0.95 (0.25 – 3.65)	
	RTX:combi	**0.11** (0.01 – 0.87)	*	**0.095** (0.012 – 0.73)	*	**0.085** (0.0091 – 0.79)	*
	ABA:combi	1.75 (0.25 – 12.2)		0.74 (0.096 – 5.75)		0.51 (0.073 – 3.62)	

* p < 0.05; ** p < 0.01; *** p < 0.001; **** p < 0.0001; †Medication as monoth. vs no medication ‡Interaction terms showing how OR of mRNA-1273 (vs BNT162b2) increases with age §Interaction terms with medications: medication in combination th. vs medication as monoth.

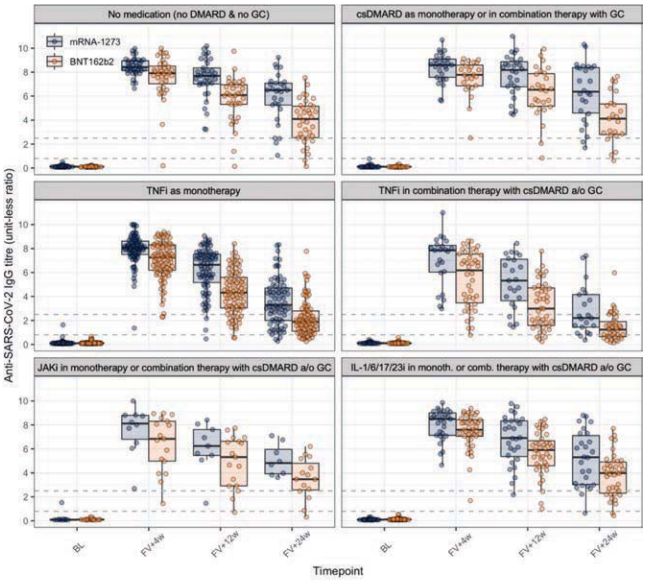

Figure 1. The variation with time of anti-S1 antibodies post mRNA COVID-19 vaccination in adult **SARS-CoV-2 naïve** IRD patients **as a function of medication** (in mono/combination therapy) **and vaccine**. Only medication groups corresponding to at least 10% of the study population are shown. Results are reported as a ratio (sample optical density/ calibrator optical density). The dashed lines indicate the thresholds below (0.8) and above (2.5) which the results are considered negative and positive for the presence of anti-SARS-CoV2 IgG, respectively; samples with results in the zone between the two thresholds were considered indeterminate and were further tested with recombinant immunofluorescence. GC = glucocorticoids; csDMARD = conventional synthetic disease-modifying antirheumatic drug; TNFi = tumour necrosis factor inhibitor; JAKi = janus kinase inhibitor; IL-1/6/17/23i = interleukin inhibitors. BL = baseline (sample taken on day before or on day of first vaccination, before vaccination), FV+4w/12w/24w = 4/12/24 weeks post full vaccination. Boxplot whiskers extend to 1.5*IQR.

Conclusion: Compared to no medication, some immunomodulatory therapies resulted in markedly lower Ab levels at all timepoints. In IRD patients, a past SARS-CoV-2 infection resulted in strikingly increased immunogenicity, as did mRNA-1273 compared to BNT162b2.

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OP0176

THE PERSISTENCE OF ANTI-SPIKE ANTIBODIES FOLLOWING TWO SARS-COV-2 VACCINES IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES USING IMMUNOSUPPRESSIVE THERAPY, COMPARED TO HEALTHY CONTROLS

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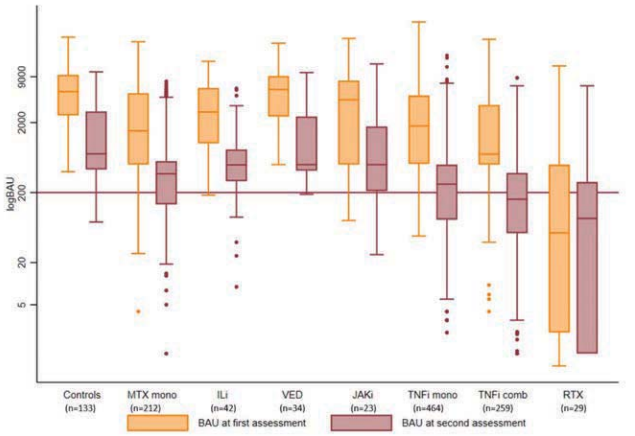
Background: Limited data is available regarding long-term effectiveness of SARS-CoV-2 vaccines in patients with immune-mediated inflammatory diseases (IMIDs) on immunosuppressive therapy. Whether the persistence of vaccine-induced humoral immunity against SARS-CoV-2 differs between this patient population and the general public is currently unknown.

Objectives: To compare the persistence of anti-Spike antibodies following two SARS-CoV-2 vaccine doses between IMID patients using immunosuppressive medication and healthy controls and identify predictors of antibody decline.
Methods: We included patients with inflammatory joint- and bowel diseases on immunosuppressive medication and healthy controls enrolled in the prospective observational Nor-vaC study. Serum samples were collected at two time points following two dose SARS-CoV-2 vaccination (first assessment within 6–48 days and second within 49–123 days). Sera were analysed for antibodies binding the receptor-binding domain (RBD) of the SARS-CoV-2 Spike protein. Anti-RBD <200 BAU /ml were defined as low levels. The estimated percent reduction in anti-RBD standardised to 30 days was calculated and factors associated with reduction were identified in multivariable regression models.
Results: A total of 1097 patients (400 rheumatoid arthritis, 189 psoriatic arthritis, 189 spondyloarthritis, 129 ulcerative colitis, 190 Crohn´s disease) (median age 54 years [IQR 43–64]; 56% women) and 133 controls (median age 45 years [IQR 35–56]; 83% women) provided blood samples within the defined intervals (median 19 days [IQR 15–24] and 97 days [86–105] after second vaccine dose). Antibody levels were significantly lower in patients compared to controls at both assessments, with median anti-RBD 1468 BAU/ml [IQR 500–5062] in patients and 5514 BAU/ml [2528–9580] in controls (p<0.0001) and 298 BAU/ml [IQR 79–500] in patients and 715 BAU/ml [28–2870] in controls (p<0.0001), at first and second assessment respectively. Figure 1 show antibody levels at both assessments after medication group. At the second assessment, anti-RBD antibody levels decreased below 200 BAU/ml in 452 (41%) patients and in 1 (0.8%) control (p<0.0001) (Table 1). The percentage change in anti-RBD levels were -86 % in patients and -77 % in controls (p<0.0001). The majority of patients using rituximab had low antibody levels at both assessments, Figure 1. In the multivariable regression analyses, patients had a greater decline in anti-RBD levels compared to controls β -3.7 (95% CI -6.0, -1.4) (p<0.001). Use of tumor necrosis factor inhibitors in mono- or combination therapy was associated with the greatest decline compared to controls, β -6.1 (95% CI -8.1, -4.1) and β -6.4 (-8.4, -4.2) respectively (p<0.001).
Conclusion: Within four months after the second vaccine dose, anti-Spike antibody levels declined considerably in both IMID patients and controls. Patients had lower antibody levels at the first assessment and a more pronounced decline compared to controls, and were consequently more likely to have low antibody levels four months after the second vaccine dose. Our results support that IMID patients lose humoral protection and need additional vaccine doses sooner than healthy individuals.

Figure 1. Level of anti-RBD antibodies at first and second assessment after medication group



MTX mono: methotrexate monotherapy; ILi: Interleukin inhibitors including tocilizumab, ustekinumab, iksekizumab, risankizumab, secukinumab; VED: vedolizumab; JAKi: janus kinase inhibitor; TNFi mono: Tumor necrosis factor inhibitor in monotherapy; TNFi comb: Tumor necrosis factor inhibitor in combination with metabolite inhibitor(s) or vedolizumab; RTX: rituximab. All groups include patients using prednisolone in doses <10mg/day in combination with other medication.
A cut-off at 200 BAU/ml is indicated.

Table 1. Serological response in patients and controls

	Controls (n=133)		Patients (n=1097)	
Anti-RBD antibodies (BAU/ml)	**1st assessment**	**2ndassessment**	**1st assessment**	**2ndassessment**
<5, n (%)	0	0	18 (1.6)	54 (5)
5-19, n (%)	0	0	4 (0.4)	60 (5)
20-199, n (%)	0	1 (1)	40 (4)	338 (31)
200-1999, n (%)	25 (19)	89 (67)	548 (50)	558 (51)
2000-8999, n (%)	71 (53)	40 (30)	398 (36)	82 (7.5)
≥ 9000, n (%)	37 (28)	3 (2)	89 (8)	5 (0.5)

1st assessment 6 - 48 days and 2nd assessment 49 -123 days after second vaccine dose.
BAU= Binding antibody Units

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OP0177

IMMUNOGENICITY INDUCED BY TWO AND THREE DOSES OF THE BNT162B2 MRNA VACCINE IN PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES AND IMMUNOCOMPETENT CONTROLS: A LONGITUDINAL MULTI-CENTER STUDY

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Background: Data on the kinetics of the immune response to SARS-CoV-2 vaccination in patients with autoimmune inflammatory rheumatic diseases (AIIRD) are limited.
Objectives: To evaluate the kinetics of the immune response induced by two and three doses of the BNT162b2 mRNA vaccine in adult patients with AIIRD and immunocompetent controls.
Methods: A prospective multicenter study investigated the antibody response to the BNT162b2 vaccine by serial measurement of serum anti-SARS-CoV-2

S1/S2 IgG titers at the following time points: 2-6 weeks (AIIRD n=720, controls n=122) and six months (AIIRD n=628, controls=116) after the second vaccine dose, and 2-6 weeks after the third vaccine dose (AIIRD n=169, controls n=45). A seropositive response was defined as a detectable anti-S1/S2 IgG titer ≥ 15 BAU/ml. T-cell immune response was evaluated in a sample of patients (n=28) and controls (n=9) by intracellular staining of S-stimulated $CD4^+$ T-cells for TNFα and IFNγ production.

Results: The two-dose vaccine regimen induced a higher humoral response in controls compared to patients, as reflected by the post-vaccination seropositivity rates of 100% vs 84.72%, p<0.0001, and 96.55% vs 74.26%, p<0.0001 at 2-to-6 weeks and at 6 months, respectively. The decline of S1/S2 IgG titers within six months was similar in controls and patients. Following the 3rd vaccine, the seropositivity rate increased to 80.47% and 100% in AIIRD and control groups, p=0.0028, with a significantly higher increase of S1/S2 IgG titers in controls compared with AIIRD patients, 284.09±76.58 vs 219.39±151.55 BAU/ml, p=0.0016. At all-time points, S1/S2 IgG titers were significantly lower in AIIRD patients compared with controls (Figure 1).

We further investigated the impact of therapies on the vaccine's immunogenicity (Figure 1). Glucocorticoids (GC) were associated with a significantly lower seropositivity rate and lower S1/S2 IgG titers compared to controls at all time points. Monotherapy with methotrexate (MTX) was associated with a comparable to controls humoral response at all time points. Anti-cytokine biologics (TNFi, IL6i, IL17i) were associated with an initial high seropositivity rate, similar to controls, followed by a steeper decline at 6 months, 79.82% vs 96.55%, p=0.0001, and restoration of seropositivity after the 3rd vaccine dose in all patients. JAKi were associated with a mildly decreased seropositivity rate after the 2nd vaccine dose and similar to controls response after the 3rd vaccine dose. Abatacept was associated with a reduced immunogenicity after the 2nd vaccine dose, but was restored to 100% seropositivity after the 3rd vaccine dose. Rituximab (RTX) significantly blunted the humoral response at all time points, with a seropositivity rate of 42% after the 2nd vaccine dose, 29% at 6 months, and with increase to 40% after the 3rd vaccine dose. A third of the RTX-treated patients who were seronegative after two vaccine doses, seroconverted after the 3rd dose. The multivariate model for predicting the seropositive response to vaccination found that higher S1/S2 IgG titers after the 2nd vaccine dose was associated with a higher seropositivity rate following the 3rd vaccine dose, OR 1.026 (1.008-1.045), p=0.0027, and that treatment with RTX was associated with a 14.3-fold risk for a negative humoral response, p≤0.0001. Cellular immune response, evaluated mainly in RTX treated patients, was preserved prior to and after the 3rd vaccine dose and was similar to controls.

Conclusion: Over a six-month period, the two dose BNTb262 vaccination was associated with a similar extent of waning of the humoral immune response in AIIRD patients and controls. The 3rd vaccine dose restored the response in all controls and in patients treated with MTX monotherapy, anti-cytokine biologics, abatacept, and JAKi. Treatment with GC and RTX was associated with an impaired humoral response at all time points.

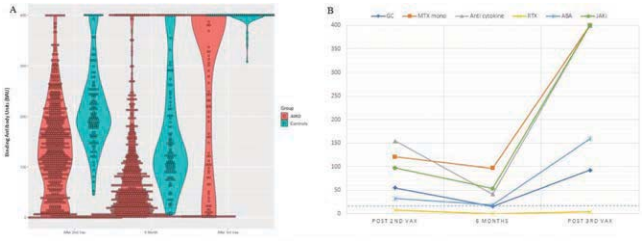

Figure. Kinetics of humoral response (S1/S2 IgG titer, BAU/mL) after two and three BNT162b2 vaccine doses. Panel A: AIIRD patients and controls. Panel B: AIIRD patients according to immunosuppressive treatment used.

BAU, binding antibody units; vax, vaccine dose; AIIRD, autoimmune inflammatory rheumatic disease; GC, glucocorticoids; MTX mono, monotherapy with methotrexate; anti cytokine includes tumor necrosis factor, interleukin 6 and interleukin 17 inhibitors, RTX, rituximab, ABA, abatacept, JAKi, janus kinase inhibitors.

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OP0178

COVID-19 BREAKTHROUGH INFECTIONS IN VACCINATED PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES AND CONTROLS – DATA FROM TWO PROSPECTIVE COHORT STUDIES

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Background: Concerns have been raised regarding risks of COVID-19 breakthrough infections in vaccinated patients with immune-mediated inflammatory diseases (IMIDs) treated with immunosuppressants, but data on COVID-19 breakthrough infections in these patients are still scarce.

Objectives: The primary objective was to compare the incidence and severity of COVID-19 breakthrough infections with the SARS-CoV-2 delta variant between fully vaccinated IMID patients with immunosuppressants, and controls (IMID patients without immunosuppressants and healthy controls). The secondary objective was to explore determinants of breakthrough infections.

Methods: In this study we pooled data collected from two large ongoing prospective multi-center cohort studies (Target to-B! [T2B!] study and ARC study). Clinical data were collected between February and December 2021, using digital questionnaires, standardized electronic case record forms and medical files. Post-vaccination serum samples were analyzed for anti-RBD antibodies (T2B! study only) and anti-nucleocapsid antibodies to identify asymptomatic breakthrough infections (ARC study only). Logistic regression analyses were used to assess associations with the incidence of breakthrough infections. Multivariable models were adjusted for age, sex, cardiovascular disease, chronic pulmonary disease, obesity and vaccine type.

Results: We included 3207 IMID patients with immunosuppressants and 1810 controls (985 IMID patients without immunosuppressants and 825 healthy controls). The incidence of COVID-19 breakthrough infections was comparable between patients with immunosuppressants (5%) and controls (5%). The absence of SARS-CoV-2 IgG antibodies after COVID-19 vaccination was independently associated with an increased incidence of breakthrough infections (P 0.044). The proportion of asymptomatic COVID-19 breakthrough cases that were additionally identified serologically in the ARC cohort was comparable between IMID patients with immunosuppressants and controls; 66 (10%) of 695 patients vs. 64 (10%) of 647 controls. Hospitalization was required in 8 (5%) of 149 IMID patients with immunosuppressants and 5 (6%) of 86 controls with a COVID-19 breakthrough infection. Hospitalized cases were generally older, and had more comorbidities compared with non-hospitalized cases (Table 1). Hospitalization rates were significantly higher among IMID patients treated with anti-CD20 therapy compared to IMID patients using any other immunosuppressant (3 [23%] of 13 patients vs. 5 [4%] of 128 patients, P 0.041; Table 1).

Table 1. Determinants of the severity of COVID-19 breakthrough infections.

	Ambulatory care (n = 222)		Hospitalized (n = 13)	
Group - no. (%)				
IMID patients with immunosuppressants	141	(64)	8	(62)
IMID patients without immunosuppressants	49	(22)	3	(23)
Healthy controls	32	(14)	2	(15)
Patient characteristics				
Age, years – mean (SD)	51	(14)	60	(11)
Female sex – no. (%)	143	(64)	4	(31)
Comorbidities – no. (%)				
Cardiovascular disease	17	(8)	5	(39)
Chronic pulmonary disease	17	(8)	4	(31)
Diabetes	15	(7)	3	(23)
Obesity	34	(15)	5	(39)
Immunosuppressants– no. (%)				
Methotrexate	36	(16)	2	(15)
TNF inhibitor	48	(22)	2	(15)
Anti-CD20 therapy	13	(6)	3	(23)
Mycophenolate mofetil	3	(1)	0	(0)
S1P modulator	5	(2)	0	(0)
Other immunosuppressants	70	(32)	3	(23)

Conclusion: The incidence of COVID-19 breakthrough infections in IMID patients with immunosuppressants was comparable to controls, and infections were mostly mild. Anti-CD20 therapy might increase patients' susceptibility to severe COVID-19 breakthrough infections, but traditional risk factors also continue to have a critical contribution to the disease course of COVID-19. Therefore, we argue that most patients with IMIDs should not necessarily be seen as a risk group for severe COVID-19, and that integrating other risk factors should become standard practice when discussing treatment options, COVID-19 vaccination, and adherence to infection prevention measures with patients.

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OP0179

CHARACTERISTICS AND OUTCOMES OF SARS-COV-2 BREAKTHROUGH INFECTIONS AMONG DOUBLE AND TRIPLE VACCINATED PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: SARS-CoV-2 vaccines offer the most effective way to reduce the risk of severe COVID-19. Recent data indicate sufficient immune response after vaccination in most patients with inflammatory rheumatic diseases (IRD) on immunomodulatory treatments.

Objectives: To investigate the clinical profile of SARS-CoV-2 breakthrough infections among double and triple vaccinated patients with IRD.

Methods: Data from the German COVID-19-IRD registry, collected by treating rheumatologists between February 2021 and January 2022 were analysed. Patients double or triple vaccinated against COVID-19 ≥14 days prior to proven SARS-CoV-2 infection were identified, and type of IRD, vaccine, immunomodulation, comorbidities and outcome of the infection were compared with 737 unvaccinated IRD-patients with COVID-19.

Results: In total, 271 cases of breakthrough infections were reported, 250 patients (91%) had received two doses of vaccines, 21 (9%) patients three. More than 70% of the patients received Pfizer/Biontech vaccine for the first, second and third vaccination. The median time from second/third vaccine dose to infection was 148 days (range 14-302) days. Most of the patients were diagnosed with inflammatory joint diseases (Table 1). Most of the patients were treated with methotrexate (Table 1). The use of Januskinase inhibitors(i) was more frequently reported in double vaccinated patients (10.4% vs 4.8%), whereas tumor necrosis (TNF)i were reported more often in triple vaccinated patients (33.3% vs. 22.8). Hospitalisation rate was higher in unvaccinated IRD-patients than in vaccinated ones, while fatality rate was similar in unvaccinated and double vaccinated patients. Although the rate of comorbidities and median age were higher in triple-vaccinated patients, infected patients showed a lower rate of hospitalisation, neither COVID-19 related complications, nor the need of oxygen treatment or death.

Conclusion: In this cohort of triple-vaccinated IRD patients no fatal courses and no COVID-19 related complications were reported, although median age and rate of comorbidities were higher compared to double-vaccinated and unvaccinated patients. These results support the general recommendations to reduce the risk of severe COVID-19 disease by administering three doses of vaccine, especially in patients with older age, presence of comorbidities, and on immunomodulatory treatment.

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Table 1. Profile of vaccinated IRD patients

	unvaccinated		2nd vaccination		3rd vaccination	
	Number (737)	%	Number (250)	%	Number (21)	%
Age	56 (18-93)		57 (22-90)		63 (35-88)	
Female	478	64.9	158	63.2	13	61.9
BMI	26.8 (17-53)		26.7 (17-55)		25.4 (18-41)	
Inflammatory rheumatic disease (multiple selections possible)						
Inflammatory joint diseases	561	75.9	186	74.4	16	76.2
Connective tissue diseases	101	12.8	30	12	2	9.6
Vasculitis	71	9.6	22	8.8	3	14.3
Other IRD	63	8.5	29	11.6	1	4.8
Immunomodulation (multiple selections possible)						
Glucocorticoid	212	28.8	67	26.8	5	23.8
Methotrexate	270	36.6	90	36	8	38.1
Azathioprine	19	2.6	7	2.8	/	/
Cyclosporine	3	0.4	1	0.4	/	/
Leflunomide	50	6.8	7	2.8	/	/
Hydroxychloroquine	79	10.7	23	9.2	1	4.8
Sulfasalazine	20	2.7	9	3.6	/	/
JAKi	54	7.3	26	10.4	1	4.8
TNFi	158	21.4	57	22.8	7	33.3
Abatacept	9	1.2	3	1.2	/	/
Rituximab	21	2.8	11	4.4	1	4.8
Other biologics	59	7.9	32	12.8	2	9.6
Mycophenolate	15	2	4	1.6	/	/
Immunoglobulines	2	0.3	1	0.4	/	/
Apremilast	4	0.5	/	/	/	/
Cyclophosphamide	1	0.1	1	0.4	/	/
No immunomodulation	74	10	22	8.8	1	4.8
No/low disease activity	625	84.8	223	89.2	18	85.7
Moderate/high disease activity	102	13.8	27	10.8	3	14.3
Comorbidities						
Cardiovascular diseases	329	44.6	130	52	13	61.9
Diabetes mellitus	76	10.3	25	10	/	/
Osteoporosis	43	5.8	21	8.4	2	9.5
Chronic renal failure	40	5.4	16	6.4	4	19
Cancer/history of cancer	15	2.0	10	4	3	14.3
COPD	25	3.4	10	4	/	/
ILD	16	2.2	7	2.8	/	/
Bronchial asthma	34	4.6	16	6.4	/	/
Pregnancy	7	0.9	1	0.4	1	4.8
No comorbidity	254	34.5	97	38.8	5	23.8
Complications due to COVID-19						
Hospitalisation	135	18.3	29	11.6	2	9.5
Oxygen treatment	114	15.5	24	9.6	/	/
Invasive ventilation	25	3.4	9	3.6	/	/
Death	16	2.2	7	2.8	/	/

Vessels glowing in the dark

OP0180

EFFECT OF AVACOPAN ON RELAPSE RATES AND RELAPSE-FREE TIME IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS, RESULTS OF THE PHASE 3 ADVOCATE STUDY

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Background: For patients with ANCA-associated vasculitis, both failure to achieve remission and relapse after achieving remission are associated with worse long-term outcomes. Avacopan, an oral selective inhibitor of the C5a receptor, is approved for the treatment of ANCA-associated vasculitis. The phase 3 ADVOCATE study tested daily avacopan as a substitute for a standard oral glucocorticoid taper regimen. At week 26, the avacopan group achieved a remission rate (72.3%) comparable to the prednisone group (70.1%) and superior sustained remission at Week 52 (65.7% avacopan vs. 54.9% prednisone groups, respectively [1]). The median (mean) total glucocorticoid dose from all sources was 400 mg (1349 mg) in the avacopan group versus 2939 mg (3655 mg) in the prednisone group, representing 86% (63%) lower glucocorticoid exposure in the avacopan group. Compared with the prednisone group, the avacopan group showed a reduction in the proportion of patients who relapsed after achieving remission and, among patients who achieved remission, a longer time to relapse (1).

Objectives: To further characterize efficacy, additional post-hoc analyses compared the avacopan and prednisone groups regarding i) failure to achieve remission and ii) relapse after achieving remission.

Methods: ADVOCATE, a phase 3, randomized, double-blind, controlled trial in 330 patients, evaluated the efficacy and safety of avacopan. Patients with ANCA-associated vasculitis (new-onset or relapsing disease) were randomized to receive avacopan 30 mg twice daily, or a standard 20-week oral prednisone taper, plus matching placebos, in addition to background immunosuppressant therapy. For the purpose of these analyses, remission was defined as the first timepoint when a BVAS of 0 was achieved. Relapse was defined as worsening of disease, after having previously achieved remission, that involved one or more major or three or more minor items in the BVAS, or one or two minor items in the BVAS recorded at two consecutive study visits.

Two post-hoc sensitivity analyses of patients in the intent-to-treat population examined: i) the proportion of patients who failed to achieve remission, or achieved remission and subsequently relapsed after achieving that remission, and ii) relapse-free time. For patients who achieved remission, relapse-free time was calculated as the number of days from the initial remission achieved to relapse. For patients who failed to achieve remission, relapse-free time was imputed as one day (remission and relapse on the same day). Patients who did not relapse were censored at the time of the last BVAS assessment.

Results: Baseline characteristics and time to achieve initial remission were similar between groups, and the incidence of BVAS 0 at any point in the study occurred approximately equally in both groups (158 avacopan vs. 157 prednisone). In the first sensitivity analysis, the avacopan group showed a reduction in the proportion of patients who failed to achieve remission, or relapsed after remission, compared with the prednisone group (24 [14.5% vs 40 [24.4%], p=0.011). In the second sensitivity analysis that included all patients in the trial, the hazard ratio of relapse-free time for avacopan vs prednisone was 0.57, 95% CI (0.35, 0.96), p=0.029 (log-rank test) (Figure 1).

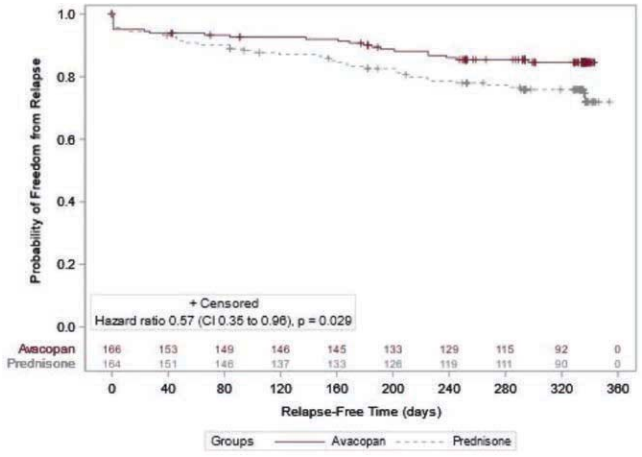

Figure 1. Relapse-free time among patients with ANCA-associated vasculitis in ADVOCATE (intention-to-treat population).

Conclusion: In the phase 3 ADVOCATE study of ANCA-associated vasculitis, more patients in the avacopan group compared to the prednisone group achieved remission, and fewer in the avacopan group relapsed after achieving remission. Patients receiving avacopan had a longer relapse-free time compared to the prednisone group. These post-hoc sensitivity analyses provide additional evidence of the efficacy of avacopan for the treatment of ANCA-associated vasculitis.

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Vessels glowing in the dark

OP0181 MORTALITY IN POLYMYALGIA RHEUMATICA: A 35-YEAR PROSPECTIVE OBSERVATIONAL STUDY FROM SOUTHERN NORWAY.

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Background: Polymyalgia rheumatica (PMR) is a common inflammatory rheumatic disease in the elderly characterized by proximal muscular pain and stiffness. Although PMR is associated with systemic inflammation, prolonged glucocorticoid therapy and probably cardiovascular diseases, previous studies have not shown increased mortality. However, the number of studies is limited.
Objectives: The aim of this study was to determine whether PMR is associated with increased mortality in a large PMR cohort followed prospectively for a period of 35 years.
Methods: All patients diagnosed with PMR according to the criteria of Bird between 1987 and 1997 in the county of Aust-Agder, Southern Norway, were identified. Further details about the inclusion process have been published previously [1]. Patients in the prospective part of this study were followed until death or December 31, 2021. Standard mortality ratios (SMR) were calculated using population data (age- and gender-matched) from Statistics Norway as reference. Difference in survival between men and women was estimated using the Kaplan-Meier method. The study was approved by the regional ethics committee.
Results: A total of 296 patients were included. Among these were 200 (67.6%) females, and the mean age at diagnosis was 71.9 (SD 8.4). The vast majority, 277 patients (93.6%), were deceased at the censoring date of December 31, 2021. Mean observation time for all patients was 13.8 years (95% CI 12.8-14.7). The overall SMR was 1.05 (95% CI 0.93-1.18), for females 1.14 (95% CI 0.99-1.31) and for men 0.91 (95% CI 0.73-1.11). SMRs and mean survival times are presented in Table 1. The Kaplan-Meier survival curve showed no pronounced difference in survival between men and women (Figure 1).

Table 1. Standard Mortality Ratios.

	n	Person-years	Observed	Expected	SMR	95% CI	Mean survival time	95% CI
All patients	296	4079	277	263.18	1.05	0.93-1.18	85.7	84.9-86.5
- Male	96	1326	89	98.04	0.91	0.73-1.11	85.0	83.5-86.4
- Female	200	2752	188	165.14	1.14	0.99-1.31	86.0	85.0-87.0
Age at diagnosis								
<60	31	678	21	17.16	1.24	0.78-1.84	78.6	78.0-81.3
60-69	91	1626	84	83.14	1.01	0.81-1.25	83.8	82.2-85.4
70-79	123	1394	121	118.39	1.03	0.85-1.22	86.8	85.7-87.9
≥80	51	380	51	50.64	1.00	0.76-1.31	90.7	89.5-91.8
Men								
2 years		185	9	8.29	1.09	0.53-1.99		
5 years		436	17	21.03	0.81	0.49-1.27		
10 years		788	36	43.67	0.82	0.59-1.13		
25 years		1272	83	88.57	0.94	0.75-1.16		
Women								
2 years		392	11	12.76	0.86	0.45-1.50		
5 years		934	32	35.80	0.89	0.62-1.25		
10 years		1678	68	74.03	0.92	0.72-1.16		
25 years		2687	172	156.21	1.10	0.95-1.28		

"Years": refer to calculated survival time from date of diagnosis; "Observed": number of deaths in the PMR cohort; "Expected": number of expected deaths in age-matched, sex-matched, and year-matched background Norwegian Population.

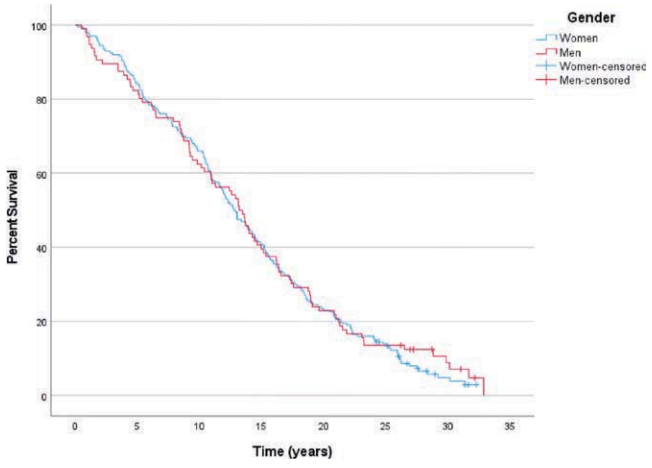

Figure 1. Kaplan-Meier survival curve.

Conclusion: To our knowledge, this is the first prospective study following a large PMR cohort from diagnosis to death. In women, overall mortality (SMR) was increased compared to the general Norwegian population. This tendency to increased mortality in women was observed during the last decades of the study period. Furthermore, increased SMR was observed in patients aged <60 at time of diagnosis and in men the first 2 years after diagnosis, although with wide confidence intervals due to the limited number of deaths in these subsets.

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OP0182 SECUKINUMAB IN GIANT CELL ARTERITIS: THE RANDOMISED, PARALLEL-GROUP, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTRE PHASE 2 TITAIN TRIAL

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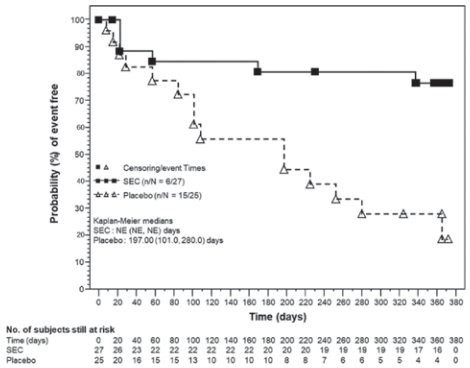
Background: Little is known about glucocorticoid-sparing agents in giant cell arteritis (GCA) except for IL-6 inhibition. Secukinumab (SEC) has shown significant improvements in the signs and symptoms of IL-17A driven medical conditions such as plaque psoriasis, psoriatic arthritis, and axial spondyloarthritis.[1,2] It has a favourable long-term safety profile.[1,2]
Objectives: TitAIN is the first randomised controlled trial investigating the potential efficacy, safety, and tolerability of SEC in GCA patients (pts).
Methods: This phase 2, randomised, double-blind, placebo (PBO) controlled, multicentre, proof-of-concept trial enrolled pts (aged ≥50 years) with new onset (diagnosed within 6 weeks (wks) of baseline) or relapsing (diagnosed >6 wks from baseline) GCA, naïve to biological therapy. Pts were randomised (1:1) to SEC 300 mg or PBO initially administered wkly (5 doses) and every 4 wks thereafter through Wk 48 (last dose), in combination with a 26-wk prednisolone taper regimen starting from baseline. Proportion of GCA pts in sustained remission until Wk 28 was the primary endpoint assessed by a Bayesian analysis of the posterior distribution with non-responder imputation. Other key endpoints included proportion of GCA pts in sustained remission until Wk 52 (based on study data with non-responder imputation) and time to first GCA flare after baseline.
Results: Out of 52 randomised pts (SEC, n=27; PBO, n=25), 71.2% (n=37) completed study treatment (SEC, 81.5%; PBO, 60.0%). Overall, 42 (80.8%) pts had new onset GCA and 10 (19.2%) pts had relapsing GCA at baseline. Proportion (posterior median with 95% credibility interval) of GCA pts in sustained remission until Wk 28 was higher with SEC, 70.1% (51.6%-84.9%), than with PBO, 20.3% (12.4%-30.0%); odds ratio (posterior median with 95% credibility interval), 9.31 (3.54-26.29) (Table 1). Until Wk 52, proportion (95% confidence interval) of GCA pts in sustained remission were 59.3% (38.8%-77.6%) in SEC group and 8.0% (1.0%-26.0%) in PBO group (Table 1). Median (95% confidence interval) time to first GCA flare after baseline was not reached for GCA pts treated with SEC and was 197.0 (101.0-280.0) days for PBO (Figure 1). Overall, treatment-emergent adverse events (AEs) occurred in 98.1% (SEC vs PBO, 100.0% vs 96.0%) and serious AEs in 32.7% (SEC vs PBO, 22.2% vs 44.0%) pts. Two pts in each SEC and PBO groups had AEs that led to study drug discontinuation and 1 pt in each group had AEs that led to death (not treatment-related). There were no new or unexpected safety signals identified with SEC treatment.

Table 1. Proportion of GCA patients with sustained remission (Full analysis set) until Week 28 and 52

Proportion of pts	Secukinumab (N=27)	Placebo (N=25)
Median percentage (95% credibility interval), Wk 28	70.1% (51.6%, 84.9%)	20.3% (12.4%, 30.0%)
Percentage (95% confidence interval), Wk 52	59.3% (38.8%, 77.6%)	8.0% (1.0%, 26.0%)

The full analysis set comprises all pts to whom study treatment has been assigned by randomisation and who received at least one dose of randomised study treatment (secukinumab or placebo).GCA, giant cell arteritis; N, number of pts in each treatment group in the full analysis set, pts, patients; Wk, Week



The triangles and rectangular shapes are showing the censoring/event times. The drop in the line of SEC or placebo patients is associated with an event (i.e., first post-baseline GCA flare). Patients who prematurely discontinued study treatment prior to Week 52 without having an event were censored at the time of premature discontinuation and patients who completed study treatment without having an event were censored at their last visit in the treatment phase. The full analysis set comprises all patients to whom study treatment has been assigned by randomisation and who received at least one dose of randomised study treatment (SEC or placebo). Time to first GCA flare after remission refers to time from first day of study treatment until first post-baseline GCA flare.
GCA, giant cell arteritis; n, total number of patients with a response; N, number of patients in each treatment group; NE, not evaluable; SEC, secukinumab.

Figure 1. Kaplan-Meier plot of time to first GCA flare from baseline up to Week 52 (Full analysis set)

Conclusion: SEC demonstrated a higher sustained remission rate and longer time to first GCA flare vs PBO through 52 wks in pts with GCA. This proof-of-concept phase 2 study supports further development of SEC as a potential treatment in combination with 26 wk glucocorticoid taper for pts with GCA.

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Disclosure of Interests: Nils Venhoff Speakers bureau: AbbVie, Novartis, Bristol-Myers-Squibb, Chugai, Roche, Vifor, Consultant of: AbbVie, Chugai, Novartis, Vifor, Grant/research support from: Bristol-Myers-Squibb, Novartis, Wolfgang A. Schmidt Speakers bureau: Abbvie, Chugai, Medac, Novartis, Roche, Sanofi, Consultant of: Advisory board member: Abbvie, Chugai, GlaxoSmithKline, Novartis, Roche, Sanofi, Grant/research support from: principle investigator in GCA trials: Abbvie, GlaxoSmithKline, Novartis, Sanofi, Raoul Bergner Speakers bureau: Abbvie, Bristol Myers Squibb, Chugai, Novartis, Roche, Consultant of: Advisory board member: Gilead, GlaxoSmithKline, Vifor, Jürgen Rech Speakers bureau: Abbvie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD; Novartis, Roche, Sanofi, Sobi, UCB, Consultant of: Abbvie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD, Novartis, Roche, Sanofi, Sobi, UCB, Leonore Unger Paid instructor for: Novartis, Hans-Peter Tony Consultant of: Abbvie, BMS, Chugai, Gilead, Lilly, Novartis, Roche, Sanofi, Meryl Mendelson Shareholder of: Novartis Pharmaceuticals Corporation, Employee of: Novartis Pharmaceuticals Corporation, Christian Sieder Employee of: Novartis Pharma GmbH, Meron Maricos Employee of: Novartis Pharma GmbH, Jens Thiel Speakers bureau: Novartis, GSK, Bristol-Myers-Squibb, Roche, AstraZeneca, Vifor, Consultant of: Novartis, Janssen, GSK; research grants: Bristol-Myers-Squibb, Novartis

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OP0183 VALIDITY OF THE EULAR RECOMMENDATIONS ON THE USE OF ULTRASOUND IN THE DIAGNOSIS OF GIANT CELL ARTERITIS

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Background: The EULAR recommendations for the use of imaging in large vessel vasculitis establish that an imaging test supported by clinical pre-test probability (PTP) is sufficient for the diagnosis of giant cell arteritis (GCA)[1].

Objectives: To determine the validity of the EULAR recommendations on the use of Colour doppler ultrasound (CDUS) in GCA after calculating the PTP based on the Southend pre-test probability score (SPTPS).

Methods: We collected data of all patients referred to our fast-track clinic between 2016 and 2020. The SPTPS was calculated and classified as low (LR), intermediate (IR) and high risk (HR) according to the values obtained by its authors, <9, 9-12 and >12, respectively[2]. All patients underwent a CDUS of the temporal arteries with their common, parietal and frontal branches, and the most also axillary (86.5%), subclavian and carotid arteries. Other diagnostic tests were performed when deemed necessary by the responsible physician. TAB was performed in 34 patients (11.4%), PET-CT in 48 (16.2%) and other imaging tests such as AngioMRI or AngioCT in 8 (2.7%). The gold standard diagnosis was made according to the physician's criteria after at least nine months of follow-up.

Results: Of the 297 referred patients, 97 (32.7%) were diagnosed with GCA. The SPTPS area under the ROC curve was 0.787. The LR category included 105 patients (35.4%), of which 10 (9.5%) had GCA. The IR category included 125 patients (42.1%), 40 with GCA (32%) and 85 without (68%). The HR category included 67 patients (22.5%), 47 with GCA (70.1%). In 4 of the 97 patients with GCA, the CDUS was negative and the diagnosis was confirmed with PET-CT. On the other hand, 6 of the 200 included patients without GCA (3%) had a false positive result of CDUS.

There were 93 patients classified as LR with negative CDUS, and 1 of them has a final clinical diagnosis of GCA. Of the 46 patients classified as HR with positive CDUS, 1 was a false positive diagnosis of GCA. And, within the IR group, of the 84 patients with negative CDUS one had a final GCA diagnosis and of those with positive CDUS 2 were not GCA (Figure 1). Therefore, the combined use of SPTPS + CDUS only miscassified 5/297 cases (<2%).

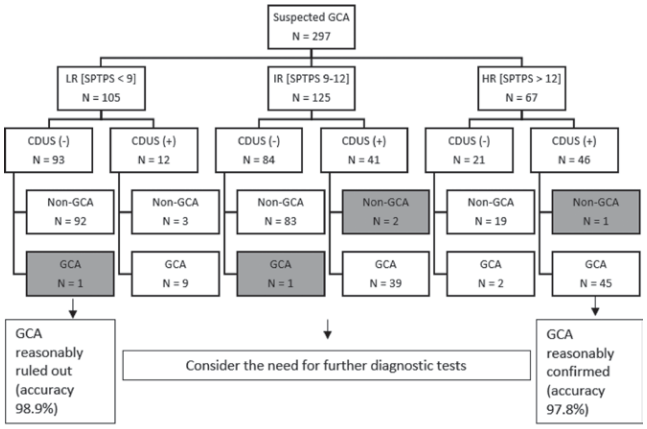

Figure 1. Flow-chart of the results of the diagnostic performance of SPTPS + CDUS.

Conclusion: Combining the results of a pre-test probability score, such as SPTPS, and the CDUS allows for an accurate diagnosis of GCA, as established by the EULAR group, with less than 2% misclassification of diagnosis. Even a negative CDUS in patients with IR shows a strong association with a negative diagnosis.

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Disclosure of Interests: None declared

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OP0184 PREVALENCE OF SUBCLINICAL GIANT CELL ARTERITIS IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are closely related diseases. PMR occurs in approximately 50 % of patients with GCA[1]; however the prevalence of subclinical GCA in PMR has not yet been widely studied.

Objectives: The aim of our multicenter, prospective study was to determine the prevalence of subclinical GCA in newly diagnosed PMR, using vascular ultrasound (US) as a diagnostic tool.

Methods: Eight European centers participated in the study. The studied cohort represented consecutive newly diagnosed patients with PMR who fulfilled 2012 EULAR/ACR Provisional Classification Criteria for Polymyalgia Rheumatica[2] without symptoms or signs suggestive for GCA. All patients underwent ultrasound (US) of both hips and shoulders, as well as of four bilateral arterial territories (i.e. temporal, common carotid, subclavian and axillary arteries). Patients with positive halo signs were considered to have subclinical GCA [3]. An intima-media thickness ≥0.34 mm for frontal and parietal TA, 0.42mm for common TA, and ≥1 mm for common carotid, axillary and subclavian arteries for positive result. Clinical demographic and laboratory characteristics of the PMR pure group were compared with the PMR/GCA patient group.
Results: A total of 258 patients were included, 137 (53.1%) females with a mean age of 73±8.4 years. Table 1 shows the main differences in PMR patients with and without subclinical GCA. The only statistical significant difference between the two groups was the higher prevalence of morning stiffness > 40 minutes in the pure PMR group (p<0.05). A halo sign was found on at least one of the examined arteries in 56/258 patients (21.7%).
The different subtypes of vessel involvement were available in 216 cases. Data compatible with the diagnosis of GCA was found in 41 cases (19%): 10 (24.3%) had only temporal artery involvement ("cranial" GCA), 27 (65.8%) had an extra-cranial artery involvement and 4 (9.8%) a mixed form with both cranial and extra-cranial artery involvement (Figure 1).

Table 1. Clinical and demographic characteristics

	PMR study n=258	PMR without GCA n=202	PMR with GCA n=56
Age (mean±SD)*	73.05±8.43	72.92±8.83	73.52±6.82
Sex (female/male)	137/121	109/93	28/28
Bilateral shoulder pain	249 (96.5%)	196(97%)	53(94.7%)
Hip pain	209 (81%)	163 (80.7%)	46 (82.2%)
Neck pain	158 (61.3%)	125 (61.9%)	33 (58.9%)
Morning stiffness*	227 (88.7%)	182 (90.1%)	45 (80.4%)
Weight loss	68 (27.6%)	49 (24.3%)	19 (35.8%)
Fever	30 (11.7%)	20 (10.0%)	10(17.9%)
Peripheral arthritis	72 (29.1%)	59(29.2%)	13 (25.0%)
Pitting edema	32 (13.1%)	26 (13.6%)	6 (11.3%)
Duration symptoms (weeks)	8.34±7.79	8.75±7.21	7.67±6.95
CRP mg/l	51.51±47.14	51.45±47.34	51.74±44.83
ESR mm/h	58.93±28.62	58.19 ±27.45	61.71±32.75

PMR= Polymyalgia rheumatica; GCA= giant cell arteritis; SD= standard deviation. * p<0.05

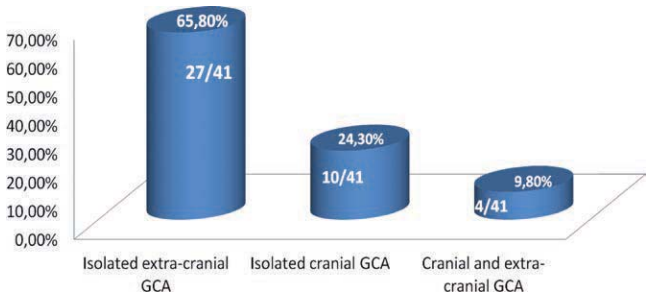

Figure 1. Subtypes of subclinical GCA in PMR in 216 patients with cranial and extra-cranial examination

Conclusion: One fifth of PMR patients without symptoms or signs of GCA have ultrasound findings consistent with the diagnosis of GCA. Subclinical GCA in PMR shows a predilection for extra-cranial artery involvement.
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Acknowledgements: To the GCA/PMR study group
Disclosure of Interests: None declared
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OP0185 TOCILIZUMAB IN COMBINATION WITH 8 WEEKS OF PREDNISONE FOR GIANT CELL ARTERITIS

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Background: Even with the use of tocilizumab (TCZ), significant glucocorticoid exposure (usually ≥ 6 months) continues to be an important problem in giant cell arteritis (GCA).
Objectives: We aimed to evaluate the efficacy and safety of tocilizumab (TCZ) in combination with 2 months of prednisone in a group of patients with GCA.

Methods: We conducted a prospective, single arm, open-label study of TCZ in combination with 2 months of prednisone for new-onset and relapsing GCA patients with active disease (ClinicalTrials.gov Identifier NCT03726749). GCA diagnosis required confirmation by temporal artery biopsy or vascular imaging. Active disease was defined as presence of cranial or polymyalgia rheumatica symptoms necessitating treatment within 6 weeks of baseline. All patients received TCZ 162 mg subcutaneously every week for 12 months and an 8-week prednisone taper starting between 20 mg and 60 mg daily (Figure 1). The primary endpoint, sustained prednisone-free remission, was defined as absence of relapse from induction of remission up to week 52 while adhering to the prednisone taper. Relapse was defined as the recurrence of symptoms of GCA requiring treatment intensification regardless of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels. Safety was also evaluated.

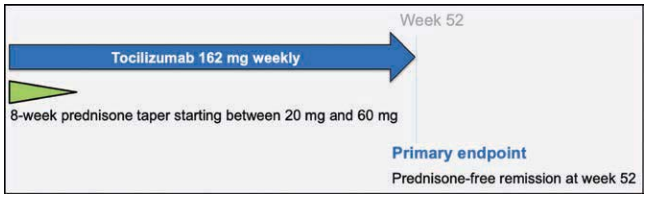

Figure 1. Clinical Trial Schema

Results: Between 11/2018 and 11/2020 we enrolled 30 patients (mean age 74 years, 60% females, 50% new-onset disease, 77% temporal artery biopsy-proven, 47% imaging-proven). The mean ESR and CRP at screening were 45 mm/hour and 48 mg/L, respectively. The initial prednisone dose was 60 mg (n = 7), 50 mg (n = 1), 40 mg (n = 7), 30 mg (n = 6) and 20 mg (n = 9). All patients entered remission within 4 weeks of baseline. The primary endpoint was achieved by 23 (77%) patients (Table 1). The mean (SD) cumulative prednisone dose in these 23 patients was 1052 (390) mg. After a mean period of 16 weeks, 7 (23%) patients relapsed (Table 1). All relapses but one occurred after the completion of the study prednisone taper. Overall, 6 of the 7 patients with relapse received a second prednisone taper over 8 weeks. Of these 6 patients, 4 achieved and maintained remission for the remainder of the trial period, and 2 withdrew from the study after having a second relapse. One patient with relapse received a second prednisone taper over 26 weeks and stayed in remission until the end of the study. The mean (SD) cumulative prednisone dose in the 7 patients with relapse was 1883 (699) mg (Table 1). Overall, 4 (13%) participants developed a serious adverse event (Table 1). No cases of ischemia-related visual symptoms including permanent vision loss occurred during the study.

Table 1. Efficacy and Safety Outcomes

	GCA patients (n = 30)
Efficacy	
Sustained, prednisone-free remission by week 52	23.0 (76.7)
Cumulative prednisone dose (mg) at week 52, mean (SD)	1051.5 (390.3)
Relapse	7.0 (23.3)
Time to relapse, weeks: mean (SD)	15.8 (14.7)
Prednisone dose (mg/day) at relapse, mean (SD)	2.1 (5.2)
Cumulative prednisone dose (mg), mean (SD)	1883.1 (699.2)
Clinical manifestations at relapse	
Cranial symptoms	4 out of 7 patients
Ischemic visual symptoms	0 out of 7 patients
PMR symptoms	4 out of 7 patients
Safety	
Serious adverse events	4.0 (13.3)
Cellulitis	1
COVID-19	1
Fragility fracture	1
Cholecystitis	1

Values represent number and (%) unless otherwise specified. SD, standard deviation; PMR, polymyalgia rheumatica

Conclusion: These results suggest that 12 months of TCZ in combination with 8 weeks of prednisone could be efficacious for inducing and maintaining disease remission in patients with GCA. Confirmation of these findings in a randomized controlled trial is required.
Disclosure of Interests: Sebastian Unizony Consultant of: Kiniksa, Sanofi, Janssen, GSK, Grant/research support from: Janssen, Genentech, Mark Matza: None declared, Adam Jarvie: None declared, Ana Fernandes: None declared, John H. Stone Consultant of: Roche/Genentech, Grant/research support from: Roche/Genentech
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OP0186

SENSITIVITY TO CHANGE OF DIFFERENT ULTRASOUND SCORES IN A PROSPECTIVE FOLLOW-UP OF NEW-ONSET TREATMENT-NAÏVE GCA PATIENTS.

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Background: The role of ultrasound (US) for monitoring giant cell arteritis (GCA) is not clarified. Follow-up assessment of number of halos (halo count) and different quantitative scores based on intima media complex (IMC) measurement of halos, have demonstrated potential to show sensitivity to change (STC)[12]. Including IMC of normalized arteries in such scores may reduce the risk of missing new arteritic lesions and assessment bias towards a response. We aimed to evaluate US scores based on halo features and scores based on IMT measurements of all assessed arteries.

Objectives: To compare different US score's 1) STC after institution of treatment and 2) correlation with disease activity.

Methods: In a prospective cohort of new-onset GCA patient, pre-treatment diagnostic evaluation including US and PET/CT and subsequently temporal artery biopsy (TAB) was performed per protocol. All patients were started on 60 mg of prednisolone and followed a routine tapering. Follow-up visits including clinical evaluation, blood tests, US, the physician's and patient's global NRS (0-10) were performed after 8 weeks, 24 weeks and in a subgroup (n=24) at 15 months. US of temporal, carotid and axillary arteries included assessment of halo and IMC measurement in all arteries.

For each visit, max IMC, max halo IMC, sum IMC, sum halo IMC, mean IMC and halo count were calculated for all and for temporal (TA) and large vessels (LV) separately. Accordingly, halo IMC scores only included positive arteries whereas other IMC scores included all arteries assessed.

The change from baseline was assessed by Student's *t*-test. Standard response means (SRM=meanΔ(visit-baseline)/SE_{Δ}) were computed for each timepoint as STC estimates. Correlation with disease activity markers was assessed by Spearman's correlation. A $p<0.05$ was considered statistically significant.

Results: In total 47 patients were included (60% women, mean (CI) age 67 (62-69) years, mean (CI) CRP 75 (63-89)). Baseline US was positive(+) in 94% (72% TA+, 72% LV+), PET/CT+ in 96% (77% cranial arteries, 85% large vessel vasculitis) and TAB+ in 72% of patients. All patients completed the per protocol planned follow-up visits. Two patients experienced a relapse at week 8 and 10 patients at week 24.

All US outcomes improved during follow-up and was apparent by week 8 (Table 1) and forward. However, only scores including TA consistently showed statistically significant change from baseline to follow-up. In accordance the magnitude of change as expressed by SRM was large in TA, whereas SRM in LV was small (Figure 1).

All TA based US scores showed significant moderate-strong correlation with disease activity markers (CRP, patient and physician global NRS). Some LV based US scored showed weak correlation with CRP but otherwise did not correlate with clinical disease activity.

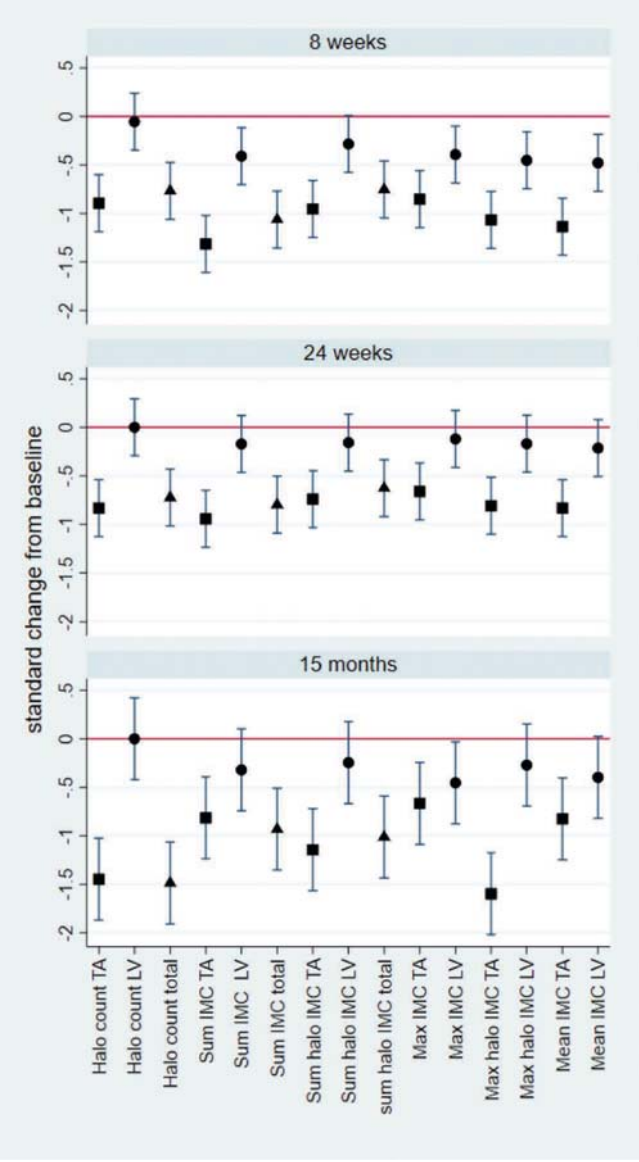

Figure 1.

Table 1.

US score changes during follow-up

		Baseline (IQR)	Δw8 (SE)	Δw24 (SE)	Δm15 (SE)
Halo count	**TA**	2 (0-4)	**-1.68 (.28)**	**-1.70 (.30)**	**-2.63 (.37)**
	LV	1 (0-2)	**-0.04 (.11)**	**0.00 (.11)**	**0.00 (.31)**
	Total	4 (2-6)	-1.72 (.33)	-1.70 (.34)	-2.63 (.36)
Sum IMC	**TA**	0.8 (0-1.8)	**-0.72 (.08)**	**-0.69 (.11)**	**-0.76 (.19)**
	LV	1.5 (0-2.8)	**-0.33 (.12)**	-0.13 (.11)	-0.33 (.21)
	Total	2.6 (1.6-4.4)	**-1.05 (.14)**	**-0.81 (.15)**	**-1.09 (.29)**
Sum halo IMC	**TA**	1.9 (1.6-2.5)	**-0.90 (.14)**	**-0.90 (.17)**	**-1.29 (.23)**
	LV	3.5 (2.8-4.0)	-0.33 (.17)	-0.15 (.14)	-0.47 (.39)
	Total	5.5 (4.6-6.3)	**-1.23 (.24)**	**-1.04 (.24)**	**-1.76 (.35)**
Max IMC	**TA**	0.5 (0.4-0.6)	**-0.17 (.03)**	**-0.14 (.03)**	**-0.17 (.05)**
	LV	1.2 (0.9-1.6)	**-0.16 (.06)**	-0.04 (.05)	**-0.20 (.09)**
Max halo IMC	**TA**	0.5 (0-0,6)	**-0.29 (.04)**	**-0.26 (.05)**	**-0.40 (.05)**
	LV	1.2 (0-1.6)	**-0.27 (.09)**	-0.09 (.08)	-0.23 (.17)
Mean IMC	**TA**	0.32 (0.27-0.43)	**-0.11 (.01)**	**-0.10 (.02)**	**-0.13 (.03)**
	LV	0.88 (0.7-1.03)	**-0.9 (0.3)**	-0.04 (.03)	**-0.10 (.05)**

Baseline medians, Δ mean difference from baseline. Bold indicates $p<0.05$.

Conclusion: STC was maintained in US scores that included all assessed arteries hereby reducing potential assessment bias. These findings confirm US as a potential tool for monitoring treatment response.

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OP0187

COMPARATIVE EFFICACY OF NON-BIOLOGIC IMMUNOSUPPRESSANTS IN TAKAYASU ARTERITIS

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Background: The choice of immunosuppressant (IS) in patients with Takayasu arteritis (TAK) is often arbitrary due to lack of comparison studies.

Objectives: In this retrospective, we aimed to compare the efficacy of 3 non biologic IS including azathioprine (AZA), mycophenolate mofetil (MMF) and methotrexate (MTX) in inducing and maintaining sustained remission in patients with TAK.

Methods: Patients with a diagnosis of TAK, attending our clinics between Jan 2000 and May 2019 were identified. Those who satisfied either ACR or Sharma's classification or EULAR PRINTO PRES criteria and/or had angiographic evidence of Takayasu arteritis with a minimum 2 follow up visits were included. Patients who received upfront biologics were excluded. The patients were matched for parameters statistically different among three groups using propensity score analysis. Clinical details at the index visit defined as the time of initiation of first IS and follow up visits were prospectively recorded and retrospectively noted from electronic medical records. The primary outcomes were attainment of complete remission and relapses. Disease activity was assessed by Indian Takayasu arteritis score (ITAS), C-reactive protein and angiograms. Relapse was defined as ITAS-A(CRP) >=2 and/or progression in angiograms and/or escalation of steroid dose and/or switching of IS due to active disease. The baseline variables of patients receiving AZA, MMF and MTX were compared using chi square test or Mann Whitney U test. The comparative efficacy of IS to induce complete remission was calculated using logistic regression and presented as odds ratio (95% CI). The cumulative risk of relapse was calculated using Cox-proportional hazards model with hazards ratio and 95% confidence interval (CI) after adjusting for duration of symptoms and juvenile onset disease. The patients were censored at the time of relapse or time of switching to another IS or last follow up whichever was the earliest. AZA was arbitrary chosen as the reference drug for all the analysis. The missing values (visits) were not included in analysis and the last observation was carried forwards. Data after switching of immunosuppressant of interest till the last follow up visit was analysed descriptively. All analysis were done for matched and unmatched patient groups. The results of matched and unmatched cohort were similar, hence the results of unmatched groups are presented here.

Results: Overall, 234 patients satisfying inclusion criteria including 53 (22.6%), 156 (66.7%) and 25 (10.7%) patients receiving AZA, MMF, Mtx respectively were studied. Complete remission (CR) was attained in 183 (78.2%) patients after initiating steroids and IS. 79.2%, 77.6% and 80% of patients receiving AZA, MMF or MTX respectively achieved CR yielding an odds ratio of 1.10 (0.52-2.37), p= 0.80 and 0.96 (0.29-3.12), p= 0.94 for MMF and MTX as compared with AZA. CR was sustained in 22 (52.4%), 80 (66.1%) and 11 (55%) of patients on AZA, MMF and MTX respectively. When compared with AZA, adjusted hazards ratio (AHR) of relapse was 1.51 (0.79-2.89), p=0.21 and 2.45 (1.00-5.99), p= 0.05 with MMF and MTX after adjusting for juvenile onset disease, type 1 and type 4 disease by angiography. The frequency of remission in patients who received MMF was significantly higher in patients who presented with type 4 disease (96%) as compared with the patients who had other types on angiography (74%), p= 0.017. Conversely, 63.6% of patients with type 1 disease responded to MMF which was significantly lower than 81.3% of patients with other angiographic types (p=0.037) while no such differential response was observed for AZA or MTX. Retrospective design and small number of patients in AZA and Mtx group were the major limitations of the study.

Conclusion: In our patients with TAK, all the three IS were comparable in inducing remission. Azathioprine was equal to MMF but superior to MTX in maintaining relapse free sustained response. The efficacy of MMF differed across various angiographic types of disease.

REFERENCES: None

Disclosure of Interests: None declared

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Active Ageing: new perspectives for RMD patients

OP0188 **CLINICAL EFFECTIVENESS OF STRATIFIED EXERCISE THERAPY COMPARED TO USUAL EXERCISE THERAPY IN PATIENTS WITH KNEE OSTEOARTHRITIS: A CLUSTER RANDOMIZED CONTROLLED TRIAL (OCTOPUS-STUDY)**

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Background: There is strong, high-quality evidence for the effectiveness of exercise therapy in people with knee osteoarthritis (OA).[1] However, although effective, the average effect size is only moderate (approximately 0.5).[1] This may be attributed to the current 'one-size-fits-all' exercise approach, while a stratified approach may yield superior clinical and economic outcomes. We are the first to test a model of stratified exercise therapy in patients in knee OA. This model was based on 3 previously identified subgroups[2] that are aligned with well-accepted OA phenotypes[3], namely a 'low muscle strength subgroup' ('age-induced phenotype'), 'high muscle strength subgroup' ('post-traumatic phenotype') and 'obesity subgroup' ('metabolic phenotype'). For each subgroup, a subgroup-specific exercise therapy intervention was developed and pilot-tested[4], which was supplemented by a dietary intervention for the 'obesity subgroup'.

Objectives: The OCTOPuS-trial aimed to determine the effectiveness of stratified exercise therapy in reducing knee pain and improving physical function, compared to usual, 'non-stratified' exercise therapy, in patients with knee OA.

Methods: We conducted a pragmatic cluster randomized controlled trial in a primary care setting in 335 people with knee osteoarthritis: 153 in the experimental arm and 182 in the control arm. Physiotherapy practices were randomized into the experimental arm providing the model of stratified exercise therapy supplemented by a dietary intervention from a dietician for the 'obesity subgroup' or the control arm proving usual, 'non-stratified' exercise therapy. Primary outcomes were knee pain severity (NRS pain, 0-10) and physical function (KOOS subscale daily living, 0-100). Measurements were performed at baseline, and 3- (primary endpoint), 6-, and 12-months follow-up. Intention-to-treat, multilevel, regression analysis was performed.

Results: We found statistically non-significant differences in knee pain (mean difference (95% confidence interval): 0.19 (-0.31, 0.69)) and physical function (-0.40 (-3.91, 3.12)) at 3-months follow-up, with within-group effect sizes ranging between 0.5 and 0.7. Non-significant differences were also found for all other time points and for nearly all secondary outcome measures. Moreover, effects of experimental and control intervention were similar in each of the 3 subgroup separately.

Conclusion: This trial demonstrated no added value with respect to clinical outcomes of our model of stratified exercise therapy compared to usual exercise therapy. This could be attributed to the experimental arm therapists facing difficulty in effectively applying the model (especially in the 'obesity subgroup') and to elements of the model possibly being applied in the control arm.

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From childhood to adulthood - growing up with an RMD

OP0189-PARE **NEW JIA-AT-NRAS RESOURCE MEDICINES IN JUVENILE IDIOPATHIC ARTHRITIS**

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Background: Biologics have been commissioned by the NHS for use to treat JIA since 2014. Many of the original biologics that were first developed have since lost exclusivity, allowing other manufacturers to produce highly similar versions (biosimilars). This difference between the originator and the biosimilar has caused confusion within the patient community, especially in how it has been communicated to them. Parents found the concept of biosimilars confusing and wanted more information about this, recommending that written material be provided. Previous conversations with healthcare professionals, parents and young people living with JIA had also found there was a lack of written information on all JIA medications so we looked into how this gap could be filled.

Objectives: Produce a new resource to clarify the confusion about the biosimilars and originators for the JIA patient community. Explain the different medications to treat JIA in a patient/parent friendly format so it can be easily referred

to. Easy to see the different categorisation of the medications e.g. pain management, DMARDS, biologics and targeting synthetic DMARDS and include information regarding how they are taken, how often and usage.

Methods: Knowing there was a need for this information, a focus group was convened with young people with JIA, parents of children with JIA and healthcare professionals. From this focus group and separate conversations with healthcare professionals it very quickly became apparent a resource not only covering medications for JIA but detailing the wider JIA journey was needed. This resource would need to cover each step from diagnosis to a young person taking control of their disease management. It would also cover how the complexity of the immune system means that some children/young people respond differently to medication; help them to learn about the unpredictability of the disease and to take control of managing their disease, particularly as they move onto adult rheumatology services.

NRAS worked collaboratively with health writer and healthcare professionals to make sure this new resource covered all the topics that were discussed at the focus group and detailed all the medications used to treat JIA, including information on the issue of differentiating between biologics and biosimilars.

Results: The Medicines in JIA booklet is now freely available to all parents, young people and healthcare professionals from the jia.org.uk website. The addition of visuals makes the information easier to navigate, clearer to understand and helps to illustrate the JIA journey. Along with the medicine directory which details all the medications to treat JIA.

Conclusion: The feedback NRAS has received from both healthcare professionals and parents has been very positive:

"We think that they're absolutely fantastic, they cover everything, and I'm so pleased I've got these to give to parents and children." **Paediatric Rheumatology Nurse Haywood Hospital**

"This is brilliant and much needed. Great piece of work much appreciated by all of us". **Lead Nurse Nottingham Children and Young People's Rheumatology Service**

"This has been my absolute saviour! It gives you support on administering the medicines and made me feel right at ease after reading it". **Parent of child with JIA**

REFERENCES:

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Figure 1. JIA-at-NRAS: Medicines in JIA resource

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Modern technology for precision medicine

OP0190

COMPREHENSIVE GENETIC AND FUNCTIONAL ANALYSES OF FC GAMMA RECEPTORS EXPLAIN RESPONSE TO RITUXIMAB THERAPY FOR AUTOIMMUNE RHEUMATIC DISEASES

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Background: Rituximab is widely used to treat rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) but clinical response varies. Efficacy is determined by the efficiency of depletion, which may depend on a variety of Fc gamma receptor (FcγR)-dependent mechanisms. Previous research was limited by complexity of the *FCGR* locus, not integrating copy number variation with functional SNP, and small sample size.

Objectives: The study objectives were to assess the effect of the full range of FcγRs variants on depletion, clinical response and functional effect on NK-cell-mediated killing in two rheumatic diseases with a view to personalised B-cell depleting therapies.

Methods: A prospective longitudinal cohort study was conducted in 873 patients [RA=611; SLE=262] from four cohorts (BSRBR-RA and BILAG-BR registries, Leeds RA and Leeds SLE Biologics). For RA, the outcome measures were 3C-DAS28CRP and 2C-DAS28CRP at 6 (+/-3) months post-rituximab (adjusted for baseline DAS28). For SLE, major clinical response (MCR) was defined as improvement of active BILAG-2004 domains to grade C/better at 6 months. B-cell depletion was evaluated by highly-sensitive flow cytometry. Qualitative and quantitative polymorphisms for five major FcγRs were measured using a commercial multiplex ligation-dependent probe amplification. Median NK cell FcγRIIIa expression (CD3-CD56+CD16+) and NK-cell degranulation (CD107a) in the presence of rituximab-coated Daudi/Raji B-cell lines were assessed using flow cytometry.

Results: In RA, for *FCGR3A*, carriage of V allele (coefficient -0.25 (SE 0.11); p=0.02) and increased copies of V allele (-0.20 (0.09); p=0.02) were associated with greater 2C-DAS28 response. Irrespective of *FCGR3A* genotype, increased gene copies were associated with a better response. In SLE, 177/262 (67.6%) achieved BILAG response [MCR=34.4%; Partial=33.2%]. MCR was associated with increased copies of *FCGR3A*-158V allele, OR 1.64 (95% CI 1.12-2.41) and *FCGR2C*-ORF allele 1.93 (1.09-3.40). Of patients with B-cells data in the combined cohort, 236/413 (57%) achieved complete depletion post-rituximab. Only homozygosity for *FCGR3A*-158V and increased *FCGR3A*-158V copy number were associated with increased odds of complete depletion. Patients with complete depletion had higher NK cell FcγRIIIa expression at rituximab initiation than those with incomplete depletion (p=0.04) and this higher expression was associated with improved EULAR response in RA. Moreover, for *FCGR3A*, degranulation activity was increased in V allele carriers vs FF genotype in the combined cohort; p=0.02.

Conclusion: FcγRIIIa is the major low affinity FcγR and increased copies of the *FCGR3A*-158V allele, encoding the allotype with a higher affinity for IgG1, was associated with clinical and biological responses to rituximab in two autoimmune diseases. This was supported by functional data on NK cell-mediated cytotoxicity. In SLE, increased copies of the *FCGR2C*-ORF allele was also associated with improved response. Our findings indicate that enhancing FcγR-effector functions could improve the next generation of CD20-depleting therapies and genotyping could stratify patients for optimal treatment protocols.

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Rheumatology in Europe

OP0191 **CONCEPTUALISING PATIENT AND PUBLIC INVOLVEMENT IN MUSCULOSKELETAL GUIDELINES IMPLEMENTATION: THE ALLIANCE FRAMEWORK**

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Background: Patient and Public Involvement (PPI), have supported high quality Rheumatology research which have now been successfully curated into widely endorsed evidence-based recommendations and guidelines. However, uptake and applicability of guidelines is less than optimal, significant variation exist in care, and health and socio-economic burdens attributed to rheumatic conditions continues to rise, suggesting an implementation challenge.
Objectives: We conducted a rapid review to investigate the role of PPI in guideline implementation.
Methods: A comprehensive search for relevant literature was undertaken (three databases - Medline, Embase, Cinahl, and two large repositories -WHO, G-IN). A priori eligibility criteria and systematic review-based methods were used to identify primary studies with explicit reference to PPI involvement in a rheumatic/musculoskeletal - MSK guideline implementation activity. Extracted data from included studies was interrogated for details regarding activities, contexts, outcomes, and impact of PPI in guidelines implementation and further discussed in review project meetings. Findings were brought together in a narrative synthesis. Recommendations for future research and practice, and a conceptual framework for PPI in Rheumatic and MSK guidelines implementation were co-developed with a public contributor.
Results: Ten papers were included, only 1 from the global south. A prevalence of consultative PPI activities in guidelines dissemination (e.g., language translations, patient versions) was found. Few studies explicitly report high-level PPI engagement in relation to care pathway adjustments, care commissioning, institutional operations and policy with a view to MSK guideline implementation. Training, development, and practice of PPI in MSK guideline implementations were not evidenced to have spread much beyond Europe and are also not well reported in literature nor rightly accrued as PPI activities in guideline implementation. The alliance framework (Figure 1) highlighting an iterative process of "creative thinking/co-production" and "strategic doing" helps to conceptualise PPI in MSK guideline implementation. The framework guides knowledge translation from guidelines to real world practice and aims to drive quality improvement for MSK care with patients, for patients, across and within care settings globally.

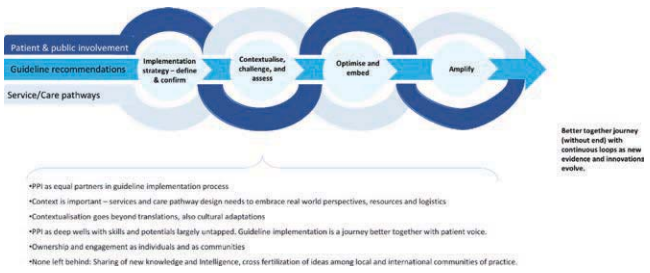

Figure 1. The Alliance framework for conceptualising Patient and Public Involvement in Rheumatic and Musculoskeletal guidelines implementation.

Conclusion: Despite success of PPI in rheumatology/MSK research, oversight or ineffective PPI in guideline implementation may hamper translation of novel advances in MSK care into real world practice and patient benefit. The Alliance framework prioritises effective PPI in MSK guideline implementation design, delivery, and evaluation, ideally applied in parallel with the development of evidence-based guidance recommendations. It highlights continuous application of innovative thinking, dynamic, and impactful collaborations for bridging the evidence-practice gap and improving quality of care for MSK patients globally through novel partnerships.
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Vaccination in rheumatic diseases with lessons from COVID

OP0192 **SEROLOGICAL RESPONSE AND SAFETY OF A THREE-DOSE SARS-COV-2 VACCINATION STRATEGY IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES ON IMMUNOSUPPRESSIVE THERAPY**

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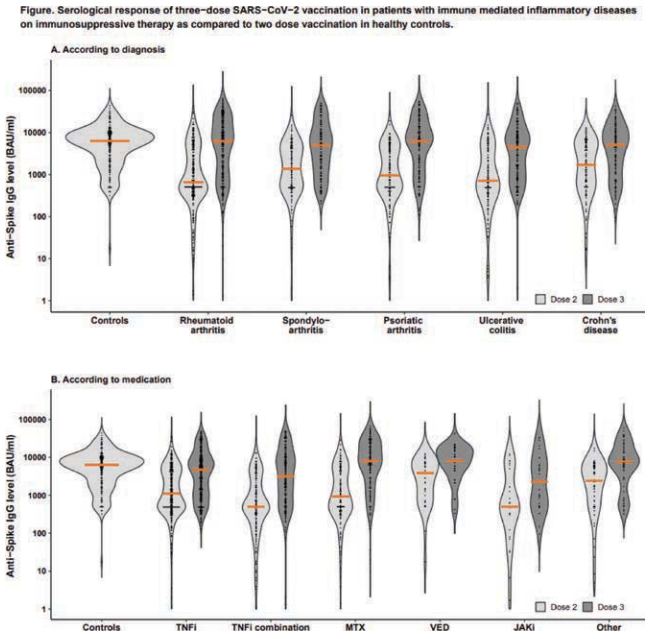
Background: Patients with immune-mediated inflammatory diseases (IMIDs) on immunosuppressive therapy have an inadequate serologic response following two-dose SARS-CoV-2 vaccination, and a standard vaccination strategy of three doses for this patient group is currently under implementation in several countries. However, the serological response and safety of this strategy has not been evaluated.
Objectives: To assess serological response and safety of a three-dose vaccination strategy in IMID patients on immunosuppressive therapy as compared to standard two-dose vaccination of healthy controls.
Methods: The prospective observational Nor-vaC study (NCT04798625) enrolled adult patients on immunosuppressive therapy for inflammatory joint- and bowel diseases. Healthy controls were health care workers from participating hospitals. All participants received standard vaccines according to the national vaccination program with three doses in patients and two doses in controls. The third dose was offered to IMID patients >4 weeks after the second dose. Analyses of antibodies binding the receptor-binding domain of the SARS-CoV-2 Spike protein were performed prior to, and 2-4 weeks after the second and third vaccine doses. Levels were compared across groups by Mann-Whitney U tests and multivariate linear regression was used to identify predictors of response.
Results: Overall, 961 patients (315 rheumatoid arthritis, 156 spondyloarthritis, 171 psoriatic arthritis, 132 ulcerative colitis and182 Crohn's disease) (median age 54 years [IQR 43-64]; 56 % women) and 227 controls (median age 44 years [IQR 32-55]; 83 % women) were included in the present analyses. TNFi monotherapy was used by 399 patients, 229 used TNFi in combination with other immunomodulators, 189 methotrexate monotherapy, 39 vedolizumab, 32 JAKi and 73 patients used other drugs. Patients on rituximab were not included. Patients were vaccinated with Pfizer BNT162b2 (54% patients, 14% controls), Moderna mRNA-1273 (16% patients, 40% controls) or a combination of vaccines (30% patients, 46% controls). Patients received the third vaccine dose a median of 120 (IQR 102-143) days after the second dose. After two doses, median anti-Spike antibody levels were significantly lower in patients (861 BAU/ml (IQR 418-4275) than controls (6318 BAU/ml (IQR 2468-9857)), p<0.001 (Figure 1). Following the third dose, patients achieved antibody levels comparable to the two-dose vaccinated controls (median 5480 BAU/ml (IQR 1081-12069), p=0.28) (Figure 1). In the patients anti-Spike antibody levels increased by a median of 2685 BAU/ml (IQR 265-9129) from the second to the third dose. Main factors associated with increased antibody level after the third dose were younger age (β -87.7 (p=0.002)), and vaccine status (mRNA-1273 vaccine (β 5549 (p<0.001)) or a combination of vaccines (β 4367.3 (p<0.001)).
Adverse events were reported by 438 (48%) of patients after the third dose as compared to 471 (54%) after the second dose and 193 (78 %) of controls. Disease flares were reported by 42 (5%) and 69 (8%) patients after the second and third dose, respectively.
Conclusion: This study suggests that a third vaccine dose for immunosuppressed patients closes the gap in serological response between patients and

the healthy population. Antibody levels following the three-dose regimen in IMID patients were comparable to healthy controls vaccinated twice, and no new safety issues emerged. This finding was consistent across all diagnoses and treatment groups, supporting the implementation of a three-dose vaccine regimen as standard in the IMID population.



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sJIA vs AOSD: Two names one disease? What have we learnt so far

OP0193

EFFICACY AND SAFETY OF EMAPALUMAB, AN ANTI-INTERFERON GAMMA MONOCLONAL ANTIBODY, IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME (MAS) IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA) WHO HAD FAILED HIGH-DOSE GLUCOCORTICOIDS

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Background: MAS is a severe, life-threatening complication of rheumatic diseases that occurs most frequently in patients with sJIA. The mainstay of treatment for MAS is high dose glucocorticoids (GCs); however, GCs do not provide adequate control in all patients. Additional treatments are used without a standardized approach; however, morbidity and mortality remain high. Data from animal models of MAS and from observational studies in patients suggest that overproduction of IFNγ is a driver of the hyperinflammation observed in MAS; neutralization of IFNγ has been shown to revert the signs and symptoms of MAS in murine models, and high IFNγ levels are strongly correlated with laboratory parameters of disease severity in patients.
Objectives: To assess the efficacy and safety of intravenous (IV) infusions of emapalumab, a fully human, anti-IFNγ monoclonal antibody, in patients with MAS in sJIA.
Methods: Open-label, single-arm, phase 2 study (NCT03311854) that included patients with MAS (2016 ACR/EULAR criteria) in sJIA who had failed high-dose IV GCs and other treatments. Emapalumab was initiated at a dose of 6 mg/kg on Day 0 and continued at 3 mg/kg every 3 days until Day 15, and then twice weekly until Day 28 to ensure rapid and complete IFNγ neutralization after initiating treatment. As per protocol, 10 infusions were planned over the 4 weeks; however, treatment could be shortened if MAS remission was achieved earlier, or extended if required to achieve remission. Complete response (CR) was defined as resolution of clinical signs and symptoms of MAS according to the investigator, and normalization of laboratory parameters relevant to MAS. All patients were followed up for 4 weeks after the last infusion of emapalumab and offered to enter a 1-year, follow-up study (NCT02069899).
Results: Fourteen patients (10 females) were enrolled (11 in Europe, 3 in the USA). Several patients had previously received cyclosporine A and/or anakinra, in addition to high-dose GCs. Six patients received emapalumab until Day 28. Seven patients discontinued emapalumab early due to MAS remission (as per investigator's assessment); one patient received treatment up to Day 38. Emapalumab treatment rapidly neutralized IFNγ, as documented by CXCL9 levels. A CR was achieved by 13/14 patients during the study. One patient stopped emapalumab after 3 doses because of achievement of MAS remission as per investigator's assessment, but lactate dehydrogenase levels remained >1.5× upper limit of normal. At Week 8, 11/14 patients had a CR; 2 achieved a CR during the study, but not at Week 8, because of a single laboratory parameter abnormality in each patient. Overall, all measured laboratory parameters related to MAS activity rapidly improved with emapalumab treatment. GCs were tapered in all patients by Week 8 (≥50% reduction, n=12; GC dose ≤1 mg/kg/day, n=8). Administration of anakinra for the treatment of underlying sJIA was maintained/introduced during the study, as required. No patients discontinued treatment for safety reasons. One treatment-related serious adverse event was reported (cytomegalovirus reactivation that resolved with antiviral treatment). All patients entered the long-term, follow-up study and were alive at last visit.
Conclusion: Emapalumab administration led to rapid IFNγ neutralization, was efficacious in controlling MAS in all patients, and was well tolerated with a favorable safety profile. These results support the pathogenic role of IFNγ in MAS in sJIA and the therapeutic value of IFNγ neutralization in MAS patients who have failed high-dose GCs.
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Autoinflammation over the course of a lifetime

OP0194

COMBINATION ANAKINRA AND TOCILIZUMAB TO TREAT REFRACTORY MACROPHAGE ACTIVATION SYNDROME TRIGGERED BY ADULT-ONSET STILL'S DISEASE.

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Background: Adult-onset Still's disease (AOSD) is associated with the development of macrophage activation syndrome (MAS) [1], sometimes termed secondary haemophagocytic lymphohistiocytosis (sHLH), a severe hyperinflammatory state with high mortality. Successful management of AOSD and MAS is contingent on early identification and treatment of the syndromes and any triggers, with aggressive immunosuppression in acutely unwell patients [2].
Objectives: To describe the case of a patient with newly diagnosed AOSD who developed severe MAS requiring ICU admission and immunosuppression with high-dose glucocorticoids, tocilizumab and anakinra.
Methods: Case report
Results: A 24-year-old woman attended hospital with a 4 month history of fever, arthralgia, rash and later dry cough. She became hypoxic and was admitted to the ICU for ventilation and vasopressor support. Imaging revealed splenomegaly, pleural effusions and lung consolidation but there was no response to antibiotics and no clear evidence of infection. Cytomegalovirus (CMV) DNA was initially absent, with IgG avidity indicating prior exposure. Bloods confirmed significant inflammation (CRP 107 mg/L, ferritin 6154 µg/L, ESR 47mm/hr) without disordered haematopoiesis. A bone marrow aspirate showed no haemophagocytosis. After extensive investigation a diagnosis of AOSD was made given the fulfilment of the Yamaguchi criteria and absence of evidence of an alternative driver of inflammation.
The patient deteriorated further, with deranged liver chemistry, rising CRP, triglycerides and ferritin (>100,000 µg /L), and trilineage cytopenia raising concern for MAS. This was managed by treating the presumed trigger (AOSD) with intravenous methylprednisolone (IVMP, 3x 500mg then 32mg daily) and anakinra (100mg twice daily). She developed a CMV viraemia that progressed despite aciclovir and later valganciclovir, which was switched to foscarnet and CMV immunoglobulin. The viraemia then stabilised and improved.
Due to persistent pyrexia, tachycardia, and elevated inflammatory markers, further IVMP (3x250mg), increased anakinra doses (100mg IV TDS) and intravenous immunoglobulin (2x60g) were given. A repeat bone marrow biopsy was consistent with MAS and testing for HLH-associated genes was negative.
The patient became increasingly hypoalbuminaemic and oedematous, developing acute kidney injury requiring continuous haemodiafiltration in the ICU. Anakinra was increased to 500mg daily in divided doses. The blood counts improved transiently, before the ferritin rose sharply again, with fevers and broad-spectrum antimicrobials continuing. Cytokine profile testing at this point revealed significant elevation in IL-1b and IL-6. Tocilizumab 8mg/kg fortnightly was added to existing therapy.
After tocilizumab initiation the inflammatory markers, blood counts and clinical state improved, though the patient remained hypertensive despite numerous antihypertensives. She left the ICU ten weeks after initial presentation. Corticosteroids and anakinra were weaned and she was discharged on tocilizumab monotherapy. Renal function did not return, and she continues outpatient haemodialysis.
Conclusion: The evidence base for effective therapies in MAS is poor. Reports exist of the use of either anakinra or tocilizumab [3] but not both agents in combination. In this case, cytokine blockade with both agents produced significant clinical improvement in a critically unwell patient.
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Challenges of fibromyalgia

OP0195

PREVALENCE OF SURVEY-BASED CRITERIA FOR FIBROMYALGIA AND IMPACT ON HOSPITAL BURDEN: A 7 YEARS FOLLOW UP STUDY FROM AN OUTPATIENT CLINIC

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Background: The prevalence of Fibromyalgia (FM) among newly referred patients to rheumatic outpatient clinics is unknown. It is well described that FM patients have increased use of the secondary healthcare facilities, however to what extent the presence of FM burdens the different medical specialties in the secondary health care sector is still unknown.
Objectives: To evaluate the prevalence of fulfilment of survey-based criteria for FM (1) among newly referred patients in a rheumatic outpatient clinic and to compare the use of secondary health care services between survey-based FM- and non-FM cases.
Methods: This is an observational cohort study. Newly referred patients with the suspicion of rheumatic inflammatory disease in an outpatient clinic were evaluated for fulfilment of 2011 FM survey criteria during a 6-month period in 2013. Demographic data were obtained at baseline. Seven years later, patients' medical files were evaluated, and comparisons between groups were made regarding the use of hospital healthcare facilities during the observation period. Results were adjusted for sex, age, and multiplicity.
Results: 248 patients of 300 invited (83%) completed the questionnaire; 90 patients (36%) fulfilled FM criteria at enrolment (Figure 1). FM cases were primarily women (80% vs. 54%) and received more public economical support (62% vs. 20%). At 7 years follow up, adjusted results shows that FM cases had higher number of hospital courses (13 vs. 9) and had undergone more invasive procedures (78% vs. 60%), however differences concerning number of diagnoses between groups were small. Neurologists (42% vs. 28%), gastroenterologists (30% vs. 13%), endocrinologists (40% vs. 21%), pain-specialists (13% vs 3%), psychiatrists (20% vs. 7%), and abdominal surgeons (43% vs. 30%) were consulted more often by FM cases than non-FM cases.
Conclusion: Fulfilment of FM survey criteria among newly referred patients with the suspicion of a rheumatic inflammatory disease to a rheumatic outpatient clinic is frequent. The burden to the secondary healthcare system in these patients is significant. The finding of a minimal difference between groups regarding the number of resulting diagnoses underlines that prolonged and excessive use of healthcare services with referral to multiple specialists should be avoided. Our study findings also support that FM continues to present a challenge for healthcare professionals as well as for patients. A timely and coordinated effort across medical specialties, including rheumatologists, could reduce diagnostic delay, facilitate management, and reduce healthcare utilisation in this patient population.
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Table 1. Highlighting primary baseline data, primary and secondary endpoints, main differences regarding invasive procedures and medical specialists consulted during seven years follow up.

	Fibromyalgia, n= 86	Non-fibromyalgia, n=151	*P*-value*
Age (years), mean (SD)	**52.5 (13.7)**	**52.8 (18.6)**	***0.432***
Female, %	**80**	**54**	***< 0.001***
Social economic support of any kind, %	**62**	**20**	***< 0.001***
Rheumatic inflammatory disease, %	**28**	**42**	***0.028***
Number of different courses at hospital, Mean (SD)	**12.7 (0.9)**	**9 (0.6)**	***< 0.001***
Number of diagnoses, Mean (SD)	**5 (0.3)**	**4 (0.2)**	***0.003***
Numbers of admissions to hospital, Mean (SD)	**2.1 (0.3)**	**1.9 (0.2)**	***0.550***
Number of Medications, Mean (SD)	**7.1 (0.5)**	**6.1 (0.3)**	***0.057***
Number of Pain Medications, Mean (SD)	**1.6 (0.1)**	**1.2 (0.1)**	***0.004***
Invasive procedures total, %	**78**	**60**	**0.003**
Joint surgery other (including arthroscopies), %	**30**	**17**	***0.026***
Gastroscopy, %	**37**	**14**	***< 0.001***
Colonoscopy, %	**38**	**21**	***0.004***
Psychiatry, %	**20**	**7**	**0.006**
Abdominal Surgery, %	**43**	**30**	**0.042**
Pain centre, %	**13**	**3**	**0.015**
Endocrinology, %	**40**	**21**	**0.003**
Gastroenterology, %	**30**	**13**	**0.003**
Neurology, %	**42**	**28**	**0.029**

Acknowledgements: Study data were collected using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at OPEN (Open Patient Data Explorative Network), Odense University Hospital, Region of Southern Denmark
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OP0196

HIGH SYMPTOM BURDEN AND LIMITED CHANGES IN FIBROMYALGIA PATIENTS' HEALTH STATUS TWO YEARS AFTER PARTICIPATION IN A MULTICOMPONENT REHABILITATION PROGRAMME

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Background: Patients with fibromyalgia (FM) suffer from high symptom burden and few available treatments. EULAR evidence-based recommendations for the management of FM state that optimal management should focus on prompt diagnosis, patient education and non-pharmacological treatments[1]. A recent systematic review of mindfulness- and acceptance-based interventions for patients with FM showed small to moderate beneficial health effects[2]. We tested a 10-session group-based mindfulness- and acceptance-based intervention, the Vitality Training Programme[3], followed by low threshold physical exercise counselling in primary health care, compared to treatment as usual (TAU) for patients diagnosed with FM.
Objectives: To explore possible changes in health status in a group of FM patients two years after participation in a multicomponent rehabilitation programme.
Methods: A total of 170 patients with confirmed FM diagnosis according to ACR 2011-criteria were randomised, 85 to intervention and 85 to control. Self-reported data were collected electronically at baseline, 3 and 12 months. There were no statistically significant health effects in any disease-related variables at 12 months. However, there were significant between-group differences in patients' tendency to be mindful[4]. All patients were asked to complete the same questionnaires two years after completion of the intervention group. Because the TAU-group had been offered the same programme after 12 months, only data from the intervention group was included in this study. Primary outcome was Patient Global Impression of Change (PGIC), scored as 1= much worse, through 4=no change, to 7=much better. Values 6 and 7 were considered clinically relevant improvement. Secondary outcomes were self-reported pain, fatigue, sleep quality, psychological distress, mindfulness, physical activity, motivation and barriers for physical activity, and work participation. Mean changes from baseline to two years were analysed by paired sample t-tests.
Results: Totally, 48 (56.5%) of the patients who had been randomised to the intervention group responded to the questionnaires, 94% female, median (range) age 47 (28 to 54), symptoms duration 12 (5 to 33) years. Only seven patients reported clinically relevant improvement on PGIC; 32 (67%) reported little better, worse or no change (Figure 1). There were small improvements in pain (p=0.048), fatigue (p=0.014) and self-efficacy for physical activity (p=0.012), but the changes were probably not clinically relevant. The improvement seen in patients' tendency to be mindful at 12 months was sustained (p=0.012). Only 58% were in paid work compared to 70% at baseline.

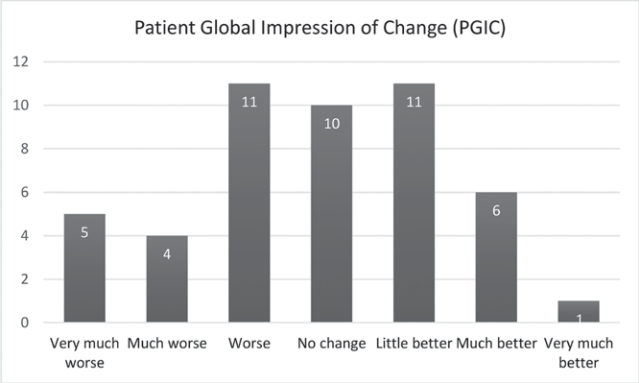

Figure 1.

Conclusion: Two years after participation in a multicomponent rehabilitation programme comprising mindfulness and acceptance training and physical activity counselling, FM patients still reported high symptom burden and no improvement in their health status. The increased tendency to be mindful was not reflected in improvements in disease-related outcomes. It was not possible to compare groups (intervention and TAU), because the TAU-group had been offered the intervention before the two-years data collection. However, there was no worsening of symptoms, which might have been the case without any intervention.
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Long-COVID

OP0197

POST-TRAUMATIC STRESS DISORDER AND SYMPTOMS IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES DURING THE COVID-19 PANDEMIC: PRELIMINARY RESULTS FROM THE PERMAS STUDY

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Background: The COVID-19 pandemic, with its uncertainties, fears of contagion, mass lockdowns and containment measures, has dramatically impacted on people's everyday lives leading to an increased risk of mental disorders, particularly Post-Traumatic Stress Disorder (PTSD). Despite evidence in general population and healthcare workers1,2, scant data emerged on vulnerable populations, such as of patients with chronic illness, particularly rheumatic and musculoskeletal diseases (RMDs)3,4, who also underwent difficulties in the management and treatment of their disorders.
Objectives: To assess PTSD and post-traumatic stress symptoms in a sample of patients with RMDs, during the COVID-19 pandemic in Italy.
Methods: PERMAS is a monocentric prospective observational study led by the Rheumatology Unit, the Psychiatric Clinic and the Institute of Management of the School of Advanced Studies. Patients with a RMD diagnosis, were consecutively enrolled from May 2021 to January 2022. During the visit, sociodemographic characteristics and psychopathological data were collected through online survey, whereas clinical data were collected by physician. The survey included the Trauma and Loss Spectrum- Self Report (TALS-SR) and the Impact of Event Scale- Revised (IES-R), aimed to assess symptomatological PTSD and post-traumatic stress symptoms related to the impact of the COVID-19 pandemic.
Results: A total of 194 eligible patients, with a mean age of 50.3±12.17 years, was included: 142 (73.19%) were females; 112 (57.74%) patients reported connective tissue diseases (CTD), 63 (32.47%) arthritis and 19 (9.8%) vasculitis. A total of 33 (17%) subjects reported a symptomatological PTSD by means of the TALS-SR. The prevalence of Partial PTSD (defined by at least 2 out of the 4 criteria for DSM-5 diagnosis of the disorder) was 56.7%, with significant higher rates among females (90, 81.8%) with respect to males (20, 18.2%) (p=.013). Accordingly, a IES-R mean total score of 21.90 ±15.98 was found in the total sample and a gender difference emerged, with higher mean scores among females rather than males (23.42 ±16.26 vs 21.90 ±15.98, p=.031).
Conclusion: The present findings point out high prevalence rates of symptomatological PTSD among patients suffering from RMDs, highlighting the potentially traumatic burden of the COVID-19 pandemic in this particular population, especially among females, suggesting the need of further investigations to address tailored prevention and intervention strategies.
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How do we overcome the research-to-practice gap? Implementation of evidence into the rheumatology practice

OP0198-HPR DEVELOPMENT OF AN INTERDISCIPLINARY NURSE-COORDINATED SELF-MANAGEMENT INTERVENTION (INSELMA) FOR PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: Up to 30% of patients with inflammatory arthritis (IA) do not respond sufficiently or tolerate the pharmacological treatment. Consequently, they may experience a substantial impact of their arthritis in everyday life. Even patients in remission or low disease activity state are at risk of substantial arthritis related symptoms and burden. These patients may need coherent interdisciplinary self-management support to manage symptoms and life with the chronic condition to increase their quality of life. A previous EULAR review on the effectiveness of self-management interventions in patients with IA (1) found that well-structured self-management programmes were lacking or were poorly reported.
Objectives: This study aimed to develop a nurse-coordinated interdisciplinary self-management intervention, delivered in routine clinical care, for patients with inflammatory arthritis and with a substantial impact of their arthritis to support their self-management ability.
Methods: The study was planned across two Danish hospitals following the British Medical Research Councils (MRC) framework for developing and evaluating Complex Interventions (2). The development process consisted of four phases: 1) a comprehensive scoping review on patients support needs and elements in self-management interventions; 2) six workshops involving health professionals (rheumatologists, nurses, physiotherapists, occupational therapists, a social worker and a psychologist) and 2 patient representatives from the two hospitals and staff from primary health care, 40 people in total; the workshops focused on ideas for the content, outline of the intervention and needs for competence development of the staff; 3) self-management, self-efficacy, health literacy and principles of Acceptance and Commitment therapy (ACT) were selected as theories to tailor the intervention and 4) development of a manual through recurrent feedback from patient research partners, clinicians and the involved researchers. Two patient research partners with IA were involved in all phases of the development of the intervention.
Results: A six month nurse-coordinated interdisciplinary self-management intervention was developed (Figure 1) consisting of: 1) an initial holistic assessment is carried out by a coordinating outpatient nurse. Patients are asked to identify up to five important activities they are unable to perform or having difficulty with in accordance with the Patient Specific Functional Scale; 2) a goal-setting and action planning process involving the patient, relatives and the coordinating nurse; 3) Ongoing support to achieve the goals. The opportunities for support include individual consultations by the coordinating nurse (telephone, online or face-to-face, 2.5 hours in total), and a maximum of four consultations by a physiotherapist and or an occupational therapist. Also, support from primary care, and an online session by a social worker about social support opportunities are offered. Two team conferences led by the coordinating nurse can be held during the intervention period. A status consultation will be held after 6 months. A manual for the initial screening, inclusion, detailing the intervention, outcomes and additional materials to support the intervention was developed. Competence development of the health professionals who are to deliver the intervention was planned and completed.

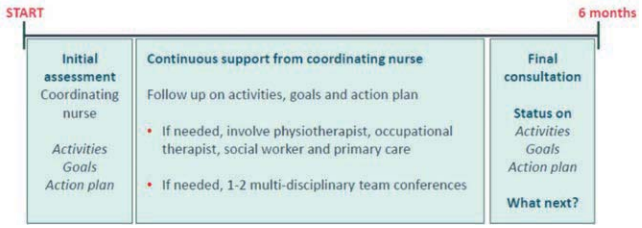

Figure 1. Illustration of the 6-month INSELMA intervention

Conclusion: A nurse-coordinated interdisciplinary self-management intervention (INSELMA) was developed and described based on MRC's framework for the development of Complex Interventions. The intervention is ready for feasibility testing before adaptation and test in a subsequent Randomized Controlled Trial.
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Strengths and weaknesses of experimental models: Moving from animals to human clinical trials

OP0199 RADIOMIC SIGNATURES REFLECT TREATMENT RESPONSE TO NINTEDANIB IN PRECLINICAL LUNG FIBROSIS MODEL

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Background: Responses to anti-fibrotic drugs in preclinical disease models are difficult to quantify by histological analysis of single tissue sections. Quantitative in-depth analysis of imaging data, termed "radiomics", may represent a more reliable and accurate measure of treatment response since the pathology of the whole organ is captured.
Objectives: To study the potential of µCT-derived radiomic features to reflect response to Nintedanib in the bleomycin (BLM)-induced murine model of fibrosing interstitial lung disease.
Methods: All C57BL/6J mice from both study groups were intratracheally instilled with 2 U/kg BLM on day 0 to induce lung fibrosis. Nintedanib was administered daily by gavage at 60 mg/kg for two weeks starting from day 7 (n=15). Controls received equivalent treatment with vehicle-only (n=19). Whole lung µCT scans (SkyScan 1176, Bruker) of each animal were acquired at baseline (day 0), pre-treatment (day 7), and post-treatment (day 21). The Ashcroft score was assessed on Sirius Red stained lung sections post-treatment. Lung volumes in µCTs were defined semi-automatically in MIM Software (6.9.2), followed by extraction of radiomic features with our in-house developed software Z-Rad (7.3.1). Each data set contained 1'386 features, describing image characteristics with histogram, texture, and wavelet functions. Data pre-processing involved removal of features sensitive to intra- and interobserver delineation variability (ICC<0.75), highly correlated features (Pearson's r>0.95), and features not

significantly changing between days 0 and 7 (p>0.05). Agglomerative clustering of radiomic temporal trajectories was performed on the Nintedanib group to identify distinct feature clusters. The identified feature sets were then used to plot average feature value trajectories for both study groups in each cluster. To identify features significantly different between a) Nintedanib vs. control, and b) pre- vs. post-treatment, Mann-Whitney U and Wilcoxon signed-rank tests were used, respectively. Samples were pooled from two independent experiments.

Results: Evaluation of tissue sections did not show a significant treatment-induced reduction of fibrosis with average Ashcroft scores of 3.7 (±1.2 s.d.) and 3.4 (±1.6 s.d.) in Nintedanib and control samples, respectively (p>0.05). Radiomics data analysis revealed two feature clusters in Nintedanib samples, composed of 52 features (cluster 1) and 96 features (cluster 2), the trajectories of which were then plotted for both study groups. In cluster 1, feature value trajectories significantly decreased in both Nintedanib and control group between pre-and post-treatment (p<0.001), whereas feature values in cluster 2 remained flat (p>0.05). Importantly, Nintedanib-treated mice displayed a much more pronounced feature value decrease post-treatment in cluster 1 compared to the control group (p<0.05). Here, feature values post-treatment resembled pre-disease baseline conditions in the Nintedanib group (p>0.05), whereas the control group remained significantly different from baseline (p<0.01). Cluster 1 was composed of 6 histogram, 11 texture, and 35 wavelet features, emphasizing the role of high-dimensional metrics for the detection of differences.

Conclusion: Histological quantification of lung fibrosis accounts only for a small fraction of the whole pathology in a spatially heterogeneous disease. We demonstrated that µCT-derived radiomic features identified significant differences on imaging level following Nintedanib treatment, which we could not reliably detect on tissue level using Ashcroft scoring. These findings hold great potential for the development of novel readouts for improved stratification of anti-fibrotic treatment effects in preclinical models.

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From abstract to concrete – the variety of activities of PARE organizations

OP0200-PARE BARING IT ALL: A REPORT ON THE SEXUAL AND REPRODUCTIVE HEALTH EXPERIENCES OF WOMEN+ WITH INFLAMMATORY ARTHRITIS, RHEUMATIC AND PSORIATIC DISEASES

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Baring it All: a report on the sexual and reproductive health experiences of women+ with inflammatory arthritis, rheumatic and psoriatic diseases

Background: Inflammatory arthritis and psoriasis commonly affect women+ in the prime of their lives with significant impacts on sexual, reproductive and mental health. There have been some efforts to provide educational resources and other support by patient organizations globally but no broad efforts to evaluate patient needs and experiences throughout their lives and disease course.

Objectives: The Canadian Arthritis Patient Alliance, Canadian Association of Psoriasis Patients, Canadian Psoriasis Network and Canadian Spondylitis Association co-developed and launched the ***Women's Sexual and Reproductive Health Survey*** on International Women's Day 2021. Findings were analyzed in the report, ***Baring it All: A survey and recommendations on sexual and reproductive health needs of women+ with rheumatic, inflammatory and psoriatic diseases.***

Methods: Survey participants were asked about their experiences with:

- sexual health
- family planning
- parenting
- perimenopause/menopause
- pain
- mental health
- accessing care and treatments (including paying for medications)

A total of 439 people across Canada who identified as female (women+) living with inflammatory arthritis, rheumatic, and psoriatic diseases participated. Results were analyzed to provide a national picture and insights based on Canadian geography, age, and identification as a member of a racialized community and/or as LGBTQ2S+.

Results: Over 60% of survey participants indicated that they did not have enough information about sexual health and their condition(s) and identified information needs relating to managing the impact of fatigue on their sex life, advice on improving sex drive, and sexual positions comfortable for their body as priorities. Less than half of survey participants indicated receiving counseling from a doctor before pregnancy. Many participants expressed a need for information about medication safety during pregnancy and breastfeeding and managing the impact of pain.

Two in five survey participants (40%) indicated they were currently experiencing symptoms of perimenopause or menopause; however, only half of them (21%) indicated they understood how menopause affects their condition(s). Over 50% of participants indicated they understand how menopause affects bone health.

Though 91% of survey participants indicated that they can honestly discuss pain with their healthcare provider, only 58% feel like their healthcare provider relates to the pain they experience from their condition. The vast majority (87%) of survey participants worry about the impact of their condition on their mental health, yet only 16% of participants identified having a mental health professional (e.g., psychiatrist, psychologist, social worker) as part of their care team.

Conclusion: There are several unmet needs in accessing care and information throughout the lives of women+ living with inflammatory arthritis, psoriatic and rheumatic diseases. A shift in models of care to focus on patient needs could assist patients in navigating a range of difficult decisions, such as choosing safe medications for pregnancy and breastfeeding, reconciling health, work and parenting demands, understanding menopause, accessing mental health support, and managing pain. A sex and gender lens can be used in the creation of resources and policies to support people with these condition(s).

REFERENCES: none

Disclosure of Interests: Laurie Proulx Grant/research support from: Laurie Proulx is 2nd vice president of the Canadian Arthritis Patient Alliance, a patient run, volunteer-based organization that receives project funding from pharmaceutical companies. CAPA received unrestricted educational grants from UCB Canada for this project. Survey design & data analysis, report preparation and dissemination were carried out independently by CAPA, CAPP, CPN, and CSA. Shannon Ketelaars Grant/research support from: Shannon Ketelaars is the Executive Director of the Canadian Spondylitis Association (CSA), a national charitable not-for-profit that receives project funding from the pharmaceutical sector. CSA received unrestricted educational grants from UCB Canada for this project. Survey design & data analysis, report preparation and dissemination were carried out independently by CAPA, CAPP, CPN, and CSA., Rachael Manion Grant/research support from: Rachael Manion is the Executive Director of the Canadian Association of Psoriasis Patients (CAPP) and the Canadian Skin Patient Alliance, both of which are national not-for-profit patient organizations that receive project funding from pharmaceutical companies. CAPP received unrestricted educational grants from UCB Canada for this project. Survey design & data analysis, report preparation and dissemination were carried out independently by CAPA, CAPP, CPN, and CSA. Antonella Scali Grant/research support from: Antonella Scali is the Executive Director of the Canadian Psoriasis Network (CPN), a national not-for-profit organization. CPN receives project funding from pharmaceutical companies including unrestricted educational grants from UCB Canada for this project. Survey design & data analysis, report preparation and dissemination were carried out independently by CAPA, CAPP, CPN, and CSA.

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OP0201-PARE DEVELOPMENT THROUGH CO-CREATION OF A PERSONALIZED, MULTIMODAL, PHYSIOTHERAPIST-LED, WORK-ORIENTED INTERVENTION TO INCREASE WORK ABILITY IN WORKING PEOPLE WITH RHEUMATOID ARTHRITIS OR AXIAL SPONDYLOARTHRITIS.

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Background: Although work ability is considered a key element of quality of life for working people, work is underexposed in current treatment in people with rheumatoid arthritis (RA) or axial spondyloarthritis (axSpA). Most people with RA or axSpA attend a physiotherapist (PT). Physiotherapy can effectively improve physical fitness, which is associated with work ability. Therefore, PTs might play an important role in optimizing work ability of people with RA or axSpA.
Objectives: Developing a personalized, multimodal, PT-led, work-oriented intervention for working people with RA or axSpA who have a reduced work ability, through a co-creation process.
Methods: A systematic co-creation process with all relevant stakeholders was conducted following the Medical Research Council (MRC)-framework for complex interventions (see Figure 1). In step 1, all relevant clinical guidelines and treatment protocols were assessed. Based on the results of this assessment, a draft version of the intervention was developed, consisting of mandatory (i.e., work-oriented intake, patient education, exercise therapy, referral-roadmap of work-related professionals) and optional treatment modalities (i.e., workplace-intervention, self-management course). In step 2, focus groups with people with RA/axSpA, PTs and occupational/rheumatology experts were organized and qualitatively analysed. In the focus groups, barriers and facilitators of work-oriented treatments and necessary adaptations to the draft intervention were discussed. In step 3, a pre-test was performed to test the feasibility of the intervention in a primary physiotherapy setting, which was evaluated in the group of PTs participating in the pre-test in step 4. Finally, in step 5, a final focus group with researchers in this field was held to discuss the findings from previous steps in this co-creation process and to agree on necessary adaptations in the final intervention.

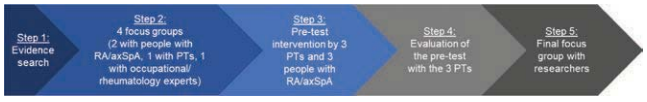

Figure 1. Process of systematic development of co-created, work-oriented physiotherapist-led intervention following the MRC-framework.

Results: After developing the draft intervention, we conducted two focus groups with people with RA/axSpA (n=16; 4 with RA, 12 with axSpA), one focus group with PTs (n=12) and one focus group with occupational/rheumatology experts (n=9; 2 rheumatologists, 2 nurse specialists, 1 physiatrists, 1 physician assistant, 1 nurse practitioner, 1 labour expert and 1 occupational therapist). People with RA or axSpA emphasized 3 aspects: i) PTs should have adequate expertise in RA/axSpA, ii) high potential for a role of 'buddy' by PTs to support them in work-related problems, and iii) most PTs currently lack adequate expertise on work-related problems. PTs and experts underlined the importance of extensive training of PTs on work-related laws and regulations and adequate (work-related) interprofessional collaboration. After revision of the draft intervention, the intervention was tested for feasibility by three PTs and three working people (2 with RA, 1 with axSpA), who indicated that the intervention was feasible and that the developed intervention facilitated PTs to support people in optimizing their work ability. However, adequate training on providing this intervention was recognized to be essential. In a final focus group with researchers (n=6), consensus was reached on minor adjustments to the intervention that were based on findings from previous steps.
Conclusion: Through a systematic co-creation process based on the MRC-framework, we have been able to develop a personalized, multimodal, PT-led, work-oriented intervention for working people with RA or axSpA and a reduced work ability. The (cost-)effectiveness of this intervention is currently being tested in a large trial (Physiotherapy WORKs study).
Acknowledgements: This study is funded by the Dutch Arthritis Society (ReumaNederland) and the Scientific College of Physical Therapy (WCF) of the Royal Dutch Society for Physical Therapy (KNGF). This study is registered in the Netherlands Trial Register under number NL9343.
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OP0202-PARE NRAS NEW2RA RIGHT START SERVICE FOR PEOPLE RECENTLY DIAGNOSED WITH RA

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Background: The National Rheumatoid Arthritis Society (NRAS) follows best practice, evidence-based standards in all we do. Huge strides have been made in the diagnosis and treatment of Rheumatoid Arthritis (RA), but impact on quality of life can be significant and for many, RA remains hard to come to terms with. Anxiety and depression are frequent co-morbidities seen in RA, and this can impede people's ability to acquire knowledge of their disease together with supported self-management skills and coping strategies.
Objectives: The aim of Right Start (RS) is to improve outcomes of the recently diagnosed with RA through a framework of emotional, educational and peer support, and access to high quality supported self-management resources tailored to individual need. RS also enables us to dispel myths and unhelpful health beliefs so that people get the 'right start' on their journey with RA to maximise health outcomes. A diagnosis of an incurable disease treated with life-long strong drugs is a life-changing event and without the right support it can be an isolating and emotionally very challenging experience for both the individual and their close family. We also wanted to give an understanding of the key role that supported self-management can play in improving quality of life, giving people back some control over their symptoms. Our goal was also to create a quick and easy way for HCPs to refer their patients to Right Start in a consented and GDPR compliant way.
Methods: HCPs are able to refer their patients via the 'Refer a patient' button on our website which takes them to a simple form which is filled in and submitted to NRAS with the patient's consent. NRAS receive the referral and the form is integrated with our Salesforce database, and we contact the patient. RS involves a simple, 4-step process and the individual receives: A call (up to 1 hr) with a member of our helpline; 1:1 peer support (phone/Teams/Zoom) from trained volunteers with RA and access to 24/7 online community support; a tailored package of hard copy information with e-links/video/webinars of interest sent by post; further follow up available from helpline and individual peer support. RS enables health professionals to meet their responsibilities against NICE Quality Standard 33, Statement 3, (patient education and access to self-management resources) on which they are audited through National Early Inflammatory Arthritis Audit (NEIAA). RS is included in the NICE shared learning database of best practice examples. RS also supports the EULAR Recommendations for implementation of self-management strategies in inflammatory arthritis.
Results: Since launch at BSR 2019, over 90 UK rheumatology units have referred over 435 patients to this service. Approx. 1/3rd cannot be contacted and after 3 attempts a letter and newly diagnosed pack are sent, inviting contact at future date. Anecdotally people are highly satisfied with this service and a number of units are referring multiple patients where the service is embedded in the patient pathway. To gather empirical data on the impact of the service NRAS has partnered with Manchester University to undertake an Enhanced Right Start pilot in 5 UK rheumatology units involving the use of validated patient reported outcome and experience measures from users recruited, and quantitative/qualitative data from health professionals. The pilot is due to commence recruitment in early Feb, 2022. Meantime, referrals to the standard service continue to grow.
Conclusion: Workforce shortages in all posts within the multi-disciplinary team), 2 years of pandemic resulting in HCPs under immense pressure and time poor with a large backlog of patients has meant it's extremely difficult for HCPs to meet Quality Standards and goals of audit. Feedback informs that HCPs find Right Start a beneficial service to refer their patients to and people with RA have found it more than helpful. We anticipate that the results of the Enhanced Right Start Service Pilot (see Results) will provide additional evidence to support HCP patient-referral to this service.
Acknowledgements: I would like to acknowledge the support of a number of UK consultant rheumatologists in the early stages of the development of this service, in particular Dr. James Galloway.
Disclosure of Interests: Ailsa Bosworth Speakers bureau: Where I have in the past the honorarium has been paid to NRAS not to me personally, Grant/research support from: Unrestricted educational grants have been paid to NRAS by a number of pharmaceutical companies in last year, Clare Jacklin Speakers bureau: Where I have in the past the honorarium has been paid to NRAS not to me personally, Grant/research support from: Unrestricted educational grants have been paid to NRAS by a number of pharmaceutical companies in the last year.
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OP0203-PARE FATIGUE IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: A SCOPING REVIEW ON ITS DEFINITION, MEASUREMENT INSTRUMENTS, DETERMINANTS, IMPACT AND INTERVENTIONS

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Background: Fatigue is one of the most important symptoms of patients with rheumatic and musculoskeletal diseases (RMDs) and numerous studies on fatigue in patients with RMDs have been published. However, no overview exists

of all topics relevant to understand and manage fatigue in patients with rheumatoid arthritis (RA), spondyloarthritis (SpA, including psoriatic arthritis (PsA)), osteoarthritis (OA) and fibromyalgia (FM).
Objectives: To scope published reviews on aspects of fatigue identified by patients in a preceding initiative as relevant for care and mapped to the following research areas: 1) definitions for fatigue, 2) measurement instruments for fatigue, 3) determinants of fatigue, 4) impact of fatigue, and 5) effect of interventions on fatigue in patients with RMDs of interest.
Methods: A methodological framework for scoping reviews was followed[1]. A systematic literature search was performed in five bibliographical databases. Data selection followed by data extraction was done by two independent researchers.

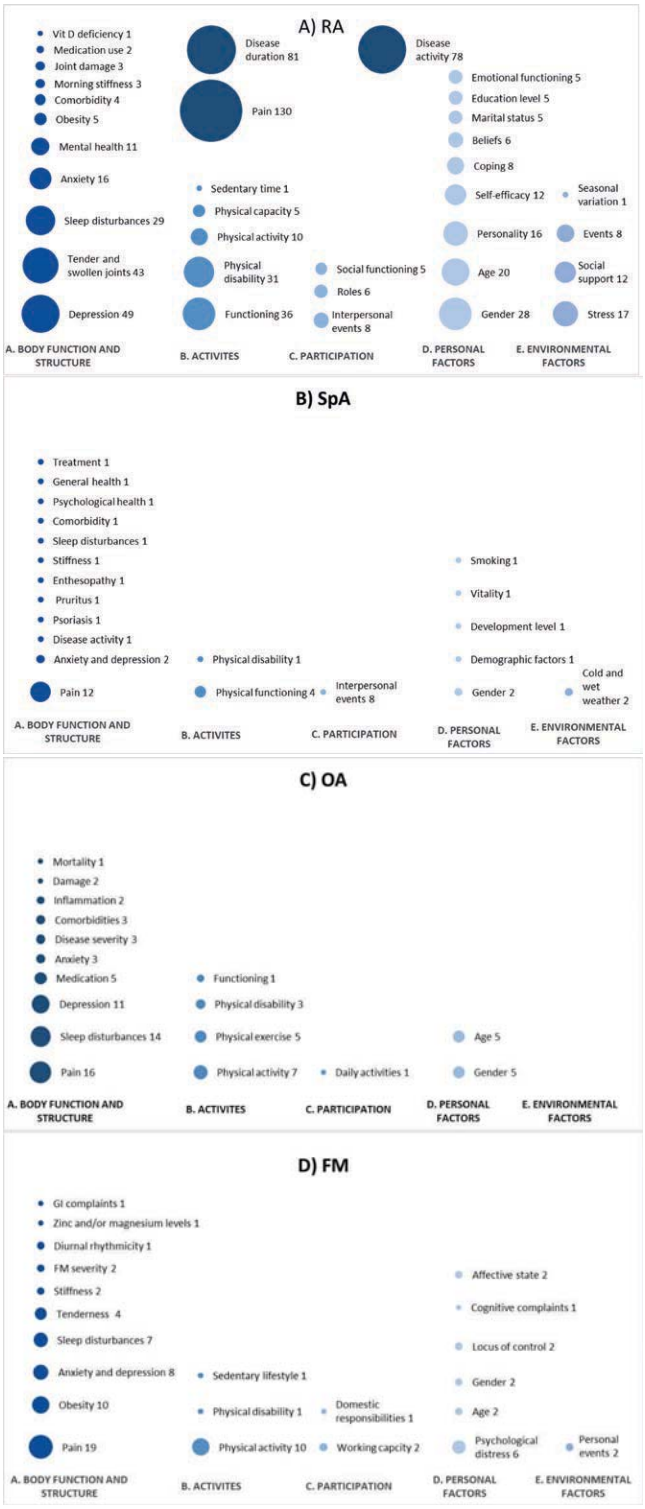

Figure 1. Determinants of fatigue and the related minimal number of underlying studies within reviews

Included reviews were categorized in Cochrane reviews (CRs), non-Cochrane systematic reviews (SRs) or narrative reviews (NRs). Data extraction was performed hierarchal based on review type (CRs followed by SRs and NRs) and year of publication. SRs and NRs were excluded if there was overlap in the underlying studies within the reviews. Data synthesis accounted for hierarchy in level of evidence by review type (CRs were considered as best evidence followed by SRs and NRs). For each research area and stratified per type of RMD, a narrative synthesis was performed. Two meetings were organized with a patient panel to discuss the results from a patient perspective.
Results: The scoping review included 144 reviews (18 CRs, 42 SRs and 84 NRs). RA was addressed most frequently (60/144 (42%)). Fatigue was a secondary outcome in the majority of these reviews.
No agreed upon definition for fatigue in any of the RMDs was found. Across reviews, there was agreement that fatigue is a complex multifactorial and highly subjective symptom, including various subtypes with specific characteristics.
Reviews discussed 23 generic and 3 disease-specific self-reported outcome instruments to measure fatigue in RA, SpA and FM, but no reviews on outcome instruments for OA were found. Four of these 23 (17.4%) instruments included validated cut-off values to diagnose or classify excessive fatigue.
Numerous factors were associated with fatigue (Figure 1), but the study design (often cross-sectional) hindered studying causality. Across RMDs, pain, physical function, and depressive symptoms were the most frequently studied disease related factors; gender and stress the most frequent contextual factors related to fatigue. The strength of association was small or moderate, but mostly not reported. Work disability was one of the most frequently studied consequences of fatigue in RMDs, followed by impact on pain, physical activity and stress. Strength of these associations was not reported.
Finally, both pharmacological and non-pharmacological interventions, including physical activity-based and psychological interventions, generally had a small positive effect on fatigue in RMDs. No reviews described the effect of pharmacological interventions on fatigue in OA.
All results were relatable for the patient panel and some missing aspects were pointed out. The patient panel advised to develop a research agenda to specifically diagnose and treat excessive fatigue in RMDs, as continuing the current path is likely to increase publications about fatigue, but unlikely to change patients' lives.
Conclusion: This scoping review emphasizes the complexity of fatigue. Only a minority of the reviews had a primary focus in fatigue, whereas to patients this prominent symptom deserves specific attention.
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1. Arksey H. Scoping studies: towards a methodological framework. Int J. Soc. Res. Methodo. 2005
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OP0204-PARE

MEANINGFUL PATIENT INVOLVEMENT IS CRITICAL TO SUCCESSFUL INTERNATIONAL GRANT APPLICATIONS: THE CASE OF THE HIPPOCRATES CONSORTIUM

L. Werner[1] on behalf of HIPPOCRATES consortium ["Health initiatives in Psoriasis and PsOriatic arthritis ConsorRTium European States"]. [1]*The Danish Psoriasis Association, Research, Copenhagen, Denmark*

Background: HIPPOCRATES is a large, international research project addressing the unmet needs of people with psoriatic arthritis (PsA). It aims to improve early identification of PsA in people with psoriasis, as well as therapeutic options and outcomes for people living with PsA. The project will run for five years with a budget of € 21 million provided by the Innovative Medicines Initiative (IMI) – a joint undertaking of the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA). During the evaluation of the HIPPOCRATES grant application, the patient involvement was highly praised: "*A strength of this proposal is that patient representative organisations seem highly integrated in the proposal and will be important avenues for dissemination.*"
Objectives: To explore the components of an effective strategy for incorporating the patient perspective in an international research consortium.
Methods: The experiences of the first six months of patient involvement in HIPPOCRATES were examined. We organized a survey and an online workshop with all participating patient research partners (PRPs) to gather data on the experiences of participation in the different working groups of the project, as well as to discuss common challenges and solutions.
Results: Patient involvement was visible and reported from the very beginning of the project, including participation of PRPs in the first consortium meeting for study design. The chosen strategy is characterized by an integrated approach containing multiple layers of patient involvement [Figure 1], with the consortium following the EULAR recommendations for the inclusion of patient representatives in scientific projects.

The active participation of 13 PRPs with well-defined roles and responsibilities ensures the preservation of the patient perspective during the entire duration of the project. Together they form the HIPPOCRATES Patient Advisory Council (PAC). PRPs are represented in the project's management team, in all work packages and in the External Advisory Board. Three patient organisations support the project: GRAPPA-EU (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) and EULAR PARE (People with Arthritis/Rheumatism in Europe) as consortium partners, and EUROPSO (European Federation of Psoriasis Patients' Associations). EULAR is co-leading the work package focusing on Communication, Dissemination, Exploitation and Sustainability, and especially those activities targeting patients, PRPs (regular educational sessions), patient organisations and the general public. Finally, people with PsO will be recruited for a large European cohort study (HIPPOCRATES Prospective Observational Study, HPOS) which aims to identify clinical and molecular risk factors for developing PsA.
Results from the PRP survey were positive. Almost all PRPs have been invited to their work package meetings and included in email exchanges, and all feel well-included in their assigned groups and roles. Nevertheless, it was reported that some PRPs may be reluctant to raise their voice or to be involved in discussions at virtual meetings. This was one of the topics addressed during the online workshop, together with discussions on ethics and recruitment strategies for HPOS.

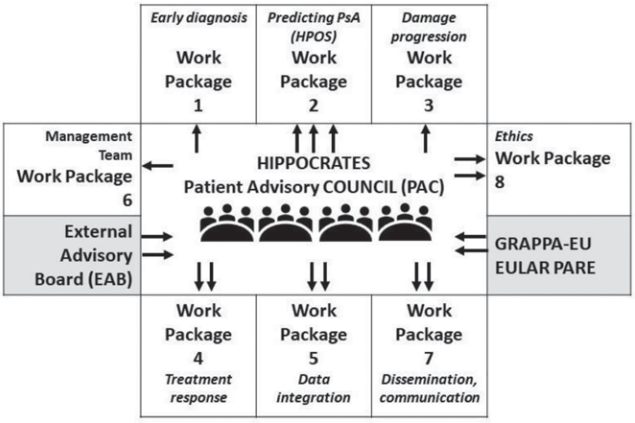

Figure 1 Multiple layers of patient involvement in HIPPOCRATES

Conclusion: It has been central to the HIPPOCRATES ethos that highly experienced PRPs were involved from its initial conception. PRPs with leading responsibilities in patient organisations or representing relevant academic backgrounds have contributed substantially to the definition of research priorities and will have active on-going engagement in the interpretation and implementation of future results. By demonstrating the pervasive benefit of the patient voice throughout the project, HIPPOCRATES will be an example for future projects in RMD and health research.
Acknowledgements: Meaningful patient involvement is critical to successful international grant applications: the case of the HIPPOCRATES consortium ["Health initiatives in Psoriasis and PsOriatic arthritis ConsorRTium European States"]
Lars Werner on behalf of the HIPPOCRATES Patient Advisory Council (PAC)
Disclosure of Interests: Lars Werner Speakers bureau: Novartis, Janssen, LEO Pharma, Consultant of: Novartis, Janssen, LEO Pharma, B-I, UCB, Grant/research support from: Novartis, Janssen, LEO Pharma, UCB, AbbVie, Sanofi, B-I, BMS, Pfizer, Employee of: LEO Pharma, AbbVie
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OP0205-PARE GREEK RMDS PATIENTS' NEED FOR SELF-MANAGEMENT AND THE USE OF NEW TECHNOLOGIES: THE CASE STUDY OF THE HELLENIC LEAGUE'S AGAINST RHEUMATISM SUPPORT LINE

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Background: The Hellenic League Against Rheumatism (ELEANA/HELAR) offer psychosocial support to its member, patients with RMDs, their families and everyone else that's interested in RMDs. More than 5000 members from all over Greece, with local ELEANA/HELAR groups in major cities such as Athens, Patras, Karditsa, Trikala, Thessaloniki and others. The helpline has been receiving incoming calls from patients with RMDs, members of ELEANA, their relatives and others that are interested in RMDs or are requesting information.
Objectives: This case study aimed at outlining that self-management is the main reason for incoming calls to ELEANA's helpline and secondly that during the pandemic and even after lockdown measures being lifted patients still use the online support offered thus making it apparent that digitalization is not a trend anymore but a necessity.
Methods: Empirical data from the helpline were gathered through the day-to-day helpline registry. This is a detailed registry containing basic info on demographics of the callers, reasons for calling and outcome of communication. Descriptive statistics as well as qualitative data have been used such as observations of the trained staff of the helpline.
Results: From 543 incoming calls, 49,91% were about self-management and the rest 50,09% were calls requesting information. 52,40% of self-management calls were about psychological issues (anxiety, depressive symptoms) and the rest were about treatment (adherence), such as the use of medication, alternative treatments, medical issues and questions on RMDs. 40,96% of patients with RMDs called again the helpline to follow up and 61,25% used online tools to communicate with the helpline both times. Psychologists receiving calls observed that patients needed counseling regarding their self-management, especially during the pandemic and that even though lockdown is lifted they keep on requesting online communication instead of face-to-face meetings.
Conclusion: The above findings show that digitalization is not a trend rather than a necessity in the self-management of RMDs. Patients seem to find it easier receiving support online and the requests for online support for their anxiety, depressive symptoms, difficulties in managing their medication makes it clear that more emphasis needs to be put on self-management programs.
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OP0206-PARE FOOD COMMUNITIES

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Background: In recent years the focus on healthy food and lifestyle has become a more important part of everyday life for many – with or without RMD. Many NGO-initiatives engaging citizens cooking and eating together has seen the light of day; people meet to talk, laugh and have a good time while making a healthy meal.
The kitchen is an often discussed topic among the volunteers and members of The Danish Rheumatism Association. "Simple" tasks as opening a can of beans or cutting bread can be complicated for people with RMDs. The fundamentals of cooking are different for this group of people; hence the idea of communities around "arthritis friendly" food unfolded during fall 2019.
Objectives: The main objective is to create "food communities" for people with RMDs, helping them to get a better understanding of how to make "arthritis friendly food", dispel the myth that it is expensive and hard, and to give them inspiration to better working positions with assistive devices - resulting in a healthier lifestyle which is important to keep the inflammation low and the quality of life high.
Methods: To obtain these objectives, a dietitian is facilitating 6 three hour "courses" guiding the participants through healthy cooking – each course with a different theme/subject which is introduced through a short presentation. Two volunteers are responsible for booking kitchen facilities (often school kitchens which is free of charge), coordination with the dietitian and making sure everything runs smoothly and that the atmosphere is top-notch. An occupational therapist is joining the group one time to ensure optimal working positions and introducing and demonstrating assistive devices.
One of our main goals is to create sustainable and longer lasting (more than 6 facilitated courses) communities, which is why an important part of the volunteer's responsibility is to initiate a talk about the opportunity of meeting without a dietitian. The 6 facilitated courses aim to give the group the ability to find recipes (provided by DRA) and being comfortable cooking with ingredients that the average Dane might not use very often. Furthermore, our assumption is that the group creates social bonds and therefore an interest in keeping these relations.
Results: About twenty groups all around Denmark has been a part of the course so far. The feedback from the participants is extremely good – they feel they are learning in an inspiring environment while having a great time with their new acquaintances. Unfortunately, only one of the groups has become a community that exists after the facilitated courses. One of the reasons is, without a doubt, that most of the groups have been affected by different Covid-19 restrictions which has had an impact on the level of social bonding and feeling of ownership. But most participants feel that the dietitian is crucial for further engagement.
Conclusion: The concept has been very successful in terms of creating a course that imparts useful knowledge about "arthritis friendly" food and lifestyle for people with RMD's. It seems we need to make corrections to create the basis for sustainable communities; small changes that helps the group visualizing how to overcome the challenge of the absence of a dietitian, the logistics of grocery shopping for a group etc. We plan to leave out the dietitian from the fifth of the six courses to prepare the group to establish their own "food community" with lots of healthy food, learning experiences and high spirit.
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HPR interventions on the spotlight

OP0207-HPR EFFECT OF FOOT ORTHOSES IN REDUCING PAIN IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A 12-MONTH RANDOMISED CLINICAL TRIAL

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children and adolescents [1]. The manifestation of JIA may include joint swelling, tenderness, and painful limitation with joint movement. Only few studies have explored the effect of foot orthoses (FOs) alone in children with JIA [2,3]. These studies showed FOs can reduce pain in children with JIA, however, further research with larger sample sizes and longer follow-ups are needed [4]. Prescribing FOs on the same day of the initial assessment may promote early clinical and targeted intervention, which is the gold standard approach in paediatric rheumatology.
Objectives: This single blinded multicentre randomised clinical trial (RCT) aims to investigate the effect of customised prefabricated FOs in reducing pain amongst children and adolescents with JIA.
Methods: Overall, 66 children and adolescents with JIA presenting with foot symptoms were recruited from the Sydney Children's Hospitals Network (Westmead and Randwick) and John Hunter Children's Hospital (Newcastle). The primary outcome measure was pain with a minimal clinical significance of 8mm on the visual analogue scale (VAS). Participants were randomly allocated to receive either customised prefabricated or sham FOs. The trial intervention was a low-density Slimflex Simple device that was customised at chair-side. The control (sham) device was made of 2mm flat leather board with no corrective modifications. Standardised tests such as the Foot Posture Index, navicular drift and drop were used to identify biomechanical abnormalities. The FOs were worn for a total of 12 months, with data collected at baseline, 4 weeks, 3, 6 months and 12 months.
Results: Reduction in self-reported pain was statistically and clinically significant at 4-weeks (p=0.018, -14.92 [-27.30, -2.55]) and 3 months (p=<0.001, -28.93 [-40.90, -16.96]) post intervention in favour of the trial group. The 6- and 12-month follow-ups were not statistically or clinically significant. Parent reported pain was statistically and clinically significant at the 3-month (p=<0.001, -21.92 [-33.16, -10.67]) in the reduction of pain in favour of the trial group. However, parent reported pain was not statistically significant at the 4-week, 6- and 12- month follow-ups. These results are similar to child reported pain with a p-value of less than 0.001 and average coefficients twice that of the clinical significance cut-off for VAS pain in paediatric rheumatology. The trial intervention was safe and tolerated well by participants with high compliance and adherence rates.
Conclusion: Results of this clinical trial indicate customised preformed FOs can be effective in reducing pain and in children with JIA experiencing foot and ankle symptoms. Significant clinical effects appear to be within the first 3-months of intervention prescription and reduce beyond 6 months. Overall, this podiatric intervention was safe, inexpensive, well tolerated and it can be easily implemented as part of the multidisciplinary paediatric rheumatology care.
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OP0208-HPR EFFECT OF AN 8-WEEK SPECIALIZED PHYSICAL THERAPY PROGRAM ON SEXUAL HEALTH IN FEMALE PATIENTS WITH SYSTEMIC SCLEROSIS AND IDIOPATHIC INFLAMMATORY MYOPATHIES: A PILOT STUDY

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Background: Systemic rheumatic diseases like systemic sclerosis (SSc) and idiopathic inflammatory myopathies (IIM) may affect all aspects of life, including sexual health However, no non-pharmacological treatment has been proposed to date.
Objectives: This is the pilot project aiming to investigate the effect of an 8-week physical therapy program on sexual function in women with SSc and IIM.
Methods: In total, 12 women with SSc and 4 women with IIM, who fulfilled the ACR/EULAR 2013 criteria for SSc and the Bohan/Peter 1975 criteria for DM/PM, respectively, were enrolled in the study. Based on patient's possibilities and willingness to participate in the program, they were divided into an intervention group (IG) (6 SSc/2 IIM, mean age: 46.8±3.1 years) and a control group (CG) (6 SSc/2 IIM, mean age: 46.3±3.0 years). The IG underwent the 8-week tailored physiotherapy program, including the pelvic floor exercise and physiotherapy of musculoskeletal problems subjectively limiting the patient's sexual function (1 hour supervised physiotherapy twice weekly), whereas the control group received no specialized therapy. At weeks 0 and 8, all patients filled in questionnaires assessing sexual function: Female Sexual Function Index (FSFI), Brief Index of Sexual Functioning for Women (BISF-W); sexual quality of life: Sexual Quality of Life-Female (SQoL-F); functional ability: Health Assessment Questionnaire (HAQ); quality of life: Medical Outcomes Short Form-36 (SF-36) and depression: Beck's Depression Inventory-II (BDI-II). At the baseline, patients in IG were assessed by a physician (medical history, mRSS, ESSG activity score, MITAX, MYOACT) and by a physiotherapist (pelvic floor function assessment–PERFECT scheme, MMT-8, Functional Index-II). Normality of data was tested, and inter-group analysis was performed with 2-way ANOVA and intra-group analysis by Friedmann's test.
Results: Compared to observed statistically significant deterioration in CG over the period of weeks 0-8, we found statistically significant improvement in both sexual function questionnaires: FSFI (p=0.043), BISF-W (p=0.040), functional status: HAQ (p=0.018), and quality of life: SF-36 Physical Somponent score (0.050). Only numerical improvement in IG compared to numerical deterioration in CG, which has not reached statistical significance, was observed in SQoL-F, BDI-II, and SF-36 Mental Component Score.
Conclusion: Our physiotherapy program not only prevented the natural course of progressive deterioration of functional abilities, but also led to a significant improvement in sexual function and overall quality of life in women with SSc and IIM. Physical therapy might become one of the possible therapeutic treatments for sexual problems in women with SSc and IIM.

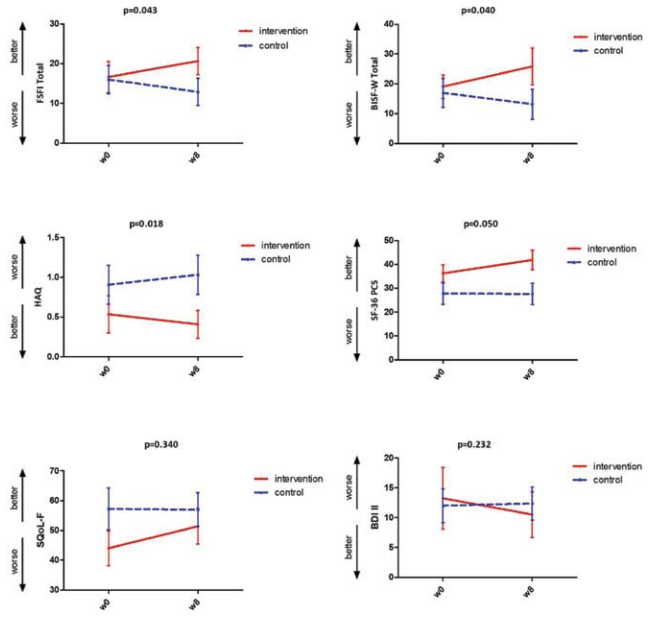

Figure 1.

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Disclosure of Interests: None declared
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OP0209-HPR BRIDGE – A QUALITY IMPROVEMENT PROGRAM IN TEAM-BASED REHABILITATION: RESULTS FROM A MIXED METHODS STUDY

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Background: There is a well-known variability in the quality of rehabilitation provided to patients with rheumatic and musculoskeletal diseases (RMDs). Elements to be improved are a higher standardization of the core content, optimal patient participation in goal setting and continuation of the process in tailored follow-up. More knowledge is needed on critical features for successful delivery of improvement programs in rehabilitation.
Objectives: To investigate how a team-based quality improvement program was implemented and how it influenced the quality in RMD rehabilitation.
Methods: This convergent mixed methods study is nested within a stepped-wedge, randomized controlled trial where providers at 8 rehabilitation-centers delivered traditional programs in the control phase (T1), and added the BRIDGE quality improvement program in the intervention phase (T2). The BRIDGE program addressed a dialog-based, multidisciplinary approach to support the patients' self-management, comprising motivational interviewing, goal setting, plans for rehabilitation, feedback and monitoring of progress, and tailored follow up. Providers answered 19 structure indicators from a quality indicator (QI) set for RMD rehabilitation [1] at T1 and T2, and a program-fidelity checklist with 18 items at T2 (both scored 0-100%, 100=best). Qualitative data was collected in three focus groups (FG) with the BRIDGE providers, and analyzed using reflexive thematic analysis. Integration and discussion of findings from the different data sources are ongoing, in our research group.
Results: Median summary pass rate for the structure QIs for all centers increased from 53 to 90% between T1 and T2. Program-fidelity was high, with a median summary score of 94% (range 6–100%), but lowest for program-components related to follow-up and communication with external services. Themes developed from the FG interviews reflected that variations in how the program was implemented related to features of the providers and institutions. More specific; the delivery of high-quality rehabilitation depended on the degree to which the providers trained their communication skills, used available tools to support their practice, and grounded their interventions in professional reasons. Critical organisational features at the institutions were dedicated time for team-work based on the patients' plans for self-management, and sufficient attention to needs for involvement of next of kin or external services. Additionally, better program-implementation occurred if providers experienced an institutional culture for quality improvement, such as educational initiatives from the leaders.
Preliminary integration of data is summarized in Figure 1. Congruent evidence in both quantitative and qualitative findings addressed the sustained needs for better quality in the area of follow-up across levels of care. However, the qualitative findings provided expanded insights on variability also in initial parts of the rehabilitation process. Presumably, these variations in delivery reported in interviews are important for the effectiveness of a quality improvement program, but difficult to capture in questionnaires.

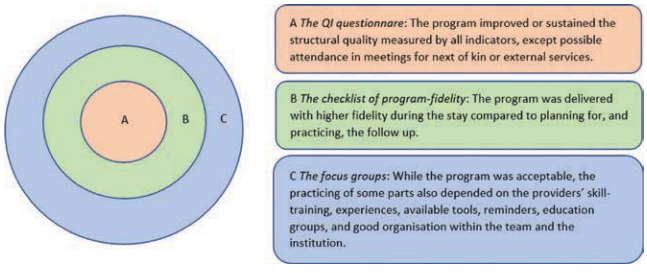

Figure 1. Complementary viewpoints on how the BRIDGE program was provided and how it influenced the quality of rehabilitation.

Conclusion: To target specific strategies for quality improvement, we suggest a combined attention not only to recommended care reflected in quality indicators and measurable aspects of fidelity, but also to contextual factors, including the providers' confidence and skills needed to provide a high-quality delivery of all components in a rehabilitation improvement program.
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OP0210-HPR

THE OCCURRENCE OF OVERWHELMING FATIGUE IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS: A DAILY DIARY STUDY

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Background: Cross sectional research shows that nearly half of the individuals with osteoarthritis (OA) experience fatigue and over one third experience severe fatigue (1). However, few studies have addressed the unpredictable and fluctuating course of fatigue in OA including the occurrence of overwhelming fatigue as evidenced from qualitative research (2). In-depth understanding of the course of fatigue and its determinants may inform clinical decision making and treatment.
Objectives: To explore 1) the occurrence of overwhelming fatigue and its determinants and 2) the variability of daily experienced fatigue in individuals with knee OA.
Methods: A daily diary design. 73 participants with a self-reported diagnosis of knee OA aged >40 years and in possession of a Smartphone completed a baseline questionnaire on demographics, health status (EQ5D-VAS), and self-efficacy (Arthritis Self-Efficacy Scale (ASES)). This was followed by daily assessments with regard to overwhelming fatigue, fatigue severity, pain, sleep, and perceived exertion of physical activities (PEPA) over a 7 day period. A yes/no format was used to assess overwhelming fatigue and a numeric rating scale (NRS, 0-10) was used to assess fatigue severity, pain, sleep, and PEPA. The variability of fatigue was assessed by calculating the standard deviation (SD) per participant over this 7 day period. Comparisons between participants with and without overwhelming fatigue were conducted by unpaired t-tests and Pearson's chi-square tests where appropriate.
Results: 47 participants were included in the analysis. Overwhelming fatigue occurred at least once in 26 (55%) participants with mean= 2.7 (SD= 1.4) over a 7 day period. Differences of participants with and without overwhelming fatigue are displayed in Table 1.

Table 1. Characteristics of participants (n=47) included in the analysis.

Characteristics*	All participants (n=47)	Participants with overwhelming fatigue (n=26)	Participants without overwhelming fatigue (n=21)	Difference (95% CI)	p-value
Age	63.4 (8.6)	61.7 (8.5)	65.5 (8.5)	-3.8 (-8.8; 1.2)	0.13
Female (n (%))	39 (83%)	23 (88%)	16 (76%)		0.47
BMI	27.4 (4.6)	28.0 (5.1)	26.5 (3.8)	1.5 (-1.1; 4.1)	0.25
Health status	67.5 (13.8)	66.0 (13.5)	69.5 (14.2)	-3.5 (-11.7; 4.7)	0.39
ASES pain	2.9 (1.0)	3.2 (0.8)	2.5 (1.1)	0.7 (0.1; 1.3)	0.02
ASES os	2.5 (0.8)	2.7 (0.8)	2.2 (0.7)	0.5 (0.1; 1.0)	0.02
Fatigue severity	4.9 (1.7)	5.5 (1.5)	4.1 (1.6)	1.3 (0.4; 2.3)	0.01
Pain	4.2 (1.9)	4.8 (1.6)	3.4 (2.0)	1.4 (0.3; 2.5)	0.01
Sleep	5.9 (1.6)	5.5 (1.7)	6.4 (1.4)	-0.9 (-1.8; -0.0)	0.05
PEPA	4.9 (1.2)	5.0 (1.2)	4.8 (1.3)	0.2 (-0.6; 0.9)	0.64

ASES, Arthritis Self-Efficacy Scale; ASES os, other symptoms; PEPA, perceived exertion of physical activities. For health status, ASES pain, ASES os, and sleep, higher scores reflect better outcomes; for PEPA, higher scores reflect more PEPA; for fatigue severity and pain, higher scores reflect higher levels. *mean (SD) unless otherwise statedg.

The variability of daily experienced fatigue per participant ranged from SD= 0.2 to 2.9 (Figure 1). This was not significantly different between participants with and without overwhelming fatigue.

Figure 1. ***Standard deviations of average fatigue severity over a 7 day period per participant (n=47).***

Conclusion: Our findings suggest that more than half of the participants experienced at least one episode of overwhelming fatigue and that this is related to self-efficacy, fatigue severity, pain, and sleep. Fatigue remained fairly stable over time by the majority of participants.
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OP0211-HPR

EXPERIENCES DURING THE COVID-19 PANDEMIC AMONG PEOPLE WITH INFLAMMATORY ARTHRITIS. "REOPENING OF SOCIETY IS HARDER THAN LOCK-DOWN" - A QUALITATIVE INTERVIEW STUDY

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Background: People with inflammatory arthritis (IA) treated with conventional or biological immunosuppressive disease-modifying anti rheumatic drugs (DMARDs), were initially considered to have an increased risk of severe illness from SARS-CoV-19 (COVID-19) infection compared to the general population. Although resent studies have not confirmed this, people with IA have reported high level of anxiety and self-isolation during the pandemic (1). Only few studies have qualitatively explored how people with IA experience the impact the COVID-19 pandemic and the SARS-CoV-19 vaccinations.
Objectives: To explore how people with IA experienced restrictions during the COVID-19 pandemic and the possible impact of vaccination on their protection against COVID-19 and their everyday lives.
Methods: Semi-structured in-depth interviews were conducted via telephone or video with 19 people with IA in May – August 2021, shortly after they were enrolled in the national COVID-19 vaccination programme (all Danish citizens >18 years of age invited for SARS-CoV-19 vaccination, free of charge, with timing depending on age and comorbidities). At the same time, society gradually reopened after a complete lock-down. Qualitative content analysis, inspired by Graneheim and Lundman (2), was applied to analyse the data. Two patient research partners were involved in development of the study protocol, an interview guide and in the interpretation of findings.
Results: The participants' age ranged from 21 to 64 years, median 50 years. 7 male and 12 female, all diagnosed with IA (Psoriatic arthritis n=4, Axial Spondyloarthropathy n=4, Rheumatoid arthritis n=9, and Juvenile arthritis n=2) and 14 were treated with DMARDs. Two had not accepted vaccination.
The analysis derived five themes: 1: *"Changing and divergent information".* The participants experienced there was an overload of general information to the public, while targeted information on the specific risk for people with IA was lacking; 2: *"Individual interpretation of own risk",* reflecting that participants had to find their own level of daily-life restrictions, a task they found to be very difficult; 3: *"Impact on everyday life".* They took self-imposed precautions to protect themselves and their families from attracting COVID-19; *4*: *"Position in society and the vaccination programme",* emphasizing that participants were affected by the inconsistent announcements from authorities whether they were considered to be in particular risk or not, and some expressed concerns regarding the DMARDs influence on the effect of the vaccine and 5: *"Reopening is somehow harder than lock down".* A societal spirit of being "in this together" emerged through the lock-down and some were concerned that fewer restrictions during reopening of the society would put them in higher risk of a COVID-19 infection and force them to continue self-isolation.

Table 1. Quotation to illustrate the findings

"… you felt like one in the crowd and then everything is easier. Even though it was difficult. But then; it was difficult for all of us. It had nothing to do with my rheumatic disease… we were in this together... But it was harder when the reopening started. Because it´s like; I'm back on the platform and can't just jump on the train, can't go anywhere, that is...I'm just not quite ready to jump into society like everyone else..."

Conclusion: The COVID-19 pandemic affected the everyday lives of people with IA due to the authorities' restrictions and further self-imposed precautions throughout lock down and reopening of society. People with IA experienced a lack of consistent information and felt alone to assess their own SARS-Cov-19 infection risk.

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OP0212-HPR

PATIENT ASSESSMENT CHRONIC ILLNESS CARE (PACIC) AND ITS ASSOCIATIONS WITH QUALITY OF LIFE AMONG SWISS PATIENTS WITH SYSTEMIC SCLEROSIS – A MIXED METHODS STUDY

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Background: Variable disease presentation and symptom burden in patients living with systemic sclerosis (SSc) require a chronic care approach including competent, coordinated, multidisciplinary collaboration as well as self-management support targeting individual patient needs. The Chronic Care Model (CCM) is a longstanding and widely adopted model guiding chronic illness management.[1] Little is known about how CCM elements are implemented in SSc care or how patients' care experiences relate to health-related quality of life (HRQoL).
Objectives: First, to describe current SSc care in Switzerland according to the CCM from the patient perspective and examine relationships with HRQoL. Second, to explain these results by patients' illness and care experiences.
Methods: We employed an explanatory sequential mixed methods design (Figure 1). First, we conducted a cross-sectional quantitative survey (n=101 Swiss patients) using the Patient Assessment of Chronic Illness Care (PACIC-20)[2] and Systemic Sclerosis Quality of Life (SScQoL)[3] questionnaires. Because PACIC has not been used in the context of SSc, we used the Mokken model to test the construct validity of the PACIC scale and its subscales. After excluding five problematic items, *H* coefficients were 'strong' for the subscales and the global scale (0.52) suggesting a robust unidimensional scale.

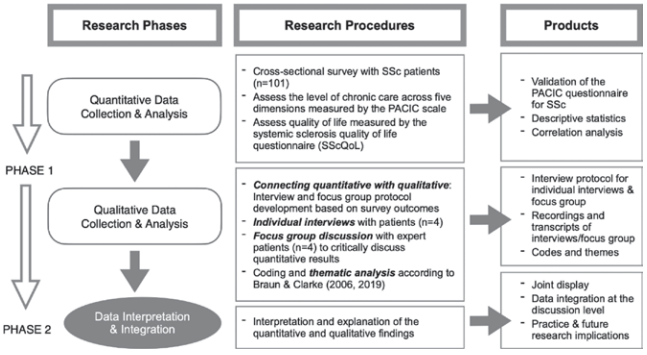

Figure 1. Schematic of the explanatory, sequential mixed methods design

Next, we used data from individual patient interviews (n=4) and one patient focus group (n=4) to further explore care experiences of people living with SSc with a focus on the PACIC dimensions.
Results: The mean overall PACIC-15 score was 3.0 / 5.0 (95% CI: 2.8–3.2, n= 100), indicating care was 'never' to 'generally not' aligned with the CCM. Lowest subscale scores related to 'goal setting/tailoring' (mean = 2.5, 95% CI: 2.2–2.7) and 'problem solving/contextual counselling' (mean = 2.9, 95% CI: 2.7–3.2) (Table 1). No significant associations were identified between the mean PACIC-15 and SScQoL scores.

Table 1. Summary of scores (n=101) for the 15-item PACIC scale (adapted version of the original 20-item scale)

	PACIC mean scores (95% CI)
PACIC 15-item mean score	3.0 (2.8–3.2)
1: Patient activation *(mean of items 1–3)*	3.4 (3.1–3.6)
2: Delivery system design/ Decision Support *(items 4–6)*	3.2 (3.0–3.4)
3: Goal setting/ Tailoring *(items 7–9)*	2.5 (2.2–2.7)
4: Problem solving/ Contextual Counselling *(items 12–15)*	2.9 (2.7–3.2)
5: Follow-up/ Coordination *(items 19–20)*	3.3 (3.0–3.5)

Note: CI=Confidence interval; PACIC=Patient Assessment of Chronic Illness Care

Interviews revealed patients frequently encounter major shortcomings in care including *experiencing organized care with limited participation, not knowing which strategies are effective or harmful and feeling left alone with disease and psychosocial consequences*. Patients often responded to challenges by *dealing with the illness in tailored measure, taking over complex coordination of care and relying on an accessible and trustworthy team.*

Conclusion: The low PACIC mean overall score is comparable to findings in patients with common chronic diseases. Key elements of the CCM have yet to be systematically implemented in Swiss SSc management. Identified gaps in care related to lack of shared decision-making, goal-setting and individual counselling –aspects that are essential for supporting patient self-management skills. Furthermore, there appears to be a lack of complex care coordination tailored to individual patient needs.

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OP0213-HPR RECOMMENDATIONS FOR NURSES IN THE MANAGEMENT OF RA PATIENTS ON TREATMENT WITH JAKINIBS

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Background: The number of new treatments available in rheumatology continues to increase. Kinase inhibitors, or jakinibs, pose an added challenge due to their variety and because they are oral. The most important role of the rheumatology nurse is patient education, especially on how to take the medication. The better the nurse understands the drugs, the better their practical recommendations and decisions will be and the better they will be able to respond to the patient. Guidelines or recommendations for inflammatory diseases do not usually include key practical details for nurses. It is our understanding that these points that will subsequently determine adherence and safety should be specially addressed in a specific document for nurses.

Objectives: To establish practical, evidence-based nursing recommendations for the management of people with RA undergoing treatment with jakinibs.

Methods: To reach an evidence-based consensus we used systematic review and Delphi survey. A multidisciplinary panel of experts was formed with 6 rheumatology nurses, 2 rheumatologists, 1 psychologist, 1 dietician-nutritionist and 1 patient on treatment with jakinibs. This panel met on 2 occasions and was kept informed at all times of the progress of the project through the Miro platform. At the preparatory meeting the scope and users, structure and PICOt questions were established (these included efficacy and adverse effects, infections, cardiovascular risk, surgery, vaccination, pregnancy and breastfeeding, interactions and switches between jakinibs).

The steering group made recommendations based on the issues raised at the first meeting. Only those that achieved 65% in favour were included as items in a Delphi survey. The Delphi survey was sent to all members of the society nurses and rheumatologists (n=60). Voting ranged from 0 to 10 (strongly disagree to strongly agree). Items with more than 75% agreement in the first round did not proceed to a second round.

Results: The Table 1 shows the recommendations with their level of evidence and level of agreement after the Delphi (n=40; 67%). One item with only 50% agreement was rejected and did not proceed to a second round.

Table 1.

Recommendation	Level of evidence	Degree of agreement
Before starting treatment with a jakinib, it should be confirmed that the patient has no contraindications.	5	100%
The patient's efficacy and outcome expectations for the drug should be explored and those that need to be adjusted.	5	85%
It should be indicated that a double dose should not be taken if one is missed.	4	100%
As with other DMARDs, the patient should be instructed that close management will follow.	5	99%
The use of contraception and discontinuation of the drug is recommended in case of gestational desire or unplanned pregnancy.	3	96%
It is recommended to explain the warning signs of infection: fever, blisters, burning pain in the ribs, itching when urinating, productive cough, diarrhoea, pus-filled wounds, phlegmon.	1a	100%
It is recommended to instruct the patient on preventive measures for infectious diseases (dental and hand hygiene, HPV, social distance, etc.).	1a	89%
Vaccination against common germs in immunocompromised persons and shingles with the current vaccine is recommended.	1a	93%
CV risk factors should be monitored, and the patient trained for signs of thrombosis, HF or ischaemic heart disease.	1a	89%
Close monitoring of elderly patients (CV risk, infections) is recommended.	2	100%
Emphasis on adherence is recommended for jakinibs to be effective.	3	100%
Before surgery, discontinuation of jakinib should be scheduled depending on the type of surgery and comorbidities.	3	89%

Conclusion: These recommendations will allow a practical approach to the management of jakinibs by nurses and enjoy an adequate consensus among potential users.

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OP0214-HPR EDUCATIONAL NEEDS AMONG HEALTH PROFESSIONALS IN RHEUMATOLOGY: LOW AWARENESS OF EULAR OFFERINGS AND UNFAMILIARITY WITH COURSE CONTENT AS A MAJOR BARRIER – A EULAR FUNDED EUROPEAN SURVEY

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Background: Health professionals in rheumatology (HPRs) should participate in post-graduate or continuous education to update and advance their knowledge and skills. This can improve patient outcomes and increase quality of care.[1] EULAR aims to become a leading provider of postgraduate education for HPRs.

Objectives: The aims of this study were to evaluate the current motivations for participating in postgraduate education of HPRs, identify barriers and facilitators for participation in postgraduate education, and evaluate participation in the current educational offerings of EULAR for HPRs across Europe.

Methods: An online survey was developed and distributed in collaboration with the EULAR Standing Committee of Education and Training (ESCET) and the Paediatric Rheumatology European Society (PReS). The questionnaire was translated by national HPR representatives in 24 languages to cover the 25 national member organisations. Barriers were assessed using 5-point Likert scales, higher scores representing higher barriers. Quantitative data were analysed using descriptive statistics. In addition, we ran the Latent Dirichlet Allocation (LDA) on the answers to the open questions. LDA is an unsupervised probabilistic topic modelling technique that extracts the meanings of a pre-defined number of topics. Design of the survey and reporting of results were done according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES).

Results: The online questionnaire was accessed 3,589 times but only 667 complete responses were recorded. HPRs from 34 European countries responded to the survey; 80% of whom were women. The highest-ranked educational need was prevention, including lifestyle interventions and professional development. Although EULAR was well known among HPRs, only 32.1% of HPRs in adult care and 18.6% of HPRs in paediatric care have ever heard of the EULAR School of Rheumatology (Table 1 A).

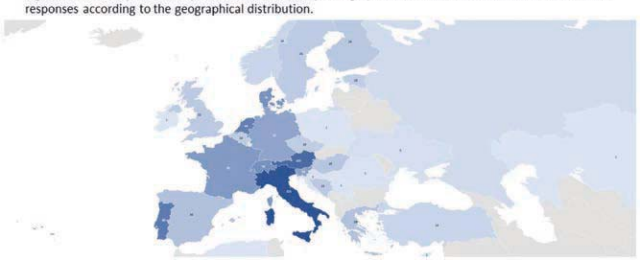
Table 1. A: Feedback on EULAR. Data are presented separately for HPRs in adult and paediatric care; except for the filter questions, no mandatory questions were included in the survey. To clarify the number of responses per question, the number of valid answers for each question was reported.

Variables	HPRs in adult care	HPRs in paediatric care
Have you ever heard of the EULAR School of Rheumatology?	614	43
I am not sure, n(%)	62 (10.1%)	7 (16.3%)
No, n(%)	355 (57.8%)	28 (65.1%)
Yes, n(%)	197 (32.1%)	8 (18.6%)
Are you aware of courses offered by the EULAR School of Rheumatology? (sub question)	197	8
I am not sure, n(%)	30 (15.2%)	2 (25.0%)
No, n(%)	63 (32.0%)	5 (62.5%)
Yes, n(%)	104 (52.8%)	1 (12.5%)
Have you ever attended one of the EULAR School of Rheumatology courses? (sub question)	103	1
I am not sure, n(%)	1 (1.0%)	0
No, n(%)	47 (45.6%)	0
Yes, n(%)	55 (53.4%)	1 (100%)
Have you ever participated in a EULAR annual congress meeting?	618	43
I am not sure, n(%)	11 (1.8%)	0
No, n(%)	457 (73.9%)	39 (90.7%)
Yes, n(%)	150 (24.3%)	4 (9.3%)

The main barriers to participation in EULAR's educational offerings were identified by HPRs in adult care and in paediatric care (respectively) as: the unfamiliarity with the course content (3.48 [±1.50]; 3.92 [±1.46]), the associated costs (3.44 [±1.35]; 3.69 [±1.28]) and English language (2.59 [±1.50]; 2.80 [±1.34]).

Conclusion: EULAR is well-known by HPRs in Europe, however, awareness of educational offerings is low and barriers to participation are numerous. To become the leading provider of postgraduate training by 2023, EULAR could use a "franchise" model that can be tailored to local conditions. This could be achieved by strengthening national organizations by actively involving them in the development of training programs and disseminating these programs and offerings through their networks.

Figure 1: Worldmap of the respondents in this survey. The graph below shows the distribution of the HPRs' responses according to the geographical distribution.



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Improving outcomes for children with JIA

OP0215

WHAT DOES THE PATIENT WELL-BEING VAS TELL US WHEN THE PHYSICIAN GLOBAL ASSESSMENT SCORE IS ZERO? ANALYSIS OF A LARGE MULTINATIONAL DATASET

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Background: Parent- and child-reported outcomes (PCROs) are measures that reflect the parent and child perception of rheumatic disease course and effectiveness of therapeutic interventions. Among PCROs for the assessment of patients with juvenile idiopathic arthritis (JIA), the most widely adopted is the parent/patient global evaluation or well-being visual analogue scale (WB-VAS). Several studies in JIA have highlighted the discrepancies in the assessment of the disease status between the physician and the parent/patient. This difference might be due to the WB-VAS measuring a broader construct than the physician global assessment (PGA).

Objectives: To evaluate, in a large multinational sample of JIA patients, the disease characteristics of subjects considered as inactive by the physician with an increased WB-VAS score.

Methods: Data from the multinational dataset of patients enrolled in the Epidemiology Treatment and Outcome of Childhood Arthritis (EPOCA) study were analyzed. We have included only subjects with a PGA score of 0. PCROs were collected through the juvenile arthritis multidimensional assessment report (JAMAR). We compared demographic features, socio-economic status, level of education, subtype of JIA diagnosis and the main PCROs (pain level, presence of morning stiffness, count of joints with swelling or pain, functional ability, disease activity level, ongoing therapy, presence of medications side effects and health related quality of life measured with the pediatric rheumatology quality of life (PRQL) scale) between subjects with WB-VAS ≤ 1 and > 1.

Results: A total of 3537 patients were sorted into two groups according to the WB_VAS score: 2862 subjects were included in a first group (WB_VAS ≤1); 675 in a second one (WB-VAS >1). Respectively, 17,6% and 18,1% of families belonged to the lower socio-economic status, 70,5% and 71% to the intermediate, 11,9% and 10,8% to the higher. The percentages of patients in the three levels of education was not different in the two groups:20,2% and 22% in the lower, 48,9% and 50,1% in the intermediate, 30,8% and 27,9% in the higher level of education. No significant difference was observed in the distribution of JIA categories in the two groups. Subjects in first group were younger at disease onset (5.6 vs 6.4 years). Comparison of main PCROs results is presented in the Table 1 below.

Table 1.

PCROs	WB_VAS ≤1	WB_VAS >1	p
VAS_Pain (mean)	0.3 (0.9)	2.4 (2.4)	<0.001
Presence of morning stiffness (%)	227 (8.0)	285 (42.4)	<0.001
Patients under treatment (%)	1919 (67.2)	540 (80.2)	<0.001
Reporting side effects (%)	421 (22.1)	236 (43.9)	<0.001
Number of adverse events to the therapy (mean)	0.2 (0.7)	0.8 (1.5)	<0.001
Juvenile Arthritis Functionality Scale (JAFS)Total Score (mean)	0.5 (1.6)	3.0 (4.4)	<0.001
JIA Quality of Life (JQL) Total Score (mean)	1.6 (2.3)	6.4 (4.4)	<0.001
VAS-Disease Activity (mean)	0.4 (1.3)	2.3 (2.4)	<0.001
Count of active joints (mean)	0.2 (0.7)	1.4 (2.2)	<0.001

Conclusion: We have analyzed the variables that might determine a difference between the physician's assessment of inactive disease and the parent's/patient's perception of well-being. In particular, socio-economic status, level of education, and gender representation seem not to impact on the general perception of well-being, while pain seems to have the greatest influence on the parent/patient quality of life assessment. Finally, children with lower WB-VAS score were younger at disease onset.

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OP0216

DEVELOPMENT, REFINEMENT AND WEIGHTING OF CANDIDATE CRITERIA FOR AXIAL DISEASE IN JUVENILE SPONDYLOARTHRITIS: AN INTERNATIONAL COLLABORATION

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Background: The lack of pediatric classification criteria for axial disease is a major impediment to the conduct of clinical trials for juvenile spondyloarthritis (JSpA).

Objectives: We aimed to develop classification criteria for axial JSpA that will enable identification of a more homogeneous group representative of children with SpA and axial disease for entry into observational or clinical trials. These criteria are not intended to capture all possible subjects, but instead most patients with shared key features of axial disease. Treatment and diagnostic decisions should adhere to evidence-based recommendations.

Methods: 304 cases with JSpA and suspected axial disease from 6 international centers were collected on a standardized case report form; all had an MRI that was reviewed by an independent team of experts in musculoskeletal imaging. Candidate criteria were developed in an earlier phase of the project through an iterative process that included an international Delphi exercise for item generation, systematic literature review, and an item reduction exercise. Using the preliminary candidate criteria, 14 international clinical SpA experts scored and rank-ordered 20 representative SpA cases. During four, 3-hour virtual meetings, the clinical expert panel reviewed the interrater reliability of case ranking, refined the criteria definitions and domain levels, and participated in a multi-criterion decision consensus methodology exercise to generate relative weights of the criteria. The expert panel assessed whether the criteria weighting was in accordance with their consensus clinical judgment as a test of face validation of the weighting/scoring system and revisions were made as necessary. Next, 30 cases from the derivation cohort were scored and ranked using the relative weights for each category and domain. Each expert independently determined the score or "threshold" below which they were no longer confident enough that a patient had axial disease to enroll the child in a Phase 3 randomized clinical trial of a drug with unclear efficacy and safety. Results of this exercise were discussed and a provisional threshold score for classification was achieved by consensus.

Results: The preliminary axial disease criteria for JSpA included the PRINTO provisional criteria for enthesitis/spondylitis-related JIA or a rheumatologist diagnosis of SpA as obligatory entry criteria as well as additive weighted criteria for 7 domains (SIJ active inflammation on imaging, SIJ structural lesions on imaging, pain chronicity, pain pattern, pain location, morning stiffness, and genetics) (Figure 1). Interrater reliability of the pre-consensus meeting case rankings was poor

(Kendall's correlation coefficient was 0.20 for clinical data-only and 0.23 for clinical plus imaging data). The multi-criterion decision analysis was repeated for the imaging domains when the initial criteria weighting was not in accordance with the expert panel's opinion. The multi-criterion decision analysis involved a total of 58 pairwise decisions agreed by expert consensus. After criteria weights and additive scores were re-calculated, experts reached consensus for axial disease in JSpA for all cases scoring 55 and greater.

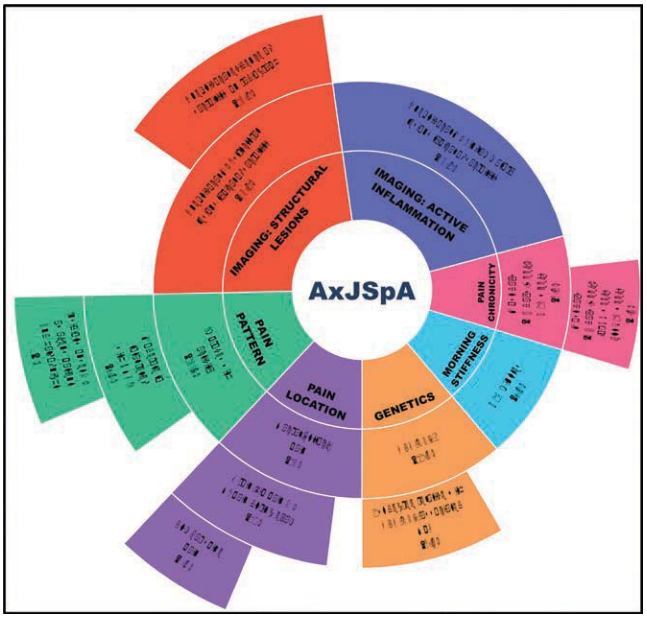

Figure 1. Axial juvenile spondyloarthritis (AxJSpA) classification criteria domains and levels. The first ring represents the domains and the items branching out are the levels moving from highest level (closest to center) to lowest level (farthest from center) in each domain. Assigned weights are shown below each item description.

Conclusion: Using an iterative process, the JSpA axial disease criteria definitions were refined, preliminary weights were generated, and a provisional threshold score for classification was determined. The most heavily weighted domains were active inflammation and structural lesions on imaging. Imaging typical of sacroiliitis was necessary, but not sufficient without any clinical criterion, to surpass the axial disease classification threshold.

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OP0217 EFFECTIVENESS AND SAFETY OF IL-6 INHIBITION (TOCILIZUMAB) VERSUS TUMOUR NECROSIS FACTOR INHIBITION IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM THE OBSERVATIONAL BIKER STUDY

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Background: Tocilizumab (TCZ) has been approved for treatment of juvenile idiopathic arthritis (JIA) for 10 years.
Objectives: Evaluation of 12-month efficacy and safety of TCZ compared to TNF inhibitors (TNFi).
Methods: BIKER WA 29358 is a 5-year multi-centre prospective, observational cohort study including polyarticular JIA patients in Germany starting treatment between 2015 and 2020 with TCZ and matched 1:1 by date of treatment start and region to patients starting an approved TNFi. Clinical disease activity (JADAS10), JADAS MDA (≦3.8)/remission (≦1.0), safety and drug adherence at 12 months were assessed and compared between cohorts.
Results: The analysis included 342 participants with 12-month treatment data (TCZ n=171; TNFi n=171). TCZ was used as 2nd line biologic in the majority of patients (84%) while TNFi were mostly 1st line biologics (86%). Patients starting TCZ had a longer disease duration. Efficacy was demonstrated by a marked decrease in JADAS10 in both cohorts (TCZ vs. TNFi at baseline: 15.0+/-6.7 vs. 14.6+/-6.3; at month 12: 3.8+/-5.1 vs. 3.4+/-4.5). Proportions of patients in TCZ/TNFi cohorts achieving JADAS remission at 12 months were 48%/41% in 1st line biologic users and 32%/33% in 2nd line biologic users. JADAS MDA was achieved in 64%/69% in 1st line and 52%/58% in 2nd line users of TCZ/TNFi.
After 12 months of treatment JADAS10 (mean +/SD) was higher in the 2nd line TNFi cohort compared to the 1st line (4.5+/-5.6 vs. 3.2+/-4.3), similar to patients receiving 2nd or 1st line TCZ (4.0+/-5.2 vs. 2.9+/-4.4). Patients receiving TCZ or TNFi as first biologic reached JADAS10 remission and MDA numerically more frequently but not statistically significant compared to 2nd line users.
Safety was assessed based on adverse event (AE) reporting. 57 (33%) patients in the TCZ cohort and 43 (25%) patients in the TNFi cohort reported AE. The AE

Table 1. Baseline characteristics and discontinuations with reasons.

Number, n	TNFi 1st 147	TNFi 2nd 24	TNFi total 171	TCZ 1st 27	TCZ 2nd 144	TCZ total 171
Female, %	119(81%)	20 (83%)	139(81%)	20(74%)	123(85%)	143(84%)
Disease duration, years	2.7+/-2.7	6.5+/-3.3	3.2+/-3.1	2.5+/-2.7	5.9+/-4.1	5.4+/-4.1
Pre-treatment	n.a.		None=147 (86%)	n.a.		None=27 (16%)
1 biologic		14 (58%)	14 (8%)		80 (56%)	80 (47%)
2 biologics		7 (29%)	7 (4%)		54 (38%)	54 (32%)
≥ 3 biologics		3 (13%)	3 (2%)		10 (7%)	10 (6%)
CHAQ-DI, mean +/- SD	0.67+/-0.64	0.31+/-0.45	0.63+/-0,63	0.43+/-0.44	0.65+/-0.65	0.61+/-0.62
JADAS 10, mean +/- SD	14.8+/-6.3	13.4+/-6.8	14.6+/-6.3	13.3+/-6.0	15.3+/-7.0	15.0+/-6.7
Concomitant						
MTX, n (%)	120 (82%)	13 (54%)	133 (78%)	17 (63%)	75 (52%)	92 (54%)
Steroid, n (%)	37 (25%)	4 (17%)	41 (24%)	8 (30%)	35 (24%)	43 (25%)
Discontinuations, n (%)	5 (3.4%)	1 (4.2%)	6 (3.5%)	4 (16%)	28 (19%)	32 (19%)
-Inefficacy	1 (0.7%)		2 (1.2%)	3 (12%)	24 (17%)	27 (16%)
-Intolerance	2 (1.4%)	1 (4.2%)	2 (1.2%)		2 (1.4%)	2 (1.2%)
-Other	2 (1.4%)		2 (1.2%)	1 (4%)	4 (2.8%)	5 (3.0%)

rate was significantly higher in the TCZ cohort (69 vs. 44.8/100 patient years, RR 1.5 [95%CI 1.1-2.0], p=0.006, Wald-test). There were 6 serious AE in the TCZ and 3 in the TNFi cohort. Injection site reactions were more common in the TNFi cohort (9 vs. 1, p=0.043). No further differences were identified to date. There was no death and no opportunistic infection.

In the TCZ cohort, 32 patients discontinued treatment, 27 due to lack of efficacy, while in the TNFi cohort only 6 patients discontinued treatment. Treatment discontinuation was more frequent among the 2nd biologic users (n=29; 17.4%) than in first line users (n= 9; 5.1%).

Conclusion: In this first interim analysis, treatment targets were reached with similar frequency after 12 months of treatment with TCZ or TNFi. TCZ was used predominantly as 2nd line biologic. Higher rates of remission /MDA were observed in 1st line compared to 2nd line biologic users. Although more AE were reported in the TCZ cohort, the occurrence of serious AE and infections was comparable in both cohorts. No new safety signals were identified. Observation is ongoing.

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OP0218

FREQUENCY OF DEPRESSIVE AND ANXIOUS SYMPTOMS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) – DATA FROM THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS WITH JIA (ICON)

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Background: Psychiatric comorbidities can be a significant additional burden in chronic diseases. The most common chronic inflammatory rheumatic disease in children and adolescents is juvenile idiopathic arthritis (JIA). Data on mental illness in children and adolescents with JIA are heterogeneous.

Objectives: To assess the frequency of depressive and anxious symptoms in patients with JIA compared to healthy peers.

Methods: Data were analysed from JIA patients and healthy controls of the same age included in the inception cohort of newly diagnosed children and adolescents with JIA (ICON). Depressive symptoms (using the Patient Health Questionnaire (PHQ-9, score 0-27) and anxious symptoms (Generalised Anxiety Disorder Scale (GAD-7, score 0-21) were captured 7 or 9 years after inclusion in ICON in patients aged thirteen years or older at the time of filling in these questionnaires. Symptom severity for both instruments was assessed by sum score with the following cut-off values: PHQ-9 score < 5: none, 5-9: mild, 10-14: moderate, 15-19: severe, ≥ 20: very severe. GAD-7 Score < 5: none, 5-9: mild, 10-14: moderate, ≥ 15: severe. Disease parameters such as Physician Global Assessment of Disease Activity (PhGA Disease Activity, numerical rating scale, (NRS),0-10, 0=best), joint count (n) and patient-reported outcomes on functional limitations ((C)HAQ, score 0-3, 0=best), Patient Global Assessment of Well-being (PGA Well-being), pain and fatigue (NRS, 0-10, 0=best) were also documented.

Results: The analysis included 344 patients, 157 (45.6%) < 18 years old (mean 15.5 ± 1.5 years, 64.3% female), 187 (54.4%) ≥ 18 years old (mean 21.5 ± 2.1 years, 65.2% female) and 224 control subjects, 115 (51.3%) < 18 years old (mean 15.2 ± 1.5 years, 60% female), 109 (48.7%) ≥ 18 years old (mean 21.4 ± 1.9 years, 58.7% female). Almost 40% of patients had oligoarthritis (26% persistent OA, 12.5% extended OA), 27% rheumatoid factor (RF)-negative polyarthritis, 6% psoriatic arthritis, 17% enthesitis-related arthritis; 3% each had systemic JIA and RF-positive polyarthritis. In the total cohort, 14% of patients and 7% of controls had a PHQ-9 ≥ 10 and 10% of patients and 2% of controls had a GAD-7 ≥ 10. Within the categories of JIA, the rate of a PHQ-9 ≥ 10 ranged from 9.3% (oligoarthritis extended) to 33.3% (RF-positive polyarthritis) and a GAD-7 ≥ 10 ranged from 0% (systemic arthritis) to 22.2% (psoriatic arthritis).

Patients aged ≥ 18 years had higher scores for both PHQ-9 (≥ 10: 18.7%) and GAD-7 (≥ 10: 14.4%) compared to patients < 18 years (PHQ-9 ≥ 10: 8.3%, GAD-7 ≥ 10: 5.1).

In patients < 18 years with PHQ-9 < 10 versus ≥ 10, there were no significant differences in either PhGA disease activity (0.8±1.6 / 1.0±2.0, p = 0.673) or joint count (0.5±1.3 / 0.5±1.6, p = 0.999). In contrast, there was a significant difference in PhGA disease activity (0.8±1.5 / 1.6±1.4, p = 0.005) but not in joint count (0.7±3.1 / 0.8±1.3, p = 0.850) in patients ≥ 18 years with PHQ-9 < 10 versus PHQ-9 ≥ 10.

Female patients were more often found to have higher scores for depression and anxiety than male patients (PHQ-9 ≥ 10: female 17.5%, male 7.4%, GAD-7 ≥ 10: female 13.5%, male 4.1%) and patients more often had higher scores for depression than controls (PHQ-9 ≥ 10: female patients 17.5%, female controls 8.3%, male patients 7.4%, male controls 4.4%). The difference in the proportion of female patients with GAD-7 ≥ 10 (13.5%) compared to control subjects (2.3%) was remarkable, but in male patients this proportion (4.1%) was only slightly higher than in male control subjects (2.2%).

Conclusion: Depressive and anxious symptoms are common in adolescents and young adults with JIA, especially in females. In the continuous care of these patients, standardised diagnostic tools should be implemented to detect

these comorbidities, to optimise therapy and thereby reduce the burden of disease. Further research is needed to identify possible predictors of the development of depression and anxiety in JIA patients in order to pursue preventive approaches.

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OP0219 HIGH INCIDENCE OF MIS-C AND OTHER AUTOIMMUNE DISEASES AFTER SARS-COV-2 INFECTION COMPARED TO COVID-19 VACCINATION IN PEDIATRIC POPULATION FROM SOUTH CENTRAL EUROPE

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Background: In contrast to adults, children are less likely to develop serious disease upon infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) but are at increased risk for inflammatory and autoimmune diseases linked to the virus (1). The reported incidence of multisystem inflammatory syndrome in children (MIS-C) varied from 0.2 to 11.4/100,000 persons under 21 years (2,3). It is yet unknown whether MIS-C can recur after SARS-CoV-2 reinfection or COVID-19 vaccination.
Objectives: To estimate the incidence and describe the spectrum of inflammatory and autoimmune diseases linked to SARS-CoV-2 infection and coronavirus (COVID-19) vaccination in pediatric patients from two neighbouring South Central European countries and regions, Slovenia and Friuli Venezia Giulia (FVG), Italy.
Methods: We performed a multi-centre prospective cohort study of all children and adolescents (under 18 years) newly diagnosed with MIS-C or other inflammatory/autoimmune diseases linked to SARS-CoV-2 infection, who were admitted to the pediatric tertiary care hospitals in Slovenia or FVG, Italy during the period from January 1, 2020, to December 31, 2021. These hospitals serve a combined population of 587,053 children and adolescents. Only patients who had positive anti-SARS-CoV-2 antibodies and/or positive SARS-CoV-2 PCR test within 3 months prior to disease onset were considered for estimating the disease incidence. We obtained the number of patients with serious adverse events (SAE) after COVID-19 vaccination and the number of patients with severe COVID-19 in the same population. This study was conducted as a part of the EU interregional Italy-Slovenia project CATTEDRA (Cross border cooperation for innovative diagnosis of rare diseases in paediatrics).
Results: 192 children and adolescents were diagnosed with inflammatory and autoimmune diseases linked to SARS-CoV-2 (Figure 1). Median age at diagnosis was 11.9 years (IQR 7.6 -14.7). All included patients were White. Incidence of MIS-C was one in 921 children and adolescents after SARS-CoV-2 infection and one in 5870 of all children and adolescents. Cumulative incidence of MIS-C since the start of the pandemic was 17/100,000 children and adolescents. Until December 31, 2021, 92,139 children and adolescents (15.7 %) received at least one dose of COVID-19 vaccine. Three patients presented with inflammatory/autoimmune disease after COVID-19 vaccination, including 2 patients with MIS-C and one patient with myositis. All 3 had evidence of recent SARS-CoV-2 infection in form of positive anti-N SARS-CoV-2 antibodies. In the same period, 15 children and adolescents were hospitalised with severe COVID-19. Seven patients from our cohort were vaccinated against COVID-19 median 8 months after MIS-C and further 6 patients had a SARS-CoV-2 reinfection 3-14 months after MIS-C. None of them experienced SAE or recurrence of MIS-C.

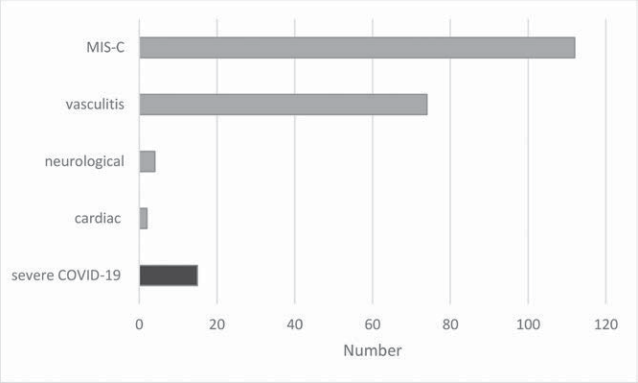

Figure 1. Inflammatory and autoimmune diseases linked to SARS-CoV-2 and severe COVID-19 in pediatric population in Slovenia and FVG, Italy

COVID-19=coronavirus disease, FVG=Friuli Venezia Giulia region in Italy, MIS-C=multisystem inflammatory syndrome in children, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2
Conclusion: MIS-C was the most common manifestation and its incidence in this predominantly white population was higher than previously reported. Based on our limited experience, MIS-C does not seem to recur after SARS-CoV-2 reinfection or COVID-19 vaccination, however long-term data are lacking. Autoimmune diseases were much more common after SARS-CoV-2 infection than after COVID-19 vaccination. Hospitalisations due to MIS-C were seven times as frequent as hospitalisations due to severe COVID-19 in children.

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OP0220 CRITERIA ASSOCIATED WITH TREATMENT DECISIONS IN JUVENILE IDIOPATHIC ARTHRITIS WITH A FOCUS ON ULTRASONOGRAPHY: RESULTS FROM THE JIRECHO COHORT.

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Background: Treatment of children with juvenile idiopathic arthritis (JIA) is a major challenge in paediatric rheumatology. The presence of synovitis, which is difficult to detect in children, is associated with structural damage. Musculoskeletal ultrasonography (MSUS) can be used in JIA patients to reveal subclinical synovitis.
Objectives: Our aim was to determine if the use of MSUS is associated with therapeutic modifications in JIA. Secondary outcomes were to identify other factors associated with therapeutic modifications.
Methods: We conducted an observational study based on the JIRECHO multicentre cohort which was developed to provide a systematic MSUS follow-up for JIA patients. Follow-up occurred every six months and included clinical and US examinations. We included children who underwent MSUS of the elbows, wrists, second metacarpophalangeal joints, knees and ankles. Synovitis in US was defined by the presence of joint effusion and/or synovial hypertrophy in B-mode (≥ grade 1) associated or not with Doppler signals (≥ grade 1). US was performed by expert sonographers with good experience in the field of JIA who previously participated in the study of the reliability of

the OMERACT paediatric US synovitis definitions and scoring system in JIA (1). Clinical and biological data, disease activity score and information on therapeutics were collected.

Results: We included 112 patients with 185 visits in total. Three groups of patients were defined according to their therapeutic status: increased(22%), decreased(14%) or stable(64%) treatment. First, we compared patients with treatment escalation with the other patients. Patients with "increased treatment" had more synovitis in B-mode US than the other patients (80% vs. 65%, p=0.06). There was no difference for the presence of synovitis in Power Doppler (PD) US (30% vs 23%, p=0.4). Patient's and physician's visual analogue scale (VAS) scores were significantly higher in patients with therapeutic escalation [3.3 vs 1.7, p<0.01 and 3.6 vs 1.6, p<0.0001] as well as disease activity score and inflammatory biological markers. Then, we compared patients with therapeutic de-escalation with the other patients. There was no difference in the presence of synovitis in US when compared with patients with stable treatment (62% vs. 69%, p=0.5) but there was less synovitis in B-mode ≥ grade 2 (8% vs. 24%, p=0.05).

We performed ROC curves analysis that showed that the sensitivity and specificity of the US in B-mode was similar to the physician's VAS, disease score activity or inflammatory biological markers (Figure 1).

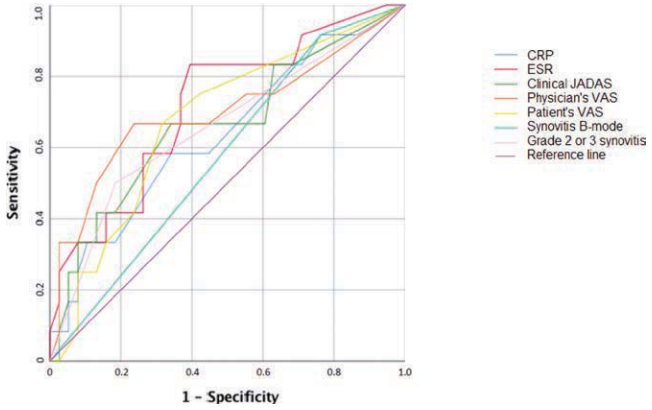

Figure 1. ROC curves for clinical and biological items and US in B-mode in patients with « therapeutic escalation »

Conclusion: In our study, MSUS of ten joints was not statistically associated with treatment escalation or de-escalation in B-mode and PD in patients with JIA.

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OP0221

EFFICACY OF SECUKINUMAB IN ENTHESITIS-RELATED ARTHRITIS: RESULTS FROM A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, TREATMENT WITHDRAWAL, PHASE 3 STUDY (JUNIPERA)

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Background: Enthesitis-related Arthritis (ERA) is a category of juvenile idiopathic arthritis (JIA) characterised by heterogeneous and insidious manifestations comprising axial and/or peripheral arthritis, and enthesitis.[1] Secukinumab (SEC) demonstrated efficacy and safety in both ERA and juvenile psoriatic arthritis (JPsA) in the JUNIPERA trial.[2]

Objectives: To evaluate the rate of flare risk reduction and efficacy of SEC on axial and peripheral manifestations in patients (pts) with active ERA.

Methods: ERA pts (2 to <18 years of age) with active disease (both ≥3 active joints and ≥1 active enthesitis site) were included. In the open-label (OL) treatment-period (TP)1, s.c. SEC (75/150 mg in pts <50/ ≥50 kg) was administered at baseline (BL), and at Week (Wk) 1–4, 8 and 12. Pts who achieved at least JIA-ACR30 response at Wk 12 were randomised into the double-blinded TP2 to continue SEC or placebo (PBO) every 4 wk until a disease flare, or up to Wk 100. The primary endpoint was time to flare in ERA and JPsA pts. The juvenile spondyloarthritis disease activity Index (JSpADA) is a disease activity assessment tool that contains 8 items to measure axial and peripheral disease activity.[3] Evaluation of axial and peripheral manifestations at the end of TP1 and TP2 in pts who experienced these symptoms at BL included modified Schober test (lumbar flexion), inflammatory back pain, FABER (Flexion, ABduction, External Rotation) test, JIA-ACR responses, Juvenile Arthritis Disease Activity Score (JADAS)-27, and resolution of enthesitis and dactylitis for peripheral disease. These outcomes were also used to assess JIA disease course at the end of TP2.

Results: A total of 52/86 (60.5%) pts with ERA were enrolled in the OL period TP1 (mean age, 13.7 years; male, 78.8%). In total, 51/52 (98.1%) pts completed TP1 and 41/44 (93.2%) completed TP2. At BL, mean JADAS-27 was 14.8, mean JSpADA index was 3.9, mean enthesitis and dactylitis counts were 2.7 and 0.4, respectively, mean number of active joints was 6.2 and of mean joints with limited range of motion 4.9. The relative risk reduction of experiencing a disease flare in TP2 was 55% (HR 0.45, 95% CI: 0.16–1.28, p=0.075) in ERA pts (Figure 1). The overall axial and peripheral disease symptoms improved over time and are presented in the Table 1. At the end of TP1, 84.6% (44/52) of pts achieved JIA-ACR 30 and 65.4% (34/52) achieved JIA-ACR 70. Clinically relevant reduction of functional ability as assessed by Childhood Health Assessment Questionnaire (CHAQ) also occurred (see Table 1).

Table 1. Resolution of axial and peripheral disease symptoms and JIA ACR responses at the end of TP1 and 2

Clinical response, mean (SD) change from BL (unless otherwise stated)	TP1-Wk 12	End of TP2*	
	SEC (N=52)	SEC (N=22)	PBO (N=22)
JSpADA index	–2.4 (1.7)	–2.7 (1.7)	–2.3 (2.1)
JSpADA Schöber, %	58.3	100.0	100.0
Inflammatory back pain, %	77.8	100.0	50.0
FABER test, %	52.6	100.0	83.3
Clinical sacroiliitis, %	53.3	100.0	50.0
Enthesitis	–2.2 (1.9)	–2.5 (2.1)	–1.3 (1.8)
Dactylitis	–0.2 (0.8)	–0.2 (1)	–0.1 (0.4)
JIA ACR30, %	84.6	90.9	68.2
JIA ACR50, %	78.8	81.8	68.2
JIA ACR70, %	65.4	68.2	54.5
JIA ACR90, %	32.7	45.5	50.0
JIA ACR100, %	26.9	36.4	45.5
Inactive disease, %	38.5	50.0	50.0
CHAQ	–0.5 (0.5)	–0.6 (0.7)	–0.4 (0.5)
CRP, median (SD) change from BL	–1.8 (38.7)	–5.8 (38.3)	0 (35.9)
JADAS-27	–9.6 (7.5)	–11.0 (8.9)	–7.6 (8.9)
Resolution of enthesitis#, %	72.3	78.6	83.3
Resolution of dactylitis#, %	50	66.7	0

*End of TP2 is based on individual pts' last visit at TP2. #At BL, in TP1, enthesitis (n= 46); dactylitis (n=5). In TP2, no. of pts who had presence at BL and showed complete resolution at the end of TP2: enthesitis, SEC 14, PBO 18; dactylitis, SEC 3, PBO, 0. CRP, C-reactive protein

Conclusion: In pts with ERA, SEC demonstrated longer time to disease flare vs PBO and exhibited rapid and sustained improvement of axial and peripheral manifestations up to Wk 104.

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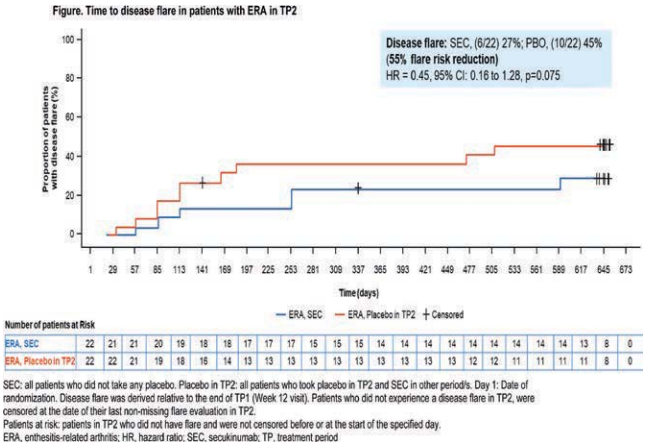

SEC: all patients who did not take any placebo. Placebo in TP2: all patients who took placebo in TP2 and SEC in other period/s. Day 1: Date of randomization. Disease flare was derived relative to the end of TP1 (Week 12 visit). Patients who did not experience a disease flare in TP2, were censored at the date of their last non-missing flare evaluation in TP2.
Patients at risk: patients in TP2 who did not have flare and were not censored before or at the start of the specified day.
ERA, enthesitis-related arthritis; HR, hazard ratio; SEC, secukinumab; TP, treatment period

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OP0222

IDENTIFICATION OF CAUSAL GENES AND MECHANISMS BY WHICH GENETIC VARIATION MEDIATES JUVENILE IDIOPATHIC ARTHRITIS SUSCEPTIBILITY USING FUNCTIONAL GENOMICS AND CRISPR-CAS9

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Background: We recently performed the largest juvenile idiopathic arthritis (JIA) genome-wide association study (GWAS) to date [1]. Disease-associated loci contain multiple single nucleotide polymorphism (SNPs), and the majority map to non-coding enhancers, making it challenging to define causal variants and genes. Functional genomics datasets in disease-relevant tissues have shown to be essential for the functional interpretation of GWAS loci. In particular, capture Hi-C (CHi-C) has been successful in detecting chromosomal interactions linking GWAS loci to their target genes. However, such datasets are lacking in JIA.
Objectives: The aim of this study is to bridge this gap and advance the knowledge of the biological mechanisms that underpin susceptibility to JIA, by integrating GWAS with public epigenomics datasets and in-house generated CHi-C from JIA patients. We focus on CD4+ T-cells, which have been shown to be one of the most relevant cell types in JIA. In addition, we use CRISPR-Cas9 to validate the regulatory effect of prioritised variants on their predicted target genes.
Methods: Credible SNP sets for the top JIA risk loci ($P < 5x10^{-6}$) were annotated using EpiMap data [2]. Low input whole genome promoter CHi-C (PCHi-C) was performed on CD4+ T-cells isolated from blood from 3 JIA oligoarthritis patients, and data was analysed using CHiCAGO [3]. GWAS and PCHi-C data were combined to prioritise causal genes using the Capture Hi-C Omnibus Gene Score (COGS) pipeline [4]. We subsequently employed CRISPR activation (CRISPRa) and CRISPR interference (CRISPRi) in Jurkats to assess whether prioritized JIA variants were capable of regulating the expression of the interacting genes.
Results: 614 credible SNPs (out of 735) were found to overlap active enhancers in CD4+ T-cells, and were prioritized for further analysis.
We identified numerous significant chromatin interactions in 19 out of 44 non-MHC JIA associated loci, linking JIA SNPs mapping to T-cell enhancers to a total of 61 target genes and revealing potential novel disease pathways. Moreover, COGS prioritised a total of 7 genes (*RGS14*, *ERAP2*, *HIPK1*, *CCR4*, *CCRL2*, *CCR2*, *CCR3*).
A JIA associated locus on chromosome 3 contains 39 SNPs. It maps to an intergenic region and the causal gene/s are unclear. Our PCHi-C data revealed that this JIA locus presents chromatin interactions with the promoters of several genes, such as *CCRL2*, *CCR2*, *CCR3* and *CCR5*, three of which were prioritised by COGS. Two variants were selected for further analysis: rs79815064, which had the highest posterior probability, and rs8005404,the only variant within a CD4+ T-cell enhancer linked to surrounding gene activity.
When both SNPs were targeted with CRISPRa and CRISPRi, we observed an increased and decreased expression, respectively, of *CCRL2*, *CCR2*, *CCR3* and *CCR5,* confirming their role in disease. These genes belong to the chemokine receptor family and are important regulators of the inflammatory response.
Conclusion: Our work shows how functional genomics can help identify biological mechanisms by which GWAS variants increase risk of JIA, which in turn will benefit patients through personalised medicine and the identification of therapeutic targets.
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Disclosure of Interests: Antonio Frantzesko: None declared, Valeriya Malysheva: None declared, Chenfu Shi: None declared, James Ding: None declared, John Bowes: None declared, Wendy Thomson: None declared, Stephen Eyre: None declared, Mikhail Spivakov Shareholder of: co-founder and shareholder of Enhanc3D Genomics Ltd, Gisela Orozco: None declared
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New developments in OA

OP0223

DISTINGUISHING OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS SYNOVIUM WITH MACHINE LEARNING USING AUTOMATED CELL DENSITY AND PATHOLOGIST SCORES

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Background: Joint damage in the knee can be severe in both rheumatoid arthritis (RA) and osteoarthritis (OA) such that total knee replacement (TKR) is often the only management option. Pathological assessment of the extent or type of

synovial tissue inflammation from joint explants or biopsies can be useful. However, an ongoing challenge in using semi-quantitative assessments of synovitis is the disagreement between human pathologist scores of the same sample. We previously developed and validated a computer vision algorithm to automatically count each cell nucleus in an H&E-stained synovial whole slide image and yield a value of cell density, defined as mean nuclei count per mm^2 of tissue[1].

Objectives: We sought to develop methods to distinguish OA from RA based on machine learning analysis of histologic features on H&E-stained synovial tissue samples.

Methods: We measured 14 pathologist-scored histology features (137 RA and 152 OA patients) and computer vision quantified cell density (60 RA and 147 OA patients) in H&E stained synovial tissue samples from total knee replacement arthroplasty explants. A random forest model was trained using disease state (OA vs RA) as classifier and histology features and/or cell density as inputs, and feature importance scores for the model were calculated.

Results: Synovium from patients with RA exhibited increased lymphocytic inflammation, lining hyperplasia, neutrophils, detritus, plasma cells, Russell bodies, binucleate plasma cells, sub-lining giant cells, synovial lining giant cells, and fibrin (all $p<0.001$), while synovium from patients with OA had increased mast cells and fibrosis (both $p<0.001$). Fourteen pathologist-scored features allowed for discrimination between RA and OA samples, producing a macro-averaged area under the receiver operating curve (AUC) of 0.85. This discriminatory ability was comparable to that of the computer vision score of cell density alone (AUC = 0.88). Combining the pathologist scores with the cell density metric improved the discriminatory power of the model (AUC = 0.91). The three most important features in this combined model were mast cells followed by cell density and fibrosis (Figure 1). AUC values for each individual feature are provided in Table 1. The optimal cell density threshold to distinguish RA from OA synovium was 3,400 cells per mm^2, which yielded a sensitivity of 0.82 and specificity of 0.82.

Table 1. Area under receiver operating characteristic curves (AUC) of the synovial features in distinguishing RA and OA patients

Feature	AUC
Automated Cell Density	0.88
Fibrosis	0.84
Mast cells	0.80
Lining hyperplasia	0.78
Lymphocytic inflammation	0.69
Fibrin	0.68
Plasma cells	0.66
Detritus	0.64
Binucleate plasma cells	0.60
Neutrophils	0.60
Synovial giant cells	0.58
Sub-lining giant cells	0.57
Russell bodies	0.56
Germinal centers	0.51
Mucoid change	0.50

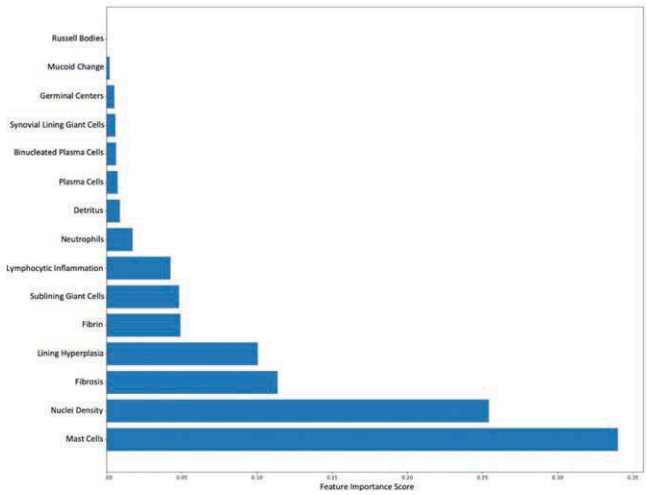

Figure 1. Importance of synovial features in distinguishing RA and OA synovium

Feature importance scores for supervised machine learning model including all 14 pathology scores and the computer vision-generated cell density.

Conclusion: H&E-stained images of RA and OA TKR explant synovium are distinct. We identified cell density, mast cells and fibrosis as the three most important features for making this distinction, with RA being characterized by increased cell density, low mast cells, and low fibrosis. Cell density greater than 3400 per mm^2 of tissue yields a sensitivity of 0.82 and a specificity of 0.82 for distinguishing RA from OA. In the future, this can have clinical and research applications as this technique removes the requirement for subjective selection of a certain field of interest, is reproducible, and is scalable as it does not require technical expertise of a pathologist.

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OP0224

DISCOVERY PROTEOMICS ANALYSIS IN THE IMI-APPROACH COHORT SHOWS THE DIFFERENTIAL MODULATION AT 24 MONTHS OF PROTEIN PROFILES ASSOCIATED WITH STRUCTURAL OR PAIN PROGRESSION IN OSTEOARTHRITIS

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Background: The characterization of differential molecular endotypes in osteoarthritis (OA) is essential for enabling patient stratification to enhance clinical trials, facilitate the development of targeted and individualized treatments.

Objectives: This study aimed to characterize the profile and dynamics over 24 months (24M) of proteins present in the sera from patients in the IMI-Applied Public-Private Research enabling OsteoArthritis Clinical Headway (APPROACH) cohort who exhibited structural (radiographic) and pain progression compared to participants who did not progressed during this period.

Methods: Forty-five patients enrolled in the IMI-APPROACH cohort were selected for the proteomic analysis. Among these, 15 showed the highest structural progression (group S) and 15 the highest pain progression (group P) at 24M, according to the APPROACH criteria [1], while 15 did not progressed neither in S nor in P. Baseline (BL) and 24M serum samples were depleted of the top 14 most abundant proteins and then analysed by liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) on a nanoElute-LC coupled to a high-resolution TIMS-QTOF (timsTOF Pro, Bruker Daltonics). Proteins were identified and quantified using the LFQ algorithm of MaxQuant software. Further statistical and bioinformatic analyses were performed using Perseus and OmicsAnalyst software.

Results: The proteomic analysis resulted in the identification of 558 proteins (10,466 peptides) in the serum samples. A label-free quantification algorithm was employed to quantify 468 proteins in the samples. Hierarchical clustering of the data showed the differences in protein abundance were more relevant longitudinally (BL to 24M) than in cross-sectional comparisons between the three groups under study (N, P or S). Sixty-three proteins were significantly altered (fold change >=1.5, p<0.05) when comparing BL to 24M in the N group (15 increased and 48 decreased), 53 in the P group (20 increased and 33 decreased) and 93 in the S group (19 increased and 74 decreased). Interestingly, two different endotypes were detected at baseline in the N and S groups, based on these protein modulations.

The overlapping of these proteomic profiles was analyzed between groups and is shown in the Figure 1. Proteins modulated specifically in the N group may be associated with mechanisms related with joint repair. On the other hand, six proteins (including two apolipoproteins) were increased at 24M only in the P group. Finally, 30 proteins were modulated only in the S group: five of them increased and 25 decreased. Remarkably, this latter group includes lubricin, chaperones and proteins related with proteoglycan binding, such as COMP, fibronectin or histidine-rich glycoprotein.

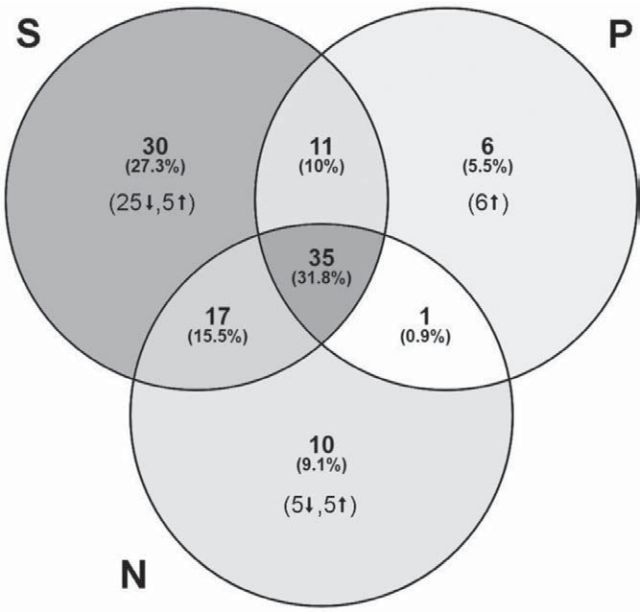

Figure 1. Circulating proteins identified as modulated after 24M follow-up in 45 patients from the APPROACH cohort that progressed in structure (S group; n=15), pain (P group; n=15) or did not progressed (N group; n=15). The numbers with arrows indicate those proteins that decrease (arrow pointing down) or increase (arrow pointing up) compared to baseline.

Conclusion: The modulation of specific protein profiles in serum were identified as associated with the progression in structure, pain or non-progression in patients from the APPROACH cohort. Proteomic changes found specifically in the S group may be interesting circulating markers of the structural affectation occurring in the joint.

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OP0225

RISK OF COMORBIDITY FOLLOWING OSTEOARTHRITIS DIAGNOSIS: A COHORT STUDY IN THE NETHERLANDS FROM THE FOREUM* INITIATIVE

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Background: Osteoarthritis (OA) is a common and disabling disease that places a significant burden on both patients and health care systems. Previous studies have already shown that patients with OA have a higher risk of developing comorbidities. However, many focused on one or a few conditions only, or did not consider the chronology of the disease onset relative to OA.

Objectives: To determine the risk of physician-diagnosed comorbidity following the diagnosis of knee or hip OA, using electronic health records in the Netherlands.

Methods: A cohort study was conducted using the Integrated Primary Care Information (IPCI) database, an electronic health record database with medical records of 2.5 million patients from Dutch general practice. The study population consisted of patients aged 18 years or older, that were at risk for incident OA and comorbidity. Diagnosis of knee or hip OA (i.e. exposure) was defined as the first registration of the corresponding diagnostic code from the International Classification of Primary Care (ICPC) coding system in the medical record. Fifty-eight long-term comorbidities (i.e. outcome) were selected and defined by their corresponding ICPC codes.

Patients' follow-up started after registration in the database, and ended at the diagnosis date of the comorbidity (i.e. event), or at deregistration, death or at December 31st, 2019 (i.e. censoring), whichever came first. Exposure to knee or hip OA was a time-varying exposure: time between the start of follow-up and diagnosis of OA was defined as unexposed time, and between diagnosis of OA and the end of follow-up as exposed time. Patients' age was used as time axis to correct for age non-linearly. Sex-adjusted hazard ratios (HRs) comparing exposed and unexposed patient status were estimated with 99.9% confidence intervals (CI).

Results: The study population consisted of 1,890,712 patients. For 11 of the 58 studied comorbidities exposure to knee OA showed a statistically significant HR larger than 1, indicating an increased risk of being diagnosed with these comorbidities after a diagnosis of knee OA. For none of the comorbidities there was a statistically significant negative association (HR<1) with exposure to knee OA. For 7 comorbidities exposure to hip OA showed a statistically significant HR larger than 1. Again, for all other comorbidities the HR of hip OA was non-significant. For an overview of the statistically significant positive associations see Table 1.

Table 1. ***Comorbidities with significant HRs of exposure to knee or hip OA***

Knee OA				Hip OA			
Comorbidity	**HR**	**99.9% CI**		**Comorbidity**	**HR**	**99.9% CI**	
Anemia	1.33	1.09	1.64	**Anemia**	1.29	1.02	1.63
Back pain	1.28	1.04	1.57	**Atrial fibrillation**	1.46	1.14	1.88
Cataract	1.27	1.02	1.59	**Fibromyalgia**	6.09	1.25	29.53
Chronic kidney disease	1.30	1.06	1.59	**Peripheral vascular disease**	1.64	1.09	2.49
Coronary heart disease	1.34	1.03	1.75	**Sleeping disorder**	1.44	1.10	1.87
Gout	1.43	1.01	2.03	**Solid malignancy**	1.32	1.11	1.55
Hearing loss	1.34	1.00	1.79	**Spinal disc herniation**	2.03	1.46	2.83
Neck pain	1.58	1.16	2.16				
Obesity	2.02	1.06	3.83				
Sleeping disorder	1.33	1.04	1.69				
Thromboembolic disease	1.40	1.01	1.94				

Conclusion: This study showed that certain comorbidities were diagnosed more often in patients exposed to knee or hip OA, and none were less frequently diagnosed in patients exposed OA. This suggests that the management of OA should consider the risk of other long-term-conditions and that further research on causality between OA and comorbidity is needed.

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[1] **https://www.foreum.org/projects.cfm?projectid=159*

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OP0226 TRAJECTORIES OF BODY MASS INDEX FROM EARLY ADULTHOOD TO LATE MIDLIFE AND INCIDENCE OF TOTAL KNEE ARTHROPLASTY FOR OSTEOARTHRITIS: FINDINGS FROM A PROSPECTIVE COHORT STUDY

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Background: There is limited evidence regarding the association between trajectories of body mass index (BMI) across adulthood and knee osteoarthritis.

Objectives: We examined the association between body mass index (BMI) trajectories across early adulthood to midlife and risk of total knee arthroplasty (TKA) for osteoarthritis.

Methods: This study examined 24,368 participants (40-70 years at recruitment) in the Melbourne Collaborative Cohort Study who had weight collected at 1990–1994, 1995–1998, and 2003–2007 and recalled weight at age 18–21 years. BMI trajectories were derived using weight data at the four timepoints. Incidence of TKA after 2003–2007 until December 2018 was determined by linking cohort records to the National Joint Replacement Registry.

Results: Using group-based trajectory modelling, six distinct trajectories (TR) of BMI from early adulthood to late midlife were identified: lower normal to normal BMI (TR1: BMI at age 18-21 years to BMI at approximately 62 years (kg/m2), 20.0±1.9 to 22.1±1.7; 19.7%); normal BMI to borderline overweight (TR2: 21.5±2.3 to 25.8±1.7; 36.7%), normal BMI to overweight (TR3: 22.0±2.2 to 29.5±1.9; 26.8%), overweight to borderline obese (TR4: 28.5±2.7 to 30.5±2.3; 3.5%), normal BMI to class 1 obesity (TR5: 22.8±2.5 to 34.3±2.3; 10.1%), and overweight to class 2 obesity (TR6: 25.6±3.9 to 39.2±2.9; 3.2%). Over 12.4 years, 1,328 (5.4%) participants had TKA. The hazard ratios for TKA increased in all TR compared with TR1: TR2 2.03 (95% CI 1.64-2.52), TR3 4.00 (3.19-4.91), TR4 5.17 (3.77-7.10), TR5 7.00 (5.54-8.80), and TR6 8.59 (6.44-11.46). It is estimated that 28.4% TKA would be reduced if individuals followed the trajectory that was one lower, a national health system savings of $AUD 373 million. Most of this reduction would occur in TR2 (population attributable fraction 37.9% (26.7%-47.3%) and TR3 PAF 26.8% (20.0%, 31.2%) (Table 1).

Conclusion: Our study suggests that prevention of weight gain from young adulthood to midlife in order to reduce overweight and obesity could have a major impact on reducing the burden of severe knee osteoarthritis and associated healthcare costs.

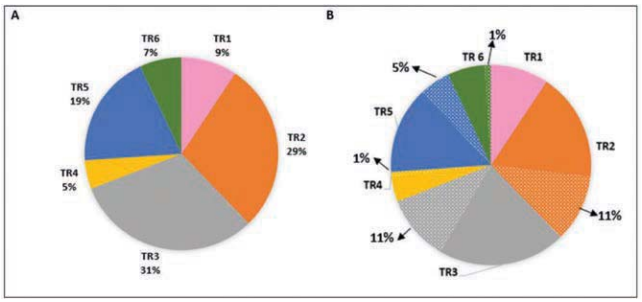

Figure 1. A. Proportion of Total Knee Arthroplasties in each trajectory category B. Speculated patters and associated percentages represents the proportion of Total Knee Arthroplasties that could be avoided in each trajectory category if the participants followed the lower trajectory category i.e. TR2 followed TR1

Disclosure of Interests: None declared

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OP0227 WEIGHT LOSS IS ASSOCIATED WITH REDUCED INCIDENCE AND PROGRESSION OF STRUCTURAL DEFECTS IN KNEE OSTEOARTHRITIS, AS ASSESSED BY RADIOGRAPHY OVER 4 TO 5 YEARS: A PROSPECTIVE MULTI-COHORT STUDY

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Table 1. Reduction in TKA if individuals followed the trajectory that was one lower

Population counterfactuals	Population at risk, n (%)	TKA under the original scenario, n (%)	TKA under the new scenario*, n (%)	Difference in risk, n (%)	PAF** (95% CI), %
TR1	4811 (19.7)	124 (2.6%)	No change 124 (2.6%)	0	-
If TR2 followed TR1 trajectory and rate of TKA*	8943 (36.7)	378 (4.2%)	2.6% of 8943 = 233	145 (10.9)	37.9 (26.7, 47.3)
If TR3 followed TR2 trajectory and rate of TKA*	6526 (26.8)	416 (6.4%)	4.2% of 6526 = 274	142 (10.7)	26.8 (20.0, 31.2)
If TR4 followed TR3 trajectory and rate of TKA*	845 (3.5)	64 (7.6%)	6.4% of 845 = 54	10 (0.8)	3.1 (0, 6.0)
If TR5 followed TR4 trajectory and rate of TKA*	2466 (10.1)	253 (10.3%)	7.6% of 2466 =187	66 (5.0)	20.2 (0, 36.3)
If TR6 followed TR5 trajectory and rate of TKA*	777 (3.2)	93 (12.0%)	10.3% of 777 = 80	13 (1.0)	0.4 (0.0, 10.0)
Total population	24368	1328	952	376 (28.4)	-

*if the trajectory is changed, ** PAFs and related 95%CIs were calculated by the Stata punafcc package using the formula $\sum pKR_i[(HR_i - 1)/HR_i]$, where pKR_i is the proportion of total knee replacements observed in the ith obesity trajectory and HR_i is the hazard ratio (HR) associated with that category. PAFs were calculated using pKR_i and HR_i estimated from the entire sample. All HR_i values were generated from Cox proportional hazards regression models adjusted for covariates (age at baseline, sex, country of birth, physical activity, smoking history, and comorbidity) and postestimation analyses.

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Background: Overweight and obesity are associated with greater incidence and progression of the structural defects of knee osteoarthritis, but it is unknown if weight loss is of benefit.
Objectives: To describe the association between change in body mass index (BMI) and the incidence and progression of structural defects in knee osteoarthritis.
Methods: Scores from radiographic analyses of knees at baseline and at 4 to 5 years' follow up were obtained from three independent data sets (the OAI and MOST data sets from the United States from America, and the CHECK data set from the Netherlands). The exposure of interest was change in BMI from baseline to 4 to 5 years' follow up. To investigate the incidence of structural defects of knee osteoarthritis, we selected a total of 9732 knees (from 5802 participants) that had a Kellgren-Lawrence (KL) grade of knee osteoarthritis at baseline of 'none' (0) or 'doubtful' (1) (the 'incidence cohort'), and determined the odds of having a KL grade at follow-up of 'minimal' (2), 'moderate' (3), or 'severe' (4). To investigate progression, we selected a total of 6084 knees (from 3996 participants) that had a KL grade at baseline of 'minimal' (2), 'moderate' (3), or 'severe' (4) (the 'progression cohort'), and determined the odds of increasing by 1 or more KL grades by follow up. The degradation of three individual structural features of knee osteoarthritis (i.e., joint space narrowing, osteophytes on the femoral surface, and osteophytes on the tibial surface), on both the medial and lateral sides of the knee, were also investigated in both the incidence and progression cohorts. Here, degradation was defined as an increase by 1 or more Osteoarthritis Research Society International (OARSI) grades.
Results: Change in BMI was positively associated with both the incidence and progression of knee osteoarthritis, as defined by KL grade. Specifically, for each one-unit change in BMI, the adjusted odds ratio for incidence was 1.05 (95% confidence interval [CI] 1.02 to 1.09), and for progression, the same adjusted odds ratio and 95% CI was also observed. Change in BMI was also positively associated with degradation (i.e., narrowing) of joint space on the medial but not the lateral side of the knee, with an adjusted odds ratio of 1.08 (95% CI 1.04 to 1.12) in the 'incidence cohort' and 1.08 (95% CI 1.03 to 1.12) in the 'progression cohort'. Degradation of the tibial and femoral surfaces (i.e., osteophytes) was also seen on the medial but not the lateral side of the knee, but only in one of the two cohorts investigated (the 'incidence cohort'), with an adjusted odds ratio of 1.07 (95% CI 1.03 to 1.12) for osteophytes on the femoral surface, and 1.05 (95% CI 1.01 to 1.09) for osteophytes on the tibial surface.
Conclusion: Each one-unit reduction in BMI is associated with a 5 to 8% decrease in the odds of the incidence and progression of the structural defects of knee osteoarthritis, with lower odds of structural degradation specific to the medial – not lateral – side of the knee.
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OAI is a collaborative informatics system created by the National Institute of Mental Health and the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) to provide a worldwide resource to quicken the pace of biomarker identification, scientific investigation and OA drug development. The OAI data repository is housed within the National Institute of Mental Health (NIMH) Data Archive (NDA). For the MOST data set, we wish to acknowledge the contributions of the study participants, investigators and research staff involved. MOST is comprised of four (4) cooperative grants: U01 AG18820 David T. Felson (Boston University); U01 AG18832 James Torner (University of Iowa); U01 AG18947 Cora E. Lewis (University of Alabama at Birmingham); U01 AG19069 Michael C. Nevitt (University of California, San Francisco), funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by MOST investigators. This manuscript was prepared using MOST data and does not claim, infer, or imply endorsement by MOST, by the MOST investigators and their respective institutions or by the University of California of the Data Recipients' use of the Data, of the entity or personnel conducting the research, or of any results of the research.
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OP0228 USE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND RISK OF COMORBIDITIES IN PEOPLE WITH AND WITHOUT OSTEOARTHRITIS - A UK PRIMARY CARE DATABASE COHORT STUDY

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Background: People with osteoarthritis (OA) are at higher risk of developing a wide array of comorbidities. Whether the use of non-steroidal anti-inflammatory drugs (NSAIDs) contributes to the increased risk of some incident comorbidities remains unknown.
Objectives: To examine the contribution of NSAIDs in the development of a wide range of comorbidities in people with and without OA.
Methods: This observational cohort study used the UK primary care Clinical Practice Research Datalink (CPRD) GOLD containing data on 20+ million people covering 937 practices. We identified 259,000 people with incident OA and 259,000 age (±2 years), sex, and practice matched controls at 1:1 ratio. Controls were assigned the same index date (the date of first diagnosis of OA) as cases for the start of follow-up. Both cases and controls were further divided into two groups according to NSAID prescriptions at any time after the index date. This allowed us to examine both the main effect of each exposure and interaction between OA and NSAID exposure after the index date. People with an NSAID prescription before the index date were excluded from the study. NSAID exposure was defined as at least two prescriptions within 90 days. Exposure status of each participant was assessed every six months as yes/no until the end of the study/outcome of interests/death/last data available, whichever came first. Comorbidities were grouped into 9 categories as cancer, cardiovascular disease (CVD), endocrine, psychological, renal, gastrointestinal (GI), genitourinary, hepatic, and neurological conditions. Propensity scores for the prescription of NSAIDs were calculated using a logistic regression model including age, sex, body mass index (BMI), musculoskeletal and pain related conditions covariates. The propensity score adjusted time varying exposure analysis was undertaken using a multivariate COX model and hazard ratio (HR) and 95% confidence intervals were calculated. Proportional hazard assumption was tested using Schoenfeld test. Smoking, alcohol, ever prescription of proton pump inhibitors (PPIs) and other comorbidities were included in the adjusted model. The additional contribution of NSAIDs

and OA towards the incident comorbidity was estimated using addictive interaction methods. We also investigated the individual risk across non-selective, and COX-2 selective NSAIDs.

Results: The mean age was 59.4±12.8 years in people with OA and 60.2±12.8 years for controls with 57.7% being female. Nearly two thirds of people with OA were prescribed NSAIDs as defined, compared to one third in the control population. People with OA and exposed to NSAIDs had highest risk of developing psychological (1.51; 1.43,1.60), CVD (1.38; 1.33,1.43), cancer (1.34; 1.25,1.44), GI (1.25; 1.16,1.34) and renal (1.17; 1.11,1.24) comorbidities after adjusting for all the covariates and PPI drugs, compared to the non-OA and non-NSAID group. (Figure 1) Interaction between OA and NSAID was significant for cancer, GI, renal, hepatic, and neurological outcomes. Within people with OA, non-selective NSAIDs increased the risk of CVD (1.25; 1.20,1.30), cancer (1.11; 1.04,1.19), endocrine (1.15; 1.10,1.19), renal (1.19; 1.13,1.26) and psychological (1.21; 1.15,1.28) comorbidities, whereas COX-2 selective NSAIDs increased risk of incident CVD (1.34; 1.25,1.44), endocrine (1.13; 1.04,1.21), renal (1.25; 1.14,1.37), and psychological (1.21; 1.09,1.34) comorbidities.

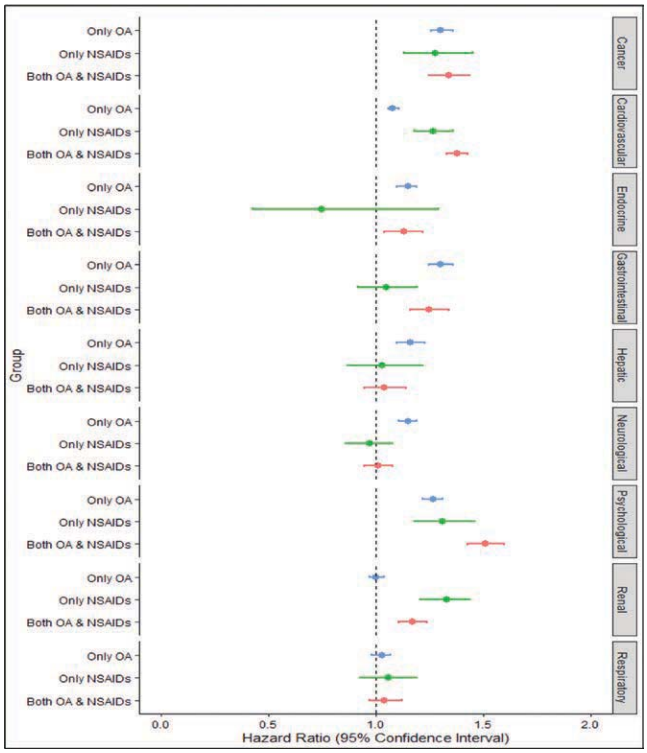

Figure 1. Hazard ratio of developing different comorbidities (reference group: no OA and no NSAIDs) OA- Osteoarthritis; NSAIDS- Non-steroidal anti-inflammatory drugs.

Conclusion: Use of NSAIDs among people with OA is associated with increased risk of a wide variety of comorbidities. Non-selective and COX-2 selective NSAIDs are both associated with increased risk of cardiovascular, renal, and psychological comorbidities.

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OP0229

OSTEOARTHRITIS OF THE KNEE, INFLAMMATION, AND THE EFFECT OF ADALIMUMAB (OKINADA): A RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Background: Cytokines such as tumor necrosis factor (TNFα) have been shown to elicit inflammatory and catabolic events in the joints of patients with osteoarthritis. Recent RCTs demonstrated that TNFα inhibition has no effect on pain and MRI-detected synovitis or bone marrow lesions in patients with erosive hand OA[1-3]. However, the progression of bone erosions was reduced in a subgroup of patients with more clinically swollen distal interphalangeal joints in one RCT[1]. Consequently, it remains possible that TNFα inhibition may have beneficial effects in specific subgroups of patients with a high inflammatory component.

Objectives: We aimed to evaluate the efficacy and safety of a TNFα inhibitor, adalimumab (ADA), in a proof-of-concept study in patients with inflammatory OA of the knee.

Methods: OKINADA was a 52-week, randomized, double-blind, placebo-controlled, parallel-group study done at 11 sites in Canada (NCT02471118). Eligible participants were adults (aged ≥18 years) with a diagnosis of OA of the index knee and classified according to American College of Rheumatology criteria, including radiological evidence of OA (Kellgren-Lawrence grades 2 or 3) with clinical signs of knee effusion. Subjects had persistent knee pain of ≥ one month duration with a pain score of ≥ 4 (0-10 NRS) in the index knee at screening and baseline despite conventional treatment with maximum tolerated acetaminophen and/or non-steroidal anti-inflammatory drug. Patients were randomly assigned (1:1) to receive subcutaneous 40 mg ADA every 2 weeks or placebo (PBO). Primary endpoint was the Outcome Measures in Rheumatology and Osteoarthritis Research Society International set of responder criteria (OMERACT-OARSI) at week 16 defined as: (1) improvement in pain or function ≥50% and an absolute change ≥20 mm; or (2) improvement of ≥20% with an absolute change ≥10 mm in at least two of the following three categories: pain, function, and patient's global assessment. Secondary endpoints included: the Knee Injury and Osteoarthritis Outcome Score (KOOS) for the domains of pain, activities of daily living (ADL), OA symptoms, sport and recreation function (SRF), and knee-related quality of life (QoL), patient's global assessment of disease status (PGAD), investigator global assessment of disease status (IGAD), and expanded Target Joint Assessment (TJA) score.

Results: A total of 59 patients were randomized (29 to PBO, 30 to ADA). The primary endpoint was not met: OMERACT-OARSI combined (ADA: 9 [30.0%] vs PBO: 7 [24.1%], p=0.62). For KOOS pain, ≥20% improvement was noted in 11 (36.7%) ADA vs 7 (24.1%) PBO patients (p=0.30), and ≥50% improvement in 5 (16.7%) ADA vs 6 (20.7%) PBO patients (p=0.69). There were no significant treatment-group differences in baseline to 16-week change in continuous secondary endpoints (ADA vs PBO: KOOS ADL 6.5 vs 8.4 (p=0.71), KOOS QoL 10.1 vs 7.4 (p=0.66), KOOS symptoms 7.8 vs 11.5 (p=0.42), KOOS SRF 5.8 vs 7.7 (p=0.76), PGAD -1.0 vs 0.1 (p=0.10), IGAD -1.5 vs -2.1 (p=0.30), TJA -2.4 vs -2.2 (p=0.87) or in lab markers (ESR, CRP). There were 11 withdrawals (4 ADA, 7 PBO) of which 2 were for adverse events (1 ADA, 1 PBO) and 2 for increasing knee pain (1 ADA, 1 PBO). No new safety signals were identified and there were no serious adverse events.

Conclusion: Although the treatment was safe, short-term treatment with anti-TNFα therapy does not appear to provide clinically meaningful improvements in OA symptoms in patients with established radiographic knee OA. Analyses of structural endpoints will be reported when results are available.

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OP0230

ANTIHISTAMINE USE AND STRUCTURAL PROGRESSION OF KNEE OA: A POST-HOC ANALYSIS OF TWO PHASE III CLINICAL TRIALS

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Background: Prior studies indicate that mast cells are involved in chronic inflammation and that their activity in the synovium may contribute to structural progression of osteoarthritis (OA), however the exact role of mast cells in OA remains unclear. Antihistamines act by blocking histamine receptors, and further are found to have anti-inflammatory effects by stabilizing mast cell membranes. Current reports describing antihistamine use in OA patients suggest that antihistamines may reduce development of OA and lead to reduced risk of structural progression.

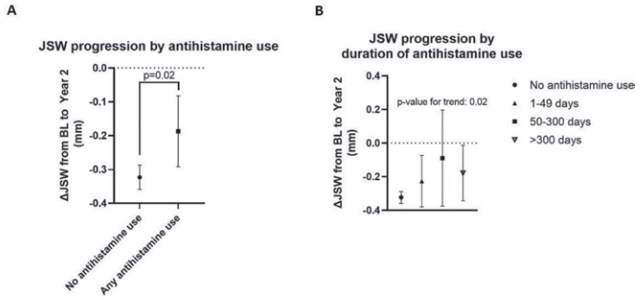
Objectives: We aimed to investigate whether antihistamine use during a two-year trial period was associated with differences in structural progression of OA, as compared with non-use.

Methods: This is a post-hoc analysis of two large phase III trials investigating oral salmon calcitonin in knee OA (NCT00486434 and NCT00704847). The primary outcome measure was structural progression defined as the change in minimum joint-space width measured by use of x-ray imaging from baseline to Year Two. In these trials, participants reported use of antihistamines, defined as medication coded with the ATC code R06A. In our study, we evaluated differences between groups of participants who reported use of antihistamines, versus those who did not, over the 2-year study period. Secondly, the duration of antihistamine use divided into categories of either no use, 1-49, 50-299 or >300 days of use was investigated to evaluate exposure-response relationships. The effect of use of antihistamines was evaluated using ANCOVA analysis adjusting for age, sex, BMI, and baseline JSW.

Results: Of a total study population of 2,206 participants, 1,485 completed the trial. Of these, 1,327 were non-users of antihistamines (mean age 64.4 years, 64.1% female, mean BMI 29.0 kg/m^2) and 158 reported use of antihistamines of any duration during the trial (mean age 64.5 years, 75.2% female, mean BMI 28.1 kg/m^2). Seventy-four participants reported use of antihistamines of a duration between 1-49 days, 21 participants between 50-299 days, and 63 reported use of 300 days or more. As illustrated in Figure 1A, the mean JSW change from baseline in the group of non-users was -0.32 mm (95% CI: -0.36 to -0.29), versus -0.19 mm (95%CI: -0.29 to -0.08, p=0.02 for difference) in the group of patients reporting antihistamine use of any duration. A trend towards an association between duration of antihistamine use and reductions in narrowing of JSW was observed (p for trend: 0.02), Figure 1B).

Conclusion: Use of antihistamines was associated with reduced structural progression in knee OA. Further research evaluating the role of antihistamines in OA is needed to further characterize this observation.

FIGURE 1



Disclosure of Interests: Asger Reinstrup Bihlet Shareholder of: Shareholder of NBCD A/S, Employee of: Employee at NBCD A/S, Claire Prener Miller Employee of: Employee at NBCD A/S, Inger Byrjalsen Employee of: Past employee at NBCD A/S, Jeppe Ragnar Andersen Shareholder of: Shareholder of NBCD A/S, Employee of: Employee at NBCD A/S, Morten Karsdal Shareholder of: Shareholder of Nordic Bioscience A/S, Employee of: Employee at Nordic Bioscience A/S, Matthew C. Baker Shareholder of: Shareholder of Mobility Bio Inc., Employee of: Employee at Mobility Bio Inc., Tharaknath Rao Shareholder of: Shareholder of Mobility Bio Inc., Employee of: Employee of Mobility Bio Inc.

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Novel etiopathogenic aspects in SLE and Sjögren's sydrome

OP0231

MASS CYTOMETRY DATA RECLASSIFY SYSTEMIC AUTOIMMUNE DISEASE PATIENTS IN PHENOTYPICALLY DISTINCTIVE GROUPS

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Background: Systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSC), Sjögren's syndrome (SJS), mixed connective tissue disease (MCTD), primary antiphospholipid syndrome (PAPS) and undifferentiated connective tissue disease (UCTD) are classified as systemic autoimmune diseases (SADs). They are diagnosed based on different clinical and laboratory criteria. Due to their high internal heterogeneity and overlapping symptoms, SADs are difficult to diagnose. Therefore, molecular and cellular-based studies need to be undertaken to precisely classify the patients. Mass cytometry is a single-cell proteomics technology that measures approximately 50 markers per cell, thus it is a suitable tool to perform deep-phenotyping studies in SADs.

Objectives: Explore differences and similarities between SADs and build reclassification framework using high-dimensional cytometry data.

Methods: The whole blood samples collected from 129 individuals, including patients and controls were stained with a 39-plex antibody panel and acquired

in 9 batches on a CyTOF (HELIOS) instrument. Data were cleaned, and normalized for batch effects using semi-automated cytof analysis pipeline. Cell frequencies and median signal intensities (MSI) for each population were extracted using FlowSOM for mononuclear cells (PBMC) and Phenograph for granulocytes. Secretion of 44 cytokines and chemokines were analyzed using a multiplexed luminex assay. Diseases were compared by Kruskal-Wallis analysis and hierarchical clustering and reclassification was done using unsupervised k-means clustering. Cytokine analysis across clusters was performed using Kruskal-Wallis test.

Results: Differently expressed features were observed between patient groups, regarding frequency of classical monocytes, B and T cells subpopulations, mature and immature granulocytes and intensities of CD38, HLA-DR and CD95 across various populations. However, none of them were disease specific. K-means clustering identified four patient clusters, which were composed by a mixture of different diagnosis. Cluster C1 was characterized by increased levels of circulating cells from PBMC compartment, and lower activation of different populations of the T cell compartment. It presented lower frequency in multiple granulocyte populations and the highest expression of CD95 and CD38. This cluster was also associated with antimalarial and steroid treatment. Clusters C1 and C2 were exactly opposite to each other, cluster C3 was characterized by intermediate features between C1 and C2 and cluster C4 could be considered as undifferentiated, mixed group. Higher production of TNFα, IL-10 and IP-10 were found in patients from C1 compared to C2, suggesting more active phenotype in C1 and physiological one in C2. The cytokine levels were independent of the treatment.

Conclusion: We constructed a patient reclassification framework using cell frequencies and expression levels of functional markers. To our knowledge this is the first time when 7 different SADs were compared using mass cytometry. In agreement with other reports we did not detect any disease-specific cellular markers. Distribution of diagnosis across different clusters confirms diseases heterogeneity. Patients can be classified into phenotypically similar groups, that could potentially benefit from the same line of treatment.

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OP0232

HIGH PLASMA C4D/C4 IDENTIFIES LUPUS NEPHRITIS PATIENTS WITH DISEASE MEDIATED BY ACTIVATION OF THE CLASSICAL COMPLEMENT PATHWAY

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Background: Proliferative lupus nephritis (LN) involves immune complex deposition in the kidney that can severely impact normal renal clearance mechanisms. Immune complexes can activate C1q and the classical complement cascade, and along with pathogenic anti-C1q antibodies (PACAs), may amplify inflammation and disease progression. Martin et al reported that circulating C4d, a marker of complement activation downstream of the C1 complex, correlated well with C4d immunohistochemistry score in kidney tissue and could be a sensitive and specific biomarker for diagnosing active LN.[1]

Objectives: To confirm and extend observations by Martin et al, and to extend a link between C4d, C1q activation, and PACA levels to identify patients most likely to have the classical complement pathway as a driving component of disease. Such patients would be potential candidates for anti-C1q therapy, such as ANX009, to dampen disease activity and slow disease progression (NCT04535752).

Methods: Plasma samples were collected from a cohort of 40 LN patients (20 with disease flare and 20 without disease flare) from the California Lupus Epidemiology Study (CLUES), a multi-racial/ethnic cohort of individuals with physician-confirmed systemic lupus erythematosus, and 20 healthy controls (Table 1). A panel of complement factors, including 15 complement protein and relevant complexes, were measured using an enzyme-linked immunosorbent assay. Clinical disease activity was measured using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and proteinuria was evaluated by a random spot urine protein to creatinine ratio (UPCR).

Table 1. Patient Demographics

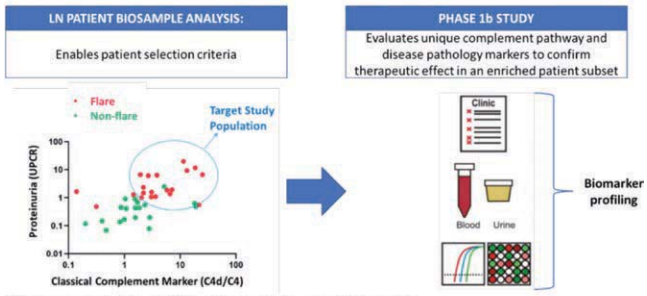
Characteristics	Healthy Control(n=20)	LN Flare(n=20)	LN Without Flare(n=20)
Median age (years)*	50 (31-60.8)	28.5 (26-34.5)	43.5 (33.5-52)
Sex, n (%)			
Female	18 (90)	17 (85)	18 (90)
Demographics, n (%)			
Caucasian	8 (40)	1 (5)	5 (25)
Hispanic	3 (15)	9 (45)	4 (20)
African American	1 (5)	3 (15)	3 (15)
Asian	8 (40)	7 (35)	8 (40)
Median UPCR (mg/mg)*	N/A	1.8 (1.3-6.5)	0.4 (0.2-0.6)
Median SLEDAI*	N/A	12 (9-16)	2 (2-4)

*Reported as median (IQR). LN, lupus nephritis; N/A, not applicable; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; UPCR, urine protein:creatinine ratio.

Results: We observed evidence of coordinated complement activation in LN patients relative to healthy controls. Specifically, levels of C4d and the C4d/C4 ratio were highly increased in LN patients with flare, while levels of C1q, C1s, and C4 were decreased, consistent with activation of the classical complement pathway (increased activation and component consumption). The C4d/C4 ratio also correlated with levels of PACA isotypes 1 and 3 that are known to activate the classical pathway. Improvements in C4 and C4d/C4 ratio were associated with improvements in proteinuria and SLEDAI following treatment for disease flare, indicating their potential value as biomarkers of treatment response.

Conclusion: A subset of LN patients exhibited high C4d/C4 ratio along with specific markers of classical pathway activation, indicating that the classical complement pathway may be a driving component of their disease. Reduction in this ratio appears to correlate with treatment response, but its levels are generally not normalized, suggesting an insufficient resolution of complement-mediated inflammation by currently available treatments. Our data support a clinical hypothesis that a subset of LN patients may benefit from a precision medicine approach targeting the classical complement pathway (Figure 1). This hypothesis will be evaluated in a forthcoming clinical trial testing the subcutaneously administered C1q inhibitor ANX009 in patients with active LN.

Figure. Unique Precision Medicine Strategy in Lupus Nephritis



LN, lupus nephritis; UPCR, urine protein:creatinine ratio.

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GSK, Ted Yednock Shareholder of: Annexon Biosciences, Consultant of: Cortexyme, Employee of: Annexon Biosciences
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OP0233 CELLULAR SENESCENCE IN A MOUSE MODEL OF LUPUS NEPHRITIS

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Background: A third of patients with lupus nephritis (LN) show a decline in renal function despite treatment, with 5-10% developing end-stage renal disease within ten years. Prognostic markers that would allow for timely treatment decisions are hence eagerly sought, as are novel therapeutic targets. It is clear that lupus kidney is not simply a passive target of systemic autoimmunity but also hosts pathogenic mechanisms determining renal disease severity. These likely involve both the infiltrating immune and resident renal cell compartments. Cellular senescence is the irreversible arrest of the cell cycle through the accumulation of cyclin dependent kinase (CDK) inhibitors such as $p16^{INK4a}$ (*CDKN2A)*. Senescent cells nevertheless remain metabolically active and undergo morphological and physiological changes including the acquisition of a pro-inflammatory, pro-fibrotic senescence-associated secretory phenotype (SASP). Aberrant accumulation of senescent cells has been observed in renal aging and pathology. We recently described the presence of $p16^{INK4a}$-positive cells (a senescence hallmark) in LN renal biopsies, and their association with baseline disease severity and 5 year outcome[1]. In addition, we observed a spatial co-distribution between tissue-infiltrating CD8 T cells, senescent kidney cells, suggesting a pathogenic functional interaction between them.
Objectives: We hypothesize that cellular senescence may contribute to tissue damage in a few different ways: **(a)** Presentation of senescence-associated antigens that attract and activate CD8 T cells. Alternatively, CD8 T cells may be summoned to the kidney by other means, and may contribute to senescence-induction through the secretion of certain cytokines; **(b)** Secretion of pro-fibrotic, pro-inflammatory molecules, and/or **(c)** Functional incapacitation of kidney cells, particularly renal progenitor cells, responsible for repairing and restoring kidney function upon damage. In parallel with our work on patient samples, we aim to establish a relevant pre-clinical model in which we may test for the effects of senescence and senescence-directed interventions, on kidney damage.
Methods: Here, we assess for whether the B6.*Sle1.Sle2.Sle3* spontaneous lupus-prone mouse may serve as an appropriate model in which to study the role of cellular senescence. We evaluated the presence and distribution of $p16^{Ink4a}$-positive cells by immunohistochemistry, and tested for an association with CD8 T cell infiltration and renal and systemic disease, in a cohort of 21 B6.*Sle1.Sle2.Sle3* female mice. This is now being followed-up by a systematic, longitudinal study for the time of onset of different renal and systemic disease parameters, as compared to the detection of renal cell senescence in this well-characterized model.
Results: As observed in renal biopsies from LN patients, staining for $p16^{Ink4a}$-positive cells was heterogenous between mouse kidney samples. Interestingly, $p16^{Ink4a}$ seems to be associated with CD8 T cell infiltration, renal impairment and damage, independently of age. This will now be confirmed using the "senescence-associated β-galactosidase" assay, the other classic measure of cellular senescence.
Conclusion: We report the occurrence of cellular senescence, and its correlation with CD8 T cell infiltration and disease severity, in the B6.*Sle1.Sle2.Sle3* mouse model of lupus. These mice provide a pre-clinical model in which to test for the role of cellular senescence in the pathogenesis of LN *in vivo* (by the induction vs. selective elimination of senescent cells). They also serve as an alternative source (alongside patient samples) of cells for *in vitro* functional assays to test for the effects of senescent renal cells on CD8 T cells and *vice versa*.
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Disclosure of Interests: Gaëlle Tilman: None declared, Laura Watteyne: None declared, Delphine Nolf: None declared, Caroline Bouzin: None declared, Frederic Houssiau Grant/research support from: Grant from GSK, Nisha Limaye: None declared
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OP0234 RNA-SEQ IN PERIPHERAL BLOOD IMMUNE CELLS IDENTIFIES MODULAR NETWORKS PREDICTIVE AND PROTECTIVE FOR PROGRESSION FROM ANA POSITIVITY TO CLASSIFIABLE SYSTEMIC AUTOIMMUNE DISEASE.

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Background: Anti-nuclear antibody (ANA) positivity represents a complex 'At-Risk' state for development of connective tissue disease (CTD). While ANA may become positive years in advance of clinically manifest CTD, they are also harboured in at least low titre by up to 25% of the wider population, of whom only a small fraction ultimately develop systemic autoimmunity. Complex immune disturbances including plasmacytoid dendritic cell exhaustion and non-haematopoietic interferon (IFN) production are evident even among ANA positive individuals who do not ultimately progress to overt disease [1].
In a prospective observational cohort of ANA positive individuals At-Risk for CTD we have shown that a validated blood IFN-Score was predictive of progression to classifiable SLE [2]. However, the wider transcriptional fingerprint of the At-Risk state and other factors modifying risk of progression are not known. We hypothesise that diverse immune processes, both independent and interacting with IFN pathway activation, could modulate risk of progression.
Objectives: To investigate how peripheral blood immune cell transcriptional signatures derived by RNA Seq associate with progression or non-progression from At-Risk ANA positivity to clinically apparent CTD.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated at baseline from ANA-positive At-Risk individuals demonstrating ≤1 clinical criterion for classifiable CTD, symptom duration <12 months and naive of glucocorticoid or immunosuppressive therapy. Progression was prospectively adjudicated at 12 months and defined as accrual of clinical/ immunological criteria sufficient to meet classification for SLE (SLICC 2012) or other relevant CTDs. Bulk RNASeq was performed on PMBCs from 16 progressors and 19 non-progressors. Weighted gene co-expression network analysis (WGCNA) was performed using WGCNA package and gene ontology enrichment was evaluated using ClusterProfiler, in R Bioconductor. The top 20% genes ranked by connectivity were defined as hub genes. Major cell subsets were quantified in parallel by multiparameter flow cytometry.
Results: 29 modules were identified by WGCNA. Eigengenes for 3 modules were significantly associated with progression status. A single, 152 gene module showed strong positive correlation with progression ($R=0.55$, $p<0.001$). Hub genes were significantly enriched for type I IFN-signalling pathway and included established interferon stimulated genes such as IFI44 and IRF7.
Two further modules had a negative, i.e. protective, association with progression; a smaller 37 gene module, correlated negatively with both blood interferon score ($R=-0.46$, $p=0.005$) and with progression ($R=-0.43$, $p=0.01$). A larger 252 gene module was also negatively related to progression ($R=-0.43$, $p=0.009$) and demonstrated significant pathway enrichment for regulation of cell morphogenesis and actin cytoskeleton organisation.
Conclusion: We identify novel modular transcriptomic signatures implicated in SLE disease initiation. We show (i) IFN-pathway activation is the single strongest transcriptomic risk marker of progression from the ANA positive At Risk state and (ii) we identify 2 novel protective signatures in peripheral blood immune cells for which further network-based characterization is ongoing.
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OP0235

GENOME-WIDE DNA METHYLATION ANALYSIS IN MULTIPLE IMMUNE CELL POPULATIONS REVEALS WIDESPREAD PROMOTER AND INTERGENIC B CELL HYPERMETHYLATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) display an aberrant DNA methylation (DNAm) pattern with a predominant interferon signature. However, the DNAm patterns in purified immune cell populations are not well described.

Objectives: To examine genome-wide DNAm changes in sorted CD4$^+$ T cells, monocytes, granulocytes and B cells in SLE patients compared to healthy controls (HC).

Methods: Genome-wide analysis was performed in 20 SLE patients with active lupus nephritis (LN) and 20 age-, sex- and ethnicity-matched HCs. Peripheral blood was processed using gradient density centrifugation for the granulocyte fraction, and CD4$^+$ T-cells, monocytes and B cells were isolated from the mononuclear cell fraction using a RoboSep device (Stemcell Technologies). DNA was extracted using the DNA/RNA/miRNA Universal kit (Qiagen). Genome-wide DNAm was evaluated using Infinium MethylationEPIC BeadChips (Illumina Inc.). Top differentially methylated CpG sites (DMC) were validated using pyrosequencing, and further analysed in follow-up samples, as well as extended to another 36 SLE patients with inactive LN, 36 SLE with never-LN and 20 HCs. Patients and HCs were compared using a paired *t*-test stratified by cell type. A false discovery rate (FDR) <0.05 was considered statistically significant. Clustering of non-gene annotated CpGs was defined as distance <5000 bp with proximity to neighbouring genes <1x10^5 bp, identified through mapping of Entrez Gene Identifiers.

Results: Overall, SLE patients with active LN compared to HCs exhibited DMCs in 22, 46, 312 and 78,068 probes in CD4$^+$ T cells, monocytes, granulocytes and B cells, respectively. In CD4$^+$ T cells, monocytes and granulocytes, the majority of DMCs were hypomethylated and related to interferon-regulated genes. In B cells, the majority of DMCs were hypermethylated with 1360 genes in the promoter region restricted to differential methylation >10% and ≥2 DMCs, of which 1087 were hypermethylated. Of these, the most significantly hypermethylated CpGs in the promoter region included *CABYR, TMPRSS7, SLC6A2, KLK10/KLK11, WIZ, LPAR1, ZNF385B* and *IL1R1* (Figure 1). Top hypomethylated genes included *IFI44L* and *MX1*. Ingenuity Pathway Analysis (IPA) predicted top upstream regulators in B cells to be *IL4*, *TNF* and *IFNG*. In addition, we identified 1437 DMCs associated with ncRNA and 4626 DMCs with no genic association. The non-gene associated DMCs were related to 275 non-coding clusters. Top non-coding clusters were in proximity to *BMP7*, *ARHGEF10*, *PRDM1, RIN2* and *CCR6,* which themselves were differentially methylated. IPA predicted *IL2, CD40LG* and *NFKB1* as the most important upstream regulators for neighbouring genes of non-coding clusters.

Pyrosequencing confirmed B cell hypermethylation in *CXCR5, DDR1, MTA3, RAB30* and *TRAF5,* and in non-coding clusters located on chromosome 3 upstream of *FGF12* and chromosome 22 downstream of *XPNPEP3* and *RBX1*. Hypermethylation in *CXCR5, DDR1, MTA3, RAB30* and hypomethylation in *IFI44L, LGALS3BP* and *PARP9* was stable at follow-up as well as in patients with inactive and never-LN. Patients in the active LN group exhibited significantly more pronounced hypomethylation in *PLSCR1* in CD4$^+$ T-cells, granulocytes and B-cells compared to the other patient groups. Greater β2 microglobulin, anti-DNA antibodies and disease activity were significantly associated with greater B cell *CXCR5* hypermethylation (p<0.001), *IFI44L* hypomethylation in all but CD4$^+$ T cells*, LGALS3BP* hypomethylation in granulocytes (p<0.0001)*, PARP9* hypomethylation in all but B cells and *PLSCR1* hypomethylation in all but monocytes. Proteinuria was related to *PLSCR1* hypomethylation in all but monocytes, as well as hypermethylation at the non-coding cluster in chromosome 3 (p=0.05) and *MTA3* (p=0.03) in B cells.

Conclusion: B cell hypermethylation in SLE patients is widespread, and may indicate a novel mechanism for SLE pathogenesis. Differential methylation of several interferon-regulated genes may be associated with disease activity.

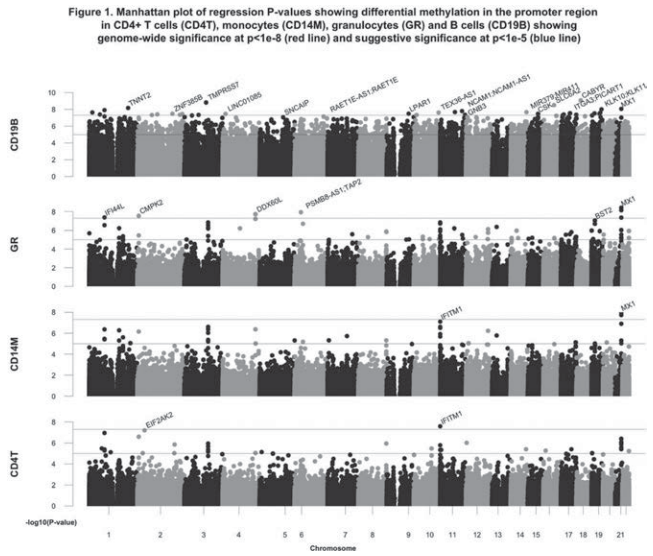

Figure 1. Manhattan plot of regression P-values showing differential methylation in the promoter region in CD4+ T cells (CD4T), monocytes (CD14M), granulocytes (GR) and B cells (CD19B) showing genome-wide significance at p<1e-8 (red line) and suggestive significance at p<1e-5 (blue line)

Disclosure of Interests: None declared

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OP0236

JAK-STAT INHIBITION RESTORES EPITHELIAL CELLS' HOMEOSTASIS IN PRIMARY SJOGREN'S SYNDROME

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Background: Although salivary gland epithelial cells (SGECs) are key players in the pathogenesis of autoimmune epithelitis that characterizes primary Sjögren's Syndrome (pSS), the mechanisms sustaining SGECs activation in pSS remain largely undetermined. Therefore, therapeutic strategies to counteract SGECs activation in pSS are also lacking. In previous studies, we revealed that maladaptive autophagy sustains survival and pro-inflammatory activation of SGECs in pSS (1).

Objectives: To determine the therapeutic potential of JAK/STAT inhibition with baricitinib to restore homeostatic regulation of SGECs in pSS, by reducing autophagy, survival, and expression of adhesion molecules.

Methods: Primary SGECs were isolated from minor salivary glands (SG) of large cohort of patients with pSS or sicca syndrome and subjected to mechanistic and functional studies including flow-cytometry, immunoblotting, and immunofluorescence to assess autophagy (autophagic-flux, LC3IIB, p62, LC3B+/LAMP1+ staining), apoptosis (annexin V/PI, Caspase-3) and activation (ICAM, VCAM). Focus score and germinal centers were determined in homologous SG biopsies to assess correlations of findings with histological disease severity. Primary SGECs of patients with pSS were treated with Baricitinib (1 mM) for 24 prior to assessment of autophagy, apoptosis and activation.

Results: SGECs from pSS patients (n=29) exhibited increased autophagy (as determined by autophagic-flux p=0.001; LC3IIB p=0.02; p62 p=0.064; LC3IIB/LAMP1+ staining), increased expression of anti-apoptotic molecules (Bcl2 p=0.006), and reduced apoptosis (Annexin-V/PI p=0.002, Caspase-3 p=0.057) compared to sicca (n=16). Induction of autophagy in pSS SGECs correlated with histologic disease severity. Treatment of pSS SGECs with baricitinib *ex vivo* suppressed autophagy, increased apoptosis, and reduced expression of adhesion molecules.

Conclusion: SGECs in the inflammatory milieu of pSS are characterized by induction of autophagy and pro-survival mechanisms, and by expression of adhesion molecules. These changes correlate with SG infiltration with immune cells and with histologic disease severity. Among clinically available therapies, the JAK/STAT inhibitor baricitinib effectively reduced autophagy, countered the state of maladaptive activation of SGECs, and restored epithelial cell homeostasis. Transcriptomics and metabolomics studies are ongoing to dissect the specific mechanisms responsible for these beneficial effects.

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Disclosure of Interests: Serena Colafrancesco Speakers bureau: Novartis Sobi, Grant/research support from: Eli Lilly, cristiana barbati: None declared, Roberta Priori: None declared, Federico Giardina: None declared, angelica gattamelata: None declared, raffaella izzo: None declared, Bruna Cerbelli: None declared, Carla Giordano: None declared, Susanna Scarpa: None declared, Massimo Fusconi: None declared, Francesca Romana Spinelli Speakers bureau: Eli Lilly Pfizer Abbvie, Giulio Cavalli: None declared, cristiano alessandri: None declared, Fabrizio Conti: None declared

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OP0237 DISTINCT IMMUNE NETWORKS STRATIFY ORGAN INVOLVEMENT AND RESPONSE TO B CELL TARGETED THERAPIES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The results from the double-blind BEAT-lupus trial comparing belimumab vs placebo, both after rituximab in systemic lupus erythematosus (SLE) have recently been reported (1). We sought to identify biomarkers of response to belimumab after rituximab to aid a personalised approach to therapy for SLE.

Objectives: To identify biomarkers of clinical response to belimumab after rituximab in the BEAT-lupus trial.

Methods: We constructed a model utilising a range of clinical, routine and exploratory laboratory data, from the BEAT-lupus trial to identify variables at baseline (screening) that could predict a major clinical response (MCR, defined as reduction to BILAG C in all domains, steroid dose of ≤7.5mg/day & SLEDAI≤2, without anti-dsDNA antibody component) at 52 weeks. Relevant serum autoantibodies and cytokines were assayed by ELISA/Simoa, and interferon signatures and BAFF expression measured by RT-PCR. A linear mixed model was applied to longitudinal data collected during the trial stratified by treatment and clinical response. An independent cross-sectional lupus cohort was recruited to validate biomarker association with organ involvement.

Results: A major clinical response (MCR) was achieved in 48% (10 responders, 11 non-responders) of patients who received belimumab after rituximab compared to 35% (8 responders, 15 non-responders) in the placebo group (i.e. rituximab alone), added to tapered standard of care, at 52 weeks. Baseline serum IgA2 anti-dsDNA antibody levels emerged as the only positive predictor of attaining MCR in belimumab treated patients (AUROC 0.8, 95% confidence interval [CI] 0.7-1.0), but negatively predicted MCR in the placebo arm (AUROC 0.2, CI 0.1-0.4). At baseline, 77% and 85% of patients were positive for serum IgA2 anti-dsDNA antibodies in belimumab and placebo arms respectively, which reduced to 30% at 52 weeks in the belimumab group but remained unchanged with placebo (Fisher exact test, p=0.007). In striking contrast, the percentage of patients who remained IgG anti-dsDNA antibody positive from baseline to 52 weeks were similar between the belimumab and placebo group, despite the serum levels significantly falling in the belimumab group (1). A significant reduction in serum IgA2 anti-dsDNA antibody levels at 24 and 52 weeks from baseline was only observed in belimumab responders (Figure 1).

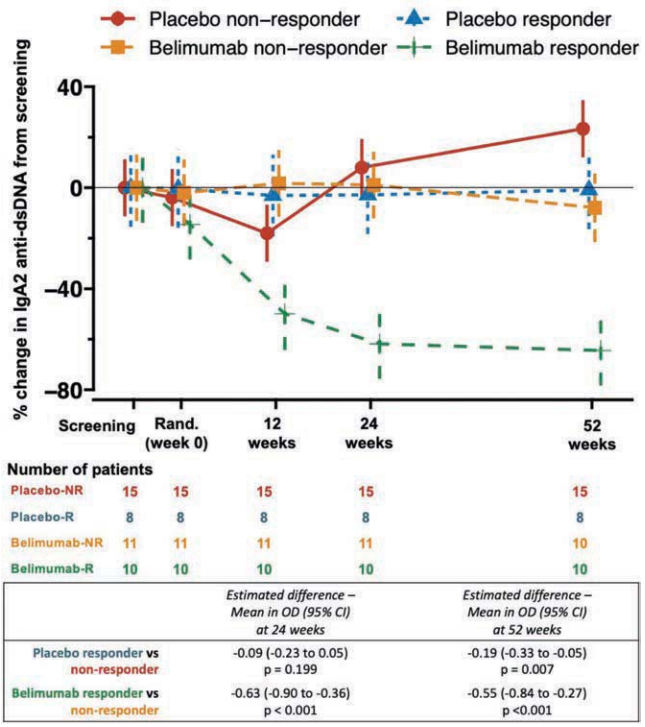

Figure 1. Percentage change in serum IgA2 anti-dsDNA antibody levels through to 52 weeks stratified by clinical response to belimumab (after rituximab) and placebo (after rituximab) at 52 weeks.

The number of circulating IgA2-secreting (but not total) plasmablasts (p=0.032) and T follicular helper cells (p=0.031) were significantly reduced at 52 weeks in the belimumab treated arm compared to placebo. Elevated serum IgA2 anti-dsDNA antibody levels were also associated with active renal disease irrespective of treatment arm (odds ratio, OR 3.2, CI 1.7-5.8, p<0.001). In contrast, serum IgA1 anti-dsDNA antibody (OR 1.3, CI 1.0-1.7, p=0.042) and interferon-alpha levels (OR 1.4, CI 1.0-2.0, p=0.041), and interferon transcriptional signature (OR 1.1, CI 1.0-1.3, p=0.027) showed a modest association with mucocutaneous disease activity; but did not predict response to B cell targeted therapy. Patients with a high baseline serum IL-6 were less likely to achieve an MCR irrespective of therapy (OR 0.4, CI 0.2-0.9, p=0.033). The associations between serum IgA2 and IgA1 anti-dsDNA antibody levels and active renal and mucocutaneous disease respectively were confirmed in an independent cross-sectional lupus cohort.

Conclusion: IgA2 anti-DNA autoantibodies is a biomarker of response to belimumab after rituximab, and of active renal disease, in systemic lupus erythematosus. Our study reveals distinct molecular networks associated with renal and mucocutaneous involvement, and response to B cell targeted therapies, which could guide precision targeting of current therapies for this heterogenous disease.

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Disclosure of Interests: Muhammad Shipa: None declared, Liliana Santos Ribeiro: None declared, Dao Nguyen: None declared, Andrew Embleton-Thirsk: None declared, Mariea Parvaz: None declared, David Isenberg Consultant of: Received consultancy fees from Astra Zeneca, Eli Lilly, Merck Serono, Servier and UCB., Caroline Gordon Speakers bureau: Speakers' bureau for GSK and

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OP0238

CLINICAL ANALYSIS OF 34 CASES OF CARDIAC COMPLICATIONS REQUIRING SURGICAL INTERVENTION IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ASSESSMENT ABOUT MECHANISM OF DEVELOPMENT WITH IMMUNOLOGICAL ANALYSIS

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Background: In cases of systematic lupus erythematosus (SLE) that lead to surgery due to the development of heart diseases such as valvular disease, ischemic heart disease and aortic aneurysm, early detection and careful monitoring are important. An absence of background diseases or immunopathological examination of the myocardial tissue in SLE cases with cardiovascular lesions demonstrates the lack of knowledge in this area. In recent years, however, there have been reports of neutrophil extracellular traps being involved in the fulminant onset of SLE.
Objectives: This study aimed to analyze clinically and immunohistopathologically the pathophysiology of heart diseases associated with SLE.
Methods: We performed left atrial appendage resection in 34 patients, including patients with cardiovascular lesions, who underwent heart surgery for SLE complications from 2012 to 2021. Tissue analysis was conducted in 9 cases. The left atrial appendage, in cases of non-collagen valvular disease, was used as the control. Tissue staining of cardiomyocytes was carried out by adding anti-neutrophil extracellular(NE) antibodies(Abs) to anti-human IgG antibody (Ab), anti-IgM Ab and anti-C3 Ab.
Results: Of the 34 SLE patients 14 had valvular disease, 8 had ischemic heart disease and 12 had aneurysms. Preoperative SLE activity was relatively stable with only 1 patient below the CH50 standard and 6 patients above the anti-DNA Ab standard. The Ab positivity rate for the patients in this study was higher than that of the 687 SLE patients who were previously tested in 2019. The presence of anti-CL Abs was 55.6%, which was higher than the 25.5% observed in previous SLE patients. In this study, anti-SS-A and anti-RNP Abs tended to be relatively numerous. An example of immunohistochemical staining of IgG in the left atrial appendage is presented (Figure 1a). IgG deposits were not observed on the left side of the myocardial fibers in the control group, whereas IgG deposits were observed on the right side in the SLE group. Deposits were also observed in tissues that were not located in the affected areas. The presence or absence of tissue deposition in the myocardial fibers and clinical findings in 2 cases of the control group and 9 cases of the SLE complication group are reported in Table 1. IgG deposits were found in the myocardial fibers of 6 of the 9 patients in the SLE complication group, and deposits were found in the left atrial appendage tissue regardless of the type of heart disease, suggesting a potential change in the heart tissue. In the SLE group, 5 cases were positive for antiphospholipid (APS) Abs, while 7 cases were positive for either anti-SS-A or anti-RNP Abs. Only 2 cases had elevated preoperative anti-DNA Ab and complement reduction. Of the SLE complication group, 2 of the 9 cases were negative for all Abs but IgG deposits were observed in a case. Of these 4 cases were selected and stained with anti-IgM, anti-C3 and anti-NE Abs. However IgM and C3 deposits were only observed in one patient who developed myocardial infarction at the age of 39 and was triple positive for APS, anti-SS-A and anti-RNP Abs (Figure 1b). There were also no NE deposits in any of the cases. Even if complement and anti-DNA Ab levels in the serum are normal, attention should be paid to heart disease complications during the long-term observation of SLE patients. In particular, attention should be paid to various autoantibody-positive cases such as APS, anti-SS-A Ab and anti-RNP Ab. The anti-NE Ab was not stained in this study because the tissue was different from the lesion site and because it occurred during the chronic course.
Conclusion: In SLE patients who developed cardiovascular lesions and required surgery, immunological abnormalities may occur in the myocardial tissue even if serum complement and anti-DNA Ab levels are stable.

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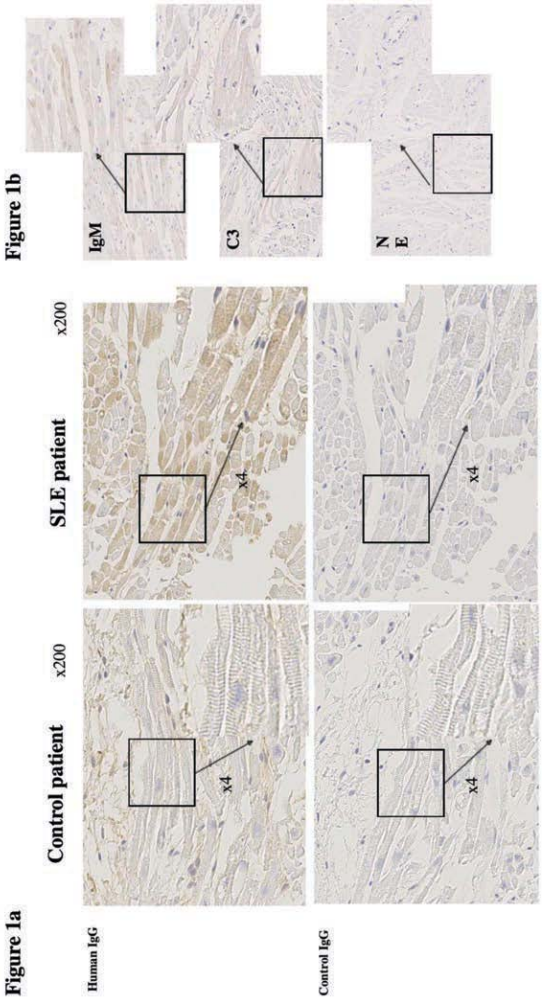
Table 1

	Subjects of operation	age	sex	cardiac muscle fiber IgG	IgM	C3	NE	CLβ2GPI	CL	LAC	SS-A	RNP	DNAab (before operation)	CH50 (before operation)
SLE	MR	61	F	++	N/E	N/E	N/E	−	+	−	+	−	−	33.9
	AS	50	F	−	N/E	N/E	N/E	−	−	−	+	−	−	46.9
	AS, AR	43	M	+	−	−	−	+	+	−	+	−	19	15.4
	AS, MR	70	F	+	−	−	−	−	−	−	−	−	−	39.3
	MR	67	F	−	−	−	−	−	−	−	−	−	−	45.3
	IHD	39	F	+++	+	+	−	+	+	+	+	+	−	45.0
	IHD	34	F	−	N/E	N/E	N/E	−	+	+	−	+	90	46.5
	IHD	59	F	+	N/E	N/E	N/E	+	+	−	−	+	−	52.4
	AR, AscAo dilatation	41	F	+	N/E	N/E	N/E	−	−	−	+	+	−	41.6
contrast	MR			−							N/E			
	MR			−										

AS : Aortic valve stenosis, MR : Mitral regurgitation, IHD : Ischemic heart disease, AR : Aortic regurgitation, AscAo : Ascending aorta, N/E : Not enforcement



Disclosure of Interests: None declared
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Osteoporosis

OP0239

REAL-LIFE SHORT-TERM EFFECTIVENESS OF ANTI-OSTEOPOROTIC TREATMENTS: A LONGITUDINAL COHORT STUDY

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Background: Data from randomized clinical trials showed that anti-osteoporotic treatments increase bone mineral density (BMD) and reduce the risk of fragility fractures. However, data on the real-life effectiveness of such medications is still scarce.
Objectives: The primary objective of the present study is to assess the real-life effectiveness of anti-osteoporotic treatment in a representative cohort of Italian women at high risk of fracture
Methods: We conducted a cohort study on women at high risk of fracture. We retrieved clinical and densitometric data from the DeFRA database, which derives from the DeFRA tool, a web-based fracture risk assessment tool. Multivariable Cox regression survival models were employed to analyze the effectiveness of

different anti-osteoporotic drugs on fracture. In sensitivity analyses we generated 1:1 matched cohorts of patients with prescription of bisphosphonates, denosumab, teriparatide or without any pharmacological prescription at baseline and 1:1 matched cohort based on the T-score variation over the time (increase in T-score vs decrease or stability in T-score values).

Results: Data from 50,862 women were available. Among these, 3,574 individuals had at least 2 consecutive visits. The crude fracture rate was 91.9/1,000 person-year for non-treated patients. The crude fracture rate in bisphosphonate users was 72.1/1,000 person-year, in denosumab users was 58.2/1,000 person-year and in teriparatide users was 19.3/1000 person-year. Overall, we found that bisphosphonates were associated with a 30% lower risk of fracture compared to no treatment (aHR 0.70, 95% CI 0.50-0.98), denosumab and teriparatide were associated with 60% and 90% lower risk of fracture, respectively (aHR 0.43, 95% CI 0.24-0.75 and aHR 0.09, 95% CI 0.01-0.70). Bisphosphonate use was associated with a lower risk of fracture only after one year of treatment. In Figure 1 are presented the Kaplan Meier curves free from fragility fracture after propensity score matching.

Conclusion: In conclusion, we found that all anti-osteoporotic medications effectively reduced the risk of fracture in the real-life. Bisphosphonate's effect on fracture risk was apparent only after the first year of treatment. Our findings do not support the use of bisphosphonates in patients at imminent risk of fracture.

Figure 1. Kaplan-Meier curves displaying the fracture (vertebral and non-vertebral fractures) probability for 1:1 matched groups of bisphosphonate users and individuals without treatment (log-rank p <0.0001)

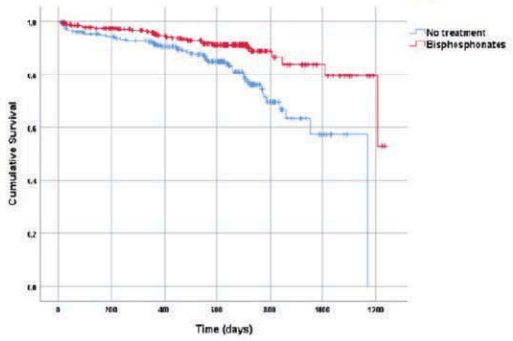


Figure 2. Kaplan-Meier curves displaying the fracture (vertebral and non-vertebral fractures) probability for 1:1 matched groups of denosumab users and individuals without treatment. (log-rank p 0.037)

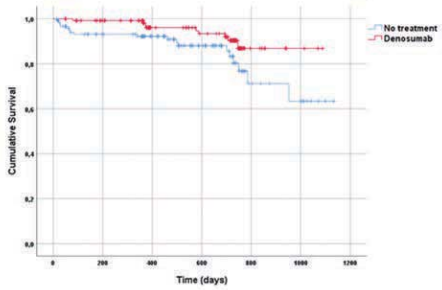
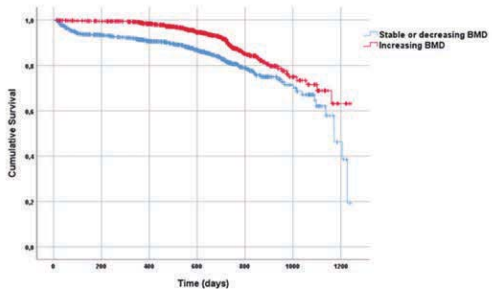


Figure 3. Kaplan-Meier curves displaying the fracture (vertebral and non-vertebral fractures) probability for 1:1 matched groups of patients with increasing BMD and stable or decreasing BMD. (log-rank p <0.0001)



Disclosure of Interests: Giovanni Adami Shareholder of: Theramex, Galapagos, IRENE GAVIOLI: None declared, Angelo Fassio: None declared, Camilla Benini: None declared, Eugenia Bertoldo: None declared, Ombretta Viapiana: None declared, Davide Gatti: None declared, Maurizio Rossini Shareholder of: Abbvie, Amgen, Bms, Eli Lilly, Galapagos, Novartis, Pfizer, Sandoz, Theramex, Ucb.

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OP0240

ZOLEDRONATE-RELATED OSTEONECROSIS OF THE JAW IN OSTEOPOROSIS: INCIDENCE, RISK FACTORS AND COMPARISON TO ORAL BISPHOSPHONATES

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Background: Mediatization of bisphosphonate(BP)-related osteonecrosis of the jaw (ONJ) has hampered the treatment of osteoporosis (OP). The risk of ONJ associated with oral BP in OP and zoledronate (ZOL) in oncology has previously been reported. However, the risk of ZOL-related ONJ in OP has only been reported in Randomized clinical trials.

Objectives: Therefore, we aimed to characterize ZOL-related ONJ in OP and compare it's incidence with oral BP in real life setting.

Methods: All reports of adverse events (AEs) of BP (ZOL, alendronate (ALN), risedronate (RIS)) were extracted from the French pharmacovigilance database (FPD) since its origin till 2020. For ZOL, cases were separated by indication, rheumatological (ZOL-R) or oncological (ZOL-K). The risk factors analyzed for ONJ were age, sex, active smoking, alcoholism, diabetes, corticotherapy, neoplasia, previous treatment by chemo or immunotherapy, recent dental care and time of exposure to BP. The association between the occurrence of ONJ and the associated BP was assessed by calculating the reporting odds ratio (ROR) in a case/non-case study. Stratification on assumed risk factors was performed to assess their impact on the risk of ONJ.

The incidence of ONJ under BP between 2011 and 2020 was estimated by relating the number of ONJ cases under BP reported to the FPD to the estimated number of patients treated with ZOL, ALN and RIS over the same period according to health insurance reimbursement data of Medic AM database. Incidence rate calculation, confidence interval calculation, and comparison of incidence rates (Fischer exact test) were performed.

Results: For ZOL 2254 AEs were reported: 568 ONJ/1103 AES with ZOL-K and 70 ONJ/1151 AEs with ZOL-R. For ZOL-R-related ONJ, 30/70 cases had recent dental care and 48.7 months of mean time of exposure to BP. Risk factors for ONJ were smoking, history of neoplasia and chemotherapy. For ALN, 1,010 AEs were reported, including 188 ONJ. 91/188 ONJ had recent dental care and 70.9 months of mean time of exposure to BP. Risk factors for ONJ were age ≥65 years, diabetes, corticotherapy, and history of neoplasia. For RIS, 771 AEs were reported including 68 cases of ONJ. 28/68 ONJ had recent dental care and 53.6 months the average time of exposure to BP. The risk factors were age ≥ 65 years, smoking, corticotherapy, history of neoplasia and chemotherapy. ROR calculation shows that corticotherapy was associated more frequently with RIS (2.10 [1.64-2.69]) and ALN (1.33 [1.04-1.70]) as compared with ZOL-R, with no other significant difference. The incidence of ONJ was significantly higher with ZOL-R than with RIS ($p<0.001$) and ALN ($p<0.001$). Indeed, between 2011 and 2020, 614 932 patients were treated with ZOL-R and 59 cases of ONJ reported yielding an incidence of 9.6/100,000 person-years; 2 233 536 patients were treated with RIS and 44 cases of ONJ reported yielding an incidence of 2.0/100 000 person-years; 2 432 373 patients were treated with ALN and 125 cases of ONJ reported yielding an incidence of 5.1/100 000 person-years.

Conclusion: Our data confirm in real-life settings and a large population, that BP-related ONJ is a rare event associated with OP. The risk of BP-related ONJ appears related to the potency of bone resorption inhibition, as RIS has the lowest and ZOL-R the highest risk. Smoking appears a consistent risk factor of ONJ, as is recent dental care. However, we must stress out the usual limitations of pharmacovigilance studies, their retrospective nature, common under-reporting of adverse-events, and the fact that the Medic AM database only refers to city reimbursements.

To our knowledge, this is the first study reporting the risk of ONJ under ZOL from the national pharmacovigilance database. Our study confirms the rarity, in OP, of BP-related ONJ. The risk of incidence of ONJ on ZOL-R is higher than on RIS and ALN, suggesting a risk associated with the inhibitory power of bone resorption.

Acknowledgements: Acknowledgements to the French Network of Pharmacovigilance Centers

Disclosure of Interests: Claire Amigues: None declared, Audrey Fresse: None declared, Christian Roux: None declared, Sophie Gauthier: None declared, Marie-Hélène Vieillard: None declared, Milou-Daniel Drici: None declared, Véronique Breuil Speakers bureau: AMGEN MSD UCB THERAMEX LILLY, Consultant of: AMGEN MSD UCB THERAMEX LILLY, Grant/research support from: AMGEN LILLY

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OP0241

BONE MICROARCHITECTURE ASSESSED BY HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (HR-PQCT) PREDICTS FRACTURE RISK IN PATIENTS WITH RHEUMATIC DISEASES ON GLUCOCORTICOIDS

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Background: Peripheral bone micro-architectural parameters assessed by high-resolution peripheral quantitative computer tomography (HR-pQCT) were able to discriminate vertebral fracture in patients with rheumatic diseases on glucocorticoid (GC) independent of areal bone mineral density aBMD. Whether these parameters could predict future fracture remained to be determined.
Objectives: The aim of this study was to compare the differences in baseline vBMD, bone microarchitecture and estimated bone strength in these patients with and without incident fragility fracture over a period of 5 years.
Methods: This was a multi-centered, retrospective, case-controlled study. Patients with rheumatic diseases on long term GC from 7 regional hospitals who had dual-energy X-ray absorptiometry (DXA) and HR-pQCT done were invited to have a 5th year follow-up assessment. X-rays were repeated. The occurrence of new fragility fracture after 5 years was documented. The baseline clinical characteristics, aBMD, FRAX and HR-pQCT parameters in patients who experienced a new fragility fracture during the 5-year follow-up period (incident fracture group) were compared with patients who did not experience a fragility fracture (control group).
Results: A total of 140 patients were recruited. The mean age of the patients, who were mostly female (80.7%), was 58.7 ± 12.5 years at baseline. SLE and RA were the commonest diagnoses. At baseline, 45.0% and 28.6% of the patients had osteopenia or osteoporosis respectively. The baseline 10-year major osteoporotic and hip fracture risks by FRAX were 13.3% and 6.0% respectively. After 5 years, 47 (33.6%) of the patients developed new fractures. The baseline clinical characteristics of incident facture group and the control group are shown in Table 1. Patients with incident fracture were older. They also had more prevalent fracture and worse mobility. The aBMD and FRAX scores were significantly higher in the incident fracture group. When comparing the HR-pQCT parameters, the incident fracture group had significantly worse vBMD, microarchitecture and bone strength particularly over the tibia at baseline. However, the changes in these parameters were not different between the 2 groups. Multivariate regression confirmed that the baseline vBMD, microarchitectural parameters and estimated bone strength over distal tibia were independent predictors of new fractures after adjusting for age, gender as well as baseline fracture, mobility and osteoporosis status.
Conclusion: A significant proportion (33.6%) of patients with rheumatic diseases on long-term GC developed new fragility fracture in 5 years, which could be predicted by the worse vBMD, microarchitecture and bone strength over tibia at baseline on HR-pQCT independent of aBMD.
Disclosure of Interests: None declared
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Table 1. Demographic and clinical characteristics at baseline

		Control group n=93	Incident fracture group n=47	*p*
Age (years)		57 ± 12	62 ± 12	**0.015**
Gender, n (%)	Female	74 (79.6%)	39 (83%)	0.629
Disease type	SLE	40 (43.5%)	21 (44.7%)	0.711
	RA	19 (20.7%)	12 (25.5%)	
	Others	33 (35.9%)	14 (29.8%)	
Mobility class, n (%)	Ambulatory	82 (88.2%)	34 (72.3%)	**0.046**
	Stick-walking	9 (9.7%)	12 (25.5%)	
	Chair-bound	2 (2.2%)	1 (2.1%)	
Previous fracture, n (%)		10 (10.8%)	12 (25.5%)	**0.023**
Medications	Cumulative prednisolone dose (g)	20.4 ± 18.7	22.0 ± 15.5	0.604
	Ever or current anti-osteoporotic treatment, n (%)	15 (16.1%)	11 (23.4%)	0.310
aBMD (g/cm^2) at	Femoral neck	0.66 ± 0.12	0.60 ± 0.12	**0.009**
	Lumbar spine	0.86 ± 0.15	0.80 ± 0.16	**0.025**
FRAX score (%)	Major osteoporotic fracture	9.9 ± 9.4	20.6 ± 17.3	**<0.001**
	Hip fracture	3.7 ± 5.6	10.8 ± 13.2	**0.001**
HR-pQCT parameters*	Distal radius: mTb.vBMD	82.0 ± 45.2	62.6 ± 42.4	**0.016**
	Distal tibia:			
	Average vBMD	258 ± 70	225 ± 70	**0.010**
	Tb. vBMD	144 ± 42	122 ± 40	**0.003**
	pTb. vBMD	221 ± 52	197 ± 46	**0.010**
	mTb.vBMD	91.3 ± 37.7	70.0 ± 40.0	**0.002**
	Tb. number	1.50 ± 0.28	1.36 ± 0.34	**0.010**
	Stiffness	162139 ± 42623	142054 ± 35375	**0.004**
	Est. failure load	-8173 ± 2083	-7200 ± 1744	**0.004**

*Only statistically significant parameters are shown

OP0242

ASSOCIATION BETWEEN EXPOSURE TO FINE PARTICULATE MATTER AND OSTEOPOROSIS: A POPULATION-BASED COHORT STUDY

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Background: Environmental air pollution has been associated with disruption of bone health at a molecular level. Particulate matter (PM) exposure can simultaneously stimulate bone resorption and halt bone formation.
Objectives: The primary aim of the present study is to describe the association between long-term exposure to PM and osteoporosis in a large cohort of women at high risk of fracture.
Methods: Clinical, demographic and densitometric data were extracted from the DeFRAcalc79 dataset, which gathers data on women at risk for osteoporosis. Data on the monitoring of PM10 and PM2.5 concentrations were retrieved from the Italian institute of environment protection and research (Istituto Superiore per la Protezione e la Ricerca Ambientale, ISPRA). Every study subject was linked to a PM exposure value, which resulted from the average concentration of urban, rural and near-traffic stations of the subject residency (ZIP code centroids 25 km) from January 2013 to December 2019. Generalized linear models with robust estimators were employed to determine the relationship between BMD and PM long-term exposure. We sequentially adjusted for confounders. Model 1 included age, body mass index (BMI), presence of prevalent fragility fractures, family history of vertebral or hip fractures, and menopause. Model 2 was further adjusted for glucocorticoid treatment and comorbidities. Model 3 (main model) added to model 2 the macro-area of residency (stratified as a categorical variable: northern Italy, central Italy and southern Italy).
Results: 59,950 women from 110 Italian provinces were included in the study. PM 2,5 exposure was negatively associated with T-score levels at the femoral neck (β -0.005, 95 CI -0.007 to -0.003) and lumbar spine (β -0.003, 95% CI -0.006 to -0.001). Chronic exposure to PM2.5 above 25 μg/m^3 was associated with a 16% higher risk of having osteoporotic T-score at any site (aOR 1.161, 95% CI 1.105 to 1.220), exposure to PM10 above 30 μg/m^3 was associated with a 15% higher risk of having osteoporotic T-score at any site (aOR 1.148, 95% CI 1.098 to 1.200).
Conclusion: Long-term exposure to air pollution was associated with higher risk of osteoporosis. Femoral neck site seemed to be more susceptible to the detrimental effect of PM exposure than lumbar spine site.

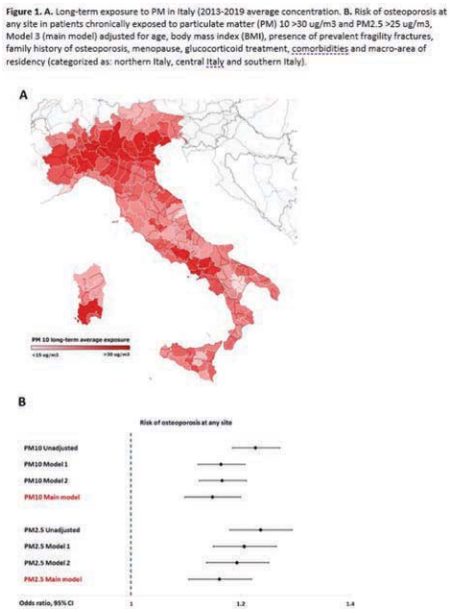

Figure 1. A. Long-term exposure to PM in Italy (2013-2019 average concentration. **B.** Risk of osteoporosis at any site in patients chronically exposed to particulate matter (PM) 10 >30 ug/m3 and PM2.5 >25 ug/m3, Model 3 (main model) adjusted for age, body mass index (BMI), presence of prevalent fragility fractures, family history of osteoporosis, menopause, glucocorticoid treatment, comorbidities and macro-area of residency (categorized as: northern Italy, central Italy and southern Italy).

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OP0243 OSTEOPOROSIS CASE-FINDING IN PEOPLE UNDERGOING ROUTINE DIAGNOSTIC CT SCANS ALMOST TRIPLED THE RATE OF OSTEOPOROSIS TREATMENT AT 12 MONTHS. A RANDOMISED, MULTI-CENTRE FEASIBILITY STUDY USING WAITING ROOM FRAX, OPPORTUNISTIC CT BONE DENSITY AND VERTEBRAL FRACTURE ASSESSMENT VERSUS USUAL CARE.

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Background: Up to 40% of all diagnostic computed tomography (CT) scans include views of the spine or hips. Among older people, osteoporosis or vertebral fractures have been found in 30% of such CT scans. Our 'PHOENIX' intervention repurposes CT scans taken for other reasons to identify fractures and measure bone density as an 'added extra'. Early detection and treatment of osteoporosis in CT-attending patients could improve health outcomes.
Objectives: To determine the feasibility and efficacy of PHOENIX versus usual care in a multi-centre, randomised, pragmatic study conducted in Eastern England involving our Cambridge Specialist Hospital 'hub' and four regional General Hospital 'spokes'.
Methods: Women ≥65 and men ≥75 years attending for routine diagnostic CT scans were invited to participate via a novel consent form incorporating FRAX Fracture Risk Assessment questions. After calculating their FRAX 10-year risk score, higher risk patients were block randomised (1:1:1) to Group 1) PHOENIX intervention, 2) Active Control, where the GP was sent the patients' FRAX answers only, or 3) Usual Care where data were only analysed after 13 months had elapsed. The CT scans of high FRAX risk patients in Group 1 were retrieved by the Cambridge team using NHS Connecting for Health (Burnbank, UK). The team performed vertebral fracture assessment and measured bone density using QCT Pro (Mindways, USA). They added patient-specific treatment and investigation management advice from 'drop down' menus before results were reviewed by a physician, authorised and sent to general practitioners (GPs). Baseline CT scans from groups 2 and 3 were assessed in the same way after 13 months to ensure no patient with osteoporosis/fractures was neglected long term. Assuming 25% attrition, the study was powered to find a superior osteoporosis treatment rate in Group 1 (estimated 20%) versus 16% (Active Control) and 5% (Usual Care). Co-primary feasibility endpoints were the ability to a) randomise 375 patients within 10 months and b) retain 75% of survivors able to complete a 1-year bone health outcome questionnaire. Secondary outcomes included osteoporosis/vertebral fracture identification rates and osteoporosis treatment rates. Stakeholder acceptability and economic aspects will be reported separately.
Results: From 1828 invites, 595 participants consented to participate of whom 213 were excluded due to 'low' FRAX score. Mortality at 12 months was 20%. Both feasibility objectives were achieved: 1) 382 people were randomised within 10 months; 2) 84.4% of survivors at 1 year (95%CI: 80.5, 88.3) were successfully followed-up. Groups were well matched at baseline. The average age of 375 patients (334 female, 41 male) was 75.2 years (74.6, 75.9). Osteoporosis of the hip/spine was present in 41% of 362 analysable CT scans. From the 264 spines that were suitable for VFA, 20% (n=53) were found to have vertebral fractures, with 8.3% having multiple vertebral fractures (n=22). Osteoporosis treatment was reported in 8.5% of Usual Care group (2.9, 14.2) and 24.2% (15.4, 33.0) of PHOENIX group participants, while in the Active Control group (FRAX only) it was 18.8% (10.9, 26.6 p=0.021). In the PHOENIX group, a recommendation to treat was sent to 50 patients' GPs at baseline. Only 18 of the 50 patients (36%) were found to be taking osteoporosis treatment 12 months after this advice was sent.
Conclusion: Osteoporosis treatment rates were almost tripled by screening patients attending for routine diagnostic CT scans with waiting room FRAX, CT-bone densitometry and vertebral fracture analysis.
Acknowledgements: This project is funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0816-20027) and by the Cambridge NIHR Biomedical Research Centre (BRC-1215-20014). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. Funding is in place to 31.03.2022. Three individuals, Mr Jeremy Dearling, Mrs Tessa Plume and Dr Ann Frost joined our trial group as PPI representatives; they were specifically involved in patient documentation design (particularly the PHOENIX pack, informed consent form which facilitated consent without having a researcher present) and contributed to suggestions for increasing patient recruitment and follow up.
Disclosure of Interests: None declared
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OP0244 AROMATASE INHIBITORS AND FRACTURE PREVENTION – DO NEW GUIDELINES WORK IN REAL WORLD?

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Background: 2,261,419 women were diagnosed with breast cancer worldwide in 2020. For postmenopausal women with hormone sensitive disease, aromatase inhibitors (AI) are recommended for their mortality benefit. However, AI bone loss (AIBL) is a recognised adverse event with resultant increase in fracture risk. In 2017, a consensus statement of 7 international bone and cancer societies was published proposing an algorithm based on clinical risk factors and different bone mineral density (BMD) threshold for bone active therapeutic intervention.
Objectives: To determine the real-world impact of the 2017 consensus guidelines on AIBL and whether bone sparing therapy utilising proposed risk stratification model is effective in fracture prevention.
Methods: Over a 7-year study period, 1001 women were prescribed AI at our university teaching hospital. The new guidelines were adopted in July 2017. We split the participants in two groups: 361 (36%) women had commenced their AI prior to the adoption of guidelines and 640 (64%) were in the post implementation group. First group were offered bone active treatment based on NOS 2009 guidelines whereas the second group followed the 2017 consensus guidelines. Women with osteoporosis were all offered treatment, however the difference in guideline is pertinent to osteopenia and we compared the results of that group.
Results: 1001 women were included. Mean age was 64 years (range 29-93). 929 (93%) were Caucasian, 57 (6%) were Asian and 15 (1%) were Afro-Caribbean. 723 women (72%) had invasive ductal carcinoma and 863 women (86%) were postmenopausal. At diagnosis, 428 women (43%) had node positive disease and 35 women (4%) had metastases. 91 women (9%) had sustained fractures prior to their cancer diagnosis.
276 women (28%) were offered oral bisphosphonates based on DEXA result, with 58 (6%) offered parenteral therapy.
First group: 361 women had a baseline DEXA with a mean left neck of femur (LNOF) BMD of 0.888 g/cm2 (range 0.552-1.222). 143 (40%) women had a normal DEXA, 174 (48%) had osteopenia and 44 (12%) had osteoporosis.
Of the women with osteopenia, 44 (25%) women were offered treatment and 33 women had a repeat DEXA after a mean of 4 years. In the treatment group, LNOF mean BMD remained relatively unchanged from 0.814 g/cm2 to 0.812 g/cm2 at the repeat DEXA (p= 0.94).
Of the 174 women with osteopenia, 22 (13%) women had a fracture.
Second group: 640 women had a baseline DEXA with a mean LNOF BMD of 0.888 g/cm2 (range 0.512-1.390). 216 (33%) women were normal, 322(50%) had osteopenia and 107 (17%) had osteoporosis.
Of the women with osteopenia, 127 (39%) women were offered treatment and 56 women had a repeat DEXA after a mean of 3 years. In the treatment group, LNOF mean BMD remained relatively unchanged from 0.822 g/cm2 to 0.829 g/cm2 at the repeat DEXA (p= 0.6169).
Of the 322 women with osteopenia, 8 (2.5%) women had a fracture.
Conclusion: Our study provides real world evidence of the success of 2017 consensus statement in lowering fracture risk. Though there has been data for positive impact on BMD decline with this approach, evidence for fracture prevention has been limited. This study showcases the success of lowering bone active therapy threshold employing alternative risk modelling strategy for women with breast cancer commenced on AI. A significant reduction in fractures pre (13%) and post guidelines change (2.5%) was demonstrated (absolute risk reduction of 10.5%) which has implications for healthcare systems worldwide as we have demonstrated this approach can reduce morbidity.
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Disclosure of Interests: None declared
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OP0245 **ASSOCIATION OF BARIATRIC SURGERY WITH THE RISK OF FRACTURE IN PATIENTS WITH OBESITY: A META-ANALYSIS OF REAL-WORLD EVIDENCE**

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Background: Evidence from published epidemiological studies found inconsistent evidence on the association of bariatric surgery with fracture risk.
Objectives: To evaluate the impact of bariatric surgery on fracture risk.
Methods: Electronic databases PubMed, and Embase were searched for studies assessing the association between bariatric surgery and fracture risk by two independent investigators. The study search period was from inception to September 2021. Study selection, data extraction, and risk of bias were assessed by investigators independently. Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias. The primary outcome was to compute the pooled fracture risk in patients with obesity who underwent bariatric surgery. Secondary outcomes include fracture risk based on follow-up duration and sites of fracture (hip, upper limb). Certainty of findings was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria.
Results: This meta-analysis was based on seven studies with a total of 156233 patients with a mean age of 41.65 ± 10.63 years. Included studies were of low risk of bias. A significantly increased risk of any fracture was found in the bariatric surgery group as compared to the non-surgical group with a pooled relative risk (RR) of 1.34 (95% CI: 1.05 – 1.70), p= 0.02 (Figure 1).

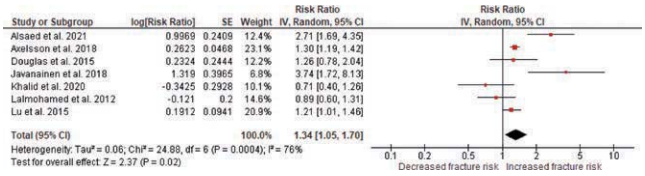

Figure 1. Forest plot showing high fracture risk in the bariatric surgery group

Subgroup analysis based on follow-up duration also revealed a significantly higher fracture risk with a RR of 1.75 (95% CI: 1.34 – 2.30), p= <0.0001 for studies with a follow-up period of >5 years. Likewise, analysis based on fracture sites revealed a significantly higher risk of hip fracture RR 1.34 (95% CI: 1.03 – 1.75), p=0.03 (Figure 2). Evidence was of low certainty as per the GRADE rating system.

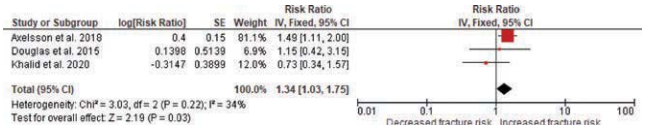

Figure 2. Forest plot showing high hip fracture risk in the bariatric surgery group

Conclusion: The current study found that bariatric surgery was associated with increased fracture risk. Clinicians should also evaluate the bone health profiling of the patients before the surgery.
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Disclosure of Interests: None declared
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OP0246 **TO SCAN OR NOT TO SCAN (BOTH HIPS) – A BRISTOL EXPERIENCE**

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Background: The current International Society of Clinical Densitometry (ISCD) recommendation for bone densitometry practice is that single hip measurement is sufficient in clinical practice, as there is overall a good correlation between the two hip bone mineral densities (BMD) (1) (2). However, discordance in individual T- scores and BMD between the 2 hips due to increasing age and osteoarthritis (3)-(5) is well recognised.
Objectives: We aimed to identify whether discordant hip BMD values would lead to differences in the FRAX risk assessment score between the two hips, and thereby impact treatment decisions in clinical practice.
Methods: We looked at all DXA scans performed at our centre for 2 months between 23/7/21 and 23/9/21. Cases in which both hips were scanned and anti-resorptive treatment was advised were included in our study. The femoral neck with the lower BMD is used to calculate the FRAX score and this was referred to as the 'reported' hip. The FRAX score for 'reported' and 'unreported' hip were calculated and the T-score of the spine was also noted. Our local treatment threshold is set at 20% for a major osteoporotic fracture and 5% for hip fracture. Cases of difference in scores crossing the 20%/5% FRAX threshold were highlighted and reviewed in more detail.
Results: DXA scans were performed in 328 patients over the 2 month period, of which 201 patients had both of their hips scanned. Of these, 50 patients were advised to start anti-resorptive treatment. The majority of the treatment decisions (60%; 30/50 cases) were based on the hip/femoral neck BMD value, while 40% (20/50 cases) were based on the spine T-score.
Where the treatment decision was based on hip/femoral neck BMD, 20% (6/30 cases) were found to have a FRAX risk above the treatment threshold at one hip only, meaning that treatment may not have been offered if both hips had not been scanned. Similarly, where treatment was advised based on spinal T-scores, 20% (4/20 cases) had a FRAX risk above treatment threshold at one hip only.
Mean age across these 10 cases with a discordant FRAX risk between the two hips was 72 years (range 59 – 83); 80% (8/10) were female. Steroid use and chronic inflammatory co-morbidities were the predominant indications for these DXA Scans.
Conclusion: A significant proportion of patients in our cohort (20%; 10/50) may not have been offered treatment if only one hip was scanned. Scanning both hips does not require much additional time and can help mitigate the risk of undertreating patients. The recommendation for best practice for DXA BMD measurements should be reviewed to consider lumbar spine and dual hip BMD as standard of care.
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Outcome of COVID-19 in Rheumatic Diseases

OP0247 **RISK FACTORS FOR SEVERE COVID-19 OUTCOMES: A STUDY OF IMMUNE-MEDIATED INFLAMMATORY DISEASES, THERAPIES AND COMORBIDITIES IN A LARGE US HEALTHCARE SYSTEM**

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Background: The risk of acquiring COVID-19, and the severity of illness if acquired, in the context of immune-mediated inflammatory diseases (IMIDs) and their therapy, remains incompletely understood. Reported infection rates and outcomes have varied depending on the IMIDs being studied, the nature and size of the study population, and the presence or absence of appropriate control populations. Having more reliable analysis on larger populations is essential for current and future pandemics.
Objectives: Health records from one of the largest health systems in the US are analyzed to determine whether specific IMIDs, including common rheumatologic conditions and specific immunomodulatory drugs, are associated with certain COVID-19 outcomes, using multivariate models that include common chronic comorbidities.
Methods: Patients (pts) with and without IMIDs who were tested for SARS-CoV-2 antigen (n=1,101,431) were identified from the EHR from Providence St. Joseph Health, which serves much of the western US. Immunomodulatory drug therapy was defined as use within three months prior to the first test. Multivariate logistic regression (LR) was applied with machine learning metrics (feature importance, p-value) reported on an 80% training set and AUROC reported on 20% test set.
Results: Rates for positive COVID-19 tests, invasive mechanical ventilation (IMV) and mortality were not greater in the IMID than non-IMID population, whilst hospitalization was similar (Table 1). Importance and statistical significance of selected factors are shown in (Figure 1). The most important risk factors for hospitalization were age and heart failure. Heart failure was the most important risk factor for IMV, and age for increased mortality. Diabetes showed weak associations with these three outcomes. Spondyloarthritis was weakly associated with decreased hospitalization, IMV, and death. The use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDS) and corticosteroids (CS) showed a weak association with hospitalization, and rituximab (RTX) showed a weak association with increased mortality. Limitations include lack of vaccination status and IMID disease severity/flare status. Testing was not universal.

Table 1. COVID-19 test results, hospitalization, invasive mechanical ventilation, and mortality

	Tested for COVID	COVID+	Hospitalized *n*, % of COVID+	IMV *n*, % of COVID+	Mortality % of COVID+
	n (%)	*n*, % of tested	*n*, % of COVID+		
All pts	1,101,431 (100%)	128,962 (11.7%)	19,704 (15.3%)	1,001 (0.8%)	2,232 (1.7%)
Pts without selected IMIDs	1,049,007 (95.3%)	123,943 (11.8%)	18,729 (15.1%)	959 (0.8%)	2,165 (1.7%)
Pts with selected rheumatologic IMIDs	28,411 (2.5%)	2,974 (10.5%)	578 (19.4%)	27 (0.9%)	51 (1.7%)
Pts with other selected IMIDs	24,013 (2.2%)	2,045 (8.5%)	397 (19.4%)	15 (0.7%)	16 (0.8%)

Selected rheumatologic IMIDs = RA, SpA, PsA, SLE, PsO, SSc; Other selected IMIDs = IBD, MS.

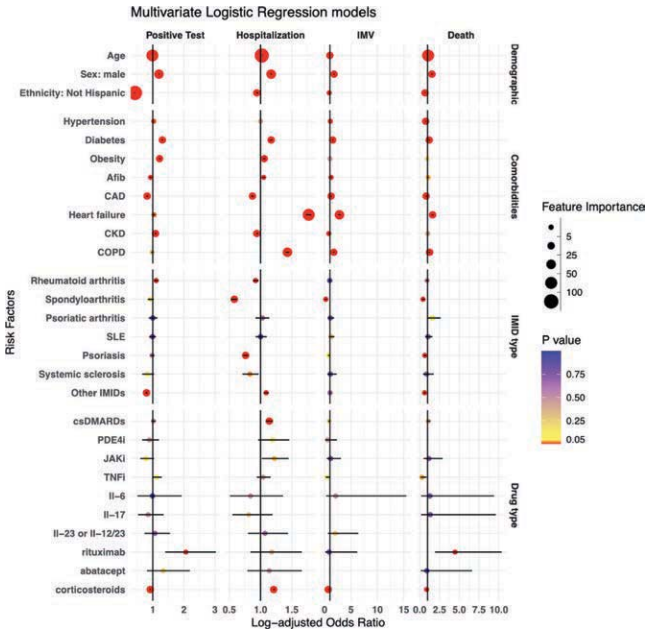

Figure 1. Odds ratio (OR) for selected risk factors for COVID-19 positive test, hospitalization, IMV, and mortality

Conclusion: This analysis of COVID+ patients (n=1,101,431) from a large US health care system analyzes outcomes of patients with *and* without IMIDs; the majority were rheumatologic IMIDs. Patients with IMIDs had a similar rate of hospitalization, IMV, and death as those without IMIDs. The strongest associations with COVID-19 severity included heart failure and age. Spondyloarthritis was weakly associated with favorable outcomes whilst other conditions, including rheumatologic, were not worse than those of non-IMID patients. csDMARDs and corticosteroids were weakly associated with hospitalization and RTX with increased mortality. Other therapies were not associated with severe adverse outcomes.
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Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Aclaris, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, Sun Pharma, UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, Swedish Medical Foundation, UCB, Qi Wei Grant/research support from: Pfizer, Swedish Medical Foundation, Michael Chiorean Speakers bureau: Pfizer, BMS, Takeda, AbbVie, Janssen, Medtronic, Consultant of: Pfizer, Lilly, Janssen, Arena, Medtronic, BMS, AbbVie, Grant/research support from: Takeda, Pfizer, Novartis, Swedish Medical Foundation, Lulu Iles-Shih Grant/research support from: Pfizer, Swedish Medical Foundation, Jennifer Hadlock Grant/research support from: Pfizer, Swedish Medical Foundation
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OP0248

SEVERE COVID-19 OUTCOMES AMONG PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: A POPULATION-BASED STUDY

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Background: Individuals with autoimmune rheumatic diseases (ARDs) may be at greater risk of severe COVID-19 outcomes than individuals in the general population.
Objectives: This study assesses the risk of COVID-19-related hospitalization, intensive care unit (ICU) admission, and COVID-19-specific mortality in patients with ARDs compared to matched general population comparators.
Methods: We conducted a population-based cohort study, using administrative datasets from British Columbia, Canada (February 2020-August 2021). Among all test-positive SARS-CoV-2 adults, we used ICD codes to identify all individuals with an **ARD**: rheumatoid arthritis (RA), psoriasis/psoriatic arthritis (PsO/PsA), ankylosing spondylitis (AS), and systemic autoimmune rheumatic diseases (SARDs), including systemic lupus erythematosus (SLE), Sjogren's syndrome, systemic sclerosis, myositis, and adult systemic vasculitides. Individuals with an ARD were matched 1:5 to general population test-positive SARS-CoV-2 individuals on age (± 5 years), sex, month/year of initial positive SARS-CoV-2 test, and health authority. Conditional logistic regression models adjusting for socioeconomic status, Charlson comorbidity index, hypertension, rural address, and number of previous COVID-19 PCR tests were performed to assess risk of COVID-19-related hospitalizations, ICU admissions, and COVID-19-specific mortality (mortality with primary ICD code for COVID-19).
Results: The risk of COVID-19-related hospitalization was significantly increased for patients with ARDs overall (aOR: 1.30) (Table 1). Within ARDs, the patient group at greatest risk of hospitalization was adult systemic vasculitides (aOR: 2.18). The risk of ICU admission was significantly increased for patients with ARDs overall (aOR: 1.30). Within ARDs, the patient group at greatest risk of ICU admission was those with AS (aOR: 2.03). The risk of COVID-19-specific mortality was significantly increased for patients with ARDs overall (aOR: 1.24). Within ARDs, the patient group at greatest risk of COVID-19-specific mortality was those with AS (aOR: 2.15).

Table 1. Risk of severe COVID-19 outcomes among patients with ARDs

	Hospitalizations		ICU admissions		COVID-19-specific mortality	
	n (%)	aOR (95% CI)	n (%)	aOR (95% CI)	n (%)	aOR (95% CI)
ARDs (6,279)	780 (12.4)	**1.30 (1.19, 1.43)**	225 (3.6)	**1.30 (1.11, 1.51)**	229 (3.7)	**1.24 (1.05, 1.47)**
ARD comparators (31,130)	2,843 (9.1)	1.00	807 (2.6)	1.00	847 (2.7)	1.00
RA *(2,067)*	321 (15.5)	**1.34 (1.15, 1.54)**	95 (4.6)	**1.30 (1.03, 1.65)**	103 (5.0)	1.18 (0.92, 1.52)
RA comparators (10,197)	1,151 (11.3)	1.00	336 (3.3)	1.00	400 (3.9)	1.00
PsO/PsA *(2,695)*	263 (9.8)	**1.17 (1.01, 1.37)**	65 (2.4)	0.90 (0.68, 1.19)	68 (2.5)	0.93 (0.68, 1.26)
PsO/PsA comparators (13,411)	1,052 (7.8)	1.00	332 (2.5)	1.00	309 (2.3)	1.00
AS *(529)*	51 (9.6)	1.36 (0.95, 1.94)	20 (3.8)	**2.03 (1.18, 3.50)**	13 (2.5)	**2.15 (1.02, 4.55)**
AS comparators (2,631)	180 (6.8)	1.00	48 (1.8)	1.00	32 (1.2)	1.00
SARDs (1,118)	168 (15.0)	**1.62 (1.32, 2.00)**	52 (4.7)	**1.74 (1.24, 2.44)**	49 (4.4)	**1.44 (1.00, 2.10)**
SARDs comparators (5,532)	490 (8.9)	1.00	135 (2.4)	1.00	157 (2.8)	1.00
SLE *(239)*	37 (15.5)	**1.88 (1.18, 3.00)**	11 (4.6)	1.67 (0.75, 3.74)	<5	0.85 (0.17, 4.29)
SLE comparators (1,187)	77 (6.5)	1.00	26 (2.2)	1.00	13 (1.1)	1.00
Sjogren's *(96)*	15 (15.6)	2.07 (0.94, 4.58)	<5	*	<5	*
Sjogren's comparators (477)	35 (7.4)	1.00	14 (2.9)	1.00	15 (3.2)	1.00
Myositis *(30)*	5 (16.7)	3.18 (0.69, 14.55)	<5	*	<5	*
Myositis comparators (150)	12 (8.0)	1.00	<5	1.00	7 (4.7)	1.00
Vasculitides *(82)*	25 (30.5)	**2.18 (1.17, 4.05)**	8 (9.8)	1.70 (0.70, 4.16)	<5	*
Vasculitides comparators (404)	64 (15.8)	1.00	21 (5.2)	1.00	16 (4.0)	1.00

Results for systemic sclerosis not presented; sample size too small. *Unable to be calculated (small sample size)

Conclusion: The risk of severe COVID-19 outcomes is increased in some ARDs, although magnitude differs across individual diseases. Strategies to mitigate risk, such as booster vaccination, prompt diagnosis, and early intervention with available therapies (e.g., oral antivirals) should be prioritized in these groups according to risk.

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OP0249

CHARACTERISTICS ASSOCIATED WITH POOR COVID-19 OUTCOMES IN PEOPLE WITH PSORIASIS AND SPONDYLOARTHRITIS: DATA FROM THE COVID-19 PSOPROTECT AND GLOBAL RHEUMATOLOGY ALLIANCE PHYSICIAN-REPORTED REGISTRIES

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Background: Some factors associated with severe COVID-19 outcomes have been identified in patients with psoriasis (PsO) and inflammatory/autoimmune rheumatic diseases, namely older age, male sex, comorbidity burden, higher disease activity, and certain medications such as rituximab. However, information about specificities of patients with PsO, psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA), including disease modifying anti-rheumatic drugs (DMARDs) specifically licensed for these conditions, such as IL-17 inhibitors (IL-17i), IL-23/IL-12+23 inhibitors (IL-23/IL-12+23i), and apremilast, is lacking.

Objectives: To determine characteristics associated with severe COVID-19 outcomes in people with PsO, PsA and axSpA.

Methods: This study was a pooled analysis of data from two physician-reported registries: the Psoriasis Patient Registry for Outcomes, Therapy and Epidemiology of COVID-19 Infection (PsoProtect), comprising patients with PsO/PsA, and the COVID-19 Global Rheumatology Alliance (GRA) registry, comprising patients with PsA/axSpA. Data from the beginning of the pandemic up to 25 October,

2021 were included. An ordinal severity outcome was defined as: 1) not hospitalised, 2) hospitalised without death, and 3) death. A multivariable ordinal logistic regression model was constructed to assess the relationship between COVID-19 severity and demographic characteristics (age, sex, time period of infection), comorbidities (hypertension, other cardiovascular disease [CVD], chronic obstructive lung disease [COPD], asthma, other chronic lung disease, chronic kidney disease, cancer, smoking, obesity, diabetes mellitus [DM]), rheumatic/skin disease (PsO, PsA, axSpA), physician-reported disease activity, and medication exposure (methotrexate, leflunomide, sulfasalazine, TNFi, IL17i, IL-23/IL-12+23i, Janus kinase inhibitors (JAKi), apremilast, glucocorticoids [GC] and NSAIDs). Age-adjustment was performed employing four-knot restricted cubic splines. Country-adjustment was performed using random effects.

Results: A total of 5008 individuals with PsO (n=921), PsA (n=2263) and axSpA (n=1824) were included. Mean age was 50 years (SD 13.5) and 51.8% were male. Hospitalisation (without death) was observed in 14.6% of cases and 1.8% died. In the multivariable model, the following variables were associated with severe COVID-19 outcomes: older age (Figure 1), male sex (OR 1.53, 95%CI 1.29-1.82), CVD (hypertension alone: 1.26, 1.02-1.56; other CVD alone: 1.89, 1.22-2.94; vs no hypertension and no other CVD), COPD or asthma (1.75, 1.32-2.32), other lung disease (2.56, 1.66-3.97), chronic kidney disease (2.32, 1.50-3.59), obesity and DM (obesity alone: 1.36, 1.07-1.71; DM alone: 1.85, 1.39-2.47; obesity and DM: 1.89, 1.34-2.67; vs no obesity and no DM), higher disease activity and GC intake (remission/low disease activity and GC intake: 1.96, 1.36-2.82; moderate/severe disease activity and no GC intake: 1.35, 1.05-1.72; moderate/severe disease activity and GC intake 2.30, 1.41-3.74; vs remission/low disease activity and no GC intake). Conversely, the following variables were associated with less severe COVID-19 outcomes: time period after 15 June 2020 (16 June 2020-31 December 2020: 0.42, 0.34-0.51; 1 January 2021 onwards: 0.52, 0.41-0.67; vs time period until 15 June 2020), a diagnosis of PsO (without arthritis) (0.49, 0.37-0.65; vs PsA), and exposure to TNFi (0.58, 0.45-0.75; vs no DMARDs), IL17i (0.63, 0.45-0.88; vs no DMARDs), IL-23/IL-12+23i (0.68, 0.46-0.997; vs no DMARDs) and NSAIDs (0.77, 0.60-0.98; vs no NSAIDs).

Conclusion: More severe COVID-19 outcomes in PsO, PsA and axSpA are largely driven by demographic factors (age, sex), comorbidities, and active disease. None of the DMARDs typically used in PsO, PsA and axSpA, were associated with severe COVID-19 outcomes, including IL-17i, IL-23/IL-12+23i, JAKi and apremilast.

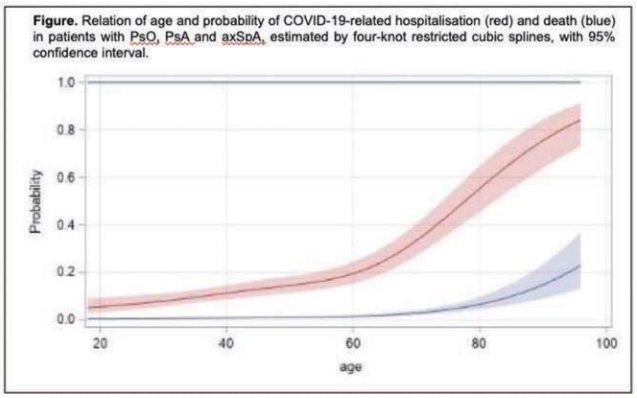

Figure. Relation of age and probability of COVID-19-related hospitalisation (red) and death (blue) in patients with PsO, PsA and axSpA, estimated by four-knot restricted cubic splines, with 95% confidence interval.

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OP0250 BREAKTHROUGH INFECTIONS AND PREDICTING SEVERE COVID OUTCOMES DURING RITUXIMAB THERAPY IN AUTOIMMUNE RHEUMATIC DISEASES

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Background: As rituximab (RTX) is a B-cell depleting agent, there are concerns regarding its safety during the COVID pandemic. Data from registries during pre-vaccination period reported increased risk of poor outcomes in RTX-treated patients vs TNFi. However, registry data could be limited by reporting bias in determining true incidence. There are also limited data on breakthrough infections following COVID vaccination.

Objectives: To assess the incidence of breakthrough infections and predictors of severe COVID outcomes in RTX-treated autoimmune rheumatic diseases (ARDs) with a view to establishing a treatment algorithm for safe RTX administration.

Methods: An observational cohort study was undertaken in the first consecutive 300 ARD patients in a single centre between index date 01/09/2019 (i.e. 6 months prior to pandemic) and 31/01/2022. Only PCR positive cases were included. COVID outcomes were categorised as Mild (i.e. not hospitalised) or Moderate/Severe (i.e. hospitalised and requiring at least oxygenation or death). Predictors of moderate/severe outcomes were analysed using Cox-regression proportional hazard.

Results: Mean (SD) at index date was 59 (14) years, 226/300 (75%) patients were female and 254 (85%) were Caucasians. The diagnoses were RA=212 (71%), SLE=33 (11%), AAV=26 (9%), Sjogren=9 (3%), IIM=8 (3%) and others=12 (4%). Therapy included concomitant DMARDs = 205 (68%) and oral prednisolone = 84 (28%). Median (range) no. of previous RTX courses was 4 (0-19). 534 RTX courses were administered. Of 294 patients with available vaccine data, 17 (6%) were unvaccinated, 4 (1%) had a single dose, 47 (16%) were double-vaccinated, 217 (74%) triple-vaccinated and 9 (3%) quadruple-vaccinated. Of those who were vaccinated, for the first dose, 11% were given within 12 weeks post-RTX, 15% within 26 weeks and 74% were >26 weeks post-RTX. The rate of overall COVID and moderate/severe infections were 11.2/100 PYs and 2.6/100 PYs respectively. Vaccinated patients had lower rate of moderate/severe infection (2.6/100 PYs) vs unvaccinated (18.6/100 PYs) [Table 1]. Over 650.7 PY follow-up, 17/300 patients (5.7%) had moderate/severe COVID including 2 deaths. Factors associated with time-to-infection in imputed multivariable analysis were number of comorbidities [HR 1.46 (95% CI 1.05-2.04)] and low IgG (<6g/L) [6.15 (1.95-19.41)]. A history of COVID vaccination reduced risk [HR 0.13 (0.03-0.51)]. Demographics including concomitant prednisolone, RTX- and vaccine-associated factors (e.g. RTX dose, time from RTX to vaccine, vaccine mode, peripheral B-cell depletion) were not predictive.

Table 1. Incidence of COVID infection

	Pre-Vaccination Programme	Post-Vaccination Programme	Overall Follow-up
Overall COVID rate	3.3/100 PY	Non-vaccinated = 37.7/100 PY Vaccinated = 18.6/100 PY	73 cases in 650.7 years] = 11.2/100 PY
Moderate/Severe COVID rate	2.1/100 PY	Non-Vaccinated = 15.1/100 PY Vaccinated = 2.6/100 PY	17 cases in 650.7 years] = 2.6/100 PY

Conclusion: The rate of moderate/severe COVID infection in this cohort is comparable to the pre-pandemic severe infection rate in rituximab trials in RA. The high vaccination uptake in our cohort was effective in preventing severe infection despite the termination of national shielding programme in March 2021 and the spread of the Delta and Omicron variants. Individualised risk–benefit assessment should be undertaken in those with comorbidities, low IgG and unvaccinated when scheduling rituximab therapy.

REFERENCES: None

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OP0251 IMPACT OF INTERSTITIAL LUNG DISEASE ON SEVERE COVID-19 OUTCOMES FOR PATIENTS WITH RHEUMATOID ARTHRITIS: A MULTICENTER STUDY

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Background: RA has been associated with poor COVID-19 outcomes, but few studies have investigated outcomes in RA features such as interstitial lung disease.
Objectives: To assess COVID-19 outcomes in patients with RA overall, and those with and without ILD, compared to general population comparators.
Methods: A multicenter, retrospective cohort study was conducted at Mayo Clinic (19 hospitals and affiliated outpatient centers in 4 states) and Mass General Brigham (14 hospitals and affiliated outpatient centers in New England). Consecutive patients with RA meeting ACR/EULAR criteria and a positive COVID-19 test from March 1, 2020 through June 6, 2021 were matched 1:5 on age, sex, race, and COVID-19 test date with general population comparators without RA. RA features assessed included: RA-ILD per Bongartz criteria [1], duration, rheumatoid factor (RF), cyclic citrullinated peptide antibody (CCP), bone erosions, and treatments. The primary outcome was a composite of hospitalization or death following COVID-19 diagnosis. We used multivariable Cox regression to investigate the association of RA, and features such as ILD, with COVID-19 outcomes compared to matched comparators.
Results: We analyzed 582 patients with RA and 2892 comparators without RA, all with COVID-19. Mean age was 62 years, 51% were female, and 79% were White. Mean RA duration was 11 years, 67% were seropositive (52% RF+ and 54% CCP+), 27% had bone erosions, 28% were on steroids, and 79% were on DMARDs. 50/582 (9%) patients with RA had ILD.
The COVID-19 hospitalization or death rate for RA patients was higher than comparators (3.0 per 1,000 days [95% CI 2.5-3.6] vs. 1.9 per 1,000 days [95% CI 1.7-2.1], respectively). Overall, RA patients had a 53% higher risk of hospitalization or death than comparators after adjustment (95% CI 1.20-1.94).
Among those with RA-ILD, the hospitalization or death rate was significantly higher than comparators (10.9 [95% CI 6.7-15.2] vs. 2.5 per 1,000 days [1.8-3.2], respectively). RA-ILD was associated with nearly 3-fold higher risk for hospitalization or death than comparators (multivariable HR 2.84 [95% CI 1.64-4.91], Table 1). There was a significant interaction between RA/comparator status and presence/absence of ILD for risk of severe COVID-19 (p<0.001, Figure 1). The elevated risk for severe COVID-19 was similar for RA subgroups defined by serostatus or bone erosions.

Table 1. Frequencies, proportions, and hazard ratios for COVID-19 outcomes, comparing all RA patients, and subgroups with or without RA-ILD, to matched comparators.

COVID-19 Outcomes	All RA Patients (n=582)	RA-ILD (n=50)	RA Patients without ILD (n=532)	Comparators (n=2,892)
Hospitalization, n (%)	121 (21)	24 (48)	97 (18)	402 (14)
Unadjusted HR (95% CI)	1.58 (1.27, 1.96)	2.65 (1.71, 4.09)	1.43 (1.12, 1.82)	Ref.
Adjusted* HR (95% CI)	1.45 (1.14, 1.83)	2.35 (1.38, 4.00)	1.31 (1.00, 1.70)	Ref.
Death, n (%)	26 (4)	9 (18)	17 (3)	63 (2)
Unadjusted HR (95% CI)	1.72 (0.98, 3.01)	5.88 (2.07, 16.71)	1.13 (0.56, 2.29)	Ref.
Adjusted* HR (95% CI)	1.24 (0.66, 2.32)	13.94 (4.30, 45.18)	0.75 (0.35, 1.63)	Ref.
Hospitalization or death, n (%)	126 (22)	25 (50)	101 (19)	419 (14)
Unadjusted HR (95% CI)	1.66 (1.33, 2.07)	3.01 (1.93, 4.70)	1.47 (1.14, 1.89)	Ref.
Adjusted* HR (95% CI)	1.53 (1.20, 1.94)	2.84 (1.64, 4.91)	1.34 (1.02, 1.77)	Ref.

*Adjusted for age, sex, race, and smoking

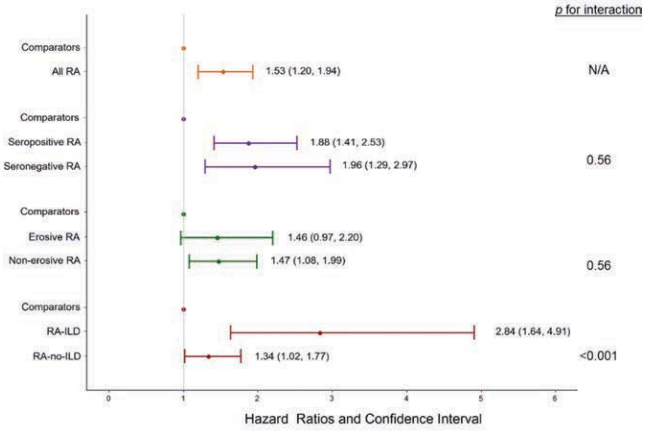

Figure 1. Multivariable hazard ratios for the composite outcome of hospitalization or death from COVID-19, comparing all RA and subgroups by serostatus, bone erosions, and ILD to matched comparators without RA.

Conclusion: We confirmed that RA was associated with severe COVID-19 outcomes compared to the general population. We found evidence that ILD may be an effect modifier for the relationship between RA and severe COVID-19 outcomes, but RA subgroups defined by serostatus and bone erosions had similarly elevated risk. These findings suggest that ILD or its treatment may be a major contributor to severe COVID-19 outcomes in RA.

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OP0252

FACTORS ASSOCIATED WITH SEVERE COVID-19 OUTCOMES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY: RESULTS FROM THE COVID-19 GLOBAL RHEUMATOLOGY ALLIANCE PHYSICIAN-REPORTED REGISTRY

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Background: There is a paucity of data in the literature about the outcome of patients with idiopathic inflammatory myopathy (IIM) who have been infected with SARS-CoV-2.
Objectives: To investigate factors associated with severe COVID-19 outcomes in patients with IIM.
Methods: Data on demographics, number of comorbidities, region, COVID-19 time period, physician-reported disease activity, anti-rheumatic medication exposure at the clinical onset of COVID-19, and COVID-19 outcomes of IIM patients were obtained from the voluntary COVID-19 Global Rheumatology Alliance physician-reported registry of adults with rheumatic disease (from 17 March 2020 to 27 August 2021). An ordinal COVID-19 severity scale was used as primary outcome of interest, with each outcome category being mutually exclusive from the other:a) no hospitalization, b) hospitalization (and no death), or c) death. Odds ratios (OR) were estimated using multivariable ordinal logistic regression. In ordinal logistic regression, the effect size of a categorical predictor can be interpreted as the odds of being one level higher on the ordinal COVID-19 severity scale than the reference category.
Results: Complete hospitalization and death outcome data was available in 348 IIM cases. Mean age was 53 years, and 223 (64.1%) were female. Overall, 167/348 (48.0%) people were not hospitalized, 136/348 (39.1%) were hospitalized (and did not die), and 45/348 (12.9%) died. Older age (OR=1.59 per decade of life, 95%CI 1.32-1.93), male sex (OR=1.63, 95%CI 1.004-2.64; versus female), high disease activity (OR=4.05, 95%CI 1.29-12.76; versus remission), presence of two or more comorbidities (OR=2.39, 95%CI 1.22-4.68; versus none), prednisolone-equivalent dose >7.5 mg/day (OR=2.37, 95%CI 1.27-4.44; versus no glucocorticoid intake), and exposure to rituximab (OR=2.60, 95%CI 1.23-5.47; versus csDMARDs only) were associated with worse COVID-19 outcomes (Table 1).

Table 1. Multivariable logistic regression analysis of factors associated with the ordinal COVID-19 severity outcomes. AZA, azathioprine; CI, confidence interval; combo, combination; CSA, ciclosporin; CYC, cyclophosphamide; DMARD, disease-modifying anti-rheumatic drug; b/tsDMARD, biologic/targeted synthetic DMARD, csDMARD, conventional synthetic DMARD; HCQ, hydroxychloroquine; IVIg, intravenous immunoglobulin; LEF, leflunomide; MMF, mycophenolate mofetil; mono, monotherapy; MTX, methotrexate; OR, odds ratio; Ref, reference; RTX, rituximab; SSZ, sulfasalazine; TAC, tacrolimus.

Variable	OR (95%CI)	P-value	Variable	OR (95%CI)	P-value
Age (per decade)	**1.59 (1.32-1.93)**	**<0.001**	**Comorbidities**		
Male sex	**1.63 (1.004-2.64)**	**0.048**	None	Ref	NA
Prednisolone-equivalent dose			One	1.46 (0.79-2.72)	0.228
None	Ref	NA	Two or more	**2.39 (1.22-4.68)**	**0.011**
>0 to 7.5mg/day	1.10 (0.57-2.11)	0.779	**Physician-reported disease activity**		
>7.5mg/day	**2.37 (1.27-4.44)**	**0.007**	Remission	Ref	NA
IVIg	0.41 (0.15-1.16)	0.093	Low/moderate	1.23 (0.67-2.28)	0.504
DMARDs			High	**4.05 (1.29-12.76)**	**0.018**
csDMARD only (mono or combi - HCQ, MTX, LEF, SSZ)	Ref	NA	**Region**		
No DMARD	1.84 (0.90-3.75)	0.094	Europe	Ref	NA
b/tsDMARD mono or combi (except RTX)	1.60 (0.49-5.26)	0.435	North America	0.89 (0.49-1.61)	0.694
CSA/CYC/TAC mono or combi (except RTX or b/tsDMARDs)	1.55 (0.52-4.58)	0.429	Other	**4.25 (2.21-8.16)**	**<0.001**
AZA mono	1.70 (0.69-4.19)	0.249	**Time period**		
MMF mono	1.22 (0.53-2.82)	0.634	Before 15 June 2020	Ref	NA
AZA/MMF combi (except RTX or b/tsDMARDs)	0.71 (0.25-2.00)	0.517	16 June - 30 September 2020	0.58 (0.26-1.27)	0.171
RTX mono or combi	**2.60 (1.23-5.47)**	**0.012**	After 1 October 2020	**0.58 (0.35-0.95)**	**0.032**

Conclusion: These are the first global registry data on the impact of COVID-19 on IIM patients. Older age, male gender, higher comorbidity burden, higher disease activity, higher glucocorticoid intake and rituximab exposure were associated with worse outcomes. These findings will inform risk stratification and management decisions for IIM patients.
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OP0253 COVID-19 ADMISSIONS AND MORTALITY IN PATIENTS WITH EARLY INFLAMMATORY ARTHRITIS: RESULTS FROM A NATIONAL COHORT

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Background: There has been a major concern about the impact of COVID-19 in patients with inflammatory arthritis during the pandemic, with recommendations from governments for patients to shield.
Objectives: Our aim was to describe the risk factors for COVID-19 hospitalisation and mortality amongst patients recruited to the National Early Inflammatory Arthritis Audit (NEIAA) in England.

Methods: An observational cohort study design was used. The population included adults in England with new diagnoses of inflammatory arthritis between May 2018 and March 2021 who enrolled in NEIAA. The outcomes were hospitalisation due to COVID-19 (primary admission reason or nosocomial acquisition) and death due to COVID-19 (COVID-19 stated on a death certificate), identified via linkage with secondary care records. Hazard ratios were calculated using Cox proportional hazards models, with adjustment for patient factors (age, gender, smoking status, and comorbidity) and disease factors (seropositivity, 28-joint disease activity score, patient-reported disability (HAQ), and functional impact (MSK-HQ)) recorded at baseline. Individuals were considered at risk from the date of diagnosis or February 2020 (whichever was later) and censored at a COVID-19 event, death or May 2021 (whichever was sooner).

Results: 14,127 patients were included. The mean age was 57 years; 62% were female; 19% were current smokers, while 29% were ex-smokers. The frequency of comorbidities at baseline were: hypertension (19%), diabetes mellitus (9%), and lung disease (9%). Overall, 20% had two or more comorbidities. Rheumatoid factor or CCP antibodies were positive in 56%. At presentation, mean scores for DAS28 were 4.6 (+/- 1.5), 1.1 (+/- 0.7) for HAQ, and 25 (+/- 11) for MSK-HQ. Initial DMARD therapy was known for 13,682/14,127 patients: methotrexate was the most common (54%), followed by hydroxychloroquine (23%), and sulfasalazine (11%).

There were 143 COVID-19 hospital admissions and 47 deaths, corresponding to incidence rates per 100 person-years for hospitalisation: 0.94 [95% CI: 0.79-1.10] and death: 0.31 [95% CI: 0.23-0.41]. Increasing age, male gender, diabetes, hypertension, lung disease and smoking status all predicted COVID-19 hospitalisation and death. Higher baseline DAS28 predicted COVID-19 hospitalisation (HR 1.24 [95% CI: 1.10-1.39]) and mortality (HR 1.33 [95% CI: 1.09-1.63]). Higher HAQ predicted both COVID-19 hospitalisation and death. Seropositivity was not a significant predictor of any COVID-19 event, nor was MSK-HQ. In unadjusted models, corticosteroids associated with COVID-19 death (HR 2.29 [95% CI: 1.02-5.13], and sulfasalazine monotherapy associated with COVID-19 hospitalisation (HR 1.93 [95% CI: 1.04-3.56]. In adjusted models, associations for corticosteroids and sulfasalazine were no longer significant. Only age, smoking status, and comorbidities independently predicted COVID-19 events.

Conclusion: The burden of COVID-19 amongst early arthritis patients was substantial during the pandemic, with concerns about the use of csDMARDs and corticosteroids.[1,2] Patient characteristics and rheumatoid disease severity at diagnosis appear to be the more important predictors of COVID-19 events than initial treatment strategy. An important limitation is that we have not looked at treatment changes over time, and must acknowledge that many patients, especially those recruited in 2019, may have changed therapy prior to the pandemic.

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OP0254

FACTORS ASSOCIATED WITH THE SEVERITY OF COVID-19 INFECTION IN PATIENTS WITH SPONDYLOARTHRITIS: RESULTS OF THE FRENCH RMD COVID-19 COHORT

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Background: To our knowledge, no published work has described precisely the severity and evolution of SARS-CoV-2 infection in patients with spondyloarthritis (SpA). Data on COVID-19 from cohorts of patients with immune-mediated inflammatory diseases concern small samples of SpA.

Objectives: Our objective was to describe the severity and course of COVID-19 in a large cohort of patients with SpA, including axial SpA (axSpA) and psoriatic arthritis (PsA), and to identify factors associated with severe forms.

Methods: Patients: individuals with Spondyloarthritis (SpA) from the French RMD COVID-19 cohort (observational, national, multicenter cohort) with a diagnosis of COVID-19 (clinical, PCR, CT or serology) were included.

Data collected: demographics, type of SpA, comorbidities, treatments, severity of COVID-19. Severity of COVID-19 was graded according to care needed: mild = outpatient care; moderate = non-intensive hospital treatment; severe = intensive care unit admission or death; severe = moderate or severe.

Statistical analyses: Logistic regression models were used to identify factors associated with these severe forms. All variables with p <0.20 in the univariate analysis were proposed in the multivariate model. Treatment variables (non-steroidal anti-inflammatory drugs (NSAIDs), methotrexate (MTX), sulfasalazine (SLZ), TNF inhibitors (TNFi), IL-17 inhibitors (IL-17i) and IL-23p19/p40 inhibitors (IL-23p19/p40i)) were included in the models, even if p≥0.20.

Results: Between March 2020 and April 2021, 626 SpAs reported COVID-19 with a mild course in 508 cases (81.1%), moderate in 93 cases (14.8%), and severe in 25 cases (3.9%), including 6 deaths.

The cohort analyzed included 349 women (55.8%), mean age 49.3 ± 14.1 years, mean BMI 27.1 ± 5.4 with 403 axSpA (64.4%), 187 PsA (29.9%) and 36 other SpA, duration of disease 11.3 ± 9.8 years; 352 (56.2%) had at least one comorbidity, of which obesity (23.6%), hypertension (15.5%), and smoking (10.4%) were the most frequent. Among them, 104 were treated with NSAIDs (16.6%), 186 with conventional synthetic disease-modifying antirheumatic drugs (DMARDs) including 156 MTX, and 460 (73.5%) with biological DMARDs (379 TNFi, 57 IL-17i, 15 IL-23p19/p40i, 9 others).

The following variables were associated with severe COVID-19 outcomes: age, body mass index, chronic obstructive lung disease, cardiovascular disease, diabetes, hypertension, interstitial lung disease, renal failure, and corticosteroids intake.

The factors independently associated with severe COVID-19 outcomes were corticosteroid intake (3.15 [CI95%: 1.46-6.76], p 0.004), and age (OR=1.06 [CI95%: 1.04-1.08], p <0.001] while anti-TNF (OR=0.26 [CI95%: 0.09-0.78], p=0.01]) was protective. NSAIDs intake (OR=0.97 [CI95%: 0.48-1.98]), SLZ (OR=7.9 [CI95%: 0.60-103]), or anti-IL17 (OR=0.37 [CI95%: 0.10-1.31]) was not associated with infection severity.

Conclusion: The course of COVID-19 was mild for the majority of SpA patients (81.1%). Corticosteroid intake was associated with more severe COVID-19 outcomes, whereas TNFi were found to be protective.

Disclosure of Interests: None declared

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Emerging treatment strategies in PsA

OP0255

BIMEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: 16-WEEK EFFICACY & SAFETY FROM BE COMPLETE, A PHASE 3, MULTICENTRE, RANDOMISED PLACEBO-CONTROLLED STUDY

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Background: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. BKZ has shown sustained efficacy and tolerability up to 152 wks in a phase 2b study in patients (pts) with active psoriatic arthritis (PsA).[1,2]

Objectives: To assess efficacy and safety of BKZ vs placebo (PBO) in pts with active PsA and prior inadequate tumour necrosis factor inhibitor (TNFi) response in the 16-wk pivotal phase 3 study, BE COMPLETE.

Methods: BE COMPLETE (NCT03896581) comprises a 16-wk double-blind, PBO-controlled period. Pts were aged ≥18 yrs, had a diagnosis of adult-onset, active PsA with ≥3 tender joints and ≥3 swollen joints, and inadequate response or intolerance to treatment with 1 or 2 TNFi. Pts were randomised 2:1 to BKZ 160 mg Q4W or PBO. From Wk 16, pts were eligible to enter an open-label extension, receiving BKZ 160 mg Q4W. The primary endpoint was a ≥50% improvement in American College of Rheumatology response criteria (ACR50) at Wk 16. Primary and ranked secondary efficacy endpoints were assessed at Wk 16.

Results: Of 400 randomised pts (BKZ: 267; PBO: 133), 388 (97.0%) completed Wk 16 (BKZ: 263 [98.5%]; PBO: 125 [94.0%]). Baseline characteristics were comparable between groups: mean age 50.5 yrs, weight 86.0 kg, BMI 29.8 kg/m^2, time since diagnosis 9.5 yrs; 47.5% pts were male.

At Wk 16, the primary endpoint (ACR50: 43.4% BKZ vs 6.8% PBO; p<0.001; Figure 1) and all ranked secondary endpoints (HAQ-DI CfB, PASI90, SF-36 PCS CfB and MDA response) were met (all p<0.001; Table 1). The ACR50 response was rapid with separation from PBO observed from Wk 4 (nominal p<0.001). Additional outcomes, including ACR20/70, TJC and SJC CfB, and PASI75/100, demonstrated numerical improvement with BKZ compared to PBO at Wk 16 (all nominal p<0.001; Table 1).

Table 1. Disease characteristics at baseline and efficacy at Wk 16

		PBO N=133	BKZ 160 mg Q4W N=267	p value
Baseline characteristics	**TJC** mean (SD)	19.3 (14.2)	18.4 (13.5)	-
	SJC mean (SD)	10.3 (8.2)	9.7 (7.5)	-
	PtGA-PsA mean (SD)	63.0 (22.0)	60.5 (22.5)	-
	PtAAP mean (SD)	61.7 (24.6)	58.3 (24.2)	-
	Psoriasis BSA n (%)			
	<3%	45 (33.8)	91 (34.1)	-
	≥3 to ≤10%	63 (47.4)	109 (40.8)	-
	>10%	25 (18.8)	67 (25.1)	-
	PASI[a] mean (SD)	8.5 (6.6)[b]	10.1 (9.1)[c]	-
	Prior TNFi n (%)			
	Inadequate response to 1 TNFi	103 (77.4)	204 (76.4)	-
	Inadequate response to 2 TNFi	15 (11.3)	29 (10.9)	-
	Intolerance to TNFi	15 (11.3)	34 (12.7)	-
	Current cDMARDs n (%)	63 (47.4)	139 (52.1)	-
Ranked endpoints in hierarchical order	**ACR50*** [NRI] n (%)	9 (6.8)	116 (43.4)	<0.001
	HAQ-DI CfB† [RBMI] mean (SE)	–0.1 (0.0)	–0.4 (0.0)	<0.001
	PASI90†[a] [NRI]n (%)	6 (6.8)[b]	121 (68.8)[c]	<0.001
	SF-36 PCS CfB† [RBMI]mean (SE)	1.4 (0.7)	7.3 (0.5)	<0.001
	MDA Response† [NRI]n (%)	8 (6.0)	118 (44.2)	<0.001
Other endpoints	**ACR20**† [NRI]n (%)	21 (15.8)	179 (67.0)	<0.001‡
	ACR70† [NRI] n (%)	1 (0.8)	71 (26.6)	<0.001‡
	TJC CfB [MI] mean (SE)	–2.4 (0.9)	–10.9 (0.8)	<0.001‡
	SJC CfB [MI] mean (SE)	–2.0 (0.5)	–7.0 (0.4)	<0.001‡
	PASI75[a] [NRI]n (%)	9 (10.2)[b]	145 (82.4)[c]	<0.001‡
	PASI100[a] [NRI]n (%)	4 (4.5)[b]	103 (58.5)[c]	<0.001‡

Randomised set (N=400). *Primary endpoint; †Secondary endpoint; ‡Nominal p value. [a]In patients with ≥3% BSA with PSO at BL; [b]n=88; [c]n=176.

Over 16 wks, 107/267 (40.1%) pts on BKZ had ≥1 TEAE vs 44/132 (33.3%) pts on PBO; the three most frequent TEAEs on BKZ were nasopharyngitis (BKZ: 3.7%; PBO: 0.8%), oral candidiasis (BKZ: 2.6%; PBO: 0%) and upper respiratory tract infection (BKZ: 2.2%; PBO: 1.5%). Incidence of SAEs was low (BKZ: 1.9%; PBO: 0%); none led to discontinuation. 2 pts on BKZ discontinued due to a TEAE (BKZ: 0.7%; PBO: 0%). No systemic candidiasis, cases of IBD, MACE, uveitis, VTE or deaths were reported.

Conclusion: Dual inhibition of IL-17A and IL-17F with BKZ in pts with active PsA and prior inadequate TNFi response resulted in rapid, clinically relevant and statistically significant improvements in efficacy outcomes vs PBO. No new safety signals were observed.[1,2]

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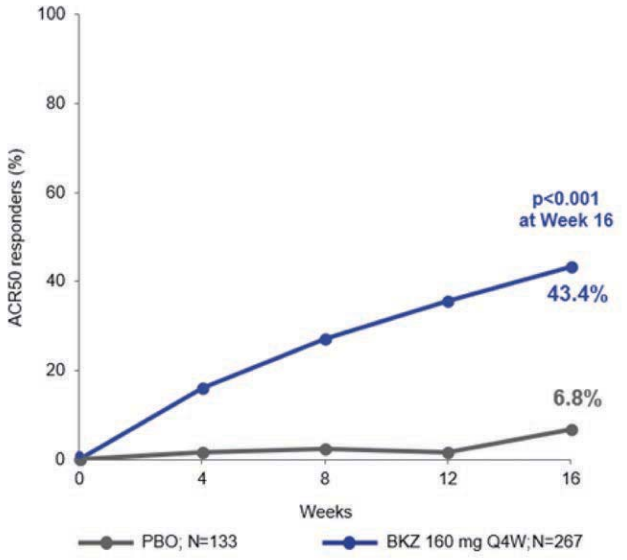
Figure. ACR50 responder rate over time to Wk 16



Randomised set (N=400). Data reported as NRI.

Abbreviations: ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; BKZ: bimekizumab; BL: baseline; BMI: body mass index; BSA: body surface area; CfB: change from baseline; cDMARD: conventional disease-modifying antirheumatic drug; HAQ-DI: health assessment questionnaire disability index; IBD: inflammatory bowel disease; IL: interleukin; MACE: major adverse cardiovascular events; MDA: minimal disease activity; MI: multiple imputation; NRI: non-responder imputation; PASI: psoriasis area and severity index; PASI75/90/100: ≥75/90/100% improvement in the psoriasis area and severity index; PBO: placebo; PsA: psoriatic arthritis; Pt: patient; PtAAP: patient's assessment of arthritis pain; PtGA: patient global assessment; PtGA-PsA: patient's global assessment of psoriatic arthritis; RBMI: reference-based multiple imputation; SF-36 PCS: 36-item short form survey physical component score; SAE: serious adverse event; SJC: swollen joint count; TEAE: treatment-emergent adverse event; TJC: tender joint count; TNFi: tumour necrosis factor inhibitor; VTE: venous thromboembolism; Wk: week; Yr: year.

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OP0256 FIBROBLAST ACTIVATION PROTEIN (FAP) PET-CT IMAGING ALLOWS TO DEPICT INFLAMMATORY JOINT REMODELING IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is characterized by substantial mesenchymal tissue activation in the context of inflammation leading to structural damage. Measuring mesenchymal tissue activation in humans in vivo is challenging but may represent a possibility to detect regions at risk for structural damage. Recently, theranostic ligands have been developed that selectively bind Fibroblast Activation Protein (FAP) and allow recognition of activated mesenchymal cells in vivo. Accumulation of such FAP-based tracers can be visualized by positron-emission tomography (PET) (1).

Objectives: In this study, we analyzed whether FAP tracer-based PET-CT can detect mesenchymal tissue activation in patients with PsA and whether this signal is associated with joint damage.

Methods: 120 consecutive PsA patients fulfilling CASPAR criteria and 100 healthy controls without musculoskeletal disease received full-body PET-CT investigation using a ^{68}Ga-labelled FAP inhibitor (^{68}Ga-FAPI-04) tracer, specifically binding FAP. For all visually identified pathological tracer-positive lesions the mean and maximum standardized uptake value (SUV mean, SUV max) was assessed. Tracer uptake was quantified in peripheral and axial joints and correlated to various composite scores of PsA. Hand MRI scans were performed in parallel to assess inflammation and structural lesions. Follow-up ^{68}Ga-FAPI-04 PET-CT scans were obtained in a subset of patients treated with cytokine inhibitors (follow-up between 3-6 months) to assess joint damage over time. In addition, FAP related tissue responses in synovial biopsy samples were evaluated on a molecular level by high-resolution slide RNA-sequencing in a subset of patients.

Results: ^{68}Ga-FAPI-04 accumulated at synovial and enthesial sites in patients with PsA compared to healthy controls ($p < 0.0001$). Active pain in peripheral as well as axial joints as measured on a visual analogue scale highly correlated with an increased ^{68}Ga-FAPI-04 uptake (peripheral pain: $R = 0.718$, $p < 0.0001$; back pain: $R = 0.875$, $p < 0.0001$). Disease Activity in PSoriatic Arthritis (DAPSA) score also correlated with the SUV mean and SUV max of FAP expression ($R = 0.774$; $p = 0.0001$). Increased ^{68}Ga-FAPI-04 uptake at baseline was associated with progression of joint damage 3-6 months later as assessed by PsAMRIS score ($R = 0.778$, $p < 0.0001$). Treatment with cytokine inhibitors partially reduced FAP expression which was associated with arrest of joint damage in MRI. In contrast, persistent FAP expression was associated with a rapid progression of joint damage in MRI. Molecular analysis of synovial biopsy samples from FAP+ lesions revealed interactions between FAP+ fibroblasts and T cells, innate lymphoid cells and macrophages, which was correlated to a strong upregulation of NF-kB related pathways fostering cartilage and bone destruction.

Conclusion: Our study presents the first in-human evidence that fibroblast activation correlates with disease progression and joint damage in patients with PsA. FAP related imaging might therefore improve the risk assessment of rapidly emerging joint damage in PsA and open new options of treat-to-target strategies in PsA.

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OP0257 RISK OF HAEMATOLOGICAL MALIGNANCY IN PATIENTS WITH PSORIATIC ARTHRITIS, OVERALL AND IN RELATION TO TNF INHIBITORS - A NORDIC COHORT STUDY

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Background: Several autoimmune inflammatory diseases, including rheumatoid arthritis (RA), are associated with increased risk of malignant lymphomas. There is also a longstanding concern of lymphoma development with tumour necrosis factor inhibitor (TNFi) treatment, but most studies in RA to date do not indicate an additionally increased risk. Corresponding studies in psoriatic arthritis (PsA), both with respect to the underlying risks, and risks in relation to treatment with TNFi, are limited. Data on myeloid malignancies in PsA are scarce.

Objectives: To estimate the risk of haematological malignancy overall and by lymphoid and myeloid types in TNFi treated versus (vs.) biologics-naïve patients with PsA across the five Nordic countries. Additionally, we investigated the underlying risk of haematological malignancies in PsA as compared to the general population.

Methods: We identified patients with PsA starting a first ever TNFi from the clinical rheumatology registers (CRR) in Sweden (SE), Denmark (DK), Norway (NO), Finland (FI), and Iceland (ICE) from 2006 through 2019 (n=10 621). We identified biologics-naïve patients with PsA from a) the CRR (n=18 705, all countries) and b) the national patient registers (NPR, n=27 286, SE and DK only). To estimate the underlying risk of haematological malignancy in PsA, we randomly sampled general population comparators in SE and DK matched on year of birth, sex, and calendar year at start of follow-up, to the patients with PsA.

Through linkage to the mandatory national cancer registers in all five countries, we collected information on haematological malignancy overall, and categorised into lymphoid or myeloid types. By applying a modified Poisson regression, we estimated pooled incidence rate ratio (IRR) with 95% confidence intervals (CI) for TNFi treated vs. biologics-naïve PsA and for PsA vs. the general population, adjusted for age (18-55, 56-65, 66-70, >70 years), sex, calendar period (2006-2010, 2011-2019) and country, and using robust standard errors.

Results: We observed 40 events of haematological malignancies (during 59 827 person-years) among TNFi treated PsA, resulting in a crude incidence rate (IR) of 67 per 100 000 person-years. The corresponding IR was 91 (63 events) for biologics-naïve PsA from the CRR, and 118 (172 events) for biologics-naïve PsA from NPR. This resulted in a pooled IRR of 0.97 (0.69 to 1.37) for TNFi-treated vs. biologics-naïve PsA patients from the CRR, and 0.84 (0.64 to 1.10) vs. biologics-naïve PsA patients from the NPR. The pooled IRR of haematological malignancies in PsA overall vs. the general population was 1.35 (1.17 to 1.55). Throughout, the estimates were largely similar for lymphoid and myeloid malignancies (Figure 1). The crude IR of haematological malignancies were substantially akin across different TNFi agents.

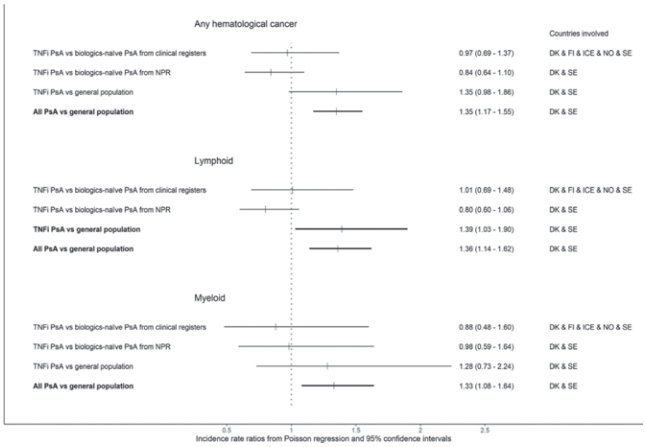

Figure 1. Pooled incidence rate ratios (IRRs) (95% CI) of haematological malignancy overall and by lymphoid and myeloid types, in first ever TNFi treated versus biologics-naïve patients with PsA, and versus general population comparators. **Legend:** Lymphoid malignancies include international classification of diseases (ICD) 10 codes C81-86, C88, C90-91. Myeloid malignancies include ICD10 codes C92-95, D45-D46, D47.1, D47.3-5. Incidence rate ratios adjusted for age (18-55, 56-65, 66-70, >70 years), sex, calendar period (2006-2010, 2011-2019) and country, and using robust standard errors.

Conclusion: In this large five-country cohort study, we did not observe any increased risk of haematological malignancies overall, nor for lymphoid and myeloid types, in patients with PsA treated with TNFi. By contrast, there were signals of a moderately increased underlying risk of haematological malignancies, both of lymphoid and myeloid types, in patients with PsA overall as compared to the general population. The findings are of importance from a patient information perspective.

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OP0258

IZOKIBEP (ABY-035) IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS – 16-WEEK RESULTS FROM A PHASE 2 STUDY

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Background: Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory disease with heterogenous musculoskeletal manifestation (arthritis, spondylitis, enthesitis, dactylitis) and extra-musculoskeletal manifestation (skin and nail psoriasis). In addition, PsA is commonly associated with comorbidities such as metabolic syndrome and cardiovascular diseases where IL-17 is a key driver of this disease.

Izokibep is a unique IL-17A inhibitor with extraordinary potency and small molecular size designed to overcome the limitations of monoclonal antibodies such as poor tissue distribution.

Here, we report 16-week phase 2 results in patients with active PsA.

Objectives: To assess efficacy, safety, pharmacokinetics and immunogenicity of izokibep versus placebo.

Methods: This is a prospective, multicenter, randomized, double-blind, placebo-controlled, parallel-groups, dose-finding trial studying bi-weekly 80 mg or 40 mg izokibep administered subcutaneously versus placebo until Week 16 (Period 1) and dose-controlled treatment until Week 46 (Period 2). PsA patients had to have ≥3 swollen and ≥3 tender joints of the 66/68 joint count, and an inadequate response to previous NSAIDs, csDMARDs or TNF inhibitor therapy. The primary endpoint was to evaluate ACR50 responses of 80 mg bi-weekly versus placebo at Week 16. Key secondary endpoints were ACR20/70, MDA, DAS28, DAPSA, SPARCC, LDI, PASI as well as tolerability and safety. Efficacy outcome measures were assessed in all patients who received at least one dose of study treatment. This trial is registered with ClinicalTrials.gov, NCT04713072.

Results: 135 patients were randomized and treated between June 2020 and July 2021 in 22 European sites located in Austria, Belgium, Czech Republic, Germany, Hungary, Poland and Spain.

At baseline, patients had a mean age of 48.5 (SD 12.0) years, a mean BMI of 29.0 (SD 4.8) kg/m^2, a mean swollen joint count (SJC) of 9.9 (SD 6.6), and a mean tender joint count (TJC) of 16.7 (SD 10.4). The mean PsA disease duration was 7.1 (SD 7.8) years. 13% failed previous TNF inhibitor treatment and 80% received a concomitant csDMARD.

At Week 16, the confirmatory primary endpoint ACR50 response rate was met (p=0.0003). ACR50 response rate was 52% in the 80 mg group, 48% in the 40 mg and 13% in the placebo group. The ACR20/50/70 response rates up to Week 16 by treatment group are presented in Figure 1.

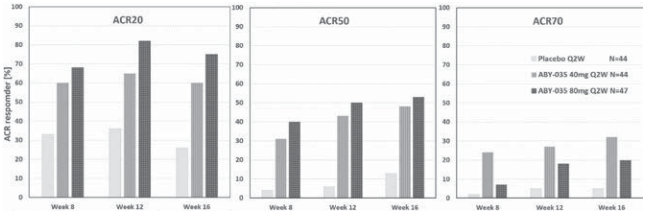

Figure 1. ACR20/50/70 response rates

SJC and TJC rapidly decreased with active treatment as indicated in Table 1.

Table 1. SJC and TJC by visit until Week 16

	Mean SJC (SD)			Mean TJC (SD)		
Study Week	Placebo Q2W N=44	40 mg Q2W N=44	80 mg Q2W N=47	Placebo Q2W N=44	40 mg Q2W N=44	80 mg Q2W N=47
BL	9.2 (6.4)	10.1 (7.0)	10.4 (6.4)	16.4 (11.3)	16.7 (10.3)	17.0 (9.7)
2	8.4 (6.1)	7.3 (6.5)	7.6 (7.6)	14.9 (10.0)	13.3 (9.5)	13.8 (10.7)
4	7.7 (7.7)	6.0 (7.0)	5.6 (6.2)	14.1 (11.8)	12.5 (11.6)	11.2 (9.2)
8	6.0 (6.2)	3.5 (4.1)	3.7 (4.7)	10.5 (7.5)	9.0 (10.5)	7.4 (7.2)
12	5.1 (5.2)	2.6 (3.4)	2.3 (3.4)	10.9 (8.7)	8.1 (8.9)	6.0 (6.7)
16	5.0 (5.7)	2.4 (3.7)	1.7 (2.7)	10.7 (9.1)	7.1 (7.7)	5.6 (6.8)

There was a dose-response relationship and a fast onset of response.

No serious or severe adverse events occurred during Period 1. The three most frequently affected System Organ Classes (SOCs) were SOC General disorders and administration site conditions comprising mainly mild injection site reactions or erythema followed by SOC Infections and infestations and SOC Metabolism and nutrition disorders. One mild, transient vulvovaginal *Candida* infection with active treatment was reported. Apart from injection site reactions there were no apparent differences in the occurrence of adverse events between active and placebo patients.

Conclusion: In this phase 2 study, izokibep showed a dose-dependent high degree of efficacy in patients with active PsA having failed previous treatment. Overall, izokibep was well tolerated.

These data strongly support further clinical development.

REFERENCES: None

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OP0259 MINIMAL DISEASE ACTIVITY RESPONSE PATTERNS IN BIO-NAIVE PATIENTS TREATED WITH GUSELKUMAB: A MACHINE LEARNING ANALYSIS

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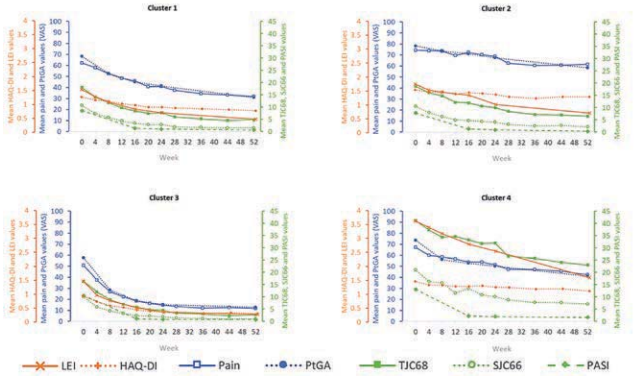
Background: Guselkumab (GUS), a human monoclonal antibody targeting the interleukin-23p19 subunit, demonstrated joint and skin efficacy in patients with active psoriatic arthritis (PsA) in the Phase III DISCOVER-1/-2 trials.[1,2] Minimal disease activity (MDA), a multi-domain composite outcome, is a clinically relevant measure of therapeutic response in PsA.[3] However, response dynamics and the effect of individual domains on achieving MDA are not well understood.
Objectives: Characterise response patterns in MDA domains over time and identify potential baseline (BL) response predictors using machine learning.
Methods: Data from bio-naïve patients with active PsA receiving GUS 100 mg every 4 or 8 weeks were pooled across DISCOVER-1/-2. Eligibility criteria are described elsewhere.[1,2] Unsupervised machine learning using the time-series K-means clustering algorithm was performed to identify clusters according to MDA domain responses over 52 weeks. MDA domain thresholds were tender joint count (TJC), swollen joint count (SJC), Psoriasis Area and Severity Index (PASI) and Leeds Enthesitis Index (LEI) each ≤1; patient global assessment (PtGA) visual analogue scale (VAS) ≤20; patient pain VAS ≤15 and Health Assessment Questionnaire-Disability Index (HAQ-DI) ≤0.5. BL characteristics were described for each cluster (Table 1). Missing data were not imputed.

Table 1. BL characteristics of four MDA response clusters (C1–4) in bio-naïve patients with active PsA treated with GUS 100 mg every 4 or 8 weeks

	Cluster			
	C1	C2	C3	C4
Patients, N	201	97	209	64
Age, years	46.1 ± 12.2	45.5 ± 11.5	46.1 ± 11.3	47.0 ± 11.1
Female, %	47.8	55.7	36.4	43.8
BMI, kg/m^2	29.4 ± 6.3	29.2 ± 6.5	28.9 ± 5.4	28.7 ± 5.7
CRP, mg/dl	1.8 ± 2.4	1.8 ± 1.6	1.4 ± 2.0	1.9 ± 2.1
PsA disease duration, years	5.5 ± 5.8	5.3 ± 5.7	5.2 ± 5.9	5.8 ± 5.9
SJC (0–66)	10.7 ± 5.4	10.6 ± 5.0	10.1 ± 6.2	21.1 ± 12.2
TJC (0–68)	18.1 ± 9.6	18.8 ± 8.8	16.3 ± 10.7	41.2 ± 13.3
Spondylitis, %	28.9	26.8	29.7	42.2
PASI score (0–72)	8.6 ± 8.9	7.8 ± 8.0	10.6 ± 12.0	13.1 ± 14.6
Dactylitis, %	42.8	42.3	35.4	71.9
Dactylitis score (0–60)	3.7 ± 6.9	1.6 ± 2.9	2.0 ± 4.4	11.7 ± 15.2
Dactylitis count (0–20)	2.1 ± 4.0	0.9 ± 1.7	1.3 ± 2.8	6.0 ± 6.8
Enthesitis, %	62.2	62.9	56.9	89.1
LEI (0–6)	1.5 ± 1.6	1.7 ± 1.8	1.5 ± 1.7	3.6 ± 2.0
HAQ-DI (0–3)	1.3 ± 0.6	1.5 ± 0.5	0.9 ± 0.6	1.5 ± 0.5
PtGA (0–100 VAS)	68.3 ± 17.8	78.2 ± 14.1	57.6 ± 21.6	73.7 ± 15.8
Pain (0–100 VAS)	62.1 ± 17.0	74.3 ± 13.7	50.8 ± 21.3	67.2 ± 15.2

Data are mean ± standard deviation or %. CRP, C-reactive protein.

Figure 1. Response patterns of individual MDA domains from Week 0 to Week 52 in four MDA response clusters (C1–4) of bio-naïve patients with active PsA treated with GUS 100 mg every 4 or 8 weeks



Data points are mean cluster values.
GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PtGA, patient global assessment; SJC66, swollen joint count 0-66; TJC68, tender joint count 0-68; VAS, visual analogue scale.

Results: This analysis included 571 of 669 patients receiving GUS and identified four distinct response clusters (C1–4; Table 1). Mean age and body mass index (BMI) were similar across clusters; C3 had a lower proportion of female patients. Relative to C3, a high burden of BL disease was observed in C4 across clinical measures and patient-reported outcomes (PROs), and across PROs only in C2. Through Week 52, MDA response rates were highest in C3 and lowest in C4, yet all clusters showed continuous improvement in mean values across all MDA domains (Figure 1). In C3, all individual domain thresholds were rapidly reached. C1, 2 and 4, met PASI threshold and showed a substantial reduction in SJC while other domains varied. In C1 and 2, improvement in clinical measures paralleled that of C3; however, PROs appeared to take longer to resolve. Responses were slowest in C4, though improvements were substantial given the high BL disease burden. Improvement in pain, PtGA and HAQ-DI occurred earlier in C1 than C2.
Conclusion: Machine learning identified four clusters of GUS-treated PsA patients based on differing response patterns in individual MDA domains. Response types may differ due to BL disease burden, especially in patients with higher pain, PtGA and functional disability scores. These results offer an innovative, complementary approach to identifying treatment response patterns across diverse clusters of bio-naïve patients with PsA, which may facilitate clinical decision-making.

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OP0260 RESPONSIVENESS OF A COMBINED POWER DOPPLER AND GREYSCALE ULTRASOUND SCORE FOR ASSESSING SYNOVITIS AT JOINT LEVEL IN PSORIATIC ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO CSDMARDS: DATA FROM THE ULTIMATE TRIAL

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Background: Power Doppler ultrasound (PDUS) is a sensitive non-invasive imaging tool that allows the visualisation of articular and periarticular inflammation in patients with psoriatic arthritis (PsA).[1] ULTIMATE (NCT02662985) was the first large randomised clinical trial that showed the responsiveness of the Global OMERACT-EULAR ultrasound synovitis score (GLOESS) in PsA and confirmed the rapid and continued benefits of secukinumab through 52 weeks.[2,3]
Objectives: To report the distribution of ultrasound-detected synovitis at joint level, by degree of severity at baseline and over time, and the contribution of each core component of GLOESS, synovial hypertrophy (SH) by greyscale (GS; B-mode) and power Doppler (PD) signal, to responsiveness.[3]
Methods: This was a 52-week study with a 12-week double-blind, placebo-controlled treatment period followed by a 12-week open-label period and a 6-month open-label extension secukinumab treatment period.[3] The number of joints with synovitis measured by GLOESS[2] was assessed up to Week 52. The assessments included distribution of synovitis based on composite PDUS score across 24 pairs of joints (with worse score of the pair of the joints used) by grade of severity (0-3) and change from baseline to Week 52 in each core component of GLOESS.[3-5] Data are presented as observed.
Results: A total of 166 patients (mean age, 46.7 years; males, 45.2%) were enrolled, of which 90% (75/83) of secukinumab and 83% (69/83) of placebo-secukinumab participants completed 52 weeks. The mean (SD) number of PDUS detected synovitis at baseline was 9.2 (4.9) and 10.2 (5.2) in the secukinumab and placebo group, respectively. The most frequent locations with synovitis at baseline were: wrist, metatarsophalangeal (MTP), knees and metacarpophalangeal (MCP) joints (Table 1). An early and continued improvement in GLOESS was observed in both secukinumab and placebo-secukinumab groups after switching to active therapy, as previously reported at Week 12 and through Week 52.[2,3] Among the two core components of GLOESS, SH was mainly responsible for the change in GLOESS from baseline to Week 52, in contrast with PD signal in this dataset. The distribution of synovitis by grade of severity showed that MTP joints, wrist, knee, MCP1/2 and tibiotalar joints mostly contributed to the composite PDUS at Week 12 (Figure 1). Similar patterns were observed through 52 weeks.

Table 1. Proportion of patients with PDUS detected synovitis at baseline*

Synovitis joint, data presented as n (%)	Secukinumab (N=83)	Placebo (N=83)
Wrist	66 (80)	66 (80)
MTP2	56 (68)	65 (78)
MTP1	58 (70)	60 (72)
MTP3	52 (63)	60 (72)
MTP4	46 (55)	59 (71)
Knee	50 (60)	47 (57)
MCP1	36 (43)	52 (63)
MCP2	35 (42)	41 (49)
MTP5	30 (36)	41 (49)

*Data for top nine pairs of joints with most frequently detected power Doppler ultrasound (PDUS) synovitis are presented here. Synovitis was scored by a OMERACT-EULAR synovitis composite score >0 for each paired joint (irrespective of right or left side). The OMERACT-EULAR composite PDUS score (for individual joints) ranged from 0 to 3 and was composed of the two core components synovial hypertrophy and power Doppler. N, total number of randomised patients; n, number of evaluable patients

Conclusion: The distribution of synovitis at baseline reflected a predominance of small joints (feet and hands) and large joints (wrist and knee) and were mostly responsive to secukinumab over time in the ULTIMATE trial. Synovial hypertrophy was the most responsive core component of GLOESS driving an early and continued reduction of synovitis with secukinumab through Week 52. This finding could be useful to select a restricted number of joints in future ultrasound trials in PsA.

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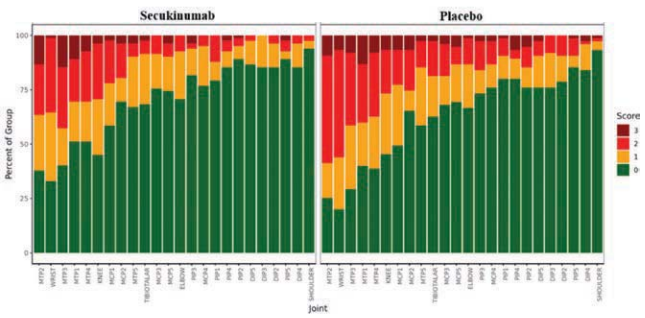
Figure. Distribution of the composite PDUS score at Week 12



Detected synovitis was determined by a OMERACT-EULAR power Doppler ultrasound (PDUS) synovitis composite score >0 for each joint irrespective of right or left side and post-baseline presence required synovitis to be present in that joint at baseline.

Disclosure of Interests: Maria-Antonietta D'Agostino Speakers bureau: Sanofi, Novartis, BMS, Janssen, Celgene, Roche, AbbVie, UCB, and Eli Lilly, Consultant of: Sanofi, Novartis, BMS, Janssen, Celgene, Roche, AbbVie, UCB, and Eli Lilly, Maarten Boers Consultant of: Novartis, Corine Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis, Carlos Gamez: None declared, LUCIO VENTURA: None declared, Javier Rosa Speakers bureau: Abbvie, Pfizer, Lilly, Janssen, Novartis and BMS, Ilaria Padovano: None declared, Peter Mandl Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Roche and UCB, Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Roche and UCB, Arnd Kleyer Speakers bureau: Abbvie, Lilly, Novartis, MEDAC; Janssen, Consultant of: Abbvie, Lilly, UCB, Novartis, BMS, Sanofi, Galapagos, Catherine Bakewell Speakers bureau: AbbVie, Novartis, Pfizer, Janssen, UCB, and Sanofi Genzyme/Regeneron, Consultant of: AbbVie, Novartis, Pfizer, Janssen, UCB, and Sanofi Genzyme/Regeneron, Weibin Bao Shareholder of: Novartis, Employee of: Novartis, Punit Goyanka Employee of: Novartis, Philip G Conaghan Speakers bureau: AbbVie, Amgen, AstraZeneca, Eli Lilly, Galapagos, Gilead, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, AstraZeneca, Eli Lilly, Galapagos, Gilead, Novartis, Pfizer and UCB, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Roche and UCB
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OP0261 TREAT-TO-TARGET DOSE REDUCTION AND WITHDRAWAL STRATEGY OF TNF INHIBITORS IN PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS: A RANDOMIZED CONTROLLED NON-INFERIORITY TRIAL

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Background: Tumour Necrosis Factor inhibitors (TNFi) are effective in Psoriatic Arthritis (PsA) and axial SpondyloArthritis (axSpA), but are associated with a somewhat increased infection risk, patient burden, and high costs. Treat-to-target (T2T) tapering might ameliorate these drawbacks, but no high quality T2T tapering studies have been done in PsA and axSpA.
Objectives: To investigate whether a T2T strategy with tapering is non-inferior to a T2T strategy without tapering.
Methods: We performed a pragmatic open-label, monocenter, randomized, controlled non-inferiority (NI) trial on T2T tapering of TNFi. PsA and axSpA patients using a TNFi with ≥6 months stable low disease activity (LDA) were randomized to a T2T tapering or no-tapering strategy, in a ratio of 2:1 and followed-up for 12 months. LDA was defined as a Psoriatic Arthritis Disease Activity Score (PASDAS) ≤3.2 for PsA and/or Ankylosing Spondylitis Disease Activity Score (ASDAS) <2.1 and/or judgement of physician and patient. Tapering consisted of 3-monthly tapering steps (66%, 50%, 0%), with re-intensification in case of flare. Primary endpoint was the difference in proportion of patients having LDA at 12 months, compared to a prespecified NI margin of 20%. The primary Bayesian analysis was adjusted for stratification factors (diagnosis and csDMARD use). Secondary endpoints included the mean percentage Daily Defined Dose (%DDD) at month 12 and mean 3-monthly disease activity and %DDD. Other endpoints included the proportion of patients discontinuing their TNFi, the cumulative incidence of flares (change from baseline PASDAS≥0.8 or ASDAS≥0.9), the use of concomitant medication and (serious) adverse events.
Results: 122 patients were included (N=81 tapering (PsA, N=42, axSpA, N=39); N=41 no-tapering (PsA, N=22, axSpA, N=19)) (Table 1). Proportion of patients in LDA at 12 months for the tapering and no-tapering group was

69% and 73%: adjusted difference 5% (Bayesian 95% credible interval: -10% to 19%), confirming NI. The mean percentage %DDD was respectively 53% and 91% at month 12 (Figure 1). At 12 months, 58 (72%) patients of the tapering group were successfully tapered, of whom 23 (28%) discontinued their TNFi. The cumulative incidence of flares was 85% in the tapering and 78% in the no-tapering group (p=0.32). Start or escalation of concomitant medication was more frequent in the tapering group, significantly so for NSAID use: csDMARDs (only for PsA): 1 (2%) vs. 1 (5%) (p=0.64); NSAIDs: 44 (54%) vs. 10 (24%) (p=0.002); glucocorticoids: 24 (30%) vs. 7 (17%) (p=0.13). For serious adverse events, similar results were seen. The risks of grade 3/4 infections and injection site reactions were respectively 46% and 23% lower in the tapering group than the no-tapering group.

Table 1. Baseline characteristics of T2T strategy treated PsA and axSpA patients with or without tapering.

Characteristic	T2T with tapering (N=81)	T2T without tapering (N=41)
Diagnosis, n (%)		
-Psoriatic arthritis	42(52%)	22(54%)
-Axial spondyloarthritis	39(48%)	19(46%)
Female, n (%)	28(35%)	20(49%)
Age in years at inclusion, mean (SD)	50(14)	52(15)
Disease duration at inclusion, years, median (IQR)	11(5-21)	12(5-21)
CASPAR Criteria, n (%)	34(81%)	17(77%)
ASAS Criteria, n (%)	35(90%)	17(89%)
Disease activity, mean (SD)		
-PASDAS - (64/64 PsA)	1.60(1.26)	1.63(0.98)
-ASDAS - (57/58 axSpA)	1.34(0.87)	1.21(0.61)
Duration of current bDMARD use, years, median (IQR)	2(1-6)	2(2-7)
Current bDMARD use, n (%)		
-Adalimumab	62(77%)	28(68%)
-Etanercept	10(12%)	6(15%)
-Certolizumab Pegol	2(2%)	1(2%)
-Golimumab	2(2%)	1(2%)
-Infliximab	5(6%)	5(12%)

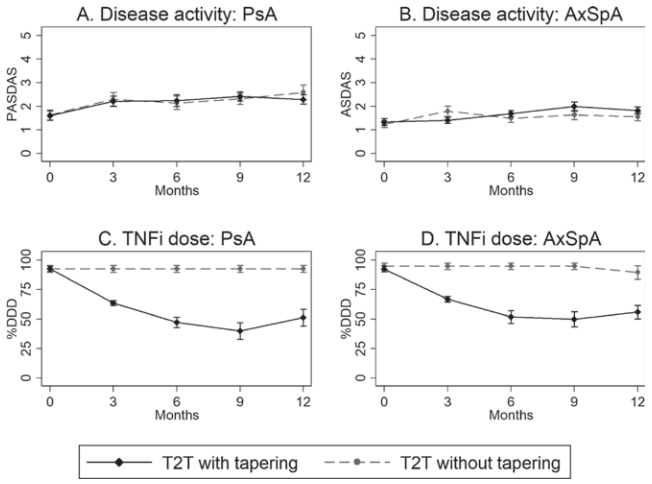

Figure 1. Mean disease activity and %DDD of T2T strategy treated PsA (A. and C.) and axSpA (B. and D.) patients with or without tapering at baseline, 3, 6, 9 and 12.

Conclusion: A T2T TNFi tapering strategy is non-inferior to a T2T strategy without tapering with regard to the proportion of patients still in LDA at 12 months and results in a substantial reduction of TNFi use, albeit with slightly more use of other medication.

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OP0262

PREVALENCE AND PREDICTORS OF ACHIEVING SUSTAINED REMISSION IN PSORIATIC ARTHRITIS

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Background: Increased availability and a wide selection of b/tsDMARDs with different mode of action has made long-term remission a realistic treatment goal in psoriatic arthritis.

Objectives: To estimate the prevalence and possible predictors of sustained remission in patients with psoriatic arthritis (PsA) treated with biologic or targeted synthetic disease-modifying anti-rheumatic drugs (bDMARD/tsDMARD) in Sweden.

Methods: All patients initiating treatment with bDMARDs or tsDMARDs for PsA in Sweden and registered in the national Swedish Rheumatology Quality Register (SRQ) were included. Data on disease and treatment characteristics from the start of the first b/tsDMARD (baseline) and all registered subsequent visits were extracted from SRQ. Sustained remission (SR) was defined as DAS28-CRP ≤ 2.6, DAPSA28 ≤ 4 or the evaluator's global assessment of disease activity (0-4 on a Likert scale) = 0, during at least two consecutive visits over at least six months. To compensate for factors that may temporarily raise disease activity measures, such as concurrent infections, one visit with higher disease activity was allowed if the treatment regimen was not altered at that point and if less than two years between adjacent visits in remission. A sensitivity analysis was performed with a more stringent SR definition, not allowing any such visits with higher disease activity. Logistic regression was used to identify possible predictors of SR.

Results: 5 459 PsA patients with 50 811 visits were included in the analysis. According to DAS28-CRP, 78% of patients achieved a state of remission at some point, and 49% achieved SR at least once. When the more stringent DAPSA28 remission criteria were applied, 27% of patients reached a state of remission at some point, and 11% ever achieved SR. Corresponding figures using the evaluator's global assessment were 64% and 34% for ever reaching remission or SR, respectively (Figure 1). The sensitivity analysis rendered similar results with a ≤3% difference from the main results for all outcomes. Higher age at start of the first b/tsDMARD therapy was associated with a lower likelihood of SR, but males were significantly more likely to achieve SR than females (OR 1,79-2,63 for reaching SR depending on the remission criteria used).

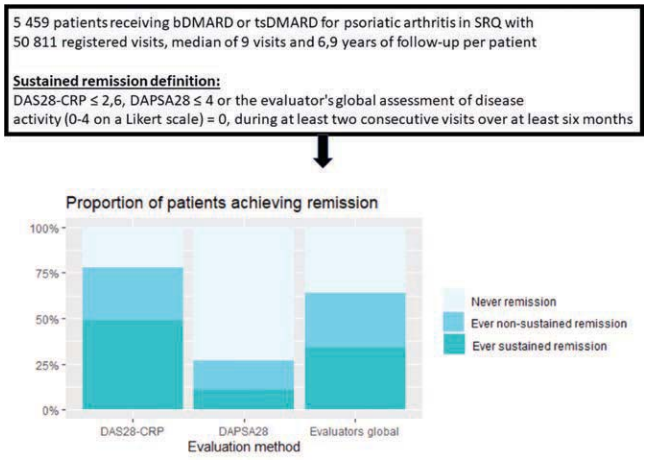

Figure 1. Proportion of patients achieving sustained and non-sustained remission at any point after SRQ registration.

Conclusion: Despite increased availability and a wider selection of b/tsDMARDs with different modes of action, a considerable proportion of PsA patients receiving such treatments never achieve a state of remission, and less than half ever achieve a more extended period of sustained remission. Males are more likely than females to enter sustained remission.

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RA treatment: modern strategies and new molecules

OP0263

FAVORABLE BALANCE OF BENEFIT AND HARM OF LONG-TERM, LOW-DOSE PREDNISOLONE ADDED TO STANDARD TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS AGED 65+: THE PRAGMATIC, MULTICENTER, PLACEBO- CONTROLLED GLORIA TRIAL

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Background: Low-dose glucocorticoid (GC) therapy is widely used in RA but the true balance of benefit and harm is still unknown.
Objectives: We studied the effects of prednisolone (5 mg/day, 2 years) in RA patients aged 65+, requiring adjustment of antirheumatic therapy (DAS28≥2.60).
Methods: Pragmatic double-blind placebo-controlled randomized trial; all co-treatments and changes therein were allowed during the trial except long-term open label GC; Ca/D supplementation was advised in all patients. Minimal exclusion criteria were tailored to seniors.
Harm outcome: the number of patients with ≥1 serious adverse event (SAE), or ≥1 'other adverse event of special interest' (other AESI). Other AESI comprised any AE (except worsening of RA) causing study discontinuation, and GC-specific events (Table 1).

Table 1. Adverse events of special interest (AESI).*

	prednisolone (n=224)		placebo (n=225)	
Events by protocol-defined category	SAE	other AESI	SAE	other AESI
Infection	26	124	16	91
Urinary tract	4	49	4	29
Pneumonia	2	17	2	13
Other	20	58	10	49
Cardiovascular	8	2	6	0
Symptomatic fracture	2	11	4	6
New onset				
Hypertension	1	4	0	7
Diabetes mellitus	0	2	0	1
Cataract	0	7	2	6
Glaucoma	0	1	0	3
Other†	43	43	35	26
Total	80	194	63	140

*AESI: Comprises serious adverse events (SAE) and other AESI, defined by protocol. †'Other' other AESI: non-serious AE outside of the above predefined categories, but associated with premature discontinuation.

Benefit outcomes: improvement in disease activity (DAS28) and joint damage progression (Sharp/van der Heijde).
Longitudinal mixed models analyzed the data. Given prior knowledge we report one-sided 95% confidence limit (95%CL) and statistical tests, performed only for the main outcomes.
Results: We randomized 451 RA patients in 7 EU countries, 449 received the intervention; of these 63% prednisolone vs 61% placebo patients completed 2 years of follow up. Discontinuations were similar in both groups: for AE (14%) and active disease (4%); the remainder mostly for 'trial fatigue' and covid-related access issues (20%). Mean time on study drug was 19 (SD 8) months.
70% of patients were female, mean age was 72 (max 88) years, RA duration 11 years; 67% were RF+, 56% ACPA+, 96% had joint damage on radiographs: mean score 20, median 8. Mean DAS28 was 4.5. Most patients (79%) were on current DMARD treatment, including 14% on biologics; 47% had previously used GC, 14% changed DMARD therapy at baseline. Patients had mean 2.1 active comorbidities, and used median 7 drugs.
Benefit: Disease activity rapidly declined to stabilize after 1 year (Figure 1), and was lower on prednisolone (adjusted mean difference in DAS28 over 2 years: 0.37, 95%CL 0.23, p<0.0001). The contrast in early (3-month) response was larger in 331 patients adherent to protocol on stable treatment: mean difference in DAS28 0.62 (95%CL 0.44), more responders on prednisolone (Figure 1). Significant time-treatment interaction in secondary analyses suggested a decrease in contrast after the first year, most likely caused by significantly more changes in DMARD treatment on placebo. Joint damage progression over 2 years was significantly lower on prednisolone: mean 0.6 (SD 1.9) v 1.8 (6.4) score points on placebo, difference 1.2 (95%CL 0.2, p=0.02).
Harm: 60% prednisolone vs 49% placebo patients experienced the harm outcome: adjusted RR 1.24, 95%CL 1.04, p=0.02; number needed to harm 9.5 (Table 1). During the study 1 vs 2 patients died, and 3 vs 0 died within 5 months of discontinuation. Per 100 patient-years, AE totaled 278 in prednisolone vs 206 in placebo patients, and the difference was most marked for infections (Table 1); these were mostly mild or moderately severe. Other GC-specific AESI were rare without relevant differences.
Conclusion: Add-on low dose prednisolone has beneficial long-term effects on disease activity and damage progression in senior RA patients on standard treatment. The tradeoff is a 24% increase in patients with mostly mild to moderate AE, suggesting a favorable balance of benefit and harm.

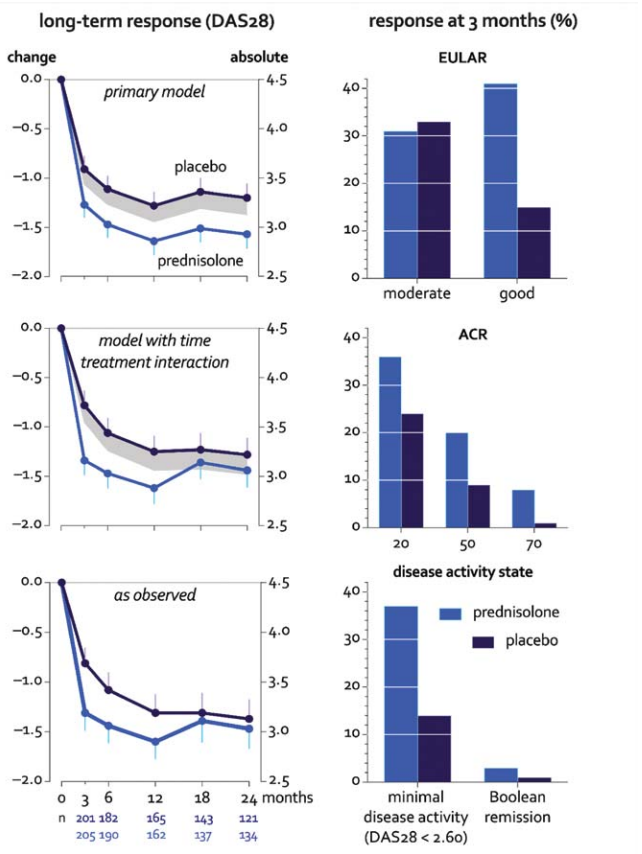

Figure. Better response in disease activity on prednisolone compared to placebo.
Left: long-term change in DAS28: primary model, model with time-treatment interactions, and as observed, with observed number of patients.
Right: response at 3 months in the stable adherent population (n=331).
Grey area: one-sided 95% confidence bound for the difference between groups at each time point.
Error bars: one half of the two-sided 95%CI for the group means.

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OP0264

IMPACT OF BASELINE CARDIOVASCULAR RISK ON THE INCIDENCE OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN THE TOFACITINIB RHEUMATOID ARTHRITIS CLINICAL PROGRAMME

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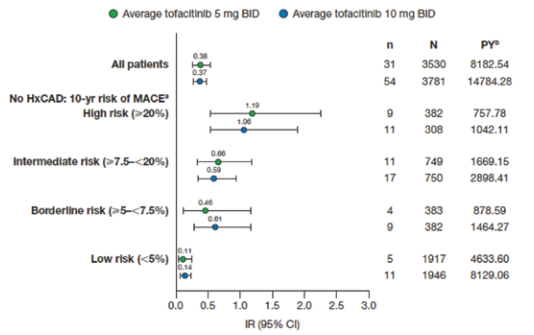
Background: Results from ORAL Surveillance, a post-authorisation safety study, indicated that patients (pts) with rheumatoid arthritis (RA) aged ≥50 yrs with ≥1 additional cardiovascular (CV) risk factor have an increased risk of major adverse CV events (MACE) with tofacitinib vs tumour necrosis factor inhibitors.[1]
Objectives: To evaluate the impact of baseline (BL) CV risk on MACE in the wider tofacitinib RA clinical programme.
Methods: Data for pts who received ≥1 tofacitinib dose in 21 Phase 1–3b/4 (excluding ORAL Surveillance) and 2 long-term extension tofacitinib RA studies were pooled and analysed post hoc as two cohorts: (1) overall cohort and (2) CV risk-enriched cohort (pts aged ≥50 yrs with ≥1 additional CV risk factor [current smoker, hypertension, HDL-cholesterol <40 mg/dL, diabetes mellitus, history of myocardial infarction (MI) or coronary heart disease (CHD)]). Data were summarised by average tofacitinib 5 or 10 mg twice daily (BID; average total daily dose of <15 or ≥15 mg, respectively). Incidence rates (IRs; pts with first events/100 pt-yrs) for adjudicated MACE were calculated. MACE IRs were stratified by pts' BL CV risk profile: pts were first categorised by history of coronary artery disease (HxCAD), then pts without a HxCAD were categorised by 10-yr risk of MACE, per the ASCVD-PCE risk calculator[2] with a 1.5 multiplier applied.[3]
Results: The overall cohort included 7964 pts (average tofacitinib 5 mg BID, n=3969; average tofacitinib 10 mg BID, n=3995); of these, 3125 (39.2%) pts were included in the CV risk-enriched cohort (average tofacitinib 5 mg BID, n=1614; average tofacitinib 10 mg BID, n=1511). In both treatment arms, as expected, higher proportions of pts in the CV risk-enriched cohort had a HxCAD or a high or intermediate 10-yr predicted risk of MACE at BL vs the overall cohort (Table 1). MACE IRs (95% CIs) were lower in the overall cohort (0.38 [0.26, 0.54] and 0.37 [0.27, 0.48] for average tofacitinib 5 and 10 mg BID, respectively) vs the CV risk-enriched cohort (0.72 [0.46, 1.09] and 0.67 [0.46, 0.93], respectively), and were similar between treatment arms. MACE IRs were lower than reported in ORAL Surveillance.[1] In the overall cohort, adjudicated MACE most commonly occurred in pts with a HxCAD (IR [95% CI] 0.98 [0.02, 5.47] and 1.05 [0.13, 3.78] for average tofacitinib 5 and 10 mg BID, respectively), or in pts with a high 10-yr risk of MACE at BL (Figure 1). A lower predicted 10-yr MACE risk was associated with lower MACE IRs (Figure 1); trends were similar for the CV risk-enriched cohort (data not shown).

Table 1. Proportions of pts with a HxCAD and pts without a HxCAD categorised by 10-yr risk of MACE, per ASCVD-PCE risk calculator[2] with a 1.5 multiplier applied[3]

	Average tofacitinib 5 mg BID		Average tofacitinib 10 mg BID	
	Overall cohort(N=3969)	CV risk-enriched cohort(N=1614)	Overall cohort(N=3995)	CV risk-enriched cohort(N=1511)
HxCAD, n (%)	61 (1.5)	61 (3.8)	65 (1.6)	60 (4.0)
No HxCAD: 10-yr risk of MACE, n (%)				
High (≥20%)	440 (11.1)	365 (22.6)	337 (8.4)	276 (18.3)
Intermediate (≥7.5–<20%)	853 (21.5)	593 (36.7)	788 (19.7)	530 (35.1)
Borderline (≥5–<7.5%)	435 (11.0)	234 (14.5)	404 (10.1)	195 (12.9)
Low (<5%)	2133 (53.7)	342 (21.2)	2058 (51.5)	307 (20.3)
Missing data	47 (1.2)	19 (1.2)	343 (8.6)	143 (9.5)

CAD is defined as any of MI or CHD. n, number of pts with specified characteristic; N, number of evaluable pts

Fig. IRs (pts with first events/100 PY; 95% CI) for adjudicated MACE, stratified by HxCAD and 10-yr risk of MACE in the overall cohort



[a]Pts without a HxCAD were categorised according to their 10-yr risk of MACE, per the ASCVD-PCE risk calculator[2] with a 1.5 multiplier applied[3]
[b]Total PY of exposure accrued during the risk period
95% CIs were constructed using Exact Poisson distribution
Includes pts from studies with CV adjudication process applied to data after 25 February 2009
Risk period was defined as the time from first study dose to last study dose +28 days, or to the death date, whichever was earlier
CAD is defined as any of MI or CHD
ASCVD-PCE, atherosclerotic CV disease-pooled cohort equations; n, number of pts with event; PY, pt-yrs

Conclusion: In the tofacitinib RA clinical programme, MACE were largely associated with BL CV risk in the overall cohort, consistent with results of ORAL Surveillance, although results should be interpreted with caution due to low pt-yrs of exposure in some pt groups. Noting this limitation, these findings emphasise the importance of assessing and addressing BL CV risk when treating pts with RA.

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OP0265

COMPARISON OF THE EFFECT OF DIFFERENT JANUS KINASE INHIBITORS ON ACTIVATION, FUNCTION AND PROPERTY OF NK CELLS TO CONTROL CANCER CELL LINES PROLIFERATION: AN EX VIVO AND IN VITRO STUDY.

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Background: Janus kinase inhibitors (JAKi) are effective targeted synthetic DMARDs licensed in rheumatoid arthritis (RA) and in other immune-mediated diseases. Among the adverse events described, the increased risk of herpes zoster is specific of this therapeutic class but variable depending on the drugs, especially lower with filgotinib (FILGO)[1]. Recently the ORAL Surveillance study highlighted an increased risk of lymphoma and lung cancer with tofacitinib (TOFA) in RA patients older than 50 years with cardio-vascular risk factors[2]. Because of their antitumor and antiviral role, especially against herpes viruses, effect of JAKi on NK cells may play a causal role in these adverse events. Our working hypothesis is that the different JAKi could have a differential impact on the activation and function of NK cells leading to the variability of the tolerance profiles observed between the molecules.

Objectives: To evaluate the phenotypic and functional impact of JAKi on NK cells.

Methods: We first performed ex vivo phenotypic analyses of NK cells in RA patients treated with TOFA or baricitinib (BARI) in comparison with patients treated with methotrexate (MTX). To go deeper, we phenotyped sorted NK cells from healthy donors after 6 days of culture with 4 JAKi (TOFA, BARI, upadacitinib (UPA) and FILGO) or control (DMSO). We used 3 different doses carefully chosen to mimic in vivo exposure [therapeutic concentration (therap) defined as mean concentration in patients at the licensed dose, infra therapeutic (infra, mean -2DS) and supra therapeutic concentration (supra, mean +2Ds)]. Thirdly, we stimulated sorted NK cells from healthy donors exposed to TOFA or BARI at therap and supra concentrations with anti-NKp30 crosslinking to assess NK cells function: intra-cellular IFNγ/TNF production and degranulation (CD107a). Finally, we challenged sorted NK cells from healthy donors exposed in vitro to TOFA or BARI at therap and supra doses with 2 different tumor cells line to assess degranulation and cytotoxicity: a lung cancer line A549 and a lymphoma cell line SU-DHL-4.

Results: Twenty-eight RA patients were included in the ex vivo assay (12 MTX, 6 TOFA, and 10 BARI). Patients under TOFA and not under BARI had a significant reduced CD69 (an activation marker) expression on NK cells ($p<0.05$) compared to MTX. After in vitro culture of NK cells with JAKi, we confirmed the negative impact of JAKi on NK cells activation (CD69), maturation markers (CD57, Tim3) and activating receptor (NKp30), more pronounced with TOFA and UPA (Figure 1A). After crosslinking with anti-NKp30, NK cells exposed to TOFA produced significantly less IFNγ/TNF and expressed less CD107a compared to DMSO ($p<0,005$). There was a non-significant trend for a dose-effect (Figure 1B). BARI did not induce any significant effect. Lastly, when NK cells were co-cultured with the cancer cell lines, previous exposition to TOFA but not to BARI led to a significant reduction of CD107a expression on NK cells ($p<0.005$) and to reduced cytotoxicity ($p<0.05$) of NK cells versus A549 at therap dose. Studies regarding SU-DHL-4 are still in progress.

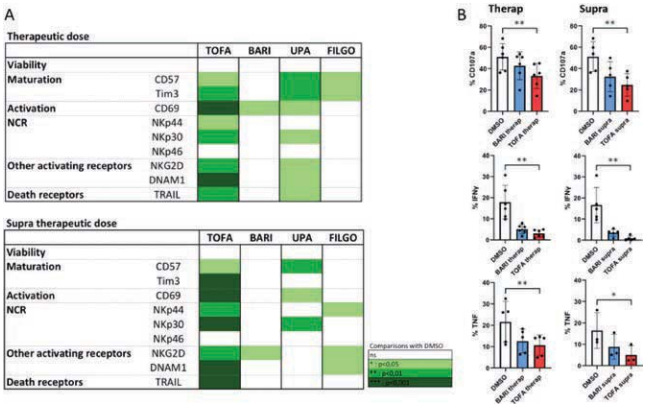

Figure 1. Impact of in vitro exposure to JAKi at therap and supra dose on NK cells regarding phenotype (A) and function after crosslinking (B)

Conclusion: JAKi have a phenotypic and functional dose-effect impact on NK cells activation, both in ex vivo and in vitro experiments. TOFA has more impact than other JAKi on NK cells phenotype and function and has the property to impair the control of proliferation of lung cancer and lymphoma cell lines by NK cells. The question remains open if this mechanism could explain the increased risk of lung cancer and lymphoma observed with TOFA in the ORAL surveillance trial.

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OP0266

TREATMENT DISCONTINUATION DUE TO ADVERSE EVENTS AS AN OVERALL MEASURE OF TOLERANCE AND SAFETY OF JAK-INHIBITORS: AN INTERNATIONAL COLLABORATION OF REGISTRIES OF RHEUMATOID ARTHRITIS PATIENTS (THE "JAK-POT" STUDY).

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Background: The recently presented "ORAL Surveillance Study" has suggested increased risk of serious adverse events (AEs) with tofacitinib, a JAK-inhibitor (JAKi), compared to a comparator TNF-inhibitor (TNFi). Currently, there is limited real world evidence for the tolerability and safety of JAKi (1).

Objectives: To assess the safety of JAKi compared to other biologic agents in rheumatoid arthritis (RA) patients in a real-world population, by evaluating treatment discontinuation for AEs.

Methods: Pooled patient database from 16 national RA registries from across Europe, Québec (Canada), Turkey, and Israel were used. Treatment discontinuation due to AEs by treatment groups, JAKi versus (vs) TNFi and JAKi vs bDMARDs with other modes of action (OMA), were compared as an overall measure of tolerability and safety of JAKi. Standard descriptive statistics were used for baseline characteristics. We plotted unadjusted cumulative incidence, then the cause-specific Cox model was used to account for competing risks, and to obtain association between covariates and the instantaneous hazard rate for AEs. Variables listed in Table 1 were used for adjustment in the fully-adjusted cause-specific Cox model.

Table 1. Baseline characteristics of the study population

	JAKi[1] (BARI, FILGO,TOFA,UPA)	OMA[2] (ABA, ANAK, SARI, TOCI)	TNFi[3] (ADA, CERT, ETAN, GOL, INFL)
	n = 9208	n = 16737	n = 64533
Treatment duration* (yrs)	0.7 [0.2, 1.7]	1.1 [0.4, 2.8]	1.5 [0.5, 3.9]
Age	57.5	56.8	53.2
Female (%)	81.3	80.7	73.2
Disease duration (yrs)	9.9	13.1	10.7
Seropositivity (%)	78.7	75.9	69.8
Previous b/tsDMARD (%)			
0	34.0	30.8	59.7
1	20.9	25.9	24.3
2	16.6	21.7	10.4
3 or more	28.5	21.5	5.6
Concomitant GC (%)	44.6	50.7	41.3
Concomitant CsDMARD (%)			
MTX	22.6	22.0	28.8
MTX + other	9.5	9.7	13.1
None	50.5	52.5	43.5
Other	17.4	15.9	14.7
CRP	13.2 (24.1)	13.3 (25.6)	12.3 (24.1)
CDAI	23.7 (13.8)	22.9 (13.5)	22.6 (14.0)
DAS 28	4.7 (1.5)	4.7 (1.6)	4.6 (1.6)
HAQ	1.2 (0.7)	1.2 (0.7)	1.1 (0.7)
BMI	27.1 (5.9)	26.8 (5.8)	26.8 (5.8)
Patients with at least one Comorbidity (%)	51.7	53.9	49.6

csDMARDs = classical synthetic DMARDs, MTX = methotrexate, GC = glucocorticoids, CRP = C-reactive protein, CDAI = Clinical Disease Activity Index, DAS 28 = Disease Activity Score 28, HAQ = Health Assessment Questionnaire, BMI = Body Mass Index, *Treatment duration (median [IQR]) = Last visit date – start date (if treatment is ongoing), treatment stop date – treatment start date (if treatment has stopped). [1]BARI (baricitinib; 44.41 %), FILGO (filgotinib; 0.23%), TOFA (tofacitinib; 49.59%), UPA (upadacitinib; 5.78%); [2]ABA (abatacept; 39.96%), ANAK (anakinra; 2.64%), SARI (sarilumab; 3.14%), TOCI (tocilizumab; 52.55%); [3]ADA (adalimumab; 31.00%), CERT (certolizumab; 8.33%), ETAN (etanercept; 38.83%), GOLI (golimumab; 9.36%), INFL (infliximab; 12.56%)

Results: 90,478 treatment courses were included in the analysis (Table 1). We observed similar crude incidence rate of treatment discontinuation due to AEs between JAKi and TNFi, but less in JAKi vs OMA (Figure 1). The fully adjusted hazard rate of treatment stop for AEs was also similar in JAKi vs TNFi (HR = 1.02 (95% CI 0.92 – 1.13)), and in JAKi vs OMA (HR= 1.08 (95% CI 0.97 – 1.20)). The rate of treatment stop for AEs was higher in women (HR = 1.29 (95% CI 1.21 – 1.37)) and with an increasing number of previous b/tsDMARDs (HR = 1.50; 1.48; 1.68 for 1, 2, and 3 or more previous b/ts DMARDs, respectively).

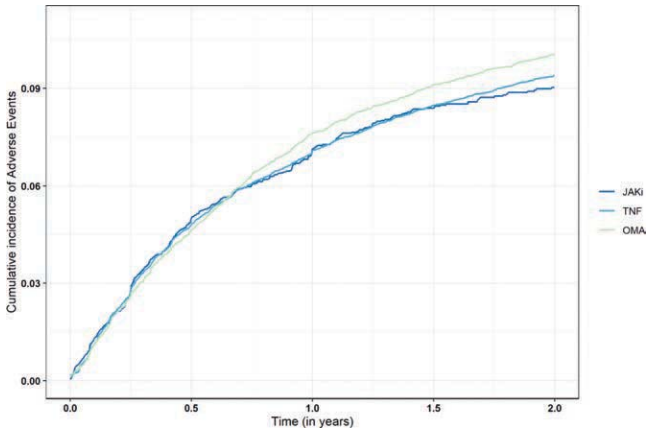

Figure 1. Comparison of cumulative incidence of treatment discontinuation for adverse events in JAKi, TNFi, and OMA group

Conclusion: After adjusting for potential confounders, the rate of treatment discontinuation for AEs was comparable between JAKi and OMA or TNFi. Treatment discontinuation for AEs comprises a wide range of AEs; future analyses will be performed to investigate specific AEs, such as cancer, serious infections or major adverse cardiovascular events.

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OP0267 A GENOME-WIDE INVESTIGATION OF PERSISTENCE TO TREATMENT WITH METHOTREXATE IN SWEDISH EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Despite being the anchor drug for treating rheumatoid arthritis (RA), methotrexate (MTX) provides a good response only in some of the treated patients [1]. If MTX treatment outcome has a substantial genetic component, genetic variants could provide useful predictors for identification of patients likely to respond and remain on treatment. So far, studies have focused mainly on primary response, and attempts to explain the inter-patient variability through genetic variants have been inconclusive or underpowered [2,3].

Objectives: We aimed to investigate whether there are genetic variants associated with persistence to treatment with MTX (at one and three years) in early RA, and to estimate any underlying heritability.

Methods: We conducted a genome-wide association study (GWAS) on persistence to treatment with MTX in DMARD-monotherapy. We included participants from the Epidemiological Investigation of RA (EIRA) study and the Swedish Rheumatology Quality Register's biobank, diagnosed with early RA and treated with MTX as their first ever DMARD. Persistence to MTX was defined as remaining on treatment at one and three years, respectively, with no additional DMARDs added during that period. Estimation of SNP-based heritability was done using restricted maximum likelihood. We performed the analyses for all RA, and two disease subsets: those positive for either ACPA or rheumatoid factor, and those negative for both.

Results: After quality control, 3403 of an initial 3609 early RA patients of European ancestry and above five million SNPs remained for the primary analysis. Among these, 65% were persistent at one year, and 44% were persistent at three years. In secondary analysis we excluded 218 patients due to missing sero-status. Of the remaining, 72% were seropositive. No SNP reached genome-wide significance, neither for persistence at one nor at three years. The SNP-based heritability was estimated to 0.35 (95%CI 0.04-0.65) for persistence at one year and 0.09 (95%CI 0.00-0.37) for persistence at three years. Analyses stratified by sero-status provided results comparable to the main analysis with similar proportions of persistent patients and no SNP reaching genome-wide significance for any of the subgroups. Point estimates of heritability for persistence in the seropositive group at one year (h^2 = 0.08, 95%CI 0.00-0.51) was lower than for seropositive persistence at three years (h^2 = 0.19, 95%CI 0.00-0.62) while point estimates for the seronegative heritability were zero for both persistence outcomes.

Conclusion: Despite being the largest GWAS on an MTX treatment outcome to date, no genome-wide significant associations were detected. The low heritability observed along with the lack of strong independent associations, may indicate that genetic influence from common genetic variants on persistence to MTX is minor, and of a polygenic nature.

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OP0268 COMPARISON OF MAJOR CARDIOVASCULAR AND THROMBOEMBOLIC EVENTS IN SAFETY REPORTS BETWEEN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH JAK INHIBITORS VERSUS ANTI-TNF: RESULTS FROM VIGIBASE

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Background: Recently, awareness has raised regarding JAK inhibitor safety in rheumatoid arthritis (RA), in particular with tofacitinib. Indeed, in a trial involving more than 4,000 patients (ORAL Surveillance), a numerically higher number of major cardiovascular events (MACEs) in patients treated with tofacitinib compared to anti-TNF (1), and a higher risk of venous thromboembolic events (VTE) in patients treated with tofacitinib 10mg twice a day compared to patients treated with tofacitinib 5mg twice a day or anti-TNF was observed. This increased risk of MACEs was also suspected in another study performed on American Health databases (2). Recently, the FDA extended warnings and use's recommendations to other JAK-inhibitor drugs (3).

Objectives: To corroborate these safety warnings, we compared the reporting MACEs and VTEs with JAK inhibitors versus anti-TNF alpha drugs from the World Health Organization (WHO) Global Individual Case Safety Report (ICSR) database (VigiBase).

Methods: We selected reports in Vigibase of patients aged between 18 and 75 years, between 01/01/2011 and 12/31/2020, with JAK inhibitors (tofacitinib, baricitinib, upadacitinib, filgotinib) or anti-TNF (etanercept, adalimumab, infliximab, certolizumab pegol, golimumab) with a diagnosis of RA. In these reports we selected MACEs including myocardial infarction, strokes and cardiovascular deaths and VTE including deep venous thromboses (DVT) and pulmonary embolisms (PE). Characteristics of reports including age of patients, country of declaration, drug involved, co-reported drugs, and type of event were described. The reporting risk was investigated using disproportionality analyses and expressed as Reporting Odds Ratios (ROR) with 95% Confidence Interval (95%CI). A sensibility analysis was performed stratifying by age category (≥ 65 years, ≥ 50 years), and by sex.

Results: Of the 11,455,891 reports in patients aged between 18 and 75 years in the period of interest, 39,097 of reports were for a JAK-inhibitor in RA (mean age 60.6 years, SD:16.3) and 231,860 of reports were for an anti-TNF in RA (mean age: 57.2 years, SD: 13.0). Most of the reports came from USA and Canada (respectively 77.4% and 12.5% for JAK-inhibitor and 86.4% and 2,6% for anti-TNF). Among the reports, 611 (1.6%) in JAK-inhibitor treated patients and 3240 (1.4%) in anti-TNF treated patients were MACEs

while 341 (0.9%) in JAK-inhibitors and 571 (0.2%) in anti-TNF treated patients were VTE. Disproportionality analyses identified an increased risk of reporting VTE events in JAK-inhibitors compared to anti-TNF (DVT: ROR = 3.99 [95%CI: 3.15-5.04], PE: ROR = 3.47 [2.90-4.13], Figure 1). This risk was not modified after stratification by age or sex. No increased ROR for MACE was found.

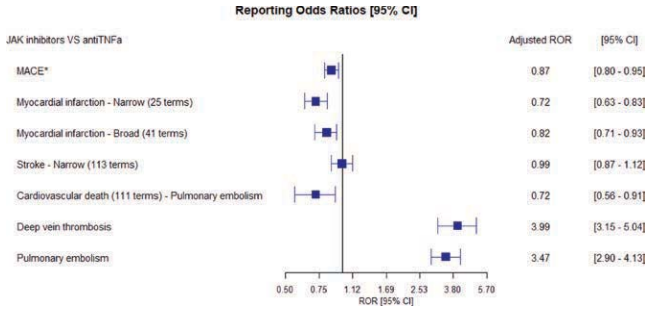

Figure 1.

Conclusion: Based on real-world data, the analysis did not identify an increase of declaration of MACEs with JAK-inhibitor compared to anti-TNF whereas we could observe more than three times declarations of VTE in Vigibase with JAK-inhibitors compared to anti-TNF.

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OP0269

BIOMARKERS TO PREDICT RISK OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB OR TUMOUR NECROSIS FACTOR INHIBITORS

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Background: In the ORAL Surveillance study of patients (pts) aged ≥50 yrs with moderate to severe rheumatoid arthritis (RA) and ≥1 additional cardiovascular risk factor (NCT02092467), the incidence of pulmonary embolism was higher with tofacitinib than with tumour necrosis factor inhibitors (TNFi).1

Objectives: To explore whether biomarkers explained the associations of tofacitinib vs TNFi with venous thromboembolism (VTE) in ORAL Surveillance.

Methods: ORAL Surveillance was a prospective, open-label, event-driven, non-inferiority, post-authorisation safety study. Pts were randomised 1:1:1 to receive tofacitinib 5 or 10 mg twice daily or a TNFi (adalimumab 40 mg every 2 weeks or etanercept 50 mg once weekly). For this exploratory post hoc analysis, 294 soluble, proteomic, genetic and antibody biomarkers were assessed (of which 79 have a known role in inflammation, coagulation, vascular biology and/or Janus kinase signalling). Biomarkers were quantified in serum collected at baseline (BL) and Month (M)12 in VTE cases and 4:1 matched controls. D-dimer was analysed with a larger control group (all eligible pts without VTE) and final adjudicated data from BL, M12 and study end.

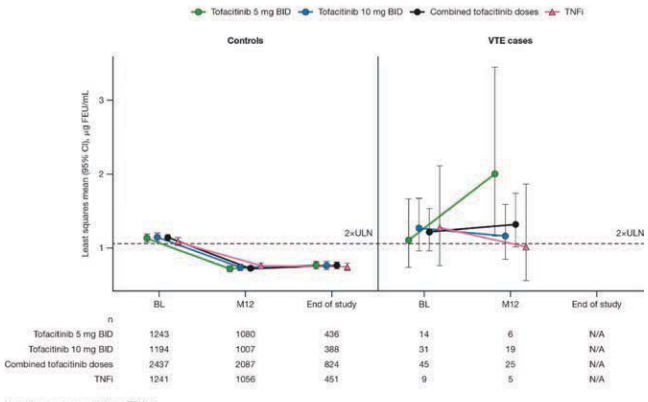
Results: Of the 4362 randomised and treated pts, D-dimer was quantified in 3732 pts (54 with VTE; 3678 without) and the remaining biomarkers were analysed in 285 pts (57 VTE cases; 228 matched controls). BL characteristics were generally similar in those with or without VTE and between treatment groups. At BL, D-dimer levels were ≥2×upper limit of normal for ~50% of controls and 67% of VTE cases. Mean D-dimer levels decreased from BL to M12 in controls across treatment groups (Figure 1). Key findings from the biomarker analyses are shown in the Table 1. No biomarker showed a clear mechanistic association with the increased risk of VTE for tofacitinib vs TNFi, or demonstrated adequate performance for prognostic use in pts with RA.

Table 1. Summary of results from biomarker analyses

Biomarker	Key results
Tier 1	
C-reactive protein	• No association with VTE in any treatment arm at BL or M12
D-dimer Thrombopoietin	• Higher M12 levels were prospectively associated with greater risk of subsequent VTE with tofacitinib 10 mg BID o For D-dimer, the same effect was observed with tofacitinib 5 mg BID • Treatment specificity of effects could not be established
Tier 2	
Factor VIII Thrombin–antithrombin complex Tissue factor pathway inhibitor Plasminogen activator inhibitor-1 Protein C Antithrombin Apolipoprotein C-III Leptin	• No clinically meaningful differences across treatment arms
Tiers 3 & 4	
Exploratory proteomic assays (276 markers from multiplex panels)	• Two biomarkers with no known relationship to VTE (angiogenin and TNFSF13B) showed significant associations with pulmonary embolism in the tofacitinib 10 mg BID arm o Treatment specificity of effects could not be established for either analyte
Genetic biomarkers	
Factor V Leiden R506Q, prothrombin G20210A and JAK2 V617F mutations	• Factor V Leiden and prothrombin risk alleles, individually or combined, were associated with increased incidence of VTE but did not explain excess events with tofacitinib • No VTE cases or matched controls had the JAK2 mutation
Antibody biomarkers	
ACA IgG and IgM, anti-β2GP1 IgG and IgM	• No statistical differences were observed between treatment arms or between VTE cases and matched controls

ACA, anticardiolipin antibody; β2GP1, beta-2-glycoprotein 1; IgG, immunoglobulin G; IgM, immunoglobulin M; JAK2, Janus kinase 2; TNFSF13B, tumour necrosis factor ligand superfamily member 13B

Fig. Least squares mean (95% CI) values of D-dimer by treatment arm in VTE cases and controls at BL, M12 and end of study



Normal assay range: <0.53 µg FEU/mL
VTE events included deep vein thrombosis and pulmonary embolism
Data collected after pts who were randomised to tofacitinib 10 mg BID had their dose reduced to 5 mg BID were included in the tofacitinib 10 mg BID group
The TNFi group received adalimumab 40 mg every 2 weeks (US, Puerto Rico and Canada) or etanercept 50 mg once weekly (rest of the world)
The end of study visit was conducted within 1 month of study completion, which was declared when the targeted number of major adverse cardiovascular events and malignancies (excluding non-melanoma skin cancer) had been met. The median duration of treatment was 44 months. To exclude the confounding effect of anticoagulant therapy, M12 samples were not analysed in pts with early VTE events (before M12) and end of study samples were not analysed in VTE cases
BID, twice daily; CI, confidence interval; FEU, fibrinogen equivalent units; N/A, not available; ULN, upper limit of normal

Conclusion: This post hoc exploratory analysis did not identify biomarkers at BL or M12 that explain the increased VTE risk for tofacitinib vs TNFi. Notably, ORAL Surveillance was neither designed nor powered to compare the risk of VTE across treatments or to identify biomarkers with a mechanistic relationship

to VTE. Individual VTE risk should be considered when making decisions about initiation or maintenance of tofacitinib treatment.

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OP0270

TAPERING OF LONG-TERM, LOW-DOSE GLUCOCORTICOIDS IN SENIOR RHEUMATOID ARTHRITIS PATIENTS: FOLLOW-UP OF THE PRAGMATIC, MULTICENTRE, PLACEBO-CONTROLLED GLORIA TRIAL

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Background: Guidelines suggest glucocorticoids (GC) should be used as bridge therapy in rheumatoid arthritis (RA), but many patients are treated chronically with low doses. The effects of withdrawal in such patients has not been studied extensively.

Objectives: To study disease activity score (DAS28), disease flares and signs of adrenal insufficiency after withdrawal of blinded trial medication (prednisolone 5 mg/day or placebo for 2 years).

Methods: The 2-year, double-blind GLORIA trial evaluated the long-term benefits and harms of low dose GC added to standard care (see main GLORIA trial abstract). Senior RA patients (≥ 65 years) were randomly assigned to prednisolone 5 mg/day or placebo.

After the final trial visit study medication was linearly tapered to zero in 3 months by adding a stop day every two weeks, and patients were reassessed. Those who successfully completed the trial and did not receive open-label GC during the 4 weeks after the final trial visit were included in this follow-up study.

The primary outcome was change in DAS28 at follow-up compared to the final trial visit. Secondary outcomes included the occurrence of disease flares (DAS28 increase > 0.6 or open-label GC between week 4 and 12 of the taper phase) and signs of adrenal insufficiency, assessed by 9 items selected from the 57-symptom list from the MDHAQ questionnaire (1) and hypotension (systolic RR < 90 or diastolic RR < 60). In a subset of patients from 3 Dutch centres, cortisol and ACTH were measured in spot serum samples during the follow-up visit.

Analysis of covariance assessed the change in DAS28. Linear regression and chi-square test were used for the remaining outcomes.

Results: 278 participants completed the GLORIA study, 21 received GC within 4 weeks after the end of the trial, 58 had missing data, leaving 199 patients eligible for this study.

34 patients received open label GC after 4 weeks and were excluded for the primary analysis. In the remaining 165 patients (80 prednisolone, 85 placebo), mean (SD) DAS28 was higher on placebo: 3.14 (1.04) vs 2.92 (1.13) prednisolone at the final trial visit. After tapering, disease activity increased significantly (p=0.02) in the prednisolone group to 3.18 (1.20) but was stable in placebo (3.14). The difference in the increase of DAS28 between the groups was 0.21 (95%CI –0.05;0.47; p=0.11).

For signs of adrenal insufficiency, 33 out of 165 had missing data, leaving 60 in the prednisolone group and 72 in placebo (Table 1). Mean (SD) number of signs for prednisolone was 1.1 (1.1) versus 0.9 (1.3) for placebo at final trial visit and 0.8 (1.2) versus 0.8 (1.0) at follow-up. Difference in the change of the number of signs was –0.1 (95%CI –0.4;0.3; p=0.66).

Table 1. Adrenal insufficiency signs and symptoms.

	prednisolone (n=60)		placebo(n=72)	
	end of trial	change after 3 months	end of trial	change after 3 months
Fatigue (unusual)	15	1	13	–1
Appetite loss	5	–1	4	4
Muscle weakness	7	–2	6	–2
Dizziness	3	2	10	1
Stomach pain	3	4	3	1
Muscle pain	19	–6	19	–1
Nausea	5	–3	2	2
Vomiting	1	0	0	1
Diarrhoea	5	–2	3	–2
Hypotension*	2	–1	4	–2
Sum**	1.1 (1.1)	–0.2 (1.3)	0.9 (1.3)	0.0 (1.3)

* Systolic RR < 90 or diastolic RR < 60. **Mean (SD)

No differences were seen in ACTH or cortisol levels: mean (SD) ACTH was 5.8 (4.1) in 23 prednisolone patients, and 5.1 (3.7) in 24 placebo patients; cortisol 296 (113) v 310 (166), cortisol/ACTH 67 (40) v 77 (54). Two prednisolone and one placebo patient had cortisol levels below 80. None developed clinical hypoadrenalism during further follow-up.

199 patients qualified for the disease flares sample, 99 prednisolone and 100 placebo; 44 patients flared on prednisolone tapering vs 31 on placebo, relative risk 1.43 (95%CI 0.99; 2.07; p=0.07).

Conclusion: Tapering prednisolone moderately increases disease activity to placebo levels (mean still at low disease activity levels) and numerically increases the risk of flare without any evidence of adrenal insufficiency. This suggests that withdrawal of low dose prednisolone is feasible after 2 years of administration.

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RA: Clinical aspects and comorbidities - II

OP0271 INCREASED RISK OF DEMENTIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Background: There have been conflicting results of previous studies on the association between rheumatoid arthritis (RA) and the risk of dementia.
Objectives: In this study, we aimed to investigate the association between RA and dementia in a large nationwide population-based cohort.
Methods: Among patients diagnosed with RA between 2010 and 2017, patients who had undergone a national health examination within two years prior to RA diagnosis were included in the study (n = 138,592). Control group included age- and sex-matched non-RA controls who received a health check-up at the same time as RA patients (n = 692,960). The primary outcome of the study was incident dementia, which was defined by an ICD-10 code and the use of dementia medications. Kaplan-Meier curves and Cox proportional hazards regression analysis were used for the analysis.
Results: Mean follow-up duration of the study was 4.7 ± 2.2 years. RA patients had a 1.2 times higher risk of dementia than controls (adjusted hazard ratio [aHR] 1.19, 95% CI 1.16–1.23). In patients with RA, the aHR for Alzheimer's disease (AD) was 1.21 (95% CI 1.67-1.25) and the aHR for vascular dementia (VD) was 1.10 (95% CI 0.99-1.21). In a stratified analysis according to age, gender, lifestyle factors and comorbidities, the association between RA and dementia was consistently found.
Conclusion: In a large nationwide population-based cohort, RA was associated with an increased risk of incident dementia. Appropriate evaluation of dementia is required when cognitive impairment occurs in RA patients. Further studies are warranted to identify mechanisms of increased risk of dementia in RA patients.
Disclosure of Interests: None declared
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OP0272 PREDNISONE USE AND THE INCIDENCE OF HYPERGLYCEMIA OR DIABETES IN PATIENTS WITH RHEUMATOID ARTHRITIS; A 10-YEAR SUB ANALYSIS OF THE BEST STUDY.

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Background: Use of prednisone in rheumatoid arthritis has been questioned because it may trigger side effects such as hyperglycemia and diabetes.
Objectives: To assess whether in RA the use of prednisone is associated with the development of hyperglycemia and diabetes.
Methods: The BeSt study is a multicenter, assessor-blinded randomized controlled 10-years follow-up trial in 508 non-diabetic early RA patients. Patients were randomised to 4 dynamic DMARD treatment strategy groups: 1) sequential monotherapy, 2) step-up combination therapy, 3) initial combination therapy including prednisone (60 mg/day, tapered to 7.5 mg/day in 7 weeks) and 4) initial combination therapy with infliximab. In groups 1, 2 and 4, prednisone had a maximum dose of 7.5 mg/day by protocol. Treatment was steered at disease activity score (DAS) ≤2.4. We performed a GEE over time to assess whether current prednisone use or cumulative prednisone dose were associated with hyperglycemia (glucose levels ≥7.8) and cox regression analyses to investigate the relationship between cumulative prednisone dose, previous prednisone use and diabetes (defined as either use of anti-diabetic medication or two instances of a glucose ≥ 11.1), assessed at 3-monthly visits. All analyses were adjusted for potential confounders.
Results: In total, 33/508 patients (6.5%) developed diabetes during the trial; 12 of these (36%) had received prior treatment with prednisone (any dose). Median (IQR) duration of prednisone use in all 508 patients was 9 (15) months and cumulative doses ranged from 0 to 27942 mg. The mean cumulative dose ranged from 55.5 mg in group 1 to 6170.0 mg in group 3. Previous prednisone use nor cumulative prednisone dose was associated with hyperglycemia or diabetes, with effect sizes ranging from a hazard ratio of 0.588 (95% CI 0.285; 1.21) for the association between any prednisone dose and diabetes to an odds ratio of 1.04 (95% CI 0.978; 1.13) for the association between cumulative prednisone dose and diabetes (Table 1). To identify potential causes for these results, we investigated the relationship between DAS and the same outcomes. We found a higher DAS was significantly associated with development of diabetes, but not with hyperglycemia.

Table 1. The relationship between prednisone dose, DAS and glucose levels, hyperglycemia and diabetes

GEE	hyperglycemia*	OR	95% CI
Any prednisone dose[1]		*0.949*	*0.805; 1.12*
Cumulative dose[1]		*1.04***	*0.978; 1.13*
DAS[2]		1.24	0.842; 1.85
Cox Regression	**diabetes (any of the definitions)**	**HR**	**95% CI**
Any prednisone dose[3]		*0.588*	*0.285; 1.21*
Cumulative dose[3]		*0.996***	*0.960; 1.03*
DAS[2]		1.60	1.13; 2.26

CI: confidence interval, GEE: Generalized Estimating Equations, OR: odds ratio, HR: hazard ratio, DAS: disease activity* hyperglycemia: glucose level above 7.8 mmol/L; diabetes: random glucose level above 11.1 mmol/L at at least two time points** odds ratio per 500mg cumulative prednisone increase: [1]adjusted for DAS, age, diabetes and BMI: [2]adjusted for cumulative prednisone dose, age, gender and BM: [3]adjusted for DAS, age and BMI

Conclusion: In early RA patients, cumulative dose nor any previous prednisone use was associated with the risk of hyperglycemia or diabetes. A higher DAS was significantly associated with increased risk of developing diabetes. Potential risks of prednisone may have been mitigated by suppression of DAS.
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OP0273 CHARACTERISTICS OF PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS IN FRANCE

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Background: Recently, EULAR has proposed a definition of difficult-to-treat rheumatoid arthritis (D2TRA). However, descriptive data on D2TRA are scarce and only one Japanese publication details the D2TRA encountered in routine practice, no similar work has been done in Europe so far.
Objectives: To describe D2TRA patients encountered in France according to two definitions and evaluate their therapeutic responses to different targeted therapies.
Methods: We reviewed all patients with RA treated in day hospital at Cochin University Hospital between 2020 and 2021. We divided our population into two groups of patients, a D2TRA group and a non-D2TRA group. This division was made on the same population according to two different definitions of D2TRA, resulting in four patient groups. The first definition is the one proposed by EULAR (EULAR D2TRA) defining D2TRAs as RAs with failure of ≥2 b/tsDMARDs (with different mechanisms of action) after failing csDMARD therapy. The second defined as D2TRA patients who have failed at least two targeted therapies, without prejudging the mechanism of action (non-EULAR D2TRA). We analyzed clinical characteristics and evaluated their response to different targeted therapies. Disease activity was assessed using the DAS for 28 joints (DAS28) at the latest visit.
Results: In total, we included 320 patients, we identified 76 EULAR D2TRA patients (mean age 59 years, 87% female) with 244 of corresponding non-DTRA patients (mean age 60 years, 85% female) and 120 non-EULAR D2TRA patients (mean age 58.7 years, 87% female) with 200 of corresponding non-DTRA (mean age 61 years, 85% female). Compared to non-D2TRA patients, there were significantly more D2TRA patients from low socioeconomic backgrounds in both D2TRA groups. In the EULAR-D2TRA group, compared to the non-D2TRA, there were significantly more patients with diabetes (14% vs 6%, p=0.024). D2TRA patients in both groups had significantly more rheumatoid factor (RF), interstitial lung disease (ILD) and a higher DAS28 than non-D2TRA patients. No difference was noted regarding ACPA and erosions. We observed a lower proportion of remission in both D2TRA groups than in non-D2TRA group (21% in EULAR-D2TRA vs 34% in non-D2TRA, p=0.034 and 23% in non-EULAR D2TRA vs 36% in non-D2TRA, p=0.024). There were significantly fewer patients on Methotrexate in the non-EULAR D2TRA group compared to the non-D2TRA group (53% vs 64%, p=0.046). In the non-EULAR D2TRA group, there were significantly more patients in remission on Rituximab than on TNF inhibitors (41% vs 5%, p=0.0032). We did not observe a significant difference in achieving remission in patients on JAK inhibitors or IL-6 inhibitors in the two groups of D2TRA.

Table 1. Clinical data of patients with D2TRA

	NON D2T RA n=200	NON-EULAR D2T RA n=120	p-value	NON D2T RA n=244	EULAR D2T RA n=76	p-value
Low socioeconomic level	69 (35)	61 (51)	**0.005**	91 (37)	39 (51)	**0.032**
TJC (0-28), mean (SD)	3.4 (4.6)	4.9 (5.8)	**0.0167**	3.5 (4.5)	5.6 (6.5)	**0.001**
SJC (0-28), mean (SD)	2.4 (3.1)	3.5 (4.3)	**0.0067**	2.6 (3.3)	3.5 (4.3)	0.0503
CRP in mg/dl, mean (SD)	6 (9.5)	7 .5 (12.1)	0.2128	6.1 (9.9)	7.9 (12.3)	0.2060
DAS28CRP, mean (SD)	3.2 (1.2)	3.6 (1.4)	**0.0044**	3.2 (1.3)	3.6 (1.4)	**0.0052**
Remission	71 (36)	28 (23)	**0.024**	83 (34)	16 (21)	**0.034**
RF positive, n (%)	156 (78)	105 (88)	**0.037**	193 (79)	68 (89)	**0.043**
Anti-CCP positive, n (%)	152 (76)	101 (84)	0.099	188 (77)	66 (87)	0.075
Erosion, n (%)	114 (57)	69 (58)	1	138 (56)	46 (60)	0.596
Interstitial Lung Disease, n (%)	16 (8)	19 (16)	**0.041**	17 (7)	18 (24)	**<0.001**
Corticosteroids, n (%)	84 (42)	64 (53)	0.064	101 (41)	46 (61)	**0.004**
Dose (mg), mean ± SD	6 (4.9)	5.5 (3.4)	0.416	6 (4.6)	5.3 (3.6)	0.374
Methotrexate, n (%)	128 (64)	63 (53)	**0.046**	149 (61)	42 (55)	0.422
Dose (mg), mean ± SD	17.3 (4.25)	17.5 (5.3)	0.786	17.2 (4.5)	18.1 (5.1)	0.291

Conclusion: The complexity of managing RA patients can be explained by socio-economic status and the presence of comorbidities such as diabetes and ILD. Our work suggests that D2TRA patients have less Methotrexate and better response to Rituximab. These data need to be confirmed in prospective studies to allow personalized management of D2TRA.

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OP0274

HOSPITALISATION FOR TUBERCULOSIS AND OTHER OPPORTUNISTIC INFECTIONS IN PATIENTS WITH INFLAMMATORY JOINT DISEASES BEFORE AND AFTER THE INTRODUCTION OF BIOLOGICAL THERAPY.

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Background: Over the last 20 years aggressive therapy for inflammatory joint diseases (IJD) has become standard of care following the acceptance of Methotrexate as anchor drug and extensive of use biologic therapy since 2003. Immunosuppression increases the risk for common and uncommon infections (1).
Objectives: To compare the temporal rates and associated mortality of hospitalisation with opportunistic infections (OI) (Table 1) for IJD patients in Western Australia between 1985 and 2015.
Methods: All patients hospitalized in Western Australia in the period 1980-2015 with ≥ 2 diagnostic codes for rheumatoid arthritis (RA, n=8490), psoriatic arthritis (PsA, n=601), axial spondylarthritis (AS, n=1419). Overall incidence rates (IR) with microbiologically confirmed OI (Mycobacterial, Fungal and viral infections) (Table 1) during 306.514 person years were expressed per 1000 person years and compared across IJD by incidence rate ratios (IRR) with 95% CI. IR trend rates across 5-year periods for each IJD were analyzed by least square regression (R^2). Mortality rate ratio (MRR) was number of deaths per 1000 observation years in patients with OI compared to patients in same disease category hospitalized without OI.

Table 1. Diagnostic codes applied to define conditions and opportunistic infections in hospital discharge database.

	ICD9CM	ICD10AM
RA	714.0-714.9	M05.0-M06.9
AS	720.0	M45, M08.10-M08.19
PsA	696.0	M07.0-M07.3, L40.5
Tuberculosis	010.x-018.x	A15–A19
Non-tuberculous mycobacteria	031.x	A30-A31
Cryptococcosis	117.5	B45
Aspergillosis	117.3	B44
Histoplasmosis	115	B39
All mycosis	114.0 - 118.9	B35.0 - B49.9
Pneumocystosis	136.3	B59
Cytomegaloviral disease	078.5	B25
Influenza	487.x, 488.x	J09, J10
Herpes zoster	053.x	B02
Varicella	052.x	B01

Results: The IR for all OI in RA patients (5.19, CI 4.8-5.6) was significantly higher than for PsA (IRR 0.56, CI 0.41-0.76 and AS (IRR 0.64, CI 0.53-0.79) with lower IRR observed especially for tuberculosis and H Zoster in PsA (0,49 and 0,47) and AS patients (0,43 and 0,49). H Zoster, TBC and other mycobacteria were the most frequent cause of OI with cryptococcal and pneumocystis only seen in RA. The IR for TBC decreased over time in RA (R^2 0.51, p=0.08), and AS (R^2 0.47, p=0.09) while the IR for H. zoster decreased in RA only (R^2 0.46, p=0.09) (Figure 1). In-hospital mortality rate in patients with OI was 4.9 % for RA, 2.6 % for PsA and 2.2% for AS, but MRR for RA (1.15; 0.71-1.97), PsA (1.64; 0.82-3.57) and AS patients (1.35; 0.68-2.89) was not significantly increased.

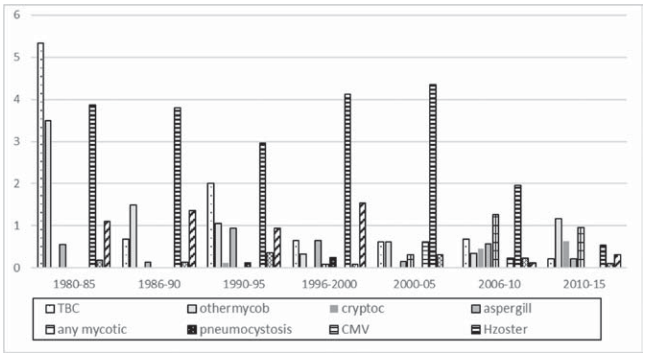

Figure 1. Incidence rate per 1000 personyears over time for hospitalisation with opportunistic infections in RA patients.

Conclusion: The IR for hospitalization with OI is twice as high for RA patients compared to AS and PsA patients. Admission rates for most OI including have decreased in RA patients over the two decades where more intensive treatment became standard of care. This suggests efficacy of preventative measures. Hospital admission with OI associated with a moderate risk of death, but did not incur a higher risk of death than admission for other medical complications in IJD patients

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OP0275

DISEASE FEATURES AND SURVIVAL OUTCOMES IN A RETROSPECTIVE COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE AFTER LUNG TRANSPLANTATION

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Background: Interstitial lung disease (ILD) is a leading cause of morbidity and mortality in patients with rheumatoid arthritis (RA). While the disease course of ILD is variable, some patients with RA have a progressive fibrosing ILD phenotype refractory to treatment. Lung transplantation (LTx) represents a life-extending option for patients with end-stage lung disease; however, data on the clinical features and outcomes of these patients are limited.
Objectives: (1) To characterize the clinical features of RA-ILD patients who received LTx at a high-volume lung transplantation center; (2) To evaluate survival and predictors of mortality in this cohort.
Methods: This retrospective study included all patients with RA-ILD who received LTx between 2004 to 2020 at UCLA. Patient demographics, RA disease features, explant pathology, pulmonary function tests (PFTs), and survival

status were extracted from the electronic medical record. Descriptive statistics were used to summarize disease features. A Kaplan-Meier curve was created to evaluate survival, and a Cox proportional hazards model was created to identify predictors of survival.

Results: 42 RA-ILD patients underwent LTx. The majority of patients were male (57.1%), seropositive (91.4%), with a mean RA disease duration of 12.9 years at LTx (Table 1). Over the study period, 16 (36%) patients died. Compared with patients who had survived, deceased patients were slightly older at the time of transplantation (59.0±9.7 vs. 57.3±11.5, respectively), and were more likely to have usual interstitial pneumonia (UIP) in the lung explant (87.7% vs. 56.0%, p <0.05). The median follow up was 2.3 years (IQR 1.3, 4.7), and median survival time was 5.3 years (IQR 2.7, 7.6; Figure 1). In the univariate Cox proportional hazards analysis, there was a relationship between the presence of UIP pathology and increased mortality, although this did not reach significance (HR 7.13, p=0.06).

Table 1. Disease features of study cohort*

	All patients (N=42)
Age at LTx	58.0±10.7
Female	18 (42.9)
BMI (kg/m2)	25.7±4.2
Race- Caucasian	28 (66.7)
Ethnicity- Hispanic	11 (26.2)
Smoking, ever	17 (40.4)
Pack years	6.5±12.8
RA Disease Duration at Time of LTx (years)	12.9±11.4
ILD Before/Concurrent to RA#	12 (28.6)
Erosive	11 (40.7)
Seropositive%	32 (91.4)
Pathology- UIP	28 (68.3)
Pathology- NSIP	7 (17.0)
Pathology- Other	13 (31.7)
FVC% at Time of LTx	46.9±14.0
DLCO% at Time of LTx	34.4±17.9
Post-Transplant Rheumatology Follow-Up	20 (47.6)

*Values are N(%) or mean ±SD #ILD diagnosis was made within 12 months of RA diagnosis %RF or CCP

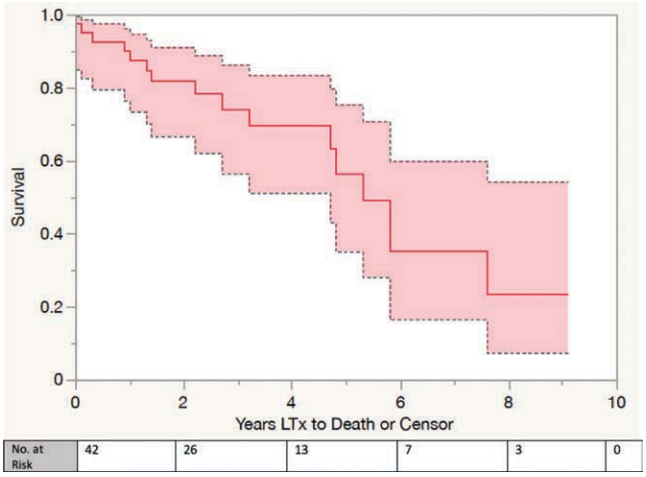

Figure 1. Kaplan-Meier survival curve for RA-LTx patients from time of LTx to death, or censor. The shaded area represents the 95% confidence interval. Median time to death was 5.3 years (IQR 2.7, 7.6).

Conclusion: This single-center study of RA-ILD patients who underwent LTx demonstrated a median survival time comparable to other LTx cohorts.[1] There appeared to be a relationship between the presence of a UIP pattern, and increased risk of mortality, though the small sample size may have precluded the ability to reach statistical significance. Future prospective studies are needed to validate these findings. Understanding the disease features of RA patients who undergo LTx may facilitate the early identification of RA patients at the greatest risk of developing progressive fibrosing phenotype.

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OP0276

PREFERENCES FOR TREATMENTS TO PREVENT RHEUMATOID ARTHRITIS: DISCRETE CHOICE SURVEY OF RHEUMATOID ARTHRITIS PATIENTS' FIRST-DEGREE RELATIVES IN THE UNITED KINGDOM AND GERMANY.

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Background: There is a growing research focus on the development of interventions to reduce risk of rheumatoid arthritis (RA) in at-risk individuals.(1) A recent survey of the general population asked to assume a 60% risk of RA established that hypothetical preventive treatments were acceptable to most participants.(2) However the preferences of individuals who actually have an elevated risk of RA, such as first-degree relatives (FDRs) of RA patients, are not well understood.

Objectives: To quantify FDRs' preferences for preventive treatments for RA.

Methods: Adult FDRs in the UK and Germany were invited to take part in a web-based survey via patients with clinician-confirmed RA either during a rheumatology clinic visit or by mail. In addition, FDRs taking part in a UK-based prospective cohort (PREVeNT-RA) were invited via email. Participants received information about RA followed by questions to check comprehension, and an introduction to the survey including warm-up questions. They were asked to imagine they were experiencing arthralgia and had positive autoantibody tests indicating a 60% chance of developing RA in the next two years. Using a discrete choice experiment, participants were offered a series of 15 choices between no treatment and two unlabeled hypothetical treatments to reduce risk of RA. Treatments were defined by six attributes with varying levels, describing benefits, risks, and frequency/route of administration (Table 1). Attribute selection and presentation was informed by qualitative research, ranking surveys, systematic literature review, and expert opinion. Survey layout was informed by patient research partners and qualitative pre-testing. A two-class latent class analysis was used to estimate preferences and calculate relative importance of treatment attributes and predicted uptake. A panel mixed logit model was used to obtain maximum acceptable risk estimates.

Table 1. Treatment attributes and levels

Attribute	Levels
Chance of developing RA reduced from 60% to	10%; 20%; 30%; 40%
How the treatment is taken	A shallow injection under the skin A drip into the vein One or two tablets
How often the medication has to be taken	Daily Weekly Monthly Every 6 months
Chance of mild side effects	2%; 5%; 10%
Chance of a serious infection due to treatment	0%; 1%; 5%
Chance of a serious side effect that is potentially irreversible	1 in 100,000 people 20 in 100,000 people 100 in 100,000 people

Results: 356 FDRs (252 female, 289 in the UK) responded. While treatment effectiveness was the most important attribute in both classes (Figure 1), the importance of other attributes differed between classes, with method and frequency of treatment administration being more important in class 2 and risk of mild side effects only impacting treatment choice in class 1. Perceived risk of developing

RA predicted class assignment; those with higher perceived risk were more likely to belong to class 1. On average, the predicted uptake of treatment profiles estimating prevention candidates: abatacept; atorvastatin; hydroxychloroquine; tolerogenic cell-based therapy; and no treatment would be 50%, 15%, 9%, 18% and 0%, respectively. Finally, the maximum acceptable risk participants were willing to accept were 81%, 25% and 3% point increases in risk of mild side effects, serious infection, and serious side effects, respectively, for medicines that would reduce their risk of developing RA in the upcoming two years from 60% to 20%.

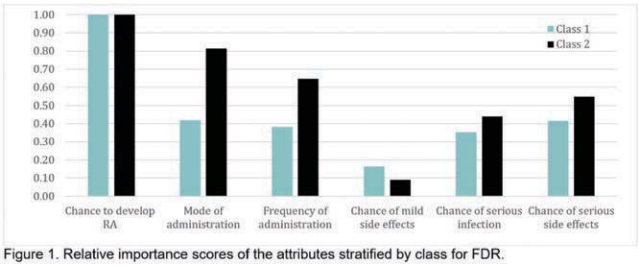

Figure 1. Relative importance scores of the attributes stratified by class for FDR.

Conclusion: Effective preventive treatments for RA were acceptable to FDRs asked to assume a 60% chance of developing RA. Mode and frequency of treatment administration had a greater impact on treatment choices for participants with a lower perceived risk of RA. These findings are informative for target product profile development, endpoint selection, benefit-risk assessment, regulatory approval, and development of informational resources for those at risk of RA.

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OP0277 PERSISTENT EXCESS OF STROKE EVENTS IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY FROM HORDALAND, NORWAY FROM 1972 TO 2014

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Background: Patients with rheumatoid arthritis (RA) have an excess risk of cardiovascular disease (CVD), including stroke [1]. After the introduction of biological DMARDs in 1999 and the treat to target strategy, more patients reach low disease activity and remission, which is associated with lower CVD risk [2]. Few previous studies have examined stroke occurrence in RA patients before and after these improvements in RA management.

Objectives: To investigate stroke events in RA patients diagnosed before and after 1999 compared with the total population.

Methods: We included 771 RA patients diagnosed during 1972-1998 and 1050 during 1999-2013 at the main rheumatological department of Hordaland county, Norway. The total population of the same county and time period were used as a comparison cohort. Data on stroke events were obtained from regional cardiovascular registries or hospital patient administrative systems during 1972-2014. Aggregated counts of stroke events and population counts from the comparison cohort were used to estimate expected counts of stroke hospitalisation in the RA cohort per 5-year age group, sex and calendar year. We then estimated standardised event ratios (SERs) by Poisson regression as a measure of excess stroke events in RA patients compared with the total population.

Results: In total, 152 stroke events occurred in 112 RA patients diagnosed during 1972-1998 over 15137 person-years of follow-up and 86 stroke events in 70 RA patients diagnosed during 1999-2013 over 8672 person-years of follow-up. RA patients diagnosed in the later period were on average 2.1 years older (56 years) at RA diagnosis, but the proportion of women was similar in both groups. Both RA patients diagnosed before and after 1998 had an excess of stroke events compared with the total population (SER 1.20, 95% CI 1.00-1.44 and SER 1.22, 95% CI 1.05-1.42 respectively). RA patients younger than 60 years of age did not appear to have significant excess stroke events in either group.

Conclusion: These results indicate a similar excess of stroke events in RA patients diagnosed before and after 1999. This warrants continued awareness regarding stroke prevention in RA patients, even after the recent improvements in RA treatment.

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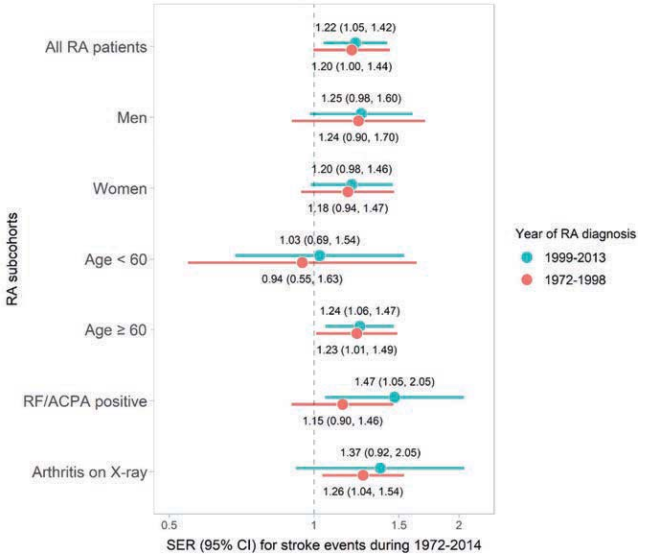

Figure 1. Standardised event ratios (SER) comparing stroke events in RA patients with the total population of Hordaland, Norway, given with 95% robust confidence intervals. Seperate estimates were calculated for the entire RA cohort and 6 RA subcohorts defined by age, sex, positive rheumatoid factor or ACPA and arthritis on x-ray during follow-up. ACPA, anti-citrullinated protein antibodies; ACR, American College of Rheumatology; EULAR, European League against Rheumatism; RA, rheumatoid arthritis; RF, rheumatoid factor.

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OP0278 MUSCULOSKELETAL IMMUNE-RELATED ADVERSE EVENTS IN 927 PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS FOR SOLID CANCER

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Background: The prevalence of the musculoskeletal immune-related adverse events (irAEs) is probably underestimated, as most studies report only severe side effects. The largest prospective study with systematic monitoring by a rheumatologist, for musculoskeletal irAEs, concerned 35 patients.
Objectives: The main objective was to describe each type of musculoskeletal irAEs: prevalence, clinical features, treatment regimen, ICI drug, time of occurrence and management of musculoskeletal irAEs. The secondary objectives were to describe IrAEs'course ant to investigated tumor response at 3 months after introduction of ICI according to IrAEs'grade, clinical features, pain patterns and the treatments used to manage musculoskeletal irAEs.
Methods: We conducted a retrospective study among patients who received ICI from 07/27/2014 to 05/08/2020 at the medical oncology department of the Institut Paoli-Calmettes, Marseille, France. All medical files were systemically reviewed by a rheumatologist who collected clinical features, time of occurrence, treatment regimen, irAEs management, course, outcomes and tumor response 3 months after introduction of ICI.
Results: In our cohort of 927 patients treated with ICI for a solid tumor, 118 patients (12.7%) presented a musculoskeletal irAE. Their median age was 66.5, 61% were male, and they mainly had a lung (57.6%) or urological cancer (27.1%). The most frequently involved ICI was an anti PD-1. Arthralgias and myalgias were the most frequent musculoskeletal irAEs (76.3%) and inflammatory rheumatic features were reported in 36 patients (30.5%) with elevated acute phase reactants and negative immunological markers. The median time of onset was 2 months (IC 95% 1.8; 2.7). Musculoskeletal irAEs were mainly mild and no deaths were related. Painkillers were the most widely used treatments (86.4%). Systemic corticosteroids were used in 38 patients (32.2%) with a mean dose of 43 ± 35 milligrams/day. Among the inflammatory rheumatic features, 20 (55.5%) were treated with systemic corticosteroids and 8 with csDMARDs (16.7%). bDMARDs were not used in our cohort. Musculoskeletal irAEs resulted in discontinuation of the responsible ICI in 23 patients (19.5%). The majority of musculoskeletal irAEs (79.7%) resolved within a median time of 3 months (IC 95% 2.2;4.0). Tumor response at 3 months did not differ according to musculo-skeletal irAE severity, type of manifestation (arthralgias/myalgias versus inflammatory rheumatic features), pain patterns (mechanical versus inflammatory) or irAE treatments.
Conclusion: Our single-center cohort is the largest to our knowledge to describe all musculoskeletal irAEs in patients treated with ICI without focusing on severe or inflammatory manifestations. These musculoskeletal irAEs are frequent, mostly mild and well tolerated, resolving and allowing possible continuation of ICI treatment. Collaboration between oncologists and rheumatologists should be further encouraged to determine whether all musculoskeletal irAEs, even non-severe and non-inflammatory ones, are associated with a good tumor response to ICI.
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Recent novelties in SLE/Sjogren and APS?

OP0279 **CAR-T CELL TREATMENT OF REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS- SAFETY AND PRELIMINARY EFFICACY DATA FROM THE FIRST FOUR PATIENTS**

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Background: While treatment of Systemic lupus erythematosus (SLE) has substantially improved, a subset of patients experiences severe progressive disease despite T- and B cell targeted therapy. Furthermore, drug-free remission and seroconversion is difficult to achieve in SLE to date
Objectives: To study the safety, tolerability, and preliminary efficacy of deep B cell depletion using autologous CD19 chimeric antigen receptor (CAR) T cells in patients with severe and treatment-refractory SLE
Methods: The CAR product was manufactured by CliniMACS Prodigy system (Miltenyi Biotec, Bergisch Gladbach, Germany). T-cells were enriched from the patients' peripheral blood apheresis product and $1x10^8$ cells were used as starting cell population. The cells were transfected with a lentiviral vector encoding an anti-CD19 CAR is composed of the FMC63 scFv, a CD8- derived hinge region, TNFRSF19-derived transmembrane domain, CD3ζ intracellular domain, and 4-1BB co-stimulatory domain (Miltenyi Biotec) and expanded for 12 days. After conditioning with cyclophosphamide/ fludarabine patients received $1x10^6$ CD19-CAR-T cells/kg body weight as a single infusion. All SLE treatments with the exception of low dose prednisolone were stopped before CAR-T cell administration. After CAR-T cell treatment, also prednisolone was stopped. Tolerability was assessed by monitoring for Cytokine-release syndrome (CRS), immune-related effector cell neurotoxicity syndrome (ICANS) and infections. Preliminary efficacy was assessed by reaching a Lupus Low Disease Activity State (LLDAS), seroconversion in dsDNA antibodies and ANA and cessation of all SLE-specific treatments
Results: As of January 22, 2022, our 4 SLE patients had been treated with CD19 CAR-T cells with a follow up of 10 months (patient 1, female aged 20, SLEDAI-2K: 16), 7 months (patient 2, male aged 22; SLEDAI-2K:8), 2 months (patient 3, female aged 22; SLEDAI 2K: 6), and 1 month (patient 4; female aged 24; SLEDAI-2K: 6), respectively. All patients had active severe SLE with failure of standard treatment including pulsed steroids, hydroxychloroquine, mycophenolate, cyclophosphamide, intravenous immunoglobulins, rituximab and belimumab before CD19 CAR-T cell administration. All patients had active kidney disease. No infections occurred. All four patients experienced fever without proof of infectious disease (CRS °I); only one patient was treated with a single dose of tocilizumab. No ICANS and no CRS of other organs occurred. In vivo, CAR-T cells rapidly expanded to a maximum of 27,6% (day 9, patient 1), 41,2% (day 9, patient 2), 11,5% (day 9, patient 3) and 59,1% (day 9, patient 4) of total circulating T cells followed by a typical decline, with circulating CAR-T cells being continuously detectable during the next months. Expansion of CAR T cells preceded the complete and sustained depletion of circulating B cells. Patient 1 experienced sustained drug-free remission (SLEDAI-2K=0) with complete loss of ANA and dsDNA antibodies despite reappearance of B cells at 6 months. Patient 2 also experienced complete loss of ANA and dsDNA antibodies with B cells not yet returned. Low-level proteinuria remained most likely due to previously accrued damage in glomerular filter function (SLEDAI-2K: 2). Patient 3 and patient 4 had a shorter observation period to date but also achieved clinical remission (both SLEDAI-2K 0). All patients met LLDAS and could successfully stop all SLE-specific medication, including glucocorticoids. No SLE flare occurred so far.
Conclusion: Taken together, these data show that CD19 CAR T-cell therapy is well tolerated and may induce rapid remission of severe refractory SLE.
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OP0280 **WEANING OF MAINTENANCE IMMUNOSUPPRESSIVE THERAPY IN LUPUS NEPHRITIS (WIN-LUPUS): A MULTICENTER RANDOMIZED CONTROLLED TRIAL.**

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Background: Lupus nephritis (LN) is a frequent complication of systemic lupus erythematosus (SLE). Severe (proliferative) forms of LN are treated with an induction immunosuppressive therapy (IST), followed by a maintenance IST, to target remission and avoid relapses. The optimal duration of maintenance IST for proliferative LN is unknown.
Objectives: The WIN-Lupus trial tested whether IST discontinuation after 2-3 years in proliferative LN was non-inferior to IST continuation for 2 more years.
Methods: WIN-Lupus is an investigator-initiated academic randomized controlled trial, conducted in 28 French centers. Patients on maintenance IST with azathioprine or mycophenolate mofetil for a minimum of 2 years and a maximum of 3 years, and who were taking Hydroxychloroquine, were randomized (1:1) between 2 groups: IST continuation and IST discontinuation. The primary endpoint was the relapse rate of proliferative LN at 24 months. Secondary endpoints were the rate of severe SLE flares, survival without renal relapse or severe flare, adverse events, kidney function, disease activity, corticosteroid exposure, patient-reported outcome and medico-economic impact.
Results: Between 2011 and 2016, 125 patients were screened and 96 were randomized in the trial: 48 in the IST continuation group, 48 in the IST discontinuation group. In the per-protocol population, a relapse of proliferative LN occurred in 5/40 (10.4%) patients with IST continuation, and in 12/44 (25%) patients with IST discontinuation (difference 14.8%, 95%CI [-1.9; 31.5]). Non-inferiority was not demonstrated for relapse rate. Time to renal relapse did not differ between groups (p=0.092). Severe SLE flares (renal or extra-renal) were less frequent in patients with IST continuation compared to IST discontinuation (5/40 vs 14/44 patients, p=0.035). IST discontinuation was associated with lower health-related costs. Adverse events did not differ between groups.
Conclusion: Non-inferiority of maintenance IST discontinuation after 2 to 3 years was not demonstrated for renal relapse. IST discontinuation was associated with a higher risk of severe SLE flare.
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OP0281 PHARMACODYNAMIC EFFECT OF SEQUENTIAL BELIMUMAB (BEL) AND RITUXIMAB (RTX) THERAPY IN PATIENTS (PTS) WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): THE PHASE 3, RANDOMISED, PLACEBO-CONTROLLED BLISS-BELIEVE STUDY

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Background: BEL is approved for active SLE and lupus nephritis (adults only). Despite failed trials,[1] RTX remains in the SLE treatment armamentarium. Sequential BEL and RTX therapy offers a promising strategy to target B cells by distinct but complementary mechanisms.
Objectives: To assess the pharmacodynamic effects of BEL and a single RTX cycle on immunologic biomarkers in adults with SLE.
Methods: In this 104-week (wk) study (NCT03312907), all pts with active SLE received subcutaneous BEL 200 mg/wk for 52 wks. Pts were randomised to receive intravenous (IV) RTX 1000 mg at Wks 4+6 (BEL/RTX), IV PBO at Wks 4+6 (BEL/PBO), or continued treatment with standard therapy (BEL/ST). For BEL/RTX and BEL/PBO pts, a 52-wk treatment-free observational phase followed the 52-wk treatment phase; BEL/ST pts continued to receive BEL for 104 wks. Changes from baseline (BL) in anti-dsDNA and C3/C4 levels, and counts of total B cells ($CD19^+$) and B-cell subsets ($CD20^+$; naïve; memory; activated B-cells), were analysed.
Results: 292 pts received ≥1 study treatment dose (BEL/PBO n=72; BEL/RTX n=144; BEL/ST n=76). For pts assessed at Wk 52, reductions from BL in anti-dsDNA levels were seen in all 3 groups with a significant difference between BEL/RTX and BEL/PBO (p=0.0495). C3/C4 levels increased from BL to Wks 52 and 104 in all groups, with trends for greater increases with BEL/RTX versus BEL/PBO (Table 1). At Wk 52, total B cells and most B-cell subsets decreased in all 3 groups (Table 1), with significant differences between BEL/RTX and BEL/PBO ($p<0.0001$ for all). During the observation period, repopulation of total $CD19^+$ B cells (comprising mostly of naïve $CD20^+CD27^-$) towards BL levels by Wk 104 was most evident with BEL/RTX, while low circulating $CD20^+CD27^+$ memory B cell levels remained relatively unchanged (Table 1).
Conclusion: An improvement in anti-dsDNA and C3/C4 levels was generally observed across all 3 treatment groups with greater reductions in anti-dsDNA antibodies following BEL/RTX versus BEL/PBO and BEL/ST. We believe that BEL induced a pharmacodynamic window for subsequent RTX treatment for a marked reduction in circulating memory B cells and other B-cell subsets. Our findings underscore the need for better understanding of the bridge from pharmacodynamic to clinical outcomes, given that BEL/RTX did not show an improvement in disease control over BEL/PBO.[1]
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Table 1. Absolute changes in biomarkers for treatment phase completers*

Median (25th, 75th percentile)	Change from BL					
	At Wk 52			At Wk 104		
	BEL/PBO	BEL/RTX	BEL/ST	BEL/PBO	BEL/RTX	BEL/ST
	n=54	n=102	n=58	n=24	n=44	n=50
Anti-dsDNA (IU/ml)	-9 (-83, 1)	-51 (-155, -3)	-5 (-61, 0)	-9.5 (-197, 2)	-55 (-329, -2)	-6.5 (-57, -1)
C3 (md/dl)	8.5 (-8, 21)	15† (0, 30)	1‡ (-6, 11)	6 (-5.5, 19.5)	11 (-7, 27)	7.5 (-5, 23)
C4 (md/dl)	2 (0, 5)	4† (2, 9)	2‡ (-1, 4)	1.5 (-1.5, 4.5)	3 (0, 8)	3 (1, 5)
B cells and B-cell subsets (cells/ml)	**n=48**	**n=93**	**n=55**	**n=20**	**n=40**	**n=47**
$CD19^+$	-57,570 (-120,810, -5861)	-95,313 (-193,946, -44,240)	-57,399 (-152,403, -12,562)	-41,343 (-105,789, 23,819)	-11,932 (-77,822, 45,773)	-48,783 (-151,528, -15,603)
$CD20^+$	-58,112 (-110,681, -3126)	-93,482 (-189,567, -42,636)	-57,428 (-147,094, -3590)	-40,773 (-95,658, 25,547)	-3986 (-75,942, 49,021)	-45,110 (-143,321, -15,063)
Naïve $CD20^+CD27^-$	-60,929 (-112,623, -15,316)	-61,405 (-152,261, -28,496)	-62,477 (-142,009, -16,191)	-22,210 (-72,131, 28,335)	6941 (-62,669, 67,355)	-51,254 (-142,712, -14,736)
Activated $CD95^+$	-5012 (-12,701, 278)	-9991 (-17,900, -5560)	-3895 (-10,068, -1347)	-3834 (-13,274, 1490)	-5821 (-11,216, -233)	-5641 (-14,810, -3341)
Memory $CD20^+CD27^+$	9,586 (1500, 30,983)	-15,076 (-42,880, -6376)	5532 (-146, 14,393)	-13,927 (-24,816, -3064)	-11,534 (-25,646, -2958)	-1229 (-8466, 7300)

*Excluded from analysis: all pts who discontinued the investigational product before Wk 52 and BEL/ST pts if discontinued before Wk 104, and BEL/PBO and BEL/RTX pts who re-started BEL after Wk 53; †n=101; ‡n=57.

OP0282

IMPACT OF ANIFROLUMAB ON NEUROPSYCHIATRIC MANIFESTATIONS OF DEPRESSION AND SUICIDALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neuropsychiatric (NP) disease is more common in patients with systemic lupus erythematosus (SLE) than in the general population.[1] Increased incidence of NP events (depression and suicidality) has been reported with biologic therapies, including SLE therapies.[2] Depression and suicidality were evaluated in patients with SLE treated with anifrolumab, a type I interferon receptor antibody, in the TULIP-1 and TULIP-2 trials.[3,4]

Objectives: To understand the impact of anifrolumab treatment on NP manifestations (depression and suicidality) in patients with SLE relative to standard therapy using pooled data from the TULIP trials.

Methods: TULIP-1/-2 were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab every 4 weeks in patients with moderate to severe SLE despite standard therapy.[3,4] Patients with active severe or unstable NP SLE were excluded. Patients who received ≥1 dose of anifrolumab 300 mg or placebo were analyzed for depression and suicidality.[3,4] The Personal Health Questionnaire Depression Scale-8 (PHQ-8) and Columbia Suicide Severity Rating Scale (C-SSRS) were used to assess clinical depression and suicidal ideation and behavior, respectively. Incidence of adverse events (AEs) within the standardized Medical Dictionary for Regulatory Activities query of depression (excluding suicide and self-injury) and antidepressant use at baseline and during the study were also assessed.

Results: In the TULIP pooled analysis, 360 patients received anifrolumab and 365 received placebo. Mean PHQ-8 scores were in the mild range (≥5 to <10); 9.7 in both groups at baseline (Table 1). Excluding patients taking antidepressants, mean PHQ-8 scores were 9.5 in the anifrolumab group and 9.7 in the placebo group at baseline. No clinically meaningful worsening in mean PHQ-8 scores was observed from baseline to Week 52 in the anifrolumab (–2.0) or placebo (–1.3) groups; excluding patients taking antidepressants, mean changes in PHQ-8 were –2.0 and –1.2, respectively. Depression AEs during the study were reported in 11 anifrolumab-treated patients (3.1%) and 9 patients who received placebo (2.5%). At baseline, antidepressant use was comparable between groups (anifrolumab group, 7 patients [1.9%]; placebo group, 9 patients [2.5%]). During the study, 8 anifrolumab-treated patients (2.2%) and 12 patients who received placebo (3.3%) used antidepressants; 1 (0.3%) and 4 (1.1%) patients, respectively, initiated antidepressant therapy during the study (1 in the placebo group stopped therapy). Suicidal ideation or behavior, as assessed by C-SSRS, during the study was reported in 5 anifrolumab-treated patients (1.4%) and 11 patients who received placebo (3.0%). Excluding patients taking antidepressants, suicidal ideation or behavior during the study was reported in 4 anifrolumab-treated patients (1.1%) and 9 patients who received placebo (2.5%) (Figure 1).

Conclusion: Patients with SLE treated with anifrolumab did not experience increased depression, suicidality, or need for antidepressants when compared with standard therapy, irrespective of baseline antidepressant use.

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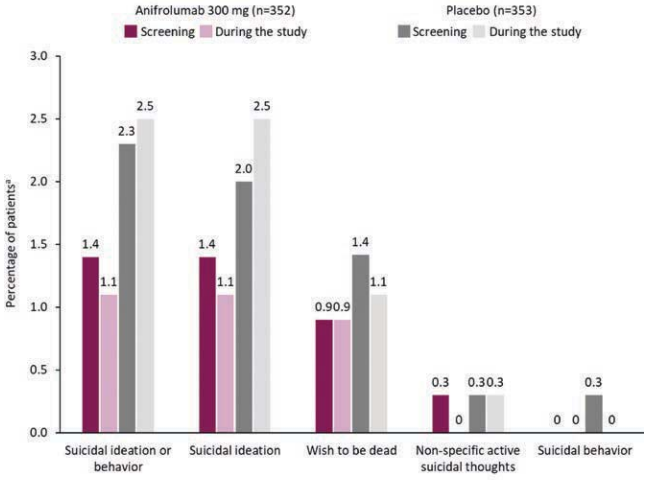
Figure. C-SSRS Summary, Excluding Patients Taking Antidepressants



[a]Percentages are based upon all patients included in the analysis within the respective pool and treatment group.

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Table 1. PHQ-8 Summary

	All patients								Excluding patients taking antidepressants							
	Anifrolumab 300 mg N=360				Placebo N=365				Anifrolumab 300 mg N=360				Placebo N=365			
	n	Mean[a]	SD	Change[b]	n	Mean[a]	SD	Change[b]	n	Mean[a]	SD	Change[b]	n	Mean[a]	SD	Change[b]
Baseline	341	9.7	6.26	–	348	9.7	6.11	–	335	9.5	6.21	–	338	9.7	6.09	–
Week 24	295	7.6	5.89	–2.1	303	8.0	6.00	–1.5	289	7.5	5.84	–2.1	293	8.1	6.00	–1.5
Week 52	266	7.8	5.99	–2.0	261	7.9	6.03	–1.3	262	7.7	6.00	–2.0	252	7.9	5.96	–1.2

SD, standard deviation.[a]PHQ-8 classifications: 0–4 = none, 5–9 = mild, 10–14 = moderate, 15–19 = moderately severe, and 20–24 = severe.[b]Mean change from baseline.

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OP0283 MYCOPHENOLATE MOFETIL VS CYCLOPHOSPHAMIDE FOR TREATMENT OF LUPUS NEPHRITIS: A SINGLE-CENTER COHORT REAL-WORLD ANALYSIS

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Background: Mycophenolate mofetil (MMF) or low-dose intravenous cyclophosphamide (CYC) are recommended as initial (induction) treatment in many recommendations for the management of lupus nephritis (LN), and randomized controlled trials have shown their similar efficacy. However, there is little to no real-world data.
Objectives: We conducted the real-world analysis to compare the efficacy and safety of MMF and CYC for the induction treatment of LN.
Methods: Our patients came from PKUFH SLE cohort, a single-center longitudinal observational cohort set up in 2007, and only patients received initial remission induction therapy for initial or recurrence LN were analyzed. The primary outcome measure was complete renal remission (CR) as defined by (proteinuria <500 mg/24 hours and serum creatinine within 10% from baseline in 12 month. All statistical analyses were performed with SPSS 26.0 and two sides $p < 0.05$ was considered statistically significant.
Results: The 237 LN patients with a median age of 35.0 years had a mean duration of disease of 5.2 years. Of these, 97 patients received CYC, 98 patients received oral MMF, and 42 patients received other immunosuppressive agents or combination therapy. The CR rate in 6-month in MMF was significantly higher than CYC group (CR 57.6% vs 45.2%, p=0.005), and that also applied to 12 month (74.7% vs 56.3%, p=0.001). MMF group patients had lower serum creatinine (76.8±14.5 vs. 93.3±62.9, p=0.012), lower dose glucocorticoid exposure (9.7±3.3vs.11.2±5.6, p<0.05), and lower 24-hour protein level (0.4±0.7 vs. 0.7±1.0, p=0.017) than CYC group. However, MMF did not showed superior to CYC in the LN induced remission (6 month:87.5% vs 73.7%, p=0.064, 12 month:87.7% vs 90.6%, p=0.632) after propensity score matching, just as the Kaplan-Meier analysis showed (Figure 1). Chinese patients usually adopted lower dose MMF (78.8% 1.5g/d,) compared Caucasian populations, and which was also effective.

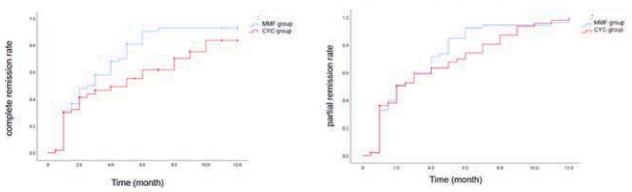

Figure 1. Kaplan-Meier analysis of complete(left) or at least partial remission rate (right)in 12 month after propensity score analysis.

97(47.5%) patients had at least one adverse event, 34% patients had experienced one or more infection. CYC group patients had higher incidence of digestive adverse reactions compared with MMF group (16.3% vs. 2.1%, p<0.001), and no evidence for a statistically significant difference in other aspects. However, patients with CYC induce-therapy are more likely to develop menstrual disturbance (11.2% vs 4.1%) and pneumonia (11.2% vs 3.1%), even failed to reach statistical significance.
No significant difference attributable to ACEIs or ARBs was found in remission rates, SLEDAI, C3 lever and prednisone dose. However, ACEIs/ARBs was benefit to decrease the urine protein (0.2±0.3 vs 0.6±1.0, p=0.031) and may increase the plasma albumin (41.8±3.8 vs 40.6±3.4, p=0.130), thus protect renal function (SCr 74.7±13.4 vs 100.4±82.0, p=0.027). There was no significant difference in remission rate and other parameters, regardless of Hydroxychloroquine (HCQ) or not.
Conclusion: This was the first real-word study to compare the effectiveness and safety of MMF in LN compared with low dose CYC. We found that MMF had similar induced remission rate, with lower gastrointestinal adverse reactions and may less influence on menstruation and less pneumonia, even at relatively low doses. ACEIs/ARBs was benefit to decrease the urine protein and protect renal function.
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OP0284 IMMUNOPHENOTYPIC CHARACTERIZATION OF PERIPHERAL BLOOD-DERIVED B LYMPHOCYTES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DURING B-CELL TARGETED THERAPY WITH ANTI-BLYS

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Background: Belimumab, the first biological drug approved for the treatment of patients with Systemic Lupus Erythematosus (SLE), is a fully human IgG1λ monoclonal antibody directed against BlyS (B Lymphocyte Stimulator). BLyS inhibition is associated with a reduction in circulating B subsets and short-lived plasmacells
Objectives: The aim of this study was to characterize the B cell phenotype in SLE patients at baseline and after B-cell targeted therapy with Belimumab in a cohort of active SLE patients.
Methods: Fifty-four SLE patients diagnosed according to the 2012 SLICC criteria (49 females, mean age 40.6±13.2 years, disease duration 12.3±9.0 years, SLEDAI-2K 6.6±3.1) who received belimumab were enrolled. Phenotyping of peripheral blood (PB)- derived B lymphocytes (using as phenotypic markers IgD, CD27 and CD38) was performed at six (T6) and twelve (T12) months in 38 SLE patients, together with the expression of BAFF and BAFF- R by flow cytometry.
Results: In the whole SLE cohort, a reduction over time was observed in the percentage of $CD19^{pos}$[T0:11.1±6.1% vs T6:6.4±3.4%,p<0.01;T12:4.2±3.4 %,p<0.01] and naïve B cells ($IgD^{pos}CD27^{neg}$) [T0:55.8±28.7% vs T6:34.9±22 .2%,p<0.01;T12:30.0±19.4%;p=0.04] and an increase of switched memory B cells ($IgD^{neg}CD27^{pos}$)[T0:21.0±20.2% vs T6:37.5±21.4%,p<0.01;T12:42.2±21.% 7,p=0.02] after B-cell targeted therapy with anti-BLyS. Moreover, a reduction of $IgD^{neg}CD27^{neg}$ memory B cells at T6(p=0.01) was observed. Conversely, BAFF and BAFFR expression in peripheral blood-derived $CD19^{pos}$ cells remained unchanged during therapy with anti-BLyS. Stratifying SLE patients based on severe (renal and/or neurological) and mild (articular and/or cutaneous) organ involvement, a significant reduction of $CD19^{pos}$ percentage[T0:10.7±4.6% vs 6:6.8±2.4%,p=0.03;T12:4.5±3.5%,p=0.03] and naïve B cells[T0:61.0±24.6% vs T6:38.9±17.5%,p<0.01;T12:36.9±16.0%,p=0.03] was found in SLE patients with mild organ involvement and a significant increase of switched memory B cell subsets in both subgroups [(severe T0:24.1±25.0% vs T6:44.9±27.4%,p=0.01) (mild T0:18.9±18.3 vs T6:31.2±12.7%,p<0.01)]. Evaluating the B cell subsets regarding the response to treatment (based on the reduction of the SLEDAI-2K), a significant reduction of naïve B cells was observed at T6 in both SLE group,[(responders T0:55.4±29.3 vs T6:32.3±19.9,p<0.01)(no responders T0:63.1±41.3% vs T6:41.4±33.5%,p=0.05)] and switched memory B cells[(responders T0:22.4±21.2% vs T6:39.6±19.4%,p<0.01)(no responders T0:20.6±26.1% vs T6:38.6±35.3%,p<0.05)], with a significant higher percentage at baseline of switched memory B cells in responder SLE than in no-responder SLE group (22.4±21.2% vs 20.6±26.1%,p=0.02). ROC curve analysis of $IgD^{neg}CD27^{pos}$ subset [AUC(95% CIs):0.761:(0.566-0.957)p=0.023] identified a cut-off of 9.94% associated with response at 6 months. Moreover, having a $IgD^{neg}CD27^{pos}$ rate ≥9.94% [OR:4.5(95% CIs:0.9-17.2)]; and the presence of anti-dsDNA antibodies at baseline[OR:5.2(95%CIs:1.2-22.1)], identified SLE patients who achieved early response within 6 months from belimumab therapy initiation.
Conclusion: Anti BLyS therapy significantly impacts on the composition of peripheral blood B-cell subpopulations in SLE patients in relation with the distinct organ involvement. Moreover, baseline immunological features and $IgD^{neg}CD27^{pos}$ B cell subset rate are novel putative biomarkers of response to anti-BLyS therapy in SLE patients.
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OP0285

VOCLOSPORIN IS EFFECTIVE IN ACHIEVING PROTEINURIA TREATMENT TARGETS IN LUPUS NEPHRITIS DEFINED BY EULAR/ERA RECOMMENDATIONS

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Background: The novel calcineurin inhibitor voclosporin was approved in 2021 for the treatment of adult patients with active lupus nephritis (LN) in combination with background immunotherapy. Voclosporin has a favorable metabolic profile and a consistent dose-concentration relationship, eliminating the need for therapeutic drug monitoring.
The Phase 2 AURA-LV and Phase 3 AURORA 1 studies demonstrated that the addition of voclosporin to mycophenolate mofetil (MMF) and low-dose steroids led to significantly higher complete renal response rates in AURA-LV at 24 weeks (32.6% vs 19.3%; odds ratio [OR] 2.03; p=0.046) and in AURORA 1 at 52 weeks (40.8% vs 22.5%; OR 2.65; p<0.0001) of treatment in patients with LN.
Objectives: The European League Against Rheumatism and European Renal Association (EULAR/ERA) published updated treatment recommendations for LN with targeted reductions in proteinuria over the course of the first year of therapeutic intervention.[1] Here we report on a post-hoc analysis of pooled data from the similarly designed 48-week AURA-LV and 52-week AURORA 1 studies based on these updated response criteria.
Methods: AURA-LV and AURORA 1 enrolled patients with biopsy-proven active lupus nephritis (Class III, IV, or V ± III/IV) and proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V). Pooled data included 268 patients in the voclosporin (23.7 mg BID) group and 266 patients in the control group, with all patients receiving MMF (target dose 1 g BID) and low-dose steroids (target dose 2.5 mg/day by week 16 according to protocol-defined steroid taper). We assessed the following EULAR/ERA treatment targets: ≥25% reduction in urine protein creatinine ratio (UPCR) by 3 months, ≥50% reduction in UPCR by 6 months, UPCR ≤0.7 mg/mg by 12 months, and steroid dose ≤7.5 mg/day by 3, 6, and 12 months.
Results: Within the first 3 months of treatment, 78.4% of patients in the voclosporin group and 62.4% of patients in the control group achieved ≥25% reduction in UPCR (odds ratio [OR] 2.25; 95% confidence interval [CI] 1.52, 3.33; p<0.0001). The percentage of patients achieving a reduction of ≥50% in UPCR by 6 months was also significantly greater in the voclosporin group compared to control (66.0% vs 47.0%, respectively; OR 2.24; CI 1.57, 3.21; p<0.0001). After 12 months of treatment, 52.6% and 33.1% of patients receiving voclosporin and control, respectively, had achieved a UPCR ≤0.7 mg/mg (OR 2.52; CI 1.75, 3.63; p<0.0001). Given the protocol-defined steroid taper, at both 3 and 6 months, a similar proportion (>90%) of patients in both groups had achieved the recommended steroid dose, with 89.6% and 82.8% in the voclosporin and control groups, respectively, on the recommended dose at 12 months. The proportion of patients meeting all three UPCR targets during the one-year study period and having a steroid dose ≤7.5 mg/day at 12 months was 37.3% in the voclosporin group and 23.3% in the control group (OR 2.11; CI 1.43, 3.10; p=0.0001).
Conclusion: The addition of voclosporin to a background regimen of MMF and low-dose steroids in patients with LN significantly increased the likelihood of achieving the 3-, 6-, and 12-month UPCR targets of therapy recommended by EULAR/ERA.
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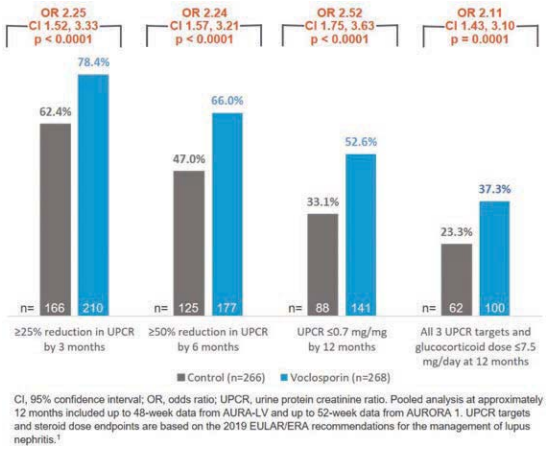

CI, 95% confidence interval; OR, odds ratio; UPCR, urine protein creatinine ratio. Pooled analysis at approximately 12 months included up to 48-week data from AURA-LV and up to 52-week data from AURORA 1. UPCR targets and steroid dose endpoints are based on the 2019 EULAR/ERA recommendations for the management of lupus nephritis.[1]

Figure 1. Integrated AURA-LV and AURORA 1 Analysis on the Achievement of UPCR Treatment Targets and Use of Low-Dose Steroids per EULAR/ERA Lupus Nephritis Recommendations

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OP0286

DEVELOPMENT AND PRELIMINARY VALIDATION OF THE SJÖGREN'S TOOL FOR ASSESSING RESPONSE (STAR): A CONSENSUAL COMPOSITE SCORE FOR ASSESSING TREATMENT EFFECT IN PRIMARY SJÖGREN'S SYNDROME

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Background: Today, there are still no DMARDs licensed for primary Sjögren Syndrome (pSS) patients. Among the explanations, are the limitations of current outcome measures used as primary endpoints: e.g; high placebo response rate, evaluation of either symptoms or systemic activity, and important features not being assessed. The NECESSITY consortium (https://www.necessity-h2020.eu/), including pSS experts from academia, pharmaceutical industry and patient groups formed to develop a new composite responder index, the Sjögren's Tool for Assessing Response (STAR) that solve the issues of current outcome measures in pSS and is intended for use in clinical trials as an efficacy endpoint.
Objectives: To develop a composite responder index in primary Sjögren's syndrome (pSS): the STAR.
Methods: To develop the STAR, the NECESSITY consortium used data-driven methods, based on 9 randomized controlled trials (RCTs), and consensus techniques, involving 78 experts and 20 patients. Based on reanalysis of rituximab trials (TRACTISS and TEARS) and literature review, the Delphi panel identified a core set of domains to include in the STAR, with their respective outcome measures. STAR options combining these domains were designed and proposed to the panel to select and improve them. For each STAR option, sensitivity to change was estimated by the C-index (derived from Effect size) in all 9 RCTs. Delphi rounds were run for selecting STAR among these options. The Delphi panel also voted to classify trials as positive, negative or "in between" in regards to primary but also key secondary endpoints. For the options remaining before the final vote, meta-analyses of the RCTs were performed separately for positive and "in between" trials together, and for negative trials.
Results: The Delphi panel identified 5 core domains (systemic activity, patient symptoms, lachrymal gland function, salivary gland function and biological parameters), and 227 STAR options, combining these domains, were selected to be tested for sensitivity to change. After two Delphi rounds, meta-analyses of the 20 remaining options were performed. The candidate STAR was selected by a final vote based on metrological properties and clinical relevance. In positive/in between trials, candidate STAR detected a difference between arms (OR 3.29, 95%-CI [2.07;5.22], whereas it did not in negative trials (OR 1.53, 95%-CI [0.81;2.91]).
Conclusion: The candidate STAR is a composite responder index, including in a single tool all main disease features, and is designed for use as a primary endpoint

in pSS RCTs. Its rigorous and consensual development process ensures its face and content validity. The candidate STAR showed good sensitivity and specificity to change. The candidate STAR will be prospectively validated in a dedicated three arms RCT of the NECESSITY consortium that will evaluate combination of synthetic DMARDs (hydroxychloroquine + lefunomide or hydroxychloroquine + mycophenolate vs placebo). We encourage the use of STAR in any ongoing and future trials.

Table 1. Candidate STAR

Domain	Point	Definition of response
Systemic activity	3	Decrease of clinESSDAI ≥ 3
Patient reported outcome	3	Decrease of ESSPRI ≥ 1 point or ≥ 15%
Lachrymal gland function	1	Schirmer: If abnormal score at baseline: increase ≥ 5 mm from baseline If normal score at baseline: no change to abnormal ***Or*** Ocular Staining Score: If abnormal score at baseline: decrease ≥ 2 points from baseline If normal score at baseline: no change to abnormal
Salivary gland function	1	Unstimulated Whole Salivary Flow: If score > 0 at baseline: increase ≥ 25% from baseline If score is 0 at baseline: any increase from baseline ***or*** Ultrasound: Decrease ≥ 25% in total Hocevar score from baseline
Biological	1	Serum IgG levels: decrease ≥ 10% ***or*** Rheumatoid Factor levels: decrease ≥ 25%
Candidate STAR responder		**≥ 5 points**

ESSDAI: EULAR Sjögren syndrome disease activity index; ESSPRI: EULAR Sjögren syndrome patient reported index; IgG: Immunoglobulin G;

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The early bird gets the worm

OP0287 **LONGITUDINAL ASSESSMENT OF THE ULTRASOUND GOUT LESIONS USING THE VALIDATED OMERACT SEMI-QUANTITATIVE SCORING SYSTEM**

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Background: In gout, ultrasound (US) is a promising tool to detect changes in monosodium urate (MSU) depositions during urate-lowering therapy (ULT). The OMERACT US group has developed definitions of gout-specific US lesions[1] and a semi-quantitative scoring system for US lesions representing MSU deposition (tophus, double contour (DC) and aggregates)[2], but the responsiveness of lesions when applying this scoring system has not yet been assessed.
Objectives: The primary aim was to evaluate the responsiveness of gout-specific US lesions in patients receiving treat-to-target ULT using both a binary (present/absent) and the OMERACT-defined semi-quantitative (0-3) scoring system. The secondary aims were to determine the most responsive US measure for MSU deposition at patient level and the optimal joint/tendon set for monitoring lesions.
Methods: US (28 joints, 14 tendons) was performed in microscopically verified gout patients initiating/increasing ULT and repeated after 6 and 12 months. Static images and videos of pathologies were stored. Tophus, DC and aggregates were scored binarily and semi-quantitatively. Individual lesion-scores were calculated at patient level as were combined crystal sum scores. Standardised response means (SRM) for lesions when scored binarily and semi-quantitatively were calculated at patient and joint/tendon level.
Results: Sixty-three patients were followed for 12 months. Plasma urate levels were effectively lowered during follow-up (Table 1). US showed statistically significant decreases in tophus and DC sum scores, both when scored binarily and

Table 1. Course and SRMs of US scores during 12 months' follow-up

	Baseline		6-months' follow-up		12-months' follow-up		P-value*			SRM
	Mean	Median [IQR]	Mean	Median [IQR]	Mean	Median [IQR]	Δ 0–6 months	Δ 6–12 months	Δ 0–12 months	12 months
P-urate (mmol/L)	0.49	0.48 [0.42;0.56]	0.33	0.32 [0.29; 0.36]	0.31	0.30 [0.27;0.35]	**<0.001**	**0.0464**	**<0.001**	-
SQ ultrasound scoring (0–3), [possible range]:										
DC sum score, [0–84]	5.5	3 [1; 8]	3.7	2 [0; 5]	2.2	1 [0; 4]	**<0.001**	**<0.001**	**<0.001**	0.80
Tophus sum score, [0–126]	9.5	6 [4; 11]	8.2	5 [3; 9]	6.4	4 [2; 7]	**<0.001**	**<0.001**	**<0.001**	0.84
Aggregates sum score, [0–126]	12.2	10 [7; 16]	12.6	10 [7; 16]	11.8	11 [6; 15]	**0.875**	**0.192**	**0.582**	0.07
SQ-TD-sum score, [0–210]	15.0	10 [6; 16]	11.9	8 [5; 12]	8.7	6 [4; 9]	**<0.001**	**<0.001**	**<0.001**	0.92
SQ-TDA-sum score, [0–336]	27.2	22 [14; 30]	24.6	18 [12; 28]	20.5	16 [9; 25]	**<0.001**	**<0.001**	**<0.001**	0.73
Binary ultrasound scoring (0–1), [possible range]:										
DC sum score, [0–28]	1.8	1 [0; 3]	1.1	1 [0; 2]	0.6	0 [0; 1]	**<0.001**	**<0.001**	**<0.001**	0.72
Tophus sum score, [0–42]	3.4	2 [1; 4]	3.0	2 [1; 3]	2.3	2 [0; 3]	**0.002**	**<0.001**	**<0.001**	0.75
Aggregates sum score, [0–42]	4.4	3 [2; 6]	4.7	4 [2; 6]	4.2	4 [2; 6]	**0.356**	**0.125**	**0.732**	0.07
Binary-TD-sum score, [0–70]	5.3	3 [2; 6]	4.2	3 [1; 4]	2.9	2 [1; 3]	**<0.001**	**<0.001**	**<0.001**	0.86
Binary-TDA-sum score, [0–112]	9.7	8 [5; 11]	8.8	7 [4; 10]	7.1	6 [3; 9]	**<0.001**	**0.001**	**<0.001**	0.70

US, ultrasound; SQ, semi-quantitative; SRM, standardised response mean; DC, double contour; TD-sum score, tophus+DC sum score, TDA-sum score, tophus+DC+aggregates sum score. * Wilcoxon signed rank test, statistically significant results are indicated by bold-face type.

semi-quantitatively, whereas aggregates were almost unchanged during follow-up (Table 1). SRMs for the semi-quantitative tophus and DC sum scores were markedly higher than those for the binary. The most responsive measure for urate deposition at patient level was a combined semi-quantitative tophus-DC-sum score (SRM 0.92, Table 1). A reduced joint/tendon set for monitoring included knee and 1st–2nd metatarsophalangeal joints and peroneus and distal patella tendons representing the most prevalent and responsive sites (SRM 1.13, Figure 1).

Conclusion: The OMERACT consensus-based semi-quantitative US gout scoring system showed longitudinal validity with both tophus and DC being highly responsive to treatment. A responsive US measure for urate deposition and a feasible joint/tendon set for monitoring are proposed.

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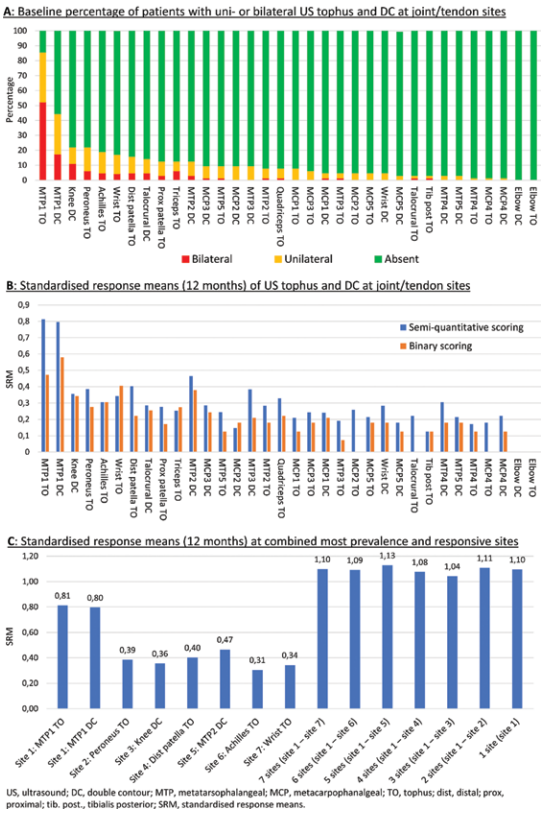
Figure: Prevalence and responsiveness of US tophus and DC at joint/tendon sites



US, ultrasound; DC, double contour; MTP, metatarsophalangeal; MCP, metacarpophanalgeal; TO, tophus; dist, distal; prox, proximal; tib. post., tibialis posterior; SRM, standardised response means.

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OP0288 IMPACT OF CARDIOVASCULAR RISK ON THE DIAGNOSTIC ACCURACY OF THE ULTRASOUND HALO SCORE FOR GIANT CELL ARTERITIS

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Background: The ultrasonographic (US) Halo Score provide a quantitative measure of the extent of vascular inflammation in patients with giant cell arteritis (GCA). High Halo Scores correlate with systemic markers of inflammation, rate of ocular ischaemia and may help to firmly diagnose GCA with high specificity. However, an increase in the intima media thickness (IMT) in patients with elevated cardiovascular risk (CVR) may lead to false-positive US findings.

Objectives: Our aim is to evaluate the impact of CVR on the diagnostic accuracy of the US Halo Score in patients with suspected GCA.

Methods: This is a retrospective observational study of patients suspected of having GCA and referred to our US fast track clinic. All patients underwent US exam within 24 hours per protocol. The IMT was measured in gray scale mode in cranial and extra-cranial (carotid, subclavian and axillary) arteries and the Halo Score was also determined to assess the extent of vascular inflammation. GCA diagnosis was confirmed after 6-month follow-up by the referring clinician. The European Society of Cardiology (ESC) Guidelines on CV Disease Prevention in clinical practice were used to define different categories of CVR. Patients were classified as very high, high, moderate or low CVR according to the Systemic Coronary Risk Evaluation (SCORE) obtained using the ESC CVD Risk Calculator app for mobile devices. Comparison between groups was performed and the diagnostic accuracy of the Halo Score in patients according to CVR was evaluated using ROC curves.

Results: Of the 157 patients referred to our US fast track clinic (67.5% female, mean age 73.7 years), 47(29.9%) had GCA confirmed after 6-month follow-up. There were no differences in CVR between patients with and without GCA (mean SCORE 20.6[21.6] vs 18.7[21];p=0.601). Among patients without GCA, extra-cranial artery IMT was significantly higher in patients with high/very high CVR than in those with low/moderate CVR (Table 1). The Halo Score was significantly higher in patients with high/very high CVR in non-GCA patients (9.38 (5.93) vs 6.16 (5.22);p=0.007). The area under the ROC curve of the Halo Score to identify GCA was 0.835 (CI95% 0.756-0.914), slightly greater in patients with low/moderate CVR (0.965 [CI95% 0.911-1]) versus patients with high/very high CVR (0.798[CI95% 0.702-0.895]) (Figure 1). A statistically weak positive correlation was found between the Halo Score and the SCORE (r 0.245;p=0.002).

Table 1. Measurements of IMT in cranial and extracranial arteries and Halo Score values according to CVR

	Patients with GCA n=47			Patients without GCA n=110		
Artery IMT mm, mean (SD)	Patients with high/very high CVR n=37(78.7%)	Patients with low/moderate CVR n=10(21.3%)	p	Patients with high/very high CVR n=79(71.8%)	Patients with low/moderate CVR n=31(28.2%)	p
Superficial temporal artery (both)	0.66(0.25)	0.45(0.11)	0.025	0.35(0.09)	0.32(0.07)	0.354
Frontal branch (both)	0.42(0.18)	0.31(0.15)	0.056	0.26(0.05)	0.26(0.06)	0.577
Parietal branch (both)	0.43(0.17)	0.35(0.12)	0.102	0.27(0.04)	0.28(0.08)	0.173
Carotid artery (both)	0.88(0.21)	1.2(0.6)	<0.001	0.83(0.16)	0.74(0.13)	<0.001
Subclavian artery (both)	0.86(0.31)	1.2(0.5)	0.001	0.74(0.18)	0.6(0.13)	<0.001
Axillary artery (both)	0.92(0.38)	1.22(0.73)	0.021	0.72(0.16)	0.59(0.15)	<0.001
Halo Score, mean (SD)	18.5(8.8)	17.2(10.6)	0.69	9.38(5.93)	6.16(5.22)	0.007

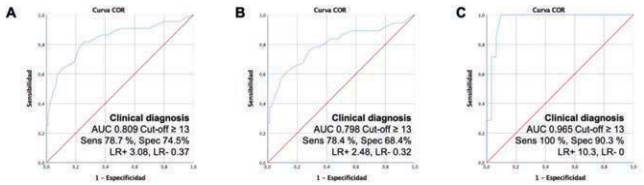

Figure 1. Diagnostic accuracy of the Halo Score for a clinical diagnosis of GCA after 6-month follow-up in (A) all GCA suspected patients, (B) patients with high/very high CVR and (C) patients with low/moderate CVR

Conclusion: High CVR may influence the diagnostic accuracy of the US Halo Score leading to false-positive findings in these patients. Higher IMT values may be found in extracranial arteries of subjects with high/very high CVR without GCA. Thus, CVR should be taken into consideration in the US vascular assessment of patients with suspected GCA. These results need to be confirmed in larger cohorts to develop a modified US Halo Score applicable to patients with high CVR.

Disclosure of Interests: None declared

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OP0289 SHORT- AND LONG-TERM EFFICACY OF ULTRASOUND-GUIDED NEEDLE FRAGMENTATION OR LAVAGE (BARBOTAGE) IN SYMPTOMATIC SHOULDER CALCIFIC TENDONITIS REFRACTORY TO SUBACROMIAL STEROID INJECTION. PROSPECTIVE LONGITUDINAL STUDY OF 181 PATIENTS.

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Background: Rotator cuff calcific tendinopathy is a common cause of shoulder pain and disability in young patients. Despite analgesics or steroid injection some patients still experience symptoms and may require surgery. Ultrasound-guided fragmentation or lavage are minimally invasive techniques that can be used instead of surgery to remove calcification and improve symptoms. However, evidence is poor because of most of published studies are retrospective or with few patients.

Objectives: To assess the short and long-term efficacy of ultrasound guided needle fragmentation or lavage (barbotage) in a large cohort of patients with symptomatic shoulder calcific tendonitis refractory to previous subacromial steroid injection.

Methods: Prospective study, including all consecutive patients referred to a Rheumatology out-patient clinic between Jul 2008-Dec 2020 because of symptomatic (visual analog scale or VAS≥4) calcific tendonitis of the rotator cuff refractory to at least one subacromial corticosteroid injection. After informed consent, all patients were treated with minimally invasive ultrasound-guided technique: fragmentation between Jul 2008-Dec 2013 or lavage (barbotage) between Jan 2014-Dec 2020. Corticoids were injected in the subacromial-subdeltoid bursa in all patients after procedure. Shoulder pain (VAS) and shoulder X-ray were assessed at baseline and after 4 months since the intervention. A new clinical assessment was made after 12 months or when clinical relapse occurred.

Results: One hundred and eighty-one subjects (56 men and 125 women), were included in the study. Mean age was 49.7 years (range 29 -72). Mean duration of symptoms was 33.0 months (2-150), with mean VAS 7.6±1.5. Right shoulder was the location most frequently affected (66,3%). Mean size of calcification by X-ray was 13.7 mm (5-40). 55 patients (30.4%) underwent fragmentation, 115 (63.5%) lavage and 11 (6.1%) both techniques. There were not significant differences between groups at baseline. 4 months after procedure, mean VAS pain was 4.5±3.8 and 82.9% of subjects experienced a X-ray resolution (56.8%) or size reduction (26.1%) of the calcification. A clinical relapse occurred in 73 patients (40.3%) in the first 4 months of follow up, and in 33 patients (18.2%) between months 4 and 12. Symptoms disappeared in most of patients with a new steroid injection. Only 31 patients (17.1%) required a second fragmentation or lavage, and 13 patients (7.2%) a rotator cuff surgery. Any patient suffered local or systemic complications after fragmentation or lavage. Patients treated with lavage had higher shoulder pain when clinical relapse (mean VAS 6.5 vs 4.0; p=0.01) and needed more frequently a new steroid injection (54.8% vs 34%; p=0.004) or ultrasound guided-procedure (17.5% vs 13.1%; p=0.008). There were no significant differences between both techniques in the radiographic resolution or size decrease of the calcification.

Conclusion: Ultrasound guided needle fragmentation and lavage (barbotage) are effective and safe at short and long-term to treat patients with symptomatic shoulder calcific tendonitis, avoiding surgery in more than 90% of cases. Fragmentation seems to have better clinical outcomes than lavage.

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Disclosure of Interests: None declared

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OP0290 WHICH INFLAMED TISSUES EXPLAIN A POSITIVE SQUEEZE TEST OF THE METATARSOPHALANGEAL JOINTS? A LARGE IMAGING STUDY TO INCREASE UNDERSTANDING OF A COMMONLY PERFORMED DIAGNOSTIC PROCEDURE

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Background: The squeeze test of metatarsophalangeal (MTP-)joints is frequently used, because it is easy and cheap, and is traditionally perceived as a test for synovitis. Besides classic intra-articular synovitis also tenosynovitis and intermetatarsal bursitis (IMB) represent synovial inflammation, albeit juxta-articularly located. Both are frequently present in RA and occasionally in other arthritides. However, the contribution of IMB to MTP squeeze test positivity is unknown and the contribution of tenosynovitis has only been partially studied.

Objectives: To assess whether tenosynovitis and IMB contribute to a positive MTP squeeze test.

Methods: 192 early arthritis patients and 693 CSA-patients underwent the MTP squeeze test and forefoot MRI at first presentation. MRI measurements in age-matched healthy controls were used to define positivity for synovitis, tenosynovitis and IMB. Logistic regression was used; multivariable models adjusted for sex and simultaneous presence of inflammation features.

Results: In early arthritis patients synovitis (OR 4.8 (95%CI 2.5–9.5)), tenosynovitis (2.4 (1.2–4.7)) and IMB (1.7 (1.2–2.6)) associated with positivity of the MTP squeeze test. Synovitis (3.2 (1.4–7.2)) and IMB (3.9 (1.7–8.8)) remained associated in multivariable analyses. Of patients with a positive MTP squeeze test, 79% had synovitis or IMB: 12% synovitis, 15% IMB and 52% both synovitis and IMB. In CSA-patients, subclinical synovitis (3.0 (2.0–4.7)), tenosynovitis (2.7 (1.6–4.6)) and IMB (1.7 (1.2–2.6)) associated with MTP squeeze test positivity. In multivariable analyses, synovitis remained independently associated (2.5 (1.5-4.1)) whilst tenosynovitis (1.5 (0.8-2.9)) and IMB did not (1.2 (0.8-1.8)). Of patients with a positive MTP squeeze test, 39% had synovitis or IMB: 10% synovitis, 15% IMB and 13% both synovitis and IMB.

Conclusion: Besides synovitis, also IMB contributes to pain upon compression in early arthritis, presumably due to its location between MTP joints. This is the first evidence showing that a positive MTP squeeze test positivity is not only explained by intra- but also juxta-articular inflammation.

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OP0291

SCORING STRUCTURAL DAMAGE IN RHEUMATOID ARTHRITIS BY ULTRASOUND: RESULTS FROM A DELPHI PROCESS AND WEB-RELIABILITY EXERCISE BY THE OMERACT US WORKING GROUP

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Background: Structural damage in rheumatoid arthritis (RA) includes bone erosion, cartilage change, and joint malalignment; historically evaluated with conventional radiography. Ultrasound (US) has been shown to be a valid tool for evaluating both cartilage change and bone erosion.
Objectives: To obtain agreement on definitions and develop semiquantitative scoring systems for assessing structural damage by US and to validate these in a web-based reliability exercise.
Methods: A Delphi survey of statements was prepared by an OMERACT US Working Group task force (USWG) based on a previously published systematic literature review (1) and circulated between group members, including definitions on normal US appearance of joint components, definitions of elementary lesions and scoring systems for bone erosions and joint malalignment. Definitions and a US scoring system for scoring cartilage change were recently developed and validated by the USWG (2) After agreement was achieved (≥75% of grades 4-5 on 1-5 Likert scale) on the statements, still images of metacarpophalangeal and proximal interphalangeal joints 2-5 in healthy controls and in RA patients with varying degrees of pathology were acquired by the USWG members. A dataset of 100 anonymized images, representing various grades of the 3 components of structural damage was created and utilized in 2 rounds of a web-based exercise. Intra- and inter-reader reliability of the scoring systems was assessed by kappa statistics.
Results: 19 USWG members needed 4 Delphi rounds to reach agreement on a total of 9 statements. 4/12 statements were approved in the first, 2/6 in the second, 1/5 in the third and 2/2 in the fourth round. Final scoring systems and representative images are shown in Table 1 & Figure 1. 22 members participated in the web-based reliability exercise. The intra-reader reliability was almost perfect for bone erosion (kappa: 0.87) and cartilage change (kappa: 0.83) and substantial for malalignment (kappa of 0.72). The inter-reader reliability was almost perfect for bone erosion (kappa: 0.85), and substantial for cartilage change (kappa: 0.79) and malalignment (0.62).

Table 1. Final definitions of scoring systems of elementary lesions of structural damage in rheumatoid arthritis

		Agreement
Bone erosion	A 4-grade semiquantitative scoring system can be used to score erosions as follows: grade 0. intact cortical bone; grade 1. single small erosion (diameter: ≤2mm); grade 2. single large erosion (diameter: >2mm) or 2 small erosions; grade 3. 2 large erosions or ≥3 erosions, regardless of size. Both longitudinal and transverse scans should be considered, and the largest measure chosen for each erosion.	100%
Cartilage change	A 3-grade semiquantitative scoring system can be used to grade hyaline cartilage change as follows: grade 0. normal cartilage; grade 1. minimal change: focal thinning or incomplete loss of cartilage; grade 2. severe change: diffuse thinning or complete loss of cartilage.	80% (2)
Malalignment	A 3-grade semiquantitative scoring system can be used to grade malalignment as follows: 0. normal alignment; 1. subluxation or partial dislocation, where the two bone endings are malaligned so that one bone ending is dislocated from its normal position, but still within the articulation; 2. luxation or total dislocation, where the luxated bone ending moves beyond the articulation and the opposing bone ending. Bone position may be compared with a contralateral or similar intact joint if available.	94%

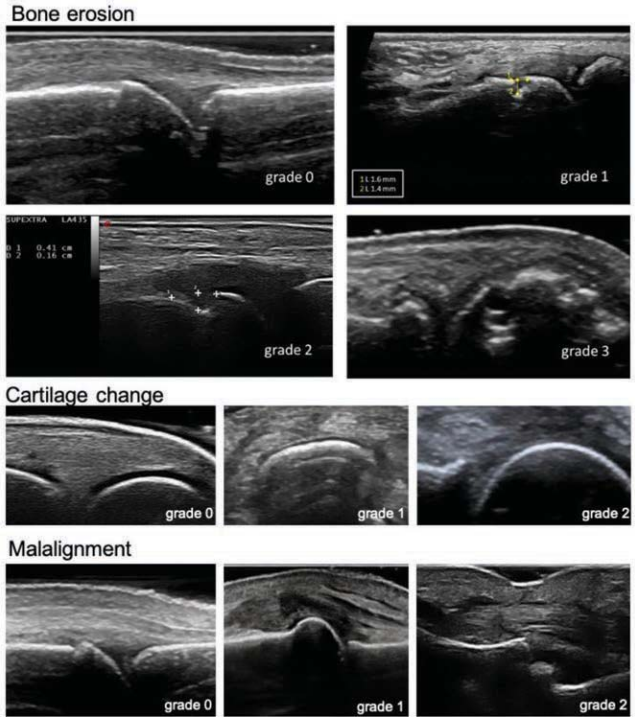

Figure 1. Representative images of the scoring systems for bone erosion (A), cartilage change (B) and malalignment (C)

Conclusion: This first attempt to create a composite US instrument based on scoring systems encompassing all aspects of structural damage, demonstrates that US is a reliable tool for evaluating and scoring bone erosion, cartilage change and malalignment in the finger joints of RA patients.
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OP0292 CLASSIFICATION OF PSORIATIC ARTHRITIS, SERONEGATIVE RHEUMATOID ARTHRITIS, AND SEROPOSITIVE RHEUMATOID ARTHRITIS USING DEEP LEARNING ON MAGNETIC RESONANCE IMAGING

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Background: While MRI evaluation of joints has been primarily used to quantify inflammation at a cross-sectional and longitudinal level, less is known about the potential of MRI in distinguishing different patterns of inflammation in the various forms of arthritis.
Objectives: To evaluate (i) whether deep learning using neural networks can be trained to distinguish between seropositive rheumatoid arthritis (RA+), seronegative RA (RA-), and psoriatic arthritis (PsA) based on structural inflammatory patterns on hand magnetic resonance imaging and (ii) to assess if psoriasis patients with subclinical inflammation fit into such patterns.
Methods: ResNet 3D [1] neural networks were trained to distinguish (i) RA+ vs. PsA, (ii) RA- vs. PsA and (iii) RA+ vs. RA- with respect to hand MRI data. Diagnosis of patients was determined using the following guidelines: ACR/EULAR 2010 [2] for RA and CASPAR [3] for PsA. Results from T1 coronal, T2 coronal, T1 coronal and axial fat suppressed contrast-enhanced (CE) and T2 fat suppressed axial sequences were used. The performance of such trained networks was analyzed by the area-under-the-receiver-operating-characteristic curve (AUROC) with and without imputation of demographic and clinical parameters (Figure 1A). Additionally, the trained networks were applied to psoriasis patients without clinical signs of PsA.

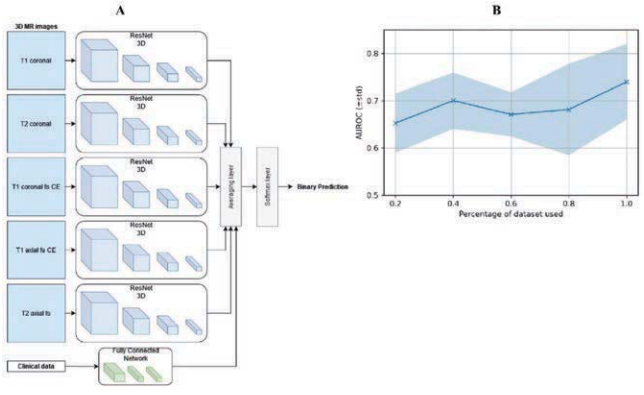

Figure 1. (A) Neural network combining MR sequences with optional additional clinical data. The prediction for a single case is formed by averaging the prediction of all sequences and the clinical data. (B) Plot of the AUROC for increasing percentages (0.6 – 60%) of training data for the differentiation between RA+ and PsA by the neural network. The light blue area around the dark blue mean indicates the uncertainty measured using a 5-fold cross-validation.

Results: MRI scans from 649 patients (135 RA-, 190 RA+, 177 PsA, 147 psoriasis) were included (Table 1). The AUROC for differentiation between disease entities was 75% (SD 3%) for RA+ vs. PsA, 74% (SD 8%) for RA- vs. PsA, and 67% (6%) for RA+ vs. RA-. All MRI sequences were relevant for classification, however, when deleting CE sequences, the loss of performance was only marginal. The addition of patient-specific data to the networks did not provide significant improvements. Increasing amounts of training data demonstrated improved performance of the networks (Figure 1B). Psoriasis patients were mostly assigned to PsA by the neural networks, suggesting that PsA-like MRI pattern may be present early in the course of psoriatic disease.

Table 1. Overview of demographic and clinical information.

		RA+	RA-	PsA	Psoriasis
Total Number (N)		649			
Number (N)		190	135	177	147
Age (years), mean±SD		56.9±12.6	60.5±10.3	56.3±12.0	49.6±13.8
Sex (female/male)		126/64	93/42	92/85	71/76
BMI (kg/m^2), mean±SD		26.6±10.5	27.6 ±9.3	29.1±11.3	26.7±6.9
Disease duration (years), mean±SD		2.6±4.9	1.3±2.3	0.8±2.3	4.2±5.1
DAS28, mean±SD		3.3±1.3	3.4±1.2	3.2±1.3	-
CRP (mg/L), mean±SD		0.9±2.5	0.7±1.2	0.5±0.8	0.5±1.3
HAQ, mean±SD		0.8±0.6	0.9±0.8	0.6±0.6	0.3±0.4
Medication	bDMARD	88.46%	83.87%	81.32%	35.01%
	csDMARD	89.52%	88.89%	80.54%	12.28%

Conclusion: Deep learning can be successfully applied to differentiate MRI inflammatory patterns related to RA+, RA-, and PsA. Early changes in psoriasis patients can be recognized by neural networks and are characterized by a pattern that allowed the networks to classify them as PsA.

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OP0293 PHOTOREALISTIC DEPICTION OF RHEUMATIC PATHOLOGIES BY CINEMATIC RENDERING FACILITATES DISEASE UNDERSTANDING OF PATIENTS WITH RHEUMATIC DISEASES

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Background: Treatment success of a rheumatic disease crucially depends on whether a patient is sufficiently informed about the disease[1]. Visual methods are suitable for explaining diseases[2]. Cinematic rendering (CR) is a new method that allows to segment standard medical images into images that illustrate disease pathologies in a photorealistic way. As such, CR provides new opportunities to visualize diseases and but could therefore be a valuable tool for patients with rheumatic and musculoskeletal disease (RMD).[3]

Objectives: We questioned, if it is possible to apply CR on images from structural lesions of patients with rheumatoid arthritis (RA), Psoriatic Arthritis (PsA) and axial Spondyloarthritis (axSpA) and to test whether such images are helpful to patients with RMDs to understand their disease process. application in doctor-patient communication.

Methods: We selected conventional computed tomography (CT) and high-resolution peripheral CT (HR-pQCT) from patients with rheumatoid arthritis (RA), Psoriatic Arthritis (PsA) and axial Spondyloarthritis (axSpA) that showed typical changes of the respective disease. HR-pQCT measurements were performed in RA and PsA at the Rheumatology Department. CT Measurements of the spine in an axSpA patient was provided from AH. All images were segmented to CR images using a prototype software by the manufacturer Siemens Healthineers. In a prospective study on consecutive patients with RA, PsA, axSpA these images were used to explain the depicted pathognomonic pathologies and compared to conventional imaging in a structured doctor-patient interview. In the last step, patients filled in a quantitative questionnaire (Likert Scale 1-5) about their perspectives answering following questions: Did you understand your disease in the provided Cinematic Rendering images? Did you understand your disease better through the presentation using Cinematic Rendering images than with a normal X-ray image? Do you think it would be reasonable to use this type of Cinematic Rendering to improve patients' understanding of their disease? Descriptive statistical methods were used.

Results: CR images of rheumatic diseases were successfully generated from above mentioned imaging data (CT, HR-pQCT). Bone erosions, osteophytes, enthesiophytes, osteoporosis and ankylosis of the spine could be visualized in photorealistic detail. Figure 1 shows examples of a images of a patient with RA and axSpA with typical bone changes.

65 patients (23 RA/23 PsA/19 axSpA; f 55%) were guided through CR images of their respective disease by an experienced rheumatologist, followed by completing the questionnaire mentioned above. Patients stated that CR was very helpful to understand their disease process (4.39±0.15), that understanding diseases by CR was better than the one obtained by conventional radiographs (4.43±0.20) and that they considered such technology helpful for improving disease understanding (4.35±0.09).

Conclusion: CR seems to be a promising teaching tool for RMD patients facilitating an improved understanding of their disease process and in consequence my also improve adherence of RMD patients to their anti-rheumatic treatment.

Figure 1 shows examples of Cinematic Rendering images from patients with rheumatoid arthritis (a/b) and axial Spondyloarthritis (c). Figure 1a shows erosions and deterioration of bone microarchitecture in MCP joints HR-pQCT. Figure 1b illustrates an os carpale with ankylosis and deformation of all carpal bones as well as the pronounced peripheral demineralization. Figure 1c shows an ankylosed spine of an axSpA patient. CR impressively visualizes the ubiquitous ankylosing process and formation of syndesmophytes.

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OP0294

REDUCED JOINT SYNOVITIS ASSESSMENT VERSUS THE GLOBAL EULAR OMERACT SYNOVITIS SCORE (GLOESS) TO PREDICT THE RESPONSE TO SECUKINUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO CONVENTIONAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS: EXPLORATORY RESULTS FROM THE ULTIMATE TRIAL

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Background: The combined use of B-mode ultrasound (US) and Power Doppler (PD; combination termed as PDUS) allows visualisation of morphological and pathophysiological changes of the synovium. ULTIMATE (NCT02662985) was the first large, randomised, double-blind, placebo-controlled PDUS phase IIIb study in psoriatic arthritis (PsA), to demonstrate that Global OMERACT EULAR Synovitis Score (GLOESS), a US score at patient level, was sensitive to detect the early and continuous decrease in synovitis in a multicenter setting using different US devices and examiners.[1] However, the US assessment for GLOESS was time-consuming owing to the number of joints assessed.

Objectives: To investigate the value of various reduced joint sets to predict the validated GLOESS score.

Methods: ULTIMATE was a 52-week study with a 12-week double-blind, placebo-controlled period followed by 12-week open-label (OL) treatment and 6-month OL extension period.[1] In the ULTIMATE trial, GLOESS for the 24 paired joints was calculated, with a potential score ranging between 0 to 144.[1] A Spearman's rank correlation matrix and a Cluster Image Map were constructed to identify highly correlated joint clusters based on the composite PDUS scores. Based on the different approaches (best correlation, model optimization, etc.), representative joints were then selected from each group, which yielded several corresponding combinations of joints. Linear models were developed with these reduced joint sets as predictors of GLOESS, using data from 60% of patients randomly selected from the

ULTIMATE study. The remaining 40% data were used for model validation and diagnostics.

Results: Five models were established with reduced pairs of joint sets (9–13 pairs). The joints included in each linear model are summarized in Table 1. All five models of reduced joint sets showed high correlation with GLOESS score of R^2 ~ 0.95. Figure 1 depicts all the 5 models of reduced joint sets for PDUS-detected synovitis versus the actual GLOESS in secukinumab and placebo-secukinumab groups, with modified GLOESS scores using reduced PDUS joint sets demonstrating changes very close to that of validated GLOESS.

Table 1. Joints included across five linear models, indicated by green shading

Joint pairs	Model 1 (N=9)	Model 2 (N=9)	Model 3 (N=9)	Model 4 (N=13)	Model 5(N=12)
Elbow					
Knee					
MTP2					
Wrist					
MCP1					
DIP4					
MTP4					
MCP2					
MCP4					
MCP5					
PIP3					
PIP4					
PIP1, PIP5					
DIP2					
DIP3, DIP5					
MTP1					
MTP5					
Shoulder					
Tibiotalar					

N, number of joint pairs used in model. DIP, distal interphalangeal; MCP, metacarpophalangeal; MTP, metatarsophalangeal;PIP, proximal interphalangeal

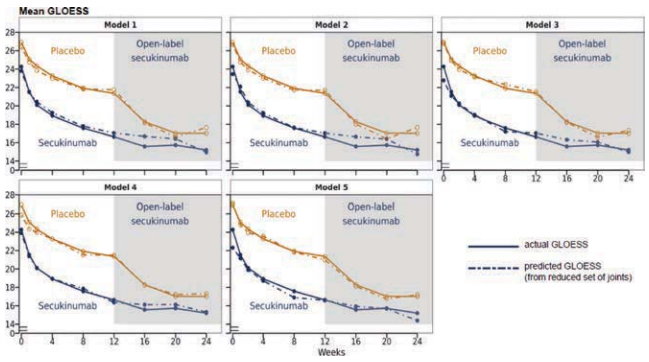

Figure 1. Reduced set of joints synovitis score vs GLOESS score

Conclusion: All models of reduced joint sets for PDUS-detected synovitis predicted GLOESS well. The next steps will be to document responsiveness and ability to discriminate between active and placebo treatment.

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Lifestyle and Disease activity in inflammatory arthritis

OP0295-HPR

THE EFFECT OF GROUP-BASED COGNITIVE BEHAVIOURAL THERAPY FOR INSOMNIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RANDOMISED CONTROLLED TRIAL

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Table 1. Primary and key secondary outcomes at week 7 and week 26, and differences between treatment groups (based on the ITT population)

	CBT-I n=31	Usual care n=31	Difference between groups (95% CI)	P-value
At week 7				
Sleep efficiency (PSG, %)[1]	88.7 (1.8)	83.7 (2.0)	5.0 (-0.4 to 10.4)	0.068
At week 26				
Sleep efficiency (PSG, %)	84.8 (1.9)	86.3 (2.0)	-1.5 (-7.0 to 3.9)	0.577
Total sleep time (PSG, minutes)	376.5 (11.8)	394.6 (12.8)	-18.1 (-52.5 to 16.4)	0.302
Sleep onset latency (PSG, minutes)	14.2 (2.2)	10.0 (2.4)	4.2 (-2.2 to 10.7)	0.197
Wake after sleep onset (PSG, minutes)	52.1 (10.7)	41.5 (11.6)	10.6 (-20.7 to 41.9)	0.505
Insomnia severity (ISI 0-28)[2]	7.6 (0.7)	17.4 (0.7)	-9.8 (-11.8 to -7.9)	<0.0001
Sleep quality global (PSQI 0-21)[3]	5.9 (0.5)	11.1 (0.5)	-5.2 (-6.6 to -3.8)	<0.0001
Fatigue (BRAF-MDQ 0-70)[4]	24.0 (1.4)	36.4 (1.5)	-12.4 (-16.5 to -8.4)	<0.0001
RA impact of disease (RAID 0-10)[5]	4.2 (0.20)	5.5 (0.20)	-1.4 (-1.9 to -0.80)	<0.0001
Depressive symptoms (HADS-D 0-21)[6]	3.8 (0.5)	6.5 (0.5)	-2.7 (-4.1 to -1.3)	<0.0001

Values are reported as least squares means (standard errors) by group, while the differences between groups are reported with 95% confidence intervals.[1]Polysomnography, [2]Insomnia Severity Index, [3]Pittsburgh Sleep Quality Index, [4]Bristol Rheumatoid Arthritis Fatigue - Multidimensional Questionnaire, [5]Rheumatoid Arthritis Impact of Disease, [6]Hospital Anxiety and Depression Scale - Depression.

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Background: Insomnia is highly prevalent in patients with rheumatoid arthritis (RA) and may exacerbate symptoms and burdens, such as fatigue, depressive symptoms, and pain[1]. Cognitive behavioural therapy for insomnia (CBT-I) has been shown to produce positive effects on sleep in other clinical populations[2,3]. However, CBT-I has not previously been investigated in patients with RA.
Objectives: The primary objective was to compare the effect of nurse-led group-based CBT-I to usual care on sleep efficiency, measured by polysomnography (PSG) immediately after the intervention (i.e. seven weeks after baseline) in patients with RA. Secondary objectives included comparing the longer-term effect of CBT-I on sleep and RA-related outcomes at 26 weeks' follow-up.
Methods: In a randomised controlled trial, using a parallel group design, the experimental intervention was six weeks' CBT-I; the control comparator was usual care. CBT-I was delivered face-to-face by a CBT-I trained nurse. The primary analyses were based on the intention-to-treat (ITT) population; missing data were statistically handled using repeated-measures linear mixed effects models adjusted for the level at baseline.
Results: The ITT population consisted of 62 patients (89% women), with an average age of 58 years (SD 10), DAS28-CRP of 3.4 (SD 1.0), Insomnia Severity Index (ISI) score of 18.9 (SD 4.4) and median Patient Global Assessment score of 55 (IQR 28;71).
When primary outcome was measured by PSG at week seven, sleep efficiency was 88.7% in the CBT-I group, compared to 83.7% in the control group (difference: 5.0 [95% CI -0.4 to 10.4]; p=0.068) (See Table 1). Secondary outcomes measured by PSG had not improved at week 26 either. However, for all secondary sleep and RA-related patient-reported outcomes, there were statistically highly significant differences between CBT-I and usual care e.g. insomnia (ISI: -9.8 [95% CI -11.8 to -7.9]), RA impact of disease (RAID: -1.4 [95% CI-1.9 to -0.80]) and Patient Global Assessment (-13.0 [95% CI -20.9 to -5.1]) at 26 weeks' follow-up.
Conclusion: Nurse-led, group-based CBT-I for two hours per week for six weeks, did not improve objectively measured sleep efficiency or any other outcomes measured by PSG. However, CBT-I showed long-term improvement on patient-reported outcomes such as fatigue, impact of disease, depression, pain, and Patient Global Assessment – a finding that could have important clinical implications.
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[3] PMID: 26434673
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Complexity of care in RMD: intersection between health and social care

OP0296-HPR HEALTH AND SOCIAL CARE PROFESSIONALS' WORK TO ACHIEVE COHERENT REHABILITATION PATHWAYS FOR PEOPLE WITH INFLAMMATORY ARTHRITIS - A QUALITATIVE INTERVIEW AND OBSERVATIONAL STUDY

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Background: 20-40% of people with inflammatory arthritis (IA) do not tolerate or do not have sufficient effect of their medication and experience substantial impact of their disease. They need rehabilitation to develop or restore functioning and become able to live an independent and meaningful life (1). Rehabilitation and the organisation of health and social care services are characterised by a high degree of complexity and many different professionals working across different departments, primary and secondary sectors.
Objectives: To investigate how health and social care professionals across different departments, levels and sectors work to achieve coherent rehabilitation pathways for people with IA.
Methods: In total, 26 professionals across primary and secondary health and social care participated in semi-structured interviews. These professionals were all pointed out by people with IA because they had made a significant difference to achieve coherent rehabilitation pathways for them. In addition, participant observations and informal interviews with the healthcare professionals were conducted during the rehabilitation stay. Formula stories (2) and institutional ethnography (3) guided the interpretation of data. In the findings, the term people is changed to users to underline their interactions with the professionals.
Results: The analysis derived three themes:
1) Interactions with users: the professional's interactions with users were predominantly characterized by the ideal of focusing on the individual human being with respect for individual's norms, values and wishes. However, this ideal was challenged when their professional knowledge contradicted the user's norms, values and wishes.
2) Dependent interactions between professionals: expresses dependency of collaboration between professionals both internally within the same department or organization but also across organizations and sectors. Dependency on information about the user to carry out examinations, deliver care or treatment or dependency on referrals to legitimize the efforts the professionals considered necessary for the user.
3) The significance of organisation within institutional frameworks for the professionals' work: the professionals experienced that they were not always able to meet the users demand for care due to organizational requirements for efficiency, economic cost reductions and documentation. These issues led to lack of time to prepare, implement, and follow up on communication with users and other professional partners.
Conclusion: The professionals want to meet the individual with a person-centred approach but sometimes they find it difficult to combine this with their own professional knowledge and values. The professionals are dependent on collaboration with other professionals across departments and sectors. This study shows that the institutional and organizational framework can hinder rather than promote the professionals' intentions to create coherent rehabilitation.
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Sjogren syndrome: from biopsy to lymphoma

OP0297 DIAGNOSTIC VALUE OF LABIAL MINOR SALIVARY GLAND BIOPSY IN THE DIAGNOSIS OF SJÖGREN'S SYNDROME: HISTOLOGIC FINDINGS OF 678 BIOPSIES AND ASSOCIATIONS WITH LABORATORY MARKERS, CLINICAL AND PATIENT ASSOCIATED PARAMETERS.

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Background: Histologic findings of salivary gland biopsy are a crucial part of the current ACR-EULAR classification criteria of Sjögren's syndrome (SS) (1). Particularly, the finding of a focal lymphocytic sialadenitis (focus

score ≥ 1/4 mm^2) corresponds to 3 scoring points out of 4 needed to reach a positive classification for SS [1]. Moreover, there is increasing evidence that salivary gland biopsy can provide prognostic information regarding systemic involvement and the development of lymphoma in the context of the disease.

Objectives: The aim of this study was to analyze the minor labial salivary gland (MLSG) biopsy findings of a large SS cohort and to examine their associations with disease specific laboratory markers, clinical and patient associated parameters.

Methods: We included all patients from two large rheumatological medical departments in Germany having undergone a diagnostic MLSG between 01/2010 and 12/2019. The data have been collected partly in a retrospective and party in a prospective manner. Next to the examination of histological results we focused on activity and chronicity parameters of the underlying disease, autoantibodies, presence of systemic and haematological involvement, as well as on current and previous comorbidities. The statistical analyses included sensitivity and specificity examinations via receiver operating characteristics (ROC), correlation analyses, Mann-Whitney-U-Tests and ANOVA.

Results: In total, 678 patients have been included (615 ♀, median age 55 years [47-63, IQR]). 306 patients (45.1%) had a positive focus score. The remaining 372 patients with a negative focus score served as a control group. There were significant correlations between the level of the focus score and nicotine use (p=0.002), hypergammaglobulinemia [1.27 (0.71-3.36, IQR) vs. 0.73 (0.0-0.76, IQR); p<0.001], ANA positivity [1.18 (0.11-3, IQR) vs. 0.64 (0-1.34, IQR); p<0.001] and rheumatoid factor positivity (p<0.001). Moreover, focus score levels correlated significantly with disease modifying antirheumatic treatment [1 (0-2.34, IQR) vs. 0.87 (0-1.8, IQR); p=0.004] and weakly significantly with erythrocyte sedimentation rate (r=0.235, p<0.001).

Within the group of patients with primary SS there were significant correlations between the level of the focus score and presence of systemic involvement [2 (1.1 - 4, IQR) vs. 1.44 (1-2.62, IQR); p=0.015], glandular involvement [4 (2.98-6.2, IQR) vs. 0.72 (1.6-3, IQR); p=0.007] and haematologic manifestations (p=0.002). SSA-antibodies showed the best diagnostic performance compared to MLSG, as examined by ROC (Table 1).

Table 1. Diagnostic value of SSA-antibodies, Sicca, Schirmer´s and Saxon´s test compared to minor labial salivary gland biopsy findings (reference focus score ≥ 1/ 4 mm^2)

	Specificity	Sensitivity	Area under the curve
SSA-Ro antibodies	88.2%	43.4%	0.658
Sicca	15%	91.9%	0.535
Schirmer´s test	27.3%	73%	0.507
Saxons´s test	57.9%	39%	0.541

Interestingly enough, among 159 patients who were admitted due to the diagnosis of primary fibromyalgia (FM), 63 (39.6%) could be diagnosed with SS on the basis of histologic findings and the ACR-EULAR classification criteria.

Conclusion: By examining one of the largest cohorts in the literature we could show that MLSG biopsy findings not only play a key role in the classification and diagnosis of SS, but could also provide important information regarding the presence of a systemic, glandular or haematological involvement. Furthermore, MLSG can help differentiate patients with FM and other chronic pain disorders from patients with subclinical SS who suffer primarily from chronic pain.

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Enhancing research through patient involvement

OP0298-PARE **EXPERIENCES AND IMPACT OF PATIENT AND PUBLIC INVOLVEMENT IN SWEDISH RHEUMATOLOGY RESEARCH: A SURVEY OF RESEARCHERS AND PATIENT RESEARCH PARTNERS**

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Background: Patient and public involvement (PPI) in research is based on the principle that research should be conducted "with" or "by" members of the public, rather than "to", "for", or "about" them.(1) Successful PPI is dependent on active partnerships between researchers and people living with rheumatic diseases throughout the research process. Such partnerships have been shown to improve the quality and relevance of the research. However, as funding bodies increase their demands for PPI, so too may the risk for tokenistic "involvement".

Since 2008, the Swedish Rheumatism Association (SRA) has trained people living with rheumatic diseases to become patient research partners (PRPs) and encouraged their involvement in research projects. The network has grown substantially in terms of the number of registered PRPs, the number of research projects aiming to include PRPs, as well as the number of active partnerships between researchers and PRPs. However, the quality of partnerships and the impact of PPI on Swedish rheumatology research is unknown.

Objectives: To examine the extent of PPI in Swedish rheumatology research, the nature of partnerships between researchers and PRPs, and the perceived impact of PRPs on the research processes.

Methods: The target population was researchers and PRPs linked to the SRA in 2021, the largest private funder of Swedish rheumatology research. In practice, this included researchers who had applied for research grants from the SRA, researchers that had sought PRPs through the SRA, PRPs trained and registered with the SRA, as well as external PRPs named in grant applications submitted to the SRA.

An online questionnaire was developed to examine the target population's understanding of the concept of PPI, their current involvement and experience of PPI, the nature of the partnerships between PRPs and researchers, and their future needs.(2,3) The survey was shared via email to the target population and remained open for one month.

PRPs were involved in the development and testing of the survey and will be involved in the interpretation and implementation of results.

Results: A total of 126 researchers that had submitted research grant applications to the SRA were identified. A further 5 researchers who had previously registered interest in collaborating with PRPs were identified from our records. Review of our internal register of trained PRPs identified 36 PRPs, whilst a further 9 external PRPs were identified from grant applications. However, contact details were unavailable for 7 of the external PRPs. As such, the survey was circulated to 131 researchers and 38 PRPs.

Preliminary response rates, one week into the survey period, were 31.3% for the researchers (41 responses) and 39.5% for the PRPs (15 responses).

Conclusion: As funding bodies increase their demands for PPI in grant applications, evaluations of the nature of PPI are required to ensure that funders' efforts do not mistakenly result in tokenistic efforts to include patients and the public in research. A better understanding of the nature of PPI, the impact of PPI on research, and the needs of the researchers and PRPs will allow appropriate support and training to be developed. This will allow growth not only in the number of partnerships, but also in the quality of partnerships between researchers and PRPs. This, in turn, is likely to improve the quality of rheumatology research.

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Facilitating work participation – why and how?

OP0299-HPR **ANALYSIS OF THE ACCEPTANCE AND USEFULNESS OF A NON-PRESENTIAL CONSULTATION, IN PATIENTS WITH CHRONIC INFLAMMATORY JOINT DISEASES USING A DIGITAL PLATFORM**

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Background: The Covid-19 pandemic has meant a modification of the patterns of the doctor-patient relationship, favoring online visits and reducing face-to-face visits. Likewise, the implementation of Patient-Reported Outcomes (PROs) that do not require the intervention of the doctor in our clinical practice and that given their close relationship with the clinical activity of chronic inflammatory joint diseases (CIJD) has favored an empowerment of patients and can allow the development of the online visit.
Objectives: Know the use and acceptance of patients with CIJD: rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthropathies (SpA) of a non-face-to-face online visit, through a digital environment.
Methods: Patients were included in a platform called Rheumanet for access by username and passwords (https://www.laconsultacercadeti.com/). At the time of inclusion, demographic variables were collected: date of birth, sex, level of education (primary education, secondary education, vocational training, further education and higher education), distance from the hospital to the patient's home, and clinical variables such as diagnosis: RA, PsA or SpA, as well as the duration of the disease. Prior to the appointment, patients were encouraged to complete a PRO survey to assess their clinical situation: Routine Assessment of Patient Index Data 3 (RAPID3) for RA, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for SpA and RAPID3 and / or BASDAI for the PsA. Both the RAPID3 and BASDAI were scored for the patient's knowledge and assigned to a color scale based on disease activity in green (remission or low activity), orange (moderate activity) or red (severe activity). Likewise, they were ordered to express through a free text what they would tell us as if they were in a face-to-face consultation. Complementary tests (analytical, radiological studies and others) are obtained simultaneously from the medical records and a joint assessment of the visit is carried out.
Results: Between September 1, 2020 and January 31, 2022, a total of 248 patients (113 RA, 53 SpA and 82 PsA) were included in the platform. 172 (69.3%) patients used the digital platform and made at least one non-face-to-face visit during follow-up. The number of online visits made by each patient ranged from 1 to a maximum of 13 visits. 80 patients (70.7%) suffered from RA, 40 (75.4%) from SpA and 52 (63.4%) from PsA. The number of patients who made non-face-to-face visits was 38 (72.3%) for a disease duration of <5 years and 137 (64.5%) for >5 years. When the ages of the patients were analyzed, the number of patients who made visits was 75 (73.5%) between 18 and 30 years old, 50 (67.7%) between 30 and 50 and 47 (66.4 %) from 50 years. According to the degree of activity of the disease, 75 patients were in remission or low activity at some point during the visits, 63 patients with moderate activity and 34 with severe activity. The distribution according to level of education was: 11 (6.3%) primary education, 21 (12.2%) secondary education, 37 (21.5%) vocational training, 63 (36.6%) further education and 40 (23.2%)higher education. The number of online visits was higher in patients who lived at a distance of 50 km or more from the hospital, reaching 100% of the visits in this subgroup of patients.
Conclusion: The online visit through a digital platform through PROs is well accepted by our population with CIJD, especially in the young population, with a higher cultural level and whose home is far from the hospital. The online visit was made by patients regardless of the severity of their disease activity. Speed and ease of use using PROs already known to the patient and clinician is an important consideration for rheumatologists working in healthcare systems where patient contact time is limited. It would be interesting to obtain this information in non-pandemic situations such as COVID-19, which would make it possible to assess actual acceptance and its use in this type of patient in circumstances in which fear of contagion is not a variable to consider.

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Crystal arthritis

OP0300 5-YEAR TRAJECTORIES OF URATE-LOWERING THERAPY AND IMPACT OF COLCHICINE ON CARDIOVASCULAR RISK: REAL-LIFE DATA ON 70,000+ PATIENTS

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Background: Urate-lowering therapy (ULT; allopurinol: ALLO and febuxostat: FBX) are recommended to treat gout on the long term, but gout management is often suboptimal. Colchicine can reduce the rate of gout flares upon ULT initiation, and several randomized clinical trials suggest that this drug is also associated with a decreased risk of cardiovascular events.
Objectives: The objectives of this study were to analyze in a real-life setting 1) ULT trajectories and maintenance following initiation and 2) the long-term impact of co-prescribing colchicine on the cardiovascular (CV) risk.
Methods: The LRx database contains the dispensing data of nearly 45% of French pharmacies. Patients who initiated ULT in 2016 (no dispensing in the previous year) and who received regular dispensing (any drug/device) from the LRx pharmacy network until the end of 2020 were included. A multivariate Cox model investigated the factors associated with ULT maintenance over time. In the same cohort, the maintenance of ULT was compared with that of other treatments for chronic diseases. The therapeutic trajectory (continuation, change of dose or type of ULT, discontinuation) was also evaluated. The impact of co-prescribing colchicine on CV risk was studied in the subgroup of patients over 50 years of age without previous delivery of CV treatment (antidiabetics, antiaggregants, antihypertensives, diuretics, statins) in the year prior to ULT initiation. The incidence of CV treatments prescription (≥ 2 deliveries) was compared between patients who initiated ULT with or without colchicine) and those treated with colchicine without ULT using logistic regression.
Results: In 2016, 74,665 patients (mean age ± SD: 70 ± 13 years, 64% men) had initiated ULT, mainly in primary care by a general practitioner (GP) (77%). ALLO was initiated in 68% of patients (100mg/d: 56%, 200mg/d: 32%, 300mg/d: 8%); FBX in 32% (80mg/d: 85%). Colchicine was co-prescribed in 34% of patients. Factors associated with better ULT maintenance were male sex, age < 70, initial prescription by a GP, and co-prescription of colchicine. Conversely, initiation in a hospital setting was associated with poorer ULT maintenance (all p<0.0000001). Half of the patients had stopped ULT after 316 days. This time was shorter than that observed in the same population with anti-diabetics (894 days), ACE inhibitors/sartans (725 days), antiaggregants (718 days). A change in the dose or type of ULT was observed in only a minority of patients. The daily dose of colchicine was associated with a lower risk of initiating a CV treatment (OR per quartile: 0.93 [0.91; 0.96], regardless of co-prescribing with ULT, suggesting a CV benefit of colchicine.
Conclusion: This study illustrates that gout management with ULT remains largely suboptimal in France, especially in comparison with other chronic conditions. In addition, our results suggests that flare prophylaxis with colchicine might lower CV risk in gout patients.

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Digital-Health and Tailored Interventions for Improving Patients' Adherence: Opportunities and Challenges

OP0301-HPR PATIENT ADHERENCE TO E-HEALTH INTERVENTIONS FOR REMOTE DISEASE MONITORING IN CHRONIC ARTHRITIS

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Background: Chronic inflammatory arthritides require lifelong follow-up and treatment. Electronic health (eHealth) could be used to remotely monitor disease, possibly improving patient self-management and lowering the burden of in-person consultations. For clinical use, it is important to understand adherence rates of patients with chronic arthritis to eHealth tools.
Objectives: To systematically review the literature on adherence to eHealth tools for remote monitoring of symptoms or disease activity in chronic arthritis.
Methods: We systematically searched the following databases: Embase, PubMed, Cochrane Central, CINAHL, Web of Science, Clinicaltrials.gov, and the International Clinical Trials Registry Platform (ICTRP). Eligible articles reported adherence rates to an eHealth tool in patients with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), spondyloarthritis (SpA), osteoarthritis (OA), or gout. Included texts were screened individually. Finally, quality assessment was done with the Newcastle-Ottawa scale (NOS) and the PEDro scale.
Results: The literature search resulted in 7027 articles. After deduplication, 4219 articles were screened for eligibility, and 47 articles were included. We found highest adherence rates in studies applying electronic diaries (81.8%), followed by text messages (79.9%), web-based platforms (74.6%), activity trackers (73%), and smartphone applications (65.5%). Highest adherence was reported in studies on patients with OA (79.7%), followed by patients with gout (73.7%), RA (71.3%), ankylosing SpA (67%), and JIA (59%). Demographic characteristics did not seem to affect patient adherence. Based on frequency of data entering, a time interval of once-daily showed highest adherence rates (72.6%), followed by entering data more than once a day (72.3%) and once a week (67.7%), or longer (59.2%). Adherence declined with longer study duration.
Conclusion: Our literature review identified declining adherence levels with longer study duration, and highest adherence rates for patients with OA, making use of electronic diaries, and requesting once-a-day completion. OA studies had an overall shorter duration than RA studies, which could be an explanation as to why OA patients showed higher adherence. Lower adherence rates were reported in studies in juvenile populations, while older age did not seem to affect reported adherence.

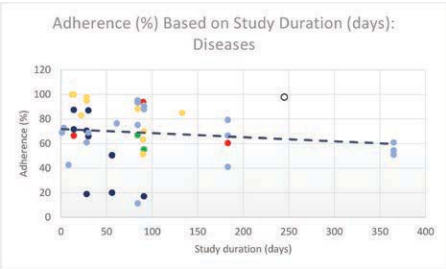

Figure 1. Linear regression model of adherence based on study duration per disease. X = study duration (days), Y = adherence (%). Y = -0.0332X + 71.84. Light blue = RA, yellow = OA, dark blue = JIA, red = Gout, green = SpA, white = >1 disease

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Rheumatology across boundaries

OP0302 IS INCREASED RISK OF UROLITHIASIS IN AXIAL SPONDYLOARTHRITIS DRIVEN BY GUT INFLAMMATION? RESULTS FROM THE SPARTAKUS COHORT

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Background: A nationwide, Swedish study found a doubled urolithiasis risk in ankylosing spondylitis (AS) compared to population controls.[1] Inflammatory bowel disease (IBD) is a known risk factor for urolithiasis, e.g. via enteric hyperoxaluria causing calcium oxalate stones.[2] With microscopic gut inflammation in around 50% of axial spondyloarthritis (axSpA) patients,[3] and overt IBD in 5-10%, gut inflammation may also drive the increased urolithiasis risk in axSpA.
Objectives: To study whether axSpA patients with a history of urolithiasis have an increased prevalence of comorbid IBD or display elevated biomarkers of gut inflammation/pathology.
Methods: AxSpA patients in the population-based SPARTAKUS cohort study in southern Sweden (non-radiographic axSpA [nr-axSpA] n=86, ASAS criteria; AS n=168, modified New York criteria) self-reported their history of prior urolithiasis (no/yes). Faecal (F) calprotectin and ASCA (anti-*Saccharomyces cerevisiae* antibodies) in serum were measured by commercially available ELISAs (Calpro AS; ORGENTEC Diagnostika). For a subgroup of patients (n=164), presence of gut dysbiosis was also assessed by the GA-Map Dysbiosis Test (Genetic Analysis). Demographics, disease/treatment characteristics, comorbid IBD and the gastrointestinal biomarkers (F-calprotectin/ASCA/dysbiosis) were compared between patients with versus without prior urolithiasis. Finally, the same biomarkers were also compared between patients with versus without urolithiasis history, after exclusion of subjects with known IBD.
Results: Urolithiasis history was reported by 13% (n=33) of the axSpA patients, and comorbid IBD was significantly more common in this group (27% versus 6.8%, p<0.001; Table 1). F-calprotectin levels were also significantly higher among patients with prior urolithiasis, as was presence of gut dysbiosis (Table 1). ASCA seropositivity did not differ between the groups. Moreover, prior urolithiasis was associated with longer disease duration and AS-phenotype. After exclusion of cases with comorbid IBD, urolithiasis history was reported by 10% (24 of 230 patients). F-calprotectin elevation ≥100 mg/kg remained significantly associated with urolithiasis history also in this population, while only being numerically increased when assessed as a continuous variable (p=0.053; Figure 1). Gut dysbiosis also remained associated with prior urolithiasis in the non-IBD population (56% [9 of 16 patients with prior urolithiasis] versus 30% [40 of 132 patients without], p=0.037), whereas ASCA status did not differ between the groups (data not shown).

Table 1. Included studies. Adh = adherence SA = smartphone app, ED = electronic diary, AT = activity tracker, OP = online platform, TM= text message. JIA= Juvenile Idiopathic Arthritis, PsA = Psoriatic Arthritis, SpA = Spondyloarthritis, OA = osteoarthritis, RA = Rheumatoid arthritis

Study	Disease	EHealth	Adh (%)	Study	Disease	EHealth	Adh (%)	Study	Disease	EHealth	Adh (%)
Skrepnik, '17	OA	AT/SA	91 AT 36 SA	Beukenhorst, '20	OA	AT/SA	75 AT 62 SA	McKenna, '18	RA	AT	43
Lee, '20	JIA	SA	51	Nowell, '20	RA	AT/SA	82 AT 72 SA	Yu, '20	OA	AT	99
Serlachius, '19	Gout	SA	67	Heiberg, '07	RA	ED	95	Zaslavsky, '19	OA	AT/SA	85
Pers, '21	RA	SA	67	Connelly, '11	JIA	ED	71	Gossec, '18	RA	OP	63
Heale, '18	JIA	AT/SA	19 AT	Connelly, '10	JIA	ED	88	Walter, '14	RA	OP	61
Reade, '17	RA	SA	77	Bromberg, '16	JIA	ED	66	Christodoulou, '14	OA	OP	98
Bellamy, '10	OA	SA	100	Bromberg, '14	JIA	ED	66	Renskers, '20	RA/SpA	OP	68
Seppen, '20	RA	SA	69	Franceschelli, '19	OA	ED	/	Tyrell, '16	SpA	OP	67
Harbottle, '18	JIA	AT/SA	17 SA	Bingham, '19	RA	ED	94	Martin, '21	RA	OP	69
Pouls, '20	Gout	SA	94	Connelly, '17	JIA	ED	87	Kai, '19	OA	OP	52
Colls, '21	RA	SA	79	Stinson, '08	JIA	ED	72	Richter, '21	RA	OP	98
Brayne, '21	RA	SA	41	Wilson, '13	OA	ED	83	Broderick, '13	OA	OP	>95
Austin, '20	RA	SA	91	Jacquemin, '18	RA/SpA	AT	88	Zuidema, '19	RA	OP	71
Crouthamel, '18	RA	SA	20	Elmagboul, '20	Gout	AT	61	Barber, '18	RA	OP	69
Nowell, '21	AS, OA, SpA, RA	SA	55	Östlind, '21	OA	AT/SA	88 AT	Christie, '14	RA/SpA	TM	98
Lee, '12	RA	TM	73								

Table 1.

	Urolithiasis history	
	No, n=221	**Yes, n=33**
Male sex	115 (52%)	23 (70%)
Age, years	50 (13)	59 (12)*
Disease duration, years	25 (14)	31 (14)*
AS (versus nr-axSpA)	141 (64%)	27 (82%)*
Inflammatory bowel disease	15 (6.8%)	9 (27%)*
ASAS 3-month NSAID score	31 (40)	37 (48)
Ongoing bDMARD therapy	87 (39%)	16 (49%)
bDMARD therapy ever	113 (51%)	20 (61%)
ASDAS-CRP	1.8 (1.0)	1.9 (0.8)
BASFI	2.0 (2.1)	2.7 (2.6)
BASMI	2.9 (1.5)	4.3 (2.1)*
F-Calprotectin, mg/kg		*#
Mean (SD)	58 (97)	115 (176)
Median (IQR)	29 (49)	39 (152)
F-Calprotectin ≥100 mg/kg	28 (14%)	10 (32%)*
ASCA IgA ≥10 U/ml	12 (5.7%)	4 (13%)
ASCA IgG ≥10 U/ml	45 (21%)	10 (33%)
Gut dysbiosis†	45 (32%)	17 (71%)*

Mean (SD) or n (%) if not otherwise stated. † GA-Map Dysbiosis Test, dysbiosis index ≥3. * p<0.05 by Chi^2-test or Student t-test, as appropriate. # Log_{10}-transformed values compared. Missing ≤13%, except for gut dysbiosis available in 140/24 patients without/with urolithiasis history.

Conclusion: The current results lend support to the hypothesis that the increased urolithiasis risk in axSpA may be driven by gut inflammation/pathology. Prospective studies are, however, needed to assess the causality.

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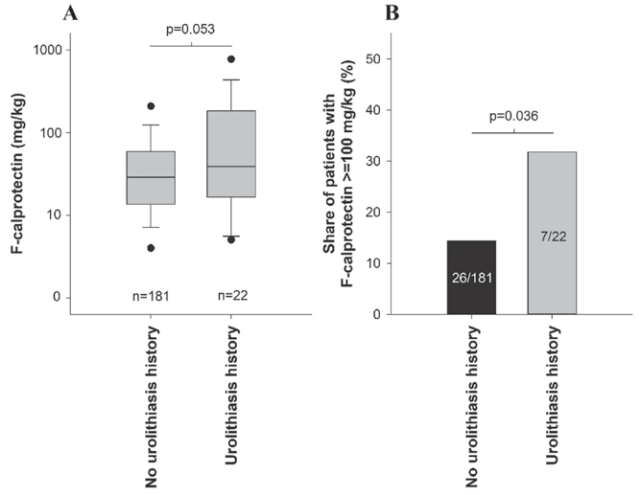

Figure. Comparison of F-calprotectin levels (**A**) and share of patients with elevated F-calprotectin ≥100 mg/kg (**B**) between axSpA patients without known comorbid IBD without versus with prior urolithiasis. Comparisons by Student t-test of Log_{10}-transformed values (A) and Chi^2-test (B), respectively. In the box-plots (A), lines represent medians, boxes 25th and 75th percentiles, whiskers 10th and 90th percentiles, and dots 5th and 95th percentiles.

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The COVID-19 pandemic – what did we learn?

OP0303-PARE

HEALTH DEMOCRACY IN THE TIME OF COVID-19: A COLLABORATIVE INITIATIVE BETWEEN PATIENT ORGANIZATIONS AND HEALTHCARE PROFESSIONALS TO SUPPORT PEOPLE LIVING WITH RHEUMATOID ARTHRITIS

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Background: Has the COVID-19 crisis overwhelmed health democracy? This question may have arisen since extraordinary measures taken in response to the pandemic were developed almost exclusively by scientific expert committees. Citizens, patients, patient organizations, healthcare professionals, and even experts from these committees have recognized a lack of health democracy in the decision-making process regarding the COVID-19 response in France. Indeed, patient voices were barely heard during the early stages of the pandemic; yet inclusive dialogue is crucial for building trust and adherence to policy. Moreover, patients also need to be assisted in handling the overabundance of COVID-19 information, particularly misleading and false information, referred to as an "infodemic" by the WHO.

Objectives: To show a practical and effective application of health democracy in rheumatology through collaboration between patient associations and rheumatologists during the COVID-19 pandemic. To collect, select, analyze, abstract, and translate COVID-19 literature to provide rheumatoid arthritis (RA) patients with useful, convenient and quality educational materials that answer patients' medical, scientific and daily life questions. This initiative is consistent with patient-centered COVID-19 response.

Methods: At the instigation of a patient association in October 2021, a working group was established to develop a COVID-19 patient education resource to meet the expectations and needs of RA patients. The working group consisted of health professionals and patients identified by the partner patient organization. A committee of rheumatologists checked the reliability and accuracy of the scientific and medical information. A committee of patients assessed materials' relevance, readability, and understandability. Materials were written in lay language without distorting the meaning of the scientific data. The methodology is detailed in Figure 1.

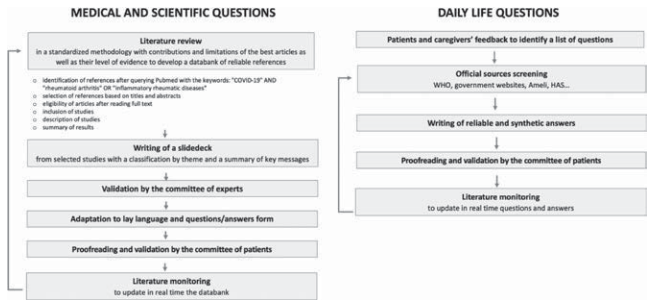

Figure 1. Process flowchart

Results: The document is available to download on www.polyarthrite-andar.com (number of unique visits on the webpage for the last version: 1176). A printed version was also provided directly to patients by rheumatologists. To provide up-to-date information, the brochure was updated 7 times between the first edition in January 2021 and the last version in August 2021. This last version included 49 questions. Each update was announced to all members of the patient organization in its monthly newsletter (number of newsletter's subscribers: 1863; number of followers: Facebook=2632; Twitter=1382; Instagram=921; LinkedIn= 590; Youtube=2907). The "Medical and scientific questions" section provided reliable and expert-reviewed information about the virus, protective measures, testing, vaccination, integrating RA specificities and its treatments for each item. The "Daily life questions" section provided practical advice during the pandemic, in particular by addressing the "TousAntiCovid" smartphone application, isolation certificates, remote working and lockdown instructions.

Conclusion: This initiative demonstrates the benefits that can be achieved by greater collaboration between patients and healthcare professionals to address population health problems. The patient could be an active contributor in improving disease management of his peers. This patient education tool is a good example of the relevance of the motto of 'nothing about us, without us'. The

COVID-19 pandemic has highlighted the importance of bringing patients' voices to affect evidence-based policies centered around the needs of patients. Health democracy needs to form the backbone of how a health system is structured.
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Disclosure of Interests: None declared
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OP0304-PARE **"THE CORONA PANDEMIC – AND HOW WE REACTED TO PATIENTS' NEEDS"**

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Background: The pandemic had major negative effects and is a big challenge to all patient organisations in Europe. Our organisation (Deutsche Rheuma-Liga) with about 270.000 members is already equipped with various tools and skills for the support of our members. We are offering not only information, but exercise-programs, self-management courses, different events to meet and exchange. But after two years of the pandemic, the problems have piled up. Our members are missing the face-to-face contact. It was impossible, due to the limitation and restriction of contact, to conduct events, meetings, consultations, and exercise programs. Most of our offers came to a standstill.
Objectives: Due to these problems, it was not only difficult to live with a chronic rheumatic disease, but there was also no possibility to get access to helpful information and advice or to use the various services, either. Especially the fear of Covid-19, which impact it has on RMDs, questions regarding the vaccination and the medication were increasing to a substantial extent.
Methods: Three different measures were taken:
Information needs:
By improving our website, it was possible to provide digital content to our members. We offer essential and understandable information with additional links to the most current expert information on COVID-19, like the EULAR recommendations and those of our national rheumatologist society (DGRh).
Activity needs:
Different digital exercise-programs were developed by our nineteen national member organisations. We shared this services on the website of our umbrella organisation with all members, nationwide. Our campaign "Keep on moving" shall encourage our members nationwide practising their exercise and developing innovative ideas into the daily routine.
Results: *Interaction needs:*
Regarding our "Rheuma-Forum" (a digital exchange format for people with arthritis)
I want to explain in detail with dates and facts how our organisation enhances the contact to our members and other people with arthritis who were looking to our organisation for information. We replied to questions and addressed the needs on an individual basis. Since the beginning of the pandemic, we implemented four Expert-Forums per year, addressing many comparable questions regarding the issues of COVID-19 (like RMDs and the covid vaccination, possible side effects). Our experts are well-known, specialized rheumatologists and trained RMD patients. The figures speak for themselves.
2020 – 4 Expert Forums with 857 Q&A within 65.396 accesses
2021 - 4 Expert Forums with 677 Q&A within 28.180 accesses
2022 – 1 Expert Forum within 242 Q&A within 10750 accesses
Conclusion: We can be pleased that our strategy to provide information to our members and other people with arthritis via the digital way was successful. We already know that this will be an ongoing process. But we are on the right path to encourage our members in difficult pandemic times and give them important and valid information. Our example of the expert forum shall encourage patient organisations to try out new digital and interactive solutions not only in pandemic times.
Disclosure of Interests: None declared
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How to review a manuscript

OP0305 **THE EMERGING EULAR NETWORK (EMEUNET) PEER-REVIEW MENTORING PROGRAM: TEN YEARS OF INITIATIVE.**

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Background: In 2012, the Emerging EULAR (European Alliance of Associations for Rheumatology) Network (EMEUNET) started a mentoring program in collaboration with the editorial board of top-leading journals in rheumatology, the Annals of the Rheumatic Diseases (ARD) and a few years later RMD Open, with the aim of improving peer reviewing skills of young researchers (mentees).[1] In this program, now in its 6th edition, senior reviewers (mentors) critically discuss manuscripts submitted to ARD or RMD Open with mentees. At the end of the program, senior reviewers certify the capability of mentees to independently conduct a good quality review. The program is organized by members of the EMEUNET Peer Mentoring Subcommittee, including facilitating communication within the groups. Several strategies, such as face-to-face meetings and periodic videoconferences, were implemented recently, following the outcome of a previous survey among mentees.[1]
Objectives: To assess the experienced benefits and challenges of the EMEUNET Peer Mentoring program of young rheumatologists and researchers and their mentors.
Methods: In November 2021, a survey was sent by email to mentors and mentees who successfully completed the first five editions of the program (launched between 2012 and 2019), asking for demographics, and potential benefits and challenges of the program. Felt change in peer-review skills before and after the program were rated on a scale from 0 (no skill) to 10 (perfect skill). Results were analysed descriptively.
Results: A response rate of 55% for mentors (11/20) and 43% for mentees (37/87) was obtained. Mentors had a mean(SD) age of 52(9.5) years, 64% were male and 7 different nationalities were included. Mentees had a mean age of 34(3.7), 43% were male and 16 nationalities were included. Mentees/mentors from all the editions were included, although recent editions were somewhat overrepresented. Almost all respondents said their overall experience with the program was positive (46/47), that the objectives of the peer-reviewing mentoring program were met (46/47) and that they would recommend the program to others (44/45).
Mentors indicated an initial average peer-review skill level of 5.2(1.8) for content and 4.2(1.9) for form, which improved by 2.7(1.3) points 3.2(1.8) points, respectively. Interestingly, improvement scores of the mentees paralleled those of mentors: content and form were initially rated at 4.9(1.7) and 5.1(1.8) and improved by 2.6(1.3) and 2.7(1.7), respectively. Nine out of ten mentors said the program had helped them improve their own skills (i.e., peer-reviewing, mentoring, and teaching). The number of peer reviews after completion of the program varied quite significantly between mentees (median 10, IQR 9.5-29). For most mentees, the number of peer-reviews stayed the same (18/32) or increased (12/32). Fifteen out of 32 respondents said they were invited as an independent reviewer for ARD and/or RMD Open after completion of the program. Potential benefits and challenges of the program are depicted in Figure 1. Added value mentioned by both mentors and mentees was the opportunity to contribute to high quality peer-review standards and improve their skills. Challenges reported by mentors were communication with mentees, stringent deadlines, and the program being time-consuming; challenges for mentees were the communication with their mentor, deadlines and insufficient clarity of the process.

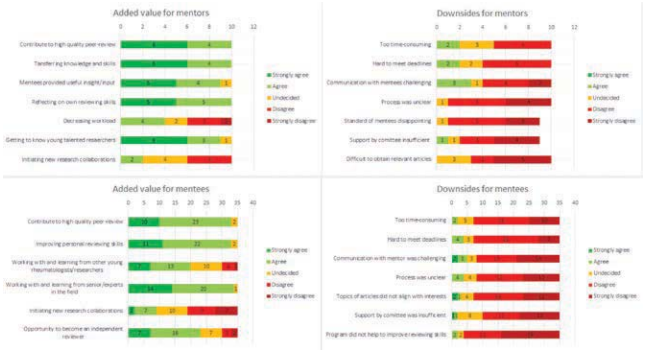

Figure 1. Rating of potential benefits and downsides of the program. X-axis: Items of the survey; Y-axis: the number of respondents (10/11 mentors and 35/37 mentees).

Conclusion: After 5 editions over 10 years, the EMEUNET Peer-Review Mentoring Program continues to be a highly valued opportunity in the field of rheumatic diseases, as both mentors and mentees experience a significant impact on their skills. Areas for improvement were identified (e.g., communication, deadlines) and will be addressed in future editions.

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Disclosure of Interests: None declared
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Interstitial lung disease in RMDs

OP0306 IMPACT OF INFLAMMATION ON INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS - AN ANALYSIS OF THE GERMAN BIOLOGICS REGISTER RABBIT

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Background: Ten percent of patients with prevalent rheumatoid arthritis (RA) develop an interstitial lung disease (ILD), which is associated with higher mortality *(1)*. A previous study identified high/moderate disease activity, but not CRP, as a risk factor for RA-ILD *(2)*.
Objectives: To analyse whether systemic inflammation (CRP and ESR) and/or disease activity measured with a composite score (DAS28-ESR) are associated with the occurrence of ILD in patients with RA.
Methods: Data from RA patients observed in the biologics register RABBIT until 10/2020 were included. Patients with incident ILD were selected as cases and matched 1:5 to controls using a modified risk-set sampling (controls had no ILD during the entire observation time). Matching criteria were age, sex, RA duration, date of enrolment and observation time. Odds ratios (OR) and 95% confidence intervals (CI) were computed by conditional logistic regression and adjusted for factors identified by a directed acyclic graph (DAG), namely smoking, rheumatoid factor (RF), chronic obstructive pulmonary disease, number of biologics until index date (date of ILD-diagnosis in cases, date after the respective observation time in controls) and mean glucocorticoid dosage (12 months prior index date). For the regression, CRP and ESR were log-transformed due to their skewed distribution, and missing values were addressed by multiple imputations (n=10).
Results: Out of 19,148 RA patients enrolled since 2001, 133 patients with incident ILD were identified. Half of the ILDs were diagnosed by computed tomography (n=67), 8% by x-ray (n=10) and in 42% the method was unknown (n=56). At baseline, cases and controls had a mean age of 61 years, 68% were female, and mean RA disease duration was 9 years. Differences were observed in smoking status (59% ever smokers in cases vs. 48% in controls), RF positivity (84% vs. 72%) and the sum of comorbidities (means 3.1 vs. 2.3).
During the 12 months prior to the index date, mean values of CRP and especially of ESR were significantly higher in cases compared to controls. This difference was not observed for DAS28 (Figure 1, upper figures). Furthermore, more cases than controls were in a high inflammatory status, but not in at least moderate disease activity (Figure 1, lower figures). The adjusted regression analyses confirmed these results: CRP and ESR were significantly associated with incident ILD both at the time of diagnosis and in the 12 previous months, and results were even more pronounced with elevated CRP and ESR, which was not the case for DAS28 (Table 1).

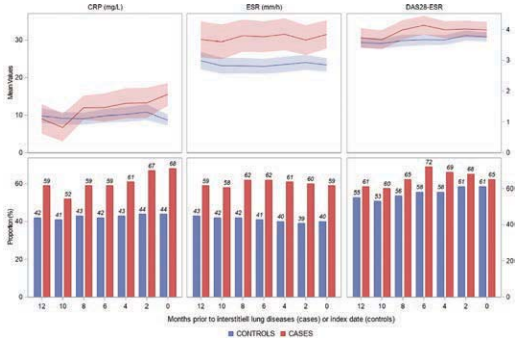

Figure 1 . Upper Figures. Unimputed and untransformed CRP, ESR and DAS28 12 months prior to the index date as means with 95% CI, computed by mixed models with matching strata as random effects. The left y-axis refers to CRP and ESR, the right to DAS28. **Lower Figures**. Percentages of patients with CRP≥5, ESR>21 and DAS28>3.2 12 months prior to the index date.

Table 1. Results of the conditional logistic regression for the risk of ILD.

	Crude OR (95% CI)	Adjusted OR (95% CI)
At index date		
Log CRP	1.55 (1.25 – 1.92)	1.55 (1.24 – 1.94)
CRP≥5 vs. CRP<5	2.43 (1.55 – 3.81)	2.41 (1.49 – 3.88)
Log ESR	1.56 (1.22 – 2.00)	1.56 (1.21 – 2.01)
ESR >21 vs. ESR ≤21	2.12 (1.40 – 3.19)	2.12 (1.37 – 3.29)
DAS28	1.17 (1.01 – 1.35)	1.16 (0.99 – 1.35)
DAS28 >3.2 vs. DAS28 ≤3.2	1.31 (0.86 – 1.99)	1.32 (0.85 – 2.06)
Within 12 months prior to index date		
Log CRP	1.41 (1.14 – 1.75)	1.38 (1.09 – 1.74)
CRP≥5 vs. CRP<5	2.60 (1.59 – 4.27)	2.60 (1.54 – 4.41)
Log ESR	1.65 (1.26 – 2.16)	1.60 (1.21 – 2.12)
ESR >21 vs. ESR ≤21	2.43 (1.53 – 3.86)	2.35 (1.45 – 3.81)
DAS28	1.16 (0.99 – 1.36)	1.13 (0.95 – 1.34)
DAS28 >3.2 vs. DAS28 ≤3.2	1.37 (0.82 – 2.30)	1.37 (0.79 – 2.35)

Conclusion: In contrast to other data, our analyses found that markers of systemic inflammation, but not the DAS28 composite score, are associated with the occurrence of incident ILD in patients with RA and can be predictors for the development of RA-ILD. Therefore, in a treat-to-target approach, rheumatologists should pay particular attention to controlling systemic inflammation.
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[2] PMID: 30951251
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Disclosure of Interests: Ronja Ramien: None declared, Tatjana Rudi: None declared, Matthias Schneider Speakers bureau: Astra-Zeneca; Biogen; BMS; Celgene; Chugai; GSK; Janssen-Cilag; Lilly; Pfizer; UCB, Paid instructor for: Lilly, Consultant of: Abbvie; Astra-Zeneca; Boehringer-Ingelheim; GSK; Lilly; Novartis; Pfizer; Protagen; Roche; Sanofi-Aventis; UCB, Grant/research support from: Abbvie; Astra-Zeneca; GSK; UCB, Sabine Balzer: None declared, Andreas Krause Speakers bureau: AbbVie, BMS, Boehringer Ingelheim, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, BMS, Boehringer Ingelheim, Galapagos, Janssen, Lilly, MSD, Mylan, Novartis, Pfizer, Roche, Grant/research support from: AbbVie, UCB, Martin Schaefer: None declared, Yvette Meissner Speakers bureau: Pfizer, Anja Strangfeld Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Janssen, Lilly, Pfizer, Roche, Sanofi, UCB.
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OP0307 PULMONARY FIBROSIS IN EARLY RHEUMATOID ARTHRITIS IN RELATION TO GENETIC LOCI AND INDIVIDUAL ACPA SPECIFICITIES

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Background: Pulmonary manifestations in rheumatoid arthritis (RA) are common comorbidities but the underlying mechanisms are largely unknown. We found in a previous study 3 SNPs associated with pulmonary fibrosis (PF); rs35705950 (MUC5B), rs111521887 (TOLLIP), and rs2609255 (*FAM13A*) besides age, rheumatoid factor positivity and methotrexate treatment.
Objectives: To evaluate for the added value of a multiplex of anti-citrullinated peptide antibodies (ACPA) for the development of pulmonary fibrosis (PF) in an inception cohort of RA patients.
Methods: A total of 1184 patients with early RA were consecutively included and followed prospectively from the date of diagnosis (index date) until death or until 31 December 2016. The diagnosis of PF was based on high resolution tomography. The presence of 21 ACPA fine specificities were analysed in plasma sampled at index date, using a custom-made microarray chip (Thermo Fisher Scientific, Uppsala, Sweden). Data on both ACPA and genetic data was available for 841 RA patients, of whom 50 developed PF. Associations were analysed using logistic regression analysis and presented as the odds ratio (OR) with the 95% confidence interval (CI). Models were adjusted for sex, age, DAS28 and presence of RF at RA diagnosis, smoking ever, and HLA-SE and in a second step for the three SNPs (.rs35705950, rs111521887 and rs2609255), respectively.

Results: In unadjusted analyses eight ACPA reactivities were found associated with PF development (p< 0.05-0.001). The number of ACPA reactivities was related to PF development, both in crude and adjusted models (p<0.05 for both). In models concomitantly adjusted for the three SNPs (rs35705950, rs111521887 and rs2609255) respectively, in addition to mentioned adjustments the number of ACPA reactivities (p<0.05 for all three nmodels), Vim60-75 (p<0.05, in all three models), Fibβ62–78 (72) (p<0.001-p<0.05) and F4-CIT-R (p<0.01-p<0.05) were all found significantly associated to PF development irrespective of the SNPs.
Conclusion: The development of PF in an inception cohort of RA patients was associated both with risk genes and, independently of the risk genes, the presence of certain ACPA, and the number of ACPA reactivities.
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Acknowledgements: I have no acknowledgements to declare. The staff and patients at the departments of rheumatology in northern Sweden.
Disclosure of Interests: None declared
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Keeping the "Dark clouds" away: Psychological distress and RMDs

OP0308-HPR

MORE THAN HALF OF RA PATIENTS WITH A LIFETIME HISTORY OF MOOD DISORDERS WERE ANXIOUS AND DEPRESSED DURING THE COVID-19 PANDEMIC: RESULTS FROM THE CANADIAN EARLY COHORT (CATCH) STUDY

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Background: A growing number of studies indicate the considerable mental health impacts of the prolonged COVID-19 pandemic in the general population as chronic stress is a risk factor for the development of depression and anxiety. Mood disorders are more prevalent in RA and a history of anxiety or depressive disorders increases the risk of recurrence in the future.
Objectives: To compare trends in prevalence of anxiety and depressive symptoms, prior to and during the COVID-19 pandemic in RA patients with and without a lifetime history of mood disorders.
Methods: Data were from RA patients diagnosed and treated for RA in rheumatology clinics across Canada enrolled in the Canadian Early Arthritis Cohort (CATCH) Study. We estimated monthly trends in prevalence of clinically significant levels of anxiety and depression (PROMIS Depression and Anxiety 4a score 55+) from all visits between Mar 2019 and Jan 2022 and compared monthly trends in anxiety and depression in the year prior to (Mar 2019- Feb 2020) and during the pandemic (Mar 2020 to Jan 2022) stratified by lifetime history of mood disorders.
Results: 4,148 visits were completed from Mar 2019 to Jan 2022 in 1,644 RA patients with a mean (SD) age of 60 (14) and disease duration of 6 (4) years. 73% were women, 84% white, 60% had completed some post-secondary education, and 77% were in CDAI REM/LDA at the visit closest to the start of pandemic. 253 (15%) reported a lifetime history of depression and 217 (13%) a lifetime history of anxiety; 8% reported prior treatment for either.
Patients with a history of mood disorders had higher levels of depression and anxiety prior-to and during the pandemic compared with patients without a history of mood disorders (Table 1). Proportions were highest during COVID waves in all and were substantially higher and more variable in people with a previous history of mood disorders as compared to those without a history (Figure 1). While depressive symptoms peaked early in the pandemic, anxiety increased with each wave, peaking in Wave 3 (May-Jun 2021).

Table 1. Prevalence of depression and anxiety symptoms prior to and during the COVID-19 pandemic in RA patients with and without a history of mood disorders.

Period Prevalence (monthly range)	Depression		Anxiety	
	No history	Prior History	No History	Prior History
N observations	3527	621	3610	538
Prepandemic (3/19 - 2/20)	21% (14%-30%)	51% (29%-64%)	27% (20%-35%)	58% (31%-89%)
Pandemic (3/20 - 1/22)	22% (15%-29%)	53% (33%-78%)	28% (20%-43%)	59% (33%-80%)

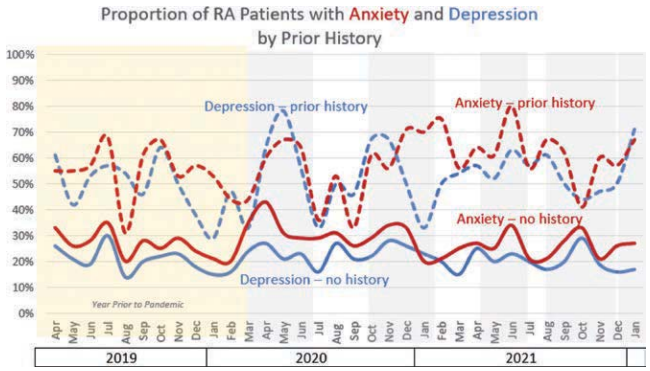

Figure 1.

During the first 22 months of the COVID-19 pandemic, the proportion of patients with depression and anxiety increased in all groups. More than half of those with a history of emotional distress had clinically significant levels of depression and anxiety; proportions were highest during COVID waves in all and were substantially higher in people with previous history as compared to those without a history (see Figure 1). Whereas depressive symptoms peaked early in the pandemic, anxiety increased with each wave, peaking in Wave 3 (May-Jun 2021).
Conclusion: Symptoms of anxiety and depression were common in Canadian adults with RA prior to and after the onset of the COVID-19 pandemic. Whereas others have found that high levels of depression and anxiety occurred early in the pandemic but declined fairly rapidly in the general population[1], emotional distress was not attenuated over time in this large cohort of RA patients. Individuals reporting lifetime history of mood disorders were more than twice as likely to report anxiety and depression, with depression peaking early in the pandemic and anxiety growing with each successive wave in the first year. The results demonstrate the importance of applying a lifetime perspective as previous episodes of anxiety and depression may be an important marker of increased vulnerability and recurrence in RA patients, particularly during the pandemic.
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[1] Fancourt D et al. Trajectories of anxiety and depressive symptoms during enforced isolation due to COVID-19 in England. Lancet Psychiatry. 2021;8:141-9.
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New lessons for rheumatology in genomics medicine

OP0309

WES ANALYSIS OF RARE FAMILIES POINTS TO A PATHOGENIC ROLE FOR THE CGAS/STING-TYPE I IFN AXIS IN SSC

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Background: Systemic sclerosis (SSc) is a rare (prevalence ±20/100,000), chronic condition characterized by vascular, immunological and connective tissue abnormalities. Genetic factors contribute to disease, as evidenced by a 15-fold increased relative risk in relatives of patients. Case-control studies have identified numerous associated loci; the identification and functional validation of risk alleles has however been elusive. No monogenic or oligogenic causes of SSc have been demonstrated, likely due to the infrequency of familial clustering (≤ 1.6% of cases) in this disease. We are fortunate to have access to DNA samples from five such families, with two affected first-degree relatives each: To our knowledge the only series of its kind.
Objectives: The goal of our research is to identify and functionally validate genes that drive SSc pathogenesis in these families, thereby shedding light on fundamental disease mechanisms. In light of the apparent lack of a multi-generational effect, we hypothesize that SSc may be transmitted as a di/oligogenic trait in these families, with two-to-a-few genes acting together to cause disease.
Methods: Whole exome sequencing (WES) was performed on all available blood-DNA (Figure 1). We filtered for variants that are (a) shared by both affected individuals within each family, (b) absent-to-rare in the general population, and (c) predicted to affect protein function by multiple *in silico* tools. Candidate gene prioritization and pathway analysis is followed by *in vitro* testing of a subset of SSc-variants, to assess for their effects on protein function. Where two strong candidate genes are identified in the same family, *in vitro* validation of both variants will be followed by the generation of single- vs. double- knock-in mice, to test for di/oligogenic effects of variant combinations on SSc-related phenotypes.

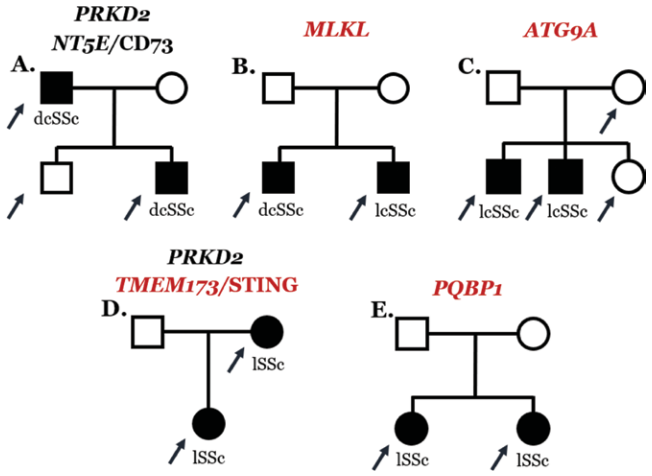

Figure 1. SSc families. Filled symbols: affected. Arrows: WES on blood-DNA. lSSc: Limited SSc; lcSSc: Limited cutaneous SSc; dcSSC: Diffuse cutaneous SSc. cGAS/STING (red) and IFN I (black) - related candidate genes.

Results: WES yielded 23-45 genes per family with variants that satisfied the above criteria. Prioritization of candidates was based on systematic annotation of all 180 genes for expression pattern, function, and potential impact of the SSc-variants. Our data suggest familial SSc is genetically heterogeneous, with little sharing of candidates between families. We therefore assessed for pathways represented in gene-lists from multiple families, and found that participants in the cGAS/STING - type I-IFN axis are identified in all (Figure 1). This would suggest a unifying disease mechanism.
cGAS/STING is a sentinel system responsible for the production of anti-viral type I interferons (IFN-α/β) and pro-inflammatory cytokines in the presence of cytoplasmic double stranded DNA (dsDNA). cGAS/STING-dependent self-dsDNA sensing has been implicated in silica-induced inflammation: a risk factor in SSc and pulmonary fibrosis. A type I IFN-response signature is identified in SSc patients and correlates with disease severity. Mutations in two of our candidates cause Mendelian diseases with phenotypic overlaps with SSc, and all but one cause disease-relevant phenotypes when perturbed in mice. Finally, preliminary *in vitro* data suggest gain-of-function effects of the variant identified in *TMEM173*/STING, and loss-of-function effects in *NT5E*/CD73 and *PRKD2* (the last with two different variants identified in two families; Figure 1). All would lead to increased IFN-I signaling.
Conclusion: We report, for the first time, WES analysis of a familial SSc series of unprecedented size for this rare disease. The identification of potential "driver" gene variants in cGAS/STING-type I IFN signaling regulators across all families points to an important pathogenic role for this pathway in SSc.
Disclosure of Interests: Pierre Maus: None declared, Vanessa Smith: None declared, Tessa Du Four: None declared, Marie Vanthuyne: None declared, Bernard Lauwerys Shareholder of: UCB Pharma, Employee of: Currently an employee of UCB Pharma, Nisha Limaye: None declared
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Volunteering for the RMD Community

OP0310-PARE **AN APP FOR VOLUNTEERS IN DENMARK**

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Background: The Danish Rheumatism Association wanted to improve its communication with and between its volunteers. We had an existing system that worked like a database of information, but our volunteers found it difficult and lacking the needed information. Furthermore, they wanted to be in closer contact with other volunteers with similar functions in the organization to be able to share ideas and learn from each other.
Objectives: We wanted to find a platform with which we could increase the connectability between our volunteers across the organization as well as making existing information more accessible for them. We also wanted an easier way of contact to our volunteers that did not require them to use their e-mails.
Methods: First we identified the tasks we wanted our "solution" to solve. Then we decided that the ideal tool for this probably would be an App that supported the connectability as well as a "database" with documents and instructions in which we could present important and useful information to our volunteers.
We searched the marked for platforms and invited three companies to make a presentation on how their product could support our ideas and wishes.
After the presentation, we settled on the solution with the best connectability functions, as we wanted to present our volunteers with a completely new experience of contact with the organization and each other.
We introduced the App on a big conference for our volunteers we have every two years. We had a big workshop planned with instruction and tests, where our volunteers could try the App and its functions. Prior to the conference, we had sent out instructions to all the participants on how to install the app, and registered them as users of the app, making sure all was in place and ready for the conference and our introduction.
Results: We found, that instructing such a large group of people all at once proved to be more demanding than we had expected. After the conference, we continued with the introduction of the app to new volunteers as well as sending information and updated instructions to existing app- users.
We have found that the introduction of this new app has been quite a success. We now have a platform for easy and fast communication to and between all our volunteers, as well as access to relevant news and important information from the organization about their roles and tasks as volunteers.
It has been quite a time-consuming task to implement the app and we have invested a great deal of working hours making sure the app would be used by our volunteers. We have found it necessary to develop a separate communication plan to ensure our volunteers accept and remember the app as an important working tool.
Conclusion: We found, that instructing such a large group of people all at once proved to be more demanding than we had expected. After the conference, we continued with the introduction of the app to new volunteers as well as sending information and updated instructions to existing app- users.
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Disclosure of Interests: None declared
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LB0001

BIMEKIZUMAB IN BDMARD-NAIVE PATIENTS WITH PSORIATIC ARTHRITIS: 24-WEEK EFFICACY & SAFETY FROM BE OPTIMAL, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED, ACTIVE REFERENCE STUDY

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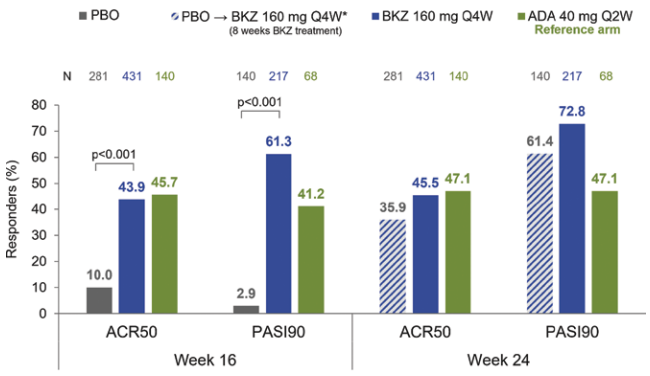
Background: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A.

Objectives: Assess BKZ efficacy and safety vs PBO in bDMARD-naïve pts with active PsA to Wk 24 of BE OPTIMAL.

Methods: BE OPTIMAL (NCT03895203) comprises 16 wks double-blind PBO-controlled and 36 wks treatment-blind. Pts were ≥18 yrs, bDMARD-naïve, with adult-onset, active PsA, ≥3 tender and ≥3 swollen joints. Pts randomised 3:2:1, subcutaneous BKZ 160 mg Q4W:PBO:adalimumab (ADA; reference arm) 40 mg Q2W. From Wk 16, PBO pts received BKZ 160 mg Q4W. Primary endpoint: ACR50 at Wk 16.

Results: 821/852 (96.4%) pts completed Wk 16 and 806 (94.6%) Wk 24. Mean age 48.7 yrs, BMI 29.2 kg/m^2; since diagnosis: 5.9 yrs; 46.8% male. BL characteristics comparable across arms. Primary endpoint met (Wk 16 ACR50: 43.9% BKZ vs 10.0% PBO, p<0.001; ADA: 45.7%; Figure 1). All ranked secondary endpoints met at Wk 16 (Table 1). As early as Wk 2, ACR20 was higher in BKZ vs PBO (27.1% vs 7.8%, nominal p<0.001; ADA: 33.6%). Outcomes continued to improve at Wk 24 (Table 1). To Wk 16, pts with ≥1 TEAE, BKZ: 59.9%; PBO: 49.5%; ADA: 59.3%. SAE rate low (1.6%; 1.1%; 1.4%). Most frequent (≥5%) AEs for all arms: nasopharyngitis (9.3%; 4.6%; 5.0%), URTI (4.9%; 6.4%; 2.1%), increased ALT (0.7%; 0.7%; 5.0%). Candida infections: 2.6%, 0.7%, 0%; no systemic candidiasis. 2 malignancies (BKZ: basal cell carcinoma; PBO: breast cancer stage 1); no MACE, uveitis, IBD or deaths.

Figure. ACR50 and PASI90 response at Wks 16 and 24



Randomised set. Data reported as NRI. *PBO→BKZ pts received PBO to Wk 16, switched to BKZ 160 mg Q4W through Wk 24 (8 wks BKZ).

Abbreviations: ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; ADA: adalimumab; AE: adverse event; ALT: alanine aminotransferase; bDMARD: biologic disease -modifying antirheumatic drug; BKZ: bimekizumab; BL: baseline; BMI: body mass index; BSA: body surface area; CfB: change from baseline; HAQ DI: health assessment questionnaire disability index; hs-CRP: high-sensitivity C-reactive protein; IBD: inflammatory bowel disease; IL: interleukin; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MACE: major adverse cardiovascular events; MDA: minimal disease activity; MI: multiple imputation; NRI: non responder imputation; PASI: psoriasis area and severity index; PASI75/90/100: ≥75/90/100% improvement in PASI; PBO: placebo; PsA: psoriatic arthritis; pt: patient; Q2W: every 2 weeks; Q4W: every 4 weeks; RBMI: reference-based multiple imputation; SAE: serious adverse event; SF-36 PCS: 36-item short form survey Physical Component Summary; SJC: swollen joint count; TEAE: treatment-emergent adverse event; TJC: tender joint count; URTI: upper respiratory tract infection; vdHmTSS: van der Heijde modified Total Sharp Score; Wk: week; yr: year.

Conclusion: Dual inhibition of IL-17A and IL-17F with BKZ in bDMARD-naïve pts with active PsA resulted in rapid, clinically relevant improvements in musculoskeletal and skin outcomes vs PBO. No new safety signals observed.[1,2]

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[1] Ritchlin CT Lancet 2020;395(10222):427–40.
[2] Coates LC Ann Rheum Dis 2021;80:779–80(POS1022).

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Table 1. Wk 16 and 24 efficacy

		BL			Wk 16				Wk 24		
		PBO N=281	BKZ 160 mg Q4W N=431	ADA 40 mg Q2W N=140†	PBO N=281	BKZ 160 mg Q4W N=431	ADA 40 mg Q2W N=140†	p value (BKZ vs PBO)	PBO→ BKZ 160 mg Q4W[a] N=281	BKZ 160 mg Q4W N=431	ADA 40 mg Q2W N=140†
Ranked endpoints[b]	**ACR50** [NRI], n (%)	–	–	–	28 (10.0)	189 (43.9)	64 (45.7)	<0.001	101 (35.9)	196 (45.5)	66 (47.1)
	HAQ-DI CfB [MI], mean (SE)	0.89 (0.04)	0.82 (0.03)	0.86 (0.05)	−0.09 (0.03)	−0.26 (0.02)	−0.33 (0.04)	<0.001[c]	−0.28 (0.03)	−0.30 (0.02)	−0.34 (0.05)
	PASI90[d] [NRI], n (%)	–	–	–	4 (2.9)[e]	133 (61.3)[f]	28 (41.2)[g]	<0.001	86 (61.4)[e]	158 (72.8)[f]	32 (47.1)[g]
	SF-36 PCS CfB [MI], mean (SE)	36.9 (0.6)	38.1 (0.5)	37.6 (0.7)	2.3 (0.5)	6.3 (0.4)	6.8 (0.8)	<0.001[c]	6.2 (0.5)	7.3 (0.4)	7.3 (0.8)
	MDA [NRI], n (%)	5 (1.8)	14 (3.2)	1 (0.7)	37 (13.2)	194 (45.0)	63 -45	<0.001	106 (37.7)	209 (48.5)	67 (47.9)
	vdHmTSS CfB (subgroup)[h] [MI], mean (SE)	15.67 (1.80)[i]	15.56 (1.69)[j]	17.39 (2.89)[k]	0.36 (0.10)[i]	−0.01 (0.04)[j]	−0.06 (0.08)[k]	<0.001[c]	–	–	–
	vdHmTSS CfB [MI], mean (SE)	13.31 (1.56)[l]	13.44 (1.47)[m]	14.55 (2.44)[n]	0.31 (0.09)[l]	0.00 (0.04)[m]	−0.03 (0.07)[n]	0.001[c]	–	–	–
Other endpoints	**ACR20** [NRI], n (%)	–	–	–	67 (23.8)	268 (62.2)	96 (68.6)	<0.001[o]	175 (62.3)	282 (65.4)	99 (70.7)
	ACR70 [NRI], n (%)	–	–	–	12 (4.3)	105 (24.4)	39 (27.9)	<0.001[o]	53 (18.9)	126 (29.2)	42 (30)
	PASI100[d] [NRI], n (%)	–	–	–	3 (2.1)[e]	103[f] (47.5)	14 (20.6)[g]	<0.001[o]	60 (42.9)[e]	122 (56.2)[f]	26 (38.2)[g]
	TJC CfB [MI], mean (SE)	17.1 (0.7)	16.8 (0.6)	17.5 (1.1)	−3.2 (0.7)	−10.0 (0.5)	−10.9 (1)	<0.001[o]	−9.4 (0.7)	−11.5 (0.5)	−11.8 (0.9)
	SJC CfB [MI], mean (SE)	9.5 (0.4)	9 (0.3)	9.6 (0.6)	−3.0 (0.5)	−6.6 (0.3)	−7.5 (0.6)	<0.001[o]	−6.8 (0.4)	−7.2 (0.3)	−7.9 (0.6)

Randomised set. Interim results. †Reference arm; study not powered for statistical comparisons of ADA to BKZ or PBO. [a]PBO→BKZ pts received PBO to Wk 16, switched to BKZ 160 mg Q4W through Wk 24 (8 wks BKZ); [b]Resolution of enthesitis/dactylitis in pts with LEI>0/LDI>0 at BL pooled with BE COMPLETE (Wk 16 LEI=0 BKZ: 124/249 [49.8%], PBO: 37/106 [34.9%], p=0.008; LDI=0 BKZ: 68/90 [75.6%], PBO: 24/47 [51.1%], p=0.002); [c]Continuous outcome p values calculated with RBMI data; [d]Pts with PSO and ≥3% BSA at BL; [e]n=140; [f]n=217; [g]n=68; [h]Pts with hs-CRP ≥6 mg/L and/or bone erosion at BL; [i]n=221; [j]n=357; [k]n=108; [l]n=261; [m]n=416; [n]n=131; [o]Nominal, not powered for multiplicity.

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LB0002

BARICITINIB IN JUVENILE IDIOPATHIC ARTHRITIS: A PHASE 3, DOUBLE-BLIND, PLACEBO-CONTROLLED, WITHDRAWAL, EFFICACY AND SAFETY STUDY

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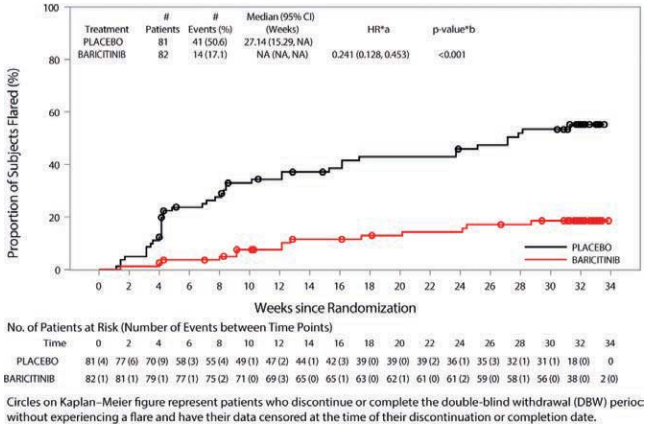
Background: Baricitinib is a JAK1/2 selective inhibitor approved for the treatment of rheumatoid arthritis. Juvenile idiopathic arthritis (JIA) is a group of diseases characterized by immune mediated chronic arthritis which often requires treatment with conventional synthetic or biologic disease-modifying antirheumatic drugs (cs or b-DMARDs).

Objectives: To investigate baricitinib efficacy and safety in pediatric patients with JIA and an inadequate response to cs or b-DMARDs.

Methods: This Phase 3 multicenter, double-blind, withdrawal, efficacy, and safety study, enrolled patients (pts) age 2 to <18 years with extended oligo- or poly-articular JIA, ERA, or JPsA, per ILAR criteria, and an inadequate response to ≥1 cs and/or b-DMARDs (NCT03773978). There were 3 periods: a 2-week (wk) pharmacokinetic/safety assessment (PKS), a 12-wk open-label lead-in (OLLI), and an up-to 32-wk double-blind withdrawal (DBW). Dosage and safety were confirmed in the PKS and then pts, including those from the PKS, enrolled in the OLLI, receiving age-based, oral, once daily doses of baricitinib. Pts with a JIA-ACR30 response at wk12, end of OLLI, entered the DBW to be randomized 1:1 to continued baricitinib or newly started placebo (PBO) and remained until flare or up to wk32. Primary endpoint was time to flare during the DBW. Secondary endpoints included JIA-ACR30/50/70/90 response rates at wk12, and proportion of pts with a flare during the DBW. Survival curves were estimated using the Kaplan-Meier method.

Results: Of 220 pts enrolled, 29 participated in the PKS, 219 entered the OLLI, and 163 entered the DBW. The JIA-ACR30/50/70/90 response at wk12 was 76.3%/63.5%/46.1%/20.1%, respectively. During the DBW, time of flare was significantly shorter with PBO vs baricitinib (hazard ratio 0.24 [95% CI 0.13,0.45], p<0.001; Figure 1). The proportion of pts with a flare during the DBW was significantly lower for baricitinib vs PBO (14 (17.1%) vs. 41 (50.6%), p<0.001). In the PKS and OLLI periods, 126 (57.3%) pts reported ≥1 treatment emergent adverse event (TEAE), while 6 (2.7%) reported ≥1 serious adverse event (SAE); Table 1. In the DBW, 38 (46.9%) and 54 (65.9%) pts reported ≥1 TEAE for PBO and baricitinib, respectively, whereas those with ≥1 SAE were 3 (3.7%) and 4 (4.9%). The mean wks of exposure was higher in the baricitinib vs PBO group during DBW (26.34 vs 18.91) due to study design. There were no deaths, cardiovascular events or uveitis and 1 case of herpes zoster.



Circles on Kaplan–Meier figure represent patients who discontinue or complete the double-blind withdrawal (DBW) period without experiencing a flare and have their data censored at the time of their discontinuation or completion date.

Table 1. Safety data

Events, N (%)		PKS and OLLI (N=220)	Events, N (%)	DBW Placebo (N=81)	DBW Baricitinib (N=82)
Discontinuations due to AEs		2 (0.9)		2 (2.5)	1 (1.2)
TEAEs		126 (57.3)		38 (46.9)	54 (65.9)
most common TEAEs	Nasopharyngitis	19 (8.6)	URTI	1 (1.2)	9 (11.0)
	Headache	14 (6.4)	Headache	3 (3.7)	9 (11.0)
	Arthralgia	12 (5.5)	Nasopharyngitis	3 (3.7)	6 (7.3)
	URTI	11 (5.0)	Arthralgia	3 (3.7)	6 (7.3)
	Nausea	11 (5.0)	Oropharyngeal pain	1 (1.2)	5 (6.1)
SAEs		6 (2.7)		3 (3.7)	4 (4.9)
All reported SAEs	Arthralgia	1 (0.5)	COVID-19	0	1 (1.2)
	Joint Destruction	1 (0.5)	Gastroenteritis	0	1 (1.2)
	Joint Effusion	1 (0.5)	Headache	0	1 (1.2)
	JIA	1 (0.5)	Pulmonary Embolism	0	1 (1.2)
	Musculoskeletal Chest Pain	1 (0.5)	Bronchospasm	1 (1.2)	0
	Decreased Appetite	1 (0.5)	JIA	1 (1.2)	0
			Suicide Attempt	1 (1.2)	0
Potential opportunistic infections		2 (0.9)		1 (1.2)	1 (1.2)
	Herpes virus	1 (0.5)	Herpes virus	1 (1.2)	0
	Herpes zoster	1 (0.5)	Candida	0	1 (1.2)

URTI= Upper Respiratory Tract Infection

Conclusion: Baricitinib significantly reduced time to and frequency of JIA flares in pts with JIA versus PBO, and improved JIA-ACR scores in the majority of pts within 12wks. Safety findings were consistent with the known safety profile in adult rheumatoid arthritis indications. These findings support baricitinib as a treatment for signs and symptoms of JIA with an inadequate response to cs or b-DMARDs.

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LB0003

WITHDRAWING METHOTREXATE AFTER BOTH VERSUS ONLY SECOND DOSE OF THE CHADOX1 NCOV-19 VACCINE IN PATIENTS WITH AUTOIMMUNE INFLAMMATORY ARTHRITIS: TWO INDEPENDENT RANDOMIZED CONTROLLED TRIALS (MIVAC I AND II)

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Background: Pausing methotrexate (MTX) for two to four weeks, improved immunogenicity of influenza vaccination in patients with rheumatoid arthritis (RA), albeit a risk of disease flare (1). This guided the framing of guidelines on MTX withdrawal for COVID-19 vaccination (2). However, evidence for MTX withdrawal for COVID-19 vaccination is limited to observational studies only.

Objectives: To compare the efficacy and safety of holding MTX after each (MIVAC 1) and only after the second dose (MIVAC II) of the ChAdOx1 vaccine versus continuation of MTX in two randomized controlled trials (RCTs).

Methods: Two single centre, investigator-blinded, RCTs were conducted in patients with RA or Psoriatic arthritis (PsA) on stable doses of MTX without prior COVID-19 (CTRI reg. no. MIVAC I: CTRI/2021/07/03463 & MIVAC II: CTRI/2021/07/035307). In MIVAC I, unvaccinated patients were randomised (1:1) to hold or continue MTX for two weeks after each dose of the vaccine. MIVAC II included patients who had continued MTX during the first dose of ChAdOx1 and were randomised (1:1) to hold or continue MTX for 2 weeks after the second vaccine dose. The primary outcome for both the trials was the anti-Receptor Binding Domain (RBD) antibody titres measured four weeks after the second vaccine dose (per protocol analysis). Secondary outcome was the flare rate, defined as an increase in disease activity scores (DAS28/cDAPSA) or physician intent to hike DMARDs.

Results: 250 patients were randomized for MIVAC 1 and 178 for MIVAC II and after due exclusions, 158 and 157 were eligible for analysis respectively (Figure 1). In MIVAC I, median anti-RBD titres were significantly high in the MTX hold group [2484 (1050-4388) versus 1147(433-2360), p=0.001] but the flare rate was higher in the hold group [20 (25%) versus 6(8%) p=0.005] compared to continue group. In MIVAC II median anti-RBD titres were significantly high for the MTX hold group [2553 (1792-4823) versus 990 (356-2252), p=0.001] when compared to continue group but there was no difference in the flare rate between the groups [9(11.8%) and 4(7.9%), p=0.15] (Table 1). Since both were parallel studies in similar population, MTX hold arms across both the trials were compared for anti-RBD titres and flare. There was no difference in the anti-RBD titres [p=0.2] between the groups. In MIVAC I, 29(36.25%) patients had reported flare (19 in either first or second dose, 10 for both doses) when compared to MIVAC II where only 9(11.84%) patients had reported flare after the second dose (P <0.001).

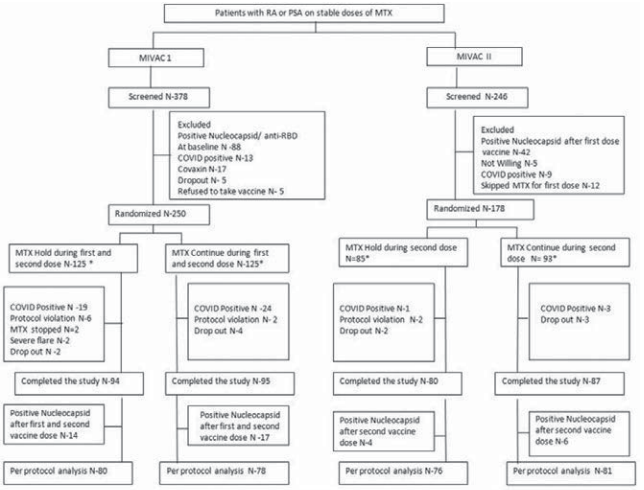

Figure 1 .Trial design *the interval between two ChadOx1 vaccines were 3 months

Conclusion: Holding MTX after both the doses or only after the second dose of ChAdOx1 yields higher anti-RBD antibody titres as compared to continuing MTX. Comparing across the trials, holding MTX only after the second dose appears to be non-inferior to holding MTX after both doses of the vaccine with a lesser risk of flare.

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Table 1. Baseline demographics and key results

	MIVAC I			MIVAC II		
	MTX Hold	MTX Continue	P	MTX Hold	MTX Continue	P value
Variable	N=80	N=78	value	N=76	N=81	
Age†	48 (38-53.3)	49 (39-59)	0.19	53 (42.3-59)	53(50-62)	0.14
Female (%) ‡	73 (91.3)	75 (96.2)	0.33	65 (85.5)	70 (86.4)	>0.99
RA (%) ‡	69(86.3)	69 (93.2)		70 (85.6)	80 (87.7)	
PsA (%) ‡	11(13.8)	6 (8.1)	0.31	6 (7.9)	1 (1.2)	0.057
DAS28†	2.7 (2.4-3.2)	2.6 (2-3.3)	0.6	2.7(2.3-3.4)	2.8 (2.1-3.5)	0.78
cDAPSA †	2(3-4.5)	2.5(1.3-3.8)	0.46	3(2.8-3)	3	0.15
Prednisolone (%) ‡	29 (36.3)	23(31.1)	0.4	24(31.6)	26 (32.1)	>0.99
MTX mg/week†	17.5 (10-25)	15 (10-20)	0.057	15 (9.4-25)	17.5(7.5-25)	0.92
Anti- RBD antibody titres post second dose (IU/mL) †	2484 (1050-4388.8)	1147.5 (433.5-2360.3)	**<0.001**	2553.5 (1792.5-4823.8)	990.5 (356.1-2252.5)	**<0.001**
Flare (N%) ‡						
Post first dose	20 (25)	6 (8)	**0.005**	NA	NA	
Post second dose	19 (23.8)	10(13.3)	0.1	9 (11.8)	4 (7.9)	0.15

All analysis as per protocol population. †Median (interquartile range): Mann Whitney U test. ‡ N (%): Fisher Exact test. Bolded if p<0.05.

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LB0004

EFFICACY AND SAFETY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE, ALLOSTERIC TYK2 INHIBITOR, IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background: Tyrosine kinase 2 (TYK2) mediates signaling of Type I interferons, IL-23, and IL-12, key cytokines involved in lupus pathogenesis. Deucravacitinib (DEUC) is an oral, selective, allosteric TYK2 inhibitor with a unique mechanism of action, distinct from Janus kinase (JAK) 1/2/3 inhibitors, and has shown efficacy in psoriasis and psoriatic arthritis.

Objectives: Assess efficacy and safety of DEUC in patients with active systemic lupus erythematosus (SLE).

Methods: This was a 48-week (wk), randomized, double-blind, placebo (PBO)-controlled, phase 2 trial (NCT03252587). Eligible patients met SLICC criteria, were seropositive (ANA/anti-dsDNA/anti-Sm), and had a SLEDAI-2K score ≥6 and ≥1 BILAG index A or >2 BILAG B manifestations from the musculoskeletal or mucocutaneous domain. Patients on standard background medications were randomized 1:1:1:1 to PBO or DEUC (3 mg BID, 6 mg BID, 12 mg QD). Oral corticosteroid tapering to 7.5 mg/day was required from wks 8-20; further tapering was optional from wks 32-40. The primary endpoint was the proportion of patients achieving SRI(4) at wk 32. Key secondary endpoints at wk 48 included SRI(4), BICLA, LLDAS, CLASI-50, and change from baseline in active (tender and swollen) joint count.

Results: A total of 363 patients were randomized, with baseline demographic and disease characteristics similar across treatment groups. Of randomized patients, 275 (76%) completed 48 wks of treatment. The primary endpoint at wk 32 was met, with significantly greater proportion of patients in DEUC 3 mg BID and 6 mg BID groups vs PBO achieving SRI(4) responses (PBO: 34.4%; DEUC 3 mg BID: 58.2%, *P*=0.0006; DEUC 6 mg BID: 49.5%, *P*=0.021; DEUC 12 mg QD: 44.9%, *P*=0.078). SRI(4) response was sustained across all DEUC groups up to 48 wks (Figure 1). At wk 48, the DEUC 3 mg BID group demonstrated statistical significance in BICLA, LLDAS, CLASI-50, and active joint count, and the two other DEUC groups demonstrated clinically meaningful differences vs PBO (Figure 1). Rates of adverse events (AEs), serious AEs, and AEs of interest were similar between DEUC and PBO groups (Table 1). Most common AEs (≥10%) with DEUC were upper respiratory tract infection, nasopharyngitis, headache, and urinary tract infection. No deaths, major cardiac events, thrombotic events, systemic opportunistic infections, or active tuberculosis occurred. Malignancies were rare with similar rates across all groups. No meaningful abnormalities in mean levels of hematology and chemistry laboratory parameters were observed.

Figure. Summary of key efficacy results

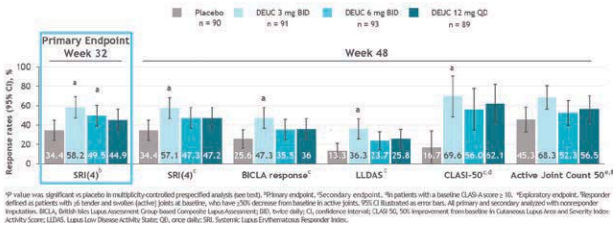

Table 1. Summary of Adverse Events Through Week 48

AE, n[a] (%)	Placebo n = 90	DEUC 3 mg BID n = 91	DEUC 6 mg BID n = 93	DEUC 12 mg QD n = 89
AE	79 (87.8)	85 (93.4)	81 (87.1)	75 (84.3)
SAE	11 (12.2)	7 (7.7)	8 (8.6)	7 (7.9)
AEs leading to treatment discontinuation	3 (3.3)	8 (8.8)	6 (6.5)	11 (12.4)
Skin-related AEs[b]	12 (13.3)	15 (16.5)	32 (34.4)	30 (33.7)
Overall infections/ infestations	48 (53.3)	60 (65.9)	60 (64.5)	45 (50.6)
Serious infections/ infestations	1 (1.1)	1 (1.1)	2 (2.2)	1 (1.1)
Infections of interest				
Tuberculosis	0	0	0	0
Herpes zoster[c]	4 (4.4)	3 (3.3)	3 (3.2)	2 (2.2)
Influenza	1 (1.1)	3 (3.3)	1 (1.1)	3 (3.4)
COVID-19	3 (3.3)	3 (3.3)	5 (5.4)	3 (3.4)
Malignancy events	1 (1.1)[d]	1 (1.1)[e]	0	1 (1.1)[f]
MACE	0	0	0	0
Thrombotic events	0	0	0	0

[a]n is the number of patients who experienced an event. [b]Includes (≤8.6% in any arm) acne, rash, dermatitis acneiform, pruritus, skin lesion, urticaria. [c]Includes herpes zoster, herpes ophthalmic, genital herpes zoster. [d]Basal cell carcinoma. [e]Breast carcinoma. [f]Vaginal squamous cell carcinoma. AE, adverse event; COVID-19, coronavirus disease 2019; DEUC, deucravacitinib; MACE, major adverse cardiac events; SAE, serious adverse event.

Conclusion: In patients with active SLE, DEUC showed statistically significant and sustained clinical efficacy in SRI(4), improvement across multiple composite and organ-specific measures up to 48 wks, and was well tolerated. DEUC shows promise as a novel therapy for SLE and warrants further investigation in phase 3 trials.

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LB0005

ORELABRUTINIB, AN IRREVERSIBLE INHIBITOR OF BRUTON'S TYROSINE KINASE (BTK), FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE IB/IIA DOSE-FINDING STUDY

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Background: Orelabrutinib is an oral, highly-selective, irreversible inhibitor of Bruton's tyrosine kinase (BTK). Orelabrutinib has been approved for the treatment of B cell malignancies in China. Two distinct lupus animal models showed significant efficacy of orelabrutinib in reducing disease activity, which supported the clinical development of orelabrutinib in Systemic Lupus Erythematosus (SLE).
Objectives: This phase Ib/IIa, randomized, double-blind, placebo-controlled, dose-finding study aimed to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), preliminary efficacy and biomarkers of orelabrutinib in patients with mild to moderate SLE who received standard of care (SoC) therapy.
Methods: Patients diagnosed with SLE by the ACR classification criteria for ≥ 6 months, who had a SLEDAI-2K score ≥5 at screening, and were autoantibody-positive, were randomized 1:1:1:1 to receive oral orelabrutinib at 50mg, 80mg, 100mg or placebo once daily for 12 weeks, respectively.
Results: This study randomized 60 patients with 55 patients who completed 12-week treatment. Age at baseline was 33.7±9.8 years and 96.7% were female. Baseline disease characteristics were generally balanced across treatment groups. Adverse events (AEs) were reported in 80%, 93.3% and 100% of orelabrutinib treated patients at doses of 50mg, 80mg and 100mg QD respectively versus 85.5% in placebo group. AEs were mostly mild or moderate. Treatment-related SAEs were reported in 3 patients treated with orelabrutinib, only 1 of which was grade 3. No deaths were reported. The plasma exposure of orelabrutinib (AUC and Cmax) was proportionally increased with doses. Nearly complete BTK occupancy was achieved at all dose levels, and the occupancy lasted for 24 hours without any decrease compared to that at 4 hour post-dosing. In all evaluable patients, the SLE Response Index (SRI)-4 response rates at week 12 were 50.0%, 61.5% and 64.3% in patients treated with orelabrutinib at 50mg (n=14), 80mg (n=13) and 100mg (n=14) respectively, compared with 35.7% in patients treated with placebo (n=14), which indicated the trend of dose-dependent improvement. Among the subgroup of patients with SLEDAI-2K≥8 at screening, SRI-4 response occurred in 70%, 70% and 66.7% of patients treated with orelabrutinib at 50mg (n=10), 80mg (n=10) and 100mg (n=9), respectively, compared with 30% who received placebo (n=10). Trends of reduced proteinuria, anti-dsDNA and IgG, total B cells and increased complements C4 were also observed following orelabrutinib treatment.
Conclusion: Orelabrutinib was generally safe and well tolerated in patients with SLE. Preliminary results also suggested encouraging efficacy which supports further development of orelabrutinib in larger and longer trials for SLE.

Table 1. Efficacy results at week 12.

	Placebo	Orelabrutinib	Orelabrutinib	Orelabrutinib
All Evaluable Patients		**50 mg**	**80 mg**	**100 mg**
N=55	14	14	13	14
SRI-4 response, n (%)	5 (35.7%)	7 (50.0%)	8 (61.5%)	9 (64.3%)
Treatment difference vs. PBO (%)		14.3%	25.8%	28.6%
SLEDAI-2K≥8, N=39	10	10	10	9
SRI-4 response, n (%)	3 (30.0%)	7 (70.0%)	7 (70.0%)	6 (66.7%)
Treatment difference vs. PBO (%)		40.0%	40.0%	36.7%

Note: All evaluable patients at week 12 efficacy data were included in the efficacy analysis.

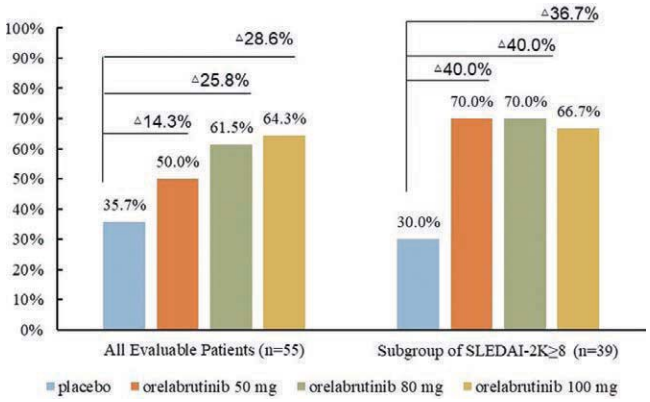

Figure 1. SRI-4 response rates at week 12.

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LB0006

SARILUMAB IN PATIENTS WITH RELAPSING POLYMYALGIA RHEUMATICA: A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL (SAPHYR)

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Background: Interleukin-6 (IL-6) is elevated in patients with active polymyalgia rheumatica (PMR) and is associated with disease activity, relapse and severity. Clinical trials with IL-6 receptor (IL-6R) inhibitors in PMR showed higher remission rates and reduced glucocorticoid (GC) use vs GC alone.[1-4]
Objectives: The SAPHYR study (NCT03600818) assessed the efficacy and safety of sarilumab (SAR), a fully human anti IL-6Rα monoclonal antibody, with a 14 week (wk) GC taper in patients with steroid resistant active PMR who flared on ≥7.5 mg/day prednisone or equivalent.
Methods: Patients were randomized (1:1) to 52 wks of treatment with SAR 200 mg every 2 wks (Q2W) + 14 wk GC tapered regimen (SAR arm) OR placebo Q2W + 52 wk GC tapered regimen (comparator arm). The primary endpoint was the proportion of patients achieving sustained remission at wk 52, defined as disease remission by wk 12, absence of disease flare, CRP normalization from wks 12 to 52 and adherence to the per protocol GC taper from wks 12 to 52.
Results: The study was terminated early due to protracted recruitment timelines during the COVID-19 pandemic, resulting in 118 of the intended 280 patients recruited between Oct 2018 and Jul 2020, and 117 were treated (SAR n=59, comparator n=58). The demographics were balanced; patients were primarily female, Caucasian, and a median age of ~70 years (Table 1). Overall, 78 patients completed the treatment (SAR n=42; comparator n=36). Primary reasons for treatment discontinuation were adverse events (AEs; SAR n=7, comparator n=4) and lack of efficacy (SAR n=4, comparator n=9). Sustained remission rate was significantly higher in the SAR arm vs the comparator arm (28.3% vs 10.3%; P=0.0193). Results of a sensitivity analysis excluding CRP from the sustained remission definition was consistent with the primary analysis (31.7% vs 13.8%; P=0.0280). All sustained remission components favored SAR (Figure 1). Patients in the SAR arm were 44% less likely to have a flare after

achieving clinical remission vs the comparator arm (16.7% vs 29.3%; HR 0.56; 95% CI 0.35–0.90; P=0.0158). The comparator arm required more additional GCs vs the SAR arm, mainly due to PMR flare (median difference in actual and expected cumulative dose 199.5 mg vs 0.0 mg; P=0.0189). The cumulative GC toxicity index scores numerically favored SAR but the difference was not statistically significant. PMR activity scores improved in the SAR arm vs the comparator arm (LS mean -15.57 vs -10.27, nominal P=0.0002). Patient reported outcomes (eg, physical and mental health component scores, disability index, etc) favored SAR (Figure 1). Incidence of treatment-emergent AEs (TEAEs) was numerically higher in the SAR arm vs the comparator arm (94.9% vs 84.5%) and included neutropenia (15.3%) and arthralgia (15.3%) in the SAR arm, and insomnia (15.5%) in the comparator arm. Conversely, the frequency of serious AEs was higher in the comparator arm vs the SAR arm (20.7% vs 13.6%). No deaths were reported.

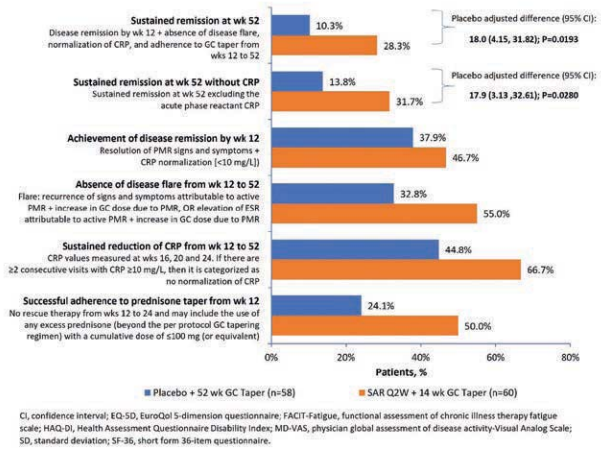
Table 1. Demographics and baseline characteristics

Parameter	SAR + 14 wk GC taper (n=60)	Placebo + 52 wk GC taper (n=58)
Age, median years (range)	69 (51–88)	70 (52–88)
Sex (female), n (%)	45 (75.0)	37 (63.8)
Race, n (%)		
Caucasian	50 (83.3)	48 (82.8)
Asian	1 (1.7)	2 (3.4)
Not reported	9 (15.0)	8 (13.8)
PMR duration (diagnosis date to baseline),* median days (range)	292 (78–3992)	310 (66–2784)
Any prior disease modifying anti rheumatic drugs, n (%)		
Methotrexate	5 (8.3)	10 (17.2)
Leflunomide	2 (3.3)	1 (1.7)
Azathioprine	0	1 (1.7)
Hydroxychloroquine	1 (1.7)	1 (1.7)
Adalimumab	1 (1.7)	0
Tocilizumab	0	1 (1.7)
CRP (mg/L), median (range)	6.8 (0.5–38.2)	5.7 (0.1–62.3)
Erythrocyte sedimentation rate (mm/h), median (range)	25.0 (2.0–115.0)	22.0 (5.0–85.0)

*SAR n = 54; comparator n= 50.

Conclusion: SAR + 14 wk GC taper demonstrated significant efficacy vs the comparator arm in steroid refractory PMR patients, including clinically meaningful improvement in quality of life. Safety was consistent with the known safety profile of SAR.

Figure. Summary of disease remission, disease flare, CRP reduction, and adherence to prednisone taper



CI, confidence interval; EQ-5D, EuroQol 5-dimension questionnaire; FACIT-Fatigue, functional assessment of chronic illness therapy fatigue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; MD-VAS, physician global assessment of disease activity-Visual Analog Scale; SD, standard deviation; SF-36, short form 36-item questionnaire.

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Poster Tours

Challenges in measuring and predicting RMDs

POS0001

CAN SINGLE IMPUTATION TECHNIQUES FOR BASDAI COMPONENTS RELIABLY CALCULATE THE COMPOSITE SCORE IN AXIAL SPONDYLOARTHRITIS PATIENTS?

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Background: In axial spondyloarthritis (axSpA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is a key patient-reported outcome. However, one or more of its components may be missing when recorded in clinical practice.
Objectives: To determine whether an individual patient's BASDAI at a given timepoint can be reliably calculated with different single imputation techniques and to explore the impact of the number of missing components and/or differences between missingness of individual components.
Methods: Real-life data from axSpA patients receiving tumour necrosis factor inhibitors (TNFi) from 13 countries in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were utilized [1]. We studied missingness in BASDAI components based on simulations in a complete dataset, where we applied and expanded the approach of Ramiro et al. [2]. After introducing one or more missing components completely at random, BASDAI was calculated from the available components and with three different single imputation techniques: possible middle value (i.e. 50) of the component and mean and median of the available components. Differences between the observed (original) and calculated scores were assessed and correct classification of patients as having BASDAI<40 mm was additionally evaluated. For the setting with one missing component, differences arising between missing one of components 1-4 versus 5-6 were explored. Finally, the performance of imputations in relation to the values of the original score was investigated.
Results: A total of 19,894 axSpA patients with at least one complete BASDAI registration at any timepoint were included. 59,126 complete BASDAI registrations were utilized for the analyses with a mean BASDAI of 38.5 (standard deviation 25.9). Calculating BASDAI from the available components and imputing with mean or median showed similar levels of agreement (Table 1). When allowing one missing component, >90% had a difference of ≤6.9 mm between the original and calculated scores and >95% were correctly classified as BASDAI<40 (Table 1). However, separate analyses of components 1-4 and 5-6 as a function of the BASDAI score suggested that imputing any one of the first four BASDAI components resulted in a level of agreement <90% for specific BASDAI values while imputing one of the stiffness components 5-6 always reached a level of agreement >90% (Figure 1, upper panels). As expected, it was observed that regardless of the BASDAI component set to missing and the imputation technique used, correct classification of patients as BASDAI<40 was less than 95% for values around the cutoff (Figure 1, lower panels).

Table 1. Level of agreement between the original and calculated BASDAI and correct classification for BASDAI<40 mm

		Level of agreement with Dif≤6.9 mm* (%)	Correct classification for BASDAI<40 mm** (%)
1 missing component	**Available**	93.9	96.9
	Value 50	73.9	96.3
	Mean	94.2	96.8
	Median	93.1	96.8
2 missing components	**Available**	83.7	94.8
	Value 50	40.7	92.8
	Mean	83.5	94.8
	Median	82.8	94.7
3 missing components	**Available**	71.9	92.6
	Value 50	28.1	87.3
	Mean	72.2	92.6
	Median	69.7	92.2

* The levels of agreement with a difference (Dif) of ≤6.9 mm between the original and calculated scores were based on the half of the smallest detectable change. Agreement of >90% was considered as acceptable. ** Correct classification of >95% was considered as acceptable.

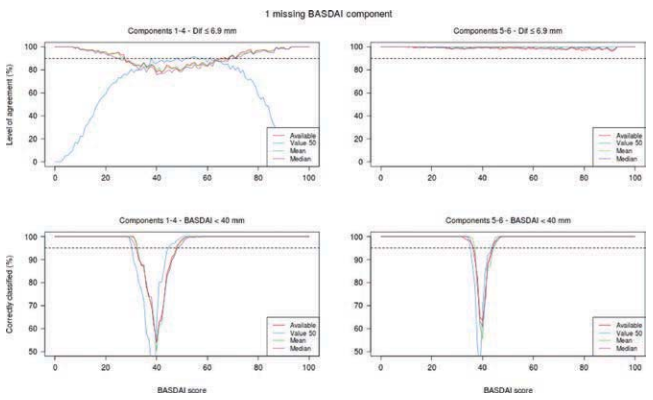

Figure 1. Level of agreement between the original and calculated BASDAI and correct classification for BASDAI<40 mm as a function of the original score

Conclusion: BASDAI calculation with available components gave similar results to single imputation of missing components with mean or median. Only when missing one of BASDAI components 5 or 6, single imputation techniques can reliably calculate individual BASDAI scores. However, missing any single component value results in misclassification of patients with original BASDAI scores close to 40.

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Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB, Grant/research support from: Abbvie, BMS, Merck, Celgene, Novartis, Simon Horskjær Rasmussen Grant/research support from: Novartis, Johan K Wallman Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, Bente Glintborg Grant/research support from: Pfizer, Abbvie, BMS, Anne Gitte Loft Speakers bureau: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Karel Pavelka Speakers bureau: Pfizer, MSD, BMS, UCB, Amgen, Egis, Roche, AbbVie, Consultant of: Pfizer, MSD, BMS, UCB, Amgen, Egis, Roche, AbbVie, Jakub Zavada Speakers bureau: Abbvie, Elli-Lilly, Sandoz, Novartis, Egis, UCB, Consultant of: Abbvie, Elli-Lilly, Sandoz, Novartis, Egis, UCB, Merih Birlik: None declared, Ayten Yazici Grant/research support from: Roche, Brigitte Michelsen Grant/research support from: Novartis, Eirik kristianslund: None declared, Adrian Ciurea Speakers bureau: AbbVie, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Consultant of: AbbVie, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Michael J. Nissen Speakers bureau: AbbVie, Eli Lilly, Janssens, Novartis, Pfizer, Consultant of: AbbVie, Eli Lilly, Janssens, Novartis, Pfizer, Ana Maria Rodrigues Speakers bureau: Abbvie, Amgen, Consultant of: Abbvie, Amgen, Grant/research support from: Novartis, Pfizer, Amgen, Maria Jose Santos Speakers bureau: Abbvie, AstraZeneca, Lilly, Novartis, Pfizer, Gary Macfarlane Grant/research support from: GSK, Anna-Mari Hokkanen Grant/research support from: MSD, Heikki Relas Speakers bureau: Abbvie, Celgene, Pfizer, UCB, Viatris, Consultant of: Abbvie, Celgene, Pfizer, UCB, Viatris, Catalin Codreanu Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Ewopharma, Lilly, Novartis, Pfizer, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Ewopharma, Lilly, Novartis, Pfizer, Corina Mogosan: None declared, Ziga Rotar Speakers bureau: Abbvie, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen, Consultant of: Abbvie, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen, Matija Tomsic Speakers bureau: Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Medis, MSD, Novartis, Pfizer, Sanofi, Sandoz-Lek, Consultant of: Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Medis, MSD, Novartis, Pfizer, Sanofi, Sandoz-Lek, Björn Gudbjornsson Speakers bureau: Amgen, Novartis, Consultant of: Amgen, Novartis, Arni Jon Geirsson: None declared, Pasoon Hellamand Grant/research support from: Novartis, Marleen G.H. van de Sande Speakers bureau: Eli Lilly, Novartis, UCB, Janssen, Abbvie, Consultant of: Eli Lilly, Novartis, UCB, Janssen, Abbvie, Grant/research support from: Eli Lilly, Novartis, UCB, Janssen, Abbvie, Isabel Castrejon: None declared, Manuel Pombo-Suarez Consultant of: Abbvie, MSD, Roche, Bruno Frediani: None declared, Florenzo Iannone Speakers bureau: Abbvie, Amgen, AstraZeneca, BMS, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Consultant of: Abbvie, Amgen, AstraZeneca, BMS, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Lykke Midtbøll Ørnbjerg Grant/research support from: Novartis

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POS0002

IS THE RHEUMATOID ARTHRITIS IMPACT OF DISEASE SCORE (RAID) AN INFORMATIVE INSTRUMENT FOR OTHER INFLAMMATORY RHEUMATIC DISEASES?

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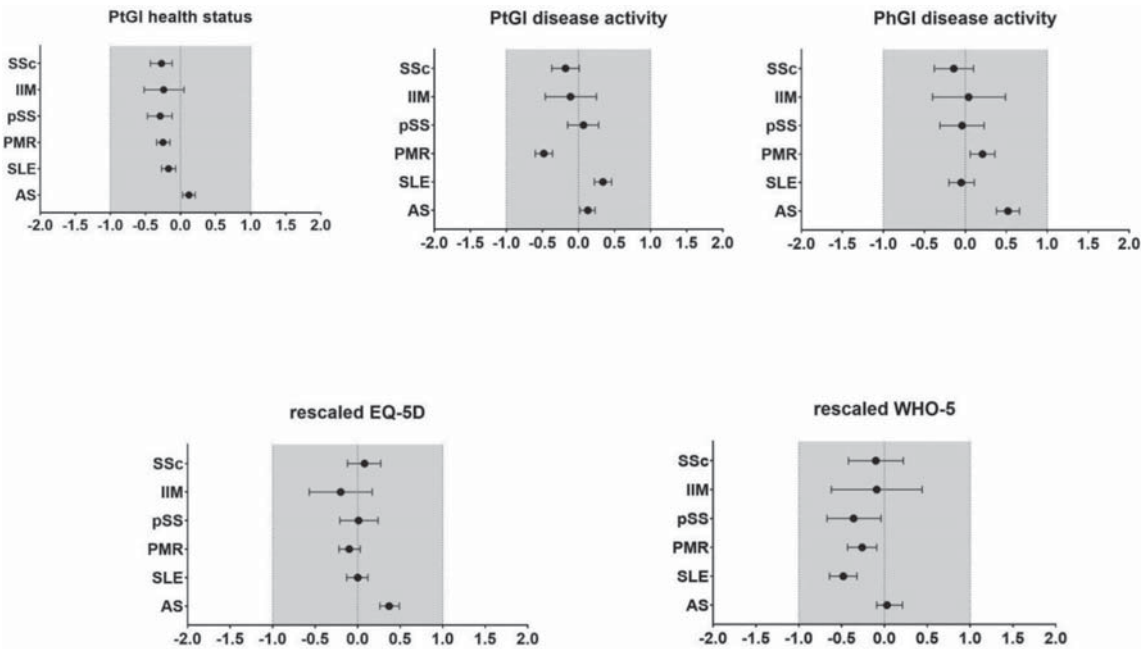
Background: The rheumatoid arthritis impact of disease score (RAID) is a patient-reported outcome measure to evaluate the impact of rheumatoid arthritis (RA) on patients' quality of life (1). While an adapted instrument has been developed for psoriatic arthritis (2), there are no comparable instruments for other inflammatory rheumatic diseases. Since the RAID includes generic questions on pain, functional capacity, fatigue, physical and emotional well-being, sleep disturbances and coping, it could be an informative instrument beyond RA.

Objectives: To analyse the performance of the RAID in ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), polymyalgia rheumatica (PMR), primary Sjögren's syndrome (pSS), idiopathic inflammatory myositis (IIM), and systemic sclerosis (SSc) compared to RA.

Methods: From 2015 to 2019, a total of 12,398 patients reported the RAID in the National Database of the German Collaborative Arthritis Centres. We calculated the age- and sex-adjusted partial correlation (0.3-0.5 weak, 0.5-0.7 moderate, > 0.7 strong correlation) between the RAID score and five other patient- or physician-reported outcomes, namely patient global (PtGl) health status, PtGl disease activity, physician global (PhGl) disease activity, the World Health Organisation Well-Being Index (WHO-5) and the EuroQoL-5 Dimensions (EQ-5D). Furthermore, for each of the diagnoses the mean difference between the RAID and the other outcomes was compared with the respective differences for RA. The EQ-5D and WHO-5 were rescaled to match the scale of the



Linear regression model: The dependent variable is the difference between RAID score and five respective outcomes. Independent variables were sex, age and diagnosis with RA as the referent category. An effect of a diagnosis was defined as clinically relevant if the mean change of difference was at least one unit.
Abbr.: PtGl, Patient Global; PhGl, Physician Global; EuroQoL-5 Dimensions (EQ-5D); World Health Organisation Well-Being Index (WHO-5)

Figure 1.

Table 1. Characteristics and patient- and physician-reported outcomes in patients with inflammatory rheumatic diseases.

	RA	AS	SLE	PMR	pSS	IIM	SSc
Number of cases	7826	1532	1142	1105	301	106	386
Female (%)	74	42	89	64	89	58	76
Age, in years (mean±SD)	63±14	51±14	47±15	73±8	53±16	58±14	58±14
Disease duration, in years (mean±SD)	13±11	18±13	15±10	5±6	12±9	11±8	12±10
RAID (mean±SD)	**3.6±2.3**	**4.0±2.3**	**3.0±2.4**	**3.2±2.3**	**3.4±2.4**	**3.5±2.5**	**3.8±2.3**
PtGl health status (mean±SD)	4.2±2.3	4.4±2.2	3.6±2.4	4.1±2.3	4.1±2.3	4.2±2.5	4.6±2.1
PtGl disease activity (mean±SD)	3.7±2.4	4.0±2.4	2.7±2.5	3.8±2.7	3.5±2.6	3.7±2.5	4.1±2.3
PhGl disease activity (mean±SD)	1.8±1.9	2.2±1.9	1.6±1.3	1.0±1.4	1.8±1.3	1.8±1.6	2.2±1.6
EQ-5D (mean±SD)	0.8±0.2	0.8±0.2	0.8±0.2	0.8±0.2	0.8±0.2	0.8±0.2	0.8±0.2
WHO-5 (mean±SD)	57±25	53±23	58±25	56±26	57±25	60±26	53±24

SD, Standard Deviation; PtGl, Patient Global; PhGl, Physician Global; EuroQoL-5 Dimensions (EQ-5D); World Health Organisation Well-Being Index (WHO-5)

RAID (range 0-10). General linear regression was used to assess the age- and sex-adjusted effect of each diagnosis on the difference between the RAID and the five other scores with RA as the referent diagnosis. We defined the effect of a diagnosis as clinically relevant if the mean change of difference was at least one unit.

Results: The mean RAID score in RA (3.6) was lower than in AS (4.0) and SSc (3.8) and higher than in SLE, PMR, pSS or IIM (Table 1). Across all diagnoses, the RAID correlated strongly with PtGl health status (0.72 to 0.83), moderately to strongly with PtGl disease activity (0.55 to 0.78) and WHO-5 (0.67 to 0.83), moderately with the EQ-5D (0.61 to 0.68), and weakly with PhGl disease activity (0.25 to 0.41). Small mean differences were found between the RAID and either PtGl disease activity (0 to -0.6), PtGl health status (-0.4 to -0.9) or WHO-5 (-0.7 to -1.3). A higher deviation was observed for EQ-5D (1.1 to 1.7) and PhGl disease activity (1.4 to 2.2). However, the discrepancies between the five outcomes and the RAID turned out to be similar across all diagnoses and, more importantly, comparable to RA. Linear regression revealed no clinically relevant effect of any of the diagnoses on the difference between RAID and the other outcomes (Figure 1).

Conclusion: The RAID score performed comparably well across all diagnoses investigated. These findings support the use of the RAID for measuring the impact of disease not only in RA, but also in AS, SLE, PMR, pSS, IIM and SSc.

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POS0003 DEVELOPMENT AND VALIDATION OF A DISEASE SPECIFIC PATIENT REPORTED OUTCOME FOR GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is caused by inflammation of the blood vessels of the head and neck; patients can present with cranial, ocular or large vessel vasculitis involvement. Treatment is with glucocorticoids, steroid sparing agents and biologics to control inflammation and protect sight.

Objectives: The aim of this study was to produce a validated disease specific PROM for patients with GCA, to capture the impact of GCA and its treatment on health-related quality of life.

Methods: Patients with clinician- confirmed GCA from the UK, either diagnosed in the last three years or with a flare in the last year, were included in the survey. A longlist of 40 candidate questionnaire items, each with a 5-point Likert scale, had previously been developed, based on a qualitative study with patients from the UK and Australia [1]. In this cross-sectional survey, patients completed the 40-item draft GCA-PROM alongside EQ5D-5L, CAT-PRO5 and self-report of GCA disease activity. Rasch and factor analysis were used in an iterative manner to determine the underlying construct validity of the new PROM. Items were fitted to the Rasch model to determine its construct validity, reliability, unidimensionality and statistical sufficiency of the total score from the scale. Factor analysis was used to establishing factor structure. Item reduction decisions were be based on clinical importance, lack of fit to the Rasch model, and redundancy detected during principal component analysis. External validity was tested by comparing the scores of the newly validated GCA-PROM (i) in participants who self-identify as having 'active disease' versus patients 'in remission' (known groups validity) (ii) with scores derived from EQ5D-5L and CAT-PRO5 (convergent validity).

Results: The survey included 428 patients; 327 (76%) cranial GCA, 114 (26.6%) large vessel vasculitis and 142 (33.2%) ocular involvement. 285 (67%) of participants were female with a mean age (SD) of 74.2 (7.2). 167 (39%) temporal artery biopsies and 177 (41.4%) temporal artery ultrasounds, and 51 (11.9%) Positron Emission Tomography and Computed Tomography (PET-CT)s were reported as positive. 108 (25%) received second-line immunosuppressants, and 34 (7.9%) anti-IL6 therapy. Active disease was reported in 197 (46%). Four factors (domains) were identified after deletion of 10 redundant items: Acute symptoms (8 items), Activities of daily living (7 items), Psychological (7 items) and Participation (8 items). The four domains were analysed as 'super-items' and shown to fit the Rasch model. The overall scale had an adequate fit to the Rasch model: X^2 = 25.219, DF=24, p=0.394 including reliability PSI=0.828. The raw-to-linear transformation scale was calibrated to enable parametric analyses if desired. Each domain was shown to have known-groups validity (p<0.001 patients reporting active versus inactive disease) and correlation with EQ5D-5L and CAT-PRO5 (Rs) ranging between 0.4.42 and 0.778.

Conclusion: The GCA-PROM is a new patient reported outcome measure for patients with GCA which demonstrates good internal and external validity.

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POS0004 WHAT DOES WORSENING IN DAPSA DISEASE ACTIVITY CATEGORIES MEAN FOR PATIENTS WITH PSORIATIC ARTHRITIS? AN ANALYSIS OF 222 PATIENTS

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Background: In psoriatic arthritis (PsA), disease activity states have been defined using the DAPSA (Disease Activity index for Psoriatic Arthritis) score (1). The disease activity states have been validated using structural progression as the gold standard (2). However, the worsening in DAPSA states has not been compared to the patient's perspective.
Objectives: To assess the association between a worsening in disease activity (i.e., change in DAPSA disease activity category) versus the patient's judgement of disease worsening.
Methods: ReFlap (NCT03119805) was a longitudinal study in 14 countries of consecutive adult patients with definite PsA and more than 2 years of disease duration. Patients were seen twice in the context of usual care, around 4 months apart (3). Worsening in disease activity between the 2 visits was defined as a transition to a more active disease category, based on the DAPSA categories [(remission, low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA)] (1).This change was compared to (a) patient perceived-flares collected according to a patient-reported question: "At this time, are you having a flare of your psoriatic arthritis, if this means the symptoms are worse than usual?"; and (b) a worsening according to the MCID (Minimal Clinical Important Difference) question. The agreement between the definitions of worsening were calculated by frequency, Cohen's kappa and prevalence adjusted bias adjusted kappa (PABAK). There was no imputation of missing data.
Results: Overall, 222 patients were analyzed: 127 (58.8%) were male, aged 53.5±12.3 years and with 10.8±8.3 years of disease duration. Disease activity was moderate: 35.9% had no current psoriasis skin lesions, mean tender joint count (TJC, 0-68) was 3.0±7.5, mean swollen joint count (SJC, 0-66) was 1.6±6.6, and mean DAPSA was 11.5±14.0.
At 4.5±2.2 months follow-up, the proportion of DAPSA worsening was 40.1% [95% confidence interval, 33.9-46.7] (n=89). Most of the changes corresponded to patients going from remission to LDA (N=24, 27.0% of worsened patients) or from LDA to MDA (N=24, 27.0%).
Patient-reported flares were reported in 27.0% [21.6-33.2] (n=60), and MCID worsening was reported in 14.0% [33.9-46.5] (n=31).
Figure 1 shows the distribution of patients with worsening in DAPSA category, versus patient-defined worsening. Of the 89 patients who worsened according to DAPSA categories, 41 (46.1%) had self-perceived flares and 20 (22.5%) had worsening according to MCID. Among patients who worsened in DAPSA category, the mean change in DAPSA was higher in patients with self-perceived flares (increase of 22.2±15.0) than in patients without self-perceived flares (increase of 14.3±12.3). Of 133 patients with no worsening according to DAPSA, 114 (85.7%) had no self-perceived flares and 122 (91.7%) had no MCID worsening. The kappa [95% confidence interval] (PABAK) coefficients between DAPSA and either patient flare or MCID worsening were 0.34 [0.21-0.46] (0.40) and 0.16 [0.05-0.27] (0.28), respectively.

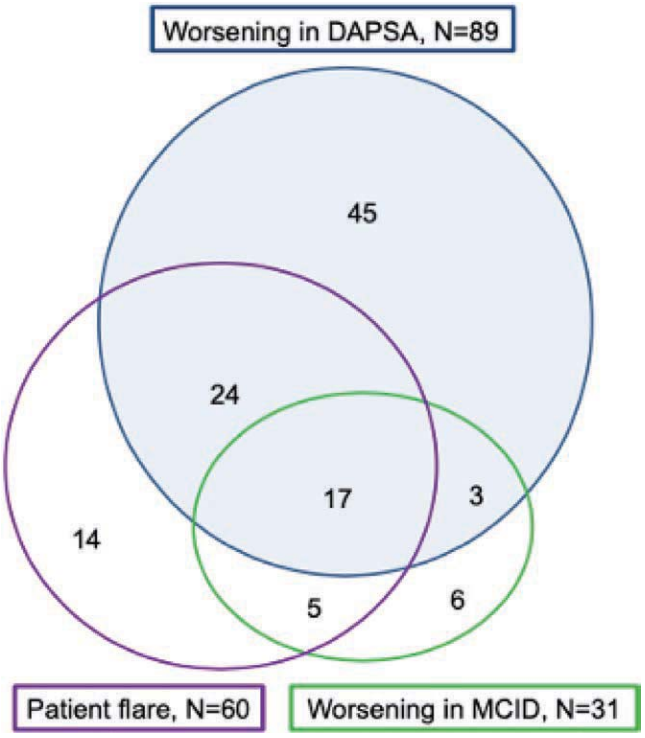

Figure 1. Venn diagram for disease worsening between 2 visits

Conclusion: After 4 months of follow-up, 40.1% patients with long-standing PsA had a change in DAPSA category corresponding to more active disease. Most of these changes reflected transitions from remission to LDA, or from LDA to MDA. Among patients changing DAPSA category, only 46.1% reported themselves in flare at the second visit and only 22.5% reported themselves as worsened by MCID, leading to only fair (for flares) to low (for MCID worsening) agreement between the assessments of worsening. It is important to assess both disease activity, and the patient's perspective of flare.
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POS0005

BASELINE BIOMARKERS PREDICT BETTER RESPONSES TO DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 (TYK2) INHIBITOR, IN A PHASE 2 TRIAL IN PSORIATIC ARTHRITIS

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Background: Deucravacitinib (DEUC) is a novel, oral, selective TYK2 inhibitor with a unique allosteric mechanism of action that has demonstrated efficacy in patients with psoriasis (PsO)[1] and psoriatic arthritis (PsA).[2] TYK2 mediates signalling of select immune cytokines, eg, interleukin (IL) 23, IL-12, and Type I interferons, whereas the related Janus kinases (JAK) 1/2/3 mediate signalling of a wider array of cytokines and mediators involved in inflammatory, developmental, metabolic, and hematopoietic pathways. DEUC reduced inflammatory markers associated with skin and joint manifestations but did not result in laboratory abnormalities associated with inhibition of JAK1/2/3 in a PsA trial.[3]
Objectives: To identify baseline biomarkers that predict response to DEUC in patients with PsA.
Methods: The double-blind Phase 2 trial (NCT03881059) enrolled 203 patients with PsA randomised 1:1:1 to placebo (PBO), DEUC 6 mg once daily (QD), or 12 mg QD.[2] Molecular profiling of baseline serum samples was performed by immunoassays. Clinical response at Week 16 was measured by ≥20% improvement from baseline in American College of Rheumatology Improvement Criteria (ACR 20) and ≥75% improvement from baseline in Psoriasis Area and Severity Index (PASI 75) scores.
Results: Biomarkers of the IL-23/T helper cell type 17 pathway, including IL-17A, IL-17–induced β-defensin 2 (BD2), and IL-19, were associated with higher PASI but not Psoriatic Arthritis Disease Activity Scores overall at baseline. PASI 75 responders in DEUC-treated groups had higher baseline levels of IL-17A compared with nonresponders. In contrast, PASI 75 responders in PBO-treated patients had lower baseline expression of IL-17A, BD2, and IL-19 compared with nonresponders. In patients treated with DEUC 12 mg QD, greater reductions in BD2 were observed in the PASI 75 responder group compared with nonresponder group. When patients were dichotomised by median baseline biomarker level, higher clinical responses in both PASI 75 and ACR 20 were achieved in those with higher baseline overall biomarker levels in the DEUC-treated groups compared with the PBO group. Higher baseline expression of IL-23 biomarkers IL-17A, IL-19, and BD2 enriched ACR 20 response in patients treated with DEUC compared with PBO (OR=5.64, 6.68, and 4.99, respectively). While greater benefit was observed in high-biomarker groups, the low-biomarker populations still manifested clinical responses although not significant (Figure 1).
Conclusion: Patients who had higher expression of IL-23 pathway biomarkers were more likely to benefit from DEUC compared with placebo in skin and joint manifestations of PsA. These results reinforce the value of TYK2 inhibition in patients with IL-23–mediated diseases. The potential value of IL-23-pathway markers in predicting higher responses to DEUC should be further explored in larger trials.
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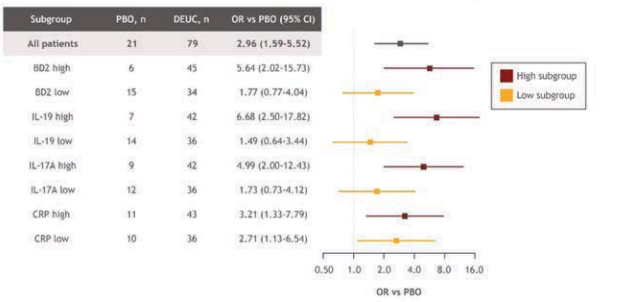
Figure. Odds ratio of ACR 20 response for DEUC (6 mg QD and 12 mg QD combined) vs PBO



ACR 20, American College of Rheumatology 20; BD2, ß-defensin 2; CI, confidence interval; CRP, C-reactive protein; DEUC, deucravacitinib; IL, interleukin; OR, odds ratio; PBO, placebo; QD, once daily.

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POS0006 IDENTIFICATION OF FIBROTIC AND FIBROLYTIC ENDOTYPES IN RHEUMATIC DISEASE COHORTS

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Background: Ankylosing spondylitis (AS), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE) are distinct diseases with common molecular features, such as an imbalance in fibrolysis and fibrosis of connective and calcified tissues. Type III, IV and VI collagens are abundant in connective tissue, and type I, II and X of the skeletal tissue. Blood biomarkers are available to measure fibrolysis (C1M, C2M, C3M, C4M, C6M, C10C) and fibrosis (PRO-C1, PRO-C2, PRO-C3, PRO-C4, PRO-C6) of these collagens.
Objectives: To profile AS, PsA and SLE patients (pts) using blood biomarkers of collagen formation and degradation.
Methods: Baseline serum samples from consenting pts of the AS (NCT02437162/NCT02438787), PsA (NCT0315828), and SLE (NCT02349061) studies were included in the analyses. Healthy donor samples were acquired from Discovery LS. Biomarkers were measured by immunoassays. Biomarker levels were compared by Kruskal-Wallis test. Before hierarchical clustering (Ward.D2), biomarker levels were log-transformed and standardized by median centering and scaling by median absolute deviation (MAD).
Results: When compared with healthy individuals, VICM was elevated in all indications (although markedly less so in SLE pts). The fibrosis marker PRO-C3 was elevated in all indications vs. healthy, while PRO-C4 and PRO-C6 were elevated only in AS and PsA. The fibrolysis markers C3M, C4M and C6M were elevated in all indications. The cartilage fibrosis marker PRO-C2, but not C2M, was elevated in AS and PsA, but not in SLE, ps. The bone fibrosis marker PRO-C1 was at the level of healthy for all. The fibrolysis marker C1M was elevated in all, while elevated C10C was seen only in PsA and SLE, pts (Table 1). Four clusters (C) of blood markers were extracted (Figure 1). C1 was characterized by low biomarker levels (68% of healthy, 1% of PsA, 3% of SLE pts). C2 was described by high levels of C10C and median levels of VICM (20% of healthy, 12% of AS, 19% of PsA, 42% of SLE pts). C3 was described by median biomarker levels (8% of healthy, 67% of AS, 48% of PsA, 46% of SLE pts). C4 had high biomarker levels (4% of healthy, 21% of AS, 31% of PsA, 9% of SLE pts).
Conclusion: Fibrosis and fibrolysis blood biomarkers were significantly elevated in AS, PsA and SLE pts. Subsets of pts from each indication were found in clusters with either low (C1/2), median (C3) or high (C4) levels of fibrosis/fibrolysis biomarkers. These findings may provide a first step towards precision medicine for guiding the use of anti-inflammatory vs. anti-fibrotic treatments in pts with rheumatological disorders.

Fig. Radar plot showing medians of standardized biomarker levels by cluster.

Cluster 1 (C1): Low turnover
Most marker levels below the median (0) of the population

Cluster 2 (C2): Low turnover, with COL10 high and VICM median levels
All marker levels at or below the median, but COL10Neo at +1MAD. VICM is higher than C1.

Cluster 3 (C3): Median turnover
Most marker levels at the median level

Cluster 4 (C4): High turnover
Most marker levels above the median

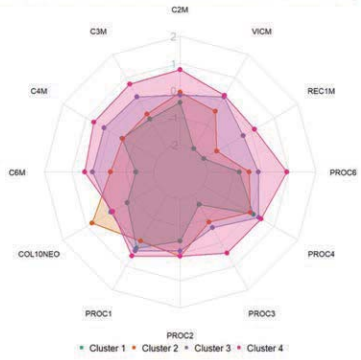

Table. Patient group description and fibrosis/fibrolysis biomarkers levels (ng/ml) in healthy and AS, PsA or SLE pts.

		Healthy	AS	PsA	SLE
	N	77	66	267	97
	Age	45 (32, 54)	41 (30, 49)	46 (37, 54)	41 (32, 49)
	Males, n (%)	38 (49.4)	53 (80.3)	145 (54.3)	9 (9.3)
	White, n (%)	51 (66.2)	47 (71.2)	260 (97.4)	66 (68.0)
Fibrosis	PRO-C1	84.3 (60.9, 116)	100 (62.5, 138)	99.6 (69.4, 139)	74.5 (46.4, 113)
Fibrosis	PRO-C2	19.2 (15.6, 23.0)	24.4 (19.9, 28.7)	22.3 (18.0, 26.6)	21.6 (17.2, 26.2)
Fibrosis	PRO-C3	7.9 (6.1, 9.9)	9.9 (8.2, 12.1)	11.1 (9.1, 14.6)	10.2 (8.6, 12.2)
Fibrosis	PRO-C4	4074 (3645, 4595)	4606 (4053, 5159)	4638 (3633, 5185)	3776 (3274, 4500)
Fibrosis	PRO-C6	6.5 (5.4, 8.3)	7.8 (6.7, 9.2)	8.9 (7.4, 11.3)	7.0 (5.7, 8.8)
Fibrolysis	C1M	23.6 (23.6, 27.9)	95.8 (65.0, 133.1)	83.3 (56.2, 130.3)	33.6 (25.8, 45.5)
Fibrolysis	C2M	0.3 (0.2, 0.4)	0.3 (0.3, 0.4)	0.3 (0.2, 0.4)	0.3 (0.2, 0.4)
Fibrolysis	C3M	10.1 (8.4, 12.0)	16.5 (13.7, 19.2)	15.6 (13.3, 19.9)	12.4 (9.8, 16.1)
Fibrolysis	C4M	29.2 (24.6, 32.9)	41.8 (35.2, 507)	41.8 (33.1, 52.9)	32.6 (26.9, 42.7)
Fibrolysis	C6M	10.1 (7.9, 16.1)	30.6 (24.3, 39.7)	29.9 (23.1, 39.8)	18.0 (14.3, 25.9)
Fibrolysis	C10C	2631 (2383, 3253)	2930 (2549, 3236)	3194 (2792, 3713)	3366 (3076, 3943)
Fibrolysis	VICM	0.7 (0.7, 1.8)	11.3 (5.7, 22.5)	8.8 (4.5, 15.3)	4.2 (2.4, 8.0)

Data as median and IQR. Kruskal-Wallis test: * p<0.05, ** p<0.01, *** p<0.001 and **** p<0.0001 vs Healthy

Disclosure of Interests: Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, Signe Holm Nielsen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, Peder Frederiksen Employee of: Nordic Bioscience A/S, Morten Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, Warner Chen Employee of: Janssen Research & Development, Sheng Gao Employee of: Janssen Research & Development
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POS0007 HLA-DQ2 IS ASSOCIATED WITH ANTI-DRUG ANTIBODY FORMATION TO INFLIXIMAB ACROSS IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Background: Immunogenicity is a leading cause of treatment failure to TNF inhibitors, and also affects drug safety. Variations in HLA class II genes have been suggested to predispose to anti-drug antibody formation (ADA), but characterisation of biologically relevant HLA haplotypes, based on high-resolution genotyping, is lacking.
Objectives: To assess associations between HLA loci and formation of ADA to infliximab across different immune mediated inflammatory diseases.
Methods: Patients with immune mediated inflammatory diseases on infliximab therapy (N=612; 181 spondyloarthritis, 120 rheumatoid arthritis, 72 psoriatic arthritis, 114 ulcerative colitis, 80 Crohn's disease and 45 psoriasis) participating in the Norwegian Drug Monitoring (NOR-DRUM) trials (1, 2) were included in the present analyses. Neutralising ADA were assessed with an automated fluorescence assay at each infusion. Next generation sequencing-based HLA typing was performed. Associations with ADA formation were assessed at locus, allele, haplotype and amino acid level. Peptide binding predictions for infliximab were performed.
Results: ADA were detected in 147 patients (24%). Significant associations were shown between ADA and several HLA loci, whereas conditional analyses indicated *HLA-DQB1* (p=1.4x10-6) as the primary risk locus. Highest risk of ADA formation was seen for patients carrying at least one of the HLA-DQ2 haplotypes; DQB1*02:01~DQA1*05:01 and DQB1*02:02~DQA1*02:01 (OR 3.18, 95% CI 2.15 to 4.69, p=5.9x10-9) (Figure 1). These findings were consistent across diagnoses (Table 1), and remained significant when adjusting for other possible predictors of ADA. Computational predictions indicated that both these HLA-DQ2 haplotypes could strongly bind two peptide motifs (INTVESEDI and VYACEVTHQ) in the infliximab heavy and light chain.

Table 1. HLA-DQ2 carrier frequencies according to the different disease phenotypes and for all diagnosis combined

Diagnosis	HLA-DQ2 carrier-frequency among patients with ADA formation	HLA-DQ2 carrier-frequency among patients without ADA formation	P-value
RA (N=120)	0.316	0.134	0.02
PsA (N=72)	0.55	0.231	0.01
SpA (N=181)	0.364	0.182	0.02
UC (N=114)	0.556	0.264	0.006
CD (N=80)	0.429	0.303	0.33
Ps (N=45)	0.867	0.267	0.0004
All disease phenotypes	0.469	0.217	$5.9x10^{-9}$

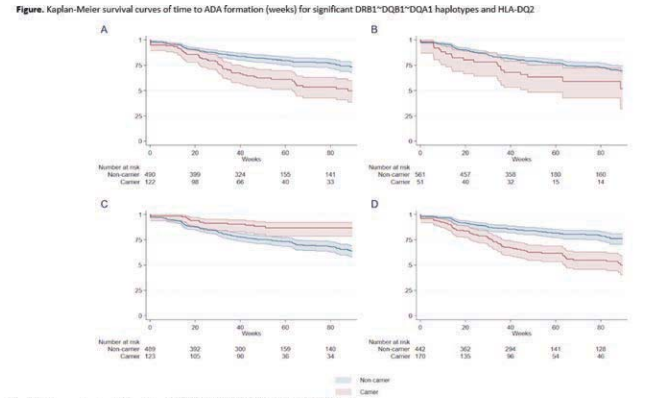

Figure. Kaplan-Meier survival curves of time to ADA formation (weeks) for significant DRB1~DQB1~DQA1 haplotypes and HLA-DQ2

(A) Patients carrying the risk haplotype DRB1*03:01~DQB1*02:01~DQA1*05:01 in red.
(B) Patients carrying the risk haplotype DRB1*07:01~DQB1*02:02~DQA1*02:01 (analysed as DRB1*07:01~DQB1*02:01~DQA1*02:01) in red.
(C) Patients carrying the protective haplotype DRB1*01:01~DQB1*05:01~DQA1*01:01 in red.
(D) Patients carrying at least one of the two HLA-DQ2 risk haplotypes in red.

Conclusion: The risk of ADA to infliximab was three-fold higher in patients carrying the HLA-DQ2 risk haplotypes across diseases. A biological role for the HLA-DQ2 molecules encoded by the two different HLA-DQ2 risk haplotypes in the formation of ADA was further supported by peptide binding predictions. These novel findings provide promise for future incorporation of HLA-DQ2 testing to facilitate personalised treatment decisions.
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POS0008 THE UTILITY OF TRANS-BRONCHIAL LUNG BIOPSIES TO GUIDE THE TREATMENT IN PATIENTS WITH RHEUMATIC INFLAMMATORY DISEASES: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Background: Rheumatic inflammatory disease associated interstitial lung disease (R-ILD) is associated with significant mortality and morbidity[1]. On a patient-to-patient level, imaging which is a cornerstone in diagnosing R-ILD may not be sufficent to determine the underlying cause of the imaging pathology or the degree of reversibilty. Furthermore the precense of co-morbidity and diffential diagnoses such as infections or malignacy needs to be taken into account when dertemining the therapeutic strategy. The role of transbronchial lung biopsies (TBB) in the diagnostic workup of R-ILD is unclear and TBB is not generally recommended[2-4].
Objectives: The study objective was to examine the utility of TBB to guide treatment in a population of patients with R-ILD reffered for bronchoscopy.
Methods: All patients from the Department of Rheumatology, Rigshospitalet, Copenhagen, Denmark referred for a TBB on the suspicion of R-ILD, from 2002 to 2016 were identified.
Patient demographics as well as smoking status, previous lung disease, pulmonary function test, CTD-diagnosis, imaging results and immunomodulatory therapy pre- and post-bronchoscopy were obtained.
Histology findings were used to dichotomize patients into a high inflammatory group or a low inflammatory group. The high inflammation group primarily consisted of non-specific interstitial pneumonia (NSIP), organizing pneumonia (OP), lymphocytic infiltrating pneumonia (LIP) and granulomatous inflammation whereas the low inflammation group primarily consisted of histological findings of usual interstitial pneumonitis (UIP) and biopsies describing fibrosis and/or sparse unspecific inflammation. Therapeutic consequence was defined as intensification of therapy. Differences in treatment intensification were calculated using a binominal logistic regression model. Differences in treatment intensification were calculated using a binominal logistic regression model adjusted for age, gender, smoking status, previous lung disease, diffusion capacity, rheumatologic diagnose, c-reactive protein level prior to TBB. Covariates with P>0.1 were excluded by a stepwise 'backwards' elimination.
Results: 96 patients had TBB performed. Biopsies from 55 patients were categorized as high-inflammatory and 41 as low-inflammatory, respectively. In the high inflammatory group thirty-eight (69%) had their therapy intensified compared to 6 (14%) in the low-inflammatory group (P <0.001). TBB inflammation type was the only covariate that was significantly associated with treatment intensification.
No procedure related complications were registered.
Conclusion: TBB findings can guide treatment strategy in R-ILD patients with suspected activity in the pulmonary disease. TBB appears safe and could be considered as part of the diagnostic workup in patients with inflammatory rheumatic diseases where clinical features, bloodsamples, imaging and/or pulmonary function test do not provide suffcient information to guide the therapeutic strategy.
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POS0009 SUBJECTIVE ASSESSMENT OF PHYSICAL FUNCTION DOES NOT SUFFICIENTLY EXPLAIN VARIANCE OF MEASURED HAND FUNCTION AND GRIP STRENGTH IN ARTHRITIS PATIENTS AND NON-ARTHRITIS CONTROLS

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Background: Monitoring disease activity in patients with inflammatory arthritis is essential for effective treatment. While the health assessment questionnaire (HAQ) is commonly used to assess physical function, additional functional tests, such as isometric grip strength and the Moberg Pick-Up-Test (MPUT), provide objective measures for hand function and allow assessing hand function across different diseases (1). It remains unclear to date, if measured hand function is already reflected by the HAQ, as the most widely used patient reported outcome measure of physical function in arthritis.
Objectives: To estimate the proportion of hand function and grip strength variability explained by HAQ, patient-reported hand function, and between-person variation in patients with inflammatory arthritis and non-arthritic controls.
Methods: Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis without PsA (PsO) and healthy controls (HC) were investigated. Subject characteristics (age, sex, disease) and HAQ were recorded. Hand function was assessed by vigorimetric grip strength, MPUT, and a patient-reported tool (Michigan Hand Questionnaire, MHQ). Mixed pure-random-effect linear regression models were used to estimate the proportion of variance in measured hand function or grip strength explained by subject characteristics (age, hand dominance, sex, reported hand function, disease group).
Results: 299 subjects were tested, 101 with RA (Age: 59.1±13.3 years, BMI: 27.2±5 kg/m^2, HAQ-DI score: 0.9±06), 92 with PsA (Age: 58.8±11.6 years, BMI: 29±6.1 kg/m^2, HAQ-DI score: 0.6±0.7) and 106 non-arthritic controls (51 with Pso (Age: 47.3±14.1 years, BMI: 29.8±7.3 kg/m^2, HAQ-DI score: 0.4±06) and 55 HC (Age: 54.6±16.5 years, BMI: 25.2±3.3 kg/m^2, HAQ-DI score: 0.1±0.2). Overall variation of MPUT is mostly accounted for by between-person variation (43.1%), followed by HAQ (20.3%) and MHQ (20.2%) (Figure 1A). Overall variation in grip strength is mostly accounted for by sex (59.8%), between-person variation (21.1%) and HAQ (11.3%) (Figure 1B). Overall variation in MHQ is mostly accounted for by HAQ (59.2%) and residual variation (28.3%). Study group specific result are summarized in Table 1.

Table 1. Variance proportions for each of the four study groups.

	Variance proportions (%)							
	Hand function (MPUT)				Grip strength			
Group	Control	PsA	PsO	RA	Control	PsA	PsO	RA
MHQ	3.4	39.0	0.0	0.0	0.0	2.1	0.0	0.0
ID	34.8	36.2	51.6	52.8	16.1	12.9	21.3	27.9
Age	0.0	13.8	0.0	0.7	8.4	8.4	0.0	0.0
HAQ	35.8	10.8	34.3	16.4	3.8	3.1	10.3	12.0
Dominant hand	0.6	0.2	0.0	0.0	3.5	0.6	1.3	0.2
Sex	12.1	0.0	0.0	4.3	64.2	68.9	63.7	55.0
Residual	13.3	0.0	14.1	25.8	3.9	4.0	3.4	5.0

Conclusion: While the variance variation in grip strength is mainly explained by sex and between-person variation for all subject groups, the proportions of explained variance for measured hand function is not similar between diseases. In all groups > 50% of the variation in measured hand function remains unexplained by the variables used. Especially in arthritis patients, HAQ explained less than 25% of the variance in measured hand function. Grip-strength can be considered a poor surrogate for hand function in this context due to its large gender dependence. The explainability of MHQ variation largely by HAQ indicates that it has limited potential to provide further information beyond overall functional impairment. In contrast, the large between-person variation in MPUT likely indicates unexplored movement patterns of hand motion that may be further dissected using sensor-based analyses (2) and can help identify movement components a potential for an in-depth assessment of subtle hand-function alterations in inflammatory arthritis.

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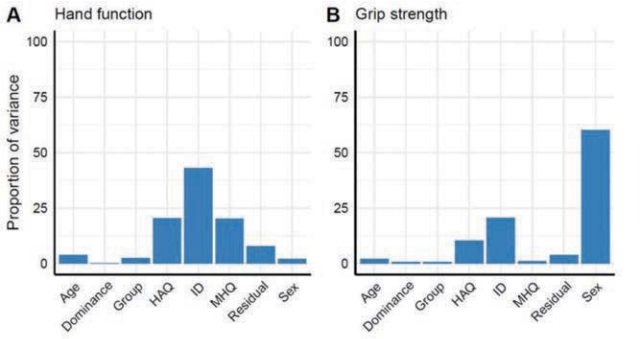

Figure 1. Overall (N=299) proportions of variance for (A) hand function by Moberg Pick-up Test (MPUT) and (B) grip strength. Dominance = dominant hand, HAQ = health assessment questionnaire, ID = individual, MHQ = Michigan Hand Questionnaire.

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POS0010 THE PSORIATIC ARTHRITIS 5-THERMOMETER SCALES (PSA-5TS): A NEW INSTRUMENT FOR ASSESSING THE STATUS OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

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Background: There are a variety of composite disease activity monitoring methods and patient-centered metrics available for psoriatic arthritis (PsA). The Psoriatic Arthritis 5-Thermometer scales (PsA-5Ts) is a new tool, proposed, with the aim of improving its diagnostic accuracy.
Objectives: The goal of this research was to evaluate data on the measurement qualities of the PsA-5Ts, a composite measure of disease activity in PsA patients, in a real-world scenario (Figure 1).

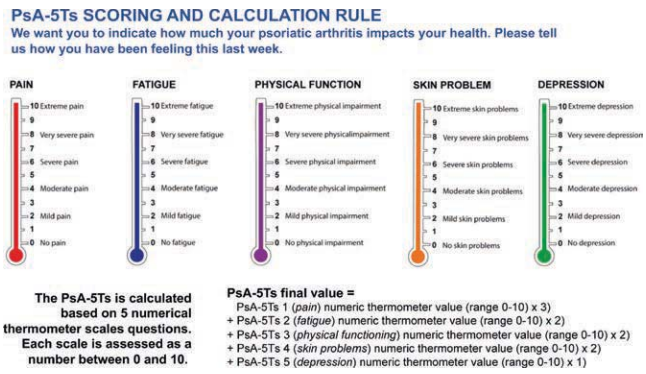

Figure 1. The Psoriatic Arthritis 5 Thermometer scales (PsA-5Ts) scoring and calculation rule

Methods: A total of 155 PsA patients were enrolled between May 2018 and December 2021. Adult-onset PsA CASPAR criteria were used to classify patients affected by PsA, while ASAS criteria were used to classify patients affected by axial-PsA (axPsA). All patients completed the PsA-5Ts, a simple instrument with five "thermometers" that incorporate pain, fatigue, physical function, skin disorders, and depression into a single assessment of disease activity. Additional continuous measures of disease activity (e.g., DAPSA, PASDAS, CPDAI) and patient-reported outcomes (PROs) measures of disease health status (e.g., PSAID and SF-36) were analyzed as comparisons. Spearman's correlations and cross-tabulations were used to examine concurrent validity. Receiver operating characteristic (ROC) curve method was used to assess discriminant validity. As an external criterion, the Minimal Disease Activity (MDA) levels were used.
Results: The 96 female and 59 male patients ranged in age from 20 to 79 years old and had been living with PsA for an average of 8.35.2 years (6 months to 22 years). The PsA-5Ts' area under the ROC curve (AUC-ROC) was 0.944. (95 percent CI 0.895 to 0.974) (Figure 2). The PsA-5Ts had same discriminant validity as the DAPSA, CPDAI, PASDAS, and PSAID, but it was better than the SF-36 (p=0.0011). PsA-5Ts subscales were highly significantly different between the MDA status (all at p<0.0001) when categorizing patients into those who rated their condition as reaching MDA (Kruskal-Wallis test). PsA-5Ts were also shown to have a remarkable (p<0.0001) correlation with known PsA activity measurement techniques.

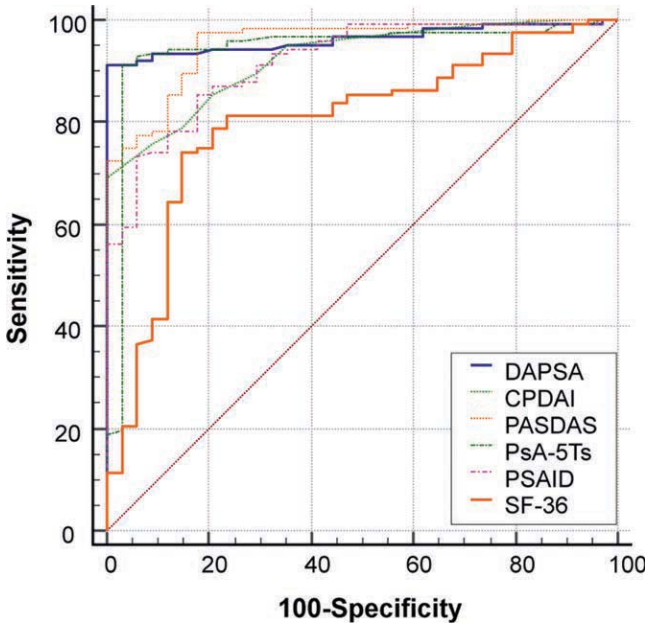

Figure 2. ROC curve analysis (AUC-ROC curves values, standard error and 95% confidence intervals) for the discriminatory power of disease activity, according to the different composite disease activity indices (DAPSA; CPDAI and PASDAS) and patient-reported outcomes (PROs) measures (PsA-5Ts, PSAID and SF-36). Receiver operating characteristic curves illustrating the relationship between sensitivity and complement of specificity (100-specificity) in PsA for activity measures using MDA as an external indicator. A line that runs diagonally across the figure from lower left to upper right will have an area of 0.5; this represents an instrument that does not discriminate.

Conclusion: For the evaluation of disease activity in PsA, PsA-5Ts is a useful alternative to continuous composite indices and other patient-centered assessments. The PsA-5Ts make data collection simpler, and they should be used in both clinical studies and everyday clinical treatment. In order to establish the tool's clinical relevance, longitudinal construct validity, which concerns the measure's capacity to identify a real change in health status as well as its accuracy in detecting changes of various magnitudes, must be addressed.

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POS0011

COMPARISON OF PSYCHOMETRIC PROPERTIES OF FOUR GLOBAL MEASURES OF PRESENTEEISM IN PATIENTS WITH OSTEOARTHRITIS AND INFLAMMATORY ARTHRITIS: A EULAR-PRO STUDY

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Background: Work is an important outcome for people with inflammatory arthritis (IA including PsA, RA, AxSpA) and osteoarthritis (OA). It is known that people with IA and OA are at increased risk of sick leave and have to stop working early due to ill health. In addition to being at increased risk of becoming work disabled and increased absenteeism, high levels of presenteeism (i.e. reduced productivity/limited ability to work due to ill health whilst at work) have also been reported. Several instruments exist to measure presenteeism, including single-item global measures and multi-item instruments. In some studies using single-item global instruments may be more feasible. However, available global instruments differ in concept, recall period and reference. It is important to understand which of the measures have good psychometric properties before using them in clinical studies.
Objectives: To assess the psychometric properties of four global presenteeism instruments.
Methods: Patients with IA or OA were recruited via rheumatology outpatient clinics to a large international, longitudinal observational study including 8 European countries and Canada. Participants completed a survey at baseline, 1, 2, 3, 4 wks, 2 months and 3 months. The four global measures of presenteeism included: Work Productivity and Activity Impairment Questionnaire (WPAI), Work Productivity Scale–Rheumatoid Arthritis (WPS-RA), Work Ability Index (WAI) and the Quality*Quantity questionnaire (QQtotal/10) scale. To facilitate score interpretation the WAI and QQtotal were reversed. Pain was measured using an 11-point Likert scale. Spearman correlations were calculated between the presenteeism measures and the Workplace Activity Limitations Scale (WALS), a validated multi-item measure of presenteeism, and HAQ to evaluate construct validity (validity: r <0.50=low; r >0.50-<0.70=moderate; r >0.70=high). Test-retest reliability of the 4 presenteeism scales (baseline-1wk) was measured applying ICC in patients with stable disease (i.e. same pain score at baseline and 1wk) (reliability: ICC<0.40=poor; ICC 0.40-0.75=fair to good; ICC >0.75=excellent). Responsiveness during 3 months was measured comparing patients with improvement in pain score (>1 point improvement in pain score (~MCID pain)) with patients with no change or worsening in pain score. The two groups were compared applying Mann Whitney U test.
Results: This international study included 550 patients with a mean age of 47.8 (SD 9.9) yrs and 61.4% were female. Mean (SD) disease duration since diagnosis was 10.8 (10.4) yrs and 91.2% had IA. Mean (SD) presenteeism scores at baseline were: WPAI=2.9 (2.7); WPS-RA=3.4 (2.7); WAI=2.7 (2.4); and QQtotal=3.1 (3.2). The correlations between the global measures and with WALS and HAQ were moderate to good, except for QQtotal and HAQ which was low (Table 1). In patients with the same stable pain scores at baseline-1wk (n=141) ICC scores were good to excellent, respectively: WPAI (0.771), WPS-RA (0.752), WAI (0.663), and QQtotal (0.650). An improvement in pain during the 3 month study duration was observed in 145/381 (38%) of the patients. In these patients a significant reduction in mean (SD) change presenteeism was observed for all four presenteeism scales compared to those with no change or worsening of the pain score: WPAI (-1.0 (2.37) vs 0.68 (2.40), p<0.01); WPS-RA (-0.76 (2.57) vs 0.43 (2.10), p<0.001); WAI (-0.09 (2.34) vs 0.41 (2.46), p<0.001); QQtotal (-0.57 (3.16) vs 0.79 (3.1), p<0.01).

Table 1.

	WPAI	WPS-RA	WAI	QQtotal	WALS	HAQ
WPAI	-	0.8164	0.5992	0.5184	0.6269	0.5592
WPS-RA		-	0.5836	0.5217	0.6055	0.5669
WAI			-	0.5866	0.5231	0.5168
QQtotal				-	0.5025	0.4367

Conclusion: The psychometric properties of all 4 global presenteeism scales were moderate to good, with slightly better scores for both the WPS-RA and WPAI instruments both measuring the impact of OA and IA on productivity.
Disclosure of Interests: Suzanne Verstappen Consultant of: EUOSHA, Grant/research support from: AbbVie, BMS. EULAR, Annelies Boonen Speakers bureau: Abbvie / Galapagos, Consultant of: Galapagos, Sarah Wilkinson: None declared, Dorcas Beaton: None declared, Ailsa Bosworth: None declared, José Canas da Silva: None declared, Gloria Crepaldi: None declared, Sabrina Dadoun: None declared, Cathie Hofstetter: None declared, Carina Mihai Speakers bureau: Boehringer-Ingelheim, Mepha, MED Talks Switzerland, Consultant of: Boehringer-Ingelheim, Janssen, Grant/research support from: Roche, Boehringer-Ingelheim, Sofia Ramiro Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB, Sanofi, Grant/research support from: Grant: AbbVie, Galapagos, Novartis, Pfizer, UCB, Garifallia Sakellariou Consultant of: Abbvie, BMS and Galapagos., Grant/research support from: Abbvie, BMS and Galapagos., Sandra Meisalu: None declared, Johan K Wallman Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, Grant/research support from: AbbVie, Amgen, Eli Lilly, Novartis, Pfizer., Diane Lacaille: None declared
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Challenging cases to make you think

POS0012 A NEW TNFRSF1A GENE MUTATION IN A TURKISH FAMILY WITH TNF RECEPTOR-ASSOCIATED PERIODIC SYNDROME (TRAPS).

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Background: Tumor necrosis factor (TNF) receptor-1 associated periodic syndrome (TRAPS) is a rare autosomal dominant autoinflammatory syndrome caused by pathogenic variants in the tumor necrosis factor receptor 1 (TNFR1) gene (TNF receptor superfamily member 1A, TNFRSF1A). For definitive diagnosis, genetic tests are needed to show variants in the TNFR1 gene (1). Information on genotype-phenotype relationships is limited due to the rarity of the disease.
Objectives: This study presents novel R97S mutation in TNFRSF1A gene and relevant clinical findings in a patient with amyloidosis of unknown etiology and his sister.
Methods: Case; Proband 33-year-old male patient presented with swelling in the legs 9 years ago. In his history, he described muscle pain, unilateral eye redness, swelling and discharge, which occurred several times in 2-3 months and lasted for up to 2 weeks. Kidney biopsy was found to be consistent with AA amylodiosis. FMF (familial Mediterranean fever) gene mutation was detected negative. Colchicine was started at 2x0.5 mg per day.
Despite colchicine treatment in the following years, acute phase reactants remained high, proteinuria continued at nephrotic level (5060 mg in 24-hour urine), progressive deterioration of kidney functions, end-stage renal failure developed. Gene analysis was performed for other autoinflammatory diseases; R97S (Nucleotide change c.290_310dup heterozygous) mutation was detected in the TNFRSF1A gene.
Sister; 31-year-old female patient was admitted to our clinic after a heterozygous mutation in the TNFRSF1A gene was detected in her brother. In her history, she described muscle pain, edema, redness and discharge around the eyes, which occurred 1-2 times a year and lasted for about 2 weeks, especially triggered by the menstrual cycle. TNF (tumor necrosis factor) receptor-associated periodic syndrome mutation was found to be heterozygous positive R97S.
Father; The father of the first two cases started having sore throat, diarrhea, muscle pain, swelling around the eyes and fever attacks starting from the age of 29. Renal biopsy revealed apple-green birefringence with congo-red stain, which was indicative of amyloidosis. When he was 32 years old, peritoneal dialysis was started first and then continued with hemodialysis due to end-stage renal disease. Three months after the start of hemodialysis, he died due to high fever, hypotension and septicemia.
Results: In this article, a novel mutation of TRAPS which has not been reported in the literature so far, is presented in a Turkish family.
Conclusion: Our patient and her sister with the R97S mutation did not have frequent clinical findings such as febrile serositis attacks and skin rashes. In addition, the incidence of conjunctivitis and periorbital edema in TRAPS cases reported in the literature is between 10-20% (1). Three members of the family presented here had periorbital edema and two had conjunctivitis. It is possible that R97S mutations in the TNFRSF1A gene are associated with the development of periorbital lesions and secondary amyloidosis.
Our country is endemic for FMF disease, a study by Bilge et al. (2) demonstrated that mutation analysis of 9% of all subjects with FMF in our country provided negative results. In our opinion genetic analysis should be performed to detect other autoinflammatory diseases in cases that classical FMF attacks are not seen, as in this case series. These and similar cases followed as FMF are likely to be associated with other autoinflammatory diseases. Diagnosing these rare diseases will provide both appropriate and effective treatment options to patients and a better definition of the clinical feature - mutation relationship.
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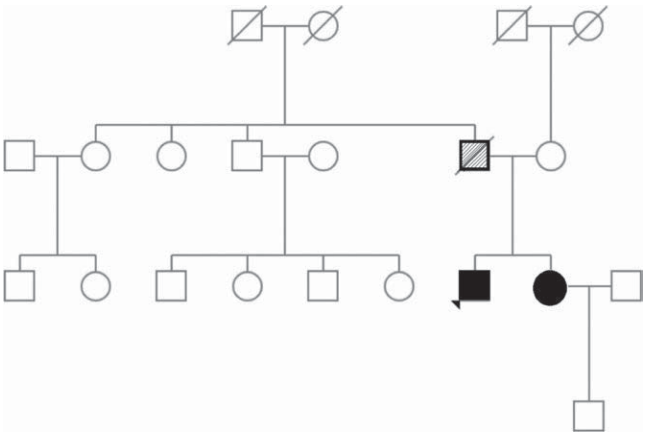

Figure 1. Family's pedigree

Disclosure of Interests: None declared
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POS0013 SJÖGREN-LIKE SYNDROME, MULTIPLE AUTOIMMUNE DISEASES, THYMOMA AND GENETIC VARIANTS IN AIRE

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Background: The autoimmune regulator gene *AIRE* is the main controlling factor for developing central immunotolerance. Variants in *AIRE* lead to autoimmunity and underly the autoimmune polyendocrine syndrome type 1 (APS-1 or APECED), defined by the clinical triad chronic mucocutaneous candiasis hypoparathyroidism and adrenal insufficiency.(1, 2) Manifold additional manifestation have been described, including Sjögren-like disease lacking the typical serology.(3) Furthermore, serological abnormalities, e.g. antibodies against IL-22, IL-17F and IFNώ are a hallmark of the disease. Due to the diversity in clinical manifestations and the genetic variants in AIRE, diagnosis is often delayed.
Objectives: Case report of a patient with 2 new variants in *AIRE* with diverse rheumatological and autoimmune disorders as well as thymoma.
Methods: Case report.
Results: The 38-year-old male patient was transferred to our clinic for immunoglobuline therapy, from his treating neurologist. His medical history included diabetes mellitus type 1, diagnosed in 1996, followed by Grave's disease in 2000, culminating in a thyroidectomy in 2017. In 2009 he underwent a thymectomy for a thymoma. He had been treated with a series of immunosuppressive therapies including prednisolone, rituximab and mycophenolate, as well as plasmapheresis and immunopheresis for his atypical, seronegative myasthenia gravis. Due to the limited effect of the previous therapeutic regimen

a trial with intravenous immunoglobulin had been initiated inducing clinical stabilization.

We diagnosed Sjogren-like syndrome based on sicca symptoms and a suspicious submandibular salivary gland in sonography, without typical serology. Family history was negative for autoimmune diseases. The clinical findings pointed towards immunodysregulation, prompting cytokine examination, lymphocyte phenotyping and genetic testing. Cytokines (IFNγ, IL-2, IL-4, IL-10, IL-17) under immunosuppression with 20 mg prednisolone and 2 g of mycophenolate were all low/below detection threshold. Flow cytometry showed no abnormalities except for a low CD20 (after Rituximab) and a slightly elevated T-reg count. Genetic testing revealed heterozygous variants in exon three (c.354C>G) and eight (c.927C>G) of *AIRE*. The patient´s mother showed the same genotype - indicating that the variants in the patient are *in cis* - but is asymptomatic. (Figure 1)

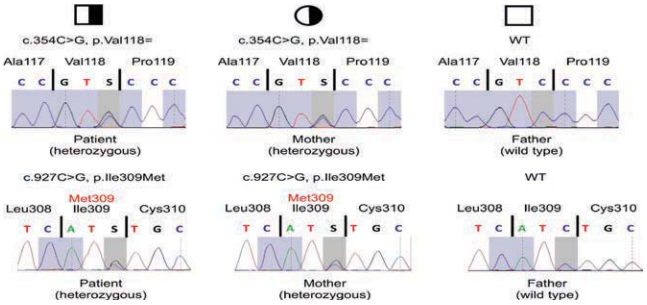

Figure 1. Electropherograms of the heterozygous patient, his heterozygous, asymptomatic mother and his asymptomatic father, who has a wildtype of AIRE.

Conclusion: To our knowledge this is the first report of a patient with thymoma and genetic variant(s) in the AIRE gene displaying several autoimmune diseases. Although clinical similarities between thymoma patients and APECED / APS1 are known (4), a genetic link between these 2 diseases has not yet been described. As rheumatic autoimmunity can be induced by either, rheumatologists should be aware of these potentially underlying causes.

An additional point of interest is the lack of autoimmunity in the mother with the same genetic variants, which suggests an additional environmental trigger (e.g. smoking, viral infection) in the patient.

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POS0014

EFFICACY AND SAFETY OF JAK INHIBITORS IN REFRACTORY OR INITIAL TREATMENT OF ADULT ONSET STILL'S DISEASE

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Background: Inappropriate activation of pro-inflammatory cytokines such as interleukin (IL)-1, IL-6 or IL-18, is a pathogenic cornerstone in adult onset Still's disease (AOSD). Beyond therapies targeting IL-1 and IL-6, Janus kinases (JAK) inhibitors have been suggested to be efficient in refractory AOSD patients [1].

Objectives: To assess the efficacy and safety of JAK inhibitors in the treatment of AOSD patient refractory to, or with initial treatment.

Methods: This retrospective study was based on our single center of the department of rheumatology and immunology. The data was collected from the patients' medical records using a standardized questionnaire and analyzed at different time points. The response to JAK inhibitors was categorized as complete remission (CR), partial remission (PR) or failure (F) [2].

Results: 7 patients were recruited (Table 1), including 4 refractory patients and 3 initial patients. Mean age at JAK inhibitor treatment start was 27.5 years for refractory patients and 35 years for initial patients; and mean disease duration was 66.5 months and 1 month respectively. All patients had fever and polyarthritis, 5 patents had rash. In addition, pulmonary hypertension, abnormal liver function tests, abdominal pain, and heart failure were also observed in our patients. Response to corticosteroids, conventional synthetic or biological Disease Modifying Anti-Rheumatic Drugs (DMARDs) had been considered inadequate in 4 refractory patients. Tofacitinib was added in the initial treatment for 3 patients for high disease activity. In total, baricitinib was used in 2 patients and tofacitinib in 5 patients. Steroids were concurrently used in 6 patients, MTX in three, SASP and NSAIDs in one. At a mean follow up of 3.8 months, complete remission was observed in one patient (with tofacitinib), partial remission was in 5 patients (4 patients with tofacitinib and one with baricitinib), and failure in one (patients with baricitinib). At the last visit, steroids could be decreased but not stopped in those 6 patients. Tolerance of JAK inhibitors was excellent, none infectious disease or other severe side effect were observed.

Conclusion: JAK inhibitors treatment may be helpful for some patients with refractory AOSD, or patients with severe disease activity at initial treatment. Different treatment responses were observed in these short series of cases, which might be due to the phenotype of patients. However, the scale of patients in our study was too low to draw a conclusion. Further study and additional information are needed to evaluate more precisely the risk-benefit ratio of this treatment, and a possible difference in efficacy among the different groups of patients or JAK inhibitors.

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Table 1. Characteristics of the AOSD patients

No.	Sex	Age (year)	Disease Duration (Month)	Main symptoms	Treatments before JAKi onset	JAKi	Steroids at onset	Conconmitant treatment	Steroids at the end of F-U	F-U (month)	Outcome
1	M	26	29	Fever, polyarthritis	Pred+MTX	Tofacitinib	0	MTX	0	4	PR
2	M	25	9	Fever, polyarthritis, rash, pulmonary hypertension	Pred+MTX	Baricitinib	16	MTX+Pred	12	4	F
3	M	38	12	Fever, polyarthritis, rash	Pred+MTX+ CsA+NSAIDs	Tofacitinib	24	Pred	12	3	PR
4	M	21	216	Fever, polyarthritis	Pred+MTX+ SASP+NSAIDs+TNFi	Baricitinib	4	Pred+MTX+ SASP+NSAIDs	4	3	PR
5	F	33	1	Fever, polyarthritis, rash, abnormal liver function tests	Pred	Tofacitinib	40	Pred	2	5	CR
6	F	47	1	Fever, polyarthritis, rash, abdominal pain	Pred	Tofacitinib	36	Pred	4	5	PR
7	F	25	1	Fever, polyarthritis, rash, heart failure	Pred	Tofacitinib	40	Pred	12	3	PR

Pred: prednisone; MTX: Methotrexate; SASP: salicylazosulfapyridine; CsA: ciclosporin A; NSAIDs: Non-Steroidal Antiinflammatory Drugs; TNFi: Tumor necrosis factor inhibitor. CR: complete remission; PR: partial remission; F: failure.

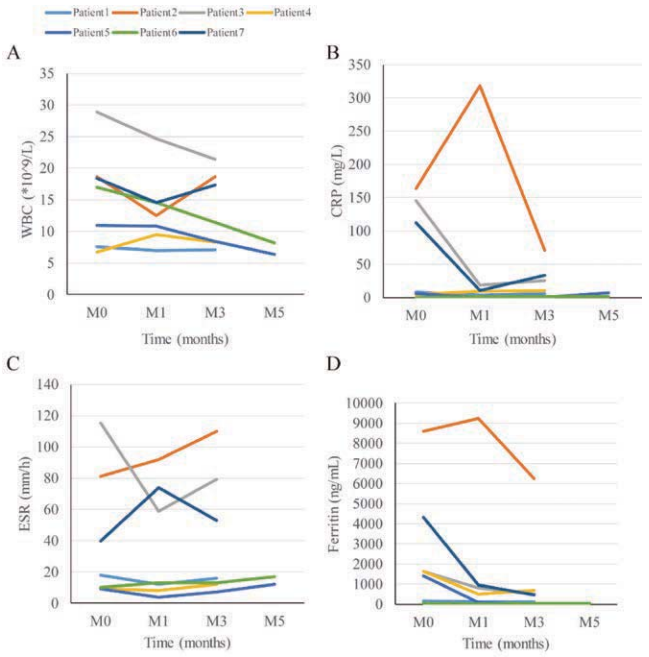

Figure 1. Changes in laboratory test (A) WBC; (B) CRP; (C) ESR;(D) Ferritin. M0: baseline; M1: month 1; M3: month 3; M5: month 5.

Acknowledgements: None
Disclosure of Interests: None declared
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POS0015

BULLOUS SYSTEMIC LUPUS ERYTHEMATOSUS SUCCESSFULLY TREATED WITH MYCOPHENOLATE MOFETIL COMBINED WITH GLUCOCORTICOID: A CASE REPORT

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Background: Bullous systemic lupus erythematosus (BSLE) is a rare subtype of systemic lupus erythematosus, accounting for less than 1% of systemic lupus erythematosus (SLE) [1]. It is common in adults aged 20 to 40, with female predominace [2]. Its skin manifestations are mainly tensive blisters, especially involving oral and genital mucosa, Nissl's sign is mostly negative, blisters break and heal to form pigmentation of varying degrees, leaving no scar. At present, the main treatment is systemic application of corticosteroids combined with immunosuppressants. Here, we report a BSLE who successfully treated with mycophenolate mofetil (MMF) combined with glucocorticoid.
Objectives: To be vigilant in the early identification of BSLE, and through the treatment experience of this case, it can provide a basis for the use of Mycophanol ester as the preferred drug for the treatment of BSLE in the future.
Methods: The clinical manifestation, laboratory test, treatment, and outcome were described.
Results: A 50-year-old female patient with systemic lupus erythematosus presented with wandering joint pain for 1 year and sporadic patchy erythema on eyelid, hands, and neck for 7 months. There are blisters on part of her erythema and normal skin, about 1mm-15mm in diameter, the blister fluid is cool, fusion is broken, and Nissl's sign is negative. She suffered from anemia, albuminuria, polyserous effusion and other system damage. Skin histopathology showed mild hyperkeratosis of epidermis, formation of subepidermal blisters and accumulation of a large number of neutrophils; direct immunofluorescence showed that the positive expressions of IgA, IgG and C3 were found in the basement membrane of the skin, leading to a diagnosis of BSLE. In the initial stage, patients were treated with high-dose glucocorticoid (160 mg, qd) combined with immunosuppressants (thalidomide and hydroxychloroquine), but the number of blisters increased. After treatment with MMF (1 g, bid), the skin lesions disappeared, joint pain relieved, anemia was corrected, and polyserous effusion was absorbed. She was followed up for half a year and there was no recurrence.
Conclusion: Patients with BSLE are often accompanied by multiple system damage [2], so it is critical to correctly identify BSLE and provide appropriate treatment as soon as possible. For patients who do not respond to single glucocorticoid therapy, combined with MMF can be used as the preferred drug for the treatment of BSLE in the future.

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Figure 1. BSLE. Blisters can be seen on the face, neck, armpits and arms.
BSLE = bullous systemic lupus erythematous.

Disclosure of Interests: None declared
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POS0016

COMMON VARIABLE IMMUNODEFICIENCY DISEASE FROM THE PERSPECTIVE OF RHEUMATOLOGY

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Background: Common variable immunodeficiency (CVID) is a primary immunodeficiency characterized by impaired B cell differentiation and immunoglobulin production. In addition to increased susceptibility to infection, patients also have an increased tendency to autoimmune disease. Since rheumatological findings usually start earlier than other autoimmunities, it is very important to increase the awareness of rheumatologists about this disease, for accurate diagnosis and to prevent delay in treatment.
Objectives: To increase the awareness of rheumatologists about the main symptoms and findings of CVID.
Methods: Adult patients referred to the rheumatology department since January 2015 were included in the study. Demographic and clinical characteristics (infections, pulmonary and extrapulmonary granulomatous involvement, autoimmune manifestations), laboratory and imaging findings and treatments of the patients were analyzed.
Results: Ten adult patients with CVID were included in the study. The gender distribution of the patients was similar and the median age was 38±10.0 years.

Table 1. Autoimmune manifestations of common variable immunodeficiency patients

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Age/Sex	36/F	43/F	40/M	25/M	23/M	36/M	41/M	57/F	35/F	48/F
Symptom duration (years)	12	11	11	4	17	12	11	13	12	7
Diagnosis duration (years)	6	11	8	3	17	10	9	1	11	2
Sinopulmonary infection	+	+	+	+	+	+	+	+	+	+
GI infection	-	+	-	+	-	+	+	-	-	-
Other infections	+	+	-	+	+	-	+	+	-	+
Pulmonary Involvement	lymphocytic ILD	nodule	*bronchiectasis	-	-	bronchiectasis	bronchiectasis cavitation	nodule	nodule	-
Extrapulmonary Granuloma	brain parenchyma, bone marrow, liver, spleen, skin	liver, spleen	-	renal°, liver	-	**bone	-	*lymph node	-	-
Autoimmune manifestations	-	monoarthritis, chronic ileitis	oligoarthritis, atrophic gastritis, chronic ileitis	alopecia, thyroiditis, bilateral anterior uveitis	-	oligoarthritis, autoimmune neutropenia, chronic ileitis, kounis syndrome	oligoarthritis, autoimmune neutropenia	oligoarthritis, thyroiditis, sicca syndrome, recurrent scleritis	colitis	-
Cirrhosis of the liver	+	+	-	-	-	+	-	-	-	-
Lymphadenopathy	+	+	+	+	-	+	+	+	+	+
Splenomegaly	+	+	+	+	-	+	+	-	+	-
Immunosuppressive Treatment	Steroid, AZA, CSA, Adalimumab	Steroid	Steroid, SSZ	Steroid, MMF, CYC	-	Steroid, SSZ, MTX, LEF, CSA	Steroid	Steroid, MTX, AZA, CSA	Steroid, AZA	-

Abbreviations: AZA-azathioprine, CSA-cyclosporine, CYC-cyclophosphamide, F-female, GI-gastrointestinal, ILD-interstitial lung disease, LEF-leflunomide, M-male, MTX-methotrexate, SSZ-sulfasalazine*right lower lobectomy, ** right foot 5th toe enucleation, * mediastinoscopic lymph node biopsy ° interstitial granulomatous nephritis

The mean duration of diagnosis was 123.5±89.3 months. At least one autoimmune manifestation was observed in 80% of the patients. In the follow-up period, 40% of the patients developed arthritis. Involvement of lower extremity joints such as knee and ankle was more prominent. While all patients were given 0.8 g/kg/3 weeks of intravenous immunoglobulin, 80% required immunosuppressive therapy for autoimmune manifestations. The demographic and clinical characteristics of the patients are summarized in Table 1.

Conclusion: Autoimmune diseases can be seen in patients with CVID, and sometimes this may be the first presentation of CVID. Heterogeneous clinical findings of the disease may lead to delay in diagnosis. Clinicians should be more careful about the different manifestations of CVID to avoid delay in diagnosis.

Disclosure of Interests: None declared

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POS0017 SEVERE GENERALIZED EDEMA AS INITIAL PRESENTING SYMPTOM IN POLYMYOSITIS

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Background: 53 year old female developed pain and swelling of the metacarpophalangeal and proximal interphalangeal joints of both hands. She was diagnosed to have possible inflammatory arthropathy since her workup showed elevated inflammatory markers with CRP 2.2 and ESR 35. Rheumatoid factor and antiCCP antibody were negative. She was treated with hydroxychloroquine, methotrexate followed by leflunomide. She had non pitting edema around both ankles at initial presentation which later spread to the thighs, abdomen and chest. There was no erythema of the skin, tenderness or skin rash. BNP was normal at 58. TSH was normal. Echocardiogram was normal. Blood and urine cultures were negative. CT scan of the chest, abdomen and pelvis showed moderate subcutaneous edema. She was noted to have elevated liver enzymes with AST 438 and ALT 245. Hepatitis panel was negative. Smooth muscle antibody and antimitochondrial antibody were negative. Ultrasound abdomen showed diffusley increased echogenicity throughout the liver. Liver biopsy showed mildly active steatohepatitis centrizonal and portal/periportal fibrosis. ANA was positive 1:640 speckled pattern. ENA showed a positive antiRNP antibody. ANCA was negative. CK was elevated at 853 U/L. Myomarker panel was negative for antiJo, Anti Mi2, antiSRP, antiNXP and anti Ku antibodies. She had a workup for malignancy including CT chest, abdomen and pelvis, mammogram and colonoscopy which were negative.

Objectives: About 4 months after she presented with edema, she developed progressive proximal muscle weakness of both lower extremities which later involved both upper extremities. She also had neck muscle weakness. She also complained of difficulty swallowing. Swallow evaluation was normal. She did not have any skin rashes.

Methods: Concentric needle electromyography showed abnormal spontaneous activity; small amplitude and often polyphasic motor unit action potentials, along with increased recruitment pattern in tibialis anterior, vastus lateralis, medial gastrocnemius, tibialis posterior and short head biceps femoris muscle in the left lower extremity. The findings were suggestive of myopathy. She underwent a muscle biopsy from the left deltoid muscle which showed dense perimysial and endomysial lymphoplasmacytic inflammatory infiltrates with degenerating myofibers.

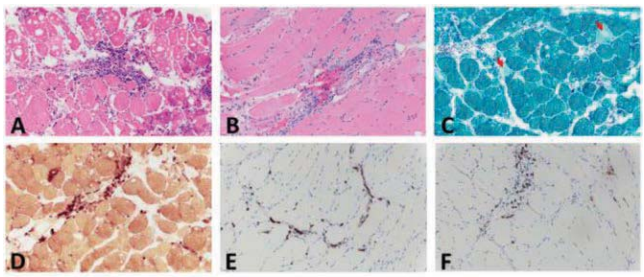

Figure. 1 Left Deltoid Muscle Biopsy. A. Dense perimysial and endomysial lympho-plasmacytic inflammatory infiltrates, with degenerating myofibers. Frozen section, H&E stain, 20x magnification. **B.** Perimysial and endomysial inflammatory infiltrates. Formalin fixed, paraffin-embedded, H&E stain, 20 x magnification. **C.** Degenerating myofibers (arrows) with pales staining on Frozen section, Gomori Trichrome, 20x magnification. **D.** Inflammatory infiltrates and degenerating myofibers are highlighted. Frozen Section, Esterase stain, 20x magnification. **E.** Endomysial mononuclear inflammatory cells are predominantly T-cells. Formalin fixed, paraffin-embedded, CD3 immunostain, 20 x magnification. **F.** The majority of T-cells have a cytotoxic (CD8+) phenotype. Formalin fixed, paraffin-embedded, CD8 immunostain, 20 x magnification.

Results: Patient has proximal muscle weakness in both upper and lower extremities along with elevated CK, EMG findings suggestive of an underlying myopathy and biopsy evidence of inflammation and a diagnosis of polymyositis was made.She was initiated on treatment with a tapering course of prednisone starting at 60 mg daily. Her edema has improved. Liver function tests and CK have improved. Muscle strength has improved in both upper extremities with some residual weakness in the proximal muscles of lower extremities.

Conclusion: Patient presented with severe generalized edema as the initial presenting symptom of polymyositis. Rheumatologists should be aware of subcutaneous edema as a presenting manifestation of inflammatory myopathy and may precede the development of muscle weakness. Previously reported cases of edematous inflammatory myopathy were mostly dermatomyositis. This case demonstrates that polymyositis could also present as subcutaneous edema.

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Chronic pain - Mechanisms, epidemiology, and treatment

POS0018 REDUCTION OF DIFFUSE NOXIOUS INHIBITORY CONTROL IN ACTIVE INFLAMMATORY RHEUMATISM: A DEMONSTRATION OF CENTRAL SENSITISATION

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Background: In rheumatoid arthritis (RA) and spondyloarthritis (Spa), persistent pain remains challenging. It is thought to result from central pain sensitisation, which can be measured by quantitative sensory testing (QST) and conditioned pain modulation (CPM).
Objectives: The main objective of the RAPID (Rheumatism Pain Inhibitory Descending pathways) study, was to assess descending pain modulation (through CPM paradigms) in patients with RA or Spa, comparing these patients with healthy sex- and age-matched controls. The secondary objectives were the measurement pain thresholds (heat and cold) in a non-articular, non-painful area in patients and controls as a means of detecting possible widespread hyperalgesia as another index of central sensitisation in our patients.
Methods: We included 50 RA and 50 Spa patients and 100 age- and sex-matched controls. We assessed clinical disease variables for patients, together with responses to various psychological questionnaires. All participants underwent QST with the determination of heat and cold pain thresholds (HPT-CPT) and CPM. In CPM, a conditioning stimulus was applied to a foot and the non-dominant hand in a randomised sequence. Descending pain control was assessed as the change in HPT (in °C) following a conditioning stimulus: the higher the CPM effect, the more efficient the inhibitory control.
Results: HPT and CPT were similar in patients and controls. Mean CPM effect was significantly weaker in patients than controls: 0.25°C (±2.57) and 2.79°C (±2.31) for patients and controls, respectively (p<0.0001) for conditioning on the foot; 0.57°C (±2.74) and 2.68°C (±2.12) (p<0.0001), respectively, for conditioning on the hand. The heat pain threshold was 42.35°C (± 3.68°C) for patients and 41.54°C (± 3.34°C) for healthy controls; this difference was not statistically significant. The cold pain threshold was 13.11°C (± 10.04°C) for patients and 13.28°C (± 9.34°C) for healthy controls; this difference was not significant. The weaker CPM effect in patients was associated with higher pain intensity. In all participants, a weak CPM effect was associated with high Central Sensitisation Inventory score, anxiety, depression, sleep disturbance and pain catastrophising.
Conclusion: Diffuse noxious inhibitory control is weaker in patients with active chronic inflammatory rheumatism than in healthy subjects, supporting the hypothesis of central sensitisation.

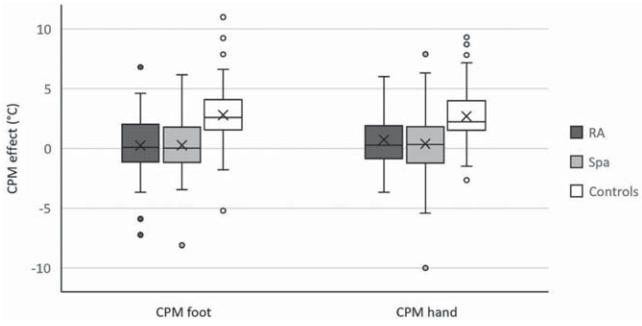

Figure 1.

Disclosure of Interests: None declared
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POS0019 CENTRAL SENSITIZATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: ASSOCIATION WITH DISEASE ACTIVITY

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Background: Rheumatoid arthritis (RA) is the most common inflammatory arthropathy with a predominance of autoimmune mechanisms of pathogenesis and pain as the main clinical manifestation. Recent evidence has found showed that Central Sensitization (CS) may be a new mechanism for the formation of pain [1]. There is insufficient data on this phenomenon in patients with RA [2].
Objectives: To determine the prevalence of the phenomenon of CS in patients with RA and evaluate its association with disease activity.
Methods: The study involved patients with RA according to the ACR / EULAR criteria (2010). RA activity was determined by DAS-28, SDAI, CDAI, and the functional ability of patients - by HAQ. Visual analog scoring (VAS) were used to evaluate the intensity of pain. The radiological stage of RA was determined according to the Kellgren-Lawrence classification. The presence of the CS phenomenon was established using the Central Sensitization Inventory (CSI) (Mayer, T. G. et al., 2012). MS Excel and SPSS22 (© SPSS Inc.) software packages were used for statistical processing of results.
Results: 110 patients (84% of women) with RA were included. The participants' mean age was (M±SD) 53.5 ± 12.2 years, with a disease duration 8.5 ± 8.1 years. Among the examined, radiological stage I was detected in 16 (15%) patients, II - in 59 (53%), III - in 23 (21%), IV - in 12 (11%). According to the DAS28-ESR index, 56 (51%) patients had high activity (DAS 28-ESR: > 5.1) and 54 (49%) patients had moderate activity (3.2 <DAS28-ESR ≤5.1). Mean values of SDAI and CDAI also showed high disease activity: 36.5 ± 10.2 and 33.3 ± 9.8, respectively. The average value of HAQ was 1.4 ± 0.7.
CS (CSI>40) was revealed in 40 (36%) patients. Correlation analysis showed that CSI was significantly correlated with disease activity, VAS pain and HAQ: DAS28-ESR (r = 0.477; p <0.01), SDAI (r = 0.559; p <0.01), CDAI (r = 0.544; p <0.01), VAS (r = 0.575; p <0.01), HAQ (r = 0.694; p <0.01). It was found that the group of patients with CS had higher rates of disease-specific values compared to patients without CS. Significance of differences between groups was at the level of p <0.01 (Table 1).

Table 1. Characteristics of the RA patients with and without CS on the indices disease activity, VAS pain and HAQ.

	CSI<40 (n=70)	CSI>40 (n=40)	P
CDAI	29,7±7,8	38,9±9,7	<0,01
SDAI	32,9±8,6	42,3±9,6	<0,01
HAQ	1,1±0,6	1,9±0,6	<0,01
DAS28-ESR	4,9±0,9	5,7±0,8	<0,01
VAS	6,3±1,3	7,8±1,2	<0,01

Notes: SDAI – The Simple Disease Activity Index, CDAI - The Clinical Disease Activity Index, DAS-28 - The Disease Activity Score-28, HAQ-DI - Health Assessment Questionnaire,VAS - Visual Analog Scoring, p – the significance of differences between groups.

Conclusion: Central sensitization is common in RA patients. The phenomenon of central sensitization is associated with higher disease activity, loss of functional ability and severity of pain.
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POS0020 PAIN PHENOTYPING IN PATIENTS WITH PSORIATIC ARTHRITIS AND HAND OSTEOARTHRITIS

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Background: Chronic pain is experienced by many patients with joint disease but underlying pain phenotypes including impact of concomitant fibromyalgia (cFM) have not been investigated in patients with psoriatic arthritis (PsA) and hand osteoarthritis (hand-OA).
Objectives: To investigate pain parameters (quantitative sensory testing) in patients with hand-OA and PsA using pressure pain thresholds (PPT), temporal summation of pain (TSP) and conditioned pain modulation (CPM) compared with healthy controls. Furthermore, to explore whether alternations in underlying pain mechanisms and psychological factors are associated with cFM compared to those patients without.
Methods: Patients with verified PsA or hand-OA and healthy controls underwent quantitative sensory testing using hand-held and cuff pressure algometry to measure PPT, TSP and CPM. Psychosocial factors were assessed via the Hospital Anxiety and Depression Scale, Pain Catastrophizing Scale, Pittsburgh Sleep

Quality Index, and disability was assessed via the Health Assessment Questionnaire Disability Index and pain quality via the painDETECT questionnaire. cFM was identified using the revised 2016 American College of Rheumatology criteria.
Results: A total of 75 patients with hand-OA, 58 patients with PsA and 20 controls were included. Patients with hand-OA or PsA had statistically significant lower PPTs and CPM, and greater TSP than controls and greater psychosocial impact. Limiting the analysis to patients without cFM yielded a similar result. Patients with cFM (58%) had greater scores of depression, anxiety, catastrophizing, disability and reduced sleep quality when compared to patients without cFM. Additionally, in cFM the TSP and painDETECT scores were higher compared to patients without cFM.
Conclusion: Patients with hand-OA and PsA experienced a greater degree of pain facilitation and psychosocial impact when compared with controls. Patients with cFM had greater TSP, painDETECT, disability, catastrophizing and reduced sleep quality, than patients without, indicating greater degree of sensitisation, psychosocial burden, and disability.

Table 1.

	Hand-OA	PsA	Controls	No cFM	cFM
N	75	58	20	74	59
Females (%)	48 (64 %)	39 (75 %)	18 (90 %)	43 (58%)	44 (75%)
Age, years	66.07 (7.73)	53.16 (11.62)	58.10 (8.32)	61 (11.53)	59 (11.56)
Pain intensity, 0 to 100 mm	56.6 (18.3)	58.6 (18.0)	NA	55.3 (17.8)	60.0 (18.4)
Quantitative sensory testing					
Pressure pain threshold joint, kPa*	215 (127)	261 (178)	370 (181)	246 (148)	220 (157)
Pressure pain threshold shin, kPa*	284 (152)	281 (154)	446 (180)	307 (160)	255 (139)
Temporal summation of pain	2.68 (2.35)	2.51 (1.91)	1.13 (1.34)	2.24 (1.74)	3.07 (2.53)
Conditioned pain modulation, kPa	3 (16)	8 (18)	19 (14)	6 (18)	4 (16)
Patient reported outcomes					
HADS depression (0-21)	2.09 (2.16)	3.43 (2.68)	0.50 (0.95)	2.09 (2.16)	3.43 (2.68)
HADS anxiety (0-21)	4.34 (3.37)	5.55 (3.32)	1.79 (2.82)	4.12 (3.07)	5.83 (3.57)
Pain Catastrophizing Scale (0-52)	16.52 (9.26)	16.95 (7.80)	3.75 (5.23)	15.03 (8.42)	18.88 (8.44)
Pittsburgh Sleep Quality Index (0 -21)	8.23 (3.84)	9.02 (4.18)	4.42 (2.41)	7.86 (3.87)	9.50 (4.01)
Health Assessment Questionnaire (0-3)	0.77 (0.56)	0.86 (0.61)	0.01 (0.04)	0.65 (0.53)	1.00 (0.59)
painDETECT questionnaire (-1-38)	17.95 (6.04)	18.73 (5.51)	-	16.67 (5.58)	20.22 (5.52)
Widespread pain index	5.81 (4.35)	6.79 (4.66)	-	3.28 (2.79)	9.95 (3.33)
cFM (%)	29 (38.7)	30 (51.7)	-	-	

Abbreviations: cFM: Concomitant fibromyalgia; HADS: Hospital anxiety and depression scale; Hand-OA: Hand osteoarthritis; PsA: Psoriatic Arthritis.

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POS0021 CHANGES OF GUT MICROBIOTA IN CONNECTIVE TISSUE DISEASE AND ITS RELATIONSHIP WITH LYMPHOCYTE SUBSETS AND CYTOKINES

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Background: Connective tissue disease (CTD) is a group of autoimmune diseases characterized by the damage of connective tissue components in various parts of the body, which involved multiple organs and systems. Dysbiosis in the gut microbiome is associated with various autoimmune diseases such as CTD.
Objectives: To explore the characters of gut microbiota and their relationship with peripheral lymphocyte subsets and cytokines in patients with CTD.
Methods: Stool samples were collected from 63 CTD patients and 63 age- and sex-matched healthy controls(HCs). Microbial genomes were extracted for 16S rRNA gene sequencing. Gut microbiota characters (alpha diversity, beta diversity, and microbial composition) were analysed by R (version 4.0.1). Peripheral lymphocyte subsets were assessed by flow cytometry. Pearson correlation analysis was used to detect the correlation between the relative abundance of genus in the sample and the activity index; correlations with $p < 0.05$ were considered significant.
Results: Shannon and Simpson index revealed a decreased alpha diversity in CTD compared with that of HCs ($p < 0.05$), though not significantly difference in ACE and Chao1 parameters ($p > 0.05$, Figure 1A). Bray curtis distance-based beta-diversity analysis indicated significant differences in microbial communities between CTD and HCs ($p = 0.0014$, ANOSIM, Figure 1B). At the genus level, CTD patients had higher abundances of Terrisporobacter ($p<0.01$), Paraprevotella ($p<0.01$), CAG–352 ($p<0.01$), et al. but lower abundances of Streptococcus ($p<0.01$), Pseudomonas ($p<0.01$), Bacteroides($p<0.01$), et al (Figure 1D). IgM was positively correlated with Lactococcus ($p<0.05$), Family_XIII_AD3011_group ($p<0.05$), Streptococcus ($p<0.05$). Th17 was positively correlated with Pseudomonas ($p<0.01$). Th2 was positively correlated with Christensenellaceae_R–7_group ($p<0.001$), UCG–010 ($p<0.001$) was positively correlated. Treg and Th2 were positively correlated with Christensenellaceae_R–7_group ($p<0.01$), UCG–010 ($p<0.01$). Treg was positively correlated with Lachnoclostridium ($p<0.05$) (Figure 1E).
Conclusion: Pattients with CTD had disbiosis of gut microbiota charaterized by impared diversity and abnomal composition,which was closely correlated with peripheral lymphocyte subsets.
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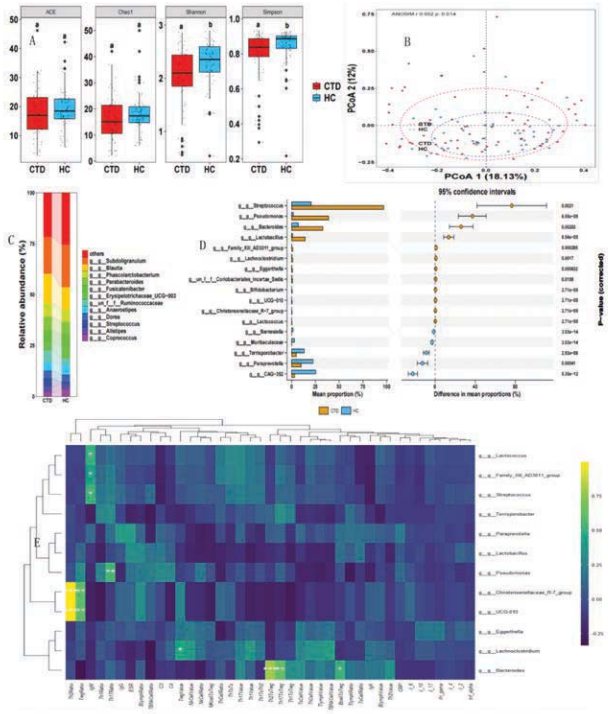

Fig1. Features of gut microbiota in CTD patients and HCs. (A) Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson), Median estimates compared across cohorts. (B) Principal component analysis (PCoA) plot generated from the Bray-Curtis distances. (C) Microbiota composition based on relative abundance at the genera levels. (D) Panel demonstrated the average relative abundance of different genus in CTD and HCs. (E) Correlation analysis of these differential phylum and lymphocyte subsets and clinical indicators between any two groups using Spearman's correlation analysis.The correlation effect is indicated by a color gradient from green (positive correlation) to purple (negative correlation).*p<0.05. ** p<0.01. ***p<0.001.

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POS0022 CHARACTERISTICS OF PAIN IN UK PATIENTS WITH BEHÇET'S SYNDROME: A PROSPECTIVE OBSERVATIONAL COHORT STUDY

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Sciences, Liverpool, United Kingdom; [6]Liverpool John Moores University, Research Institute for Sport and Exercise Sciences, Liverpool, United Kingdom

Background: Behçet's syndrome (BS) is a rare multi-organ systemic vasculitis of unknown aetiology with hallmark manifestations of mucocutaneous ulcers and skin lesions. Morbidity is high in BS; with high prevalence of pain, fatigue and poor quality of life. Fibromyalgia syndrome (FMS), a common cause of widespread musculoskeletal (MSK) pain, is more prevalent in rheumatological conditions including BS. However, there is limited research into the aetiology and characteristics of pain in BS. To our knowledge, there are no studies describing pain in a UK BS population.
Objectives: To describe the pain characteristics and incidence of comorbid FMS in patients with BS, and investigate their relationship with disease activity.
Methods: This is a prospective observational study of patients with a diagnosis of BS attending the National Centre for BS in Liverpool between February 2017 and March 2019. Patients were defined as "Complete BS" if they satisfised the International Study Group criteria and "Incomplete BS" if they met one criterion plus genital ulcers. BS severity was assessed using the Behçet's disease current activity form (BDCAF). High and low disease activity were defined as a BDCAF score ≥ 4 or < 4 respectively. FMS prevalence was determined from consultant diagnosis. To minimise inflation of disease severity in the FMS cohort, a modified BDCAF (with arthralgia and arthritis components removed) was calculated (mBDCAF). Assessments of pain included: The Pain Visual Analogue Scale (VAS), Pain Mannequin and Short Form McGill (SF-MPQ-2) questionnaires. Generalised pain data was imputed from the pain mannequin using the American College of Rheumatology 2016 definition, pain in all quadrants (upper left, upper right, lower left and lower right) plus axial distribution. Pain and FMS prevalence were compared between high and low disease activity using Chi-Square Test of Independence. The mean mBDCAF was compared between those with and without FMS using a student's T-Test. Data analysis was conducted in Microsoft Excel and STATA.
Results: 101 patients, 75 female and 26 male, of age 10-74 years were assessed. 81.2% of patients met the ISG criteria (Complete BS); The remaining 18.8% met Incomplete BS status. 90% of patients reported moderate-severe pain with a median VAS score of 68/100 [38, 81]. 35.6% of patients had a diagnosis of FMS and 46.5% experience generalized pain. 76% of patients with high disease activity reported severe pain, a VAS greater than 70, compared to 39.1% with low disease activity *(p=.003)*. Pain was more generalised in high disease activity (72%) compared to low disease activity (37.7%) *(p=.003)*. The qualitative assessment of pain (SF-MPQ-2) stratified by disease activity, Figure 1, demonstrates that pain intensity is higher in high disease activity. Continuous descriptive terms were most commonly selected indicating a chronic nature of the pain. Concomitant FMS diagnosis was more prevalent in the high disease activity group (52%) than the low disease activity group (29%) *(p=0.04)*. The mean mBDCAF of patients with FMS was 2.09 ± 1.3 compared to 1.53 ± 1.3 in patients without FMS *(p= 0.047)*.

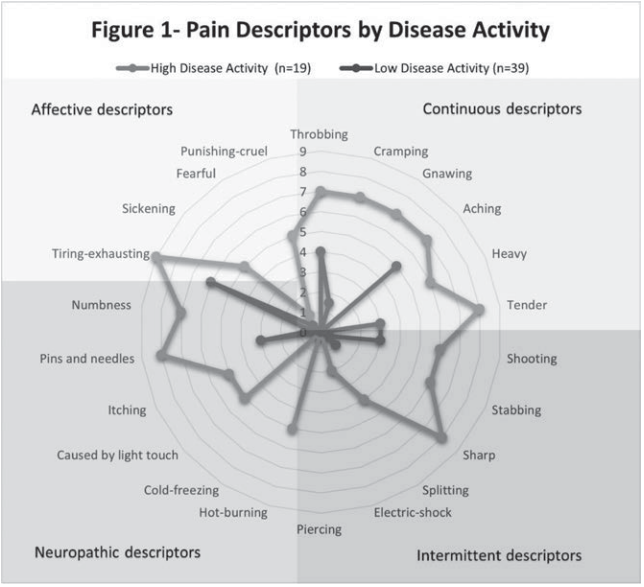

Figure 1. Pain descriptors from the SF-MPQ-2 stratified by high (BDCAF ≥4) and low disease activity (BDCAF <4). Descriptors are rated no pain to the worst pain ever (0 – 10). The median value for each descriptor is plotted. The descriptors are divided into four categories: affective, continuous, neuropathic and intermittent.

Conclusion: This the first study to describe the pain experience of a UK population of BS patients. The majority of patients experience moderate to severe chronic MSK pain. Severe generalised MSK pain is more prevalent in those with high BS disease activity. We have demonstrated a relationship between high disease activity, worse pain intensity, and comorbid FMS. Our findings pose new questions into the research of pain in BS. Further studies are required to explore the mechanism of generalised pain and its correlation with disease activity.
Disclosure of Interests: None declared
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POS0023 PREVALENCE AND IMPACT OF FIBROMYALGIA SYNDROME IN A COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Fibromyalgia (FM) is a common chronic disorder characterized by widespread pain, fatigue, sleep disturbances and functional symptoms, reaching a prevalence of 2–3% worldwide. It can present as a comorbidity in patients with concomitant chronic disease and can have a significant impact on the quality of life. There are very few studies on the prevalence and the impact of FM in patients with inflammatory bowel disease (IBD).
Objectives: The aims of this study were to assess the prevalence of FM in a cohort of patients with IBD, and to evaluate the impact of FM on the quality of life of those patients.
Methods: Consecutive patients with IBD were enrolled from August to November 2021 in two IBD units, patients with severe disease activity according to the Crohn's disease activity index (CDAI) and to the Mayo score for UC, or with other concomitant chronic diseases were excluded. Clinical and demographic data and Patient Reported Outcomes (PROs) (Widespread Pain Index (WPI), Symptom Severity Score (SSS), IBD Questionnaire (IBD-Q), Depression anxiety stress scales-21 (DASS-21), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Impact of event scale-revised (IES-R), Pittsburgh Sleep Quality Index (PSQI)) were collected. FM was diagnosed according to 2011 ACR classification criteria by an expert rheumatologist. Mann-Whitney test, chi-square test, and Student t test were used for statistical analyses. A multivariate analysis was performed to estimate the effect of independent variables (BMI, age, CRP, CDAI, Mayo score, WPI, DASS-21, FACIT-F, PSQI) on patients' quality of life (IBD-Q). A p value < 0.05 was considered as significant.
Results: A total of 196 IBD patients were enrolled (86 female (44%) with a mean age of 50 ± 15 yo), 105 with Crohn's disease (CD) and 91 with ulcerative colitis (UC). 147 patients were in remission, 35 had low disease activity and 14 moderate disease activity. The overall prevalence of FM in the IBD cohort was 17/196 (8.7%) [95% IC 5% – 13%], 10 (11.6%) women and 7 (6.3%) men; with a prevalence of 7.6% (8/105) in CD and 9.9% (9/91) in UC.
In Table 1 are indicated the characteristics of patients with IBD + FM and IBD alone. No significant demographic and clinical differences between the two groups were detected.

Table 1.

	IBD + FM (n=17)	IBD without FM (n=179)	p
Female/Male (%)	10/7 (59%/41%)	75/102 (42%/58%)	0.19
Age, years (SD)	56.8 (± 13)	48.5 (± 17)	0.06
BMI (SD)	21 (± 8.7)	23.7 (± 4.8)	0.46
CD (%)/UC (%)	8 (47%)/9 (53%)	97 (54%)/82 (46%)	0.57
CRP, median (SD)	0.16 mg/dL (± 2.8)	0.2 mg/dL (± 1.5)	0.87
IBD remission	14 (82%)	133 (74%)	0.33
IBD low disease activity	1 (6%)	34 (19%)	
IBD moderate disease activity	2 (12%)	12 (7%)	
Ongoing conventional treatment	6 (35%)	70 (39%)	0.27
Ongoing biological treatment	11 (65%)	112 (63%)	0.42
PROs			
IBD-Q	150.3	176.9	<0.001
DASS-21 DEPRESSION	15.3	8.24	<0.001
DASS-21 ANXIETY	16.6	9.13	<0.001
DASS-21 STRESS	13.4	6.13	<0.001
FACIT-F	25.5	38.2	<0.001
IES-R	36.9	16.3	<0.001

The quality of life among IBD patients and IBD + FM patients, assessed with IBD-Q, appear significantly lower (p <0.001) in the second group. Similar results were obtained evaluating depression, anxiety, stress, chronic fatigue, and patients' discomfort (Table 1).

The multivariate analysis demonstrated that the variables influencing the quality of life (IBD-Q) were the disease activity (CDAI) (p 0.0256), the chronic fatigue (FACIT-F) (p 0.0061) and sleep disturbances (PSQI) (p 0.0440), for CD; while for UC the only variable that correlate with IBD-Q was the disease activity (Mayo score) (p 0.0129).

Conclusion: FM is a common disorder especially in patients with other concomitant chronic diseases. This study reported a prevalence of FM of 8.7% in IBD patients without any significant differences between CD and UC. Moreover, the comorbidity of FM in IBD can have a considerable impact on quality of life and on measures of disease severity, with worst values in all PROs measurements.

Disclosure of Interests: None declared

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POS0024 PREDICTION OF SPONTANEOUS IMPROVEMENT IN PATIENT REPORTED OUTCOME SCORES IN OSTEOARTHRITIS USING MARKERS OF JOINT TISSUE TURNOVER

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Background: Osteoarthritis (OA) is a chronic disease characterized by pain and disability. There is no modifying treatment approved for OA today. This may be attributed to the difficulty generating a robust response based on patient-reported outcomes (PROs) linked to the drug mode of action. There is a need in drug development to test and validate biomarkers that objectively relate to PROs or even predict changes in PROs. Biomarkers of cartilage and bone turnover are associated with structural and symptomatic progression.[1] In addition, recent findings suggest that a subset of OA patients have elevated serum levels of C-reactive protein metabolites (CRPM), which is predictive of radiographic progression.[2,3]

Objectives: This explorative study aimed to investigate the association between PROs and markers of joint tissue formation and degradation in patients with either high or low levels of CRPM. In particular, whether levels could predict spontaneous improvement in PROs.

Methods: 146 knee OA patients, 62% women, from the NYU cohort were included.[4] Mean (SD) age, 62.5 (10.1); BMI, 26.6 (3.6); 32% NSAID users; and 67.6% w. radiographic OA (KL≥2). PROs were recorded at baseline (BL) and 2 years (FU), and the current investigation was: WOMAC pain, stiffness, and function. The mean (SD) for WOMAC pain, stiffness, and function were 35.4 (22.9), 40.8 (25.7), and 41.7 (28.3) mm on a 100 mm scale. Twenty-one healthy individuals were included as a reference. Eight serum biomarkers of type I, II, III, and IV collagen degradation (C1M, C2M, C3M, C4M) and formation (PRO-C1, PRO-C2, PRO-C3, and PRO-C4) as well as the inflammatory biomarker CRPM, were assessed at baseline. LN-transformed data was adjusted for race, Sec, age, BMI, and NSAID use when comparing OA to controls and in the predictive model. Marked symptomatic (S) OA was defined as ≥40 mm in either of the WOMAC scores at BL and improvement as 20 mm decreased in any of the scores from BL to FU.

Results: There was no difference in mean marker levels between controls and OA patients. Only C2M correlated with the WOMAC scores at baseline in the ALL population (p <0.001). This correlation was maintained in both the high and low CRPM groups. A high correlation was observed between the PROs and PRO-C4, C1M and C3M, but only in the high CRPM group. Next, we investigated whether the markers could predict symptomatic improvement in patients with marked SOA. A combination of C4M, Age and BMI was predictive of pain improvement in the ALL population (Table 1). Interestingly the predictors were different in the low vs. high CRPM group; PRO-C2, PRO-C3, PRO-C4 and Sex predicted a 20 mm decrease in WOMAC pain in the low group, while C2M alone predicted an improvement in the high CRPM group. Moreover, C2M predicted an improvement in stiffness in the CRPM high, but not in the low CRPM group. C1M and C3M predicted a 20 mm decrease in function only in the high CRPM group.

Conclusion: Levels of the joint tissue markers weew subtle compared to controls. However, the markers, together with sex and BMI, could predict symptomatic improvement. This may provide novel insight into the link between tissue turnover and PROs.

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POS0025 PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG ADULT PATIENTS WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) and attention deficit hyperactivity disorder (ADHD) share some clinical features, and a reduced dopamine function has been proposed for both disorders. ADHD is a chronic condition, marked by persistent inattention, impaired concentration, hyperactivity, impulsivity, emotional lability, anxiety and disorganized behaviour. High rates of comorbidity between ADHD and FM have been reported, as well as some evidence that patients with both conditions experience heightened disease severity.

Table. Prediction of symptomatic regressive OA in patients with symptomatic knee OA. Multiple variate logistic regression including ln-transformed biomarkers and baseline clinical characteristics (age, gender, race, BMI and NSAID use). Not adjusted for multiplicity.

Regressive vs. stable OA		AlL	Low CRPM	High CRPM
		20 mm change[1]	***20 mm change[1]***	***20 mm change[1]***
WOMAC pain	n (%)[2] Predictors AUC [95%-CI] P	61 (41.0) C4M, Age, BMI 0.73 (0.60 - 0.84) 0.0042	35 (34.3) PRO-C2, PRO-C3, PRO-C4, Sex 0.73 (0.62 -0.83) 0.056	26 (50.0) C2M 0.79 (0.58 - 0.92) 0.024
WOMAC stiffness	n (%)[2] Predictors AUC [95%-CI] P	57 (47.4) C2M 0.67 [0.53 – 0.79] 0.020	33 (48.5) None	24 (45.8) C2M 0.85 (0.64 - 0.96) 0.0007
WOMAC function	n (%)[2] Predictors AUC [95%-CI] P	61 (27.8) None	35 (22.7) None	26 (34.6) C1M, C3M 0.83 (0.63 – 0.95) 0.0074

[1]Regressive disease was defined as 10 or 20 mm or more decrease in VAS pain, WOMAC pain, stiffness or function, and 30 mm or 60 mm or more decrease in WOMAC total, over two-years. [2] Rate of regression in percentage in each of the sub-populations.

Objectives: Our purpose was to determine the prevalence of ADHD symptoms in patients with FM and to assess the relationship with disease impact.
Methods: Consecutive patients, older than 18 years, with diagnosis of FM (ACR 2016 criteria) without known cognitive impairment, seen at the Rheumatology Unit between April 2018 and December 2019, were included. At inclusion visit the collected data included Revised Fibromyalgia Impact Questionnaire (FIQ-R) and Health Assessment Questionnaire, Argentine version (HAQ-A). During the Neurology visit, the following tests were performed: Montreal Cognitive Assessment (MoCA) test for evaluating the presence of cognitive impairment, Conners Continuous Performance Test II (CPT II) for the assessment of ADHD, and Wender-Utah Rating Scale (WURS) to retrospectively assess childhood ADHD symptoms. Univariate analysis was performed using t-tests for normally distributed continuous variables, and Wilcoxon rank sum test for non-normally distributed continuous variables. A chi-square or Fisher test was used when appropriate for categorical variables. Predictors that were found to be related to ADHD ($p \leq 0.20$) were then entered into a multivariable logistic regression model.
Results: 60 patients with FM and 71 matched controls without FM or known cognitive impairment were included. FM patients' characteristics are shown in Table 1. 61.7% (n=37) of the patients with FM tested positive for adult ADHD. In 48.6% (18/37) of them, the diagnosis had been missed in childhood. Participants with both FM and a positive adult ADHD screening test did not score significantly higher on the FIQ-R (52.3, SD= 16.1 vs. 47.9, SD= 12.3; p= 0.2693) and HAQ-A (0.693, SD= 0.455 vs. 0.521, SD= 0.428; p=0.1523) compared with patients without ADHD. Retrospectively assessed childhood ADHD was significantly associated with adult persistence (OR 55.1, CI=3.6 to 842.6, p=0.004).

Table 1. Clinical and demographic characteristics of patients with FM.

Characteristics	n=60
Female, n (%)	53 (88.3)
Age (years), mean (SD)	58.3 (14.2)
Time from diagnosis (years), mean (SD)	5.2 (5)
Scholarity (years), mean (SD)	12.9 (3.4)
HAQ-A, mean (SD)	0.627 (0.449)
FIQ-R, mean (SD)	50.6 (14.8)
Cognitive complaint, n (%)	34 (56.7)
Depression, n (%)	35 (58.3)
Anxiety, n (%)	27 (45)
Concomitant personality disorders	39 (65)

Patients with FM had significantly higher prevalence of cognitive impairment (43.3% vs. 16.9%; p<0.0001), childhood ADHD symptoms (31.7% vs. 14.1%; p=0.016) and adult ADHD symptoms (61.7% vs. 23.9%; p<0.0001) than the control group (Figure 1).

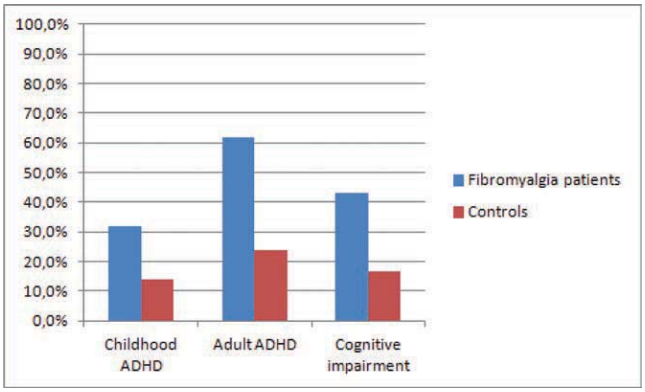

Figure 1. Percentage of FM patients with cognitive impairment, childhood and adult ADHD. Comparison with the control population.

Conclusion: The co-occurrence of adult ADHD in FM was highly prevalent. In nearly half of the patients the diagnosis had been overlooked during childhood and it was associated with adult persistence. The prevalence of cognitive impairment, and childhood and adult ADHD was higher in patients with FM compared with the control group. ADHD was not associated with the FM impact. Evaluation of ADHD symptoms in patients with FM is important for recognition and treatment of this comorbidity.
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POS0026

LOSS OF PRODUCTIVITY IN MILD, MODERATE, AND SEVERE FIBROMYALGIA FEMALE WORKERS: CROSS-SECTIONAL STUDY

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Background: Patients suffering from FM are challenged by symptoms such as chronic pain, fatigue, sleep disturbance and emotional distress. These symptoms lead to a physical capacity impairment, and FM patients report consequences on their activities of daily life and difficulties in fulfilling their work roles, resulting in reduced work capacity, presenteeism (coming to work despite health or personal issues, often resulting in a loss of productivity), absenteeism, and inability to work. Changes in ability to work are crucial to comprehend since they provide a more objective sign of function than other self-reported measures.
Objectives: To assess (a) the impacts of fibromyalgia (FM) symptoms on patients' ability to work and (b) the relationship between FM severity level and lost productivity from the perspective of patients.
Methods: FM female patients were retrospectively evaluated for this cross-sectional study. FM severity was determined using the revised Fibromyalgia Impact Questionnaire (FIQR). Work Productivity and Activity Impairment-Fibromyalgia (WPAI-FM) was used to evaluate patients' employment status. Differences across FM severity states were evaluated using the one-way analysis of variance (ANOVA) and chi-square or Fisher's exact test. The Pearson's r test was performed for the correlation analysis.
Results: The study included 209 subjects, 64 (30.6%) had mild, 64 (30.6%) had moderate, and 81 (38.8%) had severe FM; 57.9% were working full-time, and 42.1% were working part-time. According to WPAI-FM the work productivity and activity impairment resulted: absenteeism 7.03%; presenteeism 44.35%; activity impairment 47.24%; overall work productivity loss 58.23%. Disease severity was associated with decreased work productivity. Presenteeism, overall work productivity loss, and activity impairment demonstrated significant correlations with FIQR and PainDETECT Questionnaire.
Conclusion: FM severity is associated to a reduced job productivity. Early identification and treatment of FM may provide a window of opportunity for job preservation.
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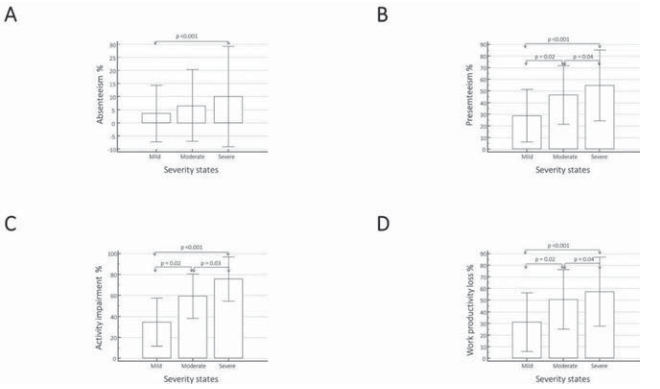

Figure 1. WPAI-FM scores (**A**, absenteeism; **B**, presenteeism; **C**, activity impairment; **D**, work productivity loss) across FM severity states.

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POS0027

SPONDYLOARTHRITIS AND COMORBID FIBROMYALGIA IN PATIENTS WITH ACUTE ANTERIOR UVEITIS: CLINICAL AND ULTRASONOGRAPHIC ASSESSMENT

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Background: Musculoskeletal pain is an important feature in patients (pts) with anterior acute uveitis (AAU), as a symptom of spondyloarthritis (SpA). Fibromyalgia (FM), which is more prevalent in pts with chronic inflammatory diseases, has a widely recognized effect on both differential diagnosis and evaluation of outcome measures in SpA.

Objectives: To estimate the prevalence of primary FM and concomitant FM and SpA in a cohort of pts with AAU, and to compare clinical and ultrasonographic findings in SpA pts with (SpAFM+) and without (SpAFM-) concurrent FM and SpA.

Methods: 152 consecutive pts affected by AAU from the Immunology Eye Unit (AUSL-IRCCS Reggio Emilia, Italy) were enrolled.

A complete rheumatological assessment, including 68/66 peripheral joint count, Leeds Enthesitis Index (LEI) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), and Fibromyalgia Impact Questionnaire (FIQ) was performed.

Using an Esaote MyLabClass, 18-6MHz linear multifrequency transducer, 6 entheses (lateral epicondyle, distal quadriceps insertion, proximal and distal patellar tendon insertions, calcaneal insertion of Achilles tendon and plantar fascia) were evaluated bilaterally for the presence of any elementary lesion, structural damage and active enthesitis, according to OMERACT definitions[2].

Pts were classified as having SpA and/or FM according to ASAS criteria and 2010 ACR diagnostic criteria for FM, respectively.

Results: 103 pts were diagnosed with anterior acute non granulomatous uveitis (AANGU) and 49 with anterior acute granulomatous uveitis (AAGU) (F/M 93/59, age 46.2±12.3 years, BMI 25±5.1, disease duration 43.8±85.2 months).

14 pts (9.2%) met the ACR criteria for FM, of whom 8 pts had concomitant FM and SpA. All FM pts had AANGU. FM pts showed significantly higher enthesitis count and report worse disease activity and function scores (Table 1). Fulfillment of ASAS criteria was associated with FM (p=0.004).

Table 1. Demographic and clinical data of FM patients (results for continuous variables expressed as mean ± standard deviations, for discrete variables as n° and percentage)

	FM + (14)	FM - (138)	p	OR (95%CI)
Age	48 ± 11.7	46.1 ± 12.4	0.569	
Female	10 (71.4%)	83 (60%)	0.409	
BMI	24.7 ± 5.5	25 ± 5.2	0.831	
AANGU	14 (100%)	89 (64.5%)	0.005	
SpA	8 (57%)	30 (22%)	0.004	4.8 (1.6 – 14.9)
ax-SpA	6 (43%)	18 (13%)	0.004	5 (1.6 – 16.1)
Psoriasis	2 (14.3%)	9 (6.5%)	0.268	
IBP	7 (50%)	19 (14%)	0.001	6.3 (2 – 19.9)
Buttock pain	9 (64%)	24 (17%)	<0.001	8.6 (2.63 – 27.8)
History of enthesitis	7 (50%)	20 (14.5%)	0.001	5.8 (1.9 – 18.6)
TJC	2.6 ± 3.8	0.6 ± 1.8	0.072	
LEI	1.9 ± 1.2	0.5 ± 1	<0.001	
MASES	3.8 ± 3.4	0.8 ± 2	0.07	
BASDAI	5.1 ± 1.7	1.8 ± 1.7	<0.001	
BASFI	2 ± 1.4	0.6 ± 1.2	<0.001	
FIQa	0.6 ± 0.6	0.3 ± 0.8	0.176	
FIQb	4.2 ± 2.3	1.1 ± 1.8	<0.001	
FIQc	1.9 ± 2.4	0.4 ± 1.3	0.044	
FIQd	38.9 ± 13.5	16.2 ± 13.9	<0.001	

SpAFM+ pts more frequently reported an history of enthesitis [75% vs 23.3% p=0.011 OR 9.9 (95% CI 1.6 – 60.2) and buttock pain [75% vs 33.3% p=0.034 OR 6 (95% CI 1.02 – 35.3)] when compared with SpAFM-, whereas no significant differences in LEI, MASES, joint count, and inflammatory back pain (IBP), as well as in sex, age and BMI were observed.

BASDAI, FIQb and FIQd were increased in SpAFM+ (6±1.1 vs 3.4±1.8 p<0.001, 4.3±2.1 vs 1.7±2.2 p= 0.005 and 43.6±11.4 vs 24.6±15.5 p=0.003 respectively).

Abnormal US findings were detected in 35/38 SpA pts (92.1%), without significant differences in elementary lesions and structural damage between SpAFM+ and SpAFM-. At patient-level, a significantly higher percentage of SpAFM+ pts had at least one active enthesitis, as compared with SpAFM- (25% vs 3.4%, p = 0.048).

Conclusion: Comorbid FM was frequent in SpA associated with AANGU, affecting both clinical presentation and outcome measures, whereas no FM patients were found in the AAGU group. In our cohort the role of ultrasonography in discriminate SpAFM- from SpAFM+ is not clear.

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POS0028

THE EFFECTS OF TELEREHABILITATION WITH REMOTELY SPINAL STABILIZATION EXERCISES ON CLINICAL VARIABLES, FUNCTIONAL ACTIVITIES, EXERCISE ADHERENCE AND MUSCLE ARCHITECTURE OF NECK MUSCLES IN INDIVIDUALS WITH CHRONIC NECK PAIN

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Background: Doing a job with functional activity may aggravate chronic neck pain(CNP). Thickness, PCSA of the neck muscles can be improved with exercise. During the Covid-19 pandemic, people has caused an increase in home workload, the frequency of performing functional activities related to performance has increased. The distance between physiotherapists and the patient should be at least 2 meters in clinics due to the risk of transmission. As a result, the importance of telerehabilitation has increased.

Objectives: Our aim is to investigate the effect of remotely spinal stabilization exercises(SSE) with telerehabilitation on clinical variables, the functional activities, exercise adherence and muscle architecture patients with CNP.

Methods: The demographic characteristics were recorded. Pain intensity with Visual Analog Scale (VAS), disability level with Neck Disability Index (NDI), neck awareness with Fremantle Neck Awareness Questionnaire (FreNAQ), the functional capacity levels with neck function capacity evaluation test, the difficulty of functional activities with VAS were assessed. Muscle thickness of M. Sternocleideomastoideus, M. Upper Trapezius, PCSA of M. Longus Colli, M. Cervical Multifidus was evaluated in the resting with 3.5-10 MHz ultrasound. The exercise adherence with Exercise Adherence Rating Scale and exercise program satisfaction with VAS were evaluated. The telerehabilitation group (TG) used exercises videos and video conferences, control group (CG) did SSE in the clinic. To study the effects of the interventions, the outcome measures were compared time-by-group interaction effects, one the within-groups factor (time) and one the between-groups factor (group) by repeated-measures two-way ANOVA. The Mann Whitney-U test was performed to compare two groups for non-parametric data.

Results: Twenty-eight patients were randomly allocated to the TG and the CG. The VAS, NDI, FreNAQ, the functional capacity levels, muscle architecture showed similar changes over time in both groups. Results showed no significant time-by-group interaction effects of VAS, NDI, FreNAQ, the functional capacity levels, the difficulty of functional activities and muscle architecture (p>0.05); a significant effect for time in the VAS, NDI, FreNAQ, the functional capacity levels, the difficulty of functional activities and muscle architecture (p<0.001). There was no difference between the groups in terms of VAS, NDI, FreNAQ, the functional capacity levels, the difficulty of functional activities and muscle architecture. Results showed no significant effect for the group in the VAS, NDI, FreNAQ, the functional capacity levels, the difficulty of functional activities and muscle architecture (p>0.05). Both groups adapted well to the exercise program and were highly satisfied with the SSE (p<0.05).

Conclusion: The VAS, NDI, difficulty of functional activities decreased; FreNAQ, functional capacity levels, architecture of neck muscles increased in both groups after 8 weeks SSE. It was determined that telerehabilitation with remotely SSE was beneficial as face-to-face SSE.

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Disclosure of Interests: None declared

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Genomics, functional genomics and genetic basis of inflammatory arthritis

POS0029 CHARACTERISING THE CLINICAL AND RADIOLOGICAL PHENOTYPE OF PSORIATIC ARTHRITIS: A CLASS I AND II HLA ALLELES STUDY

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease affecting multiple tissues including skin and joints. Few studies have fully explored the association between class I and II HLA alleles and different clinical and radiological manifestations.
Objectives: To examine the association between different class I and II HLA alleles and certain PsA phenotypes.
Methods: Cross-sectional study including patients with PsA over 18 years. All patients fulfilled the CASPAR classification criteria for PsA. Demographic, clinical, laboratory and radiology data were gathered including variables related to joint phenotype, type of skin involvement and response to biological disease-modifying drugs (bDMARDs) treatment. HLA class I (A, B, C) and II (DR, DQ, DP) determinations were performed with high-resolution techniques. We explored possible associations with univariate logistic regression and applied the Bonferroni method to correct for multiple comparisons. bDMARDs resistant patients were defined if failure to two or more bDMARDs.
Results: A total of 246 patients were included. Mean age of the cohort was 59.8 years and 53% were men. Average articular disease duration was 12.4 years. A total of 39.8% patients had axial involvement and 90.7% peripheral, being the polyarticular the most frequent subtype in 48% of cases. Considering the skin, mean disease duration was 22.2 years, being the plaque psoriasis the most frequent subtype in 75.2% of cases. 44.3% of the patients presented a history of dactylitis whilst 24% presented enthesitis. Uveitis was reported in 3.7% of patients and Crohn's disease in 0.4%. 30.9% of PsA patients had erosions in hand or feet x-ray. More than half (59.3%) were treated with bDMARDs with a median exposure of 2 different drugs.
Table 1 shows the HLA I and II alleles with a frequency greater than 5%.

Table 1. HLA class I and II alleles with frequencies greater than 5%

GEN	ALLELE	N	FREQUENCY (%)
HLA-A	02:01	79	23.87
	01:01	51	15.41
	29:02	29	8.76
	03:01	26	7.85
HLA-B	27:05	31	9.06
	44:03	26	7.6
	51:01	22	6.43
	08:01	21	6.14
HLA-C	07:01	39	11.78
	06:02	38	11.48
	04:01	34	10.27
	12:03	32	9.67
HLA-DR	07:01	60	18.13
	01:01	37	11.18
	03:01	28	8.46
HLA-DQ	05:01	60	19.8
	02:02	49	16.17
	03:01	39	12.87
	02:01	29	9.57

HLA-B*27:05 (OR 2.3, CI 95% 1.01-5.47) and HLA-C*02:02 (OR 2.8, CI 95%, 1.08-7.55) were associated with axial involvement. HLA-DRB*03:01 (OR 3.1, CI 95%, 1.22-8.36) and HLA-DQ*02:01 (OR 3.24, CI 95%, 1.3-8.82) were associated with the polyarticular subtype, HLA-B*08:01 (OR 5, CI 95%, 1.81-14.33), HLA-C*07:01 (OR 2.65, CI 95%, 1.19-5.76) and HLA-DQ*02:01 (OR 2.55, CI 95%, 1.03-6.11) with enthesitis; HLA-A*29:02 (OR 2.68, CI 95%, 1.12-6.75) and HLA-A*11:01 (OR 2.77, CI 95%, 1.06-7.78) with dactylitis; HLA-C*06:02 (OR 2.33, CI 95%, 1.09-5.06) with nail psoriasis; HLA-C*04:01 (OR 3.52, CI 95%, 1.18-9.64) with palmo-plantar psoriasis; HLA-C*06:02 (OR 4.5, CI 95%, 1.33-23.7) and HLA-C*12:03 (OR 3.59, CI 95%, 1.05-19.05) with plaque psoriasis and HLA-A*24:02 (OR 3.03, CI 95%, 1.17-7.92) with erosions. No association was found between alleles and bDMARD resistant PsA patients.
Conclusion: In our cohort, we have confirmed previously described associations in the literature[1] and found new significant associations with clinical and radiographic PsA manifestations including class II HLA analysis.
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POS0030 CLINICAL AND GENETIC FACTORS ASSOCIATED WITH RADIOGRAPHIC PROGRESSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a heritable inflammatory disease eventually leading to spinal fusion [1]. Severity of structural damage is highly variable, some patients develop almost no change in spinal structure for long disease duration, whereas others have total ankylosis even in the early stage of disease.
Objectives: To identify clinical and genetic factors associated with severe radiographic damage in patients with AS.
Methods: We newly generated genome-wide variant data (833K, KoreanChip) of 444 AS patients. The severity of radiographic damage was assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). To identify clinical and genetic factors associated with severe radiographic damage, multiple linear regression analyses were performed. Human AS osteoprogenitor cells were used for functional validation. Pathway analysis was also conducted.
Results: A total 444 AS patients (male 90.3%) were enrolled. The median mSASSS at baseline was 7.7 (5.5-16.8). The patients were observed for 9.6 (7.9-11.3) years. Within this period, the median mSASSS score increased to 14.0 (7.0-36.8). The most influential clinical factor of final mSASSS was baseline mSASSS ($\beta = 0.818$, $p < 0.001$). Peripheral joint involvement was associated with decreased possibility of severe radiographic damage ($\beta = -0.221$, $p < 0.001$). Eye involvement, longer follow up duration, and increased age at enrollment were associated with increased final mSASSS ($\beta = 0.165$, $p < 0.001$; $\beta = 0.039$, $p < 0.001$; $\beta = 0.010$, $p = 0.002$, respectively). Ryanodine receptor 3 (RYR3) gene was associated with severe radiographic damage ($\beta = 1.105$, $p = 1.97x10\text{-}06$). Treatment with Rhodamine B, a ligand of RYR3, induced extracellular matrix mineralization of AS osteoprogenitors in vitro. For the pathway analysis, PI3K-Akt signaling pathway and focal adhesion pathway were associated with severe radiographic damage in AS.
Conclusion: This study identified clinical and genetic factors that contributed to better understanding of the pathogenesis and biology associated with radiographic damage in AS.
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Genomics, functional genomics and genetic basis of inflammatory arthritis

POS0031 FUNCTIONAL GENOMICS INVESTIGATION OF THE ANKYLOSING SPONDYLITIS ASSOCIATED LOCUS RUNX3

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Background: Ankylosing Spondylitis (AS), is a highly heritable disease with >100 genomic loci incriminated. Among these, RUNX3, a transcription factor (TF) involved in diverse immunological processes, is robustly (10^{-15}) associated. [1] We have extensively investigated the single nucleotide polymorphism (SNP) *rs4648889* located in a 2kb regulatory locus upstream of the *RUNX3* promoter. We have demonstrated that the association between AS and this SNP can be explained by allele-specific effects on TF recruitment (including IRF4, IRF5 and the NuRD complex) that alter gene expression, specifically in CD8+ T-cells, and having a crucial role in CD8+ T-cells function. [2, 3]
Further, we have recently shown a clear chromatin looping event between the region encompassing SNP *rs4648889* and the RUNX3 promoter confirming the functional role of this genetic variant. [4]
Objectives: The purpose of this work is: (1) to better characterise the chromatin looping landscape of the whole AS-associated *RUNX3* genomic locus and (2) to determine the single-cell expression of the *RUNX3*-related genes identified previously [2, 3] in CD8+ T-cells lymphocytes.
Methods: (1) Chromosome conformation capture (3C) technique followed by qPCR was performed to define the chromatin looping events at the *RUNX3* genomic locus in relevant cell lines, including Jurkat T-cells and U937 monocytes-like cells. (2) 10X Chromium single-cell (sc) sequencing was performed to define *RUNX3* and *RUNX3*-related genes expression profile in CD8+ T cells obtained from AS cases.
Results: (1) In addition to the recent results published, [4] 3C-qPCR experiments revealed a high interaction frequency between the distal promoter of RUNX3 and an intronic region (called Int2), overlapping open chromatin and TF binding sites. This was highly reproducible in both cell lines analysed. (2) Four different clusters were identified in CD8+ T-cells obtained from AS peripheral blood via 10x sc-seq based on the expression of *RUNX3*. Five other genes (*TBX21*, *EOMES*, *CHD4*, *IRF5* and *IKZF3*) previously identified [2] were considered: cluster 1 showed a strong co-expression for RUNX3, IKZF3, CHD4 and EOMES. Further analysis is required to better characterize this subpopulation.
Conclusion: The AS-associated *RUNX3* genomic locus has a plausible functional role in AS, probably by regulating gene transcription and DNA looping. These observations are critically important in defining dysregulated pathways and potential therapeutic drug targets.
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POS0032 FUNCTIONAL ROLE OF SURVIVIN IN ORGANIZATION OF BIVALENT CHROMATIN REGIONS AND CONSEQUENCE FOR ARTHRITIS-RELEVANT GENE EXPRESSION

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Background: Bivalent chromatin (BvCR) is characterized by the presence of simultaneous active and repressive modifications on histone H3 proteins. Influencing expression of the genes, BvCR determine cell fate and direct differentiation and lineage commitment in primary T cells and contribute to autoimmunity. Survivin is highly expressed during cell division and in effector Th1 cells contributing to aggravation of autoimmune inflammation. Survivin can physically bind to DNA, specifically to Threonine-3 of histone H3 (1). Thus, functional, and mechanistic data point to a potential chromatin regulatory role for survivin, potentially acting in combination with histone epigenetic modifications (EMs).
Objectives: The goal of our study is to establish the colocalization of survivin with BvCRs and to deduce functional effects of this collaboration on chromatin organization and gene expression.
Methods: Chromatin from CD4+ T cells of 14 female subjects was immunoprecipitated with survivin antibodies and histone H3K27ac, H3K27me3, H3K4me3 antibodies, and coupled with DNA sequencing (ChIPseq, Hiseq2000, Illumina). BvCR were identified as exact overlaps of the three histone EM peaks and the overlapping regions were searched for co-localization with survivin using the 'ChIPPeakAnno' Bioconductor package. Tag counts K27me3>K27ac were defined as inactive/poised BvCR, while tag count K27me3<K27ac were identified asactive BvCR. Motif search was done through the MEME tool, and high/moderate complexity motifs with E-value >10e-5 were selected and scanned through the HOCOMOCO database to identify consensus transcription factor (TF) motifs. TFs co-localized with the BvCD were identified through ReMap database. To identify survivin sensitive genes, $CD4^+$ T cells were treated with survivin inhibitor YM155 and a list of reproducible DEG (log2FC>[0.4], >1 experiment) was mapped and analysed for clustering with BvCR.
Results: Co-localization of survivin ChIP peaks with individual H3-peaks was significantly less frequent compared to overlap with all three (a3)-H3 BvCR (7.1 vs 29.8%, p=8.9e-13). Overlap of a3-H3 peaks not containing survivin was less frequent (34%) compared to those which contained survivin (66%). Notably, survivin peak size was 5.5-fold higher when colocalized with a3-H3 peaks, compared to no, or any single H3 (p<2.2e-16). In contrast, no size difference for any of the H3 EM peaks was found.
Further analysis of two non-redundant groups of BvCR that contain (survivin-a3H3, n=4085), and not containing survivin (a3H3noSurv, n = 2131) demonstrated that survivin was mostly associated with inactive BvCR (OR1.29, p=6.6e-6), while no such specificity was found for BvCR with no survivin. Additionally, survivin containing BvCR contained abundant binding sites matching known consensus TF motifs. No sequence-specific motifs were identified in BvCR with no survivin. Comparison of results obtained through HOCOMOCO and ReMap databases resulted in a list of 68 unique TFs. Many of those are key regulators of adaptive immune responses, cellular metabolism, and pluripotency. Differentially expressed genes mapped to BvCR demonstrated enrichment for cellular hormone metabolic processes, regeneration and DNA biosynthesis.
Conclusion: This study provides experimental evidence that survivin defines binding specificity in bivalent chromatin regions being associated with regulation of cellular metabolism and renewal of $CD4^+$ T cells that are functionally important to resist autoimmunity.
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POS0033 GENETIC INVESTIGATION OF TUMOUR NECROSIS FACTOR INHIBITOR IMMUNOGENICITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that primarily affects the synovial joints. Tumour Necrosis Factor inhibitor (TNFi) therapy has transformed the clinical management of RA. However, monoclonal antibody derived TNFi is associated with development of immunogenicity and subsequent loss of therapeutic effects. Previous studies have observed associations between certain HLA alleles and TNFi immunogenicity. For example

HLA-DQA1 and *HLA-DRB1* have been associated with immunogenicity in inflammatory bowel disease [1,2] and RA [3,4], respectively.

Objectives: The aims of this study were to identify associations between HLA alleles and immunogenicity to TNFi in an observational cohort of RA patients and to replicate findings from previous studies.

Methods: Anti-drug antibody titres were measured using radioimmunoassay in serum samples from RA patients participating in Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). An anti-drug antibody titre of ≥12 AU/mL following six months on treatment was used to define positive immunogenicity. Genotype data were generated using Illumina HumanCoreExome Arrays. Standard quality control (QC) was applied prior to HLA imputation using SNP2HLA software before low minor allele frequency markers were removed. Logistic regression was used to study the association between HLA alleles and immunogenicity, whilst the omnibus test was applied to amino acid positions; sex and concurrent conventional synthetic DMARD use were included as a covariate in all the models.

Results: In total, 445 RA patients were analysed, 377 patients (70 immunogenicity events) were underdoing adalimumab therapy and 68 certolizumab (30 immunogenicity events) therapy. Following QC, 162 HLA alleles and 361 amino acids positions were available for analysis. The strongest HLA allele association was observed for *HLA-DQA1**03 when all patients were analysed (OR = 0.61; 95% CI = 0.43 – 0.86; p-value = 5e-3). The amino acids positions 187 (p-value = 5e-3) and 26 (p-value = 5e-3) within the *HLA-DQA1* gene were significantly associated with immunogenicity events. When both drugs were analysed separately, they produced similar effect size for HLA-DQA1*03 association; patients treated with adalimumab (OR = 0.59; 95% CI = 0.38 – 0.88; p-value = 1e-2) and certolizumab (OR = 0.52; 95% CI = 0.24 – 1.1; p-value = 1e-1). Another strong association was found in HLA-DRB1*04 (OR = 0.62; 95% CI = 0.44 – 0.88; p-value = =7e-3) and the amino acid position of 180 (p-value = 7e-3) and 33 (p-value = 7e-3) of HLA-DRB1 gene. Additionally, the similar protective effect between the two presented alleles suggested possibility of linkage disequilibrium, upon investigation the r^2 between the 2 alleles is 0.69.

Conclusion: The current study increases the evidence for association between immunogenicity development with HLA-DQA1 and HLA-DRB1 alleles in patients receiving monoclonal antibody derived TNFi therapy. Further well powered studies are now required to determine the utility of HLA markers as a potential tool to aid the clinical management of RA.

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POS0034 GENETIC FACTORS OF PREDISPOSITION TO JUVENILE IDIOPATHIC ARTHRITIS AND OTHER ARTICULAR PATHOLOGY IN BELARUSIAN POPULATION

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Background: Juvenile idiopathic arthritis (JIA) is a multifactorial autoimmune disease and. JIA exhibits clinical heterogeneity and is divided into seven phenotypic subtypes. The outcome of JIA is often difficult to predict, and differential diagnosis is significantly complicated by the variety of causes of joint pain and the similarity of the clinical picture of articular syndrome, especially in the early stages of disease development.

Objectives: to detect genetic markers, associated with the risk of developing JIA, its distinct subtypes and another joint pathology in children.

Methods: 951 individuals were divided into three cohorts: 281 children with JIA (mean age 9.14±4.84), 214 children with articular syndrome in case of another joint pathology (post-infectious, post-traumatic and reactive arthritis, osteochondropathy and arthralgia; mean age 9.50±4.75) and 456 healthy controls (mean age 14.36±2.54). The JIA patients were divided into subgroups according to IIAR classification criteria. 9 SNPs of 8 genes (*IL6* (rs1800795), *IL6R* (rs2228145 and rs4845618), *STAT4* (rs7574865), *TRAF1/C5* (rs3761847), *RUNX1* (rs9979383), *PTPN2* (rs2542151), *PTPN22* (rs2476601), *FOXP3* (rs2232365)) were genotyped using Real-time PCR or PCR-RFLP.

Results: The allele frequencies of the polymorphic loci of the *FOXP3* (rs2232365), *RUNX1* (rs9979383), *PTPN2* (rs2542151), *PTPN22* (rs2476601) genes in all three groups were comparable, indicating no association with the risk of development of joint pathology in children. It was shown that CC genotype at the rs1800795 locus of the *IL6* gene is associated with JIA (OR 1.49 [1.05–2.13], p=0.026), while the GC genotype revealed protective effect (OR 0.69 [0.51–0.93], p=0.014). In addition, a weak association of GG homozygotes at the *TRAF1/C5* locus (rs3761847) with the risk of developing JIA was found (OR 1.47 [1.00-2.16], p = 0.05). Homozygous GG genotype at the rs3761847 *TRAF1/C5* and CC at the rs1800795 *IL6* loci, as well as the corresponding G and C alleles, were associated with early JIA onset (under the age of 6 years).

At the same time, CC homozygotes (OR 2.45 [1.50–3.97], p=0.0003) and C allele (OR 1.33 [1.05–1.69], p=0, 02) at the rs2228145 locus, as well as TT homozygotes (OR 1.54 [1.06–2.23], p = 0.026) at the rs4845618 locus of the *IL6R* gene were associated with joint pathology except JIA. Moreover, minor alleles, as well as the corresponding homozygous genotypes of polymorphic *IL6R* loci were significantly more common among children with other articular pathology when compared with the JIA cohort.

The association revealed for the CC genotype at the rs1800795 locus of the *IL6* gene in the general JIA group preserved in the group of oligoarticular JIA (OR 1.59 [1.04–2.41], p=0.033) while GG genotype at rs3761847 locus of the *TRAF1/C5* gene was associated with systemic JIA (OR 2.82 [1.29 – 6.15]; p = 0.013), and rheumatoid factor-negative polyarthritis was characterized by higher frequency of GT/TT genotypes at the *STAT4* rs7574865 locus (OR 1.85 [1.06–3.24], p = 0.03).

Conclusion: Thus, the *IL6* gene polymorphism increases the sensitivity of the Belarusian population to JIA, while the *IL6R* gene polymorphism affects the development of other joint pathology.

It was found that JIA subtypes significantly differ from each other by the molecular profiles of non-HLA genes. This suggests that JIA is represented by a spectrum of genetically distinct subtypes that differ in clinical course and response to therapy.

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POS0035 GENE REGULATION IN T-CELLS FROM PSA PATIENTS DIFFERS BETWEEN PERIPHERAL BLOOD AND THE INFLAMED JOINTS: IMPLICATIONS FOR THE INTERPRETATION OF GWAS SIGNALS

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Background: Genome-wide association studies (GWAS) have identified variants that are associated with complex diseases such as Psoriatic Arthritis (PsA). The majority of these variants do not affect the coding sequence of proteins but rather regulatory elements which are highly cell type and state specific, and can affect distally located genes via chromatin interaction mechanisms.

We and others have previously analysed GWAS loci for multiple conditions (including PsA and Rheumatoid Arthrtitis) in cell lines using functional genomics techniques, providing putative mechanisms to many loci with previously unknown function [1].

However, multiple studies have identified large differences in gene regulatory mechanisms between cell lines and primary cells, which could significantly alter the proposed mechanisms. Differences between between samples from healthy volunteers and patients, in particular from the affected tissue, have although not been exhaustively investigated.

Objectives: To assess the impact of using primary cells derived from PsA patients compared to healthy volunteers in functional genomics studies.

Methods: CD4+ and CD8+ T cells were isolated from peripherial blood from 10 healthy controls and 48 PsA patients and from 6 PsA synovial fluid samples. We performed RNA-seq and ATAC-seq on these two cell types to analyse the global patterns of gene expression and chromatin activity.
Results: We find subtle differences between PsA patients and healthy controls in cells isolated from blood. RNA-seq analysis identified only a handful of differentially expressed genes whilst ATAC-seq analysis identified only 28 differential loci. On the other hand, T cells isolated from synovial fluid showed significant differences compared to T cells isolated from patient's blood. Interestingly, we find that CD4+ T cells show substantially more differentially expressed genes compared to CD8+ T cells (1168 vs 346 Log2FoldChange > 1, FDR < 0.01). Genes overexpressed in synovial CD4+ T cells are more strongly enriched for immune pathways such as cytokine signaling and T cell proliferation compared to synovial CD8+ T cells
We also find that synovial CD4+ T cells highly overexpress MHC class II genes (Figure 1).

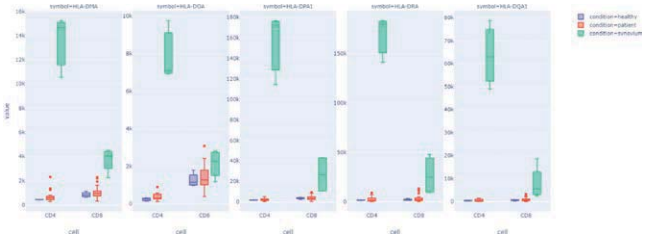

Figure 1. Normalized counts of the alpha chains of MHC class 2 genes in CD4+ and CD8+ T cells purified from blood from healthy subjects and patients and synovial fluid.

Conclusion: This preliminary analysis suggests that T cells isolated from peripherial blood do not seem to differ significantly between PsA patients and healthy controls. In contrast, cells isolated from synovial fluid are highly specialized and activated. Moreover, these cells do not resemble canonically activated T cells which means that this state can not be easily emulated in vitro.
This study indicates the importance of not only studying GWAS loci in relevant primary cells from patients, but also that attention needs to be given to cells isolated from the affected site.

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POS0036 CORRELATION BETWEEN SYSTEMIC AND LOCAL EXPRESSION LEVELS OF MIR-146A, MIR-155 AND MIR-223 AND THE ONGOING TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS

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Background: MicroRNAs (miRNAs) comprise a class of small, non-coding RNAs that serve as important negative regulators of gene expression at posttranscriptional level. Studies have shown remarkable changes in miRNA expression in autoimmune diseases, such as rheumatoid arthritis (RA) which makes them a potential systemic as well as local biomarkers for disease activity (1-3). On the other hand, regulation of miRNA on transcriptional and posttranscriptional level, as well as the effects of endogenous and exogenous factors on miRNA expression is under investigation. Of importance is the possible effect of the ongoing treatment on miRNA expression in the clinical practice.
Objectives: To analyze the expression levels of miR-146a, miR-155 and miR-223 in peripheral blood (PB) and synovial fluid (SF) from RA patients in regard to the ongoing treatment regimen.
Methods: A total number of 63 RA patients according to the 1987 ACR criteria were included in the study. Expression levels of miR-146a, miR-155 and miR-223 in 63 PB samples and matched 48 SF samples were determined by qPCR (SybrGreen technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by $2^{-\Delta\Delta Ct}$ method. 45 of the studied patients were on systemic treatment, which included non-steroidal antiinflammatory drugs (NSAIDs), glucocorticosteroids (GCS), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and original biological DMARDs. There were no patients treated with conventional target DMARDs or biosimilar DMARDs. SPSS was used for statistical analysis.
Results: RA PB showed statistically significant overexpression of miR-223 (58.73%) when compared to HCs and only miR-223 expression levels could be used to differentiate RA patients from HCs (p=0.008). RA SF showed overexpression of miR-146a (in 70.83%, p=0.007), miR-155 (in 79.17%, $p=1.63x10^{-4}$) and of miR-223 (in 79.17%, $p=1.64x10^{-3}$) when compared to HCs and the studied miRNAs could be used to differentiate RA patients from HCs ($p=4.8x10^{-4}$, $p=8.0x10^{-5}$ and $p=2.8x10^{-4}$, respectively). When we analyzed the correlation between the expression of miRNAs and the ongoing treatment we found a statistically significant correlation between the PB expression levels of miR-223 and the use of NSAIDs and GCS (p=0.015 and p=0.04, respectively) and the SF expression levels of miR-146a and miR-155 and the use of NSAIDs (p=0.011 and $7.98x10^{-4}$, respectively) and GCS (p=0.039 and p=0.009, respectively). The use of csDMARDs and bDMARDs didn't show correlation with the PB nor the SF expression of the studied miRNAs.
Conclusion: The correlation between the systemic miR-223 and the local miR-146a and miR-155 expression with the NSAIDs and GCS treatment could be due to the effect of these treatment compounds on the cells lines from which the studied miRNAs origin. In our study there was no correlation between miRNA expression and the use of biological and conventional DMARDs. Further analysis with larger sets including pre- and posttreatment samples is needed to confirm if altered miRNA expression could be influenced by the treatment regimen as well as if miRNAs could serve as biomarkers for treatment response in the clinical practice.

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POS0037 MULTIVARIABLE MENDELIAN RANDOMIZATION STUDY ON BMI-ADJUSTED LINK BETWEEN ADIPONECTIN AND RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Background: Compelling evidence suggests that adiponectin is involved in the pathogenesis of rheumatoid arthritis (RA). Nevertheless, a recent Mendelian randomization (MR) study in Europeans has shown that adiponectin does not have a causal role in the development of RA[1].
Objectives: As body-mass index (BMI) is a known risk factor for RA[2] and subjects with high BMI have lower circulating levels of adiponectin, we specifically aimed to perform a multivariable MR in both European and East Asian populations to determine if adiponectin has a causal effect on RA development independently of BMI.
Methods: We performed a range of two-sample, univariable, MR analyses to assess the causal effect of adiponectin on RA in European and East Asian individuals. Two different sets (12 in Europeans and 5 in East Asians) of adiponectin-related genetic variants were used as instruments for genetically determined adiponectin levels, to calculate its causal effect on RA risk. Multivariable MR was performed to calculate the effect of adiponectin on RA risk after adjustment for BMI.
Results: Univariable MR did not provide evidence of a causal relationship between circulating adiponectin levels and RA risk in both European (OR 1.06; 95% CI 0.87-1.31; p=0.59) and East Asian (OR 1.04; 95% CI 0.91 – 1.19; p=0.54) individuals (Figure 1). Similarly, there was no evidence of a causal effect of

adiponectin on RA in both European (OR 0.97; 95% CI 0.78 – 1.22; p=0.81) and East Asian (OR 0.97; 95% CI 0.72 – 1.31; p=0.85) populations after adding BMI as a confounder in the multivariable MR model (Figure 1).

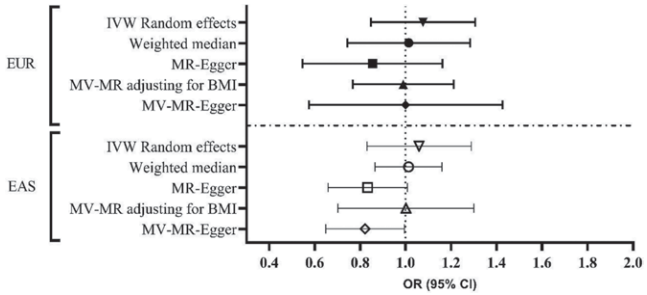

Figure 1. Forest plot of the causal effects of adiponectin-associated genetic variants on rheumatoid arthritis after adjustment for body mass index in a multivariable mendelian randomization (MR) analysis. Shown are European (EUR) and East Asian (EAS) populations. An Odds Ratio (OR) is a measure of association between an exposure and an outcome, in which the OR represents the likelihood that an outcome will occur given a particular exposure, compared to the likelihood of the outcome occurring in the absence of that exposure. Statistical analyses were performed with the use of inverse-variance weighted (IVW) estimate, MR-Egger regression weighted median analysis.

Conclusion: This MR study does not support a causal effect of genetically determined adiponectin levels on the risk of developing RA in both European and East Asian populations. By using multivariable MR to account for possible shared genetic predictors between circulating adiponectin levels and BMI we have shown that circulating adiponectin is not causally linked to RA risk after adjustment for BMI.

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POS0038 GENOMICS OF JAK-STAT SIGNALING IN VENOUS THROMBOEMBOLISM

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Background: Janus kinase inhibitors (JAKi) have been associated with an increased risk of venous thromboembolism (VTE) [1]. VTE comprises deep vein thrombosis and pulmonary embolism and is associated with complications such as recurrent VTE, post thrombotic syndrome, pulmonary hypertension, and death. These concerns limit the use of JAKi-based therapy. To improve risk stratification and drug development, it is crucial to understand the possible implication of dysregulated JAK-signal transducers and activators of transcription (STAT) signaling in the pathogenesis of VTE.

Objectives: The objective of this study is to clarify the putative genomic vulnerability to dysregulated JAK-STAT signaling in VTE.

Methods: We are systematically mine and analyze large-scale genomic datasets generated from studies comparing VTE patients with healthy controls. Using VTE genome-wide associated (GWA) summary statistics we evaluate the representation of genes encoding the JAK-STAT pathway (KEGG hsa04630) in associated loci and assess their association to VTE. Further, we examine the genetic VTE risk burden in the chromatin interactome of STAT family transcription factors (TFs). We extract available STAT family (STAT1-3) TF binding site (TFBS) consensus DNA motifs (JASPAR database) and assess the association of genes containing STAT family TFBS within their promotor sequence (TSS -2000bp) to VTE. Through mining of deposited OMICs data from VTE patients, we examine molecular characteristics related to JAK-STAT signaling, including potential enrichment of STAT family TFBSs among query promoter sequences of differently expressed genes (DEGs).

Results: We do not observe a significant overrepresentation of JAK-STAT genes (n_{total}=162) among genes annotated to VTE significant GWA loci (n_{total}=147, p=0.48). Similarly, the JAK-STAT gene set show no cumulative association to VTE (p=0.98). Applying the same gene set association approach to the STAT target gene sets (n_{total}=4570) does not reveal significant association between VTE and STAT1 ($n_{overlap}$=10, p=0.47), STAT1:STAT2 heterodimer ($n_{overlap}$=18, p=0.17) and STAT3 ($n_{overlap}$=6, p=0.20) target gene sets. At the functional molecular level, we do not see any significant overlap between molecules acting in the JAK-STAT pathway and DEGs (n_{total}=507, p=0.06) or differentially abundant proteins (DAPs; n_{total}=35, p=0.57). However, we observe a significant overlap between downregulated DEGs (n_{total}=362) and the STAT1:STAT2 heterodimer target gene set (n_{total}= 2155, $n_{overlap}$=48, p<0.0001) including downregulation of *IL-27RA* and *CCND3* (Figure 1). Supporting the biological relevance of this finding, we find a weak but statistically significant enrichment of STAT1 TFBS motifs in the promotor sequence of downregulated DEGs compared to non-DEGs (p=0.02).

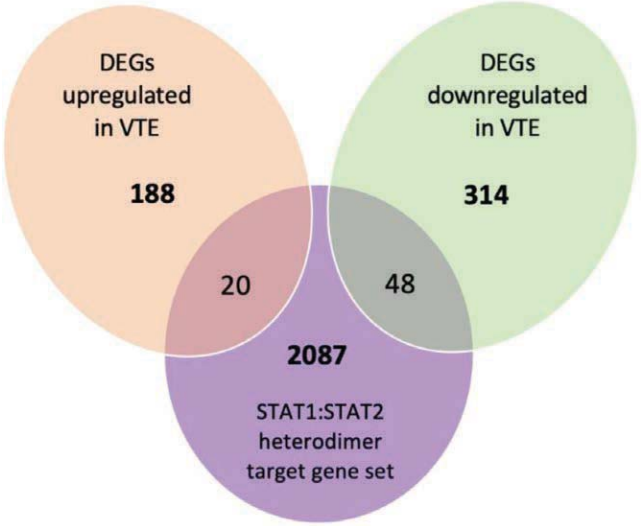

Figure 1. Overlap between STAT1:STAT2 heterodimer gene set and differently expressed genes (DEGs) in venous thromboembolism (VTE)

Conclusion: Here, we provide a coherent approach to assess the genomic basis for the reported association between JAKi treatment and VTE. Our preliminary data suggest that genes under transcriptional control of STAT family TFs may be dysregulated in VTE patients. It is conceivable, that the genomic actions of JAKi is overlapping with the molecular risk profile of VTE. *CCND3* is especially interesting because VTE occurs in up to 10% of patients treated with cyclin-dependent kinase inhibitors such as Palbociclib [2]. Obviously, genomic data mining alone cannot guide medical decision making concerning the use of JAKi. However, our results provide a basis for further investigation of adverse events seen with JAKi.

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POS0039 MONOCYTE TRANSCRIPTOMICS AND TARGETED PROTEOMICS DEFINE HETEROGENEOUS SUBGROUPS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND SUBCLINICAL ATHEROSCLEROSIS

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Background: Systemic lupus erythematosus (SLE), a chronic, inflammatory autoimmune disease, predominantly affects women with a 9:1 female:male incidence. Cardiovascular disease (CVD) is a leading cause of mortality in SLE via accelerated atherosclerosis: the build-up of cells and lipids in the vascular wall and the main pathology underlying CVD.
Objectives: To define molecular profiles of SLE with subclinical atherosclerosis using multi-omics data analysis and clinical data in a well-characterised cohort of CVD-free SLE women.
Methods: Multi-omics analyses were conducted to explore the molecular signatures of SLE patients with (SLE-P) and without (SLE-NP) subclinical atherosclerosis defined by non-invasive ultrasound scanning of the carotid and femoral arteries. SLE blood CD14+ monocyte transcriptomes were investigated by bulk RNA-sequencing (SLE-P N=13, SLE-NP N=8), and targeted serum cardiometabolic and cardiovascular proteomics (OLINK) were used to explore matched protein expression (SLE-P N=17, SLE-NP N=20) (no difference in disease activity between groups). Bioinformatics approaches, including pathway and disease module enrichment analyses and extended protein-protein interaction networks, further defined molecular profiles of SLE patients with atherosclerosis from patients that remained plaque free. Gene signature-derived interferon (IFN) scores were applied to investigate heterogeneous subgroups within the cohort as a measure of inflammation.
Results: Distinct monocyte gene and protein expression profiles were identified in SLE and enriched in biological pathways relating to extracellular mechanisms, including purinergic and cytokine signalling. Lipid regulatory mechanisms were enriched in SLE-P, whereas SLE-NP patient's transcriptome and proteome profiles were defined by pathways relating to inflammation. Specifically, the type-I IFN pathway was exclusively reduced in SLE-P compared to SLE-NP. IFN scores derived from published IFN-responsive gene expression signatures stratified patients into significantly distinct subgroups (high versus low IFN-response, p=0.0001) with 66% (N=14) of patients showing high IFN expression across multiple signatures not associated with age, ethnicity, or disease activity. However, IFN scores did not predict the presence of sub-clinical atherosclerosis and further heterogeneity was revealed with 46% of SLE-P patients showing a low IFN response (N=6). Further, a measure of plaque lipid content (echogenicity) was inversely correlated with IFN score (grey scale median, p=0.03, r=-0.8) which may reflect distinct plaque phenotypes between these subgroups relating to clinical presentation and risk of cardiovascular events.
Conclusion: Lipid dysregulation is a key mechanism that drives atherosclerosis pathology and genes and proteins relating to lipid metabolism distinguished SLE patients with and without subclinical atherosclerosis. Differences in levels of interferons and other inflammatory molecules may contribute to unique patterns of gene expression between SLE patients. A distinct subset of SLE-P patients showed low interferon expression, which may be suggestive of a dampened immune response in early subclinical CVD. Further elucidating the complexity of lipid dysregulation, inflammation and immune function in atherosclerosis in SLE will help improve patient stratification towards investigating the efficacy of anti-atherosclerotic therapies.
Disclosure of Interests: None declared
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HPR Poster Tour: Moving together towards person-centred care

POS0040-HPR **PATIENT PERCEPTIONS OF IMPACT OF GLUCOCORTICOID THERAPY IN THE RHEUMATIC DISEASES: INTERNATIONAL DEVELOPMENT OF A TREATMENT-SPECIFIC PATIENT REPORTED OUTCOME MEASURE**

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Background: Glucocorticoids (GCs) are a key treatment for inflammatory rheumatic diseases, but they cause a wide range of adverse side-effects which are of concern both to patients and clinicians.
Objectives: The objective of this study was to explore the impact of GC therapy on health-related quality of life (HRQoL) during treatment for rheumatic diseases, as a basis for development of a Patient-Reported Outcome Measure (PROM) to be used in clinical trials and practice.
Methods: Patients from the UK, USA and Australia who were treated with GCs in the last two years for a rheumatic condition were invited to take part in semi-structured qualitative interviews. Purposive sampling was used to include participants with a range of demographic and disease features. A steering committee of patient research partners, clinicians and methodologists devised an initial conceptual framework, which informed interview prompts and cues. Interviews were carried out by experienced qualitative researchers who encouraged participants to tell their stories and talk about the effects, both adverse and beneficial, of their experiences and perceptions of treatment with GCs, to identify salient physical and psychological symptoms and aspects of HRQoL. The interview data were organised using NVivo, and inductive analysis identified initial themes and domains. Candidate questionnaire items were developed and refined using cognitive interviewing, linguistic assessment, and input from patient research partners.
Results: Sixty semi-structured qualitative interviews were conducted (UK n=34, USA n=10, Australia n=16). Mean participant age was 58 years; 39 (66.1%) were female. Purposive sampling of participants provided a broad range of demographic features, GC dosages and inflammatory rheumatic conditions, with 27% having connective tissue disease, 25% inflammatory arthritis, 30% systemic vasculitis and 16% other rheumatic conditions.
Initial domains were developed to identify key themes relating to treatment using GCs and their impact on HRQoL; see Figure 1.

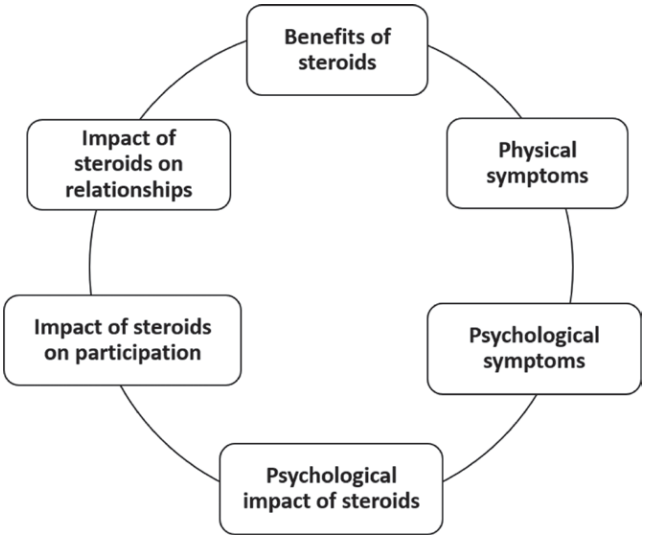

Figure 1. Steroid PRO Initial Themes

A long-list of 134 initial candidate questionnaire items was developed from the individual themes. These items were reviewed by a qualitative working group of patient research partners, researchers and clinicians to reduce duplication and ambiguity of items. The resulting 62 items were tested and refined by piloting with patient research partners, iterative rounds of cognitive interviews with patients with a range of rheumatic conditions from the UK, USA and Australia, and a linguistic translatability assessment, to define a draft questionnaire of 40 items.
Conclusion: This international qualitative study underpins the development of candidate items for a treatment-specific PROM for patients with rheumatic diseases. The draft questionnaire is currently being tested in an online large-scale survey to determine the final scale structure and measurement properties using Rasch analysis, factor analysis, test-retest, comparison with EQ5D, and known groups analysis.
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Emma Dures: None declared, Nilasha Ghosh: None declared, Elizabeth A Hoon: None declared, Suellen Lyne: None declared, Iris Navarro-Millan Consultant of: Honorarium on Swedish Orpham Biovitrum (SOBI) advisory board 2021, Diyu Pearce-Fisher: None declared, Carlee Ruediger: None declared, Joanna Tieu: None declared, Kevin Yip: None declared, Sarah Mackie: None declared, Susan Goodman: None declared, Catherine Hill: None declared, Joanna Robson Speakers bureau: EULAR Symposium 2021 for Vifor Pharma, Consultant of: Honorarium for Vifor Pharma advisory board 2021, Grant/research support from: Vifor Pharma 2020-2022

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POS0041-HPR OUTCOME MEASURES IN RHEUMATOLOGY APPLIED IN SELF-MANAGEMENT INTERVENTIONS TARGETING PEOPLE WITH INFLAMMATORY ARTHRITIS - A SYSTEMATIC REVIEW OF OUTCOME DOMAINS AND MEASUREMENT INSTRUMENTS

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Background: Self-management refers to the patient's ability to manage a large range of consequences such as symptoms, medication, emotions, and preferable life-style changes coherent with living with a chronic disease. Evaluating the effect of interventions targeting to improve people with inflammatory arthritis (IA) self-management is a challenge because self-management interventions are complex and consensus on important outcomes is lacking. Solutions to these issues could be to consensus on a Core Outcome Set (COS) describing what outcomes are relevant and should be applied in future studies hereby lessening the heterogeneity between future studies. The purpose of this study was therefore to take the first actions in identifying possible candidate outcomes for such a COS.

Objectives: The aim was to identify, and map applied outcome domains and outcome measurement instruments from previous trials measuring the effect of self-management interventions targeting people with IA.

Methods: We performed an informative systematic literature review following guidance from the Handbooks described by 'Outcome Measures in Rheumatology' (OMERACT) and 'Core Outcome Measures in Effectiveness Trials' (COMET) initiatives. Randomized and non-randomized trials describing their experimental intervention as "self-management" and included a population of adults (≥18 years) with at least 50% diagnoses with IA (Rheumatoid arthritis, Psoriatic arthritis, Spondylarthritis) was included. Both screening of possible trials and data extraction was performed independently by two reviewers. Extracted data included: study characteristics, outcome domains and the corresponding measurement instruments. During analysis two reviewers simultaneously grouped and categorized domains and subdomains, and two senior researchers approved the categorization.

Results: Searches was performed 2021.02.08 on online databases, trial registers, conference abstracts and references of included trials. From a total of 2,502 records, we included 38 trials published between 1988 and 2021. The interventions were heterogenic and patients primarily female, diagnosed with Rheumatoid Arthritis, and a calculated mean age of 54 years. We identified 12 different outcome domains, covering 39 subdomains, collected with 119 different measurement instruments. The most frequently applied outcome domains were self-efficacy, pain, physical functioning/disability, anxiety and depression, quality of life, fatigue, global assessment/disease activity and coping. Please see Figure 1 for all outcome domains identified. The applied measurement instruments varied within each outcome domain with up to 10 different instruments applied to measure the same domain. Instruments were predominantly patient-reported outcomes.

Conclusion: The outcome domains and measurement instruments used in self-management trials were widely diverse and differ from the current general OMERACT Core Outcome Sets (COS) for IA conditions. Further steps towards the establishment of a COS to be reported in all self-management intervention trials will enhance the relevance and the subsequent impact on the body of evidence from these trials.

REFERENCES: The protocol was registered in **PROSPERO** (ID CRD42021238749).

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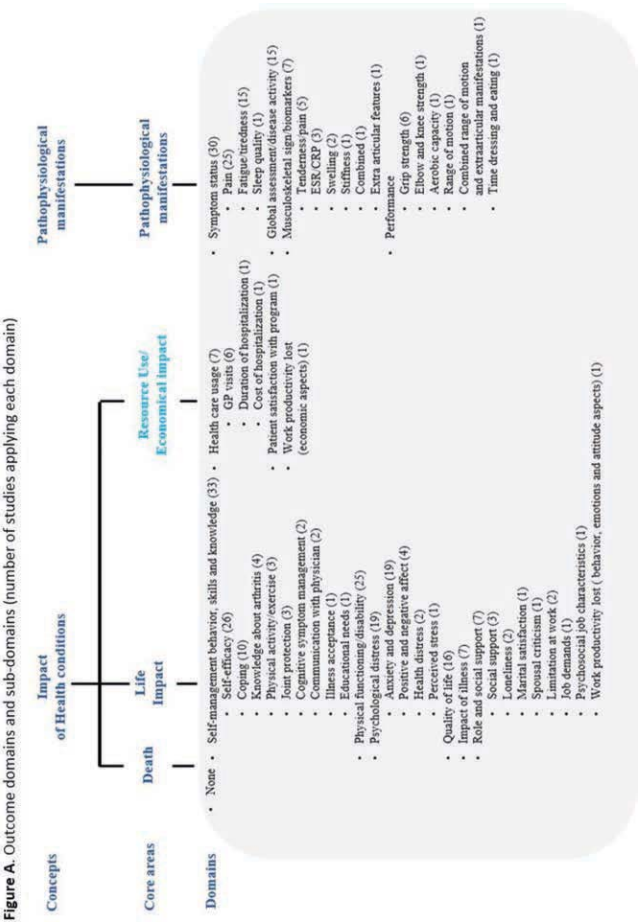

Figure A.

Disclosure of Interests: None declared

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POS0042-HPR HOW DOES WEEKLY SUPERVISED GROUP EXERCISE CONTRIBUTE TO FULFILLING EXERCISE RECOMMENDATIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS?

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Background: Supervised group exercise (SGE) has been recommended for people with axial spondyloarthritis (axSpA) since decades, but the proportion and type of axSpA patients that engage in SGE is unknown. In addition, the 2018 EULAR recommendations for physical activity advocate that people with axSpA should engage in aerobic, strength and mobility exercises according to public health physical activity guidelines. However, it is unclear if SGE contributes to fulfilment of these exercise recommendations.

Objectives: To compare characteristics, health status and fulfilment of exercise recommendations between axSpA patients with and without SGE.

Methods: Cross-sectional data from three Dutch axSpA study cohorts were analysed: two cohorts with patients recruited at rheumatology outpatient clinics (n=196 and n=153) in which participation in SGE was recorded (yes/no) and one cohort with only SGE participants (n=128). Assessments included sociodemographic and disease characteristics, health status (ASAS Health Index), spinal mobility and the 'short questionnaire to assess health enhancing physical activity'

(SQUASH). The SQUASH was used to determine fulfilment of the public health recommendations for leisure-time aerobic exercise (≥150 min/week of moderate-intensity or ≥75 min/week of vigorous-intensity exercise) and for strength and mobility exercises (≥2 sessions/week). Differences between patients with and without SGE were analysed using the Mann-Whitney U test and the Chi-Square test. Multivariate regression models were performed to correct the association between SGE and fulfilment of the exercise recommendations for age, sex, employment and health status.

Results: In the two outpatient axSpA cohorts, 17 of the 349 patients (5%) participated in SGE. The total group of SGE participants (n=145) was significantly older, had longer disease duration, was less frequently employed, used less disease related medication and had worse spinal mobility than the patients without SGE (n=332). There were no significant differences in health status. AxSpA patients with SGE performed more minutes per week of aerobic exercise (median 420; IQR 285-660) than patients without SGE (median 283; IQR 120-540), $p < 0.001$. As shown in Figure 1, SGE participants fulfilled the recommendations for moderate-intensity aerobic exercise (89% vs. 69%, $p < 0.001$) and for strength and mobility exercise (44% vs. 29%, $p < 0.01$) more often than patients without SGE. However, the recommendation for vigorous-intensity aerobic exercise was fulfilled less often by the SGE participants (5% vs. 12%, $p < 0.05$). After correcting for age, sex, employment and health status, the differences in fulfilment of the moderate-intensity aerobic and strength and mobility exercise recommendations remained significant.

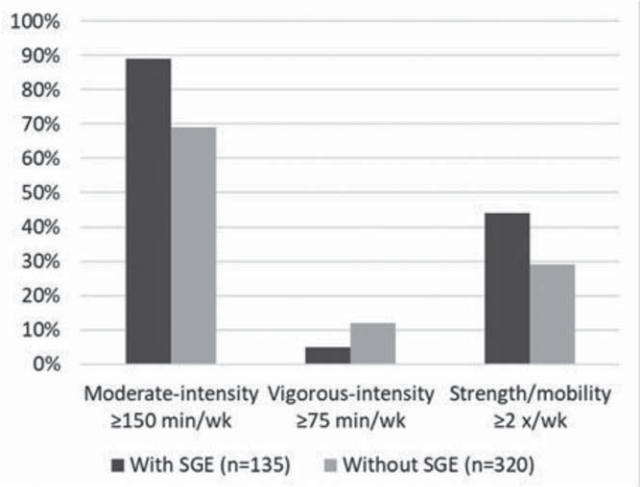

Figure 1. Differences in meeting exercise recommendations between axSpA patients with and without SGE.

Conclusion: SGE is used by just few and especially older axSpA patients and contributes to fulfilling recommendations for moderate-intensity aerobic as well as mobility and strength exercise. However, both in patients with and without SGE, only a minority fulfilled the recommendations for vigorous-intensity aerobic and strength and mobility exercises. Therefore, future promotion of physical activity should focus on implementing these types of exercise.

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POS0043-HPR DO COPING STRATEGIES, ILLNESS PERCEPTIONS AND RELATIONSHIP DYNAMICS CONTRIBUTE TO SEXUAL DYSFUNCTION FOR WOMEN WITH SJÖGREN'S SYNDROME?

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Background: Women with Sjögren's syndrome (SS) are more likely to experience vaginal dryness, dyspareunia and reduced sexual function than healthy controls[1]. There is limited data investigating relationships with psychosocial influences, such as coping mechanisms, illness perceptions, partners behaviours and relationship satisfaction.

Objectives: To investigate associations between sexual function and psychosocial parameters in women with SS.

Methods: Cisgender women aged 18+, diagnosed with SS, were invited to participate in a cross-sectional online survey. Ethical approval and informed consent were obtained. Participants completed the Female Sexual Function Index (FSFI), EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), NRS scale for vaginal dryness (0-10), Profile of Fatigue and Discomfort (ProFaD), Cognitive Emotion Regulation Questionnaire (CERQ), Brief Illness Perceptions Questionnaire (BIPQ), West-Haven Yale Multidimensional Pain Inventory (WHYMPI – Part II) and Maudsley Marital Questionnaire (MMQ – Marital subscale). Associations between the FSFI and the outcome measures were assessed using Spearman's correlations. Variables that significantly correlated with FSFI total score were entered into a backward stepwise multiple regression.

Results: The survey was completed by 98 women (M = 48.13, SD = 13.26), 70.4% were diagnosed as having primary SS (disease duration range = 3 – 348 months); 43.8% were premenopausal and 48% were postmenopausal. Vaginal dryness was reported by 92.9% of participants, and sexual dysfunction was identified in 85.2% (n = 69/81) of cases (<26.55). Participants who were not sexually active in the previous three-month period (n = 17) were excluded from analyses as inactivity may cause a low FSFI score which may be incorrectly construed as sexual dysfunction. Reduced sexual function was significantly associated with increases in age, vaginal dryness, mental fatigue (ProFaD), self-blame, rumination and catastrophising (CERQ), consequences and identity (BIPQ), negative partner responses (WHYMPI) and relationship dissatisfaction (MMQ). Reduced sexual function was also significantly associated with decreases in positive reappraisal and perspective (CERQ), personal control (BIPQ), solicitous responses and distracting responses (WHYMPI) (Table 1). No significant associations were found for disease duration, relationship duration or ESSPRI total. Results from regression analyses indicated that vaginal dryness (β = -.278, p = .004), CERQ positive reappraisal (β = .322, p = .003) and CERQ catastrophising (β = -.277, p = .009) were significantly related to sexual function and explained 42.0% of the variance in total FSFI scores (F(3,72) = 17.394, p < .001).

Table 1. Associations between sexual function and psychosocial parameters

	FSFI total			
	r_s	*p*	95% CI (LB, UB)	
Age (years)	-.270	**.015**	-.467	-.049
Disease duration (months)	-.030	.793	-.253	.196
Relationship duration (months)	-.180	.119	-.396	.054
VAS Vaginal dryness	-.350	**.001**	-.533	-.136
ESSPRI total	-.165	.141	-.376	.062
ProFaD Mental Fatigue	-.294	**.008**	-.486	-.074
CERQ Self-Blame	-.264	**.017**	-.461	-.042
CERQ Rumination	-.296	**.007**	-.488	-.077
CERQ Positive Reappraisal	.469	**.000**	.273	.628
CERQ Perspective	.341	**.002**	.126	.525
CERQ Catastrophising	-.499	**.000**	-.651	-.310
BIPQ Consequences	-.237	**.033**	-.438	-.013
BIPQ Personal Control	-.288	**.009**	-.481	-.068
BIPQ Identity	-.294	**.008**	-.487	-.075
MMQ	-.282	**.013**	-.483	-.054
WHYMPI Negative Responses	-.252	**.028**	-.457	-.021
WHYMPI Solicitous Responses	.267	**.020**	.037	.470
WHYMPI Distracting Responses	.311	**.006**	.085	.506

Note. N = 81. Associations that were not significant are not shown.

Conclusion: Women with SS using positive coping strategies have better sexual function than those with negative coping strategies. Learning positive coping strategies may be an important line of approach for managing sexual dysfunction in SS.

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POS0044-HPR FEASIBILITY OF FITNESS ASSESSMENTS IN GROUP EXERCISE THERAPY FOR INDIVIDUALS WITH AXIAL SPONDYLOARTHRITIS

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Background: Assessments should be standard in individual as well as group physical therapy. The Ankylosing Spondylitis Association of Switzerland has translated the EULAR recommendations for physical activity (PA) in a concept for group exercise therapy, which, in addition to guidance on exercising in all four fitness dimensions (aerobic, strength, flexibility, neuromotor function), also includes PA counselling and regular fitness assessments for the planning and documentation of the individual therapy progress as well for quality monitoring of the exercise groups.
Objectives: To evaluate the feasibility of the selected assessments across all four fitness dimensions, rating the acceptance, practicability, and integration by physiotherapists (PTs) and people with axSpA.
Methods: A feasibility study was conducted in four pilot exercise therapy groups. PTs performed the assessment battery, consisting of a) the Chester Step Test (CST) for aerobic fitness; b) the modified Core Strength Test for core strength, c) the Bath Ankylosing Spondylitis Metrology Index (BASMI) for spinal mobility and d) the Single Leg Stance Test (SLST) for balance, with the participants of the exercise therapy groups. Subsequently, the PTs and the participants with axSpA rated the acceptance, practicability, and integration by means of questionnaires. Acceptance was operationalised as satisfaction and perceived applicability, practicability was operationalised as feasibility and comprehensibility, and integration was operationalised as usefulness and repeatability. An ordinal scale with four answer options (very good, good, moderate, bad) and a free text field for comments was used. The categories 'very good' and 'good' were interpreted as 'positive evaluation'. The feasibility of the assessments was defined based on three levels (I-III): with a positive evaluation of >80% (level I) a specific assessment was considered suitable, with a positive evaluation of 50-80% (level II) adjustments were necessary, with a positive evaluation of <50% (level III) a specific assessment was not considered suitable for group exercise therapy and a new choice had to be made.
Results: The BASMI was rated level I by people with axSpA and PTs, no adaptations were necessary. The CST was rated level I by people with axSpA and level II by PTs (too time consuming and failure-prone software), resulting in the adaptation that the test can now be performed without software, and a training will make the testing PTs more efficient. The modified Core Strength Test was rated level I by people with axSpA and level II by PTs (instructions unclear), leading to adaptations in the instruction manual. The SLST was rated level I by people with axSpA and level II by PTs (instruction "standing on one leg as long as possible" not useful for persons without balance deficit), leading to the adaptation that the test can be stopped after 60 seconds as the normal values are below that threshold.
Conclusion: From patient perspective, the feasibility of the tests was evaluated positive in terms of acceptance, practicability and integration (all level I). From PTs' perspective some adaptations were necessary (level II, except BASMI). After the adaptations, the assessment battery can now be used in group exercise therapy for individuals with axSpA. In this way, the individual fitness status can be evaluated, and interventions can be adapted, and thus the quality of group exercise therapy can be continuously monitored and improved if necessary.
Acknowledgements: We thank all participants and the SVMB for their support.
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POS0045-HPR HEALTHCARE PROFESSIONALS' ATTITUDE TOWARDS REMOTE MONITORING

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Background: The pandemic has accelerated the use of remote monitoring of patients (1), but there is still lack of knowledge in regards to barriers and facilitators for using remote monitoring among health care professionals. Patients with rheumatic diseases are monitored frequently by healthcare professionals, and follow-up strategies with less hospital visits could reduce the resource use.
Objectives: To explore healthcare professionals' attitude, facilitators and barriers on use of remote monitoring in a specialist healthcare setting.
Methods: Approximately 100 employees at a department of rheumatology at a single Norwegian hospital were invited to complete an anonymous 22-item questionnaire in December 2021. To ensure anonymity, demographic data were limited to age (under/over 45 years of age) and current position (doctor, nurse, allied healthcare/leaders/secretaries). In addition, participants completed questions on frequency of use of video consultation, phone consultation and patient-reported software. For investigating attitudes, facilitators and barriers the participants also responded to 16 statements related to perspectives on the use of remote monitoring in patients with low and stable disease activity using a 10-point numeric rating scale (NRS) from 0="Strongly disagree" to 10="Strongly agree". We developed the statements as potential facilitators or barriers for the use of video consultations and remote monitoring based on facilitators and barriers identified in previous research (2-4). The statements that had median score for agreement >=6 were categorized as either facilitator or barrier and presented with median score and interquartile range (IQR).
Results: Seventy (70 %) participants completed the questionnaire. In the study sample 44 % were under the age of 45, 35 % were doctors, 36 % nurses and 28 % were allied health professionals, secretaries, or leaders. None used video consultation on a daily basis, while 6 % used phone consultation daily. The participants had a positive attitude towards the use of remote monitoring in patients with low and stable disease activity (median: 9 (IQR: 8-10). For the remaining 7 statements the median scores were close to 5 – which indicates that they cannot be regarded as neither facilitators nor barriers. The remaining statements focused on adequate internet connection, patients underreporting, scepticism towards new software and mistrust in technical systems. The facilitators and barriers for remote monitoring with median score >=6 among health care professionals are presented with box-plots including median score and IQR in Figure 1.

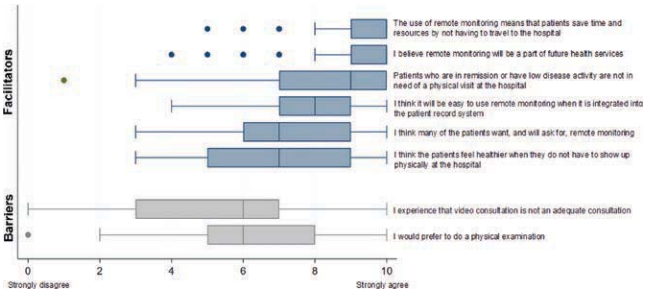

Figure 1. Facilitators and barriers presented with median score (IQR) in box-plots arrangement

Conclusion: Health care professionals showed positive attitudes towards the use of remote monitoring. Main facilitators on use of remote monitoring were: patients saving time, the belief of remote monitoring being part of future health care, remote monitoring being integrated with patient record system, patients wish to use remote monitoring and patient feeling less burdened by not visiting hospital. The main barriers were the inability to physically examine the patients and limitations related to the use of video consultation.
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POS0046-HPR THE EFFECT OF MEDITATION, MINDFULNESS, AND YOGA IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Non-pharmacological approaches additional to the pharmacological treatment of rheumatoid arthritis (RA) may include meditation, as well as yoga and mindfulness. These mind-body therapies (MBTs) create an interaction between the mind and body to enhance overall health. MBTs are perceived as valuable in RA management, but the extent of this contribution is unclear, as well as patients subgroups who benefit most from these MBTs.
Objectives: To investigate the effects of meditation, mindfulness, and yoga in patients with RA in a systematic literature review.
Methods: A search was performed in 4 databases (PubMed, Embase, Web of Science (core collection, Chinese and Korean collection) and CINAHL). All studies were screened by two independent reviewers, via title/abstract/full text. Studies included any form of meditation, mindfulness and/or yoga as an intervention

Table 1. Overview of included studies

Author (year)	Intervention	Country	Outcome	Author (year)	Intervention	Country	Outcome
Yoga				**Mindfulness**			
Haslock (1994)	Yoga	UK	Functionality	Pradhan (2007)	MBSR	USA	QoL, Disease activity, depression
Dash (2001)	Yoga	India	physiological	Zautra (2008)	MERT	USA	Disease activity, depression, pain
Badsha (2009)	Yoga	UAE	Functionality, QoL, Disease activity	Davis (2015)	MAAT	USA	depression, anxiety, pain, fatigue
Bosch. (2009)	Yoga	USA	Functionality, physiological, depression, pain	Fogarty (2015)	MBSR	New Zealand	Disease activity, pain
Evans (2010)	Iyengar Yoga	USA	Functionality, QoL, depression, anxiety, pain	Dalili (2019)	MBCT	Iran	QoL, depression, anxiety, pain, stress
Singh (2011)	Yogic package (incl. meditation)	India	Disease activity, pain	Fogarty (2019)	MBSR	New Zealand	Disease activity, depression, anxiety
Telles (2011)	Yoga	India	Functionality, Disease activity	**Relaxation**			
Evans (2013)	Iyengar Yoga	USA	Functionality, QoL, depression, anxiety, pain, fatigue, sleep quality	Bagheri-Nesami (2006)	Benson Relaxation	Iran	Disease activity, depression, anxiety, pain, fatigue
Ward (2018)	Yoga	New Zealand	Functionality, QoL, Disease activity, depression, anxiety, pain, fatigue, sleep quality	Barsky (2010)	Relaxation Response (PMR)	USA	QoL, Disease activity, depression, anxiety, pain, fatigue, sleep quality
Greysen (2019)	Yoga	USA	Functionality, depression, pain, fatigue, sleep quality				
Gautam (2020)	Yoga-based lifestyle	India	QoL, Disease activity, physiological	Yazdani (2017)	PMR	Iran	QoL
Ganesan (2020)	Yoga	India	Disease activity, physiological				
Gautam (2021)	Yoga	India	Functionality, Disease activity, physiological				
Puksic (2021)	Yoga	Croatia	QoL, depression, anxiety, pain, fatigue, stress				

MBCT = Mindfulness-Based Cognitive Therapy; PMR = Progressive muscle relaxation; MBSR = Mindfulness-based stress reduction, MERT = mindfulness-based emotion regulation therapeutic program, MAAT = mindfulness-based emotion regulation therapeutic program QoL= quality of life

for patients with RA. Animal studies, case reports, non-English articles, qualitative studies, conference abstracts and articles without full text access were excluded. Each study was assessed for quality.

Results: Out of the 1,527 records, 23 studies were included after screening (Table 1). There was considerable heterogeneity, both in applied interventions and outcome measurements. All MBTs showed limited beneficial effects on psychosocial outcomes, such as vitality, functioning, and mental health, as well as on disease activity markers. Mindfulness-based interventions mainly reduced the subjective disease activity (e.g., joint tenderness/pain), rather than objective disease activity (e.g., swollen joints/CRP). RA patients with recurrent depression seemed to benefit more from these non-pharmacological therapies than patients without recurrent depression.

Conclusion: This systematic literature review found that MBTs have added value in RA management, especially for patients with depressive symptoms. These non-pharmacological approaches as an addition to treatment can be a way to diminish polypharmacy in specific RA patient populations.

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POS0047-HPR GOALS AND ACTION PLANS ACROSS TIME AND PLACE IN PERSON-CENTRED REHABILITATION - A QUALITATIVE STUDY EXPLORING THE IMPORTANCE OF CONTEXT

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Background: Person-centeredness is increasingly addressed in relation to rehabilitation interventions (1). Collaborative goal setting and action plans are key elements in person-centered rehabilitation (2). There is a lack of knowledge about how person-centered goals and action plans developed during inpatient rehabilitation are experienced by the patients after discharge.

Objectives: This aim of the study was to explore how rheumatic patients experience the relevance of goals and action plans after discharge from an inpatient rehabilitation stay.

Methods: Individual narrative interviews were conducted with eight patients with a rheumatic disease three to five weeks after discharge from a two-week inpatient rehabilitation stay. A convenience sampling strategy was applied. In order to the exploratory nature of the study, we strived for variety in diagnoses, age and gender (3). One male and seven female patients participated, aged between 40 and 60 years. Six of the participants were active at the labor market and two were retired. Data collection, analysis and interpretation of data were performed within a phenomenological-hermeneutic framework inspired by Paul Ricoeur's interpretative philosophy (4).

Results: The analysis derived one core theme: 'The relevance of goals and action plans is contextual' and three subthemes: 'The hospitalization - a protected bubble', 'Being at home - a harsh reality', and 'Need for support after discharge'. The participants expressed that during the admission there was time and peace to exercise and to take a rest. They were relieved from everyday duties, and received support from the interdisciplinary team in how to exercise and during conversations where they focused on management of their symptoms and illness. Back home after discharge, the participants experienced how their everyday life differed from the hospital context. They found it challenging to work further with goals and actions plans in their everyday life. They described in particular challenges with incorporation of new habits in everyday life, challenges they were not prepared for. On challenging days with pain and fatigue, the participants missed having someone to talk to. The participants suggested involvement of their relatives to support action plans and called for follow-up support to enable them to continue working to achieve their goals and action plans after discharge. They suggested support by telephone calls from a nurse from the hospital after one, two or three months after discharge to ask how they felt. They believed that it would be motivating and could support the outcomes of the admission.

Conclusion: Goals and actions plans are relevant for rheumatic patients, but must be adapted to the patient's everyday life. There is a need to plan during the hospitalization how goal and action plans can be transferred to the rheumatic patient's everyday life after discharge from a rehabilitation stay. Likewise, there is a need for follow-up support after discharge to support the patients to pursue their goals and cope with challenges in everyday life.

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POS0048-HPR HEALTHCARE PROFESSIONALS' EXPERIENCES OF LIFESTYLE MANAGEMENT IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS – A QUALITATIVE STUDY

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory systemic disease that mainly affects joints and with symptoms such as stiffness, pain, and increased fatigue. RA also appears to be an independent risk factor for accelerated atherosclerosis with an increased risk of cardiovascular diseases,

why national and international guidelines recommend proper pharmacological treatment together with a healthy lifestyle (1). Supporting people with early RA to achieve and maintain a healthy lifestyle is therefore of great importance. However, few studies have explored healthcare professionals' views of working with lifestyle management. A healthy lifestyle does not only have the potential to lower cardiovascular risk but may also improve a person's quality of life.

Objectives: The aim of this study was to explore healthcare professionals´ experiences of lifestyle management in patients with early RA.

Methods: In this explorative qualitative study, individual interviews were conducted with 20 healthcare professionals who had a mean of 16 years of professional experience in the field of working with patients with RA. An interview guide with open-ended questions was used e.g.: "How do you work with lifestyle changes in patients with RA?" and "What theories do you use to support lifestyle changes?" Qualitative content analysis was used, where three categories emerged: "The importance of a well-functioning organization", "The importance of teamwork" and "The importance of person-centered care" and nine subcategories, representing the overall content of the interviews (Table 1).

Table 1. ***Overview of categories and subcategories that describes healthcare professionals´ experiences of lifestyle management in patients with early RA***

Categories	Subcategories
The importance of a well-functioning organization	Supportive leadership
	Priority of lifestyle management
	Competence development in lifestyle management
The importance of teamwork	Interdisciplinary team
	Professional expertise in lifestyle habits
	Structured approach to lifestyle management
The importance of person-centered care	Individually tailored lifestyle management
	Shared decision-making
	Patient engagement

Results: Healthcare professionals' experiences of lifestyle management in patients with early RA included the importance of a well-functioning organization with supportive leadership, priority of lifestyle management, and competence development in lifestyle management. The importance of teamwork was emphasized including interdisciplinary team, professional expertise in lifestyle habits, and structured approach to lifestyle management. The healthcare professionals also highlighted the importance of person-centered care with individually tailored lifestyle management, shared decision-making, and patient engagement.

Conclusion: Healthcare professionals' experiences of lifestyle management in patients with early RA reveal that commitment from both the management, the team, and the patient is important.

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POS0049-HPR PATIENT SATISFACTION WITH THE INTERDISCIPLINARY, RHEUMATOLOGIST-MANAGED AND RHEUMATOLOGY NURSE-CONDUCTED, DIAGNOSTIC APPROACH FOR FIBROMYALGIA PATIENTS

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Background: Based on the evidence that substituting specialized nurses for rheumatologist in the diagnostic process for fibromyalgia (FM) is safe (Kroese et al., 2008) and leads to patient satisfaction and reduction of costs (Kroese et al., 2011), the Capital Region of Denmark increased its respective capacities by introducing a rheumatologist-managed and specialized nurse-conducted diagnostic approach at the Frederiksberg Hospital in January 2018.

Objectives: The objective of this quality insurance survey was to get patients' feedback on their satisfaction with the nurse-conducted diagnostic approach.

Methods: An evaluation-questionnaire was developed. Patients were asked: *Did you feel confident in the nurse-conducted diagnostic approach? How clearly did the nurse communicate? How much did you profit from the final, diagnostic consultation with the nurse? Do you feel the need for further medical examinations?* The answers were given on a 4-point Likert scale with the points: to a high degree; to some degree; to a lesser degree; not at all. All patients that had undergone the diagnostic approach were offered to evaluate it by anonymously filling in the evaluation-questionnaire on an iPad. The data analysis consisted of counting the number and calculating the percentage of respondents in each of the response-categories.

Results: 601 patients were offered to evaluate the approach during the period from 1.1.2018 to 27.2.2020. 60% (n=358) of these patients filled in the evaluation questionnaire. 88% (n=315) of the respondents were very confident in the nurse-conducted diagnostic process, as well as thought that the nurses communicated very clearly. Furthermore, 94% (n=317) of the respondents thought that they profited from the nurse-conducted diagnostic consultation focused on the explanation of FM and treatment options. Lastly, only 11 % (n=39) felt a pronounced need for further examination. Complete overview of the results is presented in the Table 1. Number and % of respondents per each question and per each response category.

Table 1. Number and % of respondents per each question and per each response category.

Questions	Total number of respondents	Number of respondents (%) per each Likert scale point			
		to a high degree	to some degree	To a lesser degree	not at all
Confidence in the nurse	358	315 (88%)	28 (8%)	11 (3%)	4 (1%)
Clarity of nurse- communication	358	315 (88%)	39 (11%)	4 (1%)	0 (0%)
Profit from the diagnostic consultation	338	189 (56%)	128 (38%)	17 (5%)	4 (1%)
Perceived need for further examinations	357	39 (11%)	82 (23%)	114 (32%)	122 (34%)

Conclusion: The patients were confident in the nurse-conducted diagnostic process and had profited from the diagnostic consultation focused on the explanation of FM and current treatment options. Thus, specially trained nurses contribute to the effectiveness of the FM diagnostic process and to patients' satisfaction. This facilitates patients' timelier access to treatment options.

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Immunity in Rheumatic Diseases

POS0050 B CELL CHARACTERISTICS AT BASELINE PREDICT HUMORAL RESPONSE UPON SARS-COV-2 VACCINATION AMONG PATIENTS TREATED WITH RITUXIMAB

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Background: Vaccination is considered efficient in controlling infections incl. SARS-CoV-2. Prior studies showed that patients receiving rituximab (RTX) with low B cell counts are at increased infectious risk (1) and risk of inadequate vaccination responses (2, 3). Thus, the ability to further define and predict vaccination responses in these patients may guide their optimal protection.

Objectives: To assess predictive biomarkers of vaccination responses upon SARS-CoV-2 vaccination in RTX treated patients.

Methods: B cell characteristics before vaccination were evaluated to predict responses in 15 patients with autoimmune inflammatory rheumatic diseases receiving RTX. 11 patients with rheumatoid arthritis on other therapies (RA), 11 kidney transplant recipients (KTR) and 15 healthy volunteers (HC) served as controls. A multidimensional analysis of B cell subsets and a correlation matrix were performed to identify predictive biomarkers.
Results: Significant differences regarding absolute B cell counts and specific subset distribution pattern between the groups were validated at baseline. Here, the majority of B cells from vaccination responders of the RTX group (RTX IgG+) comprised naïve and transitional B cells, whereas vaccination non-responders (RTX IgG-) carried preferentially plasmablasts and double negative (CD27-IgD-) B cells (Figure 1). Moreover, there was a positive correlation between neutralizing antibodies and absolute B cell numbers with B cells expressing HLA-DR and CXCR5 (involved in antigen presentation and germinal center formation) as well as an inverse correlation with CD95 expression and CD21low expression (marker for activation and exhaustion) on B cells.
Conclusion: Substantial repopulation of naïve B cells upon RTX therapy appears to be essential for an adequate vaccination response requiring germinal center formation. In contrast, expression of exhaustion markers (CD21low, CXCR5-, CD95+) indicate negative predictors of vaccination responses. These results may guide optimized vaccination strategies in RTX treated patients clearly requiring antigen-inexperienced B cells for appropriate protection.
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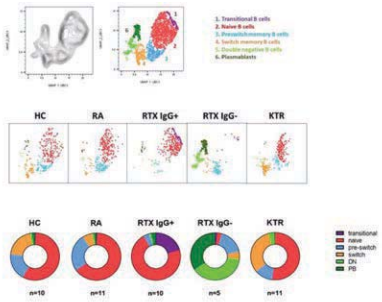

Fig. 1 Distinct B cell subsets characterize HC and patient groups. UMAP clustering performed on a concatenated file of pre-gated CD19+ B cells. Distribution of B lineage cell subsets show characteristic differences between the HC, RA, RTX IgG+, RTX IgG- and KTR group.

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POS0051

DIFFERENTIAL PHARMACODYNAMIC ALTERATIONS AFTER TREATMENT WITH ABATACEPT OR ADALIMUMAB IN MTX-INADEQUATE RESPONDER PATIENTS WITH EARLY RA: WHOLE BLOOD RNA-SEQ ANALYSIS OF THE EARLY AMPLE STUDY

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Background: Despite advances in available novel pharmacologic agents for RA,[1] the dearth of effective response predictors for specific therapies remains an unmet need. To inform clinical decision making, it is critical to define molecular signatures of these therapeutic agents by investigating their mechanisms of action (MoAs) and differential impacts on patients' immune systems. Adalimumab and abatacept are biologic DMARDs with distinct MoAs used to treat RA. A better understanding of the differential pharmacodynamic (PD) changes of these 2 agents may provide guidance for the selection of treatment options.[2] The Early AMPLE (Abatacept versus adaliMumab comParison in bioLogic-naïvE RA subjects with background MTX) study compared treatment with abatacept or adalimumab in a population of patients with early RA to explore differential PD effects; abatacept treatment resulted in numerically higher efficacy responses vs adalimumab after 24 weeks of treatment.[3]
Objectives: To investigate PD changes in response to treatment with abatacept or adalimumab, and to identify and differentiate the impact of each drug on modulation of immune cells at the molecular level.
Methods: The phase 4 Early AMPLE trial (NCT02557100) was a head-to-head comparison of treatment response to either abatacept or adalimumab in patients with early RA with an inadequate response to MTX, high anti-citrullinated protein antibody titers, and RF positivity, with or without shared epitope. Whole blood RNA sequencing (RNA-Seq) was conducted on samples collected from patients at different visits (day 1; weeks 4, 8, 16, 24, 28, 32, 40, 48). Differential gene expression analyses were performed using Limma-voom pipeline in R, adjusting for batch effect and sex. Over-representation tests were used to identify enriched Gene Ontology pathways. xCell, a gene signatures–based method learned from thousands of pure cell types, was applied for immune cell type deconvolution and enrichment analysis.
Results: PD and association analyses were performed for 14,540 protein-coding genes in 664 RNA-Seq samples (79 patients with RA at 9 visits). Baseline association analysis showed that 248 differentially expressed genes and 6 cell cycle–related pathways were significantly associated with baseline SDAI score. After treatment, gene-enrichment analysis demonstrated that twice as many genes and pathways were significantly altered in the adalimumab- vs abatacept-treated arm. Abatacept treatment decreased immune cell cycle gene expression while adalimumab treatment increased expression of these genes. The increases due to adalimumab were reversed after switching to abatacept (open-label period). Using gene signatures to identify key immune cell subsets (Figure 1), adalimumab therapy increased expression of genes defining several key immune cell types involved in RA disease development, including dendritic cells, T cells, and B cells; these effects were also reversed after switching to abatacept.
Conclusion: The differential gene expression seen after treatment with abatacept or adalimumab was noted in genes identified as correlating with RA disease activity. These findings may inform on the mechanism for the relatively greater clinical improvements seen with abatacept vs adalimumab in the Early AMPLE study. Abatacept treatment may selectively modulate genes that are relevant to disease pathology/progression, with the potential to restore the immune homeostasis dysregulated in RA. Our findings warrant further studies to investigate the potential positive correlation between RA-relevant PD effects and better therapeutic outcomes.
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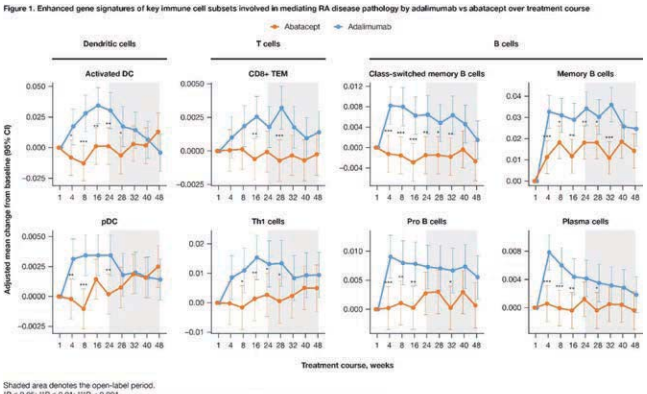

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Myers Squibb, Grant/research support from: AbbVie, Bristol Myers Squibb, Vivian Bykerk Consultant of: Amgen, Bristol Myers Squibb, Genzyme Corporation, Gilead, Regeneron, UCB, Grant/research support from: Amgen, Bristol Myers Squibb, Genzyme Corporation, Pfizer, Regeneron, Sanofi Aventis, UCB, Jane Buckner Consultant of: Bristol Myers Squibb, Hotspot Therapeutics, Janssen, Grant/research support from: Current: Bristol Myers Squibb, GentiBio; past: Amgen, Janssen, Novo Nordisk, Pfizer, Jinqi Liu Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

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POS0052 ANGIOGENIC T CELLS AS RELEVANT PLAYERS IN THE LUNG VASCULOPATHY OF RHEUMATOID ARTHRITIS, SYSTEMIC SCLEROSIS AND OTHER AUTOIMMUNE DISEASES

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Background: Interstitial lung disease (ILD) is a common and life-threatening complication in patients with autoimmune diseases (AD), mainly in those with systemic sclerosis (SSc) and rheumatoid arthritis (RA). Growing evidence indicate that vascular abnormalities constitute the early phase in the pathogenesis of these inflammatory diseases [1]. We recently reported a decrease of angiogenic T cells (TAng), that promote endothelial repair and revascularization cooperating with endothelial progenitor cells (EPC) [2], in patients with AD-ILD$^+$ [3]. Nevertheless, no studies have been conducted on the role of TAng in the presence of ILD in RA, SSc or other AD.

Objectives: To determine the contribution of TAng in the pathogenic processes of vasculopathy and lung fibrosis in RA-ILD$^+$, SSc-ILD$^+$ and other AD-ILD$^+$, as well as their relationship with EPC in all the AD-ILD$^+$ patients.

Methods: Peripheral venous blood was collected from 21 RA-ILD$^+$ patients, 21 SSc-ILD$^+$ patients and 15 patients with other AD-ILD$^+$. Furthermore, we included 4 comparative groups: 25 RA-ILD$^-$ patients, 20 SSc-ILD$^-$ patients, 21 idiopathic pulmonary fibrosis (IPF) patients and 21 healthy controls (HC). TAng were considered as CD3$^+$CD184$^+$CD31$^+$ cells by flow cytometry. Additionally, EPC data were previously published by Pulito-Cueto *et al.* [4-5].

Results: Regarding the role of TAng in vasculopathy, the frequencies of these cells were significantly lower in patients with RA-ILD$^+$, SSc-ILD$^+$ and other AD-ILD$^+$, as well as with IPF in relation to HC (p=0.007, p=0.016, p=0.005 and p<0,001, respectively, Figure 1). No differences between RA-ILD$^-$ patients, SSc-ILD$^-$ patients and HC were found (Figure 1). With respect to TAng involvement in fibrosis, TAng frequencies were similar in patients with RA-ILD$^+$, SSc-ILD$^+$, other AD-ILD$^+$ and those with IPF (Figure 1). Nevertheless, patients with RA-ILD$^+$ and SSc-ILD$^+$ showed significantly lower TAng frequencies than those with RA-ILD$^-$ and SSc-ILD$^-$, respectively (p=0.006 and p=0.044, respectively, Figure 1). In this line, a higher frequency of TAng was found in SSc-ILD$^-$ and RA-ILD$^-$ patients in relation with those with IPF (p<0.001 and p=0.003, respectively, Figure 1). Moreover, TAng frequency did not show significant correlation with EPC frequency in the whole cohort of AD-ILD$^+$ patients.

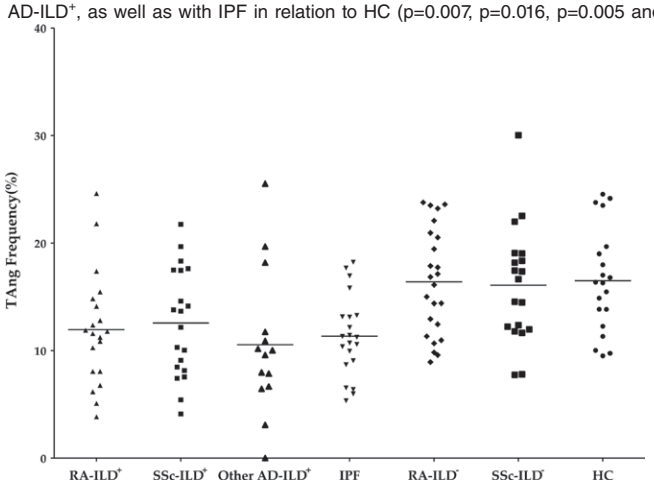

Figure 1. *Quantification of TAng population by flow cytometry in all individuals included in the study.*

Conclusion: TAng play a relevant role in the lung vasculopathy of RA-ILD$^+$, SSc-ILD$^+$ and other AD-ILD$^+$. Interestingly, circulating TAng may be considered as a useful biomarker of the presence of ILD in patients with RA and SSc.

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POS0053 ABUNDANT AUTOANTIBODY ISOTYPES IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Anti-synthetase syndrome (ASSD), a sub-group of idiopathic inflammatory myopathies (IIM) is characterized by the presence of autoantibodies targeting aminoacyl tRNA synthetases (aaRS) and specific clinical manifestations such as myositis and interstitial lung disease (ILD) [1]. Some of the most common anti-aaRS autoantibodies in ASSD are anti-Jo1, -PL7, -PL12 and-EJ. In addition, many anti-aaRS positive patients are also positive for anti-Ro52. Having the combination of anti-Jo1 and anti-Ro52 increases the risk of developing ILD [2]. The presence of autoantibodies is an important part of the classification of ASSD, however only autoantibodies of IgG isotype are usually analyzed in the clinical setting. In rheumatoid arthritis there is evidence that anti-citrullinated protein/peptide antibodies (ACPA) can be found as IgG, IgA and IgM, and importantly, specific isotypes might correlate with disease activity [3, 4].

Objectives: To verify if other autoantibody isotypes, besides IgG, might be present in sera of patients with IIM/ASSD and to compare with the corresponding frequencies in population controls (PC).

Methods: Stored sera collected from consecutive 366 IIM patients and 156 age/gender matched PC at Karolinska University Hospital were retrospectively selected. The serum samples were screened for the presence of autoantibodies of isotypes IgG, IgA and IgM, against a panel of 20 antigens representing Jo1 (HisRS), PL7 (ThrRS), PL12 (AlaRS), EJ (GlyRS), and Ro52 (TRIM21) using a multiplex bead array assay.

Results: We identified IIM patients with autoantibodies of different isotypes, and a low frequency in PC (Figure 1). For anti-Jo1 autoantibodies we could detect IIM patients with only IgG (n=13), only IgM (n=8) and only IgA (n=4), but the majority had a combination of two (n=32) or three isotypes (n=16). For the other anti-aaRS autoantibodies the distribution was more equal to each of the three isotypes with anti-PL12 and anti-PL7 being represented by a slightly higher

frequency of IgG and only a few patients had antibodies of more than one isotype targeting PL12, PL7 or EJ. The majority of anti-Ro52 positive IIM patients (n=52) only harbored IgG isotype. The combination of anti-Ro52 and anti-aaRS autoantibodies was identified in 28 patients (anti-Jo1 (n=19), -PL12 (n=2), -PL7 (n=3), and -EJ (n=4)). Most patients with such combination had anti-Ro52 IgG together with anti-aaRS IgG or IgG in combination with IgA and/or IgM. The exception was observed for three anti-Jo1 positive patients who had the combination anti-Ro52 IgG with only anti-Jo1 IgM and one anti-PL7 positive patient who had anti-Ro52 IgA together with anti-PL7 IgA and IgG.

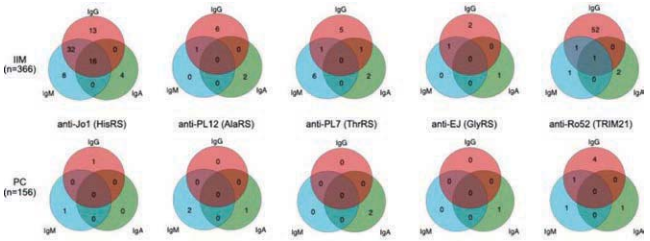

Figure 1. Venn diagrams showing reactivity in idiopathic inflammatory myopathies (IIM) (top) and population controls (PC) (bottom) for the three autoantibody isotypes IgG, IgA and IgM against five myositis antigens: Jo1 (HisRS), PL12 (AlaRS), ThrRS (PL7), EJ (GlyRS) and Ro52 (TRIM21).

Conclusion: The frequency of the different autoantibody isotypes seems to be autoantigen dependent. Our results suggest that for anti-aaRS autoantibodies it could be important to investigate additional autoantibody isotypes, as some patients only harbor autoantibodies of IgM or IgA isotypes but not IgG. The clinical relevance of the different antibody isotypes still needs to be determined.

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Table 1. Total number of individuals and percentage (n (%)) in each group for each of the isotypes and antigens.

	anti-Jo1		anti-PL12		anti-PL7		anti-EJ		anti-Ro52	
	IIM	PC	IIM	PC	IIM	PC	IIM	PC	IIM	PC
IgG	61 (16.7)	1 (0.6)	7 (1.9)	0 (0.0)	7 (1.9)	0 (0.0)	3 (0.8)	0 (0.0)	54 (14.8)	5 (3.2)
IgA	20 (5.5)	0 (0.0)	2 (1.2)	1 (0.6)	3 (0.8)	2 (1.3)	1 (0.3)	1 (0.6)	3 (0.8)	1 (0.6)
IgM	56 (15.3)	1 (0.6)	1 (0.3)	2 (1.3)	7 (1.9)	0 (0.0)	1 (0.3)	0 (0.0)	3 (0.8)	2 (1.3)

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POS0054 DYSFUNCTION OF REGULATORY B CELLS IN GIANT CELL ARTERITIS (GCA)

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Background: The pathophysiology of GCA is not clearly understood, but most research has pointed towards a major role of T cells with proinflammatory Th1 und Th17 cells as dominant drivers of disease. The role of B cells in the pathogenesis of GCA has not been much studied to date.

Objectives: To study the role of proinflammatory T cell mediators and anti-inflammatory regulatory B cells (Bregs) as their counterpart in patients with GCA compared to healthy controls (HC).

Methods: GCA Patients and HC were recruited prospectively and included after informed consent. Peripheral blood mononuclear cells were freshly isolated from whole blood and included into 3 experimental setups, using flow cytometry and fluorescent antibodies: (i) pro-inflammatory T cell mediators (IL-2, GMCSF, IL-17a, IFN-y), (ii) granzyme B production of Bregs after stimulation with different agents (anti-human IgG + IgM, IL-21, anti-CD40L) and (iii) the IL-10 production of Bregs were measured. Disease activity was defined as unequivocal evidence of cranial symptoms of GCA and/or increased concentrations of C-reactive protein and/or halo-sign, leading to a change in therapy according to the treating rheumatologist. Statistical comparisons between groups were performed by the Mann-Whitney-U-Test and Spearman's rank correlation.

Results: A total of 47 GCA patients (14 with active disease and 33 in remission) and 49 HC were included (Table 1). $CD4^+$ T cells of GCA patients with active disease produced less IFN-y than HC (p=0.016, Figure 1a). There was also a trend towards lower expression of IL-2 (p=0.18), GMCSF (p=0.1) and IL-17a (p=0.18) by $CD4^+$ T cells from GCA patients compared to HC. Bregs of GCA patients produced lower amounts of granzyme B after stimulation with anti-human IgG and IgM compared to HC, and this was similar in active patients (p=0.04, Figure 1b) and in quiescent patients (p=0.021, Figure 1b). With other stimuli, including IL-21 and anti-CD40L, there was also a trend towards a lower expression. The IL-10 production of Bregs did not show substantial differences between groups. Importantly, the dose of glucocorticoids did not influence cytokine production of T-cells or B-cells.

Table 1. Demographics

Variables	GCA Patients (n=47)	Healthy Controls (n=49)
Age, years	71 *(54-83)*	65 *(45-86)*
Sex, n (%)	31 female (65.9)	40 female (81.6)
Disease activity	14 active disease (9 first diagnosis, 5 relapse) 33 in remission	NA
Therapy	Prednisolone: n= 29 Methotrexat: n=23 Tocilizumab: n=13	none
Dosage of prednisolone	None: n=18 1-7,5 mg/d: n=15 > 7,5 mg/d: n=14	

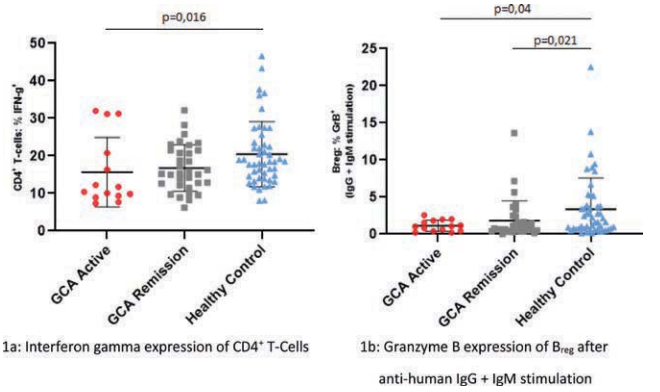

Figure 1. 1a: Interferon gamma expression of CD4+ T-Cells / 1b: Granzyme B expression of Breg after anti-human IgG + IgM stimulation

Conclusion: The *in vitro* cytokine production of proinflammatory $CD4^+$ T cells and anti-inflammatory Bregs after stimulation, especially regarding granzyme B production, showed some differences between patients and HC. A lower granzyme B production was found in patients with active disease indicating a lack of Breg–mediated suppressive capacity towards pro-inflammatory T cells. This finding may play a role in the pathogenesis of GCA.

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Disclosure of Interests: Marian Stöcker: None declared, Uta Kiltz Speakers bureau: Abbvie, Fresenius, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, Amgen, Biogen, Chugai, Eli Lilly, Fresenius, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Amgen, Biogen, Fresenius, GSK, Hexal, Novartis, Pfizer, Juergen Braun Speakers bureau: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, Fresenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Novartis, Pfizer, UCB, Paid instructor for: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, Fresenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Novartis, Pfizer, UCB, Consultant of: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, Fresenius, Hexal, Janssen, Lilly,

Medac, MSD, Mylan, Mundipharma, Novartis, Pfizer, UCB, Grant/research support from: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, Fresenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Novartis, Pfizer, UCB, Benjamin Wilde Consultant of: Alexion, Chiesi, Hexal, Otsuka, Pfizer, TEVA, Sanofi, Wyeth

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POS0055 TNF-α REGULATION OF MIR-29B EXPRESSION IN CD14+PBMS AND ITS RELEASE OF PROINFLAMMATORY CYTOKINES IN RHEUMATOID ARTHRITIS

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Background: It was found that the expression of mir-29b was significantly up-regulated in PBMs, and we tried to clarify TNF- α The production of proinflammatory cytokines was increased by inducing the overexpression of mir-29b in CD14 +PBMs in patients with rheumatoid arthritis (RA), and by using TNF-α that the expression of mir-29b was significantly urapy to reverse regulate mir-29b, and carry out relevant experiments to verify our scientific research hypothesis.
Objectives: By observing patients with RA treated with TNF-α significantly urapy to reverse regulate mir-29b, and carry out relevant experimenperipheral blood mononuclear cells (CD14+PBMs) and releases pro-inflammatory cytokines.
Methods: (1) Cell experiment: PBM cells from RA patients were collected and extracted for CD14+ cell expression labeling. Different doses of TNF-α blood mononuclear c500 ng/ml) were used for intervention. Meanwhile, the expression of mir-29b was analyzed by rt-qpcr at the level of TNF-α100 ng/ml for different periods of time (0,6,12,24h). In addition, the supernatant of cell culture was collected and human cytokines IL-1α, IL-1β, TNFα, IL-6, IFN-α and IL-8 were measured using a V-plex human cytokine 30-plex kit. (2)Grouping experiment of clinical intervention: 21 patients with RA diagnosis and 15 healthy volunteers were divided into three groups. TNF-α inhibitor group: RA patients treated with TNF-α inhibitor were collected (n=15); IL-6 monoclonal antibody group: RA patients treated with tocilizumab (n=6); Control group: healthy volunteers (n=15) were used as normal controls. PBMc was extracted from TNF-α inhibitor group for 6 months, IL-6 monoclonal antibody group for 6 months, and control group, respectively, to observe the difference of Mir-29b expression in CD14+PBMs of the three groups.
Results: The expression of miR-29b was dose-dependent and time-dependent with the incubation of TNF-α, and there was a significant difference ($P < 0.05$). Compared with the control group, the overexpression of miR-29b also led to an increase in the expression levels of a wide range of chemokines and proinflammatory cytokines (including IL-1α, IL-1β, TNFα, IL-6, IFN-α and IL-8) ($P < 0.05$). The expression of miR-29b in RA patients treated with TNF-α inhibitor was significantly reduced compared with that treated with Totuzumab ($P<0.05$).
Conclusion: TNF-α inflammatory factors can induce the overexpression of miR-29b in RA patients, and then producing a large number of proinflammatory cytokines, which can aggravate the inflammation mechanism of RA. In RA patients, TNF-α inhibitors may partially reduce the inflammatory response through the TNF-α/CD14+PBMs/ Mir-29b signaling pathway. Therefore, more attention should be paid to the expression of Mir-29b in TNF-α and CD14+PBMs in clinical practice, which may accurately indicate the state of immune disease in patients, and provide a basis for more accurate judgment of prognosis and the course of immunotherapy, as well as optimization of immunotherapy programs.
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Disclosure of Interests: None declared

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POS0056 GLOBAL STEROID METABOLISM IN MACROPHAGES: SHAPING INFLAMMATORY FUNCTION AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Macrophages are key drivers of joint destruction and disease pathophysiology in rheumatoid arthritis (RA), where their inflammatory function is influenced by steroid hormones such as androgens and glucocorticoids (GCs). Local bioavailability of these steroids is determined by both systemic adrenal/gonadal synthesis and local metabolism in peripheral target tissues. The inflammatory regulation and function of steroid hormone metabolism by key rate limiting enzymes in chronic inflammatory diseases such as RA remain poorly defined and could present new therapeutic targets.
Objectives: Characterise regulation of global steroid metabolism in macrophages in RA and determine its contribution to androgen and GC availability, macrophage function and disease activity.
Methods: Bulk and single cell RNA-sequencing of FACS-sorted macrophages were analysed using previously published datasets from RA patients (27 female, 8 male)(1, 2). Gene expression of rate limiting steroid metabolism enzymes were assessed in macrophages and their subsets and correlated to clinical parameters of disease activity. Primary human monocyte-derived macrophages were polarised to non-inflammatory (M-CSF 20ng/ml) and inflammatory activated (M-CSF 20ng/ml, IFNγ 20ng/ml, TNFα 10ng/ml) subsets and treated with active or inactive metabolites of GCs (cortisol/cortisone 100nmol/l) and androgens (androstenedione/testosterone/DHEA 100nmol/l; DHT 10nmol/l). Metabolism and functional effects were assessed in primary cultures and RA synovial fluids by liquid chromatography mass spectrometry, RT-qPCR and ELISA.
Results: Significant differentially expressed genes (DEGs) were identified in the GC and androgen metabolism pathways in synovial macrophages when stratified for high and low disease activity by DAS28-CRP. Expression of the GC-activating enzyme HSD11B1 and androgen activating enzyme SRD5A1 were significantly increased and positively correlated with disease severity. The androgen activating enzyme AKR1C3 was significantly suppressed and negatively correlated with disease severity. SRD5A1 and HSD11B1 expression were localised to $S100A12^{pos}$ and $SPP1^{pos}$ subsets associated with active RA, whilst AKR1C3 was primarily expressed by $MerTK^{pos}TREM2^{high}$ subsets associated with RA remission. Inflammatory activation of primary macrophages decreased AKR1C3, and increased HSD11B1 and SRD5A1 expression. This resulted in a shift in intracrine production of active GCs and androgens favouring increased levels of the active GC cortisol and the potent androgen DHT. The resulting changes in steroid ratios in inflammatory activated macrophages resulted in lower expression and release of the pro-inflammatory mediators TNFα, IL6 and IL12 indicating functional significance. In vivo, metabolic changes favouring increased GC activation and reduced androgen activation correlated with disease severity determined by DAS28-CRP.
Conclusion: We have shown for the first time a role for macrophages and their tissue subsets in the inflammatory metabolism and activation of GCs and androgens in RA, which influence macrophage function and disease activity. Targeting these key metabolic pathways represents a novel route to modifying and suppressing disease activity and joint destruction in chronic polyarthritis.
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Disclosure of Interests: None declared

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POS0057 INDUCIBLE REGULATORY SYNOVIAL MACROPHAGES: A PROOF-OF-CONCEPT STUDY FOR A CELL-BASED TARGETED THERAPY FOR RHEUMATOID ARTHRITIS

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Background: Infiltration of monocyte-derived macrophages into the synovial tissue (ST) is a hallmark of rheumatoid arthritis (RA) pathology. These macrophages promote inflammation, local joint effusion, and joint damage via the release of cytokines, oxygen reactive species, and tissue damaging enzymes. However, balancing these, are the 'regulatory' macrophages with inflammation-resolving properties, characterised by expression of CD206 and MerTK, dominant within the ST of healthy individuals as well as RA patients in remission (1). Indeed, these cells are believed to actively contribute to the maintenance of remission.

Macrophages are known to exhibit remarkable phenotypic plasticity and understanding the role of this characteristic in regulating inflammation and pathology remains a major challenge, as does the characterization of factors in the microenvironment such as the synovium that control such macrophage characteristics. Importantly, whether the infiltrating, inflammatory macrophages of the RA ST similarly exhibit such phenotypic plasticity, and whether this occurs during the process of reaching remission, remains to be studied.

Objectives: We investigated the phenotypic plasticity of inflammatory synovial macrophages from patients with RA in vitro, investigating their ability to convert from an inflammatory macrophage population into 'regulatory' CD206$^+$MerTK$^+$ macrophages. These findings will provide a proof-of-concept as to the utility of these macrophage for a cell-based therapy in resolving inflammation in patients with RA, and will likely extend our understanding of the mechanisms of action of currently used therapeutics.

Methods: Synovial fluid (SF) mononuclear cells were obtained from patients with active early RA (<1 year; fulfilling 2010 ACR/EULAR classification criteria). Cryopreserved SFMCs were cultured for 48hr in the presence of 10 ng/mL interferon(IFN)γ, 50 ng/mL dexamethasone, 10 µg/mL Infliximab, or diluent. Following culture, cells were immunostained and analysed using a Beckman Coulter CytoFLEX flow cytometer and FlowJo software. SF macrophages were characterised by expression of CD14, CD45, CD68 (Figure 1A), and proportions of CD206$^+$ MerTK$^+$ macrophages measured.

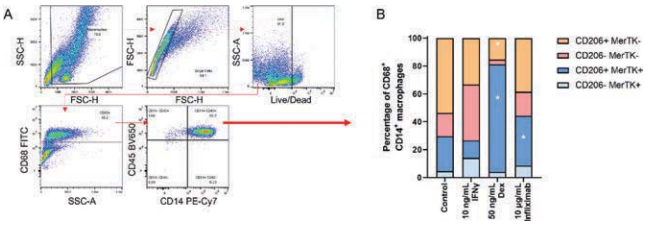

Figure 1. Synovial fluid CD68$^+$ macrophage plasticity *in vitro*. (A) Gating strategy depicting CD68$^+$ CD45$^+$CD14$^+$ SF macrophage determination. (B) Proportions of CD206 and MerTK-expressing SF macrophages after 48hr culture in the presence of 10 ng/mL IFNγ, 50 ng/mL dexamethasone or 10 µg/mL Infliximab, or absence. Data are representative of 5 individual experiments. Data were analysed by two-way ANOVA followed by Dunnett's multiple comparison test, *p<0.05.

Results: Prior to culture, the CD68$^+$ macrophage populations present in SF were found to be predominantly CD206$^-$MerTK$^-$. After 48 hours of culture, in the absence of any stimulus, there was an increase in proportions of CD206$^+$MerTK$^+$ macrophages. Treatment with either dexamethasone or anti-TNF (Infliximab) resulted in a further increase in proportions of CD206$^+$ MerTK$^+$, M2-like macrophages. In contrast, culture with IFNγ induced a reduction in this population. Importantly, we found that the generated CD206$^+$MerTK$^+$ macrophages were phenotypically stable in culture following removal of these differentiating agents.

Conclusion: Our findings demonstrate that inflammatory SF cells are indeed able to polarise to regulatory, CD206$^+$MerTK$^+$ macrophages *in vitro*. The findings provide further mechanistic insights into the basis for the therapeutic benefits of glucocorticoids and TNF inhibitors, as well as providing initial proof-of-concept in the use of regulatory macrophages as a cellular-based therapy or therapeutic target for patients with RA.

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Disclosure of Interests: None declared

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POS0058 IDENTIFICATION OF NOVEL BIOMARKERS OF DISEASE ACTIVITY IN SYSTEMIC AUTOIMMUNE DISEASES THROUGH NEXT GENERATION PROTEOMICS

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Background: Systemic autoimmune diseases such as Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) are characterised by aberrant autoimmune and inflammatory processes, which are directly associated with the development and progression of these disorders. Novel biomarkers associated with the severity of these diseases are needed to better characterise and monitor their progression as well as to develop new and more effective therapeutic strategies.

Objectives: To identify common and distinctive novel biomarkers of disease activity in SLE and RA using high-throughput proteomics.

Methods: Serum samples from 170 patients, including 100 RA and 70 SLE, were profiled with the disruptive technology "proximity extension assay" from Olink, which analysed the levels of a panel of 92 inflammatory proteins. The methodology involves protein-specific antibodies linked to DNA-encoded tags which are amplified by RT-PCR.

Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Disease activity score in 28 joints (DAS28) were assessed in SLE and RA patients respectively to characterise the disease status of all patients.

Pearson´s correlation studies were performed using molecular information and clinical data to identify biomarkers of disease activity in each disease (FDR<0.05). Gene ontology enrichment analysis were performed to gain insight about the biological meaning of the biomarker signatures.

Results: SLE patients were characterised by an average SLEDAI of 5.2 (min-max, 0-29) while RA patients exhibited an average DAS28 of 4.6 (min-max, 1.5-7.8).

Correlation studies revealed 14 proteins directly associated with SLEDAI in SLE patients, including ADA, CCL25, CD40, CDCP1, CSF1, FGF21, FLT3L, IL10RB, LAP-TGFB1, MMP20, OPG, SLAMF1, TNFRSF9 and uPA. The subsequent enrichment analysis revealed that those molecules were associated with pathways such as cytokine-cytokine receptor interaction and MAPK signalling.

In RA patients 26 proteins were directly correlated with DAS28 including AXIN1, BNGF, CASP8, CCL23, CD40, CSF1, CXCL9, CXCL10, CXCL11, EN-RAGE, FGF23, GDNF, HGF, IL10RB, IL15RA, IL6, IL7, IL19, IL20, IL33, LAP-TGFB, MCP3, OPG, SLAMF1, TNFRSF9 and TWEAK which were enriched in biological pathways such as chemokine-chemokine receptor interaction and JAK-STAT signalling.

The levels of five pro-inflammatory mediators were commonly associated with the disease activity status of both diseases such as IL10RB (receptor for IL10, IFNL2 and IFNL3), CSF1 (macrophage colony-stimulating factor 1 receptor), SLAMF1 (Signaling lymphocytic activation molecule), TNFRSF9 and OPG (both, tumor receptor factor ligand superfamily members), suggesting a key common role of these molecules in the underlying molecular mechanisms associated with both diseases.

Conclusion: The analysis of the inflammatory profile of systemic autoimmune diseases with novel high-throughput proteomic technologies in non-invasive samples allow the identification of relevant biomarkers associated with the disease activity, which can improve the monitoring of the disease and the development of new targeted therapies.

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Disclosure of Interests: None declared

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POS0059 COMPLEMENT PROTEINS ARE ELEVATED IN PATIENTS WITH AXSPA COMPARED WITH RELEVANT CONTROLS OF PATIENTS WITH LOW BACK PAIN AND SPA-FEATURES WITHOUT AXSPA.

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Background: Axial spondyloarthritis (axSpA) is associated with a certain genetic predisposition, i.e., with the presence of human leukocyte antigen (HLA)-B27. However, the pathogenesis remains largely unexplained. Animal models of ankylosing spondylitis have shown inhibition of complement to be beneficial in terms of limiting structural damage (1). The lectin pathway of complement activation serves as a key component of the innate immune system and plays a pivotal role in both homeostasis and development. The influence of complement in axSpA is mainly unexplored. We have, however, previously reported elevated plasma levels of the lectin pathway proteins L-ficolin and H-ficolin in patients with axSpA compared with blood donors (2).

Objectives: Our aim was to investigate plasma levels of lectin pathway proteins in a clinical cohort of patients with axSpA and compare them to relevant controls that we often experience significant challenges in differentiating from axSpA.

Methods: Plasma samples were obtained from individuals in a cohort of patients suffering from low back pain (LBP) including: 1) 23 patients with axSpA, 2) 55 patients without axSpA experiencing SpA-features/symptoms, and 3) 64 patients

with nonspecific LBP without SpA-features or MRI findings suggestive of axSpA. Diagnosis of axSpA was based on multidisciplinary team conference consensus after 3.5 years of follow-up (3). Plasma levels of 10 lectin pathway proteins (MBL, CL-L1, H-ficolin, L-ficolin, M-ficolin, MASP-1, MASP-2, MASP-3, MAp44, and MAp19) were measured by immunoassays developed in-house.

Results: Patient characteristics are shown in Table 1. Plasma levels of lectin pathway proteins L-ficolin, M-ficolin and CL-L1 differed significantly in the patient groups ($p \leq 0.03$). L-ficolin and M-ficolin were elevated in axSpA-patients compared with patients with SpA-features without axSpA and nonspecific LBP patients (Figure 1). CL-L1 was elevated in axSpA-patients and patients with SpA-features without axSpA compared with nonspecific LBP patients (Figure 1). No significant differences were observed for MBL, H-ficolin, MASP-1, MASP-2, MASP-3, MAp44, and MAp19. L-ficolin levels correlated with CRP in axSpA-patients (Spearman's rho=0.58 p=0.004). M-ficolin levels correlated weakly with CRP in nonspecific LBP patients (Spearman's rho=0.36 p=0.003). Lectin pathway protein levels did not correlate with disease activity (ASDAS).

Table 1. Patient characteristics

	axSpA (n=23)	Not axSpA (n=55)	Non-specific low back pain (n=64)	*p*-value
Median age, years (range)	32 (19-40)	33 (19-41)	32 (18-39)	0.75[a]
Males, n (%)	10 (43)	37 (67)	26 (41)	0.01[b]
HLA-B27 positive, n (%)	17 (74)	11 (20)	5 (8)	0.00[b]
Inflammatory back pain, n (%)	18 (78)	28 (51)		0.03[c]
Good response to NSAID	14 (61)	17 (31)		0.01[c]
Sacroiliitis on MRI acc. ASAS, n (%)	22 (96)	45 (82)		0.11[c]
Elevated CRP, n (%)	3 (13)	7 (13)		0.97
ASDAS (range)	2.5 (1.2-3.7)	2.3 (0.8-3.8)		0.52[d]

[a] compared by Kruskal-Wallis test. [b] all three groups compared by Chi2 test. [c] compared by Chi2 test. [d] compared by Mann Whitney U test.

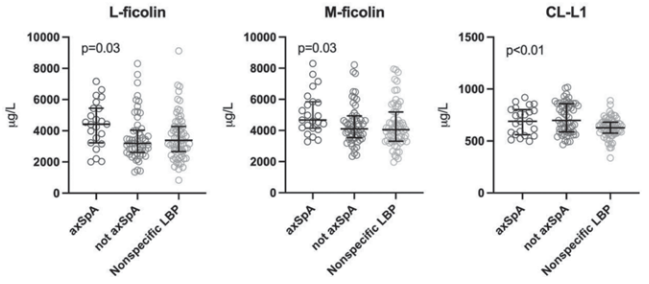

Figure 1. Plasma levels of L-ficolin, M-ficolin and CL-L1.

Conclusion: L-ficolin and M-ficolin are increased in patients with axSpA when compared with relevant control cohorts of patients with LBP or with SpA-features without axSpA. Our findings support a potential pathogenic role for complement in axSpA, however, further studies are needed to elucidate the diagnostic potential of the specific complement proteins.

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POS0060

MEASUREMENTS OF COMPLEMENT ACTIVITY SPECIFICALLY THOUGH THE LECTIN -OR THE CLASSICAL PATHWAY IN PATIENTS WITH SLE

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Background: In systemic lupus erythematosus (SLE), the complement system (CS) is activated and thought to occur primarily through the classical pathway (CP) [1]. Traditionally, when diagnosing SLE or assessing disease activity, measurement of low C3 or C4 are used as proxies for complement activation [2]. However, measurement of C3 and C4 does not differentiate which complement pathway initiated the activation (i.e., the lectin pathway (LP), the CP, or the alternative pathway) [1, 3].

C1-esterase inhibitor (C1inh) is one of the key regulators of the CS. C1inh is the exclusive inhibitor of the active CP enzymes C1r and C1s [4], and the major inhibitor of active LP enzymes MASP-1 and MASP-2 [5]. A possible way of assessing complement activation through a specific pathway, is by measuring activated enzymes complexed with C1inh in plasma, as these complexes only exist after complement enzyme activation.

Objectives: Our aim was to investigate and unravel LP and CP complement activation in SLE, by measuring the protein complexes MASP1/C1inh (LP specific activation) and C1r/C1inh (CP specific activation). Furthermore, we aimed to investigate whether there is an association between complement activity, disease activity (SLEDAI) and disease manifestations (lupus nephritis (LN)).

Methods: A cross sectional cohort of 150 patients with SLE fulfilling the 1997 ACR classification criteria for SLE were included from the out-patient clinic at the department of Rheumatology, Aarhus University Hospital (AUH), Denmark. Disease manifestations and disease activity using SLEDAI score was assessed at inclusion. Fifty healthy individuals included at the Blood Bank, AUH, were used as controls. Both C1s/C1inh and MASP1/C1inh complexes were measured in all samples using two newly developed sandwich ELISAs (C1s/C1inh: cat# HK399; MASP1/C1inh: Cat#3001, Hycult Biotech, Uden, The Netherlands). EDTA-samples from both SLE patients and controls were measured in duplicates.

Results: When comparing SLE patients to controls, we observed a difference in complement activation through the LP, where a lower mean MASP1/C1inh plasma concentration was observed ($p<0.01$).

C1s/C1inh concentrations were significantly increased in active SLE patients (SLEDAI >6) when compared to SLE patients with low disease activity (SLEDAI <6, $p<0.01$) and correlated with SLEDAI score ($r=0.285$, $p<0.01$). C1s/C1inh concentrations were increased in SLE patients with active LN compared to non-active LN, however this not statistically significant ($p=0.09$).

No differences in MASP1/C1inh plasma concentrations were observed between active SLE patients and patients with low disease activity ($p=0.11$), nor did we observe a significant correlation with disease activity ($r=0.12$, $p=0.13$). In active LN, plasma concentrations of MASP1/C1inh were significantly elevated compared to non-active LN ($p=0.02$).

Conclusion: Our data suggest that the CP and the LP is activated in SLE. CS is generally activated in active SLE disease, whereas activation of the LP might be more specific to particular disease manifestations like LN.

Our findings warrant further research into activation of the specific complement pathways in relation to specific disease manifestations in SLE.

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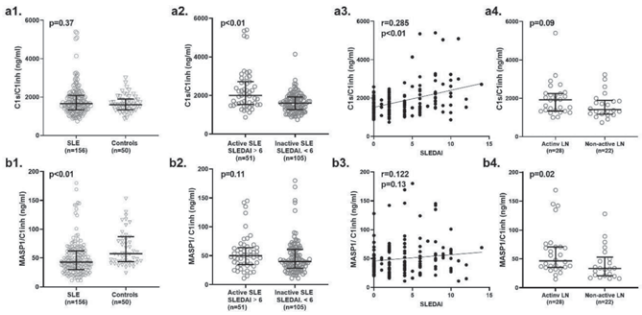

Figure 1. Measurements of plasma concentrations of C1r in complex with C1-inhibitor (C1r/C1inh) (a1-a4) and MASP1 in complex with C1-inhibitor (MASP1/C1inh) (b1-b4) in Systemic Lupus Erythematosus (SLE) patients and controls. A1 and b1 show measurements of SLE patients versus controls. A2 and b2 show measurements in SLE patients with active disease (SLEDAI >6) versus low disease activity (SLEDAI<6). A3 and b3 show correlation analysis between measurements and SLEDAI score in SLE patients. A4 and b4 show measurements in SLE patients with active lupus nephritis (LN) versus non-active LN.

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Lung involvement in Rheumatic Diseases

POS0061

THE RISK OF LUNG CANCER IN RHEUMATOID ARTHRITIS AND IN RELATION TO AUTOANTIBODY POSITIVITY AND SMOKING

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Background: Lung cancer is a common malignancy in rheumatoid arthritis (RA)[1,2]. Since smoking is a risk factor for both (seropositive) RA and lung cancer, it remains unclear whether RA, in itself, increases lung cancer risk.
Objectives: The aim of this study was to examine whether and to what extent the increased risk of lung cancer in RA may (or may not) be attributable to smoking, and to examine this association, both in terms of absolute and relative risks, specifically in relation to RA serostatus.
Methods: We performed a population-based cohort study of RA patients and individually matched general population reference individuals identified in Swedish registers and from the EIRA early RA study, prospectively followed for lung cancer occurrence 1995 through 2018. We calculated incidence rates and performed Cox regression to estimate hazard ratios (HR) including 95% confidence intervals (CI) of lung cancer, taking smoking and sero-status into account.
Results: Overall, we included 44,101 RA patients (590 incident lung cancers, 56 per 100,000), and 216,495 matched general population individuals (1,691 incident lung cancers, 33 per 100,000), corresponding to a crude HR (95% CI) of 1.76 (1.60-1.93). In subset analyses this increased risk remained after adjustment for smoking (HR=1.77, 95% CI 1.06-2.97). Compared to general population subjects who were never smokers, RA patients who were ever smokers had almost 7 times higher risk of lung cancer.
Positive autoantibody status was associated with an at least doubled risk of lung cancer in ACPA positive patients (vs. ACPA negative patients) and double seropositive (vs. double seronegative) patients after adjusting for comorbidities and smoking (Table 1).
The average absolute five-year risk of lung cancer counting from RA diagnosis was 1.3% in ever-smoking seropositive RA. At 20 years the risk was almost 3% in RA overall, and over 4% for patients who were ever smokers and had at least one autoantibody.
Conclusion: RA seropositivity is a strong and at least seemingly independent risk factor for lung cancer in RA. The absolute risks point to the potential for regular lung cancer screening, at least in seropositive RA.
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Disclosure of Interests: Katerina Chatzidionysiou Consultant of: consultancy fees from Eli Lilly, AbbVie and Pfizer, Daniela Di Giuseppe: None declared, Jonas Söderling: None declared, Anca Catrina: None declared, Johan Askling Grant/research support from: Karolinska Institutet has entered into agreements between Karolinska Institutet (JA as principal investigator) with AbbVie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, Sanofi and UCB, mainly regarding safety monitoring of anti-rheumatic therapies
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POS0062

A RISK SCORE TO DETECT SUBCLINICAL RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Despite a high morbi-mortality rate, there are no definite strategy for subclinical interstitial lung disease (ILD) screening in patients with rheumatoid arthritis (RA).
Objectives: Our objectives were: 1. to identify risk factors for subclinical RA-ILD in a prospective discovery cohort (ESPOIR) 2.to develop a risk score for subclinical RA-ILD and 3. to validate the risk score in an independent replication cohort (TRANSLATE 2).
Methods: Patients without pulmonary symptoms from 2 prospective RA cohorts who underwent chest HRCT scans were included. All patients were genotyped for *MUC5B* rs35705950. A risk score based on independent risk factors for subclinical RA-ILD was developed using multiple logistic regression in the discovery cohort. The risk score was tested for validation in the replication cohort.
Results: Discovery and replication cohorts included 163 and 89 patients, respectively. Subclinical ILD was detected in 19.0% and 16.9% of the patients, respectively. In the discovery cohort, independent risk factors for subclinical RA-ILD were the *MUC5B* rs35705950 T risk allele (odds ratio [OR]=3.74; 95% confidence interval [CI] [1.37–10.39], male sex (OR=3.93; 95%CI [1.40–11.39]), older age at RA onset (for each year, OR=1.10; 95%CI [1.04–1.16]) and increased mean DAS28-ESR (for each unit, OR=2.03; 95%CI [1.24–3.42]). We developed a risk score for subclinical RA-ILD with AUC=0.82; 95%CI [0.70–0.94] (sensitivity (Se)=71.0%) and specificity (Sp)=79.6%). The risk score was validated in the replication cohort with AUC=0.78; 95%CI [0.65–0.92] (Se=86.7%, Sp=62.2%).
Conclusion: Our risk score could help identifying patients at high-risk for subclinical RA-ILD before the onset of pulmonary symptoms.
Disclosure of Interests: Pierre-Antoine Juge Speakers bureau: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Consultant of: Bristol Myers Squibb, Benjamin Granger: None declared, Marie-Pierre Debray: None declared, Esther Ebstein: None declared, Fabienne Louis-Sidney: None declared, Joanna KEDRA: None declared, Tracy Doyle: None declared, Raphael Borie: None declared, Arnaud Constantin Consultant of: Abbvie, Amgen, Biogen, BMS, Boehringer Ingelheim, Fresenius Kabi, Galapagos, Janssen, Lilly, Medac, MSD, Mylan, Novartis, Pfizer, Procter & Gamble, Roche, Sanofi, UCB, Viatris, Bernard Combe Consultant of: AbbVie, BMS, Eli-Lilly, Gilead, Janssen, Merck, Novartis, Pfizer,

Table 1. Number of events, person-years of follow-up, number of events per 100,000 person-years, and relative risk of lung cancer according to autoantibody status in the EIRA sub-cohort. Five Hazard ratios are presented: a) crude; b) adjusted for age, sex, index year, county of residency (model A); c) age, sex, index year, county of residency and comorbidities (renal failure, heart failure, ischemic heart disease, COPD, respiratory infections, hospitalization) (model B) c) all the above plus smoking (model C) and d) as model C with packet-years instead of smoking ever vs. never.

	No of events (person years of follow-up; No of events/100 000 person years)		Crude Hazard ratio (95% CI)	Model A Hazard ratio* (95% CI)	Model B Hazard ratio** (95% CI)	Model C Hazard ratio** (95% CI)	Model D with smoking as pack-years instead of ever/never
	Positive	Negative					
RF (N=2060)	30 (49,440; 60.7)	6 (49,440; 12.1)	2.78 (1.16-6.69)	3.01 (1.25-7.26)	2.82 (1.17-6.82)	2.44 (1.01-5.89)	2.16 (0.88-5.28)
ACPA (N=2060)	30 (49,440; 60.7)	6 (49,440; 12.1)	3.13 (1.30-7.51)	3.43 (1.42-8.25)	3.22 (1.33-7.77)	2.88 (1.19-6.95)	3.29 (1.26-8.58)
RF and/or ACPA (N=2060)	34 (49,440; 68.8)	2 (49,440; 4.0)	6.38 (1.53-26.56)	7.62 (1.83-31.83)	7.20 (1.72-30.11)	6.29 (1.51-26.30)	5.76 (1.37-24.21)
RF and ACPA (positive vs. double negative) (N=1608)	26 (38,592; 67.4)	2 (38,592; 5.2)	6.67 (1.58-28.08)	7.92 (1.87-33.50)	7.08 (1.67-29.98)	6.21 (1.47-26.33)	5.86 (1.37-25.01)

Roche-Chugai, Sanofi, UCB, René-Marc Flipo Consultant of: Abbvie, Janssen, MSD and Pfizer. He reports research grants from Abbvie, Janssen, Novartis and Pfizer, Xavier Mariette Consultant of: BMS, Gilead, Janssen, Pfizer, Samsung, UCB, Olivier VITTECOQ: None declared, Alain Saraux: None declared, Guillermo CARVAJAL ALEGRIA: None declared, Jean Sibilia Consultant of: AbbVie, Lilly, MSD, Amgen, Pfizer, BMS, Janssen, Roche, Sandoz, Sanofi-Genzyme, SOBI, UCB, Novartis, Grant/research support from: AbbVie, Lilly, MSD, Amgen, Pfizer, BMS, Janssen, Roche, Sandoz, Sanofi-Genzyme, SOBI, UCB, Novartis, Francis Berenbaum: None declared, Caroline Kannengiesser: None declared, Catherine Boileau: None declared, Jeffrey Sparks Consultant of: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Gilead, Inova Diagnostics, Janssen, Optum, and Pfizer, Grant/research support from: National Institute of Arthritis and Musculoskeletal and Skin Diseases (grant numbers R01 AR077607, P30 AR070253, and P30 AR072577), The R. Bruce and Joan M. Mickey Research Scholar Fund, Bristol Myers Squibb, Bruno Crestani Speakers bureau: Boehringer Ingelheim, AstraZeneca, Roche, Sanofi, Grant/research support from: MedImmune, Roche, Boehringer Ingelheim, Bruno Fautrel Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Fresenius Kabi, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, SOBI, UCB, Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Philippe Dieudé Speakers bureau: Roche – Chugai, Bristol Myers Squibb, Consultant of: Pfizer, Roche – Chugai, Bristol Myers Squibb, Abbvie, MSD, Grant/research support from: Novartis

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POS0063

PROGRESSIVE INTERSTITIAL LUNG DISEASE IS FREQUENT ALSO IN LATE DISEASE STAGES IN SYSTEMIC SCLEROSIS PATIENTS FROM EUSTAR

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Background: Short disease duration is a predictor for progressive systemic sclerosis-associated interstitial lung disease (SSc-ILD), but studies assessing ILD progression in later disease stages are lacking. To individually tailor management of ILD in SSc patients in clinical practice it is, however, of high importance to understand disease behaviour also in patients with late disease.

Objectives: Analyse ILD progression in SSc-ILD patients from the EUSTAR cohort segregated by subgroups of disease duration.

Methods: We segregated SSc-ILD patients into four categories of disease duration (≤3 years, >3- ≤7 years, >7- ≤15 years and >15 years after onset of Raynaud's phenomenon). We assessed progressive ILD, defined as forced vital capacity (FVC) decline >10% or FVC decline ≥10% and FVC decline 5–10% and diffusing capacity of the lungs for carbon monoxide (DLCO) decline ≥15% (composite decline) over the first and second 12+/-3 months period after first registration (baseline) into EUSTAR. Clinical characteristics, pulmonary involvement, treatment at first registration and ILD progression were evaluated by descriptive statistics.

Results: In total, 2258 SSc-ILD patients were included, with 469 (20.8%) having a disease duration ≤3 years, 550 (24.4%) between >3- ≤7 years, 752 (33.3%) between >7- ≤15 years and 488 (21.6%) of >15 years (Table 1). Baseline characteristics and treatment patterns differed between the four subgroups, with more younger male patients with diffuse cutaneous SSc, anti-topoisomerase I antibody and higher Rodnan skin score having ≤3 years disease duration. Lung function with FVC and DLCO were similar between the four groups (Table 1). Notably, in the first and second 12+/-3 months periods after first registration in the EUSTAR database, there were no significant difference in FVC decline >10% or composite FVC and DLCO decline within the four subgroups. For example, patients with disease duration >7- ≤15 years and >15 years frequently showed disease progression of FVC >10%: 41/347 (11.8%) and 32/228 (14%) compared to 38/244 (15.6%) and 33/273 (15.6%) for disease duration ≤3 years and >3- ≤7 years (P=0.529), respectively (Figure 1).

Table 1. Demographics and baseline clinical characteristics of EUSTAR patients

Disease duration	≤ years (n=460)	>3- ≤7 years (n=550)	>7- ≤15 years (n=752)	>15 years (n=488)	p-value
Age, years (SD)	55 (13.5)	55 (14.1)	57 (13.1)	61 (11.5)	<0.001
Male, n (%)	123 (26.2)	115 (20.9)	112 (14.9)	38 (7.8)	<0.001
DcSSc, n (%)	228 (56.4)	262 (45.8)	311 (45.4)	163 (31.2)	<0.001
ATA, n (%)	236 (53.4)	293 (55.9)	374 (52.8)	218 (48.0)	0.099
mRSS, mean (SD)	12.3(10.1)	10.4 (8.3)	9.4 (8.1)	8.7 (7.7)	<0.001
GERD, n/N (%)	273 (58.7)	353 (64.4)	482 (64.4)	344 (71.2)	0.001
ESR, mean (SD)	26.9(21.7)	24.2 (19.5)	26.2 (19.9)	28.3 (21.2)	0.022
MMF, n/N (%)	33 (16.6)	43 (25.2)	37 (20.4)	14 (9.3)	0.002
MTX, n/N (%)	19 (10)	17 (10.1)	19 (10.6)	8 (5.2)	0.296
Any IS, n/N (%)	81 (38.6)	89 (47.1)	82 (40.8)	46 (28.7)	0.006
FVC % pred, mean (SD)	86 (20.9)	87 (21.6)	86 (21.4)	87 (22.8)	0.770
DL_{CO} % pred, mean (SD)	58 (19.3)	59 (19.3)	59 (19.9)	58 (19.7)	0.405
NYHA class 3&4, n (%)	84 (18.6)	78 (14.6)	125 (17.5)	22.6 (7.0)	0.090

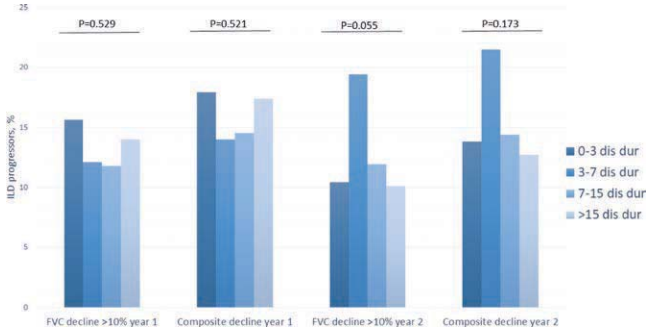

Figure 1. FVC decline >10% and composite FVC and DLCO decline in the first and second 12+/-3 months within the four subgroups segregated by disease duration

Conclusion: It was long believed that ILD burned out in late disease stages. In our analysis of ILD progression by four disease duration categories, we showed that ILD frequently progressed also in late disease stages. This has important implications for clinical practise, as SSc patients need to be regularly monitored for ILD progression independent of disease duration.

Disclosure of Interests: Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Jansen, Lilly, Medscape, Merck Sharp & Dohme, Roche, Consultant of: Actelion, ARXX, Bayer, Boehringer Ingelheim, Jansen, Lilly, Medscape, Merck Sharp & Dohme, Roche, Grant/research support from: Boehringer Ingelheim, Cathrine Brunborg: None declared, Paolo Airò Speakers bureau: Bristol-Myers-Squibb, Boehringer Ingelheim, Consultant of: Bristol-Myers-Squibb, Grant/research support from: Bristol-Myers-Squibb, Roche, Jannsen, CSL Behring, Lidia P. Ananyeva Speakers bureau: Boehringer Ingelheim, Grant/research support from: Boehringer Ingelheim, László Czirják Speakers bureau: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Actelion (now GSK), MSD, Novartis, Pfizer, Roche, Lilly, Grant/research support from: Boehringer Ingelheim, Actelion (now GSK), MSD, Novartis, Pfizer, Serena Guiducci: None declared, Eric Hachulla Speakers bureau: GSK, Roche-Chugai, Johnson & Johnson, Boehringer Ingelheim, Consultant of: CSL Behring, GSK, Roche-Chugai, Johnson & Johnson, Boehringer Ingelheim, Grant/research support from: CSL Behring, Boehringer Ingelheim, GSK, Roche-Chugai, Sanofi Genzyme, Mengtao Li: None declared, Carina Mihai Speakers bureau: MEDtalks Switzerland, Mepha, Grant/research support from: Roche, Boehringer Ingelheim, Janssen, Gabriela Riemekasten Speakers bureau: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Petros Sfikakis Consultant of: Boehringer Ingelheim, Gabriele Valentini Consultant of: Boehringer Ingelheim, Grant/research support from: Sanofi/BMS, Otylia Kowal-Bielecka Speakers bureau: Boehringer Ingelheim, Novartis, Pfizer, Gilead Sciences, Janssen-Cilag, MEDAC, MSD, Abbvie, Sandoz, Consultant of: Boehringer Ingelheim, Health Care system Navigator, CSL Behring, MSD, Novartis, Grant/research support from: CSL Behring, Boehringer Ingelheim, Abbvie, Roche, MEDAC, Yannick Allanore Speakers bureau: Boehringer, Abbvie, Consultant of: Boehringer, Bayer, Astra-Zeneca, Prometheus, Sanofi, Genentech/Roche, Boehringer, Grant/research support from: Alpine Immunosciences, OSE Immunotherapeutics, Medsenic, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Janssen, Medscape, Consultant of: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, 4P Science, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Prometheus, Roivant, Sanofi and Topadur, Grant/research support from: Kymera, Mitsubishi Tanabe, Boehringer Ingelheim

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POS0064

EPIDEMIOLOGY OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS IN FRANCE: A NATION-WIDE POPULATION-BASED STUDY OVER 10 YEARS

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Background: Data regarding interstitial lung disease (ILD) in the setting of systemic lupus erythematosus (SLE) are limited
Objectives: We used a nation-wide database to determine the incidence and the prevalence of ILD in SLE patients.
Methods: Characteristics of all SLE inpatients admitted between 2011 and 2012 in France were analyzed through the French medico-administrative database. Features associated with the presence of ILD were studied. Cox proportional hazard model was used to look for the impact of ILD on survival from the first stay to 2020. The incidence rate of ILD in SLE was estimated by analysing the onset of ILD from 2013 to 2020 in SLE patients who had no evidence of ILD in 2013.
Results: Between 2011 and 2012, 10 460 SLE patients had at least one hospital stay and could be traced until 2020. Among them, 134 (1.2%) had an ILD diagnosed at baseline. The frequency of ILD in SLE was higher in patients who had an associated autoimmune disease – such as Sjögren's syndrome or systemic sclerosis (29.9% vs 5.9%; p< 0.0001). ILD was associated with an increased risk of death in SLE after adjustment on comorbidities in the multivariable analysis (HR [CI95] 1.992 [1.420-2.794]; p <0.0001). Among the 31 029 SLE patients with no evidence of ILD at baseline, ILD occurred in 795 SLE patients (2.6%) between 2013 and 2020. The incidence rate of ILD in SLE was 10.26 for 1000 patient-years [CI95: 10.24-10.28].
Conclusion: In SLE, ILD is exceedingly rare, often associated with another systemic autoimmune disorder and appears as a major risk factor for death.
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POS0065

INTERSTITIAL LUNG DISEASE ASSOCIATED WITH PRIMARY SJÖGREN'S SYNDROME IS FREQUENTLY PROGRESSIVE

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Background: Interstitial lung disease (ILD) in primary Sjögren's syndrome (pSS) has been reported to be present in 10-15% of patients, but pSS-ILD behavior over time is not well characterized.
Objectives: Assess the pattern of ILD in pSS, its disease behavior and factors associated with disease progression in a well-characterized pSS-ILD cohort.
Methods: All pSS patients from the Oslo University Hospital (OUH) were included if ILD was diagnosed on HRCT. Clinical characteristics, lung function tests including forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO) and ILD pattern on HRCT assessed by a radiologist were evaluated. We determined ILD progression, defined as absolute FVC decline >5% or absolute DLCO decline >10% over 12 +/-6 months and increasing extent of ILD on HRCT over the observation period. Factors associated with disease progression were chosen based on expert opinion. Descriptive analyses were conducted
Results: Of 702 pSS patients followed at OUH, we identified 60 pSS patients with ILD with 33 (55%) having follow-up at 12 months (Table 1). Patients with pSS-ILD were characterized by high number of males (18%) and by frequent other extra-pulmonary organ involvement (48%) (Table 1). Mean time from pSS diagnosis to ILD diagnosis was 7.4 years. In 67% ILD was diagnosed after pSS, in 13% simultaneously, in 11% before pSS diagnosis and in 9% unknown. In total, 28 (47%) were diagnosed with lymphocytic interstitial pneumonia (LIP) and 32 (53%) with reticular pattern on HRCT. Over mean follow-up of 10.9 months (SD 4.2), 7/33 (21%) showed a FVC >5% decline, 9/32 (28%) a DLCO >10% decline and 12 (36%) had at least one of these defined lung function declines on standard of care treatment. Treatment was registered as ever used and by any indication. Over an observation period of 15.4 (SD 10.6) years, 27/47 (45%) showed any ILD progression on HRCT. HRCT pattern was not associated with risk of >10% DLCO decline or ILD progression on HCRT. >5% FVC decline occurred more frequently in patients with reticular pattern compared to LIP (6/17 (35%) vs 1/16 (6%), p=0.041). Factors significantly associated with ILD progression on lung function included higher baseline FVC (99% (SD16.4) vs 87% (SD14.9), p=0.032), higher DLCO (81% (SD13.1) vs 67% (SD17.4), p=0.020), increased CRP (2/10 (20%) vs 0/16 (0%), p=0.045) and presence of polyneuropathy (2/9 (22%) vs 1/17 (6%), p=0.045).

Table 1. Clinical characteristics, demographics and outcome of pSS with ILD

	pSS-ILD (n=60)
Age at pSS diagnosis, y (SD)	50 (21.9)
Time from pSS to ILD diagnosis, y (SD)	7.4 (8.9)
Male sex, n (%)	11 (18)
Anti-SSA AB, n/50 (%)	46 (92)
Increased CRP, n/47 (%)	7 (15)
Low complements, n/49 (%)	5 (10)
Extra-pulmonary involvement, n/46 (%)	22 (48)
Deceased, n (%)	10 (17)
Pulmonary involvement	
FVC% predicted (SD)	91 (18.7)
FVC decline>5%, n/33 (%)	7 (21)
DLCO% predicted (SD)	70 (20.7)
DLCO decline >10%, n/32 (%)	9 (32)
ILD progression on HRCT, n/47 (%)	27 (45)
Treatment during follow up	
Rituximab, n (%)	11 (18)
Any other immunosuppressive, n (%)	20 (33)
Hydroxychloroquine, n (%)	16 (27)
Nintedanib, n (%)	1 (2)
Lung transplant, n (%)	1 (2)

Conclusion: A substantial number of patients with pSS-ILD progressed during the time of observation. This highlights the importance of close monitoring and active consideration of treatment options in pSS-ILD. Recommendations for disease management including screening, diagnosis, disease monitoring and treatment for pulmonary involvement in pSS are lacking to date, but are highly needed.
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POS0066

THE PHENOTYPE OF MIXED CONNECTIVE TISSUE DISEASE PATIENTS HAVING ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Mixed connective tissue disease (MCTD) is a rare autoimmune condition characterized by Raynaud's phenomenon, positivity of autoantibodies

targeting the U1 small nuclear ribonucleoprotein particle (U1RNP), and various clinical features of other connective tissue diseases (1-2). Interstitial lung disease (ILD) is an established complication of the disease that is suspected to affect morbidity and mortality (3). However, little is known about MCTD-associated ILD (MTCD-ILD) phenotype including first presentation, outcomes and predictive factors for progression.

Objectives: To compare two distinct populations of MCTD patients with and without associated ILD and to identify predictive factors for lung progression and severity.

Methods: International multicenter retrospective study (12 tertiary hospitals). To be included, patients were required to fulfill at least one MCTD international classification criteria (4). ILD was defined by the presence of typical chest high-resolution computed tomography (HRCT) abnormalities. Patients were divided into two groups: with or without ILD, at a ratio of 1:1 and matching on disease duration (+/- 2 years).

Results: 300 patients were included. Mean age at MCTD diagnosis was 39.7±15.4 years and 191 (63.7%) were women.

At baseline, we identified several variables associated with the presence of ILD: older age (42.2 vs 37.5 years, p=0.01), scleroderma-like phenotype (38.7 vs 27.3%, p=0.03), upper gastro-intestinal (GI) symptoms (54.7 vs 30.7%, p<0.001), forced vital capacity (FVC) <80% (80.4 vs 95.3%, p<0.0001), diffusing capacity for carbon monoxide (DLCO) <80% (62.4 vs 74.8%, p<0.0001), anti-topoisomerase antibodies (6 vs 0 patients, p=0.01), SSA/Ro antibodies positivity (29.3 vs 19.3%, p=0.02), cryoglobulinemia (5.3 vs 1.3%, p=0.04) and elevated C-reactive protein (CRP) >5mg/L (54.7 vs 28.7%, p<0.001). Among the previous variables older age (OR 1.03, 95% CI 1.01 to 1.05), upper GI symptoms (OR 1.92, 95% CI 1.03 to 3.58) and CRP >5mg/L (OR 8.77, 95% CI 2.94 to 26.22) remained significantly associated with the presence of ILD by multivariate analysis.

Patients with MTCD-ILD were more likely to be treated with synthetic immunosuppressant agents (68.7 vs 49.3%, p<0.001) including mycophenolate mofetil (MMF) (7.3 vs 1.3%, p=0.03).

Mean follow-up was 7.8±5.5 years. In longitudinal analyses, mortality was higher in the MTCD-ILD group (8 vs 0 deaths, p<0.001). In the MCTD-ILD group, among 60 patients with complete data on lung function tests, we observed a FVC decline >10% in 33 (55%) patients. With regards to the risk of progression, we identified that history of digital ulcers (DU) was a risk factor for FVC decline >10% (OR 6.75, 95% CI 1.7-26.4, p=0.006).

Conclusion: In this large international cohort of patients with MTCD, we identified several factors associated with ILD development. Our findings highlight a high risk of mortality in MCTD-ILD patients and that digital ulceration seems to be at risk of more progressive ILD.

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POS0067 PULMONARY FUNCTION IN PATIENTS DIAGNOSED OF EARLY SYSTEMIC SCLEROSIS: 10 YEARS EXPERIENCE.

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Background: Interstitial lung disease (ILD) is a frequent complication of systemic sclerosis (SSc) and is often progressive and has a poor prognosis. A restrictive ventilatory defect could suggest ILD either alone or in combination with pulmonary arterial hypertension.

Nowadays, Early-SSc is well defined as preliminary stage of SSc. Patients who meet criteria for Early-SSc could benefit from an early diagnosis of pulmonary involvement.

Objectives: Our aim was to assess the pulmonary function in patients diagnosed of Early SSc.

Methods: Retrospective observational study of a wide and unselected series of patients diagnosed as Early-SSc from a single university hospital from 2012 to 2022. Patients were classified as Early-SSc following Le Roy criteria. Despite this, patients already did not meet 2013 ACR/EULAR classification criteria for SSc. We reviewed pulmonary function through conventional spirometry and diffusing capacity of lungs for carbon monoxide (DLCO).

Results: We included 61 patients with a mean age of 52.9±6.2 years (90.9% women; 9.1% men).

At the diagnosis of Early-SSc, no one of our patients evidenced a restrictive ventilatory pattern. DLCO was below normal limits in 21 patients (34.4%). Small airway obstruction expressed according decreased maximal (mid-) expiratory flow (MMEF) 25-75 was present in 26 patients (42.6%).

After a mean follow-up period of 42.4±3.2 months, 29 (47.5%) patients fulfilled 2013 ACR/EULAR criteria. The average time between diagnosis of Early-SSc and achieve SSc classification was 24.4±1.8 months. The remaining 32 patients continued classified as Early-SSc.

An analysis of the subgroup of patients which progressed to SSc showed that DLCO was decreased in 15 of those 29 patients (51.7%) and 18 of 29 patients (62.1%) presented decreased MMEF 25-75. Comparing with the subgroup of patients which not progressed to SSc were significant differences (Decreased DLCO: 51.7% vs 10.4%; p=0.01 and decreased MMEF 25-75: 42.8% vs 24.6%; p=0.05).

The analysis of pulmonary function of the subgroup of patients continued classified as Early-SSc after follow-up period did not show significative changes after follow-up.

Conclusion: In our study, a third of the patients classified as Early-SSc presented at diagnosis abnormal values of DLCO and/or signs of small airway obstruction without the presence of a restrictive ventilatory pattern. Moreover, this pulmonary disfunction was significantly more frequent in patients who progressed to definitive SSc. Patients which remains classified as Early-SSc did not experience significative changes.

Our results support the concept that pulmonary function was impaired in Early-SSc and that it should probably be considered for future Early-SSc classification criteria.

Disclosure of Interests: None declared

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POS0068 CHANGES IN QUANTITATIVE INTERSTITIAL LUNG DISEASE SCORES ON HIGH-RESOLUTION CT IN IDIOPATHIC INFLAMMATORY MYOSITIS

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Background: The idiopathic inflammatory myopathies (IIM) are autoimmune connective tissue diseases affecting skeletal muscle, skin and other organ systems. IIM-related interstitial lung disease (IIM-ILD) is the most common extra-muscular manifestation, being the leading cause of morbidity and mortality. Several studies have suggested that ILD pattern based on chest high-resolution computed tomography (HRCT) can be related to disease course and treatment response, but the results vary considerably. Moreover, the clinical impact of the quantitative ILD (QILD) score, a validated computer-aided scoring system in assessing ILD severity from HRCT, and its longitudinal changes have not yet been evaluated in IIM-ILD.

Objectives: This study aims to investigate ILD patterns and QILD scores in patients with IIM-ILD, to identify their clinical impact, and to delineate longitudinal changes of QILD measurement.

Methods: A total of 80 patients with IIM (polymyositis 22, and dermatomyositis 58) who underwent at least 2 times of serial HRCT scans were included. Visual ILD patterns were assessed by multiple thoracic radiologists. Quantitative analysis of HRCT was presented as total extent of QILD scores (%) in whole lung and most severe zone. Individual time-estimated ΔQILD score between first 2 visits was derived using a linear approximation of yearly change, where the duration of median (IQR) was 1.0 (0.4-1.6) years in the first 2 HRCT scans.

Results: The median (IQR) age of the patients was 52.0 (43.5-58.5) years and 60 (75.0%) were women. Baseline median score of whole lung-QILD and most severe zone-QILD were 28.1% (19.1-43.8) and 68.0% (45.5-81.8), respectively, and QILD score showed significant correlations with pulmonary function tests (r=-0.349, p=0.002 for % predicted forced vital capacity; and r=-0.381, p=0.001 for % predicted diffusing capacity for carbon monoxide). The individual time-estimated yearly ΔQILD score between first 2 visits presented that approximately half of the patients showed improvement or stability in QILD scores; however, when patients were sorted by visual assessment in ILD subtype on HRCT, approximately two-thirds of the patients with usual interstitial pneumonia (UIP) pattern were aggravated in QILD scores and less than half of subjects with nonspecific interstitial pneumonia and organizing pneumonia were aggravated (Figure 1, 80% for UIP vs. 44.4% for non-UIP, p=0.013). There was no immunosuppressive drugs related to meaningful improvement in QILD scores during first 2 visits. Notably, we observed significant aggravation of QILD scores in tacrolimus users (n=7, median time-estimated whole lung-yarly ΔQILD 20.3 (2.7-38.4)) compared with tacrolimus non-users (n=73, median time estimated whole lung-yearly ΔQILD -1.2 (-8.3-6.5)). Among 80 patients, 6 (7.5%) were died due to various lung complications. Higher baseline QILD scores were noted in deaths (median whole lung-QILD 45.4 (32.9-56.5)) than in survivors (median whole lung-QILD 26.9 (19.0-42.4)), albeit not significant (p=0.084). Poor survival rate was observed in patients with high grade of ground glass opacity by visual assessment in right upper lobe (log-rank test, p=0.042). Among subgroup of patients with 3 serial HRCT scans (n=41), dynamic changes of four distinct patterns (improving, worsening, convex, and concave) were observed.

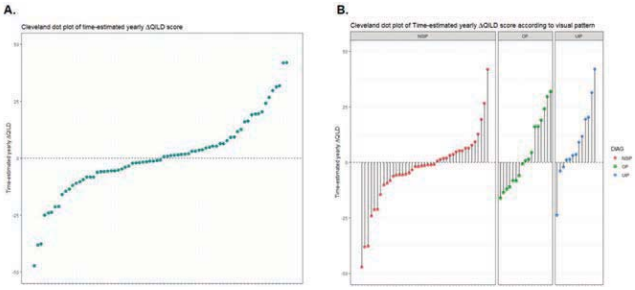

Figure 1. Cleveland dot plot of individual time-estimated yearly ΔQILD during fist 2 visits.

Conclusion: The changes in QILD score in IIM-ILD are dynamic and present different by visual assessment. QILD score has the potential for evaluation of the severity changes, prognosis and medication response in patients with IIM-ILD.

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7 truncated values in the graph A. NSIP: nonspecific interstitial pneumonia; OP: organizing pneumonia; UIP: usual interstitial pneumonia.

Disclosure of Interests: None declared

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POS0069 LONGITUDINAL CHANGES ON QUANTITATIVE CHEST HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN EARLY DIFFUSE SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION.

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Background: Since Burt *et al.* first demonstrated in the ASSIST trial (1) that lung disease high-resolution computed tomography (HRCT) volumetric measurement decreased in autologous hematopoietic stem cell transplantation (aHSCT) recipients and increased in controls receiving cyclophosphamide iv one year after starting treatment, limited data have been reported concerning the evolution of Systemic Sclerosis-Interstitial Lund disease (SSc-ILD) since and its relationship with the evolution of esophageal volume is unknown.

Objectives: To evaluate High-Resolution Computed Computed Tomography (HRCT) interstitial lung disease (ILD) and esophageal involvement in early diffuse systemic sclerosis (dSSc)-patients before and after autologous Hematopoietic Stem Cell Transplantation (aHSCT).

Methods: Overall chest HRCT, lung function and skin score changes were evaluated in 33 consecutive dSSc-patients before and after aHSCT during yearly routine follow-up between January 2000 and september 2016.Two independent radiologists blindly assessed the ILD extent using semi-quantitative Goh and Wells method (2), the widest esophageal diameter (WED) and the esophageal volume (EV) on HRCT. Patients were retrospectively classified as radiological responders or non-responders at 24 months after aHSCT according to the stability or a 5% or more decrease of HRCT ILD extent. Two by two time points comparisons after versus before aHSCT were performed using linear regressions. Survival rates were assessed for all patients by Kaplan-Meier method.

Results: Twenty-four months after aHSCT, HRCT median [IQR] ILD (-2 [-10.3; 0] points, p=0.0002) and ground-grass opacities (-2.1 [-8.3; 0] points, p=0.02) extent scores had improved, with 18 patients radiological responders (probability of response 0.78, 95% CI (0.58;0.90), whereas median WED (from 24.5 [18; 29] to 28 [19; 33] mm; p= 0.005) and EV (from 19 [13; 33] to 30 [13; 58] mm^3, p=0.01) increased significantly. Kaplan-Meier analyses showed a trend towards better 5 years survival rates (100% versus 60%; HR 0.23 95%CI 0.03 to 1.62, P = 0.11) among radiological responders versus non-responders at 24 months.

Conclusion: Real-world data analysis confirmed significant HRCT SSc-ILD improvement 24 months after aHSCT, although esophageal dilatation worsened requiring specific attention.

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POS0070 CONTINUED TREATMENT WITH NINTEDANIB IN PATIENTS WITH LIMITED CUTANEOUS SYSTEMIC SCLEROSIS (LCSSC) AND INTERSTITIAL LUNG DISEASE (ILD)

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Background: Few data are available on the progression and management of ILD, or the management of adverse events associated with drug treatment, in patients with lcSSc. SENSCIS-ON is an open-label extension trial that is collecting data on decline in forced vital capacity (FVC) and adverse events in patients treated with nintedanib over the long term.

Objectives: To assess decline in FVC and adverse events in patients with lcSSc and ILD treated with nintedanib in SENSCIS-ON.

Methods: Patients with SSc-ILD were eligible to enter SENSCIS-ON if they completed the randomized placebo-controlled SENSCIS trial (in which patients received trial drug until the last patient reached week 52 but for ≤100 weeks) or a drug–drug interaction (DDI) study of nintedanib and oral contraceptive (in which female patients received nintedanib for ≤28 days). Among patients with lcSSc, we analysed changes from baseline in FVC and adverse events over 52 weeks of SENSCIS-ON in patients who received nintedanib in SENSCIS and continued it in SENSCIS-ON ("continued nintedanib" group) and in patients who received placebo in SENSCIS and initiated nintedanib in SENSCIS-ON or who received nintedanib for a short time in the DDI study ("initiated nintedanib" group). Analyses were descriptive.

Results: There were 98 patients with lcSSc in the continued nintedanib group and 127 patients with lcSSc (114 from SENSCIS, 13 from the DDI study) in the initiated nintedanib group. In these groups, respectively, mean (SD) FVC values

at inclusion in SENSCIS-ON were 2449 (662) mL and 72.7(16.7) % predicted and 2508 (771) mL and 74.1 (17.4) % predicted. Mean (SE) changes in FVC from baseline to week 52 of SENSCIS-ON were –45.1 (19.1) mL in the continued nintedanib group, –41.5 (24.0) mL in the initiated nintedanib group, and –43.3 (15.3) mL in all patients with lcSSc, similar to the change in FVC in patients with lcSSc at week 52 of the SENSCIS trial (–39.1 [22.2] mL). The adverse event profile of nintedanib in SENSCIS-ON was consistent with that reported over 52 weeks of the SENSCIS trial (Table 1). Over 52 weeks, adverse events led to discontinuation of nintedanib in 3.1% of patients with lcSSc who continued nintedanib in SENSCIS-ON and 16.5% who initiated nintedanib in SENSCIS-ON.

Table 1. Adverse events (irrespective of causality) reported over 52 weeks in patients with lcSSc and ILD in SENSCIS and SENSCIS-ON.

	SENSCIS		SENSCIS-ON	
	Nintedanib (n=135)	Placebo (n=142)	Continued nintedanib (n=98)	Initiated nintedanib (n=127)
Most frequent adverse events*				
Diarrhoea	104 (77.0)	43 (30.3)	70 (71.4)	89 (70.1)
Nausea	45 (33.3)	20 (14.1)	19 (19.4)	32 (25.2)
Vomiting	33 (24.4)	16 (11.3)	15 (15.3)	31 (24.4)
Nasopharyngitis	21 (15.6)	29 (20.4)	18 (18.4)	23 (18.1)
Upper respiratory tract infection	18 (13.3)	19 (13.4)	13 (13.3)	18 (14.2)
Skin ulcer	11 (8.1)	18 (12.7)	11 (11.2)	14 (11.0)
Cough	17 (12.6)	25 (17.6)	13 (13.3)	8 (6.3)
Adverse event(s) leading to permanent treatment discontinuation	25 (18.5)	12 (8.5)	3 (3.1)	21 (16.5)
Adverse event(s) leading to dose reduction	47 (34.8)	5 (3.5)	17 (17.3)	62 (48.8)
Serious adverse event(s)	30 (22.2)	26 (18.3)	22 (22.4)	31 (24.4)

n (%) of patients with lcSSc with ≥1 such event reported over 52 weeks (or until 28 days after last drug intake if earlier in SENSCIS or until 7 days after last trial drug intake if earlier in SENSCIS-ON). *Adverse events reported in >10% of patients with lcSSc in either group in SENSCIS-ON. Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities.

Conclusion: The change in FVC in patients with lcSSc and ILD who received nintedanib over 52 weeks, and the safety profile of nintedanib, in SENSCIS-ON were similar to that observed in patients with lcSSc and ILD who received nintedanib in SENSCIS. These analyses support a continued effect of nintedanib on slowing decline in FVC and the ability to manage adverse events of nintedanib in patients with lcSSc and ILD over the longer term.

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POS0071

THE EFFICACY OF PIRFENIDONE COMBINED WITH IMMUNOSUPPRESSANT THERAPY IN THE CONNECTIVE TISSUE DISEASE-ASSOCIATED PULMONARY INTERSTITIAL DISEASE, A 24-WEEK PROSPECTIVE CONTROLLED COHORT STUDY

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Background: Pulmonary interstitial disease(ILD)is very common in connective tissue disease (CTD). Different subtypes display significant differentiations in prognosis. Pirfenidone (PFD), the targeted anti-fibrosis and anti-inflammatory drug, started to apply in CTD-ILD, while its strategy of combination with immunotherapy, bridging time and service time are worth discussing.

Objectives: To evaluate the efficacy and safety of PFD combined with immunosuppressant (IS) in the treatment of several CTD- ILD.

Methods: 111 CTD-ILD patients were involved from Aug 2019 to Dec 2021 (ClinicalTrials.gov Identifier NCT04928586), including systemic sclerosis (SSc, n=30), inflammatory myopathy (IIM, n=51), rheumatoid arthritis (RA, n=17) and other CTDs (such as systemic lupus erythematosus, sjogren's syndrome, n=13). Patients were treated with relative stable dose of glucocorticoid (GC) and/or IS since screening.After the evaluation of HRCT, pulmonary function (FVC% and

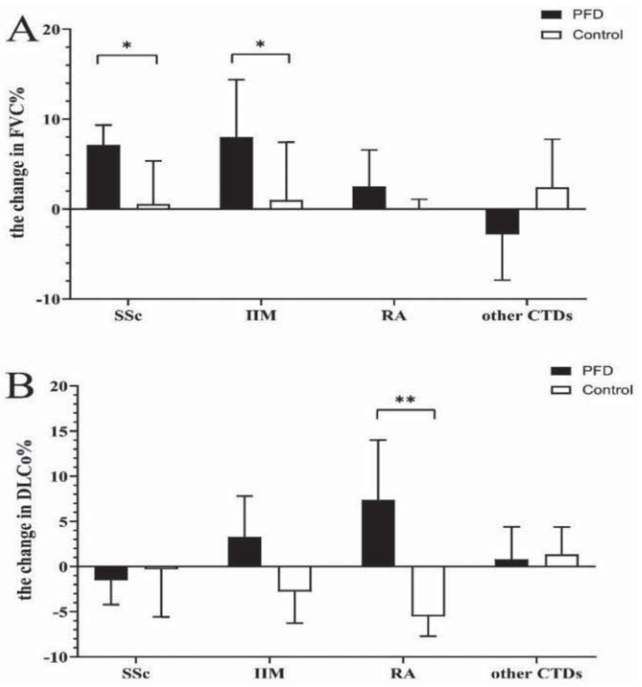

Figure 1. The changes of FVC% and DLco% in PFD treated CTD-ILD for 24 weeks. **(A)** FVC% changes in SSc, IIM, RA and other CTD-ILD from baseline.; **(B)** DLco% changes in SSc, IIM, RA and other CTD-ILD from baseline. * $p < 0.05$, compared to no PFD treatment group.

DLCo%) and basic disease activity, PFD was added or not and followed up regularly for 24 weeks. The changes of lung function and imaging were recorded in different subgroups.

Results: At baseline, The FVC% in the SSc-PFD (n=14), IIM-PFD (n=25) pts were lower than that of SSc-no-PFD (n=16), IIM-no-PFD (n=26) respectively, that was 81.06 *vs* 99.63(p=0.014), 78.23 *vs* 91.12, (p= 0.010). And IIM-PFD group present a lower baseline DLCo% than IIM-no-PFD pts (64.25 *vs* 72.82, p=0.034). DLCo% in the other CTDs was lower than SSc, IIM, RA pts (54.58 vs 65.55, 68.71, 66.89, p=0.036), while there were no significant differences in baseline FVC% among these disease.

After 24 weeks of treatment, FVC% in SSc-PFD group was improved by 7.15%, while that was -0.91% in SSc-no-PFD pts (p=0.042). The elevation in FVC% was also significant between the IIM-PFD and IIM-no-PFD control (8.00 *vs* 1.40, p=0.016). On the other hand, DLCo% of RA-PFD obviously enhanced 7.40%, compared with RA-no-PFD decrease 5.50% from baseline(p=0.002) (Figure 1).

When performing subgroup analysis with manifestations in HRCT, the change of FVC% in SSc-PFD pts with usual interstitial pueumonia tendency(SSc-PFD-UIP) was higher than SSc-PFD-non-UIP group (8.05 *vs* -3.20, p=0.014). However, the non-UIP tendency in IIM-PDF pts displayed superior therapeutic effects than IIM-PDF-UIP pts (10.50 *vs* 1.00, p=0.005). In addition, DLCo% improved significantly in RA-PDF-non-UIP subgroup, compared with RA-PDF-UIP pts (10.40 *vs* -4.45, p=0.017).

According to whether the baseline FVC% and DLCo% value was less than 70%, the improvement of FVC% was significantly higher in PFD treatment group than no-PFD pts of SSc and IIM with baseline High-FVC%(6.60 *vs* 0.10, p=0.047),(6.30 *vs* 1.10, p= 0.089).In RA-PFD pts, DLCo% showed a significant increase in baseline DLCo% less than 70% subgroup, compared to RA-no-PDF (7.40% vs -6.60%, p=0.011).The basic IS were considerable between PFD and-no-PFD pts throughout the study and no differences of GS and IS dosages at baseline and follow up among all subgroups.

Multiple linear regression analysis found that baseline FVC%<70%(HR=4.56,6.81) and prescription of PFD(HR=4.56,4.37) could positively affect the changes of FVC% and DLCo% (all p<0.05).

Conclusion: The response of pulmonary function to PFD were varied in different CTD-ILD subsets. SSc and IIM pts acquired obviously improvement on FVC%, especially with high baseline FVC group. DLco% elevated in RA-PFD, highlight those baseline Low-DLco and No-UIP pts.

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New therapeutic avenues in psoriatic arthritis

POS0072

CONSISTENT LONG-TERM GUSELKUMAB EFFICACY ACROSS PSORIATIC ARTHRITIS DOMAINS IRRESPECTIVE OF BASELINE PATIENT CHARACTERISTICS

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Background: Psoriatic arthritis (PsA) patients (pts) with differing baseline (BL) characteristics may vary in their response to treatment. In the phase 3 DISCOVER-1 and DISCOVER-2 studies, guselkumab (GUS) significantly improved joint symptoms, skin disease, enthesitis, dactylitis, physical function, and quality of life at Week (W) 24 in pts with PsA.[1,2] Clinical responses across these disease domains were maintained or increased with GUS at W52,[3,4] regardless of BL pt demographics, disease characteristics, or conventional synthetic disease-modifying antirheumatic drug (csDMARD) use.[5] Durable efficacy with GUS through W100 across multiple disease domains was observed.[6]

Objectives: Assess both BL predictors of, and by BL pt subgroups, GUS efficacy across PsA disease domains through W100 of DISCOVER-2.

Methods: Biologic-naïve adults with active PsA despite standard therapies were enrolled in DISCOVER-2 (swollen joint count [SJC] ≥5 & tender joint count [TJC] ≥5, C-reactive protein [CRP] ≥0.6 mg/dL). Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO).[2] GUS effects on joint, skin, enthesitis, dactylitis, spinal pain, and disease severity endpoints (change in Disease Activity in PsA [DAPSA], SJC, and TJC scores; Psoriasis [PsO] Area Severity Index [PASI] score [among pts with BL IGA ≥2 and body surface area [BSA] with PsO ≥3%]; Leeds enthesitis index [LEI] score [among pts with enthesitis at BL]; dactylitis score [among pts with dactylitis at BL]; spinal pain score; and PsA Disease Activity Score [PASDAS], respectively) at W100 were evaluated for GUS-randomized pts, both by treatment group and by pooling pts across Q4W and Q8W treatment arms. A multivariate linear model adjusting for BL pt characteristics assessed associations between BL predictors of interest and changes in DAPSA, PASI, and LEI scores from BL to W100, and to assess least squares mean (LSM) changes and 95% confidence intervals (CIs) in all continuous endpoints from BL to W100 within subgroups of pts defined by BL sex, body mass index (BMI), PsA duration, SJC, TJC, CRP level, %BSA, PASI score, and csDMARD use.

Results: 442 (90%) GUS-randomized pts completed study treatment through W100.[6] Among the BL predictors of long-term GUS efficacy assessed (see above), only PsA duration (p=0.032), SJC (p<0.001), and TJC (p<0.001) were significant predictors of long-term (BL to W100) DAPSA score change; %BSA (p=0.002), PASI score (<0.001), SJC (p=0.008), and csDMARD use (p=0.014) were significant predictors of long-term PASI score change; and none significantly predicted long-term LEI score change among pooled GUS pts (Figure 1). However, statistically significant improvements from BL to W100 in DAPSA, PASI, and LEI scores were observed across all BL strata, including those indicating more extensive or severe disease, in pooled GUS Q4W+Q8W pts (Figure 1, all p<0.001) and within each dosing group. Similar improvements were observed for other continuous endpoints assessed (change in Psoriatic Arthritis Disease Activity Score [PASDAS], SJC, TJC, spinal pain, and dactylitis score).

Conclusion: GUS significantly improved PsA signs and symptoms through W100 across all BL pt subgroups evaluated, including pts with highly active disease, and regardless of dosing regimen.

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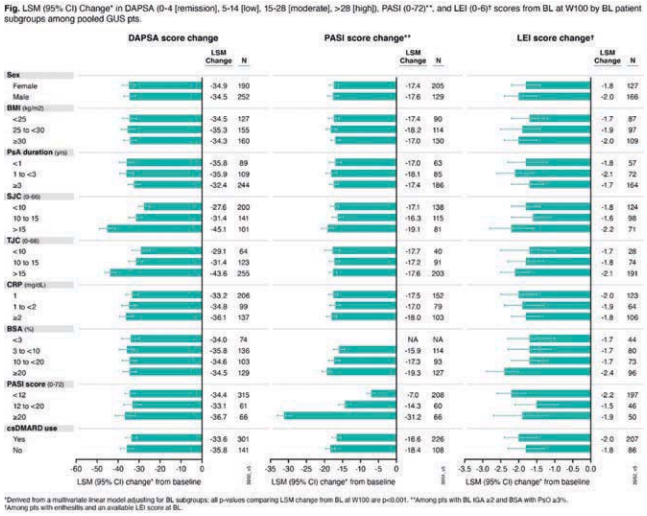

Fig. LSM (95% CI) Change* in DAPSA (0-4 [remission], 5-14 [low], 15-28 [moderate], >28 [high]), PASI (0-72)**, and LEI (0-6)† scores from BL at W100 by BL patient subgroups among pooled GUS pts.

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POS0073

COMPARISON OF TIME FROM METHOTREXATE INITIATION TO START OF A B/TSDMARD IN PSORIATIC ARTHRITIS VERSUS RHEUMATOID ARTHRITIS. A NATIONWIDE REGISTER-BASED STUDY.

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Background: In Sweden, methotrexate (MTX) is recommended as first-line DMARD for both psoriatic arthritis (PsA) and rheumatoid arthritis (RA). Whereas in RA the use of MTX monotherapy is supported by efficacy data from randomized trials, in PsA no clear efficacy has been demonstrated in placebo-controlled trials. Therefore, the use of MTX in PsA is mostly based on clinical experience and results from studies not primarily designed to evaluate MTX efficacy.

Objectives: To compare time from MTX initiation until start of a biological or targeted synthetic DMARD (b/tsDMARD), as marker of insufficient MTX response, in previously DMARD-naïve, incident cases with PsA and matched, corresponding, reference subjects with RA.

Methods: Patients with PsA, having collected a prescription of MTX as their first ever DMARD any time between 2011 through 2018, and with a first ever PsA diagnosis in the Swedish National Patient Register within two years prior to this date, were included. Each individual was required to have a visit in rheumatology, but no visit in dermatology, within 6 weeks prior to MTX initiation, to ensure that PsA rather than psoriasis was the main reason for MTX treatment. For each individual with PsA, a corresponding individual with incident RA was identified, matched on sex, age, and year of MTX initiation. Only PsA cases with an identified RA comparator were included. All individuals with a diagnosis indicating axial spondyloarthritis prior to MTX start were excluded. The data were enriched through linkage to other national registers.

Follow-up was defined as the time from MTX initiation until start of any b/tsDMARD. Censoring was performed at the first of death, migration or 31 Dec 2020. Time until start of a b/tsDMARD was compared for PsA and RA through crude survival curves and conditional Cox-regression, crude and adjusted for comorbidity, level of education and patient global health.

Results: 3098 patients with PsA, and their individually matched RA comparators were included. At initiation of MTX, PsA cases had a mean 28-joint disease activity score (DAS28) of 4.0 and RA-controls of 4.6, while patient-reported global health was 51 (of 100) for both groups and number of swollen joints (28-joint count) 4.0 for PsA and 6.8 for RA, Table 1. The comorbidity burden was similar at baseline.

Table 1. Characteristics of PsA cases and matched RA controls at start of MTX.

	Psoriatic arthritis N=3098	Rheumatoid arthritis N=3098
Age, mean (sd)	55 (14)	55 (14)
Sex, male	49%	49%
Length of education, yrs		
<10	20%	24%
10-12	51%	49%
>12	28%	26%
Diabetes[1, 2]	7.4%	6.7%
Myocardial infarction[1]	1.3%	1.8%
Malignancy[1]	4.7%	5.0%
Congestive heart disease[1]	0.2%	0.2%
Chronic lung disease[1]	1.6%	2.2%
Use of anti-depressive drugs[1, 3]	15.4%	11.4%
DAS28-CRP, mean (sd)[4]	4.0 (1.1)	4.6 (1.2)
Patient global, mean (sd)[4]	51 (23)	51 (23)
CRP, median (IQR)[4]	7 (14)	10 (21)
Tender joint count (28), mean (sd)[4]	5.2 (4.9)	7.0 (5.7)
Swollen joint count (28), mean (sd)[4]	4.0 (4.1)	6.8 (5.2)

1) Diagnosis within 5 years. 2) Also identified by collecting ≥1 prescription of anti-diabetics in 1 year. 3) Identified by collecting ≥1 prescription within 1 year before methotrexate start. 4) Data on disease activity variables available for 28-36% of PsA and 56-62% of RA.

During a mean follow-up of 4.5 and 4.4 years, 34% and 33% of PsA and RA patients, respectively, started a b/tsDMARD, of whom 63% and 84% had also used ≥1 non-MTX conventional synthetic DMARD before the b/tsDMARD initiation. The crude survival curves for time from MTX initiation until start of a b/tsDMARD were identical for PsA and RA, Figure 1A. The adjusted HR for starting a b/tsDMARD in PsA compared with RA was 0.99 (95% CI 0.90-1.09). No calendar time trends were observed (Figure 1B and C).

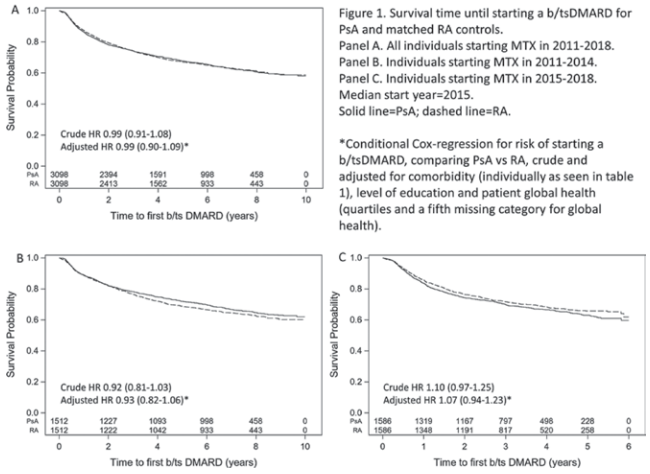

Figure 1. Survival time until starting a b/tsDMARD for PsA and matched RA controls.
Panel A. All individuals starting MTX in 2011-2018.
Panel B. Individuals starting MTX in 2011-2014.
Panel C. Individuals starting MTX in 2015-2018.
Median start year=2015.
Solid line=PsA; dashed line=RA.

*Conditional Cox-regression for risk of starting a b/tsDMARD, comparing PsA vs RA, crude and adjusted for comorbidity (individually as seen in table 1), level of education and patient global health (quartiles and a fifth missing category for global health).

Conclusion: In this study, the risk of escalating treatment from MTX, by adding or switching to a b/tsDMARD, was identical in PsA cases and matched RA controls. This supports a good response to MTX in PsA, similar to that in RA. Due to the matching, neither the results from the PsA nor the RA populations may be fully generalizable.

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POS0074

IMMUNOLOGICAL DIFFERENCES BETWEEN PSA PATIENTS WHO ARE TUMOR NECROSIS FACTOR INHIBITOR-NAIVE AND WHO HAVE INADEQUATE RESPONSE TO TUMOR NECROSIS FACTOR INHIBITORS

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Background: A better understanding of the immunological differences between psoriatic arthritis (PsA) patients (pts) who are tumor necrosis factor inhibitor (TNFi)-naïve & who have inadequate response to TNFi (TNFi-IR) may guide treatment choices. In DISCOVER-1, benefit of the IL-23p19 subunit inhibitor guselkumab (GUS) every-four-weeks (Q4W) & Q8W vs placebo (PBO) in improving PsA signs & symptoms was seen in adults with active PsA.[1] The Ph3b COSMOS study of GUS Q8W vs PBO in TNFi-IR PsA pts corroborated these findings.[2]

Objectives: Assess baseline (BL) molecular differences between TNFi-naïve & -IR PsA pts & investigate GUS pharmacodynamic (PD) effect on cytokine expression over time in these cohorts.

Methods: Serum samples collected from consenting biomarker substudy pts in DISCOVER-1[1] (TNFi-naïve [n=101] & -IR [n=17]), DISCOVER-2[3] (TNFi-naïve [n=150]), & COSMOS[2] (TNFi-IR [n=76]) were analyzed for selected serum cytokine levels. TNFi-IR pts in this post-hoc analysis had active PsA & discontinued 1-2 TNFi due to inadequate efficacy; these pts required a TNFi-specific washout period prior to starting GUS. PD effect of GUS Q8W on cytokine levels was assessed. Differential BL cytokine expression, associations between BL cytokine levels & clinical response (Psoriasis [PsO] Area & Severity Index 75% improvement from BL [PASI75] & American College of Rheumatology 20% improvement [ACR20]), & GUS effect on cytokine levels were analyzed with a General linear model & Spearman linear regression.

Results: BL pt demographics, disease characteristics, & conventional synthetic disease-modifying antirheumatic drug (csDMARD) use were comparable between TNFi-naïve (DISCOVER-1 & -2, N=251) & -IR (DISCOVER-1 & COSMOS, N=93) pts, with differences in mean PASI score (8.9 v 12.5), swollen joint count (SJC) (11.7 v 10.3), PsA duration (5.8 v 9.8 yrs), & PsO duration (16.7 v 20.4 yrs; Table 1). BL serum IL-22 & TNFα levels for pooled treatment groups were higher in TNFi-IR than -naïve pts ($p<0.05$). At W24, GUS reduced IL-22, IL-17A/F, IL-6, C-reactive protein (CRP), & serum amyloid A protein to similar levels in both cohorts ($p<0.05$; Figure 1). W24 PASI75 responders had higher BL IL-17F levels with GUS in both cohorts ($p<0.05$) & higher IL-22 levels in TNFi-IR pts only ($p<0.05$). A trend of upregulated BL IL-22 expression in W24 ACR20 responders was seen for TNFi-IR pts with GUS ($p=0.07$).

Table 1. BL demographics, disease characteristics, & drug use in TNFi-naïve & -IR cohorts with available cytokine data in DISCOVER-1&2 & COSMOS.*

	TNFi-naïve (N=251)	TNFi-IR (N=93)
Age [yrs]	47.2 (11.3)	48.5 (11.1)
Female, n (%)	132 (52.6)	46 (49.5)
Body mass index [kg/m^2]	29.6 (6.1)	30.3 (6.4)
Median (range) **CRP** [mg/dL]	0.9 (0.0-12.9)	1.0 (0.0-13.2)
Log2 IL-22 / TNFα [pg/mL]	2.0 (1.4) / 1.1 (0.6)	2.5 (1.5) / 1.9 (1.2)
Log2 IL-17A / F [pg/mL]	-0.4 (1.5) / 1.7 (1.5)	-0.1 (1.7) / 2.0 (1.6)
SJC [0-66]	11.7 (7.1)	10.3 (8.3)
TJC [0-68]	20.3 (13.1)	20.6 (14.2)
PsA duration [yrs]	5.8 (5.9)	9.8 (8.2)
PsO duration [yrs]	16.7 (12.8)	20.4 (12.0)
PsO Body surface area (%)	14.8 (18.6)	19.1 (21.3)
Investigator's Global Assessment score [0-4]	2.3 (0.9)	2.3 (1.0)
PASI score [0-72]	8.9 (10.6)	12.5 (12.0)
Enthesitis [Y], n (%)	160 (63.7)	58 (62.4)
csDMARD use [Y], n (%)	164 (65.3)	62 (66.7)
Corticosteroid use (Y), n (%)	45 (17.9)	19 (20.4)
Methotrexate use [Y], n (%)	136 (54.2)	54 (58.1)

Data are mean (SD) unless otherwise noted. *Pts with serum CRP level ≥0.3 mg/dL, SJC ≥3, & TJC ≥3 (to mimic D1 inclusion criteria[1]). *TJC*= tender joint count

Conclusion: Elevated BL IL-22 expression & association between BL IL-22 levels & W24 PASI75 response, & a W24 trend for an association between upregulated BL IL-22 & ACR20 response, in TNFi-IR pts seen in this exploratory analysis may suggest increased involvement of the IL-23 pathway in TNFi-IR pts. GUS showed comparable & significant PD effects for TNFi-naïve & -IR pts, consistent with observed clinical responses.

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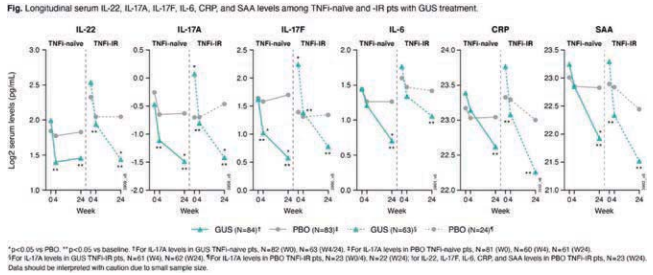

Fig. Longitudinal serum IL-22, IL-17A, IL-17F, IL-6, CRP, and SAA levels among TNFi-naïve and -IR pts with GUS treatment.

*p<0.05 vs PBO. **p<0.05 vs baseline. †For IL-17A levels in GUS TNFi-naïve pts, N=82 (W0), N=63 (W4/24). ‡For IL-17A levels in PBO TNFi-naïve pts, N=81 (W0), N=60 (W4), N=61 (W24). §For IL-17A levels in GUS TNFi-IR pts, N=61 (W4), N=62 (W24). ¶For IL-17A levels in PBO TNFi-IR pts, N=23 (W0/4), N=22 (W24); for IL-22, IL-17F, IL-6, CRP, and SAA levels in PBO TNFi-IR pts, N=23 (W24). Data should be interpreted with caution due to small sample size.

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POS0075

LONG-TERM PERSISTENCE OF FIRST-LINE BIOLOGICS FOR PSORIATIC ARTHRITIS AND PSORIASIS: A COHORT STUDY OF 23,423 PATIENTS FROM THE FRENCH HEALTH INSURANCE DATABASE (SNDS)

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Background: Treatment options for psoriasis (PsO) and psoriatic arthritis (PsA) have evolved significantly since the era of biologics. Clinical trials (mainly placebo-controlled for 12 to 16 weeks) are inadequate to assess the relative long-term efficacy of biologics and are often insufficient regarding safety.
Objectives: To assess the long-term persistence of different biologic classes to treat PsA and PsO.
Methods: This nationwide cohort study involved the administrative healthcare database of the French health insurance scheme linked to the hospital discharge database. We included, in two sub-cohorts, all adults with PsA and those with PsO, who were new users of biologics (not in the year before the index date) during 2015-2019. We excluded patients hospitalised for PsO in the PsA cohort and for PsA in the PsO cohort in the year before the index date. Persistence was defined as the time from biologic initiation to discontinuation and was estimated by the Kaplan-Meier method. Comparison of persistence by biologic class involved using propensity score-weighted Cox models (IPTW) and adjustment on specific systemic non-biologics (time-dependant variables).
Results: We included 6,531 patients with PsA (mean age 49±13 years, 45% male): 4,974 (76%) starting a TNFi, 803 (12%) an IL12/23i and 754 (12%) an IL17i. We included 16,892 patients with PsO (mean age 53±17 years, 50% male): 10,199 (60%) starting a TNF inhibitor (TNFi), 3,982 (24%) an IL12/23i, and 2,711 (16%) an IL17i. Overall 3-year persistence rates were 36% and 41% for PsA and PsO (Figure 1). After IPTW and adjustment, IL17i was associated with higher persistence than TNFi for PsA (weighted hazard ratio [HR_w] 0.70, 95% confidence interval [95%CI] 0.58-0.85) and PsO (HR_w 0.78, 95%CI 0.73-0.83) and than IL12/23i for PsA (HR_w 0.69, 95%CI 0.55-0.87). We found no difference between IL17i and IL12/23i for PsO. IL12/23i had better persistence than TNFi for PsO (HR_w 0.76, 95%CI 0.72-0.80), with no difference observed for PsA.

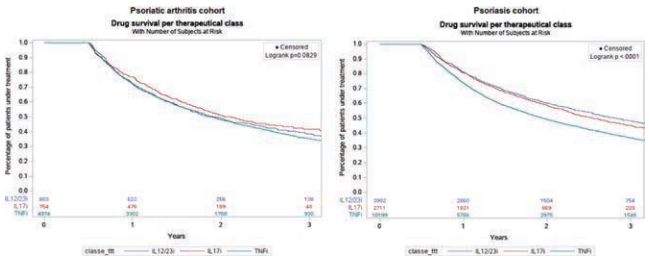

Figure 1. Kaplan Meier estimates of biologic treatment persistence in psoriasis and psoriatic arthritis cohorts *TNFi: tumor necrosis factor inhibitor; ILi: interleukin inhibitor.*

Conclusion: This real-life study suggests a higher persistence of IL17i than TNFi for PsA and PsO. IL17i also has better persistence than IL12/23i for PsA, with no difference for PsO. However, the persistence rates of all biologics remained globally low at 3 years.
Disclosure of Interests: Laura Pina Vegas: None declared, Laetitia Penso: None declared, Emilie Sbidian: None declared, Pascal Claudepierre Speakers bureau: P. Claudepierre has been an investigator for Roche Chugai, Sanofi Aventis, Celgene, Pfizer, MSD, Novartis and BMS., Consultant of: P. Claudepierre has received consulting fees from Abbvie, Amgen, Pfizer, Roche-Chugai, BMS, MSD, UCB, Novartis, Janssen, Lilly, Galapagos, Celgene (less than $10,000 each)
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POS0076 DRUG SURVIVAL OF BIOLOGICS AND NOVEL IMMUNOMODULATORS FOR RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS, PSORIATIC ARTHRITIS, AND PSORIASIS - A NATIONWIDE COHORT STUDY FROM THE DANBIO AND DERMBIO REGISTRIES

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Background: Drug survival is an important proxy measure for effectiveness of treatments for inflammatory diseases such as rheumatoid arthritis (RA), axial spondyloarthritis (AxSpA), psoriatic arthritis (PsA), and psoriasis [1-4].
Objectives: The objective of this study was to examine the real-life drug survival of biologics and novel small-molecule therapies across various disease entities such as RA, AxSpA, PsA, and psoriasis.
Methods: We performed a nationwide cohort study using the prospective nationwide registries DANBIO and DERMBIO, comprising all patients treated with biologics or novel small-molecule therapies for RA, AxSpA, PsA, and psoriasis between January 2015 through May 2021 (DANBIO) and November 2009 to November 2019 (DERMBIO). Drug survival was visualized using Kaplan-Meier curves, and Cox proportional hazards models were used to calculate adjusted Hazard Ratios (HRs) with 95% confidence intervals (CIs) for risk of discontinuing therapy.
Results: The study comprised a total of 12,089 patients (17,903 treatment series), including 5,104 RA patients (7,867 series), 2,157 AxSpA patients (3,016 series3), 2,551 PsA patients (3,313 series), and 2,577 psoriasis patients (3,707 series). In confounder-adjusted models drug survival in RA was highest for rituximab followed by baricitinib, etanercept and tocilizumab respectively. For AxSpA drug survival was high for golimumab compared to all other drugs, followed by secukinumab and etanercept and lowest for infliximab. For PsA tofacitinib and infliximab had the lowest drug survival compared to all other drugs. All other drugs performed almost equally well with a tendency of a generally higher drug survival for golimumab, followed by secukinumab and ixekizumab. For psoriasis drug survival was generally highest for guselkumab.

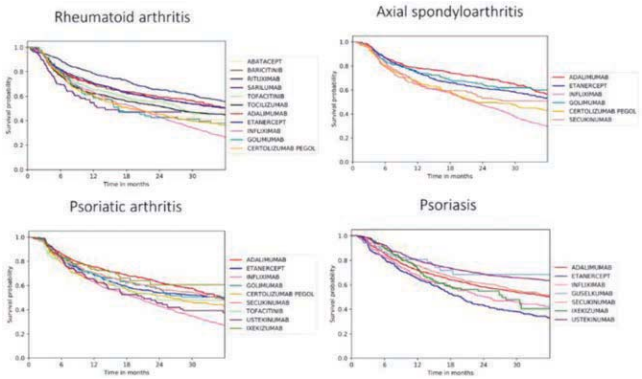

Figure 1.

Conclusion: Differing treatment responses to drugs with various types of action across RA, AxSpA, PsA and psoriasis emphasize that although these diseases have many overlaps in their pathogenesis, there is a need for an individualized treatment approach that considers the underlying disease, patient profile, and treatment history.
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Bristol-Myers Squibb, and Janssen Pharmaceuticals, Grant/research support from: Pfizer, Eli Lilly, Novartis, Bristol-Myers Squibb, AbbVie, Janssen Pharmaceuticals, Nana Lippert Rosenoe: None declared, David Aagaard: None declared, Erik Lørup: None declared, Lea Nymand: None declared, Lars Erik Kristensen Speakers bureau: Dr. LE Kristensen has received fees for speaking and consultancy from Pfizer, AbbVie, Amgen, Forward pharma, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Paid instructor for: Dr. LE Kristensen has received fees for speaking and consultancy from Pfizer, AbbVie, Amgen, Forward pharma, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Consultant of: Dr. LE Kristensen has received fees for speaking and consultancy from Pfizer, AbbVie, Amgen, Forward pharma, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Grant/research support from: Dr. LE Kristensen has received fees for speaking and consultancy from Pfizer, AbbVie, Amgen, Forward pharma, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Jacob Thyssen Speakers bureau: Dr. Thyssen has attended advisory boards for Almirall, Eli Lilly & Co, Pfizer, LEO Pharma, Asana, Regeneron, AbbVie, Union Therapeutics, and Sanofi-Genzyme and received speaker honorarium from LEO Pharma, Regeneron, Almirall, Abbvie, Eli Lilly & Co, and Sanofi-Genzyme, and been an investigator for AbbVie, Pfizer, Eli Lilly & Co, LEO Pharma and Sanofi-Genzyme., Paid instructor for: Dr. Thyssen has attended advisory boards for Almirall, Eli Lilly & Co, Pfizer, LEO Pharma, Asana, Regeneron, AbbVie, Union Therapeutics, and Sanofi-Genzyme and received speaker honorarium from LEO Pharma, Regeneron, Almirall, Abbvie, Eli Lilly & Co, and Sanofi-Genzyme, and been an investigator for AbbVie, Pfizer, Eli Lilly & Co, LEO Pharma and Sanofi-Genzyme., Consultant of: Dr. Thyssen has attended advisory boards for Almirall, Eli Lilly & Co, Pfizer, LEO Pharma, Asana, Regeneron, AbbVie, Union Therapeutics, and Sanofi-Genzyme and received speaker honorarium from LEO Pharma, Regeneron, Almirall, Abbvie, Eli Lilly & Co, and Sanofi-Genzyme, and been an investigator for AbbVie, Pfizer, Eli Lilly & Co, LEO Pharma and Sanofi-Genzyme., Grant/research support from: Dr. Thyssen has attended advisory boards for Almirall, Eli Lilly & Co, Pfizer, LEO Pharma, Asana, Regeneron, AbbVie, Union Therapeutics, and Sanofi-Genzyme and received speaker honorarium from LEO Pharma, Regeneron, Almirall, Abbvie, Eli Lilly & Co, and Sanofi-Genzyme, and been an investigator for AbbVie, Pfizer, Eli Lilly & Co, LEO Pharma and Sanofi-Genzyme., Simon F. 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POS0077

SEX DIFFERENCES IN EFFECTIVENESS OF FIRST-LINE TUMOR NECROSIS FACTOR INHIBITORS IN PSORIATIC ARTHRITIS; RESULTS FROM THIRTEEN COUNTRIES IN THE EUROSPA RESEARCH COLLABORATION NETWORK

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Background: Evidence demonstrates sex differences in disease presentation, physical function, treatment response and drug retention in patients with psoriatic arthritis (PsA). Data from observational cohort studies indicate female sex is associated with reduced effectiveness of tumor necrosis factor inhibitors (TNFis)[1,2]. Although, conflicting results are also reported[3,4]. We sought to validate prior studies using data from a large multinational cohort based on real-life clinical practice.
Objectives: To investigate sex differences in treatment response and drug retention rates in clinical practice among patients with PsA, treated with their first TNFi.
Methods: Data from biologic-naïve PsA patients initiating a TNFi in the EuroSpA registries were pooled. In the primary analysis, propensity-score weighting was applied to assess the causal effect of sex on low disease activity (LDA) according to DAS28-CRP at 6 months. A generalized linear regression model was used to estimate the causal risk difference (RD) and relative risk (RR) of sex on LDA. Possible covariates influencing the outcome were determined a priori and selected based on availability in the database (<20% missing). The final covariates included were country, age, conventional synthetic disease-modifying antirheumatic drug use at baseline and TNFi start year. In the secondary analysis, drug retention was assessed over 24 months of follow-up by Kaplan-Meier curves and log-rank test.
Results: In total, 7,679 PsA patients with available data on DAS28-CRP at 6 months were assessed for treatment response. Baseline characteristics are shown in the Table 1. In the adjusted analysis, the probability for females to have LDA was 17% (RR, 0.83; 95% confidence interval [CI], 0.81 to 0.85) lower compared to males and the difference in probability for having LDA was 13 percentage points (RD, 0.13; 95% CI, 0.11 to 0.15). The survival analysis included 18,599 PsA patients with available data on retention rates. The TNFi 6/12/24-month retention rates were significantly lower in females (81%/68%/56%) compared to males (89%/80%/69%), see Figure 1.

Table 1. Baseline characteristics of all biologic-naïve PsA patients treated with their first TNFi and available DAS28-CRP at 6 month, data pooled across all countries

	Female	Male
	Mean (SD), median [IQR] or percentages	Mean (SD), median [IQR] or percentages
Age (years)	49.7 (12.5)	47.8 (11.9)
Disease duration (years)	4.0 [1.0, 10.0]	4.0 [1.0, 10.0]
TNFi start year		
1999-2009	29%	29%
2010-2013	26%	27%
2014-2016	25%	24%
2017-2020	20%	20%
Concomittant csDMARD	75%	77%
DAS28-CRP	4.4 (1.2)	4.2 (1.2)
DAPSA28	32 (16)	29 (16)
CRP (mg/L)	7.0 [3.0, 17.0]	8.0 [3.3, 19.0]
SJC (0-28)	3.0 [1.0, 6.0]	3.0 [1.0, 6.0]
TJC (0-28)	6.0 [2.0, 10.0]	4.0 [2.0, 9.0]
VAS pain, mm	61 (23)	55 (23)
VAS fatigue, mm	62 (26)	53 (27)

Data are as observed, mean (SD), median [IQR] or percentage. TNFi, tumor necrosis factor inhibitor; csDMARD, Conventional synthetic disease-modifying antirheumatic drugs; DAS28-CRP, Disease Activity Score 28-joint count C reactive protein; DAPSA28, Disease Activity in PsA 28; CRP, C-reactive protein; SJC, swollen joint count; TJC, tender joint count.

Conclusion: Treatment efficacy and retention rates are lower among female patients with PsA initiating their first TNFi. Females presented with higher 28-tender joint count and higher scores on patient reported outcomes at baseline, reflecting differences in disease expression. Recognizing these sex differences is of relevance for customized patient care and may improve patient education.

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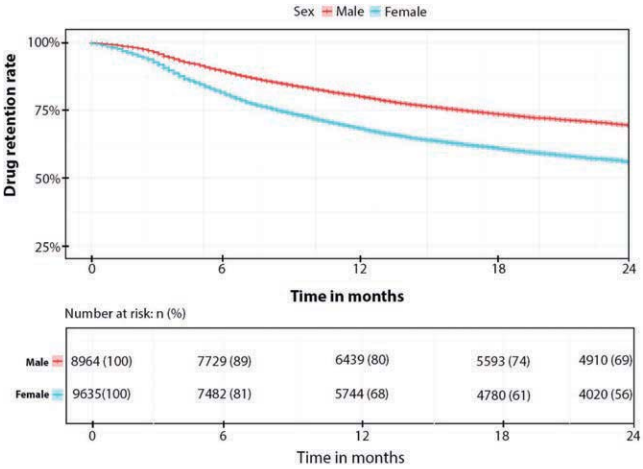

Figure. Sex differences in 24-month retention rates in first-line tumor necrosis factor inhibitors in patients with psoriatic arthritis in EuroSpA (Kaplan-Meier, log-rank test; p<0.001).

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POS0078 COMPARING METHOTREXATE MONOTHERAPY WITH METHOTREXATE PLUS LEFLUNOMIDE COMBINATION THERAPY IN PSORIATIC ARTHRITIS: A RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND CLINICAL TRIAL (COMPLETE-PSA)

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Background: Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) are the cornerstone first-line treatment in psoriatic arthritis (PsA), although there is a paucity of evidence for the effectiveness of csDMARDs and especially their combination. Assessing the efficacy and safety of combinations of csDMARDs compared with csDMARD monotherapy has been prioritized on the EULAR research agenda. We hypothesized that combining csDMARDs might be more effective than csDMARD monotherapy.
Objectives: We aimed to investigate whether a combination of methotrexate (MTX) and leflunomide (LEF) is superior to MTX monotherapy on improvement in disease activity in patients with PsA.
Methods: Patients with a clinical diagnosis of PsA and active disease (≥2 swollen joints) were included in this randomised, placebo-controlled, double-blind trial. Patients were randomised (1:1) to MTX plus LEF or MTX plus placebo. Patients received MTX 15 mg/week for four weeks and thereafter 25 mg/week, combined with two LEF 10 mg tablets or two placebo tablets daily. The primary outcome was the difference between the MTX plus LEF group and the MTX plus placebo group on the psoriatic arthritis disease activity score (PASDAS) at week 16 adjusted for baseline PASDAS. Key secondary outcomes included safety and the achievement of minimal disease activity (MDA) criteria and PASDAS low disease activity (LDA) (≤3.2).
Results: A total of 78 PsA patients (MTX + LEF n=39; MTX + placebo n=39) were included. The mean age was 53.1 (SD=12.8) years and 36% (n=28) of the patients were female. The mean PASDAS at baseline was 4.9 (SD=1) in both treatment groups. Table 1 shows that MTX plus LEF was superior to MTX plus placebo at week 16 (PASDAS 3.1, SD=1.4 vs 3.7, SD=1.3; treatment difference= -0.6, 90% CI -1.0 to -0.1, one-sided P-value=0.025). Similar and significant results were found for achievement of MDA criteria (59% vs 33%, one-sided P-value=0.013) and PASDAS LDA (59% vs 35%, one-sided P-value=0.019) (Figure 1 and Table 1). Other favorable and significant outcomes for the MTX plus LEF group included -among others- the improvement in swollen joint count (SJC) (median [IQR] = -3 [-5, -2] vs -2 [-4, 0], one-sided P-value=0.039) and the proportion of patients with active psoriasis (i.e. body surface area score >0) at week 16 (44% vs 68%, one-sided P-value=0.014). Generally mild adverse events and treatment discontinuation (MTX+LEF n/N=10/39; MTX + placebo n/N=3/39) occurred more frequently in the MTX plus LEF group.

Table 1. Primary and secondary outcomes at week 16

	MTX + LEF (N=39)	MTX + placebo (N=38)*	Absolute difference [90% CI]	P-value One-sided
Primary endpoint				
PASDAS at week 16	3.1 (1.4)	3.7 (1.3)	-0.6 [-1.0, -0.1]	**0.025**
Selected secondary endpoints				
Fulfilling PASDAS LDA, N (%)	23 (59)	13 (35)	24% [6, 42]	**0.019**
Fulfilling MDA criteria, N (%)	23 (59)	12 (33)	26% [7, 44]	**0.013**
SJC66, change from baseline, median (Q1, Q3)	-3 (-5, -2)	-2 (-4, 0)	..	**0.039**
TJC68, change from baseline, median (Q1, Q3)	-2 (-4, 0)	-2 (-5, 0)	..	0.457
VAS physician global, change from baseline, mean (SD)	-22.0 (21.9)	-12.2 (19.7)	-9.8 [-17.7, -1.9]	**0.021**
VAS patient global, change from baseline, mean (SD)	-20.9 (24.4)	-13.9 (28.3)	-7.0 [-17.0, 3.0]	0.124
Active psoriasis, N (%)	17 (44)	26 (68)	-25% [-43, -7]	**0.014**

* One patient in the MTX + LEF group was excluded from the efficacy analysis due to change of diagnosis.

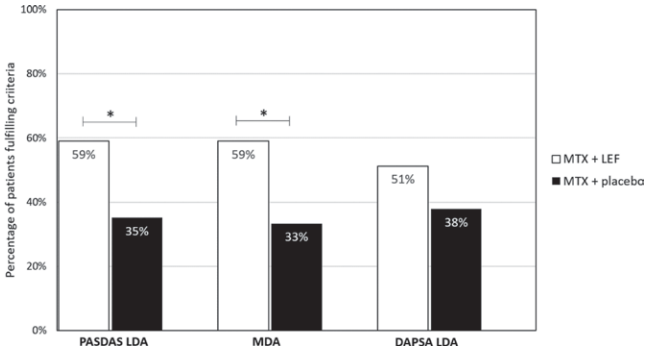

Figure 1. Proportion of patients meeting different PsA responder criteria for low disease activity at week 16* = one-sided P-value <0.05DAPSA = Disease Activity in Psoriatic Arthritis

Conclusion: MTX plus LEF combination therapy resulted in a significantly greater improvement in disease activity according to PASDAS and MDA than treatment with MTX monotherapy in patients with PsA after 16 weeks. In addition, a greater improvement in psoriasis was found for the combination group. However, there are indications that MTX plus LEF combination is less well tolerated than MTX monotherapy.
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POS0079 DOES METHOTREXATE IMPACT USTEKINUMAB IMMUNOGENICITY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS? A POST HOC ANALYSIS OF SAMPLES FROM A RANDOMIZED, PLACEBO-CONTROLLED TRIAL.

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Background: The formation of antidrug-antibodies (ADA) may reduce treatment efficacy or provoke discontinuation due to adverse reactions. Subsequent alterations in the drugs' pharmacodynamics, pharmacokinetics, safety, and efficacy are often unpredictable and can impede clinical discourse. Recent studies gave us some insights regarding the role of ADA formation against the monoclonal IL-12/-23 antibody ustekinumab (UST) and the impact of concomitant MTX treatment on immunogenicity in psoriatic arthritis (PsA) patients [1,2]. Valid measurement of ADA, particularly of neutralizing ADA (nADA) is essential to understand UST-associated immunogenicity and may help to predict clinical outcomes.
Objectives: To examine the impact of concomitant MTX on UST-immunogenicity in patients with active psoriatic arthritis (PsA).
Methods: Plasma samples were collected from a randomized controlled trial in patients with active PsA, treated with open UST and placebo-controlled methotrexate over a 52 weeks. We compared samples of 112 patients treated with

either UST and MTX (n=58) or UST and placebo (n=54). Plasma samples were obtained shortly before UST injection at weeks 0, 4, 16, 40, and 52.
Immunogenicity testing was performed as described by our group elsewhere [3], in a multitiered manner with ELISA and surface plasmon resonance analysis for the detection and quantification of ADA and UST, respectively. Neutralizing capacity was characterized in a cell-based assay. For statistical analysis, a two-way ANOVA with Sidak correction for multiple comparisons was used.
Results: Over the 52 weeks treatment period, 10 (18 %) of patients in the placebo cohort developed UST-specific ADA with one patient having non-neutralizing ADA, whereas 15 (27 %) subjects in the MTX cohort generated UST-specific ADA with 2 patients having non-neutralizing ADA. The ADA rates and concentrations at the different time points (Figure 1A, B) did not differ significantly between MTX and non-MTX users (p< 0.05). Furthermore, the presence of UST-specific ADA was not associated with decreased UST levels (Figure 1C).

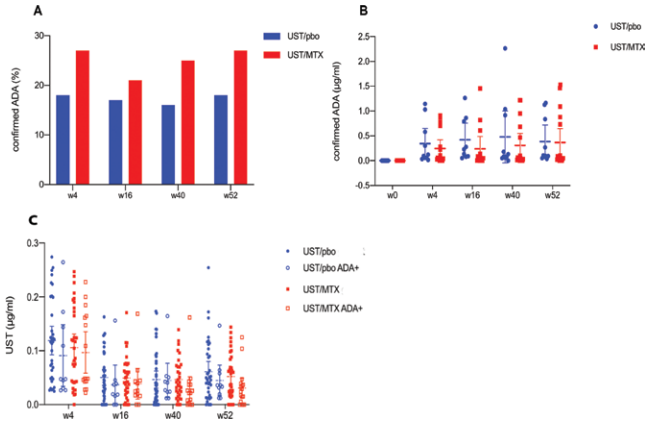

Figure 1. (A) ADA prevalence (%), (B) mean concentration (µg/ml) of confirmed ADA with 95%confidence interval and (C) mean UST concentration (µg/ml) with 95%confidence intervall in the MTX cohort (UST/MTX; n=58) and placebo cohort (UST/pbo; n=54) overall and with confirmed ADA (ADA+), respectively, at week (w) 0, 4, 16, 40, and 52.

Conclusion: The presented data yielded no statistically significant difference in ADA detection between the two analyzed groups. Our findings suggest that concomitant MTX had no impact on UST immunogenicity in PsA patients.
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POS0080 PROGNOSTIC FACTORS ASSOCIATED WITH NON-REMISSION OR LOW DISEASE ACTIVITY STATUS AFTER 1 YEAR OF PSORIATIC ARTHRITIS PATIENTS TREATMENT IN REAL PRACTICE

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Background: Remission/Low Disease Activity (LDA) are acceptable goal of psoriatic arthritis (PsA) treatment. According to registry data 32.8%- 60.3% of PsA patients (pts) are considered to be in remission under biological (b) DMARDs treatment [1, 2]. Prognostic factors for non-remission/LDA hasn't been fully studied yet and data is limited.
Objectives: to determine the prognostic factors associated with non-remission/LDA status within 1 year of treatment in PsA pts in real practice.
Methods: 292 pts (M/F=122/170) with active PsA fulfilling the CASPAR criteria were included. Mean age 46.1±12.5 years (yrs.), PsA duration 10.4±7.1 months (mos.), psoriasis (Ps) duration 19.32±12.08 mos., body mass index (BMI) 27.7±5.6 kg/m^2, Median (Me) DAPSA 23.8 [14.7; 37.4]. 182 pts was given therapy with synthetic (s) DMARDs predominantly Methotrexate (MTX), 110 pts – bDMARDs as monotherapy or with combination with MTX or other sDMARDs. At baseline (BL) and at 1 year of therapy PsA activity by tender/swelling joint count (TJC)/68, (SJC)/66, Pain (VAS), Patient global assessment disease activity (PtGA, VAS), CRP mg/l, dactylitis, enthesitis by LEI and plantar fascia, BSA (%), HAQ, DAPSA were evaluated. DAPSA>28 indicate high disease activity (HDA), 15-28 - moderate activity (MoDA), 5-14 - LDA, ≤4 - remission. By 1 year of therapy the proportion of pts who had not reached remission or LDA were calculated. The one-factor model of logistic regression was used to identify a group of features that are associated with remission or LDA nonachievement. M±SD, Me [Q25; Q75], Min-Max, %, t-test, Pearson-χ^2, Manna-Whitney tests, ORs with 95% CI were performed. All p<0.05, were considered to indicate statistical significance.
Results: At 1 year of therapy 116 pts of 292 (39.7%) have HDA/MoDA by DAPSA. Remission/LDA was reached in 176 pts (60.3%), 110 of them (62.5%) were treated with bDMARDs. Comparative analysis in both groups and one-factor model of logistic regression showed the following features at BL were associated with non-remission/LDA status: TJC>3 (p<0.001), SJC>5 (p<0.001), CRP> 10 mg/l (p<0.001), HAQ>0.5 (p<0.001), presence of entesitis (p<0.001), dactylitis (p<0.001), BMI>30 (p<0.002) and had to be treated with sDMARDs. PsA pts with combination of these clinical features at first visit have more chance to non-remission/LDA status in comparison to PsA pts without them, OR with CI 95% (Figure 1).

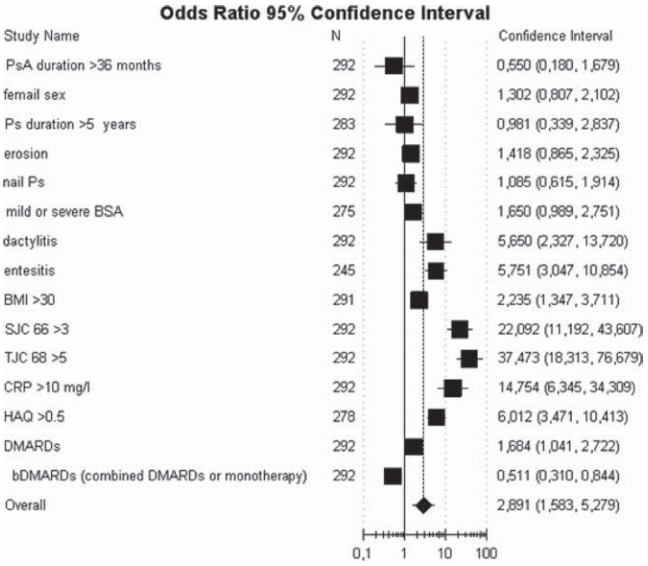

Figure 1. The prognostic factors associated with non-remission/LDA status in PsA pts

Conclusion: In real practice remission/LDA can be seen in 60% of PsA pts treated mostly with bDMARDs. But about 40% of PsA pts still have HAD/MoDA despite going through therapy. It is a combination of clinical features at BL – TJC>3, SJC>5, CRP>10 mg/l, HAQ>0.5, presence of entesitis, dactylitis, BMI>30 kg/m^2 and sDMARDs therapy - that constitutes a prognostic factor with negative impact on achievement remission/LDA after 1 year of treatment.
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POS0081 LONG-TERM EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS: 2-YEAR RESULTS FROM THE PHASE 3 SELECT-PSA 1 STUDY

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Background: In SELECT-PsA 1, patients (pts) with psoriatic arthritis (PsA) and an inadequate response or intolerance to ≥1 non-biologic disease-modifying antirheumatic drug showed improvement in the signs and symptoms of PsA with upadacitinib 15 mg (UPA15) or 30 mg (UPA30), an oral Janus kinase (JAK) inhibitor, through week (wk) 56.[1]
Objectives: To evaluate the efficacy and safety of UPA and UPA vs adalimumab (ADA) at wk 104 from the ongoing long-term extension of SELECT-PsA 1.
Methods: Pts received UPA15, UPA30, ADA 40 mg, or placebo (PBO) for 24 wks, at which point, PBO pts switched to UPA15 or UPA30. Efficacy endpoints were analyzed using non-responder imputation (NRI) and as observed (AO) (binary endpoints) or mixed-effect model repeated measures and AO (continuous endpoints), with nominal *P*-values shown, for continuous UPA and ADA treatment groups. Treatment-emergent adverse events were summarized for pts who received ≥1 dose of study drug using a visit-based cut-off at wk 104.
Results: 1704 pts received ≥1 dose of study drug. At wk 104, 25.4% of patients had discontinued study drug. The proportions of pts who achieved ACR20/50/70, MDA, PASI75/90/100, and resolution of enthesitis or dactylitis showed consistent responses, or further improvements, from wk 56[1] to wk 104 (Table 1). ACR20/50/70 and MDA responses, as well as mean change from baseline (BL) in HAQ-DI, patient's assessment of pain, BASDAI, and ASDAS, were greater with UPA vs ADA. Mean change from BL in modified total Sharp/van der Heijde Score (mTSS) was generally similar across groups and comparable to wk 56.[1] The safety profile of UPA was generally comparable to ADA (Figure 1) and consistent with wk 56[1] data. Rates of serious infection, herpes zoster, lymphopenia, and elevated CPK remained numerically higher with UPA30 vs UPA15; rates in both UPA groups were higher vs ADA. Rates of malignancies, MACE, or VTE were similar across groups, and consistent with wk 56[1] data. Two deaths were reported with UPA15, 1 with UPA30, and 1 with ADA.

Table 1. Efficacy Endpoints at Week 104

Endpoint	UPA15 (n=429)		UPA30 (n=423)		ADA (n=429)	
Proportion of Pts (%)[a]	NRI	AO	NRI	AO	NRI	AO
ACR20	69.0	87.9	69.5	87.9	63.4	85.1
ACR50	53.6	67.4	59.3*	74.1	47.1	62.3
ACR70	38.0*	47.4	43.5*	54.4	29.4	39.1
Minimal Disease Activity (MDA)	42.0	54.8	45.9*	56.8	37.8	50.3
PASI75[b]	57.9	73.4	62.4	78.6	58.8	76.5
PASI90[b]	46.7	59.0	53.3	66.5	48.8	63.3
PASI100[b]	34.1	43.4	42.4	51.4	34.1	44.0
Resolution of enthesitis by LEI[c]	53.3	75.5	52.2	72.0	49.1	73.9
Resolution of dactylitis by LDI[d]	69.9	94.5	71.7	96.2	72.4	95.2
Change from BL[e]	MMRM	AO	MMRM	AO	MMRM	AO
Health Assessment Questionnaire - Disability Index (HAQ-DI)	-0.55*	-0.57	-0.55*	-0.59	-0.45	-0.47
Patient's assessment of pain (numeric rating scale)	-3.3	-3.5	-3.4*	-3.6	-3.0	-3.2
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[f]	-3.0	-3.2	-3.3	-3.6	-2.7	-2.6
Ankylosing Spondylitis Disease Activity Score (ASDAS)[f]	-1.6	-1.8	-1.9*	-2.1	-1.5	-1.6
Modified total Sharp/van der Heijde Score (mTSS)	0.03	0.01	0.01	0.00	0.11	0.11

ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology criteria; ADA, adalimumab; AO, as observed; BL, baseline; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MMRM, mixed effect model repeated measurement; NRI, non-responder imputation; PASI75/90/100, ≥75%/90%/100% improvement in Psoriasis Area and Severity Index; pts, patients; UPA, upadacitinib. [a]Data shown as NRI and AO for binary endpoints. [b]For pts with psoriasis affecting ≥3% of body surface area at BL. [c]For pts with LEI >0 at BL; resolution LEI=0. [d]For pts with LDI >0 at BL; resolution LDI=0. [e]Data shown as MMRM (LS mean) and AO (mean) for continuous endpoints. [f]For pts with psoriatic spondylitis at BL. Nominal *$P<0.05$, UPA15 or UPA30 vs ADA for NRI and MMRM; AO descriptive only.

Conclusion: In PsA pts, efficacy responses were similar or greater with UPA15 or UPA30 vs ADA at wk 104, and inhibition of radiographic progression was maintained. No new safety signals were identified with long-term exposure to UPA up to 2 years.

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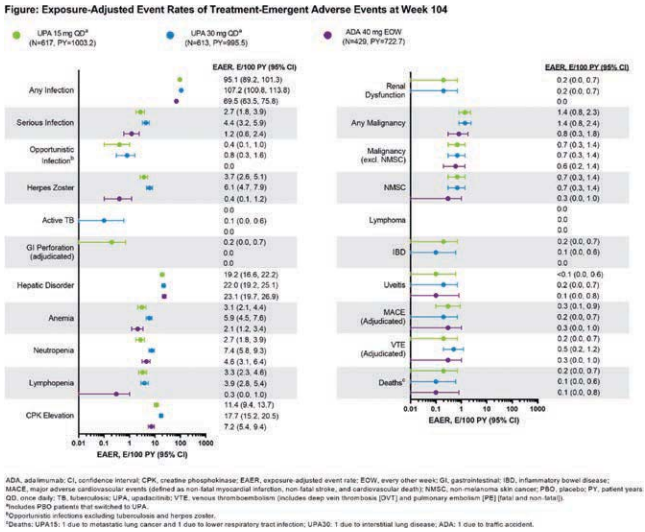
Figure: Exposure-Adjusted Event Rates of Treatment-Emergent Adverse Events at Week 104



ADA, adalimumab; CI, confidence interval; CPK, creatine phosphokinase; EAER, exposure-adjusted event rate; EOW, every other week; GI, gastrointestinal; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular events (defined as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death); NMSC, non-melanoma skin cancer; PBO, placebo; PY, patient years; QD, once daily; TB, tuberculosis; UPA, upadacitinib; VTE, venous thromboembolism (includes deep vein thrombosis [DVT] and pulmonary embolism [PE] [fatal and non-fatal]).
*Includes PBO patients that switched to UPA.
†Opportunistic infections excluding tuberculosis and herpes zoster.
‡Deaths: UPA15: 1 due to metastatic lung cancer and 1 due to lower respiratory tract infection; UPA30: 1 due to interstitial lung disease; ADA: 1 due to traffic accident.

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POS0082

A NOVEL PSORIATIC ARTHRITIS COMPOSITE ENDPOINT COMBINING TREATMENT TARGETS FOR SKIN AND JOINTS: POOLED RESULTS FROM THE GUSELKUMAB DISCOVER-1 AND DISCOVER-2 STUDIES

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Background: Psoriatic arthritis (PsA) is characterized by a range of musculoskeletal and extra-articular disease manifestations. Composite indices are valuable tools to assess the multidimensional nature of PsA. The Psoriatic Arthritis Disease Activity Score (PASDAS)[1] provides robust assessment of both joint and skin domains but is cumbersome to use in clinical practice. The Disease Activity Index for Psoriatic Arthritis (DAPSA)[2] is relatively easy to use but does not assess skin disease.
Objectives: Using pooled data from the phase 3 DISCOVER-1 and DISCOVER-2 studies of guselkumab (GUS) for the treatment of active PsA:[3,4] (1) Describe the rate of achievement of a new composite endpoint combining DAPSA low disease activity (LDA; score ≤14, including remission) and Investigator Global Assessment (IGA) of psoriasis score ≤1 (range=0 [clear] to 4 [severe]); (2) Determine whether earlier (Week [W] 16) DAPSA LDA + IGA ≤1 is predictive of future achievement of minimal disease activity (MDA) or American College of Rheumatology (ACR) 50 response criteria; and (3) Contrast the performance of DAPSA LDA + IGA ≤1 with that of PASDAS LDA (score ≤3.2).
Methods: Patients (pts) with active PsA despite standard therapies (DISCOVER-1: ≥3 swollen + ≥3 tender joints; CRP ≥0.3 mg/dL; ~30% had prior use of up to 2 TNF inhibitors; DISCOVER-2: ≥5 swollen + ≥5 tender joints; CRP ≥0.6 mg/dL; all pts were biologic-naïve) were randomized 1:1:1 to GUS 100 mg at W0, W4, then Q4W or Q8W; or placebo (PBO) with crossover to GUS Q4W at W24. In both studies, efficacy of GUS vs PBO was compared at W24 (primary endpoint). The number (%) of pts with DAPSA LDA + IGA ≤1 was determined at W24 for pts randomized to GUS or PBO. For all GUS-randomized pts, baseline variables associated with DAPSA LDA + IGA ≤1 and PASDAS LDA at W16 and the predictive value of W16 DAPSA LDA + IGA ≤1 or PASDAS LDA for achieving ACR50, MDA, and DAPSA LDA at W52 were assessed using logistic regression models.
Results: At W24, DAPSA LDA + IGA ≤1 was met by 37% (277/748) of GUS-treated pts vs 13% (48/372) in the PBO group. At W16, 27% (203/748) of GUS-randomized pts had DAPSA LDA + IGA ≤1, and 22% (164/748) had PASDAS LDA. Among the 73% (545/748) of pts who did not have DAPSA LDA + IGA ≤1 at W16, most (77% [418/545]) had IGA ≤1 but not DAPSA LDA; 4% (23/545) had DAPSA LDA but not IGA ≤1, and 19% (104/545) had neither component. Baseline predictors of DAPSA LDA + IGA ≤1 at W16 were male gender, lower dactylitis score, lower Health Assessment Questionnaire-Disability Index (HAQ-DI) score, lower tender joint count (TJC), and higher Psoriasis Area and Severity Index (PASI) score. Baseline predictors of PASDAS LDA at W16 were younger age, lower dactylitis score, lower HAQ-DI score, lower TJC, and higher PASI score. As shown (Figure 1), pts who had DAPSA LDA + IGA ≤1 and PASDAS LDA at W16 were significantly more likely to achieve ACR50, MDA, and DAPSA LDA at W52 than pts without W16 responses; odds ratios (ORs) for achievement of ACR50, MDA, and DAPSA LDA responses at W52 were similar for pts who had DAPSA LDA + IGA ≤1 and for pts who had PASDAS LDA at W16. ORs for achievement of ACR50 and MDA at W52 were higher for pts who had both DAPSA LDA and IGA ≤1 at W16 (9.5 and 10.7) than for pts who had DAPSA LDA but not IGA ≤1 (6.5 and 3.5) or IGA ≤1 but not DAPSA LDA (1.6 and 1.5).
Conclusion: DAPSA LDA at W16 predicted future (W52) achievement of the stringent treatment targets of ACR50 and MDA; associations with W52 response were greater when W16 IGA ≤1 was added to DAPSA LDA. DAPSA LDA + IGA ≤1 at W16 as a predictor of W52 ACR50 and MDA response performed similarly to PASDAS LDA. The novel composite of DAPSA LDA + IGA ≤1 may be a reliable predictor of long-term PsA skin and joint response that is more practical to implement than the PASDAS.

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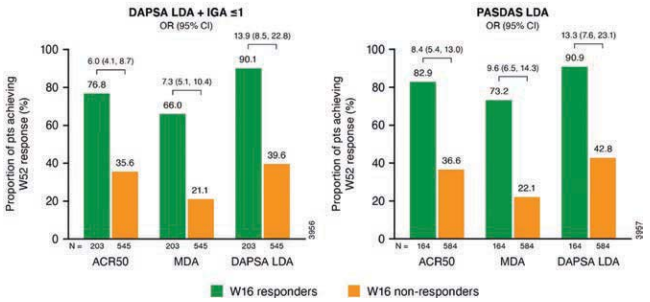
Figure. Composite Responses at W16 are Predictive of Achievement of ACR50, MDA, and DAPSA LDA at W52



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PARE Poster Tour 1

POS0083-PARE DRIVING IMPROVEMENT IN AXIAL SPONDYLOARTHRITIS SERVICES: THE USE OF QUALITY IMPROVEMENT APPROACHES AND TOOLS

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Background: Quality Improvement (QI) methods have been used in healthcare since the late 1980s across a wide range of healthcare settings. However, in the UK they have not been applied widely within rheumatology including axial Spondyloarthritis (axial SpA). In 2017, the UK healthcare regulator, NICE, produced a national clinical guideline for axial SpA, but there was no mechanism to encourage uptake of its recommendations.
The National Axial Spondyloarthritis Society created a programme to use QI approaches to help encourage uptake of the Guidelines and act as a catalyst for wider improvement in axial SpA care.
Objectives: To encourage service improvement in axial Spondyloarthritis care through the use of quality improvement theory and methods.
Methods: In late 2019 six rheumatology departments were selected to participate in the first cohort. The programme design was underpinned by:
- A framework for management grounded in systems theory[1]
- A learning system that brings healthcare organisations together[2]
- A set of tools to develop, test and implement changes: the Model for Improvement[3].

The teams met four times for training in QI methods, plus team-based online coaching. They had time to develop their projects and networking opportunities to share their data and experiences of implementation.
We conducted a qualitative review of the programme in year one. We interviewed 31 programme participants and reviewed programme documentation.
Results: The review found that:
- A proven QI framework provides a strong basis to build improvement
- A competitive programme helps foster motivation and accountability
- The programme provides the time to use tools to understand the problem and construct improvement aims
- Measurement is key to understand improvement and to create a story of change
- Collaboration and engagement is key within the team and with other stakeholders.

The teams have:
- Trained community–based physiotherapists, leading to improved rheumatology referrals
- Implemented an inflammatory back pain pathway from primary care
- Introduced an MRI spine IBP protocol to reduce variation in imaging
- Established a tertiary referral service which has improved time to diagnosis

- Implemented mental health interventions for patients and reduced the percentage of patients with abnormal scores
- Established a pathway for physiotherapy self–referral and reduced Did Not Attend rates
- Used audit to make the business case for an extended scope practitioner

Conclusion: Despite the challenges of posed by the Covid-19 pandemic, a structured QI programme has enabled clinicians to stay engaged and implement projects to reduce diagnostic delay and improve care.

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POS0084-PARE IMPACT OF OSTEOARTHRITIS ON PATIENT QUALITY OF LIFE: IS THERE AN EVOLUTION BETWEEN THE 2013 AND 2021 LARGE-SCALE SURVEYS "STOP OSTEOARTHRITIS" CONDUCTED IN FRANCE AND BELGIUM?

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Background: Osteoarthritis (OA) is the most common form of arthritis, affecting more than 500 million people globally. OA is characterized by chronic mechanical pain and stiffness in the joints, limiting patient physical activities, leading to sedentarism, and disability. The results of the French web-based survey "Stop OA" (N=4227 participants) conducted in 2013 were presented at EULAR 2014. They evidenced the heavy burden of OA in France.

Objectives: The survey was repeated in France/Belgium between 2019 and 2021 (N=3465). This study aimed at assessing the impact of OA on patient quality of life and looking at a potential evolution between the two surveys.

Methods: Participants were invited to complete the survey questionnaire online via the website www.stop-arthrose.org. The questions focused on demographic and socio-economic aspects, history of the disease, physical activities, beliefs about OA, its impact on daily life, assessment of health status and the consequences, as well as the needs and expectations of the participants.

Results: 3465 questionnaires (France N = 2822, Belgium N = 643) were thus collected between September 2019 and January 2021. The average filling time of the survey was 40 minutes. In the 2021 survey, 80.8% of participants (mean age 60 years, 80.3% women) declared that OA had a negative impact on their morale and 64.1% that they had a deteriorated self-image due to the disease. 25% of participants thought that difficulties in their couple were caused by OA and 33% reported problems in sexual life. 24.8% found it hard to cope with the discouragement generated by the disease. Even if psychological repercussions were observed in 21.2%, less than 5% consulted a psychologist. The impact on leisure (78.1%) and family life (61.9%) was also significant, as well as on social activities (58.0%) and professional life (43.7%). The disease also hindered walking (67.4%) and prevented daily actions (32.0%). Some help was necessary, mainly for gardening or tinkering (28.7%), picking up or opening objects (22.9%) as well as shopping and household chores (17.7%). 50% reported difficulty falling asleep and 67.6% were being woken up at night during their sleep because of pain caused by OA. Fatigue was difficult to live with for 47.9% of the participants. Compared to the results of the 2013 survey, there was no significant improvement evidenced in any of the areas studied.

Conclusion: OA represents a real burden that affects the mental health of patients, their relationships and the quality of their sleep. There has been no improvement of OA impact in patient' quality of life between the two surveys (i.e., 8 years). This reflects the lack of resources for research to find new treatments and implement evidence-based therapeutic strategies in the current medical practice. A better understanding of these repercussions will allow effective strategies to be adopted in order to deal with these issues.

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POS0085-PARE CURRENT NEEDS, IMPACT AND PERSPECTIVE OF PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

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Background: The impact of spondyloarthritis (SpA) and psoriatic arthritis (PsA) is enormous.

Objectives: To analyse in patients with SpA and PsA current 1) needs; 2) disease impact, and 3) patients' opinion on treatments, patients-physicians relationship and disease information.

Methods: National survey promoted by CEADE (Spanish Coordinator of Spondyloarthritis Associations). A multidisciplinary working group composed by 1 rheumatologist, 2 patients members of CEADE with SpA and PsA and a methodologist was established. They designed a structured survey (20 minutes long), in electronic format to be answered by patients with SpA and PsA, aged 18 years or above. The survey was launched on April 28, 2021, using CEADE channels to communicate with members and followers, and was closed on June 30, 2021. Sociodemographic and clinical variables were collected (age, sex, disease duration treatments), and variables related to the objectives. A descriptive analysis was performed.

Results: The survey included 543 patients with SpA (55% ankylosing spondylitis, 86% women, 61% aged 48-64 years, 25% with biological therapies) and 291 patients with PsA (89% women, 73% aged 48-64 years, 40% with biological therapies). In the last month, the reported level of fatigue, morning stiffness and sleep problems of patients with SpA and PsA was considerable. In a scale from 0 (no symptoms) to 10 (high level of symptoms) the means were greater than 8. Almost 80% of patients with SpA described low back pain within the last month and 82.5% of patients with PsA pain, stiffness and/or arthritis on the knees, ankles, feet and/or hands, and 51% dactylitis. Regarding to daily activities, practicing exercise and house cleaning were the most affected ones among patients with SpA and PsA. We found that 70%-74% of these patients were concerned about pain and almost 60%-66% about loss of mobility and autonomy. The impact of the disease on work was in general very high very high. The level of satisfaction with treatments was low in SpA, mean 5.5 (scale from 0 no satisfaction to 10 very satisfied), and moderate in PsA, mean 6.2. Across treatments, the level of satisfaction was higher with biological therapies compared with classical synthetic disease modifying antirheumatic drugs in both disease groups. Many patients (70.2% with SpA and 66% with PsA) are used to live with pain every day. Many of the survey participants (over 50%) hope that treatments will help them recover their quality of life and improve pain, stiffness and fatigue. Oral treatments are preferred over subcutaneous and intravenous drugs in SpA and PsA. Patients also consider that oral treatments have more positive influence on adherence to treatments. A total of 22% of surveyed patients with SpA and 14% with PsA said that their rheumatologists never asked them about the factors that limit their life, 14.3% and 6% that they never talked about the impact of the disease on quality of life, and 43.8% (SpA) and 31.2% (APs) that they do not stablish treatment objectives with the rheumatologist. Almost 30% of participants stated that they would like to have more time to express and discuss doubts and concerns with their rheumatologist, and around 25% would like to have more follow-up visits. Table 1 describes the most used.

Table 1. Sources and formats of information about the disease.

	SpA	PsA
Source of information		
Social networks	184 (33.9%)	68 (23.4%)
Patients associations	158 (29.1%)	77 (26.5%)
Scientific societies	70 (12.9%)	36 (12.4%)
Websites created by rheumatologists	165 (30.4%)	82 (28.2%)
Physician	197 (36.3%)	117 (40.2%)
Nurse	33 (6.1%)	10 (3.4%)
Other/s	11 (2.0%)	7 (6.9%)
Format		
Graphic or visual illustrations	184 (33.9%)	78 (26.8%)
Podcasts	47 (8.6%)	12 (4.1%)
Video	175 (32.2%)	72 (24.7%)
Written information (brochures, magazines, newspapers)	200 (37.8%)	100 (34.4%)
News	148 (27.2%)	72 (24.7%)
Chatbots	8 (1.5%)	2 (0.7%)
Other/s	10 (1.8%)	6 (0.7%)

Conclusion: Current impact of SpA and PsA on daily life is still very high. There are areas for improvement in the doctor-patient relationship and on disease treatments.

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POS0086-PARE PATIENT PREFERENCES FOR SYSTEMIC LUPUS ERYTHEMATOSUS TREATMENTS: A DISCRETE CHOICE EXPERIMENT

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Background: Fatigue, chronic pain, and skin and joint manifestations can be debilitating for people with systemic lupus erythematosus (SLE), and managing these symptoms is vital to safeguard their quality of life (QOL). In addition, oral corticosteroids (OCS) and other immunosuppressants can expose patients with SLE to severe adverse events. However, little is known about the relative importance of SLE treatment outcomes including symptom control or the extent to which treatment risks are tolerated in exchange for this.

Objectives: To quantify the relative importance of different SLE treatment outcomes and the trade-offs patients are willing to make between these outcomes.

Methods: This online discrete choice experiment (DCE) assessed how treatment choices varied with treatment outcomes. Subjects were US adults (≥18 years) with a self-reported diagnosis of moderate-to-severe SLE (≥6 months) who experienced ≥1 flare in the past year and were taking ≥1 SLE treatment. Treatment outcomes included four benefits on: 1) fatigue levels, as in the Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue, described the degree of tiredness felt by a patient in the previous 7 days, while not experiencing a flare and despite adequate sleep or rest, 2) joint and 3) non-joint pain levels as measured using the Brief Pain Inventory–Short Form (BPI-SF) scale; scores of 2, 5, and 8 correspond to mild, moderate, and severe worst daily pain on a scale of 0 (no pain) to 10 (worst imaginable pain),and 4) skin rash and itch levels, as in SLE-QOL, indicated how much patients were troubled by sore, painful, stingy, or itchy skin in the previous 7 days. Treatment outcomes also included three risks: 1) risk of infections represented by the proportion of patients who might experience an infection during treatment, 2) mild-to-moderate OCS-related side effects requiring no or only self-administered treatment and 3) severe, potentially life-threatening OCS-related side effects requiring long-term outpatient or hospital treatment. An error-component multinomial logit model was used to analyze DCE data.

Results: The DCE survey was completed by 342 subjects with SLE (mean age 39.6 years) who were predominantly female (82%). Most participants were diagnosed with SLE ≥1 year prior (84%) and experienced ≥2 SLE flares in the previous 12 months (90%). Nearly all participants experienced joint pain (92%) and non-joint pain (84%). Treatment preferences were modelled using 3,420 subject-generated observations. Over the ranges tested, more importance was attached to symptom improvement than risk reduction (Figure 1). A reduction in joint pain (8 to 2) was most important to patients (marginal utility [MU] 0.84), followed by skin rashes and itching ('extremely' to 'not at all', MU 0.66) and non-joint pain (8 to 2, MU 0.49). Reduction of infection risk (10% to 0%) was least important (MU 0.27). Regarding the maximum acceptable risk, participants would accept a 74% increase in the risk of mild-to-moderate side effects to avoid being 'extremely troubled' by skin rash and itch (Table 1).

Table 1. Maximum acceptable risk of mild-to-moderate oral corticosteroid side effects

Attribute levels	Maximum Acceptable Increase in Risk* [95% CI]
Fatigue	
A little bit	50.06% [32.41, 67.71]
Somewhat	47.51% [29.92, 65.09]
Very much	Reference
Skin rash and itch	
Not at all	73.81% [51.51, 96.11]
Moderately	50.84% [32.37, 69.32]
Extremely	Reference
Joint pain (1-level decrease)	15.63% [11.24, 20.02]
Non-joint pain (1-level decrease)	9.18% [6.06, 12.31]
Risk of infections (1% decrease)	2.99% [1.53, 4.45]
Risk of severe side effects (1% decrease)	1.72% [0.97, 2.47]

*Calculated using an error-component multinomial logit model.

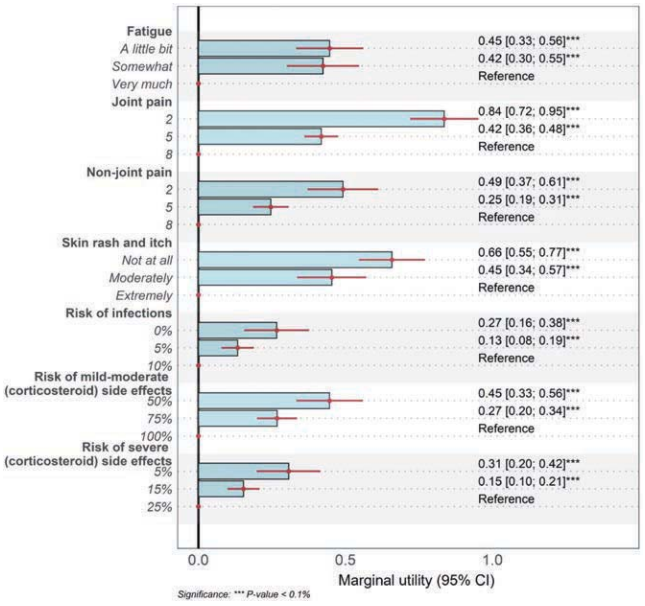

Figure 1. Marginal utilities associated with changes in SLE treatment outcomes

Conclusion: This real-world patient preference assessment provides insights into the relative importance of SLE treatment outcomes and willingness to tolerate SLE treatment risks. These results can guide endpoint prioritization in SLE clinical studies and inform the evaluation of SLE treatments.

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POS0087-PARE IMPROVED SELF-MANAGEMENT IN PATIENTS WITH OSTEOPOROSIS AND INFLAMMATORY ARTHRITIS

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Background: Self-management care services have received a great deal of attention in Switzerland lately. However, there is still a huge gap in service provision, especially with regard to rheumatic diseases. To fill this gap, the Swiss League against Rheumatism has developed a comprehensive self-management programme for patients with inflammatory arthritis (IA) and osteoporosis. In the course of this programme, eleven medical assistants in outpatient rheumatological and general practitioner clinics were trained to help osteoporosis and IA patients to strengthen their self-management capacity. This programme was implemented within the scope of a three-year pilot project (2019 – 2021) and is continuing as a regular project from 2022 onwards.

Objectives: The ultimate objective was to increase the quality of life and health status of people with osteoporosis and IA by enhancing their capacity for self-management. This included all three components of self-management, i.e. strengthening patients' knowledge of the disease, motivating them to take action

and increasing their ability to manage the disease. Furthermore, the pilot project aimed to close an important gap in the Swiss health care system.

Methods: A questionnaire was designed to measure the change in self-management abilities and the health status of patients. The questionnaire was given to patients at three points in time (t1=enrolment of patient, t2=last session of the self-management programme and t3= two months after the last session) and contained several validated scales such as the heiQ, Self-Efficacy for Managing Chronic Disease 6-Item Scale, RADAI-5 and EQ-5D-5L. Descriptive statistics were applied to analyse the data by comparing the mean values of all relevant indicators at three points in time.

Results: In total 52 patients were enrolled in the pilot project. 48 patients completed the programme and 35 took part in the follow-up questionnaire. Overall, the results show a positive trend in self-management abilities and an improvement in the patients' current health status. The slight increase in *knowledge* remained until the follow-up. Significant changes are seen in *Skill and Technique Acquisition* as well as in *Self-Monitoring and Insight* of the disease, which are two important components of self-management. Other components such as the *knowledge* and *constructive attitudes and approaches* also underwent a small but positive change that lasts up to two months after the last session of the self-management programme. *Self-efficacy* improved as well, but with a slight decrease during the follow-up. The *disease activity* also declined slightly over time. The results also indicate a small and steady improvement of the *current health status*. Using a visual analogue scale as part of the EQ-ED-EL, participants evaluated their current health status as 69 (t=1), 73 (t=2) and 74 (t=3). The *quality of life* has improved too, but the change doesn't seem to be relevant. Furthermore, the *use of health services* indicates a slight decline after taking part in the self-management programme.

Conclusion: The comprehensive self-management programme designed by the Swiss League against Rheumatism embedded in outpatient rheumatological and general practitioner clinics proved to be successful. The three components of self-management in particular, i.e. knowledge, motivation to take action and skills to manage the disease improved significantly. The results also show a positive trend in the patients' current health status, their quality of live and a decline in disease activity. However, based on the study design, it cannot be concluded that there is a correlation between the improved health status/quality of life and the self-management programme. For this purpose, a control group would be necessary to evaluate the programme's effect on the health status and quality of life of people with rheumatic disease. Nevertheless, this pilot project represents an important foundation on which further services and programmes to strengthen self-management in rheumatology can be developed.

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POS0088-PARE CHANGES IN PATIENT-REPORTED OUTCOME SCORES DURING COVID-19 PANDEMIC: DATA FROM THE ARTHRITISPOWER REGISTRY

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Background: The COVID-19 pandemic causes concern among patients with autoimmune and rheumatic disease (ARD) due to increased risk of infection and heightened isolation from social distancing.[1]

Objectives: Examine how mean patient-reported outcome (PRO) scores for mental, social and physical health fluctuated after COVID-19 vaccine availability was widespread in US.

Methods: We conducted and reported on[2] an initial analysis of January 2020 – April 2021 where US participants (pts) of the ArthritisPower (AP) registry completed PROMIS measures of physical health (Physical Function, Pain Interference, Fatigue, Sleep Disturbance), mental health (Anger, Anxiety, Depression) and social health (Social Isolation, Emotional Support). Follow-up analysis was conducted May – December 2021. Only pts from initial analysis were included in follow-up. Null hypothesis was no change in monthly average scores across 23-month pandemic period. Analysis of means compared monthly assessment mean scores to overall mean score for each measure during study period. Pts with < 2 assessment time points and osteoarthritis with no ARD were excluded from analysis.

Results: Total of 49,940 PRO scores were contributed by 2,266 pts during 23-month period, with 8,393 of the scores contributed from May – December 2021. Mean (standard deviation, SD) number of observations per pt was 5.6 (12.5). Pts were 87.6% female, 86.7% white, mean age of 52.1 (12.7) years. Rheumatoid arthritis (n=1,131, 49.9%) was the most common condition. Most commonly reported measures were Pain Interference, Fatigue, Sleep Disturbance and Physical Function, each with >11,000 total results (Table 1).

Pts' mental and social health assessment scores improved then worsened during last 8 months of 2021 (Figure 1). Overall mean scores were: Anxiety 62.4 (12.5), Social Isolation 61.9 (10.5), and Anger 61.5 (12.8). From July – August, Social Isolation decreased by 1 SD. Compared to overall assessment mean, Anger declined by > ½ SD (53.3 [19.4]) in August and Anxiety declined by ½ SD (57.7 [11.3]) in September. By December, Anger rose by > ½ SD (68.6 [5.0]) of assessment mean. Pain Interference (mean: 63.3 [7.8]), Fatigue (62.6 [9.5]), and Sleep Disturbance (58.1 [9.0]) scores were significantly lower in May, June, July and August compared to the assessment mean, though none decreased by > ½ SD.

Conclusion: ARD members of AP had mental, social and physical health scores improve during summer of 2021, corresponding with widespread availability of vaccines. However mental and social health scores worsened by December as US faced new variants of the virus.

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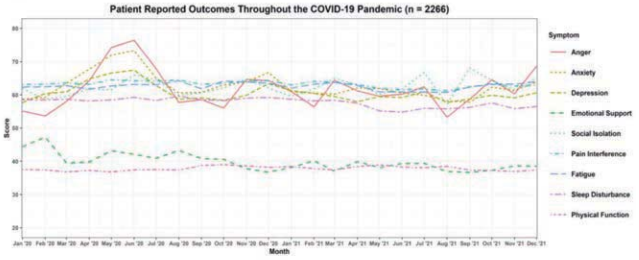
Figure. Patient Reported Outcomes (PROs) Throughout the COVID-19 Pandemic (N=2,266)



For PROMIS Measures Anger, Anxiety, Depression, Fatigue, Pain Interference, Sleep Disturbance and Social Isolation, higher scores = worsened symptoms; for Physical Function and Emotional Support, lower scores = worsened function/support

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Table 1. Avg assessment scores+ by month, mean (SD)

	Pain Interf (n= 11536)	Fatigue (n= 11591)	Sleep Disturb (n= 11257)	Physical Func (n= 11202)	Depression (n=1489)	Anxiety (n= 1066)	Social Iso (n=698)	Emot Support (n=578)	Anger (n=523)
Study Period^	63.3 (7.8)	62.6 (9.5)	58.1 (9.0)	37.7 (7.6)	60.8 (9.2)	62.4 (10.5)	61.9 (10.2)	40.8 (9.8)	61.5 (12.8)
May 2021	**61.9 (8.2)***	**60.9 (9.7)***	**55.2 (8.8)***	38.9 (8.5)	59.5 (9.2)	61.9 (9.8)	60.2 (13.3)	38.1 (8.3)	59.6 (14.5)
June	**61.6 (6.9)***	**60.9 (9.6)***	**54.8 (8.9)***	38.3 (7.8)	59.2 (7.0)	60.6 (9.6)	61.8 (12.0)	39.3 (10.3)	60.2 (10.9)
July	**61.8 (7.4)***	**60.8 (10.2)***	**56.0 (8.6)***	38.1 (7.9)	61.0 (7.8)	59.9 (12.1)	**66.8 (8.5)***	39.4 (9.7)	62.4 (9.7)
Aug	**61.2 (8.5)***	**60.7 (10.4)***	**55.8 (9.6)***	38.5 (8.5)	**57.7 (7.9)***	**58.2 (10.3)***	57.2 (11.1)	36.9 (12.2)	53.3 (19.4)
Sep	62.4 (8.5)	62.3 (10.0)	56.2 (8.3)	37.3 (7.6)	58.7 (8.0)	**57.7 (11.3)***	68.1 (12.8)	36.7 (12.1)	58.7 (12.0)
Oct	63.1 (8.4)	63.3 (9.9)	57.6 (8.6)	37.3 (8.0)	59.9 (9.9)	62.3 (9.0)	64.3 (10.3)	37.3 (11.4)	64.6 (10.2)
Nov	62.6 (6.8)	63.2 (10.0)	**55.8 (8.6)***	36.9 (7.0)	59.1 (8.8)	61.3 (6.8)	61.4 (10.9)	38.6 (11.7)	60.3 (12.4)
Dec	62.9 (8.3)	64.0 (9.6)	56.5 (8.4)	37.4 (8.1)	60.7 (8.4)	63.8 (5.3)	65.1 (7.5)	38.5 (13.5)	**68.6 (5.0)***

+PROMIS measures scored 0-100; mean 50 for general US population; 1SD = 10 points^Study period: January 2020 – December 2021. *Statistical significance (p<0.05); analysis of means (ANOM)

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POS0089-PARE THE IMPORTANCE OF ACCURATE INCIDENCE AND PREVALENCE ESTIMATES FOR FAMILIES OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is a heterogenous group of autoimmune disorders characterised by chronic joint inflammation, affecting children and young people (CYP) under the age of 16. Recent analysis in the UK [1] has provided an update to the estimated incidence and prevalence of JIA.
Objectives: Whilst the policy and health-care benefits of accurate incidence and prevalence rates are understood, this patient- and parent-led qualitative project sought views from parents of CYP with JIA to understand whether knowing accurate estimates of incidence and prevalence are important to them.
Methods: Parents of CYP with JIA, all members of a small online group on social media, were asked whether knowing accurate rates of JIA were important to them, and why. Responses were collated and summarized.
Results: Whilst a few respondents felt it did not matter to them what the overall rates of JIA were, focusing instead on their own personal experience with the condition, the majority did want to know and gave consistent reasoning.
They advised that, when your child is diagnosed with JIA, it is a very isolating experience. Most people have never heard of the condition before, and being told your child has arthritis is a frightening time (especially if you then become aware of some of the significant long-term effects, such as potential continuation of disease into adulthood and possible joint damage, and the side effects of treatment, and social impacts of the disease [2, 3]. Whilst direct support is available to families affected by JIA (www.jarproject.org/hope), understanding prevalence rates can help reduce mental health burdens on patients and parents and reduce feelings of isolation.
Families also advised that they want to know numbers of children with JIA so we collectively can get a better understanding of the cause, the trends, and the possible reasons behind changes. Knowing accurately the numbers of children with JIA can help to raise awareness; current lack of awareness in society and primary care contributes to delays in diagnosis and potentially worse clinical outcomes [4]. In addition they reported the need for appropriate resourcing of paediatric rheumatology and support services, and the political and financial discussions that must take place to enable that to happen need to be supported by evidence.
Conclusion: Overall, parents *do* want to know how many other children have JIA. It takes some of the isolation and anxiety away to know you are not alone. It matters because knowing there are other parents in the same situation as you can help reduce anxiety and loneliness. It matters, because knowing there are researchers focussing on JIA helps remind you that work is underway to better understand JIA, its causes, and improved treatments which will eventually lead to improved care for children with the condition. It matters, because it can help target resources appropriately. It matters, because raising awareness is more effective if we know how many people are affected by a chronic condition. And it matters, because as improved treatments are developed we want to be able to see the number of children categorised as having active JIA to reduce and health outcomes for each child to improve.

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POS0090-PARE ORGANIZATION, INFLUENCE, AND IMPACT OF PATIENT ADVISORY BOARD REPRESENTATION IN PRIVATE REHABILITATION INSTITUTIONS – AN EXPLORATIVE CROSS-SECTIONAL STUDY

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Background: Patient participation (PP) organised as patient advisory boards (PABs) is a statutory part of health care institutions in Norway (1). There is limited agreement on how to engage PABs in a meaningful manner (2). More knowledge on how PAB representatives experience patient engagement (PE) is needed.
Objectives: To explore how PAB representatives engage in PABs with regard to organisation, influence, and impact on decision-making processes and service delivery.
Methods: PAB representatives recruited from rehabilitation institutions, representing all four health regions in Norway completed a PE evaluation tool. The tool is tested for reliability and content validity with good results and comprises 35 items including four main domains *policies and practices, participatory culture, collaboration,* and *influence and impact* that provided responses about PE-levels (3). Categorical data were summarized to modal scores using frequencies and percentages, and response categories were collapsed from five to three. The collapsed categories were divided into PE-levels; barrier, intermediate, and facilitator (Table 1). Free-text responses were analysed according to principles of manifest content analysis, summed up, and used to complete the results of the scores. Free text responses were analysed using Quirkos version 2.4.1.
Results: Of the 150 contacted PAB representatives, 47 (32%) responded. PAB representatives' mean age was 60.5 (min-max 30 - 80), 62% were female and a majority (81%) had prior experience with PP. The results showed that 75% of the participants agreed that patient-centered care was strengthened as a result of PE. Three out of four main domains scored indicating a facilitating PE-level (Table 1). The domain, *influence and impact* scored with an intermediate PE-level. Regarding *influence and impact*, half of the participants did not know if *PE input had influenced management decisions,* and 60% had rarely *identified any PE contributions*. The results from free text analyses showed that PE was coded as a facilitator seven times, and as a barrier to PE 26 times. The most frequent barrier was exclusion of PAB (13 codes), and the most coded facilitator was inclusion of PAB (3 codes).
Conclusion: Findings indicate that PAB representatives are satisfied with how rehabilitation institutions organise PABs. Unclear adherence to the values and principles of PP may hinder influence and visibility from PE contributions.

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Table 1

Modal scores of the most common collapsed response category (PE-level) (N=47)

Items (n)	Domain	Modal PE-level	Mode n (%)	(min-max)
5	Policies and practices	Facilitating	125 (53.2)	(18-37)
8	Participatory culture	Facilitating	199 (53)	(14-35)
2	Collaboration	Facilitating	35 (36.5)	(14-19)
6	Influence and impact	Intermediate	125 (44.4)	(10-30)

Questions not presented in the table consist of *background* items, items related to *final thoughts,* and five questions with free text fields. A yes or no question related to the domain policies and practices is not included in the table.

Before collapsed, 15 items were valued: Strongly disagree, disagree, neither agree nor disagree, agree, strongly agree, don't know. Seven items valued 1-5: never, seldom, some of the time, all of the time, don't know.

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POS0091-PARE **MIG-NETWORK - A NETWORK FOR PEOPLE WITH RHEUMATISM AGED 35-55 YEARS.**

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Background: The MIG network *("MIG" is a shortening for "Midt i gigt" which means "In the middle of Reumatism" as well as mid-life. MIG also means "ME" in Danish*
The existing offers and activities in the Danish Rheumatism Association are primarily targeted towards the age group above 60 years. Often, younger members find it difficult to feel at home and see themselves as part of that particular age group. They miss activities where they can meet up with their peers, who are going through the same challenges in life.
Objectives: The objectives of the MIG network is to create a forum for people with rheumatism, who are roughly between 35 and 55 years old. The network focuses on life with rheumatism and how to keep the balance between job, family life and the disease. The ultimate goal was to create a community based on networking, shared experiences and relevant knowledge from both each other and health professionals.
Methods: First of all, the age group needed to be involved right from the start, so we initially made a series of interviews to learn about their needs and wishes. Then we gathered a group of five volunteers, who agreed to participate in defining the objectives and activities and to start up the network.
The network consists of the following:
I) an online based network with monthly webinars on the platform Zoom, where different health professionals talks about relevant subjects. The obvious advantage being, that people could participate from all over the country, from their sofa, not needing to dress up and travel after a long day of obligations.
II) The Danish Rheumatism Association have created an App for their volunteer community. In this app we offered the members of MIG "a room of resources" where they can find news on the latest research and other relevant news. The members can also ask questions and share written advice and good ideas with each other.
III) Last, but not least it was important for the volunteers to offer physical meetings once or twice a year. They long to meet up, to laugh together and share their stories and experiences on life with arthritis. These meetings always have talks and lectures by eg. Reumatologists, scientists, physiotherapists or psychologists.
Results: I) The participants in the online webinars have been very pleased with the professional presentations and found them to be very useful. At the same time, they gained useful tools to make it easier to live a life with rheumatism. But it has been difficult to create an intimate space. For many, it is difficult to share private feelings of uncertainty and inadequacy on camera in a Zoom meeting. The "room of resources" on our App has only worked and engaged a very small group of people, in spite of a great effort from our volunteers.
The physical meetings have been a great success. And they have covered a need that wasn't met before. The participants have enjoyed the professional lectures, but enjoyed the social networking even more. So now the meetings have less lectures and more networking in the program. As living with a chronic disease can make the whole family and network suffer, we also met the need to invite next of kin to join the meetings and have arranged for them to have their own workshop with a Psychologist.
Conclusion: The MIG network makes sense! And it has met a need for people with a chronic disease to meet up with peers in the same life situation. It has proven to be more difficult than intended to create an online community, whereas the physical meetings have created strong relations on a completely different level. The network continues with both the digital and the physical activities nationally. The goal is also to recruit volunteers locally, so that they can initiate local activities.
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Disclosure of Interests: None declared
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Pathogenesis of SLE, Sjöns and antiphospholipid sydrome

POS0092 **HETEROGENEITY OF THE TYPE I INTERFERON SIGNATURE AMONG ANTIPHOSPHOLIPID SYNDROME PATIENTS: A CLUSTER AND CORRESPONDENCE ANALYSIS APPROACH**

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Background: Type I Interferons (IFN) are central players in the pathogenesis, disease activity and evolution of several autoimmune conditions. To date, a limited number of evidences is available on the specific role of IFN activation in antiphospholipid antibodies (aPL) positive patients, including aPL carriers, primary antiphospholipid syndrome (PAPS) and those APS subjects who presented with an associated autoimmune disease (secondary APS, SAPS), such as systemic lupus erythematosus (SLE).
Objectives: The aim of this study was to evaluate the differential expression of IFN stimulated genes (ISG) among different subsets of aPL positive subjects and SLE patients.
Methods: For the purpose of the study, a total of 112 patients attending the San Giovanni Bosco Hospital (Turin, Italy) were enrolled, including 31 PAPS, 25 SAPS, 27 SLE patients without aPL, 29 aPL carriers (mean age 48.3±13.3 years, 76% female)[1,2]. Nineteen subjects were also recruited as healthy controls (HCs). Complete demographic, clinical, and laboratory data were collected at the time of the inclusion. Gene expression was evaluated by RT-PCR in whole blood for the following genes: IFI6, IFI44, IFI44L, MX1,IFI27, OAS1 and RSAD2. Normalized gene expression levels (Z-scores) were averaged into a global IFN signature (IFN score). Differences were measured by Kruskal-Wallis tests and associations among genes were studied by cluster and correspondence analyses. Correlations among genes were plotted by network analyses.
Results: An overall activation of ISG was noted across APS subsets, but certain differences were noted among genes. Whereas some ISG were already upregulated in the aPL positive group compared to HC (IFI44, IFI44L, MX1, IFI27, OAS1 and RSAD2, all $p<0.050$), other ISG were only in increased SLE (IFI6), MX1 differed between SLE and SAPS, and IFI27 and OAS1 showed differences between PAPS and SAPS. The composite IFN score revealed quantitative differences in the IFN pathway activation across APS subsets, being elevated in aPL carriers/PAPS groups compared to HCs (both $p<0.050$) and increasing in SAPS ($p<0.010$) and SLE ($p<0.001$) groups. Network analyses (Figure 1A) revealed qualitative differences in the gene-gene correlation networks: (i) weaker structures were found in HCs and aPL carriers, compared to stronger and higher-degree networks in SAPS and SLE groups; and (ii) the influence of each node was different across groups. Unsupervised cluster analysis identified 3 clusters (I to III) based on ISG patterns (Figure 1B). Clusters usage differed among APS subsets, thus correlating clinical status (Figure 1C). Distinct groups of ISG positively correlate to aPS/PT IgG titre in aPL carriers and PAPS groups (all rho>0.500), whereas no associations were retrieved in SAPS or SLE. No associations with previous thrombotic events were observed in any subset, although IFN composite score and several ISG correlate with the number of thrombotic recurrences under anticoagulation (all rho>0.400). No associations with GAPSS were observed.

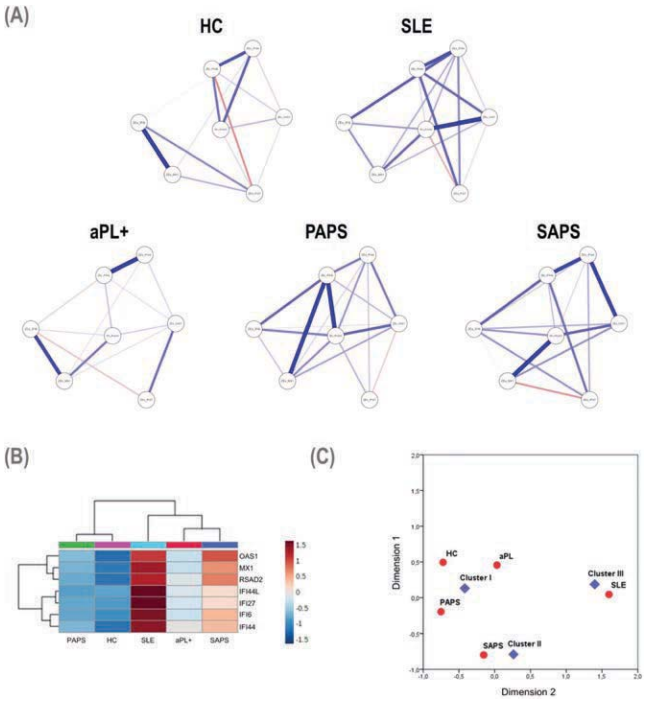

Figure 1.

Conclusion: An overall IFN pathway activation has been observed in aPL positive patients and across all APS subsets. Qualitative and quantitative differences across the APS spectrum can be identified, leading to the identification of distinct IFN signatures with different clinical value.

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POS0093 ASSESSMENT OF HISTOLOGICAL FEATURES OF CHRONICITY OF MINOR SALIVARY GLAND BIOPSY IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: The origin of the histological chronic inflammation of the salivary gland in patients with primary Sjogren's Syndrome (pSS) is questionable. It is probably a consequence of both, the evolution of the disease itself and ageing
Objectives: This study aims to evaluate histological data of chronicity of minor salivary gland biopsy with clinical characteristics and time of evolution in a series of patients with pSS.
Methods: A cross-sectional study including 98 subjects fulfilling the ACR-EULAR 2017 classification criteria for pSS. All patients underwent a minor salivary gland biopsy requested as per clinical practice. We collected the age at diagnosis and at biopsy, xeroftalmia and xerostomia evolution time, and stimulated and unstimulated salivary flow as a clinical data. We informed the following features in the minor salivary gland biopsy: the focus score (positive if ≥ 1), atrophy, fibrosis and adiposity all graded in negative, mild, moderate, and severe stages according to pathological criteria.
Results: This study included 98 patients with pSS. the median of all recruited parameters are shown in Table 1. Only 2 patients presented severe fibrosis and adiposity, so we did not consider them for the analysis. Both, the age at diagnosis and at biopsy are significantly higher between none, mild and moderate stages in the three biopsy parameters. The age at biopsy increased in negative, mild, and moderate stages, in median, 10, 9 and 6 years in atrophy, fibrosis and adiposity respectively. Although more evolution time is observed in atrophy and fibrosis regarding classification categories, it does not reach statistical signification. Focus score is associated with atrophy as a high percentage in severe stage shows negative biopsy (78% vs 22%, p = 0.046) while in negative, mild, and moderate atrophy display a positive biopsy (61%, 73% and 64%, respectively). Furthermore, we observe a significant OR of 8.75 [1.7-68] for negative, 6 [1.25-44] in mild and 9.92 [1.8-80] in moderate compared to severe atrophy. Fibrosis and adiposity are not related to focus score. A low unstimulated salivary flow is observed in the atrophy and fibrosis stages, although differences are explained when compared negative with mild and moderate (3.5 vs 2 and 1.4 for atrophy and 3 vs 2 and 1.75 for fibrosis). Regarding adiposity, a lineal statistically significant association is observed for every stage (3.5, 1.65 and 0.7, p< 0.001). No differences in the stimulated salivary flow are shown.

Table 1. Description of variables included in the study.

	Categories	N(%)Median(IQR)
Age at diagnosis(years)		55.220 (51.097, 58.407)
Age at biopsy (years)		57.719 (53.851, 61.333)
Xerostomia (months)		19.614 (10.480, 35.121)
Xeroftalmia (months)		21.487 (8.148, 38.735)
Focus score (positive)		63 (64.3%)
USF (ml/15 min)		2.000 (1.400, 3.000)
SSF (ml/ 5min)		4.500 (3.000, 5.000)
Atrophy	Negative	28 (28.7%)
	Mild	37 (38.1%)
	Moderate	23 (23.7%)
	Severe	9 (9.3%)
Fibrosis	Negative	29 (30.5%)
	Mild	40 (42.1%)
	Moderate	26 (27.4%)
Adiposity	Negative	39 (41.1%)
	Mild	38 (40%)
	Moderate	18 (18.9%)

USF: Unstimulated salivary flow, SSF: Stimulated salivary flow

Conclusion: An older age both, at diagnosis and at biopsy are associated with a severe stage of atrophy, fibrosis, and adiposity. Patient with severe atrophy shows less positive focus score, which might be noticed for biopsy interpretation

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POS0094 ALPN-303, AN ENGINEERED DUAL BAFF/APRIL ANTAGONIST, POTENTLY INHIBITS PATHOGENIC LYMPHOCYTE SUBSETS AND FUNCTION IN B-CELL- AND ANTIBODY-RELATED PRECLINICAL MODELS

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Background: B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) are tumor necrosis factor (TNF) superfamily members that bind TACI (transmembrane activator and CAML interactor), BCMA (B-cell maturation antigen), and/or BAFF-R on B cells and together support B cell development, differentiation, and survival. ALPN-303 is an Fc fusion protein of a human TACI variant TNFR domain engineered by directed evolution[1,2]. It mediates significantly improved combined BAFF and APRIL inhibition in vitro and enhanced pharmacokinetic and immunomodulatory properties in preclinical studies, as compared to wild-type (WT) TACI-Fc molecules. B-cell targeting therapies like the WT TACI-Fc fusions atacicept and telitacicept have demonstrated promising clinical potential in B cell-related diseases like systemic lupus erythematosus (SLE). ALPN-303, with enhanced inhibitory activity against BAFF and APRIL, has previously been shown to demonstrate promising efficacy in an (NZB/NZW) F_1 mouse model of lupus, and may therefore further improve clinical outcomes in such diseases.
Objectives: To further characterize the comparative activity of ALPN-303 versus an Fc matched control, a WT TACI-Fc comparator (telitacicept), and/or a B cell-depleting therapy (anti-mouse CD20 [anti-mCD20] monoclonal antibody [mAb]), in antibody-related preclinical models.
Methods: The functional activity of ALPN-303, as compared to telitacicept or a depleting anti-mCD20 mAb, was evaluated in a sheep red blood cell (SRBC) immunization mouse model. Mice immunized intraperitoneally with SRBC on Study Day 0 were administered 200 µg ALPN-303 or a molar-matched amount (240 µg) of telitacicept on Days 1 and 6 or were treated with 200 µg anti-mCD20 (rat IgG2b) on Day 1. At study termination on Day 15, serum was collected to measure levels of test article and anti-SRBC immunoglobulin (Ig) titers, and spleens and bone marrow (BM) were collected for immunophenotyping by flow cytometry. A study in the inducible bm12 mouse model of lupus was also conducted, with mice treated twice weekly with 200 µg ALPN-303 or a molar-matched dose of Fc control, starting on Day 5 after splenocyte transfer and continuing through Week 13.
Results: ALPN-303 administration rapidly and potently reduced BM plasma cells, splenic germinal center B cells, follicular T helper cells, and plasmablasts in SRBC-immunized mice, often significantly more so than telitacicept and/or anti-mCD20 mAb. ALPN-303 also significantly reduced serum titers of anti-SRBC IgM, IgG1, IgG2a, and IgG2b as compared to all other treatment groups. In the bm12 model, ALPN-303 treatment significantly impacted the same key lymphocyte subsets affected in the SRBC model, and significantly reduced circulating anti-dsDNA antibodies (Figure 1) and total IgA, IgM, IgG1, IgG2b, and IgG3, and inhibited renal IgG deposits (Figure 1).

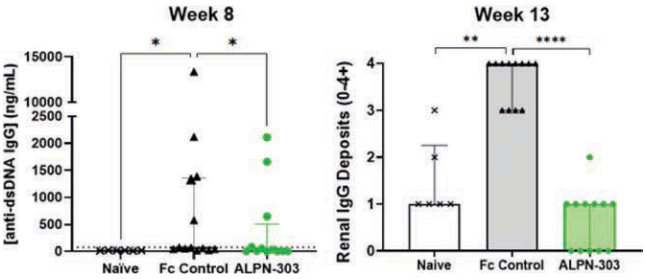

Figure 1. ALPN-303 treatment significantly reduces serum autoantibody titers and renal immune complex deposition in the inducible bm12 mouse model of lupus. *p<0.05, **p<0.01, ****p<0.0001 by the Kruskal-Wallis test.

Conclusion: ALPN-303 is an engineered, potent BAFF/APRIL antagonist that continues to consistently demonstrate encouraging immunomodulatory activity and efficacy in vitro and in vivo, as further demonstrated in the SRBC immunization and bm12 lupus models, with superiority to WT TACI-Fc and anti-CD20 comparators. ALPN-303 may thus be an attractive development candidate for

the treatment of multiple autoimmune and inflammatory diseases, particularly B cell- and/or autoantibody-related diseases such as SLE, Sjögren's syndrome, and other connective tissue diseases. A Phase 1 study of ALPN-303 in adult healthy volunteers (NCT05034484) is ongoing.

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POS0095 CAMK4 CONTROLS T REGULATORY CELL METABOLISM AND DEFINES THEIR FUNCTION AND STABILITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Calcium/Calmodulin-dependent protein kinase IV (CaMK4) is a serine kinase expressed in CD4 T cells whom activity is increased in patients with active systemic lupus erythematosus (SLE). We have shown that CaMK4 negatively impacts T regulatory (Treg) cells differentiation and function in SLE, but the underlying mechanism remains unclear. Recent, data suggest that CaMK4 impacts cellular metabolism.

Objectives: Investigate how CaMK4 impacts Treg cell metabolism and its potential effect on Treg cell function.

Methods: We harvested $CD62L^+CD4^+$ T cells from *wild-type* (WT) or *Camk4*$^{-/-}$ mice and differentiated them *in vitro* into Treg (iTreg) cells. We assessed iTreg metabolism using Seahorse XF analyzer and mass spectrometry (metabolomics). Gene expression was assessed at the mRNA (RT-qPCR) and at the protein level (Western Blot). Phosphofructokinase activity was assessed by a colorimetric assay (Abcam). *In vitro* gene knockdown was conducted by transfecting a guide RNA (gRNA) in CRISPR/Cas9-expressing T cells. Treg cell function was evaluated by *in vitro* immunosuppressive assay and *in vivo* by the adoptive transfer of T conventional T and iTreg cells (8:1 ratio) in *Rag1*$^{-/-}$ mice to induce inflammatory colitis. The relevance of CaMK4 in SLE was evaluated *in vivo* using a T-cell specific knockdown of CaMK4 in the B6.lpr mouse model, and in humans by culturing SLE patient T cells with KN-93, a CaMK4 specific inhibitor.

Results: iTreg cells from *Camk4*$^{-/-}$ mice had decreased glycolysis and increased mitochondrial metabolism compared to WT mice. Metabolomics studies suggested decreased activity of the rate-limiting glycolysis enzyme phosphofructokinase platelet-type (PFKP). While PFKP mRNA and protein levels were similar between WT and *Camk4*$^{-/-}$ iTreg, we found that PFKP activity was significantly decreased in *Camk4*$^{-/-}$ iTreg, suggesting post-transcriptional control of PFKP activity. Mechanistically, immunoprecipitation experiments confirmed that CaMK4 interacted with PFKP, and phosphoproteomic study suggested that CaMK4 phosphorylated serine residue 539 of PFKP, a site known to control PFKP activity. Excitingly, PFKP's endproduct fructose 1,6-biphosphate negatively regulates the activation of the mitochondrial metabolism masterswitch AMPK, therefore linking decreased PFKP activity/glycolysis with increased mitochondrial metabolism in *Camk4*$^{-/-}$ Treg. To confirm the importance of PFKP in Treg biology, we confirmed that PFKP knockdown significantly improved iTreg function *in vitro* ($p < 0.01$) and *in vivo* using an adoptive CD4+ T cell transfer in to *Rag1*$^{-/-}$ mice (colitis model). Interestingly, iTreg lacking PFKP were transferred *Rag1*$^{-/-}$ mice were less likely to lose FoxP3 expression and to produce IL-17A, demonstrating higher Treg stability in an inflammatory environment. On a translational basis, lupus-prone B6.*lpr* mice with a T-cell specific CaMK4 knockdown displayed significantly less lupus manifestations. In human SLE, $CD4^+$ T cells had higher PFKP activity compared to healthy donors, and PFKP activity correlated with the SLE disease activity index (SLEDAI, $r= 0.47$; $p <0.05$). Finally, culture of SLE CD4+ T cells with KN-93 led to a significant decrease in PFKP activity ($p < 0.001$).

Conclusion: Increased CaMK4 activity in human SLE mediates Treg dysfunction and instability by altering PFKP activity. Restoring normal Treg metabolism by inhibition of CaMK4 or its downstream target PFKP represents a novel strategy for the treatment of SLE.

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POS0096 SJÖGREN'S DISEASE AND SYSTEMIC LUPUS ERYTHEMATOSUS DDX6-CXCR5 RISK INTERVALS REVEAL COMMON SNPS WITH FUNCTIONAL SIGNIFICANCE IN IMMUNE AND SALIVARY GLAND CELLS

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Background: Sjögren's Disease (SjD) and Systemic Lupus Erythematosus (SLE) are autoimmune diseases with several shared characteristics and similar genome-wide significant associations with the *DDX6-CXCR5* locus. DDX6 suppresses interferon-stimulated gene expression and CXCR5 regulates T cell functions implicated in autoimmunity.

Objectives: To identify and characterize functional SNPs in the *DDX6-CXCR5* interval.

Methods: ImmunoChip data from European populations (3785 SLE cases; 1916 SjD cases; 6893 controls) were imputed and SNP-trait associations tested. Bayesian statistics defined a credible SNP set that was refined using bioinformatic analyses (RegulomeDB, Haploreg, ENCODE, promoter capture Hi-C, eQTLs, etc.). Electrophoretic mobility shift assays (EMSAs) and luciferase expression assays were used to test allele-specific SNP function in EBV-transformed B (EBV B) cells, Daudi B cells, Jurkat T cells, THP1 monocytes, and A253 salivary gland cell lines. Chromatin conformation capture with quantitative PCR (3C-qPCR) was used to assess long-range chromatin interactions.

Results: Fine mapping of the SjD and SLE associations found similar SNP associations. Bioinformatic analyses identified 5 common SNPs with strong evidence of functionality in immune cell types: rs57494551 in an intron of DDX6, and rs4938572, rs4936443, rs7117261, and rs4938573 in the promoter/enhancer region of *DDX6* and *CXCR5*. EMSAs and luciferase experiments showed cell type-specific differences in protein binding and promoter or enhancer activity, respectively, at each SNP. Risk allele of rs57494551 increased enhancer activity in B cells and A253 cells ($p<0.001$), but decreased promoter activity in T cells and A253 cells ($p<0.01$). SNP rs4938572 is an eQTL of *DDX6* in T cells, and the risk allele significantly increased protein binding, promoter and enhancer activity in T cells ($p<0.01$). Risk allele of rs4938572 also increased promoter activity in A253 cells ($p<0.001$), but had no effect on promoter or enhancer activity in B cells. SNP rs4936443 showed no promoter or enhancer activity in immune cells, but the risk allele showed

significant promoter and enhancer (p<0.001) activity in A253 cells. SNP rs7117261 showed decreased enhancer activity in EBV B cells, T cells, and A253 cells (p<0.05) and increased promoter activity in A253 cells (p<0.001). SNP rs4938573 showed decreased promoter activity in EBV B cells, T cell and A253 cells (p<0.05), decreased promoter activity in EBV B cells (p<0.05), and increased enhancer activity in A253 cells (p<0.0001). Overall, A253 cells exhibited more allele-specific effects on promoter and enhancer activity across the five SNPs compared to tested immune cells. In addition to *DDX6* and *CXCR5*, rs57494551 and/or rs4938572 are reported eQTLs for several other genes of interest in the local chromatin regulatory network: *IL10RA* in T cells, *TRAPPC4* in salivary gland and activated macrophages, and long non-coding (lnc)RNA *AP002954.1* in T cells and whole blood. 3C-qPCR in EBV B and A253 cells showed that the two regulatory regions carrying rs4938572 or rs57494551 interacted with a region upstream of *DDX6* that includes *AP002954.1*. Hi-C data showed looping between *AP002954.1* and the regulatory region carrying rs4938572 and rs57494551 in T cells.

Conclusion: SjD and SLE share similar genomic architecture across the *DDX6-CXCR5* risk interval with several common SNPs showing immune and salivary gland cell type-specific allelic effects on protein binding and/or enhancer/promoter activity. Extensive bioinformatic analyses suggest that the SNPs likely work within the local chromatin regulatory network to regulate cell type-specific expression of several genes on the interval. Ongoing studies will use 3C-qPCR to assess allele-specific chromatin interactions between the SNPs and these genes in different cells types, and CRISPR to determine how the risk alleles alters expression.

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POS0097 IDENTIFICATION OF NEW CANDIDATE DRUGS FOR PRIMARY SJÖGREN'S SYNDROME USING A DRUG REPURPOSING TRANSCRIPTOMIC APPROACH

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Background: No immunomodulatory drug has ever demonstrated its efficacy in primary Sjögren's Syndrome (pSS). Drug repurposing, or drug repositioning, refers to the use in another disease of an existing drug, originally approved or evaluated in a different disease.

Objectives: The objective of our study was to repurpose existing therapeutic drugs in pSS using a transcriptomic approach.

Methods: We generated pSS transcriptomic signatures from peripheral blood samples of patients with pSS compared to healthy controls in two cohorts (ASSESS and a Norwegian cohort) and data mined available pSS transcriptomic signatures in public databases. We compared each disease signature to transcriptomic signatures, obtained from the biological action of 2837 drugs, 2160 knock-in and 3799 knock-down genes, available in the Connectivity Map database. A median similarity score with regard to disease signatures was computed for each candidate drug/gene. Drugs and genes were selected if p<0.05 and similarity score $>|80|$. If this score is sufficiently high and statistically significant (>80, p<0.05), the tested drug or gene, mimics the signature of the disease. Conversely, if this score is sufficiently low and statistically significant (<-80, p<0.05), the tested drug or gene inverts the signature of the disease and might represent a potential treatment or therapeutic target of interest (Figure 1).

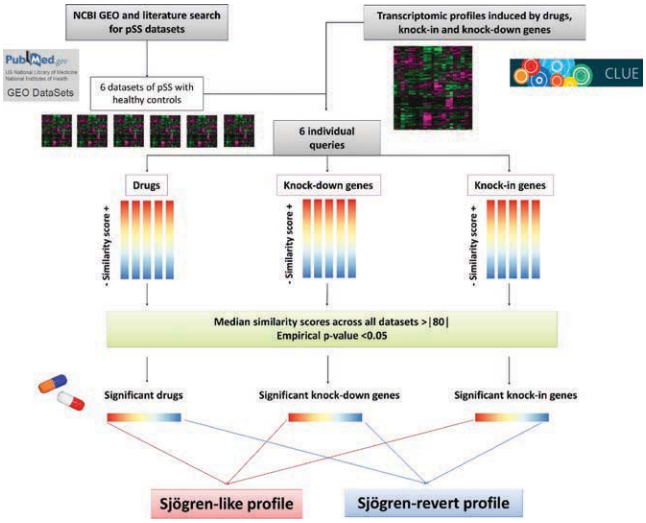

Figure 1. Methods of drug-repurposing transcriptomic analysis (adapted from Toro-Dominguez et al, Arthritis Res Ther 2017;19:54)

Results: 1091 peripheral blood transcriptomes were analyzed from 6 independent studies (906 patients with pSS and 185 healthy controls). Our analysis identified 11 transcriptomic drug signatures significantly associated with pSS signature. We identified 72 transcriptomic knock-in (11) or knock-down (61) gene signatures significantly associated with that of pSS, including 21 with a negative similarity score (Table 1).

Table 1. Knock-down and knock-in genes significantly associated with the pSS transcriptomic signatures

Type of experiment	Similarity score	Genes	Number of genes
Knock-in	+	IFNG, DUSP28, IFNB1, LYN, BCL2L2, TNFRSF1A, CD40, BCL10, NLK, ZNF398	**10**
	-	SLC52A2	**1**
			11
Knock-down	+	SLC25A14, GOLIM4, DTYMK, DCXR, RRM2, IMPA1, CLTB, F12, CAB39, ID1, ISOC1, UBAP1, HIGD2A, UFD1L, SOD2, BTG1, PRKCI, HIST2H2BE, NISCH, TEAD4, MTX2, TYK2, GTF2B, NDUFS7, NNT, ACADSB, GSTP1, HOMER2, SORBS3, PCK2, PHB2, PDXK, TES, TM9SF2, TBX2, HOXA6, KIF2C, MED1, NR2F6, CD14, BECN1	**41**
	-	TM9SF3, E2F3, PRMT3, KD, PKN2, SUCLA2, CD44, GRN, SP3, ATP5S, MYCBP2, TRAF7, POLA2, ADRB2, PSMG1, PPP2R3C, PMAIP1, ETFA, ANKRD37, SPECC1L	**20**
			61

Type I and II interferons were highly ranked (similarity score >99), and their overexpression mimicked the disease signature. CD40 appeared also as a very relevant target (similarity score = 98.8). Three drugs had a significant negative similarity score: ampicillin (-88.69, p=0.0019), amylocaine (-88.28, p=0.0026), and droxinostat (-85.42, p=0.0027). Droxinostat is a HDAC inhibitor. HDAC activity has been shown to be an essential element of the coactivation system for IFN-induced gene regulation and the IFN-induced innate immune response.

Conclusion: This first drug repositioning transcriptomic approach in Sjögren's syndrome confirms the interest of targeting interferons and identifies histone deacetylases as potential therapeutic targets.

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POS0098 LINC01871, IMPLICATED IN SJÖGREN'S DISEASE PATHOGENESIS, IS REGULATED BY INTERFERON-G AND CALCINEURIN SIGNALING

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Background: Sjögren's disease (SjD) is an autoimmune disease characterized by exocrine gland dysfunction. Long non-coding RNAs (lncRNAs) are a functionally diverse class of non-protein coding RNAs that are longer than 200 nucleotides. Our previous study using whole blood RNA-seq found that lncRNA, *LINC01871*, is overexpressed in SjD relative to controls [1]. CRISPR-Cas9 targeting in HSB2 T cells yielded a *LINC01871*$^{-/-}$ clone with altered expression of many genes implicated in immune regulation [1].
Objectives: The goal of this study was to analyze the gene expression perturbations resulting from the loss of *LINC01871* and to characterize the regulation of LINC01871 in both the *LINC01871*$^{-/-}$ clone and primary human T cells in response to immune stimuli.
Methods: Flow cytometry and LegendPlex bead assays were used to compare surface and secreted protein expression changes, respectively, in *LINC01871*$^{-/-}$ cells and the parental HSB2 cells. Parental HSB2 T cells, *LINC01871*$^{-/-}$ cells, Kasumi-3 myeloid cells, and primary human T cells were stimulated in vitro and changes in gene expression were measured over time using qRT-PCR. Responses to interferons (IFN) were assessed using universal type I IFN (IFNα) or IFNγ. TCR signaling responses were assessed using PMA/Ionomycin (PMA/I) or anti-CD3/CD28 stimulations in the presence or absence of the calcineurin inhibitor, FK506.
Results: Previous RNA-seq analysis found 1166 differentially expressed (DE) transcripts ($\log_2$FC ≥1 or ≤-1; p_{adj} ≤0.05) in *LINC01871*$^{-/-}$ cells compared to parental HSB2 cells, including many prominent immune regulatory genes. Changes in the basal expression of 7 proteins in *LINC01871*$^{-/-}$ cells were confirmed using flow cytometry (significantly decreased: CD8a (p=0.0004), CD30 (p=0.0008), CXCR3 (p=0.037), T-Bet (p=0.0002), and Aiolos (p=0.02); significantly increased: CD226 (p=0.0059) and CD44 (p=0.024)). Analysis of *LINC01871*$^{-/-}$ cells revealed a growth inhibition in *LINC01871*$^{-/-}$ cells (p=0.0014 at 72h), in which multiple secreted growth and adhesion factors were significantly reduced: GM-CSF (p=2.0e-06), M-CSF (p=2.7e-09), IGBPF4 (p=1.2e-07), s-ICAM1 (p=0.015), MMP9 (p=3.0e-14), and MMP2 (p=6e-08). In contrast, the IL-6 cytokine family member, LIF, was significantly increased in *LINC01871*$^{-/-}$ cells (p=1.2e-07). Because HSB2 cells were not responsive to all IFNs, IFN-mediated regulation of *LINC01871* expression was examined in the Kasumi-3 myeloid cell line. While *LINC01871* expression was not modulated by type I IFN stimulation, it was robustly responsive to IFNγ treatment. Since *LINC01871* was expressed in T cells and implicated in T cell pathways, responses to TCR signaling pathways were characterized in HSB2 cells or purified primary human T cells treated with PMA/I. In both cell types, *LINC01871* exhibited a prolonged decrease in expression that was abrogated by concurrent treatment with FK506, indicating that *LINC01871* is regulated by calcineurin signaling. Treatment of primary human T cells with anti-CD3/CD28 to mimic true TCR engagement resulted in a modest decrease of *LINC01871* expression at early time points, followed by an increase in expression with longer stimulation (2d).
Conclusion: Our findings suggest that *LINC01871* is a potential mediator of the dysregulated T cell inflammatory response pathways implicated in SjD pathogenesis. *LINC01871* influences the expression of many important immune cell genes and growth factors, is inducible by IFNγ, and is regulated directly by calcineurin signaling and TCR ligand engagement. Although *LINC01871* functions are still unknown, observed *LINC01871* overexpression in whole blood of SjD cases and after prolonged TCR stimulation in primary human T cells suggests that it could be a biomarker of SjD.
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POS0099 THE CELLULAR METABOLISM OF SLE NK CELLS IS PRIMARILY ALTERED AT THE LEVEL OF MITOCHONDRIAL RESPIRATION.

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Background: Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease, involving the development of autoreactive cells and autoantibodies. Natural Killer (NK) cells are innate immune cells that mediate the interaction between the innate and adaptive immune system, however their role in SLE is incompletely understood. SLE NK cells are decreased in peripheral blood, exhibit reduced cytotoxicity, and impaired cytokine production (1, 2). Furthermore, SLE NK cells present phenotypic alterations: increased expression of CD38 and altered upregulation of SLAMF7 after activation (3). To date, few studies evaluated the molecular mechanisms underlying NK cell dysfunction in SLE.
Objectives: We examined immunometabolic alterations of SLE NK cells. First, we characterized the cellular metabolism of SLE NK cells by assessing glycolysis and oxidative phosphorylation (OXPHOS) at basal level. Then, we evaluated how cellular metabolism can be manipulated to enhance NK cell function. In this perspective, we examined how the ligation of CD38 with daratumumab (DARA) and SLAMF7 with elotuzumab (ELO) modulate glycolysis and OXPHOS.
Methods: NK cells of cryopreserved PBMC from SLE patients were isolated. Glycolysis and OXPHOS were studied using XF^{e}96 Seahorse. Expression of metabolic receptors (CD71, GLUT-1, CD98), mitochondrial function (mitochondrial membrane potential, mass) and calcium influx were investigated

by FACS. Mitochondrial structure was evaluated by electron and confocal microscopy.

Results: First, we examined the cellular metabolism of SLE NK cells compared to healthy cells. We observed that OXPHOS is significantly increased in SLE NK cells (Figure 1A), whereas glycolysis was normal (Figure 1B). Furthermore, the mitochondrial mass and membrane potential (by FACS (Figure 1C) and confocal microscopy) were increased in SLE. Electron microscope imaging showed profound alterations in SLE NK cell mitochondrial ultrastructure (Figure 1D). No significant differences in the expression of key metabolite transporters involved in mitochondrial fueling (CD71, GLUT-1, CD98) was observed in SLE NK cells compared to healthy controls.

Second, we examined how ligation of DARA and ELO influences the metabolism of healthy NK cells. Our data showed that ELO primarily enhances NK cell OXPHOS (Figure 1E), whereas DARA mainly increases glycolysis. Consistently, ELO also increases mitochondrial membrane potential and expression of metabolite transporters CD71, GLUT-1 and CD98. Next, we examined the effect of DARA and ELO on SLE NK cells. While stimulation with DARA adequately increases glycolysis in SLE NK cells, engagement with ELO fails to properly increase OXPHOS (Figure 1F), expression of cell surface transporters, mitochondrial membrane potential and mass.

Conclusion: Our data suggest that SLE NK cells exhibit alterations in cellular metabolism, primarily involving mitochondrial respiration. In contrast, glucose metabolism is similar to that of healthy NK cells. Additionally, ELO and DARA mediate the activation of healthy NK cells through the engagement of different metabolic pathways: OXPHOS and glycolysis, respectively. Therefore, priming SLE NK cells with ELO is unable to adequately engage their dysfunctional mitochondrial respiration. These findings provide important insights on the alteration present in SLE NK cells and contribute to a better understanding of the pathogenesis of the disease.

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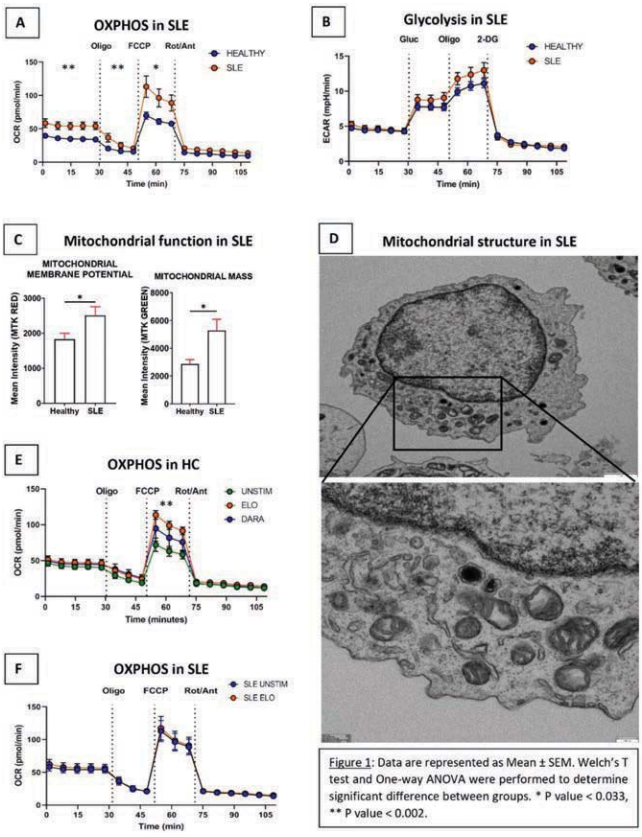

Figure 1: Data are represented as Mean ± SEM. Welch's T test and One-way ANOVA were performed to determine significant difference between groups. * P value < 0.033, ** P value < 0.002.

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POS0100 ACTIVATION OF THE CELLULAR INTEGRATED STRESS RESPONSE IN LABIAL SALIVARY GLANDS FROM SJÖGREN'S SYNDROME PATIENTS.

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Background: Sjögren's syndrome (SS) is a chronic autoimmune disease characterized by inflammation of the exocrine glands and severe symptoms of eye and mouth dryness. Disorders in the saliva secretion process have been associated with oxidative and endoplasmic reticulum (ER) stress in combination with inflammatory responses. The integrated stress response (ISR) is a mechanism that allows cells to modify their gene expression program to restore homeostasis and promote their survival against various extrinsic and intrinsic stress signals, such as hypoxia, nutrient deprivation, viral infections, inflammatory factors (cytokines, chemokines, inflammasomes), and accumulation of unfolded proteins in the ER, among others (1). The ISR is regulated by four kinases: PERK, PKR, HRI and GCN2, that dimerize and autophosphorylate to become active and each one responds to different stress stimuli. The signaling pathways that are activated in response to stress factors stimulate the phosphorylation of eIF2α, which causes a transient inhibition of global protein synthesis and induction of synthesis of some specific genes like ATF4 and NRF2. ATF4 induces the transcription of genes involved in metabolism and nutrient uptake, redox status, and regulation of apoptosis. Dephosphorylation of eIF2α is the ISR termination signal to restore protein synthesis and is mediated by the PP1 complex, which recruits the catalytic subunit PP1c and one of its two regulatory subunits: GADD34 or CREP.

Objectives: To evaluate the presence and functional state (phosphorylation) of the ISR sensing kinases: PERK, PKR, HRI and GCN2; the levels of eIF2α /p-eIF2α and the key ISR transcription factors ATF4 and NRF2, as well as subunits of the complex involved in the ISR termination: PP1c, GADD34 and CREP in labial salivary glands (LSG) of SS-patients.

Methods: Biopsies of LSG from 12 SS-patients and 11 control subjects were studied. The levels of mRNA, protein and phospho (p)-protein of the ISR components were determined by RT-qPCR and Western blotting.

Results: Our results show increased levels of p-PERK/PERK ratio (11/11), PKR (7/11), p-PKR (7/11), p-PKR/PKR ratio (7/11), eIF2α (5/11), p-eIF2α (5/11) and ATF4 (11/11) in LSG from SS-patients compared to control subjects. No significant changes were found in mRNA levels of HRI, GCN2, and GADD34 between LSG from SS-patients and control subjects. Decreased protein levels of HRI (8/12), p-GCN2 (6/11), eIF2α (6/11), p-eIF2α (6/11), NRF2 (11/12), and p-NRF2 (12/12) were found in LSG showing scarce parenchyma and high fibrosis and fat infiltration. On the other hand, PP1c and CREP showed decreased mRNA and protein levels in all SS-patients LSG. Interestingly, Ro autoantibodies and focus score were negatively correlated with PP1c and NRF2 mRNA and protein levels whereas positively correlated with PKR mRNA levels.

Conclusion: The overexpression and activation of some ISR kinases together with the decrease in the PP1c/CREP phosphatase complex suggests a continuous activation of ISR, resulting in p-eIF2α to remain activated in LSG from SS-patients. This would explain the high protein levels of ATF4 and of target genes involved in the antioxidant response in LSG from SS patients suggesting that ISR activation plays a key role in pro-survival response to cellular stress.

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Disclosure of Interests: None declared

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POS0101 POTENTIAL INVOLVEMENT OF IL-40 AND IL-40 PRODUCING CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS ASSOCIATED NEPHRITIS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder, characterized by a remarkable heterogeneity of clinical presentations. Glomerulonephritis (GN) remains a leading cause of morbidity and mortality in SLE, influencing long-term prognosis. The alteration of both innate and adaptive immune responses plays a pivotal role in SLE pathophysiology [1]. B lymphocytes are mainly involved in SLE through the production of autoantibodies but recent evidence suggests an effector role of these cells in cytokine production. IL-40 is a recently discovered cytokine, produced by B cells and involved in their homeostasis, that may participate in the pathogenesis of B-mediated autoimmune diseases, such as SLE [2].
Objectives: The purpose of this study was to evaluate the role of IL-40 in the pathogenesis of SLE, with a specific focus on renal involvement.
Methods: Peripheral blood and urine samples were collected from 10 consecutive SLE patients and 10 healthy controls; kidney biopsy specimens were obtained from 3 SLE patients and 3 controls. The concentration of IL-40 in serum and urine samples was evaluated by ELISA. IL-40 production by monocytes, B cells and T cells was assessed by flow cytometry at day 0 and after *in vitro* stimulation. Immunohistochemistry on kidney tissue was also performed to evaluate IL-40 expression.
Results: IL-40 levels were reduced in the serum of patients with active GN. This reduction was further observed in the serum of patients with previous GN. In the serum of active SLE patients, without renal involvement, the concentration of IL-40 did not change significantly compared to controls. Urinary levels of IL-40 showed no significant changes compared to controls. Consistently, immunohistochemistry on kidney showed the expression of IL-40 only in SLE patients (Figure 1). Flow cytometric analysis on T cells, B cells and monocytes isolated from peripheral blood of SLE patients with active GN did not show production of IL-40.

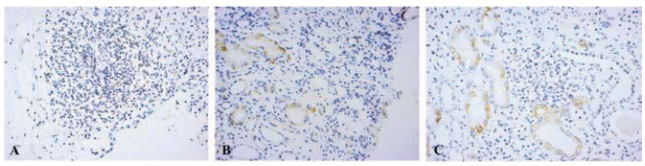

Figure 1. IL-40 overexpression in lupus nephritis at tissue level. Kidney biopsies stained for IL-40 in controls (**A**), Class III lupus nephritis (**B**) and Class V lupus nephritis (**C**) showed intense IL-40 positivity in lupus nephritis (**B, C**) compared to controls (**A**).

Conclusion: To the best of our knowledge this is the first demonstration of IL-40 expression at kidney level in SLE associated nephritis. These preliminary data suggest an active role of IL-40 in SLE, with specific focus on active kidney disease. Our results highlight a potential use of IL-40 as a marker of active GN, although its specific mechanism of action needs to be further elucidated.
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Disclosure of Interests: Chiara Rizzo: None declared, Lidia La Barbera: None declared, Marianna Lo Pizzo: None declared, Leila Mohammadnezhad: None declared, Vincenzo Luca Lentini: None declared, DENISE DONZELLA: None declared, Francesco Ciccia Speakers bureau: lilly, pfizer, novartis, celgene, abbvie, roche, janssen, UCB, SERENA FASANO: None declared, Giuliana Guggino Speakers bureau: pfizer, novartis, celgene, abbvie, roche, lilly, janssen, UCB
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POS0102 GLOBAL CHARACTERIZATION OF SALIVARY GLANDS IMMUNE MICROENVIRONMENT IN PRIMARY SJÖGREN'S SYNDROME BY SINGLE-CELL SEQUENCING

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Background: Primary Sjögren's syndrome (pSS) is a heterogeneous, chronic, complex systemic autoimmune disease. The hallmark symptom of the disease is exocrinopathy, chiefly salivary and lachrymal glands, which often results in dryness of the mouth and eyes. As of today, although a lot of genetic and epigenetic studies have reveal the complexity of pSS to a certain extent, but the knowledge of existing pSS disease heterogeneity is still limited and the immune mechanisms of salivary glands (SG) injury have been challenging to clarify.
Objectives: Single-cell RNA sequencing (scRNA-seq) is a powerful tool capable of defining cell types and states on the basis of their individual transcriptome in a given sample from health and disease. To characterize the salivary glands immune microenvironment of patients with pSS, we performed droplet-based single cell mRNA sequencing (scRNA-seq) (10X Genomics) to provide a deeper insight into the cellular and molecular characteristics of salivary glands from pSS patients.
Methods: 11 patients and 5 non-pSS controls were recruited from the The First Affiliated Hospital of USTC. The non-pSS were subjects who had experienced subjective symptoms of dryness, but no not meet any of the classification criteria of pSS. The clinical characteristics and laboratory findings of enrolled patients were also collected. After resection, salivary glands tissue samples were obtained after labial gland biopsy, rapidly digested to a single-cell suspension and subjected to scRNA-seq using the 10X platform. After rigorous quality control (QC) definition, low-quality cells were filtered. Following gene expression normalization for read depth and mitochondrial read count, we applied principle component analysis on genes variably expressed across all 72,853 cell.
Results: A total of 72,853 cells were obtained from all salivary glands samples. Our results revealed 12 major unique cell populations of salivary glands cell, including T cells, B cells, plasma cells, epithelial cells, myoepithelial cells, endothelial cells, myofibroblast, pericytes, melanocytes, fibroblast, myeloid cells and a cluster of unknown cells. As expected, lymphocytes (T and B cell populations) were significant increase in the salivary glands of patients with pSS. For further subsets analysis, we identify 41 subsets, including novel subpopulations in cell types hitherto considered to be homogeneous, as well as transcription factors underlying their heterogeneity. Strikingly, we found that differentially expressed genes (DEGs) that myoepithelial cells uniquely downregulated in pSS patients were involved in regeneration, stem cell population maintenance, cell division, and epithelial cell proliferation. This indicated an impaired stem cell property and regeneration capacity of myoepithelial cells in the SG of pSS patients which may result in the reduction of normal epithelial cells differentiation and proliferation. Our results identified three distinct endothelial subtypes according to the differentially expressed cell markers. *ACKR1*$^{+}$ endothelial cells were expanded in the SG of pSS patients which may enhance Leukocyte transendothelial migration. A clear interferon response was observed in most celltypes. We also found a significantly expand *PD-1*^{hi}*CXCR5*$^{-}$CD4^{+}T peripheral helper (Tph), *GZMK*$^{+}$CD8^{+} T cells and a patient-specific fibroblasts in pSS patients. Cellular interaction analysis of SG revealed a strong interaction between epithelial cells and immune cells from pSS patients through *CD74-MIF, MIF-TNFRSF14* and *HLA-C-FAM3C* receptor/ ligand pairs. Chemokine receptors *CXCR4* were broadly expressed in SG immune cells implying a potentially central role in cell trafficking.
Conclusion: This resource provides deeper insights into pSS salivary glands immune microenvironment that will be helpful in understanding of the disease heterogeneity and advancing pSS therapy.
Disclosure of Interests: None declared
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Rheumatoid arthritis prognosis, predictors and outcome

POS0103 IN RHEUMATOID ARTHRITIS, THE ASSOCIATION BETWEEN ANTI-MODIFIED PROTEIN ANTIBODIES AND LONG-TERM OUTCOMES IS DOMINATED BY THE EFFECT OF ANTI-CITRULLINATED PROTEIN ANTIBODIES

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Background: In rheumatoid arthritis (RA) many patients harbor autoantibodies against post translationally modified proteins (anti-modified protein antibodies (AMPA)): anti-citrullinated protein antibodies (ACPA), anti-carbamylated protein antibodies (anti-CarP) and anti-acetylated protein antibodies (AAPA). All three AMPA have been described to be associated with an increase in radiographic joint damage and ACPA also with a lower chance of obtaining sustained drugfree remission (SDFR). However, it is unclear whether the effects of these autoantibodies are independent of each other, and whether testing for all three AMPA offers additional information regarding these clinical outcomes.

Objectives: To investigate the individual and combined associations of AMPA with radiological progression and SDFR in RA.

Methods: In 612 RA patients from the Leiden Early Arthritis Clinic, we measured ACPA IgG with anti-CCP2-assays, anti-CarP IgG using homocitrullinated and native (as a control) fetal calf serum, and AAPA IgG by means of novel assays consisting of cyclic peptides with either acetylated or norleucine residues (as a control). Sharp-van der Heijde scores (SHS) were determined in 2685 sets of radiographs with yearly intervals for 7 years. The association of AMPA with SHS was assessed with a multivariate normal regression model. SDFR was defined as the absence of clinical synovitis after discontinuation of DMARD treatment. The association of SDFR with autoantibody-status was assessed with Kaplan-Meier curves. The very small number of patients single-positive for AAPA (n=4, 1%) precluded analyses in this subgroup.

Results: The prevalence of autoantibodies is shown in Table 1. A higher SHS was found in patients with autoantibodies compared to patients without antibodies, and in triple-positive versus single-positive patients (Figure 1A, p=0.04). To investigate if the higher SHS was due to the number of autoantibodies or a specific autoantibody, analyses were stratified for all three AMPAs. Interestingly, no difference was found in SHS between all ACPA-positive strata (Figure 1B). In the ACPA-negative stratum, a significant difference was found between patients with zero antibodies and solely anti-CarP (p=0.02).

Table 1. Prevalence of autoantibodies in 612 rheumatoid arthritis patients in the EAC cohort

Autoantibody status	n (%)
ACPA-positive	316 (52)
Anti-CarP-positive	270 (44)
AAPA-positive	208 (34)
ACPA-AAPA-CarP-	255 (42)
ACPA+AAPA-CarP-	46 (7)
ACPA-**AAPA+**CarP-	4 (1)
ACPA-AAPA-**CarP+**	37 (6)
ACPA+AAPA+CarP-	37 (6)
ACPA+AAPA-**CarP+**	66 (11)
ACPA-**AAPA+CarP+**	- (0)
ACPA+AAPA+CarP+	167 (27)

EAC: early arthritis clinic, ACPA: anti-citrullinated protein antibodies, anti-CarP/CarP: anti-carbamylated protein antibodies, AAPA: anti-acetylated protein antibodies

The chance to obtain SDFR was lower in all antibody-positive groups compared to the autoantibody negative group. Moreover less triple-antibody-positive patients than single-antibody-positive patients achieved SDFR (P<0.001), Figure 1C. After stratification for AMPA, no difference was found in the percentage of SDFR in all ACPA-positive strata, or in the ACPA-negative stratum, Figure 1D.

Conclusion: In ACPA-positive patients, the presence of other AMPA influences neither radiographic progression, nor the chance of SDFR. Thus, long-term clinical phenotype in RA is particularly dependent on the presence of ACPA, and less on the presence of other AMPA. Therefore, there appears to be no added value of testing the other AMPA for predicting clinical outcome in ACPA-positive patients.

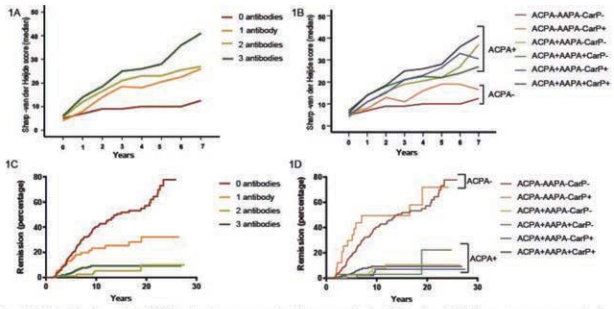

Figure 1. Sustained drug free remission (SDFR) and erosion scores according to the presence of autoantibodies. Figure 1A: Median erosion scores assessed by the Sharp-van der Heijde method (SHS) during the disease course stratified for number of autoantibodies (n=503). All comparisons between groups were statistically significant except between 1 versus 2 and 2 versus 3 antibodies. Figure 1B: Median erosion scores assessed by the SHS during the disease course stratified for anti-acetylated protein antibodies (ACPA), anti-acetylated protein antibodies (AAPA) and anti-carbamylated protein antibodies (anti-CarP) (n=499). SHS did not differ significantly between all ACPA-positive strata, in the ACPA-negative stratum a significant difference was found between 0 antibodies and anti-CarP single-positive patients, (p=0.02). Figure 1C: Kaplan-Meijer curve of the percentage of patients that achieved SDFR stratified for the number of autoantibodies (n=565). All comparisons between groups were statistically significant except between 1 versus 2 antibodies. Figure 1D: Kaplan-Meijer curve of the percentage of patients that achieves SDFR stratified for ACPA, AAPA and anti-CarP (n=561). The percentage of SDFR did not differ between all ACPA-positive strata and did also not differ between the ACPA-negative strata.

Disclosure of Interests: None declared

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POS0104 ACPA-NEGATIVE AND ACPA-POSITIVE RA-PATIENTS ACHIEVING DISEASE RESOLUTION DEMONSTRATE DISTINCT PATTERNS OF MRI-DETECTED JOINT-INFLAMMATION

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Background: Sustained DMARD-free remission (SDFR), the sustained absence of clinical-synovitis after DMARD-discontinuation, is increasingly achievable in RA. However, prevalence differs significantly between ACPA-negative (40%) and ACPA-positive RA (5-10%). In addition, early-DAS-remission ($DAS_{4months}$<1.6) associates with SDFR in ACPA-negative RA but not in ACPA-positive RA.[1] Based on these differences, we hypothesized that longitudinal patterns of local tissue-inflammation (synovitis/tenosynovitis/osteitis) might also differ between ACPA-negative and ACPA-positive RA-patients achieving SDFR.

Objectives: With the ultimate aim to increase understanding of disease-resolution in RA, we studied MRI-detected joint-inflammation over time in relation to SDFR-development in ACPA-negative RA and ACPA-positive RA.

Methods: 198 RA-patients (94 ACPA-negative and 104 ACPA-positive) underwent repeated MRIs (0/4/12/24-months) and were followed on SDFR-development. The course of MRI-detected total-inflammation, and synovitis/tenosynovitis/osteitis individually, were compared between RA-patients who did and did not achieve SDFR, using Poisson-mixed-models. 170 ACPA-positive RA-patients from the AVERT-1 were studied as ACPA-positive validation-population.

Results: In ACPA-negative RA, patients achieving SDFR had similar baseline total inflammation-levels, which declined 2.0-times stronger in the first-year of DMARD-treatment (IRR 0.50, 95%CI;0.32-0.77, p<0.01) compared to patients without SDFR. This stronger decline was seen in tenosynovitis/synovitis/osteitis. In contrast, ACPA-positive RA-patients achieving SDFR, had already lower inflammation-levels (especially synovitis/osteitis) at disease-presentation (IRR 0.45, 95%CI;0.24-0.86, p=0.02) compared to non-SDFR patients, and remained lower during follow-up (p=0.02). Similar results were found in the ACPA-positive validation-population.

Conclusion: Compared to RA-patients without disease-resolution, ACPA-positive RA-patients achieving SDFR have less severe joint-inflammation from diagnosis onwards, whilst ACPA-negative RA-patients present with similar inflammation-levels but demonstrate a stronger decline in the first year of DMARD-therapy. These different trajectories suggest that mechanisms underlying resolution of RA-chronicity in both RA-subsets might be different and indicates the relevance of the total inflammatory-load in ACPA-positive-RA.

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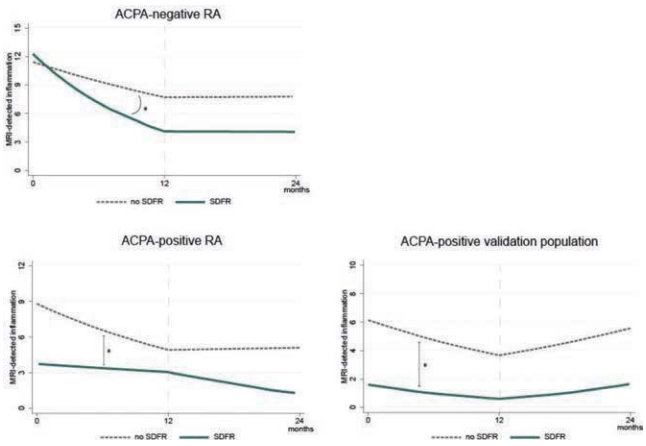

Figure 1. Patterns of MRI-detected joint-inflammation in RA-patients achieving SDFR compared to those who did not, stratified for ACPA-status

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POS0105 IMMUNOLOGICAL AND TISSUE DERIVED BIOMARKERS OF EARLY RESPONSE IN MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS TREATED WITH JAK-INHIBITORS

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Background: Among Janus kinase inhibitors (JAKi) approved for Rheumatoid Arthritis (RA) treatment, tofacitinib and baricitinib are considered as pan-JAKi (pJAKi) while upadacitinib and filgotinib as selective anti-JAK1 (sJAKi) drugs. To date, despite ≈30% of RA patients exposed to JAKi achieve DAS28-CRP remission at 12 weeks, there is still lack of predictive biomarkers of response in RA treated with distinct JAKi.

Objectives: To determine whether pre-treatment immunological and synovial tissue features can predict clinical improvement in moderate-to-severe RA treated with JAKi.

Methods: Among 174 RA patients treated with JAKi, 84 underwent peripheral blood (PB) drawing and US-guided synovial tissue (ST) biopsy. Demographic, clinical and immunological features were collected for each patient at baseline and after 12 weeks. The distribution of PB-derived B lymphocytes subsets was assessed by flow cytometry, using CD27/IgD classification. Synovitis degree assessment was determined using Krenn score (KSS) by trained pathologist, blinded to clinical characteristics.

Results: Among enrolled RA patients, 82.7% was treated with pJAKi and 17.3% with sJAKi. Moreover, 35.6% of RA patients was b/ts-DMARDs naïve, 18.4% b/ts-DMARDs non-responder and 46.0% was difficult-to-treat (D2T) RA. In the whole cohort, 49.2% and 50.8% of RA patients achieved DAS28-CRP and CDAI low disease activity (LDA), respectively, after 12 weeks of JAKi treatment. Moreover, 37.7% and 5.9% of RA patients achieved DAS28-CRP and CDAI remission (REM), respectively, after 12 weeks of JAKi treatment regardless to JAKi category. Considering the immunological profile, RA patients achieving CDAI LDA were more likely rheumatoid factor (60.0%) and ACPA positive (60.5%) compared to RA patients not achieving this outcome (RF: 40.0%, p= 0.03 and ACPA: 39.5%, p= 0.02). Considering PB-derived B cell phenotype, b/ts-DMARDs naïve RA achieving DAS28-CRP LDA at 12 week had pre-treatment lower unswitched memory B ($IgD^{pos}CD27^{pos}$) cell rate (6.91±7.70%) compared to b/ts-DMARDs naïve RA not achieving the same outcome (13.21±5.68%, p= 0.009). ROC analysis identified a cut-off value of 6.89% for $IgD^{pos}CD27^{pos}$ cells discriminating b/ts-DMARDs naïve RA achieving DAS28-CRP LDA at 12 week [AUC: 0.174±0.086; p= 0.008; OR(95%-CIs): 18.20 (1.761-188.069)]. Furthermore, b/ts-DMARDs naïve RA achieving DAS28-CRP REM at 12-week follow up visit, had PB enrichment of naïve B cells ($IgD^{pos}CD27^{neg}$: 68.08±17.38%) and lower percentage of unswitched memory B lymphocytes (5.10±4.29%) compared to RA not achieving the same outcome ($IgD^{pos}CD27^{neg}$: 54.68±16.16%, p= 0.05; $IgD^{pos}CD27^{pos}$: 13.96±8.34%, p= 0.001) [$IgD^{pos}CD27^{neg}$ cut-off: 62.6%, AUC:0.727±0.101, p=0.05; OR(95%CIs): 7.33(1.272-42.294); $IgD^{pos}CD27^{pos}$ cut-off: 6.89%, AUC: 0.139±0.073, p= 0.002; OR(95%CIs): 12.37 (1.828-83.767)]. Interestingly, considering the D2T RA subgroup, patients achieving DAS28-CRP LDA at 12 week follow up had lower rates of PB-derived $IgD^{neg}CD27^{neg}$ B cells (3.83±0.96%) compared to RA not achieving the same outcome (7.25±2.83%, p= 0.04; cut-off: 5.46%, AUC: 0.083±0.095, p=0.041). Considering the pre-treatment synovitis degree, b/ts-DMARDs naïve RA achieving CDAI LDA status had significantly higher KSS at baseline (3.8±2.2) compared to RA not achieving the same outcome [1.7±1.4, p= 0.02; KSS cut-off: 3.00, AUC: 0.795±0.097; p=0.018; OR(95%CIs): 14.0 (1.39-141.49)]. Finally, no significant associations were observed between PB-derived B cell subpopulations rate and synovitis degree both in the whole RA cohort as well as stratifying patients for disease phase.

Conclusion: Pre-treatment immunological profile, peripheral blood-derived B cell phenotype and synovitis degree are associated with the early achievement of at least DAS28-CRP/CDAI LDA in RA patients receiving JAKi despite their selectivity.

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POS0106 THE MCP2 AND WRIST PLUS 2 TENDONS ARE THE MOST AFFECTED AND RESPONSIVE JOINTS/TENDONS OUT OF THE 'US7 SCORE' IN PATIENTS WITH RHEUMATOID ARTHRITIS – AN OBSERVATIONAL STUDY

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Background: There is no international consensus on an optimal ultrasound scoring system in patients with rheumatoid arthritis (RA) yet.

Objectives: To assess the musculoskeletal ultrasound score on seven joints ('US7 score') (1) for the identification of the most frequently pathologic and

responsive joint regions during 3 and 6 months of therapy in order to optimize the score. Furthermore, to evaluate the impact of disease duration on the performance of the score.

Methods: RA patients were recruited from 54 German rheumatology centers when starting or changing DMARD therapy. Patients were assessed by the US7 score in greyscale (GS) and power Doppler (PD) at baseline, after 3 and 6 months. The frequency of pathologic joint/tendon regions and their responsiveness to therapy were assessed including the comparison of palmar vs. dorsal regions.

Differences between the palmar and the dorsal sides were analyzed using Chi-square test, the gradings of the US-joint inflammation were compared between baseline, 3 months, and 6 months by Friedman test with Dunn test as post-hoc test. We used standard response mean to determine the responsiveness of possible reduced scores and linear regression to assess the amount of information retained from the original score. Analyses were also performed separately for early and established RA.

Results: A total of 435 patients (n=138 early RA) were included (56.5 (SD 13.1) years old, 8.2 (9.1) years disease duration, 80% female). The dorsal wrist, palmar MCP2, extensor digitorum communis (EDC) and carpi ulnaris (ECU) tendons out of 7 joints were most frequently affected by GS/PD synovitis/tenosynovitis (wrist: 45%/43%; MCP2: 35%/28%; EDC: 30%/11% and ECU: 25%/11%) and significantly changed within 6 months of therapy (all $p \leq 0.003$ in GS/PD).

The dorsal vs. palmar side of the wrist by GS/PD ($p<0.001$) and the palmar vs. dorsal side of the finger joints by PD ($p<0.001$) were more frequently pathologic. The reduced US7 score (GS and PD: dorsal MCP2, dorsal wrist, EDC and ECU, only GS: palmar MCP2) showed therapy response (SRM 0.433) after 6 months and retained 76% of the information of the full US7 score. No major differences between the groups of early and established RA could be detected.

Conclusion: The wrist, MCP2, EDC and ECU tendons were most frequently pathologic and responsive to therapy, representing an optimized score for monitoring of RA patients for both early and established RA and should therefore be included in comprehensive scores for monitoring RA patients.

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POS0107

ACPA POSITIVITY DETERMINES REMISSION IN PATIENTS WITH RA TREATED WITH IV AND SC ABATACEPT: A POST HOC ANALYSIS OF THE REAL-WORLD OBSERVATIONAL ACTION AND ASCORE STUDIES

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Background: The goal of treatment for RA is achieving low disease activity and/or remission[1,2]; however, disease course and management can be complicated by additional factors that may be influenced by serostatus. Anti-citrullinated protein antibodies (ACPAs) and RF contribute to a more severe RA disease pattern[3] and may be useful in predicting response to treatment.[4] ACTION (AbataCepT In rOutiNe clinical practice; NCT02109666) and ASCORE (Abatacept SubCutaneOus in Routine Clinical PracticE; NCT02090556) were 2-year, international, observational, prospective, multicenter studies of IV and SC abatacept, respectively, for the treatment of RA in routine clinical practice.[4,5] Previous analyses have shown that ACPA/RF double-positive serostatus was associated with better treatment outcomes compared with ACPA/RF double-negative serostatus.[4–6]

Objectives: To assess the independent effect of ACPA or RF single seropositivity among patients with RA on achieving remission after treatment with abatacept for 2 years, and to compare outcomes among patients with single versus double serostatus.

Methods: This post hoc analysis included patients from ACTION and ASCORE who initiated IV (body weight–adjusted dosing) or SC abatacept (125 mg once weekly), respectively. Patients were stratified by baseline ACPA/RF status: ACPA+/RF– (ACPA+ only), ACPA/RF double positive (+/+), ACPA–/RF+ (RF+ only), and ACPA/RF double negative (–/–). DAS28 (CRP) and CDAI remission rates (defined as < 2.6 and 0–2.8, respectively) at 2 years for patients who were ACPA+ or RF+ only at baseline were assessed and compared with those who were +/+ and –/–. Patients with missing baseline ACPA/RF status were excluded. Last observation carried forward efficacy analyses were used to impute missing values.

Results: This analysis included 1679 patients from ACTION (ACPA+ only, n = 98; +/+, n = 1028; RF+ only, n = 161; and –/–, n = 392) and 1748 patients from ASCORE (ACPA+ only, n = 184; +/+, n = 1079; RF+ only, n = 142; and –/–, n = 343). Across studies and serogroups, baseline demographics and disease characteristics were similar (data not shown). In both ACTION and ASCORE, a higher proportion of patients who were only ACPA+ achieved DAS28 (CRP) and CDAI remission at 2 years compared with patients who were only RF+ (Figure 1). Additionally, a similar proportion of patients who were only ACPA+ achieved DAS28 (CRP) and CDAI remission at 2 years compared with patients who were +/+. In contrast, a lower proportion of patients who were only RF+ achieved DAS28 (CRP) and CDAI remission at 2 years compared with patients who were +/+.

Conclusion: In this post hoc analysis of real-world data from ACTION and ASCORE, ACPA positivity was associated with an increased likelihood of achieving DAS28 (CRP) and CDAI remission at 2 years. Patients who were ACPA+ only were as likely to achieve remission as +/+ patients, suggesting that RF serostatus had less influence than ACPA serostatus on remission status at 2 years. In line with this, patients who were RF+ only were less likely to achieve remission at 2 years. This is the first large, real-world study to show that ACPA positivity plays a more important role than RF positivity in achieving remission whilst on abatacept. These results highlight the importance of assessing baseline ACPA status when considering treatment options for patients with RA.

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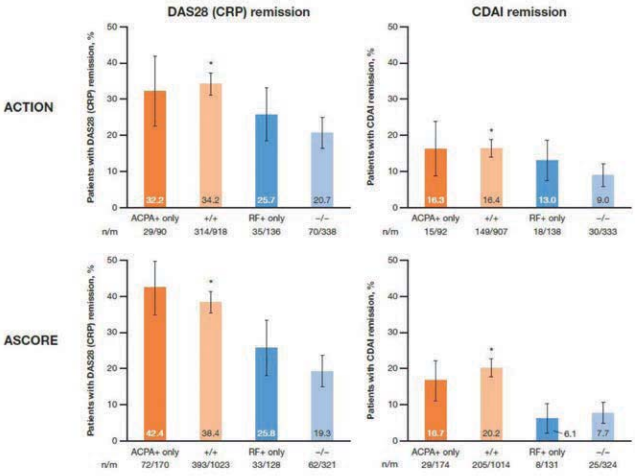
Figure 1. DAS28 (CRP) and CDAI remission at 2 years for patients with ACPA+ only,[a] +/+, RF+ only,[b] and –/– RA treated with abatacept in the ACTION and ASCORE studies



P values represent probability of association between remission and baseline ACPA/RF status.
[a]Patients with ACPA+/RF– RA; [b]Patients with ACPA–/RF+ RA.
*$P < 0.0001$.
n/m, number of patients with remission/number of patients included in the analysis.

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POS0108

REMISSION OR NOT REMISSION? THAT'S THE QUESTION, BUT WHAT'S THE ANSWER? - ILLUMINATING ON REMISSION IN ORDINARY OUTPATIENT CLINICAL RHEUMATOID ARTHRITIS PATIENTS

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Background: A recent meta-analysis by Ferreira et al. (2020) has questioned the validity of using Patient Global Assessment (PGA) to define remission in the Boolean remission criteria (4-variable remission, 4vR) [1]. This is because PGA, which presumptively reflects a patient's perception of disease activity, is influenced by both inflammatory and non-inflammatory mechanisms, thus questioning the validity of PGA-related remission definitions when treating patients to target using anti-inflammatory drugs. Further, the impact of PGA differs in the various definitions and algorithms developed to define remission in rheumatoid arthritis (RA).

Objectives: This study aims to examine remission rates by applying different definitions of remission in an outpatient cohort of RA patients and illuminate the impact of PGA on Boolean remission.

Methods: Data were obtained during 2019 from RA patients followed at an outpatient clinic in Southern Norway. The composite disease activity scores simple disease activity index (SDAI), clinical disease activity index (CDAI), and disease activity score with 28 joint count with C-reactive peptide (DAS28(3) and with PGA DAS28(4)), as well as Boolean 4vR and without PGA the 3-variable remission (3vR) were used to define remission. Cut-off remission values for CDAI, SDAI, and DAS28 are ≤2.8, ≤3.2, and ≤2.6, respectively. 4vR is attained when PGA ≤10, C-reactive peptide (CRP) ≤10 mg/L, SJC28 ≤1, and TJC28 ≤1, while 3vR when CRP ≤10 mg/L, TJC28 and SJC28 ≤1 [2]. Remission rates for 4vR were also calculated with the PGA cut-offs of ≤20, 30, 40, 50, 60, 70, 80, 90.

Results: In Figure 1, proportion rates of remission for DAS28(3), DAS28(4), CDAI, SDAI, 3vR, and 4vR with different PGA cut-offs are presented. The proportion of remission were 73% for DAS28(3), 67% for DAS28(4), 37% for CDAI, 38% for SDAI, 23% for 4vR, 65% for 3vR. When comparing the different remissions proportion rate with various cut-offs of PGA in 4vR, SDAI and CDAI lie between a cut-off of ≤20 and ≤30, while DAS28(3), DAS28(4), and 3vR all lies beyond a cut-off of ≤90.

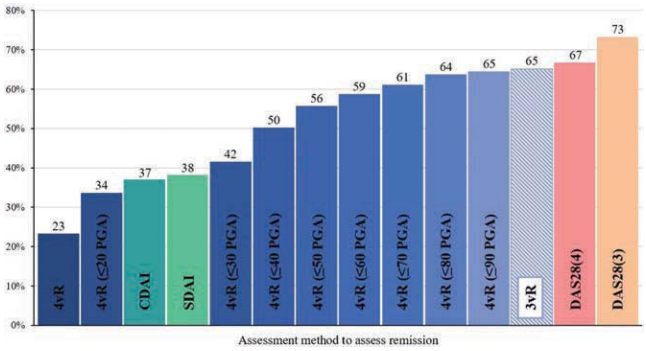

Figure 1. Remission rates using different definitions of remission in an outpatient cohort of 502 rheumatoid arthritis patients

Conclusion: Our data highlights that there is a great variation in remission rates for the different remission definitions, with DAS28(3) having the highest (73%) and the original Boolean remission the lowest (23%) remission rate. While RA patients in DAS28 remission may still have swollen joints, RA patients with no swollen and tender joints and normal CRP may not achieve Boolean remission because of even a minor elevation of PGA above ten, which may not only reflect inflammatory mechanisms. We question the value of using remission definitions where PGA has a large impact when used in ordinary clinical practice to treat patients to remission. Further studies are warranted to illuminate which remission definitions should be used both in studies and in ordinary clinical practice when treating patients with anti-inflammatory drugs.

Is it time for a paradigm shift to focus more on objective than subjective measures reflecting disease status and disease activity when aiming for remission daily clinical practice?

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POS0109 IMPACT OF EARLY AGE AT MENOPAUSE ON DISEASE OUTCOMES IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS: RESULTS FROM A LARGE OBSERVATIONAL COHORT OF KOREAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The increased prevalence of rheumatoid arthritis (RA) in women has led to studies exploring how female reproductive factors affect disease outcomes in women RA. While a few studies have investigated how early menopause (EM) affects RA outcomes, they had relatively small sample size and have shown inconsistent results [1, 2]. Moreover, none has evaluated the association between age at menopause and longitudinal changes in validated disease activity indices or patient-reported outcomes (PROs) of RA.
Objectives: We aimed to assess the differences in clinical outcomes between RA patients with EM (age at menopause <45 years) and usual menopause (UM) (age at menopause ≥45 years), and identify potential impact of EM on longitudinal changes in RA activity and PROs during follow-up period.
Methods: A total of 2,878 postmenopausal women with RA were included from the Korean Observational Study Network for Arthritis, a nationwide prospective RA cohort of Korea. Each patient was examined at baseline and for 5 consecutive years using the simplified disease activity index (SDAI), health assessment questionnaire-disability index (HAQ-DI), and other PROs. Among patients with a baseline SDAI >11, generalized estimating equation (GEE) analyses were performed to evaluate the impact of EM on longitudinal changes in RA activity and PROs during follow-up.
Results: The EM group (N=437) was younger than the UM group (N=2,441) [58.0±9.5 vs. 60.8±8.0 years, p<0.001], but RA duration was similar between the two groups. The EM group had higher education level and was more likely to be seronegative at enrollment. Moreover, the EM group demonstrated higher disease activity [SDAI 15.4±11.7 vs. 13.9±10.0, p=0.011] and patient-reported visual analogue scale (VAS) scores for global assessment, fatigue, and sleep disturbance (all p<0.05), and worse EQ-5D-VAS [59.9 ±22.2 vs. 63.0±19.5, p= 0.006] at baseline. The rate of previous fracture and neoplastic disease, especially uterine/cervical neoplasm, was higher while that of hypertension was lower among the EM group. The GEE model revealed that EM significantly influenced the rate of SDAI change (β=1.265, p=0.004), after adjusting for age, RA duration, biologic use, and SDAI at baseline. The EM group was also significantly associated with increase in HAQ-DI (β=0.088, p=0.003), and decrease in EQ-5D utility value (β=-0.031, p=0.016) during 5-year follow-up period.
Conclusion: RA patients with EM demonstrate higher disease activity and poorer health-related quality of life. EM significantly affects longitudinal changes in disease activity and PROs in RA.

Table 1. Longitudinal analysis of predictors of the SDAI, HAQ-DI, and EQ-5D utility value over time using a GEE model among patients with a baseline SDAI >11

Outcome	Independent variables	Regression coefficient (β) (95% CI)	P
SDAI	Age	0.013 (-0.024-0.049)	0.503
	RA duration	0.084 (0.046-0.122)	<0.001
	Baseline SDAI	0.580 (0.531-0.630)	<0.001
	Biologic use	0.196 (-0.924-1.315)	0.732
	Early menopause	1.265 (0.412-2.117)	0.004
	Follow-up time	-1.806 (-1.964--1.647)	<0.001
HAQ-DI	Age	0.007 (0.004-0.009)	<0.001
	RA duration	0.011 (0.009-0.014)	<0.001
	Baseline HAQ-DI	0.674 (0.638-0.711)	<0.001
	Biologic use	0.044 (-0.033-0.122)	0.264
	Early menopause	0.092 (0.030-0.154)	0.003
	Follow-up time	-0.004 (-0.016-0.007)	0.457
EQ-5D	Age	-0.002 (-0.003--0.000)	0.007
	RA duration	-0.003 (-0.004--0.002)	<0.001
	Baseline EQ-5D utility value	0.532 (0.492-0.572)	<0.001
	Biologic use	-0.012 (-0.045-0.021)	0.489
	Early menopause	-0.033 (-0.059--0.006)	0.016
	Follow-up time	0.010 (0.005-0.015)	<0.001

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POS0110 INCIDENCE OF MAJOR ADVERSE CARDIOVASCULAR EVENTS STRATIFIED BY GEOGRAPHIC REGION AND BASELINE CARDIOVASCULAR RISK: A POST HOC ANALYSIS OF ORAL SURVEILLANCE

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Background: ORAL Surveillance was a post-authorisation safety study of tofacitinib vs tumour necrosis factor inhibitors (TNFi) in patients (pts) with rheumatoid arthritis (RA) aged ≥50 yrs with ≥1 additional cardiovascular (CV) risk factor and an inadequate response to methotrexate (MTX).
Objectives: To examine associations between major adverse CV events (MACE) and the geographic region and baseline (BL) CV risk profile of pts in ORAL Surveillance.
Methods: Pts on stable MTX were randomised 1:1:1 to receive tofacitinib 5 or 10 mg twice daily (BID) or a TNFi (adalimumab 40 mg every 2 weeks in North America [NA] or etanercept 50 mg once weekly in the rest of the world [RoW]). Incidence rates (IRs; pts with first events/100 pt-yrs) were evaluated for adjudicated MACE, as well as myocardial infarction (MI) and stroke. MACE was defined as CV death (excluding CV death due to pulmonary embolism), non-fatal MI and non-fatal stroke. IRs were stratified by geographic region (NA vs RoW) and BL CV risk profile: pts were first categorised by history of coronary artery disease (HxCAD); pts without a HxCAD were then categorised by 10-yr risk of MACE (high [≥20%], intermediate [≥7.5–<20%], borderline [≥5–<7.5%] and low [<5%] risk), per the ASCVD-pooled cohort equations calculator[1] with a 1.5 multiplier applied.[2]
Results: Overall, 4362 pts were included in the study (tofacitinib 5 mg BID, n=1455; tofacitinib 10 mg BID, n=1456; TNFi, n=1451). Across treatments, a higher proportion of pts in NA vs RoW had a HxCAD (Table 1). In pts without a HxCAD, across treatments, higher percentages of pts had a high 10-yr risk of MACE in NA vs RoW (Table 1). Across treatments, overall MACE IRs were higher

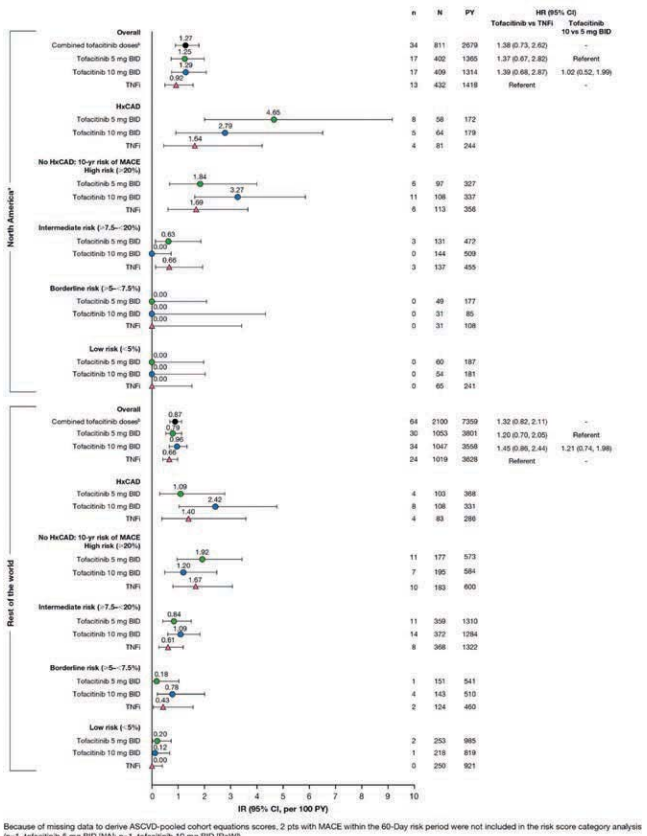
in pts in NA vs RoW (Figure 1). Incidence and risk of MACE were higher with tofacitinib vs TNFi in both NA and RoW (Figure 1). In NA, MACE IRs were higher for tofacitinib 5 mg BID vs TNFi in pts with a HxCAD, and tofacitinib 10 mg BID vs TNFi for pts with a high 10-yr risk of MACE; pts with low or borderline 10-yr MACE risk had no MACE across tofacitinib groups (Figure 1). Compared with NA, similar trends for MACE were generally observed across treatments in RoW, particularly for intermediate, borderline and low CV risk categories (Figure 1).

Table 1. Percentages of pts in NA and RoW with a HxCAD and pts without a HxCAD categorised by 10-yr risk of MACE, per ASCVD-pooled cohorts equation risk calculator[1] with a 1.5 multiplier applied[2]

	NA[a]			RoW		
	Tofacitinib 5 mg BID (N=402)	Tofacitinib 10 mg BID (N=409)	TNFi[b] (N=432)	Tofacitinib 5 mg BID (N=1053)	Tofacitinib 10 mg BID (N=1047)	TNFi[b] (N=1019)
HxCAD, n (%)	58 (14.4)	64 (15.6)	81 (18.8)	103 (9.8)	108 (10.3)	83 (8.1)
No HxCAD: 10-yr risk of MACE, n (%)						
High (≥20%)	97 (24.1)	108 (26.4)	113 (26.2)	177 (16.8)	195 (18.6)	183 (18.0)
Intermediate (≥7.5–<20%)	131 (32.6)	144 (35.2)	137 (31.7)	359 (34.1)	372 (35.5)	368 (36.1)
Borderline (≥5–<7.5%)	49 (12.2)	31 (7.6)	31 (7.2)	151 (14.3)	143 (13.7)	124 (12.2)
Low (<5%)	60 (14.9)	54 (13.2)	65 (15.0)	253 (24.0)	218 (20.8)	250 (24.5)
Missing data	7 (1.7)	8 (2.0)	5 (1.2)	10 (0.9)	11 (1.1)	11 (1.1)

HxCAD was defined as any history of MI, coronary heart disease, stable angina pectoris or coronary artery procedures. [a]United States, Puerto Rico and Canada. [b]For pts randomised to the TNFi group, adalimumab and etanercept were administered in NA and RoW, respectivelyn, number of pts with specified characteristics; N, number of evaluable pts

Fig. IRs (pts with first events/100 pt-yrs; 95% CI) for MACE, stratified by HxCAD, BL CV risk and geographic region in ORAL Surveillance



Because of missing data to derive ASCVD-pooled cohort equations scores, 2 pts with MACE within the 60-Day risk period were not included in the risk score category analysis (n=1, tofacitinib 5 mg BID [NA]; n=1, tofacitinib 10 mg BID [RoW])
Data collected after pts who were randomised to tofacitinib 10 mg BID had their dose reduced to 5 mg BID were included in the tofacitinib 10 mg BID group
Risk period was defined as the time from first study dose to last study dose +60 days, or to the last contact date, whichever was earliest
HxCAD was defined as any history of MI, coronary heart disease, stable angina pectoris or coronary artery procedures
95% CIs for IRs were constructed using Exact Poisson Distribution
ORAL Surveillance (NCT02092467)
[a]United States, Puerto Rico and Canada
[b]Includes pts who received tofacitinib 5 or 10 mg BID in ORAL Surveillance
CI, confidence interval; HR, hazard ratio; PY, pt-yrs

Conclusion: This post hoc analysis of data from ORAL Surveillance suggests that differences in MACE IRs across geographic regions are largely driven by HxCAD and high BL CV risk scores in NA vs RoW. Results should be interpreted with caution due to low pt and event numbers, particularly restricting the evaluation of tofacitinib vs TNFi in NA and RoW. Noting this limitation, these findings emphasise the importance of assessing and addressing BL CV risk when treating pts with RA.

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POS0111

MORE METICULOUSLY FOLLOWING TREAT-TO-TARGET IN RA DOES NOT LEAD TO LESS RADIOGRAPHIC PROGRESSION: A LONGITUDINAL ANALYSIS IN BIODAM

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Background: A Treat-to-Target approach (T2T) is broadly considered to lead to better clinical outcomes and recommended in patients with RA. However, very few studies have analyzed the effect of T2T on radiographic progression, and any such studies have provided inconsistent results.

Objectives: To investigate whether meticulously following a treat-to-target (T2T)-strategy in daily clinical practice leads to lower radiographic progression in RA.

Methods: Patients from the multicenter RA-BIODAM cohort with ≥2 consecutive visits with radiographs available were included. In RA-BIODAM patients were enrolled as they were initiating a new csDMARD/bDMARD treatment were followed-up with the intention to benchmark and intensify treatment. The primary outcome of this analysis was the change in Sharp-van der Heijde score (SvdH, 0-448), assessed every 6 months, using average scores from 2 readers (scores with known chronological order). Following a DAS44-T2T remission strategy, which was defined at each 3-month visit, was the main variable of interest. Patients were categorized based on the proportion of visits in which T2T was followed according to our definition: very low (≤40% of the visits, low (>40%, <62.5%), high (≥62.5%, ≤75%) and very high (>75%). Radiographic progression at 2 years was visualized across groups by cumulative probability plots. Per 3-month interval T2T could be followed zero, one or two times (in a total of 2 visits). Associations between the number of visits with T2T in an interval and radiographic progression, both in the same and in the subsequent 6-month interval, were analysed by generalised estimating equations, adjusted for age, gender, disease duration and country.

Results: In total, 511 patients were included (mean (SD) age: 56 (13) years; 76% female). After 2 years, patients showed on average 2.2 (4.1) units progression (median:1 unit). Mean (SD) 2-year progression was not significantly different across categories of T2T: very low: 2.1 (2.7)-units; low: 2.8 (6.0); high: 2.4 (4.5), very high: 1.6 (2.2) (Figure 1). Meticulously following-up T2T in a 3-month interval neither reduced progression in the same 6-month interval (parameter estimates (for yes vs no): +0.15 units (95%CI: -0.04 to 0.33) for 2 vs 0 visits; and +0.08 units (-0.06;0.22) for 1 vs 0 visits) nor did it reduce progression in the subsequent 6-month interval (Table 1).

Table 1. Effect of following DAS44-remission-T2T strategy on 6-month radiographic progression over 2 years

	Change in radiographic damage (regression coefficient (95% CI)) N=506
T2T during 3 months on radiographic progression in the same 6-month period	
2 visits vs 0 followed	0.15 (-0.04; 0.33)
1 visit vs 0 followed	0.08 (-0.06; 0.22)
T2T during 3 months on radiographic progression in the subsequent 6-month period	
2 visits vs 0 followed	-0.09 (-0.28; 0.10)
1 visit vs 0 followed	-0.10 (-0.24; 0.05)

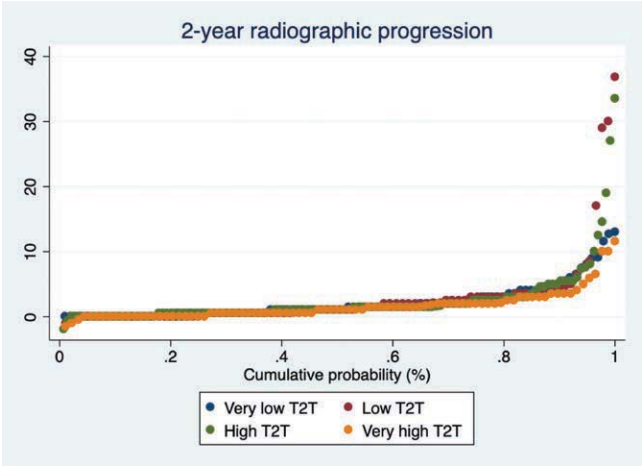

Figure 1. Cumulative probability plot with 2-year radiographic progression according to the proportion of 3-monthly visits with T2T followed

Conclusion: In this daily practice cohort, more meticulously following T2T principles did not result in more reduction of radiographic progression than a somewhat more liberal attitude toward T2T. One possible interpretation of these results is that the *intention* to apply T2T already suffices and that a more stringent approach does not further improve outcome.

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POS0112 CLASSIFYING SELF-REPORTED RHEUMATOID ARTHRITIS FLARES USING DAILY PATIENT-GENERATED DATA

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Background: Flares are an inherent part of the rheumatoid arthritis (RA) disease course and may impact clinical and patient outcomes. The ability to predict flares between clinic visits based on real-time longitudinal patient-generated data could potentially allow for timely interventions to avoid disease worsening. For intensively-collected patient-generated data, machine learning methods offer benefits over traditional statistical tools for accurate prediction, but examples in rheumatology are sparse.

Objectives: Investigate the feasibility of using machine learning methods to classify self-reported RA flares based on a small dataset of daily symptom data collected on a smartphone app.

Methods: We used data from the Remote Monitoring of Rheumatoid Arthritis (REMORA) study, which aimed to improve monitoring of disease severity in RA. Patients tracked daily symptoms (pain, fatigue, function, sleep, coping, physical and emotional wellbeing) on a 0-10 numerical rating scale, duration of morning stiffness, and weekly flares on the REMORA smartphone app for three months. The outcome was the binary yes/no answer to the weekly flare question "*Have you experienced a flare in the last week?*". Several summaries of the eight daily symptom scores collected in the week leading up to the flare question (the exposure period) were used as predictors. These included the mean, min, max, standard deviation and slope. Where exposure periods overlapped, the intersecting symptom reports were allowed to correspond to multiple outcomes.

We fitted three binary classifiers: logistic regression +/- elastic net regularization, a random forest and naïve Bayes. The models were benchmarked using the R package mlr3 and 10-fold cross-validation, with two participants comprising the test set and the remaining 18 the training set.

Finally, the performance of the classifiers was evaluated according to the area under the curve (AUC) of the receiver operating characteristic curve. The model with the highest AUC in the test dataset was considered as the best final model.

Results: Twenty patients tracked daily symptoms over three months. 60% were female, all but one were white British, and mean age was 56.9±11.1 years. The median number of days in the study was 81 (interquartile range (IQR) 80, 82). The collected data comprised an average of 60.6 daily reports and 10.5 weekly reports per participant over the study period. Participants reported a median of 2 flares (IQR 0.75-4.25) resulting in 57 flares in total.

Classifier performances are visualized in Figure 1. The best performing model was logistic regression with elastic net with an AUC of 0.82. At a cut-off point requiring specificity to be 0.80, the corresponding sensitivity to detect flares was 0.60 for this model, meaning that the prediction model correctly identified three in every five self-reported flares, and four in every five non-flares. At this cut-off, the positive predictive value, i.e. the probability that those with a predicted flare indeed go on to have a flare was 53%. The negative predictive value, i.e. the probability that those with a predicted non-flare indeed do not experience a flare, was 85%.

Conclusion: Predicting self-reported flares based on daily symptom scorings in the preceding week using machine learning methods was feasible, although regularized logistic regression outperformed the other machine learning methods in this small dataset. The perceived advantage of machine learning may therefore be attributed to overfitting. It is possible that the observed predictive accuracy will improve as we obtain more data.

Our results point to a future where regular analysis of frequently collected patient-generated data may allow us to predict imminent flares before they unfold with decent accuracy, opening up opportunities for just-in-time adaptive interventions (JITAIs). Depending on the nature and implications of a JITAI, different cut-off values should be explored: different interventions will require different levels of predictive certainty before an action is triggered (eg self-management advice vs. a patient contact).

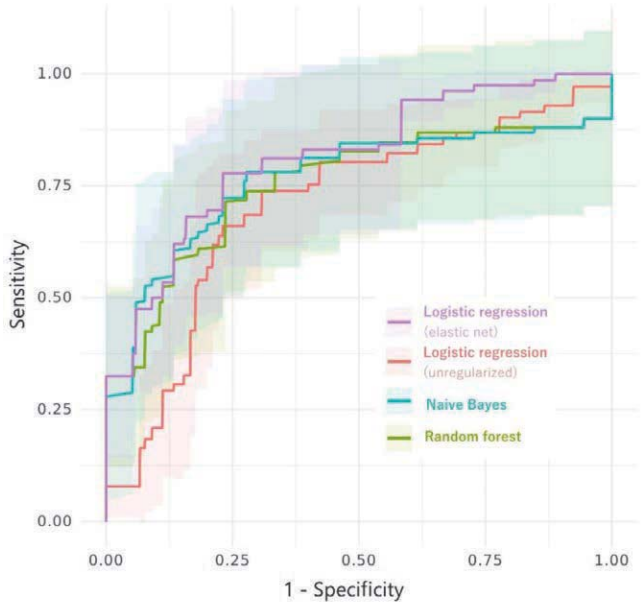

Figure 1. Performance of binary flare classifiers fitted to data from the REMORA study: Logistic regression with and without regularization, naïve Bayes and random forest.

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POS0113 THE PREDICTIVE VALUE OF HEALTH LITERACY ON DISEASE ACTIVITY AND MEDICATION USE OVER TIME IN RHEUMATOID ARTHRITIS PATIENTS.

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Background: Health literacy is a multidimensional concept comprising various individual skills and situational resources and is increasingly recognized as a critical determinant of health. Limited health literacy has been demonstrated to associate negatively with health outcomes in multiple chronic diseases, but data on the relevance of health literacy for treatment and outcomes in rheumatoid arthritis (RA) is still limited.

Objectives: The aim of this study was to explore the longitudinal association between health literacy profiles, disease activity and medication prescription in patients with RA.

Methods: We conducted a single center, retrospective, cohort study including patients from the Medisch Spectrum Twente hospital (Enschede, the Netherlands) who completed the Health Literacy Questionnaire (HLQ) and were previously clustered into 10 "health literacy profiles".[1] The 10 profiles were further aggregated, based on similarities in profile characteristics, into three groups: "several health literacy limitations", "some health literacy limitations" and "good health literacy". Up to 1 year of follow-up data on disease activity (DAS28-ESR) and medication use were obtained from patients' electronic health records. Linear mixed modelling (LMM) was used to analyze DAS28-ESR scores over time using health literacy group, time and their interaction term as fixed effects and gender and age as random effects. Drug prescriptions were constant over time, therefore chi-square tests were used to compare prescribed medication between the health literacy groups.

Results: 108 patients with RA were included and assigned to "several health literacy limitations" (n=21), "some health literacy limitations" (n=33) or "good health literacy" (n=54). LMM showed a significant main effect of health literacy group on DAS28-ESR scores over time (F (2,105) = 4.941, p=0.009). Post hoc contrast analysis showed that patients with "good health literacy" had significantly lower disease activity scores than patients with "several health literacy limitations". In addition, there was a significant effect of time on DAS28-ESR scores (F (2,141) = 4.601, p=0.012) in the total sample, indicating significantly lower scores at the 6-month follow-up. There was no significant interaction between group and

time (F (4,141) = 0.712, p=0.585). Figure 1 shows the estimated trajectories of DAS28-ESR scores over 12 months time for the three health literacy groups. Patients with "several health literacy limitations" were prescribed prednisolone significantly more often (52.4%) than patients with "some health literacy limitations" (21.2%) or "good health literacy" (22.2%) over time (p=0.019). Patients with "some health literacy limitations" were prescribed conventional DMARDs more often (72.7%) than patients with "good health literacy" (38.9%; p=0.008). There was no difference in biological DMARDs use between the health literacy groups.

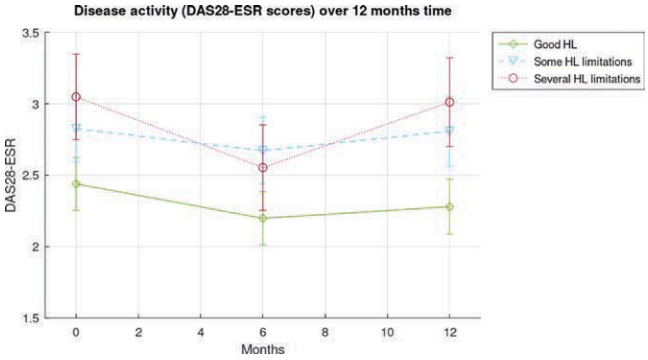

Figure 1. Mean (standard error) DAS28-ESR scores of health literacy (HL) groups over a 12-month time period.

Conclusion: We found that among patients with RA, those with several health literacy limitations have higher disease activity scores over time and use prednisolone significantly more often than patients with higher health literacy levels. No difference was observed in biological DMARD use. These results grant more insight into the role of health literacy for treatment and outcomes in patients with RA and supports existing research in other chronic diseases.

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Disclosure of Interests: None declared

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Systemic lupus erythematosus, Sjogren's syndrome and anti-phospholipid syndrome

POS0114

COMPUTATIONAL IDENTIFICATION OF SLE PATIENT RECORDS USING DATA-DRIVEN CLINICAL FINGERPRINTS

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Background: Systemic lupus erythematosus (SLE) is a chronic relapsing autoimmune disorder that is challenging to diagnose due to its heterogeneous presentation of a combination of non-specific clinical manifestations and laboratory findings. This heterogeneity and lack of granularity is a major cause of treatment failure. With the advent of precision medicine, there is a need for accurate methods to identify cases of SLE in large clinical databases, and to recognize constellations of pathological characteristics (or *fingerprints*) that allow a better understanding of the disease. Computational phenotype discovery aims to solve this problem by using unbiased, data-driven machine learning methods to disentangle the fingerprints of disease that hide within the noisy, sparse and incomplete electronic health record data.

Objectives: To generate data-driven phenotypic fingerprints of SLE and validate them by assessing their ability to distinguish records of patients with SLE vs. 'near miss' patients without the disease.

Methods: Records of 716 patients that published, expert-curated algorithms [1] indicated as likely SLE patients were reviewed by 3 clinicians and labeled as positive (490 records), negative (261), or indeterminate (55). Those labeled positive by an algorithm but negative by clinician chart review were considered 'near misses' and should be among the more difficult cases to classify. We trained an ElasticNet (regularized logistic regression) model to distinguish the true positive records from the near misses and evaluated it under 10x cross validation.

Inputs to the predictive model were the projections of each patient record into the space of 2000 latent variables. These features had been inferred separately by an unsupervised machine-learning algorithm from a much larger dataset of 646,716 randomly sampled temporal cross sections of 63,775 longitudinal records of patients with an antinuclear antibody test. Each of the 2000 variables constitutes the phenotypic fingerprint of an unobserved, independent potential disease mechanism. Formally, they represent linear combinations of demographic data, laboratory test results, billing code intensities, and medication exposures [2].

Results: Our predictive model achieved an area under the Receiver Operating Characteristic Curve of 0.90, 95% CI: [0.879, 0.922], an area under the Precision-Recall Curve of 0.94, 95% CI: [0.926, 0.954], and an Integrated Calibration Index of 0.074, 95% CI: [0.067, 0.080].

The model selected 61 of the 2000 potential latent mechanisms to distinguish positive SLE records from near-misses. All of the phenotypes selected to be predictive exhibit high face-validity from a clinical interpretation perspective. They include recognizable patterns of variables representing different clinical features of SLE (Figure 1).

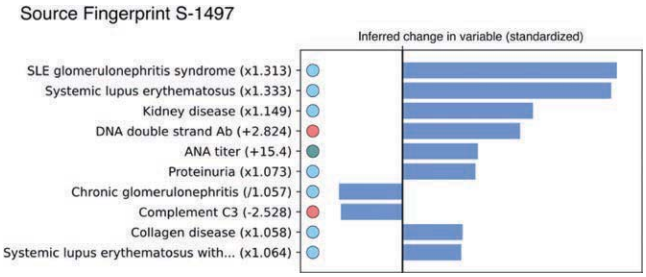

Figure 1. Detail of the estimated changes in the clinical features representing one of the 61 potential fingerprints found to distinguish records of patients with SLE vs. near misses.

Conclusion: We found unbiased, data-driven fingerprints of potential latent disease mechanisms that were highly informative in differentiating records of patients with SLE from near-miss presentations, with performance surpassing existing expert-curated algorithms. Our methods found dozens of variable constellations that may lead to a more precise understanding of this complex and heterogeneous disease. That these results were obtained from cases that should be the most difficult for an algorithm to distinguish (positive vs. near-miss) suggests that our model's accuracy is a lower bound on what would be expected from a more balanced cohort.

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POS0115

SERUM PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) AND CARDIOVASCULAR RISK IN SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL COHORT STUDY

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Objectives: To study the effect of serum PCSK9 on major cardiovascular adverse events (MACEs) in Chinese patients with systemic lupus erythematosus (SLE).

Methods: Consecutive patients who fulfilled ≥4 1997 ACR criteria for SLE and consented for a biomarker study between 2009 and 2012 were included. Stored serum samples from these patients were assayed for the levels of PCSK9 using a commercial ELISA kit (OKBB00903, Lot# 1344, Aviva Systems Biology, San Diego, US). New MACEs (acute coronary syndrome, ischemic stroke, peripheral vascular disease) documented by imaging and angiographic studies over time was evaluated. Patients were stratified into high/low PCSK9 groups according to the best cut-off level by ROC analysis for the prediction of these events. The cumulative incidence of new MACEs and mortality over time was studied by Kaplan-Meier's analysis and compared between the high and low PCSK9 subgroups. Cox regression was performed to study the effect of the PCSK9 subgroups on new MACEs and mortality, adjusted for other confounding factors.

Results: 539 SLE patients were studied (93% women, age 41.9±14.0 years; disease duration 106±90.4 months at entry). The mean PCSK level at baseline was

265±158ng/ml and a cut-off of 243.25ng/ml best predicted a new vascular event by the maximum Youden's index (ROC analysis: AUC 0.63[0.51-0.74]; sensitivity 69%; specificity 61%). 220 SLE patients had baseline PCSK9 level of ≥243.25ng/ml (high PCSK9) and 319 patients had level below 243.25ng/ml (low PCSK9). Patients with high PCSK9 (n=220) had more active SLE than those with low PCSK9 (n=319) (p<0.001). PCSK9 level was highest in active renal SLE patients and correlated with SLE disease activity index (r=0.55; p<0.001). No significant difference in SLE manifestations and autoantibody profile was observed between the high and low PCSK9 groups except the former had a significantly higher prevalence of lupus nephritis. Over 91.3±18.6 months, 31 new MACEs (13 ischemic stroke, 13 acute coronary syndrome and 5 peripheral vascular disease) developed in 29 patients. Patients with a new MACE had a significantly higher baseline PCSK9 level than those without (350±225 vs 260±153ng.ml; p=0.02). The cumulative incidence of a first MACE at 5 years from study entry was 7.8% in the high PCSK9 group and 1.9% in the low PCSK9 group (log rank test; p=0.003, univariate hazard ratio [HR] 3.08[1.39-6.80]). At last follow-up, 40 patients succumbed (10 due to vascular event [vascular death]). Kaplan-Meier's analysis showed that the high PCSK9 group had a significant higher cumulative risk of all-cause mortality (log rank test p=0.003; HR2.68[1.39-5.14]) and vascular mortality (log rank test p=0.002; HR12.4[1.56-98.4]) over time than the low PCSK9 group. Cox regression analyses showed that high PCSK9 was significantly associated with new MACEs (HR2.74[1.16-6.52]; p=0.02) independent of age, sex, SLE duration, history of nephritis, traditional atherosclerotic risk factors, antiphospholipid antibody, past history of vascular events, and the use of statins, aspirin/warfarin and immunosuppressive drugs (hydroxychloroquine, prednisolone, mycophenolate mofetil, azathioprine and the calcineurin inhibitors) at baseline. High PCSK9 was also independently associated with all-cause (HR2.55[1.27-5.12]; p=0.008) and vascular mortality (HR13.0[1.49-114]; p=0.02).

Conclusion: High circulating levels of PCSK9 increase the risk of MACEs and vascular mortality in patients with SLE.

Disclosure of Interests: None declared

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POS0116 PLASMA AND CEREBROSPINAL FLUID NEUROFILAMENT LIGHT CONCENTRATIONS REFLECT NEURONAL DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neuronal damage in systemic lupus erythematosus (SLE) is common, but the extent and mechanisms are unclear [1-2]. Neurofilament light (NfL) concentrations rise in plasma and cerebrospinal fluid (CSF) during neuronal damage and reach abnormal levels in various neurological disorders [3]. NfL is sparsely studied in SLE [4-7].

Objectives: To explore plasma and CSF concentrations of NfL in SLE patients and investigate the associations between NfL and nervous system involvement, including cognitive dysfunction, imaging findings on magnetic resonance imaging (MRI), laboratory and clinical abnormalities, and to compare the NfL levels of SLE patients with those present in healthy controls.

Methods: In this cross-sectional study, 72 consecutive SLE out-patients and 26 healthy controls, all female, aged <55 years, underwent MRI and neurocognitive testing. NfL concentrations in plasma from all individuals and in CSF from 32 patients were measured with single-molecule array technology. Patients were assessed by a rheumatologist and neurologist to define neuropsychiatric involvement (NPSLE) according to three attribution models.

Results: Plasma and CSF NfL concentrations correlated strongly (r=0.72, p<0.001). Plasma NfL concentrations were higher in SLE patients, both with and without neuropsychiatric involvement, compared with healthy controls (Figure 1A-D). Plasma and CSF NfL concentrations did not differ between NPSLE and non-NPSLE patients (Figure 1B-D). Larger white matter lesion volumes correlated with higher CSF NfL concentrations in patients aged 18-30 (r_s=0.80, p=0.005). Higher plasma NfL concentrations correlated with lower simple attention scores (r_s=-0.42, p=0.007), and were associated with dysfunction of psychomotor speed (p=0.012) and verbal memory (p=0.024). SLICC/ACR-Damage Index ≥1 was independently associated with higher plasma log-NfL concentrations when adjusting for age, SLE Disease Activity Index-2000 ≥1, low complement C3 levels, a history of renal involvement or anti-dsDNA, and ongoing treatment (β=0.080, 95% CI 0.009-0.15, p=0.028).

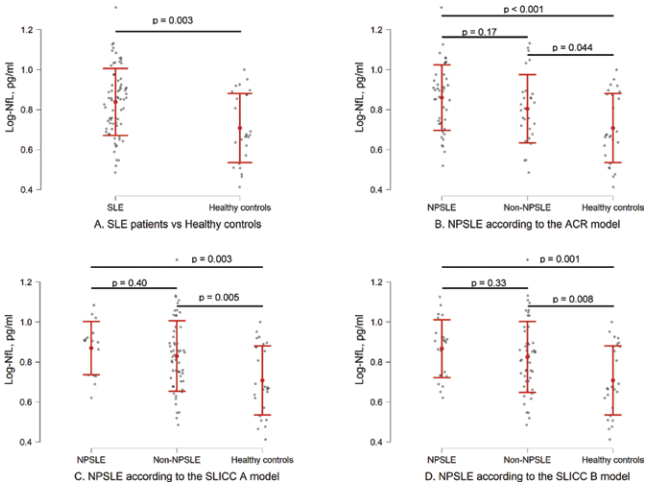

Figure 1. Plasma log-NfL concentrations between groups. The intervals illustrate means and standard deviations.

Conclusion: Higher plasma NfL concentrations in NPSLE and non-NPSLE patients may indicate a higher degree of neuronal damage in SLE in general, particularly in the lower age group, corresponding with cognitive impairment and organ damage development. NfL may serve as an indicator of neuronal damage in SLE in further studies.

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POS0117 DISEASE ACTIVITY AND CLINICAL REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARISON BETWEEN PATIENT AND PHYSICIAN PERSPECTIVES BY MEANS OF PATIENT REPORTED OUTCOMES (PROS)

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Background: In daily clinical practice, it is not rare to observe a relevant discordance between patient's global assessment (PGA) and physician's global assessment (PhGA), because of different illness perceptions.

Objectives: To evaluate the presence of PGA/PhGA discrepancy in patients with Systemic Lupus Erythematosus (SLE) who achieved clinical remission and to evaluate how this discrepancy affects PROs. In addition, to explore whether this discordance could be influenced by the presence of additional elements affecting patients' quality of life, such as comorbidities, sleep disturbances and psycho-emotional factors.

Methods: Our study included adult SLE patients consecutively followed in a single Lupus Clinic from March to July 2021 fulfilling at minimum the definition of clinical remission of treatment according to Zen et al. (1) (cSLEDAI=0, corticosteroids ≤5mg/die, stable dosage of DMARD). Medical records including demographic data, clinical characteristics and outcomes measures were collected. Pain assessment, PGA and PhGA were rated on a visual analogue scale

(0-100 mm) on the same day of the clinical evaluation. To analyse the discrepancy between PGA and PhGA, the [PGA-PhGA] variable was calculated, considering as discordant a difference ≥ 25 mm as previously proposed (2) All the subjects completed the following questionnaires: Health Assessment Questionnaire (HAQ), SF36 Health Survey, State-Trait Anxiety Inventory (STAI-Y1/Y2), Self-rating Depression Scale (SDS Zung) and Insomnia Severity Index. Statistical analysis was performed to compare concordant and discordant groups.

Results: The study included 106 patients, (93 women, 13 men) with a median age of 48 (41-58) and a median SLE duration 227 months (124-330). At the last evaluation median SLEDAI was 0 (0-2) and median SLICC was 1 (0-1). According to Zen definitions of remission, 51 patients (48%) and 20 (19%) also fulfilled the criteria of clinical remission off corticosteroids and complete remission respectively. Nevertheless, in 24 patients (22,7%) [PGA-PhGA]≥25. Patients in the discordant group were older (median 58 years, IQR 49-62 vs 46, IQR 39-57; p=0,0043) and less frequently achieved the definition of clinical remission off corticosteroids (n=4, 16,7% vs n=47, 57,3%,p<0.001;OR6,7; CI95%2.1-21) than concordant. No differences were found in gender, SLE duration, serology, disease activity or damage and other treatment. Data about differences in PROs between two groups are reported in Table 1: discordant patients had a worse performance in all the PROs included. At multivariate analysis SF-36 Physical Component Summary (PCS) resulted associated with [PGA-PhGA] ≥25 (p=<0,0001).

Table 1. Data are expressed as median and interquartile range (IQR) and compared using Mann-Whitney test.

	TOTAL N=106 (%)	CONCORDANT GROUP (PGA-PhGA) <25 N=82 (%)	DISCORDANT GROUP (PGA-PhGA) ≥25 N=24 (%)	P value
VAS-pain [0-100],	10 (0-30)	10 (0-20)	50 (40-60)	< 0.001
SF-36 Physical Component Summary (PCS)	50 (37,5-53)	51 (44-54)	30 (27,5-39)	< 0.001
SF-36 Mental Component Summary (PCS)	48 (38-55)	51 (40-55)	40 (36-48,5)	0,015
STAI-Y1 [20-80]	35 (30-47)	33 (28,3-45,5)	42 (36,5-49,5)	0,013
STAI-Y2 [20-80]	37 (30-46)	35 (29-43,3)	42 (36-46)	0,021
Test di Zung [20-80]	34,5 (29-43)	33 (27-43)	39 (35,5-44,5)	0,008
Insomnia severity index [0-28]	6 (2-12)	4 (1-9)	9 (6,8-14,3)	<0,0001
HAQ	0 (0-0,1)	0 (0-0)	0,38 (0-0,6)	< 0.001

Conclusion: In our study we found that, even in patients considered in remission, in more than 20% of patients there is a considerable discordance between the global disease assessment reported by patients and their physicians. Patients that had a higher PGA also presented worse score at PROs. Our data seems to confirm that potential causes for discordance could be more related to the presence of non-inflammatory processes, depression, or anxiety than clinical manifestations or damage related to SLE.

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Disclosure of Interests: None declared

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POS0118

SMALL FIBER NEUROPATHY EVALUATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A SINGLE CENTER STUDY.

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Background: Neuropsychiatric involvement represents one of the most relevant Systemic Lupus Erythematosus (SLE) manifestations and it is characterized by a protean spectrum of clinical disorders. Among them, small fiber neuropathy (SFN) could represent a relevant reason for chronic pain and somatosensorial dysfunctions, even if not included in ACR 1999 nomenclature yet.

Objectives: In the present study we aimed at evaluating the prevalence of SFN among SLE patients with neuropathic pain and identifying significant associations with clinical and laboratory disease features.

Methods: Consecutive SLE patients (according to ACR 1987 criteria), were screened for neuropathic pain through a specific questionnaire (DN4). Subjects were enrolled to the full protocol in the presence of bilateral limb pain and one of the following: hypoesthesia to touch or prick; pain caused or increased by brushing; tingling, numbness and itching; electric shocks, painful cold or burning pain. We excluded SLE patients with other possible explanation for SFN including diabetes, Sjogren's syndrome and kidney impairment (eGFR <30 ml/m). For each patient the following data were collected: demographics, medical history, treatments, disease activity (SLEDAI-2K) chronic damage (SLICC *damage index)*, clinical and laboratory data, including complement level and the main autoantibodies. Each patient enrolled underwent different tools specific for neuropathic pain (such as SFN-SIQ and NPSI), nerve conduction study, quantitative sensory testing (QST) and skin biopsy performed at proximal thigh and distal leg. SFN was diagnosed when intraepidermal nerve fiber density (IENFD) reduction was associated with at least one thermal detection threshold abnormality at QST. A concomitant fibromyalgia (FM) was evaluated by different tools including FIRST, FibroDetect and ACR 2016 criteria.

Results: Among the 114 recruitable subjects, 58 were excluded because of confounding factors and 25 declined the study. Therefore we enrolled 31 patients (M/F 3/28, median age 50.0 years, IQR 21.0; median disease duration 132.0 months, IQR 197.0; median SLEDAI-2k 0, IQR 4 and median SDI 1, IQR 1.2). FM was identified in 81.8% of subjects according to ACR criteria. SFN was diagnosed in 35.5% of patients; among them, in 81.8% a non-length dependent distribution was recognized while in 18.2% a length-dependent pattern and the large fiber dysfunction were found. SFN was associated with anti-Sm (p=0.03), Raynaud's phenomenon (p<0.01), low complement levels (p=0.04) and SLEDAI-2k≥4 (p=0.04). Neurovegetative symptoms and pain intensity correlated with distal (p<0.001) and slightly with proximal IENFD reduction (p=0.02 and p=0.04). No significant association was found between FM and SFN or IENFD.

Conclusion: The present study suggests that SFN is a common finding in SLE and it should be considered in patient with neuropathic pain, somatosensorial and neurovegetative dysfunctions, especially in subjects with low complement levels, high disease activity and Raynaud's phenomenon.

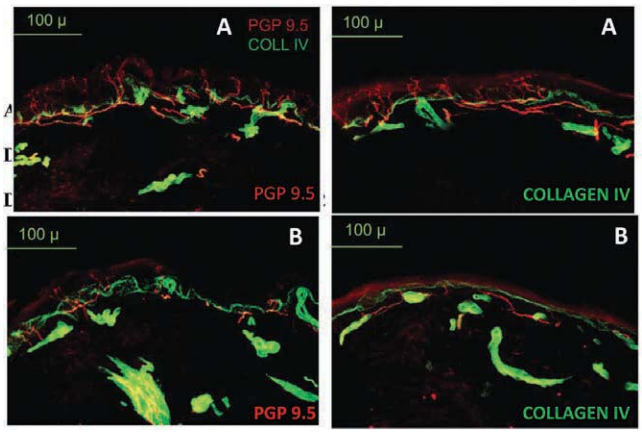

Figure 1. A: SLE patient with normal IENFD. B: SLE patient with low IENFD, consistent with SFN.

Disclosure of Interests: None declared

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POS0119

SLE-DAS REMISSION AND LOW DISEASE ACTIVITY STATES ARE ASSOCIATED WITH IMPROVED HEALTH-RELATED QUALITY OF LIFE AND FATIGUE: POST-HOC ANALYSIS OF THE BLISS-52 AND BLISS-76 PHASE III TRIALS.

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Background: Accurate and practical outcome measures for clinical trials in systemic lupus erythematosus (SLE) are lacking. The SLE Disease Activity Score (SLE-DAS) is a recently validated 17-item instrument, with high accuracy and sensitivity to changes in SLE disease activity. The SLE-DAS definitions of remission and low disease activity (LDA) were newly validated against disease activity physician-applied measures in the clinical setting [1, 2]. Criterion validity of

SLE-DAS for Patient Reported Outcomes, namely health-related quality of life (HR-QoL) and fatigue needs to be assessed.

Objectives: To evaluate if the attainment of SLE-DAS remission and LDA states is associated with improvements in HR-QoL and fatigue.

Methods: Post-hoc analysis of the merged study population in the BLISS-52 and -76 trials (NCT00424476; NCT00410384) of intravenous belimumab versus placebo for moderate to severe SLE disease activity. We analysed the Functional Assessment of Chronic Illness Therapy (FACIT) and 36-Item Short Form Survey (SF-36) trial data. Fulfillment of SLE-DAS remission (defined as absence of all SLE-DAS clinical items and prednisone ≤5mg/day) and LDA (defined as SLE-DAS≤2.48 and prednisone ≤7.5mg/day) definitions were retrospectively assessed from the individual participants' data. Mean changes from study baseline to week 52 in FACIT and SF-36 physical component summary (PCS) and mental component summary (MCS) and domain scores were compared between patients attaining at week 52 the SLE-DAS remission *vs* non-remission and the SLE-DAS LDA *vs* non-LDA using multivariate regression analysis adjusted for baseline scores.

Results: A total of 1684 SLE patients were included. Few patients were in SLE-DAS remission (0.5%) and LDA (0.8%) at study entry. At week 52, 12.5% patients attained SLE-DAS remission and 17.5% attained SLE-DAS LDA. Mean improvements in SF-36 PCS and MCS scores were greater in patients that attained SLE-DAS remission *vs* non-remission (5.4 *vs* 3.4, and 4.6 *vs* 2.7, respectively; multivariate p<0.005 for both) and SLE-DAS LDA *vs* non-LDA (5.0 *vs* 3.4 and 4.6 *vs* 2.6, respectively; multivariate p<0.005 for both), at week 52 (Figure 1). Similarly, improvements in all individual domain scores were greater in SLE-DAS remission *vs* non-remission patients (all multivariate p<0.005) and SLE-DAS LDA *vs* non-LDA patients (all multivariate p<0.005) (Figure 1). Importantly, improvements in the summary scores and in all the individual domain scores largely exceeded the minimum clinically important differences (MCIDs) of 2.5 and 5 points, respectively, in those patients attaining SLE-DAS remission or LDA.

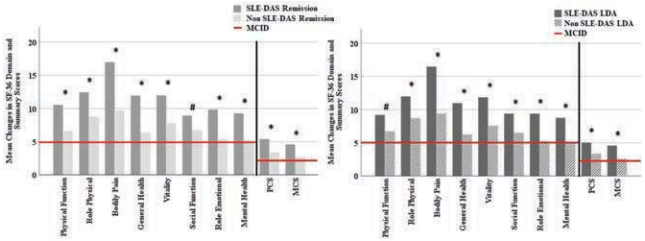

Figure 1. Mean changes in SF-36 domains and summary scores from baseline to week 52. #p<0.005; *p<0.001; MICD, Minimum Clinically Important Difference; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Medical Outcomes Survey Short Form; SLE-DAS, Systemic Lupus Erythematosus Disease Activity Score.

Additionally, mean improvements in FACIT scores were higher in SLE-DAS remission than non-remission (6.3 *vs* 3.6, multivariate p<0.001) and in SLE-DAS LDA than non-LDA (5.9 *vs* 3.6, multivariate p<0.001), and exceeded the MCID of 4 points.

Conclusion: Attainment of SLE-DAS remission and LDA is associated with meaningful improvement in HR-QoL and fatigue.

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POS0120 NEUROLOGICAL INVOLVEMENT IN A MONOCENTRIC COHORT OF PATIENTS WITH SERONEGATIVE ANTIPHOSPHOLIPID SYNDROME

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Background: The nervous system is affected in a relevant number of patients with antiphospholipid syndrome (APS), being responsible for high morbidity and mortality rates. The identification of neurological manifestations is crucial since those symptoms may benefit from anticoagulation treatment. Noteworthy, the prevalence and the characteristics of neurological manifestations in the subset of patients with "seronegative APS" (SN-APS) still need to be investigated.

Objectives: The aim of this study was to assess the neurological involvement in patients with SN-APS. Secondly, association between non-conventional antiphospholipid antibodies (aPL) and clinical characteristics were investigated.

Methods: We included all consecutive patients referred to the Lupus Clinic and to the Stroke Unit of our Hospital, presenting clinical features consistent with a diagnosis of APS despite the evidence of persistently negative tests for anti-cardiolipin antibodies (aCL), anti-β2 glycoprotein I, and lupus anticoagulant. Patients with an identified cause of thrombosis and/or pregnancy morbidity were excluded. Patients' sera were analyzed for the detection of aCL using thin layer chromatography (TLC), while ELISA test was used to detect antibodies directed against the anti-vimentin/cardiolipin complex (aVim/CL).

Results: From January 2015 to October 2019, 40 patients with SN-APS and neurological involvement were enrolled. Clinical and demographic characteristics are reported in Table 1. Thirty-three patients (82.5%) resulted positive for at least one non-conventional test (62.5% positive on two occasions) while 17.5% were negative. The occurrence of aCL by TLC immunostaining was 33/40 (82.5%), while a Vim/CL were found in 10/40 (25%). Double positivity for aCL by TLC-immunostaining and aVim/CL was observed in 8/40 patients (20%). Patients who tested positive for non-conventional aPL on two occasions had a five-fold increased risk of developing venous thrombosis (LR 5.24; p=0.022). The positivity for aCL by TLC immunostaining determined an augmented risk of sinus vein thrombosis (LR 5.49; p=0.019) while positivity for aVim/CL raised the likelihood of epilepsy (LR 4.133; p=0.042). Almost all (16/18, 88%) patients with ischemic stroke resulted positive at least one test, 15 tested positive for aCL by TLC-immunostaining and 3 for aVim/CL. In this subset of patients, the positivity for non-conventional aPL on two occasions determined an increased risk of venous thrombosis (LR 8.905; p=0.003) and recurrent stroke (LR 6.321; p=0.012). In particular, those who tested positive for aVim/CL were at higher risk of developing recurrent stroke (LR 6.659; p=0.01).

Table 1.

Characteristics	Patients N= 40 (%)
Female/Male	35/5
Mean age in years (S.D.)	48 (12.5)
Thrombosis	34 (85)
Arterial	23 (57.5)
Venous	17 (42.5)
Recurrent	13 (32.5)
Pregnancy morbidity	12 (34.3)
Recurrent miscarriage	11 (31.4)
Foetal deaths	2 (5.7)
Premature births	2 (5.7)
Thrombosis + Pregnancy morbidity	6 (17.1)
Neurological manifestations	
Stroke	18 (45)
Recurrent stroke	7 (17.5)
Transient ischemic attack	4 (10)
Venous sinus thrombosis	5 (12.5)
Headache	18 (45)
Epilepsy	7 (17.5)
Transverse myelitis	2 (5)
Other manifestations	
Livedo reticularis	5 (12.5)
Low platelets	3 (7.5)

Conclusion: The nervous system is one of the most frequently affected in APS, however only few data exist about prevalence, characteristics and outcome of its involvement in SN-APS patients. In this work, using TLC immunostaining and ELISA for aVim/CL, we identified non-conventional aPL antibodies in 62,5% SN-APS patients. This subset of patients presented a wide spectrum of neurological manifestations, with frequencies and features that resemble those observed in APS patients. Furthermore, we demonstrated the association between non-conventional aPL and neurological manifestations, such as sinus vein thrombosis, recurrent stroke and epilepsy. In conclusion, testing for non-conventional aPL antibodies may contribute to the evaluation of the stratification of risk for neurological manifestations in SN-APS.

Disclosure of Interests: None declared

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POS0121

ASSOCIATION OF LUPUS LOW DISEASE ACTIVITY STATE ATTAINMENT WITH REDUCED ORGAN DAMAGE AND FLARE IN SLE PATIENTS WITH HIGH DISEASE ACTIVITY

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Background: In SLE patients, episodes of high disease activity state (HDAS, SLEDAI-2K≥10) are associated with worse outcomes even if only experienced once. We investigated whether attainment of the lupus low disease activity state (LLDAS) was associated with protection against adverse outcomes in SLE patients after an episode of HDAS.

Objectives: To compare LLDAS attainment between HDAS and non-HDAS patients.

Methods: Data on 4,106 SLE patients from a multinational cohort, collected prospectively between 2013 and 2020, were analysed. Disease activity was assessed using SLEDAI-2K. Patients who had SLEDAI-2K≥10 at least once were defined as HDAS patients. For the purpose of evaluating long term outcomes, each HDAS patient's first visit with SLEDAI-2K≥10 was assigned as baseline, and for non-HDAS patients, recruitment was considered as baseline. Patients in LLDAS continuously for ≥6 months were defined as in sustained LLDAS (≥6months- and ≥12months-sustained LLDAS). Survival analyses were performed to examine the association between LLDAS attainment and damage accrual and flare.

Results: 1076 patients (26%) had HDAS at least once (HDAS-ever). Compared to patients who never experienced HDAS (HDAS-never), HDAS-ever patients were younger, had shorter disease duration at enrolment, and a longer study follow-up period. HDAS-ever patients had higher disease activity across the observation period measured by time-adjusted mean SLEDAI-2K and PGA; higher PNL and IS use, more flares, organ damage, and damage accrual.

None of the HDAS cohort and 42% of HDAS-never group were in LLDAS at baseline (HDAS-never/not LLDAS BL). 66% of HDAS-ever and 57% of 'HDAS-never/not LLDAS BL' patients attained LLDAS at least once during the study observation period. Proportions of patients in sustained LLDAS and who had cumulative LLDAS ≥ 50% of observed time (LLDAS-50) were lower in HDAS-ever patients (Table 1). LLDAS-50 attainment was protective from damage accrual and flare in both HDAS-ever and HDAS-never patients (Table 1). Sustained LLDAS was similarly protective from damage accrual and flare in both 'HDAS-ever' and 'HDAS-never/not LLDAS BL' groups (Table 1).

Table 1.

	HDAS-never/not LLDAS BL n=1215 n (%)	HDAS-ever n=1076 n (%)
Patients with organ damage accrual	212 (18.8%)	269 (27.5%)
patients with flare	613 (50.5%)	894 (83.1%)
LLDAS-ever (at least once)	688 (56.6%)	713 (66.4%)
≥50% cumulative time in LLDAS (LLDAS-50)	371 (33.1%)	182 (18.6%)
≥6-months in sustained LLDAS	391 (32.2%)	287 (26.7%)
≥12-months in sustained LLDAS	243 (20.0%)	143 (13.3%)
Longitudinal associations with	**HR (95% CI), p-value**	**HR (95% CI), p-value**
Organ damage accrual$_t$		
LLDAS$_{t-1}$	0.54 (0.41,0.71), p<0.001	0.49 (0.36,0.67), p<0.001
LLDAS-50$_{t-1}$	0.67 (0.49,0.90), p=0.009	0.61 (0.38,0.98), p<0.04
≥6m sustained LLDAS$_{t-1}$	0.68 (0.45,1.01), p=0.06	0.43 (0.26,0.73), p=0.002
≥12m sustained LLDAS$_{t-1}$	0.54 (0.31,0.94), p=0.03	0.29 (0.11,0.74), p=0.01
Flare$_t$		
LLDAS$_{t-1}$	0.83 (0.71,0.97), p=0.019	0.67 (0.59,0.77), p<0.001
LLDAS-50$_{t-1}$	0.84 (0.69,1.01), p=0.059	0.59 (0.48,0.72), p<0.001
≥6m sustained LLDAS$_{t-1}$	0.47 (0.37,0.60), p<0.001	0.48 (0.38,0.60), p<0.001
≥12m sustained LLDAS$_{t-1}$	0.41 (0.30,0.56), p<0.001	0.29 (0.20,0.42).p<0.001

Conclusion: Sustained or majority LLDAS was less achievable in SLE patients after an episode of HDAS in HDAS-ever compared to HDAS-never patients, but protective associations of LLDAS against organ damage accrual and flare were similar regardless of HDAS. LLDAS attainment is protective from adverse outcomes even after high disease activity.

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POS0122

CENTRAL NERVOUS SYSTEM DEMYELINATING SYNDROMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM "ATTIKON" LUPUS COHORT

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Background: Central nervous system (CNS) demyelinating syndromes that occur in the context of SLE may represent a manifestation of neuropsychiatric lupus, or an overlap of SLE and multiple sclerosis (MS). The differential diagnosis between the two entities has important clinical implications, because the therapeutic management differs between the two conditions.
Objectives: To characterize CNS demyelinating syndromes in a large SLE cohort as neuropsychiatric SLE or SLE-MS overlap, using a multidisciplinary approach and existing diagnostic (MS) and classification criteria (SLE)
Methods: Patients from the "Attikon" lupus cohort (n=707) were evaluated for demyelinating syndromes. Clinical, laboratory and neuroimaging data were recorded for each patient. Following multidisciplinary evaluation and application of criteria, the demyelinating syndrome was attributed to either SLE or MS. Patients with transverse myelitis were not included in this study.
Results: We identified 26 patients with demyelinating syndromes (3.7%) with mean age at diagnosis 46.9 (SD 12.3) years and median disease duration at last follow-up 60 (IQR 52) months. Of them, 12 were diagnosed as primary SLE-demyelination (46.2%) and 14 as overlap SLE-MS (53.8%). The two groups did not differ with respect to rheumatologic and neurologic manifestations, or serologic findings (ANA, dsDNA, C3/C4, aPL, ENA). SLE patients with demyelination manifested mild extra-CNS disease mainly involving joints and skin, while severe non-CNS manifestations were rare. However, patients with SLE-demyelination were less likely to have elevated IgG index (OR 0.055 95% CI: 0.008-0.40) and positive oligoclonal bands (OR 0.09 95% CI: 0.014-0.56). SLE patients with primary demyelinating syndrome were less likely to exhibit brain lesions in the spinal cord, infratentorial, periventricular and juxtacortical regions. A single brain region was affected in 9 SLE-demyelination patients (75%), while all MS-SLE patients had multiple affected brain regions. MS-SLE overlap was associated with increased likelihood of neurologic relapses (OR 18.2, 95% CI: 1.76-188), while SLE-demyelination patients were less likely to exhibit neurological deficits (EDSS>0) at last follow-up visit (50% vs. 78.6%in SLE-MS, respectively).
Conclusion: Demyelination in the context of SLE follows a more benign course compared to a frank SLE-MS overlap. Prolongation of follow-up will ascertain whether SLE-demyelination patients evolve to MS, or this is a *bona fide* NPSLE syndrome.
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POS0123

MAJOR SALIVARY GLAND ULTRASONOGRAPHY AND MRI WITH DIFFUSION WEIGHTED IMAGING (DWI) AS COMPLEMENTARY TOOLS TO IDENTIFY FEATURES OF MALT IN PRIMARY SJÖGREN'S SYNDROME (PSS): A SINGLE CENTER CROSS SECTIONAL STUDY

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Background: Salivary MALT lymphoma represents the major complication of primary Sjögren's Syndrome (pSS). However, the early recognition of MALT lymphoma may be challenging due to its indolent, slow clinical course.
Objectives: 1. to identify salivary gland ultrasonographic (SGUS) features and magnetic resonance (MRI) abnormal findings with Diffusion Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC) of MALT in pSS patients 2. To evaluate the correlation between salivary gland ultrasonography (SGUS) and MRI in pSS patients with suspected lymphoma.
Methods: consecutive patients with pSS (2016 ACR/EULAR criteria) and suspected MALT lymphoma undergoing histological examination were included in this cross sectional study from September 2017 to November 2021. The US echostructure of each gland on B-mode images was graded using the latest 2019 OMERACT semiquantitative SGUS scoring systems (0-3). Sonographic features of focal lesions were described. Conventional MRI techniques (i.e T1WI, T2WI, and STIR images) combined with MR sialography was performed in all the cases. DWI was acquired at b-value 0, 500 and 1000. ADC values were calculated. Patients' clinical and histological data were collected. Data were presented as mean±SD, or percent frequency as appropriate. Intergroup comparisons were made using the t-test/Mann–Whitney test for continuous variables and Fisher's exact test for categorical variables.
Results: 45 pSS (mean age, S.D=55±15 yrs) were included. MALT lymphoma was histologically confirmed in 14/45 pSS patients and, specifically in 18/180 major salivary glands (17 parotids and 1 submandibular glands). At SGUS examination, MALT salivary glands presented an OMERACT grade 3 in 16/18 and a grade 2 in 2/18, significantly higher than the OMERACT scoring observed in no-MALT pSS glands (p=0.0001). The sonographic features more commonly detected in MALT were: hypoecoich macroareas with posterior enhancement, presence of septa or hyperechogenic strands and anarchic intralesional vascularization. At MRI, 15/18 (83.3%) MALT lymphoma appeared as intraglandular solid lesions: 9/15 (60%) were solid-cystic lesions and 6/15 (40%) were solid lesions without cystic changes. The frequency of solid lesions in pSS patients without lymphoma was 3/124 (2.4%), significanlty lower than in MALT-pSS. Furthermore 15/18 (83.3%) MALT lymphoma showed glandular fatty substitution. The presence of fatty substitution did not differ in MALT lymphoma and in no-MALT pSS glands. The mean (SD) ADC value of MALT lesions was significantly lower than the ADC of the parotid glands in pSS without lymphoma (0.63±0.07 x 10^-3 mm^2/s vs 1.13± 0.19 x 10^-3 mm^2/s, p =0.001). A negative correlation between SGUS OMERACT score and mean glandular ADC values (r = – 0.776, p < 0.001) was found; patients with OMERACT score 3 presented the lowest mean salivary gland ADC when compared to the other OMERACT scores (0-2) (p=0.001).
Conclusion: OMERACT semiquantitative SGUS scoring systems and MRI with DWI represent promising complementary tools in the differential diagnosis of pSS MALT lymphoma, particularly useful to guide parotid biopsy. Patients with an OMERACT score 3 in their SGUS deserve a careful screening for lymphoma.
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Through the looking glass

POS0124

DIAGNOSTIC VALUE OF LIVER STIFFNESS AS MARKER OF HEPATIC MARKER OF HEPATIC AMYLOID DEPOSITION IN SYSTEMIC AL AMYLOIDOSIS

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Background: Hepatic involvement in AL amyloidosis is often asymptomatic but does affect prognosis and should be taken into account during follow-up. An increased plasma level of alkaline phosphatase (ALP) or increased liver span are part of the conventional diagnostic criteria for establishing hepatic involvement[1], however these markers are nonspecific. ^{123}I-labeled serum amyloid P component (SAP) scintigraphy is a specific and sensitive method to establish hepatic involvement but is not widely available. Liver stiffness measured by transient elastography is increased in AL amyloidosis patients with hepatic involvement and could be useful in establishing liver involvement and monitoring treatment response in AL-amyloidosis.
Objectives: To assess the diagnostic value of liver stiffness (LS) for liver involvement in AL amyloidosis and the utility of LS to monitor treatment effect using SAP scintigraphy as gold standard.
Methods: LS was measured prospectively in 49 treatment naive patients with systemic AL amyloidosis and 9 patients with wild type transthyretin amyloidosis (ATTRwt) with cardiomyopathy (cardiac controls). In addition, LS was longitudinally measured in 10 AL amyloidosis patients of whom 9 patients had liver involvement. SAP scintigraphy, laboratory assessments including ALP and measurement of liver span was performed in all patients.
Results: Of the 49 patients, 27 patients had liver involvement (of whom 24 also had heart involvement), 10 patients had heart involvement, 12 patients had no heart or liver involvement. Median LS was significantly higher in AL amyloidosis patients with liver involvement (22.8 kPa, range 4.3-75), than in AL amyloidosis patients without liver involvement (6.3 kPa, range 4.4-35.8) (p=0.000). Also a significant difference was seen between AL amyloidosis patients with liver involvement (22.8.9, range 4.3-75) versus, heart involvement (9.0, range 4.5-35.8) (p=0.02), no liver or heart involvement (5.7, range 4.4-10.1) (p=0.0001), and ATTRwt patients (9.9 kPa, range 4.0-14.6) (p=0.01). Furthermore, LS values seemed to significantly decrease over time in AL amyloidosis patients with liver involvement with a good hematologic response to treatment.
Conclusion: LS is a non-invasive tool which seems to be useful in clinical practice to establish liver involvement in patients with AL amyloidosis. In addition, it is a promising marker in the follow up of AL amyloidosis patients for establishing hepatic response over time.
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POS0125 EXTRA-ARTICULAR FINDINGS WITH FDG-PET/CT IN RHEUMATOID ARTHRITIS PATIENTS: MORE HARM THAN BENEFIT.

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Background: Whole-body Positron Emission Tomography with CT-scanning using fluorine-18 fluorodeoxyglucose (18F-FDG) is occasionally used in Rheumatoid Arthritis (RA) patients. Reasons to use FDG-PET/CT-scans are to diagnose arthritis or guide decisions on systemic therapy, as FDG uptake in affected joints may reflect disease activity [1]. FDG-PET/CT might also detect malignancies, but the frequency of incidental findings and the proportion of relevant malignant disease that could be missed are currently unknown.
Objectives: To study the malignancy screening performance of whole-body FDG-PET/CT in longstanding RA patients with low disease activity.
Methods: FDG-PET/CT-scanning was done in the intervention arm of the Dose REduction Strategy of Subcutaneous TNF-inhibitors (DRESS) study, a randomized controlled trial on dose-tapering of biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) [3]. Baseline and if applicable follow up whole-body FDG-PET/CT-scans were performed in consenting patients in the tapering arm to assess predictive value of subclinical PET-arthritis for risk of flaring [4]. The scans were also read by experienced nuclear medicine specialists immediately after they were performed for any unexpected extra-articular finding, conform routine clinical care.
The reference standard was clinical diagnosis of malignancy during the 3 year follow-up. Prevalence of extra-articular abnormalities, follow-up, and received treatments were summarized post-hoc.
Results: 121 scans were made in 79 patients. Extra-articular abnormalities were found in 59/121 (48.8%) scans (Table 1) in 45/79 (57%) patients.

Table 1. ***Abnormalities found on FDG-PET/CT scans***

	# abnormal results found on scans (%)
No PET/CT result obtained	3 (2.5)
No abnormalities found on any scan	59 (48.8)
One or more abnormalities found per scan*	59 (48.8)
Total number of scans	**121**
Inflammatory	7 (5.7)
Suspected malignancies	9 (7.4)
Cardiovascular	2 (1.6)
Pulmonary	7 (5.8)
Gastrointestinal	10 (8.3)
Muscles/tendons	3 (2.5)
Bone-related	3 (2.5)
Hypermetabolic lymph nodes (non-specific)	16 (13.2)
Thyroid	4 (3.3)

* Fifteen of these abnormalities were found on the second PET/CT, the rest was found on the first scan. 11 abnormalities on the second PET/CT were the same as the one seen on the first scan, and 7 abnormalities resolved after the first scan. One scan can show multiple abnormalities, from different categories.

Follow-up action occurred in 21 (26.6%) patients, consisting of referral to a specialist or reassessing and/or scheduling diagnostics directly by the treating rheumatologist. In 5 (6.3%) patients, the rheumatologist followed-up. In 17 (21.5%) patients a consultation with a different specialist was scheduled. In five patients surgical/invasive intervention took place. In one patient a hemi-thyroidectomy was performed revealing a follicular adenoma. This resection was complicated by persistent recurrent laryngeal nerve paresis and hoarseness. In a second, an intra-uterine myomectomy took place. In a third, a colonoscopy was performe revealing two low-grade adenomas. In a fourth a benign cyst in the neck was extracted. A fifth patient underwent spinal marginal myotomy which turned out to be a benign schwannoma.
Nine patients (7.4%) were suspected of malignancy, none turned out to be malignant. Six clinical malignancies (bladder, penile, lymphoma, 2x melanoma and prostate) that developed during follow-up were all negative on baseline FDG-PET/CT. The malignancies were diagnosed after an interval of between 5 and 34 months (mean 13 months).
Conclusion: Whole-body FDG-PET/CT-scanning for arthritis imaging in RA patients results in frequent incidental extra-articular findings, while some who apparently had normal scans developed malignancies.
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POS0126 UTILITY OF THE SUBCHONDRAL BONE ATTENUATION COEFFICIENT OF THE SACROILIAC MARGINS TO DIFFERENTIATE SPONDYLOARTHRITIS AND OSTEITIS CONDENSANS ILII

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Background: Differentiating ankylosing spondylitis (AS) from osteitis condensans ilii (OCI) remains challenging for clinicians.
Objectives: The aim of this study was to determine whether Subchondral Bone Attenuation Coefficient of the Sacrolliac margins (SBAC-SI) is different in AS, OCI and diffuse idiopathic skeletal hyperostosis (DISH).
Methods: A monocentric retrospective observational study was performed at a French University Hospital. Patients included were followed for AS, DISH or OCI and underwent CT scan including sacroiliac joint. Patients with tumor lesion of bone or a history of pelvic radiotherapy were excluded. AS and OCI patients were matched with a control of the same age and sex. All scans were acquired on the same CT-scan unit (Somatom 64 definition AS+, Siemens Healthineers, Erlangen, Germany), with a slice thickness of 0.625 mm. In the coronal oblique plane of the SIJ, three slices (anterior, middle and posterior) and four quadrants per joint were defined. Twenty-four identical circular regions of interest (ROIs) (30 mm2), 8 per slice, were manually placed separately subcortical to the SIJ, four on the sacral side and four on the iliac side. The distance between the circle of the ROI and the cortical bone was 2 to 3 mm. An overall score was obtained from

the sum of all ROIs. For every ROI, an Attenuation Coefficient was measured and expressed in Hounsfield Unit. The total SBAC-SI score was the sum of the 24 ROI. The sacral and iliac SBAC-SI scores were the sum of the sacral or the iliac ROI.

Results: Thirty AS and AS controls, 31 DISH, 29 OCI and OCI controls were included. SBAC-SI score was 9727 (±2430) in the OCI group (p<0.001), 3563 (±1860) in the AS group, 3899 (±1937) in the DISH group, 4224 (±1693) in the AS control group and 5445 (±1205) in the OCI control group. A threshold of 7500 HU had the best discriminative value between OCI and AS (youden index: 0.89). In AS, disease duration is negatively associated with SBAC-SI (r: -0.623; p< 0.01) and HLA B27 is associated with lower SBAC-SI (6523 [5198; 7137]VS 2809 [1568; 3371]; p <0.001).

Conclusion: SBAC-SI is significatively different between AS and OCI and could help to distinguish these two diseases.

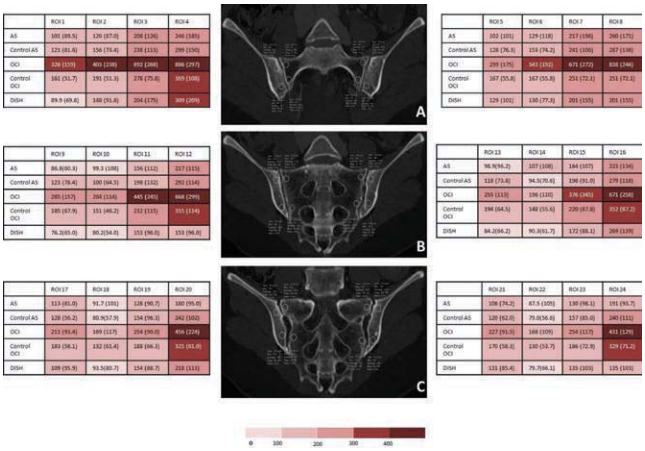

Figure 1. Distribution of the Subchondral Bone Attenuation Coefficients of the Sacroiliac Margins of the 24 ROI in the anterior (A), middle (B) and posterior (C) slices in the coronal oblique plane of the sacroiliac joints

Disclosure of Interests: None declared

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POS0127 QUANTITATIVE ASSESSMENT OF FINGER VASCULARITY IN SYSTEMIC SCLEROSIS PATIENTS WITH RAYNAUD'S PHENOMENON USING ULTRASOUND VASCULAR IMAGING

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Background: In patients with Systemic Sclerosis (SSc), vasculopathy plays an important pathophysiological role and it is almost universally expressed as Raynaud's Phenomenon (RP). Assessment of vasculopathy/microangiopathy is crucial for early diagnosis of SSc and also is considered in the SSc classification criteria. Currently, this evaluation is performed by nailfold capillaroscopy. However, nailfold capillaroscopy is limited to the nail fold area and is mainly qualitative since is based on the shape, size, and density of the observed capillaries.

Objectives: The objective of this study is to detect and quantify finger vascularity of SSc patients with RP using four ultrasound vascular imaging techniques. Additionally, the diagnostic performance of quantified finger vascularity was assessed.

Methods: This prospective IRB approved study has enrolled 20 SSc patients fulfilling the 2013 ACR/EULAR classification criteria and presenting RP. Age and sex matched normal volunteers (16 subjects) without RP, were also enrolled. All fingers except thumbs were imaged at room temperature in the seated position. The blood flow of each finger was evaluated on the dorsal (showing nail) and ventral (showing palm) sides using an i24LX8 probe (9-24 MHz) on an Aplio i800 system (Canon Medical Systems, Tustin, CA, USA). Blood flow images were obtained using color Doppler imaging (CDI), power Doppler imaging (PDI), monochrome Superb Microvascular Imaging (mSMI), and color-coded Superb Microvascular Imaging (cSMI) keeping the same imaging settings for all subjects. The percent area of vascularity observed by each technique was quantified offline by counting pixels of blood flow in a 5 x 5 mm square centered at the nail fold for the dorsal side and in a 1 x 1 cm square from the fingertip for the ventral side using Matlab (MathWorks, Natick, MA, USA). The percent vascularity areas from dorsal and ventral sides were averaged over fingers, then t-tests and receiver operating characteristic (ROC) analyses were performed (Youden Index) to assess the ability of the different methods for classifying disease status (RP-SSc from normal controls), allowing to assign diagnostic accuracy.

Results: Two patients' data were excluded due to technical errors. The data from 18 RP-SSc patients and 16 normal volunteers were analyzed. The percent vascular areas in patients with RP were significantly lower than those in normal volunteers at both dorsal ($p < 0.03$) and ventral ($p < 0.01$). For each imaging technique, the ventral side vascularity showed a higher diagnostic accuracy compared to the dorsal side. Among the four imaging techniques, CDI showed the highest diagnostic accuracy. The mean percent areas by CDI were 6.8 ± 7.1% (mean ± standard deviation) and 15.3 ± 8.9% on the dorsal side ($p < 0.01$) and 5.3 ± 5.6% and 16.7 ± 7.4% on the ventral side ($p < 0.0001$) for RP patients and normal volunteers, respectively. The ventral side vascularity by CDI showed the highest diagnostic accuracy of 90% with 88% specificity and 78% sensitivity.

Conclusion: Ultrasonic vascular imaging demonstrated the potential to quantify microangiopathy of RP-SSc. Additionally, the mean percent vascular area averaged across the fingers showed to be accurate (70 to 90%) to differentiate patients with RP-SSc from normal controls, albeit based on small sample size.

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POS0128 MICROVASCULAR INVOLVEMENT IN BEHÇET'S DISEASE. STUDY OF NAILFOLD CAPILLAROSCOPY AND ENDOTHELIAL PROGENITOR CELLS IN A NATIONAL REFERRAL CENTER

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Background: Ocular manifestations of Behçet's disease (BD) are globally recognized and widely studied **[1]**. Vascular lesions are also frequent but less explored **[2]**. Microvascular involvement may be clinical (as Raynaud's phenomenon) or subclinical. Vascular microcirculation is studied with Nailfold Capillaroscopy (NFC) that may show capillary abnormalities such as dilated loops, megacapillaries and microhemorrhages. Endothelial progenitor cells (EPCs) have been implied in the pathogenesis of multiple cardiovascular disorders and vasculitis, including BD and could be used as biomarkers.

Objectives: To assess the microvascular involvement and EPCs in patients with BD.

Methods: Observational study of unselected consecutive patients with BD assessed in a national referral center from March to May 2021. All patients fulfilled the 2014 ICBD criteria **[2].** They were evaluated sequentially with a scheduled clinic visit after signing an informed consent. The main variables collected were **a)** periungual capillaries features (loop diameter, tortuosity, vascular density, microhemorrhages and blood flow), and **b)** serum EPCs levels. NFC was performed from the second to fifth fingers of both hands using a 500x magnification digital microscope. The following features were considered abnormal: diffuse enlarged capillaries (≥2 capillaries with a diameter of 20-50 µm in at least 2 different fingers), megacapillaries (>50 µm in diameter), reduced vascular density (<9 capillaries/mm or avascular areas), diffuse microhemorrhages (≥2 hemorrhages in at least 2 different fingers) and granular/slow flow. EPCs were studied in unselected BD patients in whom instant blood samples were available and compared with sex-aged matched healthy controls (HC). EPCs from peripheral venous blood were quantified by direct flow cytometry and characterized by simultaneous expression of cell surface markers of stemness (CD34), immaturity (CD133), endothelial commitment (CD309) and a low expression of the pan-leukocyte marker (CD45).

Results: From a cohort of 120 patients with BD, 42 were evaluated during the period of the study (Table 1). NFC was performed in the 42 cases, being abnormal in 54.8% of them. The most common findings were capillary loop dilation (45.2%), capillary tortuosity (31%), megacapillaries (21.4%) and microhemorrhages (16.7%) (Table 1). Instant blood samples to study EPCs levels were available in 18 BD patients and 12 HC. The median [IQR] frequency of EPCs levels were higher in BD than in HC (p=0.011) (Figure 1).

Table 1. Collected data of 42 patients with Behçet's disease.

Demographic data	n (%)
Women/Men	19 (45.2)/ 23 (54.8)
Age (years), mean ± SD	47.86±12.99
Clinical vascular involvement	**n (%)**
Deep vein thrombosis	4 (9.52)
Superficial thrombophlebitis	1 (2.38)
Arterial aneurysms	2 (4.76)
Acute myocardial infarction	3 (7.14)
Arterial thrombosis	1 (2.38)
Raynaud's phenomenon	10 (23.81)
Nailfold capillaroscopy Findings	**n (%)**
Abnormal	23 (54.8)
Dilated loops (20-50 µm) ≥2 in at least 2 fingers	19 (45.2)
Megacapillaries (>50 µm)	9 (21.4)
≥2 in at least 2 fingers	3 (7.1)
Capillary tortuosity	13 (31)
Microhemorrhages	7 (16.7)
≥2 in at least 2 fingers	1 (2.4)
Reduced vascular density	3 (7.1)
Granular flow	1 (2.4)

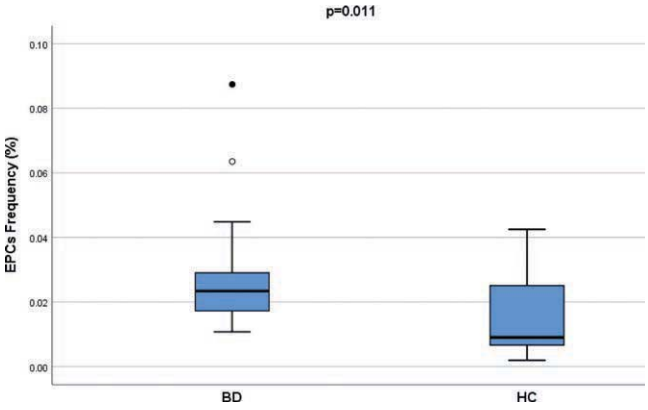

Figure 1. Quantification of endothelial progenitor cells population by flow cytometry in 18 patients with Behçet's disease and 12 healthy controls. Mann-Whitney U test. BD: Behçet's disease. EPCs: endothelial progenitor cells. HC: healthy controls.

Conclusion: Microvascular involvement is common in BD and can be easily assessed by NFC. Furthermore, EPCs quantification may be a useful serum biomarker of the disease.

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POS0129 TO CONTRAST OR NOT TO CONTRAST? ON THE ROLE OF CONTRAST ENHANCEMENT IN HAND MRI STUDIES OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Currently, clinical indications for application of gadolinium-based contrast agents (GBCA) in magnetic resonance imaging (MRI) are increasingly being questioned[1]. Rheumatoid arthritis is a disease which is characterised by joint inflammation and due to various existing therapies, early diagnosis and sensitive monitoring is beneficial for assessing disease progression, therapy response and optimizing the individual therapy.

Objectives: This study aimed to evaluate the necessity of contrast enhancement in MRI of the hand in patients with rheumatoid arthritis (RA).

Methods: 31 patients with RA (mean age, 50±14 years [range, 18–72 years]) from the German ArthroMark cohort underwent morphologic high-field MRI scans on a clinical 3T scanner. MRI studies were analyzed based on (1) the Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS[2]) and (2) the GBCA-free RAMRIS version, termed RAMRIS **S**ine-G**a**dolinium-**F**or-**E**xperts (RAMRIS-SAFE), in which synovitis and tenosynovitis were assessed using the short-tau-inversion-recovery (STIR) sequence instead of the post-contrast T1-weighted sequence.

Results: Correlation between RAMRIS and RAMRIS-SAFE in terms of Spearman's ρ was almost perfect (ρ=0.976; p<0.001). The synovitis subscores, as based on RAMRIS and RAMRIS-SAFE, were equally strongly correlated (ρ=0.937; p<0.001), while the tenosynovitis subscores were less strongly correlated (ρ=0.380 p=0.035). Inter-rater reliability in terms of Cohen's κ was high ($0.963 \leq \kappa \leq 0.925$).

Conclusion: In conclusion, RAMRIS-SAFE as the GBCA-free version of the well-established RAMRIS is a patient-friendly and resource-efficient alternative for assessing disease-related joint changes in RA. As patients with RA are subject to repetitive GBCA applications, non-contrast imaging protocols should be considered.

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Table 1. Composition of both scores: RAMRIS-SAFE and RAMRIS

Imaging Feature	Anatomic Location	MRI Sequence:	
		RAMRIS-SAFE (without contrast enhancement)	RAMRIS (with contrast enhancement)
Erosion	•distal radius and distal ulna •all carpal bones and metacarpal bases •MCP joints (II-V)	coronal T1	coronal T1
Osteitis	•distal radius and distal ulna •all carpal bones and metacarpal bases •MCP joints (II-V)	coronal STIR	coronal STIR
Synovitis	•Distal radio-ulnar joint •Radiocarpal joint •Intercarpal and carpometacarpal joints •MCP (II-V) joints	coronal STIR, axial T1	coronal and axial T1 + contrast
Tenosynovitis	•flexor tendons at the level of MCP joints	coronal STIR, axial T1	coronal and axial T1 + contrast
Joint space narrowing	•all radiocarpal, intercarpal, carpometacarpal, . . and MCP joints (n=17)	coronal T1	coronal T1

Abbreviations are "RAMRIS" (rheumatoid arthritis MRI scoring system), "RAMRIS-SAFE" (RAMRIS sine gadolinium for experts), "MCP" (metacarpophalangeal), and "STIR" (Short-Tau-Inversion-Recovery).

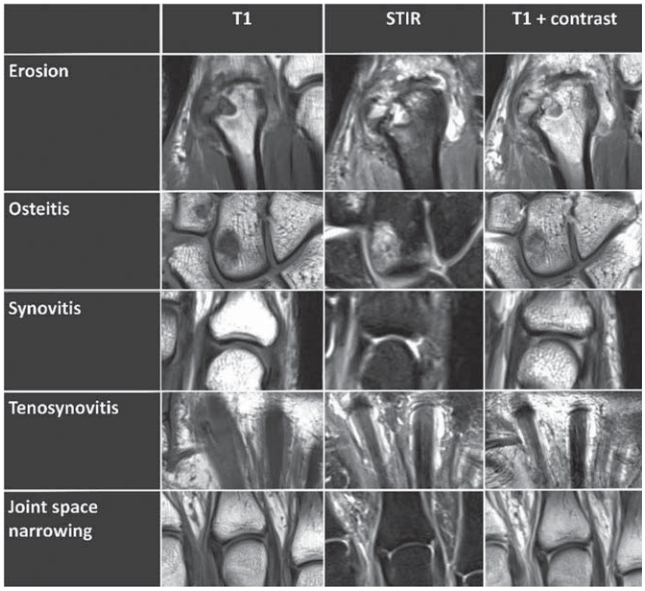

Figure 1. Exemplary imaging features (erosion, osteitis, synovitis, tenosynovitis, and joint space narrowing) that are scored semiquantitatively based on RAMRIS, shown in (i) unenhanced MRT T1-weighted sequence (left column), (ii) STIR sequence (middle column), and enhanced T1-weighted postcontrast sequence (right column).

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POS0130 NEAR INFRARED FLUORESCENCE OPTICAL IMAGING (NIR-FOI) CAN SUPPORT THE DIFFERENTIAL DIAGNOSES OF CONNECTIVE TISSUE DISEASES

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Background: Differentiation between degenerative osteoarthritis (OA) and autoimmune caused connective tissue diseases (CTD), or rheumatoid arthritis (RA) is important for effective therapy. Anamnesis, clinical examination, and analysis of laboratory parameters are helpful for diagnosis, but do not always lead to clear results. One problem is that patients often show overlapping symptoms. Particularly, imaging techniques as NIR-based fluorescence optical imaging (FOI) are playing an increasingly role as quantifiable and sensitive diagnostic methods. After injection of a fluorescent dye, changes in the microcirculation caused by inflammation can be detected due to altered blood flow and accumulation in anatomical structures of the hands. Analyses of enrichment features can be used to identify pathological changes and to support the diagnosis of degenerative and autoimmune diseases.

Objectives: The present work investigates the potential of NIR-FOI feature assessment to differentiate between various rheumatic diseases, which are accompanied by pathological changes in connective tissues.

Methods: NIR fluorescence imaging comprised 360 images/6 min. after injection of the dye. Analyses of patients with the clinical diagnosis of OA (n = 236) were compared with RA patients (n = 235), and patients diagnosed with autoimmune CTD (collagenoses) (n = 149). 17 features known to occur in FOI images were analyzed in both hands in three time periods (P1-3) after injection in two independent passes. In some cases, Prima Vista images (PVI), representing the sum of images 1-240 were also analyzed (n = 45, 33, 33 for OA, RA, CTD). Signals compared to the background were assessed as positive or negative (Figure 1). The data were analyzed statistically.

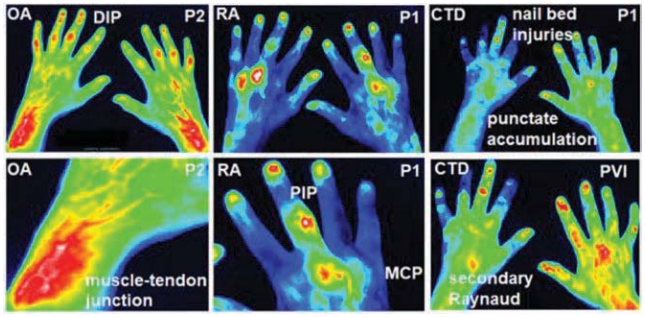

Figure 1. Examples of significantly different features in NIR-FOI images of patients with clinically diagnosed OA, RA, or CTD. Top: the whole hands, also with nail bed injuries in phase 1 (P1) for a CTD patient (right), bottom: increased intensity in muscle-tendon junction in the forearm in phase 2 (P2) for an OA patient, increased intensity in MCP joint in phase 1 (P1) for an RA patient and a secondary Raynaud syndrome for a CTD patient in PVI.

Results: Comparing the analyses of all phases of the OA cohort with those of the RA cohort, 14 of 51 features were identified as significantly different ($p<0.05$). The dye accumulation in metacarpophalangeal joints (MCP) has high specificity and diagnostic odds ratio (DOR) for RA patients (91%, 4.32). Patients in the OA cohort showed an increase in the signal at the muscle-tendon junction in the forearm (80% specificity, DOR 3.11). A comparison of the RA and CTD cohorts revealed 24 significant differences, most prominent changes in the nail bed in P1 (100% specificity, DOR 8.27) and a punctate accumulation pattern in P2 (98% specificity, DOR 2.61) for the CTD cohort. Comparing the RA and CTD cohorts, 22 features were significantly different. The strongest differences were found in the PIP joints of RA patients (78% sensitivity, DOR 2.97) and in the nail bed of CTD patients (100 % specificity, DOR 8.18). In the cumulative PV images a high specificity for a secondary Raynaud's syndrome in CTD patients was found as compared to RA (97%, DOR 17.7) and OA (91%, DOR 5.9). Further, DIP signals for OA comparing to CTD show significant differences (76 % sensitivity, DOR 2,73).

Conclusion: The present work demonstrates the detection and localization of specific, significant features in NIR-FOI of patients with different rheumatic diseases and can thus make an important contribution to diagnosis and optimization of therapy. In future, multivariate analysis and artificial intelligence algorithms can combine these features to further improve the diagnostic value.

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POS0131 CONCORDANCE BETWEEN LOCATION OF SELF-REPORTED SITE OF MUSCULOSKELETAL PAIN IN PSORIASIS AND FINDINGS OF INFLAMMATION BY ULTRASOUND

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Background: Patients with psoriasis (PsO) often report muskuloskeletal (MSK) pain without clinical findings of inflammation. Ultrasound (US) is more sensitive than clinical evaluation in detecting synovitis and enthesitis, and we have previously found that patients with PsO and pain more often have US signs of inflammation in joints and entheses than patients without pain (1), indicating possible psoriatic arthritis (PsA). Whether the area of reported pain in these patients correspond to inflammation by US has not yet been investigated.
Objectives: In patients with PsO with self-reported MSK pain, to investigate if the area of reported of pain corresponds to synovitis and/or enthesitis.
Methods: PsO patients with self-reported MSK pain (n=79, Table 1), recruited from a Danish nationwide survey, were evaluated in one of four rheumatology departments with greyscale (GS) and color Doppler (CD) US of 48 joints and 12 entheses, applying the OMERACT scoring systems (2) for US synovitis (defined as GS score ≥2 or CD≥1) and enthesitis (defined as ≥1 GS inflammatory finding (hypoechogenicity/thickening) and CD score ≥1). Patients indicated the location of current pain in 21 areas on a homunculus, out of which shoulder (joint), elbow (joint and common extensor enthesis), hand (wrist and MCP, PIP, and DIP-joints 1-5), knees (joint and quadriceps- and patellar entheses), feet (ankle and MTP-joints 1-5) and heel (Achilles- and plantar fascia entheses) were evaluated by US, se Figure 1. Association between self-reported pain and US inflammation (synovitis/enthesitis) was explored using Fisher's exact test and odds ratios (OR) for 2x2 tables. Agreement was calculated using Cohen's kappa (κ).

Table 1. Population characteristics (n=79)

Sex (female)	33 (42)
Age (years)	57 (47-66)
Body Mass Index (kg/m^2)	28.4 (24.8-34.8)
Disease duration PsO (years)	25 (11-39)
Swollen joint count (0-66)	0 (0-1)
Tender joint count (0-68)	2 (0-5)
Tender enthesis count (0-16)	1 (0-2)
Fibromyalgia tender point count (0-18)	1 (0-5)
Psoriasis Area and Severity Index (0-72)	1.5 (0.2-4.2)
Nail psoriasis (presence)	26 (33)
Physician VAS (0-100)	3 (1-6)
CRP (mmol/l)	2.1 (0.5-4.1)
Global VAS (0-100)	16 (4-45)
Pain VAS (0-100)	20 (5-39)
Health Assessment Questionnaire (0-3)	0.25 (0.00-0.69)
DAS28-CRP (0-10)	1.6 (1.5-2.6)
Disease Activity in Psoriatic Arthritis (0-164)	5.2 (4.1-20.7)

Numbers are median (IQR) or no. (%). CRP: C-reactive protein, DAS28: Disease Activity Score - 28 joints, VAS: Visual Analog Scale

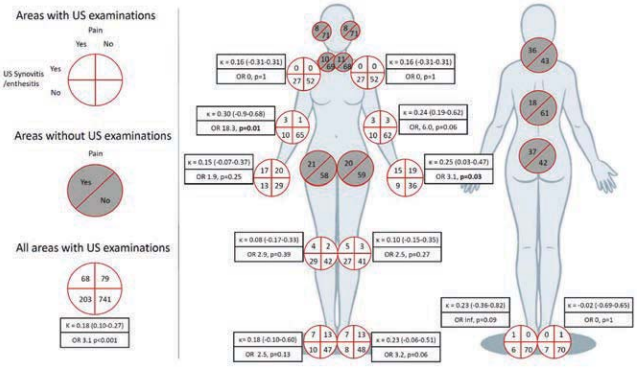

Figure 1. Self-reported pain versus ultrasound (US) inflammation in different areas, and in all areas considered together, presented as 2x2 tables and corresponding odds ratios (OR, p-value) (Fisher's exact test), and agreement (Cohens Kappa (κ (95% confidence interval)).

Results: Of the areas examined by US, pain was most frequent in the knees (41% of patients), while US inflammation was most frequent in the hand/wrist (55%). In total, US inflammation was found in of 72% patients (synovitis in 71%, enthesitis in 17%). In 47% of patients, US inflammation was found in one or more of the painful sites. Figure 1 shows 2x2 tables of pain versus US inflammation in different areas and corresponding ORs and κ-values. Self-reported pain was significantly related to US inflammation in that area, both overall (OR=3.1, p>0.001) and for the specific areas of the left hand (OR 3.1, p=0.03) and right elbow (OR 18.3, p=0.01). Agreement between self-reported pain and US inflammation, as measured by κ, was overall low, κ =0.18(95% confidence interval 0.10-0.27), with highest agreement found for the right elbow (κ = 0.30(-0.9-0.68)). Pain only in areas not examined by US (back/hips/breastbone/jaw) was indicated by 16% of patients.
Conclusion: While US signs of synovitis and enthesitis is frequent in patients with PsO and pain, concordance between US inflammation and the specific location of pain is only seen in half of the patients.

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POS0132

THE FIRST ALGORITHM TO INTEGRATE ULTRASONOGRAPHY IN THE DIAGNOSTIC PROCESS OF DIFFERENTIAL DIAGNOSIS OF INFLAMMATORY ARTHROPATHY IN CLINICAL PRACTICE: A STUDY FROM THE MSUS WORKING GROUP OF THE ITALIAN SOCIETY OF RHEUMATOLOGY

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Background: Musculoskeletal ultrasonography (MSUS) is a useful tool for the diagnosis of several Rheumatic and Musculoskeletal Diseases (RMDs) but its role in the diagnostic pathways in clinical practice is still unclear as feasibility issues limit its application as a bed side technique.
Objectives: To optimize the use of US in clinical practice, the MSUS Study Group of the Italian Society for Rheumatology aimed to develop an algorithm combining US with clinical and laboratory findings to improve the differential diagnosis among patients presenting with joint swelling.
Methods: Based on a systematic literature review[1] and experts' opinion, MSUS Study Group Members attempt to identify a set of statements including the main US elementary lesions useful for US scanning in the suspicion of Rheumatoid arthritis (RA), Psoriatic arthritis (PsA), Rheumatic Polymyalgia (PMR), Gout, Calcium Pyrophosphate Deposition Disease (CPPD), Osteoarthritis (OA). Then, the MSUS Study Group defined through a survey and ranked in a 1000minds exercise the most important clinical/laboratory findings for the differential diagnosis of those diseases. Higher-ranked items were fitted in an algorithm driving the differential diagnosis of RMDs to a reduced spectrum of 2 to 4 possible diseases. Finally, the algorithm supported the performance of US according to the established scans for those specific diseases. To assess the algorithm's performance, a pilot study was conducted on 59 patients, comparing the algorithm-based diagnosis with the final diagnosis based on rheumatologist's experience and/or on classification criteria.
Results: Sets of elementary US lesions and a scanning protocol for each included pathology were created (Table 1), optimized towards high sensibility and specificity. Among the findings evaluated, the age (<50 / ≥50 years old), the number of the involved joints (monoarticular/polyarticular), the serology (Rheumatoid Factor [RF] and anti-citrullinated protein antibody [ACPA]); the acute-phase reactants (C-reactive protein [CRP]; erythrocyte sedimentation rate [ESR]) reached the higher ranking in the survey and were introduced in the algorithm, showed in Figure 1. In the pilot study, the algorithm-based diagnosis was consistent with the final diagnosis in 52 cases (accuracy 88.1%). Among the 7 cases in which the algorithm misclassified patients, four patients had a final diagnosis of OA (3 diagnosed by the algorithm as PMR/RA/PSA and one as PSA), one gout (algorithm diagnosis: OA/CPPD/PSA), one RA (algorithm diagnosis: Gout/CPPD/PSA) and one CPPD (algorithm diagnosis: PMR/RA/PSA).

Table 1. Elementary ultrasound lesions and joints to be scanned for each included pathology

Disease	Sites to scan	US elementary lesions
RA	II-IV MCPs	Synovial Hypertrophy (SH), Power Doppler (PD), erosions
	Wrist	
	V MTP	
PsA	II-III MCPs	Peritendonitis
	PIPs	Enthesitis
		Soft tissue oedema
	Flexor tendons of the hands	Tenosynovitis
		Soft tissue oedema
	Achille's tendon enthesis	PD, erosions
	Proximal patellar tendon enthesis	
CPPD	Knees (menisci and Hyaline Cartilage)	CPP deposits
	Wrist (triangular fibrocartilage complex)	
	Any involved sites	CPP deposits, SH, PD
Gout	Knees	Double contour, tophi
	I MTP	
	Involved sites	SH
		PD
OA	Involved sites	Osteophytes
		Cartilage changes
PMR	Shoulders	Bursitis
		Arthritis
		Rotator cuff integrity

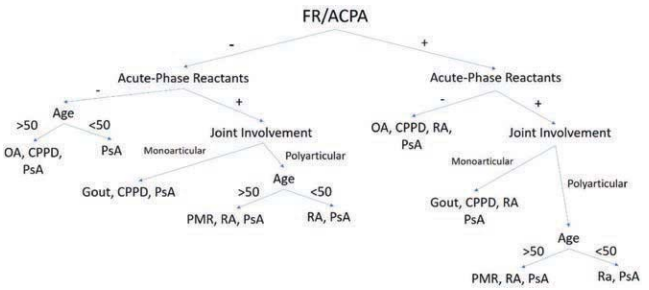

Figure 1. The final algorithm

Conclusion: The diagnostic algorithm produced in this pilot study correctly classified patients with the most prevalent RMDs in clinical practice. A longitudinal study on a large sample size is ongoing to evaluate the added value of US when implemented in this algorithm regarding diagnostic certainty, accuracy and early diagnosis.

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POS0133

HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY FOR THE EVALUATION OF BONE EROSIONS OF METATARSOPHALANGEAL JOINTS IN RHEUMATOID ARTHRITIS: A PILOT STUDY

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Background: Bone erosion in rheumatoid arthritis (RA) is most commonly detected in the wrist, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints. High-resolution peripheral quantitative computed tomography (HR-pQCT) has successfully been used to quantify bone erosions in the wrist and MCP joints. A recent study highlights that HR-pQCT of only two MCP joints has equal accuracy to detect erosive disease in RA patients compared to conventional radiography (CR) of the hands, wrists, and feet (44 joints)[1]. However, no study has evaluated the MTP joints by HR-pQCT.

Objectives: To characterize the localization, size and frequency of erosions in the 4th and 5th MTP joints. Furthermore, to evaluate the sensitivity for the detection of erosion in the 4th and 5th MTP joints by HR-pQCT, compared to CR.

Methods: This single-centre cross-sectional study included 42 patients with established RA (disease duration ≥ 5 years). The right foot was imaged by HR-pQCT in a 2.7 cm long region corresponding to the 4th and 5th MTP joint. Blinded to patient data, the number and volume of bone erosions by HR-pQCT were measured and scored according to the SPECTRA criteria[2]. CR of 44 joints was evaluated according to the Sharp/van der Heijde (SHS) method.

Results: The patients (62% women) had a median disease duration of 12 years (interquartile range (IQR): 7 – 20). HR-pQCT of the 4th and 5th MTP joints identified erosions in 38 (90%) patients. The total erosion volume (V_{tot}) was 2610 mm^3 in all quadrants of the 4th and 5th MTP joints. Erosions were most frequently found at the lateral aspect of the 5th metatarsal head (MH), including 1261 mm^3 (48%) of V_{tot} (Figure 1). CR of 44 joints detected erosions in 30 (71%) patients with a median SHS erosion score of 9 (5 – 28). The sensitivity and specificity (95% CI) of classifying patients with erosive RA by HR-pQCT and CR is displayed in Table 1. McNemar's χ^2 test showed a significantly higher sensitivity of patients classified as having erosive RA by HR-pQCT of the 4th and 5th MTP joints than by CR of 44 joints (4.6, p = 0.03).

Table 1. Comparing CR and HR-pQCT for classifying patients as having erosive RA, and for identifying erosions in the 4th and 5th MTP joints.

Sensitivity & specificity of classifying patients with erosive RA by HR-pQCT when CR of the hands, wrist and feet was used as reference

	CR Hands, wrists, and feet Erosive RA	CR Hands, wrists, and feet Non-erosive RA	Total	Sensitivity (95% CI)
HR-pQCT 4th and 5th MTP joints Erosive RA	27	11	38	90.0 (73.5 – 97.9)
				Specificity (95% CI)
HR-pQCT 4th and 5th MTP joints Non-erosive RA	3	1	4	8.3 (0.2 – 38.5)
Total	30	12	42	

Sensitivity & specificity of classifying patients with erosive RA by CR when HR-pQCT was used as reference

	HR-pQCT 4th and 5th MTP joints Erosive RA	HR-pQCT 4th and 5th MTP joints Non-erosive RA	Total	Sensitivity (95% CI)
CR Hands, wrists, and feet Erosive RA	27	3	30	71.0 (54.1 – 84.6)
				Specificity (95% CI)
CR Hands, wrists, and feet Non-erosive RA	11	1	12	25.0 (0.6 – 80.6)
Total	38	4	42	

Conventional Radiography (CR), High-resolution peripheral Quantitative Computed Tomography (HR-pQCT), Metatarsophalangeal (MTP), Rheumatoid Arthritis (RA), Confidence Interval (CI).

Conclusion: This is the first study to evaluate erosions with HR-pQCT of the 4th and 5th MTP joints, including a comparison to CR. Erosions were frequent at the lateral aspect of the MTP joints, suggesting that mechanical and biomechanical demands may play a role in the development of erosions in the MTP joints. The superiority of HR-pQCT compared to CR for detecting erosions provide a basis for larger studies assessing bone changes in the MTP joints.

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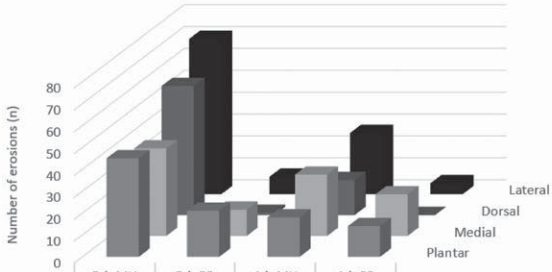

	5th MH	5th PB	4th MH	4th PB
Plantar	45	21	18	14
Medial	40	12	28	19
Dorsal	59	1	16	0
Lateral	71	8	28	5

Figure 1: Total number and distribution of erosions in the 4th and 5th MTP joints by HR-pQCT. Metatarsal Head (MH), Proximal Base (PB), Metatarsophalangeal (MTP), High-resolution peripheral Quantitative Computed Tomography (HR-pQCT).

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POS0134

RELATIONSHIP BETWEEN RETINAL VASCULAR DENSITY DETECTED THROUGH OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY AND INTIMAL MEDIAL THICKNESS: A NEW POTENTIAL MARKER OF CARDIOVASCULAR INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) patients have a 3- fold risk of CV events compared to the general population, mainly due to accelerated atherosclerosis that is not completely explained by the presence of traditional CV risk factors. Individuals with increased Intimal medial thickness (IMT) carry a higher risk to develop carotid atherosclerosis. Accordingly, IMT acts as a marker of subclinical atherosclerosis. In recent studies, SLE patients showed a significant higher IMT compared to healthy subjects. On the other side, SLE retinal involvement can be detected in 7-29% of cases, it is characterized mainly by retinal vasculopathy and it can be a marker of systemic vascular involvement. Optical Coherence Tomography Angiography (OCTA), a new diagnostic technique that can visualize retinal blood flow and evaluate the Fovea Avascular Zone (FAZ), has been investigated as an instrument for early detection of subclinical retinal vascular impairment in SLE.
Objectives: Aim of this study is to examine a possible correlation between IMT and retinal vascular impairment assessed through OCTA in SLE.
Methods: We recruited SLE patients fulfilling 2019 EULAR/ACR classification criteria. Patients with other rheumatic, ophthalmological diseases, diabetes or history of CV diseases were excluded. We also collected patients' demographic and clinical data, including sex, age, smoking habit, BMI, systolic and diastolic blood pressure (BP), C-Reactive Protein (CRP), total cholesterol, LDL, HDL, triglycerides. All patients underwent an ophthalmological evaluation, including OCTA estimation of superficial and deep retinal vessel density (VD), considering both the whole image and the foveal region, and FAZ area. Carotid ultrasound (US) comprising IMT assessment was also performed. Statistical analysis was accomplished using unpaired t-test or Mann Whitney U test, Pearson or Spearman rank correlation when appropriate.
Results: We enrolled 37 SLE patients; demographic, clinical and US data are displayed in Table 1. Nine patients (24.3%) had uncontrolled arterial hypertension. According to US evaluation, carotid plaques were detected in six patients (16.2%). OCTA data were correlated with IMT values showing a negative correlation between IMT and both superficial and deep fovea VD (p=0.003, r=-0.4 and p=0.004, r=-0.4), while a positive correlation was found with FAZ area (p=0.02, r=0.4).

Table 1. Demographic, clinical and US data of the study population

Female sex n(%)	28 (75.6)
Age, yrs	49.2±14.7
Smokers n(%)	12 (32.4)
BMI	25.1±5.2
SBP, mmHg	118.5±15.7
DBP, mmHg	73.3±11.6
IMT, μM	549.6±124

IMT positively correlated with traditional CV risk factors, particularly age (p<0.0001, r=0.7), BMI (p=0.007, r=0.3) and systolic BP (p=0.001, r=0.4). Patients with high BP levels showed not only a significant higher IMT compared to the group with normal BP values (p=0.04), but also a significant increased FAZ area (p=0.02). FAZ area correlated positively with CRP levels (p=0.0001, r=0.5). Triglycerides showed a positive correlation with IMT values (p=0.001, r=0.4) and FAZ area (p=0.04, r=0.3) while correlated negatively with deep fovea VD (p=0.04, R=-0.4). A reduction in deep whole retinal VD was detected among patients with carotid plaques compared to the group without (p=0.02), together with higher IMT values (p=0.04).
Conclusion: Retinal vascular impairment in SLE has been associated with IMT, atherosclerotic plaques and some CV risk factors as hypertension, hypertriglyceridemia and CRP levels. Search for new markers of preclinical CV damage in SLE is currently ongoing and OCTA might be an additional instrument to assess preclinical cardiovascular involvement in SLE.
Disclosure of Interests: None declared
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Biomarkers in pathogenesis, monitoring and treatment of rheumatic diseases

POS0135

DOWNREGULATION OF MIR-885-5P AS A KEY EFFECTOR IN CUTANEOUS LUPUS ERYTHEMATOSUS PATHOGENESIS

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Background: Skin involvement is common in systemic lupus erythematosus (SLE), with up to 70% of patients developing skin lesions at some point during the course of their disease. Moreover, cutaneous lesions are the first sign of systemic disease in 20% of SLE patients [1]. Skin requires a regulated and undisrupted miRNA profile for a correct development and function. Studies show that miRNAs play a pathogenic role in autoimmune skin diseases such as Psoriasis [2]. Understanding of the role of deregulated miRNAs in CLE may enhance our knowledge about CLE pathogenesis which is currently not understood.
Objectives: Identify differentially expressed miRNAs in skin lesions to determine their role in CLE pathogenesis.
Methods: Paired skin biopsies from CLE lesional (n=20) and non-lesional skin (n=20) were obtained. MiRNA microarray screening was performed using TaqMan MicroRNA Array. Validation was performed in a new cohort of FFPE skin samples by qRT-PCR (n=20). *In situ* hybridization was performed to identify the skin cell type involved in selected miRNAs. Next, *in vitro* experiments using primary skin and immune cells were performed in order to discover their role in CLE pathogenesis. A microarray screening and luciferase assay were performed to find miR-885-5p altered gene expression, molecular pathways and target genes.
Results: MiR-885-5p was found downregulated in CLE lesional skin (-4.45 fold, pvalue<0,01, respectively). Results were confirmed in a validation cohort. *In situ* hybridization revealed miR-885-5p was located in the epidermal keratinocytes in CLE non-lesional skin. Healthy keratinocytes presented an increased miR-885-5p expression compared with other relevant cell types such as fibroblasts (p<0.001) or PBMCs (p<0.001). Moreover stimulation with IFNα and UVB promoted a marked long-lasting downregulation of miR-885-5p (IFNα, 24h -67 fold (p<0.001); UVB, 24h -70 fold (p<0.001)).
Gene microarray of anti-miR-885-5p keratinocytes showed that the unique gene that was upregulated in all anti-miR-885-5p conditions was PSMB5. In *vitro* experiments demonstrated that PSMB5 is a direct target of miR-885-5p (74% of reduction p<0.001) and it is involved in epidermal inflammation by enhancing NFKB and inflammatory cytokines IL-1β, TNFα and CXCL8. In addition, we observed immune recruitment in UVB stimulated anti-miR885-5p keratinocytes and we found that this immune migration is mediated via miR-885-5p

direct binding of TRAF1 and subsequent chemokine CCL5, CCL20, CXCL8 and S100A7 secretion.

Conclusion: Our findings demonstrate that CLE lesions present a downregulation of miR-885-5p that is strongly implicated in CLE pathogenesis. Moreover, miRNA applicability as therapeutics makes the discovered miRNAs promising candidates for novel therapy in CLE, as there is a need to develop new therapies for refractory cases and to avoid current treatment significant side effects.

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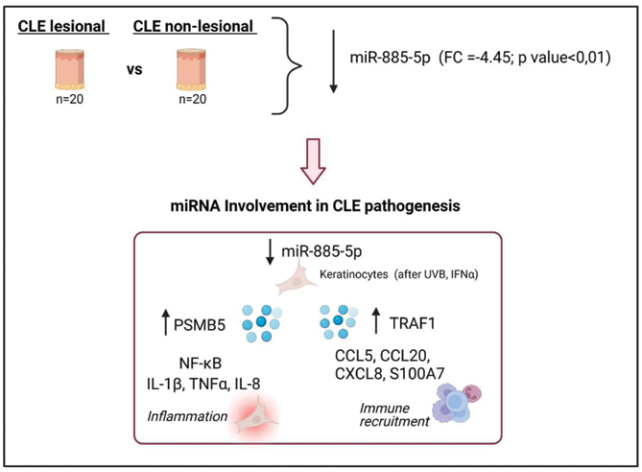

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POS0136

COMPLEMENT C1Q PROMOTES MITOCHONDRIA RESPIRATION AND SECRETION OF IL-6 AND IL-1B BUT NOT TNF-A BY SYNOVIAL MACROPHAGE IN RHEUMATOID ARTHRITIS

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Background: Complement C1q (C1q), predominantly synthesized by myeloid cells such as macrophages, has elusive functions in the pathogenesis of rheumatic arthritis (RA). Binding to its receptor gC1qR, C1q can activate mitochondria, the dysfunction of which may result in tissue inflammatory disease [1]. Bone marrow derived macrophages in RA patients have elevated OXPHOS activity [2], while the reason remains to be discovered.

Objectives: The objectives of the study were to explore the expression of C1q and its receptor gC1qR in synovial macrophages in RA and whether C1q contributes to tissue inflammation via affecting pro-inflammatory cytokines (IL-1β, IL-6 and TNF-α) and mitochondria respiration in synovial macrophages.

Methods: Tissue transcriptome analysis for C1q(C1qA, C1qB and C1qC), C1q receptors (including gC1qR) in rheumatoid synovium and and pro-inflammatory cytokines (IL-6, IL-1β and TNF-α) in rheumatoid synovium and synovium macrophages were quantified by RT-PCR. Concentrations of C1q in the plasma of RA and healthy controls (HC) were analyzed by ELISA and the correlation between plasma C1q and disease activty measured by DAS28 were calculated. gC1qR protein expression was detected by flow cytometric analysis and immunoblotting. Synovial macrophages were isolated and stimulated with or without C1q for 24 h. Function of gC1qR was analysed by knockdown experiment using siRNA. Transcripts for inflammatory cytokines were quantified by RT-PCR. Mitochondrial respirometer was evaluated with Seahorse Bioscience XF96 analyzer after C1q treatment or gC1qR knockdown.

Results: C1qA, C1qB,C1qC and gC1qR were all upregulated in both rheumatoid synovium and synovial macrophages compared to healthy controls. Meanwhile, RA patients had a higher level of C1q concentration in plasma, which positively correlated with DAS28. Moreover, an increased expression of gC1qR protein was confirmed by flow cytometric analysis and immunoblotting. Besides, C1q could increase the expression of IL-6 and IL-1β but not TNF-α in synovial macrophages. We also found that C1q could increase basal OCR, ATP-coupled OCR, max respiration and reserve capacity of healthy macrophages. Comparatively, gC1qR knockout could down-regulate mitochondria respiration of RA macrophages.

Conclusion: Synovial macrophages in RA patients have significantly elevated expression of C1q and its receptor gC1qR. C1q could promote mitochondria respiration through gC1qR, thus leading to hyper-metabolism in macrophages from RA patients. C1q could promote synovitis through enhanced pro-inflammatory cytokines IL-6 and IL-1β but not TNF-α secreted by synovial macrophages, which represents a novel therapeutic target in RA.

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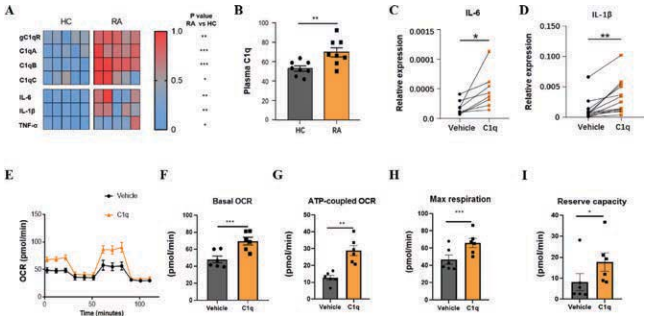

Figure 1. The expression and function of C1q in RA macrophage. A.Transcripts for gC1qR, C1qA, C1qB and C1qC and pro-inflammatory cytokines were quantified by RT-PCR in synovial macrophage of RA and healthy control (HC), n=6; B. Concentrations of C1q in the plasma of RA and HC were measured by ELISA, n=8; C-D. Transcripts for pro-inflammatory cytokines were quantified by RT-PCR after C1q treatment, n=9; E-I. Mitochondrial respirometer was evaluated with Seahorse Bioscience XF96 analyzer by adding test agents in order of 1, oligomycin; 2, FCCP; 3, anti-mycin A/rotenone. Total trend and each segmentation of oxygen consumption rates (OCR) were shown after treated with C1q, n=6. *P < 0.05; **P < 0.01; ***P < 0.001.

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POS0137

FREQUENCIES OF WNT PATHWAY GENE VARIANTS ASSOCIATED WITH ANTI CARBAMYLATE PROTEIN IN EARLY RHEUMATOID ARTHRITIS

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Background: Increased bone resorption and impaired bone formation characterize the pathogenesis of rheumatoid arthritis (RA). Wnt/β-catenin pathway regulates osteoblast function. Since bone mineral density (BMD) and RA joint destruction are partially inherited, we studied the association of Dickkopf-1 (DKK-1), sclerostin (SOST), Kremen-1 and lipoprotein receptor-related protein-5 (LRP-5) genes single nucleotide polymorphisms (SNPs).

Objectives: To establish the genotypic frequency of variants of the DKK-1 (rs1896368, rs1896367, rs1528873), SOST (rs6503475), Kremen-1 (rs132274) and LRP-5 (3736228) genes in patients with early RA (eRA) and first degree relative (FDR) with healthy controls (HC), and its association with autoimmunity profile.

Methods: Colombian individuals were matched by age and gender. Serological and clinical indices were measured. Variants associated with the Wnt pathway; DKK-1, SOST, LRP-5, and Kremen were analyzed using High Resolution Melting and confirmed by Sanger sequencing. A bivariate analysis was conducted in eRA and FDR. A logistic regression was performed.

Results: 232 individuals were evaluated; 66 eRA patients, 50 FDR, and 116 HC. For eRA, 78.8% were female, with a median age 52 years (IQR: 38,8-56). Higher levels of CRP: 4,2 (IQR: 1,6-11,6), RF: 30,2 (IQR: 1,2-74,1), anti-CCP: 7,81 (IQR: 7,81-104,9) and anti-Carbamylate protein (CarP): 17,7 (IQR: 12,3-31,8) were observed.

Among eRA, FDR, and HC genotypic frequencies are listed in Table 1, there were significant differences among DKK-1 rs1528873 GA and AA (p<001), Kremen GG and GA (p<0,001), and LRP5 GG and GA (p=0,038), and GG with AA (p=0,023). In haplotype analysis between eRA and HC for DKK-1 rs1896368 GA and LRP-5 AA (p=0,033) and for LRP5 GG and AA DKK-1 rs1528873 (p<0,001).

Table 1. Population genotypic frequencies

	eRA	FDR	HC	
	n(%)	n(%)	n(%)	p value*
DKK-1 rs1896367	27 (40,9)	25 (50)	57 (49,1)	
GG Native	39 (59,1)	25 (50)	59 (50,9)	0,528
GA Homozygous	4 (6,1)	4 (8)	8 (6,9)	0,890
AA Heterozygous	23 (34,8)	21 (42)	49 (42,2)	0,597
DKK-1 rs1896368	59 (89,4)	45 (90)	98 (84,5)	
GG Native	7 (10,6)	5 (10)	18 (15,5)	0,543
GA Homozygous	30 (45,5)	21 (42)	54 (46,6)	0,882
AA Heterozygous	29 (43,9)	24 (48)	44 (37,9)	0,450
DKK-1 rs1528873	25 (37,9)	24 (48)	59 (50,9)	
TT Native	42 (62,1)	26 (52)	57 (49,1)	0,233
TG Homozygous	24 (36,4)	5 (10)	6 (5,2)	**<0,001**
GG Heterozygous	1 (1,5)	19 (38)	53 (45,7)	**<0,001**
SOST rs6503475	51 (77,3)	35 (70)	85 (73,3)	
GG Native	15 (22,7)	15 (30)	31 (26,7)	0,657
GA Homozygous	13 (19,7)	9 (18)	28 (25)	0,580
AA Heterozygous	38 (57,6)	26 (52)	56 (48,3)	0,488
KREMEN rs132274	62 (93,9)	28 (56)	102 (87,9)	
CC Native	4 (6,1)	22 (44)	14 (12,1)	**<0,001**
CT Homozygous	35 (53)	6 (12)	54 (46,5)	**<0,001**
TT Heterozygous	27 (40,9)	22 (44)	48 (41,4)	0,953
LRP-5 rs3736228	23 (34,8)	16 (32)	22 (19)	
CC Native	43 (65,2)	34 (68)	94 (81)	**0,038**
CT Homozygous	3 (4,5)	10 (20)	3 (2,6)	**0,038**
TT Heterozygous	20 (30,3)	6 (12)	19 (16,4)	**0,023**

In eRA SOST rs6503475 was associated with anti-CarP (AOR 3,4 [95%IC 1,1-10,8] p=0,037). LRP-5 with former smoking (AOR 8,6 [95%IC 2,0-36,4] p=0,004). Additionally, in patients with a combination of at least three SNPs with a lower frequency of anti-Carp peptide (AOR 0,09 [95%IC 0,012-0,608], p=0,014), meanwhile a combination of at least five SNPs with a higher frequency of anti-Carp (AOR 4,7 [95%IC 1,27-17,1] p=0,020) were observed. There were no differences in FDR group.

Conclusion: Significant associations between Wnt pathway genes variants, haplotypes, and antibody profile could reinforce evidence to relation of high titters of anti-CarP with decreased BMD in eRA patients.

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POS0138 RHEUMATOID SYNOVIAL FIBROBLASTS DISPLAY IMPRINTED MEMORY OF THEIR SYNOVIAL ENDOTYPE WHICH CAN BE PLASTICALLY MODULATED BY B-CELLS CROSSTALK

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Background: Despite advances in the treatment of Rheumatoid Arthritis (RA), synthetics and biologicals drugs are ineffective in ~40% of patients. The origin of this refractoriness is unclear, but several clues point at the synovial microenvironment (SE) and the relative cellular heterogeneity between patients. We previously described the existence of different RA endotypes such as the lympho-myeloid, LM, which is B-cell rich and the fibroid-paucimmune, FPI, which is devoid of B-cells. While there is clear evidence that the crosstalk between stromal and immune cells in rheumatoid joints is critical for the perpetuation of chronic inflammation and autoimmunity, it is currently unknown whether transcriptional signatures identified in synovial fibroblasts (SFs) derived from different RA endotypes are driven by "imprinted" properties of the SFs or are shaped by the interaction with infiltrating immune cells in the RA joints.

Objectives: I) to identify "imprinted" vs "inducible" RASFs signatures trough the comparison of freshly isolated SFs and primary established SFs cultures obtained from LM vs FPI RA synovial biopsies and ii) to investigate the identified RASF signature as predictive biomarkers of disease evolution and of response to conventional and biological DMARDs.

Methods: We performed flowcytometry and single cell RNA sequencing (sc-RNAseq) on SFs obtained from LM and FPI biopsies, in isolation or in co-culture with RA B cells. Next, supernatant has been screened trough Multiplex and ELISA. Furthermore, we compared our results to publicly available sc-RNAseq datasets on freshly isolated SFs and to our bulk-RNAseq data from clinical trials patients.

Results: Hierarchical clustering from sc-RNAseq transcriptional profiling of LM vs FPI RASF - after several cell passages - identified profoundly different gene signatures: whereby LM-RASF were characterised by genes involved in inflammation, proteoglycan formation and integrin binding, FPI-RASF were defined by genes related to collagen biosynthesis. Comparing the above signatures with those of freshly isolated RASF we identified both imprinted (i.e. maintained through several in vitro passages) and inducible (i.e. loss after long term culture) gene signatures. Notably, RA B-cells co-cultured with FPI-RASF profoundly altered the FPI-RASF transcriptional profile including the ex-novo expression of gene signatures typical of LM-RASF. Consensus gene modules constructed on LM vs FPI RASF imprinted gene signatures could be tracked in longitudinal whole tissue bulk RNA-seq data obtained from both early arthritis and established RA and were associated with synovial pathotype-specific histological and clinical features. Finally, modulation of FPI-RASF related genes following B-cell depletion identified poor responders to Rituximab in the R4RA randomised clinical trial.

Conclusion: Our work demonstrates that RASFs from different endotypes display imprinted memory of their original synovial tissue when maintained in culture over several months. We also demonstrated that imprinted memory typical of RASF isolated from B-cell rich LM synovial tissues can be dynamically modulated in FPI RASF following crosstalk with RA B cells. Finally, consensus gene modules based on FPI vs LM RASF-gene signatures were able inform on response/resistance to targeted biologic therapies.

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POS0139 RELATIONSHIP BETWEEN SYNOVIAL FLUID IMMUNE CELL PHENOTYPES AND CLINICAL OUTCOMES IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis (KOA) is a highly heterogeneous and multifaceted disease with many clinical phenotypes that often overlap. So far, phenotypes based on the composition of immune cells in synovial fluid (SF) have not yet been defined, although these cells, their activation and the mediators they produce play a central role in the pathophysiology of OA.

Objectives: This study aimed to investigate the relation between SF-derived immune cells and SF protein patterns in patients with KOA and its relationship to disease trajectory. Special emphasis was given to chemokine receptor expression on macrophages.

Methods: Immune cell phenotype and protein pattern from 119 KOA patients were analysed using flow cytometry. KOA phenotypes were determined by multivariate network analysis and related to clinical outcome 3-6 months post-sampling. The chemokine receptor pattern on macrophages was analysed using the FlowSOM algorithm and verified by manual gating.

Results: Four KOA-phenotypes were detected based on the distribution of T-lymphocytes, monocyte-macrophage lineage cells and activated CD8+ T-lymphocytes. The "healing" phenotype (n=17) had a high proportion of T lymphocytes, but low NK cells, monocyte-macrophage lineage and neutrophils, showing improved symptoms in 70% of patients. The "pain-less" phenotype (n=31) characterised by a higher percentage of neutrophils and a lower percentage of lymphocytes and monocyte-macrophage lineage as well as its activation, showed lower levels of pain. Next, the "progressive" phenotype (n=35) was represented by high NK percentage and monocyte-macrophage lineage representation yet low lymphocyte percentage and T-lymphocyte activation. From the „inflammatory progressive" phenotype (n=36) with a high proportion of activated lymphocytes, macrophages, NK cells and neutrophils, only 39% of patients improved during follow-up. The phenotypes obtained showed differences in CXCL10 expression, with high levels in the "healing" KOA1 compared to the "inflammatory progressive" KOA4 phenotype (1106 vs 126 pg/ml, p=0.001). In general, high CXCL10 levels were associated with improved disease trajectory compared to patients with

worsening symptoms (339 vs 222 pg/ml, p=0.002). CXCL10 levels in patients with improved symptoms showed a decreasing trend between phenotypes from KOA1 > KOA2 > KOA3 > KOA4. Regarding macrophages, low expression of chemokine receptors CXCR4 and CCR7 on macrophages was associated with improved symptoms regardless of KOA phenotype.

Conclusion: We identified four KOA phenotypes differing in immune cell percentage and activation associated with different clinical trajectories. Low expression of chemokine receptors CXCR4 and CCR7 on macrophages and high CXCL10 in SF was linked to KOA symptom improvement. How these phenotypes can be targeted therapeutically deserves future investigations.

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POS0140 PREDICTING OUTCOMES IN SYSTEMIC SCLEROSIS: STRATIFICATION BY AUTO-ANTIBODIES OUTPERFORMS CUTANEOUS SUBSETTING IN THE EUSTAR COHORT

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Background: Risk-stratification is key in a heterogeneous disease like systemic sclerosis (SSc). Until now, SSc patients are stratified according to the extent of skin involvement into limited cutaneous, diffuse cutaneous and sine scleroderma subtypes. However, this classification remains inaccurate to capture disease heterogeneity. Autoantibodies are found in more than 90% of the patients and can be detected before onset of the disease. Among them, three predominant and specific antibodies are used: anti-centromere, anti-Scl70 and RNA polymerase III antibodies.

Objectives: To compare the performances of stratification into LeRoy's cutaneous subtypes versus autoantibody status in SSc versus combination of cutaneous subtypes and autoantibodies status.

Methods: Patients from the EUSTAR database were classified either as (i) limited cutaneous, diffuse cutaneous or sine scleroderma (based on the recording made by the treating physician) or (ii) according to autoantibodies with the following subclassifications: (1) no specific autoantibodies, (2) isolated ANA, (3) anti-centromere antibodies, (4) anti-Scl70 antibodies and (5) anti-RNA polymerase III antibodies or (iii) according to combination of cutaneous subset and auto-antibodies. The respective performance of each model to predict overall survival (OS), progression-free survival (PFS), disease progression and different organ involvements was assessed and the three models were compared by the area under the receiver operating characteristic curve (AUC 95%CI) and the net reclassification improvement (NRI). Missing data were imputed through multiple imputation using chain equations.

Results: In all, 10'711 patients were included: 84.6% females, mean age: 54.4±13.8 years, mean disease duration: 7.9±8.2 years. In the prospective analysis (n= 6'467 to 7'829 according to the outcome), after a mean follow-up of 56 months and a mean of three visits per patient, we did not identify any difference in AUC between the cutaneous-based model and the antibody-based model for prediction of OS and disease progression. However, the NRI showed a significant improvement in prediction of OS (0.57 [0.46-0.71] vs. 0.29 [0.19-0.39]) and disease progression (0.36 [0.29-0.46] vs. 0.21 [0.14-0.28]) at 4 years using the antibody-based model. Regarding prediction of each organ involvement in longitudinal analyses, the antibody-based model showed better performance than the cutaneous-one for renal crisis (AUC: 0.719 [0.696-0.742] vs. 0.664 [0.643-0.685]), with the highest association observed with anti-RNA polymerase III (OR: 7.47 [1.63-34.24], p= 0.010). Similarly, the antibody-based model was better than the cutaneous model in predicting lung fibrosis (AUC 0.719 [0.715-724] vs. 0.653 [0.647-0.659]) and restrictive lung fibrosis (AUC 0.759 [0.749-0.766] vs. 0.711 [0.701-0.721]) which were both associated with anti-Scl70 antibodies (OR: 9.29 [8.17-10.55] and 7.92 [5.37-11.69], respectively, p<0.0001 for both). Although there was no difference in the AUC to predict digital ulcers, NRI showed an improvement using the antibody-based model (0.31 [0.29-0.33] vs. 0.24 [0.22-0.26]) with the highest association with anti-Scl70 antibodies (OR: 3.57 [2.68-4.75], p<0.0001). The two models had similar performances in assessing occurrence of intestinal involvement, heart dysfunction or elevated sPAP. Combining both antibody status and cutaneous subtype did not improve the performance of our models. In the exploratory analysis, there was no change using modified Rodnan skin score to define cutaneous form.

Conclusion: Auto-antibody status outperforms the common cutaneous subsetting to risk-stratify SSc patients in the EUSTAR cohort. This easily performed subclassification using autoantibodies specific status can be used by the clinicians to risk-stratify their patients and to adapt disease monitoring in routine practice.

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POS0141 PLATELET-SELECTIN PRIME LUPUS NEUTROPHILS TO PRODUCE MITOCHONDRIAL ROS AND PARTICIPATE IN SLE PATHOGENESIS

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Background: In patients with active systemic lupus erythematosus (SLE), circulating platelets have an activated phenotype characterized by the expression of P-selectin (CD62P). We have shown that in human SLE, platelets interact with T regulatory cells and repress their immunosuppressive functions through a P-selectin/CD15s-dependent interaction (1). Preliminary results showed that neutrophils express high level of CD15s, predicting a possible platelet/neutrophil interaction in SLE.

Objectives: Investigate platelet/neutrophils interaction in human SLE and evaluate its impact on neutrophil functions, and lupus pathogenesis.

Methods: Patients with SLE responding to the 2019 ACR/EULAR criteria were recruited for blood sampling (n = 30). Disease activity was measured using

SLE disease activity index (SLEDAI-2K), and patients were considered active if SLEDAI-2K ≥ 6. Platelet-neutrophils aggregates were identified as (platelet) $CD61^+$ (neutrophil) $CD66b^+$ cells using flow cytometry on fresh blood samples. Single-cell cytosolic calcium and ROS imaging was performed by incubating cell with either a fluorescent calcium dye (cali-520), or a mitochondrial specific dye (MitoSox). Coverslips were mounted in an Attofluor cell chamber positioned on the stage of an inverted epifluorescence microscope (Olympus, IX70). Mitochondrial polarization of human neutrophil was evaluated by incubating cells with TMRM (100 nM) for 30 minutes. Platelet-free plasma was isolated by two sequential centrifugations (3500xg) of EDTA-anticoagulated blood and stored for subsequent evaluation of soluble P-selectin (using ELISA) and (platelet-derived) microparticular P-selectin (using flow cytometry).

Results: In healthy donors (HD) and patients with SLE, circulating neutrophils expressed significantly higher levels of the P-selectin ligand CD15s compared to lymphoid subsets ($p < 0.001$), predicting platelet/neutrophil interactions. In contrast to HD and patients with inactive SLE, those with active disease had a significant increase of circulating platelet-neutrophils aggregates ($p < 0.05$), and these aggregates correlated with the SLEDAI ($r = 0.59$, $p < 0.001$). The incubation of human neutrophils with recombinant P-selectin induced a strong intracellular calcium signaling which was inhibited by preincubating neutrophil with anti-PSGL1 antibody (blocking P-selectin/CD15s interaction) or with a Syk kinase inhibitor. Similarly, P-selectin induced a mitochondrial ROS release in a CD15s- and Syk-dependent manner. Interestingly, incubation of neutrophils with anti-dsDNA IgG and P-selectin induced mitochondrial depolarization, which was absent with either stimulus alone. Soluble and platelet-derived microparticular P-selectin levels were significantly increased in patients with active SLE compared to inactive patients or healthy donors ($p < 0.05$ and $p < 0.001$, respectively). In a longitudinal analysis of SLE patients, soluble and microparticular P-selectin levels closely followed clinical (SLEDAI) and biological (C3 levels) markers of SLE disease activity.

Conclusion: P-selectin levels are increased in active SLE and follow hallmark of disease activity. P-selectin induces calcium/mitochondrial ROS signaling in lupus neutrophils which are key players in SLE pathogenesis. We hypothesize that the inhibition of P-selectin pathway might be a promising target in SLE.

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POS0142

DISTINCT EXPRESSION CLUSTERS OF INTERFERON-REGULATED GENES ASSOCIATE DIFFERENTLY WITH DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background: Systemic lupus erythematosus (SLE) is a complex multiorgan autoimmune disease that primarily affects women during child-bearing years. The aetiology of SLE involves inadequate clearance of nuclear material released from apoptotic cells. The persistence of host DNA and RNA triggers the immune system to react as seen in a viral infection, causing persistent activation of anti-viral interferon (IFN) signalling pathways. Aberrant production of IFN cytokines, type 1 in particular, results in elevated levels of >1000 IFN-regulated gene (IRG) expression in the blood, termed an IFN signature. The IFN signature is typically measured as a score combining the expression levels of a subset of 3-4 IRGs. Several cross-sectional studies have pointed to an association between the IFN signature and disease activity, however subsequent longitudinal studies and a recent systematic review by our group[1] have failed to reproduce these findings. It was suggested that the lack of association between the IFN signature and disease activity was because the IRGs that are sensitive to disease activity are not typically included in the subset of IRGs used to determine an IFN score[2]. Uncovering the significance of the IFN signature in SLE disease activity is particularly relevant for evaluating the scope of IFN pathway inhibitors and may explain why these fail to have a significance for the primary endpoint in clinical trials[3].

Objectives: -Determine the mRNA expression of a broad subset of IRGs (>100) in a cross-sectional study of SLE patients with diverse clinical manifestations
-Investigate the association between IRG expression and disease activity
-Validate the findings from a cross-sectional study in a longitudinal study of SLE patients with fluctuating disease activity

Methods: In a cross-sectional study, peripheral blood samples from 34 SLE patients and 15 healthy controls were collected in PAXgene tubes. Ten SLE patients were followed longitudinally, and peripheral blood samples were collected in PAXgene tubes at time of inclusion and after 12 months. Disease activity was assessed by SJ in all patients and determined by means of SLE Disease Activity Index 2000 (SLEDAI-2K) and European Consensus Lupus Activity Measurement Index (ECLAM). RNA from peripheral blood cells (PBCs) was extracted using the PAXgene Blood RNA kit. The mRNA transcripts of 128 IRGs were measured using the multiplexed NanoString nCounter Gene Expression platform. Bioinformatics and statistical analyses were performed using nSolver and SPSS software.

Results: Out of 128 IRGs, 46 were highly expressed in SLE patients as compared to controls and seemed to co-express in mainly two distinct clusters, Figure 1. Expression scores for cluster K1 did not correlate with SLEDAI or ECLAM in a cross-sectional setting, whereas K2 expression scores did ($p<0.01$). These findings were confirmed by correlation analysis of changes in K1 and K2 expression scores with scores of disease activity in a longitudinal setting.

Conclusion: Interferon signatures may express differentially with varying associations with disease activity.

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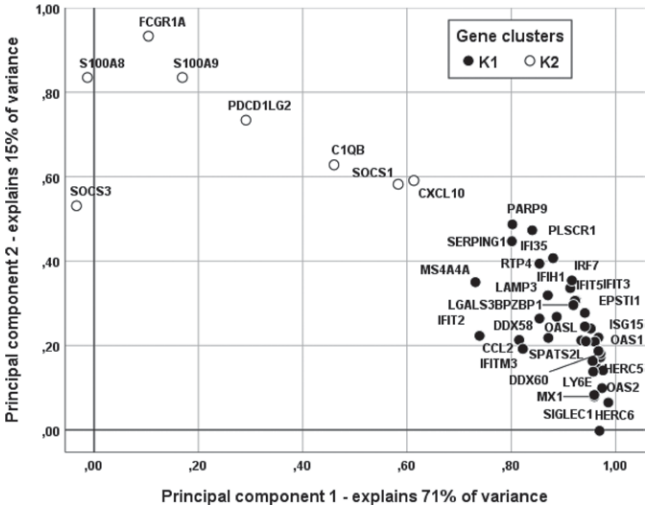

Figure 1.

Disclosure of Interests: None declared

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POS0143

COMPOSITION AND ASSOCIATIONS OF THE GUT MICROBIOTAWITH PERIPHERAL LYMPHOCYTE SUBSETS AND CYTOKINES IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: The idiopathic inflammatory myopathies (IIM) are a group of acquired myopathies characterized by inflammatory lymphocytes infiltrates in muscle tissue[1].Gut microbiota serves as a critical environmental component of autoimmune disease pathogenesis such as IIM[2].

Objectives: This study sought to investigate the composition of gut microbiota and the relationship between microbiota structure and lymphocyte subpopulations and cytokines in IIM patients to recommend feasible intervention strategies.

Methods: Faecal samples were taken from 37 IIM patients and 37 age- and gender- matched healthy controls (HCs) in a sterile environment placed into the Second Hospital of Shanxi Medical University. Microbiome profiling was performed by sequencing of the V3-V4 variable regions of the 16S rRNA gene and the peripheral T lymphocyte subsets of these participants were assessed by flow cytometry. The clinical laboratory data such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and immunoglobulin were also determined. In terms of gut microbia, the diversity and richness was evaluated from two aspects: alpha diversity and beta diversity with the indices of ACE, Chao1, Shannon and Simpson. Analyses were conducted using R version 4.0.1. Pearson correlation was applied to assess the relationship between the relative abundances of bacterial genera and clinical parameters, and $p < 0.05$ was considered to be statistically significant.

Results: The α-diversity analysis of the richness (Chao1) and diversity (Shannon and Simpson) were reduced in IIM samples compared with those of HCs (Figure 1A, $p < 0.05$). Bray curtis distance-based beta diversity analysis revealed significant differences in the microbial community between IIM and HCs (Figure 1B, $p = 0.001$,

ANOSIM). Detailly, at the genera level, IIM patients had a higher abundance of Enterococcus, Veillonella, Streptococcus, et al. and a lower abundance of Roseburia, Lachnospira, Klebsiella, et al(Figure 1D, $p < 0.05$). In IIM patients, Fusobacteriota correlated positively with the ratio of Th1 cells (Figure 1E, $p < 0.01$), and there was a significant positive correlation between Synergistota and B lymphocyte (Figure 1E, $p < 0.01$). Besides, Euryarchaeota and Cyanobacteria were both positively and significantly related to IL-6, IFN-γ and C-reactive protein (CRP) (Figure 1E, $p < 0.001$).

Conclusion: Richness and diversity of intestinal flora in IIM patients were impaired, which might participate in the pathogenesis of IIM by disturbing lymphocyte subpopulations and cytokines. Regulating intestinal flora and restoring homeostasis might become a critical therapeutic methods of IIM.

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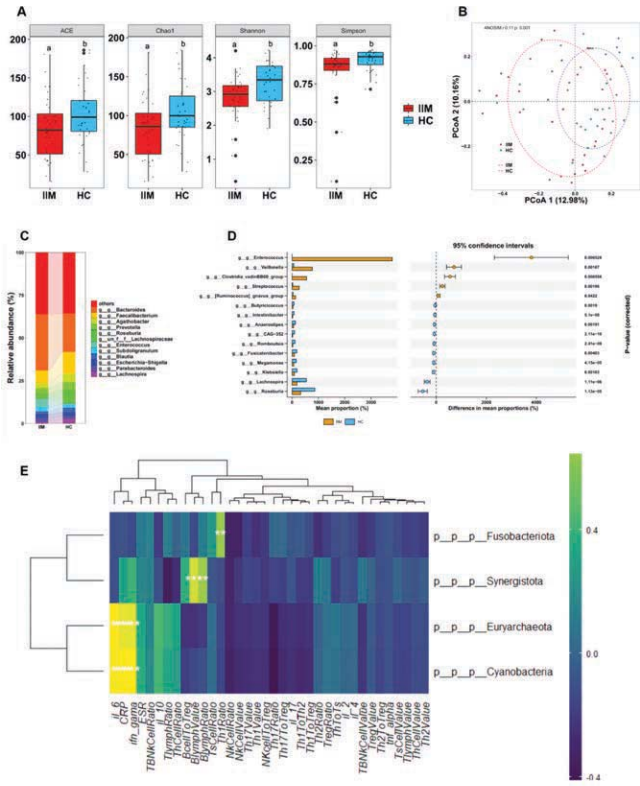

Figure 1: Feature of gut microbiota in IIM patients and HCs. (A) Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson). Median estimates compared across cohorts. (B) Principal component analysis (PCoA) plot generated from the Bray-Curtis distances. (C) Microbiota composition based on relative abundance at the genera levels. (D) Panel demonstrated the average relative abundance of different genus in IIM and HCs. (E) Correlation analysis of these differential phylum and lymphocyte subsets and clinical indicators between any two groups using Spearman's correlation analysis.The correlation effect is indicated by a color gradient from green (positive correlation) to purple (negative correlation). *p<0.05. **p<0.01. ***p<0.001.

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POS0144 NOVEL ANTIBODY BIOMARKERS THAT PREDICT FAILURE TO ACHIEVE EARLY AND SUSTAINED DISEASE REMISSION OR LOW DISEASE ACTIVITY AFTER INTENSIVE FIRST-LINE THERAPY IN RHEUMATOID ARTHRITIS

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Background: Current EULAR guidelines for the management of rheumatoid arthritis (RA) recommend the use of classical synthetic disease-modifying anti-rheumatic drugs (csDMARDs), combined with short-term use of glucocorticoids (GC) as first-line therapy. Still, finding out which patients will show a poor response to such intensive first-line therapy is currently based on trial and error. Therefore, we recently performed a screening for novel antibody biomarkers that could predict the lack of response to csDMARD/GC combination therapy, resulting in identification of antibodies to 6 novel University Hasselt (UH)-RA antigens.

Objectives: The aim of this study was to validate these novel antibody biomarkers for their potential to identify at baseline, which RA patients fail to reach remission (rem-), or low disease activity (LDA), after intensive csDMARD therapy.

Methods: Presence of antibodies to the identified UH-RA antigens was measured using ELISA in 179 baseline samples from participants of the CareRA trial, which evaluated the efficacy of different first-line combination therapies[1]. Baseline antibody reactivity was correlated with remission or LDA, over a two-year follow-up period, according to the Disease Activity Score based on 28 joints with C-reactive protein (DAS28CRP), the DAS28 with erythrocyte sedimentation rate (DAS28ESR), and the clinical/simplified disease activity index (CDAI/SDAI).

Results: Baseline antibody reactivity against a panel of 3 antigens was higher in patients failing to reach DAS28CRP (31 vs 15%, p=0.007) or DAS28ESR (30 vs 14%, p=0.007) remission at week 8, or those failing to reach SDAI (36 vs 17%, p=0.018) or CDAI (37 vs 17%, p= 0.01) LDA at week 8, compared to RA patients that did reach these respective disease states. Baseline antibody reactivity correlated with lack of DAS28CRP remission after 8, 16, 40 and 52 weeks of first-line therapy, and was present in one in three DAS28CRP rem- patients, and in one in two DAS28CRP rem- patients that were seronegative for RF and ACPA. For each of the remission criteria studied (DAS28CRP, DAS28ESR, SDAI and CDAI), baseline antibody reactivity against these antigens was significantly higher in RA patients that did not maintain sustained remission (resp. 25 vs 12%, p=0.029; 24 vs 11%, p=0.041; 24 vs 4%, p=0.009; 24 vs 4%, 0.011), or sustained LDA (resp. 29 vs 13%, p=0.007; 27 vs 11%, p=0.008; 29 vs 14%, p=0.018; 29 vs 14%, p=0.013) between week 8 and week 52, compared to patients that did reach these respective disease states.

Conclusion: We have identified a set of 3 antibody biomarkers that predict the failure to achieve early and sustained remission and LDA in response to intensive first-line RA therapy. Therefore, the presence of these antibodies might indicate the need for another first-line treatment option in a personalized medicine approach.

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POS0145 CLINICAL RESPONSE TO RITUXIMAB IS ASSOCIATED WITH PREVENTION OF B-CELL DRIVEN SALIVARY GLAND INFLAMMATION AND EPITHELIAL RESTORATION AS REVEALED BY MOLECULAR PATHOLOGY: RESULTS FROM THE TRACTISS TRIAL IN PRIMARY SJOGREN'S SYNDROME

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Background: The TRial for Anti-B-Cell Therapy In patients with pSS (TRACTISS) is the largest multi-centre, placebo-controlled, phase-III trial with the administration of 2 cycles of Rituximab (RTX) or placebo at week 0 and 24, with trial clinical endpoints at week 48. Despite the primary endpoints (30% reduction in fatigue or oral dryness) were not met, RTX treated patients showed an improvement in secondary endpoints, such as unstimulated whole salivary flow

(UWSF), and salivary gland (SG) total ultrasound score[1,2]. Additionally, recent post-hoc analysis of TRACTISS using novel CRESS composite endpoints[3], highlighted a significantly increased response rate in the RTX vs placebo arm.

Objectives: To perform the first longitudinal analysis of matched transcriptomic and histological data of SG biopsies of pSS patients treated with RTX vs placebo at 3 time points, over 48 weeks, from the TRACTISS cohort, in order to identify mechanisms of response/resistance to B cell depletion.

Methods: 29 pSS patients randomised to RTX or placebo arm consented for labial SG biopsies at week 0, 16 and 48. Patients received two 1000mg cycles of RTX or placebo at week 0 and 24. SG focus score, inflammatory aggregate area fraction, B-cells (CD20+), T-cells (CD3+), follicular dendritic cells (FDCs) (CD21+) and plasma cells (CD138+) density were assessed using quantitative digital image analysis. RNA sequencing with deconvolution and pathway analysis was performed to identify genes signatures and consensus gene modules as biomarkers of disease evolution and response/resistance to therapy.

Results: Placebo-treated SGs showed worsening of SG inflammation highlighted by the increment of aggregate size, B-cell density, development of new FDC networks, and a higher ectopic GC prevalence over 48 weeks, compared to RTX-treated patients. No difference in focus score, total T-cell and plasma cell infiltration was observed. RTX downregulated genes involved in immune cell recruitment and inflammatory aggregate organisation (e.g. CXCL13, CCR7 and PDCD1). Gene signature-based analysis of 35 immune cell types using XCell highlighted how RTX blocked class-switched and memory-B-cells accumulation in SGs over 48 weeks. Pathway analyses confirmed the downregulation of leukocyte migration, MHC-II antigen presentation, and T-cell co-stimulation immunological pathways, such as the CD40 receptor complex pathway. Among RTX-treated patients, only CRESS-responders demonstrated prevention of worsening B cell-driven molecular pathology signatures over time and a significant improvement in UWSF, in parallel with the upregulation of molecular pathways associated to SG restoration of the glandular epithelium. None of the above effects were observed at week 16 after the first RTX cycle.

Conclusion: Two RTX infusions repeated at week 24 exerted beneficial effects on labial SG inflammatory infiltration in pSS by downregulating genes involved in immune cell recruitment, activation and organisation in ectopic GCs. Conversely, all the above parameters showed significant evolution in placebo treated patients over 48 weeks demonstrating progression of SG immunopathology. Clinical responders to RTX based on CRESS response criteria were characterised by preservation of exocrine function which appear driven by SG epithelial restoration.

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Disclosure of Interests: None declared

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Clinical aspect of spondyloarthritis

POS0146 INCREASED RISKS OF AORTIC REGURGITATION AND ATRIAL FIBRILLATION IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS: A 10 YEAR NATIONWIDE COHORT STUDY

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Background: Radiographic axial spondyloarthritis (r-axSpA) has increased risk of cardiovascular disease. Other cardiac manifestations such as conduction disturbance and valvular diseases were also suggested as co-morbidities in r-axSpA patients, however, the risk of these cardiac manifestation in r-axSpA were seldomly evaluated in large cohort.

Objectives: To compare the incidences of aortic regurgitation, atrial fibrillation (AF), and atrioventricular (AV) block II–III between r-axSpA patients and the general population (GP).

Methods: National Health Insurance Services data were used. R-axSpA patients (N = 8,877) and the age- and sex-matched GP (N = 26,631) were followed from August, 2006 to December, 2019. Incidence rates and standardized incidence ratios (SIR) of aortic regurgitation, AF, and AV block II–III were compared between these groups. Ten year incidence rates and hazard ratios (HRs) were calculated by the Kaplan–Meier method and Cox regression analysis.

Results: Incidence rates of aortic regurgitation, AV block II–III, and AF in the r-axSpA group were 0.42, 0.21, and 4.0 per 1000 person-years, respectively. In the r-axSpA group, the SIR for aortic regurgitation was highest among 40–49-year-old men (4.11). Incidence rates of aortic regurgitation and AF were higher in the r-axSpA group than in the GP group (both $p < 0.001$), whereas the difference was insignificant for AV block II–III. In multivariate analysis, HRs for aortic regurgitation and AF were higher in the r-axSpA group than in the GP group (HR (95% confidence interval) = 2.55 (1.49–4.37) and 1.20 (1.04–1.39), respectively), but the difference was insignificant for AV block II–III.

Conclusion: Compared with the GP, r-axSpA patients are at increased risk of aortic regurgitation and AF, but not AV block II–III. These patients should be carefully monitored for occurrence of aortic regurgitation and AF.

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POS0147 DETERMINANTS OF GENERAL HEALTH AND HEALTH RELATED QUALITY OF LIFE IN AXIAL SPONDYLOARTHRITIS, PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: RESULTS FROM THE ASAS-PERSPA STUDY

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Background: Axial Spondyloarthritis (axSpA), peripheral Spondyloarhritis (pSpA) and Psoriatic arthritis (PsA) are different types of SpA, with large heterogeneity in clinical manifestations. It is crucial to understand which are the determinants of health-related quality of life (HRQoL) and general health (GH, global functioning and health) in axSpA, pSpA and PsA, which can lead to differential approaches and interventions, to attain better outcomes.

Objectives: This study aims to identify and compare determinants of HRQoL and GH in axSpA, pSpA and PsA, using data from the PerSpA study.

Methods: Data from the ASAS-PerSpA study, a cross-sectional and multicenter study with 24 participating countries, was used. Patients with either axSpA, pSpA or PsA were enrolled. Sociodemographic, lifestyle, anthropometric, and clinical characteristics were collected. Univariable and multivariable regression models for the three groups were performed separately, to explore factors associated with HRQoL, assessed by EuroQoL-5 Dimensions 3 level (EQ-5D), and similar analysis was performed for GH, assessed by the Assessment of SpondyloArthritis international Society Health Index (ASAS-HI).

Results: 4185 patients were included in the analyses. For the final models, only patients with complete data were included (results summarized in Table 1). Regarding HRQoL, worse HRQoL in axSpA was associated with female gender, fibromyalgia (FM), peripheral disease (PD), worse function and higher disease activity (DA) and patient's global assessment (PGA), in pSpA with worse function, higher DA and higher non-steroidal anti-inflammatory drugs intake score (NSAIDs-IS), and in PsA with female gender, axial involvement, worse function, higher DA and glucocorticoid therapy. On the contrary, better HRQoL was

associated in axSpA with a history of uveitis, in pSpA with older age (with a trend in axSpA and PsA, but not statistically significant) and in PsA with biologic therapy. Regarding GH, in axSpA, worse GH was associated with female gender, FM, PD, worse function and higher DA and PGA, in pSpA, with female gender, inflammatory bowel disease, worse function, treatment with conventional synthetic disease-modifying anti-rheumatic drug and higher NSAIDs-IS, in PsA with female gender, alcohol intake, FM, axial involvement, worse function and higher DA. On the contrary, better GH was associated in axSpA with university education (UE), higher BMI and higher NSAIDs-IS, in pSpA with UE, and in PsA with older age and UE.

Table 1. Factors associated with HRQoL and GH stratified by diagnostic category (summarized)

	EQ-5D			ASAS-HI		
	axSpA n= 2698 R^2=0.548	pSpA n= 418 R^2=0.520	PsA n= 1017 R^2=0.551	axSpA n= 2700 R^2=0.539	pSpA n= 418 R^2=0.545	PsA n= 1016 R^2=0.560
	p-value	p-value	p-value	p-value	p-value	p-value
Female gender		0.146	**0.017**	**<0.001**	**0.001**	**<0.001**
Age	0.054	**0.048**	0.076	0.056	0.496	**0.003**
University education	0.060	NS	0.875	**0.039**	**0.044**	**<0.001**
BMI	0.428	0.116	0.207	**0.004**	0.646	0.309
Ever alcohol intake	0.072	NS	0.796	0.531	0.539	**0.035**
Fibromyalgia	**<0.001**	0.473	0.052	**<0.001**	0.692	**<0.001**
Uveitis	**0.028**	NS	0.832	NS	NS	0.225
IBD	NS	NS	0.341	NS	**0.025**	0.657
Axial disease	NS	0.867	**0.003**	NS	NS	**0.006**
Peripheral disease	**0.039**	NS	NS	<0.001	NS	**NS**
PGA	**<0.001**	*	*	**<0.001**	*	*
BASFI	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
ASDAS-CRP	**<0.001**	NA	NA	**<0.001**	NA	NA
DAS44-CRP	NS	**<0.001**	**<0.001**	NA	0.349	**<0.001**
csDMARD	0.156	0.796	NS	0.233	**0.002**	NS
bDMARD	0.491	0.896	**0.021**	0.901	NS	NS
Glucocorticoids	0.295	0.988	**0.035**	0.692	0.803	0.814
NSAID intake score	0.998	**<0.001**	0.659	**0.011**	**0.028**	0.685

NS – not significant in univariable model; NA – not applicable; * - colinear with DAS44-

Conclusion: In all types of SpA, DA and function are major determinants of HRQoL, passible of tight monitoring and therapeutic intervention. In GH, besides DA and function, socio-demographic factors, like gender and education, also play an important role, in all forms of SpA, highlighting the importance of a holistic approach of the individual patient in order to achieve better outcomes.

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POS0148

SPARCC, MASES, LEI AND MEI INDEXES CAPTURE DIFFERENT PATIENTS WITH ENTHESITIS IN AXIAL SPONDYLOARTHRITIS, PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS.

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Background: Spondyloarthritis, (axial (axSpA), peripheral (pSpA)) and psoriatic arthritis (PsA)) share enthesitis as a hallmark clinical feature. Reliable clinical instruments have been developed to assess enthesitis: Spondyloarthritis Research Consortium of Canada Enthesitis (SPARCC), Leeds Enthesitis Index (LEI), Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) and MEI (Mander Enthesitis Index). Since these four indexes include different enthesis locations, they may capture a different number of patients with enthesitis in the different SpA entities.

Objectives: a) To describe the individual locations of enthesitis in axSpA, pSpA and PsA; b) to evaluate whether the prevalence of patients with at least one enthesitis across the three groups differs depending on the use of SPARCC, LEI, MASES and MEI indexes; c) to evaluate the level of agreement between these indexes for detecting patients with at least one enthesitis in axSpA, pSpA and PsA populations.

Methods: PerSpA was a multinational observational, cross-sectional study with 24 participating countries worldwide. A total of 4185 patients with a diagnosis of axSpA (2719), pSpA (433) and PsA (1033) according to the Rheumatologist's opinion were included in this analysis. Information on the location of enthesitis collected during the study visit was used according to the SPARCC, LEI, MASES and MEI indexes.

The prevalence of patients with at least one enthesitis according to the different indexes were compared across the diseases (axSpA, PsA and pSpA), and pairwise agreement between indexes were evaluated using the Cohen's kappa in the global population and in the three groups.

Results: Out of 36 locations, the most prevalent enthesitis in the overall population were the lumbar spinous processes (6.5%), the thoracic spinous processes (4.9%) and the insertion of the Achilles tendon right (4.8%) and left (3.9%). A total of 10.7%, 8.3%, 13.5% and 17.2% of patients in the overall population showed at least one enthesitis according to the SPARCC, LEI, MASES and MEI indexes, respectively. Figure 1 shows that, among patients with axSpA, MEI and MASES indexes capture the majority of patients with at least one enthesitis (98.7% and 82.4%, respectively), while in pSpA and PsA, MEI and SPARCC are the indexes which capture the majority of patients with enthesitis (100% and 84.6% for MEI and SPARCC in pSpA, and 97.3% and 77% for MEI and SPARCC in PsA, respectively). In PsA, the LEI only captured 57.2% of the patients with at least one enthesitis. In the total population, MASES and MEI showed the strongest agreement for patients with at least one enthesitis (absolute agreement 96.3%; Cohen's kappa: 0.86). Similarly, among axSpA patients, MASES and MEI showed an almost perfect agreement (97.3%; 0.90), while LEI and MEI showed a moderate agreement (90.4%; 0.54). In pSpA patients, SPARCC and MEI showed the strongest agreement (97.2%; 0.90), as well as among PsA patients (95.4%; 0.82). However, MASES and SPARCC showed a less agreement in PsA patients (94.2%; 0.67).

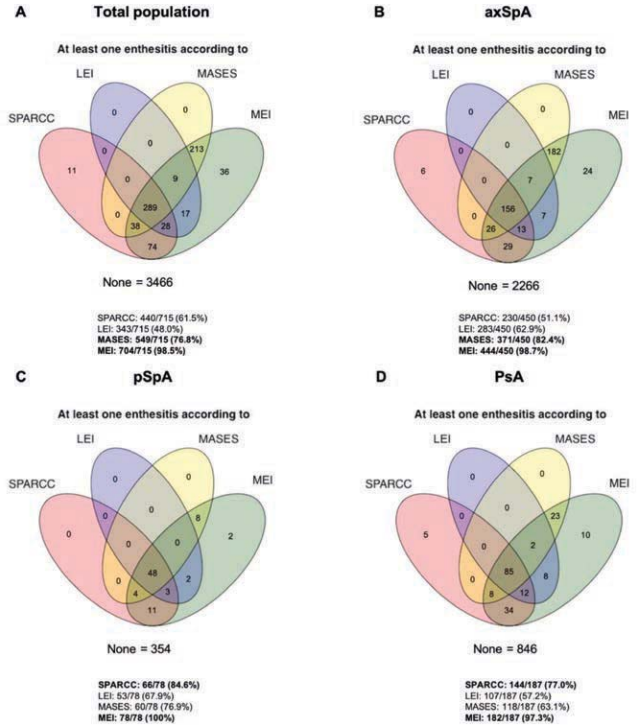

Figure 1. Prevalence of enthesitis captured by different indexes.

Conclusion: The most prevalent locations of enthesitis on the global SpA population are the lumbar spinous processes, the thoracic spinous processes and Achilles tendon. MEI and MASES are the two index that capture more patients with enthesitis in axSpA, while MEI and SPARCC are the two index that capture more patients in pSpA and PsA. The LEI index may underestimate the prevalence of enthesitis in these patients. MASES and MEI showed the largest level of agreement in the overall population and in axSpA, while MEI and SPARCC showed the largest level of agreement in pSpA and PsA. These results suggest that the prevalence of enthesitis across entities differs depending on the disease and on the use of the different index.

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POS0149

WHAT IS BACKFILL? - DETAILED CT / MRI ANALYSIS OF NEW BONE FORMATION IN AXIAL SPONDYLOARTHRITIS

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Background: Several magnetic resonance imaging (MRI) findings of the sacroiliac joint space in axial spondyloarthritis (axSpA) were previously described such as inflammation or fatty metaplasia inside an erosion, i.e. "backfill". However, it is incompletely understood if one or all of these changes represent calcified bone matrix.
Objectives: This study aims to one-by-one link the aforementioned changes to computed tomography (CT) measurements and to understand, which of those findings represents new bone formation.
Methods: Out of 178 patients from two prospective studies that included CT and MRI of the sacroiliac joints all patients with the final diagnosis of axSpA were selected. MRI was screened by two senior musculoskeletal radiologists in consensus for joint-space related MRI findings and grouped into three categories, Type A: hyperintense in STIR and hypointense in T1 (inflammation inside erosion), Type B: hyperintense in both sequences and Type C: hypointense in STIR and hyperintense in T1 (backfill). By using image fusion techniques and one-by-one comparison, the Hounsfiled Units (HU) of those lesions as well as normal cartilage and spongeous and cortical bone were measured in CT.
Results: Ninety-nine patients with axSpA were identified and 48 Type A, 88 Type B and 84 Type C lesions were assessed. Please see Figure 1 for CT measurements. The HU values of cartilage were 73.6±15.0, spongious bone 188.0±69.9, cortical bone 1086.0±100.3, Type A 341.2±96.7, Type B 359.3±153.5 and Type C 446.8±123.0, respectively. The lesion values were significantly higher than cartilage and spongious bone but lower than cortical bone (p<0.001). Type A and B showed similar HU (p=0.93), whereas Type C lesions where denser (p<0.001).

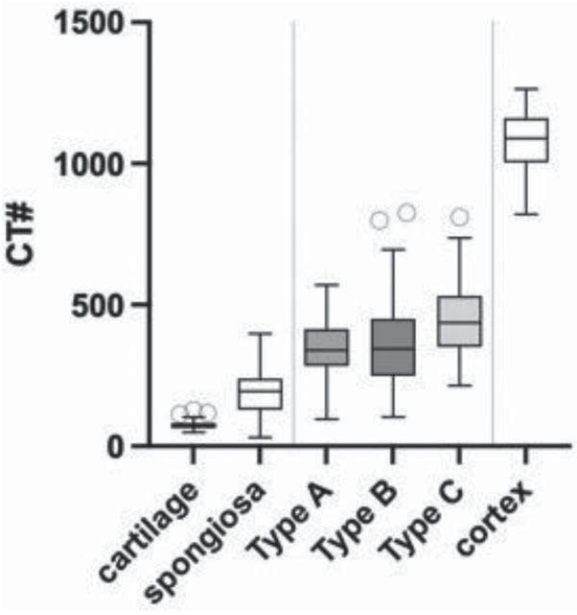

Figure 1. CT-Measurements of cartilage, bone and lesions.

Conclusion: All joint space lesions (Type A to C) show calcified matrix and, thus, resemble new bone formation with gradually more calcified matrix in Type C lesions, i.e. typical backfill. Therefore, the nomenclature of those lesions should be critically re-assessed.
Disclosure of Interests: None declared
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POS0150

ANKYLOSING SPONDYLITIS RELATED STRUCTURAL CHANGES IN THE SPINE INDEPENDENTLY INFLUENCE PATIENT REPORTED PHYSICAL FUNCTION IN MEN BUT NOT IN WOMEN. A COMPREHENSIVE CROSS-SECTIONAL ANALYSIS OF BATH ANKYLOSING SPONDYLITIS FUNCTIONAL INDEX AND ITS RELATION TO SEX

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Background: Patient reported physical function assessed by Bath Ankylosing Spondylitis Functional Index (BASFI) is an important outcome in ankylosing spondylitis (AS) and is associated with health-related quality of life.
Objectives: To improve health care efforts, we aimed to investigate which demographic and disease related factors that influence BASFI in AS patients overall and stratified by sex. Further, we sought to elucidate if there are differences between sexes regarding specific BASFI items.
Methods: Patients fulfilling the modified New York criteria for AS were included in two geographically separate regions in Sweden for this observational cross-sectional study. Patients were assessed with 66/68 joint count and Bath Ankylosing Spondylitis Metrology Index (BASMI) measurements. Lateral X-rays of the spine were performed for modified stoke ankylosing spondylitis spine score (mSASSS) and BASFI, BASDAI, ASDAS CRP were registered. Multiple linear regression analyses were used to investigate influencing factors on BASFI. Independent variables were chosen based on what is previously known and on hypothetical reasoning. Models were performed overall and stratified by sex.
Results: A total of 353 patients, age (median, range) 53 (17-78) years, symptom duration 27 (2-56) years, men 62.3% and HLAB27 91.8 % were included. In multiple linear regression analysis age, BMI, ASDAS CRP, mSASSS, fatigue (BASDAI Q1) and tenderness (BASDAI Q4) were found to significantly associate with BASFI. In models separated by sex, mSASSS independently influenced BASFI in men (p<0.0001) but not in women (p=0.124)(Table 1). Further, separate BASFI items were compared between sexes. The ability to look over shoulder was scored the worst among men while getting up from the floor was hardest for women (Figure 1). Differences between sexes were found in the ability to look over shoulder (p=0.05) and the ability to climb stairs without handrail (p<0.001). Among the separate BASFI items, the ability to look over shoulder showed the highest correlation with mSASSS (r= 0.532, p<0.001).

Table 1. Multiple linear regression analysis exploring factors associated with BASFI

	All		Men		Women	
R^2	0.58		0.62		0.54	
	B (95% CI)	p-value	B (95% CI)	p-value	B (95% CI)	p-value
Age	0.06 (0.04;0.08)	<0.0001	0.05 (0.03;0.07)	<0.0001	0.08 (0.05;0.11)	<0.0001
BMI	0.05 (0.01;0.09)	0.024	0.04 (-0.01;0.09)	0.093	0.05 (-0.03;0.13)	0.209
ASDAS CRP	1.04 (0.74;1.34)	<0.0001	0.84 (0.48;1.20)	<0.0001	1.39 (0.86;1.93)	<0.0001
mSASSS	0.03 (0.02;0.04)	<0.0001	0.03 (0.02-0.05)	<0.0001	0.02 (-0.01;0.06)	0.124
Fatigue	0.34 (0.24;0.43)	<0.0001	0.41 (0.29;0.53)	<0.0001	0.27 (0.11;0.42)	0.001
Tenderness	0.17 (0.07;0.26)	0.001	0.14 (0.02;0.27)	0.027	0.18 (0.02-0.34)	0.027
Women	-0.29 (-0.74;0.17)	0.214	N/A		N/A	

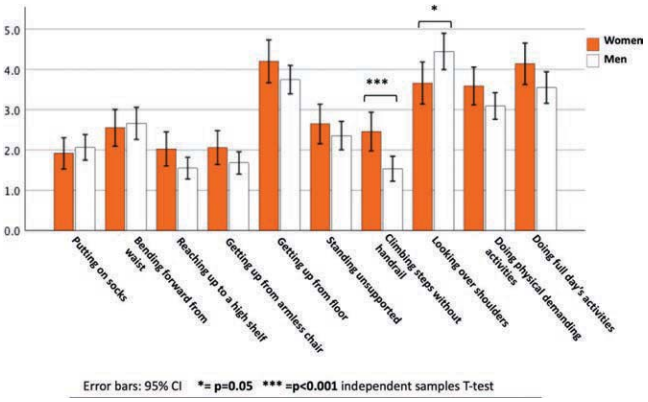

Figure 1. Separate BASFI items women compared to men

Conclusion: AS related self-reported physical function measured by BASFI was influenced by disease activity, fatigue and tenderness in both men and women. Interestingly, structural changes in the spine, evaluated by mSASSS, independently influenced BASFI in men but not in women with AS.
The ability to look over the shoulder was worse in men vs women and excelled as more disease specific than other individual BASFI items in both sexes.
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POS0151

PREGNANCIES IN PATIENTS WITH SPONDYLOARTHRITIS: DATA FROM 2 EUROPEAN CENTERS.

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Background: There is growing interest in reproductive issues in patients with Spondyloarthritis (SpA) and Psoriatic arthritis (PsA).
Objectives: To describe a real-life cohort of prospectively-followed pregnancies in SpA and PsA patients, focusing on obstetric outcome and on flare during pregnancies and post-partum.
Methods: Data on SpA and PsA pregnancies prospectively-followed in 2 European pregnancy clinics from 2010 to 2021 were retrospectively analysed.
Disease activity was assessed using ASDAS-CRP or DAS28-CRP according to the main involvement (peripheral or axial). Disease flare was defined as the need to treatment modification (introduction or increase ≥5mg/day of prednisone, introduction of cDMARD or bDMARD). Miscarriages were excluded from the analysis of flares.
Results: Data on 122 pregnancies (53 PsA and 69 'other SpA': 39 axialSpA, 20 undifferentiated SpA, 6 IBD-related SpA, 4 reactive arthritis) in 102 patients (median age at conception: 34 [IQR: 31-36] years; median disease duration: 72 [24-132] months) were collected.
We recorded 98 (86%) live births and 16 (14%) miscarriages (8 missing data).
Cesarean section was performed in 15/98 (15%) cases. Median week of gestation at delivery was 39 [38-40]; 8 preterm births (<37 week of gestation) and 2 severe preterm births (<34 week of gestation) occurred. There was no difference between PsA or 'other-SpA' concerning pregnancy outcome and route of delivery.
Fourty-two pregnancies (40%) had at least 1 flare during pregnancy; 7 pregnancies had more than 1 flare. Overall, there were 13, 24 and 12 flares in the 1st, 2nd and 3rd trimester, respectively.
A higher frequency of patients with axial involvement was observed in the 'flare' group as compared to pregnancies without flare (83% vs 59%, p=0.02) (Table 1).

Table 1. Comparison between 'flare' and 'without flare' groups.

	FLARE (42)	WITHOUT FLARE (64)	*p*
Age at conception (years)	33 (31-37)	33 (31-35)	0.88
Disease duration at conception (months)	71 (24-120)	60 (24-137)	0.74
PsA	13 (31%)	31 (48%)	0.11
'Other SpA'	29 (69%)	33 (52%)	0.11
Axial involvement	**35 (83%)**	**38 (59%)**	**0.02**
Peripheral involvement	30 (%)	54 (%)	0.17
bDMARD use			
Any time before pregnancy	16 (38%)	19 (30%)	0.49
Stop at + pregnancy test/1st trimester	8 (19%)	4 (6%)	0.09
Start/continue 1st trimester	7 (17%)	10 (16%)	0.89
Start in 2nd trimester	**5 (12%)**	**0**	**0.02**
Start in 3rd trimester	2 (5%)	0	0.30
Post-partum flare	11/34 (32%)	22/49 (45%)	0.36

Continuous variables were compared using Mann-Whitney test; categorical variables were compared using Chi-square with Yates' correction or Fisher's exact test.

Medications resumed to treat flare were steroids (29 pregnancies), csDMARDs (14 pregnancies) and TNF-inhibitors (7 pregnancies: 5 during the 2nd and 2 during the 3rd trimester).
A post-partum flare was registered in 33/83 (40%) of cases, without difference between 'flare' group vs 'without flare' group (Table 1), as well as between PsA vs 'other SpA' pregnancies (47% vs 33%, p=0.2).
Conclusion: In this cohort of SpA pregnancies, 40% experienced a flare during pregnancy and 40% during post-partum. Flares occurred more frequently in the 2nd trimester and especially in patients with axial involvement, requiring the start of a TNF-inhibitor during the 2nd or the 3rd trimester in 7 pregnancies. Having a flare during pregnancy was not associated with a post-partum flare.

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POS0152

DIRECT AND INDIRECT EFFECT OF TNF INHIBITORS ON SPINAL MOBILITY IN PEOPLE WITH AXIAL SPONDYLOARTHRITIS AND THE MEDIATOR ROLE OF DISEASE ACTIVITY

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Background: Although it may be difficult to detect changes in spinal mobility on the short term, spinal mobility is considered an important measure to assess the efficacy of drugs used to treat axial spondyloarthritis (axSpA). However, few studies evaluated the long-term impact of biologic treatment on spinal mobility.
Objectives: To describe the long-term effect of TNF inhibitors (TNFi) on spinal mobility in patients with axSpA, and to determine whether the use of TNFi treatment influences spinal mobility, and if this due to a direct or indirect effect (mediated by disease activity).
Methods: We performed a retrospective observational study, using data collected from patients with a clinical diagnosis of axSpA treated with TNFi at a tertiary care centre where disease activity and metrology assessments are routinely done. Adult patients with at least two Bath Ankylosing Spondylitis Metrology Index (BASMI) measurements were included. Disease activity was measured using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score C-reactive protein (ASDAS). The longitudinal association between TNFi and improvement in BASDAI/ASDAS was tested using a linear mixed effects model with BASMI as dependent variable. To test whether TNFi had a direct effect on BASMI, not mediated by disease activity, we tested that TNFi treatment was not conditionally independent of BASMI given BASDAI/ASDAS (Figure 1). We tested whether the nodes TNFi and BASMI were disconnected if we removed BASDAI and ASDAS. To test this conditional independence, we first built a linear mixed effects model for BASMI given BASDAI or ASDAS when the patient was under TNFi and used this model to predict a 95% confidence interval (CI) for BASMI given the data for BASDAI/ASDAS when the patient was without TNFi. We checked whether the true value of BASMI lay within this 95% CI and performed a hypothesis test for binomial distribution where H0: p=0.95. To test for the indirect effect of TNFi on BASMI reduction, mediated through the disease activity, we regressed BASMI on BASDAI/ASDAS, TNFi (if there was a direct effect), demographics, presence of radiographic (r-) axSpA and HLA-B27 positivity, using a linear mixed effects model adjusted for within-patient correlation.

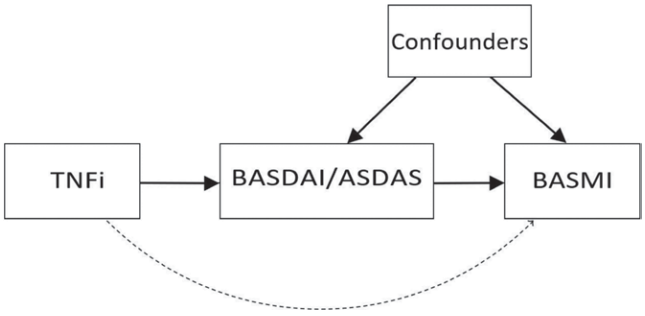

Figure 1. Indirect effect of TNFi on BASMI (represented by the full line), through the influence of TNFi on disease activity, adjusted by other confounders and direct effect of TNFi on BASMI (dashed line), independently of disease activity.

Results: Data from 188 patients and 1326 visits were analysed. Mean age was 45.6 (SD 11.6) years, mean disease duration was 15.8 (SD 9.64) years, 152 (80.9%) were male, 120 (73.6%) had r-axSpA, and 83 (74.8%) were HLA-B27 positive. Mean follow-up time was 8.0 (SD 4.4) years, ranging from 0.8 to 18.2 years. Treatment with TNFi was significantly associated with long-term improvement in BASMI (B=-0.423, 95% CI=[-0.553,-0.292], p<0.001). An indirect effect of TNFi on BASMI improvement was observed, mediated by reduction in disease activity, measured by BASDAI (B=0.146, 95% CI=[0.092, 0.200], p<0.001) or ASDAS (B=0.405, 95% CI=[0.260, 0.549], p<0.001). Using conditional independence tests, a direct effect of TNFi on BASMI improvement was also observed, independently of disease activity, when BASDAI was used (p<0.001) as a covariate, but not when ASDAS was used (p=0.3104). The direct effect of TNFi (B=-0.300, 95% CI=[-0.576,-0.025], p<0.001) on BASMI was estimated in the BASDAI-adjusted mixed effects model.

Table 1. Frequency of Spinal MRI lesions According to SIJ Imaging Positive for AxSpA

MRI Spinal Lesions, N (%)	MRI_{global} SIJ+ (n=19)	MRI_{global} SIJ- (n=32)	P value	MRI_{global} SIJ+ and/or mNY+ (n=22)	MRI_{global} SIJ- and mNY- (n=29)	P value	MRI_{global} SIJ- and SpA Diagnosis+ (n=17)	MRI_{global} SIJ- and SpA Diagnosis- (n=15)	P value
MRI_{global} consistent with axSpA (≥2/9 readers agree)	8 (42.1%)	4 (12.5%)	0.04	8(36.4%)	4(13.8%)	0.10	4 (23.5%)	0 (0%)	0.10
MRI_{global} consistent with axSpA (≥5/9 readers agree)	6 (31.6%)	1 (3.1%)	0.01	6 (27.3%)	1 (3.4%)	0.03	1 (5.9%)	0 (0%)	1.0
VC BME ≥1	9 (47.4%)	15 (46.9%)46.9% RT 62.5% CT 29.4% GT	1.0	10(45.5%)	14(48.3%)	1.0	11 (64.7%)	4 (26.7%)	0.04
VC BME ≥2	6 (31.6%)	10 (31.3%)31.2% RT 55.6% CT 19.6% GT	1.0	6(27.3%)	10(34.5%)	0.76	9 (52.9%)	1 (6.7%)	0.007
VC BME ≥3	6 (31.6%)	7 (21.9%)21.9% RT 53.8% CT 13.7% GT	0.52	6(27.3%)	7(24.1%)	1.0	7 (41.2%)	0 (0%)	0.008
VC BME ≥4	5 (26.3%)	5 (15.6%)	0.47	5(22.7%)	5(17.2%)	0.73	5 (29.4%)	0 (0%)	0.046
Vertebral Endplate BME ≥1	2 (10.5%)	3 (9.4%)	1.0	2(9.1%)	3(10.3%)	1.0	2 (11.8%)	1 (6.7%)	1.0
Lateral vertebral BME	3 (15.8%)	3 (9.4%)	0.66	3(13.6%)	3(10.3%)	1.0	3 (17.6%)	0 (0%)	0.23
Facet BME ≥1	4 (21.1%)	1 (3.1%)3.1% RT 20.0% CT 2.0% GT	0.06	4(18.2%)	1(3.4%)	0.15	1 (5.9%)	0 (0%)	1.0
Posterior BME ≥1	5 (26.3%)	2 (6.3%)	0.09	5(22.7%)	2(6.9%)	0.22	1 (5.9%)	1 (6.7%)	1.0
VC Fat ≥1	8 (42.1%)42.1% RT 44.4% CT 15.7% GT	10 (31.3%)31.2% RT 55.6% CT 19.6% GT	0.55	8(36.4%)	10(34.5%)	1.0	5 (29.4%)	5 (33.3%)	1.0
VC Fat ≥2	7 (36.8%)	5 (15.6%)	0.10	7(31.8%)	5(17.2%)	0.32	3 (17.6%)	2 (13.3%)	1.0
VC Fat ≥3	6 (31.6%)31.6% RT 66.7% CT 11.8% GT	3 (9.4%)	0.06	6(27.3%)	3(10.3%)	0.15	1 (5.9%)	2 (13.3%)	0.59
VC Fat ≥4	6 (31.6%)	1 (3.1%)	0.01	6(27.3%)	1(3.4%)	0.03	0 (0%)	1 (6.7%)	0.47
Lateral Fat ≥1	6 (31.6%)	2 (6.3%)	0.04	6(27.3%)	2(6.9%)	0.06	0 (0%)	2 (13.3%)	0.21
Erosion ≥1	3 (15.8%)	2 (6.3%)	0.35	3(13.6%)	2(6.9%)	0.64	1 (5.9%)	1 (6.7%)	1.0
Bone Spur ≥1	4 (21.1%)	5 (15.6%)	0.71	4(18.2%)	5(17.2%)	1.0	4 (23.5%)	1 (6.7%)	0.34
Ankylosis ≥1	2 (10.5%)	0 (0%)	0.13	2(9.1%)	0(0%)	0.18	0 (0%)	0 (0%)	-

Conclusion: TNFi are effective at improving BASMI in patients with axSpA, in a real-life setting. This effect is mainly explained by the reduction in disease activity. However, a direct effect of TNFi on BASMI could also be demonstrated, when disease activity was measured by BASDAI, suggesting that ASDAS captures additional factors that can influence spinal mobility. These potential factors deserve further investigation, but they could for example include biomechanical properties of tendons and myofascial tissue.

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POS0153 MRI SPINAL LESIONS IN PATIENTS WITHOUT MRI OR RADIOGRAPHIC LESIONS IN THE SACROILIAC JOINTS TYPICAL OF AXIAL SPONDYLOARTHRITIS

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Background: There are limited data as to the frequency of spinal lesions on MRI in patients without MRI or radiographic features typical of sacroiliac joint (SIJ) disease and to what degree spine MRI might enhance diagnostic evaluation.

Objectives: To assess the frequency of MRI lesions of the spine in the ASAS-Classification Cohort according to the presence of MRI SIJ lesions typical of axSpA and/or radiographic sacroiliitis (mNY+).

Methods: MRI spine lesions were recorded by 9 central readers in an eCRF that captures global assessment of the spine ("Is the MRI consistent with axSpA: yes/no") (yes=MRI_{global} spine+) and detailed anatomical-based scoring of each discovertebral unit plus lateral and posterior structures. Independently, readers globally assessed SIJ scans for active and/or structural lesions typical of axSpA. We compared the frequency of MRI_{global} spine+ and frequencies of different types of spinal lesions according to the presence/absence of axSpA on global evaluation of SIJ scans by ≥5 of 9 readers (MRI_{global} SIJ+) and mNY+ sacroiliitis using Fisher's exact test. Analysis was also stratified by rheumatologist diagnosis.

Results: Among 51 cases with SIJ as well as spine MRI scans and radiographs of the SIJ,19 (37.3%) had MRI_{global} SIJ+, and 12 (23.5%) and 7 (13.7%) had MRI_{global} spine+ by ≥2 and ≥5 reader agreement, respectively. MRI_{global} spine+ occurred significantly more frequently in the presence of mNY+ sacroiliitis and MRI_{global} SIJ+ but was also recorded in 4 of 32(12.5%) (≥2 readers) and 1 of 32(3.4%) (≥5 readers) cases that were MRI_{global} SIJ- ***and*** x-ray negative, all 4 cases being diagnosed with axSpA. Moreover, vertebral corner BME lesions, but not spinal structural lesions, were significantly more frequent in MRI_{global} SIJ- cases that had been clinically diagnosed as axSpA versus non-axSpA (Table 1).

Conclusion: Spinal lesions on MRI indicative of axSpA per majority read occurred in about 3% of patients without positive imaging in the SIJ. Frequency of spinal BME lesions was higher in cases with negative SIJ imaging but clinically diagnosed with axSpA.

Disclosure of Interests: None declared

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POS0154 INFLAMMATION IS ASSOCIATED WITH INCIDENT HYPERTENSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A LONG-TERM FOLLOW-UP STUDY

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Background: Axial spondyloarthritis (axSpA) patients have increased risks of developing cardiovascular diseases (CVD) compared to the general population. Hypertension (HT) as the most common CV risk factor in these patients. Whether chronic, low-grade inflammation predispose to the development of incident hypertension in axSpA remained uncertain.

Objectives: To examine the association between markers of systemic inflammation and incident hypertension in axSpA patients.

Methods: A cohort analysis was performed in patients with axSpA who had been followed since January 2001. Patients diagnosed with hypertension and/or on anti-hypertensives at baseline were excluded. The primary outcome was first diagnosis of HT occurring between January 2001 and December 2020. Three different CVD risk scores including Framingham risk score (FRS), QRISK3 and SCORE were computed at baseline. Baseline demographic data and clinical inflammatory and disease activity parameters were assessed using Cox proportional hazard regression. The association between disease activity measures, inflammatory markers, medications, and the occurrence of incident HT was assessed using time-varying Cox proportional hazard models after adjusting for baseline CVD risk scores.

Results: 413 patients [34(25-43) years, male: 319 (77.2%)] were recruited. After a median follow up of 12 (6-17) years, 58 patients (14%) developed incident HT (IHT+group). In baseline multivariable Cox regression analysis, ESR and CV risk scores were significantly associated with developing IHT ($p<0.05$) (Table 1). Using time-varying multivariate analysis, higher inflammatory burden (ESR≥20) was significantly associated with developing IHT after adjusting for FRS and SCORE respectively. Use of csDMARDs was significantly linked to develop IHT after adjusting for baseline FRS, while a trend suggesting that csDMARDs was associated with an increased risk of IHT after adjusting for baseline SCORE was observed (Table 2).

Table 1. Multivariable analysis with Cox proportional hazard regression for the baseline predictors of incident HT.

Table 1a.

	Model 1		Model 2	
	HR (95%CI)	p-value	HR (95%CI)	P-value
BASDAI≥5	1.44 (0.78, 2.67)	0.244	1.39 (0.75, 2.59)	0.3
ESR	1.01 (1.00, 1.02)	0.003*	1.01 (1.00, 1.02)	0.003*
BASFI	1.03 (1.00, 1.02)	0.616	1.03 (0.92, 1.16)	0.572
Baseline disease duration	1.04 (1.00, 1.08)	0.102	1.03 (0.98, 1.08)	0.215
Symptom duration	1.01 (0.98, 1.05)	0.513	1.02 (0.98, 1.05)	0.386
FRS	1.05 (1.03, 1.08)	<.001*		
SCORE			1.23 (1.12, 1.36)	<.001*

Table 1b.

	Model 1		Model 2	
	HR (95%CI)	p-value	HR (95%CI)	P-value
BASDAI≥6	1.53 (0.84, 2.78)	0.166	1.47 (0.81, 2.69)	0.209
ESR	1.01 (1.00, 1.02)	0.003*	1.01 (1.00, 1.02)	0.003*
BASFI	1.03 (0.92, 1,15)	0.646	1.03 (0.92, 1.16)	0.599
Baseline disease duration	1.04 (1.00, 1.08)	0.121	1.03 (0.98, 1.07)	0.244
Symptom duration	1.01 (0.98, 1.05)	0.530	1.02 (0.98, 1.05)	0.391
FRS	1.05 (1.03, 1.08)	<.001*		
SCORE			1.23 (1.11, 1.35)	<.001*

Conclusion: Higher baseline and time-varying inflammatory burden predict the development of IHT in addition to traditional CV risk scores in axSpA patients. While exposure to csDMARDs may be associated with the development of IHT, NSAIDs and biologic DMARDs use were not associated with the development of IHT.

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Table 2. Multivariable analysis with Cox proportional hazard regression for the time-dependent predictors of incident HT.

Table 2a.

	Model 1		Model 2	
	Time-dependent HR (95%CI)	p-value	Time-dependent HR (95%CI)	P-value
ESR	1.01 (1.00, 1.03)	0.085	1.01 (1.00, 1.03)	0.074
csDMARDs	2.24 (1.04, 4.82)	0.04*	2.16 (1.00, 4.68)	0.05
FRS	1.05 (1.01, 1.08)	0.008*		
SCORE			1.24 (1.09 1.41)	0.001*

Table 2b.

	Model 1		Model 2	
	Time-dependent HR (95%CI)	P-value	Time-dependent HR (95%CI)	P-value
ESR≥20	2.22 (1.05, 4.72)	0.038*	2.27 (1.06,4.82)	0.034*
csDMARDs	2.17 (1.01, 4.64)	0.047*	2.09 (0.97, 4.50)	0.059
FRS	1.05 (1.01, 1.08)	0.01*		
SCORE			1.23 (1.08, 1.41)	0.002*

Disclosure of Interests: None declared
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Health services research: scoping the landscape

POS0155

WHAT DRIVES RACIAL DISPARITIES IN GOUT IN THE US? – POPULATION-BASED, SEX-SPECIFIC, CASUAL MEDIATION ANALYSIS

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Background: Traditionally viewed as a disease of White men, global frequency and disability burden of female gout are rising disproportionately to male gout.[1] Moreover, emerging US cohort data suggest gout and hyperuricemia impart larger burdens on Black adults than Whites.[2] These racial disparities may be largely attributable to differences in non-genetic, mainly modifiable gout risk factors e.g., BMI, diet,[3,4] and chronic kidney disease (CKD). However, national-level, general population data on racial differences in burden of gout, and potential mediators, are lacking.

Objectives: To determine and quantify sex-specific mediators of racial disparities in gout prevalence among a nationally representative sample of US adults.

Methods: Using recent decadal data (2007-2016) on physician-diagnosed gout and hyperuricemia from the National Health and Nutrition Examination Survey, we compared contemporary sex- and race-specific prevalences and conducted sequential causal mediation analysis (adjusting for upstream mediators following causal pathways)[5] to determine the proportion of the racial differences attributable to 7 potentially mediating social and clinical factors (see DAG in Figure 1): low education, poverty, body mass index (BMI), alcohol, poor quality diet (poor DASH adherence), diuretic use, and CKD (eGFR <60 mL/min, using the latest equations that do not include a coefficient for Black race[6], per National Kidney Foundation and American Society of Nephrology recommendations.[7])

Results: Age standardised prevalence of gout was 3.5% and 2.0% in Black and White women, respectively (age-adjusted OR =1.8 [95% CI: 1.3 to 2.5]), and 7.0% and 5.4% in Black and White men (age-adjusted OR =1.3 [1.0 to 1.6]). Most risk factors were more frequent/elevated in Blacks than Whites, except alcohol consumption, which was lower in Blacks (both sexes). BMI levels and poverty were higher in Black women, but similar between Black and White men.

Largest mediating factor of excess gout cases among Black women was excess BMI, accounting for 56% of the racial difference (independent of education, poverty, diet, and alcohol), followed by CKD (24%), poverty (17%), and poor diet (12%) (see Table 1).

Table 1. Indirect (mediation) effects of potential mediators, using sequential mediation analysis, for the association between Black race and odds of gout in US women and men.

	WOMEN		MEN	
	Effect Estimate (OR), 95% CI	Proportion Mediated, %	Effect Estimate (OR), 95% CI	Proportion Mediated, %
Indirect (Mediation) Effect				
Education (high school or less)	1.01 (0.98 to 1.03)	2.4%	1.01 (0.98 to 1.03)	3.3%
Poverty	1.07 (1.04 to 1.10)	16.9%	1.00 (0.99 to 1.00)	0.53%
Alcohol consumption *(# drinks/ week, continuous)*	0.99 (0.96 to 1.01)	-3.4%	0.99 (0.98 to 1.00)	-4.5%
DASH diet score *(continuous; higher scores = ↓ adherence)*	1.05 (0.96 to 1.01)	12.0%	1.05 (1.01 to 1.10)	19.8%
Body mass index *(continuous)*	1.25 (1.14 to 1.37)	55.9%	1.03 (1.02 to 1.04)	11.9%
Diuretic use	1.03 (1.01 to 1.05)	7.6%	1.04 (1.02 to 1.06)	14.2%
Chronic kidney disease	1.10 (1.04 to 1.16)	23.9%	1.12 (1.08 to 1.17)	45.6%
Direct Effect	0.94 (0.68 to 1.30)[a]	–15.2%	1.02 (0.83 to 1.26)[b]	9.2%
Total Effect	1.49 (1.12 to 1.98)	100%	1.29 (1.05 to 1.57)	100%

DASH=Dietary Approaches to Stop Hypertension; [a]p=0.52, [b]p=0.83

Among men, CKD was the largest mediator (46%), followed by poor diet (20%) and diuretic use (14%). BMI (12%) and poverty (0.5%) mediated smaller proportions of the racial difference among men compared to women. Mediators of racial differences in hyperuricemia closely agreed with gout results.

Conclusion: Contrasting with historical views, gout is more frequent among Black adults in the US than their White counterparts, especially women (two-times greater in Black women vs. White). Culturally informed efforts to reduce these disparities should focus on excess adiposity, diet quality, and kidney disease while recognising the impact of poverty in female gout.

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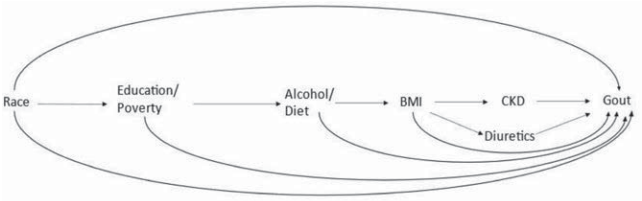

Figure 1. Assumed causal diagram of the association between race and gout or hyperuricemia. BMI=body mass index; CKD=chronic kidney disease.

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POS0156 PATIENT INVOLVEMENT IN REGISTRIES BASED RESEARCH

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Background: Patient research partners (PRPs) are increasingly included in research as well as guideline development task forces in rheumatology. In observational and registry studies the role and involvement of PRPs is not clear.
Objectives: We aimed to evaluate current PRP involvement in registry research as well as benefits and barriers of implementation in practice.
Methods: Based on a round table discussion during the EULAR Registries and observational drug studies meeting (RODS) in 2019 we used mixed methods methodology (survey and focus groups) to study the role of PRPs and involvement in research. The survey was sent to investigators of registries across Europe, participants of RODS meetings and members of the EULAR PARE (People with Arthritis / Rheumatism across Europe) network. Interested survey participants were further invited to one of three focus groups. The conduction of the focus groups (FG) was guided by a semi-structured guide based on the survey results. An inductive thematic analysis approach was applied to qualitative data.
Results: We received 45 survey responses with around half of them from patients. The mean importance of PRP involvement was scored VAS±SD: 75±24mm (on a 100mm VAS), but the actual involvement was rather low (VAS: 32±20mm) and 12 participants had no experience with PRPs. The most common current practice was patient involvement in design of studies (32%), cooperation with patient organisation for recruitment (32%) and involvement of PRPs in the management board (32%). The most important need of PRP integration was attributed in the stages of design and preparation before recruitment. 11 survey participants even indicated that PRPs should be involved in all stages/tasks of research. During the focus groups 5 main themes (Table 1) could be identified. Complementary perspectives lead to greater synergy between researchers and patients and further the aim of deriving more valid outcomes. For successful involvement of PRPs, ideally PRPs should be heterogeneous in regard to their lived experience, education ought to be provided and researchers are responsible to offer an environment where PRPs feel comfortable. All FGs elaborated on different roles that PRPs can take on, although the researcher FGs outlined more different tasks of involvement than the PRP group. One theme summarised different barriers for PRP involvement, which have not been a topic of discussion in the FG composed of PRPs only.

Table 1. Overview of themes, sub-themes, and presence of theme according to which focus group discussion.

Theme	Sub theme	Focus Groups		
		Researcher	Researcher and Professionals	PRPs
1.Current experiences of PRPs involvement in research	Researcher experiences of involving PRPs	X		X
	Patient experiences of being involved as PRPs		X	X
2.The role of PRP in registries and research	Complementary perspectives between researchers and PRPs	X	X	X
	The aim of patient involvement in research	X		
3.Points to consider for involving PRPs in research	Consider professional and social backgrounds		X	
	Provide PRPs education and training		X	X
	A welcoming environment for PRPs to contribute		X	X
4.PRP involvement in different phases of the research process	Give PRPs a voice in research committees	X		X
	Identify questions that are most relevant to patients	X	X	
	Select the most relevant outcomes to patients	X		X
	Improve recruitment strategies		X	
	analysis, interpretation and dissemination of results	X	X	
5.Barriers to involving PRPs in research	Recruiting PRPs from ethnic minorities		X	
	Researchers' preconceptions of patients' ability to be involved in research	X		
	Challenging to ask patients to help analyse quantitative data	X		
	Limited financial resources	X		

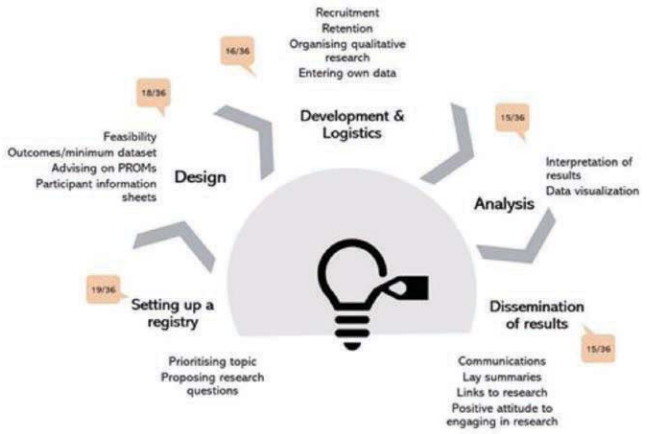

Figure 1. the empirical research cycle - basis for discussion of the role, opportunities & challenges for patient research partners in registry and observational drug study research. X/Y indicates the number of votes for including PRPs at the respective stage.

Conclusion: There is room and much appreciation of PRP involvement in registry research. Researchers and PRPs could use the strategies proposed in this study to define PRP roles and plans of ongoing and future studies.
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POS0157

IMPLEMENTATION OF A VACCINATION TOOL IN THE ELECTRONIC PATIENT HEALTH RECORD COINCIDES WITH A SIGNIFICANT INCREASE IN VACCINATION COVERAGE.

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Background: Patients with immune-mediated inflammatory diseases (IMID) are at higher risk for infectious diseases. Despite this increased risk and the available guidelines[1,2], we reported a suboptimal vaccination rate of 27 % of IMID patients in 2018. In the meantime, a vaccination module was introduced in the electronic patient medical record (EMR) of our hospital to accurately document and monitor vaccination status of patients.
Objectives: To evaluate the impact of a new vaccination module in the patient health record on vaccination coverage in a previously included IMID cohort.
Methods: Between Aug and Oct 2021, the vaccination status of 1435 (out of the original 1488) IMID patients (45 % male, median age 53.6 years) was collected (790 patients with IBD (inflammatory bowel diseases), 607 with rheumatologic inflammatory conditions (RHEU)(RA or SpA), and 38 with dermatologic inflammatory conditions(DER)) and was compared to that of 2018. The vaccination status for influenza (FLU), pneumococci (Pnc), hepatitis B (Hep B) and tetanus (TT) was obtained mainly through the patients' electronic medical records. Missing data were added after contacting patients or their general practitioner.
Results: From 2018 to 2021, the overall vaccination coverage (excluding TT) of all IMID patients significantly increased from 42 % to 66 % (p<0.001, Figure 1).

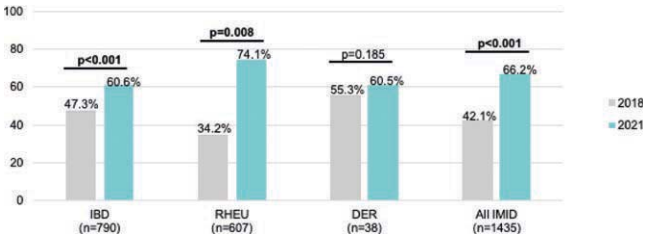

Figure 1. Percentages of total vaccination coverage in 2018 vs. 2021 in patients with IMID – TT vaccination excluded

For patients with RHEU, the vaccination coverage significantly increased, namely from 69.0% to 75 % for FLU (p<0.001), from 36 % to 89 % for Pnc (p<0.001), from 57 % to 73 % for Hep B (p<0.001) and from 34 % to 74 % overall (p=0.008) (Figure 1 and Table 1).

Table 1. Vaccine coverage in 2018 vs. 2021 in patients with IMID

	FLU (%)	Pnc (%)	Hep B*(%)	TT (%)
IBD (n=790)	2018: 76	2018: 73	2018: 67	2018: 80
	2021: 87	2021: 82	2021: 79	2021: 67
	p-value < 0.001	**p-value < 0.001**	**p-value < 0.001**	**p-value < 0.001**
RHEU (n=607)	2018: 69	2018: 36	2018: 57	2018: 65
	2021: 75	2021: 89	2021: 73	2021: 41%
	p-value < 0.001	**p-value < 0.001**	**p-value < 0.001**	**p-value = 0.038**
DER (n=38)	2018: 74	2018: 61	2018: 47	2018: 79
	2021: 71	2021: 82	2021: 65	2021: 71
	p-value = 0.116	p-value = 0.401	**p-value < 0.001**	p-value = 0.394
All IMID (n=1435)	2018: 73	2018: 58	2018: 63	2018: 74
	2021: 81	2021: 85	2021: 77	2021: 56
	p-value < 0.001	**p-value < 0.001**	**p-value < 0.001**	**p-value < 0.001**

*recommended in all seronegative IMID patients with IBD and patients at risk for other IMIDs

Similarly, the vaccination coverage in IBD patients increased significantly from 76 % to 87 % for FLU (p<0.001), from 73 % to 82 % for Pnc (p<0.001), from 67 % to 79 % for Hep B (p<0.001) and from 47 % to 61 % overall (p<0.001) (Figure 1 and Table 1).
For patients with DER, vaccination coverage significantly increased from 47 % to 65 % for Hep B (p<0.001) (Table 1). TT vaccination coverage decreased in all 3 IMID groups from 2018 to 2021.

Conclusion: The implementation of a vaccination tool integrated in the EMR coincided with a significant increase in vaccination rates and also in the total amount of IMID patients that were fully vaccinated according to guidelines. Quite likely, the suboptimal vaccination rate measured in 2018 and the COVID-19 pandemic also raised awareness among patients and healthcare professionals about the importance of following vaccination guidelines.
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POS0158

ADHERENCE TO TELEMONITORING DISEASE ACTIVITY BY ELECTRONIC PATIENT REPORTED OUTCOMES IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A PROSPECTIVE COHORT STUDY

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Background: The use of electronic patient reported outcome measures (ePROM's) enables telemonitoring disease activity in patients with inflammatory arthritis in between consultations. However, recent telemonitoring studies report declining long-term adherence to reporting ePROM's[1,2]. What factors are associated with a decline in adherence is not known.
Objectives: To investigate the factors that are associated with adherence to telemonitoring by an ePROM in patients with inflammatory arthritis.
Methods: We performed a prospective cohort study in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) at Reade Amsterdam, The Netherlands. Patients telemonitored their disease activity weekly for 6 months with a modified Multidimensional Health Assessment Questionnaire including the Routine Assessment of Patient Index Data 3 (RAPID3) that was completed in the "MijnReuma" Reade smartphone application[2]. Adherence was defined as the percentage of weekly completed ePROM and time to dropout as ≥4 weeks nonresponse. Based on literature and through expert meetings, 13 baseline factors were selected to assess their association with dropout through multivariable Cox-regression analysis. The association with the system usability score (measured at 3 months, 1-100) was analyzed with a linear regression for patients who dropped out in month 1, month 2-3 and month 4-6.
Results: A total of 220 consecutive patients was included (mean age 54, 55% females, median disease duration 9 years), of which 99 had RA, 81 PsA, and 40 AS. Adherence to telemonitoring declined from 81% (week 1) to 39% (week 26). Median time to dropout was 17 weeks; a total of 141 patients (64%) stopped

telemonitoring their disease activity. Women had a higher chance to dropout over time compared to men (HR 1.6, p=0.02). The reported usability of the app was higher for patients who were adherent throughout the study (82) compared to patients who dropped out in the 1st month (68, p<0.001), 2nd-3rd month (71, p<0.001) and 4-6th month (78, p=0.18).

Conclusion: Women stopped reporting the ePROM sooner than man and the usability score of the app differed between the adherence and drop-out group. Future research is needed to investigate if the association between the usability score of the app and adherence is causal, and thus if improvements in the usability will lead to lower dropouts. Furthermore, we will perform focus group discussions to identify why women tend to dropout sooner, since this is in contrary to previous research[3].

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Table 1. Hazard ratios for dropout

Variable	HR	95%CI		p
Women	**1,58**	**1,06;**	**2,36**	**0,02**
Higher education	1,36	0,92;	2,02	0,13
Biological usage	1,18	0,83;	1,68	0,35
High medication adherence	1,14	0,80;	1,63	0,47
Diagnosis (relative to RA)				
PsA	1,14	0,77;	1,69	0,53
AS	1,09	0,63;	1,90	0,76
Smartphone usage	1,08	0,94;	1,23	0,29
Charlson Comorbidity index	1,05	0,78;	1,40	0,76
Resident in Amsterdam	1,02	0,72;	1,44	0,93
Disease duration	1,01	0,99;	1,02	0,49
Interaction patient-physician	1,00	0,92;	1,09	1,00
Self-management	1,00	0,98;	1,02	0,72
Age	0,99	0,96;	1,02	0,39
RAPID3	0,97	0,89;	1,06	0,51

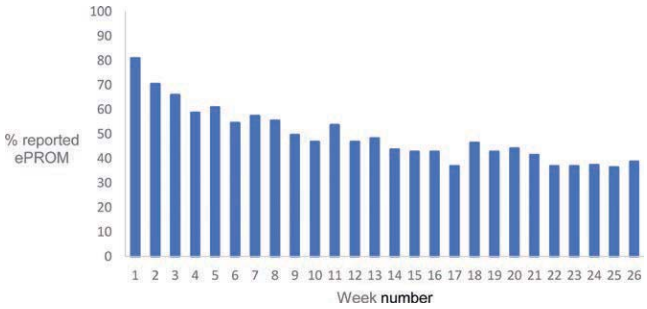

Figure 1. Percentage weekly completed ePRO's during the study.

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POS0159

SEX-RELATED DISPARITIES IN HEALTHCARE UTILIZATION IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A POPULATION-BASED STUDY

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Background: Delayed diagnosis of inflammatory arthritis (IA) such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) is associated with joint damage and disability. So regular timely assessment by both family physicians and specialists is necessary for favorable disease outcomes. Sex (biology) and gender (socio-cultural) related factors influence clinical patterns of IA, patient behavior and their interaction with care providers. This influence could be reflected in patterns of healthcare utilization.

Objectives: To compare patterns of musculoskeletal (MSK)-related healthcare utilization before and after diagnosis between male and female patients with IA in Ontario, Canada.

Methods: We assembled 3 inception cohorts of adult RA, AS and PsA patients diagnosed between April 2010 and March 2017 using Ontario health administrative data. MSK-related healthcare utilization patterns in terms of visits to physicians, MSK imaging and laboratory tests were assessed yearly for 3 years before and after the diagnosis date, and compared between male and female patients. Among individuals ≥ 66 years, prescriptions for rheumatic drugs (NSAIDs, corticosteroids, csDMARDs, advanced therapy (bDMARDs and tsDMARDs)) and opioids were ascertained. Regression models were used to compare healthcare utilization indicators between males and females after adjusting for demographics and comorbidities.

Results: A total of 41,277 patients with RA (69% females), 8,150 patients with AS (51% females) and 6,446 patients with PsA (54% female) were analyzed. Male patients were significantly older than female patients only in the RA cohort (mean age M 60.4 y, F 57.1 y). Multimorbidity, depression and osteoporosis were more common in female patients and cardiovascular disease in male patients across the 3 cohorts.

Similar trends of sex-related differences were observed in all three cohorts. Female patients were more likely to visit rheumatologists and family physicians than male patients especially in earlier pre-diagnosis periods (Figure 1). Male patients were more likely to visit emergency department immediately before diagnosis. A similar female predominance was observed in imaging modalities of X-rays and ultrasounds (adjusted ORs for F:M 1.15 - 1.2 for X-rays and 1.07 -1.44 for ultrasounds), and laboratory tests before diagnosis (adjusted ORs for F:M 1.10 to 2.17) across the three cohorts.

Overall DMARD prescription patterns in older male and female patients were similar across the three cohorts except more csDMARD prescriptions in female AS patients (Table 1). Female RA patients were more likely to use NSAIDs and opioids.

Table 1. Odds ratios for prescription patterns in inflammatory arthritis for older female to male patients after diagnosis

Medication Class	Adjusted Odds Ratio (95% Confidence Interval)		
	Rheumatoid Arthritis	Ankylosing Spondylitis	Psoriatic Arthritis
csDMARD			
Yr 1	1.00 (0.92, 1.09)	**1.82 (1.38, 2.41)**	1.05 (0.81, 1.37)
Yr 2	1.00 (0.92, 1.08)	**1.66 (1.24, 2.22)**	0.94 (0.73, 1.20)
Yr 3	1.05 (0.97, 1.14)	**1.51 (1.12, 2.04)**	0.85 (0.66, 1.09)
Advanced therapy			
Yr 1	0.99 (0.78, 1.25)	0.79 (0.49, 1.25)	0.75 (0.47, 1.19)
Yr 2	1.17 (0.99, 1.39)	0.80 (0.53, 1.23)	0.91 (0.61, 1.37)
Yr 3	**1.23 (1.05, 1.45)**	1.04 (0.67, 1.61)	0.88 (0.6, 1.30)
NSAID			
Yr 1	**1.14 (1.04, 1.25)**	1.22 (0.91, 1.63)	0.94 (0.71, 1.24)
Yr 2	1.1 (0.99, 1.22)	1.04 (0.77, 1.43)	0.98 (0.73, 1.32)
Yr 3	**1.16 (1.04, 1.30)**	1.35 (0.96, 1.89)	1.02 (0.73, 1.41)
Opioid			
Yr 1	**1.39 (1.22, 1.58)**	1.23 (0.85, 1.78)	1.32 (0.87, 1.98)
Yr 2	**1.51 (1.32, 1.72)**	1.22 (0.85, 1.76)	1.14 (0.75, 1.75)
Yr 3	**1.46 (1.27, 1.68)**	1.42 (0.96, 2.09)	1.45 (0.95, 2.23)

Bolded results are statistically significant (p < 0.05). Odds ratios for female to male patients adjusted for age, residence, income quintiles, comorbidities and access to rheumatologists

Conclusion: Female patients with IA have higher MSK-related healthcare utilization which may indicate biological differences in disease course or sociocultural differences in healthcare seeking behavior between male and female patients.

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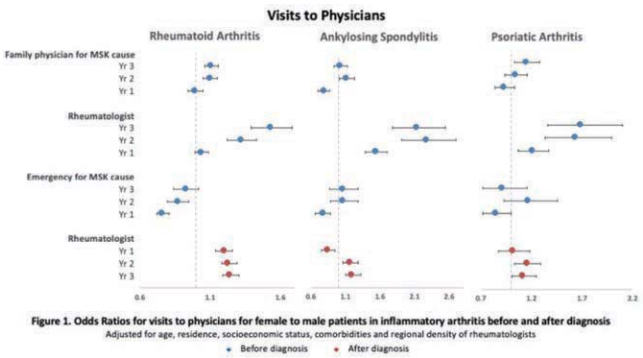

Figure 1. Odds Ratios for visits to physicians for female to male patients in inflammatory arthritis before and after diagnosis
Adjusted for age, residence, socioeconomic status, comorbidities and regional density of rheumatologists

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POS0160 THE EMPLOYMENT GAP IN PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES COMPARED WITH THE GENERAL POPULATION: A SYSTEMATIC LITERATURE REVIEW

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Background: Many people with rheumatic and musculoskeletal diseases (RMDs) experience problems at work and some may even have to stop working due to ill health. In most countries, RMDs are a major cause of worker productivity loss. The peak age of onset of many adult onset RMDs is between ~30-50 years, meaning that the majority of patients are still in employment when diagnosed with their chronic disease. Uncertainty about employment prospects and job attainment is also a major concern for young adults with juvenile idiopathic arthritis (JIA) for whom their first job may influence their future employment prospects. From both a societal and patient perspective it is important to gain an understanding about the impact of juvenile and adult onset RMDs on work outcomes. Data comparing productivity loss with the general population are more relevant for care and healthcare planning. However, these data are more scarce and have not been summarized recently across RMDs.
Objectives: To systematically summarize the literature on work outcomes in people with RMDs compared with the general population.
Methods: A systematic literature review (SLR) was conducted to compare work outcomes in people with various RMDs (i.e. JIA, RA, PsA, AxSpA, SSc, SLE, gout, FM, and OA) with the general population or healthy controls as part of the EULAR Task Force on work. A search for eligible observational studies was performed in Medline, Embase and PsycInfo between 2000 and May 2021. Work outcomes were categorizedaccortding to employment status, work disability/stopped working due to ill health, absenteeism, presenteeism and other.
Results: 541 abstracts were extracted and screened for eligibility. Results of 65 studies fulfilling the inclusion criteria were evaluated for this study, including 28 prospective/retrospective longitudinal cohort studies, 34 cross-sectional studies and 3 (nested) case-control studies. The majority of the studies were conducted in Europe (63.1%). The most common RMD evaluated was RA (26.2%) followed by OA (15.4%), SLE (15.4%), AxSpA (12.3%), FM (9.2%), mixed population (7.7%), JIA (7.7%), PsA (3.1%), SSc (1.5%), and gout (1.5%). In papers reporting disease duration (n=38), the majority of the study population had established disease (76.3%). Several work outcomes were evaluated with some papers reporting more than one work outcome: employment/work status (41.5%), unemployment (9.2%), work disability/pension or stopping work due to ill health (38.5%), absenteeism (52.3%), presenteeism (10.8%), and other (e.g. reduced working hours) (29.2%). Fifty-two papers applied statistical tests (e.g. indirect standardisation, logistic regression analysis, Cox regression analysis) to compare work outcomes in people with RMDs with a control/general population. The percentage of papers reporting the work outcomes to be worse, not significantly different or better in the RMD population compared to the control population (n papers included per work outcome; %) was, respectively: employment/work status (n=26; 73.1%, 23.0%, 3.8%), unemployment (n=6; 66.7%, 33.3%, 0%), work disability/stopping work (n=22; 90.9%, 9.4%, 0%), absenteeism (n=26; 92.3%, 7.7%, 0%), presenteeism (n=8; 87.5%, 12.2%, 0%), other (n=19; 84.2%, 15.8%, 0%).
Conclusion: Despite better disease management during the last two decades there is still a significant employment gap between people with RMDs and the general population. It is therefore essential that health professional organisations, policy makers, patient organisations and employers should collaborate to minimize the employment gap and optimize employment opportunities among people with juvenile and adult onset RMDs.
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POS0161 WORK STATUS IN PATIENTS WITH INFLAMMATORY RHEUMATIC MUSCULOSKELETAL DISEASES: RESULTS OF A BELGIAN COMPARATIVE STUDY

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Background: Inflammatory Rheumatic Musculoskeletal Diseases (RMD) constitute a heterogeneous group of chronic disorders with a potential major individual and socio-economic burden. RMD patients often report work-related difficulties (e.g. productivity loss, sick leave, work disability) which contribute significantly to indirect costs and may lead to additional premiums or exclusion when contracting private insurances. However, work-related epidemiological data in Belgium date back to a pre-biologics era, albeit that diagnosis, management and treatment strategies have drastically improved in the last decade.
Objectives: To investigate actual work participation status of inflammatory RMD patients in Belgium, and to benchmark these data to the general Flemish population.
Methods: During an outpatient visit at the rheumatology clinic of Ghent University Hospital, a tertiary hospital in the Flemish region, adult patients with spondyloarthritis (SpA), rheumatoid arthritis (RA), and systemic sclerosis (SSc) were questioned on their socio-economic status (May 2018 to June 2021). SpA patients fulfilled the ASAS classification criteria for axial or peripheral SpA. RA patients fulfilled the 2010 ACR/EULAR classification criteria or had undifferentiated arthritis most suggestive for RA. SSc patients fulfilled the LeRoy and Medsger's criteria. Employment rate, weekly working hours and work disability were compared to the general Flemish population (Dutch-speaking part of the country) in 2019 (https://statbel.fgov.be/en); data on sick leave were deduced from the 2018 national Health Interview Survey.
Results: Among the 483 participants, 262/275 (95%) SpA, 63/102 (62%) RA, and 83/106 (78%) SSc were at a work-productive age (<65 y/o). Table 1 summarizes socio-demographic and clinical characteristics.

Table 1.

	SpA (n=262)	RA (n=63)	SSc (n=83)
Male	148 (56%)	15 (24%)	18 (22%)
Age (y)	40.7±11.0	53.5±10.8	49.9±10.6
Symptom duration (y)*	7.8 (4.7-15.7)	3.9 (1.4-5.8)	5.8 (2.8-11.5)
Age at diagnosis (y)	32.6±11.1	48.3±12.0	43.9±10.7
Biomarker†	170 (70%)	52 (82%)	46 (55%)
Disease activity††	1.9±1.0	2.1±1.0	4 (1-8)
Functional index**	2.3±2.2	67±14	-
EQ-5D scale	0.79±0.22	0.80±0.18	0.74±0.24
Biologics treatment	123 (58%)	15 (24%)	7 (8%)
Educational level			
Low	100 (38%)	36 (57%)	53 (64%)
High	162 (62%)	27 (43%)	30 (36%)
Classification criteria	ASAS: axSpA: 192 (73%) perSpA: 70 (27%)	ACR/EULAR 2010: 46 (73%)	Leroy & Medsger: LSSC: 21 (25%) LcSSc: 47 (57%) DcSSc: 15 (18%)

† HLA B27 (SpA), RF/ACPA (RA), SSc-related auto-antibodies (SSc). †† ASDAS-CRP (SpA), DAS28 (RA), mRSS (SSc). *Disease duration from first non-Rayneud phenomenon in SSc. **BASFI (SpA), Michigan Hand Outcomes Questionnaire (RA).

Crude employment rates were 82% in SpA, 56% in RA and 63% in SSc. Age- and sex-adjusted employment rates (indirect standardization) were respectively 75%, 68%, and 66%, corresponding to a standardized employment ratio of 1.00 (95% CI 0.87 – 1.14) for SpA, 0.89 (0.64 – 1.24) for RA, and 0.88 (CI 0.67 – 1.15) for SSc.

SpA patients worked 39.5±10.9h/week, compared to 40.9±16.9h in RA and 33.0±12.4h in SSc (p=0.003). Flemish employees worked on average 39.7h (full-time) and 25.7h (part-time) per week.

In the working population, 48% of SpA patients, 53% RA and 78% SSc reported sick leave in the previous year, compared to 42% in Flanders. Long-term work disability was reported by respectively 10%, 17% and 20% of patients (p=0.03) compared to 9% in the reference population.

The median retention time on the labour market was not significantly different between SpA (42.1 years), RA (42.1 years) and SSc (41.2 years) (p=0.94, Figure 1).

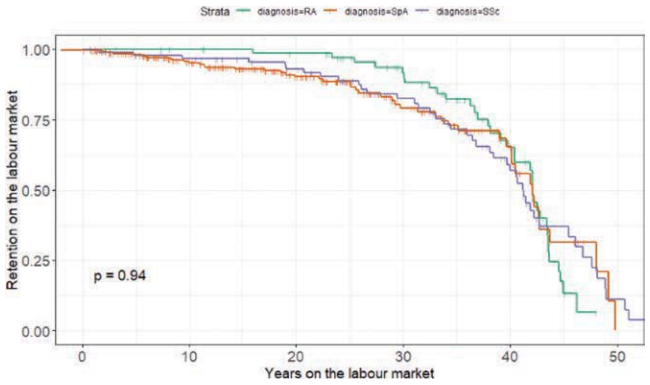

Figure 1. retention time on the labour market since start of patient's professional career.

Conclusion: Our data refute the common perception that patients with RMDs, especially inflammatory joint diseases, have significantly worse work outcomes compared to the general population. In an era of early diagnosis and treatment, more recent datasets could be used to realistically estimate the odds of these important health economic outcomes.

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POS0162 HOW ACCURATELY CAN WE IDENTIFY RHEUMATOID ARTHRITIS BY ICD-10 CODES? A LINKAGE OF CROSS-SECTIONAL SURVEY DATA WITH CLAIMS DATA

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Background: Claims data from health insurance companies are a valuable source in health services research to provide insights on health care provision for an unselected patient collective. However, the available ICD-10 diagnoses have been collected for billing purposes and their validity is not clear.

Objectives: The aim of this analysis was to assess the positive predictive values (PPV) of a ICD-10 diagnosis of rheumatoid arthritis (RA) and additional criteria (specific medication, measurement of inflammatory markers, contact to a rheumatologist) in German claims data using patient-reported confirmed diagnosis as reference/gold standard.

Methods: Within the PROCLAIR project (Linking Patient-Reported Outcomes with CLAims data for health services research In Rheumatology), data from a large German statutory health insurance with 6.6 million persons aged 18 to 79 were used. We identified a random sample of persons for which an ICD-10 code for RA (M05/M06) was available in at least two quarters in outpatient care. The sample was stratified for age (18 to 49, 50 to 64, 65 to 79 years), sex and seropositive (M05)/ seronegative RA (M06). Persons were asked to confirm their RA diagnosis ("What does your attending physician call the disease you are suffering from?") with answer options "chronic polyarthritis", "rheumatoid arthritis", "rheumatism of the joints" "other (please specify)". The answer was used as the gold standard for RA diagnosis. Analyses were weighted to represent the total RA population of the database. Patient-reported information was linked to the claims data given patient consent. PPVs (% of confirmed RA diagnosis) were calculated for ICD-10-diagnosis or additional examination of inflammatory markers (erythrocyte sedimentation rate/C-reactive protein), prescription of specific medication (disease-modifying anti-rheumatic drugs, non-steroidal anti-rheumatic drugs and glucocorticoids) and contact to a rheumatologist, in the respective year.

Results: We contacted 6,193 persons with a claims diagnosis of RA. Of these 3,184 responding (51%), N=2,535 (81%) confirmed that they had RA. PPVs were 81% for ICD-10 only, 94% in M05 and 76% in M06. When additional criteria were taken into account, PPVs increased to 82% (measure of inflammatory markers), 85% (rheumatologist) and 89% (medication), respectively (Figure 1). However, PPVs ranged from 72% to 76% even if the additional criteria were not fulfilled. PPVs were lowest in men aged 18-49 years and relatively stable among women of all age groups.

Figure 1.

Positive predictive values (PPVs) for different criteria additional to ICD-10 codes to identify rheumatoid arthritis patients in claims data

% RA-Diagnosis Confirmed	No additional criterion	ESR/CRP		Specific Medication		Rheumatologist contact		ESR/CRP + Medication + Rheumatologist	
		Yes	No	Yes	No	Yes	No	Yes	No
All	81	82	73	89	72	85	76	89	76
Women	81	83	73	90	73	85	77	89	77
Men	79	80	72	88	67	82	74	85	74
Age 18-49	75	76	73	81	67	79	70	79	72
Age 50-64	81	84	66	90	71	87	73	90	75
Age 65-79	82	83	78	91	75	85	80	91	78
Women, Age 18-49	78	78	76	85	69	82	72	82	75
Women, Age 50-64	81	85	63	90	72	88	74	90	76
Women, Age 65-79	82	83	79	91	75	85	80	91	78
Men, Age 18-49	64	65	62	68	58	66	62	68	61
Men, Age 50-64	78	79	76	89	63	83	73	87	71
Men, Age 65-79	83	84	74	93	74	88	79	91	79

ESR: erythrocyte sedimentation rate CRP: C-reactive protein

Conclusion: The ICD-10 codes M05 and (less optimal) M06 have high PPVs and are therefore feasible to identify RA in claims data. The prerequisite of specific medication seems to be the most useful one in identifying RA.

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Disclosure of Interests: Johanna Callhoff Paid instructor for: Rheumatologische Fortbildungsakademie GmbH, Grant/research support from: Abbvie, AstraZeneca, BMS, GSK, Galapagos, Lilly, Medac, MSD, Pfizer, Sanofi, UCB, Katinka Albrecht: None declared, Ursula Marschall Employee of: Employee of BARMER, Falk Hoffmann: None declared

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POS0163 USEFULNESS OF WEARABLE DEVICES TO ASSESS PHYSICAL ACTIVITY IN NON-INFLAMMATORY AND INFLAMMATORY RHEUMATIC DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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Background: In the last years, the rise of personalized medicine has grown up. So, patient-oriented wearable technologies have been developed. Wearable devices (WD) are useful to collect objective data related to physical activity. In the management of rheumatic musculoskeletal disorders (RMDs) a regular physical activity is an important recognized non-pharmacological intervention [1].

Objectives: This systematic review aims at evaluating how the use of WDs impacts physical activity in patients with non-inflammatory and inflammatory rheumatic diseases.

Methods: A systematic review and meta-analysis were performed. A comprehensive search of articles was performed in the following databases: MEDLINE via PubMed, EMBASE, CINAHL, and Scopus. A random-effect meta-analysis has been carried out on the number of steps and moderate to vigorous physical activity (MVPA). Univariable meta-regression models have been computed to assess the possibility that the study characteristics may act as effect modifiers on the final meta-analysis estimate. The primary outcome is the level of physical activity evaluated with a wearable device as a number of daily steps and MVPA. The secondary outcome is the comparison of both a number of steps and MVPA to reference value for healthy people. The number of steps per day and the time spent in MVPA considered as a mean or median were collected. Missing information was calculated from available data when possible.

The reference value for steps was 7000 steps per day, this value was derived by a literature review commissioned by the Public Health Agency of Canada on the number of steps/day suitable for adults [2]. MVPA reference value was of 150 min/week and was derived by WHO guidelines [3].

Results: An overall of 1788 studies was considered in the title/abstract screening. In the analysis, 51 articles were included, with an overall of 7488 participants. Twenty-two studies considered MVPA outcome alone, 16 studies number of steps alone and 13 studies reported information on both outcomes.
The results of this meta-analysis show that there is a high level of I^2 heterogeneity, 99%, according to diagnosis.
Recommended threshold for daily steps was reached for MVPA (36.35, 95% CI 29.39 - 43.31) but not for daily steps (-1092.60, 95% CI -1640.42 - -544.77), with fibromyalgia reporting a higher number (6290, 95% CI 5198.65 – 7381.62) of daily steps compared to other RMDs. Patients affected by chronic inflammatory arthropathies seem to fare better in terms of daily steps than the other categories. Patients with rheumatoid or other chronic arthritis reported a higher number of steps, respectively 6361 (95% CI 5382.51; 7340.35) and 6290.14 (95% CI 5198.65; 7381.62).
Non-elderly people show a higher overall level of physical activity compared to the elderly, 6796.11 (95% CI 5974.10; 7618.13) versus 5431.85 (95% CI 4633.76; 6229.95). Non-elderly group show higher level MVPA compared to the reference value 38.96 (95% CI 18.35; 59.68) vs 11.77 (95% CI 3.32; 20.21).
Conclusion: RMDs suffer of low level of physical activity and WDs are useful and affordable instruments to support the increase of it. WDs can be used in daily monitoring of physical activity in RMDs.
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Improving our care and understanding of paediatric RMDs

POS0164 GENETIC ANALYSIS OF WHOLE EXOME SEQUENCING IN A COHORT OF CHILDREN WITH REFRACTORY JIA REVEALS GENETIC RISK FACTORS FOR RARE JUVENILE DISEASES.

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Background: Juvenile idiopathic arthritis (JIA) encompasses a group of heterogeneous rheumatic diseases of childhood onset. JIA can result in long term disability and remission is the main goal of treatment. However refractory disease can occur, which is defined as the absence of response to a standard disease therapy. A genetic basis for refractory disease has yet to be explored, where deleterious rare variants can complicate diagnosis or treatment outcome.
Objectives: To investigate, through genetic analysis, whether children with JIA that is refractory carry rare genetic risk factors in genes linked to monogenic diseases.
Methods: Whole exome sequencing of 99 children with JIA was performed with the Agilent SureSelect Human All ExonV6 kit. All quality control, variant filtering and annotation was performed in Varseq (version 2.2.1). Variants with a read depth <30 and genotype quality <80 were removed. Rarity and pathogenicity filters were then applied to remove variants with an allele frequency >1% (based on ExAC, gnomAD, gnomAD exome, NHLBI and 1KGp phase 3), classified as benign or likely benign on ClinVar, with a CADD PHRED score <15 and a REVEL score >0.7. Variants were annotated if they appeared in a gene from the primary immunodeficiency PanelApp (Martin et al., 2019), in a gene associated with an arthritis phenotype or in a gene that appeared on a paediatric monogenic gene list. The variants were then classified using ACMG guidelines (Richards et al., 2015) and benign, or likely benign, classified variants were removed.
Results: A total of 628 variants were identified and we found that 20 out of the 99 children screened were heterozygous for at least one recognised variant in a gene linked to a monogenic disease. Five of these children carried more than one recognised variant linked to monogenic genes. Here we provide a number of illustrative examples: three genes, *ADAR, ATP7B and MVK,* were prioritised based on prior evidence of associated disease. The variant p.Pro193Ala (gnomAD allele frequency (GAD) $2.2x10^{-3}$) of *ADAR* has previously been deemed pathogenic in a homozygous or compound heterozygous state for Aicardi-Goutières syndrome. Adenosine deaminases (ADARs) catalyse the hydrolytic deamination of adenosine to inosine in dsRNA and is suggested to act as a suppressor of type 1 interferon-stimulated genes. Within *ATP7B*, two distinct variants were detected; p.Gln1142His (GAD $1.6x10^{-5}$) and p.Ile1148Thr (GAD $4.0x10^{-5}$) have previously been reported as pathogenic, in combination with a third variant, for Wilson's disease and were carried by one individual in this cohort. *ATP7B* encodes copper-transporting ATPase 2, which supplies copper to ceruloplasmin. Variant p.Val377Ile (GAD $1.6x10^{-3}$) of *MVK* was detected in eight individuals in this cohort, interestingly five of these individuals also carried at least one *HLA-DRB1* stop-gained variant. This *MVK* mutation has been confirmed as pathogenic in a homozygous or compound heterozygous state for mevalonate kinase deficiency. MVK converts mevalonic acid into mevalonate-5-phosphate in the cholesterol synthesis pathway. Additionally, two stop-gained loss of function *HLA-DRB1* variants, p.Tyr107Ter and p.Gln125Ter, were detected in five and 20 individuals, respectively, in this cohort. *HLA-DRB1* is a recognised susceptibility locus for JIA.
Conclusion: Screening of a cohort of 99 children with JIA that have refractory disease has revealed that individuals carry deleterious variants in genes linked to monogenic forms of disease. These results highlight that the genetic basis for refractory disease needs to be further investigated. Carrying additional genetic risk factors to disease may complicate disease outcome and genetic screening of children with refractory JIA may improve treatment outcome in the future.
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POS0165 WHOLE EXOME SEQUENCING TO IDENTIFY RARE INFLAMMATORY VARIANTS IN AN IRISH COHORT WITH CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO)

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Background: Chronic nonbacterial osteomyelitis (CNO) is a rare inflammatory disease affecting bone which predominantly occurs in the paediatric population. It is frequently associated with pustulosis, psoriasis, inflammatory bowel disease and arthritis, in particular enthesitis-related arthritis. Activation of the *NLRP3* inflammasome has been implicated in both human and mouse models of the disease.
Objectives: To identify a candidate list of rare, deleterious variants in known inflammatory genes in an Irish cohort with CNO.
Methods: 41 unrelated Irish children with CNO were recruited. Whole exome sequencing was performed on blood using Agilent SureSelect XT Human All Exon V6 kits and Illumina HiSeq 3000 with 150bp paired-end reads. Reads were aligned to the hg19 reference genome. After preprocessing, variants were hard filtered using quality by depth(QD) > 2.0, read depth (DP) >10 and genotype quality (GQ) >20. Synonymous variants and variants with MAF > 0.01 were excluded from further analysis. Remaining variants were filtered against existing databases of genes known to be associated with inborn errors of immunity, autoimmunity or autoinflammation. The Gene Damage Index (GDI) was used to identify genes which are least tolerant to variance and CADD phred-like scores to identify variants predicted to be deleterious. Genes with variants in >=2 CNO patients were included in the candidate list and variants manually checked using the Integrative Genomics Viewer (IGV).
Results: After filtering low-quality, synonymous and common variants, 17,293 variants were filtered against a database of 581 known inflammatory genes. 350 rare variants in 201 genes predicted to be intolerant to variance were identified. After excluding those present in one individual only, ranking by CADD phred-like scores and manual inspection on IGV, a candidate list of 25 genes remained. The same variant in *IL17RA, NLRP1* and *KMT2D* was present in 3 unrelated individuals (Table 1). *IL17RA* belongs to the Th17 pathway which is involved in psoriasis pathogenesis. *NLRP1* is implicated in several autoinflammatory diseases including psoriasis. None of the individuals carrying these variants in *IL17RA* or *NLRP1* have psoriasis. One individual with *IL17RA* variant has 1st-degree family history of psoriasis. Rare variants which are predicted to be deleterious were found in two individuals in each of the following genes in the IL-17 signalling/Th17 differentiation pathway: *IL17RB, IL17RE, IL25, HIF1A* (Table 1). This suggests that the Th17 pathway may play a role in disease pathogenesis in a proportion of children with CNO.
Conclusion: *IL17* +/- the IL-17 signalling/Th17 differentiation pathways, and *NLRP1* provide targets for further investigation in CNO. The role of these candidate genes may be further elucidated through gene-/pathway-based burden testing against a matched control population.
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Table 1.

Sample	Gene	Variant	Effect	CADD	CNO MAF	gnomAD MAF	OR	p-value
16 37 42	*IL17RA*	22- 17586757-T>C	Nonsynonymous p.W320R	24.5	0.04	0.0034	11.06	0.003
5 9 38	*NLRP1*	17- 5462417- C>A	Nonsynonymous p.Q533H	26.2	0.04	0.0058	6.47	0.01
2 11 21	*KMT2D*	12- 49434409-G>A	Nonsynonymous p.P2382S	21.3	0.04	0.0056	6.75	0.01
10 40	*IL17RB*	3-53889368-G>A	Nonsynonymous p.G177R	29.7	0.024	0.0061	4.05	0.09
7 43	*IL17RE*	3-9957033-C>A	Nonsynonymous pL400M	24.9	0.024	0.0086	3.19	0.13
11 24	*IL25*	14-23845076-G>A	Nonsynonymous p.R174H	34	0.024	0.0085	3.02	0.15
9 15	*HIF1A*	14-62187212-G>C	Nonsynonymous p.V74L	23.7	0.024	0.0026	9.9	0.02

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POS0166 POLYARTICULAR JIA HAS A DISTINCT CO-INHIBITOR RECEPTOR PROFILE AMONG OTHER JIA SUBTYPES

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Background: Juvenile idiopathic arthritis (JIA) is the most common inflammatory joint disease in children, driven by continuous T-cell activation.[1] T cell activation is counter-balanced by signals generated by co-inhibitory receptors (co-IRs) such CTLA-4, PD-1, LAG-3, and TIM-3.[2]

Objectives: We aimed to identify the role of co-IRs in the pathogenesis of different subtypes of JIA.

Methods: In total, we included 107 patients with oligoarticular JIA (n=67), polyarticular JIA (n=12), enthesitis related arthritis (n=17), systemic JIA (n=11) and healthy controls (HC, n=10). We collected plasma samples from the patients during the active phase of their disease. We measured the soluble plasma levels of co-IRs by commercial pre-defined cytometric bead array kits and their cellular expression by flow cytometry in blood mononuclear cells. We compared the plasma levels and cellular expressions of different coIRs within different JIA subgroups.

Results: IL-2 levels were lower than HC in all JIA subgroups. The polyarticular JIA group distinguished from the four different JIA subgroups, by having different co-IR pattern. In this specific subgroup, CTLA4, PD-1 and 4-1BB levels were higher than other groups. Polyarticular JIA is the more chronic and severe form of JIA, especially when compared to oligoarticular JIA. (Figure 1).

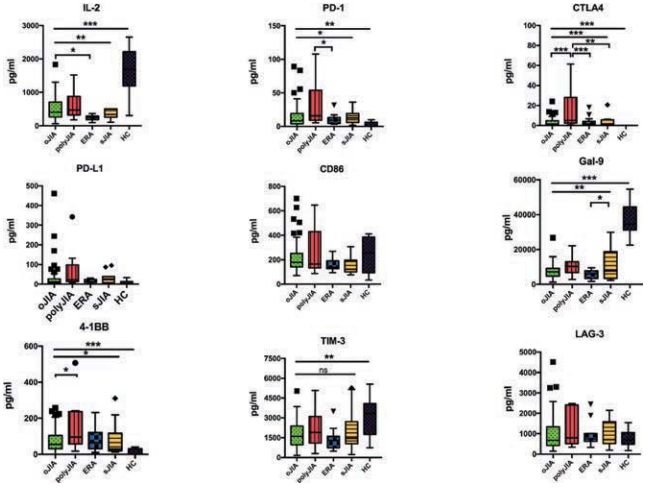

Figure 1.

We investigated the correlations between disease activity markers and plasma co-IRs. Plasma TIM3 levels correlated with erythrocyte sedimentation rate, C-reactive proteins and JADAS in the polyarticular JIA group. In oligoarticular JIA group, JADASs correlated with plasma PD-1 levels, C-reactive protein with PD-L1 plasma levels. Erythrocyte sedimentation rates correlated with IL-2, CD86, PD-L1 and PD-1 plasma levels. There was no correlation between disease activity markers and co-IRs levels in the systemic JIA group and enthesitis related arthritis group.

Finally, we analysed the cellular surface expression of different co-IRs on the PBMCs of different JIA subtypes. Similar to plasma levels, both the percentage and the MFI (mean fluorescence intensity) of CTLA4 expression was higher in polyarticular JIA subgroup.

Conclusion: This is the first report studying the effects of different co-IRs in different subtypes of JIA. Polyarticular JIA patients had a different coIR profile, having more CTLA-4, PD-1 and 4-1BB in their plasma than the other subtypes of JIA

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Disclosure of Interests: None declared

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POS0167 A PROTEOGENOMIC MAP OF NATURAL KILLER CELLS IN OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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Background: Natural Killer (NK) cells are innate lymphocytes which are specialised for recognising stressed cells, classically divided into cytotoxic (CD56dim) and cytokine-producing (CD56bright) populations. During oligoarticular Juvenile Idiopathic Arthritis (oligo-JIA), an unknown trigger induces the recruitment of peripheral immune cells into synovial joints, which in turn creates a chronic inflammatory environment. This can result in joint contractures and extraarticular complications, highlighting the requirement for early disease intervention. The contribution of NK cells toward immunopathology during the early stages of disease and in subsequent arthritic flares is unknown, providing a potential avenue for understanding disease course and therapeutic intervention.

Objectives: We aimed to assess the contribution of NK cells to the early pathogenesis of oligo-JIA by identifying inflammatory signatures present in patient synovia, and which signals could induce them.

Methods: Peripheral blood (PB) and synovial fluid (SF) were drawn from 4 patients at the first clinical presentation of oligo-JIA. Flow-cytometry Activated Cell-Sorting (FACS) was used to unbiasedly isolate NK cells (CD3-CD7+), and single cell RNA-sequencing (scRNA-Seq) paired with

oligonucleotide-tagged antibodies (CITE-Seq) performed, allowing us to generate a proteogenomic dataset of 35,609 NK cells. Antibody-derived-tags were used to delineate whether cells were isolated from PB or SF, and a community detection algorithm was used to cluster neighbours of cells for differential gene expression.

Results: We identified 468 differentially expressed genes (>0.2 log2 fold change) between peripheral and synovial NK cells, among which were CD56bright- and CD56dim-specific genes, and a synovia-specific signature. Antibody-tag measurements confirmed the majority of synovial NK cells to be phenotypically CD56bright, with a spectrum of modified gene expression patterns compared of those in the periphery. 6 distinct synovial clusters were identified by community detection, among which were a large number of proliferating cells, a transitionary CD56bright population, and 2 uniquely activated signatures.

Conclusion: Synovial NK cells possess a significantly different transcriptomic identity compared with those in the periphery. However, though they share a gene signature that is most comparable to blood CD56bright NK cells, it is not identical. Uniquely activated subpopulations also provide the first evidence of NK cell activation during oligo-JIA pathogenesis, suggesting that these cells could hold therapeutic potential.

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Disclosure of Interests: None declared

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POS0168 NON-INVASIVE IMAGING IN JUVENILE LOCALISED SCLERODERMA: HIGH-FREQUENCY ULTRASOUND, THERMOGRAPHY, LASER DOPPLER & MULTISPECTRAL IMAGING

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Background: Outcome measures which can differentiate activity (inflammation) from damage (fibrosis/atrophy) would facilitate development of new treatment strategies in juvenile localized scleroderma (JLS) to target the inflammatory phase of the disease.

Objectives: To evaluate whether in JLS, non-invasive imaging modalities (high frequency ultrasounds (HFUS), multispectral imaging (MSI), laser doppler imaging (LDI) & infra-red thermography (IRT)) can detect differences between affected & non-affected skin, as a next step in developing these as outcome measures. Our hypothesis was that blood flow (and therefore temperature & oxygenation) would be increased in lesional skin.

Methods: Participants aged 4-17 were recruited from 3 paediatric rheumatology centres in the UK. For each participant, a single lesion was selected. HFUS (30MHz), MSI (bespoke camera and tuneable liquid crystal filter, coupled to custom analysis software, 500nm/710nm wavelengths), LDI and IRT imaging were performed at four sites relating to each lesion: two of affected skin (centre & inner edge of lesion) and two of non-affected skin (one cm from edge of lesion ('outer') & contralateral unaffected side). Imaging was performed at 4 visits at 3 monthly intervals. Mean values were compared between the four sites using data from all visits by mixed-effects linear regression to account for individual-level clustering.

Results: 24 participants completed all 4 visits and 1 attended 3. 20 participants were female (80%) & 5 male (20%). Mean age at diagnosis was 7.6 years & disease duration 4.9 years. Subtype of disease was linear head in 5/25 (20%), linear limb 12/25 (48%), generalised morphea 1/25 (4%), mixed 5/25 (20%) and superficial plaque in 2/25 (8%).

Table 1 shows a subset of data. All 4 imaging techniques could detect differences between healthy (outer/contralateral) & affected skin (centre/inner edge). For HFUS, there was strong evidence of a difference between affected & unaffected skin ($p<0.001$) indicating affected skin is thinner than unaffected. Higher mean values of oxygenation, perfusion & temperature were observed in affected compared to non-affected skin in MSI, LDI and IRT respectively. There was no statistical difference seen between inner edge and centre of the lesion in any of the methods.

Table 1. Mean differences between different locations for each imaging technique

Imaging technique	Location	Overall mean difference (95% CI)	p-value
HFUS	Centre - Contralateral	-0.34 (-0.46, -0.22)	<0.001
	Inner edge - Contralateral	-0.30 (-0.40, -0.20)	<0.001
(mm)	Centre - Outer	-0.35 (-0.46, -0.24)	<0.001
	Inner edge - Outer	-0.31 (-0.40, -0.21)	<0.001
	Centre - Inner edge	-0.04 (-0.10, 0.02)	0.168
MSI	Centre - Contralateral	0.06 (0.03, 0.10)	<0.001
	Inner edge - Contralateral	0.06 (0.03, 0.09)	<0.001
(rel units)	Centre - Outer	0.04 (0.01, 0.07)	0.012
	Inner edge - Outer	0.03 (0.00, 0.06)	0.028
	Centre - Inner edge	0.01 (0.00, 0.02)	0.251
LDI	Centre - Contralateral	44.8 (24.4, 65.2)	<0.001
	Inner edge - Contralateral	47.9 (21.0, 74.8)	<0.001
Relative perfusion	Centre - Outer	19.1 (1.0, 37.1)	0.039
units	Inner edge - Outer	24.8 (6.7, 42.9)	0.007
	Centre - Inner edge	-3.5 (-20.3, 13.2)	0.679
IRT	Centre - Contralateral	0.58 (0.24, 0.91)	0.001
	Inner edge - Contralateral	0.44 (0.13, 0.75)	0.005
°C	Centre - Outer	0.44 (0.22, 0.66)	<0.001
	Inner edge - Outer	0.30 (0.09, 0.52)	0.006
	Centre - Inner edge	0.14 (-0.05, 0.32)	0.153

The overall mean difference is the measurement of the first location minus the measurement from the second location (e.g. centre minus contralateral), averaged across the four visits.

Conclusion: Our results suggest non-invasive imaging can detect differences between healthy & unaffected skin in JLS. Whether each technique is only measuring activity & not damage requires further evaluation. The leading edge of lesions has historically been considered as most active compared to the centre. However, no difference was seen between centre & inner edge measurements suggesting that in future studies, imaging protocols can be simplified.

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POS0169 OPEN-LABEL, LONG-TERM (10-YEAR) STUDY OF THE SAFETY OF ETANERCEPT IN CHILDREN AND YOUNG ADULTS WITH EXTENDED OLIGOARTICULAR, ENTHESITIS-RELATED, OR PSORIATIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: CLIPPER2 was an 8-year, open-label extension of the phase 3b, multicenter, 2-year CLIPPER study of the safety and efficacy of etanercept (ETN) in the treatment of patients (pts) with juvenile idiopathic arthritis (JIA) categorized as extended oligoarticular arthritis (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA).

Objectives: The objective of this analysis was to describe the safety of ETN in this population after 10 years of follow up.

Methods: Pts (n=127) with eoJIA (2-17 years), ERA, or PsA (each 12-17 years) who received ≥1 ETN dose (0.8 mg/kg once weekly [max, 50 mg]) in CLIPPER were eligible to enter CLIPPER2. The primary outcome measure was the occurrence of malignancy. Long-term safety was assessed as the total incidence of events from CLIPPER baseline (BL) to month (mth) 120, frequency of events per 100 patient-years (EP100PY), and frequency of events in each study year.

Results: A total of 109/127 (86%) pts entered CLIPPER2; 99 (78%) continued in the active treatment period. At mth 120, 84 (66%) pts had completed the study; 27 (21%) while actively taking ETN; 7 (6%) had withdrawn from treatment due to low/inactive disease; 5 (4%) had re-started ETN following an earlier withdrawal from treatment; and 45 (35%) had stopped ETN (but remained under observation); 25 (20%) pts permanently discontinued from the CLIPPER2 study. In CLIPPER/CLIPPER2, 1 case of malignancy (Hodgkin's disease) was reported (1 pt with eoJIA in Year 3). There was 1 case of uveitis (1 pt with eoJIA in Year 8) and 3 of Crohn's disease (2 pts with ERA, Year 1/Year 6; 1 pt with eoJIA, Year 5). There were 2 cases of opportunistic infections (both herpes zoster), and no deaths. Overall, there were 559 (81.82 EP100PY) treatment-emergent adverse events

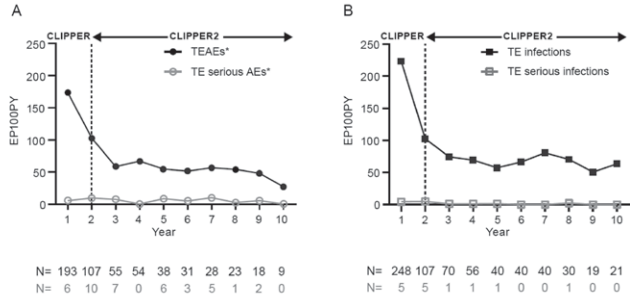
(TEAEs) excluding infections and injection-site reactions (ISRs). The overall rate of TE serious infections was low (N=14; 2.05 EP100PY) (Table 1), with the most common TE serious infection being gastroenteritis (N=2; 0.29 EP100PY). The most frequently reported TEAEs (N [EP100PY]) were headache (28 [4.10]), arthralgia (24 [3.51]), pyrexia (21 [3.07]), diarrhea (14 [2.05]), and leukopenia (12 [1.76]). Overall, 39 patients reported serious AEs (excluding infections/ISRs). The number and frequency (N [EP100PY]) of TEAEs (excluding infections/ISRs) decreased over the 10-year study period from 193 [173.81] in Year 1 to 9 [27.15] in Year 10. The number and frequency of TE infections and TE serious infections also decreased over the 10-year study period. There was no clear trend of a decrease over time for the incidence of TE serious AEs (Figure 1).

Table 1. ETN Safety Summary (from CLIPPER BL to mth 120), N (EP100PY) (FAS)*

	eoJIA, n=60 (EXP=313.667 PY)	ERA, n=38 (EXP=206.971 PY)	PsA, n=29 (EXP=162.576 PY)	Total, n=12 (EXP=683.214 PY)
TEAEs†	269 (85.76)	176 (85.04)	114 (70.12)	559 (81.82)
TE serious AEs†	16 (5.10)	17 (8.21)	7 (4.31)	40 (5.85)
TE ISRs	23 (7.33)	29 (14.01)	12 (7.38)	64 (9.37)
TE infections	418 (133.26)	99 (47.83)	155 (95.34)	672 (98.36)
TE serious infections‡	5 (1.59)	4 (1.93)	5 (3.08)	14 (2.05)
Opportunistic infections§	0	1 (0.48)	1 (0.62)	2 (0.29)
TEAEs causing withdrawal†	7 (2.23)	9 (4.35)	2 (1.23)	18 (2.63)
TE infections causing withdrawal	2 (0.64)	0	1 (0.62)	3 (0.44)

*While on active ETN treatment or within 30 days of last dose†Excluding infections/ISRs‡Gastroenteritis, 2 (0.29); acute tonsillitis, anal abscess, bronchopneumonia, gastrointestinal infection, helicobacter gastritis, influenza, peritonitis, pharyngitis, pyelocystitis, sepsis, urinary tract infection, viral infection, all 1 (0.15)§Both herpes zosterEXP, exposure to ETN; FAS, full analysis set; n, number of patients; N, number of events

Figure. Incidence of TEAEs (A) and TE Infections (B) in CLIPPER/CLIPPER2 by Study Year, N (EP100PY)



*Excluding infections/ISRs

Conclusion: ETN treatment to mth 120 was well tolerated in this patient population and consistent with the known safety profile. Frequency of TEAEs and TE infections decreased over time. Over 10 years, there was 1 reported event of malignancy and the overall rate of TE serious infections was low.

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POS0170 EXPERIENCES WITH COVID-19 INFECTIONS IN GERMAN PEDIATRIC RHEUMATOLOGY CENTERS

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Background: Although the risk for severe COVID-19 progression in children is low, this may be aggravated by the underlying disease and/or immunosuppressive drugs.

Objectives: We analyzed clinical data of COVID-19 cases among paediatric patients with rheumatic diseases reported to the BIKER registry.

Methods: The main task of the German BIKER (Biologics in Pediatric Rheumatology) registry is to monitor the safety of biologics therapies in JIA. After the onset of the COVID-19 pandemic, the survey was expanded with a standardized form to proactively interview all participating centers about the occurrence, presentation, and outcome of SARS-CoV-2- infections in children with rheumatic diseases. Interviews were conducted with 68 centers initially weekly and later biweekly.

Results: A total of 68 centres participated in the survey. Clinical data from 194 COVID-19 cases reported to the BIKER registry from 41 German and 1 Austrian pediatric rheumatology institutions between February 2020 and December 2021 were analyzed. Juvenile idiopathic arthritis (JIA, n=144) was the most common diagnosis followed by genetic autoinflammation (n=18; i.e. FMF, TRAPS, CAPS, HIDS, DADA2), systemic autoimmune diseases (n=11; i.e. SLE, dermatomyositis, vasculitis) and 16 with other rheumatic diseases (i.e. CRMO, Uveitis). 5 patients with no rheumatic disease were excluded. 104 (54%) patients were receiving conventional DMARDs, 81 (43%) received biologics, mainly TNF inhibitors (n=66 (35%)). Of the 189 rheumatic patients with SARS-CoV2 infection, 123 (63%) were female. The mean age was 12.4+/-4.4 years in females and 13.2+/-4.1 in males. The duration of SARS-Co2 infection associated symptoms was 13.8+/-15.3 days (max. 113 days), in 35 (43%) patients they lasted for > 12 days. 46 (24%) were asymptomatic. Patients with autoinflammation and systemic autoimmunopathies reported more symptoms such as fever, head and throat ache. 4 patients only complained about dyspnea. Only 3 patients were hospitalized and received Oxygen-supplementation. The only patients admitted to ICU, received ventilation but succumbed. This 3½-year-old patient, initially diagnosed with systemic JIA, developed fatal disease with intracranial edema and respiratory failure, as well as typical pulmonary texture changes. Prior to her SARS-CoV-2 infection, the patient was treated with MTX and low-dose steroids. Genetic testing revealed a so far unrecognized congenital immunodeficiency. In the total JIA cohort, treatment with corticosteroids, conventional DMARDs, biologics or combinations did not influence the number of reported symptoms or the favorable outcome of the cohort. However, the duration of symptoms was lower in the TNF-treated cohort (10.4+/-6.4 days vs. 15.7 +/- 19.7 days). In the cohort with autoinflammation, fever was observed in 11 (61%). Those 6 who received IL-1-inhibitors did not show a different outcome than those 12 who did not. No case of PIMS/MISC in children with rheumatic diseases was reported.

Conclusion: Except for one patient with congenital immunodeficiency who died from her COVID-19 infection, no case of severe COVID-19 was reported in our cohort. At the time of infection, over 80% of patients in our cohort had been treated with conventional DMARDs and/or biologics. This did not appear to have a negative impact on the severity or outcome of SARS-CoV2 infection. Interestingly, no case of PIMS/MISC was observed.

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Dressler Speakers bureau: Pfizer, Novartis, Abbvie, Paid instructor for: Advisory boards Novartis, Mylan, Daniel Windschall Speakers bureau: Pfizer, Novartis, Abbvie, MEDAC, Canon, Grant/research support from: Novartis, Pfizer, Sonja Mrusek: None declared, Toni Hospach: None declared, Alexander Kühn: None declared, Maria Haller: None declared, Philipp von Bismarck: None declared, Wolfgang Emminger: None declared, Peggy Ruehmer: None declared, Markus Hufnagel: None declared, Ariane Klein Speakers bureau: Novartis

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POS0171 A STANDARDIZED ASSESSMENT OF TREATMENT AND OUTCOME OF NEWLY DIAGNOSED PATIENTS WITH JIA WITHIN THE PROKIND PROJECT – PATHWAYS FOR POLYARTICULAR JIA

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Background: The ProKind Commission of the Society for Paediatric and Adolescent Rheumatology (GKJR) has developed evidence- and consensus-based protocols for the diagnosis and therapy of children and adolescents with defined rheumatic diseases (e.g., [1]). In the ProKind-Rheuma project, it is now investigated whether the protocols are followed in everyday clinical practice and what the treatment-associated outcomes are.

Objectives: To investigate the mode of treatment and treatment response in patients with polyarticular juvenile idiopathic arthritis (pJIA).

Methods: ProKind-Rheuma is a multicenter prospective non-interventional observational study. Patients with pJIA enrolled until 17/1/2022 were included into this analysis. Treatments and outcomes up to the 3-month follow-up visit (3FU) were analyzed. Disease states were categorized based on the 2021 cJADAS10 cutoffs [2].

Results: To date, 18 pediatric rheumatology facilities have participated in ProKind-Rheuma. Data from 203 patients with JIA are available. Of those, 44% have oligoarthritis, 36% polyarthritis, 9% systemic JIA, 6% enthesitis-related arthritis and 3% psoriatic arthritis. In total, 76 patients were diagnosed with pJIA, 38 with already completed 3FU: For 23 patients with pJIA and completed 3FU, we were able to analyze the protocol-defined [1] treatment goal of at least "minimal improvement". In total, 18 (78%) achieved minimal improvement, 5 (22%) missed it. For 4 of those 5 patients, the underlying MTX therapy was escalated to a bDMARD (3 changed to MTX+bDMARD-combi, 1 to bDMARD-mono). In 3 other patients, therapy was also escalated to an MTX-+bDMARD-combi. Between baseline and 3FU, 72% achieved cJADAS10-disease state improvement (Table 1) by at least one category (range 1 - 2), 0% decreased.

Table 1.

*based on non-missing values	At Baseline all	At Baseline with 3FU	At 3FU
Total	76	38	
Female, n (%)	58 (76)	30 (79)	
Age (years), *Mdn* (IQR)	9 (3-12)	7 (2-12)	7.5 (3-12)
Time since diagnosis (months), *Mdn* (IQR)	0 (0-1)	0 (0-1)	4 (3-4)
RF-positivity, n (%)	8 (11)	3 (8)	
Number of active joints (arthritis), *Mdn* (IQR)	7 (4-12)	7 (5-12)	2 (0-4)
JADAS10 (0-40), *Mean* (SD) (N_{BL+3FU}= 23)	18.6 (7.4)	19.6 (7.6)	7.2 (4.2)
cJADAS10 (0-30), Mean (SD) (N_{BL+3FU}= 29)	16.3 (5.9)	16.7 (6.1)	7.1 (4.1)
State of inactive disease (cJADAS10≤2.5), n (%*)	0 (0)	0 (0)	4 (13)
State of minimal disease activity (2.5<cJADAS10≤5), n (%*)	1 (2)	1 (3)	9 (28)
State of moderate disease activity (5<cJADAS10 ≤16), n (%*)	33 (54)	17 (50)	18 (56)
State of high disease activity (cJADAS10>16), n (%*)	27 (44)	16 (47)	1 (3)
CHAQ (0-3), *Mean* (SD)	0.8 (0.8)	0.9 (0.8)	0.3 (0.5)
Pain (NRS 0 - 10), *Mean* (SD)	4.3 (3)	4.7 (3)	2.2 (2.7)
PedsQL 4.0 total score, *Mean* (SD)	66.3 (22.2)	65.4 (21.8)	78.4 (17.6)
Intraarticular glucocorticoids > 4 joints (ever), n (%)	12 (16)	5 (13)	7 (18)
Glucocorticoid pulses (ever), n (%)	22 (29)	12 (32)	13 (34)
Methotrexate, n (%)	56 (74)	31 (82)	34 (90)
bDMARDs, n (%)	7 (9)	2 (5)	9 (24)

Within the first 3 months after diagnosis, the treatment pathways proposed by the ProKind Commission [1] were followed in about three-quarters of patients: i) 5 (13%) received MTX and intra-articular glucocorticoid injections in more than 4 joints (IAGC), but no high-dose intravenous glucocorticoid pulse (HDGC) or bDMARD; ii) 8 (21%) received MTX and HDGC (no bDMARD, no IAGC); iii) 16 (42%) patients received MTX, of whom 4 received a bDMARD up to or at the 3FU (no HDGC, no IAGC). Nine (24%) patients were not treated with MTX or did not fit any of these categories, mostly due to starting bDMARD therapy in conjunction with HDGC or IAGC.

Conclusion: In the routine care of JIA patients with polyarthritis, the proposed treatment protocol and treat-to-target strategy are followed in most patients. At 3FU, improvements of JADAS10 and other outcomes were evident, with 41% having achieved inactive or minimal active disease.

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POS0172 DIFFUSE JUVENILE SYSTEMIC SCLEROSIS PATIENTS SHOW DISTINCT ORGAN INVOLVEMENT AND HAVE MORE SEVERE DISEASE IN THE LARGEST JSSC COHORT OF THE WORLD. RESULTS FROM THE THE JUVENILE SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children (1). In adult patients there are significant differences between the clinical presentation of diffuse and limited subtypes (2). We reviewed clinical differences in presentation of subtypes in patients in the juvenile systemic scleroderma inception cohort up to 2021.
Objectives: To study the clinical presentation of jSSc patients with diffuse (djSSc) and limited (ljSSc) subtypes.
Methods: We reviewed the clinical baseline characteristics of the patients, who were recruited to the juvenile scleroderma inception cohort (jSScC) (3, 4) till 1st of December 2021. jSScC is a prospective cohort of jSSc patients, who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion.
Results: 210 patients with jSSc were included in the cohort, 71% (n=162) had diffuse subtype. The median age at onset of Raynaud phenomenon was 10.4 years (7.3 – 12.9) and the median age at the first non-Raynaud symptom was 10.9 years (7.4 – 13.2). Median disease duration was 2.5 years (1 – 4.4) at the time of inclusion. The female/male ratio was significantly lower in the djSSc subtype (3.7:1 versus 5:1, p<0.001). Antibody profile was quite similar, with the exception of a significantly higher number of anticentromere positive patients in the ljSSc (12% versus 2%, p=0.013). Decreased FVC < 80% was found in approximately 30% and decreased DLCO < 80% was found in around 40% in both subtypes. Pulmonary hypertension assessed by ultrasound was identified in 5% in both groups. Patients with diffuse subtype had significantly higher modified Rodnan Skin Score (mRSS) (16 versus 4.5, p<0.001), sclerodactyly (84% versus 60%, p<0.001), history of digital ulceration (62% versus 31%, p<0.001), decreased Body Mass Index (BMI) < -2 z score (20% versus 4%, p=0.003) and decreased joint range of motion (64% versus 46%, p=0.019). Patients with ljSSc had significantly higher rate of cardiac involvement (13% versus 2%, p=0.001). Regarding patient related outcomes djSSc patients had more severe disease, looking at patient reported global disease activity (VAS 0 – 100) (40 versus 25, p=0.039), patient reported global disease damage (VAS 0 – 100) (40 versus 25, p=0.021) and patient reported assessment of ulceration activity (10 versus 0, p=0.044). Regarding physician related outcomes the physician reported global disease activity (VAS 0 – 100) (32 versus 20, p<0.001) and physician reported global disease damage (VAS 0 – 100) (30 versus 15, p=0.014) was significantly higher in djSSc.
Conclusion: In this jSSc cohort, the largest in the world, djSSc patients have a significantly more severe disease than ljSSc patients. Interestingly, we found no differences regarding interstitial lung disease and pulmonary hypertension.

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POS0173 DATA-DRIVEN MRI DEFINITIONS FOR ACTIVE AND STRUCTURAL SACROILIAC JOINT LESIONS IN JUVENILE SPONDYLOARTHRITIS TYPICAL OF AXIAL DISEASE

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Background: For classification in juvenile spondyloarthritis (JSpA), it is important to develop cut-offs for active and structural lesions typical of axial disease on MRI that are readily and consistently interpreted. Since the maturing sacroiliac joint (SIJ) looks different from the adult SIJ, the criteria developed for positive MRI in adults may not be applicable in JSpA.
Objectives: As part of a study developing classification criteria for axial disease in JSpA, we aimed to determine quantitative SIJ imaging lesion cut-offs for inflammatory and structural lesions typical of axial JSpA using majority imaging expert decision as the reference criterion.
Methods: Subjects were a retrospective cohort of children with SpA who met the provisional Pediatric Rheumatology International Trials Organization criteria for enthesitis/spondylitis-related juvenile idiopathic arthritis or had a rheumatologist JSpA diagnosis. All subjects had symptom onset prior to age 18 years and underwent MRI as part of a diagnostic evaluation for axial disease. To enable SIJ quadrant-based scoring, all MRIs included semi-coronal slices through the cartilaginous part of the joint on fluid sensitive sequences and on T1-weighted sequences for the assessment of inflammation and structural lesions, respectively. MRIs were reviewed by 6 musculoskeletal imaging experts who were blinded to clinical details. MRI evaluation of the SIJ was based on standardized lesion definitions that were decided by consensus of the central imaging team and represented a mix of definitions from ASAS and the Juvenile Arthritis MRI Score Outcome Measures in Rheumatology working group. Using a web-based interface, raters globally assessed the presence or absence of lesions typical of axial SpA and performed SIJ quadrant or joint based scoring. Lesion scores were generated by averaging the scores of all raters. Sensitivity and specificity of lesion cut-offs were calculated using rater majority (≥4/6 raters) on a global assessment of the presence/absence of active or structural lesions typical of axial SpA with high confidence (confidence of ±3 or stronger on confidence scale from -5, "Definitely No" to +5, "Definitely Yes") as the reference standard.
Results: Imaging from 243 subjects, 61% male, median age 14.9 years, had sequences available for detailed MRI scoring. Active inflammatory lesion typical of axial disease in JSpA was defined as bone marrow edema (BME) in at least 3 SIJ quadrants (sensitivity 98.6%, specificity 96.5%). For structural lesion typical of axial JSpA, the optimal cut-off was erosion in at least 3 quadrants or at least one of the following lesions in at least 2 SIJ quadrants: sclerosis, fat lesion, backfill, ankylosis (sensitivity 98.6%, specificity 95.5%).
Conclusion: We propose data-driven cut-offs for active inflammatory and structural lesions on MRI typical of axial disease in JSpA that have high specificity and sensitivity using central imaging global assessment as the reference standard.

Table 1. Performance of cut-offs for inflammatory and structural lesions of axial disease

Cut-offs for number of SIJ quadrants (any location)	Sensitivity (95% CI)	Specificity (95% CI)
Definite active lesion		
BME score ≥2	100 (95.0-100)	93.5 (88.7-96.7)
BME score ≥3	98.6 (92.5-100)	96.5 (92.5-98.7)
BME, same location on ≥3 consecutive slices	88.6 (78.7-94.9)	98.8 (95.8-99.9)
Definite structural lesion		
Erosion ≥2	95.7 (88-99.1)	96.8 (92.7-99)
Erosion, same location on ≥2 consecutive slices	94.3 (86-98.4)	98.1 (94.5-99.6)
Erosion ≥3	91.4 (82.3-96.8)	98.7 (95.4-99.8)
Sclerosis ≥2	62.9 (50.5-74.1)	98.1 (94.5-99.6)
Fat lesion ≥2	22.9 (13.7-34.4%)	98.7 (95.4-99.8%)
Backfill ≥2	20 (11.4-31.3)	100 (97.7-100)
Ankylosis ≥2	1.3 (0.2-4.7)	100 (94.9-100)
ANY of the following in ≥2 SIJ quadrants: erosion, sclerosis, fat lesion, backfill, ankylosis	98.6 (92.3-100)	93.6 (88.5-96.9)
Erosion ≥3 quadrants *OR* ≥2 quadrants of at least one of the following lesions: sclerosis, fat, backfill, ankylosis	98.6 (92.3-100.0)	95.5 (91.0-98.2)

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New insights into the associations of outcomes and biomarkers in OA

POS0174 **PAIN SEVERITY ACROSS HAND OA PHENOTYPES BASED ON A BIOPSYCHOSOCIAL APPROACH**

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Background: Hand osteoarthritis (OA) pain is heterogeneous and multifactorial, involving biological, psychological and social aspects extending beyond the OA disease process. Different phenotypes may differ in prognosis and treatments requirements, and thus be of clinical importance. The presence of hand OA phenotypes has not previously been examined.

Objectives: To explore classes based on a biopsychosocial framework as possible phenotypes in a hand OA population, and examine whether pain severity differ between the classes.

Methods: Biological, psychological, and social domains were assessed including self-reported questionnaires, clinical assessment and imaging in 300 persons with hand OA. Central pain sensitization was tested by pressure pain thresholds (PPT; kg/cm^2) and temporal summation (TS). Variables used for comparison across the classes included age, sex, hand and overall bodily pain severity (Numeric Rating Scales (NRS) last 24h (0-10)). We used Latent Class Analysis followed by posterior fit statistics. Differences in age, sex and pain between classes were assessed by one-way ANOVAs and chi-squared tests.

Results: We identified 4 classes (Table 1): Class 1 had the lowest hand OA severity, high levels of pain sensitization, comorbidities, sleep problems, psychological distress and the lowest frequencies of working participants. Class 2 had the lowest pain sensitization levels and the highest proportion of participants with university education and living with a partner. Class 3 had the highest level of hand OA severity, and the lowest levels of comorbidity burden and psychological distress. Class 4 was similar to class 1 with high levels of pain sensitization, comorbidities and sleep problems and fewer with university education. Compared with class 1 they had less psychological distress and more severe hand OA.

Table 1.

	Class 1: n=25 (8%)	Class 2: n=53 (18%)	Class 3: n=103 (34%)	Class 4: n=119 (40%)	P-value
Biological domain					
OA severity	22.2 (15.8)	28.4 (15.6)	33.6 (20.1)	29.7 (20.0)	0.05
(Kellgren-Lawrence; 0-128)					
PPT tibialis anterior	3.9 (1.8)	9.4 (1.9)	5.6 (1.9)	4.2 (1.6)	< 0.001
PPT trapezius	2.8 (0.9)	7.2 (1.8)	4.5 (1.4)	3.4 (1.5)	< 0.001
TS change	2.6 (1.7)	0.8 (1.0)	1.4 (1.5)	1.9 (1.6)	< 0.001
BMI	28.4 (5.2)	25.7 (4.5)	24.9 (3.6)	27.9 (5.6)	< 0.001
Comorbidity burden (0-45)	10.7 (4.7)	7.2 (3.5)	4.9 (2.9)	9.8 (3.9)	< 0.001
Poor sleep, n (%)	24 (96%)	30 (57%)	57 (55%)	112 (94%)	< 0.001
Psychological domain					
HADS (0-42)	20.9 (5.9)	5.1 (4.4)	4.6 (4.2)	8.0 (4.5)	< 0.001
ASES (10-100)	47.7 (13.6)	73.8 (9.5)	76.6 (12.7)	63.6 (10.1)	< 0.001
PCS (0-52)	23.5 (8.3)	9.6 (7.0)	6.3 (5.3)	12.9 (7.1)	< 0.001
Social domain					
University education, n (%)	13 (52%)	40 (77%)	72 (70%)	48 (41%)	0.01
Working, n (%)	8 (32%)	38 (72%)	68 (66%)	45 (38%)	< 0.001
Living with partner, n (%)	16 (64%)	34 (71%)	70 (61%)	76 (64%)	0.03

SD=standard deviation; BMI= Body Mass Index; HADS=Hospital Anxiety and Depression Scale; PCS=Pain Catastrophizing Scale; ASES=Arthritis Self Efficacy Scale.

Hand and overall pain severity differed significantly between the classes. Class 3 reported the lowest mean (SD) NRS hand and overall pain (2.7 (1.8) and 2.8 (1.7), p=0.01). The highest mean (SD) for NRS hand and overall pain (5.8 (2.7) and 5.8 (2.4), p=0.05) where reported by Class 1, which also had the lowest mean age of 56.9 (SD 6.5), p< 0.001. Class 2 held the highest proportion of men (n=15; 29%), although not significantly different from the other classes.

Conclusion: Four potential hand OA phenotypes that differed in hand and overall pain severity were identified. The phenotypes with higher levels of pain sensitization, comorbidities, psychological and social burden tended to have more severe hand pain than persons with lower levels. The phenotypes with lowest hand OA severity reported the highest pain severity which may reflect the discordance between OA severity and pain experience. Biopsychosocial factors are likely important in defining hand OA phenotypes and may present a possibility for improved clinical outcomes.

Biopsychosocial characteristics across the proposed hand OA phenotypes. Data presented as mean (SD) unless otherwise indicated.

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POS0175

ASSOCIATIONS BETWEEN CHRONIC WIDESPREAD PAIN, PRESSURE PAIN THRESHOLDS AND LEPTIN IN INDIVIDUALS WITH KNEE PAIN

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Background: Previous studies have reported associations between obesity, chronic pain and increased pain sensitivity. The adipokine leptin has been suggested to be involved in the osteoarthritis process as well as in pain sensitisation.
Objectives: The aim was to study associations between chronic widespread pain, pain sensitivity and leptin in individuals with knee pain.
Methods: In all, 306 individuals with knee pain were included in the Halland osteoarthritis cohort, ClinicalTrials.gov NCT04928170. Of those, 265 were included in this cross-sectional baseline study. The mean age (sd) was 51.6 (8.8) years, and 71% was women. The participants marked their painful areas on a pain figure with 18 predefined areas. They were categorised in three different pain groups according to the modified WP2019 definition (1), with knees excluded (due to highest goodness of fit): Chronic widespread pain (CWP), chronic regional pain (ChRP) if CWP was not met, and no chronic pain (NCP). The group with CWP were compared with those reporting no CWP (ChRP and NCP). The pressure pain thresholds (PPT) were measured using a computerised pressure algometry (AlgoMed, Medoc) on eight predefined tender points (trapezius (bilateral), right second rib, right lateral epicondyle, knees, gluteal (bilateral)) (2). Increased pain sensitivity was defined as having PPT in the lowest third in all tender points. Obesity was measured via waistline measurement and a bioimpedance (InBody 770) measuring BMI and visceral fat area (VFA). Serum-Leptin were analysed with an ELISA method (Alpco). Knee Injury and Osteoarthritis Outcome Score (KOOS) was used to describe the groups.
Results: In this baseline study, 16% reported CWP, and 15% had low pain pressure thresholds at baseline in the study. Those fulfilling CWP were more often women, had higher BMI, VFA, and increased leptin levels and worse KOOS in four of five subscores, see Table 1A. The age and gender-adjusted leptin levels were 21.6 ng/ml (95% CI 18.2-25.0) in the group with no CWP vs. 35.5 ng/ml (95% CI 27.6-43.4) in the CWP group, p=0.002. In a logistic regression adjusting for age and gender, leptin was associated with reporting CWP OR 1.015 (95% CI 1.004-1.027, p= 0.008). The participants with low PPT were younger and had a mean (sd) leptin 31.8 ng/ml (31.6) vs 23.0 (26.0), p=0.061 in the group not having low PPT, Table 1B. In a logistic regression adjusting for age and gender, leptin was associated with low PPT OR 1.016 (95% CI 1.004-1.029, p= 0.012).
Conclusion: The pathophysiological mechanism causing widespread pain is probably multifactorial, involving both biological and physical factors. The adipokine leptin could be involved in some of these mechanisms, but longitudinal studies are needed to be able to study causal relationships.
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Table 1. A Comparisons between those without CWP and those fulfilling CWP and table 1B comparisons between those not having low PPT and those with low PPT.

	A			B		
	No CWP Mean (sd)	CWP Mean (sd)	p-value	Not Low PPT Mean (sd)	Low PPT Mean (sd)	p-value
n	210	40		226	39	
Age	51.8 (8.7)	52.8 (7.6)	0.465	52.1 (8.5)	48.8 (9.9)	0.030
Gender, female n(%)	67	90	0.004	72	67	0.524
BMI (kg/m^2)	26.2 (4.6)	28.0 (5.0)	0.022	26.4 (4.9)	27.5 (4.3)	0.213
VFA (cm^2)	107 (50)	137 (56)	0.001	110 (54)	127 (49)	0.088
Leptin (ng/ml)	21.0 (23.9)	39.0 (36.6)	<0.001	23.0 (26.0)	31.8 (31.6)	0.061
CRP (mg/L)	1.9 (2.7)	2.2 (2.3)	0.602	2.0 (2.7)	1.9 (1.8)	0.825
KOOS						
Pain (0-100, worst to best)	74 (15)	61 (17)	<0.001	73 (15)	65 (18)	0.002
Symptom (0-100, worst to best)	72 (17)	64 (18)	0.016	71 (17)	67 (19)	0.188
ADL (0-100, worst to best)	84 (13)	69 (19)	<0.001	84 (14)	72 (21)	<0.001
Sport/rec (0-100, worst to best)	49 (26)	34 (27)	0.001	49 (26)	36 (25)	0.009
QoL (0-100, worst to best)	53 (18)	46 (20)	0.050	53 (18)	45 (21)	0.017

BMI, body mass index; VFA, visceral fat area; CRP, C-reactive protein; KOOS, knee injury and osteoarthritis outcome score; ADL; function in daily living; sport/Rec, Function in sport and recreation; QOL, knee-related Quality of life

POS0176

A COMPARISON OF ULTRASOUND-DETECTED PATHOLOGIES IN PERSONS WITH AND WITHOUT KNEE OSTEOARTHRITIS AND THE ASSOCIATIONS WITH PAIN

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Background: Ultrasound can evaluate osteophytes and synovitis in persons with knee OA. However, albeit the literature demonstrates a positive association between knee pain and synovitis, the instruments used to report pain, the number of patients included, the strengths of associations and the overall quality of the studies varies greatly (1).
Objectives: 1) To compare the degree of OA changes by ultrasound among people with and without clinical knee OA according to established classification criteria. 2) Study the associations between ultrasound findings and pain.
Methods: We included 286 of 300 participants from the NOR-HAND study, a hospital-based observational cohort after excluding participants with knee prostheses or arthrodesis.
The participants reported the levels of knee/hip pain using the Western/Ontario McMaster University index (WOMAC) and marked their painful joints (including the bilateral knees) during the last 24 hours and last 6 weeks on two separate homunculi. An experienced rheumatologist (BSC) examined whether the participants fulfilled the clinical ACR criteria for knee OA or not (n=7 missing).
A trained medical student performed the ultrasound examination of the knees using a General Electric (GE) Logic E9 ultrasound machine with a 6-15Mz probe. Both knees were scored for 1) osteophytes in the medial and lateral tibia and femur on 0-3 semi-quantitative scales (0=no, 1=small, 2=medium, and 3=large), and 2) grey-scale synovitis on 0-3 semi-quantitative scales (0=no, 1=mild, 2=moderate, and 3=severe pathology). The highest score of osteophytes and grey-scale synovitis (range: 0-3) and the sum scores of both knees together (range: 0-24 for osteophytes and 0-6 for synovitis) were calculated.
We compared the degree of ultrasound pathologies in persons with vs. without clinical knee OA using Chi square tests and Mann-Whitney U test or T test as appropriate. The associations between ultrasound pathologies and pain scores were explored by logistic regression analyses, adjusted for age, sex and BMI. Generalized Estimating Equations were applied to account for two knees belonging to the same person.
Results: Knee osteophytes, but not grey-scale synovitis, were more common in persons with vs. without clinical knee OA (median sum score of osteophytes: 2 vs. 0, p<0.001) and were associated with higher levels of WOMAC pain (beta=0.18, 95% confidence interval (CI) 0.03-0.32). The same association to WOMAC pain was not found for synovitis (beta=0.03, 95% CI -0.33-0.40). However, in analyses on joint level, both osteophytes and synovitis were associated with pain in the same joint in both a short (24 hours) and longer term (6 weeks), with stronger associations for more severe ultrasound scores (Table 1).

Table 1. Associations between ultrasound pathologies and a) WOMAC pain and b) joint pain in the same joint previous 24 hours and c) previous 6 weeks, adjusted for age, sex and BMI.

	a) WOMAC pain both knees Beta (95%CI)	b) OR (95% CI) of pain in the same knee joint previous 24 hours	c) OR (95% CI) of pain in the same knee joint previous 6 weeks
Osteophyte sum score (both knees; range 0-24)	0.18 (0.03-0.32)		
Highest osteophyte score			
-Grade 0	0.0 (ref)	1.00 (ref.)	1.00 (ref.)
-Grade 1	1.13 (-1.3, 2.4)	1.85 (1.20, 2.84)	1.79 (1.19, 2.68)
-Grade 2	0.67 (-0.74, 2.07)	2.77 (1.64, 4.70)	2.98 (1.76, 5.06)
-Grade 3	1.87 (0.04, 3.7)	9.02 (4.04, 20.10)	6.50 (2.95, 14.30)
Grey-scale synovitis sum score (both knees; range 0-6)	0.03 (-0.33, 0.40)		
Highest GS synovitis score			
-Grade 0	0.0 (ref)	1.00 (ref.)	1.00 (ref.)
-Grade 1	0.24 (-0.99, 1.47)	1.00 (0.66, 1.53)	0.95 (0.61, 1.47)
-Grade 2	0.27 (-1.33, 1.87)	1.67 (0.96, 2.91)	1.32 (0.78, 2.25)
-Grade 3	0.46 (-1.73, 2.65)	6.63 (2.26, 19.43)	4.32 (1.59, 11.71)

Conclusion: Both osteophytes and grey-scale synovitis were associated with pain in the same joint, supporting the validity of ultrasound in knee OA. Grey-scale synovitis was commonly present in people not fulfilling the ACR criteria for clinical knee OA and seems to be less specific for clinical knee OA than osteophytes.
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POS0177

HETEROGENOUS CARTILAGE DAMAGE SEEN ON MRI AMONG KNEES WITH KELLGREN-LAWRENCE 2 & 3 OSTEOARTHRITIS: WHAT ARE THE IMPLICATIONS FOR CLINICAL TRIALS?

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Background: The most recent update of the Global Burden of Disease figures (GBD 2013) estimated that 242 million people were living in the world with symptomatic and activity-limiting OA of the hip and/or knee. Many potential disease-modifying osteoarthritis drugs (DMOADs) have been investigated, but to date no DMOADs that slow or stop disease progression have been approved by the Food and Drug Administration (FDA) or the European Medicines Agency (EMA). A potential reason for the lack of demonstrated efficacy may be reliance on radiographs for defining structural inclusion and exclusion criteria for clinical trials, such as use of joint space width and Kellgren-Lawrence (KL) grade as surrogates for cartilage damage.

Table 1.

Cartilage damage seen on 3T MRI, by Kellgren-Lawrence grade

Knee MRI Findlings	Kellgren-Lawrence Grade			
	KL2 (n=2,318)		KL3 (n=1,128)	
	Percent	(95%CI)	Percent	(95%CI)
Medial TFJ				
Normal	52.4	(50.1, 54.6)	14.4	(12.2, 16.6)
Focal PT/FT	9.4	(8.2, 10.7)	2.6	(1.6, 3.5)
Diffuse PT lesion	32.1	(30.1, 34.2)	40.6	(37.5, 43.6)
Diffuse FT lesion	6.1	(5.0, 7.1)	42.5	(39.4, 45.6)
Lateral TFJ				
Normal	61.0	(58.8, 63.2)	53.6	(50.4, 56.7)
Focal PT/FT	16.4	(14.8, 18)	14.2	(12.1, 16.3)
Diffuse PT lesion	14.6	(13.1, 16.2)	12.1	(10.1, 14.0)
Diffuse FT lesion	7.9	(6.8, 9.1)	20.1	(17.6, 22.7)
Medial/lateral TFJ (maximum score)				
Normal	34.8	(32.7, 36.9)	4.3	(3.0, 5.5)
Focal PT/FT	15.1	(13.5, 16.6)	1.2	(0.6, 1.9)
Diffuse PT lesion	36.9	(34.8, 39.0)	35.4	(32.4, 38.4)
Diffuse FT lesions	13.3	(11.8, 14.8)	59.1	(56.0, 62.2)
PFJ				
Normal	22.0	(20.2, 23.9)	23.0	(20.3, 25.6)
Focal PT/FT	4.4	(3.5, 5.3)	3.9	(2.7, 5.1)
Diffuse PT lesion	24.9	(23, 26.9)	36.3	(33.3, 39.2)
Diffuse FT lesions	48.6	(46.2, 50.9)	36.9	(33.8, 40.0)
Whole knee				
Normal	9.8	(8.5, 11.1)	2.0	(1.1, 2.9)
Focal PT/FT	5.4	(4.4, 6.4)	1.0	(0.4, 1.5)
Diffuse PT lesion	28.8	(26.8, 30.8)	23.6	(20.9, 26.3)
Diffuse FT lesions	55.9	(53.7, 58.2)	73.4	(70.6, 76.2)
Number of compartments with diffuse FT lesions				
0	44.0	(41.7, 46.3)	26.6	(23.8, 29.4)
1	49.8	(47.5, 52.1)	48.9	(45.8, 52)
2	5.8	(4.8, 6.8)	22.9	(20.3, 25.5)
3	0.4	(0.2, 0.7)	1.6	(0.9, 2.3)
Number of TFJ compartments with diffuse FT lesions				
0	86.7	(85.2, 88.2)	40.9	(37.8, 44.0)
1 (medial or lateral)	12.5	(11.0, 13.9)	55.5	(52.5, 58.6)
2 (medial and lateral)	0.8	(0.4, 1.1)	3.5	(2.4, 4.7)

PT: Partial-thickness, FT: Full-thickness, TFJ: Tibiofemoral Joint, PFJ: Patellofemoral Joint

Objectives: To estimate the distribution of cartilage damage seen on knee MRI in a sample of knees with radiographic KL 2 and 3 OA that would potentially qualify for a DMOAD trial.
Methods: We selected knees from the Osteoarthritis Initiative (OAI), a longitudinal cohort study of knees with or at risk of developing symptomatic radiographic OA, that met common structural inclusion criteria for DMOAD trial enrollment at OAI baseline: knees with radiographs centrally graded as KL 2 or 3 and medial minimum joint space width (mJSW) ≥ 1.5mm. A musculoskeletal radiologist with 10 years of experience in semi-quantitative MRI assessment scored knee cartilage damage in the medial and lateral tibiofemoral and patellofemoral compartments using WORMS (Whole-Organ Magnetic Resonance Imaging Score). Coronal intermediate weighted (IW) TSE and sagittal fat-suppressed IW TSE sequences on 3T MRI were used. The WORMS cartilage scores, which are based on both the extent and depth of cartilage damage, were collapsed into 4 categories: no cartilage damage (WORMS 0 and 1), focal partial or full-thickness (PT/FT) cartilage damage (WORMS 2 and 2.5), diffuse partial thickness (PT) cartilage damage (WORMS 3 and 4), and diffuse full-thickness (FT) cartilage damage (WORMS 5 and 6). We estimated the prevalence of each category of cartilage damage in KL2 and KL3 knees; 95% confidence intervals (CI) accounted for clustering at the participant-level since some participants contributed two knees to the analysis.
Results: We identified 2,372 participants contributing 3,446 knees with radiographic OA (KL 2 and 3) and medial mJSW ≥ 1.5mm. There were 2,318 KL2 knees and 1,128 KL3 knees. The distribution of cartilage damage in each compartment by KL grade is presented in Table 1. We found no cartilage damage in any compartments in 9.8% (95%CI: 8.5, 11.1) of KL2 knees and 2.0% (95%CI: 1.1, 2.9) of KL3 knees. Cartilage damage was absent in the medial tibiofemoral compartment in 52.4% (95%CI: 50.1, 54.6) of KL2 knees, and 14.4% (95%CI: 12.2, 16.6) of KL3 knees, versus 61% (95%CI: 58.8, 63.2) of KL2 knees and 53.6% (95%CI: 50.4, 56.7) of KL3 knees in the lateral compartment. When medial and lateral compartments were combined, cartilage damage was absent in 34.8% (95%CI: 32.7, 36.9) of the KL2 knees, and 4.3% (95%CI: 3.0, 5.5) of the KL3 knees. Diffuse FT cartilage lesions in the medial compartment were found in 6.1% (95%CI: 5.0, 7.1) of KL2 knees and 42.5% (95%CI: 39.4, 45.6) of KL3 knees.
Conclusion: MRI screening prior to clinical trial enrollment may identify a substantial percentage of knees with normal cartilage, as well as knees with diffuse FT cartilage lesions that may not be responsive to DMOADs, depending on the mode of action of a given pharmacological compound.
Disclosure of Interests: Mohamed Jarraya: None declared, Frank Roemer Shareholder of: Boston Imaging Core Lab, Consultant of: California Institute of Biomedical Research, Erin Ashbeck: None declared, John Lynch: None declared, C. Kent Kwoh Consultant of: Novartis, Regeneron, LG Chem, Kolon Tissue Gene, Avalor, Grant/research support from: Pfizer, Lilly, Cumberland, Ali Guermazi Shareholder of: Stock options in BICL, Consultant of: Pfizer, TissueGene, MerckSerono, Regeneron, Novartis, AstraZeneca
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POS0178 ASSOCIATION BETWEEN KNEE MR IMAGING MARKERS AND KNEE SYMPTOMS OVER 7 YEARS IN YOUNG ADULTS

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Background: Knee magnetic resonance imaging (MRI)-based morphological markers (quantitative biomarkers) and structural abnormalities (semi-quantitative biomarkers) are known to be associated with the progression of knee osteoarthritis (OA). However, there is conflicting evidence on the association between knee MRI-based morphological markers and knee symptoms. Besides, there is a lack of evidence on the clinical significance of MR imaging markers in the general population-based young adults. Hence, our aim was to investigate the associations between MR imaging biomarkers and knee symptoms in middle-aged adults followed over seven years.
Objectives: To describe the associations of cartilage volume, cartilage thickness, subchondral bone area, cartilage defects, and bone marrow lesions (BML) with knee symptoms in young adults followed up over 6-9 years.
Methods: Knee symptoms (pain, stiffness, and dysfunction) were assessed using the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) scale during Childhood Determinants of Adult Health (CDAH)-knee study at baseline (year: 2008-10, age: 30–40 years) and 6-9 year follow-up (CDAH-3; year: 2014–2019, age: 36–49 years). Knee MRI scans were obtained at baseline and were assessed quantitatively for morphological markers such as cartilage volume, cartilage thickness, subchondral bone area using semi-automated segmentation (Chondrometrics, Germany). Cartilage defects and BMLs were assessed using semi-quantitative scoring systems. Univariable and multivariable (adjusted for age, sex, and body mass index (BMI)) zero-inflated Poisson (ZIP) regression model with random effects were used to describe the cross-sectional and longitudinal associations.
Results: The prevalence of knee pain at baseline (mean age (SD): 34 (2.7); female 49%) was 34% that increased to 50% over 6-9 year follow-up (mean age (SD): 43 (3.2)). Cross sectionally, there was a weak but statistically significant negative association between medial femorotibial compartment (MFTC) [Ratio of Mean (RoM)= 0.99971084; 95% CI: (0.9995525, 0.99986921; p<0.001], lateral femorotibial compartment (LFTC) [RoM=0.99982602; 95% CI: 0.99969915, 0.9999529; p=0.007], and patellar cartilage volume [RoM=0.99981722; 95% CI: 0.99965326, 0.9999811; p=0.029] with knee symptoms.
Similarly, there was a negative association between patellar cartilage volume (RoM=0.99975523; 95% CI: 0.99961427, 0.99989621; p=0.014), MFTC cartilage thickness (RoM= 0.72090775; 95% CI: 0.59481806, 0.87372596; p=0.001) and knee symptoms assessed after seven years.
The total bone area was consistently and negatively associated with knee symptoms at baseline [RoM= 0.9210485; 95%CI: 0.8939677, 0.9489496; p<0.001] and over seven years (RoM=0.9588811; 95% CI: 0.9313379, 0.9872388; p=0.005). Presence of any cartilage defect or BML was associated with higher knee symptoms at baseline and after seven years.
Conclusion: In the middle-aged adult population, BML and cartilage defects were positively associated with knee symptoms, whereas cartilage volume and thickness at MFTC and total bone area were weakly and negatively associated with knee symptoms. These results suggest that the quantitative and semi-quantitative MR imaging biomarkers can be explored as a marker of the clinical progression of OA in a young adult population.
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POS0179 IMPLICATIONS OF BRAIN ACTIVITY IN THE TREATMENT DECISION OF KNEE OSTEOARTHRITIS

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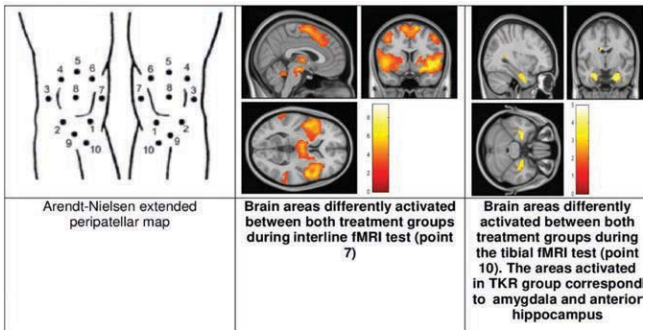
Background: Chronic pain related to knee osteoarthritis (KOA) is a common health problem and functional magnetic resonance imaging (fMRI) is a useful technique which can determine different brain activation (1).
Objectives: The main purpose of our study was to observe whether there is different risk to central sensitization and different brain activation in patients with KOA according to the treatment followed (conservative (CNV) Vs. total knee replacement (TKR))
Methods: Patients diagnosed of primary KOA following a CNV treatment or undergoing TKR were recruited. The two groups were matched by age, sex and BMI. Clinical central sensitization was considered if patients presented spread tenderness, evaluated with an algometer, in more than 1 site of the extended peripatellar map (2) (notice that pain at points 3, 7 and 8 were not counted) fMRI testing involved pressure painful stimulation to the articular interline and to a commonly sensitized site (tibial surface, point 10).To evaluate the associations between central sensitization and the risk to undergo a TKR; logistic regression was performed to estimate OR and 95% confidence intervals (95%CI). Models were adjusted by sex, age and BMI (R (R v.3.5.2).Whole-brain activation maps were compared between groups using Statistical Parametric Mapping software (SPM12 http://www.fil.ion.ucl.ac.uk/spm).
Results: Women have a significant higher risk to present central sensitization than men (OD 12,11 (95% CI 4,32-33,95) p-value:$2,09*10^6$), but no differences were observed between CNV and TKR group (OR TKR 0,69 (95% CI 0,24-1,98)) (Table 1). The differences observed in brain activation between the treatment groups in the interline fMRI test (point 7) did not correspond to any specific brain

area. However, TKR group showed a higher activation that implicated the region of the amygdala and anterior hippocampus during the tibial fMRI test (point 10).

Table 1. Central sensitization Odds Ratio (OR) with 95% Confidence Interval (95%CI)

	O.R. (95% CI)	p-value
Treatment	0.69 (0.24- 1.98)	0,494
Sex	12.11 (4.32- 33.95)	$2{,}09*10^{-6}$
Age	0.72 (0.26- 1.97)	0,525
BMI	1.88 (0.69- 5.17)	0,219

Conclusion: Presenting central sensitization is not a risk for KOA patients to undergo a TKR, but the mechanism underlaying sensitization in both treatment groups might be different, with amygdala playing an important role in TKR patients. The amygdala is an important element of the brain systems that both express emotions and modulate pain. The activation of the amygdala in response to pressure stimulation on a sensitized knee site is interpreted as a failure of the descending pain inhibitory systems, and the occurrence of a major emotional response during the painful experience in patients that ultimately received TKR.



Arendt-Nielsen extended peripatellar map

Brain areas differently activated between both treatment groups during interline fMRI test (point 7)

Brain areas differently activated between both treatment groups during the tibial fMRI test (point 10). The areas activated in TKR group correspond to amygdala and anterior hippocampus

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Extended peripatellar map including the points tested for tenderness, and brain areas differently activated between both treatments groups during painful stimulation to point 7 (interline) and point 10 (tibial surface, a commonly sensitized site).

Disclosure of Interests: None declared

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POS0180

THE EFFICACY AND SAFETY OF A FIXED-DOSE COMBINATION OF APOCYNIN AND PAEONOL IN SYMPTOMATIC KNEE OA: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED CLINICAL TRIAL

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Background: There is a great unmet need for the development of effective treatments to treat the symptoms of OA. Nuclear-Factor Kappa-B (NF-κB) and Nrf2 play a key roles in OA pathogenesis and have been identified as potential targets. A fixed-dose combination of apocynin and paenol in a ratio of 2:7 (APPA) has been shown to inhibit activation of NF-κB and upregulate Nrf2. [1]

Objectives: We report the results of a phase 2a study evaluating the efficacy and safety of APPA in patients with symptomatic knee OA.

Methods: The trial was a 28-day randomized, placebo-controlled, double-blind study comparing 800 mg of APPA twice daily with matched placebo capsules. Patients with radiographic knee OA KL-grade 2-3, and a WOMAC pain score ≥40 and ≤90/100 of target knee at screening and baseline were randomized 1:1 to APPA or placebo. Main exclusion criteria included recent intraarticular surgery or injection therapy, hip pain greater than the target knee, and BMI ≥40 kg/m^2. The primary endpoint was change from baseline to Day 28 in the WOMAC pain score. Safety outcomes included reported adverse events (AE), clinical laboratory parameters, ECG, and vital signs.

A pre-defined subgroup analysis in subjects with a baseline PainDETECT score >12 indicated a positive effect. Accordingly, post-hoc analyses were undertaken to further assess the effects of APPA in subgroups of participants with higher disease severity.

Results: 152 participants were randomized, and 149 (98%) completed the trial. The mean (SD) WOMAC pain score at baseline was 55.3 (10.2). The two groups were comparable in terms of baseline pain score, gender, age, and BMI.

The primary endpoint was not met, mean difference (MD) between APPA and placebo was -0.89 (95 % CI: -5.62, 3.84, p=0.71, Figure 1A). Similarly, no significant differences were found on other key secondary endpoints (WOMAC Function and WOMAC total Figure 1B and C, respectively.) APPA was well tolerated and no differences in frequencies of reported AEs were noted, apart from a higher proportion of subjects reporting mild to moderate gastrointestinal discomfort reported with APPA compared to placebo (12% vs. 6.5 %).

In the pre-defined subgroup of participants with baseline PainDETECT ≥ 13 (N=45), the difference in mean change in pain from baseline favored the APPA-group (MD: -11.20, 95 % CI: -20.29 to -2.11, p=0.02). Analysis of participants > 50 WOMAC pain at baseline (Group 1, N=95, Figure 1D), and a KL-grade of the non-target knee >2 (Group 2, N=105, Figure 1E), and a combination of these two criteria (Group 3, N=64, Figure 1F) found a positive effect of APPA compared to placebo (Group 1 MD: -2.61, 95 % CI: -8.98 to 3.76, p=0.42, Group 2 MD: -4.01, 95 % CI: -9.35 to 1.33, p=0.14, and Group 3 MD: -8.32, 95 % CI: -15.48 to -1.16, p=0.02).

Conclusion: Treatment with APPA 800 mg twice daily for 28 days in patients with symptomatic knee OA overall was not associated with significantly improved outcomes compared to placebo. The treatment was well-tolerated and safe. Subgroup analyses, however, showed a significant effect of APPA in patients with moderate to severe OA, indicating that further research in the effects of APPA in appropriate patients is warranted.

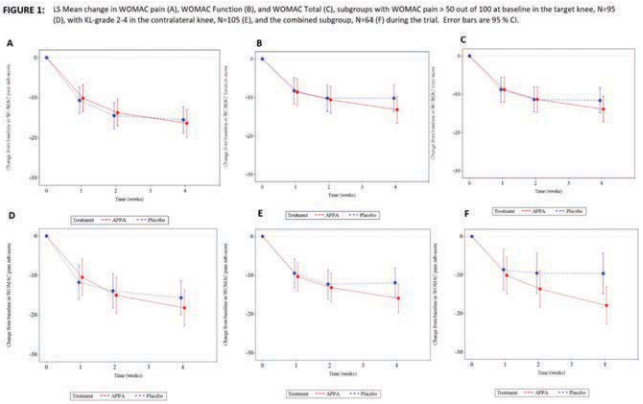

FIGURE 1: LS Mean change in WOMAC pain (A), WOMAC Function (B), and WOMAC Total (C), subgroups with WOMAC pain > 50 out of 100 at baseline in the target knee, N=95 (D), with KL-grade 2-4 in the contralateral knee, N=105 (E), and the combined subgroup, N=64 (F) during the trial. Error bars are 95 % CI.

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POS0181

EFFECT OF A MULTIDISCIPLINARY LIFESTYLE PROGRAM ON PATIENTS WITH METABOLIC SYNDROME-ASSOCIATED OSTEOARTHRITIS: THE PLANTS FOR JOINTS RANDOMIZED CONTROLLED TRIAL

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Background: Metabolic syndrome with low grade inflammation is associated with chronic diseases including osteoarthritis (OA) (1). Nonpharmacological treatment with a combination of an intensive diet and exercise produced better results in people with osteoarthritis (OA) than either treatment alone (2). We further developed the concept of an integrated lifestyle intervention in people with metabolic syndrome-associated osteoarthritis (MSOA) by combining a whole food plant-based diet with physical activity and stress management.

Objectives: To determine the effect of a multidisciplinary lifestyle program on pain, stiffness, and physical function in patients with MSOA.

Methods: In the "Plants for Joints" (PFJ) parallel-arm, randomized clinical trial, patients with MSOA were assigned to the PFJ group or the control group. Patients with metabolic syndrome (according to NCEP criteria) and OA in the knee and/or hip (according to clinical ACR criteria) were eligible for participation. The PFJ group followed a 16-week lifestyle program based on a whole food plant-based diet, physical activity, and stress management in addition to usual care. The control group received usual care.

Prior to the start of the study, it was hypothesized that the lifestyle program would lower pain and stiffness and improve physical function, based on the Western Ontario and McMaster Universities Arthritis Index (WOMAC) score (primary outcome). Secondary outcomes included anthropometric, and metabolic markers. Patient partners selected the patient-reported outcome measures (PROMIS©) depression, fatigue, pain interference and physical function as additional secondary outcomes.

An intention-to-treat analysis with a linear mixed model, adjusted for baseline values (and age, sex, and body mass index [BMI] in additional analyses), was used to analyze the between-group differences of continuous outcomes.

Results: Of the 92 people screened, 66 were randomized and 64 completed the study (PFJ group: n = 32). Participants were 84% female, had a mean (SD) age of 63 (6) and a mean (SD) BMI of 33 (5) kg/m^2. After 16 weeks the PFJ group had a mean 11-point greater improvement of the total WOMAC score (range 0-96) over time (95% CI 6 to 16; p = 0.0001) with significant improvements in all three components pain, stiffness, and physical function compared to the control group (Figure 1). Also, compared to the control group, the PFJ group lost more body weight (–3.9 kg, 95% CI –5.8 to –2.0; p < 0.001), fat mass as measured with dual-energy x-ray absorptiometry (–3.9 kg, 95% CI –5.3 to –2.5; p < 0.0001) and waist circumference (–4 cm, 95% CI –7 to –1; p = 0.01). HbA1c and fasting glucose improved in the PFJ versus control group, but not significantly. LDL decreased by 0.38 mmol/l (95% CI 0.07 to 0.69; p = 0.02) and triglycerides by 0.32 (95% CI 0.01 to 0.63; p = 0.04) in favour of the PFJ group. HDL and blood pressure remained unchanged. Of the patient reported outcome measures (PROMIS©) only fatigue showed a significant improvement. Based on a baseline mean (SD) value of 55 for all the participants, fatigue improved with 4 (95% CI 1 to 6; p = 0.03) in the PFJ group when compared with the control group. Additional analyses adjusted for age, sex, and BMI did not lead to different outcomes.

No serious adverse events occurred.

Conclusion: The 16-week "Plants for Joints" lifestyle program substantially decreased pain and stiffness and improved physical function in people with metabolic syndrome associated osteoarthritis of hip and/or knee. In addition, following the lifestyle program resulted in lower weight, fat mass and smaller waist circumference in comparison with usual care.

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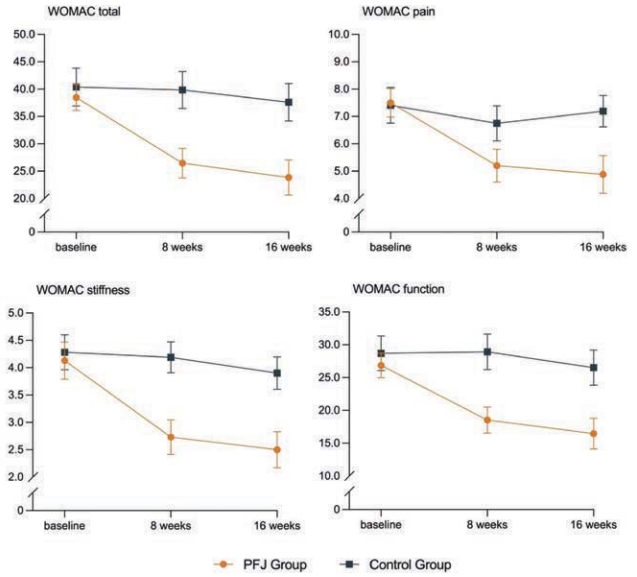

Figure 1. Change in Western Ontario and McMaster Universities Arthritis Index (WOMAC) total score (p = 0.0001) and WOMAC component scores for pain (p = 0.04), stiffness (p < 0.001) and function (p = 0.0001) for the Plants for Joints group (n = 32) when compared with the control group (n = 32). Graphs present mean ± standard error.

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POS0182

WHO ARE LIKELY TO BENEFIT FROM THE GOOD LIFE WITH OSTEOARTHRITIS IN DENMARK (GLAD) EXERCISE AND EDUCATION PROGRAM? AN EFFECT MODIFIER ANALYSIS OF A RANDOMISED CONTROLLED TRIAL

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Background: EULAR clinical guidelines have identified moderators of knee osteoarthritis (OA) outcomes as an important research priority to optimize individualized treatment. In our recent trial the GLAD exercise and education program was proved equivalent to open-label placebo (OLP) in 206 people with knee OA, which calls for evaluation of factors that may predict differential treatment response to GLAD versus OLP.

Objectives: To identify contextual factors that might modify the treatment effect of the '*Good Life with osteoArthritis in Denmark*' (GLAD) exercise and education programme on knee osteoarthritis (OA) pain compared to that of open-label placebo (OLP) in individuals with knee OA, i.e. explore who are likely to benefit from participating in exercise and education programs.

Methods: Secondary effect modifier analysis of a randomised controlled trial, in which 206 adults aged ≥ 50 years, with symptomatic and radiographic knee OA were randomised to either an 8-week exercise and education programme (GLAD; n=102) or OLP in the form of 4 intra-articular saline injections over 8 weeks (n=104). Primary outcome was change from baseline to week 9 in the Knee injury and Osteoarthritis Outcome Score questionnaire (KOOS) pain subscale (range 0 (worst) to 100 (best)). Subgroups were created based on baseline information: BMI, swollen study knee, bilateral radiographic knee OA, sports participation as a young adult, sex, median age, *a priori* treatment preference, regular use of analgesics (NSAIDs or paracetamol), radiographic disease severity, and presence of constant and intermittent pain using the Intermittent and Constant Osteoarthritis Pain questionnaire. Analyses were based on the intention-to-treat principle with simple conservative non-responder imputation of missing outcome data.

Results: Participants who at baseline reported use of analgesics at baseline seem to benefit from the GLAD programme over OLP (subgroup contrast: 10.3 KOOS pain points (95% CI 3.0 to 17.6)). Further, participants with constant pain at baseline also seem to benefit from GLAD over OLP (subgroup contrast: 10.0 KOOS pain points (95%CI 2.8 to 17.2; P=0.007)). Further, *a priori* preference for GLAD also seemed to predict treatment effect in favour of GLAD. Presence of

intermittent pain predicted beneficial effects of OLP, albeit the precision of the estimate was low. See Figure 1.

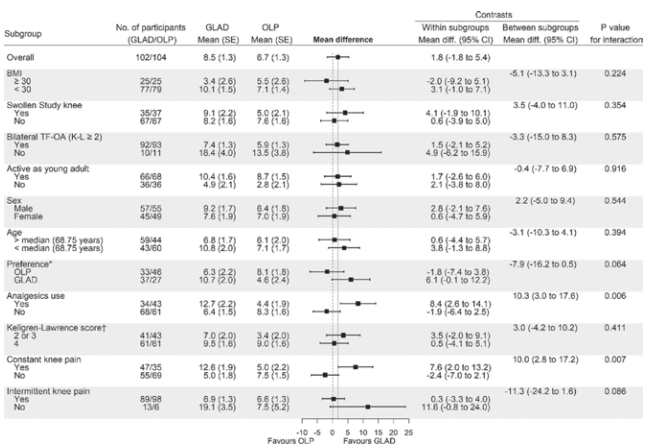

Figure 1. Forest plot showing the results of the subgroup analyses based on the intention-to-treat population with missing outcome data at week 9 replaced with the baseline observation (non-responder imputation). The outcome is change from baseline in KOOS pain at week 9 (after 8 weeks of intervention). GLAD: The Good Life with osteoArthritis in Denmark exercise and education programme. OLP: Open-label placebo consisting of 4 intra-articular saline injections. K-L: Kellgren-Lawrence grading of radiographic disease severity.The full vertical line indicates the overall treatment effect, and the dashed line indicates zero effect. *24 GLAD and 26 OLP had no preference and are not included in the analyses, and 8 GLAD and 5 OLP had missing data; †For study knee.

Conclusion: These results imply that GLAD should not be considered as a one-size-fits-all intervention. For patients who take analgesics for their knee pain or report constant knee pain, GLAD seems to yield clinically relevant benefits when compared to an open-label placebo. The results support a stratified recommendation of GLAD as management of knee OA.

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New options in SLE-Sjogren and APS

POS0183

THE EFFECT OF BELIMUMAB ON SRI-4 RESPONSE IN MULTIPLE SUBGROUPS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A LARGE INTEGRATED ANALYSIS

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Background: Belimumab (BEL) is approved for the treatment of active autoantibody-positive systemic lupus erythematosus (SLE).[1] Four Phase 3 studies have consistently demonstrated greater SLE Responder Index (SRI) response rates with BEL vs placebo (PBO).[2-5] This robust dataset allows for additional exploration of the onset of efficacy of BEL and response rates by patient (pt) characteristics.
Objectives: To perform a *post hoc* analysis evaluating the effect of BEL on SRI-4 response across a large, pooled population and pt subgroups.
Methods: The Belimumab Summary of Lupus Efficacy (Be-SLE) integrated analysis evaluated data from adults with SLE from 5 double-blind, PBO-controlled BEL trials: BLISS-76, BLISS-52, BLISS-NEA, BLISS-SC, and EMBRACE.[2-6] Pts were randomised to BEL (monthly intravenous 10 mg/kg or weekly subcutaneous 200 mg) or PBO, plus standard therapy. Data were collected every 4 weeks (wks) from baseline (BL) to Wk 52. The SRI-4 response rate (a composite measure that includes ≥4-point reduction in Safety of Estrogens in Lupus Erythematosus National Assessment - SLE Disease Activity Index [SELENA-SLEDAI] score, stable Physician Global Assessment [PGA] increase of <0.3, and no new British Isles Lupus Assessment Group [BILAG] 1A/2B organ domain scores) by visit and time to first SRI-4 response maintained through Wk 52 were determined for both treatment groups. SRI-4 response rates at Wk 52 were evaluated by BL characteristic subgroups: SELENA-SLEDAI score; SLE International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) score; disease duration; biomarker levels (anti-dsDNA, complement [C]3/C4); glucocorticoid (GC), immunosuppressant (IS), and antimalarial (AM) use.
Results: Overall, 3086 pts were included (BEL, n=1869; PBO, n=1217). Most were female (94.4%); mean (standard deviation [SD]) age was 37.0 (11.6) years. Mean (SD) SLE duration was 6.4 (6.4) years.
At Wk 52, in the overall population, significantly more BEL vs PBO pts were SRI-4 responders (Figure 1). A significantly greater proportion of SRI-4 responders was observed with BEL vs PBO as early as Wk 8 (38.4% vs 33.3%; odds ratio, OR [95% confidence interval, CI] 1.25 [1.07, 1.46]; p=0.0060), which continued to increase to Wk 52 (54.8% vs 41.6%; OR [95% CI] 1.70 [1.46, 1.98]; p<0.0001). At Wk 52, more BEL vs PBO pts had a 4-point reduction in SELENA-SLEDAI (56.3% vs 43.1%; OR [95% CI] 1.71 [1.47, 2.00]; p<0.0001), no worsening in PGA (76.6% vs 67.9%; OR [95% CI] 1.52 [1.28, 1.79]; p<0.0001), and no new BILAG 1A/2B organ domain scores (77.1% vs 69.4%; OR [95% CI] 1.47 [1.25, 1.74]; p<0.0001). Pts on BEL were 52% more likely to experience an SRI-4 response that was maintained through Wk 52 (hazard ratio, HR [95% CI] 1.52 [1.36, 1.69]; p<0.0001).

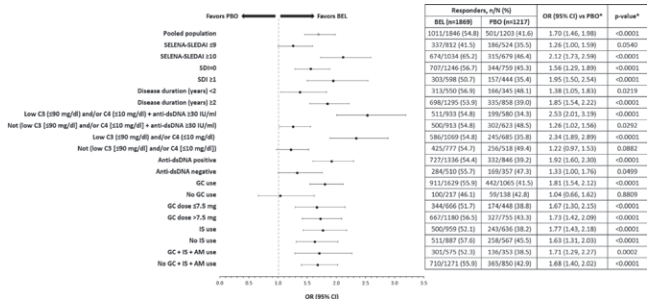

Figure 1. SRI-4 response at Wk 52 in the overall population and by BL characteristic subgroups. *OR (95% CI) and p-value are from a logistic regression model for BEL vs PBO comparison with covariates of treatment group, study and BL SELENA-SLEDAI score (≤9 vs ≥10)

SRI-4 response rates were significantly higher with BEL vs PBO in most subgroups, with the highest response rates observed in pts with SELENA-SLEDAI score of ≥10, low C3 and/or C4 + anti-dsDNA ≥30 IU/ml, and low C3 and/or C4 at BL (Figure 1).
Conclusion: Significantly more pts receiving BEL had SRI-4 response rates that occurred from Wk 8 and were maintained through Wk 52 compared with pts receiving PBO. The efficacy of BEL was consistent across multiple pt subgroups, with higher response rates in pts with SELENA-SLEDAI scores of ≥10, low C3 and/or C4 + anti-dsDNA ≥30 IU/ml and low C3 and/or C4 at BL. These results further substantiate the benefits of BEL in the treatment of adults with SLE.

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POS0184

EFFICACY OF BIIB059 ON SKIN MANIFESTATIONS IN PARTICIPANTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN THE PHASE 2 LILAC STUDY (PART A)

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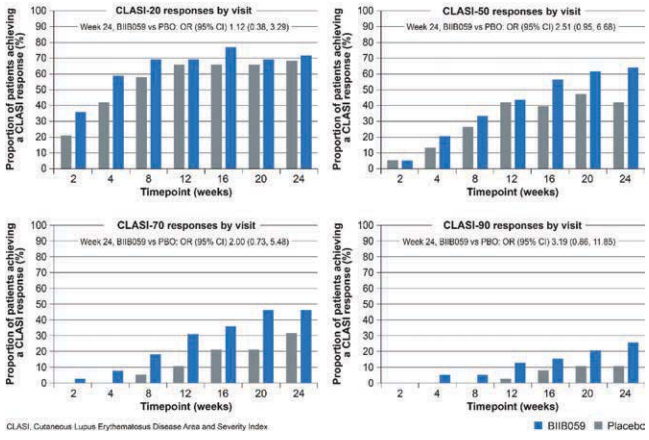
Background: SLE is a heterogeneous disease with diverse clinical presentations, and up to 70–80% of patients develop skin manifestations.[1–3] In SLE, plasmacytoid dendritic cells (pDCs), a major source of Type I interferon (IFN), accumulate in the skin.[4] Treatment with BIIB059, a humanized monoclonal antibody targeting blood dendritic cell antigen 2 (BDCA2) that is expressed on pDCs, leads to rapid internalization of BDCA2 from the surfaces of pDCs and inhibits the production of Type I IFNs, pro-inflammatory cytokines, and chemokines.[5] Part A of the randomized, two-part, Phase 2 LILAC study (NCT02847598) enrolled participants with SLE and active skin and joint disease. The primary endpoint was met, with a greater reduction in total active joint count at Week 24 in the BIIB059 treatment group vs placebo (PBO), and more participants achieved a ≥50% improvement from baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity (CLASI-A) score with BIIB059 vs PBO.[6]
Objectives: To further evaluate the effect of BIIB059 vs PBO in reducing skin disease activity, as measured by various CLASI-A response thresholds.
Methods: Adults with an SLE diagnosis according to the revised ACR 1997 SLE classification criteria, with ≥4 tender and ≥4 swollen joints (28-joint assessment), active skin disease (as defined by the SLE Disease Activity Index 2000 [SLEDAI-2K]), and positive anti-nuclear antibodies and/or anti-double-stranded DNA antibodies, were enrolled. Participants were randomized to receive BIIB059 450 mg or PBO, administered subcutaneously every 4 weeks with an additional dose at Week 2. Improvements in skin disease were assessed in participants with baseline CLASI-A score ≥8. The proportion of participants achieving a ≥7-point reduction from baseline in CLASI-A score was assessed at Week 24, and CLASI-20, -50, -70, and -90 responses were assessed over time. Achievement of CLASI-A scores of 0–1 was also assessed at Week 24. These analyses used non-responder imputation with logistic regression, without correction for multiplicity. The proportions of participants achieving CLASI-A scores of 0–3 and with resolution of SLEDAI-2K skin rash at Week 24 were evaluated *ad hoc* in the same population. Non-responder imputation was applied to visits post treatment failure and treatment discontinuation. Improvement from baseline in British Isles Lupus Assessment Group index (BILAG-2004) A or B mucocutaneous domains was similarly assessed at Week 24. P-values were calculated based on the odds ratios (ORs) for BIIB059 compared with PBO.
Results: At Week 24, a significantly greater proportion of participants receiving BIIB059 (n=39) vs PBO (n=38) had a ≥7-point reduction in CLASI-A score from baseline to Week 24 (56.4% vs 34.2%, OR [95% confidence interval {CI}] 2.71 [1.03, 7.17], P=0.044). Numerically greater proportions of participants receiving BIIB059 vs PBO achieved CLASI-50, CLASI-70, or CLASI-90 responses (Figure 1). Similarly, the proportion of participants who achieved CLASI-A scores of 0–1 was greater in the BIIB059 group vs PBO (25.6% vs 13.2%), as was the proportion who achieved CLASI-A scores of 0–3 (48.7% vs 28.9%). A greater proportion of BIIB059- vs PBO-treated participants had resolution of SLEDAI-2K skin rash at Week 24 (28.6% vs 10.7%), with similar findings seen in the BILAG-2004 mucocutaneous domain.

Figure. Patients achieving CLASI-20, -50, -70, and -90 responses by visit



Conclusion: Numerically greater reductions in skin disease activity were consistently observed with BIIB059 treatment vs PBO in participants with SLE and active skin disease, supporting a potential benefit of BIIB059 treatment for skin manifestations in SLE.

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POS0185 BELIMUMAB DISRUPTS MEMORY B-CELL TRAFFICKING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Belimumab (BEL), a recombinant human monoclonal antibody directed against B-cell activating factor (BAFF), is the first approved biological agent for patients with active systemic lupus erythematosus (SLE) and lupus nephritis (LN).[1] BEL inhibits primary humoral immune responses by depleting naïve B cells that are dependent on BAFF for their survival while secondary humoral immune responses by memory B cells (MBCs) remain intact. Indeed, some studies reported an increase of circulating MBCs following neutralisation of BAFF.[2-4] So far, these effects of BEL on the MBC compartment in SLE patients have not been investigated.
Objectives: This study aimed to establish the dynamics of circulating MBCs in patients with SLE treated with BEL and to perform an in-depth analysis of the impact of BEL on the MBC compartment.
Methods: First, a retrospective meta-analysis was performed by pooling individual patient MBC flow cytometry data from 1245 patients with SLE treated with BEL 10 mg/kg IV or placebo (PBO) from four randomised clinical trials (NCT00071487, NCT00410384 [BLISS-76],[3] NCT01632241 [EMBRACE],[5] NCT01649765 [PLUTO][6]). Second, extensive B-cell subset phenotyping was performed prospectively by employing high-sensitivity flow cytometry (HSFC) based on EuroFlow protocols[7] in patients with active SLE (from the BLISS-BELIEVE trial [NCT03312907])[8] and with severe SLE/LN (from the SynBioSe-2 trial [NCT03747159])[9] treated with BEL. Additionally, in-depth characterisation of surging MBCs in circulation was performed by single-cell RNA sequencing (scRNA-seq).
Results: By comparing BEL-treated with PBO-treated patients with SLE, a substantial increase in circulating MBC counts was established 4 weeks after BEL initiation, gradually returning to baseline by Week 52. The increase of MBCs was most prominent in BEL-treated patients with higher SLE disease activity (SLE

Disease Activity Index >9), serologically active patients (dsDNA positive and/or low complement levels) and with younger age (below 18 years). HSFC established that the increase was non-specific and observed in a broad range of MBC subclasses peaking as early as 2 weeks after BEL initiation. Subsequent scRNA-seq analysis of the emerging MBCs revealed a non-proliferating phenotype with a prominent decrease in activation status. In these circulating MBCs, a large amount of migration and adhesion genes were downregulated suggesting that the accumulation of MBCs following BEL treatment was related to their impaired cell-cell adhesion, disrupting cell-trafficking and preventing extravasation.

Conclusion: After initiation of BEL treatment, a substantial increase of circulating MBCs was firmly established and was most notable in patients with severe, serologically active SLE/LN. The surge of circulating MBCs appeared to be associated with disrupted lymphocyte trafficking of MBCs, thereby suggesting a new potential therapeutic mechanism of BEL on MBCs in SLE. These findings have important implications to our understanding and consequent improvement of B-cell targeted treatment strategies in patients with active SLE and LN, as MBC accumulation in circulation might allow for more efficient targeting of the B-cell compartment.

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POS0186 VOCLOSPORIN FOR LUPUS NEPHRITIS: RESULTS OF THE TWO-YEAR AURORA 2 CONTINUATION STUDY

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Background: Voclosporin (VCS), a novel calcineurin inhibitor, was approved in the US in January 2021 for the treatment of adult patients with active lupus nephritis (LN) in combination with background immunosuppressive therapy. The Phase 3 AURORA 1 study showed that the addition of VCS to mycophenolate mofetil (MMF) and low-dose steroids in patients with LN significantly increased rates of complete renal response at 52 weeks.

Objectives: Here we report the results of the completed continuation study, AURORA 2, which assessed the long-term safety and tolerability of VCS compared to placebo in patients with LN receiving treatment for an additional 24 months following completion of the AURORA 1 study

Methods: Key inclusion criteria for the parent AURORA 1 study included a diagnosis of biopsy-proven active LN (Class III, IV, or V ± III/IV), proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V) and estimated glomerular filtration rate (eGFR) >45 mL/min/1.73 m^2. Patients who completed AURORA 1 and who elected and were eligible to enter AURORA 2 continued on the same blinded therapy as at the end of AURORA 1 (either VCS or placebo twice daily in combination with MMF and low-dose steroids). Safety and tolerability were monitored, and eGFR, serum creatinine (SCr), and urine protein creatinine ratio (UPCR) were also assessed.

Results: In total, 116 and 100 patients in the VCS and control arms enrolled in AURORA 2, with 92 (79.3%) and 73 (73.0%) patients in each respective arm receiving treatment to the end of AURORA 2. There were no unexpected safety signals in the VCS arm compared to control, with similar rates of serious adverse events reported in both arms (VCS [18.1%] vs. control [23.0%]; Table 1). Eight patients in each arm experienced serious adverse events of infection; serious coronavirus infections were observed in 2 patients in the voclosporin arm and 5 patients in the control arm. There were 4 and 2 adverse events by preferred term of renal impairment reported in the VCS and control arms, respectively, none of which were considered serious, and no reports of acute kidney injury by preferred term in either arm. There were no deaths in the VCS arm during AURORA 2; four deaths were reported in the control arm (pulmonary embolism [n=1], coronavirus infection [n=3]). Mean eGFR and SCr levels remained stable through the end of AURORA 2. The difference between the VCS and control arms in LS mean change from baseline in eGFR was 2.7 mL/min/1.73 m^2 at 4 weeks following study drug discontinuation (Figure 1). The mean reductions in UPCR observed in patients treated with VCS in AURORA 1 were maintained in AURORA 2 with no increase in UPCR noted at the follow-up visit 4 weeks after study drug discontinuation.

Table 1. Overall Summary of Adverse Events

	Control (n=100)	Voclosporin (n=116)
	n (%)	n (%)
Any AE	80 (80.0)	100 (86.2)
Renal Impairment	2 (2.0)	4 (3.4)
Acute Kidney Injury	0	0
Treatment-related AE	21 (21.0)	28 (24.1)
Serious AE	23 (23.0)	21 (18.1)
Serious Treatment-related AE	2 (2.0)	1 (0.9)
AE Leading to Study Drug Discontinuation	17 (17.0)	11 (9.5)
Death	4 (4.0)	0
Treatment-related Death	0	0

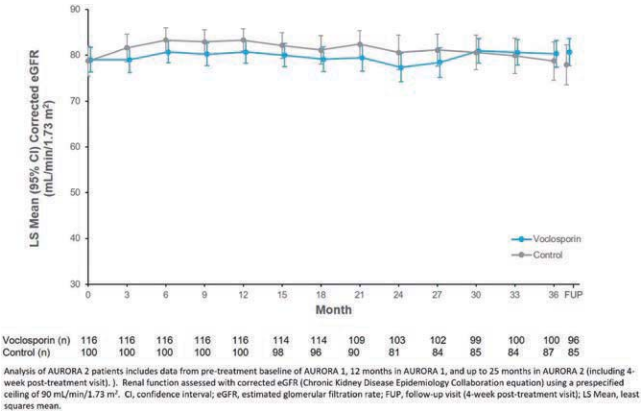

Figure 1. LS Mean eGFR over Time

Conclusion: Voclosporin was well-tolerated over 3 years of treatment with no unexpected safety signals detected. Further, eGFR remained stable throughout the study period, and the significant and meaningful reductions in proteinuria achieved in AURORA 1 were maintained. These data provide evidence of a long-term treatment benefit of VCS in patients with LN.

Includes adverse events starting on or after the first dose of study drug in AURORA 2 up to 30 days after the last dose and all events of death reported during study follow-up. Adverse events were aggregated by System Organ Class and Preferred Term and coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 20.0. AE, adverse event.

Disclosure of Interests: Amit Saxena Speakers bureau: Aurinia Pharmaceuticals Inc., Consultant of: Aurinia Pharmaceuticals Inc., Y.K. Onno Teng Consultant of: Aurinia Pharmaceuticals Inc., Chris Collins Shareholder of: Aurinia Pharmaceuticals, Employee of: Aurinia Pharmaceuticals, Nicole England Shareholder of: Aurinia Pharmaceuticals, Employee of: Aurinia Pharmaceuticals, Henry Leher Shareholder of: Aurinia Pharmaceuticals, Employee of: Aurinia Pharmaceuticals

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POS0187

DRUG REPURPOSING FOR TREATING LUPUS NEPHRITIS BASED ON TRANSCRIPTOME PROFILING AND AUTOIMMUNITY-RELATED SEROLOGICAL MARKERS

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Background: Lupus nephritis (LN) is one of the most severe organ manifestations of systemic lupus erythematosus (SLE) and constitutes an important cause of morbidity and death among patients with SLE [1]. The associated renal injury, and ultimately damage, is the result of an immune-mediated process which involves leukocytes, immune complexes, complement and cytokines [2].
Objectives: Lupus nephritis (LN) is one of the most severe organ manifestations of systemic lupus erythematosus (SLE) and constitutes an important cause of morbidity and death among patients with SLE [1]. The associated renal injury, and ultimately damage, is the result of an immune-mediated process which involves leukocytes, immune complexes, complement and cytokines [2].
Methods: We analysed differentially expressed genes (DEGs), pathways and their druggability via the Drug Gene Interaction database (DGIdb) [3] in active LN (n=41) versus healthy controls (HC; n=497), and eQTLs in active or past LN (n=87), based on validated (identified in two independent SLE populations) DEGs in SLE (n=350) vs HC (n=497), in whole blood collected within the frame of the European PRECISESADS consortium [4]. Genome-wide RNA-sequencing and genotyping was previously performed by Illumina assays, and serum levels of 17 cytokines and 18 autoantibodies were analysed using a Luminex assay, ELISA, IDS-iSYS and SPAPLUS analyser [4].
Results: A total of 6 869 significant and validated DEGs were identified in active LN patients compared with HC. Of these, 1010 validated DEGs were tagged to 34 KEGG pathways including 24 DEGs with a lfold change (FC)l > 1.5, genes of 18 cis-eQTLs and 3 trans-eQTLs, and 1 gene from cytokines that differed significantly between active LN and HC. Moreover, 2446 validated DEGs were tagged to 216 Reactome pathways included 85 DEGs with a lFCl > 1.5, genes of 21 cis-eQTLs and 5 trans-eQTLs, and 1 gene from cytokines that differed significantly between active LN and HC. These genes could be targeted by 203 different drugs, with the proteasome inhibitor bortezomib interfering with cathepsin B (CTSB) regulation and cyclophosphamide interfering with the regulation of tumour necrosis factor receptor superfamily member 1A (TNFRSF1A) being of particular interest.
Conclusion: Integrated multilevel omics analysis in LN revealed a set of enriched pathways of potential interest for future drug investigation. A prospect for proteasome inhibition was implicated.

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POS0188

TRANSCRIPTOME PROFILING AND AUTOIMMUNITY-RELATED SEROLOGICAL MARKERS IDENTIFY TP53 AND C3AR AS DRUG TARGETS IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Involvement of the nervous system is a common but poorly understood manifestation of systemic lupus erythematosus (SLE), termed neuropsychiatric SLE (NPSLE). Although studies have reported varying prevalence estimates [1], NPSLE affects at least 20% of patients with SLE within the first years of the disease course [2]. The management of neuropsychiatric SLE (NPSLE) is poorly optimised and specific treatment is lacking.
Objectives: The aim of this study was to investigate expression quantitative trait loci (eQTLs), the transcriptome, and autoimmunity-related cytokines and autoantibodies in patients with central nervous system (CNS) lupus to gain insights into underlying genetics and biologic mechanisms towards identification of novel drug targets.
Methods: We analysed differentially expressed genes (DEGs), pathways and their druggability via the Drug Gene Interaction database (DGIdb) [3] in active CNS lupus (n=26) versus healthy controls (HC; n=497), and eQTLs in active or past CNS lupus (n=53), based on validated (identified in two independent SLE populations) DEGs in SLE (n=350) versus HC (n=497), in whole blood collected within the frame of the European PRECISESADS consortium [4]. CNS lupus was defined according to SLE Disease Activity Index 2000 (SLEDAI-2K) [5] CNS items or by CNS manifestations such as chorea, acute confusional state, transverse myelitis, aseptic meningitis, and optic neuritis in the absence of predisposing conditions unrelated to SLE. Genome-wide RNA-sequencing and genotyping was previously performed by Illumina assays, and serum levels of 17 cytokines were analysed using a Luminex assay and ELISA [4].
Results: Among 5631 significant and validated DEGs in active CNS patients compared with HC, 1922 unique DEGs were tagged to 21 and 176 significant KEGG [6] and Reactome [7] pathways, respectively. Pathways included "Interferon signalling", "TNF signalling" and "Toll-like Receptor Cascades". The pathways included 29 of 59 DEGs with a lfold change (FC)l > 1.5, 6 genes from 14 significant cis-eQTLs and 10 genes from 22 trans-eQTLs, and 2 genes from 8 cytokines that differed significantly between active CNS lupus and HC. These genes could be targeted by 496 different drugs, with the Bruton tyrosine kinase (BTK) inhibitor ibrutinib and the anti-CD20 B cell depleting monoclonal rituximab with ability to interfere with tumour protein P53 (TP53) activity, and a complement C3a Receptor (C3aR) antagonist being of particular interest.
Conclusion: Integrated multilevel omics analysis revealed a set of enriched pathways of potential interest for future drug investigation in CNS lupus, including BTK and C3aR inhibition, and B cell depletion.

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POS0189

EFFECT OF ATACICEPT ON RENAL FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Atacicept is a fusion protein that blocks B-lymphocyte stimulator and a proliferation-inducing ligand, which are increased in patients with SLE. APRIL-SLE was a double-blind, placebo-controlled, Phase 2 study that randomized patients with moderate-to-severe systemic lupus erythematosus (SLE) to atacicept 75 mg, atacicept 150 mg, or placebo twice-weekly for 4 weeks, then weekly for 48 weeks.
Objectives: The primary results of the APRIL-SLE study – the effect of atacicept compared to placebo in preventing new flares in patients with moderate-to-severe SLE – have been reported (Isenberg et al., 2013). We performed a post hoc analysis to describe the effect of atacicept compared to placebo on measures of renal function in patients with SLE; this effect has not been reported previously.
Methods: The APRIL-SLE study excluded patients with moderate to severe glomerulonephritis, as defined by either of the following: urinary protein/creatinine ratio (UPCR)>1 mg/mg and/or hematuria or a significant renal impairment as defined by estimated glomerular filtration rate (eGFR)<50 mL/min/1.73 m2. Patients with proteinuria and mild to moderate chronic kidney disease, as assessed by KDIGO criteria were eligible. UPCR and eGFR were measured at baseline, week 2, and then every 4 weeks until week 52. The median change from baseline to each of these timepoints was calculated for eGFR and UPCR using the Safety Analysis Set, comprised of all randomized patients who received at least 1 dose of study medication. Enrollment in the atacicept 150 mg group was discontinued prematurely due to 2 deaths from pneumonias. When treatment was discontinued, 62 of 144 patients in this group had completed 52 weeks of treatment; 27 other patients had already been withdrawn for various reasons; and, in the remaining 55 patients, treatment was stopped early as a safety precaution. Patients in the other two groups completed the protocol.
Results: In total, 111 patients in the placebo group, 112 patients in the atacicept 75 mg group, and 62 patients in the atacicept 150 mg group completed 52 weeks of treatment. The eGFR time course was stable for the atacicept groups compared to a 4.4% decline in the placebo group from baseline at week 52 (Figure 1 and Table 1). UPCR from baseline at week 52 declined in the atacicept groups and increased in the placebo group.

Table 1. Median Percent Change from Baseline of Estimated Glomerular Filtration Rate (eGFR) and Proteinuria at Week 52 – Safety Analysis Set

Variable	Placebo	Atacicept 75 mg	Atacicept 150 mg
eGFR (mL/min)	n=110	n=111	n=62 [b]
median	-4.35	-1.49	0.57
UPCR (mg/mg)	n=108	n=108	n=63
median	6.29	-6.27	-12.72
UPCR (mg/mg) [a]	n=12	n=15	n=8
median	26.11	-54.42	-12.15

eGFR=estimated glomerular filtration rate; UPCR=urinary protein/creatinine ratio. [a]Among patients with screening UPCR ≥0.2 mg/mg. [b]Enrollment in the atacicept 150 mg arm was discontinued prematurely (described in Isenberg et al., 2015).

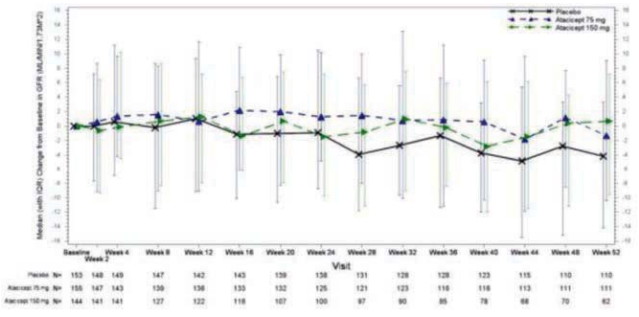

Figure 1. Median Change from Baseline in eGFR. eGFR= estimated glomerular filtration rate; IQR=interquartile range

Conclusion: Results from this double-blind, placebo-controlled, Phase 2 study suggest a potential for improved renal function with atacicept treatment of patients with moderate-to-severe SLE.

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Disclosure of Interests: David Isenberg Consultant of: Professor Isenberg has consulted for Veratx, Servier, Astro-Zeneca, Idorsia, Merck Serono, and Amgen. His honoraria are passed onto a local arthritis charity., Celia J. F. Lin Shareholder of: Dr. Lin is an employee of Vera Therapeutics, Inc., Employee of: Dr. Lin is an employee of Vera Therapeutics, Inc., Amy Kao Shareholder of: Dr. Kao own stocks of Merck KGaA, Darmstadt, Germany, Employee of: Dr. Kao is an employee of EMD Serono Research & Development Institute, Inc (a business of Merck KGaA), Aida Arselan Aydemir Employee of: Ms. Aydemir is an employee of EMD Serono Research & Development Institute, Inc (a business of Merck KGaA), Caroline Gordon Speakers bureau: Dr. Gordon reports personal fees for speakers bureau from UCB, Consultant of: Dr. Gordon reports personal fees for honoraria from consultancy work from the Center for Disease Control and Prevention, Amgen, Astra-Zeneca, AbbVie, EMD Serono, MGP, Sanofi, and UCB, Grant/research support from: Dr. Gordon reports an educational grant from UCB to Sandwell and West Birmingham Hospitals NHS Trust that supported previous research work unrelated to any specific drug (last payment July 2019).
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POS0190 EFFICACY AND SAFETY OF BARICITINIB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM TWO RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP, PHASE 3 STUDIES

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Background: In a 24-week, phase 2 clinical study (NCT02708095) in patients with systemic lupus erythematosus (SLE), baricitinib (BARI), an oral selective inhibitor of Janus kinase 1 and 2 approved for the treatment of rheumatoid arthritis and atopic dermatitis, inhibited the type I interferon gene signature, multiple other cytokine pathways, and improved disease activity (1) (2).
Objectives: To further evaluate the efficacy and safety of BARI in patients with SLE.
Methods: Patients with active SLE receiving stable background therapy were randomised 1:1:1 to BARI 2-mg, 4-mg, or placebo (PBO) once daily in two identically designed, 52-week, phase 3 randomised, PBO-controlled studies. In SLE-BRAVE-I (NCT03616912) and -II (NCT03616964), 760 and 775 patients, respectively were enrolled in a balanced manner across regions, although different countries per region participated in each study. The primary endpoint for both studies was the proportion of patients achieving an SLE Responder Index-4 (SRI-4) response at week 52. Glucocorticoid tapering was encouraged but not required per protocol.
Results: The mean Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at baseline was 10.1 for both SLE-BRAVE-I and -II participants; musculoskeletal and mucocutaneous domains were the most common domains involved at baseline. In SLE-BRAVE-I, the proportion of SRI-4 responders at week 52 among patients treated with BARI 4-mg (56.7%), but not BARI 2-mg (49.8%), was significantly greater than in patients treated with PBO (45.9%, p = 0.016) (Table 1). No difference was seen in SLE-BRAVE-II (47.1%, 46.3%, and 45.6%, BARI 4-mg, 2-mg, and PBO, respectively). None of the key secondary endpoints, including glucocorticoid tapering or time to first severe flare (SFI), were met in either study. The proportions of patients with serious adverse events (SAEs) were 7.1% and 8.6% for PBO, 9.4% and 13.4% for BARI 2-mg and 10.3% and 11.2% for BARI 4-mg in SLE-BRAVE-I and II, respectively.

Table 1. Efficacy and safety of baricitinib in patients with SLE-BRAVE-I and -II

	SLE-BRAVE-I			SLE-BRAVE-II		
Efficacy measure	PBO (N=253)	BARI 2-mg (N=255)	BARI 4-mg (N=252)	PBO (N=256)	BARI 2-mg (N=261)	BARI 4-mg (N=258)
SRI-4 (W52)	116 (45.9)	126 (49.8)	142 (56.7)*	116 (45.6)	120 (46.3)	121 (47.1)
SRI-4 (W24)	99 (39.1)	114 (44.8)	117 (46.5)	98 (38.6)	104 (40.0)	108 (42.1)
Severe Flares (n, events)	38 (15.0)	34 (13.3)	26 (10.3)	26 (10.2)	29 (11.1)	29 (11.2)
HR for time to first severe flare (SFI) HR [CI]	NA	0.8 [0.52, 1.32]	0.65 [0.40, 1.08]	NA	1.1 [0.65, 1.89]	1.1 [0.67, 1.94]
Glucocorticoid sparing	36 (30.8)	31 (29.2)	36 (34.0)	33 (31.7)	34 (29.8)	36 (34.3)
LLDAS (W52)	66 (26.2)	65 (25.7)	74 (29.7)	59 (23.2)	62 (24.0)	65 (25.4)
Safety measure						
TEAE	210 (83.0)	210 (82.4)	208 (82.5)	198 (77.3)	199 (76.2)	200 (77.5)
SAE	18 (7.1)	24 (9.4)	26 (10.3)	22 (8.6)	35 (13.4)	29 (11.2)

Data are n (%) patients, unless otherwise indicated. BARI=baricitinib; CI=confidence interval; HR=hazard ratio compared with PBO; LLDAS=lupus low disease activity state; N=number of patients in the analysis population; n=number of patients in the specified category; PBO=placebo; TEAE=treatment-emergent adverse event; SAE=serious adverse event; W=week. *p≤0.05 vs PBO.

Conclusion: Although phase 2 data suggested BARI as a potential treatment for patients with SLE (2), the SLE-BRAVE-I and -II phase 3 study results were discordant for the primary outcome measure, with only SLE-BRAVE-I positive, making it difficult to elucidate benefit. Additional analyses are being performed to understand this discordance. No new safety signals were observed.

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Disclosure of Interests: Eric F. Morand Speakers bureau: Astra Zeneca, Eli Lilly, Novartis, Sanofi, Consultant of: Amgen, AstraZeneca, Asahi Kasei, Biogen, BristolMyersSquibb, Capella, Eli Lilly, EMD Serono, Genentech, Glaxosmithkline, Janssen, Neovacs, Sanofi, Servier, UCB, Wolf, Grant/research support from: Janssen, AstraZeneca, BristolMyersSquibb, Eli Lilly, EMD Serono, GlaxoSmith-Kline, Yoshiya Tanaka Speakers bureau: Gilead, Abbvie, Behringer-Ingelheim, Eli Lilly, Mitsubishi-Tanabe, Chugai, Amgen, YL Biologics, Eisai, Astellas, Bristol-Myers, Astra-Zeneca, Consultant of: Eli Lilly, Daiichi-Sankyo, Taisho, Ayumi, Sanofi, GSK, Abbvie, Grant/research support from: Asahi-Kasei, Abbvie, Chugai, Mitsubishi-Tanabe, Eisai, Takeda, Corrona, Daiichi-Sankyo, Kowa, Behringer-Ingelheim, Richard Furie Consultant of: Eli Lilly, Edward Vital Consultant of: Eli Lilly (consultant and honoraria), Ronald van Vollenhoven Consultant of: Abbvie, Biotest, BMS, Celgene, Crescendo, Eli Lilly and Company, GSK, Janssen, Merck, Novartis, Pfizer, Roche, UCB, Vertex, Grant/research support from: Abbvie, Amgen, BMS, GSK, Pfizer, Roche, UCB, Kenneth Kalunian Consultant of: Eli Lilly, Marta Mosca Consultant of: Eli Lilly, GSK, Astra Zeneca, Thomas Dörner Speakers bureau: AbbVie, Eli Lilly, BMS, Novartis, BMS/Celgene, Janssen, Consultant of: AbbVie, Eli Lilly, BMS, Novartis, BMS/Celgene, Janssen, Daniel J. Wallace Consultant of: Amgen, Eli Lilly and Company, EMD Merck Serono, and Pfizer, Maria Silk Shareholder of: Eli Lilly, Employee of: Eli Lilly, christina dickson Shareholder of: Eli Lilly, Employee of: Eli Lilly, Inmaculada De La Torre Shareholder of: Eli Lilly, Employee of: Eli Lilly, Gabriella Meszaros Shareholder of: Eli Lilly, Employee of: Eli Lilly, Bochao Jia Shareholder of: Eli Lilly, Employee of: Eli Lilly, Brenda Crowe Shareholder of: Eli Lilly, Employee of: Eli Lilly, Michelle A Petri Consultant of: Eli Lilly

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POS0191

ANTIMALARIAL DRUGS AND ELECTROCARDIOGRAPHIC ALTERATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background: During the first months of the Sars-CoV-2 pandemic, antimalarial drugs were the central axis of the treatment of patients with acute respiratory infection. After that, several studies reported a risk of prolongation of corrected QT interval (QTc) at the electrocardiogram (ECG).
Historically, these drugs, have been the common denominator in the treatment of patients with Systemic Lupus Erythematosus (SLE).

Objectives: To analyze the possible relationship between the use of antimalarial drugs ant the electrocardiographic alterations in patients diagnosed with SLE.

Methods: Cross-sectional study in patients diagnosed with SLE (SLICC 2012). In all of them, we performed a 12-lead ECG at rest. We measured the QT interval: manually and automatically, ant its correction was made according to the Hodge formule (QTc).

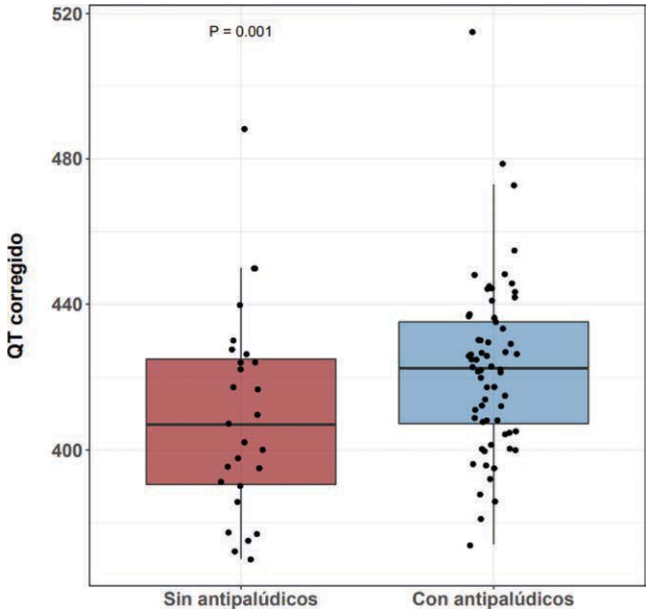
Results: 91 patients diagnosed with SLE were included in the study. Of the total of patients included in the study, 64 were in current treatment with an antimalarial drug, with a mean of 9.09 (5.73) years of treatment, and a mean cumulative dosage of 813.16 (436.12) gr.
Of the patients on current treatment with antimalarial drugs, 4.69% had a prolonged QTc, compared to 3.7% of the patients without current treatment with these drugs.

Table 1.

	NO antimalarial n= 27	YES antimalarial n= 64
Heart disease	7 (25,93%)	5 (7,81%)
Cumulative dosage HCQ (gr)	316,41 (457,28)	813,16 (436,12)
ECG disorders	5 (18,52%)	12 (18,75%)
Structural disorders	1 (3,7%)	6 (9,38%)
Electrical conduction disorders	2 (7,41%)	6 (9,38%)

We analyzed the possible relationship between the QTc interval, the current treatment with antimalarial drugs, and the cumulated dosage of this medication. We corrected the lineal regression models by the years of disease evolution, the presence or absence of known heart disease, the women gender, and other treatments such as antiarrhythmics or beta-blockers.
We found a statistically significant association between taking antimalarial drugs and the elongated QTc interval (p= 0,001). Nevertheless, in the multivariate analysis, we did not found a significant relationship between the ECG alterations and the treatment with antimalarial drugs.

Figure 1.



Conclusion: In our study, we did not observe a direct relationship between the intake of antimalarial drugs and the alteration of the corrected QT interval.

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N/A

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POS0192 IMPACT OF CORTICOSTEROID DISCONTINUATION ON SYMPTOM CONTROL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Corticosteroid (CS) treatment effectively reduces swelling and pain caused by inflammation in patients with systemic lupus erythematosus (SLE). However, prolonged CS treatment is associated with adverse events including weight gain, infections, bone loss, and premature atherosclerosis. CS treatment should be minimised to ≤7.5 mg/day prednisone or equivalents for chronic use and withdrawn when possible. Available data on the impact of CS discontinuation on patients with SLE are limited.
Objectives: To understand CS treatment patterns and impact of CS discontinuation on flares using a real-world cohort of patients with SLE from the United States.
Methods: This retrospective cohort study used the IBM MarketScan Commercial/Medicare supplemental claims database. Patients with SLE receiving CS who subsequently discontinued treatment during 2015 through 2019 were included. The index date was the completion date of the last CS prescription prior to discontinuation. The duration of CS exposure, daily oral CS dose, and CS medication types prescribed, converted into a prednisone-equivalent dose (PEQ), were evaluated during a 12-month pre-index (baseline) period. Outcomes were evaluated during the follow-up period, which started on the date of CS discontinuation and continued until health plan disenrollment or last day of data. Outcomes included flares, CS treatment restarts, and CS-free period prior to resuming therapy. A published algorithm, which draws on SLE-related healthcare resources and medication use, was used to identify and classify flares as mild, moderate, or severe.[1] Multivariable Cox regression models evaluated the association between oral CS dose and occurrence of flare.
Results: Overall, 17,759 patients were included in the study (Table 1). The most frequently prescribed oral CS treatments were prednisone (62.7%) and methylprednisolone (23.8%). The mean (SD) duration of CS use prior to discontinuation was 104 (130) days. Most patients (86.6%) received ≥6 mg/day oral daily CS PEQ prior to discontinuation. During a mean follow-up of 27.7 months, nearly all patients (90%) had at least one flare and 73.2% resumed CS treatment following discontinuation. Three-quarters of patients (76%) had no CS treatment for a continuous period of ≥6 months after discontinuation. The mean (SD) number of flares during follow-up was 6.9 (6.4) and approximately 50% experienced a severe flare. In Cox proportional hazards models with adjustment for baseline characteristics, the high baseline cumulative oral CS dose tertile was associated with the greatest risk of flare (hazard ratio 1.2 vs. low dose, p<0.001) followed by the middle dose tertile (hazard ratio 1.1 vs. low dose, p<0.001).

Table 1. Outcomes in patients with SLE treated with CS

Measure Mean (SD) or %	Commercial Health /Medicare (N=17,759)
Prior to initial CS discontinuation	
Duration CS use in days	103.6 (129.5)
Oral CS dose tertile	26.6 (126.3)
≤5 mg/day	13.5%
6–20 mg/day	58.6%
>20 mg/day	28.0%
After initial CS discontinuation	
CS treatment restart	73.2%
No CS treatment ≥6 months	76.7%
Any flare	90.4%
Mild to moderate	72.4%
Severe	50.7%
Number flares	6.9 (6.4)

CS, corticosteroid; SD, standard deviation.

Conclusion: Flares were common in patients with SLE who discontinued CS and most patients restarted CS treatment over an average follow-up of 28 months. Patients in the highest cumulative oral CS dose tertile were most at risk of disease flares following CS withdrawal.
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POS0193 EVALUATION OF CRESS IN THE PHASE 2 RANDOMISED PLACEBO-CONTROLLED STUDY OF SEQUENTIAL BELIMUMAB/RITUXIMAB ADMINISTRATION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: EULAR Sjögren's syndrome disease activity index (ESSDAI) assesses systemic disease activity in patients (pts) with primary Sjögren's syndrome (pSS); however, weaknesses include exclusion of patient-reported symptoms, tear and salivary gland function, and a marked placebo (PBO) response. Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS) is a recently developed composite outcome measure validated using data from three Phase 3 randomised controlled trials of pts with pSS.[1] Concise CRESS (cCRESS) is used when ocular staining score and salivary gland ultrasonography are unavailable. ESSDAI was an endpoint in a Phase 2, PBO-controlled study, evaluating the safety and efficacy of belimumab (BEL) and rituximab (RTX) sequential administration (BEL/RTX), and BEL and RTX monotherapies in pts with pSS. Although the results numerically favoured BEL/RTX over PBO, this was not statistically significant.
Objectives: To evaluate the efficacy of BEL/RTX and monotherapies using cCRESS overall responses at Weeks (Wks) 24, 52, and 68, and individual item responses at Wk 24 in pts with pSS who completed the Phase 2 study.
Methods: In the Phase 2, double-blind, 68-Wk study (NCT02631538) adults were randomised (2:2:2:1) into 4 treatment arms: BEL/RTX (n=24; weekly BEL 200 mg subcutaneous [SC] to Wk 24 followed by weekly PBO SC to Wk 52 + RTX 1000 mg intravenous [IV], Wk 8 + 10), BEL monotherapy (n=24; weekly BEL 200 mg SC to Wk 52), RTX monotherapy (n=25; RTX 1000 mg IV, Wk 8 + 10), or PBO (n=13). Pts were classified *post hoc* as cCRESS responders when ≥3 of the following 5 items were met: 1) Clinical (Clin)ESSDAI score <5 (low disease state); 2) decrease of ≥1 point or ≥15% from baseline (BL) in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI); 3) increase of ≥5 mm from BL in abnormal Schirmer's test, or no change to abnormal if normal at BL; 4) unstimulated whole saliva (UWS) increase of ≥25% from BL, or any increase from BL if score was 0 at BL; 5) decrease of ≥25% in the rheumatoid factor (RF) titre from BL, or decrease of ≥10% in IgG from BL.[1]
Results: Of 86 randomised pts, 60 completed follow-up to Wk 68 (completer population) and were included in the analysis. Most pts were female (95%, n=57); mean (SD) age was 49.6 (13.0) years. BL disease characteristics are presented in the Table 1.

Table 1. Clinical, functional, and laboratory parameters at BL and cCRESS responders at Wks 24, 52, and 68 (completer population)

	PBO (n=8)	BEL/RTX (n=17)	BEL (n=19)	RTX (n=16)
Pt parameters at BL, mean (SD)				
ClinESSDAI	11.1 (3.76)	11.7 (5.47)	9.2 (3.77)	11.7 (4.76)
ESSPRI	6.4 (2.05)	6.0 (1.97)	6.5 (1.68)	5.9 (2.20)
Schirmer, mm/5 min	2.7 (3.25)	5.3 (6.44)	3.3 (3.16)	2.8 (3.15)
UWS, ml/min	0.1 (0.11)	0.1 (0.12)	0.1 (0.09)	0.1 (0.14)
RF, KU/l	60.8 (42.24)	30.9 (38.20)	37.0 (34.98)	105.0 (200.97)
IgG, g/l	20.4 (6.65)	16.7 (5.00)	18.1 (7.19)	16.5 (6.09)
cCRESS responders, n (%)				
Wk 24	4 (50.0)	9 (52.9)	7 (36.8)	5 (31.3)
Wk 52	4 (50.0)	10 (58.8)	8 (42.1)	4 (25.0)
Wk 68	1 (12.5)	6 (35.3)	7 (36.8)	3 (18.8)

At Wks 24 and 52, the proportion of cCRESS responders was numerically higher with BEL/RTX than with either BEL, RTX, or PBO, but the difference was not significant (Table 1). At Wk 68, the proportion of cCRESS responders was numerically higher with BEL/RTX than with RTX or PBO (Table 1). The 5 cCRESS items contributed relatively equally to total cCRESS response, with the highest response observed in the RF/IgG item and the lowest in the tear gland item (Schirmer's test; Figure 1).

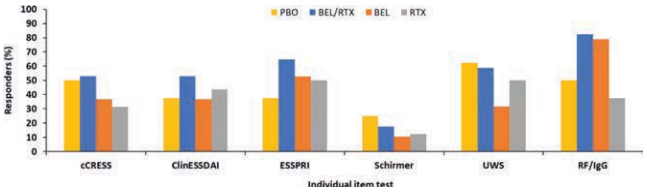

Figure 1. cCRESS and individual item responders at Wk 24 (completer population)

Conclusion: At Wks 24, 52, and 68, BEL/RTX was generally associated with a numerically higher cCRESS response rate compared with the monotherapies or PBO. The PBO response for cCRESS was notable and similar to the PBO response for ClinESSDAI. The PBO response in the tear and salivary gland items was greater than in the other treatment arms, perhaps due to the use of cCRESS instead of CRESS. Due to the small sample size, the results should be interpreted with caution.

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Outcome of COVID-19 in patients with rheumatic diseases

POS0194 MORBIDITY AND MORTALITY OF BREAKTHROUGH COVID-19 IN PATIENTS WITH IMMUNE MEDIATED CONDITIONS ON B CELL DEPLETING THERAPIES AND THE EFFECTS OF MONOCLONAL ANTIBODY TREATMENT

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Background: Among immunocompromised patients with immune mediated inflammatory diseases (IMIDs), those undergoing therapy with B cell depleting agents are among the most vulnerable to both severe COVID-19 disease and sub-optimal response to COVID-19 vaccines(1). Numerous studies have documented suppressed humoral, but relatively maintained cell mediated, responses to COVID-19 vaccines in these patients. However, the clinical significance of such immunity in terms of protection from infection and its sequelae are poorly understood. We have analyzed a large cohort of vaccinated IMIDs patients undergoing B cell depleting therapy for the presence of breakthrough infection and assessed their outcomes.

Objectives: To define the frequency and outcomes of COVID-19 breakthrough infection in fully or partially vaccinated IMIDs patients receiving B cell depleting therapies. To assess the characteristics and risk factors for severe outcomes and death.

Methods: All pharmacy records from within a large health care system were electronically searched for patients undergoing B cell depleting therapies with approved monoclonal antibodies in 2020. Records with ICD codes for IMIDs but not malignancies were included; patients must also have had at least one documented COVID-19 vaccine. From this cohort all patients with breakthrough COVID-19 disease from time of 1st vaccination through December 15, 2021 were identified; each record was hand-reviewed to extract clinical data including vaccine history, demographics, comorbidities, use of monoclonal antibodies, dose and timing of B cell depleting therapy, and outcomes as assessed by an 8 point NIH ordinal scale. Univariate and multivariable logistic/proportional-odds regression models were used to examine the risk factors for severe outcomes.

Results: A total of 1677 IMIDs patients were identified who received any B cell depleting monoclonal antibody and at least one COVID-19 vaccine in 2021. From this cohort 74 patients (4.4%) experienced a breakthrough COVID-19 infection. Among the breakthrough patients 34 (46%) had a rheumatic disease (RA 11, AAV 15, SLE 2), 34 (46%) had CNS inflammatory disease (MS 32, 2 other), and 6 (8%) had immune hematologic/miscellaneous diseases. Four patients had a previous history of COVID-19 infection. Overall 24 (35%) were hospitalized with 11 patients requiring critical level care (15%) and 6 deaths (8 %). All fatal cases had rheumatic diseases. Monoclonal antibodies were given as outpatient therapy to 21 patients and among these only 1 patient was hospitalized without requiring O2 and none died. In univariate analysis only number of comorbidities had a significant positive effect (p=.001) on severe outcomes (i.e. groups 1-4 vs. groups 5-8: Table 1) while monoclonal antibody therapy was associated with more favorable outcomes (p=.005 group 1-2 vs.3-8, Table 1). There were no associations between the dose, duration or timing of the B cell therapy, concomitant therapies including glucocorticoids, vaccine status (incomplete, complete, boosted) or date of vaccination with severe outcomes.

Conclusion: In IMIDs patients treated with B cell depleting therapies breakthrough infections are common with many experiencing severe outcomes. Concomitant comorbidities were associated with risk of severe disease. Monoclonal antibody therapy was used in only 28% but was associated with enhanced clinical outcomes with only 1 in 21 requiring hospitalization and zero mortality. This population of immunocompromised patients remains vulnerable to COVID-19 disease despite vaccination. More aggressive use of outpatient management with monoclonal antibody therapy and other preventive and therapeutic measures are urgently needed.

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Disclosure of Interests: cassandra calabrese Speakers bureau: Sanofi-regeneron, Consultant of: Sanofi-regeneron, Elizabeth Kirchner Consultant of: Janssen, M Elaine Husni Consultant of: Abbvie, BMS, Novartis, Lilly, Pfizer, UCB, Regeneron, Janssen, Brandon Moss Consultant of: Biogen advisory board, Grant/research support from: Genentech/Roche and Novartis as part of investigator-initiated studies, Anthony Fernandez Consultant of: Consulting: AbbVie, Novartis, Mallinckrodt, UCB, BMS, Boehringer Ingelheim, Alexion, Grant/research support from: Research: AbbVie, Novartis, Pfizer, Corbus, Mallinckrodt, Yuxuan Jin: None declared, Leonard Calabrese Speakers bureau: Sanofi, Janssen, AbbVie, ChemoCentryx, GSK, AstraZeneca, Consultant of: Sanofi, Janssen, AbbVie, ChemoCentryx, GSK, AstraZeneca, BMS, Genentech

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POS0195 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS HAVE AN INCREASED RISK OF MORTALITY, MECHANICAL VENTILATION, AND HOSPITALIZATION FROM COVID-19

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Background: Patients with systemic lupus erythematosus (SLE) may have an increased risk of mortality from COVID-19 due to underlying immunosuppression, comorbidities, and abnormalities in the innate immune system. Studies have shown that autoimmune diseases and some immunosuppressive agents are risk factors for hospitalization, ventilation, and mortality from COVID-19.

Objectives: To compare the outcomes of patients with or without SLE who were diagnosed with COVID-19 and to identify the factors associated with 30-day hospitalization, mechanical ventilation, and mortality. We hypothesized that patients with SLE had a higher risk of adverse outcomes.

Methods: This retrospective cohort study used the deidentified Optum COVID-19 electronic health record dataset to identify adult patients with COVID-19 diagnosis from 1/1/2020 – 12/31/2020. The SLE cohort was defined as patients who had two or more international classification of diseases (ICD) 9 or 10 diagnosis codes of 710.0 or M32.xx but not M32.0 within one year before COVID-19 diagnosis and were on either antimalarial or immunosuppressive therapy. The general cohort excluded patients with SLE. We matched SLE cases with controls at a ratio of 1:10 by age, sex, race and ethnicity, and month of COVID-19 diagnosis via a propensity score matching with exact matching for the latter three variables. Outcomes included 30-day mortality, hospitalization, and mechanical ventilation after COVID-19 diagnosis. We performed multivariable logistic regression models to estimate the odds of 30-day mortality,

hospitalization, and mechanical ventilation after adjusting for age, sex, race and ethnicity, COVID-19 diagnosis quarter, insurance, region, severe obesity, smoking status, and comorbidities.

Results: We included 687 SLE cases matched with 6,870 controls. After matching, the 30-day mortality for SLE and control was 3.6% and 1.8% (p <0.001), the 30-day mechanical ventilation was 6.0% and 2.5% (p <0.001), and 30-day hospitalization was 31.0% and 17.7% (p <0.001). After multivariable adjustment (Table 1) for age, sex, race, COVID-19 diagnosis quarter, insurance, region, severe obesity, and smoking status, patients with SLE had higher odds of death (Odds Ratio (OR)=2.09; 95% CI 1.31-3.32), mechanical ventilation (OR=2.43; 95% CI 1.67-3.54) and hospitalization (OR=2.06; 95% CI 1.71-2.49). After additionally adjusting for comorbidities, the OR decreased to 1.39 (95%CI 0.79-2.44), 1.81 (95%CI 1.16-2.82), and 1.32 (95%CI 1.05-1.65) for mortality, mechanical ventilation, and hospitalization respectively. Older age, male sex, Hispanic ethnicity or Black race, severe obesity, and smoking had increased risk of adverse outcomes.

Table 1. Multivariable logistic regression model of 30-day mortality, 30-day mechanical ventilation, and 30-day hospitalization on matched cohort adjusting for demographic and comorbidity score

Variables	Model 1* Odds Ratio (95% CI)	Model 2** Odds Ratio (95% CI)
Mortality		
Control	1	1
SLE	2.09 (1.31 to 3.32)	1.39 (0.79 to 2.44)
30-day mechanical ventilation		
Control	1	1
SLE	2.43 (95% CI 1.67 to 3.54)	1.81 (1.16 to 2.82)
Hospitalization		
Control	1	1
SLE	2.06 (1.71 to 2.49)	1.32 (1.05 to 1.65)

SLE: systemic lupus erythematosus; CI: confidence interval. *Model 1 includes adjustments for age, sex, race, COVID-19 diagnosis date (by quarter), insurance, region, severe obesity, smoking status, and skilled nursing facility stay three months before COVID-19 diagnosis. **Model 2 includes adjustments from model 1 and comorbidities (excluding SLE).

Conclusion: Patients with SLE have an increased risks of mortality, mechanical ventilation, and hospitalization within 30 days of COVID-19 diagnosis. The risks decreased after adjustment for comorbidities but remained statistically significant for mechanical ventilation and hospitalization.

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All unrelated to the topic of this study.

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POS0196 NINE PERCENT OF PATIENTS PRESENT WITH MUSCULOSKELETAL SYMPTOMS AFTER A SEVERE SARS-COV2 INFECTION: A DESCRIPTIVE ANALYSIS OF THE ASSISTANCE PUBLIQUE - HÔPITAUX DE PARIS CLINICAL DATA WAREHOUSE.

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Background: the main and most severe manifestation of the SARS-CoV2 infection is pneumonia, but other organ-specific symptoms have been described (myocarditis, encephalitis,..), and some sparse cases have reported musculoskeletal (MSK) symptoms following such an infection.

Objectives: to determine the prevalence of MSK symptoms appearing after a SARS-CoV2 infection.

Methods: this was an observational cohort based on data available at the Assistance Publique-Hôpitaux de Paris (APHP) Clinical Data Warehouse (which includes data from patients admitted in the 39 APHP hospitals). Data collected included both ICD-10 codes in discharge summaries, and 'key-words' search on electronic medical records (EMR). To be included in the analysis, patients had to have a positive RT-PCR for SARS-CoV2 performed in APHP and be admitted in any APHP department between 1st March 2020 until 31st December 2020. Patients with past history of any MSK condition were excluded. MSK conditions were considered only if coded or reported in an EMR up to 90 days after the positive RT-PCR. Demographics and disease characteristics including treatment were compared in both groups (MSK yes/no) by T-test or ChiSquare test, accordingly.

Results: Among the 55872 patients with a positive SARS-CoV2 RT-PCR performed in APHP, 17771 were admitted in APHP hospitals. Among them, 2170 had a previous history of MSK condition and were therefore excluded from this analysis. Among the remaining 15601 patients, 1370 (8.8%) presented with MSK symptoms. The most prevalent MSK symptoms were low back pain (32.9%), followed by joint pain (29.9%), radicular pain (20.2%) and joint effusion/arthritis (22.8%). Patients with MSK symptoms were older (67y vs. 64y, p<0.01), more frequently obese (29% vs. 25%, p=0.03), hypertensive (34% vs. 30%, p<0.01) and with diabetes (21% vs. 18%, p<0.01). There were no differences on gender nor on the ICU admission rate between groups (31% vs. 29%, NS); 30-days mortality was significantly lower in the MSK+ group probably due to selection bias (i.e. only patients who survived could present with MSK symptoms up to 90 days later) (7.8% vs. 16.9%, p<0.01). Treatment for SARS-CoV2 was slightly different in both groups, with higher corticosteroids (40.7% vs. 29.0%, p<0.01), antivirals (21.5% vs. 15.3%, p<0.01) and immunosuppressive drugs (8.5% vs. 4.5%, p<0.01) prescription rates in the MSK+ group.

Conclusion: MSK symptoms occurred in almost 9% of patients admitted to the hospital after a SARS-CoV2 infection, particularly in older and more comorbid patients. Further analysis evaluating the persistence of these symptoms are needed.

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POS0197 SARS-COV-2 INFECTION CAUSED THROMBOSIS IN THE LUPUS MODEL WITH ANTIPHOSPHOLIPID ANTIBODY, WHEREAS COVID-19 ASSOCIATED THROMBOSIS WAS IRRELEVANT IN PATIENTS WITH POSITIVE ANTIPHOSPHOLIPID ANTIBODY

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Background: Thrombosis is a unique complication in coronavirus disease 2019 (COVID-19). We have reported that elevated ferritin and D-dimer on admission were the risk factors of thromboses by analyzing the patients sequentially admitted to our hospital due to COVID-19 (1). However, we have not analyzed thrombotic complications in the view of the antiphospholipid antibodies (aPLs), which are frequently detected in the COVID-19 patients.

Objectives: To elucidate the thrombogenic effects of aPLs in COVID-19, we analyzed the development of thrombosis in three lupus models after SARS-CoV-2 infection. Additionally, we evaluated the association of thrombotic events and the serum profile of aPLs in Japanese patients with COVID-19.

Methods: Three animal models of lupus (MRL-*lpr*/*lpr*, NZBxNZW F1 and NZW×BXSB F1) were evaluated in this study. NZW×BXSB F1 was also considered as a model of antiphospholipid syndrome (APS) since aPLs were detected with a high titer (2). Experimental SARS-CoV-2 infection was induced using mouse-passaged virus strain (3). The incidence of thromboses in the lungs and kidneys were identified by evaluating H&E staining and PTAH staining of paraffin-embedded sections. We have experienced 44 thrombotic events in 34 out of 594 patients admitted to our institute. As a non-thrombotic COVID-19, 68 patients were selected to make a 1 to 2 matched-pair based on the propensity score. In total 102 patients, seven types of aPLs (anti-cardiolipin (CL) IgG/IgM, anti-β2GP1 IgG/IgA/IgM, and anti-phosphatidyl serine/prothrombin complex (PS/PT) IgG/IgM) were measured using specific ELISA kits. The patients' clinical characteristics and serological profile of aPLs were further evaluated.

Results: We identified the development of thromboses in the lungs or kidneys in 6 out of 12 (50%) NZW×BXSB F1 mice after the SARS-CoV-2 infection, whereas no thrombosis was observed in non-infected mice. Further, there was no thrombosis in the other lupus models (0%) after the infection. These findings might suggest the pathogenic role of aPLs under the SARS-CoV-2 infection.

Among our COVID-19 patients, 39 out of 102 (38%) were tested positive for one or more aPLs. The positive ratios of any aPLs were statistically indifferent between the patients with or without thrombosis; anti-CL IgG (8.8% vs 5.9%)/IgM (0% vs 5.9%), anti-β2GP1 IgG (21% vs 12%)/IgA (8.8% vs 15%)/IgM (0% vs 1.5%), and anti-PS/PT IgG (0% vs 2.9%)/IgM (12% vs 13%), respectively. In addition, their titers were relatively lower than those observed in APS patients. The patients' characteristics and the prognosis of COVID-19 were comparable

regardless of the detection of any aPLs. These findings suggested that COVID-19 associated aPLs were irrelevant to thrombotic complications.

Conclusion: Thromboses were induced after the infection of SARS-CoV-2 only in the APS model. However, aPLs detected in COVID-19 patients have little impact on the development of thrombosis. SARS-CoV-2 infection might have a high risk of thrombosis, especially in APS patients, as shown in the case report (4). The discrepancy of its thrombogenic effects of aPLs might be explained by the low titer of the antibody or the diversity of antibody epitope. Further analyses are required to clarify the mechanisms of aPLs production and the development of thrombosis in COVID-19.

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POS0198 COVID-19 OUTCOMES IN PATIENTS WITH DERMATOMYOSITIS: A REGISTRY-BASED COHORT ANALYSIS

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Background: Dermatomyositis (DM) patients have fewer risks of COVID-19 infection compared to the general population, however, certain subgroups with DM have worse outcomes. Men. African Americans, those with interstitial lung disease, exhibited higher risks of severe COVID-19. DMARD and glucocorticoid use was associated with frequent hospitalisations and severe sepsis.

Objectives: Rheumatic diseases (RDs) like DM, are previously known to be vulnerable towards various types of infections due to its aggressive activity mandating high dose immunosuppressive therapy. The severity of COVID-19 in RDs is limited in literature due to the heterogeneous nature of the condition. Therefore, specific details on mortality is essential to navigate any precautions required in the treatment.

Methods: Retrospective data of individuals with DM and COVID-19 and the general population with COVID-19 between January 2020 to August 2020 was retrieved from the TriNetX database. A one-to-one matched COVID-19 positive control was selected using propensity score (PS) matching. We assessed COVID-19 outcomes such as mortality, hospitalisation, ICU admission, severe COVID-19, mechanical ventilation (MV), acute kidney injury (AKI), venous thromboembolism (VTE), ischemic stroke, acute respiratory distress syndrome (ARDS), renal replacement therapy (RRT) and sepsis. Subgroup analyses included gender, race, ILD, cancer patients, disease-modifying rheumatic drugs (DMARDs) use, and glucocorticoids (GC) use (Figure 1).

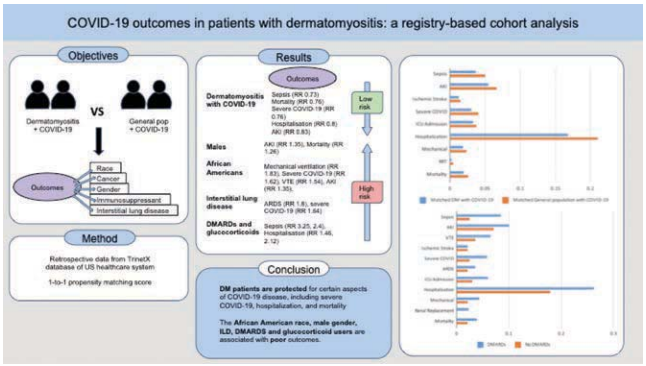

Figure 1. Overview of study

Results: We identified 5,574 DM patients with COVID-19, and 5,574 general population with COVID-19 (controls). DM with COVID-19 had a lower risk of mortality in comparison to controls [RR 0.76], hospitalisation [RR 0.8], severe COVID-19 [RR 0.76], AKI [RR 0.83], and sepsis [RR 0.73]. Males and African Americans were more likely to develop AKI [RR 1.35, 1.65], while African Americans had higher odds for severe COVID-19 [RR 1.62] and VTE [RR 1.54]. DM with ILD group also experienced higher odds for severe COVID-19 infection [RR 1.64], and VTE [RR 2.06] (Figure 1).

DM patients receiving DMARDs and glucocorticoids had higher odds for hospitalisation [RR 1.46, 2.12], and sepsis [RR 3.25] Subgroup analysis of neoplasms amongst DM patients with COVID-19 was inadequate for meaningful comparison (Figure 1).

Conclusion: DM patients are protected for certain aspects of COVID-19 disease, including severe COVID-19, hospitalization, and mortality. The African American race, male gender, ILD, DMARDS and glucocorticoid users, are associated with poor outcomes.

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POS0199 DETECTION OF SARS COV-2 ANTIBODIES FOLLOWING VACCINATION IN PATIENTS WITH RHEUMATIC MUSCULOSKELETAL DISEASE (DECODIR) – AN INTERIM REPORT FROM A DANISH PROSPECTIVE COHORT STUDY

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Trust, Thrombosis and Haemostasis, London, United Kingdom; [4]University Hospital of Copenhagen Rigshospitalet, Glostrup, DANBIO, The Danish Rheumatologic Biobank and Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre of Head and Orthopedics, Copenhagen, Denmark; [5]Faculty of Health and Medical Sciences, University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark

Background: During the COVID-19 pandemic, it remains a major concern whether patients with rheumatic musculoskeletal disease treated with conventional (cs) or biologic (b) disease modifying drugs (DMARDs) exhibit an adequate immune response to the currently available SARS-CoV2 vaccines. There remains an urgent need for more data on SARS-CoV-2 vaccine efficacy to inform healthcare providers on the efficiency of the applied vaccination, potential need of and period for booster and/ or re-vaccination.

Objectives: To assess and compare the efficacy of the SARS-CoV2 vaccines BNT162b2 vaccine (Pfizer/BioNTech) and mRNA-1273 vaccine (Moderna). (*The vaccines were administered as part of the Danish vaccine roll out and offered each with two doses and approximately four weeks apart*).

Patients' SARS-CoV2 IgG serum level was used as proxy to determine vaccination response.

Methods: We established the 'Detection of SARS-CoV2 antibodies in Danish Inflammatory Rheumatic Outpatients' study (DECODIR) as a longitudinal prospective cohort study. Patients with rheumatoid arthritis (RA), spondyloarthropathies (SpA) or psoriatic arthritis (PsA) receiving their outpatient treatment and monitored in the Danish DANBIO registry at the Danish Hospital for Rheumatic Diseases (DG), Sonderborg were included (April - June 2021).

Bloods, patient reported outcome measurements (PROMS), clinical data and treatment information (cs/bDMARD) were collected at baseline (prior to vaccination) and after six weeks and six months. SARS-CoV2 IgG levels in serum were assessed by ELISA (ThermoFischer), and manufacturer's cut-off (>=10 EliA U/mL) selected as definition of sufficient IgG response.

Associations between antibody response, age, gender, disease (RA/PsA/SpA), treatment with no or cs/bDMARDs and disease activity were tested using proportional odds regression and bootstrapped tests of medians. Results were reported using mean, median (IqR) and bootstrapped 95% confidence interval (CI) of the median.

Results: A total of 243 patients were included at baseline and after six weeks; at six months' follow-up data were available for 233 patients.

After six weeks, vaccination was followed by a significant increase in IgG levels (median of <0.7 EliA U/mL at baseline *versus* 36.5 EliA U/mL). Patients treated with a combination of both cDMARD and bDMARD had significantly lower IgG levels compared to patients without any DMARD treatment (8,2 EliA U/mL vs 19.5 EliA U/mL (p<0.001)). Patients treated with oral prednisolone (any dose) also showed significantly lower median IgG levels compared to patients without DMARD treatment (3,8 EliA U/mL vs 19.5 EliA U/mL (p<0.01)).

The actual measurements six months after baseline demonstrated a significant decrease of IgG levels for the whole study population (median of 16 EliA U/mL at six month vs 36.5 EliA U/mL at six weeks, p < 0.001) (Figure 1).

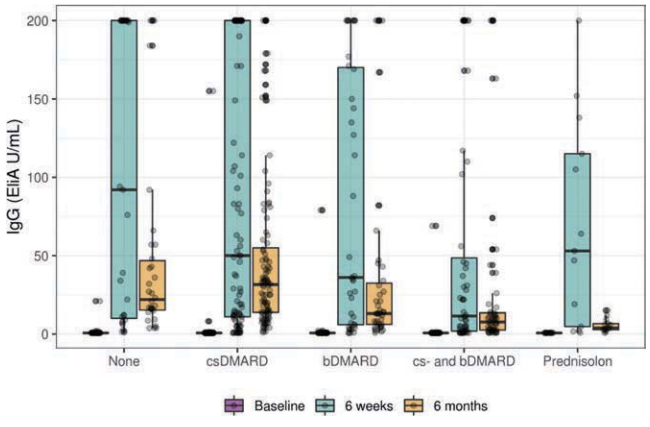

Figure 1. IgG-level stratified by treatment

Similar to week 6, lowest response rates were found in patients treated with prednisolone or combination of csDMARD and bDMARD. After 6 months, the proportional odds model revealed significantly lower median IgG antibody level in patients who received Pfizer compared to Moderna (median 15 EliA U/mL (95%CI: 13-18) vs 44.5 EliA U/mL (95%CI: 36-83) (p<0.001).

Conclusion: IgG levels decreased markedly six months after the initial double dose regimen. Patients treated with a combination of cs/bDMARD or oral prednisolone are at higher risk of inadequate vaccine response as measured by IgG level.

Our results support the decision for the need of a third booster vaccine in patients with inflammatory rheumatic diseases, especially in the case of cs/bDMARD combination treatment and prednisolone. The data may indicate a need for further revaccination in these patients.

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POS0200

POST-MRNA VACCINE FLARES IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES: INTERIM RESULTS FROM THE CORONAVIRUS NATIONAL VACCINE REGISTRY FOR IMMUNE DISEASES SINGAPORE (CONVIN-SING)

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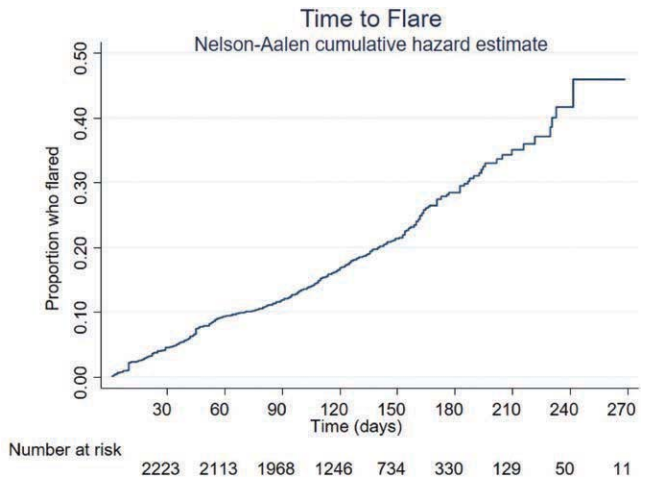

Figure 1. Nelson-Aalen curve of flares over time

Hospital, Rheumatology, Singapore, Singapore; [11]Khoo Teck Puat Hospital, Rheumatology, Singapore, Singapore

Background: Published data suggest no increased rate of flare of autoimmune inflammatory rheumatic diseases (AIIRD) after COVID-19 mRNA vaccination; however, the studies are limited by small sample size, short follow up or at risk of selection bias (voluntary physician reports or patient surveys).
Objectives: To study flares of AIIRD within three months of the first dose of an anti-SARS-COV2 mRNA vaccine.
Methods: A retrospective cohort study of consecutive AIIRD patients ≥ 12 years old, across six public hospitals in Singapore who received at least one dose of an mRNA (Pfizer/BioNTech or Moderna) vaccine. Data were censored at the first post-vaccine clinic visit when the patient had flared or if ≥ three months had elapsed since the first dose of the vaccine, whichever came first. Predictors of flare were determined by Cox proportional hazards analysis and time to flare was examined using a Nelson Aalen cumulative hazard estimate (Figure 1).
Results: 2339 patients (74% Chinese, 72% female) of median (IQR) age 64 (53, 71) years were included in the interim analysis (Table 1). 2112 (90%) had the Pfizer/BioNTech vaccine and 195 (8%) had Moderna, with a median (IQR) interval of 21 (21, 23) days between the two doses. The most common AIIRD diagnoses were Rheumatoid arthritis (1063, 45%), Psoriatic arthritis (296, 12.6%) and Systemic lupus erythematosus (SLE) (288, 12.3%). 186 (8%) were treated with biologics/ targeted disease modifying agents. 2125 (91%) patients were in low disease activity or remission. Treatment was interrupted for vaccination in only 18 (0.8%) patients. Seven (0.3%) patients had previous COVID-19 infection.

Table 1. Patient characteristics

Baseline characteristics	No flares (n = 1887, %)	Flares within 0—3 months of 1st vaccine dose (n= 272, %)	Flares outside of 0 – 3 months after 1st vaccine dose (n = 180, %)
Age (median years, IQR)	64 (53, 71)	61 (50, 69)	65 (55, 71)
Race			
Chinese	1386 (73)	206 (76)	129 (72)
Malay	193 (10)	28 (10)	20 (11)
Indian	195 (10)	27 (10)	26 (14)
Gender	1367 (72)	200 (74)	117 (65)
Female			
Vaccine type			
Pfizer/BioNTech	1713 (92)	239 (90)	160 (90)
Moderna	149 (8)	28 (10)	18 (10)
Diagnosis			
Rheumatoid Arthritis	831 (44)	139 (51)	93 (52)
Systemic Lupus Erythematosus	269 (14)	20 (7)	9 (5)
Psoriatic Arthritis	225 (12)	42 (15)	29 (16)
Spondyloarthropathies	141 (7)	21 (7)	17 (9)
Sjogren's Syndrome	114 (6)	15 (6)	8 (4)
Systemic sclerosis	94 (5)	4 (1)	6 (3)
Baseline Physician Disease Activity			
Remission	1007 (53)	99 (36)	63 (35)
Low Disease Activity	731 (39)	128 (47)	97 (54)
Moderate Disease Activity	134 (7)	40 (15)	20 (11)
High Disease Activity	15 (1)	5 (2)	0

452 (19%) flares were recorded during 9798.8 patient-months [4.6/100 patient-months, median (IQR) follow up duration 4.2 (3.3, 5.3) months], of which 272 (11.6%) patients flared within the 3-month period of interest and 180 (7.7%) flared outside of the 3-month period (Table 1). Median (IQR) time-to-flare was 40.5 (18, 56.6) days. 60 (22.1%) were mild and self-limiting, 170 (62.5%) were mild-moderate and 42 (15.4%) were severe. 190 (69.8%) of those who flared required escalation of treatment and 15 (5.5%) required hospital admission. 239 (10.2%) had improved disease activity after the vaccine.
On multivariate Cox regression analysis, patients in the oldest age tertile [median (IQR) 74 (71, 79) years] were less likely to flare [HR 0.80 (95% CI 0.63, 1.00), p = 0.05] Patients with inflammatory arthritis (compared with connective tissue disease, vasculitis and others) and patients with baseline active disease were more likely to flare [HR 1.72 (95% CI 1.35, 2.20), p < 0.001 and 1.82 (95% CI 1.39, 2.39), p < 0.001 respectively]
Conclusion: There was a moderately high rate of AIIRD flares after mRNA vaccination; however, there was no clustering of flares in the immediate post-vaccine period to suggest causality. Older patients were less likely to flare, while those with inflammatory arthritis and active disease at baseline were more likely to flare.
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POS0201

COVID-19 SEVERITY AND VACCINE BREAKTHROUGH INFECTIONS IN IDIOPATHIC INFLAMMATORY MYOPATHIES, OTHER SYSTEMIC AUTOIMMUNE AND INFLAMMATORY DISEASES, AND HEALTHY INDIVIDUALS: RESULTS FROM THE COVID-19 VACCINATION IN AUTOIMMUNE DISEASES (COVAD) STUDY.

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Background: Significant gaps are present in the evidence of the spectrum and severity of COVID-19 infection in idiopathic inflammatory myopathies (IIM). IIM patients typically require immunosuppressive therapy, may have multiple disease sequelae, and frequent comorbidities, and thus may be more susceptible to severe COVID-19 infection and complications (1). The possibility of attenuated immunogenicity and reduced efficacy of COVID-19 vaccines due to concomitant immunosuppressive medication is a major concern in these patients, and there is little data available on COVID-19 vaccine breakthrough infections (BI) in IIM (2).

Objectives: This study aimed to compare disease spectrum and severity and COVID-19 BI in patients with IIM, other systemic autoimmune and inflammatory diseases (SAIDs) and healthy controls (HCs).

Methods: We developed an extensive self-reporting electronic-survey (COVAD survey) featuring 36 questions to collect respondent demographics, SAID details, COVID-19 infection history, COVID-19 vaccination details, 7-day post vaccination adverse events and patient reported outcome measures using the PROMIS tool. After pilot testing, validation, translation into 18 languages on the online platform surveymonkey.com, and vetting by international experts, the COVAD survey was circulated in early 2021 by a multicenter study group of >110 collaborators in 94 countries. BI was defined as COVID-19 infection occurring more than 2 weeks after receiving 1st or 2nd dose of a COVID-19 vaccine. We analyzed data from the baseline survey for descriptive and intergroup comparative statistics based on data distribution and variable type.

Results: 10900 respondents [mean age 42 (30-55) years, 74% females and 45% Caucasians] were analyzed. 1,227 (11.2%) had IIM, 4,640 (42.6%) had other SAIDs, and 5,033 (46.2%) were HC. All respondents included in the final analysis had received a single dose of the vaccine and 69% had received 2 primary doses. Pfizer (39.8%) was the most common vaccine received, followed by Oxford/AstraZeneca (13.4%), and Covishield (10.9%). IIM patients were older, had a higher Caucasian representation and higher Pfizer uptake than other SAIDs, and HC. A higher proportion of IIM patients received immunosuppressants than other SAIDs.

IIMs were at a lower risk of symptomatic pre-vaccination COVID-19 infection compared to SAIDs [multivariate OR 0.6 (0.4-0.8)] and HCs [multivariate OR 0.39 (0.28-0.54)], yet at a higher risk of hospitalization due to COVID-19 compared to SAIDs [univariate OR 2.3 (1.2-3.5)] and HCs [multivariate OR 2.5 (1.1-5.8)]. BIs were very uncommon in IIM patients, with only 17 (1.4%) reporting BI. IIM patients were at a higher risk of contracting COVID-19 prior to vaccination than ≤2 weeks of vaccination [univariate OR 8 (4.1-15)] or BI [univariate OR 4.6 (2.7-8.0)]. BIs were equally severe compared to when they occurred prior to vaccination in IIMs, and were comparable between IIM, SAIDs, and HC (Figure 1), though BI disease duration was shorter in IIMs than SAIDs (7 vs 11 days, p 0.027). 13/17 IIM patients with BI were on immunosuppressants.

Conclusion: IIM patients experienced COVID-19 infection less frequently prior to vaccination but were at a higher risk of hospitalization and requirement for oxygen therapy compared with patients with HC. Breakthrough COVID-19 infections were rare (1.4%) in vaccinated IIM patients, and were similar to HC and SAIDs, except for shorter disease duration in IIM.

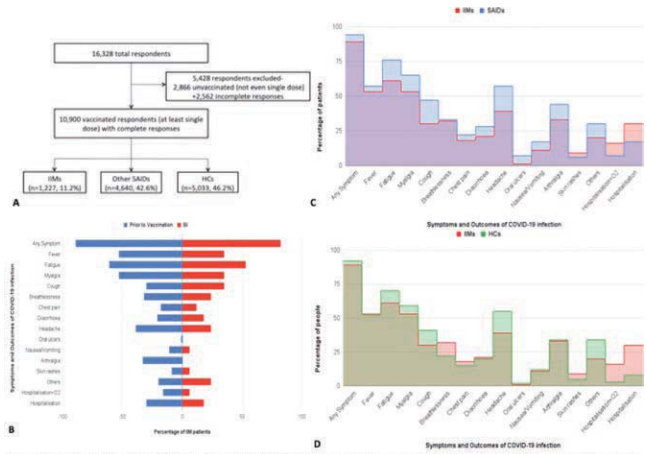

Figure 1. A. Flow diagram of study participants. B. Symptomology of COVID-19 infection in IIM prior to vaccination compared to BI. C. Symptomology of COVID-19 infection prior to vaccination in IIMs compared to other SAIDs. D. Symptomology prior to vaccination in IIMs compared to other HCs. IIMs: Idiopathic Inflammatory myopathies, SAIDs: systemic autoimmune inflammatory diseases, HCs: Healthy controls, BI: vaccine breakthrough COVID-19 infection

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Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos, Glenmark, GSK, Horizon (Curzion), Inventiva, iQvia, Kymera, Lupin, Medac, Medscape, Mitsubishi Tanabe, Novartis, Roche, Roivant, Sanofi, Serodapharm, Topadur and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Consultant of: OD has/had consultancy relationship with and/or has received research funding from or has served as a speaker for the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three years: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, Baecon, Blade, Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos, Glenmark, GSK, Horizon (Curzion), Inventiva, iQvia, Kymera, Lupin, Medac, Medscape, Mitsubishi Tanabe, Novartis, Roche, Roivant, Sanofi, Serodapharm, Topadur and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Grant/research support from: OD has/had consultancy relationship with and/or has received research funding from or has served as a speaker for the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three years: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, Baecon, Blade, Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos, Glenmark, GSK, Horizon (Curzion), Inventiva, iQvia, Kymera, Lupin, Medac, Medscape, Mitsubishi Tanabe, Novartis, Roche, Roivant, Sanofi, Serodapharm, Topadur and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Hector Chinoy Speakers bureau: HC has been a speaker for UCB, Biogen., Consultant of: HC has received consulting fees from Novartis, Eli Lilly, Orphazyme, Astra Zeneca, Grant/research support from: HC has received grant support from Eli Lilly and UCB, Vikas Agarwal: None declared, Rohit Aggarwal Consultant of: RA has/had a consultancy relationship with and/or has received research funding from the following companies-Bristol Myers-Squibb, Pfizer, Genentech, Octapharma, CSL Behring, Mallinckrodt, AstraZeneca, Corbus, Kezar, and Abbvie, Janssen, Alexion, Argenx, Q32, EMD-Serono, Boehringer Ingelheim, Roivant., Grant/research support from: RA has/had a consultancy relationship with and/or has received research funding from the following companies-Bristol Myers-Squibb, Pfizer, Genentech, Octapharma, CSL Behring, Mallinckrodt, AstraZeneca, Corbus, Kezar, and Abbvie, Janssen, Alexion, Argenx, Q32, EMD-Serono, Boehringer Ingelheim, Roivant.

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POS0202

CONTROL OF RHEUMATIC DISEASE AND COVID-19: RESULTS FROM THE INTERNATIONAL COVID-19 EUROPEAN PATIENT REGISTRY

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Background: A major concern across rheumatology in recent years is how contracting COVID-19 may impact the control of rheumatic diseases.
Objectives: To quantify any difference in rheumatic disease control between those who did and did not contract COVID-19 between March and December 2020 and whether rheumatic disease control changed after COVID-19 was contracted.
Methods: Adults with rheumatic diseases recruited to the COVID-19 European Patient Registry, a patient-led, online, self-referred prospective cohort recruiting participants from around the globe, were included if enrolled between March and December 2020. Rheumatic disease control was self-reported weekly on a scale of 0 (very poor) to 10 (very well). Dates of contracting COVID-19 were self-reported.
Differences in rheumatic disease control trends between those who did and did not contract COVID-19 over the study period were tested via multilevel linear regression. Within those who contracted COVID-19, differences in rheumatic disease control trends were tested via segmented multilevel, multivariable linear regression, adjusting for month of COVID-19 contraction and with the interruption point set at the point of COVID-19 contraction.
Results: Of 3646 adults with rheumatic diseases, the majority were female (89%), most commonly from the UK (82%) and the most common rheumatic disease diagnosis was RA (63%). Between March and December 2020, 3% of the cohort contracted COVID-19 (n=103).
Over the study period, rheumatic disease control for adults who did not contract COVID-19 decreased weekly by 0.01 points (95% CI 0.01, 0.02, p<0.001). In those who contracted COVID-19, rheumatic disease control decreased weekly by 0.03 points (95% CI 0.2, 0.05, p<0.001), with a significant weekly difference of 0.86 points between groups (95% CI 0.28, 1.44, p=0.004) (Figure 1a).
Within those that contracted COVID-19, there were significant differences in rheumatic disease control trends before and after contracting COVID-19 (p=0.001). In the run up to contracting COVID-19, rheumatic disease control significantly decreased weekly by 0.03 points (95% CI 0.02, 0.04, p<0.001), dropped significantly by 0.53 points (95% CI 0.23, 0.83, p=0.001) at the point of COVID contraction and then stabilised with no further reductions or improvement in rheumatic disease control for the remainder of follow-up (p=0.831) (Figure 1b).
Conclusion: People who contracted COVID-19 had initial decreases in rheumatic disease control before contracting the virus, after which their disease control stabilised at a lower level. Those with disease flares should consider increased screening for COVID-19 and COVID-19 mitigation measures. The stabilising lower disease control post-COVID is concerning and should prompt further work into restoring disease control pre-COVID-19 levels.
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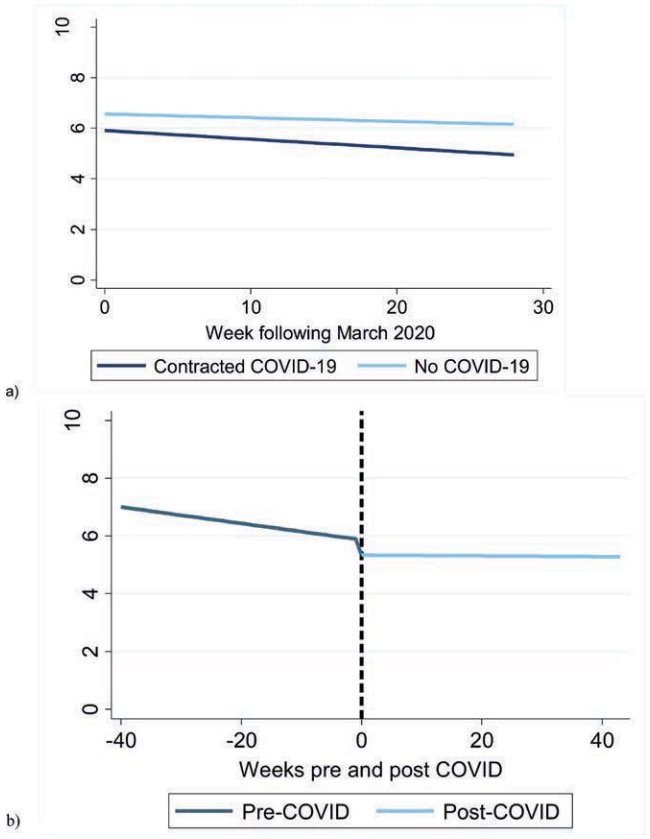

Figure 1. Trends in rheumatic disease control in those who did and did not contract COVID-19 between March and December 2020 a) overall and b) before and after contracting COVID-19

Table 1. General features patients with R-IMID and COVID-19

General features	Overall patients (n=274)	Critical COVID (n=21)	General features (continuation)	Patients (n=274)	Critical COVID (n=21)
Age, years	59 ±18	76.32 ± 13.4	**Analytical values, mean ± SD**		
Female, n (%)	185 (67)	11 (52.4)	-CRP (mg/dl)	4.7 ± 5.25	11.7 ± 8.6
CV risk factors, n (%)			-Creatinine (mg/dl)	0.91 ± 0.4	1.4 ± 0.7
-Current smoker	27 (10)	2 (9.5)	-Platelets (x103/ul)	179 ± 78	163 ± 72
-Obesity	49 (18)	5 (23.8)	-Hemoglobina (g/l)	13.0 ± 1.8	12.5 ± 2.1
-Hypertension	119 (43)	18 (85.7)	-Neutrophils (x103/ul)	4.5 ± 2.5	4.9 ± 3.2
-Diabetes Mellitus	36 (13)	5 (23.8)	-Lymphocytes (x103/ul)	1.1 ± 1	0.7 ± 0.5
-Dyslipidemia	119 (43)	15 (71.4)	-Ferritin (ug/L)	426 ± 417	664 ± 469
Comorbidities, n (%)			-LDH (U/L)	257 ± 92	314 ± 143
-Chronic pulmonary disease	12 (4.4)	3 (14.3)	-D-Dimer (ng/ml)	999±1256	1890 ± 1893
-Established cardiovascular disease	45 (16.4)	10 (47.6)	**Underlying R-IMID, n (%)**		
-Cancer	21 (8)	6 (28.6)	-RA	79 (28.8)	9 (42.9)
-Chronic kidney disease	27 (10)	6 (28.6)	-PsA	55 (20.1)	3 (14.3)
-Chronic liver disease	11 (4)	3 (14.3)	-SpA	34 (12.4)	0
Treatments received, n (%)			-PMR	22 (8)	6 (28.6)
-Methotrexate // Hydroxychloroquine	62 (23) // 50 (18)	3 (14.3) // 2 (9.5)	-SLE	22 (8)	0
-TNFi	31 (11.3)	0	-Vasculitis	8 (2.9)	1 (4.8)
-Anti-CD20	8 (2.9)	3 (14.3)	-Sjogren's syndrome	8 (2.9)	2 (9.5)
-Other biologic DMARDs // JAKINIBs	16 (5.8) // 6 (2.2)	1 (4.8) // (4.8)	-Others	46 (16.8)	0

CRP: C-reactive protein; ILD: Interstitial lung disease; LDH: Lactate dehydrogenase; PMR: Polymyalgia rheumatica¸PsA: Psoriatic arthritis, RA: Rheumatoid arthritis; SLE: Systemic lupus erythematosus; SpA: Axial spondyloarthritis*Adjusted by age, cardiovascular risk factors and comorbidities

POS0203

PREDICTIVE SEVERITY FACTORS OF COVID-19 IN PATIENTS WITH RHEUMATIC IMMUNE MEDIATED DISEASES

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Background: COVID-19 has become a common disease in patients with rheumatic immune-mediated diseases (R-IMID). A risk stratification of the patients at COVID-19 onset is important to predict possible unfavorable results.

Objectives: To identify predictive severity factors in patients with COVID-19 with R-IMID.

Methods: Cross-sectional study in a single University Hospital. We included all consecutive patients with a R-IMID and COVID-19 up to November 6th, 2020. Confirmed infection was defined if the patient had a positive nasopharyngeal swab for SARS-CoV-2.

COVID-19 case severity was divided into mild, moderate, severe and critical according to the United States National Institute of Health (NIH) COVID-19 guidelines **(1).**

We performed a multivariable analysis and calculated de odds ratio of critical COVID in patients with R-IMID, adjusting by age, sex and comorbidities.

Results: We included 274 patients with R-IMID complicated with COVID-19. At COVID-19 onset, the main comorbidities, analytical values, underlying R-IMID and treatments received are shown in Table 1.

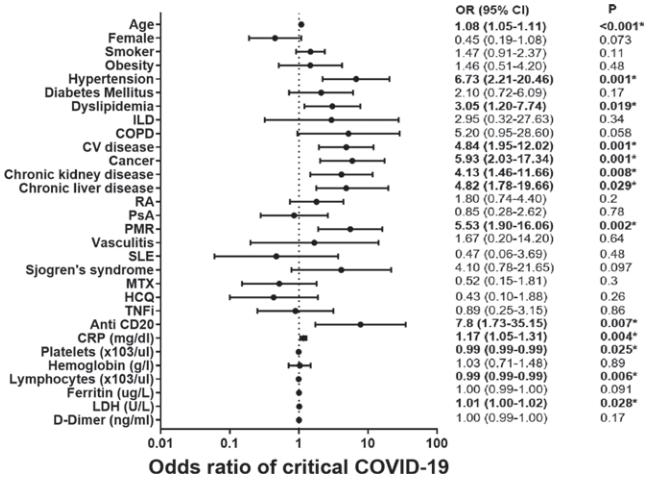

Figure 1. Predictive factors for critical COVID-19 in R-IMID (Multivariable analysis)COPD: Chronic obstructive pulmonary disease; CRP: C-reactive protein; CV: Cardiovascular; HCQ: Hydroxychloroquine; ILD: Interstitial lung disease; LDH: Lactate dehydrogenase; MTX: Methotrexate; PsA: Psoriatic arthritis; RA: Rheumatoid arthritis; SLE: Systemic lupus erythematosus; TNFi: TNF inhibitors. *p< 0.005Data in graphic are presented in a logarithmic scale.

According to COVID-19 severity, patients were mild (n=209; 76.3%), moderate (n=35; 12.8%), severe (n=9; 3.3%) and critical (n=21; 7.7%).

The predictive variables at COVID-19 onset related statistically to critical COVID were older patients, hypertension, dyslipidemia, previous cardiovascular disease, cancer, chronic kidney disease, and chronic liver disease. The only underlying R-IMID and treatment was polymyalgia rheumatica and Rituximab, respectively. Regarding analytical values were higher values of C-reactive protein, LDH, platelets and lymphopenia (Figure 1).

Conclusion: We identified various factors associated with a worse prognosis of COVID-19 in patients with R-IMID. This can help to identify which patients can present a worse course of the disease at the moment of the diagnosis.

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POS0204

RETROSPECTIVE STUDY OF THE COVID-19 COURSE IN CHILDREN WITH RHEUMATIC DISEASES: SINGLE CENTER EXPERIENCE

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Background: The study of the features of the course and mutual influence of the new coronavirus disease COVID-19 and various rheumatic diseases (RD) in children can still give us new lessons, warnings and fears.

Objectives: To update the analysis in a retrospective study the course of covid-19 in children with RD based on the results of two years of the pandemic. To analyze the impact of COVID-19 on the course of RD in children.

Methods: Retrospective analysis based on data from single center. The study included patients with RD and confirmed COVID-19 for 2 years (2020-2021).

Results: Were registered 320 cases of COVID-19 in children with RD. 158 (49%) patients were asymptomatically infected, 162 (51%) had clinical symptoms. A detailed description of the groups is presented in Table 1. Clinical symptoms were fever (67%), anosmia (47%), rhinitis (34%), cough (19%), arthralgia/myalgia (16%), dyspepsia (5%), rash (2.5%), pneumonia (3%). In the majority of cases (98%), COVID-19 proceeded in mild to moderate severity. Hospitalization due to COVID-19 was required just in 5 cases. 2 children were admitted to the intensive care unit. First, an 11-year-old girl with sJIA with the history of recurrent episodes of MAS resolved by regular administration of canakinumab. 2nd, a 12-year-old girl with Sjogren's syndrome, who received

Table 1. Clinical characteristics of children with COVID-19 and RD

	Covid-19 with symptoms (n= 162)	Covid-19 asymptomatic (n=158)	Worsening of RD after Covid-19 (n=51/320)
Sex (F/M)	96/66	109/49	33/18
Age, years (Me[25;75]) *	15 [9;17]	11 [8;14]	13 [10;16]
IgG Covid-19 positive	91	126	30
IgM Covid-19 positive	8	6	4
PCR Covid-19 positive	106	48	22
Diagnosis of RD			
JIA non-systemic	110	104	30
sJIA	11	10	9
SLE	6	5	2
JDM	9	6	3
Scleroderma	8	15	3
Sjögren's syndrome	8	6	2
Overlap syndrome	0	4	0
AIDs (CAPS, FMF, Behçet's disease)	9	7	2
FOP (Fibrodysplasia ossificans progressive)	1	1	0
Treatment of RD			
NSAID monotherapy	23	27	4
DMARDs	107	125	29
Systemic glucocorticoids	36	29	13
bDMARDs	73	72	21
Etanercept	22	33	8
Adalimumab	15	11	3
Golimumab	12	3	2
Infliximab	0	1	0
Abatacept	9	7	3
Tocilizumab	6	6	3
Sarilumab	2	2	1
Canakinumab	3	3	1
Rituximab	3	3	0
Tofacitinib	1	1	0
Baricitinib	0	2	0
Immunoglobulin human normal (in last 6 month)	7	3	2
Duration of disease, years (Me[25;75])	5 [2;8]	4 [2;8]	5 [2;7]
Duration of treatment DMARDs, years (Me[25;75])	4 [2;7]	4 [2;7]	4 [2;5]
Duration of treatment bDMARDs, years (Me[25;75])	4 [1;5,5]	3 [2;6]	2 [0,6;5]
The activity stage of RD by the start of COVID-19			
Remission	91	90	33
Low disease activity	60	49	16
High disease activity	11	19	2
Temporary withdrawal of DMARD and bDMARDs during COVID-19	58	8	18
Worsening/flare of RD	42	9	51

*- p<0,05

Rituximab and 1 month later she developed the COVID-19 with MIS-like clinical picture, pneumonia with 25%CT lessions. Both cases have a favorable outcome.

The clinical characteristics of the patients are presented in Table 1. COVID-19 didn`t affect the course of RD in the 86% of pts. However, 15% developed a flare of the RD with average of 3 months after COVID-19. In this group for 13 pts (girls mostly F/M-9/4, mean age 15 years [9;16]), COVID-19 triggered the new onset of RD (non-systemic JIA – 4, Uveitis – 1, non-bacterial osteomyelitis – 3, systemic JIA – 2, Scleroderma – 2, Sjögren's syndrome – 1. 12 from 13 these children had clinical symptoms on COVID-19. Whether this is Long-COVID syndrome or an independent RD is not known.

Conclusion: Our study suggests that the new coronavirus infection in most cases in children with RD, had mild or asymptomatic course, regardless of therapy with immunosuppressive drugs and bDMARD, except of 1 observation with the previous therapy of Rituximab. Worsening of RD after coronavirus infection developed in 15% of cases, regardless of its clinical manifestations. In 13 patients, the RD were started just after COVID-19. The explosive increasing of the incidence of a new strain of COVID-19 for a past month may change the current results and conclusions.

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RA comorbidities

POS0205

SAFETY AND TOLERABILITY OF NINTEDANIB IN PATIENTS WITH AUTOIMMUNE DISEASE-RELATED INTERSTITIAL LUNG DISEASES (ILDS) IN SUBGROUPS BY SEX AND AGE

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Background: Nintedanib slows the progression of fibrosing ILDs, with a safety profile characterised predominantly by gastrointestinal events.
Objectives: Assess the safety and tolerability of nintedanib in patients with autoimmune disease-related ILDs by sex and age.
Methods: The SENSCIS trial was conducted in patients with ILD associated with systemic sclerosis. The INBUILD trial was conducted in patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis. Patients were randomised to receive nintedanib 150 mg bid or placebo. Dose reductions to 100 mg bid and treatment interruptions were permitted to manage adverse events (AEs). Data from all patients in SENSCIS and patients with autoimmune disease-related ILDs in INBUILD were pooled. In subgroups based on sex and age (<65 and ≥65 years) at baseline, we analysed AEs, irrespective of causality, over 52 weeks.
Results: Among 746 patients; 70.1% were female; 29.1% were aged ≥65 years. Mean (SD) exposure to nintedanib or placebo was 10.8 (3.2) and 11.1 (2.9) months in females and males, and 11.0 (3.0) and 10.6 (3.5) months in

Table 1. Adverse events in patients with autoimmune disease-related ILDs in the SENSCIS and INBUILD trials in subgroups by sex and age at baseline.

	Female		Male		Age <65 years		Age ≥65 years	
	Nintedanib (n=268)	Placebo (n=255)	Nintedanib (n=102)	Placebo (n=121)	Nintedanib (n=267)	Placebo (n=262)	Nintedanib (n=103)	Placebo (n=114)
Most frequent adverse events*								
Diarrhoea	198 (73.9)	77 (30.2)	73 (71.6)	38 (31.4)	197 (73.8)	85 (32.4)	74 (71.8)	30 (26.3)
Nausea	92 (34.3)	35 (13.7)	21 (20.6)	14 (11.6)	86 (32.2)	38 (14.5)	27 (26.2)	11 (9.6)
Vomiting	73 (27.2)	22 (8.6)	12 (11.8)	14 (11.6)	61 (22.8)	27 (10.3)	24 (23.3)	9 (7.9)
Skin ulcer	42 (15.7)	37 (14.5)	12 (11.8)	13 (10.7)	42 (15.7)	45 (17.2)	12 (11.7)	5 (4.4)
Nasopharyngitis	34 (12.7)	41 (16.1)	12 (11.8)	21 (17.4)	33 (12.4)	43 (16.4)	13 (12.6)	19 (16.7)
Weight decreased	34 (12.7)	8 (3.1)	10 (9.8)	6 (5.0)	29 (10.9)	9 (3.4)	15 (14.6)	5 (4.4)
Decreased appetite	29 (10.8)	9 (3.5)	13 (12.7)	4 (3.3)	25 (9.4)	10 (3.8)	17 (16.5)	3 (2.6)
Abdominal pain	32 (11.9)	18 (7.1)	8 (7.8)	5 (4.1)	27 (10.1)	19 (7.3)	13 (12.6)	4 (3.5)
Upper respiratory tract infection	30 (11.2)	31 (12.2)	9 (8.8)	8 (6.6)	31 (11.6)	33 (12.6)	8 (7.8)	6 (5.3)
Cough	23 (8.6)	39 (15.3)	13 (12.7)	19 (15.7)	27 (10.1)	46 (17.6)	9 (8.7)	12 (10.5)
Liver-related investigations, signs and symptoms	49 (18.3)	11 (4.3)	13 (12.7)	6 (5.0)	42 (15.7)	12 (4.6)	20 (19.4)	5 (4.4)
Adverse event(s) leading to dose reduction	101 (37.7)	9 (3.5)	18 (17.6)	3 (2.5)	81 (30.3)	9 (3.4)	38 (36.9)	3 (2.6)
Adverse event(s) leading to treatment discontinuation	44 (16.4)	21 (8.2)	17 (16.7)	13 (10.7)	39 (14.6)	18 (6.9)	22 (21.4)	16 (14.0)
Serious adverse event(s)	57 (21.3)	53 (20.8)	40 (39.2)	37 (30.6)	63 (23.6)	54 (20.6)	34 (33.0)	36 (31.6)

n (%) of patients with ≥1 such adverse event over 52 weeks. Adverse events were coded based on preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA), except for liver-related investigations, signs and symptoms, which was based on a standardised MedDRA query. *Adverse events reported in >10% of patients with autoimmune disease-related ILDs in the nintedanib or placebo group.

patients aged <65 and ≥65 years, respectively. The AE profile of nintedanib was similar between males and females, but nausea, vomiting, hepatic adverse events and dose reductions were more frequent in females. The AE profile of nintedanib was similar between patients aged <65 and ≥65 years, but nausea, decreased appetite, and weight loss were more frequent in patients aged ≥65 years. AEs leading to treatment discontinuation were more frequent in patients aged ≥65 years in both treatment groups. Serious AEs were more frequent in males and in patients aged ≥65 years in both treatment groups.

Conclusion: In patients with autoimmune-disease related ILDs, the AE profile of nintedanib in subgroups by sex and age was generally consistent with the known safety profile, but certain types of AE and dose reductions were more frequent in female patients, while serious AEs were more common in male patients.

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POS0206 EVALUATION OF SALIVARY GLANDS ULTRASOUND IN THE FRENCH RHEUMATOID ARTHRITIS COHORT BCD

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Background: The prevalence of salivary glands ultrasound (SGUS) abnormalities in Sjögren's syndrom (SS) is well described[(2)]. However, the prevalence is still unknown in rheumatic inflammatory conditions such as rheumatoid arthritis (RA).

Objectives: The main objective of this study was to describe the prevalence of SGUS parenchymal structural abnormalites in patients with RA. Secondary objectives were: i) to study correlation between disease duration and the SGUS OMERACT score and ii) to study correlation between duration of sicca syndrome and the SGUS OMERACT score.

Methods: 561 patients with RA satisfying ACR/EULAR 2010 classification criterias were included in 10 french centers in the prospective cohort BCD, comparing joint ultrasonography to clinical follow-up. Cross sectionnal SGUS examination (parotid and submandibular) was performed in a substudy of this cohort. The new OMERACT-SGUS scoring system[(1)] was used and clinical, biological, immunological and radiological data were collected.

Results: 100 patients agreed to be included in this substudy of BCD cohort, and a total of 98 SGUS patients data were evaluated (lack of SGUS data for 2 patients). Most patients were women (81%), mean age 59 years, with time from RA diagnosis of 11 years on average. The mean CRP-DAS-28 at baseline was at 3.2 with a third of patients in remission at inclusion. Anti-CCP antibodies or RF was positive in 92 patients (92%). 27 patients (27%) complained of eye dryness and 20 (20%) of mouth dryness. 12 (12%) suffered from both. The levels of self-reported fatigue was higher than in the general group of RA included in the study. Two thirds of patients benefited from csDMARD, with a third treated with bDMARDS. 33 (33%) also benefited from a corticosteroid treatment. Among 98 patients, 22 (22.5%) had at least one salivary gland scored grade 1 or more, this number was reduced to 18 patients (18.4%) when considering only the parotid glands. 7 patients (7.1%) had at least one salivary gland scored grade 2 or more, with a number reduced to 4 patients (4.1%) when considering only the parotids. Only one patient (1%) had a parotid gland scored 3. In the 7 patients presenting significant abnormalities in SGUS (grade 2 or more), 5 patients had either dry eye or dry mouth symptoms (71,4%).

Conclusion: Our findings suggest that 7% of RA patients present significant SGUS abnormalities according to OMERACT scoring system, associated with clinical sicca syndrome in 71% of cases. There was no significant association between the duration of rheumatoid arthritis and the OMERACT score (Spearman coefficient for correlation -0,028, p = 0,99). There was also no significant association found between the duration of sicca symptoms and the OMERACT score (Spearman coefficient for correlation 0,025, p = 0,89). This study highlights the importance of SGUS assessment in RA sicca patients to improve monitoring and follow-up in routine clinical practice.

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POS0207 UNRAVELING THE COMPLEX INTERACTION BETWEEN DISEASE ACTIVITY AND FATIGUE IN EARLY RA: A MEDIATION ANALYSIS WITH DATA FROM THE CARERA TRIAL

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Background: Fatigue is recognized as one of the most important symptoms of rheumatoid arthritis (RA). Although inflammation is often proposed as the predominant pathophysiological mechanism, many patients with RA continue to experience fatigue despite inflammatory disease control. The relationship between RA disease activity and fatigue appears to be complex and is likely confounded by cognitive, emotional and social aspects.

Objectives: To unravel the complex interaction between disease activity and fatigue in early RA.
Methods: Data were analyzed from the 2-year treat-to-target trial Care in early RA (CareRA), which compared different remission-induction DMARD regimens, either with or without bridging glucocorticoids, in treatment-naïve patients with early RA. Fatigue was measured on a visual analog scale (VAS) at every study visit. The association between inflammatory disease activity (DAS28-CRP) and fatigue (VAS) over time was studied with a multilevel mediation analysis, including as mediators the individual components of the DAS28-CRP, pain (VAS), disability (HAQ), psychosocial aspects (Short-Form 36 [SF-36]), illness perceptions (Revised Illness Perception Questionnaire [IPQ-R]), and sleep quality (Pittsburgh Sleep Quality Index [PSQI]).
Results: A total of 356 patients were included in these analyses, with a mean (SD) fatigue (VAS) of 48/100 (24) at study initiation. Although there was a consistently positive association between DAS28-CRP and fatigue over time, this association was fully mediated by patient global assessment (PGA) and pain, and to a lesser extent by SF-36 Mental Health and the PSQI global score (Figure 1). Full mediation implies the absence of a significant direct association between DAS28-CRP and fatigue after adjusting for these mediators. In addition, no mediating effect was found for tender/swollen joint counts or CRP.

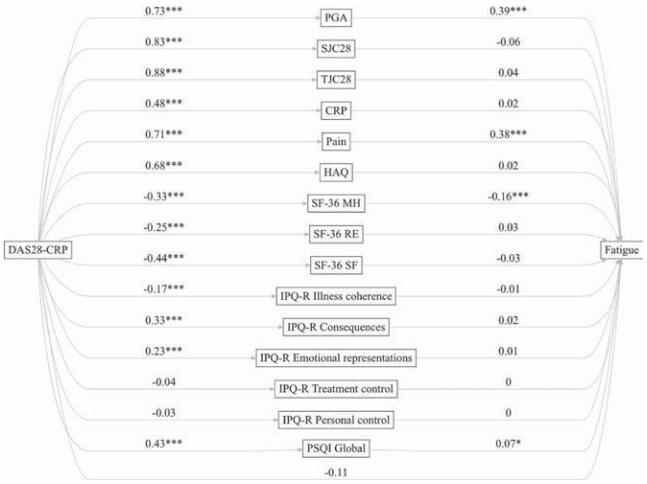

Figure 1. Mediation analysis of the association between DAS28-CRP and fatigue (VAS) over time.Reported are the standardized regression coefficients with indicators of significance (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$). *DAS28-CRP = Disease Activity Score in 28 joints with C-reactive protein, SJC28/TJC28 = swollen/tender joint count in 28 joints, HAQ = Health Assessment Questionnaire, SF-36 = Short-Form 36, MH = mental health, RE = emotional role functioning, SF = social functioning, IPQ-R = Revised Illness Perception Questionnaire, PSQI = Pittsburgh Sleep Quality Index*

Conclusion: Our mediation analysis suggests that the relationship between disease activity and fatigue in early RA is complex and fully mediated by aspects of wellbeing like pain, mental health, sleep quality, and the patient's overall assessment of disease. These results imply a mainly indirect relation between fatigue and inflammation. Clinicians should reserve specific attention for the psychosocial determinants of fatigue, particularly when no improvement is seen with DMARDs.
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POS0208

STRESS AT HOME IS COMMON AND HAS SIGNIFICANT ASSOCIATION WITH MARITAL STATUS, HIGHER DISEASE ACTIVITY, COMORBIDITIES, AND WORSE QUALITY OF LIFE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: SINGLE CENTRE RESULTS FROM THE PRIME REGISTRY COHORT

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Background: In chronic inflammatory diseases like rheumatoid arthritis (RA), psychological stress is widely recognised as an important risk factor to negatively affect the disease course. Perceived stress can potentially induce the disease exacerbation, but on the other hand, the disease itself might produce significant stress to patients thus the vicious circle is formed and maintained.
Objectives: We aimed to examine the prevalence of mental/emotional stress at home and its associations among patients with Rheumatoid arthritis. We addressed this question using real-world data from the PRIME registry.
Methods: This was a cross-sectional study conducted using data collected at the time of patient enrolment in the PRIME registry. The PRIME Registry is a large, independent, prospective, observational cohort initiated in October 2019 that comprises patients diagnosed with RA, SLE, PsA or AS by a rheumatologist, and is being actively followed up. IRB approval and informed consent was obtained. We assessed the data for RA patients. The clinical variables studied were gender, age, smoking habits, body mass index, education status, marital status, disease duration, comorbidities (using Charlson Comorbidity Index). Education status was stratified by whether participants completed secondary (high) school education. The SF-12 Physical Component Score (PCS-12) and Mental Component Score (MCS-12) was also measured. Evaluation of disease activity and severity was made as per internationally agreed definitions, such as: swollen joint counts, tender joint counts, deformed joint counts, and DAS-28. All participants were directly inquired at the interview during the time of patient enrolment about the presence or otherwise of mental/emotional stress at home, and to rate it from 1-3 (mild, moderate, severe). For better understanding and ease of statistical analysis, dichotomous variable was made with moderate-to-severe stress patients were categorised into one group and none-to-mild stress patients into second group.
Results: The data from consecutive 1016 RA patients (mean age 40.8±13 years, 78.6% female, disease duration of 65±67 months) was reviewed. Forty-nine percent of patients accepted to have moderate-severe stress at home. Female gender (p=0.003), low education status (p=0.050), being unmarried (p=0.051), and MCS, PCS, CCI (p<0.001) were associated with moderate-severe stress. However, no statistical association of age and disease duration was noted. On univariate analysis, significant association of moderate-severe stress at home was noted with deformed joint counts (p=0.003), higher DAS-28 scores (p<0.001), low education status (p=0.02) and being married (p<0.001). Weak statistical association of age (p=0.30), disease duration (p=0.12), low education status (p=0.14), female gender (p=0.24) was noted. On multiple logistic regression analysis, a significant association of moderate-severe stress at home was observed with higher DAS-28 scores (OR 2.38, CI 2.00-2.84, p<0.001), MCS-12 (OR 0.65, CI 0.61-0.69, p<0.001), comorbidities-CCI (OR 1.41, CI 1.15-1.74, p=0.001) and being unmarried (OR 0.55, CI 0.36-0.83, p=0.005). The final regression model resulted in a statistically significant improved association/prediction of worse moderate-severe stress at home (R square=71%). Following variables were included in multiple stepwise regression analysis: age, disease duration, gender, education status, marital status, comorbidities index, major trauma/stress in last one year, DAS-28, MCS-12 and PCS-12 scores.
Conclusion: Nearly half of the cohort was noted to have moderate-severe level of stress at home, and is associated with important adverse clinical outcomes. These findings demonstrate an important need for integration of rheumatologic, social workers and mental health services
Disclosure of Interests: Muhammad Haroon Speakers bureau: Novartis, Abbvie, Pfizer, Roche, Grant/research support from: Abbvie, Sadia Asif: None declared, Saadat Ullah: None declared, Farzana Hashmi: None declared, Saba Javed: None declared
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POS0209

CLINICAL AND DIAGNOSTIC SIGNIFICANCE OF INTIMA-MEDIA THICKNESS, LEVELS OF SOLUBLE CELL ADHESION MOLECULES AND CD40 LIGAND IN RHEUMATOID ARTHRITIS PATIENTS WITH LOW CARDIOVASCULAR RISK

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease leading to significant increase in cardiovascular morbidity and mortality. Development of atherosclerotic lesions of the carotid arteries in RA patients is associated with the accumulation of traditional risk factors and immunological disorders.
Objectives: To evaluate the detection rate of subclinical carotid atherosclerosis and clinical significance of immunoinflammatory markers in RA patients with low cardiovascular risk (CVR) in comparison with the control group.
Methods: The study included 275 RA patients (with low CVR and no established cardiovascular diseases) and a control group comprising 100 people without autoimmune diseases. The groups were comparable in terms of sex, age, traditional risk factors, and CVR value. CVR was calculated using the QRISK3 scale. All study participants had a low CVR (QRISK3<20%). All patients and control group members undertook carotid duplex ultrasonography. Atherosclerotic lesions of the carotid arteries are assessed by the detection of of atherosclerotic plaque (ASP) - the cause of IMT ≥ 1.2 mm. Concentration of sICAM-1, sVCAM, and sCD40L in blood serum was determined by enzyme immunoassay using reagent kits and according to Bender MedSystems protocols (USA).
Results: Carotid ASP were observed more frequently in RA patients (27%) with low CVR than in the control group (17%), p=0.03. ASP were detected more frequently in men with RA than in women with RA (50% versus 24%, p<0.01). The frequency of ASP in RA patients with low CVR did not depend on the disease's stage or activity.
In RA patients, there was a significant correlation between carotid IMT and age (R=0,48), CVR value determined by QRISK3 (R=0,36), level of total cholesterol (R=0,28), LDL cholesterol (R=0,18), systolic blood pressure (R=0,37), diastolic blood pressure (R=0,38), p<0,05 in all cases. No correlation between carotid IMT and blood concentrations of sCD40L, sVCAM, and sIACAM was found in RA patients or controls.
A higher concentration of sVCAM was detected in RA patients compared with the control group (1520 [945; 1915] ng/mL versus 790 [605; 1307] ng/mL, p=0.01); and in RA patients with carotid ASP compared with patients without carotid ASP (1680 [1460; 3350] ng/mL versus 1210 [865; 1810] ng/mL, p=0.01).
In RA patients with carotid ASP, sCD40L level was associated with carotid IMT (R=0.40, p=0.04) and cholesterol concentration (R=0.38, p=0.01). In RA patients without ASP, sCD40L level was associated with cholesterol concentration (R=0.41, p=0.02) and diastolic blood pressure level (R=0.3, p=0.04).
Conclusion: Subclinical atherosclerotic lesions of the carotid arteries were observed in a quarter of RA patients with low CVR and were detected at a significantly more frequent rate compared to the control group. The evaluation of carotid IMT is recommended for RA patients with low CVD. These results suggest that there is an association between carotid IMT and traditional CVR factors and immunoinflammatory markers in RA patients.

Disclosure of Interests: None declared
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POS0210

A PREDOMINANT NON-SPECIFIC INTERSTITIAL PNEUMONIA PATTERN AND ABERRANT TRANSCRIPTOMIC NEUTROPHIL-MEDIATED IMMUNITY CHARACTERIZE A CONTEMPORARY RA-ILD COHORT

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Background: Lung involvement is the most common extra-articular manifestation. Rheumatoid arthritis related interstitial lung disease (RA-ILD) comprises a heterogeneous group of parenchymal lung disorders classified by distinct clinical, pathologic, and radiographic features. According to the current paradigm, circulating immune complexes and aberrant neutrophil extracellular trap formation (NETosis) contribute to disease pathogenesis.
Objectives: To characterize the pattern of lung disease in "Attikon" RA-ILD cohort and develop insights about the pathophysiologic mechanisms via whole blood RNA sequencing.
Methods: Retrospective and prospective study to identify clinical, laboratory and radiologic characteristics of patients with RA and pulmonary manifestations in the "Attikon" RA-ILD cohort. Changes in pulmonary function tests (PFTs), pattern of lung involvement (chest HRCT), disease activity (DAS28-ESR) and incidence of complications and comorbidities, were prospectively analyzed during the one-year follow-up period. Peripheral blood was collected in a subset of RA-ILD (n=11) and control RA patients (n=9) for RNA isolation and RNA sequencing. The gene expression profile of RA-ILD was inferred through differential gene expression analysis, followed by pathway and enrichment analyses.
Results: 114 patients with RA-ILD were included [67% female, mean (SD) age at diagnosis 71.5 (9) years, 58% seropositive]. Non-specific interstitial pneumonia (NSIP) was the radiologic pattern most frequently observed (52%), followed by usual interstitial pneumonia (UIP) (24%). RA was diagnosed after ILD in 40% of patients. Mean (SD) FVC and DLCOsb at baseline was 80.5 (19.2) and 55.4 (19.5), respectively. Disease activity was lower in seropositive compared to seronegative both at baseline and at 1-year follow-up (p=0.025). PFTs at 12 months from baseline had been stabilized. Respiratory infections were observed in 17.6% of patients during the first year of follow-up, more common in the NSIP vs UIP group (p=0.01), possibly due to the higher doses of glucocorticoids in NSIP patients. RNA-sequencing analysis revealed a distinct gene expression profile in RA-ILD, characterized by the activation of type I interferon response, neutrophil activation and degranulation, and CCR1 chemokine interactions.
Conclusion: NSIP is the most frequent pattern of ILD in this RA-ILD cohort, carrying a higher risk for respiratory infections probably related to higher doses of glucocorticoid used. Myeloid cells' migration via CCR1 and the formation of pro-inflammatory and pro-fibrotic NETs by activated neutrophils may contribute to RA-ILD pathogenesis.

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Table 1. Patients' characteristics with RA-ILD in Attikon cohort

Patients Characteristics	N=114
Mean age	71.5±9
Female: Male	76/38
Smoking (current/ex)	23/43
Arterial hypertension	71
Diabetes mellitus	32
Dyslipidemia	52
COPD/BA	17
Thyroid disease	30
Latent TB	17
Seropositive	66
Diagnosis RA before ILD	34
Diagnosis RA after ILD	45
NSIP	59
UIP	27
Mixed NSIP-UIP	5
Organizing Pneumonia (OP)	17
Nodules	21

Disclosure of Interests: None declared
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POS0211

ASSOCIATION BETWEEN CARDIOVASCULAR OUTCOME AND RHEUMATOID ARTHRITIS: NATIONWIDE POPULATION-BASED COHORT STUDY

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Background: Many studies have shown increased risk of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA). Despite a growing burden posed by CVD in RA patients, large scale studies which examined the association between characteristic of RA patients and CVD risks, and studies which adjusted for various confounding factors are lacking.
Objectives: This study aimed to investigate the association between CVD risk and RA in large-scale, nationwide cohort of Korean population, and to examine which characteristics of RA patients are associated with increased CVD risk.
Methods: We enrolled 136,469 patients with RA who participated in national health examinations within 2 years of RA diagnosis between 2010 and 2017 and non-RA controls matched by age and sex (n= 682,345). The cohort was followed until the end of 2019. The outcome was occurrence of myocardial infarction (MI) or stroke. MI was defined as one hospitalization or two outpatient visit with ICD-10-CM codes I21 or I22. Stroke was defined as one hospitalization with ICD-10-CM codes I63 or I64 and a claim for brain imaging (CT or MRI). The Cox proportional hazard model and Kaplan Meier curve were used for the analysis.
Results: Mean follow up duration was 4.7 years. The incidence rate of CVD was higher in RA group than control (MI: 3.20 vs 2.08; stroke: 2.84 vs 2.33 per 1,000 person-years). The risk of CVD was higher in RA patients. (MI: adjusted HR 1.54, 95% CI 1.46-1.61; Stroke: adjusted HR 1.22, 95% CI 1.16-1.28). The association between RA and CVD was prominent in female (MI: adjusted HR 1.41 in male, 1.60 in female, *p* for interaction = 0.0293; Stroke: adjusted HR 1.13 in male, 1.27 in female, *p* for interaction = 0.03) and younger-age subgroups (MI: adjusted HR 2.9 in <40 years, 1.52 in 40-64 years, 1.51 in ≥65 years, *p* for interaction<0.0001; Stroke: adjusted HR 2.35 in <40 years, 1.21 in 40-64 years, 1.21 in ≥65 years, *p* for interaction = 0.0100) after adjusting for confounding variables. The association between RA and risk of MI was significant in those without DM. (adjusted HR 1.30 in DM, 1.61 in non-DM, *p* for interaction = 0.0005)
Conclusion: RA patients had increased risk of CVD events compared to age- and sex-matched control group, and this association was stronger in female and younger-age subgroups. Therefore appropriate screening for CVD would be important in all RA patients including female and younger patients.
Disclosure of Interests: None declared
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POS0212

THE REDUCTION OF TURICIBACTER IN GUT MICROBIOTA ASSOCIATED WITH SJOGREN'S SYNDROME SECONDARY TO RHEUMATOID ARTHRITIS

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Background: Secondary Sjogren's syndrome(SS) is a common extra-articular manifestation of rheumatoid arthritis (RA)[1]. RA patients combined with SS have different outcomes from those without SS[2]. However, the studies investigated the characteristics of gut microbiota in patients with RA and SS is limited.
Objectives: To investigate the characteristics of gut microbiome and the associations between flora and peripheral lymphocyte subpopulations in RA patients with or without Sjogren's syndrome.
Methods: A total of 326 samples from 145 RA patients without SS, 23 RA combined with SS patients(RA-SS) and 168 healthy controls (HCs) were recruit in this study from The Second Hospital of Shanxi Medical University (Taiyuan, Shanxi, China). The gut microbiota were investigated via 16s rRNA sequencing and the peripheral T lymphocyte subsets of these participants were assessed by flow cytometry. The Wilcoxon rank-sum test was used to compare alpha diversity indicesbetween groups. Differential abundance analysis was carried out the STAMP software. Spearman's correlation analysis was used to assess the correlations between the relative abundances of bacterial genera and clinical meatures.

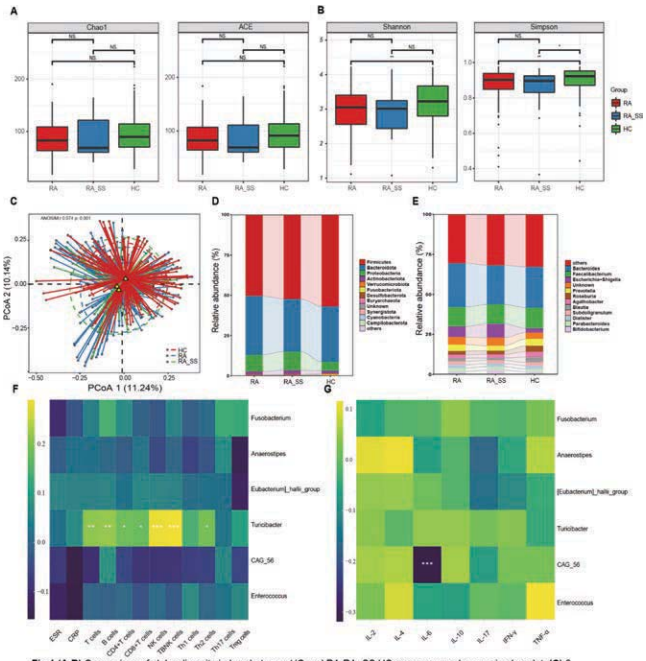

Fig 1 (A-B) Comparison of alpha-diversity indexs between HC and RA,RA_SS,HCs groups was shown using boxplot. **(C)** β diversity of the gut microbiome in RA,RA_SS patients and HCs.**(D-E)** Distribution of gut microbiota at phylum and genus level in RA,RA_SS,HCs.**(F-G)** Relationship between gut microbiota, and Lymphocyte subsets as well as cytokines. the correlation effect is indicated by a color gradient from green (positive correlation) to purple (negative correlation). *p<0.05 **p<0.01 ***p<0.001

Results: Patients with RA and RA-SS exhibited a significant reduction in the richness and diversity of gut microbiota compared with those of HCs (Figure 1 A-B, p < 0.05), whereas there was no significant difference between RA and RA-SS patients. Principal co-ordinates analyses based on bray curtis distance suggested that these there microbiota states explained a definable proportion of observed variance in microbiota composition (ANOSIM R2 = 0.074, p < 0.001; Figure 1 C). Compared with HCs, 58 species of flora were discovered to be distinctly different in RA patients without SS at the genus level of which 6 species of flora unique to RA-SS patients were presented much fewer ([Eubacterium]_hallii_group, Anaerostipes, CAG-56, Fusobacterium, Turicibacter and Enterococcus). Among these RA-SS patients' unique species of flora, it seems that Turicibacter is the key species of flora, owing to whose has a positive correlation with most of lymphocytes such as T, B, CD4+T, CD8+T and NK cells suggesting a close association with intestinal immunity.(Figure 1 F-G,P<0.05)
Conclusion: RA patients with deficiency of Turicibacter in flora had higer occurrence of Sjögren's syndrome sjogren's syndrome complication, which was correlated with peripherial lymphocyte subpopulations and cytokines.
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POS0213

EFFECT OF EARLY ETANERCEPT TREATMENT ON CIRCULATING LIPOPROTEINS DIFFERS TO TREATMENT WITH METHOTREXATE AND IS MODULATED BY CLINICAL DISEASE ACTIVITY

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Background: A reduction in serum lipids such as total cholesterol (TC) and low-density lipoprotein (LDL) has been associated with increased risk of cardiovascular events in active RA, paradoxical to the general population[1]. The effect of DMARDs and active inflammation on lipid profiles has been investigated in RA

but detailed lipid profiling has been lacking in very early disease and across the spectrum of disease activity.

Objectives: In a treatment naïve early RA trial cohort, we sought to compare circulating lipid profiles between patients treated with first line etanercept + methotrexate (ETN+MTX) versus methotrexate treat-to-target (MTX-TT) regime and between clinical remission and high disease activity.

Methods: VEDERA trial (Very early Etanercept and Methotrexate versus Methotrexate with/without Delayed Etanercept in RA) randomised 120 treatment-naïve RA patients to either first-line ETN+MTX or MTX-TT regime with escalation to ETN+MTX if not in DAS28ESR remission at week 24[2]. TC, triglycerides (TG), high density lipoprotein (HDL) and LDL were measured; apolipoproteins and atherogenic indices such as TC/HDL, atherogenic index of plasma (AIP) and apolipoprotein B/A-i ratio (aporatio) were calculated at baseline, weeks 12, 24 and 48. Linear mixed effects regression was used to test the effect of treatment on lipids and atherogenic indices in states of remission (DAS28-ESR ≤ 2.6) and high disease activity (DAS28-ESR > 5.1).

Results: Baseline clinical characteristics of individuals[1] and lipid profiles including atherogenic indices were comparable between the two treatment groups (Table 1).

Table 1. Baseline lipids (mmol/L) and atherogenic indices in VEDERA. Median with interquartile range and n/N (%) reported.

	Total, N = 120	MTX_TT, N = 60	ETN+MTX, N = 60
TC	4.69 (4.03,5.25)	4.70 (4.04,5.42)	4.69 (4.01,5.18)
TG	1.15 (0.90,1.41)	1.18 (0.92,1.32)	1.10 (0.89,1.55)
HDL	1.28 (1.04,1.53)	1.29 (1.04,1.57)	1.27 (1.05,1.48)
LDL	2.87 (2.22,3.27)	2.87 (2.27,3.19)	2.84 (2.01,3.29)
TC/HDL	3.53 (3.01,4.16)	3.53 (3.00,4.14)	3.58 (3.08,4.17)
AIP	-0.06 (-0.20,0.09)	-0.06 (-0.22,0.08)	-0.06 (-0.17,0.13)
Aporatio	0.63 (0.54,0.74)	0.62 (0.54,0.74)	0.64 (0.55,0.74)

In clinical remission, a lowering of atherogenic indices and TC, TG, LDL levels as well as a rise in predicted HDL levels were observed. In high disease activity, both HDL and LDL were increased along with the atherogenic indices TC/HDL-C, AIP and aporatio. However, the predicted values at different weeks did not reach statistical significance (not shown).

Treatment with MTX-TT and ETN+MTX had opposing effects on predicted HDL levels in remission and high-disease activity (Figure 1). In remission, MTX-TT treatment resulted in a predicted rise in HDL whilst with ETN+MTX a small reduction was observed (estimate 0.004, p 0.02). Similar trends were observed for HDL in high disease activity (p 0.5). In remission, both treatments resulted in a reduction in LDL (p 0.5), whilst in high disease activity ETN+MTX treatment resulted in a modest rise in LDL compared to MTX-TT (p 0.06). At weeks 24 and 48, significant differences were observed in LDL values between treatment groups in high disease activity (estimate 0.57, p 0.05 and estimate 1.13, p 0.04 respectively).

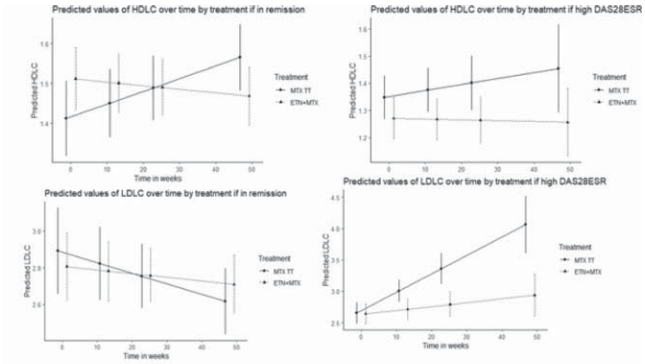

Figure 1: Predicted trends in HDL and LDL if in remission (left) vs high disease activity in MTX-TT and ETN+MTX groups

Conclusion: Effect of early ETN treatment on HDL, and to a lesser extent LDL, differs from MTX and is modulated by clinical disease activity. Further investigation is needed to understand the basis for these findings and the clinical implication of observed differences in LDL and HDL. These data may indicate direct effect of therapies on the qualitative and functional components of metabolic lipid pathway.

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POS0214

CORONARY MICROVASCULAR DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND DIABETES MELLITUS: A CROSS-SECTIONAL STUDY WITH 13NH3 MYOCARDIAL PET/CT

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Background: Patients with rheumatoid arthritis (RA) are at increased risk of cardiovascular disease. This risk is similar to that of diabetes mellitus (DM). There have been no studies comparing the coronary microvascular dysfunction assessed with coronary flow reserve (CFR) of RA patients to both patients with DM and a control group (=patients without RA, without DM and no cardiovascular event).

Objectives: To assess the difference in coronary microvascular dysfunction in patients with RA in comparison to patients with DM and control group.

Methods: From our 13NH3 myocardial PET/CT registry we included all patients that were included from December 2013 until March 2019. A total of 33 patients with RA, 299 patients with DM and 179 control patients (=patients without RA and without DM) were analyzed. Myocardial blood flow was quantified at rest and under stress induced by administrating adenosine. Coronary flow reserve was calculated by dividing MBF under stress by MBF in rest. CFR < 2 was indicative for coronary microvascular dysfunction.

Results: The mean age of patients was 66, with more females in the RA and control group vs the DM group (67% and 69% vs 49% respectively). The total MBF, under adenosine administration, measured in RA patients was higher than DM patients albeit that this did not reach statistical significance (2.26 ± -,70 vs 2,05 ± 0,63 mL/min/g, p=0.08). When compared to controls, the MBF of RA patients was significantly lower (2,94 ± 0,44 vs 2,26 ± 0,70, p < 0.001). The coronary flow reserve (CFR) of patients with RA was similar to patients with DM (2.20 ± 0,69 vs 2,21 ± 0,70 mL/min/g, p=0.977). The CFR of the control group was significantly higher than those of the RA patients (3,03 ± 0,64 vs 2.20 ± 0,69 mL/min/g, p<0.000) and of the DM patients (3,03 ± 0,64 vs 2.21 ± 0,70 mL/min/g, p<0.000). 42% of RA- and 38% of DM patients had coronary microvascular dysfunction, compared to 4% in the control group.

Conclusion: Our results indicate an impaired coronary blood flow in both patients with RA and DM in similar levels. Both patient groups had significantly more coronary microvascular dysfunction.

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Recent advances in orphan rheumatic diseases

POS0215

PHENOTYPES AND DISEASE CHARACTERISTICS OF IGG4-RELATED DISEASE IN NORWAY

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Background: Milestones in the field of IgG4-related disease (IgG4-RD) include the 2011 Comprehensive Diagnostic Criteria (CDC) (1), the 2019 ACR/EULAR classification criteria (2), and the recent identification of four distinct clinical phenotypes (3). Performance of the criteria and phenotypic disease expression in Scandinavian populations are largely unknown.

Table 1.

	All (60)	Pancreato-Hepato-Biliary (14)	Retroperitoneum and aorta (12)	Head and Neck-Limited (17)	Mikulicz and Systemic (17)
Male, n (%)	44 (73)	11 (79)	9 (75)	10 (59)	14 (82)
Caucasian, n (%)	52 (87)	14 (100)	11 (92)	13 (77)	14 (82)
Age at diagnosis, years (SD)	60 (14)	66 (9)	64 (10)	50* (17)	61 (11)
Time from onset to diagnosis, years (SD)	2 (3)	2 (3)	2 (4)	1 (1)	4 (5)
Serum IgG4, g/L (SD) (n=51)	8 (9)	5 (5)	3 (2)	7 (5)	16* (13)
Elevated baseline serum IgG4, n (%) (n=51)	44 (86)	9 (69)	10 (91)	11 (92)	14 (93)
CRP, mg/dL (SD)	11 (26)	4 (7)	36* (52)	9 (17)	5 (4)
ESR, mm/h (SD)	35 (32)	16 (11)	63* (36)	29 (29)	39 (30)
Eosinophilia, n (%) (n=46)	17 (37)	2 (22)	0	6 (38)	9 (64)
CDC definite, n (%)	32 (53)	10 (71)	3 (25)	8 (47)	11 (65)
CDC probable, n (%)	10 (17)	3 (21)	1 (8)	5 (29)	1 (6)
CDC possible, n (%)	14 (23)	0	6 (50)	4 (24)	4 (24)
ACR/EULAR classification criteria, n (%)	42 (70)	13 (93)	5 (42)	8 (47)	16 (94)
Number of involved organs (SD)					
Active, all	4 (2)	3 (2)	2 (2)	3 (1)	6* (2)
Active, symptoms	2 (1)	2 (1)	1 (0)	2 (1)	3* (1)
Active, urgent	1 (1)	1 (1)	1 (1)	0* (0)	1 (1)
Damage	2 (1)	2* (1)	1 (1)	1 (1)	2* (2)
IgG4-RD RI (SD)	10 (5)	9 (4)	7 (4)	7 (3)	15* (4)

*p < 0,05 by one-way ANOVA

Objectives: Describe disease characteristics, phenotypes, and performance of the 2011 CDC and 2019 ACR/EULAR classification criteria in patients with IgG4-RD in Norway.

Methods: Consenting, adult patients with a clinical diagnosis of IgG4-RD, seen at the Department of Rheumatology, Oslo University Hospital were included. Two experts (JV, ØMi) assigned patients to phenotypes ("Pancreato-Hepato-Biliary", "Retroperitoneum and Aorta", "Head and Neck-Limited" or "Mikulicz and Systemic") based on pattern of organ involvement. Fulfillment of the CDC and classification criteria were assessed. Disease activity and damage were scored with the IgG4-RD responder index (IgG4-RD RI). We used descriptive statistics.

Results: We identified 60 patients with IgG4-RD (Table 1). Clinical characteristics were as expected, with approximately equal number of patients in each phenotype group. Of all patients diagnosed by expert opinion, 42 (70%) fulfilled the ACR/EULAR classification criteria. Reasons for not fulfilling the criteria were (i) failure to meet the inclusion criterium (n = 3) due to "atypical" organ involvement: tonsils (n = 1), nasal cavity (n = 1); coronary artery (n = 1); (ii) presence of ≥ 1 exclusion criterium (n = 5): fever (n = 1), leukopenia (n = 1), thrombocytopenia (n = 1), positive anti-MPO-ANCA (n = 3), anti-SSA (n = 1) and/or anti-RNP (n = 1) antibody; and (iii) score < 20 points (n = 10). In the latter group, 8 (80%) were not biopsied, and 1 (10%) had only performed fine needle biopsy. Among the patients not meeting the inclusion criterium or having ≥ 1 exclusion criteria, 1 (33%) and 4 (80%) scored ≥ 20 points, respectively. Of all patients, 56 (93%) fulfilled CDC, with 32 (53%), 10 (17%) and 14 (23%) patients characterized as "definite", "probable" and "possible" IgG4-RD, respectively. Of the 18 patients not fulfilling the ACR/EULAR classification criteria, 15 (83%) fulfilled CDC (4 "definite", 3 "probable", 8 "possible"). Of the 4 patients not fulfilling CDC, 1 fulfilled the ACR/EULAR classification criteria.

Conclusion: Despite expected clinical characteristics, phenotype distribution and fulfilment of CDC in our cohort, the performance of the ACR/EULAR classification criteria was lower than expected, especially in the "Retroperitoneum and Aorta" and "Head and Neck-Limited" phenotypes. This may have important implications for the comparability across studies and inclusion in future clinical trials.

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POS0216

CARDIAC SARCOIDOSIS: AN UNDERDIAGNOSED, LIFE-THREATENING YET TREATABLE DISEASE

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Background: Cardiac sarcoidosis (CS) is potentially life-threatening and it typically causes heart failure, ventricular arrhythmia, AV block or sudden death. CS has been reported to account for 25% of sarcoidosis patient deaths, thus highlighting the importance of early diagnosis and treatment. Diagnostic challenges and lack of a unified screening approach make it difficult to estimate its prevalence. Immunosuppression is the mainstay of treatment, but there is paucity of data on optimal dose, duration and efficacy of steroids and synthetic (s) or biologic (b) disease-modifying anti-rheumatic drugs (DMARDs).

Objectives: To describe the demographic and clinical characteristics of our CS patients, and to study their clinical response to steroids, synthetic and biologic DMARDs.

Methods: A retrospective cohort study with a prospective ongoing phase was conducted. ICD-10 codes were used to identify patients over 18 years old with sarcoidosis and CS followed at Montefiore Medical Center from 2017 to 2021. The following variables were recorded: demographics (age, sex, ethnicity), BMI, smoking status, presenting manifestations, histopathology (cardiac and extracardiac), imaging, treatment (corticosteroids and s/bDMARDs), dose and duration of therapy, steroid-sparing effect, response to treatment based on clinical and imaging improvement (echocardiogram, cardiac MRI, PET).

Results: 220 patients with sarcoidosis were identified. 154 (70%) female and 124 (56.4%) Black. 42 out of 220 (19.1%) met diagnostic criteria for CS [1,2]. Mean age of CS patients was 61.6 years. 23 (54.8%) were male and 24 (57.1%) Black. Heart

Table 1. Treatment of cardiac sarcoidosis

Agent	Treated with DMARDs (N=21)*	Duration of treatment (months, x̄)	Max dose (mg, x̄)	Prednisone dose at 12 months (mg, x̄)	Response to treatment
Methotrexate (Weekly)	16/21 (76.1%)	16.0	16.9	3.67	14/16 (87.5%)
Mycophenolate mofetil (Daily)	6/21 (28.6%)	16.9	2000	5.1	3/6 (50%)
Hydroxychloroquine (Daily)	1/21 (4.8%)	17.5	400	5	1/1 (100%)
Infliximab (q 8 weeks)	1/21 (4.8%)	6.0	5 (mg/kg)	5	1/1 (100%)
Adalimumab (q 2 weeks)	2/21 (9.5%)	10.0	40	7.5	2/2 (100%)

*2 patients switched from MTX to MMF and 3 from sDMARDs to bDMARDs

failure (54.8%), arrhythmias (47.6%) and heart block (28.6%) were the most common presenting manifestations. 28.6% had isolated CS. 5 (11.9%) underwent endomyocardial biopsy and 2 of them (40%) had histopathologic evidence of CS. Mean left ventricular ejection fraction (LVEF) was 40.6 % on echocardiogram, and 29 patients (69%) had PPM/ICD placed for arrhythmia prevention. 35 (83.3%) underwent cardiac MRI, 37 (88.1%) cardiac PET scan and 23 (62.3%) had a follow up PET. 33 (78.6%) CS patients were treated with corticosteroids for a mean duration of 17.3 months. 21 of them were also treated with sDMARDs and 3 were subsequently switched to bDMARDs (Table 1). Mean prednisone dose at 12 months was 4.8mg, and 11 patients (33%) were tapered off corticosteroids.

Conclusion: In our sarcoid patient population, the prevalence of CS is 19.1%, which is higher than previously reported in the literature, suggesting CS may be underdiagnosed. There was a greater proportion of male patients in the CS population (54.8%) than the generalized sarcoidosis population (30%). This indicates that males with sarcoidosis may be more likely to have cardiac involvement. Patients treated with s/bDMARDs had a high response rate as reflected by clinical and imaging improvement. Steroid-sparing effect is suggested by the low prednisone dose at 12 months (Table 1). Methotrexate was the most commonly used DMARD (76.2%). Randomized clinical trials are needed to establish robust guidelines for the treatment of CS.

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POS0217 ALL-CAUSE AND CAUSE SPECIFIC MORTALITY AMONG PATIENTS WITH BEHCET'S DISEASE VERSUS GENERAL POPULATION

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Background: Behcet's disease (BD) is a systemic vasculitis with multiorgan involvement.

Objectives: To compare the risk of all-cause and cause specific mortality among patients with BD compared to general population

Methods: Using the 2002-2017 Korea National Health Insurance database, we conducted a cohort study among BD patients compared to general population matched on age and sex at a 1:5 ratio. The primary outcome was death of any cause, and the secondary outcomes were cause-specific mortality for top 5 causes of death. Cox proportional hazards models estimated hazard ratios (HRs) and 95% confidence intervals (CIs), comparing BD patients versus general population.

Results: The PS-matched study cohort (mean age 42.1 years; 32.0% male) included 32288 BD patients and 161440 controls. During a mean follow-up of 9.6 years, 2214 deaths occurred. The HR [95%] for all-cause mortality was 10.6 [9.6-11.6]. The Top 5 causes of death derived from malignancy, cardiovascular disease, infection, respiratory disease, and injury: the HR [95%] for mortality from these causes were 8.5 [7.2-10.1], 10.8 [8.6-13.6], 14.6 [8.1-26.3], 12.0 [8.5-17.0], and 8.0 [5.0-13.0], respectively.

Conclusion: This population-based cohort study warns exceptionally heavy burden of the disease showing approximately 10 times higher mortality of BD patients compared to general population. In line with this, risk of cause specific mortality was also significantly higher among the BD patients, for 5 top causes of death.

Disclosure of Interests: None declared

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POS0218 DECREASED MIR-122-5P IN NEUTROPHIL-DERIVED EXOSOMES ATTENUATED IMMUNOREGULATORY FUNCTION ON MACROPHAGES BY TARGETING IRF5 EXPRESSION IN BEHCET'S DISEASE

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Background: Behçet's disease (BD) is a chronic systemic vasculitis characterized by the overactivation of neutrophils and macrophages. Exosomes are membrane-derived vesicles that mediate intercellular communications and neutrophil-derived exosomes account for the major portion of serum exosomes in BD. However, the role of neutrophil-derived exosomes in BD remains unknown.

Objectives: 1) To investigate the production of exosomes by BD neutrophils; 2) To elucidate the regulation of macrophage by BD neutrophil-derived exosomes; 3) To explore the mechanism of immunoregulatory functions of BD neutrophil-derived exosomes.

Methods: BD and healthy control (HC) neutrophil-derived exosomes were extracted and quantified. Human monocyte-derived macrophages (HMDM) were stimulated with BD and HC neutrophil-derived exosomes, and TNF-α and IL-6 production were examined. Differently expressed miRNAs in BD neutrophil-derived exosomes were analyzed using miRNA sequencing. LPS-induced HMDM were treated with miRNA mimics or inhibitors, and TNF-α and IL-6 production were detected. miRNA was overexpressed in macrophages, and RNA sequencing was performed to analyze regulating pathways. Dual-luciferase assays were performed to confirm miRNA-mRNA interaction.

Results: BD neutrophils produced a significantly lower level of exosomes than HC ones. Both BD and HC neutrophil-derived exosomes suppressed TNF-α and IL-6 production by macrophages, but to a lesser extent by BD neutrophil-derived exosomes. Six downregulated miRNAs were presented in BD neutrophil-derived exosomes, including miR-122-5p. miR-122-5p mimics inhibited IL-6 and TNF-α production while miR-122-5p inhibitor promoted IL-6 and TNF-α production by HMDMs. Overexpression of miR-122-5p attenuated TLR4 and IFN-β signaling. miR-122-5p directly targeted 3'UTR of IRF5, the TF regulating TLR4 pathway and autocrine of IFN-β, and downregulated IRF5 expression confirmed by dual luciferase assay. Knocking down IRF5 dampened IL-6 and TNF-α production in HMDMs.

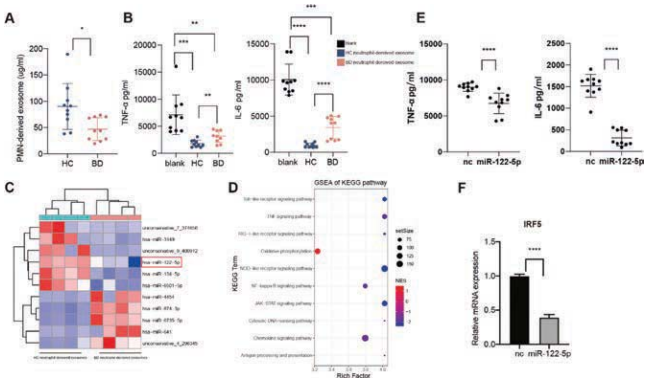

Figure 1. (A) Decreased production of BD neutrophil-derived exosomes. (B) Reduced suppression of macrophage activation by BD neutrophil-derived exosomes. (C) Differentially expressed miRNAs (downregulated) in BD neutrophil-derived exosomes. (D) miR-122-5p suppressed TLR4 and JAK-STAT signaling in HMDM. (E) miR-122-5p inhibited activation of HMDM. (F) miR-122-5p inhibited IRF5 expression in HMDM.

Conclusion: Our findings suggested the reduced production and immunoregulatory function of BD neutrophil-derived exosomes, mediated by lower levels of miR-122-5p in neutrophil-derived exosomes. Impaired BD neutrophil-derived exosomes might be implicated in the overactivation of macrophages in BD.

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POS0219 EARLIER AND MORE AGGRESSIVE TREATMENT OF MAJOR ORGAN INVOLVEMENT WITH BIOLOGICS MAY PREVENT RELAPSES OR FURTHER NEW ORGAN INVOLVEMENT IN A SUBGROUP OF BEHÇET'S DISEASE PATIENTS

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Background: Conventional immunosuppressives (cIS) are the choice of treatment for major organ (ocular, vascular, central nervous (CNS) and gastrointestinal (GIS)) involvement to prevent relapses and organ damage in patients with Behcet's disease (BD).

Objectives: We aimed to investigate the rate of new major organ involvement in BD patients under cIS treatments during follow-up and to assess the characteristics and treatment protocols of these patients.

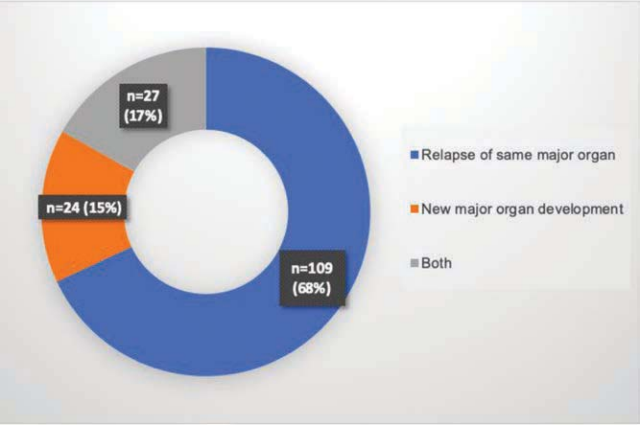
Methods: The files of 1114 patients diagnosed with BD and followed (1992-2019) in the Marmara University Behcet's Clinic were overviewed retrospectively. Patients with follow-up duration less than 6 months were excluded. A total of 806

patients, of whom 56% were male were included in the analysis. Demographic and clinical characteristics, follow-up and treatment data of the patients were recorded from files. Relapse of the same organ and/or new major organ development during the follow-up period of patients receiving cIS was defined as "event under cIS".

Results: Median age at diagnosis was 29 (10-65) years and median follow-up duration was 68 months (6-272). Genital ulcer, erythema nodosum and arthritis/arthralgia were more common in women, whereas papulopustular lesions, vascular and ocular involvement were more common in men (p<0.005 for all). Presence of major organ involvement was 56.9% (n=459) and the frequencies of vascular, ocular, CNS and GIS involvement were 29.8%, 33,5%, 9.7%, and 2%, respectively. At diagnosis 232 (50.5%) patients had major organ involvement, whereas it developed in 227 patients during a follow-up of median 3 years (0.5 - 32) after diagnosis. Major organ involvement developed earlier in males compared to females (median 2 years vs 4 years, p = 0.012). In patients with a first-degree relative history of BD, major organ involvement also developed earlier, however without reaching significance (median 1 year vs 3 years) (p= 0,066). 440 patients had follow-up data under cISs with the follow-up duration of median 65.5 months (6-272). Main reason for cISs use was major organ involvement (86.8%), less frequent reasons were mucocutaneous disease (9.3%) and joint involvement (3.8%). An event under ISs (mainly relapses) occurred in 160 (36.4%) patients with median 23 months after cISs initiation. Majority of events (68%) were relapses of the same major organ (Figure 1). The most commonly used cIS agent was azathioprine (87%). Among patients having an event under cISs, 91% of the relapses and 75% of new major organ involvement developed under azathioprine treatment. In patients with an event under cISs, treatment mostly switched to other ISs such as cyclophosphamide, interferon-alpha, and high dose corticosteroids. In 22% of patients, azathioprine was switched to tumor necrosis factor (TNF) inhibitors.

Conclusion: In our study, major organ involvement developed in 57% of the 806 BD patients. We observed that disease course was more severe under cIS treatment in male patients diagnosed at a younger age and with the history of familial BD. In one third (36%) of the patients under cIS treatment, a relapse or a new major organ involvement developed despite the cISs use, mainly under azathioprine. TNF-inhibitor use was approved for BD treatment within the last decade in Turkey. Therefore, azathioprine was switched to a TNF inhibitor in only 22%. Our results suggest that earlier and more aggresive treatment of major organ involvement with biologics may be an option in young male patients especially with the history of familial BD, who had the highest risk for severe disease course.

Figure 1: Distribution of events under immunosuppressive treatments.



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POS0220

LONG-TERM SAFETY AND EFFECTIVENESS OF CANAKINUMAB IN CRYOPYRIN-ASSOCIATED PERIODIC SYNDROMES – 36-MONTH DATA FROM THE RELIANCE REGISTRY

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Background: The cryopyrin-associated periodic fever syndromes (CAPS) are hereditary monogenic autoinflammatory diseases with severe systemic and organ inflammation due to increased production of Interleukin-1β (IL-1β). The subcutaneously administered monoclonal antibody canakinumab (CAN) effectively inhibits IL-1β and results in rapid remission of CAPS symptoms in clinical trials as well as in real-life.

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

Methods: This prospective, non-interventional, observational study with a 3-year follow-up enrolls patients in Germany with clinically confirmed diagnoses of CAPS routinely receiving CAN. In 6-monthly visits, clinical data, physician assessments and patient-reported outcomes are evaluated starting at baseline.

Results: 98 CAPS patients (52% female; 15 [15%] NOMID/CINCA subtypes) were enrolled by December 2021 (Table 1). At baseline, median age was 20 years and median duration of prior CAN treatment was 6 years. At the 36 months visit, 74% of patients reached disease remission by physicians´ assessment along with increasing rates of absent disease activity (patient's assessment, median 2.0 at baseline and 0.0 month 36). In addition, patients reported low levels of fatigue (absent to mild/moderate: 87% at baseline and 95% at month 36). At baseline, CAPS impaired social life in 47% of patients (37% at month 36) and 33% (23% at month 36) reported days off from school/work. Lab parameters were within normal limits. Remission and disease control were sustained as evaluated parameters remained stable or even decreased over time.

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

	Baseline	12 months	36 months
Number of patients, N	98	72	40
Number (%) of patients in disease remission (physician assessment)	64 (68)	48 (70)	28 (74)
Patient's assessment of current disease activity; 0–10, median (min; max)	2.0 (0; 7)	2.0 (0; 7)	0.0 (0; 6)
Patient's assessment of current fatigue; 0–10, median (min; max)	3.0 (0; 9)	2.0 (0; 8)	1.0 (0; 8)
Number (%) of patients without impairment of social life by the disease	34 (53)	35 (65.0)	17 (63)
CRP (mg/dl) I SAA (mg/dl); median	0.1 I 0.3	0.1 I 0.5	0.1 I 0.3
Number (%) of patients with disease-related symptoms	prior to inclusion into the study I at baseline	12 months	36 months
Fever	75 (80) I 14 (15)	19 (28)	4 (11)
Fatigue	84 (89) I 49 (52)	36 (52)	17 (46)
Conjunctivitis/Uveitis	63 (67) I 27 (29)	21 (30)	7 (19)
Headache	68 (72) I 30 (32)	30 (43)	9 (24)
Arthralgia/arthritis	80 (85) I 32 (34)	30 (43)	14 (38)
Impairment of hearing	35 (37) I 23 (25)	18 (26)	11 (30)
Trigger (cold, stress, infections, vaccinations, hormones)	71 (76) I 32 (34)	21 (30)	3 (8)
SAE	**Number of events**	**Incidence rate* per 100 patient years**	
All types of SAE I SADR	63 I 28#	25.98 I 11.55	

CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; n. a., not annotated; SAA, serum amyloid A; SADR, serious adverse drug reaction; SAE, serious adverse event*Incidence rate = number of events * 36,525 / sum of observation days (=88,558)#Abdominal pain, Alport's syndrome, appendicitis, arthralgia, blister, cardiovascular disorder, chest pain, circulatory collapse, dehydration, diplopia, dyspnoea, erythema, febrile convulsion, gastroenteritis, glomerulonephritis, haemophilus test positive, myalgia, oedema, pneumonia, premature delivery, skin discoloration, tonsillectomy, tonsillitis bacterial, tonsillitis streptococcal, vision blurred (all N=1 event), pyrexia (3 events)

Table 1. Baseline characteristics and interim analysis data of patients with TRAPS.

	Baseline (N=19)	12 months (N=15)	24 months (N=8)
Number (%) of patients in disease remission (physician assessment)	9 (53)	11 (79)	4 (67)
Physician assessment of disease activity, percentage of absent/mild-moderate/severe rating	35 / 59 / 0	57 / 36 / 7	67 / 33 / 0
Patient´s assessment of current disease activity; 0–10, median (min; max)	1.5 (0; 8)	1.0 (0; 6)	0 (0; 7)
Patient´s assessment of current fatigue; 0–10, median (min; max)	1.0 (0; 8)	1.0 (0; 8)	0 (0; 8)
Number (%) of patients without impairment of social life by the disease	5 (56)	4 (44)	2 (100)
Number (%) of patients with days absent from work/school during last 6 months	8 (44)	6 (40)	1 (14)
CRP, median (mg/dl)	0.2	0.1	0.2
SAA, median (mg/dl)	0.5	0.4	0.4
ESR, median (mm/h)	7.0	5.5	6.0
SAE	**Number of events**	**Incidence rate# per 100 patient years**	
All types of SAE	9	24.2	
SADR	0	0.0	

CRP, c-reactive protein; SAA, serum amyloid A; ESR, erythrocyte sedimentation rate; #Numbers/percentage do not sum up to N=19/100%, due to unknown weight of some patients

Conclusion: The 36-month interim analysis of the RELIANCE study demonstrates that long-term CAN treatment is safe and effective in patients with CAPS, independent of subtype severity.

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POS0221 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH TRAPS (TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME) – INTERIM ANALYSIS OF THE RELIANCE REGISTRY

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Background: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is a rare hereditary autoinflammatory disease characterized by periodic fever as well as severe systemic and organ inflammation. Successful treatment was achieved with the interleukin-1β inhibitor canakinumab (CAN) in a pivotal phase 3 study, in which 45% of patients reached clinical remission after 16 weeks (primary endpoint)[1]. CAN has been approved and applied for the treatment of TRAPS patients since 2017[2].

Objectives: The present study explores the long-term efficacy and safety of CAN under routine clinical practice conditions in pediatric (age ≥2 years) and adult TRAPS patients.

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany. Patients with clinically confirmed diagnosis of TRAPS who routinely receive CAN are enrolled in order to evaluate efficacy and safety of CAN under standard clinical practice conditions at baseline and at 6-monthly intervals.

Results: The interim analysis of TRAPS patients enrolled by December 2021 includes baseline (N=19, 1 patient with atypical TRAPS) and preliminary 24-month data. Of these patients, N=12 (63%) were females and median age at baseline was 16 years (3–43 years).

Preliminary results indicate stable remission by physicians´ assessment and laboratory parameters. Disease control by patients´ assessment showed no major changes over time (Table 1). In total, N=7 adverse drug reactions where observed, of which none was classified as severe.

Conclusion: Baseline characteristics and interim data of TRAPS patients are available from the RELIANCE study. Further interim and end-of-study data will be analyzed to assess efficacy and safety of long-term treatment as well as dosing effects in TRAPS patients.

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POS0222 POLYARTICULAR ARTHRITIS AND ADULT-ONSET OSTEOLYSIS CAUSED BY MUTATIONS IN THE ASAH1 GENE: FARBER DISEASE CLINICAL PRESENTATIONS IN THE CONTEXT OF A FIRST-EVER NATURAL HISTORY STUDY

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Background: Farber disease is frequently misdiagnosed as polyarticular juvenile idiopathic arthritis or seronegative rheumatoid arthritis which leads to a delay in diagnosis for many patients. Farber disease is an ultra-rare lysosomal storage disease caused by mutations in the *ASAH1* gene. The resulting deficiency of the acid ceramidase enzyme leads to accumulation of the pro-inflammatory and pro-apoptotic sphingolipid ceramide. Accumulation of ceramide throughout the body leads to the symptoms of Farber disease. Cardinal symptoms include joint disease (polyarticular arthritis and contractures), subcutaneous nodules, and a hoarse or weak voice due to laryngeal nodules. The phenotypic spectrum of Farber disease ranges from rapidly progressive disease causing death in infancy to moderate or slowly progressive disease with survival into late adulthood. Symptoms may vary in severity across patients and phenotypes.

Objectives: To further define the symptoms of Farber disease, including joint disease, subcutaneous nodules, dysphonia, and osteolysis, which can lead to referral to rheumatology or related specialties. To understand the clinical presentation and broad phenotypic spectrum of this rare disease to aid in clinical diagnosis and reduce diagnostic delay.

Methods: The Observational and Cross-Sectional Cohort Study of the Natural History and Phenotypic Spectrum of Farber Disease (NCT03233841) was the first systematic clinical study of the natural history of Farber disease. The study collected retrospective and prospective data on living and deceased patients, including demographics, clinical presentation, phenotype, diagnostic history, and patient reported outcomes.

Results: 45 patients with Farber disease (27 living, 18 deceased) who had or had not undergone hematopoietic stem cell transplant (HSCT) were enrolled from 16 centers in 9 countries. A cohort of 24 living non-HSCT patients were followed prospectively. The patients represented the broad phenotypic spectrum of Farber disease, from rapidly progressive (severe) to slowly progressive (attenuated). In patients whose data was available for analysis, the average age of patients at enrollment was 7.2 years (range 1 to 28 years). The average age of onset of joint disease (arthritis and/or contractures) was 15 months (range 3 months to 7 years), of subcutaneous nodules was 13 months (range 3 months to 5 years), and of dysphonia was 13 months (range birth to 8 years). The average time from onset of symptoms to Farber disease diagnosis was 2 years (range <1 to 12 years). At baseline, the mean number of joints affected with active arthritis was 11.3 (range 0-36) and the mean number affected with contractures was 18 (range 0-38). 12.5% of patients were reported to have a bone disorder such as osteoporosis or osteolysis. The Child Health Assessment Questionnaire Disability Index (CHAQ) ranging from 0 (no impairment) to 3 (unable to do) was high, with mean scores of 2.62-3.00 across visits.
Conclusion: Data from the Farber disease natural history study further defined the cardinal symptoms, phenotypic spectrum, and high disease-related burden in patients with Farber disease. The large number of joints affected with arthritis or contractures reflects that patients with Farber disease are often referred to rheumatology and can be misdiagnosed with polyarticular juvenile idiopathic arthritis or seronegative rheumatoid arthritis. Demographic information and numbers of patients enrolled indicate that Farber disease is likely not as rare as previously thought. *ASAH1* genetic testing for adult and pediatric patients referred to the rheumatology clinic with symptoms including polyarticular arthritis, subcutaneous nodules, dysphonia, or osteolysis, may shorten the time to diagnosis in patients with Farber disease.
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POS0223 AMYLOID BURDEN AND ASSOCIATED FACTORS PREDICT HIGHER MORTALITY AND POOR OUTCOME IN FAMILIAL MEDITERRANEAN FEVER-ASSOCIATED AA AMYLOIDOSIS: DATA FROM A TERTIARY REFERRAL AMYLOIDOSIS CENTER WITH 137 PATIENTS

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Background: AA amyloidosis (AA-a) is a rare condition while the most common cause is Familial Mediterranean Fever (FMF) in Turkey. There is limited evidence about the impact of AA-a burden on prognosis and outcome in AA-a.
Objectives: We herein aimed to evaluate the AA-a burden and its association with outcome in patients (pts) with FMF-associated AA-a (FMF-AA)
Methods: We retrospectively evaluated FMF-AA pts from our AA-a cohort. Diagnosis of AA-a was confirmed by histologically. Heart involvement (inv.) was defined by documenting increased (>12mm) septal wall thickness (CSWT) and at least one of three appropriate echocardiography findings (decreased ejection fraction, increased granular echogenicity or valvulopathy, diastolic dysfunction). The pts were divided in three groups according to AA-a burden: pts had only renal inv. (Group 1, G1), renal and gastrointestinal (GIS) (Group 2, G2); renal and GIS and heart (Group 3, G3)
Results: Data of 137 pts with FMF-AA (55% male) were analyzed. We classified 79 pts in G1, 20 in G2, and 14 in G3. CSWT, troponin (trop) and pro-BNP levels were higher in G3 than G1 and G2 but trop levels were not statistically (sts) significant (sig.) between G3 and G2. Overall mortality was in 15.3 %. While mortality rate increased gradually with higher AA-a burden (10 % in G1, 15 % in G2 and 43 % in G3), the difference was sts sig. between G3 and G1.
The number of MEFV variants was lower in pts with higher AA-a burden, especially those with M694V homozygosity were 93% and 72% in G1, 83% and 67% in G2, and 75% and 50% in G3 rsp; but the differences were not sts sig. (p=0.2 and p=0.7 for G1-G2, p=0.06 and p=0.2 for G1-G3, p=0.6 and p=0.4 for G2-G3).
The number of organ inv. was correlated with CSWT (r=0.559' 'p<0.001), trop (r=0.646'), pro-BNP (r=0.572'), bsl creatinine (Cre) (r=0.511'), bsl proteinuria (prt) levels (r=0.321 p=0.008) and negatively correlated with bsl e-GFR (r=-0.437') and biologic DMARD duration (r=-0.235 p=0.03)
ROC analyses revealed 56% sensitivity (SS) and 70 % specificity (SP) for bsl Cre (cut off value [COV] 0.95, AUC=0.726 p=0.03 95% CI 0.56-0.9), 83.3 % SS and 74 % SP for trop (COV 35.5 AUC=0.864 p=0.006 CI 0.73-0.99), 100 % SS and 85.5 % SP for pro-BNP (COV 7246 AUC=0.897 p=0.024 CI 0.79-1.0), 79% SS and 58 % SP for CSWT (COV 11.5 AUC=727 p=0.007 CI 0.61-0.84) to be able to predict higher mortality.
Conclusion: This study showed the association of AA-a burden with higher morbidity such as ESRD and higher mortality in pts with FMF-AA. Bsl Cre, prt, trop and pro-BNP levels were correlated with extent of AA-a burden and predicted higher mortality. Lower frequency of pts with two exon 10 variants or M694V homozygosity in pts with higher AA-a burden indicates that additional genetic and environmental factors may play a role in the development and progression of AA-a in FMF.

Table 1. Clinical and laboratory features of pts with FMF-AA according to AA-a burden

Variables	G1 (n=79)	G2 (n=20)	G3 (n=14)	p1 (OR)	p2	p3
Age * ǂ	42.8±13	43.2±13	48.9±11	0.9	0.1	0.2
Gender, male**	36 (45.6)	15 (75)	7 (50)	***0.02 (5.5)***	0.8	0.1
Diagnosis age of AA-a * ǂ	30.7±13	34.1±14	34.9±15	0.3	0.3	0.9
Duration of AA-a * ǂ Baseline	13.8±9	10.8±6	14.3±8	0.15	0.8	0.2
CRP (mg/L) ǂ	20±13	24±19	13±7	0.4	***0.05***	0.07
Prt (g/dL) ǂ ǂ	3.8 (5.8)	12.4 (16)	5 (4.2)	***0.03***	0.3	0.2
Cre (mg/dL) ǂ	0.8±0.4	1.5±1	1.8±1.3	***<0.001***	***<0.001***	0.6
e-GFR ǂ#	104±31	104±31	59±39	***0.02***	***0.004***	0.5
CRF at admission**	28/74 (38)	13/19 (68)	9/12 (75)	***0.02 (5.7)***	***0.03 (6)***	0.7
ESRD at admission**	7/62 (11)	6/18 (33)	4/11 (36)	***0.03 (5)***	***0.03 (4.6)***	0.9
CSWT ǂ	10.2±1.7	10.6±1.1	13.9±1.6	0.3	***<0.001***	***<0.001***
Trop κ ǂ ǂ	9 (13)	28 (68)	75 (85)	0.4	***0.005***	0.1
pro-BNP κ ǂ ǂ	288 (1040)	766 (1967)	4968 (33800)	0.5	***0.003***	***0.026***
ESRD (overall)**	35 (45)	10 (50)	13 (93)	0.7	***0.001 (11)***	***0.01 (7)***
Duration of b-DMARD (months) ǂ##	66±29	67.7±37	41.8±30	0.9	***0.02***	0.08
Mortality **	8 (10)	3 (15)	6 (43)	0.5	***0.006 (10)***	0.1

#estimated glomerular filtration ratep1: G2-G1p2: G3-G1p3: G2-G3ǂ mean±std dev. ǂ ǂmedian (IQR) *years ** n, % κ pg/mL

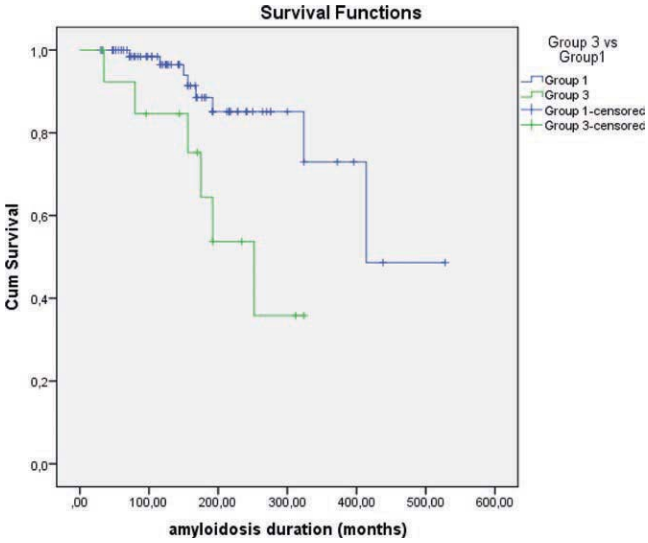

Figure 1. Comparison of survival rate between G3 and G1Log-Rank: p=0.007

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POS0224 A NOVEL TNFRSF1A MUTATION ASSOCIATED WITH TNF-RECEPTOR ASSOCIATED PERIODIC SYNDROME AND ITS METABOLIC SIGNATURE

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Background: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is an autosomal dominant periodic fever syndrome characterized by prolonged episodes of fever, arthralgia, myalgia, abdominal pain and erythematous rash.1 We report a new mutation in the TNFRSF1A gene which is associated with TRAPS and AA-amyloidosis. Furthermore we analyzed the metabolic changes using a metabolomics approach.
Objectives: To describe a novel mutation in the TNFRSF1A gene that causes TRAPS.
Methods: Case series. For pathogenicity predictions we used the PolyPhen-2 web-software2 and PROVEAN3. Metabolomics: Mass spectrometry was performed

on patient plasma and healthy controls using an UHPLC system (Vanquish, Thermo Fisher Scientific, Bremen, Germany) coupled to an HRAM mass spectrometer (Q-Exactive Plus, Thermo Fischer Scientific GmbH, Bremen, Germany).
Results: A 44-year-old man (patient 1) presented to our hospital with abdominal pain, elevated inflammation parameters, renal failure and large proteinuria. Renal biopsy revealed AA amyloidosis. Further anamnesis showed he had suffered from recurrent attacks of abdominal pain with fever and elevation of inflammation markers since he was 16 years old. He also reported that his father, aunt, sister and daughter have had similar problems. His daughter (patient 2) reported recurrent episodes of abdominal pain with fever since she was 11 years old and his 46-year-old sister (patient 3) reported similar symptoms starting at 12 years of age. Upon presentation patient 3 showed proteinuria of 2000 mg/g creatinine (albuminuria 1500 mg/g creatinine) strongly indicating early renal AA-amyloidosis. All symptomatic family members underwent genetic testing that revealed the yet uncharacterized TNFRSF1A-variant c.332A>G (p.Q111R). In silico analysis of the mutation by PolyPhen-2 software and PROVEAN classified the mutation as probably pathogenic culminating in the diagnosis of TRAPS. All patients received canakinumab for treatment and responded with normalization of the inflammatory parameters. Patient 3 showed a marked reduction of proteinuria after 6 months of treatment. Using a metabolomics approach we were able to detect 158 distinct metabolic compounds of which 32 were up- and 35 downregulated, respectively. Two patients were analyzed before and after treatment with canakinumab. The treatment with canakinumab, however, appears to have no effect on the metabolic changes caused by TRAPS. Significantly upregulated metabolic pathways included purine metabolism, glycolysis/glyconeogenesis, glutathione metabolism, pyrimidine metabolism and phenylalanine, tyrosine and tryptophan biosynthesis. Downregulated pathways included Aminoacyl-tRNA biosynthesis, arginine and proline metabolism, arginine biosynthesis among others.
Conclusion: Here we present a novel mutation in the TNFRSF1A gene that causes TRAPS and is associated with AA-amyloidosis. Canakinumab is an effective treatment in this variant and led to improvement in proteinuria in one of the patients with presumed early renal AA-amyloidosis. We observed significant changes in the metabolome in comparison to healthy controls. Treatment with canakinumab appeared to have no effect on these metabolic changes caused by TRAPS.
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Remodelling in OA

POS0225 FLUIDIC SHEAR STRESS REDUCES TNFA-MEDIATED CARTILAGE DAMAGE IN A 3D MODEL OF DEGENERATIVE JOINT DISEASE

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Background: Pathomechanisms of degenerative joint diseases such as osteoarthritis (OA) ultimately result in the breakdown of cartilage tissue. To date, the exact underlying mechanisms of both cause and progression of OA remain unclear. Therefore, developing complex and long-lasting *in vitro* components of a human joint including cartilage, subchondral bone, synovial membrane and tendons that simulate the 3D architecture and the metabolic, humoral and cellular interplay of the joint components is needed to study the long-lasting course of OA pathogenesis. Beside the impact of metabolic components and 3D architecture, mechanical forces are well-known to be important modulators of joint health, while aberrant forces are primary etiological factors leading to cartilage degeneration.
Objectives: Here, we aimed to (i) develop a long-lasting human *in vitro* 3D cartilage model using alternated perfused cultivation and (ii) simulate TNFα-mediated cartilage degradation. As a mechanical force we used the perfusion-mediated fluid shear stress (FSS) to enhance chondrogenesis and mimic FSS during joint movement.
Methods: Human bone marrow-derived mesenchymal stromal cells (MSC) were used to develop an *in vitro* 3D cartilage model incubated in a bioreactor with a perfusion cycle that facilitates mechanical stimulation via FSS and daily sampling. Within the bioreactor, MSC mass cultures were subjected to FSS at 10 dyn/cm^2 by medium circulation three times a day for 1.5 hours. The approach of using optimized FSS rate, cycles and cultivation period of 18 days for MSC mass cultures was compared to a non-perfused control based on cell viability (live-dead- and viability-assay), apoptosis (TUNEL-assay, caspase-3/7-activity, *BCL2*/*BAX*), metabolic activity (oxygen and glucose consumption, lactate production), chondrogenic gene expression (*ACAN, COMP*, *COL2A1, COL1A1*, *COL2A1*/*COL1A1*) and matrix metalloproteinase expression *(MMP-1, -3, -13)*.
Results: Alternate perfused long-term cultivation at 10 dyn/cm^2 did not affect cell survival; it rather reduced apoptosis, did not affect oxygen consumption but reduced glucose consumption and lactate production and enhanced chondrogenic gene expression with reduced *MMP13* and *COMP* gene expression compared with non-perfused conditions. Mimicking pathophysiology of OA we stimulated the 3D cartilage model with 100 ng/mL TNFα for 6 hours under non-perfused and perfused long-term cultivation with FSS at 10 dyn/cm^2 as a mechanical stimulus. Compared to untreated perfused conditions, TNFα stimulation (i) did not affect overall cell survival but enhanced apoptosis (demonstrating efficacy of stimulation), (ii) did not affect oxygen consumption and glycolysis, and (iii) enhanced *COMP* and *MMP1* expression as markers of matrix protein turnover. In comparison to TNFα treated cells under non-perfused conditions, TNF stimulation under perfused conditions (i) did not affect cell survival but reduced apoptosis, (ii) did not affect oxygen consumption but reduced glucose consumption and lactate production as a measure of glycolysis, and (iii) reduced the expression of *IL6* and soluble amounts of IL-6 but not of *TNFA* whereas soluble amounts of TNFα were enhanced. Furthermore, TNFα stimulation (iv) reduced the expression of matrix degrading enzymes but (v) enhanced anabolic chondrogenic matrix proteins on mRNA.
Conclusion: In a 3D model that mimics OA, FSS as a mechanical stimulus provides a metabolic "feel-good" niche that reduces chondrocyte apoptosis, metabolic activity, and matrix metalloproteinase expression, increases matrix protein expression and protects against TNFα-mediated cartilage degradation.
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POS0226 DEFICIENT CHAPERONE-MEDIATED AUTOPHAGY CONTRIBUTES TO JOINT DAMAGE IN OSTEOARTHRITIS

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Background: In Osteoarthritis (OA), defects in macroautophagy are evident and precede joint damage. Indeed, pharmacological activation of macroautophagy protects against joint damage and disease.
Objectives: Therefore, identifying hallmarks associated with specific autophagy subtypes could shed light to fundamental mechanisms of joint disease and facilitate the development of therapeutic strategies to prevent OA progression.
Methods: A gene expression analysis of 35 autophagy genes was performed from blood from a Prospective OA Cohort of A Coruña (PROCOAC) of non-OA (Age:61,44±1,16 years; BMI:25,25±0,52; Females, n=18) and knee OA subjects (Age:65,50±1,05 years; BMI:29,55±0,67; Females, n=18, OA grade III-IV) by using SYBR green array. The differential expression of candidate genes in blood (n=30/group) and knee cartilage (Non-OA, n=12; Knee OA donors, n=21) was confirmed by using Taqman Technology. HSP90AA1, a chaperone mediated autophagy (CMA) mediator, was evaluated in human knee joint tissues (i.e. cartilage, meniscus, ACL and synovium) with different KL grades (0, 2 and 4, n=3/each KL grade) and in both spontaneous aging mice (2, 6, 12, 18, and 30 months old, n=3/each time) and surgically-induced OA mice (10 weeks after surgery, n=4/each) by immunohistochemistry. The functional consequences of HSP90AA1 deficiency on inflammation, oxidative stress, senescence and apoptosis were studied in human OA chondrocytes by gene and protein expression and flow cytometry. The potential contribution of CMA to chondrocyte homeostasis was studied by assessing the capacity of CMA to restore proteostasis upon macroautophagy deficiency by ATG5 knockdown. To study the therapeutic potential of targeting CMA, HSP90AA1 was overexpressed in human OA chondrocytes.
Results: 16 autophagy-related genes were significantly downregulated in knee OA subjects ($p<0.05$). Macroautophagy-related genes ATG16L2, ATG12, ATG4B and MAP1LC3B, were significantly downregulated ($p<0.05$). Interestingly, HSP90AA1 and HSPA8, CMA mediators involved in stress response and protein folding, were significantly downregulated ($p<0.001$). Confirmatory studies showed a downregulation of MAP1LC3B and HSP90AA1 in blood ($p<0.001$) and cartilage ($p<0.05$) from

knee OA subjects. Moreover, HSP90A was reduced in human joint tissues (i.e. cartilage, meniscus, ACL, $p<0.05$) and associated to OA severity. In mice, HSP90A reduction was observed not only in OA ($p<0.05$) but also in aging ($p<0.01$). LAMP2A, a key CMA mediator, was also reduced in human OA cartilage and associated with aging in mice ($p<0.05$). Remarkably, HSP90AA1 deficiency was functionally linked to inflammation, oxidative stress, senescence and apoptosis ($p<0.05$). Moreover, LAMP2A activity was decreased upon HSP90AA1 deficiency, while mTOR signaling pathway, p62 and active caspase 3 were increased ($p<0.05$), indicating a failure in the autophagy flux that may lead to impaired lysosomal degradation and apoptosis. Human OA chondrocytes with impaired macroautophagy through ATG5 knockdown show reduced LC3II expression and induced activation of prbs6, p16 and p21 ($p<0.05$). Interestingly, HSP90A was increased, suggesting a compensatory activation of CMA in response to specific macroautophagy defects. Remarkably, HSP90AA1 overexpression itself is sufficient to protect against joint damage by decreasing mTOR signaling and senescence in human OA chondrocytes.

Conclusion: Taking together, we identified HSP90A, a marker of CMA, as a key regulator of chondrocyte homeostasis underlying a relevant mechanism in OA. A better definition of the cross-talk between CMA and macroautophagy defects might reveal its role as a hallmark of OA.

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POS0227 MUSSEL ADHESIVE PROTEIN-BASED ADHESIVE TO RETAIN STEM CELLS FOR CARTILAGE REGENERATION

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Background: Cartilage has limited intrinsic healing capacity, motivating the application of stem cells for regenerative therapies. Therapies to treat osteochondral defects using stem cell therapy-based tissue engineering have been developed and used for more than 20 years; however, the low viability and high possibility of dispersion of injected cells to target defect sites have remained challenge. Mussel adhesive protein (MAP) receiving increasing attraction as functional biomedical materials on tissue and biomedical engineering field. Because of functional underwater adhesive ability if the bioengineered MAP, therefore it could be applied on various environment of lesion site.

Objectives: We developed biocompatible adhesive which enables implanted chondrogenic-enhanced hASCs being strongly fixed to the lesion site of defected cartilage, and thus, the implanted cells can survive lengthily in defect site allowing cells to differentiate directly to chondrocytes.

Methods: MAP was produced and purified for in vivo applications using a bacterial expression system as previously reported [1]. The cell encapsulated coacervate was formulated with two polyelectrolyte, the MAP and 723 kDa hyaluronic acid (HA). The DiD labeled cell was dispensed into the solution in which the MAP solution and the HA solution were mixed in a ratio of 7:3 (v/v). MAP formed liquid microdroplets with hyaluronic acid and subsequently gelated into microparticles, which is highly viscous and strongly adhesive.

In vivo efficacy of MAP in rats - the osteochondral defects were created on the patellar groove of distal femora in rats with sharp excision. After transplantation of human adipose derived stem cells (hASCs), the fluorescents image was taken in every 7 days. Animals were allocated into two groups as follows: MAP with hASCs; fibrin with hASCs.

The MAP with chondro-induced hASCs were implanted on the osteochondral defect created in the patellar groove/condyle of OA-induced rabbits. Rabbits were allocated to three different groups as follows: Group 1 - Fibrin only; Group 2 - Fibrin with hASCs (1.5×10^6 chondro-induced hASCs); Group3; MAP with hASCs. After 12 weeks of implantation, rabbits were sacrificed for analysis.

Results: The fluorescence cell images exhibit the viability of cells under encapsulated condition in coacervate. The cell viabilities were determined with Live/Dead fluorescent staining. The implanted cells were labeled with DiD for in vivo visualization. After 35 days, fluorescent signals were more potently detected for MAP with hASCs group than Fibrin with hASCs group in osteochondral defect model. Implanted hASCs had been remained in target defect rather than diffused to other sites of the knee. Moreover, histological assessment showed that MAP with hASCs group had the best healing and covered with hyaline cartilage-like tissue. The staining image shows that MAP with hASCs group were filled with perfectly differentiated chondrocytes. Although Fibrin with hASCs group had better healing than fibrin only group, it was filled with fibrous cartilage which owes its flexibility and toughness. As MAP with hASCs group has higher possibility of differentiating to complete cartilage, Fibrin only group and Fibrin with hASCs group have failed to treat OA by rehabilitating cartilage. In order to clarify the evidence of remaining human cell proving efficacy of newly developed bioadhesive, human nuclear staining was proceeded with sectioned rabbit cartilage tissue. The results explicitly showed MAP with hASCs group have retained more human cells than Fibrin only and Fibrin with hASCs groups.

Conclusion: We investigated the waterproof bioadhesive supporting transplanted cells to attach to defect lengthily in harsh environment, which prevents cells from leaked to other region of cartilage. Collectively, the newly developed bio-adhesive, MAP, could be successfully applied in OA treatment as a waterproof bioadhesive with the capability of the strong adhesion to target defect sites. Our study suggests a new effective strategy for cartilage regeneration using MAP in tissue engineering fields

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POS0228 HYPOXIA AND INHIBITION OF WNT SIGNALING PROMOTE EXPRESSION OF THE PROTECTIVE MOLECULE ANP32A IN CARTILAGE

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Background: Osteoarthritis (OA) is the most common chronic joint disease and is characterized by damage to the articular cartilage. To date, no cure exists (1). Previously, an association between polymorphisms in the acidic leucine-rich nuclear phosphoprotein-32A (ANP32A) gene and OA was described (2). Our group showed that ANP32A plays a key protective role in OA by preventing oxidative stress (3). In OA cartilage, ANP32A is downregulated as compared to non-OA cartilage (3).

Objectives: Maintaining levels of ANP32A seems crucial to preserve joint health, yet the factors that regulate ANP32A in the joint remain unknown. In this study, we aim to investigate factors that regulate ANP32A expression since such knowledge may lead to the identification of specific novel targets for OA therapy.

Methods: A bioinformatic analysis pipeline was applied to identify potential regulatory factors of ANP32A expression. We then investigated two selected pathways *in vitro*, using pharmacological compounds and incubation in a hypoxia chamber in the human articular chondrocyte cell line C28/I2 and in primary human articular chondrocytes (hACs). The effects on ANP32A expression were evaluated using RT-qPCR and Western blot analysis. For *in vivo* validation, we performed immunohistochemistry to determine ANP32A protein levels in several mouse models.

Results: The bioinformatic analysis pipeline identified the Wnt signaling pathway and the hypoxia pathway as likely regulatory pathways of ANP32A expression. Wnt hyper-activation is known to contribute to OA (4). We found that Wnt hyper-activation with CHIR99021 decreased ANP32A expression at the mRNA level and at the protein level in hACs. *In vivo*, ANP32A protein expression was decreased in *Frzb* knockout mice and wild-type mice that were treated with CHIR99021 intra-articularly (two Wnt gain-of-function mouse models). ANP32A protein levels increased in wild-type mice upon intra-articular injection of the Wnt inhibitor XAV939. In healthy conditions, cartilage is in hypoxic status but in OA, hypoxia is lost (5). Treatment with the hypoxia mimetic IOX2 and incubation in a hypoxia chamber increased ANP32A expression *in vitro* in both the C28/I2 cell line and in hACs. *In vivo*, ANP32A expression was increased in wild-type mice treated with the hypoxia mimetic IOX2 intra-articularly after induction of OA by destabilization of the medial meniscus (DMM).

Conclusion: Limiting activation of Wnt signaling and maintaining the homeostatic hypoxic environment within the joint are strategies to sustain ANP32A levels and its protective effect against the development of osteoarthritis.

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POS0229 ELUCIDATING THE MECHANISM OF ACTION DOWNSTREAM OF ROR2 BLOCKADE: A PHOSPHOPROTEOMIC APPROACH

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Background: Osteoarthritis (OA) affects 12% of the population, and yet we still have no disease-modifying treatment. Cartilage breakdown is the hallmark of OA, and patients suffer from pain and loss of joint function/independence, severely affecting quality of life. Therefore, there is a huge unmet clinical need.
Receptor tyrosine kinase–like orphan receptor 2 (ROR2) is a non-canonical WNT receptor that regulates the planar cell polarity pathway, controlling limb outgrowth. During skeletal development chondrocytes require ROR2 to undergo hypertrophy in the process of endochondral bone formation (1). Loss of function mutations in humans causes Recessive Robinow Syndrome (limb shortening and brachydactyly (2,3)).
Although absent from healthy adult articular cartilage, our initial studies identified high ROR2 expression in chondrocytes from patients with OA, suggesting a role in the disease process.
In a murine model of OA, blocking ROR2 in therapeutic regime using siRNA resulted in reduced cartilage destruction and rapid and sustained pain relief. Due to the limited expression pattern of ROR2 in adulthood, no systemic or local toxicity were expected, nor were any observed. We also found that blocking ROR2 supports cartilage formation in a human cartilage organoid model in nude mice using chondrocytes from patients with OA, and proposed ROR2 blockade as a potential disease-modifying OA treatment.
The mechanism of action of ROR2 blockade was independent of modulation of canonical WNT signaling. YAP inhibition was required, but not sufficient, for the chondrogenic effect (4). Therefore, additional, yet unknown mechanisms must be involved downstream of ROR2 blockade.
Objectives: To study the phosphorylation events downstream of ROR2, to further our understanding of the mechanism of action of ROR2 blockade.
Methods: Phosphoproteomics (label free liquid chromatography tandem-mass spectrometry with TiO2 based phospho-enrichment), in vitro studies in cells, CRISPR.
Results: WNT5A is the most well established ligand for ROR2. We confirmed that WNT5A stimulation leads to time-dependent phosphorylation of ERK in C3H10T1/2 cells.
We then deleted ROR2 in C3H10T1/2 cells by CRISPR, and performed phosphoproteomics analysis on wildtype (control) C3H10T1/2 cells and ROR2-CRISPR C3H10T1/2 cells stimulated with 100ng/ml recombinant WNT5A for 5 or 15 minutes.
ROR2-dependant phosphorylation targets were defined as proteins differentially phosphorylated in control cells upon WNT5A stimulation, but that did not occur in ROR2-CRISPR cells.
YAP was phosphorylated by WNT5A in a ROR2-dependant manner. WNT5A/ROR2 also modulated the YAP signaling pathway at other levels.
KEGG analysis revealed that other pathways with known roles in the pathogenesis of OA were enhanced, including NF-KB, mTOR signaling and cellular senescence.
With the current technology, ROR2 blockade requires intra-articular injections of siRNA conjugated to atelocollagen every 5 days. Preliminary efficacy data of potentially longer-acting ROR2 blockers are promising.
Conclusion: ROR2 blockade has potential as a disease-modifying treatment for OA, resulting in cartilage protection and rapid and sustained pain relief in a murine model. Here, we studied the mechanism downstream of ROR2 blockade using a phosphoproteomics approach. We confirmed that YAP signaling was modulated by ROR2, and identified novel pathways and cellular processes regulated by WNT5A/ROR2. Further studies are needed to clarify their role downstream of ROR2 blockade in OA.
Our current siRNA-atelocollagen based technology requires intra-articular injections too frequently to be acceptable for patients. We are developing ROR2 blockade which can be administered systemically or intra-articularly not more often than every 3 months.
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POS0230 THE MIR-320 FAMILY IS UPREGULATED IN FAST-PROGRESSING RADIOGRAPHIC KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: There is an outstanding need for prognostic biomarkers to reliably detect fast-progressing knee osteoarthritis (OA) such that preventative interventions can be targeted to this patient population. MicroRNA-sequencing is an unbiased approach for comprehensive profiling of circulating microRNAs in liquid biopsies to discover novel biomarkers of disease. As negative regulators of gene expression, microRNAs hold potential not only as biomarkers, but also as mechanistic drivers of knee OA.
Objectives: To apply microRNA-sequencing to identify unique circulating microRNAs as potential biomarkers that distinguish fast-progressing radiographic knee OA from both slow- and non-progressing radiographic knee OA.
Methods: Leveraging the Osteoarthritis Initiative (OAI) longitudinal cohort, we applied our customized microRNA-sequencing pipeline [1] to blood plasma samples collected at both baseline and 4-year follow-up from 106 participants. The disease trajectory for each participant was constructed by plotting their Kellgren-Lawrence (KL) grades over an 8-year follow-up period. Based on these trajectories, we defined fast-progression as an increase from KL 0/1 at baseline to KL 3/4 by 4-year follow-up, slow-progression as an increase from KL 0/1 at baseline to KL 2/3/4 by 8-year follow-up, and non-progression as no increase from KL0/1 at baseline throughout the 8-year follow-up. Following differential expression analysis, we assessed predictive performance and identified putative gene targets for prioritized microRNAs.
Results: Comparing fast-progressors to both slow-progressors and non-progressors, we identified differentially expressed microRNAs within timepoints (i.e., 48 microRNAs at baseline and 2 microRNAs at 4-year follow-up) and across timepoints. Among these microRNAs were four members of the miR-320 family, with miR-320d showing an increase in fast-progressors at both timepoints, compared to both slow- and non-progressors. The predictive models we constructed included miR-320 members and had good accuracy (area under the receiver operating characteristic curves ranging from 82.6 to 91.9) in distinguishing fast-progressors. Putative gene targets of the miR-320 family included members of the 14-3-3 gene family (Table 1), including *YWHAE*, whose downregulation in OA cartilage was reported to promote deterioration [2].

Table 1. Predicted gene targets of the miR-320 family include members of the 14-3-3 gene family.

14-3-3 gene family member	hsa-miR-320b	hsa-miR-320c	hsa-miR-320d	hsa-miR-320e
SFN	M	M	M	L
YWHAB	M	M	M	M
YWHAE	V	**V**	V	**H**
YWHAG	V	V	V	M
YWHAH	**V**	**V**	**V**	M
YWHAQ	**V**	**V**	**V**	M
YWHAZ	**V**	**V**	**V**	M

All mirDIP results with bold text indicating the prediction was among the top 1% for that microRNA/gene target pair. Letters denote the mirDIP score class with V=very high, H=high, M=medium, and L=low.

Conclusion: This microRNA-sequencing study is the first of its kind, profiling circulating microRNAs at two timepoints in 106 participants with data-driven construction of knee OA trajectories. We identify the miR-320 family of microRNAs to be associated with fast-progressing radiographic knee OA over time. While our data suggest this microRNA family could have applications as prognostic biomarkers for knee OA, and could be regulating gene targets to impact OA severity, validation of these findings in independent longitudinal cohorts is required.
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POS0231 GENETIC BIOMARKERS, SNP GENES AND MTDNA HAPLOGROUPS, PREDICT OSTEOARTHRITIS STRUCTURAL PROGRESSORS THROUGH THE USE OF SUPERVISED MACHINE LEARNING

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Background: Knee osteoarthritis is the most prevalent chronic musculoskeletal debilitating disease. Current treatments are only symptomatic and to improve this, we need a robust prediction model to stratify patients at an early stage according to the risk of joint structure disease progression. Some genetic factors, including single nucleotide polymorphism (SNP) genes and mitochondrial (mt) DNA haplogroups/clusters, have been linked to this disease.
Objectives: For the first time, we aim to determine, by using machine learning, whether some SNP genes and mtDNA haplogroups/clusters alone or combined could predict early knee osteoarthritis structural progressors.
Methods: Participants (901) were first classified for the probability of being structural progressors. Genotyping included SNP genes TP63, FTO, GNL3, DUS4L, GDF5, SUPT3H, MCF2L, TGFA, mtDNA haplogroups H, J, T, Uk, others, and clusters HV, TJ, KU, C-others. They were considered for prediction with major risk factors of osteoarthritis, namely, age and body mass index (BMI). Seven supervised machine learning methodologies were evaluated. The support vector machine was used to generate gender-based models. The best input combination was assessed using sensitivity and synergy analyses. Validation was performed using 10-fold cross-validation as well as an external cohort (TASOAC).
Results: From 277 models, two were defined. Both used age and BMI in addition for the first one of the SNP genes *TP63, DUS4L, GDF5, FTO* with an accuracy of 85.0%; the second profits from the association of mtDNA haplogroups and SNP genes *FTO* and *SUPT3H* with 82.5% accuracy. The highest impact was associated with the haplogroup H, the presence of CT alleles for rs8044769 at *FTO*, and the absence of AA for rs10948172 at *SUPT3H*. Validation accuracy with the cross-validation (about 95%) and the external cohort (90.5%, 85.7%, respectively) was excellent for both models.
Conclusion: This study introduces a novel source of decision support in precision medicine in which, for the first time, two models were developed consisting of i) age, BMI, TP63, DUS4L, GDF5, FTO and ii) the optimum one as it has one less variable: age, BMI, mtDNA haplogroup, FTO, SUPT3H. Such a framework is translational and would be of benefit to patients at risk of structural progressive knee osteoarthritis.
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POS0232 IDENTIFICATION OF THE CORE REGULATORY GENE NETWORKS REGULATING SUBCHONDRAL BONE AND MARROW ADIPOSE TISSUE REMODELING IN HUMAN KNEE OA

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Background: Subchondral bone and the marrow adipose tissue (BMAT) contained therein undergo elevated turnover and remodeling during progression of osteoarthritis (OA). BMAT changes, detected as bone marrow lesions (BML) on MRI images, are considered important diagnostic and prognostic imaging biomarkers for OA. However, a comprehensive understanding of the regulatory mechanisms in individual BMAT-resident cell populations that mediate marrow fibrosis and subchondral bone sclerosis is still lacking. Recently generated single-cell transcriptomic atlas of human adipose tissue has opened new avenues for computational bulk tissue cell type deconvolution and dissecting gene regulatory networks.
Objectives: To infer core gene regulatory networks underlying subchondral bone sclerosis and BMAT remodeling in human knee OA.
Methods: We conducted comparative transcriptomics on bulk transcriptomic profiles of human subchondral bone tissue from three independent studies[1,2,3] comprising tibial plateaus from non-OA controls (*n*=20) and BMLs (*n*=14), non-sclerotic (*n*=45) and sclerotic (*n*=45) regions from patients with medial knee OA. Cell type deconvolution (adipocyte/pre-adipocyte/fibroblast/endothelial/macrophage) of differentially expressed genes (DEGs) was performed using single-cell atlases of human brown and white adipose tissue[4]. Cell type annotated DEGs were functionally annotated using Gene Ontology enrichment. To infer transcription factors (TFs) regulating gene networks we performed ChIP-Seq enrichment analyses and assessed the presence of TF binding sites in the proximal promoter (-500/+100) sequence of DEGs. Tissue explants were stained en bloc with Oil red O and Hoechst to evaluate distribution of neutral lipids and nuclei in BMAT from non-sclerotic and sclerotic regions.
Results: 534 upregulated and 363 downregulated DEGs were shared between at least two independent datasets. Cell deconvolution revealed the majority of upregulated DEGs were expressed in fibroblasts (38%), pre-adipocytes (27%) and endothelial cells (22%). Dowregulated DEGs were predominantly expressed by endothelial (31%), adipocyte (25%) and fibroblast (16%) cell populations. We inferred major TF regulatory networks driving upregulated DEGs in pre-adipocytes (*PRRX1*/*SNAI2*/*TWIST1*) and fibroblasts (*SP7*/*SMAD4*/*RUNX2*/*DLX5*) and loss of *PPARG*/*SOX17*/*SNAI1*-driven gene expression in adipocytes and endothelial cells. Pre-adipocyte genes were functionally enriched for collagen fibril organization, ossification and cell migration. Fibroblast genes associated with biomineral tissue development and negative regulation of angiogenesis. Downregulated DEGs were enriched for triglyceride catabolism and sequestration (adipocytes) and regulation of vascular permeability and endothelial cell differentiation (endothelial). Whole mount staining displayed homogenous distribution of neutral lipids in adipocytes and low cell abundance in BMAT from non-sclerotic tissue. In contrast, BMAT from sclerotic tissue showed heterogeneously distributed and lower neutral lipid content as well as high cell abundance (Figure 1).

Figure 1.

Conclusion: These data provide detailed insight into the cellular and molecular mechanisms underpinning subchondral bone and BMAT remodeling in OA. An expansion of pre-adipocyte populations along altered function of BMAT adipocytes might represent a previously unrecognized mechanism regulating subchondral bone sclerosis. TFs driving core gene regulatory networks might be promising therapeutic targets for knee OA.

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POS0233 COMPARISON OF 3D QUANTITATIVE OSTEOARTHRITIS IMAGING BIOMARKERS: A STUDY USING PAIRED CT AND MR IMAGES FROM THE IMI-APPROACH STUDY.

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Background: MRI bone surface area and femoral bone shape (B-score) measures have been employed as quantitative endpoints in DMOAD clinical trials. The B-score (typical range -2 to +7) has been shown to be an objective, automated assessment of OA status, with clinical risk defined for current and future pain, functional limitation and total knee replacement. Computerized Tomography (CT) imaging is more commonly used for 3D visualization of bony anatomy due to its high bone-soft tissue contrast. Also, CT images are not subject to the geometric distortion in MR images due to field inhomogeneities, a problem addressed in DMOAD clinical trials by positioning the knee near the magnet isocenter. Measurement of 3D joint space width (3DJSW) has been previously reported using CT images but is possible from MR images.

Objectives: To test the robustness of the B-score, bone area and 3DJSW imaging endpoints to the choice of imaging modality, we compared the results of automated analysis of CT and MR image pairs acquired at baseline and 24-month timepoints.

Methods: We used image data from the IMI-APPROACH exploratory, 2-year prospective cohort study. High resolution CT images were acquired at baseline and 24-months. These were matched with 3D T1w MR images with fat-sat or WE sequences. CT and MR images were acquired within a mean of 12 days of each other. Additional test-retest MR images with repositioning were available from 37 subjects. Kellgren-Lawrence Grades (KLG) were read centrally from screening weight-bearing x-rays.

Femur and tibia bones were automatically segmented with sub-voxel accuracy from CT or MR images using active appearance models, a machine learning model trained to search images (Imorphics, Manchester, UK). Bone area measurement was produced for MF.tAB, LF.tAB, MT.tAB and LT.tAB regions. Average 3DJSW was measured in central regions of the medial or lateral tibial plateaus, normal to the tibial surface

Linear regression was used to test for correlation between measures. Limits of agreement and systematic bias were tested using Bland-Altman analysis. Smallest detectable difference (SDD) for MR B-score was computed from test-retest image pairs using Bland-Altman analysis. Images acquired from the same subject at both baseline and 24-month timepoints were treated as independent.

Results: Baseline and 24-month CT-MR pairs of the same knee were available from 231 and 203 subjects respectively. 338 were female knees (78%). KLG was KLG0 (19%); KLG1 (31%); KLG2 (30%); KLG3 (16%); KLG4 (3%) with 5 knees ungraded (1%). SDD of the B-score measure was 0.227. Table 1 presents summary statistics for shape, area, and 3D JSW measures. Figure 1 shows linear regression and Bland-Altman analysis for B-score.

Table 1. Bland-Altman and linear regression statistics.

Measure	Bias [95% CI]	Limits of Agreement	R^2
B-score	0.10 [0.05, 0.14]	-0.90, 1.10	0.94
MF.tAB (mm^2)	-54.983 [-61.22, -48.75]	-184.52, 74.56	0.96
LF.tAB (mm^2)	-42.792 [-47.02, -38.57]	-130.56, 44.98	0.97
MT.tAB (mm^2)	-5.86 [-9.24, -2.48]	-76.00, 64.38	0.96
LT.tAB (mm^2)	-21.33 [-23.90, -18.77]	-74.66, 32.00	0.97
Med 3DJSW (mm)	1.04 [0.98, 1.11]	-0.32, 2.40	0.58
Lat 3DJSW (mm)	0.42 [0.34, 0.51]	-1.30, 2.14	0.47

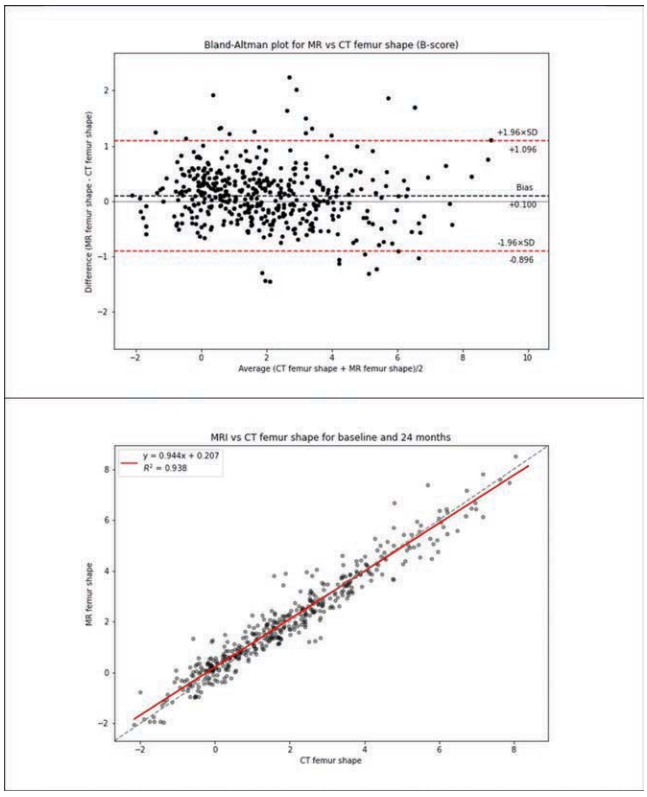

Figure 1. B-score. Top: Bland-Altman plot; Bottom: linear regression

Conclusion: B-score measures were highly correlated with CT and showed good agreement with a relatively small bias of 0.1 suggesting that B-score may be measured reliably using either modality. All 4 area measures were highly correlated and showed negative bias (MR smaller); it is likely that the bone surface identified using MR and CT will be at slightly different positions within the bone/cartilage boundary. A consistent negative bias suggests the MR bone boundary is inside the CT boundary. This is consistent with the positive bias in favour of MR for 3DJSW. However, the MR-CT difference for medial 3DJSW is larger than for lateral 3DJSW, possibly due to a difference in knee pose during acquisition (fully extended for CT, flexed for MR) – the tibia is more externally rotated with respect to the femur in the fully extended knee.

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Disclosure of Interests: Alan Brett Shareholder of: Stryker Corporation, Employee of: Stryker Corporation, Michael A Bowes Shareholder of: Stryker Corporation, Employee of: Stryker Corporation, Philip G Conaghan Speakers bureau: AbbVie, Amgen, Contura, Galapagos, Consultant of: AbbVie, Eli Lilly, Galapagos, GSK, Grunenthal, Novartis, Pfizer, UCB

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Rheumatoid arthritis: JAKi and beyond

POS0234 HOW CLOSELY DO GERMAN RHEUMATOLOGISTS FOLLOW THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS WHEN MAKING THERAPEUTIC DECISIONS?

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Background: EULAR developed recommendations for the management of rheumatoid arthritis (RA) suggesting treatment escalation and changes at different stages of the disease to reach at least low disease activity with latest updates in 2013[(1)], 2016[(2)], and 2019[(3)]. The recommendation to *consider adding* a biologic disease-modifying anti-rheumatic drug (bDMARD) – or, since 2016, a Januskinase inhibitor (JAKi) – after the first conventional synthetic (cs) DMARD had failed and if poor prognostic factors (PPF) are present, was strengthened 2019. Since then, it is recommended that a bDMARD or a tsDMARD *should be added*.

Table 1. Number and percentages of treatment changes at different stages of the disease.

Patients with	1 previous csDMARD & no PPF	1 previous csDMARD & ≥1 PPF	2 previous csDMARDs	1 previous bDMARD/ JAKi	≥2 previous bDMARDs/ JAKi
EULAR Recommendation	change/add csDMARD	add bDMARD/ JAKi**	add bDMARD/ JAKi	change to another bDMARD/JAKi	
Total numbers of treatment changes	61	2073	2220	1700	1863
Period [I] 01/2014 – 12/2016* N=2,922	n=25	n=848	n=986	n=543	n=520
csDMARD	21 (84.0%)	594 (70.0%)	134 (13.6%)	199 (36.6%)	275 (52.9%)
bDMARD	4 (16.0%)	254 (30.0%)	852 (86.4%)	344 (63.4%)	245 (47.1%)
Period [II] 01/2017 – 06/2020 N=4,580	n=32	n=1,090	n=1,136	n=1,054	n=1,268
csDMARD	16 (50.0%)	469 (43.0%)	96 (8.5%)	261 (24.8%)	274 (21.6%)
bDMARD	13 (40.6%)	509 (46.7%)	822 (72.4%)	403 (38.2%)	288 (22.7%)
JAKi	3 (9.4%)	112 (10.3%)	218 (19.2%)	390 (37.0%)	706 (55.7%)
Period [III] 07/2020 – 04/2021 N=415	n=4	n=135	n=98	n=103	n=75
csDMARD	0	43 (31.9%)	7 (7.1%)	15 (14.6%)	9 (12.0%)
bDMARD	1 (25.0%)	64 (47.4%)	60 (61.2%)	36 (35.0%)	23 (30.7%)
JAKi	3 (75.0%)	28 (20.7%)	31 (31.6%)	52 (50.5%)	43 (57.3%)

*EULAR treatment recommendations are indicated in green. *JAKi were not available. **Recommendation in period [I]: Addition of a bDMARD should be considered; in [II]: Addition of a bDMARD or a tsDMARD should be considered, current practice would be to start a bDMARD; in [III]: a bDMARD or a tsDMARD should be added. PPF, poor prognostic factor.*

Objectives: How closely are EULAR recommendations followed in daily rheumatologic practice in Germany?

Methods: Data were used from the long-term observational cohort RABBIT, which enrols patients with RA starting a bDMARD or JAKi, or a csDMARD after at least one previous csDMARD failure. According to the publication of the recommendations, periods from [I] 01/2014 – 12/2016, [II] 01/2017 – 06/2020 and [III] 07/2020 – 04/2021 were investigated. Patients who were in at least moderate disease activity (DAS28≥3.2) were selected and analysed, if they started a csDMARD, a bDMARD or a JAKi. Patients were further stratified by prior treatments and by the presence of PPF (≥4 swollen joints, positive rheumatoid factor or ACPA, erosions).

Results: Of the 15,150 patients with RA enrolled since 2007, 2,922 treatments were initiated in period [I], 4,580 in [II] and 415 in [III] (see Table 1). The proportion of patients with 1 previous csDMARD and ≥1 PPF who – in agreement with the recommendations – switched to bDMARD or JAKi, increased from 30% (only bDMARDs) in period [I] to 68% (bDMARDs + JAKi) in [III]. The proportions were even higher in patients with 2 previous csDMARDs (86% in [I], 93% in [III]). As recommended, JAKi were used more often as first line therapy (after csDMARD) in period [III].

Conclusion: JAKi have become more established, especially in bionaive patients, but have not reached the significance of biologics in certain patient groups. The early decision for a bDMARD or JAKi has been made more frequently in recent years, yet one third of patients did not receive the recommended treatment escalation. We cannot conclude from the data, which considerations led to the decision not to escalate. Of note, German rheumatologists should rather follow the German treatment guidelines[(4)], which are, however, very similar to the EULAR recommendations.

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[1] *PMID: 24161836;*
[2] *PMID: 28264816;*
[3] *PMID: 31969328;*
[4] *PMID: 29968101*

Acknowledgements: RABBIT is supported by a joint, unconditional grant from AbbVie, Amgen, BMS, Fresenius-Kabi, Galapagos, Hexal, Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis, VIATRIS and UCB.

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POS0235 INTEGRATED SAFETY ANALYSIS UPDATE FOR FILGOTINIB (FIL) IN PATIENTS (PTS) WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS (RA) RECEIVING TREATMENT OVER A MEDIAN OF 2.2 YEARS (Y)

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Background: The preferential Janus kinase-1 inhibitor FIL significantly improved signs and symptoms of RA in Phase 2 and 3 trials.[1–5] FIL is approved for treatment of moderate to severe active RA in Europe and Japan. Integrated safety analysis of FIL with patient data through 2019 was presented at the 2020 ACR virtual meeting.[6]

Objectives: To report updated, as-treated data from the FIL integrated safety analysis with increased study drug exposure.

Methods: Data were integrated from 2 Phase 2 (NCT01668641, NCT01894516), 3 Phase 3 (NCT02889796, NCT02873936, NCT02886728), and 2 long-term extension (LTE) (NCT02065700, NCT03025308) trials. Phase 2 and 3 LTE data were through Nov 2020 and Jan 2021, respectively. The as-treated analysis set included all available data for pts receiving ≥1 dose FIL 200 (FIL200) or 100 mg

Table 1. TEAEs of special interest, as-treated set

TEAE, n (%) and EAIR per 100 PYE (95% CI)	FIL 200 mg n=2267 PYE=5302.5	FIL 100 mg n=1647 PYE=2782.6	Total FIL N=3691 PYE=8085.1
Infectious AEs	1206 (53.2)	747 (45.4)	1927 (52.2)
EAIR	21.1 (19.7, 22.5)	30.2 (26.8, 34.0)	21.0 (19.9, 22.3)
Serious infectious AEs	80 (3.5)	57 (3.5)	137 (3.7)
EAIR	1.5 (1.1, 1.9)	2.7 (1.9, 3.9)	1.6 (1.3, 2.0)
Opportunistic infections	5 (0.2)	4 (0.2)	9 (0.2)
EAIR	0.1 (0, 0.2)*	0.1 (0.1, 0.4)*	0.1 (0.1, 0.2)*
Active tuberculosis	0	3 (0.2)	3 (<0.1)
EAIR	0	0.1 (0, 0.3)*	0 (0, 0.1)*
Herpes zoster	84 (3.7)	30 (1.8)	114 (3.1)
EAIR	1.6 (1.2, 2.0)	1.1 (0.8, 1.5)*	1.4 (1.1, 1.7)
Major adverse cardiovascular events[a]	19 (0.8)	14 (0.9)	33 (0.9)
EAIR	0.3 (0.2, 0.5)	0.5 (0.3, 0.8)*	0.4 (0.2, 0.6)
Venous thromboembolism[b]	11 (0.5)	4 (0.2)	15 (0.4)
EAIR	0.2 (0.1, 0.4)*	0.1 (0.1, 0.4)*	0.2 (0.1, 0.3)*
Atrial systemic thrombotic events[a]	1 (<0.1)	1 (<0.1)	2 (<0.1)
EAIR	0 (0, 0.1)	0 (0, 0.3)	0 (0, 0.1)
Malignancy excluding NMSC	32 (1.4)	17 (1.0)	49 (1.3)
EAIR	0.6 (0.4, 0.9)	0.6 (0.4, 1.0)*	0.6 (0.4, 0.8)
NMSC	15 (0.7)	5 (0.3)	20 (0.5)
EAIR	0.3 (0.2, 0.5)*	0.2 (0.1, 0.4)*	0.2 (0.2, 0.4)*
Gastrointestinal perforations	3 (0.1)	1 (<0.1)	4 (0.1)
EAIR	0.1 (0, 0.2)*	0 (0, 0.3)*	0 (0, 0.1)*

*Except when any study had 0 event within the treatment, the Poisson model was not adjusted by study. PYE was defined as (last dose date – first dose date + 1)/365.25.
[a]Positively adjudicated.
[b]Adjudicated as deep vein thrombosis or pulmonary embolism.
NMSC, nonmelanoma skin cancer

(FIL100), including those rerandomized to FIL for LTE. Exposure-adjusted incidence rates (EAIR)/100 patient-y exposure (PYE) of treatment-emergent adverse events (TEAEs; onset after first dose and no later than 30 days after last dose or new drug first dose date –1 day) and TEAEs of special interest (AESIs) are presented.

Results: 3691 pts received FIL200 or FIL100 for 8085.1 PYE (median 2.2, maximum 6.8 y). In the as-treated set, 61% of FIL200 and 45% of FIL100 pts received FIL for ≥2 y, 19% and 5% for ≥3 y, and 11% and 0.5% for ≥4.5 y, respectively. EAIR for TEAEs was higher with FIL100 than FIL200; EAIRs for deaths were 0.5 and 0.3 for FIL200 and FIL100 (Figure 1). Incidences of infections and serious infections were numerically greater for FIL100 vs FIL200, while EAIRs for other AESIs were comparable between doses (Table 1). EAIRs for AESIs tended to decrease since the previous update, except for venous thromboembolism (total FIL 0.1 to 0.2) and malignancies excluding NMSC (total FIL 0.5 to 0.6).

Conclusion: With 1 additional year of exposure since the 2020 report, FIL continues to be well tolerated with no new safety concerns emerging. EAIRs of TEAEs, including deaths, and AESIs remained stable or decreased since the 2020 report, except for slight increases in rates of NMSC and malignancies excluding NMSC. In the context of demonstrated efficacy, both FIL doses had an acceptable risk/benefit profile.

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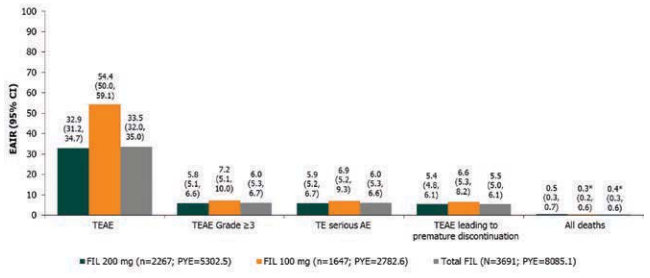
Figure. Overall summary of EAIRs of TEAEs (as-treated set)



EAIRs and 95% CIs were estimated with Poisson models. with treatment and study as covariates and natural log of exposure as offset, unless otherwise specified. *Except when any study had 0 event within the treatment, the Poisson model was not adjusted by study. PYE was defined as (last dose – first dose date +1)/365.25. AE, adverse event; CI, confidence interval; EAIR exposure-adjusted incidence rate per 100 PYE; FIL, filgotinib; PYE, patient-years of exposure; TE, treatment-emergent; TEAE, treatment-emergent adverse event

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Disclosure of Interests: Kevin Winthrop Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly and Co., Galapagos NV, Gilead Sciences, Inc., GlaxoSmithKline, Pfizer, Roche, Regeneron, Sanofi, and UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, and Pfizer, Yoshiya Tanaka Speakers bureau: Daiichi-Sankyo, Eli Lilly, Novartis, YL Biologics, Bristol Myers Squibb, Eisai, Chugai, AbbVie, Astellas, Pfizer, Sanofi, Asahi-Kasei, GSK, Mitsubishi-Tanabe, Gilead Sciences, Inc., and Janssen, Consultant of: AbbVie, Ayumi, Daiichi-Sankyo, Eli Lilly, GSK, Taisho, and Sanofi, Grant/research support from: AbbVie, Asahi-Kasei, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, and Takeda, Tsutomu Takeuchi Speakers bureau: AbbVie, AYUMI, Bristol Myers Squibb, Chugai, Daiichi Sankyo, Dainippon Sumitomo, Eisai, Eli Lilly Japan, Gilead Sciences, Inc., Mitsubishi-Tanabe, Novartis, Pfizer Japan, and Sanofi, Consultant of: Astellas, Chugai, and Eli Lilly Japan, Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi Sankyo, Eisai, Mitsubishi-Tanabe, Shionogi, Takeda, and UCB Japan, Alan Kivitz Shareholder of: Amgen, Gilead Sciences, Inc., GlaxoSmithKline, Pfizer, and Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, and Sanofi, Paid instructor for: Celgene, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, and Sanofi, Consultant of: AbbVie, Boehringer Ingelheim, Flexion, Genzyme, Gilead Sciences, Inc., Janssen, Novartis, Pfizer, Regeneron, Sanofi, and SUN Pharma Advanced Research, Mark C. Genovese Shareholder of: Gilead Sciences, Inc., Consultant of: AbbVie, Amgen, Beigene, Eli Lilly and Co., Genentech, Inc., Gilead Sciences, Inc., Sanofi Genzyme, RPharm, and SetPoint, Employee of: Gilead Sciences, Inc., Alena Pechonkina Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Franziska Matzkies Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Beatrix Bartok Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Kun Chen Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Deyuan Jiang Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Iyabode Tiamiyu Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Robin Besuyen Shareholder of: Galapagos BV, Employee of: Galapagos BV, Sander Strengholt Shareholder of: Galapagos BV, Employee of: Galapagos BV, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Eli Lilly and Co., Galapagos, Gilead Sciences, Inc., and Pfizer, Consultant of: AbbVie, Eli Lilly and Co., Galapagos, Gilead Sciences, Inc., and Pfizer, Jacques-Eric Gottenberg Speakers bureau: AbbVie, Eli Lilly and Co., Galapagos BV, Gilead Sciences, Inc., Roche, Sanofi Genzyme, and UCB, Consultant of: Bristol Myers Squibb, Sanofi Genzyme, and UCB, Grant/research support from: Bristol Myers Squibb and Pfizer

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POS0236 SAFETY AND EFFICACY OF NEUROSTIMULATION WITH A MINIATURIZED VAGUS NERVE STIMULATION DEVICE IN PATIENTS WITH MULTIDRUG-REFRACTORY RHEUMATOID ARTHRITIS: 24-WEEK FOLLOW-UP OF A RANDOMIZED CONTROLLED FIRST-IN-HUMAN TRIAL

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Background: Vagus nerve stimulation (VNS) activates innate neuroimmune reflexes that have been shown to reduce pro-inflammatory cytokines and clinical disease activity in subjects with rheumatoid arthritis (RA).[1] We previously reported primary clinical outcomes from a first-in-human, double-blind study of a novel, implanted VNS device called a MicroRegulator (MR). That study showed 5/10 subjects with drug-refractory RA met or exceeded the minimal clinically important difference (MCID) in DAS28-CRP; 2 subjects achieved DAS28 remission (DAS28-CRP < 2.6); and pro-inflammatory cytokines were decreased by >30% following 12 weeks of VNS.[2] We now report 24-week efficacy and safety findings from this study.

Objectives: Determine the long-term safety and exploratory efficacy of neurostimulation using a novel, miniaturized VNS device in patients with multiple drug refractory RA who were previously enrolled in a first in human study.

Methods: The primary study enrolled adult patients with active moderate-to-severe RA with incomplete response or intolerability to at least two biologic and/or targeted synthetic DMARDs having at least two different mechanisms of action. The study was enrolled in 2 Stages: Stage 1 (n=3) was open-label, and Stage 2 (n=11) was randomized and sham-controlled (Figure 1). Three weeks after MR implantation, the first 3 subjects in Stage 1 received active VNS for 1 minute, once per day (QD). Following safety review board approval, 11 patients in Stage 2 were implanted with the MR and randomized 1:1:1 into one of two active VNS groups (1 minute of VNS QD or 1 minute of active VNS four times per day [QID]) or a sham group. At Week 12, the blind was lifted, sham subjects were re-randomized and crossed over to either QD or QID active VNS dosing, and all actively treated subjects remained on their dosing through Week 24. Safety and tolerability were determined, and several secondary efficacy endpoints were evaluated measuring the change in disease activity from the start of active VNS to Week 24.

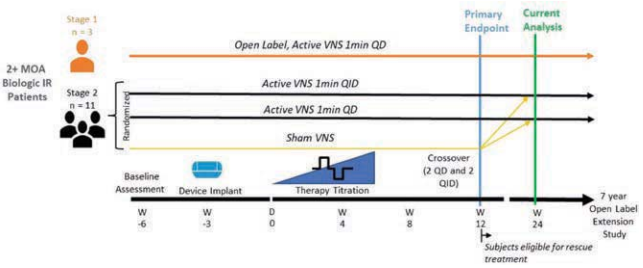

Figure 1. Study Schematic

Results: There were no device-related adverse events from Week 12 through Week 24. Improvement in clinical disease activity was sustained through Week 24: 5/9 patients within the original, active VNS treatment groups met or exceeded

EULAR response criteria for DAS28-CRP at Week 24 (Table 1) vs. 5/10 at Week 12 (one Week 12 responder was lost to follow-up). Similarly, 6/9 patients in the original, active VNS treatment groups met or exceeded the MCID in CDAI at Week 24 vs. 5/10 at Week 12. In the long-term extension, 1/4 sham crossover patients had both EULAR and CDAI response after 12 weeks of VNS (1/2 QD, 0/2 QID). Co-therapy with a b/tsDMARD was initiated in 2 subjects (Table 1). One crossover subject was treated with oral methylprednisolone at week 19 due to worsening RA disease activity. VECTRA composite scores and component analysis revealed an 18-point decrease in median multi-analyte disease activity index in the QD group over 24 weeks of VNS with a decrease in serum levels of several analytes in key component categories (IL-6, serum amyloid A, and VCAM-1). Erosion progression by hand MRI was stabilized or decreased in all but 1 of the stimulated patients at Week 24.

Table 1. Change in DAS28-CRP at Week 24

Subject	Treatment	DAS28-CRP (MCID -1.2) *added b/tsDMARD co-therapy
005-01	QD	-2.4
005-03	QD	-2.21
006-01	QD	-0.07
002-01	QD	-4.95 *
005-06	QD	-0.72 *
006-03	QID	-0.69
008-01	QID	0.49
008-03	QID	-3.14
008-04	QID	1.43
005-05	Sham to QD	0.39
006-04	Sham to QD	-0.78
006-02	Sham to QID	-0.22
008-02	Sham to QID	-0.09

Conclusion: Improvements in clinical disease activity and pro-inflammatory cytokine suppression were maintained through 24 weeks of VNS treatment. Safety outcomes continue to support the risk/benefit profile of VNS as a treatment option for patients with multiple-drug refractory RA.

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POS0237

MAJOR ADVERSE CARDIOVASCULAR EVENTS, MALIGNANCIES AND VENOUS THROMBOEMBOLISM BY BASELINE CARDIOVASCULAR RISK: A POST HOC ANALYSIS OF ORAL SURVEILLANCE

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Background: ORAL Surveillance was a post-authorisation safety study of tofacitinib vs TNF inhibitors (TNFi) in rheumatoid arthritis (RA) patients (pts) aged ≥50 yrs with ≥1 additional cardiovascular (CV) risk factor and an inadequate response to methotrexate (MTX). CV disease has overlapping risk factors with malignancies and venous thromboembolism (VTE), including older age, smoking, hypertension and diabetes.[1,2]

Objectives: To evaluate the impact of pts' baseline (BL) CV risk on the incidence and risk of major adverse CV events (MACE), malignancies and VTE in ORAL Surveillance.

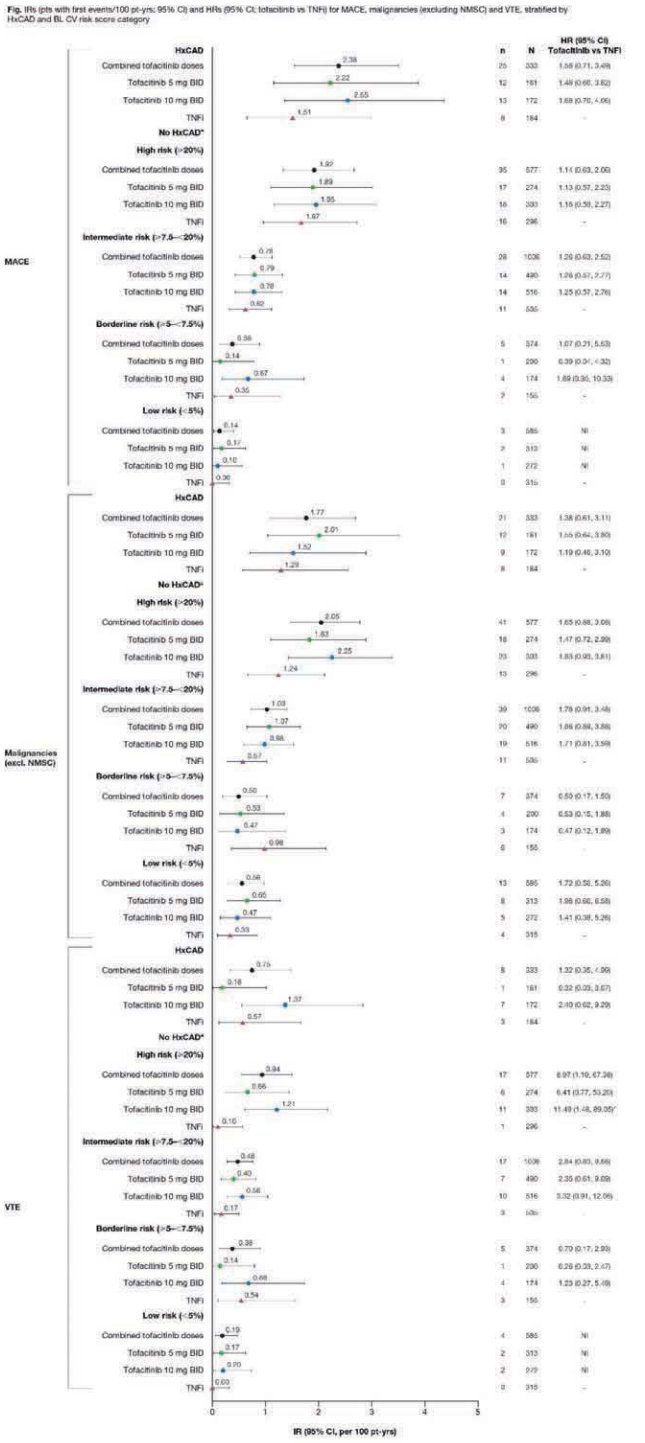
Methods: Pts on stable MTX were randomised 1:1:1 to receive tofacitinib 5 or 10 mg twice daily (BID) or a TNFi (adalimumab 40 mg every 2 weeks or etanercept 50 mg once weekly). Incidence rates (IRs; pts with first events/100 pt-yrs) and hazard ratios (HRs; tofacitinib vs TNFi) were evaluated for adjudicated MACE (defined as CV death [excluding CV death due to pulmonary embolism (PE)], non-fatal MI and non-fatal stroke), malignancies (excluding NMSC) and VTE (including fatal/non-fatal deep vein thrombosis and PE). Across safety outcomes, IRs/HRs were stratified by BL CV risk score: pts were first categorised by history of coronary artery disease (HxCAD); pts without a HxCAD were further stratified by BL CV risk score categories (high [≥20%], intermediate [≥7.5–<20%], borderline [≥5–<7.5%] and low [<5%] risk), with a 1.5 multiplier applied per EULAR recommendations.[3]

Results: 4362 pts were included: tofacitinib 5 mg BID, n=1455; tofacitinib 10 mg BID, n=1456; TNFi, n=1451. In these treatment groups, during a median follow-up of 4.0 yrs, MACE was reported in 47 (3.2%), 51 (3.5%) and 37 (2.6%) pts, malignancies in 62 (4.3%), 60 (4.1%) and 42 (2.9%) pts, and VTE in 17 (1.2%), 34 (2.3%) and 10 (0.7%) pts, respectively. Approximately two-thirds of pts had intermediate to high CV risk, or HxCAD, and risk was well-balanced across treatment groups (Table 1). Across treatments, MACE and malignancies IRs were highest in pts with a HxCAD or a high BL CV risk score (Figure 1). IRs/HRs for MACE, malignancies and VTE were generally higher with tofacitinib vs TNFi. Differences between tofacitinib vs TNFi in MACE and malignancy IRs/HRs were typically more pronounced in pts with a HxCAD or at least intermediate BL CV risk score, and less so in pts with lower BL CV risk score (Figure 1). In tofacitinib 10 mg BID-treated pts, VTE IRs/HRs (vs TNFi) were clearly highest in pts with a HxCAD or high BL CV risk score; no association between VTE and BL CV risk scores was observed with tofacitinib 5 mg BID or TNFi (Figure 1).

Table 1. Percentages of pts with a HxCAD and pts without a HxCAD categorised by BL CV risk scores, per ASCVD-PCE risk calculator[4] with a 1.5 multiplier applied[3]

	Tofacitinib 5 mg BID (N=1455)	Tofacitinib 10 mg BID (N=1456)	TNFi (N=1451)
HxCAD, n (%)	161 (11.1)	172 (11.8)	164 (11.3)
No HxCAD: BL CV risk score, per ASCVD-PCE risk calculator, n (%)			
High (≥20%)	274 (18.8)	303 (20.8)	296 (20.4)
Intermediate (≥7.5–<20%)	490 (33.7)	516 (35.4)	505 (34.8)
Borderline (≥5–<7.5%)	200 (13.7)	174 (12.0)	155 (10.7)
Low (<5%)	313 (21.5)	272 (18.7)	315 (21.7)
Missing data	17 (1.2)	19 (1.3)	16 (1.1)

HxCAD is defined as any history of MI, coronary heart disease, stable angina pectoris or coronary artery procedures n, number of pts with specified characteristics; N, number of evaluable pts



Conclusion: In this post hoc analysis of data from ORAL Surveillance, IRs for MACE and malignancies (excluding NMSC) were highest across treatments, and increased with both tofacitinib doses vs TNFi, in pts with a HxCAD or high BL CV risk score; a similar finding was observed for VTE IRs in pts treated with tofacitinib 10 mg BID. These findings support recommendations to regularly assess and address CV risk in RA pts.

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POS0238

SIDE EFFECT PROFILE OF HYDROXYCHLOROQUINE USE IN PATIENTS WITH RA, SLE, AND OTHER RMDS OVER 20 YEARS

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Background: During the pandemic, hydroxychloroquine (HCQ) became a household name, yet despite more than 70 years as a csDMARD treatment, relatively little is known about its overall side effect (SE) profile.
Objectives: To understand the types, severity, and rates of patient-reported side effects of HCQ in adults with RA, SLE, and other RMDs alone and in comparison with methotrexate (MTX).
Methods: Adult participants in the Forward Databank observational registry reported all medication use and medication side effects through biannual questionnaires from 1999 through 2021. Incident use of HCQ and MTX were measured at enrollment and longitudinally with additional reporting of severity of side effects, certainty of medication as cause of side effect, and affected body systems. We analyzed incident rates of side effects overall and by HCQ or MTX categorical use, respectively: monotherapy, with concomitant use of another csDMARD, or with concomitant use of a bDMARD or tsDMARD. Finally, the likelihood of having any side effects was analyzed in Cox regression models by comparing HCQ initiators to MTX initiation, and within each, combination MTX or HCQ with csDMARD or bDMARD to monotherapy; these

Table 1. Incidence rates (IR) per 1000 patient-years of SEs by diagnoses for HCQ and MTX initiators

	RA		SLE		Other	
	Pt-yrs	IR (95% CI)	Pt-yrs	IR (95% CI)	Pt-yrs	IR (95% CI)
Any HCQ SE	12711	26 (23, 29)	1305	25 (18, 36)	567	41 (27, 61)
Mono HCQ	3397	28 (24, 33)	797	28 (18, 42)	347	52 (32, 82)
HCQ + csDMARDs	5473	28 (24, 33)	416	24 (13, 45)	127	32 (12, 84)
HCQ + bDMARDs	3841	22 (17, 27)	93	11 (2, 77)	93	11 (2, 76)
SE stopping HCQ	12711	13 (11, 15)	1305	12 (7, 19)	567	14 (6, 35)
Mono HCQ	3397	12 (9, 16)	797	11 (6, 22)	347	14 (6, 35)
HCQ + csDMARDs	5473	15 (12, 18)	416	13 (5, 31)	127	24 (8, 73)
HCQ + bDMARDs	3841	12 (9, 16)	93	0	93	0
HCQ SE hospitalization	12711	0.31 (0.12, 0.84)	1305	0.77 (0.1, 5.4)	567	0
Any MTX SE	81234	51 (49, 52)	1516	59 (48, 72)	2145	72 (61, 84)
Mono HCQ	22980	49 (46,52)	369	41 (25, 67)	802	62 (47, 82)
MTX + csDMARDs	15447	72 (68, 77)	872	69 (53, 89)	229	131 (91, 187)
MTX + bDMARDs	42748	43 (41, 45)	265	49 (29, 85)	1106	67 (53, 84)
SE stopping MTX	91477	26 (25, 27)	1638	41 (32, 52)	2335	44 (36, 53)
Mono MTX	26060	19 (17, 20)	390	33 (19, 57)	885	27 (17, 39)
MTX + csDMARDs	17430	38 (36, 42)	933	48 (36, 65)	255	90 (60, 136)
MTX + bDMARDs	47832	25 (23, 26)	305	26 (13, 53)	1188	47 (36, 61)
MTX SE hospitalization	96436	2.4 (2.1, 2.8)	1674	5.4 (2.8, 10.3)	2502	3.2 (1.6, 6.4)

By body system, the patterns of any SE were similar between HCQ or MTX initiators. Gastrointestinal SEs were the most common for both. Only ocular SEs were higher for HCQ vs. MTX. Multivariable Cox regression models of HCQ vs MTX SEs had a HR 0.46 (0.41 - 0.51) for RA, HR 0.47 [0.27 – 0.82] for SLE, and HR 0.51 [0.25 – 1.02] for other RMDs. While there was no difference in HCQ SEs by concomitant category or diagnoses, there was consistently higher SE rates in MTX for those on concomitant csDMARD vs monotherapy: RA HR 1.27 (1.16 - 1.38), SLE HR 1.97 (1.03 - 3.52), and other RMDs HR 2.04 (1.28 - 3.24).

models were adjusted for age, sex, RD Comorbidity Index, patient global, pain, disease duration, and number of bDMARDs used.

Results: Overall, 5874 patients initiated HCQ and 10420 initiated MTX, with RA as the predominant diagnosis. Mean baseline characteristics were similar for RA: 59 years old, 80% female and 12 years of RA duration. HCQ was mostly used with other csDMARDs, while MTX was mostly used with bDMARDs. In the other RMD and SLE groups, most were on HCQ monotherapy. For all RMDs, SE incidence for HCQ (16 – 17%) was lower than MTX (26 – 39%). The Table 1 provides incidence rates by HCQ/MTX for any SE, a SE that forces medication discontinuation, and SE leading to hospitalization. Reported SE rates were always higher for MTX vs. HCQ for all SE severity and diagnoses.

Conclusion: This is the largest study yet to review patient-reported SEs from HCQ and MTX in RA and other RMDs over a 20-year period. While validating SEs was beyond the scope of the current study, we found an overall low incidence of SEs from HCQ use, with an adjusted rate half of those reported for MTX, and that this low rate did not differ by diagnosis or concomitant DMARD use.

Disclosure of Interests: None declared

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POS0239

RISK OF VENOUS THROMBOEMBOLIC EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS AGED ≥50 YEARS WITH ≥1 CARDIOVASCULAR RISK FACTOR: RESULTS FROM A PHASE 3B/4 RANDOMISED STUDY OF TOFACITINIB VS TUMOUR NECROSIS FACTOR INHIBITORS

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Background: ORAL Surveillance (NCT02092467) was a randomised, open-label, non-inferiority, Phase 3b/4 study assessing the relative risk of major adverse cardiovascular (CV) events (MACE) and malignancies with tofacitinib vs TNF inhibitors (TNFi) in patients (pts) with moderate to severe rheumatoid arthritis despite methotrexate (MTX) and a high risk of MACE (aged ≥50 yrs; ≥1 additional CV risk factor).

Objectives: To assess risk of venous thromboembolic events (VTE; including deep vein thrombosis [DVT] and pulmonary embolism [PE]) in ORAL Surveillance.

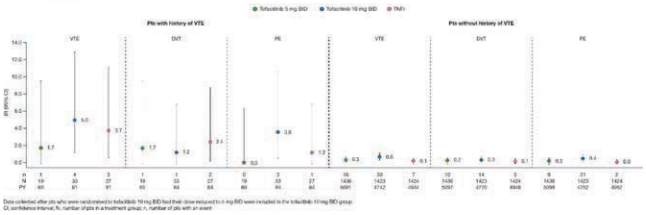
Methods: Pts on stable MTX received tofacitinib 5 or 10 mg twice daily (BID) or a TNFi (etanercept 50 mg weekly or adalimumab 40 mg once every 2 weeks). Incidence rates (IRs; pts with first events/100 pt-yrs [PY]) and 95% CIs were calculated for adjudicated VTE, DVT and PE (overall by 6-month interval and for pts with/without history of VTE). For overall VTE, DVT and PE, numbers needed to harm (NNH; tofacitinib 5 or 10 mg BID vs TNFi) were calculated post hoc. Multivariate Cox models were used post hoc to identify overall independent baseline (BL) risk factors for PE. Censoring time was a 28-day on-treatment period (minimum of last contact date or last study treatment dose date +28 days).

Results: Analysis included 1455, 1456 and 1451 pts receiving tofacitinib 5 mg BID, 10 mg BID and TNFi, respectively. Generally, across 6-month intervals to >54 months, VTE, DVT and PE IRs were numerically higher with both tofacitinib doses vs TNFi, and with tofacitinib 10 vs 5 mg BID; IRs were consistent across time (data not shown). Across treatments, VTE, DVT and PE IRs were higher in pts with vs without history of VTE; however, only a small number

Table 1. Multivariate Cox analyses to identify overall independent BL risk factors for PE across treatments

	HR (95% CI)	p value
BL covariate		
History of VTE	7.06 (2.46, 20.25)	0.0003
Antidepressant use[a]	2.94 (1.44, 6.02)	0.0032
Body mass index ≥30 kg/m^2	2.97 (1.40, 6.32)	0.0047
Corticosteroid use[b]	3.01 (1.40, 6.46)	0.0047
Proton pump inhibitor use	0.32 (0.15, 0.71)	0.0052
Male sex[c]	2.18 (1.06, 4.48)	0.0340
Age ≥65 yrs	2.00 (1.03, 3.88)	0.0401
Oral contraceptives/HRT use	3.56 (1.05, 12.10)	0.0422
History of hypertension	2.57 (0.98, 6.76)	0.0554

[a]BL antidepressant use was an indicator of an underlying condition of depression, and subgroup analysis did not identify the difference in HRs for depression across treatments[b]Proxy for elevated BL disease activity; HRs for BL corticosteroid use were similar between all tofacitinib doses combined and TNFi; includes any BL corticosteroid use[c]Impact of sex on PE risk considered inconclusiveMultivariate Cox model using backward selection included treatment effects (not subject to model selection) and overall potential independent risk factors (those affecting PE IRs equally across treatments; subject to model selection) identified from a prior set of Cox regression analyses (which included treatment and a single candidate risk factor in each model fitting, cycling through a predetermined set of risk factors); cut-off for risk factor to stay in multivariate model was p<0.10; nominal p value and HR (95% CI) based on this modelHR, hazard ratio



of pts per treatment had history of VTE (Figure 1). NNH for tofacitinib 5 and 10 mg BID, respectively, vs TNFi were 763 and 198 PY for VTE, 1347 and 589 PY for DVT, and 870 and 229 PY for PE, or, over 5 yrs, 153 and 40 pts for VTE, 269 and 118 pts for DVT, and 174 and 46 pts for PE. Identified BL risk factors for PE across treatments included history of VTE, antidepressant use, body mass index ≥30 kg/m^2, corticosteroid use, male sex, age ≥65 yrs, oral contraceptives/hormone-replacement therapy (HRT) use, and history of hypertension (Table 1).

Conclusion: Generally, in ORAL Surveillance, VTE, DVT and PE IRs were numerically higher for tofacitinib (10 > 5 mg BID) vs TNFi across 6-month intervals, and for pts with vs without history of VTE. Multivariate Cox models identified BL risk factors for PE that may help support future treatment decisions.

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POS0240 WHICH FACTORS DRIVE THE CHOICE BETWEEN A 1ST AND 2ND GENERATION TSDMARD THERAPY IN RA THERAPY?

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Background: Tofacitinib and Baricitinib are Janus Kinase Inhibitors (JAKi) considered first generation targeted synthetic DMARD (tsDMARDs) for the treatment of Rheumatoid Arthritis (RA). The second generation of JAKi (Upadacitinib and Filgotinib) seem to target JAK1 more selectively. Choice of JAKi is left to the treating rheumatologist as no head-to head-study or guidelines exist on this choice in RA.

Objectives: To investigate differences in demographics and clinical variables of patients with RA receiving either a 1st or a 2nd generation JAKi in daily practice.

Methods: Patients were included from the electronic platform "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS). Data from all Belgian RA patients on biologic (b) and tsDMARDs are here collected for drug reimbursement. Patients were selected for this analysis if starting a JAKi in 2021. Differences in demographic and clinical data were compared by χ^2-tests and t-tests. Stepwise logistic regression models with tsDMARD choice as dependent variable was constructed with variables with $p<0.05$ in univariate analyses. Sensitivity analyses for bionaïve and bioexperienced patients were performed.

Results: In total, 1643 patients with RA starting JAKi therapy in 2021 were included. Of these, 433 (26.4%) were 1s generation and 1210 (73.6%) were 2nd generation. Patients starting a 1st generation JAKi were older, had higher Health Assessment Questionnaire (HAQ) scores, had a higher erythrocyte sedimentation rate (ESR), and less patients starting a 1st generation JAKi were bioexperienced (Table 1).

The final logistic regression model included older age (OR(95%) =1.0(1.0-1.0)) and number of previous b/ts DMARDs ((OR(95%) =0.9(0.8-0.9))) as predictors of choice of 1st generation tsDMARDs (Table 2). In bionaive patients, only ESR (OR(95%) =1.0(1.0-1.0)) was predictive. In bioexperienced patients, older age (OR(95%) =1.0(1.0-1.0)), number of previous b/ts DMARDs ((OR(95%) =0.8(0.7-0.9)) and TJC (OR(95%) =1.0(1.0-1.1)) were predictors for choice of 1st generation tsDMARDs. HAQ was not included as it was missing in 90% of patients.

Conclusion: The high uptake of 2nd generation JAKi, just launched in 2021, is remarkable. Some variables effecting the choice of JAKi were found, yet these effects seemed to be small-sized. These drug choices could also be driven by other factors such as socio-economic status, illness perceptions or other patient reported outcomes, and also by marketing and sales.

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Table 1. Comparison of baseline demographic and clinical characteristics between 1st and 2nd generation tsDMARDs

	All population		Bionaïve patients		Bioexperienced patients	
	1st generation tsDMARDs	2nd generation tsDMARDs	1st generation tsDMARDs	2nd generation tsDMARDs	1st generation tsDMARDs	2nd generation tsDMARDs
number	433	1210	207	482	226	728
Age (years)	60.8 ± 12.6*	57.5 ± 13.1*	60.5 ± 12.5*	57.9 ± 13.5*	60.8 ± 12.8*	57.2 ± 12.7*
Gender (women)	304 (72.6%)	833 (74.6%)	137 (66.2%)	344 (71.4%)	175 (77.4%)	550 (75.6%)
Weight (kg)	73.3 ± 15.3	74.2 ± 15.3	74.7 ± 16.4	74.2 ± 14.4	72.4 ± 13.8	74.6 ± 16.1
Disease duration (years)	9.0 ± 8.9	10.0 ± 9.7	5.6 ± 6.6	5.7 ± 7.1	11.9 ± 9.7	12.5 ± 10.1
HAQ (0-3)	1.9 ± 0.6*	1.3 ± 0.8*	1.8 ± 0.7	1.4 ± 0.7	1.9 ± 0.5*	1.2 ± 0.8*
PGA (0-100)	63.5 ± 19.2	63.0 ± 21.5	65.0 ± 17.6	66.0 ± 20.1	62.0 ± 21.0	61.0 ± 21.8
CRP (mg/l)	12.8 ± 11.0	11.7 ± 10.7	16.3 ± 19.5	13.3 ± 15.4	10.5 ± 16.0	10.1 ± 13.5
ESR (mm/h)	25.3 ± 20.1*	22.5 ± 18.3*	28.1 ± 20.2*	23.7 ± 17.5*	21.9 ± 19.3	21.4 ± 19.3
TJC28	8.8 ± 5.5	8.4 ± 5.7	8.7 ± 5.2	9.4 ± 5.4	8.9 ± 5.9*	7.7 ± 5.8*
SJC28	6.1 ± 4.6	5.9 ± 4.6	6.1 ± 4.1	6.6 ± 4.1	6.1 ± 4.9	5.5 ± 4.8
DAS28	4.8 ± 1.0	4.7 ± 1.1	5.0 ± 0.9	5.0 ± 4.9	4.7 ± 1.1*	4.5 ± 1.2*
Bio-Experienced (yes)	226 (51.1%) *	728 (60.2%) *	-	-	-	-
N previous b/tsDMARDs	2.0 ± 1.9*	2.3 ± 2.2*	-	-	2.8 ± 1.0*	3.1 ± 1.4*

Number given are mean ± SD or number, proportion. b=biologic; ts= targeted synthetic, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints; N= number. * Signifies $p<0.05$.

POS0241

JAK INHIBITORS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: EXPLORING EARLY RESPONSE ON CENTRAL SENSITIZATION AND CATASTROPHISM SYMPTOMS

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Background: Catastrophizing has been demonstrated to be linked with central sensitization (CS), although few studies have investigated the potential of interactions between catastrophizing and CS in patients receiving JAK inhibitors.

Objectives: To explore the link between changes in Simplified Disease Activity Index (SDAI) and changes in pain catastrophizing, pain intensity, neuropathic pain component (NPC) and CS symptoms that occur with the introduction of a novel treatment targeting the JAK/STAT signalling pathway.

Methods: 115 patients in an ongoing prospective observational analysis filled out questionnaires at the start and conclusion of the research, using the Pain Catastrophizing Scale (PCS) and Central Sensitization Inventory (CSI). The study included 22 patients on tofacitinib monotherapy (5 mg BD), 19 on tofacitinib and MTX, 19 on baricitinib monotherapy (4 mg OD), 14 on baricitinib and MTX, 17 on upadacitinib monotherapy (15 mg OD), 16 on upadacitinib and MTX, and 8 on filgotinib (200mg OD) and MTX. The disease activity index was evaluated by the simplified disease activity index (SDAI). The US scoring system validated in the US-CLARA was used. The Semantic Questionnaire for Rheumatology (SQR) and PainDETECT questionnaire (PDQ), were used to assess pain severity and NPC. Using multivariable linear regression models, we investigated the connection between changes in SDAI and in CSI, PCS, PDQ, SQR and US score.

Results: At baseline, the percentage of RA patients who exceeded the thresholds for the presence of NPC (PDQ > 19 points) of the CSI (> 40 points) and PCS (> 30 points) were 43.5%, 36.5%, and 62.6%, respectively. After 4 weeks of treatment, the patient-reported scores and the disease composite index decreased significantly, SRQ (p<0.0001), PDQ (p=0.0084), PCS (p=0.0066), CSI (p=0.0165) and SDAI (p<0.0001).The US score did not change significantly (5.25 to 5.03; p=0.248). SDAI achieved 10.6% remission and 15.2% low disease activity at week 4. Multivariate regression analysis indicated that changes in SDAI were exclusively connected to changes in catastrophizing (coefficient=0.500, P=0.0224).

Conclusion: After starting a Jak inhibitor, pain catastrophizing, but not articular inflammation on US, diminishes along with disease activity. These findings provide credence to the concept of catastrophizing as a dynamic construct that may be adjusted by therapy aimed at reducing inflammatory disease activity and pain levels in the RA patient.

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Table 1. ***Multivariate regression analysis, using SDAI*** **(Simplified Disease Activity Index)** ***changes as dependent variable.***

Independent variables	Coefficient	Std. Error	T	P
(Constant)	*-0.7239*			
ACPA, titre	-0.0002410	0.002528	-0.0953	0.9242
Age, yrs	-0.09063	0.1028	-0.881	0.3803
BMI	-0.1600	0.2787	-0.574	0.5671
Disease duration, yrs	-0.1003	0.1611	-0.623	0.5347
Educational level, yrs	-0.1072	0.3703	-0.289	0.7728
Diff. CSI	0.3194	0.1984	1.610	0.1105
Diff. SRQ	0.07018	0.3726	0.188	0.8509
Diff US score	1.2248	0.7024	1.744	0.0842
Diff PCS	0.5009	0.2160	2.318	0.0224
Diff PDQ	0.1860	0.2271	0.819	0.4146

Abbreviations: ACPA= Anti-Citrullinated Protein/peptide Antibody; BMI= Body Mass Index; CSI= Central Sensitization Inventory; SRQ= Semantic Questionnaire for Rheumatology; US= Ultrasonography; PCS= Pain Catastrophizing Scale; PDQ= PainDETECT Questionnaire.

Disclosure of Interests: None declared
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POS0242

THE EFFECT OF ANTIMALARIALS ON THE OVERALL SAFETY AND PERSISTENCE OF TREATMENT WITH BIOLOGIC AGENTS OR JAK INHIBITORS IN RHEUMATOID ARTHRITIS

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Background: Antimalarials (AM) are frequently part of the initial scheme of conventional synthetic DMARDs in the treatment of rheumatoid arthritis (RA), and have been associated with lower incidence of diabetes and better lipid profile in these patients (1). However, the role of AM in schemes involving biologic (b-) or targeted synthetic (ts-) DMARDs has been much less extensively studied. In addition, a recent large scale study (2) and a consensus article (1) casted doubt on the long-term cardiovascular safety of AM.

Objectives: To evaluate the association of concomitant use of AM with the overall safety and survival of
treatment course among patients receiving one or multiple courses of bDMARDs or tsDMARDs

Methods: BiobadaBrasil is a multicentric registry-based cohort study of Brazilian patients with rheumatic diseases starting their first bDMARD or tsDMARD (3). The present analysis includes RA patients recruited from Jan 2009 to Oct 2019, followed-up over one or multiple (up to six) courses of treatment (latest date, Nov 19, 2019). A treatment course is defined as a period during which the medication scheme does not change. The primary outcome was the incidence of serious adverse events (SAEs). Total and system-specific adverse events (AEs), treatment interruption for any reason, interruption due to AEs and due to inefficacy served as secondary outcomes. Negative binomial regression with generalized estimating equations (to calculate the incidence rate ratios [IRRs]) and extended (frailty) Cox proportional hazards models were used for statistical analyses (both types of analyses including time-varying covariates over multiple courses of treatment).

Results: In total, 1316 patients (2335 treatment courses, 6711 patient-years [PY]) were enrolled. The overall incidence of serious adverse events was 9.2/100 PY. AM were used over 354 courses (1254.5 PY) of therapy. The IRRs for the primary and secondary outcomes are presented in Table 1. AM were also associated with better treatment course survival (Figure 1), reducing the risk of interruption due to AEs (multivariate hazard ratio: 0.56, 95% CI: 0.39 to 0.81, P=0.002) and inefficacy (0.65, 0.48 to 0.87, P=0.003).

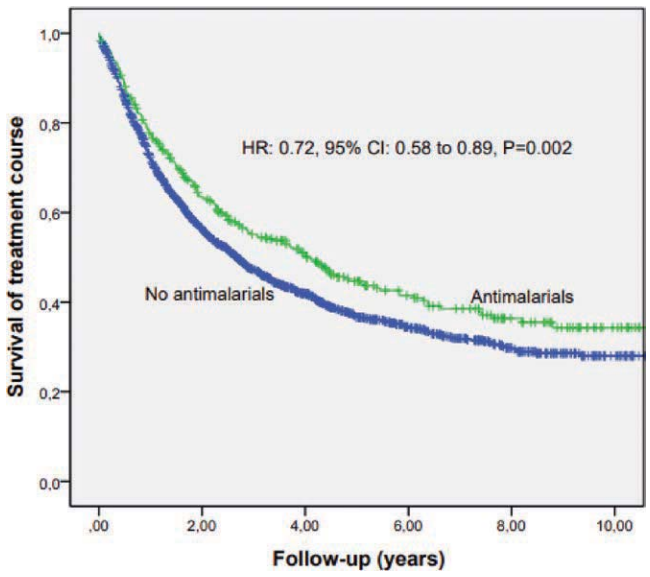

Figure 1.

Table 1. Univariate and multivariate incidence rate ratios (IRRs) of adverse events comparing use versus non-use (reference category) of antimalarials. Results are IRRs, 95% CIs, and P values.

Type of adverse event (n of events)		Crude analysis	Adjusted covariates*
Serious adverse events (617)		0.60 (0.41 to 0.87), P=0.007	0.51 (0.37 to 0.69), P<0.001
Any adverse event (3494)		0.65 (0.54 to 0.77), P<0.001	0.68 (0.57 to 0.81), P<0.001
Cardiovascular‡	Serious (52)	1.04 (0.49 to 2.20), P=0.924	1.06 (0.45 to 2.50), P=0.891
	Total (163)	0.90 (0.59 to 1.38), P=0.642	0.93 (0.59 to 1.45), P=0.737
Infections	Serious (277)	0.78 (0.44 to 1.39), P=0.404	0.53 (0.34 to 0.83), P=0.006
	Total (1400)	0.77 (0.61 to 0.98), P=0.033	0.75 (0.60 to 0.94), P=0.014
Hepatic‡	Total (66)	0.20 (0.07 to 0.64), P=0.007	0.16 (0.04 to 0.57), P=0.005
Glicemic control-related	Total (34)	0.74 (0.29 to 1.92), P=0.540	0.73 (0.26 to 2.00), P=0.535
Dyslipidemia	Total (83)	0.60 (0.31 to 1.13), P=0.114	0.55 (0.28 to 1.06), P=0.074

*Age, baseline DAS28, disease duration, gender, smoking, seropositivity (RF or anti-CCP), previous malignancy, interstitial lung disease, diabetes, hypertension, hypercholesterolemia, renal failure, ischemic cardiomyopathy, COPD, heart failure, concomitant use of each cs-, b-, and tsDMARDs, corticosteroids, starting year, osteoporosis, hepatitis B and C, and treatment sequence. ‡ Excluding infections.

Conclusion: Among RA patients on treatment with bDMARDs or tsDMARDs, concomitant use of antimalarials reduced the incidence of serious and total AEs, including infections and hepatic AEs, and prolonged treatment course survival. No significant increase in the risk of cardiovascular AEs was observed.

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POS0243

THE EFFECT OF A MEDITERRANEAN DIET ON PHYSICAL FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS – THE MEDRA STUDY

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Background: The immunomodulatory and anti-inflammatory effects of the Mediterranean Diet (MedDiet) suggest a protective role in rheumatic conditions[1]. A small but increasing body of evidence from randomised controlled trials demonstrates that increased adherence to a MedDiet in patients with Rheumatoid Arthritis (RA) can have a beneficial effect on disease activity, pain levels and physical function[2].

Objectives: The primary aim of the MEDRA study was to determine the effects of a MedDiet compared to the current food based dietary guidelines in Ireland (Healthy Eating Guidelines/HEG) on the physical function and quality of life in patients with RA.

Methods: In this randomised controlled trial, 44 patients with RA were randomly allocated to either the MedDiet or the HEG arm of the study. The 12-week dietary intervention study was delivered online by a Registered Dietitian (RD) and included data collection at three time points: baseline, mid-intervention (6 weeks) and post-intervention (12 weeks). Participants in both dietary intervention groups attended three video consultations with the RD, at baseline, weeks 6 and 12, and two follow up reviews by telephone at weeks 3 and 9. All participants were provided resources designed to specifically explain the assigned diet and how it can be successfully adhered to. Primary outcomes were changes in physical function and quality of life measured using the validated Health Assessment Questionnaire - Disability Index (HAQ-DI) and Rheumatoid Arthritis Quality of Life Questionnaire (RAQoL), respectively. Secondary outcomes included changes in physical activity and patient-reported pain levels.

Results: Forty patients with RA completed the study (mean age:47.5 SD10.9 years, females: 87.5%). No significant differences were found in the distribution of age, anthropometric measures, disease duration, physical activity, and quality of life between the two diet groups at baseline. However, the group assigned to the MedDiet had better mean values for quality of life compared to the HEG group; 0.9 ± 0.5 vs. 1.4 ±0.7, p<0.001, respectfully. Compared to baseline, there was a significant improvement in HAQ-DI scores in participants following both the MedDiet (0.9 ±0.5 to 0.5 ± 0.4, p<0.001) and HEG (1.4 ± 0.7 to 1.0 ± 0.6, p<0.001). Significant improvements in RAQoL scores were also seen in both the MedDiet (10.1 ±7.5 to 4.0 ± 4.7, p<0.001) and HEG (11.25 ± 7.2 to 7.9 ± 6.4, p=0.02) groups. At 12 weeks, participants in the MedDiet group reported a significantly better physical function status (mean difference -0.5, 95% CI -0.8 to -0.1, p=0.007) and quality of life (mean difference -3.9, 95% CI -7.5 to -0.2, p=0.04) compared to the HEG group. Participants in the MedDiet group demonstrated a significant increase in physical activity levels (56.7 ± 28.6 to 70.6 ± 33.5, p=0.01). Conversely, a non-significant decrease in physical activity levels was observed in the HEG group from baseline to post-intervention.

Conclusion: The study indicates positive effects of a Mediterranean and low-fat diet as per the Healthy Eating Guidelines on physical function and quality of life in patients with RA. The MedDiet may be superior in improving physical activity levels. Further studies and a larger cohort are needed to confirm these findings.

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Disclosure of Interests: None declared

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Small vessels on fire

POS0244

ASSOCIATION OF PROTEINASE 3 GENE (PRTN3) VAL119ILE POLYMORPHISM (SNP RS351111) WITH RISK OF RELAPSE AMONG HOMOZYGOUS PATIENTS WITH PR3 ANCA-ASSOCIATED VASCULITIS

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Background: The frequency of the proteinase 3 gene (PRTN3) polymorphisms in patients with ANCA-associated vasculitis (AAV) is not well characterized. We hypothesize that PRTN3 gene polymorphisms induce allosteric changes in PR3 conformation which may alter its interaction with ligands and PR3-ANCA during inflammation with potential implications for disease presentation and clinical outcomes.

Objectives: To analyze the association of PRTN3 Val119Ile polymorphism (SNP rs351111) with risk of relapse risk among homozygous patients with PR3 ANCA-associated vasculitis.

Methods: DNA variant calling for SNP rs351111 (chr.19:844020, c.355G>A) in PRTN3 gene assessed the allelic frequency in patients with PR3-AAV included in the Rituximab versus Cyclophosphamide (RAVE) trial. This was followed by RNA-seq variant calling to characterize the mRNA expression. We compared clinical presentation and outcomes between patients homozygous for PR3-Ile^{119} or PR3-Val^{119}.

Results: Serum samples for DNA calling were available in 188 of the 197 patients with AAV in the RAVE cohort. 75 PR3-AAV patients had the allelic variant: 13 patients were homozygous for PR3-Ile^{119} and 62 patients were heterozygous PR3-Val^{119}Ile with an allele frequency threshold of 29.3 – 55.1% of reads (Figure 1A and 1B). RNA-seq was available for 89 patients and the mRNA corresponding to the allelic variant was found in 35 PR3-AAV patients: 13 patients were homozygous for PR3-Ile^{119} and 22 patients were heterozygous PR3-Val^{119}Ile with an allele frequency threshold of 11.1 – 62.8% of reads (Figure 1A and 1C). The agreement between the DNA calling results and the mRNA expression of the 86 patients that overlapped was 100%. We found an additional homozygous patient for PR3-Val^{119} in which blood was not available for DNA calling.

We compared the clinical presentation and outcomes of 74 patients with PR3-AAV: 13 homozygous for PR3-Ile^{119} and 51 homozygous for PR3-Val^{119} (Table 1). The frequency of severe flares at 18 months in homozygous PR3-Ile^{119} was ≥ 2x higher when compared with homozygous PR3-Val^{119} (46.2% vs. 19.6%, p=0.048). We found no differences in clinical presentation.

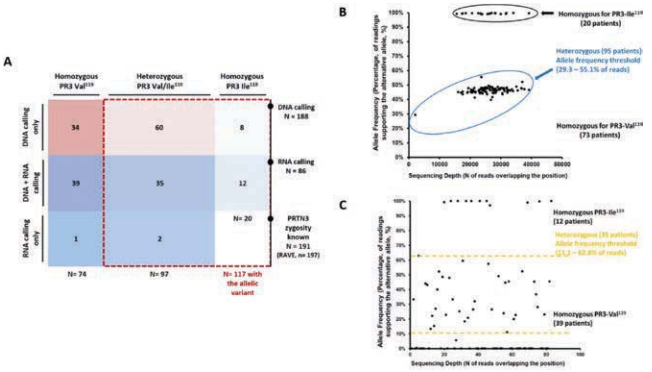

Figure 1. RAVE trial population distribution according to the zygosity status for PRTN3 gene (PR3 and MPO-ANCA patients) and DNA or RNA variant calling (panel A). Allelic frequency for rs351111, chr.19:844020 (c.355G>A) in PRTN3 among patients with AAV (PR3 and MPO-ANCA) in the DNA (panel B) and RNA (panel C) variant calling.

Table 1. Outcomes of patients with PR3-ANCA according with PRTN3 zygosity.

PR3-ANCA (n=64)	Homozygous PR3-Val^{119} (n=51)	Homozygous PR3-Ile^{119} (n=13)	p-value
Remission, n (%)	45 (88.2)	13 (100)	0.194
Complete remission, n (%)	36 (70.6)	10 (76.9)	0.650
Any flare 18 months, n (%)	30 (58.8)	7 (53.8)	0.746
Severe Relapse* 18 months, n (%)	10 (19.6)	6 (46.2)	0.048

* Relapse was considered "Severe" if Birmingham Vasculitis Activity Score for Wegener's Granulomatosis (BVAS/WG) > 3 or one major item as per the RAVE trial definition.Abbreviations: ANCA - anti-neutrophil cytoplasmic antibody; Ile – isoleucine; n- number; PR3 - proteinase 3; Val - valine.

Conclusion: In patients with PR3-AAV the presence of PRTN3 Val^{119}Ile polymorphism was associated with higher frequency of severe relapse. Further studies are necessary to understand the association of this observation with the risk of severe relapse.

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Disclosure of Interests: None declared

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POS0245 PROTEIN PROFILING IN PRE-SYMPTOMATIC ANCA-ASSOCIATED VASCULITIS INDIVIDUALS.

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Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a rare chronic relapsing condition, with unknown etiology.

Objectives: This study was undertaken to gain insight to the molecular processes and to find potential biomarkers in blood samples collected prior to the onset of symptoms of AAV.

Methods: The National Patient Register and Cause of Death register were searched for AAV-ICD codes and linked to the registers of five biobanks. Eighty-five AAV cases were identified (34 males, 51 females) with samples >1month <10years from AAV symptom onset. For each case two controls matched for sex, age, and sampling date were included. Samples were analyzed using ELISAs for PR3- or MPO-ANCA specificities. Ninety-two protein markers were analyzed using Olink Inflammation panel, (OLINK, Uppsala, Sweden) with 73 eligible after quality control.

Results: Eight protein markers were significantly altered between pre-AAV and controls, with higher levels of CCL23, CXCL5 (p< 0.01-0.05) and lower levels of Flt3L, STAMBP, ADA, TNFB, CX3CL1 and IL-15RA (p< 0.01-0.05) in the pre-AAV individuals. Nine protein markers were found significantly associated with time to symptom onset; CXCL9, CD244, VEGFA, CXCL1, TNFSF9, OPG, CSF-1, IFN-gamma and CD40 (p< 0.01-0.05). In pre-AAV individuals, six proteins were associated with MPO-ANCA-positivity compared with the MPO-ANCA-negative pre-AAV individuals which showed no overlap with the seven proteins related to PR3-ANCA-positivity.

Conclusion: To our knowledge our study is the first to analyze for and identify protein markers before symptom onset in AAV. This allowed for further studies of underlying cellular and molecular mechanisms in AAV pathogenesis as well as the diversification into PR3-ANCA and MPO-ANCA subphenotypes.

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POS0246 SEQUENTIAL RITUXIMAB AND MEPOLIZUMAB IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Rituximab (RTX) is an effective remission-induction treatment in ANCA-associated vasculitides (AAVs). Some reports have suggested that it might be effective also in Eosinophilic Granulomatosis with Polyangiitis (EGPA), to induce and maintain remission of vasculitic manifestations [1,2]. However, its effects for preventing respiratory relapses seem to be poor. Mepolizumab (Mepo) (both 100 and 300mg/month) is effective in improving respiratory manifestations and lung function, while partially controlling also systemic activity [3,4]. Isolated case reports further indicate that the sequential therapy with RTX and Mepo might be effective [5-7].

Objectives: The study aimed to investigate the efficacy and safety of a therapeutic regimen based on sequential RTX and Mepo for the control of EGPA.

Methods: A multicenter, retrospective, cohort study was conducted on adult patients diagnosed with EGPA according to the ACR classification criteria [8] or MIRRA trial criteria [3]. Only patients who received induction therapy with RTX (any dosage), and subsequent treatment with Mepo (100-300 mg/4 weeks) within 12 months from last RTX administration were included. Patients receiving other induction therapies between RTX and Mepo were excluded. The effectiveness of sequential RTX and Mepo was assessed in terms of disease activity (by the Birmingham Vasculitis Activity Score, BVAS) and daily corticosteroid dosage. Safety data were also collected.

Results: Thirty-four EGPA patients treated with sequential RTX and Mepo were included (59% females, median age of 51 years (IQR 40-58); 41% ANCA positive).

In most cases (26/34; 76%), RTX was started at the dosage of 1g q2w, and all except two patients had active disease at time of RTX beginning [median BVAS of 9 (IQR 6-14)]. Specifically, most patients started RTX for the control of

systemic manifestations (19/34; 56%), or of both systemic and respiratory symptoms (11/34; 32%). All except one patient were receiving oral corticosteroids, at a median dosage of 25 mg/day (10-38).
Mepo was started after a median of 14 months (6-23) from RTX initiation and after a median of 5 months (IQR 3-11) from the last RTX administration. Mepo was used at the dosage of 100mg/4 weeks in 32/34 (94%), mostly for the control of respiratory manifestations (25/34, 74%). At the time of starting Mepo, the median BVAS was 4 (2-8), and median prednisolone dose 10 mg/day (7-15). After a median follow-up of 28 months (IQR 23-33) from starting Mepo, the median BVAS decreased to 1.5 (IQR 0-4) and the median corticosteroid dosage to 5 mg/day (2.5-5), with 7/34 (21%) patients being off steroids. At last follow-up, most patients were off-RTX (28/34), typically due to stable disease remission (20/34; 59%).
Both RTX and Mepo were well-tolerated; 5 patients had adverse events on RTX (none serious), and 5 on Mepo (including one serious infection).
Conclusion: Sequential use of RTX and Mepo seems to be effective for remission induction and maintenance in EGPA.
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Table 1. ***Effectiveness of sequential RTX and Mepo in the 34 patients included in the study***

	RTX beginning	Mepo beginning	Last follow-up
Median time elapsed (IQR)	-	14 months (6-23) from RTX beginning	28 months (23-33) from Mepo beginning
Dosage	1g q2w (26/34);	100mg/4 weeks (32/34)	6 patients off Mepo; 28 patients off RTX
	375mg/m^2 for 4 weeks (8/34)	300mg/4 weeks (2/34)	
Reason for treatment beginning (manifestations)	Systemic (19/34);	Respiratory (25/34);	-
	Systemic + respiratory (11/34);	Systemic (4/34);	
	Only respiratory (3/34);	Remission maintenance (5/34)	
	Other (1/34)		
BVAS (median, IQR)	9 (6-14)	4 (2-8)	1.5 (0-4)
Prednisolone dosage (median, IQR), mg/day	25 (10-38)	10 (7-15)	5 (2.5-5)

Disclosure of Interests: Alessandra Bettiol: None declared, Maria Letizia Urban: None declared, Federica Bello: None declared, Davide Fiori: None declared, Irene Mattioli: None declared, Giuseppe Lopalco: None declared, Florenzo Iannone: None declared, Allyson Egan: None declared, Luca Moroni: None declared, Lorenzo Dagna Consultant of: Consultation honoraria from GSK outside the current work, Marco Caminati: None declared, Simone Negrini: None declared, Paolo Cameli: None declared, Marco Folci: None declared, Paola Toniati: None declared, Roberto Padoan: None declared, Oliver Flossmann: None declared, Roser Solans-Laqué: None declared, Laura Losappio: None declared, Jan Schroeder Consultant of: Advisory Board fees from AstraZeneca and GSK, Marc André: None declared, Laura Moi: None declared, paola parronchi Consultant of: Consultation honoraria from GSK and Novartis, Fabrizio Conti: None declared, Savino Sciascia: None declared, David Jayne Consultant of: Consultant for Astra-Zeneca, Aurinia, BMS, Boehringer-Ingelheim, Chemocentryx, Chugai, CSL, GSK, Infla-RX, Janssen, Novartis, Roche/Genentech, Takeda and Vifor, Augusto Vaglio Consultant of: Consultation honoraria from GSK outside the current work, Giacomo Emmi Consultant of: Consultation honoraria from GSK outside the current work
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POS0247

GLUCOCORTICOID TAPERING STRATEGY FOR ANCA-ASSOCIATED VASCULITIS: ADDRESSING THE GAP BETWEEN RECOMMENDATIONS AND REAL-WORLD PRACTICE

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Background: Antineutrophil cytoplasmic antibody -associated vasculitis (AAV) is usually treated with combination of high-dose glucocorticoid (GC) and immunosuppressive agents, followed by tapering GC dose. Although the European League Against Rheumatism (EULAR) has specific recommendations for tapering the GC dose, clinicians often taper it slower than recommended due to concerns of potential disease relapse. However, such slower taper may prolong GC exposure for the patients, increasing the risk of adverse events, particularly infection.
Objectives: The aims of our study were (1) to clarify GC dose tapering in the treatment of AAV in a real-world setting, in contrast to the EULAR recommendation of 2015 and (2) to compare the incidence of AAV relapse and severe infection between patients underdoing EULAR-recommended tapering and those undergoing slower tapering than the recommendation.
Methods: In this multicenter (25 sites in Japan), observational, retrospective study of AAV, 541 patients who had initial or severe relapse were enrolled between January 2017 and June 2020. Of these, 349 patients with microscopic polyangiitis (MPA) or granulomatosis with polyangiitis (GPA) who entered in GC tapering phase after successful induction treatment were included. These patients were then grouped on the pace of GC tapering, defined as the GC dose at 12 weeks after treatment initiation: (1) EULAR group: 7.5-10 mg/day of GC, according to the EULAR recommendation of 2015, and (2) SLOWER group: >10 mg/day of GC. Their baseline characteristics and clinical outcomes were compared. Primary outcome was defined as relapse-free days from treatment initiation, whereas secondary outcome included the incidence of infectious events requiring hospitalization within 48 weeks from treatment initiation. Multivariable analysis was performed to assess the relationship between tapering pace and clinical outcomes.
Results: There were 44 patients (12.6%) in the EULAR group and 290 (83.2%) in the SLOWER group. Regarding baseline characteristics, compared with the EULAR group, the SLOWER group had significantly higher serum C-reactive protein level (EULAR, 5.89 ± 6.89 mg/dL vs SLOWER, 7.56 ± 6.01 mg/dL; p = 0.03), as well as a trend toward higher Birmingham Vasculitis Activity Score

(version 3) (EULAR, 11.80 ± 7.01 SLOWER, 13.93 ± 7.06; p = 0.08) We did not observe any significant differences in the frequency of relapses between the two groups (EULAR, 8/44, 18.2% vs SLOWER, 55/290, 19.0%; p = 0.63). Multivariable Cox proportional hazard analysis revealed no relationship GC dose at 12 weeks from treatment initiation and incidence of relapse. However, upon logistic regression analysis, the SLOWER group was found to have significant higher risk of a severe infectious event within 48 weeks from treatment initiation (p = 0.046; hazard ratio, 1.27; 95% confidence interval, 1.004 – 1.601).

Conclusion: Our finding indicates that clinicians tended to taper GC slower for patients with higher disease activity. However, slower GC taper was not found to reduce the frequency of relapse. In addition, slower GC taper was found to increase the risk of a severe infection. Hence, clinicians should pay attention not only relapsing but also late GC taper resulting in the risk of serious infection, especially in patients with higher disease activity of AAV.

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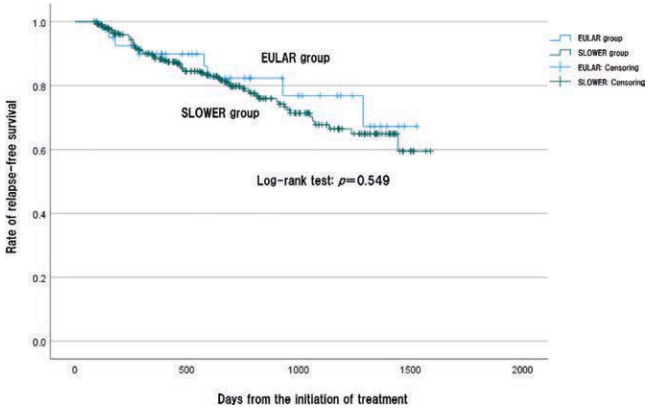

Figure 1.

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POS0248 SUBCLINICAL GIANT CELL ARTERITIS IN PATIENTS WITH POLYMYALGIA RHEUMATICA SHOWS A DIFFERENT ULTRASONOGRAPHIC PATTERN THAN PATIENTS WITH CLASSICAL GIANT CELL ARTERITIS

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Background: Polymyalgia rheumatica (PMR) can be associated with giant cell arteritis (GCA), even in the absence of clinical suspicions of vasculitis. In addition, some studies have shown an association of PMR with the predominantly large vessel involvement.

Objectives: The objective of our study was to assess the presence of subclinical GCA in patients with PMR and to compare its pattern of vascular involvement to patients with classical GCA.

Methods: Eight rheumatology European centers participated in the study. Cohort A represented consecutive newly diagnosed patients with PMR who fulfilled the 2012 EULAR/ACR Provisional Classification Criteria for Polymyalgia Rheumatica[2] and had no symptoms or signs suggestive of GCA. Ultrasound (US) examination of four vessel territories (i.e. temporal, carotid, subclavian and axillary arteries) was performed bilaterally. Cohort B included all consecutive patients with the diagnosis of GCA evaluated on the fast-track clinic of one of the hospitals (HULP). The halo sign was considered as positive US finding for GCA[3]. In addition, intima-media thickness of arteries was measured, with a cut-off ≥0.34 mm for temporal arteries (TA) frontal and parietal, 0.42mm for common TA, and ≥1 mm for common carotid, axillary and subclavian arteries for positive result. The clinical characteristics of PMR patients were recorded and the frequency of subclinical GCA determined.

Results: Cohort A included 41 PMR patients with subclinical GCA. Cohort B was formed by 97 GCA. The characteristics of the patients are shown in the Table 1. Figure 1 shows the different subtypes of vessel involvement in patients with PMR and subclinical GCA and in patients of the fast-track clinic with the diagnosis of GCA in a single hospital.

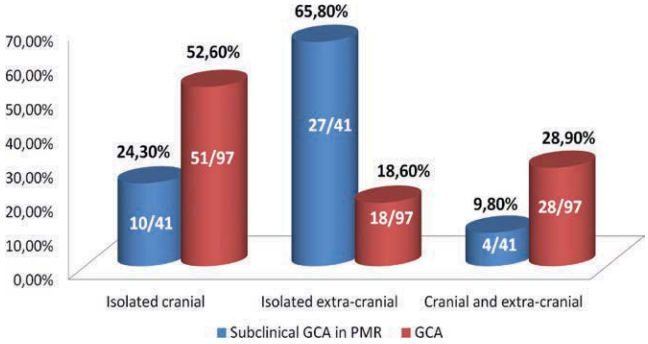

Figure 1. Subtypes of vessel affectation in Subclinical GCA in PMR and in classical GCA

Table 1. Clinical characteristics of patients of Cohort A (Subclinical GCA in PMR n = 41/216) and B (GCA in the fast-track clinic n = 97)

	Cohort A (n = 41)	Cohort B (n = 97)
Sex female (%)	17 (41.5%)	53 (54.6%)
Age (years) mean ± SD	74±6.7	79 ± 12
CRP mg/L	49.6±49.1	46 ± 81.6
Polymyalgia rheumatica	41 (100%)	47 (48.5%)
Constitutional symptoms	19 (35.18%)	35 (36.1%)

Subclinical PMR has a predilection for affectation of large vessels, followed by isolated cranial pattern (ie. Isolated temporal artery involvement) and by the mixed (cranial and extra-cranial) form. On the contrary, in classical GCA an isolated cranial involvement represents the more common pattern, followed by the mixed and finally isolated large vessel involvement.

Conclusion: Subclinical GCA in PMR shows a principal isolated extra-cranial involvement and with clearly different pattern than classical GCA.

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POS0249 FIBROBLAST ACTIVATION PROTEIN AS A LINK BETWEEN INFLAMMATION AND VASCULAR REMODELING IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) can present with serious complications such as blindness, stroke and aortic aneurysm that are related to both inflammation and remodeling of the vessel wall. GCA frequently overlaps with polymyalgia rheumatica (PMR). The pathogenesis of GCA starts in the adventitia where fibroblasts are the major stromal cell population. A preliminary study [1] reported the migration of adventitial fibroblasts to the intima, contributing to intimal hyperplasia in GCA. Fibroblast activation protein (FAP) is a non-classical serine protease which can be present in both a membrane-bound form and a soluble form and has been demonstrated to promote inflammation and fibrosis in coronary artery disease and rheumatoid arthritis [2-3]. We hypothesize that FAP is involved in GCA vasculopathy due to its pro-inflammatory and pro-fibrotic effects.

Objectives: As a first step to unravel the contribution of FAP to the vasculopathy in GCA, we determined FAP plasma levels and FAP protein expression at the site of vascular inflammation in GCA.

Methods: In our prospective cohort of GCA, PMR and healthy elderly (GPS), we measured the plasma FAP levels with ELISA in new-onset, treatment-naïve GCA (N=62), and PMR (N=63) patients and 42 age-matched healthy controls (HC). In addition, we measured the plasma FAP levels at follow-up (3-months, 1-year, 1.5-year and treatment-free remission (TFR)). Temporal artery biopsies (TAB) from treatment-naïve GCA patients (n=9) and non-GCA patients (n=9), aorta samples from GCA-related aneurysm (n=9) and atherosclerosis (n=11) were stained for FAP using immunohistochemistry. Immunofluorescence staining for CD90, CD68, αSMA and FAP was performed to detect FAP expression in fibroblasts, macrophages and vascular smooth muscle cells (VSMC), respectively.
Results: Baseline plasma FAP levels were significantly lower in GCA patients (52.72±2.93 ng/ml) than in PMR patients (66.42±2.86 ng/ml) and HC (80.47±3.38 ng/ml). FAP levels at baseline correlated inversely with C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin (IL)-6, macrophage-associated protein YKL-40 (Chitinase 3-like 1/CHI3L1) levels and monocyte counts. Plasma FAP levels in GCA patients decreased even further at 3 months (37.23±2.10 ng/ml) upon glucocorticoid-induced remission, and gradually increased to the level of HC (76.84±5.43 ng/ml) when patients were in TFR. Increased FAP expression in GCA TAB (adventitia, media, intima) and aorta (media) compared with tissues from non-GCA was documented. FAP was abundantly expressed in fibroblast- and macrophage-rich areas but not in VSMC-rich areas in TAB and aorta of GCA patients.
Conclusion: FAP expression is clearly modulated both in plasma and at the site of vascular inflammation in GCA and may represent a pathogenic link between the inflammatory and remodeling processes in GCA. As such, FAP may have utility as a biomarker and should be further investigated as target for therapeutic intervention.

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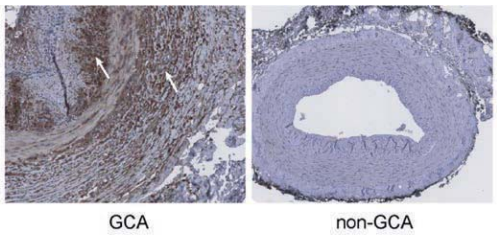

Figure. Immunohistochemistry staining of fibroblast activating protein (FAP) in temporal artery. Abundant expression of FAP (brown staining, white arrow) is seen in giant cell arteritis (GCA) as opposed to negative staining in a non-GCA biopsy.

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POS0250 PLASMA MITOCHONDRIAL DNA AS A BIOMARKER IN THE DIAGNOSIS AND FOLLOW-UP OF ANCA-ASSOCIATED VASCULITIDES

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Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) include granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) (1, 2). ANCA recognize the antimicrobial proteins proteinase 3 (PR3) or myeloperoxidase (MPO) (1,2) and trigger the formation of neutrophil extracellular traps (NETs), which release DNA into the extracellular space and systemic circulation. This cell-free (cf)DNA induces endothelial damage, vascular inflammation and necrosis (3).
Objectives: The nature, diagnostic and prognostic value of cfDNA in AAV is still unknown. The aim of the present study was to examine the clinical utility of cfDNA quantification as a biomarker in AAV.
Methods: Total DNA was isolated from platelet-free plasma samples of healthy controls (HC) and consecutive AAV patients. Plasma and clinical data were collected at baseline and follow-up. Copy numbers were quantified by qPCR for mtDNA (ATP-6 gene) and nuclear (n) DNA (GAPDH gene) (4). Patients with eosinophilic GPA (EGPA) were excluded.
Results: Ninety-two HC (median age 51 ± 9, 48.2% female) and 104 AAV patients (median age 64 ± 10, 48% female, mean BVAS: 0; range: 0-40) were available for analysis. Eighty-four (80.8%) of these patients were diagnosed with GPA, and 20 with MPA (19.2%).
mtDNA levels were significantly elevated in AAV plasma ($8.7x10^7$ copies/ml plasma, 95% CI: $5.3x10^7$ to 1.3 $x10^{8)}$), compared to HC plasma ($6.7x10^6$ copies/ml plasma, 95% CI: $5.4x10^6$ to $9.1x10^7$, p<0.0001). nDNA levels in contrast did not differ between AAV ($4.0x10^6$ copies/ml plasma, 95%CI: $2.7x10^6$ to $5.0x10^6$) and HC ($3.3x10^6$ copies/ml plasma, 95%CI: $2.4x10^6$ to $4.7x10^6$, p=0.30). ROC analysis showed that a cut-off value of $1.3x10^7$ mtDNA copy numbers differentiated between AAV and HC with 89.4% sensitivity, 82.6% specificity and an AUC of 0.94. For AAV patients with active AAV, a cut-off value of $2.9x10^7$ mtDNA copy numbers differentiated between AAV and HC with 96.1% sensitivity, 98.9% specificity and an AUC of 0.99 (Figure 1a).

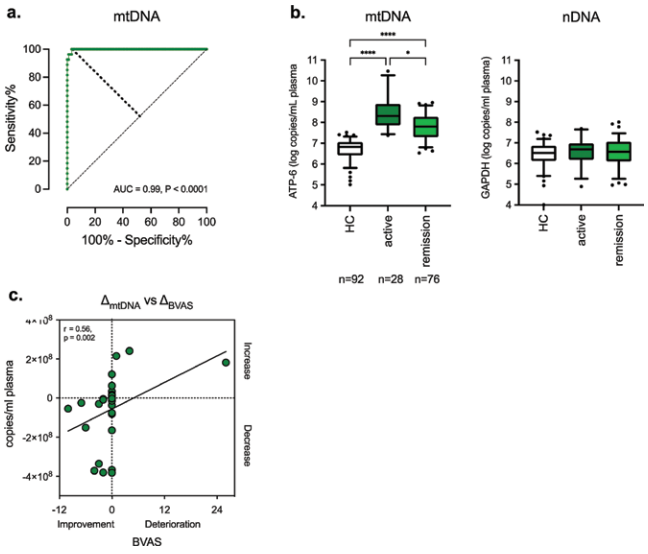

Figure 1. (**a.**) ROC curve for mtDNA plasma concentrations to discriminate between HC and active AAV patients (BVAS>0). AUC: area under the curve. (**b.**) Plasma mtDNA levels distinguish between AAV patients with active disease versus patients in a state of remission. Whiskers represent 95% CI. (**c.**) Plasma mtDNA levels in AAV patients correlate with the evolution of disease activity at follow-up.

With the exception of the peripheral nervous system involvement, there was no association of mtDNA elevation with any particular type of active organ involvement at the time of blood sampling. A positive correlation between all cell-free DNA species and anti-MPO antibody titres was observed, as expected (for cfDNA, nDNA and mtDNA - r=0.25, p=0.01; r=0.21, p=0.02; r=0.22, p=0.02, respectively).
AAV patients with active disease (BVAS>0) had a mean of $2.0x10^8$ copies/ml of mtDNA in plasma which was higher compared to HC (p<0.0001) and AAV patients in remission (BVAS=0) ($6.2x10^7$copies/ml, p=0.03). For nDNA on the other hand, there were similar levels in active disease as in remission ($5.3x10^6$ and $4.8x10^6$ copies/ml, respectively; p=0.64) (Figure 1b).
Follow-up data were available for 27 AAV patients (median follow-up: 6 ± 6 months, IQR: 12). Longitudinal changes in mtDNA levels robustly correlated with changes in BVAS (r=0.56, p=0.002, Figure 1c).
Conclusion: The quantification of cell free mtDNA - but not nDNA - copy numbers allows a sensitive and specific distinction between healthy individuals and patients with active AAV. mtDNA levels correlate cross sectionally with disease activity in AAV patients. Plasma mtDNA quantification may therefore aid in the diagnosis of AAV and in monitoring AAV activity.

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Disclosure of Interests: None declared
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POS0251 TRANSCRIPTOMIC CHANGES INDUCED BY MAVRILIMUMAB VERSUS TOCILIZUMAB IN EX-VIVO CULTURED ARTERIES FROM PATIENTS WITH GIANT-CELL ARTERITIS

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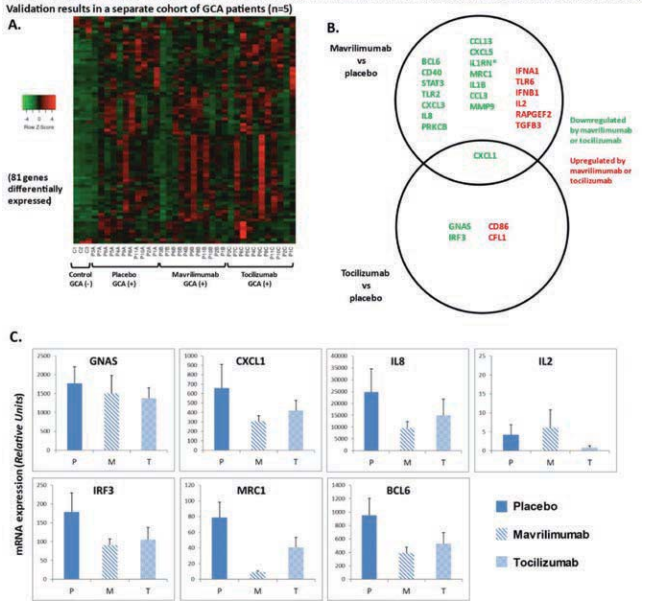
Background: Giant cell arteritis (GCA) is a chronic disease, and affected patients suffer from relapses and glucocorticoid (GC)-related toxicity. Targeted therapies are emerging with the aim of achieving better disease control and reducing GC exposure. Blocking IL-6 receptor with tocilizumab has been a major advance in the treatment of GCA. However, approximately 40% of patients treated with tocilizumab in combination with GCs experience a flare or tocilizumab-related adverse event. Blocking GM-CSF receptor α with mavrilimumab significantly reduced risk of relapse and improved sustained remission at week 26 vs placebo in a Phase 2 trial. Not all patients satisfactorily respond to any therapy, indicating heterogeneity in leading pathogenic pathways among patients. For these reasons, it is crucial to understand the specific impact of targeted therapies on vascular lesions.

Objectives: In this study we investigated transcriptomic changes induced by tocilizumab or mavrilimumab in *ex-vivo* cultured arteries from patients with GCA.

Methods: Temporal artery sections obtained for diagnostic purposes from 11 patients with histopathologically-confirmed GCA and 3 controls were cultured *ex-vivo* and exposed to placebo, mavrilimumab, or tocilizumab (both at 20 µg/mL) for 5 days. Of 11 GCA donors, 2 had received no treatment prior to biopsy, 2 had received a single prednisone (60 mg) dose, 1 had received 2 daily doses, and the remaining 6 had extended treatment; in prednisone-treated patients, mean (SEM) treatment duration was 17.9 ±8.7 days. A separate cohort of patients (consisting of five newly diagnosed patients with GCA, age- and sex-matched with the previous cohort) was used to validate 7 transcripts by real time PCR. Genes were selected for validation based on high level of expression and differential expression with each treatment. All samples were homogenized, and total RNA was extracted with TRIzol reagent. 100 ng of RNA per sample were processed with Nanostring Inflammation gene expression assay (256 transcripts) and hybridized using nCounter Prep Station. Barcode counts from nCounter Digital Analyzer were processed with nSolver 4.0 Software. Normalised data were analyzed using R Studio 4.0.5 and IBM SPSS 22.0, and paired Wilcoxon tests were applied individually to each treatment comparison group for each analysed gene. One µg of RNA per sample from the validation cohort was retrotranscribed; subsequent real time PCRs were normalised against endogenous control GUSb and analysed using SDS 2.3 software.

Results: 67 out of 250 transcripts were differentially expressed between arteries from GCA patients and arteries from control patients (all placebo-treated).

Figure 1. (A) Heat map of differential expression of 81 genes in GCA (-) control and GCA (+) treated with placebo, mavrilimumab, or tocilizumab. (B) Venn diagram of genes differentially expressed in mavrilimumab versus placebo and tocilizumab versus placebo. (C) Validation results in a separate cohort of GCA patients (n=5)



Of those, only 9 transcripts remained significant after correction for multiple comparisons, with a false discovery rate ≤0.05. 81 transcripts were differentially expressed in at least one comparison across groups (Figure 1A). 15 transcripts were lower, and 6 were higher in the mavrilimumab group vs placebo; 3 transcripts were lower, and 2 were higher in the tocilizumab group vs placebo. Most changes elicited between treatments were unique, but CXCL-1 was common (Figure 1B). None remained significant after correction for multiple comparisons. The effects of mavrilimumab and tocilizumab on GNAS, CXCL1, IL8, IL2, IRF3, MRC1 and BCL6 expression by Nanostring were consistent with the effect assessed using real time PCR in the separate validation cohort (Figure 1C).

Conclusion: Mavrilimumab and tocilizumab have a different transcriptomic impact on cultured arteries from patients with GCA, with some overlapping effects, although differential effects may have been attenuated by prior GC use. A better understanding of the impact of targeted therapies on vascular inflammation is needed to improve treatment options for patients with GCA.

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POS0252 MYOFIBROBLASTS MAINTAIN TH1 AND TC1 POLARIZATIONS IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a large-vessel vasculitis mainly involving the aorta and cranial arteries. It is the most frequent vasculitis in adults over 50 years. When they are stimulated by interferon-gamma (IFN-γ), vascular smooth muscle cells (VSMC) contribute to GCA pathogenesis by producing chemokines triggering the recruitment of pro-inflammatory T cells and monocytes (1).

Objectives: Current knowledge about the interaction between resident cells of the vascular wall (VSMC, myofibroblasts [MF]) and immune cells is limited. The aim of our research was to better characterize the interactions between VSMC, MF and T cells in GCA.

Methods: Fresh fragments of temporal artery biopsies (TAB) performed at Dijon university hospital (France) were prospectively sent to our research unit. Fresh sections of positive and negative TAB were fixed and embedded in optimal cutting temperature OCT and stored at -80°C. Then, cryostat sections were fixed, permeabilized, blocked and incubated with primary antibodies (anti-alpha smooth muscle actin [α-SMA], anti-myosin heavy chain 11 [MHC11], anti-Desmin, anti CD90, anti-CD45, anti-HLA-DR, anti-phospho STAT1 [pSTAT1] and anti-pSTAT3) and secondary antibodies for confocal microscopy analyses. Fresh sections of healthy TAB were embedded in MATRIGEL and covered by DMEM to obtain vascular cells in culture. Cells were treated with trypsina-EDTA between each passage. Vascular cells were used after 4-7 doubling passages. Cells were analyzed by immunofluorescence, flow cytometry and RT-PCR and their proliferation was evaluated by impedancemetry (iCELLigence system). Peripheral blood

mononuclear cells (PBMC) and vascular cells thus obtained were co-cultured for 7 days in different conditions. Vascular cells were cultured in the presence or absence of IFN-γ and tumor necrosis factor alpha (TNF-α) or interleukin-6 (IL-6) and soluble receptor of IL-6 for 72 hours. When cells reached confluence, they were cultured alone or with allogenic PBMC activated with anti-CD3/CD28 microbeads. After 7 days of culture, cells were separated with a treatment with EDTA and studied by flow cytometry.

Results: Confocal microscopy analyses of GCA arteries showed that neointima was mainly composed of myofibroblasts (MF) (α-SMA$^+$Desmin$^+$MHC11^{low}CD90$^+$) in contact with CD45$^+$ cells and that MF expressed HLA-DR, the phosphorylated form of STAT1 (pSTAT1) and in a lesser extent pSTAT3, strongly suggesting the activation of the IFN-γ signaling pathway rather than the IL-6 pathway. The phenotype of cultured vascular cells isolated from fresh TAB was consistent with MF. When MF were exposed to IFN-γ and TNF-α *in vitro*, their proliferation capacity decreased and their levels of expression of HLA-DR and CD86 increased (median fluorescence intensity [MFI] from 0 to 57 [p=0.03] and from 34 to 103 [p=0.03], respectively). In addition, co-cultures of MF and activated PBMC revealed that MF maintained the polarization of T cells into Th1 and Tc1 cells (p≤0.001) and to a lesser extent into Th17 and Tc17 cells (p=0.03). This effect was even more significant when MF were previously exposed to IFN-γ and TNF-α but not when they were exposed to IL-6.

Conclusion: Our results show that myofibroblasts are present in the neointima of GCA patients and that these MF activate signaling pathways indicative of IFN-γ exposure. Moreover, these MF, especially when exposed to IFN-γ, maintain the polarization of T cells into Th1 and Tc1 cells, which contributes to amplify the production of IFN-γ and thus initiate a pro-inflammatory amplification loop that likely participates in vascular inflammation and remodelling.

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Disclosure of Interests: None declared

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POS0253 **PERSONALIZED RISK EVALUATION FOR OUTCOME PREDICTION IN ANCA ASSOCIATED VASCULITIS (AAV) USING LATENT CLASS ANALYSIS AND MACHINE LEARNING.**

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Background: ANCA associated vasculitides (AAV) are a heterogeneous group of rare diseases with unknown etiology. In the most severe cases AAV can lead to end stage kidney disease or death. Since etiology and detailed pathogenesis of AAV is not known, the prediction of disease outcome at the time of diagnosis is challenging. Thus, there is an unmet need for tools to identify patients with the highest risk of organ dysfunction and death and apply effective personalized therapy.

Objectives: The aim of this work was to search for tools allowing outcome prediction at the time of AAV diagnosis. Early identification of patients, who are likely to develop severe organ dysfunction and death is crucial for appropriate disease management. Induction therapy in AAV relays on immunosuppressive drugs characterized by a high risk of severe side effects. Thus, their administration in high doses should be limited only to individual patients with an especially high risk of poor outcome.

Methods: We applied here two methods of identification of AAV patients at risk to develop severe organ dysfunction and death. First method (latent class analysis [LCA] followed by logistic regression) was meant to subcategorize patients and identify a subgroup at subjects at risk to develop chronic renal replacement therapy (CRRT) and death [1]. Second, served to assess individual poor outcome risk and was based on two machine learning (ML) classifiers, which by analyzing clinical information allow assigning computed risk for CRRT and death in an individual patient allowing to identify subjects with high risk of chronic replacement therapy (CRRT) and death. We have evaluated a number of different approaches to build the ML models (including logistic regression, support vector machines, random forests), and obtained the best results for the gradient boosting algorithm implementation called LightGBM [2]. It works as a sequential ensemble of so-called weak learners (decision trees) finally combined in a one prediction model. Both analyses were based on retrospective data from Polish national AAV registry (POLVAS) [3] including presently 565 GPA and 135 MPA patients. The parameters used were: demographic data and laboratory parameters, specific organ involvement, ANCA specificity and time between selected stages of the disease.

Results: LCA used on our AAV cohort identified four subphenotypes – three already previously proposed - and revealing a fourth clinically relevant subphenotype. This new subphenotype includes only GPA patients, usually diagnosed at a younger age as compared to other groups, and characterized by multiorgan involvement, high relapse rate, relatively high risk of death, but no end-stage kidney disease. Logistic regression analysis revealed significant differences in the risk of CRRT and death between those subphenotypes – the worst prognosis was found for severe MPO AAV. On the other hand, using ML approach we obtained an individual prediction model with potentially relevant clinical performance (ROC AUC of 0.85 for CRRT and 0.82 for death).

Conclusion: We consider results obtained encouraging. They may offer a new insight into AAV course based on data available at diagnosis, and create a solid foundation for potential clinical decision support system.

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Disclosure of Interests: None declared

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Vaccination against SARS-CoV-2

POS0254 **IMMUNE RESPONSE TO SARS-COV-2 INFECTION IN PATIENTS WITH RHEUMATIC MUSCULOSKELETAL DISEASES: THE MAINSTREAM STUDY**

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Background: Rheumatic musculoskeletal diseases (RMD) are pathological conditions characterized by an impaired immunological system that is determinant both in the pathogenesis and in the inadequate response to infections. The use of disease-modifying anti-rheumatic drugs (DMARDs), which include conventional synthetic (cs) or biologic and targeted synthetic (b/ts) DMARDs, contribute to compromise immunological reactivity.

Objectives: To analyze the immune response to SARS-CoV-2 in patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA) receiving treatment with DMARDs and to investigate the effect of the different classes of drugs on humoral and cellular response.

Methods: Patients were tested for anti-SARS-CoV-2 IgG, IgM and IgA antibodies to nucleoprotein (N) and receptor-binding domain (RBD) through ELISA and neutralization assays. Then, we performed a flow cytometry analysis of monocytes, NK cells, B and T lymphocytes from PBMCs of serologically positive patients. We also included a cohort of non-RMD individuals recovered from COVID-19 as a reference group of non-immunosuppressed subjects. A first recruitment occurred in May-June 2020 (T1) and a second recruitment, 3-4 months after (T2), allowed to evaluate the persistence of the antibody response over time and to investigate the cellular immune response to SARS-CoV-2 in RMD patients having resolved the infection.

Results: During T1, 358 patients with RA (n=200) or SpA (n=158) were recruited. Mean age was 52.8, 64% were female. All patients were treated with DMARDs, 299 with b/tsDMARDs and 59 received csDMARDs alone. One third was also receiving corticosteroids (CS). At T2, 36 subjects were recruited. We found a seroprevalence rate of 18.4%, which did not significantly differ between RA and SpA groups, and between patients treated with b/ts-DMARD or csDMARDs, either alone or in combination with CS (Table 1). Antibody levels of RMD patients were lower than non-RMD individuals (Figure 1), with CTLA4-Ig-treated patients having the lowest IgG levels. This difference was less marked in symptomatic RMD patients. 72% of seropositive patients elicited neutralizing sera. Despite an overall decrease in anti-RBD and anti-N titers, more than two-third of patients maintained antibodies titers above positivity threshold at T2. Concerning cellular response, we found that CD8+ T-cells frequency was overall comparable between RMD and non-RMD convalescents, and did not differ in b- or cs-DMARD treated ones. Conversely, CD4+ T-cell frequencies were significantly lower in RMD patients, especially those treated with anti-IL6R and CTLA4-Ig. B-cell subpopulations (class-switched, memory, and IgG+ memory B-cells) had sustained frequencies in anti-TNFα treated patients, while they had a trend of reduction in patients treated with anti-IL6R and CTLA4-Ig.

Table 1. Anti-RBD seroprevalence

	Total	Seropositive, n	(%)	IgM (n)	(%)	IgG (n)	(%)	IgA (n)	(%)
COVID19 symptomatic	**77**	25	32.5	19	24.7	17	22.1	17	22.1
COVID19 asymptomatic	**281**	41	14.6*	23	8.2*	13	4.6 *	26	9.3*
RA	**200**	36	19	23	11.5	20	10	27	13.5
SpA	**158**	30	19	19	12	10	6.3	16	10.1
b/ts-DMARD	**299**	55	18.4	35	11.7	24	8	36	12
cs-DMARD	**59**	11	18.6	7	11.9	6	10.2	7	11.9
csDMARD+b/tsDMARD	**112**	26	23.2	8	7.1	8	7.1	9	8
a-TNFa	**173**	37	21.4	25	14.5	16	9.1	21	12.1
a-IL-6R	**35**	8	22.9	5	14.3	6	17.1	8	22.9
CTLA4-Ig	**42**	5	11.9	3	7.1	1	2.4	4	7.1

**P value < 0,005*

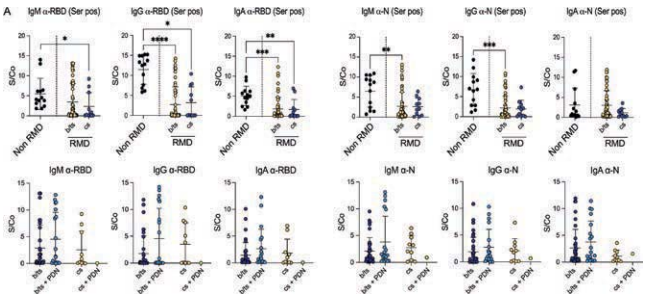

Figure 1. Magnitude of the anti-RBD and anti-N antibody response

Conclusion: Our data provide a comprehensive picture of the humoral and cellular immune responses to SARS-CoV-2 infection in RMD patients. We showed that DMARDs treatments did not alter a successful antibody response to the virus and did not hamper the antibody neutralizing ability. However, the magnitude of antibody response was slightly reduced compared to non-RMD individuals, especially in patients receiving CTLA4-Ig. We did not observe marked differences in the B- and T-cell populations between RMD patients compared to non-RMD individuals. However, in patients receiving anti-TNFα we found a higher relative abundance of effector adaptive population compared to other bDMARDs.

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POS0255 PREDICTORS OF ANTIBODY RESPONSE TO COVID-19 VACCINE IN RITUXIMAB TREATED PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES. A SWEDISH NATIONWIDE STUDY (COVID19-REUMA)

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Background: In line with other reports, our group showed that patients treated with rituximab had significant impaired antibody response compared to patients treated with other biologic and targeted and synthetic disease modifying anti-rheumatic drugs (csDMARD).

Objectives: To investigate predictors of response to COVID-19 vaccination (2 doses of mRNA vaccines, 2 doses of virus vector vaccines or combinations of these) in patients with inflammatory rheumatic diseases (IRD) treated with rituximab and controls.

Methods: Antibody levels to three antigens: Spike protein full length, Spike S1 and Nucleocapsid C-terminal fragment (to confirm previous COVID-19 infection) were measured in sera collected before vaccination and 2-12 weeks after the second vaccine using a multiplex bead-based serology assay. The antigen-specific cut-off was defined as the median fluorescence intensity signal plus 6x standard deviations across 12 pre-pandemic controls. A good vaccine response was defined as having antibodies over the cut-off level for both spike antigens. Proportion (%) responders was compared between patients and controls (Chi2 test). Patients with IRD receiving last rituximab treatment within a mean (range) 193 (23-501) days before first vaccination participated. Individuals without IRD served as a control group. Predictors of a good vaccine response were explored using multivariate logistic regression analysis adjusted for age, sex, disease duration, diagnosis (systemic vasculitis/RA/JIA/other), concomitant csDMARD, rituximab dose and prednisolone dose. Hazard ratio (chanse) of a good antibody response in relation to time between the last rituximab treatment and vaccination was studied by Kaplan-Meier survival analysis.

Results: In total, 145 patients receiving rituximab and 61 controls were inclyded. Of these, 82 received rituximab as monotherapy (67% women; mean age 66 years, mean disease duration 13 years; 33% had RA/JIA and 60% vasculitis) and 63 received rituximab+csDMARD (62% women; mean age 66 years; mean disease duration 17 years; 76% had RA/JIA and 10 % vasculitis). Controls (n=61) were 74% women and mean age 49 years. Compared to controls, rituximab patients had lower antibody levels for both spike proteins (p<0.001). Proportion (%) responders among patients receiving rituximab as monotherapy (40.2%) and rituximab+DMARDs (25.4%) was significantly lower than in controls (98.4%) (p<0.001, Chi2). Higher age, concomitant csDMARD at vaccination and shorter time from last rituximab treatment predicted impaired antibody response (multivariate logistic regression model) (Table 1). Longer time between the last rituximab course and vaccination was associated with better antibody response (Figure 1).

Table 1. Predictors of good antibody response to two doses of COVID-19 vaccine defined as antibodies over the cut-off level for both spike antigens

	B	p-value	OR	95% CI
Age at vaccination (years)	-0.04	0.009	0.96	0.93-0.99
Sex (male/female)	-9.55	0.209	0.58	0.24-1.36
csDMARD at vaccination (yes/no)	-1.08	0.026	0.34	0.13-0.88
Prednisolone (mg/dag)	-0.10	0.103	0.90	0.80-1.02
Rituximab dos (1000 mg vs 500 mg)	-0.01	0.370	0.99	0.99-1.00
Time between the last rituximab and vaccination (months)	**0.20**	**0.001**	**1.31**	**1.11-1.55**
Diagnosis at vaccination (systemic vasculitis vs others)	-0.51	0.315	0.60	0.21-1.64

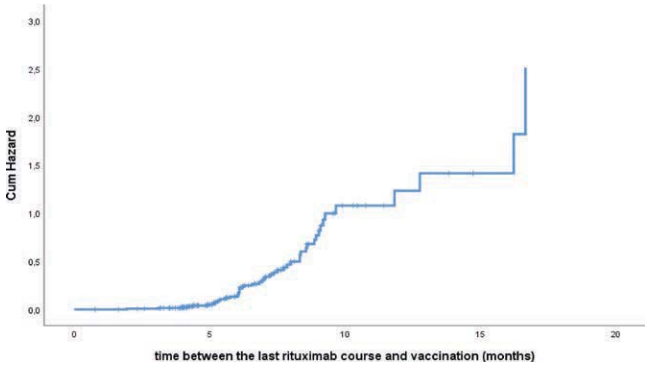

Figure 1. The chance of good antibody response following two doses of COVID-19 vaccine in relation to time between the last rituximab course and vaccination.

Conclusion: Patients with IRD getting vaccinated with two doses of COVID19 vaccine during the treatment with rituximab have the ability to develop antibody response although the response is impaired. For each month passed after the last rituximab course, the chance of good antibody response increases with 30%. Younger patients receiving rituximab as monotherapy and vaccinated preferably several months after the last rituximab treatment have the highest chance of achieving a good antibody response.

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POS0256

CLINICAL PREDICTORS OF ATTENUATED ANTIBODY RESPONSE TO PRIMARY SARS-COV-2 VACCINATION IN A LARGE PROSPECTIVE STUDY OF PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: An attenuated humoral response to SARS-CoV-2 vaccination has been observed in some patients with rheumatic and musculoskeletal diseases (RMD) (1). We sought to identify clinical factors associated with poor humoral response following primary (two-dose mRNA or single adenoviral vector dose) SARS-COV-2 vaccination in patients with RMD on immunosuppression.

Objectives: To identify clinical predictors of an attenuated antibody response to primary SARS-CoV-2 vaccination in RMD patients on immunosuppression.

Methods: We included patients ≥18 years old with RMD on immunosuppression who received either two-dose mRNA or single dose Janssen/Johnson and Johnson (J&J) vaccination. Demographics, diagnoses, and therapeutic regimens were collected via participant report; those with prior COVID-19 infection were excluded. One month after vaccination, participants underwent SARS-CoV-2 antibody testing on the semi-quantitative Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay, which measures antibody to the SARS-CoV-2 S-receptor binding domain (RBD) protein (ceiling >250U/mL later expanded to >2500U/mL). Associations were evaluated using Fisher's exact and Wilcoxon rank sum tests. Logistic regression analyses were performed to evaluate for clinical factors associated with antibody response. We adapted survival methods to address right-truncation of titers; this methodology was used to calculate medians. Participants provided informed consent electronically and the study was approved by the local Institutional Review Board.

Results: We studied 1138 RMD participants on immunosuppression; most were female (93%) and white (91%) (Table 1). One-hundred and fifteen (10%) had anti-RBD response in the negative range at a median (IQR) of 29 days (28-34) following completion of vaccine series. A greater proportion of participants with negative response were non-white, received J&J vaccine, reported use of mycophenolate, rituximab, or glucocorticoids. Antibody response differed by immunosuppressive regimen, with those receiving rituximab having poorest response (Figure 1). Use of mycophenolate (aOR 9.92, p=0.001), rituximab (aOR 56.99, p=0.001), glucocorticoids (aOR 2.99, p=0.001) or receipt of J&J (aOR 3.13, p=0.039) were associated with negative antibody response.

Table 1. Clinical characteristics stratified by anti-SARS-CoV-2 RBD response

	Negative (n=115)*	Positive (n=1023)*	p-value†
Age,median(IQR)	49(42, 58)	47(37, 58)	0.07
Female sex,no.(%)	108(94%)	952(93%)	0.78
Non-white,no.(%)	16(13.9%)	83(8.1%)	0.04
Diagnosis,no.(%)	22(19.1%)	469(45.8%)	<0.01
Inflammatory arthritis			
SLE	27(23.5%)	193(18.9%)	0.27
Sjögren's syndrome	5(4.3%)	46(4.5%)	0.53
Myositis	13(11.3%)	49(4.8%)	<0.01
Systemic sclerosis	2(1.7%)	9(0.9%)	0.55
Vasculitis	12(10.4%)	16(1.6%)	<0.01
Overlap connective tissue disease¶	34(29.5%)	24(23.6%)	0.65
Vaccine,no.(%) Pfizer/BioNTech	66(57.4%)	548(53.6%)	0.01
Moderna	38(33.0%)	438(42.8%)	
J&J	11(9.6%)	37(3.6%)	
Non-biologic in regimen	89(77.4%)	725(70.9%)	0.52
Biologic in regimen	84(73.0%)	570(55.7%)	0.01
Mycophenolate**	56(48.7%)	120(11.7%)	<0.01
Rituximab	54(47.0%)	29(2.8%)	<0.01
Glucocorticoid**	61(53.0%)	284(27.8%)	<0.01
Withheld immunosuppression	18(21.2%)	260(39.6%)	<0.01

* Negative defined as anti-RBD titer <0.8 U/mL.† Comparisons between negative and positive groups.¶ Denotes a combination of two or more of the above conditions** Mycophenolate: mycophenolic acid and mycophenolate mofetil. Corticosteroid: prednisone and prednisone equivalents

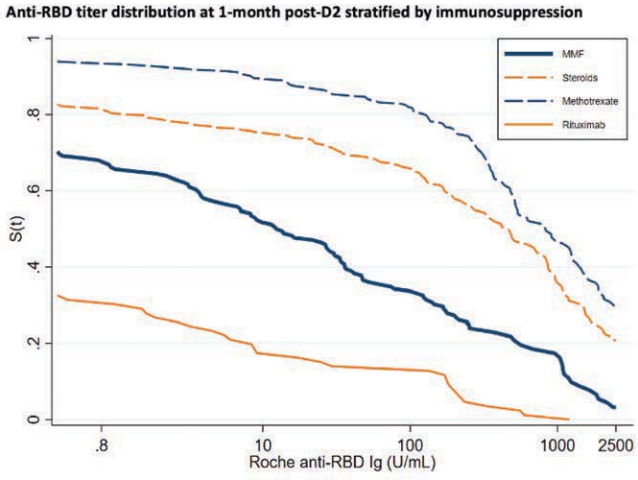

Figure 1.

Conclusion: Use of mycophenolate, glucocorticoids, rituximab and receipt of J&J vaccine were the strongest predictors of an attenuated antibody response to primary SARS-CoV-2 vaccination; these data support use of an additional primary dose in RMD patients.

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Disclosure of Interests: Caoilfhionn Connolly: None declared, Teresa Po-Yu Chiang: None declared, Mayan Teles: None declared, Sarah Frey: None declared, Jennifer Alejo: None declared, Allan Massie: None declared, Lisa Christopher Stine Consultant of: Janssen, Boehringer-Ingelheim, Mallinckrodt, EMD-Serono, Allogene, and ArgenX., William Werbel: None declared, Dorry Segev Speakers bureau: Sanofi, Novartis, CSL Behring, Jazz Pharmaceuticals, Veloxis, Mallincrodt, Thermo Fisher Scientific, Regeneron, and Astra-Zeneca, Consultant of: Sanofi, Novartis, CSL Behring, Jazz Pharmaceuticals, Veloxis, Mallincrodt, Thermo Fisher Scientific, Regeneron, and Astra-Zeneca, Julie Paik: None declared
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POS0257 COMPARISON OF SARS-COV-2 VACCINE RESPONSE IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASE; MRNA-1273 VACCINE INDUCES HIGHER HUMORAL IMMUNOGENICITY THAN BNT162B2

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Background: The SARS-CoV-2 messenger RNA (mRNA) vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) have benefitted all countries amid the coronavirus disease 2019 (COVID-19) crisis. Whereas both of them have shown efficacy in preventing COVID-19 illness in healthy participants, there is paucity of data about immunogenicity and safety of mRNA COVID-19 vaccines in patients with autoimmune, inflammatory rheumatic disease. Recent observational studies evaluated mainly BNT162b2, suggesting that glucocorticoids, immunosuppressive agents impair SARS-CoV-2 vaccine responses. However, difference in immune reactions and safety between BNT162b2 and mRNA-1273 have not been clarified in patients with inflammatory rheumatic diseases.
Objectives: To assess humoral and T cell immune responses and safety profiles after two doses of different mRNA vaccine against SARS-CoV-2; BNT162b2 and mRNA-1273.
Methods: We enrolled consecutive, previously uninfected patients with inflammatory rheumatic diseases receiving mRNA vaccine including BNT162b2 and mRNA-1273. Healthy participants receiving BNT162b2 were also recruited as control. Blood samples were obtained 3weeks, 2 months, 3 months, 4 months, and 6 months after second dose of vaccines. We measured titres of neutralizing antibodies against SARS-CoV-2 and calculated seroconversion rates to evaluate humoral responses. We also assessed T-cell immunity responses by using interferon releasing assay against SARS-CoV-2 in a part of the patients. Answers to questionnaires about adverse reactions were obtained from participants.
Results: A total of 974 patients with inflammatory rheumatic diseases and healthy 630 control participants were enrolled. Among them, 796 patients received BNT162b2, 178 patients received mRNA-1273, and all control participants received BNT162b2. Seroconversion rates and neutralizing antibody titres 3 weeks after vaccination were significantly higher in patients with mRNA-1273 and healthy participants with BNT162b2 compared with patients with BNT162b2; seroconversion rates, 97.2% vs 99.5% vs 83.3%, p<0.001; titers of neutralizing antibodies, 29.4±33.9 IU/mL vs 23.9±14.2 IU/mL vs 10.8±16.5 IU/mL, p<0.001, respectively. On another front, T cell reaction against SARS-CoV-2 was similar in both patients with mRNA-1273 and BNT162b2; interferon gamma levels for antigen 1, 1.2±2.1 IU/mL vs 0.8±2.5 IU/mL, p=0.23; and for antigen 2, 1.4±1.9 IU/mL vs 1.0±2.1 IU/mL, p=0.11, respectively. Regarding adverse reaction of each mRNA vaccine, the frequency of systemic adverse reactions including fever and general fatigue are also significantly higher in patients with mRNA-1273 and healthy controls than patients with BNT162b2; fever, 48.0% vs 44.9% vs 10.2%, p<0.001; general fatigue, 70.4% vs 61.8% vs 31.2%, p<0.001, respectively). In longitudinal measurement, neutralizing antibody titres in patients with BNT162b2 were decreased more rapidly than those in healthy controls; 3.3±3.2 IU/mL in patients with BNT162b2 at 4 months and 3.2±4.7 IU/mL in healthy controls with BNT162b2 at 6 months. We identified age, glucocorticoid dose (prednisolone > 7.5mg), use of immunosuppressants including methotrexate, mycophenolate, cyclophosphamide, and tacrolimus are associated with rapid attenuation of humoral responses in patients with BNT162b2.
Conclusion: Our results demonstrated a significant higher humoral immunogenicity and frequency of systemic adverse reaction of the SARS-CoV-2 mRNA-1273 (Moderna) compared with the BNT162b2 (Pfizer-BioNTech) in inflammatory rheumatic disease patients. Glucocorticoid and immunosuppressive agents impaired induction and sustention of neutralizing antibody, and earlier third booster vaccination may be required within 4 months, especially for those receiving BNT162b2.
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POS0258 SAFETY AND IMMUNOGENICITY OF BNT162B2 MRNA COVID-19 VACCINE AMONG ADOLESCENTS WITH RHEUMATIC DISEASES TREATED WITH IMMUNOMODULATORY MEDICATIONS

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Background: Adolescents with juvenile-onset autoimmune inflammatory rheumatic diseases (AIIRD) could be at risk for disease flare secondary to SARS-CoV-2 infection or to withholding anti-inflammatory therapy. While vaccination can protect against COVID-19, safety and immunogenicity data regarding anti-SARS-CoV-2 vaccines among adolescents with AIIRD are limited.
Objectives: This international, prospective, multicentre study evaluated the safety and immunogenicity of the BNT162b2 anti-SARS-CoV-2 vaccine among adolescents and young adults with juvenile-onset AIIRD, 80% of whom are on chronic immunomodulatory therapy.
Methods: Vaccine side effects, disease activity, and short-term efficacy were evaluated after 3 months in 91 patients. Anti-spike S1/S2 IgG antibody levels were evaluated in 37 patients and 22 controls, 2–9 weeks after the second dose.
Results: Ninety-one patients and 40 healthy controls were included. Safety profile was good, with 96.7% (n=88) of patients reporting mild or no side-effects, and no change in disease activity. However, 3 patients had transient acute symptoms: 2 following the first vaccination (renal failure and pulmonary haemorrhage) and 1 following the second dose (mild lupus flare vs. viral infection). Seropositivity rate was 97.3% in the AIIRD group compared with 100% among controls. However, anti-S1/S2 antibody titres were significantly lower in the AIIRD group compared with controls (242±136.4 vs. 387.8±57.3 BAU/ml, respectively; p<0.0001). No cases of COVID-19 were documented during the 3-month follow-up.
Conclusion: Vaccination of juvenile-onset AIIRD patients demonstrated good short-term safety and efficacy, high seropositivity rate, but lower anti-S1/S2 antibody titres compared to healthy controls. These results should encourage vaccination of adolescents with juvenile-onset AIIRD, even while on immunomodulation.
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POS0259 A RANDOMIZED CLINICAL TRIAL OF 2-WEEK METHOTREXATE DISCONTINUATION IN RHEUMATOID ARTHRITIS PATIENTS VACCINATED WITH INACTIVATED SARS-COV-2 VACCINE

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Background: Patients with rheumatoid arthritis (RA) on methotrexate have reduced vaccine responses. Temporary discontinuation has improved immunogenicity of anti-influenza vaccine, but this strategy has not been evaluated in anti-SARS-CoV-2 vaccines.

Objectives: To evaluate the effect on immunogenicity and safety of 2-week methotrexate (MTX) discontinuation after each dose of the Sinovac-CoronaVac vaccine versus MTX maintenance in rheumatoid arthritis (RA) patients.

Methods: This was a single-center, prospective, randomized, investigator-blinded, intervention study (#NCT04754698, CoronavRheum), including adult RA patients (stable CDAI≤10, prednisone ≤7.5mg/day), randomized (1:1) to withdraw MTX (MTX-hold) for 2 weeks after each vaccine dose or maintain MTX (MTX-maintain), evaluated at D0, D28 and D69. Co-primary outcomes were anti-SARS-CoV-2 S1/S2 IgG seroconversion(SC) and neutralizing antibody (NAb) positivity at D69. Secondary outcomes were geometric mean titers (GMT) and flare rates. For immunogenicity analyses, we excluded patients with baseline positive IgG/NAb, and, for safety reasons, those who flared at D28 (CDAI>10) and did not withdraw MTX twice.

Results: Randomization included 138 patients with 9 exclusions (5 COVID-19, 4 protocol violations). Safety evaluation included 60 (MTX-hold) and 69 (MTX-maintain) patients. Further exclusions: 27 patients [13 (21.7%) vs. 14 (20.3%), p=0.848] with positive baseline IgG/NAb and 10 patients (21.3%) in MTX-hold with CDAI>10 at D28. At D69, MTX-hold (n=37) had a higher rate of seroconversion than MTX-maintain (n=55) group [29 (78.4%) *vs* 30 (54.5%), p=0.019], with parallel augmentation in GMT [34.2 (25.2-46.4) *vs* 16.8 (11.9-23.6), p=0.006]. No differences were observed for NAb positivity [23 (62.2%) *vs* 27 (49.1%), p=0.217]. At D28 flare, rates were comparable in both groups (CDAI, p=0.122; DAS28-CRP, p=0.576), whereas CDAI>10 was more frequent in MTX-hold at D69 (p=0.024).

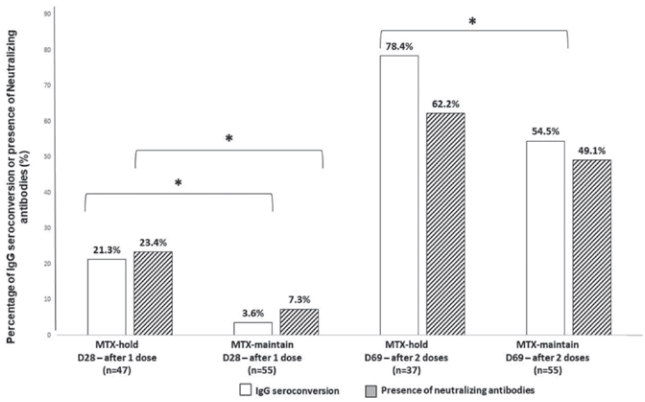

Figure 1.

Conclusion: We provide novel data that 2-week MTX withdrawal after each Sinovac-CoronaVac vaccine dose improves anti-SARS-CoV-2 IgG response. The increased flare rates after second MTX withdrawal may be attributed to the short-term interval between vaccine doses. This strategy requires close surveillance and shared decision making due to the possibility of flares.

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POS0260 LONG-TERM HUMORAL RESPONSE TO SARS-COV-2 VACCINATION IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASE

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Background: The first vaccine against SARS-CoV-2 was approved in December 2020. Immunogenicity of SARS-CoV2 vaccines in patients with immune-mediated inflammatory disease (IMID) have so far been evaluated in the 2-6 weeks following complete vaccination and risk groups for poor early vaccine response have been identified leading to specific vaccination recommendations. However, data on the long-term course and persistence of vaccine response in IMID patients, as well as the outcomes of the specific recommendations are lacking.

Objectives: To evaluate the long-term course of humoral response to SARS-CoV-2 vaccination in a large prospective cohort of IMID patients and non-IMID controls with a follow-up duration of up-to to 10 months after the first vaccine dose.

Methods: We have initiated a prospective dynamic cohort of IMID patients and healthy controls in February 2020 to monitor immune response to SARS-CoV-2 and respiratory infections including COVID-19 (1). Participants who contributed data starting from the 4 weeks before their first vaccination onwards were included in this analysis. Antibodies against SARS-CoV-2 spike protein were quantified with an ELISA from Euroimmun (Lübeck, Germany) with an optical density cutoff of 0.8. We fitted linear mixed-effect models for log-transformed antibody levels using time splines with adjustment for age and sex. Marginal mean antibody levels with 95% confidence intervals (CI) were estimated at selected time points for IMID patients and controls with double vaccination. We descriptively analyzed the observed antibody levels over time in cohort participants receiving two vaccinations vs. three vaccinations.

Results: Among 5076 cohort participants, 3147 IMID patients and healthy controls (mean (SD) age 49 (16)) provided 4756 samples for this analysis between December 2020 and 2021, with a median (IQR) 28 (14-31) weeks of follow-up after the first vaccination (Table 1). 2965 (94%) participants had received at least 2 and 223 (7%) participants had received three vaccine doses by the date of their latest sampling.

In IMID patients, age and sex-adjusted estimated marginal mean antibody levels waned after week 16 and were substantially reduced at all time points compared to the controls, finally dropping to the borderline range (1.01, 95%CI 0.86 to 1.19) at week 40 (Figure 1A, Table 1). A third dose was given to 128 (7%) of IMID patients with a poor response to 2 vaccine doses after a median 20 weeks of the second dose (IQR 10 to 26 weeks). After the third dose, antibody levels in IMID patients were comparable to those of healthy controls at 40 weeks who had three vaccine doses. These were also higher than that of IMID patients and controls who did not receive a third dose (Figure 1B).

Table 1. Participant characteristics and antibody levels

	Healthy controls	IMID
N	1199	1948
Age, mean (SD)	40.8 (13.5)	54.3 (14.8)
Follow-up, weeks, median (IQR)	31.1 (23.8-36.6)	19.6 (12.3-26.6)
Follow-up range, weeks,	1.6-46.1	1.7-46.3
Sex, n(%)		
Female	554 (46.2)	1136 (58.3)
Vaccine intervals, ´median (IQR)		
1st to 2nd dose	4.6 (3.0-6.0)	6.0 (5.0-6.1)
2nd to 3rd dose	29.6 (26.9-36.4)	19.9 (10.0-26.1)
Diagnosis, n (%)		
Spondyloarthritis	-	713 (36.6)
Rheumatoid arthritis	-	489 (25.1)
Autoimmune disease, systemic+	-	420 (21.5)
Inflammatory bowel disease	-	219 (11.2)
Psoriasis	-	107 (5.5)
Mean* antibody levels after 1st dose		
Week-8	4.16 (3.89 to 4.45)	2.97 (2.83 to 3.12)
Week-16	8.39 (7.81 to 9.02)	5.04 (4.81 to 5.28)
Week-32	5.02 (4.73 to 5.33)	2.52 (2.32 to 2.74)
Week-40	2.14 (1.95 to 2.35)	1.01 (0.86 to 1.19)

+ Systemic lupus, systemic sclerosis, Sjögren's syndrome, vasculitis* Estimated marginal means adjusted for age and sex.

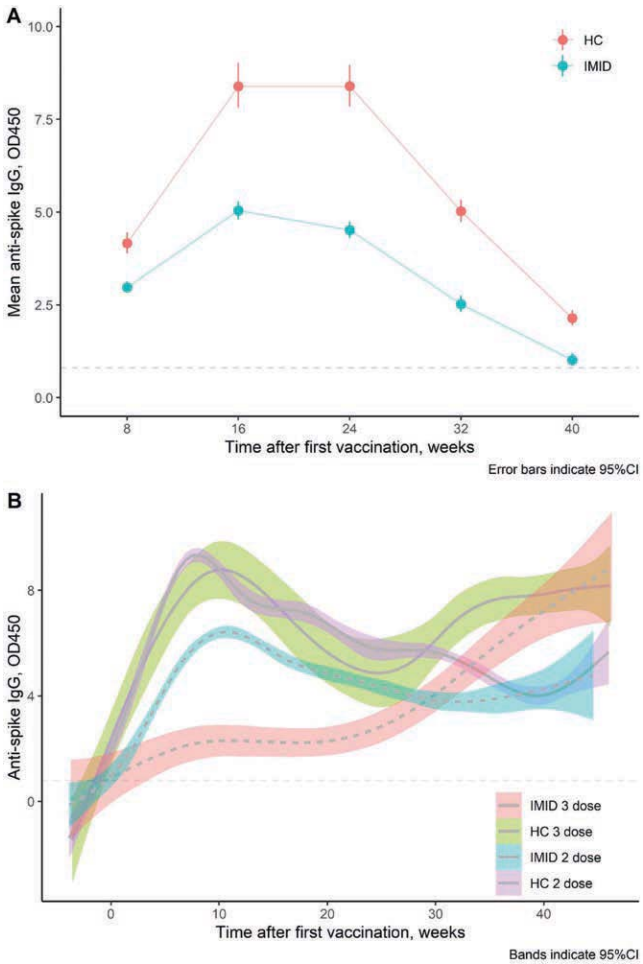

Figure 1.

Conclusion: Humoral response to vaccination against SARS-CoV-2 was weaker in IMID patients compared to controls at all time points after the first vaccine dose and practically disappeared after 1 year. IMID patients can still achieve a good antibody response with a third dose even after a weak response with two doses.

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POS0261

TIME SINCE LAST RITUXIMAB TREATMENT IS ESSENTIAL FOR DEVELOPING A HUMORAL RESPONSE TO THE COVID-19 MRNA VACCINE IN PATIENTS WITH RHEUMATIC DISEASES.

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Background: Concerns about Rituximab (RTX) treatment and potentially inadequate vaccine response were aired early in the pandemic, and initial data seem to support this concern (1). So far, studies regarding rheumatic patients and the COVID-19 vaccines have included a relatively small number of patients receiving rituximab.

Objectives: We aimed to investigate if patients with rheumatic diseases treated with RTX raise a serological response towards the COVID-19 mRNA vaccines and to elucidate the influence of time since the last dose RTX before vaccination on this response.

Methods: We included 201 patients followed at the Department of Rheumatology, Aarhus University Hospital. All had been treated with RTX in the period 2017-2021, and had finished a two-dose COVID-19 mRNA vaccination. All patients and 44 blood donors had total antibodies against SARS-CoV2 spike protein measured. Univariate and multivariate logistic regression were used.

Results: Patients were predominantly female (67%) with a median age of 62 years. The most frequent diagnosis was ANCA-associated vasculitis (32%), rheumatoid arthritis (31%), and myositis (14%), and 97% had the Pfizer/Biontic vaccine. Median number of RTX infusions were 5 (IQR 2-8), with a cumulative dose of 4g (2-8), and 72% had received RTX within the last 15 months. Prednisone was used by 43%, followed by methotrexate (25%), hydroxychloroquine (11%) and azathioprine (10%). We observed a time-dependent increase in antibody response as the interval from the last RTX treatment to vaccination increased (Table 1). Only 17.3% of patients developed a detectable antibody response after receiving their vaccination 6 months or less after their previous RTX treatment (Figure 1). Positive antibody response increased to 66.7% in patients who had RTX 9-12 months before vaccination. Neither cumulative treatment time nor cumulative RTX dose seemed to influence the serological response to the vaccine (Table 1). Thus, even in patients who have received RTX for a substantial time, expanding time-since-last-RTX treatment could prove beneficial for increasing the chance of a serological response. We further found that "months between last Rtx and vaccination", prednisone and azathioprine treatment were alle negatively associated with antibody response in a multivariate logistic regression analysis(Table 1). All blood donors (100%) had detectable antibodies after vaccination.

Table 1. Logistic regression analysis with precense of SARS-CoV-2 antibodies after mRNA vaccination as dependent varaible.

Univariate	OR	95% CI	P-value
Sex, female = ref.	0.91	0.50 - 1.67	0.77
Age, years	0.98	0.96 - 1.00	0.09
Diagnosis	1.05	0.99 – 1.13	0.08
Months between last RTX and vaccination	1.06	1.03 - 1.09	**<0.001**
Total number of RTX infusions	0.96	0.92 - 1.01	0.10
Total dose of RTX, mg	0.97	0.92 - 1.02	0.18
Time from first to last RTX treatment	1.00	1.00 - 1.00	0.57
No DMARD treatment	0.94	0.50 - 1.78	0.85
Prednisone, dose in mg	0.91	0.85 - 0.99	**0.02**
Methotrexate	1.71	0.90 - 3.25	0.10
Hydroxychloroquine	0.87	0.35 - 2.19	0.77
Azathioprine	0.23	0.06 - 0.80	**0.02**
Multivariate model			
Months between last Rtx and vaccination	1.08	1.04 - 1.11	**<0.001**
Prednisone treatment, mg	0.91	0.84 - 0.99	**0.03**
Azathioprine treatment	0.10	0.02 - 0.44	**0.002**

All significant variables in the univariate analysis were included in the multivariate model.

Conclusion: In conclusion, patients with rheumatic diseases treated with RTX have a severely impaired serological response towards the COVID-19 mRNA vaccine. This is especially true if the interval between RTX treatment and vaccination is

less than 9 months. For the majority of RTX treated patients, the recommended six months since last RTX is insufficient to develop a humoral response to COVID-19 mRNA vaccines. Our data suggest that the current recommendations of a 6 months interval should be revised.

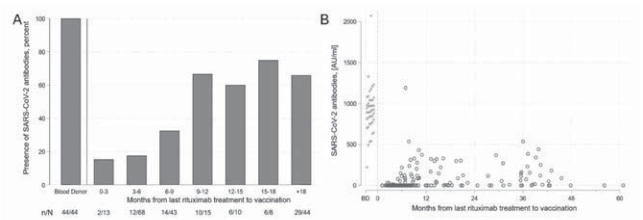

Figure 1. Total SARS-CoV-2 antibody response after receiving two vaccinations with COVID-19 mRNA vaccine in patients with rheumatic diseases treated with rituximab and controls. A) Percent of patients and controls with a measurable antibody response post-vaccination. B) Levels of measured total anti-SARS-CoV-2 antibodies in patients (circles) and controls (crosses). The X-axis shows time since the patients' last treatment with rituximab prior to vaccination. n=number of individuals with SARS-CoV-2 antibodies, N= total number of individuals. Blood donors (BD)

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POS0262 HUMORAL AND CELLULAR SARS-COV-2 VACCINE RESPONSES IN PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are overlapping autoinflammatory diseases affecting people over 50 years. The diseases are treated with immunosuppressive drugs such as prednisolone, methotrexate, leflunomide and tocilizumab. Even though GCA and PMR patients have a substantially higher risk for infections, little is known about humoral and cellular immune responses after vaccination in these patients.
Objectives: In this study we assessed the immunogenicity and safety of SARS-CoV-2 vaccinations in these diseases.
Methods: Patients (n=45 GCA, n=33 PMR) visited the outpatient clinic twice: pre-vaccination and 4 weeks post-vaccination (BNT162b2 or ChAdOx1 vaccine). Patients with previous SARS-CoV-2 infection were excluded. In both pre- and post-vaccination samples, anti-Spike antibody concentrations were assessed and compared to age-, sex- and vaccine-matched control groups (n=98). In addition, the frequency of SARS-CoV-2 Spike-specific T-cells was assessed by IFN-γ ELIspot assay, and side-effects and disease activity were recorded.
Results: The GCA/PMR patients, as a group, did not have reduced antibody concentrations compared to controls. However, linear regression analysis revealed a significant association of methotrexate and >10mg/day prednisolone use with lower antibody concentrations in GCA/PMR patients. Evidence of cellular immunity, as assessed by ELIspot assay, was found in 67% of GCA/PMR patients, and was correlated with humoral immunity (Figure 1). Patients using >10mg/day prednisolone had reduced cellular immunity. Importantly, vaccination did not lead to significant side-effects or changes in disease activity.

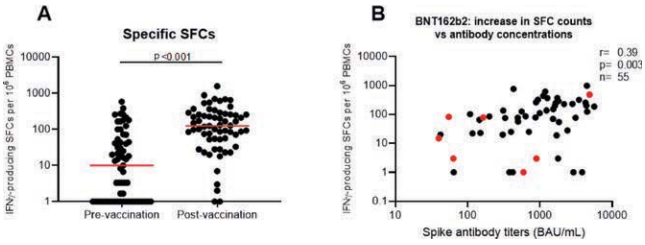

Figure 1. Spot-forming cell (SFC) counts in the ELIspot assay. SFC counts, indicating IFNγ producing cells, increased significantly (Mann Whitney U) at post-vaccination compared to pre-vaccination. Red line indicates the median (A). SFC counts correlated with Spike antibody concentrations in GCA/PMR patients vaccinated with BNT162b2 (B). GCA/PMR patients using >10 mg/day prednisolone are indicated in red. For the correlation, the specific SPC counts are used in the post-vaccination sample after subtracting the SPC count in the pre-vaccination sample. Statistical analysis by the Spearman correlation coefficient. BAU: binding antibody units

Conclusion: SARS-CoV-2 vaccination was safe for GCA/PMR patients and immunogenicity was comparable to other older individuals. However, patients using methotrexate and particularly >10mg/day prednisolone did show lower vaccine responses, which corroborates findings in other autoinflammatory patient populations. These patients may therefore be at higher risk of (potentially even severe) breakthrough SARS-CoV-2 infection.
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POS0263 RE-VACCINATION COMPARED TO BOOSTER COVID-19 MRNA VACCINATION SIGNIFICANTLY INCREASES THE SEROLOGICAL RESPONSE IN RITUXIMAB-TREATED PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES WITHOUT A PRIMARY DETECTABLE SEROLOGICAL COVID-19 VACCINE RESPONSE

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Background: Reports of an impaired humoral response after COVID-19 vaccination in patients treated with rituximab (RTX) have raised particular concern for patients with inflammatory rheumatic diseases (IRD) receiving RTX (1). This calls for strategies to enhance a humoral response in RTX-treated patients. At present, there is no data on whether it is best to increase the humoral response with a third vaccine dose (a booster) or with a third and fourth dose (re-vaccination).
Objectives: In IRD patients treated with RTX, without a detectable humoral response after the first vaccination course (two shots), we aimed to investigate the difference of either a booster vaccine (dose 3) or a new re-vaccination course (dose 3+4) on the serological response of the COVID-19 mRNA vaccines.
Methods: We included 84 patients with IRD treated with RTX, all without measurable total SARS-CoV-2 antibodies after a full primary COVID-19 vaccination course (2 doses three weeks apart). All patients were offered a new re-vaccination course with the mRNA vaccine not used primarily (Pfizer/Biontec or Moderna). A small number of patients declined the revaccination, and recieved a booster with the mRNA vaccine used initially. Serum total antibodies were measured before and six weeks after the last dose against recombinant SARS-CoV-2 spike S1 protein (VITROS). In addition, CD19+ B-cells were measured at inclussion.
Results: Patient characteristics are in Table 1. The median age was 64 years; 68% were female with a disease duration of 5 years. Sixty-nine out of 84 were re-vaccinated (3+4 dose). Details previous exposure to RTX are given in Table 1. CD19+ B-cells were measurable in 12/81 at inclussion.

Table 1. ***Patient Characteristics***

	Booster, n=15	Revaccination, n=69
Age, years median (IQR)	60 (45 - 69)	65 (54 - 70)
Female	47%	72%
Disease duration, years (IQR)	5 (2-8)	6(2 - 13)
ANCA-vasculitis	47 %	45 %
Rheumatoid Arthritis	47 %	17 %
Poly- Dermatomyositis	6 %	19 %
SLE, Scleroderma, other diagnoses	-	19 %
No DMARD treatment	27 %	35 %
Prednisone	33 %	46 %
Methotrexate	40 %	16 %
Azathioprine	7 %	12 %
Mycophenolate	7 %	7 %
Other	20 %	9 %
Rituximab treatment, (IQR)		
Months from last RTX to vaccination	3.9 (1.3 - 9.3)	5.4 (4.2 - 7.3)
Number of infusions	6 (4 - 8)	7 (5 - 12)
Cummulativ total dose, gram	4 (2.5 - 7.5)	6 (3.5 - 10)
Total treatment time with RTX, months	15 (9 - 54)	27 (13 - 63)
Patients with measurable CD19+ B-cells in peripheral blood at the time of booster or re-vaccination (positive/total)	3/14	9/67

We found a combined seroconversion rate of 33% six weeks after the last shot. There was no statistical difference between the booster (38,5%) and the re-vaccination group (32,3%), p=0.67 (Pearson's chi-squared). IRD patients with a humoral response in the re-vaccination group had significantly higher levels of total SARS-CoV-2 antibodies (median(IQR) 306(49-464) AU/ml) compared to the booster group (14(4-15) AU/ml) p=0.02, Figure 1A. In multiple logistic regression model, we found that levels of CD19+ B-cells were the only variable able to predict a humoral response, Figure 1B. However, only 39% of the patients with

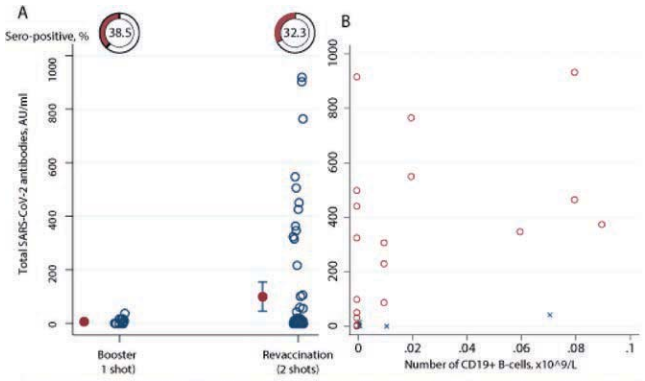

Figure 1. Concentration of total SARS-CoV-2 antibodies measured 6 weeks after last COVID-19 revaccination or booster shot. A) Total antibody concentration presented by vaccination group, either 1 shot (booster) or 2 shots (revaccination). Pie chart present percent of patients with a positive total antibody measurement post-vaccination. Circle with whiskers indicate mean concentration with confidence intervals. B) Total antibody concentration presented by pre-vaccination measurement of circulating CD19+ B-cells in peripheal blood. (x) indicate booster and (0) indicate revaccination group.

Figure 1.

a humoral response to vaccination had measurable CD19+ B-cells before vaccination. We found no effect of age, sex, diagnosis, treatment, and RTX exposure on the chance of seroconversion in multiple logistic regression models when corrected for CD19+ B-cells.

Conclusion: We found that re-vaccination (dose 3+4) with COVID-19 mRNA vaccines favored a high humoral response in patients with IRD treated with RTX, who did not have a detectable humoral response after the first two vaccine doses, compared to a booster shot (dose 3). A detectable humoral response after re-vaccination was seen in more than half of the patients with no measurable CD19+ B-cells before vaccination. Presence of circulating CD19+ B-cells are a significant predictor of humoral response to mRNA COVID-19 vaccination.

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POS0264

CHARACTERIZATION OF THE IMMUNE RESPONSE IN PATIENTS WITH INFLAMMATORY IMMUNE-MEDIATED DISEASES ON IMMUNOSUPPRESSIVE TREATMENT AFTER ONE MONTH OF SARS-COV-2 VACCINATION

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Background: The relevance of studying immune response after SARS-CoV-2 vaccination in patients with inflammatory immune-mediated diseases (IMIDs) represents a deep concern regarding the risk estimation and management of patients with these diseases on immunomodulatory drugs. It is well known that certain treatments as anti CD20 therapies results in a diminished immunogenicity against common vaccines but it is a scarce data regarding the cellular protection obtained upon vaccination between patients with different IMID and between different treatments.

Objectives: To compare a potential detriment on cellular and antibody-mediated protection upon SARS-CoV-2 vaccination in patients with IMIDs treated with immunosuppressive drugs.

Methods: We recruited 73 patients with rheumatoid arthritis-RA-(n=49), spondylarthritis-SpA-(n=19), inflammatory bowel disease-IBD-(n=5), idiopathic juvenile arthritis-IJA- (n=2) and heterogenous group composed of sclerodermia, lupus, uveitis…(n=6). They were treated mainly with rituximab (n=27), TNFi (n=37) or JAKi (n=3). We collected data of age,sex, csDMARDs, previous SARS-CoV-2 infection, last RTX infusion and prednisone use.

After one month of vaccination, we assessed the humoral response performing the Thermo Scientific EliA SARS-CoV-2-Sp1 IgG Test (positivity cut-off >0.70 IU/ml) which was also compared with the data with of 35 healthy controls. In addition, in 40 patients who had serum antibody levels under 100UI/ml, we analysed the cellular response by the use of the QuantiFERON SARS-CoV-2 Starter Pack (Quiagen). A cut-off value of 0.15 IU/ml discriminate between positive or negative cell-mediated immune responses. We compared differences among the different IMIDs and between the different immunosuppressive treatments through non-parametric test (p<0.05)

Results: Regarding demographic characteristics of patients, older patients (>56 years) and female sex were factors which were associated with low titles of serum antibodies.

Anti-spike IgG antibodies were present in an 86% of the IMIDs patients and in 100% healthy controls with significant different IgG titre (median [IQR]): 51[11-184] vs 700[440-940]; p<0.0001.

The differences between (median [IQR]) serum antibody levels were statistically different between IMID type: 33[1-138] in RA vs 94[34-191] in SpA vs 204[187-204] in IBD vs 133[61-204] in IJA vs 13[1.5-31.8] in the rest; p=0.04. Remarkably, patients with IBD who had the highest antibodies titles were the youngest compared with the other patients.

Target of the therapy played also an important role in serum antibody levels being these: 3.6 [0.7-51] in RTX patients vs 156 [45-204] in TNFi vs 40 [18-58] in JAKi patients; p<0.0001. In those patients who the last infusion of rituximab was, at least, one year before vaccination presented CD19+ B cells detected by flow cytometry and anti-spike IgG antibodies as well.

Cell-mediated responses to SARS-CoV-2 were positive in 33% of IMIDs patients, indeterminated in 3% and negative in 65% of the patients. Strikingly, out of the 33% positive patients, 85% were treated with RTX. A 61% of the RTX patients had inducible cell-mediated responses vs 14% of the patients treated with TNFi; p<0.01. On the other hand, there were not differences in cell-mediated responses between positive and negative antibody patients.

Conclusion: Titres of serum antibodies against spike protein of SARS-CoV-2 were lower in IMIDs patients than in controls. Patients with RTX had lower rates of positivity humoral response as well as lower serum titles than patients treated with other therapies regardless the patients 'age. Neverthless, in those patients in whom RTX infusion was delayed because of vaccination they conserved a humoral response.

On the other hand, more patients treated with RTX had inducible cell-mediated responses compared with patients with TNFi.

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Achy-Breaky vessels

POS0265

SERUM PROTEOMICS IN GIANT CELL ARTERITIS IN RESPONSE TO A THREE-DAY PULSE OF GLUCOCORTICOID FOLLOWED BY TOCILIZUMAB MONOTHERAPY (THE GUSTO TRIAL)

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Background: Measuring disease activity in Giant Cell Arteritis (GCA) remains a challenge, particularly, if Tocilizumab (TCZ) is prescribed which blunts the acute phase response. A proteome analysis may not only serve to identify biomarkers, but also to shed light on pathophysiology. The sequential administration of Glucocorticoids (GC) and TCZ as done in the GUSTO study (GCA treatment with ultra-short GC and TCZ) provides a unique opportunity to dissect the effects of GC and TCZ.

Objectives: To investigate the effects of pulse GC-treatment and of ensuing long-term TCZ monotherapy on serum proteins in GCA; to compare the serological findings with clinical response; to search for proteins which are not under control of IL-6 and may be suitable as biomarkers of disease activity.

Methods: Eighteen patients with newly diagnosed GCA received 500 mg methylprednisolone intravenously for 3 consecutive days (NCT03745586). Thereafter, GC treatment was discontinued and a single dose of TCZ (8 mg/kg body-weight) was administered intravenously, followed by weekly subcutaneous TCZ injections (162 mg) from day 10 until week 52. Serum samples were collected prior to treatment (day 0), at day 3 (after GC treatment), day 10 and at weeks 4, 24, and 52

(Lancet Rheumatology, https://doi.org/10.1016/S2665-9913(21)00152-1). Sera of patients were analyzed on Olink Explore 1536, capturing over 1400 proteins. Protein wise t-tests (threshold, adjusted p-value < 0.05) with adjustment for multiple testing (Benjamini-Hochberg) were performed to identify differentially expressed proteins (DEPs) between day 0 vs day 3 (referred to as GC treatment) and day 0 vs week 52 (referred to as TCZ treatment, remission). DEPs were grouped in pathways identified in the KEGG database.

Results: Successful treatment resulted in the upregulation of 254 proteins and the downregulation of 245 proteins from day 0 to week 52. Protein levels did not change between week 24 and 52 during established full remission.

In response to GC pulse therapy the ten most significant DEPs included ANGPTL7, AREG, IL1RL1, MATN3, MMP3, SPARCL1 (upregulated) and IL12A, IL12B, KLK10, SIGLEC6 (downregulated). Conversely, under treatment with TCZ, SIGLEC6 was continuously up- and MMP3 and AREG were continuously down-regulated from day 3 to week 4.

KEGG pathways of interest in GCA (day 0 vs day 3 and day 0 vs week 52, respectively) included: cytokine-cytokine receptor interaction, the PI3K-AKT, JAK-STAT, IL17, TNF, NF-kappa B, Toll-like receptor and MAPK signaling pathways. Figure 1 displays the top 5 KEGG pathways enriched in TCZ-treated GCA patients in remission.

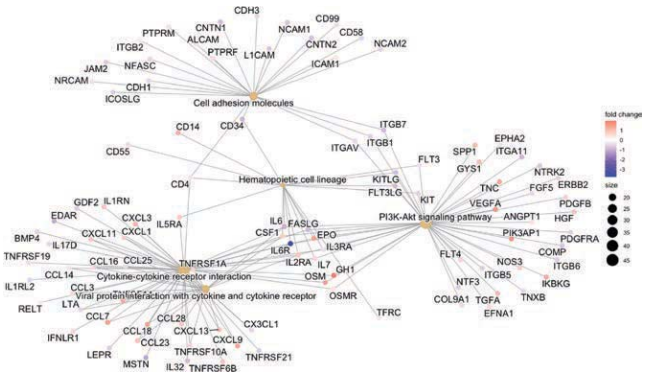

Figure 1. Network plot of the top 5 KEGG pathways from day 0 vs week 52. Size in the figure legend refers to the number of proteins in each pathway. Estimate in the figure legend indicates the log2 fold change from day 0 vs week 52.

Conclusion: One third of the measured proteins covering a wide spectrum of pathways changed in response to pulse GC-treatment followed by TCZ monotherapy. Several proteins were inversely induced by GC or TCZ. Osteopontin, CSF1 and CCL18 as markers of macrophage activation should be explored as biomarkers of disease activity in TCZ-treated GCA-patients.

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POS0266 EFFECTIVENESS OF A SPACING-UP STRATEGY AFTER ONE-YEAR COURSE OF WEEKLY TOCILIZUMAB IN PATIENTS WITH GIANT CELL ARTERITIS: A SINGLE-CENTRE PROSPECTIVE STUDY

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Background: Although tocilizumab (TCZ) is extensively used for the treatment of giant cell arteritis (GCA), there is still uncertainty with regard to optimal treatment duration. The GiACTA open-label extension phase showed that 58% of patients treated with a 12-month course of weekly TCZ had a disease flare in the 2 years following therapy suspension[1], suggesting that some patients may need a more prolonged duration of this therapy.

Objectives: To evaluate efficacy and safety of low-dose TCZ maintenance in GCA patients who achieved remission after one year of standard TCZ therapy.

Methods: GCA patients eligible for TCZ according to the 2018 EULAR recommendations[2] and who achieved remission after one year of weekly subcutaneous TCZ were prospectively enrolled. TCZ was administered every-other-week (EOW) for additional 12 months, and eventually suspended. Patients were evaluated 4-monthly during TCZ therapy, and 1 and 6 months after TCZ suspension (Figure 1). In patients with large-vessel (LV) involvement at baseline, PET scan was performed 12 and 24 months after TCZ start. Primary outcome was relapse-free survival at month 6 since TCZ suspension. Relapse-free survival during TCZ therapy and imaging response at PET scan were also evaluated. Adverse events were recorded.

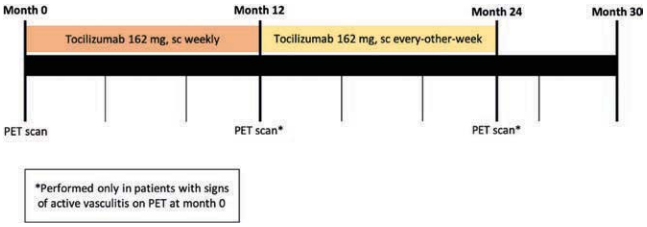

Figure 1. Study design.

Results: 17 patients were enrolled (12 women, 71%; mean age 71.5±8.7 years). Disease features at diagnosis and TCZ start are listed in Table 1. Reasons for TCZ start were clinical or imaging disease flare (n=9), persistence of disease activity (n=5), and steroid-related adverse events (n=3). At TCZ start, median disease duration was 8 (3-22) months, serum C-reactive protein (CRP) was 13 (6-22) mg/L, daily prednisone (PDN) dose was 25 (15-37.5) mg; 4 patients were already on methotrexate (MTX) which was maintained in 1 of them; 10 patients (59%) had LV involvement on PET scan. At TCZ EOW start, no patient was on PDN and 1 patient was on MTX; MTX was added in another patient due to persistence of LV involvement at PET scan. All patients completed the 24-month TCZ course. Two patients (12%) had a polymyalgic flare while on EOW TCZ: one patient at month 1 and one patient at month 6; of note, one of them had a polymyalgic flare also while on weekly TCZ. Both flares were managed with a PDN course with complete clinical remission. No patient had active LV involvement at 24-month PET scan. Adverse events on EOW TCZ were zoster reactivation (n=1) and neutropenia (n=1). At TCZ stop, no patient was on PDN and 2 patients were on MTX. One month after TCZ stop, all patients were in remission. Six months after TCZ stop, 4 patients (24%) experienced a flare, which was successfully managed in all cases with TCZ weekly re-introduction; in 2 patients, a PDN course was also started.

Table 1. ***Patients' characteristics at giant cell arteritis diagnosis and at study entry.***

	GCA diagnosis, n=17 n (%)	TCZ start, n=17 n (%)
Headache	16 (94)	5 (29)
Scalp tenderness	11 (65)	5 (29)
Jaw claudication	9 (53)	2 (12)
Ocular ischemic manifestations	3 (17)	0 (0)
Polymyalgia rheumatica	8 (47)	0 (0)
Constitutional symptoms	14 (82)	7 (47)
Active vasculitis on PET	10 (59)	10 (59)
Modality of diagnosis		
Vascular ultrasound	7 (47)	-
Temporal artery biopsy	3 (17)	-
PET	10 (59)	10 (59)

Conclusion: In this proof-of-concept study, low-dose TCZ maintenance in GCA showed excellent disease control, which was maintained in most patients after therapy suspension. Longer follow-up and replication in larger cohorts are required.

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POS0267 OUTCOMES DURING AND AFTER LONG-TERM TOCILIZUMAB TREATMENT IN PATIENTS WITH GIANT CELL ARTERITIS

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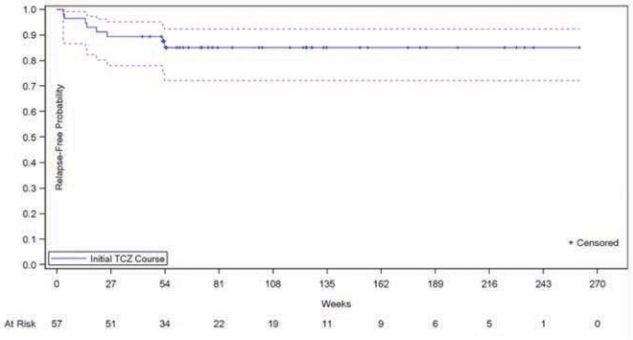
Background: Data on the long-term efficacy and safety of tocilizumab (TCZ) for giant cell arteritis (GCA), including incidence and timing of disease relapse after TCZ discontinuation, is limited.
Objectives: We aimed to evaluate the long-term outcomes of GCA patients treated with TCZ in a real-world setting.
Methods: Retrospective analysis of GCA patients treated with TCZ for >9 months at a single center between 2010-2021. Time to relapse and annualized relapse rate during and after TCZ treatment, prednisone use and safety were assessed. Relapse was defined as the re-appearance of clinical manifestations of GCA that required treatment intensification regardless of the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) levels. The duration of TCZ treatment was determined as per the best clinical judgement of the treating rheumatologist.
Results: A total of 57 GCA patients were followed for a mean (SD) period of 3.4 (1.7) years. Baseline characteristics and treatments received are shown in Table 1. Patients were maintained on their initial TCZ course for a mean (SD) period of 2.0 (1.3) years. The initial TCZ course lasted >12 months in 50 (88%) patients. During the initial TCZ course, 8 (14.0%) patients relapsed. Kaplan-Meier (KM) estimated relapse rates on TCZ were 10.5% and 14.9% at 12 and 18 months, respectively (Figure 1**A**). TCZ was discontinued due to long-term remission in 37 (64.9%) patients and after an adverse event in 6 (10.5%) patients. Of the 43 patients stopping TCZ due to remission or adverse event, 19 (44.2%) subsequently relapsed. KM estimated relapse rates after TCZ discontinuation were 30.4% and 44.0% at 12 and 18 months, respectively (Figure 1**B**). Overall, 12 patients received more than one TCZ course. The aggregation of all TCZ courses (mean 2.5 years) and all periods off TCZ following the initial TCZ treatment (mean 0.9 years) showed that 11 (19.3%) patients relapsed while on TCZ and 20 (35.1%) patients relapsed during time off TCZ. An analysis adjusting for age, sex, prednisone dose at initiation of first TCZ course, and disease type (new onset vs. relapsing) at initiation of first TCZ course showed an annualized relapse rate (95% CI) of 0.1 (0.0-0.2) during TCZ treatment and 0.4 (0.3-0.7) off TCZ (rate ratio 0.2, p<0.0001). By the end of follow up, 42 (73.7%) patients were able to wean off prednisone. During the study, 12 serious adverse events occurred in 11 (19.3%) patients. Among those 12 events, 3 (25%) were related or possibly related to TCZ exclusively (i.e., soft tissue infection, bacteremia, and COVID-19), 3 (25%) to prednisone exclusively (i.e., osteoporotic fracture, diabetic ketoacidosis and stroke), and 2 (16.7%) to either TCZ or prednisone (i.e., pneumonia and sepsis).
Conclusion: Long-term TCZ treatment was efficacious in maintaining disease remission and sparing the use of prednisone in patients with GCA. Over 40% of patients stopping TCZ after long-term remission or adverse event relapsed following TCZ discontinuation.

Table 1. Baseline characteristics and treatments

	GCA patients (n = 57)
Age, mean (SD)	70.1 (9.3)
Female sex	39 (68.4)
New onset disease at TCZ initiation	18 (31.6)
Initial TCZ treatment	
4 mg/Kg intravenously monthly	2 (3.5)
8 mg/Kg intravenously monthly	13 (22.8)
162 mg subcutaneously every 2 weeks	6 (10.5)
162 mg subcutaneously weekly	36 (63.2)
On prednisone at TCZ initiation	57 (100)
Prednisone dose (mg) at TCZ initiation, mean (SD)	32.3 (21.7)
Patients receiving >1 TCZ course	12 (21.1)
Duration of initial TCZ course (years), mean (SD)	2.0 (1.3)
Total duration of TCZ treatment (years), mean (SD)	2.5 (1.6)*

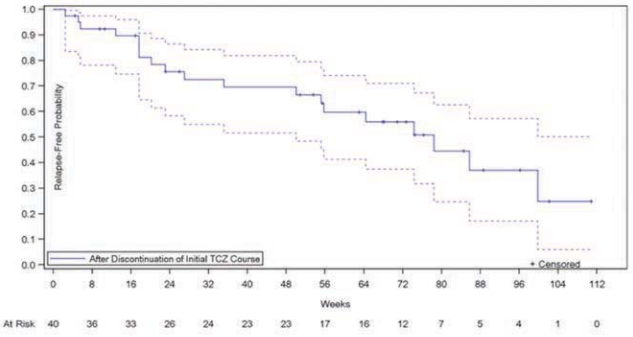
Values represent number and (%) unless otherwise specified. *Aggregated time on tocilizumab (TCZ)for those patients that received more than 1 TCZ course. GCA, giant cell arteritis; SD, standard deviation.

Figure 1A. Time to relapse on initial TCZ treatment*



* Patients were censored if tocilizumab (TCZ) was discontinued for any reason or the patient was lost to follow-up.

Figure 1B. Time to relapse after discontinuation of initial TCZ treatment*



* Time to relapse in patients that discontinued TCZ due to either long-term remission or an adverse event and who had follow-up beyond their TCZ discontinuation date. Patients were censored if TCZ was re-started for any reason other than relapse or the patient was lost to follow-up

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Disclosure of Interests: Mark Matza: None declared, Nicholas Dagincourt Employee of: Working for Genentech, Inc., as employees of Everest Clinical Research, Shalini Mohan Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Andrey Pavlov Employee of: Working for Genentech, Inc. as an employee of Everest Clinical Research, Jian Han Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., John H. Stone Consultant of: Roche, Grant/research support from: Roche, Sebastian Unizony Grant/research support from: Research funding from Genentech, Inc.
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POS0268 INTRAVENOUS TOCILIZUMAB FOR THE TREATMENT OF GIANT CELL ARTERITIS: A PHASE IB DOSE-RANGING PHARMACOKINETIC BRIDGING STUDY

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Background: Subcutaneous (SC) tocilizumab (TCZ), a recombinant humanized anti-interleukin-6 receptor (IL-6R) monoclonal antibody, is approved globally for

the treatment of giant cell arteritis (GCA), with once weekly injections, based on the GiACTA trial.

Objectives: This Phase Ib study (NCT03923738) investigated the pharmacokinetics (PK), pharmacodynamics (PD), safety and exploratory efficacy of 2 doses of TCZ given intravenously (IV) in patients with GCA. The purpose was to explore an IV dose resulting in a minimum exposure level within the range of effective trough concentrations achieved with TCZ SC dosing in GCA and not exceeding the exposure of the well-tolerated 8 mg/kg IV every 4 weeks (Q4W) in rheumatoid arthritis (RA).

Methods: This study enrolled patients with GCA in Switzerland who had received ≥5 consecutive doses of TCZ IV 8 mg/kg (off label) Q4W and were in remission. Patients received 5 or 6 doses of TCZ IV 7 mg/kg Q4W in period 1 and, if still in remission, then received 5 or 6 doses of 6 mg/kg Q4W in period 2. Glucocorticoid use was at the investigator's discretion. PK endpoints were maximum concentration (C_{max}), minimum (trough) concentration (C_{trough}), area under the curve (AUC_τ) over a dosing interval (τ) and average concentration (C_{mean}) calculated as AUC_τ/τ of TCZ after the last dose of each period. Other endpoints included PD markers (IL-6, soluble IL-6R [sIL-6R], C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]), safety (adverse events [AEs], serious AEs [SAEs]) and exploratory efficacy (rates of flare and remission).

Results: In 24 patients enrolled, median (range) age was 65.5 (57-90) years and the majority were female (62.5%). All patients had a history of elevated ESR and/or CRP and evidence of GCA by temporal artery biopsy and/or evidence of large vessel vasculitis at GCA diagnosis. The mean PK profile following TCZ IV 7 mg/kg Q4W in Period 1 was of a similar shape to mean PK profile following TCZ IV 6 mg/kg Q4W in Period 2, with a slightly lower exposure at the 6-mg/kg dose level (Figure 1). Compared with the 7-mg/kg dose, TCZ exposures (C_{max} and AUC_τ) were on average 11.2% and 20.0% lower at the 6-mg/kg dose (Table 1). Mean IL-6 serum concentrations were elevated at baseline due to previous TCZ treatment and remained elevated throughout the study, with slightly higher concentrations in Period 1 (7 mg/kg) than Period 2 (6 mg/kg). Mean sIL-6R concentrations were elevated at baseline and comparable between the 2 doses at steady state. As expected for patients in remission, CRP levels and most ESRs were within the normal ranges at baseline and throughout the study. Overall, 22 patients (91.7%) had ≥1 AE; infections were the most frequently reported AEs. Two patients (8.3%) experienced a Grade ≥3 AE. The majority of AEs (70.8%) were not TCZ-related. Four patients (16.7%) reported an SAE; 1 (pneumococcal pneumonia) was considered TCZ-related by the investigator and 3 led to treatment interruption. There were no deaths. No patients experienced a GCA flare, and all patients remained in remission throughout the study.

Table 1. Steady-State PK Parameters of TCZ IV 7 and 6 mg/kg Q4W

PK Parameters, mean, median (range)	7 mg/kg IV (Period 1) n=22*	6 mg/kg IV (Period 2) n=22
C_{max}, µg/mL	205	182
	197 (118-352)	178 (115-320)
AUC_τ, day•µg/mL	2150	1720
	2130 (1120-4300)	1610 (921-3070)
C_{mean}, µg/mL	76.9	61.5
	76.0 (40.1-154)	57.5 (32.9-110)
C_{trough}, µg/mL	35.3	22.7
	37.2 (6.59-69.0)	22.7 (3.38-54.5)

AUC_τ, area under the curve over a dosing interval (τ); C_{max}, maximum concentration; C_{mean}, mean concentration (AUC_τ/τ); C_{trough}, minimum (trough) concentration; IV, intravenous; PK, pharmacokinetics; Q4W, every 4 weeks; TCZ, tocilizumab. *n=21 for C_{max}.

Conclusion: Both dose levels of TCZ-IV (6 and 7 mg/kg) Q4W were generally well tolerated in patients with GCA. The C_{max} and C_{mean} achieved with 6 mg/kg IV Q4W in patients with GCA were similar to those seen in patients with RA treated with 8 mg/kg IV Q4W, and C_{trough} was within the range observed in patients with GCA treated with once weekly and every 2 weeks SC dosing.

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Disclosure of Interests: Christophe Schmitt Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: F. Hoffmann-La Roche Ltd, Laura Brockwell Employee of: F. Hoffmann-La Roche Ltd, Mylène Giraudon Employee of: F. Hoffmann-La Roche Ltd, Mauro Zucchetto Employee of: Working for F. Hoffmann-LaRoche Ltd as an employee of Parexel International, Lisa Christ Shareholder of: Gilead Sciences and F. Hoffmann-La Roche Ltd, Consultant of: Bristol-Myers Squibb, Novartis, and Sanofi, Grant/research support from: Gilead Sciences, F. Hoffmann-La Roche Ltd, and Pfizer, Bettina Bannert: None declared, Thomas Daikeler Speakers bureau: Novartis, Consultant of: Advisory fees from Novartis, Grant/research support from: Research support from Novartis, Peter Villiger Speakers bureau: Roche, MSD, AbbVie, Pfizer, Novartis, Grünenthal, Amgen, Sanofi, Chugai, BMS, and Gilead, Consultant of: Advisory fees from Roche, MSD, AbbVie, Pfizer, Novartis, Grünenthal, Amgen, Sanofi, Chugai, BMS, and Gilead, Grant/research support from: Research support from Roche, MSD, AbbVie, and Pfizer

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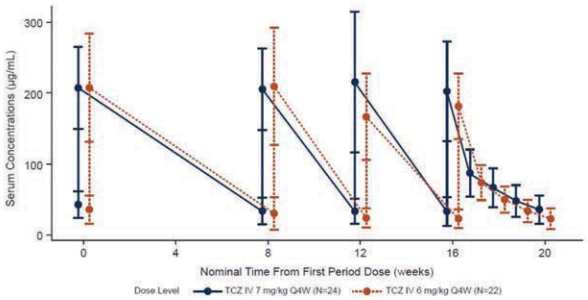
Figure. Arithmetic Mean (SD) Serum Concentration of TCZ vs Time Profiles Following TCZ IV 7 mg/kg Q4W in Period 1 and TCZ IV 6 mg/kg Q4W in Period 2, Linear Scale



POS0269 RESULTS OF ONE YEAR OBSERVATIONAL EXTENSION OF THE BRIDGE-PMR STUDY, A RANDOMIZED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL WITH RITUXIMAB IN POLYMYALGIA RHEUMATICA.

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Background: Glucocorticoids (GC) are the cornerstone of treatment in Polymyalgia rheumatica (PMR) [1]. However, they are associated with considerable toxicity and inefficacy in part of the patients. Rituximab (RTX) was effective for PMR in a 21-week randomized controlled trial (RCT), however results from longer follow-up is still absent [2].

Objectives: To assess, in a randomized double blinded fashion, the clinical and GC-sparing effects one year after RTX.

Methods: In the BRIDGE-PMR, an RCT of 38 recently diagnosed and 9 relapsing PMR (2012 EULAR/ACR classification criteria) patients recruited from the Sint Maartenskliniek, patients were randomly allocated in a 1:1 ratio and treated with 1x 1000mg RTX / placebo (PCB) iv, identical pre-medication and an accelerated GC tapering protocol. After the 21-week study, patients were assessed in a double blinded prospective extension study up to one year after infusion. The primary outcome at one year was between group difference in GC-free remission (PMR-activity score < 10). Analysis was performed with Fischer's exact test and a two-tailed p-value < 0.05 was considered significant. Secondary outcomes were proportion of relapsing patients during the extension, proportion of patients with CRP > 5mg/l during the extension, cumulative GC dose, DMARD use, EQ-5D score, and adverse events (AE).

Results: The proportion of patients in GC-free remission after one year was significantly higher in the RTX group (48%, 11/23) compared to the PCB group (17%, 4/24), with an absolute difference of 31% (95%-CI 6-56), a relative risk of 2.9 (95%-CI 1.1-7.7), p=0.03. The secondary outcomes showed statistically significant differences in RTX versus PCB in median GC cumulative dose: 1595 versus 2302 mg (p = 0.04) and median PMR-AS: 6 versus 15 (p = 0.02) (Table 1 and Figure 1). No differences were seen in other secondary outcomes.

Table 1. Primary and Secondary Outcomes for Rituximab Versus Placebo Treatment One Year After Infusion

	Placebo [n=24]	Rituximab [n=23]	p-value
Remission, number (%)	10 (42%)	15 (65%)	0.15
GC-free remission, number (%)	4 (17%)	11 (48%)	0.03
Cumulative GC dose 0-52 weeks, in mg	2302 (1595 - 2881)	1595 (1275 – 2260)	0.04
Cumulative GC dose 21-52 weeks, in mg	959 (91 – 1442)	160 (0 - 902)	0.10
Relapse patient 21-52 weeks, number (%)*	14 (58%)	12 (52%)	0.77
PMR-AS**	15.25 (7.75 - 22.5)	6.3 (4.7 - 12.1)	0.02
CRP serum level, in mg/L	3.5 (2 - 5)	3 (1 - 4)	0.29
physicians' VAS, 0-10	2 (0.2 - 3.7)	1 (0 - 2)	0.08
Morning stiffness, in minutes	25 (4 - 60)	10 (0 - 30)	0.06
VAS pain, 0-10	3 (1.45 - 6.4)	1.8 (0.7 - 5)	0.16
EQ5D-5L, score at week 52#	0.71 (0.65 – 0.77)	0.71 (0.63 – 0.77)	0.87
EQ5D-5L, change week 21-52#	0 (-0.03 - 0.09)	0.07 (-0.05 - 0.10)	0.56
Methotrexate use, number (%)	4 (17%)	2 (9%)	0.67
Adverse events, total, % of patients	8, 26%	6, 33%	0.75

Notes. * Relapse was defined as therapy intensification, based on either a) an increase in oral prednisolone, b) adding intramuscular methylprednisolone, or c) starting or switching a DMARD due to treatment inefficiency ** Remission is based on the PMR-AS, calculated by CRP +VASp +VASph + (MST *0.1) + EUL, and a PMR-AS < 10 was considered remission or low disease-activity. # Number of patients for placebo versus RTX were n=23 versus n=23 respectively at week 52, and for comparison of change between week 21-52 total number of patients were n=21 versus n=23 respectively

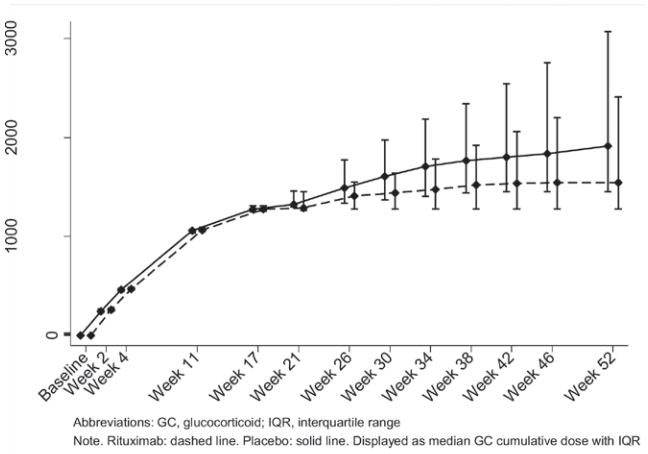

Figure 1. Cumulative GC Dose 0-52 Weeks, in mg

Conclusion: Efficacy of 1x1000 mg RTX in PMR was maintained up to 1 year follow-up, while also demonstrating a GC sparing effect. A larger trial, also assessing effect of on demand retreatment, is needed to confirm our results, and provide insight in which patients most likely benefit from RTX.

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POS0270

DEVELOPMENT OF AORTIC ANEURYSM/DILATATION IN A PROSPECTIVE COHORT OF PATIENTS WITH BIOPSY-PROVEN GIANT-CELL ARTERITIS: EARLY IDENTIFICATION OF PATIENTS AT RISK.

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Background: Up to 10-33% of patients with giant-cell arteritis (GCA) develop aortic structural damage (ASD) (aneurysm or dilatation), typically involving the ascending aorta (1,2). Systematic use of imaging reveals radiological features of aortitis in 45-65% of patients at diagnosis (3). This finding has been associated with future aortic dilatation in retrospective studies (4).

Objectives: To investigate the prevalence of thoracic ASD in a large prospective cohort of patients with GCA subjected to periodic imaging. To evaluate the association between features at diagnosis with ASD development.

Methods: Patients were included in the study if consented, had biopsy-proven GCA and met the 1990 ACR criteria for GCA classification. Patients were prospectively followed and treated according to uniform criteria. Since 1995 patients were subjected to systematic imaging screening aimed to detect thoracic ASD. Until November 2006 it consisted of a chest X-ray that was performed at least 4 years after diagnosis and repeated every 4 years. When aortic dilatation was minimally suspected, patients underwent contrast-enhanced computed tomography (CT) scan. Since November 2006, most of patients were prospectively studied with CT angiography at diagnosis, after 1 year and every 4 years.

The diagnosis of ASD was confirmed by CT, defined as an aortic diameter > 4 cm at the ascending aorta or ≥4 cm at the aortic arch or the descending aorta. Data regarding demographic characteristics, cardiovascular risk factors, GCA symptoms, laboratory tests, chronic medication at time of GCA diagnosis and corticosteroid tapering were recorded.

Kaplan-Meier survival plot was used to present the cumulated incidence of thoracic ASD over time and patients were censored at the time of ASD diagnosis or at the time of the last screening in those without ASD.

We also investigated which variables present at the time of GCA-diagnosis were associated with future development of ASD. Patients were classified in two groups according to whether they developed ASD or not during a follow-up period of 8 ± 1 years from the time of diagnosis.

Results: Thoracic ASD was confirmed by CT in 58 patients (21.6% of the patients with systematic screening diagnosed from 1994 to 2018) after a median follow-up of 4.7 years (0.05-7.5). Ascending aorta was involved in 56 patients (96.5%), followed by the aortic arch in 11 patients (18.9%), and descending aorta in 5 (8.6%). 14 patients (24.1%) had more than 1 aortic segment involved. Figure 1 shows the number of patients with thoracic ASD detected during follow-up.

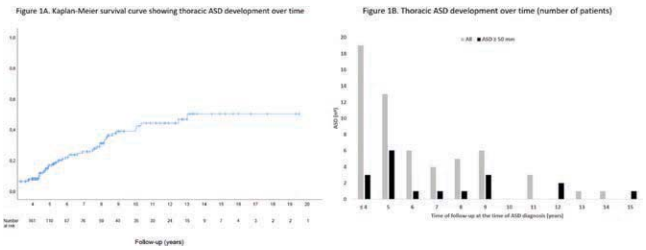

Figure 1. Thoracic ASD was detected within the fir

st 4 years from GCA-diagnosis in 19 out of the 58 patients who developed ASD (32.7%) but was severe (≥ 50 mm) in only 3 (15.8% out of those 19 patients). Most ASD was detected between 5 and 9 years after GCA-diagnosis.

Patients who developed ASD during follow-up experienced less often cranial ischemic symptoms (14.8% vs 41.1%; p=0.003) or polymyalgia (33.3% vs 51.8%; p=0.057), and less frequently had a previous diagnosis of hypertension (66.7% vs 82.1%; p=0.081). Age, sex, clinical or laboratory findings or chronic therapies used at time of GCA-diagnosis were not significantly different between groups.

After multivariate analysis, the presence of cranial ischemic symptoms (HR 0.180, 95% CI 0.065-0.495, p=0.001) and polymyalgia rheumatica (HR 0.329, 95% CI 0.136-0.793, p=0.013) remained inversely associated with thoracic ASD development.

Conclusion: ASD is frequent and probably an underdiagnosed complication of GCA. There is no consensus yet regarding the optimal screening protocol during follow-up and early identification of patients at risk is crucial for this purpose. The presence of cranial ischemic symptoms or polymyalgia rheumatica were inversely associated with thoracic ASD development in our prospective cohort.

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POS0271

CLINICAL SYMPTOMS AT GIANT CELL ARTERITIS DIAGNOSIS AS PREDICTORS OF PERMANENT VISUAL LOSS.

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Background: Giant cell arteritis (GCA) is the most prevalent vasculitis in the elder. Nearly 20% of patients experience transient or permanent visual loss (PVL). It has been reported that erythrocyte sedimentation rate (ESR), haemoglobin (Hb), constitutional syndrome (CS) and fever are prognostic factors that predict PVL but models have shown poor diagnostic performance.
Objectives: To evaluate if clinical signs, symptoms and blood tests can predict PVL at GCA diagnosis.
Methods: We retrospectively included patients from the Spanish Vasculitis Registry (REVAS) from 2005 to 2009. Clinical and blood tests data were obtained from medical records. We randomly split the cohort using shrinkage function to create a derivation and a validation cohort. In the derivation set we compared data and we built a multivariable logistic regression model to predict PVL. Internal validity was evaluated with 1000 bootstrap. External validity was evaluated using the validation set of data. Performance of the model was determined using the area under the curve (AUC) with 95% confidence interval. Calculations were done using StataBE 17.0.
Results: We included 620 patients (derivation cohort: 397 patients). Clinical signs, symptoms and blood tests results according to the presence or absence of PVL (Table 1). Mean age at diagnosis was 76.3 years and PVL was present in 86 (21.7%) patients. Significant predictors at baseline were age (p=0.000), hypertension (p=0.04), fever (p=0.001), jaw claudication (0.000), transient visual loss (TVL, p=0.000) and decreased temporal artery (TA) pulse (p=0.004). Multivariable logistic regression showed that age older than 75 years (OR 2.7, p=0.000), jaw claudication (OR, 2.75; p=0.000) and TVL (OR 7.2, p=0.000) were risk factors for PVL. CS was the only protective factor (OR 0.57, p=0.017). Hypertension (OR 1.4, IC95%: 0.88 – 2.3) and diabetes (OR 1.63, IC95%: 0.94 – 2.8) were not statistically significant. Our model showed an AUC 0.8 (IC 95%: 0.75 – 0.84). A 1000 bootstrap analysis showed good internal validity (AUC 0.79, IC95%: 0.74 – 0.83). Validation cohort comprised 223 patients and the AUC of the model in this dataset showed an AUC 0.81. We compared our model to previously published models and we found that our model had a higher AUC (AUC 0.8, IC 95%: 0.75-0.84 vs. AUC 0.65, IC95%: 0.6 – 0.7; p < 0.0001).

Table 1. Baseline date according to the presence or absence of permanent visual loss.

	Permanent Visual Loss		No Permanent Visual Loss		
Variable	Mean/ Proportion	SD	Mean/ Proportion	SD	Significance
Female	69.8%		72.0%		0.68
Age >75 y.o.	72.1%		53.4%		**0.000**
Hypertension	64.3%		51.6%		**0.04**
Diabetes	25.9%		16.9%		0.06
Fever	18.6%		36.8%		**0.001**
Constitutional syndrome	42.4%		53.2%		0.075
Polymyalgia	40.7%		39.7%		0.87
Headache	79.1%		79.2%		0.987
Jaw claudication	68.2%		39.7%		**0.000**
Tenderness of the TA	38.6%		31.4%		0.22
Transient visual loss	39.0%		10.5%		**0.000**
Stroke	3.5%		3.9%		0.86
Transient ischaemic attack	0.0%		4.2%		0.053
Decreased TA pulse	66.7%		48.0%		**0.004**
TA enlargement	55.1%		50.9%		0.51
Haemoglobin	11.1	1.2	11.4	1.4	0.37
Erythrocyte sedimentation rate	95.0	26.2	96.4	26.8	0.67
C Reactive protein	9.7	6.2	10.4	8.6	0.8

SD: Standard deviation. TA: Temporal artery.

Conclusion: Age > 75 years, jaw claudication and TVL can predict PVL, being the CS a protective factor for this complication. Blood test data are not good PVL predictive factors.

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POS0272

INTRAVENOUS VERSUS SUBCUTANEOUS TOCILIZUMAB IN A SERIES OF 471 PATIENTS WITH GIANT CELL ARTERITIS

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Background: Tocilizumab (TCZ) has shown efficacy in large-vessel vasculitis, including Giant Cell Arteritis (GCA) **(1-3)**. Clinical trials with TCZ in GCA was performed with intravenous (iv) TCZ in a phase 2 trial **(3)**, and with subcutaneous (sc) TCZ in the phase 3 GiACTA **(4)**. However, in GCA there are no studies comparing IV vs SC TCZ.
Objectives: To compare the efficacy of TCZ in GCA patients according to the route of administration IV-TCZ vs SC-TCZ.
Methods: Multicentre study of 471 patients diagnosed with GCA and treated with TCZ. They were divided into 2 groups according to the route of administration: **a)** IV, and **b)** SC. GCA was diagnosed by: **a)** ACR criteria, and/or **b)** temporal artery biopsy, and/or **c)** imaging techniques. Sustained remission was established according to EULAR definitions **(5)**.
Results: We studied 471 patients (mean age, 74±9 years) treated with TCZ, 238 with IV-TCZ and 233 with SC-TCZ (Table 1). The time between diagnosis of GCA and TCZ onset was shorter in the SC TCZ group. Regarding acute phase reactants at the beginning of TCZ, no differences were found between both groups. There were no significant differences in sustained remission or in glucocorticoid-sparing effect of TCZ (Figure 1). Patients on IV TCZ treatment suffered more relevant adverse effects during follow-up.

Table 1. Main characteristics of GCA patients treated with intravenous and subcutaneous tocilizumab

	IV TCZ (n= 238)	SC TCZ (n=233)	P
Baseline characteristics at TCZ onset			
Age(years), mean±SD	73.3±8.7	73.7±9.3	0.63
Sex, female/male (% female)	175/63 (73)	167/66 (72)	0.65
Time from GCA diagnosis to TCZ onset (months), median [IQR]	8 [3-23.5]	5 [2-15]	**0.016**
ESR, mm 1st hour, median [IQR]	30.5 [12.5-53]	28 [10-56.5]	0.66
CRP, mg/dL, median [IQR]	1.4 [0.5-2.8]	1.4 [0.4-4]	0.92
Prednisone dose, mg/day, median [IQR]	20 [10-40]	20 [10-36.2]	0.69
Safety after TCZ onset			
Follow-up, (months), median [IQR]	27 [16-44]	14 [6-26.7]	**<0.001**
Relevant adverse events, n (%)	80 (34)	46 (19)	**<0.001**
Relevant adverse events per 100 patients-year	12.7	15.2	NS
Serious infections, n (%)	44 (18)	21 (9)	0.44
Serious infections per 100 patients-year	6.7	7.2	NS
MACEs, n (%)/	1 (0.4)	0 (0)	-
MACEs per 100 patients-year	0.1	0	NS
Malignancies, n (%)	4 (1.7)	1 (0.4)	0.20
Malignancies per 100 patients-year	0.6	0.3	NS

Abbreviations: CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GCA: giant cell arteritis; IQR: interquartile range; IV: intravenous; MACEs: major adverse cardiovascular events; NS: non significant; SC: subcutaneous; SD: standard deviation

Conclusion: In GCA, TCZ seems equally effective and safe regardless of the route of administration IV or SC.

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POS0273 THE ROLE OF FACIAL, OCCIPITAL, SUBCLAVIAN AND CAROTID ARTERIES ULTRASOUND IN THE DIAGNOSTIC ASSESSMENT OF GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is the most common form of primary systemic vasculitis in patients aged >50 years. It predominantly affects the cranial arteries; however, extra-cranial disease involving the aorta and its major branches can also be present. Currently, ultrasound of the temporal (TA) and axillary (AX) arteries is the first imaging modality recommended in patients with suspected predominantly cranial GCA. Nevertheless, other arteries such as facial (FA), occipital (OC), subclavian (SC), and common carotid (CC) arteries can also show vasculitic changes on ultrasound. However, there are still conflicting data to support the inclusion of these arteries in the routine ultrasound assessment of patients with suspected GCA.

Objectives: To assess the value of adding the evaluation of the FAs, OCs, SCs and CCs in the ultrasonographic diagnosis of patients with GCA.

Methods: Single-center observational retrospective study, using data from patients diagnosed with GCA registered at the Rheumatic Diseases Portuguese Registry (Reuma.pt). All patients underwent ultrasound of the TAs and AXs ± FAs, OCs, SCs or CCs at the time of diagnosis. The halo sign was considered a positive ultrasonographic finding for GCA. Only patients with the presence of halo sign in at least one of the arterial segments evaluated were included. Binary logistic regression modelling was performed to explore associations between the presence of halo sign in different arterial segments.

Results: We included 84 patients, 57 (67.9%) females, with a mean ± standard deviation age at diagnosis of 75.6 ± 8.8 years. Halo sign was found in the TAs of 66/84 (78.6%) patients, AXs of 40/84 (47.6%) patients, FAs of 37/74 (50.0%) patients, OCs of 15/61 (24.6%) patients, SCs of 30/49 (61.2%) patients and CCs of 13/60 (21.7%) patients. Of the 18/84 patients with GCA without the presence of TA halo, 17/18 (94.4%) showed halo in the AXs, 1/18 (5.6%) in the FAs, 3/18 (16.7%) in the OCs, 15/17 (88.2%) in the SCs and 6/16 (37.5%) in the CCs. Of the 44/84 patients with GCA without the presence of AX halo, 43/44 (97.7%) showed halo in the TAs, 24/39 (61.5%) in the FAs, 12/32 (37.5%) in the OCs, 4/18 (22.2%) in the SCs and 3/33 (9.1%) in the CCs. A total of 83/84 (98.8%) patients had halo sign on the ultrasound of either the TA or AX arteries. The patient with normal TA and AX ultrasound had the presence of halo sign in the SCs. Table 1 shows the proportion of patients with positive TA and AX ultrasounds according to the presence of halo in the FA, OC, SC or CC arteries. Patients with involvement of the cranial arteries were more likely to have a TA halo (FA: OR 30.6, 95%CI 3.8-247.3; OC: OR not applicable) and less likely to have an AX halo (FA: OR 0.37, 95%CI 0.14-0.95; OC: OR 0.19, 95%CI 0.05-0.77). As opposed to patients with involvement of the extra-cranial arteries in whom the halo sign was more frequently found in the AXs (SC: OR 18.2, 95%CI 4.2-78.9; CC: OR 5.9, 95%CI 1.4-24.4) but not in the TAs (SC: OR 0.12, 95%CI 0.02-0.60; CC: OR 0.32, 95%CI 0.09-1.15).

Table 1. Differences in the presence of halo sign in the temporal and axillary arteries according to the arterial segment affected.

Arterial segment with halo	Temporal arteries with halo	Axillary arteries with halo
Facial arteries (n=37)	36/37 (97.3%)	13/37 (35.1%)
Occipital arteries (n=15)	15/15 (100.0%)	3/15 (20.0%)
Subclavian arteries (n=30)	15/30 (50.0%)	26/30 (86.7%)
Common carotid arteries (n=13)	7/13 (53.8%)	10/13 (76.9%)

Conclusion: Our results support the need to assess both TAs and AXs in patients with suspected GCA, resulting in a diagnostic sensitivity of 99%. Only by adding the evaluation of the SCs to the already recommended TAs and AXs increased the diagnostic sensitivity of ultrasound to 100%. All patients with a positive FA, OC or CC ultrasound for GCA also showed a halo sign in either the TAs or AXs. Hence, the additional assessment of these arteries did not improve the diagnostic yield of ultrasound and, therefore, should not be recommended in routine practice.

Disclosure of Interests: None declared

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POS0274 PREDICTION OF VASCULAR COMPLICATIONS IN TAKAYASU ARTERITIS BY MACHINE LEARNING: A PROOF-OF-CONCEPT STUDY BASED ON A PROSPECTIVE COHORT

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Background: Vascular complications are common poor prognosis in Takayasu arteritis (TAK). A reliable prediction model for this outcome has not been performed using machine learning (ML) due to the lack of a dataset with sufficient sample size.

Objectives: We aimed to develop ML models for prediction of vascular complications in TAK based on the prospective data of the largest sample in China from the East China Takayasu Arteritis (ECTA) cohort.

Methods: Data were collected from the ECTA cohort in which patients were enrolled from January 2009 to August 2020 and followed till February 2021 (n = 517). Predictor variables included 53 baseline features and outcome of interest was incident vascular complications. Data were randomly split into a training (85%) and test (15%) set. Logistic regression (LR), support vector machine, random forest (RF), k-nearest neighbors, XGBoost (XGB), and light gradient boosting machine models were trained using five-fold cross validation, and evaluated on the test set for recall, specificity, precision and area under ROC (AU-ROC) and precision-recall curves (AU-PRC). Permutation score was applied to assess feature importance to the outcome.

Results: Over a median follow-up of 30 (15–44) months, incident vascular complications were observed in 29.0% (150/517) patients. The RF model demonstrated the best overall predictive performance (AU-ROC = 0.84, AU-PRC = 0.63). Both the RF and LR models had the highest specificity (0.98), and the XGB model had the highest recall (0.87). Progressive clinical course was an important feature significantly associated with the outcome for all models.

Conclusion: It demonstrated the feasibility of developing ML models for prediction of vascular complications in TAK. The XGB model could help for early identification of high-risk patients, and RF and LR models could further confirm.

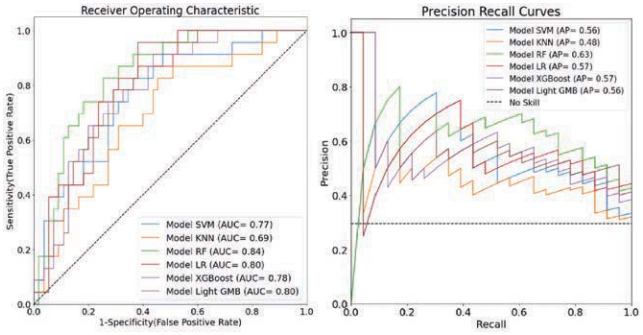

Figure 1.

Disclosure of Interests: None declared

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POS0275 SEROLOGICAL RESPONSE FOLLOWING THREE DOSES OF SARS-COV-2 MRNA VACCINE IN PATIENTS WITH GIANT CELL ARTERITIS: EXPERIENCE OF A SINGLE-CENTRE COHORT

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Background: The spread of COVID-19 pandemic raised the need to perform an additional vaccine dose to overcome the diffusion of the infection and possible

life-threatening disease complications. Certain population subsets seem to be at increased risk of developing such complications, such as elderly and/or immunocompromised patients.

Objectives: To assess the persistence of immunity following SARS-CoV-2 mRNA vaccine and the magnitude of the humoral response after the booster dose in a cohort of patients affected by giant cell arteritis (GCA).

Methods: Patients with GCA regularly followed at the Rheumatology Department of the University of Pavia, Italy, who received a booster dose of SARS-CoV-2 mRNA vaccine (BNT162b2 Pfizer/BioNtech or mRNA-1273 Moderna) between October 1st and December 31st, 2021 were included. Humoral response was assessed by measuring SARS-CoV-2 Trimeric S (TSAbs) and Neutralizing (NAbs) antibodies, with a cut-off of 33.8 Binding Antibody Units (BAU)/mL and 1:10 dilution, respectively. Blood samples from each patient were drawn at least 4 months after the second and three weeks after the third vaccine dose.

Results: Forty-two patients who received the booster dose of SARS-CoV-2 mRNA vaccine were enrolled. Thirty (71.4%) were females, mean age 73.2±4.7 years, disease duration 58±38 months, 19 (45.2%) had large-vessel vasculitis. Thirty-two (76.2%) were on glucocorticoids (GCs) at a mean dose of 4.9±7.8 mg/day prednisone equivalent, with 7 (16.7%) receiving ≥7.5 mg/day. Eighteen (42.9%) were on methotrexate (MTX) (mean dose 14.2±3.5 mg/week) and 8 (19.0%) were treated with subcutaneous tocilizumab (TCZ) 162 mg/week.

SARS-CoV-2 serology was tested prior to the third vaccine dose at an average of 5.4±0.4 months from the former vaccination scheduled: 37 (88.1%) retained TSAbs and 30 (71.4%) NAbs. The median TSAb titre was 134 BAU/mL (IQR 97-292). Four out of 5 patients (80.0%) without TSAbs and 7 out of 12 (58.3%) without NAbs were on both GCs and MTX. Moreover, those on GCs plus MTX had lower pre-third dose TSAb titres as compared to other treatment subgroups (Figure 1A). GC doses ≥7.5 mg/day prednisone equivalents seemed to blunt NAb levels along time: 28.6% patients on GCs ≥7.5 mg/day prednisone equivalents had negative NAbs before the third dose vs. 80.0% of those taking <7.5 mg/day (p=0.007) as well as lower NAb titres (Figure 1B).

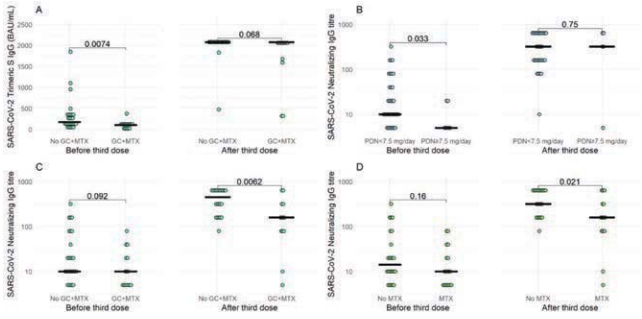

Figure 1. (A) TSAb levels before and after the booster dose among patients on GC + MTX. (B) NAb titres before and after the booster dose according to treatment with prednisone ≥7.5 mg/day or (C) MTX in combination with GCs or (D) MTX alone.

Data regarding antibody response after the booster dose were available for 35 patients (83.3%). Blood collection occurred at a median of 25 days (IQR 24-32) after the third vaccine dose. All patients developed TSAbs, even those who did not respond to the previous shots. The median TSAb titre rose to 2080 BAU/mL (IQR 2080-2080) (p<0.001), while the median NAb titre increased from 1:10 to 1:320 (p<0.001). One patient (2.9%) treated with prednisone 8.75 mg/day plus MTX 12.5 mg/week did not develop NAbs. NAb levels were lower in patients taking MTX as compared to those who did not (Figure 1C,D), whereas treatment with TCZ or GCs, along with the GC dose, did not affect the magnitude of the antibody response.

There were no serious adverse events from the vaccine. However, 3 patients (8.6%) experienced a disease relapse 24±5 days after the booster dose.

Conclusion: In our cohort, most patients who seroconverted after the second dose of vaccine retained the humoral immunity, with excellent seroconversion rates following the booster dose. However, GCs, especially at doses ≥7.5 mg/day prednisone equivalents, may contribute to the waning of NAb titres. On the other hand, immunosuppressants like MTX, especially when combined with GCs, might impair the magnitude of the humoral response to the booster dose.

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Advances in Crystal Arthritis

POS0276

TRADITION VS INNOVATION! CONVENTIONAL RADIOGRAPHY AND ULTRASOUND IN THE DIAGNOSIS OF CPPD: INSTRUCTIONS FOR USE

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Background: Conventional radiography (CR) is widely used as the first-line investigation for calcium pyrophosphate deposition (CPPD) disease, given its widespread use and the low cost. Next to it a series of advanced imaging techniques have been evaluated for accuracy and reliability. Among them, ultrasound (US) has been thoroughly tested and demonstrated to be accurate and reliable for CPPD diagnosis. However, even if there are data on the diagnostic accuracy of US and CR alone, it is not clear if performing both diagnostic tests and in which sequential order provides an added value for the diagnosis of CPPD.

Objectives: The aim of this study was to assess which diagnostic test performs better for the diagnosis of CPPD and if a combination of the two exams provides an additional value.

Methods: This is an ancillary study of the criterion validity of US in CPPD study[1]. Consecutive patients with knee osteoarthritis requiring total joint replacement were enrolled in 8 centres. Participants underwent US and CR of the affected knee prior to surgery. US was performed by experienced sonographers following the same scanning protocol described in the main study, while CR were performed in weight bearing AP and lateral views and were read by 2 experienced radiologists that reached a consensus on the presence/absence of CPPD. The evaluation of CPPD at the level of menisci and hyaline cartilage (HC) was based on the OMERACT definitions for US and on the new definitions developed by the ACR/EULAR CPPD classification criteria working group for CR [paper under submission]. Patients were classified as having CPPD considering histological examination as reference standard. Diagnostic indexes were calculated for US and CR alone and combined. Poisson models with robust estimation were used to estimate the best sequence of these diagnostic methods for a more accurate diagnosis of CPPD.

Results: 51 pts were enrolled (63% F, mean age 74y ± 8). Diagnostic indexes of US and CR alone and combined are indicated in Table 1. Compared to histology, US demonstrated to be a sensitive tool for identification of CPPD at the knee, with a good sensitivity in all sites and in the overall evaluation. Instead, CR was less sensitive, but it was a highly specific exam for CPPD identification. Combining US and CR led to a higher sensitivity compared with CR alone, but a lower specificity compared to both CR and US alone, and it offered no additional increase in diagnostic accuracy. The Figure 1 shows the results of the

appropriate sequence of use of US and CR in patients with suspected CPPD: in case of a positive CR at any of the 3 sites (menisci and HC) no additional exam is necessary, and the same in case of a positive US in at least two sites; however in case of a negative CR, US could help in a statistically significant way to identify CPPD patients, and further in case of a positive US in a single site CR can offer additional information.

Table 1. ***diagnostic indexes of US, CR and US + CR in the identification of CPPD. MM: medial meniscus, LM: lateral meniscus, HC: hyaline cartilage, SN: sensitivity, SP: specificity, PPV: positive predictive value, NPV: negative predictive value, ACC: accuracy.***

US		SN	SP	PPV	NPV	ACC
	MM	0.88	0.81	0.82	0.88	0.84
	LM	0.88	0.73	0.76	0.86	0.80
	HC	0.78	0.86	0.82	0.83	0.82
	Overall	**0.92**	**0.64**	**0.73**	**0.89**	**0.78**
CR	MM	0.32	1	1	0.61	0.67
	LM	0.40	0.96	0.91	0.63	0.69
	HC	0.48	0.93	0.85	0.68	0.73
	Overall	**0.54**	**0.92**	**0.88**	**0.66**	**0.73**
US + CR	MM	0.88	0.81	0.82	0.88	0.84
	LM	0.92	0.69	0.74	0.90	0.80
	HC	0.87	0.82	0.80	0.89	0.84
	Overall	**0.92**	**0.56**	**0.67**	**0.88**	**0.75**

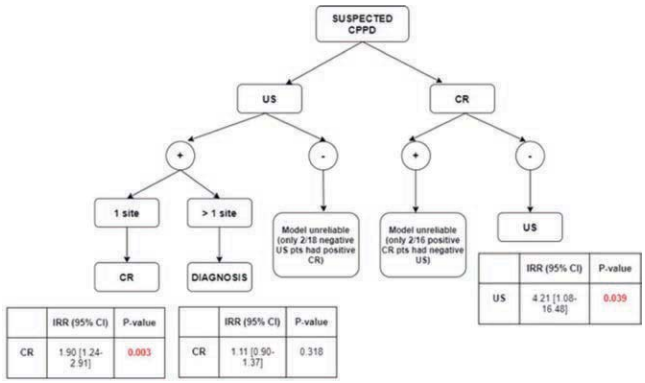

Figure 1. evaluation of sequence of US and CR

Conclusion: US confirmed a high diagnostic accuracy in identifying patients affected by CPPD at knee level, while CR demonstrated a high specificity but a low sensitivity. Performing both diagnostic tests could make sense in case of a negative CR or in case of an inconclusive US (only one positive site). To our knowledge, this is the first study that investigates the role of the combination of the two exams in CPPD. Further studies in a large number of patients and in different joints would be helpful to address this point.

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POS0277 EFFECT OF COLCHICINE THERAPY ON ATHEROSCLEROSIS-RELATED CARDIOVASCULAR OUTCOMES IN PATIENTS WITH CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION DISEASE

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Background: anti-inflammatory therapy supposed to influence the rate of cardiovascular events development in pts with calcium pyrophosphate deposition disease (CPPD).

Objectives: To assess the effect of colchicine, hydroxychloroquine, and methotrexate on cardiovascular outcomes (CVO) in CPPD pts.

Methods: The study included 305 pts with CPPD: 115 (37.70%) men, 190 (62.30%) women. The average follow-up period was 3.9±2.7 yrs. Among the factors influencing CVO were considered: gender, age, smoking, alcohol intake ≥20 standard doses/week, hypertension, history of cardiovascular disease (CVD): (ischemic heart disease (CHD), acute myocardial infarction myocardial infarction (AMI), acute cerebrovascular insufficiency (ACV), chronic heart failure (CHF) >3 grade, NYHA), diabetes mellitus (DM), BMI >25 kg/m^2 and >30 kg/m^2, cholesterol level >5.1 mmol/l, GFR <60 ml/min/1.73 m^2, serim uric acid (sUA) > 360 µmol/l, hypercalcemia (serum calcium> 2.62 mmol/l), CRP> 2 mg/l, hyperparathyroidism (parathyroid hormone> 65 pg/ml), phenotypes of CPPD (asymptomatic, osteoarthritis with calcium pyrophosphate crystals (OA with CPP crystals), chronic arthritis, acute arthritis), taking colchicine, hydroxychloroquine and methotrexate, glucocorticoids (GCs) and non-steroidal anti-inflammatory drugs (NSAIDs).
Information about mortality, regardless of cause, was noting down throughout the follow-up period.
The causes of death were determined on the patient's death certificate, and then classified according to the International Classification of Diseases of the 10-th Revision (ICD-10) All newly developed cases of non-fatal cardiovascular events were identified on the basis of medical documentation. The odds ratio (OR) with a 95% confidence interval of developing cardiovascular events was calculated. Statistica 12.0 package was used for statistical data processing.

Results: The mean age at inclusion was 58.9±12.5 yrs. 264 patients were available for follow-up. Any of the studied cardiovascular events were registered in 79 (29.9%) pts. During the follow-up period, 46 (17.4%) pts died; 35 of 46 (76.1%) pts died because of CVD; 11 (23.9%) pts died due to other causes. Non-fatal cardiovascular events were registered in 44 (16.7%) pts.
The risk of cardiovascular events was higher for ps aged >65 years (OR 5.97, 95% CI 3.33-10.71), serum cholesterol level ≥5.1 mmol/l (OR 1.95, 95% CI 1.04-3.65]), GFR <60 ml/min/1.73 m^2 (OR 2.78, 95% CI 1.32-5.56]), history of CVD (OR 2.32, 95% CI 1.22-4.44) Colchicine therapy was associated with the lower risk of cardiovascular events (OR 0.20, 95% CI 0.11-0.39]). Therapy with methotrexate and hydroxychloroquine did not exert an influence on opportunity of CVO.

Conclusion: Adverse CVD outcomes in CPPD pts are associated with age, hypercholesterolemia, CKD, and a history of CVD. The intake of colchicine, but not methotrexate and hydroxychloroquine, by patients with CPPD is associated with decline of risk of cardiovascular events.

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Disclosure of Interests: Elena Cheremushkina: None declared, Maxim Eliseev Speakers bureau: Berlin Chemie Menarini Group, Sobi, EGIS, CSC, MosFarma, Alium Group, Olga Sheliabina Speakers bureau: Berlin Chemie Menarini Group, Aleksandra Novikova: None declared, Svetlana Glukhova: None declared

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POS0278 COMPARISON OF ULTRASOUND BEAM ATTENUATION BY CALCIUM PYROPHOSPHATE, HYDROXYAPATITE AND MONOSODIUM URATE CRYSTALS: A PROOF-OF-CONCEPT STUDY

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Background: Ultrasound (US) demonstrated to be reliable and accurate for the diagnosis of crystal induced arthropathies, especially gout and calcium pyrophosphate deposition disease (CPPD) and validated definitions for uric acid and calcium pyrophosphate deposition in joints were released by the Outcome Measures in Rheumatology (OMERACT) US group. Less is known regarding hydroxyapatite (HA) deposition disease (HAAD) and the role of US in the assessment of HA crystal deposition.
It is general belief that HA crystals create posterior acoustic shadowing, monosodium urate could create or not US beam attenuation while CPP crystals generally do not attenuate the US beam.

Objectives: Aim of this proof-of-concept study was to investigate the US appearance in terms of beam attenuation due to increasing concentrations of MSU, CPP and HA crystals.

Methods: Sixteen synthetic crystal suspensions with known concentrations of CPP (26-109 mg/mL), HA (31-153 mg/mL) and MSU (90-500 mg/mL) were prepared. These specific concentrations were selected to replicate the X-ray attenuation characteristics of those crystals when imaged by conventional radiography,

computed tomography (CT) and dual-energy CT (DECT) in vivo[1]. The density of the agar-based lipogel background was intentionally increased to mimic the X-ray attenuation of hyaline cartilage (i.e., 100-120 HU at 120 kVp). Each crystal suspension was placed in a plastic container filled with US gel, next to the control (i.e., crystal-free background) calibration phantom. We acquired all US images using a Samsung RS80A system equipped with a high-frequency linear array transducer (4-18 MHz) set at the maximum frequency, by applying the same settings. US scans were performed by a single experienced sonographer, blinded to the crystal type and concentration. For each of the 16 crystal suspensions, at least two images were recorded both in the long- and short-axis views, the latter including the control phantom in the field of view. Interpretation of US images for the extent of US beam attenuation and the presence of acoustic shadowing was performed in consensus with a second experienced sonographer.

Results: None of the five CPP phantoms generated posterior acoustic shadowing or US beam attenuation regardless of CPP concentration. HA 31mg/mL did not generate US beam attenuation, while HA 62, 92 and 123mg/mL generated a progressively increasing US beam attenuation with posterior acoustic shadow clearly generated by HA 153mg/mL. Similarly, MSU 90mg/mL did not generate US beam attenuation. MSU 195mg/mL generated only a very faint US beam attenuation that became progressively more visible at 270 and 345mg/mL even if a clear posterior acoustic shadow was detectable only with MSU 420 and 500mg/mL (Figure 1).

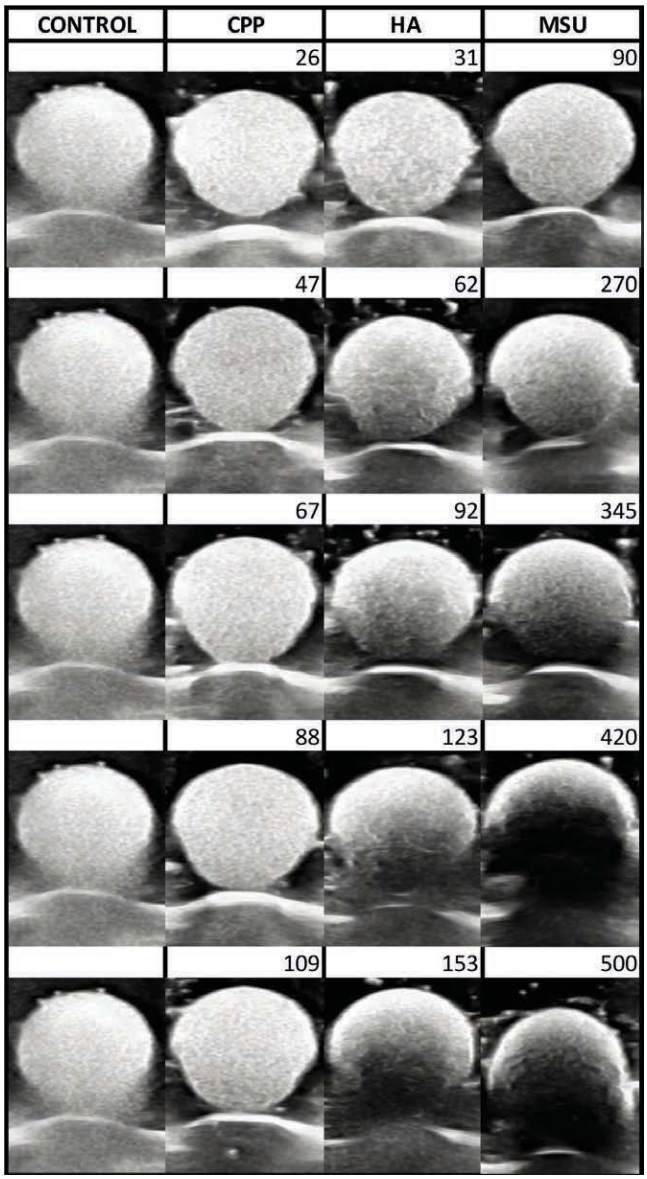

Figure 1. Short-axis views comparing the US attenuation characteristics, including acoustic shadowing, of increasing concentrations (in mg/mL) of CPP, HA and MSU crystals. The left column shows the US attenuation of the crystal-free (0mg/mL) agar-based lipogel background for reference

Conclusion: This proof-of-concept study confirmed that in the concentrations of crystals encountered in vivo, CPP do not generate posterior shadowing, while MSU and HA determine US beam attenuation proportionally to the concentration of the crystals. Being this a proof-of-concept study, attenuation of the US beam was assessed empirically and not in a quantitative or semi-quantitative way. However, this study highlights the potential of US to differentiate between CPP, MSU and HA crystals based on their appearance on gray scale imaging. Future studies should be carried out with different crystal concentrations, different US equipment and settings, in order to create a scoring system for US beam attenuation that is actually lacking.

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POS0279

THE ABCG2 RS2231142 POLYMORPHISM ARE ASSOCIATED WITH RISK OF NEPHROLITHIASIS IN A TAIWANESE POPULATION.

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Background: In genome-wide association studies (GWAS), the strong association of ABCG2 *rs2231142* variant with hyperuricemia and gout was confirmed in Asian population. Additionally, the obesity, diet, lifestyle, genetics and underlying comorbidities are important risks factors predisposing to hyperuricemia and gout. The systematic reviews revealed a significant link between obesity, systemic comorbidities and hyperuricosuria for predisposition of kidney stones (nephrolithiasis). However, whether ABCG2 plays an important role in the phathogenesis of nephrolithiasis remain unclear. The interaction between genetic factors and other risk factors of nephrolithiasis is still elusive.

Objectives: In this study, we want to explore the association between *ABCG2* rs2231142 variant and the risk of nephrolithiasis in modern Taiwanese population, and clarify the role of uric acid in nephrolithiasis formation.

Methods: This retrospective case-control study was conducted using the Taiwan Biobank database. A total of 120,267 individuals of Taiwanese Han Chinese aged 30-70 years were enrolled in the study. The primary outcome was the incidence of self-reported nephrolithiasis. Odds ratio (OR) of incident nephrolithiasis was analyzed by multiple logistic regression models and the interaction between ABCG2 *rs2231142* variants, serum uric acid level, on the nephrolithiasis was explored. The multifactorial confounding factors for prediction of nephrolithiasis were also re-examined in our study.

Results: Finally, we identified 8,410 participants with nephrolithiasis and the prevalence was 11.52% and 4.37% in men and women, respectively. Older age (OR=1.08, 95% CI: 1.02-1.03, p<0.001) and male gender (OR=2.21, 95% CI: 2.08-2.36, p<0.001) showed an independent predictor for development of incident nephrolithiasis. The risk of nephrolithiasis markedly increased resulting from the interaction of ABCG2 rs2231142 and nephrolithiasis. In comparison with GG genotype, the risk of nephrolithiasis also demonstrated a significant association with TT and GT genotype (TT: OR=1.18, 95% CI: 1.09-1.28, p<0.001; GT: OR=1.12, 95% CI: 1.06-1.18, p<0.001). The variant comorbidities significantly associated with susceptibility to nephrolithiasis are hyperlipidemia (OR=1.40, 95% CI: 1.29-1.51, p<0.001), hypertension (OR=1.67, 95% CI: 1.57-1.78, p<0.001), diabetes mellitus (OR=1.16, 95% CI: 1.06-1.26, p=0.002), and hyperuricemia (OR=1.06, 95% CI: 1.04-1.08, p<0.001) with significant difference. The interaction of lifestyles and the risk of nephrolithiasis revealed significant differences in smoking (OR=1.15, 95% CI: 1.09-1.22, p<0.001) and overweight (OR=1.22, 95% CI: 1.15-1.28, p<0.001) rather than alcohol use(OR=0.92, 95% CI: 0.84-1.01, p=0.083). Participants with regular physical exercise is a protective factor from nephrolithiasis (OR=0.95, 95% CI:0.9-1.0, p=0.048).

Conclusion: Our study demonstrated the risk of nephrolithiasis is significant association with ABCG2 *rs2231142* variants. This risk also increased with systemic comorbidities (hyperlipidemia, hypertension, diabetes mellitus, and hyperuricemia), and lifestyle (obesity, and smoking). Regular physical exercise is associated with protective factor for incident nephrolithiasis.

Table 1. Adjusted Odds ratio of kidney stone.

Variable	OR	95% CI	*p*-value
Age, years	1.03	(1.02-1.03)	<0.001
Gender			
female	1.00	–	–
male	2.21	(2.08-2.36)	<0.001
ABCG2 *rs2231142*			
GG	1.00	–	–
GT	1.12	(1.06-1.18)	<0.001
TT	1.18	(1.09-1.28)	<0.001
Hyperlipidemia			
No	1.00	–	–
Yes	1.40	(1.29-1.51)	<0.001
Hypertension			
No	1.00	–	–
Yes	1.67	(1.57-1.78)	<0.001
Diabetes			
No	1.00	–	–
Yes	1.16	(1.06-1.26)	0.002
Hyperuricemia >7.0 mg/dL			
No	1.00	–	–
Yes	1.06	(1.04-1.08)	<0.001
Smoking			
No	1.00	–	–
Yes	1.15	(1.09-1.22)	<0.001
Alcohol use			
No	1.00	–	–
Yes	0.92	(0.84-1.01)	0.083
Regular physical exercise			
No	1.00	–	–
Yes	0.95	(0.90-1.00)	0.048
Overweight, BMI ≥24 kg/m^2			
No	1.00	–	–
Yes	1.22	(1.15-1.28)	<0.001

OR was adjusted for all variables in table.

Disclosure of Interests: None declared
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POS0280 EXCESS RISK OF ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN FEMALES WITH GOUT – A PROSPECTIVE COHORT STUDY OF 105,502 WOMEN

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Background: Despite the disproportionately worsening disease burden of female gout in recent years[1] and its frequent associations with key cardiovascular risk factors (more often than male gout[2,3]), there remains a paucity of specific data about female gout, particularly about its impact on mortality and fatal coronary heart disease (CHD).
Objectives: To prospectively examine the relation of female gout and risk of all-cause and cardiovascular and coronary heart disease-specific deaths.
Methods: Using data from the Nurses' Health Study (NHS), an ongoing prospective cohort study in which female nurses in the United States completed detailed mailed questionnaires regarding their medical history, lifestyle, and other risk factors at baseline and every two years thereafter, we prospectively analyzed the relation between gout status at baseline and during the follow-up period and the risk of all-cause and cardiovascular mortality using Cox proportional hazards regression to adjust for cardiovascular risk factors such as comorbidities, body mass index, postmenopausal status, medication use, and dietary factors.
Results: The analysis included 105,502 women without gout and 1602 women with gout. Women with gout at baseline in 1982 tended to be older (mean age 54 vs. 50 years), and more likely to report a history of hypertension (44% vs. 22%), hypercholesterolemia (17% vs. 8%), and diabetes (11% vs. 6%). During 24 years of follow-up, we documented 15,255 deaths from all causes, including 3,128 deaths from cardiovascular disease (CVD) and 1,405 deaths from coronary heart disease (CHD). Compared to women without history of gout or CHD at baseline, the multivariable relative risks (RRs) among women with history of gout at baseline were 1.33 (95% CI, 1.21 to 1.46) for total mortality, 1.40 (95% CI, 1.17 to 1.67) for CVD deaths, and 1.49 (95% CI, 1.17 to 1.91) for fatal CHD (Table 1). The corresponding RRs for gout at baseline and during the follow-up were 1.33 (95% CI, 1.23 to 1.44), 1.43 (95% CI, 1.24 to 1.66), and 1.34 (95% CI, 1.08 to 1.66), respectively.

Table 1. Relative Risks of Death from All-Causes, Cardiovascular Disease, and Coronary Heart Disease According to Gout Status at Baseline in 1982 in the Nurses' Health Study

	No CHD	
	No Gout	Gout
Deaths from all causes		
Cases, n	14,810	445
Age-adjusted RR (95% CI)	1.0	1.58 (1.43, 1.73)
Multivariable-adjusted* RR (95% CI)	1.0	1.33 (1.21, 1.46)
All cardiovascular deaths		
Cases, n	3,001	127
Age-adjusted RR (95% CI)	1.0	2.06 (1.72, 2.46)
Multivariable-adjusted* RR (95% CI)	1.0	1.40 (1.17, 1.67)
Fatal CHD		
Cases, n	1,335	70
Age-adjusted RR (95% CI)	1.0	2.53 (1.99, 3.22)
Multivariable-adjusted* RR (95% CI)	1.0	1.49 (1.17, 1.91)

*Adjusted for age (continuous), history of hypertension, history of hypercholesterolemia, history of diabetes, aspirin use (yes, no), diuretic use (yes, no), smoking (never, past, current <15, current ≥15 cigarettes/day), body mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥35), physical activity (quintile), alcohol intake (nondrinker, <5, 5-9, 10-29, ≥30g/day), family history of MI (yes, no), menopausal status (premenopause, post menopause), hormone replacement therapy use (premenopause, never user, current user, past user). total energy intake (quintile), trans fat (quintile), dietary cholesterol (quintile), protein (quintile), linoleic fatty acid (quintile), and ratio of polyunsaturated fat/saturated fat.CHD = coronary heart disease; CI = confidence interval; RR = relative risk.

Conclusion: These prospective data indicate that women with gout have a higher risk of all-cause mortality, which is primarily driven by higher risk of CVD deaths. These findings closely agree with the UK general population data of both sexes that showed unclosing mortality gap over the past two decades.[4] Together, these findings provide support for rigorous cardiovascular risk factor modification specifically in female gout to help curtail the rising disease burden of gout worldwide.[1]
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Disclosure of Interests: Chio Yokose: None declared, Natalie McCormick: None declared, Na Lu: None declared, Amit Joshi: None declared, Gary Curhan Consultant of: AstraZeneca, Allena Pharmaceuticals, Shire/Takeda, Dicerna, and Orfan, Grant/research support from: Decibel Therapeutics, Employee of: Chief Medical Officer at OM1, Inc., Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, and Vaxart, Grant/research support from: Ironwood and Horizon
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POS0281 FLUCTUATIONS IN SERUM URATE ARE RELATED TO GOUT FLARES IN THE NOR-GOUT STUDY

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Background: Urate lowering therapy (ULT) is expected to prevent new gout flares, but flares still do occur during the first year, and could be related to fluctuations in serum urate (SUA), being a result of proinflammatory signals. Knowledge on the relationship between fluctuation in SUA and gout flares is limited.
Objectives: To study how fluctuation in SUA is related to gout flares in the first year of ULT.
Methods: In a prospective observational 2-year study 211 included patients with crystal-proven gout were evaluated for flare frequency. Patients were frequently followed during ULT (allopurinol or febuxostat) with monthly dose escalation until SUA was at target (<360 µmol/L or <300 µmol/L if tophi), and met also for visits at 3, 6, 9, 12 during year 1 and at year 2. Self-reported flares were continuously registered at all study visits.
Fluctuations in SUA were defined with various measures of SUA: a.) sum of changes between all consecutive visits over the whole 2-year period as a global measure, b. SUA change during 3-month visits at year 1 and during year 2. Further, the frequency of patients exceeding SUA changes with threshold >30, >60 and >90 µmol in these periods was calculated.
Fluctuations in SUA were then related to self-reported flares during the same 3-month periods year 1, and the whole years 1 and 2.
Results: Age was 56.4 (SD 13.7) years, 95.3% were males, disease duration 7.8 (SD 7.6) years.

SUA decreased from mean 500 µmol/L at baseline to 311 µmol at 1 year and 324 µmol/L at year 2. Flares were seen in year 1 in 81.2% (155/186) and year 2 26.0% (45/173) of patients.
The total sum of SUA changes over 2 years as a global measure for individual SUA fluctuation was related to flares in all 3-month periods during year 1 (Table 1) and for year 1 overall (Figure 1), but not for year 2.

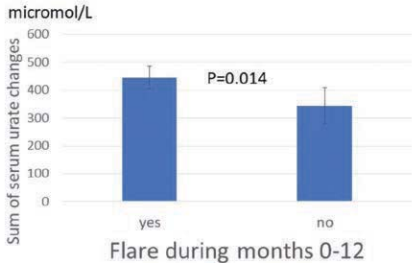
Table 1. Flares and fluctuation of serum urate (SUA) measures during defined observation periods.

Flare period (Mths)		N	Sum of all SUA changes (mean)	SUA change (mean)	>30 µmol/L SUA change (% patients)	>60 µmol/L SUA change (% patients)	>90 µmol/L SUA change (% patients)
0-3	Flare +	63	467*	141*	88.1	83.1	67.8
	Flare -	148	388	165	95.5	91.5	80.8
3-6	Flare +	91	459**	19	38.8	28.2	10.6
	Flare -	120	375	17	39.4	24.5	14.9
6-9	Flare +	56	482*	10	49.0**	25.5	25.5
	Flare -	155	386	26	26.5	15.5	15.5
9-12	Flare +	70	470*	4	32.2	16.9	11.9
	Flare -	116	406	9	22.6	9.4	6.6
0-12	Flare +	155	445*	193	98.0	94.0	90.7*
	Flare -	36	345	160	91.7	86.0	75.0
12-24	Flare +	45	411	13	24.4	11.1	6.7
	Flare -	128	449	14	25.8	11.7	4.7

*P<0.05, **P<0.01 for comparisons +/-Flare

Other measures of SUA fluctuation (SUA change during periods, and exceeding thresholds of change) were generally not related to incidence of flares, neither were sensitivity analyses for incidence of flares in periods succeeding observed SUA fluctuations.
Conclusion: Fluctuation in SUA, defined as the total sum of mean SUA changes between all study visits, was related to gout flares during year1. Our findings support that a pattern of SUA fluctuation is related to gout flares.

Figure. Fluctuation of serum urate and flare during months 0-12



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POS0282 UPDATE ON COMPARATIVE CARDIOVASCULAR SAFETY OF FEBUXOSTAT VERSUS ALLOPURINOL AMONG PATIENTS WITH GOUT

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Background: Gout is associated with an increased risk of cardiovascular (CV) disease.
Objectives: To update comparative CV safety of febuxostat versus allopurinol among patients with gout
Methods: Using the 2011-2019 Korea National Health Insurance database, we conducted a cohort study comparing gout patients initiating febuxostat versus allopurinol, with study participants matched on a propensity score (PS) for>60 covariates at a 1:1 ratio. The primary outcome was composite CV outcome of myocardial infarction, coronary revascularization, and stroke. Secondary outcomes were CV and all-cause mortalities in addition to individual components of the primary outcome. Cox proportional hazards models estimated hazard ratios (HRs) and 95% confidence intervals (CIs), comparing febuxostat versus allopurinol initiators.
Results: We included 160,930 febuxostat users PS-matched on 160,930 allopurinol users (mean age 59.3 years, 79.6% male). During a mean follow-up of 250 days, the incidence rate of the primary outcome was 2.27 and 2.06 per 100 person-years for allopurinol and febuxostat users respectively, with the PS-matched HR [95% CI] of 1.03 [0.95-1.12]. Analysis on secondary outcomes also showed a similar result except for all-cause mortality with a significantly reduced risk among febuxostat users with a PS-matched HR [95% CI] of 0.84 [0.78-0.91] (Table 1).

Table 1. Comparative cardiovascular safety between febuxostat and allopurinol

	Febuxostat N = 160,930			Allopurinol (Ref) N= 160,930			HR
	Events	PY	[a]IR [95% CI]	Events	PY	[a]IR(95% CI]	(95% CI)
Composite CV endpoint	2635	128,193	2.06 [1.98-2.13]	2,099	92,512	2.27 [2.17-2.37]	1.03 [0.95-1.12]
MI	468	129,873	0.36 [0.33-0.39]	341	93,808	0.36 [0.33-0.40]	1.13 [0.91-1.39]
Coronary revascularization	1085	129,233	0.84 [0.79-0.89]	856	93,293	0.92 [0.86-0.98]	1.10 [0.96-1.26]
Stroke or TIA	1490	129,163	1.15 [1.10-1.21]	1,187	93,252	1.27 [1.20-1.35]	0.99 [0.90-1.10]
Death	2558	130,176	1.97 [1.89-2.04]	2,201	94,007	2.34 [2.24-2.44]	0.84 [0.78-0.91]

[a]IR is per 100 person-years. IR=incidence rate, HR=hazard ratio, CI=confidence interval, MI=myocardial infarction, PY=person-years, TIA=transient ischemic attack

Conclusion: This large population-based cohort study showed a similar CV safety profile between febuxostat and allopurinol users but found a 16% reduced all-cause mortality among febuxostat users compared to allopurinol, primarily derived from non-CV death reduction.
Disclosure of Interests: None declared
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POS0283 DOES A GOUT STIGMA AMONG RHEUMATOLOGISTS INFLUENCE PERCEPTIONS OF PATIENTS AND TREATMENT DECISIONS?

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Background: Gout is an inflammatory condition caused by chronic hyperuricemia, often causing physical and emotional distress and a lower quality of life (QOL).[1-3] Gout stigma is common and impactful,[4] with physicians often perceiving gout as a "lifestyle" disease caused by personal dietary and exercise choices. Further, patients can internalize and anticipate this stigma, influencing how they seek healthcare and adhere to medical therapies.[5]
Objectives: This study investigated whether or not a gout stigma exists among rheumatologists and, if so, how it influences physicians' perceptions of patients and treatment decisions. Rheumatoid arthritis (RA) was used as a comparator disease.
Methods: 106 practicing rheumatologists completed an online survey regarding perceptions of, experiences with, and recommendations for patients with controlled gout, uncontrolled gout, and rheumatoid arthritis (RA). Disease states were presented in random order. Each set of measures examined rheumatologists' perceptions and judgments of each disease condition on a range of dimensions, including (a) perceptions of patient's compliance with treatment recommendations and responsibility for their disease condition, (b) causal attributions for contributing factors to disease condition, and (c) efficacy of recommended treatment decisions. Answers were provided using a 7-point Likert scale (e.g., patient compliance: 1 = will not comply, 7 = will comply; patient responsibility for condition: 1 = not responsible, 7 = responsible). Prior to analyses, all responses were converted to a 0 to 1 scale for ease of comparison and interpretation.
Results: Responses regarding controlled and uncontrolled gout patients were not significantly different, so these two groups were pooled. Compared to patients with RA, rheumatologists perceived patients with gout as significantly more responsible for their disease (p<0.05) and significantly less likely to comply with prescribed treatment regimens (p<0.05, Figure 1). Further, rheumatologists perceived patient personal behavior, diet, BMI, and patient adherence as

greater contributing factors to gout than to RA (all p<0.01). Similarly, change in diet, increased exercise, and weight loss were perceived as more beneficial for managing gout than RA (all p<0.01), and biological treatments were perceived as more effective for managing RA than gout (p<0.01).

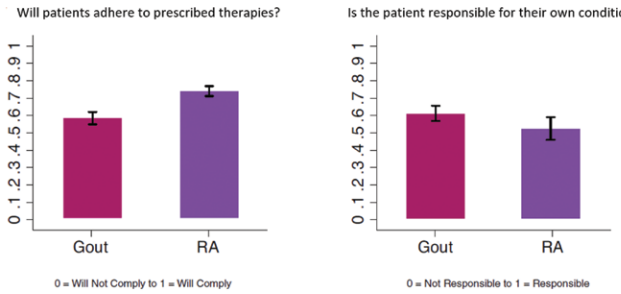

Figure. Rheumatologist's mean-level perceptions of patient treatment compliance (left) and responsibility for their condition (right). Error bars represent 95% confidence interval.

Conclusion: Despite good intentions when treating gout patients, rheumatologists appear to have causal beliefs and illness perceptions that reflect negative gout-related stereotypes. Compared to RA patients, gout patients were perceived as being more responsible for their condition and were expected to be less compliant with medications and less likely to benefit from biological therapies. Interestingly, there were no differences in rheumatologists' judgments between patients with controlled and uncontrolled gout, suggesting that their beliefs may refer to gout itself rather than the degree of control or management. Educating physicians, particularly rheumatologists, on the myths surrounding gout may improve clinical care and, therefore, patient outcomes.

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POS0284 CHANGES OF ESTIMATED GLOMERULAR FILTRATION RATE AFTER LONG-TERM FEBUXOSTAT OR ALLOPURINOL TREATMENT IN GOUT PATIENTS

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Background: Under the hypothesis that hyperuricemia is a potentially modifiable risk factor for progression of CKD, there has been numerous small, single-center studies that have shown that use of urate-lowering therapy (ULT) delayed CKD progression in patients with hyperuricemia or CKD. However, recent three multicenter, randomized controlled trials have not shown beneficial effect of ULT on the progression of CKD among CKD patients without gout and in DM patients with albuminuria.

Objectives: We investigated whether ULT may have a beneficial effect on the progression of CKD in gout patients.

Methods: Gout patients who took the study medication for more than 1 year were identified from the Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout (CARES) trial, which is a large, multicenter, randomized controlled trial. We analyzed the estimated glomerular filtration rate (eGFR) slope (mL/min/1.73 m^2 per year) using the CKD-EPI equation. Using logistic regression, we investigated risk factors for CKD progression, defined as eGFR slope of lower than 0 mL/min/1.73 m2 per year.

Results: During the study period [median (interquartile range, IQR) 3.1 (2.0-4.8) year], 4,144 patients performed median (IQR) 12 (9~15) creatinine tests, the GFR slope was analyzed as median (IQR) 0.5 (-0.8-1.6). The median (IQR) values of the GFR slope were -1.2 (-2.3--0.5) in the CKD progression group (n=1,590) and 1.3 (0.7-2.2) in the CKD progression delayed group (n=2,554). After adjusting well known factors associated with CKD progression, average level of serum uric acid ≥ 6 mg/dL during study period was significantly associated with CKD progression (adjusted odds ratio 1.73; 95% confidence interval 1.49-2.01, p < 0.0001).

Conclusion: This study showed that eGFR did not decrease in more than half of gout patients after long term febuxostat or allopurinol administration. ULT may have a beneficial effect on slowing the progression of CKD in gout patients.

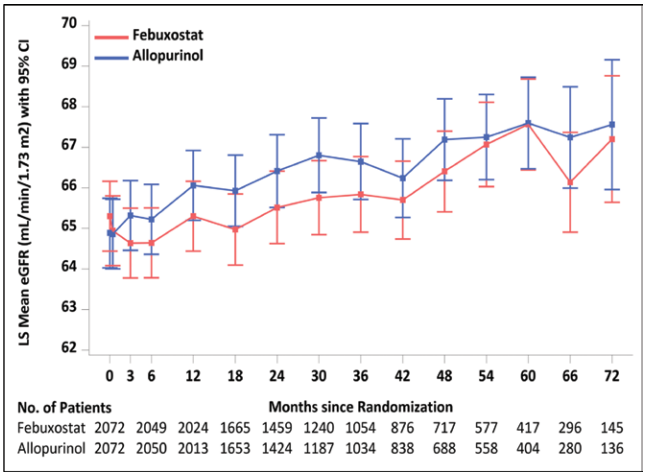

Figure 1. Changes of estimated glomerular filtration rate during febuxostat or allupurinol administration.

Acknowledgements: We were able to access the CARES trial data through the Vivli company, and re-analyzed data of the CARES trial without financial support from any company.

Disclosure of Interests: None declared

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POS0285 SUB-STANDARD CARE FOR PATIENTS WITH GOUT, DESPITE UPDATED GUIDELINES: A UK-WIDE, POPULATION-BASED COHORT STUDY

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Background: Treat-to-target urate-lowering therapy (ULT) is highly effective at preventing flares and improving quality of life for patients with gout.[1] However, in 2012, only 27% of patients with gout in UK primary care received prescriptions for ULT within 12 months of diagnosis.[2] Since then, EULAR and BSR gout management guidelines have been updated, to recommend that all patients with gout should have ULT discussed and offered to them, with uptitration of dosing until target urate levels are achieved. We investigated whether gout management has improved in recent years.

Objectives: To assess temporal trends in the initiation of ULT and attainment of serum urate targets following new gout diagnoses in UK primary care from 2004 to 2020.

Methods: The Clinical Practice Research Datalink (CPRD) Gold database was used to assess the management of patients with index diagnostic codes for gout in UK primary care between January 2004 and October 2020. We analysed the proportion of patients with the following outcomes within 12 months of diagnosis: i) initiation of ULT (allopurinol, febuxostat, benzbromarone, probenecid or sulfinpyrazone); ii) serum urate ≤360 µmol/L; iii) serum urate ≤300 µmol/L; iv) treat-to-target urate monitoring (defined as two or more serum urate levels performed within 12 months of diagnosis and/or one or more urate ≤300 µmol/L). Interrupted time-series analyses (ITSA) were used to estimate the impact of updated EULAR and BSR gout management guidelines on these outcomes. Multivariate logistic regression was used to analyse predictors of ULT prescription and target attainment following new gout diagnoses.

Results: 129,972 patients had index gout diagnoses between January 2004 and October 2020, of whom only 37,529 (28.9%) had ULT initiated within 12 months of diagnosis. ULT initiation improved modestly over the study period, from 26.8% for those diagnosed in 2004 to 36.6% in 2019, decreasing to 34.7% in 2020 (Figure 1). Of patients diagnosed in 2020 who had a serum urate performed within 12 months of diagnosis, 36.0% attained a urate ≤360 µmol/L, while 17.1% attained a urate ≤300 µmol/L. Of all participants, 18.9% received treat-to-target urate monitoring. In ITSA models, no statistically significant improvements in ULT prescription or urate target attainment were observed after publication of updated

EULAR (2016) or BSR (2017) gout management guidelines, relative to before publication of these guidelines. In multivariate logistic regression models, comorbidities including chronic kidney disease, heart failure and obesity, and diuretic use were associated with increased odds of ULT initiation but decreased odds of attaining target urate levels by 12 months.

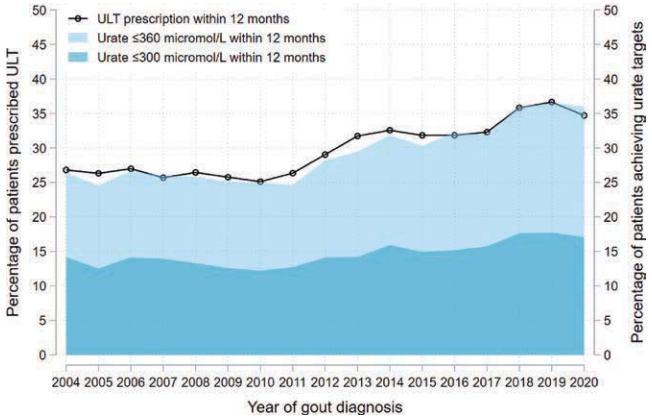

Figure 1. Proportion of patients newly diagnosed with gout who: i) were initiated on urate-lowering therapy (ULT) within 12 months of diagnosis (black line); ii) had a serum urate performed and attained a level ≤360 µmol/L (light blue) or ≤300 µmol/L (dark blue) within 12 months of diagnosis.

Conclusion: In this UK-wide study, we demonstrate that the initiation of ULT and attainment of serum urate targets following new gout diagnoses remain poor, despite the introduction of updated management guidelines. If the evidence-practice gap in gout management is to be bridged successfully, strategies to implement best practice gout care are urgently needed.

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All you want to know about bDMARDs in RA.

POS0286

CAN PATIENTS WITH CONTROLLED RA RECEIVING ANY CLASS OF TARGETED THERAPY WITH METHOTREXATE (MTX) SUSTAIN DISEASE CONTROL AFTER TAPERING MTX? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Patients with RA frequently struggle with intolerance of MTX and adherence to MTX remains highly variable. Guidelines conditionally recommend the tapering of MTX before tapering biologic (b)DMARDs, but acknowledge there is an absence of direct evidence. Prior reviews on this topic have focused on tapering of MTX from combination treatment with TNF-inhibitors(i) only[1]. There have been no updated reviews addressing MTX tapering from other targeted therapies such as IL6-i or JAK-i, nor has there been a systematic review addressing this question.

Objectives: To determine the feasibility of tapering MTX to targeted therapy (bDMARDs or JAKi) alone in patients whose RA is controlled (LDA or remission).

Methods: A systematic literature search combing MeSH terms and keywords was conducted in Medline, Embase and Cochrane Library for studies reporting remission outcomes after tapering MTX from targeted therapies in RA. Non-English and animal studies were excluded. Meta-analyses were conducted using random effects models. Forest and funnel plots were created and heterogeneity was calculated.

Results: Our search identified 5762 citations. After removal of duplicates and screening title/abstract using the COVIDENCE platform, 504 full-text articles were reviewed. Of the 10 articles meeting our inclusion criteria of tapering MTX to monotherapy with a targeted therapy, 3 studies tapered to etanercept, 3 to tocilizumab, 1 to tofacitinib, 1 to certolizumab pegol, 1 to adalimumab and 1 to abatacept monotherapy. Nine studies were RCTs and one was a long-term extension study (LTE) (Table 1). Disease duration was longer in 7 studies (6-11 years) and early in 3 studies (1-9 months). The MTX tapering strategy was gradual in 2 and rapid in 8 studies. Follow-up ranged from 3 -18 months in RCTs, and up to 3 years in the LTE. Studies reporting outcomes up to 1 year after tapering had remission rates ranging 48-76%, but this dropped to 40% in one study reporting 18- month remission outcomes. Our meta-analysis conducted in 2000 RA participants from 10 studies showed that patients who tapered MTX to targeted therapy alone could maintain remission with an overall pooled OR of 0.81 (0.68, 0.97) (Figure 1). There was no heterogeneity among the studies in this group (I^2=0.0%, p=0.788). Our funnel plot indicated high precision and potentially less publication bias. No significant difference in remission outcomes between early RA [OR 0.63 (0.33, 1.18)] and established RA [OR 0.84 (0.69, 1.03)] was observed.

Table 1. Included Studies

Author/ Year	n	Early RA	Baseline treatment	MTX Taper Strategy	REM measure	Follow-up
Curtis 2020	253	no	ETA+MTX	Stop	SDAI	48 wks
Emery 2019	147	yes	ABA+MTX	Stop	SDAI	48 wks
Cohen 2019	533	no	TOFA+MTX	Stop	DAS28-CRP	48 wks
Emery 2019	411	yes	ETA+MTX	Taper 4 wks	DAS28	52 wks
Pablos 2019	165	no	TCZ+MTX	Stop	DAS28	28 wks
Pope 2019	88	no	CZP+DMARD	Stop	DAS28	18 mos
Kremer 2018	296	no	TCZ+MTX	Stop	DAS28	52 wks
Edwards 2017	272	no	TCZ+MTX	Taper 24 wks	DAS28	48 wks
Keystone 2016	205	no	ETA+MTX	Stop	DAS28	18 mos
Keystone 2018	140	yes	ADA+MTX	Stop	DAS28-CRP	3 years

ETA etanercept, ABA abatacept, TOFA tofacitinib, TCZ tocilizumab, CZP certolizumab pegol, ADA adalimumab, REM remission, wk week, mo month, DAS28 Disease Activity Score 28, SDAI Simplified disease activity index.

Conclusion: Patients with controlled RA have a high probability of maintaining disease control after tapering their MTX to targeted therapy alone, up to 18 months. This review may inform patients with controlled disease on any of a range of targeted therapies and MTX, but who are struggling with MTX-related adverse effects and wish to taper it. Longer follow-up studies with attention to radiographic, functional and patient reported outcomes are needed. The possibility of disease worsening must be discussed with the patient in advance with careful follow-up and prompt re-treatment of disease worsening.

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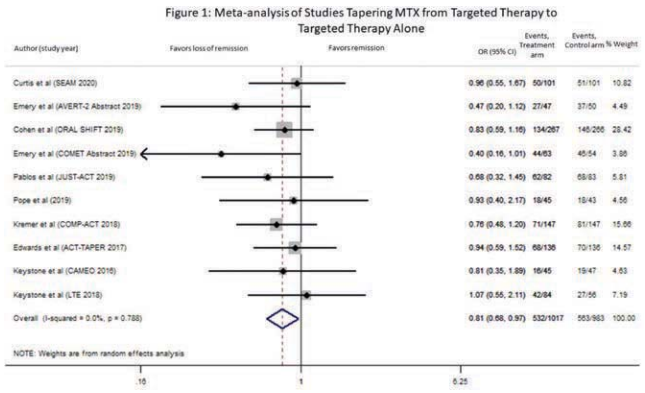

Disclosure of Interests: Charis Meng: None declared, Diviya Rajesh: None declared, Deanna Jannat-Khah Shareholder of: AstraZeneca, Cytodyn, Walgreens, Omar Bruce: None declared, Bridget Jivanelli: None declared, Vivian

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POS0287

A PHASE III, RANDOMISED, DOUBLE-BLIND, ACTIVE-CONTROLLED CLINICAL TRIAL TO COMPARE BAT1806/BIIB800, A PROPOSED TOCILIZUMAB BIOSIMILAR, WITH TOCILIZUMAB REFERENCE PRODUCT IN SUBJECTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS WITH AN INADEQUATE RESPONSE TO METHOTREXATE THERAPY

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Background: BAT1806/BIIB800 is a proposed biosimilar to reference tocilizumab (TCZ). A Phase III randomised, double-blind, active-controlled clinical trial was conducted as part of a biosimilar development programme.
Objectives: To evaluate the efficacy, pharmacokinetics (PK), safety and immunogenicity of BAT1806/BIIB800 in comparison with EU-sourced TCZ in subjects with moderate to severe rheumatoid arthritis with inadequate response to methotrexate (MTX).
Methods: The study was conducted at 55 centres in China and Europe, between June 2018 and January 2021. Eligible subjects were randomised in a 2:1:1 ratio to one of three treatment groups: (1) BAT1806/BIIB800 up to Week 48, (2) TCZ up to Week 48, or (3) TCZ up to Week 24, followed by BAT1806/BIIB800 from Week 24 to Week 48, administered intravenously every 4 weeks at a dose of 8mg/kg. The primary endpoint was the proportion of subjects achieving an ACR20 response at timepoints pre-specified to meet the requirements of different Regulatory Agencies: Week 12, for EMA; Week 24, for FDA and NMPA. Equivalence margins applied to differences in ACR20 response rates in the BAT1806/BIIB800 and TCZ treatment groups were pre-specified as follows: +/- 14.5% for EMA (95% confidence interval (CI)); -12.0%,15% for FDA (90% CI); +/- 13.6% for NMPA (95% CI). Secondary endpoints included pharmacokinetics, safety and immunogenicity.
The ICH E9(R1) estimands framework including intercurrent events (related or unrelated to the COVID19 pandemic) was implemented for the ACR20 evaluation. A logistic regression model including 'region' (China and Eastern Europe) and 'previous biologic or targeted synthetic DMARD use' (Yes/No) as captured in Interactive Web Response System as stratification factors was utilised to assess equivalence for the primary endpoint. The difference in response rates was estimated and corresponding confidence intervals were derived to assess equivalence for the primary endpoint. This abstract presents results up to Week 24.
Results: In total, 621 subjects were randomised to receive BAT1806/BIIB800 (N=312), TCZ (N=155), or TCZ followed by BAT1806/BIIB800 (N=154). The groups were comparable in terms of baseline demographics and disease characteristics, including age, gender, disease activity and disease duration. The estimated proportions of subjects achieving an ACR20 response in the BAT1806/BIIB800 vs. the TCZ groups, respectively, were 68.97% vs. 64.82% at Week 12 and 69.89% vs. 67.94% at Week 24. The estimated difference between ACR response rates was 4.15% (95% CI -3.63, 11.93) at week 12, and 1.94% (90% CI -4.04, 7.92; 95% CI -5.18, 9.07) at Week 24. The CIs for the estimated differences between the treatment groups were within the pre-defined equivalence margins (Figure 1). The treatment groups were comparable in terms of serum trough levels, incidence of TEAEs and ADA/NAb positivity (Table 1).

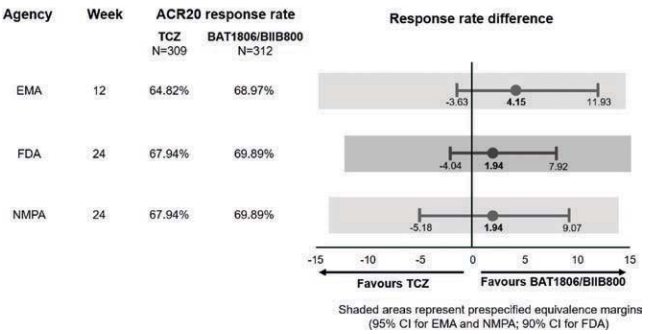
Table 1. Safety and Immunogenicity up to Week 24, and Pharmacokinetics at Week 24

	TCZ (N =309) n (%)	BAT1806/BIIB800 (N=312) n (%)
TEAE	196 (63.4)	201 (64.4)
Related TEAE	151 (48.9)	148 (47.4)
Serious TEAE	13 (4.2)	11 (3.5)
Related Serious TEAE	7 (2.3)	2 (0.6)
Fatal TEAE	1 (0.3)	3 (1.0)
ADA positive [a]	42 (13.6%)	64 (20.5%)
NAb positive [a]	42 (13.6%)	63 (20.2%)
PK, n	271	276
Serum trough level (ug/mL), mean (SD)	15.4 (17.1)	15.8 (12.3)
Serum trough level (ug/mL), geometric mean (CV%)	12.3 (140.3)	12.9 (121.3)
Below limit of quantification, n (%)	43 (15.9)	28 (10.1)

TEAE, treatment emergent adverse events[a] subjects with ≥1 ADA/NAb positive results up to week 24

Conclusion: BAT1806/BIIB800 has demonstrated equivalent efficacy at Week 12 and Week 24 and a similar PK, safety and immunogenicity profile as reference tocilizumab up to Week 24.

Figure 1. Forest Plot of Primary Efficacy Results



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POS0288

A CANADIAN RETROSPECTIVE CHART REVIEW EVALUATING CONCOMITANT METHOTREXATE DE-ESCALATION PATTERNS IN RA PATIENTS TREATED WITH BIOLOGIC OR TARGETED SYNTHETIC DMARDS

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Background: Rheumatoid arthritis (RA) guidelines recommend methotrexate (MTX) as anchor therapy in combination with biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs). However, its tolerability is challenging with a significant proportion of patients not adhering to their prescribed MTX regimen following b/tsDMARD initiation. Rates of MTX tapering and withdrawal have been reported elsewhere but Canadian data are lacking.
Objectives: This multi-centre, retrospective chart-based cohort study assessed the frequency of MTX withdrawal or tapering following initiation of a b/tsDMARD in Canadian adults with RA.

Methods: Patients were eligible if they received MTX for ≥3 months before initiation of a b/tsDMARD that was then prescribed continuously for ≥18 months and was initiated in combination with MTX. Patients taking oral prednisone or equivalent at a dose >10 mg per day, and those whose b/tsDMARD was prescribed prior to 2014, were excluded.
Results: Data from 889 patients were included in the analysis. Mean age was 50.6 years and 72.6% were female. Mean time since diagnosis was approximately 8 years. Of the 46.1% of patients with a documented assessment of disease status at baseline, 62.7% of patients had high disease activity. Baseline mean (SD) MTX dose was 18.9 (6.63) mg/week, administered orally (57.4%), subcutaneously (41.3%), or intramuscularly (1.2%). Overall, 270 (30.4%) patients either tapered (123, 13.8%) or discontinued (147, 16.5%) their MTX within 2 years of initiating the b/tsDMARD. Methotrexate dose was unchanged for 582 (65.5%) subjects and increased for 37 (4.2%) subjects. The prescribed b/tsDMARD was most often a tumor necrosis factor inhibitor (TNFi,52.1%), followed by a Janus kinase inhibitor (JAKi, 18.3%), other modes of action (OMA) which included abatacept and rituximab (17.7%) and interleukin-6 inhibitor (IL-6i, 11.9%). The b/tsDMARD type with the highest frequency of MTX Taper or Discontinued was IL-6i (37 patients, 34.9%) followed by TNFi (144 patients, 31.1%), JAKi (47 patients, 28.8%) and OMA (44 patients, 28.0%). In the MTX Discontinued group, the most common reasons for MTX discontinuation were patient decision (27.2%) and adverse events (24.5%). In the MTX Tapered group, the most common reasons for MTX dose change were planned tapering (36.6%) and adverse events (29.3%). In the MTX Increased group, insufficient clinical response (73.0%) was the most common reason provided for MTX dose change. Baseline factors associated with MTX dose discontinuation and tapering by multiple logistic regression were a shorter time since diagnosis (Odds ratio [OR]: 0.981; 95% confidence interval [CI]: 0.964 – 0.999. P=0.0401), use of non-DMARD medications excluding steroids (OR: 0.683; 95%CI: 0.503 – 0.929. P=0.0150) and a greater number of comorbidities (OR: 1.054; 95%CI: 1.001 – 1.110. P=0.0444). The mean (SD) weekly MTX dose at the end of the data extraction period was 14.13 (4.81) mg for the MTX Tapered group, with 109 (88.6%) subjects taking a weekly MTX dose ≥10 mg. In the MTX Increased group the mean (SD) weekly MTX dose was 22.3 (3.74) mg. Interpretation of the effect of MTX dose on disease activity, fatigue, pain and functional status is challenging due to missing data, but most patients in all 4 groups transitioned to low disease activity or remission during the study period.
Conclusion: Methotrexate withdrawal or tapering occurred in 30.4% of Canadians with RA within two years following b/tsDMARD initiation. There was no evidence of worsening disease activity in these patients. These proportion of Canadian RA patients who reduce or discontinue MTX after the initiation of a ts/bDMARD are generally consistent with those reported in other regions of the world.
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POS0289

A CONCEPTUAL FRAMEWORK OF THE COURSE AND TIMEFRAME OF PATIENT-REPORTED ADVERSE DRUG REACTIONS OF BIOLOGICS IN IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Background: Patients with immune-mediated inflammatory diseases (IMIDs) need chronic drug treatment, including biologics, which may cause adverse drug reactions (ADRs). Information about ADRs is usually restricted to the type of ADRs that may occur with drug use. Common patterns in the course and timeframe of ADRs are often not described while this information may provide valuable insights for patients and healthcare professionals.
Objectives: To identify common and corresponding items with thematic analysis in the described course of ADRs of biologics reported by patients with IMIDs.
Methods: We used qualitative data from the Dutch Biologic Monitor (DBM) to assess the patient's descriptions of the course of ADRs they experienced. IMID patients were asked to fill out a bimonthly questionnaire on experienced ADRs they attributed to the use of a biologic [1, 2]. Inclusion criteria were: patients reporting an ADR and elaboration on the course of the ADR in an open-ended text field. Answers of the patients on the course of the experienced ADR were analysed by two pharmacovigilance assessors with a thematic analysis with an inductive approach to develop a conceptual framework which was visualised using an Ishikawa diagram.
Results: From 1382 consecutive participants, 730 patients reported 2035 ADRs. Six themes with multiple subthemes were identified from patient descriptions on the course of the ADRs they experienced (Figure 1). Four themes included descriptive items of the course of ADRs: the moment or period of ADR occurrence (e.g. a specific moment of the day or in a specific season), the frequency of an ADR episode (e.g. once, sometimes, often, always or recurring with or without specified frequency), the duration of an ADR episode (e.g. specified duration, constant, variable increasing or decreasing duration) or an association in time with the administration moment (e.g. before, during or after biologic administration or a specific time to onset in relation to the moment of biologic administration). Two themes included factors influencing the course of ADRs: triggering factors for ADR occurrence or aggravation (e.g. administration method, social, physical or mental status, nutrition, external factors, (co)medication or daily activities) and improving factors (e.g. administration method, treatment, physical or mental status, nutrition or selfcare).

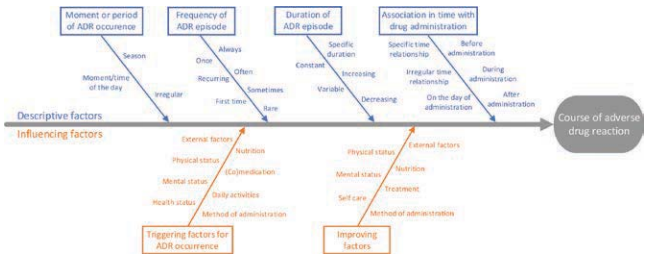

Figure 1. A conceptual framework of descriptions of the course and timeframe of adverse drug reactions reported by patients using a biologic for immune-mediated inflammatory diseases

Conclusion: We identified six themes in patient-reported descriptions of the course of ADRs of biologics. These themes provide information about ADRs on a broader level than the currently available information on nature and frequency. Information about ADRs enriched with details on the course and timeframe of ADRs may support healthcare professionals in improving clinical practice by discussing ADRs with patients and finding practical solutions in dealing with ADRs. This will ultimately lead to more optimised medical treatment.
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POS0290 THE EFFECTS OF TREATMENT RESPONSE AND RISK FACTOR TO INHIBIT THE CLINICAL RESPONSE IN PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS TREATED WITH IL-6 RECEPTOR INHIBITOR, ABATACEPT AND JAK INHIBITOR

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Background: Recently, the disease activity of rheumatoid arthritis (RA) was improved due to the 'treat-to-target' strategy. However, some patients remain various symptoms despite recommended treatment was performed. Then, the term of 'difficult-to-treat RA (D2TRA)' is widely recognized. It is unknown how the difference of type of biological disease-modifying anti rheumatic dugs (bDMARDs)/Janus kinase inhibitor (JAKi) will affect clinical efficacy in patients with D2TRA. Moreover, the risk factor to inhibit the clinical response in patients with D2TRA is unknown.

Objectives: The aim of this study was to evaluate the treatment response in patients with D2TRA who were treated with interleukin 6 receptor inhibitor (IL-6Ri), abatacept and JAKi.

Methods: This study used the multicenter database included 673 RA patients treated with bDMARDs/JAKi (tocilizumab 240, sarilumab 67, abatacept 146, tofacitinib 101, baricitinib 83, upadacitinib 20, peficitinib 14, filgotinib 2). Two hundred forty-two patients were treated as first line bDMARDs/JAKi (IL-6Ri 117, abatacept 63, JAKi 62), 211 patients were treated as second line bDMARDs/JAKi (IL-6Ri 117, abatacept 37, JAKi 57), 220 patients were treated as third and more bDMARDs/JAKi. In these 220 patients, 82 patients did not meet D2TRA criteria (IL-6Ri 42, abatacept 15, JAKi 25) and 138 patients met D2TRA criteria (IL-6Ri 31, abatacept 31, JAKi 76). In all patients, we analyzed 138 patients with D2TRA (113 female, mean age was 63.1 ± 13.7 years). Drug retention rate and effectiveness of bDMARDs/JAKi in patients with D2TRA were evaluated for 24 weeks. Multivariate linear regression analysis was performed to clarify the risk factors to inhibit the clinical response.

Results: Drug retention rate of patients with D2TRA at 24 weeks was 67.7% in IL-6Ri group, 74.2% in abatacept group, 61.8% in JAKi group. Drug retention rate in patients with D2TRA was not different between groups (IL-6Ri vs abatacept: p=0.86, IL-6Ri vs JAKi group: p=0.39, abatacept vs JAKi group: p=0.33). DAS28-CRP at 4, 12, 24 weeks decreased in all group (Figure 1). Abatacept showed lower improvement ratio of DAS28-CRP at 24 weeks compared to IL-6Ri group (IL-6Ri vs abatacept: p<0.01, IL-6Ri vs JAKi: p=0.1, abatacept vs JAKi: p=0.07). Good responder (defined as decrease in DAS28-CRP score > 1.2 with a score < 3.2) was 52.4% patients in IL-6Ri, 17.4% patients in abatacept, 29.8% patients in JAKi. SDAI and CDAI at 4, 12, 24 weeks decreased in all group (Figure 1). There were no diferences between the groups in improvement ratio of SDAI (IL-6Ri vs abatacept: p=0.11, IL-6Ri vs JAKi: p=0.81, abatacept vs JAKi: p=0.08) and CDAI (IL-6Ri vs abatacept: p=0.31, IL-6Ri vs JAKi: p=0.82, abatacept vs JAKi: p=0.13) at 24 weeks. HAQ was 1.42, 1.15, 1.39 at baseline, 1.27, 1.07, 1.22 at 4 weeks, 1.17, 1.07, 1.17 at 12 weeks, 1.26, 1.06, 1.14 at 24 weeks in IL-6Ri group, abatacept and JAKi, respectively. Multivariate linear regression analysis revealed that high HAQ (β=0.28, p=0.02) and high dosage of glucocorticoid (β=0.67, p<0.01) inhibited the improvement of DAS28-CRP. Type of bDMARDs/JAKi (β=-0.09, p=0.36) did not affect the DAS28-CRP improvement for 24 weeks.

Figure. Clincal responce in patients with D2TRA treated with different type of bDMARDs/JAKi

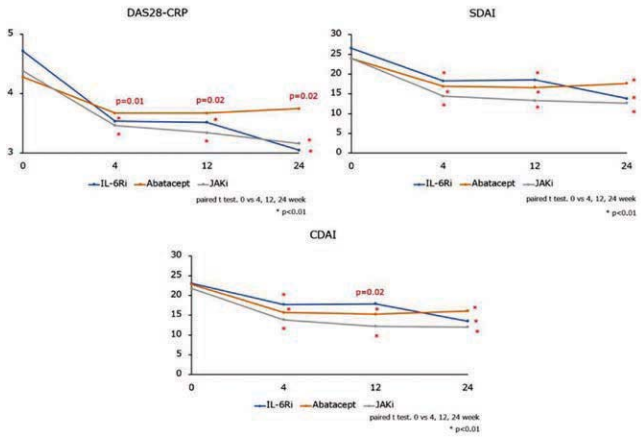

Table 1. Multivariate linear regression analysis of risk factor to inhibit the clinical response in patients with D2TRA.

	β	95% CI	p
Age (years)	-0.037	-0.025, 0.017	0.74
male	-0.047	-0.788, 0.486	0.64
Disease durations (years)	-0.048	-0.028, 0.017	0.63
RF (IU/ml)	-0.082	-0.0004, 0.0002	0.41
Anti CCP antibody (U/ml)	0.111	-0.0005, 0.002	0.26
DAS28-CRP	-0.063	-0.265, 0.142	0.55
HAQ	0.279	0.059, 0.717	0.02
MTX (mg/day)	0.136	-0.018, 0.081	0.21
Glucocorticoid dose (mg/day)	0.669	0.174, 0.324	< 0.01
Type of bDMARDs/JAKi	-0.088	-0.415, 0.151	0.36

Conclusion: Drug retention rate and clinical efficacy of D2TRA patients were not different among IL-6Ri, abatacept and JAKi. DT2RA patient with functional disorder and high dosage of glucocorticoid were risk factor to inhibit the clinical response.

Disclosure of Interests: None declared

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POS0291 OLOKIZUMAB IMPROVED PATIENT REPORTED OUTCOMES IN TNF INCOMPLETE RESPONDER (TNF-IR) RHEUMATOID ARTHRITIS PATIENTS: RESULTS FROM THE PHASE 3 RANDOMIZED CONTROLLED TRIAL, CREDO 3

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Background: Olokizumab (OKZ) is an interleukin-6-inhibitor for treatment of rheumatoid arthritis (RA). In these analyses we present patient reported outcomes (PROs) reported by TNF-IR patients with moderate to severely active RA receiving OKZ or placebo in a phase 3 randomized controlled trial (RCT) (ClinicalTrials.gov number, NCT02760433).

Objectives: To assess the effect of OKZ treatment compared with placebo in patient global assessment of disease activity (PtGA), pain, physical function (HAQ-DI), fatigue (FACIT-F) and health related quality of life (SF-36 physical (PCS) and mental (MCS) component summary and domain scores) at 12 weeks.

Methods: 368 patients were randomized 2:2:1 to receive subcutaneously administered OKZ 64 mg once every 2 weeks (q2w), OKZ 64 mg q4w, or placebo, plus

Table 1. Mean baseline values and LSM changes from baseline to week 12 for PROs

	Baseline, mean (standard deviation)			12 weeks LSM changes (standard error)		
	OKZ q2w, N=138	OKZ q4w, N=161	Placebo, N=69	OKZ q2w, N=138	OKZ q4w, N=161	Placebo, N=69
PtGA-VAS (mm)	64.8 (20.5)	68.1 (19.1)	72.1 (18.5)	-24.9 (2.1)	-25.0(1.9)*	-16.9 (2.9)
Pain-VAS (mm)	67.2 (19.5)	69.3 (19. 1)	69.6 (21.9)	-28.2 (2.2)**	-27.5(2.0)**	-15.0 (3.0)
HAQ-DI†	1.79 (0.53)	1.78 (0.56)	1.78 (0.64)	-0.49 (0.05)*	-0.39(0.04)	-0.32(0.07)
SF-36 PCS score	31.4 (6.8)	30.6 (7.2)	30.6 (5.9)	6.9 (0.7)**	5.7 (0.6)	3.9 (0.9)
SF-36 MCS score	44.3 (12.6)	44.5 (11.1)	45.1 (10.2)	4.1 (0.8)*	3.4 (0.8)*	0.5 (1.1)
Physical functioning	29.9 (7.9)	29.8 (8.5)	29.6 (8.4)	6.1 (0.8)	5.2 (0.7)	3.7 (1.1)
Role physical	32.8 (6.9)	33.1 (7.4)	33.7 (6.8)	6.0 (0.7)	5.0 (0.7)*	3.3 (1.0)
Bodily pain	34.5 (6.9)	33.2 (6.0)	33.0 (6.6)	8.5 (0.7)***	7.8 (0.7)***	3.7 (1.0)
General health	38.3 (8.3)	36.5 (8.6)	36.9 (8.5)	4.7 (0.7)*	3.3 (0.6)	2.1 (1.0)
Vitality	40.8 (10.1)	40.7 (9.5)	41.1 (8.1)	5.7 (0.8)	6.0 (0.7)*	3.0 (1.1)
Social functioning	38.8 (9.9)	38.7 (9.8)	39.6 (9.3)	6.7 (0.8)***	3.6 (0.8)*	0.2 (1.2)
Role emotional	39.1 (12.5)	39.1 (11.2)	38.9 (11.1)	4.3 (0.9)*	3.4 (0.8)	1.0 (1.2)
Mental health	41.4 (11.6)	41.4 (10.5)	42.2 (10.3)	4.4 (0.8)	4.6 (0.8)	1.9 (1.1)
FACIT-Fatigue	27.0 (10.2)	26.6 (10.6)	27.3 (9.9)	7.8 (0.9)*	6.8 (0.8)	4.6 (1.2)

Footnotes: NRI for Missing data.†, secondary endpoint; *p≤0.05, **p<0.01, ***p<0.001 vs placebo;

MTX. PROs were assessed at baseline, weeks 12 (primary endpoint) and 24. At week 16, all patients receiving placebo were switched to either OKZ dose. Between groups differences in least-squares mean (LSM) changes from baseline were analyzed, p < 0.05 considered significant; nominal p-values for PROs not in the hierarchy.

Results: Baseline demographics and disease characteristics were comparable between groups. At week 12, treatment with OKZ q2w compared with placebo resulted in significantly greater LSM changes from baseline in Pain, HAQ-DI, FACIT-F, SF-36 PCS, MCS and 4 domains; with OKZ q4w in PtGA, Pain, SF-36 MCS and 4 domains (Table 1, Figure 1). Improvements reported at week 12 in PROs continued or increased with both doses of OKZ until week 24. Post hoc analyses demonstrated that a higher proportion of patients receiving OKZ reported improvements ≥minimum clinically important differences vs placebo (p<0.05) in FACIT-F, SF-36 PCS and MCS scores, indicating that these changes translated into clinically meaningful benefits on an individual patient basis. Numbers needed to treat to gain these benefits in fatigue and physical function ranged from 9.2 - 15.4 with OKZ q2w vs 10.5 - 13.3 with OKZ q4w, respectively.

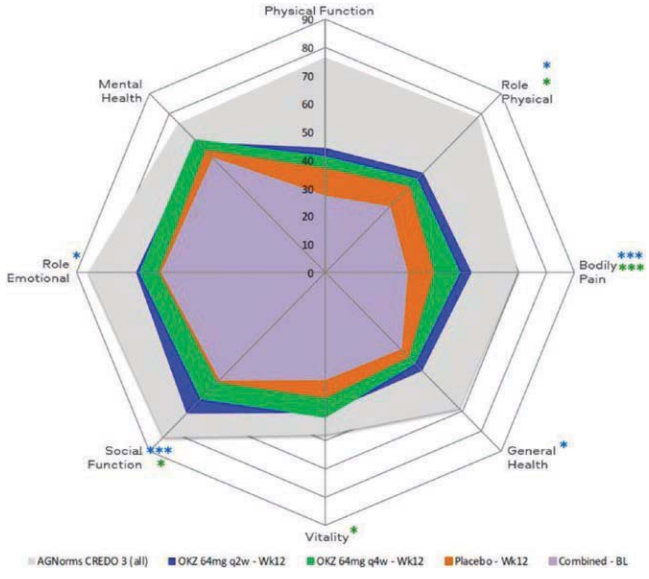

Figure 1. SF-36 domain changes from baseline to week 12. *p≤0.05, **p<0.01, ***p<0.001 for OKZ q2w vs placebo; *p≤0.05, **p<0.01, ***p<0.001 for OKZ q4w vs placebo; AGNorms, age- and gender-matched normative values; BL, baseline.

Conclusion: Treatment with OKZ over 12 weeks resulted in statistically significant improvements in PROs vs placebo reported by TNF-IR RA patients. Benefits were more frequently reported by patients receiving OKZ q2w than q4w in this phase 3 RCT of limited size in treatment experienced patients.

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POS0292

INCREASE OF PRO-INFLAMMATORY CYTOKINES IS ASSOCIATED WITH ANTI-IDIOTYPE EVENTS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH INFLIXIMAB OR ADALIMUMAB

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Background: A significant percentage of rheumatoid arthritis (RA) patients undergoing Infliximab (IFX) or Adalimumab (ADA) treatment develop antidrug antibodies with potential negative effects over their clinical activity; however, it is unknown if these anti-idiotype events could be associated with changes in cytokines levels

Objectives: To evaluate the association between blood cytokine levels, anti-idiotype events and clinical activity in RA patients treated with IFX or ADA.

Methods: All patients complied with ACR/EULAR 2021 criteria for RA and received anti-TNFa agents. Blood samples were collected during the drug trough and kept at -75ºC until analysis. Clinical activity was based on DAS28-ESR. Specific anti-drug antibodies to IFX and ADA were evaluated by sandwich ELISA. Cytokine blood levels were quantified using a multiplex system or sandwich ELISA.

Results: 57 patients with RA were recruited, 17 treated with IFX and 40 with ADA. According to the presence of anti-drug antibodies and sub-optimal levels of the biologic drug, patients were classified as immunogenic (29.8%; n=17) and non-immunogenic (70.2%; n=40), the first showed significantly higher ESR (p<0.001) and DAS28 (p<0.005). A significant association was seen between antidrug antibodies and increases of IFNg (2.1 OR, CI95%:1.2-3.8, p<0.01); MCP-1 (3.9 OR, CI95%:1.1-14.5, p<0.05); MIF (2.8 OR, CI95%:1.3-5.7, p<0.01) and TNFa 3.0 OR, CI95%:1.3-6.6, p<0.01 (see Table 1). Although anti-idiotype events were more frequent in IFX treated patients (41%), a significant difference was not seen when comparing with ADA treated patients (25%).

Table 1. Association analysis between anti-Idiotype events with cytokine levels.

Anti-Idiotype events vs	Crude results OR (IC, 95%)	p	Model 1* OR (IC, 95%)	p	Model 2** OR (IC, 95%)	p
IL-1β	**2.04 (1.26-3.30)**	**0.004**	**2.18 (1.27-3.74)**	**0.005**	**2.72 (1.41-5.24)**	**0.003**
IL-6	**1.29 (1.02-1.64)**	**0.03**	**1.30 (1.00-1.69)**	**0.04**	**1.33 (1.03-1.72)**	**0.02**
IL-8	1.20 (0.80-1.79)	0.37	1.24 (0.81-1.88)	0.32	1.22 (0.79-1.90)	0.35
IL-10	1.18 (0.91-1.51)	0.20	1.16 (0.89-1.53)	0.26	1.22 (0.92-1.62)	0.15
IL-12p40	**1.73 (1.09-2.76)**	**0.02**	**1.67 (1.00-2.80)**	**0.04**	**1.90 (1.12-3.22)**	**0.01**
IL-17A	1.39 (0.95-2.02)	0.08	1.31 (0.90-1.91)	0.15	**1.51 (1.01-2.25)**	**0.04**
INF_{γ}	**2.38 (1.37-4.12)**	**0.002**	**2.36 (1.32-4.23)**	**0.004**	**2.97 (1.57-5.61)**	**0.001**
Leptina	6.15 (0.77-48.72)	0.09	4.79 (0.63-1.07)	0.12	7.30 (0.78-68.37)	0.08
MIF	**3.94 (1.07-14.48)**	**0.04**	**5.86 (1.28-26.65)**	**0.02**	3.45 (0.87-13.68)	0.07
MCP-1	**2.98 (1.34-6.62)**	**0.007**	**3.28 (1.38-7.78)**	**0.007**	**3.74 (1.47-9.49)**	**0.005**
TNFα	**2.79 (1.38-5.63)**	**0.004**	**2.55 (1.27-5.14)**	**0.008**	**2.72 (1.30-5.71)**	**0.008**
Anti-Idiotype events vs	**Crude results*** OR (IC, 95%)**	***p***	**Model 1* OR (IC, 95%)**	***p***	**Model 2** OR (IC, 95%)**	***p***
IL-1β	1.07 (1.02-1.12)	**0.004**	1.08 (1.02-1.13)	**0.005**	1.10 (1.03-1.17)	**0.003**
IL-6	1.02 (1.00-1.05)	**0.03**	1.02 (1.00-1.05)	**0.04**	1.02 (1.00-1.05)	**0.02**
IL-8	1.02 (0.98-1.06)	0.37	1.02 (0.98-1.06)	0.32	1.01 (0.97-1.06)	0.35
IL-10	1.02 (0.99-1.04)	0.20	1.01 (0.99-1.04)	0.26	1.01 (0.99-1.04)	0.15
IL-12p40	1.05 (1.01-1.10)	**0.02**	1.05 (1.00-1.10)	**0.04**	1.06 (1.01-1.11)	**0.01**
IL-17A	1.03 (0.99-1.07)	0.08	1.03 (0.99-1.06)	0.15	1.03 (1.00-1.08)	**0.04**
INF_{γ}	1.09 (1.03-1.14)	**0.002**	1.08 (1.02-1.14)	**0.004**	1.10 (1.04-1.17)	**0.001**
Leptina	1.19 (0.98-1.45)	0.09	1.16 (0.95-1.40)	0.12	1.20 (0.97-1.49)	0.08
MIF	**1.14 (1.01-1.29)**	**0.04**	**1.18 (1.02-1.36)**	**0.02**	1.12 (0.98-1.28)	0.07
MCP-1	1.11 (1.03-1.20)	**0.007**	**1.12 (1.03-1.21)**	**0.007**	**1.13 (1.03-1.23)**	**0.005**
TNFα	1.10 (1.03-1.18)	**0.004**	1.09 (1.02-1.16)	**0.008**	1.10 (1.02-1.18)	**0.008**

*Model 1: Adjusted by age + Body mass index; **Model 2: Adjusted by Time since onset of disease + Time with biologic + complementary treatment with MTX; ***Adjusted to 10% increase of cytokine.

Conclusion: Patients with antidrug antibodies to IFX or ADA had higher ESR and DAS28 and a showed a significant association with higher levels of IFNg, MCP-1, MIF and TNFa.

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POS0293 IN VITRO RESPONSE TO DISEASE MODIFYING ANTIRHEUMATIC DRUGS LINK MOLECULAR DRUG TARGET WITH SYNOVIAL TRANSCRIPTIONAL SIGNATURE

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Background: Immune-mediated inflammatory arthritis (IMIA) is a group of diseases characterized by chronic synovitis including rheumatoid arthritis (RA), psoriatic arthritis (PsA), and spondyloarthritis (SpA). Some disease modifying antirheumatic drugs (DMARDs) have demonstrated efficacy in several of these diseases (e.g. TNFα inhibitors) while others have not (e.g. IL-17A inhibitors in RA). Furthermore, within each disease there are patient subgroups experiencing different responses to the same drug, which underlines the need for further elucidation of pathogenic processes to guide personalized in IMIAs.

Objectives: Here we investigated if clinical features and synovial transcriptional signature could predict *in vitro* efficacy of specific DMARDs across different IMIAs.

Methods: Synovial fluid mononuclear cells (SFMCs) from patients with SpA (n=13), RA (n=16), PsA (n=13), juvenile idiopathic arthritis (JIA) (n=7) or undifferentiated arthritis (n=5) were included. SFMCs from each patient were cultured for 48 hours (drugs listed in Table 1). Culture medium and DMSO were used as negative controls. In vitro drug response was assessed by measuring monocyte chemoattractant protein 1 (MCP-1) by ELISA. SFMC baseline gene expression of 270 genes related to inflammation was measured using the NanoString nCounter Human Inflammation V2 Panel. Drug responses (ΔMCP-1) were compared with clinical diagnosis, serostatus in RA patients, HLA-B27 status in SpA patients, DAS28-CRP score, years since diagnosis, failed modes of action and transcriptional signatures.

Table 1.

Drug	Target
Adalimumab	TNFα
Etanercept	TNFα
Tocilizumab	IL-6
Anakinra	IL-1β
Ustekinumab	IL-12/23
Secukinumab	IL-17A
Tofacitinib	JAK1/3
Baricitinib	JAK2/3

Results: DMARDs with a similar molecular target had comparable effects on ΔMCP-1. The TNFα inhibitors adalimumab and etanercept (r=0.86) had similar drug responses, and so had the JAK inhibitors tofacitinib and baricitinib (r=0,71). In contrast, drugs with different modes of action had diverse responses (Figure 1). High HLA-DRA gene expression associated with high responses to TNFα inhibitors (both p<0.05). JAK inhibitors reduced MCP-1 secretion significantly more in SFMCs from seropositive than seronegative RA patients (p<0.05). Drug response was greater in SFMCs from patients with low DAS28-CRP scores (DAS28-CRP <2.5) compared with patients with a high DAS28-CRP score (DAS28-CRP >5.2) for TNFα inhibitors, tocilizumab and JAK inhibitors (all p<0.05). Patients clustered with either an overall high or an overall low response to almost all DMARDs, or with a significant response to only one or a few of the DMARDs. Transcriptional signature of patient SFMCs primarily responding to TNFα inhibitors was different compared with the signature of patient SFMCs primarily responding to JAK inhibitors. Diagnosis, HLA-B27 status, failed modes of action and years since diagnosis did not affect ΔMCP-1 in this in vitro setup.

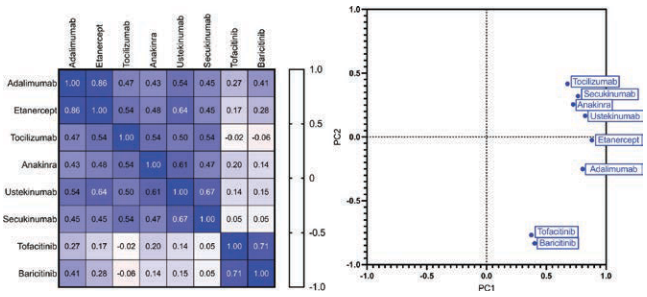

Figure 1. *Association between DMARD molecular target and in vitro response as measured by change in MCP-1 secretion.*

Conclusion: Similarities and differences in mode of action for 8 different DMARDs were captured in drug response as measured by MCP-1 change in SFMC cultures from 54 patients with inflammatory arthritis. We were able to identify interesting differences in gene expression when comparing cells responding to TNF inhibitors to cells responding to JAK inhibitors. Drug responses were only to a minor extent associated with clinical features.

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POS0294 ARTIFICIAL INTELLIGENCE TO CONNECT THE USE OF BIOLOGICS AND SMALL MOLECULES IN RHEUMATOID AND PSORIATIC ARTHRITIS WITH A MULTIDISCIPLINARY EVALUATION: A REAL WORLD EVIDENCE APPROACH THROUGH NATURAL-LANGUAGE PROCESSING

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Background: The management of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) is often relying on a multidisciplinary approach with different specialists evaluating the patient for treatment choices. The ultimate impact of such management on the use of systemic glucocorticoids and more innovative drugs such as biologics and small molecules, however, is unclear. Artificial intelligence tools, particularly natural language processing and machine learning, allow to manage large datasets and investigate associations between variables.
Objectives: To use a natural language processing approach to demonstrate whether a multidisciplinary approach to RA or PsA changes treatment choices.
Methods: We analysed the clinical notes of hospital encounters between 2017 and 2020 of patients with a terminated or ongoing care process at outpatient clinics included in the Humanitas Center for immune-mediated disease. To extract structured information from text data we used regular expressions (RegEx), a technique that allows to define elastic search patterns. RegEx were also used to detect negations to consider only affirmative citation of diseases or prescribed therapy. Care processes were described by binary flags which express the presence of RA or PsA and the prescription of glucocorticoids and biologics /small molecules for each patient. Working with only categorical data, we relied on the chi squared test to detect possible correlations between prescribed treatments and the characteristics of the care process, including whether a multidisciplinary evaluation had occurred.
Results: Our analysis included 1839 patients with RA (77% women, mean+-standard deviation age 58±16 years) and 1652 patients with PsA (46% women, age 57±15 years), accounting for 5517 and 3992 outpatient visits with different specialists over the study period, respectively. Among patients with RA and PsA, 378 (22%) and 371 (25%) were prescribed biologics or small molecules, respectively, while 830 (47%) RA and 431 (29%) PsA cases received a prescription for systemic glucocorticoids during one of the visits and patients seen three of more times by the rheumatologists received significantly more biologics / small molecules. Importantly, 4.5% of patients with RA and 9.4% of patients with PsA were evaluated also by dermatology, gastroenterology, allergy and pulmonary disease specialists and these patients were treated more frequently with glucocorticoids (70% vs.47% for RA, P<0.001; 60% vs. 29% for PsA, P<0.001) as well as with biologics / small molecules (42% vs. 22% for RA, P<0.001; 58% vs. 25% in PsA, P<0.001).
Conclusion: Natural language processing and machine learning were applied to unstructured electronic clinical charts in a large Center dedicated to immune-mediated diseases and allowed to demonstrate that patients with RA or PsA undergoing multiple evaluations are more likely to receive biologics or small molecules.
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POS0295

OCCURRENCE OF SERIOUS INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS CONCURRENTLY TREATED WITH A BIOLOGIC AGENT AND DENOSUMAB: A RETROSPECTIVE STUDY WITH PROPENSITY SCORE

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Background: Denosumab is a monoclonal antibody used in patients with osteoporosis. It inhibits the receptor activator NF-kB ligand (RANKL), an essential cytokine mediator of osteoclastogenesis. Some concerns have been raised about Denosumab safety profile, especially when it is administered concurrently with biologic drugs for rheumatoid arthritis (RA) (1,2). Indeed, RANK and RANKL have a known immunomodulatory effect (2). In a retrospective study, Lau et al. (1) showed that patients concurrently treated with Denosumab and biologic disease modifying anti-rheumatic drugs (bDMARDs) had a higher rate of serious infections compared to patients taking bDMARDs only, but no adjustment was made for any observed imbalances in potential confounders, such as age and disease activity, between the groups.
Objectives: This study aims to evaluate, in a monocentric cohort of RA patients concurrently treated with bDMARDs and Denosumab, the safety of such combination.
Methods: We retrospectively observed RA patients on bDMARDs ± methotrexate and denosumab (DEN group) for comorbid osteoporosis and RA patients treated with bDMARDs±methotrexate (noDEN group) who started treatment in a tertiary care centre from 2015 to 2020. Clinical characteristics were gathered at baseline and at 12-month follow up. We also recorded the occurrence of serious infections between groups (defined as infections requiring hospitalization and/or parenteral antibiotics). We deployed the nearest-neighbour matching algorithm (1:4), based on Propensity Score (PS), in order to adjust for non-randomization. The McNemar's test was used to compare the frequency of serious infection in the two groups.
Results: DEN group consisted of 36 patients were recruited, while the cohort of patients in noDEN group consisted of 547 individuals (Table 1). After PS matching only 58 patients were noDEN group, matched for disease duration, presence/absence of ACPA antibodies, baseline BMI, baseline DAS28 and daily prednisone dosage. In the matched cohort, we found an increase in terms of frequency of serious infections in DEN group, even if not statistically significant (Figure 1). All the infections were completely resolved after hospitalization and/or parenteral antibiotic treatment, without fatal events or irreversible complications. Both groups were not stratified for bDMARDs mechanism of action (MoA). Of note, in the DEN group Rituximab therapy was admnistered in 22% of patients, while in noDEN group in 12% of them.

Table 1. Patients' characteristics at baseline.

	Av. Obs.	bDMARDs Only	Av. Obs.	bDMARDs + Denosumab
Female, n (%)	547	466 (85.2%)	38	34 (89.4%)
Age, y (mean±sd)	547	53.3±13.2	38	63.4±11.1
Disease duration, m (mean±sd)	472	120.2±105.3	38	207.9±126.5
DAS28, n(mean±sd)	532	4.55±1.39	38	2.90±1.44
PCR, mg/dL (mean±sd)	539	1.77±4.51	38	0.81±1.22
HAQ, n (mean±sd)	516	1.28±0.86	38	1.54±0.87
ACPA, n. (%)	541	416 (76.8%)	38	17 (44.7%)

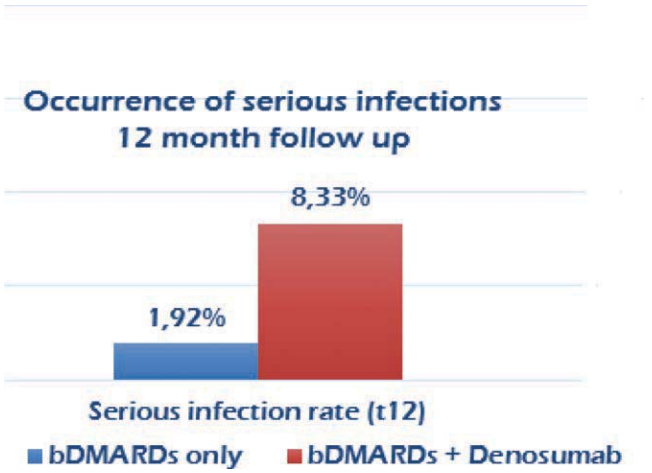

Figure 1. Occurrence of serious infections at 12-months follow-up.

Conclusion: The occurrence of serious infections among RA patients receiving denosumab in combination with bDMARDs ± MTX for RA was not significantly increased compared to those receiving bDMARDs ± MTX alone at 12 months from treatment baseline. Further studies powered for detecting difference between bDMARDs MoA are necessary in order to assess the infection risk of denosumab co-administration.

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[1] Occurrence of Serious Infection in Patients with Rheumatoid Arthritis Treated with Biologics and Denosumab Observed in a Clinical Setting. J Rheumatol. 2018 Feb;45(2):170-176. doi: 10.3899/jrheum.161270. Epub 2017 Nov 15.
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AxSpA: About treatments and outcomes

POS0296

INTEGRATED SAFETY ANALYSIS OF TOFACITINIB IN ANKYLOSING SPONDYLITIS CLINICAL TRIALS

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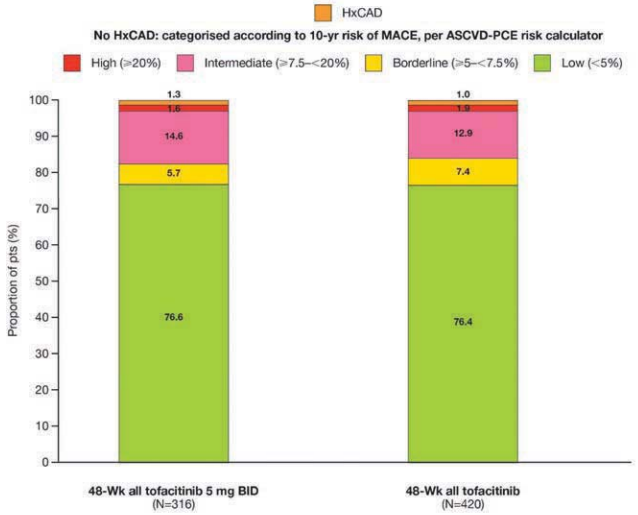
Background: Tofacitinib is an oral JAK inhibitor for the treatment of adults with ankylosing spondylitis (AS).
Objectives: To describe the tofacitinib safety profile from an integrated analysis of randomised controlled trials (RCTs) in patients (pts) with active AS.
Methods: Pooled data from Phase (P)2 (NCT01786668) and P3 (NCT03502616) RCTs in pts with AS were analysed in 3 cohorts (Table 1): the 16-Week (Wk) placebo (PBO)-controlled cohort (pts receiving tofacitinib 5 mg twice daily [BID] or PBO from Wks 0–12 [P2 RCT] or Wks 0–16 [P3 RCT]), the 48-Wk all tofacitinib 5 mg BID cohort and the 48-Wk all tofacitinib cohort (pts receiving ≥1 dose of tofacitinib 2, 5 or 10 mg BID), including pts receiving tofacitinib from Wks 0–12 (P2 RCT) or Wks 0–48 (P3 RCT). Pts receiving tofacitinib 5 mg BID were included in the 16-Wk PBO-controlled cohort and both 48-Wk tofacitinib cohorts. Adverse event (AE)/AEs of special interest incidence rates (IRs; pts with events/100 pt-yrs) were reported based on a 28-day risk period (time of first to last study drug dose +28 days). Baseline (BL) cardiovascular (CV) risk was calculated post hoc by the atherosclerotic CV disease (ASCVD)-pooled cohort equations calculator for pts without history of coronary artery disease (48-Wk tofacitinib cohorts).
Results: At BL, most pts (>76%) in the 48-Wk tofacitinib cohorts had <5% (low) 10-yr ASCVD risk (Figure 1). The most common treatment-emergent AEs were nasopharyngitis/upper respiratory tract infection. Serious AE IRs were higher with tofacitinib 5 mg BID vs PBO in the 16-Wk PBO-controlled cohort, and similar in the 48-Wk tofacitinib cohorts (Table 1). Discontinuation due to AEs was similar between groups in the 16-Wk PBO-controlled cohort and between the 48-Wk tofacitinib cohorts (Table 1). One pt receiving tofacitinib 5 mg BID (included in the 16-Wk PBO-controlled and both 48-Wk tofacitinib cohorts) had a serious infection (SI; meningitis; Table 1). No SIs with PBO. Herpes zoster (HZ; all non-serious) occurred in the 48-Wk all tofacitinib 5 mg BID (5 pts [1.6%]) and 48-Wk all tofacitinib cohorts (7 pts [1.7%]; Table 1) only. Most cases involved a single dermatome, but 1 pt (tofacitinib 10 mg BID) had HZ involving 2 adjacent dermatomes. Across cohorts, there were no deaths or adjudicated opportunistic infections (OIs), OIs excluding tuberculosis (TB), TB, malignancies excluding non-melanoma skin cancer (NMSC), NMSC, major adverse CV events, thromboembolic events, gastrointestinal perforation or interstitial lung disease. Uveitis was reported in 1 (0.5%), 3 (1.6%), 4 (1.3%) and 6 (1.4%) pts in the tofacitinib 5 mg BID, PBO, 48-Wk all tofacitinib 5 mg BID and 48-Wk all tofacitinib groups, respectively; all but 1 pt (tofacitinib 2 mg BID) had history of uveitis. Psoriasis occurred in 1 (0.5%) pt (PBO) with history of psoriasis. There were no AEs of inflammatory bowel disease.

Fig. Proportions of pts with a HxCAD and pts without a HxCAD categorised according to their 10-yr risk of ASCVD, per the ASCVD-PCE risk calculator, in the 48-Wk all tofacitinib 5 mg BID and 48-Wk all tofacitinib cohorts



CAD was defined as having ≥1 of the following: myocardial infarction, coronary heart disease, coronary artery procedure or stable angina pectoris
Pts without a HxCAD were scored according to the ASCVD-PCE calculator, developed by the ACC and the AHA. Scores were calculated based on pts' age, sex, race (White, Black, other), smoking status (yes/no), systolic blood pressure, antihypertensive treatment (yes/no), total cholesterol, high-density lipoprotein cholesterol and diabetes (yes/no). Pts were assigned to one of the following categories based on these risk scores (per ACC/AHA guidelines): high risk (≥20%), intermediate risk (≥7.5–<20%), borderline risk (≥5–<7.5%) and low risk (<5%)
The proportion of pts without a HxCAD, but with missing ASCVD-PCE risk category data, are not shown in the figure: 48-Wk all tofacitinib 5 mg BID, n=1 (0.3%); and 48-Wk all tofacitinib, n=2 (0.5%)
ACC, American College of Cardiology; AHA, American Heart Association; CAD, coronary artery disease; HxCAD, history of CAD; N, number of pts per cohort in the Safety Analysis Set; PCE, pooled cohort equations

Conclusion: Tofacitinib 5 mg BID was well tolerated over 48 Wks in pts with AS, and safety was consistent with the established safety profile of tofacitinib.
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Disclosure of Interests: Atul Deodhar Consultant of: AbbVie, Amgen, Aurinia, Boehringer Ingelheim, Bristol-Myers Squibb, Celegene, Eli Lilly, GlaxoSmithKline, Janssen, MoonLake, Novartis, Pfizer Inc and UCB, Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer Inc and UCB, Servet Akar Speakers bureau: AbbVie, Amgen, Eli Lilly, MSD, Novartis, Pfizer Inc and UCB, Consultant of: AbbVie, Amgen, Eli Lilly, MSD, Novartis, Pfizer Inc and UCB, Grant/research support from: Pfizer Inc, Jeffrey Curtis Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, CorEvitas, LLC (formerly Corrona, LLC), Eli Lilly, Janssen, Myriad, Pfizer Inc, Radius,

Table 1. AEs and AEs of special interest

	16-Wk PBO-controlled cohort		48-Wk tofacitinib cohorts	
	Tofacitinib 5 mg BID N=185	PBO N=187	48-Wk all tofacitinib 5 mg BID N=316	48-Wk all tofacitinib N=420
AE, n (%), IR [95% CI per 100 pt-yrs]				
Serious AE	3 (1.6) 5.28 [0.00, 11.25]	2 (1.1) 3.56 [0.00, 8.49]	8 (2.5) 3.49 [1.51, 6.87]	9 (2.1) 3.45 [1.58, 6.55]
Discontinuation due to AEs	4 (2.2) 7.04 [0.14, 13.94]	4 (2.1) 7.10 [0.14, 14.05]	11 (3.5) 4.77 [2.38, 8.54]	12 (2.9) 4.58 [2.37, 8.00]
SI	1 (0.5) 1.77 [0.00, 5.89]	0 0.00 [0.00, 3.31]	1 (0.3) 0.43 [0.01, 2.41]	1 (0.2) 0.38 [0.01, 2.12]
HZ	0 0.00 [0.00, 3.28]	0 0.00 [0.00, 3.31]	5 (1.6) 2.18 [0.71, 5.08]	7 (1.7) 2.68 [1.08, 5.53]
All-cause mortality	0 0.00 [0.00, 3.28]	0 0.00 [0.00, 3.31]	0 0.00 [0.00, 1.59]	0 0.00 [0.00, 1.40]
Malignancies excluding NMSC	0 0.00 [0.00, 3.28]	0 0.00 [0.00, 3.31]	0 0.00 [0.00, 1.59]	0 0.00 [0.00, 1.40]
Major adverse CV event	0 0.00 [0.00, 3.28]	0 0.00 [0.00, 3.31]	0 0.00 [0.00, 1.59]	0 0.00 [0.00, 1.40]
Venous thromboembolism	0 0.00 [0.00, 3.28]	0 0.00 [0.00, 3.31]	0 0.00 [0.00, 1.59]	0 0.00 [0.00, 1.40]

CI, confidence interval; n, number of pts with event within 28-day risk period

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POS0297

EFFECTIVENESS AND SAFETY OF SECUKINUMAB IN AXIAL SPONDYLOARTHRITIS: A 24-MONTH PROSPECTIVE, MULTICENTER REAL-LIFE STUDY

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Background: Axial Spondyloarthritis (axSpA) can be distinguished in radiographic axSpA (r-axSpA) and non-radiographic (nr-axSpA). Secukinumab (SEC) is a novel treatment for axSpA, but data from real-life are still missing.

Objectives: To evaluate, in a multicentric-Italian-cohort of axSpA patients on SEC followed for 24-months: a)the long-term effectiveness and safety of SEC; b)the drug-retention-rate and low-disease-activity (LDA) measured as BASDAI<4/ASDAS<2.1 and very-low-disease-activity (VLDA) measured as BASDAI<2/ASDAS<1.3; c)any differences in outcomes according to: line of biological treatment (naïve/non-naïve), gender (male/female), subtype of axSpA (r-axSpA/nr-axSpA).

Methods: Consecutive patients with active axSpA (diagnosis according Assessment of SpondyloArthritis International Society ASAS criteria), who started SEC treatment, were evaluated prospectively. Data on disease characteristics, previous/ongoing treatments and imaging were collected. Disease-activity/functional/clinical scores and biochemical values were recorded at baseline (T0), at 6 (T6), 12 (T12), and 24 (T24) months. Effectiveness was evaluated over-time with descriptive statistics; multivariate Cox and logistic regression models were used to evaluate predictors of drug-discontinuation and LDA at T6. Infections, adverse events were recorded.

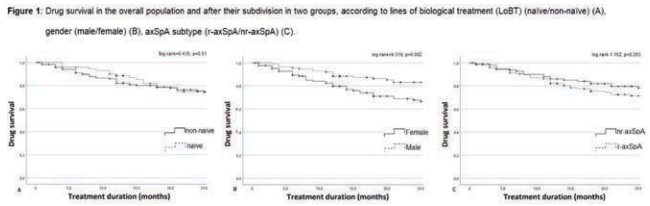
Results: 249 patients (47.8% male; median age 51 years) were enrolled; 40.9% had HLA-B27; 53.8% had r-axSpA and 46.2% nr-axSpA. SEC was prescribed in 28.9% naïve and in 71.1% non-naïve patients. SEC effectiveness was shown as an improvement in several outcomes, such as ASDAS [T0=3.5(2.9-4.4) vs. T24=1.9(1.2-2.4);p=0.02] and BASDAI [T0=6.5(5.0-7.5) vs. T24=2.8(1.8-4.0);p=0.03]. After 24-months of treatment, 90.7% of naïve and 75.3% of non-naïve patients achieved LDA (BASDAI<4). At T24 naïve-patients showed better physical-functioning and lower disease-activity than non-naïve (Table 1). Similarly, at T24 we observed better physical functioning and lower inflammatory activity in males vs. females and in nr-axSpA vs. r-axSpA subjects. Retention-rate at T24 was 75% in the whole population, with some difference depending on gender (log-rank 9.319; p=0.002) (Figure 1). Treatment was discontinued in 61 patients (24.5%), mainly due to primary/secondary loss of effectiveness events (20 and 24 subjects, respectively), and only 17 patients (6.8%) due to adverse events (7 for reactions at the injection site or skin manifestations, 1 for gastro-intestinal complications, 1 for relapsing uveitis, 1 for hypertransaminasemia, 4 for severe recurrent infections, 3 due to the onset of new cancer).

Table 1. Clinical, functional, disease activity and serological parameters of *naïve* (n=72) and *non-naïve* (n=177) axSpA patients during the 24-month follow-up

	T0	T6	T12	T24
BASMI [0-10], median (IQR)				
naïve	2.0 (1.0-4.0)	2.0 (0.0-3.3)	1.0 (0.0-2.8)	1.0 (0.0-2.0)
non-naïve	4.0 (1.0-7.0)	4.0 (1.0-7.0)	2.0 (1.0-4.0)	2.0 (1.0-3.0)
p	*p=0.03*	*p=0.04*	*ns*	*ns*
HAQ-S [0-8], median (IQR)				
naïve	0.8 (0.5-1.3)	0.5 (0.0-1.0)	0.3 (0.0-1.0)	0.1 (0.0-0.5)
non-naïve	1.1 (0.8-1.5)	1.0 (0.4-1.3)	0.6 (0.4-0.9)	0.7 (0.1-0.9)
p	*p=0.04*	*p=0.04*	*p=0.04*	*p=0.04*
ASDAS [0-6], median (IQR)				
naïve	3.3 (2.7-3.9)	2.1 (1.6-2.7)	2.0 (1.2-2.8)	1.3 (1.0-2.2)
non-naïve	3.7 (2.9-4.7)	2.9 (2.0-3.7)	2.1 (1.9-3.1)	2.3 (1.6-2.3)
p	*ns*	*ns*	*ns*	*p=0.04*
ESR [0-25](mm/h), median (IQR)				
naïve	14.0 (6.0-27.0)	10.0 (4.0-19.5)	8.0 (3.1-12.8)	5.0 (2.0-15.0)
non-naïve	18.5 (10.0-31.3)	15.0 (8.0-25.0)	12.0 (6.0-20.0)	12.0 (6.0-19.0)
p	*p=0.04*	*p=0.04*	*p=0.04*	*p=0.04*

Legend: BASMI: Bath Ankylosing Spondylitis Metrology Index; HAQ: Health Assessment Questionnaire modified for spondyloarthritis; ASDAS: Ankylosing Spondylitis Disease Activity Score; ESR: erythrocyte sedimentation rate

Conclusion: In a real-life clinical-setting, SEC proved to be safe and effective in axSpA, mainly in naïve-patients, with a notable drug-retention-rate. No differences were observed between r-axSpA and nr-axSpA.



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POS0298

OCCURRENCE AND PREDICTION OF FLARE AFTER TAPERING OF TNF INHIBITORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Patients with axial spondyloarthritis (axSpA) in clinical remission tapered Tumor Necrosis Factor inhibitor (TNFi) therapy according to a clinical guideline and had 2 years´ follow-up [1].

Objectives: We aimed to investigate flare frequency, dose at which flare occurred, type of flare (clinical/ Bath ankylosing spondylitis disease activity index (BASDAI)/magnetic resonance imaging (MRI)) and predictors of flare.

Methods: Patients in clinical remission (BASDAI<40, physician global score<40 and without disease activity the previous year) tapered TNFi to 2/3 standard dose at baseline, 1/2 at week (w)16, 1/3 at w32 and 0 (discontinuation) at w48. Patients who flared were increased to previous dose. Predictors of flare at each dose step were investigated by regression analyses.

Results: Of 108 patients, 106 (99%) flared before year 2 (flare occurring mean (SD) 99(44.3) days after last tapering). Twenty-nine patients (27%) flared at 2/3 standard dose, 21 (20%) at 1/2 dose, 29 (27%) at 1/3 dose and 27 (25%) after discontinuation. One-hundred-and-five (99%) had clinical flare, 25 (24%) BASDAI flare and 23 (29% of patients with MRI at flare) MRI flare; and forty-one patients (41%) fulfilled the ASAS-definition of clinically important worsening (≥0.9 increase since baseline) (Figure 1). Most common flare symptoms were back/buttock pain (n=93 (89%)) and pain in peripheral joints/entheseal regions (n=48 (46%)). Higher baseline physician global score was an independent predictor of flare after tapering to 2/3 (Odds ratio=1.19 (95% Confidence Interval=1.05-1.41); p=0.011) (Table 1). Changes in clinical and/or imaging variables in the 16 weeks prior to tapering did not predict flare (data not shown).

Conclusion: Almost all (99%) axSpA patients in clinical remission flared during tapering to discontinuation, but above half not before receiving 1/3 dose or less. Higher physician global score was the only independent predictor of flare.

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Figure 1. Venn diagram showing flare types (n=106)

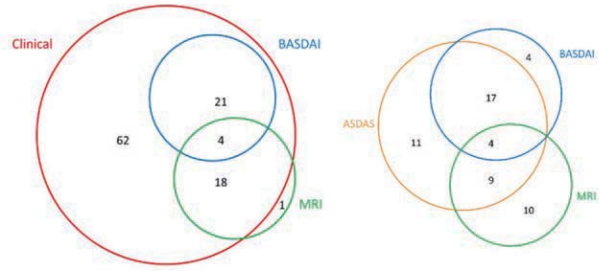

Figure 1. The left schematic shows the overlap between the 3 flare types (i.e BASDAI, clinical and MRI flare). The right schematic shows overlap between BASDAI flare, MRI flare and clinically important worsening according to ASDAS. BASDAI flare: change in BASDAI ≥20 since inclusion and an absolute BASDAI ≥40. Clinical flare: signs of inflammatory back pain, development of musculoskeletal manifestations such as peripheral arthritis, enthesitis or dactylitis and/or development of extra-articular manifestations as anterior uveitis, psoriasis or inflammatory bowel disease, and/or an increase in ASDAS-CRP ≥0.9. MRI flare: ≥2 new or worsened inflammatory lesions in the sacroiliac joints or spine according to a predefined MRI-flare definition.
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Index; MRI, magnetic resonance imaging.

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Table 1. Prediction of flare within 16 weeks after tapering to 2/3 dose (n=74)

Values are from timepoint of tapering from full dose to 2/3 dose	Univariate analyses			Final multivariable analyses*		
	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Male gender	0.96	(0.25 - 4.14)	0.955			
Age	1.00	(0.96 - 1.04)	0.880			
Time since diagnosis	1.00	(0.95 - 1.06)	0.863			
Current smoker	0.70	(0.20 - 2.20)	0.543			
HLA-B27 positive	0.66	(0.18 - 2.41)	0.515			
Previous bDMARDs	1.28	(0.66 - 2.49)	0.458			
Patient pain VAS	1.02	(0.98 - 1.06)	0.310			
Physician global VAS	1.19	(1.04 - 1.41)	**0.012**	1.19	(1.04 - 1.41)	0.011
ASDAS	1.66	(0.70 - 4.10)	0.251			
mNYc positive	0.78	(0.29 - 2.09)	0.615			
SPARCC SIJ Inflammation Index	1.01	(0.90 - 1.12)	0.861			
CANDEN Total inflammation	0.95	(0.65 - 1.25)	0.702			
SPARCC SSS Erosion	1.11	(0.91 - 1.37)	0.293			
CANDEN Fat	0.99	(0.96 - 1.02)	0.705			
AUC (95% CI)				0.66 (0.54 - 0.78)		

Predictors were selected by applying backward selection in stacked data. p-values by likelihood ratio tests. Bold indicates p-values<0.1 in univariate analyses. Predictors were selected by backward selection in stacked imputed datasets after applying a fixed weight to all observations, accounting for the average fraction of missing data across all variables under consideration. *Results were derived in non-imputed data (no missing values in selected predictors). CIs given as profile likelihood CIs. AUC estimated based on internal validation by bootstrapping with 1000 samples.ASDAS, Ankylosing Spondylitis Disease Activity Score; bDMARDs, biological disease modifying anti-rheumatic drugs; AUC, Area Under the receiver operating characteristic Curve; CANDEN, Canada-Denmark MRI scoring system of the spine in patients with axial spondyloarthritis; CI, confidence interval; mNYc, modified New York criteria; SIJ, sacroiliac joint; SPARCC SIJ inflammation, Spondyloarthritis Research Consortium of Canada Sacroiliac joint inflammation; SPARCC SSS, Spondyloarthritis Research Consortium of Canada Sacroiliac joint Structural Score; VAS, visual analogue scale.

Bioepis, and Janssen Biologics BV, Grant/research support from: MSD, Biogen, Pfizer, Bristol-Myers Squibb, AbbVie, Roche and Novartis, Anne Duer: None declared, Mikael Boesen Speakers bureau: Image Analysis Group, Esaote, AbbVie, Celgene, Eli-Lilly, Janssen, Novartis, Pfizer, UCB, Novo, GSK, Takeda, Geurbet, Biogen, Radiobotics and Chondrometrics, Consultant of: Image Analysis Group, Esaote, AbbVie, Celgene, Eli-Lilly, Janssen, Novartis, Pfizer, UCB, Novo, GSK, Takeda, Geurbet, Biogen, Radiobotics and Chondrometrics, Grant/research support from: Image Analysis Group, Esaote, AbbVie, Celgene, Eli-Lilly, Janssen, Novartis, Pfizer, UCB, Novo, GSK, Takeda, Geurbet, Biogen, Radiobotics and Chondrometrics, Kasper K Gosvig: None declared, Jakob Møllenbach Møller: None declared, Mads Bakkegaard: None declared, Cecilie Heegaard Brahe: None declared, Niels Steen Krogh: None declared, Bente Jensen: None declared, Ole Madsen: None declared, Jan Christensen: None declared, Annette Hansen Speakers bureau: speaker fees from Elly Lilly, Jesper Noerregaard: None declared, Henrik Røgind: None declared, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Consultant of: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB

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POS0299

EFFECT OF SECUKINUMAB ON RADIOGRAPHIC PROGRESSION AND INFLAMMATION IN SACROILIAC JOINTS AND SPINE IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 2-YEAR IMAGING OUTCOMES FROM A PHASE III RANDOMISED TRIAL

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Background: Axial spondyloarthritis (axSpA) is characterised by inflammation of the sacroiliac joints (SIJ) and the spine. Secukinumab (SEC) treatment was clinically efficacious and reduced SIJ bone marrow oedema as detected by magnetic resonance imaging (MRI) in patients (pts) with non-radiographic (nr)-axSpA through 52 weeks in the PREVENT (NCT02696031) study.[1]

Objectives: To report radiographic progression and the course of inflammation as assessed by X-ray and MRI of SIJ and spine over 2 years in the PREVENT study.

Methods: Study design and key endpoints have been reported earlier.[1] In total, 555 pts were randomised (1:1:1) to receive SEC 150 mg, with (LD) or without loading (NL) doses, or placebo (PBO). Switch to open-label (OL) SEC or standard of care (SoC) was permitted after Week (Wk) 20. All pts (except those who switched to SoC) received OL SEC from Wk 52. Radiographs of the spine and SIJ were collected at baseline (BL) and Wk 104; MR images of the spine and SIJ were collected at BL, Wk 16, 52, and 104. Spinal radiographs were scored using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) and SIJ radiographs according to modified New York criteria (mNYC). Pts whose screening SI joint radiographs fulfilled mNY criteria during the eligibility reading session were excluded from the study. Spinal MR images were assessed for signs of inflammation with the Berlin score. SIJ bone marrow oedema was assessed according to the Berlin Active Inflammatory Lesions Scoring. All images were evaluated in blinded fashion independently by 2 central readers. All data are reported from the Wk 104 reading session and are presented as observed.

Results: The vast majority (98%) of pts treated with SEC 150 mg (pooled LD and NL) showed no structural progression, defined as change in total mSASSS score ≤ smallest detectable change (SDC) of 0.76 (80% agreement level) over 2 years. At BL, 62 pts (43 in SEC, 19 in PBO) presented with ≥1 syndesmophyte (≥1 vertebral unit scored by ≥1 reader). Among these pts, 9 in SEC (20.9%) and 7 in PBO (36.8%) groups had developed ≥1 new syndesmophyte by Wk 104. Among 237 SEC and 117 PBO pts without syndesmophytes at BL, only 4 pts on SEC (1.7%) and 4 pts on PBO (3.4%) developed ≥1 new syndesmophyte by Wk 104. SIJ radiographs showed that 88% of pts on SEC and 86% on PBO had no progression in SIJ (defined as change ≤ SDC (0.46) in total mNYC score) by Wk 104. No patient had an increase in total mNYC score of 2 or more. When screening radiographs of eligible pts were scored alongside post-BL images in the final reading campaign, approximately 25% of pts (68/277 and 34/139 pts in the SEC and PBO groups, respectively) were evaluated as mNY-positive at screening (pts were considered mNY-positive if ≥1 reader evaluated them as mNY-positive). Of these, 11/68 pts in the SEC (16.2%) and 5/34 in the PBO (14.7%) groups were evaluated as mNY-negative at Wk 104. In the SEC and PBO groups, 202 (96.7%) and 102 (97.1%) pts who were mNY-negative at screening stayed negative through Wk 104, respectively. Only 7 pts in the SEC (3.3%) and 3 in the PBO (2.9%) groups who were mNY-negative at BL were scored as mNY-positive at Wk 104. In both groups, fewer pts progressed from mNY-negative to mNY-positive than had a change in the opposite direction (from positive to negative), resulting in an overall negative net progression. Spinal inflammation on MRI (Berlin score) was low at BL with a mean of 0.82 in SEC and 1.07 in PBO groups with no meaningful change up to Wk 104 (mean of 0.56, SEC). SEC reduced SIJ bone marrow oedema score versus PBO at Wk 16 and Wk 52 with sustained reduction through Wk 104 in the overall patient population, with greater reduction in pts with BL score >2 (Figure 1).

Conclusion: Most pts initially randomised to SEC or PBO showed no radiographic progression through 2 years. There was some discrepancy between SIJ eligibility and efficacy reads. SEC reduced SIJ inflammation (bone marrow oedema) on MRI in pts with active nr-axSpA.

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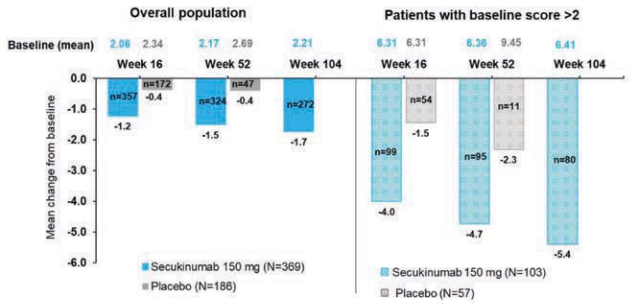
Figure. Mean change in SIJ bone marrow oedema score by MRI in the overall population and in patients with baseline score >2 through Week 104



Data presented as observed. Secukinumab (pooled) included patients who continued on secukinumab to Week 104. Placebo included only patients randomised to placebo who remained on placebo to Week 52. At each time point, only patients with a value at both baseline and that time point are included. MRI, magnetic resonance imaging; N, total number of randomised patients; n, number of evaluable patients; SIJ, sacroiliac joint

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POS0300

FACTORS ASSOCIATED WITH SECUKINUMAB (SEC) RETENTION IN AXIAL SPONDYLOARTHRITIS (AXSPA): RESULTS OF THE FRENCH RETROSPECTIVE STUDY FORSYA

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Background: While data on real-life SEC retention rate in patients (pts) with axSpA is accumulating, there are no data on predictive factors for this retention. Presence of objective sign of inflammation (OSI) are known to be predictive of efficacy of anti-TNFs and their retention in axSpA.
Objectives: To assess whether OSI were predictive of SEC retention at 1 year in axSpA.
Methods: French retrospective study collecting between October 2019 and September 2020 data from axSpA pts a) having initiated and received at least one dose of SEC between August 11th 2016 and August 31st 2018, b)with at least a one year follow-up period. Retention of SEC at 1 year was estimated by the Kaplan Meier (KM) method. OSI were defined by at least one of the following: CRP> N, MRI-inflammation at the sacroiliac or spine level. Preselected factors of SEC retention at 1 year (≥1 OSI, age, sex, BMI, smoking, HLA B27, non-radiographic vs radiographic axSpA, past or present uveitis / Inflammatory Bowel Disease (IBD) / psoriasis / arthritis or synovitis, diagnostic delay, disease duration, SEC line of biologic therapy, SEC maintenance dose, concomitant csDMARD / oral corticosteroids / proton pomp inhibitor, history of depression / fibromyalgia) were analyzed by multivariate cox model regression. Only variables with <20% missing data were included in the model after imputation and stepwise selection (significance level for entering variables = 20%; for removing variables = 10%). OSI was forced into the model whatever its significance level or rate of missing data.
Results: In total, 906 pts from 47 centers (male: 42.2%, mean age: 46.2 ± 11.7 years, mean disease duration: 9,3 ± 9.1 years), were included in the analysis. At initiation of SEC, 86.3% of pts had ≥ 1 OSI and respectively 8.0%, 14.9% and 77.1% were in 1st, 2nd and ≥ 3rd line (L) of biologic/targeted synthetic DMARD. The 1 year KM survival rate for SEC was 59% [95%CI:55%-62%] overall, 58% [54%-62%] and 63% [53%-73%] for pts with or without OSI, and was numerically greater in 1st L vs 2nd and ≥3rd L (70% [59%-81%], 62% [54%-70%], 57% [53%-61%] respectively). In multivariate analysis absence of OSI, lack of prior exposure to anti-TNF inhibitors, absence of IBD, and absence of history of depression were associated with a better SEC retention at 1 year (Table 1).

Table 1. Predictive factors of SEC 1 year retention identified by multivariate cox regression analysis (multiple imputation + stepwise selection)

Predictive factors (* reference)		Still on SEC at 1 Year (%)#	HR [95% CI]	p vs ref	p type III
≥ 1 objective sign of inflammation	No (N=165)*	65.3%			
	yes (N=711)	58.8%	1.44 [1.08; 1.93]	0.014	
SEC treatment line	1st L (N=68)*	72.2%			0.084
	2nd L (N=132)	62.7%	1.53 [0.91; 2.57]	0.107	
	≥ 3rd L (N=676)	57.6%	1.67 [1.06; 2.62]	0.028	
Past or present history of IBD	No (N=854)*	59.8%			
	Yes (N=22)	40.9%	1.76 [1.01; 3.07]	0.047	
History of depression or anti-depressive concomitant treatment	No (N=716)*	60.8%			
	Yes (N=160)	54.5%	1.25 [0.97; 1.60]	0.090	

without imputation for missing dataInterpretation HR > 1: the hazard of discontinuation at 1 year is X times higher vs reference

Conclusion: The overall retention of SEC at 1 year in daily practice at the time of its launch in France was 59% for axSpA patients and OSI, prior exposure to TNF inhibitors, IBD and history of depression were identified as predictive factors of SEC retention.
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POS0301

STRUCTURAL OUTCOMES IN THE SACROILIAC JOINT AFTER IXEKIZUMAB TREATMENT FOR 16 WEEKS IN PATIENTS WITH ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS STRATIFIED BY GENDER, HLA-B27, AND BASELINE MRI INFLAMMATION

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Background: Ixekizumab (IXE) has demonstrated clinical efficacy in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) together with significant repair of structural lesions in the sacroiliac joint (SIJ) on MRI. There is, however, a paucity of data as to which patients may be most responsive.

Objectives: We aimed to evaluate whether patients' gender, HLA-B27 status, and presence of MRI inflammation impacted the effect of treatment with IXE versus placebo (PBO) on MRI structural lesions in the SIJ in patients with nr-axSpA.

Methods: Patients with active nr-axSpA, biologic-naïve (COAST-X, NCT02757352) were randomized 1:1:1 to ixekizumab 80 mg every 4 (Q4W) or 2 weeks (Q2W) or PBO. Structural lesions on SIJ MRI were assessed by the Spondyloarthritis Research Consortium of Canada (SPARCC) MRI SIJ structural score (SSS). Treatment comparisons used analysis of covariance based on observed cases. SPARCC SSS subgroup analyses were performed according to baseline gender, HLA-B27 status, and SPARCC MRI SIJ bone marrow oedema (BME) <4 and ≥4 subgroups, which reflects a definite MRI for inflammation in the SIJ typical of axSpA.

Results: Of 303 randomized patients, 266 patients (Q4W: n=85, Q2W: n=91, PBO: n=90) had an MRI scan at baseline and week 16. At baseline, SPARCC scores were consistently higher in males, and mostly higher in HLA-B27 and BME≥4 positive subgroups. Significant differences between patients treated with IXE versus PBO were observed for male patients, HLA-B27 positives, and those with baseline SPARCC BME ≥4. Numerically similar changes were observed in female patients, patients with negative HLA-B27, and patients with SPARCC BME<4, though not statistically significant.

Conclusion: Effects of IXE on structural repair are most evident in males, HLA-B27 positives, and patients with definite MRI inflammation at baseline.

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POS0302

TREATING SPONDYLOARTHRITIS EARLY: DOES IT MATTER? RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

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Table 1. MRI SIJ Structural Lesion Outcomes.

		PBO		IXE Q4W		IXE Q2W	
Lesion	**Analysis**	**Male (n=39)**	**Female (n=51)**	**Male (n=44)**	**Female (n=41)**	**Male (n=43)**	**Female (n=48)**
Erosion	BL mean	5·167	1·980	3·545	2·817	3·523	2·594
	LS mean CFB (SE)	0·51 (0·20)	-0·11 (0·17)	-0·63 (0·18)	-0·11 (0·19)	-0·51 (0·18)	-0·32 (0·17)
	P value vs PBO	NA	NA	p<0·001	p>0·99	p<0·001	p=0·37
Fat	BL mean	2·051	0·912	2·091	1·293	1·465	0·677
	LS mean CFB (SE)	-0·02 (0·09)	-0·03 (0·08)	0·29 (0·08)	0·03 (0·08)	0·21 (0·08)	0·04 (0·08)
	P value vs PBO	NA	NA	p=0·01	p=0·65	p=0·062	p=0·51
Backfill	BL mean	1·154	0·167	0·663	0·415	0·791	0·323
	LS mean CFB (SE)	-0·20 (0·13)	0·01 (0·11)	0·39 (0·12)	0·01 (0·12)	0·34 (0·12)	0·14 (0·11)
	P value vs PBO	NA	NA	p<0·001	p>0·99	p=0·002	p=0·38
Lesion	**Analysis**	**HLA-B27+ (n=64)**	**HLA-B27- (n=25)**	**HLA-B27+ (n=61)**	**HLA-B27- (n=23)**	**HLA-B27+ (n=65)**	**HLA-B27- (n=26)**
Erosion	BL mean	3·820	2·100	3·467	2·543	3·515	1·827
	LS mean CFB (SE)	0·27 (0·15)	-0·10 (0·24)	-0·49 (0·15)	-0·01 (0·25)	-0·50 (0·15)	-0·17 (0·24)
	P value vs PBO	NA	NA	p<0·001	p=0·79	p<0·001	p=0·84
Fat	BL mean	1·578	1·020	1·328	2·783	1·285	0·462
	LS mean CFB (SE)	-0·06 (0·06)	-0·06 (0·10)	0·22 (0·06)	0·01 (0·10)	0·13 (0·06)	0·10 (0·10)
	P value vs PBO	NA	NA	p=0·002	p=0·65	p=0·027	p=0·25
Backfill	BL mean	0·742	0·240	0·542	0·565	0·762	0
	LS mean CFB (SE)	-0·12 (0·10)	0·01 (0·16)	0·28 (0·10)	0 (0·17)	0·27 (0·10)	0·16 (0·16)
	P value vs PBO	NA	NA	p=0·005	p=0·96	p=0·005	p=0·52
Lesion	**Analysis**	**BME ≥4 (n=40)**	**BME <4 (n=50)**	**BME ≥4 (n=27)**	**BME <4 (n=58)**	**BME ≥4 (n=38)**	**BME <4 (n=53)**
Erosion	BL mean	4·863	2·160	5·352	2·190	5·276	1·425
	LS mean CFB (SE)	0·42 (0·19)	-0·06 (0·17)	-0·70 (0·23)	-0·23 (0·16)	-0·71 (0·20)	-0·19 (0·17)
	P value vs PBO	NA	NA	p<0·001	p=0·47	p<0·001	p=0·57
Fat	BL mean	0·775	1·910	1·926	1·603	1·671	0·604
	LS mean CFB (SE)	-0·02 (0·08)	-0·02 (0·07)	0·54 (0·10)	-0·01 (0·07)	0·28 (0·08)	0·01 (0·07)
	P value vs PBO	NA	NA	p<0·001	p=0·90	p=0·013	p=0·74
Backfill	BL mean	0·750	0·470	1·019	0·328	0·763	0·387
	LS mean CFB (SE)	-0·21 (0·12)	0·01 (0·11)	0·41 (0·15)	0·11 (0·10)	0·49 (0·13)	0·05 (0·11)
	P value vs PBO	NA	NA	p=0·002	p=0·52	p<0·001	p=0·80

CFB=change from BL. BL=baseline, LS=least squares.

Background: So far, no consensus has been reached on a definition of early SpA. The ASAS-SPEAR (SPondyloarthritis EARly definition) project aims to develop a consensual definition. Therefore, it is important to know whether treatment earlier in the disease course compared to treatment of established disease leads to better outcomes in axSpA.

Objectives: To summarize the evidence on the relationship between symptom duration or the presence of radiographic damage and clinical response in patients with axSpA treated with NSAIDs, bDMARDs or tsDMARDs.

Methods: A SLR was conducted using Medline, EMBASE and the Cochrane Library (April 28, 2021), supplemented by hand-searches in the FDA website. Randomized controlled trials (RCTs) and cohort studies in patients with axSpA addressing the impact of symptom duration or disease duration and presence of radiographic damage on treatment response (to NSAIDs, b/tsDMARDs) were included. Based on a cut-off of symptom/disease duration or the absence/presence of radiographic damage, groups of 'early' and 'established' disease were compared. Treatment outcomes were measures of disease activity, function or quality of life. Two reviewers independently identified eligible studies and extracted the data, including the risk of bias (RoB) assessment. For categorical outcomes we calculated relative risk (RR), relative risk ratio (RRR) and number needed to treat (NNT), and differences in differences (DID) for continuous outcomes.

Results: From the 8769 articles retrieved, 23 were included and 3 added by hand-search, most of them with low RoB. Nineteen studies (9 RCTs) compared groups based on symptom (n=6)/disease duration (n=13) and 7 studies (4 RCTs) based comparisons on absence/presence of radiographic damage in posthoc analyses. When early axSpA was defined by symptom duration in RCTs (n=4), in patients with nr-axSpA, early treatment was associated with higher RR and RRR and lower NNT for ASAS40 in two studies (Table 1); a third study showed that patients achieving ASDAS-ID and ASAS-PR had shorter symptom duration than those not achieving this. Lastly, in one study including patients with axSpA patients, no difference in treatment response was observed based on symptom duration. In most of the cohort studies using a definition based on symptom/disease duration (n=10), no association was found between symptom/disease duration and treatment response (n=8). Only in one cohort study, disease duration was a significant predictor of quality of life, and in another cohort study, it was a predictor of functional improvement.

Table 1. Assessment of treatment response in RCTs based on symptom duration

Study	Population	Early vs established (years)	RR (early vs established)	RRR (95%IC)	NNTs (early vs established)
ASAS20					
Landewé 2014	axSpA	<5 vs ≥5	1.5 vs 1.5	0.96 (0.53-1.73)	5.5 vs 4.8
ASAS40					
Sieper 2012	nr-axSpA	<5 vs ≥5	8.2 vs 1.6	5.24 (1.12-24.41)	2.4 vs 9.1
Kay 2019	nr-axSpA	<5 vs ≥5	5.0 vs 3.3	1.52 (0.60-3.87)	2.1 vs 3.9
			3.6 vs 3.5	1.01 (0.46-2.20)	2.1 vs 2.9
ASDAS-MI					
Kay 2019	nr-axSpA	<5 vs ≥5	5.1 vs 6.5	0.78 (0.19-3.16)	2.7 vs 4.9
			7.1 vs 6.4	1.11 (0.34-3.66)	2.1 vs 3.0
Study	**Population**	**Symptom duration**			***p* value**
		Responders	**Non responders**		
ASDAS-ID					
Sieper 2019	nr-axSpA	6.1±6.2	8.3±8.1		<0.001
ASAS-PR					
Sieper 2019	nr-axSpA	5.3±5.7	8.0±7.8		<0.001
Cell colours	In favor of early disease	In favor of established disease	Non significant		

When early axSpA was defined based on disease duration or the presence of radiographic damage, there was no significant difference in response to treatment between early and established axSpA.

Conclusion: Studies addressing treatment response based on symptom duration or radiographic damage in axSpA are scarce. When defining early axSpA based on symptom duration, in nr-axSpA, treatment with bDMARDs may lead to better outcomes compared to established axSpA whereas in axSpA there is no difference in response to treatment between early and established disease. When early axSpA is defined based on disease duration or radiographic damage, no differences in response to treatment are found between early and established disease.

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POS0303 TREATMENT DECISIONS IN AXIAL SPONDYLOARTHRITIS ARE MORE THAN TREAT TO TARGET

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Background: Several guidelines advise treating axial spondyloarthritis (axSpA) patients according to the 'treat-to-target principles' (T2T)1 although a clear target has not yet been defined. Disease activity measures, which are often used as targets, do not always reflect pure inflammatory disease activity. Currently is it not known if T2T is applied in axSpA clinical practice and what factors influence treatment decisions.

Objectives: To assess residual disease activity according to the physician's opinion, patient's opinion and disease activity measures and the subsequent treatment decisions made in axSpA patients.

Methods: This cross-sectional multicentre study included 249 patients with a clinical diagnosis of axSpA ≥ 6 months. Remission and low disease activity according to Bath Ankylosing Spondylitis Disease Activity Index (BASDAI <1.9 and <3.5 respectively), physician's, and patient's opinion was assessed. Questionnaires including patient reported outcomes (PROs) such as the Patient Global Assessment (PGA) of disease activity, Bath Ankylosing Spondylitis Functional Index (BASFI), ASAS-Health Index (ASAS-HI), central sensitization inventory (CSI), Brief Illness Perception Questionnaire (B-IPQ), and satisfaction with treatment; or questions regarding motivations for treatment decisions were filled in by patients and physicians respectively.

Results: In this cohort, 115/249 patients were in remission according to the physician. Of these 115 patients, 67% (n=80) indeed perceived their disease as being inactive, but only 37% (n=43) reached remission according to the BASDAI. This shows a significant level of discrepancy in comparison with the physician's opinion. Of note, 30% (n=35) even reported a BASDAI >3.5. In 93% (n=107) treatment-intensity remained unchanged and in 6% (n=5) treatment was tapered. Physicians motivated that treatment was left unchanged in the majority of these patients because of remission (n=55, 48%), low disease activity (n=28, 24%), or complaints not related to axSpA (n=13, 12%). The latter two motives were most frequently mentioned for the patients with a BASDAI >3.5 (respectively n=13, 39% and n=9, 27%). Residual disease activity was present in 134/249 patients according to the physician's opinion and 67% (n=90) of these patients also perceived their disease as active. In 89% (n=119) BASDAI score was >1.9 and in 62% (n=83) >3.5. In 61% (n=51) of these patients with residual disease and a BASDAI >3.5, treatment remained unchanged, as well as in 84% (n=43) of the patients with a BASDAI between 1.9 and 3.5. Physician's most frequently mentioned motives for not changing treatment in the residual disease activity group were: low disease activity achieved (n=29, 25%), the need to await the effect of the current treatment (n= 23, 20%), or complaints that were not related to axSpA (n=9, 8%). The second (n=20, 39%) motive was most frequently mentioned for unchanged treatment in the BASAI >3.5 group and additionally, physicians mentioned that these patients had a preference to continue their current treatment despite high disease activity (n=5, 10%). Analyses of PROs showed significantly higher scores for PGA of disease activity, several subdomains of the B-IPQ, general fatigue and morning stiffness in patients with remission according to the physician despite a

BASDAI >3.5 compared to patients with residual disease according to the physician with a BASDAI <1.9.

Conclusion: This study shows that physicians in daily clinical practice do not always adjust treatment according to the T2T-principles in patients with residual disease activity when measured by BASDAI scores, either because low disease activity is achieved, because they classify the patient as being in remission, as having low disease activity, or because there was a need to await the efficacy of the current treatment. Further studies are needed to investigate if treatment choices made in clinical practice result in under-treatment of axSpA patients with worse outcome in comparison to the T2T approach.

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POS0304 THE EFFECT OF ANTI-INFLAMMATORY TREATMENT ON DEPRESSION IN SPONDYLOARTHRITIS: DOES THE TYPE OF DRUG MATTER?

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Background: Patients with spondyloarthritis (SpA) are at increased risk of depression compared to the general population. Currently, it is unknown whether this increased risk is only secondary (due to SpA-related symptoms), or also due to a shared inflammatory pathway. From both clinical and pathophysiological perspectives, it is relevant to know whether comorbid depressive symptoms improve with treatment of SpA, and if so, whether such an improvement depends on drug type/mechanism of action.

Objectives: To investigate the effect of pharmacological treatment of SpA on depressive symptoms, and to explore whether this effect differs between drug types.

Methods: Data from the international ASAS Health Index Validation Study were used. Included patients had a diagnosis of SpA and fulfilled the ASAS classification criteria for axial/peripheral SpA. Patients were assessed at baseline, and for those who required a therapeutic change (initiation of NSAID, conventional synthetic (cs)DMARD or TNFi) due to high disease activity, a follow-up assessment was conducted. The current analysis included only those with a therapeutic change. Data on demographics, disease characteristics and disease activity (ASDAS, BASDAI, CRP) were available. Depressive symptoms were assessed with the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D, range 0-21 [best-worst]). HADS-D scores ≥8 and ≥11 indicated possible and probable depression, respectively. Change in depressive symptoms from baseline was compared between treatments (NSAID, csDMARD, TNFi) with ANOVA and linear regression analysis, adjusting for potential confounders.

Results: In total, 1548 patients were assessed at baseline. A therapeutic change was initiated in 304 patients (n=102/45/157 initiated an NSAID/csDMARD/TNFi). Of these, 260 (85%) had axSpA, 190 (63%) were male, mean age was 37.3 (SD 12.6) years and mean ASDAS at baseline 3.3 (1.1). The mean HADS-D was 6.9 (4.2); 126 (42%) were possibly depressed and 66 (22%) probably depressed. At baseline, there were no significant differences in demographics, disease parameters or depressive symptoms between treatment groups. At follow-up, mean HADS-D had improved to 5.1 (change -1.9 (3.8), p<0.01). Improvement in HADS-D was greater for TNFi (-2.4) than NSAIDs (-1.3, p=0.05) or csDMARDs (-1.2, p=0.15). Also, the proportion of patients with possible depression decreased more for TNFi (from 48% at baseline to 29% at follow-up) compared to NSAIDs (from 38% to 32%). In multivariable regression, initiation of TNFi was associated with greater improvement in HADS-D compared to NSAID (B = -1.27, 95%CI -2.23 to -0.32, base model) (Table 1). However, after additional adjustment for change in ASDAS/BASDAI, drug type was no longer associated with HADS-D improvement (Table 1). Adjustment for CRP in addition to BASDAI did not change results, and CRP itself was not associated with depressive symptoms (not shown). Of note, csDMARDs did not differ from NSAIDs in any of the analyses regarding their effect on HADS-D.

Table 1. Multivariable regression analysis of change in HADS-D from baseline

	Base model		ASDAS model		BASDAI model	
Variable	**B**	**95%CI**	**B**	**95%CI**	**B**	**95%CI**
Age, years	**0.04**	**0.00 to 0.07**	0.03	-0.01 to 0.07	**0.03**	**0.00 to 0.06**
Male gender	0.23	-0.67 to 1.14	0.55	-0.39 to 1.49	0.28	-0.54 to 1.10
HLA-B27 (vs negative)						
Positive	**1.56**	**0.46 to 2.67**	**1.38**	**0.27 to 2.49**	**1.17**	**0.17 to 2.18**
Unknown	**1.70**	**0.19 to 3.22**	**2.21**	**0.66 to 3.75**	**1.41**	**0.04 to 2.77**
Therapy initiated (vs NSAID)						
csDMARD	0.19	-1.16 to 1.54	0.02	-1.34 to 1.39	0.14	-1.07 to 1.36
TNFi	**-1.27**	**-2.23 to -0.32**	-0.51	-1.58 to 0.55	-0.23	-1.13 to 0.67
ASDAS, change			**1.27**	**0.84 to 1.71**	†	
BASDAI, change			†		**0.78**	**0.60 to 0.96**

Associations in bold are statistically significant (p<0.05) †Due to collinearity, ASDAS and BASDAI were tested in separate models

Conclusion: Treatment of active SpA also improves depressive symptoms. TNFi have a larger effect than NSAIDs, which can mainly be explained by a stronger effect on disease activity. This analysis did not find evidence for a direct link between CRP-mediated inflammation and depressive symptoms in SpA.

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POS0305 TIME TO IMPROVEMENT OF FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS IN A STUDY OF TOFACITINIB

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Background: Fatigue is common in patients (pts) with ankylosing spondylitis (AS) and is associated with higher levels of pain and functional disability.[1] Tofacitinib is an oral JAK inhibitor approved for the treatment of AS. In pts with AS, greater improvements in fatigue were seen with tofacitinib vs placebo (PBO).[2]

Objectives: To estimate the time to improvement in fatigue in pts with AS treated with tofacitinib.

Methods: This post hoc analysis used data from a Phase 3 trial (NCT03502616) in pts with AS receiving tofacitinib 5 mg twice daily (BID) or PBO for 16 weeks; after Week (W)16, all pts received open-label tofacitinib until W48.[2] Fatigue was assessed by Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) total score (range 0–52; higher scores indicate less fatigue[3]). A series of time to event analyses were performed using non-parametric Kaplan–Meier models. Median times to initial improvements in FACIT-F total score were assessed based on different thresholds. The initial improvement event was defined as time to first post-baseline week with an improvement in FACIT-F total score of at least 5%, 10%, 15% etc, up to 100%. Median times to events based on absolute changes in FACIT-F total score were also investigated.

Results: Overall, 269 pts were assessed; baseline demographics/disease characteristics have been previously reported.[2] The median times to initial improvements in FACIT-F total score were significantly (p<0.05) shorter in pts receiving tofacitinib 5 mg BID vs PBO (Figure 1). For example, median time to

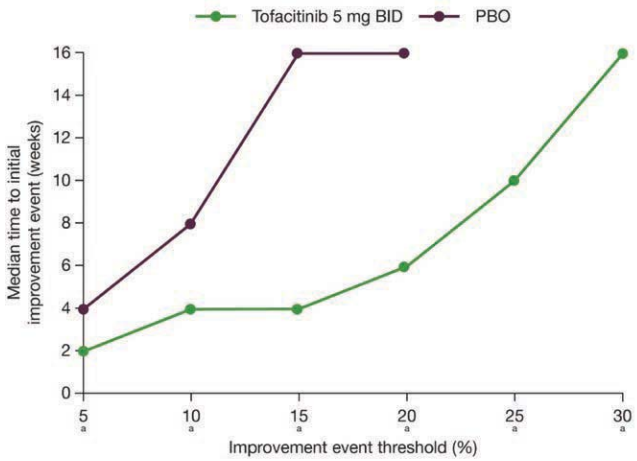
initial improvement of 30% in FACIT-F total score was 16 weeks in pts receiving tofacitinib 5 mg BID; however, in pts receiving PBO, the median time for this event was not achieved up to W16. More pts receiving tofacitinib 5 mg BID vs PBO experienced initial improvement events up to W16 (Table 1). For example, 36.1% of pts receiving tofacitinib 5 mg BID experienced 50% improvement of fatigue up to W16, compared with 19.9% of pts receiving PBO.

Table 1. Proportions of pts who experienced initial improvement events in FACIT-F total score up to W16

Fatigue improvement threshold	Initial improvement, n (%)	p value[a]
25%		
Tofacitinib 5 mg BID	82 (61.7)	0.0009
PBO	58 (42.6)	
50%		
Tofacitinib 5 mg BID	48 (36.1)	0.0031
PBO	27 (19.9)	
75%		
Tofacitinib 5 mg BID	30 (22.6)	0.0626
PBO	19 (14.0)	
100%		
Tofacitinib 5 mg BID	23 (17.3)	0.1233
PBO	15 (11.0)	

N=133 (tofacitinib 5 mg BID); N=136 (PBO) [a]Test of equality over strata log-rank test, p<0.05
n, number of pts achieving an initial improvement event; N, total number of pts in each treatment group

Fig. Median times to initial improvement events in FACIT-F total score



[a]Test of equality over strata log-rank test, p<0.05
Initial improvements in fatigue were evaluated from baseline based on the first post-baseline week with an improvement in FACIT-F total score of at least 5%, 10%, 15% etc, up to 100%

Conclusion: In pts with AS, initial improvements in fatigue, as determined by FACIT-F total score, occurred faster and were larger in magnitude with tofacitinib vs PBO up to W16. These results may help physicians better understand the speed and magnitude for fatigue benefit in pts receiving tofacitinib.

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POS0306

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS REFRACTORY TO BIOLOGIC THERAPY: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL

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Background: Upadacitinib (UPA) was shown to be safe and effective through 2 years in patients (pts) with active ankylosing spondylitis (AS) naïve to biologic disease-modifying antirheumatic drugs (bDMARDs) in the pivotal phase 2/3 SELECT-AXIS 1 trial.[1,2]

Objectives: To assess the efficacy and safety of UPA in pts with active AS with an inadequate response (IR) to bDMARDs.

Methods: SELECT-AXIS 2 (NCT04169373) was conducted under a master protocol and includes two separate studies (one for AS bDMARD-IR and one for non-radiographic axial spondyloarthritis [nr-axSpA]). The AS bDMARD-IR study is a randomized, double-blind, placebo (PBO)-controlled, phase 3 trial that enrolled adults ≥18 years with AS who met modified New York criteria, had BASDAI and pt's assessment of total back pain scores ≥4 (numeric rating scale 0–10) at study entry, and had an IR to one or two bDMARDs (TNF inhibitor or IL-17 inhibitor). Pts were randomized 1:1 to receive oral UPA 15 mg once daily (QD) or PBO during the 14-week (wk) double-blind treatment period. The primary endpoint was ASAS40 response at wk 14. Multiplicity-controlled secondary endpoints evaluated at wk 14 were improvements from baseline in disease activity (ASDAS [CRP], ASDAS ID [<1.3], ASDAS LDA [<2.1], BASDAI50, ASAS20, and ASAS PR), pain (total and nocturnal back pain), function (BASFI), objective measure of inflammation (SPARCC MRI score of the spine), spinal mobility (BASMI), enthesitis (MASES), and quality of life (ASQoL and ASAS HI). Non-responder imputation incorporating multiple imputation (NRI-MI) was used to handle intercurrent events and missing data for binary endpoints. Cochran-Mantel-Haenszel (CMH) test and mixed-effect model for repeated measures (MMRM) were used for analyzing binary and continuous endpoints, respectively. Treatment-emergent adverse events (TEAEs) assessed through wk 14 are reported for pts who had ≥1 dose of study drug.

Results: All 420 randomized pts with active AS received assigned treatment (UPA 15 mg, n=211; PBO, n=209); 409 (97%) received study drug through wk 14. Baseline demographic and disease characteristics were generally similar between treatment groups and reflective of an active AS bDMARD-IR population (74% male; mean age 42.4 years; mean disease duration 7.7 years; 83% HLA-B27 positive; mean BASDAI 6.8). Significantly more pts achieved the primary endpoint of ASAS40 response at wk 14 with UPA vs PBO (45% vs 18%; $P<0.0001$; Figure 1); UPA showed onset of effect in ASAS40 as early as wk 4 (nominal $P\leq0.05$). All multiplicity-controlled secondary endpoints met statistical significance for UPA vs PBO at wk 14 across multiple clinical domains of AS ($P<0.0001$; Figure 1). The rate of TEAEs was similar between treatment groups through wk 14 (UPA, 41%; PBO, 37%). TEAEs led to discontinuation in 3 (1.4%) pts treated with PBO and none with UPA. Serious infections occurred with UPA (2.4%) but not with PBO and included 4 events of COVID-19 and 1 event of uveitis. Additional events of uveitis were reported in 3 (1.4%) pts treated with PBO. Inflammatory bowel disease (IBD) occurred in 1 (0.5%) pt on UPA and none on PBO. No malignancy, major adverse cardiovascular events, venous thromboembolic events, or death were reported with UPA; 1 event of malignancy was observed with PBO.

Conclusion: UPA 15 mg QD was significantly more effective than PBO over 14 wks of treatment in pts with active AS and IR to bDMARDs. No new safety risks were identified with UPA compared with its known safety profile.[3,4] These findings are consistent with and complementary to those of SELECT-AXIS 1 (bDMARD-naïve AS population),[1,2] and support the use of UPA in pts with active AS, including those who had a previous IR to bDMARD therapy.

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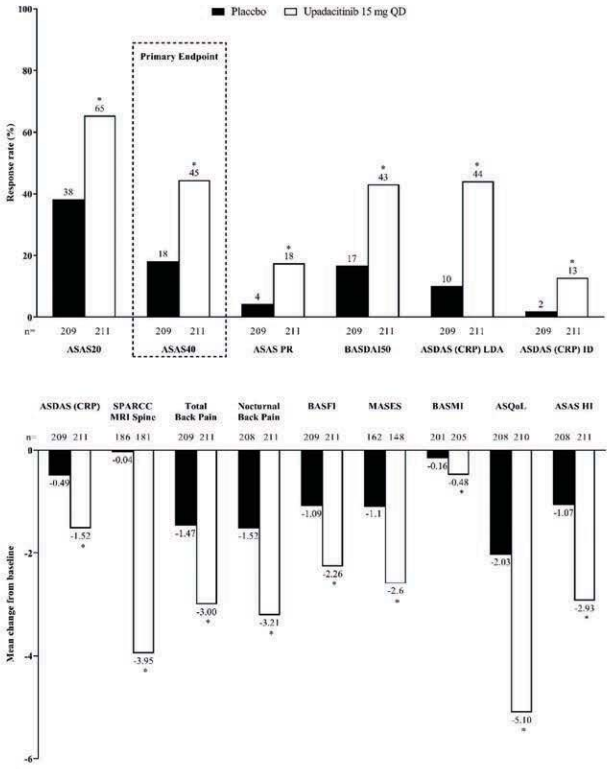

Figure. Analysis of Primary and Multiplicity-Controlled Secondary Endpoints at Wk 14

ASAS20=Assessment of SpondyloArthritis international Society 20 response; ASAS40=Assessment of SpondyloArthritis international Society 40 response; ASAS HI=Assessment of SpondyloArthritis international Society Health Index; ASAS PR=Assessment of SpondyloArthritis international Society partial remission; ASDAS (CRP)=Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS (CRP) ID=Ankylosing Spondylitis Disease Activity Score C-reactive protein inactive disease; ASDAS (CRP) LDA=Ankylosing Spondylitis Disease Activity Score C-reactive protein low disease activity; ASQoL=Ankylosing Spondylitis Quality of Life; BASDAI50=at least 50% improvement from baseline in Bath Ankylosing Spondylitis Disease Activity Index; BASFI=Bath Ankylosing Spondylitis Functional Index; BASMI=Bath Ankylosing Spondylitis Metrology Index; MASES=Maastricht Ankylosing Spondylitis Enthesitis Score; QD=once daily; SPARCC=Spondyloarthritis Research Consortium of Canada.
*P<0.0001; Significant in multiplicity-adjusted analysis.
ASDAS LDA was defined as ASDAS (CRP) <2.1 and ASDAS ID as ASDAS (CRP) <1.3.
MASES was assessed in pts with baseline enthesitis.

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Clinical aspects in Psoriatic Arthritis

POS0307

IMPAIRED GLYCAEMIC CONTROL IS ASSOCIATED WITH INCREASED RISK OF PSORIATIC ARTHRITIS: MENDELIAN RANDOMISATION STUDY

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Background: Psoriatic arthritis (PsA) and psoriasis are both strongly associated with impaired glycaemic control and type 2 diabetes. The risk of developing type 2 diabetes is estimated to be ~40% higher in PsA compared to controls [1]. However, these observational findings are susceptible to bias from reverse causation: Insulin resistance and impaired glycaemic control are evident well over a decade before clinical onset of type 2 diabetes [2]. Therefore, whether impaired glycaemic control is a cause or consequence of PsA is unclear. Testing this hypothesis using traditional observational designs is challenging since longitudinal assessments of glycaemic control before PsA onset are often not available. Mendelian randomisation (MR) is an epidemiologic method that provides evidence about putative causal relationships between modifiable exposures and disease outcomes using genetic variants as instrumental variables. MR is less likely to be affected by confounding or reverse causation than conventional observational designs because genetic variants are randomly allocated at conception.
Objectives: To estimate the effect of genetically predicted glycaemic traits - glycated haemoglobin (HbA1c), 2-hour glucose after oral glucose challenge (2hG), fasting glucose (FG), and fasting insulin (FI) - on risk of PsA and psoriasis compared to controls using two-sample MR.
Methods: We selected 320 independent (r^2<0.001) genome-wide significant ($p<5x10^{-8}$) variants as instruments for HbA1c from a UK biobank genome-wide association study (GWAS) of 344,182 individuals, and 14 variants for 2hG, 67 for FG and 38 for FI from up to 200,622 individuals from a MAGIC consortium meta-analysis that adjusted for body mass index. Genetic associations for PsA were obtained from a GWAS comprising 3,609 cases (majority fulfilling CASPAR criteria) and 9,192 controls. Psoriasis data were obtained from 5,278 cases (96% European, defined using ICD and phecodes) and 650,391 controls from the UK biobank, FinnGen and BioBank Japan [3]. We used the inverse-variance weighted method to combine effect estimates from each variant using fixed-effect meta-analysis.
Results: Genetically predicted HbA1c increased risk of PsA (OR 1.18 per standard deviation (6.7 mmol/mol) increase in HbA1c; 95%CI 1.02, 1.36). 2hG (OR 1.55 per SD (0.6 mmol/L) increase; 95%CI 1.26, 1.89) and FG (OR 1.73 per SD (1.6 mmol/L) increase; 95%CI 1.35, 2.21) similarly increased PsA risk (Figure 1). FI was not associated with PsA risk. 2hG was the only glycaemic trait significantly associated with psoriasis (OR 1.21; 95%CI 1.04, 1.40).

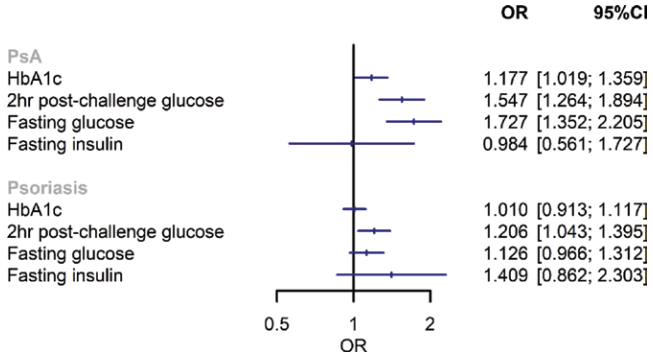

Figure 1. Mendelian randomisation estimates of the effect of glycaemic traits on risk of psoriatic arthritis and psoriasis.

Conclusion: This study provides supportive genetic evidence that impaired glycaemic control increases risk of PsA. By contrast, estimates were smaller when comparing psoriasis against controls with confidence intervals including the null. Improving glycaemic control may reduce PsA risk, although further studies are required to confirm these findings and to compare PsA directly against cutaneous only psoriasis.
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POS0308

EFFECT OF GUSELKUMAB ON SERUM BIOMARKERS IN PSORIATIC ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE OR INTOLERANCE TO TUMOR NECROSIS FACTOR INHIBITORS: RESULTS FROM THE COSMOS STUDY

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Background: Guselkumab (GUS), a selective IL-23 inhibitor, is efficacious in treating bio-naïve and TNFi-experienced active PsA patients (pts).[1,2] In the COSMOS study of active PsA pts with lack of efficacy/intolerance, i.e., inadequate response (IR), to 1-2 TNFi, GUS demonstrated significantly greater response rates and mean improvements in PsA signs and symptoms vs. placebo (PBO) at Week (W) 24.[3]

Objectives: Evaluate baseline (BL) serum levels of pro-inflammatory biomarkers (CRP, serum amyloid A [SAA], TNFα, IFNγ, IL-6, IL-10, IL-17F, IL-17A, IL-22) and their relationship to BL disease activity, GUS treatment (tx), and clinical response in COSMOS TNFi-IR pts.

Methods: TNFi-IR pts ≥18 yrs with active PsA (≥3 swollen & ≥3 tender joint counts [SJC/TJC]) were randomized 2:1 to GUS 100 mg every 8W (Q8W) through W44 or PBO with early escape (W16) or crossover (W24) to GUS Q8W. Samples for serum biomarker analyses, collected at W0, 4, 16, 24, and 48 from consenting pts, were compared with healthy controls (HC; independent of COSMOS). Associations between early biomarker changes and BL disease activity, GUS tx, and clinical response at W24 were assessed.

Results: Among 285 COSMOS pts, 50/95 PBO and 100/190 GUS pts had available biomarker data. BL characteristics of the biomarker cohort were similar to the overall COSMOS population and well balanced across tx arms. At BL, levels of TNFα, IFNγ, IL-6, IL-10, IL-17A, IL-17F, and IL-22 were significantly upregulated in TNFi-IR pts vs. HC (Table 1). IL-6, CRP, and SAA levels were associated with BL joint disease severity per Disease Activity Score (DAS) 28-CRP (but not with SJC [0-66]/TJC [0-68]). IL-17A and IL-17F levels were associated with BL PASI score. Through W24, significant decreases from BL in levels of CRP, SAA, IL-6, IL-17A, IL-17F, and IL-22 were seen in GUS-, but not PBO-tx pts. Reductions in IL-17A, IL-17F and IL-22 with GUS were significant by W4, decreased further by W16, and were sustained through W24 and W48. In GUS-tx pts, serum levels of IL-17F (from W16) and IL-22 (from W4) were not significantly different vs. HC. At W48, reductions in these same markers were seen in PBO-tx pts who crossed over to GUS at W16/24 (Figure 1; IL-17A, IL-17F, & IL-22 data shown). In these TNFi-IR pts, GUS-tx pts achieving ACR20 at W24 exhibited higher IL-22 and IFNγ levels at BL than nonresponders (NR). All other biomarkers evaluated were not significantly associated with ACR20 response to GUS. In the subset of pts with IGA of psoriasis assessed, BL IL-6 and SAA levels were upregulated in W24 IGA 0/1 responders (R) vs. NR in the GUS arm. ACR20 and IGA 0/1 R at W24 exhibited an early greater reduction in IL-6 expression (at W4) than did respective NR in the GUS arm. No BL biomarkers were associated with ACR50 or PASI75 responses to GUS at W24.

Table 1. Select Serum Biomarkers at BL in TNFi-IR pts vs. HC¤

Biomarker, pg/mL	HC N=24	TNFi-IR N=150	Fold difference	p-value
CRP	22.1 (1.5)	22.8 (2.2)	1.6	0.2895
SAA	21.7 (1.2)	22.8 (2.4)	2.1	0.0794
IL-6	0.07 (1.1)	0.98 (1.7)	**1.9**	**0.0314***
IL-10	-2.3 (1.1)	-1.7 (1.0)	**1.5**	**0.0272***
IL-17A	-2.1 (1.3)	-0.3 (1.5)	**3.3**	**<0.0001***
IL-17F	0.05 (1.1)	1.3 (1.5)	**2.4**	**0.0007***
IL-22	1.9 (1.1)	3.1 (1.3)	**2.4**	**0.0002***
TNFα	0.5 (0.75)	1.4 (1.1)	**1.8**	**0.0002***
IFNγ	2.4 (0.84)	2.9 (1.3)	**1.5**	**0.0259***

Data are mean (SD); *p<0.05 and |fold difference| >1.4; ¤adjusted for confounding factors age & sex.

Conclusion: GUS-tx TNFi-IR pts showed response-specific associations with BL biomarkers (IL-22, IFNγ, IL-6, and SAA). GUS resulted in decreased levels of elevated CRP, SAA, IL-6, IL-17A, IL-17F, and IL-22, while no significant change was observed with PBO tx. Reductions in these biomarkers were evident as early as W4 and approximated levels seen in HC from W16 onward (W4 for IL-22), suggesting apparent normalization of effector cytokines associated with the IL-23/Th17 axis following GUS tx.

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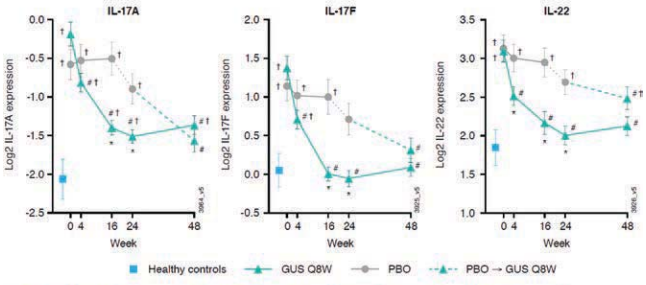
Figure. Reductions in Serum Levels of IL-17A, IL-17F, & IL-22 With GUS



PBO includes pts who had an early escape to GUS at W16 (dotted line; n=24), and a planned cross-over to GUS at W24 (dashed line; n=26)
Statistics based on general linear model. Error bars represent 1 standard error.
* Indicates statistical significance vs. PBO by p<0.05 & |fold difference| >1.4.
# Indicates statistical significance vs. baseline by p<0.05 & |fold difference| >1.4.
† Indicates statistical significance vs. healthy controls by p<0.05 & |fold difference| >1.4.

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POS0309 ARE PATIENTS' AND RHEUMATOLOGISTS' PERCEPTIONS OF THE BURDEN AND TREATMENT OF PSORIATIC ARTHRITIS ALIGNED? RESULTS FROM THE UPLIFT SURVEY

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Background: Alignment of patient and clinician goals and perceptions of psoriatic arthritis (PsA) burden and treatment are important to improving disease management.

Objectives: To describe patient and rheumatologist perceptions on factors contributing to PsA severity, treatment goals, and attributes of ideal therapy.

Methods: Understanding Psoriatic Disease Leveraging Insights for Treatment (UPLIFT) was a multinational Web-based survey that included adults who reported a healthcare provider (HCP) diagnosis of PsA and/or psoriasis, as well as rheumatologists and dermatologists. This analysis focused on survey responses from patients with PsA and rheumatologists. Respondents ranked their top 3 contributing factors for PsA severity, treatment goals, and ideal attributes for therapy. Results were analyzed using the sum of scores.

Results: In all, 1256 patients with PsA and 450 rheumatologists completed the respective surveys between March and June 2020. An oligoarticular (≤4 joints involved) pattern of involvement was prevalent in 43.8% of patients (Table 1). Involvement of large joints (78.8%) was most common, followed by intermediate (69.3%) and small (51.8%) joints. Only half of patients reported seeing an HCP for PsA in the last year (Table 1). Patients and rheumatologists agreed that joint pain is a top factor contributing to disease severity; patients also ranked the impact on quality of life and type of symptoms as top factors whereas rheumatologists placed greater importance on the number of joints involved and joint erosion or deformity (Figure 1). Top treatment goals for patients were reducing joint pain and stiffness and stopping the progression of joint damage or erosion (Figure 1). Rheumatologists agreed that inhibiting progression of joint damage or erosion and reducing joint pain were among the top treatment goals, and they rated disease remission or low disease activity (LDA) as the most important goal (Figure 1). Rheumatologists identified consistent treatment goals for patients

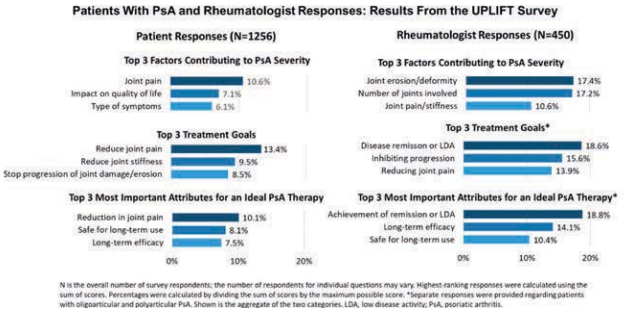
regardless of degree of joint involvement (oligoarthritis vs polyarthritis). Patients and rheumatologists agreed that long-term safety and efficacy are key attributes of an ideal PsA therapy. The top attribute for patients was joint pain reduction, whereas achievement of remission or LDA was the top attribute identified by rheumatologists (Figure 1). Despite general alignment between patient and rheumatologist responses across metrics, 87.1% of patients reported they did not feel that their treatment goals matched those of their current HCP.

Table 1.

Characteristic	UPLIFT Global PsA Patient Subgroup N=1256
Age, mean (SD), years	42.9 (15.3)
Men, n (%)	674 (53.7)
Joint count, n (%)	
>4 joints (polyarthritis)	706 (56.2)
≤4 joints (oligoarthritis)	550 (43.8)
Seen an HCP in the past year, n (%)*	626 (49.8)
Type and location of practice, n (%)	**UPLIFT Rheumatologists N=450**
Single or solo specialty	267 (59.3)
Multi-specialty	183 (40.7)
Canada	41 (9.1)
France	53 (11.8)
Germany	50 (11.1)
Italy	54 (12.0)
Japan	50 (11.1)
Spain	51 (11.3)
United Kingdom	50 (11.1)
United States	101 (22.4)

The N represents the total sample. The number of patients with data available may vary. *COVID-19 restrictions may have impacted a patient's ability to have an HCP visit from March 2 to June 3.

Conclusion: In the UPLIFT survey, patients with PsA and their rheumatologists generally agreed on the top factors contributing to disease severity, treatment goals, and attributes of ideal PsA therapy. However, the majority of patients with PsA did not feel aligned with their current HCP regarding treatment goals. Development of methods for treatment goal discussion and alignment are important to improving patient outcomes.



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POS0310 DO AXIAL PSORIATIC ARTHRITIS PATIENTS MEET ASAS CLASSIFICATION CRITERIA FOR AXIAL SPONDYLOARTHRITIS?

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Background: There isn't any generally accepted definition and diagnostic criteria for axial psoriatic arthritis (axPsA). According to most recent data, classification criteria for axial spondyloarthritis (axSpA) may not be applied to axPsA (1).
Objectives: To analyze, in clinical practice, whether axPsA patients (pts) meet classification criteria for axSpA and ankylosing spondylitis (AS).
Methods: 52 pts (M/F–32/20), a hospital cohort, with PsA according to CASPAR criteria were observed. All pts had back pain at one time or another, which rheumatologist suspected to be axial involvement. Pts' age 43.0 [35.0; 54.0], disease duration 3.4 yrs [0.2; 32.0]. Me BASDAI 5.3 [3.6; 7.0]; ASDAS-CPБ 3.3 [2.2; 4.1]; DAPSA 36,3 [19,3; 50,5]; CRP 9.6 [0.1; 86.6] mg/L; ESR 31 [3; 99] mm/h. Enthesitis was found in 69.2% and dactylitis in 61.5% of pts. All pts had psoriasis with Me BSA (body surface area) of 4 [1; 9]%, Me PASI (Psoriasis Area Severity Index) of 9.6 [5.6; 17.4]. Nail psoriasis was found in 38 (73.1%) pts, 40.4% of them had onycholysis. All pts were evaluated for presence of inflammatory back pain (IBP) by ASAS criteria. Pts underwent sacroiliac joints (SIJ) X-ray (pelvic radiographs), cervical and lumbar spine, hands and feet X-rays, so that 50 pts had complete sets of radiographs. Radiographic sacroiliitis (rSI) was defined as bilateral grade ≥ 2 or unilateral grade ≥ 3. Pts without rSI underwent SIJ MRI on Philips Multiva 1.5 T scanner. Active MRI sacroiliitis (MRI-SI) was categorized using ASAS 2016 criteria. Radiographic spondylitis (rSp) was defined as ≥1 marginal/paramarginal syndesmophyte(s) of the cervical and/or lumbar spine. All radiographs and MRI results were interpreted by two experienced musculoskeletal radiologists. 45 pts underwent HLA B27 examination. Me [Q25; Q75] and Pierson-χ2 tests were performed. All $p<0.05$ were considered to indicate statistical significance.
Results: IBP was found in 34 (66.7%) and rSI in 30 (57.7%) pts. 15 (30.0%) pts had rSI along with rSp, while in 15 (30.0%) pts rSI was without it, and 9 (18.0%) pts had rSp alone. 2 pts of the 17 examined, had MRI-SI. HLA B27 was present in 15 (33.3%) pts examined. 37 (71.2%) pts met ASAS criteria for axSpA as follows: 22 pts met the imaging arm (rSI or MRI-SI + ≥ 1SpA feature), 5 pts met the clinical arm (HLA B27+ ≥ 2 other SpA features) and 10 pts met both of those. 10 (19.2%) pts didn't meet ASAS criteria for axSpA: they had neither rSI/MRI-SI nor HLA B27; however, 9 of them had syndesmophytes. 30 pts had rSI with 21 of them (40.4% of all pts) meeting modified New York (mNY) criteria for AS, because along with rSI, they had at least 1 of the 3 clinical criteria (IBP for > 3 months, limitation of lumbar motion in sagittal and frontal planes, limitation of chest expansion). The pts who met both CASPAR and mNY criteria, however had typical axPsA features: 85.7% of them had polyarthritis with multiple joint erosions, 61.9% had osteolysis and/or juxtaarticular new bone formation, 61.9% dactylitis, 33.3% non-marginal asymmetrical syndesmophytes, 44.4% were HLA B27 negative, 43.3% didn't have IBP; all pts developed psoriasis many years before the onset of PsA.
Conclusion: Among PsA pts with axial involvement there is an alternative phenotype group (18% of our cohort) with neither sacroiliitis (rSI/ MRI-SI) nor HLA B27. Such pts do not meet ASAS criteria for axSpA. The alternative phenotype is characterized by isolated spondylitis (syndesmophytes) without sacroiliitis. Axial disease cannot be ruled out in PsA pts without spinal radiographs, regardless of symptoms. Pts meeting both CASPAR and mNY criteria and featuring typical axPsA symptoms cannot be diagnosed as having AS along with concomitant psoriasis, because axPsA and AS with psoriasis seem to be two different diseases. There is an urgent need for a unified definition of axial involvement in PsA.
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Disclosure of Interests: ELENA GUBAR: None declared, Tatiana Korotaeva Speakers bureau: Pfizer, MSD, Novartis, AbbVie, Janssen, Lilly, Celgene, JSC BIOCAD and Novartis-Sandoz, Elena Loginova Speakers bureau: Janssen, Yulia Korsakova Speakers bureau: Novartis, Svetlana Glukhova: None declared
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POS0311 FLARES IN PATIENTS WITH RECENT-ONSET PSORIATIC ARTHRITIS. PREDICTIVE MODEL BASED ON MACHINE LEARNING

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Background: An important aspect in the clinical care of patients with PsA is to be able to predict the occurrence of a flare using tools and information that are readily available in daily clinical practice. This information would provide added value in disease management, yet, unfortunately, scarcely any studies provide it.
Objectives: To identify patient- and disease-related characteristics that make it possible to predict flares in recent-onset PsA.
Methods: We performed a multicenter observational prospective study (2-year follow-up, regular annual visits), promoted by the Spanish Society of Rheumatology [1]. The study population comprised patients aged ≥18 years who fulfilled the CASPAR criteria [2], with less than 2 years since the onset of symptoms. The intention at the baseline visit was to reflect the patient's situation before disease progress was modified by the treatments prescribed in the rheumatology department.
All patients gave their informed consent. The study was approved by the Clinical Research Ethics Committee of the Principality of Asturias.
Flares were defined as inflammatory episodes affecting the axial skeleton and/or peripheral joints (joints, digits or entheses) and diagnosed by a rheumatologist between the previous and the current visit.
The dataset contained data for the independent variables from the baseline visit and from follow-up visit number 1. These were matched with the outcome measures from follow-up visits 1 and 2, respectively. We trained logistic regression models and a random forest–type machine learning algorithm to analyze the association between the outcome measure and the variables selected in the bivariate analysis (statistical significance was defined as p value <0.05). We used a confusion matrix to visualize the performance of the final model. This matrix shows the real class of the data items, together with the class predicted by the machine learning algorithm, and records the number of hits and misses.
Results: The sample comprised 158 patients. 14.6% were lost to follow-up. At the first follow-up visit, 37.6% of the patients who attended the clinic had experienced flares since the baseline visit. Of those who attended the second visit, 27.4% had experienced flares since the first visit. Table 1 shows the results of the logistic regression analysis. The variables predicting flares between visits selected in this analysis were age-adjusted Charlson comorbidity index, PsAID score, number of digits with onychopathy, and level of physical activity. The direction of the association was negative for the Charlson index and physical activity and positive for PsAID score and onychopathy.

Table 1. Variables associated with flares between visits selected in the logistic regression analysis.

Variable	Regression coefficient	95% CI	p value (Wald test)
Age-adjusted Charlson comorbidity Index	-4.655	(-7.021, -2.289)	<0.001
PsAID score	2.212	(1.171, 3.254)	<0.001
No. of digits with onychopathy	1.420	(0.331, 2.511)	0.011
Level of physical activity	-1.221	(-1.87, -0.572)	<0.001

When the random forest machine learning algorithm was trained with these 4 variables, the order of importance (from more to less) attributed by the model was as follows: PsAID score, number of digits with onychopathy, age-adjusted Charlson comorbidity index, and level of physical activity. The percentage of hits in the confusion matrix was 78.38%.
Conclusion: PsAID score was the first variable in the predictive hierarchy generated in our model, supporting its importance in the management and follow-up of PsA patients.
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POS0312 REAL-WORLD EVIDENCE ON ASSESSING PSORIATIC ARTHRITIS BY DISEASE DOMAIN: AN EVALUATION OF THE COREVITAS PSORIATIC ARTHRITIS/ SPONDYLOARTHRITIS REGISTRY

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Background: Psoriatic arthritis (PsA) is a burdensome, chronic disease that can impact patient functionality and quality of life. Real-world data are limited regarding the most common disease domain combinations in patients with PsA receiving biologic disease-modifying anti-rheumatic drugs.
Objectives: The objective of this study was to describe PsA disease domain frequency, the most common disease domain combinations of PsA manifestations, and pairwise disease domain prevalence in patients initiating treatment with tumor necrosis factor inhibitors (TNFis) or interleukin-17 (IL-17) inhibitors.
Methods: The CorEvitas PsA/Spondyloarthritis (SpA) Registry is a prospective, observational registry for patients with PsA or SpA under the care of a rheumatologist. The current analysis included adults with PsA who initiated treatment with a TNFi (adalimumab, etanercept, certolizumab pegol, infliximab, golimumab), etanercept (ETN; independent exploratory evaluation as a subset of the TNFi group), or an IL-17 inhibitor (ixekizumab, secukinumab) from January 2013 through December 2020. Baseline disease characteristics among the total population and by therapy group were examined for 6 PsA domains, including enthesitis (ET), dactylitis (DA), peripheral arthritis (PA), nail psoriasis (NP), axial PsA (AX), and skin disease (SD). The top 5 most common domain combinations and frequency of other concomitant disease domains within each domain subpopulation are presented.
Results: Among 1005 patients initiating treatment for PsA (mean age, 52.9 years; 57% female, 90% white), the prevalence of disease domains was PA (86%), SD (82%), NP (57%), ET (38%), DA (23%), and AX (20%); these proportions were similar among the therapy groups. The frequency of high skin disease (body surface area [BSA] ≥10%) at baseline was highest in IL-17 initiators (23% vs 16% for TNFi and 9% for ETN). TNFi (40%) and ETN (48%) were more frequently observed as first-line therapy compared with IL-17 inhibitors (14%). The most common disease domain combination overall (14%) was PA, NP, and SD; frequency of the top 3 most common domain combinations were similar among therapy groups (Table 1). Overall, PA and SD were the most common concomitant disease domains observed within each PsA disease domain subpopulation (Figure 1). Results were similar by therapy group (data not shown).

Table 1. Most common PsA domain combinations overall and by therapy

Domain Combination Ranking by Frequency, n (%)	Overall (N=1005)	TNFi[a] (n=631)	ETN (n=112)	IL-17 (n=374)
#1	PA, NP, SD 138 (14)	PA, NP, SD 91 (14)	PA, SD 17 (15)	PA, NP, SD 47 (13)
#2	PA, SD 122 (12)	PA, SD 84 (13)	ET, PA, NP, SD 13 (12)	ET, PA, NP, SD 41 (11)
#3	ET, PA, NP, SD 95 (9)	ET, PA, NP, SD 54 (9)	PA, NP, SD 12 (11)	PA, SD 38 (10)
#4	ET, PA, SD 64 (6)	DA, PA, NP, SD 38 (6)	SD 7 (6)	ET, PA, SD 33 (9)
#5	DA, PA, NP, SD 61 (6)	ET, PA, SD 31 (5)	ET, PA, NP, AX, SD 6 (5)	ET, PA, NP, AX, SD 24 (6)

Matching domain combinations are shaded across each therapy group.ET, enthesitis; DA, dactylitis; PA, peripheral arthritis; NP, nail psoriasis; AX, axial PsA; SD, skin disease; TNFi, tumor necrosis factor inhibitors; ETN, etanercept; IL-17, interleukin-17 inhibitors.[a]TNFi includes ETN initiators.

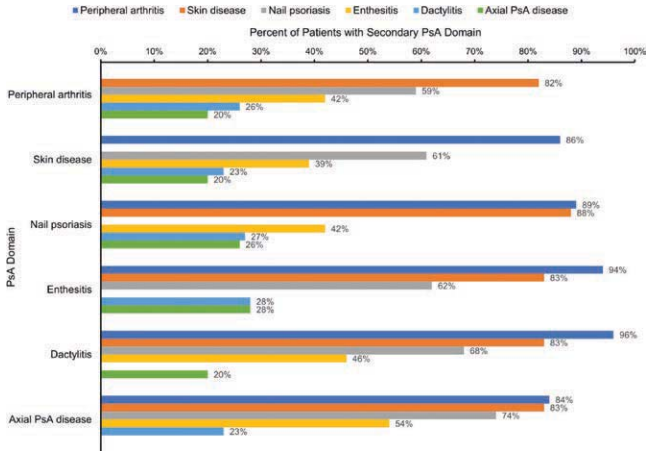

Figure 1.

Conclusion: The most common disease domains and domain combinations were similar among initiators of TNFis, ETN, and IL-17s. IL-17 initiators had high skin disease (BSA ≥10%) more often and initiated as first-line therapy less frequently than TNFi initiators. Assessing all PsA domains is important for optimal disease management.

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POS0313 THE ASSOCIATION BETWEEN BODY COMPOSITION AND PHYSICAL ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS: THE TRØNDELAG HEALTH STUDY

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Background: Persons with psoriatic arthritis (PsA) have an altered body composition compared to the general population, including overweight, which may increase the risk of several comorbidities. However, the associations of physical activity (PA) with body composition among persons with PsA is not well described.

Objectives: The aim of the study was to investigate the relationship between visceral fat mass (VFM) and percentage body fat (PBF), respectively, with PA in persons with PsA.

Methods: The study utilized data from the population-based Trøndelag Health Study (HUNT4, 2017-2019), where all inhabitants ≥ 20 years of age in northern Trøndelag were invited. Data comprised questionnaires, measurements, and blood sample analyses. Persons with PsA (n=291, CASPAR criteria) were identified from hospital case notes. The remaining participants with complete data for relevant variables (n=38 955) were used as controls.

Body composition was measured using bioelectrical bioimpedance including 30 values for 5 body segments. The primary outcomes were VFM (Model 1) and PBF (Model 2). PA was quantified using an index based on self-reported frequency, duration, and intensity (1), and categorized as low, moderate, or high.

Data were analyzed with multivariable linear regression including PsA and PA as exposures. The models were adjusted for age (<40, 40-59 >60 years), sex, alcohol consumption (once a week/more vs. less/none), smoking status (present/former vs. never smoker), diabetes, hypertension, heart disease, lung disease and cancer; and height (Model 1 only). To achieve appropriate model fit, an interaction term between age and PsA was included.

Results: Persons with PsA had higher weight, body mass index, VFM and PBF than controls, and they were less physically active (Table 1). The interaction term between PsA and age was statistically significant in both models (p<0.05), showing that the difference in VFM and PBF with PsA compared to controls was relatively larger in persons < 40 years (VMF difference: 3.6kg (95% CI 1.4, 5.9 kg) vs. ~1.1 kg in older age groups, PBF difference: 5.2% (1.9, 8.5%) vs. ~1.5% in older age groups).

Table 1. Demographic and clinical characteristics

Variable	PsA (n=291)	Controls (n=38 955)	p-value
Age (years), mean (±SD)	58 (12)	53 (17)	p<0.001
Male, n (%)	174 (59.8)	21 875 (56.2)	p =0.21
Diabetes, n (%)	28 (9.7)	1 876 (4.8)	p<0.001
Cardiovascular disease, n (%)	11 (3.8)	1 349 (3.5)	p=0.77
Lung disease, n (%)	45 (15.5)	4 904 (12.6)	p=0.14
Cancer, n (%)	29 (10.0)	2 746 (7.1)	p=0.053
Alcohol (once a week/more), n (%)	71 (24.4)	8 234 (21.1)	p=0.18
Smoking (present/former), n (%)	208 (71.5)	20 915 (53.7)	p<0.001
Education (college or higher), n (%)	164 (56.4)	25 166 (64.6)	p=0.003
Height (cm), mean (±SD)	171 (9.1)	171 (9.2)	p=0.31
Weight (kg), mean (±SD)	83 (16.5)	79 (15.7)	p<0.001
Body mass index (kg/m^2), mean (±SD)	28.3 (4.7)	26.9 (4.5)	p<0.001
Percentage body fat, mean (±SD)	33.7 (8.8)	30.5(9.3)	p<0.001
Visceral fat mass (kg), mean (±SD)	13.5 (5.5)	11.4 (5.4)	p<0.001
Physical activity			p=0.004
Low	139 (47.8)	16 648 (42.8)	
Moderate	104 (35.7)	14 491 (37.2)	
High	48 (16.5)	7 816 (20.1)	

The associations between PA and VFM or PBF were similar with and without PsA. In Model 1 (R^2=0.17), moderate or high physical activity was significantly associated with lower VFM. The moderate activity group had 0.8 kg (0.7, 0.9 kg, p<0.001) and the high activity group had 2.6 kg (2.5, 2.7, p<0.001) lower VFM compared to the low physical activity group. In Model 2 (R^2=0.38), moderate or high physical activity was significantly associated with lower PBF. The moderate activity group had 1.4% (1.2, 1.5%, p<0.001) and the high activity group had 4.3% (4.1, 4.5%, p<0.001) lower PBF compared to the low physical activity group.

Conclusion: Patients with PsA had increased PBF and VFM, and moderate or high physical activity was associated with significant reductions in both endpoints. Physical activity may reduce the comorbidity burden among persons with PsA and should be a focus in clinical treatment plans.

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POS0314 IDENTIFICATION OF CIRCULATING MICRORNA SIGNATURES IN PATIENTS WITH PSORIASIS WITH SUBCLINICAL JOINT DISEASE AND PATIENTS WITH PSORIATIC ARTHRITIS

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Table 1.

	PsA vs HC		PsO vs HC		PsA vs PsO	
	Discovery Phase	Validation Phase	Discovery Phase	Validation Phase	Discovery Phase	Validation Phase
miRNAs	**p-adj.**	**p-adj.**	**p-adj.**	**p-adj.**	**p-adj.**	**p-adj.**
miR-93-5p	**0.0001**	**<0.001**	**0.008**	**0.005**	**0.039**	0.947
miR-29b-3p	**0.0001**	**<0.0001**	**0.004**	**0.0002**	0.191	0.522
miR-19b-3p	**0.007**	0.708	**0.0002**	**0.020**	0.138	0.147
miR-320d	**0.001**	0.619	**<0.0001**	0.135	0.941	0.247
miR-144-5p	**0.003**	**0.006**	**0.0001**	0.169	0.350	0.444
miR-188-5p	**0.014**	0.990	0.975	0.647	**0.053**	0.839
let-7b-5p	**0.025**	**0.0003**	0.889	**0.026**	**0.0003**	0.472
miR-92a-3p	**0.043**	**0.001**	**0.005**	0.773	**<0.0001**	**0.0005**
miR-324-3p	0.138	1.000	0.257	0.392	0.814	0.518
miR-126-3p	**0.014**	0.169	**0.013**	0.598	0.922	0.654
miR-223-3p	0.169	0.872	0.617	0.746	0.519	1.000
miR-130a-3p	**0.039**	**0.035**	0.556	**0.009**	**0.006**	0.724
miR-140-3p	0.350	**0.053**	**0.002**	**0.006**	0.118	0.683
miR-155-5p	0.159	0.995	0.169	0.549	0.922	0.604
miR-21-5p	0.297	0.990	**0.003**	0.116	0.08	**0.014**
miR-146a-5p	0.706	**0.004**	0.836	**0.038**	0.905	0.941
miR-122-5p	0.960	0.734	0.695	0.799	0.905	0.444

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Background: MicroRNAs (miRNAs) are small non-coding RNAs that control gene expression. Specific miRNA signatures have been identified in numerous diseases and may serve as potential biomarkers or new drug targets. Whether certain miRNA signatures are associated with psoriatic joint disease is currently unknown.
Objectives: To search for circulating miRNA signatures in psoriasis patients with subclinical joint disease and in patients with psoriatic arthritis (PsA).
Methods: Analyses of serum miRNA were done in three groups: (1) PsA patients fulfilling CASPAR criteria (PsA), (2) healthy controls without past or present signs of musculoskeletal disease (HC) and (3) psoriasis patients with musculoskeletal pain but no signs of clinical PsA (PsO). PsO and PsA patients received a hand MRI, which was scored according to PsAMRIS method. miRNA analysis of serum samples was performed stepwise using RT-qPCR (TAmiRNA Vienna). In the discovery phase 192 miRNA assays were analyzed in 48 samples (N=16 each group). In the validation phase 17 miRNAs (Table 1) were selected and analyzed in 94 samples (N=35 PsA, N=24 PsO, N=35 HC) based on results of discovery phase and previous reports in literature. Results presented as mean±SD/median (IQR), p-values are adjusted for multiple testing.
Results: 51 PsA patients (age: 51.3±11.4 years; 56.9% females), 40 PsO patients (51.4±11.0; 37.5%) and 50 HC (51.0±10.5; 52.9%) were assessed. Duration of psoriasis was 12(25) years in PsA and 15(22.8) years in PsO. Duration of joint disease in PsA was 1.0(4.8) year. 51% of PsA and 5% of PsO patients were on biological disease modifying drugs (bDMARDs), 49% vs. 10% on conventional DMARDs. The most frequent findings in the MRI were erosions (PsA 59.6%; PsO 40%) and synovitis (PsA 48.9%; PsO 42.5%). PsA patients had higher number of tenosynovitis compared to PsO (p=0.04). In discovery phase 51 miRNAs in PsO and 64 miRNAs in PsA were down- or upregulated compared to HC, with an overlap of 33 miRNAs changed in PsA and PsO (p<0.05). Results of the selected 17 miRNAs are presented in Table 1. The top candidates to differentiate PsA and HC were miR-29b-3p (AUC=0.87), miR-93-5p (AUC=0.83) and let-7b-5p (AUC=0.79). For differentiating PsO and HC, they were miR-29b-3p (AUC=0.82), miR-140-3p (AUC=0.81) and miR-19b-3p (AUC=0.80) and for PsO vs. PsA miR-92a-3p (AUC=0.87), let-7b-5p (AUC=0.72) and miR-21-5p (AUC=0.70). miR-93-5p was lower in patients with erosions (p=0.01). miR-92a-3p, let-7b-5p and miR-21-5p were lower in patients with tenosynovitis, bone proliferations or erosions.
Conclusion: PsA and PsO patients show miRNA signatures different from HC. Top candidate miRNAs differentially regulated in PsA and PsO have been previously reported in alteration of bone metabolism and osteoarthritis indicating the intimate association of psoriatic inflammation with bone and cartilage changes.

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POS0315 DIAGNOSTIC PERFORMANCE OF CASPAR CRITERIA FOR PSORIATIC ARTHRITIS WITH OR WITHOUT INTEGRATION OF ULTRASOUND

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Background: Although the CASPAR criteria in the diagnosis of psoriatic arthritis (PsA) have been validated, CASPAR based on physical examination (PE) is not "gold standard". The ultrasound (US) could improve the diagnostic accuracy as compared to clinical examination alone.
Objectives: To evaluate the diagnostic performance of CASPAR criteria for psoriatic arthritis (PsA) with or without integration of ultrasound (US).
Methods: The patients with hint of PsA were enrolled. Tender and swollen joint counts, presents of enthesitis and dactylitis were collected by physical examination (PE). US was performed to evaluate peripheral joints, entheses and tendons. The additional value of US to CASPAR criteria were analysed.
Results: 326 consecutive patients were enrolled, with 164 PsA and 162 non-PsA. Significantly higher frequencies of tenosynovitis and enthesitis on US and new bone formation on X-ray were found in PsA than non-PsA patients (56.7% vs. 13.0%; 62.2% vs. 14.2%; 62.2% *vs*. 8.0%, $p<0.01$ for all). Logistic regression analysis showed that dactylitis (OR=12.0, $p<0.01$), family history of PsO/PsA (OR=3.1, $p<0.05$), nail involvement (OR=3.5, $p=0.01$), new bone formation (OR=14.8, $p<0.01$) and tenosynovitis on US (OR=21.3, $p<0.01$), enthesitis on US (OR=21.7, $p<0.01$) were independent risk factors for PsA. Adding US tenosynovitis and/or enthesitis to CASPAR criteria showed better performance by improving the specificity (91.4% *vs.* 67.9%) and meanwhile keeping sensitivity (92.1% *vs.* 96.3%). When replacing hand X-ray by US in CASPAR criteria, the sensitivity and specificity were comparable to CASPAR criteria adding with US. The diagnostic accuracy was 82.2% for CASPAR criteria based on PE, 91.7% for CASPAR integrated with US, and 91.4% for CASPAR with US to replace X-ray.
Conclusion: CASPAR criteria based on US improve the diagnosis utility of PsA than CASPAR criteria based on PE. US assessment is valuable in the diagnosis of PsA.

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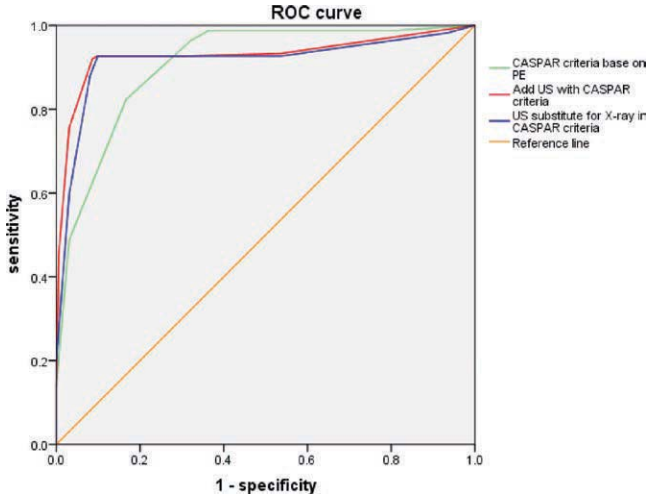

Figure 1. ROC curves for adding US or substituting X-ray by US in CASPAR criteria. Receiver operating characteristic (ROC) curve illustrates the diagnosis performance of CASPAR criteria adding US or substituting X-ray by US in CASPAR criteria and CASPAR criteria based on PE alone. The area under the curve of the ROC curve (AUC) was 0.929 (95%CI 0.897, 0.961) (p<0.01) for adding US to CASPAR criteria. AUC was 0.908 (95%CI 0.876, 0.940) (p<0.01) for CASPAR criteria based on PE. And AUC was 0.916 (95%CI 0.880, 0.951) (p<0.01) for substituting X-ray by US in CASPAR criteria. CASPAR: ClASsification criteria for Psoriatic ARthritis; PE: physical examination; US: ultrasound.

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POS0316

SEMIQUANTITATIVE ASSESSMENT OF SYNOVITIS ON US-GUIDED SYNOVIAL MEMBRANE BIOPSIES IS CONTINGENT ON DISEASE PHASE AND PREDICTIVE OF TREATMENT RESPONSE IN NAIVE TO TREATMENT PSORIATIC ARTHRITIS

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Background: Ultrasound (US)-guided minimally invasive Synovial Tissue (ST) biopsy serves as a safe and well tolerated procedure for basic and translational research on chronic inflammatory joint disease.
Objectives: (i) to assess the diagnostic value of the Krenn score (KSS) on ST samples obtained from US-guided biopsies in a large bio-samples dataset of patients with Psoriatic Arthritis (PsA) across different disease phases; (ii) to develop a multiparametric nomogram integrating clinical and histological characteristics enabling treatment response prediction in naïve to treatment PsA.
Methods: 410 patients fulfilling the CASPAR criteria for PsA who underwent US-guided ST biopsy were enrolled. At baseline, patients were categorized based on their disease phase and treatment: n=207 naïve to DMARDs; n=101 resistant to c-DMARDs; n=48 resistant to b-DMARDs and n=54 in sustained clinical and ultrasound remission or in low disease activity (LDA) state (DAPSA ≤ 4 or among 4-14, respectively). Clinical, demographic, and immunological characteristics were recorded for each patient. All ST specimens were stained with H&E and classified by a pathologist, blinded to clinical characteristics, using the Krenn score to assess ST inflammation degree (1) implemented with the determination of lymphocytes, plasma cells, granulocytes and tissue oedema presence. Each naive to treatment PsA was treated according to the EULAR recommendations (2) and DAPSA remission rate at 6 months was recorded.
Results: Considering the whole enrolled cohort, the distribution of KSS was significantly different among patients across the different PsA phases (ANOVA p<0.001). In particular, among the different phases, KSS was significantly higher in b-DMARDs resistant (p<0.0001) and c-DMARDs resistant (p<0.0001) compared to remission/LDA disease patients as well as naive to treatment PsA (p<0.0001). Interestingly, regardless to the disease phase, KSS of the biopsied joint directly correlated to disease activity in terms of DAPSA (r=0.476, p<0.001) and DAS28 scores (r=0.476, p<0.001). Considering the naïve to treatment PsA cohort, patients achieving DAPSA defined-LDA/remission had, before treatment, significantly lower KSS (p<0.001), lower rate of ST plasmacells presence (p<0.001) and shorter symptoms duration (p=0.01) as compared to naïve to treatment PsA not achieving this clinical outcome. Moreover, considering distinct clinical phenotype domains, naive to treatment PsA patients with concomitant dactylitis and skin disease were less likely to achieve DAPSA LDA/remission (p<0.001), regardless of treatment scheme. On logistic regression, at baseline, having a KSS <5 [OR: 5.30 (95%CI:2.21-12.74) p<0.001], absence of plasma cells ST infiltrate [OR: 3.87 (2.11-7.10 95%CI) p<0.001], concomitant dactylitis [OR: 2.55 (95%CI:1.24-5.25) p=0.01] and skin involvement [OR: 2.06 (95%CI:1.17-3.62) p=0.01] were independent factors associated with DAPSA score-LDA/remission achievement at 6 months. Finally, a multiparametric nomogram integrating baseline clinical and histological characteristics of naïve PsA enabling to predict up to 75% of probability to achieve DAPSA remission at 6 months was developed.
Conclusion: KSS is a reliable tool for synovitis assessment in PsA, being contingent on disease phases, related to disease burden and included within a treatment response predictive multiparametric nomogram in naïve PsA.

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Mortality, Co-morbidity and disease burden

POS0317

WORLD MORTALITY OF SPONDYLOARTHRITIS AND INFLAMMATORY BOWEL DISEASES IN 2015 AND ITS EVOLUTION BETWEEN 2001 AND 2015

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Background: There is little epidemiological data on mortality in spondyloarthritis (SpA).
Objectives: To determine countries' mortality rates of ankylosing spondylitis (AS) and psoriatic arthritis (PsA), as well as chronic inflammatory bowel diseases (IBDs), which are physiologically related to SpA, and to describe their evolution between 2001 and 2015.
Methods: We used mortality data from the World Health Organisation (WHO), freely available on its website, which shows the number of deaths classified by age, sex, and cause of death coded by ICD-10. The code M45 was used for AS, L405 for PsA, K50 for Crohn's disease (CD), and K51 for ulcerative colitis (UC). Age-standardized mortality rates (ASMR) were constructed using the 2015 WHO reference population and are expressed as deaths per million inhabitants. Temporal trend analyses of ASMR were performed between 2001 and 2015, considering only countries with up to 3 years of missing data, using joinpoint regression.
Results: In 2015, the global ASMR of AS was 0.13 (0.11-0.14), ranging from 0.02 in Japan to 2.00 in Iceland (Figure 1A). The ASMR was 0.20 (0.18-0.23) for men and 0.07 (0.06-0.09) for women (p<0.0001). The trend analysis did not show any significant variation between 2001 and 2015. The ASMR in Europe (0.17 (0.15-0.20)) was significantly higher than in North America (0.12 (0.09-0.14)) (p=0.008), South America (0.09 (0.06-0.12)) (p=0.0001) and Asia (0.08 (0.05-0.10)) (p<0.0001).

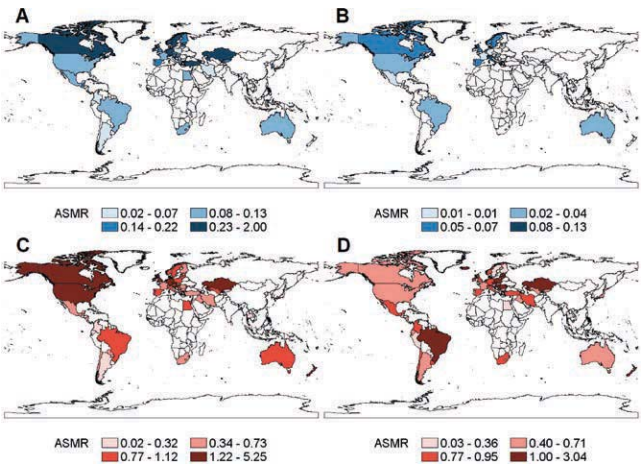

Figure 1. 2015 ASMR by country for ankylosing spondylitis (A), psoriatic arthritis (B), Crohn's disease (C) and ulcerative colitis (D).

For PsA, the global ASMR in 2015 was 0.04 (0.03-0.05), ranging from 0.01 in Mexico to 0.13 in Greece (Figure 1B). The ASMR was 0.06 (0.04-0.07) for men and 0.03 (0.02-0.04) for women (p=0.01). The trend analysis showed a significant increase from 2004 to 2015 with a mean annual percent change (APC) of 5.94% (p=0.02). The ASMR in Europe (0.05 (0.03-0.06)) was significantly higher than in South America (0.02 (0.00-0.03)) (p=0.02).

For CD, the global ASMR in 2015 was 0.86 (0.82-0.89), ranging from 0.02 in Thailand to 5.25 in Luxembourg (Figure 1C). The ASMR was 0.41 (0.38-0.43) for men and 0.38 (0.36-0.41) for women (p=0.17). The trend analysis showed a significant decrease from 2001 to 2015 with a mean APC of -0.82% (p=0.048). The ASMR in Europe (1.12 (1.05-1.19)) was significantly lower than in North America (1.31 (1.21-1.41)) (p=0.001), but significantly higher than in Latin America (0.57 (0.51-0.64)) (p<0.0001) and Asia (0.27 (0.23-0.32)) (p<0.0001).

For UC, the global ASMR in 2015 was 0.76 (0.73-0.79), ranging from 0.03 in Thailand to 5.48 in Saint Lucia (Figure 1D). The ASMR was 0.37 (0.35-0.39) for men and 0.23 (0.21-0.24) for women (p<0.0001). The trend analysis showed a significant decrease from 2001 to 2015 with a mean APC of -1.29% (p=0.01). The ASMR in Europe (1.00 (0.93-1.06)) was significantly higher than in North America (0.64 (0.57-0.71)) (p<0.0001), Africa (0.57 (0.41-0.72)) (p<0.0001), South America (0.84 (0.76-0.91)) (p=0.003)), Asia (0.47 (0.93-1.06)) and Oceania (0.58 (0.38-0.79)) (p=0.003).

Conclusion: ASMR for IBD are higher than those for SpA and are decreasing over time, in contrast to SpA where they remain essentially stable. There are geographical disparities which must be interpreted with caution due to the declarative nature of the data.

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POS0318 CHRONIC WIDESPREAD PAIN AND MORTALITY - A 25 YEAR FOLLOW UP

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Background: Chronic widespread pain (CWP) has been suggested as a risk for mortality in especially cardiovascular diseases and malignancies (1, 2). Most studies are based on the CWP definition that is part of ACR1990 criteria for fibromyalgia (3). The ACR1990 definition has been criticized for being too including, and recently a more stringent definition, the WP2019, has been suggested (4). It is yet to be investigated how the more stringent WP2019 definition compares to the ACR1990 definition regarding excessed mortality and certain causes of death.

Objectives: To study if overall mortality and common causes of death are increased among people with CWP in a 25 year follow up of a cohort from the general population. Additionally, to study if the definition of CWP, according to ACR1990 or WP2019, influences these outcomes.

Methods: A 25-year follow up of the EPIPAIN cohort study that in 1995 included 2425 person from the general population (5). They were at baseline divided into three pain groups: CWP, chronic regional pain (CRP) and no chronic pain (NCP). CWP was defined according to both the ACR1990 ($CWP_{ACR1990}$) and the more stringent WP2019 (CWP_{WP2019}) criteria. Deaths and causes of death were derived from the official national Swedish register. Mortality, adjusted for age, sex, socioeconomic status, and smoking habits, was analyzed with Cox regression and presented as Hazard Ratios (HR).

Results: An overall increased mortality was predicted by CWP_{WP2019} (HR 1.32, p = 0.033), but not by $CWP_{ACR1990}$ (HR 1.08, p = 0.484), compared to NCP. An increased mortality in diseases of the circulatory system was predicted by CWP_{WP2019} (HR 1.70, p= 0.016), but not by $CWP_{ACR1990}$ (HR 1.35, p=0.128). Neither definition of CWP, CWP_{WP2019} (HR 1.35, p= 0.176) or $CWP_{ACR1990}$ (HR 1.21, p=0.327) predicted a significantly increased mortality for neoplastic diseases overall.

Conclusion: The WP2019 definition of CWP enhanced the association between CWP and increased mortality, and especially mortality in diseases of the circulatory system. This suggests that the CWP_{WP2019} definition captures a more vulnerable subset of the population that should be assessed for other cardiovascular risk factors in the clinic.

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POS0319 DISEASE BURDEN OF PRIMARY SJOGREN SYNDROME: A RETROSPECTIVE UNITED STATES CLAIMS DATABASE STUDY

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Background: Primary Sjögren's syndrome (pSjS) is a chronic and complex systemic autoimmune disease, primarily characterised by inflammation and progressive destruction of the exocrine glands (ie, autoimmune epithelitis) [1].

Objectives: We evaluated disease progression, treatment patterns, mortality, and healthcare resource utilization (HCRU) of pSjS patients in the United States (US) to understand the real-world experiences of patients with pSjS.

Methods: This retrospective cohort study utilised data from US Optum Clinformatics claims between 01 May 2000 and 31 December 2020. The study included pSjS patient cohort and general population cohort, matched (1:1) on age, sex, and index date. Baseline period of 365 days prior to the index date was used for assessment of baseline comorbidities. Descriptive statistics were used to describe baseline characteristics, HCRU, and treatment pattern while multivariable models were used to assess hazard ratios (HRs) and risk factors.

Results: Overall, 23,168 patients with pSjS (ICD-9 710.2 Sicca syndrome and ICD-10 M 35.0 Sjogren Syndrome and excluding patients with Rheumatoid arthritis [RA], Systemic sclerosis [SS] and Systemic lupus erythematosus [SLE] diagnoses codes) were included in the cohort (mean [SD] age: 61.5 [15.3] years; females: 85%). At baseline, 79.4% and 8.2% of pSjS patients had systemic complications and organ-specific autoimmune comorbidities, respectively. In a subset of the cohort including patients with at least 5 years of follow-up, by the end of 5 years 96.8% and 16.5% of patients developed systemic complications and organ-specific autoimmune comorbidities, respectively (Table 1). The most frequently occurring organ-specific autoimmune comorbidities over the 5-year follow-up included Graves disease (5.4%), Hashimoto disease (3.7%), and discoid/ subacute cutaneous lupus erythematosus (3.5%). Mortality was reported in 7.4% of the patients during 5-year follow-up. Risk factors associated with higher mortality included systemic complications in renal (HR [95% CI]: 2.29 [2.09–2.52]), cardiovascular (HR [95% CI]: 2.42 [2.19–2.67]), lungs (HR [95% CI]: 3.73 [3.41–4.09]) and haematological domains (HR [95% CI]: 2.83 [2.56–3.13]), non-Hodgkin's lymphoma (HR [95% CI]: 2.58 [2.12–3.14]), and primary biliary cirrhosis (HR [95% CI]: 2.17 [1.60–2.96]). Corticosteroids (28.2%), hydroxychloroquine (15.7%), and cyclosporine (10.9%) were most frequently used medications. During the year following the first pSjS diagnosis, defined as the first claim with the Sjogren Syndrome ICD code (index date), the mean all-cause healthcare costs have increased by 27% from $21,634 to $27,526 per patient per year.

Table 1. Occurrence of systemic complications and organ-specific autoimmune comorbidities over follow-up of 5 years

Variable, n (%)	Baseline (N=6000)	Within 5 years (N=6000)
Any systemic complication	**4,555 (75.9%)**	**5,806 (96.8%)**
Articular involvement	3,176 (52.9%)	5,026 (83.8%)
Renal involvement	352 (5.9%)	1,185 (19.8%)
Cardiovascular complications	342 (5.7%)	826 (13.8%)
Muscles	1,390 (23.2%)	2,732 (45.5%)
Pancreatic	31 (0.5%)	88 (1.5%)
Lungs	373 (6.2%)	1,383 (23.1%)
Peripheral nervous system	766 (12.8%)	2,109 (35.2%)
Haematological	1,016 (16.9%)	2,507 (41.8%)
Glandular	542 (9.0%)	2,274 (37.9%)
Central nervous system	212 (3.5%)	556 (9.3%)
Biological	153 (2.6%)	408 (6.8%)
Skin	517 (8.6%)	1,327 (22.1%)
Lymphadenopathy	374 (6.2%	959 (16.0%)
Non-Hodgkin's lymphoma	59 (1.0%)	131 (2.2%)
Any organ-specific autoimmune disease	**464 (7.7%)**	**992 (16.5%)**

Conclusion: These results provide additional evidence that pSjS is associated with substantial morbidity and clinical burden supporting the need for safe and efficacious disease modifying treatment options in this patient population.

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POS0320 EPIDEMIOLOGY AND HEALTHCARE RESOURCE UTILIZATION OF PATIENTS WITH EGPA IN THE UNITED KINGDOM

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is characterized by eosinophilic inflammation of small with or without medium arteries. EGPA is a rare disease with varying prevalence and incidence rates globally. To date, limited information is available on the prevalence, incidence and burden of disease in the United Kingdom (UK).

Objectives: The objectives were to estimate the prevalence and incidence of EGPA, and to describe the healthcare resource utilization (HCRU) among patients with EGPA in the UK.

Methods: This retrospective database study used the UK-based Clinical Practice Research Datalink (CPRD)-AURUM database linked to the Hospital Episode Statistics (HES). Prevalence was estimated from 2005 to 2019, and incidence was estimated from 2006 to 2019. HCRU was assessed in the 12-months following the first recorded diagnosis of EGPA (index date), and included hospitalizations, emergency room visits, procedures, outpatient specialist visits, primary care visits, and oral corticosteroid use.

Results: 764 people were identified with EGPA in the UK. The prevalence of EGPA, reported in the database, increased from 22.7 to 45.6 per 1,000,000 persons from 2005 to 2019 (Figure 1), whereas the incidence of EGPA from 2006 to 2019 ranged from 2.28 to 4.00 per 1,000,000 person-years. 377 patients with EGPA were successfully linked to the CPRD-HES database. Patient characteristics were as follows: mean age (SD) was 57 years (14.2); 49% were male; 81% had asthma; and 11% had peripheral neuropathy prior to the index date. For patients with EGPA, 19% had an EGPA-related hospitalization and 50% had any-cause hospitalization within 1 year of the index date (Table 1). The mean length of stay was, 18 days and 16 days for EGPA-related and any-cause hospitalizations, respectively. 52% of patients with EGPA had undergone a medical procedure, 89% of patients with EGPA had an outpatient visit to a specialist. Almost all patients with EGPA visited a general practitioner within 1 year of their EGPA diagnosis (97%) and averaged 16.0 visits in 1 year. A significant proportion of the EGPA population were prescribed OCS; most EGPA patients had a prescription in the 0–3 months after the index date (64%), and patients on average had a prescription for OCS for 6 out of the 12 months after the index date.

Table 1. HCRU among patients with EGPA

HCRU	Number of patients N (%) [total days]	Number of events per patient, Mean (SD)
Total EGPA cohort (N)	377	
EGPA-specific hospitalizations	72 (19.10)	1.2 (1)
EGPA-specific hospitalizations	[1283]	17.8 (23.3)
length of stay		
Any-cause hospitalizations	188 (49.87)	1.7 (1)
Any-cause hospitalizations length of stay	[2992]	15.9 (23.7)
Any-cause A & E events	19 (5.04)	1.8 (2)
Any-cause outpatient visits	334 (88.59)	9.8 (7)
Any procedures undertaken	196 (51.99)	6.8 (6)
General Practitioner visits	366 (97.08)	16.0 (11)

A&E, Accident and Emergency; EGPA, eosinophilic granulomatosis with polyangiitis; HCRU, healthcare resource utilization.

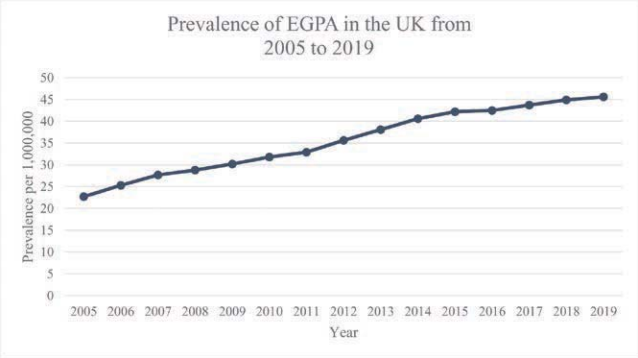

Figure 1. Prevalence of EGPA in the UK from 2005 to 2019Prevalence is expressed as cases per 1,000,000 persons. EGPA, eosinophilic granulomatosis with polyangiitis; UK, United Kingdom.

Conclusion: The prevalence of EGPA increased over the study period in the UK, and the data show significant HCRU within 1 year of the first recorded diagnosis of EGPA. Almost all of the patients with EGPA were found to frequently visit the primary care physician and seek specialist care, and almost half required hospitalization. Funding: GSK [207888]

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POS0321 CO-MORBIDITY IN POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) is the most common autoimmune musculoskeletal condition in the developed world, with UK prevalence of 1.7% in those aged older than 55 years. Current guidelines recommend glucocorticoid treatment for one to two years. Since PMR affects older individuals and is associated with prolonged treatment with glucocorticoids, patients are at risk of developing or worsening co-morbidity.

Objectives: This national study aimed to establish the prevalence of PMR from routinely recorded administrative care records from community-based primary care practices; secondly to calculate the most common comorbidities and their relative risk amongst those diagnosed with PMR.

Methods: The ECLIPSE databased covers over 23m patients across 2400 general practices in England and provides insights for enhanced clinical pathway management and to support patient safety in primary care. Routinely recorded diagnoses from primary care data are updated daily, along with administrative prescribing data. Using standardised nationally agreed disease coding frameworks, all diagnoses of PMR were retrieved from the live patient population of 23.3m individuals registered with general practices across England. Comorbidity was recorded similarly. Diagnoses of PMR were categorised in 12-month bands since their date of diagnoses to examine the rates of prednisolone prescription by time since diagnosis.

Results: Amongst the 23.3 million patient care records there were 146,252 diagnoses of PMR, resulting in a prevalence of 2.2% for those aged older than 55 years. The average age of those with PMR was 77.5 years. There were between 9863 to 11036 diagnoses of PMR made each year over the past five years. The proportion of those receiving prednisolone were highest amongst those most recently diagnosed: 76.4% for those in the last year; 48.4% for those diagnosed between a year and two years ago; 33.0% for those diagnosed between two to three years ago; 28.8% for those diagnosed between three to four years ago, and 24.9% for those diagnosed between four to five years ago. On average each patient with PMR had 3.5 co-morbid conditions and was prescribed 5.4 different medications. The top ten co-morbid conditions were, in rank order: hypertension (53.6%), osteoarthritis (48.6%), anxiety and depression (27.5%), chronic kidney

disease (24.3%), type II diabetes (18.9%), ischaemic heart disease (14.9%), atrial fibrillation (13.7%), asthma (12.7%), COPD (7.9%), and heart failure (6.2%).
Conclusion: Routinely recorded GP records provide prevalence estimates that are similar to previously published descriptive epidemiological studies, and despite guidelines recommending shorter courses of treatment, show the rates of prednisolone prescription remain high, years after diagnosis. Furthermore, due to the age of onset of PMR, this results in a patient population with high levels of co-morbidity many of whom are at increased risk due to prolonged glucocorticoid use. These data are crucial for developing risk stratification and population health management tools.
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POS0322 CARDIOVASCULAR RISK FACTORS AND RISK OF GIANT CELL ARTERITIS AND/OR POLYMYALGIA RHEUMATICA: RESULTS FROM THE FRENCH E3N COHORT STUDY

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two associated inflammatory diseases with incompletely known common pathophysiological mechanism. Cardiovascular (CV) risk factors have been thought to play a role in the underlying chronic vascular inflammation involved in GCA and PMR pathophysiology. However, available data on CV risk factors are conflicting.
Objectives: To investigate the association between CV risk factors and the risk of GCA and/or PMR in a large prospective cohort of French women.
Methods: The E3N cohort study (*Etude Epidémiologique auprès des femmes de la Mutuelle générale de l'Education Nationale*) is a French prospective cohort including 98,995 French women born between 1925 and 1950, recruited in 1990. They completed biennially mailed questionnaires to update their health-related information. A validation study based on the use of a specific GCA/PMR questionnaire and medication reimbursement database was conducted prior to this study. The history of CV risk factors (hypertension, type 2 diabetes, dyslipidemia, active smoking status and family history of cardiovascular disease) was self-reported at each questionnaire. Hazard ratios (HRs) and their 95% confidence intervals (95%CIs) for incident GCA and/or PMR were estimated by Cox proportional hazards regression models with age as the time scale. Multi-adjusted models included all CV risk factors and educational level. Further analyses were conducted to separately analyse the risk of incident GCA and of PMR.
Results: The overall population included 79,804 women, during a total follow-up of 1,899,742 person-years. Among them, 399 incident GCA and/or PMR cases were identified (incidence 31/100,000 person-years): 282 PMR alone, 112 GCA cases, and 5 patients who could not be classified. Incident GCA/PMR cases were diagnosed after a mean of 17.9 (± 5.2) years after recruitment. Mean age at diagnosis was 69 (± 7.2) years. Type 2 diabetes was inversely associated with risk of incident GCA/PMR in age-adjusted and multivariable models (HR 0.41; 95%CI 0.2–0.9 in multivariate model). Other CV risk factors such as hypertension, smoking status, dyslipidaemia, familial history of cardiovascular events were not associated with incident GCA/PMR (Table 1). The inverse association remained statistically significant when studying separately the risk of incident PMR (HR 0.3; 95%CI 0.09–0.91) but no longer with incident GCA (HR 0.5; 95%CI 0.1–2.0), probably due to a reduced statistical power.
Conclusion: Type 2 diabetes was associated with a decreased risk of subsequent GCA/PMR development. Further work should be carried out to determine potential mechanisms, and especially to analyze the respective role of diabetes itself and its treatments.
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POS0323 RISK FACTORS FOR MAJOR CARDIOVASCULAR EVENTS (MACE) IN INFLAMMATORY ARTHRITIS: A TIME-DEPENDENT ANALYSIS ON INFLAMMATORY BURDEN, USE OF NSAIDS, STEROID AND DMARDS

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Background: Inflammatory arthritis (IA) including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylarthritis (AS) are associated with accelerated atherosclerosis due to systematic inflammation.
Objectives: To elucidate whether inflammatory burden (c-reactive protein [CRP] and erythrocyte sedimentation rate [ESR] levels) and drugs used to suppress inflammation (disease modifying anti-rheumatic drugs [DMARDs] and non-steroidal anti-inflammatory drugs [NSAIDs]) over time are independently associated with major cardiovascular events (MACE) in patients with IA.
Methods: A population-based cohort of IA patients were identified in the city-wide Clinical Data Analysis and Reporting System (CDARS) of the Hong Kong Hospital Authority. IA patients recruited from 2006 to 2016 were followed until the end of 2018. The outcome was occurrence of a first MACE, defined as unstable angina, acute myocardial infarction, stroke/transient ischemic attack or death from cardiovascular causes. Cox proportional hazard models with time-varying

Table 1. Hazard ratios for the risk incident GCA and/or PMR according to cardiovascular risk factors

	NON-CASES N=79,405	GCA/PMR CASES N=399	M1	M2
	Number (%)	Number (%)	HR [95%CI]	HR [95%CI]
Smoking status				
Never-smoker	42,2745 (53.2)	233 (58.4)	Reference	Reference
Past smoker	30,824 (38.8)	134 (33.6)	0.91 [0.74;1.13]	0.90 [0.73; 1.12]
Current smoker	6,307(7.9)	32 (8.0)	1.05 [0.72; 1.52]	1.04 [0.72; 1.51]
High-blood pressure				
No hypertension	38,813 (48.9)	210 (52.6)	Reference	Reference
Hypertension	40,592 (51.1)	189 (47.4)	0.84 [0.89; 1.03]	0.85 [0.69; 1.04]
Type 2 diabetes				
No diabetes	75,704 (95.3)	386 (96.7)	Reference	Reference
Diabetes	3,701 (4.7)	13 (3.3)	**0.41 [0.18; 0.91]**	**0.41 [0.18; 0.92]**
BMI				
<25 kg/m2	52,054 (65.6)	269 (67.4)	Reference	Reference
≥ 25 kg/m2	27,351 (34.4)	130 (32.6)	1.01 [0.82; 1.25]	1.06 [0.85; 1.31]
Dyslipidemia				
No	43,944 (55.3)	237 (59.4)	Reference	Reference
Yes	33,169 (41.8)	147 (36.8)	1.17 [0.94; 1.44]	1.18 [0.95; 1.45]
Familial history of cardiovascular disease				
No	64,878 (81.7)	336 (84.2)	Reference	NA
Yes	3,121 (3.9)	20 (5.0)	1.30 [0.85; 2.09]	NA

M1: Adjusted for age and educational level educational level (<high school, up to 2 years of university, > 3 years of university),M2: M1+ smoking status, body mass index(kg/m2), hypertension, diabetes, dyslipidemia

CRP and ESR levels and drugs used were analyzed to identify the risk of having MACE in IA patients.

Results: A total of 17,732 (12050 RA patients, 1789 PsA patients and 3893 AS patients) patients with IA were recruited. After a mean follow-up of 8.7 ± 3.1 years, 1,069 (6.0 %) patients developed a first MACE. At baseline, the MACE group were older (68±12 vs 53±15, p<0.001), had more traditional cardiovascular risk factors, higher levels of CRP (2.7±1.5 vs 1.7±1.3, p<0.001) and ESR (57.8±32.4 vs 42.5±29.2, p<0.001), and less exposure to biologic DMARDs (bDMARDs) (1.0% vs 3.0%, p<0.001) and non-selective NSAIDs (nsNSAIDs) (63.4% vs 71.1%, p<0.001). After adjusting for age, sex, baseline cardiovascular comorbidities using multivariable Cox regression analysis, IA patients with higher inflammatory burden (as reflected by the time-varying CRP [hazard ratio {HR} 1.11, 95% confidence interval {CI} 1.10-1.12, p<0.001] and ESR levels (HR 1.02, 95% CI 1.01-1.01, p<0.001) and the use of steroid (HR 1.79-1.88) were independently associated with a higher risk of developing MACE (Table 1). In contrast, exposure to nsNSAIDs had a protective effect against MACE (HR 0.76, 95% CI 0.66-0.89, p<0.001), while bDMARDs were not associated with MACE.

Table 1. Multivariable time-varying Cox regression models for the predictors of incidence of MACE in the IA patients (n=17732)

	Model 1 †		Model 2 ‡	
Variables	**HR (95% CI)**	***p* value**	**HR (95% CI)**	***p* value**
Male	1.92 (1.65-2.23)	<0.001*	1.52 (1.33-1.76)	<0.001*
Age	1.06 (1.05-1.06)	<0.001*	1.06 (1.05-1.06)	<0.001*
Disease duration	1.04 (0.97-1.08)	0.056	1.04 (1.01-1.08)	0.016*
Baseline DM	1.25 (0.95-1.64)	0.108	1.44 (1.13-1.84)	0.003*
Baseline HT	1.77 (1.52-2.08)	<0.001*	1.85 (1.59-2.16)	<0.001*
Baseline LP	1.14 (0.92-1.41)	0.232	1.19 (0.98-1.46)	0.081
Time-varying inflammatory markers				
ESR	1.02 (1.01-1.01)	<0.001*		
CRP			1.11 (1.10-1.12)	<0.001*
Time-varying treatment				
bDMARDs	0.93 (0.68-1.27)	0.657	0.89 (0.65-1.22)	0.478
CoxII	0.71 (0.53-0.96)	0.027*	0.79 (0.59-1.04)	0.104
nsNSAIDs	0.76 (0.66-0.89)	<0.001*	0.76 (0.66-0.88)	<0.001*
Steroids	1.88 (1.63-2.17)	<0.001*	1.79(1.56-2.04)	<0.001*

*Statistically significant at p < 0.05. † and ‡ Adjusted for Age, Sex, Hypertension at baseline, diabetes mellitus at baseline, dyslipidemia at baseline, bDMARDs, CoxII, non-selective NSAIDs, Steroids. CRP, C-reactive protein; ESR: Erythrocyte sedimentation rate; HT: hypertension; DM: diabetes mellitus; LP: Dyslipidemia; bDMARD, biological disease-modifying anti-rheumatic drug; COXII: cyclooxygenase -2 inhibitors; nsNSAIDs: non-selective nonsteroidal anti-inflammatory drugs.

Conclusion: Increased inflammatory burden as reflected by elevated ESR and CRP level over time, and increased exposure to steroid were independently associated with increased risk of MACE, while the risk was significantly reduced with non-selective NSAIDs use in IA patients.

Disclosure of Interests: None declared

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POS0324 RISK OF CARDIOVASCULAR COMORBIDITIES IN RHEUMATIC DISEASES

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Background: Cardiovascular diseases (CVD's) are the most significant comorbidities in rheumatic diseases, causing also increased mortality. [1,2] However, there is only limited data on how the risk of CV comorbidities varies between different rheumatic diseases.

Objectives: The aim of our study was to estimate the risk of certain CV comorbidities across rheumatic diseases.

Methods: The ongoing FinnGen project links nationwide healthcare register data with genome data. The study (data freeze 7) included 321 302 individuals, and from this group we identified patients with seropositive (N=4293) and seronegative (N=1733) rheumatoid arthritis (RA), ankylosing spondylitis (AS, N=1247), psoriatic arthritis (PsA, N=1235), systemic lupus erythematosus (SLE, N=386), primary Sjogren's syndrome (pSS, N=557) and gout (N=2178). Each patient was matched based on age, sex and municipality of residence with twenty individuals without any rheumatic conditions. The CV comorbidities studied were any CV disease (CVD), major coronary heart disease event (myocardial infarction and/or revascularization; CHD), ischemic stroke, atrial fibrillation and flutter (AF), deep vein thrombosis of lower extremities (DVT) and pulmonary embolism (PE), chronic heart failure (CHF) and valvular heart disease excluding rheumatic fever (VHD). From the prevalence of each CV disease among rheumatic disease cohorts, we calculated the risk ratio (RR) for each CV disease by comparing the prevalence of these diseases between rheumatic diseases and controls.

Results: The average age at the time of diagnosis ranged from 39.6 to 64.4 years, and the average duration of follow-up varied from 9 to 19.5 years in different rheumatic diseases. The risk for any CVD was elevated in all rheumatic disease cohorts with RR varying from 1.14 in seropositive RA to 1.65 in SLE. SLE patients carried the highest relative risk for CV comorbidities, demonstrating over 2.5-fold risk for DVT/PE (RR 3.57), stroke (RR 2.57), CHF (RR 2.64) and VHD (RR 2.98). At least two-fold risk compared to controls was identified for AF (RR 2.03), DVT/PE (RR 2.44) and CHF (RR 3.03) in patients with gout, for DVT/PE (RR 2.15) and CHF (RR 2.0) in patients with pSS, and for DVT/PE (RR 2.03) in patients with PsA. Seropositive and seronegative RA demonstrated similar CV risk profiles. In patients with seropositive or seronegative RA, PsA, pSS or SLE, DVT/PE demonstrated the highest RR's among various CV comorbidities.

Conclusion: The risk of CV comorbidities is increased in all studied rheumatic diseases, with the largest effects observed in patients with SLE and gout. Among CV comorbidities, DVT/PE displayed the largest effect sizes in several rheumatic diseases. The current results further strengthen the importance of evaluating and treating risk factors for CV comorbidities across rheumatic diseases, focusing also to the excess risk for thromboses.

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POS0325 THE ASSOCIATION BETWEEN OBESITY, SOCIOECONOMIC POSITION AND KNEE JOINT REPLACEMENT SURGERY IN PATIENTS WITH OSTEOARTHRITIS: RESULTS FROM THE ENGLISH LONGITUDINAL STUDY OF AGEING

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Background: Evidence suggests that associations of lower socioeconomic position (SEP) with increased incidence of osteoarthritis (OA) are partially mediated by obesity. Obesity and lower SEP are also associated with increased symptoms in OA (i.e. pain/function). However, few studies have investigated whether obesity and lower SEP are also associated with increased risk of knee joint replacement surgeries (kJRS).

Objectives: To investigate the relationships of obesity and SEP at time of diagnosis with kJRS at follow-up in people with knee OA (kOA).

Methods: The English Longitudinal Study of Ageing is a nationally representative panel study of adults aged ≥50 years with biannual waves of data collection (2002–2019). Participants who self-reported OA diagnosis for the first time

in waves 2–8 and knee pain in the same or previous wave of diagnosis were defined as having kOA (baseline). Participants with at least one body mass index (BMI) measurement and one follow-up assessment were included. Underweight/normal weight, overweight and obesity were defined using BMI <25 kg/m^2, 25–30 kg/m^2 and ≥30kg/m^2, respectively. Education, occupation (current or last occupation if retired), wealth quintiles (all individual-based) and index of multiple deprivation quintiles (area-based) were used as SEP indicators. Outcome was the first self-reported kJRS (left or right knee) in waves 3–9. Cox proportional hazards models were used to investigate the associations of obesity and SEP with kJRS, controlling for baseline covariates. Person year follow up was calculated from baseline to either a) date of self-reported kJRS, b) loss to follow-up, c) end of follow-up (wave 9).

Results: The analysis sample included 1499 people who reported kOA and had ≥1 BMI measure (62.3% female; mean age 66.5y (SD 9.4); 96% white; 47.4% obese). Number of person-years included in the analysis was 8427. Over a mean follow-up of 4.7 years (SD 2.8), 144 (9.6%) reported having kJRS. Obese kOA patients were more likely to report kJRS than non-obese patients (adjHR 1.89 (95% CI 1.33, 2.68)), independent of age, gender, SEP, cardiovascular disease (self-reported) and HbA1c values (measured from collected blood samples). Education and occupation were not associated with kJRS. However, those living in the most deprived areas and with the least amount of wealth were less likely to undergo kJRS compared with the least deprived and wealthiest (HRs adjusted for age and gender 0.37 (95% CI 0.19, 0.73) and 0.55 (95% CI 0.33, 0.93), respectively). There was no evidence of interactions between obesity and SEP indicators.

Conclusion: Obesity increased the likelihood of undergoing kJRS in kOA patients. Therefore, reducing obesity in kOA patients may help to reduce the need for kJRS. Area-deprivation and lower wealth were associated with lower likelihood of kJRS. Taken together with findings from other studies which report associations between lower SEP and worse OA symptoms, our results suggest that there may be social inequalities in the provision of kJRS in England.

Table 1. The relationships between obesity at baseline and rates of knee joint replacement surgery over a mean of 4.7 (SD 2.8) years in follow-up in those with knee OA at baseline in the English Longitudinal Study of Ageing

	HR (95% CI)			
Predictors	Unadjusted	Adjusted for age and gender	Adjusted for age, gender and SEP	Adjusted for age, gender, SEP, CVD and HbA1c
Obesity	1.56 (1.12, 2.17)	1.63 (1.17, 2.28)	1.77 (1.26, 2.50)	1.89 (1.33, 2.68)
Non-obesity	ref	ref	ref	ref
Obesity	3.53 (1.77, 7.02)	3.58 (1.80, 7.12)	4.01 (2.01, 8.03)	4.35 (2.16, 8.74)
Overweight	2.91 (1.43, 5.91)	2.81 (1.38, 5.73)	2.93 (1.44, 5.98)	2.98 (1.46, 6.09)
Underweight/normal weight	ref	ref	ref	ref
BMI per 1 kg/m^2 increment	1.05 (1.02, 1.07)	1.05 (1.03, 1.08)	1.06 (1.04, 1.09)	1.07 (1.04, 1.10)

HR, hazard ratio; CI, confidence interval; SEP, socioeconomic position; CVD, cardiovascular disease; ref, reference category; BMI, body mass index.

Disclosure of Interests: None declared

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New data on pathophysiology of spondyloarthritis including psoriatic arthritis

POS0326 THE TRANSCRIPTOMIC LANDSCAPE OF ACTIVE PSORIATIC ARTHRITIS: ACTIVATED INNATE IMMUNITY, EXTRACELLULAR MATRIX (ECM) TURNOVER, ABERRANT METABOLISM AND HEMOPOIETIC CELL - SKIN CROSSTALK.

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease whereby activated T lymphocytes and myeloid cells interact with tissue-resident cells in the skin and joints. Gene expression studies, mainly based on the microarray platforms, have provided an initial glimpse into disease pathogenesis highlighting, among others, the role of the TNFα and IL17 cytokine axis. Yet, the transcriptomic landscape of PsA remains largely unexplored, and the specific contribution of skin fibroblasts to disease pathogenesis remains elusive.

Objectives: To comprehensively characterize the gene expression profile in PsA, specifically in the blood and skin fibroblasts through next-generation RNA sequencing.

Methods: Peripheral blood (PB) was collected from PsA patients (n=30) after informed consent. Healthy individuals (HC) and patients with rheumatoid arthritis (RA) were used as healthy and disease controls (n=10/group) respectively. Psoriatic skin biopsies were obtained from a subset of three PsA patients and three HC. All PsA patients fulfilled the CASPAR criteria and displayed peripheral polyarthritis of moderate- to high- disease activity. Patient's clinical and laboratory data were recorded at the time of sampling. Disease activity in PsA and RA was assessed using the Disease Activity Index for Psoriatic arthritis (DAPSA) and the Disease Activity Score-28 (DAS28), respectively. RNA from PB and skin fibroblasts was extracted, RNA libraries were prepared and sequenced. EdgeR package was used to call differentially expressed genes (DEGs). Statistical significance was set at p value<0.05 and fold-change |FC| >1.5. Functional enrichment analysis and weighted gene co-expression network analysis (WGCNA) was implemented. Inference and analysis of blood immune cells-skin fibroblasts communication were performed with CellChat.

Results: 8 males and 22 female patients with PsA were included with median age 49 years old and median disease duration 4 years. The median DAPSA score was 44.3 and the median DAS28 score was 5.5 for RA patients, suggesting high disease activity in both groups. We found 466 DEGs in PsA versus HC blood (303 up- and 163 down-regulated). DEGs were significantly enriched in biological pathways related to immunity (i.e. *inflammatory response, TNFa signaling via NFkB, IFNa & IFNγ response, complement, IL2 signaling*), metabolism (i.e. *oxidative phosphorylation, adipogenesis, fatty acid metabolism*) and other signaling cascades of pathophysiologic relevance (i.e. *WNTb catenin signaling, TGFβ signaling, MTORC1 signaling*). WGCNA in blood revealed four gene modules containing highly correlated genes. These modules were enriched in *myeloid leukocyte mediated immunity*, *neutrophil-mediated immunity*, *ECM and collagen metabolism, TGFβ and PDGF signaling*. Next, we characterized the "PsA specific activity signature", taking the intersection of DEGs in 'PsA vs. HC' and 'PsA vs. RA', which resulted in 67 DEGs enriched in *response to TGF* and *PDGF*, *ECM organization and degradation.* CellChat analysis identified a higher number of interactions between blood immune cells and skin fibroblasts and increased strength of interactions in PsA compared to healthy state. Aberrant interactions between blood and skin fibroblasts in PsA included, among others, ligand-receptor pairs of the WNT, Notch, and GDF11 signaling pathways.

Conclusion: Our findings confirm the presence of an IFNα signature and complement activation in PsA. The increased cardiometabolic burden and enhanced bone remodeling are reflected by the presence of pathways related to aberrant metabolism and ECM metabolism, respectively. The myeloid cell signature in active disease supports the emerging role of monocytes/macrophages in driving inflammation in PsA, while the aberrant blood-skin fibroblast interactions suggest a novel role for these resident cells in disease pathophysiology.

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POS0327 IRISIN: A NEW MARKER OF SUBCLINICAL ATHEROSCLEROSIS, CARDIOVASCULAR RISK AND DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS?

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Background: Axial spondyloarthritis (axSpA) is an inflammatory disease with detrimental effects on the health status of the individuals affected by this condition [1]. axSpA patients also exhibit high cardiovascular (CV) risk, mainly due to accelerated atherosclerosis [2]. Interestingly, the adipomyokine irisin was described to play a beneficial role in several physiological and pathophysiological processes such as inflammation, angiogenesis, oxidative stress, as well as lipid and bone metabolism [3]. However, studies on the role of irisin in CV risk in the setting of axSpA or in the pathogenesis of axSpA are limited [4].

Objectives: In this study we evaluated the role of irisin as a genetic and serological biomarker of subclinical atherosclerosis and CV risk in a large cohort of patients with axSpA. We also assessed its role as a marker of axSpA susceptibility and severity.

Methods: 725 patients who fulfilled the Assessment of SpondyloArthritis international Society classification criteria for axSpA were included in this study [5]. In these patients, the presence of subclinical atherosclerosis (plaques and/or abnormal carotid intima-media thickness values) was assessed by carotid ultrasound. Four *irisin* polymorphisms (rs16835198 G/T, rs3480 A/G, rs726344 G/A and rs1570569 G/T) were genotyped by TaqMan probes in all the patients and in 656 age, sex and ethnically-matched healthy controls. Additionally, serum irisin levels were determined by ELISA in all the patients. All analyses were performed using STATA v.11.1 statistical software, adjusting for potential confounding factors. The strength of associations is indicated as odds ratios (OR) [95% confidence intervals].

Results: Low levels of serum irisin were linked to the presence of plaques ($p=0.002$) and with atherogenic index values indicative of an adverse lipid profile ($p=0.01$). Serum irisin levels also negatively correlated with visual analogue scale (VAS) patient, VAS physician and Bath Ankylosing Spondylitis Metrology Index (BASMI) values ($p<0.05$). Moreover, the presence of sacroiliitis was related to lower serum irisin levels ($p<0.001$). Furthermore, the minor alleles of rs3480 (G) and rs1570569 (T) were associated with higher values of Ankylosing Spondylitis Disease Activity Score (ASDAS) in axSpA patients ($p\leq0.01$ in both cases). In this line, the frequency of the minor allele of rs1570569 (T) was higher in patients with ASDAS values >2.1 (indicative of high disease activity) (OR: 1.46 [1.08-1.97], $p=0.01$), while the minor allele of rs16835198 (T) was less frequent in this group of patients (OR: 0.73 [0.57-0.92], $p=0.01$).

Conclusion: Low serum irisin levels could be indicators of the presence of subclinical atherosclerosis, high CV risk and more severe disease in axSpA patients. In addition, irisin may also constitute a genetic biomarker of disease activity in axSpA.

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POS0328 AUTOPHAGY MODULATION BY TOFACITINIB IMPROVES PSORIATIC ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES FUNCTION.

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory systemic disease, and peripheral joints involvement is responsible of significant morbidity for patients, leading to damage accrual. Different drugs are available for the systemic management of this condition, with different mechanisms of action. Nevertheless, the rules driving the correct therapeutical choice in each individual patient are not completely defined. Janus kinases (JAK) inhibitors are a class of drugs able to reduce synovial inflammation, and tofacitinib, a JAK1/3 inhibitor, is the most studied. Preliminary evidence suggest an effect of tofacitinib on fibroblast-like synoviocytes (FLS) from PsA patients, reducing pro-invasive and pro-inflammatory properties. The link

between JAK inhibition and FLS function improvement at synovial level is not fully understood.

Objectives: To evaluate the effect of tofacitinib on spontaneous autophagic activity of PsA FLS, and to confirm its effect on anti-inflammatory and anti-invasive properties of PsA FLS and synovial explants.

Methods: This is an in vitro study. Patients with active PsA underwent ultrasound-guided synovial biopsy. Histological evaluation was performed according to Krenn's synovitis score. FLS, PBMCs and synovial explants cultures were set up, and cells were treated in vitro with tofacitinib 1 µM or vehicle control for 24h. Protein levels in cellular homogenates were analysed by western blot for relevant autophagy markers. Autophagy was also studied by fluorescence microscopy using GFP-LC3. Chemokines/cytokines levels into culture supernatants were quantified by ELISA. Migration assays were used to investigate the effect of tofacitinib on invasive properties of FLS. Differences were determined adopting the non-parametric Wilcoxon signed rank test.

Results: 16 patients with moderately active PsA were enrolled (Table 1). Mean (SD) Krenn's synovitis score was 4.4. (1.9). Tofacitinib significantly increased LC3-II and ATG7 levels in PsA FLS compared to vehicle control, while p62 levels were not significantly affected, suggesting an increase in spontaneous autophagy activity, confirmed by LC3-autophagic vesicles count (Figure 1). No effect was highlighted in PBMCs and synovial explants cultures. Tofacitinib significantly reduced migration properties of PsA FLS, as well as MCP-1 and IL-6 release into FLS and synovial explants cultures supernatants.

Table 1. Baseline demographic and clinical data of included patients (N=16).

Variables	Frequency
Age (years), mean (SD)	59.8 (7.9)
Female, N (%)	5 (31.3%)
Disease duration (years), mean (SD)	9.7 (7.9)
CRP (mg/dl), mean (SD)	1.5 (2.0)
Patient Global Activity (0-100), mean (SD)	73.4 (16.9)
Physician Global Activity (0-100), mean (SD)	56.3 (18.1)
DAPSA, mean (SD)	25.6 (6.8)
HAQ (0-3), mean (SD)	0.9 (0.5)
Previous csDMARDs treatment, N (%)	13 (81.3%)
Previous bDMARDs treatment, N (%)	6 (37.5%)
Grey scale synovitis - joint to be biopsied (0-3), mean (SD)	1.9 (0.8)
Joint effusion - joint to be biopsied (0-3), mean (SD)	1.4 (0.7)
Power Doppler - joint to be biopsied (0-3), mean (SD)	0.5 (0.6)
Krenn's synovitis score (0-9), mean (SD)	4.4 (1.9)

Abbreviations: SD, standard deviation; CRP, C reactive protein; DAPSA, Disease Activity Index for Psoriatic Arthritis; HAQ, Health Assessment Questionnaire; csDMARD, conventional synthetic disease modifying antirheumatic drugs; bDMARD, biological disease modifying antirheumatic drugs.

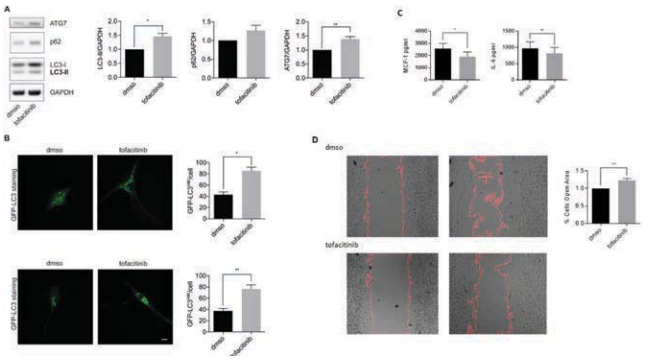

Figure 1. Tofacitinib significantly increased LC3-II and ATG7 levels in PsA FLS homogenates (A), and LC3-autophagic vesicles (B). Tofacitinib significantly reduced MCP-1 and IL-6 release into FLS cultures supernatants (C), and reduced PsA FLS migration properties at 24h (D).

Conclusion: The induction of autophagy by tofacitinib might permit a better functioning of PsA FLS, with a coherent reduction in pro-invasive and pro-inflammatory properties. This may contribute to the rationale for tofacitinib use in PsA management.

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POS0329 ABERRANT GLOBAL DNA METHYLATION IN PERIPHERAL BLOOD CELL SUBPOPULATIONS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) corresponds to a group of chronic inflammatory diseases mainly affecting the axial skeleton. TNFα and IL-17A have been identified as key inflammatory mediators driving the inflammatory process of axSpA. Epigenetics refers to different mechanisms that alter gene expression without involving changes in DNA sequence. DNA methylation is an important epigenetic mechanism, playing a role in gene expression regulation. It is recognized that aberrant DNA methylation can result in immune cell autoreactivity.

Objectives: epigenetic features have been rarely evaluated in axSpA. Prior studies have identified DNA methylation changes at both the gene-specific and genowe-wide levels in radiographic ax-SpA (r-axSpA). In this study, we aimed to evaluate the global DNA methylation of patients with axSpA.

Methods: case-control study (NCT03092583). Patients with r-axSpA or non radiographic (nr) axSpA (ASAS criteria) and healthy controls (HC) were evaluated. All the patients were biologic naïve and under NSAIDs. Disease activity was evaluated by BASDAI and ASDAS. CD4+T cells and CD14+ monocytes were isolated from peripheral blood and then DNA was extracted. Global DNA methylation (5-mC) was determined using MethylAmp global DNA methylation quantification kit (Epigentek) using 150 ng of total DNA.

Results: 104 patients with axSpA including 59 with r-axSpA (45 M; age [mean ± SD]: 47.1 ± 15 y; disease duration: 15.2 ± 13 y; B27: 86.4%) and 45 nr-axSpA (21 M, age: 39.6 ± 13.2; disease duration: 7 ± 7.8; B27: 65.1%) and 79 healthy controls (HC) (51 M; age: 43.4 ± 12.2 y) were evaluated. Patients had active disease (BASDAI and ASDAS in r-axSpA and nr-axSpA: 5.1 ± 1.8 and 3.04 ± 1.1; 5.04 ± 1.1 and 2.8 ± 1.0, respectively). In CD4+ T lymphocytes, global DNA methylation was higher in the whole SpA group compared to HC (1.45 ± 3.6 *vs* 0.44 ± 0.9 of 5-mC (p= 0.0092). Similarly, DNA methylation was higher in monocytes from patients with ax-SpA compared to HC (1.94 ± 2.3 *vs* 0.62 ± 0.9 of 5-mC)(p= 0.0004). When analysing the results between ax-SpA subgroups, DNA methylation remains higher in both CD4 T lymphocytes and monocytes of each patient subgroup compared to HC (p< 0.05 for all comparisons) (Figure 1). The levels of DNA methylation did not correlate with laboratory (ESR, CRP) or clinical (BASDAI) measures of disease activity, excepting ASDAS which was weakly correlated with DNA methylation in CD4+ T lymphocytes from the whole group of axSpA (r = 0.18, p = 0.08). History of uveitis was associated with higher DNA methylation in monocytes (p= 0.017). Previous smoker patients had higher DNA methylation in their monocytes compared to current or never smoker patients (p = 0.06). In a limited number of patients (N = 15) who started a TNFi, DNA methylation decreased in both CD4 T lymphocytes and monocytes after 3 months of treatment.

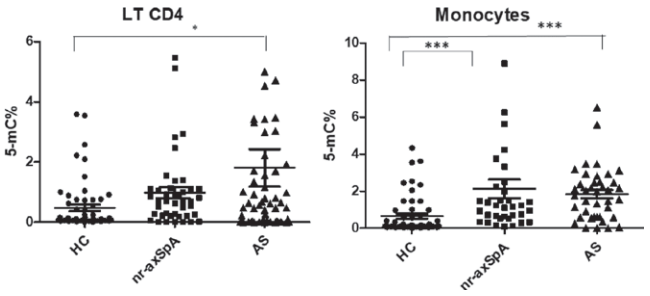

Figure 1. global DNA methylation of CD4+ T lymphocytes and monocytes from patients with ankylosing spondylitis (AS or radiographic axial spondyloarthritis) and non radiographic axial spondyloarthritis (nr-axSpA) and healthy controls (HC) (* p <0.05; *** p <0.001)

Conclusion: a global DNA hypermethylation was observed in patients with axSpA, both in T CD4 lymphocytes and monocytes. These modifications involved both the radiographic and non radiographic forms. These results were weakly correlated with disease activity and only in monocytes. Collectively, these changes in DNA methylation could alter recruitment of methyl binding proteins (MBP) that regulate chromatin structure and/or impair binding of transcription factors, resulting in down regulation of gene expression relevant to the pathogenesis of axSpA. We currently evaluated the level of expression of DNA methyltransferase (DNMT) and MBP proteins and specific DNA methylation status of the promoters of gene involved in inflammation such as TNFa.

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POS0330

DIFFERENCES IN GUT MICROBIOTA ASSOCIATED WITH LYMPHOCYTE SUBSETS, CYTOKINES AND DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS), a common chronic inflammatory disease, is a prototype of spondyloarthritis affecting sacroiliac joints and spine with or without peripheral arthritis and other systemic symptoms[1]. Environmental factors, especially microorganisms have been suggested to implicate with AS pathogenesis[2].

Objectives: Utilizing 16S rRNA genes sequencing on the feces of untreated AS patients and healthy controls (HCs), our study aimed to provide an in-depth understanding of AS gut microbiota and identifying a feasible diagnostic strategy for AS.

Methods: Fecal samples were collected from 62 AS patients and 62 age-and-gender- matched HCs. Microbial genome was extracted from approximately 250mg fresh fecal samples from all participants using QIAamp PowerFecal DNA Kit (Qiagen). The V3-V4 variable regions of bacterial 16S rRNA genes were sequenced with the Illumina Miseq PE300 system. QIIME2 based pipeline was used to process the raw sequence data. Alpha and beta diversities were assessed using result from QIIME2, and comparisons of gut microbiome profile were performed using linear discriminant analysis (LDA) effect size (LEfSe) to examine differences between AS and HCs. R (version 4. 0.1) was used for comparative statistics, and pearson's correlation was used to assess the correlations between the relative abundances of bacterial genera and clinical parameters; correlations with p<0.05 were considered significant.

Results: AS for alpha-diversity, ACE and Chao1 indices were lower in AS compared with those HCs(Figure 1**A**, p<0.05), though no significant differences observed in Shannon and Simpson index. Bray curtis distance-based beta-diversity analysis revealed significant differences in the microbial community between AS and HCs (Figure 1**B**, p=0.003, ANOSIM). Fecal microbial communities in AS differed significantly from those in HCs, driven by higher abundances of Escherichia-Shigella, Turicibacter, Enterococcus, et al. and a lower abundance of Agathobacter, Roseburia, Eubacterium_eligens_group, et al (Figure 1**C**, p<0.05). There was a significant positive correlation between ESR and Klebsiella, Butyricicoccus, Roseburia, CRP and Faecalibacterium, Muribaculaceae, ASDAS-CRP score and Faecalibacterium, Ruminococcus, total lymphocyte cells and Agathobacter, Ruminococcus, T cell and Agathobacter, $CD4^+$T cell and Agathobacter, B cell and Agathobacter, Streptococcus, Th1 and Prevotella, CAG–352, Th2 and Agathobacter, Th17 and Prevotella, Agathobacter, IL-2 and Agathobacter, IL-4 and Agathobacter, IL-6 and Lachnospiraceae_UCG–004, Muribaculaceae, IL-17 and Eubacterium_hallii_group, IFN-gama and Phascolarctobacterium.There were negative correlations between total lymphocytes and Escherichia–Shigella, $CD4^+$T cell and Enterobacteriaceae, Th2 cell and Escherichia–Shigella, IL-10 and CAG–352, Ruminococcus (Figure 2, p<0.05).

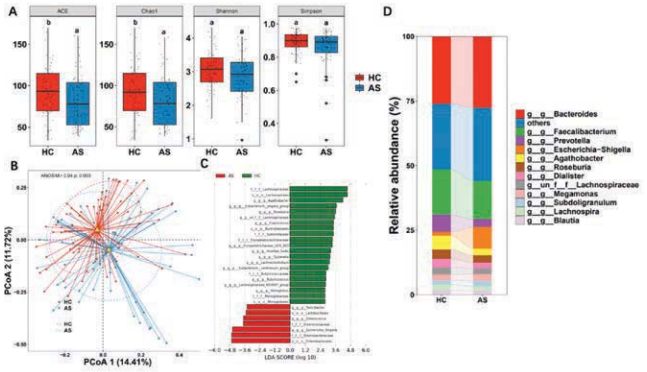

Figure 1. Feature of gut microbiota in AS patients and HCs. (A) Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson), Median estimates compared across cohorts. (B) PCoA plot based on the Bray curtis distance of gut microbiota samples from AS patients vs. HC group(p=0.003, ANOSIM). (C) Panel demonstrated the average relative abundance of different genus in AS and HCs. (D) Distribution of gut microbiota at genus level.

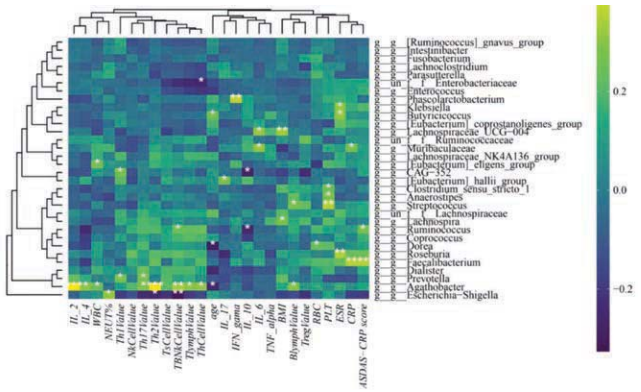

Figure 2. Correlations between the relative abundance of significantly different bacteria and clinical variables. *p<0.05, **p < 0.01, ***p <0 .001, ****p < 0.0001.

Conclusion: Human gut microbiome in patients with AS differed from that of the HCs. Characters of bacteria communities were associated with disease activity.

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POS0331

UPADACITINIB EFFECTIVELY LIMITS IL-23 DRIVEN INFLAMMATION AT THE ENTHESIS BY INHIBITING T CELL STAT1 PHOSPHORYLATION, IL-17A AND TNFA PRODUCTION

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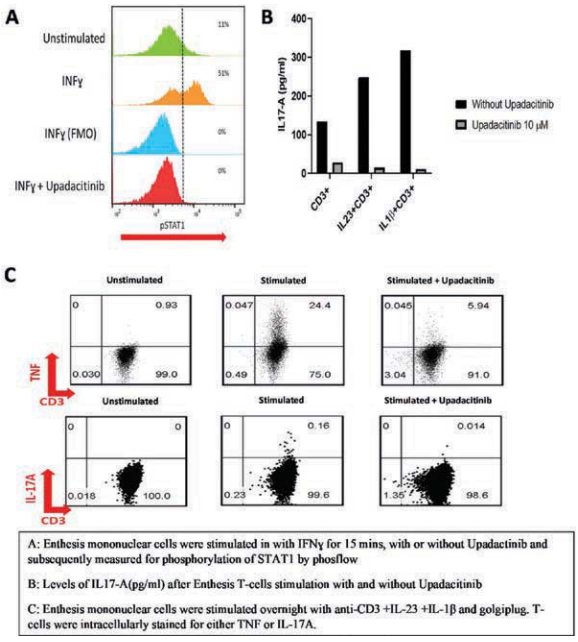
Background: Enthesitis or inflammation of the tendon/ligament anchorage points is the cardinal lesion in spondyloarthritis (SpA)[1]. Several key mediators have been shown to have a role in SpA including TNFα, IL-23, IL-17A and IL-17F [1]. There is a need for new therapeutic agents to treat SpA as current therapeutics fail to adequately target all its manifestations. Janus kinase (JAK) inhibitors have shown promise as disease modifying drugs and by targeting signaling components shared amongst several inflammatory pathways may be advantageous in treating inflammatory diseases with complex overlapping pathological mechanisms, as seen in SpA[2]. Upadacitinib is an oral selective JAK inhibitor (JAK1 over JAK2/3) which in phase II/III trials has shown efficacy for both psoriatic arthropathy and ankylosing spondylitis, suggesting specific JAK1 targeting may be superior[3, 4]. The role of JAK/STAT signaling in enthesis has not been extensively explored and given the importance of the enthesis in the development of SpA it is crucial to gain a mechanistic understanding of how JAK inhibitors affect entheseal inflammation.
Objectives: To determine if upadacitinib could suppress innate and adaptive immune responses in an in vitro human enthesis model and elucidate mechanisms of suppression.
Methods: Normal spinous process enthesis was obtained from patients undergoing spinal decompression or surgery for scoliosis correction as previously described[5]. Enthesis cells were subsequently isolated by mechanical digestion. Entheseal cells were stimulated with IFNγ (JAK1 activator) with and without upadacitinib and STAT 1 activation measured by phos-flow cyometry. Entheseal T-cells were stimulated with anti-CD3, anti-CD3 with IL-23 and anti-CD3 with IL-1β with and without upadacitinib. IL-17A and TNFα were quantified using intracellular flow cytometry and ELISA of supernatants. Entheseal cells were also stimulated with LPS with and without upadacitinib, and IL-23 and TNFα quantified by ELISA.
Results: Upadacitinib inhibited phosphorylation of STAT1 in entheseal cells, following IFNγ stimulation (Figure 1-A). Following stimulation of entheseal T cells upadacitinib inhibited both TNFα and IL-17A production as assessed by both ELISA and intracellular flow cytometry (Figure 1-B, 1-C). Upadacitinib did not attenuate LPS induced IL-23 or TNFα from entheseal myeloid cells.
Conclusion: Upadacitinib inhibition of entheseal T cell derived TNFα and IL-17A, therefore interrupting the IL-23/IL-17/TNFα axis so prominent in SpA, may offer a mechanistic explanation for upadaticintib's efficacy treating enthesitis.



A: Enthesis mononuclear cells were stimulated in with IFNγ for 15 mins, with or without Upadactinib and subsequently measured for phosphorylation of STAT1 by phosflow

B: Levels of IL17-A(pg/ml) after Enthesis T-cells stimulation with and without Upadacitinib

C: Enthesis mononuclear cells were stimulated overnight with anti-CD3 +IL-23 +IL-1β and golgiplug. T-cells were intracellularly stained for either TNF or IL-17A.

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POS0332

CD71 RECEPTOR APICAL EXPRESSION IN ILEUM IS RELATED WITH HIGH LEVELS OF SERUM SIGA AND ACTIVITY DISEASE IN SPA PATIENTS

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Background: Currently, mucosal immunity research has been investigated whether the serum levels of SIgA reflects the over-activation immune system in gut associated lymphoid tissues (GALT) and if the antigenic stimuli in the mucosa are responsible for inducing and maintaining the inflammatory response in Spondyloartrhitis (SpA). Based on our previous results, variances on levels of SIgA might influence in disease activity. SIgA Reverse transcytosis (retrotranscytosis) has been demonstrated as a GALT mechanism which enhance systemic inflammation in some autoimmune pathologies such as celiac disease.
Objectives: This study proposes the evaluation of receptors associated with retrotranscytosis CD71 and Dectin-1 (Dec-1) in gut tissues from SpA without IBD patients to explore a possible mechanism responsible of gastrointestinal inflammatory imbalance.
Methods: In total, 180 patients with SpA (ASAS/criteria) were assessed by rheumatologists, of which (n=65, 36.1%) met the selection criteria and from them (n=41, 63.1%) by a gastroenterologist to perform digital chromoendoscopy with magnification for colon e ileum and histological analysis. Pregnant and lactating women, and cancer patients, patients with other autoinflammatory diseases, autoimmune diseases, immunodeficiency, chronic pancreatitis, or chronic liver disease, and those who had received antibiotic treatment in the last 3 months were excluded from the study. Furthermore, those patients with SpA and concomitant IBD were excluded. All included patients were between 18 and 65 years old. CD71 and Dec-1 apical expression were identified by indirect immunofluorescence. Fecal Calprotectin (FC), Serum SIgA in house and clinical indices BASDAI, BASFI, ASDAS-CRP, ASDAS-ESR were measured. The association were evaluated using the Chi-square or Fisher's exact test and a multiple correspondence discriminant analysis (MCDA) was performed including those variables with significant associations from bivariate analysis and some that are considered clinically relevant to explain the impact of SIgA and CD71 in SpA.
Results: The average age of the patients included was 44,6±10.2 years, 56.1% were men, 39.0% were HLA-B*27:05 positive, 90.2% had axial involvement. Serum levels of SIgA were 62.3±24.1 gr/mL, CRP 1.7±2.4 and ESR 14.1±12.0 mm/h. Positive levels of FC (>120ng/mL) were observed in 31.7%. BASDAI >4 was found in 58.5% of patients and ASDAS-CRP >2.1 in 75.6%. Apical expression of CD71 and Dec-1 in the ileum was observed in 48.8% and 36% respectively, the expression of both receptors in colon tissues were irrelevant. CD71 expression was associated with high levels of serum SIgA (p=0.05). However, no associations were observed between retrotranscytosis receptors and any of the clinical and histological variables. The MCDA showed a Cronbach's Alpha reliability coefficient of 0.763 and showed two dimensions: a main

dimension (Dim 1) related to the presence of loss of the vascular pattern in the ileum (CC 0.325), FC + diarrhea (CC 0.695), FC + abdominal distension (CC 0.883) and FC + abdominal pain (CC 0.885) and a secondary dimension (Dim 2) that collected the variables serum SIgA (CC 0.513), ASDAS-CRP >2.1 (CC 0.311), CD71 (CC 0.424), please see Figure 1.

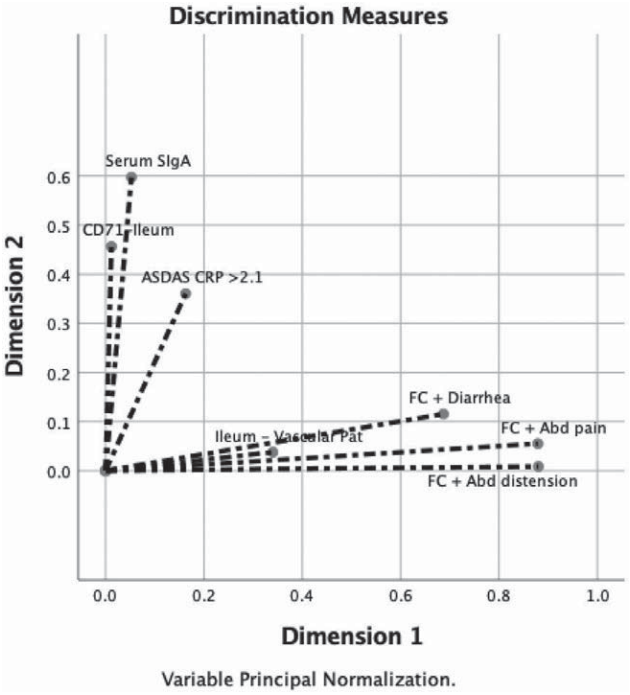

Figure 1. Multiple correspondence discriminant analysis for CD71, serum SIgA and activity index in SpA patient

Conclusion: The findings reflect a possible relationship among the apical expression of CD71in ileum with high levels of serum SIgA and activity, suggesting that retrotranscytosis mediated by this receptor might be a mechanism that mediate the intestine-joint axis in SpA.

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Disclosure of Interests: None declared

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POS0333

CIRCULATING NON-CLASSICAL CD14LOW/-CD16+ MONOCYTES AND THEIR EXPRESSION OF ARGINASE-1 ARE ASSOCIATED WITH THE ACTIVITY OF AXIAL SPONDYLOARTHRITIS

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Background: Human peripheral blood monocytes represent heterogeneous population and can be divided into three major populations, classical ($CD14^{++}CD16^{-}$), intermediate ($CD14^{++}CD16^{+}$) and non-classical ($CD14^{+}CD16^{++}$) monocytes. All three monocyte populations are thought to have different functional activity, including their pro- and anti-inflammatory activity. The ratio between monocyte populations could change in inflammatory conditions that it is thought to be important for the development of adequate immune responses. Axial spondyloarthritis (axSpA) being autoimmune diseases is currently classified as an autoinflammatory disease based on a strong inflammatory component. It is accepted that increased concentration of pro-inflammatory mediators can cause an impairment of myelopoiesis.

Objectives: The present study aimed to analyze the frequency of blood monocyte subpopulations and their expression of the suppressor molecule arginase-1 (Arg1) in patients with axSpA.

Methods: The study included 14 healthy donors and 19 axSpA patients aged 23 to 59 years, including 15 men and 4 women. Ankylosing Spondylitis Disease Activity Score (ASDAS) was used to assess disease activity and high activity was determined as ASDAS≥2.1. The disease duration at the time of the study was 12 years (median). Phenotypic analysis of blood monocytes was performed by flow cytometry based on CD14 and CD16 expression.

Results: The frequency of monocyte subpopulations in patients with low/moderate activity of axSpA did not differ from the donor group. Patients with high/very high disease activity showed an increased relative number of non-classical $CD14^{low/-}CD16^{+}$ monocytes (vs donors p_U=0.007). All donor monocyte subpopulations expressed suppressor intracellular molecule Arg1 with higher expression in intermediate and non-classical monocytes. The expression of Arg1 in $CD14^{low/-}CD16^{+}$ monocytes was significantly reduced in patients with high activity (vs donors Me 41.5 vs 76.5%, p_U=0.01). Patients with the presence of peripheral articular manifestations of axSpA were characterized by a decreased Arg1 expression in non-classical monocytes compared with the donor group (p_U=0.02). However, patients without peripheral manifestations demonstrated a significant reduction of Arg1 expression in all monocyte subpopulations (p_U<0.05).

Conclusion: Shifting of monocyte subpopulation toward a higher number of non-classical monocytes with the decrease in the expression of the suppressor molecule Arg1 in the high activity of axSpA can play important role in terms of the possible involvement of monocytes in maintaining inflammation and its regulation in autoinflammatory disease.

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Disclosure of Interests: None declared

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New insights into the management of JIA

POS0334

DRIVERS OF NON-ZERO PHYSICIAN GLOBAL SCORES DURING PERIODS OF INACTIVE DISEASE IN JUVENILE IDIOPATHIC ARTHRITIS

A. I. Rebollo Giménez[1], A. Alongi[2], G. Giancane[1], R. Naddei[1], V. Natoli[1], N. Ruperto[1], A. Consolaro[1], A. Ravelli[3]on behalf of Pediatric Rheumatology Internationals Trials Organization (PRINTO). *[1]Istituto Giannina Gaslini, Pediatric and Rheumatology Clinic, Genoa, Italy; [2]Azienda Ospedaliera di Rilievo Nazionale e di Alta Specializzacione Civico Di Cristina e Benfratelli, Pediatric Clinic, Palermo, Italy; [3]Istituto Giannina Gaslini, Scientific Director, Genoa, Italy*

Background: The ACR provisional criteria for defining inactive disease (ID) in Juvenile Idiopathic Arthritis (JIA) requires that the physician's global assessment of disease activity (PhGA) is marked as 0 on the visual analog scale (VAS). However, some investigators have noticed the tendency of some clinicians to mark the PhGA>0 even on resolution of active disease. Due to the fact that the PhGA and the count of active joints are the two main physician-centered measures included in ID criteria the analysis of their discordance may be of importance to address the issue.

Objectives: To investigate the frequency in which the physician provides a global assessment of disease activity (PhGA)>0 and an active joint account (AJC)=0 in children with juvenile idiopathic arthritis (JIA) and search for determinants of divergence between the two measures.

Methods: Data were extracted from a multinational cross-sectional dataset of 7265 patients who had JIA by ILAR criteria, were recruited between 2011 and 2016 and had both PhGA and AJC recorded by the caring paediatric rheumatologist at the study visit. Determinants of discordance between PhGA and AJC=0 were searched for by multivariable logistic regression and dominance analysis.

Results: The PhGA was scored >0 in 1211 (32,4%) of 3668 patients who had an AJC of 0. In 536 patients (14,6%) the PhGA was the single most frequent reason for not meeting the ID definition in patients with AIJ=O. Independent associations with discordant assessment were identified for tender or restricted joint count>0, history of enthesis, presence of active uveitis or systemic features, enthesitis-related or systemic arthritis, increased acute phase reactants, pain visual analog scale (VAS)>0, and impaired physical or psychosocial wellbeing. In dominance analysis, tender joint count accounted for 35,43% of PhGA variance, followed by VAS>0 (17,72%), restricted joint count >0 (16, 14%) and physical health score >0 (11,42%) (Figure 1).

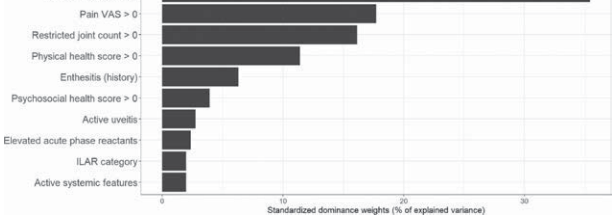

Figure 1. Dominance analysis of relative importance of predictive factors in explaining the variance in PhGA.

Conclusion: We found that many paediatric rheumatologists did not mark a score of 0 for patients who they found not to have active joints. The presence of pain in joints not meeting the definition of active joint used in JIA was the main determinant of this phenomenon.

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Disclosure of Interests: Ana Isabel Rebollo Giménez: None declared, Alessandra Alongi: None declared, Gabriella Giancane: None declared, Roberta Naddei: None declared, Valentina Natoli: None declared, Nicolino Ruperto Speakers bureau: NR has received honoraria for consultancies or speaker bureaus from the following pharmaceutical companies in the past 3 years: 2 Bridge, Amgen, AstraZeneca, Aurinia, Bayer, Brystol Myers and Squibb, Celgene, inMed, Cambridge Healthcare Research, Domain Therapeutic, EMD Serono, Glaxo Smith Kline, Idorsia, Janssen, Eli Lilly, Novartis, Pfizer, Sobi, UCB., Consultant of: NR has received honoraria for consultancies or speaker bureaus from the following pharmaceutical companies in the past 3 years: 2 Bridge, Amgen, AstraZeneca, Aurinia, Bayer, Brystol Myers and Squibb, Celgene, inMed, Cambridge Healthcare Research, Domain Therapeutic, EMD Serono, Glaxo Smith Kline, Idorsia, Janssen, Eli Lilly, Novartis, Pfizer, Sobi, UCB., Alessandro Consolaro Consultant of: AC has received honoraria from Abbvie in the past 3 years., Angelo Ravelli Speakers bureau: AR has received honoraria for speaker bureaus from the following pharmaceutical companies in the past 3 years:Abbvie, Angelini, Pfizer, Novartis, Reckitt Benckiser, Sobi, Alexion, Roche

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POS0335 IMPROVED PAIN COPING SCALE FOR CHILDREN AND THEIR CAREGIVERS

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Background: Pain can be a problem in a subgroup of juvenile idiopathic arthritis (JIA) patients even though in clinical remission. This can at least partly be due to their pain coping strategy of catastrophizing [1]. In a chronic disease such as JIA, the quality of coping with pain is crucial. The importance of coping with pain is well recognized in children [2]. The understanding of the parental role in supporting the child in pain is growing [3]; yet measuring the precise mechanism of parental pain coping is less studied. Thus, it seems important to measure also parental coping quality.

Objectives: The aim of this study was to develop a pain coping scale (PCSpar) for assessing the parents' coping strategies to their child´s pain and a shorter improved PCSped for children feasible for use in clinical practice.

Methods: The original pain coping questionnaire (PCQ) [4] has been validated in Finnish [5] resulting in a 38-item, eight-factor structured PCQ. The items in the new version of PCQ were reduced into twenty by an interdisciplinary team (mPCQped). A corresponding scale was created for parental use (mPCQpar). Consecutive patients aged 8-16 years, visiting pediatric rheumatology outpatient clinic, reporting musculoskeletal pain during the last week before visit or longer, were recruited to participate in this study. Both the patient and the caregiver rated the child's pain VAS from 0 to 100, completed the mPCQped /the mPCQpar and Children´s Depression Inventory (CDI) [6]/the Beck´s depression Inventory (BDI) [7] as appropriate. The selection process of pain questionnaire items was performed with factor analyses. The construct validity, the associations of the mPCQ factors, CDI, BDI and pain VAS, were tested by Spearman´s correlation coefficient.

Results: The study was conducted in all five tertiary and four secondary hospitals evenly distributed throughout Finland. Of the 153 families invited to the study, 130 attended. The average (SD) age of the attending patients was 13.0 (2.3) years. Of the patients, 91 (70%) were girls. Several steps in the exploratory factor analyses preceded the final factor analyses mPCQped and mPCQpar results. The four factors retained in the new improved Pain Coping Scale for children (iPCSped) were named positive cognitive distraction, catastrophizing (CATped), seeking social support (SSSped) and behavioral distraction. The factors in the improved Pain Coping Scale for caregivers (iPCSpar) were positive self-statement, catastrophizing (CATpar), seeking social support and distraction. In both iPCSped and iPCSpar there are a total of 15 items, 2-5 items/factor. The factor´s Cronbach´s alpha reliability coefficients were satisfactory, and the goodness-of-fit statistics were good. The CATpar correlated to BDI Rs= 0.33, $p<0.05$ and parent's assessment of the child's pain Rs= 0.23, $p<0.05$ in caregivers. The CATped correlated to CDI Rs= 0.49, $p<0.05$ and SSSped Rs= 0.26, $p=0.05$ but not to patient pain VAS Rs= 0.08, $p>0.05$.

Conclusion: In this study, we created a shorter pain coping scale for children (iPCSped) and a novel scale for caregivers (iPCSpar). Both showed good validity and reliability.

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Disclosure of Interests: None declared

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POS0336 COURSE OF UVEITIS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS WITH JIA (ICON-JIA) STUDY

J. Klotsche[1], C. Sengler[1], F. Dressler[2], D. Foell[3], I. Foeldvari[4], J. P. Haas[5], G. Horneff[6], T. Hospach[7], T. Kallinich[8], I. Liedmann[1], K. Moenkemoeller[9], M. Niewerth[1], F. Weller-Heinemann[10], D. Windschall[11], A. Heiligenhaus[12], K. Minden[1], K. Baquet-Walscheid[12]. *[1]German Rheumatism Research Center Berlin, Epidemiology, Berlin, Germany; [2]Medizinische Hochschule Hannover, Paediatric Rheumatology, Hannover, Germany; [3]University Hospital Münster, Department of Paediatric Rheumatology and Immunology, Münster, Germany; [4]Hamburg Centre for Pediatric and Adolescence Rheumatology, Paediatric Rheumatology, Hamburg, Germany; [5]German Centre for Child and Adolescent Rheumatology, Paediatric Rheumatology, Garmisch-Partenkirchen, Germany; [6]Asklepios Kinderklinik St. Augustin, Centre for General Paediatrics and Neonatology, St. Augustin, Germany; [7]Olgahospital Stuttgart, Center for Pediatric Rheumatology, Stuttgart, Germany; [8]Charité - Universitätsmedizin Berlin, Department of Paediatric Respiratory Medicine, Immunology and Intensive Care Medicine, Berlin, Germany; [9]Kliniken Köln - Kinderkrankenhaus, Paediatric Rheumatology, Köln, Germany; [10]Klinikum Bremen-Mitte, Prof-Hess-Kinderklinik, Paediatric Rheumatology, Bremen, Germany; [11]St. Josef-Stift Sendenhorst, Clinic for Paediatric and Adolescent Rheumatology, Sendenhort, Germany; [12]Franziskus Hospital, Department of Ophthalmology, Münster, Germany*

Background: Uveitis is an extra-articular manifestation of Juvenile idiopathic arthritis (JIA) with a prevalence of up to 20% developing most frequently in young girls and patients positive for antinuclear antibodies (ANA). Untreated and uncontrolled uveitis may lead to vision-threatening complications and even blindness.

Objectives: The main objectives of the analyses were to determine the visual prognosis, uveitis complications and necessity of ocular surgery during the first five years of ocular disease. The likelihood of achieving an inflammation-free phase or even a remission without medication were investigated.

Methods: The Inception Cohort of Newly diagnosed patients with JIA (ICON) was initiated in 2010 in order to prospectively follow JIA patients up to 10 years after JIA disease onset. 953 Patients were assessed at enrollment, three-monthly during the first year, and six-monthly afterwards by a standardized physician's and patient's case report form including clinical parameters, treatment data and several laboratory parameters such as ESR, CRP or S100A12. Patients who developed uveitis underwent a regular ophthalmological assessment. The treating ophthalmologist three-monthly completed an additional questionnaire, documenting the anterior chamber (AC) cell grade, current uveitis activity (UA) and UA during the previous three months, best corrected visual acuity (BCVA), uveitis-related complications, previous ocular surgery, current topical treatment

and clinical course of uveitis and additional parameters. Inactive uveitis was defined by AC cell grade of 0, quiescence of uveitis by inactive uveitis for at least 6 months, and remission by inactive uveitis for at least 6 months without topical steroids or systemic anti-inflammatory medication (steroids or DMARDs).

Results: A total of 133 children developed uveitis in the JIA disease course, of which 97 patients were documented via the ophthalmological questionnaire for at least two years resulting in a mean follow-up of 5.8 years (SD 1.8). 76% were female, 86% ANA positive, 70% oligoarthritis, and 22% rheumatoid factor negative polyarthritis and mean age at JIA onset was 3.1 (SD 2.1) and uveitis onset at 4.4 (SD 2.2) years. The mean duration between JIA onset and uveitis onset was 15.7 (SD 15.6) months. At least one ocular complication was reported for 24% of patients at first uveitis documentation and 47% of patients had at least one ocular complication until the five year follow-up. Among those, posterior synechiae (31%) and cataract (27%) were the most frequent, followed by an increased IOP (12%) with or without glaucomatous changes. Ocular surgery was rarely necessary, and visual acuity remained quite good in the majority of patients: After five years, >90% had BCVA of <0.4 LogMAR (Logarithm of the Minimum Angle of Resolution), and 63.5% even of <0.1 LogMAR. About half of the uveitis patients were already treated with DMARDs at uveitis onset. The rate of treatment with biological DMARDs increased from 10% at first uveitis documentation up to 20% at 5-year follow-up. Three in four patients were treated with topical steroids at first assessment, whereas this proportion decreased to 43%. 80 of 97 patients (83%) achieved uveitis quiescence during the first five years of disease, with more than 50% experiencing more than one episode (mean 1.5 episodes (SD 1.0)) during this time period. The mean duration of uveitis quiescence was 23.2 (SD 15.6) months. A total of 39 (40%) patients achieved uveitis remission during follow-up. The likelihood of remission was associated with a lower JIA disease activity (cJADAS10), lower erythrocyte sedimentation rate (ESR) and a higher age at JIA disease onset.

Conclusion: The rate of ocular complications is already remarkable at uveitis diagnosis, and increases during uveitis disease course despite anti-inflammatory treatment. However, the visual acuity frequently remains unaffected, and the majority of patients achieve uveitis quiescence and even 40% uveitis remission within 5 years of follow-up.

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POS0337 DISTINCT CLUSTERS OF JIA AT METHOTREXATE INITIATION IDENTIFIED USING TOPOLOGICAL DATA ANALYSIS

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Background: Stratified medicine requires the identification of unique strata of a disease within which to base prognostic and treatment decisions. Juvenile idiopathic arthritis (JIA) offers a unique challenge in its inherent heterogeneity. The current ILAR classification, whilst useful for clinical categorisation, does not correlate with treatment outcomes. Therefore, further refinement, clustering and correlation of patient characteristics with treatment response are urgently required.

Objectives: To identify novel, phenotypically consistent subgroups of children and young people (CYP) with JIA at the point of starting methotrexate, across 19 patient and disease characteristics.

Methods: MTX-naïve CYP with JIA were selected if enrolled prior to April 2021 in one of four national JIA studies contributing to the UK CLUSTER consortium. Data from 19 harmonised study variables were extracted at point of starting MTX. Topological data analysis using a Gower similarity metric was used to identify clusters with distinct characteristics. Intervals and percent overlap between clusters were varied until an optimal model identified stable, potentially clinically plausible clusters. Significant differences in characteristics between identified clusters were tested using Kruskall-Wallis and Chi-Squared statistics.

Results: Of 2915 CYP included, the majority were female (68%), of white ethnicity (90%); with the most common ILAR categories being oligoarthritis (35%) and RF-negative JIA (34%).

The optimal TDA model identified six clusters which significantly differed across 16 of the 19 clinical variables at MTX initiation: Adolescents with low-moderate disease (Cluster 1, 41%), adolescents with predominantly sJIA and moderate-high disease (Cluster 2, 4%), children with predominantly sJIA and high disease (Cluster 3, <1%), children with oligo/RF-polyarthritis and low-moderate disease (Cluster 4, 43%) and two ANA-positive groups of largely females with moderate (Cluster 5, 11%) and high (Cluster 6, 1%) disease (Figure 1). Clustered groups also significantly differed in gender proportions (p<0.001), ethnicities (p<0.001), history of uveitis (p<0.001) and disease duration to both diagnosis (p<0.001) and MTX initiation (p<0.001), but did not differ in limited joint count (p=0.117), height (p=0.245) or BMI (p=0.394) z-scores.

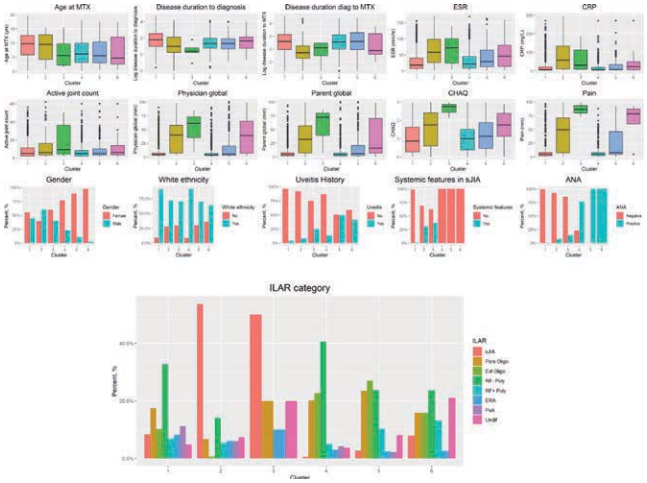

Figure 1. Clusters identified at MTX initiation in children and young people recruited to the UK BSPAR-ETN, BCRD, CAPS and CHARMS studies.

Conclusion: This study shows substantial heterogeneity in JIA at the point of MTX initiation, with six clusters identified across 19 demographic and clinical variables. ILAR categories across clusters were not always indicators of disease activity or symptom burden. Future analyses will correlate MTX treatment response within each cluster to understand what role these combined factors may have on initial treatment response.

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POS0338 TRANSITION COMPETENCE IN YOUNG PEOPLE WITH JUVENILE IDIOPATHIC ARTHRITIS HAS IMPROVED OVER TIME

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Background: In recent years, transition clinics have been set up at an increasing number of paediatric rheumatology sites in Germany to reduce identified deficits in the care of young people with rheumatic diseases[1]. In addition, the German Rheumatic Diseases League (Deutsche Rheuma-Liga, DRL), the largest self-help organisation in Germany, has been offering support services for young people in transition since 2016, including the interactive website www.mein-rheuma-wird-erwachsen.de.

Objectives: To assess the transition competence of young people with juvenile idiopathic arthritis (JIA) and their knowledge of self-help services.

Methods: Cross-sectional data of the National Paediatric Rheumatology Database (NPRD) from 2016 to 2020 were used to evaluate the health-related transition competence of young people with JIA aged ≥16 years. Health-related knowledge and health-care competence were assessed using a modified self-report instrument[2] on a 4-point Likert scale as part of routine documentation in the NPRD. Young people were also asked about their information behaviour and knowledge of new support services. Linear mixed models were used to determine whether health-related transition competence changed between 2016 and 2020, adjusted for disease duration.

Results: During the years 2016 to 2020, between 1.908 to 2.536 patients with JIA aged ≥16 years were annually recorded in the NPRD from 56 to 61 paediatric rheumatology sites. The annual patient collectives comprised 34-39% oligoarthritis, 23-26% RF-negative or RF-positive polyarthritis and 22-27% enthesitis-related arthritis cases. In the years from 2016 to 2020, about one-third of patients had inactive disease (cJADAS-10≤1) and about 60% had no functional limitations (CHAQ=0).

Over the years, the proportions of patients who rated their disease knowledge and health care competence as "very well" increased significantly in most areas. Although over time, no increase in numbers of patients seeking information about their disease outside of rheumatology consultations were recorded (2016: 22.8%; 2020: 20.9%), awareness of the DRL's new website for young people with rheumatic diseases increased from 7.7% in 2016 to 26.9% in 2020. Compared to those who were unaware of the new website, those who knew about the website were more likely to have received care in rheumatology settings that offer transition clinics and were more likely to be girls (75% vs 65%), to attend high school (51% vs 46%) and to be slightly older (17.6 vs 17.1 years).

Conclusion: The transition competence of young people with JIA seems to have improved over the last five years. During this time, more transition services were made available for young people with rheumatic diseases. However, most young people are not yet aware of these services. Moreover, the effectiveness of the different measures/interventions has yet to be evaluated.

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Table 1. Health-related transition competence in JIA patients ≥16 years who participated in the NPRD

	2016	2018	2020	p (difference over time)
Patients	N=2536	N=2068	N=1908	
Disease duration, years	6.7±4.9	7.2±5.0	7.6±5.1	
DMARDs at documentation, %	57	62	63	
Disease-related knowledge (best answer "very well"), %	N=1992	N=1598	N=1265	
name of illness	35	42	42	**0.001**
names of medicines	54	59	56	0.717
what medicines are for	50	54	52	0.357
who to contact in case of health problems	59	65	65	**0.015**
influence of smoking, drugs, and alcohol on disease	49	55	54	**0.002**
how to make a doctor's appointment	68	68	65	0.087
which doctors are responsible after leaving paediatric care	42	46	49	**0.031**
Health-care competence (best answer "most of the time"), %	N=1784	N=1443	N=1143	
inform my doctor of any unusual changes in my health	66	72	69	**0.038**
keep information about my illness	81	84	84	0.281
ask my own questions	51	56	55	**0.016**
answer the questions I am asked	69	73	74	**0.014**
take care of my health concerns and needs	66	71	69	**0.041**
attend the consultation alone	59	61	61	0.599
speak up for myself and say what I need	64	68	68	0.537

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POS0339 POINTS TO CONSIDER AT THE EARLIEST STAGES OF THE DIAGNOSIS AND MANAGEMENT OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS/ MACROPHAGE ACTIVATION SYNDROME (HLH/MAS)

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Background: Hemophagocytic Lymphohistiocytosis (HLH) and Macrophage Activation Syndrome (MAS) are life-threatening systemic hyperinflammatory syndromes that occur in many contexts and are often called by many names. They nevertheless can progress rapidly, and early identification and management are critical for preventing organ failure and mortality.

Objectives: The purpose of this effort was to develop a series of 'points to consider' to assist clinicians at the earliest stages of evaluation and diagnosis, management, and monitoring of patients with HLH/MAS in order to improve patient outcomes.

Methods: A working group of adult and pediatric rheumatologists (14), hematologist/oncologists (4), immunologists (2), infectious disease specialists (2), intensivists (3), allied health care professionals (1), and patients/parents (2) formulated relevant research questions for a systematic literature review (SLR). We then used the SLR results, Delphi questionnaires, and consensus methodology to devise and refine overarching and specific 'points to consider' statements.

Results: The group arrived at six overarching statements and 24 specific points-to-consider relevant to early decision-making in diagnostics, initial management, and monitoring of HLH/MAS. Major themes included the a) need for prompt recognition, evaluation, and management of underlying triggers and conditions, b) multi-disciplinary/expert input, and c) early, tailored intervention with the goals of halting disease progression and preventing life- and organ-threatening immunopathology

Conclusion: These 2022 EULAR/ACR Points to Consider provide guidance on the initial evaluation, management, and monitoring of patients during the initial consideration of HLH/MAS.

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POS0340 PREDICTORS OF CLINICAL RESPONSE TO ABATACEPT IN CHILDREN WITH POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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Background: For children with polyarticular juvenile idiopathic arthritis (pJIA) and inadequate response or intolerance to initial treatment with MTX, treatment options include abatacept.[1] Abatacept, a selective T-cell co-stimulation modulator, has a distinct mechanism of action from other current treatments for rheumatic diseases,[2] and factors predicting clinical response can help determine optimal treatment strategy. Two phase 3 studies demonstrated the efficacy and safety of IV and SC abatacept in patients with pJIA and an inadequate response to other DMARDs.[2,3]

Objectives: To determine baseline and post-baseline factors that may predict a clinical response in children and adolescents with pJIA treated with abatacept for 2 years.

Methods: Baseline demographic and disease characteristics and post-baseline factors (50% and 70% improvement in ACR criteria [ACR50, ACR70] at days 57 and 85) were analyzed using data from 2 phase 3 studies of abatacept in patients with JIA aged 2–17 years (SC administration) and 6–17 years (IV administration). Efficacy endpoints were Juvenile Arthritis Disease Activity Score in 10 joints based on CRP (JADAS10-CRP) inactive disease (ID; score of ≤ 2.7),[4] and remission, defined as 6 consecutive months of post-baseline JADAS10-CRP ID. Data were analyzed over the entire 2-year study period. The earliest time point at which patients achieved these outcomes was reported. The aforementioned study factors were subjected to a time-to-event analysis, including Cox proportional hazards univariate regression analysis and Cox proportional hazards multivariate regression analysis using stepwise regression; results of the multivariate analysis are reported. Kaplan–Meier analysis was used to estimate time to achieve clinical response. Receiver operating characteristic curves were used to determine threshold values for continuous variables.

Results: Overall, 347 patients were included in the analysis (SC, n = 219; IV, n = 128; 73.8% female; mean [SD] age, 11.3 [4.0] years). Following abatacept treatment, both time to JADAS10-CRP ID and time to JADAS10-CRP remission were predicted (nominal $P \leq 0.05$) by age (≤ 11 years: hazard ratio [HR], 1.52 [95% CI, 1.14–2.02] and ≤ 10 years: HR, 1.73 [95% CI, 1.20–2.48], respectively), high-sensitivity CRP (hsCRP; ≤ 0.6 mg/dL: HR, 1.67 [95% CI, 1.22–2.28] and ≤ 0.21 mg/dL: HR, 1.67 [95% CI, 1.15–2.42], respectively), Parent/Patient Global Assessment of well-being (≤ 35.86: HR, 1.88 [95% CI, 1.41–2.51] and ≤ 43.16: HR, 2.05 [95% CI, 1.35–3.10], respectively), and Childhood HAQ-DI (CHAQ-DI; ≤ 1.63: HR, 2.23 [95% CI, 1.47–3.39] and ≤ 0.75: HR, 1.84 [95% CI, 1.24–2.73], respectively) (remission data shown in Figure 1). Disease duration ≤ 2 years from baseline (HR, 1.66 [95% CI, 1.25–2.21]) and SC route of administration (HR, 2.05 [95% CI, 1.45–2.91]) also predicted ID. Among the post-baseline factors, ACR50 at days 57 and 85 predicted both ID (HR, 1.57 [95% CI, 1.04–2.36] and HR, 1.88 [95% CI, 1.41–2.51], respectively) and remission (HR, 1.96 [95% CI, 1.11–3.45] and HR, 3.05 [95% CI, 1.47–6.34], respectively); ACR70 at day 57 also predicted ID (data not shown). Patients with predictive factors for age, hsCRP, Parent/Patient Global Assessment of well-being, and CHAQ-DI, and with lower disease activity achieved ID and/or remission earlier than patients with high disease activity.

Conclusion: We identified baseline and post-baseline factors that predicted JADAS10-CRP ID and remission in patients with pJIA treated with abatacept for 2 years. Screening of abatacept-treated patients with pJIA for such factors may help predict earlier achievement of ID and/or remission.

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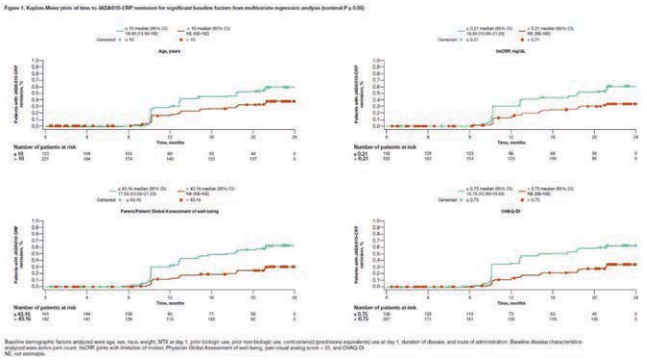

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POS0341 CONSENSUS-DRIVEN DEFINITION FOR UNEQUIVOCAL SACROILIITIS ON RADIOGRAPHS IN JUVENILE SPONDYLOARTHRITIS

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Background: Radiographs are not a sensitive or reliable imaging tool for detection of early sacroiliitis in juvenile spondyloarthritis (JSpA). However, radiographs are still commonly performed in some areas due to difficulty in accessing MRI. As such, radiographs were included in the imaging data considered for an axial disease classification criteria development study, but only when there was no suitable MRI available.
Objectives: We aimed to define criteria for unequivocal evidence of sacroiliitis on pelvic radiography in skeletally immature children and adolescents for use in classification criteria.
Methods: Subjects were a cohort of JSpA patients with suspected axial disease. All subjects had symptom onset prior to age 18 years and underwent MRI as part of a diagnostic evaluation for axial disease; a subset of subjects also had a dedicated pelvic radiograph. Using a web-based interface, 6 musculoskeletal imaging experts, blinded to clinical details, reviewed the radiographs and graded them according to the modified New York (mNY) criteria. A two-way random effects intraclass correlation coefficient (ICC) was used to assess agreement. Next, the central imaging team underwent an iterative consensus process to define unequivocal evidence of sacroiliitis on pelvic radiography in skeletally immature children. Radiographs with at least two raters assigning a non-zero mNY grade were re-reviewed for the presence/absence of "unequivocal evidence of sacroiliitis" according to the consensus definition. Agreement was assessed with Fleiss's kappa statistic with agreement interpreted as poor ≤0.40, fair 0.41-0.59, good 0.60-0.74, and ≥0.75 excellent. Sensitivity, specificity, and positive and negative predictive values (PPV, NPV) were calculated to assess performance of the novel definition using structural lesion typical of juvenile axial disease on MRI as the reference standard (erosion in ≥3 sacroiliac joint (SIJ) quadrants *or* at least one of the following lesions in ≥2 SIJ quadrants: sclerosis, fat lesion, backfill, ankylosis).
Results: Radiographs from 120 subjects, 61% male, median age 14.7 years (range 6.7-20.1 years), had an AP dedicated pelvic radiograph available for scoring. The ICC for mNY grade amongst 6 central raters was fair for joints with at least one rater reporting a non-zero grade (0.45, 95% CI: 0.34-0.57). After multiple iterations and discussion, the consensus definition of unequivocal sacroiliitis by radiograph in skeletally immature children and adolescents was deemed "Unequivocal lesion (erosion, sclerosis, or ankylosis [partial or complete]) that must include at least one iliac bone. When sclerosis is present in isolation, if measurable, should extend ≥5mm from the joint surface. The decision may be influenced by the presence of other lesions, which in themselves do not suffice to meet the criterion." Sixteen radiographs were assessed using the consensus definition. 8 (50%) were rated as unequivocal sacroiliitis and Fleiss' kappa statistic was good at 0.61 (95% CI: 0.41-0.80). Across raters, the sensitivity, specificity, PPV and NPV of the consensus definition on radiograph using structural lesions typical of sacroiliitis on MRI as the reference standard were 80% (95%CI: 44.4-97.5), 100% (95% CI: 54.1-100), 100% (63.1-100) and 75% (95% CI:34.9-96.8), respectively.
Conclusion: We propose a consensus-derived definition of unequivocal sacroiliitis by radiography in skeletally immature children and adolescents with good expert rater agreement. Additionally, the consensus-definition had moderate to high sensitivity and PPV and high specificity and NPV with typical structural lesions on MRI as the reference standard. This definition has applicability to JSpA axial disease classification criteria when MRI is unavailable.

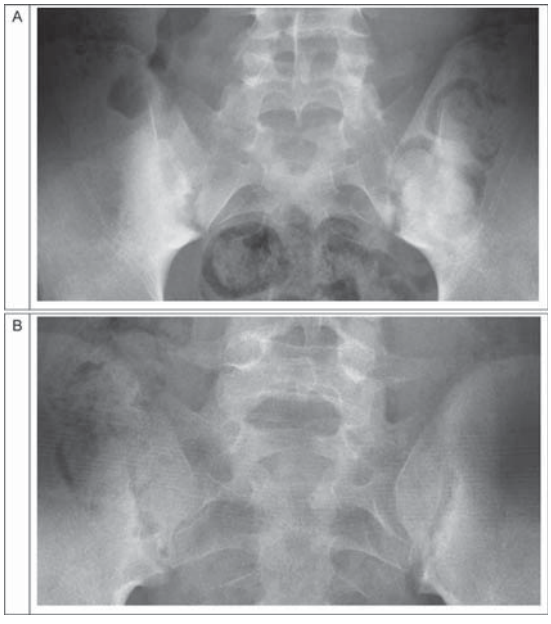

Figure 1. Examples of radiographs with unequivocal evidence of sacroiliitis in skeletally immature children as indicated by definite erosions of both iliac bones (A and B) and definite iliac sclerosis (A).

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POS0342 ANTI-TUMOUR NECROSIS FACTOR (ATNF) WEANING STRATEGY IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): DOES LONGER DURATION MATTER?

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Background: The efficacy of aTNF in the treatment of children with JIA has been demonstrated. However, once the disease is under control, strategy towards discontinuing aTNF should be considered. Thus far, there is no convincing information regarding how biologics should be weaned.
Objectives: To compare the outcomes of a short- and long-weaning strategies of aTNF in our prospective observational JIA cohort
Methods: Children with JIA taking aTNF with at least 6 months follow-up duration were recruited from our JIA registry (May 2010-Jan 2022) at KK Women's and Children's Hospital, Singapore. Once remission on medication, ROM[1] (including no enthesitis and sacroiliitis by MRI for ERA) was achieved, aTNF was weaned according to 2 different protocols– short (Etanercept every 2 weeks, and Adalimumab every 4 weeks, for 6 months) and long (extending frequency by every 2 weeks for 3 cycles until reaching 12 weekly interval for another 3 cycles then stop biologic thereafter) protocols. Flare (recurrent of arthritis, enthesitis or uveitis) rates were compared, and potential predictors were assessed. Nonparametric statistics were used to described data and logistic regression and Kaplan-Meier analyses were used to assess clinical parameters and outcome association and cumulative probability of disease flare, respectively.
Results: Out of 143 JIA patients, 105 (78% male, 82% Chinese; enthesitis related arthritis 78%, oligoarticular JIA 9%, polyarticular JIA 11%, psoriatic arthritis 1%, undifferentiated JIA 1%) underwent aTNF weaning with 53% on short- and 47% on long-weaning protocol. Median disease duration at aTNF start was 13.5 (10.6-15.8) and duration of follow-up was 6.6 (3.9-9.5) years. There was no significant difference in demographic and clinical parameters between groups. There was none of the short- but 49% of the long-weaning group flared during the weaning period, Table 1. However, no significant difference in the total flare rate (during and after stopping aTNF) was observed between the 2 groups despite less patient flare after stopping aTNF in the later, p=0.004. Median time to flare after stopping aTNF was not different, p=0.270. Furthermore, probability of flare after stopping aTNF was not different as well, Log Rank p=0.095, Figure 1. Positive ANA predicts flare during weaning (OR 5.2, 95%CI: 1.224-22.416, p=0.026), but none of clinical parameters were associated with risk of flare after discontinuing aTNF therapy in our cohort.

Table 1. Rate of flare and duration related to aTNF between short- and long-weaning groups

FLARE	Total (n=105)	Short (n=56)	Long (n=49)	p
Number of JIA patients flared during wean (%)	24 (22.9)	0 (0.0)	24 (49.0)	<0.001
Time to flare during aTNF weaning after starting (month)*			6.5 (4.5-14.5)	
Number of JIA patients flared after DC aTNF (%)	50 (47.6)	34 (60.7)	16† (32.7)	0.004
Time to flare after stopping aTNF (month)*		6.2 (2.7-11.8)	6.9 (5.5-11.6)	0.270
Total number of patients who flared	68 (64.8)	34 (60.7)	34 (69.4)	0.353

*Median (interquartile range), †included 6 patients who flare during weaning and after stopping aTNF, aTNF = anti-tumour necrosis factor

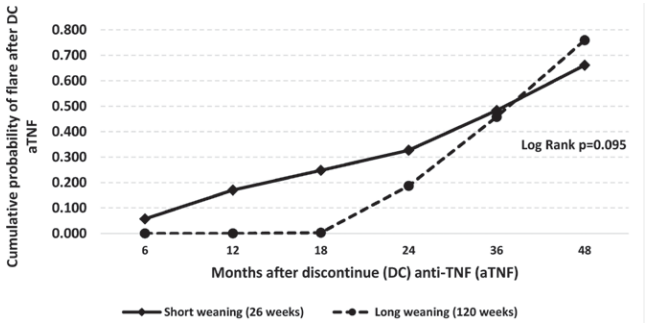

Figure 1. Cumulative probability of flare between the short- and long-weaning group after discontinuing aTNF therapy

Conclusion: Duration of spacing out the aTNF therapy after achieving ROM may not minimize the flare rate or delay time to flare after stopping the therapy in JIA patients. Further validation in larger multinational longitudinal cohorts is required to confirm our initial findings.

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Disclosure of Interests: None declared

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POS0343 TREATMENT PERSISTENCE AND ADHERENCE AMONG PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS RECEIVING ABATACEPT OR TNF INHIBITORS USING US CLAIMS DATA

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic condition among children and teens[1] and contributes to a diminished quality of life.[2] Previous data underscore the potential for abatacept to improve health-related outcomes in patients with JIA after demonstrating poor responses to other DMARDs.[3] Patients with RA show greater persistence on abatacept vs TNF inhibitors (TNFi), and this should also be confirmed in patients with JIA.[4]

Objectives: To evaluate treatment persistence and adherence at 12- and 18-month follow-up in patients with JIA newly initiating either abatacept or a TNFi.

Methods: This analysis used data from the IQVIA PharMetrics Plus claims database from Jan 2008–Apr 2021. We identified patients with ≥ 1 claim of JIA diagnosis after Jan 2008, who were < 18 years old at initial diagnosis, had ≥ 1 claim of abatacept or TNFi treatment (adalimumab, etanercept, golimumab) following diagnosis, had continuous enrollment in medical and pharmacy benefits for ≥ 12 months before index date (first prescription of abatacept or TNFi), and had 12 or 18 months' continuous medical and pharmacy enrollment after index date. Patients receiving abatacept or TNFi treatment ≤ 12 months prior to index date and patients initiating combined abatacept + TNFi treatment on the index date were excluded. Specific outcomes included: discontinuation (absence of a new prescription for index treatment within the gap of 5× treatment half-life), persistence rate (proportion of patients continuing index medication without any gaps exceeding 5× treatment half-life), and treatment adherence (defined as medication possession ratio [MPR, proportion of follow-up period where medication supply is available] and proportion of days covered [PDC, proportion of follow-up period where a patient is covered by a given drug]). All outcomes were reported at 12 and 18 months. All statistical analyses are descriptive with the intent for hypothesis generation.

Results: There were 2847 patients (abatacept, n = 111; TNFi, n = 2736) at 12-month follow-up; fewer completed the 18-month follow-up (2403 patients: abatacept, n = 94; TNFi, n = 2309). At index date, treatment groups were similar for sex, geographic location, and comorbidities (Table 1). Numerically higher persistence was observed in patients prescribed abatacept compared with TNFi overall at both time points. Abatacept persistence was higher than etanercept but similar to adalimumab (Figure 1). At 12 months, the percent of patients with PDC ≥ 0.8 was 57% for abatacept, 51% for adalimumab, and 38% for etanercept, while MPR ≥ 0.8 was 63% for abatacept, 55% for adalimumab, and 42% for etanercept. Patients prescribed abatacept had numerically greater proportions of PDC ≥ 0.8 (abatacept, 48%; adalimumab, 40%; etanercept, 29%) and MPR ≥ 0.8 (abatacept, 53%; adalimumab, 44%; etanercept, 33%) at 18 months.

Table 1. Baseline characteristics of patients with 12-month follow-up data

Characteristic	Abatacept (n = 111)	TNFi (n = 2736)
Age, years, mean (SD)	14.4 (3.8)	12.6 (4.6)
Female sex	89 (80.2)	1930 (70.5)
Geographic region		
South	43 (38.7)	865 (31.6)
Midwest	40 (36.0)	818 (29.9)
West	9 (8.1)	408 (14.9)
East	19 (17.1)	540 (19.7)
Unknown	0 (0)	105 (3.8)
Comorbidities		
Asthma	9 (8.1)	275 (10.1)
COPD	11 (9.9)	323 (11.8)
Cardiovascular disease	14 (12.6)	222 (8.1)
Uveitis	14 (12.6)	321 (11.7)
Iridocyclitis[a]	12 (10.8)	216 (7.9)
CCI score, mean (SD)	0.58 (0.73)	0.46 (0.68)

Data are shown as n (%) unless otherwise specified. [a]Subgroup disease under uveitis. CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease.

Conclusion: The present findings suggest that patients with JIA initiating abatacept treatment display numerically higher persistence and adherence compared with patients treated with TNFis at both 12- and 18-months' follow-up.

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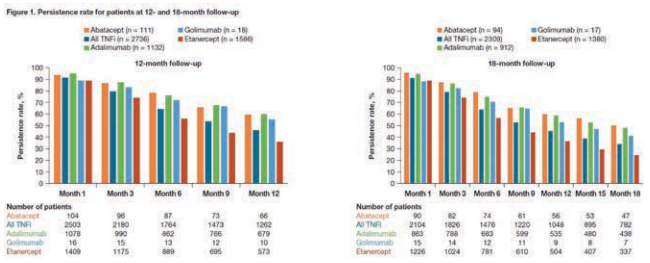

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Novel molecular regulators of bone turnover

POS0344 O-GLCNACYLATION ON NUP153 REGULATES THE EARLY STAGES OF OSTEOCLASTOGENESIS THROUGH MYC NUCLEAR TRANSLOCATION

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Background: Bone homeostasis is maintained by the balance between bone formation and resorption. In inflammatory arthritis, such as rheumatoid arthritis (RA), the pro-inflammatory environment promotes osteoclast differentiation and skews this balance towards bone resorption, leading to destructive bone erosion and bone loss. O-GlcNAcylation is one of the most common post-translational modifications, which attaches a single N-acetylglucosamine (GlcNAc) molecular to the serine or threonine of the target protein. O-GlcNAcylation is controlled by the activities of a single pair of enzymes: OGT, which facilitates the transfer of GlcNAc onto proteins; OGA, which removes GlcNAc from proteins. The activity of O-GlcNAcylation has been reported to be involved in several cellular events, such as transcription, translation, intracellular trafficking, and differentiation. We previously showed that the dynamics of O-GlcNAcylation are essential for osteoclast differentiation. TNF-α, a key pro-inflammatory factor in RA, intensified the O-GlcNAcylation dynamics. Inhibition of OGT arrests osteoclast precursors at early stages, whereas OGA inhibition blocks osteoclast maturation. However, the molecular mechanism of these regulations remains unclear.

Objectives: We aimed to identify the O-GlcNAcylation targets in osteoclast precursors in a pro-inflammatory milieu and to decipher the molecular mechanism of O-GlcNAcylation mediated regulation of osteoclastogenesis.

Methods: We first identify the O-GlcNAc-dependent molecular pathways in osteoclast precursors with pharmacological OGT and OGA inhibition by RNA sequencing. Then, we identified the O-GlcNAcylated proteins by mass spectrometry-based proteomics analysis and confirmed by immunoprecipitation. We found the potential molecular mechanism by combining the data from transcriptomics and proteomics. The proposed mechanism was further validated through siRNA-mediated knockdown and high-content screening analysis.

Results: Our transcriptomics data showed that OGT inhibition arrested osteoclast differentiation at early stages through interfering the cytokine signaling and metabolic adaption. The upstream analysis proposed MYC as the most potent regulator for the transcriptomic profile under OGT inhibition. Recent studies proposed MYC as a master regulator for metabolic reprograming during osteoclast differentiation. However, O-GlcNAcylation of MYC was not detected by mass spectrometry, suggesting indirect effects of O-GlcNAcylation on MYC signaling in osteoclast precursors. We detected upregulated levels of O-GlcNAc on NUP153, MTDH, RBM27, IFI207 upon RANKL+TNFα stimulation. An integrated analysis of transcriptomic and proteomic data by Ingenuity Pathway Analysis indicated that NUP153 might regulate the most DEGs among all the identified targets and indicated potential of NUP153 to regulate nuclear shuttling of MYC. Subcellular fractionation and confocal microscopy showed enhanced MYC nuclear translocation upon RANKL+TNFα stimulation, which could be blocked by NUP153 knockdown or OGT inhibition. Functionally, knockdown of NUP153 arrested cells at similar stages to OGT inhibition and reduced bone resorption ability. Together, these results suggest a model, in which O-GlcNAcylation regulates the shuttling activity of the nuclear pore component NUP153 to control the access of MYC to the nucleus during osteoclast differentiation.

Conclusion: Our results indicated that OGT inhibition arrests osteoclastogenesis at early stages through hampering MYC-dependent metabolic adaption. NUP153 was proposed as the most potent O-GlcNAcylation target by multi-omics data integration. NUP153-mediated MYC nuclear trafficking is required for osteoclast differentiation. These findings reveal the molecular mechanism of O-GlcNAcylation-dependent osteoclastogenesis and provide therapeutic insights on targeting O-GlcNAcylation in pathologic bone resorption.

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POS0345 ASSESSMENT OF THE EFFECT OF TOFACITINIB ON BONE MARROW ADIPOCYTES AND BONE-FORMING OSTEOBLASTS UNDER NON-INFLAMMATORY AND INFLAMMATORY CONDITIONS

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Background: Systemic inflammation is the main factor underlying secondary osteoporosis in patients with rheumatoid arthritis (RA). The JAK inhibitors, such as Tofacitinib (Tofa), can control systemic inflammation and have beneficial effects on bone in various models. This might be due to direct effects on the bone microenvironment and not exclusively based on their anti-inflammatory function. Bone marrow adipocytes (BMAds) are abundant in the bone microenvironment. The effect of JAK inhibitors on BMAds is unknown, but evidence suggests that there is competition between human bone marrow-derived stromal cell (hBMSCs) differentiation routes toward BMAds and osteoblasts (Ob) in osteoporosis.

Objectives: To determine in various models whether Tofa influences directly bone marrow cell committment toward adipogenesis and osteoblastogenesis. Then, in a prospective pilot study, to investigate the potential effects of Tofa on bone marrow adiposity in patients with RA.

Methods: To study the effect of Tofa on cellular commitment, hBMSCs were cultured for 3 days in appropriate Ob- and BMAd- differentiation media (Ob-3d and BMAd-3d), together with Tofa at 200, 400 (equivalent to a therapeutic dose of 5 mg twice a day in RA patients) or 800 nM. To mimic inflammatory conditions, TNFα was added to the media at a dose of 1 ng/ml. This study was also conducted on mature BMAds and a similar treatment was applied for 6 days to mature BMAds at 14 days of differentiation (BMAd-20d). The impact of Tofa was determined by gene expression profile analysis, western-blot analysis and cell density monitoring. In parallel, in a pilot study of 9 RA patients treated with Tofa 5 mg twice a day (TOFAT study: NCT04175886), proton density fat fraction (PDFF) was measured by MRI (Dixon technique) at the lumbar spine at the start of treatment and at 6 months.

Results: In non-inflammatory conditions, the gene expression of Runx2 decreased in Ob-3d treated with Tofa 400 and 800 nM($p<0.05$). Conversely, BMAd-3d treated with Tofa (at 200, 400 and 800 nM) exhibited a substantial increase in the gene expression of PPARγ2, C/EBPα and Perilipin 1 (a marker associated with lipid droplet formation) compared to controls ($p<0.05$). The increase in the expression of Perilipin 1 was also confirmed at the protein level. In inflammatory conditions, BMAd-3d and Ob-3d markers decreased considerably (PPARy2 and RUNX2, respectively, $p<0.05$), but the addition of Tofa did not change the expression profiles of Ob-3d compared to TNFα controls. On the contrary, the analysis of PPARy2 gene expression showed that Tofa limited the negative effect of TNFα on BMAd differentiation ($p<0.05$). The positive effect of Tofa on mature adipocyte (BMAd-20d) under inflammatory conditions was also supported by an increase in the density of differentiated BMAds ($p<0.001$). These findings were consolidated by an increase in PDFF at 6 months of treatment with Tofa in RA patients (+6.9%, $p<0.01$).

Conclusion: Overall, *in vitro* and clinical results suggest a stimulatory effect of Tofa on BMAds commitment and differentiation, which does not support a positive effect of Tofa on bone

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POS0346

IDENTIFICATION OF NEW MUTATIONS IN THE SQSMT1 GENE IN PATIENTS WITH PAGET'S DISEASE OF BONE. GENOTYPE-PHENOTYPE CORRELATION

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Background: The Paget's disease of Bone (PDB) is characterized by a chronic and focal disorder of bone remodeling. PDB is currently considered a complex and multifactorial disease, as a result of a synergistic association of genetic variants with environmental risk factors. The genetic component would explain certain epidemiological traits such as the predisposition to develop in certain ethnic groups and the strong tendency to family aggregation. The most important susceptibility gene for PDB is the Sequestosome-1 (*SQSTM1*), and encodes a 440-amino-acid protein called p62 protein. *SQSTM1* gene occur in between 20 and 40% of patients with a family history of PDB, and 5 and 10% of patients with 'sporadic' disease, according to the series studied. Thus far, 29 *SQSTM1* mutations have been identified in patients with PDB[1-4].
Objectives: To analyze the importance of SQSTM1 gene (p62) variants in the susceptibility to develop PDB, as well as to evaluate the genotype-phenotype correlation in our PDB population.
Methods: The molecular study was carried out by sequencing the SQSTM1 gene (p62) in a population of 200 PDB affected patients and 200 *hypernormal* controls. An "*in silico*" functional analysis of the different genetic variants was performed using the information provided by the splicing prediction algorithms, the miRNA target prediction algorithms, the gene-specific algorithms for predicting pathogenicity (SIFT, PolyPhen, PMut) and the interspecific evolutionary conservation study. The statistical analysis was *performed using SPSS statistical software* Windows (v23) and the R software version 2.15.0 for Windows. The study was approved by the CEIC (Hospital del Mar-Parc de Salut Mar (2007/2885/I)) and all participants signed an informed consent agreeing to participate in the study.
Results: The 27% of the PDB affected patients were carriers of different gene *SQSMT1* mutations, being the most frequent identified the p.P392L, described in the 20% of cases. In terms of genotype-phenotype relation, being a carrier of gene *SQSMT1* mutations is associated to a more severe phenotype based on a greater disease activity and a greater extent at diagnosis as well as higher complications during the course of it, without the presence of an associated family history positive. In our patient cohort 17 mutations have been identified in coding regions of the SQSMT1, with six newly described "*missense*" genetic variants (p.R161W, p.H163Y, p.K238E, p.G262R, p.E274D,p.G405S), all of them associated to a greater susceptibility in the development of PDB and distributed in the different structural and functional domains of the p62 protein, being able to cause dysfuntions in the different cell signalling processes where intervenes (apoptosis, autophagy, proteic degradation through the ubiquitin-proteasome system, the regulation of antioxidant response and the cell survival mediated by RANK-TRAF6-NF-κB signaling pathway), implicated in the pathogenesis of Paget's disease of bone.
Conclusion: In the molecular study of the *SQSTM1* gene, seventeen mutations were identified in the coding regions of the gene, being six "*missense*" genetic variants of new description, associated all of them to a higher risk of developing PDB and distributed in different structural and functional domains of the p62 protein.
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POS0347

CHARACTERIZATION OF THE TRANSCRIPTOMIC SIGNATURE OF BONE MARROW CELLS IN OSTEOPOROSIS ASSOCIATED WITH SYSTEMIC MASTOCYTOSIS

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Background: Systemic mastocytosis (SM) is a rare monoclonal mast cell disease, associated with vertebral osteoporosis (OP) in ~30% of the patients. This OP frequently leads to multiple vertebral fractures, in particular in young or premenopausal patients. Soluble mediators secreted by the pathogenic mast cells and subsequent activation of osteoclasts are thought to explain the development of such OP. However, data about the nature and the regulation of the pro-osteoporotic factors is limited. We hypothesize that a transcriptomic approach, assessing bone marrow cells involved in this pathological condition, can identify the specific determinants of fragility fractures in SM.
Objectives: To identify a bone marrow transcriptomic profile associated with osteoporosis in SM.
Methods: We analysed clinical data and bone marrow samples collected at diagnosis in SM patients from our Reference Centre for Mastocytosis (CEREMAST) and fulfilling the SM WHO criteria. All patients signed an informed consent. Twelve SM patients with OP and fragility fracture (OP group) were age- and gender-matched with 12 SM patients without OP or fragility fracture (non-OP group). We used a Nanostring nCounter approach to compare the bone marrow mRNA profile. We used a predefined panel of 800 transcripts relevant for an osteo-immunological analysis. Genes expressions were normalized and compared by a Wilcoxon test with R software. We performed a pathway analysis with C5, C7, KEGG and Reactome databases.
Results: Both OP and non-OP groups included 8 women and 4 men, with similar average age (OP 56.1 +/- SD 8.7 vs non-OP 57.1 +/- 9.3). The 12 patients from the OP group had at least 1 vertebral fracture (VF) with an average number of VF of 4.9 +/- 2.6. Lumbar and hip bone mineral density was significantly lower in the OP group. The transcriptomic analysis revealed a specific profile associated with osteoporotic vertebral fractures in SM, with 26 differentially expressed genes (see Figure 1). The analysis highlighted an involvement of NECTIN2 and of IL6/STAT3. Pathway analysis suggested a role for genes involved in cell cycle regulation, T cell activation, protein kinase activity and differentiation and activation of monocytic cells.

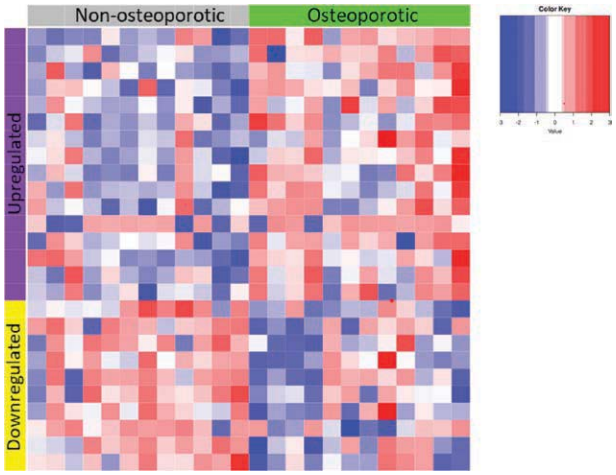

Figure 1. Heatmap of the differentially expressed genes in bone marrow from SM patients with osteoporosis and fragility fracture versus without osteoporosis

Conclusion: Our results highlight that a transcriptomic analysis of bone marrow is relevant to identify biomarkers associated with OP in SM. In addition to the pathogenic role of clonal mast cells and of monocytic lineage, this condition may involve non-clonal immune cells such as T cells.
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POS0348

DEVELOPING A WHOLE MOUNT FLUORESCENT OSTEOCLAST ACTIVITY ASSAY USING THE ELF97 PHOSPHATASE SUBSTRATE TO VISUALISE AND QUANTIFY IN SITU OSTEOCLAST ACTIVITY IN ZEBRAFISH (DANIO RERIO)

E. L. S. Fong[1], E. L. Prabha[1], T. Carney[1]. *[1]Lee Kong Chian School of Medicine (LKCMedicine), Singapore, Singapore*

Background: Osteoporosis is a mineral bone disease arising from the predominance of osteoclastic bone resorption. Bisphosphonates which inhibit osteoclasts are commonly used in osteoporosis treatment, but are not without severe adverse effects like osteonecrosis of the jaw. The mechanisms behind the development of such phenomena is not well understood. Bone homeostasis is achieved through an intimate cross-talk between osteoclasts and osteoblasts. Thus, it is important to visualise activities of these cells simultaneously in situ. Currently, there are means to visualise osteoclast shape and numbers with tartrate-resistant alkaline phosphatase (TRAP) staining but no practical and accurate methods to quantify osteoclast activity *in situ*.

Objectives: This investigation aims to establish the use of ELF97, a substrate of TRAP, to visualise and quantify osteoclast activity. This provides vital clues to mechanisms of various bone disorders. TRAP dephosphorylation of ELF97 results in a detectable fluorescent product at areas of osteoclast activity.

Methods: Osteoclastic activity was initiated in zebrafish by inducing crush injuries in tail fin rays. Colocalisation of ELF97 fluorescence with osteoclast-specific DsRed in transgenic zebrafish, visualised under confocal microscopy, is used to further establish the specificity of ELF97 to sites of osteoclastic activity. Quantification is established by comparing fluorescence between wild type, osteoclast-deficient mutants and bisphosphonate-treated zebrafish. The utility of ELF97 will also be investigated in terms of the stability of the florescent product.

Results: The investigation revealed that ELF97 and DsRed fluorescence were found commonly at crush sites with osteoclastic activity. Wild type zebrafish had greater fluorescence compared to osteoclast-deficient ($p<0.0001$) and bisphosphonate-treated zebrafish ($p<0.0001$) after 7 and 14 days post-crush, revealing that fluorescence from ELF97 corresponds to expected osteoclastic activity. Fluorescence of tail fins treated with ELF97 did not diminish over a period of 21 days of storage, demonstrating its stability.

Conclusion: ELF97 is thus a useful means to visualise osteoclast activity, potentially crucial in more advanced investigations to understand bone disorders. It could be used in combination with other cellular markers in whole biological samples to study and experimentally manipulate bone remodelling.

Disclosure of Interests: None declared

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POS0349 DECOY RECEPTOR 3 AND ITS SIGNAL PATHWAY CONTRIBUTE TO PATHOGENESIS IN PRIMARY GOUTY ARTHRITIS

Y. Jiang[1], X. Liao[1], S. B. Wang[1], Y. X. He[1], Y. F. Qing[1]on behalf of Institute of Research Center of Gout and Hyperuricemia of the Affiliated Hospital, North Sichuan Medical College. *[1]Affiliated Hospital of North Sichuan Medical College, Department of Rheumatology, Nanchong, China*

Background: Gouty arthritis (GA) is an autoinflammatory disease caused by the deposition of monosodium urate crystal (MSU) in the joints and surrounding tissues, which lead to a series of complex inflammatory cascade amplification reactions.The clinical symptoms of acute GA attack rapidly, but often alleviate spontaneously within 7 ~ 10 days, which is one of the significant characteristics different from other joint diseases or autoimmune diseases. However, the exact molecular mechanism of its inflammatory self limitation is still unclear. The phenotypic imbalance of Th1 / Th2 cells and the M1/ M2 polarization of macrophages may be involved in the inflammatory self limitation of gout[1].Decoy receptor 3 (DCR3) can differentiate T cells into Th2 phenotype, promote M2 polarization of macrophages, and play the functions of immune regulation and repair[2].DCR3 and its Signal Pathway are involved in the pathogenesis of tumors and a variety of autoimmune diseases, and have become an important research target of tumors and immune related diseases.However, studies on DcR3 related molecular pathway and GA are scarce, and the specific regulatory mechanism is unknown.

Objectives: To assess the contribution of DcR3 and its signal pathway to gout and the clinical importance of these genes in primary gouty arthritis.

Methods: The mRNA expression levels of DCR3 and its signal pathway(DR3, TL1A, Fas, FasL, Ligth, LigthR, LTgthRNA expression levels of DCR3 and its signal pathway(DR3gout and the clinical importance of these genes in primary gouty arthritis.nt research target of tumors and immune related diseases.However, studies on DcR3 related moathway expression levels and laboratory features was analyzed in GA patients.

Results: The expression levels of DCR3, FasL were much lower in the AG and IG group than in the HC groups ($p<0.05$), and no significant difference was detected between AG and IG groups($P>0.05$)(a,e). The expression levels of DR3 were much lower in the AG and IG group than in the HC groups ($p<0.05$), and much lower in the AG group than in the IG groups ($p<0.05$)(b). The expression levels of TL1A were much higher in the AG group than in the IG and HC groups ($p<0.05$), and no significant difference was detected between IG and HC groups($P>0.05$)(c).The expression levels of Light, LightR were much lower in the AG group than in the HC groups ($p<0.05$), and no significant difference was detected between AG and IG groups, IG and HC groups($P>0.05$)(f,g).The expression levels of LTlower in the AG and IG group than in the HC groups ($p<0.05$($p<0.05$), and no significant difference was detected between AG and IG groups, IG and HC groups($P>0.05$)(h).In GA patients, the levels of DcR3 related molecular pathway gene correlated with laboratory inflammatory and metabolic indexes.

Conclusion: Altered DCR3 and its signal pathway expression suggests that DCR3 related molecular pathway is involved in the pathogenesis of GA and participates in regulating inflammation and metabolism.

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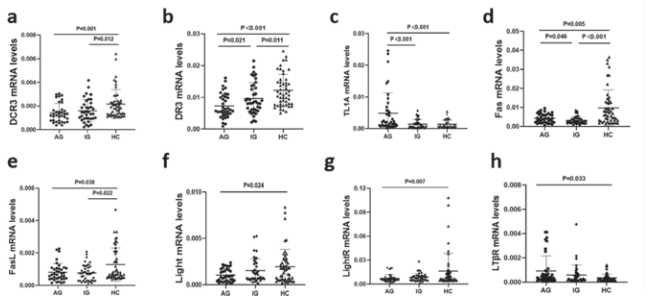

Figure 1. Relative Expression of DcR3 related molecular pathway gene in the PBMCs of Patients.The expression levels of DCR3, FasL were much lower in the AG and IG group than in the HC groups ($p<0.05$)(a,e). The expression levels of DR3 were much lower in the AG and IG group than in the HC groups ($p<0.05$), and much lower in the AG group than in the IG groups ($p<0.05$)(b). The expression levels of TL1A were much higher in the AG group than in the IG and HC groups ($p<0.05$)(c).The expression levels of Light, LightR were much lower in the AG group than in the HC groups ($p<0.05$)(f,g). The expression levels of LTβR were much higher in the AG group than in the HC groups ($p<0.05$)(h).

Acknowledgements: Institute of Research Center of Gout and Hyperuricemia of the Affiliated Hospital, North Sichuan Medical College

Disclosure of Interests: None declared

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POS0350 MICRORNAS ASSOCIATED WITH OSTEOPOROSIS IN PATIENTS WITH HAEMOCHROMATOSIS ARTHROPATHY

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Background: Haemochromatosis arthropathy (HA) is one of the most frequent manifestations of hereditary haemochromatosis (HH). Moreover, frequency of osteoporosis is increased in HH. MicroRNAs (miRNAs) are small non-coding RNAs involved in gene silencing, and onset and progression of disease is often reflected in aberrant miRNA expression patterns including osteoarthritis and osteoporosis. Active or passive release of miRNAs from cells enables minimal-invasive detection in biofluids such as plasma (“circulating miRNAs”).

Objectives: We aimed to investigate whether circulating miRNAs involved in osteoporosis as well as liver disease in healthy elderly individuals are also elevated in patients with HH.
Methods: Plasma of 28 HA patients homozygeous for C282Y (60.71% female), 8 HA patients heterozygeous for C282Y (50% female), and 12 controls (66.67% female), was analyzed using the osteomiR and the hepatomiR RT-qPCR kits. Levels were normalized using spike-in controls and non-parametric analyses were performed to associate miRNAs to other clinical parameters and test for differential regulation of miRNAs between the groups.
Results: Even though mean age was different between the three groups (70.64, 52.38, 61.92 years), correlation analysis identified only weak or no associations to miRNA levels. In patients with osteoporosis (n=9, all female, all homozygeous) miR-203a-3p, 214-3p (both bone-related), and 122-5p (liver-related) were significantly downregulated (Kruskal Wallis p=0.024, p=0.037, and p=0.00024). Interestingly, miR-122-5p also showed a clear trend for down-regulation in homozygous HH compared to heterozygous HH and controls (p=0.087).
Conclusion: This is the first study reporting miRNAs involved in osteoporosis and liver diseases in patients homozygeous for C282Y.
Disclosure of Interests: None declared
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POS0351 **NEITHER ANTI-CITRULLINATED PROTEIN ANTIBODIES (ACPA) NOR POLYCLONAL IGG ARE ASSOCIATED WITH BONE MASS, IN ELDERLY MEN**

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Background: Bone loss is associated with anti-citrullinated protein antibodies (ACPA) positivity in rheumatoid arthritis (RA) patients. This is shown in both in pre-clinical RA, and in more pronounced bone loss in serum positive patients compared to serum negative patients. Further, both ACPA and activated IgG stimulate osteoclastogenesis *in vitro* and in murine arthritis-mediated bone loss.
Objectives: Whether polyclonal IgG or autoantibodies are important for general bone architecture, and not only in arthritis-mediated bone loss, has not been determined but they may represent an important link between the immune system and bone.
Methods: Polyclonal IgG and ACPA were measured with ELISA in serum of 600 elderly men (mean age 80.2±3.5 years), in the cohort MrOS Gothenburg. In this cohort, bone was investigated with Dual-energy-x-ray absorptiometry (DXA) and high-resolution 3D peripheral quantitative computed tomography (HR-pQCT). In C57/BL6 mice, high dose heat-activated polyclonal IgG was repetitively injected systemically or intraarticularly, and the bone was investigated with DXA and micro-CT.
Results: No association was determined between existing serum polyclonal IgG and ACPA, with the measured bone parameters, not total bone density, trabecular or cortical bone in the MrOS cohort. Systemic injection of activated IgG in mice did not affect general bone health, not total, trabecular, or cortical bone. Intraarticular injection of activated IgG was shown to give a local reduction in trabecular bone density of the tibia.
Conclusion: These data indicate that serum polyclonal IgG and ACPA do not influence general bone health in elderly men. However, in mice injection with activated IgG intraarticularly leads to a local reduction in trabecular bone. In conclusion, our data imply that ACPA and activated IgG need to be present in close connection to the bone, e.g., in the synovial area, to be able to mediate a reduction in bone mass.
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PARE Poster Tour 2

POS0352-PARE **PODCAST FOR RHEUMATISM SUFFERERS AND THEIR RELATIVES**

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Background: Two million people in Switzerland suffer from rheumatic diseases. The Swiss League against Rheumatism is committed to helping those affected. It provides them and their relatives with professional, neutral information on the subject of rheumatism. The Swiss League against Rheumatism has been publishing the podcast series "Rheumatism in person" since 2021. In it, affected people discuss relevant and current topics about living with rheumatism with experts. Another aim is to devote time to the personal experiences of sufferers. The pool of experts includes medical specialists, nutritionists, social counsellors and psychologists.

Objectives: The Swiss League against Rheumatism, as the national umbrella organisation, is expanding its communication services via the podcast in order to reach even more people with rheumatism in Switzerland. This makes it is possible to increasingly address a younger, digital-savvy target group and to expand the service proposed for this target group. The podcasts are primarily aimed at people with chronic forms of rheumatism between the ages of 25 and 50 and their relatives in German-speaking Switzerland. A further aim is to bring the opinions of those affected to the attention of the public, as well as to provide information from specialists, thereby creating greater awareness of the disease.

Methods: Each podcast episode is about 30 minutes long. According to experience, this length is the most popular with most listeners, whilst also allowing complex topics to be explored in depth. The podcasts are issued monthly. This enables listeners to be prepared for a fixed release date. The episodes are produced in cooperation with a podcast agency. The advantage of an agency lies in its expertise and experience, especially in the technical field. Funding for the podcast episodes can be secured from sponsors.

"When things get complicated – social counselling for rheumatism", "Sport and rheumatism – anything but a contradiction" or "Rare forms of rheumatism – lupus, EDS & co." are popular episode titles, to name but a few.

The podcasts are available on various international podcast platforms. The episodes are distributed via blog posts, existing newsletters and social media (Facebook, Instagram and LinkedIn). External distribution channels are used in the form of the interviewees' networks, the "Junge mit Rheuma" (young people with rheumatism) group, national patient organisations, cantonal/regional rheumatism leagues, the Swiss Society of Rheumatology and any media coverage attracted.

Results: So far, the eleven episodes and accompanying trailer have been downloaded or streamed over 8,200 times by 5,300 unique listeners.

All eleven topics were of great interest. The episode on "Anti-inflammatory nutrition" generated the most downloads (1,550), closely followed by the episode on "The coronavirus pandemic with rheumatism", which reached just under 1,300 downloads (as of 21 January 2022). On 15 March 2021, the podcast series also made it onto the podium of a well-known podcast chart in the field of medicine. This clearly shows that there is a need among rheumatism sufferers and their relatives to obtain information via podcasts.

The large quantity of positive feedback from patients, rheumatologists and other health professionals is particularly noteworthy. "From the first second: very interesting topics, well produced and a great voice," shared a listener.

Conclusion: The podcast series has proved successful and will therefore be continued as a complementary communication tool for the Swiss League against Rheumatism. In addition to the episodes already released, another ten episodes are planned in German.

The Swiss League against Rheumatism is keen to extend the podcast series to the French-speaking part of Switzerland. The idea is therefore to include French episodes in 2022. There are specific plans to record three episodes, which will be broadcast in the second half of the year. The aim is to add more episodes to the French podcast series in the long term.

REFERENCES: None

More information: Podcast: Rheuma persönlich - Rheumaliga Schweiz

Disclosure of Interests: Monika Siber Grant/research support from: The Swiss League against Rheumatism has a sponsorship agreement with MSD Merck Sharp & Dohme AG and Pfizer AG for the production of the podcasts. The two companies have no influence on the content of the podcast., Tina Spichtig Grant/research support from: The Swiss League against Rheumatism has a sponsorship agreement with MSD Merck Sharp & Dohme AG and Pfizer AG for the production of the podcasts. The two companies have no influence on the content of the podcast.
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POS0354-PARE **THE POLITICAL WORK FOR BETTER TREATMENT OF MUSCULOSKELETAL DISEASES IN DANISH MUNICIPALITIES**

K. Hammenfors[1] on behalf of The Danish Rheumatism Association. [1]*The Danish Rheumatism Association, Department for Politics and Knowledge, Gentofte, Denmark*

Background: Historically most treatment of musculoskeletal diseases in Denmark has taken place in hospitals. Today, treatment is split between different sectors, where the requirements are widely different.

Physiotherapists, occupational therapists and dietitians are, to a certain extent, no longer found in the rheumatic sections of the hospitals, but rather expected to take care of rehabilitating treatment in one of the 98 municipalities. With the clinical guidelines, the Health Authorities has indicated which treatment areas the individual groups of patients will benefit from – however, there is lack of provision of these in many of the municipalities across the country.

Objectives: To secure that treatment guidelines - within the field of musculoskeletal diseases - made by The National Board of Health, are transformed into national quality standards for treatment in the municipalities.

Methods: To ensure that patients get the treatment needed, we have worked with external consultants resulting in two research papers (visible at link) on the subject at hand. One paper mapped how many of the 98 municipalities provides each of four treatment guidelines made by The National Board of Health. The four being – weight loss, education and physical training for hip- and knee osteoarthritis, education and physical training for patients with back conditions and interdisciplinary treatment for people with pain conditions. The other paper uncovered the potential economic gains for the public sector by introducing the treatment guidelines.

The Danish Rheumatism Association has used these research papers as a significant driver for a large conference in October 2021 at the Danish Parliament – Christiansborg. Essential national politicians where present and they acknowledged the need for an increased focus on the treatment areas.

The results of the reports has also been shared with government officials, an existing commission on labor supply as well as municipalities etc.

In connection with the recently held elections in Danish municipalities and regions, we have reached out to the local politicians experiencing a gap in the offerings either directly or through local media which will hopefully result in an uplift of the focus. In addition, we have made debate posts with among others - unions sharing our point of view.

Results: Essential national politicians acknowledged the need for an increased focus on the treatment areas.

We hope that both from the municipalities as well as from a national level initiative will be taken to introduce a set of national quality standards within the field of musculoskeletal diseases because of our forceful approach.

Conclusion: The increased focus on treatment of musculoskeletal diseases is the result of strong collaboration between The Danish Rheumatism Associations department for Politics and Knowledge, Internal Communications and external partners.

We believe that our work can inspire other European NGO's who has a need to increase their political agenda and awareness. We made a long-term goal, allocated the finances and employees needed and it seems that the structured approach we have taken have increased the focus for our patients in the public debate and will help us achieve the goals.

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Disclosure of Interests: None declared
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POS0355-PARE **LONGITUDINAL INVESTIGATION AND VISUALIZATION OF COURSE AND BURDEN OF ADVERSE DRUG REACTIONS IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES USING TNFα INHIBITORS**

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Background: Patients are increasingly involved in the decision process regarding their medicines, but a discrepancy exists between the information provided and preferred. Information on adverse drug reactions (ADRs) focuses on frequency, but little is known about the course and burden of ADRs.

Objectives: We aimed to investigate the course and burden of ADRs over time attributed to using TNFα-inhibitors in patients with inflammatory rheumatic diseases (IRDs) and to assess whether Sankey diagrams and polar plots are suitable to provide visualization of these aspects.

Methods: We used data of the Dutch Biologic Monitor [1], in which biologic users with an immune-mediated inflammatory disease filled out bimonthly surveys about ADRs experienced and specifically the ADR course and burden. ADRs were coded according to the MedDRA terminology. ADR course was scored as worsening, improving, remaining stable or resolving over time, with room to give a description. Furthermore, it was assessed whether an ADR was recurrent or not. Patients scored burden on a scale ranging from 1 (no burden) to 5 (very high burden). We selected patients with rheumatoid arthritis (RA), psoriatic arthritis or axial spondyloarthritis using a TNFα inhibitor (adalimumab, certolizumab pegol, etanercept, golimumab or infliximab). They also had to report an ADR belonging to the system organ classes 'Infections and infestations' or 'Skin and subcutaneous tissue disorders', or the high-level term 'Injection site reactions' and completed ≥2 consecutive questionnaires (representing circa ≥4 months). These types of ADRs were chosen as they impose the highest burden for patients. [2]

Results: A total of 202 patients met the inclusion criteria (71.8% female, mean age 54.8 years (±12.7 years)). The majority of the patients (61.9%) was diagnosed with RA. Most frequently used TNFα inhibitors were adalimumab (37.1%) and etanercept (54.0%). In total 353 ADRs were reported, of which 76 (21.5%) were categorized as 'Skin and subcutaneous tissue disorders', 122 (34.6%) as 'Infections and infestations' and 155 (43.9%) as 'Injection site reactions'. The course of the ADRs is visualized in Sankey diagrams (Figure 1a-c); the flows show possible ADR courses, the width of each is proportional to the number of ADRs following that course. Most skin reactions did not change during follow-up (25.0%, Figure 1a), only a few were recurrent. Most infections resolved over time (50.8%, Figure 1b), with some remaining stable and some being recurrent. Most injection site reactions (72.3%, Figure 1c) were recurrent, and resolved in only a minority of the patients (13.4%) during follow-up. The polar plots (Figure 1d-f) visualizes the burden of the ADRs over time. For skin reactions and infections a decreasing trend was observed, represented by fading of the colors to the periphery. Infections had the highest burden at the start of the ADR, indicated by the darker colors in the inner circle. Injection site reactions had a relatively low and stable burden over time, shown by the lighter colors continuing over the circles.

Conclusion: Skin reactions attributed to the use of TNFα-inhibitors by IRD-patients show a stable course over time with a slightly diminishing burden over time. Infections have the highest burden at start but decrease over time and most of them resolve during follow-up. Injection site reactions are mostly recurrent with a low and stable burden over time. We propose that Sankey diagrams and polar plots are suitable to visualize the course and burden of ADRs over time.

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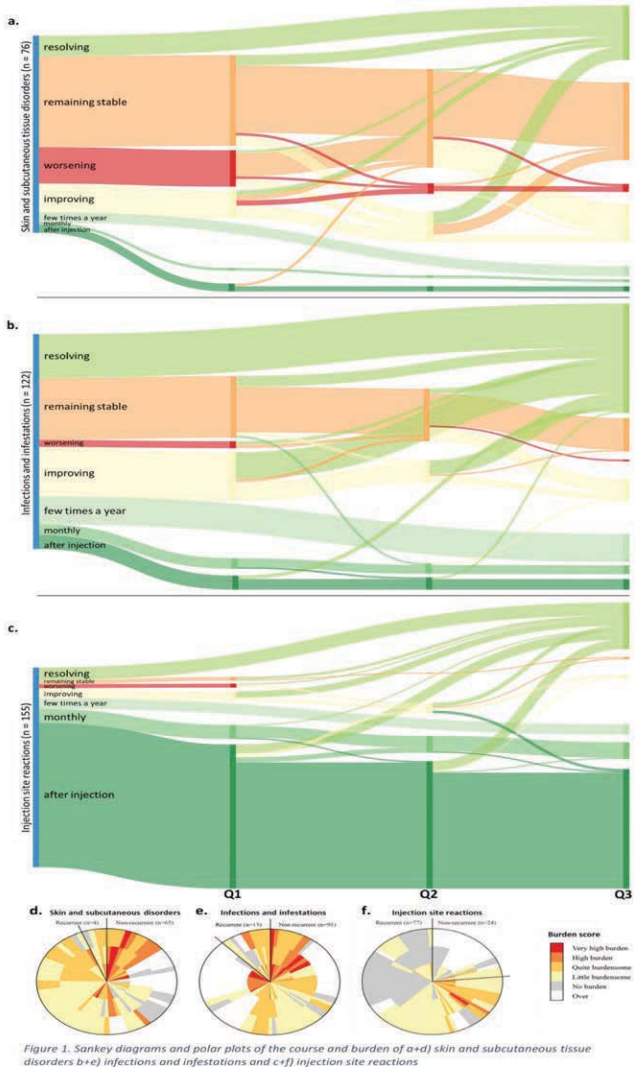

Figure 1. Sankey diagrams and polar plots of the course and burden of a+d) skin and subcutaneous tissue disorders b+e) infections and infestations and c+f) injection site reactions

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POS0356-PARE IN OUR HAND – SELF MANAGEMENT COURSE (FOR PEOPLE WITH CHRONIC RHEUMATIC DISEASES

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Background: Since 2016 we had a dream to construct a self-management course for members of The Israeli association for RMDs patients *Mifrakim Tz'eirim*. On September 2018, our CEO heard a lecture by Mrs. Mary Vella, the president of ARAM Malta, and the rest is history.

We approached PARE through AGORA for the Knowledge Transfer Program Grant and got approved in February 2019. The need to develop such a course came from members of the association, as well as posts in Facebook groups. Concerns, fears, and uncertainties about how to live with a chronic illness.

Mifrakim Tz'eirim is committed to reaching out to children, youth, adults and seniors with autoimmune and inflammatory joint diseases and rare autoimmune and various inflammatory diseases and to their families. The association assists its members and provides them with support and available tools on a personal, family, and social level. Our goal is to act for increasing public awareness of these diseases and their day-to-day impact on patients, to expand knowledge and disseminate information about them, patient rights and innovations in treatment, as well as to promote access to a variety of advanced treatments and medications for the members.

Objectives: Providing tools for daily coping and optimal conduct in chronic illness situations in a wide range of aspects: a self-management triangle:

a. Medical / biological (better / helpful understanding of the situation)
b. Emotional (Identify and manage the emotional impact)
c. Social (adjusting the way you manage your daily life)

METHODS:

1. Receiving a grant from PARE - The Knowledge Transfer Program Grant, through AGORA
2. Cooperation with ARAM - Arthritis & Rheumatism Association Malta
3. A study visits to Malta
4. Monitoring the process in Israel by ARAM
5. Founding a management team for the course
6. Localizing adaptation of the learned content for Israelis and introducing new content of our own
7. Promotion of the course to the association members, selecting participants
8. December 2019 the first course started. In 2020-2021 we had 3 more cycles of the course to the members. We had 40 participations
9. Following the pilot course - generating conclusions, lessons, and adjustment of the syllabus accordingly
10. Three more courses are planned for 2022

RESULTS:

1. Excellent feedback from ARAM during the control performed
2. Participants provided outstanding feedback on the course
3. Course graduates established designated WhatsApp groups for ongoing mutual support, thus creating empowerment circles, including periodic physical meetings

CONCLUSION:

1. *In My Hands* course provides a highly efficient and relevant toolbox.
2. The course should be continually offered to people coping with chronic diseases
3. *Finger on the pulse* - ongoing drawn conclusions to be implemented for adjusting the syllabus
4. The course should be promoted gently, since it marks a change in life, which can threat some people's perception
5. We have expanded and offered participation to members of other patient associations that we collaborate with
6. Graduates of the course become ambassadors, spreading the benefits received by the course
7. Graduates of the course are a vivid example of the chance of improving your life even when you cope with chronic diseases
8. Graduates of the course influence their immediate circles to adapt and adopt changing habits

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2. AGORA Board platform for South European organizations of Patients with RMDs
3. Mrs. Mary Vella, President, ARAM
4. Dr. Mariella Borg Buontempo, Consultant in public health medicine, Maltese Ministry for Health
5. Prof. Gleb Slobodin, Senior Rheumatologist, medical supervisor to the Israeli course
6. Mrs. Hily Wollach, Chairwoman of Mifrakim Tze'irim, and the Association Board members
7. The Israeli course Management Team and lecturers
8. Last but not least - Mifrakim Tze'irim members who took part in the courses

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POS0357-PARE EXPLORING THE IMPACT OF THE PANDEMIC ON ITALIAN RHEUMATIC DISEASE PATIENTS: A PATIENT ADVOCACY SURVEY

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Background: Patients with rheumatic diseases show impaired quality of life (QoL): disease activity, comorbidities and treatment-related side effects contributes to decrease physical, emotional, and social functioning. The COVID-19 pandemic challenged health care systems and patients with chronic conditions: hospital and outpatient clinics delayed access, unpredictable changes like non-adherence to medication, but also negative emotions, psychological conditions recognized as risk factors for the poor QoL [1-2].
Objectives: To describe the impact of the COVID-19 pandemic on the Qol of Italian patients with rheumatic diseases in the first period of the national lockdown.
Methods: APMARR (Associazione Nazionale Persone con Malattie Reumatolgoche e Rare) invited Italian patients and caregivers to participate to an online structured survey in the period March-June 2020. Informed consent was retrieved. The questionnaire, promoted by the patient advocacy website, collected demographics, emotional and healthcare pattern information.
Results: 87,44% (N=215) complete questionnaires were retrieved (96.3% patients; 3.7% caregivers; 87.77% female; 2% aged <18 years, 16% aged 18-30 years, 82% aged >31 years; 0.53% missing data). Respondents were illustrative of the Patient Advocacy regional distribution (Puglia Region predominant). Rheumatoid arthritis regarded 29% of respondents, ankylosing spondylitis 17%, psoriasis 16%, remaining 38% other rheumatoid diseases. 96% of respondents were employed, 39% of which had to discontinue/change working activity during pandemics.
60% of respondents reported being worried about their disease. The deriving sense of fragility was the main cause of anxiety, which was not controlled even by compliance to the treatment plan (88%). 30% of respondents was worried about virus infection. Irritability, appetite and sleep disorders were also reported: anxiety had effects on irritability (46% sometimes more irritable) and sleep quality (38% always disturbed). GPs visits access was limited (40% considered it absent and 76% had to postpone it). Only 32% of specialist centers provided facilitated patterns of care.
Respondents suggested possible solutions to improve QoL during COVID-19 pandemic and over it. Psychologist support was suggested as useful by 44% of respondents to manage therapies and by 56% to effort daily life. The home infusion would be of support according to 44% of respondents (18% already got access to it).
Patient Advocacy had a main role in the new care and life context: 80% would consider it useful to participate to and 81% was satisfied by the prompt and continuous support received during pandemics.
Conclusion: Similar results as far as distress were reported by Italian and foreign evidence, which demonstrated considerable COVID-19 related psychosocial burden in rheumatic disease patients [3-5]. Potential solutions are also with EULAR recent guidelines, which underlined how psychological interventions were found to reduce pain and fatigue even in difficult-to-treat patients [6] and how mental health needs should be periodically assessed, due to the link between better emotional well-being and better self-management [7]. Besides, the reported picture of reorganised care during pandemic corresponded to the real-world experience of the Italian Regions [8]. New approaches of care like home infusions and telemedicine supported by patient organisations should become routinary and may therefore benefit patients.
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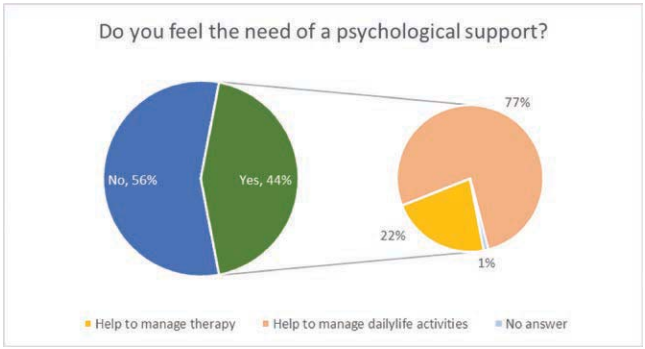

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POS0358-PARE THE IRISH 'WEAR RED' FOR VASCULITIS CAMPAIGN – LAUNCHING AN ANNUAL AWARENESS CAMPAIGN IN A RESTRICTED PANDEMIC WORLD.

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Background: Vasculitis is an umbrella term for a number of conditions which are caused by inflammation of the blood vessels. It presently affects approx. 1,000 people in Ireland. Vasculitis is one of the rare rheumatic diseases which are quite often overlooked and unknown as it does not have the recognition that Lupus has created especially with the recent celebrity diagnoses. It is often mistakenly thought to be a heart condition among members of the public due to the vasc sound in the word Vasculitis often being associated with the word vascular. May is Vasculitis Awareness month and the 15th of May is now celebrated as World Vasculitis Day. Due to being in a pandemic due to Covid 19 we couldn't plan face to face events for our first awareness day due to restrictions within Ireland and medically enforced restrictions for members of our committee so online was the only viable option.
Objectives: To celebrate May as Vasculitis month on behalf of those with Vasculitis. To increase awareness among the public of Vasculitis nationally in a memorable way on World Vasculitis Day May 15th 2021. To create brand awareness of our organisation the Irish Vasculitis Organisation (IVO) and increase our Facebook page membership.
Methods: We decided to celebrate the month by posting a fact about Vasculitis every second day starting the 1st of May until the end of the month skipping the 15th which is when we would run our first Wear Red campaign. We approached a number of famous Irish buildings to light up in red to support the day. We also ran a Facebook campaign which looked for people's support on the day by wearing red and posting it online on May 15th encouraging people to wear red and we reposted their efforts on our Facebook page.
Results: We had six famous Irish buildings across Ireland including the Rock of Cashel and the Dublin Mayor's residence light up in red to support the day.
The Vasculitis facts were interesting to some but the Wear Red campaign was the most successful activity we did. In the 14 days running up to the 15th we were reaching on average 28 people a day and on the 15th, we reached an amazing 526 people. We also saw our interactions (comments, shares, likes) go from an average of one a day in the 14 days prior to the campaign to 167 people on the 15th. The videos with children achieved the most interactions.
Unexpectedly the campaign received support from abroad as well with many of the 15% increase in members joining our Facebook page on the 15th being from the UK The Vasculitis Foundation in the USA heard about one of our light up buildings and they advertised it on the newsletter to their many subscribers.
Conclusion: The Wear Red campaign was evidence that even in a pandemic while there were severe limitations to people meeting up and having no ability to go out to advertise, a successful awareness campaign could still be run from a volunteer's kitchen as long as there was careful planning and support.
It is also clear to see that while informative facts may be the answer to those who run organisations and have the condition in order to educate the public it is important to recognise that the public learn through fun activities and if you want to generate real interest keeping it light fun and informative is the way to go.
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POS0359-PARE YOUTUBE AS A SOURCE OF INFORMATION ON AUTOINFLAMMATORY DISEASES

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Background: Getting access to specialists for autoinflammatory diseases (AIDs) is challenging. Therefore, an increasing number of patients and healthcare professionals are seeking information on this topic via the internet, e.g., on the video platform YouTube, which has attracted a huge audience in recent years (1). However, not much is known about the quality of videos pertaining on AIDs.
Objectives: To assess videos about AIDs uploaded on YouTube and to evaluate the quality and usefulness of available information from both the patient's and professional healthcarer´s perspective.
Methods: A YouTube.com search was conducted in January 2022: Selected keywords were "autoinflammatory diseases" (AID), "periodic

fever syndrome" (PFS), "familial mediterranean fever" (FMF), "cryopyrin associated periodic syndrome" (CAPS), "tumor necrosis factor associated periodic syndrome" (TRAPS), "adult onset of still´s disease" (AOSD) and "systemic juvenile idiopathic arthritis"(sJIA). For every keyword, the top 20 videos in their order of relevance were included. Video duration, number of views, likes, dislikes, comments and uploading source were extracted. The quality of a video´s information was evaluated independently by two physicians based on the modified global quality scale (GQS) (2). Subgroup analyses were performed classifying healthcare professionals and patients as target group.

Results: In total 140 videos were screened. We excluded 5 videos due to language other than English, 7 duplicates and 23 not suitable ones. 105 videos met the inclusion criteria for further analysis. Video characteristics are presented in Table 1. Based on the GQS, overall quality of videos for patients was found to be low in 64,8%, intermediate in 27,6%, and high in 7,6% of videos. The quality of videos for professionals was similar: 54,3% were judged to be of low, 23,8% of intermediate, and 21,9% of high quality (Figure 1). Subgroup analyses focusing on videos for professionals found sJIA videos to achieve the highest scores (31,6% with high quality) whereas videos regarding CAPS were rated the least useful ones (15,4% with high quality). In videos for patients, sJIA videos also ranked highest (42,1% with high quality) whereas no high quality videos could be identified for TRAPS. Videos are more often aimed at specialists such as doctors or medical students (65.7%) and less often at affected patients or relatives (34.3%). Video duration was significantly longer in videos targeting a professional audience ($p < 0.001$). In videos for professionals, length was significantly correlated with higher quality ($p < 0.001$).

Table 1. Video Characteristics

	Median (range)							
	Total included (n=105)	AID (n=19)	PFS (n=15)	FMF (n=16)	CAPS (n=13)	TRAPS (n=3)	AOSD (n=20)	SJIA (n=19)
Video duration (minutes)	6,75 (0,58-86,33)	16,13 (0,63-75,18)	3,78 (1,18-54,02)	10,80 (1,58-51,35)	3,48 (0,58-23,27)	6,10 (3,03-86,33)	9,88 (1,47-48,28)	7,28 (1,65-59,67)
Total views	1569 (24-102928)	1672 (223-32930)	2560 (24-36732)	2182,50 (40-24842)	635 (26-32932)	1392 (520-2963)	1029 (192-20011)	2317 (202-102928)
No. of likes	15 (0-1275)	18 (0-357)	26 (0-271)	22 (0-323)	8 (0-357)	11 (8-14)	20,50 (3-133)	15 (0-1275)
No. of dislikes	0 (0-17)	0 (0-7)	0 (0-0)	0 (0-17)	0 (0-7)	0 (0-0)	0 (0-0)	0 (0-0)
GQS (patients)	2 (1-5)	3 (1-4)	3 (1-4)	2 (1-5)	2 (1-4)	2 (1-2)	1,50 (1-4)	2 (1-3)
GQS (professionals)	2 (1-5)	3 (1-5)	1 (1-5)	2 (1-5)	1 (1-5)	2 (1-4)	2 (1-4)	3 (1-5)

Abbrevations: GQS= Global Quality Scale 1(low quality) - 5 (high quality)

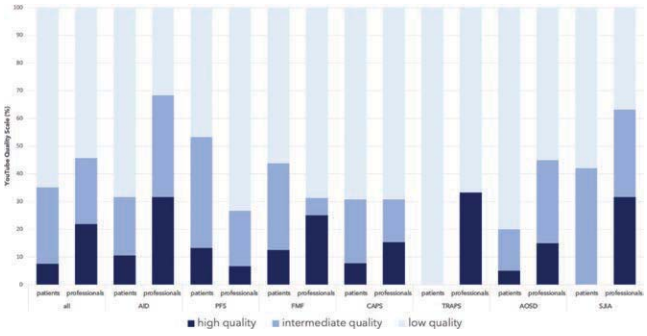

Figure 1. Quality Scale

Conclusion: YouTube as a source of information could have great potential for rare diseases. However, this study demonstrates that the majority of videos regarding AIDs is of limited quality and available videos more often adress users with a professional medical background. Only a small proportion of existing videos provide understandable and useful information for AID patients.

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POS0360-PARE EDUCATIONAL NEEDS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AND HEALTH PROFESSIONALS IN RHEUMATOLOGY: A SWISS CROSS-SECTIONAL QUALITATIVE ANALYSIS

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Background: The content and delivery of patient education (PE) should be individually tailored and needs-based for people with inflammatory arthritis[1]. Therefore, a patient trained in PE joined forces with a rheumatology clinical nurse specialist to explore the needs for the management of patients with RA in a Swiss local context (rheumatology department of a university hospital).

Objectives: To identify the difficulties and needs of patients with RA regarding their disease and its management in a local context, from both perspectives: patients and health professionals (HPs).

Methods: We developed 2 different semi-structured questionnaires for each surveyed group. They were distributed to 93 patients and 62 HPs during Summer 2020. Only the fully completed surveys were analysed. A qualitative analysis of the answers to the open questions was carried out and the phenomena thus highlighted were then quantified.

Results: We collected 38 patient (40%) and 35 HP (56%) questionnaires, and 23 patients (25%) and 21 HPs (34%) filled them completely out.

Participants among patients were mostly female (74%) with a mean (SD) age of 54,8 (10,9). Mean (SD) number of years of illness after diagnosis was 11,9 (12,6). HPs were nurses (57,1%), medical doctors (19%), occupational therapists (14,3%), physiotherapists (4,8%) and assistant nurses (4,8%).

Almost half of HPs (48%) and 39% of patients experience difficulties to talk about sensitive topics like sexuality, financial or emotional difficulties.

A third of patients (30%) wished a more supportive attitude from HPs and HPs (62%) would like patients to be more involved in their care, more specifically regarding autonomy and treatment adherence. A few HPs (9%) and patients (19%) want to improve patient-centred and personalised care. Most of HPs (81%) and patients (87%) state that they have no objection or reluctance to PE being developed in the department. Some HPs see PE as an additional workload (19%) and others as a tool to involve the patients more in their care (43%).

HPs (43%) express a need for patient's and disease's management training and wish to acquire additional tools and methods to better assist their patients (43%). A third of them (33%) report a lack of communication, collaboration and interdisciplinarity to support patients. Furthermore, due to the lack of time and availability, 67% of them are not able to provide adequate time for meeting the patients' needs. Some HPs feel powerless to help their patients (19%). Some others (18%) highlight the difference of perspectives and concerns between patients and HPs.

Patients and HPs agreed on most of the main difficulties related to the disease and follow-up. It should be noted that HPs were not aware of the difficulties related to their patients' sleep. The painful and distressing psychological and emotional impact of RA is the difficulty most cited by patients (74%) and the second most mentioned by HPs. More than half of patients (61%) have difficulty managing their pain.

Conclusion: The results of this study confirm the need for PE in the department. Communication is a challenge for both populations. HPs know their patients well, but patients and HPs have different expectations regarding disease's management and follow-up. This work shows the importance of analysing educational needs: it brings out dimensions of the disease and its management that are sometimes hidden or underinvestigated. It thus helps to have a better understanding of the reality and difficulties as they are experienced by people in order to propose appropriate solutions. This work provides a basis for reflection and discussion for the future development and implementation of a PE program, based on the paradigm of the patient-HP partnership. In addition to being an example of an advanced and successful patient-HP partnership, it also demonstrates the benefits of such collaboration.

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POS0361-PARE **THE MEDIATING EFFECT OF PAIN CATASTROPHIZING ON WORK PRODUCTIVITY**

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Background: Work disability is a major patient outcome for spondyloarthritis (SpA) patients since SpA mostly appears in younger adults.
Objectives: we examined the influence of catastrophizing as a negative psychological factor on work productivity and activity impairment in SpA.
Methods: We conducted a cross-sectional study over a 3 months period. We included patients treated with SpA (Assessment of SpondyloArthritis International Society (ASAS) 2009 criteria). Patients related data, and disease characteristics were collected. Pain catastrophizing were assessed by the pain catastrophizing score (PCS). Work productivity and activity impairment were evaluated by Work productivity and Activity Impairment Questionnaire (WPAI). WPAI score examined four aspects of the patient's life: Absenteeism due to SpA and presenteism at work, work productivity loss and activity impairment.
Results: Sixteen SpA patients were enrolled (22 females and 38 males). Mean age was 39,4 years ± 11,08. Mean disease duration was 11,37 years ±7,23; 28 were unemployed. Among workers, absenteeism due to SpA was reported in 7 cases (21,9%). Mean absenteeism rate was 2,35% [0-20]. Both mean work productivity loss and mean activity impairment were 50,23% [20-90].
Mean PCS was 15,73 ± 13,893. Thirteen patients (21,7%) had PCS >30 which indicates a clinically relevant level of catastrophizing, and only two of them reported absenteeism at work. PCS score was higher in patients with absenteeism (mean score=26), compared to patients without absenteeism (mean score=16,96), (p=0,166). Presenteeism was lower in patients with higher pain catastrophizing scores, without reaching a significant difference (p=0,066). A higher PCS was significantly correlated with a greater work productivity loss (p= 0,036, r=0,371) and greater activity impairment (p=0,005, r=0,36).
Conclusion: In our series, pain catastrophizing affected work productivity and daily activity in patients with SpA.
Disclosure of Interests: None declared
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Systemic Lupus Erythematosus: monitoring and management

POS0362 **FACTORS ASSOCIATED WITH CHANGES IN COPING BEHAVIOUR IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS - A LONGITUDINAL STUDY OF THE LULA COHORT**

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Background: Patients with Systemic Lupus Erythematosus (SLE) experience both physical and psychosocial restrictions that negatively impact their quality of life. Coping mechanisms have turned out to be important contributors to health-related outcomes, not only in SLE but also other chronic conditions. However, there is limited understanding of factors that enhance or hamper coping in SLE.
Objectives: To analyse parameters associated with longitudinal changes in coping behaviour in patients with SLE who take part in a long-term SLE patient cohort study.
Methods: Since 2001, the German nationwide SLE patient longitudinal (Lupus Langzeit 'LuLa') study annually administers self-reported questionnaires to SLE patients.
In addition to demographic and the annually probed extended clinical data (e.g., medication, disease activity, fatigue, depression), in both 2009 and 2014 we assessed the Pain-related Self Statements Scale (PRSS) to perceive information related to coping behaviour. This includes 'positive coping' as well as catastrophizing as a dysfunctional form of coping behaviour.
Statistical analysis was accomplished by a linear regression model adjusting for age, pain, number of comorbidities and net income. The PRSS score difference from 2009 and 2014 was used as the dependent variable. Factors from the i) medical (involvement of the skin, pain, fatigue), ii) activity (basic, leisure, sports), iii) intrinsic (depression, kinesiophobia, perceived health control), and iv) social participation categories were entered as independent variables.
Results: 272 patients (96.7% female) provided valid PRSS questionnaires in both 2009 and 2014. In 2009 the mean age in this cohort was 51 years (SD 11.2) with an average disease duration of 16.2 years (SD 8.3). The mean reported lupus activity (VAS 0-10) during the last three months was 3.7 (SD 2.4). During the six-year observation period, the proportion of improvement (46.2%) and deterioration (47.4%) in coping score was almost balanced, while in catastrophizing score more participants improved (50.0%) than deteriorated (37.0%).
A perceived high internal control, thus the belief that health outcomes are contingent on personal behaviour, was associated with an improvement in the coping score [HLC, b=0.061 (95%-CI 0.014; 0.109), p=0.012]. Conversely, high external control convictions, e.g., the belief that doctors and other third parties determine health outcomes, were associated with a worse coping score [HLC, b=-0.090 (95%-CI -0.154; -0.026), p=0.006]. Deterioration in depression [ADS-L, b=0.015, (95%-CI 0.006; 0.025), p=0.002] and impaired social participation [IMET, b=0.043, (95%-CI 0.000; 0.085), p=0.050] were associated with a deterioration of catastrophizing, whereas better internal control [HLC, b=-0.046, (95%-CI -0.080; -0.012), p=0.009] was associated with its improvement.
Mucocutaneous involvement, fatigue and the extent of physical activity were not significantly associated with either coping or catastrophizing scores in the regression analysis.
Conclusion: In line with data from other chronic diseases, our findings in a longitudinal SLE cohort emphasise the role of intrinsic factors, such as mental health status and self-efficacy, improving the quality of life in SLE patients via successful coping behaviour. Affirmative action measures and programs to improve social participation may yield additional benefits.
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POS0363 **THE SIMPLE INDEX FOR SELF-ASSESSMENT OF DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL COHORT VALIDATION**

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Background: The SIMPLE (SIMple Disease Assessment for People with Lupus Erythematosus) index is a composite numeric tool that captures disease activity from patients' self-assessment with minimal physicians' input. The SIMPLE index consists of 2 components: patient self-reported survey questionnaire (3 items from the lupus symptoms domain from the validated LupusPRO, 10 items from Lupus Impact Tracker [LIT], change in the health status and current glucocorticoids use [and dose]) and two laboratory tests (low complements [C3/C4] and urine protein-creatinine ratio >0.5). The values are put in an equation to derive a number, which is transformed to a 0- to 100-point scale by a formula using weighted scores of the above parameters. The SIMPLE index has been validated in US with good correlation with physicians' assessment of disease activity.
Objectives: To validate the SIMPLE index for systemic lupus erythematosus (SLE) disease activity assessment in a longitudinal cohort of Chinese patients.
Methods: Adult patients (age ≥18 years) who fulfilled the 2012 SLICC criteria for SLE and were followed in the Rheumatology clinics of Tuen Mun Hospital, Hong Kong were recruited. Patients were followed for a total of 3 consecutive visits, including hospitalization. Participants were invited to complete the SIMPLE questionnaire before seeing doctors on the same day of clinic visit or hospital stay. The two laboratory results were supplemented by research nurses. Physicians, who were blinded to the SIMPLE results, were asked to complete disease activity assessment by the SELENA-SLEDAI and physicians' global assessment (PGA) after consultation. Correlation was made between the SIMPLE score and the SLEDAI/PGA scores by Spearman's rank correlation test. Correlation was also performed for the changes in total/clinical SLEDAI, PGA with the change in SIMPLE index during subsequent visits relative to baseline.
Results: 399 SLE patients were studied (93.7% women; age 45.3±13.4 years; disease duration 13.3±8.0 years). The proportion of patients having a history of neuropsychiatric and renal disease that required immunosuppressive therapies was 9.8% and 55.6%, respectively. At visit 1, 18 (4.5%) patients had

clinical SLEDAI ≥5 and 98 (24.6%) had clinical SLEDAI 1-4. The mean total SLEDAI was 3.02±2.87 and PGA score was 0.60±0.53. A total of 178 patients (44.6%) had SDI score ≥1. The mean SIMPLE index was 25.6±12.8. SIMPLE index correlated significantly with clinical SLEDAI (ρ=0.56; p<0.001), total SLEDAI (ρ=0.75; p<0.001) and PGA score (ρ=0.41; p<0.001). At visit 3, 87 and 38 patients, respectively, had a drop in total SLEDAI score by ≥1 and ≥4, and the corresponding change in SIMPLE index was 35.3±13.7 to 25.0±10.1 (p<0.001) and 42.9±11.9 to 26.0±11.1 (p<0.001). Conversely, 103 and 29 patients, respectively, had an increase in total SLEDAI score by ≥1 and ≥4. The corresponding increase in SIMPLE index was 23.5±11.3 to 25.7±10.1 (p=0.007) and 25.3±13.7 to 27.3±11.6 (p=0.27). Change in SIMPLE index from visit 1 to 3 correlated significantly with the change in total SLEDAI (ρ=0.35; p<0.001), clinical SLEDAI (ρ=0.19; p<0.001) and PGA (ρ=0.14; p=0.005). ROC analysis performed with pooled data from all the 3 visits showed that a SIMPLE index of >24 points best predicted a clinical SLEDAI score of 1-4 (area under the curve [AUC] 0.72[0.68-0.75]; sensitivity 0.65; specificity 0.64), and >31 points best predicted a clinical SLEDAI score of ≥5 (AUC 0.84[0.77-0.91]; sensitivity 0.76, specificity 0.81).

Conclusion: The SIMPLE index shows a good correlation with SELENA-SLEDAI and PGA. It is also sensitive to change in SLEDAI and PGA score during subsequent visits. The SIMPLE index is a simple tool that enables patients to self-report disease activity and communicate with the health care team more efficiently.

Disclosure of Interests: None declared

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POS0364 UNMET NEEDS IN THE TREATMENT OF EXTRA-RENAL FLARES IN SLE PATIENTS: REAL LIFE EXPERIENCE VS ARTIFICIAL APPROACH

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous disease which can affect various organs and is characterized by different clinical phenotypes. While the treatment of renal involvement is quite standardized, the therapeutic approach to extra-renal manifestations is subjected to a degree of variability.

Objectives: 1. To describe extra-renal disease flares in terms of clinical phenotype and outcomes in SLE patients 2. To compare data from a real-life setting with a machine learning (ML) approach.

Methods: This study is a retrospective analysis of data from a monocentric cohort of SLE patients who experienced a disease flare between 2015 and 2020. Each flare was followed for one year and was classified according to the organ involvement and categorized according to the BILAG definition of flare. At baseline and at 3,6,12 months the following variables were collected: disease activity (SELENA-SLEDAI score), ongoing therapy and disease state (DORIA definition of remission). Demographic data and previous organ involvement were retrieved from clinical charts. Flares' features at baseline and during follow up were analyzed in terms of explained variance across the dataset's Principal Components and clustered with a hierarchical unsupervised learning approach. A ML model based on neural networks was built to early detect flares' therapeutic difficulty: it was validated after data augmentation to satisfy statistical requirements during the training phase.

Results: 66 extra-renal flares were investigated (Table 1); 5 flares (7.5%) were treated with glucocorticoid (GC) pulses and 61 (92.5%) with oral GC therapy, while an immunosuppressive (IS) treatment was prescribed in 44 flares (66.7%). The remission rate at 12 months for the whole group was 50%, with musculo-skeletal (MS) flares, mucocutaneous (MC) flares and others (neuropsychiatric, cardiopulmonary, constitutional, haematologic) that was respectively 63.6%, 31.3% and 41.2%, showing lower rate of remission for MC flares. In 12 months, 17 flares (25.8%) did not respond to treatment (non-responders), requiring an increase in the dose of GC or the introduction of a new IS therapy. Using a machine learning approach, we were able to identify 4 flare clusters, grouping flares in relation to phenotypic characteristics (Figure 1), and recognized statistically relevant features for patients' stratification (cluster 1 "flare in systemic disease with high activity", cluster 2 "outcast flares", cluster 3 "flare in polymorphic disease with mild activity" and cluster 4 "recurrent skin flares"). Interestingly, cluster 4 (recurrent skin flares) was associated with the lowest rate of remission at 12 months with respect to clusters 1, 2, and 3 (33% vs 40%, 76.5% and 56% respectively). Moreover the neural network model correctly predicts difficult to treat flares in up to 80% of the cases

Figure 1. Flare clusters.

Conclusion: These data suggest that, in a real-life setting, the clinical response rate to therapy of patients with an extra-renal flare is not satisfactory, thus identifying an unmet need in the treatment of SLE and highlighting the absence of a standard treatment. Both the real-life data and the machine learning approach identify flares with MC manifestations as the most difficult to treat with the lower rate of remission after one year. Further prospective studies are necessary to improve the neural network model; ML techniques could help in the early identification of difficult to treat flares to be candidates for new and more aggressive therapeutic strategies for extra-renal manifestations.

Disclosure of Interests: None declared

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POS0365 RELAPSES ARE COMMON IN SEVERE HEMATOLOGICAL SLE: REAL-LIFE EXPERIENCE FROM THE "ATTIKON" LUPUS COHORT

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Background: Hematological manifestations are common in systemic lupus erythematosus (SLE), and are thought to result from immune-mediated peripheral cell destruction or bone marrow failure(1,2).

Objectives: To assess the clinical characteristics and outcomes of severe hematological disease in a large cohort of lupus patients.

Methods: Retrospective analysis of the "Attikon" lupus cohort (over 800 patients total) (3) for the identification of patients with a history of severe hematological manifestation. The latter were defined as: thrombocytopenia with a platelet count <30.000/mm3, hemolytic anemia with an hemoglobin <8 g/dL, neutropenia with less than 500 neutrophils/mm3, history of thrombotic microangiopathy (TMA) or macrophage activation syndrome (MAS). Treatments and long-term outcomes (relapses, mortality) were recorded.

Results: Among 300 patients with hematologic manifestations, 40 patients had severe disease. Most of them were women (75%). Mean age at SLE diagnosis was 41,1 years and mean disease duration at diagnosis of cytopenia was

Table 1.

	WHOLE GROUP	MUSKEL	MUCOCUT	CONSTITUTIONAL	CARDIOPULM	HAEMATOL	NEURO	p
NUMBER (%)	66	33 (50)	16 (24.2)	7 (10.6)	4 (6.1)	5 (7.6)	1 (1.5)	
SLEDAI at baseline median (IQR)	7 (4-29)	8 (6-10)	5.5 (4-10)	5 (4-9)	9 (4.5-12)	5 (5-6)	29 (29-29)	
SLEDAI 12 mos median (IQR)	2 (0-20)	0.5 (0-4)	3 (0-4)	3 (2 – 4)	0 (0-0)	2 (0-3)	14 (14 – 14)	
REMISSION 12 mos number (%)	33 (50)	21 (63.6)	5 (31.3)	4 (57.1)	2 (40)	2 (40%)	1 (100)	0.217
NON RESPONSE 12 mos number (%)	17 (25.8)	8 (25)	5 (31.3)	2 (28.6)	1 (20)	1 (20%)	1 (100)	0.467

3.8 years. Hematologic manifestation preceded SLE diagnosis in 13 patients (32,5%).
Autoimmune thrombocytopenia was the most common (57,5%), followed by hemolytic anemia (17.5%), TMA (12.5%) and Evans syndrome (7,5%). All patients received glucocorticoids (GC). Rituximab (15%) and cyclophosphamide (12,5%) were the most frequently used GC-sparing agents during the first episode. Nine patients (22,5%) received intravenous immunoglobulin (IVIg). Relapse occurred in 23 patients (57,5%), most of which (N=17, 73,9%) were treated with GC alone or in combination with IVIg or plasma exchange at initial presentation, without the use of GC-sparing agents. Most of the flares (60,8%) were severe. No deaths were observed.
Conclusion: Hematological disease in SLE is treatment-responsive. GC remain the mainstay of treatment, but the high relapse rates underscore the need for more efficient GC-sparing agents.
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Table 1. Characteristics of patients with hematological manifestations

Age at diagnosis, mean (years)	41,1
Women N(%)	30(75)
Mean disease duration at cytopenia diagnosis (years)	3,8
Thrombocytopenia, N=23, (mean platelet count,/mm3)	11682
Hemolytic anemia,N=7 (mean Hb,g/dL)	6,75
Neutropenia N=1,(mean neutrophil count)	450
Evans syndrome, N=3 (mean Hb, g, mean platelet count)	7 /46600
TMA,N=5, (mean platelet count)	8750
MAS, N=1	
Immunosuppressive treatment at initial presentation	Azathioprine (N,%) 4(10) Corticosteroids (N,%) 40 (100) Cyclophosphamide (N,%) 5(12,5) IgIV (N,%) 9 (22,5) Mycophenolate mofetil (N,%) 2(5) Rituximab (N,%) 6(15)
Relapse N(%)	23(57,5)
Severe relapse (N,%)	14(60,8)
Non responder to corticosteroids/IgIV (N,%)	1(2,5)

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POS0366 MODERATE RATES OF TREATMENT INTENSIFICATION IN SLE PATIENTS WITH RESIDUAL DISEASE ACTIVITY

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Background: The treat-to-target (T2T) strategy has gained significant attention in SLE,[1] while EULAR has set remission or low disease activity as the goal of treatment.[2] Nevertheless, the degree to which T2T is followed in real-life clinical settings has not been extensively studied.
Objectives: To assess the proportion of lupus patients with residual disease activity that had their therapy intensified during their most recent visit, identify associated factors, and assess the validity of the SLEDAI-2k as a predictor of this intensification.
Methods: Cross-sectional study of SLE patients who were evaluated in three tertiary centers in Greece during their last visit. Patients were categorized in four disease activity states (remission on and off treatment, low disease activity and non-optimally controlled), according to definitions used in previous studies.[3] Intensification of treatment was defined as addition/increase of glucocorticoids (GC) or addition/increase of immunosuppressive (IS) agent (conventional or biologic). Logistic regression analysis was used to identify factors associated with treatment intensification and ROC analysis to calculate sensitivity, specificity of different SLEDAI-2k cut-off values to predict this escalation.
Results: 332 patients were included [93.1% female, mean (SD) age 48.5 (14.7) years, median (IQR) disease duration 6.5 (12.4) years]. Regarding disease activity states, 23.2% (n=77) of patients were in remission (off or on therapy), 36.7% (n=122) were in LDA, while 40.1% (n=133) were categorized as non-optimally controlled disease.
Within patients with residual disease activity, therapy intensification was offered to 25.8% and 48.9% of those with low disease activity and non-optimally controlled disease, respectively. In multivariable analysis, proteinuria (OR 6.78, 95% CI 2.06 – 22.25), arthritis (OR 5.48, 95% CI 3.20 - 9.40) and rash (OR 3.23, 95% CI 1.81 - 5.75), were associated with intensification of therapy. The AUC of the ROC analysis for total SLEDAI-2k to predict therapy escalation was 0.761, indicating only fair accuracy; the cut-off value with the best combination of sensitivity and specificity was 3 (sensitivity 87%, with a specificity of 55%). For clinical SLEDAI-2k, the respective AUC was marginally better (0.779), with a cut-off of 3 being associated with the best sensitivity (80%), with compromised specificity (64%). (Figure 1).

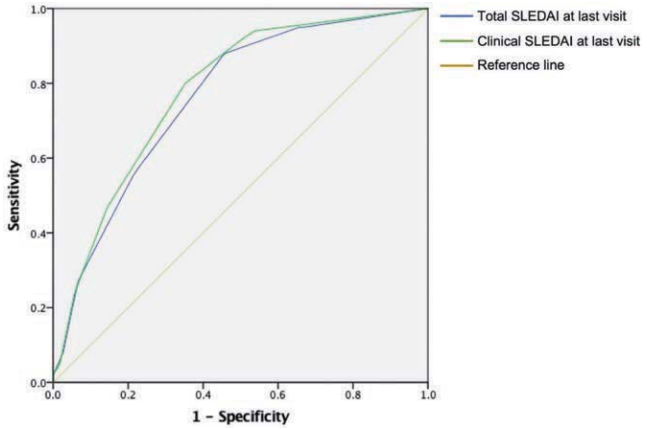

Figure 1. ROC analysis of total and clinical SLEDAI to predict any increase in therapy

Conclusion: In real-life clinical settings, no therapy intensification was offered in more than half of patients categorized as non-optimally controlled disease. Total and clinical SLEDAI-2k showed only fair accuracy to predict therapy escalation, reflecting the role of additional parameters in the decision to escalate therapy in an individual patient.
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POS0367 IMPROVEMENT OF INDIVIDUAL MUCOCUTANEOUS MANIFESTATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH ANIFROLUMAB

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Background: Patients with cutaneous lupus erythematosus (CLE) experience disfiguring and painful lesions that can lead to psychological distress and significant impacts on quality of life.[1] Treatment of patients with systemic lupus erythematosus (SLE) with anifrolumab, a type I interferon receptor antagonist, was associated with CLE Disease Area and Severity Index–Activity (CLASI-A) improvements compared with placebo through Week 52 in the phase 3 TULIP-1

and TULIP-2 SLE trials.[2,3] CLASI assesses overall skin improvement and may be driven by erythema over the other components.[4]

Objectives: To better understand the effect of anifrolumab on mucocutaneous SLE manifestations by analyzing the individual domains of CLASI-A using pooled data from the TULIP trials.

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were randomized, double-blind, placebo-controlled, 52-week trials that evaluated efficacy and safety of intravenous anifrolumab administered every 4 weeks in patients with moderate to severe SLE despite standard therapy.[2,3] In a post hoc analysis, individual CLASI-A domains (erythema, scale/hypertrophy, alopecia, and mucosal) were assessed at Week 24 (time point chosen to ensure adequate duration for improvement in slow-remitting manifestations [eg, scale, alopecia]) in 2 patient subgroups: 1) the "chronic" mucocutaneous subgroup (resembling chronic/discoid CLE), defined as patients with a baseline erythema score ≥4 and scale score ≥2, and alopecia score ≥1 or baseline mucosal lesions or ulceration score of 1; and 2) the "extended" mucocutaneous subgroup (resembling all CLE subtypes), defined as patients who met the "chronic" criteria or those who had a baseline erythema score ≥8.

Results: Across the pooled TULIP trials, 360 patients received anifrolumab 300 mg and 366 patients received placebo. In patients with assessments at Week 24 in the "chronic" (anifrolumab n=58, placebo n=50) and "extended" (anifrolumab n=104, placebo n=96) subgroups, anifrolumab led to a greater mean percent reduction from baseline compared with placebo in erythema (chronic: −63.6% vs −39.9%; extended: −63.7% vs −41.2%) and scale/hypertrophy (chronic: −72.2% vs −42.6%; extended: −45.3% vs −7.3%). Anifrolumab-treated patients in both subgroups had no worsening in alopecia (chronic: 93.3% [56/60] vs 96.0% [48/50]; extended: 95.3% [102/107] vs 95.8% [92/96]) or mucous membrane (chronic: 95.0% [57/60] vs 96.0% [48/50]; extended: 96.3% [103/107] vs 94.8% [91/96]) from baseline vs placebo (Table 1).

Table 1. Skin Responses at Week 24 Compared With Baseline

Criteria, n (%)	Chronic subgroup		Extended subgroup	
	Anifrolumab 300 mg (n=60)	Placebo (n=50)	Anifrolumab 300 mg (n=107)	Placebo (n=96)
Erythema score reduction				
≥25%	53 (88.3)	32 (64.0)	93 (86.9)	68 (70.8)
≥50%	42 (70.0)	22 (44.0)	71 (66.4)	47 (49.0)
≥60%	34 (56.7)	18 (36.0)	61 (57.0)	32 (33.3)
Scale/hypertrophy score reduction				
≥10%	49 (81.7)	34 (68.0)	55 (51.4)	38 (39.6)
≥25%	47 (78.3)	30 (60.0)	53 (49.5)	34 (35.4)
≥50%	46 (76.7)	28 (56.0)	51 (47.7)	31 (32.3)
No new/worsened lesions in any individual body area	44 (73.3)	26 (52.0)	81 (75.7)	56 (58.3)
Alopecia				
≥1-point decrease[a]	25 (41.7)	19 (38.0)	35 (32.7)	27 (28.1)
No worsening	56 (93.3)	48 (96.0)	102 (95.3)	92 (95.8)
Mucosal lesion/ulceration				
1-point decrease[b]	25 (41.7)	13 (26.0)	39 (36.4)	23 (24.0)
No worsening	57 (95.0)	48 (96.0)	103 (96.3)	91 (94.8)

[a]If baseline score ≥1. [b]If baseline score =1.

Conclusion: In the phase 3 TULIP trials, SLE patients with mucocutaneous manifestations treated with anifrolumab experienced numerical improvements in erythema and scale/hypertrophy and no worsening in alopecia or mucous membrane CLASI-A domains compared with placebo, regardless of whether skin disease was classified by chronic or extended definitions. These encouraging data support further evaluation of anifrolumab in patients with CLE.

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POS0368

EARLY (3 MONTHS) IMPROVEMENT IN PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY PREDICTS LONG-TERM RETENTION OF BELIMUMAB TREATMENT IN SLE: A MULTICENTRE OBSERVATIONAL STUDY OF 184 PATIENTS

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Background: Belimumab has been introduced in the management of SLE for more than 10 years, however long-term efficacy and safety data are still limited and mostly derive from the extended phase of randomized clinical trials.

Objectives: To evaluate the long-term survival of belimumab treatment, reasons for treatment cessation and associated predictors in routine care setting.

Methods: Multicentre observational study of adult SLE patients who were treated with belimumab according to physician discretion and in line with the EULAR recommendations. Disease activity (Physician Global Assessment [PGA]: scale 0-3; SLE disease activity index-2000 [S2K]), flares (SELENA-SLEDAI Flare Index), organ damage (SLICC damage index [SDI]), co-administered treatments and dosage, adverse events and causes of belimumab discontinuation were monitored prospectively at 3–6-month intervals. Cox-regression analysis was performed to identify factors associated with reduced drug survival.

Results: A total 184 patients treated with belimumab for at least 3 months were included (women 95.6%; mean ± SD age 48.8 ± 13.4 years; disease duration 9.2 ± 11.3 years). Baseline S2K and PGA were 7.5 ± 3.0 and 1.64 ± 0.42, respectively, both demonstrating significant improvement at 6 months (4.5 ± 3.5 and 1.02 ± 0.69, respectively; p<0.001) and 12 months (3.5 ± 3.1 and 0.68 ± 0.55, respectively; p<0.001). Of patients receiving glucocorticoids at onset, 49.0% tapered the dose and 17.6% completely withdrew them. After a median (interquartile range) follow-up of 15.1 (16.9) months, 44.0% of patients discontinued belimumab due to suboptimal efficacy as judged by the treating physician (28.3%), adverse events (including infections) (9.8%) or other causes (e.g., pregnancy, patient decision). Accordingly, efficacy-related drug survival rates at 1 and 2 years were 70% and 61%, respectively, with corresponding safety-related survival rates of 94% and 87%, respectively. Baseline factors associated with belimumab discontinuation due to suboptimal efficacy included PGA >1.50 (hazard ratio [HR] 3.66; 95% confidence interval [95% CI] 1.14–11.73; p=0.029) and severe (RA-like) arthritis (HR 2.56; 95% CI 1.16–5.68; p=0.020) but not disease duration, use of glucocorticoids, active serology or organ damage. Notably, patients with early (3 months) improvement (i.e., any decrease in PGA) showed significantly lower risk for treatment cessation (HR 0.38; 95% CI 0.22–0.67; p=0.001) (Figure 1) and this effect was independent of the initial PGA level. Baseline use of hydroxychloroquine was associated with prolonged safety-related belimumab survival (HR 0.32; 95% CI 0.12–0.88; p=0.028).

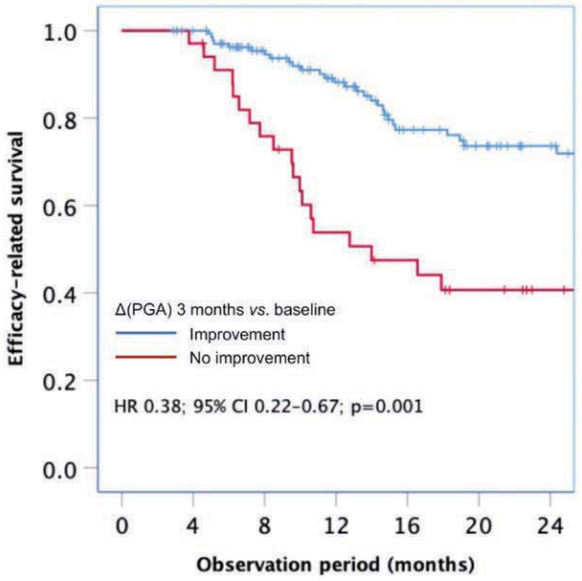

Figure 1. Efficacy-related survival of belimumab according to improvement or not of PGA at 3 months since treatment initiation.

Conclusion: In real-life setting, about 28% of SLE patients discontinue belimumab due to suboptimal treatment response per physician judgement, especially those with moderate-to-high activity and severe arthritis. Improvement in PGA at 3 months predicts long-term drug maintenance, therefore suggesting its value for patient monitoring. Our data confirm the very good tolerability of belimumab and identify hydroxychloroquine co-administration as a predictor for prolonged safety-related drug survival.

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POS0369 IMPACT OF HYDROXYCHLOROQUINE LEVEL ON ECG QTC INTERVAL IN PATIENTS WITH RHEUMATIC SYSTEMIC AUTOIMMUNE DISEASES: A REAL-LIFE STUDY

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Objectives: To analyze the impact of the serum level of hydroxychlroquine (OHCLQ) on the QTc interval of the ECG, in patients with rheumatic systemic autoimmune diseases (SARD), treated with this drug for a long time

Methods: Retrospective study, among patients with SARD, treated with OHCLQ ≥ 1 year, dose 200-400 mg/day. Serum OHCLQ level was measured by liquid chromatography and QTc interval by ECG (Welch Allyn 200; SF, N York, USA). Two control groups for QTc are included: Group-1: patients with SARD not treated with OHCQ; Group-2: healthy subjects without SARD. In both, weight and current treatment and an ECG were recorded.

In patients with SARD was collected: 1) Epidemiological data: age, sex, weight, concomitant diseases, current treatment. 2) SARD: diagnosis, year of diagnosis, disease evolution time, clinical and autoimmunity data, treatment and dose. 3) OHCLQ: time in treatment, toxicity, symptoms (dizziness, syncope) and serum level. 4) ECG; QTc and heart rate (HR).

Results: 65 patients treated with OHCLQ, mean 10.8 (6.5) years are included, diagnosed with SLE: 43 (66%) patients, RA: 15 (23%), palindromic rheumatism: 4 (6%), SS1º: 2 (3 %) and PsA: 1 (1%). 63 (97%) patients are women, with a mean age (SD): 58 (14.7) years, weight: 69 (15) kg. Mean dose of OHCLQ: 221 mcg/L (64), 3.24 (1) mg/kg/day.

Mean serum OHCLQ level: 166 mcg/L (6.5): 18 (28%) patients with level <100 mcg/L (mean: 63 [0.7] mcg/L) and 47 (72%) with level >100 mcg/L L (mean 195 mg/XX [94]). On ECG, mean HR: 69 bpm (10) and mean QTc interval: 429.7 (84) ms, prolonged (>440 ms) in 23 (35%) of the patients.

12 (18%) patients reported dizziness at some time and 29 (45%) were being treated with a drug related to the risk of QTc prolongation: Possible (P: at authorized doses no risk of TdP): 1 (2%) patient, Conditional (C: risk under excessive dose, interactions): 13 (20%), P+C: 4 (8%), C+C: 11 (17%).

When comparing the mean QTc result of the group with OHCLQ and the control groups without OHCLQ (n: 41), the QTc is higher (p=0.062) than the group of healthy subjects (n: 23) and without differences with the control group EASR (n: 18), not treated with OHCLQ (p=0.70). Among patients with OHCLQ level >100 mcg/L (n: 47) vs <100 mcg/L (n: 18), patient weight (p=0.012), level (p<0.0001), and dose in mg /kg (p=0.03), is significantly higher at levels >100 mcg/L. No relationship was observed between the OHCLQ level and the QTc result.

In 6 (9%) patients the OHCLQ dose is >3 mg/kg (mean: 5.35 [1] mg/kg, HR: 73 [14] bpm, OHCLQ dose: 367 [71] mcg/L), no detected significant differences in QTc (1 patient presented QTC >440). In patients with QTc >440 ms, older patient age, QTc result, and heart rate were significant. However, the dose in mg/kg of OHCLQ was lower in the group with QTc <440 ms (p=007).

Conclusion: In patients with SARD treated with maintenance doses of OHCLQ of about 3 mg/kg/day, 1) The serum level of OHCLQ is not associated with QTc prolongation on the ECG. 2) QTc is significantly related to age and heart rate. 3) The EASR per se does not affect the QTc result.

Table 1. Characteristics of patients with QTc greater than or less than 440 ms and with an OHCLQ level greater than or less than 100 mcg/L.

	QTc >440 ms N: 23 (35%)	QTc ≤440 ms N: 42 (65%)	p
Age, mean (SD)	64 (15)	56 (14.5)	**0.007**
Female, n (%)	22 (96)	40 (95)	0.85
QTc, mean (SD)	454 (23.9)	416 (23.7)	**0.0001**
Symptoms, n (%)	4 (17)	4 (10)	0.77
Heart rate, mean (SD)	74 (10.3)	67 (10.3)	**0.016**
Weight, mean (SD)	69 (15.1)	67 (15.6)	0.61
Risk factors QTc prolongation			
Concomitant disease, n (%)	4 (17)	4 (10)	0.77
Drugs, n (%)	14 (61)	15 (36)	0.18
OHCLQ;			
Dosis, mean (SD)	209 (64.5)	229 (15.8)	0.15
Mg/kg OHCLQ, media (SD)	2.91 (1.06)	3.43 (1.08)	**0.07**
Years in treatment, mean (SD)	9.3 (6.6)	10.5 (6.5)	0.48
OHCLQ serum level, media (SD)	174.27 (94.6)	162,4 (80)	0.51
	OHCLQ >100 mcg/L N: 47 (72%)	**OHCLQ ≤100 mcg/L N: 18 (28%)**	**p**
OHCLQ serum level, mean (SD)	166 (94)	63 (96.5)	**0.0001**
QTc, mean (SD)	430 (24)	431 (23)	0.87
Dosis mg, mean (SD)	221 (65)	208 (66.5)	0.48
Mg/kg OHCLQ, mean (SD)	3.32 (1.1)	2.65 (1.08)	**0.03**
Years in OHCLQ, mean (SD)	10.8 (6.8)	11.5 (6.9)	0.71
Weight, mean (SD)	69 (15.3)	80 (15.2)	**0.012**

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POS0370 COMPARATIVE RETINOPATHY RISK OF HIGH- VS LOW-DOSE HYDROXYCHLOROQUINE AMONG 4,677 INCIDENT LONG-TERM USERS: EMULATED TARGET TRIAL ANALYSES

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Background: Hydroxychloroquine (HCQ) is a key treatment for patients with lupus, but the major long-term toxicity is HCQ retinopathy. A large cross-sectional study found a prevalence of HCQ retinopathy of 7.5% overall and 5 times higher odds associated with HCQ dose >5 mg/kg/day, which led to ophthalmology guidelines recommending the avoidance of HCQ dosing >5 mg/kg.[1] However, whether this dosing recommendation is applicable to the future risk of HCQ retinopathy is unknown, as is the incidence of severe bullseye retinopathy vs. the mild, pre-symptomatic stage. Furthermore, recent studies have indicated that the use of lower doses of HCQ may increase the risk of lupus flares and hospitalizations.[2]

Objectives: To determine the incidence of HCQ retinopathy associated with long-term HCQ use and compare them according to HCQ dose.

Methods: We emulated a hypothetical target trial using observational data[3] from the US integrated health network Kaiser Permanente Northern California to compare two HCQ weight-based dosing strategies, >5 vs ≤5 mg/kg/day, based on dispensed tablets per year. A secondary analysis evaluated >80% of prescription days covered by dispensed tablets per year with HCQ dose >5 vs ≤5 mg/kg. We included 4,677 patients who initiated and continued HCQ for at least 5 years between 1997-2020. We emulated randomization of treatment strategy by cloning each subject and assigning a replicate to each treatment group.[3] We censored replicates if and when they deviated from the assigned treatment group, assessed as the average dose in the first 5 years and annually thereafter. We used inverse probability weighting to account for censoring. The primary outcome was HCQ retinopathy, assessed by expert adjudication of spectral domain-optical coherence tomography (SD-OCT) and graded by severity. All SD-OCTs were prospectively reviewed by an expert ophthalmologist (RM), and a second expert ophthalmologist (MM) reviewed all abnormal scans and a random subset of normal scans. We assessed intra-rater reliability of SD-OCT findings. We used pooled logistic regression to estimate the cumulative incidence of HCQ retinopathy for each HCQ dose strategy from initiation. The odds ratios approximated hazard ratios (HRs) because the outcome at each one-year time block is <5%.

Results: Among 4,677 patients, the mean age at HCQ initiation was 52 years; 83% were female. The racial/ethnic composition included 51% non-Hispanic White, 19% Hispanic, 14% Asian, and 11% Black patients. 756 (16.2%) and 3,921 (83.8%) patients initiated HCQ with the primary definition of the treatment strategies >5 and ≤5 mg/kg/day, respectively. The weighted kappa was 0.80 for SD-OCT reliability. 164 patients developed HCQ retinopathy (100 mild, 38 moderate, and 26 severe cases). The cumulative incidence of retinopathy over 18 years was 37.6% for >5 and 5.7% for ≤5mg/kg of HCQ in our primary analysis. The corresponding risk was 26.5% for >5 and 3.2% for ≤5 mg/kg in our secondary analysis using >80% of prescription days. Compared with ≤5 mg/kg of HCQ, the HRs of retinopathy were 9.65 (95% CI 5.73-16.65) and 10.79 (95% CI 6.40-20.07) for >5 mg/kg using the primary and secondary definitions of HCQ dose categories, respectively (Figure 1).

Conclusion: The risk of HCQ retinopathy associated with long-term adherence to >5 mg/kg dosing was high, approximately 10 times that of ≤5 mg/kg dosing. However, most cases identified during the study were mild and pre-symptomatic, supporting the value of regular screening. These data should be incorporated into individualized decisions about long-term use of HCQ.

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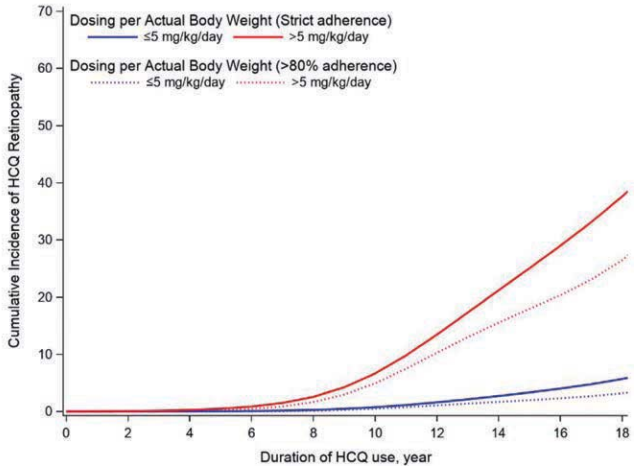
Figure 1. Cumulative Incidence of HCQ Retinopathy According to Weight-Based Dose



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POS0371 CAN WE ENHANCE ADHERENCE TO MEDICATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS? RESULTS FROM A QUALITATIVE STUDY

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Background: Medication non-adherence is common among patients with systemic lupus erythematosus (SLE) [1] and may lead to poor clinical outcomes [2,3].

Objectives: Our aim was to identify influenceable contributors to medication non-adherence to suggest interventions that could increase adherence.

Methods: Patients with SLE from two Swedish tertiary referral centres (N=205) participated in a survey assessing self-reported adherence to medications. Medication adherence was self-reported and measured using the generic instrument Medication Adherence Self-Report Inventory (MASRI) and the rheumatic disease-specific instrument Compliance Questionnaire Rheumatology (CQR). Responses were used to select patients for qualitative interviews (N=15). Verbatim interview transcripts were analysed by two researchers using content analysis methodology.

Results: The mean age of the interviewees was 39 years, 87% were women, and their mean SLE duration was 11.6 years. Patients' medications and adherence levels are detailed in Table 1. We categorised reasons for non-adherence thematically into (i) patient-related e.g., unintentional non-adherence due to forgetfulness or intentional non-adherence due to disbelief in medications, (ii) healthcare-related e.g., untrustworthy relationship with the treating physician, authority fear, and poor information about the prescribed medications or the disease, (iii) medication-related e.g., fear of side-effects, and (iv) disease-related reasons e.g., lacking acceptance of a chronic illness or perceived disease quiescence. Interventions identified that healthcare could implement to improve patients' adherence to medications included (i) increased communication between healthcare professionals and patients, (ii) patient education, (iii) accessible healthcare, preferably with the same personnel, (iv) smooth transition from paediatric to adult care, (v) regularity in addressing adherence to medications, (vi) psychological support, and (vii) involvement of family members or people who are close to the patient.

Table 1. Characteristics of the fifteen interviewees.

Patient	Prescribed medications	Overall medication adherence according to: MASRI (0–100%)	CQR (0–100%)	Direct question (Y/N) *	Intentional non-adherence (Y/N)
1	PRED HCQ AZA	96 96 96	61	N	Y
2	PRED HCQ MTX (pills)	100 100 100	77	Y	NA
3	PRED	100	81	Y	NA
4	HCQ	90	58	N	Y
5	HCQ	100	54	N	Y
6	PRED HCQ AZA	70 70 69	65	N	N
7	PRED HCQ AZA	67 50 20	47	N	Y
8	HCQ	88	72	N	N
9	PRED HCQ MMF RTX (iv)	95 96 99	74	N	Y
10	PRED HCQ AZA BEL (sc)	100 100 80	66	N	N
11	PRED HCQ MMF RTX	96 100 98	54	N	N
12	PRED HCQ	89 92	58	N	N
13	PRED CYS	100 100	84	Y	NA
14	HCQ MTX (pills)	100 100	74	Y	NA
15	PRED HCQ MMF	90 90 80	67	N	N

[1] MASRI: Medications Adherence Self Report Inventory; CQR: Compliance Questionnaire Rheumatology; F/M: female/male; Y/N: yes/no; NA: not applicable; iv: intravenous; sc: subcutaneous; PRED: prednisolone; HCQ: hydroxychloroquine; AZA: azathioprine; MTX: methotrexate; MMF: mycophenolate mofetil; RTX: rituximab; BEL: belimumab; CYS: cyclosporine; * Y= Adherence assent to direct question; N= Non-adherence assent to direct question.

Conclusion: The reasons for medication non-adherence are complex and multifaceted. From the patients' perspective, multiple different strategies could be implemented in healthcare with the goal of improving adherence, including increased communication, patient education and psychological support.

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POS0372

USE OF TELEMEDICINE FOR FOLLOW-UP OF LUPUS NEPHRITIS IN THE COVID-19 OUTBREAK: ONE-YEAR, PRAGMATIC RANDOMISED CONTROLLED TRIAL

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Background: Patients with systemic lupus erythematosus (SLE) are at increased risk of severe COVID-19 due to the underlying disease, comorbidities and use of immunosuppressants (IS). An alternative option would be to adopt telemedicine (TM) to maintain medical care while minimizing exposure. Despite being widely adopted during the pandemic, the evidence supporting the use of TM in rheumatology has been limited.
Objectives: We primarily aimed to evaluate the effectiveness to maintain disease activity control using TM delivered care compared to conventional in-person follow-up in patients with lupus nephritis (LN). The secondary objectives were to compare the patient reported outcomes, safety and cost-of-illness from the patient's perspective between the 2 modes of health care delivery.
Methods: This was a 1-year, single-center, RCT conducted at a regional hospital in Hong Kong. From May 2020, consecutive adult patients with a SLE according to the 2019 EULAR/ACR classification criteria followed up at the LN clinic were invited to participate in the study. Participants were randomized 1:1 to either TM (TM group) or standard FU (SF group). Patients randomized to receive TM FU were scheduled for a video consultation via a commerical software ZOOM. Patients in the SF group received standard in-person outpatient care. SLE disease activity at each consultation was assessed by SLEDAI-2k and physician global assessment (PGA).
Results: A total of 144 patients with LN were randomized and 3 patients self-withdrew from the study. The mean age was 44.5±11.4 years and the median time from diagnosis to randomization was 168 months (range: 1-528). Most of the patients had class III, IV or V LN (87.2%) and were on prednisolone (89.4%, median dose 5mg daily). Many of them (68.1%) were on IS. While 66.0% of the patients were in lupus low disease activity state (LLDAS), none had disease remission. There were no baseline differences, including demographics, SLEDAI-2k (TM: 3.8±2.3, SF: 3.2±2.2, p=0.13, PGA (TM: 6.2±6.5, SF: 4.6±5.9, p=0.13) and SLE damage index (TM: 1.1±1.3, SF: 0.8±1.1, p=0.10), between the 2 groups.
At one year, 80.0% and 80.2% of the patients in the TM group and SF group were in LLDAS or remission respectively. SLE disease activity indices including SLEDAI-2k, PGA, proteinuria amount and serum anti-ds-DNA level remained similar between the 2 groups. Within the study period, 28 (40%) patients in the TM group and 21 (29.6%) patients in the SF group had disease flare (p=0.20). There were no differences in the SF-36, lupusQoL and HADS scores between the 2 groups at the end of the study. The overall patient satisfaction score was higher in the TM group with a significantly shorter waiting time before seeing doctors. At the end of the study, 67.9% of the overall participants agreed to (versus 15.0% who did not agree to) use TM as a mode of future FU. The mean indirect costs of illness (HKD26,681 vs HKD12,016, p=0.20) and the out-of-pocket costs for health care services were similar between the 2 groups (TM: HKD13,547 vs SF: HKD12,297, p=0.83) in one year. The total number of FU was similar (TM: 6.0±2.0, SF: 5.7±1.7, p=0.40). However, significantly more patients in the TM group (29/70, 41.4% vs 4/71, 5.6%; p<0.01) requested change mode of FU. The proportion of patients requiring hospitalization during the study period was also higher in the TM group (TM: 23/70, 32.9% vs 11/71, 15.5%; p=0.02). After adjusting for age and prednisolone dosage, not being in LLDAS at baseline was the predictor of hospitalization (OR 3.4, 95%CI 1.20-9.65). None of the participants was tested positive for COVID-19.
Conclusion: TM FU resulted in similar 1-year disease activity control and better satisfaction in patients with LN compared to standard care. However, a significant proportion of patients cared by TM required in-person visits or were hospitalized. The results of the study suggest that TM delivered care could help minimizing exposure to COVID-19, but it needs to be complemented by physical visits, particularly in those with unstable disease.
Acknowledgements: We would also like to thank the University of Central Lancashire & East Lancashire Hospitals NHS Trust for granting us permission to use the LupusQoL questionnaire.
Disclosure of Interests: None declared
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Telemedicine what does it tell us

POS0373

WHO ARE IN AND WHO ARE NOT? CHARACTERISTICS OF PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES ACCEPTING AN ONLINE SYSTEM FOR REMOTELY ENTERING PATIENT REPORTED OUTCOMES. EXPERIENCE FROM THE DANISH DANBIO REGISTRY

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Background: Digital solutions for online monitoring of chronic diseases are increasingly implemented in health care, but not all patients might have access, skills, or interest in using them. Fueled by the COVID-19 pandemic and the urgent need for remote consultations, an online website to enter patient-reported outcomes (PROs) from home (DANBIO-from-home, https://danbio.dk) was implemented on May 15th 2020 for patients with inflammatory rheumatic diseases (IRD) followed in the Danish nationwide DANBIO registry.
Objectives: To explore the use of DANBIO-from-home during the first 1½ year after launching, with focus on a) characteristics of patients who did versus who did not access the webpage, and b) impact of patient age on time to first entry.
Methods: DANBIO-from-home allows PROs to be entered remotely by computer, tablet, or smartphone after secure log-on. All patients followed in DANBIO were informed about this option by invitations sent through eBoks, a national infrastructure for electronic communication, available to 80-90% of Danish citizens. Patients were encouraged to access DANBIO-from-home before planned rheumatology consultations, or when participating in the voluntary questionnaire survey 'You and your rheumatic disease during times with corona-virus' (on three occasions: May 2020, Nov 2020, June 2021) (ref). Follow-up ended Dec 1st 2021. Characteristics of patients who did/did not access DANBIO-from-home during follow-up are explored by multivariable logistic regression analyses adjusted by clinical factors (gender/age-group/diagnosis/disease duration/use of biologics/HAQ/PASS). Time to first entry of PRO using DANBIO-from-home is presented as cumulative incidence curves by age group.
Results: Among 33,776 patients with inflammatory rheumatic diseases followed in DANBIO, 68% used DANBIO-from-home at least once during follow-up (Table 1). Patients who used the system were less frequently below 40 years or above 80 years old, more frequently biologically treated and had lower HAQ-score than patients who did not use it.

Table 1.

		Data entry, DANBIO-from-home solution N=33,776	
		YES, 68%	NO, 32%
Gender, female		64	36
Gender, male		78	22
Age strata, yrs	< 40	62	38
	40-60	73	27
	61-80	72	28
	>80	39	61
Diagnosis	RA	67	23
	AxSpA	69	31
	PsA	70	30
Biologic treatment, yes*		73	27
PASS, yes		71	29
Age, yrs, median (IQR)		62 (52-71)	65 (50-77)
Time since diagnosis, yrs, median (IQR)		9 (5-16)	10 (5-17)
HAQ, median (IQR)		0.5 (0.125-1.0)	0.625 (0.125-1.25)

Row percentages unless otherwise shown* latest visit before March 2020AxSpA: Axial spondyloarthritis, HAQ: health assessment questionnaire, PASS: patient acceptable symptom scale, PsA: psoriatic arthritis, RA: rheumatoid arthritis

In logistic regression analyses, factors associated with DANBIO-from-home access were: female gender (odds ratio, OR 1.2 (1.1;1.3)), age group 40-60

(1.8 (1.6;2.0)) or 61-80 yrs (1.9 (1.7;2.19) and not age >80 yrs (0.6 (0.5;0.7) with age <40 as the reference), biologic treatment (1.4 (1.3;1.5)), higher HAQ (1.3 (0.3;1.4)), scoring PASS 'no' (1.1 (1.02;1.2)) (all p <0.001), whereas disease duration and diagnosis had no impact.

Time to first entry was longest in in patients >80 yrs followed by the <40 yrs group. For all age-groups, and most pronounced for age <40 yrs, the use increased when invitations to questionnaire surveys were sent out. (Figure 1)

Conclusion: A web-based system for secure remote entry of PROs was well-received after a nationwide launch. Patient-related factors had a substantial impact on the use. Lower use in the elderly might indicate lack of technical skills or facilities, whereas low use in younger age groups, which improved over time, is likely driven by other factors. Further analyses are planned to explore if lack of use impacts treatment outcomes.

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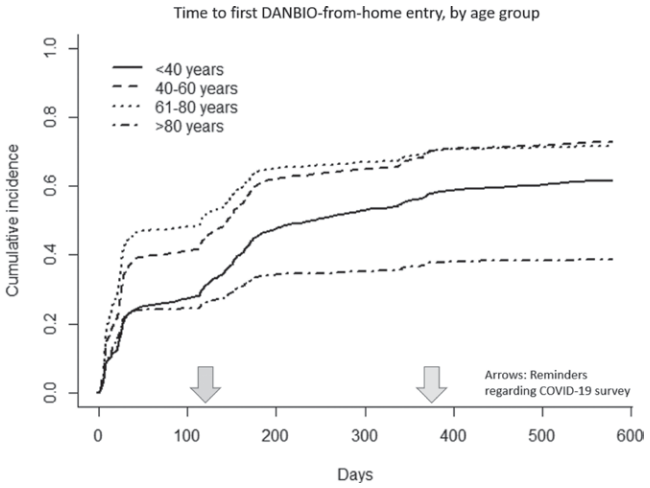

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POS0374

MONITORING CHRONIC INFLAMMATORY MUSCULOSKELETAL DISEASES WITH A PRECISION DIGITAL COMPANION PLATFORM(TM)–RESULTS OF THE DIGIREUMA FEASIBILITY STUDY

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Background: Patients with rheumatic and musculoskeletal diseases (RMDs) require a tailored follow-up that is limited by the capacity of healthcare professionals. Innovative tools need to be implemented effectively in the clinical care of patients with RMDs.

Objectives: To test the feasibility of a Precision Digital Companion Platform™ for real-time monitoring of disease outcomes in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA).

Methods: Digireuma was a prospective study including patients with RA and SpA, using the digital Precision Digital Companion Platform, Adhera for Rheumatology (ISRCTN11896540). During a follow-up of 3 months, patients were asked to report disease specific electronic patient reported outcomes (ePROs) on a regular basis in the mobile solution. Two rheumatologists monitored these ePROs and, patients were contacted for online or face-to-face interventions when deemed necessary by clinicians (Figure 1). Assessment measures included patient global assessment (PGA) of disease activity, tender joint count (TJC), swollen joint count (SJC), Health Assessment Questionnaire (HAQ) and pain visual analogue scale (VAS), for patients with RA; VAS, PGA, TJC, SJC, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and ASAS Health Index (ASAS-HI), for patients with SpA. In addition, flares, changes in medication and recent infections were asked. Usability of the digital solution was measured by the Net-Promoter Score (NPS).

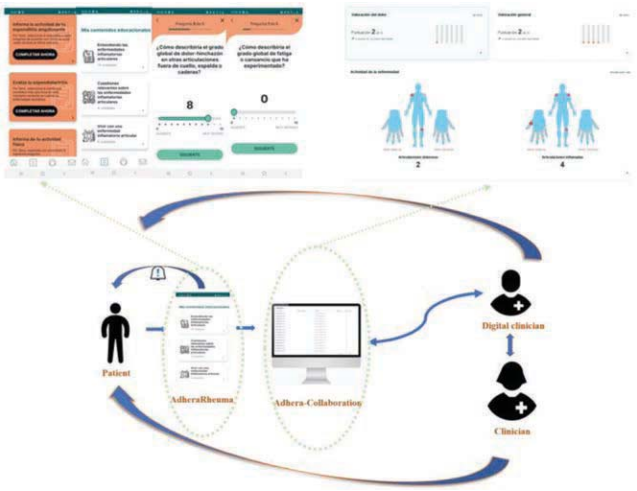

Figure 1. Digital monitoring in the study powered by Adhera for Rheumatology. Screenshots in top depict the mobile interface (left) and clinical web application (right)

Results: Forty-six patients were recruited of whom 22 had RA and 24 SpA. Mean age was 48 ± 12 and 42 ± 9 years in the RA and SpA groups, respectively. 18/22 (82%) patients with RA and 9/24 (38%) with SpA were female. Among the total included patients, 41 (89%) completed the onboarding (18/22 (82%) RA, 23/24 (96%) SpA) and 37 (80%) submitted at least one entry. In the RA group who completed the onboarding (n=18) there were a total of 4019 total interactions (2178 questionnaire items, 648 accesses to educational units, 105 quizzes, 1088 rated messages), while patients with SpA (n=23) had a total of 3160 interactions (1637 questionnaire items, 684 accesses to educational units, 77 quizzes, 762 rated messages). ePROs measurements completion rates for RA and SpA patients that completed any data during follow-up are shown in Table 1. Patients with RA completed a median of 9.5 ePROs during follow-up, whereas patients with SpA completed a median of 3. Regarding alerts, 15 patients generated a total of 26 alerts, of which 24 were flares (10 RA, 14 SpA) and 2 were problems with the medication (1 RA, 1 SpA). 18 (69%) of the alerts were managed remotely, 5 (19%) required a face-to-face intervention and in 3 (12%) patients did not respond before the consultation. Regarding usability and patient satisfaction, 14 patients provided feedback. According to the NPS, 9/14 were considered promoters, 4/14 passives and 1/14 detractor. The overall rating of these 14 patients for the app was 4.3 out of 5 stars.

Table 1. Onboarded patient engagement with regards to e-PROs

Rheumatoid Arthritis (n=18)						
	PGA	TJC	SJC	VAS	HAQ	Total
ePROs completed	1.5 (0.25, 3)	2 (0.25, 3)	2 (0.25, 3)	2 (0, 3)	2 (1, 3)	9.5 (4.3, 15.8)
Patients with ≥ 1 entry	13 (72.2)	13 (72.2)	13 (72.2)	12 (66.7)	16 (88.9)	16 (88.9)
Spondyloarthritis (n=23)						
	PGA	TJC	SJC	BASDAI	ASAS-HI	Total
ePROs completed	1 (0,3)	1 (0,3)	1 (0,3)	1 (0,2)	1 (0,2)	3 (1, 12)
Patients with ≥ 1 entry	16 (69.5)	16 (69.5)	16 (69.5)	14 (60.8)	14 (60.8)	21 (91.3)

Follow-up period was 3 months. Results are expressed in median (Q1, Q3) and n (%)

Conclusion: This study shows that the use of a digital health solution is feasible in clinical practice. Based on these preliminary results, the next step will be to further implement the Precision Digital Companion Platform, Adhera for Rheumatology, in a multicentric setting to analyze the added value for monitoring patients.

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Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie and Novartis, María Sanz: None declared, Enrique Calvo Aranda Speakers bureau: Abbvie, LETICIA LOJO: None declared, Alejandro Balsa Speakers bureau: Pfizer, Abbvie, Lilly, Galapagos, BMS, Sandoz, Nordic Pharma, Gebro, Roche, Sanofi, UCB, Consultant of: Pfizer, Abbvie, Lilly, Galapagos, BMS, Nordic Pharma, Sanofi, UCB, Grant/research support from: Pfizer, Abbvie, BMS, Nordic Pharma, Gebro, Roche, UCB, Chamaida Plasencia Speakers bureau: Pfizer, Abbvie, Lilly, Sandoz, Sanofi, Biogen, Roche, Novartis, Grant/research support from: Pfizer y Abbvie
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POS0375 EVALUATION OF PATIENTS WITH RHEUMATOID ARTHRITIS IN TELECONSULTATION DURING THE FIRST WAVE OF THE COVID-19 PANDEMIC

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Background: The sudden emergence of SARS-CoV-2 onto the world stage has accelerated a major change in the management of patients with chronic rheumatic diseases and has catalyzed the rapid emergence of telemedicine.
Objectives: Our aim was to describe which parameters were used by rheumatologists to monitor patients with rheumatoid arthritis (RA) in teleconsultation during the first wave of the pandemic and identify the most relevant for decision making.
Methods: Retrospective monocentric routine care cross-sectional study including RA patients seen in teleconsultation between March and September 2020. Available parameters assessing disease status were collected in teleconsultation files. Clinician intervention was defined by treatment escalation and/or the need for a rapid face-to-face consultation or day hospitalization.
Results: 143 RA patients were included (117 females, mean age of 58±16 years, mean disease duration of 14±11 years). The presence or absence of patient self-reported RA flares was mentioned in all medical files, followed by the presence and/or the number of tender joints (76%), the duration of morning stiffness (66%), the number of pain-related nocturnal awakenings (66%) and the CRP value (54%). Patient self-reported RA flares concerned 43/143 patients (30%). The presence of self-reported RA flares was associated with a more detailed evaluation of patient in teleconsultation: The presence (or number) of tender joints and swollen joints were more significantly reported in patients who presented a flare (39/43, 91% vs. 70/100, 70%, p=0.008 and 25/43, 58% vs. 23/100, 23%, p<0.001, respectively).
Teleconsultation led to a clinician intervention in 22/143 patients (14%), representing 51% of patients with self-reported flares (22/43 patients). Therapeutic escalation was necessary in 13 patients: introduction or dose increase of corticosteroids in 8 patients, introduction or dose increase of methotrexate in 4 patients and introduction of hydroxychloroquine in 1 patient. Face-to-face consultation or day hospitalization were organized for 10 patients. Active disease was confirmed during this next face-to-face visit in 9 patients, with DAS28 ranging from 3.35 to 5.62, leading to therapeutic modification. The 133 other patients were seen in face-to-face consultation 6±2 months after the teleconsultation. No DMARD modification was recorded during this next face-to-face consultation.
The following variables were associated with clinician intervention during the teleconsultation in univariate analysis: patient self-reported RA flares since the last visit (p<0.001), CRP >10 mg/mL (p=0.012) and a morning stiffness > 30 minutes (p<0.001). Multivariate analysis confirmed RA flares (Odds Ratio, OR: 15.6 95% CI 3.37-68.28) and CRP values >10 mg/L (OR: 3.32, 95% CI % 1.12-13.27) as the variables independently associated with clinician intervention.
Conclusion: Our study identified patient reported RA flares and increased CRP values as 2 red flags in teleconsultation, independently associated with therapeutic modification and/or the need for a rapid face-to-face consultation. These indicators may help clinician's decision making in teleconsultation.
Disclosure of Interests: Jerôme Avouac Speakers bureau: Bristol Myers Squibb, SANOFI, galapagos, Lilly, Abbvie, Pfizer, Novartis, Biogen, Fresenius Kabi, Janssen, MSD, Roche-Chugai, Medac, Consultant of: galapagos, Abbvie, Pfizer, Bristol Myers Squibb, SANOFI, Nordic-Pharma, Grant/research support from: Bristol-Myers Squibb, Pfizer (Passerelle), Novartis (Dreamer), Fresenius Kabi, Anna Moltó: None declared, CAMELIA FRANTZ: None declared, Sarah Wanono: None declared, Elise Descamps: None declared, Olivier Fogel: None declared, Alice Combier: None declared, Lucile Poiroux: None declared, Corinne Miceli Richard: None declared, Yannick Allanore: None declared
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POS0376 THE ROLE OF ELECTRONIC CONSULTATION IN THE EARLY DIAGNOSIS OF INFLAMMATORY ARTHROPATHIES IN A THIRD LEVEL HOSPITAL

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Background: The relevance of early diagnosis in rheumatic inflammatory diseases is well known. Electronic consultation (e-Consults) is a tool for communication between primary health care (PHC) and hospital care (HC) physicians in order to present the cases of patients. It has proven to resolve cases without on-site consultations and to facilitate quick access to conventional consultations.
Objectives: To evaluate whether e-Consults is an effective tool in the early diagnosis of inflammatory arthropathies
To evaluate whether the clinical suspicion of the rheumatologist correspond to the final diagnosis.
Methods: Retrospective, observational study of all e-Consults carried out during 2021 in the hospital area *Virgen Macarena*. All e-Consults were carried out by means of a computer program as a clinical extension of the research project E-Hermes for the implementation of e-Consults. The analysis focused on those e-Consults in which the rheumatologist suspected rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondylarthritis (SpA) in comparison with the final diagnosis. The on-site consultations and waiting time for appointments were also analyzed.
Results: During 2021, the number of e-Consults received was 733. Inflammatory arthropathy was suspected in 54 (7.4%). RA was suspected in 55.9% of the cases, PsA in 17.6% and SpA in 26.5% of the cases. 67.6% of the patients were women with an average age of 53.15 (± 17.06). 87.3% were recalled for an on-site consultation. Of these, 76.5% were given a preferential appointment and 11.8% were given a regular appointment. The waiting time for the preferential appointment was 18.5 days on average and 39 days for the regular appointment.
73.7% of the patients with suspected RA were women with an average age of 55.16 years (± 16.8). The reasons for consultation were: joint swelling (89.5%), polyarthralgia (5.3%) and hand pain (5.3%). The diagnosis of RA was confirmed in 47.4% of the suspected cases and only 27.7% showed no inflammatory joint pathology.
83.3% of the suspected PsA cases were women with an average age of 53 years (± 12.6). Joint swelling was the most frequent reason for consultation (50%) followed by polyarthralgia, lumbar back pain and hand pain (16.7%, respectively). The diagnosis of PsA was confirmed in 33.3% of the suspected cases.
55.6% of the patients with suspected SpA were men with an average age of 49 years (± 20.8). The most frequent reasons for consultation were: joint swelling (44.4%) and lumbar back pain (33%). The suspected diagnosis of SpA was confirmed in consultation in 44.4% of the patients and only 33.3% of the suspected cases showed no inflammatory pathology.
After all 733 e-Consults performed in 2021, 14 patients (2%) were diagnosed with RA, 5 (0.7%) were diagnosed with PsA and y 6 (0.9%) with SpA, which means a 3.5% diagnosis of inflammatory arthropathy by means of e-Consults.
The hospital area *Virgen Macarena* serves 481,296 inhabitants. Considering that the incidence per 100,000 patients/year is 8.3 for RA, 3.6 for PsA and 7.2 for SpA [1-2], the number of new cases expected in our area are as follows: 40 for RA, 17 for PsA and 5 for SpA. The proportion of cases diagnosed by TC were 36% for AR, 27.7% for PsA and 18.5% for SpA, corresponding to the reference population.
Conclusion: The suspected diagnosis of the rheumatologist in the e-Consults was confirmed for inflammatory joint pathologies in almost half of the cases.
E-Consults is a useful tool to identify inflammatory joint processes that need evaluation in an on-site consultation.
E-Consults is an efficient method for the early detection of high-impact rheumatic diseases, facilitating quick access to those patients and minimizing diagnostic time.
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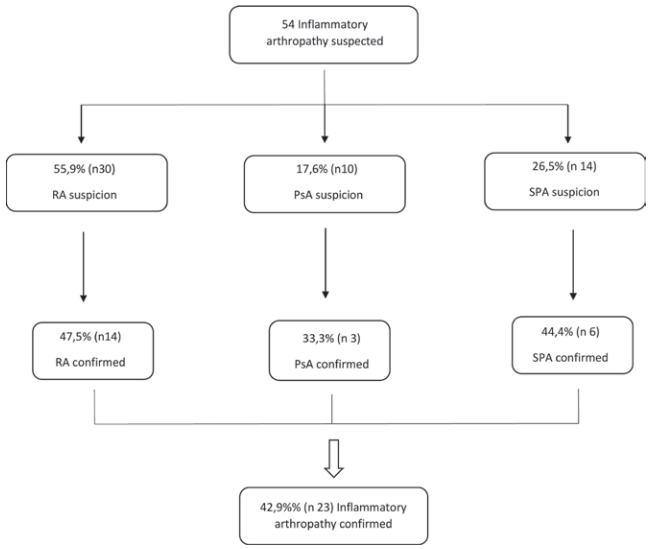

Disclosure of Interests: None declared
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POS0377

ONE YEAR OF DIGITAL HEALTH APPLICATIONS (DIGA) IN GERMANY – RHEUMATOLOGISTS' PERSPECTIVES

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Background: Based on given legislation (§§ 33a and 139e SGB V, Social Code Book V) the German approach to digital health applications (Digitale Gesundheitsanwendungen, DiGA) allows reimbursed prescription of approved therapeutic software products (listed in the DIGA directory https://diga.bfarm.de/de/verzeichnis) for patients since October 6th, 2020.
Objectives: To evaluate the level of knowledge on DiGA among members of the German Society for Rheumatology (DGRh) after one year of DiGA under the conditions of the COVID-19 pandemic using the DiGA Toolbox of the 'health innovation hub' (hih), a think tank and sparrings partner of the German Federal Ministry of Health.
Methods: Anonymous cross-sectional online survey using LimeSurvey (https://limesurvey.org). The survey was promoted by newsletters sent out to DGRh newsletter recipients and Twitter posts. Ethical approval was obtained.
Results: 75 valid participants reported that they care more than 80% of their working time for patients with rheumatic diseases. Most were working in outpatient clinics (54%) and older than 40 years of age (84%). Gender distribution was balanced (50%).
70% were aware of the possibility to prescribe DiGA. Most were informed on this for the first time via trade press (63%), and only 8% via the professional society. 46% expect information on DiGA from professional societies and the medical chambers (36%) but rarely from the manufacturer (10%) and the responsible ministry (4%). Respondents would like to be informed about DIGA via continuing education events (face-to-face 76%, online 84%), trade press (86%), and manufacturers test accounts (64%).
Only 7% have already prescribed a DiGA, 46% planned to do so, and 47% did not intend DiGA prescriptions. Relevant aspects for prescription are given in Figure 1.

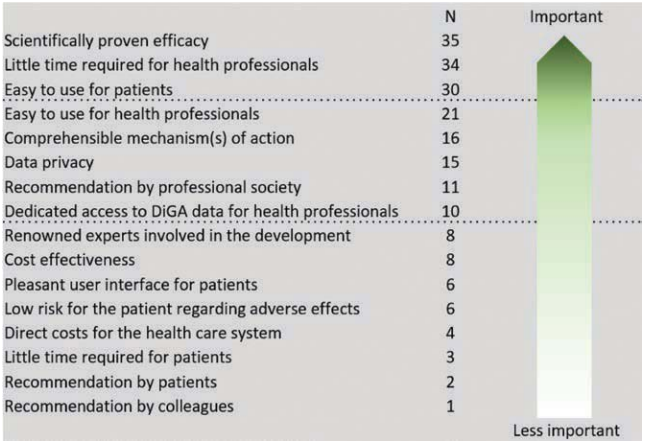

Figure 1. Aspects relevant for DiGA prescriptions; sorted by importance/number of mentions (participants needed to pick their three most relevant aspects from a pre-given list)

86% believe that using DiGA / medical apps would at least partially be feasible and understandable to their patients.
83% thought that data collected by the patients using DiGA or other digital solutions could at least partially influence health care positively.
51% appreciated to get DiGA data directly into their patient documentation system resp. clinical electronic health record (EHR) and 29% into patients' owned EHR.
Conclusion: DiGA awareness was high whereas prescription rate was low. Mostly, physician-desired aspects for DiGA prescriptions were proven efficacy and efficiency for physicians and patients, risk of adverse effects and health care costs were less important. Evaluation of patients' barriers and needs are warranted. Our results will contribute to the implementation and dissemination of DIGA.
Disclosure of Interests: Jutta G. Richter: None declared, Gamal Chehab: None declared, Philipp Stachwitz: None declared, Julia Hagen: None declared, Denitza Larsen: None declared, Johannes Knitza Consultant of: Vila Health, ABATON, Medac, Matthias Schneider: None declared, Anna Voormann: None declared, Christof Specker: None declared
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POS0378

EVALUATION OF THE USE OF VIDEO CONSULTATION IN GERMAN RHEUMATOLOGY CARE BEFORE AND DURING THE COVID-19 PANDEMIC WAVES

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Background: During the COVID-19 pandemic telemedicine tools rapidly and widely gained acceptance as indispensable management tools for the continuum of clinical care in rheumatic diseases. They have been adopted in position papers and guidelines for the management of rheumatic diseases in adult patients.
Objectives: Evaluation of the use of video consultation as one form of telemedicine before and during the COVID-19 pandemic and associated lockdowns among Rheumatology physicians in Germany. The survey results are expected to support the optimization and implementation of video consultation (VC) into routine clinical practice in rheumatology, providing long-term benefits for both parties, patients and their treating rheumatologists.
Methods: Cross-sectional nationwide online survey among German rheumatologists and rheumatologists in training. The survey was promoted by newsletters sent by means of mail and Twitter posts to members of the German Society for Rheumatology (n=1,650) and German Professional Society for Rheumatology (n=527).
Results: Reported data refer to 205 participants. The majority of respondents was male (59%), older than 40 years (90%) and specialized in internal medicine/rheumatology (85%).
They were divided into two groups: 'digital users' (38%) and 'digital non-users' (62%). Users employing telemedicine (TM) but never VC were defined as 'TM-users' (10%). Those using TM and VC were classified as 'VC-users' (27%). 'Non-users' negated the use of VC and TM respectively.
Knowledge on telemedicine was self-rated as 4 (median on a Likert Scale 1 (very high) to 6 (very low)) with a significant difference between user (VC-user 2.7±1.2, TM-user 3.2±1.1) and non-user (4.4±1.3).
The Figure 1 shows a significant increase in the use of VC during the lockdown periods. Even between the lockdown phases, VC use was higher than in the pre-pandemic phase.

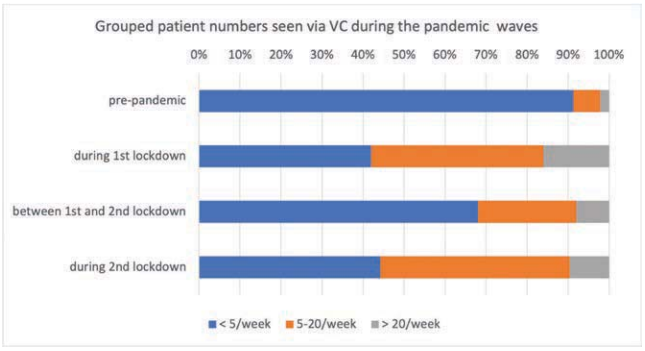

Figure 1. Grouped patient numbers seen via VC during the pandemic waves

Reasons for VC non-use in TM-user and non-user were administrative/technical efforts (21%), lack of technical equipment (15%), time constraints (12%), time required for individual VC sessions (12%), inadequate reimbursement (11%), lack of demand from patients (11%), data security concerns (9%), poor internet connection (8%), and lack of scientific evaluation/evidence (5%).
Based on the experience gained, physicians considered the following clinical situations to be particularly suitable for VC: follow-up visits (VC-user 79%, TM-user 62%, non-user

47%), emergency consultations (VC-user 20%, TM-user 33%, non-user 20%), and patients presenting for the first time (VC-user 11%, TM-user 19%, non-user 8%).

Table 1. Evaluation of the VC in comparison to other patient interaction (VC-user) on a Likert Scale with 1 (I agree completely) to 6 (I do not agree at all)

VC is	Mean ± standard deviation (median)
… comparable to a face to face meeting (n=52)	4.3 ± 1.3 (4.5)
… comparable to a telephone consultation (n=51)	3.3 ± 1.3 (3.0)
… suitable as an additional means of communication with the patient (n=51)	2.3 ± 1.5 (2.0)

Conclusion: Despite the fact that the current pandemic situation, with social distancing and several lockdowns, provides an ideal environment for the implementation of new remote care forms such as VC, their use and acceptance remained below expectations. Given the reported decline in physician face-to-face consultations during the pandemic, these findings are even more concerning. The identified reasons for non-utilization should be addressed by policy makers, payers and medical societies to provide better foundations for future innovative care models.

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POS0379

SMARTPHONE-ASSISTED PATIENT-INITIATED CARE VERSUS USUAL CARE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND LOW DISEASE ACTIVITY: A RANDOMIZED CONTROLLED TRIAL

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Background: Most patients with rheumatoid arthritis (RA) visit their rheumatologist every 3-6 months to evaluate their disease activity. This may be inefficient, as research shows that many patients have minimal disease activity.[1] When patients monitor their disease and initiate care at the right moment, they may be able to reduce the number of clinic visits, with a lower health care burden and costs. We developed a smartphone app that allows patients to self-monitor their disease activity through a weekly assessment of patient index data (RAPID-3).

Objectives: To assess safety (non-inferiority in disease activity, DAS28) and efficacy (reduction in number of visits) of patient-initiated care assisted by a smartphone app compared to usual care.

Methods: A twelve month, randomized, non-inferiority clinical trial was conducted in RA patients with low disease activity, on stable treatment for at least 6 months prior to entry. Patients were randomized (1:1) to either app supported patient-initiated care with a scheduled follow-up consultation after a year (app-group), or usual care, see Figure 1. The primary outcomes were non-inferiority in terms of change in disease activity (ΔDAS28) after 12 months and the number of consultations with a rheumatologist. The non-inferiority limit was set at 0.5 difference in ΔDAS28 between the groups.

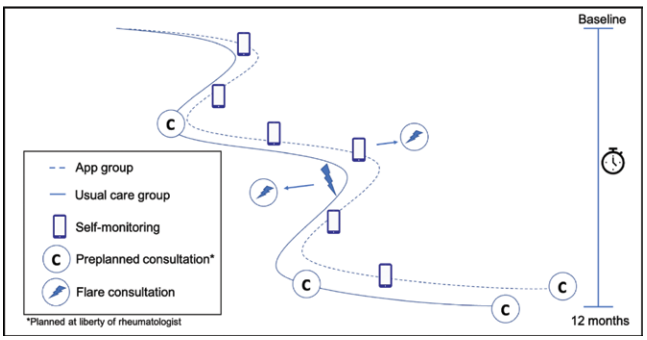

Figure 1. Typical routine care versus app-supported self-initiated care.

Results: 102 of 103 randomized patients completed the study. The mean age was 58, 60 were female and the mean disease duration was 12 years. At baseline mean (SD) DAS28 was 1.67 (0.68) in the app group, and 1.54 (0.72) in the usual care group. After a year, ΔDAS28 was 0.27 in the app group vs 0.35 in the usual care group: the difference in ΔDAS28 was –0.04 in favor of the app group (95%CI –0.39; 0.30) documenting non-inferiority. The number of rheumatologist consultations was significantly lower in the app group: mean (SD) 1.7 (1.8) vs 2.8 (1.4) visits/year; visit rate ratio: 0.62 (95% CI 0.47;0.81, p<0.001).

Conclusion: Patient-initiated care supported with self-monitoring via a smartphone app was non-inferior to usual care in terms of ΔDAS28 and led to a 38% reduction in rheumatologist consultations rate.

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Disclosure of Interests: Bart Seppen: None declared, Jim Wiegel: None declared, Marieke ter Wee: None declared, Dirkjan van Schaardenburg: None declared, Leo Roorda: None declared, Maarten Boers: None declared, Michael Nurmohamed: None declared, W.H. Bos Grant/research support from: AbbVie sponsored this trial

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POS0380

EFFECTIVENESS OF REMOTE CARE INTERVENTIONS: A SYSTEMATIC REVIEW INFORMING THE 2022 EULAR POINTS TO CONSIDER FOR REMOTE CARE IN RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: While the number of patients with rheumatic musculoskeletal diseases (RMDs) is increasing worldwide, there is no adequate increment in the number of health care professionals, leading to the urgent need for new forms of care to take pressure from health care systems.[1] [2] Telehealth comprises a number of different types of interventions with the scope of performing certain steps of care, ranging from diagnostics to follow-up visits, in a remote manner. The use of remote care is heterogenous and guidance is needed to optimize the combination with conventional face-to-face (F2F) visits.

Objectives: To perform a systematic literature review (SLR) on different outcomes of remote care compared to F2F care, its implementation into clinical practice and to identify drivers and barriers in order to inform a task force formulating the European Alliance of Associations for Rheumatology (EULAR) Points to Consider for remote care in RMDs.

Methods: Prospective, retrospective, and qualitative studies testing different types of remote care in patients with RMDs were included. Medline, Embase and the Cochrane Library were searched through February 28th, 2021. Two reviewers independently performed standardized data extraction, synthesis, and risk of bias assessment.

Results: A total of 2,240 references were identified. Forty-seven studies, consisting of 26 randomized controlled trials, 8 prospective cohort studies, 8 cross sectional studies, and 5 qualitative studies were included.

Fifty-one percent of the studies involved patients with inflammatory RMDs, including rheumatoid arthritis, and spondyloarthritis, while 49% were on patients with non-inflammatory conditions, such as osteoarthritis and fibromyalgia. Remote monitoring (n=35) was most frequently studied, with telephone/video calls being the most common mode of delivery (n=30). Thirty-four studies investigated outcomes of remote care in comparison to F2F care. The most frequently assessed outcomes concerned efficacy and user perception of remote care, with 34% and 21% of studies, respectively, reporting superior results for the remote care intervention.

Time savings and flexibility were reported as major drivers, while inadequate technical knowledge and concerns in data security were the main barriers to

implementing remote care. Implementation of remote care methods into clinical practice was not reported by the included studies. The main limitations were the heterogeneity of outcomes and interventions, and the substantial risk of bias (50% of studies with high risk of bias).

Conclusion: Studies on remote care reported similar to partially better results compared to F2F care concerning efficacy, and user perception outcomes, with the limitation of heterogeneity and considerable risk of bias.

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POS0381 ALLOCATION OF VISITS ACCORDING TO NEED: SCREENING RHEUMATOID ARTHRITIS PATIENTS WITH PATIENT REPORTED OUTCOMES

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Background: Currently, patients with rheumatoid arthritis (RA) require frequent consultations to monitor their disease activity. However, since a majority of patients is in remission during routine follow up, it should be possible to reduce the number of consultations for them.[1] Patients that are meeting their treatment goal, based on the results of their electronic patient reported outcome measures (ePROMs), could be eligible to skip their visit. Research revealed that patients who indicate to be in remission or have a low disease activity (remission/LDA) on their ePROMs, such as the routine assessment of patient index data (RAPID3), also have a low disease activity score 28 (DAS28).[2] However, in clinical practice the decision to intensify treatment is more complex than not meeting a DAS28 threshold. Therefore, ePROM-results should be compared with treatment intensifications to assess the safety of screening with ePROMs.

Objectives: To assess the probability that patients with low scores on disease activity assessment with ePROMs do not need medication intensification.

Methods: This retrospective study compared results of three ePROMs (RAPID3, patient acceptable symptom state (PASS) and asking patients if they experienced a flare (flare question)) answered during routine care with (disease modifying anti-rheumatic drug) DMARD or steroid intensifications collected from anonymised electronic medical records at Reade. We calculated the positive predictive value (PPV) for not receiving a DMARD or steroid intensifications within two weeks and three months for 1) being in remission/LDA according to the RAPID3, 2) being in PASS and 3) not reporting a flare. The secondary aim of the study was to assess which combination of ePROM-results led to the best PPV for DMARD or steroid intensifications.

Results: A total of 321 records were included that regarded 302 unique patients (77% female, mean age (SD) was 60 (12) years). The PPV for not receiving a DMARD or steroid intensification within 2 weeks of the RAPID3, PASS and flare-question were 99%, 95% and 83%, respectively, and after 3 months 95%, 88%, 85%, for all test characteristics see Table 1. The combination of a RAPID3 < 2 and a negative flare-question resulted in a PPV of 100%; this combination was present in 29% (93/321) of the total study population.

Table 1. Predictive values of ePROMs for DMARD or steroid intensifications

ePROMs	PPV	Specificity	NPV	Sensitivity
Direct (<2 weeks)				
RAPID3	99	99	28	37
PASS	95	85	42	71
FLARE	93	74	52	83
RAPID3 + Flare	100	100	36	29
Follow up (<3 months)				
RAPID3	95	95	39	40
PASS	88	75	54	74
FLARE	85	62	63	85
RAPID3 + Flare	96	96	39	39

All numbers are percentages. ePROMs: electronic Patient Reported Outcome Measures, NPV: Negative Predictive Value, PPV: Positive Predictive Value, RAPID3: Routine Assessment of Patient Index Data-3, PASS: Patient Acceptable Symptom State.

Conclusion: Our results show that the RAPID3, PASS and flare have a high diagnostic accuracy to identify individuals that will not receive a DMARD or steroid intensification up to 3 months after their initial consultation and are therefore possibly eligible to skip their outpatient clinic visit. The combination of the RAPID3 and the PASS yielded the best combination of diagnostic accuracy and highest number of eligible patients.

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What's new in scleroderma and myositis?

POS0382 RNA-SEQUENCING ANALYSIS TO IDENTIFY POTENTIAL FUNCTIONAL PATHWAYS INVOLVED IN SYSTEMIC SCLEROSIS PATHOGENESIS: OUR PRELIMINARY EXPERIENCE

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Background: Systemic Sclerosis (SSc) is a connective tissue disease, characterized by endothelial dysfunction, autoimmunity abnormalities and fibrosis of the skin and internal organs. The exact pathogenetic mechanisms that propagate SSc vasculopathy are still not completely understood. A complex network of interactions between endothelial cells, pericytes, myofibroblasts, and the extracellular matrix (ECM) has been implicated but it is currently unclear what drives the activation of fibroblasts and the increased ECM deposition responsible for the fibrotic changes well known in SSc.

Objectives: Using RNA sequencing (RNA-seq), our goal was to identify potential functional pathways possibly involved in SSc pathogenesis and markers that could potentially be used to better understand endothelial dysfunction and fibrosis mechanisms in SSc patients.

Methods: RNA-seq analysis was performed on RNA obtained from biopsies from 3 SSc patients and 3 age- and sex-matched healthy controls (HC) enrolled in our University Hospital between January 2019 and December 2020. The samples were transferred to a labelled cryovial and immediately stored in liquid nitrogen. RNA extraction followed standard methodologies. RNA from each sample was used to generate sequencing libraries that were sequenced according to proper transcriptomic analyses. To identify potential functional pathways that could be involved in SSc pathogenesis, we performed gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs). GSEA was applied on the entire list of genes that compose the RNA-seq expression matrix. Genes were ranked based on their fold change calculated between groups of each pairwise comparison and analyzed by GSEA in pre-ranked mode. We adopted the

"classic" enrichment statistic, the recommended approach for RNA-sequencing data.

Results: According to GSEA analysis of DEGs applied to SSc and HC, we identified 305 DEGs that were upregulated or downregulated at least 2-fold. In particular, 175 genes were upregulated and 130 genes were downregulated. A marked upregulation of genes involved in Wnt signaling, including Wnt family members, was present in HC if compared with SSc. The upregulation of collagen type VI, extracellular matrix protein 2, vascular endothelial growth factor D, among others, was also observed. Conversely, a marked downregulation of late cornified envelope and of genes encoding for keratins, was present in HC versus SSc samples. GSEA revealed that HC were characterized, among others, by gene signatures related to stromal stem cells proliferation, cytokine-cytokine receptor interaction, macrophage-enriched metabolic network, whereas SSc tissues were enriched in signatures related to keratinization, cornification, retinoblastoma (RB) 1 and tumour suppressor (TP) 53 signaling. Figure 1 displays GSEA in HC *vs* SSc tissues.

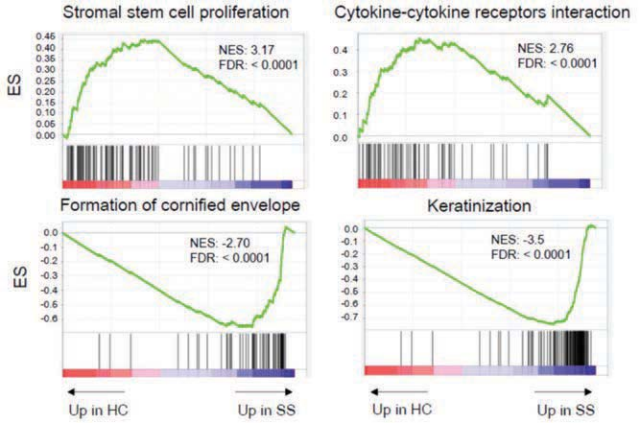

Figure 1. GSEA in HC vs SSc tissues.Enrichment of gene signature was analyzed in transcriptomic data from HC and SSc samples.ES=enrichment score. NES=normalized enrichment score. FDR=false discovery rate.

Conclusion: According to our preliminary data, RNA-seq, differential gene expression and pathway analysis revealed that SSc patients show a discrete pattern of gene expression associated with keratinization, extracellular matrix generation, and negative regulation of angiogenesis and stromal stem cells proliferation. Further analysis on larger numbers of patients are needed; however, our results provide an interesting framework for the development of biomarkers representing vascular injury and fibrotic changes in SSc in order to explore potential future therapeutic targets.

Disclosure of Interests: None declared

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POS0383 CLINICAL CHARACTERISTICS AND PROGNOSIS OF PATIENTS WITH SYSTEMIC SCLEROSIS SINE SCLERODERMA: DATA FROM THE INTERNATIONAL EUSTAR DATABASE.

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Background: LeRoy's classification defines two main subsets of Systemic Sclerosis (SSc) based on the extent of skin fibrosis: limited cutaneous SSc (lcSSc) with skin thickening sparing the trunk and distal to the elbow and knees, and diffuse cutaneous SSc (dcSSc) with proximal and distal skin thickening. These two subsets notably differ in terms of survival and frequency of visceral involvement, dcSSc being less prevalent but having a higher mortality rate with more frequent visceral manifestations. SSc sine scleroderma (ssSSc) is a third subset initially described by Rodnan *et al.* and characterized by the absence of skin fibrosis but with the existence of SSc-associated visceral manifestations.

Objectives: This study aimed to characterise the main clinical features of patients with ssSSc in comparison with the lcSSc and dcSSc subsets within the international EUSTAR database.

Methods: All patients from the EUSTAR database fulfilling the ACR2013 or 1980 classification criteria for SSc assessed by the modified Rodnan Skin score (mRSS) at inclusion and with at least one follow-up visit were eligible. Sine scleroderma (ssSSc) was defined by the absence of skin thickening (mRSS=0 and no sclerodactyly) at all available visits. The clinical characteristics of these ssSSc patients were compared to those of patients with lcSSc and dcSSc with similar disease duration at last follow-up visit. Descriptive statistics were applied.

Results: Among the 4263 patients fulfilling the inclusion criteria, 376 (8.8%) were classified as ssSSc. Among them, 40.3% had puffy fingers, 39.4% had interstitial lung disease (ILD), 1.6% had a history of scleroderma renal crisis at inclusion visit. At last available visit, in comparison with 708 lcSSc and 708 dcSSc with the same disease duration, ssSSc patients had a lower prevalence of previous or current digital ulcers (28.2% versus 53.1% in lcSSc (P<0.001) and 68.3% in dcSSc (P<0.001)), of joint synovitis (16.9% versus 24.3% in lcSSc (P<0.01) and 30.8% in dcSSc (P<0.0001)), and of elevated sPAP on echocardiogram (15.2% versus 23.9% in lcSSc (P<0.01) and 28.7% in dcSSc (P<0.0001)). Despite similar disease duration, disease activity at follow up visit (assessed by the EScSG disease activity index 2001 and 2016) was lower in ssSSc in comparison with lcSSc and dcSSc. By contrast, the prevalence of ILD was almost similar in ssSSc and lcSSc (49.8% and 57.1% (P=0.03)) but significantly higher in dcSSc (75.0%, P<0.0001). Based on forced vital capacity, ILD was less severe in ssSSc in comparison with the other subsets (mean FVC 100% (SD=22)(%pred) versus 93% (SD=21) in lcSSc and 82% (SD=23) in dcSSc (P<0.0001 for both)). Anti-centromere antibodies were most represented in ssSSc (61.7% versus 41.9% in lcSSc (P<0.0001) and 16.3% in dcSSc (P<0.0001), whereas the opposite distribution was observed for anti-Scl70 antibodies. Survival was significantly higher in ssSSc patients compared to lcSSc (P<0.05) and dcSSc (P<0.0001).

Conclusion: This study highlights that ssSSc patients account for almost 10% of SSc patients with milder disease severity compared to both lcSSc and dcSSc.

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POS0384 ULTRA SHORT ECHO TIME MRI (UTE) SEQUENCE IN THE ASSESSMENT OF INTERSTITIAL DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS: CORRELATION WITH DISEASE EXTENSION AT CT AND WITH PULMONARY LUNG FUNCTION TESTS.

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Background: Interstitial lung disease (ILD) is the major cause of death in Systemic sclerosis (SSc). Computed tomography (CT) is the gold standard imaging

technique to diagnose ILD and to assess ILD prognosis. ILD extent assessment at lung CT has shown to correlate with functional lung capacity: extensive lung disease (> 20%) correlate with significant lung capacity decline (forced vital capacity ((FVC) <70%) that is, in fact, associated with a higher mortality. Unfortunately, it is burdened by exposure to ionizing radiations that limits its use for the follow-up. For this reason, new MRI sequences were recently investigated, and Ultra Short Echo Time (UTE) emerged promising for ILD assessment.

Objectives: The aim of the study is to evaluate the reliability of an MRI-UTE sequence in the assessment of ILD extent in patients with SS in comparison with standard high-resolution CT images and to correlate the extension with pulmonary function tests (PFT).

Methods: Patients with SSc and ILD underwent a CT and UTE-MRI (1.5 T) acquisition on the same day. In the same week, they carried out PFT, with FVC and the diffusion capacity of carbon monoxide (DLCo) evaluation. Two thoracic radiologists assessed in consensus, on CT and UTE-MRI, the extent of ILD. Extensions were calculated as the mean percentage of lung involvement, evaluated at five levels, with an approximation of 5%. ILD extension were classified as limited (<20%) or extensive (> 20% or 20% with FVC <70%). The ANOVA test was adopted to compare the CT and MRI extensions of the ILD. Correlations of the extent of CT and UTE-MRI alterations with FVC and DLCo were calculated with Pearson's correlation coefficient *r*. Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (VPN) of UTE-MRI were also calculated for UTE-MRI in determining ILD extension.

Results: The mean ILD extension was 20.9% in CT and 17.9 % in UTE-MRI (p-value=0.64). The correlation of ILD extension in CT with FVC and DLCo were significant (r=-0.66 (p<0.0001) and r=-0.59 (p<0.0008), respectively). The correlation of ILD extension in UTE-MRI with FVC and DLCo were significant (-0.68 (p<0.0001) and -0.57 (p<0.002), respectively) too. The UTE-MRI assessments agreed with CT in identifying limited or extensive ILD in 25/29 patients (19 limited and 6 extended) and discordant in 4 (1 limited and 3 extended to CT). UTE-MRI sensitivity and specificity in identifying extended ILD were high (86.4% (65.1% -97.1%) and 85.7% (42.1% -99.6%), respectively). PPV and NPV were 95.0% (75.4% -99.2%) and 66.7% (40.7% -85.7%), respectively.

Conclusion: UTE-MRI sequence, compared to CT, has shown high correlation with PFR and comparable ability in identifying patients with extensive ILD. Therefore, UTE-MRI seems new promising imaging sequence for the evaluation of ILD extension in SSc patients.

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POS0385 "EFFECTIVE LUNG AGE" IN SUBJECTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) IN THE SENSCIS TRIAL

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Background: FVC declines gradually with aging. The loss of lung function in patients with progressive SSc-ILD mimics an accelerated ageing process.

Objectives: Using reference equations, we estimated the "effective lung age" of subjects in the SENSCIS trial (*i.e.* the age of healthy individuals with the same FVC) and compared these estimates to their real age.

Methods: The SENSCIS trial enrolled subjects with SSc-ILD with first non-Raynaud symptom within the prior ≤7 years, extent of fibrotic ILD on HRCT ≥10%, FVC ≥40% predicted, DLco 30–89% predicted. Evidence of recent decline in FVC was not an inclusion criterion. Subjects were randomised to receive nintedanib or placebo. Using reference equations published by the European Respiratory Society Global Lung Function Initiative, based on FVC data from over 70,000 healthy individuals aged 3–95 years from 26 countries, [Quanjer et al. Eur Respir J 2012;40:1324–1343], we estimated the effective lung age of subjects at baseline and at week 52 based on their FVC, sex, ethnicity and height, and compared these effective lung ages with the subjects' real ages. Three subjects aged <25 years were excluded. The upper limit of effective lung age was considered to be 95 years.

Results: Mean time since onset of first non-Raynaud symptom was 3.5 years in both the nintedanib and placebo groups. At baseline, mean (SD) effective lung age was 83.1 (14.4) years in the nintedanib group (n=287) and 82.9 (14.8) years in the placebo group (n=286). In these groups, respectively, the mean (SD) difference between effective lung age and real age was 28.4 (17.7) and 29.3 (18.5) years and the difference was >20 years in 71.4% and 72.4% of subjects. In the nintedanib and placebo groups, respectively, median (Q1, Q3) effective lung age was 88.4 (74.6, 95.0) and 88.5 (74.7, 95.0) years at baseline and 91.0 (75.2, 95.0) and 95.0 (75.9, 95.0) years at week 52.

Conclusion: At entry into the SENSCIS trial, subjects with SSc-ILD had an effective lung age that was much higher than their real age. Over 52 weeks, the increase in effective lung age was numerically lower in subjects treated with nintedanib than placebo. These data show that marked loss of lung function that can occur in the few years following onset of SSc-ILD and support a benefit of nintedanib in slowing the progression of SSc-ILD.

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POS0386 A NOVEL ECHOCARDIOGRAPHY METHOD FOR THE DETECTION OF SUBCLINICAL MYOCARDIAL FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY.

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Background: Scar imaging echocardiography with ultrasound multi-pulse scheme (eSCAR) is a novel technique allowing detection of myocardial scars. eSCAR has never been explored in patients with systemic sclerosis (SSc).

Objectives: The aim of our study was to examine whether eSCAR may detect subclinical myocardial fibrosis in SSc.
Methods: In this cross-sectional study conducted between 11/2020 and 02/2021, consecutive SSc patients from the University of Verona underwent cardiovascular disease (CVD) screening procedures including standard transthoracic echocardiography (TTE) and myocardial scars detection through the eSCAR technique. We excluded patients with prior history of structural heart disease and pulmonary hypertension. To validate eSCAR findings, we assessed myocardial function through global longitudinal strain (GLS) analysis by speckle tracking echocardiography (STE). We also conducted a case-control study comparing eSCAR findings in randomly selected SSc patients and non-SSc controls matched 1:1 for age, sex and number of CVD risk factors. The primary outcome was the proportion of patients with myocardial scars. Principal component analysis (PCA) was used to determine main eSCAR patterns. Multivariable linear regression analysis was used to minimise confounding.
Results: Scar imaging echocardiography revealed that 42/92 (44%) SSc patients had myocardial scars involving a median [25th-75th percentile] of 4 [1-7] segments. PCA identified that myocardial scars localised mostly at the inferior and septal segments (inferoseptal pattern; Figure 1). STE validation confirmed that GLS was significantly reduced in SSc patients with inferoseptal scars (Table 1). Otherwise, all standard echocardiography measures were normal in both groups. In multivariable regression analysis, prior digital ulcerations (B=0.41, 95% CI 0.008 to 0.809, p=0.045) and body mass index (B=-0.06, 95% CI -0.113 to -0.015, p=0.012) were both significantly and independently associated with inferoseptal myocardial scars. Myocardial scars were found in 38% of SSc patients and no matched controls (p<0.0001).

Table 1. Comparison of speckle tracking echocardiography (longitudinal myocardial strain) in eSCAR-positive (inferoseptal pattern) and eSCAR-negative (no inferoseptal pattern) patients.

Speckle tracking echocardiography	eSCAR-positive (n= 8)	eSCAR-negative (n=31)	P-value
GLS global (%)	- 20.24 (2.39)	- 20.42 (3.65)	0.895
GLS 4-chambers (%)	- 20.66 (1.91)	- 20.09 (4.12)	0.720
GLS 2-chambers (%)	- 23.02 (5.23)	- 21.97 (3.89)	0.924
GLS 3-chambers (%)	- 17.11 (2.60)	- 19.31 (5.26)	0.015
GLS apical			
- anterior	- 19.60 (6.12)	- 17.72 (4.42)	0.857
- inferior	- 26.89 (7.79)	- 23.65 (5.46)	0.581
- lateral	- 18.91 (2.04)	- 18.13 (5.12)	0.508
- septal	- 22.68 (7.14)	- 21.76 (7.04)	0.844
GLS basal			
- anterior	- 23.35 (3.82)	- 22.75 (8.36)	0.752
- anteroseptal	- 14.09 (4.74)	- 18.66 (7.46)	0.109
- inferior	- 22.69 (8.49)	- 22.78 (6.94)	0.818
- lateral	- 19.99 (7.68)	- 22.55 (7.01)	0.218
- septal	- 14.26 (4.63)	- 18.07 (8.79)	0.081
GLS mid			
- inferior	- 23.09 (6.12)	- 22.58 (5.07)	0.917
- septal	- 14.80 (5.69)	- 17.50 (7.53)	0.056
- anterior	- 20.54 (3.28)	- 19.73 (6.52	0.026
- anteroseptal	- 14.70 (4.96)	- 18.13 (5.20)	0.010
- lateral	- 18.64 (5.79)	- 20.09 (5.73)	0.270

Data are reported as mean (S.D.). GLS, global longitudinal strain.

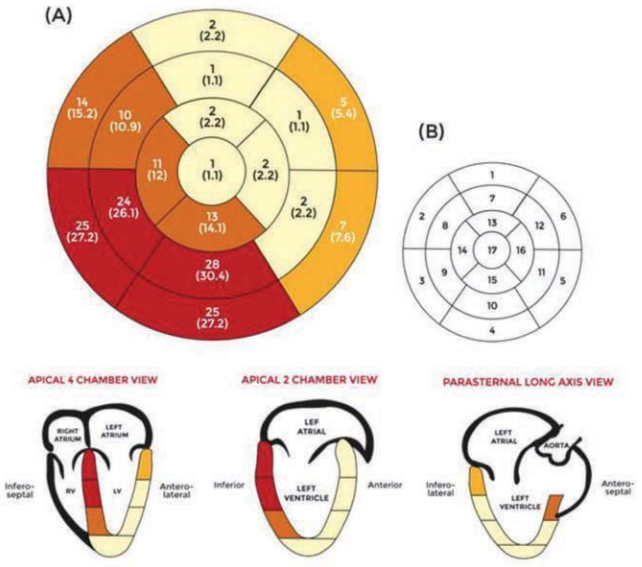

Figure 1.

Conclusion: This simple ultrasound technique allows detection of myocardial dysfunction associated with scars in SSc patients, or its absence in matched controls. Patients with prior digital ulcerations and low body weight have the strongest association with inferoseptal myocardial scars. eSCAR may help detect subclinical myocardial fibrosis in SSc.
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POS0387 RISK STRATIFICATION APPROACHES PERFORM DIFFERENTLY IN SSC-ASSOCIATED PAH IN EUSTAR

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Background: Pulmonary arterial hypertension (PAH) is a major clinical challenge in systemic sclerosis (SSc), and is associated with high mortality. Risk stratification provides an estimate for individual patient risk of 1-year mortality. The aim is to detect patients with the worst prognosis to optimize management strategies. Nine risk stratification approaches have been proposed in PAH, but have not been validated in SSc-PAH.
Objectives: To assess four risk stratification models and their performance to predict 1- and 3- year mortality and to identify the best risk assessment approach for SSc-PAH.
Methods: We included all patients with SSc diagnosed with PAH by right heart catheterization (RHC) from the European scleroderma trial and research (EUSTAR) database from 2001 to February 2021. PAH was defined as mean pulmonary arterial pressure (mPAP) ≥25 mmHg, pulmonary artery wedge pressure (PAWP) ≤15mmHg, and pulmonary vascular resistance (PVR) >3 Wood units (WU) in the absence of significant interstitial lung disease. We applied four different approaches for risk stratification at time of PAH diagnosis. Risk parameters included New York Heart Association (NYHA) class, 6-minute walk distance (6MWD), NT-proBNP or BNP, and echocardiographic and hemodynamic parameters with cut-off values based on the 2015 ESC/ERS Guidelines. Model 1 and 2 stratified patients into low, intermediate and high-risk categories; while Model 3 and 4 stratified the patients into four categories (low, intermediate-low, intermediate-high and high).
Model 1: Patients with ≥ 1 high-risk parameter were considered at high risk; with ≥ 1 intermediate-risk parameter at intermediate risk, otherwise at low risk[1]
Model 2: Each variable was graded from 1 to 3 representing low to high risk. The mean of available risk parameters was rounded to the nearest integer to define the risk category[2]
Model 3: Equals Model 2, but the intermediate risk group was divided into intermediate-low and intermediate-high based on the mean score[3]
Model 4: Stratifies patients into four risk categories based on the proportion of low-risk parameters[3]
We performed analysis of 1- and 3- year mortality in patients with a minimum follow-up of 1 and 3 years, respectively.

Table 1. Demographic and clinical characteristics of patients segregated by risk stratification (Model 3)

	N	All patients (n=273)	Low-risk (n=78)	Intermediate-low (n=118)	Intermediate-high (n=56)	High-risk (n=21)
Age, years (SD)	273	65 (10.7)	65 (10.3)	65 (10.7)	65 (10.8)	67 (12.8)
Female sex, n (%)	273	230 (84)	64 (82)	98 (83)	48 (86)	20 (95)
lcSSc, n (%)	263	221 (84)	60 (80)	99 (86)	47 (90)	15 (71)
NYHA 3 or 4, n (%)	261	155 (59)	12 (16)	75 (68)	49 (89)	19 (95)
NT-proBNP, pg/ml (IQR)	111	1941 (230-1485)	215 (103-377)	763 (325-1418)	1926 (1051-5681)	3314 (1129-6553)
6MWD, m (SD)	196	321 (124.1)	404 (119.7)	314 (99.9)	262 (128.6)	215 (96.0)
RHC:						
- mPAP, mmHg (SD)	273	40 (11.0)	35 (8.8)	41 (11.5)	41 (10.8)	45 (11.6)
- PAWP, mmHg (SD)	273	9 (3.2)	9 (3.0)	9 (3.4)	9 (3.2)	8 (3.1)
- Cardiac index, l/min/m^2 (SD)	260	2.8 (0.8)	3.2 (0.7)	2.7 (0.8)	2.6 (1.0)	2.0 (0.5)
- PVR, WU (SD)	273	7.4 (4.1)	5.3 (2.8)	7.9 (4.0)	7.9 (4.2)	11.3 (4.7)

Results: Of 911 patients who conducted RHC, 273 (30%) were diagnosed with SSc-PAH according to the inclusion criteria (Table 1). Median follow-up time was 2.8 years (IQR 1.3-5.3). The models varied in their ability to predict mortality (Figure 1). Model 1 and 4 either over- or underestimated mortality. Model 2 stratified patients according to the expected 1-year mortality of <5%, 5-10% and >10% suggested by the ESC/ERS Guidelines. Model 3, which divided the intermediate risk group in two different risk groups, segregated the risk of mortality further within this group.

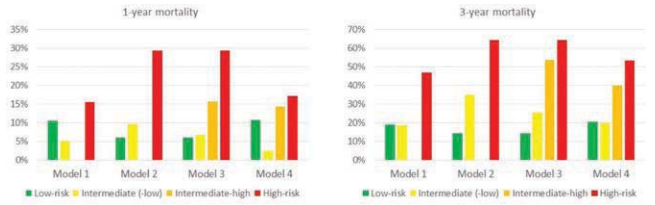

Figure 1. 1- and 3-year mortality according to risk category in the four different models

Conclusion: Model 3 provides signals for a better risk stratification of patients with newly diagnosed SSc-PAH, with progressively increasing mortality across the categories. This may provide guidance for optimized management in clinical practice.

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[3] Kylhammar, ERJ open 2021

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POS0388

DEVELOPING A SCREENING TOOL FOR THE DETECTION OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS: THE ILD-RISC RISK SCORE

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Background: High resolution computed tomography (HRCT) is the gold standard for the diagnosis of systemic sclerosis associated interstitial lung disease (SSc-ILD). Although there is agreement in performing HRCT as a screening test at time of SSc diagnosis, some physicians do not regularly perform baseline HRCTs. In addition, it is unclear according to which criteria HRCTs should be repeated during the follow-up of baseline ILD negative patients.

Objectives: To develop a risk score for the presence of SSc-ILD (the ILD-RISC), to guide physicians in ordering both baseline and follow-up HRCTs.

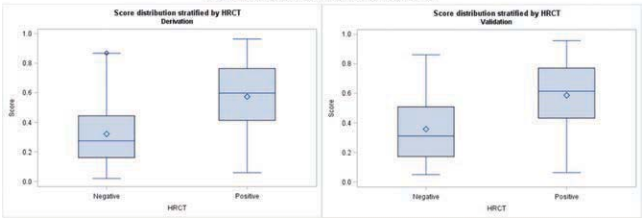
Methods: The steering board included six SSc-ILD experts from referral centers, two fellows and a patient research partner. Items for regression analysis were selected according to face validity, feasibility, scientific background, and personal experience using the nominal group technique (NGT). The prediction model for the presence of ILD was developed from baseline visits of SSc patients from the six centers using multivariable logistic regression with backward selection. Patients were randomly divided into a derivation and validation cohort consisting of 66% and 34% of patients respectively. Patients with missing data in the selected covariates and in the ILD status (outcome) were excluded. After identifying a cut-off favoring sensitivity >85% from the ROC curve analysis, the derived ILD-RISC score was applied first in the validation cohort and then longitudinally in a cohort of SSc patients with negative baseline HRCT.

Results: The steering board selected 13 variables deemed important in the identification of SSc-ILD: sex, age, disease duration from first non-Raynaud's phenomenon symptom, skin subset (diffuse/limited), presence of esophageal symptoms, digital ulcers (DU) ever, arthritis ever, smoking ever, increased inflammatory markers, NYHA functional class, SSc autoantibody status (SSc_Atb), FVC% and DLCO%. Among 780/3240 patients fulfilling the inclusion criteria, 533 (43% ILD) and 247 (48% ILD) respectively constituted the derivation and the validation cohort. In the derivation cohort, a model including FVC%, DLCO%, DU ever, age and SSc_Atb (Table 1A) showed an OR of 133.9 (95% CI 53.4-335.9) and an AUC of 79.1% (95% CI 75.3-83.0%) for the presence of ILD on HRCT (Figure 1). An ILD-RISC score ≥0.3 showed sensitivity of 85.6% and specificity of 53.6%, NPV of 83.2% and PPV of 58.2%, which were replicated in the validation cohort (Table 1B). Among 819 patients with negative baseline HRCT, 170 (20.8%) developed ILD during a 3.8±3.0 years follow up (1988 visits). Longitudinally, the ILD-RISC score showed comparable sensitivity and specificity (Table 1B).

Table 1.

A)ILD-RISC MODEL VARIABLES	OR	95% CI	p value
Digital ulcers, ever	2.058	1.347-3.145	<0.001
Age	1.026	1.010-1.042	0.001
SSc_ATB			
Anti-centromere	0.334	0.198-0.563	<0.001
Anti-topoisomerase I	2.379	1.326-4.267	0.004
Anti-RNA-polymerase III	1.407	0.636-3.113	0.399
Anti-Pm/Scl	2.556	0.916-7.135	0.073
None of the above	Comparator		
FVC%	0.990	0.979-1.002	0.091
DLCO%	0.971	0.960-0.982	<0.001
B)ILD-RISC SCORE PERFORMANCE	**Derivation cohort**	**Validation cohort**	**Longitudinal cohort**
All Patients/ILD patients	533/229	247/119	819/170
AUC %, 95% CI	79.1 (75.3 – 83.0)	76.4 (71.0 – 82.7)	72.6 (68.9 – 76.2)
Sensitivity %, 95% CI	85.6 (80.4 – 89.9)	85.7 (78.1 – 91.5)	80.4 (73.9 – 86.0)
Specificity %, 95% CI	53.6 (47.8 – 59.3)	49.2 (40.3 – 58.2)	50.5 (48.2 – 52.9)
Negative Predictive Value %, 95% CI	83.2 (77.2 – 88.1)	78.8 (68.2 – 87.1)	96.3 (94.9 – 97.4)
Positive Predictive Value %, 95% CI	58.2 (52.7 – 63.5)	61.1 (53.2 – 68.5)	13.9 (11.8 – 16.1)

Figure 1. Distribution of the ILD-RISC score between patients with and without ILD on HRCT, in the derivation and validation cohorts.



Conclusion: We developed and validated the ILD-RISC score to predict the presence of ILD at time of diagnosis and evaluated its performance during follow-up. The ILD-RISC may be useful in routine practice when resources for HRCTs might be limited. In particular, it may also help to decide when to order HRCTs at follow up, thus limiting unnecessary HRCTs and reducing the burden for patients and institutions.

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POS0389 MUSCULAR EXPRESSION OF CD163 AND MAJOR HISTOCOMPATIBILITY COMPLEX CLASS I AS DIAGNOSTIC MARKERS IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Various inflammatory markers have been suggested for detecting idiopathic inflammatory myopathies (IIMs); however, their diagnostic utility remains inconclusive.

Objectives: Muscle tissues from patients diagnosed with IIMs from January 2001 to March 2017 in a tertiary hospital were investigated. Muscular expression of CD3, CD4, CD8, CD20, CD68, CD163, MX1, MHC class I, MHC class II, and HLA-DR in muscle biopsy specimens from patients with IIMs and controls were evaluated using immunohistochemical staining. Classification and regression tree analyses were used to classify patients with IIMs who met the 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies (2017 EULAR/ACR criteria for IIMs) using various staining results as predictor variables.

Methods: Muscle tissues from patients diagnosed with IIMs from January 2001 to March 2017 in a tertiary hospital were investigated. Muscular expression of CD3, CD4, CD8, CD20, CD68, CD163, MX1, MHC class I, MHC class II, and HLA-DR in muscle biopsy specimens from patients with IIMs and controls were evaluated using immunohistochemical staining. Classification and regression tree analyses were used to classify patients with IIMs who met the 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies (2017 EULAR/ACR criteria for IIMs) using various staining results as predictor variables.

Results: Among the total 146 patients diagnosed with IIMs by expert neurologist or rheumatologist, 129 patients with IIMs met the 2017 EULAR/ACR criteria for IIMs. Histopathologic features consistent with IIMs using HE staining was observed in 104 of 129 (80.6%) patients who met the 2017 EULAR/ACR criteria for IIMs (dermatomyositis, n = 46/66, 69.7%; polymyositis n = 58/63, 92.1%; sensitivity 80.6%, specificity 100.0%). Muscular expression of CD163 (99.2% vs. 20.8%, p < 0.001) and MHC class I (87.6% vs. 23.1%, p < 0.001) were significantly higher in patients with IIMs who met the 2017 EULAR/ACR criteria for IIMs than in controls. Combined CD163 and MHC class I expression provided the most significant stratification for the control group (sensitivity 96.1%, specificity 94.5%). This combination was able to classify 16 of 17 (94.1%) patients who were diagnosed with IIMs by an expert physician but did not meet the 2017 EUALR/ACR criteria for IIMs.

Conclusion: Combined CD163 and MHC class I muscular expression may be useful in diagnosing IIMs.

Table 1. Sensitivity, specificity, and predictive values of various inflammatory marker expressions and their optimal combinations for the diagnosis of idiopathic inflammatory myopathies.

	Sensitivity	Specificity	PPV	NPV	Patients who were diagnosed by an expert physician but did not meet the 2017 EULAR/ACR classification criteria for IIMs are classified by each combination
Muscle biopsy features consistent with IIMs on H/E staining	80.6%	100.0%	100.0%	74.5%	7/17 (41.2%)
CD3 expression	91.5%	51.4%	77.6%	76.6%	7/17 (41.2%)
CD163 expression	99.2%	79.2%	89.5%	98.3%	16/17 (94.1%)
MHC class I on myofibers	87.6%	76.9%	88.3%	75.8%	12/17 (70.6%)
HLA-DR on myofibers	69.8%	81.5%	88.2%	57.6%	8/17 (47.1%)
MHC class II on myofibers	13.2%	72.3%	45.6%	29.6%	6/17 (35.3%)
Combination of CD163 pattern and MHC class I on myofibers	96.1%	94.5%	96.9%	93.2%	16/17 (94.1%)
Combination of histopathologic examination using HE staining, CD163 pattern, and MHC class I on myofibers	97.7%	94.5%	95.8%	96.5%	16/17 (94.1%)

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POS0390 GENES OF "DEFENSE RESPONSE TO VIRUS" IN PERIPHERAL BLOOD OF ANTI-MDA5 POSITIVE DERMATOMYOSITIS WERE UPREGULATED AS COMPARE WITH OTHER FORMS OF DERMATOMYOSITIS. ~SUPPRESSING RIG-I LIKE RECEPTOR SIGNALING OR TYPE 1/2 INTERFERON SIGNALING WERE THE KEYS FOR SURVIVAL.

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Background: Anti-melanoma differentiation-associated gene 5–positive dermatomyositis (MDA5 DM) is a rare but distinct subtype of idiopathic inflammatory myopathy (IIM) that is characterized by high mortality due to rapid progressive interstitial lung disease (ILD). MDA5 is a cytosolic protein and a family of retinoic-acid inducible gene-I (RIG-I) like receptor, which functions as a virus RNA sensor and induces the production of type I interferons (IFN-I) and proinflammatory cytokines. This leads to the death of infected cells and the activation of the antigen-specific antiviral immune response. Although the pathogenesis of MDA5 DM is largely unknown, a hypothesis that pathogenic involvement of anti-MDA5 antibodies has been proposed. Recently, similarities have been noted between multifaceted features of COVID-19 and MDA5 DM, which suggests shared underlying autoinflammatory mechanisms.
Objectives: To detect the critical actors in the pathogenesis of MDA5 DM by gene expression analysis of peripheral blood.
Methods: Total of 31 DM cases were investigated, including anti-aminoacyl-tRNA synthetase positive (ARS) DM (n=12), MDA5 DM (n=7, survivor=3) and others (n=12). Peripheral blood was drawn at baseline and 2 to 3 months after treatments. Total RNAs were then extracted with using PAXgene miRNA kit. After quantifying the expressions of transcripts by multiplex sequencing. And then, hierarchical clustering analysis, enrichment analysis using gene ontology (GO) terms, single sample gene set enrichment analysis (ssGSEA) and weighted gene co-expression network analysis (WGCNA) were performed.
Results: The hierarchical clustering with expression profiles of peripheral blood at baseline showed major 3 clusters. Interestingly, ARS DM cases were segregated into right side of the 3rd cluster while MDA5 DM cases fell into 1st and 2nd clusters. ARS and MDA5 DM were clearly discriminated if differentially expressed genes (DEGs) between these subtypes of DM were analyzed. By GO enrichment analysis, the terms, such as related to "defense response to virus" including "type1 interferon signaling pathway" were found in the DEGs. In the MDA5 DM cases, ssGSEA revealed that genes of "Fcγ receptor mediated phagocytosis pathway" or "complement and coagulation cascade" were significantly enriched and WGCNA showed that pathways of "T-cell antigen receptor signaling" or "lung fibrosis" were significantly upregulated. Next, we also investigated the DEGs of peripheral blood at 2-3 months after treatment between survival and fatal cases in MDA5 DM. We found that suppressing RIG-I like receptor and type 1 and type 2 interferon (IFN) signaling were the keys for survival.
Conclusion: MDA5 is a key sensor of several RNA viruses including coronavirus families and then activate antiviral gene transcription such as type 1 IFN genes, leading to establish an antiviral host response. As the pulmonary damage of COVID-19 is known to be difficult to distinguish from the ILD associated with anti-MDA5 DM, the life-threating ILD of MDA5 DM may be caused by the over-activation of RIG-I like receptor signaling via MDA5. The hypothesis is supported by our findings that the defining features of MDA5 DM are activation of "type 1 IFN pathways" and antigen-specific antiviral immune responses including "Fcγ receptor mediated phagocytosis pathway" or "T-cell antigen receptor signaling". As the levels of anti-MDA5 antibodies reported to be important prognostic parameter, it may be involved in pathogenesis of MDA5 DM. As we found that suppression of type 1 and type 2 IFN signaling were the keys for survival, it seems to be reasonable to use inhibitors of Janus Kinases (JAK) for treatment of MDA5 DM.
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POS0391 TRENDS IN THE DIAGNOSIS OF MYOSITIS AND ASSOCIATION WITH THE CORONAVIRUS-19 PANDEMIC AND VACCINES: DATA FROM THE VENETO RARE DISEASE REGISTRY, 2014-2021

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Background: There are uncertainties regarding the occurrence of idiopathic inflammatory myopathies (IIM) after infection by Severe Acute Respiratory Syndrome (SARS)-CoronaVirus2(CoV2) or in recipients of Coronavirus disease-19 (Covid-19) vaccines.
Objectives: Herein, the main objective was to assess temporal trends of newly diagnosed IIM in the past eight years, including the effects of the Covid-19 pandemic.
Methods: We extracted data of IIM patients from the Veneto Rare Disease Registry from 01/01/2014 and 31/12/2021. This regional registry has to be considered comprehensive of all patients with IIM in a specific geographical area. Hence, we extracted the following information: age; sex; date of diagnosis; type of IIM including dermatomyositis (DM), polymyositis (PM), anti-synthetase syndrome (ASS), inclusion body myositis (IBM); place of residence. We restricted the analysis to IIM patients certified by expert rheumatologists belonging to the Regional Centre for Study and Treatment of Connective Tissue and other Rare Diseases at the Division of Rheumatology, University of Padua, Veneto, Italy. Finally, we compared new IIM cases before and after 04/01/2021 as the starting date for the vaccination campaign in Veneto. We reported descriptive statistics (median and interquartile range) and results of non-parametric tests to compare cases of IIM across the study period.
Results: Database extraction retrieved 192 people with IIM diagnosed during the study period (DM 85, PM 82, ASS 23, IBM 2; females 67.2%; median [25th-75th percentile] age at diagnosis 58.5 [49.6-68.5] years). There was a median of 2 [1-4] newly-diagnosed IIM monthly, with a non-significant increase in the post-pandemic two-year period 2020-2021 (Figure 1**A**). Numerically, 2020 had the most IIM diagnosis (N=30), mainly clustered in the second (N=12) and third (N=11) trimesters. Trends of new IIM diagnoses over one year course were similar during the study period, with visually identified higher IIM occurrence in February, April and September (Figure 1**B**). There was no difference in incident IIM cases in the 12 months before (N=31) and after (N=29) the initiation of the vaccination campaign (7 [5-9.8] vs 8 [3-12] new cases for each trimester; Mann-Whitney U test p=0.884). Finally, there was a significant trend for median age at diagnosis increasing by 6.46 years from 55.4 to 61.8 years between 2014 and 2021 (p=0.015, R^2=0.344; repeated measures ANOVA with post test for linear trend).

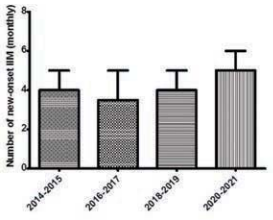

Figure 1A. New diagnoses of IIM certified at the Division of Rheumatology, University of Padua, for each biannual period between 2014 and 2021. Boxes represent median and error bars interquartile range. Kruskal-Wallis statistic (4.699, p=0.195) with Dunn's multiple comparison test (p>0.05 for all comparisons). IIM, idiopatic inflammatory myopathy.

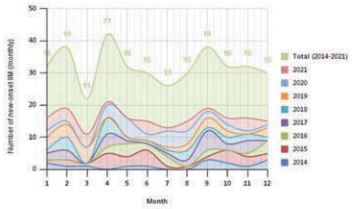

Figure 1B. Seasonal trends of idiopatic inflammatory myopathies. Data are presented as the number of new cases of myositis diagnosed each month (horizontal axis: from 1 [January] to 12 [December]) and total counts between 2014 and 2021.

Conclusion: We found no significant change in patterns of IIM diagnoses between 2014 and 2021 besides a slight numerical increase in the second and third trimesters of 2020. In addition, we noted no signals of increased IIM diagnoses after introducing Covid-19 vaccines. This data encourage further analyses of larger, multicentre datasets from other geographical areas to clarify whether there has been variation in specific myositis subtypes across new-onset IIM after the pandemic.
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POS0392 ROLE OF SEMIQUANTITATIVE THIGH MAGNETIC RESONANCE IMAGING (TMRI) IN DETERMINING SKELETAL MUSCLE OUTCOMES AT BASELINE AND ON FOLLOW UP IN IDIOPATHIC INFLAMMATORY MYOPATHIES (IIMS)

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Background: Idiopathic Inflammatory Myopathies (IIMs) are characterized by muscle inflammation and associated muscle weakness. Semiquantitative scoring of thigh Magnetic Resonance Imaging (tMRI) has shown contradictory results in associating muscle inflammation, damage, and clinically assessed muscle weakness. Moreover, there are no studies assessing the role of tMRI detected muscle damage in determining long-term recovery of muscle strength and endurance.

Objectives: To correlate tMRI scores for muscle edema, fascial edema, muscle atrophy, and fatty infiltration with consecutively collected manual muscle testing 8 (MMT-8) scores and muscle enzymes. To determine the role of baseline tMRI changes in achieving maximum muscle power during follow-up.

Methods: This is a retrospective analysis of a single-center myositis cohort. IIM patients (n=55) who underwent baseline tMRI (STIR and T1 sequences) at the time of diagnosis were included. Baseline demographic, clinical, and serological parameters were noted. MRI T1 weighted sequence and STIR sequence axial and coronal images were assessed for intramuscular and fascial edema, atrophy and fatty replacement using a semiquantitative score and the percentage of muscle involvement for each parameter was calculated. MMT-8 values and muscle enzyme levels which remained unchanged at least for 6 months during follow-up were noted for 42 patients. MMT-8 ≥74 was taken as near normal muscle power based on the fact that 75% of IIM patients in remission for a long duration achieved MMT-8 of≥74 in our cohort. Spearman correlation was done between clinical parameters, muscle enzymes, and tMRI scores. Baseline parameters of patients who achieved and did not achieve MMT8≥74 were compared. Multiple linear regression was performed to assess the tMRI variables predicting a higher MMT-8 during follow-up

Results: The median age was 36 (27.25-44.75) years, median duration of disease at presentation was 4 months (2-10), median duration of follow up was 24 months (6.75-38.25). Dermatomyositis, Polymyositis and Antisynthetase syndrome comprised of 58.2%, 7.3% and 30.9% cases respectively. Baseline muscle enzymes CPK(r=0.531), AST(r=0.535) and ALT(r=0.442) showed significant positive correlation($p<0.01$) with muscle edema. Baseline MMT-8 showed significant negative correlation with muscle edema(r=-0.657) and fascial edema(r=-0.522) ($p<0.01$). Follow up MMT-8 showed significant negative correlation with muscle edema(r=-0.359), muscle atrophy (r=-0.319) and fatty infiltration(r=-0.308) ($p<0.05$) (Figure 1). Baseline MMT-8 and MRI fatty infiltration were significantly different between patients who achieved and did not achieve MMT-8 of ≥74 on follow-up (Table 1). Multiple regression analysis revealed adjusted R^2 value of 0.386. Baseline MMT-8(β=0.372) and muscle atrophy(β=-0.459) significantly predicted MMT-8 on follow-up

Table 1. Comparison between those who achieved near-normal muscle power versus others

	Follow up MMT-8<74 (n=8)	Follow up MMT-8 ≥74 (n=34)	P-value
Age (years) (median, IQR)	36.5(27-47.5)	36(28.75-44.25)	1.000
Duration of disease (months) (median, IQR)	6(4-10.5)	3.5(2.75-9.75)	0.459
Baseline muscle enzymes and MMT-8 (median, IQR)			
CPK (IU/L)	1758(116-6160)	680(57.5-3595)	0.410
LDH (IU/L)	496(240-823)	616.50(289.25-753)	0.672
AST (IU/L)	112(76-201.5)	69.5(40.5-226.25)	0.352
ALT (IU/L)	74.50(65.5-139.75)	69(36-142.25)	0.560
MMT-8 baseline (0-80)	49.5(47.25-56)	63(53.75-73.25)	**0.007**
MRI thigh scores (median, IQR)			
Muscle edema%	22.41(5.65-63.33)	10.37(0.00-28.70)	0.070
Fascial edema %	43.33(18.61-78.06)	33.89(11.49-50.56)	0.478
Muscle atrophy %	2.22(0.28-20.83)	0.00(0.00-2.50)	0.081
Fatty infiltration %	6.67(2.78-18.61)	0.56(0.00-3.61)	**0.010**

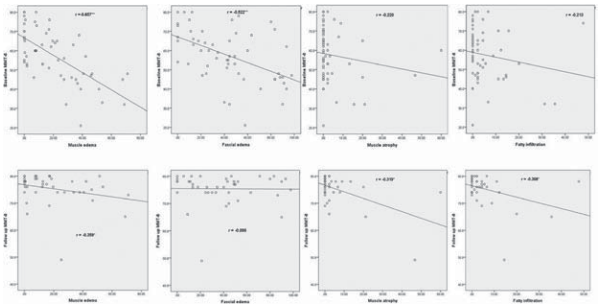

Figure 1. Correlation between baseline and Follow up MMT-8 with tMRI scores.

Conclusion: Low baseline MMT-8 and presence of muscle atrophy at baseline are predictors of poor outcome. Hence performing a baseline MRI will help in the prognosis.

Disclosure of Interests: None declared

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POSTERS only

Genomics, genetic basis of disease and functional genomics

POS0393 ASSOCIATION BETWEEN GENETICALLY PREDICTED EXPRESSION OF TPMT AND AZATHIOPRINE ADVERSE EVENTS IN PATIENTS WITH INFLAMMATORY CONDITIONS

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Background: Azathioprine is a widely used immunosuppressant for the treatment of inflammatory conditions such as systemic lupus erythematosus (SLE), systemic vasculitis, dermatomyositis, and inflammatory bowel disease. However, its use is often limited by myelotoxicity. Variants in the gene encoding thiopurine-S-methyltransferase (TPMT), an enzyme in the metabolic pathway of azathioprine, increase the risk for myelotoxicity[1]. We know little about the relationship between the genetically predicted expression of *TPMT* and side effects of azathioprine.
Objectives: To examine whether genetically predicted expression of *TPMT* in liver tissue is associated with azathioprine adverse effects.
Methods: We assembled a retrospective cohort of new users taking azathioprine for inflammatory conditions at a tertiary care center. We performed genotyping with Illumina Infinium Expanded Multi-Ethnic Genotyping Array plus custom content data, and we then used Michigan Imputation servers for genetic imputation and PrediXcan models trained with GTEx/Genotype-Tissue Expression Project version 8 data to impute *TPMT* expression in liver tissue. We prespecified nine groups of phecodes (comprised of ICD9 and ICD10 codes) corresponding to known adverse effects of azathioprine. We then tested the association between the predicted expression of *TPMT* and these adverse events; for outcomes significant in the Wilcoxon ranksum tests ($p<0.05$), each case was reviewed in clinical records for confirmation. Finally, we grouped the predicted expression of *TPMT* in liver tissue into tertiles and conducted logistic regressions to assess the associations between predicted expression and side effects. We conducted a sensitivity analysis restricted to patients with EHR-reported White race.
Results: The cohort included 1034 patients (Table 1). Phecodes for 3 side effects—leukopenia (n=29), skin cancer (n=13), and rash (n=52)—were identified as associated with predicted *TPMT* expression in liver tissue. Of these, cases of side effects attributed to azathioprine were validated by chart review: leukopenia (96.6%; n=28), skin cancer (92.3%; n=12), and rash (9.6%; n=5) and used for analysis. When assessed by tertile of predicted *TPMT* expression, patients in the highest tertile had lower odds of having leukopenia (OR=0.35, 95%CI: 0.12-0.98, p=0.045) and a trend towards higher odds for skin cancer, but the number of cases was small (OR=3.56, 95%CI: 0.73-17.27, p=0.115). Confirmed cases of rash attributed to azathioprine were too few for meaningful analysis. We found similar results when restricted to patients with reported White race.

Table 1. Characteristics of patients by *TPMT* expression

	Lowest Tertile	Middle Tertile	Highest Tertile
	N=345	N=345	N=344
Female sex, n (%)	228 (66.1)	244 (70.7)	238 (69.2)
EHR-reported White race, n (%)	306 (88.7)	293 (84.9)	290 (84.3)
Age, median [IQR]	42 [29-58]	43 [30-55]	46 [30-56]
Indication, n (%)			
Systemic lupus erythematosus	38 (11.0)	42 (12.2)	38 (11.0)
Inflammatory bowel disease	191 (55.3)	185 (53.6)	190 (55.2)
Other connective tissue disorder/autoimmune	92 (26.7)	96 (27.8)	100 (29.1)
Other	24 (7.0)	22 (6.4)	16 (4.7)
Verified leukopenia attributed to azathioprine, n (%)	14 (4.1)	9 (2.6)	5 (1.5)
Verified skin cancer attributed to azathioprine, n (%)	2 (0.6)	3 (0.9)	7 (2.0)
Verified rash attributed to azathioprine, n (%)	2 (0.6)	3 (0.9)	0 (0)

Conclusion: This analysis suggests that PrediXcan may be useful for examining the association between gene expression and side effects of medications. Moreover, this approach successfully identified leukopenia as a side effect associated with predicted *TPMT* expression.
Acknowledgements: None to declare.
Disclosure of Interests: None declared.
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POS0394 VALIDATION OF THE SLE SUSCEPTIBLE GENE LOCI IN THE MULTI-ETHNIC MALAYSIAN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COHORT AND THEIR ASSOCIATIONS WITH CLINICAL MANIFESTATION

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Background: Systemic Lupus erythematous (SLE) is an autoimmune disease with a wide spectrum of clinical manifestations. Asian patients including Malaysia tend to have more severe disease with renal involvement. The differences could be due to the interactions between genetic and environmental factors. Thus, identifying the genetic associations from diverse populations provides a better understanding on the genetic architecture of this heterogeneous disease.
Objectives: The primary objective of this study was to validate the previously described SLE susceptibility gene loci among other population in the multi-ethnic Malaysian SLE patients. The secondary objective was to determine the association between the gene loci with organ-specific involvement across different Malaysian ethnicities.
Methods: This was a case-control study involving the recruitment of SLE patients who attended the outpatient clinic in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from July 2019 until March 2021. Their medical records were reviewed to record the socio-demographic characteristics and SLE clinical manifestations. The SLE susceptible gene loci from the NHGRI-EBI Catalog of human genome-wide association studies were reviewed. The gene loci with *p* values less than $5x10^{-8}$ tested in a total sample size of at least 1000 individuals were included in the genotyping study in our SLE patients. Healthy controls with frequency matching by gender and ethnicity-matched were also recruited in this study. Their peripheral blood samples were genotyped using the Agena MassARRAY system (Agena Bioscience). The genotype frequencies of susceptibility loci in all patients and controls were tested for Hardy–Weinberg equilibrium. Associations between phenotype and genotype were performed by logistic regression analysis.
Results: A total of 202 SLE patients and 206 healthy controls were recruited. The SLE cohort consisted of predominant Malay ethnicity (n=126,62.6%) followed by Malaysian Chinese (n=69, 34.2%) and Indian (n=7, 3.5%). After quality control and Hardy–Weinberg equilibrium test, a total of 27 candidate SNPs were genotyped in our study population. Meta-analysis revealed 5 gene loci at SNP rs4544377 (*RNU6-546P*), rs4917014 (*IKZF1*), rs1878186 (*SLC12A1*), rs4728142 (*IRF5*) and rs5029937 (*TNFAIP3*) were associated with SLE in Malaysian population (all *p* value <0.05). In Malay group, rs4544377 (*RNU6-546P*) and rs4728142 (*IRF5*) were found to be associated with SLE with adjusted OR 0.42 (95% CI: 0.24-0.74), *p*=0.002 and OR 3.08 (95% CI: 1.71-5.54), p=0.000169, respectively. In Malaysian Chinese group, rs4917014 (*IKZF1*) was found to be associated with SLE with OR 0.45 (95% CI: 0.23-0.86), *p*=0.016. Among Malay patients, rs1878186 (*SLC12A1*) was found to be associated with skin rash with OR 2.01 (95% CI: 1.20-3.35), *p*=0.008 while rs4544377 (*RNU6-546P*) and rs4917014 (*IKZF1*) were associated with lupus nephritis, with OR 0.48 (95% CI: 0.24-0.96), *p*=0.039 and OR 3.29 (95% CI: 1.18-9.20), *p*=0.023. In Malaysian Chinese patients, rs4544377 (*RNU6-546P*) was associated with muco-cutaneous manifestation with OR 2.82 (95% CI: 1.15-6.92), *p*=0.023 while rs4728142 (*IRF5*) was associated with haematological manifestation with OR 5.61 (95% CI: 1.69-18.60), *p*=0.005.
Conclusion: Our exploratory study demonstrates the associations of the established SLE genes in Malaysian SLE populations. There are variations in the SLE susceptible gene loci with clinical manifestations of SLE between Malay and Malaysian Chinese populations.
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Disclosure of Interests: None declared.
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POS0395

EXPLORING THE POTENTIAL OF GENOMIC RISK PREDICTION FOR CORONARY ARTERY DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) have a higher prevalence of coronary artery disease (CAD) than the general population which contributes to early mortality. However, CAD screeing tools developed in the general population are less effective for estimating CAD risk in RA patients. This is mainly due to the differing contribution from traditional risk factors and the contribution from disease-specific factors. Understanding of the genetic basis of CAD has improved over recent years and shows promise for improving risk prediction in the form of genetic risk scores (GRs), in particular with the development of the metaGRS approach, which combines multiple polygenic risk scores.
Objectives: This study hypothesise that the metaGRS approach can help us improve CAD risk prediction in patients with RA.
Methods: Patients were recruited from the Norfolk Arthritis Register (NOAR), a longitudinal observational study focused on the cause and outcome of inflammatory polyarthritis. Analysis was restricted to patients who satisfied the 2010 ACR criteria cumulatively over five years and had detailed clinical history at baseline and follow-up for ten years. We developed a prediction model based on traditional risk factors[1], and explored the inclusion of a metaGRS. We used a meta-analytic approach to calculate a new metaGRS for CAD, using the effect-sizes from three large-scale, genome-wide, and targeted GRs derived from 1,745,179 [2], 6,630,150 [3], and 40,079 SNPs [4]. We tested the metaGRS in combination with available data on traditional risk factors in a subset of patients with available genetic data. Cox proportional hazards models were used to derive risk equations for evaluation of 10-year risk of CAD. We applied multiple imputations with chained equations to replace missing values. Calibration and discrimination were determined in a separate cohort of 423 individuals.
Results: A total of 2123 patients were included in the analysis with 136 incident cases of self-reported CAD (defined as a composite outcome of myocardial infarction, angina, heart attack, arrhythmia, angioplasty, and coronary artery bypass grafting). The model using only traditional risk factors achieved an AUC of 0.81 (95% CI 0.80, 0.82), with a calibration slope of 1.10, and explained approximately 71% (95% CI 69, 72%) of the variance of the outcome. The hazard ratio for age was found to be 1.00 (95% CI 0.99, 1.01) indicating risk remains the same across all age groups. Inclusion of a CAD metaGRS improves the AUC to 0.82 (95% CI 0.80, 0.83), explains more of the variance at 81% (95% CI 79, 82%) but worsens calibration slope to 0.93. A likelihood ratio test indicates that the integrated model is a better fit (p = 0.04).
Conclusion: An integrated risk score, that combines traditional risk factors with a metaGRS, improves CAD prediction in patients with RA. Further research is required to better understand the role of heritable components contributing to CAD risk in RA patients. By refining the underlying GRS, we hope to further improve risk prediction, through this integrated approach.

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Disclosure of Interests: None declared.
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POS0396

IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Characterizing differentially expressed genes (DEGs) of systemic lupus erythematosus (SLE) is necessary to understand immunogenic interactions, and how several key immune genes were closely associated with the susceptibility of SLE.
Objectives: This study aimed to identify DEGs of SLE using gene expression-based computational methodologies to analyze disease-immune interactions, which affect the development and progression of SLE.
Methods: Twenty-six patients with SLE and 46 healthy controls were selected from the Gene Expression Omnibus database. The significantly enriched immune and virus related gene lists were computed and visualized by using the DEGs from the Gene Set Enrichment Analysis. Quantification of 38 immune cells were performed in determining the impact of immune cells on the virus mediated immunity in SLE by using ImmQaunt algorithm.
Results: Thirty nine upregulated and 57 downregulated were identified in SLE patient compared to the healthy controls. Upregulated genes were significantly implicated in Gene Ontology gene sets as cytokine mediated signaling, secretion, and exocytosis in immune response pathways. In addition, these genes were enriched in hepatitis C, influenza A, measles, Epstein–Barr virus, and

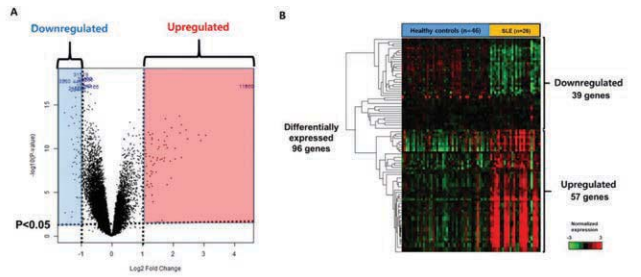

Figure 1. Gene expression analysis of SLE patients vs. healthy control samples. (A) The volcano plot represents differentially expressed gene expression with the significance criteria (adjusted p < 0.05, |Log2 (fold change)| ≥ 1). The x-axis indicates the log 2-fold change of gene expression (SLE patients/healthy controls), and the y–axis indicates the –log 10 (p-value). (B) Heatmap of the expression of selected differentially expressed genes with the computed p-value between the SLE and healthy control samples.

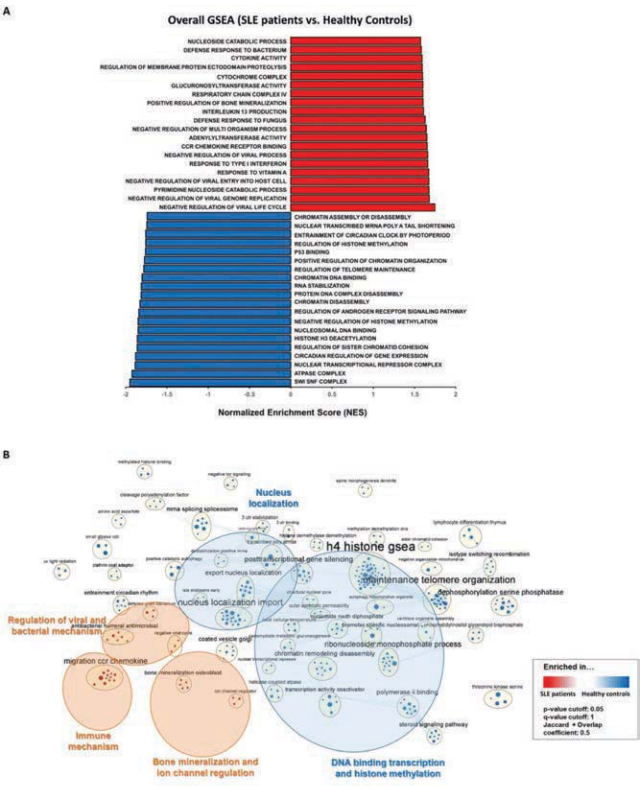

Figure 2. Gene set enrichment analysis (GSEA) of SLE patients vs. healthy control samples. (A) A forest plot was generated showing the overall GSEA pathways that were positively or negatively enriched according to the normalized enrichment score. (B) Network visualization based on the gene enrichment analysis. Blue and red nodes represent the downregulated and upregulated gene sets in SLE patients, respectively. Genes in significant networks were annotated and grouped with simplified Gene Ontology terms.

herpes simplex virus 1 infection in Kyoto Encyclopedia of Genes and Genomes pathways. Especially, FCGR1A, IRF7, OAS2, CAMP, MX1, OAS3, OAS1, DEFA3, ISG15, and RSAD2 were involved in virus mediated SLE mechanism, and the expression for OAS1, OAS2, and IRF7 was closely associated with the quantities of colony forming unit-monocyte and colony forming unit-granulocyte.
Conclusion: Identifying virus mediated SLE genes and quantifies of immune cells were used to understand the pathological process and perform early diagnosis of SLE, and will lead to clinical tools for treating SLEs in patients.
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Adaptive immunity (T cells and B cells) in rheumatic diseases

POS0397 SSD6453, A NOVEL AND HIGHLY SELECTIVE BTK/JAK3 DUAL INHIBITOR IS EFFICACIOUS IN MULTIPLE PRE-CLINICAL MODELS OF INFLAMMATION

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Background: The mechanism of inflammatory diseases is complicated and dysfunction of multiple immune cells is thought to be directly related to the pathogenesis. Targeting either JAK-STAT or BCR signaling has been proved solid clinical efficacy in multiple inflammatory diseases, such as rheumatoid arthritis (RA) and multiple sclerosis (MS). And the combination of BTK and JAK inhibitors demonstrated synergistic effects for the treatment of inflammation models in pre-clinic. JAK3 expression is largely restricted to leukocytes and involves functions in JAK1/JAK3 heterodimer in signal transduction, it might be a more effective and safer target. Meanwhile, both BTK and JAK3 possess a cysteine residue in their active site and this feature makes it possible to design a dual inhibitor. SSD6453 is a highly selective and irreversible JAK3/BTK dual inhibitor which may have synergistic effects for the treatment of RA and other inflammatory diseases such as MS.
Objectives: To develop a potent, oral, highly selective JAK3/BTK inhibitor for treatment of multiple inflammatory diseases.
Methods: ADP-GLO based biochemical assays were performed to determine the enzymatic inhibitory effect and selectivity for JAK family. The target engagement was evaluated by IgM induced pBTK and IL-2 induced pSTAT5 in human PBMCs. In vivo efficacy was evaluated by rat collagen-induced arthritic (CIA) model and mice experimental autoimmune encephalomyelitis (EAE) models induced by MOG1-125 or MOG35-55, respectively. BTK occupancy in spleens post last dose 24h and IL-2 induced pSTAT5 in whole blood post last dose 0.5h were used to evaluate targets inhibitions. Osteoclast was stained by IHC in pathological section of rat paws.
Results: In biochemical assays, SSD6453 inhibited BTK and JAK3 with the IC_{50} values of 3.4 nM and 1.1 nM, respectively. Notably, SSD6453 displayed high selectivity against JAK1 (510 fold), JAK2 (75 fold) and TYK2 (525 fold). In cellular assays, SSD6453 inhibited anti-IgM induced pBTK and IL-2 induced pSTAT5 in human PBMCs with the IC_{50} values of 18.8 nM and 168.8 nM, respectively. SSD6453 demonstrated favorable PK properties in broad pre-clinical species. Single oral administration of SSD6453 in rat or mouse, resulted in dose-dependent inhibition of BTK and JAKs concurrently. In the rat CIA model in which disease development was accompanied by a robust T-cell and B-cell inflammation response to collagen, SSD6453 dose-dependently inhibited paw edema. And SSD6453 at 10mpk achieved complete (95%) BTK occupancy and JAK3 inhibition and superior efficacy in comparison of tofacitinib (JAK@10 mpk) or evobrutinib (BTK @30mpk) alone, suggesting that concurrent inhibition of JAK3 and BTK lead to synergistic anti-inflammation effects. In addition, ED-1+ osteoclast count decrease was observed in paws, suggesting the prevention of SSD6453 in joint destruction. In two EAE models either induced by MOG1-125 or MOG35-55, which represented T or B dominant inflammation model, respectively, SSD6453 robustly ameliorated disease in both two models. In comparison, BTK inhibitor is efficacious only in the MOG1-125 induced model.
Conclusion: SSD6453 is a novel and high selective BTK/JAK3 dual inhibitor, and demonstrated synergistic efficacy in multiple pre-clinic inflammation models. SSD6453 showed good pharmacokinetic characteristics and well-tolerant in multiple pre-clinical species, and is moving to IND in 2022.
Disclosure of Interests: Feng Zhou Shareholder of: I own the shares of Simcere, Grant/research support from: The work is financially support by Simcere, Employee of: Simcere, Lei Jiang Shareholder of: I own the shares of Simcere, Grant/research support from: The work is financially supported by Simcere, Employee of: I am employee of Simcere, Yuxi Yan Grant/research support from: The work is financially supported by Simcere, Employee of: I am employee of Simcere, Wenqing Yang Shareholder of: I own the shares of Simcere, Grant/research support from: the work is financially supported by Simcere, Employee of: I am employee of Simcere, Feng Tang Shareholder of: I own the shares of Simcere, Grant/research support from: The work is financially supported by Simcere, Employee of: I am employee of simcere, Ping Chen Shareholder of: I own the shares of Simcere, Grant/research support from: The work is financially supported by Simcere, Employee of: I am employee of Simcere, Renhong Tang Shareholder of: I own the shares of Simcere, Grant/research support from: The work is financially supported by Simcere, Employee of: I am employee of Simcere.
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POS0398 IDENTIFICATION OF THE HLA-B*51:01 IMMUNOPEPTIDOME IN BEHÇET'S DISEASE

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Background: Immunopeptidomes are peptides, bound to human leukocyte antigens (HLA), that play a key role in immune responses. HLA-B*51:01 is an HLA allele associated with Behçet's disease (BD)[1]. However, the characteristics and the role of HLA-B*51:01 immunopeptidome are not revealed in Behçet's disease.
Objectives: To investigate the difference of HLA-B*51:01 immunopeptidome between Behçet's disease and healthy controls (HCs) and to select candidate peptides which have a pathogenic role in Behçet's disease.
Methods: HLA-bound peptide profiles were established through analysis of plasma samples from HLA-B*51:01–positive BD patients and HCs. HLA-class I molecules were immunoprecipitated, and liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed. Then, HLA-B*51:01–binding peptides were assessed in terms of binding affinity using NetMHCpan. Finally, the

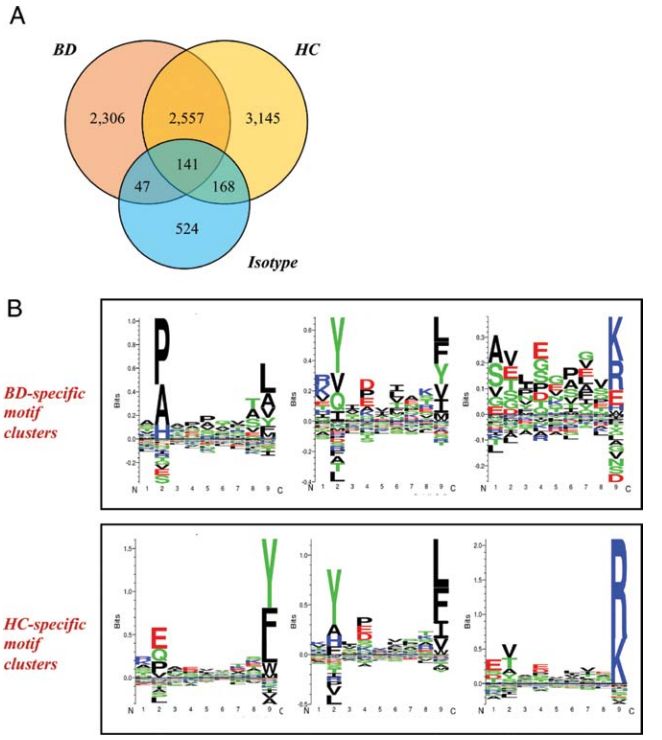

Figure 1. Venn diagram of the identified 8–13-mer peptides and graphs showing the motif clusters. (A) Venn diagram showing the numbers of peptides detected by immunoprecipitation with BD patients or HCs. The number of peptides isolated with isotype antibodies were also depicted. (B) Motif clusters of human leukocyte antigen (HLA)-B*51:01-positive BD patients and HCs.

immunological characteristics of selected peptides were analyzed in BD patients and HCs, using ELISpot, flow cytometry, and dextramer staining.
Results: 2,306 peptides were present only in BD patients, while 3,145 peptides were detected only in HCs. Immunopeptidome of BD patients preferentially showed hydrophobic amino acids at amino acid position 2 (Figure 1). Ten peptides were selected which were confirmed to be preferentially expressed in BD patients compared with HCs. When bound to HLA-B*51:01 in monocyte-derived dendritic cells (Mo-DCs) or peripheral blood mononuclear cells, these peptides activated T cells and induced surface expression of CD69 and CD107, as well as the secretion of inflammatory cytokines such as interferon (IFN)-γ and tumor necrosis factor (TNF)-α.
Conclusion: HLA-B*51:01 immunopeptidome can play a critical role in the development of BD by activating T cells and inducing the secretion of inflammatory cytokines.
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POS0399 CHARACTERIZATION OF HSP60, A STROMAL-DERIVED AUTOANTIGEN, RECOGNIZED BY RA SYNOVIAL RECOMBINANT MONOCLONAL ANTIBODIES

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Background: Up to 50% of rheumatoid arthritis (RA) patients display synovial ectopic lymphoid structures (ELS) supporting B-cell autoreactivity toward locally generated citrullinated and other translationally modified antigens. Recently, screening a large number of recombinant monoclonal antibodies (rmAbs, n=71) which we derived from locally differentiated B-cells from RA ELS+ synovium [1], we identified a subset of antibodies which specifically recognise fibroblast-like-synoviocytes (FLS) (10 out of 71), suggesting FLS as a cellular source of autoantigens fuelling the local autoimmune response. We reported that calreticulin is one of the antigenic targets of these anti-FLS rmAbs, while the nature of other FLS-derived autoantigens is still unclear [2].
Objectives: Here we aimed to define other stromal-derived autoantigens from RA-FLS targeted by RA-rmAbs.
Methods: Western blotting/mass-spectrometry were used to identify potential autoantigens from RA-FLS protein extracts. Putative candidates were validated using colocalization immunofluorescence confocal microscopy/ELISA/immunoprecipitation assay. Finally, both serum and synovial fluid (SF) from RA patients (OA patients used as control) were tested for immunoreactivity towards the putative antigen.
Results: Following immunoprecipitation and mass-spectrometry analysis, among the anti-FLS antibodies we identified a subset of RA-rmAbs which display strong reactivity towards heat shock protein 60 (HSP60). Three RA-rmAbs confirmed a clear immunoreactivity towards HSP60 in ELISA assay in a dose-dependent manner. Confocal microscopy did not show co-localization between anti-HSP60 RA-rmAbs and HSP60, suggesting that HSP60 act as autoantigen when released from the RA-FLS in stress condition. Finally, anti-HSP60 Abs were preferentially detected in RA-SF versus OA-SF, with an accumulation of HSP60 in RA-SF versus RA sera.
Conclusion: Here, we identified synovial B cell-derived RA-rmAbs locally differentiated within the ELS+ RA synovium reacting toward HSP60, suggesting that FLS-derived HSP60 may contribute to fuel the local autoimmune response. Elucidating the mechanisms involved in RA-FLS activation *in vitro/in vivo* will be important to clarify the anti-FLS rmAbs functional role in modulating inflammation.
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POS0400 MODULATION OF HUMAN EARLY B CELL DEVELOPMENT THROUGH TARGETED DEGRADATION OF IKAROS AND AIOLOS WITH IBERDOMIDE

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Background: B differentiation in the bone marrow (BM) is impaired in patients carrying mutation in the IKFZ1 gene, coding for Ikaros a zinc-finger transcription factor. High Ikaros expression is on the contrary associated with systemic lupus erythematosus[1] and multiple myeloma[2]. Targeted treatment with iberdomide, a cereblon modulator which enhances degradation of Ikaros and Aiolos, is under clinical investigation in multiple myeloma patients and systemic lupus erythematosus. However, consequences of the treatment on human early B cell development remain elusive. Immature B cells develop in the BM from hematopoietic stem cells. An intricate network of transcription factors regulates the maturation process. Ikaros and Aiolos regulate gene expression during B cell development. As reported in mice, Ikaros is essential for the commitment to the lymphoid lineage and later, together with Aiolos, ensures the transition from pre-BII large to pre-BII small cells.
Objectives: Investigate the effect of iberdomide (CC-220) on human early B cell development simulated in vitro.
Methods: We tested the impact of iberdomide on short term culture of BM-derived lymphocytes and in a unique in vitro modeling of early B cell development starting from cord blood (CB)- CD34+ progenitors [3, 4]. We used multi-dimensional spectra flow cytometry (17-color pan-el) to dissect early B cell subpopulations.
Results: Iberdomide treatment led to enhanced degradation of Ikaros and Aiolos in both BM- and CB-derived cultures. Addition of iberdomide early (day 7) to the CB-derived culture impaired the specification to the lymphoid lineage and later also the commitment to the B cell lineage. These observations were confirmed by reduced E2A and PAX5 gene expression, respectively. Treatment with iberdomide on B cell precursors (pro- and pre-B cells, day 28 of culture) on one side it enhanced the proliferation of early progenitors resulting in increased amount of CD10+CD38+ lymphoid-committed cells. On the other side, it resulted in a accumulation of pre-B cells and inefficient development of immature B cells.
Conclusion: Iberdomide impairs the commitment to the lymphoid lineage by enhancing Ikaros' degrada-tion. When targeting already committed B cells, iberdomide treatment undermines the transition of pre-BII large to pre-BII small cells due to increased Aiolos' degradation, conse-quently impairing the development of immature B cells. Our data can instruct immunologi-cal monitoring of patients treated with iberdomide, and provide insights in the mechanisms of therapeutic efficacy.
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POS0401 SERUM ANTIBODIES TO TYPE I COLLAGEN IN PERIPHERAL ARTHROPATHY ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

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Background: Immunological disorders play an important role in the pathogenesis of inflammatory bowel disease (IBD). Type I collagen (COL1) is the main component of the intercellular matrix of connective tissue. It can be assumed that the immune disorders leading to the production of autoantibodies to collagen play a role in the pathogenesis of arthropathy associated with IBD.
Objectives: to study the level of IgM and IgG to type I collagen (COL1) in peripheral arthropathy associated with IBD.

Methods: We prospectively included 91 patients with IBD [61 ulcerative colitis (UC), 30 Crohn's disease (CD)] and 30 healthy controls. 82 patients with IBD were in disease attack and 9 in the remission Mean age in IBD was 36 [28; 47] years and in control group – 35 [25; 48]. Joint involvement (arthralgia, arthritis) was observed in 33 patients (36%). Affected joints were the knees 17 (51%), shoulders 6 (18%), feet 6 (18%), hands 5 (15%), elbows 4 (12%), ankles 3 (9%), wrists 2 (6%). Levels of serum IgM and IgG to COL1 were assessed by enzyme immunoassay.
Results: Levels of IgM to COL1 in active IBD (0,18 [0,10; 0,2] mkg/ml; p<0,01) and in remission (0,15 [0,11; 0,20] mkg/ml; p<0,05) were increased compared with healthy (0,09 [0,07; 0,12] mkg/ml). There were no differences between stage of disease (remission and exacerbation), IBD severity (p>0,05). IgM antibodies to COL1 in patients with peripheral arthropathy (0,174 [0,12; 0,28] mkg/ml) were significantly higher than in patients without joint involvement (0,12 [0,08; 0,19] mkg/ml; p<0,01). The levels of IgG to COL1 in active IBD (14,4 [10,22; 33,34] mkg/ml; p<0,05) and in remission (28,82 [16,36; 78,9] mkg/ml; p<0,005) were higher than in the control group 11,36 [6,93; 19,83] mkg/ml. We didn't find any differences in IgG levels depending on the severity of disease. IgG levels to COL1 in patients with peripheral arthropathy (16,18 [9,46; 26,21] mkg/ml) were higher, than without them (12,78 [8,81; 28,31] mkg/ml), also not significant.
Conclusion: In active IBD the level of serum antibodies of class IgM and IgG to COL1 increased compared with healthy. The maximum increase was found in the patients with peripheral arthropathy, which can be explained by the high content of this collagen in the structural components of the joints and by joint inflammation in patients with IBD.
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POS0402 CLONALLY EXPANDED CD38hi CYTOTOXIC CD8 T CELLS DEFINE THE T CELL INFILTRATE IN CHECKPOINT INHIBITOR-ASSOCIATED ARTHRITIS

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Background: Immune checkpoint inhibitor (ICI) therapies that promote T cell activation have improved outcomes for advanced malignancies yet can also elicit harmful autoimmune reactions. The T cell mechanisms mediating these iatrogenic autoimmune events remain unclear.
Objectives: To investigate the immunophenotype, transcriptomic feature and clonotypes of T cells from joints of patients affected by ICI-induced inflammatory arthritis (ICI-arthritis).
Methods: Detailed immunophenotyping was performed on mononuclear cells from synovial fluid (SF) using mass cytometry and flow cytometry to identify significantly altered populations in ICI-A compared to seropositive rhrumatoid arthritis (RA) and psoriatic arthritis (PsA) (p<0.05). Bulk RNA-seq was performed on altered SF CD8 T cell subsets from ICI-A, RA and PsA to investigate their transcriptomic features. Cytokine profile and pathways enriched in ICI-A CD8 T cells were examined using differentially expressed genes, intracellular staining, and in vitro culture. TCR clonotypes were examined using single cell RNA-seq of T cells from synovial fluid, tissue and blood of ICI-A.
Results: Compared to the autoimmune arthritides RA and PsA, ICI-arthritis joints contained an expanded $CD38^{hi}$ $CD127^{-}$ $CD8^{+}$ T cell subset that displays cytotoxic, effector, and interferon (IFN) response signatures. Exposure of synovial T cells to Type I IFN, more so than IFN-γ, induced the $CD38^{hi}$ cytotoxic phenotype. Single cell transcriptomic and T cell repertoire (TCR) analyses indicated that the abundance of $CD38^{hi}$ CD8 T cells in ICI-arthritis resulted from proliferation of a limited number of clones. The $CD38^{hi}$ population appeared distinct from dysfunctional T cells and clonally most related to $TCF7^{+}$ memory populations. Comparison of synovial tissue from bilateral knees of the same patient demonstrated considerable sharing of TCR clonotypes among $CD38^{hi}$ CD8 T cells between the two joints. Further, TCR clonotypes expanded in synovial fluid of ICI-arthritis patients were detected in circulating T cells, and circulating $CD38^{hi}$ CD8 T cells are also expanded in ICI-arthritis patients.
Conclusion: These results define a distinct CD8 T cell subset in the synovial fluid and in the circulation of patients with ICI-A that may be directly activated by ICI therapy to mediate a tissue-specific autoimmune response.
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POS0403 DYNAMIC CHANGES IN AUTOREACTIVE MEMORY B CELLS IN RHEUMATOID ARTHRITIS: KEY TO UNDERSTANDING IMMUNOLOGICAL DISEASE ACTIVITY

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Background: Rheumatoid arthritis (RA) patients with autoantibodies against citrullinated antigens (ACPA) are characterized by poor chances to achieve sustained DMARD free remission. We have previously observed that autoreactive ACPA-expressing memory B cells (MBC) display an activated phenotype and frequently maintain this state of activation even in patients in clinical remission in whom joint inflammation is absent through treatment. Conceptually, these observations could reflect ongoing immunological activity. In fact, they indicate that most current therapeutic interventions do not induce immunological remission and could explain why disease frequently flares when treatment is stopped. ACPA-expressing MBC display the phenotype of recent germinal centre emigrants, actively proliferating (Ki-67 positive), expressing CD95 and co-stimulatory markers CD80 and CD86, and the signature cytokine IL-8.[1] Notably, in autoantibody-positive individuals with arthralgia that did not progress to inflammatory arthritis within 2 years, the autoreactive B cells were readily detectable in the circulation and proliferated but lacked, in most cases, the upregulation of CD80 seen at the onset of disease. Now, we studied these autoreactive B cells longitudinally in the 'at-risk' phase of clinically suspect arthralgia (CSA) and in a population of patients in sustained (>1 year) drug-free remission (SDFR).
Objectives: To define dynamic changes of the ACPA-expressing B cell compartment throughout clinical disease stages with the aim to evaluate this response as a possibly predictive biomarker of immunological disease activity.
Methods: ACPA-expressing MBC were identified by flow cytometry in peripheral blood of RA patients with chronic disease or at disease-onset (treatment-naïve), in ACPA-positive CSA patients 'at-risk' for RA, and in patients in SDFR. B cells were characterized by a combination of markers to classify B cell subpopulations and activation- and germinal centre related markers. Tetanus-toxoid-specific B cells were analysed in the same individuals as antigen-specific comparators.
Results: In patients in SDFR, significantly less autoreactive B cells expressed CD80 compared to active disease, while they persistently showed signs of proliferation, similar to the phenotype observed in CSA patients that did not progress to RA. ACPA-specific plasmablasts (defined as $CD20^{-}CD27^{hi}$) were practically absent in SDFR and CSA non-progressors, while they were readily detectable in patients with RA at disease onset, during treatment, and in CSA-individuals that later progressed to RA. Notably, two arthralgia patients that developed RA within one year showed high CD80 expression in the autoreactive MBC compartment already in the 'at-risk' phase, whereas patients that so far did not progress to RA during the time of follow-up, showed less CD80-positive autoreactive MBC.
Conclusion: The phenotype of autoreactive B cells is dynamic in different disease phases of RA. By studying extremes of clinical phenotypes ('at-risk' phase, disease onset, SDFR), we found evidence for dynamic expression of CD80 by ACPA-expressing MBC in relation to clinical disease stage. Intriguingly, CD80-positive B cells, but not CD80-negative B cells, have been shown to be able to differentiate into antibody secreting cells in mice.[2] Our finding that plasmablasts were practically absent in ACPA-positive arthralgia patients that did not progress to RA and in SDFR would fit with this notion and suggests that in SDFR autoreactive MBC lack, although actively proliferating, triggers that induce CD80 upregulation, differentiation to plasmablasts and, possibly, their active participation in processes causing joint inflammation. Based on this observation, it is possible that induction of this $CD80^{lo}$ phenotype in autoreactive MBC may be an important step towards achieving immunological remission, a conceptual proxy for cure.
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Innate immunity in rheumatic diseases

POS0404 IFNα-MEDIATED METABOLIC REPROGRAMMING IN HUMAN SLE MONOCYTES INVOLVES PERTURBATIONS IN GLYCOLYTIC AND LIPID METABOLISM TO REGULATE PROINFLAMMATORY MARKERS AND CYTOKINES

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Background: Systemic Lupus Erythematosus (SLE) is a prototype interferonopathy characterized by multiple organ damage[1]. Metabolomic analyses of patient-derived sera indicate distinct metabolic pertubations in oxidative and lipid metabolism[2,3]. Among innate effectors, monocytes (Mo) are implicated in SLE pathogenesis and also display a perturbed metabolic phenotype[4].
Objectives: Based on previous data indicating a prominent IFNα-gene signature in SLE monocytes even during disease remission[5], we herein sought to delineate the metabolic repercussion of IFNα signaling contributing to SLE autoimmunity.
Methods: Using transcriptomic data, we compared the enriched metabolic categories of IFNα(+) and IFNα(-) SLE-Mo[6]. In order to compare metabolic perturbations pertaining to SLE, we performed transcriptomic Gene Set Enrichment Analysis (GSEA)[7] from *in vitro* cultured IFNα-activated Mo. We supplemented the analysis with selective *ex vivo* biochemical inhibition of the metabolic pathways arising from the GSEA and evaluated the effect on inflammatory markers of healthy IFNα-Mo.
Results: We found a statistically significant enrichment of transcripts associated with glycolytic metabolism and lipid biosynthetic and catabolic processes in both IFNα(+)-SLE Mo and healthy IFNα-Mo, but not in IFNα(-)-SLE Mo, which in turn resembled healthy-Mo. Additionally, transcripts associated with cholesterol biosynthetic processes such *PMVK*, *SQLE*, *LSS*, *DHCR7*, and *LDLR*, *MVK*, *FFT1* were significantly upregulated in IFNα(+)-SLE Mo and healthy IFNα-Mo respectively. In accordance, blockade of either glycolysis with the use of 2-DG hexokinase inhibitor, or mevalonic acid synthesis with the use of fluvastatin, attenuated proinflammatory cytokine secretion (IL6, CXCL10) associated with IFN-response in both IFNα(+)-SLE Mo and healthy IFNα-Mo.
Conclusion: Our results link IFNα mediated metabolic shifts in Mo with corresponding metabolic perturbations found in SLE patient-Mo. Pending further confirmation with targeted metabolomics, these data further rationalize the use of IFN blockade and also suggest the potential use of specific metabolites as novel therapeutic targets in SLE.
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POS0405 INCREASED LEVELS OF CELLULAR ADHESION MOLECULES ARE LINKED TO THE PRESENCE OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH AUTOIMMUNE DISEASES

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Background: Intercellular adhesion molecule-1 (ICAM-1) and E-Selectin are adhesion molecules considered as markers of underlying endothelial activity and damage. These molecules are known to play an important role in autoimmune disease (AD) [1]. Accordingly, they may contribute to the development of interstitial lung disease (ILD), one of the main causes of death in patients with AD [2]. In fact, they have been proposed as prognostic biomarkers in idiopathic pulmonary fibrosis (IPF) [3]. However, studies on the role of ICAM-1 and E-Selectin in AD-ILD$^+$ are scarce.
Objectives: To study the role of ICAM-1 and E-Selectin in the pathogenesis of AD-ILD$^+$.
Methods: Peripheral venous blood was collected from 57 patients with AD-ILD$^+$ and three comparative groups: 45 AD-ILD$^-$ patients, 21 IPF patients and 21 healthy controls (HC). All the subjects were recruited from the Rheumatology and Pneumology departments of Hospital Universitario Marqués de Valdecilla, Santander, Spain. ICAM-1 and E-Selectin levels were measured in serum samples by enzyme-linked immunosorbent assay.
Results: Higher levels of ICAM-1 and E-Selectin were found in patients with AD-ILD$^+$ compared to AD-ILD$^-$ patients ($p<0.001$ and $p=0.001$, respectively) and HC ($p<0.001$ in both cases). Likewise, IPF patients showed increased levels of ICAM-1 and E-Selectin in relation to AD-ILD$^-$ patients ($p<0.001$ and $p=0.002$, respectively) and HC ($p<0.001$ in both cases). However, no statistically significant difference in ICAM-1 and E-Selectin concentrations was observed between AD-ILD$^+$ and IPF patients.
Conclusion: Our study suggests that increased levels of ICAM-1 and E-Selectin are associated with the presence of ILD in AD patients.
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POS0406 CHARACTERISATION OF ENHANCER RNAS IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: Rheumatoid arthritis synovial fibroblasts (SF) exhibit a prolonged histone 3 lysine 27 acetylation (H3K27ac) after stimulation with TNF, leading to a sustained inflammatory response. Enhancer RNAs (eRNAs) are short-lived non-coding RNAs transcribed from cell type-specific H3K27ac-marked enhancers that facilitate the transcription of their linked coding genes. The interrelation of eRNAs and their linked coding genes in SF has not been studied yet.
Objectives: To analyze the expression and regulation of inflammatory eRNAs in SF.

Methods: The expression of eRNAs in SF (n=9), stimulated with TNF (24h; 10 ng/µl) or left untreated, was detected by cap analysis of gene expression followed by sequencing (CAGEseq). To further investigate eRNA expression in SF, the expression of selected eRNAs and their linked coding genes (*CXCL1*, *CCL20*, *IL6*, *CCL2*, *CXCL12*, *IL8*) was analyzed by real-time PCR in SF that were stimulated with TNF (1, 3, 6, 24h; 10 ng/µl), IL1 (1, 24h; 1 ng/ml), or the Toll-like receptor agonists Pam3 (1, 24h; 1 ng/ml), pIC (1, 24h; 10 µg/ml) and LPS (1, 24h; 100 ng/µl). Samples containing the untranscribed RNA were measured in parallel. To study eRNA regulation, SF were treated with the bromodomain inhibitor I-BET (1 µM; 24h), or silenced for the histone acetyltransferases CBP and p300 by transfection of antisense LNA gapmeRs (12.5 nM) prior to stimulation with TNF (1, 24h).
Results: We have selected four potential eRNAs for CCL2 and IL8, three for CXCL12, two for IL6 and CXCL1 and one for CCL20 from CAGEseq analysis. They were located upstream (eCCL2#1, eCCL2#2, eCXCL1#2, eCXL12#3, eIL6#1+2, eIL8#1-4), downstream (eCCL2#3, eCCL2#4, eCXCL1#1, eCXL12#1) and intronic (eCCL20, eCXL12#2) at distances between 300 bp to 35.6 kb relative to the transcription start sites of the corresponding coding genes. None of the eRNAs was present in all nine samples in CAGEseq data sets, indicating a patient-dependent variability in eRNA expression. The majority of eRNAs were not detected in unstimulated SF, with the exception of eRNAs for CXCL12. By performing TNF time course experiments (Figure 1), we have detected different patterns of eRNAs: (a) eRNAs, that peaked at 1h (eCCL20, eIL8#2, eCCL2#1), (b) at 6h (eCXCL1#1), (c) or at 24h (eIL8#1, eIL8#3, eIL8#4, eCXCL1#2) after stimulation, (d) eRNAs that were stably expressed over the time points (eCCL2#2, 3, 4), and (e) eRNAs that were down regulated by TNF

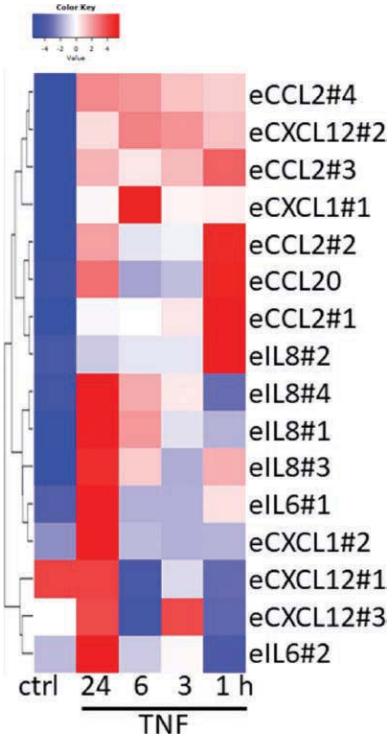

Figure 1.

stimulation (eCXCL12#1, eCXCL12#3). All inflammatory stimuli induced eRNA expression in SF, with LPS and IL1, followed by TNF, being the most potent inducers of eRNAs. I-BET suppressed the TNF-induced expression of all eRNAs tested. The effects on the expression of eRNAs after silencing of p300 but not of CBP mirrored to a large extent those of the respective coding genes.
Conclusion: In SF, the expression of some eRNAs is maintained for up to 24h, contradicting previous reports that eRNAs are short-lived. Our data suggest that different eRNAs orchestrate the early and sustained expression of cytokines and chemokines in SF. eRNA expression is controlled by p300 and BET bromodomain proteins.
Disclosure of Interests: Larissa Moser: None declared, Miranda Houtman: None declared, Oliver Distler Consultant of: Abbvie, Britta Maurer Speakers bureau: Boehringer-Ingelheim, Consultant of: Novartis, Boehringer Ingelheim, Janssen-Cilag, Grant/research support from: AbbVie, Protagen, Novartis Biomedical Research, Caroline Ospelt: None declared, Kerstin Klein Grant/research support from: Novartis Foundation for biomedical research (2019)
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Osteo arthritis, aetiology, pathology and animal models

POS0407

OXYSTEROL 7-KETOCHOLESTEROL CAN RE-PROGRAM SYNOVIAL TISSUE MACROPHAGES AND SUPPORT M1 POLARIZATION

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Background: Oxidized low-density lipoprotein (oxLDL) particles support low-grade inflammation and have been found in synovial fluid from osteoarthritis (OA) joints [1]. Their component is 7-ketocholesterol (7-KC), which arises as the result of the oxidation of cholesterol [1]. 7-KC acts proinflammatory and it binds to Toll-like receptor (TLR) 4 expressed on macrophages [1]. Activation of TLR4 stimulates the classical macrophage maturation program, resulting in a specific phenotype of inducible nitric oxide synthase positive (iNOS+) and macrophage (M) 1 function, which produce and secrete proinflammatory chemokines and cytokines [2]. M2 macrophages are associated with wound healing by the production of arginase-1 [2,3]. Synovial macrophages are of critical importance in the symptomatology and structural progression of OA since M1 polarized macrophages accumulate in human OA synovial tissue during exacerbation [3]. However, it is not known whether 7-KC can re-program synovial tissue macrophages and support M1 polarization.
Objectives: We analyzed the influence of 7-KC on the polarization of CD68+ macrophages in the suspension of synovial mononuclear cells (SMCs) in respect to lipopolysaccharide (LPS), as M1 inducer.
Methods: Mature synovial tissue samples were obtained during alloarthroplasty of the knee (N = 56). Paraffin embedded tissue sections were labelled by double immunofluorescence using a combination of antibodies directed toward CD68 and iNOS, arginase-1, CCL2 or CCL22. Suspension of SMCs was prepared by enzymatic digestion of tissue samples using collagenase IV and gradient density centrifugation. We analyzed intracellular (iNOS, arginase-1, CCL2, and CCL22) and surface (CD91, mannose receptor, HLA-DR, CD80, CD86 and decoy D6) antigens expression in CD68+ cells in the suspension of freshly isolated or 18 hour-cultured SMCs with 7-KC (25 µM), LPS (10 ng/ml), their combination or in the medium only.
Results: iNOS and CCL2 were more frequently labelled in lymphocyte clusters, while arginase-1 and CCL22 were labelled in synovial lining CD68+ cells. Phenotype of CD68+ cells did not change significantly after the 18 hour- culture in the medium only, except the decrease of mannose receptor and CD91, when compared with freshly isolated cells. 7-KC increased the percentage of CD86 expressing CD68+ cells, whereas decreased surface expression of CD91 and chemokine decoy D6, like in the culture with LPS, when compared with cells cultured in the medium only. 7-KC decreased the frequency of arginase-1+/CD68+ cells in the suspension and did not change iNOS+ in CD68+ cells, thus increasing the ratio of iNOS+/arginase-1+ in CD68+ subset. 7-KC was unable to increase CCL2 like LPS in comparison with cells cultured in the medium only. Neither 7-KC nor LPS affected CCL22 expression in the CD68+ subset.
Conclusion: These data provide a new perspective in understanding the polarization of macrophages toward the M1 phenotype mediated with oxysterol 7-KC *in vitro*.
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Disclosure of Interests: None declared.
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Rheumatoid arthritis - aetiology, pathogenesis and animal models

POS0408 TRANSFER OF HUMAN RHEUMATOID ARTHRITIS MONONUCLEAR CELLS INDUCES ARTHRITIS IN IMMUNODEFICIENT HLA-DR4 TRANSGENIC MICE

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease leading to erosive joint destruction. Although the exact pathogenesis is still elusive, the strong association of certain HLA class II molecules, such as HLA-DRB1*0401 (HLA-DR4), suggest involvement of $CD4^+$ T cells (1,2). Mouse models of RA mimic specific aspects of the disease but are limited by the differences between human and murine immune systems.
Objectives: We aimed to establish a humanized mouse model (humice) carrying $DR4^+$ RA PBMCs to study its role in the pathogenesis of RA without putting patients at risk.
Methods: Peripheral blood mononuclear cells (PBMC) of HLA-DR4 positive RA patients or controls were isolated and injected into NSG-Ab^0 DR4 mice (NOD-scid IL2Rgamma^{null} mice lacking MHC class II while expressing the human HLA-DR4) to create humice. Human immune cell composition within humice was profiled using flow cytometry. Development of RA was monitored by examination of the joints and micro computed tomography analysis. Joints were analysed by histology regarding pannus formation, bone erosions, cartilage damage, and human cell infiltration.
Results: Transfer of RA PBMCs induced arthritis in humice recapitulating hallmarks of RA including immune cell infiltration, pannus formation, increased osteoclastogenesis, cartilage damage, and bone erosions. Arthritis was dependent on the implanted human cells as NSG-Ab0 DR4 mice without transfer of human PBMCs did not develop arthritis. T-helper 1 (Th1) cells, dominated the human immune cell composition in humice, while regulatory T cells (Tregs) were diminished compared to donor PBMC composition. Mice humanized with cells from RA patients were more likely to develop inflammatory joint disease, compared to healthy HLA-DR4 positive controls (RA donor 70% vs. healthy control 20%, p=0.00196). CTLA-4 Ig treatment prevented arthritis development in this model (p=0.0055).
Conclusion: Humice carrying $DR4^+$ RA PBMCs developed an RA-like erosive joint disease driven by the implanted human immune system. The data implies that the disease can be transferred by arthritogenic cells found in the peripheral blood of RA patients. This model will allow new insights into the pathogenesis of RA.
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POS0409 INTESTINAL HIF1α EXPRESSION PROTECTS AGAINST EPITHELIAL CELL DEATH IN ARTHRITIS

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Background: While a so-called *gut-joint axis* is supported by many clinical observations, the current knowledge on such axis is mostly confined to descriptive and correlative data, e.g. showing the microbiota changes are associated with arthritis. In contrast, mechanistic data on how molecular changes in the intestinal epithelium influence the development of arthritis are scarce.
Objectives: To investigate, whether the mucosal barrier in the intestine dependent of the epithelial cell survival maintenance, influences the development of arthritis.
Methods: Intestinal hypoxia inducible factor (HIF)-1α expression was assessed before, at onset and during experimental arthritis and human rheumatoid arthritis (RA). Intestinal epithelial cell-specific HIF1α conditional knock-out mice were generated ($HIF1\alpha^{\Delta IEC}$) and subjected to collagen-induced arthritis (CIA). Clinical and histological courses of arthritis were recorded, and T and B cell subsets were analyzed in the gut and secondary lymphatic organs, and intestinal epithelial cells were subjected to molecular mRNA sequencing in $HIF1\alpha^{\Delta IEC}$ and littermate control mice. Furthermore, pharmacologic HIF1α stabilization by PHD inhibitor was used for the treatment of arthritis.
Results: Intestinal HIF1α expression peaked at onset and remained high in experimental arthritis and RA. Conditionally deletion of HIF1α in gut epithelial cells strongly exacerbate arthritis and was associated with increased gut epithelial cell death, intestinal and lymphatic Th1 and Th17 activation. Mechanistically, HIF1α inhibits the transcription of necroptotic and apoptotic markers, which leads to a defect in the intestinal barrier integrity. Furthermore, treatment with HIF1α stabilization reinforced the gut epithelial cell survival and inhibited arthritis.
Conclusion: These findings show that the HIF1α regulating epithelial cells survival is critical for the breakdown of the intestinal barrier function in arthritis highlighting the functional link between intestinal homeostasis and arthritis.
Disclosure of Interests: None declared.
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POS0410 THE ROLE OF IL-6 IN ENDOTHELIAL DYSFUNCTION: RHEUMATOID ARTHRITIS AND COVID-19, TWO PATHOGENIC MODELS IN COMPARISON

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Background: Rheumatoid arthritis (RA) is the most common systemic autoimmune disease that primarily affects joints but is also often characterized by extra-articular involvement[1]. Cardiovascular diseases are the most important causes of sudden death in these patients, which present a risk of developing cardiovascular events increased by 48%[2]. The causes of increased cardiovascular risk are several and not completely understood, but recent evidence supports the key role of endothelial dysfunction in pathogenesis. In this complex scenario, it is known that IL-6 receptors are present at the endothelial level and can be activated leading to endothelial dysfunction. SARS-Cov-2 is a coronavirus responsible for the disease called 'coronavirus disease 2019' (CoViD-19) characterized by clinical manifestations ranging from a flu-like syndrome up to severe lung damage associated with systemic hyper cytokine syndrome that can lead to multiple organ failure and death. Therefore, both RA and Covid-19 are associated with an increased pro-thrombotic and cardiovascular risk and IL-6 might be crucial in the pathophysiological mechanisms of both diseases.
Objectives: The main hypothesis of this study was to evaluate the possible role of IL-6 as a promoter of endothelial dysfunction in RA and CoViD-19.
Methods: In vitro experiments were conducted on the endothelial cell line EA. hy926. Cells were treated for 24 h with fetal bovine serum (FBS), a pool of RA patients' sera or a pool of CoViD-19 patients' sera. The expression levels of adhesion molecules (V-CAM1/CD-106, I-CAM/CD-54, p-selectine/CD-62, tissue factor/CD-142) and apoptosis were analyzed using cytofluorimetric technique. In addition, the autophagy level, using the autophagy markers p62 and LC3II, were evaluated through a western-blot analysis. The same experiments were conducted co-treating cells with the same pool of sera in addition to tocilizumab (TCZ), an anti-IL-6 drug, to verify the reversibility of the process and test the role of the aforementioned cytokine. Data are reported as interquartile median values. The Kruskal Wallis test was used for unpaired samples and the Mann-Whitney test for paired samples. $P<0.05$ values were considered statistically significant.
Results: EA. hy926 cells, when treated with both RA and CoViD-19 patients' sera, showed increased levels of activation molecules and apoptosis compared to FBS treated cells. In addition, we observed increased levels of both p62 and LC3 proteins after both rheumatoid arthritis and CoViD-19 patients' sera treatment. All these findings were reversible in the presence of TCZ. The results are presented in Figure 1.

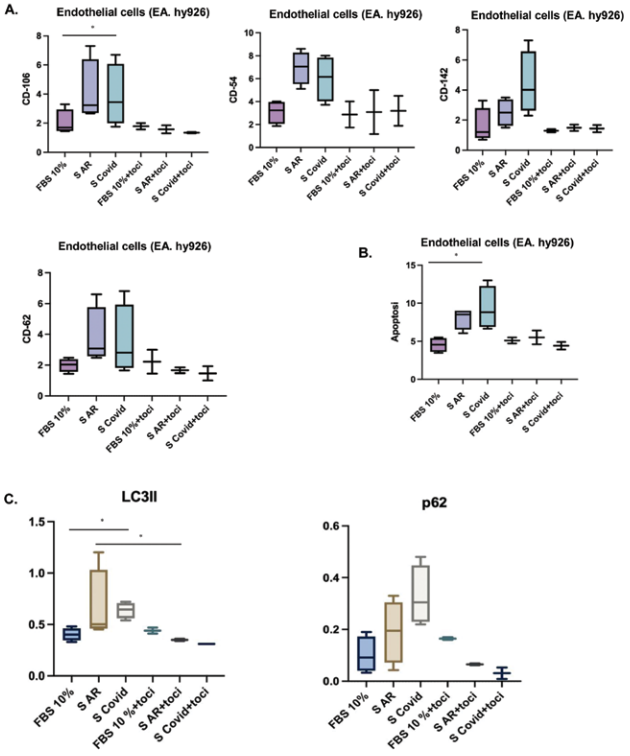

Figure 1. Figures show the adhesion molecules levels (**A**), apoptosis levels (**B**), p62 and LC3II levels (**C**), in all experimental conditions. FBS 10% (cells treated with FBS at 10% concentration), S AR (cells treated with a pool of RA patients' sera); S Covid (cells treated with a pool of COVID-19 patients' sera); FBS 10%+toci (cells co-treated with FBS at 10% concentration and TCZ); S AR+toci (cells co-treated with a pool of RA patients' sera and TCZ); S Covid+toci (cells co-treated with a pool of CoViD-19 patients' sera and TCZ).

Conclusion: Our data showed that treatment with RA and CoViD-19 patients' sera increase the activation and death of endothelial cells in vitro. The increased level of cells death is possibly due to a block of autophagy. The reversibility of the process after blocking IL-6 with TCZ co-treatment confirms the hypothesis that IL-6 can play a key role in the pathogenesis of endothelial damage in patients with RA and CoViD-19.

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Disclosure of Interests: None declared.

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POS0411

COMPARISON OF MTX-POLYGLUTAMATE ACCUMULATION PROFILES IN PERIPHERAL BLOOD MONONUCLEAR CELLS AND ERYTHROCYTES DURING 6 MONTHS MTX-THERAPY IN THE METHOTREXATE MONITORING (MEMO) TRIAL

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Background: Optimal dosing of methotrexate (MTX) in rheumatoid arthritis (RA) remains challenging. To this end, monitoring of intracellular MTX polyglutamates (MTX-PGs) in red blood cells (RBCs) has been investigated as a potential marker of MTX (non-)response, with contradictory results. As enucleated, non-proliferative cells, mature RBCs lack regulated folate metabolism and are devoid of folylpolyglutamate synthetase (FPGS) activity catalyzing the conversion of MTX to MTX-PGs. Therefore, it has been argued that analysis of MTX-PG in immune-effector cells, represented by peripheral blood mononuclear cells (PBMCs), would be more relevant. However, no prospective study has been performed measuring MTX-PG levels in PBMCs nor in comparison with RBCs.

Objectives: To investigate the pharmacokinetics of MTX-PG accumulation in RBCs and PBMCs in newly diagnosed RA patients in the early phase of MTX treatment.

Methods: In a clinical prospective cohort study (Methotrexate Monitoring (NTR7149)), RA patients were administered MTX op to 25 mg/week, as described before. (1) At 1, 2, 3 and 6 months after start of therapy, blood was collected and RBCs were isolated by centrifugation and PBMCs after Ficoll density gradient centrifugation. MTX-PG_{1-6} concentrations in these cells were analyzed using a UPLC-MS/MS method with including custom-made stable isotopes of MTX-PG_{1-6} as internal standards. (2) UPLC-MS/MS measurements for MTX-PG_{1-6} were performed with a Waters Acquity BEH C18 column coupled to an AB Sciex 6500+ with the ESI operating on the positive mode. MTX dosing and concomitant treatments were in conformity with clinical practice. (3)

Results: 46 consecutive patients were included in this study; 76% female, mean age: 57.8 years, mean baseline DAS28-ESR: 3.5, as described before. (1) Mean dosage was 10.5 mg (SD: 1.5) at baseline, 16.3 mg (2.5) at month 1, 22.7 mg (4.5) at month 2, 19.5 mg (6.3) at month 3 and 19.1 mg (6.2) at month 6.

MTX-PG accumulation in PBMCs and RBCs revealed a disparate profile in both MTX-PG distribution and absolute accumulation levels (Figure 1A/B). Remarkably, MTX-PG distribution in PBMCs was mainly composed of MTX-PG_1 (58%), and to a lesser extent MTX-PG_2 (27%) and MTX-PG_3 (15%). Longer chain MTX-PG_{4-6} were also detectable in PBMCs, but at lower levels (mean: 4.0 – 6.7 fmol/10^6 cells) than MTX-PG_{1-3}. Moreover, this MTX-PG distribution profile in PBMCs remained constant over a MTX therapy period of 6 months (Figure 1A). The RBC MTX-PG accumulation profile shows mainly MTX-PG_1 and lower levels of MTX-PG_{2-6} at 1 month after the start of therapy. After 3 months of therapy, MTX-PG_3 is the main PG-moiety with also MTX-$PG_{4,5,6}$ being detected. This profile is largely similar after 6 months of therapy. With respect to total intracellular MTX-PG_{1-6} accumulation, PBMCs had significantly ($p<0.001$) 10-20-fold higher levels than RBCs at all analyzed time points (Figure 1A/B). Total MTX-PG_{1-6} levels in RBCs and PBMCs at all time points were weakly correlated ($r=0.41$, $p<0.01$) (Figure 1C).

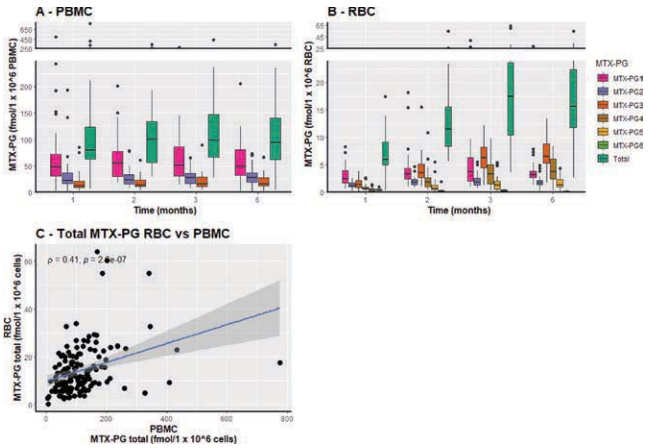

Figure 1. Individual MTX-PG concentrations in PBMCs (A) and RBCs (B) during the first 6 months of MTX administration (note the different scaling of the y-axes). At 6 months, 36 patients were still on MTX treatment. Panel (C): Spearman's correlation plot of total MTX-PGs in RBCs versus PBMCs of all time points.

The disparate MTX-PG accumulation and distribution profiles in PBMCs versus RBCs of RA patients may be associated with the shorter life span of PBMCs and the low FPGS activity in RBCs. (4)

No significant relation between MTX-PGs and DAS28 was found (data not shown).

Conclusion: This study shows that in newly diagnosed RA patients starting MTX therapy, MTX-PG concentrations in PBMCs are significantly 10-20-fold higher than in RBCs over a period of 6 months, with a disparate MTX-PG distribution profile in PBMCs (highest: MTX-PG_1) than RBCs (highest: MTX-PG_3).

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POS0412 ENHANCING SURVIVAL AND THERAPEUTIC EFFECT OF MESENCHYMAL STEM CELLS IN RAT MODEL OF RHEUMATOID ARTHRITIS VIA NANOMODIFICATION

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Background: Mesenchymal stem cells (MSCs) have immunomodulatory, multilineage differentiation, and inflammatory/injury site-homing properties. These unique therapeutic features enable MSCs to be used in the treatment of rheumatoid arthritis (RA). However, MSCs therapy is still facing multiple obstacles in RA. First, MSCs are sensitive to inflammatory microenvironment (e.g., high level of reactive oxygen species [ROS]) and hence lose viability and immune regulatory effect when exposed in the inflamed joint. Second, uncontrolled differentiation of MSCs leads to the failure of cartilage repair.
Objectives: The aim of this study was to develop nanoparticle (NP)-modified MSCs that can maintain their biofunctions under the RA-associated oxidized stress and chondrogenically differentiate to repair cartilage.
Methods: Copper sulfide@manganese dioxide (CuS@MnO_2) NPs were sythesized, then modified with an MSC-targeting peptide (VTAMEPGQ, termed VQ) and loaded with metformin (MET) to produce VQ-CuS@MnO_2/MET (termed VCMM) NPs. After cellular uptake, the NP-modified VCMM-MSCs were obtained. The basic functions, chondrogenesis, anti-inflammatory effect and cell viability under oxidized stress of VCMM-MSCs were studied in vitro. Further, VCMM-MSCs were intravenously (i.v.) injected into rat models of collegan-induced arthritis (CIA) and adjuvant-induced arthritis (AIA) to evaluate their survival and therapeutic effect in vivo.
Results: The NP-modified VCMM-MSCs exhibited stronger capabilities of cell migration and chondrogenesis relative to bare MSCs. VCMM-MSCs were also better than bare MSCs in terms of anti-inflammation towards lipopolysaccharide-induced M1 macrophages (RAW264.7). Moreover, VCMM-MSCs could survive under the RA-associated oxidized stress through catalyzing intracelluar ROS into oxygen by the superoxide dismutase (SOD)- and catalase (CAT)-like activities of the NPs, whereas approximately half of bare MSCs were dead. After i.v. injection into CIA and AIA rats, VCMM-MSCs lived longer and accumulated more abundant in the inflamed joints relative to bare MSCs (determined by in vivo fluorescence imaging). They promoted the repolarization of macrophages from M1 to M2 type in synovium, thereby inhibiting synovial inflammation in vivo. Further, VCMM-MSCs enhanced the sythesis of glycosaminoglycan and type II collegan in cartilage and thus promoted joint reapir.
Conclusion: The NP-modified VCMM-MSCs alleviated arthritis syndrome of both CIA and AIA models through reducing synovial hyperplasia and cartilage destruction. Nanomodification of MSCs may provide a new strategy to improve stem cell therapy in RA and other inflammatory diseases.
Acknowledgements: This study was supported by National Natural Science Foundation of China (81902198).
Disclosure of Interests: None declared.
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POS0413 IGURATIMOD AMELIORATES BLEOMYCIN-INDUCED PULMONARY FIBROSIS VIA INHIBITINGEMT PROCESS AND NLRP3 INFLAMMASOME ACTIVATION

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Background: Interstitial pulmonary fibrosis is the deadliest manifestation of rheumatoid arthritis (RA), and its pathogenesis is complicated. As a new drug for controlling RA, clinical studies have found that iguratimod (IGU) has certain advantages in improving lung function and shows great potential for pulmonary fibrosis therapy[1]. However, the specific mechanism of IGU in treating pulmonary fibrosis is not clear.
Objectives: This study was designed to observe and investigate the therapeutic effects of IGU on bleomycin-induced pulmonary fibrosis in mice and further investigate its underlying mechanism, aiming to provide a further theoretical basis for clinical rational drug use.
Methods: A mouse model of pulmonary fibrosis was induced by intratracheal injection of bleomycin (BLM)[2]. Model mice were randomly assigned to receive Sodium carboxymethyl cellulose (CMC) or different concentrations of IGU. HE staining and immunohistochemical staining were performed to observe the therapeutic effects of IGU on mouse fibrosis. TGF-β induced A549 EMT cell model was utilized to investigate the effects of IGU on EMT *in vitro*[3]. NLRP3 inflammasome was activated by the co-stimulation of TGF-β+LPS+ATP (TLA) to evaluate the effects of IGU *in vitro*[4].
Results: We found that IGU resulted in favorable therapeutic outcomes by affecting the inflammation infiltration (Figure 1A) and collagen deposition (Figure 1B). Immunohistochemical results showed that IGU downregulated the levels of α-SM and NLRP3. Additionally, the markers of BLM-mediated EMT (Figure 1C) phenotype and NLRP3-activated (Figure 1D) phenotype in the lung were also attenuated after IGU administration. *In vitro* experiments, the results confirmed its anti-EMT effects of reducing the expression of interstitial proteins Vimentin and α-SMA and restoring the content of epithelial protein E-cadherin. Besides, IGU could inhibit NLRP3 activation by downregulating NLRP3 related marker proteins, reducing the secretion of IL-1β, and attenuating caspase-1 activity. We then found that IGU anti-EMT and anti-NLRP3 effect was accompanied by decreased ROS production.

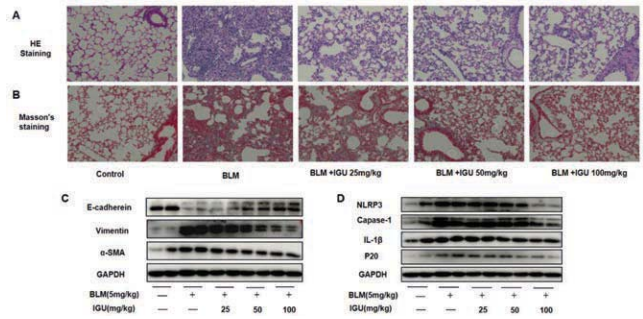

Figure 1. IGU ameliorates BLM-induced pulmonary inflammation and pulmonary fibrosis. **(A)** Representative lung micrographs of lung tissues stained with HE. Magnification, ×200. **(B)** Representative photographs of lung tissues stained with Masson's trichrome staining. Magnification, ×200. **(C)** Representative results of western blot for E-cadherin, Vimentin, α-SMA expression in lung tissues. GAPDH was used as the endogenous control. **(D)** Representative results of western blot for NLRP3, caspase-1, cleaved-caspase-1 p20, IL-1β expression in lung tissues. GAPDH was used as the endogenous control.

Conclusion: IGU can inhibit the EMT process and NLRP3 inflammasome activation, reduce ROS production to ameliorate pulmonary fibrosis, which may provide new insights into the further application of IGU in Interstitial pulmonary fibrosis.
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POS0415 PLASMA GALECTIN-9 IS ASSOCIATED WITH CLINICAL DISEASE ACTIVITY IN TREATMENT NAÏVE EARLY RHEUMATOID ARTHRITIS, UNAFFECTED BY DMARD TREATMENT, AND IN VITRO MODULATES THE SECRETION OF MCP-1 AND IL-6 IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: Fibroblast-like synoviocytes (FLS) are pivotal mediators of rheumatoid synovitis expansive growth and invasiveness which respond insufficiently to disease-modifying antirheumatic drugs. Galectin-9 (Gal-9) is a lectin with well-conserved carbohydrate-recognition domains. Gal-9 has been reported to have both pro- and anti-inflammatory properties based on its ability to modulate RA FLS. Gal-9 levels are elevated in serum of rheumatoid arthritis (RA) patients, and high levels of Gal-9 have been identified in both the synovial fluid and in the inflamed synovial tissue of patients with RA.

Objectives: To investigate the role of Gal-9 as a biomarker for disease severity in treatment naïve patients with early RA and to study aspects of Gal-9 effects on inflammatory RA FLS.
Methods: Soluble plasma Gal-9 was measured in patients with newly diagnosed, treatment-naïve RA (n = 98) and in Healthy (HC) (n = 48) (Table 1). Over a 2-year period patients were randomized to either MTX alone or MTX and anti-TNF antibody treatments. Serial measurements of disease activity (DAS28CRP) were collected to evaluate the disease course. In another cohort of patients with established RA, plasma and synovial fluid samples were also examined for Gal-9 (n = 18) (Table 1). Synovial fluid mononuclear cells (SFMC) from established RA patients were used to harvest RA FLS (n=7). Osteoarthritis FLS were used as disease controls and obtained from patients with knee OA undergoing joint replacement surgery (n = 5). Monocultures of synovial fluid derived FLS (SF-FLS) (n= 6) and autologous co-cultures of SF-FLS and peripheral blood mononuclear cells (PBMC) were established (n=7) and subsequently analyzed by flow cytometry, MTT assay, and ELISA. *In vitro,* cultures were treated with a neutralizing anti-Gal-9 antibody.

Table 1.

Patient characteristics	Early RA (n=98)			Established RA (n=18)	HC (n=48)
Time after treatment initiation (months)	0	3	24	84 (12-288)	
Disease activity					
DAS28CRP (0-10)	5.7 (5.1-6.4)	2.1 (1.8-3.2)	2.0 (1.8-2.7)	5.0 (3.2-5.5)	-
Gal-9 levels (pg/ml)					
Plasma	3315 (2683-4421)	3217 (2706-4250)		2904 (2639-3411)	2190 (1652-2852)
Synovial fluid				21246 (13832-34727)	

Patient characteristics. Data are expressed as median with IQR range unless otherwise indicated.

Results: Patients with early and established RA had increased plasma levels of Gal-9 compared with HCs ($P < 0.05$) (Table 1) and levels of Gal-9 correlated positively with swollen joint counts at baseline (rho = 0.344, $P < 0.05$). The levels remained unaffected by treatment with MTX alone or by a combination of MTX and anti-TNF antibodies. Gal-9 levels were markedly elevated in the synovial fluid of chronic RA patients compared with the corresponding plasma samples ($P < 0.05$) (Table 1). *In vitro,* a neutralizing Gal-9 antibody mediated a 40% decrease in MCP-1 secretion ($P < 0.05$) and a 30% decrease in IL-6 secretion ($P < 0.05$) in RA FLS monocultures. In OA FLS, addition of anti-Gal-9 antibodies comparably decreased the production of both MCP-1 ($P < 0.05$) and IL-6 ($P < 0.05$). The changes in cytokine production were not attributable to reduction in the fraction of inflammatory FLS ($CD34^-PDPN^+THY1^+$), decreased viability or proliferation. We further investigated if the effect of neutralizing Gal-9 persisted in co-cultures between FLS and autologous PBMC. Also in this setting, neutralization of Gal-9 mediated a 40% reduction in both MCP-1 and IL-6 ($P < 0.05$, $P < 0.05$).
Conclusion: Pretreatment plasma Gal-9 levels in patients with newly diagnosed RA were increased and correlated with baseline clinical disease activity but remained elevated during goal directed synovitis suppressive therapy. In addition, in vitro neutralization of Gal-9 decreased MCP-1 and IL-6 production in a subset of FLS linked to RA pathology. Collectively these findings indicate that Gal-9 overexpression is a co-player in the causation of acute and persistent RA synovitis by enhancing pro-inflammatory FLS pathways.
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POS0416 PRECLINICAL EFFICACY OF AN OXAZOLOPYRIDINE IRAK4 INHIBITOR IN RODENT MODELS OF INFLAMMATION

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Background: Interleukin-1 receptor-associated kinase 4 (IRAK-4) is involved in Toll-Like Receptor (TLR) and Interleukin-1 Receptor (IL-1R) signaling pathways regulating innate immunity. Inhibition of IRAK4 could block the expression of cytokines involved in autoimmune disorders such as rheumatoid arthritis. CA-4948 is a member of the oxazolopyridine class of IRAK4 inhibitors and has been shown to suppress TLR agonist-induced NF-kappaB activation, TNF-alpha and IL-1beta expression in the THP-1 monocytic cell line.
Objectives: Determine whether a highly specific oxazolopyridine IRAK4 inhibitor demonstrates efficacy in mouse models of arthritis and systemic inflammation; compared to an isoquinoline inhibitor PF-06650833.
Methods: We used the mouse model of collagen induced arthritis (CIA) and lipopolysaccharide (LPS)-induced cytokine release mouse model of systemic inflammation. Mice were treated with CA-4948 or PF-06650833. In the CIA mouse model, disease activity was determined by measuring inflammation swelling in the affected joints (paw volume) and clinical score over time. Histopathological evaluation of the sum of hindpaws was performed for CIA study. A single oral dose of IRAK4 inhibitor was administered to CD-1 mice followed by intraperitoneal administration of LPS at 3 hours. ELISA kits were used to evaluate cytokine levels in mouse serum samples at 1 and 3 hours after LPS challenge.
Results: Treatment with CA-4948 or PF-06650833 resulted in inhibition of arthritis severity in the CIA mouse model and a decreased expression of proinflammatory cytokines as measured in mouse blood after LPS challenge. Consistent with CIA in-life data, treatment with CA-4948 decreased the score of all histopathological parameters (inflammation, cartilage erosion, synovial hyperplasia and pannus, bone degeneration/resorption, periosteal/exostotic changes, and composite scores) when compared to vehicle control and the differences attained statistical significance for all histopathological parameters. Treatment with CA-4948 resulted in a significant reduction of cytokine levels by 72% for TNF-alpha and 35% for IL-6 in LPS-induced cytokine release mouse model.
Conclusion: A highly specific oxazolopyridine IRAK4 inhibitor, CA-4948, demonstrated potent therapeutic efficacy in mouse models of arthritis and systemic inflammation.
Disclosure of Interests: Andrey Ugolkov Employee of: I am employed by Curis., Reinhard von Roemeling Employee of: I am employed by Curis, Robert Martell Employee of: I am employed by Curis.
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POS0417 LESS ACPA EPITOPE EXPANSION IS FOUND IN ACPA-POSITIVE IMMUNE CHECKPOINT INHIBITOR ARTHRITIS PATIENTS COMPARED TO ACPA-POSITIVE RHEUMATOID ARTHRITIS PATIENTS

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Background: Immune checkpoint inhibitors (ICI) have markedly improved the treatment of many advanced cancers; however, they can result in immune-related adverse events (irAE) including ICI arthritis (ICI-A). ICI-A often resembles rheumatoid arthritis (RA) and ~9% of ICI-A patients are anti-citrullinated peptide antibody (ACPA) positive. In RA, ACPA epitope expansion occurs over the years prior to onset of clinical disease. In this study we examined the degree of ACPA epitope expansion in seropositive ICI-A patients in order to determine whether it is similar to early RA, or more suggestive of the pre-clinical phase of disease[1].
Objectives: To compare the number of ACPA epitopes targeted in seropositive ICI-A versus RA.
Methods: We used clinical data and serum from 12 ACPA+ ICI-A patients enrolled in a prospective registry and 39 ACPA+ RA patients enrolled in the CATCH-US early RA cohort. ACPA screening was done using a commercial ELISA (positive >20 units/mL). A custom, bead-based antigen array was used to identify antibody reactivities to 16 putative RA associated citrullinated proteins. Synovial fluid (SF) samples from 3 of the ICI-A patients were also tested using the bead-based microarray. Hierarchical clustering software was used to create heatmaps to identify ACPA levels. Z-scores for fluorescence intensity were also calculated separately for each peptide, and a fluorescence level above the mean (Z-score>0) was defined as a positive ACPA. The number of positive epitopes for each patient was determined and compared categorically between the ICI-A and RA patients using Fischer's exact test.
Results: Characteristics of ICI-A and early RA patients are listed in Table 1. Compared to RA patients, ICI-A patients were older (mean 71 years vs. 48 years), more likely to have ever smoked (67% vs. 36%) and less likely to have positive rheumatoid factor (RF) (8% vs. 69%). Median symptom duration for ICI-A patients was 3.7 months compared to 6.7 months in RA patients. The median ACPA titer was lower in ICI-A patients than RA patients (42 units/mL vs. 250 units/mL). As demonstrated in Figure 1, lower signal intensities (level of ACPA) and a lower number of distinct ACPA epitopes were seen in the serum of ICI-A patients compared to RA patients. Of ICI-A patients, 67% were positive for 0-4 ACPA epitopes, 8% for 5-10 epitopes and 25% for >10 epitopes, as opposed to

23% of RA patients positive for 0-4 epitopes, 36% for 5-10 epitopes, and 41% for >10 epitopes (p=0.02). The one ICI-A patient who was also RF positive had 12 positive ACPA epitopes. There was no significant difference in the number of ACPA epitopes in ICI-A patients who were smokers vs. nonsmokers, RA-like vs. PMR-like, or who received ICI combination vs. ICI monotherapy. In the 3 ICI-A patients with synovial fluid samples, SF ACPA was not demonstrated.

Table 1. Baseline Characteristics of ACPA+ ICI-A and RA Patients

	ICI-A (N=12)	Early RA (N=39)
Age in years, mean (SD)	71.0 (8.3)	48.2 (14.6)
Female Sex	7 (58%)	33 (85%)
White/Caucasian	9 (75%)	27 (69%)
Symptom Duration in months, median [IQR]	3.7 [1.0,11.3]	6.7 [4.0,9.7]
RF Positive	1 (8%)	27 (69%)
ACPA level (units/mL), median [IQR]	42.2 [29.4,70.5]	250 [107.5,251.0]
Obese (BMI≥30)	3 (25%)	9 (23%)
Current/Past Smoker	8 (67%)	14 (36%)
Cancer Type[†]		
Melanoma	4 (33%)	
Renal Cell Carcinoma	3 (25%)	
ICI Regimen		
PD-1/PD-L1	7 (58%)	
CTLA-4+PD-1	5 (42%)	
ICI-A Phenotype		
RA-like	9 (75%)	
PMR-like	3 (25%)	

[†] *Other cancer types in ICI-A patients included urothelial carcinoma (n=2), non-small cell lung cancer (n=2), and head and neck cancer (n=1).*

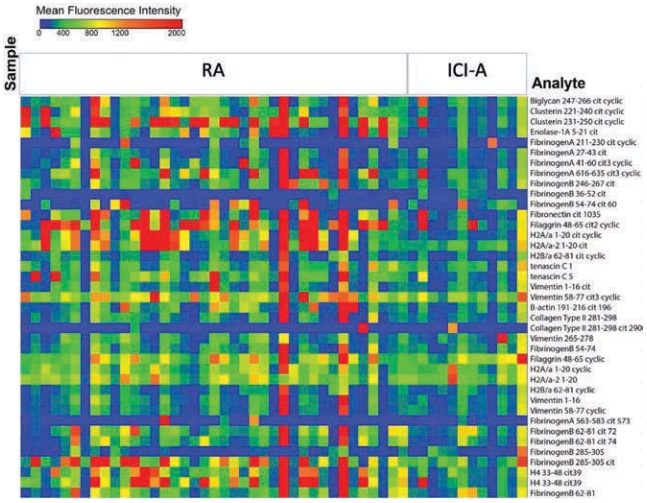

Figure 1. Heat Map of ACPA repertoire in RA Patients and ICI-A Patients.

Conclusion: ICI-A patients had lower ACPA titers and targeted fewer ACPA epitopes than early RA patients. It remains to be determined if ICI-A represents an accelerated model of RA pathogenesis with ICI triggering an early transition from pre-clinical to clinical disease. This would require sequential sampling and analysis.

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POS0418 ICE CRYOTHERAPY: A NEW STRATEGY TO REDUCE ARTERIAL INFLAMMATION IN RHEUMATOID ARTHRITIS? A STUDY IN ADJUVANT-INDUCED ARTHRITIS MODEL

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Background: Rheumatoid arthritis (RA) is characterized by endothelial activation (EA), endothelial dysfunction and vascular inflammation, leading to accelerated atherosclerosis. In the last decade, a renewed interest in cryotherapy - local or whole body - has emerged. Although growing evidence demonstrated that ice cryotherapy reduces not only pain but also disease progression, whether such therapy might blunt disorders of the systemic vasculature is unknown.

Objectives: The aim of our study was to determine the effects of a subchronic treatment with ice cryotherapy on aortic leucocyte infiltration and markers of endothelial activation in the rat adjuvant-induced arthritis (AIA) model.

Methods: AIA was induced by injection of *Mycobacterium butyricum* in Freund's incomplete adjuvant at the base of the tail in 6-week-old male Lewis rats. AIA rats were treated or not with ice applied on paws, from the onset of arthritis to the acute inflammatory stage of the disease, twice a day for 14 days. Arthritis score and paw skin temperature were daily monitored. At the end of the treatment, leucocyte infiltration and the different cell subsets (monocytes/macrophages, neutrophils, $CD4^+$ and $CD8^+$ T cells producing or not IL-17A) were measured in thoracic aorta using flow cytometry. Relative mRNA expression of cytokines/chemokines (IL-6, TNF-α, CXCL-1, MIP-1α (CCL-3), MCP-1 (CCL-2)) and adhesion molecules (ICAM-1, VCAM-1) was analyzed in thoracic aorta by RT-qPCR. X-Ray analysis of hind paws was performed to assign a radiographic score.

Results: Treatment with ice cryotherapy, that decreased skin surface temperature from 28.6 ± 0.3°C to 18.5 ± 0.2°C, reduced arthritis score (-36%, $p<0.001$) and radiographic score (-34%, $p<0.05$) with a positive effect on osteoporosis, cartilage and bone destruction. These effects were associated with a dramatic decrease in $CD4^+$, $CD8^+$ and Tc17 cell aortic infiltration as compared to untreated AIA. By contrast, ice had no effect on endothelial activation markers except VCAM-1 mRNA expression that was significantly increased ($p<0.05$). A positive correlation was found between the number of total leucocytes, monocytes/macrophages, $CD4^+$ and $CD8^+$ T cells in aorta and arthritis score.

Conclusion: In the model of AIA that reproduces arterial wall inflammation recently characterized in rheumatoid arthritis by PET/CT [1], local ice cryotherapy exerts not only local beneficial effects on the joints but also systemic benefits on vascular inflammation in large vessels. These results suggest that reduction of vascular comorbidities might be a new output of ice cryotherapy used as an adjunctive therapy in RA.

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Disclosure of Interests: None declared.

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POS0419 DIFFERENTIAL MIRNA EXPRESSION AND ENDOTHELIAL CELL FUNCTION IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Rheumatoid arthritis (RA) and Psoriatic arthritis (PsA) constitute forms of inflammatory arthritis (IA) characterised by enhanced angiogenesis, immune cell infiltration, and generation of a hypoxic microenvironment leading to an invasive synovial pannus that results in bone and cartilage destruction. However, significant differences in circulating biomarkers in addition to disease pathogenesis at the clinical, immunological, cellular, and molecular levels have been identified that differentiate the two pathotypes.

Objectives: The aim of this study was to examine circulatory miRNA as cellular biomarkers that can distinguish RA form PsA and to evaluate the potential implication for disease pathogenesis. Furthermore, this study aimed to examine the differential effect of the joint microenvironment on endothelial cell (EC) function in both RA and PsA.

Methods: RA, PsA and healthy controls (HC) were recruited from St. Vincent's University Hospital, and serum was collected. Multiplex analysis of 68 serum miRNAs was performed using the FirePlex miRNA Immunology-V2 panel (FirePlex Bioworks Inc). Receiver operator characteristic (ROC) curves were generated to determine sensitivity and specificity of specific miRNAs whilst DNA intelligent analysis (DIANA)-mirPath and STRING software were used to analyse pathways targeted by the dysregulated miRNAs. Additionally, human umbilical vein endothelial cells (HUVEC) were cultured with RA and PsA synovial fluid (SF). Angiogenesis, invasion, and cellular adhesion were quantified by Matrigel tube formation assays, wound healing assays, and adhesion assays. Real-time cellular bioenergetics was analysed in HUVEC in response to RA and PsA SF using the Seahorse XFe96 Analyser.

Results: 7 miRNAs; miR-126-3p, miR-29b-3p, miR-22-3p, miR-223-3p, miR-320a, let-7g-5e, and let-7g-5p (all**$p\leq0.01$), were significantly elevated in RA

serum compared to both PsA patients and HC, with ROC curve analysis demonstrating the predictive accuracy with which each miRNA differentiated between RA and PsA (all <0.05). Biplot analysis further identified that three miRNA, miR-29b-3p, miR-22-3p, and miR-223-3p demonstrated the greatest separation between RA and PsA (all p<0.05). DIANA and STRING analysis identified the P13K-Akt pathway as being the primary target of these 3 miRNAs with specific gene targets involved in this pathway including factors all importantly associated with endothelial cell migration, proliferation, invasion, and angiogenesis. Next, we examined the effect of the joint microenvironment on endothelial cell function and demonstrated that PsA SF significantly enhanced EC tube formation (p<0.05) and EC leukocyte adhesion (p<0.05), with RASF only significantly inducing EC leukocyte adhesion. Finally, metabolic analysis of endothelial cells demonstrated that PsA SF significantly induced baseline glycolysis (p<0.05), baseline OCR (p<0.05), maximal respiratory capacity (p<0.05) and spare respiratory capacity (p<0.05), with no effect observed for RA SF.

Conclusion: Circulating miRNAs may be valuable as diagnostic biomarkers that can distinguish RA from PsA. Additionally, the joint microenvironment induces EC function and metabolic capacity, with these effects more pronounced in response to PsA SF compared to RA SF.

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Disclosure of Interests: None declared.

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POS0420 A 10-COLOR FLOW CYTOMETRIC PANEL FOR IDENTIFYING SYNOVIAL FIBROBLAST SUBSETS IN RHEUMATOID ARTHRITIS

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Background: Synovial fibroblasts are key players in the disease pathology of rheumatoid arthritis and specific fibroblast subsets have been linked to joint inflammation and joint destruction[1]. These synovial fibroblasts can be cultured from both the easily obtained synovial fluid or the more time-consuming synovial biopsy or resection. Recently, cultured synovial fibroblasts from synovial fluid where confirmed to possess a similar phenotype to that of the synovial fibroblast podoplanin+/CD90+/human leukocyt antigen(HLA)-DR+ subset from biopsies[2].

The present advancement in our knowledge of synovial fibroblasts have been spearheaded through bulk and single cell RNA transcriptomics. Expensive techniques that may require supplementary identification of phenotype clusters and cell function on protein level.

Objectives: The objective of this work was to plan, optimise and test a multi-color flow cytometry panel for identification of known synovial fibroblast subsets linked to arthritis pathology. The primary focus was well established markers; podoplanin, CD90, CD55, HLA-DR, CD34 and fibroblast activation protein alpha (FAPa).

Methods: Several cell types were used in optimizing the panel. The majority of antibody titration was conducted on immortalized synovial fibroblasts from a patient with rheumatoid arthritis. Exclusion markers such as CD45 (blood cells) and CD31 (endothelial and monocytes/macrophages) were titrated on synovial fluid mononuclear cells and peripheral blood mononuclear cells. Finally, full panel testing on synovial fibroblasts cultured from synovial fluid was compared with immortalized synovial fibroblasts. All tests were carried out on a commercially available flow cytometer with 4-lasers (405, 488, 561 and 637nm) and 27 detectors.

Results: Several panel iterations were tested during the optimization process. Two markers, cadherin-11 and receptor activator of nuclear factor kappa-b ligand, were abandoned after testing different antibody clones for staining and several detaching solutions on fibroblasts prior to staining. Initial compensation issues were overcome by rearranging fluorochromes and using cells as CD90 compensation controls.

The final flow cytometry panel contained 10 markers; podoplanin, CD90, CD55, CD34, HLA-DR, FAPa, CD45, CD31, complement C3a receptor and a viability marker. Final testing on synovial fibroblasts cultured from synovial fluid yielded an acceptable viability > 90%. Within the synovial fibroblasts cultured from synovial fluid, the panel was able to identify podoplanin+/CD90+/FAPa+ synovial fibroblasts previously linked with joint inflammation. The panel was, furthermore, able to identify a podoplanin+/CD90+/HLA-DR+ population in the immortalized synovial fibroblasts.

Conclusion: The optimized flow cytometry panel presented here enables researchers to identify synovial fibroblasts subsets which have been linked with disease traits in rheumatoid arthritis. This panel could therefore both be useful as a supplement to transcriptomic data and as a primary interrogation tool when investigating fibroblast subsets and cell function on a protein level.

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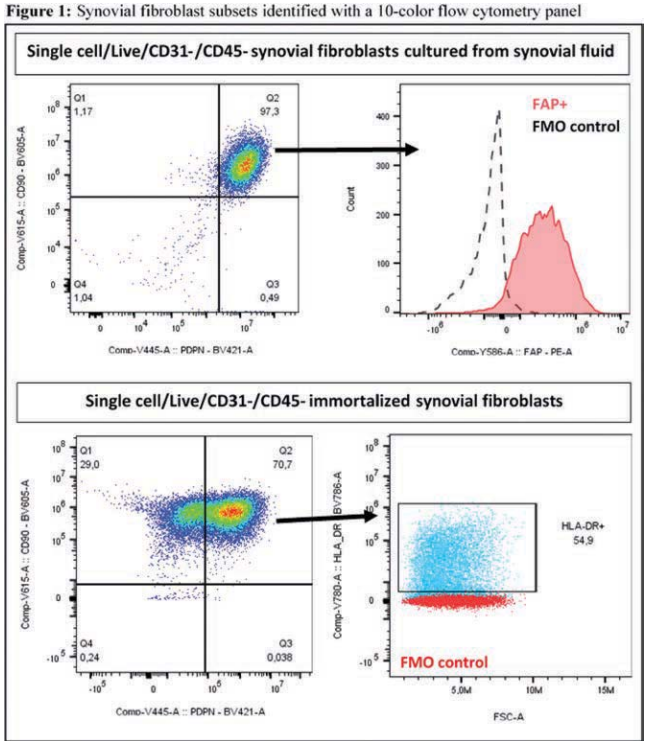
Figure 1: Synovial fibroblast subsets identified with a 10-color flow cytometry panel



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POS0422 A HISTORY OF CHLAMYDIAE INFECTION IN RHEUMATOID ARTHRITIS DEVELOPMENT

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Background: Current hypotheses for the ethiopathogenesis of rheumatoid arthritis (RA) postulate an infectious agent initiating autoimmunity, which is thought to be at the mucosal level. *Chlamydiae* infections have been previously associated to development of an acute inflammatory arthritis, which can become chronic in some patients. *Chlamydia trachomatis* was detected in synovial fluid and tissue of RA patients, at least in early disease, suggesting that this organism could be involved in initiating RA onset, at least in a subset of patients.

Objectives: To investigate the association between *Chlamydiae* infection and the development of autoimmunity and pre-clinical manifestations associated with RA.

Methods: This study was performed in an ongoing prospective study of individuals genetically at risk of developing RA, namely first-degree relatives of RA patients (RA-FDR). Individuals without clinical evidence of RA

are enrolled, and assessed yearly, clinically and biologically. We included all RA-FDRs who responded to a *Chlamydiae* infection questionnaire, and the exposure of interest was self-reported *Chlamydiae* infection. The primary outcome was autoimmunity associated with RA (seropositivity) defined by the presence of anti-citrullinated peptide antibodies (ACPA) and/or rheumatoid factors (RF) at the last visit. Seropositive inflammatory arthritis at the last visit was a secondary outcome. We used logistic regression to analyze univariable and multivariable associations, adjusting for age and gender as potential confounders.

Results: A total of 1254 RA-FDRs were analyzed, of which 168 (13.4%) had developed seropositivity. The prevalence of self-reported Chlamydia infection was significantly higher in seropositive individuals as compared to controls (17.9% versus 9.8%, P<0.01) (Table 1). A significant association between the self-reported history of *Chlamydiae* infection and the seropositivity was observed in both univariate and multivariate analyses (OR=2.00, 95% CI: 1.27-3.09; OR=1.91, 95% CI: 1.20-2.95, respectively). A sub-group of 48 RA-FDRs (4 %) presented inflammatory arthritis in conjunction with seropositivity. This subgroup, considered at highest risk for RA, reported significantly more often prior infections with *Chlamydiae* than the negative subgroup (20.8% versus 10.5%, P<0.05). The ORs for the association of self-reported history of *Chlamydiae* infection and inflammatory arthritis coupled to RA-associated autoimmunity were 2.23 (95% CI: 1.03-4.43, P<0.01, univariate analysis) and 1.91 (95% CI: 0.88-3.82, P=0.08, multivariate analysis).

Table 1. A potential association between a self-reported history of *Chlamydiae* infection and RA development

	RA-FDR with a self-reported chlamydia infection anamnesis (n=1254)		
		Univariate analysis	Multivariate analysis[1]
Study Groups	**Self-reported "infection"**	**OR (95% CI)**	**OR (95% CI)**
Seropositive RA-FDR (n=168)	30 (17.9%)	2.00** (1.27 - 3.09)	1.91** (1.20 – 2.95)
Seronegative RA-FDR (n=1063)	104 (9.8%)		
RA-FDR with seropositive inflammatory arthritis [2] (n=48)	10 (20.8%)	2.23* (1.03 – 4.43)	1.91 (0.88 – 3.82)
RA-FDR without seropositive inflammatory arthritis (n = 1206)	127 (10.5%)		

[1]Logistic regression model adjusting for age and gender.[2]Seropositive inflammatory arthritis was defined by being either: seropositive RA; seropositive "arthritis" (defined by at least one swollen joint at physical examination); seropositive with MSUS (musculoskeletal ultrasound) inflammatory activity.* P-value < 0.05** P-value < 0.01

Conclusion: Our results suggest that a history of *Chlamydiae* infection may be a risk factor for the development of RA in a subset of individuals at genetic risk for the disease. Serological analyses to assess the prevalence of antibodies to *C. trachomatis* major outer membrane protein (MOMP) are under way to confirm these preliminary data.

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POS0423 CYCLIC CITRULLINATED PEPTIDE APTAMER TREATMENT ATTENUATES COLLAGEN INDUCED ARTHRITIS

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Background: Anti-citrullinated peptide antibodies (ACPA) appear 10–15 years before the diagnosis of rheumatoid arthritis (RA) and are associated with a more severe disease course. In previous work, we rationally designed and screened ACPA-binding peptide aptamer sequences in silico and constructed a nanoparticle with chitosan and hyaluronic acid(1). A developmental stage version of this nanoparticle was able to reduce disease activity in the collagen-induced arthritis (CIA) and the serum transfer arthritis mouse models (2).

Objectives: Here, we investigated the effect and potential toxicity of three different versions of the aptamer nanoparticle (loading of 20%, 10% and 5% aptamer, respectively) in the CIA rat model.

Methods: Wistar rats (males and females) were given a single intravenous dose (100 mg/kilo) of type II collagen in PBS in the tail vein. The dosing was repeated three times with one day interval, followed by blood sample collection at day 7 after the initial collagen injection. To evaluate route of administration and dosing, we injected a single intravenous and subcutaneous dose (2.5 mg/kg) of aptamer-nanoparticles (A/N ratio 20%) in PBS in the tail vein/abdomen, and plasma concentration–time profiles were followed for 2 days after dosing with weekly blood sampling. To evaluate organ uptake, rats were given a single intravenous and subcutaneous dose (2.5 mg/kg) of aptamer-nanoparticles (A/N ratio 20%) in PBS in the tail vein/abdomen. The procedure was repeated after 24 hours. Blood and urine samples were taken once a week. A group of 10 animals was sacrificed every week over a three-week period, and the organs were processed. To examine efficacy, rats were given a single subcutaneous dose (2.5 mg/kilo) of aptamer-nanoparticles and nanoparticle controls without aptamer or PBS alone in the abdomen. The procedure was repeated once a week over a course of three weeks. Weight, joint measurement, blood, and urine samples were taken once a week. Paw swelling was measured on a weekly basis. In the plasma samples we measured CPEP2 and anti-collagen II by enzyme linked immunosorbent assay (ELISA).

Results: Using a rather high dose of collagen (100 mg/kilo) via an intravenous administration route, ACPA was measurable in all CIA rats with rapid development of RA in 82% of the included animals. Intravenous administration resulted in an immediate high plasma concentration post injection, which decreased rapidly to low levels. The s.c. administration route gave a steady, long-term aptamer release with a maximum availability 8 hours post-injection. After three aptamer-nanoparticle doses (2.5 mg/kg; either 20%, 10% or 5% aptamer), we observed a dose-dependent reduction in swollen joint count for the aptamer-nanoparticle treated groups (10 rats in each group) compared with the healthy control group (10 rats) (P-value = 2,1E-6). We observed decreased ACPA IgG levels in the rats treated with aptamer-nanoparticle. The decrease in ACPA levels correlated with the aptamer-nanoparticle having higher loading. Anti-collagen II IgG levels slightly increased towards the end of the study.

Conclusion: We developed and tested a novel peptide aptamer-based drug candidate for seropositive rheumatoid arthritis in CIA rats. Over a 3-week course of treatment with subcutaneous administration of aptamer-nanoparticles, joint swelling was decreased during treatment, and completely reversed at the end of the observation period. The reduction of joint swelling was associated with decreased levels of ACPA in the blood.

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POS0424 THE ROLE OF IL-25 REGULATING IL-17 AND ROR-γT ON TH17 IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a prevalent common autoimmune disease characterized by chronic inflammation of the joint and synovial hyperplasia and progressive destruction of articular cartilage and bone, which seriously influences a patient's quality of life.Interleukin-25 belongs to the IL-17 cytokine family newly identified. IL-25 is widely produced between tissues, IL-25 is reported to play an anti-inflammatory role in autoimmune and inflammatory diseases through the downregulation of Th1 and Th17 cell responses[1]. However, the exact role of IL-25 in the pathogenesis of RA remains to be elucidated.
Objectives: Set up CIA model to evaluated IL-25 influence in RA disease. Discuss the molecular mechanism of IL-25 how to regulate IL-17A, ROR-γt and Th17.
Methods: ①male DBA/1 mice (n=12) were induced with immunized intradermally twice with type II chick collagen (2 mg/ml) emulsified in Complete Freund's adjuvant or Incomplete Freund's adjuvant containing by tail intravenous injection.CIA mouse model was constructed. CIA were then divided into two groups, for the use of PBS (n=6) and IL-25 (0.5μg, n=6) respectively, and follow-up daily. After 42 days, mice were sacrificed and collected articular tissues, proceed pathological staining and pathological score of arthritis. ②Male DBA/1 mice were immunized with CII to induce arthritis and consecutively received rmIL-25 (1 μg/mice) or PBS for 5 days beginning from day 1 after the second immunization with CII, and the incidence of arthritis was calculated. Spleen $CD4^+$ T cells were isolated from CIA mice using Mouse $CD4^+$ T Cell Isolation Kit. Cells were stimulated with plate-bound anti-CD3 (5 μg/ml) plus anti-CD28 (2 μg/ml) in the presence or absence of recombinant mouse (rm) IL-25 (100 ng/ml) for 24 h. In some cases, control IgG (10 μg/ml) were added to the cultures. The expression of IL-17A were examined using ELISA assay and ROR-γt mRNA in the cells were measured by real-time quantitative qPCR.
Results: In vivo studies indicated that, the RA incidence and symptoms of arthritis in IL-25-treated mice were significantly reduced compared with PBS controls. Histopathologic examination showed that the knee joints of IL-25-treated mice with CIA exhibited a significant reduction in synovial hyperplasia, cartilage damage and bone erosion compared with PBS controls. The serum levels of IL-17A in IL-25-treated mice were markedly reduced compared with those in WT mice. RT-qPCR also demonstrated that the transcription levels of IL-17A and ROR-γt were decreased in the Spleen of IL-25-treated mice.
Conclusion: Systemic injection of IL-25 can reduce the onset of arthritis and joint injury in CIA mice. IL-25 can inhibit Th17 cells of CIA mice, and its target is to regulate IL-17 cytokines and Expression of ROR-γt mRNA. CIA protection is mediated by the inhibition of Th17 by IL-25.
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POS0425 METABOLIC ALTERATIONS IN ACTIVATED FIBROBLAST-LIKE SYNOVIOCYTES FROM NON-INFLAMED SUBJECTS - MIMICKING EARLY STAGE OF RHEUMATOID ARTHRITIS

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Background: Proliferative cells, such as inflamed cells, depend on altered metabolic pathways to support their active proliferation. Synovial samples from patients with rheumatoid arthritis (RA) show reprogramming of different metabolic pathways such as glucose and glutamine metabolism [1]. However, it is unknown which metabolic pathways are altered in the early phases of RA pathogenesis, when non-inflamed fibroblast-like synoviocytes (FLS) are activated to a pro-inflammatory state. Our group has created an in-vitro cell model using FLS from subjects without inflammatory arthritis (non-inflamed FLS) after activation with adiponectin and tumour necrosis factor (TNF) to mimic the early stage of RA [2].
Objectives: We aim to determine if the stimulation of non-inflamed FLS upregulates the expression of key-enzymes involved in glucose and glutamine metabolism and how the inhibition of those enzymes affects FLS activation.
Methods: FLS (passage 6-8) were isolated from synovial tissues of patients without inflammatory arthritis or osteoarthritis who underwent diagnostic arthroscopy due to a previous injury. FLS were cultured in DMEM medium (high glucose and GlutaMAX) containing 10% FBS and stimulated by known FLS-activators, i.e. TNF, interleukin 1 beta (IL-1 β), or adiponectin. For the inhibition experiments, cells were pre-treated with 25 mM 2-DG or 300 nM CB-839 for 4 hours before stimulation. Expressions of the enzymes were measured by western blot in whole-cell lysates and IL-6 was measured using ELISA in cell culture supernatants at 24 hours after stimulation. Cell proliferation was determined using MTT assay after 48 hours of stimulation.
Results: First, we compared the expression of hexokinase 2 (HK2), glutaminase C (GAC), and PFKFB3 in non-inflamed FLS before and after activation with adiponectin, TNF, and IL-1β. Expression of HK2 and GAC were upregulated in adiponectin- and TNF-activated FLS compared to unstimulated FLS. PFKFB3 was not affected by any of the stimuli. IL-1β did not affect the expression of the analysed enzymes (Figure 1A-C). As IL-1β did not affect the expression of metabolic enzymes, we continued stimulation only with adiponectin and TNF. TNF but not adiponectin significantly enhanced the proliferation of FLS without inhibition (Figure 1D). However, FLS proliferation was significantly reduced by pre-treatment with 2-DG, a glycolysis inhibitor, in unstimulated as well as TNF- and adiponectin-stimulated cells. CB-839, a glutaminase inhibitor, did not affect the proliferation of FLS (Figure 1D). Both TNF and adiponectin significantly upregulated the production of IL-6 in FLS. Pre-treatment with 2-DG significantly reduced the production of IL-6. CB-839 pre-treatment significantly reduced the production of IL-6 only in unstimulated FLS (Figure 1E).

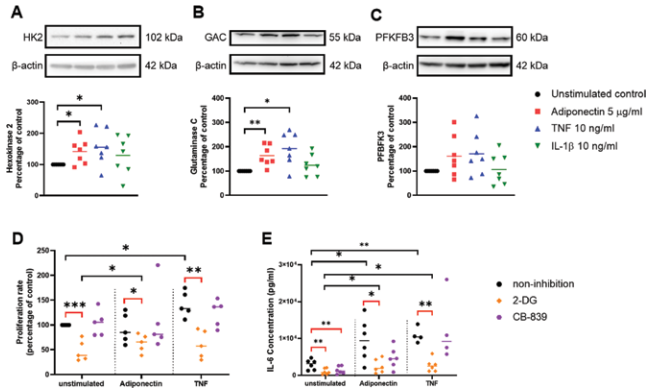

Figure 1. Metabolic alterations in non-inflamed FLS. Expression of hexokinase 2 (HK2; A), glutaminase C (GAC; B) and PFKFB3 (C) in non-inflamed FLS measured by western blot. Proliferation assay (MTT assay; D) and production of IL-6 (ELISA; E) was performed using cells treated with HK2 inhibitor 2-DG and glutaminase inhibitor CB-839. Statistical significance was determined as by one sample t test (A-C; n=7) or paired t test (D-E; n=4-6).

Conclusion: Our results show that the expression of key-enzymes regulating metabolic pathways can be enhanced by adiponectin and TNF in non-inflamed FLS. Moreover, we also show that inhibition of specific metabolic pathways can affect FLS activation differently depending on the cytokine stimulation. These results provide a deeper understanding of metabolic reprogramming in FLS in early RA.
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POS0426 BRD3 REGULATES THE INFLAMMATORY AND STRESS RESPONSE IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: Small molecule inhibitors targeting members of the bromodomain and extra-terminal (BET) protein family (BRD2, BRD3, BRD4) have anti-inflammatory properties in rheumatoid arthritis (RA). BET proteins are readers of acetylated histone side chains and activators of transcription. BRD3 is an understudied member of BET proteins.

Objectives: To analyse individual functions of BET proteins and mechanisms underlying BET inhibition in RA synovial fibroblasts (SF).
Methods: The expression of BRD2, BRD3, and BRD4 was silenced by lenti-viral transduction followed by TNF stimulation (10 ng/µl, 24h). Silencing was confirmed by Western blotting. Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000, n=3). Pathway enrichment analysis for KEGG and Reactome databases was conducted with significantly affected genes (± fold change > 1.5, FDR < 0.05). SF were treated with I-BET (1 µM) and TNF (10 ng/µl, 24h). Autophagy was evaluated by Western blotting using the conversion of LC3B as a marker (n=9). I-BET-induced global changes on post-translational histone modifications were analysed by mass spectrometry (Mod Spec, Active Motif; n=2; 120h protocol) and Western blotting (H3K27ac, H3K18ac, total acH3; n=7; 24h and 120h protocol). For this purpose, SF were stimulated with I-BET (1 µM) for 24h, and either co-stimulated with TNF (24h protocol), or washed with PBS, followed by a 24h stimulation with TNF 120h after the I-BET treatment (120h protocol).
Results: Silencing of BRD2 and BRD4 in SF was, in contrast to silencing of BRD3, associated with high levels of cell death, and therefore not analyzed further. We detected 257 and 324 differentially expressed genes (DEG) that were affected by BRD3 silencing in unstimulated and TNF-stimulated SF, respectively. 105 DEG overlapped between the two groups. DEG were enriched in inflammatory pathways such as "TNF signaling pathway", "rheumatoid arthritis", "Toll-like receptor cascades", "MAPK signaling pathway", "IL-17 signaling pathway" and "signaling by interleukins". Furthermore, pathway enrichment analysis suggested a role for BRD3 in different stress-associated pathways, including "DNA repair", "chaperone mediated autophagy", "cellular responses to stress", and "autophagy". In line with the pathway enrichment analysis, I-BET induced levels of LC3B-II in unstimulated (4.3 fold, p=0.07) and TNF-stimulated (2.9 fold, p=0.07) SF, indicating a role of BET proteins in the regulation of autophagy. To further study the mechanisms underlying I-BET-mediated suppression of gene expression, we analyzed potential effects of I-BET on histone modifications. Mod Spec analysis indicated that I-BET induced profound changes in chromatin modifications, with a global reduction of acetylation on different histone side chains. We confirmed some of these differences in independent samples. I-BET treatment reduced mean TNF-induced levels of total acH3 by 25.2% (120h; p=0.0303), of H3K18ac by 35.3% (24h; p=0.0288) and by 29.3% (120h; p=0.0373) and of H3K27ac by 41.7% (120h; p=0.0587).
Conclusion: BRD3 acts as an upstream regulatory factor that integrates the response to inflammatory stimuli and stress conditions in SF. Our data suggest that BET inhibitors do not only prevent the reading of acetylated histone side chains, but also directly affect the chromatin structure, in particular by downregulating global levels of histone acetylation.
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POS0427 PRE-INFLAMMATORY MESENCHYMAL (PRIME) CELLS IDENTIFIED BY MASS CYTOMETRY IN THE PERIPHERAL BLOOD OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Experimental evidence suggests that synovial fibroblasts (SFs) may play a central pathogenetic role in chronic inflammatory arthritis in humans. RNA of the mesenchymal marker cadherin-11 characterising SFs is overexpressed in the peripheral blood of rheumatoid arthritis (RA) patients compared to healthy donors and correlates with established polyarthritis [1]. Recently, Orange et al. using RNA sequencing and flow cytometry have identified in the peripheral blood of RA patients PRIME (PRe-Inflammatory MEsenchymal) cells, considered as the precursors to inflammatory sublining SFs, that could be used as predictors of RA flares [2].
Objectives: To test the hypothesis that circulating PRIME cells can be identified by mass cytometry in patients with active RA, as well as in patients with active psoriatic arthritis (PsA).
Methods: The expression of markers suggestive of PRIME cells, namely, cadherin-11 and/or podoplanin (both expressed on SFs), and/or CD90 (Thy-1, expressed on sublining SFs), and/or Notch-3 (expressed on endothelial cells and sublining SFs), and/or CD34 (expressed on stem cells and SFs) was evident in all 10 RA and 5 PsA-derived blood samples. Circulating PRIME cell levels were elevated in patients (0.019%±0.003%) than healthy donors (0.008%±0.002%, p=0.004). The increased PRIME cell levels were more pronounced in PsA (0.023%±0.007%, p=0.003) than RA (0.017%±0.003%, p=0.03), when compared to healthy donors. PRIME cells were also present in 2 RA synovial fluid samples, being at three-fold higher levels than in the paired blood samples. Interestingly, a fraction of circulating PRIME cells exhibited expression of HLA-DR, suggestive of antigen-presenting capacity.
Results: The expression of markers suggestive of PRIME cells, namely, cadherin-11 and/or podoplanin (both expressed on SFs), and/or CD90 (Thy-1, expressed on sublining SFs), and/or Notch-3 (expressed on endothelial cells and sublining SFs), and/or CD34 (expressed on stem cells and SFs) was evident in all 10 RA and 5 PsA-derived blood samples. Circulating PRIME cell levels were elevated in patients (0.019%±0.003%) than healthy donors (0.008%±0.002%, p=0.004). The increased PRIME cell levels were more pronounced in PsA (0.023%±0.007%, p=0.003) than RA (0.017%±0.003%, p=0.03), when compared to healthy donors. PRIME cells were also present in 2 RA synovial fluid samples, being at three-fold higher levels than in the paired blood samples. Interestingly, a fraction of circulating PRIME cells exhibited expression of HLA-DR, suggestive of antigen-presenting capacity.
Conclusion: Rare circulating mesenchymal cells with antigen-presenting properties may be of pathogenetic importance in patients with RA and PsA. Whether their measurement is clinically relevant, as well their function during chronic inflammatory arthritis, merits further studies.
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POS0428 PATHOGENETIC ROLE OF MICROPARTICLES IN RHEUMATOID ARTHRITIS

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Background: Microparticles (MPs) are fragments of surface membranes of activated eukaryotic cells. They are characterized by different dimensions (from 0.1 to 1µm) and expression of surface antigens, depending on their origin. MPs are important mediators of cell-to-cell communication as they can be internalized in a dose-dependent manner by macrophages, endothelial cells and other cell types, influencing both functional and phenotypic characteristics of the target cells. Even if MPs formation is enhanced by cell activation or apoptosis, constitutive exocytosis is a continuous ongoing process in vivo for many cells, and MPs originating from different cells can be always found in the plasma. In various autoimmune diseases, it has been found an increased number of MPs derived from activated platelets, leukocytes, vascular endothelium cells and other cell types. In Rheumatoid Arthritis (RA) an excessive production of MPs may predispose to autoimmune manifestations. Moreover, it has been speculated that MPs can stimulate the production, secretion, and transport of inflammatory factors in RA.

Objectives: We investigated the presence on the surface of RA-MPs of antigens derived from post-translationally modified proteins (citrullinated peptides and carbamylated peptides). We assumed that these specific antigens carried on the surface of RA-MPs could participate in RA pathogenetic process.
Methods: We enrolled 20 RA patients naïve for biological therapy fulfilling the 2010 American College of Rheumatology RA criteria and 20 healthy controls (HC), matched for age and sex. For each patient, laboratory and clinical data were recorded and clinical indexes were measured (TJ, SJ, CDAI, VAS pain, CDAI, SDAI, DAS28). A fasting blood sample, obtained from RA patients and HC, was centrifugated in order to obtain platelet-poor plasma (PPP), rich in MPs. Thereafter, MPs in RA patients and HC were measured using nanoparticle tracking analysis. Later on, MPs were incubated with unconjugated anti-citrullinated/carbamylated proteins antibodies and processed by flow cytometry and western blot to evaluate the surface expression of citrullinated/carbamylated antigens.
Results: Nanoparticle tracking analysis revealed a significant increase of number of MPs in RA compared to HC. Moreover, densitometric analysis showed a significative higher expression of citrullinated antigens on MPs' surface in RA than controls ($p < 0.0001$), while no substantial difference was found in the expression of carbamylated antigens. The data obtained were confirmed with the western blot which identified the cytoskeletal protein vimentin, the cytoplasmatic glycolytic enzyme alpha-enolase1 and type II collagen as the main citrullinated and carbamylated proteins carried by MPs. Finally, a relevant correlation between the expression of citrullinated and carbamylated antigens and disease activity was found (Figure 1).

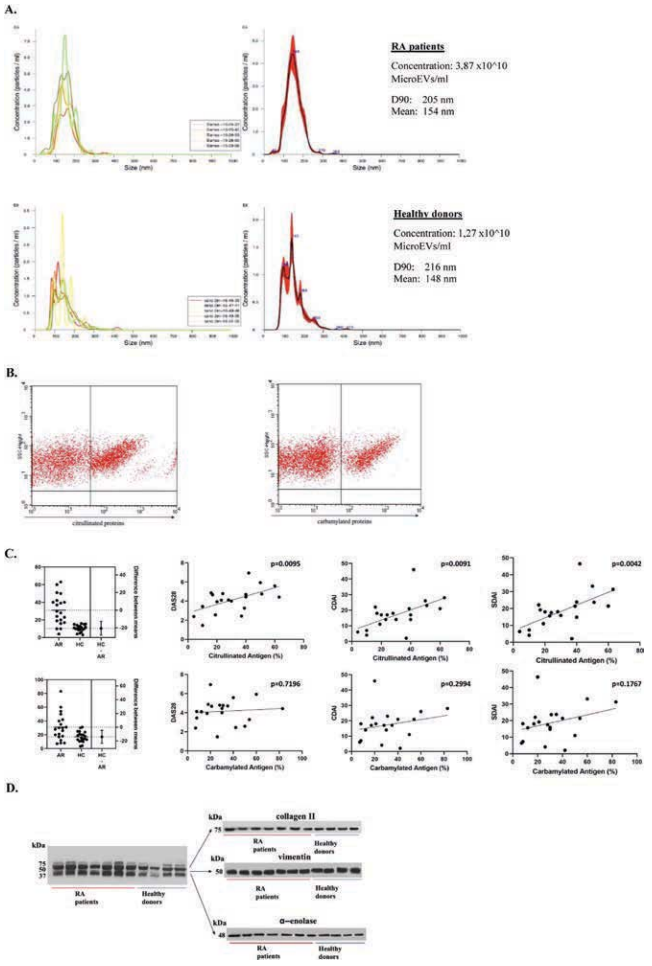

Figure 1. The figure shows: (A) concentration of MPs in RA patients and HC (nanoparticle tracking analysis); (B) expression of citrullinated and carbamylated antigens on MPs' surface in RA patients (flow cytometry analysis); (C) expression of citrullinated antigens in RA patients and HC and correlation between expression of citrullinated and carbamylated antigens on MPs' surface in RA patients and DAS28, CDAI, SDAI; (D) cytoskeletal protein vimentin, cytoplasmatic glycolytic enzyme alpha-enolase1 and collagen type II (western blot).

Conclusion: The results of this study confirm an important role of MPs in the pathogenesis of RA not only as markers of disease activity but also as possible inducers of autoimmunity.
Disclosure of Interests: None declared.
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POS0429 ACTIVATED RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS ALTER OSTEOCLAST DIFFERENTIATION AND ACTIVITY

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Background: In rheumatoid arthritis (RA), osteoclasts are one of the most important mediators of bone erosion. In addition, RA synovial fibroblasts (RASF) have a major influence on joint erosion in RA. They affect osteoclast differentiation e.g. by increased RANKL production or secretion of other pro-osteoclastogenic factors such as IL-6. In addition to the pro-osteoclastogenic effect of soluble factors such as RANKL and IL-1, visfatin inhibits osteoclast differentiation. Furthermore, visfatin increases the secretion of pro-inflammatory factors by RASF, such as IL-6 or matrix degrading enzymes.
Objectives: In this study, the effect of RASF with/without activation by visfatin and IL-1 on osteoclastogenesis was evaluated.
Methods: Blood from healthy donors and RA patients was used for PBMC isolation. RANKL, TGF-β and hM-CSF were added to induce osteoclast differentiation. RASF-conditioned media (CM) were prepared from confluent RASF cultured for 48h. Differentiating PBMCs in monoculture were compared to PBMC cultured with CM from RASF (CM: 10%, 20%, 30%) as well as in direct co-culture with RASF with/without stimulation with IL-1 (0.05ng/ml), visfatin (25ng/ml). After two weeks in culture, cells were stained using TRAP staining. 3-5 images per well were used for quantification dependent on the variability of the wells. IL-6 was measured by ELISA in supernatants collected at day 14.
Results: IL-6 production increased by IL-1 (e.g. co-culture: 2,8-fold) and visfatin (CM-visfatin: 10%=4,3-fold, 20%=5,4-fold, 30%=4,2-fold; co-culture: 9,5-fold) compared to unstimulated control in all settings. In addition, IL-6 was increased with the addition of CM compared to unstimulated controls (healthy donors CM 30%: unstimulated p=0.0342, IL-1 p=0.0133, visfatin p=0,0133; RA: unstimulated p=0.0133, IL-1 p=0.0342, visfatin p=0.0133, n=3 each). Of note, baseline IL-6 concentrations were higher in PBMC from RA patients compared to healthy donors. Co-culture showed an additional increase in IL-6 levels in all settings (e.g. monoculture: IL-1 4.71±5.75pg/ml, visfatin 141.09±182.79pg/ml; co-culture: IL-1 7241±10398pg/ml, visfatin 24535±16994pg/ml;). During osteoclast differentiation, addition of CM showed similar osteoclastogenesis with similar proportion of osteoclasts with 2 and 3-5 vs. higher numbers of nuclei per cell compared to control. In coculture with RASF osteoclasts showed a stronger TRAP signal compared to monoculture especially for unstimulated and IL-1 stimulated co-cultures.
Conclusion: Both, in monoculture with CM and in coculture, IL-6 levels were increased compared to control, whereas in RA patients the IL-6 levels were higher compared to healthy donors. The CM containing secreted factors of RASF did not have a prominent influence on osteoclastogenesis. However, the presence of RASF increased the TRAP signal showing an increased activity of differentiated osteoclasts especially in unstimulated and IL-1 stimulated co-cultures but not with addition of visfatin.
REFERENCES: None.
Disclosure of Interests: None declared.
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POS0430 SYNOVIAL FLUID-DERIVED EXTRACELLULAR VESICLES FROM RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS MODULATE DIFFERENT HIPPOCAMPAL SYNAPTIC ACTIVITIES

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Background: Accumulating evidence suggests that poor mental health is one of the most common comorbidities of both rheumatoid arthritis (RA) and osteoarthritis (OA) [1]. Even if underpinning RA and OA are different genetic, structural, mechanical, and immunologic pathways involved in their pathogenesis, poor mental health, and joint involvement are intertwined and negatively affect their mutual course by contributing to global disability. Thus, new insights into mechanisms that link these disorders are needed to identify new actionable biomarkers to drive more personalized therapeutic strategies. Amidst potential mediators, extracellular vesicles (EVs) play a central role in terms of communication between cells, they cross the blood-brain barrier and based on their cargos can affect the recipient cell function [2].
Objectives: To isolate EVs from synovial fluid (SF) in RA and OA patients and to evaluate if and how these EVs can alter in vitro synaptic transmission of murine hippocampal neurons.
Methods: In this cross-sectional pilot study, consecutive adult RA and primary OA who were referred to the Rheumatology Unit for aspiration of joint effusion were enrolled. Demographic and clinical variables and mental health rating scales were collected. Discarded SF were collected and EVs were isolated and analyzed by Malvern NanoSight NS300 system to obtain information on their number and size. Afterwards, DIV14 cultured wild-type hippocampal neurons were exposed for two hours to OA- and RA-EVs at low and high concentration EVs. Thus, miniature excitatory and inhibitory postsynaptic currents (mEPSCs and mIPSCs), which reflects glutamatergic and GABA-ergic activity respectively, were examined by exploiting patch-clamp recordings in the whole-cell configuration. Frequency and amplitude were analyzed to evaluate potential changes at the presynaptic or postsynaptic compartment. Mann Whitney test was used to compare two different samples.
Results: Eight RA patients (7 female, mean age 57 yrs), and 5 primary OA (4 female, mean age 60 yrs) were recruited for SF aspiration. The mean VAS pain was 7.25 in RA and 6.5 in OA. No statistically significant differences were found between the two groups in mean rating scale scores although patients affected by RA had more severe depressive symptoms (Montgomery Asberg Depression Rating Scale -MADRS- means scores: 16.57) with respect OA group (MADRS mean scores: 10). The Nanoparticle tracking analysis showed that RA-EVs were significantly more in number compared to OA-EVs (Figure 1 A), mimicking more inflammation, while no significant difference in size was observed. Analysis of miniature events revealed the occurrence of two different changes. High concentration of OA-EVs has led to an increased amplitude of excitatory events, meaning an increased susceptibility of neurons to glutamate in the post-synaptic compartment (Figure 1 B). Whereas low concentration of RA-EVs has led to a decreased frequency of inhibitory events, which reflects a reduced function of GABA-ergic synapse in the pre-synaptic compartment (Figure 1 C).

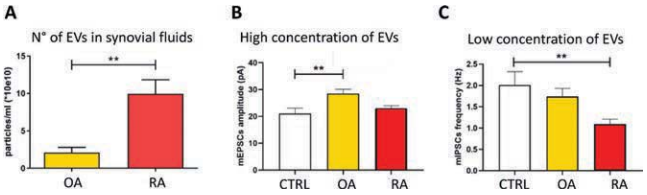

Figure 1.

Conclusion: Our results suggest that SF-derived EVs from OA and RA patients lead to different specific changes of neurotransmission, with different concentration needed to alter neuronal spontaneous activity in post-synaptic and pre-synaptic compartment, respectively. EVs may provide insight into the pathogenesis of joint-brain communication in RA and OA, unraveling specific pathways thus allowing targeted therapies for neuropsychiatric involvement.
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[2] FASEB Bioadv 2021;3(9):665-675

Disclosure of Interests: Lavinia A. Coletto: None declared, Francesca Ingegnoli: None declared, Clara Cambria: None declared, Laura Cantone: None declared, Orazio De Lucia: None declared, Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Lilly, Pfizer, Fresenius-Kabi, MSD, UCB, Roche,Janssen, Novartis, Sandoz, Consultant of: Abbvie, Amgen, BMS, Celltrion, Galapagos, Lilly, Pfizer, MSD, UCB, Janssen, Novartis, Sandoz, Valentina Bollati: None declared, Massimiliano Buoli: None declared, Flavia Antonucci: None declared.
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POS0431 PDGF-BB, TNF-α, AND LT-β REGULATE FOLLICULAR DENDRITIC CELL DEVELOPMENT IN THE RHEUMATOID SYNOVIUM

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Background: Follicular dendritic cells (FDCs) fundamentally contribute to the formation of synovial ectopic lymphoid-like structures in rheumatoid arthritis (RA) which is associated with poor clinical prognosis. Despite this critical role in RA pathogenesis, FDC development in the RA synovium has not been fully elucidated.
Objectives: To investigate the role of TNF-α/LT-β and PDGF-BB in the ontogeny of RA synovial FDCs and the differentiation of lymphoid and fibroid RA synovitis.
Methods: RA Synovial tissues were obtained from the Pathobiology of Early Arthritis Cohort (PEAC) of the Centre for Experimental Medicine and Rheumatology of Queen Mary University of London. RNA-Seq analysis and confocal imaging of early and late FDC differentiation markers were carried out and the stromal cell subsets were sorted by flow cytometry. The stromal cell subsets were treated with TNF-α/LT-β and/or PDGF-BB and the expression of FDC differentiation genes was assessed by qPCR. Germinal centre reactions were setup *in vitro* using TNF-α/LT-β activated stromal cells, and antibody production by naive human B cells stimulated with anti IgM was measured by ELISA.
Results: Our results indicate that PDGF-BB induces the FDC marker CNA.42$^+$ on NG2$^+$/αSMA$^+$ type-1 pericytes, stimulates THY-1 and αSMA gene expression, and strongly correlates with fibroid synovitis using RNA-Seq analysis. On the other hand, TNF-α/LT-β downregulate PDGFR-β, THY-1, αSMA; induce CD21, FcγRIIB expression, and significantly correlate with lymphoid synovial pathotype. Ultrastructural examination of antigen trapping on TNF-α/LT-β-activated RA synovial fibroblasts (RASFs) showed periodically retained surface antigens and these fibroblasts were able to induce T cell independent B cell activation in *in vitro* germinal centre reactions. The transition from an early PDGFR-β$^+$ pre FDCs to a late TNF-α/LT-β-responsive mature FDCs is promoted by PDGF-BB. PDGF-BB induces TNF-αR expression in RASFs and facilitates B cell recruitment via pericyte CXCL13 expression and stromal cell migration.
Conclusion: To the best of our knowledge, this is the first report describing the crosstalks between PDGF-BB and TNF-α/LT-β in FDC development in the rheumatoid synovium and its association with the evolution of lymphoid and fibroid synovitis. Selective targeting of this interplay could inhibit FDC differentiation and potentially ameliorate RA in clinically severe and drug-resistant patients.
Disclosure of Interests: None declared.
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POS0432 MDSCS IN THE INFLAMMATORY JOINT OF SKG MICE HAVE BOTH T CELL SUPPRESSIVE ABILITY AND OSTEOCLAST DIFFERENTIATION POTENTIAL

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Background: Myeloid-derived suppressor cells (MDSCs) are heterogeneous immature myeloid cells with suppressive functions (1). It is known that MDSCs are expanded in inflammatory sites after migrating from bone marrow (BM) or spleen. Rheumatoid arthritis (RA) is an autoimmune disease characterized as polyarthritis. Although previous reports indicate that MDSCs are increased in BM

and spleen of arthritis model mice, detailed analysis of MDSCs in inflammatory joints is limited.

Objectives: The purpose of this study is to characterize the MDSCs in the joints of autoimmune arthritis.

Methods: We isolated $CD11b^{+}Gr1^{+}$ cells as MDSCs from joints (Jo-MDSCs), bone marrow (BM-MDSCs) and spleen (Sp-MDSCs) of arthritis-induced SKG mice, and investigated differential expressed genes (DEGs) among MDSCs from three tissues by microarray expression analysis. Furthermore, we analyzed the suppressive function of each MDSCs by investigating the effect of them on T cell -proliferation and the osteoclast differentiation of each MDSCs stimulated by M-CSF and RANKL.

Results: Microarray analysis revealed that Jo-MDSCs highly expressed immunosuppressive DEGs (*Pdl1, Arg1, Egr2* and *Egr3*) compared to BM MDSCs or Sp MDSCs. In addition, Jo-MDCSs highly expressed NF-κB non-canonical pathway DEGs (*Nfkb2* and *Relb*), which are related to osteoclast differentiation. BM-MDSCs differentiated into osteoclasts but didn't suppress T cell-proliferation and Sp-MDSCs suppressed T cell-proliferation but didn't differentiate into osteoclasts. On the other hand, Jo-MDSCs was found to have both functions: T cell suppression and osteoclast differentiation potential.

Conclusion: Jo-MDSCs have a strong inhibitory effect on T cell proliferation and have the ability osteoclast differentiation potential.

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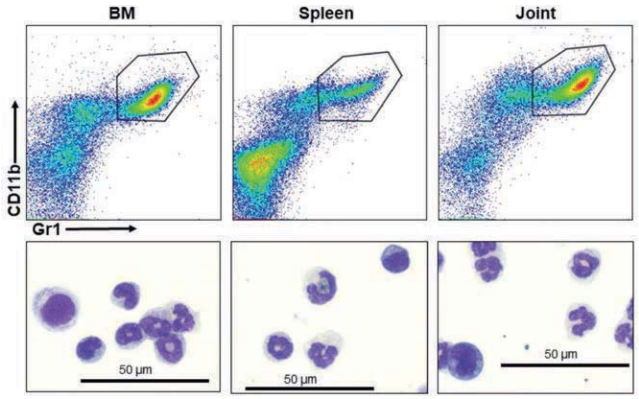

Figure1 Detection of BM-, Spleen- and Joint-MDSC from autoimmune arthritis-induced SKG mice. Representative flow cytometry plots of total MDSCs (CD11b+Gr1+ cells) (upper), May-Giemsa staining of CD11b+Gr1+ cells (MDSC) isolated from BM, spleen and joints of arthritic SKG mice (lower).

Disclosure of Interests: None declared.

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POS0433 POTENTIAL THERAPEUTIC EFFECTS OF NARINGENIN ON RA THROUGH SUPPRESSING P2X7R/NLRP3 MEDIATED PYROPTOSIS BY TARGETING ESR

H. Wang[1], Y. Zhang[1]. [1]*Qilu Hospital, Department of Clinical Laboratory, Jinan, China*

Background: Naringenin (NAR), a partial agonist on estrogen receptor, is naturally occurring flavonoids in grapes and grapefruits. We previously reported that NAR in patients with Rheumatoid arthritis (RA) have changed significantly [1]. However, the role and mechanism of action of NAR in RA remain unclear.

Objectives: This study aimed to determine the roles and mechanisms of NAR on RA and provides a basis for NAR to become a potential therapeutic agent for RA.

Methods: This study employed bovine type II collagen-induced arthritis (CIA) rats, in vitro mononuclear cells (MNCs) as models to explore the potential therapeutic effects and mechanisms of NAR on RA.

Results: Rats following NAR injections showed significantly alleviated CIA, while the proportion of NK cells decreased. After CIA rats were injected with both NAR and NK cells, the rats remained joint inflammation. NAR decreased the proportion of NK cells in RA MNCs. However, NAR did not directly affect the NK cell activation and their cytokine production. NAR suppress pyroptosis in THP-1 cells (Figure 1). The NAR activate the ESR1 in macrophage. NAR significantly increased histone deacetylase 1 gene (HDAC1) activation in macrophage. NAR significantly increased P2X7R expression and decreased NLRP3 expression in macrophage.

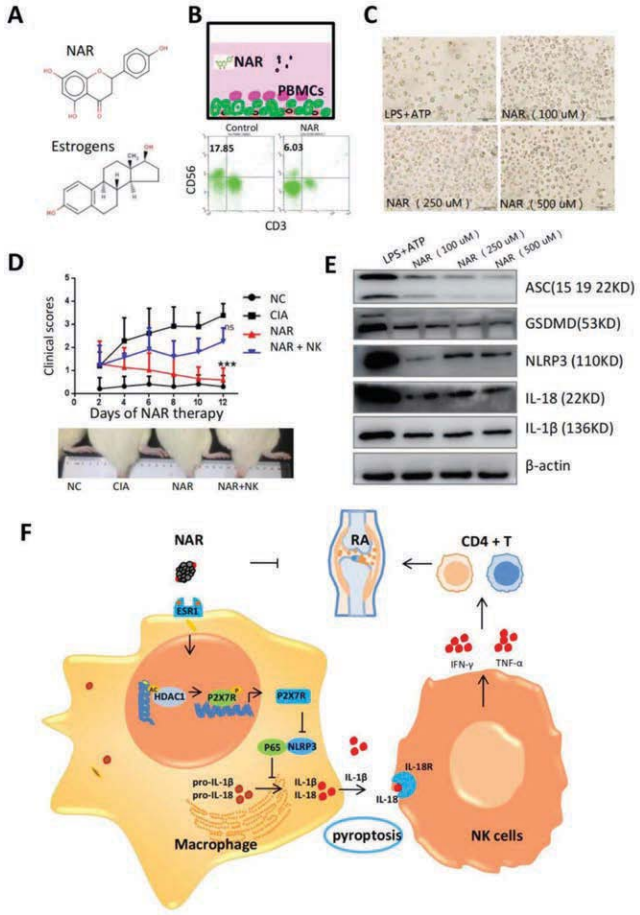

Figure 1. Effect of NAR on RA in vitro and in vivo. A The chemical structures of NAR and Estrogen. **B** Flow cytometry assay of NK cells in MNCs with treatment of NAR. **C** The morphology of THP-1 cells with treatment of NAR. **D** Joint inflammation of CIA rats with treatment of NAR and NK cells. **E** The expression level of pyroptosis -related protein was tested by western blot (WB). **F** Pattern diagram explaining therapy mechanism of NAR to RA.

Conclusion: NAR has therapeutic effects for CIA and RA through suppressing P2X7R/NLRP3 mediated pyroptosis by targeting ESR.

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Disclosure of Interests: None declared.

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POS0434 A NOVEL TARGET FOR TREATMENT OF INFLAMMATORY JOINT DISEASES

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Background: A significant number of patients with inflammatory joint disorders do not respond or experience a waning effect to currently available pharmaceuticals, which emphasizes a high medical need for new efficacious drugs operating through novel targets and modes of action. One unexplored novel target is Bile Salt-Stimulated Lipase (BSSL). We have shown that patients with rheumatoid arthritis (RA), psoriasis arthritis (PsA), and juvenile idiopathic arthritis (JIA) have increased BSSL plasma levels compared to healthy controls, and that these levels correlate with disease activity scores. Moreover, conventional BSSL knockout mice are protected from developing disease in several recognized in vivo arthritis models and antibodies targeting BSSL prevent or mitigate arthritis in rodent models[1].

We have further shown that BSSL is secreted from activated granulocytes, binds to monocytes and stimulates their migration in vitro. With that knowledge, we developed a humanized anti-BSSL antibody (SOL-116) that blocks BSSL from binding to monocytes and we are now evaluating SOL-116 as candidate drug for treatment of chronic inflammatory joint diseases, including RA, PsA and JIA in man.

Objectives: The aim of the present study was to characterize SOL-116's biological activity in vitro and verify the therapeutic efficacy in the pristane induced arthritis (PIA) rat model.

Methods: The affinity of SOL-116 to human, mouse and rat BSSL was measured by surface plasmon resonance biosensor technology. The epitope on human BSSL was mapped by hydrogen deuterium exchange mass spectrometry (HDX-MS) and confirmed by crystallization of SOL-116 Fab-fragments with human BSSL. For efficacy evaluation, arthritis was induced in DA rats by administration of pristane. SOL-116 at three different doses (10, 30 and 90 mg/kg) or vehicle control were administered subcutaneously on day 5, 10 and 15 after disease induction. Disease activity was evaluated daily from day 7 in a blinded fashion using a macroscopic scoring system of the four limbs. To gain knowledge about the mechanism of action, the effect of SOL-116 on BSSL induced cell migration was evaluated using a transwell migration assay.

Results: SOL-116 binds to human, mouse, and rat BSSL, although a single amino acid deviation in the BSSL epitope results in approximately 80-fold lower affinity to rodent compared to human BSSL protein. In the efficacy validation study, treatment with highest dose SOL-116 (90 mg/kg) significantly mitigated disease severity in the PIA rats (Figure 1A). The relatively high doses of SOL-116 were chosen to compensate the low affinity for rat BSSL. A decrease in disease severity was also seen with SOL-116 at 30 mg/kg and 10 mg/kg, indicating a dose response, albeit not statistically significant. The plasma concentration of SOL-116 at day 19 correlated significantly to the arthritis score (Figure 1B). Mechanistic studies show that BSSL stimulates migration of CD14+ monocytes, and that SOL-116 prevents this effect in a dose dependent manner.

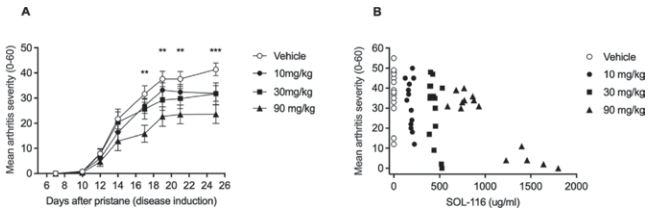

Figure 1. Arthritis development and SOL-116 exposure in rats following pristane injection. (**A**) Animals treated with SOL-116 (90 mg/kg) show significantly lower disease severity compared to vehicle treated animals. Results are presented as mean ± SEM. (**B**) Plasma concentration of SOL-116 at day 19 in animals treated with 90 mg/kg correlates to disease severity.

Conclusion: The present study verifies that BSSL plays an important role in inflammation and that SOL-116 is a promising biologic drug candidate for novel treatment of chronic inflammatory joint diseases.

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POS0435

IMPACT OF COMBINATION THERAPY WITH CSDMARDS ON THE EFFECTIVENESS OF BIOLOGIC OR TARGETED SYNTHETIC DMARDS IN A REAL-LIFE SETTING: RESULTS FROM THE SWISS RHEUMATOID ARTHRITIS REGISTER (SCQM-RA)

B. Gilbert[1], D. Mongin[1], E. Nham[1], D. Courvoisier[1], K. Lauper[1,2], C. Laedermann[3], R. Müller[4], A. Finckh[1]. *[1]Geneva University Hospitals, Division of Rheumatology, Geneva, Switzerland; [2]Centre for Musculoskeletal Research University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom; [3]Eli Lilly, (Suisse) SA, Vernier, Switzerland; [4]Kantonsspital, Division of Rheumatology, Aarau, Switzerland*

Background: Management guidelines of RA suggest to administer biological or targeted synthetic DMARD (b/tsDMARD) in combination with conventional synthetic DMARD (csDMARD). Limited data exists about the impact of such csDMARD combination therapy (co-therapy) in real life settings, in particular for baricitinib use compared to other types of b/tsDMARD.

Objectives: To assess the impact of concomitant csDMARD prescription on b/tsDMARD maintenance, in a real-world setting.

Methods: This is a nested cohort study within the Swiss registry of RA patients (Swiss Clinical Quality Management (SCQM-RA)), of treatment courses with bDMARDs or baricitinib (BARI) initiated between 2017-09-01 and 2020-06-01, with at least one follow-up visit. We compared the time-to-drug-discontinuation (drug maintenance), as a measure of drug effectiveness of b/tsDMARDs, with or without csDMARD co-therapy. Our exposure of interest was the impact of csDMARD co-therapy compared to monotherapy in 3 categories of b/tsDMARDs: baricitinib (BARI), TNFi inhibitors (TNFi) and other modes of action bDMARDs (OMA). Co-therapy was defined as receiving at least one csDMARD during at least 40% of the b/tsDMARD treatment courses (TC) duration. Baseline characteristics were compared using t-tests or χ^2. Survival Kaplan-Meier curves, with Log-rank test, were used to assess time-to-discontinuation. Cox models were applied to obtain adjusted hazard ratios (HR) using age, BMI, corticosteroid treatment, CDAI score, disease duration, smoking, line of therapy, seropositivity, gender as covariates. Missing baseline CDAI values were imputed using linear model with quadratic regression time.

Results: 1065 TC were included (273 BARI, 319 OMA, 473 TNFi), about half of which were initiated with csDMARD co-therapy (Table 1). In the co-therapy groups, csDMARD were taken on average 98% of the TC duration. Methotrexate was the most prescribed csDMARD (Table 1). Even after adjustment, we found no difference in drug maintenance with and without concomitant csDMARD in the BARI group (crude p = 0.67; HR co-therapy 2.17, 95% CI [0.61;7.77], p = 0.16) and in the TNFi group (crude p = 0.13; HR co-therapy 1.24, 95% CI [0.56;2.74], p = 0.60). Adjusted drug maintenance with or without csDMARD was also similar in the OMA group, despite non-adjusted p-value in favor of monotherapy (Figure 1) (crude p = 0.007; HR co-therapy 0.66, 95% CI [0.25;1.80], p = 0.39).

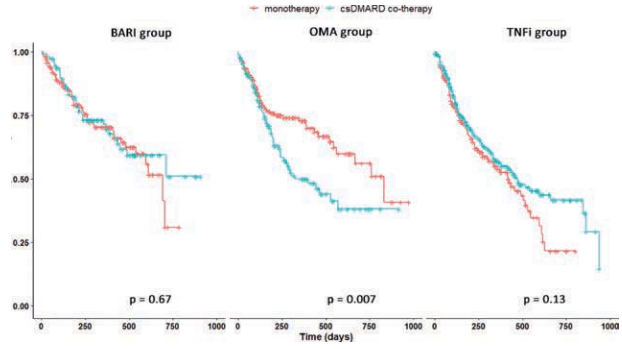

Figure 1. Drug maintenance of monotherapy vs csDMARD co-therapy (Non-adjusted Kaplan-Meier).

Conclusion: Our data suggest that drug maintenance of BARI, OMA and TNFi, were not significantly modified by concomitant csDMARD therapy.

Disclosure of Interests: Benoit GILBERT Speakers bureau: Once for Lilly, outside of the presented work., Denis Mongin: None declared, Eric Nham: None declared, Delphine Courvoisier: None declared, Kim Lauper Speakers bureau: for Pfizer, Viatris and Celltrion, outside of the submitted work., Consultant of: for Pfizer, outside of the submitted work., Cedric Laedermann Employee of: Currently employed by Eli Lilly., Rüdiger Müller: None declared, Axel Finckh Speakers bureau: Lilly, Grant/research support from: Research Grant by Lilly, to the rheumatology division.

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Table 1. Baseline characteristics of studied population

	BARI			OMA			TNFi		
	BARI	BARI + csDMARD		OMA	OMA + csDMARD		TNFi	TNFi + csDMARD	
	n = 164	n = 109		n = 170	n = 149		n = 183	n = 290	
	Mean (SD)			Mean (SD)			Mean (SD)		
Variable	Otherwise: %*		p values	Otherwise: %*		p values	Otherwise: %*		p values
Prednisone	21 %	24 %	0.73	22 %	29 %	0.18	20 %	20 %	1.00
Line of Therapy									
- 1st (= bio-naive)	17 %	18 %	**0.04**	19 %	22 %	0.51	42 %	51 %	0.15
-2nd	17 %	24 %		24 %	22 %		26 %	20 %	
-3rd	24 %	11 %		27 %	20 %		14 %	10 %	
-4th or later	42 %	48 %		31 %	36 %		19 %	18 %	
Female	82 %	73 %	0.14	75 %	71 %	0.42	81 %	70 %	**0.01**
Age	60 (15)	57 (11)	**0.05**	60 (13)	57 (12)	**0.03**	52 (16)	53 (14)	0.66
Disease duration (years)	13 (10)	12 (9)	0.82	11 (9)	11 (10)	0.58	9 (10)	8 (8)	0.36
CDAI baseline	19 (10)	18 (8)	0.53	20 (14)	21 (12)	0.53	18 (10)	18 (11)	0.64
Seropositivity	77 %	72 %	0.35	74 %	75 %	0.96	68 %	71 %	0.64
csDMARD type									
- MTX	-	48 %	-	-	50 %	-	-	60 %	-
- MTX + other	-	2 %		-	5 %		-	4 %	-
- Other	-	50 %		-	45 %		-	36 %	-

TC = treatment course, BARI = baricitinib, TNFi = TNF inhibitors, OMA = Other Mode of Action drugs, DMARDs = Disease Modifying Anti-Rheumatic Drugs, csDMARDs = classical synthetic DMARDs, SD = standard deviation. CDAI = Clinical Disease Activity Index. csDMARD = conventional synthetic DMARD. MTX = Methotrexate. Other: Other csDMARD. * Percentages relate to total n treatment courses. p values in bold highlight statistically significant difference between respective groups. All % mean and SD values are rounded to integers.

POS0436

EFFECT OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS ON LUNG MICROENVIRONMENT IN RHEUMATOID ARTHRITIS-ASSOCIATED LUNG DISEASE ANIMAL MODELS

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Background: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is one of the pivotal extrapulmonary conditions. However, the pathophysiology of RA-ILD, including the effect of disease-modifying anti-rheumatoid drugs (DMARDs) is largely unknown.
Objectives: To study the effect of methotrexate and TNFα inhibitor on lung microenvironment of SKG mice using single-nucleus RNA sequencing.
Methods: At age eight to ten weeks, male SKG mice received a single intraperitoneal zymosan A (ZyA) injection to induce arthritis and pneumonitis. We gave them twice-weekly intraperitoneal injections of PBS, methotrexate (7.5 mg/kg; MilliporeSigma), or TNFα inhibitor (100 μg/kg; R&D Systems, Inc., Minneapolis, MN, USA). Nuclei were prepared from frozen lung tissue under ribonuclease-free conditions by a method adapted from an existing protocol.
Results: Macroscopically, pneumonitis was most evident in SKG mice with ZyA and methotrexate treatment; multiple inflammatory cell aggregations were observed. In mice with ZyA and TNFα inhibitor, there were a few perivascular inflammatory cell aggregations as in the mice with ZyA and PBS, compared with the mice without ZyA. A total of 59,860 nuclei were obtained from sixteen mice, four mice from each of the four groups. We classified each cell type using previous reports on the single-nucleus cells of mouse lungs. The most frequently observed cell was the type 2 alveolar (AT2) cell among all four groups. Alveolar epithelial cells were further subclustered into six clusters (Figure 1). Cluster 2 highly expressed type 1 alveolar (AT1) cell marker genes. In mice without ZyA, cluster 0 predominated relative to cluster 1. This proportion was inverted in mice with the ZyA injection, where cluster 1 predominated. TNFα inhibitor treatment reversed the proportion, with cluster 0 predominating in this group. On the other hand, methotrexate treatment further accentuated the predominance of cluster 1 over cluster 0. Interestingly, a distinct cluster 3 was observed after methotrexate treatment. This distinctive alveolar epithelial cell cluster (cluster 3) showed IL-1, TNF, IFNα, and IFNγ perturbation-response signatures using Library of Integrated Network-Based Cellular Signatures (LINCS) 1000 ligand perturbation analysis. In addition, enrichment analysis revealed that cluster 3, as well as cluster 2 (i.e., AT1 cells) significantly enriched genes of BMI1 knockout mice that fail to self-renew their lung cells after damage.
Conclusion: The current study shows that methotrexate exacerbates lung inflammation via attenuation of the regenerative potential of AT2 cells.

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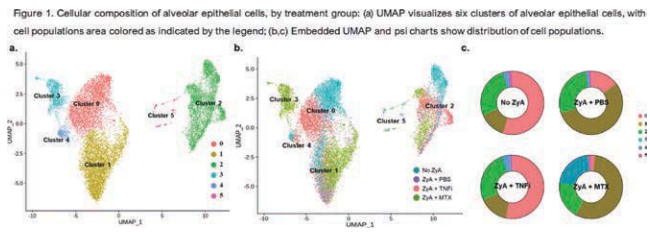

Figure 1. Cellular composition of alveolar epithelial cells, by treatment group: (a) UMAP visualizes six clusters of alveolar epithelial cells, with cell populations area colored as indicated by the legend; (b,c) Embedded UMAP and psi charts show distribution of cell populations.

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POS0437

CIRC_ 0003972 STUDY ON FIBROBLAST LIKE SYNOVIAL CELLS IN RHEUMATOID ARTHRITIS THROUGH IMMUNE REGULATION

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Background: Rheumatoid arthritis (RA) is a common chronic autoimmune disease involving multiple joint symmetry. The main pathological changes are fibroblast like synovial (FLS) cell proliferation and bone destruction. Circular RNA (circrna) is a special type of noncoding RNA formed by reverse splicing of linear RNA, which has high stability in organisms. Research shows that circ_ 0003972 is a circrna found to be significantly up-regulated in RA patients in recent years, and its level is significantly positively correlated with DAS28 score and patients with joint tenderness (Wen et al, 2020b)[1]. However, The role of CIRC_0003972 in the pathological progression of RA synovium has not been confirmed. Our research aims to reveal Role of Circ_0003972.
Objectives: Circular RNAs (circrnas) have been shown to play an important role in the progression of RA. The purpose of this study is to explore Circ_ 0003972 Role and mechanism of in the progression of RA.
Methods: The gene expression was determined by real-time quantitative PCR. The proliferation and apoptosis of human RA fibroblast like synovial (fls-ra) cells were measured by cell counting kit 8, edu staining and flow cytometry. Western blot analysis was performed to measure protein expression, and ELISA was used to check

the concentration of inflammatory factors. Double luciferase reporter gene detection and rip detection confirmed mir-654-5p and Interaction between Circ_0003972.
Results: Circ_0003972 is expressed in RA patients and fls-ra cells. Circ_ 0003972 knockdown inhibits proliferation and inflammation and promotes TNF-α Flra-induced apoptosis. Mir-654-5p is down regulated in RA patients and fls-RA cells, and it can be expressed by Circ_ 0003972 absorption. Mir-654-5p inhibitor reversed Circ_0003972 silencing on TNF-α Effects of induced hfls-RA on cell proliferation, inflammation and apoptosis.
Conclusion: Circ_0003972 may promote the proliferation and inflammation of FLS-RA cells and accelerate the pathological progress of RA by regulating mir-654-5p.
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POS0438 IDENTIFICATION OF ANTI-CYTOKINE AUTOANTIBODIES WITH POTENTIAL TO PREDICT FLARE IN RHEUMATOID ARTHRITIS PATIENTS UNDERGOING BIOLOGICAL THERAPIES: A DISCOVERY STUDY

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Background: The presence of anti-cytokine autoantibodies (ACAAs) seems to be a physiologic mechanism to control the immune response and regulate cytokine activity. Biological therapies also regulate cytokine activities and have greatly improved the quality of life of RA patients. However, alteration of the cytokine network by the use of these treatments may lead to a disbalance in the regulatory system of ACAAs. We hypothesize the ACAAs network may influence the course of immune response in RA patients and may be useful to predict the therapy efficacy.
Objectives: We aimed to explore the potential of circulating ACAAs to predict flare in a cohort of RA patients treated with biological therapy.
Methods: We employed sera at baseline from 194 RA patients of the clinical trial OPTIBIO[1] (A Coruña), whose primary endpoint is to evaluate the usefulness of standardized protocol strategies of dose reduction in patients with RA in clinical remission treated with biologics. These patients were treated with TNF inhibitors (Etanercept, N=47; Infliximab, N=12; Adalimumab, N=35; Certolizumab (CTZ), N=17; Golimumab, N=5), Tocilizumab (TCZ, N=60) and Abatacept (ABA, N=18). Patients were in clinical remission (DAS 28 <2.6 or SDAI <5 or ACR/EULAR 2011 criteria) at least from 6 months. Patients were followed during a minimum period of one year and maximum period of 3 years. Flare was considered when remission criteria were not fulfilled. The bead-based antigen array MILLIPLEX MAP Human Cytokine Autoantibody Magnetic Bead Panel was used for the simultaneous detection and quantification in sera of anti-BAFF, anti-G-CSF, anti-IFNβ, anti-IFNγ, anti-IL-1α, anti-IL-6, anti-IL-8, anti-IL-10, anti-IL-12 (p40), anti-IL-15, anti-IL-17A, anti-IL-17F, anti-IL-18, anti-IL-22, and anti-TNFα. Non-parametrical tests, ROC curves and logistic regressions were performed for the statistical data analysis using SPSS. P-value < 0.05 was considered statistically significant.
Results: The levels of anti-17A and anti-IL-1α were increased in the sera from patients who suffered a flare during the follow-up period (N= 76), compared to those who remained in remission (N= 118), showing an area under the curve (AUC) of 0.586 and 0.594, respectively. Segregating by treatment, the levels of anti-17A were specifically increased in those relapsing patients under CTZ (N=6), ABA (N=12) and TCZ (N=20) treatment. The AUC of anti-17A within these three therapies was 0.867, 0.903 and 0.682, respectively. Logistic regression analysis also associated the levels of anti-17A with the risk of suffering a flare in TCZ-treated patients (OR=1.11; p=0.015, for 100 MFI increase). In addition, the TCZ-treated patients who suffered a flare also showed higher levels of anti-IL17F, anti-IL-1α, and anti-IL-18 compared to those that remained in remission, showing AUCs of 0.689, 0.657 and 0.698, respectively. Anti-IL-18 was also associated with the risk of flare in these patients (OR=1.65; p=0.028, for 100 MFI increase). The presence of these three ACAAs was also higher in the TCZ-treated patients who suffered a flare compared to those in remission.
Conclusion: Although further validation of our results is needed, we present a ground-breaking study showing the potential of anti-IL17A, anti-IL-1α, and anti-IL18 to predict flare in RA patients under biological therapies.
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Table 1. Table showing a summary of the results. CI: confidence interval

• Treatments	• ACAAs	• AUC (CI 95%; p)
All	anti-IL17A	0.586 (0.504-0.668; 0.044)
	anti-IL-1α	0.594 (0.512-0.676; 0.028)
CTZ	anti-IL17A	0.867 (0.675,1.000; 0.017)
ABA	anti-IL17A	0.903 (0.761-1.000; 0.007)
TCZ	anti-IL-1α	0.657 (0.494-0.820; 0.049)
	anti-IL-17F	0.689 (0.551-0.827; 0.018)
	anti-IL17A	0.682 (0.528-0.835; 0.023)
	anti-IL18	0.698 (0.545-0.850; 0.013)

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POS0439 STROMAL B-CELL CROSSTALK PROMOTES THE ESTABLISHMENT OF SYNOVIAL B CELL NICHES THROUGH THE SELECTION, ACTIVATION OF NATURALLY OCCURRING EBV+ B CELLS

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Background: Rheumatoid Arthritis (RA) is characterized by the formation of ectopic lymphoid structures (ELS) in the synovial tissue, which can promote B cells activation and local production of autoantibodies. B cells exert an essential role in RA immunopathogenesis, as demonstrated by therapeutical effects of Rituximab (1). We previously showed that ELS in the RA joints frequently accumulate Epstein Barr virus (EBV)-infected B cells displaying evidence of both latent (LMP2A) and early lytic viral reactivation in locally differentiated plasma cells (PCs)(2). RA synovial fibroblasts (SFs) can sustain B cells activation, proliferation and maturation into high affinity antibodies producing cells, mimicking B cells physiological differentiation in germinal centres (3). Whether RASFs can also promote preferential selection of naturally-occurring EBV+ B cells is currently unknown.
Objectives: Here, we aim to a) demonstrate SFs role in EBV+ B cells selection b) phenotypically characterize B cells after co-culture with SFs c) dissect the molecular mechanisms behind the B cells SFs crosstalk.
Methods: Long-term *in vitro* B cells SFs co-cultures have been established, followed by phenotypical characterization of B cells in flowcytometry. Supernatant were then screened by ELISA at different timepoints, to measure IgG, IgM and IgA production. EBV infection status on B cells were analysed by qRT-PCR after gDNA extraction. Single cells RNA sequencing was finally performed at 28 days of co-culture.
Results: Preliminary results confirmed RASFs role in sustaining B cells activation and maturation, showing B cells survival up to 90 days, production of IgG and an increased IgG/IgM ratio overtime. Interestingly, we identified a particular B cells phenotype occurring in long term *in vitro* co-cultures, characterized by CD38 expression and the subdivision into two functional subsets, CD58+/CD23^{high} and CD58+/CD23^{low}. These two subpopulations - previously described by Megyola et al. in *in vitro* EBV infected B cells - are characterized by two different functional states: an highly proliferating (CD58+/CD23^{high}) population and an IL-6 producers (CD58+/CD23^{low}) one(4). We also observed that RASFs preferentially support EBV+ clones expansion, showing a preferential expression of EBV markers in CD58+/CD23^{high} cells. The high proliferation rate of these B cells allowed – on a specific experiment - the establishment of a cell line, named

"Carejavi", that we are currently employing as tool for functional investigation of RASFs primed EBV+ B-cells. Finally, the transcriptomic analysis revealed the selection of a relatively small number of clonotype at the VDJ analysis at the end of co-culture. In addition, we observed the upregulation of genes related to GC formation (such as EBI3, LTA and LTB), B cells proliferation (mki67) and viral oncogenic transformation (MYC).

Conclusion: Here, we demonstrated that RA SFs not only support B cells maturation and activation in local autoantibodies producing cells, but they are also able to preferentially induce selection and proliferation of EBV+ clones, characterized by a peculiar expression of CD58 and CD23. The molecular mechanisms behind this phenomenon are currently under investigation.

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POS0440 THE ANALYSIS OF THE INFLAMMATORY PROTEOME IN RHEUMATOID ARTHRITIS IDENTIFIES COMMON SIGNATURES ASSOCIATED WITH THE CLINICAL RESPONSE TO DMARDS AND TNFI THERAPIES

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Background: The clinical outcome of the most common therapeutic options of rheumatoid arthritis (RA) patients, such as conventional disease-modifying antirheumatic drugs (DMARDs) and TNF inhibitors (TNFi) is still unpredictable, since a high percentage of patients do not response to the therapy. Innovative analyses combining high-throughput technologies and thorough clinical assessments are needed to gain insight about the management of this prevalent autoimmune disorder.

Objectives: To evaluate the systemic inflammatory proteome of RA patients, to identify useful biomarkers associated with distinctive clinical outcomes.

Methods: Serum samples from 140 subjects, including 40 healthy donors (HC) and 100 RA patients with high activity disease (mean DAS28=4.7), were profiled with the innovative proteomic methodology "proximity extension assay" (Olink) which analyses one panel of 92 pro-inflammatory proteins. Samples from RA active patients included 40 from newly-diagnosed RA patients before taking conventional DMARDs and 60 from biologics-naïve patients (mean disease duration=10 years) before receiving TNFi drugs. Clinical outcomes were evaluated following EULAR criteria after 6 months of treatment and patients were classified as responders or non-responders to the different therapeutic interventions. Unsupervised hierarchical clustering methodologies were applied to identify subgroup pf patients based on the proteomic profiles. Gene ontology enrichment were used to interrogate the biological meaning of the distinctive molecular signatures identified.

Results: The inflammatory proteome analysis identified 33 proteins differentially expressed and upregulated in RA patients compared with HC including several chemokines (CCL-11, -19, -20, -23, -28; CXCL-10, -11, -9; MCP-1, -3), interleukins (IL-6, -8, -18, -10, -17c), and other relevant proinflammatory mediators (VEGFA, CD40, MMP-1, CSF-1, OPG, FGF23) among others (FDR<0.05). Most of these molecules were associated with disease activity (DAS28) and the autoimmunity profile (Rheumatoid factor and ACPAs antibodies) of RA patients. The unsupervised clustering analysis using the proteomic profile of RA patients before TNFi identified two subgroups of patients. Cluster 1 (C1) was characterised by patients with higher levels of several pro-inflammatory mediators compared with Cluster 2 (C2), where a signature of 16 chemokines was significantly enriched (CCL-3, -4, -10, -11, -20, -23; CX3CL1; CXCL-1, -10, -11, -5, -6, -9; MCP-1, -3, -4). Clinically, 25% of the non-responders' patients was included in C2, while 75% was located in C1, suggesting that a prominent circulating chemotaxis profile prior therapy is associated with a poor clinical outcome. These data were similarly observed in patients before receiving DMARDs, where a signature of upregulated chemokines and pro-inflammatory mediators characterised a cluster with a high % of non-responder patients.

Conclusion: A pro-inflammatory signature, where chemokines are predominantly up-regulated in the serum of RA patients before therapy, is associated with a poor clinical outcome. This newly identified signature, which deserves a more in-depth analysis, might be clinically useful guiding precision medicine and novel therapeutic approaches.

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POS0441 IN-DEPTH ANALYSIS OF AXL AND MERTK EXPRESSION PATTERNS AND REGULATION BY BIOLOGIC TREATMENTS IN RHEUMATOID ARTHRITIS

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Background: Tyrosine kinases receptors MerTK and Axl have been implicated in the pathogenesis of several autoimmune diseases. Despite sharing significant structural homology and having common ligands, Axl and MerTK have distinct features and biological functions [1]. A growing body of evidence suggests that both Axl and MerTK play a crucial role in Rheumatoid Arthritis (RA) pathogenesis and progression and may be exploited as novel therapeutic targets [2]. However, numerous unanswered questions remain to be addressed.

OBJECTIVES:

i. To define common and distinct gene-partners of Axl/MerTK and quantify their expression in RA synovial tissue.
ii. To assess the co-expression of Axl/MerTK by synovial cells.
iii. To outline the longitudinal variation in Axl/MerTK expression upon treatment intervention.

Methods: Synovial tissue samples were collected by US-guided synovial biopsy from: i. Patients with early (<12 months) RA DMARDs/steroid-naïve [n=87]; and ii. RA patients who failed the first-line biologic with TNF-inhibitors (TNFi) before and 16 weeks after receiving either Rituximab (RTX) or Tocilizumab (TOC) [n=164] [3]. Gene expression was obtained by bulk RNAseq performed on an Illumina HiSeq2500 platform. Axl-/MerTK-modules were defined using STRING networks and the module expression determined by the mean z-score of regularized log transformed expression for all genes in the set. Axl, MerTK, CD55, CD90, CD68 protein expression was analysed by multiplex immunofluorescence staining.

Results: Using STRING network analysis, we defined an Axl- and a MerTK-module composed of 31 predicted gene-partners of either Axl or MerTK. Thirteen genes were common to both modules and included the ligands Gas6 and ProteinS, and EGFR. Conversely, eighteen genes were uniquely present in the Axl-module (e.g., PIK3-family, IGF1R, IFNAR1 and STAT3) or the MerTK-module (e.g., Galectin3 and TULP, recently discovered MerTK ligands, FCGR1A/CD64, PTPN1and MEGF10). Axl/MerTK-modules quantified in the early-arthritis treatment-naïve RNAseq dataset showed a significant negative correlation with the synovitis score (Axl r=−0.33, p=0.0032; MerTK r=-0.33, p=0.003). At protein level, CD68+macrophages of the Lining showed notable heterogeneity between patients: they could express either Axl or MerTK alone, or co-express both. Axl was also present in most CD55+ Lining Fibroblast-Like-Cells (FLS) but not by CD90+ Sublining FLS while MerTK, as expected, was restricted to macrophages, including intra-aggregate tingible-body-macrophages. To define how Axl and MerTK vary depending on disease stage and treatment exposure, we quantified their gene expression in active RA patients inadequately responding to TNFi, prior and 16 weeks after starting second-line biologic (RTX or TOC) [3]. Differently from the early-arthritis cohort, MerTK was significantly up-regulated in synovia characterised by higher degree of tissue inflammation (lympho-myeloid > diffuse-myeloid > pauci-immune, p<0.0001) and significantly positively correlated with several cytokines' genes such as TNF, IL-6, CCL8 and IL-10. MerTK expression was dependent on clinical response to RTX but not TOC as assessed by EULAR response (DAS28CRP, good vs none/mod, FDRresp 0.048). Conversely, Axl expression

significantly increased upon IL-6 blockade by TOC independently of the clinical response (FDRtime 0.016).

Conclusion: Our data further corroborate that Axl and MerTK constitute a dynamic axis influenced by the synovial tissue inflammatory features, the disease stage, the exposure and the response to targeted treatment and the blockade of critical inflammatory pathways over time. A better understanding of the individual features of these tyrosine kinases as well as their interaction would be beneficial to define novel treatment approaches.

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POS0442 GLPG4399: SELECTIVE SIK3 INHIBITION AS A NOVEL MODE OF ACTION FOR THE TREATMENT OF INFLAMMATORY ARTHRITIC DISEASES (PRECLINICAL)

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Background: Salt-inducible kinases (SIKs) is a family of kinases with immunomodulatory function identified using a proprietary adenoviral shRNA knockdown target discovery platform. Moreover, SIK inhibition has previously been shown to have a role in inflammatory signalling.[1–3] These findings suggest a therapeutic potential for SIK inhibition in inflammatory indications. A medicinal chemistry effort resulted in the development of a first-in-class, oral, selective SIK3 inhibitor: GLPG4399. This compound may be beneficial in inflammatory diseases such as rheumatoid and psoriatic arthritis which are chronic disorders characterized by impaired joint synovial inflammation.

Objectives: Our research aimed to characterize GLPG4399 and explore its impact in arthritis-relevant inflammatory *in vitro* phenotypic cell assays, and to evaluate the therapeutic potential of selective SIK3 inhibition in *in vivo* experimental models of arthritis.

Methods: The selectivity and potency of GLPG4399 was profiled using biochemical and target-based cell assays. The mode of action of selective SIK3 inhibition in inflammation was explored in an *in vitro* panel of innate (monocytes, macrophages, dendritic cells) and adaptive (B and T lymphocytes) immune phenotypic assays and in a lipopolysaccharide (LPS)-stimulated human whole blood assay by measuring the production of inflammatory cytokines. *In vivo* target engagement was evaluated in an acute LPS-stimulated cytokine release mouse model by measuring plasma tumour necrosis factor (TNF) α levels. The therapeutic efficacy of GLPG4399 was evaluated *in vivo* in collagen-induced arthritis (CIA) and IL-23-induced psoriatic arthritis mouse models by assessing disease activity endpoints.

Results: GLPG4399 was shown to be a SIK3 inhibitor with high selectivity against a panel of 370 kinases. The wide effect of SIK3 inhibition on key immune cell types was demonstrated by GLPG4399's reduction of pro-inflammatory cytokines produced by monocytes, macrophages, dendritic cells, B and T lymphocytes in a panel of *in vitro* innate and adaptive immune phenotypic assays. The biological activity and target engagement of GLPG4399 was further demonstrated by dose-dependent inhibition of TNFα production *in vitro* in LPS-stimulated human whole blood and *in vivo* in the blood of LPS-challenged mice. Oral treatment with GLPG4399 in mice resulted in a significant and dose-dependent improvement of disease activity score in both CIA and the psoriatic arthritis disease model. Moreover, bone erosion in CIA and new bone formation in the psoriatic arthritis disease model were significantly reduced.

Conclusion: Our preclinical findings demonstrate the strong immunomodulatory effect of SIK3 inhibition in arthritis-relevant inflammatory cell assays and highlight the significant preclinical efficacy of GLPG4399 in two experimental arthritis mouse models. The novel mechanisms of action of GLPG4399 represents a promising approach for the treatment of arthritis.

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POS0443 INSIDE THE JOINT OF INFLAMMATORY ARTHRITIS PATIENTS: HANDLING AND PROCESSING OF SYNOVIAL TISSUE BIOPSIES FOR HIGH THROUGHPUT ANALYSIS

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Background: Inflammatory arthritis (IA) is a chronic systemic autoimmune disease of unknown aetiology, which affects the joints. While studies of immune cell populations in peripheral blood have been informative regarding potential immune cell dysfunction and possible patient stratification, there are considerable limitations in identifying the early events that lead to synovial inflammation. The joint, as the site of inflammation and the local microenvironment, exhibit unique characteristics that contribute to disease pathogenesis. The limited availability of synovial tissue (ST) biopsies is a key incentive for the utilisation of high-throughput techniques in order to maximise information gain.

Objectives: This work aims to provide an overview of key methods and novel techniques that are used in the handling, processing and analysis of ST biopsies and the potential synergy between these techniques.

Methods: We describe the utilisation of high dimensionality flow cytometric analysis, single cell RNA sequencing, *ex vivo* functional assays, including T cell activation, endocytosis and two-photon fluorescent lifetime imaging microscopy (FLIM).

Results: When comparing different methods for ST cell suspension generation we observed that the combination of mechanical and enzymatic digestion resulted in the release of considerably higher numbers of total viable cells when compared to mechanical digestion alone, although consideration should be taken in the cleaving of extracellular markers, like CD27. We next compared two different cryopreservation methods to that of freshly digested ST and observed similar viability and frequency of immune cells. Functional characterisation of ST cells can be challenging due to the high number of cells required for analysis, herein, we utilised the above protocols to establish ST viable cell suspensions and optimised different experimental approaches for phenotypical/functional characterisation. To investigate the functional consequence of OxPhos inhibition on ST T-cell polyfunctionality, ex-vivo ST cell suspensions from IA patients were stimulated with PMA/Ionomycin in the presence/absence of FCPP followed by metabolic profile characterisation via FLIM and high dimensionality flow-cytometric analysis for T cell-derived cytokines. Treatment with FCPP resulted in a decreased in T-cell polyfunctionality specifically in co-expression of TNF-α,-IL-2,-IFN-γ,IL-17A, -GM-CSF, an effect associated with a shift in their metabolic profile. In addition, freshly digested ST cell suspensions were subjected to an optimized assay to evaluate endocytosis in multiple populations simultaneously without the need for cell sorting. Briefly, digested cells were incubated in parallel at 4°C (passive endocytosis) and 37°C (active endocytosis) with DQ OVA(Ovalbumin). ST cells were then stained for multiple populations, demonstrating differential endocytosis capacity across pathotypes and disease controls. Finally, utilisation of novel bioinformatics analysis of RNAseq a data showed differential gene expression and pathway enrichment involved in IA pathogenesis and allowed for the comparison of cell specific enrichment scores and transcription factor usage based on pathotype and gender.

Conclusion: The introduction of new powerful techniques in the study of ST inflammation, brings new challenges and significant opportunities. These approaches will accelerate our path towards understanding of the mechanisms involved in the pathogenesis of IA and lead to the identification of new avenues of therapeutic intervention.

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POS0444 PROFILING OF CIRCULATING MIRNAS IN DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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Background: Biologic (b-) and targeted synthetic (ts-) disease-modifying antirheumatic drugs (DMARDs) have brought significant progress in the treatment of rheumatoid arthritis (RA), but a significant proportion of RA patients still remain symptomatic despite treatment according to current recommendations. These patients have recently been defined as "difficult-to-treat (D2T)" RA (1). There is evidence that miRNA expression may play a role in the diagnosis and therapy of RA (2).

Objectives: In a retrospective study, we analyzed patients' blood samples prior to b-/ts-DMARD treatment and profiled circulating miRNAs to predict the development of D2T-RA.

Methods: A total of 36 patients fulfilling the EULAR definition of D2T-RA (1) (mean age 59.1±10.7 yrs, 78% females), 36 patients with RA in sustained clinical remission on b-/ts-DMARDs at two consecutive examinations 12 wks apart (mean age 66.3±9.6 yrs, 78% females), and 36 healthy controls (mean age 61.1±7.7 yrs, 68% females) were included in the study. Blood samples were collected before initiation of b-/ts-DMARD. We profiled circulating miRNAs using the sequencing approach and differential expression analysis was performed using DESeq2 algorithm.

Results: The massive parallel sequencing of circulating miRNAs detected 814 quantifiable miRNAs and DESeq2 algorithm revealed 35 miRNAs with different concentrations in patients who developed D2T-RA compared to patients with RA who achieved sustained remission or healthy controls. Out of these miRNAs, miR-16-5p (1.5x) and miR-451a (2.1x) were downregulated and miR-126-3p (1.4x) was upregulated in D2T RA patients compared to controls. In addition, miR-101-3p (1.5x) was downregulated in D2T RA compared to RA patients. Except for miR-101-3p, these miRNAS have been previously associated with RA and might predict development of D2T disease prior to initiation of b-/ts-DMARD therapy.

Conclusion: We found four miRNAs as potential biomarkers differentiating patients who are at risk to develop difficult-to-treat disease compared to patients who have a chance of sustained remission even before initiation of biological or targeted synthetic DMARDs. Further studies with larger sample size are needed to validated these data.

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POS0445 DISSECTING THE ROLE OF PLATELET FUNCTION IN INFLAMMATORY ARTHRITIS

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Background: Inflammatory autoimmune diseases such as rheumatoid arthritis (RA) show an increase in atherosclerotic cardiovascular disease, and are commonly associated with an increase in platelet counts. Thus, platelets fill a central role in the tenet: Inflammation begets coagulation, and coagulation begets inflammation. We have previously reported that induction of arthritis by the Streptococcal cell wall component peptidoglycan-polysaccharide (PGPS) results in increased platelet numbers, aggregation, activation, and increased expression of P-selectin (CD62-P) and of the costimulatory molecule CD40. These platelets are also more sensitive to stimuli such as ADP and thrombin, which induce dense granule release of serotonin and aggregation. We have also described increased P-selectin expression limited to the joints in mice with acute arthritis. Platelets, generally considered elements of the hemostatic system, are underappreciated for their pro-inflammatory potential.

Objectives: To further understand the role of platelets in inflammatory arthritis, and distinguish their biochemical and adhesive features we set out to characterize the impact of modulating platelet activity in acute and chronic rodent models of arthritis.

Methods: Chronic inflammatory arthritis was induced in Lewis rats by a single i.p. injection of PGPS which results in an early phase non-T cell dependent arthritis, and a chronic T cell dependent phase after day 10. An acute inflammatory arthritis was induced in Balb/c mice by the same method. Joint scoring and volume measurement were carried out daily to determine an arthritis severity score. The role of platelets on PGPS arthritis was assessed using a) depletion of platelets using periodic intraperitoneal (IP) anti-platelet antibody, b) blockade of the integrin GPIIb/IIIa with the monoclonal antibody (mAb) abciximab to inhibit activation and aggregation via vWF and fibrinogen. In the acute murine arthritis c) P-selectin deficient mice were assessed for severity of arthritis, and d) wild-type mice were pre-treated with a single IP injection of anti-CD41 (GPIIb) antibody.

Results: Depletion of platelets in rats during the PGPS treatment resulted in amelioration of both the early and chronic phases of disease. We previously demonstrated that TNF is elevated in this model following PGPS injection, so for comparison animals were treated with infliximab, a monoclonal antibody to TNF, with equivalent suppression of both acute and chronic phases of disease. Abciximab, targeting the dual function adhesion and signaling molecule GPIIb/IIIa, did not decrease arthritis, and in fact increased the severity of the chronic phase of arthritis. In the acute murine model, despite the previously described expression of CD62-P in joints and on platelets, the CD62-P knockout mice had no significant difference in arthritis severity. Conversely treatment of wild-type mice with the anti-CD41 to block GPIIb resulted in suppression of the arthritis.

Conclusion: Platelet depletion had a dramatic impact on both acute and chronic phases of inflammatory arthritis, which is not unexpected given that platelets carry an array of pro-inflammatory and procoagulant mediators including IL-1, chemokines, vWF, and fibrinogen, as well as an array of adhesion molecules for binding to endothelium, leukocytes, and to other platelets. The increase in chronic arthritis severity despite inhibiting platelet aggregation by blockade of GPIIb/IIIa was unexpected, but may have been due to increased platelet-endothelial binding or platelet-leukocyte aggregation thus exacerbating the chronic T cell phase. Lack of CD62-P appeared to have no influence on acute phase arthritis development. Interestingly anti-CD41, which blocks one part of the GPIIb/IIIa integrin, was effective at ameliorating arthritis in the murine model. Platelets play an often underappreciated role in inflammatory processes, but understanding the mechanisms will require further dissection of the complex nature of these cellular elements which have dual inflammatory and hemostatic roles.

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POS0446 ARP2/3 AS A LASP1 INTERACTION PARTNER REGULATES CELL-TO-CELL CONTACT FORMATION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RA

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Background: In rheumatoid arthritis (RA), fibroblast-like synoviocytes (FLS) undergo a stable transformation resulting in an aggressive phenotype mediating cartilage damage by increased levels of adhesion molecules. In this context, Lasp1 and the Arp2/3 complex are of interest because they modulate actin organization and focal adhesion turnover.

Objectives: In this study, the effects of Arp2/3 on cadherin-11 mediated cell-to-cell contact formation have been investigated using the arthritic hTNFtg mouse model.

Methods: Expression levels of Lasp1 and Arp2/3 protein complex were investigated in synovial tissue of wild type (wt) and hTNFtg hind paws by immunohistochemistry. Primary FLS were analysed, respectively and co-immunoprecipitation experiments were performed. In addition, *lasp1*$^{-/-}$ mice were interbred with hTNFtg animals and offspring were evaluated for disease progression and joint destruction. To further study the role of Arp2/3 in the function of the cadherin-11 adhesion complex, the effects of an Arp2/3 inhibitor (CK666) on cell-to-cell contact formation in FLS derived from hTNFtg and *lasp1*$^{-/-}$hTNFtg mice were investigated by stainings. To assess signaling pathway activation, cells were stimulated with the growth factor PDGF.

Results: Upregulated Lasp1 levels were found in synovial tissue and FLS of hTNFtg compared to wt mice. Assays showed that Arp2/3 is part of the adherens junction (AJ) machinery in FLS although Arp2/3 expression levels were not changed between the genotypes. *In vivo* evaluation of *lasp1*$^{-/-}$hTNFtg mice revealed a milder arthritis score, less cartilage degradation and reduced FLS attachment to articular cartilage compared to hTNFtg mice. *In vitro*, the loss of Lasp1 led to clear alterations in AJ arrangement indicated by altered β-catenin pattern. As expected, β-catenin expression was mainly located at adhesion sites between adjacent cells. In hTNFtg FLS, these structures were characterized by a zipper-like pattern. In contrast, these structures were disrupted in *lasp1*$^{-/-}$hTNFtg FLS. Interestingly, CK666 induced zipper-like structures in hTNFtg FLS comparable to the pattern found in *lasp1*$^{-/-}$hTNFtg cells. Furthermore, *lasp1*$^{-/-}$hTNFtg FLS showed decreased Src phosphorylation following PDGF stimulation in comparison to hTNFtg FLS.
Conclusion: Lasp1 represents an interesting target involved in RA-caused joint destruction, because its loss results in significantly reduced cartilage destruction and altered FLS contacts mediated by Arp2/3.
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POS0447 TREATMENT WITH UPADACITINIB IN RA PATIENTS FOR WHICH BIOLOGIC THERAPY FAILED

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Background: Upadacitinib is a JAK inhibitor recently approved for rheumatoid arthritis treatment with promising results in its studies for severe moderate RA for which conventional therapies failed.
Objectives: To study and describe the evolution of patients diagnosed with RA and treated with Upadacitinib who had inadequate response to biological therapy in association or not with DMARDs and GC for 6 months.
Methods: A population of 23 patients (19 of them female) with RA on treatment with Upadacitinib was analyzed over 6 months. Using patient-reported outcomes (PROs) to measure disease activity by visual analogue scale (VAS), the HAQ Disability Index (HAQ-DI), Disease Activity Score (DAS28), and morning stiffness duration. The age´s (average ± SD) = 53 ± 10 years and time of disease evolution (average ± SD) = 17.6 ± 23.3 years. Pretreatment HAQ (average ± SD) = 2.2 ± 0.5. All patients received previous biologic treatments and 61% (14 patients) combined therapy with DMARDs. Only 2 cases had no glucocorticoid treatment prior to treatment with Upadacitinib.
Results: In 3 months' time, most patients (81%, n = 21) treated with Upadacitinib were able to reduce GC dose, and this reduction was maintained 6 months from the beginning of the treatment. After 3 months of treatment, most patients experienced an enhancement in DAS28 (89%, n = 18), with an average improvement in DAS28 of (± SD) 1.87±1.09 units. Regarding the pain (VAS), 67% of the patients showed improvement after 3 months (n=18), reaching 71% after 6 months (n=17). Sixty-eight percent of treated patients showed a reduction in morning stiffness after 3 months (n = 19), and this improvement increased up to 84% of treated patients at 6 months (n = 19). Side effects were observed in five patients, consisting of dizziness and nausea. In no case were they a reason for the withdrawal of the drug. Treatment was withdrawn in three patients due to primary failure.
Conclusion: Treatment with Upadacitinib allows GS dose reduction, as well as an improvement in DAS28, VAS and morning stiffness at three months and six of treatment. These data are in line with the evidence published in Upadacitinib pivotal studies, meaning a good alternative in the treatment of patients with moderate or severe RA.
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POS0448 SYNOVIAL TRANSCRIPTOMIC PROFILES CORRELATE WITH DISEASE ACTIVITY IN EARLY UNTREATED RHEUMATOID ARTHRITIS

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Background: Synovitis is the common feature across all individuals with a diagnosis of rheumatoid arthritis (RA). Yet, cellular and transcriptomic alterations occuring in RA synovium are highly variable amongst patients. So far, most data on clinical-tissue correlations either rely on hypothesis-driven approaches or are potentially biased by heterogeneous clinical characteristics (e.g. disease duration or disease-modifying antirheumatic drugs).
Objectives: We used transcriptomic profiling of synovial tissue from early, untreated rheumatoid arthritis patients (ERA) to 1/ identify the genes with the most variable expression amongst patients and 2/ explore the ability of unbiased (data-driven) approaches to define clinically relevant ERA subgroups.
Methods: Synovial biopsies were harvested from clinically involved joints of ERA patients using needle arthroscopy or ultrasound-guided biopsy. Data on disease activity were collected at inclusion. For each sample, 350ng total RNA was sent for RNAsequencing using a standardized protocol (Macrogen Europe). After quality control (Fast QC) and genome alignement (HiSat2), normalized read counts were analyzed on Qlucore Omics Explorer. To focus on inter-sample heterogeneity, genes were filtered based on variance (σ/σ_{max}). Unbiased approaches (Principal Component Analysis, Unsupervised Clustering) were applied to define patients' clusters. Pathway enrichment analysis were performed on Metascape. CibersortX was used to extrapolate the immune cell subsets relative composition from gene expression data. All other statistical analyses were performed on GraphPad Prism v9.
Results: Total RNA was obtained from synovial biopsies from 74 patients. We first applied variance filtering to identify the genes whose expression showed the greatest variation between patients (n = 894 most variable genes). PCA analysis on the level of expression of these genes did not divide samples into distinct groups, instead yielding a continuous distribution broadly associated with baseline disease activity, as measured by DAS28CRP. Consequently, we used unsupervised clustering to allow for unbiased definition of two patient clusters (PtC): PtC1 (n=52) and PtC2 (n=22) based on their expression of these 894 genes. Pathway analysis of these genes revealed significant enrichment of immune system genes, in the *Inflammatory response* and *Rheumatoid Arthritis* pathways (gene cluster 1: GC1), B cell & plasma cell-related pathways (GC2) and metabolic processes-related genes (GC3). Interestingly, PtC1 and PtC2 were characterized by very different clinical features. More specifically, patients from the group with a strong B & plasma cell signature (PtC1) displayed higher baseline indices of all disease activity score components (median DAS28CRP: 5.56 *vs* 4.09; p-value = 0.0003). They also had higher rates of baseline radiological erosions (erosive disease in 34.6 % *vs* 10%; p-value = 0.0252) but similar rates of seropositive disease. In line with our pathway analyses, we found a higher signature (inferred relative frequency) of B & plasma cells, T cells and M1-like macrophages in PtC1 compared to PtC2 synovia. PtC2 synovia instead had relatively higher M2-like macrophage and resting mast cell signatures.
Conclusion: In this large synovial biopsy study, we found that synovial transcriptomic profiles in ERA patients distribute continuously based on the expression of inflammatory and immune cell transcriptomic pathways. These synovial transcriptomic signatures correlate strongly with systemic disease activity.
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Spondyloarthritis - aetiology, pathogenesis and animal models

POS0449 CHARACTERISTICS OF GUT MICROBIOTA AND ITS RELATIONSHIP WITH LYMPHOCYTE SUBSETS AND CYTOKINES IN PATIENTS WITH UNDIFFERENTIATED SPONDYLOARTHRITIS

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Background: Gastrointestinal microbiota, particularly dysbiosis of gut microbiota composition have been correlated with the progression of autoimmune disorders, such as undifferentiated spondyloarthritis (USPA).
Objectives: This study aimed to identify the changed gut microbiota and its relationship with lymphocyte subsets and cytokines in USPA Patients.
Methods: A total of 210 participants were recruited in this study, comprising 105 USPA patients and 105 age and sex-matched healthy controls (HCs). Microbial genome was extracted from approximately 250mg fresh fecal samples from all participants using QIAamp PowerFecal DNA Kit (Qiagen). The V3-V4 variable regions of bacterial 16S rRNA genes were sequenced with the Illumina Miseq PE300 system. QIIME2 was used to process representative sequence clusters with a similarity cutoff of 100% (ASVs)[1]. Microbial diversity was estimated by the alpha diversity (observed, chao1, ACE, shannon, simpson, and ivsimpson) and beta diversity (bray distance). Biomarker species were identified based on STEMP between USPA and HC group. Correlations were analyzed with the Spearman rank correlation test.
Results: The alpha-diversity indices have no significant different between two groups (P >0.05, Figure 1A). Gut microbial community structure differed between USPA and HC, as revealed by ASV Bray–Curtis distances (P <0.05, Figure 1B). As for composition of gut microbiota, there were the increased levels of Escherichia_Shigella, Flavonifractor, Hungatella in the USPA group, and Lachnospirales, Roseburia, and Lachnospiraceae in HCs (Figure 1C). The relative abundance of Lachnospiraceae_UCG_001 and Enterobacter was negatively correlated with the absolute numbers of Th17 (P<0.05). Bifidobacterium was positively correlated with the absolute number of Th1 and Tregs (P<0.01, Figure 1D). The relative abundance of Fusobacterium, Incertae_Sedis, and Colidextribacter were negatively correlated with the absolute numbers of Il-10, IL-4, and IL-2 (P<0.05). Prevotella and Enterobacter were positively correlated with the absolute number of IL-6 and IL-4 respectively (P<0.05, Figure 1E). Bifidobacterium and Bilophila were neagtively correlated with the absolute number of NK cell (P<0.05, Figure 1F).
Conclusion: Gut dysbiosis in USPA patients mainly characterized by reduced the diversity and impaired abundance of the intestinal flora, which was closely related to the disturbance of lymphocyte subpopulations and cytokines.

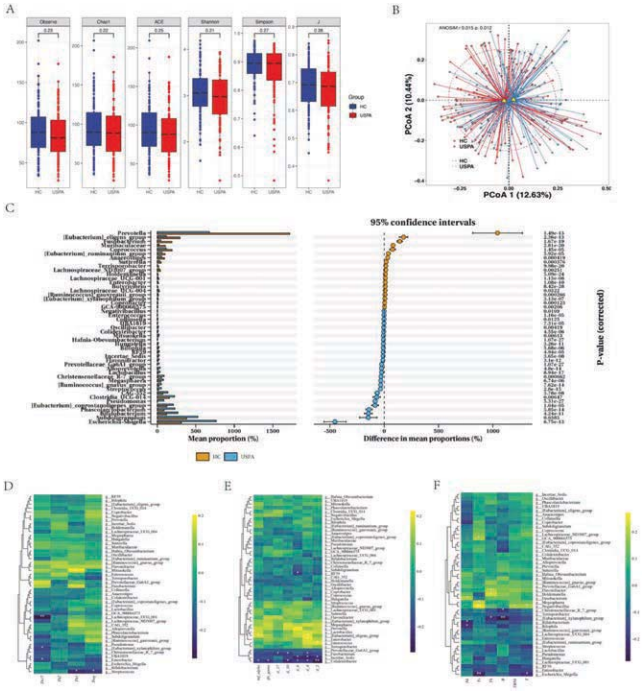

Figure 1. (A) Comparison of alpha-diversity indexs between HC and USPA groups was shown using boxplot. (B) β diversity of the gut microbiome in USPA patients and HCs. Principal coordinate analysis plot generated from the bray distance analyse. (C) STEMP was used to detect difference in Flora according to USPA and HC. (D-F) Relationship between gut microbiota, and Lymphocyte subsets as well as cytokines. *P<0.05, **P<0.01.

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POS0450 TEMPORAL MIGRATION OF IMMUNE CELLS FROM PSORIATIC SKIN TO JOINTS INITIATING SYNOVIAL INFLAMMATION IN PSORIATIC ARTHRITIS

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Background: Spreading of inflammation from skin to joint is a key question behind the pathogenesis of psoriatic arthritis (PsA). Psoriasis (PsO), being one of the most prevalent skin diseases, usually anticipates joint manifestations, suggesting spreading of skin to joint disease, which happens in about 30% of the patients with psoriasis.[1] To date, it is still obscure why the inflammatory process in some patients with PsO remains restrained to the skin, whereas in other patients it extents to tendons and joints.
Objectives: Using a pre-clinical model of PsA, we aimed to unveil the skin-joint axis, i.e. the spreading of psoriatic inflammation from the skin to the joints.
Methods: KAEDE transgenic mice expressing a photo-convertible fluorescent reporter were used to assess cell trafficking from inflamed skin to other organs in the mouse model of IL-23 overexpression (IL-23OE) induced PsA. Psoriatic skin lesions were irradiated with UV light to trigger the photoswitch from KAEDE^{GREEN} to KAEDE^{RED}. Migration to different organs was determined by flow cytometry. Imaging flow cytometry was used to characterize the type of cells migrating from the skin to the joints. Migrating cells were further characterized by single-cell RNA-sequencing (scRNAseq) and functional analyses.
Results: MRI imaging and histological evaluation of IL-23OE mice revealed skin inflammation preceding joint inflammation in both wild-type and KAEDE-transgenic mice. Specific leukocyte migration from the skin to the joints started shortly after the onset of skin inflammation and before onset of inflammation within the joints of KAEDE transgenic mice. No migration was observed in healthy control animals. Other organs such as spleen or lymph nodes showed no model-dependent migration. Imaging flow cytometry revealed that the cells migrating to the joints were predominantly CD45+ CD11b+ cells. ScRNAseq analysis of sorted KAEDE^{RED} cells from inflamed joints confirmed that approximately 80% of the migrating cells were macrophages. Differential gene expression and pathway analysis revealed an imbalance between pro- and anti-inflammatory macrophages in the joints of experimental psoriatic arthritis.
Conclusion: We describe IL-23-mediated migration of skin-derived macrophages from the skin to the joints during the onset of experimental psoriatic arthritis. This process may explain the spreading from psoriatic skin to joint disease as these cells foster the development by local cytokine production once arrived in the joints.

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SLE, Sjöns and APS - aetiology, pathogenesis and animal models

POS0451 DEFICIENCY OF PPM1A IN MACROPHAGE AGGRAVATES PRISTANE-INDUCED LUPUS-LIKE DISEASE

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Background: Protein phosphatase Mg^{2+}/Mn^{2+}-dependent 1A (PPM1A) is a phosphatase which regulates various intracellular cell signaling pathways including inflammation. We previously suggested that the inflammatory signal decreased the PPM1A protein level in macrophage and this reduction had correlation with the chronic inflammatory bone disease, implying the possible role of PPM1A in inflammatory responses of macrophage.

Objectives: In this study, we aim to elucidate the potential role of PPM1A in macrophage to regulate inflammatory response during the disease progression of systemic lupus erythematosus.

Methods: We generated macrophage-specific conditional gene-knockout ($PPM1A^{fl/fl}$;LysM-Cre) mice and developed a lupus-like disease with immune complex glomerulonephritis in these $PPM1A^{fl/fl}$;LysM-Cre mice by intraperitoneal pristane injection. Mouse serum was collected every 4 weeks after pristane injection. Serum anti-dsDNA IgG, anti-ssDNA IgG, interleukin-17 (IL-17) and tumor necrosis factor-α (TNF-α) was quantified by ELISA. After 41 weeks from pristane injection, histological changes in the kidney, spleen, and lung tissues were observed. To analyze M1/M2 polarization in vitro, LysM-Cre and $PPM1A^{fl/fl}$;LysM-Cre mouse bone marrow-derived macrophages were cultured with lipopolysaccharide (LPS)/interferon-γ (IFN-γ) or interleukin-4 (IL-4) to check M1 or M2 related genes.

Results: We found that macrophages of $PPM1A^{fl/fl}$;LysM-Cre mice displayed different gene expression with LPS stimulation especially in M1/M2 related genes through the RNA-seq analysis and showed a decrease in both M1 and M2 polarization induced by LPS/IFN-γ or IL-4 stimulation. Notably, we found that $PPM1A^{fl/fl}$;LysM-Cre mice with pristane injection showed a significant increase of anti-ssDNA IgG compared to LysM-Cre mice. $PPM1A^{fl/fl}$;LysM-Cre mice showed severe lupus-like phenotypes such as global glomerular enlargement indicated by endocapillary proliferation and glomerular cellularity in kidney and lung inflammation accompanied by fibrosis, compared to LysM-Cre mouse by pristane injection. Together, serum IL-17 and TNF-α, which are proinflammatory cytokines, were increased in $PPM1A^{fl/fl}$;LysM-Cre after pristane injection. These results indicate that PPM1A depletion in macrophage deteriorates inflammation and contributes to the tissue damage in a lupus-like disease.

Conclusion: Our findings suggest that the deficiency of PPM1A in macrophages impairs M1/M2 macrophage polarization leading to an immune imbalance in lupus-like disease model, providing a potential link between the loss of function of PPM1A in macrophages and its molecular target for treatment of systemic lupus erythematosus.

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POS0452 ABNORMALITY OF TYPE I INTERFERON SIGNALLING IN B CELLS IN PRIMARY SJÖGREN´S SYNDROME AND THE IMPACT ON LABORATORY AND CLINICAL FINDINGS

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Background: B cell hyperactivity (1), autoantibody production (anti-SS-A, anti-SS-B) and hypergammaglobulinaemia as well as interferon (IFN) signature (2) play a central role in the pathogenesis of primary Sjögren´s Syndrome (pSS). The link between these hallmarks is still elusive. While treatment of pSS remains limited, an improved understanding of IFN and JAK/STAT signalling on B cells may hold promise to improve potential treatment targets and related biomarkers.

Objectives: To investigate downstream molecules of the IFN signalling pathway on B cells and their clinical impact in pSS.

Methods: Peripheral blood from 47 pSS patients and 36 matched healthy controls (HC) was obtained and permeabilized for intracellular staining. Here B and T cell markers were applied together with Signal Transducers and Activators of Transcription 1 (STAT1), STAT2, pSTAT1 and 2, Interferon Regulatory factor 9 (IRF9), IRF7 and IRF1 and analysed by using flow cytometry. Cell subsets and correlations with all markers and clinical information were subjected to statistical analyses.

Results: Compared to HC the pSS group showed significantly elevated STAT1 expression among all B cell subsets ($p>0.0001$) including naïve (CD27-IgD+), pre-switched (CD27+ IgD+), switched-memory (CD27+IgD-), double negative (CD27- IgD-) B cells and plasmablasts (CD27++ CD38++). Furthermore, IRF9 and STAT2 were increased among most B cell subsets. Positive correlations were found between STAT1 and IRF9 with Siglec-1 (CD169), an IFN signature marker expressed on the surface of CD14+ monocytes ($p>0.0001$; $r=0.633$). Notably, increased levels of IRF9 positively correlates with STAT1. Upregulated STAT1 and IRF9 within pSS B cells were associated to extraglandular manifestations, high anti-SS-A and anti-SS-B autoantibodies, high anti-nuclear antibody titers (ANA) and rheumatoid factors (IgA, IgM) in pSS patients.

Patients treated with prednisolone showed dose dependent inverse correlations of IRF9 expression among naïve-, memory-, and double negative B cells suggesting its treatment responsiveness.

Conclusion: The current data provide evidence of type I IFN on B cell subsets in pSS. Elevated STAT1, STAT2 and IRF9 expression suggest transcriptionally activity, which was evident in patients with extraglandular manifestations and elevated serologic activity.

Targeting JAK/STAT in pSS could be beneficial for patients with high STAT1 levels leading to a personalized approach for this specific subgroup of patients.

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POS0453 EXPLORATORY IMMUNOPHENOTYPE OF THE RARE DISEASE JUVENILE SJÖGREN'S SYNDROME REVEALS A DYSREGULATION OF B AND T MEMORY CELL FREQUENCIES

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Background: Sjögren's syndrome (SS) is an autoimmune rheumatic disease characterised by dryness resulting from chronic lymphocytic infiltration of the exocrine glands. Patients also present with other extraglandular manifestations such as arthritis, anemia and fatigue or various organ and systems involvement. The disease is more frequent in women aged 30-50. However, in rare cases, the disease starts in childhood and is known as juvenile SS (JSS) or childhood SS. Children have different clinical manifestations compared to adults, with dryness being less common, making the diagnosis very challenging[1].

Objectives: To investigate in depth the immune cell profile of patients with JSS for better understanding of disease pathogenesis.

Methods: Peripheral blood was collected from a cohort of patients with JSS while attending appointments at UCLH clinics. None had received B-cell depletion therapy. Immune-phenotyping of 29 immune-cell subsets, including B and T cells, in peripheral blood from patients with JSS (n=10) and age and sex-matched healthy controls (n=10) was performed using flow cytometry as we have performed previously for patients with adult onset SS[2]. Data were analysed using multiple t-tests and compared with the adult SS immune phenotype.

Results: Patients with JSS had an average age of 18 years (range 16-21) with an average age of disease onset at 14 years (range 12-18). Up to 60% of patients presented Anti-Ro autoantibodies while 50% presented Anti-La autoantibodies.

Patients with JSS had an altered immune profile compared to age matched healthy controls (average of 18 years, range 15-25). In the B cell compartment,

JSS patients had higher frequencies of Total CD19+ B cells (p=0.0044), Naïve B cells (CD19+IgD+CD27-) (p=0.0183) and bm2 (CD19+IgD+CD38+) (p=0.0490) whereas memory B cell subsets such as early bm5 (CD19+IgD-CD38+) and late bm5 (CD19+IgD-CD38-) were significantly reduced (p=0.0249, and p=0.0117 respectively), similar to the profile seen in patients with adult-SS. Interestingly, in the CD4+ T cell compartment, central memory (CD4+CD27+CD45RA-) T cells were significantly reduced (p=<0,0001) but effector memory (CD4+CD27-CD45-) and effector memory-re-expressing-CD45RA (EMRA, CD4+CD27-CD45RA+) T-cell subsets were significantly elevated (p=0.0171 and p=0.0002 respectively). These changes were not identified in adult-SS patients. Finally, unlike our observations in patients with adult-onset SS there was no widespread deregulation of CD8+ T cell subsets in JSS patients; only a significant increase in CD8+CD25-CD127+ responders T cells (p=0.0392) was observed in JSS patients versus healthy.

Conclusion: This is the first pilot study investigating the immunophenotype profile of patients with JSS. Our preliminary findings suggest altered immune phenotypes in both B-cell and T cell compartments and for B cells are in concordance with previous immunophenotyping studies in adult SS (predominance of naïve and lower frequencies of memory B cells), suggesting an immunological rationale for the use of similar therapies. Further studies, comparing the adult with the juvenile phenotype could help stratify patients for targetted therapies and improve treatment in this rare disease in children for which no evidence-based recommnedations exist.

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POS0454 DIGITAL IMAGE ANALYSIS OF INTRAEPITHELIAL B-LYMPHOCYTES AS AN OBJECTIVE ALTERNATIVE TO ASSESS LYMPHOEPITHELIAL LESIONS IN SALIVARY GLANDS OF SJÖGREN'S SYNDROME PATIENTS

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Background: Salivary glands of primary Sjögren's syndrome (pSS) patients characteristically contain periductal lymphocytic infiltrates. Associated with these infiltrates, lymphoepithelial lesions (LELs) can be formed. LELs are composed of hyperplastic ductal epithelium with infiltrating lymphocytes and may assist in the diagnostic process of pSS[1]. However, manual identification of LELs on H&E staining is a subjective process and can be challenging. A more objective histological parameter that could assist in identification of LELs is the presence of intraepithelial lymphocytes within striated ducts, since we previously showed an association between intraepithelial B-lymphocytes and hyperplasia of the ductal epithelium[2]. These results, however, warrant validation in a larger cohort. Furthermore, associations between clinical parameters of pSS patients and presence of intraepithelial lymphocytes are not yet known.

Objectives: To investigate if detection of intraepithelial lymphocytes using digital image analysis can be used as an objective alternative to assess LELs, and to correlate presence of intraepithelial lymphocytes to clinical parameters of pSS patients.

Methods: Paired labial and parotid salivary gland biopsies of 109 patients clinically suspected for pSS were serially sectioned and stained for CD3 (T-lymphocytes), high molecular weight cytokeratin (striated ducts) and CD20 (B-lymphocytes). We developed a virtual triple staining digital image analysis (DIA) algorithm using the Visiopharm Integrator System (Visiopharm, Hørsholm, Denmark) to detect intraepithelial T- and B-lymphocytes within regions of interest comprising striated ducts. A maximum of 10 regions of interests was selected per biopsy. Presence of ductal hyperplasia was assessed on consecutive H&E stained slides. Patients were classified as pSS or non-SS according to the ACR-EULAR criteria.

Results: The DIA algorithm presented in this study was an accurate and objective method to detect intraepithelial lymphocytes within striated ducts in salivary gland tissue. Presence of intraepithelial B-lymphocytes, in contrast to intraepithelial T-lymphocytes, was a specific finding in salivary gland biopsies of pSS patients. In total, 59% of labial and 68% of parotid gland biopsies of pSS patients contained intraepithelial B-lymphocytes, against only 2% of patients classified as non-SS. Intraepithelial B-lymphocytes were not only detected within striated ducts with hyperplasia (LELs), but also in around 25% of analyzed striated ducts without hyperplasia of pSS patients (precursor stage of LEL). PSS patients with presence of intraepithelial B-lymphocytes in the labial gland showed lower stimulated whole salivary flow (p=0.011) and higher ocular staining scores (p=0.048), compared to patients without intraepithelial B-lymphocytes. Serological parameters, such as, rheumatoid factor-, IgG- and ESR levels were significantly higher in pSS patients with presence of B-lymphocyte containing ducts, irrespective whether the labial or parotid gland was taken into account.

Conclusion: Presence of B-lymphocyte containing ducts is a specific finding in salivary gland biopsies of pSS patients and is associated with clinical parameters of pSS. Together, identification of B-lymphocyte containing ducts by using DIA could be used as an objective marker in the diagnostic histopathological work-up of patients suspected of pSS.

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POS0455 TOFACITINIB DECREASES INFLAMMATORY MARKERS AND MITOCHONDRIAL MORPHOLOGICAL DAMAGE IN SALIVARY GLANDS OF A MURINE MODEL OF SJÖGREN'S SYNDROME

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Background: Altered homeostasis of salivary gland (SG) epithelial cells in Sjögren's syndrome (SS) patients could be the initiating factor that leads to inflammation, as well as secretory dysfunction. Mitochondria are important organelles involved in cellular metabolism and their dysfunction can induce a loss of homeostasis and inflammation. Altered mitochondrion can release mitochondrial components that can act as damage-associated molecular patterns (DAMPs) and induce an inflammatory response via pattern recognition receptors (PRRs) such as the NLRP3 inflammasome, TLR9, cGAS/STING, and ZBP1 (1). Previously we determined that SG from SS patients showed and altered autophagy, which is associated to an increased pro-inflammatory cytokines expression. Interestingly, increased expression of pro-inflammatory markers such as IL-6, was reversed by JAK inhibitor tofacitinib in three-dimensional (3D)-acini deficient in autophagy (2). It is not clear whether the alterations in autophagy found in SG patients include alterations in mitochondrial clearance (mitophagy) that may lead to the accumulation of damaged mitochondria and enhanced inflammation. In this context, recent results of our laboratory showed, for the first time, severe ultrastructural alterations of mitochondria in SG cells from SS patients (1). However, it remains to be determined if these alterations are related to inflammation and if an anti-inflammatory agent could regulate these processes.

Objectives: To analyze the effect of tofacitinib on the mitochondrial ultrastructure in submandibular glands of a murine model of SS. In addition, to evaluate the effect of tofacitinib on the expression and activation of some PRRs involved in the recognition of mitochondrial DAMPs in the same murine model.

Methods: Six-month-old female NOD.B10Sn-H2b/J mice (Jackson Laboratories, USA) were used with 4-5 mice per group. Procedures were approved by the Universidad de Chile Animal Care and Use Committee. 30 mg/kg/day tofacitinib citrate was administered by oral gavage. After 28 days of tofacitinib or vehicle administration, their submandibular glands were obtained, which were processed to evaluate the mitochondrial ultrastructure by electron microscopy or lysed in

RIPA buffer to obtain proteins. The protein levels of PRRs: NLRP3, TLR9, ZBP-1, and cGAs, as well as molecules activated downstream of cGAS and ZBP-1 such as TBK1, pTBK1, pSTING, and STING were determined by Western blotting.

Results: The results show that the mitochondria of the glandular epithelial cells of NOD.B10Sn-H2b/J mice treated with vehicle (control) present alterations such as swelling, disruption of membranes and crest disorganization that previously were reported in patients with SS (1). Interestingly, tofacitinib treatment improves the architecture of mitochondria. On the other hand, the protein levels of PRRs such as NLRP3 and cGAS decreased in mice treated with tofacitinib, as well as pTBK1.

Conclusion: The altered morphology of mitochondria together with the increased protein levels of PRRs and downstream markers of these PRRs suggests release of mitochondrial DAMPs in submandibular glands of NOD.B10Sn-H2b/J mice. The improvement in mitochondrial morphology as well as the decrease in PRRs activation under tofacitinib treatment suggest a potential use of this anti-inflammatory agent in mitochondrial alterations associated with inflammation. Many questions remain to be addressed, such as determining which mitochondrial DAMP might be being released and whether this is associated with impaired mitochondrial function in SS.

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POS0456 AUTOPHAGY-RELATED RISK LOCI IN SLE AND THEIR ROLE IN NEUTROPHILS

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Background: Systemic lupus erythematous (SLE) is an autoimmune disease with ~150 established susceptibility risk loci. Genome wide-association (GWA) studies in SLE cases and controls of Korean ancestry identified the SLE risk locus ATG16L2-P2RY2, and rs11235604 as a SLE-associated missense variant (R220W) of Autophagy Related 16 Like 2 (ATG16L2) [1]. PRDM1-ATG5 is also an SLE risk locus in European populations that is implicated in autophagy. Autophagy plays a crucial role in neutrophil extracellular trap (NET) formation, degranulation, and limiting autoantigens in blood. Dysregulated autophagy has been implicated in SLE pathology and poor disease outcomes. The function of ATG16L2 is unknown, but evidence suggests it may function as a negative regulator of autophagosome formation [2].

Objectives: To identify autophagy-related SLE risk variants shared across different ancestry populations and define the role of ATG16L2 in SLE and autophagy.

Methods: SLE case-control GWA scans from European (7568 cases; 1082 controls), African American (4336 cases; 935 controls), Hispanic (3752 cases; 1840 controls), and Korean (1173 cases; 4213 controls) populations were imputed and SNP associations tested. Meta-analysis was performed, then Bayesian statistics were used to define a credible SNP set. Bioinformatic analyses (RegulomeDB, promoter capture Hi-C, eQTLs, etc.) further prioritized SNPs based on predicted functionality. The functional significance of autophagy SLE risk genes, ATG16L1, ATG16L,2 and ATG5, were tested by CRISPR knockout (KO) in PLB-985 cell line. CRISPR-targeted single cell clones were screened for ATG16L1, ATG16L2 or ATG5 deletion using qPCR, NanoPore sequencing, and Western blotting. Changes in autophagy were assessed by Western blotting and confocal microscopy.

Results: Transracial fine-mapping of PRDM1-ATG5 locus identified two SNP associations shared across the credible sets in all populations: rs56886418 (p=1.38x10-5) located in the intron of PRDM1 and rs77791277 (p=1.38x10-5) that tagged a group of SNPs in strong linkage disequilibrium. Cross comparison of the credible SNP sets and bioinformatic analyses of shared SNPs identified rs533733 and rs9373843 as additional likely functional variants. Bioinformatic analyses prioritized rs56886418, an eQTL for ATG5 (p=0.05) and PRDM1 (p=4.75x10-7) in blood cells positioned in a topologically associated domain (TAD) that may interact with ATG5 and PRDM1 promoters in EBV-transformed B cells. SNP rs533733 is an eQTL for ATG5 in neutrophils (p=0.006) and is in a TAD 6.4kb 3' of PRDM1 that interacts with the ATG5 promoter region where rs9373843 (eQTL of ATG5 in neutrophils (p=0.04)) is positioned. These data suggest that risk SNPs on the PRDM1-ATG5 locus may modulate ATG5 expression and autophagy in specific cell types by modulating the local chromatin regulatory network. To assess the roles of ATG5, ATG16L1 and ATG16L2 in autophagy, PMA/I-induced hallmarks of autophagy, LC3-I and LC3-II conversion and p62 protein aggregation, were assessed in homozygous and heterozygous ATG5, ATG16L1, or ATG16L2 CRISPR KO PLB-985 cells by Western blotting and confocal microscopy. Loss of ATG5 or ATG16L1 impaired PMA/I-induced autophagosome formation in myeloid-like and differentiated neutrophil-like PLB-985 cells. In contrast, loss of ATG16L2 elevated the conversion of LC3-I to LC3-II and p62 protein aggregation in both cell types, suggesting that ATG16L2 may inhibit autophagy.

Conclusion: Functional characterization of SNPs on the PRDM1-ATG5 and ATG16L2-P2RY2 loci, and the functional characterization of ATG16L2 in myeloid and neutrophil cell lines, provide new insights into the mechanisms that regulate autophagy in health and disease. Ongoing studies will focus on in vitro validation of predicted functional SNPs and will introduce ATG16L2 rs11235604 risk variant in PLB-985 cells to assess its importance in autophagy.

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POS0457 LABIAL AND PAROTID SALIVARY GLAND HISTOPATHOLOGY IN PRIMARY SJÖGREN'S SYNDROME

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Background: Salivary gland involvement is a hallmark of disease in primary Sjögren's syndrome (pSS). This is reflected by the prominent role of a positive biopsy within the ACR-EULAR classification criteria, which is solely based on the focus score (FS)[1]. In pSS all salivary glands might be involved in the disease process. For this reason, both labial and parotid salivary gland biopsies can be used for diagnosis and evaluation. Although nearly all clinical centres obtain labial gland biopsies for classification and diagnosis of pSS, a parotid biopsy is also a safe and effective procedure. Furthermore, it has a comparable diagnostic potential in pSS, might be associated with less morbidity, and may even detect presence of subclinical MALT lymphomas[2]. However, histopathological differences between both types of salivary glands should potentially be taken into account.

Objectives: The aim of this study was to get histopathological insight in minor (labial) and major (parotid) salivary glands in pSS patients in comparison with non-SS sicca patients.

Methods: Both labial and parotid salivary gland biopsies were obtained from 99 patients. According to the expert opinion of three experienced rheumatologists, 36 patients were classified as pSS patients and 63 as non-SS sicca patients. Salivary gland biopsies were formalin fixed, paraffine embedded and serially sectioned at 3-4µm. Sections were stained with H&E and for CD3, CD20, CD45, hmwCK, CD21, Bcl6, IgA/IgG and IgM. Focus score (FS), relative area of lymphocytic infiltrate, level of lymphoid organization and presence of a plasma cell shift were determined. In addition, number of lymphoepithelial lesions, germinal centers, follicular dendritic cell networks, B-cells and T-cells were analyzed.

Results: All histopathological parameters differed significantly between pSS and non-SS sicca patients in both labial and parotid salivary gland sections. Comparison of the two salivary gland types of non-SS sicca patients revealed more signs of inflammation in labial gland biopsies as shown by a significantly higher FS, $CD3^+$ T-cells, $CD20^+$ B-cells and relative area of $CD45^+$ infiltrates compared to non-SS parotid salivary gland biopsies. Other histopathological parameters were comparable between the two types of salivary glands. In pSS patients, a higher FS and relative area of $CD45^+$infiltrates was observed in labial gland biopsies compared to parotid gland biopsies. Nevertheless, relative and absolute $CD20^+$ B-cell counts, GCs/mm^2 and LELs/mm^2 were higher in parotid gland parenchyma.

Conclusion: This study shows in labial salivary gland biopsies of non-SS sicca patients more signs of (unspecific) inflammation compared to parotid biopsies. In parotid gland biopsies signs of B-cell hyperactivity, such as number of $CD20^+$B-cells, GCs/mm^2 and LELs/mm^2, are more pronounced, compared to labial gland biopsies. These histopathological differences should be taken into consideration in diagnosis and classification of Sjögren's disease.

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POS0458 ENRICHMENT OF COMPLEMENT, IMMUNOGLOBULINS, AND AUTOANTIBODY TARGETS IN THE PROTEOME OF PLATELETS FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Systemic Lupus Erythematosus (SLE) is characterized by autoimmunity towards apoptotic/necrotic cells, complement activation and excessive amounts of circulating immune complexes. Platelets are recognized as immune cells that interacts with innate and adaptive immune functions. They are activated in SLE patients and contribute to an increased susceptibility to thrombosis [1]. Decreased platelet size has been observed in patients with SLE [2], but the mechanism(s) remains unclear. In this study, we have analyzed the complete proteome of platelets with normal and decreased size from SLE patients and from healthy controls (HC).
Objectives: Our aim was to find clues that could explain the morphological differences observed in platelets from SLE patients and to better characterize the role of platelets in SLE.
Methods: We included 23 consecutive patients with SLE, median SLEDAI-2K score was 2, and 10 HC. Blood count, serum complement levels and the presence of antiphospholipid or dsDNA antibodies were analyzed in all patients. Platelet size (forward scatter) and activation status (CD154, PAC1, CD32, PAR1, CD62P and Annexin V) was determined using flow cytometry. The proteome of 10 platelet isolates from SLE (five with smallest and the five with largest average size) and five HC were analyzed using liquid chromatography with tandem mass spectrometry (LC-MS/MS). Data were analyzed using ANOVA, t-test, hierarchical cluster analysis, protein interactions using the STRING software and correlation analysis using spearman correlation.
Results: We identified a total of 2572 proteins from the platelet isolates. Out of the identified proteins, 396 had significantly different levels, meeting an ANOVA q-value ≤ 0.01. Pairwise t-test analysis, using a fold difference (FD) of ≥ 1.5 and a p-value of ≤ 0.05 as cut off reveled significant differences in the distribution of proteins between groups. Platelets of both SLE groups (small and normal sized) shared higher levels of forty proteins and twenty proteins were reduced, compared to HC. Cytoskeletal functions were overrepresentation in the group of reduced proteins, while proteins with higher levels in platelets from SLE patients included proteins associated with complement and autoantibody targets such as Beta-2-glycoprotein 1, Annexin A5, and Prothrombin. Platelets from SLE patients also shared an abundance in immunoglobulin proteins, with even greater accumulation in the normal sized platelets. SLE platelet heavy constant alpha 1 (r -0.85, p=0.003), heavy constant mu (r -0.64, p=0.05) and heavy constant gamma 3 (r -0.80, p=0.008) was inversely correlated with complement C4 in serum and heavy constant gamma 2 (r -0.648, p=0.049) with complement C3.
Conclusion: This study revealed an accumulation of complement proteins, immunoglobulins and known autoantigens in platelets from SLE patients compared to HC. The signature was largely independent of platelet size, but the enrichment of proteins involved in SLE pathogenesis indicates that the composition is influenced by SLE disease mechanisms. This was supported by the inverse correlation between platelet immunoglobulin and serum levels of complement protein C3 and C4. Platelets are known to interact with complement and express the low-affinity immunoglobulin gamma Fc region receptor IIA (CD32), suggesting a role in the clearance of immune complexes [3]. Future studies will have to determine if platelets play a role in the turnover of complement and immune complexes and the potential role of platelets as a source of autoantigens.
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POS0459 APTAMER-BASED PROTEOMIC SCREENING IN IDENTIFICATION OF PATHOGENIC SIGNAL PATHWAY AND URINARY BIOMARKERS ASSOCIATED WITH HISTOLOGICAL FINDINGS IN LUPUS NEPHRITIS

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Background: The current gold standard for the diagnosis and classification, assessment of the severity of lupus nephritis (LN) is a renal biopsy. On the other hand, since the procedure is highly invasive, there is a pressing need to identify biomarkers for predicting the presence and its histological severity of LN. In addition, the background pathogenesis of each histological findings is not clearly understood.
Objectives: The purpose of this study was to elucidate the urine biomarkers for predicting the presence and the severity of histological findings of LN, and to search the pathogenic signal pathway.
Methods: Urine samples from 24 biopsy-proven active LN patients were initially screened for the levels of 1305 distinct human proteins using an aptamer-based-targeted proteomic assay. We developed histological scoring system based on ISN/RPS lesion definitions and classification, NIH activity and chronicity score. Two experienced evaluators assessed the histological scores. Cluster analysis and pathway analysis were performed.
Results: A total of 24 LN patients were included: 20 (83%) had a proliferative histological class (III or IV +/-V), 4 (17%) pure membranous (V). Through cluster analysis, several histological subgroups were extracted according to correlation with each histological finding, and proteins which corelated with each histological scores were analyzed. We focused on two subgroups: one in which including active glomerular histological findings (endocapillary hypercellularity, karyorrhexis, neutrophil infiltration, subendothelial deposits) and the other in which including interstitial histological findings (interstitial inflammation, interstitial fibrosis, tubular atrophy). Histological scores in the former group showed strong positive correlation with protein group which contained 59 proteins (Group A), including CCL21, CXCL10, VCAM1. Histological scores in the latter group corelated with another protein group which contained 85 proteins (Group B), including MCP-1, CCL11. Ingenuity Pathway Analysis showed 16 pathways (PDGF Signaling, Granulocyte Adhesion and Diapedesis, etc) were upregulated in Group A and 11 pathways (IL-17 signaling, Fibrosis signaling pathway, etc) upregulated in Group B. Among group A and group B urine proteins, those showed strong correlation between respective histological findings were validated with ELISA assays.
Conclusion: An aptamer-based-targeted proteomic assay screening by combining with renal histological scoring system suggested several urine proteins can predict the severity and the presence of major renal histological findings, and suggested to be related with the pathogenesis in patients with LN.
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POS0460 METABOLOMICS ACROSS AGE IDENTIFIES UNIQUE CHANGES IN THE SERUM METABOLIC PROFILE IN PATIENTS WITH SLE

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Background: Cardiovascular disease (CVD) is a leading cause of mortality in patients with systemic lupus erythematosus (SLE, female:male ratio of 9:1) through accelerated atherosclerosis, the build-up of lipids and inflammation in the major artery walls, compared to age and sex matched healthy individuals. This is due to chronic inflammation, dyslipidaemia and other cardiometabolic defects that exacerbate with age (1). SLE in women aged of 35-44 increases the risk of coronary artery disease by 50 times and there is a 100-300-fold increased CVD-related mortality risk in young patients that develop SLE before the age of 18. Investigating metabolic defects in young patients and how they progress with age could help us understand the progressive mechanisms of atherosclerosis in SLE.

Objectives: This study investigated detailed changes in the metabolomic profile of female patients with SLE and matched healthy controls across age.

Methods: Serum NMR metabolomics (>250 metabolites, Nightingale) covering glycolysis metabolites, amino acids and 130 lipid measures was performed on serum from a cohort of female SLE patients (n=164, 13-72 years of age, median 35) and matched healthy controls (HCs, n=120, 15-76 years of age, median 36) and analysed by linear regression and Venn analysis. Multiple t-tests (corrected for multiple comparisons by false discovery rate) were used to assess unique metabolic changes by age group between SLE patients and HCs (≤25, n=62/43; 26-49, n=50/46; ≥50, n=52/31) and dysregulated metabolic pathways were assessed using metaboanalyst software. The metabolic impact of disease activity measures and treatments was assessed by Spearman correlations and unpaired t-tests respectively.

Results: Twenty-five metabolites were significantly altered in all SLE age groups compared to HCs, dominated by atheroprotective high density lipoprotein (HDL) subsets and their surface-bound peptide, apolipoprotein(Apo) A1, all of which were significantly decreased in SLE compared to HCs ($p<0.0001$ in ages combined). In addition, the concentration of glycoprotein acetyls (GlycA, inflammatory biomarker) was increased in SLE in all age groups compared to HCs ($p<0.0001$ in ages combined). Importantly, ApoA1 correlated negatively with disease activity measures (SLEDAI, p=0.005; BILAG, p=0.0009; dsDNA, p=0.003; ESR, p=0.0006) and positively with lymphocyte count (p=0.0005), whilst GlycA correlated positively with ESR ($p<0.0001$) and CRP ($p<0.0001$). Alternatively, metabolites unique to specific age groups in SLE compared to HCs included reduced amino acid subsets in the ≤25 age group, increased atherogenic very low density lipoproteins and reduced polyunsaturated fatty acids in the 26-49 age group, and increased atherogenic low density lipoproteins in the ≥50 age group. Separately, metabolites associated with the glycolysis pathway (p=0.004, metaboanalyist), including acetone, citrate, creatinine, glycerol, lactate and pyruvate, had significant positive correlations with age in SLE patients, but not in HCs. These metabolites were not significantly associated with disease activity measures. However, pyruvate (p=0.01) and lactate (p=0.009) were significantly upregulated in prednisolone treated patients, whilst citrate (p=0.002) and creatinine (p= 0.005) were downregulated in hydroxychloroquine treated patients.

Conclusion: Increasing HDL (ApoA1) levels whilst maintaining low disease activity in patients with SLE from a young age could improve cardiometabolic risk outcomes. This could be achieved through improved nutrition, lipid targeted therapies and better treatment strategies. Focusing on understanding and monitoring biomarkers of the glycolytic pathway could aid treatment decisions and help avoid adverse metabolic effects of current anti-inflammatory therapies in SLE (1).

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POS0461 DISRUPTED HIPPOCAMPAL NEUROGENESIS MEDIATED BY IL-6 AND IL-18 INDUCE NEUROPSYCHIATRIC CHANGES IN MURINE LUPUS

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Background: Systemic lupus erythematosus (SLE) frequently affects the nervous system (NPSLE), however, its pathogenesis is only partly understood. We have previously characterized the behavioral phenotype of the NZB/W-F1 lupus-prone mouse which recapitulates the NPSLE phenotype exhibiting hippocampal-linked behavior including depressive-like disorder, anxiety and cognitive impairment both at early and late stages of the disease characterized by a profound hippocampal inflammatory response1,2. Defective hippocampal neural stem cell (hNSC) response is associated with cognitive dysfunction, depression and anxiety, all of which represent common neuropsychiatric features of both human and murine SLE.

Objectives: To further investigate the hippocampal neurogenesis in lupus mice and determine its involvement in disease pathogenesis.

Methods: All experiments were performed in female NZW/NZB F1 and C57BL/6 (WT) mice at the age of 3 months (pre-nephritic) and 6 months (nephritic stage) (n=5-8/condition/experiment). Neurogenesis was assessed in sagittal sections of hippocampus by immunohistochemical staining (DCX, Sox2, GFAP, Iba1) and morphological criteria. RNA-sequencing was performed in hippocampal tissue followed by pathway and enrichment analysis. Apoptosis (cleaved-caspase 3) and immune cell infiltration (CD11b, CD45, Ly6G, Ly6C, MHC-II, CD4, CD8, B220, Iba1, CD80, CD86, Argianse-1, iNOS) were assessed by flow-cytometry. Cytokines levels were measured by Legendplex. Ex vivo assays were performed in adult hippocampal neural stem cells extracted by 2-month-old female WT mice.

Results: We identified a profound disruption (~2-fold) of hippocampal neurogenesis (decreased DCX+ cells) both at 3 ad 6 month-old lupus mice together with decreased differentiated cells in both time-points, suggesting that lupus mice exhibit impaired neuronal differentiation. Although the number of the neuronal precursors radial glial-like cells (RGLs) was normal at pre-nephritic stage, lupus mice express increased number of both activated RGLs (Sox2+/GFAP+) and proliferating neuronal progenitors (Sox2+ cells) indicating enhanced self-renewal ability of neural precursors and augmented proliferation. Levels of cleaved-caspase 3 were elevated in lupus hippocampus supporting increased hippocampal apoptosis. Transcriptomic analysis of hippocampal tissue revealed a profound inflammatory response in lupus mice. Flow-cytometry analyses showed a pronounced immune cell trafficking in lupus hippocampus with a myeloid predominant response –involving predominantly the microglia- both at early and late stages of the disease. Multiplex assays revealed elevated levels of IL-6 and IL-18 in lupus hippocampus. Ex vivo exposure of adult hNSCs to IL-6 or IL-18 promoted cell proliferation and induced apoptosis.

Conclusion: The NZB/W-F1 mouse model of SLE exhibits defective neurogenesis due to increased apoptosis, and decreased differentiation of neuronal progenitors. Inflammation in lupus hippocampus results in elevated levels of IL-6 and IL-18 with both cytokines negatively affecting the hNSCs response. IL-6 and IL-18 may induce behavioral changes in NZB/W-F1 lupus mediated by altered neurogenesis and may represent therapeutic targets in NPSLE.

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POS0462 HYDROXYCHLOROQUINE REDUCES THE TITERS OF ANTI-DOMAIN 1 ANTIBODIES OVER TIME IN PATIENTS WITH PERSISTENTLY POSITIVE ANTIPHOSPHOLIPID ANTIBODIES: RESULTS FROM THE APS ACTION CLINICAL DATABASE AND REPOSITORY ("REGISTRY")

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Background: Data on fluctuation of antibodies directed against domain 1 (anti-D1) of β_2-glycoprotein I (β_2GPI) are scarce. Patients with antiphospholipid syndrome (APS) and all three criteria tests for antiphospholipid antibodies (aPL) display higher titers of anti-D1, which correlate with anti-β_2GPI levels.
Objectives: This project aims at evaluating predictors of the variation of anti-D1 titers over time in a large international cohort of persistently aPL positive patients.
Methods: AntiPhospholipid Syndrome Alliance For Clinical Trials and InternatiOnal Networking (APS ACTION) Registry was created to study the course of persistently aPL-positive patients with or without autoimmune disorders over at least 10 years. Inclusion criteria are positive aPL by Updated Sapporo Criteria tested within one year prior to enrolment. Patients are followed every 12±3 months with clinical data and blood collection. Patients with available blood samples from at least three time points were included in this analysis. Anti-β_2GPI and anti-D1 IgG were tested by chemiluminescence (BioFlash, Werfen) at APS ACTION core laboratories. Positive results were defined as >20 CU, according to the manufacturer. Clinical data were retrieved from APS ACTION online database. Anti-D1 titers within the same subject were compared by Friedman's test. A mixed linear model was built to identify predictors of the fluctuation of anti-D1 antibody titers over time.
Results: In this longitudinal study, 230 patients with anti-D1 tested at 4 time points were included (Table 1). Patients with thrombotic APS had anti-D1 titers significantly higher than those without thrombosis (p=0.022). Among 135 patients with at least one anti-D1 positive result, anti-D1 titers varied significantly over time (Friedman statistics: 508.5, p<0.0001; anti-D1 geometric mean at baseline 189.0; T1 132.3 [-15%]; T2 113.8 [-17%]; T3 109.2 [-6% versus T2, -38% versus T1]). Anti-D1 titers were significantly higher at baseline compared to T3 (p=0.029). In the 4 years of follow-up, 18 new thrombotic events occurred. Patients with double/triple aPL positivity displayed 12.5 fold increase [95%CI 7.4-20.0] in baseline anti-D1 titers. After adjustment for age, gender and number of positive aPL tests, the fluctuation of anti-D1 titers was associated with treatment with hydroxychloroquine (HCQ) at each time-point. In particular, treatment with HCQ, but not those with conventional immunosuppressors, was associated with a 1.3-fold decrease in anti-D1 titers [95%CI 1.1-1.5]. In the same multivariable model, incident vascular events were associated with a 1.5 fold increase of anti-D1 titers. A concomitant diagnosis of systemic lupus erythematosus did not affect the fluctuation of anti-D1 titers.
Conclusion: Treatment with HCQ and vascular events during follow-up were identified as significant predictors of the fluctuation of anti-D1 antibody titers over time.

Table 1. Demographic and Clinical Characteristics of 230 APS ACTION Registry Patients with anti-D1 tested ≥3 time points during the follow-up

	Anti-D1 pos samples	Anti-D1 neg samples	p-value	Overall sample
	(n=135)	(n=95)		(n=230)
Age [years] *mean (SD)*	42.3 (11.8)	48.8 (13.0)	0.0001	45.0 (12.7)
%Female *(n)*	71.9 (97)	65.3 (62)	0.358	69.1 (159)
Associated systemic autoimmune disease	39.3 (53)	44.2 (42)	0.539	41.3 (95)
aPL without APS	19.3 (26)	34.7 (33)	0.010	25.7 (59)
Thrombotic APS	54.1 (73)	53.7 (51)		53.9 (124)
Obstetric APS	11.9 (16)	5.3 (5)		9.1 (21)
Thrombotic/+obstetric APS	14.8 (20)	6.3 (6)		11.3 (26)
aCL IgG	89.5 (119/133)	25.5 (24/94)	<0.0001	63.0 (143/227)
aCL, IgM	36.1 (48/133)	27.7 (26/94)	0.234	32.6 (74/227)
Anti-2GPI, IgG	93.2 (124/133)	39.4 (37/94)	<0.0001	70.9 (161/227)
Anti-2GPI, IgM	34.6 (46/133)	21.3 (20/94)	0.043	29.1 (66/227)
LA	82.8 (82/99)	59.5 (44/74)	0.001	72.8 (126/173)

Disclosure of Interests: None declared.
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POS0463 REENGINEERING CHIMERIC ANTIGEN RECEPTOR T CELLS FOR TARGETED THERAPY OF LUPUS NEPHRITIS

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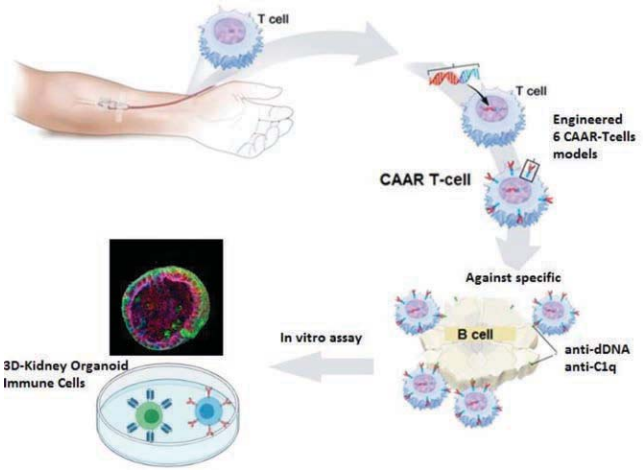
Background: Although the pathogenesis of lupus nephritis (NL) is not completely clear, it is known that the production of anti-dsDNA or anti-C1q antibodies is related to its activity [1]. Despite treatment, approximately 30-40% of patients continue to present a significant number of renal outbreaks [2]. Therefore, there is a growing interest in the development of more specific drugs. As B cells play a central role in the pathogenesis of SLE, the therapy CAR-T cells has been studied reporting good results for the prevention and also for as treatment in murine lupus models [3,4]. Recently, a new selective immunotherapy for autoimmune diseases has been demonstrated by modifying the T cells with a chimeric autoantigen receptor (CAAR) [5]. This novel therapeutic approach could be beneficial in NL with the aim of depleting only anti-DNA producing B cells. In this way, the benefits of anti-CD20 biologics would be obtained, but it would be much more specific, personalized and, surely, effective since only the self-reactive B cells would be destroyed.
Objectives: To study CAAR-Tcell anti-dsDNA and anti-C1q therapy in NL through *in vitro* experiments (primary cells and kidney organoids).
Methods: Synthesis of 6 CAAR anti-dDNA that will be transfected in the primary T cells extracted from patients with NL and healthy controls (N = 10 per group). Through *in vitro* experiments their ability to lyse the B cells that produce anti-dsDNA or anti-C1q will be evaluated. The two CAAR-Tcell models that is most effective will be evaluated using kidney organoid models obtained from human samples.
Results: We engineered six human T cells models to express a chimeric autoantibody receptor (CAAR), consisting lupus nephritis autoantigen. As antigens for anti-DNA produced B cells, we designed Heparanase1/2, Histone1 and alpha actinin 1/2 CAAR-Tcells. For anti-C1q produced B cells, we used C1q protein fused to CD19-CD3 signaling domains. The CAAR-Tcells models that exhibited specify cytotoxicity *in vitro* againts B cells producing



anti-dDNA were Heparanase2 and alpha actinin1 CAAR-Tcells (selectivity of 75% vs 45%). C1q CAAR-T cells also presented specificy cytotoxicity for anti-C1q B cells (selectivity of 80%). In *vivo* imaging assay reveals that C1q or Heparanase2 CAAR-Tcells depleted completly B cells at 48 hours (ratio 1:10, Bcells:CAAR T-cells). We developed 3D in vitro organoid culture using human kidney organoid and B cells from lupus nephritis patients. We evaluated Heparanase2 and C1q CAAR-Tcells using them and we demostrated that C1q CAAR-Tcells could resolved better local kidney inflammation (reduction of IL6, TNF and INF cytokines levels).

Conclusion: Taken together, these results show that C1q CAAR-Tcells could be an effective and selective immune therapy for treatment of lupus nephritis. Currently, we are evaluated this therapy using NZWB/F1 murine models.

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POS0464 DIFFERENTIAL MOLECULAR PROFILES IN THE SYNOVIAL TISSUE AND SYNOVIAL FLUID OF PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: The differential diagnosis of Rheumatoid Arthritis (RA) and Psoriatic arthritis (PsA) is often difficult due to the similarity of symptoms and the unavailability of reliable clinical biomarkers. Molecular alterations have been suggested to contribute to the pathophysiological processes in the knee joint, and it is known that chronic inflammation induces significant changes in the synovial tissue (ST) and synovial fluid (SF) lipidome and proteome.

Objectives: We aimed to evaluate whether specific characteristics in the molecular profiles from ST and SF could support the differential diagnosis of these diseases.

Methods: ST frozen samples of patients affected by RA (n=6), PsA (n=12) and control donors (n=10) were compared using Matrix-Assisted Laser Desorption Ionization Mass Spectrometry Imaging (MALDI-MSI) for spatially resolved lipid analysis. To this end, tissue sections were measured on a RapifleX MALDI-TOF/TOF instrument. Next, a targeted approach based on multiple reaction monitoring (MRM-MS) was performed to further validate the lipidomic alterations reported by MALDI-MSI between RA and PsA tissues. In this case, lipids extracted from SF (control donors (n=4), RA (n=21) and PsA (n=27)) were analyzed in a QTRAP 4000 mass spectrometer for the targeted analysis of 84 lipid species. Finally, a quantitative proteomic analysis was carried out on FFPE ST from RA (n=13), PsA (n=13) and controls (n=8) by nLC-MS/MS analysis using a TimsTOF Pro system (Bruker). Statistical analyses were performed using GraphPad Prism, Metaboanalyst and Perseus software.

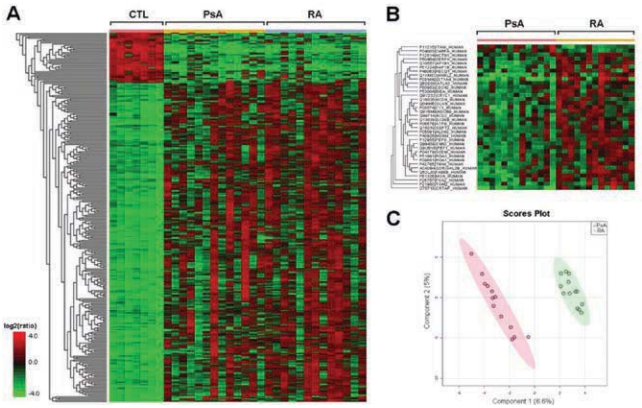

Figure 1. Results from the proteomic analysis carried out on synovial tissues. A) Heatmap showing the differential protein profiles between synovial tissues (PsA and RA) and healthy controls (CTL), at FDR 0.01. B) Characteristic protein panel discriminating PsA and RA tissues (p-value < 0.01). C) Discriminant analysis performed using this protein panel.

Results: Lipid profiles in ST from PsA and RA were unequivocally distinguished by MALDI-MSI followed by PCA-DA, and were also different comparing with control tissues. Interestingly, several lipid species, including sphingomyelins, phosphatidylcholines (PC) and phosphatidylethanolamines (PE), presented the greatest separation power to classify RA and PsA tissue samples. ANOVA analysis found 35 lipid species significantly different among the study groups, most of them significantly increased in RA and PsA compared to controls. Particularly, 11 lipids showed higher levels in PsA tissues compared with RA, including several PC and PE. The spatial distribution of these PE species was associated with areas of the sublining layer with increased vascularity and inflammatory cell infiltrates, according to MALDI-MSI images. On the other hand, RA and PsA patients were also correctly classified based on the SF levels of all quantified lipid species according to PCA and clustering analysis. Finally, the proteomic analysis quantified around 2,500 distinct proteins in the ST, including several related with lipid metabolism. Near 300 proteins showed altered abundance in the pathological tissues compared to healthy controls (FDR 0.01%, Figure 1A), being the small subset increased in controls mainly extracellular matrix proteins. The comparison between RA and PsA ST led to the identification of a panel of 36 proteins discriminating the two tissues with high statistical significance (p-value <0.01). In this comparison, all proteins except two appeared increased in RA (Figure 1B). A discriminant analysis shows the usefulness of this protein panel to differentiate the two diseases (Figure 1C).

Conclusion: Our study shows distinct molecular profiles between RA and PsA synovial tissue and synovial fluid, and reports potential clinically useful lipid and protein markers for the differential diagnosis of these diseases.

Disclosure of Interests: None declared.

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POS0465 UNSUPERVISED CLUSTERING ANALYSIS OF THE SERUM PROTEOME IDENTIFIES SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH DISTINCTIVE DISEASE SEVERITY AND LUPUS NEPHROPATHY

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Background: Systemic lupus erythematosus (SLE) is a remarkably heterogeneous autoimmune disease. Despite great efforts, our knowledge of serum protein patterns in severe SLE phenotypes is still limited.

Objectives: This study investigated the serum proteomic profile of SLE, in order to identify relevant clinical patterns.

Methods: Proximity extension immunoassay (PEA, Olink) was used to assess the serum levels of one hundred and eighty-four inflammation and organ damage-related proteins in patients with SLE (n = 72) and age-matched healthy donors (HD) (n = 18). In parallel, an extensive clinical and analytical profile of recruited subjects was performed. To evaluate the contribution of molecular profiles to the disease severity, unsupervised clustering analyses were developed. Gene ontology enrichment analysis were

also carried out to interrogate the biological meaning associated with the molecular signatures identified.

Results: Several circulating proteins related to inflammation and organ damage were coordinately altered in the serum of SLE patients in relation to HD. Unsupervised clustering analyses differentiated 2 patients clusters presenting different proteomic profiles. Clinically, although no differences were found in terms of age or disease duration, patients belonging to cluster 1 were characterized by a significantly higher status of disease activity (SLEDAI > 6) and prevalence of positivity for anti-ENA and anti-dsDNA antibodies than patients belonging to cluster 2, along with preponderance of patients with biopsy-diagnosed lupus nephritis (LN), abnormal creatinine and proteinuria. Twenty-three serum proteins were found deregulated between clusters. Interestingly, in parallel to well-recognized inflammatory cytokines, chemokines and regulatory proteins of leukocyte activity [Interferon (IFN)-gamma, interleukin (IL)-15RA, IL-20, sCD40, macrophage colony-stimulating factor-1 (CSF-1), leukemia-inhibitory factor receptor (LIF-R), monocyte chemotactic protein (MCP)-1, MCP-4, C-C motif chemokine (CCL)-4, C-X-C motif chemokine (CXCL)-5, CXCL-6, metalloproteinase (MMP)-1, programmed cell-death ligand (PDL)-1, eukaryotic translation initiation factor 4E-bindign protein 1 (4E-BP1)], a number of key proteins involved in renal damage, not previously reported in serum from SLE, were further found significantly deregulated in patients belonging to cluster 1 when compared with cluster 2 (kidney injure molecule 1 (KIM1), Linker for activation of T-cells family member-2 (LAT2), C-type natriuretic peptide (NPPC), Erbin-2 interacted protein (ERBB2IP)].

Conclusion: 1) This highly sensitive proteomic analysis in the serum of SLE identified molecular patterns distinguishing patients with high disease activity and active LN, and including several novel candidate proteins, whose exact role and suitability as biomarkers in SLE deserve further investigation. 2) Combination of novel and traditional disease-specific biomarkers may improve diagnosis and management of SLE.

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Disclosure of Interests: None declared.

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POS0466

RESISTANT STARCH DIET IMPROVES DISTINCT GUT MICROBIOTA STRUCTURES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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Background: Fiber-poor diets are linked to a reduction in gut microbiota diversity and gut barrier integrity, which is thought to promote the susceptibility to chronic inflammatory disorders[1,2]. We have previously shown that dietary resistant starch (RS) improves lupus-like disease in a murine model of SLE[3] through the modulation of microbiota composition. If similar dysbiotic microbial community structures exist in subsets of SLE patients and if a RS intervention may be efficacious in those patients remains unclear.

Objectives: To test if the dietary RS content in SLE and SLE-related antiphospholipid syndrome (APS) affect gut microbial taxa associated with SLE in published cohorts to date.

Methods: We obtained stool and blood samples as well as diet history for up to 3 visits (0, 4 and 8 weeks) from 12 SLE (n=28) and 15 APS (n=44) patients as well as 20 controls (n=48) as previously published[4-6]. Microbiota composition was defined by 16S rRNA V4 region sequencing on the Illumina platform and correlated with dietary fiber content extracted from a diet questionnaire. We used the FDA reference list to determine dietary RS contents in patients` regular diets and defined RS quantities as being low if less than 2.5 g/day and as medium if 2.5 to 15 g/day. None of the patients achieved high RS greater than 15 g/day. Mann-Whitney or Kruskal-Wallis tests were performed to compare bacteria relative abundances among the different groups. Simple linear regression was performed to relate the bacterial abundance to RS content and other metadata.

Results: Medium intake of RS was associated with beneficial *Bifidobacterium* spp. in SLE patients (p=0.016) but not APS (p=0.509). Instead, APS patients who consumed medium quantities of RS in their diets had less gut bacterial taxa that are capable of producing cardiolipins (among them *Collinsella*; p=0.009) and *Ruminococcus gnavus* (p=0.0142), a species previously associated with lupus nephritis[7]. A recent Japanese metagenome-wide study[8] associated *Streptococcus* spp. and related redox reaction genes with SLE, which may also affect oxidative processes in APS[9]. We therefore also explored *Streptococcus* levels in SLE and APS patients and found unexpectedly a significant reduction of streptococci in a subset of APS (p=0.004) but not SLE patients (p=0.451) in medium compared to low RS dietary content. *Streptococcus* abundance was correlated with both *Collinsella* (R^2=0.3141; p=<0,0001) and *Ruminococcus gnavus* (R^2=0.1687; p=<0,0056) in APS patients.

Conclusion: Medium compared to low RS quantities in the regular diets of SLE and APS patients were associated with unique alterations in gut microbial community structures. *Bifidobacterium* increased in SLE patients with diets containing medium RS whereas APS patients with medium RS carried less cardiolipin-synthesizing taxa and lupus-related pathobionts. In particular, *Streptococcus* species recently strongly associated with SLE and redox reactions in Japanese patients in a metagenome-wide study[8], were significantly suppressed in APS patients on medium RS diets. This modulatory effect was not seen in SLE patients or control subjects consuming medium RS. Together, these findings support distinct dietary effects on autoimmune gut microbiomes depending on the disease state. They also suggest potential beneficial effects of increased RS content on gut microbiota in SLE and APS patients. Fully resolving gut microbial signatures and clinical characteristics in these patients may identify the ideal subset to benefit from an interventional pilot trial with RS.

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Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models

POS0467 DERSIMELAGON, A NOVEL ORAL MELANOCORTIN 1 RECEPTOR AGONIST, DEMONSTRATES DISEASE-MODIFYING EFFECTS IN PRECLINICAL MODELS OF SYSTEMIC SCLEROSIS

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Background: Activation of melanocortin 1 receptor (MC1R) is known to have broad anti-inflammatory and anti-fibrotic effects. The bleomycin (BLM)-induced skin fibrosis murine model is well-established for systemic sclerosis (SSc). α-melanocyte-stimulating hormone, an endogenous ligand of MC1R, inhibits skin fibrosis and MC1R knock-out enhances skin fibrosis in this model. These pieces of evidence suggest that MC1R agonism has potential in the treatment of SSc.
Objectives: Dersimelagon phosphate (MT-7117) is an investigational small molecule that is an orally administered, selective agonist for MC1R. The purpose of this study is to investigate the potential of MT-7117 as a therapeutic agent for SSc by evaluating its efficacy and mechanism of action in complementary preclinical models. The expression and distribution of MC1R in the skin of SSc patients was investigated.
Methods: The effects of MT-7117 on skin fibrosis and lung inflammation were evaluated in BLM-induced SSc murine models that were optimized for prophylactic and therapeutic evaluation. Microarray-based gene expression analysis and serum protein profiling were performed to investigate the mechanism of action of MT-7117 in the BLM-induced SSc models. The effect of MT-7117 on TGF-β-induced activation of human dermal fibroblasts was evaluated *in vitro*. Immunohistochemical analyses of MC1R expression in skin samples from SSc patients were performed.
Results: Prophylactic treatment with MT-7117 (≥0.3 mg/kg/day p.o.) significantly inhibited the increase in collagen content of the skin, the serum level of surfactant protein D, and the weight of the lungs from BLM-induced skin fibrosis and lung inflammation model. Therapeutic treatment with MT-7117 (≥3 mg/kg/day p.o.) significantly suppressed skin thickening and the numbers of myofibroblasts in pre-established BLM-induced skin fibrosis model. Gene array analysis using the BLM-induced SSc model demonstrated changes in numerous categories related to macrophages, monocytes, and neutrophils, followed by endothelial cell-related categories after treatment with MT-7117. In the analysis that focused on biological functions, categories of inflammatory response, activation of antigen-presenting cells, angiogenesis, atherosclerosis, vasculogenesis, and vaso-occlusion were suppressed by MT-7117. In the analysis that focused on molecular signaling pathways, triggering receptor expressed on myeloid cells-1, IL-6, and oncostatin M involved in inflammation, and peroxisome proliferator-activated receptor that is related to fibrosis were all affected by MT-7117. Serum protein profiling using BLM-induced SSc model revealed that multiple SSc-related biomarkers including P-selectin, osteoprotegerin, cystatin C, growth and differentiation factor-15 and S100A9 were suppressed by MT-7117. MT-7117 inhibited the activation of human dermal fibroblasts by suppressing TGF-β-induced *ACTA2* (encoding α-smooth muscle actin) mRNA elevation in vitro. Immunohistochemical analyses showed that MC1R positivity was observed in 40 of 50 diffuse cutaneous SSc patients. MC1R was expressed by monocytes/macrophages, neutrophils, blood vessels (endothelial cells), fibroblasts, and epidermis (keratinocytes) in the skin of SSc patients.
Conclusion: MT-7117 demonstrates disease-modifying effects in preclinical models of SSc. Investigations of its mechanism of action and target expression analyses indicate that MT-7117 exerts its positive effects by affecting the pathologies of inflammation, vascular dysfunction, and fibrosis through inflammatory cells, endothelial cells, and fibroblasts. In view of its potent beneficial impact on all these three main pathologies of SSc, MT-7117 is a potential therapeutic agent for the treatment of clinically challenging SSc, which has diverse and difficult to treat symptoms. A phase 2 clinical trial investigating the efficacy and tolerability of MT-7117 in patients with early, progressive diffuse cutaneous SSc is currently in progress.
Disclosure of Interests: Masahiro Kondo Employee of: Mitsubishi Tanabe Pharma Corporation, Tsuyoshi Suzuki Employee of: Mitsubishi Tanabe Pharma Corporation, Yuko Kawano Employee of: Mitsubishi Tanabe Pharma Corporation, Shinji Kojima Employee of: Mitsubishi Tanabe Pharma Corporation, Masahiko Miyashiro Employee of: Mitsubishi Tanabe Pharma Corporation, Atsuhiro Matsumoto Employee of: Mitsubishi Tanabe Pharma Corporation, Gabriela Kania: None declared, Przemyslaw Blyszczuk: None declared, rebecca ross: None declared, Panji Mulipa: None declared, Francesco Del Galdo Grant/research support from: Prof. F. Del Galdo received fees and research support from Abbvie, AstraZeneca, Boehringer-Ingelheim, Capella, Chemomab, Kymab, Janssen and Mitsubishi-Tanabe., Yun Zhang: None declared, Jörg H.W. Distler Grant/research support from: Prof. J.H.W. Distler received consulting fees, lecture fees, and/or honoraria from Actelion, Active Biotech, Anamar, ARXX, aTyr, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, Sanofi-Aventis, RedX, RuiYi and UCB. J. H. W. Distler is stock owner of 4D Science and Scientific head of FibroCure.
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POS0468 EXTRACELLULAR VESICLES FROM SERUM OF MYOSITIS PATIENTS AS CIRCULATING BIOMARKERS AND DISEASE MEDIATORS

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Background: Inflammatory myopathies (IM) are a heterogeneous group of disorders characterized by autoimmune inflammatory destruction of skeletal muscles. It is many times associated with lung, skin and joint involvement. Identifying biomarkers that can differentiate IM from other muscle disorders may elucidate the pathophysiology of IM, guide novel therapies, monitor disease activity/response to treatments and predict prognosis. Exosomes are membrane-bound nanovesicles with diameters of 30-150 nm that contain multiple proteins, nucleic acid, lipids and other molecules in a tissue- and cell-specific manner. Exosomes are secreted by a large variety of cells, play major roles in cell-cell interactions, and have recently emerged as circulating biomarkers in a variety of pathological conditions, including several autoimmune diseases.
Objectives: To characterize exosomes from serum of IM patients, analyze protein expression and study their potential mediators of disease pathologies.
Methods: Serum was collected from patients suffering from IM(n=5) and from patients suffering from Becker (BMD) and Duchenne (DMD) muscular dystrophies (n=6). Exosomes were isolated by Exoquick precipitation and analyzed for size distribution and by nanoparticle tracking analysis (NTA) and by Western blot for exosome markers. The effects of the isolated EVs on human satellite cell proliferation and differentiation and macrophage activation were examined.
Results: Exosomes from IM patients decreased human satellite cell proliferation (51%, P<0.01) and inhibited their myogenic differentiation as indicated by lower fusion index (24% inhibition, P<0.01) and expression of myosin heavy chain (72% inhibition, P<0.001). Similar results were obtained also with exosomes derived from DMD and BMD patients; however, their inhibitory effect were more pronounced on MyoG expression. Treatment of macrophages with exosomes from IM patients significantly increased the expression of IL-10 (3-fold, P<0.001), compared to exosomes of healthy controls and DMD patients. Another significant difference was in the expression of signaling molecules: Thus, exosomes from BMD patients increased the phosphorylation of Erk and p38, whereas a smaller effect was induced by IM exosomes.
Conclusion: Exosomes from IM patients decrease satellite cell proliferation and myogenic differentiation compared to healthy exosomes. In addition, these exosomes increased the expression of IL-10 in macrophages. These effects are unique to exosomes of IM patients compared to muscular dystrophies. These promising results suggest that serum exosomes should be further investigated as a novel biomarker with potential therapeutic implications.
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POS0469 ENDOTHELIAL TO MESENCHYMAL TRANSITION AND SENESCENCE ARE PART OF THE FIBROTIC PATHOGENESIS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterised by inflammation, vasculopathy and fibrosis. Several mechanisms, including endothelial to mesenchymal transition (EndMT) and cellular senescence, may be included in the fibrosis process, especially in response to inflammation and vasculopathy.
Objectives: Our study aimed to identify how EndMT and cellular senescence manifest in SSc skin fibrosis.
Methods: We performed a cross-sectional biobank study on formalin-fixed, paraffin-embedded skin biopsies from patients meeting the ACR/EULAR 2013 classification criteria for SSc. The extent of dermal fibrosis and inflammatory cell infiltration was scored on haematoxylin-eosin stained samples. Fibrosis severity was semi-quantified by the compactness of collagen bundles and scored from one to three. The presence of senescence was defined by P21 or P16 positivity without co-localised Ki-67. The expression of P16, P21, and CTGF on fibroblasts and endothelia was scored from zero to two. The semi-quantitative score was evaluated independently in the superficial and deep dermis by agreement of two researchers (MRD and YHC). EndMT was assessed by co-localisation of CD31 and α-SMA double staining by immunofluorescence, and enclosure of ERG positive endothelial cell nuclei by α-SMA stained cytoplasm under bright field. Lymph vessels were identified by D2-40 (podoplanin) staining, and density was assessed.

Results: In total, skin biopsies from 18 SSc patients and four age-matched healthy controls were investigated. The characteristics of the patients are listed in Table 1. The dermal fibrosis score revealed a correlation with modified Rodnan skin score (Figure 1A).

Table 1. Clinical features of 18 patients with systemic sclerosis

Age, median (IQR)	47 (21)
Female, n (%)	11 (61)
Biopsy site, n (%)	
Upper limb	3 (17)
Trunk	6 (33)
Lower limb	8 (44)
Type of SSc, n (%)	
Limited cutaneous SSc	13 (72)
Diffuse cutaneous SSc	5 (28)
mRSS, median (IQR)	4 (9)
Anti-topoisomerase I antibody positive, n (%)	3 (17)
Anti-RNA polymerase 3 positive, n (%)	2 (11)
Anti-centromere positive, n (%)	3 (17)

SSc, systemic sclerosis; IQR, interquartile range; mRSS, modified Rodnan skin score.

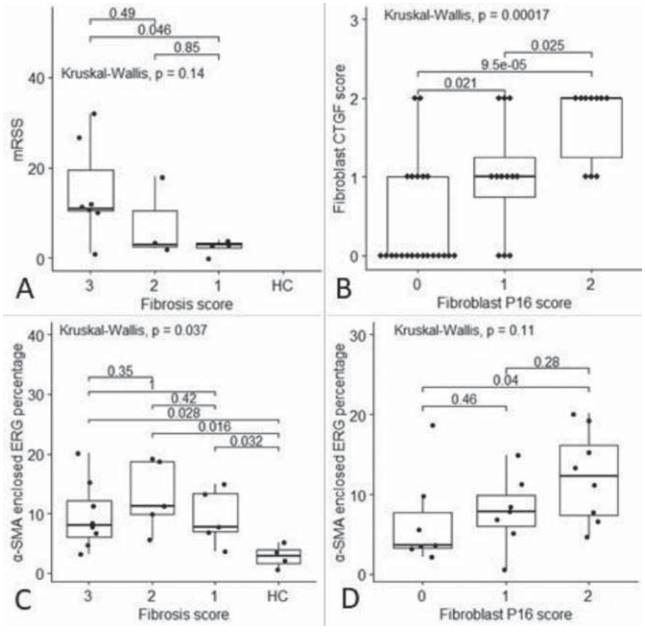

Figure 1. (A) The modified Rodnan skin score (mRSS) was higher in skin biopsies with severe fibrosis. (B) While merging superficial and deep dermis semi-quantitative scores, increased senescence marker was associated with increased CTGF expression on fibroblasts. (C) Endothelial to mesenchymal transition (EndMT) was more in systemic sclerosis skin without difference between groups with various fibrosis severity. (D)EndMT was associated with increased senescence markers on fibroblasts.

Senescence markers showed higher expression on fibroblasts from highly fibrotic dermis than healthy control. The median (IQR) percentage of P16 positive fibroblasts in dermis was 0.7 (0.5) in healthy controls, 0.9 (0.7) in grade one fibrosis, 0.5 (0.5) in grade two fibrosis, and 6.0 (4.6) in grade three fibrosis (p = 0.144). The median (IQR) percentage of P21 positive fibroblasts in dermis was 3.3 (7.0) in healthy controls, 10.3 (11.8) in grade one fibrosis, 33.2 (19.2) in grade two fibrosis, and 32.9 (40.7) in grade three fibrosis (p = 0.042). Moreover, increase of senescence markers on fibroblasts was associated with increased CTGF expression (Figure 1B). The density of blood and lymphatic vessels did not correlate with fibrosis severity. Still, the frequency of EndMT was significantly higher in patients with SSc, although it did not differ between groups with various fibrosis severity (Figure 1C). EndMT was not observed in lymphatic vessels (i.e. there was no co-localisation of D2-40 and α-SMA). Finally, the frequency of EndMT was increased with stronger fibroblast senescence (Figure 1D).
Conclusion: EndMT and fibroblast senescence were more prominent in SSc skin compared to healthy control skin. Strong fibroblast senescence was associated with EndMT. Fibroblast senescence might facilitate EndMT and be involved in SSc fibrosis.
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POS0470 FOSL-2 TRANSCRIPTION FACTOR REGULATES MACROPHAGE POLARIZATION AND PHAGOCYTOSIS IN SYSTEMIC SCLEROSIS

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Background: Macrophages play a crucial role in the development and progression of systemic sclerosis (SSc). Pathological effects of the AP-1 transcription factor Fos-related antigen 2 (Fosl-2) have been associated with SSc. However, the exact role of Fosl-2 in macrophage function in SSc has not been clarified.
Objectives: To study macrophage functions in SSc with a focus on Fosl-2 as a potential regulator.
Methods: Human monocyte-derived macrophages (hMDM) were differentiated from $CD14^+$ blood-derived monocytes from healthy controls and SSc patients. Published data of single cell RNA sequencing (scRNAseq) of human explanted lung tissue from SSc-ILD patients[1] and skin from dcSSc patients[2] was further analyzed using the R package Seurat V2.3.4. Peritoneal macrophages were isolated from Fosl2 overexpressing transgenic (Fosl2tg), $Csf1R^{Cre}Fosl2^{fl/fl}$, wild-type (wt) and $Fosl2^{fl/fl}$ mice. Protein expression was detected by Western Blot. Phagocytic activity in hMDM was detected using pHrodo Red *E.coli* particles and *in vivo* phagocytosis of phagocytic dye aggregates in peritoneal macrophages was assessed 4 hours post injection and detected by flow cytometry. Surface marker expression was measured using human or mouse macrophage polarization panels by flow cytometry.
Results: SSc hMDM (n=18-25) showed increased Fosl-2 protein expression (untreated: p<0.01, LPS stimulated: p<0.01) compared to healthy hMDM (n=11-18). Phenotypical characterization of untreated SSc hMDM (n=17) displayed an increased percentage of $CD40^+CD86^+CD206^+PD\text{-}L2^+CD163^+$ cells (p<0.05) compared to healthy hMDM (n=7). Additionally, we found enhanced phagocytic activity in untreated (p<0.01) and LPS stimulated (p<0.05) SSc hMDM (n=29-34) compared to healthy hMDM (n=12-16). To assess the role of Fosl-2 in other macrophage types, we performed scRNAseq analysis of the SSc-ILD lung dataset, which lead to the identification of differentially expressed macrophage polarization (*CD206*) and phagocytosis-associated genes (*MARCO*/*C1QA*/*C1QB*/*C1QC*) in $SPP1^{hi}$ macrophages from SSc-ILD patients when comparing $FOSL2^{hi}$ and $FOSL2^{null}$ cells. Moreover, independent of *FOSL2* expression phagocytosis-associated *ARPC1B*/*ARPC2*/*ARPC5* genes were upregulated in $SPP1^{hi}$, $FABP4^{hi}$ and $FCN1^{hi}$ macrophages in SSc-ILD patients (p.adj.≤0.05; log2 ratio≥0.5). Similarly, to the alternatively-activated macrophages in SSc-ILD lungs, scRNAseq of dcSSc skin tissue revealed increased expression of *CD204*/*CD163*/*CD36* in $CCR1^+$ macrophages. Further, $FOSL2^{hi}$ $CCR1^+$ skin macrophages showed higher expression of phagolysosome-associated *CARO1A* and *ARL8B* genes compared to $FOSL2^{null}$ cells (p.adj.≤0.05; log2 ratio≥0.5). In the immunofibrotic animal model of SSc, Fosl2tg peritoneal macrophages showed enhanced expression of alternatively-activated CD206 (p=0.0591) and PD-L2 (p<0.05) polarization markers compared to wt cells (n=5-9). $Csf1R^{Cre}Fosl2^{fl/fl}$ peritoneal

macrophages displayed a reduced expression of CD206 ($p<0.05$) and PD-L2 ($p<0.01$) markers compared to $Fosl2^{fl/fl}$ controls (n=5-9). Preliminary data indicated that Fosl2tg $MHCII^+$ and $CD36^+$ peritoneal macrophages showed a trend towards elevated phagocytic activity compared to wt cells (n=3). $Csf1R^{Cre}Fosl2^{fl/fl}$ peritoneal macrophages did not show a significant difference in phagocytic activity (n=3) compared to $Fosl2^{fl/fl}$ controls.

Conclusion: For the first time, we showed an increased expression of Fosl-2 and boosted phagocytic activity in SSc hMDM. scRNAseq analyses revealed upregulated phagocytosis-related genes with association to alternatively-activated macrophage polarization in different macrophage clusters in SSc-ILD lungs and dcSSc skin. Moreover, our animal data indicated an involvement of Fosl-2 regulating alternatively-activated macrophage polarization and phagocytosis. Therefore, targeting this alternative/pro-phagocytic phenotype represents an effective tool to counteract disease progression.

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POS0471

INDUCED ANTIBODIES DIRECTED TO THE ANGIOTENSIN RECEPTOR TYPE 1 PROVOKE SKIN AND LUNG INFLAMMATION AND DERMAL FIBROSIS AND ACT SPECIES OVERARCHING

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Background: Antibodies directed to the angiotensin receptor type 1 (AT1R) were found to be increased in patients with SSc ad they predict mortality and SSc complications (1, 2). In vitro studies suggested an involvement in the pathogenesis of systemic sclerosis (SSc).

Objectives: Here, we aim to determine the contribution and functions of AT1R autoantibodies (Abs) in vivo and in vitro as well as their capacity to recognize AT1R from different species.

Methods: C57BL/6J mice were immunized with membrane-embedded human AT1R or empty membrane as control. Phenotypic properties of various organs were examined by immunohistochemistry, immunofluorescence, and TUNEL apoptosis assay. A monoclonal (m)AT1R Ab was generated based upon this mouse model by hybridoma technology and transferred into C57BL/6J mice. Mice deficient for CD4+ and CD8+ T cells, B cells and AT1Ra/b served as controls. In vitro, Abs responses towards AT1R were measured using rat cardiomyocytes, human epithelial cells, AT1R-transfected HEK293 cells and primary human monocytes.

Results: AT1R-immunized mice developed perivascular skin and lung inflammation, lymphocytic alveolitis, weak endothelial apoptosis and skin fibrosis, not present in controls or mice deficient for CD4+ T and B cells. The contribution of AT1R Abs to skin manifestations and interstitial lung disease was demonstrated by application of a mAT1R Ab, which induced skin and lung inflammation, not observed in the AT1Ra/b knockout mice. IgG from immunized mice containing AT1R Abs and/or the mAT1R Ab activated rat cardiomyocytes and human monocytes. Treatment of AT1R-transfected HEK293 cells with the mAT1R Ab enhanced AT1R signaling in the presence of the endogenous agonist Angiotensin II.

Conclusion: Our immunization strategy successfully induced AT1R Abs, contributing to inflammation and most likely to fibrosis via activation of AT1R. Therefore, AT1R Abs are valuable targets for future therapies in SSc and possibly other AT1R Ab-related diseases.

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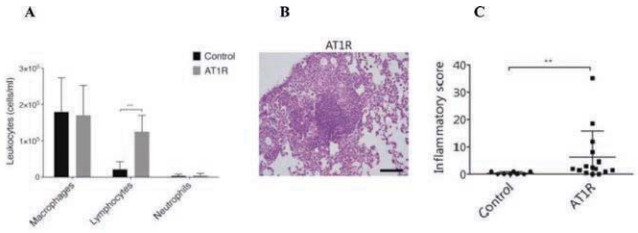

Figure 1. AT1R immunization and induction of AT1R Abs in C57BL/6J mice induced lymphocytic alveolitis in bronchoalveolar fluid (A), interstitial lung disease (B) with increased inflammatory score (C)

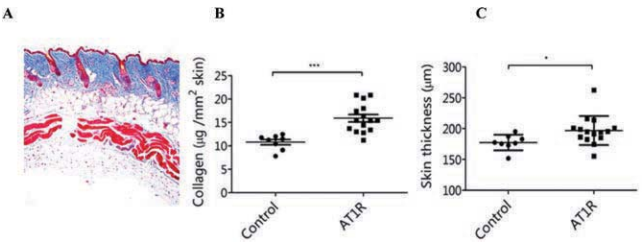

Figure 2. AT1R immunization and induction of AT1R Abs in C57BL/6J mice induced skin fibroses (A) as determined by collagen content (B) and skin thickness (C).

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POS0472

AGONISTIC STIMULATION OF GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AMELIORATED INFLAMMATORY MYOPATHIES THROUGH SUPPRESSING MUSCLE FIBER NECROPTOSIS

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Background: While glucocorticoids (GC) are the cornerstone of the treatment for polymyositis (PM), GC-induced myopathy is inevitable, which further deteriorates muscle weakness. Therefore, novel therapeutic strategy that not only suppresses muscle inflammation but also improves muscle strength is awaited. We recently found that injured muscle fibers in PM undergo FASLG-mediated necroptosis[1], a form of regulated cell death accompanied with release of pro-inflammatory mediators such as HMGB1, which contributes to accelerate muscle inflammation and muscle weakness. We also showed that inhibition of necroptosis or HMGB1 ameliorated the muscle weakness and muscle inflammation[1] in C protein-induced myositis (CIM), a murine model of PM. Glucagon-like peptide-1 receptor (GLP-1R) agonists, which have been developed as an anti-diabetic therapy, have pleiotropic actions including anti-inflammatory effects[2], suppression of muscle wasting[3], and inhibition of cell death[4]. Accordingly, we hypothesized that GLP-1R agonists have beneficial effects on PM to recover muscle strength and to suppress muscle inflammation.

Objectives: The aims of this study are to examine the role of GLP-1R in PM and the effect of a GLP-1R agonist on in vivo and in vitro models of PM.

Methods: Muscle specimens of PM patients and CIM were examined with immunofluorescence staining for the expression of GLP-1R. The effect of PF1801, a GLP-1R agonist, on CIM was examined in monotherapy or in combination with prednisolone (PSL). As an in vitro model of PM, C2C12-derived myotubes were treated with FAS ligand (FASLG) to induce necroptosis. The levels of HMGB1, TNF-α, and IL-6 in the serum of CIM and in the culture supernatant of the in vitro model were measured by ELISA. The effect of PF1801 on the myotube necroptosis was examined using time lapse imaging [5] and its effect on the activation of AMP-activated protein kinase (AMPK), the expression of PGAM5, and ubiquitination of PGAM5 was assessed with immunoblotting. The levels of reactive oxygen species (ROS) in the myotubes were analyzed with CellROX assay. The

effect of PF1801 on the expression of antioxidant molecules in the myotubes was analyzed with quantitative real-time PCR.

Results: GLP-1R was expressed on the inflamed muscle fibers of PM and CIM. The treatment with PF1801 in monotherapy or in combination with PSL suppressed CIM-induced muscle weakness and the muscle weight loss as well as the severity of histological myositis while the monotherapy with PSL did not suppress muscle weakness and muscle weight loss. PF1801 decreased the levels of inflammatory mediators such as HMGB1, TNF-α, and IL-6 in the serum of CIM. In vitro, PF1801 inhibited FASLG-induced myotube necroptosis and decreased the levels of HMGB1, TNF-α, and IL-6 in the supernatant. PF1801 activated AMPK and decreased the levels of PGAM5, which was crucial for FASLG-induced necroptosis of the myotubes. The inhibitory effect of PF1801 on myotube necroptosis was cancelled by compound C, an AMPK-kinase inhibitor, or MG132, a proteasome inhibitor, suggesting that PF1801 promoted ubiquitin-proteasome-mediated PGAM5 degradation through the activation of AMPK. Furthermore, PF1801 suppressed FASLG-induced reactive oxygen species (ROS) accumulation in myotubes, which was also crucial for the execution of necroptosis, thorough up-regulating the antioxidant molecules such as *Nfe2l2*, *Hmox1*, *Gclm*, and *Nqo1*.

Conclusion: GLP-1R agonist could be a novel therapy for PM that restores muscle strength as well as suppresses muscle inflammation through inhibiting muscle fiber necroptosis.

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POS0473 INFLAMMATORY-PRIMED MUSCLE CELLS INFLUENCE MACROPHAGE CYTOKINE SECRETION IN A MYOSITIS CONTEXT

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Background: Sporadic inclusion body myositis (sIBM) is a progressive disease causing muscle weakness and mobility issues. It is characterised by inflammatory and degenerative features; however there is no clear single cause for sIBM symptoms. Inflammatory factors include macrophage infiltration into muscle fibres and presence of high levels of inflammatory cytokines such as IFNγ [1]. Degenerative features within muscle fibres include sarcoplasmic inclusions containing aggregated proteins. p62 and TAR DNA-binding protein 43 (TDP-43) are two proteins that are found in inclusion bodies, and these have been suggested as sensitive diagnostic markers differentiating sIBM from other inflammatory myopathies [2]. Currently there is limited understanding of the pathogenic mechanisms underlying sIBM, and no effective treatments.

Objectives: The aim of this study is to investigate the interplay between inflammatory and degenerative features of sIBM with a focus on macrophage secreted factors, p62 and TDP-43 sarcoplasmic aggregation. Firstly, to examine whether skeletal muscle cells that have previously been exposed to an inflammatory environment can in turn influence the inflammatory response of macrophages. Secondly, by investigating if macrophage-secreted inflammatory factors influence p62 and TDP-43 sarcoplasmic aggregates. This will give insight into whether macrophage inflammation precludes skeletal muscle degeneration in an sIBM context or vice versa.

Methods: Primary human myogenic cells from healthy individuals were differentiated into myotubes for 7 days, with further 48-hour 20 ng/mL IL-1β and 750 ng/mL IFNγ incubation to form inflammatory-primed myotubes. Conditioned media (CM) was collected from washed myotubes after 24 hours. $6x10^5$ THP-1 cells/mL were differentiated to unprimed M(PMA) macrophages with 150 nM phorbol 12-myristate 13-acetate (PMA) for 24 hours, followed by 72-hour PMA-free rest. Inflammatory-primed M(IFNγLPS) THP-1 were generated from M(PMA) with 48-hour IFNγ and lipopolysaccharide (LPS) incubation. 20 % CM from myotubes was added to M(PMA) or M(IFNγLPS) THP-1 for 24 hours, before washing and measuring IL-6 and TNFα release from macrophages via ELISA. 20 % CM from M(PMA) or M(IFNγLPS) was added to myotubes for 48 hours before quantifying TDP-43 and p62 aggregates with image analysis.

Results: M(IFNγLPS) THP-1 secreted higher levels of IL-6 and TNFα than M(PMA). M(PMA) or M(IFNγLPS) exposed to conditioned media from control or inflammatory-primed myotubes had no detectable TNFα secretion. For both M(PMA) and M(IFNγLPS), addition of inflammatory-primed myotube CM caused higher IL-6 secretion than adding control myotube CM. Incubating unprimed myotubes with M(PMA) or M(IFNγLPS) CM had no effect on the presence, size, or frequency of p62 or TDP-43 sarcoplasmic aggregates compared to control conditions.

Conclusion: Inflammatory priming myotubes with IL-1β and IFNγ caused a response in macrophages that increased IL-6 production. However, CM from inflammatory-primed myotubes did not influence TNFα secretion from macrophages compared to control myotube CM. IL-6 has pleiotropic effects on skeletal muscle [3], promoting both hypertrophy and atrophy under different conditions. Therefore the effects of macrophage IL-6 upregulation on muscle is unclear. Culturing myotubes in unprimed or inflammatory-primed macrophage conditioned media did not influence p62 or TDP-43 sarcoplasmic aggregation. This suggests macrophage secretory factors are not responsible for the sIBM degenerative features of p62 and TDP-43 aggregation.

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POS0474 ACTIVATION AND HYPERSENSITIZATION OF THE ANGIOTENSIN II TYPE 1 AND ENDOTHELIN-1 TYPE A RECEPTORS BY AGONISTIC AUTOANTIBODIES CONTRIBUTES TO VASCULAR INJURY IN SCLERODERMA RENAL CRISIS

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Background: Scleroderma renal crisis (SRC) is a vascular complication of systemic sclerosis (SSc) with substantial risks for end-stage renal disease and death. Activating autoantibodies (Abs) targeting the angiotensin II type 1 (AT1R) and the endothelin-1 type A receptor (ETAR) are suggested to contribute to the vasculopathy in SSc (1, 2).

Objectives: Here, we sought to determine their pathogenic significance for acute renal vascular injury.

Methods: IgG from patients with SRC was studied for AT1R and ETAR dependent biologic effects on isolated rat renal interlobar arteries and vascular cells including contraction, signaling, and mechanisms of receptor activation. A cohort of ten patients with refractory SRC received multimodal treatment including AT1R and ETAR inhibition and plasma exchange and was followed for improvement of kidney function.

Results: In myography experiments, patient IgG exerted vasoconstriction (mean 6.5% of KCl induced contraction [95% confidence interval (95 CI) 5.0-8.1]) whereas control IgG did not (0.6% [95 CI 0.3-1.0]). The response was sensitive to inhibition of AT1R (3.0% [95% CI 1.4-4.7]) and ETAR (1.0% [95 CI 0.6-1.3]) and relied on MEK-ERK signaling. Contraction induced by angiotensin II and endothelin-1 was amplified by anti-AT1R and anti-ETAR Abs with substantial crosstalk between both receptors implicating autoimmune receptor hypersensitization. Co-immunoprecipitation experiments indicated heterodimerization between both receptor types enabling functional interrelation by structural interactions. 30% of patients with refractory SRC had improved kidney function after multimodal therapy.

Conclusion: We provide experimental and clinical evidence that agonistic Abs may contribute to SRC. Novel therapies targeted at autoimmune hyperactivation of AT1R and ETAR might improve outcomes in severe cases of SRC.

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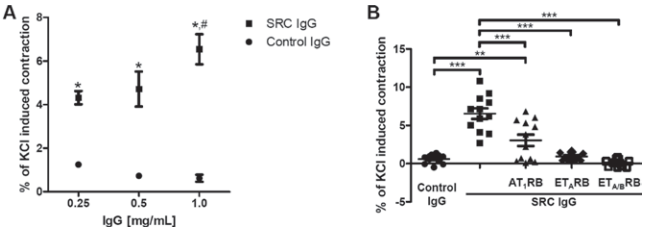

Figure 1. Contraction of isolated rat renal interlobar arteries in response to IgG isolated from patients with scleroderma renal crisis (SRC) is dependent on angiotensin II typ 1 (AT1R) and endothelin-1 type A receptors (ETAR). Small vessel myography of artery rings exposed to (a) different concentrations of IgG isolated from healthy controls (Control IgG) or patients with SRC (SRC IgG). n = 12. *P<0.001 for SRC IgG versus Control IgG, #P<0.01 for 1.0 mg/mL versus 0.25 mg/mL and P<0.05 for 1.0 mg/mL versus 0.5 mg/mL. (b) Myography of vessels exposed to 1.0 mg/mL Control IgG or SRC IgG after pretreatment with an AT1R blocker (AT1RB, valsartan), an ETAR blocker (ETARB, sitaxsentan) or a dual endothelin-1 type A and type B receptor blocker (ETA/BRB, bosentan). n = 12. **P<0.01, ***P<0.001. Contraction is expressed as % of the maximal contraction in response to 60 mM KCl of each individual vessel. Mean±SEM.

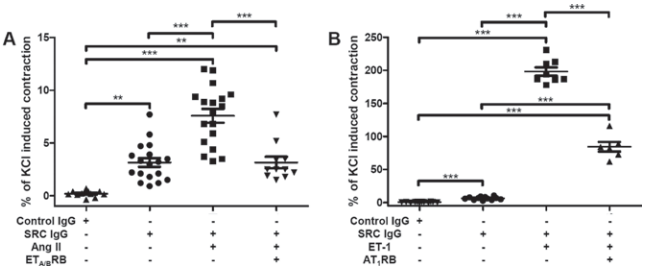

Figure 2. Interdependence of the angiotensin II (AngII) type 1 receptor (AT1R) and endothelin-1 (ET-1) receptors (ETA/BR) in the contractile response of isolated rat renal interlobar arteries to AngII and ET-1 in the presence of anti- AT1R and anti-ETAR activating autoantibodies.Small vessel myography of artery rings exposed to 1.0 mg/mL IgG isolated from healthy controls (Control IgG) or patients with scleroderma renal crisis (SRC IgG) and natural ligands with and without pretreatment with receptor blockers as indicated. (a) Additional stimulation with 1000 nM AngII ± ETA/BR blocker (ETA/BRB) bosentan. n = 11-18. (b) Additional stimulation with 100 nM ET-1 ± AT1R blocker (AT1RB) valsartan. n = 6-12. Contraction is expressed as % of the maximal contraction in response to 60 mM KCl of each individual vessel. Mean±SEM. **P<0.01, ***P<0.001.

Disclosure of Interests: None declared.
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POS0475

ROLE OF IL-33/ST2 AXIS IN SYSTEMIC SCLEROSIS PATIENTS WITH ELECTROCARDIOGRAPHIC ABNORMALITIES

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Background: Electrocardiographic (EKG) abnormalities are described in 25-75% Systemic Sclerosis (SSc) patients and they are associated with other systemic manifestations[1] as well as with a worse prognosis.[2] There is an increasing need for clinical and laboratory biomarkers to ameliorate the diagnostic approaches to patients with EKG abnormalities.[3] In the last decade, many studies focused on the components of the interleukin (IL)-33/ST2 axis. Under physiological conditions, IL-33 is released by apoptotic cardiac cells, promoting a protective mechanism of cell survival, thanks to the binding with its transmembrane receptor ST2.[4] During pathological cardiovascular events, an abnormal secretion of the IL-33 soluble receptor (sST2) by Th2 cells occurs. It binds IL-33 not allowing the physiological mechanism driven by the IL-33/ST2 binding previously described.[4] For these reasons, sST2 has been proposed as a biomarker of cardiac injury in a variety of diseases.[5]

Objectives: Aim of this study was to analyse clinical and demographical parameters in a group of SSc patients, trying to define any possible feature associated with EKG abnormalities. Furthermore, the role of IL-33/ST2 axis components as biomarkers of cardiac injury in patients with SSc-related EKG abnormalities was evaluated, also assessing the possible correlation with serum concentration of NT-pro-BNP, a well-known cardiac injury biomarker in SSc.

Methods: Data from 277 SSc patients, fulfilling the 2013 ACR/EULAR classification criteria,[6] attending our Scleroderma Clinic were retrospectively analysed. We selected patients with EKG trace and a blood sample available, collected after the SSc diagnosis. The sera levels of sST2 (ELISA Kit, Abcam), IL-33 (ELISA kit, RayBiotech) and NT-pro-BNP (ELISA Kit, Abcam) were measured. Patients with a history of heart diseases occurring before the diagnosis of SSc or features of secondary cardiac involvement (pulmonary arterial hypertension, severe interstitial lung disease or renal disease) were excluded.

Results: Forty-six SSc patients showed significant EKG abnormalities (rhythm and conduction disorders). Thirty-one SSc patients without pathologic finding at EKG traces were recruited as the control group. From the analysis of the clinical characteristic of the disease at the moment of serum collection, patients with EKG anomalies have more frequently both a diffuse form of disease (*n*°-%: 23-50 vs 7-23; *p* 0.01), with a mean value of mRSS higher than controls (11±9 vs 6±6; *p* 0.01), and a scleroderma "late" pattern at the nailfold capillaroscopy (*n*°-% 23-50 vs 6-19; *p* 0.027). Significantly higher median values of serum levels of sST2 in SSc patients with EKG disorders compared to the control group (4289pg/mL, IQR 2383 vs 2560 pg/mL, IQR 1455; *p 0.0002*) were detected, while opposite results were found analyzing serum levels of IL-33 (2.89 pg/mL IQR 101 vs 9 pg/mL IQR 277; *p* 0.032) (Graph 1). Serum NT-pro-BNP median values were significantly higher in the group of patients with EKG abnormalities than in the control group (149 pg/mL, IQR 354 vs 26 pg/mL, IQR 62; *p* 0.0007). These values correlated with sST2 serum levels (rho Spearman correlation 0.37; *p* 0.0006).

Conclusion: SSc patients with EKG abnormalities showed an increased skin and vascular involvement with respect to the control group. These associations could help clinicians in clinically stratifying SSc patients at risk of EKG abnormalities. To our knowledge, this is the first report evaluating the serum concentration of sST2 in SSc patients. Based on these results, we can speculate on the role of this molecule as potential biomarkers of early cardiac injury during SSc, although further studies involving a larger cohort of patients are needed.

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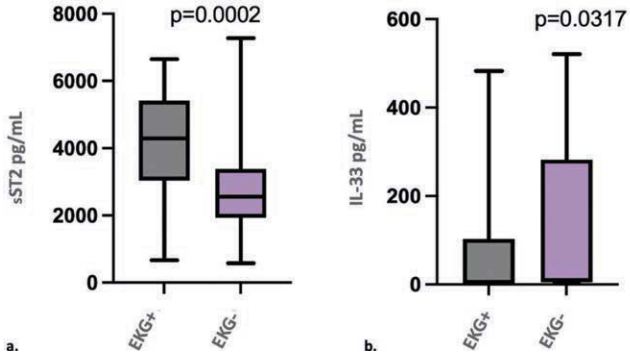

Figure 1: Graph 1. Serum sST2 (**a**) and IL-33 (**b**) concentrations in patients with EKG abnormalities (EKG+) vs control group (EKG)

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POS0476

THE NUCLEAR RECEPTOR TR4 ORCHESTRATES CYTOSKELETAL ORGANIZATION IN A Gα12/ ROCK-DEPENDENT MANNER TO PROMOTE MYOFIBROBLAST DIFFERENTIATION AND TISSUE FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Nuclear receptors (NR) are a family of transcription factors. Several members of the NR family are candidates for targeted intervention in inflammatory and fibrotic diseases (1-2). Testicular receptor 4 (TR4), also known as Nr2c2, has been shown to regulate fundamental cellular processes such as differentiation, proliferation and growth factor signaling (3-4). However, its role in fibrotic diseases has not been investigated so far.
Objectives: The aim of the present study was to characterize the role of TR4 in the pathogenesis of fibrotic tissue remodeling in SSc and to interrogate its underlying mechanism.
Methods: Expression of TR4 was quantified by RT-PCR, Western blot and immunofluorescence. The effects of TR4 knockdown on collagen production and myofibroblast differentiation were analyzed in cultured human fibroblasts and in three mouse models with fibroblast-specific knockout of TR4. RNA sequencing was performed in TGFβ-stimulated human dermal fibroblasts transfected with TR4 siRNA or non-targeting siRNA. The implication of TR4 in cytoskeleton regulation was analyzed by ROCK activity assays, stress fiber formation and quantification of the ratio of filamentous (F)-actin/ globular (G)-actin. The functional role of ROCK and Gα12 was analyzed using small molecule inhibitors and siRNA, respectively.
Results: TR4 expression was upregulated in fibroblasts in the skin of SSc patients and fibrotic mouse models. The expression of TR4 was upregulated in a TGFβ- and SMAD3-dependent manner. TR4 knockdown inhibited TGFβ-induced myofibroblast differentiation and collagen release, whereas overexpression of TR4 promoted fibroblast activation. Fibroblastspecific knockout of TR4 ameliorated experimental dermal fibrosis induced by bleomycin, adTBR and in sclGVHD with decreases in dermal thickening, myofibroblast counts and hydroxyproline content. The RNASeq of TR4 knockdown fibroblasts stimulated with TGFβ identified 651 differentially expressed genes as compared to control fibroblasts. Differentially expressed genes included central profibrotic genes such as ACTA2, COL3A1, CCL12. gProfiler enrichment analysis of the TR4-DEGs revealed enrichment of multiple GO, GSEA and Reactome terms related to ECM release, cytoskeleton organization and Rho GTPases activity. Indeed, knockdown of TR4 ameliorated the induction of ROCK activity by TGFβ stimulation and reduced the shift in the ratio from globular (G) actin to filamentous (F) actin. Knockdown of TR4 strongly reduced the expression of the G-protein alpha-12 (Gα12). ROCK inhibition by Y27632 or knockdown of Gα12 inhibited the induction of αSMA and stress fiber formation induced by overexpression of TR4.
Conclusion: TR4 is upregulated in SSc in a TGFβ-dependent manner to promote fibroblast activation. Inhibition of TR4 interferes with TGFβ-induced activation of ROCK, prevents cytoskeletal remodeling and fibroblast-to-myofibroblast transition and ameliorates experimental fibrosis. As nuclear receptors are common targets for therapeutic intervention, TR4 may offer potential for antifibrotic therapies.
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POS0477 ATTENUATION OF FIBROBLAST ACTIVATION AND FIBROSIS BY ADROPIN IN A HEDGEHOG-DEPENDENT MANNER

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Background: Adropin is a secretory protein encoded by the energy homeostasis-associated (*ENHO*) gene. Emerging evidence indicate its role in metabolism and energy homeostasis, which is known to be deregulated in SSc. However, adropin/*ENHO* has not been linked to the pathogenesis of fibrosis, tissue remodeling or fibroblast activation so far.
Objectives: The aim of the current study was to investigate the role of adropin/*ENHO* in the pathogenesis of fibroblast activation and fibrosis in SSc.
Methods: Machine learning and bioinformatics models were used to identify candidate genes regulating fibroblast activation in SSc. The expression of adropin/*ENHO* in skin samples of SSc patients and healthy individuals was analyzed by quantitative PCR, immunofluorescence and western blot, and validated by *in silico* data mining. The effects of adropin were analyzed in cultured human fibroblasts, 3D skin equivalents, and complimentary murine models of SSc, including sclerodermatous GvHD (sclGvHD) and bleomycin-induced lung fibrosis mice. RNA sequencing (RNAseq) was performed to identify downstream regulatory pathways.
Results: Biostatistical screening of publically available datasets identified adropin/*ENHO* as a potential molecular mediator involved in fibroblast activation with pronounced downregulation in SSc skin. We first confirmed the impaired expression of adropin/*ENHO* in SSc patients and SSc models. TGFβ reduced adropin/*ENHO* expression in a JNK-dependent manner. Recombinant Adropin peptides in turn inhibited TGFβ-induced fibroblast activation and subsequent fibrosis. Treatment of biologically active peptides adropin$^{34-76}$ inhibited TGFβ induced fibroblast activation and extracellular matrix (ECM) production in cultured primary dermal fibroblasts, as well as in 3D skin equivalents. Moreover, therapeutical administration of adropin$^{34-76}$ in mice with preestablished fibrosis exerted potent antifibrotic effects in skin and lungs of two complimentary murine SSc models, sclGvHD and bleomycin-induced lung fibrosis mice. RNAseq demonstrated the antifibrotic effects of adropin were functionally linked to hedgehog signaling and GLI1 deactivation, which experimentally confirmed *in vitro* and *in vivo*. Knockdown of *GPR19*, a putative receptor of adropin, abrogated the therapeutic effect of adropin on αSMA- and GLI1-expression in fibroblasts, indicating adropin may regulate GLI1 signaling and fibroblast activation via GRP19.
Conclusion: We demonstrate a novel regulatory loop of adropin/*ENHO* in TGFβ signaling: TGFβ inhibits the expression of adropin/*ENHO*, while recombinant adropin peptides inhibited fibroblast activation by GPR19-dependent inhibition of hedgehog/GLI1 signaling. Our findings characterize adropin peptides as a potential approach to interfere with aberrant fibroblast activation and tissue fibrosis in SSc.
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Disclosure of Interests: Minrui Liang: None declared, Jörg H.W. Distler Shareholder of: stock owner of 4D Science, Consultant of: consultancy relationships with Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Medac, Novartis, Pfizer, RuiYi and UCB, Grant/research support from: has received research funding from Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, Inventiva, Kiniksa, Sanofi-Aventis, RedX, UCB.
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POS0478 TOPICAL CALCIUM CHELATORS FOR TARGETING CUTANEOUS CALCIFICATION: PRECLINICAL EVIDENCE OF EFFICACY

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Background: Cutis calcinosis, defined as sub-epidermal deposition of calcium salts, is a painful, disabling, disfiguring, problem in 20-40% of patients with systemic sclerosis. Its pathogenesis remains poorly understood and currently there is no effective disease-modifying pharmacotherapy. One potential strategy is topical application of calcium chelating agents, able to penetrate the epidermal barrier and dissolve subcutaneous calcinotic deposits *in situ*. To date, the only

compound reported for this application has been sodium thiosulfate (STS), with often-contradictory results.

Objectives: To test the hypothesis, in pre-clinical studies, that polycarboxylic acids can induce calcium dissolution without skin toxicity, with the long-term aim of developing an effective topical treatment for cutis calcinosis.

Methods: We compared the metal ion-chelating agents citric acid (CA) and ethylenediaminetetraacetic acid (EDTA) - polycarboxylic acids with well-characterised chelation profiles – to STS for their ability to chelate calcium, without inducing cytotoxicity or inflammation (pro-inflammatory cytokine expression and release), using in vitro 2D (keratinocyte [HaCaT]; fibroblast ([HCA2]) and recombinant human epidermal (RHE) models. The resultant data was subsequently used to predict therapeutic concentrations for assessment in a validated skin irritation model (SkinEthicTM; Episkin SA) and to assay maximal percutaneous absorption. At relative dermal concentrations, the dissolution performance of each chelator was further assessed using two different models of calcinosis: 1) pharmaceutical dissolution of a hydroxyapatite (HAp) tablet (1) and; 2) dissolution of a calcified extracellular matrix laid down by mineralising SaOS2 in vitro monolayer culture (2).

Results: Incubation with CA, EDTA and STS induced cytotoxicity in both *in vitro* cell lines studied at concentrations of >10 mM; only EDTA (10 mM) resulted in inflammatory cytokine release (IL8) from cells at these higher concentrations (*cf* positive control, Lipopolysaccharide 10 mg/mL). When applied topically to RHE models as near-saturated solutions, none of the chelators were categorised as skin irritants. Due to differences in their relative aqueous solubility, higher concentrations of CA (1600 mM) and STS (1200 mM) could be delivered through the RHE model than EDTA (200 mM). Using a simple linear regression model, the rate of compound absorption was: CA, 0.43 ± 0.05; STS, 0.26 ± 0.03 and; EDTA, 0.05 ± 0.01 g/L/hr. At each time-point, the cumulative concentration of compound in the receptor media was CA > STS > EDTA. Incubation with chelators had no effect on the integrity of the RHE by standard histology. Based on the rate of percutaneous absorption, the dissolution performance of each chelator was tested at relative dermal concentrations for phosphate dissolution (nmoles) of HAp (CA, 9.61 ±0.97; EDTA, 5.38 ± 0.28; 3.78 ± 0.58) and in the calcified *in vitro* model (Figure 1; CA, 3285 ± 105, STS, 947 ± 95, EDTA, 1174 ± 89), showing the superiority of CA in both model systems.

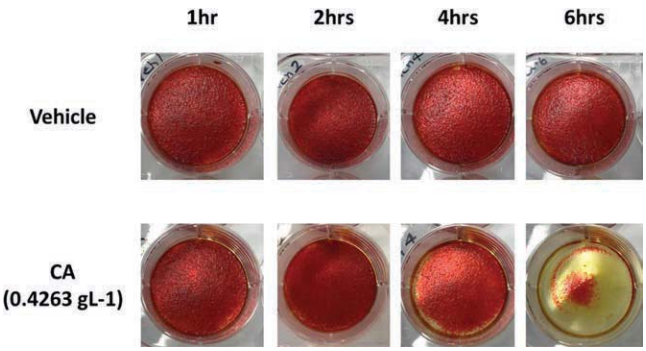

Figure 1. Dissolution of a calcified extracellular matrix by citric acid

Conclusion: Overall, this study highlights the promise of polycarboxylic acids, particularly CA, to target subcutaneous calcification, which are neither toxic nor inflammatory to the skin. Specifically, we have identified CA as a potentially more efficacious alternative to STS for the topical treatment of cutis calcinosis.

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POS0479

STAT3 DEGRADERS PROTECT FROM IMMUNOFIBROTIC CHANGES IN PRECLINICAL MODELS

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Background: The ubiquitin-proteasome system (UPS) is the endogenous intracellular mechanism for maintaining protein homeostasis through protein degradation and turnover. Heterobifunctional small molecules are a new class of compounds that form a ternary complex with an E3 ligase and protein of interest leading to ubiquitination and subsequent degradation of the protein of interest in a process known as Targeted Protein Degradation. This new therapeutic modality enables targeting of "undruggable" proteins such as STAT3, a transcription factor activated in immunofibrotic diseases.

Objectives: Kymera has developed heterobifunctional molecules that potently and selectively target STAT3 for degradation and elimination by the ubiquitin-proteasome pathway. The aim of these studies was to evaluate the therapeutic potential of pharmacologically removing STAT3 by targeted protein degradation in various human cell types in vitro, and to prevent the development of skin and lung fibrosis in vivo.

Methods: Dermal fibroblasts obtained from healthy and systemic sclerosis patients activated with TGF-β were analyzed for development of α-smooth muscle actin (α-SMA)-positive stress fibers and for contractility using collagen gel contraction assay. Contraction assay was also performed using human dermal smooth muscle cells. Human aortic endothelial cells (HAECs) were activated with LPS, and their adhesive properties were assessed in the microcapillary system by the ability to bind peripheral blood mononuclear cells (PBMCs) under shear stress. HAECs proliferation was induced with VEGF. THP-1 cells and $CD14^+$ monocytes were activated with IL-6 or LPS, and secreted cytokines were assessed by CBA. PBMCs activated with LPS, IL-6, IL-21, or IL-23 alone (pSTAT3 induction), or with a combination of anti-CD3/CD38 beads and a pro-Th17 cocktail comprised of cytokines and antibodies to evaluate the development of a Th17 and Treg phenotype by flow cytometry. Cytokines were analyzed by ELISA. All cell types were pre-treated with STAT3 degraders 20h prior to experiment start. Intratracheal instillation of bleomycin was used to induce pulmonary fibrosis. Transgenic Tsk-1 mice were used as a model of spontaneous skin fibrosis.

Results: STAT3 degraders completely ablated STAT3 in all analyzed cell types with DC50 ranging from 0.25-0.8 nM. STAT3 degradation prevented TGF-β-induced formation of α-SMA-positive stress fibers in dermal fibroblasts (IC50 = 0.35nM) and 2 and 10nM degrader completely abrogated their contractility. Similarly, STAT3 degradation reduced the constitutive contractility of dermal smooth muscle cells of 13% ($p<0.05$, n=6). Treatment of HAECs with STAT3 degraders resulted in anti-adhesive 178±21 for LPS and 93±12 for LPS +degrader, $p<0.05$, n=6) and anti-proliferative 1.2±0.1 for VEGF and 0.95±0.1 for VEGF +degrader, $p<0.05$, n=10-11) effects. In monocyte-focused assays (CD14+ monocytes and THP-1 cells), STAT3 degradation potently and dose-dependently inhibited IL-6 and LPS-induced pSTAT3 levels and the ensuing release of MCP-1/CCL2 (24.3±3.7 for LPS and 20.2±3.2 for LPS +degrader, $p<0.05$, n=6). In CD4+ T lymphocytes, STAT3 degradation promoted a Treg phenotype and suppressed the development of Th17 cells. Systemic treatment in vivo showed that prophylactic STAT3 degradation (7 mg/kg twice a week, i.p.) reduced disease severity in the bleomycin-induced pulmonary fibrosis model (Ashcroft's score, 4.7±1.9 vs. 3.1±1.6, $p<0.05$, n=11). In Tsk-1 mice that show co-occurrence of spontaneous skin thickening and robust STAT3 activation, STAT3 degrader treatment (2 or 7 mg/kg twice a week, i.p.) for 7 weeks significantly reduced thickness of the skin (701±238 vs. 480±205 vs. 365±107, $p<0.05$, n=6-8).

Conclusion: STAT3 degraders that selectively and potently eliminate STAT3 show robust anti-inflammatory and anti-fibrotic potential in vitro and in vivo. Our results suggest that targeted protein degradation is a promising approach to modulate the STAT3 pathway, making it a novel therapeutic opportunity to treating multiple immunofibrotic diseases.

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POS0480 VITAMIN D AND ITS RECEPTOR (VDR) GENE EXPRESSION IN SKELETAL MUSCLE ASSOCIATE WITH DISEASE AND MUSCLE FUNCTION PARAMETERS IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IIM) are chronic inflammatory disorders characterised, apart from extramuscular manifestations, by symmetrical progressive muscle weakness that may persist even after pharmacological suppression of inflammation, suggesting a significant involvement of nonimmune mechanisms. Low levels of vitamin D have been associated with several autoimmune diseases. Vitamin D is essential for the maintenance of skeletal muscle, and mounting evidence supports its relation to muscle damage, regeneration, and energy metabolism.
Objectives: The aim was to analyse vitamin D and the mediators of its function in muscle tissue of IIM patients, and to associate it with muscle health parameters.
Methods: A total of 46 IIM patients (40 females, 6 males; mean age 56.7±12.4; disease duration 6.5±6.0 years; dermatomyositis (21), polymyositis (18), necrotizing myopathy (7)) and 67 healthy controls (HC) (56 females, 11 males; mean age 50.9±14.7) were recruited. In total, 27 IIM patients participated in a 24-week intervention combining activities-of-daily-life, resistance and stability training [1]. Muscle biopsies from *m. vastus lateralis* (by Bergström needle) were obtained from 7 IIM patients before/after the 24-week training program, and from 13 control IIM patients, and 21 HC. Primary muscle cell cultures were established from these samples. Disease-associated parameters were evaluated by MYOACT/MITAX, MDI, VAS, HAQ, MMT8, FI-2 and CK, myoglobin, LD, ALT, AST, and CRP levels. Myostatin, as a myokine involved in muscle atrophy, was determined from serum samples by ELISA. Circulating concentrations of 25(OH) vitamin D (calcidiol) and active 1,25(OH) vitamin D (calcitriol) were measured by routine biochemistry techniques. Gene expression of vitamin D receptor (VDR) and 25-hydroxyvitamin D 1-alpha-hydroxylase (CYP27B1), an enzyme catalysing calcidiol conversion to hormonally active calcitriol, was determined by real-time PCR in muscle tissue and primary muscle cell cultures. Data are presented as mean ± standard deviation.
Results: Decreased levels of active 1,25(OH)D were observed in IIM patients compared to HC (125.0±45.4 vs. 164.7±49.2 pmol/l; p<0.0001). No difference was found for 25(OH)D. The 24-week training program did not have an effect on 25(OH)D or 1,25(OH)D serum levels. 25(OH)D was significantly associated with CRP (r=-0.322, p=0.040), MITAX (r=-0.380, p=0.021) and HAQ (r=-0.370, p=0.017) in IIM patients, even after correction for BMI, gluccocorticoid (GC) and vitamin D daily supplementation dose. After 24 weeks of exercise, active 1,25(OH)D was positively associated with MMT8 (r=0.866, p<0.0001), FI2 (r=0.608, p=0.013) and HAQ (r=-0.537, p=0.032) (corrected for BMI, GC and vit.D supplementation). Numerically higher gene expression of VDR and CYP27B1 was found in muscle tissue and primary muscle cells in IIM compared to HC. After the 24-week training, gene expression of both VDR and CYP27B1 in primary muscle cells decreased (p=0.031 and p=0.078, respectively). Associations of VDR gene expression with myoglobin (IIM: r=0.510, p=0.026; HC: r=0.473, p=0.035), MMT8 (IIM: r=-0.559, p=0.013), myostatin (IIM: r=-0.519, p=0.023; HC: r=0.586, p=0.005), and CK (HC: r=0.484, p=0.031) were observed in muscle tissue. CYP27B1 gene expression in the muscle was also associated with myoglobin (HC: r=0.501, p=0.024), MMT8 (IIM: r=-0.555, p=0.011) and VDR (IIM: r=0.561, p=0.012; HC: r=0.632, p=0.002).
Conclusion: Decrease of the biologically active form of vitamin D in circulation suggests an impairment of its metabolism in IIM. Vitamin D serum levels and gene expression of its receptor and activating enzyme in muscle tissue associate with disease activity and muscle function parameters indicating an important role of vitamin D in physical fitness and disease manifestations in IIM patients.
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POS0481 DEFINING DISTINCT RESIDENT AND MIGRATORY FIBROBLAST POPULATIONS FROM SKIN BIOPSIES IN SYSTEMIC SCLEROSIS

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Background: Recent studies using single cell RNA sequencing have delineated distinct subpopulations of fibroblasts in skin and other organs. To improve understanding of functional differences between fibroblast subpopulations, we have developed a novel technique to selectively isolate "migratory" fibroblasts, and non-migratory "resident" fibroblasts from heathy control (HC) and SSc skin.
Objectives: To compare migratory and resident populations of dermal fibroblasts in systemic sclerosis by their differential gene or protein expression, and through functional assays of fibrotic potential.
Methods: Forearm skin punch biopsies were collected from dcSSc(n=3), and healthy control skin(n=3).
Migratory fibroblasts were first isolated by standard explant culture, then the residual biopsy fragments underwent collagenase digestion to yield a population of resident fibroblasts that retained in the biopsy fragments. These populations were further expanded for use at passage 3-6. Functional characterisation included 3-D collagen gel contraction, and migratory scratch-wound assays. Expression of pro-collagen I (Col1), CTGF and αSMA was compared by western blot. Bulk RNAseq on each fibroblast population was performed. Statistical analysis was carried out using Rsoftware "tidyverse". Criteria for significant differences in gene expression were a fold change of ≥1.5, and adjusted p-value (FDR) of <0.05
Results: Compared with HC, all SSc fibroblast populations showed a hallmark fibrotic phenotype with increased gel contraction, faster migration, and overexpression of Col1, CTGF and αSMA compared with HC. However, SSc resident fibroblasts showed attenuated contraction, migration, and reduced levels of αSMA compared to migratory SSc fibroblasts. Bulk RNAseq performed on each fibroblast population confirmed 5579 significantly differentially expressed genes between SSc resident and SSc migratory fibroblasts, whereas no genes were significantly differentially expressed between HC resident and migratory fibroblasts. SSc and HC migratory fibroblasts and resident fibroblasts were then compared, to understand disease-related differences between the two fibroblast populations. 739 genes were significantly overexpressed in the migratory fibroblast population (including ASPM, TRIP3), whereas 745 genes were significantly upregulated in the resident fibroblast population. The genes upregulated in resident fibroblasts included CCL2, CXCL8, and ICAM1. Many genes typically associated with SSc (such as SERPINE1, COMP), were not significantly different between the SSc fibroblast subpopulations, but were significantly elevated in both SSc subpopulations compared to HC fibroblast populations, suggesting that these reflect a more generic SSc phenotype.
Conclusion: Migratory and resident SSc fibroblast populations exhibit distinct functional and transcriptional differences that are much less apparent for HC biopsies. Further work is required to understand the precise contribution these distinct SSc fibroblast populations in pathogenesis, and how they might be targeted therapeutically. Our findings also highlight that conventional explant culture techniques may ignore important fibroblasts populations and highlight the importance of more detailed analysis such as single cell analysis to better understand pathobiology of SSc.

Table 1. Table of the most significantly differentially expressed genes with highest fold change and adjusted p-value (FDR) between the migratory and resident SSc fibroblast population

Significantly upregulated genes in SSc migratory fibroblasts			Significantly upregulated genes in SSc resident fibroblasts		
	Fold change	Adjusted p value		Fold change	Adjusted p value
GPR1	5.99	0.01	CCL2	38.66	<0.0001
PPME1	4.86	0.011	CXCL8	24.36	0.0001
KIF20A	4.34	0.015	ICAM1	15.38	<0.0001
CENPF	4.31	0.018	EGR1	15.19	0.0002
STC2	4.18	0.01	EGR2	12.77	0.0002
ASPM	3.88	0.02	IFI44L	11.5	0.002
TRIB3	3.60	0.011	CXCL6	11.43	<0.0001
HAPLN1	3.36	0.039	PDGF-D	10.14	0.0003
CCNB2	3.29	0.025	OAS3	8.94	0.0009
KIF14	3.24	0.027	IFIT1	8.58	0.004

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POS0482 LONG NON-CODING RNA H19X IS A MEDIATOR OF ENDOTHELIAL CELL ACTIVATION IN SYSTEMIC SCLEROSIS

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Background: In one of our previous studies, we demonstrated that long non-coding RNA (lncRNA) *H19X* plays a crucial role in the development of TGFβ driven fibrosis in systemic sclerosis (SSc) and other fibrotic diseases[1].
Objectives: To define the functional relevance of *H19X* in endothelial cell (EC) activation as a decisive process in SSc vasculopathy.
Methods: Correlation of *H19X* expression and microvascular gene signature was computed on bulk RNA-Seq data derived from SSc skin biopsies of patients enrolled in the multicentre Prospective Registry of Early Systemic Sclerosis cohort (PRESS, n=48 SSc vs. n=33 healthy controls, HCs). Single cell RNA sequencing (scRNA-seq) data were collected from 27 diffuse cutaneous SSc (dcSSc) and 10 HC skin biopsies. Single cells were barcoded and encapsulated in droplets using a 10X Genomics system. After cDNA synthesis, the libraries were prepared and sequenced using Illumina NovaSeq-500 platform. Seurat package in R (v.3.0) was used to perform data analysis. EC were identified by enrichment of EC markers *CLDN5*, *VWF* and *PECAM1*. One thousand five hundred eighty-three and 3398 EC were identified from HC and SSc patients, respectively. Cells were analysed for the expression of *H19X* and EC activation markers. Additionally, differential expression and pathway enrichment analysis between *H19X* expressing cells and *H19X* negative cells was carried out. The function of *H19X* was investigated in human dermal microvascular EC (HDMEC) by silencing, using locked nucleic acid antisense oligonucleotides (LNA GapmeRs). Gene expression was measured by qPCR. Protein levels of endothelial adhesion molecules were analysed by Western Blot. Endothelial adhesion was evaluated by co-culture of HDMEC and fluorescently labelled peripheral blood mononuclear cells (PBMCs).
Results: *H19X* expression was found significantly upregulated in SSc skin biopsies of the PRESS cohort (p<0.0001). The expression of *H19X* positively correlated with the microvascular endothelial cell gene signature in all subjects (SSc and HC, R=0.43, p<0.0001), confirming that *H19X* is expressed in this cell type. To determine if *H19X* might be an important factor in SSc EC dysfunction scRNAseq was performed. This analysis revealed a significant upregulation of *H19X* in SSc EC as compared to HC EC (p=0.0095). *H19X* was found to be upregulated in several EC subclusters including arterial (*SEMA3G*, *HEY1*), capillary (*CA4*, *RGCC*), venous (*ACKR1*, *VCAM1*) and lymphatic (*PROX1*, *LYVE1*). *H19X* displayed highest expression in injured SSc EC and capillary SSc EC. Co-expression analysis of the scRNA-seq data revealed higher expression of several adhesion molecules in EC expressing *H19X*, including *VCAM1*, *ICAM* and *JAM3*. KEGG pathway analysis revealed that differentially expressed genes in *H19X* expressing cells were highly associated with the 'Cell adhesion molecule' pathway (p=2.209e-7). *H19X* silencing lead to a significant downregulation of mRNA levels of genes encoding adhesion molecules VCAM1 (n=7, p<0.05) and E-selectin (n=7, p<0.01) at 48h after transfection. VCAM1, but not E-Selectin, was also reduced at protein level as revealed by Western Blot (n=3). The functional relevance of *H19X* on endothelial adhesion was confirmed by PBMCs with *H19X* silenced HDMEC where we were able to demonstrate a significant decrease in leucocyte-to-endothelial cell adhesion (n=5, p<0.05).
Conclusion: Our results show that lncRNA *H19X* could contribute to EC activation in SSc vasculopathy, acting as a regulator of expression of adhesion molecules in EC.
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POS0483 THE EFFECT OF VITAMIN D3 AND A-TOCOPHEROL ACETATE IN THE PRECLINICAL MODEL OF SYSTEMIC SCLEROSIS

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Background: The pathogenesis of systemic sclerosis (SSc) is characterized by complex damage of an organism due to the development of mechanisms of autoimmunity. Dysregulation of immune system, development of fibrosis, and vasculopathy play a significant role in this process.
Objectives: This study aimed to investigate the effect of antioxidant α-tocopherol acetate and immunomodulator vitamin D 3 in the preclinical model of SSc.
Methods: To perform this study, three groups of laboratory animals were formed: a control group (20 animals), an experimental group #1 (25 animals) and an experimental group #2 (25 animals). Experimental animals were mature laboratory rats of the Wistar line weighing 180-220 g. Modeling of SSc was performed in the experimental group #1 using sodium hypochlorite (NaClO) according reported previously method [1]. Laboratory animals of the control group were injected with the isotonic solution according to the same scheme. In the experimental group #2, in addition to NaClO, laboratory rats received a solution of α-tocopherol acetate 10 mg / 100 g of body weight, IV and a solution of vitamin D3 1000 IU / 100 g of body weight, IV for 3 weeks (second half of the experiment). The level of surfactant protein D (Elabscience SP-D ELISA-Kit), the vascular cell adhesion molecule (Elabscience VCAM-1 ELISA-Kit), and interleukin 13 (Elabscience IL-13 ELISA-Kit) was determined by enzyme-linked immunosorbent assay. ELISA was performed on an enzyme-linked immunosorbent assay STAT FAX 303 plus. Data distribution was evaluated with the Shapiro-Wilk test. Mann-Whitney U test and unpaired t test were used for comparisons between groups, a p-value <0.05 was considered statistically significant.
Results: The level of IL-13 (pg/ml) in the experimental group was higher than in the control 136,4± 56,23 vs 9,43± 4,01 (p<0.001). The serum concentration of SP-D (pg/ml) among the experimental group of laboratory animals was significantly higher compared to the control subjects 490,20 [228,75–568,73] vs 70,13±33,21, (p<0,05). VCAM-1(pg/ml) was also higher in the experimental group VCAM-1 91,25 [85,63–143,75] vs 17,35±7,47, (p<0,05). The administration of vitamin D3 and α-tocopherol acetate has shown a positive effect for all three investigated parameters. We have found a statistical difference between the two experimental groups regarding IL-13, SP-D, and VCAM-1. The SP-D level in the experimental group #2 was 124.93 ± 18.96, which was significantly lower than in the experimental group #1 (p=0.04). The concentration of IL-13 and VCAM were also lower in the group of vitamins D3 and α-tocopherol acetate administration (22.88±5.11, p<0.001 and 38.73±12.13, p=0.02 respectively).
Conclusion: This study provided evidence that administration of vitamins D3 and α-tocopherol acetate, given in combination, has a beneficial effect on IL-13, SP-D, and VCAM-1 levels in the organism of the experimental animals.
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POS0484 LUNG ORGANOIDS: A NOVEL APPROACH TO STUDY THE MOLECULAR PATHOLOGY OF PULMONARY FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Pulmonary fibrosis is one of the major manifestations in Systemic Sclerosis (SSc) associated with high mortality. Mesenchymal transformation of the airway epithelial cells has been implicated as one of the causes for

developing pulmonary fibrosis. Though several animal models shed light towards some of these aspects, an *in vitro* airway epithelial model would provide a novel experimental platform for the understanding and molecular and genetic changes that occur in SSc associated pulmonary fibrosis.

Objectives: To establish a functional model for airway epithelium from patient with diffuse cutaneous SSc (dSSc)and healthy volunteers derived nasal stem cells. Subsequently to induce Epithelial Mesenchymal transformation (EMT).

Methods: Nasal stem cells harvested from healthy volunteers(HV) and dSSc patients were differentiated into ciliated airway epithelium in an Air -Liquid Interface (ALI) using a transwell system. 4 HV cultures were then stimulated with TGF beta (5ug/ml) for 10 days at a basal stage and when differentiated. Markers of mesenchymal transformation including loss of E cadherin, and gain of N cadherin, fibronectin and vimentin were analysed by flow cytometry and image stream, and mean expression intensities given as (MFI). Secreted Type 1 collagen and fibronectin were measured by ELISA.

Results: Ciliated epithelial cultures could successfully be established from nasal stem cells (Figure 1).

TGF beta induced a phenotypic change in the epithelial cells towards a mesenchymal one in HV cultures. This was observed by significantly increased expression of fibronectin and vimentin and loss of expression of E cadherin on the ciliated cells with 7 days of stimulation with TGF beta at a basal stage (Figure 1b). When cells, stimulated with TGF beta for 7 days, were analysed at Day 35 a similar trend was seen in their Delta MFI (Figure 1c). Stimulating the ALI cultures with TGF beta for 20 days completely repressed epithelial cell growth and disrupted their microstructure.

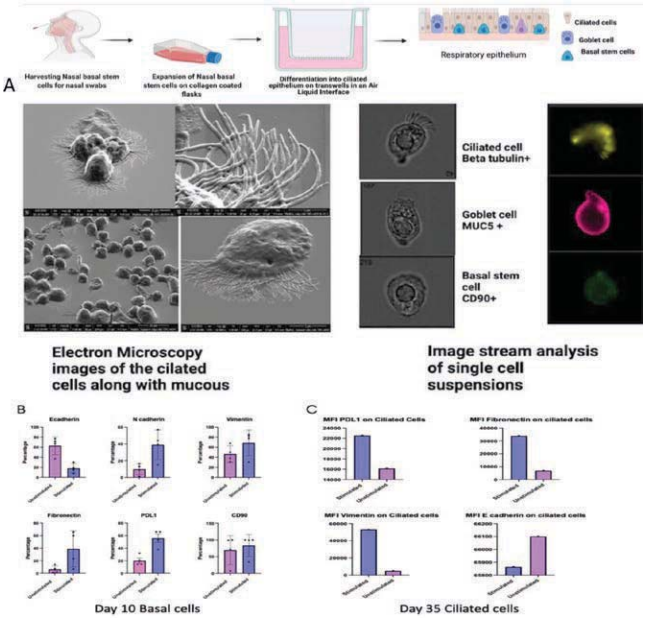

Figure 1.

Conclusion: This novel ALI differentiated Airway epithelial model serves as a functional organoid to test various pulmonary manifestations of Systemic Sclerosis. The ability to induce Epithelial Mesenchymal Transformation of these cultures provides a proof of concept for TGF beta mediated fibrosis in dSSc. Moreover, this model can be utilized to explore, at the cell and molecular level, the impact of various autoantibodies and therapeutics on epithelial cells.

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POS0485

PLATELET-DERIVED MICROPARTICLES IN SYSTEMIC SCLEROSIS: POTENTIAL NEW PROFIBROTIC BIOMARKER?

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Background: Systemic sclerosis (SSc), the most lethal autoimmune rheumatic disorder, is characterized by vascular damage, immune dysregulation and progressive tissue fibrosis [1]. Microparticles (MP) are membrane-derived vesicles released from cells undergoing activation or apoptosis, that participate in regulation of inflammatory responses, homeostasis and vascular function [2]. Prior studies have reported elevated plasma levels of MP in SSc [3,4], but its association with clinical SSc features and its role in the disease pathogenesis has still not been completely elucidated.

Objectives: We aimed to compare serum levels of platelets-derived microparticles (PMP), endothelial cells-derived microparticles (EMP), and monocytes-derived microparticles (MMP) between SSc patients and healthy controls. Also, we aimed to evaluate the association of MP and SSc clinical features.

Methods: In this cross-sectional study, 70 SSc patients and 35 age- and sex-matched healthy controls were recruited. After staining with fluorescent cell-specific monoclonal antibodies (PMP $CD42^+/31^+$, EMP $CD105^+$, and MMP $CD14^+$), plasma MP were quantified by flow cytometry. Clinical and nailfold capillaroscopy data from patients were obtained. All of them fulfilled the 2013 ACR/EULAR classification criteria for SSc.

Results: Clinical features of studied population are shown on Table 1. Serum MP levels were significantly increased in SSc patients compared to healthy controls (mean ± SD): 79.2% ± 17.3% vs 71.0% ± 19.8% for PMP (p = 0.033); 43.5% ± 8.7% vs 37.8% ± 10.4% for EMP (p = 0.004); and 3.5% ± 1.3% vs 1.1% ± 0.5% for MMP (p < 0.001) (Figure 1). We observed significantly higher PMP levels in patients with positive anti-topoisomerase-I antibodies compared to those with negative anti-topoisomerase-I antibodies (p = 0.030) and in patients with disease duration > 3 years compared to patients with disease duration ≤ 3 years (p = 0.038).

Table 1. Demographic and clinical data of studied population

Variable	SSc (n=70)	Healthy controls (n=35)	*p*
Female/Male	63 (90) / 7 (10)	31 (88.5) / 4 (11.4)	0.68
Age, yr.	48.9 ± 13.4	47.6 ± 14.0	0.63
Limited SSc/Diffuse SSc	44 (62.9) / 26 (37.1)	--	--
Disease duration, yr.	6.4 ± 4.0	--	--
Modified Rodnan skin score	6.5 ± 9.6	--	--
Active digital ulcers	15 (21.4)	--	--
FVC, *(n=63)*	80.9 ± 17.4	--	--
ILD	38 (54.3)	--	--
PAH	4 (5.7)	--	--
Esophageal dyskinesia	42 (60)	--	--
Cardiac involvement	8 (11.4)	--	--
Autoantibodies			
Anticentromere	13 (18.6)	--	--
Anti-topoisomerase-I	13 (18.6)	--	--
Nailfold capillaroscopy, *(n=61)*			
SD Early	23 (37.7)	--	--
SD Active	15 (24.5)	--	--
SD Late	23 (37.7)		
Calcium channel blockers in use	49 (70)	--	--
Phosphodiesterase-5 inhibitors in use	9 (12.9)	--	--
Immunosuppressors in use			
Glucocorticoids	8 (11.4)	--	--
Cyclophosphamide	3 (4.3)	--	--
Mycophenolate	15 (21.4)	--	--
Azathioprine	3 (4.3)	--	--
Rituximab	1 (1.4)	--	--
Methotrexate	12 (17.1)	--	--

Data are mean ± SD or n (%) unless otherwise stated. FVC: forced vital capacity; ILD: interstitial lung disease; PAH; pulmonary arterial hypertension.

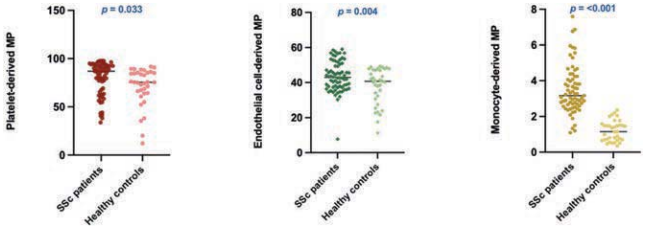

Figure 1. MP plasma levels in SSc patients vs healthy controls

Conclusion: Serum levels of PMP, EMP and MMP are elevated in scleroderma patients, thus indicating a possible role of these agents in SSc pathogenic mechanisms. The higher plasma titles of PMP observed in patients with longer

disease duration and presence of anti-topoisomerase-I, a well-established factor of worse prognosis in SSc, might suggest a profibrotic function for this new potential biomarker.

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POS0486 IDENTIFICATION OF NEW CANDIDATE TARGETS INVOLVED IN ACTIVATION OF CARDIAC FIBROBLASTS UNDER IMMUNOFIBROTIC CONDITIONS

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Background: Inflammatory dilated cardiomyopathy (iDCM) often leads to heart failure (HF), which is the main cause of mortality in patients with systemic diseases. Fibroblast activation, driven by the activator protein 1 family member Fos-related antigen 2 (FOSL2), represents a critical step in cardiac fibrogenesis. The existing antifibrotic therapies, based on known fibrotic markers, failed to demonstrate efficacy against myocardial fibrosis.
Objectives: To identify new candidate targets implicated in cardiac fibrogenesis under immunofibrotic conditions.
Methods: Cardiac fibroblasts were isolated from the left atria of patients (n=5) undergoing heart transplantation due to HF associated with iDCM and from unaffected hearts of brain-dead donors (UDs, n=5). Protein identification and quantification was performed using liquid chromatography tandem-mass spectrometry (LC–MS/MS). The data were analysed with MaxQuant v1.6.2.3 software. Bulk RNA sequencing (RNA-seq) was conducted using the Illumina HiSeq platform. Differentially expressed genes were identified using DESeq2. Additionally, we analysed publicly available single-cell (sc) RNA sequencing datasets (GSE109816, GSE121893) [1] on adult hearts from HF patients (n=6) and UDs (n=14) using Seurat package (V.2.3.4). Specific gene knockdown was achieved by siRNA transfection of human foetal cardiac fibroblasts (HCFs, Sigma), untreated or stimulated with TGF-β for 48-72h. The profibrotic marker expression was assessed using RT-qPCR and Western Blot. Cell viability was measured using PrestoBlue HS reagent (Invitrogen), and ATP production was quantified with CellTiter-Glo assay (Promega) in untreated and TGF-β-stimulated HCFs 48h after transfection.
Results: The LC–MS/MS analysis revealed 14 differentially expressed proteins (absolute log2FC>1, adj. p<0.05) in the HF group compared to UDs. The most upregulated protein in HF fibroblasts was dysferlin (DYSF, log2FC=5.78, adj. p<0.004), which is known to play a role in the sarcolemma repair of both skeletal muscle fibres and cardiomyocytes. Bulk RNA-seq analysis identified a total of 67 significantly differentially expressed genes (absolute log2FC>1, adj. p<0.05). The comparative analysis of bulk RNA-seq results and publicly available scRNA-seq datasets revealed two commonly upregulated genes in HF fibroblasts or their subclusters, encoding transcription factor FOXF1 (log2FC=3.51, adj.p<0.05) and matrix remodelling-associated protein MXRA5 (log2FC=2.91, adj. p<0.05). Further *in vitro* studies on HCFs (n=4) showed that TGF-β upregulated *DYSF* (p<0.001) and *MXRA5* (p<0.01) but downregulated *FOXF1* (p<0.05). *DYSF* silencing in HCFs (n=4) upregulated *MXRA5* after 48h of TGF-β stimulation (p<0.05), downregulated *ACTA2* (48h and 72h of TGF-β stimulation, p<0.05), and upregulated FOSL2 protein levels in untreated HCFs and 72h after TGF-β stimulation (n=3, p<0.05). *MXRA5* knockdown (n=8) resulted in the upregulation of *DYSF* (p<0.05), *ACTA2* (p<0.05) and *COL1A1* (p<0.001) in untreated HCFs, and also upregulated *DYSF* (p<0.01) and *COL1A1* (p<0.05) after 48h of TGF-β stimulation. *FOXF1* silencing in HCFs (n=8) followed by 48h of TGF-β stimulation downregulated *MXRA5* (p<0.01) and *ACTA2* (p=0.06), and upregulated *DYSF* (p<0.001) and *COL1A1* (p=0.05). Candidate targets knockdown reduced cell viability in untreated (n=4, *DYSF*: p<0.01, *MXRA5*: p<0.001, *FOXF1*: p<0.01) and TGF-β stimulated (n=4, *DYSF*: p<0.05, *MXRA5*: p<0.05, *FOXF1*: p<0.01) HCFs. ATP levels were decreased in TGF-β-stimulated HCFs after *DYSF* silencing (n=6, p=0.05).
Conclusion: Based on transcriptomics, proteomics and *in vitro* analysis of human cardiac fibroblasts, we identified *DYSF*, *MXRA5* and *FOXF1* as candidate targets implicated in profibrotic phenotype development, including profibrotic transcription factor FOSL2 regulation. These newly proposed candidates may serve as potential therapeutic targets for the treatment of cardiac fibrosis.

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POS0487 THE CROSSTALK OF THE SKIN-ORAL-GUT MICROBIOME AXIS IN LIMITED AND DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a complex and still unclear rare disease. Microbiota has recently emerged as an important environmental factor in SSc pathogenesis, either at gut, oral and skin level.
Objectives: To investigate the role of microbiota in SSc subsets, focusing on the skin-oral-gut microbiota axis and serum and fecal free fatty acids (FFA) profile.
Methods: Twenty-six consecutive SSc patients (22 females) (mean disease duration (SD): 13 ± 6.91 yrs), classified according to the ACR/EULAR2013 criteria, were enrolled. Demographic, clinical and laboratory data were recorded. Gastrointestinal symptoms were investigated with UCLA GIT-2.0-questionnaire. Fecal, unstimulated saliva and superficial epidermal samples were collected. Microbiota was assessed through 16S ribosomal RNA Next Generation gene-sequencing analysis. Gas Cromatography-Mass Spettroscopy was used to measure FFAs in serum and fecal samples.
Results: Thirteen patients had limited cutaneous SSc (lcSSc), 13 diffuse cutaneous (dcSSc). The two subsets displayed a different cutaneous and fecal microbiota profile. In detail, the class of cutaneous *Sphingobacteria* was significantly higher in lcSSc (p<0.05), while the phylum of *Lentisphaerae*, the family of *Victivallaceae* and the genus of *Victivallis* were significantly higher in fecal samples of lcSSc (all p<0.05). A significant increase of fecal propionic acid was observed in lcSSc patients (p<0.05). Moreover, all fecal medium-chain FAs and hexanoic acids were significantly higher in lcSSc (p<0.05 and p<0.001, respectively). The analysis of serum FFAs levels showed an increase of valeric and octanoic acids in lcSSc (both p<0.05). A negative correlation between UCLA-GIT-2.0 total score and fecal octanoic acid (rho=-0.61; p=0.03), and a positive correlation with serum propionic acid (rho=0.55; p=0.05) was found in lcSSc.
Conclusion: Our findings show a different microbiota signature in the skin and gut, and a different FFAs profile in lcSSc and dcSSc. Such a differential regulation of microbiota composition and bacterial metabolite production suggests different dynamics of skin-oral-gut microbiota axis in SSc subsets. This data could be useful to develop personalized therapies targeting gastrointestinal and skin involvement.

Disclosure of Interests: None declared.
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POS0488 IDENTIFICATION OF NOVEL DISEASE BIOMARKERS IN SYSTEMIC SCLEROSIS THROUGH HIGH-THROUGHPUT PROTEOMICS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, tissue fibrosis and activation of the innate and adaptive immune

system. Clinical features of the disease consist of skin thickening and internal organ involvement. Due to the heterogeneous nature of the disease, there is an unmet need of biomarkers for diagnosis, disease progression and response to treatment.

Objectives: The aim of this study was to explore new serum proteomic fingerprints of clinically defined forms of SSc.

Methods: Highly specific detection of nighty two proteins from a panel related to organ damage was performed, by using the breakthrough technology proximity extension immunoassay (PEA, Olink), in the serum of 72 patients with SSC and 18 age-matched healthy donors (HD). Main disease complications in the SSC cohort, including lung fibrosis, skin fibrosis, renal, vascular, and esophageal involvement were assessed, and prevalence of circulating autoantibodies was tested, along with standard demographic and inflammatory parameters. Unsupervised hierarchical clustering methodologies were applied to identify subgroups of patients based on their proteomic profiles. Gene ontology enrichment was used to interrogate the biological meaning of the distinctive molecular signatures identified.

Results: Sixteen circulating proteins related to organ damage were coordinately altered in the serum of SSc patients in relation to HD. Unsupervised clustering analyses differentiated 3 patients clusters presenting different proteomic profiles. Clinically, patients belonging to cluster 1 were characterized by a significant prevalence of multiple organ involvement (84%) in relation to clusters 2 (52%) and 3 (43%), mostly encompassing lung and skin fibrosis and esophageal dysmotility. Immunologically, cluster 1 further displayed the highest percentage of positivity for anti-scl70 antibodies. Nineteen serum proteins, not previously reported in the serum of SSC patients (BANK1, BID, CALR, ERBB2IP, FGR, FOSB, FOXO1, INPPL1, MAEA, MAGED1, MAP4K5, NBN, NCF2, PRKAB1, RASSF2, RCOR1, SMAD1, STXBP3, VASH1) were found deregulated between clusters, with a significant increase in the levels of all of them in cluster 1 compared with clusters 2 and 3. These deregulated proteins were mostly involved in biological processes such as cell proliferation, apoptosis, cell adhesion, migration, and immune response. Among them, two were functionally linked with cutaneous diseases [Calreticulin (CALR) and B-cell scaffold protein with ankryn repeats (BANK1)], two with digestive disorders (Tyrosine-protein kinase Fgr (FGR) and syntaxin-binding protein 3 (STXBP3)] and three with lung disfunction [protein FosB (FOSB), mothers against decapentaplegic homolog 1 (SMAD1) and forkhead box protein O1 (FOXO1)]. Interestingly, levels of some overexpressed proteins in C1 [BH3-interacting domain death agonist (BID), phosphatidylinositol 3,4,5-triphosphate 5-phosphatase 2 (INPPL1), Erbin (ERBB2IP), BANK1 and FOSB] were further related to the positivity for anti-scl70, the specific SSC-autoantibody known to be mostly associated to a bad prognosis and multiple organ involvement in SSC patients.

CONCLUSION:

1) Stratification based on serum proteomic profile could be of use for a better clinical classification of SSc patients, adding new insights to the underlying pathophysiological mechanisms.
2) Combination of disease classifying autoantibodies with principal pathophysiological processes and serum proteomic profiles can help to elucidate and strengthen the diagnosis as well as the prognosis in SSC.

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Disclosure of Interests: None declared.

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POS0489 CCL24 SERUM CONCENTRATION CORRELATES WITH DISEASE ACTIVITY AND WORSE PROGNOSIS IN DIFFUSE CUTANEOUS SSC: A PROMISING BIOLOGICAL TARGET TO PREVENT DISEASE PROGRESSION

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Background: Linking novel therapeutic targets for diffuse cutaneous Systemic Sclerosis (dcSSc) to markers of disease severity and clinical outcome will enable directing the right therapeutic agents to the appropriate patient populations. Such correlation will also support patient stratification in clinical trials, increasing their informative value and success rates. CCL24 is a chemokine within the Eotaxin family, that has been shown to have a dual pro-inflammatory and pro-fibrotic role in SSc. CCL24 and its receptor, CCR3, were found to be over-expressed in SSc skin and serum samples. In-vivo CCL24 blockage was associated with reduction of bleomycin induced skin and lung injury.

Objectives: We aimed to study the role of CCL24 in dcSSc using patient cohorts, by correlating its serum levels to disease activity markers and disease progression.

Methods: Retrospective and longitudinal dSSc patients' cohorts were analyzed for CCL24 circulating levels, clinical measurement and disease related bio-markers.

Results: In a retrospective cohort of 56 dcSSC patients, CCL24 serum levels were significantly higher in patients that had positive anti topoisomerase antibody (ATA) compared to patients with negative ATA. In addition, within the ATA positive patients, ones that had high serum CCL24 levels (≥1500 pg/ml) also presented significantly higher fibrotic activity reflected by a higher enhanced liver fibrosis (ELF) score compared to ATA positive patients with low CCL24 (<1500 pg/ml). In a second longitudinal cohort of 66 patient, baseline CCL24 levels positively correlated with ELF score (r=0.42, p≤0.0005). Patients with high baseline CCL24 serum levels were also more likely to experience lung disease progression, measured by reduction in forced vital capacity (FVC) during 12 months(7 out of 17 patients with CCL24 ≥ 1500 pg/ml had at least -5% reduction of FVC). Consistent with these data, patients with normal FVC at baseline (>80% predicted) which experienced worsening in the next 12 months (at least 7%) had a statistically significant higher baseline serum CCL24 (Average 2,275 pg/ml) compared to patients that had no worsening in FVC over time (average 962 pg/ml, p≤0.001). Interestingly, the same group showed an even steeper reduction in DLCO % predicted (-6.8% vs -0.2%, p≤0.05).

Conclusion: We show here using two dcSSc patient cohorts, that CCL24 serum levels are correlated with disease activity and worse prognosis reflected by high fibrotic activity and deterioration of lung function over time. This reverse translational study supports the role of CCL24 as a therapeutic target for dcSSc and it has informed a phase 2 study testing CM-101, a CCL24 neutralizing antibody, in dcSSc patients to be started in 2022.

Disclosure of Interests: Michal Segal Salto Employee of: Chemomab Therapeutic Ltd., Adi Mor Employee of: Chemomab Therapeutics Ltd., Francesco Del Galdo Consultant of: Chemomab Therapeutic Ltd., Grant/research support from: Chemomab Therapeutic Ltd.

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POS0490 USEFULNESS OF MHC-II IMMUNO-STAINING ON MUSCLE BIOPSIES IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IIMs) constitute a group of acquired muscular diseases that occur during childhood and adulthood, exhibit a variety of phenotypes and are potentially life-threatening. IIM diagnosis considers clinical, serological, and histological data. Muscle pathological analysis of IIM patients gives relevant elements for the diagnosis (immune cell infiltrate, vascular and connective tissues, as well as myofiber morphology). Immunochemistry (IHC) labeling for major histocompatibility complex class I (MHC-I), and C5b9, that are negative in normal muscle, appeared of interest in IIM diagnosis and the understanding of IIM pathogenesis. In normal muscle, myofibers are negative for MHC-II IHC. Its interest in the neuropathological exam of IIM muscle remains to be better characterized.

Objectives: This study aims to analyze the pattern of MHC-II expression in various IIMs.

Methods: A historical cohort was designed using the MYOLYON register (IIM patients diagnosed between 2016 and 2020 at the University Hospital of Lyon, France). Inclusion criteria were IIM diagnosis that was established histologically and available frozen muscle samples for additional analyses. Exclusion criterium was any treatment before muscle biopsy. Demographical data and final diagnosis were collected retrospectively from medical records. A centralized, standardized, and blind analysis of muscle MHC-II immuno-staining was conducted to define the various patterns of MHC-II by myofibers and by capillaries. The study complied with ethical requirements.

Results: Seventy-three patients were included: 23 dermatomyositis (DM), 13 anti-synthetase syndrome (ASS), 13 immune-mediated necrotizing myopathies (IMNM), 13 inclusion body myositis (IBM), and 11 overlap myositis (OM). MHC-II immuno-staining of myofibers or capillaries was abnormal for 91.8% of the analyzed biopsies (Figure 1). The analysis of MHC-II myofiber immuno-staining

revealed distinguishable patterns according to IIM subtype: the labeling was diffuse in IBM (69.2%, n=9/13), perifascicular in ASS (61.5%, n=8/13), and variable in OM (patchy for 27.3% n=3/11 or clustered for 36.4%, n=4/11). MHC-II immuno-staining was negative in IMNM (84.6%, n=11/13) and in DM (47.8%, n=11/23). DM exhibiting positive MHC-II myofibers (n=12) were associated with the presence of anti-TIF1γ, anti-NXP2 and anti-SAE auto antibodies (n=5, n=3 and n=2, respectively). Among the 12 patients, there were juvenile cases (n=5, 41.7%) or DM associated with ongoing neoplasia (n=4, 33.3%). Three main architectures were described for capillaries: giant, leaky and capillary dropout. Patterns of MHC-II positive capillaries were the following: DM was characterized by capillary dropout (68.2%), IMNM showed leaky capillaries (75.0%), IBM giant capillaries (66.7%), ASS exhibited both giant (61.5%) and/or leaky (58.3%) capillaries, while OM showed giant (63.6%) or/and leaky (80.0%) capillaries and capillaries dropout (60.0%).

Conclusion: The present work establishes the usefulness of MHC-II immuno-staining for IIM diagnosis, and gives additional elements on the impairment of myofibers and capillaries in the various IIM subgroups. MHC-II expression is known to be induced by inflammatory cytokine such as interferon type II. This could be linked to myofiber and/or capillary impairment in some IIMs, such as IBM, ASS and OM. These results also support the implication of vasculopathy in IIM pathogenesis, with various structural and cellular consequences regarding the different subgroups. Finally, MHC-II immuno-staining in IIM muscle biopsies enables a foremost analysis of myofibers and capillaries, and represents an additional biomarker to distinguish IIM subgroups.

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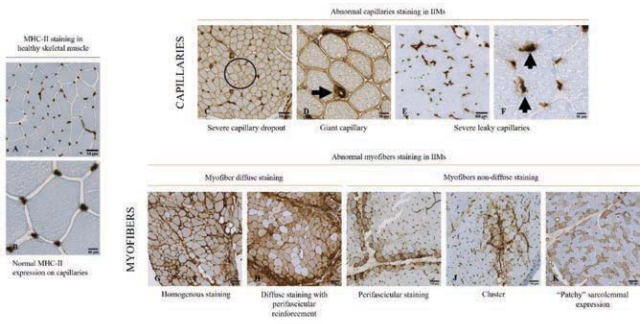

Figure 1. Major histocompatibility complex class II immunostaining in idiopathic inflammatory myopathies.
In normal skeletal muscle, major histocompatibility complex class II (MHC-II) is expressed on capillaries and highlights their regular and "round" shape on axial sections, while there is no sarcolemmal MHC-II expression ((A, scale bar 50μm and B, scale bar 10μm). In idiopathic inflammatory myopathies (IIMs), MHC-II staining highlights either capillary dropout (C, circle, scale bar 50μm)), giant capillaries ((D, arrow, scale bar 10μm) characterized by a widen lumen and a thickened wall, as well as leaky capillaries characterized by a blurred staining with undefined borders (E, scale bar 50μm, and F, arrow, scale bar 10μm). Sarcolemmal expression of MHC-II can be diffuse (G, scale bar 100μm), with for some cases perifascicular reinforcement (H, scale bar 100μm); or non-diffuse: perifascicular (I, scale bar 100μm), clusters (sarcolemmal expression around inflammatory infiltrates) (J, scale bar 100μm), or "patchy" (K, scale bar 100μm).

Disclosure of Interests: None declared.
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Vasculitis - aetiology, pathogenesis and animal models

POS0491 A COMPREHENSIVE PROFILE OF CHEMOKINES IN THE PERIPHERAL BLOOD AND VASCULAR TISSUE OF PATIENTS WITH TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic granulomatous large vessel vasculitis with multiple immune cells involved [1]. In TAK, vascular lesions originate from the vascular adventitia. The vascular adventitia is rich in vasa vasorum, which can transport peripheral immune cells to active vascular lesions in the early stage of lesion development [2]. Thus, chemokines played critical roles in the pathogenesis of TAK. It has been reported that the levels of RANTES, CCL2, CCL20, CXCL8, and CXCL10 were elevated in TAK, and their levels were correlated with disease activity [3, 4]. However, the profile of chemokines in TAK has not been clearly elucidated.

Objectives: This study aimed to investigate chemokine profile in peripheral blood and vascular tissue of patients with TAK.

Methods: A total of 58 patients with TAK and 53 healthy controls were enrolled. Chemokine array assay was performed in five patients with TAK and three controls. Chemokines with higher levels were preliminarily validated in 20 patients and controls. The validated chemokines were further confirmed in another group of samples with 25 patients and 25 controls. Their expression and distribution were also examined in vascular tissue from 8 patients and 5 controls. Correlations between these chemokines and peripheral immune cells, cytokines, disease activity parameters were analyzed. Their serum changes were also investigated in these 45 patients after glucocorticoids and immunosuppressive treatment.

Results: Patients and controls were age and sex-matched. Twelve higher chemokines and 4 lower chemokines were found based on the chemokine array. After validation, increase of 5 chemokines were confirmed in patients with TAK, including CCL22, RANTES, CXCL16, CXCL11, and IL-16. Their expressions were also increased in vascular tissue of patients with TAK. In addition, levels of RANTES and IL-16 were positively correlated with peripheral CD3+CD4+ T cell numbers. Close localization of CCL22, CXCL11 or IL-16 with inflammatory cells were also observed in TAK vascular tissue. No correlations were found between these chemokines and cytokines (IL-6, IL-17, IFN-γ) or inflammatory parameters (ESR, CRP). No differences were observed regarding with these chemokines between active and inactive patients. After treatment, increase of CCL22 and decrease of RANTES, CXCL16 were found, while no changes were showed in levels of CXCL11 and IL-16.

Conclusion: CCL22, RANTES, CXCL16, CXCL11, and IL-16 were identified as the major chemokines involved in the recruitment of immune cells in the vascular tissue of patients with TAK. Additionally, the persistently high levels of CCL22, CXCL11, and IL-16 observed after treatment indicate their role in vascular chronic inflammation or fibrosis and demonstrate the need for developing more efficacious treatment options.

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POS0492 MALADAPTIVE ACTIVATION OF TRAINED IMMUNITY IN THE PATHOGENESIS AND TREATMENT OF GIANT CELL ARTERITIS

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Background: Trained immunity (TI) is a *de facto* innate immune memory program of monocyte/macrophages, mechanistically characterized by immunometabolic and epigenetic changes sustaining persistent inflammatory activation with enhanced cytokine production. TI evolved as a protective mechanism against infections; however, maladaptive activation can cause detrimental inflammation and might be implicated in the pathogenesis of rheumatic and musculoskeletal diseases (RMDs).

Objectives: In this study, we investigated the role of maladaptive TI in the pathogenesis of Giant Cell Arteritis (GCA), a disease characterized by aberrant macrophage activation.

Methods: Monocytes from a large cohort of clinically active GCA patients (ie, at diagnosis or during disease flares, n=20) and from age- and sex-matched healthy donors were subjected to polyfunctional determinations, including

intracellular metabolomics, chromatin immunoprecipitation PCR, ATAC and RNA sequencing, and cytokine production assays. Arteries from GCA patients were evaluated with immunohistochemistry (IHC) to assess immunometabolic activation. Pharmacologic inhibition of immunometabolic changes underlying TI (ie, glycolysis) was evaluated *ex vivo* as a therapeutic strategy to suppress cytokine production.

Results: GCA monocytes exhibited hallmark molecular features of TI. Specifically, these included typical immunometabolic changes (eg, increased glycolysis and glutaminolysis through the TCA cycle), epigenetic changes promoting transcription of genes governing pro-inflammatory activation, and enhanced IL-6 production upon inflammatory challenge. IHC revealed that GCA lesions are highly glycolytic microenvironments, and pharmacologic inhibition of glycolysis with 2-deoxy-glucose effectively dampened IL-6 production.

Conclusion: This study reveals the deleterious potential of maladaptive TI in the pathogenesis of GCA, and the therapeutic potential of inhibiting TI for the treatment of this condition.

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POS0493 1H-NMR BASED METABOLOMIC PROFILE OF PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA IN ACTIVE AND INACTIVE DISEASE STATE

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Background: Giant cell arteritis (GCA) is the most common form of systemic vasculitis in the elderly. The disease is characterized by a remarkable heterogeneity in terms of clinical picture, histologic pattern of the affected vessels, pathogenetic mechanisms and treatment selection strategies. Approximately half of GCA patients present with polymyalgia rheumatica (PMR), while 20% of PMR patients will develop GCA during follow-up. Organ or life-threatening complications of GCA, include vision loss, strokes, aneurysm formation and accelerated atherosclerosis. The clinical heterogeneity along with the increased relapse rate, even under treatment and the fact that ESR and C-Reactive Protein are the only laboratory tools for the assessment of active disease suggest that the definition of new biomarkers with diagnostic, prognostic and predictive value is an unmet need (1). Among the high throughput approaches towards this direction, ^{1}H NMR spectra of serum samples provides a direct, untargeted, and holistic metabolic profile offering a wealth of information that could be proved useful to discover outcome tools for the management of the disease (2).

Objectives: 1. To characterize and compare the metabolic profile of GCA/PMR serum samples, as captured in ^{1}H NMR spectra, in 3-time points: diagnosis, 1 and 6 months of treatment with steroids (remission), 2. evaluate whether ^{1}H NMR-based metabolomics in serum from patients with GCA/PMR associate with response to treatment and 3. identify potential discriminatory serum metabolic profiles correlating with disease activity.

Methods: One-hundred and ten serum samples from 50 consecutive patients (33-GCA and 17-PMR) were evaluated in the study. GCA serum samples consisted of 33 naïve, 22 in 1 and 21 after 6 months of treatment (25 females, mean age 73.0 ± 7.6 years and 8 males, mean age 69.5 ± 4.9 years), while PMR of 15 naive, 10 in 1st and 8 respectively (9 females, mean age 65.0 ± 5.3 years and 8 males, mean age 77.0 ± 6.6 years). The serum metabolic profiles of patients were obtained at a 600 MHz NMR spectrometer and analysed by means of uni- and multivariate statistical methods.

Results: Multivariate analysis showed metabolic differences between GCA/PMR patients in activity and in remission using unsupervised principal component analysis (PCA: R2X= 0.698, Q2= 0.561) and supervised partial least squares discriminant analysis (PLS-DA: R2X= 0.596, Q2= 0.219) (Figure 1). In accordance with univariate analysis ($p<0.05$), the following discriminatory metabolites were identified: N-acetyl glycoproteins, 3-hydroxybutyric acid and phenylalanine were increased in inflammation, while cholines, lipoproteins, and lipids were decreased in these patients.

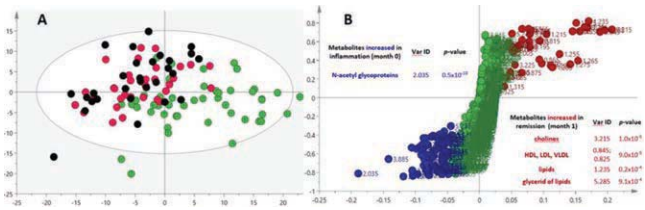

Figure 1. (A) PLS-DA scores plot and (B) S-plot from OPLS-DA of ^{1}H NMR profiling of GCA/PMR serum samples before treatment (green dots) and after 1 (red dots) and 6 months (black dots) of treatment. Characteristic metabolites in inflammation and remission are annotated and the corresponding p-values are given. PLS-DA: partial least square discriminant analysis, OPLS-DA: orthogonal partial least squares discriminant analysis.

Conclusion: ^{1}H NMR-based serum metabolomics revealed a clear discrimination of GCA/PMR metabolic profiles before (active inflammation) and after treatment with steroids (remission), suggesting that the metabolomic analysis may serve as a useful tool to identify potential biomarkers related to disease activity in both GCA and PMR, as well as give further insights into pathogenetic mechanisms mediating the inflammatory response. Further validation studies to dissect the clinical value of specific metabolites are ongoing in our laboratory.

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Disclosure of Interests: None declared.

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POS0494 ARTERIAL WALL DENDRITIC CELLS IN GIANT CELL ARTERITIS (GCA) AND POLYMYALGIA RHEUMATICA (PMR)

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Background: Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disease (1) associated in 16 to 21% of cases with giant cell arteritis (GCA). The association of these two conditions raises the question of a pathophysiological *continuum* between PMR and GCA. An early study reported mature arterial wall dendritic cells (DC) in patients with GCA or PMR leading, during GCA, to $CD4^+$ T cell recruitment and the development of vasculitis (2). However, these data have never been confirmed in other studies. There are 3 main types of DC: plasmacytoid DC (expressing CD123), conventional DC (cDC) expressing CD141 (cDC1) or CD1c (cDC2) and monocyte-derived DC (mo-DC) expressing CD14.

Objectives: The aim of this study was to describe the arterial wall infiltrating DCs, their phenotype and maturation state, during PMR and GCA.

Methods: Using temporal artery biopsies (TAB) from patients with PMR, GCA and healthy controls, the level of expression of *CD11c, CD83, CCR7, CCR6, CD1c, CCL18, CCL19, CCL20, CCL21, GM-CSF, CD3, CD68* genes was assessed by RT-PCR. Expression of markers of DC lineage (CD209), DC maturation state (CD83 and CCR7) and DC origin (CD14, CD68, CD1c, CD141) were studied by confocal microscopy.

Results: Fourty-one patients were included (14 GCA, 16 PMR, 11 controls). Within the arterial wall, DCs were identified in GCA patients, with a mature DC phenotype ($CD209^+CD83^+CCR7^+$). DC were present in all three layers of the arterial wall and also expressed CD14 and often CD68 but neither CD1c nor CD141, which could be explained by a monocytic/macrophage origin. TAB from GCA patients were characterized by a high level of expression of *CD83, CCR7, CCR6, CCL18, CCL19, CCL20, CD11c, GM-CSF, CD3 and CD68* gene. This expression was significantly higher ($p<0.05$) compared to the control and PMR groups. Confocal microscopy analyses of arteries from the PMR and controls did not detect the presence of DCs into the arterial wall. In addition, level of

expression of *CD83, CCR7, CCL18, CCL19, CCL21 and CD68* genes in temporal arteries was comparable between PMR and healthy controls.

Conclusion: This work confirms the presence of mature $CD209^+CD83^+CCR7^+$ DCs within the arterial wall in GCA. The phenotype of these DCs mainly fits with DC of monocytic origin (mo-DCs). However, both by RT-PCR and confocal microscopy, we did not identify DCs in the arterial wall of PMR patients. This discrepancy with previous work (3) could be explained by a better diagnosis of GCA in PMR patients since the development of imaging techniques.

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Basic and translational science in paediatric rheumatology

POS0495 CYTOKINE SYNERGY ENHANCES SYNOVIAL FIBROBLAST ACTIVATION IN CHILDREN WITH DOWN'S SYNDROME-ASSOCIATED ARTHRITIS

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Background: We have previously shown that children with Down's syndrome-associated arthritis (DA) display a more aggressive form of inflammatory arthritis compared to that of Juvenile Idiopathic Arthritis (Shih *et al.*, 2019). DA is associated with an increase in polyfunctional T-cells coexpressing TNF-α DA is associated with an increase in polyfunctional T-cells coexpressing TNF-fibroblasts (FLS) (Foley *et al.*, 2019).

Objectives: In this study we examine the effect of cytokine synergy on primary DA FLS function.

Methods: Primary DA FLS were cultured and stimulated with TNF-α (0.1 and 1ng/ml), IL-17A (20 and 50ng/ml), IFN-γ (10 and 50ng/ml) and GM-CSF (20 and 100ng/ml) or a combination of these cytokines and the following functional experiments performed. Chemokine and adhesion molecule cell surface expression were quantified by flow cytometry, in addition to quantification of leukocyte-DA-FLS adhesion assays. Gene and protein expression of proinflammatory and metabolic mediators were quantified by ELISA and RT-PCR. Furthermore, real-time metabolic activity in response to cytokine stimulation was assessed by measuring the two major energy pathways: glycolysis (ECAR) and oxidative phosphorylation (OCR), by the Seahorse XFe96 Analyser.

Results: We examined the effects of T cell derived cytokines, TNF-α, IL-17A, IFN-γ and GM-CSF, alone and in combination on DA FLS function. TNF-α, IL-17A and IFN-γ induced IL-6, RANTES and MCP-1 production, with no effect observed for GM-CSF. Furthermore, TNF-α, IFN-γ and IL-17A increased leukocyte adhesion to DA FLS. TNF-α and IFN-γ induced cell surface expression of CXCR3, CXCR4, ICAM-1 and VCAM-1 on DA FLS. Next, we investigated the potential synergistic relationship that these cytokines could have on proinflammatory mediators. IL-17A and IFN-γ potentiated the effects TNF-α on IL-6 and MCP-1 secretion compared to stimulation alone. Furthermore, cytokine synergy significantly induced IL-6, IL-8, RANTES and LDHA mRNA expression compared to basal. IL-17A and IFN-αL-17A and IFN- eeased ts TNF-α on IL-6 and MCP-1 secretion compared to stimulation alone. Additionally, IFN the ECAR:OCR ratio demonstrating a shift in the metabolic profile of DA FLS to glycolysis. Overall DA FLS are transformed from a quiescent metabolic state to an energetic phenotype.

Conclusion: TNF-αNF-lusion:OCR ratio demonstrating a shift in the metabolhe aggressive phenotype of DA FLS through increased cytokine, adhesion molecule and chemokine expression, which is pathways for the treatment of DA.

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POS0496 CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS HAVE ALTERATIONS IN B AND T FOLLICULAR CELL SUBSETS IN PERIPHERAL BLOOD

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children[1]. Our group has recently demonstrated that extended oligoarticular (eoJIA) and polyarticular JIA (pJIA) mostly evolve to a rheumatoid arthritis (RA) like phenotype in adulthood[2]. Disturbances in B cells, T follicular helper (Tfh) and T follicular regulatory (Tfr) cell immune responses are associated with the pathogenesis of RA[3,4], but their exact role in JIA development is not entirely known.

Objectives: The main goal of this study was to characterize the frequency and phenotype of B, Tfh and Tfr cells in peripheral blood of children with eoJIA and pJIA when compared to healthy controls and children with persistent oligoarticular JIA (poJIA).

Methods: Blood samples were collected from children with eoJIA (n=5), pJIA (n=11) and poJIA (n=19) treated with disease modifying anti-rheumatic drugs. A group of age-matched healthy individuals (n=8) was used as control. Peripheral blood mononuclear cells were isolated and the frequency and phenotype of B, Tfh and Tfr cells were evaluated by flow cytometry.

Results: The frequency of B, Tfh and Tfr cells was similar between JIA patients and controls. Children with eoJIA and pJIA, but not poJIA, had higher levels of naïve B cells and lower frequencies of post-switch memory B cells and plasmablasts when compared to controls. Th17-like Tfh cells were significantly increased in all JIA patients when compared to controls. B cell phenotype was similar between JIA patients and controls, but a reduced activated phenotype of Tfh cells was observed in JIA patients in comparison to controls.

Conclusion: Changes in B and Tfh cell subpopulations, but not in Tfr cells, were found in peripheral blood of children with JIA when compared to controls. The increased frequencies of Th17-like Tfh cells detected in JIA when compared to controls suggests a potential role of these cells in JIA pathogenesis. A treatment effect on the activation state of B, Tfh and Tfr cells cannot be excluded.

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POS0497

A STUDY ON THE IMMUNOREGULATORY ROLE OF THE PD1 PATHWAY IN JUVENILE IDIOPATHIC ARTHRITIS - PRELIMINARY RESULTS

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Background: The Programmed cell Death protein-1 (PD1) pathway promotes self-tolerance, by inhibiting immune responses. The PD1 soluble form (sPD1), by antagonizing the binding of the membrane-bound PD1 with its ligands, may lead to the blocking of the pathway's functions. Data regarding the role of the PD1 pathway in Juvenile Idiopathic Arthritis (JIA) are still limited.
Objectives: To investigate the immunoregulatory role of the PD1 pathway in JIA patients.
Methods: JIA patients and healthy controls participated in this study with peripheral blood (PB) and/or synovial fluid (SF) samples. sPD1 levels in serum and SF were determined by ELISA. The PD1 expression on T-helper (CD4+) and T-cytotoxic (CD8+) cells in PB and SF was analyzed by flow cytometry. A search for any association between the above biomarkers, as well as their relation with JIA activity was then performed. Inactive disease was defined according to Wallace criteria.
Results: 77 Caucasian patients (52 female) participated so far in this study, with a median (range) age of 13 (2-19) years; their JIA subtypes were: oligoarthritis (33%), polyarthritis (26%), psoriatic (12%), enthesitis-related (16%), systemic (10%) and undifferentiated (3%). Ten healthy children served as controls. As compared to controls, a subpopulation of these JIA patients (n=46) had a significantly higher median percentage of PD1+CD4+ (1.15 *vs*. 0.32%, p=0.029) and PD1+CD8 T cells (1.34 *vs.* 0.4%, p=0.006) in PB. In regard to the JIA status, patients with activity (n=33) had a significantly higher median percentage of both PD1+CD4+ and PD1+CD8 T cells in PB, as compared to those with inactive disease (n=13) (1.36 *vs*. 0.87%, p=0.034 and 2.03 *vs*. 0.45%, p<0.001, respectively). Additionally, in a sample of the patients with disease activity (n=22), the median serum sPD1 level was statistically significantly higher, as compared to a sample of those with inactive JIA (n=10) (218.3 *vs.* 186.7pg/ml, p=0.035). In patients with concurrent serum and SF samples (n=7), the median sPD1 level was statistically significantly higher in the SF than in the serum [1104.4 *vs.* 773.4pg/ml, p=0.028). No correlation was though found between the sPD1 levels and the PD1 cellular surface expression (n=16 PB/serum, n=11 SF).
Conclusion: These preliminary results indicated an sPD1 compartmentalization in active JIA, as sPD1 levels were more prominently raised in the inflamed joint than in the PB. A higher number of circulating T-helper and T-cytotoxic cells expressing PD1 were also detected in active JIA. Further investigation in a larger sample of JIA patients may verify these observations and contribute to unraveling the precise role of the PD1 pathway in the pathogenesis and persistence of the joint inflammation.
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Basic and translational pain science

POS0498

MOLECULAR DOCKING AND PHARMACOLOGICAL ANALYSIS OF ALPHA-PHELLANDRENE IN CHRONIC PAIN: THE ROLE OF SEROTONINERGIC SYSTEM

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Background: Pain is an unpleasant sensory and emotional experience that causes human suffering.[1] Its prevalence has increased, as well as the abuse and dependence on strong opioids.[2,3] The α-phellandrene is a terpene that exerts antinociceptive and immunostimulant effects,[4] however, its mechanisms remain to be elucidated. In this way, bioinformatics may assist in developing new therapeutic approaches for pain management.
Objectives: To investigate the action of a-PHEL in chronic pain, focusing on the role of the serotoninergic system, to develop a new therapeutic tool without the side effects of conventional drugs.
Methods: Molecular docking is an important method for the investigation of the mechanism of action of natural compounds. It is possible to evaluate the molecular dynamics, elucidating the stability of complexes. The software PyMOL and AutoDock Vina 1.5.7 were used to predict interactions of a-PHEL and 5-HT_{2A}R. The mechanism of action of a-PHEL in chronic pain was analyzed *in vivo* as well. The Ethics Committee of UFPI approved this project (protocol n° 305/17). Female Swiss mice (25-30 g) underwent partial sciatic nerve ligation surgery to induce neuropathy. The neuropathic mice (N=6) were pre-treated with 5-HT_{2A} receptor antagonist Ketanserin (0,3 mg/kg, i.p.) or Saline (10 mL/kg, p.o.). After 20min, they were treated with α-phel (6,25 mg/kg, p.o.) and after 1h they were evaluated by the Von Frey test.
Results: The serotoninergic system has a complex and important role in pain modulation especially through descending inhibitory pathways. The Molecular docking predicted the positioning of a-PHEL in the 5-HT_{2A}R, aiding the understanding of its biological activity. The analysis identified 9 key positions for the ligand binding in 5-HT_{2A}R. The lowest Gibbs free energy ΔG= -6.9 kcal/mol. The negative binding energy indicates a strong and stable bond, therefore, α-PHEL has a high affinity for the receptor (Figure 1).

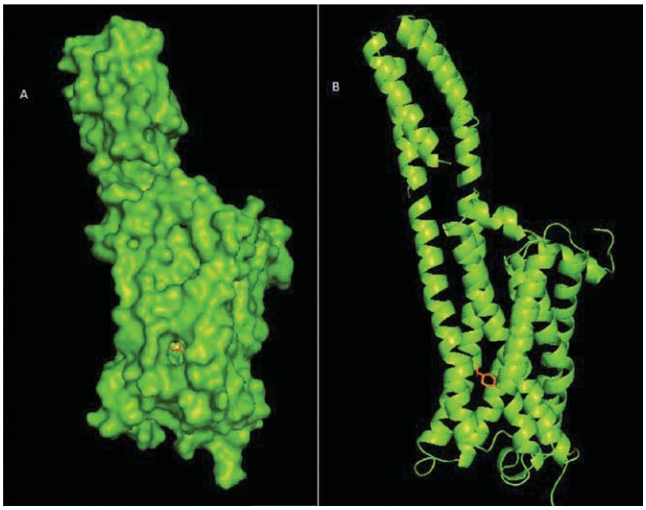

Figure 1. Graphical 3D representation of the binding mode of α-PHEL with 5-HT_{2A}R. A - The ligand (orange) is shown surrounded by a molecular surface of the receptor (green). B – Representation of the best-scoring docked pose (-6.9 kcal/mol) of a-PHEL (orange).

Excellent in vivo therapeutic effects were observed in the animal model of neuropathic pain. Regarding the pharmacological in vivo analysis, the a-PHEL significantly decreased the pain threshold (P<0.05), exhibiting an anti-hypersensitive effect. The inhibition of serotonergic transmission by pretreatment with Ketanserin significantly reduced the antinociceptive effect of a-PHEL in mice. The data indicate that a-PHEL exerts its antinociceptive effect on chronic neuropathic pain model by activation of the 5-HT2AR receptor. Its analgesic effect seems to be mediated by descending inhibitory serotonin system interfering with pain impulse transduction.
Conclusion: Chronic pain is often resistant to medical treatment and the cheminformatics techniques may facilitate the discovery of new compounds, guiding towards specific molecular targets. The a-PHEL may act as a serotoninergic agonist, reducing mechanical sensitivity. It is a promising compound for chronic pain treatment, with lower cost and fewer adverse effects than opioids. Future investigations are expected to highlight the in-depth effects of the interaction of a-PHEL with other receptor subtypes.
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Rheumatoid arthritis - prognosis, predictors and outcome

POS0499 A NEW SERUM ASSAY MEASURING SYNOVIAL TURNOVER IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is characterized by synovial tissue (ST) inflammation leading to pain, joint destruction, impaired mobility and ultimately increased morbidity and mortality. These various components of disease etiology can be monitored by pain scores and imaging technologies. Noninvasive assessment of joint tissues metabolism can be performed by measuring serum metabolites of tissue matrix turnover. Specific biochemical markers (BM) of bone and cartilage have been developed, but there is still a lack of a sensitive index of ST metabolism abnormalities, although there are early and key drivers of joint destruction.
Objectives: To develop a sensitive ELISA-based serum BM of ST turnover (SynHelix) and evaluate its performance in patients with RA.
Methods: We identified a 11 amino-acid sequence (HELIX-III) within the triple helical portion of type III collagen, a main component of ST matrix which is released during ST turnover and can be measured in the serum. A highly specific rabbit polyclonal antibody raised against the synthetic HELIX-III peptide was produced to develop a competitive ELISA. Specificity of the antibody was evaluated by competitive inhibitions with homologous sequences of type I, IV and XI collagens which are also present in ST, but in minor quantities for the two later. Immunohistochemistry analysis of human ST obtained during hip surgery was performed to investigate in situ localisation of the HELIX-III peptide. ELISA was then used to quantify serum HELIX-III fragments in two samples of patients with low (n= 40, median DAS 28: 2.1) and moderate (n=11, median DAS28: 3.5) RA activity participating in clinical trials. Levels in RA subjects were compared to sex and age-matched healthy controls randomly selected from epidemiological cohorts (n=70).
Results: The ELISA for SynHelix demonstrated adequate analytical performances with intra and interassay variations below 10 and 15%, respectively; analytical and functional limits of quantification of 0.21 and 2.5 ng/ml, respectively and dilution recovery of human serum ranging from 80 to 108%. Competitive inhibition experiments demonstrated that the antibody does not recognize HELIX-III peptide shortened or elongated by one amino-acid, indicating that immunogenicity is dependent on the presence of a neopitope resulting from the cleavage of the collagen molecule. The antibody does not recognize the homologous sequence of type I collagen, but shows significant immunoreactivity with the homologous sequences of type IV (alpha 5) and type XI (alpha 2) collagens with however a lower affinity than for type III collagen (a 2.2 and 4-fold higher concentration, respectively, is needed to displace 50% of the immune signal). Immunohistochemistry of ST tissue from RA subjects showed increased staining in the interstitial tissue and around vessels which are rich in type IV collagen. Median serum levels of SynHelix were significantly higher in patients with low (p=0027, +17%) and moderate RA activity (+220%, p=00004 vs healthy controls; +164% p=0.16 vs low RA) compared with those in age-matched controls, although CRP did not discriminate RA patients with low and moderate activity (2.2 mg/L for both groups, p=0.90). In RA subjects, serum SynHelix correlates modestly with CRP (r=0.59, p <0.0001), but not with DAS28.
Conclusion: The new SynHelix ELISA measures precisely circulating degradation fragments of Helix-III peptide-containing collagens. Serum SynHelix levels are already increased in patients with low activity RA, values correlating modestly the degree of systemic inflammation. Larger longitudinal studies are needed to further evaluate the value of SynHelix to predict disease outcome in RA.
Disclosure of Interests: Patrick Garnero: None declared, Evelyne Gineyts: None declared, Jean-Charles Rousseau: None declared, Hubert MAROTTE: None declared, Roland Chapurlat Consultant of: BMS, abbvie, Lilly, Galapagos, fresenius-Kiabi, novartis.
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POS0500 LEVELS OF IL-6 AND OTHER INFLAMMATORY PROTEINS IN EARLY RA PREDICT JOINT DAMAGE PROGRESSION OVER 5 YEARS

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Background: Joint damage in rheumatoid arthritis (RA) remains a significant problem. Identification of biomarkers associated with joint destruction can improve our understanding of underlying disease processes and future management.
Objectives: To evaluate inflammatory proteins as potential predictors of radiographic progression of joint damage.
Methods: Consecutive early RA patients (symptom duration <12 months), recruited 1995-2005 from a defined area, were followed through 5 years in an observational study. Radiographs of hands and feet were scored in chronological order by a trained reader according to the modified Sharp-van der Heijde score (SHS). Stored plasma samples from the baseline visit were analyzed for levels of 92 inflammatory proteins (Inflammation panel by O-link). Statistical analyses were pre-designated as hypotheses-driven or exploratory. For the latter, principal component analysis was used to identify groups of proteins that explain the variance in the proteome. Within components selected based on Eigenvalues, proteins with a factor loading of >0.50 were investigated as potential predictors of radiographic progression. Logistic and linear regression models were used to assess associations with rapid radiographic progression (RRP; ≥5 SHS/year) and progression of SHS over 5 years.
Results: Data on baseline levels of proteins, and radiographs at baseline and 5 years were available for 114 patients. The median progression of SHS was 11 (interquartile 2-19). For potential biomarkers with an a priori hypothesis, IL-6 significantly predicted both RRP and progression of SHS over 5 years analyzed as a continuous variable [adjusted ß = 0.09 per SD, p=0.032, adjusted for rheumatoid factor (RF) and baseline SHS]. A significant positive association for matrix metalloproteinase 1 (MMP-1) was observed in the unadjusted analysis for SHS progression, but not for RRP (Table 1). In the exploratory analyses, S100 calcium-binding protein A12 (EN-RAGE) was positively, and TNF-related apoptosis-inducing ligand (TRAIL) negatively associated with both outcomes.
Conclusion: Plasma levels of IL-6 at RA diagnosis predict degree of future joint damage. EN-RAGE and TRAIL, both modulators of NF-κB which is known to regulate immune response, are potential biomarkers that need further investigation.

Table 1. Baseline inflammatory protein biomarkers and progression of joint damage over 5 years in rheumatoid arthritis

Rapid radiographic progression									SHS progression (continuous)							
	Crude				Adjusted*				Crude				Adjusted*			
Variables	OR	95% CI	P	P (corr)§	OR	95% CI	P	P (corr)§	Beta	95% CI	P	P (corr)§	Beta	95% CI	P	P (corr)§
A priori hypothesis°																
IL-6	**1.83**	**1.11-3.01**	**0.018**	0.14	1.62	0.96-2.75	0.072	0.58	**0.14**	**0.06-0.23**	**0.002**	**0.016**	**0.09**	**0.01-0.17**	**0.032**	0.26
MMP-1	1.56	0.92-2.66	0.10	0.55	1.44	0.84-2.47	0.19	0.96	**0.11**	**0.02-0.20**	**0.019**	0.13	0.08	-0.01-0.16	0.072	0.50
Exploratory analyses†																
MCP-3	**1.64**	**1.01-2.65**	**0.045**		**1.99**	**1.14-3.49**	**0.016**		0.03	-0.07-0.12	0.57		0.04	-0.05-0.12	0.39	
CDCP1	**1.76**	**1.07-2.91**	**0.027**		**2.14**	**1.22-3.78**	**0.009**		0.06	-0.03-0.15	0.19		0.08	-0.00-0.16	0.063	
SLAMF1	**1.64**	**1.05-2.57**	**0.031**		**1.61**	**1.01-2.56**	**0.047**		0.06	-0.02-0.15	0.16		0.05	-0.02-0.13	0.15	
TNFSF14	**1.67**	**1.08-2.60**	**0.022**		1.53	0.98-2.37	0.060		0.07	-0.02-0.15	0.12		0.04	-0.04-0.11	0.30	
EN-RAGE	**2.77**	**1.56-4.94**	**0.001**		**2.44**	**1.34-4.43**	**0.004**		**0.16**	**0.08-0.25**	**<0.001**		**0.10**	**0.02-0.19**	**0.014**	
LIF	**1.96**	**1.13-3.40**	**0.017**		1.73	0.95-3.14	0.073		**0.11**	**0.02-0.20**	**0.019**		0.06	-0.03-0.15	0.18	
Flt-3L	**0.60**	**0.36-0.98**	**0.040**		0.68	0.40-1.14	0.15		**-0.11**	**-0.20-'-0.03**	**0.011**		-0.07	-0.15-0.01	0.075	
DNER	0.72	0.42-1.25	0.25		0.69	0.37-1.27	0.23		**-0.10**	**-0.19-'-0.00**	**0.049**		-0.08	-0.17-0.00	0.054	
CD8A	0.74	0.49-1.12	0.16		0.85	0.55-1.31	0.45		**-0.09**	**-0.17-'-0.01**	**0.031**		-0.05	-0.12-0.03	0.23	
TRAIL	**0.50**	**0.30-0.83**	**0.007**		**0.51**	**0.29-0.88**	**0.016**		**-0.12**	**-0.20-'-0.03**	**0.007**		**-0.08**	**-0.16-0.00**	**0.048**	

Variables per SD. * Adjusted for RF and baseline SHS. § Holms correction for multiple testing for a priori hypotheses only. ° No significant associations for TNF-alpha, Osteoprotegerin, IL-17A, CCL11, CCL19 or VEGFA. † Only biomarkers with significant associations shown.

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POS0501 SEQUENTIAL ULTRASOUND IN ARTHRALGIA PATIENTS AT RISK FOR INFLAMMATORY ARTHRITIS; IS IT HELPFUL FOR RISK STRATIFICATION IN DAILY PRACTICE?

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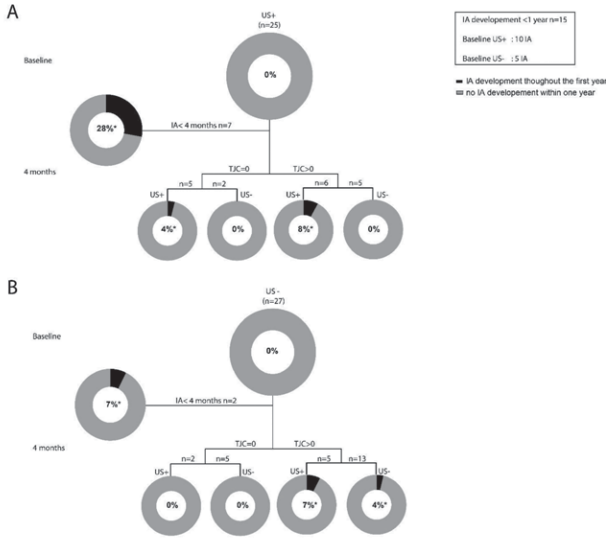
Background: Musculoskeletal Ultrasound (MSUS) is often used to assess the presence of subclinical joint inflammation in patients presenting with arthralgia suspicious for progression to inflammatory arthritis (IA). Even though evidence-based guidelines for these patients are still absent, presence or absence of subclinical joint inflammation often influences management decisions in daily clinical practice. Studies so far focused on MSUS results at presentation with arthralgia. However, it is unknown if and how MSUS results change over time, and whether repeating MSUS is helpful in demonstrating or ruling out impending RA with greater certainty.
Objectives: To investigate whether sequential imaging at 4-months, in addition to baseline evaluation, is helpful in the risk stratification of arthralgia-patients.
Methods: Arthralgia-patients suspicious for progression to IA were included in the Rotterdam clinically suspect arthralgia cohort. At baseline and at 4-months a bilateral MSUS-examination was performed of the joints and tendons in both hands and feet. Subclinical inflammation was defined as GS>1 and/or PD>0, this was scored according to the latest OMERACT- guidelines.(1, 2) Based on a large US study carried out in a symptom-free population, the cut-off value in MTP 2-3 was considered present if GS ≥3 and/or PD ≥1.(3) Patients were followed for one-year on development of IA, identified with joint examination by experienced rheumatologists. The value of MSUS was studied separately for patients with and without subclinical joint inflammation at baseline. In a sensitivity analysis, ACPA-stratification was applied.
Results: A total of 52 consecutive patients were studied; 29% developed IA after one year. At baseline, 25 patients had subclinical inflammation and 27 patients did not have subclinical inflammation. In these groups respectively 28% and 7% developed IA before the 4-month-visit and therefore did not have repeated MSUS (Figure 1 A/B). In the patients with a positive MSUS at baseline, 28% had a negative MSUS at four months, all these patients did not progress to IA, irrespective of tender joints count(Figure 1A). In the group of patients with a negative MSUS at baseline, 26% achieved a positive MSUS at 4-months. All patients with a negative MSUS at baseline and no tender joints at 4-months did not progress to IA, regardless of the MSUS results. Patients with a negative MSUS at baseline and tender joints at 4-months developed IA infrequently, without relevant differences between those that did or did not develop a positive MSUS at 4-monthts. Overall, only a minority of patients whose MSUS progressed from negative to positive indeed developed IA, whereas this repeated MSUS was falsely positive in most cases(Figure 1B). Despite the small numbers, ACPA-stratification was performed, this showed a similar trend.
Conclusion: Within arthralgia patients with a positive MSUS at baseline, a negative MSUS after 4-months may be an incentive to exclude arthralgia-patients from further follow-up. Within the patients with a negative MSUS at baseline, repeating MSUS may induce more false positive than correct positive results.



* percentage IA developement is calculated based on the group at baseline (n=25 for US+ and n=27 for US-)

Figure 1. Sequential ultrasound at baseline and after 4-months of follow-up in arthralgia-patients at risk for inflammatory arthritis with subclinical inflammation at baseline (A) and without subclinical inflammation at baseline(B).

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POS0502 ULTRASOUND THRESHOLDS FOR INFLAMMATORY AND STRUCTURAL LESIONS TODISTINGUISH OSTEOARTHRITIC FROM RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatic disease affecting small and medium-sized joints symmetrically, leading to poor functional outcomes and structural damages with time. The RA elementary inflammatory lesions, synovitis and tenosynovitis, have been associated with the development and worsening of bone erosions leading to loss of joint function and pain. The median age at diagnosis of RA patients, ranged between 50-60 years old, age at which degenerative and inflammation lesions relative to osteoarthritis (OA) damages may be present and interfere to establish a diagnosis of inflamed and/or structural RA disease.
Objectives: To assess prevalence, topography and severity of inflammation and erosion on ultrasound (US) in RA and OA patients and to propose US thresholds to classify RA patients.
Methods: Patients fulfilling ACR 1987 and/or ACR/EULAR 2010 criteria for RA or ACR criteria for hand OA were reprospectively included. Synovitis and tenosynovitis (TS) in B and Power Doppler (PD) modes on seven bilateral joints (carpus, MCP2, 3, 5, MTP2, 3, 5) were scored according to a four-grade scale of severity. Erosive disease was defined by the presence of at least one erosion >2 mm confirmed in 2 perpendicular plans on 30 targeted facet joints. Sensitivity, specificity and OR for the diagnosis of RA were calculated for each elementary (inflammatory and erosive) US lesion.
Results: 153 patients were included: 107 (31 early <2 years) RA and 46 OA patients. Synovitis (B and PD modes) was observed in 92 (85.9%) RA and 12 (26%) OA patients, respectively (p <0.0001). TS (B and PD modes) was depicted in 61(57%) RA and 4 (8.7%) OA patients, respectively (p <0.0001). 71 (66%) RA and 5 (11%) OA patients responded to the definition of erosive disease (p<0.001). The combination of US erosion and PD+ synovitis provided the best compromise to classify RA patients: sensitivity 49.1% (39.7-58.4)), specificity 97.8% (87.4-99.5) and OR= 43.8 (CI95: 8.2-230.2). For early RA, PD+ TS provided the best compromise: sensitivity 54.8% (37.8-58.4), specificity 97.8% (87.4 -100) and OR= 54.6 (CI95: 9.3- 320.5).
Conclusion: The combination of PD+ synovitis and erosion in RA and PD+ tenosynovitis alone in early RA offered the best compromise to classify RA versus OA patients.

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POS0503

RISKS OF CARDIOVASCULAR EVENTS AFTER THE INTRODUCTION OF BDMARDS IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENTS: A POPULATION-BASED INTERRUPTED TIME-SERIES ANALYSIS

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Background: Rheumatoid arthritis (RA) is associated with increased risk of cardiovascular (CV) events. Biological disease-modifying anti-rheumatic drugs (bDMARDs) are effective in suppressing inflammation and preventing joint damage and may help lower the risk of CV events. However, recent epidemiological studies have shown mixed results with some suggesting a lower risk of CV events, while others reporting no significant differences.
Objectives: To determine the impact of the introduction of bDMARDs on incident cardiovascular disease (CVD) among patients newly diagnosed with RA compared with matched non-RA individuals.
Methods: In this age- and gender-matched cohort study using administrative health data for the population of BC, Canada, all incident RA patients diagnosed between 1995–2007 were identified. Non-RA individuals were randomly selected from the general control population to match with RA. Incident RA and non-RA individuals were then divided into quarterly cohorts according to their diagnosis date. The outcome of interest was incident CVD event after RA onset, which include acute myocardial infarction, cerebrovascular accident, and venous thromboembolism. We calculated the 8-year incident CVD rate for each cohort. We conducted interrupted time-series analyses to compare levels and trends of CVD in RA and non-RA individuals diagnosed during pre-bDMARDs (1995–2001) and post-bDMARDs (2003–2007) periods with intervention time set at year of 2002. Adjusted 8-year CVD rates for RA and non-RA cohorts diagnosed five years after bDMARDs introduction were compared with expected rates assuming no bDMARDs introduction, based on extrapolation of pre-bDMARDs trends.
Results: A total of 60,226 and 588,499 incident RA and non-RA individuals were identified. We identified 6,740 and 48,653 incident CVD events in total in RA and non-RA individuals, respectively. We observe no change in the secular trends of the 8-year CVD rates in both RA and non-RA individuals diagnosed in pre- and post-bDMARDS periods (Figure 1): the adjusted difference between the post- and pre-bDMARDs secular trends of 8-year CVD rates was 0.23 (p=0.26) for RA patients and -0.07 (p=0.33) for non-RA individuals (Table 1). However, we observed a reduction in the level of CVD rates among RA patients diagnosed in the post-bDMARDs period and no change in non-RA (Figure 1): the adjusted difference in level comparing points immediately before and after the intervention, and accounting for pre-intervention trend was -1.61 (p=0.03) in RA, while it was -0.02 (p=0.93) in non-RA (Table 1).
Conclusion: Arthritis onset after bDMARDs introduction is associated with a significant reduction in the risk of incident CVD events among RA patients, but not in the matched non-RA individuals.
Acknowledgements: We would like to thank the Ministry of Health of British Columbia and Population Data BC for providing access to the administrative data. All inferences, opinions, and conclusions drawn in this publication are those of the authors, and do not reflect the opinions or policies of the Data Stewards or the [British Columbia] Ministry of Health. No personal identifying information was made available as part of this study. Procedures used were in compliance with British Columbia's Freedom in Information and Privacy Protection Act. Ethics approval was obtained from the University of British Columbia's Behavioral Research Ethics Board (H15-00887).
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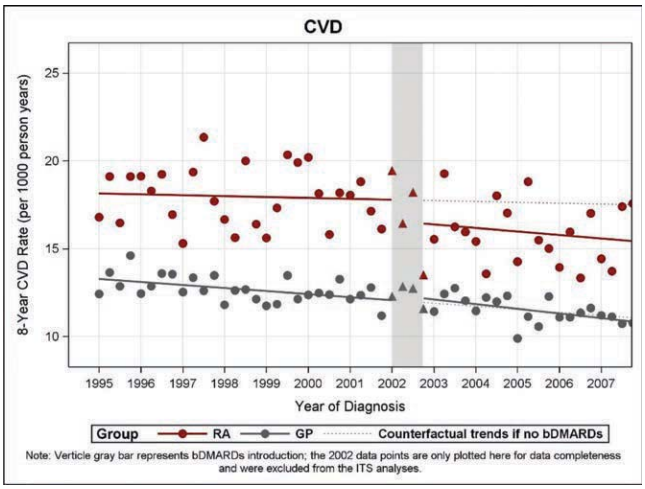

Figure 1. Unadjusted rates.

POS0504

LOW SOCIAL SUPPORT, WORSE FINANCIAL STATUS AND LIMITED PHYSICAL ACTIVITY AT RHEUMATOID ARTHRITIS ONSET PREDICTS EXCESS DISABILITY OVER 10 YEARS

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Background: Previous research has identified trajectory groups of people with rheumatoid arthritis (RA) characterised by excess disability (with respect to inflammation)[1]. These excess disability trajectories were relatively fixed from symptom onset, indicating that sociodemographic and lifestyle factors prior to onset may partially determine the disability trajectories of people with RA, potentially mediated by patient reported outcomes (PROMs).
Objectives: To (i) investigate the relationship between social support, financial status and lifestyle factors and excess disability group membership in RA, and (ii) evaluate the mediating effect of pain, fatigue, anxiety and depression on this relationship.
Methods: Data came from the *Etude et Suivi des Polyarthrites Indifférenciées Récentes* (ESPOIR) study, a prospective cohort from 14 centres across France. Inclusion criteria were: >2 swollen joints for 6 weeks-6 months, certain / possible diagnosis of RA, aged 18-70 years, and no disease modifying treatments or glucocorticoids for >2 weeks. A previous study applying trajectory analysis to the 10-year disability and inflammation scores of the ESPOIR participants identified pairs of trajectories characterised by similar inflammation but different disability[1]. For the current analysis, those in the higher disability trajectories of each pair were allocated into the "excess disability" group. At baseline, participants reported demographics, patient reported outcomes (pain / fatigue visual analogue scales;

Table 1. Results of interrupted time-series analysis of incident CVD rates, adjusting for age, gender, chronic obstructive pulmonary disease, Romano Charlson Comorbidity Index, diabetes, angina, hypertension, chronic kidney disease, peripheral vascular disease, atrial fibrillation, glucocorticoid, non-steroidal anti-inflammatory drugs, CVD medications, fibrates, contraceptives, and aspirin use at disease diagnosis year, using stepwise model selection

Outcome	Parameter	RA		Non-RA	
		Unadj. Diff (95% CI)	Adj. Diff (95% CI)	Unadj. Diff (95% CI)	Adj. Diff (95% CI)
		p-value	p-value	p-value	p-value
CVD					
	Trend	-0.15 (-0.72, 0.42) 0.6086	0.23 (-0.17, 0.64) 0.2620	-0.09 (-0.27, 0.08) 0.3084	-0.07 (-0.20, 0.07) 0.3290
	Level (1 year post-intervention)	-1.36 (-3.17, 0.45) 0.1474	-1.61 (-2.96, -0.25) 0.0251	0.22 (-0.41, 0.84) 0.5011	-0.02 (-0.44, 0.40) 0.9345
	5 years post-intervention	-1.96 (-4.48, 0.55) 0.1332	-0.67 (-2.80, 1.46) 0.5418	-0.15 (-1.06, 0.75) 0.7421	-0.29 (-0.97, 0.39) 0.4102

anxiety / depression: Arthritis Impact Measurement Scales), social support (availability of financial and accommodation support, family contact, married / co-habiting), financial status (personal and family income, job status and level, home owner, ability to go to the cinema/shows / go on holiday) and lifestyle factors (smoking, alcohol, body mass index [BMI; from height and weight], physical activity). Structural equation modelling was used to combine the social support and financial status data into latent variables, and then assess the direct and indirect (mediated by PROMs) effects of these variables as well as lifestyle factors on excess disability (adjusted for age and gender).

Results: In total, 538 people with RA were included (mean [standard deviation] age: 48.3 [12.2] years; 79.2% women), 200 (37.2%) of whom had excess disability over 10 years. The excess disability group were older, included more women, and had worse PROMs at baseline compared with the no excess disability group (Table 1). Less social support (β 0.17, 95% CI 0.08, 0.26) and worse financial status (β 0.30, 95% CI 0.19, 0.41) both predicted excess disability group membership, as did lower physical activity (β 0.17, 95% CI 0.09, 0.25) (Figure 1), whereas smoking, alcohol and BMI at baseline did not. Only a small proportion of this effect was mediated by the PROMs (social support: 21%, financial status: 31%, physical activity: 28%; Figure 1).

Table 1. Baseline characteristics

	Excess disability,	No excess disability,
	Mean (SD) / N (%)	Mean (SD) / N (%)
N	200	338
Age, years	50.4 (10.7)	47.0 (12.8)
Women, N(%)	174 (87.0%)	252 (74.6%)
Symptom duration, months	3.63 (2.02)	3.36 (1.62)
Pain VAS	47.1 (27.4)	37.0 (26.9)
Fatigue VAS	59.3 (27.2)	46.5 (26.5)
AIMS anxiety	5.61 (2.25)	4.71 (2.27)
AIMS depression	4.47 (2.24)	3.47 (1.97)
Health Assessment Questionnaire	1.39 (0.64)	0.93 (0.61)
DAS28-2C	4.04 (1.28)	3.99 (1.34)

AIMS = Arthritis Impact Measurement Scales, DAS28-2C = two-component Disease Activity Score, SD = standard deviation, VAS = visual analogue scale

Conclusion: Disability resulting from RA is a complex phenomenon, arising from more than just joint inflammation. This analysis indicates that lack of social support, financial instability and lower physical fitness at symptom onset may explain the excess disability associated with RA. As only a small portion of the effect is mediated by PROMs, health and social inequalities may need to be targeted directly by interventions.

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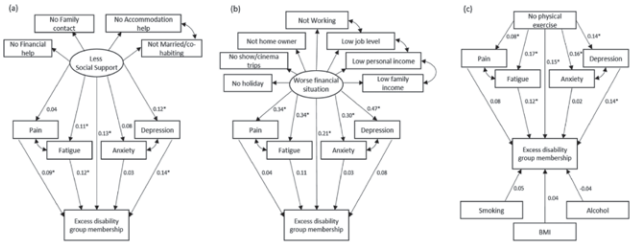

Figure – SEM diagrams of direct and mediating paths between latent variables (a) less social support, (b) worse financial status as well as (c) lifestyle factors and excess disability group membership (indicates statistical significance)*
Ovals represent latent constructs, rectangles observed variables. The total effects referred to in the abstract combine both the direct effect from the latent constructs to the outcome (excess disability), and the indirect effects through the PROMs. For example, the total effect of social support on excess disability (panel a) was 0.17, calculated as the direct effect (0.13) plus the indirect effects through the PROMs ((0.04 x 0.09) + (0.11 x 0.12) + (0.08 x 0.03) + (0.13 x 0.14)). Proportion mediated by the PROMs is the indirect effect divided by the total effect.
BMI = body mass index, PROMs = Patient reported outcome measures, SEM = structural equation model

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POS0505

NO EXCESS MORTALITY IN CONTEMPORARY UNDIFFERENTIATED ARTHRITIS, IN CONTRAST TO RHEUMATOID ARTHRITIS; A STUDY WITH A FOLLOW-UP OF AT LEAST 10 YEARS

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Background: Undifferentiated arthritis (UA) is traditionally considered an early phase of rheumatoid arthritis (RA),[1] and management strategies of RA are often transferred to UA-patients assuming outcomes are comparable. Importantly, the UA population changed with the introduction of 2010 RA criteria as part of the conventional UA population became classified as RA. Consequently, contemporary UA-patients (not fulfilling the 1987 nor 2010 RA-criteria) are largely autoantibody negative and present with relatively mild disease.[2] Subsequently, contemporary UA might no longer represent a group of patients in a pre-phase of RA but a population with intrinsically different characteristics than RA. We therefore hypothesized that mortality, a long term outcome which is increased in RA, is not increased in contemporary UA.

Objectives: To asses mortality rates in contemporary UA-patients, and to compare this to RA and conventional UA during at least 10 years of follow up.

Methods: We studied 860 conventional UA-patients (no 1987 RA-criteria or other diagnosis), 561 contemporary UA-patients (no 1987/2010 RA-criteria or other diagnosis) and 762 RA-patients according to the 1987 criteria and 826 patients fulfilling the 2010 criteria, included in the Leiden Early Arthritis Clinic (EAC) between 1993-2008 to ascertain 10-years of follow-up. Mortality data were obtained from the civic registries (June 2018). Standardized-mortality-ratios (SMRs) were adjusted for age, gender and calendar-year, and additionally stratified for ACPA-positivity (anti-CCP2, cut-off>10 mg/L) and DMARD-treatment.

Results: The contemporary UA-population was for 93% ACPA-negative and the SJC was 1 (median) and TJC 2. This presentation was milder than that of patients with conventional UA. In RA (both 1987-RA and 2010-RA) we observed excess mortality compared to the general population (Figure 1). In conventional UA, a trend towards excess mortality was observed: SMR 1.11 (95%CI:0.96-1.27). However, part of this UA population is currently classified as 2010-RA. Subsequently, in contemporary UA, which does not include these 2010 RA-patients, no excess mortality was observed: SMR 1.05 (95%CI:0.87-1.26). ACPA-stratification suggested excess mortality in ACPA-positive contemporary UA, but not in ACPA-negative contemporary UA (Figure 1). Mortality rates in contemporary UA-patients who did and did not receive DMARD-treatment were comparable (SMR 0.93 (95%CI:0.66-1.24) and SMR 1.08 (95%CI:0.82-1.36)).

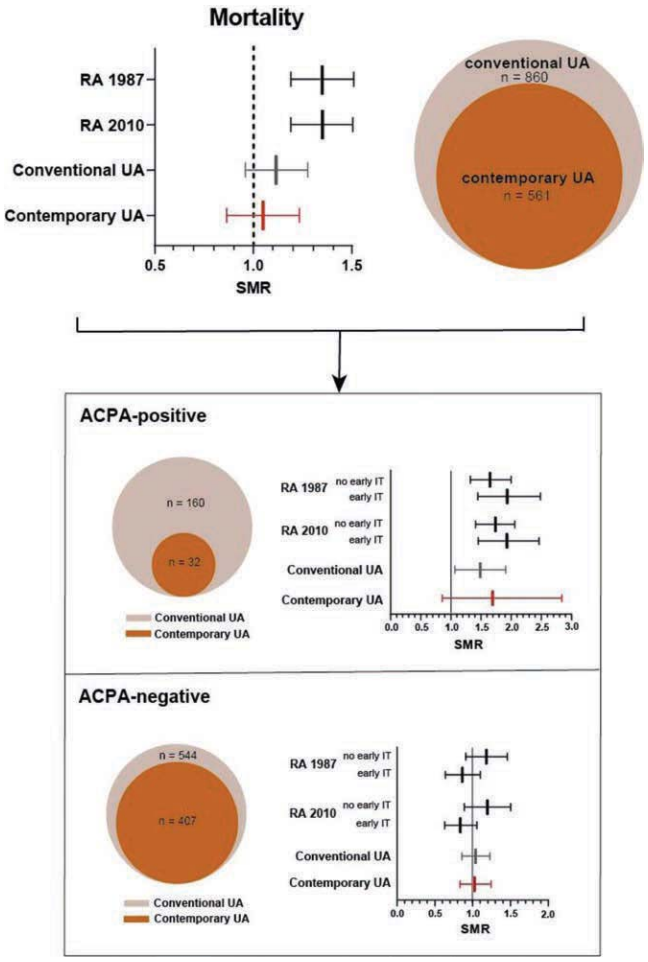

Figure 1. SMRs in UA and RA-patients with minimally 10-years of follow-up. Additionally, mortality was stratified for ACPA-status. In RA, SMRs were also stratified for early treat-to-target DMARD-therapy, which has been shown relevant for mortality analysis in RA.[3] *ACPA: anticitrullinated autoantibody protein, UA: undifferentiated arthritis, RA: rheumatoid arthritis, SMR: Standardized mortality rate, IT: intensive treatment.*

Conclusion: Contemporary UA has no excess mortality, in contrast to RA. So, besides milder disease at presentation within contemporary UA, also the long-term outcome mortality is more favorable and comparable to the general population. This supports the notion that contemporary UA-patients have intrinsically different characteristics than RA-patients, rather than representing an early stage of RA. Future studies are warranted to determine whether contemporary UA should be treated as RA; our results suggest that this population may deserve separate guidelines.

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Disclosure of Interests: None declared.
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POS0506 DIFFERENT BIOACTIVE LIPID PROFILES PREDICT RESPONSE TO TNF OR IL6 INHIBITORS IN RHEUMATOID ARTHRITIS: RESULT OF THE COREVITAS CERTAIN COMPARATIVE EFFECTIVENESS STUDY

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Background: Circulating bioactive lipids can provide information about the pathogenesis of specific diseases and potentially help predict therapeutic response. Choosing the right biological therapy earlier in the course of rheumatoid arthritis (RA) could help reach the goal of remission.
Objectives: We hypothesized that circulating bioactive lipids at baseline would identify specific metabolic profiles that predict patient response to therapy and define elements of metabolic pathobiology in arthritis.
Methods: Bioactive lipids were measured in plasma from two cohorts of RA patients from the CorEvitas (formerly known as Corrona) CERTAIN registry (1) at baseline prior to treatment with TNF inhibitors (all biologic naïve, N=102) or anti-IL6 (all previously exposed to biologics, N=114). Response to treatment was categorized by minimal clinically important difference (MCID) in Clinical Disease Activity Index (CDAI) (2) at 6 months after treatment initiation. Patients had to have a 6 month follow up visit and plasma available at both the baseline and the f/u time points. Liquid chromatography (LC) system coupled with high resolution QExactive orbitrap mass spectrometer (LC/MS) was used for bioactive lipids profiling. Around 300 spectral features were identified as potential oxylipins by searching against an in-house MS/MS library. Logistic regression analyses adjusted for gender, age and BMI was perfomed using R software.
Results: 102 patients (average age 54, standard deviation [SD] 12.6, 82% female [83], average BMI 29.7, SD 6.7, average CDAI 27.1, SD 13.7) starting anti-TNF therapy and 114 patients (average age 57, SD 13, 90% female [102], average BMI 30.5, SD 7.4, average CDAI 28.7, SD 13.8) starting tocilizumab were analyzed. Twenty-five bioactive metabolites discriminated between RA patients classified as anti-TNF responders (R, n = 74) and non-responders (NR, n = 28). Among these, the anti-inflammatory oxylipin maresin 2 was higher in R while the pro-inflammatory oxylipins 15d PGJ2 and 5,6-diHETE were higher in NR. Twenty different metabolites discriminated anti-IL6 R (n=73) and NR (n=41) as shown in Figure 1. The anti-inflammatory oxylipin 14-15EET was higher in R while the pro-inflammatory oxylipins 16-HETE and 5S-HpETE were higher in NR.
Conclusion: Circulating bioactive lipid analysis using LC/MS provided a rapid analysis of a wide range of metabolites and can be used to describe metabolic signatures that predict response to therapies. These results lay the groundwork for more deliberate investigations novel metabolic-based interventions to predict response to therapy and reduce arthritis morbidity.

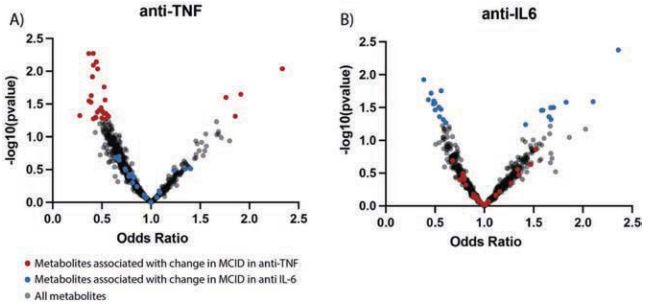

Figure 1. Volcano plots visualizing baseline metabolites associated with responders vs. non responders in a) anti-TNF and b) anti IL-6 therapy groups. Results are derived from multivariate logistic regression analysis of baseline metabolites and response to treatment categorized by MCID. Data plotted as the metabolite against its statistical significance, respectively reported as odds ratio (OR) and -log10(pvalue).

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Disclosure of Interests: Mona Alotaibi: None declared, Roxana Coras: None declared, Dimitrios A Pappas Speakers bureau: Sanofi, Novartis, Paid instructor for: Novartis, Consultant of: Roche, Sanofi, Joel M Kremer Speakers bureau: Pfizer, Consultant of: BMS, Geoffrey Thiele: None declared, Ted Mikuls Consultant of: Pfizer, Gilead, BMS, Sanofi, Mohit Jain Employee of: Sapient Bio, Monica Guma Grant/research support from: Pfizer, Novartis.
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POS0507 TAILORING ORAL THERAPY IN RHEUMATOID ARTHRITIS: THE TUTOR APP

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Background: Medication non-adherence has a significant impact on the health and well-being of individuals with chronic diseases. Indeed, with respect to important risk factors of Rheumatoid Arthritis (RA), such as cardiovascular risk factors, it is known that up to 50% of patients will stop taking medication for these conditions during the first year of prescription [1].
Objectives: To support the management of RA patients treated with Tofacitinib, we designed the TuTOR (Tailoring Tofacitinib Oral therapy in Rheumatoid arthritis) Mobile App.
Methods: A prospective-controlled study evaluated the impact of TuTOR App on medical adherence in 20 RA patients, that began treatment with Tofacitinib jointly with the App. We used a crossover design alternating Paper-Diary and TuTOR App, with monthly clinical assessments.
Results: Seventeen patients with RA (mean age at inclusion 59±13yrs; 88% females) the study. A statistically significant decrease of DAS28 was observed since the first month of therapy with Tofacitinib (mean DAS28 at baseline 3.9±1 vs. 1° month 3.1±1, p=0.0016). Similarly, Numerical Rating Scale(NRS) of perceived activity of disease (5.8±2.1 vs.3.7±2.5, p=0.02), and subjective fatigue (6.1±2.3 vs 4.3±2.6; p=0.01) progressively decreased. No differences were reported in DAS28 and in all the NRS between the use of the TuTOR App and the Paper-Diary. A significant decrease was observed also in HAQ during the follow-up (baseline 1.38±1.11 vs.six months 0.83±0.9; p=0.01). Most of the patients (82%) when filling out the self-reporting questionnaires preferred the TuTOR App in helping them to remember to take the pills. Further 82% of patients used the TuTOR App regularly (vs.53% Paper-Diary) and 76% of patients would use it in the future (vs.53% Paper-Diary). Three patients suspended the therapy with Tofacitinib due to gastrointestinal intolerance.
Conclusion: Both digital- and paper-devices can help maximize the adherence to therapy, leading to an improvement in disease's activity, highlighting the need of supports for medication adherence.

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Table 1. Baseline demographic and clinical characteristics of the patients enrolled in the study, who completed follow-up. *RA – Rheumatoid Arthritis*

	Patients with RA
	(N=17)
DEMOGRAPHICS	
Age (mean ± S.D.)	59,4 ± 13,5
Sex (n; %)	M (2; 11,8), F (15; 88,2)
Etnicity (caucasian; n; %)	16; 94
Etnicity (Hispanic; n; %)	1; 6
CLINICAL CHARACTERISTICS	
Age at diagnosis (mean ± S.D.)	44,7±14,47
Follow-up length (years; mean ± S.D.)	6,33± 5,17
Positive Rheumatoid Factor (n; %)	17; 100
Positive Anti-Cyclic citrullinated peptides (n;%)	15; 88.2
Structural articular damage at radiography (n; %)	11; 7

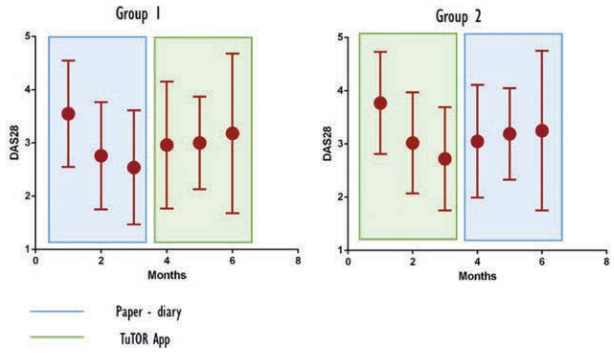

Figure 1. Decrease of disease activity assessed by DAS28 in the paper-diary and TuTOR App groups.

Disclosure of Interests: Massimo Radin Grant/research support from: The study is supported by the Investigator-Initiated Research Studies Grant—CREARE (Pfizer)., Marta Arbrile: None declared, Irene Cecchi Grant/research support from: The study is supported by the Investigator-Initiated Research Studies Grant—CREARE (Pfizer)., Alice Barinotti: None declared, Simone Baldovino: None declared, Elisa Menegatti: None declared, Daniela Rossi Grant/research support from: The study is supported by the Investigator-Initiated Research Studies Grant—CREARE (Pfizer)., Savino Sciascia Grant/research support from: The study is supported by the Investigator-Initiated Research Studies Grant—CREARE (Pfizer)., Dario Roccatello Grant/research support from: The study is supported by the Investigator-Initiated Research Studies Grant—CREARE (Pfizer).
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POS0508

PREDICTORS OF PERSISTENT DISEASE IN EARLY ARTHRITIS: 12 MONTHS RESULTS

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Background: Early arthritis is an inflammatory disease with the potential to progress to persistent arthritis, such as established Rheumatoid Arthritis (RA) or other articular disease, to resolve spontaneously or remain undifferentiated for indefinite periods of time.
Objectives: To identify predictors of persistent RA after 12 months follow up in the Argentinean early arthritis clinic (CONAART).
Methods: We conducted an observational, prospective longitudinal study, including patients with early arthritis (at least 1 swollen joint with <2 years of evolution) who had at least one year of follow-up. Sociodemographic and clinical data and characteristics of the disease were recorded at baseline, at 3, 6 and 12 months. After 1 year of follow-up, each patient was classified according to diagnosis: self-limited arthritis, persistent non-erosive arthritis, or persistent erosive arthritis. The association between the different predictors of diagnosis at 12 months was evaluated using multiple logistic regression, adjusted by potential confounders. Rheumatoid Factor (RF) and Anti Citrullinated Peptide Antibodies (ACPA) were included in separate models in order to avoid multicollinearity. A value of $p<0.05$ was considered significant.
Results: We included 839 patients, 83% females, mean age of 57±14 years and mean disease duration of 8.2±6.2 months; 67.5% were rheumatoid factor positive and 59% ACPA positive. Disease characteristics at baseline were DAS28 5.1±1.4, swollen joints 6±5, erythrocyte sedimentation rate (ESR) 34±25 mm/h, C Reactive Protein (CRP) 4±6 and Health Assessment Questionnaire-Argentinean (HAQ-A) 1.2±0.8. After 12 months follow up, 11% of the patients were diagnosed as self-limited disease, whereas 89% were diagnosed as persistent disease. For the persistent disease, 34% presented radiograph erosions and therefore were catalogued as persistent erosive disease. The seropositivity for both, RF and ACPA, together with baseline DAS28, were the variables independently associated with the development of persistent disease at 12 months. [Model 1a: RF OR 2.33 (95% CI 1.44, 3.78) and DAS28 1.27 (1.06, 1.52); Model 2a: ACPA 2.61 (1.38, 4.93) and DAS28 1.59 (1.24, 2.04)]. (Table 1). In the patient prediction model, it can be observed that a patient with female gender, ACPA negative, and a low activity at baseline (DAS28 <3.1) presents a 62.3% of likelihood of developing persistent arthritis after 12 months, while a male patient, ACPA positive, with a high baseline activity level, the probability of having persistent disease rises to 97.5%. (Figure 1)

Gender	Female	62.3 (42.4, 82.1)	81.3 (67.7, 94.8)	<3.2	**Baseline DAS28**
	Male	69.7 (47.4, 92.1)	85.8 (72.6, 99.0)		
	Female	82.5 (75.1, 89.8)	92.5 (88.4, 96.7)	>3.2-5.1	
	Male	86.8 (76.6, 97.0)	94.5 (89.7, 99.3)		
	Female	91.3 (86.5, 96.1)	96.5 (94.2, 98.8)	>5.1	
	Male	93.6 (87.8, 99.4)	97.5 (95.0, 100)		
		ACPA negative	**ACPA positive**		

Figure 1. Matrix prediction model. Probability of diagnosis of Persistent Rheumatoid Arthritis after 12 months of follow-up. Colors represents predictive probability of achieving the outcome as follow: grey: 0-69.9%; blue: 70.0-89.9%; purple: 90.0-100%.DAS28, Disease Activity Score 28; LDA, low disease activity; MDA, Moderate Disease Activity; HDA, High Disease Activity.

Table 1. Predictors of Persistent Rheumatoid Arthritis at 12 months

Outcomes	Persistent RA	Persistent RA	Persistent RA	Persistent RA
	OR (95 IC)	OR (95 IC)	OR (95 IC)	OR (95 IC)
	Model 1a	Model 1b	Model 2a	Model 2b
n	**708**	**708**	**507**	**507**
Age (years)	**0.99 (0.98, 1.01)**	**0.99 (0.98, 1.01)**	**0.99 (0.97, 1.01)**	**0.99 (0.97, 1.01)**
Female gender	**1.06 (0.57, 2.00)**	**1.06 (0.56, 1.99)**	**0.72 (0.30, 1.71)**	**0.72 (0.30, 1.70)**
RF positive	**2.33 (1.44, 3.78)*****	**2.45 (1.52, 3.98)*****	**-**	**-**
ACPA positive	**-**	**-**	**2.61 (1.38, 4.93)****	**2.63 (1.39, 4.98)****
DAS28 at baseline	**1.27 (1.06, 1.52)****		**1.59 (1.24, 2.04)*****	
Categorical DAS28				
MDA (vs LDA)	**-**	**1.81 (0.85, 3.86)^**	**-**	**2.86 (1.68, 6.99)***
HDA (vs LDA)	**-**	**2.83 (1.30, 6.15)^**	**-**	**6.39 (2.42, 16.82)*****

^ $p<0.1$, * $p<0.05$, ** $p<0.01$, *** $p<0.001$RF, Rheumatoid Factor; ACPA, Anti Citrullinates Protein Antigen; DAS28, Disease activity Score-28; LDA, low disease activity; MDA, moderate disease activity; HDA, high disease activity.

Conclusion: Predictors of persistent arthritis after 12 months of follow up since AT diagnosis were RF and ACPA seropositivity and higher baseline disease activity level.
Disclosure of Interests: None declared.
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POS0509 DEVELOPMENT OF A MULITNOMIAL PREDICTION MODEL OF TREATMENT RESPONSE TO ETANERCEPT IN A MULTI-CENTRE COHORT OF PATIENTS WITH ESTABLISHED RA

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Background: Treatment response in rheumatoid arthritis (RA) is assessed through EULAR response groups of good, moderate, and poor response. Clinical prediction models from the literature typically frame this as a binary model, to differentiate poor from good and moderate responders. Here, we develop a multinomial model, to predict each group separately, after 3 months on the anti-TNF drug Etanercept (ETN).
Objectives: Develop and validate a multinomial prediction model of treatment response to ETN in RA, based on baseline clinical covariates.
Methods: We identified patients treated with ETN or biosimilars (N = 778) from the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS). Response groups were derived from the CRP based 4C-DAS28 at baseline and 3 month follow up, yielding 310 good, 320 moderate, and 148 poor responders. A multinomial logistic regression model was fitted, using good responders as reference category. Multiple imputation by chained equations was used to impute missing data, and models were internally validated via bootstrapping. We report model accuracy, as well as calibration, and compare effect sizes across response groups. Table 1shows the baseline statistics, and odds ratios for the included covariates.

Table 1. Baseline covariate statistics and odds ratios (in bold: significant at p < 0.05); HADS: Hospital Anxiety and Depression Scale

Variable	Mean (± SD) or % Yes	$OR_{Moderate}$ [95% CI]	p	OR_{Poor} [95% CI]	p
Swollen Joint Count (SJC)	8.8445 (± 5.20)	0.98 [0.95 1.02]	0.35	**0.94 [0.89 0.98]**	**8e-3**
Tender Joint Count (TJC)	14.6877 (± 6.74)	**1.07 [1.04 1.10]**	**6e-6**	**1.05 [1.01 1.08]**	**0.01**
General Health Visual Analog Scale (GHVAS)	74.7429 (±17.79)	1.00 [0.99 1.01]	0.6	**0.98 [0.97 0.99]**	**1e-3**
CRP	19.0739 (±25.07)	1.00 [1.00 1.01]	0.22	0.99 [0.98 1.00]	0.26
BMI	30.3035 (±23.28)	1.00 [0.99 1.01]	0.48	1.00 [0.99 1.01]	0.41
Age of onset	47.3330 (±13.86)	1.01 [1.00 1.03]	0.12	1.02 [1.00 1.04]	0.06
Disease duration	9.9401 (±10.35)	1.00 [0.98 1.02]	0.84	0.99 [0.96 1.02]	0.45
HAQ	1.6085 (± 0.65)	**1.48 [1.06 2.08]**	**0.02**	**2.95 [1.91 4.54]**	**1e-6**
HADS-Anxiety	8.0868 (± 4.54)	1.04 [0.98 1.10]	0.19	1.06 [0.99 1.13]	0.12
HADS-Depression	7.3841 (± 4.02)	1.06 [0.99 1.13]	0.12	0.97 [0.89 1.06]	0.55
Concurrent DMARD	81.49%	**0.41 [0.26 0.66]**	**2e-4**	**0.52 [0.28 0.94]**	**0.03**
Female	78.66%	1.39 [0.92 2.10]	0.12	1.11 [0.65 1.87]	0.71
Seropositive	77.89%	**0.54 [0.33 0.89]**	**0.02**	**0.47 [0.26 0.86]**	**0.01**
1st Biologic	90.62%	1.06 [0.55 2.06]	0.86	**0.48 [0.24 0.94]**	**0.03**

Results: Adjusted for optimism, the multinomial model achieves an accuracy of 50.7% (IQR: 50 – 51.3%), with calibration slopes of 0.574 (IQR: 0.569 - 0.579) and 0.534 (IQR: 0.525 - 0.544) for moderate and poor response, respectively. Figure 1 shows a comparison of odds ratios (OR) for the different outcome groups. The Health Assessment Questionnaire (HAQ) score is the biggest driver of both moderate and poor response. Previous biologic treatment also predicts poor but not moderate response. Compared to the multinomial model, a binary model, that discriminates poor from moderate and good responders, underestimates the effect size of HAQ.

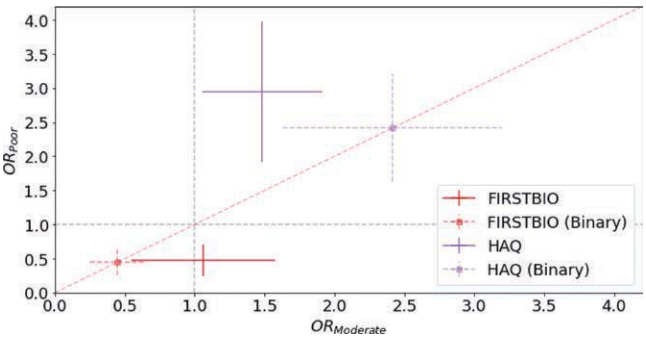

Figure 1. Odds ratios of FIRSTBIO and HAQ for moderate and poor response. Size of crosses indicate 95% confidence intervals.

Conclusion: The model predicts EULAR response groups moderately well but is poorly calibrated, which can partly be explained by the generally higher sample size requirement of multinomial modelling. In the multinomial model, moderate and poor response is largely driven by the same covariates, which leads to blurred boundaries between good and poor responders, when response groups are merged to create a binary problem. Future research should consider the most appropriate model choice to describe data, including the use of multinomial instead of binomial models. More research and bigger sample sizes are required to improve on this multinomial model.
Disclosure of Interests: Michael Stadler: None declared, Stephanie Ling: None declared, Nisha Nair: None declared, John Isaacs Speakers bureau: Abbvie, Gilead, Roche, UCB, Grant/research support from: GSK, Janssen, Pfizer, Kimme Hyrich Speakers bureau: Abbvie, Grant/research support from: Pfizer and BMS, Ann Morgan Speakers bureau: Roche/ Chuga, Consultant of: GSK, Roche, Chugai, AstraZeneka, Regeneron, Sanofi, Vifor, Grant/research support from: Roche, Kiniksa Pharmaceuticals, Anthony G Wilson: None declared, Darren Plant: None declared, John Bowes: None declared, Anne Barton Grant/ research support from: Pfizer, Galapagos, Scipher Medicine, and Bristol Myers Squibb.
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POS0510 INFLUENCE OF CMV INFECTION ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The causes of the onset and progression of rheumatoid arthritis (RA) are complex and not yet understood. Some studies suspect viruses as triggers of inflammatory processes (1). Increased numbers of immunomodulatory cells have already been detected in patients with RA infected with the cytomegalovirus (CMV) (2) (3). Understanding the role this infection has on RA-specific disease parameters could help clarify predisposing and prognostic factors.
Objectives: The aim of this study was to determine the relationship between CMV serostatus and disease activity in patients with rheumatoid arthritis.
Methods: We performed a retrospective study in adult patients diagnosed with RA. The data was collected between 2008 and 2021 in the rheumatological outpatient department of the University Hospital in Leipzig, Germany. The parameters examined included age, gender, CMV-IgG and CMV-IgM, and the following parameters to record the disease activity of RA: disease duration, joint erosions, rheumatoid factor, anti-CCP antibodies, CRP, disease activity score (DAS28), visual analog scale (VAS) for pain detection, Health Assessment Questionnaire (HAQ), medication with DMARDs and prednisolone.
Results: A total of 89 RA patients were included, 78.7% of them were female. The mean age was 61.44 ± 10.89 years and the mean duration of illness was 9.48 ± 9.13 years. 56.2% of the patients were CMV-IgG positive, 2.2% CMV-IgM positive. With an OR of 5.04 (95% CI 1.63-15.64), the CMV-IgG titer in women was significantly higher than in men (115.16 vs. 50.75

p = 0.007). This has already been shown in other studies (4). One of the reasons discussed is the women's closer relationship with children at work. It has also been shown that among women those medicated with DMARDs had significantly higher CMV-IgG titers (126.82 vs. 58.84 p = 0.036). This could be explained by an increased predisposition for CMV reactivation due to the intake of medication. Women with joint erosions were also more likely to be CMV-IgG positive (OR = 3.2; 95% CI 1.02-10.03) and had higher CMV-IgG titers (147.44 vs. 97.23 p = 0.024). Furthermore, seropositive RA women were significantly more likely to be CMV-IgG positive (p = 0.05). This association supports the assumption that CMV may play a role in the pathogenesis of RA.

Conclusion: The data presented shows that there is indeed a relationship between infection with CMV and parameters for disease activity in patients with RA. In summary, the integration of a CMV status determination into everyday clinical practice in patients with high disease activity could be quite useful and should be discussed.

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POS0511

PERIODONTAL STATUS BEFORE DIAGNOSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS PREDICTS CUMULATIVE DISEASE ACTIVITY IN YEARS AFTER TREATMENT INITIATION

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Background: Transversal cohort studies demonstrated an association between periodontal disease (PD) and rheumatoid arthritis (RA), but it is unknown how this association evolves during the course and treatment of both conditions[1].

Objectives: In this study we compared RA and PD before and after RA diagnosis in patients versus controls and analyzed the relationships between disease course and treatment of both conditions.

Methods: Retrospective dental and RA data were analyzed of 95 RA patients from 10 years before up to 10 years after RA diagnosis. Dental data were acquired from general practices and matched healthy control patient data from the university dental college. PD was analyzed via radiographic assessment using the new periodontal classification system from 2017. The relationship was analyzed between PD and RA parameters and treatment.

Results: More RA patients had severe or very severe PD compared to matched healthy controls, already before RA diagnosis. The fraction of RA patients with severe/very severe PD increased from 23% before diagnosis to 43% 5-10 years after diagnosis. Patients with a more severe PD before RA diagnosis had more tooth loss at last dental follow-up and a higher cumulative DAS28 in the years after diagnosis. Two-thirds of patients with severe/very severe PD received appropriate dental care less frequently than advised by guidelines. Suboptimal dental care was associated with a higher cumulative DAS28.

Conclusion: PD occurs before RA diagnosis in a proportion of patients. This proportion increases in the years after diagnosis. PD is associated with a decreased response to treatment of RA. A significant number of RA patients with PD receives suboptimal dental care, which is associated with diminished response to RA treatment.

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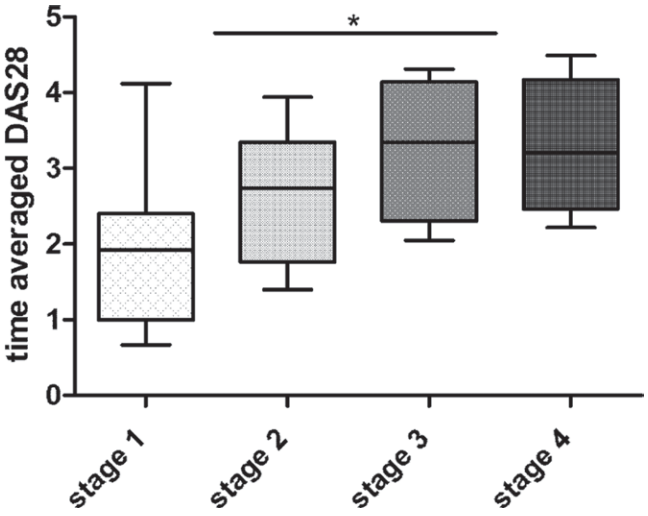

Figure 1. periodontitis severity in the years before RA diagnosis was scored from stage 1 to 4 (mild, moderate, severe, very severe) according the periodontal classification system from 2017. The time averaged DAS28 was calculated by taking the mean of the available DAS28 scores in the first 10 years after diagnosis and correcting this for the time intervals during which these were acquired. Linear regression analysis was performed. * = P < 0.05.

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POS0512

ANTI-CITRULLINATED PROTEIN ANTIBODY SEROSTATUS DETERMINES 2-YEAR RETENTION OF IV AND SC ABATACEPT IN PATIENTS WITH RA IN A REAL-WORLD SETTING

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Background: A treat-to-target approach for RA management is recommended.[1,2] However, up to half of patients discontinue DMARD treatment within 18 months.[2] Predictive biomarkers, such as anti-citrullinated protein antibodies (ACPAs) and RF, may be useful to stratify patients to the most appropriate treatment. ACTION (AbataCepT In rOutiNe clinical practice; NCT02109666) and ASCORE (Abatacept SubCutaneOus in Routine Clinical PracticE; NCT02090556) were 2-year, international, observational, prospective, multicenter studies of IV and SC abatacept, respectively, for the treatment of RA in routine clinical practice.[3,4] Higher

retention has been previously reported in patients with double ACPA/RF seropositive RA compared with double ACPA/RF seronegative RA.[3,4]

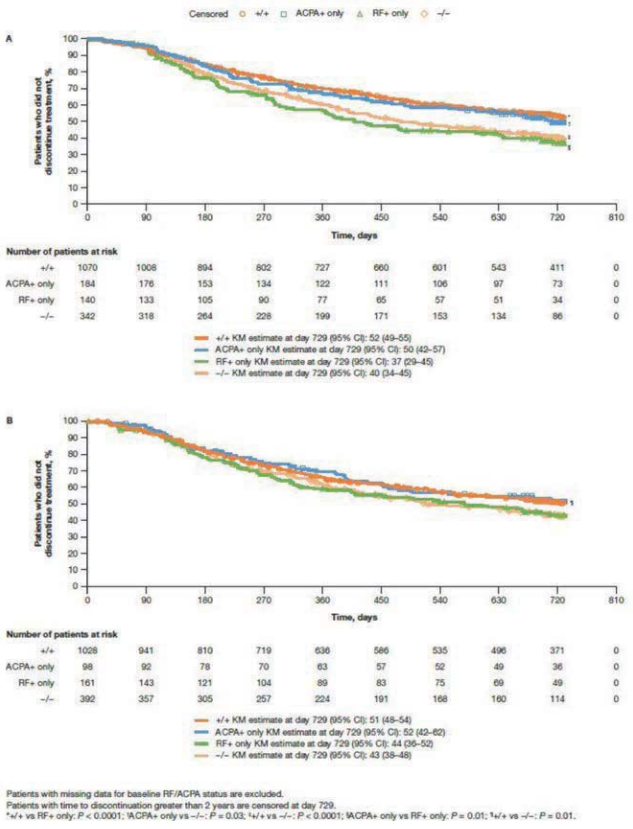
Objectives: To assess the independent effect of ACPA or RF single seropositivity on abatacept retention in patients with RA receiving abatacept in a post hoc analysis of ACTION and ASCORE.

Methods: This post hoc analysis included patients aged ≥ 18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria) who initiated IV (body weight–adjusted dosing) or SC (125 mg once weekly) abatacept.[3,4] Patients were stratified by baseline ACPA/RF status: ACPA+/RF– (ACPA+ only), ACPA/RF double positive (+/+), ACPA–/RF+ (RF+ only), and ACPA/RF double negative (–/–). Abatacept retention rate at 2 years was estimated by Kaplan–Meier (KM) analysis.

Results: Patients with ACPA/RF serostatus data from the ACTION and ASCORE studies (N = 1679 and N = 1748, respectively) were evaluated. Baseline demographic and disease characteristics were similar across studies and serostatus groups (Table 1). In patients with ACPA+ only RA, abatacept retention rates were similar to the +/+ group and greater than the RF+ only and –/– groups (Figure 1). In ASCORE (Figure 1A), retention rates were significantly higher in ACPA+ only and +/+ groups when compared with the –/– group. In contrast, retention rates for patients with RF+ only RA were not significantly different vs –/– patients. Results were similar in ACTION, although the higher retention in the ACPA+ group did not reach statistical significance (Figure 1B).

Conclusion: In this post hoc analysis of the real-world ACTION and ASCORE studies, ACPA positivity was associated with an increased likelihood of retention over 2 years. Patients with ACPA+ only RA were equally as likely to be retained on abatacept as patients with ACPA/RF double positivity. In contrast, patients with RF+ only RA were less likely to be retained on abatacept over 2 years. These findings suggest that ACPA positivity played a more important role than RF positivity in abatacept retention. The higher retention seen in patients with ACPA+ only vs RF+ only disease demonstrates the key role of ACPA in RA and supports the importance of precision medicine in treating patients.

Figure 1. Retention rates for patients with ACPA+ only, RF+ only, +/+, and –/– RA treated with abatacept in the (A) ASCORE and (B) ACTION studies



Patients with missing data for baseline RF/ACPA status are excluded.
Patients with time to discontinuation greater than 2 years are censored at day 729.
*+/+ vs RF+ only: $P < 0.0001$; †ACPA+ only vs –/–: $P = 0.03$; ‡+/+ vs –/–: $P < 0.0001$; §ACPA+ only vs RF+ only: $P = 0.01$; ¶+/+ vs –/–: $P = 0.01$.

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POS0513

SAFETY OF FILGOTINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: ANALYSIS OF LYMPHOCYTES IN THE LONG-TERM EXTENSION FINCH 4 STUDY

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Table 1. Baseline demographics and disease characteristics by ACPA/RF status for the ASCORE and ACTION studies

ASCORE	+/+ (n = 1079)	RF+ only (n = 142)	ACPA+ only (n = 184)	–/– (n = 343)
Age, years	57.1 (12.8)	58.2 (11.8)	57.4 (13.5)	57.8 (13.9)
DAS28 (CRP)	4.7 (1.2)	4.6 (1.1)	4.4 (1.0)	4.8 (1.2)
CDAI	26.6 (12.5)	25.8 (12.0)	23.6 (10.9)	28.2 (13.2)
SDAI	28.1 (13.0)	27.2 (12.4)	24.4 (10.8)	29.7 (13.9)
ACTION	**+/+ (n = 1028)**	**RF+ only (n = 161)**	**ACPA+ only (n = 98)**	**–/– (n = 392)**
Age, years	58.2 (12.0)	58.4 (13.4)	58.5 (14.0)	57.0 (13.3)
DAS28 (CRP)	4.9 (1.1)	5.0 (1.1)	4.9 (1.0)	5.0 (1.1)
CDAI	28.7 (12.2)	29.2 (12.4)	28.7 (11.5)	30.1 (12.9)
SDAI	30.4 (13.1)	31.2 (13.4)	29.8 (11.5)	31.7 (13.4)

Data are mean (SD). Patients with missing data for baseline ACPA/RF status are excluded.

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Background: Filgotinib (FIL) is a Janus kinase 1 preferential inhibitor approved for the treatment of moderate to severe rheumatoid arthritis (RA) in patients (pts) with an inadequate response to disease-modifying antirheumatic drugs.[1] In a pooled analysis of Phase 3 FINCH 1–3 studies of FIL in RA, median lymphocyte levels were relatively stable over 1 year with lymphocyte decreases observed in individual FIL-treated pts. Lymphocyte levels should be monitored.[1]
Objectives: To assess the effect of FIL on lymphocyte levels and lymphopenia in the FINCH 4 long-term extension (LTE) study in RA.
Methods: Safety data of FIL 100 mg (FIL100) and 200 mg (FIL200) from LTE baseline to data cut off (01 June 2020) are reported overall and by prior FIL exposure for pts who received ≥1 FIL dose in FINCH 4 (NCT03025308; adults with RA who had completed FINCH 1/2/3). Adverse events (AEs) of lymphopenia were graded based on clinical severity; laboratory abnormalities (decreased lymphocytes) were graded per Common Terminology Criteria for Adverse Events v4.03 (CTCAE). Frequencies of both measures and exposure-adjusted incidence rates (EAIRs) of AEs are reported. Median lymphocyte levels are reported to LTE Week 48.
Results: The safety analysis set included 2729 pts (FIL200: n=1530; FIL100: n=1199). Of these, 75.4% (n=2058) had prior FIL exposure in FINCH 1/2/3. Median FIL exposure to LTE Week 48 was 600 (FIL200: 696; FIL100: 533) days. In both treatment groups, median laboratory lymphocyte levels remained relatively stable to LTE Week 48 for pts with prior FIL exposure. Pts without prior exposure had numerically higher median lymphocyte levels at LTE baseline vs pts with prior exposure (Figure 1). These decreased over time, but medians remained within normal range. The frequency and EAIR of graded decreases in laboratory lymphocyte levels were higher with FIL200 vs FIL100 (Table 1); incidence was slightly higher in pts with vs without prior FIL exposure, with the difference most apparent for Grade 2 decreases.

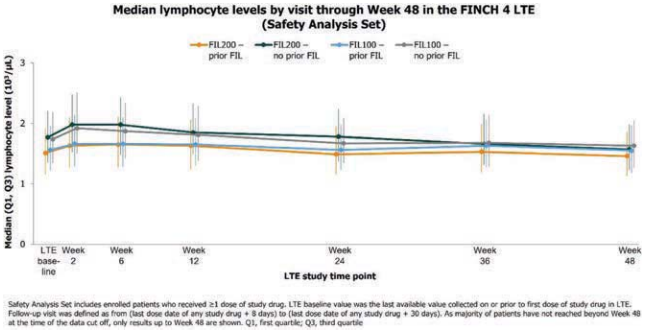

Figure 1.

Of all pts receiving FIL, 43 (1.6%) reported a lymphopenia AE; frequencies and EAIRs of lymphopenia AEs were slightly higher with FIL200 (1.9%; EAIR [95% CI]: 1.2 [0.9–1.8]) vs FIL100 (1.2%; 0.8 [0.4–1.3]). Most were Grade 1 or 2 in severity. Grade 3 lymphopenia AEs occurred in 4 (0.3%) vs 1 (<0.1%) pts receiving FIL200 vs FIL100. There were no Grade 4 AEs in either group. No serious AEs of lymphopenia or treatment discontinuations due to lymphopenia were reported. In total, 8 (0.3%) pts interrupted study treatment due to lymphopenia. Infection rates, but not serious infections, were slightly higher for pts with lymphopenia, however no relationship between lymphopenia severity and infection AE grade was seen.
Conclusion: In FINCH 4, lymphopenia AEs were infrequent but numerically greater with FIL200 vs FIL100, suggesting a dose–response relationship. While exposure at either dose may be associated with decreased lymphocytes, median lymphocyte levels were comparable in both groups and all remained within normal range at LTE Week 48, similar to observations in FINCH 1–3.

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POS0514 PREDICTION OF RESPONSE TO METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A MACHINE LEARNING APPROACH USING CLINICAL TRIAL DATA

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Background: Methotrexate (MTX) is the preferred initial disease-modifying drug (DMARD) for rheumatoid arthritis (RA). However, up to 50% of patients respond inadequately to MTX (1). Clinically useful predictors that effectively identify patients with RA who are likely to respond to MTX are lacking. Whether machine learning (ML) can provide robust and clinically useful prediction of response to MTX monotherapy in the first months of treatment in patients with early RA using uniformly collected baseline demographics and clinical data has not been investigated in large patient populations.
Objectives: We aimed to identify clinical predictors of response to MTX as the first DMARD among patients with RA using ML methods.
Methods: Randomized clinical trials (RCT) of patients with RA who were DMARD-naïve and randomized to placebo plus MTX were identified and accessed through the Clinical Study Data Request Consortium and Vivli Center for Global Clinical Research Data. Studies with available Disease Activity Score with 28-joint count and erythrocyte sedimentation rate (DAS28-ESR) at baseline, 12 and 24 weeks were included. Latent class modeling of MTX response was performed. Least absolute shrinkage and selection operator (LASSO) and random forest were used to identify predictors of response.
Results: A total of 775 patients from 4 RCTs were included (mean age 50 years, 80% female). Two distinct classes of patients were identified based on DAS28-ESR change over 24 weeks: "good responders" and "poor responders" to MTX

Table 1. Frequencies of treatment-emergent laboratory decreases in lymphocytes

	Prior FIL exposure		No prior FIL exposure		Overall		Total
	FIL200	FIL100	FIL200	FIL100	FIL200	FIL100	(N=2729)
	(n=1195)	(n=863)	(n=335)	(n=336)	(n=1530)	(n=1199)	
Decreased lymphocytes (any grade), n (%)	228 (19.1)	125 (14.5)	41 (12.3)	40 (12.0)	269 (17.6)	165 (13.8)	434 (16.0)
Grade 1	48 (4.0)	35 (4.1)	14 (4.2)	7 (2.1)	62 (4.1)	42 (3.5)	104 (3.8)
Grade 2	159 (13.3)	82 (9.5)	21 (6.3)	26 (7.8)	180 (11.8)	108 (9.1)	288 (10.6)
Grade 3	21 (1.8)	8 (0.9)	6 (1.8)	7 (2.1)	27 (1.8)	15 (1.3)	42 (1.5)
Grade 4	0	0	0	0	0	0	0

A treatment-emergent laboratory decrease in lymphocytes was defined as an increase of ≥1 toxicity grade from baseline at any time post-baseline up to and including the date of last study drug dose + 30 days. Severity grades were defined per CTCAE (lower limit of normal: <0.8 × 10^9/L [Grade 1]; <0.8–0.5 × 10^9/L [2]; <0.5–0.2 × 10^9/L [3]; <0.2 × 10^9/L [4]).

treatment (Figure 1). Baseline DAS28-ESR, anti-citrullinated protein antibody (ACPA) and health assessment questionnaire (HAQ) score were the top predictors of good response to MTX using LASSO (Area Under the Curve [AUC] 0.79) and Random Forest models (AUC 0.68) in the external validation set. DAS28-ESR≤7.4, ACPA positive and HAQ≤2 provided the highest likelihood of response (Table 1). Among patients with 12-week DAS28-ESR>3.2, at least 1 point improvement in DAS28-ESR baseline-to-12-week was predictive of achieving DAS28-ESR≤3.2 at 24 weeks.

Table 1. Matrix prediction model: Probability of achieving a good response to methotrexate at 24 weeks

DAS28ESR		HAQ ≤2	HAQ >2	ACPA Status
	≤7.4	80.1 (76.4, 83.8)	77.3 (70.6, 84)	Positive
		77.1 (68.6, 85.6)	74.1 (63.3, 84.9)	Negative
	>7.4	40.3 (32.1, 48.5)	36.5 (29.3, 43.6)	Positive
		36.2 (23.3, 49.1)	32.5 (20.9, 44.1)	Negative

Footnote: The number in each cell represents the percentage and 95% CI of achieving the outcome, based on the combination of predictors at baseline. DAS28-ESR: Disease Activity Score with 28-joint count with erythrocyte sedimentation rate; HAQ: Health assessment questionnaire score; ACPA: Anti-citrullinated protein antibody.

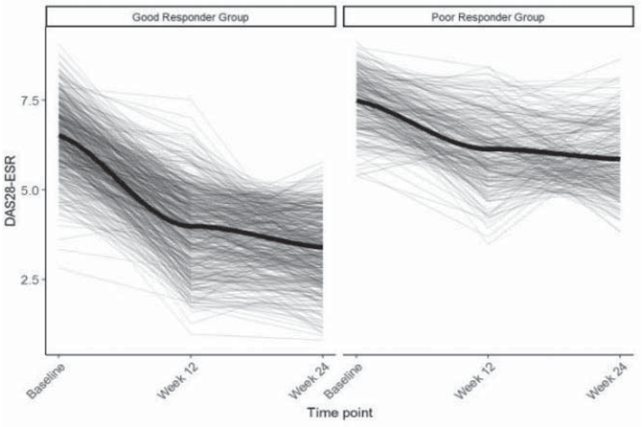

Figure 1. Two patient class trajectories identified with latent class modeling of DAS28-ESR (N=775)

Conclusion: We have developed and externally validated a prediction model for response to MTX within 24 weeks in DMARD-naïve patients with RA, providing variably weighted clinical features and defined cut-offs for clinical decision-making. Trajectory of DAS28-ESR change over 24 weeks in patients with moderate-to-high RA disease activity at baseline who are starting MTX can be predicted by baseline DAS28-ESR, ACPA status and HAQ-score. Patients with at least 1 unit decline in DAS28-ESR within the first 12 weeks of treatment who have not achieved low disease activity by week 12, may be more likely to achieve low disease activity at 24 weeks. These parameters should be considered as part of the clinical decision-making process when initiating MTX in DMARD-naïve patients with RA.

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POS0515 THE ASSOCIATION BETWEEN AUTOANTIBODIES AND RISK FOR VENOUS THROMBOEMBOLIC EVENTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) have an increased risk for cardiovascular disease, including venous thromboembolic events (VTE)[1]. The reason behind the increased VTE risk is incompletely understood, but inherent features of RA, such as RA specific autoantibodies, could potentially play a role. For example, studies have linked occurrence and levels of rheumatoid factor (RF) in the general population to increased VTE risk[2]. We and others have demonstrated an association between ACPA and risk of later ischemic cardiovascular events[3]. There are also potential mechanistic links; citrullinated fibrinogen (cFib) has been associated to clot stability[4].

Objectives: We aimed to examine the association between anti-modified protein antibodies (AMPAs) and risk of VTE in RA.

Methods: We included 2809 individuals newly diagnosed with RA and included in the Swedish EIRA study 1996-2009. Through linkage to nationwide health care registers we identified past and incident events of VTE based on validated ICD code algorithms. We centrally typed baseline sera for anti-CCP2, 20 different ACPA sub-specificities, RF isotypes, carbamylated antibodies and 10 additional post-translational modifications. We followed all individuals from RA diagnosis up until their first ever VTE event, migration, death or end of study (2020-12-31) whichever occurred first. We used a Cox regression to estimate hazard ratios (HR) with 95% confidence intervals (CI). Individuals with a history of a VTE event (n=27) at RA diagnosis were excluded.

Results: We included 2782 individuals; 72% were women, median age at RA diagnosis was 54 years (inter quartile range (IQR) 18 years) and median follow-up time was 15.5 (IQR 6.8) years. During follow-up 177 incident VTE events were observed corresponding to an incidence of 5.0 per 1,000 person years.

1797 (64.6%) patients were positive for IgG anti-CCP2 and the HR for VTE (vs. being negative for anti-CCP2) was 1.33 (95%CI 1.00-1.78). The risk of VTE increased with the level of anti-CCP2, with an HR of 1.49 (95%CI 0.99-2.22) for the group with extreme levels compared to those negative for anti-CCP2 (p-value for trend 0.048). For IgA anti-CCP2 the HR was 1.35 (95% CI 0.99-1.84) when comparing those expressing IgA anti-CCP2 against those who did not. Of 20 ACPA fine-specificities studied, 18 occurred with a frequency > 10% in our sample. The median number of fine-specificities expressed was 6 (IQR 11). The risk of VTE increased with the number of ACPA fine-specificities expressed (p-value for trend 0.033). At the 0.05 significance level, two fine-specificities were each associated with VTE; cPept Z1 [HR=1.40 (95%CI 1.06-84)] and cPept-1 [HR=1.47 (95%CI 1.12-1.93)]. None of the six antibodies against cFib assessed were statistically significantly associated with VTE risk. No associations were observed for other AMPAs. Among the three RF isotypes, only IgM RF was statistically associated with VTE [HR=1.38 (95%CI 1.04-1.83)].

Conclusion: RA-related antibodies analysed in clinical practice (anti-CCP2 IgG, RF) are associated not only with risk of myocardial infarction, stroke and cardiovascular death as previously demonstrated but also with VTE. There were no clear specific signals with ACPA fine-specificities, other AMPAs, or IgA RA autoantibodies.

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declared, Lars Alfredsson: None declared, Linda Mathsson-Alm Employee of: LMA an employee of Thermo Fisher Scientific producing the ACPA sub-specificity test, Guy Serre: None declared, Martin Cornillet: None declared, Rikard Holmdahl Consultant of: historically several. Currently paid advisor for Lipum AB and Cyxone AB, Per-Johan Jakobsson Consultant of: UCB – Nov 2021 to Feb 2022., Karl Skriner: None declared, Holger Bang Employee of: HB is an employee of Orgentec Diagnostica, an IVRc company, Lars Klareskog: None declared, Saedis Saevarsdottir Employee of: SS is a part-time employee of deCODE genetics Inc., Karin Lundberg: None declared, Caroline Grönwall: None declared, Johan Askling Grant/research support from: AbbVie, AstraZeneca, Bristol Myers Squibb, Eli Lilly, Janssen, Merck, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB.

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POS0516 PLASMA CALPROTECTIN WAS ASSESSED IN MULTIPLE BIOLOGICAL TREATMENT STRATEGIES FOR EARLY RHEUMATOID ARTHRITIS

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Background: Plasma calprotectin is a sensitive inflammatory marker in patients with rheumatoid arthritis (RA) and reflects activation of granulocytes and macrophages. Plasma calprotectin has not previously been studied in a head-to-head trial of multiple biological mechanisms of action versus active conventional therapy (ACT) with methotrexate and prednisolone.

Objectives: To assess the effect of treatment on plasma calprotectin levels in patients with early RA by determining the 24-week change in the four arms of the NORD-STAR Study, a large multicenter randomized head-to-head clinical trial of ACT versus tumor necrosis factor inhibition, T-cell co-stimulation inhibition, and interleukin-6 inhibition (1).

Methods: Calprotectin was analyzed in plasma samples at baseline, week 4 and week 24 from 400 treatment naïve patients with early RA in the NORD-STAR Study. Samples were analyzed using a calprotectin ELISA alkaline phosphatase (ALP) kit from CalproLab (Oslo, Norway) in a Dynex DS2 processing system (normal levels <910 µg/L). Patients were assessed by clinical (CRP, 28 SJC/TJC, physician global) and patients' reported assessments. Crude and adjusted linear regression analyses were performed in R 4.0.3 with calprotectin levels at week 24 as the outcome. The four arms were represented by three dummy variables. The adjustment variables were age, sex, anti-CCP status and country. Both analyses were adjusted for baseline calprotectin levels.

Results: At baseline, the mean time since diagnosis was 15.7 days (SD) (22.9), mean age 53.7 (15.0) years, ACPA positive 81%, and female 66%. Mean calprotectin levels were 1931 (1495) µg/L at baseline, 866 (951) µg/L at week 4, and 629 (661) µg/L at week 24. At baseline, normal calprotectin levels (<910 µg/L) were observed in 27% of all patients (ACT 22%, certolizumab-pegol and methotrexate 30%, abatacept and methotrexate 25%, tocilizumab and methotrexate 31%). At week 24, normal calprotectin levels were observed in 82% of all patients (ACT 68%, certolizumab-pegol and methotrexate 91%, abatacept and methotrexate 80%, tocilizumab and methotrexate 90%). Observed calprotectin levels at week 24 were significantly lower in patients treated with certolizumab-pegol and methotrexate -336µg/L (97) ($p < 0.006$) or tocilizumab and methotrexate -284 (99) ($p < 0.004$), versus ACT when adjusted for age, sex, anti-CCP status, baseline calprotectin level, and country; however, a significant difference was not observed in patients treated with abatacept and methotrexate -110 (96) ($p = 0.25$). The Figure 1 shows the average percentage change in calprotectin levels from baseline to week 24 for all treatment groups.

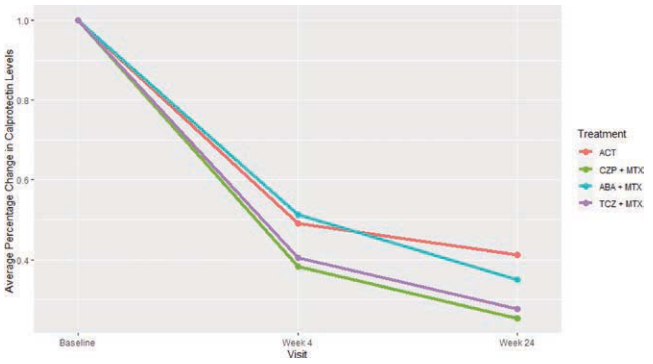

Figure 1. Average percentage change in calprotectin levels from baseline to week 24. ACT: active conventional therapy, CZP+MTX: certolizumab-pegol and methotrexate, ABA+MTX: abatacept and methotrexate, TCZ+MTX: tocilizumab and methotrexate.

Conclusion: Calprotectin, a sensitive biomarker of inflammation, normalized in the majority of patients. The decline differed between treatment groups and was largest in patients treated with a TNF inhibitor and methotrexate, suggesting that calprotectin reflects the activity of specific inflammatory pathways rather than overall inflammation. The findings of this study should be further explored.

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POS0517 IGA ACPA ARE ASSOCIATED WITH PROGRESSION TO RHEUMATOID ARTHRITIS IN INDIVIDUALS AT-RISK AND DECLINE IN LEVELS AROUND THE DISEASE ONSET

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Background: Anti-citrullinated protein antibodies (ACPA) can precede the diagnosis of rheumatoid arthritis (RA) up to a decade. However, while some ACPA-positive individuals rapidly develop the disease, a considerable proportion are not progressing to RA, and the events triggering the disease outbreak are still poorly understood. While a lot is known about ACPA of IgG class, the role of IgA ACPA is still not defined.

Objectives: We aimed to look into IgA ACPA isotypes in individuals at-risk for RA and their role in RA development.

Methods: IgA1 and IgA2 ACPA were measured cross-sectionally in 30 seropositive (IgG ACPA-positive) RA patients, 29 seronegative RA patients, 63 individuals at-risk for RA (positive for IgG ACPA and/or anti-modified citrullinated vimentin antibodies and with joint complaints) and 32 healthy controls. In addition, IgA ACPA levels were compared in 24 RA at-risk individuals who developed RA during a follow-up of 14 months and in 21 individuals who did not. Furthermore, longitudinal measurements of IgA1 and IgA2 ACPA levels 1-28 months prior to, at and 1-18 months after the onset of RA were performed in 14 at-risk individuals and in 9 individuals from a confirmation retrospective cohort of RA patients from the Medical University of Vienna. Cut-offs were set based on the comparison of

IgA ACPA levels in RA patients versus healthy controls. Rather than prioritizing specificity, as is done for diagnostic tests, we aimed to define reliably detectable amounts of IgA ACPA, with both sensitivity and specificity not under 70% – 3 µg/ml for total IgA ACPA; 2.46 µg/ml for IgA1 and 0.6 µg/ml for IgA2 ACPA.

Results: Serum levels of both IgA ACPA subclasses were elevated in individuals at-risk, with no significant difference to patients with established IgG ACPA-positive RA. Interestingly, 41.4% of IgG ACPA-negative patients had detectable amounts of IgA ACPA. IgA1 ACPA, but not IgA2 ACPA levels were higher in individuals at-risk who developed RA in the next 14 months than in those who did not (4.54 vs. 2.05 µg/mL, p=0.03); and the percentage of those developing RA was higher in IgA1 ACPA-positive at-risk individuals (64.3% versus 35.3%). Interestingly, during the transition to RA, in the majority of IgA ACPA-positive individuals a decline in IgA1 ACPA levels at the time of RA diagnosis (-26%; p=0.085), as well as in the first months after the RA diagnosis (-38%; p=0.0002) was observed. This observation was confirmed in an independent cohort. IgA2 ACPA declined only after the diagnosis (33%; 10-64%; p=0.0237), and no significant change was observed for IgG ACPA.

Conclusion: Both IgA ACPA subclasses were elevated in individuals at-risk for RA. Positivity for IgA1 ACPA was associated with the progression to RA in the next 14 months. IgA1 ACPA levels declined in the months preceding the diagnosis of RA and in the months after the diagnosis, which might reflect pathophysiological events happening at the time of the disease outbreak.

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POS0518 EFFECT OF FILGOTINIB (FIL) ON BODY WEIGHT (BW) AND BODY MASS INDEX (BMI) AND EFFECT OF BASELINE BMI ON THE EFFICACY AND SAFETY OF FIL IN RHEUMATOID ARTHRITIS (RA)

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Background: FIL is a Janus kinase (JAK) 1 preferential inhibitor approved for the treatment (tx) of moderate to severe RA. Weight gain has been reported with other JAK inhibitors[1–3]; it is important to describe the effect of FIL on BW/BMI for physicians to correctly inform and appropriately treat patients.

Objectives: Our primary aim was to assess the effect of FIL on BW/BMI using data from the FINCH 1–3 studies. Secondary aims were to assess the efficacy and safety of FIL according to baseline BMI.

Methods: FINCH 1–3 (NCT02889796, NCT02873936, NCT02886728) were phase 3, randomised, double-blind, active/placebo (PBO)-controlled studies of FIL 100/200 mg (FIL100/FIL200) ± methotrexate (MTX) in patients with active RA who had an inadequate response to MTX (FINCH 1) or biologic DMARD (FINCH 2), or were MTX naïve (FINCH 3). We assessed changes from baseline (CFB) in BW and BMI by tx group and baseline BMI, and the efficacy and safety of FIL by baseline BMI (<25, 25–<30 or ≥30 kg/m^2). Efficacy measures included American College of Rheumatology (ACR)20/50/70 response, Disease Activity Score 28 with C-reactive protein (DAS28-CRP) and health assessment questionnaire disability index (HAQ-DI). Safety data were from 7 RA clinical trials (FINCH 1–4, DARWIN 1–3)[4].

Results: In FINCH 1–3, baseline disease characteristics such as HAQ-DI, DAS28-CRP and clinical disease activity index were similar across BMI subgroups for each tx group. There were no clinically relevant CFB in median BW or BMI in any tx group or differences between tx groups. Mean CFB in BMI (kg/m^2) were 0.4 with FIL200 and FIL100 and 0.3 with adalimumab (ADA) at Week 52 in FINCH 1; 0.2, 0.6 and –0.1 with FIL200, FIL100 and PBO, respectively, at Week 24 in FINCH 2; and 0.5, 0.6, 1.1 and 0.3 with FIL200+MTX, FIL100+MTX, FIL200 and MTX, respectively, at Week 52 in FINCH 3. CFB in BMI did not appear dependent on baseline BMI. FIL200±MTX was efficacious vs controls regardless of baseline BMI for most measures at each timepoint. In FINCH 1, in the <25, 25–<30 and ≥30 kg/m^2 BMI subgroups, DAS28-CRP <2.6 was achieved by 38%, 29% and 33% of the FIL200 group, 29%, 19% and 21% of the ADA group, and 7%, 10% and 11% of the PBO group at Week 12, respectively. Figure 1 shows ACR20 responders by baseline BMI in FINCH 1–3. Integrated safety data across baseline BMI subgroups are summarised in Table 1. VTE rate was numerically higher with FIL200 in the ≥30 than 25–<30 or <25 kg/m^2 BMI subgroups; serious infection rate was numerically higher with FIL100 in the <25 mg/m^2 subgroup vs other BMI subgroups.

Table 1. Exposure-adjusted incidence rate (95% CI) of AEs per 100 PYE by baseline BMI

	FIL dose (mg)	BMI (kg/m^2)		
		<25	25–<30	≥30
		PYE 3062.8	PYE 2640.1	PYE 2382.2
TEAEs	200	34.5 (32.0, 37.1)	35.7 (33.0, 38.6)	36.6 (33.7, 39.8)
	100	44.3 (40.4, 48.6)	43.0 (38.9, 47.5)	45.3 (41.1, 50.0)
Serious TEAEs	200	5.3 (4.4, 6.4)	5.8 (4.8, 7.1)	7.1 (5.8, 8.5)
	100	7.6 (6.0, 9.4)	6.5 (5.0, 8.4)	8.1 (6.4, 10.2)
Deaths	200	0.3 (0.2, 0.7)	0.5 (0.3, 1.0)	0.5 (0.2, 1.0)
	100	0.4 (0.1, 1.0)	0.3 (0.1, 1.0)	0.2 (0.1, 0.9)
Venous thrombotic and embolic events	200	0.1 (0.0, 0.4)	0.1 (0.0, 0.5)	0.5 (0.2, 1.0)
	100	0.1 (0.0, 0.7)	0.1 (0.0, 0.8)	0.2 (0.1, 0.9)
Major adverse cardiovascular events	200	0.3 (0.2, 0.7)	0.3 (0.1, 0.7)	0.5 (0.2, 1.0)
	100	0.6 (0.3, 1.3)	0.3 (0.1, 1.0)	0.6 (0.2, 1.4)
Serious infections	200	1.1 (0.7, 1.7)	1.7 (1.2, 2.5)	1.8 (1.2, 2.6)
	100	2.6 (1.8, 3.9)	1.2 (0.7, 2.2)	2.2 (1.4, 3.4)
Herpes zoster	200	1.6 (1.1, 2.2)	1.4 (1.0, 2.1)	1.8 (1.2, 2.6)
	100	1.0 (0.5, 1.8)	1.2 (0.7, 2.2)	1.0 (0.5, 2.0)
Malignancy excluding non-melanoma skin cancer	200	0.5 (0.3, 1.0)	0.7 (0.4, 1.3)	0.5 (0.3, 1.1)
	100	0.6 (0.3, 1.3)	0.4 (0.2, 1.2)	0.8 (0.4, 1.7)

BMI, body mass index; FIL, filgotinib; PYE, patient years of exposure; (TE)AE, (treatment-emergent) adverse event

Conclusion: FIL did not substantially affect CFB in BW or BMI. FIL200±MTX was generally more efficacious vs controls regardless of baseline BMI, and the rate of TEAEs was similar across baseline BMI subgroups.

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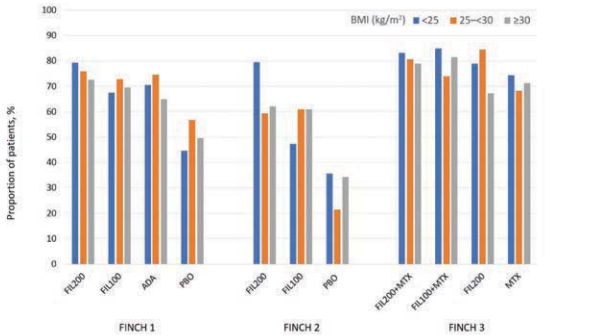
Figure 1. Proportion of patients to achieve ACR20 response at Week 12 (FINCH 1 and 2) or Week 24 (FINCH 3)



ACR, American College of Rheumatology; ADA, adalimumab; BMI, body mass index; FIL, filgotinib; MTX, methotrexate; PBO, placebo

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POS0519

RELATIONSHIP BETWEEN DISEASE ACTIVITY AND MAJOR ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS ON TOFACITINIB OR TNF INHIBITORS: A POST HOC ANALYSIS OF ORAL SURVEILLANCE

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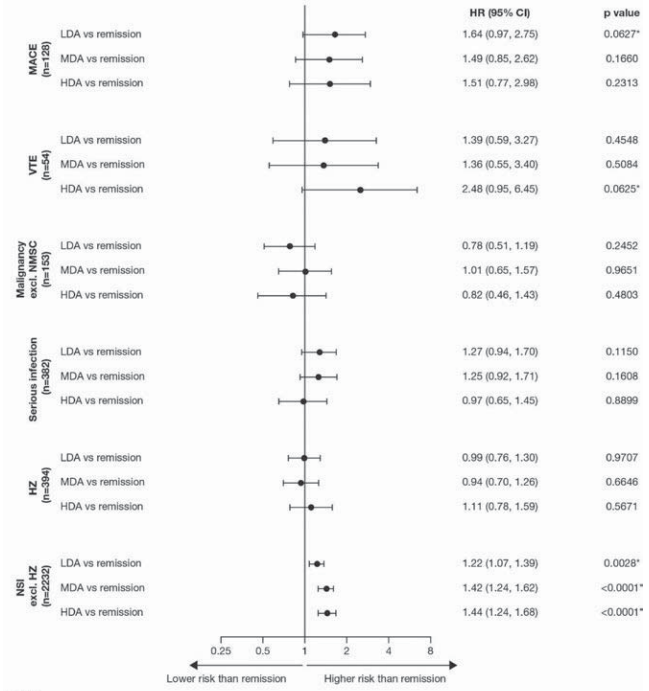
Background: Uncontrolled rheumatoid arthritis (RA) activity and acute disease flares are associated with higher risk of adverse outcomes such as cardiovascular (CV) disease, venous thromboembolism (VTE), malignancy and infection.[1-4]

Objectives: To evaluate associations of acute and cumulative Clinical Disease Activity Index (CDAI) measurements with major CV, malignancy, or infectious adverse events (AEs) of special interest in ORAL Surveillance.

Methods: ORAL Surveillance (NCT02092467) was a post-authorisation safety study of tofacitinib vs TNF inhibitors (TNFi) in patients (pts) aged ≥50 yrs with active RA despite methotrexate (MTX), and ≥1 additional CV risk factor. Pts were randomised 1:1:1 to tofacitinib 5 or 10 mg twice daily (BID) or subcutaneous TNFi. Two post hoc analyses were performed: (1) a time-varying multivariate Cox model examined risks of major AEs when pts were in CDAI-defined low (>2.8–≤10; LDA), moderate (>10–≤22; MDA) or high (>22; HDA) disease activity vs remission (≤2.8). The Cox model also included pt demographics, medical history, RA characteristics, prior treatments, baseline (BL) medications and treatment arm, pre-selected using backward selection; (2) area under the curve (AUC) per yr for CDAI prior to event or to study end (pts without event) was calculated and compared using an analysis of variance model with treatment arm, event status and interaction (supportive). Nominal p values <0.10 were considered evidence of associations.

Results: 4362 pts were included. Mean RA duration at BL was approximately 10 yrs. All pts were on MTX at BL, and 28% had previously been on one other synthetic disease-modifying antirheumatic drug (DMARD). Overall, 10% of pts had been on one biologic DMARD. Hazard ratios suggested that when pts had LDA, MDA or HDA vs remission, they were potentially at higher risk of developing major adverse CV events (MACE), VTE and non-serious infections (NSIs) excluding herpes zoster (HZ), but not malignancies, serious infections or HZ (Figure 1). Similarly, mean CDAI AUC trended higher for MACE, VTE and NSIs (Table 1).

Fig. HRs for major AEs of special interest during active RA vs remission as defined by CDAI



*p<0.10
HRs (95% CI) are shown on a logarithmic scale
CI, confidence interval; HR, hazard ratio; n, number of pts who experienced each AE; NMSC, non-melanoma skin cancer

Table 1. Cumulative CDAI (from BL to event) for pts with vs without events (AUC/yr)

Major AE	Pts with events		Pts without events		LS mean difference in pts with vs without events	p value
Treatment	n	LS mean AUC/yr	n	LS mean AUC/yr		
MACE						
Tofacitinib 5 mg BID	42	6275.4	1336	4607.3	1668.1	0.0018*
Tofacitinib 10 mg BID	50	5237.4	1306	4482.6	754.8	0.1253
TNFi	36	5234.5	1312	4851.5	383.0	0.5069
VTE						
Tofacitinib 5 mg BID	15	6546.7	1363	4614.4	1932.3	0.0293*
Tofacitinib 10 mg BID	31	6688.2	1323	4458.5	2229.7	0.0003*
TNFi	8	6423.6	1339	4839.4	1584.1	0.1907
Malignancy excl. NMSC						
Tofacitinib 5 mg BID	59	5249.3	1319	4618.9	630.4	0.1655
Tofacitinib 10 mg BID	55	4793.7	1301	4482.2	311.5	0.5077
TNFi	39	5561.4	1308	4826.3	735.1	0.1854
Serious infections						
Tofacitinib 5 mg BID	127	5710.2	1242	4577.5	1132.7	0.0004*
Tofacitinib 10 mg BID	150	5425.2	1197	4476.4	948.8	0.0013*
TNFi	105	6058.4	1240	4807.7	1250.7	0.0003*
HZ						
Tofacitinib 5 mg BID	175	5184.5	1199	4738.1	446.4	0.1101
Tofacitinib 10 mg BID	163	5549.1	1186	4481.3	1067.8	0.0002*
TNFi	56	5667.2	1291	4875.5	791.8	0.0930*
NSIs excl. HZ						
Tofacitinib 5 mg BID	760	6608.3	463	5122.5	1485.8	<0.0001*
Tofacitinib 10 mg BID	750	6587.8	426	5009.6	1578.2	<0.0001*
TNFi	722	6737.6	521	5217.5	1520.1	<0.0001*

*p<0.10. Data collected after pts who were randomised to tofacitinib 10 mg BID had their dose reduced to 5 mg BID were included in the tofacitinib 10 mg BID groupLS, least squares; n, number of pts in analysis of variance model

Conclusion: In ORAL Surveillance, the risk of MACE, VTE and NSIs excluding HZ appeared higher when pts had active disease than when in remission. Greater cumulative RA disease activity was seen in pts who suffered these AEs vs those who did not. Our findings support treat-to-target recommendations for RA.

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POS0520

ASSOCIATION BETWEEN BASELINE STATIN TREATMENT AND MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF ORAL SURVEILLANCE

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Background: ORAL Surveillance (NCT02092467) was a post-authorisation safety study of tofacitinib vs tumour necrosis factor inhibitors (TNFi) in patients (pts) with rheumatoid arthritis (RA) aged ≥50 years (yrs) with ≥1 additional cardiovascular (CV) risk factor and an inadequate response to methotrexate (MTX). Statins are used to treat coronary artery disease (CAD) and are recommended by the American College of Cardiology/American Heart Association (ACC/AHA) for the management of pts at risk of atherosclerotic CV disease (ASCVD),[1] such as those with ≥7.5% 10-yr risk of major adverse CV events (MACE) or diabetes mellitus.

Objectives: To examine the association between baseline (BL) statin use and MACE in ORAL Surveillance.

Methods: Pts with RA on stable MTX were randomised 1:1:1 to receive tofacitinib 5 or 10 mg twice daily (BID) or TNFi (adalimumab 40 mg every 2 weeks or etanercept 50 mg once weekly). Pts were stratified post hoc by BL statin use (yes/no). Pts were further categorised by history of CAD (HxCAD), BL CV risk score per ACC/AHA guidelines[1] (for pts without HxCAD; 10-yr risk of MACE per the ASCVD-pooled cohort equations risk calculator[2] with a 1.5 multiplier applied[3]), and separately by BL diabetes status. CV risk score/BL diabetes status categories were: high (≥20%)/HxCAD (yes), intermediate (≥7.5–<20%) or low-borderline (<7.5%), and diabetes status (yes). For the overall population and each treatment group, risk of MACE was compared between BL statin use (yes vs no) via Cox analyses for each CV risk category and diabetes status (yes). Incidence rates (IRs; pts with first events/100 pt-yrs) and hazard ratios (HRs; BL statin use: yes vs no) were evaluated for adjudicated MACE.

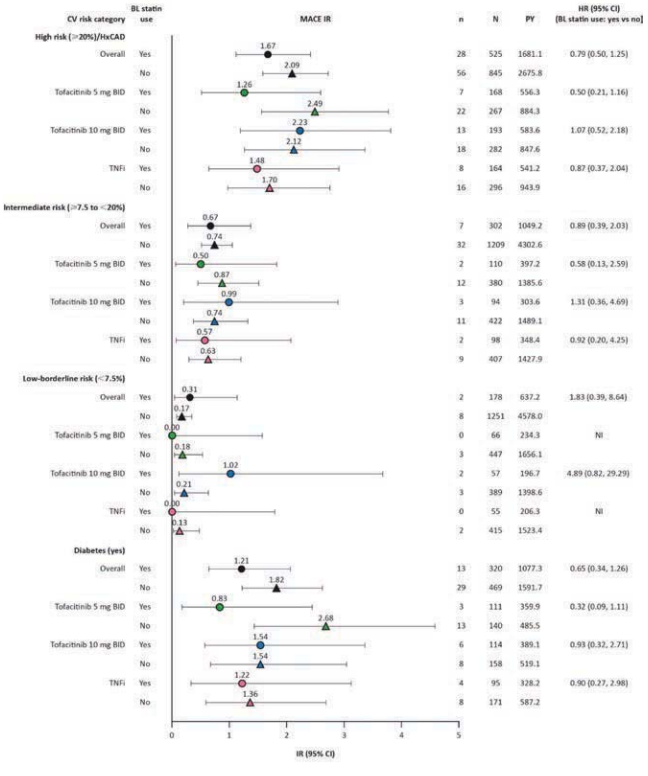
Results: Of 4362 pts (tofacitinib 5 mg BID, n=1455; tofacitinib 10 mg BID, n=1456; TNFi, n=1451), 497 had a HxCAD, and 3813 without a HxCAD had CV risk scores determined; 789 had BL diabetes. Overall, 1020 (23.4%) pts reported BL statin use. Across CV risk score categories for all treatment groups, <50% of pts received statins at BL, with statin use highest in the high/HxCAD category pts (35.7–40.6%) and pts with diabetes (35.7–44.2%) (Table 1). Across categories, no interpretable associations between BL statin use and MACE were found. However, in the overall population, MACE IRs were lower in pts with vs without BL statin use in the high/HxCAD category, and in pts with diabetes (Figure 1). In pts receiving tofacitinib 5 mg BID and TNFi, MACE IRs were lower in pts with vs without BL statin use across all categories (Figure 1).

Table 1. Proportion of pts receiving statins at BL, by CV risk category and presence of diabetes

n/N (%)	Overall	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi
High (≥20%)/HxCAD	525/1370 (38.3)	168/435 (38.6)	193/475 (40.6)	164/460 (35.7)
Intermediate (≥7.5–<20%)	302/1511 (20.0)	110/490 (22.4)	94/516 (18.2)	98/505 (19.4)
Low-borderline (<7.5%)	178/1429 (12.5)	66/513 (12.9)	57/446 (12.8)	55/470 (11.7)
Diabetes (yes)	320/789 (40.6)	111/251 (44.2)	114/272 (41.9)	95/266 (35.7)

N, number of pts in each category; n, number of pts receiving BL statins

Fig. MACE IRs (pts with first events/100 pt-yrs) and HRs (BL statin use: yes vs no) across treatment groups, by CV risk category and presence of diabetes in ORAL Surveillance



Data collected after pts who were randomised to tofacitinib 10 mg BID had their dose reduced to 5 mg BID were included in the tofacitinib 10 mg BID group
For MACE, risk period was defined as the time from first study dose to last study dose +60 days, or to the last contact date, whichever was earliest
95% CIs for IRs (per 100 PY) were constructed using Exact Poisson distribution. HRs (95% CIs) comparing BL statin use (yes vs no) were generated using a Cox model with BL statin use as the only covariate at each CV risk category and BL diabetes (yes) within each treatment group
CI, confidence interval; N, number of pts in each category; n, number of pts with events; NI, non-informative (HRs [95% CI] were NI when comparator group had 0 events); PY, pt-yrs

Conclusion: In this post hoc analysis of data from ORAL Surveillance, most pts did not receive BL statin treatment. This suggests suboptimal CV risk management, particularly in pts at high risk of CV events. There was no interpretable association

between BL statin use and MACE. However, pts in the higher risk categories, particularly those receiving tofacitinib 5 mg BID, had lower MACE IRs with vs without BL statin use. This analysis did not take into account initiation or dose adjustment of statin treatment during the study, and had low yrs of exposure in some categories.

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POS0521

RISKS OF SEVERE INFECTION AFTER THE INTRODUCTION OF BDMARDS IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENTS: A POPULATION-BASED INTERRUPTED TIME-SERIES ANALYSIS

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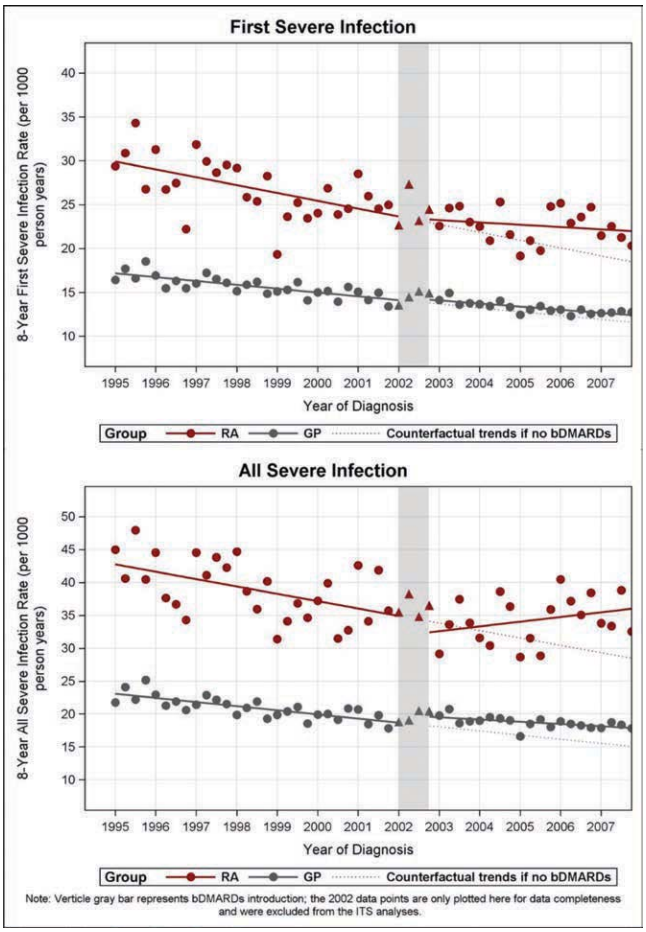

Figure 1. Unadjusted rates.

Background: Biological disease-modifying anti-rheumatic drugs (bDMARDs) are effective in suppressing inflammation and preventing joint damage. But bDMARDs may be associated with increased risk of severe infection. Evidence on this is contradictory with some studies showing increased risk, whereas others reporting no significant changes.

Objectives: To determine the impact of the introduction of bDMARDs on severe infection among patients newly diagnosed with RA compared with non-RA individuals.

Methods: In this age- and gender-matched cohort study using administrative health data for the population of BC, Canada, all incident RA patients diagnosed between 1995–2007 were identified. Non-RA individuals were randomly selected from the general control population to match with RA. Incident RA/non-RA individuals were then divided into quarterly cohorts according to their diagnosis date. Two outcomes were examined: (1) first severe infection (FSI) after RA onset necessitating hospitalization or occurring during hospitalization; and (2) all severe infections (ASI) after RA onset. We calculated the 8-year FSI and ASI rate for each cohort. We conducted interrupted time-series analyses to compare levels and trends of FSI and ASI in RA and non-RA individuals diagnosed

Table 1. Results of interrupted time-series analysis of FSI/ASI rates, adjusting for age, gender, chronic obstructive pulmonary disease, Romano Charlson Comorbidity Index, diabetes, chronic kidney diseases, alcoholism, cancer, prior hospitalization with infection and socio-economic status at disease diagnosis year, using stepwise model selection

Outcome	Parameter	RA		Non-RA	
		Unadj. Diff (95% CI)	Adj. Diff (95% CI)	Unadj. Diff (95% CI)	Adj. Diff (95% CI)
		p-value	p-value	p-value	p-value
FSI	Trend	0.63 (0.03, 1.22) 0.0441	0.68 (0.09, 1.27) 0.0292	0.08 (-0.08, 0.25) 0.3237	0.03 (-0.12, 0.19) 0.6728
	Level (1 year post-intervention)	0.50 (-2.00, 2.99) 0.6989	0.31 (-1.88, 2.49) 0.7847	0.41 (-0.21, 1.03) 0.2041	0.26 (-0.24, 0.75) 0.3103
	5 years post-intervention	3.01 (-0.85, 6.87) 0.1331	3.02 (-0.48, 6.52) 0.0986	0.75 (-0.24, 1.73) 0.1433	0.39 (-0.46, 1.25) 0.3721
ASI	Trend	1.84 (0.83, 2.84) 0.0009	1.85 (0.81, 2.89) 0.0011	0.28 (0.04, 0.53) 0.0305	0.12 (-0.10, 0.34) 0.2877
	Level (1 year post-intervention)	-1.21 (-5.41, 3.00) 0.5763	-1.44 (-5.44, 2.56) 0.4850	1.46 (0.42, 2.49) 0.0085	1.20 (0.38, 2.02) 0.0064
	5 years post-intervention	6.14 (0.26, 12.01) 0.0466	5.97 (0.02, 11.93) 0.0560	2.60 (1.08, 4.12) 0.0017	1.69 (0.45, 2.92) 0.0109

during pre-bDMARDs (1995–2001) and post-bDMARDs (2003–2007) periods. Adjusted 8-year FSI and ASI rates for RA and non-RA cohorts diagnosed five years after bDMARDs introduction were compared with expected rates assuming no bDMARDs introduction, based on extrapolation of pre-bDMARDs trends.
Results: A total of 60,226 and 588,499 incident RA/non-RA individuals were identified. We identified 8,954 FSI and 14,245 ASI in RA, and 56,153 FSI and 79,819 ASI in non-RA. The 8-year FSI rates among RA patients diagnosed in the pre-bDMARDs period decreased over time but leveled off among those diagnosed in the post-period (Figure 1). The adjusted difference between the post- and pre-bDMARDs secular trends of 8-year FSI rates was 0.68 (p=0.03) in RA and 0.03 (p=0.67) in non-RA (Table 1). The 8-year ASI rates among RA patients diagnosed in the pre-bDMARDs period decreased over time but increased significantly among those diagnosed in the post-period (Figure 1). The adjusted difference between the post- and pre-bDMARDs secular trends of 8-year ASI rates was 1.85 (p=0.001) in RA and 0.12 (p=0.29) in non-RA (Table 1). For RA cohort diagnosed 5 years after bDMARDs introduction, ASI rate increased by 20.4% than expected rates assuming no bDMARDs introduction. In contrast, ASI rate in non-RA increased by only 10.9%.
Conclusion: Arthritis onset after bDMARDs introduction is associated with an elevated risk of severe infection in RA patients, compared with matched non-RA individuals.
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POS0522 ASSOCIATED FACTORS WITH PHYSICAL DYSFUNCTION OF ELDERLY-ONSET RHEUMATOID ARTHRITIS TREATED WITH A TREAT-TO-TARGET STRATEGY

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Background: Achievement of normal physical function is an important outcome for older patients. Previous studies of younger cohorts showed that aging, comorbidities, and joint damage influenced the physical function of patients with RA who achieved clinical remission or low disease activity (LDA). We previously demonstrated that a treat-to-target (T2T) strategy for methotrexate (MTX)-naïve elderly-onset RA (EORA) was effective with an acceptable safety profile. It showed that 60.9% of 197 patients achieved HAQ Disability Index (HAQ-DI) ≤0.5 at three years by following the T2T strategy targeting LDA (1).
Objectives: We aimed to evaluate associated factors with HAQ-DI in the T2T strategy targeting LDA for patients with EORA during three-year observational period.
Methods: Treatment was adjusted to target LDA with conventional synthetic disease-modifying antirheumatic drugs (DMARDs), followed by biological DMARDs (bDMARDs) in 197 MTX-naïve EORA patients (mean age 74.9 years) with moderate-to-high disease activity. HAQ-DI was evaluated at week 0, 24, 52, 76, 104, 128, and 156. To evaluate associated factors with SDAI and HAQ-DI over the 36-month follow-up, Bayesian hierarchical logistic regression modeling was applied for 1067 periods from the 197 patients.
Results: At baseline, the enrolled 197 patients with EORA who had normal physical function (HAQ-DI ≤0.5) in 29.4%, HAQ-DI >0.5 and <1.5 in 36.5%, and HAQ-DI ≥1.5 in 33.0%, and the mean age (standard deviation [SD]) in each group was 72.7 (5.9), 74.8 (7.3), and 75.6 (6.7), respectively. Baseline SDAI increased in the group with higher HAQ-DI. The proportions of patients with each comorbidity and estimated creatinine clearance at baseline were not significantly different across the 3 groups. In the multilevel logistic model, the association of MTX, bDMARDs, and GC use with changes in SDAI in each period was evaluated. Age, sex, and comorbidities (chronic lung disease, cardiovascular disease, history of malignancy, osteoporosis, history of serious infections, and osteoarthritis) were included as inter-individual factors. The model indicated that the use of bDMARDs was associated with a reduction of the SDAI (ΔSDAI: -9.75, SD 0.75, p<0.001), while neither MTX (ΔSDAI: -1.25, SD 1.13, p=0.270) nor GCs (ΔSDAI: -0.78, SD 0.88, p=0.372) was associated with changes in SDAI. Chronic lung diseases (ΔSDAI: 4.64, SD 1.44, p=0.001) and osteoporosis (ΔSDAI: 3.78, SD 1.46, p=0.001) at baseline were associated with the increment of SDAI. The association of age, sex, the comorbidities, and MTX, bDMARDs, and GC use with physical function in each period was evaluated by the multilevel logistic model. The model indicated that older age (ΔHAQ-DI: 0.03, SD 0.01, p <0.001), chronic lung diseases (ΔHAQ-DI: 0.15, SD 0.10, p=0.001), and osteoporosis (ΔHAQ-DI: 0.30, SD 0.10, p=0.010) at baseline were associated with the increment of HAQ-DI. When the mean SDAI during the observation period was added to the model as an inter-individual factor, the associations of HAQ-DI with the chronic lung diseases and osteoporosis at baseline were not statistically significant.
Conclusion: These data indicate that bDMARDs had a central role in reducing disease activity in the T2T strategy targeting LDA in EORA patients. Chronic lung diseases and osteoporosis at baseline were associated with increase in disease activity and worsening of physical function. However, disease activity had a greater impact on physical function than the comorbidities at baseline.
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POS0523 FATIGUE TRAJECTORIES IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: A LONGITUDINAL ANALYSIS OF DATA FROM THE CARERA TRIAL

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Background: Fatigue is a common and impactful symptom of rheumatoid arthritis (RA). Given its heterogeneity and unpredictable nature, studies on contributing factors of RA-related fatigue should include multidimensional measures of

Table 1. Predictors of fatigue trajectory membership

	Gradual improvement		Transient improvement		Early deterioration	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Fatigue (0-100)	1.01 (0.99; 1.04)	0.32	0.99 (0.97; 1.01)	0.16	0.98 (0.96; 1.00)	0.07
PGA (0-100)	0.98 (0.95; 1.01)	0.11	0.96 (0.94; 0.99)	**0.003**	0.95 (0.92; 0.98)	**<0.001**
Tender joints (0-28)	1.00 (0.91; 1.13)	0.82	1.00 (0.91; 1.09)	0.97	0.99 (0.88; 1.11)	0.80
Swollen joints (0-28)	1.01 (0.90; 1.15)	0.82	0.99 (0.89; 1.10)	0.83	0.93 (0.81; 1.06)	0.30
CRP (mg/dL)	1.00 (0.98; 1.01)	0.67	0.99 (0.98; 1.01)	0.36	1.00 (0.97; 1.02)	0.66
Pain (0-100)	0.99 (0.96; 1.02)	0.36	0.96 (0.94; 0.98)	**0.002**	0.95 (0.92; 0.98)	**<0.001**
HAQ (0-3)	1.07 (0.52; 2.20)	0.85	0.55 (0.30; 1.01)	**0.05**	0.24 (0.11; 0.51)	**<0.001**
SF-36 Mental Component Score (0-100)	1.00 (0.96; 1.04)	0.97	1.02 (0.99; 1.06)	0.23	1.02 (0.98; 1.06)	0.34
Treatment response						
Secondary failure	2.22 (0.78; 6.32)	0.13	3.87 (1.57; 9.55)	**0.003**	7.88 (2.68; 23.13)	**<0.001**
Delayed response	2.93 (0.70; 12.15)	0.14	6.82 (1.91; 24.44)	**0.003**	11.14 (2.33; 53.19)	**0.003**

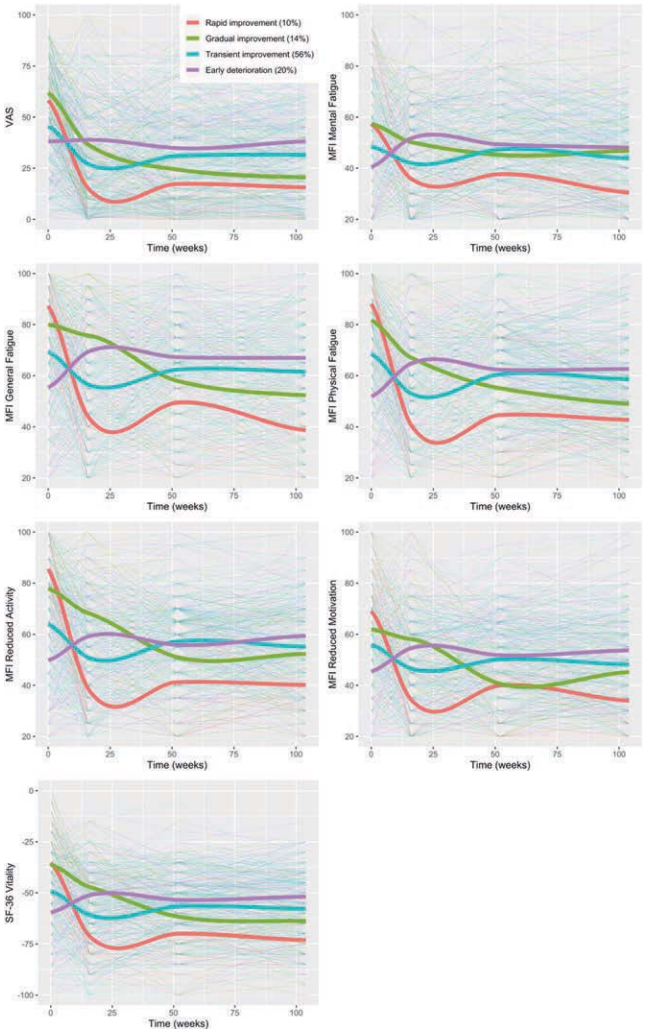

Figure 1. Latent trajectories of fatigue evolution over the first 2 years in CareRA (n = 356).

fatigue and assess these longitudinally with multivariate methods, starting early in the disease.

Objectives: We aimed to explore the longitudinal course of fatigue and its predictors among patients with early RA starting DMARD therapy.

Methods: Data came from the 2-year treat-to-target trial Care in early RA (CareRA) and its 3-year extension. Fatigue was measured based on visual analog scale (VAS), Multidimensional Fatigue Inventory (MFI), and Short-Form 36 (SF-36). Longitudinal fatigue trajectories were identified with multivariable growth mixture modeling. Baseline and early predictors of trajectory membership, including treatment response, were studied with multinomial logistic regression adjusted for age, gender, and treatment type. Patient global assessment (PGA), pain (VAS), and disability (HAQ) were studied in separate models because of collinearity (Spearman r > 0.60). For all models, posterior probabilities of trajectory assignment were included in the regression as weights to account for classification uncertainty. Treatment response was defined, based on whether remission (DAS28-CRP < 2.6) was achieved by week 16 and sustained until year 2, as either early persistent response, secondary failure, or delayed response.

Results: In total, 356 and 244 patients were included in the 2-year and 5-year analyses, respectively. Mean (SD) fatigue (VAS) at inclusion was 48/100 (24). Four fatigue trajectories were identified: Rapid, Gradual, and Transient Improvement, and Early Deterioration, consisting of 10%, 14%, 56%, and 20% of patients, respectively (Figure 1). Higher PGA, pain and HAQ at baseline were associated with increased probability of Rapid Improvement compared to Transient Improvement or Early Deterioration (Table 2). Secondary treatment failure and delayed treatment response strongly increased the probability of less positive fatigue trajectories when compared to early persistent response.

Conclusion: The longitudinal course of fatigue in early RA is dynamic but highly refractory, with less than 25% of patients making lasting improvements and 20% even experiencing worsening fatigue despite intensive DMARD therapy. Remarkably, a higher perceived disease impact at baseline was associated with an increased probability of fatigue improvement, possibly reflecting the fluctuating nature of this complex symptom. However, early inflammatory disease control appears to be the most important contributor to improved long-term fatigue outcomes, illustrating the far-reaching impact of the therapeutic window of opportunity in early RA.

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POS0524

THE VALUE OF ULTRASOUND AND MAGNETIC RESONANCE IMAGING SCORING TECHNIQUES FOR DETECTING JOINT INFLAMMATION AND DAMAGE IN RHEUMATOID ARTHRITIS PATIENTS IN EXPLAINING FUNCTIONAL IMPAIRMENT AND HANDGRIP STRENGTH: A PILOT STUDY

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Background: Composite disease activity ratings, which are used to assess the severity of rheumatoid arthritis (RA), may not effectively reflect the illness's spatial impact on the hands. In RA, assessments of handgrip strength (HGs) and functional deficits are a kind of objective examination that focuses on the hands.

Objectives: The goal of this study was to see if there was a link between joint inflammation and damage in the wrists and hands, as measured by ultrasound (US) and magnetic resonance imaging (MRI), functional disability as measured by hand-specific self-report questionnaires, and composite disease activity indices.

Methods: Sixty-six female patients with RA were investigated (age 55.6 ± 12.2 years, range 20-80 years; disease duration 4.4 ± 3.0 years). The DAS28-CRP, the SDAI, the CDAI, and US and MRI scoring techniques such as the UltraSound-CLinical ARthritis Activity (US-CLARA) and modified Simplified Rheumatoid Arthritis Magnetic Resonance Imaging Score [SAMIS] were all used as baseline assessments (mod SAMIS) (Figure 1). Without contrast injection, the mod SAMIS score was rated for the presence/absence and semiquantitative assessments of synovitis, bone erosion (ERO), and bone marrow edema (BME). All patients had HGs and completed the shortened Disability of Arm, Shoulder, and Hand Questionnaire (QuickDASH), the Arthritis Impact Measurement Scales hand and finger function subscale, and the upper extremity function sub-score of the ROAD.

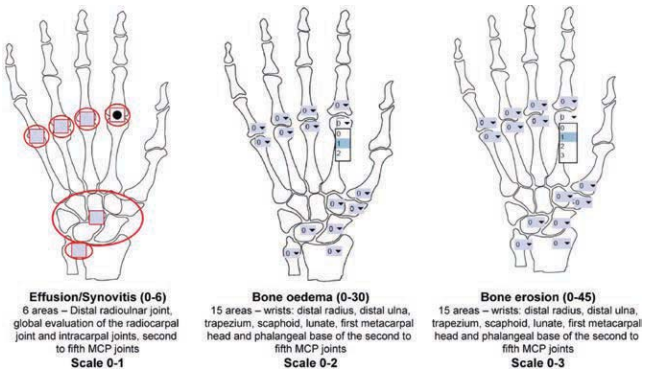

Figure 1. The modified simplified SAMIS magnetic resonance score (mod SAMIS) scoring spreadsheet. The MRI was graded for the presence/absence of synovitis and semiquantitative ratings of bone marrow oedema and bone erosion, without contrast injection.

Results: The mod SAMIS total score and the US-CLARA had a strong correlation (rho=0.377, p=0.0018) for all patients. Among the SAMIS subscores, there was a significant relationship between mod SAMIS bone oedema (SAMIS-BME) and US-CLARA (rho=0.799, p<0.001) and mod SAMIS synovitis (SAMIS-synovitis) and US-CLARA (rho=0.539, p<0.001). There were also significant negative relationships between the HGs score and the mod SAMIS total score and US-CLARA (rho = -0.309, p=0.011 and rho = -0.775, p<0.0001, respectively). The HGs and disease activity composite indices, as well as hand-specific self-report questionnaires, were shown to have high relationships (p<0.0001) in individuals with RA. The hand and finger function sub-scales, as well as the mod SAMIS erosion (SAMIS-ERO) and HGs, exhibited no significant relationship. For each of the three components, interobserver agreement was good to excellent (intraclass correlation values = 0.713, 0.912, and 0.821, respectively) (synovitis, BME, and BME) (Figure 2).

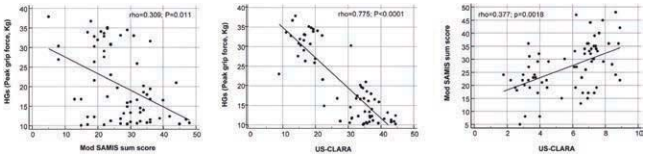

Figure 2. Scatterplot with linear regression lines displays the relationship between (A) mod SAMIS total score vs HGs, (B) US-CLARA vs HGs, and (C) US-CLARA vs mod SAMIS total score.

Conclusion: BME and synovitis have an impact on upper-extremity function. The US-CLARA and mod SAMIS total score are promising solutions for semi-quantitative evaluation of joint inflammation and damage in RA. These shortened scores might cut down on image processing time in US and MRI-controlled RA investigations, as well as make using these imaging modalities in RA treatment response evaluation studies simpler.

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POS0525

ARE BIOLOGIC AND TARGETED SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS ASSOCIATED WITH WORK PARTICIPATION IMPROVEMENT IN EARLY RHEUMATOID ARTHRITIS? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: In early RA, the benefit of treatment with b-/tsDMARDs on work participation (WP), a top-three social role in RA, has seldom been studied.

Objectives: To review the effect of treatment with b-/tsDMARDs on employment status (ES), presenteeism and sick leave (SL), in patients with early RA.

Methods: A systematic literature review (SLR) was conducted in key electronic databases up to October 2021, to include RCTs assessing the effect of treatment with b-/tsDMARDs vs any comparator on ES, presenteeism and SL in patients with RA (≤ 3y). Two reviewers independently identified eligible studies and extracted data. Random-effects meta-analysis was only performed if ≥3 studies were conducted in comparable populations, assessing WP outcome similarly. Statistical heterogeneity was assessed with I^2.

Results: From 7129 records (65 full-text articles screened), 11 RCTs were included in the SLR (7 in csDMARD naïve patients; 2 in inadequate responder to csDMARDs; 1 bDMARD tapering after initial combination with MTX, and 1 strategy study). Large heterogeneity was found across WP outcomes, measurement instruments, interventions and comparators (Table 1), which together with insufficient data reporting hampered meta-analysis of most outcomes. For ES, to allow meta-analysis, all outcomes were converted to employment loss, for which individual study Odds ratios (OR) were computed. The pooled OR of 4 studies with 779 patients treated with adalimumab, infliximab or baricitinib (Figure 1) showed a lower likelihood of employment loss at weeks 56 to 104 in those treated with MTX+b/tsDMARDs compared to MTX+PBO (OR: 0.65; 95% CI:0.43-0.99). For presenteeism and SL, 33/40 (83%) between-group comparisons showed improvement in favour of b-/tsDMARDs, but an effect size was reported or possible to compute for only 12 comparisons, of which 8 (67%) were statistically significant.

Table 1. Overview of between-group results

Author, year Study name	Intervention (I) Comparator (C)	Assessed Outcome	Instrument	Follow-up (weeks)	Favours intervention (+ yes; - no) [$]
csDMARD naïve					
Smolen 2006	**IFX+MTX**	ES	SCMI[‡]	54	+[*]
ASPIRE	PBO+MTX	SL			+[*]
Bejarano 2008	**ADA+MTX**	ES	Weekly diaries[‡]	56	+[*]
	PBO+MTX	SL			+[*]
Anis 2009	**ETN+MTX**	SL	SCMI[‡]	52	+[*]
COMET	MTX				
van den Hout 2009	**I: IFX+MTX**	SL	SCSI[‡]	104	56w: + I vs $C_{1/2}$
BeSt	C1: seq. monotherapy	Pres	VAS (0-100)		104w: + I vs C_1 I
	C2: step-up comb. Therapy + IFX				+[*] I vs C_3
	C3: initial comb. Therapy + IFX				
van Vollenhoven 2010	**I_1: ADA+MTX**	ES	SCMI[‡]	104	+[*] I_1 vs C I + I_2 vs C
	I_2: ADA+PBO	Pres			+[*] I_1 vs C I + [*] I_2 vs C
PREMIER	C: PBO+MTX	SL			+[**] I_1 vs C I + [**] I_2 vs C
Emery 2016	**ADA+MTX**	ES	WPAI-RA	24-26	OPTIMA & PROWD +
OPTIMA					
PROWD	PBO+MTX	Pres			OPTIMA +[*]
		SL			OPTIMA -
Wiland 2016	**I: ETN25/MTX**	Pres	WPAI-RA	117	39W & 65 W: + I vs $C_{1/2}$
PRIZE					39W & 65 W: + I vs $C_{1/2}$
	C_1: PBO+MTX	SL			
	C_2: PBO+PBO				
Schiff 2017	**I_1: BARI+MTX**	Pres	WPAI-RA	52	24w: + $I_{1/2}$ vs C
RA-BEGIN¶	**I_2: BARI+PBO**	SL			52w: + I_2 vs C
	C: PBO+MTX				24w: + $I_{1/2}$ vs C
					52w: + I_2 vs C
Strand 2021	**I_1: UPA 30**	Overall work impairment	WPAI-RA	12	+ $I_{1/2}$ vs C
SELECT-EARLY¶	**I_2: UPA 15**				
	C: MTX				
csDMARD Inadequate responders					
Eriksson 2015	**IFX + MTX**	SL	Registry	7 y	+
Swefot	csDMARD + MTX				
Fleischmann 2016	**ABA+MTX**	Pres	WPAI-RA	104	24, 56 & 104w: +
AMPLE¶	ADA+MTX	SL			24 & 104w: +

SCMI – self composed multiple items; **SCSI** – self composed single item; **WPAI –** Work Productivity Activity Impairment questionnaire; [*] $p \leq 0.05$ [**] $p \leq 0.001$ vs C; [‡] non-validated instrument; [$] when > 1 I/C or time-point, between-group comparisons and time-points are presented if I vs C differences were observed; **¶** insufficient data reporting to compute effect sizes.

Conclusion: A protective effect against employment loss was observed in patients with early RA treated with MTX+b-/tsDMARDs compared to MTX monotherapy. The methodological heterogeneity and insufficient reporting hampers clear conclusions regarding the beneficial effects of b-/tsDMARDs on presenteeism and SL. Efforts to uniformize future studies with WP as outcome by following recently developed points to consider are crucial[1].

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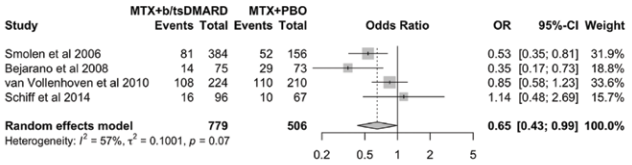

Figure 1. Random-effects meta-analysis of the employment loss in early Rheumatoid Arthritis csDMARD-naïve patients treated with MTX plus b-/tsDMARDs *versus* MTX in monotherapy. **b-/ts** biologic/targeted synthetic; **cs –** conventional synthetic; **DMARD –** disease-modifying antirheumatic drugs; **MTX –** methotrexate; **PBO –** placebo.

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POS0526

HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY AND PREDICTION OF EROSIVE PROGRESSION AS ASSESSED BY THE GOLD STANDARD CONVENTIONAL RADIOGRAPHY IN ESTABLISHED RHEUMATOID ARTHRITIS: A 1-YEAR COHORT STUDY

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Background: High-Resolution peripheral Quantitative Computed Tomography (HR-pQCT) is a promising imaging technique for assessing erosive disease in rheumatoid arthritis (RA). We have shown that the diagnostic accuracy in detecting erosive disease of HR-pQCT of two joints corresponds to conventional radiography (CR) of 44 joints in established RA (1). No data assessing HR-pQCT as a tool for predicting erosive radiographic progression in a large cohort of established RA has been published.

Objectives: To assess the association between erosive disease identified using either CR or HR-pQCT at baseline and erosive progression using CR during 1-year follow-up in established RA.

Methods: This observational cohort study included 220 patients with RA (disease duration ≥ 5 yrs) at the Department of Rheumatology, Aarhus University Hospital, between Mar. 2018 and Oct. 2020. All participants had demographic information collected, together with HR-pQCT at baseline and CR made at baseline and 1-year follow-up. Erosive assessment using HR-pQCT was performed at the second and third metacarpophalangeal (MCP) joint (2). The Sharp/van der Heijde score (SHS) method was used to assess erosive status and erosive progression using CR of hands, wrists and feet (3).

Results: In total, 220 participants with RA (median age 66 yrs, interquartile range (IQR) 57-72; 71% women) were included and 212 completed their follow-up visit in Dec. 2021 (dropout n=8 (4 %)). During follow-up (median 1 yrs, range 0.7-1.4), erosive progression on CR was detected in 24 of 211 (11%) (missing baseline CR, n=1). Characteristics of the study population by erosive progression are shown in Table 1. In unadjusted regression analyses, number of erosions on HR-pQCT at baseline and erosion score (per 10) using CR at baseline were associated with erosive progression (yes/no) on CR at 1-year (Odds ratio (OR) 1.1; 95%CI 1.0-1.1; *p<.05* and OR 1.1; 95%CI 1.0-1.2; *p<.01*). After adjusting for age and sex, erosion score remained associated with erosive progression (OR 1.1; 95%CI 1.1-1.2; *p<.01*), but number of erosions did not (OR 1.0; 95%CI 1.0-1.1; *p=.07*).

Table 1. Demographics at baseline

	Progression on CR	*No progression on CR*	*P value*
No	24/211 (11)	187/211 (89)	
Age, yrs	66 (57-73)	66 (57-71)	*.80*
Women	15/24 (63)	134/187 (72)	*.35*
Disease Duration, yrs	20 (8-28)	15 (9-23)	*.44*
DAS28-CRP	1.7 (1.5-2.5)	1.8 (1.5-2.5)	*.53*
Erosive on CR	24/24 (100)	141/187 (75)	***< .01***
Erosive 2nd/3rd MCP on CR*	17/23 (74)	62/185 (34)	***< .001***
Erosive on HR-pQCT	22/23 (96)	153/185 (83)	*.14*
Erosion score (per 10)	4 (2-7)	1 (0-3)	***< .0001***
Erosion number	10 (5-17)	3 (1-10)	***< .01***
Total erosion volume, mm³	128 (19-201)	26 (2-111)	***< .05***

Data are no. (%) or median with interquartile range. P-values: Mann-Whitney *U* or Fisher's exact test. Missing HR-pQCT, n=3. CR = conventional radiography, DAS28-CRP = disease activity score of 28 joints based on C-reactive protein, HR-pQCT = high-resolution peripheral quantitative computed tomography* Same hand as HR-pQCT scanned

Conclusion: In established RA, baseline CR of 44 joints is superior to baseline HR-pQCT of two joints in identifying individuals at risk of erosive progression on CR. This underlines the need for a head-to-head comparison between progression identified by HR-pQCT and CR to fully assess the clinical utility of HR-pQCT in predicting erosive progression compared to CR.

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POS0527

ANTI-CCP POSITIVE INDIVIDUALS AT RISK OF PROGRESSION TO INFLAMMATORY ARTHRITIS: WHAT HAPPENS TO BIOMARKERS PRIOR TO PROGRESSION?

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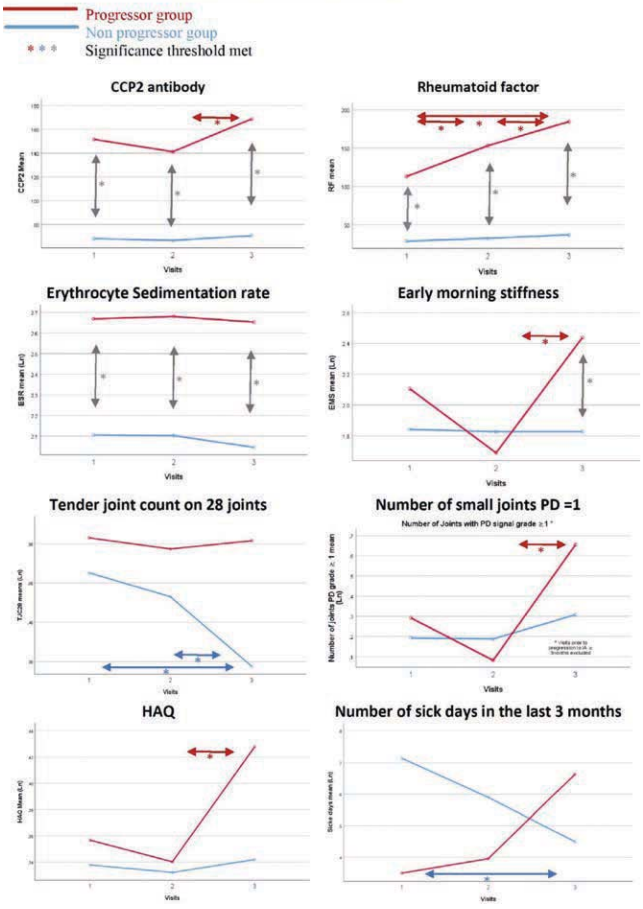
Background: Although many predictors of progression to inflammatory arthritis (IA) have been identified at first visit in individuals at risk of developing IA, their fluctuation during follow-up is largely unknown.

Objectives: To describe the changes in relevant biomarkers, which precede arthritis development in anti-CCP positive at risk individuals.

Figure 1: Mixed model ANOVA on repeated measures



Methods: In a single centre prospective observational cohort of anti-CCP positive individuals with new musculoskeletal symptoms but without clinical arthritis, 394 individuals with at least 3 available longitudinal datapoints including first, second and last records (progression excluded), were selected. Data on anti-CCP2 antibodies (CCP2), rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), early morning stiffness duration (EMS), tender joint count on examination (TJC28), health assessment questionnaire (HAQ), absence from work in the last 3 months (sick days), and ultrasound power Doppler signal (PD) grade ≥ 1 in small joints, were assessed. Mixed model analysis on repeated measures (MANOVA) were performed, missing data were not imputed.

Results: Of the 394 selected individuals, 82 (21%) progressed to IA. In those who progressed, last visit was at a mean (SD) of 6.1 (8) months prior to progression, and total follow-up duration was 33.7 months (26.7) versus 46.5 months (30.2) for those who did not.

Within group analysis: *in the progressor group* there was a significant increase in the value of biomarkers at the visit prior progression for CCP2 +, RF +, EMS, HAQ, and the number of joints with a PD grade ≥ 1 (Figure 1, Table 1). For sick days from work prior last visit, the increase was non-significant.

Table 1. Mixed model ANOVA on repeated measures: pairwise comparison

		Analysis between groups	Analysis within groups		
Biomarker	Mean (SD) at last visit	P-value between groups at last visit	P-value between second and last visit within the progressor group	P-value between second and last visit within non-progressor group	Within subject effect
CCP2	NP: 71 (108) P: 169 (131)	**p<0.001**	**P=0.008**	P=1.000	F(2/257)=3 $P\eta^2$= 0.017 P=0.077
RF	NP: 37 (73) P: 185 (180)	**P<0.001**	**P=0.012**	P=0.973	F(2/304)=15 $P\eta^2$= 0.084 **P<0.001**
ESR	NP: 11 (9) P: 22 (21)	**p<0.001**	P=1.000	P=0.614	F(2/580)=0.1 $P\eta^2$< 0.001 P=0.877
EMS	NP: 26 (68) P:58 (120)	**P=0.010**	**P=0.006**	P=1.000	F(2/710)=4 $P\eta^2$= 0.018 **P=0.011**
TJC28	NP: 0.5 (1.5) P: 3 (5.5)	**P<0.001**	P=1.000	**P<0.001**	F(2/784)=10 $P\eta^2$< 0.025 **P<0.001**
Number of joints PD ≥1	NP: 0.7 (2) P: 1 (2)	**P=0.020**	**P=0.001**	P=0.055	F(2/318)=4 $P\eta^2$= 0.025 **P=0.014**
HAQ	NP: 0.5 (0.6) P: 0.7 (0.8)	P=0.105	**P=0.016**	P=1.000	F(2/494)=2.5 $P\eta^2$= 0.0.009 P=0.086
Number of sick days	NP: 2 (6) P: 4 (13)	P=0.204	P=0.457	P=0.492 (Between visit 1 and 3: **p=0.042**)	F(2/360)=4 $P\eta^2$= 0.021 **P=0.021**

NP: Non progressors, P: progressors, $P\eta^2$: Partial η^2+ *for these results the assumption of homogeneity of variance was violated, as assessed by Levene's test for equality of variances*.

In the non-progressor group, only TJC28 and sick days showed significant decrease between first and last visit.

Between groups analysis showed significant differences at last visit for the following biomarkers -CCP2 +, RF +, ESR, EMS, TJC28, and number of joints PD grade ≥ 1. The difference in HAQ and sick days was non-significant (Figure 1, Table 1). A significant difference was also shown in all visits for CCP2 + and RF +, and at the second visit for TJC28.

For PD grade ≥ 1, differences at last visit *within progressor group* and *between groups* were only significant after selection of last visits < 3 months before progression.

Conclusion: These results show for the first time significant changes in relevant biomarkers prior to progression to IA with individual biomarkers having different trajectories. Clinical markers (EMS, TJC28, and HAQ) and ultrasound changed late, whilst immunological (CCP2 and RF values) and inflammation biomarkers (ESR) were different from baseline. These data provide valuable information for longitudinal monitoring of biomarkers, further analysis will show if these changes have predictive value for imminent progression to IA.

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POS0528 EARLY OPTIMISATION OF METHOTREXATE THERAPY PREVENTS DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: A SINGLE-CENTRE, RETROSPECTIVE COHORT STUDY

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Background: According to the current EULAR recommendations for the management of rheumatoid arthritis (RA), methotrexate (MTX) should be started as soon as RA is diagnosed and rapidly optimized to achieve remission. Nonetheless, it has been estimated that a difficult-to-treat (D2T) disease occurs in 3-10% of RA patients[1]. Herein, we hypothesized that D2T-RA can be prevented with an optimal MTX treatment in early stages.
Objectives: The main objective of this study was to demonstrate an association between successful optimization of MTX treatment within two years of RA diagnosis and development of a status of D2T-RA later in the disease course.
Methods: In 2016 we started a 'Refractory RA' clinic at the Rheumatology Unit, University of Padua, Italy. In this retrospective cohort study conducted in December 2021, we enrolled patients fulfilling both the ACR/EULAR 2010 criteria for RA and the EULAR definition of D2T-RA[2] diagnosed after 2000. We compared D2T-RA patients with non-D2T-RA controls from the same clinic having similar sex distribution and year of diagnosis. The primary outcome was the status of DT2-RA. The exposure was 'MTX optimization' after two years from diagnosis, as assessed with a numeric score (the sum of the following binary variables concerning MTX therapy: started within 3, 12 or 24 months from diagnosis; adequate dose (≥15 mg weekly); treatment duration≥6 months; early intolerance (≤3 months); range 0 to 6, with higher scores reflecting better optimization). We used multiple logistic regression analysis to examine the association (odds ratio (OR)) between MTX optimization scores and the outcome, controlling for potential modifiers (age, sex, body mass index, age at onset, and anti-citrullinated peptides antibodies [ACPA]).
Results: There were 37 DT2 RA patients and 107 non-D2T RA controls for the analysis (mean (SD) disease duration 12.8 (4.1) vs. 12.6 (4.6), p=0.621). Per protocol, gender (females 77.3 vs. 82.0%, p=0.247) and year of diagnosis (median [25th, 75th percentile]: 2008 [2004, 2011] vs. 2008 [2003, 2012]) were comparable between groups. Optimization of MTX therapy was poor overall, yet MTX optimization scores were significantly higher in D2T-RA than in non-D2T-RA patients (1.06 (0.21) vs. 0.56 (0.14), p<0.001). In multiple logistic regression, MTX optimization was protective against DT2-RA. Indeed, the likelihood of D2T-RA was decreased by 34%-54% according to MTX optimization scores. Other disease characteristics significantly associated with D2T-RA were an older age at diagnosis and female sex (Table 1). In December 2021 (last follow-up), D2T-RA patients were receiving a significantly higher daily dose of prednisone (4.3 (1.4) vs. 0.5 (0.2), p<0.001), and had a numerically greater burden of comorbidities (median 3 [1, 4] vs. 2 [1, 3], p=0.252) and disease activity (DAS28-ESR: 3.41 (0.40) vs. 2.6 (0.19), p=0.053) than non-D2T-RA patients.

Table 1. Early factors associated with difficult-to-treat rheumatoid arthritis (multivariable logistic regression)

	B	SE	P-value	Odds ratio	95% IC
MTX optimization score	-0.599	0.092	<0.001	0.549	0.459, 0.657
Age, years	0.033	0.008	<0.001	1.034	1.017, 1.051
Sex (female vs males)	0.723	0.287	0.012	2.061	1.174, 3.615
BMI, kg/m^2	-0.006	0.018	0.748	1.006	0.970, 1.043
ACPA (positive vs negative)	0.431	0.2450	0.079	1.539	0.952, 2.487

ACPA, anti-citrullinated peptide antibodies; B, unstandardised beta coefficient; BMI, body mass index; MTX, methotrexate; SE, standard error.

Conclusion: DT2-RA may be prevented by optimization of MTX therapy within two years of RA management.
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POS0529 LONG-TERM LOCAL JOINT DAMAGE PROGRESSION IN RHEUMATOID ARTHRITIS IS RELATED TO CUMULATIVE LOCAL CLINICAL JOINT INFLAMMATION

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Background: Previously we showed that joint inflammation in rheumatoid arthritis (RA) tends to recur in the same joint, suggesting local factors contributing to joint inflammation. In the same study population, we now investigated whether cumulative local joint inflammation is associated with local radiographic damage progression.
Objectives: To investigate whether there is an association between long-term cumulative joint swelling and progression of radiographic damage in treated-to-target patients with RA.
Methods: Data from the BeSt study were used, in which newly diagnosed patients with RA (ACR 1987 criteria) were treated-to-target (DAS ≤2.4) during 10 years. Local joint swelling (yes/no) was determined by clinical evaluation by trained nurses of all hand and foot joints at 3-monthly study visits. Yearly radiographs of hand and feet were scored for radiographic joint damage (Sharp-van der Heijde method) in random order by two independent readers who were blind for clinical results. Per joint, damage was expressed as the percentage of the maximum possible damage score, to account for differences in maximal scores per joint. Missing values were imputed using the last observation carried forward method. A generalized linear mixed model was used to assess the association between local joint swelling over time (i.e., percentage of study visits with observed local joint swelling) and degree of joint damage at the end of follow-up. Joints were clustered within patients. The model was adjusted for baseline damage and follow-up duration. To test the association between cumulative local joint swelling and joint damage as a local or a general inflammation effect, we did two analyses. First, we additionally adjusted the primary analysis for the mean disease activity score (DAS) over time. Second, we did a permutation test to study whether joint damage progression was better predicted by joint swelling in the joint itself than by joint swelling in randomly selected other joints, which is indicated by a p-value of <0.05.
Results: Of the 16,150 joints of 475 patients with at least one year follow-up with both radiographic and joint swelling assessment available, 16% (2,564) had radiographic joint damage (damage score ≥ 0.5) at the end of follow-up. Median (IQR) follow-up time was 10 (6-10) years. Of the joints with damage at the end of follow-up, 46% (1,163) was swollen at baseline, versus 36% (4,818) of the joints without damage. The median (IQR) percentage of visits at which joint swelling was observed was 6 (0-17) and 3 (0-8) for joints with and without joint damage respectively. We found a β of 0.13 (95% CI 0.12 to 0.14) for the association between cumulative local joint swelling and local progression, that is, with each 1% increase in the number of visits with local joint swelling, local radiographic joint damage progression on average increased with 0.13 percent. In an analysis with 10-years completers only (both baseline and year 10 damage score available, n = 9,520) we also found an association between cumulative local joint swelling and local radiographic damage (β 0.24, 95% CI 0.22 to 0.26). The association was also found in a subset of joints that were swollen at least once (β 0.20, 95% CI 0.18 to 0.22), indicating that joint damage is not only associated with ever-occurrence but also with the frequency of joint swelling. This association was found for both erosions (β 0.07, 95% CI 0.07 to 0.08) and joint space narrowing (β 0.21, 95% CI 0.19 to 0.22). The results of the primary analysis did not change after adjustment for DAS over time. The permutation test showed that local joint damage progression was better predicted by the frequency of joint swelling of that joint, than by joint swelling frequency of other joints (p<0.001). These results indicate a local, rather than a general, inflammation effect.
Conclusion: Cumulative local joint swelling over time is associated with joint damage progression in the same joint in treated-to-target (DAS ≤2.4) patients with RA. Our results indicate that this is a local effect rather than an effect of general disease activity.
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POS0530

MOLECULAR SIGNATURE IN SUSTAINED CLINICAL REMISSION INDUCED BY TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Clinical remission is a clinical goal in the treatment of rheumatoid arthritis (RA). Sustained, biologics-free and true remission is an unachieved goal of the "treat-to-target" approach in most patients, and the determinants for achievement are still unclear. In our recent prospective study using multiomics analysis, we proposed that a molecular signature in peripheral whole blood can be a predictor for subsequent disease activity or activities of daily living.[1] We also showed that tocilizumab (TCZ) induced deep clinical remission associated with gene expression in peripheral CD4+ T cells.[2]
Objectives: To consolidate and expand our hypothesis, we investigated the significance of molecular signatures in sustained remission in a larger scale cohort.
Methods: To build and validate the diagnostic model, we collected 73 peripheral blood samples from 30 patients with active RA, 30 patients in clinical remission induced by TCZ and 13 healthy controls. We then collected another 23 samples at a point before TCZ was halted due to sustained clinical remission. In total, 96 samples were analyzed by a multiomics platform, which included RNA sequencing and comprehensive proteomics.
Results: We first developed an optimized partial least-squares regression (PLSR) model using data from 5,436 genes and 255 proteins extracted in our previous model.[1] The odds ratio in the model clearly reflected the clinical state with high fidelity (Figure 1). In that study, TCZ induced nearly half of the patients with clinical remission into molecular remission, with an odds ratio of less than zero. To clarify the characteristics of the molecular signature at sustained clinical remission under TCZ continuation, 23 samples were applied to the model. The odds ratio was largely the same as that for clinical remission. Next, we investigated the association with disease flare after cessation of TCZ. At some points before cessation, the median odds ratio in patients who experienced disease flare after stopping TCZ tended to be higher than that in patients with sustained remission after stopping TCZ in the transcriptomics model but not in the proteomics model. Thirty-five differentially expressed genes were identified between the two groups under the conditions of a >1.5-fold change and P-value<0.05.

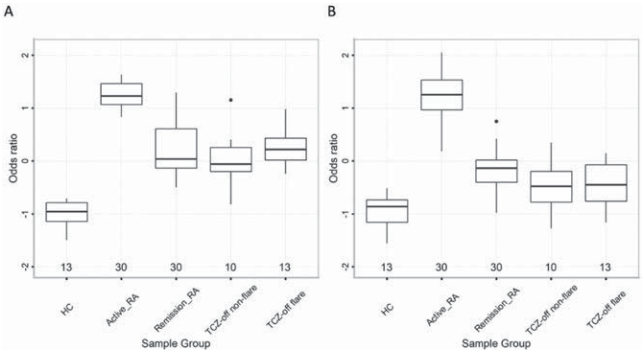

Figure 1. Odds ratio in the partial least-squares regression model using transcriptomics (A) and proteomics (B) data from rheumatoid arthritis and healthy control groups

Conclusion: Our larger scale study validated the idea in our previous study that TCZ induces molecular remission. A certain substantial gap associated with prognosis after quitting TCZ may exist as a molecular signature of sustained clinical remission induced by TCZ. These multiomics data sets enable us to understand sustained clinical remission at a molecular level.

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Graphs:

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POS0531

ABATACEPT DELAYS THE DEVELOPMENT OF RA– CLINICAL RESULTS AFTER 18 MONTHS FROM THE RANDOMIZED, PLACEBO-CONTROLLED ARIAA STUDY IN RA-AT RISK PATIENTS

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Background: The development of RA is described by a preclinical phase of autoimmunity, that precedes clinical disease. This autoimmune phase is characterized by the presence of anti-modified protein antibodies that recognize citrullinated proteins (ACPA). A subset of individuals with ACPA develops RA, i.e. those with imaging signs of subclinical inflammation in the joints. As T cell mediated B cell activation is a key step in developing autoimmunity and RA, interventions that target this process may be useful for preventing the onset of RA. In this context, abatacept seems being an attractive therapeutic tool as it interrupts the activation of T cells and has a favourable safety profile in the treatment of RA.
Objectives: To test whether treatment of abatacept, as compared to placebo, delays the onset of RA in ACPA positive individuals with a high risk to develop RA.
Methods: ARIAA is an international, randomized double-blinded placebo-controlled multi-center study in RA-at risk individuals, being ACPA positive and showing MRI signs of inflammation. The study was composed of a 6 months treatment phase with either abatacept s.c. 125 mg weekly or placebo and a 12 months observation phase with no treatment. Primary endpoint was the improvement of MRI inflammation after 6 months, secondary endpoints were the progression to RA after 6 and 18 months. The primary analysis was done on the ITT population and missing values were classified as treatment failures.
Results: Between November 2014 and December 2019 139 RA-at risk individuals were included into ARIAA by 14 study sites (11 in Germany, 1 in the Czech Republic and 2 in Spain). Of them, 100 patients were randomized to receive either abatacept or placebo. Two patients were excluded and 98 patients could be evaluated for efficacy and safety. The primary endpoint was met: 61% of abatacept and 31% of placebo treated individuals (p=0.0043) improved in MRI inflammation. Furthermore, only 4 patients (8.2%) in the abatacept group but 17 patients in the placebo group (34.7%) progressed to RA after 6 months (p= 0.0025). Even 1 year after cessation of treatment (18 months after inclusion) the number of patients progressing to RA was lower in the abatacept group (35%) than in the placebo group (57%; p=0.0421). With respect to safety, 12 serious adverse events (each one gastritis, cellulitis, pneumonia, tendinitis calcificans, rotator cuff syndrome,

cholelithiasis, peripheral artery disease, idiopathic pain syndrome, prostate cancer, penile neoplasm; trabeculectomy, cataract surgery) were reported, with only one (pneumonia) being considered to be related to treatment.
Conclusion: Abatacept significantly reduces subclinical joint inflammation and delays the development of RA in at-risk individuals.

Table 1.

	ABA	PBO	All
N	49	49	98
Females, N (%)	31 (63.3)	39 (79.6)	70 (71.4)
Age (ys); mean (±SD)	51.3 (±10.8)	48.5 (±12.6)	49.9 (±11.7)
SJC (N); mean (±SD)	0	0	0
TJC (N); mean (±SD)	3.06 (± 3.75)	3.51 (± 4.42)	3.29 (±4.08)
VAS Pain (mm) mean (±SD)	42.2 (± 27.1)	42.8 (± 33.2)	42.5 (± 30.2)
VAS PG (mm) mean (±SD	42.2 (±28.7)	43.0 (± 33.8)	42.6 (± 31.2)
MRI improvement, N (%)	30 (61.2)	15 (30.6)	45 (45.9)
RA at 6 months, N (%)	4 (8.2)	17 (34.7)	21 (21.4)
RA at 18 months, N (%)	17 (34.7)	28 (57.1)	45 (45.9)

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POS0532

DRUG RETENTION OF BIOLOGICS OR JAK INHIBITORS IN PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: RESULTS FROM THE ANSWER COHORT

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Background: Difficult-to-treat rheumatoid arthritis (D2T RA) is defined as RA in which disease activity is uncontrolled despite the use of two or more biologics or Janus kinase inhibitors (JAKi) with different mechanisms of action (MOA).
Objectives: To explore the optimal treatment strategy for D2T RA, we evaluated the drug retention, efficacy, and reasons for discontinuation of biologics or JAKi used for patients with D2T RA in a longitudinal multicenter cohort.
Methods: RA patients with clinical disease activity index (CDAI) >10 despite the use of at least two biologics or JAKi with different MOA and further treated with biologics or JAKi were included. The drug retention rates of biologics (TNFi, IL-6Ri, and CTLA4-Ig) or JAKi were estimated at 12 months using the Kaplan-Meier method and adjusted for potential confounders (age, sex, disease duration, concomitant MTX and PSL use, and the number of switched biologics or JAKi) using Cox proportional hazards models.
Results: A total of 251 treatment courses (TCs) from 167 patients were included (TNFi: 97 TCs, IL-6Ri: 67 TCs, CTLA4-Ig: 27 TCs, JAKi: 60 TCs). Baseline characteristics showed no difference in age, sex, disease duration, ACPA positivity, CDAI, and concomitant MTX and PSL use between the four groups. Drug retention excluding non-toxic reasons and remission was significantly higher in patients treated with JAKi or IL-6Ri than in patients treated with TNFi or CTLA4-Ig (P=0.00172). Multivariate analysis using Cox proportional hazards models demonstrated that discontinuation of the drug was associated with the use of TNFi or CTLA4-Ig (HR: 3.29, 95%CI: 1.15-9.42, P=0.027) and concomitant PSL use (HR: 1.14, 95%CI: 1.04-1.26, P=0.0084). In terms of disease activity evaluated with CDAI, no difference was observed between the four groups at 3 months (P=0.90), at 6 months (P=0.77), and at 12 months (P=0.75).
Conclusion: In patients with D2T RA, JAKi or IL-6Ri may have treatment advantages compared with TNFi or CTLA4-Ig.
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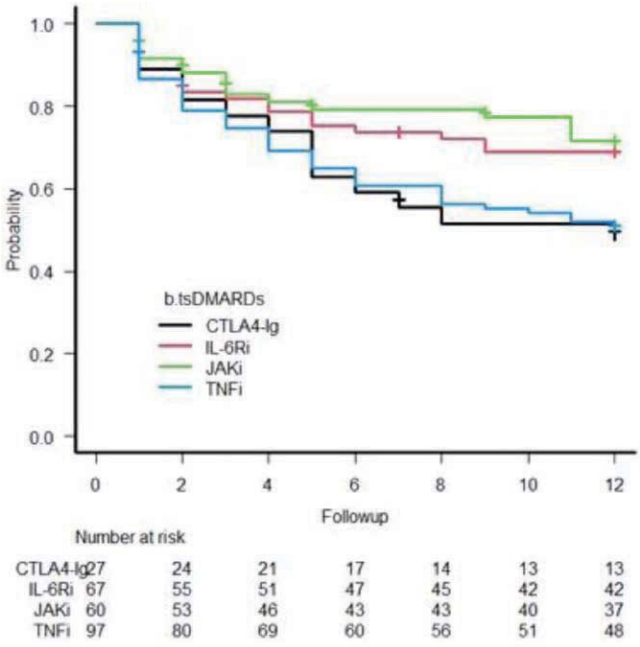

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POS0533 REPURPOSING FIB-4 SCORE IN RHEUMATOID ARTHRITIS: DATA FROM THE ESPOIR COHORT

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Background: The Fibrosis-4 (FIB4) score, including age, transaminases and platelets, can detect severe fibrosis (F3-F4) in patients with Non Alcoolic Steato Hepatitis (NASH) and could be of interest in the follow-up of patients with RA. Indeed, platelets contribute to the pathophysiology of RA, transaminases are used in the liver monitoring of our treatments. In addition, retrospective data suggested the association between FIB4 and mortality in RA (1).
Objectives: We aimed to evaluate the value of the FIB4 score as a prognostic factor in RA in the prospective ESPOIR cohort.
Methods: Patients of the ESPOIR cohort diagnosed with RA according to ACR-EULAR criteria were included in our analysis. The formula for the FIB-4 score is as follows: [Age (years) × ASAT (U/L)] / [Platelet count (10^9/L) × ALT (U/L)1/2]. The analyses were based on linear mixed-effects models with a random effect on the subject to account for repeated measures throughout time.
Results: 633 of the 813 patients included met the ACR/EULAR criteria for RA and had a calculable FIB4 score. Median FIB4 was 0.75 IQR (0.53-0.99) and 61 patients (9.6%) had a high FIB4 score at baseline. Baseline FIB4 was significantly higher in patients with a chronic alcohol consumption (p=0.021) or viral hepatitis (p<0.001). In multivariate analysis, including the main baseline prognostic factors for progression of RA (swollen Joint Count, CRP, Presence of ACPA, Rheumatoid Factor and modified Sharp score), FIB4 was not independently associated with progression of DAS28 during 10 years of follow-up, unlike baseline CRP and SJC. Baseline FIB4 was not associated with the modified Sharp score at 10-year follow-up unlike age and the presence of ACPA (Table 1). FIB4 was not associated with mortality (p=0.77) or major adverse cardiovascular events (p=0.22) during the 10-year follow-up. No significant change in FIB4 score over time was related to the use of NSAIDs, methotrexate, tocilizumab or other DMARDs.

Table 1. Associations of FIB4 score with DAS28 and modified Sharp score evolutions in multivariate analyses

Variable	Variables included in model	p-value
DAS28	Time	**<0.0001**
	Age	0.97
	Baseline number of swollen joints	**<0.0001**
	Baseline Rheumatoid Factor	0.51
evolution over time	Baseline ACPA (presence)	0.97
	Baseline CRP	**<0.0001**
	Baseline modified Sharp score > 0	0.15
	Baseline FIB4	0.26
Modified Sharp score	Time	0.052
	Age	**0.0005**
	Baseline number of swollen joints	0.38
evolution over time	Baseline Rheumatoid Factor	0.61
	Baseline ACPA (presence)	**0.012**
	Baseline CRP	0.84
	Baseline FIB4	0.25

Conclusion: Our study was the first to evaluate the value of FIB4 in a prospective cohort of RA patients. The present prospective cohort study with a 10-year follow-up did not find a prognostic role of FIB4 in RA, in contrast to previous retrospective studies. Reassuringly, FIB4 score was not increased by DMARD treatment after 10 years of follow-up, confirming the absence of long-term DMARD-related hepatotoxicity.

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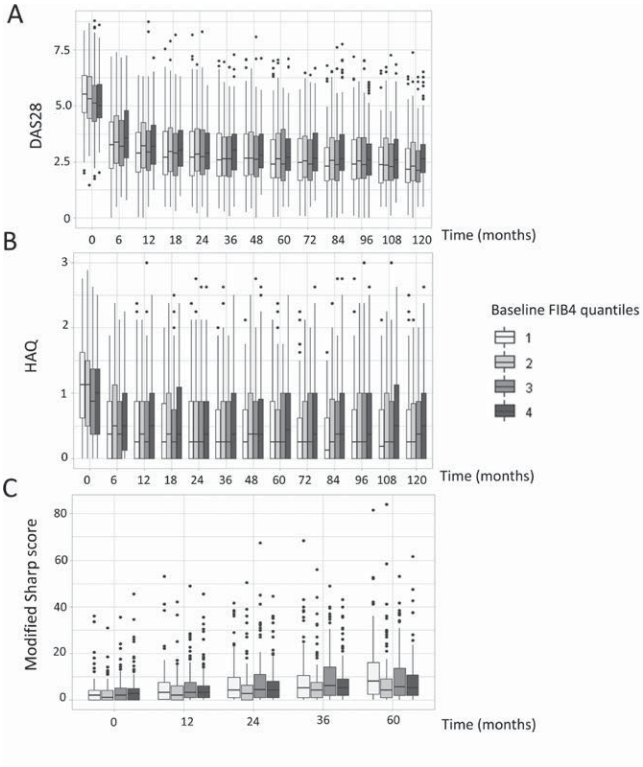

Figure 1. Impact of baseline FIB4 score on DAS28, HAQ and total modified-Sharp score over time.

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POS0534 TRAJECTORY ANALYSIS OF RHEUMATOID ARTHRITIS PROGRESSION USING CLINICAL DATA

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Background: Given the different symptom duration at first presentation of patients who are developing rheumatoid arthritis, we hypothesize that patients progress towards RA at a different speed, possibly going through different clinical stages. By identifying those stages and the pace at which patients transition from one to the other we could get a better understanding of the disease course as well as define a better timing for medical intervention.
Objectives: To identify clinically distinct disease stages and trajectories within Rheumatoid Arthritis.
Methods: We used clinical data (ESR, TJC, MCH, MCHC, MCV, leukocytes, thrombocytes, hemoglobin, and hematocrit) of 1595 outpatient visits in the first one and a half years of treatment of 426 patients. To facilitate trajectory comparison, we normalized data per patient. Building on previous work in the single-cell analysis field, we employed the Seurat[1] pipeline running an unsupervised cluster

analysis in the higher dimensions using the SLM (smart logical moving) algorithm. Different baseline definitions were explored; the date of first visit, RA diagnosis, and DMARD initiation. Using these different baselines we can examine whether a cluster contains mostly late or early visits.

Results: Using only clinical variables, we identified eleven distinct clinical clusters that represent early, mixed, and late clinical visits (Figure 1) with approximately 105, 220, and 300 days after baseline respectively.

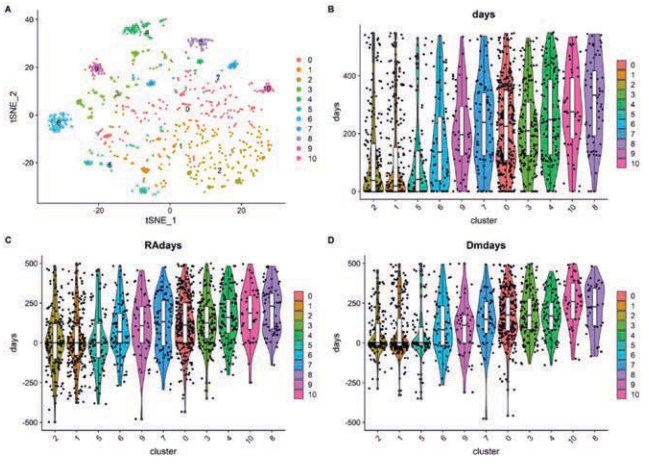

Figure 1. Violin plots for the different baselines. A) tSNE plot color indicating cluster, B) baseline defined by first clinic visit, C) baseline is RA diagnosis, D) baseline is DMARD initiation. The colors correspond to the different clusters. (y-axis: days since baseline, x-axis: cluster)

For each patient, we also had access to the number of days relative to the date of the first visit, RA diagnosis, and DMARD initiation that the different samples were taken from. Using this information we can show that some clusters are enriched for late time points while others are enriched for early time points (Figure 1B, C, and D), suggesting that the different clusters correspond to different disease stages. Considering the clinical values in the different clusters showed a lower disease activity in the later clusters than in the earlier clusters (Figure 2), which is in line with expected treatment efficacy. For example, in cluster 1 which is an early cluster, the average ESR was 28.6 in comparison with late cluster 8 which had an average ESR of 6.0. Interestingly, some clusters are defined by the different clinical variables even when they have a comparable number of days since baseline(Figure 2).

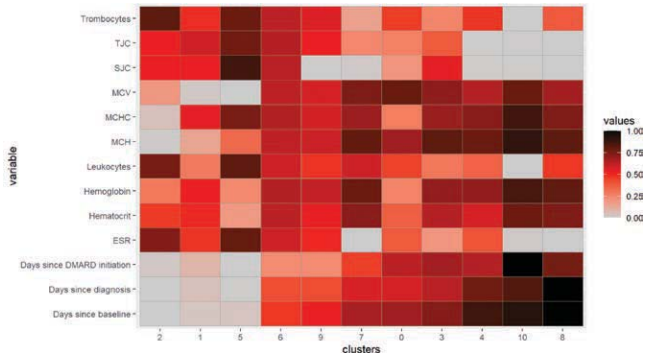

Figure 2. Interpreting the clusters and their values. ESR, Erythrocyte Sedimentation Rate; SJC, Swollen Joint Count; TJC, Tender Joint Count

Conclusion: With unsupervised clustering on clinical parameters, we can differentiate early and late outpatient visits even when the duration between first visit and RA diagnosis or DMARD initiation differed. Subsequently, the clustering identified different clinical groups amongst the first and later clinical visits. Our analysis is the first step into defining disease trajectories in patients who develop RA and represents a new way to integrate longitudinal patient data. The next step is to explore whether patients follow different trajectories.

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POS0535 OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING THERAPY WITH ETANERCEPT, ADALIMUMAB, OR JANUS KINASE INHIBITORS

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Background: Ongoing debate exists regarding the optimal sequence of tumor necrosis factor inhibitors and Janus kinase inhibitors (JAKis) in patients with rheumatoid arthritis (RA) as first-line biologic or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD) therapy following conventional therapies.

Objectives: To describe baseline characteristics, effectiveness, persistency, and treatment patterns among first-line b/tsDMARD-naive initiators of etanercept (ETN), adalimumab (ADA), or JAKis (tofacitinib, baricitinib, and upadacitinib).

Methods: Data on patients who initiated b/tsDMARD from 11/2012 to 6/2021 were obtained from the CorEvitas RA Registry, a prospective, multicenter, observational, disease-based registry. Patients ≥18 years with rheumatologist-diagnosed RA and 6- and/or 12-months' (M) follow-up were included. We report descriptive statistics at baseline, persistency on therapy, escalation/de-escalation of therapy, details on patterns of drug switching, and effectiveness outcomes using regression models adjusted for baseline covariates (demographic/socioeconomic/lifestyle characteristics, comorbidities, medication history, disease activity, and patient-reported outcomes). Outcomes were evaluated at 6M and 12M follow-up.

Results: First-line initiators of ETN, ADA, and JAKis with baseline and follow-up visits were identified: 803, 984, and 361 patients at 6M, respectively; 589, 749, and 264 patients at 12M, respectively. Baseline characteristics were similar among ETN, ADA, and JAKi initiators with the exception of disease duration, which was longer among first-line JAKi initiators (mean, 8.6 y) versus ETN (5.9 y) and ADA (5.8 y) initiators. Unadjusted mean improvement in Clinical Disease Activity Index (CDAI) was generally similar between groups at 6M and 12M (Table 1). Adjusted effectiveness results were similar at 6M and 12M (Figure 1). At 6M, 68% of ETN, 69% of ADA, and 67% of JAKi initiators remained on the same therapy; at 12M, 53% of ETN, 57% of ADA, and 57% of JAKi initiators remained on the same therapy. The frequency of switching to another b/tsDMARD was similar across initiators.

Table 1. Patient Description at Time of Initiation and Unadjusted Disease Activity Results

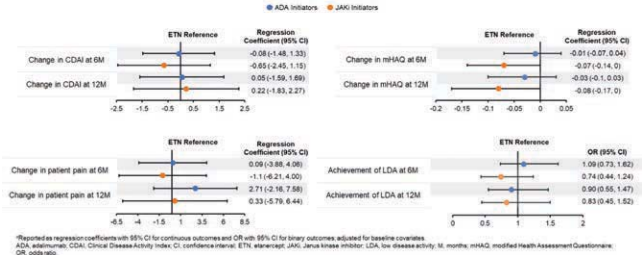
	ETN	ADA	JAKis
Age, years	54.4 (12.8)	55.5 (12.1)	60.9 (12.5)
Female, n (%)	666 (77)	843 (76)	303 (77)
BMI, kg/m^2	30.4 (7.6)	31.3 (7.9)	30.8 (7.6)
Duration of RA, years	5.9 (7.6)	5.8 (7.3)	8.6 (10.0)
BL disease activity[a]			
CDAI	19.9 (14.3)	18.9 (12.7)	18.8 (13.2)
mHAQ	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)
Patient pain[b]	48.0 (28.8)	49.2 (28.5)	45.2 (29.2)
Disease activity decrease from BL at 6M			
CDAI	6.9 (13.6)	6.4 (12.1)	4.7 (12.3)
mHAQ	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)
Patient pain[b]	9.7 (30.2)	10.6 (28.4)	8.9 (29.5)
Disease activity decrease from BL at 12M			
CDAI	7.4 (13.5)	6.1 (13.0)	5.1 (13.0)
mHAQ	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)
Patient pain[b]	8.8 (29.7)	8.7 (30.1)	7.5 (28.6)
Achievement of LDA[c], %			
6M	43.4	41.9	32.5
12M	41.0	39.6	38.3

[a]Baseline for combined population with 6M and 12M follow-up. [b](range: 0–100). [c]CDAI ≤10 among those with moderate or high disease activity at baseline.Data are mean (SD) unless otherwise specified.ADA, adalimumab; BL, baseline; CDAI, Clinical Disease Activity Index; ETN, etanercept; JAKis, Janus kinase inhibitors; LDA, low disease activity; M, months; mHAQ, modified Health Assessment Questionnaire; RA, rheumatoid arthritis; SD, standard deviation.

Conclusion: In this real-world study in patients initiating first-line b/tsDMARD therapy with ETN, ADA, or JAKis, we did not observe differences in

clinical effectiveness/patient-reported outcomes and treatment persistency at 6M and12M after treatment initiation.

Figure. Adjusted Mean Differences in Change in Effectiveness and Patient-Reported Outcomes Relative to Etanercept Initiators[a]



[a]Reported as regression coefficients with 95% CI for continuous outcomes and OR with 95% CI for binary outcomes; adjusted for baseline covariates.
ADA, adalimumab; CDAI, Clinical Disease Activity Index; CI, confidence interval; ETN, etanercept; JAKi, Janus kinase inhibitor; LDA, low disease activity; M, months; mHAQ, modified Health Assessment Questionnaire; OR, odds ratio.

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POS0536

REFINING THE SEROLOGICAL SCORES OF THE ACR/EULAR 2010 RHEUMATOID ARTHRITIS CLASSIFICATION CRITERIA: AN INTERNATIONAL STUDY

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Background: Rheumatoid factor (RF) and anti-cyclic citrullinated protein/peptide antibodies (ACPA) are included in the ACR/EULAR 2010 classification criteria for rheumatoid arthritis (RA)(1). Both markers are given the same weight in the criteria.
Objectives: As the performance characteristics differ significantly between RF and ACPA(2), we set out to refine the serological scores for RA classification.
Methods: Diagnostic samples from 398 RA patients and from 1073 diseased controls were evaluated with five RF assays (two RF IgM isotype-specific assays and three total RF assays) and five ACPA IgG assays from five different manufacturers.
Results: Firstly, we harmonized thresholds between manufacturers based on predefined specificity for low positive (at 92.5% specificity for RF and at 97.5% specificity ACPA) and high positive results (at 97.5% specificity RF and at 99.0% specificity for ACPA). Next, we determined likelihood ratios (LRs) for RF, ACPA, and combinations of both, for negative, low positive, and high positive results. The LR was higher for ACPA than for RF, for high positive results than for low positive results and for double positivity than for single positivity. Based on these data we refined the weights of serological scores for classification (Table 1).

Table 1. Refined weights of serological scores for RA classification

	RF negative	RF low positive	RF high positive
ACPA negative	0	1	1
ACPA low positive	2	3	3
ACPA high positive	3	4	4

Application of such refined serological weights significantly increased the area under the curve of receiver operating characteristics analysis to distinguish RA from controls, significantly reduced the serological scores in the controls as well as the number of RA misclassifications without affecting the diagnostic sensitivity. Besides, we showed that combining predefined specificity thresholds with the refined serological scoring, reduced manufacturer-dependent variability in RA classification impacting RA classification for controls from 18.0-29.0% by ACR/EULAR to 11.0-13.0% (significantly increasing specificity) and for RA patients from 67.8-74.0% to 67.6-71.5% (without significantly affecting sensitivity).
Conclusion: Serological weight factors for RA classification can be improved by taking into account the antibody type (RF versus ACPA), the antibody level, and single or combined positivity.

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POS0537

MORTALITY IN RHEUMATOID ARTHRITIS: CHANGING CAUSES AND PREDICTIVE FACTORS. STUDY OF A COHORT FOLLOWED PROSPECTIVELY

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Background: Patients with Rheumatoid Arthritis (RA) present an increased risk of mortality. In the last decades, mortality rates tended to decrease but cardiovascular (CV) events remained as the leading cause of death in most series (1).
Objectives: To assess mortality rates and leading causes of death, as well as predictors of mortality related to disease activity in a prospectively followed-up cohort of RA patients.
Methods: We conducted a prospective longitudinal study that included 673 RA patients from a single tertiary center. Univariate and multivariate Cox proportional hazards regression were used to identify predictors of mortality.
Results: We studied 673 patients with RA (75% women), mean age 61±13 years. The main general characteristics, CV risk factors, RA disease activity data and current treatment are summarized in the Table 1.

Table 1. Baseline characteristics of 673 RA patients

Age, years, (mean±sd)	61 ± 13
Female/Male, n (%)	505 (75) /168 (25)
Past or Current smoker, n (%)	338 (50)
Obesity, n (%)	226 (34)
Hypertension, n (%)	310 (46)
Diabetes Mellitus, n (%)	85 (13)
Dyslipidemia, n (%)	310 (46)
BMI, kg/m2 (mean±sd)	28 ± 6
Abdominal circumference, cm (mean±sd)	97 ± 15
Total/HDL/LDL cholesterol, mg/dl (mean±sd)	204±38/62±18/120 ± 31
Disease duration, years (median, [IQR])	13 [10-20]
CRP, mg/l (median, [IQR])	3.0 [0.8-7.0]
ESR, mm/ 1º hour (median, [IQR])	12 [5-21]
Rheumatoid factor/ ACPA, n (%)	376 (56) / 314 (48)
DAS28-ESR/ DAS28-PCR (mean±sd)	3.18 ± 1.41/3.00 ± 1.23
NSAIDs / Prednisone, n (%)	265 (39) /341 (51)
Prednisone dose, mg/day (median, [IQR])	5 (2.5-5)
c-DMARDS: Metotrexate/ Leflunomide/ Hydroxychloroquine/ Salazopyrin, n (%)	406 (60) /52 (8) / 178 (26) / 10 (1)
b-DMARDS: TNFi/ Tocilizumab/ Rituximab/ Abatacept, n (%)	88 (13) / 43 (6) / 13 (2) / 8 (1)
JAK inhibitors, n (%)	12 (2)

After a follow-up of 4,367 person-years (mean 6.4±1.4), 67 deaths were recorded. Considering all causes of mortality, the cumulative incidence was 14% (95% CI 11-18) with a mortality incidence rate of 0.015 (95% CI 0.012-0.020) patient/year. The main causes of mortality in decreasing order of frequency were infections (N=23) (34%), incidence rate-IR: 0.005 [95% CI 0.003-0.008]), cancer (N=18) (27%), IR: 0.004 [95% CI 0.002-0.007]), CV events (N= 12) (18%), IR: 0.003 [95% CI 0.001-0.005]), respiratory diseases (N=2) (3%), IR: 0.0005 [95% CI 0.00007-0.002] and other causes (N=12) (18%), IR: 0.003 [95% CI 0.001-0.005l]. The statistically significant predictive factors of mortality in the univariate analysis were male gender (HR 1.97[95%CI 1.20-3.21, p=0.007), abdominal circumference (HR 1.03 [95% CI 1.01-1.05], p=0,0006), diabetes (HR 2.85 [95%CI 1.68-4.86], p<0.001) and hypertension (HR 2.92 [95%CI 1.73-4.94], p<0.001). Also, baseline data of variables associated with disease activity such as increased CRP, ESR, DAS28-CRP, DAS28-ESR were predictors of mortality (Figure 1). Disease related parameters were adjusted by CV risk factors in a multivariate analysis. Following this procedure, the predictive factors that reached statistical significance; (Hazard Ratio [95%CI]), were an increased in DAS28-VSG (1.40 [1.07-1.83], p=0.016), DAS- 28-PCR (1.40 [1.07-1.83], p=0.016), CRP (1.02 [1.01-1.05] p=0.002), and ESR (1.03 [1.01-1.05], p=<0.001) (Figure 1).

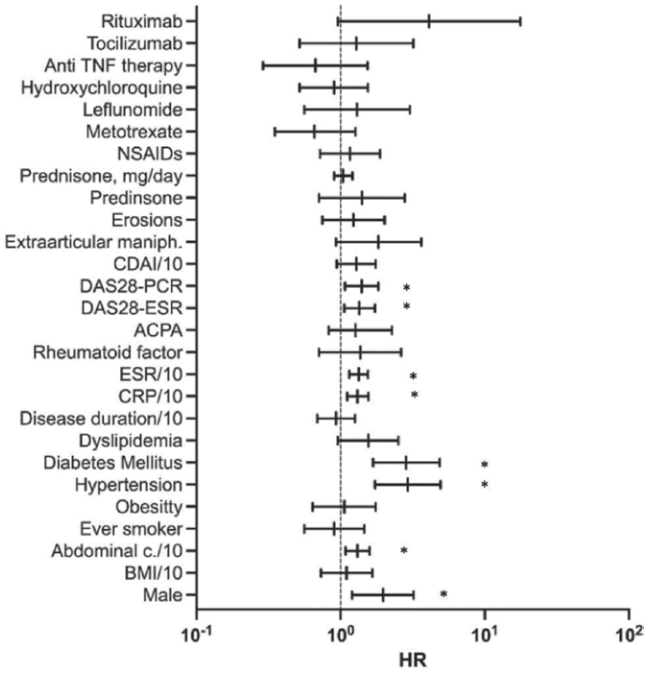

Figure 1. Forest Plot of mortality (Univariate and multivariate analysis). *Results expressed in logarithmic scale. Multivariate analysis: Disease activity related parameters adjusted by age, gender, disease duration, smoker, diabetes, hypertension and abdominal circumference. CDAI, ESR and CPR expressed value/10. (*) p<0.05.*

Conclusion: In a cohort of patients with RA followed prospectively in a tertiary hospital, infections and malignancies are the main cause of mortality rather than CV events. Disease activity parameters are associated with an increased risk of mortality in these patients with RA.

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POS0538

PREDICTING VALUE OF CIRCULATING SEMAPHORIN 4A FOR RHEUMATOID ARTHRITIS PROGRESSION

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Background: The lack of validated tools to predict rheumatoid arthritis (RA) disease course warrants the development of new reliable biomarkers. We have previously detected increased SEMA4A expression in endothelial cells, synovial tissue, and serum of patients with RA. In addition, SEMA4A serum levels correlated with multiple clinical, biological, and power doppler ultrasound markers of disease activity and angiogenesis (1).
Objectives: To evaluate the merit of circulating semaphorin 4A (SEMA4A) for the prediction of disease progression in RA patients.
Methods: Prospective monocentric observational study including consecutive RA patients between May 2016 and February 2018 with available SEMA4A concentrations, measured by quantitative ELISAs (Coud-Clone Corp, Katy, TX). Increased SEMA4A concentrations were defined as values >94 ng/mL, as previously reported (*1*). Patients were followed up on an annual basis until August 2021. Primary endpoints were the occurrence of patient-reported flares with swollen joints and the necessity to initiate or change a targeted biologic or synthetic disease-modifying anti-rheumatic drugs.
Results: A total of 101 patients (85 females, 84%) were included, with a mean age of 58±13 years and a mean disease duration of 14±11 years. During a follow-up period of 41±15 months, disease flares occurred in 38 patients and targeted therapy was added or modified in 26 patients because of insufficient disease control. Increased baseline SEMA4A levels were predictive of flares and treatment escalation (hazard ratio, HR: 2.43, 95% confidence interval, CI 1.27-4.68 and 2.73, 95%CI 1.24-5.96, respectively) (Figure 1**A-B**). Multivariate

Cox analyses confirmed that SEMA4A was an independent predictors of flares and treatment escalation (HR: 2.12, 95%CI 1.04-4.32 and 2.71, 95%CI1.14-6.43, respectively), and revealed that DAS28-CRP and synovial hyperhemia were independent predictors of flares. Baseline age, disease duration, ACPA or RF positivity, smoking status, presence of erosions, line of targeted DMARDs, treatment with corticosteroids and CRP levels were not predictive of these outcomes. SEMA4A remained predictive of flares and treatment escalation in the 58 patients with a DAS28 <3.2 at baseline (HR: 3.68, 95%CI 1.33-10.17 and 3.50, 95%CI 1.02-12.01, respectively). Baseline SEMA4A levels also identified more active and difficult to treat patients who maintained higher mean DAS28-CRP values during the follow-up period (Figure 1**C**). The highest predictive value of flares and treatment escalation was obtained with the combination of increased circulating SEMA4A and/or DAS28-CRP>3.2 and/or the presence of synovial hyperemia on power-doppler ultrasound (HR:4.88, 95%CI 1.50-15.89 and 10.42, 95%CI 1.41-76.94, respectively).

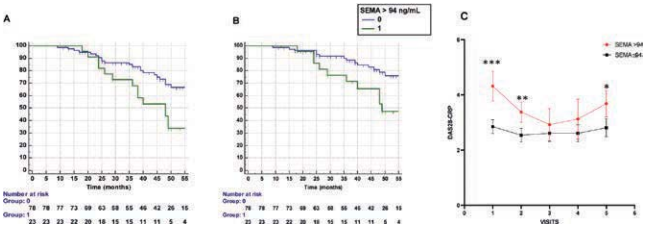

Figure 1. A-C: Predictive value of SEMA4A for the progression of rheumatoid arthritis. A, Disease flare-free survival according to circulating SEMA4A concentrations (≤ or > 94 ng/mL). B, Time to treatment escalation according to circulating SEMA4A concentrations (≤ or > 94 ng/mL). C, Course of the DAS28-CRP during the follow-up period according to baseline SEMA4A concentrations (≤ or > 94 ng/mL). All data are shown as the mean ± SEM. * p<0.05, ** p<0.01 and *** p<0.001, determined by Student's t test.

Conclusion: Circulating SEMA4A was a robust biomarker of disease progression in this cohort, complementary of the DAS28 and synovial hyperemia on power-doppler ultrasound. These results need to be confirmed in replication cohorts.

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POS0539

LATE ONSET RHEUMATOID ARTHRITIS HAS A SIMILAR REMISSION RATE AS YOUNGER ONSET RHEUMATOID ARTHRITIS: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE

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Background: The prevalence of rheumatoid arthritis (RA) in persons 60 years or older is estimated to be 2%. Late onset rheumatoid arthritis (LORA) is a sub-group of patients traditionally defined as onset of RA after the age of 60 years. Compared to younger onset rheumatoid arthritis (YORA) which occurs before the age of 60 years, LORA has unique characteristics and disease manifestations. The prognosis of LORA patients is less clear based on prior studies.

Objectives: We compared the clinical characteristics, time to remission and treatment regimen at remission between LORA and YORA patients.

Methods: The Ontario Best Practices Research Initiative (OBRI) is a clinical registry of RA patients followed in routine care. This analysis used the OBRI database from 2008 to 2020. Patients were included if they had active RA disease (≥1 swollen joint) and were enrolled in the study within 1 year of diagnosis. LORA was defined as diagnosis of RA after age of 60, YORA as under age of 60. Remission was defined by Disease Activity Score 28 (DAS28) ≤2.6. A multivariable Cox proportional hazards model was used to estimate time to remission.

Results: The Ontario Best Practices Research Initiative (OBRI) is a clinical registry of RA patients followed in routine care. This analysis used the OBRI database from 2008 to 2020. Patients were included if they had active RA disease (≥1 swollen joint) and were enrolled in the study within 1 year of diagnosis. LORA was defined as diagnosis of RA after age of 60, YORA as under age of 60. Remission was defined by Disease Activity Score 28 (DAS28) ≤2.6. A multivariable Cox proportional hazards model was used to estimate time to remission.

Table 1. Cox proportional hazards model predicting time to remission

	Univariate		Multivariable	
Baseline characteristics	HR (95% CI)	p-value	HR (95% CI)	p-value
Sociodemographic				
Female gender	0.71 (0.60-0.84)	<.0001	0.87 (0.70-1.09)	0.2256
Post-secondary education	1.26 (1.08-1.47)	0.0039	1.04 (0.87-0.70)	0.6744
Ever smoked	0.87 (0.75-1.02)	0.076	0.93 (0.77-1.12)	0.4269
RA family history	0.89 (0.74-1.07)	0.2176	0.87 (0.70-1.70)	0.1817
Disease characteristics				
Positive rheumatoid factor	1.01 (0.85-1.19)	0.9182	0.94 (0.78-1.14)	0.5381
*HAQ-DI	0.62 (0.55-0.69)	<.0001	0.71 (0.61-0.84)	<.0001
Morning stiffness (>30 mins)	0.71 (0.61-0.83)	<.0001	0.89 (0.73-1.08)	0.2366
Joint erosion	0.94 (0.77-1.14)	0.5224	0.87 (0.70-1.08)	0.1954
DAS28	0.77 (0.72-0.82)	<.0001	0.88 (0.80-0.96)	0.0048
Number of comorbidities	0.83 (0.77-0.88)	<.0001	0.88 (0.81-0.95)	0.0019
Treatment				
Biologic or JAK inhibitor (time variant)	0.86 (0.71-1.03)	0.09	1.53 (0.63-3.69)	0.3485
LORA	0.83 (0.71-0.97)	0.0194	1.10 (0.90-1.34)	0.3593

*HAQ-DI = health assessment questionnaire disability index

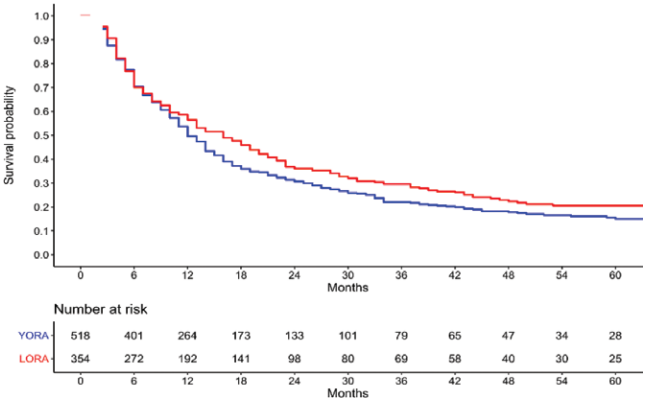

Figure 1. Kaplan Meier survival curve of time to remission.

Conclusion: LORA and YORA patients had similar prognosis in terms of time to remission. At remission, LORA patients were more likely to be on a single csDMARD without biologic or JAK inhibitor. Clinicians should take the same approach for all RA patients targeting remission regardless of age of onset.

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POS0540

CLINICAL OUTCOMES ASSOCIATED WITH GLUCOCORTICOID DISCONTINUATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB OR ADALIMUMAB

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Background: Patients (pts) with rheumatoid arthritis (RA) are often administered glucocorticoids (GCs) as bridging therapy when initiating or adjusting disease-modifying antirheumatic drugs (DMARDs). Due to their systemic effects, short-term use of GCs at the lowest possible dose is recommended with rapid tapering.[1]
Objectives: We describe GC discontinuation patterns and the associated clinical outcomes in pts with RA receiving upadacitinib (UPA) or adalimumab (ADA).
Methods: SELECT-COMPARE is a randomized phase 3 trial of UPA vs placebo and ADA with a 48-week (wk) double-blind treatment period and a 10-year long-term extension in pts with RA receiving concomitant methotrexate (MTX) who had an inadequate response to MTX.[2] Background GCs (≤10 mg/day prednisone or equivalent) were permitted and could be tapered or discontinued starting at wk 26 per physician discretion. This post hoc analysis included pts who received ≥1 dose of UPA 15 mg once daily or ADA 40 mg every other wk while on concomitant GCs at baseline. The proportion of pts with disease worsening (Clinical Disease Activity Index [CDAI] >2 and Disease Activity Score 28-joint count C-reactive protein [DAS28-CRP] >0.6) following GC discontinuation through follow-up is described. Maintenance of clinical response, including remission and low disease activity based on CDAI ≤2.8 and ≤10, respectively, as well as DAS28-CRP <2.6 and ≤3.2, were assessed among pts who discontinued GCs. Adverse events (AEs) were assessed before and after GC discontinuation through follow-up. Data were analyzed descriptively.
Results: Of 1,629 pts randomized, 978 (60%) used GCs at baseline; 128 (13%) discontinued use at/after wk 26 (UPA, n=97; ADA, n=31). Baseline demographics and clinical characteristics were broadly similar between pts who continued or discontinued GCs. Median follow-up time after GC discontinuation was 60 wks for UPA and 84 wks for ADA. At the time of GC discontinuation, a numerically higher proportion of pts treated with UPA vs ADA were in disease control (CDAI ≤2.8: 55% vs 32%; CDAI ≤10: 85% vs 68%; DAS28-CRP <2.6: 71% vs 48%; DAS28-CRP ≤3.2: 87% vs 62%) (Table 1). Few pts receiving UPA experienced disease worsening following GC discontinuation (1% CDAI increase >2; 7% DAS28-CRP increase >0.6) and none on ADA (Table 1). At 6 months follow-up after GC discontinuation, most pts treated with UPA and ADA maintained CDAI ≤2.8 (74% vs 88%) and ≤10 (92% vs 95%) and DAS28-CRP <2.6 (89% vs 85%) and ≤3.2 (91% vs 94%), respectively (Table 1). GCs were reintroduced (albeit usually temporarily) in 14% of pts on UPA and 19% on ADA (Figure 1). AEs were generally similar across treatment groups. Rates of serious infection before and after GC discontinuation were 0.8 (95% CI 0.0–4.2) and 1.5 (0.2–5.4) events per 100 patient-years (E/100 PY) for UPA and 7.7 (1.6–22.4) and 0 E/100 PY for ADA, respectively. Interpretation of results is limited by small pt numbers and different exposure times.
Conclusion: In pts who achieved disease control and discontinued GCs, disease control was maintained in almost all without worsening disease activity over time following GC discontinuation.

Table 1. Clinical outcomes of pts who discontinued GCs at/after wk 26

	Pts who discontinued GCs N=128	
n/N (%)	UPA n=97	ADA n=31
CDAI		
≤10 at discontinuation	79/93 (85%)	21/31 (68%)
Maintained at 6 months post discontinuation[a]	61/66 (92%)	18/19 (95%)
≤2.8 at withdrawal	51/93 (55%)	10/31 (32%)
Maintained at 6 months post discontinuation[a]	32/43 (74%)	7/8 (88%)
Increase >2 any visit after withdrawal	1/93 (1%)	0
DAS28-CRP		
≤3.2 at withdrawal	78/90 (87%)	18/29 (62%)
Maintained at 6 months post discontinuation[a]	58/64 (91%)	15/16 (94%)
<2.6 at withdrawal	64/90 (71%)	14/29 (48%)
Maintained at 6 months post discontinuation[a]	47/53 (89%)	11/13 (85%)
Increase >0.6 any visit after withdrawal	6/92 (7%)	0

[a]As a proportion of pts achieving outcome at GC discontinuation and with observed data 6 months post GC discontinuation.

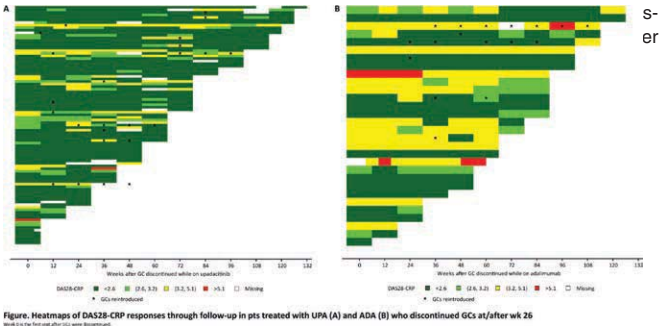

Figure. Heatmaps of DAS28-CRP responses through follow-up in pts treated with UPA (A) and ADA (B) who discontinued GCs at/after wk 26

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POS0541

PREDICTORS OF REMISSION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH UPADACITINIB OR ADALIMUMAB IN THE SELECT-COMPARE PHASE 3 STUDY: CLINICAL STATUS AT WEEK 12, BUT NOT STANDARD LABORATORY MEASURES, PROVIDES THE BEST CURRENT PREDICTOR OF REMISSION AT WEEK 26

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Background: Upadacitinib (UPA, 15 mg QD), an oral JAK1 selective inhibitor, showed greater efficacy compared to adalimumab (ADA, 40 mg EOW) at week 12 in patients with active rheumatoid arthritis (RA) on background methotrexate (MTX) in the SELECT-COMPARE phase 3 study[1]. Treatment with UPA compared to ADA resulted in a larger proportion of patients reaching CDAI Remission (REM) at week 26 (23% vs. 14%, p-value ≤ 0.001). Because remission is the goal in managing RA, it is of clinical relevance to identify early during the treatment course who might be able to achieve this state. It has been reported that early response to therapy with UPA was associated with achieving CDAI REM at week 26[2]. In parallel, it has been reported that reduction in monocyte can predict DAS28-ESR REM in RA patients treated with anti-TNF therapy[3]. However, the relative predictive values of clinical and standard laboratory measures have not been compared side-by-side.
Objectives: To determine post-hoc the relative predictive values of selected clinical and standard laboratory measures collected at week 12 for identifying RA patients who will be in CDAI REM at week 26 upon treatment with UPA or ADA.

Methods: Clinical (CDAI, SDAI, and DAS28-CRP) and laboratory data (CRP, ESR, CBC with differential, and Lipids) for all available patients enrolled in the SELECT-COMPARE phase 3 study were included in this post-hoc analysis (UPA: n =623 [CDAI REM at wk26 = 23.8%]; ADA: n = 316 [CDAI REM at wk 26 = 14.2%]). Patients who switched treatment between weeks 14 and 22 due to not reaching at least 20% improvement in tender and swollen joints were classified as non-responders for CDAI REM at week 26. The predictive value of clinical and laboratory endpoints recorded at week 12 for determining CDAI REM status at week 26 was assessed by univariate logistic regression. We report the performance of each model as ROC AUC with a cutoff of 0.75 for meaningful predictive value.
Results: For both patients treated with UPA and those treated with ADA, clinical disease activity status measures (CDAI, SDAI, and DAS28-CRP) and relative change in disease activity measures (Percent Change [PCHG] in CDAI, PCHG in DAS28-CRP, and PCHG in SDAI) at week 12 resulted in the highest predictive performance for determining CDAI REM status at week 26 (Figure 1). In contrast, none of the selected standard laboratory measures (CRP, ESR, CBC with differential, and Lipids) reached a meaningful predictive value (ROC AUC < 0.75). Of note, cell numbers and changes in cell numbers (including Neutrophils Lymphocytes, Basophils, Eosinophils, and Monocytes) at week 12 had no meaningful predictive value for determining CDAI REM at week 26.

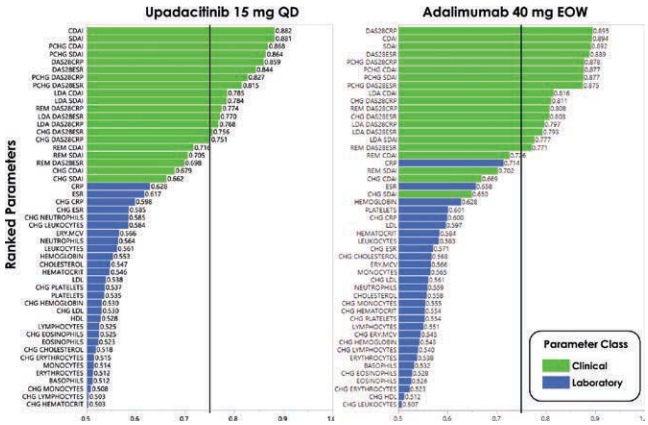

Figure 1. Univariate Logistic Models to Predict CDAI REM at Week 26 in Active RA Patients who had an Inadequate Response to MTX: ROC Analysis AUC. **Legend**: All evaluated parameters were recorded at Week 12; CHG = Change from Baseline to Week 12; PCHG = Percent Change from Baseline to Week 12

Conclusion: This analysis suggests that standard laboratory measures (CRP, ESR, CBC with differential, and Cholesterol) at week 12 do not represent useful predictors for REM at week 26 in csDMARD-IR RA patients. In particular, blood cell numbers and the changes in these measures at week 12 do not provide additional predictive value in our analyses, contrasting with the results from Amarnani and colleagues[3]. Hence, clinical disease activity levels and changes in these measures at week 12 remain adequate predictors of CDAI REM at week 26. Still, the absolute predictive performance of clinical measures remains suboptimal, highlighting the need to dedicate continued efforts to identify and validate improved predictors of long-term REM in RA.

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Disclosure of Interests: Thierry Sornasse Shareholder of: AbbVie, Employee of: AbbVie, Fang Cai Shareholder of: AbbVie, Employee of: AbbVie, Feng Hong Shareholder of: AbbVie, Employee of: AbbVie, Samuel Anyanwu Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie, Marwan Bukhari Speakers bureau: Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Sanofi-aventis, Eli-Lilly, Janssen, Amgen, Novartis and Gilead, Paid instructor for: honoraria from educational groups revalidaid and TREG consultants.

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POS0542

MACHINE LEARNING PREDICTS RESPONSE TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS: RESULTS ON THE ESPOIR AND ABIRISK COHORTS

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Background: Thirteen drugs with different mechanisms of action may be considered to treat patients with methotrexate (MTX) inadequate response in rheumatoid arthritis (RA). TNF inhibitors (TNFi) are frequently the first choice in this situation. Unfortunately, 30% to 40% of RA patients do not respond to TNFi, resulting in a delay for beginning the appropriate targeted DMARD (tDMARD). Predicting the patient response to TNFi before prescribing the treatment is therefore a major goal and could help physicians to prescribe a tDMARD suited to the patient.
Objectives: We aimed to build machine learning models based on simple clinical and biological data to predict patient response to TNFi.
Methods: We used data from the ESPOIR early arthritis cohort (1) to train the models, and the ABIRISK cohort (2) to validate the results. We included patients that fulfilled the EULAR/ACR 2010 criteria and that were treated with a TNFi. The models take as inputs patient's characteristics at treatment initiation and predicts the therapeutic response, defined as the EULAR response 12 months (+/- 6 months) after treatment initiation. We compared the performances of four models (Linear Regression, Random Forest, XGBoost, and Catboost) on the training set by cross-validated them using the Area Under the ROC Curve (AUCROC). The best model was then evaluated on the validation dataset (ABIRISK cohort). We conducted the methodology both on all TNFi together and on etanercept and monoclonal anti-TNF antibodies separated. We analyzed how clinical and biological variables impacted response to provide explainability of the prediction.
Results: We included 164 patients from the ESPOIR cohort and 118 patients from the ABIRISK cohort. Better results were obtained when etanercept and monoclonal anti-TNF antibodies were analyzed separately. These models predict a probability for a patient to respond to TNFi. This probability is compared to a decision threshold to obtain the binary outcome. Two decision thresholds were tested. The first prioritizes a high confidence when identifying responders (Strategy 1) while the second prioritizes a high confidence when identifying non-responders (Strategy 2). The model's results are presented in Table 1.
Using SHAP, we were able to analyze how each variable impacted the predictions. In particular, a DAS28 around 5 had the highest positive impact on response. Higher and lower values of DAS28 had either less impact or even negative impact on the patient response to TNFi treatment (Figure 1). This allows to identify non-linear relations between variables and patient response.
Conclusion: The machine learning models developed in this study can predict RA patients' response to TNFi using exclusively data available in clinical routine. These models also allow to analyze how these variables are used to predict response. Along with similar models for other tDMARDs, such algorithms could lead to a personalized therapeutic strategy.

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Figure 1: Each point represents a patient which is plotted with his DAS 28 on horizontal axis; and positive or negative influence on probability response to TNFi treatment on vertical axis.

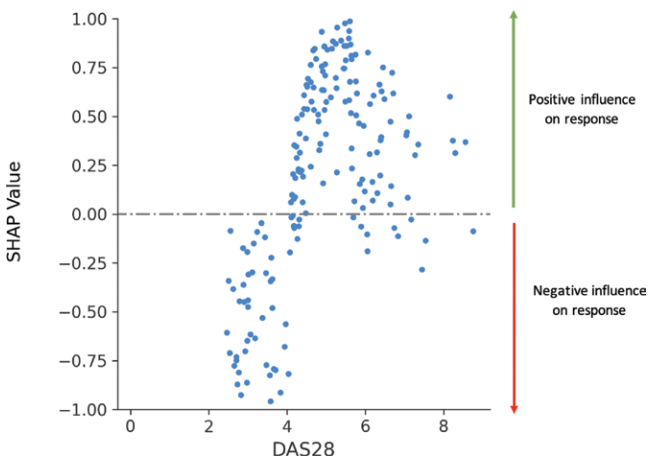

Table 1. Sensitivity, Specificity, PPV and NPV are computed on the ABIRISK validation cohort for each strategy

Drug	AUC (ESPOIR)	AUC (ABIRA)	STRATEGY 1 (high confidence in response) SensitivitY	Specificity	PPV	NPV	STRATEGY 2 (high confidence in non-response) Sensitivity	Specificity	PPV	NPV
Overall TNFi	0.72 (0.68-0.73)	0.65 (0.54 - 0.75)	18% (10%-27%)	**91% (82%-98%)**	**76% (54%-95%)**	42% (32%-51%)	**90% (83%-96%)**	30% (18%-44%)	67% (58%-76%	**67% (45%-86%**
Etanercept	0.74 (0.68-0.75)	0.70 (0.57- 0.82)	60% (44%-74%)	**73% (55%-89%)**	**78% (63%-92%)**	53% (36%-69%)	**95% (88%-100%)**	15% (4%-30%)	64% (52%-76%)	**67% (20%-100%)**
Monoclonal anti-TNF antibodies	0.74 (0.69-0.77)	0.71 (0.55-0.86)	37% (20%-55%)	**95% (83%-100%)**	**92% (73%-100%)**	50% (35%-66%)	**90% (78%-100%)**	40% (19%-62%)	69% (54%-84%)	**73% (44%-100%)**

[2] Anon. ABIRISK Anti-Biopharmaceutical Immunization: Prediction and Analysis of Clinical Relevance to Minimize the RISK. 2019.

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SB was supported by FHU CARE.
Disclosure of Interests: None declared.

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POS0543 MACHINE LEARNING PREDICTS RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS: RESULTS ON THE ESPOIR, T-REACH AND LEIDEN COHORTS

V. Bouget[1], J. Duquesne[1], P. H. Cournède[2], B. Fautrel[3], F. Guillemin[4], P. De Jong[5], J. Heutz[5], A. Van der Helm-van Mil[6], M. Verstappen[6], S. Bitoun[7], X. Mariette[7]. *[1]Scienta Lab, Research department, Paris, France; [2]Université Paris-Saclay, CentraleSupélec, Lab of mathematics and computer science (MICS), Gif-sur-Yvette, France; [3]Sorbonne Université – Assistance Publique Hôpitaux de Paris, Groupe Hospitalier Pitié Salpêtrière, Service de Rhumatologie, Paris, France; [4]Université de Lorraine, APEMAC, Nancy, France; [5]University Medical Center, Department of Rheumatology, Rotterdam, Netherlands; [6]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands; [7]Université Paris Saclay, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service de Rhumatologie, Le Kremlin-Bicêtre, France*

Background: Methotrexate (MTX) is the first line of treatment for rheumatoid arthritis (RA) patients. Unfortunately, 30% to 40% of RA patients do not respond to MTX, resulting in uncontrolled joint pain and potential joints destruction. At the same time, many efficient second-line treatments exist and can be given to the inadequate responder patients. Predicting patient response to MTX before prescribing the treatment is therefore a major goal and could enable physicians to directly prescribe second-line treatments if inadequate response to MTX is predicted.
Objectives: We aimed to build machine learning models based on simple clinical and biological data to predict patient response to MTX.
Methods: We used data from the ESPOIR early arthritis (1) and Leiden cohorts (2) to train the models, and the tREACH cohort to validate the results. We included patients that fulfilled the EULAR/ACR 2010 criteria and that were treated with MTX in monotherapy as their first treatment for RA. The models take as inputs patient's characteristics at treatment initiation and predict the therapeutic response, defined as the EULAR response 3 to 12 months after treatment initiation. We evaluated four missing data imputation methods (median, mean, MICE, KNN); we used the backward feature selection algorithm to select the most relevant variables; and compared the performances of four models (Linear Regression, Random Forest, XGBoost, and Catboost) on the training set by cross-validated them using the Area Under the ROC Curve (AUCROC). The best model was then evaluated on the validation dataset.
Results: We included 435 patients from the ESPOIR cohort, 243 patients from the Leiden cohort and 143 patients from the t-REACH cohort. Results of the model are displayed in Table 1. The variables automatically selected to perform prediction were Sex, DAS28, White blood cells, AST, ALT and lymphocytes. Our model performs well on unseen data, this result comes from the fact that we included two different cohorts in our training set which reduces the overfitting of our model and helps him generalize. Our model predicts a probability for a patient to respond to MTX. This probability is compared to a decision threshold to obtain the final binary outcome. Two decision thresholds were tested. The first prioritizes a high confidence when identifying responders (Strategy 1) while the second prioritizes a high confidence when identifying non-responders (Strategy 2). This second strategy would enable physicians to identify highly probable inadequate responders to methotrexate and propose them directly a targeted DMARD such as TNF inhibitors, while still treating more than 70% of patients with MTX as first-line treatment.
Conclusion: The machine learning models developed in this study can predict RA patients' response to methotrexate with a good accuracy exclusively using data available in clinical routine. It paves the way for personalized therapeutic strategies in rheumatoid arthritis.

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POS0544 REMOTE MONITORING TOOLS IN RA PATIENTS: FACIT-FATIGUE AND HAQ

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Background: The need to avoid the transmission of COVID19 infection has forced to promote teleconsultations for rheumatic diseases follow-up. However, remote monitoring for rheumatic diseases which require clinical examination, as rheumatoid arthritis (RA), may affect to the evaluation of clinical activity, including the biological therapies follow-up. Due to that, count on tools as Patient Reported Outcomes (PROs) could help the remote monitoring of patients when it is not advisable their physical presence in health centers, being a great help in RA control.
Objectives: We aim to assess the association among the tiredness, disability and pain perception with the clinical activity in RA patients.
Methods: We performed a prospective observational study of three months of follow-up in RA patients (ACR/EULAR 2010) who are newly on biological or anti-JAK therapy. A basal visit and 1, 3 months follow-up visits were conducted. We analyzed changes during follow-up in the PROs parameters reported by patients through FACIT-fatigue and HAQ questionnaires, as well as pain VAS (0-10). Moreover we measured clinical activity through Das28, Das28-CRP, SDAI and CDAI index.
Results: We included 60 patients (83.3% female), with a mean age of 55 (13) and mean disease evolution of 13 (11) years. At the basal visit, 55% of them exhibited increased levels of CRP and the 48.3% of ESR, showing moderate or high clinical activity the 83.3% of the total patients.

Table 1. Sensitivity, Specificity, PPV and NPV are computed on the T-REACH validation cohort for each strategy

AUC (ESPOIR, LEIDEN)	AUC (T-REACH)	STRATEGY 1 (High confidence in responders) SensitivitY	Specificity	PPV	NPV	STRATEGY 2 (high confidence in non-responDeRS) Sensitivity	Specificity	PPV	NPV
0.72 (0.70-0.73)	0.73 (0.64-0.81)	20% (12%-28%)	**98% (83%-100%)**	**95% (82%-100%)**	40% (32%-49%)	**91% (85%-97%)**	33% (20%-47%)	71% (63%-79%)	**68% (48%-86%)**

39 patients started anti-JAK therapy and 21 with TNF-α inhibitors. The 33.34% of patients were under monotherapy, and the 46.67% previously have been treated with biological therapy. The 77.36% of the total number of patients was on the biological therapy at 6 months of follow-up, while the 22.64% discontinued at 6 months of follow-up (9 due to inefficacy and 3 due to adverse effects). 48 patients continued the treatment in the 6 months after, and 12 patients discontinued due to ineffectiveness or drug intolerance. Clinical activity, fatigue, disability and pain perception are shown in Table 1.

Table 1.

Variable	VISIT 0 N=60	VISIT 1 N=57	VISIT 3 N=45
	Mean (SD)	Mean (SD)	Mean (SD)
Pain VAS	6 (2)	4 (3)	5 (3)
HAQ	1.33 (0.61)	1.06 (0.64)	1.06 (0.69)
FACIT-fatigue	25.52 (12.19)	31.03 (12.9)	32.76 (12.46)
DAS28	4.78 (1.2)	3.6 (1.33)	3.54 (1.44)
DAS28-CRP	4.31 (1.06)	3.19 (1.14)	3.05 (1.28)
SDAI	22.72 (9.88)	13.58 (8.58)	12.97 (9.32)
CDAI	21.75 (9.62)	12.88 (7.96)	12.36 (9.11)

Using a mixed linear regression model the association among the fatigue, disability and pain perception with clinical activity was conducted, corrected by age, smoking habits, time of disease evolution, BMI, previous biological/anti-JAK therapy administration and current dose of steroids. We observed a significant association among clinical activity and fatigue (P<0.001), disability (P<0.001) and pain perception (P<0.001). The statistical analyses showed a significant association where a high fatigue is increased in cases with high pain perception (P>0.001) and high number of swollen joints (P=0.002), but not in high levels of CRP and ESR. Fatigue was higher in those cases whom discontinued treatment (P=0.044) regardless of which therapy was chosen. No effect of age, time of disease evolution, steroid dose, BMI or previous therapy and smoking habits in the PROs values was observed.

Conclusion: PROs would be helpful in the disease control in those cases where a remote monitoring is needed, since HAQ or FACIT-FATIGUE index showed a significant association with clinical activity index in RA. Because of its ease for shipping and handling by the health professional, PROs could be a useful tool in the disease control. Its implementation in the remote monitoring of RA patient, as has been the case of Covid19 pandemic, results in an improvement of the clinic evaluation of RA patient, due to required information to clinical management is reported, avoiding presence consultation in those situations when it is required.

Disclosure of Interests: None declared.

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POS0545 A NEURAL NETWORK BASED CLUSTERING MODEL OF A COLOMBIAN COHORT OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid Arthritis (RA) is a chronic disease characterized by inflammation and joint pain. In daily clinical practice, it is usual to have multiple variables of different nature to define the current state of the disease, the patient's risk profile, and the subsequent optimal treatment.

Objectives: We aimed to identify the most influential variables from a suitable multivariable clustering and its labeling for an outpatient clinic-based cohort of Colombian RA patients.

Methods: We execute a clustering model (Kohonen's self-organizing map – SOM), applied to 23 variables (17 continuous and 6 discrete) obtained from 14,811 related follow-up visit records hosted on a previously preprocessed database of a cohort with data prospectively collected between 2013 and 2020. The included variables were the disease activity indexes (DAS28-ESR/CRP, CDAI, and SDAI; as outcome variables), serological status (autoantibodies positivity), and patients' sociodemographic and clinical characteristics. Clustering method used for generating the groups was SOM with a size of 25 x 25 neurons and 10000 iterations. SOM allows us to generate the groups by the comparison of the Euclidean distance in the hyperspace generated by the dimensions composed by the variables. After clustering, a discrete label built upon the categorization of the disease activity allowed us to identify the behavior of the included variables regarding the aforementioned outcomes, without affecting the clustering process. We evaluated the corresponding weights and their influence on the proposed neural network.

Results: Data from a total of 1,277 patients were included in the analysis. When both continuous and discrete variables were integrated, discrete data were transformed using the one-hot encoding method, creating new variables according to the corresponding number of categories. Dissimilarity between groups was very low when considering only the continuous variables, and it increases when adding all the other variables; likewise, regardless of the clinimetric index used for labeling, the clustering organization remains (Figure 1a).

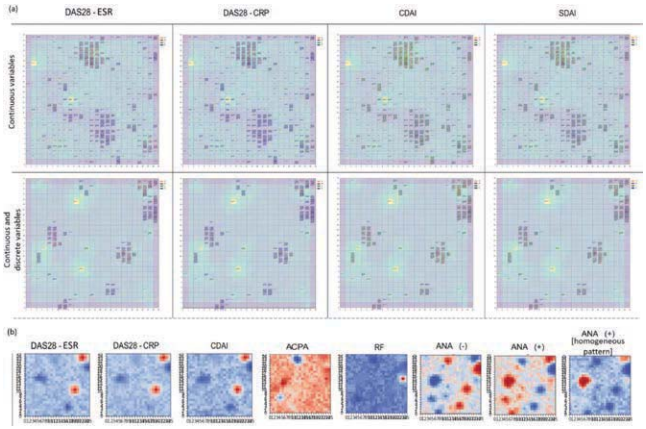

Figure 1. Clusters and heatmaps of variables' weights

In the construction of the groups, the influence of the RF and ACPA positivity was confirmed; furthermore, the antinuclear antibodies (ANAs) delivered a significant effect, especially those with negative ANAs or positive ANAs with a homogeneous pattern, on disease activity (Figure 1b).

Conclusion: SOM, as well as other artificial neural networks (ANN) are important methods for clustering and 2D visualization, due to the multivariate nature of the clinical data and its difficult visualization in the generated n-dimensional hyperspace. The utilized labels confirm that the clustering is adequate when considering that there was an identical grouping behavior for those registers with similar characteristics and an equivalent disease activity score. The findings of this research provide insights into a potentially pivotal role of the influence of RF, ACPA, and ANAs and their interaction with the proposed outcome variables in the understanding and development of future classification or prediction models; based on artificial intelligence and big data methods rather than on classical epidemiological approaches.

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POS0546 URINARY METABOLOMIC BIOMARKER CANDIDATES FOR SKELETAL MUSCLE WASTING IN PATIENTS WITH RHEUMATOID ARTHRITIS

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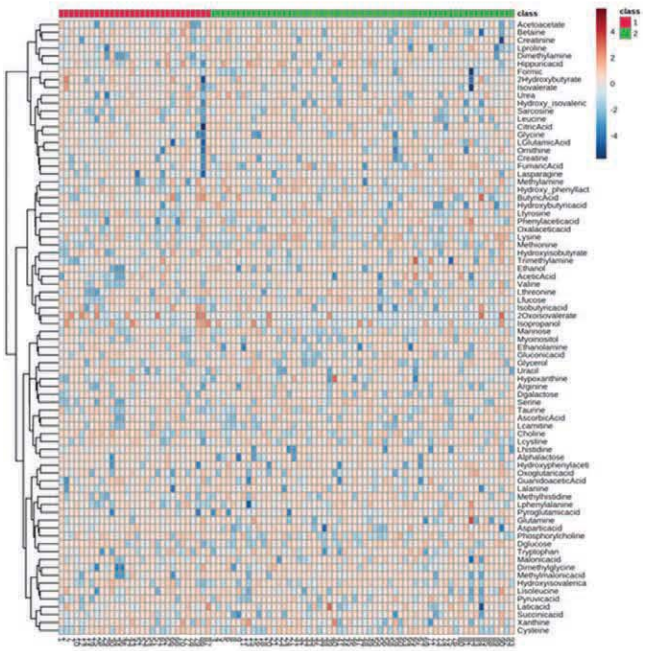
Background: Rheumatoid arthritis (RA) is an autoimmune disease that affects the joints, leading to chronic synovial inflammation and local tissue destruction. Extra-articular manifestations may also occur, such as changes in body composition. Skeletal muscle wasting is often observed in patients with RA, but methods for assessing loss of muscle mass are expensive and not widely available, limiting their use in clinical practice and their evaluation in longitudinal studies. Metabolomic analysis has shown great potential for identifying changes in the metabolite profile of patients with autoimmune diseases and can advance our understanding of pathogenic mechanisms, early diagnosis, treatment, and follow-up. In this setting, urine metabolomic profiling in patients with RA may be a useful tool to identify skeletal muscle wasting.

Objectives: To evaluate the urinary metabolomic profile of patients with rheumatoid arthritis and associate it with skeletal muscle loss.

Methods: We recruited patients aged 40–70 years with RA according to the 2010 ACR/EULAR classification criteria. We measured disease activity by the

A.



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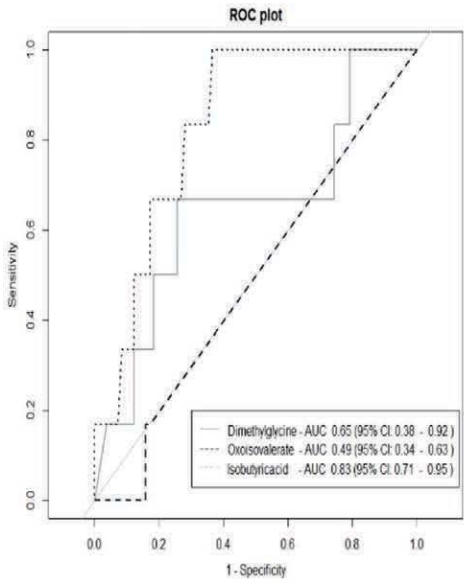

Figure 1.

Disease Activity Score in 28 joints using the C-reactive protein level (DAS28-CRP). We determined muscle mass according to DXA-derived appendicular lean mass index (ALMI) by summing the lean mass measurements for both arms and legs and dividing them by height squared (kg/height^2). We performed urine metabolomic analysis by nuclear magnetic resonance (NMR) spectroscopy using the BAYESIL and MetaboAnalyst software packages. We performed principal component analysis (PCA) and partial least squares-discriminant analysis (PLS-DA), followed by Spearman's correlation analysis. We set the significance level at $p<0.05$ for all analyses. We combined Receiver Operating Characteristic Curve (ROC) and logistic regression analyses to establish a diagnostic model.

Results: We included 90 patients with RA. Most patients were women (86.7%), with a mean age of 56.5 (SD, 7.3) years and a median DAS28-CRP of 3.0 (IQR, 1.0–3.0). We identified 15 metabolites that showed high variable importance in projection (VIP scores) by MetaboAnalyst. Of these, dimethylglycine (r=0.205; p=0.053), oxoisovalerate (r=−0.203; p=0.055) and isobutyric acid (r=−0.249; p= 0.018) were significantly correlated with ALMI. Based on low muscle mass (ALMI ≤6.0 kg/m^2 for women and ≤8.1 kg/m^2 for men), we established a diagnostic model with dimethylglycine (Area Under the Curve - AUC=0.65), oxoisovalerate (AUC=0.49) and isobutyric acid (AUC=0.83), with significant sensitivity and specificity.

Conclusion: Isobutyric acid, oxoisovalerate and dimethylglycine from urine samples were associated with low skeletal muscle mass in patients with RA. These findings suggest that this group of metabolites may be further tested as biomarkers for identification of skeletal muscle wasting.

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POS0547

THE ADVANTAGE OF TIGHT CONTROL AND TREAT TO TARGET IN NEW-ONSET RA PATIENTS IN DAILY RHEUMATOLOGY PRACTICE: RESULTS FROM A CONTEMPORARY UNIVERSITY CLINIC INCEPTION COHORT

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Background: Since 2018, all patients with new-onset rheumatoid arthritis (RA) at the Department of Rheumatology, Skane University Hospital, Lund, Sweden, are offered to participate in a "tight control" and "treat to target" (TC+T2T) follow-up strategy. This strategy includes regular follow-up visits to a rheumatologist (at diagnosis and 3, 6, 12, 18, 24 months) plus physical/telephone consultations with a rheumatology nurse between physician visits, both with disease activity assessments and, if needed, adjustment/intensification of anti-rheumatic treatment aiming for remission.

Objectives: To explore the possible advantages of integrating this TC+T2T strategy over routine care, aiming more systematically for remission (DAS28<2,6 or CDAI≤2,8), in clinical practice of new-onset RA.

Methods: Patients followed by the TC+T2T strategy were compared to new-onset RA patients followed according to routine care at the same department and during the same period. Data on disease and treatment characteristics, as well as outcome measures during follow-up were retrieved from the Swedish Rheumatology Quality register (SRQ). In total, 156 patients with at least 3 months follow-up between 2018 and 2021 were included; 95 followed according to the TC+T2T strategy and 61 according to routine care. Percentage females/mean age at onset/mean symptom duration at diagnosis were 79%/57 years/4 months (TC+T2T) and 62%/62 years/7 months (routine care). The change in DAS28 and CDAI from baseline to 12 months follow-up were compared between the two strategies by linear regression analyses, adjusted for sex, age, symptom duration, and DAS28 or CDAI, respectively, at baseline. In addition, changes in patient-reported outcomes (fatigue, pain and HAQ) are calculated.

Results: Disease and treatment characteristics at inclusion (diagnosis) are summarized in the Table 1.

Table 1.

	TC+T2T group (n=95)	Controls (n=61)
Swollen 28 joint count,	6,6 (4)	5,1 (5)
Tender 28 join count	8,2 (5)	6,2 (6)
ESR	48,1 (29)	37,7 (25)
CRP	21,3 (29)	16,9 (23)
DAS28	5,5 (1)	4,6 (1)
CDAI	24,5 (11)	18,3 (11)
HAQ	1,01 (0,6)	0,98 (0,7)
Fatigue (VAS)	50,1 (29)	46,6 (30)
Pain (VAS)	57,9 (24)	47,3(30)
ACPA positive (%)	77%	53%
Radiographic changes in hands or feet at inclusion (%)	12%	18%
Smoker (%)	16%	7%
Methotrexate started at inclusion (%)	78%	85 %
Prednisolone started at inclusion (%)	100%	97%

Mean and standard deviation (SD) if not otherwise stated.

The TC+T2T strategy resulted in greater improvements in DAS28 and CDAI scores from inclusion to 12 months follow up (p=0,025 and p=0,026; respectively; Figure 1). Beyond improvements in DAS28 and CDAI, a significant decrease in patient-reported outcomes (fatigue and pain) during 12 months from diagnosis was observed (Figure 1).

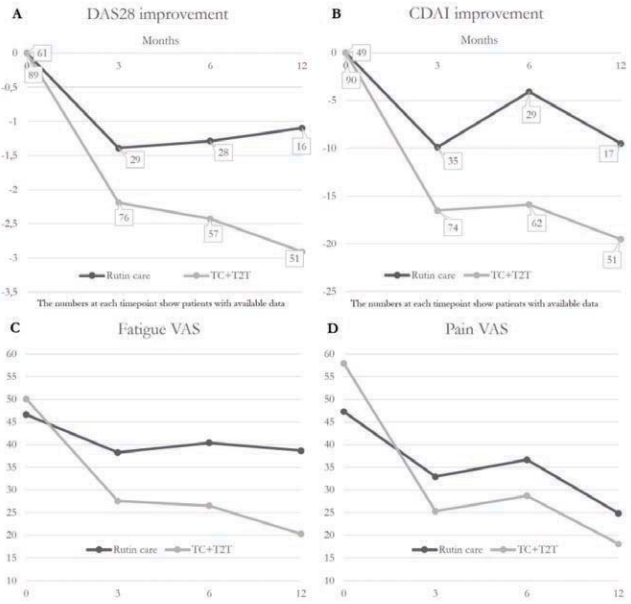

Figure A and B show the mean improvement in DAS28 and CDAI respectively from baseline, 3, 6, and 12 months from diagnosis.
Figure C and D show the mean fatigue and pain respectively at baseline, 3, 6, and 12 months from diagnosis.

Conclusion: Compared to routine rheumatology practice, the implementation of a "tight control" and "treat to target" strategy resulted in a greater improvement in disease activity and an early and sustained improvement in patient-reported outcomes. Our results suggest that this type of strategy should be integrated into daily clinical practice of new-onset RA.

Disclosure of Interests: Jon Thorkell Einarsson: None declared, Katarina Friberger Pajalic: None declared, Caroline Bengtsson: None declared, Elisabeth Mogard: None declared, Elisabet Lindqvist: None declared, Carmen Roseman: None declared, Olafur Palsson: None declared, Johan K Wallman Consultant of: Consultant of AbbVie, Amgen, Celgene, Eli Lilly, Novartis, Grant/research support from: Research support from AbbVie, Amgen, Eli Lilly, Novartis, Pfizer. Tor Olofsson Consultant of: consultant of MSD, Meliha C Kapetanovic Consultant of: Abbvie, Pfizer, GSK, Grant/research support from: unrestricted grants from Pfizer and Roche.

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POS0548

EVALUATION OF PHYSICIAN GLOBAL ASSESSMENT IN PATIENTS WITH B/TSDMARD THERAPY SELECTION ALIGNED WITH A MOLECULAR SIGNATURE RESPONSE CLASSIFIER RESULTS: AN ANALYSIS FROM THE STUDY TO ACCELERATE INFORMATION OF MOLECULAR SIGNATURES (AIMS) IN RHEUMATOID ARTHRITIS

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Background: Despite drug therapies that improve lives, tens of millions of patients annually are prescribed therapy using a "trial and error" approach because, until recently, it was not possible to personalize treatment using a patient's unique molecular profile. A blood-based molecular signature response classifier (MSRC) was shown to predict non-response to TNFi therapies in patients. MSRC integrates disease-associated RNA transcripts, and clinical features (anti-CCP, sex, BMI, PGA).[1] A recent study demonstrated that patient response to treatment informed by MSRC was more than 3 times better when MRSC informed therapy selection (predicted non-responders [alt-MOA] =34.8% vs predicted non-responders [TNFi] = 10.3%, p-value = 0.05).[1] Furthermore, when patients without a non-response signal from MSRC were prescribed a TNFi for treatment, their outcomes were improved by 5 times compared to the cohort receiving TNFi therapy despite a signal of non-response from MSRC (no prediction -[TNFi] = 45.8% vs predicted non-responder[TNFi]= 10.3%, p-value = 0.005) [1]

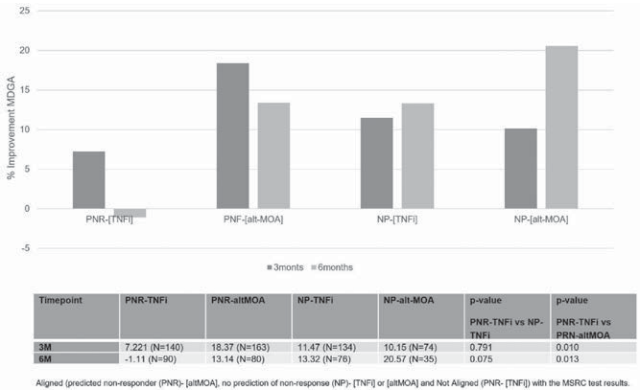
Objectives: The objective of the Study to Accelerate Information of Molecular Signatures (AIMS) in RA is to build a clinical/molecular database of longitudinal data from RA patients managed a real-world, settings with a focus on utilization of the MSRC test (PrismRA Scipher Medicine). Physician Global Assessment scores were measured and assessed as the objective of this analysis.

Methods: This analysis reports on data from patients enrolled in AIMS who initiated a new b/tsDMARD, or continued existing therapy, following MSRC testing (n = 560). Patients were ≥18 years of age with a clinical diagnosis of RA. The cohort was divided into patients whose targeted therapy selection was Aligned (predicted non-responder (PNR)- [altMOA], no prediction of non-response (NP)- [TNFi] or [altMOA] and Not Aligned (PNR- [TNFi]) with the MSRC test results. Improvement from baseline of MDGA was evaluated at 3 & 6ms and swollen joints at 3ms.

Results: Predicted non-responders prescribed an alt-MOA had significant improvement in MDGA scores at 3 & 6ms compared to predicted non-responders prescribed a TNFi (3m: PNR-[altMOA]- 18.4% (n=163) vs PRN-[TNFi] 7.2% (n=140), p-value – 0.010, 6m: PNR-[altMOA]- 13.1% (n=80) vs PRN-[TNFi] -1.11% (n=90), p-value – 0.013). Patients without the molecular signature prescribed a TNFi showed a trend of more improvement in MDGA scores at 3 & 6ms compared to patients with the molecular signature prescribed a TNFi (3m: NP-[TNFi]- 11.5% (n=134) vs PRN-[TNFi] 7.2% (n=140), p-value – 0.791, 6m: NP-[TNFi]- 13.3% (n=76) vs PRN-[TNFi] -1.11% (n=90), p-value – 0.075) (Figure 1). Moreover, predicted non-responders prescribed an alt-MOA showed a trend of improvement in swollen joints at 3ms compared to predicted non-responders prescribed a TNFi (PNR-[altMOA]- 3.15% (n=163) vs PRN-[TNFi] 1.7% (n=140), p-value – 0.08). Patients without the molecular signature prescribed a TNFi showed significantly more improvement in swollen joints at 3ms (NP-[TNFi]- 3.71% (n=134) vs PRN-[TNFi] 1.7% (n=140), p-value – <0.001). Characteristics of the cohort are reported in the Table 1.

Table 1.

Characteristic	PNR-TNFi n=159	PNR-altMOA n=176	NP-TNFi n=145	NP-altMOA n=80	P-value (PNR-TNFi vs NP-TNFi)	P-value (PNR-TNFi vs PNR-altMOA)
Age,mean (SD)	53.5 (13.8)	57.6 (12.9)	55.9 (14.4)	59.7 (13.2)	0.135	0.005
Race, n (%)					0.346	0.896
White	128 (81)	142 (81)	124 (86)	64 (80)		
Black	11 (7)	11 (6)	9 (6)	5 (6)		
Other	20(13)	23(13)	12(8)	11 (14)		
CDAI at baseline (SD)	34.1 (15.8)	38.5 (16.3)	28.5 (15)	26.5 (15.6)	0.002	0.012
TNFi Navie at baseline, n (%)	128 (81)	148 (84)	120 (83)	71 (89)	0.672	0.473



Timepoint	PNR-TNFi	PNR-altMOA	NP-TNFi	NP-alt-MOA	p-value PNR-TNFi vs NP-TNFi	p-value PNR-TNFi vs PRN-altMOA
3M	7.221 (N=140)	18.37 (N=163)	11.47 (N=134)	10.15 (N=74)	0.791	0.010
6M	-1.11 (N=90)	13.14 (N=80)	13.32 (N=76)	20.57 (N=35)	0.075	0.013

Aligned (predicted non-responder (PNR)- [altMOA], no prediction of non-response (NP)- [TNFi] or [altMOA] and Not Aligned (PNR- [TNFi]) with the MSRC test results.

Figure 1.

Conclusion: The incorporation of MSCR testing into the b/tsDMARD selection process can improve patient outcomes and can help identify which patient may be more or less responsive TNFi therapies.

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POS0549

IMBALANCED TFR/TFH IN PERIPHERAL BLOOD OF NEW-ONSET RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a kind of autoimmune disease characterized with chronic aggressive arthritis, presence of abnormal antibodies and persistent synovitis[1]. However, the pathogenesis of RA remained unclear by now. Several observations have showed that the breakdown of immune tolerance was involved in the development of RA. T follicular regulatory (Tfr) cells and T follicular helper (Tfh) cells, as a new subset of CD4+T cell, can exert an opposite effect in the regulation of humoral immunity[2]. Intensive researches have showed that the imbalance of Tfr/Tfh cell is related to the pathogenesis and development of autoimmune disease. There is still a lack of understanding of the relationship between Tfr/Tfh and RA, which needs further exploration.

Objectives: To detect the expression of Tfh and Tfr cells in thr peripheral blood of patients with new-onset RA and healthy controls, and to explore the role of Tfh and Tfr cells in the pathogenesis and development of RA.

Methods: We enrolled 26 patients with new-onset RA who hospitalized at the Second Hospital of Shanxi Medical University from the June 2021 to the November 2021. And 17 age and gender-matched healthy adults were anticipated as controls. The absolute number of Tfh and Tfr cells in peripheral blood was detected by flow cytometry. Disease activity indicators were collected including erythrocyte sedimentation rate (ESR, mm/h) and Disease Activity Score in 28 joints (DAS28). Then we compared the expression of Tfh and Tfr cells between the patients and healthy controls and conducted the correlation analysis with disease activity.

Results: There was significant decreased level of Tfr cells in the patients with new-onset RA compared with healthy controls (P<0.001) and a lower ratio of Tfr/Tfh in the patients (P<0.01). The reduced Tfr cells and Tfr/Tfh were significant negative correlation with the disease activity indicators including ESR and DAS28 (r=-0.305, P=0.033). There was no statistically significant in the absolute number of Tfh cells between patients and healthy controls, but the level of Tfh cell showed an increasing trend in new-onset RA.

Conclusion: The results we investigated here showed that new-onset RA exhibited an imbalance of Tfr/Tfh, specifically reduced Tfr cells, compared with healthy controls, which were negatively correlated with higher disease activity in RA. It was likely that the imbalance of Tfr/Tfh in peripheral blood played an important role in the development of RA, which may be a target to treat RA.

Table 1. A summary of data of all enrolled patients with RA and healthy controls

	HC(n=17)	New-onset RA(n=26)	P value
Age(years)	51.94±13.03	55.88±13.56	P=0.35
Sex(male/female)	4/13	7/19	P=0.81
ESR(mm/h) [a]	-	54.85±32.71	-
DAS28 [a]	-	5.09±1.56	-
Tfh cell count(cell/UL)[b]	43.156(23.277,106.638)	83.914(38.133,119.662)	0.214
Tfr cell count(cell/UL)[b]	1.422(0.882,1.893)	0.441(0.116,2.888)	0.025*
Tfr/Tfh[b]	0.030(0.014,0.049)	0.011(0.001,0.024)	0.001**

[a] Results are expressed as the mean ± standard error. [b] Results are expressed as the median(Q1,Q3).Normally distributed continuous variables were analyzed by the independent-samples Student's t-test. And nonparametric variables were analyzed by Mann–Whitney U test

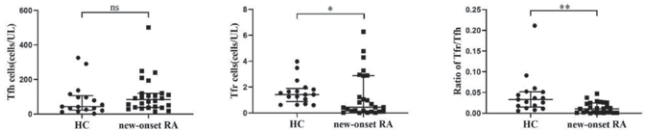

Figure 1. The differences of Tfr and Tfh cells in peripheral blood between the healthy controls and patients with RA. Tfr cells were higher in new-onset RA leading to an imbalance of Tfr/Tfh. Statistical analyses were performed by the Mann-Whitney U test. (*P<0.05, **P<0.01)

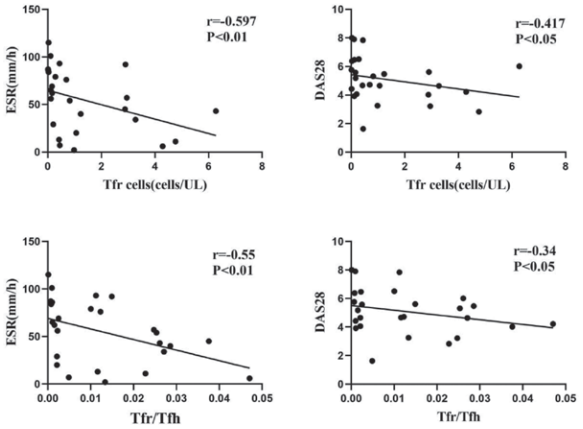

Figure 2. The correlation of disease activity with the level of Tfr cells and Tfr/Tfh. Tfr cells and Tfr/Tfh were negative associated with ESR and DAS28. Statistical analyses were performed by the Spearman correlation analysis.

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POS0550

LONG TERM EFFICACY OF A 2-YEAR MRI TREAT-TO-TARGET STRATEGY ON DISEASE ACTIVITY, MRI INFLAMMATION AND PHYSICAL FUNCTION IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION: FIVE YEAR FOLLOW-UP OF THE IMAGINE RA-COHORT

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Background: Targeting MRI remission in rheumatoid arthritis (RA) patients in clinical remission may improve long term clinical, functional and MRI outcomes.

Objectives: To investigate whether a 2-year treat-to-target (T2T) strategy, based on structured MRI assessments targeting absence of osteitis combined with clinical remission, compared with a conventional clinical T2T strategy targeting clinical remission only, improves disease activity, physical function and suppresses MRI-inflammation over 5 years in RA patients.

Methods: The IMAGINE-more trial was designed as an extension protocol to the 2-year IMAGINE-RA randomised controlled trial (RCT). IMAGINE-RA included 200 RA patients, in clinical remission (DAS28-CRP<3.2 and no swollen joints), who received conventional synthetic disease-modifying antirheumatic drugs (csDMARD) and investigated whether an MRI T2T strategy targeting absence of osteitis in combination with clinical remission (DAS28-CRP≤3.2 and no swollen joints) could increase remission rates and prevent erosive progression compared with a conventional T2T strategy targeting clinical remission only. If target was not met, treatment was escalated according to a predefined treatment algorithm starting with increment in csDMARDs and then adding biologics. At the end of the study, participants were invited to participate in the IMAGINE-more follow-up study. Patients were managed in routine outpatient clinic and had three IMAGINE-more visits including clinical examination (year 3, 4 and 5) and contrast-enhanced MRI of the dominant wrist and 2nd-5th metacarpophalangeal joints (year 3 and 5). The primary clinical endpoint was the proportion of patients achieving DAS28-CRP remission (DAS28-CRP<2.6) at year 5. Predefined key secondary outcomes were disease activity (DAS28-CRP), and changes in MRI osteitis (OMERACT RA MRI scoring system (RAMRIS)) and functional level (Health Assessment Questionnaire (HAQ)) from baseline to 5-years follow up. Endpoints were analysed by logistic regression models and repeated measures mixed effects models adjusted for propensity scores corresponding to (remaining in) group allocation.

Results: Fifty-nine patients in the MRI T2T arm and 72 patients in conventional T2T arm consented to participate. Of these, 47 patients (80%) in the MRI T2T group and 54 patients (75%) in the conventional T2T group reached the primary clinical endpoint (p=0.161) (Table 1 and Figure 1). No statistically significant differences between treatment strategies in key secondary outcomes were seen.

Table 1. Primary and key secondary outcomes at 5 years

	MRI T2T	Conventional T2T	Difference between groups	P value
	N=59	N=72		
Primary endpoint				
DAS28-CRP remission (DAS28-CRP<2.6), No. (%)	47 (80%)	54 (75%)	2.00 (0.76 to 5.28)	0.161
Key secondary endpoints				
DAS28-CRP	1.79 (0.08)	1.94 (0.08)	-0.15 (-0.38 to 0.07)	0.176
Change from baseline in MRI osteitis (RAMRIS)	-0.17 (0.58)	0.18 (0.54)	-0.35 (-1.96 to 1.25)	0.663
Change from baseline in HAQ	-0.02 (0.03)	0.05 (0.03)	-0.07 (-0.15 to 0.01)	0.080

Group estimates are presented as No. (%) for dichotomous data and least squares means (SE) for continuous data. For the primary endpoint, adjusted odds ratio and 95%CI between groups were calculated from a logistic regression model including a fixed factor for treatment arm, and an adjustment for propensity score as a covariate. For endpoints with continuous data, least squares mean differences between groups were calculated based on repeated-measures mixed linear models adjusted for baseline values and propensity scores.

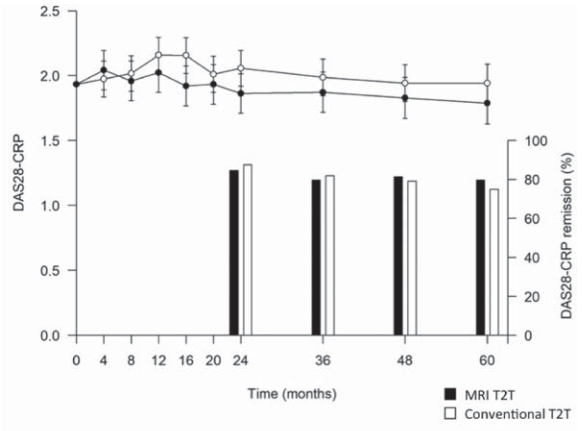

Figure: Absolute scores from baseline to 5 years in DAS28-CRP and proportions in remission
Illustrating the trajectory of absolute scores from baseline to month 60 (i.e. 5 years) in DAS28-CRP based on a mixed model with adjustment for baseline and propensity scores, as well as proportions in DAS28 remission over time for each group, with non-responder imputation.

Conclusion: A 2-year MRI T2T strategy targeting absence of MRI osteitis combined with clinical remission as compared to a conventional clinical T2T strategy in RA patients had no effect on the long-term probability of achieving DAS28-CRP remission. These findnings do not support the use of an MRI-guided strategy for treating patients with RA.

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POS0551 CLINICAL SIGNIFICANCE OF SERUM MPO-DNA COMPLEX IN RHEUMATOID ARTHRITIS

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Background: Tumor necrosis factor inhibitors (TNFi) have been widely used in the treatment of RA. Few researches offered solid solution to predict the response of TNFi treatment. NETs formation (NETosis) is a key process participant in RA. NETs and their components also work as a source of auto-antigens for RA.

Objectives: To explore the relationship between serum MPO-DNA complex, which is one of the components of NETosis, and disease activity of RA, and to explore the possibility for serum MPO-DNA complex to predict the therapy response of anti-TNF therapy in RA patients.

Methods: RA patients were enrolled from a randomized controlled clinical trial (EScoRT study, ClinicalTrials.gov identifier: NCT02320630) conducted from Oct. 2014 to Oct. 2018. The clinical and demographic data and blood samples were collected at baseline and every 4 weeks. Serum levels of MPO-DNA complex were detected by a modified enzyme-linked immunosorbent assay (ELISA) kit. The Association between MPO-DNA complex level and disease activity was analyzed. The predictive value of baseline MPO-DNA complex for treatment response of RA patients was analyzed.

Results: 86 RA patients were enrolled. The level of serum MPO-DNA was higher in patients with high disease activity (HDA) than that in patients with medium disease activity (MDA) (1.10±0.32 vs. 0.86±0.29, p=0.001). After 4 weeks of treatments, the level of seurm MPO-DNA complex decreased significantly (1.0±0.3vs. 0.6±0.2, p<0.001). Changes of MPO-DNA complex at week 4 (ΔMPO-DNA) was postively and linearly correlated with changes of TJC, SJC, PGA, EGA, ESR, CRP, DAS28ESR, DAS28CRP, SDAI and CDAI(r 0.270-0.495, all p-value<0.05). Receiver operating characteristic (ROC) analysis revealed that baseline MPO-DNA complex (95% CIs 0.57-0.79 for ACR50 and 0.66-0.85 for ACR70, all p-value<0.05) and ΔMPO-DNA complex at week 4 against baseline (95% CIs 0.63-0.83 for ACR 50 and 0.74-0.97 for ACR70) could predict the achievement of ACR50 and ACR70 within 12 weeks. ΔMPO-DNA complex at week 4 against baseline could predict the achievement of low disease activity (LDA) (95%CIs 0.57-0.79, p=0.03) and remission (95%CIs 0.54-0.8, p=0.024) within 12 weeks.

Conclusion: Serum MPO-DNA is associated with disease activity and can predict treatment response of RA.Serum MPO-DNA could serve as a powerful tool for clinicians to forecast the effectiveness of anti-TNF treatment in RA patients.

Disclosure of Interests: None declared.

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Table 1. Predictive ability of MPO-DNA for treatment response at week 12

	AUCs for ACR50 at week 12				AUCs for ACR70 at week 12			
Measures	**AUC(95%CIs)**	**P**	**AUC difference**	**p**	**AUC(95%CIs)**	**P**	**AUC difference**	**p**
b-MPO-DNA	0.68(0.57-0.79)	0.003	Reference	-	0.77(0.66-0.85)	<0.001	Reference	-
b-ESR	0.48(0.36-0.61)	0.848	0.20	0.085	0.57(0.40-0.75)	0.332	0.20	0.036
b-CRP	0.55(0.43-0.68)	0.062	0.13	0.072	0.65(0.52-0.79)	0.044	0.12	0.135
ΔMPO-DNA	0.73(0.63-0.83)	<0.001	reference	-	0.86(0.74-0.97)	<0.001	reference	-
ΔESR	0.56(0.48-0.68)	0.33	0.17	0.017	0.64(0.48-0.80)	0.072	0.22	0.007
ΔCRP	0.59(0.47-0.71)	0.14	0.14	0.056	0.68(0.53-0.83)	0.019	0.18	0.068
	AUCs for DAS28ESR LDA at week 12				**AUCs for DAS28ESR remission at week 12**			
Measures	**AUC(95%CIs)**	**P**	**AUC difference**	**p**	**AUC(95%CIs)**	**P**	**AUC difference**	**p**
ΔMPO-DNA	0.68(0.57-0.79)	0.03	Reference	-	0.67(0.54-0.8)	0.024	Reference	-
ΔESR	0.59(0.47-0.71)	0.14	0.09	0.226	0.54(0.41-0.68)	0.532	0.13	0.131
ΔCRP	0.60(0.47-0.72)	0.11	0.08	0.271	0.58(0.44-0.72)	0.274	0.08	0.258

Values are presented as areas under curve (95%CIs). Abbreviations: b-MPO-DNA/ESR/CRP, Serum MPO-DNA complex/ESR/CRP at baseline; ΔMPO-DNA/ESR/CRP, change of serum MPO-DNA/ESR/CRP at week 4 against baseline; ΔMPO-DNA/ESR/CRP%, reduction rate of serum MPO-DNA/ESR/CRP at week 4 against baseline.

POS0552

RELATIONSHIP BETWEEN PAINLESS MYOCARDIAL ISCHEMIA WITH LEVEL WILLEBRAND FACTOR AND INFLAMMATORY MARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In a patient with rheumatoid arthritis (RA) manifestations of coronary heart disease occur gradually, at the same time "painless" myocardial ischemia is detected in 50 - 70% of cases according to the literature. According to modern ideas, the formation of endothelial dysfunction, development of early atherosclerosis and vascular thrombosis are closely associated with the increase level of von Willebrand factor (VWF) and inflammatory markers.
Objectives: The aim of this study was to investigate the frequency and duration of painless myocardial ischemia and its association with VWF levels and inflammatory markers in patients with RA.
Methods: 63 patients with RA (44 women) aged 27 - 65 years (mean age - 46.8 ± 9.8 years) and 69 ages and sex-matched controls were examined. Serum levels of VWF, CRP and TNF-α were determined by enzyme-linked immunosorbent assays. Daily (Holter) ECG monitoring was performed by Holter ECG monitoring systems "DiaCard", registrar: model 02100, software version 1.0.40, developed by JSC "Solveig" (Ukraine).
Results: It was found, that the part of patients with painless myocardial ischemia among patients with RA was significantly higher (58.7%) than in the control group (13%). At the same time, in patients with RA the duration of painless myocardial ischemia was in averaged 10.9 ± 8.1 minutes per day. It was significantly more than in the control group 2.88±1.25 minutes per day (p <0,05). It was found, that in patients with RA there was an increased levels of VWF (162.2 ± 9.3% vs. 86.2 ± 2.7% in control). It was found, that the duration of painless myocardial ischemia had close correlations with VWF (r = 0.28), CRP (r = 0.41) and TNF-α (r = 0.40).
Conclusion: The severity the duration of painless myocardial ischemia in RA patients is associated with elevated levels of VWF, CRP, and TNF-α, indicating the possible involvement of VWF and inflammatory markers in cardiovascular disease in RA patients.
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POS0553

NEW BIOMARKERS IN RHEUMATOID ARTHRITIS: ROLE OF HOMOCYSTEINYLATED ANTI-ALPHA1 ANTITRYPSIN ANTIBODIES

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Background: Rheumatoid Arthritis (RA) is a multifactorial, chronic, systemic, inflammatory disease that can lead to progressive joint destruction (Alamanos et al, Autoimmun Rev 2005). Positivity for Rheumatoid Factor (RF) and antibodies against citrullinated proteins (ACPA) is useful for diagnostic and prognostic purposes. Nevertheless, in about 20% of patients, it is not possible to detect the presence of these autoantibodies. This has led to the identification of new antibody specificities, such as antibodies directed against carbamylated proteins (Mastrangelo A et al, J Immunol Res 2015) and, more recently, against homocysteinylated alpha 1 antitrypsin (anti-HATA) (Colasanti T et al, J Autoimmun 2020).
Objectives: To evaluate the prevalence of anti-HATA in a large cohort of patients with RA and their correlation with serological, clinical and erosive bone damage assessed by musculo-skeletal ultrasound (US).
Methods: Consecutive outpatients with RA, diagnosed according to the 2010 ACR/EULAR criteria, were enrolled. Demographic and clinical-laboratory data were recorded, including FR and ACPA determination. Disease activity was assessed by DAS28. The presence of anti-HATA antibodies was investigated by homemade ELISA using native alpha 1 antitrypsin modified *in vitro* to obtain homocysteinylated alpha 1 antitrypsin. US assessment was performed at the level of bilateral metacarpophalangeal and proximal interphalangeal joints; the presence of erosions and inflammatory features was identified according to OMERACT definitions (Wakefield RJ et al, J Rheumatol 2005).
Results: The present analysis included 91 RA patients (M/F 22/69; mean age 62 years; mean disease duration 12.5 years). Overall, the prevalence of anti-HATA was 69.2%. Anti-HATA antibodies were found in 63/91 (69.2%) of the entire patient cohort, whereas 68/91 (74.3%) patients were positive for ACPA and 63/91 (69.4%) for FR. 41.4% of patients had concomitant positivity for the three autoantibodies (FR, ACPA, anti-HATA). The analysis of patients with triple positivity for related arthritis antibodies (FR, ACPA, anti-HATA) was particularly interesting: indeed, in this subgroup, 80% of patients presented erosive damage, compared to 42.1% of patients who did not present simultaneously the three autoantibodies (p=0.0001). Patients with simultaneous positivity for RF, ACPA and anti-HATA showed a more aggressive disease phenotype (p=0.0001). Finally, a positive correlation was also found between disease activity (expressed by DAS28) and total inflammatory and erosive ultrasonographic score (p=0.005 and p=0.001, respectively).
Conclusion: The results of the present study confirm a high prevalence of anti-HATA in RA patients; furthermore, patients with concomitant presence of anti-HATA, ACPA and RF showed a more aggressive disease phenotype, in terms of erosive damage. Our analysis underlines as the characterization of new antibody specificities in RA could help in the early diagnosis of this disease and in the characterization of the different severity degrees.
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POS0554

CLINICAL CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS IN PRE-DIFFICULT-TO-TREAT STATUS

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Background: Patients with rheumatoid arthritis (RA) who have a difficult-to-treat condition (D2T RA) are often a burden to both patients and rheumatologists.
Objectives: The aim of this study was to determine the risk factors for failure to treat in patients with refractory conditions and to find them relevant to prevention.
Methods: Patients with RA who were treated under treat-to-target (T2T) strategy more than one year were picked up. Their background characteristics such as sex, age, disease duration, anti-citrullinated polypeptide antibodies titer (ACPA), and disease duration, were collected, and their simplified disease activity index (SDAI) score, Health Assessment Questionnaire Disability Index (HAQ) score, pain score measured with visual analog scale (PS), EuroQol 5th-dimensions score (EQ5D) were monitored every three months. Sharp/van der Heijde score (SHS) was calculated annually. Difficult-to-treat status was determined in according to the EULAR definition of D2T RA [1], and pre-D2T RA status was determined as follows: (Category-1) a failure history of one kind of action in biologic or targeted synthetic disease modifying anti-rheumatic drug (b/tsDMARD) and switched to another b/tsDMARD with other action mechanism or (Category-2) one or more of following status; mean SDAI score in recent three months exceeded 11 (MDA), three consecutive administration of glucocorticoid steroid no less than 7.5mg in prednisolone equivalent (GCS), rapid radiographic progression with 5 or more in SHS than last time (RRP), or decrease of EQ5D score less than -0.2 in recent 6 months (dEQ5D). Patients were recruited when Category-1 or -2 was matched in treating, and their results were determined in the last observation for each category. When second d/tsDMARD was failed until last observation in patient matched Category-1, the patient was judged as "failure," and the other patient was judged as "success." When Category-2 continued until last observation, the patient was judged as "failure," and escaped from the category, the patient was judged as "success." Risk factors for failure in background characteristics and monitored items in treating were evaluated for each category using binary logistic regression analysis.
Results: A total of 47 in Category-1 and 491 patients in Category-2 were recruited. In Category-1 matched patients, female were 83.0% and mean age was 71.3. Mean SDAI score, HAQ score, PS, EQ5D score, and SHS at failure of b/tsDMARD (baseline) were 15.5, 0.457, 40.1, 0.811, and 72.9, respectively. Numbers of the first b/tsDMARD were 32 TNF inhibitors, 8 IL-6 inhibitors, 6 abatacepts, and 1 JAK inhibitor. Numbers of the second after the first were 13 IL-6 inhibitors and 19 JAK inhibitors after THF inhibitor, whereas 3 TNF inhibitors, 2 abatacepts, and 3 JAK inhibitors after IL-6 inhibitor failure, 1 TNF inhibitor, 1 IL-6 inhibitor, and 4 JAK inhibitors after abatacept failure, and 1 TNF inhibitor after 1 JAK inhibitor failure. In these, success counted 18 and failure counted 29. Significant risk factors for Category-1 failure were higher ACPA, higher SDAI score, higher HAQ score, and higher SHS at baseline ($p<0.05$). There was no significant difference between drugs.
In Category-2 matched patients, numbers of each status at first (baseline) were 455 MDAs, 20 GCSs, 17 RRPs, and 9 dEQ5Ds. Numbers in success and failure for each status at baseline were 315 and 140 for MDA, 16 and 4 for GCS, 9 and 0 for RRP, and 7 and 2 for dEQ5D, respectively. Significant risk factors for each failure status were higher mean SDAI score after baseline for MDA, higher HAQ score at baseline for GCS, and higher mean PS after baseline for dEQ5D ($p<0.01$).
Conclusion: Clinical background factors besides disease activity such as ACPA, HAQ score, and SHS at baseline were important for preventing fall-in D2T_RA. However, most weighted factor was disease activity control after falling in MDA status. Tight disease activity control is the overriding factor.
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POS0555

THE NON-APOPTOTIC PROGRAMMED-CELL-DEATH-RELATED SIGNATURE PREDICTS ANTI-TNF THERAPY NONRESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: EULAR guideline in rheumatoid arthritis (RA) recommended the primary failure of the first-line conventional synthetic modifying anti-rheumatic drugs (csDMARDs) patients switching to tumor necrosis factor alpha inhibitors (TNFi) [1]. Nevertheless, approximately 30-40% csDMARDs-IR patients also experience inefficacy of TNFi [2]. There is still no index to predict whether TNFi would be responded or not. Moreover, only few studies had focused on the relationship between TNFi nonresponse and other cell programmed deaths except apoptosis.
Objectives: To predict the possibility of TNFi response prior to prescript in RA patients with the biomarkers of non-apoptotic programmed cell death in synovial cells.
Methods: The datasets of 22 TNFi treated RA synovial samples were enrolled from the Gene Expression Omnibus (GEO) database (GSE140036 and GSE15602). And the differentially expressed genes (DEGs) and modules related to TNFi treatment through weight gene correlation network analysis (WGCNA) were identified with the R packages "limma" and "WGCNA". Then the enrichment analysis among the shared genes was performed through the R.4.1.2, Metascape website, and WebGestalt website. Following with the confirmation of the non-apoptotic programmed cell death (NAPCD) genes in the shared genes with Student's T-Test. Furthermore, the TNFi treatment cohort was clustered based on the hub genes, making the receiver operating characteristic (ROC) curve analysis. Moreover, the least absolute shrinkage and selection operator (LASSO) model was constructed to identify the predictive genes.
Results: 2624 DEGs were identified significantly, including 161 upregulated genes and 2463 downregulated genes. One module with TNFi treatment was constructed in WGCNA, significant in both response and nonresponse. Then the gene signatures for TNFi nonresponse were collected from overlaps 2260 genes in above. And we found 38 NAPCD genes might play role in TNFi nonresponse, but reserved 33 genes which statistically significant with T-Test. 22 TNFi treated synovial samples in GEO database could be classified into response or nonresponse subgroups. The ROC curve showed that the AUC for 32 genes in these samples ranged from 0.7 to 0.9, expected for CD46. At last, the LASSO model indicated that CASP5, CAPN10, ITGB4, NLRP2, and SLC2A8 could predict the TNFi nonresponse, as the risk score = CASP5 × 0.028 + CAPN10 × 0.064 + ITGB4× 0.080+ NLRP2 × 0.317+ SLC2A8 × 0.090 (Figure 1).

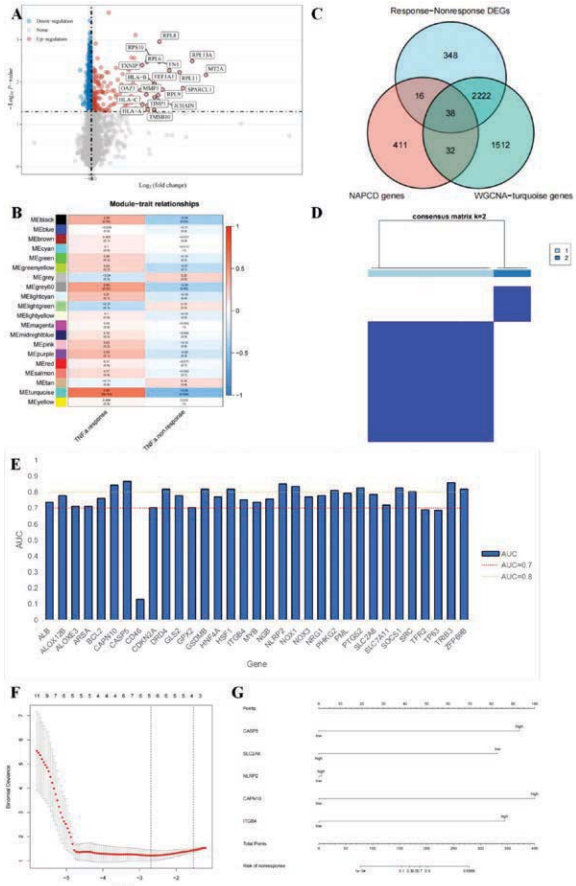

Figure 1. Predictive model of TNFi nonresponse based on NAPCD genes. (A) Volcano map of differential expressed genes; (B) Correlation heat map of gene modules and phenotypes, the red is positively correlated with the phenotype, blue is negatively correlated with the phenotype; (C) The shared 38 genes of TNFi response & nonresponse DEGs, among the WGCNA turquoise module and cell programmed death genes; (D) Consensus clustering matrix for k = 2; (E) The ROC curve of 33 genes; (F) LASSO regression of the 32 genes,except for CD46; (G) Nomogram for predicting TNFi nonresponse in TNFi treatment RA cohort, indicated five possible indicators (CASP5, CAPN10, ITGB4, NLRP2, and SLC2A8) were closely related to TNFi nonresponse.

Conclusion: Our study firstly screened out the 38 NAPCD candidate genes signatures in RA synovial tissues which took part in TNFi nonresponse through WGCNA and DEGs. Further analysis confirmed that five possible indicators (CASP5, CAPN10, ITGB4, NLRP2, and SLC2A8) were closely related to TNFi nonresponse.
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POS0556

ALTERATION OF THE GUT MICROBIOTA IN CHINESE POPULATION WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an aggressive immune-mediated joint disease characterized by synovial proliferation and inflammation, cartilage destruction, and joint destruction. Growing evidences suggests a chronic inflammatory response induced by gut microbiome critically contribute to the development of rheumatoid arthritis.
Objectives: The aim of this study was to evaluate and quantify differences in the composition of gut microbiota in RA patients and investigate the associations between flora and clinical variables in RA patients.
Methods: Fecal samples from 145 RA patients and 145 age- and gender-matched healthy controls (HCs) were collected for bacterial 16S rRNA genes sequencing. The alpha-diversity, beta-diversity and the microbial composition (at the phylum and genus level) analysis of the gut microbiome were used to define the difference of gut microbiota profiles between RA patients and HCs. The peripheral lymphocytes of these patients were assessed by flow cytometry, and inflammatory biomarkers (ESR, CRP), auto-antibodies(ACPA, MCV) and cytokines measured by ELISA were recorded. Correlations between different taxa and clinical variables, were calculated by Spearman's rank test.
Results: Consistent with trends observed for diversity, patients with RA had a lower richness compared with those of HCs ($p < 0.01$, Figure 1a), suggesting gut microbiome was markedly less diverse in composition in RA. Bray curtis distance-based beta diversity analysis revealed significant differences in the microbial community between RA and HCs (ANOSIM, R2=0.061, p=0.001, Figure 1b). Ten selected taxonomic biomarkers at different phylogenetic levels showed great discriminant ability, with Log10 LDA score > 4.0 (Figure 1e-g). Detailly, at the phylum level, RA patients had a lower frequency of Firmicutes while higher Proteobacteria. RA patients presented fewer Faecalibacterium but more Escherichia_Shigella at the genus level (Figure 1c-d). PICRUSt analysis found that in the KEGG pathways, the microbial gene functions related to Propanoate metabolism were higher in the fecal microbiome of RA patients (Figure 1h). Escherichia_Shigella positively correlated with ACPA antibodies ($r=0.176$, $p < 0.05$) and IL-4 ($r=0.204$, $p < 0.05$, Figure 1i), wheras Faecalibacterium as a probiotic showed no significant correlation with our clinical measures.

Conclusion: Specific gut microbiota played an important role in the pathogenesis of RA, which may aid in the diagnosis or determination of the susceptibility of individuals to RA via detection of the gut microbiome.

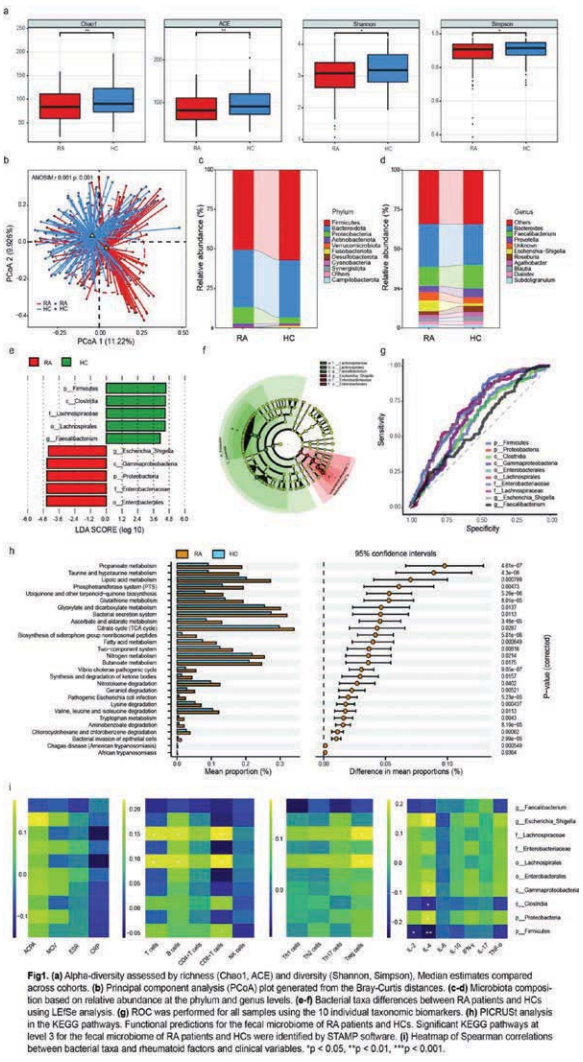

Fig1. **(a)** Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson). Median estimates compared across cohorts. **(b)** Principal component analysis (PCoA) plot generated from the Bray-Curtis distances. **(c-d)** Microbiota composition based on relative abundance at the phylum and genus levels. **(e-f)** Bacterial taxa differences between RA patients and HCs using LEfSe analysis. **(g)** ROC was performed for all samples using the 10 individual taxonomic biomarkers. **(h)** PICRUSt analysis in the KEGG pathways. Functional predictions for the fecal microbiome of RA patients and HCs. Significant KEGG pathways at level 3 for the fecal microbiome of RA patients and HCs were identified by STAMP software. **(i)** Heatmap of Spearman correlations between bacterial taxa and rheumatoid factors and clinical variables. *p < 0.05, **p < 0.01, ***p < 0.001.

Figure 1.

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POS0557

ASSOCIATION BETWEEN ANTI CITRULLINATED PEPTIDES ANTIBODIES, BONE MINERAL DENSITY, AND FRACTURE RISK IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Recent literature reported Anti Citrullinated Peptides Antibodies (ACPA) associated with bone loss in patients with rheumatoid arthritis (RA).
Objectives: To study if ACPA positivity was associated with bone mineral density and the ten-year probability of fracture (FRAX) in RA patients.
Methods: We performed a cross-sectional study on patients with RA diagnosis according to ACR-EULAR 2010 classification recruited from January 2021 till January 2022. Patients aged from 40 to 90 years were included. Those with prior cancer, hyperparathyroidism, hyperthyroidism, diabetes, chronic kidney disease, and cirrhosis were excluded. Clinical data and results of laboratory tests were collected simultaneously with bone mineral density (BMD) acquisition. The latter was measured with dual-energy X-ray absorptiometry (DXA). BMD of the femoral neck (FN) was used to calculate the ten-year probability of major osteoporotic fracture (FRAX MOF) and femoral neck risk fracture (FRAX FN). Patients were grouped by positivity or quartile of ACPA level (I-IV). We used logistic regression, parametric and non-parametric tests for statistical analysis with SPSS20.
Results: Eighty-two RA patients were enrolled. In total, 69 (84.1%) were women, 16 (19.5%) reported a previous personal fracture, and 37 (45.1%) had osteoporosis. Seventy-two (87.8%) patients were ACPA positive. The mean body mass index (BMI; kg/m^2) and lumbar spine BMD in ACPA-positive patients were 25.44 ± 4.79 and 0.791 ± 0.138, respectively. We found a significant association between ACPA positivity and BMI over 25 ($p = 0.01$; OR = 0.132 [1.527; 6.785]). Comparison between ACPA positive/negative patients did not find a significant difference for osteoporosis, history of fracture, DAS28CRP, lumbar spine BMD, FN BMD, FRAX MOF BMD, and FRAX FN BMD. Lumbar spine BMD was significantly different ($p = 0.035$) among subgroups of ACPA levels, whereas there was no significant difference for FRAX MOF, FRAX FN, and FN BMD.
Conclusion: In this study, lumbar spine BMD was significantly different among subgroups of ACPA levels.

Disclosure of Interests: None declared.
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POS0558

A INFLAMMATORY FACTOR-BASED NOMOGRAM PREDICTS FIRST REMISSION TIME OF RHEUMATOID ARTHRITIS PATIENTS WITH BASELINE GALECTIN-9

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Background: Rheumatoid arthritis (RA) is an autoimmune disease. The core treatment principle of RA is to achieve remission or low disease activity as soon as possible to ensure optimal outcomes. Predicting the first remission time according to the patient's risk factors is very important for the choice of treatment scheme.
Objectives: We aimed to verify the prognostic value of inflammatory factors in RA and establish a nomogram based on Human Interleukin-6(IL-6), Galectin-9(Gal-9)and disease activity to predict the first remission time after conventional synthetic DMARDstreatment.
Methods: 184 RA active patients(DAS28-ESR> 3.2, ACR 1987 criteria or EULAR 2010 criteria) were enrolled in the rheumatology department of Qilu Hospital of Shandong University from June 2014 to June 2020.129 patients were assigned to the development cohort and 55 patients were assigned to the validation cohort randomly. Baseline clinical data and plasma were collected. The expressions of Tumour Necrosis Factor α (TNF-α), Vascular Endothelial Growth Factor (VEGF), IL-6 and Gal-9 in plasma of RA patients were detected by ELISA. All patients were treated with csDMARDs and we recorded activity of each follow-up visit until 36 months. Lasso regression and Cox regression analysis were used to screen the 14 variables (including activity indices and cytokines) at baseline, and the prediction model was established to draw the nomogram.
Results: Patient age, CRP, IL-6, Gal-9, HAQ and DAS28-ESR were the significant prognostic factors in the lasso and Cox regression analyses, especially Gal-9. The multivariate analysis revealed that IL-6≤ 9.04 pg/ml(*HR* =0.54, 95% *CI*:0.31–0.95), Gal-9≤ 4490 pg/ml(*HR* =0.43, 95% *CI*:0.21–0.89) were independent protective factors (Table 1). Above-mentioned six factors were included in our model as predictors (Figure 1). The resulting model containing six factors had good discrimination ability in both the development cohort (C-index, 0.729) and the validation cohort (C-index, 0.710). Time-dependent ROC curve (Figure 2), calibration analysis (Figure 3) and decision curve analysis (DCA) show that the nomogram has significant discriminant power, stability and clinical practicability in predicting the first remission time.
Conclusion: We constructed and validated a nomogram with baseline activity indices and cytokines that can predict first remission time in RA patients after csDMARDs treatment. Using this simple-to-use model with plasma Gal-9 at baseline, the remission rate can be determined for an individual patient and could be useful for the early identification of high-risk patients.

Figure1. The nomogram for predicting first remission time of RA after treatment.

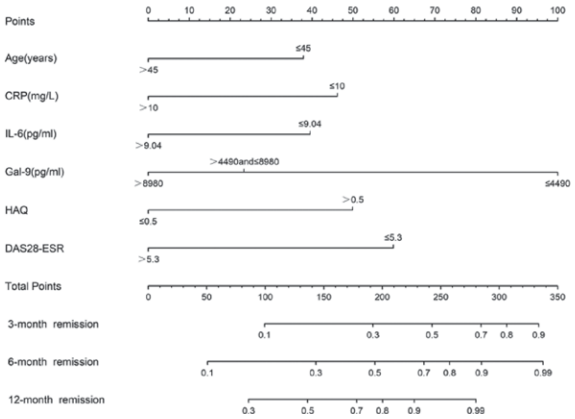

Figure2. ROC curve analysis showed the discriminatory ability of nomogram for predicting 3, 6, 12 months remission rate after treatment.

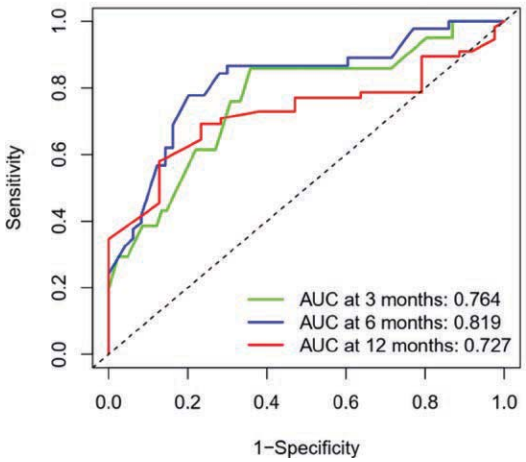

Figure3. The calibration curves for predicting RA patients' postoperative 3, 6, and 12 months remission rate.

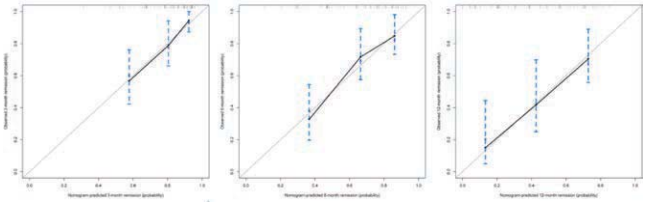

Table1. Univariate and multivariate analysis of factors associated with first remission time according to the Cox Proportional Hazards Model.

Variable	Univariate			Multivariate		
	HR	95%CI	P value	HR	95%CI	P value
Age，years						
≤45 vs.>45	0.69	0.43-1.12	0.13	0.75	0.46-1.21	0.24
CRP，mg/L						
≤10 vs.>10	0.87	0.53-1.42	0.57	1.56	0.87-2.82	0.14
IL-6，pg/ml						
≤9.04 vs.>9.04	0.58	0.34-0.97	0.04	0.54	0.31-0.95	0.03
Gal-9，pg/ml			<0.01			0.03
≤4490 vs.>4490and≤8980	0.37	0.18-0.73	<0.01	0.43	0.21-0.89	0.02
≤4490 vs.>8980	0.44	0.26-0.77	<0.01	0.51	0.29-0.90	0.02
HAQ						
≤0.5 vs.>0.5	1.71	1.01-2.9	0.05	0.65	0.36-1.17	0.15
DAS28-ESR						
≤5.3 vs.>5.3	0.56	0.34-0.93	0.02	0.50	0.28-0.87	0.01

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POS0559

COMPLIANCE WITH RECOMMENDATIONS OF LOW INTAKE OF RED MEAT AND HIGH FIBER INTAKE IS ASSOCIATED WITH A REDUCED RISK OF RHEUMATOID ARTHRITIS

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Background: Diet has received much attention as a factor that may contribute to the development of rheumatoid arthritis (RA). Several different nutrients, food components and dietary patterns have been studied in different populations. There is limited information on the importance of compliance with diet recommendations in this context.
Objectives: The aim of this study was to investigate the relation between overall dietary quality, diet components, and the risk of RA.
Methods: Participants in a population-based survey conducted in 1991-1996 who were subsequently diagnosed with RA (from inclusion until December 2004) were identified through register linkage and validated in a structured process. Four controls for each case, matched for sex, year of birth, and year of inclusion, were selected from the study cohort. The controls were alive and RA-free when the index person was diagnosed with RA. At inclusion, diet was assessed using a modified diet history method, consisting of a seven-day food record, a food questionnaire, and a supplementary interview. The New Diet Score (NDS) reflects the recommendations in the Swedish dietary guidelines (SDG) from 2015, produced developed by the Swedish Food Agency, which in turn are based on the Nordic Nutrition Recommendations from 2012. According to the SDG, it is recommended to eat more fiber, vegetables and fruits and fish, and less red meat and added sugars. The mentioned dietary components are all included in the NDS, with a range 0-5. A score of 1 was assigned to each component where the individual complied with the recommendation. Non-compliance was assigned a score of 0. The cutoff values for the

recommendations are based on a previously validated Diet Quality Index, except for red meat (based on SDG) and added sugars (based on World Health Organization guidelines from 2015 for sugar intake).
We used conditional logistic regression analysis to study the relation between NDS, its components, and RA. The NDS was divided into categories, defined as low (0–1), moderate (2–3) and high (4-5), with "low" as reference, and also assessed as a continuous variable. All models were adjusted for reported total energy intake, and potential misreporters of total energy intake were excluded.
We designed multivariable-adjusted models in which we included covariates that had been associated with diet and RA (smoking, alcohol and leisure time physical activity).
Results: In the study population, 172 RA cases were identified. Low red meat intake (<500 g/week) was significantly associated with a decreased risk of RA (Table 1). Compliance with the recommendations for intake of fiber and vegetables and fruit were inversely associated with RA, with a similar trend for the total NDS (Table). In additional multivariable analysis, including both variables and relevant confounders, compliance with recommendations for red meat intake (odds ratio (OR) 0.43; 95% CI 0.22-0.85) and for fiber intake (OR 0.53; 95% CI 0.30-0.94) were both associated with a reduced risk of RA.

Table 1. Multivariable-adjusted odds ratios (ORs) describing the relation between New Diet Score (NDS) and its components and the risk of developing rheumatoid arthritis

		Adjusted for reported energy intake, smoking, alcohol, leisure time physical activity	
NDS components	Recommendation	OR	95% CI
Fibre	≥2.4 g/MJ	**0.51**	**0.29–0.90**
Vegetables and fruits	≥400 g/day	**0.55**	**0.32–0.95**
Fish	≥300 g/week	1.25	0.76–2.05
Added sugar	≤10 E%	1.10	0.68–1.78
Red meat	<500 g/week	**0.42**	**0.22–0.81**
NDS			
0–1		**1.00**	**(Ref)**
2–3		0.65	0.38–1.10
4–5		0.67	0.30–1.46
Per point increment		0.82	0.67–1.00

Conclusion: These preliminary results indicate that low intake of red meat and higher fiber intake, in line with current recommendations, are independently associated with reduced risk of developing RA, suggesting that components found in meat and fiber-rich foods may affect very early disease mechanisms.
Disclosure of Interests: None declared.
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POS0560 ASSESSMENT OF THE SWOLLEN TO TENDER JOINT COUNT RATIO AS A PREDICTOR OF RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS: A COHORT STUDY

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Background: Several response predictors have already been studied in rheumatoid arthritis, especially since the introduction of biological therapies. The swollen to tender joint count ratio (STR) has been proposed as a predictor of response in patients receiving anti-TNF therapy, but its usefulness in other therapies is not yet well established.
Objectives: To assess whether STR can be a predictor of response in patients with rheumatoid arthritis under b/tsDMARD.
Methods: Longitudinal and retrospective study that included patients diagnosed with rheumatoid arthritis followed in the Rheumatology Department of a tertiary hospital, under therapy with b/tsDMARD. Demographic, laboratory, and clinical data were collected, including tender and swollen joint counts (as included in DAS 28), Visual Analog Scale (VAS), DAS28 4V, SDAI, CDAI, ACR and EULAR responses, and HAQ. All patients were evaluated at 0, 6 and 12 months after starting the first b/tsDMARD therapy performed after 2015. The variation in each parameter compared to baseline was calculated at 6 and 12 months and represented as a delta. A cutoff of 1 was defined for comparison between STR groups. The correlations between the continuous variables were assessed by Pearson's test and comparison between groups of ratios using t test (continuous variables) and chi-square test (categorical variables). Multiple linear regression and multivariate logistic regression were performed to determine response predictors.
Results: A total of 287 patients were included, 238 (82.9%) females, aged 55.7±10.8 years and diagnosed with rheumatoid arthritis for 11.2±8.1 years. Two hundred and sixty-nine (93.7%) were on csDMARD; with regard to b/tsDMARD therapy, 66 started etanercept (23.0%), 62 tocilizumab (21.6%), 58 rituximab (20.2%), 44 adalimumab (15.3%), 17 golimumab (5.9%), 14 abatacept (4.9%), 7 certolizumab (2.4%), 5 upadacitinib and baricitinib (1.7%), 4 infliximab (1.4%), 3 tofacitinib (1.0%), and 2 anakinra (0.7%). At the start of therapy with b/tsDMARD, the mean DAS28 4V was 4.7±1.5, CDAI 20.4±12.2, SDAI 22.8±16.4, erythrocyte sedimentation rate 31.8±24.4, C-reactive protein (CRP) 1.5±1.7, patient VAS 62.6±1.5, physician VAS 41.4±29.7, pain VAS 62.5±24.8, and HAQ 1.5±0.6; median tender joint count was 4 (interquartile range - IQR - 6), swollen joint count was 3 (IQR 6), and STR joint count was 0.9 (IQR 0.5). When the STR < 1 and STR ≥1 groups were compared, it was found that there were no differences in these variables when starting b/tsDMARD, nor in the therapies they performed. At 6 months, the STR ≥1 group showed a higher proportion of patients in CDAI remission (CDAI ≤2.8 – 15.3% vs 6.9%, p=0.033) and in DAS28 4V remission or low disease activity according to DAS28 4V (DAS28 4V ≤3.2 – 36.5% vs 22.4%, p=0.008). At 12 months, the STR ≥1 group exhibited less disease activity (mean DAS28 4V 3.2±1.2 vs 3.6±1.3, p=0.028) and a higher proportion of patients in DAS28 4V remission (25.2% vs 19.7%, p=0.047). No significant differences were found between the groups in the other variables studied. In the correlation studies, a weak correlation was identified between STR and CRP at 12 months (r=0,28, p<0,001). In multiple linear regression studies, when adjusted for sex, age, prednisolone, csDMARD, inflammatory parameters, b/tsDMARD, STR was not shown to be a predictor of DAS28 4V disease activity at 1 year; in multivariate logistic regression studies, when adjusted for the same variables previously described, STR was not shown to be a predictor of remission or remission or low disease activity according to DAS28 4V at 1 year.
Conclusion: The STR is a practical, easy-to-use index that can be used as an adjunct in clinical practice in the evaluation of patients with rheumatoid arthritis, as it is associated with a better response to b/tsDMARD therapy, regardless of patient status and therapy, although it should not be used alone, as it does not appear to be a predictor of response, according to the indices that are currently used.
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POS0561 PREVALENCE AND CHARACTERISTICS OF PATIENTS WITH "ARTHRALGIA AT-RISK" DEFINED ACCORDING TO THE RHEUMATOLOGIST AND THE NEW EULAR DEFINITION: A PILOT RETROSPECTIVE STUDY FOCUSSED ON REFERRAL TO A STRUCTURED EARLY ARTHRITIS CLINIC

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Background: The phase preceding the development of rheumatoid arthritis (RA) may contain a novel window of opportunity for disease prevention and control. Investigation of this phase at population level remain, however, very challenging in epidemiological terms due to the rarity of the events. Patients seeking medical attention with arthralgia at-risk, defined by an expert rheumatologist (clinically suspect arthralgia, CSA) or by the recent EULAR definition represent an attractive platform for the identification of both seropositive and seronegative disease subsets.
Objectives: The objective of this study was to explore the prevalence and characteristics of patients with different types of arthralgia, focusing on referral to the screening visit of an early arthritis clinic (EAC) as a putative enrichment strategy for pre-RA.
Methods: EAC first referrals from January 1st 2019 to June 30th 2021 were systematically reviewed through a retrospective evaluation of medical charts. Patient's history, comorbidities, PROs and clinical examination were recorded by two expert rheumatologists blind to immunological, ultrasound and radiological data. Arthralgia cases, sub-classified according to risk-definitions, were recorded. Categories at-risk, according to the rheumatologist's opinion and the EULAR definition, were characterized and compared to other arthralgia cases for clinical characteristics, imaging data and autoantibody status.
Results: Of the 363 patients referred to the EAC, 178 were characterized by peripheral arthralgia (swollen joint count=0) at screening visit (49%). Of these patients, 130 cases were characterized by recent-onset arthralgia (ROA) (<12 months symptoms' duration) (73% of the total). CSA, according to the rheumatologist's opinion, was applicable to 71/178 total arthralgia patients (40%) and to 61/130 ROA patients (47%, recent-onset CSA, RO-CSA). Patients without

CSA were characterized by undefined concomitant conditions or by "clinically suspect psoriatic or spondylarthritis arthralgia" (20/178, 11%). EULAR definition of arthralgia at-risk (>2 items) was fulfilled by 53/71 CSA patients (74.6%) and by 52/107 (49%) patients not characterized by CSA (p=0.001 Chi-square test) (Figure 1).

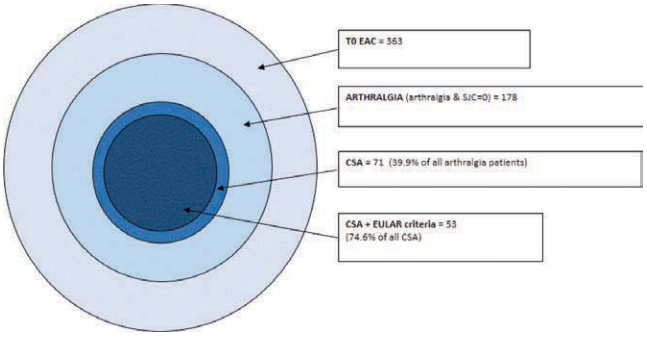

Figure 1. Early Arthritis Clinic first referrals from January 1st 2019 to June 31th 2021.

Despite a similar clinical phenotype, comparative analysis between different arthralgia categories demonstrated a significant enrichment of RF and ACPA positivity (21% vs 4%, p=0,001, and 15% vs 3%, p=0.01) in both CSA and RO-CSA vs other groups. RO-CSA showed also an enrichment of hypogammaglobulynemia compared to other groups (13% vs 3%, p=0.03). After a stratification according to the fulfillment of the EULAR definition, both CSA and RO-CSA increased their differences compared to other groups regarding the elevation of C-reactive protein (CRP ≥0.5 mg/dl, p=0.006 and p=0.02 respectively). No epidemiological, clinical or imaging differences were observed through patient stratification according to the EULAR definition *per se* in the whole population.

Conclusion: Results of our pilot study provide evidence of the applicability of patient selection according to current arthralgia at-risk definition in the real-life setting of an EAC. Both CSA and RO-CSA appears as suitable niches for the enrichment of primary immunological and serological risk factors for RA (RF/ACPA, hypogammaglobulynemia and C-reactive protein). Current data confirm in an independent setting the importance of the rheumatologist's perspective as a platform for appropriate application of the EULAR definition.

Disclosure of Interests: None declared.

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POS0562 AUTOANTIBODIES TO JOINT PROTEINS AS NOVEL BIOMARKERS FOR THE DIAGNOSIS OF UNTREATED EARLY RHEUMATOID ARTHRITIS

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Background: Autoantibodies to citrullinated protein (ACPA; measured as anti-CCP; aCCP) and rheumatoid factor (RF) appear years before clinical onset of RA and are essential tools in today's classification criteria for RA. In animal models, antibodies to joint specific proteins (JP) can induce arthritis, and they are also present at onset of RA [1]. As there is a need for increased precision for early diagnosis of RA as well as identification of different subtypes of the disease, we aim to assess whether autoantibodies to native or modified JP can be used for early and precise diagnosis of RA.

Objectives: To study whether antibodies to JP, alone or in combination with ACPA/RF, could increase the diagnostic sensitivity and specificity in untreated early (ue)RA patients.

Methods: Antibodies to JP were analysed in serum from patients in three independent ueRA cohorts as well as from population controls without rheumatic diseases (WINGA, Gothenburg and MFM-ÅUS, Malmö n=1062). ERAp (n=66), the smallest and most recent cohort was chosen for screening, and BARFOT and TIRA-2 (n=1939) for validation. We have developed a bead-based multianalyte flow immunoassay [2] and screened approx. 350 peptides derived from JPs of interest. We included monoclonal antibodies as assay calibrators and determined limit of detection (LoD). To assess positivity for autoantibodies to JP of interest above LoD, we used 5MAD (median absolute deviation) of the control populations as the cut-off.

Results: In the ERAp cohort, 5 autoantibodies discriminated RA patients from controls with 81% sensitivity and 100% specificity (Table 1). The same autoantibodies had 68% sensitivity and 98% specificity in the combined BARFOT and TIRA-2 cohorts. Together with RF and aCCP, only 2 of the 5 autoantibodies added statistically significant diagnostic value, increasing the sensitivity from 48% to 61% with 99% specificity. In aCCP- and RF-negative ueRA patients (n=536), the novel biomarkers identified 22.5% of the patients with 99% specificity compared to controls.

Table 1. Diagnostic capacity of the joint-specific antibodies

	Test panel			Performance		
Group of patients	**aCCP+**	**RF+**	**JP+**	**Sensitivity**	**Specificity**	**AUC(ROC)**
ERAp						
All patients (n=66)	-	-	X	81%	100%	89%
RF and aCCP-neg patients (n=7)[1]	-	-	-	-	-	-
BARFOT and TIRA-2, combined data						
All patients (N=1939)	-	-	X	68%	98%	86%
All patients (N=1939)	X	-	-	58%	99%	78%
All patients (N=1939)[2]	X	X	-	48%	100%	84%
All patients (N=1939)[2, 3]	X	X	X	61%	99%	86%
RF and/or aCCP-pos patients (N=1403)	-	-	X	84%	99%	93%
RF and aCCP-neg patients (N=536)	-	-	X	22%	99%	67%
RA, literature values						
Anti-CCP test	X	N/A	N/A	53–71%	95–96%	N/A

[1]*Not analysed due to lack of power* [2]*This patient population is both aCCP+ and RF+* [3]*Only 2 of the 5 autoantibodies added statistically significant to the diagnostic valueAUC, Area under the curve; ROC, receiver operating characteristic curve; N/A, not applicable. Controls without rheumatic diseases: N=935 for BARFOT / TIRA-2 and N=27 for ERAp.*

Conclusion: Autoantibodies to JP discriminate ueRA patients better then aCCP and RF alone and add an increased diagnostic value in particular for seronegative patients.

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POS0563 INFLUENCE OF ACTIVE VERSUS PLACEBO CONTROL ON TREATMENT RESPONSES IN RANDOMIZED CONTROLLED TRIALS IN RHEUMATOID ARTHRITIS

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Background: Randomised placebo controlled double-blind clinical trials are the mainstay of testing drugs for efficacy and safety and ultimately drug approval in medicine.[1] They are performed to ensure the efficacy of the active intervention against the effects of interventions without expected efficacy (placebo). Patients have to be fully consented to the risk of being (randomly) allocated to placebo by good clinical practice guidelines.[2] Knowledge about this risk may reduce the expectations about efficacy on both the patient and the investigator side.

Once many therapeutic options are available, active control interventions are often used as comparators instead of placebo in trials. In such studies, placebo

effects are still in place by the mere expectation of a response, but one could hypothesise that the observable effect of each intervention may be higher simply because of patients' awareness of an active treatment (i.e. no risk of placebo).
Here we investigated this hypothesis by comparing the effects of active controlled trials versus placebo controlled trials on the efficacy for the same therapeutic intervention in patients with rheumatoid arthritis (RA), in a systematic approach using all published trials in the field.
Objectives: To assess whether there is a systematic difference in response rates when investigating treatments in randomised controlled trials (RCTs) with active control compared to placebo control in RA clinical trials.
Methods: A systematic literature search was performed. We identified and matched RCTs that used comparable regimens, patient populations, background therapy and outcome reporting, but were different in terms of control group (active or placebo). Included studies were explored for potential risk of bias and mixed-model logistic regression was used to estimate odds ratios (OR) for achieving an American College of Rheumatology (ACR) 20, 50 and 70% response at week 12 in active-controlled studies compared to corresponding placebo-controlled studies.
Results: 7477 studies were screened, 576 of which underwent detailed review. Finally, 39 studies (45 study arms) were included for analysis. ACR response rates were higher in active controlled trials. The OR for achieving an ACR response when investigating the same treatment was consistently higher in studies with active control group than in corresponding studies with placebo control group: ORs were 1.64 (95% Confidence Interval, CI: 1.44-1.86; p<0.001) for ACR20 (Figure 1), 1.46 (95% CI: 1.28-1.71, p<0.001) for ACR50 and 1.61 (95% CI: 1.28-2.02; p<0.001) for ACR70 at week 12.

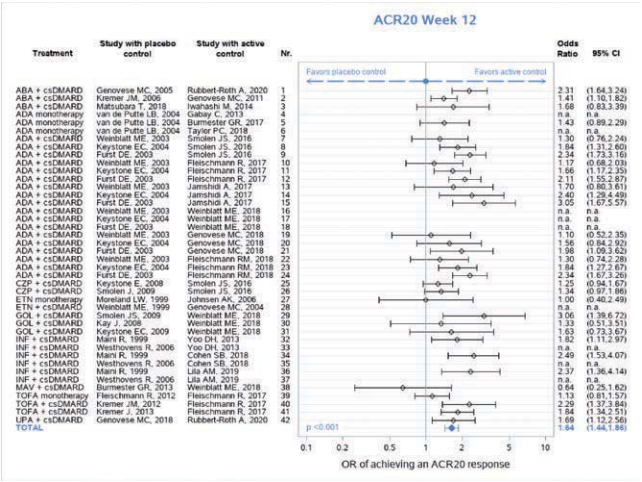

Figure 1. Forest plot showing ORs (with 95% CI) of achieving an ACR20 response at week 12 in studies with active control compared to studies with placebo control.

Conclusion: A systematic difference in response rates favouring head-to-head trials compared to placebo-controlled trials exists in RA clinical trials. This finding calls for consideration when interpreting and planning clinical trials and has implications for patients, investigators, sponsors and regulatory agencies.
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POS0564

SHOULD WE USE PHYSICIAN'S GLOBAL TO DEFINE REMISSION IN RHEUMATOID ARTHRITIS AND CONSIDER A SEPARATE PATIENT-CENTRED TARGET?

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Background: The definitions of remission play a crucial role in the treat-to-target strategy in rheumatoid arthritis.The patient's and physician's global assessment (PGA|PhGA) of disease activity are considered in current definitions, but PGA has been criticized for its poor relationship with actual disease activity. This leads to a considerable risk of overtreatment in patients who are otherwise in remission but fail this target solely because of PGA: PGA-near-remission. A dual-target strategy, excluding PGA from the definition of biological remission and the creation of a second target focused on disease impact has been proposed.[1] Another proposal is to substitute PGA by PhGA with the purpose of strengthening the definition with a fourth variable capable of conveying relevant unaccounted factors, such as comorbidity.[2]
Objectives: To assess the relationship of PGA and PhGA with objective measures of disease activity (DAS3v) and their impact upon near-remission and risk of overtreatment.
Methods: This is a cross-sectional analysis of data from RAID.PT, an observational, prospective and multicenter study, including adult patients fulfilling RA classification criteria. Tender (TJC28) and swollen (SJC28) 28 joint counts, C-Reactive Protein (CRP), Pain score, Health Assessment Questionnaire (HAQ), the Rheumatoid Arthritis Impact of Disease (RAID) total score, Hospital Anxiety and Depression Scale (HADS) scores, PGA and PhGA were collected. Disease Activity Score (DAS28-3v-CRP) was calculated and taken as the reference measure of current disease activity. Correlation between PGA and PhGA with other continuous variables was evaluated through Pearson´s Correlation Coefficient and variables with p<0.10 in univariate analysis were included in multivariable linear regression models.
Results: We included 299 patients, 81.3% women, mean age of 57.4±12.0 years and disease duration 9.4±9.5 years. Average DAS28-3v-PCR 2.4 (±1.9).
DAS3v-CRP is the strongest factor associated with PhGA, explaining 45% of its variance. Inversely, it only explains 2% of the variance of PGA, which is more affected by disease impact. In this clinical cohort, 13% of patients were in full Boolean remission and 41% in PGA-near-remission. Only 49 of 123 patients in the latter group had a PhGA >1. Considering PhGA instead of PGA in the Boolean definition of remission would increase the proportion of remission from 13 to 37.5% of the whole cohort.

Table 1. Factors Associated with PGA and PhGA in multivariate regression analysis

	PGA	PhGA(β, 95% CI)
	(β, 95% CI)	(β, 95% CI)
	ΔR^2	ΔR^2
DAS28-3v-CRP	**3.7 (1.9-5.5)**	**10.9 (9.4 to12.5)**
	0.02	**0.45**
RAID	**7.7 (6.7-8.8)**	**3.4 (2.5 to 4.3)**
	0.61	**0.09**
HAQ	**5.6 (1.0-8.1)**	**-3.4 (-6.4 to -0.4)**
	0.01	**0.01**
R^2	**0.64***	**0.55***

DAS28-3v-CRP: Disease Activity Score-3 variables C-Reactive Protein. PGA: Patient global assessment; PhGA: Physician Global Assessment; HAQ (health assessment questionnaire); RAID: Rheumatoid Arthritis Impact Disease score. ΔR^2 change of R^2associated with the inclusion of the variable in the model. *p<0,01

Conclusion: PhGA is a closer representation of actual disease activity than PGA, thus providing a more valid basis for treatment decisions aimed at disease activity. These observations support the substitution of PGA by PhGA in the Boolean definition of remission as it would strengthen the representation of disease activity and significantly reduce the risk of overtreatment in comparison to current definitions. The consequences of this change upon the prediction of long-term function and structural stability warrant evaluation. The patient's perspective will remain central to disease management in the form of a distinct target.
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POS0565 WORSE OUTCOMES LINKED TO ETHNICITY FOR EARLY INFLAMMATORY ARTHRITIS IN ENGLAND AND WALES: A NATIONAL COHORT STUDY

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Background: Patients from ethnic minority backgrounds suffer considerable health inequality, with generally poorer health outcomes relative to the rest of the population.[1] Further exploration of these differences is essential if we are to deliver the best care for all, and close the health gap for our patients.
Objectives: We used the National Early Inflammatory Arthritis Audit (NEIAA) to assess variability in care quality and treatment outcomes across ethnicities for patients diagnosed with early inflammatory arthritis (EIA) in England and Wales.
Methods: NEIAA is an observational cohort design. Data were from adult patients newly diagnosed with EIA, and seen by rheumatology in England and Wales between May 2018 and March 2020. Quality of care outcomes were assessed against six metrics contained within the National Institute for Health and Clinical Excellence (NICE) Quality Standard for Rheumatoid Arthritis.[2] Clinical outcomes were measured using DAS28. Outcomes were compared between ethnic groups (White, Black, Asian, Mixed, Other), and adjusted for confounders (age, sex, smoking, comorbidity, seropositivity and disease severity at presentation) using Logistic regression models with multiple imputation for missing data.
Results: Data for 35,807 eligible patients were analysed, of whom 30,643 (85.6%) were White and 5,164 (14.6%) were from ethnic minority backgrounds: 1,035 (2.8%) Black; 2,617 (7.3%) Asian; 238 (0.6%) Mixed; 1,274 (3.5%) Other. A total of 12,955 patients had confirmed EIA. Of those, 11,315 were White and 1,640 were from ethnic minority backgrounds: 314 (2.4%) Black; 927 (7.1%) Asian; 70 (0.5%) Mixed; 329 (2.5%) Other. Of 35,160 eligible patients who had data available, 14,803 (42.1%) were assessed by rheumatology within three weeks of referral. Of 9,900 EIA-eligible patients with data available, 5,642 (57.0%) started treatment within six weeks of referral. There were no significant differences in these outcomes by ethnicity. Ethnic minority patients did, however, have lower odds of disease remission at three months, relative to patients of White ethnicity (adjusted odds ratio 0.79; 95% CI: 0.65-0.96; p=0.02). This difference was due to lower odds of disease remission in Black and Asian patients, relative to White patients (Table 1). Ethnic minority patients were significantly less likely to receive initial treatment with methotrexate (0.68; 95% CI: 0.52-0.90; p=0.008) or with glucocorticoids (0.63, 95% CI: 0.49-0.80; p< 0.001).

Table 1. Associations between ethnicity and disease remission at three months in EIA patients

Model	Odds ratio	95% CI	P-value
Unadjusted			
All ethnic minority backgrounds	0.76	(0.62,0.93)	0.01
Black	*0.48*	*(0.34,0.67)*	*<0.001*
Asian	*0.74*	*(0.59,0.93)*	*0.01*
Mixed	*0.61*	*(0.28,1.35)*	*0.22*
Other	*1.09*	*(0.71,1.68)*	*0.67*
Age and sex-adjusted			
All ethnic minority backgrounds	0.78	(0.63,0.96)	0.01
Black	*0.49*	*(0.35,0.69)*	*0.00*
Asian	*0.75*	*(0.60,0.94)*	*0.01*
Mixed	*0.63*	*(0.28,1.39)*	*0.25*
Other	*1.11*	*(0.71,1.71)*	*0.63*
Fully-adjusted			
All ethnic minority backgrounds	0.79	(0.65,0.96)	0.02
Black	*0.57*	*(0.41,0.79)*	*0.001*
Asian	*0.76*	*(0.62,0.93)*	*0.009*
Mixed	*0.63*	*(0.27,1.46)*	*0.29*
Other	*1.04*	*(0.71,1.54)*	*0.80*

Conclusion: The results from this large cohort demonstrate that some minority ethnic groups are less likely to reach disease remission in the early months following an EIA diagnosis. Our results are not explained by delays in referral or treatment. Intitial treatment strategies varied across ethnic groups. These data highlight the need for investigation into the possible drivers of these inequitable outcomes and reappraisal of EIA management pathways.
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POS0566 PREDICTORS OF RESPONSE TO METHOTREXATE MONOTHERAPY IN ACTIVE RHEUMATOID ARTHRITIS: RESULTS FROM A MULTICENTRE, RANDOMIZED CONTROLLED TRIAL (MEIRA)

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Background: Methotrexate (MTX) is the gold standard, first-line therapy for rheumatoid arthritis (RA). However, not all patients respond to MTX, and the predictors of its response or non-response have not yet been reliably identified. Identification of these predictors will facilitate personalized therapeutic choices, and improve patient outcomes.
Objectives: To identify the clinico-laboratory predictors of response to MTX monotherapy in active RA.
Methods: This study included patients with active RA (SJC≥2 and TJC≥4) aged 18-55 years, with disease duration <5 years, who were not receiving DMARDs (except HCQ and low-dose prednisolone) and had been enrolled in the multicentre, parallel group RCT comparing two different MTX escalation strategies in RA (MEIRA)[1]. All these patients received MTX monotherapy which was started at 15 mg/week, escalated to 25 mg/week by 4-8 weeks, and continued till 16 weeks. MTX response was defined as EULAR good or moderate response (based on DAS28-CRP-3v) at 16 weeks. Stepwise, multivariable logistic regression was done using key demographic (age, gender, BMI, comorbidities), clinical (disease duration, DAS28, HAQ), and laboratory parameters (RF, anti-CCP, ESR, CRP, RBC MTX-polyglutamates 1-4, IL-6, MMP-3) as independent variables to identify predictors of MTX response. A two-tailed p-value <0.05 was used for defining statistical significance. (Trial Reg: CTRI/2018/12/016549)
Results: Out of a total of 178 included patients [84% females, mean age 40 (9) years, mean DAS28-CRP=5.4 (1.1)], 113 (63.5%) were classified as MTX responders at 16 weeks. Age (OR=0.95, p=0.01), BMI (OR=1.12, p=0.006), and RF (OR=0.34, p=0.045) were found to be independent predictors of MTX response on multivariable analysis (Table 1). On sensitivity analysis with DAS28-ESR-based EULAR response, age (OR=0.94, p=0.003) and RF (OR=0.42, p=0.059) were replicated as independent predictors of MTX response, in addition to pre-treatment swollen joint count (OR=0.94, p=0.05).

Table 1. Results of multivariable logistic regression analysis for prediction of response (as defined by DAS28-CRP-based EULAR good or moderate response) to methotrexate monotherapy in RA

Variable	OR (unadjusted)	Unadjusted p-value	OR (adjusted)	Adjusted p-value
Age	0.97 (0.93-1.002)	0.06	0.95 (0.91-0.99)	0.01
Male sex	0.78 (0.35-1.76)	0.55	-	
BMI	1.1 (1.02-1.19)	0.01	1.12 (1.03-1.22)	0.006
Presence of comorbidities	0.67 (0.31-1.44)	0.31	-	
Disease duration	0.98 (0.79-1.22)	0.87	-	
Baseline DAS28	1.1 (0.81-1.49)	0.54	-	
Baseline HAQ	1.04 (0.66-1.64)	0.86	-	
Baseline TJC	1.01 (0.96-1.05)	0.72	-	
Baseline SJC	0.97 (0.91-1.02)	0.24	-	
Baseline ESR	1.01 (1.00-1.02)	0.27	-	
Baseline CRP	1.00 (0.99-1.01)	0.85	-	
RF positive	0.31 (0.11-0.85)	0.02	0.34 (0.12-0.98)	0.045
Anti-CCP positive	0.73 (0.27-1.99)	0.54	-	
MTX PG1 (16 weeks)	0.99 (0.94-1.04)	0.69	-	
MTX PG2 (16 weeks)	0.98 (0.95-1.02)	0.37	-	
MTX PG3 (16 weeks)	0.99 (0.96-1.02)	0.43	-	
MTX PG4 (16 weeks)	0.99 (0.95-1.03)	0.62	-	
Serum IL-6 (baseline)	0.98 (0.95-1.02)	0.33	-	
Serum MMP-3 (baseline)	1.00 (1.00-1.00)	0.48	-	

BMI= Body Mass Index, CCP= Cyclic Citrullinated Peptides, CRP= C-reactive protein, DAS= Disease Activity Score, ESR= Erythrocyte Sedimentation Rate, HAQ= Health Assessment Questionnaire, MTX= Methotrexate, PG= polyglutamate, OR=Odds Ratio, RF=Rheumatoid Factor, SJC= Swollen Joint Count, TJC= Tender Joint Count Note: Only variables with p-value <0.2 on univariable analysis were included in the multivariable analysis.

Conclusion: Younger age, RF negativity, higher BMI, and lower pre-treatment swollen joint count are potential predictors of response to MTX monotherapy in RA.

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POS0567 SELF-PERCEIVED GENERAL HEALTH AT START OF ANTI-TNF THERAPY PREDICTS THERAPEUTIC RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS: ANALYSIS FROM THE CZECH BIOLOGICS REGISTRY ATTRA

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Background: SF-36 and its components, as well as other PROs have been shown to predict various disease outcomes. We hypothesized that positive responses to questions (Q) 11A "I seem to get sick a little easier than other people" and 11C "I expect my health to get worse" from the general health (GH) domain of the SF-36 v1 questionnaire may correspond to a more fragile self-perceived GH status, and thus serve as possible predictors of future disease outcomes in patients with rheumatoid arthritis (RA).

Objectives: We aimed to investigate whether these 2 questions could predict therapeutic response in patients with RA starting their first anti-TNF therapy.

Methods: We have used two separate datasets from the Czech biologics registry ATTRA to validate our hypothesis. Dataset D1 included RA patients with at least 1 year follow-up and all relevant data available starting their first-line anti-TNF treatment within period 01/01/2012-31/12/2017 (N=1808), and dataset D2 pts starting in in 01/01/2018–01/01/2020 (N=734). Our primary outcome was DAS28-ESR remission (REM) at 12 months. REM was defined as DAS28<2.6. Patients were grouped according their response (definitely/mostly yes vs. definitely/mostly no) to Q11A and Q11C at baseline. REM rates after 12 months of 1st-line anti-TNF treatment were compared across patients' groups with Pearson chi-squared test. Firstly, odds ratios (ORs) using logistic regression (univariate, and then adjusted to baseline DAS28 and HAQ) were calculated to predict REM at 12M. Secondly, ORs were calculated after matching pts with positive or negative responses by a propensity score (PS) using sex, age, disease duration, baseline DAS28, calendar year and co-medication to balance baseline differences.

Results: At baseline, 79% and 80% pts were female, mean (SD) age was 52(12) and 54(13) years, DAS28 6.3 (0.9) and 6.2 (1.1), HAQ 1.5(0.6) and 1.5(0.6), 74% and 68% were RF+, 70% and 69% ACPA+ in D1 and D2 resp. In D1 34% and 31% pts, and in D2 32% and 30% responded positively to Q11A and 11C resp. Patients with positive responses to Q11A and 11C tended to have slightly (but statistically significantly) higher DAS28, HAQ, CRP or ESR, and patient- and physician global activity assessment at baseline. At 12 months, 40% (49%), 31% (37%), and 30% (40%) patients with positive, negative and neutral response to Q 11A reached REM; p<0.001 (p=0.018) in D1 (D2) resp. At 12 months, 42% (51%), 31% (37%), and 30% (40%) patients with positive, negative and neutral response to Q 11C reached REM; p<0.001 (p=0.04) in D1 (D2) resp. Crude and adjusted ORs for reaching REM according to responses to Q11A and Q11C are shown in the Table 1.

Conclusion: We provide a robust evidence that self-perceived general health at start of anti-TNF therapy predicts reaching remission at 12 months in pts with RA.

Dataset	D1 (N=1808)		D2 (N=734)	
Baseline parameter	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
Analysis 1: Patients' responses and occurrence of DAS28 remission after 12 months - Univariate logistic regression models (Remission (DAS28-ESR < 2.6) after 12 months (1 – yes vs. 0 – no)				
Q11A: yes vs. no	1.62 (1.27; 2.05)	< 0.001	1.74 (1.20; 2.52)	0.004
Q11C: yes vs. no	1.48 (1.15; 1.91)	0.003	1.66 (1.13; 2.45)	0.010
Analysis 2: Patients' responses and occurrence of remission after 12 months - Adjusted ORs using logistic regression				
Q11A: yes vs. no	1.86 (1.24; 2.79)	0.003	2.04 (1.37; 3.03)	< 0.001
HAQ	0.48 (0.35; 0.64)	< 0.001	0.45 (0.33; 0.62)	< 0.001
DAS28-ESR	0.74 (0.61; 0.88)	< 0.001	0.89 (0.76; 1.05)	0.165
Q11C: yes vs. no	1.65 (1.28; 2.13)	< 0.001	1.91 (1.26; 2.88)	0.002
HAQ	0.59 (0.49; 0.71)	< 0.001	0.46 (0.34; 0.62)	< 0.001
DAS28-ESR	0.73 (0.64; 0.83)	< 0.001	0.91 (0.77; 1.06)	0.232
Analysis 3: Patients' responses and occurrence of remission after 12 months - Univariate logistic regression models after PS matching				
Q11A: yes vs. no	1.45 (1.12; 1.87)	0.004	1.70 (1.12; 2.59)	0.013
Q11C: yes vs. no	1.33 (1.00; 1.77)	0.050	1.51 (0.97; 2.34)	0.066

yes vs. no = definitely yes / mostly yes vs. definitely no / mostly no

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POS0568 HOW DOES INSTANTANEOUS RA DISEASE ACTIVITY AFFECT THE SHORT-TERM RISK OF ACUTE CORONARY SYNDROME? – A REGISTER-BASED STUDY

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Background: Rheumatoid arthritis (RA) patients have a reduced life expectancy, with cardiovascular disease (CVD) being the most frequent cause of death. The mechanisms behind the increased CVD morbidity and mortality in RA are not fully understood. Systemic inflammation is an important contributor to the accelerated arteriosclerosis in RA, and traditional risk factors for CVD are usually more prevalent in RA patients than in the general population. How much the current state of RA disease control impacts the short-term risk of CVD events remains unclear.

Objectives: To estimate the short-term risks and relative risks of acute coronary syndrome (ACS) in patients with RA as a function of RA disease activity, with particular focus on remission.

Methods: We identified patients with RA from the clinical rheumatology registers (CRR) in Sweden (SE) and Norway (NO), and for these patients we retrieved all registered clinical rheumatology visits from January 1st, 2012 to December 31st, 2020. At each visit, we assessed whether the patient was in remission or not according to multiple definitions including DAS28, ACR criteria, and SDAI. We also categorised the disease activity at each visit into categories (remission, low, moderate and high) using DAS28-ESR. Patients had to be free of any history of ACS in a five-year look back window (assessed at the visit date), and were followed for 6 months from each visit date until ACS event (defined as hospitalization due to ACS or death due to either ACS or sudden death) or censoring (death due to other causes, migration, end of the study). We compared the risk of ACS between patients who were (vs. were not) in remission using Cox regression with robust standard errors (accounting for the correlated data structure), adjusted for covariates (including age at the visit, sex, number of previous treatment courses, use of prednisolone, the expanded risk score in RA (ERS-RA), and defined co-morbidities: diabetes, malignancy, respiratory failure, liver failure and kidney disease) and stratified by country.

Results: We included 43,338 RA patients and their 223,197 visits (211,158 (SE), 12,039 (NO)). 74% of the visits were from women, with a mean age (SD) at visit of 62 (14) years. Several clinical characteristics including treatments and

comorbidity history varied with disease activity (Table 1). By contrast, age, number of previous DMARDs, disease duration and smoking habits were relatively similar across categories of disease activity (Table 1).

Table 1. Median [Q1-Q3] or percentage for clinical characteristics in remission (DAS28-ESR<=2.6) and high disease activity (DAS28-ESR>5.1) categories

Variable	Remission	High disease activity
N (visits)	91,497	25,364
Age, years	65[53-72]	63[53-72]
Disease duration	10[4-18]	8[2-17]
N treatment courses	0[0-0]	0[0-1]
Prednisolon	28%	58%
Tender joint count, 28-joints (TJC)	0[0-0]	10[6-14]
Swollen joint count, 28-joints (SJC)	0[0-0]	7[4-10]
Erythrocyte sedimentation rate, ESR	10[6-18]	28[15-47]
C-reactive protein (CRP)	3[1-4]	14[5-32]
Patient global assessment, PGA	13[4-27]	70[55-82]
Pain	12[4-27]	70[55-82]
ERS-RA	8[3-16]	12[5-23]
Ischemic heart disease	6%	7%
Diabetes	9%	13%
Hypertension	39%	42%
Hyperlipidemia	23%	25%
Ever smoking	45%	50%

We observed 598 ACS events (in 554 patients) during the 6-month follow-up window. Comparing patients not in remission to patients in remission, adjusting for the covariates described above, indicated that not being in remission increased the risk of ACS occurrence (Figure 1). Similarly, there was an association between DAS28-ESR at the visit and the risk of ACS during the coming six months.

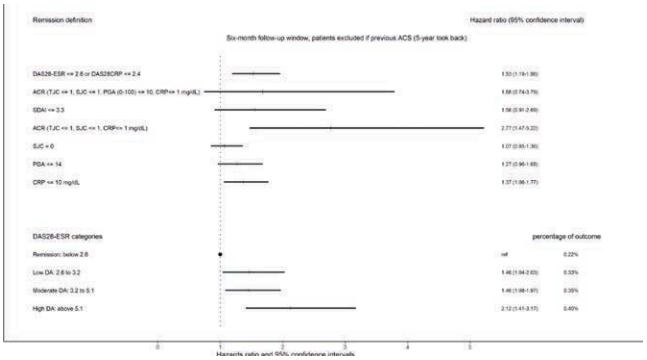

Figure 1. Hazard ratio (95% confidence interval) comparing patients not in remission to patients in remission, using several remission definitions. Percentage of visits with an ACS event within 6 months (bottom panel).

Conclusion: Being in RA remission at any visit is associated with a noticeably lower risk of ACS during the following months, suggesting that RA disease activity not only affects CVD risk in the longer term but also in the short term.
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POS0569 IDENTIFICATION OF JOINT LOCATIONS IN AN EARLY RHEUMATOID ARTHRITIS COHORT AS A CHARACTERISTIC OF DISEASE SEVERITY. DATA FROM THE ERA-UCLOUVAIN BRUSSELS COHORT

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Background: Early RA patients (ERA pts) often present with different areas of joint involvement, but limited data exist to identify which specific joint locations may be indicative of greater disease severity[1].
Objectives: This analysis investigated the baseline (BL) prevalence of swelling in individual joint locations and their possible association with disease characteristics and prognostic factors in a cohort of ERA pts.
Methods: This analysis was based on data from the ERA UCLouvain Brussels cohort in which patients were included according the ACR/EULAR 2010 criteria, naïve to DMARDs and followed in our daily clinic. The physician assessed prevalence of baseline individual swollen joint status (present, absent) through a physical examination. The joint count includes 44 joints. Similarly, all patient and RA characteristics were analyzed.The association between BL swelling and disease characteristics was investigated for each individual joints.
Results: 453 ERA pts were analyzed, BL swelling was most frequently observed in the wrist (71.1%) followed by IPP 3 and 2 joints (52.5 and 50.1%) (Table 1). MTP4 et 5 was more present in younger and MCP 2-4 in older pt *. BL swelling in the large size joint (knee, elbow, shoulder and ankle), in the medium size joint (wrist) and the small size joint (only MCP3, IPP 1, 2 and MTP5) was highly associated with higher DAS28 (CRP) *. Pts with BL swelling MCP1, 3, 4; MTP 1,2, 5 was associated with erosive disease*. In contrast, swelling of the knee was correlated with non erosive and also seronegative RA*. Swelling of many joints locations (knee, shoulder, ankle, MCP 1-5, MTP1, 5 and IPP 1, 2) were correlated significantly with a higher HAQ*. Only swelling of MTP1, 2, 5 was associated with the presence of ACPA antibodies*. No difference was observed for smoking habits and gender. *(*) - p≤0.001.*
Conclusion: In our cohort of ERA, small joints swelling was associated with erosive and seropositive RA (only MTP). Swelling of the large joint and the wrist seems to be associated with higher disease activity. In ERA, a difference in joint location presentation may identify pts with poor pronostic factors to be eligible for an intensive treatment or a personalized treatment approach. Further analysis are planned to analyze the correlation with erosion in each joint location and response to Methotrexate.
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Disclosure of Interests: None declared.
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POS0570 UNSUPERVISED DEEP-LEARNING IDENTIFIES SIX CLINICAL SUBTYPES OF RHEUMATOID ARTHRITIS AT BASELINE THAT ASSOCIATE WITH METHOTREXATE FAILURE DURING FOLLOW-UP

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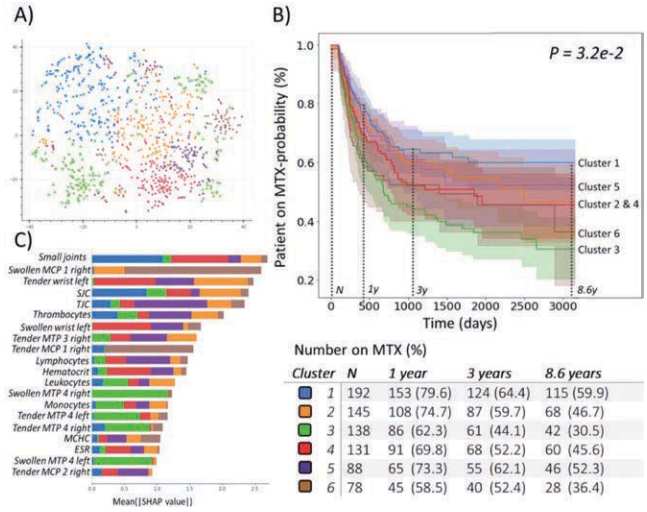
Background: Currently methotrexate (MTX) is the prevailing baseline treatment for Rheumatoid Arthritis (RA). Treatment response varies since RA is a highly heterogeneous disease. A tantalizing idea is that the factors causing clinical heterogeneity can already be elucidated at baseline.
Objectives: Disentangle clinical heterogeneity of RA patients at baseline to identify likely MTX failure during follow-up.
Methods: We constructed patient-specific profiles, featuring baseline clinical measurements which we split into three layers: 1) joint counts, 2) numerical hematology work up, and 3) categorical features (binary serological markers (aCCP/RF) and localization of joint inflammation and tenderness). We applied Z-score scaling on the numerical data and one hot encoding on the categorical features. To identify hidden structure across these layers we used Maui (Multi-omics Autoencoder Integration) [1], and Phenograph [2] for subsequent clustering of patients within the extracted latent space. We examined the most discriminatory features post-hoc with SHAP. With Kaplan Meier curves we assessed MTX efficacy using treatment switch as proxy for failure. We calculated hazard ratios (HR) with univariate Cox-regression.
Results: We had 944 RA patients with baseline health record data. MAUI identified 23 latent factors from 335 baseline variables. Phenograph showed 6 RA-subgroups (Table 1 & Figure 1).
The baseline clusters (C) are characterized by a different joint involvement or lab value: C1 had a low aCCP-positivity (37%) and high median ESR of 33. C1 had the most affected joints (primarily the small joints) with a swollen- (SJC) and tender joint count (TJC) of 15 and 19 respectively. C2 had mediocre aCCP-positivity (50%) and low median SJC=6 and TJC=9. C3 had MTP involvement, high aCCP-positivity (64%), and low ESR=19 but relatively high joint counts; SJC=9 and TJC=12. C4 had no wrists, high aCCP-positivity (65%), high ESR=28 and low joint counts; SJC=2, TJC=4. C5 had low lymphocyte numbers and a low median ESR=23, SJC=4 and TJC=3. C6 had MCP1 involvement, was mostly aCCP-positive (59%) and had a slightly higher median ESR=25, SJC=9 and TJC=11.

Table 1. Baseline characteristics of the different clusters

	C1	C2	C3	C4	C5	C6
N	224	179	171	162	116	92
Sex (F)*	131 (59)	122 (68)	125 (73)	112 (69)	71 (61)	57 (62)
RF*	95 (42)	89 (50)	106 (62)	107 (66)	68 (59)	55 (60)
aCCP*	82 (36.6)	89 (50)	110 (64)	105 (65)	65 (56)	54 (59)
DAS44(3)	3.6 (2.7-4.2)	2.7 (2.2-3.1)	2.4 (1.9-2.9)	2.1 (1.7-2.6)	2.2 (1.7-2.6)	2.8 (2.4-3.2)
SJC	15 (11-20)	6 (3-8)	9.0 (6-12)	2 (1-5)	4 (2-6)	9 (6-12)
TJC	19 (14-27)	9 (6-12)	12.0 (9-18)	4 (2-6)	3 (2-6)	11 (7-13)
ESR (mm/hr)	33 (14-53)	33 (14-48)	19 (9-35)	28 (14-39)	23 (11-38)	25 (9-36)
Age (yr)	63 (14)	60 (13)	53 (16)	59 (15)	63 (13)	58 (16)
MTX prescription*	192 (85)	146 (81)	138 (80)	131 (80)	88 (75)	78 (85)
Follow up (days)	1308 (743-2060)	1458 (880-2567)	1821 (982-2566)	1590 (1022-2245)	1566 (787-2000)	1468 (832-2211)
Symptom duration (days)	124 (52-334)	155 (46-537)	155 (62-365)	217 (77-775)	186 (62-548)	155 (62-365)

Presented are *binary variables as n(%) and continuous as median (Q1-Q3) or mean (SD).



Number on MTX (%)

Cluster	N	1 year	3 years	8.6 years
1	192	153 (79.6)	124 (64.4)	115 (59.9)
2	145	108 (74.7)	87 (59.7)	68 (46.7)
3	138	86 (62.3)	61 (44.1)	42 (30.5)
4	131	91 (69.8)	68 (52.2)	60 (45.6)
5	88	65 (73.3)	55 (62.1)	46 (52.3)
6	78	45 (58.5)	40 (52.4)	28 (36.4)

Figure 1. Overview of the distinct RA-clusters: A) 2D UMAP, B) Kaplan Meier plot of MTX-probability across 8.6 years (defined by cluster with shortest follow up), C) SHAP plot of most discriminatory features per cluster.

Clusters differed in MTX failure: 40%, 53%, 69%, 54%, 48% and 64% (for cluster 1-6, *P=3.2e-2*). Examining the local differences, we observed the biggest difference between C1 and C3 (HR 0.5 (95% CI 0.36-0.7), *P=4.4e-5*).

Conclusion: Using baseline data, we identified 6 putative novel RA subtypes which were associated with differences in MTX failure. Our study demonstrates the applicability of unsupervised deep learning and cluster analysis to elucidate hidden structure in the multi-modal EHR.

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POS0571

THE ROLE OF PROINFLAMMATORY CYTOKINES (IL-6 AND IL-17) IN PREDICTING 6-YEAR RESULTS OF EARLY RA THERAPY

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Objectives: To evaluate the dynamics of indicators of the cytokine profile and determine their role in predicting long-term results of early rheumatoid arthritis (RA) therapy.

Methods: The research included 93 patients with early RA (16 men and 77 women), average age Me;IQR (58 [49; 66] years), the duration of the disease 7 [4-11,5] months, DAS28-ESR high 59.7% and moderate activity 38.8%. All patients were prescribed a subcutaneous form of methotrexate (MT) at an initial dose of 10 mg / week with a rapid escalation of the dose to 20-30 mg / week. If the effectiveness of the therapy was insufficient, biologics were prescribed. The concentration of 27 cytokines in the blood serum: IL-1b, IL-1Pa, IL-2,-4,-5,-6,-7,-8,-9,-10,-12,-13,-15,-17, Eotaxin, FGF-basic, IFN-γ, IP-10, MCP-1, MIP-1α, MIP-1β, RANTES, TNF-α, VEGF (pg/ml) were determined with the help of the multiplex xMAR technology on the Bio-Plex array system analyzer (BIORAD, USA).

Results: Before the start of the therapy, the DAS 28-ESR was 5.31 [4.79; 6.14], SDAI – 28.27 [18.79; 40.73], after 6 years, the DAS28-ESR was 4.0 [3.4; 4.59], SDAI - 15.06 [9.32; 21]; remission of the disease: DAS 28-ESR was detected in 7.8%, SDAI-5.3%; the low activity: DAS28-ESR in 21%, SDAI in 30.1 %, moderate activity: 60% according to DAS28-ESR, 56% according to SDAI, high activity: 11.2% according to DAS28-ESR, 8.6% according to SDAI. Prior to the start of therapy, the group of patients with RA had a higher level of pro-inflammatory cytokines (IL -6, IL -12, IL -15, IL -17), anti-inflammatory (IL -5, IL -13), chemokines (IP- 10, MIP-1ß, IL-8) and growth factors (IL -7, PDGF-BB, VEGF) compared with healthy donors ($p<0.05$) Table 1. After 6 years, the patients were divided into groups: remission/low activity and moderate/ high activity. Among the patients who achieved remission/low SDAI activity by the 6th year after the initiation of the therapy, a lower level of IL -6, IL -17 after 12 weeks, IL -9 after 24weeks $p<0.05$ was observed. There was a low level of IP-10 ($p=0.06$) 12 weeks after the start of therapy. (Table 2)

Table No. 1 Initial cytokine level of patients with early RA compared with healthy donors (pg/ml)

Parameters	Patients with RA(n=23)	Donors (n=30)
IL-1b	2,52 [2,21; 4,95]	4,07 [2,61;4,9]
IL-1Pa	219,36 [100,29;599,77]	150,64 [111,19; 253,83]
IL-2	7,12 [2,94; 23,12]	10,765 [5,53; 13,87]
IL -4	2,71 [2,33; 4,4]	3,315 [0,21;5,85]
IL -5	6,06 [3,65; 7,66]	2,92 [0,2; 5,24] *
IL -6	36,09 [20,38; 82,02]	7,78 [4,5;13,09] *
IL -7	33,83 [24,74; 64]	8,15 [0,5; 21,52] *
IL -8	27,99 [22,92; 40,54]	12,47 [4,76; 16,25] *
IL -9	23,01 [14,78; 46,54]	34,17 [26,3; 42,36]
IL -10	13,61 [5,24; 33,46]	13,22 [5,83; 37,47]
IL -12	38,14 [19,98; 92,89]	5,775 [2,24; 9,94] *
IL -13	4,53 [0,01; 14,99]	16,685 [9,93; 22,44] *
IL -15	0,37 [0,01; 2,28]	6,695 [3,92; 17,42] *
IL -17	11,24 [5,81; 16,71]	22,87 [5,23; 90,3] *
Eotaxin	263,51 [179,96; 442,95]	102,415 [19,39; 585,69]
FGF-basic	20,83 [15,79; 23,89]	27,25 [19,32; 44,3] *
IFN-γ	111,21 [86,27; 358,6]	285,345 [112,29; 1037,9] *
IP-10	5616,05 [3123,44; 9901,46]	717,8 [188,68; 4064,81] *
MCP-1	36,99 [19,81; 93,85]	48,595 [22,26; 120,74]
MIP-1α	9,51 [8,62; 10,09]	10,815 [8,84; 18,1]
MIP-1β	140,72 [116,05; 174,44]	66,045 [49,36; 99,42] *
PDGF-BB	4975,53 [3031,33; 8994,55]	26024,51 [5854,75; 58715,04]*
TNF-α	42,66 [34,01; 110,11]	38,9 [17,2; 64,87]
VEGF	84,02 [56,71; 160,84]	205,56 [63,85; 312,77] *

p<0,05 from baseline

Table No. 2. The relationship between the dynamics of the cytokine concentration (after 12 and 24 weeks) and the results of therapy after 6 years

	After 12 weeks		After 24 weeks	
Parameters	Remission/low activity according to SDAI (n=30)	Moderate/ high activity according to SDAI (n=63)	Remission/low activity according to SDAI (n=30)	Moderate/ high activity according to SDAI (n=63)
IL -6, pg/ml	7,7 [7,4; 23,3] *	23,5 [12,4; 69,5]	13,8 [5,8; 28,6]	33 [17,4; 45,8]
IL -9, pg/ml	13,5 [9,1; 18,9] *	17,8 [15; 29]	12,6 [6,8; 16,2] *	18,5 [14,2; 22,8]
IL -17,pg/ml	0,01 [0,01; 5,5] *	12,4 [0,01; 24,2]	3,7 [1,4; 9,2]	12,4 [0,01; 23,1]
IP-10, pg/ml	1319 [936; 2586]	2430 [2074; 4023],p=0,06	1358,1 [817; 2504]	1489 [1332; 3005]

*p<0,05 from baseline

Conclusion: The evaluation of the level of proinflammatory cytokines (IL -6, IL -17), chemokines IP-10, immunoregulatory cytokine IL -9 after 12 weeks and 24weeks of the initiation of therapy allows to identify a group with the worst long-term prognosis.

Disclosure of Interests: None declared.

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POS0572 ARE WOMEN WITH RHEUMATOID ARTHRITIS REALLY LESS LIKELY TO ACHIEVE REMISSION WITH BIOLOGICS? A COHORT STUDY IN THE SWISS CLINICAL QUALITY MANAGEMENT COHORT

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Background: Rheumatoid arthritis (RA) affects women three time more frequently than men. However, compared to men, women may have a lower likelihood of achieving clinical response, but data related to this topic are controversial.

Objectives: We aimed to compare the likelihood of achieving remission across men and women with RA, who started their first biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARDs).

Methods: This observational cohort study in the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry included adult RA patients who started their first b/tsDMARDs (from 1997 to 31/April/2018). Patient characteristics at start of the b/tsDMARD were compared between men and women. Subsequently, logistic regression was used to assess the likelihood of achieving remission during the first year after b/tsDMARDs start, defined by disease activity score 28 (DAS28) <2.6, in men compared to women (reference group). Secondary analyses were adjusted for age and seropositivity as prognostic factors, and we investigated the role of potential mediators or factors that could explain the findings from the main analysis.

Results: The study included 3722 RA patients, of which 2839 (76.3%) were women and 883 (23.7%) were men. Compared to women, men were older at diagnosis and start of b/tsDMARDs, and had shorter time from diagnosis to their first b/tsDMARD (3.4 vs 5.0 years, p<0.001). At baseline (b/tsDMARD initiation), women had significantly more active disease activity (DAS28) and worse patient-reported outcomes (Health Assessment Questionnaire, tender joints). Concomitant osteoporosis and depression/anxiety were more frequent among women, while men had more frequent diabetes and prior or current smoking record. Physician's global disease assessment and swollen joints were similar across groups. Compared to women, men were 21% more likely to achieve DAS28-remission, with an odds ratio (OR) 1.21, 95% confidence interval (CI) 1.02-1.42. Secondary analyses adjusting by for age and seropositivity did not change the findings (adjusted OR 1.24, 95% CI 1.05-1.46). Our analyses of potential mediators suggested that the observed effect may be explained by the shorter disease duration and lower DAS28 at treatment initiation in men vs women.

Conclusion: Men started b/tsDMARDs at an earlier stage of disease than women, particularly regarding disease duration and disease activity (DAS28) at b/tsDMARD initiation, and they presented higher odds of remission. This highlights the importance of an earlier treatment, and it suggests to target an earlier stage of disease in women to match the benefits observed in men.

Acknowledgements: We thank all patients and rheumatologists contributing to the SCQM registry, as well as the entire SCQM staff. A list of rheumatology offices and hospitals which contribute to the SCQM registry can be found at http://www.scqm.ch/institutions. A list of financial supporters of SCQM can be found at http://www.scqm.ch/sponsors. We would like to add a personal thank you to Axel Finckh (University Hospitals of Geneva) for his input regarding the database. AMB acknowledges that her professorship is partly endowed by the Swiss National Pharmacy Association (PharmaSuisse) and the ETH Foundation.

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POS0573 MUSCULOSKELEATAL ULTRASOUND STUDIES ARE CRITICAL FOR DETECTING SERONEGATIVE INFLAMMATORY ARTHRITIS

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Background: The autoantibody status of rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (anti-CCP Ab) has gained widespread recognition for its role in the diagnosis of rheumatoid arthritis (RA) based on the latest diagnostic criteria for RA.[1] However, in early disease, the rates of antibody expression have been reported as low as 50%[2], rendering early diagnosis of RA difficult. Furthermore, the nature of seronegative rheumatoid arthritis is unknown, though it is presumed to have less aggressive disease course as compared to its seropositive counterparts. Musculoskeletal (MS) ultrasound studies have been widely used in recent clinical practice to assess soft-tissue abnormalities of the joints and disease states in RA, such as synovitis and bone erosions. MS ultrasound studies were recently shown to be more sensitive to detect early synovial changes and erosions than other radiographic methods while maintaining cost-effectiveness.[3-5] We hypothesize that MS ultrasound studies are more sensitive to detecting inflammatory changes in seronegative inflammatory arthritis, which is often subclinical in presentation.

Objectives: To assess the role of MS ultrasound studies in detecting early inflammatory changes in the joints and diagnosing seronegative inflammatory arthritis.

Methods: A retrospective electronic medical record review was performed of all patients at the two University at Buffalo rheumatology clinics who underwent MS ultrasound studies after complaining of multiple joint pain. All these patients were previously seen and evaluated by at least one other medical provider, who found no evidence of inflammatory arthritis on physical examination. These patients did not meet diagnostic criteria for rheumatoid arthritis due to a lack of gross joint swelling and/or positive serological makeup. As part of their clinical care, they were referred to obtain MS ultrasound studies to rule out inflammatory arthritis. All patients were de-identified at initial data collection. Information pertaining to the patients' 1) demographics (gender, age, ethnicity, etc.), 2) findings of MS ultrasound studies, and 3) serological studies (RF, anti-CCP Ab, HLA-B27) was collected and tabulated.

Results: Of the 363 patients who underwent MS ultrasound studies, 280 of them (77.1%) of them were found to have synovial hypertrophy [minimal = 23%, mild = 46%, moderate = 29%, severe = 2%] in bilateral MCP, PIP, carpal, and/or MTP joints, therefore conferring a diagnosis of inflammatory arthritis. The average age of these 280 patients was 48.35 ± 14.86 years old at the time of diagnosis, with female to male ratio of 4.38:1. Surprisingly, of these 280 patients with evidence of inflammatory arthritis, 69 (24.6%) of them were found to have joint erosions with either MCP or MTP joints, supporting a diagnosis of advanced inflammatory arthritis with erosive disease. The erosions were predominantly located in MTP joints (77.1%) as compared to MCP joints (22.9%). Therefore, our findings clearly demonstrated distinct clinical and ultrasonography features of seronegative inflammatory arthritis (SNIA) as compared to seropositive RA.

Conclusion: MS ultrasound studies are more sensitive to and critical for detecting inflammatory changes and joint damages in SNIA due to its subclinical presentation. Based on our findings, SN IA is underdiagnosed in individuals who complain of joint pain without gross synovitis. SNIA also likely has distinct pathophysiology that needs further characterization.

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Disclosure of Interests: Clarice Lin: None declared, Richard Chou Consultant of: Sun Pharmaceuticals Industries Limited.
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POS0574 FEMALE GENDER AND STRESS ARE MAIN DETERMINANTS OF NON-ADHERENCE AND NEGATIVE ILLNESS PERCEPTION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: SINGLE CENTRE RESULTS FROM THE PRIME REGISTRY COHORT

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Background: Adherence to medications among patients with RA is traditionally considered to be low. Little is known about the indicators and the outcomes of patients having good adherence to medications among Pakistani RA patients.
Objectives: We aimed to assess the level of non-adherence and its associations with clinical indicators and outcomes using validated measures in a large consecutive Pakistani RA population. Moreover, we measured illness perception using additional validated tools to help us better understand this concept.
Methods: This was a cross-sectional study conducted using data collected at the time of patient enrolment in the PRIME registry. IRB approval and informed consent was obtained. The clinical variables studied were gender, age, smoking habits, body mass index, education status, marital status, disease duration, Charlson Comorbidity Index. Education status was stratified by whether participants completed secondary (high) school education. Evaluation of disease activity and severity was made as per internationally agreed definitions. To measure adherence, the instrument used in the study was the Urdu version of the General Medication Adherence Scale (GMAS), which has been validated for RA patients. Brief Illness Perception Questionnaire (BIPQ) is the simplified version of the Illness Perception Questionnaire (IPQ). BIPQ is a nine-item scale designed to rapidly assess the cognitive and emotional representations of illness. To facilitate interpretation of results in daily clinical practice and to identify patients with the most negative illness perception, we dichotomized the BIPQ scores using the 75th interquartile range score as cutoff, as previously done.
Results: The data of consecutive 320 RA patients enrolled in PRIME registry (mean age 37.4±13.4 years, 74% female, disease duration of 73±68 months, 30% rural residents, 32.5% had low education status of ≤primary school, and 35% of the cohort was employed) was reviewed. Thirty six percent of the cohort (n=116) was noted to have non adherence. On multiple logistic regression analysis, a significant association of moderate-severe stress (OR 1.85, CI 1.04-3.2, p=0.03), DAS-28 scores (OR 1.83, CI 1.52-2.21, p<0.001), HAQ scores (OR 1.77, CI 1.07-2.92, p=0.02), deformed joint counts (OR 1.30, CI 1.15-1.46, p<0.001). We further examined the concept of non-adherence among our cohort across three domains or components of GMAS questionnaire individually. Firstly, on multivariate regression analysis showed that non-adherence due to patient behavior had significant association with male gender (OR 0.48, p=0.01), unemployment (OR 1.82, p=0.02), stress (OR 2.17, p=0.001), DAS-28 (OR 1.15, p=0.050), worse HAQ scores (OR 1.83, p=0.005). Secondly, multivariate regression analysis showed that non-adherence due to comorbidity and pill burden was associated with age of onset of arthritis (OR 1.02, p=0.006), DAS-28 (OR 1.18, p=0.03), and HAQ (OR 1.81, p=0.008). Thirdly, multivariate regression analysis showed that cost-related non-adherence had no significant association with patient related demographics and traits, but was noted to have significant association with worse DAS-28 and HAQ scores. The mean total BIPQ score of the cohort was 62±8.8. Twenty six percent of the cohort (n=86) was noted to have the most negative illness perception (BIPQ score of >68). On multiple logistic regression analysis, a significant protective association of male gender (OR 0.24, CI 0.11-0.53, p<0.001) and age of onset of arthritis (OR 0.96, CI 0.94-0.99, p=0.01), along with significant association of worse HAQ scores (OR 3.7, CI 2.2-6.1, p<0.001) was noted with the most negative illness perception.
Conclusion: Non-adherence is common and its main determinants were female gender and stress, along with associated adverse clinical outcomes. Gender-based discrimination in low socioeconomic states along with associated stress is a plausible explanation.
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POS0575 CAPACITY OF SIX DIFFERENT CARDIOVASCULAR RISK ALGORITHMS FOR THE DETECTION OF CAROTID PLAQUE IN RHEUMATOID ARTHRITIS

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Background: Current EULAR recommendations for cardiovascular risk (CVR) assessment in rheumatoid arthritis (RA) indicate that the CVR evaluation should be performed according to national guidelines; however, there was no algorithm designed for the Mexican population until 2019, when the World Health Organization (WHO) published the CVR charts for 21 world regions, including Mexico (1).
Objectives: To determine the capacity of the WHO and other five algorithms for the detection of carotid plaque (CP) in RA patients.
Methods: Cross-sectional study. We included 164 patients with RA diagnosis according to the 2010 ACR/EULAR classification criteria, aged 40-75 years. CVR was calculated with six algorithms: WHO, FRS-lipids, FRS-BMI, SCORE, ACC/AHA and QRISK3. Carotid ultrasound was performed in all patients to identify the presence of CP. A ROC-curve analysis was performed, and the cutoff points of each algorithm were determined using the Youden Index. Area under the curve (AUC), sensitivity, specificity, and likelihood ratios (LR) were calculated. A *p*-value <0.05 was considered statistically significant.
Results: The prevalence of CP was 35.9%. The WHO algorithm showed AUC: 0.729 (0.649-0.809), cutoff point: 5.25, sensitivity: 72.9%, and specificity: 64.8%. FRS-lipids showed AUC: 0.684 (0.601-0.767), cutoff point: 8.62, sensitivity: 67.8%, and specificity: 61.0%. FRS-BMI showed AUC: 0.700 (0.618-0.781), cutoff point: 11.55, sensitivity: 72.9%, and specificity: 61.0%. SCORE showed AUC: 0.687 (0.601-0.773), cutoff point: 1.5, sensitivity: 79.7%, and specificity: 45.7%.

Table 1. Capacity of cardiovascular risk algorithms to detect presence of carotid plaque in rheumatoid arthritis patients

		CI 95%					Likelihood radio	
Algorithms (cut-off points)	**AUC**	**Inferior limit**	**Superior limit**	*p*	**Sensibility**	**Specificity**	**+**	**-**
WHO (5.25)	0.729	0.649	0.809	<0.001	72.9%	64.8%	2.07	0.42
FRS-lipids (8.62)	0.684	0.601	0.767	<0.001	67.8%	61.0%	1.74	0.53
FRS-BMI (11.55)	0.700	0.618	0.781	<0.001	72.9%	61.0%	1.87	0.44
SCORE (1.5)	0.687	0.601	0.773	<0.001	79.7%	45.7%	1.47	0.44
ACC/AHA (3.82)	0.687	0.604	0.770	<0.001	62.7%	61.0%	1.61	0.61
QRISK3 (6.05)	0.733	0.654	0.811	<0.001	71.2%	61.0%	1.82	0.47

AUC, area under the curve; WHO, World Health Organization; FRS, Framingham Risk Score; BMI, body mass index.

ACC/AHA showed AUC: 0.687 (0.604-0.770), cutoff point: 3.82, sensitivity: 62.7%, and specificity: 61.0%. QRISK3 showed AUC: 0.733 (0.654-0.811), cutoff point: 6.05, sensitivity: 71.2%, and specificity: 61.0%. All algorithms had a *p*-value <0.001 (Figure 1 and Table 1).

Conclusion: The WHO calculator was one of the best algorithms for the detection of CP, with the best positive and negative likelihood ratios; however, like the other algorithms, a lower cut-off point than the one established by official guidelines was needed to identify high-risk patients with the presence of CP, who were initially classified as low-moderate risk by the CVR algorithm.

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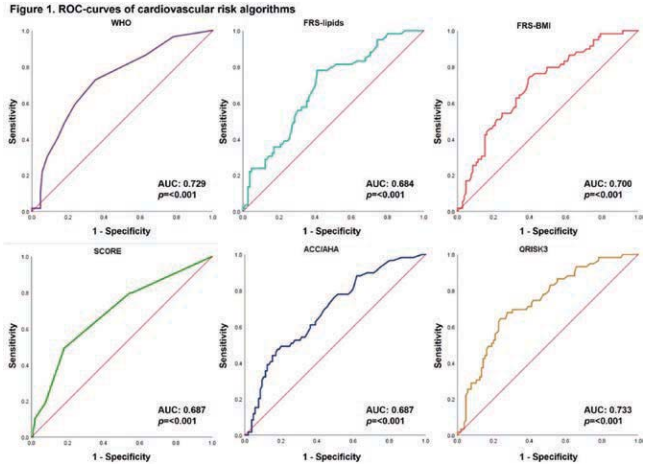

Disclosure of Interests: None declared.
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POS0576

ASSOCIATION BETWEEN POTENTIAL PROGNOSTIC FACTORS AND ADVERSE HEALTH OUTCOMES IN RHEUMATOID ARTHRITIS: A STUDY OF 5658 UK BIOBANK PARTICIPANTS

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Background: There is a pressing need to identify simple prognostic factors, which are readily available in primary and secondary care settings, that can predict adverse health outcomes in people with rheumatoid arthritis (RA). Exploring various clinical, physiological and patient-reported measures as prognostic factors may enhance risk stratification and promote more personalised care for RA patients.

Objectives: To determine the association, if any, between selected prognostic factors and all-cause mortality and major adverse cardiovascular events (MACE; including myocardial infarction and stroke) in an RA population.

Methods: UK Biobank participants that self-reported RA were included in this study. Prognostic factors were selected from the literature based on relevance, predictive potential, simplicity and accessibility in a primary/secondary care setting. Those included were categorised into the following domains: anthropometric measures (body mass index (BMI), body fat percentage, waist circumference, waist-to-hip ratio), functional measures (hand grip strength (HGS), usual walking pace (UWP)), inflammatory markers (C-reactive protein (CRP)), patient-reported measures (pain), physiological measures (blood pressure (BP), heart rate (HR)) and serological markers (rheumatoid factor (RF)), with normal ranges used as reference categories. Associations between individual factors and outcomes were explored using Cox proportional hazards models. Models were adjusted for age, sex, socioeconomic status, number of additional long-term conditions and smoking status in the first instance to identify potential individual predictors. Models were then further adjusted for any identified individual predictors to determine the most important prognostic factors.

Results: 5658 (1.1%) UK Biobank participants self-reported RA (mean age 59 (standard deviation 7.13); 69.8% female). 670 deaths (median 11 years) and 370 MACE (median 8 years) were recorded during the follow-up period. Several significant individual associations with all-cause mortality (Figure 1A) and MACE (Figure 1B) were found. After further adjustment for these significant individual predictors, the following factors demonstrated significant associations with risk of all-cause mortality, independent of the other significant predictors: underweight BMI (<18.5kg/m^2) (hazard ratio (HR) 2.96 [95% confidence intervals (CI) 1.59-5.51]), obese BMI (≥30.0kg/m^2) (HR 0.52 [95% CI 0.36-0.76]), 3-10mg/L CRP (HR 1.41 [95% CI 1.14-1.75]), >10mg/L CRP (HR 1.77 [95% CI 1.39-2.26]), low HGS (<16kg female or <27kg male) (HR 1.28 [95% CI 1.05-1.56]) and slow UWP (patient-reported) (HR 1.31 [95% CI 1.06-1.62]). Likewise, the following factors were found to be significantly associated with MACE, independent of other significant factors: >10mg/L CRP (HR 1.62 [95% CI 1.19-2.20]), low HGS (HR 1.61 [95% CI 1.26-2.07]) and slow UWP (HR 1.50 [95 % CI 1.15-1.97]).

Conclusion: In this RA population, the risk of all-cause mortality was approximately three-fold higher in those who have an underweight BMI when compared to those who have a BMI in the normal range, when adjusted for all other significant factors, while an obese BMI appeared to lower this risk, consistent with the "obesity paradox" reported in RA [1]. Increased levels of CRP, low HGS and slow UWP were also all independently associated with an increased risk of all-cause mortality and MACE. Our findings highlight the potential value of these factors for predicting adverse outcomes in RA populations. A simple, yet multidimensional approach to risk assessment, combining well-tolerated, easily repeatable measures such as those included here may provide important prognostic information at both primary and secondary care levels, while limiting excessive and overly invasive testing on RA patients.

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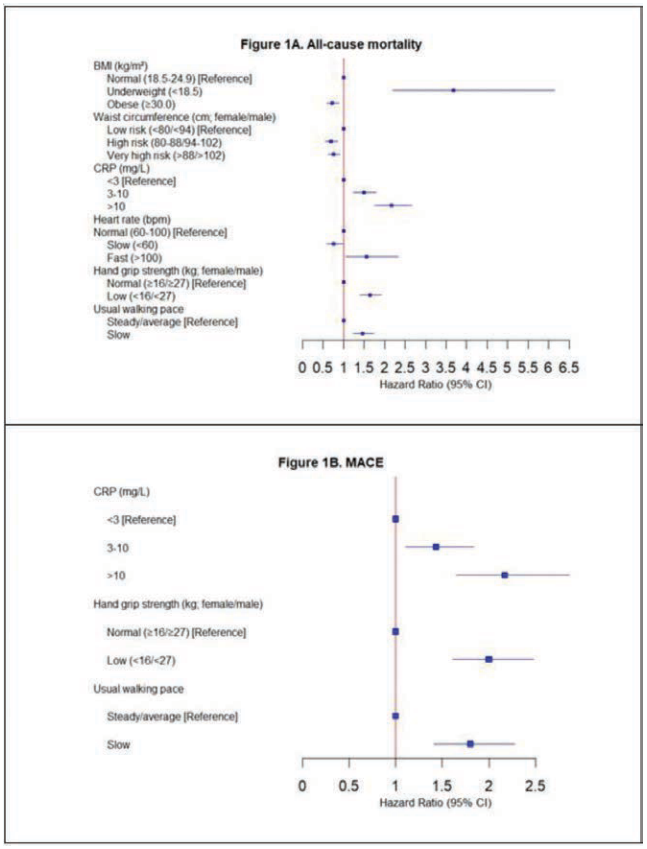

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POS0577 COMPARISON OF THE WHO AND ACC/AHA CARDIOVASCULAR ALGORITHMS TO DETECT CAROTID PLAQUE IN RHEUMATOID ARTHRITIS

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Background: Cardiovascular disease is the major cause of death in rheumatoid arthritis (RA) patients. Cardiovascular risk algorithms are used to estimate the probability for the development of a cardiovascular event in 10 years, according to patients' characteristics, however, no algorithm existed for the Hispanic population until the World Health Organization (WHO) published the cardiovascular disease risk charts for 21 regions (1).
Objectives: To compare the capacity of the 2019 WHO algorithm and the 2013 American College of Cardiology/American Heart Association (ACC/AHA) algorithm for detecting the presence of carotid plaque (CP) in RA patients.
Methods: Cross-sectional study. We recruited a total of 164 patients with RA diagnosis, according to the 2010 ACR/EULAR classification criteria, aged 40-75 years. Patients with a previous cardiovascular event were excluded. Cardiovascular risk was evaluated with the 2019 WHO algorithm for the Mexican population and the 2013 ACC/AHA cardiovascular algorithm. The results were multiplicated by 1.5, according to current guidelines. A carotid ultrasound was performed to all study subjects by a certified radiologist blinded to clinical information. Distribution was evaluated with the Kolmogorov-Smirnov test. Correlations were performed with the Spearman-rho coefficient (rho). A ROC-curve analysis was performed for both algorithms. The areas under the curve (AUC) of the algorithms were compared using the method of DeLong.
Results: The presence of CP was detected in 59 (36.0%) patients. Demographic characteristics are shown in Table 1. There was a large positive correlation between the WHO and the ACC/AHA algorithms (rho=0.880, p=<0.001). Both algorithms showed significant discrimination for the presence of CP in RA patients, the WHO algorithm had an AUC 0.729 (95% CI 0.649-0.809, p=<0.001) and the ACC/AHA algorithm had an AUC 0.687 (95% CI 0.604-0.770, p=<0.001). However, there was a difference when comparing both AUC, which was higher with the WHO algorithm (p=0.042) (Figure 1).

Table 1. Demographic characteristics of RA patients

Characteristics	RA patients (n=164)
Age, years, mean ± SD	55.82 ± 8.94
Women, n (%)	157 (95.73)
T2DM, n (%)	27 (16.46)
Hypertension, n (%)	53 (32.32)
Dyslipidemia, n (%)	58 (35.36)
Obesity, n (%)	56 (34.15)
Active smoking, n (%)	15 (9.15)
WHO algorithm, median (IQR)	4.5 (3.0-9.0)
ACC/AHA algorithm, median (IQR)	3.75 (1.80-9.26)
Carotid plaque, n (%)	59 (36.0)

RA, rheumatoid arthritis; T2DM, type 2 diabetes mellitus; WHO, world health organization; ACC/AHA, American College of Cardiology/American Heart Association.

Conclusion: Our results showed that although both algorithms had significant discrimination for the presence of CP, the 2019 WHO algorithm had a better capacity for the detection of CP than the 2013 ACC/AHA algorithm, for this specific Hispanic RA population. This could be attributed to the fact that the WHO algorithm was designed for 21 different regions, including the Mexican population.
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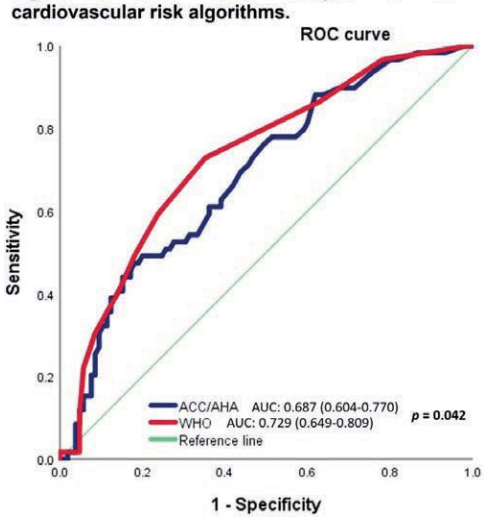
Figure 1. ROC curve analysis of the cardiovascular risk algorithms.



Disclosure of Interests: None declared.
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POS0578 RISK AND RISK FACTORS OF MORTALITY IN RHEUMATOID ARTHRITIS PATIENTS WITH INTERSTITIAL LUNG DISEASE: A NATIONWIDE, POPULATION-BASED COHORT STUDY

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Background: Recent meta-analysis by Meihua Qiu et al [6] has shown ten factors associated with increased risk of mortality in rheumaoitd arthritis associated interstitial lung disease (RA-ILD): older age, male sex, smoking history, lower diffusing capacity of the lung for carbon monoxide, lower forced vital capacity predicted, higher composite physiological index, usual interstitial pneumonia pattern on high-resolution computed tomography, emphysema presence and acute exacerbation of ILD. However majority of the studies were single-centre studies. There were very limited studies on influence of treatment, especially disease-modifying anti-rheumatic drugs on mortality in RA-ILD.
Objectives: To examine the risk and risk factors of mortality among RA patients with ILD.
Methods: Using the 1997-2013 Taiwanese National Health Insurance Research Database, we identified 32,289 newly diagnosed RA patients from 2001 to 2013. Of them, 214 subsequently developed ILD. We then matched RA patients with ILD at a ratio of 1:10 to RA patients without ILD by sex, age at RA diagnosis, year of RA diagnosis date and disease duration. We further conducted propensity score matching (PSM) at a 1:1 ratio for selected comorbidities using the greedy algorithm to select RA-ILD patients and controls. We examined the association of mortality with ILD in RA patients using the Cox proportional hazard model shown as adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs). Among 214 RA-ILD patients, we assessed factors associated with mortality using the multivariable Cox regression analysis.
Results: Before PSM, a total of 164 RA-ILD patients and 1,640 RA patients without ILD were selected. After PSM, 155 RA-ILD patients and non-ILD RA controls were included. The incidences of mortality were 2,975 per 10^5 years and 2,981 per 10^5 years in the RA-ILD group before and after PSM, respectively. The incidence rate ratios (95% CIs) of mortality were 2.66 (1.95–3.63) and 2.55 (1.51–4.29) in the populations before and after PSM, respectively. Using the multivariable Cox regression analysis and the conditional Cox regression analysis, the risk of mortality was associated with ILD in RA patients (before PSM: aHR, 3.17 [2.17–4.63]; after PSM: 7.16 [1/76–29.15]). Among 214 RA-ILD patients, significant predictors for mortality included male gender (aHR, 2.59), age (aHR, 1.04), residence in suburban region (aHR, 2.29), peripheral vascular disease (PVD) (aHR, 83.26) and chronic pulmonary obstructive disease (COPD) (aHR, 2.73). The risk of mortality was not associated with use of non-steroidal anti-rheumatic drugs, corticosteroid, methotrexate, sulfasalazine, leflunomide, hydroxychloroquine, immunosuppressants, tumor necrosis factor inhibitors and rutixumab.
Conclusion: This population-based, cohort study demonstrated that ILD was associated with increased risk of mortality in RA patients, and risk factors for mortality in RA-ILD patients included male, age, residence in suburban region, PVD and COPD. Use of DMARDs was not associated with the risk of mortality in RA-ILD patients.
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Disclosure of Interests: None declared.
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Rheumatoid arthritis - comorbidity and clinical aspects

POS0579

ABSENCE OF ASSOCIATION BETWEEN ABATACEPT EXPOSURE LEVELS AND INITIAL INFECTION IN PATIENTS WITH RA: A POST HOC ANALYSIS OF THE RANDOMIZED, PLACEBO-CONTROLLED AVERT-2 STUDY

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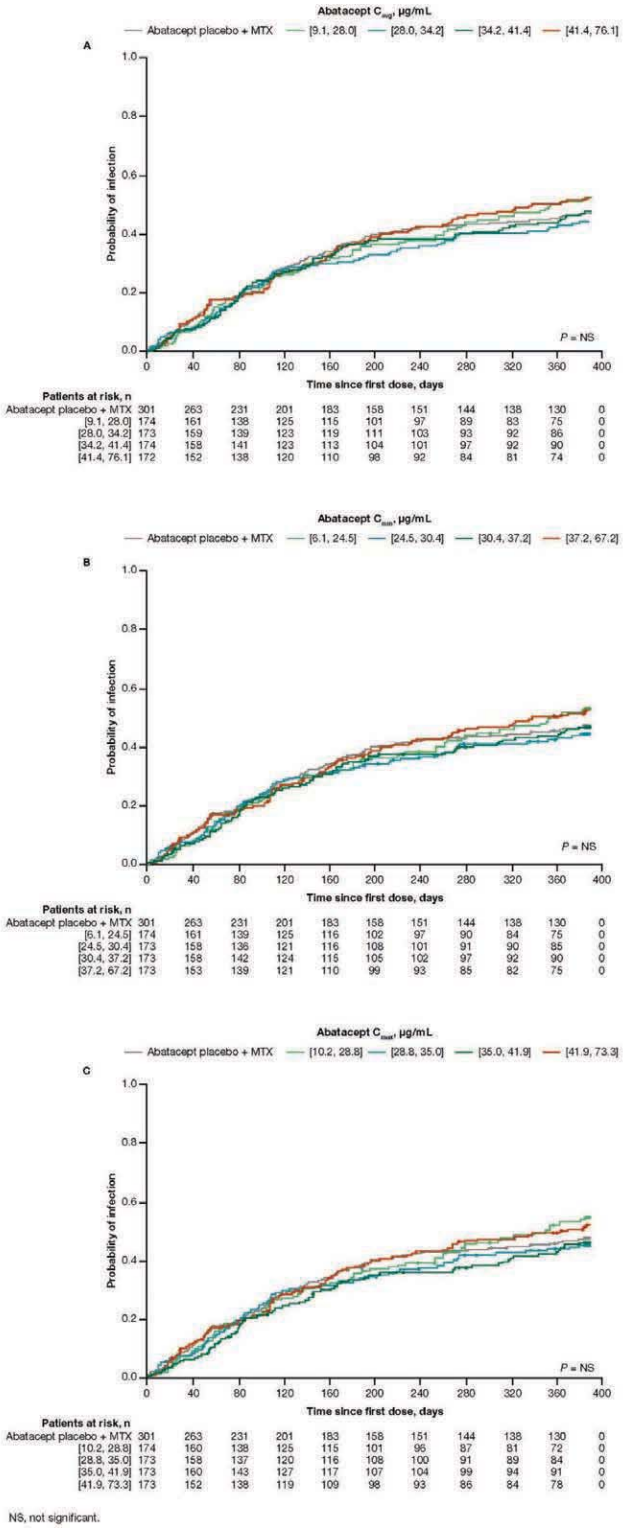
Background: Infections are the most commonly reported AE observed in patients with RA treated with immunosuppressive therapies and can be clinically significant. A recent review reported differences in the risk of infection for some biologics such as tocilizumab and TNF inhibitors.[1] Abatacept selectively modulates T-cell co-stimulation and is approved for the treatment of RA. In patients with polyarticular-course juvenile idiopathic arthritis, no association was found between higher serum abatacept exposure and the incidence of infection.[2] This has not been evaluated for adult patients with RA.

Objectives: To determine if higher serum abatacept exposure during treatment with SC abatacept was associated with increased risk of infection in adult patients with RA.

Methods: AVERT-2 (Assessing Very Early Rheumatoid arthritis Treatment-2) was a randomized, placebo-controlled study of SC abatacept + MTX vs abatacept placebo + MTX in MTX-naive, anti-citrullinated protein antibody–positive patients with early, active RA.[3] A post hoc population pharmacokinetic (PK) analysis was performed using PK-evaluable patient data from the induction period (year 1) of AVERT-2. Association between steady-state abatacept exposure (min plasma concentration [C_{min}], max plasma concentration [C_{max}], and average plasma concentration [C_{avg}]) and first infection was evaluated using Kaplan–Meier plots of probability vs time on treatment by abatacept exposure quartiles and Cox proportional-hazards models.

Results: PK of SC abatacept was defined as a linear 2-compartment model with first-order absorption and first-order elimination. The findings of the updated PK analysis were consistent with those reported in prior population analyses of abatacept PK in adults with RA. The final model included effects of baseline body weight, estimated glomerular filtration rate, sex, age, albumin, MTX use, NSAID use, SJC, and race on abatacept clearance. The only covariate with a clinically relevant effect was higher body weight, which caused an increase in clearance and volume. Infections occurred in a total of 330/693 (47.6%; serious, 1.6%) patients treated with abatacept, and 134/301 (44.5%; serious, 1.3%) with placebo during the first year of AVERT-2. In patients taking abatacept, the mean (SD) study exposure to abatacept was 376 (60) days, while mean (SD) prednisone equivalent dose was 6.7 (3.8) mg/day and mean (SD) MTX dose was 9.6 (3.0) mg/week. No exposure–response relationship was observed between the probability of first infection and steady-state abatacept exposure quartiles (C_{avg}, C_{min}, and C_{max}), or compared with placebo (Figure 1A–C). Kaplan–Meier assessment also showed no increase in risk of infection with concomitant use of MTX and glucocorticoids.

Conclusion: No association was found between initial infection and steady-state abatacept exposure (C_{avg}, C_{min}, C_{max}) or MTX and glucocorticoid use in patients with RA treated with SC abatacept.



NS, not significant.

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POS0580

TRENDS IN THE OCCURRENCE OF ISCHEMIC HEART DISEASE OVER TIME IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY FROM NORWAY OF 1821 PATIENTS FROM 1972 TO 2014

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Background: Previous studies have shown that rheumatoid arthritis is associated with a 1.5 to 2.0 times increased risk of acute myocardial infarction (AMI) and ischemic heart disease (IHD) compared with the general population [1,2]. RA treatment has improved vastly over the last two decades, due to the focus on early and aggressive treatment and the use of synthetic and biologic DMARDs. Several studies have documented higher rates of remission and better long-term outcomes in patients with early introduction of DMARDs [3]. This "window of opportunity" may also be a critical phase for intervention against the development of atherosclerosis in RA. There is little information about the occurrence of AMI and IHD in RA patients diagnosed after the introduction of modern RA treatment.
Objectives: To evaluate trends of AMI and IHD in RA patients compared with the general population over time.
Methods: We performed a retrospective cohort study of 1821 RA patients diagnosed from 1972 to 2013. The total population of Hordaland, Norway was used as a comparison cohort. Information on AMI and IHD events was obtained from hospital patient administrative systems or cardiovascular registries during 1972-2014. Aggregated counts of AMI, IHD and population counts of the comparison cohort were used to calculate expected counts of AMI and IHD in the RA cohort per 5-year age group, sex and calendar year. We then used Poisson regression with expected counts as an offset to estimate standardized event ratios (SER) as a measure of excess events.
Results: The difference in events (excess events) in RA patients compared with the general population declined on average 1.3% per year for AMI and 2.3% for IHD from 1972 to 2014. There was no significant excess AMI (SER 1.05, 95% CI 0.82–1.35) and IHD events (SER 1.02, 95% CI, 0.89–1.16) for RA patients diagnosed after 1998 compared with the general population.
Conclusion: RA patients have historically had an excess risk of IHD compared with the general population. Our study did not find excess AMI or IHD events in RA patients diagnosed after 1998. Our findings may reflect improved management of RA, CVD prevention or changes in the case-mix of RA patients over time.

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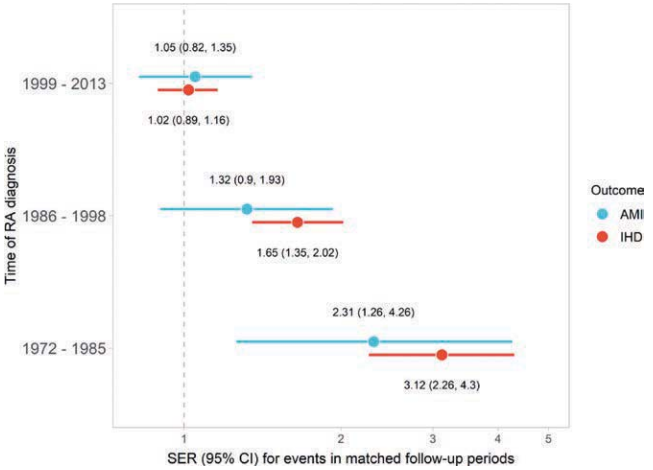

Figure 1. Excess AMI and IHD events in RA patients compared with the general population. RA patients are divided into three groups by the time of RA diagnosis. End of follow-up was set to 1 year after the end of each diagnostic period (1986, -99 and 2014 respectively) to allow for equal RA duration between groups. Point estimates are standardized event ratios comparing the number of events in the RA cohort to the expected number of events calculated from reference rates in the general population and standardized for age, sex and year of the event. All estimates are given with robust 95% confidence intervals (CI). Both the RA and general population were obtained from Hordaland, Western Norway. AMI, acute myocardial infarction; IHD, ischemic heart disease.

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POS0581

HIGHER SKIN AUTOFLUORESCENCE IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS: RESULTS FROM A LARGE POPULATION BASED COHORT

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Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease which is associated with increased mortality, mostly because of a higher incidence of cardiovascular disease (CVD), which cannot be explained by traditional risk factors alone. (1,2) Also studies showed that the cardiovascular events can already occur at a higher than expected rate shortly after the first symptoms of RA. (3)This raises the question if individuals with clinical suspect arthralgia (CSA) but not yet diagnosed with RA, already have an increased risk for developing cardiovascular disease compared to healthy controls and if this is also true for ACPA positive individuals without symptoms of clinical suspect arthralgia. In our study we used skin autofluorescence (SAF), measured with the AGE reader, as an early non-invasive tool to identify subjects who are at increased risk for developing cardiovascular disease. (4) SAF measures the accumulation of AGEs in the skin and thereby offers a simple alternative to invasive measurement of AGE accumulation. (5)
Objectives: To investigate skin autofluorescence (SAF) levels, as an early indicator for cardiovascular disease, in relation to the presence of anticitrullinated

protein antibodies (ACPA), clinical suspect arthralgia (CSA) and rheumatoid arthritis (RA) in a large population-based cohort.
Methods: Cross-sectional data were used from 17346 participants of the Dutch Lifelines Cohort Study, of whom baseline SAF and ACPA levels were available. The presence of CSA was determined using EULAR questions from the connective tissue disease screening questionnaire (CSQ). Individuals were divided into four groups: ACPA negative controls (n=17211), ACPA positive without CSA (n=49), ACPA positive with CSA (n=31) and defined RA (n=52). Multinomial regression was used to compare SAF levels and correct for potential confounders.
Results: SAF levels were higher in the ACPA positive with CSA group (OR 2.04, p=0.034) and the defined RA group (OR 3.10, p<0.001) compared to controls, but not in the ACPA positive without CSA group (OR 1.07, p=0.875). The difference in SAF levels remained statistically significant in the defined RA group after adjusting for age (OR 2.09, p=0.011), smoking status, renal function or HbA1c. In the ACPA positive with CSA group, the effect was found to be comparable (corrected for age: OR 2.09).
Conclusion: Our results indicate that ACPA positive individuals with CSA have elevated SAF levels, which is regarded as an early marker for oxidative stress and a possible indicator for development of cardiovascular disease. Therefore it is important to conduct further studies to explore if, in individuals with clinical suspect arthralgia, cardiovascular risk management should be considered in future clinical practice.
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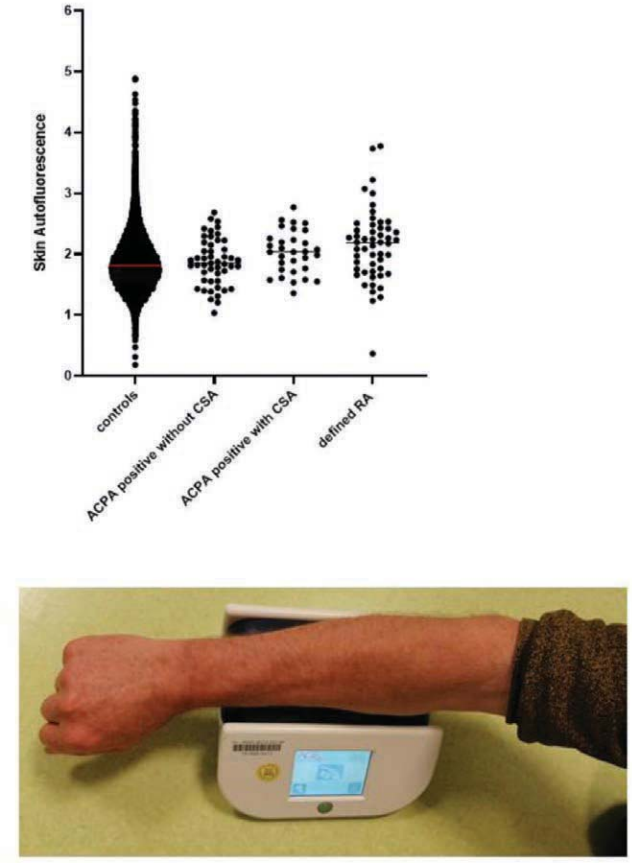

Figure 1. The top chart shows SAF levels measured with the AGE reader in the 4 groups: ACPA negative controls, ACPA positive without CSA group, APCA positive with CSA group and defined RA group.The lower picture shows the AGE reader we used from DiagnOptics Technologies BV, Groningen, the Netherlands: https://www.diagnoptics.com/

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POS0583

RHEUMATOID ARTHRITIS BENEFITS FROM FASTING AND PLANT-BASED DIET: AN EXPLORATORY RANDOMIZED CONTROLLED TRIAL (NUTRIFAST)

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Background: Fasting has been shown to be beneficial in many diseases, including rheumatoid arthritis (RA). Among other effects, fasting stimulates ketogenic metabolism, induces autophagy, and harbors immunomodulatory functions. Recent studies have highlighted the role of the intestinal microbiota in the still unclear etiology of RA[1]. This could be a potential target for additional dietary therapy in RA.
Objectives: To investigate the effect of therapeutic fasting followed by a plant-based diet compared to standard dietary recommendations in patients with RA.
Methods: In this pilot study[2] patients with RA were randomized to either a 7-day fast (≤250kcal/d) followed by 11 weeks of plant-based diet or to conventional nutritional counselling according to the recommendations of the German Society for Nutrition (Deutsche Gesellschaft für Ernährung, DGE) for 12 weeks. Disease activity and treatment response in RA (including Health Assessment Questionnaire, HAQ; EULAR Response Criteria, ACR Response Criteria) were measured at baseline (T0), day 7 (T1), 6 weeks (T2) and 12 weeks (T3).
Results: A total of 50 from 53 enrolled participants were included into the per-protocol analysis. The mean age was 51.98 ± 9.4 years with symptoms duration of 6.8 ± 8.1 years; 92% were females and 78% were ACPA and/or RF IgM positive. At baseline, participants presented HAQ 0.8 ± 0.5, DAS28CRP 4.0 ± 1.3, CRP 3.1 ± 3.8 mg/L, and a BMI of 25.0 ± 3.7 kg/m^2. The primary endpoint did not become significant. However, post-hoc analyses revealed clinically relevant improvements in the HAQ after 12 weeks in both the fasting and the DGE group (Δ-0.29; 95% CI, -0.45 to -0.13; p = 0.001; and Δ-0.23; 95% CI, -0.45 to -0.22; p = 0.032; respectively). Furthermore, the effect already set on by day 7 in the fasting group compared to week 6 in the DGE group (Figure 1). This effect was independent of antibody status, delivery mode of the intervention or previous dietary forms. CV risk factors including weight and total cholesterol levels improved stronger in the fasting group compared to the DGE group (Δ-3.9 kg vs. -0.7kg; 95% CI, 1.4 to 5.0; p = 0.001 and Δ-18.60 mg/dl vs Δ6.44 mg/dl; 95% CI, 7.3 to 42.8, p=0.007).

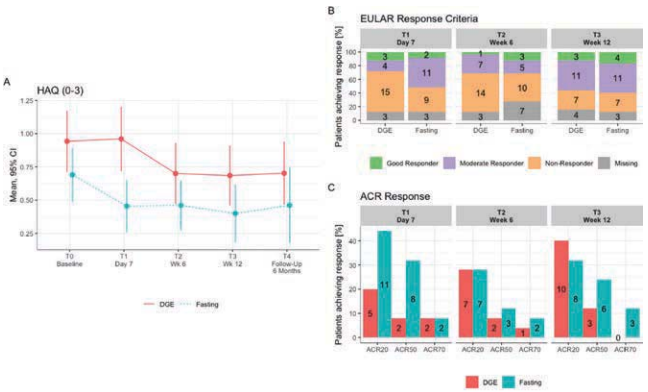

Figure 3. EULAR and ACR Response until week 12 and HAQ up to 6 months. ACR, American College of Rheumatology; CI, confidence interval; HAQ, health assessment questionnaire.

Figure 1. EULAR and ACR Response until week 12 and HAQ up to 6 months. ACR, American College of Rheumatology; CI, confidence interval; HAQ, health assessment questionnaire.

Conclusion: Fasting followed by a plant-based diet positively impacts disease activity and CV risk factors in RA, comparable to and no lesser than those of an anti-inflammatory diet according to the DGE. These results may open new perspectives by dietary interventions in an integrative therapeutic approach. Further confirmatory clinical studies with larger patient numbers are needed to confirm these exploratory findings.

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POS0585

INCIDENCE AND CLINICAL CHARACTERISTICS OF MALIGNANCY IN RHEUMATOID ARTHRITIS PATIENTS – DATA FROM THE MALAYSIAN NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR)

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Background: Patients with rheumatoid arthritis (RA) are at increased risk of developing malignancies, particularly hematologic malignancies. This predisposition for malignancy is attributed to the immune dysregulation, chronic inflammation and the long-term use of disease-modifying anti-rheumatic drugs(DMARDs).

Objectives: This study was undertaken to determine the incidence, patterns of malignancy and identify risk factors of malignancy among RA patients.

Methods: Individuals diagnosed with cancer after the onset of RA between year 2008 and 2020 from the NIAR RA registry were retrospectively examined. Standardized incidence ratios (SIR) and 95% confidence intervals of various cancers were calculated based on the expected and observed frequencies. The expected number of cases were extracted from the Malaysian National Cancer registry report. ANOVA, Chi-squared, and Student's t test were used to analyze the risk factors for developing malignancy.

Results: Of the 3995 patients in the registry, 97 patients developed malignancies at a mean interval of 9.1 years after RA onset. The total follow-up time was 26841.9 person-years. The mean age of patients was 59.3 (± 9.25) years, of which 89.7%(n=87) were women and 40%(n=39) were Chinese. 87.6%(n=84) had solid-organ tumours while 12.4%(n=13) had hematological malignancies. Women showed increased risks of non-Hodgkin's lymphoma (SIR = 13.1, 95% CI = 9.78 – 17.08), followed by lung cancer (SIR = 12.7, 95% CI = 10.01-15.77) and breast cancer (SIR = 8.8, 95% CI = 7.84 – 9.83). Men showed increased risks of lung cancer (SIR = 3.79, 95% CI = 2.81 – 4.92) and colorectal cancer (SIR = 1.69, 95% CI = 1.09 – 2.42). The risk factors for developing malignancy ($p<0.05$) include age above 60 years, long duration of RA disease, and higher disease activity states. There were no associations between gender, ethnicity, autoantibodies and DMARDs exposure.

Conclusion: The overall malignancy incidence was increased among RA patients, with women having a 4-fold higher risk. Though the incidence of solid-organ malignancies is higher, the SIR once adjusted was highest for non-Hodgkin's lymphoma which is consistent with literature review. Hence, cancer screening with continued vigilance among RA patients is recommended.

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Table 1. SIR of Malignancy among Rheumatoid Arthritis Patients by Sex and Age Groups

Sex and Age Group	Number of Patients (%)	Person-Years	Incidence		SIR (95% CI*)
			Observed	Expected	
Sex (Age Group)					
Males	10 (10.31%)	48	6	4	1.5 (0.54 - 2.94)
Age at Diagnosis					
50-60	4 (10.31%)	12	2	2	1 (0.09 - 2.87)
60-70	6 (60%)	36	4	2	2 (0.52 - 4.44)
Females	87 (89.69%)	540	59	18	3.28 (2.49 - 4.17)
Age at Diagnosis					
30-50	12 (13.79%)	31	7	5	1.4 (0.55 - 2.63)
50-60	34 (39.08%)	228	24	10	2.4 (1.54 - 3.46)
60-70	41 (47.13%)	281	28	3	9.33 (6.2 - 13.11)

SIR, standardized incidence ratios; CI, confidence interval.Acknowledgements*CI = (√observed number of cancer cases ± 1.96 × 0.5)^2/(expected number of cancer cases).

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POS0586

DIAGNOSIS OF MENTAL DISORDER COMPLICATED BY RHEUMATOID ARTHRITIS: A STUDY OF THE VALIDITY OF A PSYCHIATRIST'S DIAGNOSIS AND QUESTIONNAIRE METHOD

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Background: It has been reported that about 15% of patients with rheumatoid arthritis (RA) have depression, and most of these studies have used questionnaire methods. Most of the studies have used questionnaires for depression. Because the depression questionnaire includes questions about physical symptoms, it is necessary to be careful in interpreting the results when there is an underlying disease. In addition, there are no studies on other mental disorders.
Objectives: In this study, we examined the validity of the questionnaire method for the diagnosis of RA complicated by psychiatric disorders.
Methods: Forty-nine outpatients with RA who agreed to participate in this study were included. Age, gender, type of Disease-modifying anti-rheumatic drugs, prednisolone use, presence of diabetes, hypertension, dyslipidemia, and CRP were investigated. The Patient Health Questionnaire-9 (PHQ-9) and Center for Epidemiologic Studies Depression Scale (CES-D) questionnaires were used; a score of 10 or more on the PHQ-9 and 16 or more on the CES-D was considered a cutoff. The psychiatrist was blinded to the results of the questionnaire and conducted a structured interview in a separate room. The psychiatrist's diagnosis was defined as the Gold Standard, and was compared with the PHQ-9 and CES-D.
Results: Psychiatrist's diagnosis was abnormal in 9 patients. This included one patient with major depression, one patient with moderate depression, two patients with minor depression, and two patients with adjustment disorder. The PHQ-9 had a specificity of 98%, a sensitivity of 33%, a positive predictive value of 75%, and a negative predictive value of 87%. The CES-D had a specificity of 82%, a sensitivity of 100%, a positive predictive value of 56%, and a negative predictive value of 100%.
Conclusion: The PHQ-9 and CES-D may be useful in screening for psychiatric disorders including associated with RA.
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POS0587

TRAJECTORIES AND FACTORS INFLUENCING THE EVOLUTION OF HAND GRIP AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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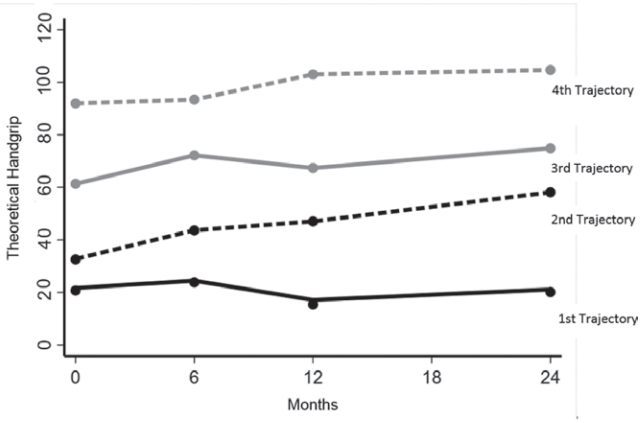
Background: Rheumatoid arthritis (RA) is characterized by an early reduced grip strength which persists over time despite the remission of the disease suggesting the presence of a sarcopenia.
Objectives: To study the evolution of the grip strength measured by the handgrip. by identifying different trajectories and associated factors.
Methods: Patients with active RA who visited the Rheumatology Department of Clermont-Ferrand University Hospital for initiating bDMARD were invited to participate to the longitudinal cohort RCVRIC analyzing cardiovascular risk and chronic inflammatory rheumatic disease. Within the RCVRIC cohort 175 RA initially underwent a handgrip determination. 143 patients had at least 2 handgrip measurements over 2 years, allowing analysis of trajectories by the "Group Based Trajectory Modeling" method. For the trajectories, handgrip was expressed in terms of percentage of the theoretical value defined according to age and sex. The clinical characteristics of the disease, the therapeutic response, and the body composition associated with each trajectory were analyzed.
Results: At inclusion, the handgrip was normal among only 4% of patients, with an alteration of 51% of its theoretical value. After 2 years of follow-up, a majority of patients improved their handgrip trajectory to reach an average of 68% of the theoretical one, but only 15.7% of the patients normalized their handgrip. Four trajectories have been identified along with associated factors:



1st trajectory consists of low handgrip with little improvement and was composed of: 9 patients (6.3%), median age 60 years [53.6;69.3], 88% women, disease duration 17.99 years [6.78;24.9], DAS 28 ESR 4.68 ± 1.29, and initial handgrip 21% of the theoretical value [8;24].
2nd trajectory shows good improvement (+72%) and was composed of: 70 patients (49%), median age 58.9 years [54.4;64.3], 84% women, disease duration 5.99 years [1.46;14.8], DAS 28 ESR 4.43 ± 1.07, and initial handgrip 32% of the theoretical value [17.8;46.4].
3rd trajectory shows moderate improvement (+25%) and was composed of: 43 patients (30%), median aged 60.7 years [45.7;69.4], 79% women, disease duration 3.5 years [1.25;9.9], DAS 28 ESR 4.0 ± 1.03 and initial handgrip 60% of the theoretical value [48.2;76].
4th trajectory shows high handgrip and was composed of: 21 patients (14.7%), 57% women, median age 57.9 years old [49.7; 67.4], disease duration 3.81 years [2.14; 10.7], DAS 28 ESR 3.68 ±1.29 and initial hand grip 92% of the theoretical value [85; 100].
Significant differences at inclusion between the 4 trajectories were observed. The 4th trajectory was characterized by a higher proportion of men (p=0.05), lower disease activity (DAS 28 ESR (p=0.02), SDAI (p=0.04)), better initial handgrip (p=0.03) and 6 min walk test (p=0.0001), and a lower percentage of fat mass (p=0.04). In contrast, a higher disability (HAQ, p=0.002), a lower total lean body mass (p=0.001) and poorer therapeutic response (p=0.04) were noted in trajectories 1 and 2.
Conclusion: After 2 years of follow-up, a majority of patients improved their handgrip trajectory. However, very few patients normalized their hand grip. Four trajectories of handgrip were identified; the main indicators of hand grip's improvement were the control of the disease activity, low functional disability, walking performance, a low percentage of fat mass and high lean mass.
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POS0588 SEASONALITY OF FLARE AND REMISSION PATTERNS IN RHEUMATOID ARTHRITIS: A POPULATION-BASED COHORT STUDY

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Background: Flare of rheumatoid arthritis (RA) disease activity is an important aspect of RA disease experience for patients with RA, associated joint damage and comorbidity. Major advancements in treatment of RA in recent decades resulted in improving trends in RA disease activity and increasing rates of remission. However, flares in RA remain common and some patients are still unable to achieve remission. Disease-modifying antirheumatic drugs have a major impact on controlling RA disease activity, minimizing the likelihood of flares. The effect of environmental factors on the pattern of flares and remissions in RA is less studied. Previous studies showed conflicting results regarding the likelihood of flare and remission occurrence across the seasons of the year.

Objectives: To assess the seasonal pattern in the occurrence of flares and remissions in a population-based cohort of patients with RA.

Methods: This retrospective population-based cohort study included patients with RA (age ≥30 years) who met 1987 ACR criteria in 1988-2007. A retrospective review of each clinical visit in the medical records was performed to ascertain flare or remission status. A flare was defined as an episodic worsening of RA disease activity that leads to initiation, change or increase of treatment. Remission was defined as the absence of disease activity based on a tender joint count of 0, a swollen joint count of 0 and an ESR less than 10 mm/h. Seasons were defined as: winter (Dec, Jan, Feb), spring (Mar, Apr, May), summer (June, July, Aug) and autumn (Sep, Oct, Nov). All subjects were followed until death, migration or July 1, 2012. Generalized linear models with random effects to account for multiple visits per patient were used for data analyses.

Results: The study included 650 RA patients (mean age 55.8 years; 69% female) with a mean follow up of 10.3 years. In a total of 17,323 clinical visits, patients were flaring in 2887 (17%) visits. The incidence of RA flares was 15% higher in the spring than in the winter (OR 1.15: CI: 1.02-1.29, p=0.045) after adjusting for age, sex and RA duration. There was no change in flare pattern between winter and summer or autumn. Remission rate did not differ between the seasons. (3df test p=0.65).

Conclusion: Patients with RA were more likely to experience flares in spring as compared to winter, and there were no differences in flare rates for the rest of the seasons. Remission rates were similar between the seasons of the year. The reasons for this seasonal effect on flare pattern is unknown, and the role of patient-related and environmental risk factors remains to be investigated. Our findings on the seasonality in flare occurrence can be used to inform patients about the risk of RA disease flares throughout the year.

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POS0589 CARDIOVASCULAR DISEASE RISK IN INFLAMMATORY ARTHRITIS STILL ELEVATED IN 2021!

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Background: Patients with inflammatory rheumatic diseases as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA) are at higher risk for developing cardiovascular diseases (CVD) than the general population. This is due to a higher prevalence of 'traditional' CV risk factors as hypertension and dyslipidemia, and the underlying systemic inflammation. During the past two decades, the burden of inflammation has been reduced by more efficacious anti-rheumatic treatment, leading to a reduced CVD risk, albeit still elevated in comparison to the general population. Therefore, it remains important to monitor the presence of CVD in rheumatic patients in systematically controlled cohorts.

Objectives: To evaluate whether, nowadays, the CVD risk of patients with inflammatory rheumatic diseases still differs from the general population.

Methods: In March 2020, all adult patients with an inflammatory rheumatic disease from the Amsterdam Rheumatology and Immunology Center, location "Reade" were systematically asked to participate in a prospective cohort study, which focused on the impact of the COVID-19 pandemic. The patients were compared with age and sex matched controls. In the third questionnaire, sent out in January 2021, questions regarding CV risk factors and comorbidities were added. Baseline characteristics and prevalence of CV risk factors and CVD were compared between RA, PsA or SpA patients, and healthy controls.

Results: 2050 consecutive patients with an inflammatory rheumatic disease (1312 RA patients, 353 PsA patients, 385 SpA patients), and 939 healthy controls completed the questionnaires (Table 1). The prevalence of at least one CV comorbidity was more frequently reported in RA, PsA and SpA patients compared to healthy controls: 69 (5%), 24 (7%), 17 (4%) compared to 31 (3%), respectively. Events were primarily cardiac (i.e. myocardial infarction and coronary angioplasty). Inflammatory arthritis patients more often had hypertension or hypercholesterolemia than healthy controls, which were untreated in nearly half the cases. RA patients most often used anticoagulant medication.

Table 1. Baseline characteristics. Values are displayed as mean ± standard deviation (SD) or frequencies with percentages (%). RA = rheumatoid arthritis, PsA = psoriatic arthritis, SpA = spondyloarthritis, CV = cardiovascular, DMARD = disease modifying anti-rheumatic drug

Patient characteristics	All patients (n = 2050)	RA (n = 1312)	PsA (n = 353)	SpA (n = 385)	Control (n = 939)
Mean age – yr	57 ± 13	60 ± 12	57 ± 12	51 ± 13	55 ± 13
Female sex - no (%)	1266 (63)	923 (70)	164 (47)	179 (47)	636 (69)
CV risk factors - no (%)					
Hypertension	746 (37)	482 (38)	134 (39)	130 (34)	213 (23)
Antihypertensive med	411 (20)	271 (21)	78 (22)	62 (16)	131 (14)
Hypercholesterolemia	594 (30)	391 (31)	102 (30)	101 (27)	197 (21)
Statins	335 (16)	223 (17)	59 (17)	53 (14)	98 (10)
Anticoagulants	246 (12)	180 (14)	34 (10)	32 (8)	74 (8)
CV diseases - no (%)					
Overall	110 (5)	69 (5)	24 (7)	17 (4)	31 (3)
Cardiac	91 (4)	60 (5)	17 (5)	14 (4)	26 (3)
Cerebral	27 (1)	12 (1)	9 (3)	6 (2)	4 (0)
Peripheral	14 (1)	10 (1)	3 (1)	1 (0)	3 (0)
Anti-rheumatic drugs - no (%)					
Prednisone	202 (10)	175 (13)	17 (5)	10 (3)	n/a
Conventional synthetic DMARD	1118 (55)	902 (69)	184 (52)	32 (8)	n/a
Biological DMARD	895 (44)	512 (39)	166 (47)	217 (56)	n/a
Targeted synthetic DMARD	20 (1)	11 (1)	5 (1)	4 (1)	n/a

Conclusion: The prevalence of CVD was approximately 1.5 times higher in patients with inflammatory rheumatic diseases compared to healthy controls (5% vs 3%), similar to older investigations. The prevalence of CV risk factors also remained elevated, and often undertreated. This indicates that the CVD risk in arthritis patients is still elevated in 2021 compared to the general population, despite improved anti-rheumatic treatment. Therefore, adequate and timely treatment of CV risk factors and optimization of anti-rheumatic drug treatment remains important in all inflammatory arthritis patients.

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POS0590 ASSOCIATIONS BETWEEN SELF-REPORTED RHEUMATOID ARTHRITIS, RHEUMATOID FACTOR POSITIVITY AND STRUCTURAL BRAIN PHENOTYPES IN UK BIOBANK

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Background: There is very limited research on structural brain health in people with rheumatoid arthritis (RA).

Objectives: To investigate whether there are differences in brain volume in people with self-reported RA or positive rheumatoid factor (RF+).

Methods: Cross-sectionally tested for associations with several MRI brain volume measures in UK Biobank (n=37,379 of whom 432 RA and 1833 RF+). The partially adjusted regression models controlled for age and sex, while the fully adjusted models further controlled for deprivation index, smoking status and

cardiometabolic diseases. For all subcortical volumes analyses we also controlled for total brain volume.

Results: Those that self-reported RA were more likely to have increased WMH (White Matter Hyperintensities) (β= 0.08, 95% CI= 0.022; 0.14, p<0.01), and smaller volumes of the amygdala (β=-0.09, 95% CI= -0.16; -0.02, p<0.01), pallidum (β=-0.07, 95% CI= -0.13; -0.005, p<0.05) and thalamus (β= -0.06, 95% CI= -0.12; -0.01, p<0.05) in the partially adjusted analyses. In the fully adjusted model only amygdala volume remained negatively associated with RA (β=-0.09, 95% CI= -0.16; -0.02, p<0.01).

Conclusion: We provide evidence of differences in structural brain phenotypes known to underpin cognitive and psychological health, in RA. Since the amygdala may play an important role in pain modulation and mental health, while WMH are associated with a higher risk of stroke, the observed differences may be of clinical relevance in RA which is associated with a higher prevalence of these conditions. Further research is required to confirm these findings and asses their functional implications.

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POS0591 TREATMENTS TO PREVENT RHEUMATOID ARTHRITIS IN FIRST DEGREE RELATIVES: DEMOGRAPHIC AND PSYCHOLOGICAL PREDICTORS OF RISK TOLERANCES

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Background: There is a growing research focus on the development of interventions to reduce risk of rheumatoid arthritis (RA) in at-risk groups.(1) RA patients' first-degree relatives (FDRs) have an elevated risk of developing RA and are potential candidates for preventive interventions. Recent studies have quantified the preferences of at risk groups for preventive treatments. (2-4) Little is known about predictors of preference heterogeneity in this context.

Objectives: Assess the extent to which FDR characteristics and beliefs predict risk tolerances for preventive treatments.

Methods: Adult FDRs of patients with confirmed RA in the UK were invited to take part in a web-based survey. FDRs enrolled in a UK prospective cohort (PREVeNT-RA) were also invited. Survey development, including attribute selection and presentation, was informed by qualitative research, ranking surveys, literature review, and expert opinion including patient research partners. Respondents received information about RA, questions to check comprehension, and an introduction to the survey. Participants were asked to imagine they were experiencing arthralgia and had positive autoantibody tests indicating a 60% chance of developing RA within two years. Using a probabilistic threshold technique, participants made choices between no treatment (no benefit and no risks) or a preventive treatment option. Treatment options were defined by a fixed level of benefit (reduction in risk of RA from 60% to 20%) and varying levels of risks (Table 1). For each treatment risk, participants made a series of choices where the risk was systematically increased or decreased until they switched their choice. This procedure was repeated for each of the remaining risks. Participants also completed items assessing demographics, perceived risk of developing RA, health literacy, subjective numeracy, the Brief Illness Perception Questionnaire (IPQ) and the Beliefs about Medicines Questionnaire General (BMQ-G). The maximum acceptable risk (MAR) respondents were willing to accept for a 40% (60% to 20%) point risk reduction in developing RA was summarized across participants using descriptive statistics. Associations between MARs and participants' characteristics and illness/medication beliefs were assessed using interval regression. Independent variables were dichotomized and effects coded.

Table 1. Attributes and levels of treatment options

Treatment attribute	Levels describing no treatment option	Levels describing treatment option
Chance of developing RA	60%	20%
Chance of mild side effects	0%	2%; 4%; 5%; 7% or 10%
Chance of a serious infection due to treatment	0%	1%; 1.5%; 2%; 3% or 5%
Chance of a serious side effect that is potentially irreversible	0%	0.001%; 0.01%; 0.02%; 0.05% or 0.1%

Results: 289 FDRs (80 male) responded. The mean (SE) MAR for mild side effects, serious infection, and serious side effects was 29.08 (1.52), 9.09 (0.60) and 0.85 (0.27), respectively. Participants aged over 60 years were less tolerant of risk of serious infection than average (mean MAR - 2.06 (0.78)) and younger participants were more tolerant of risk of serious infection than average (mean MAR + 2.06 (0.78)). Risk of mild side effects was less acceptable to participants who perceived they were likely/very likely to develop RA (mean MAR - 3.34 (1.55)) than to those who did not (mean MAR + 3.34 (1.55)). Education level, health literacy, numeracy, IPQ and BMQ-G subscales were not predictors of risk tolerance.

Conclusion: Age and perceived risk of RA had a significant impact on FDRs' tolerance for specific, but not all, included risks. Cognitive ability and beliefs about RA/medicine did not explain preference heterogeneity. This is informative for drug development and the development of tailored risk communication resources to support preventive approaches.

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POS0592 PREDICTING LIVER ENZYME ELEVATION IN PATIENTS WITH RHEUMATOID ARTHRITIS ON TREATMENT WITH METHOTREXATE USING SUPERVISED MACHINE LEARNING

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Background: Methotrexate (MTX) is the most used disease-modifying anti-rheumatic drug (DMARD) in the treatment of rheumatoid arthritis (RA). (1) Chronic use of this medication warrants close laboratory monitoring given its propensity for liver damage and myelosuppression. (2) MTX associated hepatic dysfunction is a well-described adverse effect and has been seen in up to a quarter of

patients on long term treatment. (3) Recent advances in health care coupled with the extensive use of electronic health records (EHR) has resulted in the accumulation of large amounts of patient data. Approaches like machine learning (ML) allows us to leverage these large data sets to predict outcomes and support clinical decision making. (4) We hypothesized that a ML model trained on conventionally available EHR data would be able to identify patients at the greatest risk of developing MTX related hepatotoxicity.

Objectives: To develop a machine learning model to accurately predict liver enzyme elevation in rheumatoid arthritis (RA) patients on treatment with methotrexate (MTX) using electronic health record (EHR) data from a real-world RA cohort.

Methods: Demographic, clinical, biochemical, as well as prescription information from 569 RA patients were retrospectively collected. Liver transaminase elevation above the upper limit of normal following initiation of MTX, was the primary outcome. The total dataset was randomly split into a training (80%) and test set (20%) and used to develop a Random Forest Classifier model. The best model was selected after hyper-parameter tuning and fivefold cross-validation.

Results: 104 patients (18.2%) developed hepatic dysfunction while on MTX therapy. The best performing predictive model had an accuracy/F1 score of 0.87. The top ten predictive features were then used to create a limited feature model that retained most of the predictive accuracy, with an accuracy/F1 score of 0.86.

Conclusion: Our proof-of-concept study suggests the possibility of building a well-performing ML model to predict liver enzyme elevation in RA patients being treated with MTX. Similar ML models could be used to identify 'high risk' patients who can then be potentially targeted for closer monitoring with the aim of preventing these adverse outcomes. Conversely, patients at low risk can avoid extra outpatient visits, thereby reducing costs.

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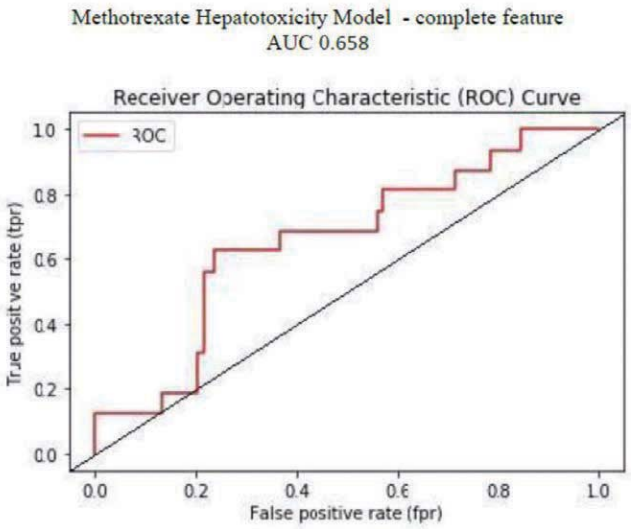
	Occurrence of Hepatic Dysfunction		*p*
	No (n= 465)	Yes (n=104)	*value*
Age (Mean ± SD)	52.33 ± 13.27	53.19 ± 10.61	0.194
Gender			
• Male	64	18	0.352
• Female	401	86	
NAFLD on Ultrasound	5 (1.1%)	6 (5.7 %)	1.00
MTX prescription patterns			
Intial MTX Dose prescribed			
• ≤ 12.5 mg/week	321 (69.3 %)	70 (67.3 %)	0.821
• > 12.5 mg & < 20mg/ week	131 (28.2 %)	30 (28.8 %)	
• 20mg or more / week	13 (2.5 %)	4 (3.8 %)	
Maximal MTX Dose prescribed			
• ≤ 12.5 mg/week	24 (5.1%)	3 (2.9 %)	0.647
• > 12.5 mg & < 20mg/ week	119 (25.6 %)	26 (25.0 %)	
• 20mg or more / week	322 (69.3 %)	75 (72.1 %)	
Duration of MTX therapy more than 1.5 years	200 (43 %)	70 (67.3 %)	<0.001
Pattern of Combination Drug therapy with MTX			
MTX Monotherapy	454 (97.6%)	104 (100 %)	1.00
MTX plus Sulfasalazine	48 (10.3%)	22 (21.2 %)	0.002
MTX plus Leflunomide	172 (37.0 %)	41 (39.4 %)	0.643
MTX plus Mycophenolate Mofetil	6 (1.3%)	1 (0.9 %)	1.00
MTX plus Hydroxychroloquine	208 (44.7%)	41 (39.4 %)	0.315
MTX plus > 1 DMARDs (Triple regimen)	10 (2.2%)	3 (2.9 %)	0.714

Table 1: MTX -RA cohort stratified for occurrence of liver enzyme elevation



Disclosure of Interests: None declared.

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POS0593

THE COURSE OF FATIGUE AND ITS RELATION WITH INFLAMMATION DURING THE DEVELOPMENT OF RHEUMATOID ARTHRITIS: A LONGITUDINAL STUDY

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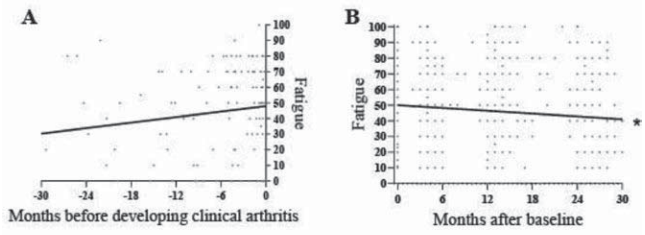
Background: Fatigue is a prominent and disabling symptom in patients with rheumatoid arthritis (RA), that is only partially explained by inflammation and responds poorly to DMARD-therapy. We hypothesized that inflammation explains fatigue to a larger extent in the phase of clinically suspect arthralgia (CSA), when clinical arthritis is still absent and fatigue has not yet become chronic.

Objectives: To study the course of fatigue in CSA during progression to RA and the association with inflammation at CSA-onset and at RA-diagnosis.

Methods: 600 consecutive CSA-patients were followed for RA-development (median follow-up 25 months). Additionally, 710 early RA-patients were studied at diagnosis. Fatigue was assessed every study visit and expressed on a scale of 0-100. The DAS44-CRP was used to measure inflammation (with SJC=0 in CSA). The course of fatigue over time was studied with linear mixed models. Associations between fatigue and inflammation were studied with linear regression, corrected for sex. Analyses were stratified by ACPA-status.

Results: In 88 CSA-patients who developed RA, pre-arthritis fatigue-levels increased gradually with 7/year (95%CI= -2 to 16, p=0.13), towards 48 at RA-development. Fatigue decreased in CSA-patients who did not develop RA (-4/year, 95%CI= -6 to -3, p<0.001) (see Figure 1). At CSA-onset, inflammation was associated with fatigue (β=18, meaning 18 points more fatigue

Figure 1. Course of fatigue in CSA-patients developing RA (A) and in CSA-patients not developing RA (B)



Legend: lines depict the average course derived from linear mixed model analysis. Timepoint zero was defined as time of clinical arthritis in CSA-patients who developed RA and as the first visit in the CSA-patients who did not develop RA. Figure 1B contains data of 475 patients at baseline (t=0), but most dots overlap. Fatigue increased in CSA-patients who developed RA with 7/year. *Fatigue decreased in CSA-patients who did not develop RA with -4/year.

per point increase DAS-score, 95%CI=7-28, p=0.001). This association was stronger than at RA-diagnosis (β=5, 95%CI=3-7, p<0.001). Fatigue-levels increased towards RA-development in both ACPA-subtypes, but were on overall average higher in ACPA-negative CSA than ACPA-positive CSA (mean difference in fatigue of 13, 95%CI=1-24, p=0.027). However, the association between fatigue and inflammation was stronger in ACPA-positive compared to ACPA-negative CSA.

Conclusion: Fatigue increased gradually during progression from arthralgia to clinical arthritis, and fatigue was better explained by inflammation in CSA than in RA. This implies a 'phase-dependent relation' between inflammation and fatigue.

REFERENCES: -

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POS0594 FACTORS ASSOCIATED WITH THE 6-MINUTE WALK TEST AMONG PERSONS WITH RHEUMATOID ARTHRITIS

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Background: Persons with rheumatoid arthritis (RA) are less physically active than the general population. A 6-minute walk test (6MWT) measures how far a person can walk in 6 minutes, testing overall functional capacity. This can inform clinicians before initiating potential interventions.

Objectives: To assess psychological, patient- and disease-related factors associated with 6MWT results among persons with RA.

Methods: Patients were recruited in 2019 and 2021 from the Rheumatology outpatient clinics at St. Olavs Hospital and Levanger Hospital, Norway (n=225). They answered questionnaires, and a subgroup (n=86) performed a 6MWT according to guidelines from the American Thoracic Society (1). Diagnostic characteristics and medical history were collected from hospital records. Participants with data for 6MWT but missing data for other variables in the main model were excluded (n=7). Physical function was measured with the Modified Stanford Health Assessment Questionnaire (mHAQ, range 0-3, lower score indicating better physical function). For the patient global assessment (PGA) patients rated their overall disease activity in the past week on a 100 mm visual analogue scale; higher score indicates more symptoms. Presence of depressive symptoms was measured with the Hospital Anxiety Depression Index Depression score (HADS-D, range 0-21, higher value implying more depressive symptoms). Perceived stress was measured with Cohen's Perceived Stress Scale (range 0-40, higher score indicates more stress). The belief in one's ability to be physically active under different circumstances was measured by the Self-Efficacy for Exercise score (range 5-35, higher score indicates higher self-efficacy). Data were analyzed with multiple regression with 6MWT as dependent variable. Model 1 included age (categorized into tertiles to improve model fit: <59, 59-69, or ≥70 years), sex, mHAQ, PGA, HADS-D, Cohen's Perceived Stress Scale, Self-Efficacy for Exercise, smoking habit and body mass index (BMI, categorized ≤25 or >25 kg/m^2). Model 2 included only the variables significantly associated with 6MWT in Model 1, but keeping adjustment for sex. The regression coefficients of Model 2 were standardized.

Table 1. Patient characteristic

	Rheumatoid arthritis patients (N=79)
Female sex, n (%)	60 (76)
Age (years), median (IQR)	65 (55, 71)
Ever smoker, n (%)	49 (62)
Body mass index (kg/m^2), median (IQR)	26.3 (23.6, 28.9)
Rheumatoid arthritis duration (years), median (IQR)	10 (5, 23)
Seropositive (anti-CCP and/or RF), n (%)	68 (86)
Uses conventional DMARDs, n (%)	67 (85)
Uses biological DMARDs, n (%)	42 (53)
Uses corticosteroids, n (%)	21 (27)
Cardiovascular disease (HT, angina, MI, arrhythmia or stroke), n (%)	38 (48)
Respiratory disease (COPD, CRPD or asthma), n (%)	21 (27)
DAS28-CRP	2.3 (1.8, 2.9)
Modified Health Assessment Questionnaire, median (IQR)	0.38 (0.13, 0.63)
Patient global assessment (mm), median (IQR)	27 (12, 40)
Hospital Anxiety Depression Scale Depression score, median (IQR)	3 (1, 4)
Cohen's Perceived Stress Scale, median (IQR)	15 (9, 19)
Self-Efficacy for Exercise, median (IQR)	25 (17, 30)
6-Minute Walk Test (m), mean (±SD)	507 (±88)

Results: In model 1, the variables associated with 6MWT were mHAQ (p=0.04), Self-Efficacy for Exercise (p=0.001), BMI (p=0.01) and age (oldest versus youngest age tertile p<0.001, middle versus youngest age tertile p=0.11). Sex was not significantly associated with 6MWT (p=0.82). The standardized coefficients in Model 2 were: mHAQ -0.27 (p=0.002), Self-Efficacy 0.27 (p=0.002), categorized BMI -0.27 (p-value=0.002), middle age group versus youngest age group -0.17 (p=0.08), oldest age group versus youngest age group -0.55 (p<0.001), male gender 0.08 (p=0.33). The R^2 of Model 1 and Model 2 were 0.54 and 0.52 respectively.

Conclusion: Self-Efficacy for Exercise, mHAQ, BMI and age had the largest impact on 6MWT, explaining 52 % of the observed variation in 6MWT in a model adjusted for sex.

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POS0595 THE ASSOCIATION BETWEEN AXIAL AND PERIPHERAL BONE IN PATIENTS WITH RHEUMATOID ARTHRITIS, INCLUDING THE IMPACT OF EROSIVE DISEASE. A HR-PQCT STUDY.

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Background: The severity of Rheumatoid Arthritis (RA) is associated with increased fracture risk (1). Areal bone mineral density (aBMD) by dual-energy absorptiometry (DXA) is the gold standard for diagnosis of osteoporosis as well as fracture risk assessment. High resolution peripheral quantitative computed tomography (HR-pQCT) of the distal radius yields volumetric BMD (vBMD) of trabecular and cortical bone compartments, as well as micro-architectural parameters and may prove useful for fracture risk prediction. The association between aBMD by DXA and HR-pQCT derived vBMD and microarchitecture have only been sparsely investigated in patients with RA, and it is not known if erosive disease, measured by the gold standard Heijde-modified Sharp Scores (HSS) (2) affects HR-pQCT derived parameters.

Objectives: To assess the associations between aBMD by DXA and bone parameters of the distal radius by HR-pQCT, in both male and female patients with RA, and the impact of erosive disease on the bone parameters of the distal radius.

Methods: We measured aBMD by DXA of the lumbar spine and hip, HR-pQCT of the distal radius and assessed HSS in 162 patients with RA. Using multivariate linear regression models, we explored the association between HSS and HR-pQCT parameters, adjusted for sex and age. The associations between aBMD by DXA and vBMD and microarchitecture by HR-pQCT were assessed by Spearman correlation coefficients, interpreted as negligeable (0.00-0.10), weak (0.10-0.39), moderate (0.40-0.69), strong (0.70-0.89) or very strong (0.90-1.00).

Results: Mean age for the included patients was 63 years, 75% were women and median disease duration was 18 years. Erosive disease (HSS) was negatively associated with trabecular number and density, but not with cortical bone parameters. This association was stronger for HSS of the wrist joints, than for HSS of the hands and total HSS (Table 1). Trabecular density of the distal radius correlated moderately with aBMD at the total hip, and weakly with aBMD at the lumbar spine. Trabecular numbers also correlated moderately with aBMD at the total hip. Cortical bone parameters at the distal radius correlated weakly with aBMD at the hip, but only among women.

Table 1. Multivariate linear regression model exploring the effect of Heijde-modified Sharp Score on selected HR-pQCT (distal radius) parameters, adjusted for age and sex.

		R^2	Effect	p-value
HSS total (n=146)	Tt. BMD (mg HA/cm^3)	0.129	-0.052	0.519
	Ct. BMD (mg HA/cm^3)	0.138	0.060	0.642
	Ct. Th (mm)	0.096	0.001	0.084
	Tb. BMD (mg HA/cm^3)	0.284	-0.173	<0.001
	Tb. N (1/mm)	0.319	-0.003	<0.001
HSS of the hands (n=145)	Tt. BMD (mg HA/cm^3)	0.124	-0.073	0.522
	Ct. BMD (mg HA/cm^3)	0.132	0.046	0.801
	Ct. Th (mm)	0.087	0.001	0.122
	Tb. BMD (mg HA/cm^3)	0.279	-0.242	0.001
	Tb. N (1/mm)	0.324	-0.005	<0.001
HSS of the wrists (n=146)	Tt. BMD (mg HA/cm^3)	0.127	-0.121	0.614
	Ct. BMD (mg HA/cm^3)	0.136	-0.029	0.939
	Ct. Th (mm)	0.089	0.001	0.158
	Tb. BMD (mg HA/cm^3)	0.273	-0.467	0.003
	Tb. N (1/mm)	0.311	-0.010	<0.001

HR-pQCT: high resolution peripheral quantitative computed tomography,HSS: Heijde-modified Sharp Score, Tt.: total, Ct.: cortical, Tb.: trabecular, BMD: bone mineral density, HA: hydroxyapatite, Th.: Thickness, N: number

Conclusion: Among patients with RA, the correlation between axial and peripheral bone is strongest between trabecular bone parameters of the radius and aBMD at the hip, which suggests that prediction of hip fractures is maintained. However, the degree of erosive disease negatively impacts the trabecular bone parameters. This may potentially interfere with the hip fracture prediction abilities of HR-pQCT in patients with high degree of erosive disease.

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POS0596 SERUM CHOLESTEROL LOADING CAPACITY ON MACROPHAGES IS LINKED TO OXIDIZED LOW-DENSITY LIPOPROTEIN AND REGULATED BY SEROPOSITIVITY AND C-REACTIVE PROTEIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Excessive cholesterol accumulation in macrophages underlies foam cell formation, initiation and progression of atherosclerosis. LDL oxidation and unregulated uptake of oxidized LDL by macrophages are critical in foam cell development. Cholesterol loading capacity (CLC) is the ability of serum to deliver cholesterol to cells and is related to foam cell formation. Rheumatoid arthritis (RA) serum increased cholesterol content in macrophages and promoted foam cell formation significantly more than control serum[1]. Although inflammation, LDL oxidation and antibodies to oxidized LDL (anti-oxLDL) may be higher in RA, their relationships and their individual and synergistic contributions to CLC in RA are unknown.

Objectives: To explore determinants and moderators of serum CLC in patients with RA. We also investigated whether oxidized LDL influences CLC directly or indirectly through anti-oxLDL IgG and proprotein convertase subtilisin/Kexin type-9 (PCSK9), independently or conditionally on RA-related autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) or level of inflammation.

Methods: In an observational study of 104 patients, CLC was measured fluorimetrically as intracellular cholesterol content in human THP-1-derived macrophages after incubation with patient serum. Oxidized LDL was measured as oxidized phospholipids on apoB100 particles (oxPL-apoB100). Anti-oxLDL, PCSK9 and C-reactive protein (CRP) were also quantified. Associations of oxPL-apoB100, anti-oxLDL IgG and PCSK9 with CLC were examined with multivariable linear regression. A two-stage dual moderated mediation model explored whether an indirect association of oxPL-apoB100 with CLC through parallel mediators anti-oxLDL IgG and PCSK9 varied as a function of moderators CRP and RF/ACPA positivity.

Results: OxPL-apoB100, anti-oxLDL IgG and PCSK9 positively associated with CLC (all adjusted p<0.020). In the final dual moderated mediation model oxPL-apoB100 was directly linked to CLC only in dual seropositive patients (unstandardized b [95% bootstrap confidence interval]=2.08 [0.38-3.79], Figure 1). An indirect effect of oxPL-apoB100 on CLC through anti-oxLDL IgG was present and increased along with level of CRP (index of moderated mediation=0.55 [0.05-1.17]). CRP also moderated the other indirect effect of oxPL-apoB100 on CLC through PCSK9, but only in dual seropositive patients (conditional indirect effect=0.64 [0.13-1.30]).

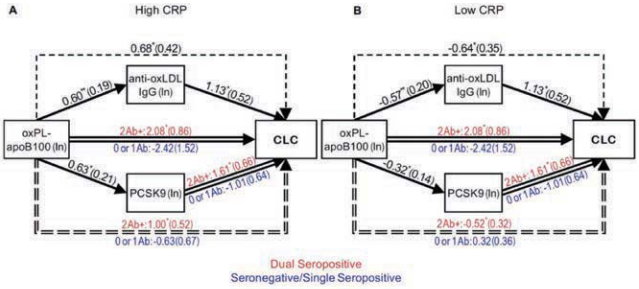

Figure 1. Determinants of CLC in RA. Unstandardized regression coefficients (standard errors) for paths of the dual moderated mediation model at **(A)** high (+1 SD above the mean) and **(B)** low (-1 SD below the mean) levels of the moderator CRP. ASCVD score, statin use, LDL-C, anti-oxLDL IgM, obesity, and age at diagnosis were included as covariates. Double lines are paths moderated by RF/ACPA seropositivity. Single dashed lines are the indirect effect of oxPL-apoB100 on CLC through anti-oxLDL IgG. Double dashed lines are the indirect effect of oxPL-apoB100 on CLC through PCSK9.
*p<0.05, **p<0.01

Conclusion: Oxidized LDL can directly influence CLC in dual seropositive RA patients, regardless of CRP. This suggests that targeting LDL oxidation in addition to inflammation may enable a more comprehensive reduction of atherosclerotic risk in these patients. Depending on CRP level, oxidized LDL also affected CLC indirectly via anti-oxLDL IgG and via PCSK9 in dual seropositive patients. If externally validated, our findings may have clinical implications for cardiovascular risk stratification and prevention.

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POS0597 PREDICTORS OF PERCEIVED RISK IN FIRST DEGREE RELATIVES OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Risk of rheumatoid arthritis (RA) is 3-5 times higher in first-degree relatives (FDRs). Efforts are increasing to develop preventive interventions for this at risk group. Risk perception is a key predictor of health behaviours, including FDRs' interest in predictive testing[1] and preventive intervention for RA. Effective risk communication is essential for RA prevention studies and clinical translation[2].
Objectives: To define variables associated with perceived risk of developing RA in FDRs of RA patients.
Methods: RA patients attending outpatient clinics (West Midlands, UK) were asked to invite their FDRs to complete a cross-sectional printed survey. Patients were also invited to complete a survey. Unique survey numbers enabled linkage of FDR and proband responses. FDRs' perceived absolute risk, comparative risk, experiential risk, and worry about risk were assessed using 5-point Likert scales. Predictor variables included demographics, the Single Item Literacy Screener, Brief Illness Perception Questionnaire, Brief Approach/Avoidance Coping Questionnaire, Life Orientation Test Revised and the Short Health Anxiety Inventory. Patient predictors of FDR perceived risk included demographics, time since RA diagnosis and Rheumatoid Arthritis Impact of Disease Score. Outcome measure responses were grouped into 'low' and 'high' for regression analyses. Univariable analysis used independent samples T-tests, chi-square tests and Mann-Whitney U Tests. Backwards stepwise binary logistic regression examined the relationship between FDR characteristics and perceived risk of RA. Generalised Estimating Equations assessed whether patient variables predicted FDR's perceived risk.
Results: 396 FDRs returned a survey. Paired data from 213 patients were available for 292 of these FDRs. The distributions of risk perception scores are shown in Figure 1. All measures of perceived risk were inter-correlated ($p<0.001$; ranging from r=0.48 to r=0.80). 65.2% of FDRs perceived themselves to be 'Likely' or 'Very Likely' to develop RA in their lifetime. FDR's ethnic group, deprivation index, employment status, education level, smoking status, cohabitation with index patient status, coping style and dispositional optimism were not significantly different between high and low perceived risk groups. Characteristics significant in univariable analyses were used in multivariable analyses (Table 1). Children were 3.89 times more likely than siblings to perceive themselves at high risk of RA. Higher health anxiety scores were associated with increased perceived risk. Female gender, and beliefs that RA would last a long time, and cause higher concern and negative emotional impact predicted increased risk perceptions. Higher perceptions of how well treatment would control RA was associated with a reduced likelihood of perceiving oneself at high risk.Index patient characteristics did not associate with FDRs' risk perceptions.

Table 1. Multivariable analysis

FDR Characteristic	Perceived Risk [Odds Ratio (95% Confidence Interval)]			
	Absolute	**Comparative**	**Experiential**	**Worry about Risk**
Gender				1.98 (1.19-3.27)*
Male[$]				
Female				
Relationship to index patient	2.80 (1.70-4.61)***	3.43 (2.04-5.78)***	3.89 (2.24-6.75)***	2.26 (1.30-3.94)**
Child				
Sibling[$]				
Health Literacy			1.50 (1.00-2.25)	
Illness Perceptions	0.89 (0.79-0.99)*	1.25 (1.05-1.48)*	1.17 (0.99-1.38)	0.84 (0.74-0.94)**
Timeline		0.91 (0.81-1.01)	0.87 (0.77-0.98)*	1.36 (1.13-1.63)**
Treatment control				1.20 (1.02-1.40)*
Concern				
Emotion				
Health Anxiety	1.04 (1.01-1.07)*	1.05 (1.01-1.07)*	1.07 (1.03-1.11)**	1.06 (1.02-1.09)**

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, [$] Reference

Conclusion: FDRs' perceived risk of RA was high. Key predictors included being a child of a patient with RA, higher health anxiety and lower perceptions of RA treatment control. An understanding of these predictors will inform the development of effective risk communication and preventive strategies.

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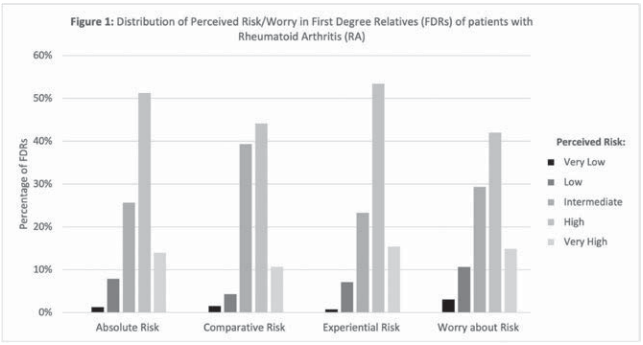

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POS0598

PERSISTING PAIN IN RHEUMATOID ARTHRITIS: DO WE NEED TO RECONSIDER OUR IDEA OF PAIN ALLEVIATION DESPITE ANTI-INFLAMMATORY TREATMENT?

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Background: Pain significantly impacts life of patients with rheumatoid arthritis (RA) (1). Besides articular pain due to systemic inflammation, neuropathic pain (NeP) represents another challenge that can pose a considerable burden on the life of patients (2).
Objectives: To investigate persisting pain in RA patients and to analyse NeP along with patient-reported outcomes (PROs).
Methods: PAIN-CONTROL is a prospective, non-interventional study in rheumatology centres in Germany. Inclusion criteria were fulfilment of the 2010 ACR/EULAR RA classification criteria, disease duration ≤ 8 yrs, DAS28 > 3.2, SJC > 3, CRP normal or above reference range, and pain rating ≥ 50 (0-100 VAS). Eligible subjects had to be scheduled for escalation of anti-inflammatory treatment according to national guidelines. At wk 24 subjects were allocated to three subgroups given DAS28-CRP change and VAS pain: i) reference group: VAS pain < 50 with either DAS28 improvement > 1.2 or DAS28 ≤ 3.2, ii) non-responders: DAS28 improvement ≤ 1.2 and DAS28 > 3.2 with or without pain alleviation, iii) persisting pain: VAS pain ≥ 50 with either DAS28 improvement > 1.2 or DAS28 ≤ 3.2. For groups 1 and 2 end of study was at week 24, patients with persisting pain continued until wk 48. Patients were assessed for NeP using a score of ≥ 19 in the painDETECT questionnaire (PD-Q) (3). Pain-related PROs, i.e. the Rheumatoid Arthritis Impact of Disease Questionnaire (RAID) and the Patient Health Questionnaire (PHQ-9), were analysed along with demographic background information (1,4). Descriptive results are presented as mean (SD) or mean (SD) | N_{valid}, as well as n (%) or n (%) | N_{valid}, respectively.
Results: 567 subjects were analysed with the following distribution: Reference group 337 (59.4%), non-responders 102 (18.0%), and persisting pain 128 (22.6%), of which 115 patients were available at wk 48. Subgroups showed similar demographic baseline characteristics but differed in PROs (Table 1). Until wk 24, proportion of patients with NeP indication decreased in the reference group (-19.8%) and slightly in non-responders (-6.0%) and persisting pain group (-9.5%). Non-responders showed the highest NeP proportion at wk 24 (35.0%) (Table 1). Of 115 patients with

persisting pain at wk 24, 47 (40.9%) tested NeP negative at wk 48, 21 (18.3%) tested unclear, 28 (24.3%) were missing and 19 (16.5%) tested positive. Of the latter 9 patients (47.4%) still had persisting pain at week 48, while this was the case for 14 patients (29.8%) in the former group. 49 (42.6%) of 115 patients with severe persisting pain at wk 24 reported pain alleviation at wk 48 and fulfillment of reference group criteria. RAID and PHQ-9 scores improved in the reference group but only slightly in the other two subgroups.

Table 1. Demographic background and PROs

Characteristic	Reference group (N = 337)	Non-responders (N = 102)	Persisting pain (N = 128)
Gender (f/m)	233 (69.1%) / 104 (30.9%)	65 (63.7%) / 37 (36.3%)	87 (68.0%) / 41 (32.0%)
Age	57.1 (13.2) | 337	59.9 (12.0) | 102	57.1 (13.0) | 128
Disease duration (yrs)	2.5 (2.6) | 337	2.7 (2.8) | 102	2.5 (2.5) | 128
PD-Q (≥ 19) (BI)	82 (28.6%) | 287	32 (41.0%) | 78	40 (36.0%) | 111
PD-Q (≥ 19) (wk 24)	21 (8.8%) | 239	28 (35.0%) | 80	27 (26.5%) | 102
PD-Q (BI)	14.0 (6.8) | 287	15.5 (7.1) | 78	15.5 (6.5) | 111
PD-Q (wk 24)	8.8 (5.8) | 239	14.8 (6.7) | 80	13.8 (7.2) | 102
RAID (BI)	5.8 (2.0) | 332	6.0 (1.9) | 100	6.6 (1.7) | 125
RAID (wk 24)	2.4 (1.8) | 321	5.4 (1.9) | 97	5.1 (1.9) | 123
PHQ-9 (BI)	7.3 (5.1) | 328	8.4 (5.4) | 98	7.9 (5.1) | 123
PHQ-9 (wk 24)	3.8 (3.5) | 318	7.3 (4.5) | 95	6.6 (4.5) | 122

Conclusion: NeP is common among RA non-responders to anti-inflammatory treatment and in patients with persisting pain, meriting a routine NeP screening to more adequately address persisting pain in these patients. However, even late improvements (after 24 wks) regarding persisting pain seem likely during anti-inflammatory treatment.

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POS0599 IMPACT OF TREAT-TO-TARGET THERAPY ON BONE MINERAL DENSITY LOSS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE COHORT STUDY

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Background: Osteoporosis is a common comorbidity of rheumatoid arthritis (RA). Although RA disease activity has been demonstrated to be associated with bone loss in previous studies, most of them were cross-sectional studies and not in the context of treat-to-target (T2T) strategies.

Objectives: To evaluate the association of disease activity with bone mineral density (BMD) changes in the context of T2T strategies in a prospective RA cohort.

Methods: RA patients were enrolled from a prospective CENTRA cohort of Peking University First Hospital. BMD was repeated at baseline, 1-year and then every other year. Time-adjusted mean disease activity scores were adopted to reflect the overall disease activity during follow-up. The influence of univariable associations between predictors and BMD was investigated using linear regression.

Results: A total of 268 patients were included in our analysis. Their mean age was 50 (12.9) years old. At enrollment, the mean (SD) DAS28-ESR was 3.70 (1.17), and the median (IQR) CDAI and SDIA was 10 (14.45) and 10.30 (16.53), respectively. Osteoporosis at lumbar spine was observed in 23.1% patients and 9.3% at femoral neck at enrollment. Older age, higher SDAI score and lower BMI were found to be associated with osteoporosis at baseline. Reevaluations of BMD at 1 year was applied in 144 patients. Mean decreases of BMDs were 1.75 % at the lumbar spine and 1.40 % at femoral neck at 1 year form baseline, respectively. Patients who achieved remission had less yearly bone loss at lumbar spine (p=0.036). Female gender was identified as a risk factor in the multiple linear regression analyses, and lower disease activity and bisphosphonates were protective factors of continuous bone loss.

Conclusion: Disease activity is associated with bone loss in RA patients in the context of T2T strategies, and those who achieved remission had less yearly bone loss.

Disclosure of Interests: None declared

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POS0600 ANGIOGENIC T-CELL DEPLETION OCCURS DURING THE EARLIEST PHASES OF RHEUMATOID ARTHRITIS LINKED TO SUBCLINICAL VASCULAR STIFFNESS

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Background: vascular insult accounts for the cardiovascular (CV) risk excess in rheumatoid arthritis (RA). Angiogenic T cells (Tang), which are responsible of vascular repair, have been described to be reduced in established RA with overt CV disease. However, whether Tang are altered during the earliest stage of the disease and related to subclinical CV findings is unknown.

Objectives: to evaluate circulating Tang levels in the very early stage of RA, including clinically suspect arthralgia (CSA), and their associations with subclinical CV endpoints (subclinical atherosclerosis and vascular stiffness).

Methods: 84 RA patients (2010 EULAR/ACR classification criteria), 14 CSA individuals (EULAR criteria) and 28 matched healthy controls (HC) were recruited. All patients were untreated at the time of sampling. Tang (CD3+CD31+CXCR4+) frequency was assessed by flow cytometry in peripheral blood samples. Plaque occurrence, cIMT and stiffness parameters were analyzed by Doppler ultrasound in internal carotid, middle cerebral and basilar arteries. Lipoprotein analyses were performed by NMR.

Results: Tang were decreased in RA and CSA groups compared to HC (both p<0.010). Whereas Tang frequency was negatively correlated with very low density lipoproteins features (cholesterol and triglyceride content, size distribution and particle number) in HC and positively with HDL (cholesterol content and particle number), these associations were lacking in RA

and CSA groups. Tang levels were not related to individual traditional CV risk factors, body mass index, wait circumference (all p>0.050) nor with the modified SCORE (r=-0.070, p=0.542) or Framingham Risk Score (r=-0.013, p=0.907). On the contrary, disease activity accounted for the Tang depletion observed in RA (b[95% CI]; DAS28: -0.436 [-0.306, -0.109], p=<0.001; SDAI: -0.020 [-0.032, -0.008], p=0.002). Tang levels were unrelated to the duration of the symptoms both in RA and CSA. In RA patients, Tang frequency was not associated with atherosclerosis plaque occurrence (p=0.556) or cIMT (r=0.136, p=0.245). However, Tang paralleled stiffness parameters: vascular strain (VS, r=0.373, p=0.013), vascular distensibility (VD, r=0.479, p=0.004), vascular stiffness (VSf, r=-0.400, p=0.007) and pressure-strain elastic modulus (PSEM, r=-0.373, p=0.013). Finally, Tang frequency was an independent predictor of stiffness parameters after adjusting for mSCORE, body mass index, DAS28, RF and ACPA positivity: VS (β=0.415, p=0.035), VD (β =0.361, p=0.028), VSf (β =-0.322, p=0.033) and PSEM (β =-0.346, p=0.016).

Conclusion: Tang depletion is an early event along RA development, associated with disease-related parameters and unrelated to traditional risk factors. Tang may be the missing, functional link between disease activity and CV outcomes. Altered Tang levels may be an early biomarker of premature vascular stiffness during the first stages of the disease.

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POS0601 CRANIOCERVICAL JUNCTION INVOLVEMENT ASSESSED BY COMPUTED TOMOGRAPHY AND/OR MAGNETIC RESONANCE IMAGING IN INFLAMMATORY ARTHRITIS: SINGLE CENTER CASE-CONTROL STUDY

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Background: Craniocervical involvement is generally overlooked clinically.

Objectives: The aim of this study is to investigate the craniocervical involvement in inflammatory arthritidies and compare with patients without inflammatory arthritidies.

Methods: In this retrospective analysis, cervical CT and/or MRI scans -taken for any reasons between 2010 and 2020 - of patients with rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsA) (M05, M06, M07 and M45) according to ICD-10 codes were scanned from the hospital database. The diagnosis of RA, AS, and PsA was confirmed by an experienced clinician with medical history, laboratory, and treatment history. Of these patients, those who underwent CT and/or MRI before the definitive diagnosis of inflammatory arthritis were included in the analyses. Demographic data of the included patients were recorded. Craniocervical involvements (anterior, posterior, lateral, and rotational atlantoaxial subluxation; vertical subluxation; subaxial subluxation; odontoid process involvement [resorption or pannus], atlantoaxial and atlantooccipital involvement) were evaluated by an experienced radiologist on CT or MRI, as appropriate. Control group was consisted of consequent patients without inflammatory arthritidies and who undergone cervical CT or MRI with any reasons out of trauma. p<0.05 was considered statistically significant.

Results: From a total of 4442 records (1558 individual patients), 459 patients (204 RA, 200 SpA, and 55 PsA patients) and 78 patients for control group were included in the study. **In** Table 1, comparison of RA, SpA and control groups was given. The percentage of female gender and age at diagnosis were lower in SpA patients. Craniocervical junction involvement was detected in 101 (49.5%) RA, 53 (26.5%) SpA, 4 (5.1%) of control group, p<0.001. The odontoid process appears to be one of the main targets at the craniocervical junction, especially in RA patients (69 (33.8%)) which was significantly higher than SpA and control groups. Atlantoaxial subluxation and atlantoaxial joint involvement were significantly higher in RA and SpA groups than control group. Although vertical subluxation (VS) was numerically higher in RA nd SpA groups compared to control group, VS-related brainstem compression was relatively uncommon (6 (2.9%) in RA, 1 (0.5%) in AS, none of the control group. Spinal cord compression was detected in 8 (7.9%) RA patients and 2 (1.0%) AS patients and none of the control group. Regarding PsA, percentage of overall craniocervical involvement was higher than control group (16.4% vs 5.1%) without precedence of any specific involvement.

Table 1. Comparison of RA, SpA and control groups for spesific types of craniocervical involvements

	RA (n=204)	SpA (n=200)	Control group (n=78)	p; RA vs SpA vs Contol	p; RA vs Control	p; SpA vs Control	p; RA vs SpA
Female, n (%)	166 (81,4)	124 (62,0)	55 (70.5)	<0,001	0.048	0.18	<0,001
Age at the time of CT	50 (41-60)	38 (32-47)	46 (18-86)	<0,001	<0,001	0.45	<0,001
Any type of involvement	101(49,5)	53 (26,5)	4 (5.1)	<0,001	<0,001	<0,001	<0,001
Odontoid process involvement	69(33,8)	24 (12,0)	0	<0,001	<0,001	0,001	<0,001
Odontoid process resorption	62(30,4)	19(9,5)	0	<0,001	<0,001	0,005	<0,001
Odontoid process pannus	37(18,1)	9(4,5)	0	<0,001	<0,001	0.065	<0,001
Atlantoaxial subluxation (AAS)	17(8,3)	10 (5,0)	0	0.022	0.004	0.067	0.018
Spinal cord compression due to AAS	5 (2,5)	1 (0,5)	0	0.12			
Vertical subluxation (VS)	24 (11,8)	20/197 (10,2)	3 (3.8)	0.13			
Brainstem compression due to VS	6 (2,9)	1 (0,5)	0	0.06			
Subaxial subluxation (SAS)	12 (5,9)	4 (2,0)	1 (1.3)	0.054			
Spinal cord compression due to SAS	3 (1,5)	1 (0,5)	0	0.38			
Atlantoaxial joint involvement	23/186 (12,4)	13 (6,5)	0	0.002	0.001	0.023	0.32
Atlantooccipital joint involvement	6/187 (3,2)	3 (1,5)	0	0.19			

CT: Computarized tomography, RA: Rheumatoid arthritis, SpA: Spondyloarthritis

Conclusion: Craniocervical junction involvement can often be detected in patients with inflammatory arthritis, especially in patients with RA. Odontoid process seems as the main target of inflammation. Craniocervical involvement has the potential to be overlooked clinically, and needs to be evaluated more carefully.

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POS0602 PULMONARY RHEUMATOID NODULES: DOES SEROLOGIC STATUS MATTER?

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Background: The frequency of pulmonary rheumatoid nodules closely relates to the diagnostic modality and changes from <0.4% to 32%. Also, it is known that seropositive RA patients tend to have more extra-articular disease.

Objectives: We aimed to compare the disease and pulmonary rheumatoid nodule characteristics of seropositive and seronegative RA patients.

Methods: In this study, all RA patients - according to ICD-10 code - and had at least one chest computerized tomography (CT) were examined and revealed 4117 individual patients. First, RA diagnosis was confirmed according the patients' history, physical examination, radiography and laboratory assessment. Then, chest CTs were examined by an experienced radiologist. To classify pulmonary nodules as ''pulmonary rheumatoid nodule'', following inclusion and exclusion criteria were used; For inclusion: 1) nodules with changing dimension on follow-up, 2) At least two nodules with different dimensions, 3) Cavitary nodule at any chest CT. For exclusion: 1) Solitary nodules OR all nodules ≤ 5mm and without follow-up OR no change on follow-up. Biggest nodule was named as **dominant nodule.** Then, patients were grouped according to rheumatoid factor and anti-CCP status as seropositive (RF ± anti-CCP) and seronegative. Demographics, comorbidities, RA-spesific treatments and nodule characteristics were compared.

Results: Of 680 RA patients who had pulmonary nodule in chest CT, 208 (30.6%) patients were classified as having pulmonary rheumatoid nodule. 167 (80.3%) patients were seropositive. Demographic and comorbidity characteristics were similar among seronegative and seropositive patients (Table 1). Regarding RA-spesific treatments, methotrexate, leflunomide and rituximab were prescribed more frequently in seropositive patients. For nodule characteristics, seropositive patients had higher number of nodules (5 [1-48] vs 3 [1-27]; p=0.004), bigger dominant nodule (8 [3-95] vs 6 [3-45] mm; p=0.011), and higher percentage of cavitary nodule (28.7% vs 12.2%; p=0.03). Localization of the nodule was compareble.

Table 1. Comparison of demographic, disease and nodule characteristics of seropositive and seronegative patients (n=208)

	Seropositive (n=167, 80.3%)	Seronegative (n=41, 19.7%)	P value
Female, n(%)	113 (67.7)	28 (68.3)	0.94
Age at the time of CT (median, min-max)	61 (24-83)	59.7 (20-83)	0.28
Smoking (n=73)	26 (43.3)	4 (30.8)	0.40
- **Never smoked**	34 (56.7)	9 (69.2)	
- **Ever smoked**			
Comorbidity (n=188)	127 (84.7)	30 (78.9)	0.40
- **Hypertension**	72 (55.0)	18 (58.1)	0.91
- **Diabetes (n=166)**	25 (18.5)	7 (22.6)	0.79
- **CAD (n=165)**	30 (22.6)	7 (21.9)	0.93
- **Heart Failure (n=164)**	15 (11.4)	6 (18.8)	0.41
- **COPD (n=163)**	20 (15.2)	1 (3.2)	0.13
- **Asthma (n=160)**	15 (11.6)	5 (16.1)	0.54
- **CKD (n=169)**	20 (14.5)	8 (25.8)	0.22
- **ILD (n=202)**	54 (33.1)	10 (25.6)	0.37
RA-spesific treatments (ever)	90 (72.6)	16 (55.2)	0.07
- **Methotrexate (n=153)**	105 (64.0)	12 (30.8)	**0.001**
- **Leflunomide (n=208)**	117 (70.5)	25 (61.0)	0.06
- **Hydroxchloroquine (n=169)**	65 (47.4)	11 (36.7)	0.28
- **Sulfasalazine (n=167)**	39 (39.0)	6 (27.3)	0.30
- **TNFi (n=122)**	41 (39.8)	2 (9.5)	0.008
- **Rituximab (n=124)**	11 (9.9)	2 (8.0)	0.77
- **Tofacitinib (n=136)**	12 (11.9)	2 (10.5)	0.86
- **Abatacept (n=120)**	9 (8.5)	2 (8.7)	0.98
- **Tocilizumab (n=129)**			
Number of nodules at baseline CT (median, min-max)	5 (1-48)	3 (1-27)	**0.004**
Diameter of dominant nodule (median, min-max) (mm)	8 (3-95)	6 (3-45)	**0.011**
Localization of dominant nodul	64 (38.3)	15 (36.6)	0.84
- **Left or right?**	64 (38.3)	12 (29.3)	0.48
◦ **Left**	51 (30.5)	16 (39.0)	0.28
- **Upper, middle or lower?**	52 (31.1)	13 (31.7)	
◦ **Upper**	69 (41.3)	21 (51.2)	
◦ **Middle**	22 (13.2)	7 (17.1)	
◦ **Lower**	76 (45.5)	13 (31.7)	
-Peripheral, central or subpleural			
◦ **Peripheral**			
◦ **Central**			
◦ **Subpleural**			
Cavitation	48 (28.7)	5 (12.2)	**0.03**
Calcification	54 (32.5)	12 (29.3)	0.69

CAD: Coronary artery disease, CKD: Chronic kidney disease,; ILD: Interstitial Lung Disaese,

Conclusion: Autoantibodies seem to have impact on the characteristics of pulmonary rheumatoid nodules. As there were different prescription patterns were seen in our study, effects of these treatment differences need to be determined.

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POS0603 CARDIOVASCULAR RISK FACTORS BEFORE ONSET OF RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH CARDIOVASCULAR EVENTS AFTER DISEASE ONSET – A CASE CONTROL STUDY

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Background: Increased comorbidity and mortality in rheumatoid arthritis (RA) patients are highly due to cardiovascular disease (CVD). The etiology of this increased morbidity and mortality in patients with RA compared with the general population is not fully understood. We have previously shown that individuals who subsequently develop RA have increased frequencies of several risk factors for CVD, such as elevated BMI, elevated Apoliprotein (Apo) B/ApoA1 ratio, and cigarette smoking compared with matched controls, already before symptom onset of RA.
Objectives: We aimed to assess the impact of CV risk factors, already present before onset of symptoms of RA, for future CV events (CVE) in comparison with matched controls.
Methods: A case-control study including 521 individuals before symptoms of RA and 1,566 matched controls identified in the Health Surveys of the Medical Biobank of Northern Sweden was performed. Information regarding the presence of the selected risk factors for CVD was based on surveys with data collected in the Västerbotten Intervention Programme (VIP) and the Northern Sweden Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA). Selected CVD risk factors were: hypertension, elevated Apolipoprotein B/A1 ratio, elevated body mass index, diabetes, and smoking. Information on comorbidities (coded according to the International Statistical Classification of Diseases and Related Health Problems ninth or tenth revision (ICD-9 and/or -10)) was requested from the Swedish National Patient Register and the Cause of Death Register. Statistics were performed using SPSS version 26.0 (IBM Corp., NY, USA), Cox proportional hazard regression was used and presented with calculated hazard ratios (HRs) and 95% confidence intervals (CI). Adjustments were performed for risk factors developed after RA onset.
Results: Pre-RA individuals had a higher risk for CVE after RA onset compared with matched controls (HR (95% CI)= 1.70 (1.31-2.21)) which remained after adjustment for various risk factors for CVD, (HR (95% CI)= 1.69 (1.24-2.30)). Also, treatment with biological disease modifying anti rheumatic drugs (bDMARDs) were associated with CVE (HR (95% CI)=2.06 (1.05-4.03), adjusted for CV risk factors). Most of the risk factors present prior to RA were associated with CVE after diagnosis, The significant association of risk factors present before RA onset for a CVE after onset remained after adjustments for risk factors that developed after RA onset. A combination of risk factors resulted in a higher risk in RA compared with controls (OR (95% CI); two risk factors 3.30 (1.16-9.36), vs. 1.21 (0.62-2.37), and three-four risk factors, 7.32 (2.71-19.74), vs. 4.16 (2.27-7.67).
Conclusion: Known risk factors for CVD present in individuals prior to onset of RA were associated with future CVE and even after adjustments for the risk factors, patients with RA had a higher risk for CVE compared with controls. In addition, risk factors present before RA was associated with future CVE even after adjustment for risk factors developed after RA onset. These findings further enlighten the importance of early assessment of risk for CVD in RA.

REFERENCES: -

Disclosure of Interests: None declared
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POS0604 THE EFFECT OF TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION AND DEEP BREATHING EXERCISES ON HEART RATE VARIABILITY IN HEALTHY PARTICIPANTS AND PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are chronic autoimmune diseases associated with a reduced function of the autonomic nervous system including an impaired function of the vagus nerve (VN). The VN has potential anti-inflammatory effects, which could be utilized in a new treatment approach using vagus nerve stimulation (VNS). Different types of VNS exist, but no direct comparison has been made of the methods in patients with RA and SLE.
Objectives: The aim of this study was to compare the effect of transcutaneous auricular VNS (taVNS) and deep breathing (DB) on vagal tone in patients with RA or SLE and healthy participants and to investigate the washout effect assessed through time domain heart rate variability (HRV) measures (RMSSD (root-mean-square of successive differences), SDNN (standard deviation of N-N intervals), and PNN50 (percentage of adjacent N-N intervals that differ from each other by more than 50 milliseconds)).
Methods: The study was designed as an open label cross-over study. 42 healthy participants and 52 patients with RA or SLE performed two interventions, 30 minutes of taVNS and 30 minutes of DB. The interventions were separated by at least 24 hours. Before each intervention, two 5-minutes ECG-recordings were made to determine the participants' baseline HRV. After each intervention three 5-minutes ECG-recordings were conducted in the following 30 minutes to investigate the potential washout effect.
Results: Healthy participants: A significant increase in SDNN, RMSSD, and PNN50 were found after DB. SDNN increased significantly immediately after taVNS. SDNN was significantly higher after DB compared to taVNS. Otherwise, there were no significant differences between the effects of the two interventions. Patients: A significant increase in SDNN, RMSSD, and PNN50 were present after both DB and taVNS. No significant differences were found between the effects of the two interventions. The effects of the interventions were still measurable 30 minutes after intervention, indicating no washout.

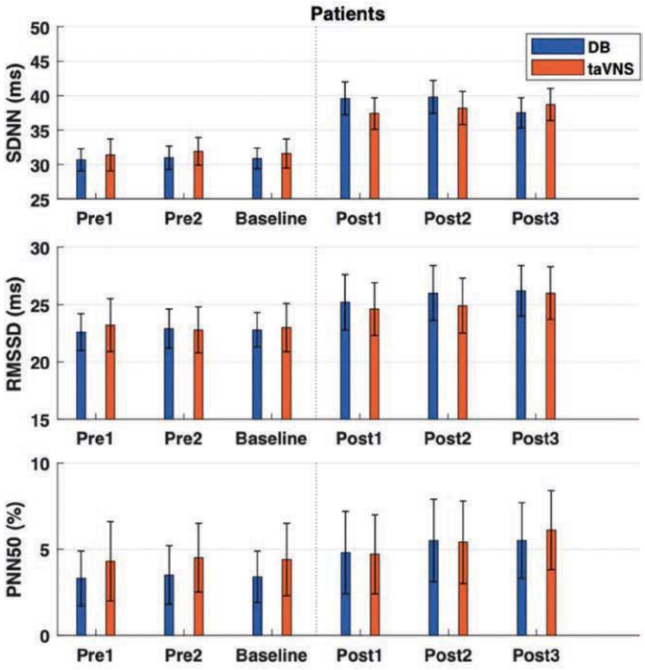

Figure *HRV-data for the patient population. Baseline shows mean values of Pre1 and Pre2. Data are displayed as mean ± standard er ror across participants.*

Conclusion: DB causes the greatest increase in HRV for healthy participants, while both DB and taVNS can equally elevate HRV in patients with RA and SLE, which support their use as a potential new treatment approach. However, their clinical effect needs to be investigated in future studies.

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POS0605

IN PATIENTS WITH RHEUMATOID ARTHRITIS, CLINICAL EXAMINATION OF THE FEET IS IMPORTANT FOR UNDERSTANDING INDIVIDUAL DISEASE BURDEN, BUT DOES NOT PROVOKE A CHANGE IN THERAPY IN MOST CASES

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Background: Disease activity scores like CDAI, SDAI or DAS28, are essential for measuring rheumatoid arthritis (RA) disease activity. These do not contain foot joints. However, foot pain is an important aspect of morbidity for RA patients, which leads to reduced mobility and quality of life.

Objectives: To analyse the impact of synovitis in ankle and metatarsophalangeal joints on RA scores and RA disease activity states.

Methods: Joint scores of 545 RA outpatients were followed from August 2004 through December 2020. Informed consent for the analysis of their routine data was obtained for every patient. The standard CDAI cut-offs used were CDAI ≤ 2.8 for remission (REM), CDAI > 2.8 - 10.0 for low disease activity (LDA), CDAI > 10.0 - 22.0 for moderate disease activity (MDA) and CDAI > 22.0 for high disease activity (HDA). Foot involvement (FI) was defined as having at least one swollen (SJ) or tender (TJ) foot joint in patients who ever had palpable synovitis in any of these joints. The visits were grouped according to the number of swollen joints (SJ 0-28). The mean Physician Global Assessment of disease activity (PhGA) was calculated for each SJ group and the difference between the mean PhGA in patients with and without FI (as defined above) was calculated for each SJ group (ΔPhGA). Statistical analysis was performed in IBM SPSS Statistics Version 28.0.1.0.

Results: A total of 7,577 visits of 545 patients were included, for a mean of 14 visits per patient. 413 (75.8%) of the patients were female, the mean age at visit was 59 years, mean disease duration was 13 years, 284 (52.1%) were ACPA positive. 247 (45.3%) were on glucocorticoid therapy, 50 (9.2%) were on biological DMARDs. The median CDAI at visit was 4.3 (interquartile range IQR 1.6 - 9.0), the median DAS28 was 2.56 (IQR 1.89 - 3.37), the median CRP was 2.5 (IQR 1.0 - 6.2) mg/L. At 2,853 (37.7%) visits the patient was in REM, at 3,134 (41.4%) visits in LDA, at 1,265 (16.7%) visits in MDA and at 324 (4.3%) visits in HDA. Patients with FI were more active and scored higher on CDAI (9.1 vs. 3.4, p<0.001) and DAS28 (3.19 vs. 2.45, p<0.001), even though the indices do not include the foot joints. This was mainly due to higher patient global assessment of disease activity (3.1 vs. 2.0, p<0.001). Involvement of the feet also led to a higher physician estimate of global disease activity. The mean difference of PhGA between patients with and without involvement of their feet (ΔPhGA) was meaningful for joint counts 0-10, with an unweighted mean ΔPhGA of 0.273. Of the 217 patients with FI, 3,776 visits were analyzed. For patients with FI, the potential change in disease activity was calculated by subtracting ΔPhGA from the CDAI at each visit. For 3,662 (97.0%) of the visits, this did not result in a change of disease activity state. For 90 (2.4%) visits, disease activity changed from LDA to REM, for 21 (0.6%) from MDA to LDA, and for only 3 (0.1%) visits from HDA to MDA. At 83 (1.1%) visits of a total of 59 (10.8%) patients, only swollen foot joints without tender foot joints were recorded.

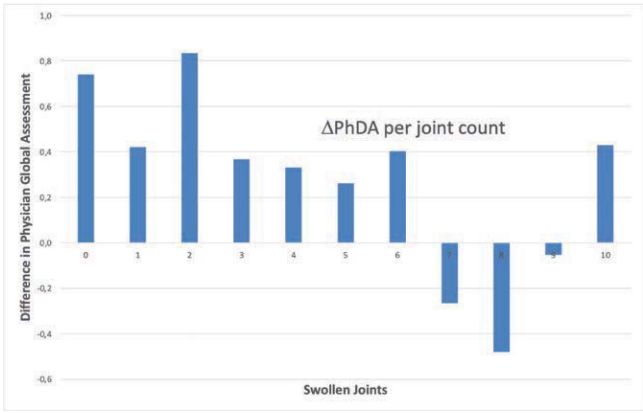

Figure 1.

Conclusion: Patients with foot involvement are more active and score disproportionally high on disease activity indices, even though these do not include foot joints. While patients suffer significantly from foot involvement, underestimating disease activity by not assessing the feet would have changed the disease activity state for 3.1% of the visits only. Palpable synovitis without tenderness, which would be missed by performing only a metatarsophalangeal squeeze test, was found at one in a hundred visits.

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Consultant of: Abbvie, AstraZeneca, BMS, Boehringer Ingelheim, Chugai, GSK, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi, UCB., Christoph Weinert: None declared, Martin Aringer Speakers bureau: AbbVie, Astra Zeneca, BMS, Boehringer Ingelheim, Chugai, Galapagos, GSK, HEXAL, Lilly, MSD, Mylan, Novartis, Otsuka, Pfizer, Roche, Sanofi, UCB., Consultant of: AbbVie, Astra Zeneca, BMS, Boehringer Ingelheim, Galapagos, GSK, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB.

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POS0606

HOW DO GLUCOCORTICOIDS, BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS AND DISEASE ACTIVITY IMPACT THE RISK OF STAPHYLOCOCCUS AUREUS BACTEREMIA IN RHEUMATOID ARTHRITIS PATIENTS? A NATIONWIDE NESTED CASE CONTROL STUDY IN THE DANISH DANBIO COHORT

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Background: *Staphylococcus aureus* bacteremia (SAB) has high mortality and rheumatoid arthritis (RA) patients are at increased risk,[1] however, the role of anti-rheumatic treatments and disease activity is unclear.[2,3]
Objectives: To explore the impact of treatment with glucocorticoids and biologic disease-modifying anti-rheumatic drugs (bDMARDs) and disease activity on the risk of SAB in RA patients.
Methods: Nested case control study in a nationwide cohort of RA patients (DANBIO) with no history of SAB. Cases had a first-time microbiologically verified SAB between 2010-2018. Controls were incidence density matched (age and sex) at time of SAB (index date). We linked data from DANBIO (e.g. disease activity, anti-rheumatic treatment) to other national registries (comorbidities, prescriptions, socioeconomic status, etc). Treatments were redeemed prescriptions or registrations in DANBIO (oral glucocorticoids, bDMARDs) 0-2 years before the index date. Dose of oral glucocorticoids was retrieved from either DANBIO or estimated from the latest prescription. Risk associated with treatment and disease activity was assessed by multivariate conditional logistic regression. For treatments, excess cases/10,000 exposed/year were calculated by multiplying the fully adjusted OR (95%CI) with the incidence rate in the cohort. Missing data was handled by multiple imputation.
Results: We identified 180 cases in 30,479 RA patients (IR 106.7/100,000 person-years) and matched 720 controls (53% women, median age 73 years, IQR 65;80). For cases, orthopedic implants were frequent (53%/34% for cases/controls), many had recent surgery (38%/5%), longstanding RA (13 years (6;21)/8 (4;14)), joint erosions (48%/39%), moderate (29%/16%) or high (10%/7%) disease activity, and used glucocorticoids (41%/19%) and bDMARDs (31%/20%). Adjusted ORs were high for current use of oral glucocorticoids, especially for doses >10mg/day (OR=14.5 (4.0; 52.2)). For bDMARDs, adjusted OR was 1.9 (1.1; 3.2). Correspondingly, the treatments increased risk with 144 and 9 excess cases/10,000/year, respectively (Table 1). For disease activity, adjusted ORs were >1 (non-significant) for moderate and high disease activity compared with remission (Figure 1).

Table 1. Use of oral glucocorticoids and biologic disease-modifying anti-rheumatic drugs (bDMARDs) 0-2 years before the index date and risk of *Staphylococcus aureus* bacteremia (SAB)

	SAB cases, n=180	Controls, n=720	OR (95% CI)*	Number of excess cases/10,000 exposed/year (confidence limits)
Glucocorticoids	n (%)	n (%)		
No	67 (37)	450 (63)	ref	
Yes	113 (63)	270 (38)	**2.4 (1.5; 3.8)**	15 (6; 30)
Former user[a]	39 (22)	133 (19)	1.7 (0.9; 3.0)	NA
Current user[b]	74 (41)	137 (19)	**3.2 (1.9; 5.3)**	23 (9; 46)
Current daily dose				
>0-5 mg	44 (24)	108 (15)	**2.1 (1.1; 3.8)**	11 (1; 30)
>5-10mg	18 (10)	26 (4)	**3.5 (1.4; 8.6)**	26 (4; 81)
>10mg	12 (7)	8 (1)	**14.5 (4.0; 52.2)**	144 (32; 46)
bDMARDs				
No	111 (62)	558 (78)	ref	
Yes	69 (38)	162 (23)	**1.9 (1.1; 3.2)**	10 (1; 24)
Former user[a]	14 (8)	18 (3)	2.1 (0.8; 5.8)	NA
Current user[b]	55 (31)	144 (20)	**1.9 (1.1; 3.2)**	9 (1; 23)

[a] >3 to 24 months before (rituximab >12 to 24 months), [b] 0-3 months before (rituximab 0-12 months)*adjusted for sex, age, comorbidities, implants, recent surgery, RA disease duration, time since entry, csDMARDs, socioeconomic-, sero-, erosive-, functional- and smoking status, body mass index, and disease activity (high/low/moderate/remission)

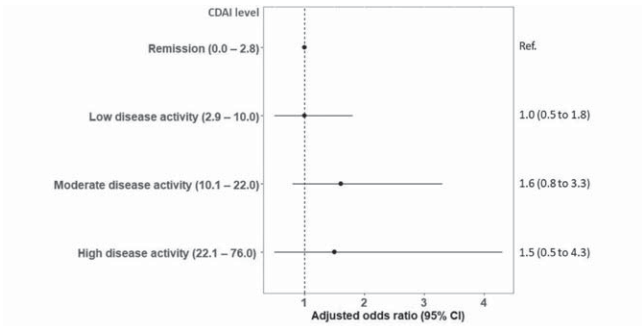

Figure 1. Disease activity and risk of *Staphylococcus aureus* bacteremia

Conclusion: Oral glucocorticoids and bDMARDs increased relative risk of SAB, with number of excess cases being high for oral glucocorticoids (>10 mg/day) and low for bDMARDs. Disease activity had minor impact on the risk. This emphasizes that high dose glucocorticoids should be used with caution.
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POS0607

IMPROVING TREAT-TO-TARGET IMPLEMENTATION IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW OF BARRIERS, FACILITATORS, AND INTERVENTIONS

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Background: Treat-to-target (T2T) is integral to international recommendations for managing patients with rheumatoid arthritis (RA),[1,2] but its implementation in clinical practice is suboptimal.[3] Understanding T2T barriers and facilitators may inform strategies for improving T2T implementation in RA.
Objectives: To review published evidence on barriers to and facilitators of T2T implementation in RA, and interventions designed to improve T2T implementation.
Methods: Two systematic literature searches were conducted to identify barriers to or facilitators of, and interventions designed to improve, T2T implementation in RA (Jan 1, 2015–Mar 1, 2021 and Jan 1, 2010–Jul 1, 2021, respectively). The quality of each study was assessed using the appropriate Critical Appraisal Skills Programme (CASP) checklist.[4] Barriers/facilitators and interventions were grouped into categories and summarized descriptively.
Results: The barriers/facilitators literature search retrieved 235 articles. Seventy-seven of these, which described primary studies mentioning a total of 331 T2T barriers/facilitators in RA, were included in the analysis. The interventions literature search identified 451 articles, including 70 primary studies reporting a total of 56 unique interventions to improve T2T implementation in RA. The quality of the studies varied; however, most addressed at least half of the information evaluated in the CASP checklists. Barriers/facilitators were categorized into 18 key target areas for patients (n=7), healthcare professionals (HCPs; n=6), or patients and HCPs (n=5). These related to: HCPs' or patients' knowledge or perceptions; patients' clinical or social conditions; patient–HCP communication or alignment; and time or resources (Figure 1). The 56 interventions were grouped into 18 types (Table 1). More than half of the interventions (n=30; 53.6%) were designed to improve or streamline disease activity or patient-reported outcome assessments or increase patient–HCP alignment on disease activity. Interventions designed to improve shared decision-making were also common (n=23; 41.1%); these included patient and HCP education (n=15), decision aids (n=7), and shared decision-making prompts (n=3). Of the 56 interventions, 20 (35.7%) reported improvements in T2T implementation and/or patient outcomes in RA. However, as most interventions were evaluated in single centers, their effectiveness, feasibility, and generalizability across other regions or healthcare settings were unclear.

Table 1. Interventions for improving T2T implementation in RA, by type

Type of intervention	Number of unique interventions (n=56)[a]
Electronic disease assessment recording	11
Disease assessment process/quality improvement initiative	8
Allied HCP-supported T2T strategy	8
Patient educational tools	7
Patient decision aid	7
HCP performance feedback	7
Integrated PRO assessment	6
Ultrasound assessment	5
HCP learning collaborative (structured learning sessions + performance feedback)	4
Patient PRO dashboard/visual feedback tool	4
Telehealth monitoring	3
HCP T2T/shared decision-making prompt	3
Nurse-led patient education	3
Multidisciplinary team program	3
HCP training	2
Patient telehealth education	2
HCP decision-making tool	1
Patient group sessions	1

[a]Interventions may be assigned to more than one categoryPRO, patient-reported outcome

Conclusion: While practical methods designed to improve T2T implementation in RA are available, their effectiveness and feasibility will likely vary by region and healthcare setting. More primary research is required to identify the most relevant barriers/facilitators and prioritize the most appropriate interventions to optimize T2T implementation both globally and locally.

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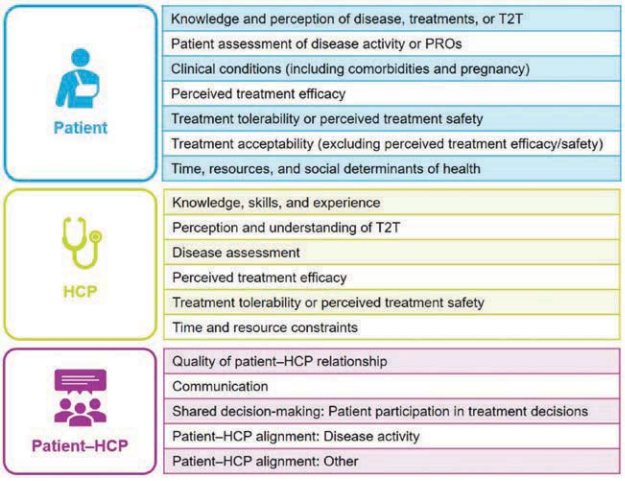
Figure. Key barriers to/facilitators of T2T implementation in RA by stakeholder



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POS0608

PROGRESSIVE INCREASE IN THE DIAGNOSTIC DELAY AND PERSISTENTLY SEVERE CLINICAL PRESENTATION OVER THE YEARS IN AUTOANTIBODY-NEGATIVE PATIENTS WITH RHEUMATOID ARTHRITIS IN THE SETTING OF AN EARLY ARTHRITIS CLINIC

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Background: Over the past 20 years, despite the widespread diffusion of dedicated early arthritis clinics (EAC) and more sensitive classification criteria, the percentage of patients seen within the window of opportunity remains low, and the new RA criteria, heavily weighted on autoantibodies, may have further hindered the recognition and treatment of seronegative patients.
Objectives: we analysed changes in the diagnostic delay and clinical presentation of patients with RA admitted to the EAC of the Division of Rheumatology of the San Matteo University Hospital, Pavia, Italy, from its institution in 2005 to 2017.
Methods: Referral criteria to the EAC have remained stable over the years and include ≥3 swollen joints (SJs) or, in case of <3 SJs, a positive squeeze test or morning stiffness >30 min. From all early arthritis patients (n=1.553), we selected 668 patients fulfilling at enrolment at least the 1987 ACR criteria for RA before

December 2010 (n=345, 88.4% also fulfilling 2010 criteria), and at least the 2010 ACR/EULAR criteria after January 2011 (n=323, 63.5% also fulfilling 1987 criteria). Time from first self-reported joint symptom to referral (diagnostic delay) was compared across different time periods: (i) 2005-2007; (ii) 2008-2010; (iii) 2011-2013; (iv) 2014-2017. Clinical characteristics were collected according to standardised assessments. Data were analysed in the total population and after stratification for the autoantibody status (double negative for rheumatoid factor, RF, and anti-citrullinated protein antibodies, ACPA vs RF and/or ACPA positive).
Results: In all, the diagnostic delay collectively increased from a mean (SD) of 20.8 (20.5) weeks before 2010 to 24.4 (20.6) weeks thereafter (p=0.02), and the proportion of patients diagnosed within 12 weeks non-significantly decreased from 39.3% to 35.3%. Still, patients presented with progressively milder inflammatory markers despite unchanged joint tenderness and patient-reported outcomes (PROs). Trends were, however, remarkably different in different autoantibody subgroups. In RF/ACPA-positive patients, a stable proportion of 41-44% was diagnosed within 12 weeks (Figure 1**A**). At presentation, patients had fewer SJs and lower C-reactive protein (CRP) levels; the mean decrease of SJs and CRP from 2005-2007 to 2014-2017 were -5.6 and -1.1 mg/dl, respectively (Figure 1**B**). The improvement in PROs was smaller but still significant over time (Figure 1**C**). In contrast, in autoantibody-negative patients, the proportion of patients diagnosed within 12 weeks progressively decreased from 37.9% to 25.6% (p=0.08) (Figure 1**D**). Furthermore, the improvement over time of inflammatory features, especially of SJs, was significant but smaller than autoantibody-patients, and PROs such as pain and global assessment of disease activity remained severely impacting with mean values of up 60 mm even in recent times (Figure 1**E,F**).

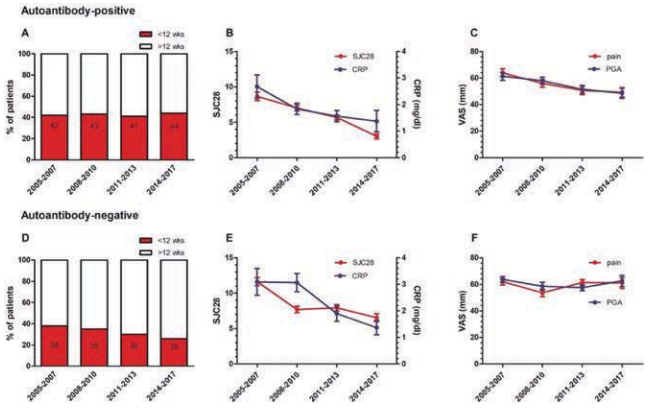

Figure 1. Time to diagnosis and clinical presentation of autoantibody-positive and –negative patients with early rheumatoid arthritis. (**A**, **D**) Proportion of patients diagnosed within 12 weeks from symptoms' onset among autoantibody-positive (**A**) and autoantibody-negative (**D**) rheumatoid arthritis (RA) in different time periods. (**B**, **C**, **E**, **F**) Values of swollen joints (SJC28), C-reactive protein (CRP) (**B**, **E**), and visual analogue scales (VAS) for pain and patient global assessment (PGA) of disease activity (**C**, **F**) in autoantibody-positive (**B**, **C**) and autoantibody-negative (**E**, **F**) RA in different time periods. Values are expressed as means and standard errors.

Conclusion: Collectively, our data indicate that a large proportion of patients with RA still lack early diagnosis despite dedicated early access to rheumatology care; from 2010 onwards, autoantibody-positive patients are diagnosed with a milder and less disabling disease, while autoantibody-negative patients are at increased risk of delayed diagnosis, and remain burdened with severe disease
Disclosure of Interests: Ludovico De Stefano Speakers bureau: Gilead, Bernardo D'Onofrio: None declared, Garifallia Sakellariou: None declared, Antonio Manzo: None declared, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, Pfizer, Roche, Sanofi, Serena Bugatti Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, Pfizer, Sanofi, Grant/research support from: Pfizer
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POS0609 STRESS-ASSOCIATED INCREASES IN RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND FLARES DURING THE COVID-19 PANDEMIC

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Background: The novel coronavirus disease 2019 (COVID-19) pandemic has spurred global action. Beginning in March of 2020, the Southern California COVID-19 pandemic response to limit virus transmission was characterized by mandated lockdowns and quarantines, resulting in significant stressors for rheumatology patients and potentially threatening their disease.
Objectives: To examine factors associated with changes in rheumatoid arthritis (RA) disease activity and flares in the COVID-19 pandemic.
Methods: RA patients identified by ICD-9/10 codes and active email addresses within a University of California, Los Angeles (UCLA) Rheumatology database were sent surveys via email in July and November of 2020. The survey was UCLA Institutional Review Board approved and included electronic consent and questions related to: perceptions of disease activity/remission via Routine Assessment of Patient Index Data 3 (RAPID3), flare frequency, RA flare questionnaire (RA-FQ), Perceived Stress Scale (PSS-4), and pandemic impact on stress (i.e. emotional state, apprehension, panic, helplessness, work, home, financial, and social distancing stress). Demographics were extracted from electronic medical records. Results were examined via descriptive analyses, Pearson correlations, and chi-square test for comparisons plus linear stepwise regressions where appropriate to evaluate the relationship between stress measures, RA disease activity, and flare frequency and severity.
Results: Among 5037 patients surveyed, 361 in July and 4676 in November,1128 (22.4%) responded. The study population demographics were: mean age of 57.5 ± 15.1 years, 79.4% female, racially diverse (69.6% Caucasian, 13.7 % LatinX, 9.5 % Asian, and 4.9% Black), and 62% seropositive (CCP and/or RF). Perceived disease activity and remission remained stable in most patients with 719 reporting no flares, and 409 in current flares at the time of the survey (Table 1). A minority reported perceived increases in disease activity which were associated with multiple aspects of perceived stress. At survey completion, 346 had not experienced flares, 290 had experienced one flare, and 492 had experienced multiple flares. Use of DMARDs was associated with lack of flare versus current flare (77.8% versus 71.6%, p = 0.02). The use of conventional synthetic, biologic, or targeted synthetic DMARDs were not associated with flare while current corticosteroid use was associated with flare (9.3% without flare and 20.8% with flare, p < 0.0001). Current flare was associated with increased PSS-4 scores (odds ratio (OR): 1.17 (95% confidence interval: 1.12 – 1.22, p < 0.0001). Figure 1 describes the odds ratio of experiencing aspects of stress with the presence of RA flare.

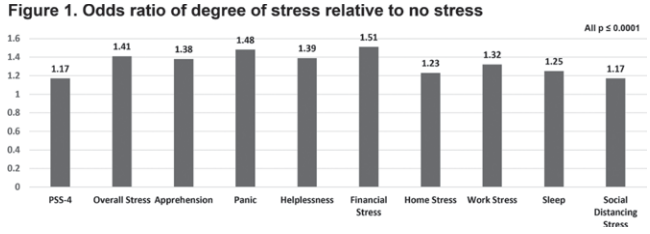
Table 1. Current RA flare at time of survey completion

	Current Flare No N=719	Current Flare Yes N=409	P-Value
RA duration (mean ± SD) years	15.6 ± 12.3	14.9 ± 11.6	0.3133
Patient Global (mean ± SD), range 0-10	3.5 ± 2.5	6.1 ± 2.2	<0.0001
RAPID3 (mean ± SD) range 0-30	6.1 ± 5.6	13.7 ± 5.7	<0.0001
Patient-Reported Remission, no. (%)	404 (57.1%)	49 (12.1%)	<0.0001
RA-FQ Score, (mean ± SD), range 0-50	13.4 ± 11.4	29.7 ± 10.8	<0.0001
PSS-4, (mean ± SD)	5.2 ± 3.1	6.9 ± 3.1	<0.0001
Overall stress level (%)			0.0004
Increased	62.3%	72.9%	
Unchanged	26.9%	21.8%	
Decreased	10.7%	5.4%	
Current RA Therapy			
Any DMARD	77.8%	71.6%	0.0218
csDMARD Only	31.4%	26.7%	0.0911
bDMARD Only	18.1%	16.9%	0.6082
tsDMARDs Only	3.3%	3.4%	0.9394
bDMARD + csDMARD Only	19.8%	19.8%	0.9823
tsDMARD + csDMARD Only	4.6%	4.9%	0.8188
Current Corticosteroid	9.3%	20.8%	<0.0001

SD = standard deviation; No. = number; RA = rheumatoid arthritis; RAPID3 = routine assessment of patient index data 3; RA-FQ = rheumatoid arthritis flare questionnaire; PSS-4 = perceived stress scale; D/C = discontinued; DMARD = disease modifying antirheumatic drugs; csDMARD = conventional synthetic DMARD; bDMARD = biologic DMARD; tsDMARD = targeted synthetic DMARD

Conclusion: In a large survey population of RA patients during the COVID-19 pandemic, multiple aspects of stress were found to correlate with RA disease activity and flare.

Figure 1. Odds ratio of degree of stress relative to no stress



Disclosure of Interests: Daniel Furst Consultant of: Corbus; Galapagos; Novartis; Amgen, Grant/research support from: Actelion; Galapagos; National Institutes of Health; GlaxoSmithKline; Sanofi; Corbus; Pfizer; Novartis; Amgen; Bristol Myers Squibb; Roche/Genentech, Nicolette T Morris: None declared, Angela Q Pham: None declared, Thasia Woodworth: None declared, David Elashoff: None declared, Jenny Brook: None declared, Veena Ranganath Grant/research support from: Bristol Myers Squibb; Mallinckrodt Pharmaceuticals
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POS0610 THE RELATIONSHIP BETWEEN SYSTEMIC MANIFESTATIONS OF RHEUMATOID ARTHRITIS AND THE STRUCTURAL GEOMETRY OF THE MYOCARDIUM.

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Background: In recent years, chronic inflammatory diseases, including rheumatoid arthritis (RA), have been perceived as independent risk factors for cardiovascular diseases. In addition to influencing the development of atherosclerosis, rheumatic diseases are accompanied by changes in the myocardium.
Objectives: to determine the relationship between systemic manifestations of RA and structural changes of the heart.
Methods: The 282 patients (240 women and 42 men) with verified RA were examined. In addition to standard diagnostic tests, all patients underwent echocardiography with tissue Dopplerography of the myocardium.
Results: Structural and geometric remodeling of the heart was detected in 146 patients (51.8%), of which 29 had concentric remodeling, 35 had concentric hypertrophy, and most often, 82 people had eccentric hypertrophy. The average age was 57.9±8.55 years in the group with cardiac remodeling and 47.2±11.92 years in individuals with normal heart geometry, respectively (p<0.0001). Among 136 patients (48.2%) with normal heart geometry, 39 people suffered from arterial hypertension, 79 patients had various systemic manifestations of rheumatoid arthritis (Sjogren's syndrome, rheumatoid nodules and/or cryoglobulinemia). Among those with cardiac remodeling, arterial hypertension was diagnosed more often – in 107 people (p<0.0001), and systemic manifestations of rheumatoid arthritis - in 87 patients (p<0.1). A comparison was made between a group with eccentric hypertrophy (82 people) and a combined group of patients with concentric remodeling and concentric hypertrophy (64 people). In the first group, the age was higher and amounted to 58.6±8.52 years, and in the second – 57.2±7.96 years (p<0.05). In the first group, systemic extra-articular manifestations of rheumatoid arthritis were found in 56 individuals (68.3%), and in the second group – in 33 people (51.6%) (p=0.04).
It is worth noting that in the second group, patients with concentric hypertrophy made the greatest contribution: out of 35 people, systemic manifestations of rheumatoid arthritis were detected in 23 people (65.7%), which is comparable to the frequency among people with eccentric hypertrophy. In this regard, for the research purpose, we combined individuals with normal geometry and concentric remodeling into one group (165 people), and patients with concentric and eccentric hypertrophy into another group (117 people). When compared, it was found that regardless of the type of myocardial hypertrophy these individuals are significantly more likely to suffer from systemic manifestations of rheumatoid arthritis: 53,9% and 67.5%, respectively (p=0.02).
Conclusion: the formation of myocardial hypertrophy in patients with rheumatoid arthritis is associated with more frequent development of extra-articular manifestations of this disease.
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POS0611 THE SIGNIFICANCE OF DETERMINING THE LEVEL OF THE ST-2 MARKER OF HEART FAILURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The heart failure in patients with rheumatoid arthritis differs in its genesis from that in the general population. It has been established that the increased risk of congestive heart failure in patients with RA cannot be explained by the high frequency of risk factors for cardiovascular diseases, including coronary heart disease. While 80% of chronic heart failure in the general population is associated with classical risk factors for cardiovascular diseases, in RA these same predictors explain only 40% of cases
Objectives: to establish the prevalence of diastolic dysfunction of preclinical signs of heart failure in patients with rheumatoid arthritis.
Methods: The 282 patients with verified rheumatoid arthritis were examined, including 240 women and 42 men. All patients underwent standard diagnostic tests, two-dimensional transthoracic echocardiography with tissue dopplerography of the myocardium, determination of the level of ST-2, stimulating growth factor, a marker of heart failure, in blood serum.
Results: The Tissue Dopplerography in combination with two–dimensional echocardiography allowed us to identify patients with diastolic myocardial dysfunction and form the following subgroups. 1 – with normal heart geometry and without diastolic myocardial dysfunction (91 people), 2 – with normal heart geometry and with diastolic dysfunction (45 people), 3 - with structural and geometric remodeling of the heart and without diastolic myocardial dysfunction (73 people), 4 – with structural -geometric remodeling of the heart and with diastolic dysfunction (73 people). Among patients with altered heart geometry (3rd and 4th subgroups), the prevalence of diastolic dysfunction was higher than among those with normal geometry (1st and 2nd subgroups): 50% and 33.1%, respectively (p=0.004). We conducted a comparison between the subgroups depending on the presence of diastolic myocardial dysfunction. The average age of patients with rheumatoid arthritis who showed signs of diastolic dysfunction with normal heart geometry was higher (54 [49; 57] years) than in the compared subgroup (45.5 [33.5; 53.5]) (p<0.0001). They also had significantly higher levels of the ST-2 marker, which indicates an early preclinical sign of heart failure: 70.1 [39.5; 106.5] and 42.2 [29.6; 61.5]ng/ml (p<0.01). Apparently, despite the absence of cardiac remodeling, with age, patients with rheumatoid arthritis are more likely to develop not only diastolic dysfunction, but also diastolic type of heart failure.
Conclusion: Thus, in patients with rheumatoid arthritis, it is advisable to conduct tissue Dopplerography in addition to standard echocardiography to detect diastolic dysfunction, which in these patients may develop in the absence of structural and geometric changes.
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POS0612 COMORBIDITIES IN RHEUMATOID ARTHRITIS DO NOT INFLUENCE BIOLOGICS DRUG RETENTION: DATA FROM THE NATIONAL HEALTH INSURANCE FUND OF TUNIS

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Background: The advent of biologics in the late 1990s radically changed the profile of inflammatory diseases, in particular rheumatoid arthritis (RA). The survival of these innovative therapies is an indicator, in clinical practice, of their long-term efficiency in patients with RA.
Objectives: To study the influence of comorbidities on biologics drugs retention rates.
Methods: We conducted a cross-sectional, observational study. Data were identified from the files of the National Health Insurance Fund of Tunis. It included patients with RA on biologics. Epidemiological characteristics such as age, sex, and comorbidities, were collected. Comorbidities were assessed by the Charlson Comorbidity Index (CCI). The therapeutic maintenance rate at 12, 24, 36, and 48 months as well as the biologics survival were analyzed using Kaplan-Meier survival curves and compared using the Log-Rank test.
Results: Three hundred and seventy-four files were selected. The average age of our cohort was 55±12.54 years [20-90]. A female predominance was noted with a sex ratio M/F=0.147. The average duration of RA was 11.7±6.76 years

[2-41].First biogics prescription was: etanercept 54%, adalimumab 14%, certolizumab pegol 13%, infliximab 6%, tocilizumab 6% and rituximab 7%. First-line survival rates at 12, 24, 36, and 48 months were 85.8; 69.9; 60.6, and 55.9% respectively. Biologics drug survival was, on average, 41.7 months [39.47-43.91]. Comorbidities were assessed by the CCI in 373 patients (99.7%). Ninety patients had an ICC of 0 and 103 patients had an ICC of 1. Only one patient had an ICC of 8. The median value of this score was equal to 1, the mean was 1.64 ± 1.48. Osteoporosis was the most observed comorbidity with 78 patients (20.9%). The study of drug survival according to the ICC did not show any significant difference between the different curves (p=0.809). The Hazard Ratio was 0.999. Similarly, we did not find a discriminating threshold for the Charlson score, allowing it to be decisive for the survival of biologic drugs.

Conclusion: This study did not identify the influence of comorbidities on the biologics survival during RA. Comorbidities can have an impact not only on our therapeutic choice but also on the efficacy and maintenance of biomedicines as well as the quality of life of patients and consequently the prognosis of RA (1). The few studies that have looked at this subject have produced variable results.

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Disclosure of Interests: None declared

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POS0613 IDENTIFICATION OF PREDICTORS OF SUDDEN CARDIAC DEATH IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease with a high cardiovascular risk, increasing the incidence of coronary artery disease, ventricular arrhythmias and sudden cardiac death (SCD). The annual incidence of SCD among the general population is 0.2%, and patients with RA are twice as likely to develop it as healthy people. The well-known predictors of the development of SCD are the variance of the QT interval and the alternation of the T-wave.

Objectives: to study the prevalence of predictors of the risk of SCD among patients with RA.

Methods: 282 patients with verified RA were examined, including 240 women and 42 men. All patients underwent standard laboratory and instrumental diagnostic tests. In addition, electrocardiography was performed with the calculation of the QT interval variance and determination of the T-wave alternation, two-dimensional transthoracic echocardiography with tissue Dopplerography of the myocardium.

Results: The echocardiography allowed us to identify patients with diastolic dysfunction and form the following groups. 1 group – with normal heart geometry and without diastolic myocardial dysfunction (91 patients), 2 – with normal heart geometry and with diastolic dysfunction (45 pts), 3 - with structural and geometric remodeling of the heart and without diastolic myocardial dysfunction (73 pts), 4 – with structural -geometric remodeling of the heart and with diastolic dysfunction (73 pts). Both groups of patients with rheumatoid arthritis, who had remodeling of the heart, practically did not differ in age. But in the group with diastolic dysfunction, a high variance of the QT interval was significantly more often detected than among individuals without myocardial dysfunction, 54.8 and 38.4%, respectively (p<0.05). Thus, the development of diastolic dysfunction with altered heart geometry is more often accompanied by an increase in the variance of the QT interval, which is a predictor of sudden death in people with heart failure. In this regard, we conducted a comparison between individuals with a high variance of the QT interval (1st subgroup - 139 people) and without it (2nd subgroup - 143 people). We did not obtain significant differences between the subgroups in the prevalence of structural and geometric myocardial remodeling (51.8% and 51.7%, respectively), left ventricular hypertrophy (40.3% and 42.7%, respectively) and diastolic dysfunction (45.3% and 38.5%, respectively). However, in the subgroup with high QT interval variance, T wave alternation was more often recorded: 55.6% and 29.3%, respectively (p=0.0001).

Conclusion: The presence of diastolic dysfunction in patients with cardiac remodeling on the background of rheumatoid arthritis is accompanied by an increase in the variance of the QT interval, which, in turn, is associated with a more frequent occurrence of T-wave alternation. Therefore, patients with diastolic dysfunction and myocardial remodeling on the background of RA belong to the category of increased risk of SCD.

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POS0614 THE RELATIONSHIP BETWEEN DISEASE ACTIVITY AND FINANCIAL TOXICITY IN PATIENTS WITH RHEUMATOID ARTHRITIS ON BIOLOGICS: A CROSS-SECTIONAL STUDY USING THE JAPANESE RHEUMATOID ARTHRITIS REGISTRY

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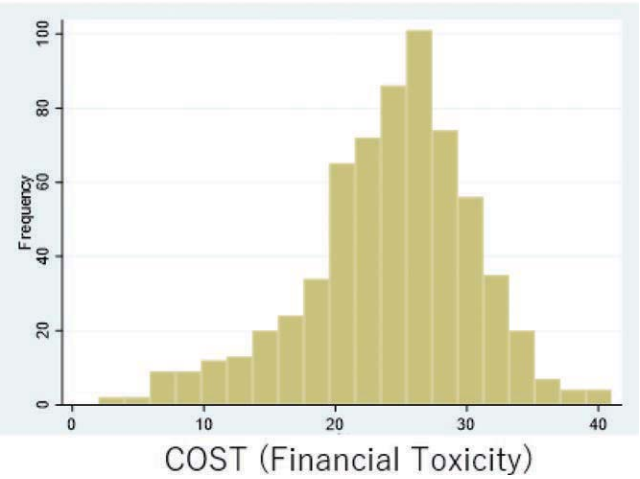
Background: As the number of rheumatoid arthritis (RA) patients using biologics increases, the health financial issues posed by biologics become more important. The health financial issues posed by biologics have been discussed using health economic indicators such as incremental cost-effectiveness ratios (ICERs), but have not been evaluated using the financial burden of medical expenses (financial toxicity). In the field of malignancies, evaluations using financial burden have been conducted and have shown that the stage of malignancy is associated with financial toxicity. It is not known whether disease activity and financial toxicity are similarly associated in RA patients.

Objectives: This study aims to evaluate the relationship between RA activity and financial toxicity in RA patients using biologics, who are especially likely to feel the financial burdens.

Methods: We conducted a cross-sectional study of biologic users enrolled in NinJa2020, a database of rheumatoid arthritis patients in Japan collected from April 1, 2020 to March 31, 2021. We defined the users of TNF inhibitor, IL-6 receptor antagonists, T-cell costimulation blocker, Janus kinase inhibitor and biosimilar as biologic users. The main exposure was the disease activity of RA and was measured using DAS28-CRP. Outcome measure was a financial toxicity and was measured using COmprehensive Score for financial Toxicity (COST). This scale is a patient-reported outcome measure (PROM) consisting of 11 items. The responses are recorded on 5-point Likert Scales (ranging from 0 = strongly disagree to 4 = strongly agree). The score by domains ranges from 0 to 44. Higher scores indicated better results and lower financial toxicity. Multiple linear regression models adjusted for age, sex, disease duration, co-payments for anti-rheumatic drugs, work status, financial support systems were conducted to assess the relationship between the disease activity of RA and financial toxicity. As a

Figure.1



secondary analysis, we excluded patients with zero copayments and performed the same analysis as in the main analysis. We used multiple imputation to deal with missing values.
Results: Among 15553 cases in the NinJa database, 649 cases for which RA disease activity and COST were available were included. The median age of the patients was 70 (interquartile range [IQR],56 -77), 83.7% were female. The median copayment amount was ¥12978 per month (IQR 637.2 to 24204.1). The median DAS28-CRP was 1.99 (IQR, 1. - 2.72). The median financial toxicity (COST score) was 21 (IQR 0-27) (Figure 1). In the main analysis using multiple linear regression, COST significantly decreased with disease activity of RA (per 1-pt DAS28-CRP, -1.16 [95% CI -2.04 - -0.28]). In the secondary analysis, COST significantly decreased with disease activity of RA (per 1-pt DAS28-CRP, -1.69 [95% CI -2.29 - -1.10]). Statistical significance was defined as a two-sided p-value < 0.05. All statistical analyses were conducted using STATA 17.0 (Stata Corp LP, College Station, TX). The National Hospital Organization's research ethics committees evaluated and authorized the NinJa study.
Conclusion: High disease activity of RA was associated with high financial toxicity in biologic users. We reaffirmed the importance of financial considerations and empathy for RA patients using biologics, and suggested a potential demand for more financial support for RA patients who are refractory to treatment.
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POS0615 CLINICAL DEMOGRAPHICS AND FACTORS AFFECTING DRYNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Sjogren's syndrome (SS) is known to coexist with rheumatoid arthritis (RA). However, the prevalence of RA with SS varies widely, from 2.4% to 30%, and some patients with RA without SS also show dryness. The prevalence and clinical demographics of dryness in patients with RA are not well recognized.
Objectives: The aim of this study was to clarify the prevalence, clinical demographics, and related factors of dryness in patients with RA who have not been diagnosed with (SS).
Methods: We enrolled 166 patients with RA (129 females, 37 males; mean age 65.8±14.3 years; disease duration 14.1±10.9 years; DAS28-CRP 2.30±0.92) who were not diagnosed with SS. We analyzed CRP, the estimated glomerular filtration rate (eGFR), RF, anti-CCP antibody, antinuclear antibody, anti-SS-A antibody (SSA), and disease activity score (DAS) 28-CRP, and identified treatments for RA. We used each question item of the EULAR SS Patient Reported Index (ESSPRI) to clarify dryness, somatic and mental fatigue, and pain. History of smoking, comorbidities, such as interstitial pneumonia, fibromyalgia, and psychiatric disorders, and narcotic and/or psychotropic medication use were determined from the medical records. We defined patients with dryness as greater than or equal to one point, and those with severe dryness as greater than or equal to five points, of the visual analog scale (VAS).
Results: Dryness was observed in 93/166 (56.0%) patients and severe dryness was identified in 57/166 (34.4%) patients, and SSA was positive in 23/139 patients(13.9%). We divided our patients into dryness and non-dryness groups and compared their clinical demographics. The dryness group was relatively younger (64.0±14.5 vs. 68.1±13.8 years, p=0.052), had a female predominance (89.2% vs. 63.0%, p<0.001), had severe fatigue (4.06±2.59 vs 2.60±2.78, p<0.001), and had severe pain (3.52±2.41 vs. 2.73±2.32, p=0.020). However, the prevalence of SSA did not significantly differ in this cohort, compared with the non-dryness group (19.3% vs. 11.8%, p=0.248). Next, we analyzed the clinical characteristics of the patients with severe dryness. The severe dryness group was younger (61.9±15.5 vs. 67.9±13.2 years, p=0.022), had higher eGFR (76.1±15.5 vs. 68.9±22.7, p=0.020), had more severe fatigue (4.89±2.42 vs. 2.85±2.63), p<0.001), and had more severe pain (4.16±2.51 vs. 2.65±2.18, p<0.001), compared with non-severe dryness group. The prevalence of SSA was also significantly higher in the severe dryness group (91.2% vs. 70.6%, p=0.002). We then performed a multifactorial analysis using logistic regression analysis with a stepwise method. Female sex (OR 3.739, 1.247-11.207) and VAS of fatigue (OR 1.269, 1.054-1.526) were found to independently relate to dryness.
Conclusion: More than half of the patients with RA had dryness, although only 13.9% of patients were SSA positive. Dryness was related to female predominance and fatigue. Simon et al. reported that SS was found in 2.42% of patients with RA (1). On the other hand, Harrold et al. reported that SS was found in 30% of patients with RA, and the prevalence of SS increased with duration of RA (2). Our data indicate that patients with fatigue, regardless of pain, tend to have dryness, which may be a key factor in diagnosing SS in patients with RA.
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POS0616 EFFECT OF TOCILIZUMAB ON THE TRIGLYCERIDES METABOLISM PATHWAYS CONSTITUTED BY ANGIOPOIETIN LIKE-PROTEIN 4, APOLIPOPROTEIN CIII AND LIPOPROTEIN LIPASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tocilizumab is a humanized immunoglobulin G antibody to the interleukin 6 (IL-6) receptor that is used in the treatment of patients with rheumatoid arthritis (RA). Patients receiving TCZ are more likely to experience an elevation in total cholesterol, triglycerides and the ratio of low-density lipoprotein to high-density lipoprotein cholesterol. Elevated triglycerides or triglyceride-rich lipoproteins are cause of cardiovascular disease. Although the pathways for the synthesis and metabolism of triglycerides are complex and diverse, three molecules play a central role in their metabolism: apolipoprotein C-III (ApoC3), angiopoietin-like protein 4 (ANGPLT4), and lipoprotein lipase (LPL). LPL hydrolyzes the triglycerides core of chylomicrons and has a crucial role in regulating plasma triglycerides levels. Besides, ApoC3 and ANGPLT4 participates in the regulation of triglycerides metabolism by the inhibition of LPL, thereby also decreasing the lipolysis of circulating triglycerides.
Objectives: The objective of this study was to evaluate the influence that TCZ has on the TG metabolism axis constituted by ANGPTL4, ApoC3 and LPL. In a second step we have assessed whether the changes that TCZ exerts on the lipid profile can be justified by a modification of this axis.
Methods: TOCRIVAR (*ClinicalTrials.gov:* NCT01752335) is a one-year prospective clinical trial that analyzes the influence of TCZ on different cardiovascular risk factors including lipid pattern. Twenty-seven RA patients receiving TCZ (8 mg/kg IV/q4w) were assessed at baseline and weeks 12, 24, and 52. Disease activity indexes, serum levels of ApoC3, ANGPLT4 and LPL, and lipoproteins serum concentrations were assessed at every visit.
Results: Acute phase reactants and disease activity were significantly reduced during study visits and at the end of treatment after one year with TCZ. While total and LDL cholesterol initially increased in plasma concentration, then decreased to baseline, lipoprotein (a) was significantly lower, and HDL higher, than baseline at all study visits. TG showed a trend to be significantly higher at 6 months (net increase 29 (95%CI -45-68) mg/dl, percentage increase 36 (95%CI -27-52) %, p=0.079). However, TG did not show significant differences at any visit compared to baseline levels. ANGPLT4 (baseline 387 ± 203 vs final 257 ± 32 wk52 ng/ml, p=0.016) and ApoC3 (baseline 10.1 ± 6.7 vs final 6.3 ± 3.7 mg/dl, p=0.023) were significantly lower at the end of the study (week 52) compared to their initial concentrations. LPL also showed a gradual decrease at each visit (baseline 345 ± 289 vs. final 291 ± 197 ng/ml, p=0.57), although statistical significance was not reached (trend test p=0.56). The decrease in DAS28-ESR at each visit was not associated with the changes produced in the three molecules, thus showing that the decrease in the TG metabolism axis does not depend on the lower activity of the disease produced by TCZ. In contrast, the decline in ApoC3 was significantly correlated with the increase in TG at month 3 (Pearson r -0.494, p=0.037) but not at 6 and 12 months.
Conclusion: TCZ decreases serum levels of ANGPTL4, ApoC3 and LPL. At 3 months, the increase that occurs in TG seems to depend on the inhibition that TCZ exerts over ApoC3. Our findings suggest that the effect of TCZ on the lipid profile in patients with RA could be mediated by the modification that this drug exerts on the ANGPTL4-ApoC3-LPL axis.
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POS0617 SYNOVITIS OF THE FIRST METACARPOPHALANGEAL JOINT HAS A MAJOR IMPACT ON GRIP FORCE IN EARLY RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) has a major impact on hand function in many patients. Information on the contribution of individual joints to impaired grip strength may be helpful for guiding individualized management.
Objectives: The objective of this study was to investigate the relation between swelling and tenderness of individual finger joints and grip force in patients with early RA.
Methods: An inception cohort of patients with early RA (symptom duration ≤12 months), recruited in 1995-2005, was investigated and followed in a structured program, with follow-up evaluations after 1 and 5 years. All patients were examined by the same rheumatologist according to a structured protocol. Grip force (Newton) was measured using the electronic instrument Grippit (AB Detektor, Gothenburg, Sweden). Average grip force values of each hand were evaluated and compared to the expected, based on age- and sex-specific reference values from the literature (1). Grip force was expressed as % of expected values. Linear regression analyses were used to assess the relation between involvement of individual finger joints and grip force. Synovitis and joint tenderness were assessed in separate models. As wrist involvement, high erythrocyte sedimentation rate (ESR) and severe patient reported pain have been independently associated with reduced grip force in early RA (2), the analyses were adjusted for these covariates.
Results: A total of 215 patients with early RA (71 % women; mean age 60 years) were investigated. The median symptom duration at inclusion was 7 months; interquartile range 5-10. In the right hand, synovitis of the first metacarpophalangeal (MCP) joint was consistently associated with reduced grip force at all evaluations (Table 1). Patients with MCP II and MCP III synovitis also had reduced grip force at inclusion, but not after 1 and 5 years. Proximal interphalangeal (PIP) joint swelling (Table 1), and tenderness of MCP or PIP joints, had a lower impact on grip force. Results were largely similar for the left hand.

Table 1. Relation between synovitis of individual MCP and PIP joints and grip force of the right hand (% of expected) in patients with early RA; β (95 % CI), adjusted for wrist synovitis, ESR and VAS pain

	Inclusion	1-year follow-up	5-year follow-up
MCP I	**-10.8 (-17.1 to -4.4)**	**-8.0 (-14.8 to -1.2**)	**-8.2 (-16.4 to 0)**
MCP II	**-7.5 (-13.9 to -1.1)**	-0.6 (-7.6 to 6.4)	-0.6 (-8.2 to 9.5)
MCP III	**-7.4 (-13.5 to -1.3)**	-1.3 (-9.4 to 6.8)	-4.5 (-13.4 to 4.5)
MCP IV	-8.9 (-18.5 to 0.7)	-8.8 (-25.7 to 8.1)	-4.0 (-22.1 to 14.0)
MCP V	-2.5 (-12.6 to 7.6)	-2.6 (-16.5 to 11.2)	7.4 (-5.2 to 20.0)
IP I	2.0 (-6.4 to 10.9)	-1.6 (-14.0 to 10.7)	-5.1 (-23.3 to 13.2)
PIP II	-0.8 (-7.7 to 6.2)	-3.9 (-13.3 to 5.5)	-3.2 (-16.2 to 9.8)
PIP III	-5.6 (-12.1 to 1.0)	2.5 (-6.5 to 11.6)	1.9 (-9.0 to 12.9)
PIP IV	-4.1 (-11.8 to 3.6)	-1.9 (-12.8 to 9.0)	-0.1 (-14.2 to 14.1)
PIP V	-7.2 (-16.0 to 1.7)	-10.3 (-22.8 to 2.3)	-5.6 (-21.2 to 9.9)

Conclusion: MCP I synovitis is a major contributor to reduced grip force in patients with early RA during the first 5 years after diagnosis, independent of wrist synovitis, general pain and systemic inflammation. This underlines the importance of involvement of the thumb for impaired hand function in RA.
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POS0618 CLASSICAL PATHWAY OF THE COMPLEMENT SYSTEM RELATES TO SUBCLINICAL ATHEROMATOSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is associated with arteriosclerosis. The inflammation present in the disease is responsible for this cardiovascular (CV) comorbidity. The complement system (C) is an essential component of the immune response that has the function of enhancing the inflammatory response. C has been implicated in the etiopathogenic mechanisms of CV disease and RA.
Objectives: Our objective was first to determine the serum levels of different molecules of the classical C pathway to fully characterize it in patients with RA. In a second step, we analyzed the relationship of this classic C pathway with the CV comorbidity and subclinical atheromatosis of a large series of patients with RA.
Methods: Cross-sectional study of 430 patients with RA. Clinical and analytical information related to CV disease was collected: presence of CV risk factors, lipid profile, indices of insulin resistance (HOmeostatic Model Assessment - HOMA2-), as well as measurement of intima media thickness and detection of carotid plaque by ultrasound. Plasma levels of C3, C4, C1-inhibitor and CH50 assay were assessed. Multivariable linear and logistic regressions was performed to study the relation of these molecules of the classical C pathway to the characteristics of the disease, CV comorbidity and subclinical atheromatosis.
Results: C3, C4 y C1-inh were highly and positively correlated with each other ($p<0.001$). However, although CH50 functional test was strongly interrelated to C3 and C1-inh, correlation index to C4 was found to be weak (Pearson r 0.126, $p=0.049$). In the univariable analysis the four parameters (C3, C4, C1-inh and CH50) were, in general, associated with classical CV risk factors. In this sense, C3 and C4, but not C1-inh and CH50, were positively associated with body mass index, and abdominal circumference. Similarly, hypertension and the use of statins were associated with significant higher serum levels of C3, C4 and C1-inh, but not CH50; and the presence of dyslipidemia was related to higher circulating C3 and CH50. Likewise, in non-diabetic RA patients, C3, but not the other parameters, were significantly related to higher HOMA2-insulin resistance, and beta cell function indices after adjustment for covariates. Besides, after fully multivariable analysis, disease activity and acute phase reactants were positively related with significant higher serum levels of the three C component and the CH50 assay. Similarly, the use of NSAIDs, anti-TNF therapies, and tocilizumab, but not other therapies, were related to lower circulating C3, C4 and C1-inh, but not CH50. After adjustment for covariables that included traditional CV risk factors, CH50, but not the other C components, was positively associated with higher carotid intima-media thickness (beta coef. 1 [CI95% 1-2] microns, $p<0.001$). Similarly, C3 (OR 1.01 [CI95% 1.00-1.02], $p<0.021$), C1-inh (OR 1.05 [CI95% 1.01-1.08], $p<0.007$), and CH50 (OR 1.02 [CI95% 0.99-1.03], $p=0.067$) were associated with the presence of carotid plaque.
Conclusion: Classical pathway of the C system is activated in patients with RA. Its serum components and functional assay are associated with disease activity and several disease-related data. Moreover, C's classical pathway is related to traditional CV risk factors and to the subclinical carotid atherosclerosis present in the disease. Our findings highlight the role of C system in RA, and propose its therapeutical inhibition as a tool to control both the disease activity and the CV comorbidity that accompanies the disease.
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POS0619

CLINICAL AND SUBCLINICAL INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS: ASSOCIATED FACTORS.

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Objectives: To evaluate the differences between patients with rheumatoid arthritis (RA) with and without interstitial lung disease (ILD), to identify factors associated with the development of ILD and to evaluate subclinical ILD; prevalence and factors associated with its development.
Methods: Observational and cross-sectional study of a cohort of patients with RA (ACR/EULAR 2010) and with ILD and a control group of patients without ILD. Both groups with HRCT performed in the last 18 months. The date of the last HRCT was considered as the study date. The % of patients who had subclinical ILD was retrospectively evaluated, defining this as pulmonary involvement due to a requested HRCT without any previous respiratory symptoms. Demographic variables, activity data (DAS28VSG, SDAI and CDAI on the study date), RF and ACPA levels, RA severity data and treatments they were receiving were collected. Descriptive analysis, χ^2 or t-Student and multivariate logistic regression analysis was performed to find predictive variables of the development of ILD.
Results: 66 patients with RA (41 with ILD and 25 without ILD) were included. The main differences between both groups are shown in Table 1. In the group of patients with ILD, the male sex predominated, they were older, with a longer duration of the disease and a longer diagnostic delay of RA. They made more use of biological therapies with better control of the disease by DAS28, SDAI and CDAI. Pulmonary function preserved by respiratory function tests. Of the total number of patients with ILD, 15 (36.6%) did not present any respiratory symptoms when the HRCT was requested. The reasons for their request were: finding abnormalities on chest X-ray (66.7%) and dry crackles on examination (33.3%). Subclinical ILDs were diagnosed with less evolution time of RA than clinical ones. In the rest of the variables there were no differences with the clinical ILD. The variables independently associated with the development of ILD, adjusted for age, tobacco use and ACPA at high titers, were male sex [OR = 4.2 (95% CI 1.05-19.7), p = 0.049] and time of evolution of RA [OR = 1.08 (95% CI 1.02-1.17), p = 0.014].
Conclusion: In our cohort, the prevalence of subclinical ILD was high (36%). Clinical characteristics, disease activity and ILD data (PFT and HRCT patterns) were similar between clinical and subclinical ILD, but prospective studies are needed to assess whether the course and prognosis in both groups is also similar. Bearing in mind that ILD is an important cause of death in our patients, we must actively search for this condition in order to treat it early and improve its prognosis.

Table 1. Differential characteristics between the different groups.

Variables	RA with ILD (n= 41)	RA with clinical ILD (n=26)	RA with subclinical ILD (n=15)	RA without ILD (n=25)	*p-value ILD vs. no ILD*	*p-value clinical ILD vs. subclinical ILD*
Age (years), mean (SD)	64.9 (10.6)	64.8 (10.7)	65.3 (10.7)	59.5 (8.05)	**0.022**	0.878
Age at ILD diagnosis, mean (SD)	61.3 (11.2)	60.3 (11.7)	63.1 (10.3)	-	-	0.434
Sex (male), n (%)	19 (46.3)	10 (38.5)	9 (60)	5 (20)	**0.031**	0.182
Tobacco, n (%)	25 (60.9	14 (53.8)	11 (78.6)	12 (48)	0.251	0.123
RA evolution time (years), mean (SD)	16.0 (10.2)	19.7 (9.7)	9.6 (7.5)	10.9 (9.7)	**0.048**	**<0.001**
Time from diagnosis of RA to ILD (years), mean (SD)	12.8 (9.4)	16.1 (9.2)	7.3 (7.2)	-	-	**<0.001**
Diagnosis delay (years), mean (SD)	1.4 (2.3)	1.9 (3)	0.9 81.3)	0.5 (0.6)	**0.050**	0.299
Positive Rheumatoid factor, n (%)	37 (90.2)	23 (88.5)	14 (93.3)	24 (96)	0.391	0.612
Title Rheumatoid factor, mean (SD)	271.4 (321.5)	227.8 (252.9)	349.3 (416.9)	170.2 (172.7)	0.110	0.337
ACPA positive, n (%)	37 (90.2)	24 (92.3)	13 (86.7)	20 (80)	0.239	0.557
ACPA, mean (SD)	338 (482)	262.4 (145.5)	471.6 (780.6)	186 (196)	0.110	0.377
Erosions, n (%)	11 (26.8)	7 (26.9)	4 (26.7)	6 (24)	0.798	0.985
Rheumatoid nodula, n (%)	6 (14.6)	4 (15.4)	2 (13.3)	3 (12)	0.762	0.857
Secondary Sjogren's syndrome, n (%)	2 (4.8)	2 (7.7)	0	2 (8)	0.606	0.270
Osteoporosis, n (%)	8 (19.5)	7 (26.9)	1 (6.7)	5 (20)	0.961	0.115
DAS28-ESR, mean (SD)	2.7 (1)	2.4 (0.8)	3.0 (1.1)	3.4 (1.4)	**0.034**	0.117
SDAI, mean (SD)	9.4 (6.7)	8.08 (7.1)	11.7 (5.5)	13.9 (8.5)	**0.045**	0.105
CDAI, mean (SD)	8.7 (6.2)	7.4 (6.3)	11.1 (5.6)	12.9 (8.2)	**0.050**	0.084
DMARDs, n (%)	32 (78.1)	19 (73.1)	13 (86.7)	23 (92)	0.140	0.311
Methotrexate, n (%)	13 (31.7)	7 (26.9)	6 (40)	13 (52)	0.107	0.386
Leflunomide, n (%)	17 (41.5)	11 (42.3)	6 (40)	9 (36)	0.659	0.885
Hydroxycloroquine, n (%)	6 (14.6)	1 (3.8)	5 (33.3)	5 (20)	0.570	**0.010**
Sulfasalazine, n (%)	0	0	0	2 (8)	0.065	-
bDMARD, n (%)	24 (58.5)	16 (61.5)	8 (53.3)	7 (28)	**0.015**	0.607
Rituximab, n (%)	7 (17.07)	5 (19.2)	2 (13.3)	1 (4)	0.114	0.628
Abatacept, n (%)	15 (36.5)	10 (38.5)	5 (33.3)	1 (4)	**0.002**	0.743
Anti-TNFα, n (%)	1 (2.43)	1 (3.8)	0	3 (12)	0.114	0.442
Anti- IL6, n (%)	2 (4.9)	1 (3.8)	1 (6.7)	1 (4)	0.868	0.686
Jakinibs, n (%)	0	0	0	1 (4)	0.196	-
Glucocorticoids, n (%)	32 (78.1)	21 (80.9)	11 (73.7)	19 (76)	0.847	0.579
Glucocorticoids dose, mean (SD)	5.8 (2.9)	5.6 (2.6)	6.3 (3.6)	5.1 (1.3)	0.233	0.539
HRCT pattern						0.243
UIP, n (%)	18 (43.9)	13 (50)	5 (33.3)	-	-	
Indeterminate UIP, n (%)	15 (36.6)	7 (26.9)	8 (53.3)	-	-	
NSIP, n (%)	5 (12.2)	3 (11.5)	2 (13.3)	-	-	
Others, n (%)	3 (7.3)	3 (11.5)	0	-	-	
DLCO, mean (SD)	76.0 (20.9)	73.8 (24.5)	80 (12.5)	-	-	0.387
CVF, mean (SD)	89.5 (20.8)	88.9 (22.9)	90.8 (16.5)	-	-	0.784
FEV1, mean (SD)	91.5 (19.9)	91.8 (21.4)	90.8 (17.5)	-	-	0.886

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POS0620

RHEUMATIC DISEASE COMORBIDITY INDEX: IT IS A PREDICTOR OF OUTCOMES IN RHEUMATOID ARTHRITIS?

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Background: Comorbidities are frequent among patients with rheumatoid arthritis (RA). They influence clinical outcomes and treatment response. Comorbidity indices are developed to study their impact on different outcomes [1].
Objectives: The aim of our study was to assess comorbidity among RA patients and to explore the association between comorbidities and the clinical profile of the rheumatic disease.
Methods: We conducted a retrospective study in our rheumatology department including 255 patients with established RA according to the ACR/EULAR 2010 criteria. The Disease Activity Scale (DAS28) and the functional impairment (HAQ) were noted. Comorbidities were collected. Rheumatic Disease Comorbidity Index (RDCI) was calculated for each patient. It is rated from 0 to 9 and comprises 11 comorbid conditions including lung disease, cardio-vascular disease, hypertension, diabetes, fracture, depression, cancer, and gastrointestinal ulcer [2].
Results: There were 255 RA with sex ratio M/F at 0.2. The mean age was 58.92 ± 10.72 years [25-85]. The mean age at onset of disease was 43.78 ± 14.28 years [13-81]. The mean disease duration was 16.32 ± 14.3 [1-72]. Identified comorbidities were: hypertension (31.4%), lung disease (27.1%), diabetes (19.6%), cardio-vascular disease (16.8%), gastrointestinal ulcer (9.2%), depression (8.8%), and chronic renal failure (8%). The mean RDCI was 1.14 ± 1.25 [0-6]. A statistically significant correlation was found between RDCI and age ($p<10^{-3}$, r=0.277), RDCI and age at disease onset ($p<10^{-3}$, r=0.3). RDCI was not correlated to the disease duration (p=0.27). RDCI was not associated with the DAS28 (p=0.5) nor with the HAQ (p=0.4). RCDI was not significantly different in terms of sex (female: 1.2 vs male: 1.3, p=0.09). This comorbidity index was associated with the presence of extra articular manifestation (presence: 1.4 vs absence: 0.8, p=0.004). It was associated with pulmonary involvement (presence: 1.7 vs absence: 0.6, $p<10^{-3}$). There was an association between the presence of radiographic erosions and RDCI (1.2 vs 1, p=0.001). RDCI was also associated with atlanto-axial dislocation (p=0.009) and with coxitis (p=0.009). Comorbidity index was statistically different between patients on biologic drugs and patients without biologic drugs (1.6 vs 0.9, $p<10^{-3}$).
Conclusion: Our study showed that comorbidity index was associated with a severe disease and signs of poor prognosis (erosions, coxitis, andatlanto-axial dislocation). This confirmed the hypothesis that comorbidity can be a threat to the improvement in the long-term prognosis in RA patients.
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POS0621

MORE THAN 40% OF WOMEN WITH RHEUMATOID ARTHRITIS HAVE A TIME-TO-CONCEPTION LONGER THAN 1 YEAR: ANALYSIS OF THE PROSPECTIVE GR2 COHORT

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Background: Rheumatoid arthritis (RA) is one of the most common chronic inflammatory diseases and regularly affects women of childbearing age[1]. However, there is limited knowledge about the impact of the disease and its treatment on fertility.
Objectives: The aim of the study was to determine factors associated with time-to-conception in women with RA.

Methods: All RA patients (diagnosis according to the Rheumatologist) included in the national multicenter GR2 cohort from 2015 to June 2021 were included in the analysis. Patients could be included either with a pregnancy wish (i.e., preconceptional period) or because of a clinical pregnancy (<12 weeks of gestation): for this analysis, only patients included preconceptionally were included. The main endpoint was time-to-conception, and the secondary endpoints were the number of subfertile patients (i.e., time-to-conception >12 months or non-achievement of pregnancy), as well as the number exposed to csDMARDs and biologics in the preconception period. We performed survival analyses, using a Cox model including a random effect for the center to account for heterogeneity of practices among participating centers. We used a multiple imputation to address missing data among the explanatory variables. Results are presented as a hazard ratio (HR) with confidence interval (CI) to assess associations between the factors studied and time-to-conception.

Results: Among the 167 patients with RA included in the GR2 cohort, 78 were selected for the main analysis of time-to-conception. Of these, 40 (51.3%) had a clinical pregnancy during follow-up. Subfertility was observed in 33 (42.3%) women and median time-to-conception was 19.1 months; mean preconception DAS28-CRP score was 2.3 (+/- 1.2). Patients were treated during the preconceptional period with NSAIDs, corticosteroids, csDMARDs and biotherapy in 10 (12.8%), 35 (44.9%), 24 (30.8%), and 32 (41.0%) cases, respectively. The multivariate model adjusted for age, BMI, DAS28-CRP, disease duration, ACPA positivity, and exposure to corticosteroids and biologics in the preconception period found an association between increased preconception delay and age (HR (per year) 1. 12 95% CI [1.04-1.16] p = 0.01) as well as disease duration (HR (per year) 1.06 95% CI [1.02-1.15] p = 0.03).

Conclusion: This study provides original results on fertility in women with RA. It found a median time-to-conception of 19.1 months, with a subfertility rate of 42.3%, which is significantly higher than the general population[2]. In this context, it seems essential to discuss this topic from the beginning of the disease in women of childbearing age.

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Table 1. ***Survival analyses (Cox model): factors associated with time-to-conception in women with RA.***

	Univariate analyses		Multivariate analyses	
	Crude HR 95% CI	p	Adjusted HR 95% CI	p
Age	**1.11 [1.04-1.18]**	**0.002**	**1.12 [1.04-1.16]**	**0.015**
BMI	1.06 [0.99-1.16]	0.103	1.08 [0.99-1.16]	0.062
ACPA positivity	1.75 [0.90-3.39]	0.107	1.44 [0.65-2.86]	0.310
Disease duration	1.03 [0.98-1.08]	0.267	**1.06 [1.02-1.15]**	**0.032**
DAS28-CRP score	1.08 [0.81-1.45]	0.592	1.08 [0.92-1.32]	0.170
Corticosteroids	0.91 [0.51-1.65]	0.769	0.86 [0.42-1.68]	0.620
Biologics	1.52 [0.82-2.81]	0.189	1.30 [0.62-2.78]	0.630

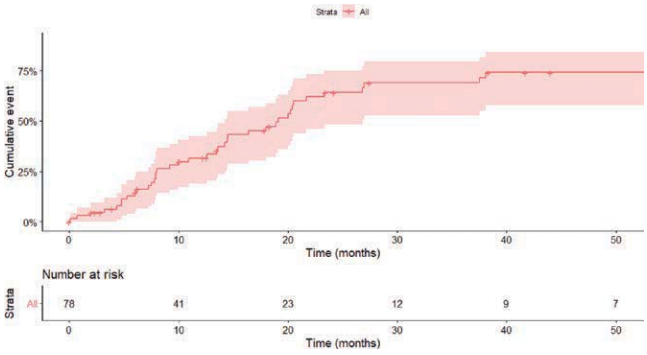

Figure 1. *Cumulative incidence curves for pregnancies in women with RA.*

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POS0622 ASSOCIATION OF DIURNAL FLUCTUATION OF THE SOLUBLE TOLL-LIKE RECEPTORS 2 (STLR2) WITH COMORBIDITY AND QUALITY OF LIFE IN WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Disorders of circadian rhythms in the production of inflammatory mediators play an important role in the pathogenesis of rheumatoid arthritis (RA) [1]. Innate immune factors, in particular toll-like receptors 2 (TLR2), are involved in the formation of the inflammatory pattern in RA. Recently was shown that TLR2 play an important role in the development of atherosclerosis and hypertension [2]. Chronobiological aspects of innate immunity, in particular circadian rhythms of the soluble form of TLR2 (sTLR2) in RA and its comorbidity, requires further study.

Objectives: The aim of the study was to assess the daily variability of sTLR2 in RA patients depending on comorbid conditions and quality of life indexes.

Methods: In the study were enrolled 173 females with RA aged 45.9 (8.79) years and disease duration 7.96 (6.38) years. High activity of the RA (DAS28-ESR > 5.1) were registered in 114 (66%) cases, moderate activity (DAS-28 3.2-5.1) - in 59 (34%) cases. 144 (83%) patients were seropositive by anticyclic citrullinated peptide (ACCP). Among enrolled subjects 140 (81%) had II-III radiographic stage. There were 89 (51%) patients with comorbid pathology, including arterial hypertension (AH) - 59 (34%). Serum sTLR2 level was determined at 8:00 and 20:00 using Cloud-Clone Corp kits (USA). All stages of the study were carried out in compliance with bioethical standards and provisions of the WHO, Helsinki Declaration of the General Assembly of the World Medical Association (1989), Bioethical protocol No 1, 01 November 2016. *Data are mean (SD) or n (%).

Results: In patients with RA, daily fluctuations in sTLR2 levels were detected: indexes at 8:00 at 20:00 were lower than at 8:00 (343 (93.7) vs 272 (99.2) ng/L, p<0.001). The mean difference between sTLR2 levels at 8:00 and 20:00 was -21.6 (13.2) %. In RA patients with AH, the average daily level of sTLR2 was higher (in 1.42 times, p <0.001) than in RA patients without AH. Differences between RA with AH and RA without AH groups were more significant in the evening sTLR2 level (320 (112) vs 246 (81.3) ng/L, p<0.01), than in the morning (378 (90.6) vs 321 (89.0) ng/L, p<0.05). In the group RA with AH decrease in sTLR2 in the evening was less than in the group RA without AH (1.36 times, p <0.05). An increase in sTLR2 at 20:00 was associated with a deterioration in mental health according to SF-36 (VT, SF, MH) in 1.2-1.3 times (highest quartile vs lowest quartile, p<0.01). An increase in sTLR2 at 8:00 was associated with a decrease in physical health PF, RP, BP and GH (in 1.3-1.6 times, p<0.01). Patients with high levels of sTLR2 showed more severe pain, impaired function, fatigue and sleep, decreased physical and emotional comfort, and control of symptoms according to RAID (in 1.3-1.4 times, p<0.01).

Conclusion: In RA patients daily fluctuations in sTLR2 levels has been registered with the decrease of this index in the evening. In the case of comorbid AH production of sTLR2 is higher, especially in the evening time. Disorders of sTLR2 production are one of the factors that deteriorate the quality of life in patients with RA.

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POS0623 SUBCLINICAL ATHEROSCLEROSIS IS NOT RELATED WITH ACID URIC IN RHEUMATOID ARTHRITIS. STUDY OF 1005 PATIENTS OF A SINGLE UNIVERSITY HOSPITAL

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Background: Rheumatoid Arthritis (RA) and Gout are associated with an increase of cardiovascular (CV) disease **(1,2).** Carotid plaques and increased carotid intima-media thickness (cIMT) are surrogate markers of CV mortality **(3)**. The association of serum uric acid (SUA) levels as an independent factor of subclinical Atherosclerosis and mortality in RA remains not fully clarified **(4,5).**
Objectives: In a wide cohort of patients with RA our aims were to assess the relationship of SUA with **a)** CV risk factors and **b)** presence of atherosclerosis.
Methods: Cross-sectional study including 1005 patients with RA from a Single University Center. The presence of Atherosclerosis (c-IMT and carotid plaque) was explored by Carotid Ultrasonography. The relationship between SUA and markers of subclinical atherosclerosis was studied through linear regression and logistic multivariate analysis.
Results: We studied 1005 RA patients (741 women, 74%), mean age 61±13. The main general features, CV risks factors, RA activity data and current therapy are summarized in Table 1.

Table 1. Main features of 1005 RA patients

GENERAL FEATURES	RESULTS	GENERAL FEATURES (CONTINUATION)	RESULTS (CONTINUATION)
Age, years, mean±SD	60±13	**RA features**	
Female/ Male, n (%)	741 (74) / 264 (26)	RA duration, years; mean±SD	17±12
		CRP, mg/L, median, [IQR]	3.0 [0.9-7.5]
CV risk factors		ESR, mm/ 1st hour; median, [IQR]	14 [6-24]
Past or Current smoker, n (%)	539 (54)	Rheumatoid factor, n (%)	528 (53)
Obesity/ Dyslipidemia, n (%)	307 (31)/ 560 (56)	ACPA, n (%)	492 (50)
Hypertension, n (%)	453 (45)	DAS28-ESR; mean±SD	3.3 ± 1.5
Diabetes Mellitus, n (%)	127 (13)	DAS28-CRP; mean±SD	3.1 ± 1.3
BMI, kg/m2, mean±SD	28±5/93±15	**Uric acid**	
Abdominal circumference cm; mean±SD		Uric acid level (mg/dl); mean±SD	4.8 ± 1.4
Previous CV Events, n (%)	125 (12)		
Chronic Kidney Disease, n (%)	58 (6)	**Carotid Ultrasonography**	
Gout / using drugs for hyperuricemia; n (%)	20 (2)	cIMT microns; mean±SD	708 ± 157
Total cholesterol, mg/dl; mean±SD	201±39	Carotid plaque¸ n (%)	617 (62)
HDL cholesterol, mg/dl; mean±SD	61±17		
LDL cholesterol, mg/dl; mean±SD	119 ± 32		

Abbreviations: ACPA: Anti–citrullinated protein antibody; BMI: Body mass index; CV: Cardiovascular; cIMT: carotid intima-media thickness; cm: centimeter; CRP: C Reactive protein; DAS28-ESR: Disease Activity Score-28 for Rheumatoid Arthritis with Erythrocyte Sedimentation Rate; DAS28-PCR: Disease Activity Score-28 for Rheumatoid Arthritis with C reactive protein; dl: deciliter; ESR: Erythrocyte Sedimentation Rate; HDL: high-density lipoprotein; IQR: Interquartile range; Kg: kilogram; LDL: Low-density lipoprotein; mg: milligram; m2: square meter; n: number; RA: Rheumatoid Arthritis; SD: Standard Deviation.

SUA as a dependent variable was significantly correlated with age, male gender and most of CV risk factors (body mass index, abdominal circumference and obesity) (single-variable analysis). Similarly, a significative beta coef. [95%CI] positive relationship with SUA was observed with hypertension (0.7 [0.5-0.8], p<0.001), diabetes (0.5 [0.2-0.7], p<0.001), dyslipidemia (0.2 [0.04-0.4], p=0.016), renal chronic insufficiency (1.5 [95CI 1.1-0.8], p<0.001) and previous CV events (0.8 [0.4-1.2], p<0.001). Subclinical Atherosclerosis, as dependent variable, was significantly correlated with SUA (single-variable analysis). In addition, SUA showed a positive significative beta coef. [95%CI] relationship with cIMT (18 [12-25], p<0.001) and the presence of carotid plaques (1.29 [17-1.42], p<0.001). However, statistical significance was not observed in the multivariable analysis adjusted by Classic CV Risk Factors.
Conclusion: In RA, SUA is related with most of CV risk factors. However, SUA is not associated with Subclinical Atherosclerosis.
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POS0624 RHEUMATOID ARTHRITIS AND ORAL MICROBIOME RELATED TO PERIODONTAL DISEASE

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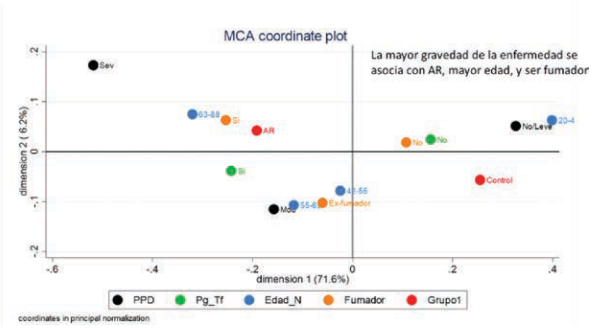
Background: Rheumatoid Arthritis (RA) is a prevalent systemic autoimmune disease with an unknown etiology. Its onset has been related with chronic immune activation.[1] Oral microbiome (OM) could be one trigger for this beginning, due to its implication in periodontal disease (PD) and chronic gum inflammation.[2]
Objectives: To correlate OM species potentially harmful and RA disease activity.
Methods: During a 6-month period (June to December 2021), RA patients (from the daily practice in a Rheumatology Department) and healthy controls were recruited. Healthy controls proceed from outpatient Orthopaedic Surgery Department (with no autoimmune diseases). A specialized odontologist made an oral evaluation and took samples. OM was assessed by a semiquantitative reactive-chain protein. Species evaluated were Porphyromonas gingivalis, Tanerella forthsytia, Treponema denticola, Prevotella intermedia y Aggregatibacter actinomycetemcomitans (PerioPOC, Austria).
Results: 237 RA patients and 83 healthy controls were recruited. 100% RA patients have, at least, one oral germ, as opposed to healthy controls (57.8%, p<0.001). P. gingivalis was present in 60.2% RA patients treated with biological therapies, most of them anti-TNF. No healthy patients were carriers of P. gingivalis. 41% RA patients had the association of T. denticola and P. gingivalis, regardless of therapies used. The association of T. denticola, T. forsythia and P. gingivalis was also frequent. No relationship between biological therapies used and germs were found (p<0.12). The coexistence of P. gingivalis and T. forsythia increases exponentially the risk of having a severe PD (x5, Figure 1). This is influenced also by higher age and smoking status. As well, this association was observed more frequently in RA patients versus healthy controls (x2.5).

Figure 1:



Conclusion: RA is related with OM, regarding healthy controls. P. gingivalis is more frequent in RA patients that needed biological therapies. These therapies seem to not influence the presence of OM, being frequent the association of several species (symbiosis) causing PD. An OM and PD examination in RA patients could be beneficial to assess disease development and response to treatments, mainly if an eradication protocol is developed (based on local hygiene and periodontal treatment).

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POS0625 VASCULAR EFFECT OF INFLAMMATORY BURDEN IN EARLY RHEUMATOID ARTHRITIS PATIENTS - A 5-YEAR PROSPECTIVE STUDY

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Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are associated with accelerated atherosclerosis driven by chronic Inflammation. We have previously reported that cumulative inflammatory burden, as reflected by cumulative averages of repeated measures of erythrocyte sedimentation rate (ca-ESR), was associated with increased arterial stiffness in PsA patients (1).

Table 1. Univariable analysis on baseline clinical characters and progression of subclinical atherosclerosis parameters

	AP+				ba PWV change			
	Univariate model		Multivariate model		Univariate model		Multivariate model	
	OR		OR		β		β	
	95% CI	*p* Value	95% CI	*p* Value	95% CI	*p* Value	95% CI	*p* Value
Symptom duration	0.99 0.92-1.06	0.704			5.62 -0.88-12.131	0.089*		
RF positive	0.99 0.92-1.06	0.692			84.04 -6.48-174.55	0.068*	84.25 0.38-168.12	0.049
Baseline Triglycerides	3.19 1.34-7.61	0.009*	3.48 1.38-8.76	0.008*	-39.05 -108.25-30.14	0.266		
FRS, 20%	5.97 1.17-30.39	0.031*	5.65 1.00-31.80	0.500	-164.11 -292.67- -35.55	0.013*	-149.48 -1.25-10.87	0.017*
ca-ESR	1.02 1.00-1.04	0.106	1.03 1.00-1.06	0.038*	3.12 0.97-5.27	0.005*	2.78 0.73-4.82	0.008*

*Statistically significant at $p < 0.05$.RF positive: Rheumatoid factor positive, FRS, 20%: Framingham risk score ≥20%, caESR: cumulative average-Erythrocyte sedimentation rate.

Objectives: To ascertain whether inflammatory burden over time is associated with long-term vascular outcome in early RA (ERA) patients.

Methods: In this 5-year prospective study, consecutive ERA patients without overt cardiovascular disease were recruited. All patients received tight-control treatment in the first year followed by stand-of-care management subsequently. Subclinical atherosclerosis and arterial stiffness progression were assessed using high-resolution carotid ultrasound (US) and brachial-ankle pulse wave velocity (PWV) respectively at baseline, year 1 and year 5. The primary outcome was subclinical atherosclerosis progression (AP+), defined as incident plaque in a segment without plaque before, or an increased number of plaques in a segment, and/or maximum carotid intima-media thickness (max cIMT) over 0.9 mm at year 5. Secondary outcome was the change in PWV over a period of 5 years. ESR level was measured during each clinic visit. Inflammatory burden was measured by cumulative averages of the area under the curve for erythrocyte sedimentation rate (ESR) over a period of 5 years.

Results: One-hundred and four ERA patients (age: 52±11 years, 81(78%) female) who completed 5 years of follow-up were included in this analysis. Significant improvement in disease activity was observed (DAS-ESR at baseline: 5.8±0.9 vs 3.2±1.2 at year 5, $p<0.001$). Forty-two patients (40.4%) had AP+. The AP+ group had higher ca-ESR (37.6±16.4 vs 32.0±17.1, $p=0.106$) and baseline Framingham risk score (FRS) (13.3±12.5 vs 5.5±6.6, $p<0.001$). Multivariate logistic regression analysis revealed that a higher ca-ESR was associated with AP+ (OR=1.03, 95%CI: 1.00-1.06, $p=0.038$) after adjustment for baseline high risk Framingham risk score (FRS≥20%) and baseline triglycerides level (Table 1). Similarly, PWV increased from 1461±285cm/s to 1559±309cm/s ($p<0.001$) after 5 years. Higher ca-ESR correlated with PWV progression (r=-0.211, $p=0.032$). Using multivariate logistic regression analysis, ca-ESR was associated with arterial stiffness progression ((β=2.94, 95%CI: 0.80 to 5.08, $p=0.007$) after adjusting for symptom duration, presence of rheumatoid factor and FRS.

Conclusion: Persistent inflammation was an independent predictor of subclinical atherosclerosis and arterial stiffness progression in ERA. Effective long-term suppression of inflammation is required to minimize cardiovascular risk.

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POS0626 CREATININE-BASED CKD-EPI EQUATION LEADS TO OVERESTIMATION OF GLOMERULAR FILTRATION RATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Accurate calculation of glomerular filtration rate (GFR) is an important aspect of clinical care for rheumatologic patients [1, 2, 3].

Objectives: To choose the optimal method of determining the GFR to assess the severity of renal dysfunction in patients with rheumatoid arthritis (RA).

Methods: An open cross-sectional study was performed involving 96 patients with a reliable diagnosis of RA (mean age 54.4±11.6 years, duration of disease 10.7±8.56 years, 57.3% with moderate RA activity).

For comparative assessment of renal function, we used the estimated glomerular filtration rate (eGFR) using the CKD-EPI formulas on the National Kidney Foundation website (USA): creatinine-based equation (eGFRcr), cystatin C-based equation (eGFRcyst) and calculated creatinine and cystatin C equation (eGFRcr-cyst). The 2009 CKD-EPI creatinine equation (eGFRcr) was used as a reference for comparative calculations of GFR. Based on the eGFRcr measurements, patients with RA were divided into four groups: I, >90 ml/min/1.73 m^2; II, 89-60 ml/min/1.73 m^2; III, 45-59 ml/min/1.73 m^2; and IV, <45 ml/min/1.73 m^2.

Results: The mean eGFRcr, presented as a reference in this study, was 70.0±18.7 ml/min/1.73 m^2. Signs of hyperfiltration using eGFRcr (>90 ml/min/1.73 m^2) were observed in 16 (10.1%) patients with RA, mild decrease of renal function (60-89 ml/min/1.73 m^2) was registered in 52 (32.9%), moderate/severe decrease (<59 ml/min/1.73 m^2) - in 28 (17.8%) patients with RA. Decreased eGFRcr was differentially associated with increased patient age (r=0.46; p=0.003), disease duration (r=0.24; p=0.017), cumulative dose of hormones (r=0.66; p=0.007), lower height (r= 0.35; p=0.001).

Analysis of eGFR values demonstrated significant differences using the selected methods (χ^2=9.91, p= 0.007). Intergroup differences (in degree of decrease in eGFR) were statistically significant for all variants of eGFR calculation (eGFRcr, eGFRcyst, eGFRcr-cyst; H-test and Median-test, p<0.001). According to the eGFRcr formula, an absolute majority of patients with RA (83.3%) had a decrease in GFR of varying severity (a slight decrease was registered in 54.2% of cases) (Table 1).

Table 1. Group distribution of RA patients according to eGFR, n(%)

	Group I	Group II	Group III	Group IV
eGFRcr	16 (17.0)	52 (54.2)	20 (20.8)	8 (8.33)
eGFRcr-cys	22 (22.9)	39 (40.6)	20 (20.8)	15 (15.6)
eGFRcyst	29 (30.2)	29 (30.2)	22 (22.9)	16 (16.7)

The use of eGFRcyst showed that only 12 of 29 people in the first group had optimal (>90 ml/min/1.73 m^2) eGFRcr (p=0.031), and 17 patients entered the group with slightly decreased (60-89 ml/min/1.73 m^2) eGFRcr. A similar, but less significant situation (12 of 22 people and 10 patients, p=0.02) was also observed with eGFRcr-cyst. In the second group of RA patients 19 patients corresponded to the chosen criteria in determination of eGFRcyst, and 8 patients entered groups (III and IV) with more severe decrease of renal function (2 patients were included into group I) (p=0,011). Significant differences in this group were also noted when comparing the proportions according to eGFRcr with eGFRcr-cyst (p=0.044). A probable decrease in renal filtration function with eGFRcr (compared with the alternative use of eGFRcr-cyst or eGFRcyst) can be observed in 11-18% of RA patients in group 1 (high/optimal renal function) and up to 10% of RA patients in group 2 (slight decrease). No significant differences were found using the three estimated CKD-EPI formulas in RA patients with moderate/significant decrease in GFR (p>0.05).

Conclusion: Currently, the overall diagnostic performance of the CKD-EPI equation based on creatinine and cystatin C may be the most optimal (in comparison with other calculated CKD-EPI formulas) in patients with RA, and may also be useful for confirming eGFRcr results >60 ml/min/1.73m^2.

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POS0627 SUBOPTIMAL MANAGEMENT OF RHEUMATOID ARTHRITIS IN FRANCE: A REAL-WORLD STUDY BASED ON DATA FROM THE FRENCH NATIONAL HEALTH DATA SYSTEM

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Background: Currently, real-world data on rheumatoid arthritis (RA) treatment patterns in France are limited.
Objectives: The aim of this study was therefore to describe, between 2013 and 2017, the sequence of therapies used in the treatment of patients with RA and to characterize RA treatment patterns using real-world data.
Methods: A non-interventional, longitudinal study was conducted using the Echantillon Généraliste des Bénéficiaires (EGB) between 1 January 2013 and 31 December 2017. EGB is a 1/97th representative random sample from the French National Healthcare Database (SNDS) which includes claims data covering 99% of the total French population. Treatment patterns, adherence and persistence of RA treatments were described in a cohort of patients with RA, identified between 2013 and 2017.
Results: Between 2013 and 2017, 2,553 patients with RA were identified, including 2,314 in 2017. Of the 2,314 RA patients identified in 2017 (mean age 66.2 ± 15.4 years; 73.7% female; mean Charlson comorbidity score 4.2), 1,102 (47.6%) did not receive any disease-modifying anti-rheumatic drug (DMARD). Of these, 944 (85.7%) had received at least one symptomatic treatment, including 862 (91.3%) an analgesic, 509 (53.9%) an oral corticosteroid and 384 (40.7%) non-steroidal anti-inflammatory drugs. Of the 2,553 RA patients monitored between 2013 and 2017, 1,512 (59.2%) patients received a DMARD, of which 721 (47.7%) patients received only one treatment sequence, mainly methotrexate (n=529, 35.0%), and did not discontinue or switch treatment. Switching treatment to a targeted DMARD was reported for 144 (9.5%) patients. During follow-up, 377 (25%) patients discontinued treatment. In total, 1,142 RA treatment initiations were recorded, 62.4% of which were conventional synthetic DMARDs (csDMARDs). Persistence rates (95% confidence interval) for csDMARDs, TNF inhibitors (TNFi) and other targeted DMARDs (tDMARDs) were 63.4% (59.6–67.0), 55.9% (49.2–62.0) and 59.4% (51.2–66.6) at 12 months, respectively; Medication Possession Ratio (MPR), an adherence indicator, was 80.5%, 90.8% and 71.9%, respectively. Long-term oral corticosteroids (≥6 months) were also associated with csDMARD for 42.6% of cases (n=304/713), TNFi for 39.7% (n=100/252) and another tDMARD for 53.1% (n=94/177). The average doses of long-term oral corticosteroids were 7.5 mg, 6.5 mg and 7.8 mg of prednisone equivalent per day, respectively.
Conclusion: Using data obtained from the EGB, this study estimated the number of patients with RA in France to be 307,612 in 2017. Approximately half of the patients identified in the EGB cohort were not treated with a DMARD. For a substantial proportion of patients receiving DMARDs, therapeutic escalation, a switch in treatment, or long-term corticosteroid co-therapy with an average daily dose greater than 5 mg were needed. Furthermore, median persistence for most targeted DMARDs was less than 2 years, and the early discontinuation rates of up to 46.6% suggest poor DMARD tolerance in many patients.
This study highlights that the medical need for RA treatment is not covered by current therapeutic strategies.

Table 1. Characteristics of DMARD treatments initiated between 2013–2017 in the EGB database (N=1,142)

	csDMARD	TNFi	Other targeted DMARD
Treatments initiated, n (%)	713 (62.4)	252 (22.1)	177 (15.5)
Median duration of treatment, months	26.7	18.5	14.6
Rate of early treatment discontinuation (≤2 dispensations within 2 months of initiation), %	15.5	10.7	11.9
Mean treatment adherence (MPR), %	80.5	90.8	71.9

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POS0628 CLINICAL AND LABORATORY FEATURES OF RHEUMATOID ARTHRITIS IN COMBINATIONS WITH SJOGREN'S SYNDROME IN CLINICAL PRACTICE OF RHEUMATOLOGICAL HOSPITAL.

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Background: Overlap syndrome of rheumatoid arthritis (RA) and Sjogren`s syndrome (SjS) characteristically manifested with more visceral involvements and has his own features of the articular syndrome. This issue is not well covered in the literature.
Objectives: To determine the clinical and laboratory features of RA in combination SjS, in cases where biologic therapy was prescribed.
Methods: 505 patients (pts) were enrolled in observational cross-sectional study. These patients were examined and treated in our clinic in 2021 year. RA was diagnosed according to the 2010 ACR/EULAR criteria. SjS was diagnosed on ECR/EULAR 2016 criteria in 155 (30.7%) pts. Thus, 2 groups (grs) were identified for comparative analysis: pts with RA in combination with SjS (n=155) (group S) and pure RA (n=350) as a control group (gr C).
Results: In gr S there were two times less men (8.4% and 17.7%, p=0.004) and pts were older (53.6±12.5 and 48.8±15, p<0.001), while the duration of disease didn`t differ significantly and amounted 10 (5-16) years. Tender joints score and the duration of morning stiffness in the joints were comparable. Other indicators of RA activity (swollen joints score, VAS of pts, ESR, CRP), as well as calculated activity indices (DAS28ESR, DAS29CRP) in gr S were significantly lower than in gr C (Table 1). The frequency of erosive arthritis was similar for this grs. Leukopenia was more common in the gr S (p=0.004). Pts of gr S had positive values of RF and ACCP more often (p≤0,005).

Table 1. Indicators of RA activity at study entry.

	S (n=155)	C (n=350)	p
tender joints score, M±SD; Me [25; 75]	9,1±5,3; 8[4;12]	9,5±5,8; 8[5;13]	p>0.05
swollen joints score, M±SD; Me [25; 75]	5±4,5; 4[2;7]	6±4,1; 5[3;9]	0,02
VAS pts, M±SD; Me [25; 75], mm	58,9±16,1; 60[50;70]	63,9±13,2; 65 [60;70]	0,0003
ESR, M±SD; Me [25; 75], mm/h	27,9±28,4; 18[9;34]	36,3±35; 22[11;51]	0,009
CRP, M±SD; Me [25; 75], g/l	14±20,2; 5[1,4;17,8]	23,8±29,5; 11,7[3,5;33,8]	0,0002
DAS28COЭ, M±SD; Me [25; 75]	5±1,3; 4,9[3,9;6,2]	5,4±1,2; 5,4[4,5;6,3]	0,005
DAS28CPБ, M±SD; Me [25; 75]	4,7±1,2; 4,6[3,7;5,6]	5±1,1; 5,1[4,3;5,8]	0,0007
Morning stiffness M±SD; Me [25; 75], min	109,8±98; 60[30;140]	122,7±96,4; 90[42,5;180]	p>0.05

The frequency of prescribing methotrexate or leflunomide at the onset of the disease was comparable. Hydroxychloroquine was more often prescribed in the gr S at the onset of the disease (16% and 6%, p<0.001) and at the time of analysis (22.6%, 8.6%, p<0.001). The frequency and duration of oral glucocorticoids (GCs) in the grs were comparable, but at the time of hospitalization GCs were received at lower doses in gr S (p=0.02). The first biological drugs,

prescribed at the onset of the disease were more often TNFα blockers in gr C and rituximab in gr S.
Conclusion: According to our observations, the combination of RA with SjS leads to a milder course of the RA. Early diagnosis of SjS in RA pts is important for understanding the course of the disease and determining the prognosis.
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POS0629 PREVALENCE AND FACTORS ASSOCIATED WITH SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Sarcopenia is a progressive and generalized skeletal muscle loss associated with falls, fractures, physical disability, and mortality, described as age-related or secondary. Systemic inflammatory diseases, such as rheumatoid arthritis (RA), are well-known causes of secondary sarcopenia. However, the exact prevalence of sarcopenia in patients with RA is still unknown, partly due to the heterogeneous definitions of sarcopenia adopted in different studies.
Objectives: To assess the prevalence of sarcopenia in a cohort of patients affected by RA, and to evaluate the influence of age, sex, comorbidity, disease duration and activity, antibody status and therapies on sarcopenia.
Methods: We conducted a retrospective observational study on adult patients affected by RA undergoing evaluation at our outpatient clinic from January 2009 and July 2021. All patients underwent dual-energy X-ray absorptiometry (DXA) for assessment of body composition; diagnosis of sarcopenia was defined using Skeletal Muscle Mass Index (SMI), as proposed by consensus EWGSOP2 (1). We collected relevant demographic, clinical, therapeutic, and laboratory data at the time of DXA. We excluded patients affected by neoplastic disorders and/or malnutrition. Binary logistic regression analysis was employed to define predictors and protective factors of developing sarcopenia.
Results: A total of 266 patients (82.7% women) with a median age of 58.4 (IQR 14.4) years were included in the study. The prevalence of sarcopenia was 27.44%. From the binary logistic regression analysis, we found that the use of oral glucocorticoids (GCs) at a daily dose > 3.25 mg of prednisone-equivalent was significantly associated with sarcopenia (β 0.68, p = 0.047, aOR 1.98, 95% CI 1.009 – 3.881) (Figure 1). We found a significant inverse correlation between conventional disease-modifying antirheumatic drug (c-DMARDs) and sarcopenia (β -0.71, p = 0.027) as well. Age, sex, disease duration, mean disease activity - expressed as disease activity score based on 28 joints (DAS-28), erosive and seropositive disease - and biologic disease-modifying antirheumatic drug (b-DMARDs) therapy were not predictors of sarcopenia, albeit seropositive status showed a correlation trend with increased prevalence of sarcopenia (p = 0.092).

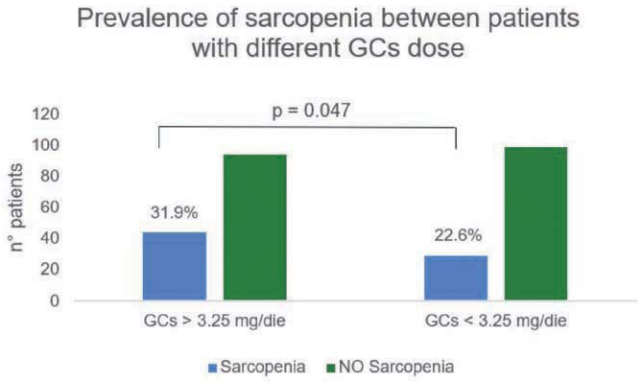

Figure 1.

Conclusion: Our study showed that sarcopenia is a common complication in RA. Glucocorticoid therapy was associated with an increased prevalence of sarcopenia, while c-DMARDs acted as protective factors, possibly decreasing chronic inflammation. No correlation was found with b-DMARDs, possibly due to association with longer and more aggressive rheumatic disease.

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POS0630 INCIDENCE AND ASSOCIATED FACTORS OF CANCER IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease primarily characterized by joint inflammation along with systemic manifestations and increased risk of cardiovascular disease. Furthermore, it has been suggested that RA itself and medications administered might increase the risk of cancer.
Objectives: To assess cancer incidence in RA patients and factors associated with cancer development in RA patients.
Methods: In this single centre retrospective cohort study, the data of 2000 patients (76.3% female, mean age at the last follow-up: 59.5 ± 13.4 years) who were followed up between 2005 and 2020 and fulfilled 2010 ACR/EULAR classification criteria were scrutinised. Patients' demographic, clinical and serological characteristics, and smoking history were recorded. Multivariable logistic regression analysis was performed to determine the associated factors with cancer development. The standardized incidence rate (SIR) was calculated by dividing the number of cancer cases observed in a given age and gender group by the expected number.
Results: After a median follow-up of 9 years, 71 (3.6%) patients were diagnosed with cancer and the number of patients with more than one malignancy was 5 (0.5%). Cancer types in each sex were demonstrated in Table 1. Seropositivity rate of the cohort was 86.0% and 376 out of 1102 (34.1%) patients were smokers. Glucocorticoids were the most common used agent in the treatment of RA (75.2%), followed by methotrexate (68%), hydroxychloroquine (65.1%), sulfasalazine (37.7%), leflunomide (35.5%), biological disease-modifying antirheumatic drugs (11.4%) and tofacitinib 4%. In multivariable logistic regression analysis performed of 1102 patients without missing data of smoking history, only smoking and age were independently associated with malignancy (Odds Ratios were 2.11 (95% Confidence Interval (CI) 1.07-4.14 and 1.05 (95% CI 1.02-1.07), respectively). Treatment modalities and RA-related clinical factors were not related to cancer development (data not shown). When compared with the 2017 Cancer Statistics of Turkey, the incidence of malignancy in our RA cohort was similar to the corresponding age and gender groups. The SIRs in male and female patients were calculated as 0.93 (95% CI: 0.82-1.05 p= 0.25) and 0.92 (95% CI: 0.77-1.09 p= 0.34), respectively.

Table 1. Number of malignancy distribution by gender of patients

	Female	Male
	n=47	n= 24
Breast, n (%)*	15 (100.0)	0 (0.0)
Urogenital system, n (%)*	8 (53.4)	7 (46.6)
Prostate, n (%)*	0 (0.0)	5 (100.0)
Lung, n (%)*	3 (30.0)	7 (70.0)
Lymphoma, n (%)*	4 (57.1)	3 (42.9)
Thyroid, n (%)*	6 (100.0)	0 (0.0)
Skin, n (%)*	5 (83.3)	1 (16.7)
Colorectal, n (%)*	2 (50.0)	2 (50.0)
Head and Neck, n (%)*	0 (0.0)	3 (100.0)
Multipl Myeloma, n (%)*	1 (50.0)	1(50.0)
Others, n (%)*	7 (87.5)	1 (12.5)

*Row Percent

Conclusion: Our results show that patients with RA do not require additional screening beyond the nationally recommended guidelines. Medications used, including tumor necrosis factor inhibitors, did not increase the risk of cancer. In conclusion, all patients with RA should receive standard age- and sex-appropriate cancer screening.
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POS0631 EVEN LOW-DOSE GLUCOCORTICOID USE IS A RISK FACTOR FOR CLINICAL FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS: TEN-YEAR FINDINGS OF THE TOMORROW STUDY

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Background: Patients with rheumatoid arthritis (RA) who have sarcopenia and stiff or painful joints might be at increased risk of falls and fractures.
Objectives: The present study aimed to prospectively identify the incidence of clinical fractures and associated risk factors in patients with RA in a cohort study named the TOMORROW (UMIN000003876) that started in 2010.
Methods: We evaluated anthropometric parameters, bone mineral density (BMD), disease activity, RA medication at entry and observed the incidence of clinical fractures during ten years in 202 patients with RA (mean age, 58.6 y; medication with biological agents, 54.9%) and 202 age- and sex-matched non-RA volunteers (Vo) (mean age, 57.4 y). We compared the incidence of clinical fractures between patients with RA and Vo for ten years, and analyzed the risk factors for clinical fractures using Cox proportional hazard model.
Results: The incidences of clinical fractures were 0.036 and 0.024/person-year in patients with RA and Vo, respectively. Cox proportional hazard model revealed that low BMD at the thoracic vertebrae (< 0.7 g/cm^2) and history of fractures at entry were significantly associated with the incidence of clinical fractures (Hazard ratio [HR]1.737, p=0.020 and HR1.514, p=0.047, respectively) in all participants. RA morbidity, however, was not (HR1.398, p=0.112). In patients with RA, medication with GC at entry was a significant risk factor for clinical fractures (HR1.898, p=0.017). Additionally, a mean GC dose (≥ 2 mg/day) at entry and during the ten-year period increased risk for fractures (HR 2.189, p=0.004, 1.866, p=0.022, respectively).
Conclusion: RA per se was not a risk factor for clinical fractures in this cohort. Low BMD at the thoracic vertebrae at entry and the use of GC with even low dose at entry and during ten years were significantly associated with an increased frequency of clinical fractures among patients with RA.
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POS0632 EXPRESSION OF PD-1 AND PD-L1 IN DIFFUSE LARGE B-CELL LYMPHOMA PATIENTS WITH PRE-EXISTING RHEUMATOID ARTHRITIS – A POSSIBLE ASSOCIATION WITH HIGH RHEUMATOID ARTHRITIS DISEASE ACTIVITY

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Background: Patients with rheumatoid arthritis (RA) are at increased risk of developing diffuse large B-cell lymphoma (DLBCL). Immunotherapy blocking programmed cell death protein 1 (PD-1) and its ligand PD-L1 has substantially improved outcome in a number of malignant diseases but has so far been disappointing in DLBCL. However, current research seeks to identify DLBCL subgroups responsive to PD-1 blocking agents. Whether patients with pre-existing rheumatoid arthritis (RA) might constitute such a subgroup is unknown. Expression of PD-1 and PD-L1 has not previously been studied in a cohort of RA-DLBCL patients.
Objectives: To determine intratumoural expression of PD-1 and PD-L1 in DLBCL patients with pre-existing RA and relate the expression to clinical characteristics and survival outcome.
Methods: We included 103 RA-DLBCL patients and 74 DLBCL controls without rheumatic disease. PD-1 and PD-L1 immunohistochemical markers were applied on tumour tissue microarrays. The number of PD-1+ tumour infiltrating leukocytes (TILs) and proportions of PD-L1+ tumour cells and TILs were calculated and correlated to clinical data. For RA patients, disease activity had been individually scored repeatedly over time based on swollen and tender joint counts, erythrocyte sedimentation rate (ESR), and the treating physician's global assessment of disease activity from onset of RA until lymphoma diagnosis(1). Values of cumulative disease activity for each patient were calculated as area under the curve (AUC). To investigate a possible influence of RA disease severity on the expression of PD-1 and PD-L1, RA patients with DLBCL were divided in two groups using the upper quartile of the AUC values as cut off for the highest disease activity group.
Results: Expression of PD-1 in TILs and PD-L1 in tumour cells was similar in RA-DLBCL and DLBCL controls. In RA-DLBCL, high expression of PD-L1 in tumour cells was significantly more common in patients with the most severe RA disease (45% vs 20%, p=0.04) (Table 1) and was associated with inferior overall survival in multivariable analysis (HR 4.62, 95% CI, 1.55-13.71).

Table 1. Clinical and lymphoma related parameters and their distribution in the RA-DLBCL patients according to high and low expression of PD-L1 in tumour cells

	Entire cohort	High PD-L1 in tumour cells[1]	Low PD-L1 in tumour cells	P-value*
All patients, n (%)	**103 (100)**	**11 (100)**	**89 (100)**	
Women, n (%)	**61 (59)**	**6 (55)**	**54 (61)**	**0.70**
Age ≥60, n (%)	**85 (83)**	**10 (91)**	**72(81)**	**0.68**
DLBCL subtype, n (%)				**0.35**
GCB	**30 (29)**	**2 (18)**	**27 (30)**	
Non-GCB	**69 (67)**	**9 (82)**	**57 (64)**	
Missing	**4 (4)**	**0 (0)**	**5 (6)**	
Ann Arbor stage III-IV, n (%)	**65 (63)**	**5 (45)**	**57 (64)**	**0.31**
Missing	**4 (4)**	**1 (10)**	**3 (3)**	
EBV status, n (%)				**<0.001**
Positive	**9 (9)**	**4 (36)**	**5 (6)**	
Missing	**2 (2)**	**0 (0)**	**2 (2)**	
RA highest disease severity group, n (%)				**0.04**
Yes	**25 (25)**	**5 (45)**	**18 (20)**	
Missing	**4 (4)**	**1 (10)**	**3 (3)**	
Active RA treatment, n (%)†				**0.96**
Yes	**39 (38)**	**4 (36)**	**34 (38)**	
Missing	**3 (3)**	**1 (10)**	**2 (2)**	

RA, rheumatoid arthritis; DLBCL, diffuse large B-cell lymphoma; GCB, germinal centre B-cell like;EBV, Epstein-Barr virus; DMARD, disease modifying anti-rheumatic drug; TIL, tumour-infiltrating leukocytes; [1] High expression ≥17% PD-L1+ tumour cells of all tumour cells; *According to chi-square or Fischer's exact test; †Active RA treatment= DMARD and/or corticosteroids;

Conclusion: Our results indicate an association between a more severe RA disease and increased expression of PD-L1 in DLBCL tumour cells. This might have implications for the prognosis of the lymphoma as well as the chance of response to immunotherapy and warrants further studies also in other chronic inflammatory condidions.
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POS0633 HIGH SENSITIVITY TROPONIN I IS ASSOCIATED WITH FOCAL FIBROSIS AS DETECTED BY CARDIAC MR IN EARLY, TREATMENT-NAIVE RA

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Background: RA individuals are known to have excess CVD risk, equivalent to that of type 2 diabetes mellitus[1]. We recently reported vascular and

myocardial abnormalities on cardiac magnetic resonance imaging (CMR) in an early RA cohort compared with control subjects, and improvement with DMARD treatment[2]. Non-invasive assays for high-sensitivity troponin and NT-pro-BNP have been evaluated in RA cohorts. No study has investigated these in early, treatment-naïve RA and in association with subclinical CMR findings.

Objectives: In a treatment-naïve, early RA trial cohort, we examined serum cardiac markers of ventricular stretch (NT-pro-BNP) and myocardial injury (high-sensitivity troponin-I (hs-Tn-I)) and change with treatment, and whether these associated with cardiac MRI abnormalities.

Methods: In CADERA (a unique early RA RCT derived study), out of a total of 120 patients randomised to either first-line TNFi+MTX (n=60) or MTX and conventional synthetic DMARDs (n=60), 81 subjects with no previous history of CVD or diabetes and with only a maximum of 1 other traditional risk factor, underwent baseline and year 1 CMR. Corresponding levels of NT-pro-BNP (pg/ml) and hs-Tn-I (ng/L) were measured at baseline and year 1. CADERA reported CMR measures of vascular stiffness [aortic stiffness index (AoSI), and aortic distensibility (AD)]; tissue oedema/fibrosis [native T1 values (T1), myocardial extracellular volume (ECV), and late gadolinium enhancement (LGE)] and ventricular function [2]. Bayesian linear and logistic regression models with mixed effects for overall data were used to test association between serum cardiac markers and CMR parameters.

Results: CADERA trial already reported baseline demographics and comorbidity data of patients. The most common risk factor was smoking history (55%) followed by hypertension (7%) and family history of ischaemic heart disease (5%)[2]. 7 patients had abnormal findings on LGE imaging at baseline and 4 at year 1.[2] From baseline to year 1, NT-pro-BNP remained within normal limits although a numerical improvement was noted at year 1(76.4 to 59.4, p = 0.038). Hs-Tn-I was within normal limits (<3ng/L) with no significant change noted (1.62 to 1.7). At baseline, median hs-Tn-I was 2 (IQR 1.4 - 3.05) in patients with abnormal LGE findings compared to 1.60 (0.95 – 2.52) in those without (p = 0.3). At year 1, median hs-Tn-I was 2.70 (IQR 1.08 – 4.82) in patients with abnormal LGE findings versus 1.7 (IQR 1 – 2.5) in those without (p = 0.5). Table 1 outlines the association of serum cardiac markers with CMR parameters. At baseline, hs-Tn-I positively associated with LGE. This association was also demonstrated when considering overall data (baseline + week 48). Association of NT-pro-BNP with CMR was not significant.

Table 1. Association of serum Hs-Tn-I with CMR parameters (posterior estimates with 95% credible intervals reported)

	Hs-Tn-I		
CMR parameter	Overall	Baseline	Year 1
Measures of myocardial tissue oedema/fibrosis			
LGE	**0.56(0.1 to 1.11)**	**0.6(0.04 to 1.27)**	0.54(-0.13 to 1.17)
T1	-4.42(-10.5 to 1.5)	-0.38(-6.7 to 6.2)	-6.02(-14.9 to 3.15)
ECV	0.002(-0.04 to 0.08	0.001(-0.05 to 0.07)	0.001(-0.04 to 0.04)
Measures of vascular stiffness			
AoSI	0.01(-0.23 to 0.25)	0.05(-0.22 to 0.33)	0.05(-0.33 to 0.42)
AD	-0.05(-0.23 to 0.13)	-0.02(-0.18 to 0.14)	-0.06(-0.37 to 0.25)

Conclusion: Our data suggest hs-Tn-I is within normal limits in a treatment-naïve, RA cohort but with numerical differences that associated with presence of focal fibrosis on CMR. Modest numbers of those with focal fibrosis may account for normal range values for hs-Tn-I.

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POS0634

SAFETY PROFILE OF B/TSDMARD IN RHEUMATOID ARTHRITIS PATIENTS WITH IMPAIRED GLOMERULAR FILTRATION RATE. AN ANALYSIS FROM THE GISEA REGISTRY.

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Figure 1.

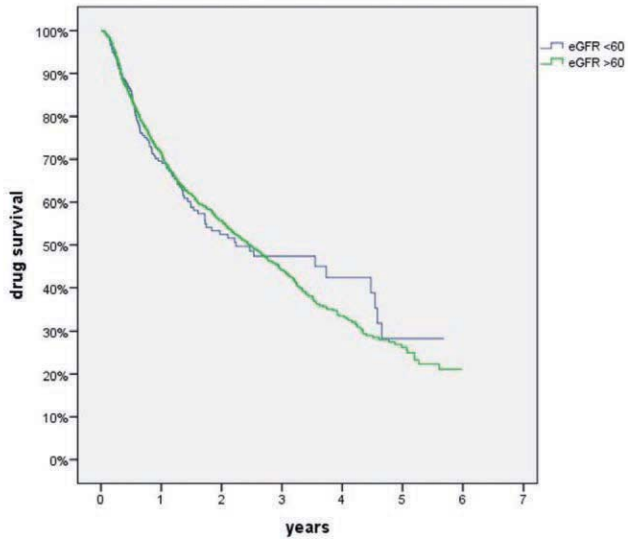

Table 1. Disease characteristics at b/tsDMARD prescription of RA patients with impaired glomerular filtration rate (eGFR ≤60) and normal (eGFR>60) glomerular filtration rate

	eGFR ≤60 n. 288	eGFR>60 n. 2155
DAS28-ESR	4 (1.3)	4 (1.5)
CDAI	16 (12)	17 (12)
HAQ-DI	1.3 (0.8)	1 (0.8)***
csDMARD, n. (%)	220 (76.4)	1790 (83.1)**
Glucocorticoid, n. (%)	231 (80.2)	1568 (72.8)**
Anti-TNF antagonists, n. (%)	84 (29.2)	748 (34.7)
Anti-IL6Ri	48 (16.7)	374 (17.4)
JAKi	69 (24)	569 (26.4)
CTLA4-Ig	75 (26)	368 (17.1)*
Anti-CD20	12 (4.2)	96 (4.5)
First-line b/tsDMARD treatment	90 (31.3)	753 (34.9)
Second-line b/tsDMARD treatment	72 (25)	487 (22.6)
Other-line b/tsDMARD treatment	126 (43.8)	915 (42.5)

*p<0.05, p<0.01, p<0.001

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Background: In real-life setting, a greater number of elderly rheumatoid arthritis (RA) patients with impaired glomerular filtration rate (GFR) needs treatment with biologic or target synthetic disease-modifying anti-rheumatic drugs (b/tsDMARD) to achieve disease control and reduce NSAIDs intake. Long-term observational data from the real-life on the use of b/tsDMARD in these patients are scarce.

Objectives: The aim of this study was to evaluate the retention rate of b/tsDMARD in RA patients with impaired GFR in real-life setting.

Methods: Data of RA patients treated with at least one b/tsDMARD were retrospectively analyzed form the national Italian GISEA registry from January 2016 to December 2021. Estimated-GFR (eGFR) was calculated with the Cockcroft-Gault equation at the time of any b/tsDMARD prescription. For the purpose of this study, patients were divided in two groups, patients with impaired GFR (eGFR ≤60) and patients with normal GFR (eGFR >60). The retention rate was calculated by the Kaplan-Meier method and compared between these two groups by a log-rank test.

Results: The study population included 2443 treatment-line with b/tsDMARD from 1888 patients (female 80.4%, age 57±12 years, mean baseline CDAI 17±12, FR/ACPA+ 69.5%) who started a new b/tsDMARD. Disease characteristics are shown in Table 1. 288 treatments with b/tsDMARD were started in patients with impaired eGFR and 2155 in patients with normal eGFR. Compared to patients with eGFR >60, patients with eGFR ≤60 showed higher HAQ-DI (1.3±0.8 vs 1±0.8, p<0.001) at the start of b/tsDMARD treatment. Glucocorticoids were more prescribed in patients with impaired eGFR (80.2% vs 72.8%, p<0.01), while csDMARDs were more prescribed in association with b/tsDMARD in patients with normal eGFR (83.1% vs 76.4%, p<0.01). Of note, CTLA4-Ig treatment was more prescribed in patients with impaired eGFR (26% vs 17.1%, p<0.05), while no difference in b/tsDMARD prescription was observed for other mechanism of actions. Drug survival was similar between RA patients with impaired eGFR [58.2%, mean survival time 35 months (CI95% 31-39)]and RA patients with normal eGFR [55%, mean survival time 34.4 months (CI95% 33-36), log rank: 0.88] (Figure 1). Cox regression model adjusted for age, sex and b/tsDMARD showed no impact of eGFR on drug survival [HR: 0.9 (CI95%: 0.7-1.2).

Conclusion: Our data show that impaired eGFR seems to not influence the persistence of b/tsDMARD treatment in RA patients.

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POS0635 DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: EXPERIENCE IN A RHEUMATOLOGY OUTPATIENT PRIVATE CENTRE

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Background: Patients with difficult-to-treat rheumatoid arthritis (D2T RA) have not achieved treatment target despite treatment according to EULAR recommendations. Information on the incidence rates of D2T RA in a real-life setting is lacking.

Objectives: To estimate the prevalence of D2T RA in a well-characterized cohort.

Methods: This was a cross-sectional analytical study of patients with RA (1987 ACR criteria). Each patient was evaluated and followed by a rheumatologist from January 2014 to December 2021 in a single rheumatology outpatient private center in Bogotá, Colombia. RA patients were classified as D2T RA according to EULAR definition.

Results: A total of 783 patients were evaluated. Baseline characteristics were as follows: female gender 91.1%, mean age 54.4±13 years, mean disease duration 13.9±9.3 months, RF positive 92.4%, ACPA positive 59.5%, and erosions 44.3%. 32.9% have extra-articular manifestations and 31.6% at least one comorbidity. Most of patients have received conventional synthetic DMARDs (97.8%), being prednisone and methotrexate the most frequently prescribed. Seventy-nine (10%) patients were classified as D2T RA. The current treatments were conventional synthetic DMARD alone 18.9%, combination with bDMARD 79.4%, and 78.5 with glucocorticoids. Main characteristics of the patients are shown in Table 1.

Table 1.

	D2T RA (n=79)
Demographics	
Age, years	54.4
Female, %	91.1
Comorbidity	31.6
Smoking	37.9
Disease characteristics	
Disease duration, months	13.9
RF positivity, %	92.4
ACPA positivity, %	59.5
PAI	10.1
EAM	32.9
Drugs	
Number of previous bDMARDs, mean	2.89
Glucocorticoid therapy, mean dose per day (mg)	18.4

RF: rheumatoid factor; ACPA:anti-citrulinated protein antibodies; PAI: poliautoimmunity, EAM: extra-articular manifestations, bDMARD: disease-modifying biologic antirheumatic drug; D2T: difficult-to-treat; n: number; mg miligrams

Conclusion: D2T AR is common and represents a phenotype with a significant burden of comorbidities and a high prevalence of poor prognostic factors. This concept should be recognized and taken into account to bring a personalized approach.

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Rheumatoid arthritis - biological DMARDs

POS0636

PATIENT GROUPS IN RHEUMATOID ARTHRITIS IDENTIFIED BY DEEP LEARNING RESPOND DIFFERENTLY TO BIOLOGIC OR TARGETED SYNTHETIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS

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Background: Cycling of biologic or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs) in rheumatoid arthritis (RA) patients due to non-response is a problem preventing and delaying disease control.
Objectives: To assess and validate treatment response of b/tsDMARDs among RA patient groups identified by deep learning.
Methods: In the Swiss Clinical Quality Management of Rheumatic Diseases registry (SCQM), between 1998 and 2018, we identified all RA patients with a DAS28-erythrocyte sedimentation rate (esr) record within 6 months before start of the first b/tsDMARD. This first-time b/tsDMARD was the cohort entry at which patients were clustered through several runs of deep embedded clustering. Features, measured at cohort entry, included demographics, RA disease burden/duration, life-style factors, and other RA medication. To increase robustness of the obtained clusters, we grouped similar patient clusters together (further referred to as groups). Our outcomes were b/tsDMARD stop due to non-response, and separately a ≥20% reduction in DAS28-esr (RA disease activity in 28 joints using esr measures) as a proxy for treatment response. We followed all patients from cohort entry until b/tsDMARD stop or a maximum of 15 months follow-up. We assessed comparative effectiveness of b/tsDMARDs (ref. adalimumab) using Cox proportional hazard regression in each patient group by estimating hazard ratios (HR) with 95% confidence intervals (CI). We validated results obtained per patient group through stratified analyses according to most distinctive patient characteristics of the respective group, i.e. the characteristics that led to the respective grouping were also used to stratify the overall population by in this validation analysis.
Results: We obtained 24 clusters which comprised between 362 and 1481 patients (among 3516 unique patients). These clusters were grouped into 5 groups according to most distinct characteristics at b/tsDMARD initiation: 1) ≥2 csDMARDs and prednisone use, 2) male sex, 3) seronegativity, female sex, and no prednisone use, 4) rather low disease burden, 5) seropositivity, female sex, and a rather high disease burden/duration.
Comparative effectiveness results among validation strata confirmed comparative effectiveness results observed among the 5 groups: Patients with ≥2 csDMARDs and prednisone at b/tsDMARD initiation, men, as well as patients with a lower disease burden responded better to tocilizumab than to adalimumab (HRs of reaching ≥20% reduction in DAS28-esr: 5.46, 95% CI [1.76-16.94], HR 8.44 [3.43-20.74], and HR 3.64 [2.04-6.49], respectively). Furthermore, seronegative women without use of prednisone at b/tsDMARD initiation as well as seropositive women with a higher disease burden and longer disease duration had a higher risk of non-response with golimumab (HRs of b/tsDMARD discontinuation: 2.36 [1.03-5.40] and HR 5.27 [2.10-13.21], respectively) than with adalimumab.
Conclusion: Our results suggest that RA patient groups identified by deep learning may respond differently to individual first-line b/tsDMARDs. Thus, our results can possibly support the decision on the best choice of first-time b/tsDMARD for certain RA patients, which is a step forward towards personalizing treatment. However, further research in other cohorts is needed to verify our results.
Acknowledgements: We thank all patients and rheumatologists contributing to the SCQM registry, as well as the entire SCQM staff. A list of rheumatology offices and hospitals which contribute to the SCQM registry can be found at http://www.scqm.ch/institutions. A list of financial supporters of SCQM can be found at http://www.scqm.ch/sponsors. The professorship of Andrea M Burden is partially supported by PharmaSuisse and the ETH Foundation.
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POS0637

SAFETY OF B/TSDMARDS FOR RA AS USED IN CLINICAL PRACTICE - RESULTS FROM THE LAST DECADE OF THE ARTIS PROGRAM

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Background: While the relative efficacy of treatments can be demonstrated in relatively small studies with limited follow-up, most safety concerns are infrequent, requiring longer follow-up and larger populations. This is recognized by the regulatory framework, where data from pivotal randomized controlled trials are usually considered sufficient for demonstrating efficacy and non-toxicity, but post-approval safety studies are required for many years to fully evaluate drug-associated risks. Though such regulatory safety-studies often focus on one drug (vs. all others), clinical decision-making requires data across all available treatment options. Long-standing longitudinal clinical registries, like the Anti-Rheumatic Therapies in Sweden (ARTIS) database, thus have a key role in assessing the relative safety of b/tsDMARDs, allowing simultaneous comparison of all drugs used in clinical practice, with consistent definitions of treatment cohorts, follow-up, and outcomes.
Objectives: To assess incidence rates of critical safety endpoints for individual b/tsDMARDs used to treat RA, updating previously published reports and including more recently introduced treatments.
Methods: Nationwide register-based cohort study including all RA patients in Sweden registered as starting any b/tsDMARD between Jan 1st 2010 and Dec 31st 2019, and followed until Dec 31st 2020. The incidence rates of selected outcomes, identified through national healthcare registers, were compared between individual b/tsDMARDs while adjusting for a range of potential confounders (covering demographics, RA-related characteristics and disease activity, and comorbidity) using Inverse Probability of Treatment Weighting. Probabilities were predicted by multinomial logistic regression, regressing all covariates on treatment status. Exposure time was counted from treatment start until stop (+90 days' lag time), censored at emigration and death.
Results: There were clear differences between patients starting individual b/tsDMARDs, in particular with TNF inhibitors more often used as a first line b/tsDMARD; sarilumab, baricitinib, and tofacitinib predominantly used later in the treatment course; rituximab used more often for older patients, and non-TNFi generally used more frequently for patients with higher disease activity or comorbidity. Expectedly, these differences translated into differences in the crude rate of safety endpoints. Several differences remained after confounder-adjustment (Table 1), including a higher rate of treatment discontinuation due to adverse events on baricitinib, tofacitinib, and sarilumab. Rituximab was associated with higher rates of several outcomes, but the confounder-adjustment markedly reduced risks and residual confounding likely explain part of the remaining increase. Baricitinib and tofacitinib were associated with higher rates of hospitalised herpes zoster, but not with similarly elevated rates of other serious infections. There were no clear differences in the rate of cardiovascular events or severe depression. Low number of events limit the comparison, in particular for sarilumab and tofacitinib.

Table 1. Weighted incidence rate per 1,000 person-years of selected safety outcomes.

DMARD	N	Discont. due to. adverse event	ACS	Stroke	Liver disease	Hosp. infection	Hosp. Herpes zoster	Hosp. depression	Any hosp.	All-cause mortality
ETA	8244	45	6.2	4.5	1.4	32	2.9	2.3	156	10.8
ADA	5069	46	5.9	5.6	1.1	36	3.5	1.5	166	9.5
INF	2832	50	8.2	5.8	3.1	43	3.2	2.0	197	12.7
CER	2072	54	6.4	7.0	2.5	34	3.6	1.7	172	11.0
GOL	1796	51	5.9	6.8	-	32	2.8	-	154	11.5
ABA	3254	56	7.3	4.7	1.9	36	2.3	1.6	172	13.9
RTX	3990	31	8.4	6.2	2.2	41	3.3	2.4	194	15.1
TCZ	2619	30	5.7	5.0	2.1	31	2.9	1.6	163	15.7
SAR	271	100	-	-	-	18	-	-	298	-
BARI	1665	69	3.0	4.2	1.4	37	8.8	2.6	173	16.7
TOFA	392	82	-	-	-	32	12.9	-	129	-

Note: Rates based on <5 events set to '-'

Conclusion: We found large differences in the rate of treatment discontinuations due to adverse events across b/tsDMARDs, which were not generally mirrored by corresponding differences in the rates for specific serious adverse events.
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Bénédicte Delcoigne: None declared, Nils Feltelius Employee of: NF is employed by the Medical Products Agency (MPA), which is a governmental body. The views in this abstract may not represent the views of the MPA, Helena Forsblad-d'Elia: None declared, Elisabet Lindqvist: None declared, Ulf Lindström: None declared, Johan Askling Grant/research support from: Karolinska Institutet has entered into agreements with the following companies, with JA as PI: Abbvie, BMS, Eli Lilly, Galapagos, Janssen, Pfizer, Roche, Samsung Bioepis and Sanofi.

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POS0638 RECOMMENDATIONS FOR COST-EFFECTIVE USE OF BIOLOGICAL AND TARGETED SYNTHETIC DMARDS IN INFLAMMATORY ARTHRITIS: RESULTS FROM AN INTERNATIONAL DELPHI STUDY

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Background: Biological and targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs) are effective treatments for rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA), but associated with high costs. Therefore, various strategies for safe and cost-effective use of these drugs have been developed, such as tapering and biosimilar use. However, overarching recommendations on how clinicians or hospitals can use these strategies in clinical practice are absent.
Objectives: To develop evidence-based multidisciplinary recommendations on strategies for cost-effective use of b/tsDMARDs in the treatment of RA, PsA and SpA.
Methods: A task force was formed consisting of 13 experts in rheumatology, epidemiology and/or pharmacology from seven European countries. Relevant strategies for cost-effective use were collected and defined using one-to-one interviews with each task force member followed by group discussion. Next, a scoping review in PubMed and Embase was performed to summarize the evidence on each strategy, followed by a Delphi procedure and five online meetings, to form a set of overarching principles and recommendations. Levels of evidence and strengths of recommendations were determined in accordance with the 2018 EULAR additional guidance.[1] If consensus was reached on the formulation of the recommendation in the group meeting, voting on level of agreement was performed by every task force member separately using an online form. Level of agreement varied from 0 (completely disagree) to 10 (completely agree).
Results: Twelve strategies for cost-effective use of b/tsDMARDs were identified and four overarching principles were formulated (Table 1). For 10 strategies, there was enough evidence available to form one or multiple recommendation(s). In total, 20 recommendations were formulated, focussing on: the use of loading doses (2); the use of biosimilars where available (2); combining a csDMARD with a b/tsDMARD to maximise efficacy (3); the use of disease activity guided dose optimisation (4); the use of a drug formulary policy in clinical practice (1); considering using a lower dose where approved (2); improving medication adherence (1); non-medical drug switching within or between drug classes (1); therapeutic drug monitoring and other predictors for selecting or tapering a b/tsDMARD (2); and the use of different routes of administration of the same b/tsDMARD (2). The level of agreement for the recommendations varied between 7.9 (SD 1.2) and 9.8 (0.4).

Table 1. Overview of strategies (A) and overarching principles (B) for cost-effective use of b/tsDMARDs in RA, PsA and SpA

A.Strategies	
Avoid dose loading	Biosimilar/generic drug use
Combination therapy	Disease activity guided dose optimisation
Drug formulary policy	Drug wastage
Initial lower dose	Medication adherence
Nonmedical drug switching	Optimizing pharmacokinetic exposure
Response prediction	Route of administration
B.Overarching principles	
Cost-effectiveness considerations are an important aspect of treatment, and rheumatologists should have a leading role regarding this.	
Treat-to-target is the cornerstone of b/tsDMARD based treatment in RA, PsA and axSpA.	
Treatment choices must be based on shared decision making between the patient and the rheumatologist.	
Reimbursement policies should cover cost-effective use of pharmacological treatments, both on- and off-label, when they are evidence based and supported by (inter)national guidelines.	

Conclusion: These evidence-based recommendations provide caregivers in rheumatology with a consensus on strategies for cost-effective use of b/tsDMARDs in RA, PsA and SpA. Because high-quality evidence was limited, we were not able to formulate recommendations on all strategies.

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POS0639 PHARMACOKINETIC BOOSTING TO ENABLE A ONCE-DAILY REDUCED DOSE OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Tofacitinib is an effective drug for rheumatoid arthritis (RA) and psoriatic arthritis (PsA). As tofacitinib is metabolized by the CYP3A4-enzyme, the manufacturer recommends to reduce the dose with 50% when combined with CYP3A4-inhibitors. This creates an opportunity to improve cost-effectiveness and patient experience by deliberately combining tofacitinib 5 mg once daily with a registered CYP3A4-inhibitor, cobicistat.
Objectives: Primary: pharmacokinetic (PK) bioequivalence of tofacitinib 5 mg and cobicistat 150 mg once daily (intervention) to tofacitinib 5 mg twice daily (control). Secondary: clinical efficacy (DAS28-CRP), safety, patient preference, and predictive modelling of long-term DAS28 and ACR20 response.
Methods: This open-label, cross-over, monocentre study (Sint Maartenskliniek, The Netherlands) included patients with RA or PsA, using tofacitinib 5mg twice daily for ≥ 14 days without co-medication affected by CYP3A4-inhibition. At the first sampling day, plasma samples of tofacitinib were collected pre-dose and 0.5, 1, 2, 3, 4, 6, 9 and 12 hours post-dose. Subsequently, patients switched treatment to tofacitinib 5 mg and cobicistat 150 mg once daily, and 2-6 weeks thereafter, another PK sampling was performed at the same timepoints and additionally at 24 hours post-dose. PK bioequivalence was defined as the 90% confidence interval of the average tofacitinib concentration ($C_{avg,ss}$) geometric mean ratio (GMR) falling between 80-125%. Secondary endpoints included efficacy (change in mean DAS28-CRP between sampling days), safety, and patient preference (7-point Likert scale at study end). Additionally, differences between both regimens in DAS28 and probability of ACR20 response were predicted using a validated PK/PD model.[1]
Results: Between September 2019 and March 2021, 27 participants were included. Twenty-five participants completed both PK measurements and were included in the primary analysis. The $C_{avg,ss}$ GMR was 84.8%, 90% CI 75.1% to 95.6%. The difference in absolute DAS28-CRP was 0.05 (95% CI -0.50 to 0.59, intervention to control). There were no significant or relevant

differences in adverse events between both regimens. Patient preference was 56% for intervention (Likert score 5-7), versus 18% for control (score 1-3). Median differences in predicted DAS28 and probability of ACR20 response were 0.03 (95% CI -0.16 to 0.22; intervention-control) and -0.01 (-0.07 to 0.05), respectively.

Conclusion: Due to slightly lower tofacitinib concentrations during combination therapy, pharmacokinetic bioequivalence could not formally be established. However, because of comparable short-term clinical efficacy and safety, a clear patient preference and no relevant differences in predicted DAS28 and ACR20-response at maximum efficacy, pharmacokinetic boosting seems an attractive strategy to improve cost-effectiveness of tofacitinib treatment.

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Table 1. Baseline characteristics

	Participants (n=27)
Age (years)	57 ± 11
Female gender	15 (56%)
Weight (kg)	85 ± 21
GFR calculated by CKD-epi (ml/min/1.73m^2)	80 ± 14
Disease	
• RA	17 (63%)
• RF and/or ACPA positive (RA only)	14 (82%)
• PsA	10 (37%)
Disease duration (years)	11 (4-18)
Tofacitinib use ≤ 3 months	22 (81%)
DAS28-CRP at baseline	3.27 ± 1.41
Concomitant csDMARD use	8 (30%)
• methotrexate	4 (15%)
• leflunomide	4 (15%)
Previous b/tsDMARDs (n)	3 (2-4)

Either displayed as number (%), mean ± standard deviation or median (interquartile range). Percentages were calculated over the total number of participants unless indicated otherwise.

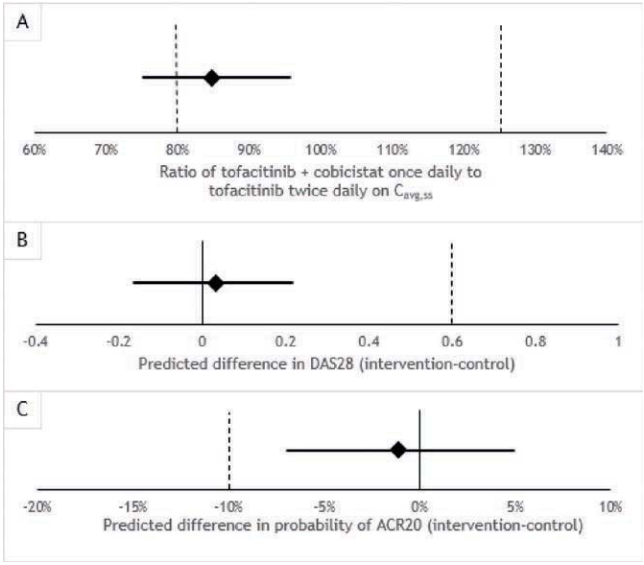

Figure 1. Visual representation of measured bioequivalence (A), and predicted difference in DAS28 response (B) and probability of ACR response (C)

A: GMR (diamond) with 90% CI; vertical dotted lines: equivalence margin (80-125%). B/C: median predicted value (diamond) with 95% CI; vertical dotted line: post-hoc noninferiority margins (+ 0.6 for DAS28 and -10% for ACR20).

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POS0640

REAL-WORLD EFFECTIVENESS AND SAFETY OF GP2015 IN PATIENTS WITH RHEUMATIC DISEASES: FINAL RESULTS OF THE COMPACT STUDY

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Background: COMPACT is a non-interventional study evaluating the effectiveness and safety in patients (pts) with rheumatoid arthritis (RA), axial-spondyloarthritis (axSpA) or psoriatic arthritis (PsA) treated with GP2015 (an etanercept [ETN] biosimilar) in real-world conditions.

Objectives: We present the effectiveness and safety data from the final analysis of the COMPACT study for all patient groups.

Methods: Pts aged ≥18 years on treatment with GP2015 were enrolled. Baseline visit corresponded with date of study inclusion and not with date of GP2015 treatment start. Pts were categorised based on prior treatment status: pts on clinical remission or low disease activity under treatment with reference ETN or biosimilar ETN (initial ETN: [iETN]) and switched to GP2015 (Group A) or pts who received non-ETN targeted therapies and switched to GP2015 (Group B) or biologic-naïve pts who started GP2015 after conventional therapy failure (Group C) or DMARD-naïve pts with recent diagnosis of RA considered suitable for treatment initiation with a biologic and started on treatment with GP2015 (Group D). Effectiveness assessments included Disease Activity Score 28-joint count Erythrocyte Sedimentation Rate (DAS28-ESR) or Ankylosing Spondylitis Disease Activity Score (ASDAS) until Month 12 after enrolment (baseline) in the study.

Results: Of the 1466 pts enrolled, 572 were switched from iETN (Group A), 171 were switched from other targeted therapies (Group B), 713 were biologic-naïve (Group C), and 10 were RA DMARD-naïve (Group D). Comorbidities were more frequent in pts with RA (68.7%,) followed by pts with PsA (59.4%) and axSpA (52.1%). After 12 months of treatment with GP2015, pts with RA or PsA achieved comparable DAS28-ESR scores irrespective of whether they switched from iETN, or from other targeted therapies or were biologic-naïve. At Month 12, the mean ASDAS scores were comparable between the treatment groups in pts with axSpA (Table 1). Across all pt groups, no major differences were observed in the disease activity scores between baseline and Month 12 that may be explained by the ongoing GP2015 treatment at the time of enrolment for an observed average of 138 days. Overall, the proportion of patients with at least one adverse event (AE) and serious AE (SAE) was 47.6% and 7.7% in pts who were switched from iETN, 56.7% and 9.9% in pts switched from other targeted therapies, 56% and 8.7% in biologic-naïve pts, and 60% and 0% in DMARD-naïve pts. Rate of injection site reaction was low across the groups (Figure 1).

Table 1. Effectiveness outcomes in patients treated with GP2015

Effectiveness outcomes			Group A	Group B	Group C	Group D	Overall (A-D)
RA	DAS28-ESR, n, mean (SD)		N=295	N=88	N=451	N=10	N=844
		Baseline	n=259	n=70	n=392	n=8	n=729
			2.5 (1.1)	3.6 (1.3)	3.3 (1.5)	3.8 (1.2)	3.0 (1.4)
		Month 12	n=135	n=47	n=238	n=2	n=422
			2.5 (1.3)	2.7 (1.0)	2.8 (1.4)	4.3 (2.5)	2.7 (1.3)
PsA			N=117	N=36	N=135	N=0	N=288
		Baseline	n=80	n=30	n=116	-	n=226
			2.1 (1.0)	2.9 (1.6)	2.9 (1.6)		2.6 (1.5)
		Month 12	n=32	n=13	n=60	-	n=105
			2.6 (1.9)	2.6 (1.6)	2.3 (1.4)		2.4 (1.5)
AxSpA	ASDAS, n, mean (SD)		N=160	N=47	N=127	N=0	N=334
		Baseline	n=77	n=18	n=59	-	n=154
			1.6 (0.6)	1.8 (0.8)	2.3 (0.9)		1.9 (0.8)
		Month 12	n=39	n=8	n=23	-	n=70
			1.8 (0.9)	1.9 (0.6)	1.9 (1.0)		1.8 (0.9)

N, total number of patients in the treatment group; n, number of patients with available data at each time point, SD, standard deviation

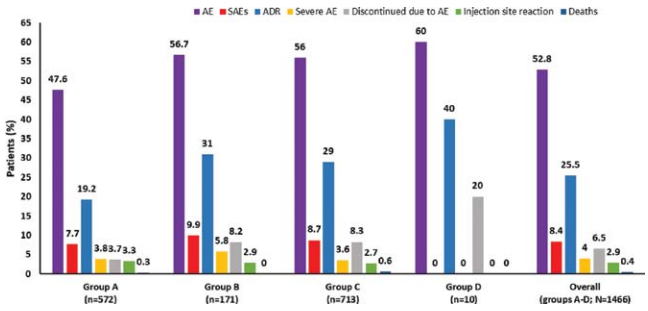

Figure 1. Overall safety outcomes in patients treated with GP2015Figure 1 represents the adverse events reported during GP2015 treatment.N, total number of patients in the treatment; n, number of patients in each treatment group

Conclusion: The results show comparable disease activity scores between pts who were switched from iETN, pts switched from other targeted therapies and biologic-naïve pts after 12 months of treatment with GP2015. No impact on the effectiveness of ETN was observed in pts with RA, axSpA or PsA who switched to GP2015. No new safety signals were reported.

Disclosure of Interests: Marc Schmalzing Speakers bureau: Novartis, AbbVie, Chugai/Roche, Janssen-Cilag, Lilly, Consultant of: AstraZeneca, Chugai/Roche, Hexal/Sandoz, Gilead, AbbVie, Janssen-Cilag, Boehringer/Ingelheim, Grant/research support from: Chugai/Roche, Boehringer/Ingelheim, Celgene, Medac, Herbert Kellner: None declared, Ayman Askari: None declared, Javier de Toro Santos: None declared, JULIO CESAR VAZQUEZ PEREZ-COLEMAN Speakers bureau: Sandoz, Abbvie, Sanofi, Fresenius, Rosario Foti Speakers bureau: Abbivie, Gilead, Lilly, Pfizer, UCB, Roche, Novartis, Pfizer, UCB, Sławomir Jeka: None declared, Boulos Haraoui Consultant of: Abbvie, Amgen, Fresenius Kabi, Lilly and Pfizer, Grant/research support from: Abbvie, Amgen, Fresenius Kabi, Lilly and Pfizer, Yannick Allanore Consultant of: Sandoz Hexal, Mylan, Astra-Zeneca, Masiur Rahman Employee of: Sandoz Hexal AG, Fabricio Furlan Employee of: Sandoz Hexal AG, Sohaib HACHAICHI Employee of: Sandoz Hexal AG, Tom Sheeran Speakers bureau: Pfizer, UCB, Roche, Consultant of: Novartis, Pfizer, Grant/research support from: Novartis, UCB, Roche

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POS0641 A RANDOMISED PHASE I PHARMACOKINETIC STUDY COMPARING HIGH-CONCENTRATION, LOW-VOLUME, AND CITRATE-FREE SB5 (40 MG/0.4 ML) WITH PRIOR SB5 FORMULATION, AND ADALIMUMAB BIOSIMILAR, IN HEALTHY MALE SUBJECTS

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Background: SB5, an adalimumab (ADL) biosimilar, was developed in a low-concentration (40 mg/0.8 mL, SB5-LC) aligned with the reference ADL product. Pharmacokinetics (PK) equivalence of SB5 and reference ADL was demonstrated in a Phase I study conducted in healthy subjects[1]. Equivalent efficacy and comparable safety between 40 mg/0.8 mL SB5 and 40 mg/0.8 mL reference ADL were demonstrated in a Phase III study conducted in patients with rheumatoid arthritis[2]. High-concentration, low-volume, citrate-free SB5 (40 mg/0.4 mL, SB5-HC) has been developed as a part of life cycle management in line with the reference ADL formulation.

Objectives: To compare the PK, safety, and tolerability of the newly developed SB5-HC (40 mg/0.4 mL) to prior SB5-LC (40 mg/0.8 mL) in healthy male subjects.

Methods: This study was a randomised, single-blind, two-arm, parallel group, single-dose study in healthy male subjects. Subjects were randomised in a ratio of 1:1 to receive a single dose of either SB5-HC or SB5-LC by subcutaneous injection on Day 1 and then observed for 57 days during which the PK, safety, and immunogenicity were evaluated. The serum concentration of ADL was measured using an enzyme-linked immunosorbent assay. The primary PK parameters were area under the concentration-time curve from time zero to infinity (AUC_{inf}) and maximum serum concentration (C_{max}). Equivalence for the primary PK parameters was to be concluded if the 90% confidence intervals (CIs) for the ratio of geometric least squares means (LSMeans) of the treatment groups compared were completely contained within the pre-defined equivalence margin of 0.80 to 1.25 using an analysis of variance.

Results: Of 188 randomised subjects, 187 subjects were analysed as PK Analysis Set (PKS) (n=93 in SB5-HC and n=94 in SB5-LC). One subject was excluded from the PKS in SB5-HC group (major protocol deviation for not being withdrawn in the event of confirmed COVID-19). The geometric LSMeans ratios for the comparison of SB5-HC and SB5-LC for AUC_{inf} and C_{max} were 0.920 and 0.984, respectively, and the corresponding 90% CIs were within the pre-defined equivalence margin of 0.80 to 1.25 (Table 1), indicating the two treatment groups are bioequivalent. There were no deaths, serious adverse events or discontinuation of the study due to treatment-emergent adverse events (TEAEs) during the study. The proportions of subjects who experienced TEAEs were comparable between the two treatment groups (44.7% in SB5-HC vs 51.1% in SB5-LC). The most frequent TEAEs were headache (10.6% in SB5-HC vs 12.8% in SB5-LC).

Table 1. Comparison of Primary PK Parameters between the Treatments

PK Parameter	Treatment	Geometric LSMean	Ratio	90% CI
AUC_{inf} (h·µg/mL)	SB5-HC	2616.1	0.920	0.8262; 1.0239
	SB5-LC	2844.3		
C_{max} (µg/mL)	SB5-HC	4.1	0.984	0.9126; 1.0604
	SB5-LC	4.1		

Conclusion: This study demonstrated PK equivalence between SB5-HC and SB5-LC in healthy subjects. Both SB5-HC and SB5-LC were generally well tolerated with similar safety profiles.

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Disclosure of Interests: None declared

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POS0642 THE PROBABILITY OF SUSTAINING RHEUMATOID ARTHRITIS REMISSION IN PATIENTS TAPERING TARGETED THERAPY USED AS MONOTHERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Up to 30% of RA patients receive monotherapy with biologic (b) DMARDs or JAK inhibitors (i), often due to intolerance of methotrexate (MTX). Monotherapy with IL-6i and JAK-i has been reported to be effective. The EULAR research agenda includes addressing the question of whether tapering of targeted therapy (bDMARDs and JAK-i) used as monotherapy (targeted monotherapy) is possible[1].

Objectives: To assess if it is feasible to taper (stop or reduce) targeted monotherapy with controlled RA using existing clinical trial data.

Methods: A systematic review of the literature (2014-2021), cited in Medline, Embase and the Cochrane Library, was performed. Meta-analyses were conducted using random effects models. Forest and funnel plots were created and heterogeneity calculated.

Results: Our search yielded 5762 citations. After de-duplication, screening of titles/abstracts and review of full text articles, we identified 5 studies comparing tapering of targeted monotherapy (TNF-i, tocilizumab (TCZ), abatacept (ABA) and baricitinib) to continuing therapy or other tapering regimens (Table 1). In our meta-analysis of data from 800 patients we observed a trend for lower odds of remission when tapering of targeted monotherapy vs comparator treatment regimen [pooled OR 0.72 (0.35, 1.48)]. In one study comparing stopping monotherapy to continuing MTX, we saw the lowest OR 0.55 (0.20, 1.48). In studies comparing two tapering regimens the pooled OR was higher 2.17 (1.13, 4.16). There was no heterogeneity in the studies which compared tapering to continuing therapy (I^2=0.0%, p=0.437) and moderate heterogeneity in the studies that tapered different treatments in both arms (I^2=53.7%, p=0.115). Trials using a gradual tapering strategy had a numerically higher odds of remission [OR 2.15 (0.94, 4.92); 3.61(1.85, 7.04)] compared to a trial implementing abrupt withdrawal [OR 1.19 (0.53, 2.68)]. There was a trend for higher remission outcomes in studies of early RA [pooled OR 1.71 (0.72, 4.05)] compared to established RA [pooled OR 1.12 (0.29, 4.27)] (Figure 1). Funnel plots indicate a paucity of studies, and perhaps publication bias.

Conclusion: There are no trials designed to compare tapering targeted monotherapy to continuing it, indicating a significant gap in knowledge in an area of increasing clinical relevance for our patients. There was insufficient evidence to demonstrate the significant effects of tapering targeted monotherapy in RA. Only one study out of 5 compared stopping targeted monotherapy to continuing therapy (MTX), and reported a low OR of remission. Three studies tapered therapy in both arms and one study performed a dose reduction. Our review suggests that stopping targeted monotherapy is unlikely to maintain disease control. More gradual tapering schemes, dose reduction and early treatment of disease may be associated with more successful tapering. More studies are needed to better inform our patients. Currently, we do not recommend stopping targeted monotherapy in RA.

Table 1. Included studies.

Author/year	n	Early RA	Mean Age Range	Baseline treatment	Tapering strategy	Comparison arm intervention	Remission Outcome	Follow up
van Mulligen 2020	189	No	56-57	csDMARD + TNFi	Taper csDMARD then TNFi	Taper in reverse order	DAS44 < 1.6	24 mos
Kaneko 2018	102	No	54-58	TCZ+MTX vs TCZ	Stop TCZ	Continue MTX	DAS28 < 2.6	104 wks
Bijlsma 2016	299	Yes	54	TCZ+MTX vs TCZ vs MTX	Gradual taper MTX 1st then TCZ	Gradual taper MTX	DAS28 < 2.6+SJC≤4	104 wks
Emery 2015	176	Yes	45-49	ABA+MTX vs ABA vs MTX	Stop ABA	Stop ABA Taper MTX off	DAS28-CRP<2.6	18 mos
Takeuchi 2019	69	Yes	48-53	Bari 4mg	Reduce 2mg	Continue 4mg	CDAI < 2.8	48 wks

ABA abatacept, Bari baricitinib, CDAI Clinical disease activity index, csDMARDS conventional synthetic DMARDs, DAS28 Disease Activity Score 28, MTX methotrexate, SJC swollen joint count, TCZ tocilizumab, wks weeks, mos months.

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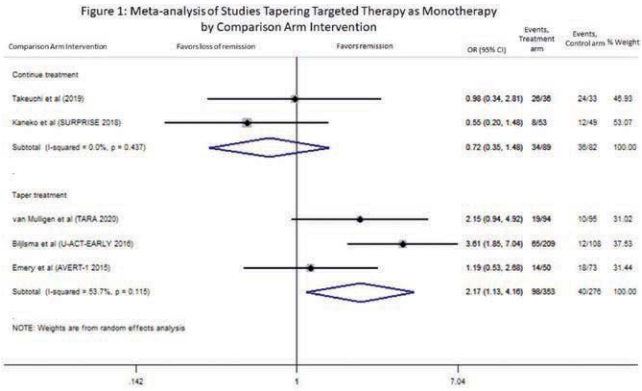

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POS0643

SUSTAINABILITY OF RESPONSE BETWEEN UPADACITINIB AND ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS THROUGH 3 YEARS FROM THE SELECT-COMPARE TRIAL

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Background: The primary treatment target for patients with active rheumatoid arthritis (RA) is sustained clinical remission (REM) or low disease activity (LDA).[1,2] A greater proportion of patients with RA and inadequate response to methotrexate (MTX) receiving the JAK inhibitor, upadacitinib (UPA), achieved REM/LDA compared with adalimumab (ADA), both with background MTX, through 26 weeks in the phase 3, SELECT-COMPARE trial.[3]

Objectives: We assessed sustainability of response over 3 years in UPA-treated patients with RA.

Methods: SELECT-COMPARE included a 26-week, double-blind, placebo (PBO)-controlled period, a 48-week, double-blind active comparator-controlled period, and an ongoing long-term extension for up to 10 years. Patients on background MTX received UPA 15 mg once daily, PBO, or ADA 40 mg every other week. Patients who did not achieve at least 20% improvements in tender and swollen joint counts (Weeks 14-22) or LDA (CDAI ≤10 at Week 26) were rescued from UPA to ADA or PBO/ADA to UPA. This post hoc analysis evaluated clinical REM (CDAI ≤2.8; SDAI ≤3.3), LDA (CDAI ≤10; SDAI ≤11), and DAS28(CRP) <2.6/≤3.2 at first occurrence (prior to treatment switch [rescue]), as well as over 3 years following initial response in patients randomized to UPA or ADA. For those patients who achieved REM/LDA, Kaplan-Meier was used to define the time from when the response was first achieved to the earliest date at which the response was lost at two consecutive visits, discontinuation of study drug, or losing response at the time of rescue. The predictive ability of time to CDAI REM/LDA was assessed using Harrell's concordance (c)-index (range: 0 [all predictions wrong] to 1.0 [perfect predictive ability]. Non-responder imputation was used for missing data.

Results: Through 3 years, a significantly higher proportion of patients receiving UPA + MTX vs ADA + MTX achieved CDAI REM (47% vs 35%, $P = 0.001$) as well as CDAI LDA (70% vs 60%, $P = 0.001$). At 30 months after first occurrence of response, CDAI REM/LDA was sustained in 19%/42% of patients randomized to UPA and 10%/30% of patients randomized to ADA (Figure 1). Time to initial clinical response did not appear to be predictive of sustained disease control. The c-index for CDAI REM/LDA was 0.50/0.60 on UPA vs 0.49/0.56 on ADA. Through the last follow-up visit, 37%/58% of patients receiving UPA and 27%/48% on ADA remained in CDAI REM/LDA, respectively (Figure 2). Of patients who lost CDAI REM, 68% on UPA and 55% on ADA remained in LDA. Additionally, roughly similar proportions on UPA and ADA recaptured CDAI REM/LDA (UPA, 40%/17%; ADA, 48%/19%). Similar results were observed for REM/LDA based on SDAI and for DAS28(CRP) <2.6/≤3.2.

Conclusion: Among patients with inadequate response to MTX, a higher proportion receiving UPA + MTX achieved remission or LDA across disease activity measures vs ADA + MTX. UPA-treated patients demonstrated a consistently higher sustained response rate over 3 years compared to those receiving ADA. Furthermore, significant proportions of patients who lost response on either UPA or ADA were able to recapture remission or LDA.

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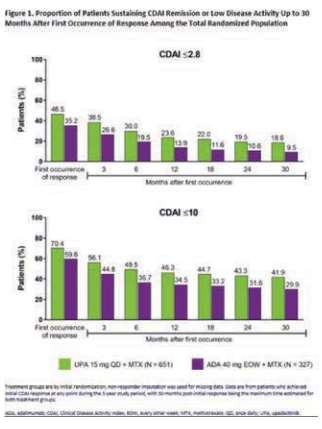

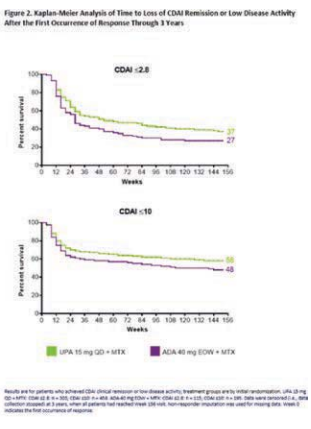

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POS0644

IMPACT OF FIBRE AND RED/PROCESSED MEAT INTAKE ON TREATMENT OUTCOMES AMONG PATIENTS WITH CHRONIC INFLAMMATORY DISEASES INITIATING BIOLOGICAL THERAPY: A PROSPECTIVE COHORT STUDY

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Background: Crohn's disease (CD), Ulcerative Colitis (UC), Rheumatoid Arthritis (RA), Axial Spondyloarthritis (axSpA), Psoriatic Arthritis (PsA), and Psoriasis (PsO) are known as Chronic Inflammatory Diseases (CID). These CID's are prevalent diseases that share pathophysiological pathways, genetics, environmental factors and pharmacological therapies. Biologic disease-modifying drugs have revolutionised the treatment of CIDs but unfortunately up to 60% of the patients have no or only suboptimal response to the treatment. Aside pharmacologic treatment, many patients are interested in self-management strategies for their symptoms and often request dietary recommendations. However, sound evidence for such recommendations is lacking [1].

Objectives: To investigate if the treatment outcome of biological therapy (e.g. a TNF inhibitor) is associated with the habitual dietary intake of fibre and red/processed meat in patients with a CID [2].

Methods: In this prospective multicentre cohort study we consecutively enrolled 233 adult patients with a diagnosis of CD, UC, RA, axSpA, PsA or PsO for whom biologic therapy was planned. The Intention-to-Treat (ITT) population was defined as those with completed baseline food frequency questionnaires enabling stratification into a high fibre/low red and processed meat exposed group (HFLM) and an unexposed group (low fibre/high red and processed meat intake = LFHM). This was determined by the ratio of fibre to red/processed meat intake whereby HFLM constituted the upper tertile of the study sample and LFHM constituted the two lower tertiles of the study sample. The primary outcome was the proportion of patients with a clinical response to biologic therapy after 14-16 weeks of treatment. Based on the ITT population, differences between the dietary phenotypes in terms of the clinical response rate were analysed (while adjusting for the specific CID) in logistic regression models. **Trial registration** ClinicalTrials.gov NCT03173144.

Results: Of 193 patients included in the ITT population, we had outcome data on 176 (i.e. data from 17 patients were imputed): 114 (59%) had a clinical response to biologic therapy. In the HFLM group, 41 (64%) patients responded to treatment compared to 73 (56%) in the LFHM group, but the difference proved not to be statistically significant (Odds ratio, OR: 1.48, 95% confidence interval 0.72 to 3.05). For RA patients however, HFLM diet was associated with a clinical response in 82% compared to 28% in the LFHM group (OR: 9.84, 1.35 to 71.56). The same picture was seen for the 'As Observed' population (i.e. excluding the 17 patients without outcome data), see Figure 1. Changes in measures of health-related quality of life, physician's global assessment and C-reactive protein were comparable between groups and across conditions.

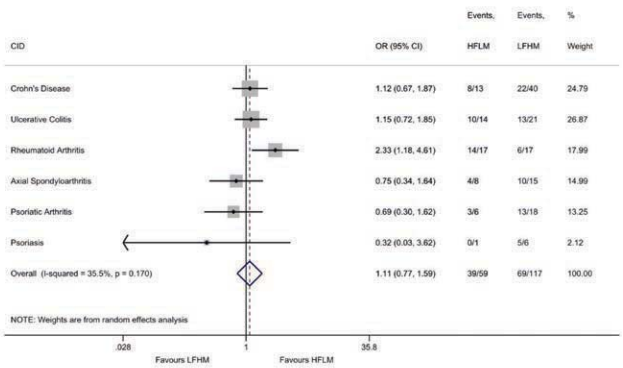

Figure 1. Meta-analysis (random effects model) of the included Chronic Inflammatory Diseases (CIDs) on the 'As Observed' population comparing clinical response to biologics in patients with a high intake of fibre and low intake of red/processed meat (HFLM) versus patients with a low intake of fibre and high intake of red/processed meat (LFHM). The horizontal lines represent the OR ± 95% CI. Event= clinical response according to the specified criteria for each CID.

Conclusion: Overall, habitual HFLM intake did not affect the clinical response to biological treatment across CIDs. However, a HFLM diet in RA patients might be associated with a better response following biological treatment.

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POS0645 LONG-TERM SAFETY AND EFFICACY OF OLOKIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS – RESULT OF AN OPEN-LABEL EXTENSION STUDY, CREDO4

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Background: Olokizumab (OKZ), an IL-6 ligand inhibitor, demonstrated significant improvements in signs and symptoms of RA vs placebo (PL) and non-inferiority to adalimumab (ADA) in doses of 64 mg every two weeks (q2w) or every 4 weeks (q4w).[1-3] Patients (pts) who completed core phase III studies, were enrolled in an open-label extension study (OLE) (ClinicalTrials.gov number, NCT03120949).
Objectives: To report long-term safety and efficacy results of OKZ in combination with MTX.
Methods: During the OLE study, pts continued OKZ 64 mg q2w or q4w, and those who were on PBO or ADA were randomized to OKZ 64 mg q2w or q4w. Adverse events (AE) were assessed through 82 weeks of the OLE treatment and an additional 20 weeks of safety follow-up. All AEs were analyzed using descriptive statistics. Efficacy assessments included proportions of pts who achieved ACR20/50/70 responses, SDAI ≤3.3, improvement in HAQ-DI ≥0.22, mean change in CDAI, and DAS-28-CRP using descriptive statistics.
Results: 2105 eligible pts were enrolled, 1709 (81.2%) pts completed the OLE treatment period and 394 (18.7%) pts discontinued treatment, mainly due to adverse events 180 (8.6%), due to subject decision 158 (7.5%) and due to lack of efficacy 9 (0.4%). Treatment emergent AE occurred in 1546 (73.5%) pts, the most common AE 809 pts (38.5%) were infections (Table 1). The most common AE leading to treatment discontinuation were infections (53 [2.5%]), investigations (43 [2.0%]) including 1% with ALT increase and blood and lymphatic system disorders (13 [0.6%]) including leuko- and lymphopenia (0.2%-0.1%). Serious AE were reported by 249 (11.8%) pts, serious infections - by 87 (4.1%) pts.

All cases, n (%)	OKZ 64 mg q2w (OLE), N=1061	OKZ 64 mg q4w (OLE), N=1043
Any AE	793 (74.7%)	753 (72.2%)
Any serious AE	120 (11.3%)	129 (12.4%)
Any AE leading to discontinuation of study drug	90 (8.5%)	87 (8.3%)
Any death	13 (1.2%)	13 (1.2%)
Any AE of special interest	611 (57.6%)	598 (57.3%)
Infections	398 (37.5%)	389 (37.3%)
Opportunistic infections	22 (2.1%)	19 (1.8%)
Malignancies	6 (0.6%)	9 (0.9%)
Basal cell carcinomas	1 (<0.1%)	2 (0.2%)
Hyperlipidemia	138 (13.0%)	120 (11.5%)
Systemic injection and hypersensitivity reactions	100 (9.4%)	99 (9.5%)
Anaphylactic reactions	0	0
Gastrointestinal perforation	2 (0.2%)	1 (<0.1%)
Neutro-, thrombocyte-, leukocyte-, pan-cytopenias	168 (15.8%)	146 (14.0%)
Potential hepatotoxicity (ALT >3 ULN)	63 (5.9%)	68 (6.5%)
Injection site reactions	34 (3.2%)	34 (3.3%)
Demyelination in peripheral or central nervous system	1 (<0.1%)	0
Autoimmune disorders	41 (3.9%)	48 (4.6%)
Serious infection	47 (4.4%)	40 (3.8%)
Any potential adjudicated major adverse cardiac events	7 (0.7%)	15 (1.4)

AE, adverse event; ALT, alanine aminotransferase; n, number of subjects; %, percentage of subjects calculated relative to the total number (N) of subjects in the population; ULN, upper limit normal

Deaths occurred in 1.2% of pts, equally distributed between the two groups with the most frequent reason being infections. Efficacy of OKZ was maintained throughout the OLE (Figure 1) and pts who switched from PBO or ADA showed the same level of improvement as those who were treated with OKZ in the core studies (data not shown).

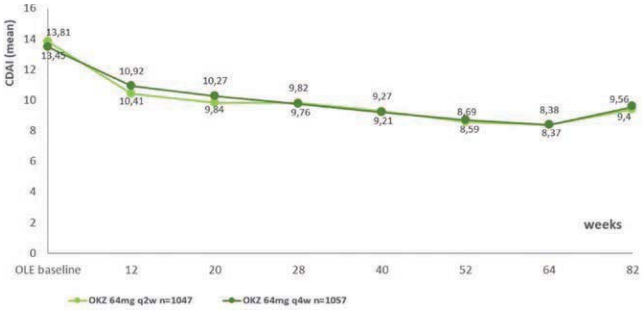

Figure 1. Mean CDAI over time (modified Intent-to-treat population). **Abbreviations**: CDAI, clinical disease activity index.

There were no apparent differences in safety and efficacy outcomes between OKZ arms, except incidence of major adverse cardiovascular events appeared slightly higher in q4w arm (Figure 1, Table 1).
Anti-drug antibodies occurred infrequently and neutralizing antibodies were rare.
Conclusion: OKZ was safe and well-tolerated that is consistent with the results of previously reported studies of OKZ and IL-6 inhibitors. Efficacy of OKZ was maintained through Wk 82 and discontinuation rates were low.

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POS0646 NON-MEDICAL SWITCHING FROM TOCILIZUMAB TO SARILUMAB IN RHEUMATOID ARTHRITIS PATIENTS WITH LOW DISEASE ACTIVITY

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Background: Tocilizumab (TCZ) and sarilumab (SRL) are IL6-receptor antagonists registered for the treatment of rheumatoid arthritis (RA). Data from extension of the ASCERTAIN trial showed that patients responding to blinded intravenous (IV) TCZ rarely experienced a loss of response when switching to open label SRL [1]. This within-class, between-drug switch has gained relevance given the recent pandemic-driven shortage of several bDMARDS including TCZ.
Objectives: To assess the efficacy and persistence of switching to sarilumab in RA patients responding well to tocilizumab.
Methods: SAARTOOS (SArilumab Actively Replacing TOcilizumab, an Open label Study) is an open, observational single arm study. RA patients doing well (DAS28-CRP<2.9 or <3.5 with clinical judgement of low disease activity) on a stable dose (>6 months) of TCZ were offered to switched to SRL in clinical care (because of lower injection frequency). Patients who switched and consented were followed for 6 months. SRL was prescribed at a dose of 200mg. The SRL dosing interval was determined by doubling patient's last TCZ dosing interval. All treatment decisions, including adjusting dose of or stopping SRL, were left to the treating physician. Co-primary outcomes were 1) the 90% confidence interval (CI) of DAS28-CRP change from baseline to month 6 compared to the non-inferiority

margin of 0.6 and 2) the 90% CI of the proportion of patients persisting with SRL at month 6, compared to a pre-specified minimum persistence of 70% at month 6. Secondary outcomes included the CDAI, proportion of patients experiencing DAS28-CRP based flare (and post-hoc the proportion of patients remaining on SRL at month 6 without flare), changes in co-medication, expectations both patient and physician on SRL efficacy and tolerability.

Results: Of 50 invited patients, 25 agreed to attempt a switch to SRL, of whom 23 patients switched and were included. Switching and therefore inclusion was halted at this point due to an observed increase in disease activity and lack of SRL persistence. One patient was lost to follow up immediately after inclusion, therefore 22 patients are included in analyses (Table 1).

Table 1. Baseline characteristics

Baseline characteristics	N=22
Age, mean (SD)	66 (11)
Female, n (%)	17 (77%)
Rheumatoid factor positive, n (%)	18 (82%)
Anti-CCP positive, n (%)	18 (82%)
Erosive disease, n (%)	14 (67%)
2010 ACR/EULAR classification criteria, n (%)	21 (95%)
DAS28-CRP, mean (SD)	1.9 (0.6)
CDAI, mean (SD) (n=15)	4.7 (3.1)
Disease duration, years, median (IQR)	20 (10-24)
Duration of tocilizumab use, years, median (IQR)	2.7 (2.1-7.3)
Tocilizumab dose, n (%)	
162mg per week	10 (45%)
162mg per 10 days	2 (9%)
162mg per 2 weeks	9 (41%)
162mg per 3 weeks	1 (5%)
Concomittant csDMARD use, n (%)	7 (32%)

DAS28-CRP changed significantly from baseline to month 6: mean 0.48 (90% CI: 0.1 to 0.9). 15 of 22 patients maintained SRL at month 6, leading to a persistence of 68% (90% CI: 51% to 82%). Both co-primary outcomes therefore failed to meet their non-inferiority criteria. DAS28-CRP change was driven by both objective and subjective components. Median (IQR) CDAI at month 6 was 7 (3-10). During the study, 8 (36%) patients experienced 1 or more DAS28-CRP based flare. Only 11 (50%) patients remained on SRL for 6 months without experiencing flare. Expectations of patients and physicians at baseline were positive, with no patients or physicians expecting worsening of either disease activity or adverse effects prior to switching. Patient preference after using SRL (n=20, 2 missings) was inconsistent, with 5 (25%) patients strongly preferring TCZ, and 5 (25%) patients somewhat or strongly preferring SRL. In terms of (co-)medication, 4 (18%) patients required additional corticosteroids (oral or intramuscular), 5 (23%) patients switched back to TCZ and 2 (9%) switched to baricitinib.

Conclusion: Non-medical switching from tocilizumab to sarilumab in patients doing well on tocilizumab is associated with a non-negligible risk of flare and non-persistence.

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POS0647

DOES TNF INHIBITOR MOLECULAR STRUCTURE MATTER? ANALYSIS OF IMPACT OF BASELINE RHEUMATOID FACTOR TITERS ON DRUG LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Elevated rheumatoid factor (RF) in patients with rheumatoid arthritis (RA) is associated with higher disease activity and increased risk for disease progression[1]. Recent publications indicate significantly lower efficacy of TNF inhibitors (TNFi) in RA patients with high RF levels compared with low/negative RF subgroup[2,3]. Fab therapy with Certolizumab pegol (CZP), a PEGylated, Fc-free monoclonal antibody (mAb), has shown comparable efficacy and consistent serum levels irrespective of baseline RF[4]. RF binds the Fc region of IgG1, the subtype used to engineer the majority of mAbs[5]. Formation of large immune complexes may likely explain the inceased clearance of mAbs in patients with high RF titers and reported reduced TNFi efficacy.

Table 1. Baseline characteristics.

Characteristics	Total (n=168)	IFX (n=90)	ADL (n=48)	CZP (n=32)	p value
Age, years*	55.5(45.3-66)	57(46-65)	50(42-64)	61(47-70)	0.08
Body mass index, Kg/m^2*	24.5(21.7-29)	24.2(21.8-27.7)	24.7(21.5-30.3)	24.6(22.2-30.3)	0.3
Male, n(%)	28(17%)	14(15%)	9(19%)	5(17%)	0.2
Disease duration, years*	8.7(4.5-14.3)	8.4 (4.4-14.3)	8.8 (3.9-16)	9.7(5-12)	0.06
Smoking status, n(%)					0.03
Currently/ex-smoker	66(39%)	29(32%)	22(48%)	16(57%)	
Non-smoker	96(57%)	61(68%)	24(52%)	12(43%)	
RF, n(%)	128(76%)	75(83%)	28(58%)	25(81%)	0.002
ACPA, n(%)	134(80%)	73(81%)	35(73%)	27(84%)	0.3
DAS28**	5.1(1.3)	5.4(1.3)	4.5(1.3)	4.9(1.3)	0.002
CRP levels*	7.8(3-21.8)	10.3(3.2-25.2)	5.1(1.4-10.1)	7.8(2.3-18.2)	0.1
Prior bDMARDs, n(%)	26(15%)	10 (11%)	10 (21%)	6(20%)	0.2
Monotherapy, n(%)	16(10%)	8(9%)	8(17%)	0	0.2
csDMARDS, n(%)	152(90%)	82(91%)	82(91%)	32(100%)	
Methotrexate, n(%)	112(67%)	64(78%)	33(83%)	17(53%)	0.2
Other csDMARDs, n(%)	24(24%)	18(22%)	7(18%)	15(50%)	0.0008
Prednisone, n(%)	85(51%)	49(54%)	21(44%)	16(50%)	0.6

*Median and interquartile range;**mean and standard deviation

Objectives: We aimed to evaluate in clinical practice whether RF levels in RA patients influence serum drug levels of 3 TNFi with different molecular structures.

Methods: We evaluated retrospectively a cohort of RA patients from La Paz University Hospital (RA-Paz Registry, 1999-2019) treated with Infliximab (IFX), Adalimumab

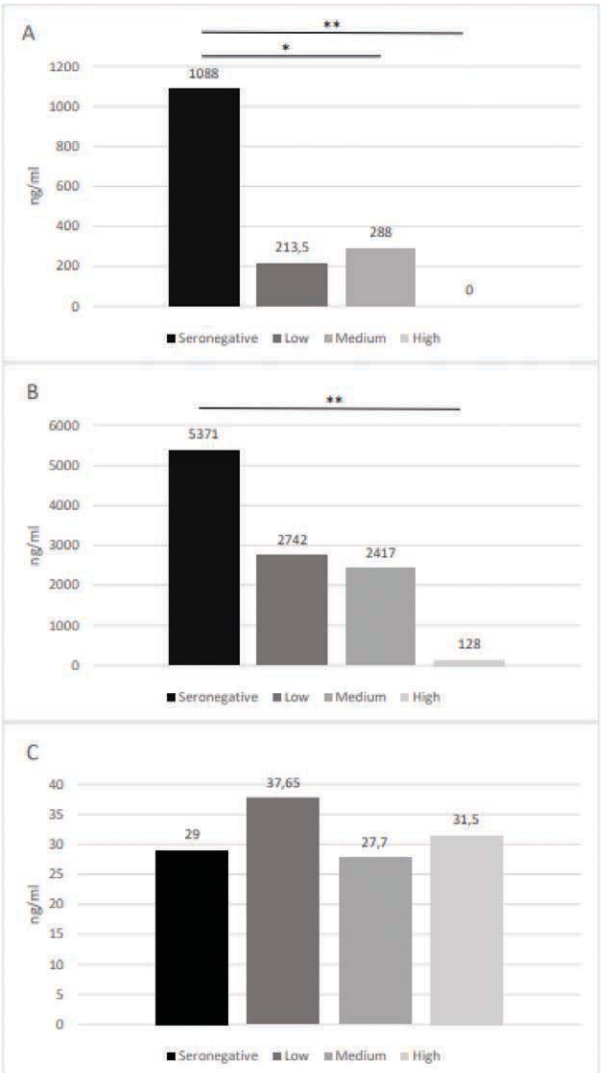

Fig. 1: Median drug levels (ng/ml) at 6 months by baseline RF titer. A: Infliximab; B: Adalimumab; C: Certolizumab pegol. *p<0.05; **p<0.01

(ADA) or CZP. Clinical and demographic data were collected at baseline (T0) and after 6 months (T6) of treatment. RF titers and serum drug levels were measured at T0 and T6 using nephelometry and ELISA respectively. Association between baseline RF titers and drug levels was assessed using non-parametric test (Mann-Whitney).

Results: 168 patients were evaluated: 90 received IFX, 48 ADA and 32 CZP. Characteristics at T0 are shown in Table 1. All patients had active disease at baseline and 76% were RF positive: ADA subgroup had lower percentage of positive RF than IFX and CZP subgroups. Patients were stratified into quartiles based on baseline RF titers: low (20-57 IU/ml), medium (57-380 IU/ml), high (>380 IU/ml) and seronegative (<20 IU/ml). Drug levels of IFX and ADA at T6 were significantly lower in those patients who had higher RF titers at T0 compared to seronegative. In contrast, CZP levels remained stable irrespectively of baseline RF titers, without significant differences among quartiles (Figure 1).

Conclusion: Higher baseline RF titers are associated with lower IFX and ADA levels at T6 in a cohort of RA patients. A concentration-response association has been clearly established for TNFi, and baseline RF levels appear to influence drug levels. Reduced immune complexes formation with CZP may result in a limited impact of baseline RF titers on drug levels.

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POS0648

SEX DIFFERENCES IN ADVERSE DRUG REACTIONS FROM BIOLOGICAL USE IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Background: Women generally report more adverse drug reactions (ADRs) than men. Information on sex differences concerning the frequency and the nature of ADRs is still limited and sex differences are often not considered in research on ADRs. Consequently, no sex specific distinction is made when reporting results of ADR analyses or when providing information to patients.

Objectives: To examine sex differences in regard to the nature and frequency of reported ADRs in patients with immune-mediated inflammatory disease (IMIDs) treated with adalimumab or etanercept.

Methods: Patients with rheumatoid arthritis (RA), psoriatic arthritis or axial spondyloarthritis using etanercept or adalimumab, were included from the Dutch Biologic Monitor (DBM). Questionnaires concerning experienced ADRs were filled out bimonthly. ADRs were coded according to Medical Dictionary for Regulatory Activities (MedDRA) terminology. Sex specific ADRs (e.g. concerning menstruation) were excluded. MedDRA Preferred Terms (PTs) were analyzed to assess the nature and frequency of ADRs. Only PTs that were reported at least four times were analyzed. Discrepancies in the distribution of the nature of reported ADRs between male and female patients were assessed using Fisher Freeman Halton with Monte Carlo simulation. Subsequently, differences in frequencies at PT level were examined using Fisher's exact tests, corrected for multiple testing using Bonferroni correction.

Results: In total 748 consecutive patients were included of which the majority (59%) was female (Table 1). 362 participants (48%) reported at least one ADR during the study. Relatively more female patients (55%) reported at least one ADR compared to male patients (38%, p<0.001). In total 882 ADRs were reported comprising 264 distinct ADRs, of which the majority (74%) was reported by female patients. The ADR distribution differed significantly between male and female patients (p=0.025). 'Injection site pruritus' (p=0.004), 'injection site inflammation' (p=0.028), 'injection site hematoma' (p=0.017), 'injection site erythema' (p=0.026), 'hematoma' (p=0.011) and 'cystitis' (p=0.044) were reported relatively more often by female patients (Figure 1). These differences were no longer statistically significant upon correction for multiple testing.

Table 1. Demographics of included patients from the Dutch Biologic Monitor stratified on sex

Participants	Male	Female
N	304	444
Age, mean ± SD[a]	58.2 ± 11.9	56.6 ± 12.9
Indication[b], N(%)		
Bechterew's disease/axial SpA	71 (23.4)	39 (8.8)
Bechterew's disease/axial SpA and PsA	4 (1.3)	8 (1.8)
Bechterew's disease/axial SpA and RA	8 (2.6)	3 (0.7)
PsA	89 (29.3)	84 (18.9)
RA	132 (43.4)	310 (69.8)
bDMARDs, N(%)		
Adalimumab	138 (45.4)	199 (44.8)
Etanercept	159 (52.3)	232 (52.3)
Switched adalimumab/etanercept	7 (2.3)	13 (2.9)
Comedication, N(%)[c]		
Methotrexate	107 (35.2)	250 (56.3)
Corticosteroids	27 (8.9)	49 (11.0)
Thiopurines	3 (1.0)	10 (2.2)
Aminosalicylates	14 (4.6)	33 (7.4)

[a]Age was missing for 1 male and 1 female patient. [b]Patients could report multiple indications. 5 male and 14 female participants also reported other indications.[c]Reported comedication is from the moment of inclusion. Eleven patients (male=3, female=8) did not start with etanercept or adalimumab at the moment they were included. For these, comedication is from the moment they reported to be treated with adalimumab or etanercept for the first time.

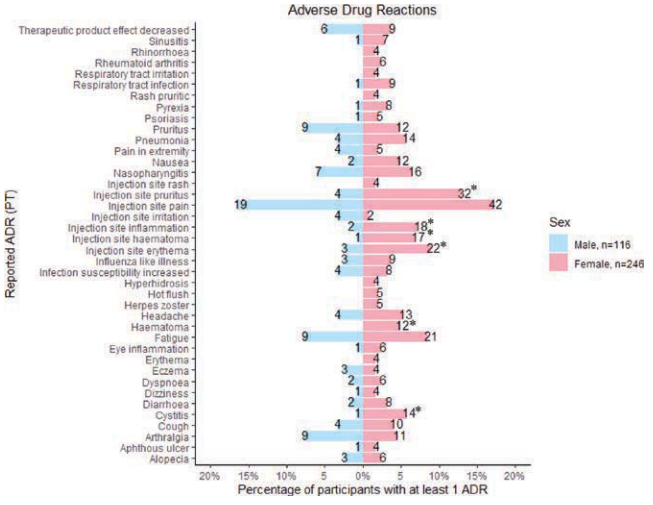

Figure 1. Top reported ADRsPercentages on the x-axis were calculated separately for sex, divided by the number of male or female patients with at least one ADR. *p-value<0.05.

Conclusion: Female patients reported relatively more ADRs than male patients. Also, the distribution of the nature of the ADRs significantly differed for male and female patients. In particular injection site reactions were reported relatively more often in female patients than in male patients. Therefore, sex differences in experiencing ADRs may exist and should be taken into consideration when investigating and reporting results on ADRs or when informing patients.

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POS0649 EFFICACY AND SAFETY OF LEVILIMAB IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: 1-YEAR RESULTS OF PHASE III, DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED TRIAL

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Background: Previously, 24-week results of phase III double-blind, placebo-controlled randomized clinical study (SOLAR) of levilimab in subjects with active rheumatoid arthritis (RA) proved a superiority of levilimab over placebo[1]. Here we present 1-year efficacy and safety data of the open-label period of the SOLAR study.
Objectives: To evaluate the efficacy and safety of levilimab in combination with methotrexate (MTX) in subjects with MTX resistant active RA.
Methods: The study was conducted at 21 clinical sites in Russia and Belarus. All randomized subjects had completed the study between November 2019 and October 2021. 154 adults, aged ≥ 18 years with confirmed diagnosis of RA[1] were randomly assigned (2:1) to receive either levilimab, 162 mg, SC (LVL QW) + MTX (n=102) or placebo (PBO) + MTX (n=52). After W24 of the study all subjects continued to receive open label levilimab +MTX. Subjects who had achieved DAS28-CRP ≤ 2.6 at W24 were switched to maintenance (Q2W) regimen of levilimab + MTX at W28: LVL QW/Q2W arm (n=27) and PBO/LVL Q2W arm (n=1). Those with DAS28-CRP > 2.6 at W28 continued with levilimab QW regimen + MTX: LVL QW/QW arm (n=75) and PBO/LVL QW arm (n=51). The efficacy analysis was done in a population of all randomized subjects (n=154). Those with missing data due to study discontinuation or rescue therapy prescription were considered non-responders. Otherwise, the analysis was performed on complete cases. Safety was assessed through monitoring of adverse events (AEs) in a population of those, who received at least one dose of LVL (n=152). Two subjects randomized to receive placebo were discontinued within first 24 weeks of the study, thus did not received any dose of levilimab and were excluded from safety analysis.
Results: Obviously, better response to the treatment was observed in LVL QW/Q2W arm as it was composed of those who had reached DAS28-CRP ≤ 2.6 at W24. At this time point 15/27 (55.6%) of them achieved ACR70; 23/27 (85.2%) achieved DAS28-CRP remission (< 2.6) and 7/27 (25.9%) achieved ACR/EULAR2011 remission of RA. After switching to LVL Q2W, rates of ACR70 and DAS28-CRP < 2.6 did not significantly changed until W52: 17/27 (63.0%) and 21/27 (77.8%), respectively, yet the proportion of subject with ACR/EULAR 2011 remission further increased and reached 12/27 (44.4%). LVL QW/QW arm was diminished by subjects who had achieved high response to treatment at W24 and composed LVL QW/Q2W arm. Thus, the ACR70, and remissions rate in this arm were close to zero at W24. However, continuation of LVL QW in those who had not achieved DAS28-CRP ≤ 2.6 at W24 induced ACR70 response in 37/75 (36.0%), DAS28-CRP remission in 35/75 (46.7%) and ACR/EULAR 2011 remission in 8/75 (10.7%) at W52. The most common adverse events (reported in ≥5% of subjects) were blood cholesterol increase (30.3%), ALT increase (23.0%), lymphocyte count decrease (17.1%), ANC decrease (16.4%). blood triglycerides increase (13.8%), bilirubin increase (11.2%), AST increase (9.9%), WBC decrease (9.9%), IGRA with M.tb antigen positive (7.2%) and injection site reactions (5.9%). No deaths were occurred.
Conclusion: Open label period confirmed the lasting efficacy and safety of levilimab in combination with MTX in subjects with MTX resistant active RA and suggested the possibility of switching to maintenance (Q2W) regimen of levilimab in those who achieved remission of RA at week 24.
Trial registration: Clinicaltrials.gov identifier NCT04397562

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POS0650 THE IMPACT OF OLD AGE ON THE PERSISTENCE AND SAFETY OF TREATMENT WITH BIOLOGIC AGENTS OR JAK INHIBITORS IN RHEUMATOID ARTHRITIS

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Background: The effect of age on persistence and safety of treatment with biologic disease modifying anti-rheumatic drugs (bDMARDs) in rheumatoid arthritis has been a subject to research interest. Two recently published studies did not observe significantly different survival of treatment with bDMARDs among older age (≥ 65 years) individuals (1,2); incidence of serious adverse events was higher in these patients (2).
Objectives: to evaluate association of the age with treatment survival and overall safety among patients receiving one or multiple courses of bDMARDs or targeted synthetic (ts-) DMARDs.

Methods: BiobadaBrasil is a multicentric registry-based cohort study of Brazilian patients with rheumatic diseases starting their first bDMARD or tsDMARD (3). The present analysis includes RA patients recruited from Jan 2009 to Oct 2019, followed-up over one or multiple (up to six) courses of treatment necessarily involving a bDMARD or tsDMARD (latest date, Nov 19, 2019). Treatment course is defined as a period during which the medication scheme does not change, except for dose adjustments. Primary outcome was the incidence treatment interruption for any reason (except for pregnancy or disease remission), while interruption due to adverse events (AEs; including death) and due to inefficacy served as secondary outcomes. Incidence of serious adverse events (SAEs) also served as a secondary outcome. Extended (frailty) multivariate Cox proportional hazards models and negative binomial regression with generalized estimating equations (to calculate incidence rate ratios [IRRs]) were used for statistical analyses (both types of analyses including time-varying covariates over multiple courses of treatment).
Results: In total, 1316 patients (2335 treatment courses, 6508 patient-years [PY]) were enrolled. Of these, 160 patients (643 PY; 237 treatment courses) were ≥ 65 years old, mean age at starting treatment = 71 ± 5 yrs (84% female). Old age was not significantly associated with treatment interruption for any reason, but presented higher risk of interruption due to adverse events (after multivariate adjustment) and lower risk of stopping because of inefficacy (see Table 1). Older patients presented higher incidence of SAEs than younger ones (16.0 vs 8.4/100 PY, respectively; multivariate IRR: 2.06, 95% CI: 1.51 to 2.80, P<0.001). Among old patients, tocilizumab (HR: 2.73, 95% CI: 1.13 to 6.64, P=0.026), etanercept (2.13, 1.12 to 4.07, P=0.022), and infliximab (2.39, 1.19 to 4.79, P=0.014) presented higher risk of treatment termination as compared with adalimumab. In this subgroup (age ≥65 yrs), there was no significant difference in the risk of SAEs between different bDMARDs/tsDMARDs.

Table 1. Univariate and multivariate hazard ratios (HRs) of interruption of treatment course comparing older (≥65 years) versus younger patients (reference category). Results are HRs, 95% CIs, and P values.

Cause of interruption (n of events)	Crude analysis	Adjusted covariates*
Interruption - any reason (1321)	0.96 (0.75 to 1.23), P=0.760	1.09 (0.82 to 1.43), P=0.550
Interruption - adverse events (368)	1.33 (0.75 to 0.89), P=0.160	1.59 (1.07 to 2.35), P=0.020
Interruption - inefficacy (680)	0.56 (0.39 to 0.80), P=0.002	0.57 (0.38 to 0.87), P=0.009

* Age, baseline DAS28, disease duration, gender, smoking, RF or anti-CCP, previous malignancy, interstitial lung disease, diabetes, hypertension, hypercholesterolemia, renal failure, ischemic cardiomyopathy, COPD, heart failure, concomitant use of each cs-, b-, and tsDMARDs, corticosteroids, starting year, osteoporosis, hepatitis B,C, treatment sequence.

Conclusion: The overall risk of treatment interruption with biologic or targeted synthetic DMARDs is not higher in older patients. Higher risk of interruption due to AE was balanced by a lower risk of stopping treatment due to inefficacy. Older patients had a higher incidence of SAEs.
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POS0651 IMPACT OF ADVERSE DRUG REACTIONS ON THE TREATMENT PATHWAYS OF EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients frequently pass through several medications in order to achieve and maintain acceptable disease control The clinical heterogeneity and variable course of the disease, plus the availability of multiple classes and subclasses of DMARDs may lead to very different and complex treatment sequencing in individual patients. Limited real-world data exists regarding treatment pathways among patients with RA. Adverse drug reactions (ADRs) belong to the stop reasons of medication, but the impact of ADRs on treatment pathways has not been quantified.
Objectives: To assess differences in treatment pathways between RA patients with and without adverse drug reactions (ADRs).
Methods: Single center retrospective observational study, using real-world data collected in the Dutch Rheumatoid Arthritis Monitoring (DREAM-RA) registry from Medisch Spectrum Twente (Enschede, the Netherlands). From all early RA patients enrolled between 16 July 2006 and 30 April 2020, the first four consecutive courses of treatment were assessed. Patients were selected from the DREAM early RA treat-to-target cohort I.[1] The use of corticosteroids per protocol was allowed but not considered as a DMARD treatment. Any alteration in (a combination of) medication was viewed as a separate treatment, and thus any addition, subtraction or change in medication was the start of a new treatment. If a patient was without continuous treatment for 90 days or more in between treatments, this was considered a temporary stop of treatment. Treatment pathways were stratified for occurrence of at least one 'ADR or 'No ADR'. Differences in duration of treatment, number of treatments, and the proportion of treatments with csDMARDs, bDMARDs and a combination of csDMARDs and bDMARDs between patients with and without ADRs are assessed.
Results: Treatment pathways of 372 RA patients (66.1% females) were assessed (Table 1). The average duration of treatment was shorter in patients that experienced at least one ADR (1.8 vs. 2.7 years, p<0.001), and the number of treatments was higher (3.5 vs. 2.5, p<0.001), than in those that experienced no ADR. Furthermore, there was a difference between these groups in the proportion of treatments with csDMARD(s), bDMARD(s) or a combination of the two (p<0.001). This was for the 'No ADR' group respectively 93%; 1%; 6%, and for the 'ADR' group respectively: 77%; 8%; 15%.

Table 1. Characteristics of patient with and without adverse drug reactions (ADRs) and treatment pathways

		All patients	Females	Males	Patients without ADRs	Patients with ADRs
Total, n (% of all patients)		372 (100.0)	246 (66.1)	126 (33.8)	285 (76.6)	87 (23.3)
Female, n (% of total)		246 (66.1)	N/A	N/A	183 (64.2)	63 (72.4)
Age at start of treatment in years, mean ±SD		57.8 ±14.0	57.3 ±14.3	59.0 ±13.2	58.4 ±14.4	56.0 ±12.3
Follow-up time in years, mean ±SD		6.7 ±3.7	6.8 ±3.6	6.6 ±3.9	6.9 ±3.8	6.2 ±3.4
Duration per treatment in years, mean ±SD		2.4 ±2.9	2.4 ±2.8	2.4 ±2.9	2.7 ±3.0	1.8 ±2.2*
Distribution of treatments:	**1**	113 (30.4)	72 (29.3)	41 (32.5)	104 (36.5)	8 (9.2)
number of patients that received 1, 2, 3 or 4 treatments, n (%)	**2**	25 (6.7)	18 (7.3)	7 (5.6)	20 (7.0)	5 (5.8)
	3	83 (22.3)	53 (21.5)	30 (23.8)	70 (24.6)	13 (14.9)*
	4 or more	151 (40.6)	103 (41.9)	48 (38.0)	91 (31.9)	61 (70.1)
Number of treatments, mean ±SD		2.7 ±1.3	2.8 ±1.3	2.7 ±1.3	2.5 ±1.3	3.5 ±1.0*
Number of patients stopped with treatment, n (% of total)		84 (22.6)	56 (22.8)	28 (22.2)	71 (24.9)	18 (20.7)

* p<0.001

Conclusion: Treatment pathways for patients with and without ADRs differ significantly. Patients that experience ADRs have shorter duration of treatments and have more consecutive treatments utilizing more bDMARDs.
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Disclosure of Interests: Fenna Poppelaars: None declared, Jurriaan Jansen: None declared, Peter ten Klooster: None declared, Tristan Coppes: None declared, Kimberly Velthuis: None declared, Harald Vonkeman Speakers bureau: Amgen, BMS, Celgene, Galapagos, GSK, Janssen-Cilag, Lilly, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Grant/research support from: Abbvie, Sanofi-Genzyme, Naomi Jessurun: None declared
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POS0652 LONG-TERM EFFECTIVENESS OF ULTRA-LOW DOSES OF RITUXIMAB IN RHEUMATOID ARTHRITIS

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Background: The optimal rituximab (RTX) dose for the treatment of rheumatoid arthritis remains unclear. RTX treatment of 1000mg per 6 months and 2000mg per 6 months were shown to be similarly efficacious (1). The REDO trial showed comparable the 6-month efficacy of continued treatment with 500mg and 200mg compared to 1000mg, though formal non-inferiority could not be established (2).
Objectives: To assess the long-term effects of ultra-low dose RTX (1×500mg and 1×200mg) in RA patients previously responding well to conventional low dose RTX (1×1000mg).

Methods: Patients from the REDO trial were invited to participate in this study. Treatment decisions were left at the discretion of the rheumatologist and patient. Disease activity (DAS28-CRP), and medication use (b/tsDMARD, csDMARD, gluccocorticoids [GC]) were collected from start of the trial to censoring in April 2021. The primary outcome was disease activity, secondary outcomes were RTX persistence, RTX doses and intervals, and use of comedication. Disease activity was analyzed using a longitudinal mixed model with random intercepts to account for intra-patient correlations, in two ways: 1. By original randomization and stratification factors (RF/ACPA and csDMARD use). 2. By time-varying total RTX dose received in the year preceding each disease activity measurement, adjusted for current csDMARD or GC use, and RF/ACPA. The original DAS28-CRP non-inferiority (NI) margin of 0.6 was used.

Results: 118 out of 142 REDO patients were included in current analyses (Table 1) Reasons for exclusion were: continuing treatment elsewhere (n=3), no informed consent (n=9) and data yet to be collected in 2 study centers (n=12). Mean follow up was 3.2 years (total of 377 patient-years), with 7 patients switching to another b/tsDMARD (Figure 1) upon which they were censored from disease activity analyses.

Table 1. Patient characteristics by original randomization

	1000mg (n=24)	500mg (n=48)	200mg (n=46)
Age (years)	65 (9)	64 (11)	64 (12)
Female	15 (63%)	28 (58%)	34 (74%)
Meeting ACR1987 or ACRU/EULAR 2010 RA criteria	22 (92%)	47 (98%)	43 (93%)
Disease duration (years)	14 (9-24)	14 (7-21)	13 (8-20)
RF or ACPA positive	22 (92%)	44 (92%)	40 (87%)
Duration of rituximab use (years)	3.0 (1.6-5.5)	2.0 (1.0-5.5)	3.7 (2.0-5.7)
Concomitant csDMARD	17 (71%)	29 (60%)	27 (59%)
Previous number of b/tsDMARDs used	2 (2-2)	2 (1-3)	2 (1-2)
Previous number of csDMARDs used	3 (1-3)	2 (1-4)	3 (1-3)
Oral GC use at baseline	3 (13%)	8 (17%)	5 (11%)
Baseline DAS28-CRP	2.3 (0.9)	2.3 (0.9)	2.5 (1.1)

Data are n (%), mean (SD), or median (IQR).

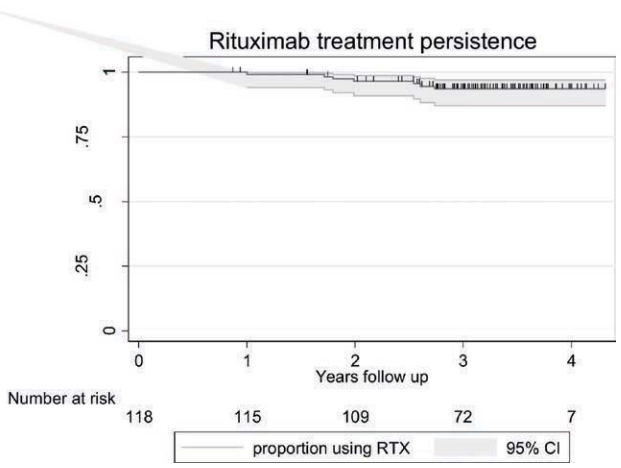

Figure 1. Rituximab treatment persistence during follow up.

Disease activity in both ultra-low dose groups was non-inferior to the 1000mg group, with a mean DAS28-CRP (95% CI) during follow-up of 2.2 (2.0-2.4) in the 1000mg group, 2.2 (2.1-2.4) in the 500mg group and 2.3 (2.2-2.5) in the 200mg group. Analyzed by received RTX dose, lower RTX dose was significantly associated with a higher DAS28-CRP: 0.15 (95% CI: 0.04-0.26) points higher per 1000mg more RTX. The upper limit for relevant RTX doses was below the prespecified NI margin, excluding a relevant effect of RTX dose on disease activity. Median (IQR) yearly RTX dose was 978mg (704mg-1425mg). Final RTX dose per infusion was 200mg in 37 patients (31%), 500mg in 47 (40%) and 1000mg in 34 (29%), with a median (IQR) final interval between infusions of 6.0 (5.7-6.5), 6.2 (6.0-7.4) and 6.4 (6.0-9.6) months respectively. The rate of GC injections was 0.38 (95% CI: 0.32-0.44) per patient-year and initiation rate of oral GC was 0.05 (0.03-0.08) per patient-year.

Conclusion: A majority of patients treated with ultra-low dose RTX remained on ultra-low doses for up to 4 years, while disease activity remained low and did not relevantly differ between RTX doses, either according to original randomization or by received dose. Switching to other b/tsDMARDS or use of GC was rarely required.

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POS0653

CAN DOSAGE OF INFLIXIMAB BE ADJUSTED TO 8 WEEK INTERVALS WITHOUT LOSING EFFICACY IN ARTHRITIS PATIENTS ON MAINTENANCE THERAPY WITH MORE FREQUENT INFUSIONS?

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Background: Infliximab is usually given every 8 weeks. To increase dosage, the dose can be increased or the interval between infusions shortened. To minimize patient visits and workload for the medical staff during the Corona pandemic, we intended to change all infliximab infusions to 8 week intervals. For patients with inflammatory bowel disease, a trough level of serum (s-) concentration of infliximab of 3-7 µg/ml is recommended. In Rheumatology the usefulness of assessing s-concentration is controversial. (1, 2)

Objectives: To evaluate if 8 week interval infliximab dosage, with retained weekly dose, can be used in arthritis patients, without worsening of disease activity or general health and study if s- concentration of infliximab is related to disease activity and general health.

Methods: All arthritis patients on stable infliximab treatment were evaluated at the time for infliximab infusion. Disease activity, DAS28-CRP, VAS pain, global, fatigue, doctors' global, HAQ, and ASDAS-CRP, BASFI for spondyloarthritis (SpA) patients were registered in the Swedish Rheumatology Quality registry (SRQ). Blood tests for CRP, ESR and s-concentration of infliximab were taken before infusion start. S-concentration was analysed at Karolinska Hospital, Solna, Sweden with an in-house ELISA. Antibodies were assessed if s-concentration was <0.5 µg/ml.

Patients with infusion intervals less than 8 weeks were recommended a switch to 8 week intervals with maintained weekly dose of infliximab. The new dose was given the same day and patients with changed doses were re-evaluated after 24 weeks. Paired samples T-test and Wilcoxon signed rank test for paired data were used for comparison of disease activity and general health after dosage change. Linear regression analyses were used to explore associations between s-concentration, disease activity and general health.

Results: Of 91 assessed patients, 66 with shorter intervals were recommended dosage change. The remaining 25 patients had infliximab every 8 weeks and served as controls. For baseline characteristics see Table 1. Dosage was changed in 58 patients and 90% (n=52) remained on 8 week intervals after 24 weeks, with a mean (SD) dose of infliximab of 5.3 (1.9) mg/kg. All assessed disease variables (DAS28-CRP, VAS pain, global, fatigue, Dr global, HAQ, ASDAS-CRP, BASFI, CRP and ESR) remained unchanged (p=0.051 (pain) – 0.83) (Figure 1 A, B) while S-concentration was lower (p<0.001) at follow up. S-concentration of infliximab did not relate to disease activity neither at baseline nor at follow up (p=0.15-0.24). (Figure 1 C, D)

Table 1. Patient characteristics at inclusion

Interval	4-7 w, n=66	8 w, n=25
Age, years	56 (15)	58 (14)
Female sex	42 (64%)	11 (44%)
Disease duration, years	20 (12)	20 (10)
Clinical diagnosis: RA/JIA+arthritis UNS	14 (21%)/ 5 (8%)	7 (28%)/2 (8%)
SpA/PsA	31 (47%)/16(24%)	10 (40%)/6 (24%)
S-concentration infliximab µg/ml	9.0 (4.6-14.0)	3.4 (1.1-5.1)
Antibodies against infliximab	2 (3%)	3 (12%)
ESR	24 (16-37)	24 (15-42)
CRP	1.3 (0.8-2.3)	1.1 (0.6-2.9)
DAS28-CRP	2.8 (1.1)	2.6 (1.2)
HAQ	1.0 (0.38-1.38)	0.38 (0.25-0.85)
Patients' VAS pain	23 (8-50)	20 (3-32)
Patient's VAS global health	31 (11-49)	15 (2-48)
Doctors' VAS global health	9 (6-11)	7 (2-12)
ASDAS-CRP	1.8 (0.7-2.5)	1.2 (0.6-1.5)
BASFI	3.3 (1.3-6.1)	1.4 (0.3-2.4)
Concomitant csDMARD	39 (59%)	16 (64%)
Glucocorticoids	12 (18%)	1 (4%)

Mean (SD), median (interquartile range (IQR)) or n (%). ASDAS-CRP and BASFI; 41 SpA patients.

Conclusion: Adjustment of infliximab dosage to every 8 weeks worked for a majority of the arthritis patients in this clinical setting without worsening of

disease activity or general health. S-concentration of infliximab did not relate to disease activity or general health.

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Figure

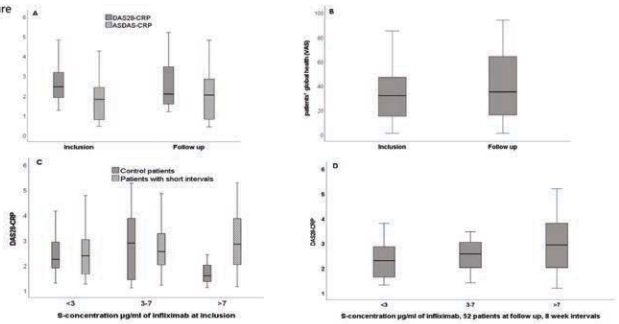

Figure. A. DAS28-CRP and ASDAS-CRP for 52 patients (27 RA/PsA and 25 SpA) before and after dosage change of infliximab. **B.** Patients' VAS global for 52 patients before and after dosage change of infliximab. **C.** DAS28-CRP for control patients and patients with shorter intervals divided on low/moderate/high trough values of s-concentration of infliximab at inclusion. **D.** DAS28-CRP in relation to low/moderate/high trough values of s-concentration of infliximab at follow up for 52 patients after dosage change.

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POS0654 EFFECTIVENESS OF ABATACEPT IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS.

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Background: Interstitial Lung Disease (ILD) is the most common lung involvement in rheumatoid arthritis (RA) and leads to increased morbidity and mortality. Some retrospective observational studies suggest that abatacept (ABT) could be effective and safety, although there are no clinical trials and prospectively collected data are scarce.

Objectives: To evaluate prospective the effectiveness and safety of ABT in patients with ILD associated RA (ILD-RA).

Methods: Design and Protocol: We performed a multicenter, prospective, observational study of patients with interstitial lung disease secondary to rheumatoid arthritis (ILD-RA) receiving ABT between 2015 and 2021. The patients were assessed using high-resolution computed tomography and lung function tests at the beginning of treatment (V0), at 12 months (V12), and at the end of follow-up in 2021 (fV). The study was approved by the Ethics Committee (Code 1719-N-15). **Main variable**: effectiveness of ABT according to evolution of ILD at the end of follow-up: (1) improvement (ie improvement of FVC ≥10% or DLCO ≥15% and no radiological progression), (2) no progression (stabilization or improvement in FVC ≤ 10% or DLCO <15% and no radiological progression), (3) progression (worsening of FVC >10% or DLCO >15% and radiological progression) or (4) death**. Other variables:** clinical and analytical characteristics, treatments and safety (infections, hospitalization and mortality). **Statistical analysis**: Cox regression analysis to identify factors associated with worsening of ILD-RA treated with ABT.

Results: Thirty-eight ILD-RA patients started ABT treatment during prospective follow-up. A total of 22/38 (57.9%) were men and the mean (SD) age was 66.1 (9.1) years. The mean (SD) evolution of ILD was 43.9 (30.0) months and the median (IQR) time with ABT was 17.0 (12.1-34.8) months. The baseline clinical-epidemiological characteristics and pulmonary progression of the patients are shown in Table 1. At the end of follow-up (fV) 28/38 (73.6%) had improvement/stabilization and 7/38 (18.4%) progressed and 3/38 (7.8%) of them died (COVID-19 pneumonia, respiratory infection and ILD progression, respectively). There were no significant differences in FVC (75.3 [8.7] vs 77.7 [14.6]; p=0.775) or in FEV1 (83.9 [10.7] vs 84.7 [13.2]; p=0.416) nor in the DLCO (61.0 [17.4] vs 60.7 [15.2]; p=0.789) at the end of follow-up. There was a greater numberwith improvement/stabilization among the patients who were in combination with Methotrexate compared to those who were in monotherapy (83.3% vs 39.1%; p=0.046). The baseline variables that were independently associated with progression-mortality of ILD-RA in fV were: baseline FVC (OR [95% CI], 0.895 [0.805-0.996]; p=0.042) and duration of ILD-RA (OR [95% CI], 1.204 [1.148-2.112; p=0.046]). Two patients discontinued ABT during follow-up due to insufficient joint and pulmonary response.

Table 1. Characteristics of patients with ILD-RA treated with Abatacept.

Variable	ILD-RA n=38
Baseline clinical-epidemiological characteristics	
Sex, man, n (%)	22 (57.9)
Age in years, mean (SD)	66.1 (9.1)
Race, caucasian, n (%)	38 (100.0)
Smoking history	
No smoker, n (%)	23 (60.5)
Smoker, n (%)	15 (39.5)
Time of evolution RA, months, median (IQR)	139.1 (68.1-218.7)
RF, n (%)	36 (94.7)
Anti-CCP, n (%)	32 (84.2)
ANA, n (%)	8 (22.9)
Radiological pattern	
UPI, n (%)	26 (68.0)
NSIP, n (%)	12 (32.0)
Treatment	
DMARDs, n (%)	33 (86.8)
Methotrexate, n (%)	19 (50.0)
Leflunomide n (%)	11 (22.9)
Sulfasalazine, n (%)	2 (5.3)
Hydroxychloroquine, n (%)	6 (15.7)
Immunosuppressants, n (%)	11 (297)
Antifibrotic, n (%)	1 (2.6)
Corticosteroids, n (%)	32 (84.2)
Corticosteroids, median (IQR)	5.0 (2.5-10.0)
Pulmonary progression (fv)	
Improvement-Stabilization, n (%)	22 (73.6)
Progression-Mortality, n (%)	10 (26.4)

Conclusion: More than half of the patients with ILD-RA treated with ABT manage to stabilize or improve their lung disease after a median follow-up of 17 months. Patients who worsen or die have lower baseline FVC values and ILD-RA with a longer evolution time.

Disclosure of Interests: None declared

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POS0655 SURVIVAL AND SAFETY OF BIOLOGICAL AND TARGETED SYNTHETIC THERAPIES AS REGARDS TO AGE GROUPS. BIOBADASAR 3.0 REGISTRY.

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Background: Advances in rheumatology and new therapeutic options have certainly impacted patient survival, changing the age range, from youth to seniors. The differences between the age groups could influence the evolution of the disease and the adverse events (AEs) related to the treatments. There are few real-world data on the safety and efficacy of treatments in different age groups.
Objectives: To evaluate the frequency of AEs and the survival of treatments according to the age in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis (AS).
Methods: Retrospective, observational, multicenter study of real-life data of patients included in the BIOBADASAR 3.0 registry; exposed and not exposed to original biological treatments (b-DMARDs), biosimilars, targeted synthetic drugs (ts-DMARDs). The unexposed group received treatment with conventional disease-modifying drugs (cDMARDs). A Kaplan-Meier and Log Rank Test analysis was performed to study AEs-free survival and treatment in different age groups (young people <25; young adults 25-34; mature adults 34-65; old adults >65). Factors related to treatment survival were evaluated using Cox regression models.
Results: 5,297 patients were included, 80.3% female, mean age 43.7 years (SD 15.6) and median disease progression 14.3 [IQR 11.5]. RA 4658 (87.9%); APs 490 (9.25%) and EA 149 (2.8%). The main reason for treatment discontinuation was ineffectiveness, in 624 patients in the exposed group and in 53 (2.5%) patients in control group, followed by the presence of AEs in 352 (11.2%) and 83 (3.9%), respectively (p=0.001). A mean Charlson Score of 0.268 (SD 0.6) in the exposed group and 0.306 (SD 0.7) in the control group (p=0.095). Median EAs-free survival in the exposed group was 12.5 years [IQR 16.6] while in controls was 28 years [IQR 11], p<0.0001. Median AEs-free survival was 12 years (IQR 11) in young people, 11.5 years [IQR: 4.9] in young adults, 10 years [IQR: 3.25] in mature adults and 7.6 years [IQR: 6] in old adults with a difference statistically significant (p>0.017). The exposed group presented a median treatment survival in years of 11.25 years [IQR: 10] in young people; 12.5 years [IQR: 4.7] in young adults, 7.5 years [IQR: 12.1] in mature adults and 4.5 years [IQR: 1.14] in old adults (p>0.0001). Considering only the first line of treatment, a median survival of 11.5 years [IQR: 10] was evidenced in the age group <25; 12 years [IQR: 2.6] between 25-34 years old, 10 years [IQR: 12] in the group between 34-65 years old and 5.5 years [IQR: 1.14] in the group > 65 years old (p>0.004). (Figure 1). Considering the second line of treatment, the differences between the groups were not statistically significant (p=0.57). In the multivariate regression model for patients with RA, the factors with the greatest impact on treatment survival were female sex (HR 1.3, 95% CI 1.2-1.4), old age (HR 1.01, 95% CI 1.008-1.01), treatment with steroids (HR 1.19, 95% CI1.1-1.2) and longer disease duration (HR 1.01, 95% CI1.01 – 1.02).
Conclusion: In the present study we were able to demonstrate a greater occurrence of AEs in old adults and mature adults compared to young people and young adults. Conversely, survival for b-DMARDs and ts-DMARDs were greater in youth and young adults. In patients with RA, female sex, corticosteroid therapy, old aged and longer disease duration were associated with treatment discontinuation.
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POS0656 FRAILTY AND RISK OF ADVERSE OUTCOMES IN BIOLOGIC OR TARGETED-SYNTHETIC DMARD TREATED PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Recently, it has been recognized that frailty and pre-frailty are common in patients with rheumatoid arthritis (RA) [1]. Whether frailty status portends an increased risk of adverse outcomes in patients with RA on biologic or targeted synthetic disease modifying anti-rheumatic drugs (b- or tsDMARDs) remains unknown.
Objectives: To evaluate the association between frailty and adverse outcomes in patients with RA exposed to b- or tsDMARDs.
Methods: Using the IBM/Watson MarketScan Commercial Claims and Encounters Databases, we identified all patients with RA who filled new prescriptions (or received infusions) for TNFα antagonists (TNFi), non-TNFi biologics (rituximab, abatacept, tocilizumab) or Janus Kinase inhibitors (JAKi) between 2008-2019. We used a 1-year lookback period without the use of these drugs to identify new users. The date of the first prescription within these three drug categories was the index date. Patients' frailty risk score was calculated using the Claims-Based Frailty Index (CFI) [2], which estimates a deficit-accumulation frailty index using International Classification of Diseases codes, Current Procedural Terminology codes, and Healthcare Common Procedure Coding System codes in administrative claims data in the 1-year baseline period. The index ranges from 0 (not at all frail) to 1 (severely frail). The primary outcome was time to serious infections (those requiring hospitalization); secondary outcomes: any infection (outpatient or inpatient encounters) and all-cause hospitalizations. Patients were followed until 1) outcome occurrence; 2) disenrollment; 3) >90 days elapsed (or >180 days for rituximab) without further fills of the first drug categories; 4) they filled/received infusions of b-/tsDMARDs from a different drug category; or 5) 2 years after index. Cox proportional hazards adjusting for demographics, calendar year, serious and/or opportunistic infections in the 12-months prior to index were used to estimate the adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) for each outcome. In separate model, we additionally adjusted for comorbidity burden, and health care utilization (HCU).
Results: A total of 62,246 patients with RA met our inclusion criteria of whom 50,910 (82%) started TNFi as their first biologic, 9525 (15%) non-TNFi biologics, and 1811 (3%) JAKi. Among these, 3928 (6%) were considered frail. In multivariable analyses, frail patients had higher risk of serious infections compared to non-frail patients (aHR 2.37, 95% CI 2.05-2.74) which decreased to aHR 1.34, 95% CI 1.13-1.58 (Table 1) after adjusting for comorbidity burden and the HCU. Similarly, frailty was associated with increased risk of any infection (aHR 1.18, 95% CI 1.11-1.25), and all-cause hospitalizations (aHR 1.34, 95% CI 1.21-1.49) relative to non-frail individuals.

Table 1. Multivariable models evaluating the association between frailty status and inpatient infections as the outcome

Variable	#Hazard Ratio (95% Confidence Interval)	@Hazard Ratio (95% Confidence Interval)
Frail	**2.37 (2.05, 2.74)**	**1.34 (1.13, 1.58)**

#Model adjusts for age, sex, major infection requiring inpatient admission in 12 months prior, concomitant baseline drugs such as csDMARDs, glucocorticoids, NSAIDs and opioids@ Model additionally adjusts for Charlson comorbidy score and healthcare utilization

Conclusion: Frailty is an important predictor for the risk of adverse outcomes among patients with RA treated with b- or tsDMARDs. Our findings underscore the need for considering this parameter in patient evaluations (even among younger patients) in the clinic.
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POS0657 SURVIVAL OF BARICITINIB VS ANTI-TNF AS THE FIRST BIOLOGICAL DRUG IN PATIENTS WITH RHEUMATOID ARTHRITIS, IN CLINICAL PRACTICE: RESULTS OF A LOCAL REGISTRY

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Objectives: To evaluate survival in the first 4 years of treatment with Baricitinib (BARI) vs anti-TNF (TNFi), as the first biological drug (BIO-1), in patients with rheumatoid arthritis (RA).
Methods: Retrospective study of patients with RA, treated with the first BIO-1, with BARI or TNFi, from September-2017 to December-2021. General data (current age, at diagnosis of RA and at the start of BIO-1) were collected; RA: evolution time, RF, ACPA; type of BIO-1: dose received, time in treatment, reason for withdrawal. Univariate analysis of drug survival was performed using Kaplan-Meyer curves and the Long Rank test to differentiate by groups. For the multivariate study, Cox regression with proportional hazards.
Results: The study includes 96 patients with RA, who have started treatment for > 1 month with BIO-1: BARI (n: 63/66% patients) or TNFi (33/34% patients): women: 82 (96%), current mean age (SD): 62 (1) years, at diagnosis: 51 (1) years and at the start of BIO-1: 59 (1) years. 36 (37%) patients are ≥65 years old, the mean time

in AR is 7.6 years and the time in BIO-1: 1.34 (2.2) years. BIO-1 was withdrawn in 34 (40%) patients: Inefficacy: 17 (18%) patients, Complications: 14 (15%) [Cardiovascular/thrombosis: 2 (2%), rash: 2 (2%), infection-neoplasia-immunogenicity: 1 (1%) patient in each], loss to follow-up: 5 (5%) and others: 2 (2%). When comparing the BARI vs. TNFI group, no differences were detected between the general data, the percentage of patients >65 years of age, or the mean time in treatment or the reasons for drug withdrawal (Table 1). However, survival in the BARI group was significantly superior to TNFi throughout the period (p=0.04; HR: 0.47, 95% CI: 0.24-0.91, p=0.026) (Figure 1A).

Table 1. Characteristics of patients who receive Baricitinib (BARI) or anti-TNF as first BIO-1 (TNFi).

	All N: 96	BARI N: 63 (66%)	TNFi N: 33 (34%)	P
Female, n (%)	82 (85%)	56 (89)	26 (79)	0.2
Current age, mean (SD)	62 (4.2)	63 (6)	59 (11)	**0.057**
Age at diagnosis RA, mean (SD)	51 (4.9)	52.5 (7.8)	48.6 (15.5)	0.17
Age at start of BIO-1, mean (SD)	59 (2.1)	60 (4.9)	55.9 (9.9)	0.23
≥ 65 years, n (%)	36 (37)	27 (43)	9 (27)	0.39
RF positive, n (%)	77 (80)	54 (86)	23 (70)	0.1
ACPA positive, n (%)	74 (77)	50 (79)	24 (73)	0.56
Average time in BIO-1, years (DE)	1.34 (2.2)	1.85 (0.5)	1.32 (2.4)	0.21
BARI 2 mg, n (%)	-	23 (36)	-	-
Withdrawal of BIO-1, n (%):	38 (40)	20 (32)	18 (55)	0.15
- Complication	14 (15)	7 (13)	7 (21)	-
- Loss of efficacy	17 (18)	8 (13)	9 (27)	-
- Loss of follow up	5 (5)	5 (8)	-	-
- Other	2 (2)	-	2 (6)	-

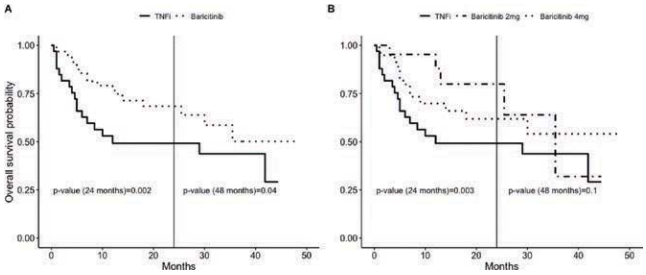

Figure 1. Survival probability in patients with rheumatoid arthritis who receive the first BIO-1. **A**. Between TNFi drug vs Baricitinib. **B**. Between TNFi vs Baricitinib 2 mg or 4 mg.

In patients <65 years, the greatest survival of BARI is maintained (p=0.05), being significant in the first 24 months of treatment (p=0.02). In patients ≥65 years, significance was not reached throughout the overall period (p=0.5) and in the first 24 months of treatment (p=0.06). When comparing the BARI 2 mg (n: 23/36%) and 4 mg (n: 40/64%) groups, the 2 mg group is significantly older at RA diagnosis (73 [SD: 2] years vs 56 [SD: 3] years; p<0.0001) and at the start of BIO-1 (72 [SD: 1.4] years vs 54 [SD: 2.8] years; p<0.0001). However, survival in the BARI 2 mg group was significantly higher in the first 24 months (p=0.003;) (Figure 1B): BARI 2 mg HR: 0.14, 95% CI; 0.04-0.56, p=0.005, HR BARI 4 mg: 0.44 (95% CI; 0.20-0.96, p=0.038).

Conclusion: 1. Survival of BARI is superior to TNFi during the first 4 years of treatment, especially during the first 24 months of treatment. 2. There are no differences between the cause that causes drug withdrawal. 3. The use of the 2 mg dose of BARI predominates in patients older than 65 years, with survival being greater than TNFi, especially in the first 24 months of treatment.

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POS0658 TUMOR NECROSIS FACTOR BLOCKERS INDUCED SARCOIDOSIS: DESCRIPTION OF 31 CASES FROM THE FRENCH PHARMACOVIGILANCE DATABASE

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Background: Development of Tumor Necrosis Factor blockers (TNFb) whose drug class has several mechanistic and pharmacologic sub-classes, have improved the management of autoimmune and inflammatory diseases, including sarcoidosis. With their increasing use, paradoxical reactions are described and one of the most frequent is sarcoidosis. However, the description of TNFb-induced sarcoidosis (TIS) remains poor, because reported in few and only short case-series.

Objectives: We aimed to better describe the clinical spectrum of TIS, and the differential involvement of TNFb sub-classes.

Methods: French pharmacovigilance database was used to collect data on TIS, excluding patients with previous idiopathic sarcoidosis. Statistical analyses were performed using the Mann-Whitney test for quantitative data and Fisher test for qualitative data. A p value < 0.05 was considered statistically significant.

Results: Data were obtained from 2002 to 2019 for infliximab, adalimumab, golimumab, certolizumab and etanercept. Thirty-one TIS patients were collected from the database, including 12 women (38.7%). In most cases, TNFb was introduced for ankylosing spondylitis (58%), psoriasis (19.3%) or rheumatoid arthritis (16.1%). Median age at TIS occurrence was 54 [43.5; 61.5] years, with a median time to onset of 24 [6.0; 72.0] months. The most frequent involved TNFb was etanercept (n=21, 67.8%). The two mains clinical TIS manifestations were lymph node (n=27, 87.1%) and lung involvement (n=16, 51.6%). The culprit drug was discontinued in 26 (84%) patients, and a double-barreled inflammatory gun to control both initial and induced disorders was proposed in 19 of them (90.5 %), mostly glucocorticoids (n=13, 68.4%) alone or combined with methotrexate (n=3, 15,8%). Among the 14 patients with the available data, the TIS had completely resolved in 11 (78.6%); for all these lasts, the TNFb was discontinued. No significant differences were observed between the TNFb sub-classes of monoclonal antibodies or fusion proteins, regarding clinical presentation, median time to onset or outcome.

Conclusion: This second largest case-series shows that TIS are mostly encountered with etanercept, but without any difference in clinical or prognostic implications with the other TNFb-subclasses.

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POS0659 LONG-TERM DYNAMICS OF ANTIBODY RESPONSE TO ADALIMUMAB DETECTED WITH A DRUG TOLERANT ASSAY

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Background: Immunogenicity of adalimumab (ADL) has been the subject of extensive research, with the primary focus on its incidence, antibody titers and effects on clinical outcome. However, the temporal evolution of antibodies, i.e. dynamic and variation in titers, time point of emergent and persistence or transience of the response, remains under elucidated. To investigate this further, it is essential to collect samples at regular intervals and over a longer period of time. Also, a drug tolerant assay should be used to conquer with the phenomenon of drug interference (1).

Objectives: To evaluate the temporal evolution and to distinguish dynamic patterns of antibody response. Secondly, to assess the clinical impact and factors influencing these dynamic patterns.

Methods: ADA and adalimumab concentration were measured in sera of 511 consecutive ADL treated rheumatoid arthritis patients. Serum samples were drawn at week 0, 4, 16, 28, 52, 78 and 104. ADA were measured with a drug tolerant assay (Acid dissociation RadioImmunoAssay). Logistic regression analysis was carried out. Benjamini-Hochberg was used to correct for multiple testing.

Results: Baseline characteristics are depicted in Table 1. Fifty-nine percent of patients (n=300) developed ADA. Based on visual observations patients were

clustered in 9 groups, taking the next features in to account (Figure 1); the presence or absence of ADA, the height of ADA titers (higher or lower than 100AU/mL), emergent (early vs. late; cutoff week 28) and its persistence. Based on these features 397 (77%) patients were assigned to one of the groups. Due to missing data at crucial time points the remainder of patients were excluded. In the 'High early' and High early LTF' group was the rate of MTX use (adjusted odds ratio (AOR) 0.033 [95%CI 0.01-0.09] P<0.0001 respectively 0.79 [95%CI 0.03-0.22] P <0.0001), adalimumab concentration above 5mg/L (AOR 0.022[95%CI 0.01-0.08] P<0.001 respectively 0.026 [95%CI 0.01-0.09] P<0.001) and low disease activity (DAS28 <3.2) at week 52 (AOR 0.191[95%CI 0.07-0.56] P<0.002 respectively 0.102 [95%CI 0.03-0.31] P<0.001) significantly lower, compared to the negative group. Furthermore, the failure rate was in both groups significantly higher (AOR 9.19 [95%CI 3.7-22.87] P<0.0001 respectively 23.94 [95%CI 8.13-70.53] P<0.0001). In contrast to forgoing studies, our data does not show any differences in clinical outcomes between groups with persistent and transient ADA response.

Table 1. Baseline characteristics

Totaal N=511	
Follow-up	
Median weeks (IQR)	78 (28-104)
Demographics	
Age mean SD	53,7; ± 12,5
Female No (%)	409 (79.8)
Disease status	
Disease duration years median (IQR)	6,7 (3-13)
IgM rheumatoid factor + (%)	327 (68.2)
Anti-citrullinated protein antibody + (%)	315 (73.2)
Erosive (%)	296 (61.6)
DAS28-score mean SD	4.5 ± 1.5
Medication	
Methotrexate use no (%)	378 (73)

Conclusion: The majority of patients have an immune response to ADL. Based on ADA concentration, time point of emergence and its persistence, certain patterns of ADA response can be distinguished. Only high ADA concentration at early time points, causing low ADL concentration, are associated with unfavorable clinical effects. All the remaining distinctive patterns does not have any association with clinical outcomes. This suggests a regulated immune response in the majority of patients.

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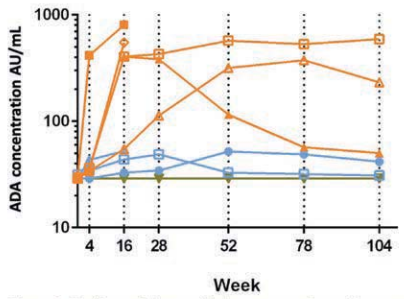

Figure 1. Median antidrug antibody concentration of 9 groups of patients during 2 years of adalimumab treatment. Each curve represents a group with a certain pattern of ADA formation.

- High persistent (n=47)
- HigHigh transient (n=23)§
- High late (n=31)
- High early (n=40)*
- High early LTF (n=33)*
- Low transient (n=45)§
- Low late (n=30)
- Low LTF (n=23)*
- ADA Negative (n=125)

§ Transient; a peak in ADA titers is followed by a 4-fould decrease.
* The majority of these patients discontinued treatment after week 16. Hence, a curve through week 16 LTF, lost to follow-up

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POS0660

SURVIVAL AND SAFETY OF BIOLOGICAL AND TARGETED SYNTHETIC THERAPIES. 10 YEARS OF REAL-LIFE DATA. BIOABASAR 3.0 REGISTRY

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Background: The use of biological and targeted synthetic drugs has changed the outcomes of rheumatic diseases. The information on efficacy and safety provided by randomized controlled clinical trials does not always reflect the conditions of patients in real life. Data obtained from prospective registries, over extended periods and with real-world evidence, is a great contribution to the pharmacovigilance of these drugs.

Objectives: The aim of this study is to describe adverse events (AE) and survival of treatments of patients included in the Argentine Registry of Adverse Events of Biological Therapies and Target Synthetic Drugs (BIOBADASAR 3.0).

Methods: Observational, prospective and multicenter study of ten years of follow-up in patients with rheumatic diseases treated with original biological drugs, biosimilars or original and generic targeted synthetic therapies in Argentine. Those patients who received biological therapies were considered exposed while non-exposed patients represent the control group. All patients were evaluated at least once a year and whenever they experienced an AE or a change in treatment. Survival of treatments was evaluated by Kaplan Meier curves and the comparison between them was made by Log Rank Test analysis.

Results: A total of 6010 patients were included and 8810 treatment periods from 56 centers. 79.7% were female, mean age of 43.7 (SD 15.6) years. The most frequently reported rheumatological disease was rheumatoid arthritis (RA) (77.5%), followed by psoriatic arthritis (PsA) (8.2%), systemic lupus erythematosus (SLE) (3.1%), juvenile idiopathic arthritis (JIA) (2.6%) and ankylosing spondylitis (AS) (2.5%). The b-DMARD use frequencies were etanercept in 32.2%, followed by adalimumab in 18.7%, abatacept in 9.7%, certolizumab pegol in 8.7%, tofacitinib in 7.9%, rituximab in 7.3% and tocilizumab in 5.5%. The frequency of AE was 11.7% in the exposed group and 4.9% in controls (p=0.001). Infections were present in 41% in the exposed group vs 34% in controls (p<0.001). AE-free survival was 23 years [IQR: 18.2] in controls vs 10 years [IQR: 8.8]) in the exposed group p<0.0001). In the multivariate regression model, age (HR: 1.005, 95% CI 1.001-1.009) and corticosteroid treatment (HR:

1.18, 95% CI 1.05-1.34) were associated with a higher risk of AE in exposed patients. Treatment survival was 15 years [IQR: 28] in unexposed group vs 4.7 years [IQR: 10] in exposed patients (p<0.0001). In the multivariate analysis, female sex (HR 1.1, 95% CI 1.09-1.2), older age (HR 1.0, 95% CI: 1.010-1.014), corticosteroid treatment (HR 1.16, 95% CI 1.09-1.2), the diagnosis of systemic lupus erythematosus (HR1.547, CI95%1.3-1.8) and disease duration (HR1.01, CI95%1.008-1.015) were associated with a higher risk of treatment discontinuation while the diagnosis of rheumatoid arthritis (HR 0.83 CI95% 0.75-0.93) was associated with a lower risk of suspension.

Conclusion: We found that the use of steroids and elderly patients are still being associated with a higher risk of presenting an AE and treatment discontinuing. This could be related to the fact that the use of steroids is frequently associated with active disease or severe conditions. Exposed patients have a lower AE-free survival and a lower treatment survival. This could be since unexposed patients have a longer follow-up time and a longer duration of their disease. This data from real-world Latin American patients of ten years of follow-up are extremely useful for monitoring and pharmacovigilance of biological therapies in patients with rheumatic diseases.

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POS0661 MAJOR COST SAVINGS ASSOCIATED WITH BIOLOGIC DOSE REDUCTION IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: Anti-TNF drugs have dramatically improved the management of inflammatory arthritis (IA). Although the introduction of biosimilars have reduced the cost, chronic use of biologic agents has a high impact on healthcare expenditure. This study evaluated the cost effectiveness of a dose reduction strategy for the most commonly used anti- TNF drugs over a period of 10 years in patients with IA in remission.

Objectives: The purpose of this study was to explore whether patients with Inflammatory Arthritis (IA) (Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS) would remain in remission after 10 year period, following a reduction in biologic dosing frequency and to calculate the cost savings associated with dose reduction.

Methods: This prospective, non-blinded, non-randomised study was commenced in 2010. Patients with IA, Rheumatoid arthritis (RA),ankylosing spondylitis (AS) and Psoriatic arthritis (PsA) who were in remission as defined by disease activity indices (DAS28<2.6, BASDAI<4), and were offered Anti TNF dose reduction. Patients on etanercept were reduced from 50mg weekly to fortnightly, adalimumab 40mg once monthly instead of fortnightly. Patients were assessed for disease activity at 1, 4 and 10 years following reduction in dosing frequency.Cost saving was calculated by deducting the total annual cost of the biologic agent used over 10 years compared with the cost if the dosing interval had not changed.

Results: Seventy nine patients with inflammatory arthritis in remission were recruited. 57% had rheumatoid arthritis (n=45), 13% psoriatic arthritis (n=10) and 30% ankylosing spondylitis (n=24). 57% (n=45) were taking etanercept and 43% (n=34) adalimumab. The percentage of patients who maintained dose reduction at 10 years was 9% (n=7). Of the total 48 patients who were successfully dose reduced at year 1 (n=42), (69%, n=29) were able to maintain the dose reduction up to 4 years and 9% (n=7) maintained this dose reduction up to year 10. The estimated cost saving was €4,928 per patient per year. Estimated cost savings for 7 patients on reduced dose was €344,952.88 over 10 years.

Conclusion: Anti TNF dose reduction strategy in patients with IA results in substantial cost savings. Implementation of a dose reduction strategy while monitoring of disease activity reduces the financial impact of the use of biologic therapies. Further studies should be done to identify which patients are more likely to remain in remission while on dose reduction.

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POS0662 BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS PRESCRIPTION OVER TIME IN A COHORT OF EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: According to 2019 updated EULAR recommendations, therapy of Early Rheumatoid Arthritis (ERA) with biological disease-modifying antirheumatic drugs(bDMARDs) is adviced in presence of poor prognostic factors,i.e. persistently moderate/high disease activity, high acute phase reactants, high swollen joint count, autoantibody positivity, presence of early erosions, failure of two/more conventional synthetic DMARD.

Objectives: To evaluate over time prevalence of bDMARD therapy and factors associated to rapid initiation in our EA Clinic (EAC), comparing two different periods: from 2004 to 2012 and from 2012 to 2020. The last two years were not considered because of the adverse influence of COVID19 pandemia on early access to EAC and on timely scheduled visits.

Methods: A total of 281 ERA patients with less than 12 months of disease duration (53.9 years mean age, 75% female, 77% seropositive), followed according to the treat-to-target (T2T) strategy, were enrolled in the study. At baseline, and every three months, the ACR/EULAR core data set variables were recorded. At baseline and every year, hand and foot radiographs were examined according to modified Total Sharp score (mTSS). At each visit, clinical improvement and remission were evaluated according to EULAR criteria. The achievement of Comprehensive Disease Control (CDC) (28-joint Disease Activity Score using C reactive protein <2.6, Health Assessment Questionnaire <0.5 and change from baseline in mTSS ≤0.5) was assessed every year.

Results: We examined 164 patients from 2004 to 2012 and 117 subjects from 2012 to 2020. In the first group 72 patients (43.9%) initiated bDMARDs during the 8-year FU, with a mean delay of 41.8 months. In the second group 37 patients (31.6%) started biotechnological drugs over time, with a mean delay of 50.4 months.
Analyzing the period from 2004 to 2012, ERA patients starting bDMARDs were younger (*p<0.0001*), had longer disease duration (*p=0.02*) and higher body mass index (BMI) (*p=0.01*) compared to subjects not undergoing to biological therapy. Moreover, ERA patients in bDMARDs were in higher percentage anti-citrullinated peptide antibody (ACPA) positive (80.6%) and reached to a lesser extent CDC at 12months of FU (26.1%) compared to patients that didn't initiate bDMARDs (60.9% ACPA positive, *p=0.01*; 63% achieving CDC, *p<0.0001*, respectively). Examining the period from 2012 to 2020, bDMARD-treated ERA patients were younger (p=0.06),in higher percentage ACPA positive (81.1%) and erosive at baseline (35.1%) compared to patients that didn't initiate bDMARDs (64% ACPA positive, *p=0.02*; 17.5% erosive, *p=0.04*, respectively). As previously, patients in bDMARD reached to a lesser extent CDC at 12 month of FU (35.1%) compared to subjects not undergoing to biological therapy (55% achieving CDC, *p=0.05*). On multivariate analysis, ACPA positivity was associated with initiation of bDMARD in both patient groups *(p=0.02)*, whereas older age at onset and reaching CDC at 12 month were inversely associated (*p=0.001*; *p<0.0001*, respectively).

Conclusion: Despite the widest choice of bDMARDs currently available in the last 8 years, we did not observe an increase in the prescription of these drugs from 2012 to 2020. As in other ERA cohorts, bDMARD initiation is associated to poor prognostic factors, in particular ACPA positivity, presence of erosions at baseline and not achieving CDC at 12 months of FU. In the last 8 years, the decreased influence of disease duration at onset and of BMI could be a consequence of the improvement in strategies of early referral and control of modifiable risk factors.

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Rheumatoid arthritis - non biologic treatment and small molecules

POS0663 THE USE OF EXPOSURE-ADJUSTED EVENT RATES VERSUS EXPOSURE-ADJUSTED INCIDENCE RATES IN ADVERSE EVENT REPORTING: INSIGHTS FROM FILGOTINIB INTEGRATED SAFETY DATA IN RHEUMATOID ARTHRITIS

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Background: Reporting of treatment-emergent adverse events (TEAEs) in rheumatoid arthritis (RA) clinical trials can be summarized as exposure-adjusted incidence rates (EAIRs) or exposure-adjusted event rates (EAERs). Censored EAIR (EAIR), weighing exposure up to a patient's first event, is commonly reported; uncensored EAIR (EAIRu), using total exposure time for all patients, can also be used. For EAIR, exposure time can vary by event. In contrast to EAIR(u), the total number of events are used to calculate EAER. The three methods account for different exposures and/or multiple events, which can impact the outcome evaluation. Studies of filgotinib (FIL) in RA[1] report safety data as EAIR/100 patient-years of exposure (PYE) for TEAEs, which is uncensored.

Objectives: To describe the outcome of long-term FIL integrated safety data in RA by applying different statistical methodologies: EAER, EAIRu and EAIR.

Methods: Integrated FIL safety data from seven clinical trials were assessed[1]. Predefined adverse events of special interest (AESI) included serious infections (any), herpes zoster (HZ), major adverse cardiac events (MACE), malignancies (excluding nonmelanoma skin cancer [NMSC]), NMSC and venous thromboembolism (VTE). The number of patients with an event, number of events, EAER, EAIRu and EAIR were summarized. The data extraction date was January 2021 for the DARWIN 3 (NCT02065700) long-term extension (LTE) and November 2020 for the FINCH 4 (NCT03025308) LTE.

Results: In total, 3691 patients received ≥1 FIL dose for 8085 PYE. In this population, 176 serious infections were reported in 137 patients, 125 HZ events were reported in 112 patients, 39 MACE were reported in 33 patients, 20 cases of VTE were reported in 15 patients, 60 malignancies excluding NMSC were reported in 49 patients and 21 cases of NMSC were reported in 20 patients. Within each treatment arm (FIL 200 mg [FIL200], FIL 100 mg [FIL100] or combined FIL), rates for most AESI were similar when reported as EAER, EAIRu or EAIR (Table 1). For serious infections, EAER was higher than EAIRu or EAIR. The total exposure time to first event (censored PYE) was high and comparable to total exposure (PYE) (>2700 years and >5100 years for the total populations in the FIL100 and FIL200 groups, respectively).

Table 1. Exposure-adjusted event and incidence rates for AESI

		FIL200	FIL100	FIL combined
Number of patients/PYE		2267/5302.5	1647/2782.6	3691/8085.1
Serious infections	**EAER**	1.9 (1.5, 2.4)	3.2 (2.2, 4.5)	2.0 (1.7, 2.4)
	EAIRu	1.5 (1.1, 1.9)	2.7 (1.9, 3.9)	1.6 (1.3, 2.0)
	EAIR	1.5 (1.2, 1.9)	2.8 (1.9, 4.0)	1.7 (1.4, 2.0)
HZ	**EAER**	1.6 (1.3, 2.1)	1.3 (0.9, 1.8)	1.5 (1.2, 1.8)
	EAIRu	1.5 (1.2, 2.0)	1.1 (0.8, 1.5)	1.4 (1.1, 1.7)
	EAIR	1.6 (1.2, 2.0)	1.1 (0.8, 1.6)	1.4 (1.1, 1.7)
MACE	**EAER**	0.3 (0.2, 0.5)	0.6 (0.4, 1.0)	0.4 (0.3, 0.6)
	EAIRu	0.3 (0.2, 0.5)	0.5 (0.3, 0.8)	0.4 (0.2, 0.6)
	EAIR	0.3 (0.2, 0.5)	0.5 (0.3, 0.9)	0.4 (0.2, 0.6)
VTE	**EAER**	0.3 (0.2, 0.5)	0.1 (0.1, 0.4)	0.2 (0.2, 0.4)
	EAIRu	0.2 (0.1, 0.4)	0.1 (0.1, 0.4)	0.2 (0.1, 0.3)
	EAIR	0.2 (0.1, 0.4)	0.1 (0.1, 0.4)	0.2 (0.1, 0.3)
Malignancies excluding NMSC	**EAER**	0.8 (0.5, 1.1)	0.8 (0.5, 1.2)	0.7 (0.2, 2.8)
	EAIRu	0.6 (0.4, 0.9)	0.6 (0.4, 1.0)	0.6 (0.4, 0.8)
	EAIR	0.6 (0.4, 0.9)	0.6 (0.4, 1.0)	0.6 (0.4, 0.8)
NMSC	**EAER**	0.3 (0.2, 0.5)	0.2 (0.1, 0.5)	0.3 (0.2, 0.4)
	EAIRu	0.3 (0.2, 0.5)	0.2 (0.1, 0.4)	0.2 (0.2, 0.4)
	EAIR	0.3 (0.2, 0.5)	0.2 (0.1, 0.4)	0.2 (0.2, 0.4)

Data are rate (95% CI) unless otherwise stated.

Conclusion: These data confirm that using different methods to analyze FIL safety data (EAER, EAIRu, EAIR) does not result in different safety outcomes, reinforcing the previously reported FIL safety profile in patients with RA. As the AESI reported in the long-term safety database with FIL are rare, patients commonly have long exposure times before experiencing an event, which are often associated with end of treatment. As such, EAIRu, EAIR and EAER are similar.

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POS0664 RADIOGRAPHIC CHANGE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ESTIMATED BASELINE YEARLY PROGRESSION ≥5 OR <5: POST HOC ANALYSIS OF TWO PHASE 3 TRIALS OF FILGOTINIB

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Background: In some patients (pts) with rheumatoid arthritis (RA), especially those with joint damage early in the disease, first-line methotrexate (MTX) treatment may not suffice to prevent further rapid radiographic progression (RRP).[1] In FINCH 1 (NCT02889796), filgotinib 200 mg (FIL200) and 100 mg (FIL100) reduced change in modified total Sharp score (mTSS) vs placebo (PBO) in pts with RA and inadequate response to MTX (MTX-IR).[2] In FINCH 3 (NCT02886728), FIL200 and FIL100 reduced change in mTSS vs MTX monotherapy (MTX mono) in MTX-naïve pts.[3]

Objectives: To evaluate, via post hoc analysis of 2 trials, filgotinib's effects on radiographic progression vs MTX mono in pts with estimated baseline (BL) yearly progression ≥5 or <5 mTSS units/year.

Methods: The double-blind 52-week (W) FINCH 1 study randomised MTX-IR pts with moderate–severe active RA to FIL200 or FIL100, subcutaneous adalimumab (ADA) 40 mg, or PBO; at W24, PBO pts were rerandomised blinded to FIL200 or FIL100; all took stable background MTX.[2] In FINCH 3, MTX-naïve pts were randomised, blinded, to FIL200 + MTX, FIL100 + MTX, FIL200 alone, or MTX mono for up to W52.[3] This analysis examined subgroups by estimated BL yearly progression (BL mTSS/duration in years of RA diagnosis), based on ≥5 or <5 mTSS units/year,[4] a threshold commonly used to define RRP. We assessed effects of filgotinib vs ADA or PBO in mTSS change from BL (CFB) at W24/W52 (using a mixed model for repeated measures) and percentages with no W24 progression (mTSS change ≤0, ≤0.5, ≤smallest detectable change [SDC], using Fisher's exact test).

Results: At BL, 558/1755 MTX-IR and 787/1249 MTX-naïve pts had BL estimated yearly progression ≥5. Median mTSS in pts with BL yearly progression ≥5 and <5 was 53.25 vs 5.00 respectively in the MTX-IR trial and 6.00 vs 2.50 in the MTX-naïve trial. At W24, the mTSS CFB in pts with BL yearly progression ≥5 and <5 was 0.84 and 0.22 in MTX-IR pts taking PBO + MTX, and 0.67 and 0.25 in MTX-naïve pts taking MTX mono. At W52, in pts with BL yearly progression ≥5, FIL200 + MTX reduced mTSS change vs PBO + MTX in the MTX-IR trial and vs MTX mono in the MTX-naïve trial (Figure 1). At W24, among pts with estimated BL yearly progression ≥5, FIL200 + MTX increased odds of no

Table 1. Ratio of no radiographic progression at W24

FINCH 1: MTX-IR	FIL200 + MTX		FIL100 + MTX		ADA + MTX		PBO + MTX	
BL yearly progression	≥5 (n = 138)	<5 (n = 267)	≥5 (n = 139)	<5 (n = 265)	≥5 (n = 91)	<5 (n = 180)	≥5 (n = 101)	<5 (n = 250)
% with no progression (≤0.5)	87.7	97.0	88.5	92.5	87.9	93.9	76.2	91.6
OR	2.22*	2.97*	2.40*	1.12	†	†	†	†
% with no progression (≤0)	80.4	91.8	81.3	88.3	80.2	89.4	67.3	86.4
OR	2.00*	1.75	2.11*	1.19	†	†	†	†
% with no progression (≤SDC [1.36])	91.3	98.1	92.1	96.6	92.3	95.6	81.2	94.0
OR	2.43*	3.35*	2.70*	1.82	†	†	†	†
FINCH 3: MTX-naïve	FIL200 + MTX		FIL100 + MTX		FIL200 mono		MTX	
BL yearly progression	≥5 (n = 221)	<5 (n = 134)	≥5 (n = 121)	<5 (n = 63)	≥5 (n = 115)	<5 (n = 58)	≥5 (n = 224)	<5 (n = 132)
% with no progression (≤0.5)	86.9	94.0	83.5	93.7	89.6	89.7	78.6	87.9
OR	1.81*	2.17	1.38	2.03	2.34*	1.20	†	†
% with no progression (≤0)	78.7	83.6	72.7	84.1	80.0	87.9	67.9	80.3
OR	1.75*	1.25	1.26	1.3	1.89*	1.79	†	†
% with no progression (≤SDC [1.53])	93.7	97.8	91.7	96.8	95.7	96.6	89.3	95.5
OR	1.77	2.08	1.33	1.45	2.64	1.33	†	†

MTX-IR ORs are FIL vs PBO + MTX; MTX-naïve are FIL vs MTX. *Nominal *P*<.05. †Not applicable.ADA, adalimumab; FIL, filgotinib; IR, inadequate response; mTSS, modified total Sharp score; MTX, methotrexate; OR, odds ratio; SDC, smallest detectable change; W, week.

progression (≤0.5 or ≤0) vs PBO + MTX in MTX-IR pts and vs MTX mono in MTX-naïve pts (Table 1).

Conclusion: These data suggest filgotinib's inhibition of radiographic progression was numerically greater than MTX monotherapy in RA pts with high estimated BL yearly progression. In those with a more moderate estimated rate of progression, filgotinib suppressed progression comparably to ADA and/or MTX.

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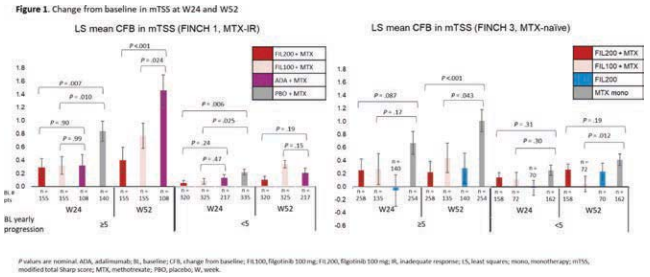

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POS0665 DEVELOPMENT OF A BIOCHEMICAL TOFACITINIB ADHERENCE ASSAY IN RHEUMATOID ARTHRITIS: THE ORAL ADHERE STUDY

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Background: Tofacitinib is a potent inhibitor of the JAK1/JAK3 tyrosine kinases effective in the treatment of rheumatoid arthritis (RA). Unlike biologic DMARDs, tofacitinib is administered orally. Oral administration offers a major benefit to patients, removing the risk of injection site reactions and previous research has shown that patients prefer an oral DMARD which may affect patient's adherence (1). Non-adherence is a health behaviour that results in reduced response and increased healthcare costs but can be challenging to accurately measure. Direct tofacitinib measurement may be an accurate measure of adherence that could, in the future, be used in a clinical setting as part of a behaviour change intervention. Tofacitinib can be measured using High Performance Liquid Chromatography Selected Reaction Monitoring Mass Spectrometry (HPLC-SRM-MS). Previous tofacitinib studies have demonstrated an assay sensitivity of 0.1ng/ml may be sufficient for the detection of adherence following 5mg twice daily administration (2).

Objectives: The aim of this study is to develop a HPLC-SRM-MS assay to measure biochemical tofacitinib adherence in patients with RA.

Methods: Human serum for method development was obtained from volunteers recruited to the collection of blood and urine samples from volunteers for the development of analytical methods study (UREC 12346) and the National Repository Study (REC 99/8/84) following informed consent. Samples were spiked with Tofacitinib/Tofacitinib-d3 and subjected to protein precipitation. LC-MS/MS analysis was performed on a TSQ Vantage triple quadrupole mass spectrometer coupled with an Accela UHPLC system (Thermo Fisher Scientific, USA). Validation of the assay was tested as adapted from European Medicines Agency guidelines on Bioanalytical Validation. Specifically, the lower limit of quantification (LLOQ), carryover, accuracy, linearity, precision, recovery and stability of the assay was determined.

To investigate the ability of the assay to detect adherence, serum samples (n=10) of patients prescribed tofacitinib from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS) were analysed (REC reference: 04/Q1403/37). Participants self-reported date and time of tofacitinib ingestion prior to venepuncture. Samples were analysed in triplicate.

Results: The assay demonstrated a tofacitinib LLOQ of 0.1ng/ml, carryover of sample following injection of a 1000 ng/ml tofacitinib was <1%, linearity of r2=0.998, within run accuracy was between 81-85% at LLOQ and between 91-107% at all other levels. Between run accuracy was within 14.9% at LLOQ and within 0.2-5.1% of the nominal concentration at all other levels. Samples of tofacitinib spiked in whole blood and left at room temperature for seven days were within 0.98-10.25% of serum samples spiked on the day of analysis for all concentrations. To demonstrate the potential of the assay to determine adherence, all 10 BRAGGSS samples revealed tofacitinib levels above 0.1ng/ml with CV<15% (Table 1).

Table 1.

Sample ID	Time difference between self-reported tofacitinib ingestion and blood sample (hours)	Mean Tofacitanib (ng/ml, n=3)	CV (%)
49	7.0	26.43	2.82
40	2.8	100.55	5.51
70	3.6	73.23	2.27
68	1.5	150.37	8.09
20	1.5	137.46	9.09
30	1.8	117.85	14.97
33	1.4	90.89	1.18
79	5.4	217.47	11.40
17	2.8	108.43	7.43
37	2.5	335.04	3.48

Conclusion: A novel tofacitinib LC-MS/MS assay has been developed. The ability of the assay to measure biochemical adherence has been explored. Further research to establish the sensitivity of the assay and the ability of the assay to detect non-adherence are required.

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POS0666

A MULTINATIONAL, PROSPECTIVE, OBSERVATIONAL STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING BARICITINIB, TARGETED SYNTHETIC OR BIOLOGIC DISEASE-MODIFYING THERAPIES: 12 MONTH TIME TO DISCONTINUATION, EFFECTIVENESS AND PATIENT REPORTED OUTCOME DATA FROM THE EUROPEAN COHORT

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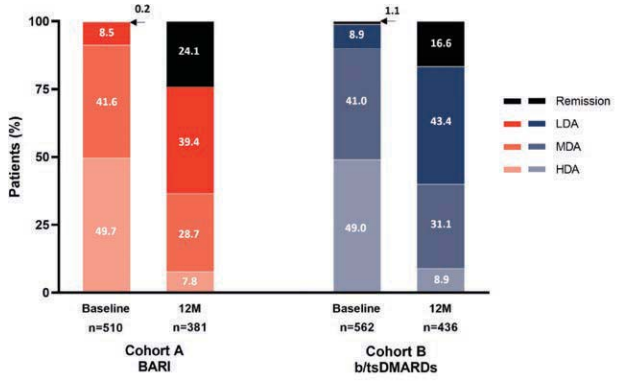
Background: Baricitinib (BARI), an oral selective JAK 1/2 inhibitor, is approved for treating adults with moderate to severe active rheumatoid arthritis (RA). RA-BE-REAL is a 3-year, multinational, prospective, observational study of adult patients with RA evaluating time to discontinuation of initial RA treatment for all causes (excluding sustained clinical response) over 24 months (M).

Objectives: This analysis reports time to discontinuation in the European (France, Germany, Italy, Spain, UK) subgroup, treated with either BARI, biologic (b) disease-modifying anti-rheumatic drugs (DMARDs) or any other targeted synthetic (ts)DMARDs, as well as, the effectiveness of RA treatment, at 12M.

Methods: In the two cohorts, patients were initiated with BARI 2-mg or 4-mg (cohort A), or any bDMARD or tsDMARD (b/tsDMARDs; cohort B). Treatment initiation and changes are at the discretion of the patient or physician. Response rates for remission, low disease activity (LDA), moderate disease activity (MDA) or high disease activity (HDA) were determined using the Clinical Disease Activity Index (CDAI) at 12M. Quality of life using the EQ-5D-5L and patient reported outcome (PRO) measures for pain (pain visual analogue scale; VAS) and physical functioning (Health Assessment Questionnaire Disability Index; HAQ-DI) were also assessed at 12M. This pre-specified interim analysis reports descriptive 12M data using summary statistics, without any inferential testing.

Results: This analysis involved 1073 adult RA patients with a mean age (standard deviation; SD) of 59.1 (13.2) (cohort A) and 57.0 (13.9) yrs (cohort B), respectively, and a mean disease duration (SD) of 10.0 (9.1) (cohort A) and 8.9 (9.6) yrs (cohort B), respectively. At baseline, 50.9% of patients in cohort A and 31.2% in cohort B initiated treatment as a monotherapy. At 12M, 26.7% of patients in cohort A and 44.1% of patients in cohort B had discontinued treatment. The most common reason for discontinuation in both cohorts was primary non-response. At 12M, 24.1% of patients in cohort A and 16.6% in cohort B achieved CDAI remission (Figure 1). The mean CDAI reduction was -14.5 and -12.0, respectively in cohorts A and B. Mean reductions from baseline in physician global assessment (PhGA) and in patient global assessment (PGA) were -3.4 and -2.5, respectively in cohort A and -3.0 and -2.1, respectively in cohort B. Improvements from baseline in EQ-5D-5L, HAQ-DI, and pain (VAS) were reported in both cohorts at 12M. The mean pain (VAS) reduction from baseline was -24.6 and -19.3 in cohort A and cohort B, respectively.



Footnote: Values are presented as percent of each cohort at each timepoint.

BARI; Baricitinib, b/tsDMARDs; biologic or any other targeted synthetic disease-modifying anti-rheumatic drugs, M; months, LDA; low disease activity, MDA; moderate disease activity, HDA; high disease activity.

Figure 1. Percentage of pts in cohorts A and B achieving remission and LDA at 12M

Conclusion: The majority of BARI-treated patients were in remission or had low disease activity and continued treatment at 12M.

Table 1. Disease activity and patient reported outcomes at baseline and 12M

	Cohort A Baricitinib			Cohort B b/tsDMARDs		
	Baseline	12M	CFB	Baseline	12M	CFB
CDAI	24.0 (11.7)	9.1 (8.2)	-14.5 (12.4)	23.8 (12.4)	10.7 (9.8)	-12.0 (12.6)
SJC	5.2 (4.8)	1.3 (2.4)	-3.9 (4.8)	4.7 (4.9)	1.3 (2.8)	-3.0 (4.6)
TJC	7.3 (6.1)	2.2 (3.6)	-4.7 (6.0)	7.8 (6.5)	3.0 (4.8)	-4.0 (6.1)
PhGA	5.6 (2.0)	2.3 (2.1)	-3.4 (2.5)	5.5 (2.1)	2.5 (2.1)	-3.0 (2.6)
PGA	5.9 (2.3)	3.4 (2.5)	-2.5 (2.9)	5.8 (2.4)	3.8 (2.6)	-2.1 (3.0)
HAQ-DI	1.4 (0.7)	1.0 (0.8)	-0.4 (0.6)	1.3 (0.7)	1.0 (0.8)	-0.3 (0.6)
Pain (VAS)	59 (23.1)	33.2 (26.2)	-24.6 (28.7)	56.5 (24.3)	36.6 (26.5)	-19.3 (30.4)
EQ-5D-5L	0.5 (0.3)	0.7 (0.2)	0.1 (0.3)	0.5 (0.3)	0.7 (0.2)	0.1 (0.3)

Values represent observed mean (SD)b/tsDMARDs; biologic/targeted synthetic disease-modifying anti-rheumatic drugs, CFB; change from baseline, CDAI; clinical disease activity index, SJC; swollen joint count, TJC; tender joint count, P(h)GA; patient (physician) global assessment of disease activity, HAQ-DI; health assessment questionnaire disability index, VAS; visual analogue scale (mm), EQ-5D-5L; European quality of life 5 dimensions 5 levels

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POS0667 CHARACTERIZING NON-RESPONSE TO METHOTREXATE MONOTHERAPY AMONG RHEUMATOID ARTHRITIS PATIENTS IN A LARGE REAL-WORLD LONGITUDINAL COHORT

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Background: Methotrexate (MTX) monotherapy is the first choice among disease-modifying drugs (DMARDs) for most moderate-to-severe rheumatoid arthritis (RA) patients, consistent with treatment guidelines.[1] However, response to, and tolerability of, MTX varies among patients.[2] Understanding the proportion of patients with MTX non-response in a real-world setting and identifying its predictors could enable earlier access to alternative or additional medications and improve management of disease progression.

Objectives: The objectives of this study were, using data from a large, geographically representative US cohort of RA patients, to describe the pattern of non-response among patients initiating MTX monotherapy and to identify predictors of non-response to MTX.

Methods: The OM1 RA Registry (OM1, Inc; Boston, MA) follows more than 210,000 RA patients in the US managed by rheumatologists longitudinally with deep clinical data, including laboratory, patient-reported and disease activity information, and linked administrative claims starting from 2013. In this retrospective observational study, patients aged ≥ 18 years initiating MTX between 01 January 2014 and 01 August 2020 without previous bDMARD/tsDMARD utilization were identified. The first MTX date was the index date, with ≥1 Clinical Disease Activity Index (CDAI) measurement and ≥2 all-cause healthcare encounters required in the preceding 12 months (baseline). Patients initiating a bDMARD/tsDMARD within 30 days of the index date or with a history of other conditions where the same bDMARD/tsDMARDs are indicated were excluded. MTX non-response was defined as failing to attain remission or low disease activity (i.e., CDAI >10) within 4 to 8 months and/or the initiation of a bDMARD/tsDMARD within 8 months following the index date (with or without continuing MTX; non-response could include patients discontinuing MTX due to tolerability). Baseline characteristics were summarized with descriptive statistics. Multivariate logistic regression with age, gender, region, race, payor, year of index, the most recent CDAI and body mass index (BMI) measurements from the baseline, and Charlson comorbidity index (CCI) was used to investigate risk factors of non-response. *P* value was considered significant if <0.01.

Results: Among 6,648 eligible RA patients, 3,748 (56.4%) were classified as non-responders. Baseline charactesistics are summarized in Table 1. Being female (OR=1.3), increasing baseline CDAI (OR: Low activity=1.9, moderate activity=8.1, high activity=13.0) and higher BMI (OR=1.01) were significantly associated with non-response. Being older was found protective of non-response (OR=0.98). The C-statistic was 0.74.

Table 1. Baseline Characteristics Overall and by Response Status

Statistic	Overall	Responders	Non-responders
Age	61.6 (13.3)	63.9 (13.0)	59.8 (13.3)
Female	5,059 (76.1%)	2,096 (72.3%)	2,963 (79.1%)
Region			
MIDWEST	905 (13.6%)	366 (12.6%)	539 (14.4%)
NORTHEAST	1,115 (16.7%)	520 (17.9%)	595 (15.9%)
SOUTH	4,063 (61.1%)	1,759 (60.7%)	2,304 (61.5%)
WEST	565 (8.5%)	255 (8.8%)	310 (8.3%)
Race			
BLACK	597 (9.0%)	243 (8.4%)	354 (9.5%)
WHITE	4,305 (64.8%)	1,935 (66.7%)	2,370 (63.2%)
OTHER	166 (2.5%)	73 (2.5%)	93 (2.5%)
UNKNOWN	1,580 (23.8%)	649 (22.4%)	931 (24.8%)
Payor			
COMMERCIAL	3,768 (56.7%)	1,516 (52.3%)	2,252 (60.1%)
MEDICARE	2,590 (39.0%)	1,273 (43.9%)	1,317 (35.1%)
MEDICAID	290 (4.4%)	111 (3.8%)	179 (4.8%)
CDAI	15.6 (10.4)	11.3 (9.5)	18.9 (9.8)
CCI	1.4 (1.1)	1.4 (1.1)	1.4 (1.1)
BMI	30.4 (7.1)	29.7 (6.8)	30.9 (7.3)

Conclusion: We found that over half of patients qualified as MTX non-responders at approximately 6 months. Significant predictors of non-response were younger age, female gender, higher CDAI score and BMI. Maximizing improvement as quickly as possible and deploying more tailored escalation of care may be aided by identifying RA patients at higher risk of early MTX treatment failure.

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POS0668 THE EFFICACY OF TOFACITINIB ON CLINICAL DYNAMIC AND CONCENTRATION OF CYTOKINES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Pathogenesis of RA includes numerous interactions of genetic and acquired defects in normal immunoregulation, one is disbalance of pro- and anti-inflammatory cytokines production. Basic treatment conception in RA is «treat-to-target», including biological agents and Janus kinase (JAK) inhibitors. Tofacitinib is one of the first JAK-inhibitors in clinical practice, but data on its influence on cytokine profile during course of treatment are still limited.

Objectives: To study the dynamics of clinical signs, laboratory parameters of inflammatory activity and cytokines profile in RA patients treated with tofacitinib.

Methods: A total of 10 adults with valid diagnosis of RA (ACR/EULAR, 2010) and high disease activity (DAS28 5,88 [5,53; 5,94], CDAI 33.0 [29.0; 36.0], SDAI 33.72 [30.75; 36.85] score) were enrolled to the study. Mean age was 51,0 [48,0; 62,0] years, median disease duration 7.0 [3,0;20.0] years. All patients received TOFA 5 mg bid, methotrexate, non-steroidal anti-inflammatory drugs. There were 3 control points: before treatment, 3 and 6 months of tofacitinib treatment. Concentration of IL-1β, IL-4, IL-6, TNF-α, INF-γ, IL-10, IL-17A, IL-17F, IL-21, IL-22, IL-23, IL-25, IL-31, IL-33, sCD40L were studied using multiplex technology (BioPlexTM 200 System, BIO-RAD, USA).

Results: Significant decrease in RA activity was marked after 3 and 6 months of treatment with tofacitinib - DAS28 of 4.55 [3.47; 5.16], 3.92 [3.80; 4.60]; CDAI 16.5 [11.0; 23.0], 18.0 [15.0; 19.0]; SDAI 16.6 [11.23; 23.06], 18.07 [15.06; 19.10]; ESR 19.0 [11.0; 26.0], 7.0 [4.0; 18.0]; CRB 0.56 [0.50; 1.99], 0.71 [0.51; 1.1], respectively. IL-6 levels decreased after 3 and 6 months of therapy ($p<0.05$). The concentration of IFN-γ significantly decreased after 3 months ($p<0.05$) but remained unchanged thereafter. Concentrations of IL-25 and IL-31 decreased after 3 months ($p<0.05$), and by the 6th month of treatment there was an increase, but not reaching the initial values. The results of the study are shown in Table 1

Table 1. Levels of cytokines in RA patients receiving tofacitinib, pg/ml, Me [25;75 percentile].

Cytokine	Initial	After 3 months of tofacitinib treatment	After 6 months of tofacitinib treatment
IL-1β	0,07 [0,03;0,13]	0,05 [0,03;0,08]	0,08 [0,06;0,11]
IL-4	4,28 [3,32;10,42]	3,96 [2,49;13,25]	7,03 [3,69;13,46]
IL-6	3,43 [2,44;11,02]	2,28 [1,62;3,85]*	1,55 [1,33;2,07]*
TNF-α	1,35 [0,68;2,41]	1,11 [0,68;1,76]	0,95 [0,49;1,57]
IFN-γ	2,05 [1,48;3,19]	0,99 [0,49;2,05]*	0,99 [0,49;2,62]*
IL-10	2,96 [1,20;2,56]	2,10 [1,50;3,04]	2,41 [1,80; 3,99]
IL-17A	1,57 [0,42;2,17]	1,20 [0,71;1,72]	1,27 [0,85;1,27]
IL-17F	2,49 [1,25;12,38]	1,56 [0,0;3,30]	2,49 [1,87;5,97]
IL-21	4,74 [1,19;49,36]	2,07 [0,0;5,93]	4,75 [4,75;10,46]
IL-22	2,76 [0,63;4,10]	1,18 [0,94;2,21]	2,21 [0,32;3,94]
IL-23	13,54 [7,34;46,27]	10,26 [4,41;19,74]	13,90 [8,80;20,46]
ИЛ-25	1,11 [0,32;2,18]	0,31 [0,0;1,25]*	0,42 [0,21;1,4]*
IL-31	6,95 [3,85;17,72]	3,00 [1,50;3,85]*	5,09 [3,85;6,33]*
IL-33	13,66 [8,72;38,48]	8,10 [3,90;22,37]	14,07 [9,96;26,09]
sCD40L	72,77 [8,90;201,18]	15,31 [4,29;34,80]	40,17 [26,53;68,55]

*p<0,05 (comparing with initial concentration)

Conclusion: The data obtained indicate the efficacy of tofacitinib in patients with RA, including decreasing of disease activity and concentrations of clue pro-inflammatory cytokines. Further studies are needed to investigate pathogenic role of cytokine-mediated inflammation in RA and the efficacy of targeted oral medications on the course of the disease.

Disclosure of Interests: None declared

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POS0669

TAPERING SUBCUTANEOUS METHOTREXATE CAUSES MORE DISEASE FLARES COMPARED TO ORAL ADMINISTRATION IN ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS.

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Background: Thanks to improved treatment strategies, disease remission in rheumatoid arthritis(RA) patients has become more common. Therefore, current guidelines recommend to consider tapering DMARDs, including methotrexate(MTX), in patients who are in sustained remission. Previous research has shown that subcutaneous methotrexate(MTXsc) has a better bioavailability, efficacy and tolerability in active RA than oral MTX[1]. However, these advantages might be a disadvantage when tapering of MTXsc is considered.
Objectives: To compare the 1-year cumulative flare rates between established RA patients who taper subcutaneous and oral MTX.
Methods: Data from the TApering strategies in Rheumatoid Arthritis(TARA) trial were used[2]. In this trial, established RA patients with a well-controlled disease, defined as Disease Activity Score(DAS)≤2.4 and swollen joint count(SJC)≤1, using ≥1 csDMARD and TNF-inhibitor(TNFi) were included. Participants were randomized into two groups which gradually tapered their csDMARD first followed by the TNFi, or vice versa. The csDMARD was tapered by reducing the dosage by a half at baseline, by a quarter at 3 months and was stopped at 6 months. Patients who tapered MTX were included in this analysis. If a disease flare(DAS>2.4 or SJC>1) occurred, the last effective therapy was restarted and intensified every 3 months, until DAS≤2.4 and SJC≤1. Following an intention-to-treat principle, flare rates were compared between patients who tapered subcutaneous and oral MTX, using a chi-square test. Two sensitivity analyses were performed were we 1) only included patients with a complete follow-up; and 2) assumed that patients developed a flare at the moment of drop-out.
Results: A total of 71 and 17 patients respectively used oral and subcutaneous MTX. The median disease duration was 5.9 years and 70% was female. The median MTX dosage for both administration routes was 20 milligrams per week. After 12 months, 53% of patients who tapered MTXsc developed a flare compared to 27% who tapered oral MTX (OR 3.1(1.0-9.1, 95%CI), p=0.037)(Figure 1). Respectively 68% and 67% of the patients who developed a flare and were using oral and subcutaneous MTX had a well-controlled disease 3 months after restarting their treatment(p=0.93). Both sensitivity analyses showed similar results.

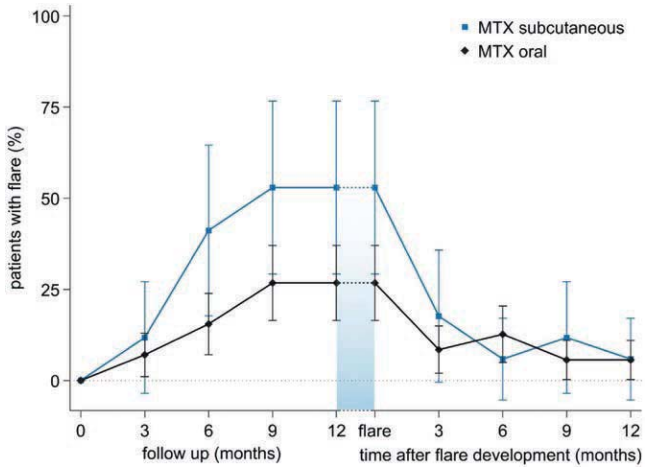

Figure 1. Flare development and resolution over time for different administration routes of methotrexate.*The first part on the X-axis illustrates the cumulative % of patients that develop a disease flare during follow up, the second part illustrates the cumulative % of patients that still has active disease (DAS>2.4 +/ SJC44>1) from point of flare development and after restarting the last effective treatment.Abbreviations: DAS, Disease Activity Score; MTX, methotrexate; SJC44, swollen joint count measured in 44 joints.*

Conclusion: Patients who tapered MTXsc have a higher chance at developing a disease flare compared to those who tapered oral MTX. This could be explained by a higher efficacy of MTXsc when similar dosages are used[1]. Alternatively, the better tolerability of MTXsc, especially regarding gastro-intestinal side effects[1], may lead to a difference in adherence. When deciding to taper MTX, the administration route should be taken into account. Because of the increased risk of flare after tapering MTXsc, these patients could be monitored more closely than those tapering oral MTX.

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POS0670

EVALUATION OF UPADACITINIB IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO FIRST-GENERATION JANUS KINASE INHIBITORS

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Background: Janus kinase inhibitors (JAKi) are effective in the treatment of patients with difficult-to-treat rheumatoid arthritis (D2T RA), regardless of previous use of biological disease-modifying antirheumatic drugs (bDMARDs), and receive equal billing with biological therapies in the latest version of the EULAR recommendations for treatment of RA[1]. However, as with bDMARDs, cases of discontinuation due to intolerance or inadequate response have been observed in patients treated with the so-called first-generation JAKi, leading to the development of a new generation of JAKi that aims to maximize efficacy and improve safety by enhancing kinase selectivity. The results of randomized controlled trials and meta-analyses suggest that the efficacy and safety of Upadacitinib (UPA) treatment are favorable. Although there have been no head-to-head trials between JAKi, a matched-adjusted indirect comparative study has shown a difference in efficacy between JAKi[2], suggesting that the new generation of JAKi may be effective in rheumatoid arthritis patients with intolerance or inadequate response to first-generation JAKi. It is already apparent that a clear need exists for a JAK-IR trial to give guidance in those difficult patients who are JAKi non-responders[3].
Objectives: To evaluate real world efficacy of a second-generation JAK1-selective JAKi UPA in single-center cohort of RA patients who had discontinued first-generation JAKi.
Methods: Patients with RA who had discontinued tofacitinib and/or baricitinib due to inadequate response or intolerance, regardless of whether they had used bDMARDs or not, were eligible for the study if they had received UPA by October 2021 and had been followed up for at least 12 weeks. Endpoints were Kaplan-Meier survival rate with inadequate response or intolerance as reasons for discontinuation, various disease activity assessments (DAS28-ESR, SDAI, CDAI, etc.), and patient reported outcomes (visual analogue scales (VASs) such as pain and stiffness, HAQ-DI, FACIT-Fatigue Scale, etc.) at 12 weeks. In addition, the reasons for discontinuation were investigated.
Results: Fifty-one patients were included in the study, all of whom had D2T RA and had used at least one bDMARD as well as JAKi. The mean (median) age was 72.7 (77) years, disease duration 18.0 (17) years, number of bDMARDs used 3.34 (3), number of JAKi used 1.3(1), 5 patients with methotrexate, 6 patients with prednisolone, and DAS28-ESR 3.83 (3.9). At 12 weeks, the overall survival rate was 94% (94.6% in 37 cases used as 2nd JAKi and 92.9% in 14 cases used as 3rd JAKi). For reference, there was no significant difference from the 100% of the 15 cases used as the 1st JAKi (P=0.49). DAS28-ESR <3.2 and <2.6 were achieved in 60.8% and 29.4%, VASs for pain and stiffness decreased by a mean of 12.9 mm (9 mm) and 12.1 mm (7 mm), respectively, and FACIT-Fatigue scale improved by a mean of 3.0 (1). The reasons for discontinuation in the three patients were inadequate efficacy in two and leg cramps due to venous thromboembolism in one.
Conclusion: UPA is more selective for JAK1 than first generation JAKi, and is expected to reduce adverse reactions caused by inhibition of JAK family members other than JAK1. The present study suggests that UPA is effective and well tolerated, regardless of the number and type of first-generation JAKi used in the past, albeit for a short period of time. Limitations include the small number of cases and the short time frame for discussing adverse reactions.

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POS0671

IMPACT OF RACE ON THE EFFICACY AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF PHASE 2, 3 AND 3B/4 CLINICAL TRIALS

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Background: While racial disparities in clinical outcomes for rheumatoid arthritis (RA) patients (pts) have been described,[1] there is a paucity of data on racial differences in response to advanced therapies.

Objectives: To evaluate impact of self-reported race on tofacitinib efficacy/safety in RA pts.

Methods: This post hoc analysis used pooled data from 8 Phase (P)2, 6 P3 and 1 P3b/4 randomised controlled trials (RCTs) of RA pts treated with tofacitinib 5 or 10 mg twice daily (BID), adalimumab (ADA; 40 mg once every 2 weeks) or placebo (PBO), stratified by self-reported pt race (White, Black, Asian, Other) at baseline (BL). Efficacy outcomes (Month [M]3): ACR20/50/70 and CDAI/DAS28-4(ESR) low disease activity (LDA; scores ≤10 and ≤3.2, respectively) rates, and least squares (LS) mean change from BL (Δ) in DAS28-4(ESR) and HAQ-DI. Incidence rates (IRs; unique pts with events/100 pt-yrs) were estimated for adverse events (AEs) and serious AEs.

Results: 6355 pts were included (White, n=4145; Black, n=213; Asian, n=1348; Other, n=649). BL characteristics were generally similar across treatment/racial groups, excepting higher prior bDMARD exposure rates in White/Black vs Asian/Other pts. Across treatments, White, Black, Asian and Other pts most commonly enrolled from Europe (40.9%), North America (68.1%), East/South Asia (97.9%) and Latin America (80.6%), respectively; most Other pts self-reported as Hispanic and/or Latino (52.4%), followed by mixed race (36.8%) and unspecified (4.6%). At M3, ACR50 rates were higher in Other vs White pts with tofacitinib, similar across racial groups with ADA, and numerically higher in Black vs White/Asian/Other pts with PBO (Figure 1); broadly similar trends were seen with ACR20/70 and CDAI LDA rates (data not shown [DNS]). DAS28-4(ESR) LDA rates, and LS mean ΔDAS28-4(ESR) and ΔHAQ-DI were generally comparable across racial groups with active treatment, and numerically higher in Black vs White/Asian/Other pts with PBO (DNS). Across efficacy outcomes, PBO-adjusted response rates and improvements generally supported the trends observed with active treatments (Figure 1; DNS). Safety outcomes were broadly similar across treatment arms, with some higher IRs for AEs observed with Black/Other vs White/Asian pts (Table 1). Results should be interpreted with caution due to low pt numbers in some groups and the heterogenous nature of the Other pts group.

Table 1. AEs and SAEs, stratified by race

	White		Black		Asian		Other	
	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)
Tofacitinib 5 mg BID	**N=1699; PY=1588.3**		**N=93; PY=81.8**		**N=560; PY=548.8**		**N=257; PY=245.9**	
AE	1150	141.9 (133.8, 150.3)	76	244.1 (192.4, 305.6)	382	150.0 (135.4, 165.9)	205	227.1 (197.1, 260.4)
SAE	146	9.1 (7.7, 10.7)	15	19.1 (10.7, 31.4)	61	11.3 (8.6, 14.5)	17	6.7 (3.9, 10.8)
Tofacitinib 10 mg BID	**N=1264; PY=1175.4**		**N=60; PY=49.8**		**N=462; PY=487.2**		**N=238; PY=239.8**	
AE	919	188.5 (176.5, 201.1)	48	434.3 (320.2, 575.8)	338	178.4 (159.9, 198.5)	190	234.3 (202.2, 270.1)
SAE	103	8.9 (7.3, 10.8)	2	3.9 (0.5, 14.3)	47	9.7 (7.1, 12.9)	15	6.2 (3.5, 10.2)
ADA	**N=484; PY=390.4**		**N=22; PY=18.6**		**N=73; PY=60.1**		**N=64; PY=49.5**	
AE	318	140.4 (125.4, 156.7)	16	162.2 (92.7, 263.4)	51	157.0 (116.9, 206.5)	44	161.6 (117.4, 216.9)
SAE	31	7.6 (5.2, 10.8)	2	10.3 (1.3, 37.4)	9	14.5 (6.6, 27.5)	1	1.9 (0.1, 10.4)
PBO	**N=698; PY=177.3**		**N=38; PY=10.0**		**N=253; PY=72.3**		**N=90; PY=24.5**	
AE	369	311.6 (280.6, 345.1)	23	424.9 (269.4, 637.6)	122	251.5 (208.9, 300.3)	48	271.4 (200.1, 359.8)
SAE	23	12.5 (7.9, 18.7)	1	9.4 (0.2, 52.2)	8	10.9 (4.7, 21.4)	3	11.5 (2.4, 33.6)

n, number of pts with events; PY, pt-yrs; SAE, serious AE

Conclusion: Across racial groups, tofacitinib efficacy/safety was consistent with previous tofacitinib RA clinical programme findings. Some racial differences in clinical outcomes were observed, which may reflect regional practice norms or demographic differences. Future analyses should focus on the impact of socioeconomic, cultural, genetic or practice-based differences that may underpin these results.

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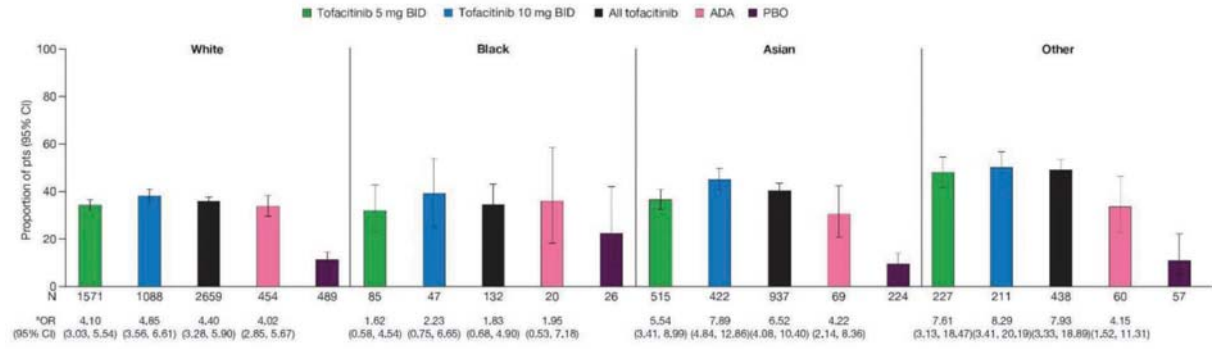
Fig. Proportions of pts achieving ACR50 response across treatment groups at M3, stratified by race



*OR (95% CI) for active treatment vs PBO from a logistic regression model including treatment and disease duration
ACR50, improvement in American College of Rheumatology criteria of ≥50%; CI, confidence interval; N, number of evaluable pts; OR, odds ratio

POS0672

ASSESSMENT OF THE DRUG-DRUG INTERACTION POTENTIAL OF BRANEBRUTINIB (BMS-986195), A HIGHLY POTENT AND SELECTIVE IRREVERSIBLE COVALENT INHIBITOR OF BRUTON'S TYROSINE KINASE, IN HEALTHY PARTICIPANTS

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Background: Branebrutinib (BMS-986195) is a highly potent and selective irreversible small-molecule covalent inhibitor of Bruton's tyrosine kinase (BTK),[1] a non-receptor tyrosine kinase involved in the pathophysiology of immune-mediated diseases. Branebrutinib has the potential to be best in its class, as it achieves ~100% BTK occupancy in humans, sustained over a 24-hour dosing interval at low doses (≤ 10 mg once daily [QD]) despite its short half-life (≤ 2 hours),2 and demonstrates potent efficacy in murine models of immune-mediated diseases.1 Branebrutinib is under clinical study in multiple autoimmune inflammatory disorders such as RA, systemic lupus erythematosus, primary Sjögren's syndrome, and atopic dermatitis. In vitro drug-drug interaction (DDI) studies with branebrutinib predicted pharmacokinetic DDI potential with substrates of cytochrome P450 (CYP)3A4 and the breast cancer resistant protein drug transporter.
Objectives: To assess the DDI potential of branebrutinib when co-administered with potential concomitant medications and probe substrates of major drug-metabolizing enzymes (DMEs) and drug transporters.
Methods: DDI risk with branebrutinib was assessed in 3 single-sequence, cross-over clinical studies in healthy participants. In the first 2-part study, MTX was administered alone or with steady-state (SS) branebrutinib (10 mg QD) in part 1; in part 2, caffeine, montelukast, flurbiprofen, omeprazole, midazolam, digoxin, and pravastatin were taken with or without SS branebrutinib (9 mg QD). In the second study, rosuvastatin was taken alone or with SS branebrutinib (9 mg QD). In cycle 1 of the third study, the oral contraceptive (OC) loestrin (1.5 mg norethindrone/30 µg ethinyl estradiol) was taken alone; in cycle 2, SS branebrutinib (9 mg QD) was taken alone or with the OC.
Results: Weak DDI with montelukast (CYP2C8) was observed, leading to a mild increase in montelukast exposure (max concentration [C_{max}], 56%; area under the curve [AUC], 27%). A mild increase in digoxin exposure (P-glycoprotein [P-gp] substrates; C_{max}, 57%; AUC, 21%) was also observed. There was no potential DDI with MTX (Table 1). No other clinically relevant DDIs with branebrutinib were observed. No serious AEs or other significant AEs occurred during these studies. All AEs were mild to moderate in intensity.

Table 1. Results from clinical DDI studies of branebrutinib

		Adjusted geometric mean ratios with (test) and without (reference) branebrutinib	
Concomitant medication or probe substrate	DME or drug transporter tested	C_{max} ratio (90% CI)	AUC ratio (90% CI)
Digoxin (0.25 mg)	P-gp	1.57 (1.36–1.80)	1.21 (1.11–1.32)
MTX (7.5 mg)	BCRP, OATP1B1, OATP1B3, OAT1, OAT3, MRP2, MRP4	1.00 (0.92–1.09)	0.94 (0.90–0.99)
Pravastatin (40 mg)	OATP1B1, OATP1B3	1.25 (1.00–1.57)	1.06 (0.90–1.25)
Rosuvastatin (10 mg)	BCRP, OATP1B1, OATP1B3	0.81 (0.71–0.93)	0.96 (0.88–1.04)
Montelukast (10 mg)	CYP2C8	1.56 (1.24–1.95)	1.27 (1.10–1.47)
Caffeine (200 mg)	CYP1A2	0.98 (0.94–1.01)	1.16 (1.08–1.24)
Flurbiprofen (50 mg)	CYP2C9	1.06 (0.97–1.16)	1.12 (1.09–1.15)
Omeprazole (50 mg)	CYP2C19	1.05 (0.85–1.30)	0.97 (0.84–1.13)
Midazolam (5 mg)	CYP3A4	0.95 (0.82–1.11)	1.00 (0.84–1.19)
Ethinyl estradiol (30 µg)	CYP3A, CYP2C9, UGAT1A1, SULT1E1	1.16 (1.09–1.23)	1.17 (1.12–1.22)
Norethindrone (1.5 mg)	CYP3A4, CYP2C19	1.10 (1.04–1.15)	1.06 (1.01–1.12)

BCRP, breast cancer resistant protein; MRP, multidrug resistance-associated protein; OAT, organic anion transporting polypeptide; SULT, estrogen sulfotransferase; UGAT, uridine diphosphate glucuronosyltransferase.

Conclusion: In all 3 studies, co-administration of SS branebrutinib was generally well tolerated. The only potentially significant DDIs with substrates of major DMEs or transporters were mild increases in montelukast (CYP2C8) and digoxin (P-gp) exposures.
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POS0673

ENDOTHELIAL INFLAMMATION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB

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Background: Systemic inflammation in rheumatoid arthritis (RA) seems to accelerate atherosclerosis process and increased cardiovascular (CV) events. An adequate joint inflammation control is correlated with endothelial inflammation (EI) improvement. 18F-fluorodeoxyglucose positron emission tomography with computed tomography (FDG PET/CT) has been shown as a non-invasive, sensitive, and specific tool to show EI. Maximum standardized uptake value (SUV(max)) greater than 1,6 has been correlated with vascular and joint inflammation. Tofacitinib is a Jak inhibitor (JaKi) approved for RA that improves activity and function. The aim of this study is to evaluate the EI outcome by FDG-PET in RA patients treated with tofacitinib.
Objectives: To assess the EI by FDG-PET/CT in RA patients at baseline and after 12 weeks of tofacitinib treatment initiation. To correlate the vascular findings with disease activity, lipid profile and carotid atherosclerosis by echo Doppler.
Methods: Prospective, observational study. Inclusion criteria: RA (ACR 2010) patients >18 years old, with high activity score (DAS 28 >3,2) and with biologics or synthetic Dmards requirement by Treat to Target strategy and who tofacitinib was prescribed. Exclusion Criteria: Biologics or Jaki previous use or major CV history known. A baseline Visit evaluating disease activity (DAS 28 and CDAI), functional status by Health Assessment Questionary (HAQ), CV and smoking history, treatments and lipid lab assessment was performed. EI was measured by PET-FDG/CT, showing the SUVmax and target-to-background ratio (TBR) in: right primitive carotid, left primitive carotid, ascendent aorta, descendent aorta and abdominal aorta. Carotid echo Doppler for showing plaque presence was done. During baseline visit tofacitinib was started. After 12 weeks the initial parameters were re-evaluated.
Results: Consecutively, 30 patients were included. Mean age 57 yo (21-79). Female 70%. Mean disease duration 8,3 years (1-40), mean Body mass index (BMI) 24,5. Clinical history: Hypertension 27%, smoking 6,6%, methotrexate treatment 46,6%, methotrexate plus leflunomide 50%, corticosteroids 7,6% (mean dosis 7,6 mg/day).
Mean values of DAS 28, CDAI and HAQ were 5.21, 26,6 y 1,56 in baseline and 3,04, 8,80 y 1,09 in the final visit respectively (p:< 0,001 in all comparations) showing statistical significance activity improvement. Echo doppler showed Carotid plaque in 40% of patients without change between visits. Mean cholesterol levels were 188,5 y 207,53 mg/dl in baseline and final visit respectively (p: 0,0039), showing statistical significance. Endothelial uptake by PET-FDG in the 5 areas measured, considering baseline and final visit was: Right Primitive Carotid: SUV Max 2,03 and 1,93 (p: 0,32) and TRB Max 0,94 and 0,85 (p:1,0); Left Primitive Carotid Suv Max 2,07 and 1,94 (p:1,0) and TRB Max 0,92 and 0,90 (p:0,57); Ascendent Aorta SUV Max 2,63 and 2,57 (p:1,0) and TRB Max 1,18 and 1,15 (p:1,0); Descendent Aorta SUV Max 2,77 and 2,57 (p:0,26) and TRB Max 1,27 and 1,17 (p:0,26) and Abdominal Aorta SUV Max 2,59 and 2,43 (p:0,85) and TRB Max 1,15 y 1,11 (p:0,32). None of the endothelial uptake comparisons showed a significant difference between baseline and final visit after 12 weeks.
Conclusion: This work shows that, despite the significant improvement in joint activity and function values, there was no modification in EI measured by FDG-PET during tofacitinib treatment along 12 weeks. It is noteworthy that all patients initially presented high inflammatory endothelial uptake values, which reinforces the hypothesis of vascular compromise associated with active joint disease. Studies with more observation time and evaluating the role of different treatments related to endothelium will be of clinical utility in the future.
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POS0674

RISK FACTORS FOR MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS AGED ≥50 YEARS WITH RHEUMATOID ARTHRITIS AND ≥1 ADDITIONAL CARDIOVASCULAR RISK FACTOR: A POST HOC ANALYSIS OF ORAL SURVEILLANCE

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Background: ORAL Surveillance (NCT02092467) was a post-approval safety study of tofacitinib vs TNF inhibitors (TNFi) in rheumatoid arthritis (RA) patients (pts) aged ≥50 yrs with ≥1 additional cardiovascular (CV) risk factor and an inadequate response to methotrexate (MTX).

Objectives: To identify independent risk factors for major adverse CV events (MACE) in ORAL Surveillance.

Methods: Pts on stable MTX were randomised 1:1:1 to receive tofacitinib 5 or 10 mg twice daily (BID) or a TNFi (adalimumab 40 mg every 2 weeks or etanercept 50 mg once weekly). Incidence rates (IRs; pts with first events/100 pt-yrs) and hazard ratios (HRs; tofacitinib vs TNFi) were assessed for adjudicated MACE (total/fatal/non-fatal), sudden cardiac death, and total/fatal/non-fatal myocardial infarction (MI) and stroke. Post hoc univariate Cox model analyses identified potentially independent baseline (BL) risk factors for MACE across treatments; those with p<0.10 were entered into a multivariate Cox model using backward selection (p<0.10 stay criteria). MACE HRs were produced for subgroups for BL risk factors with p<0.05 in the final multivariate Cox model.

Results: 4362 pts were included (tofacitinib 5 mg BID, n=1455; tofacitinib 10 mg BID, n=1456; TNFi, n=1451). IRs for total/fatal/non-fatal MACE, sudden cardiac death, and total/non-fatal MI were higher with tofacitinib vs TNFi (Table 1). Fatal MI and stroke (including fatal/non-fatal events) IRs were similar across treatments (Table 1). Total MACE and MI IRs and risk were higher with tofacitinib vs TNFi (HRs >1) and higher for non-fatal MI for tofacitinib 5 mg BID (Table 1). Current smoking, aspirin use, history of chronic lung disease, history of diabetes, male sex and older age were BL risk factors for MACE. While MACE risk was generally higher with tofacitinib vs TNFi across all BL risk factors, increased risk was clearest in current/past smokers (vs never smoked) and aspirin users (vs non-users) (Figure 1). When age and smoking status were considered in combination, pts aged ≥65 yrs or who had ever smoked had a particularly elevated MACE risk vs never smokers aged ≥50–<65 yrs (Figure 1).

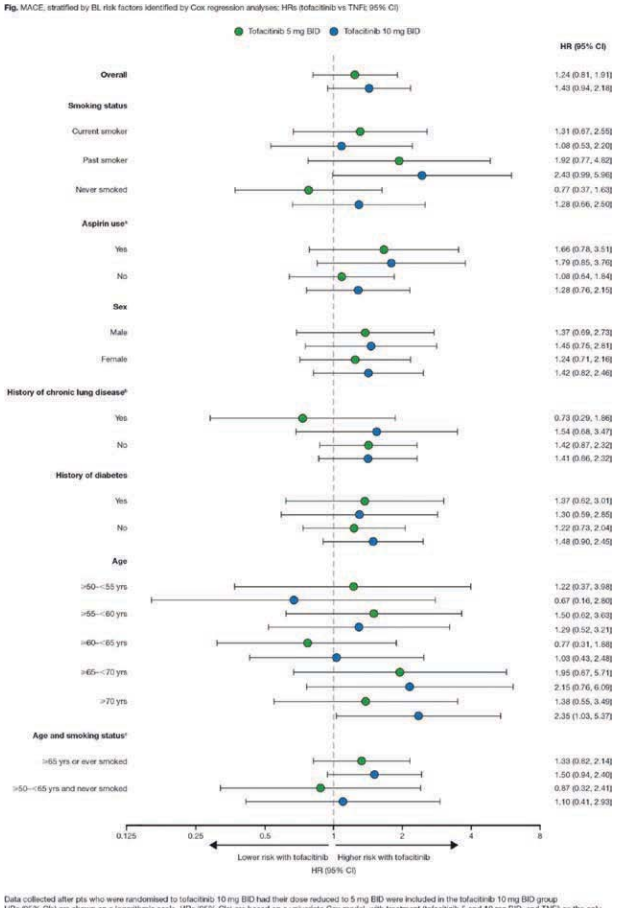

Table 1. MACE, MI and stroke IRs (pts with first events/100 pt-yrs; 95% CI) and HRs (tofacitinib vs TNFi; 95% CI)

	Tofacitinib 5 mg BID (N=1455)			Tofacitinib 10 mg BID (N=1456)			TNFi (N=1451)	
	n	IR (95% CI)	HR (95% CI)	n	IR (95% CI)	HR (95% CI)	n	IR (95% CI)
MACE	47	0.91 (0.67, 1.21)	1.24 (0.81, 1.91)	51	1.05 (0.78, 1.38)	1.43 (0.94, 2.18)	37	0.73 (0.52, 1.01)
Fatal MACE	14	0.27 (0.15, 0.45)	1.14 (0.53, 2.47)	19	0.39 (0.23, 0.60)	1.63 (0.79, 3.36)	12	0.24 (0.12, 0.41)
Non-fatal MACE	33	0.64 (0.44, 0.90)	1.29 (0.77, 2.17)	32	0.66 (0.45, 0.93)	1.33 (0.79, 2.24)	25	0.50 (0.32, 0.73)
Sudden cardiac death	10	0.19 (0.09, 0.35)	1.22 (0.48, 3.10)	13	0.26 (0.14, 0.45)	1.67 (0.69, 4.04)	8	0.16 (0.07, 0.31)
MI	19	0.37 (0.22, 0.57)	1.69 (0.80, 3.55)	19	0.39 (0.23, 0.61)	1.80 (0.85, 3.77)	11	0.22 (0.11, 0.39)
Fatal MI	0	0 (0.00, 0.07)	NI	3	0.06 (0.01, 0.18)	1.03 (0.21, 5.11)	3	0.06 (0.01, 0.17)
Non-fatal MI	19	0.37 (0.22, 0.57)	2.32 (1.02, 5.30)[a]	16	0.33 (0.19, 0.53)	2.08 (0.89, 4.86)	8	0.16 (0.07, 0.31)
Stroke	18	0.35 (0.21, 0.55)	1.03 (0.53, 2.00)	18	0.37 (0.22, 0.58)	1.10 (0.57, 2.13)	17	0.34 (0.20, 0.54)
Fatal stroke	4	0.08 (0.02, 0.20)	NI	2	0.04 (0.00, 0.15)	NI	0	0.00 (0.00, 0.07)
Non-fatal stroke	14	0.27 (0.15, 0.45)	0.80 (0.40, 1.63)	16	0.33 (0.19, 0.53)	0.97 (0.49, 1.93)	17	0.34 (0.20, 0.54)

[a]HR 95% CI excludes 1. Data collected after pts who were randomised to tofacitinib 10 mg BID had their dose reduced to 5 mg. BID were included in the tofacitinib 10 mg BID group. HRs (95% CI) were not informative when one of the treatments in the comparison had 0 events. Risk period was defined as time from first dose to last dose +60 days or to the last contact date, whichever was earlier. CI, confidence interval; NI, non-informative

Conclusion: MACE IRs and risk were higher with tofacitinib vs TNFi in ORAL Surveillance. BL risk factor findings could aid identification of RA pts with potentially highest risk for MACE, with a view to informing treatment decisions.
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POS0675 IMPACT OF PAST USE OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS ON JAK INHIBITOR TREATMENT FOR RHEUMATOID ARTHRITIS - DATA FROM THE FUKUI ISHIKAWA TOYAMA DATABASE OF RHEUMATOID ARTHRITIS

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Background: Currently, five types of Janus kinase inhibitors (JAKis) are used for rheumatoid arthritis (RA) treatment. The number of cases in which multiple JAKis have been prescribed is increasing. However, the real-world efficacy and safety of JAKis and related factors require further evaluation.
Objectives: The primary objective of this study was to elucidate the impact of past use of disease-modifying anti-rheumatic drugs on RA treatment using JAKis. The secondary objective was to investigate the safety profiles of these agents in a real-world setting.
Methods: Of the 303 JAKi-treated patients in the Fukui Ishikawa Toyama Database of RA included in this study, 30 had switched from one JAKi to another (JJ group), 214 switched from a biologic agent to a JAKi (BJ group), and 47 were naïve to either biologics or JAKis (NJ group). We compared baseline factors, treatment response, and JAKi continuation rates among the three groups. Factors related to JAKi discontinuation were assessed using Cox regression analysis. Furthermore, we investigated adverse events and reported them using exposure-adjusted incidence rates (EAIR; incidence rates per 100 patient-years).
Results: Data from the 303 cases were analyzed (mean age = 63.6 years; female, 82%; mean RA duration, 176 months). Of the 303 patients, 118, 106, 50, and 29 were treated with tofacitinib, baricitinib, peficitinib, and upadacitinib, respectively, on initial observation. Rate of concomitant use with methotrexate and prednisolone was 52% and 49%, respectively.
Regarding efficacy, no significant differences were observed among the three groups in terms of treatment response and JAKi continuation rates, except for the 6-month treatment response between the JJ and NJ groups. Cox regression analysis of the 303 cases revealed that only past use of JAKis during the disease history was significantly associated with JAKi discontinuation. The Kaplan–Meier method showed that patients who previously used JAKis had significantly shorter median JAKi treatment duration than those without such a history (20.9 vs. 54.7 months; p = 0.012). Treatment response was significantly poor in patients who had previously used JAKis, especially 6 months after treatment initiation. In terms of safety, the total exposure period for the 303 cases was 495 person-years, and the total number of adverse events was 161 (EAIR, 32.5). There were 12 cases (EAIR, 2.5) of serious infections, 23 cases (EAIR, 5.1) of herpes zoster, 7 cases (EAIR, 1.4) of malignant tumors, and 4 cases (EAIR, 0.8) of MACE. Adverse events led to JAKi discontinuation in 34 patients (EAIR, 6.9); the main causes of adverse events leading to treatment discontinuation were infectious diseases in 10 cases (EAIR, 2) and neoplasms in 4 cases (EAIR, 0.8). Within 1 year of initiating JAKi therapy, 21 patients discontinued treatment owing to adverse events, which accounted for 27% of the reasons for treatment discontinuation. We also investigated cases of JAKi dose reduction, observed in 42 of the 303 cases. Among them, 10 patients required a re-increase in the JAKi dose, and 13 patients (56.5%) were able to maintain the reduced dose for more than 1 year. The remaining 19 patients were excluded from the analysis because the treatment duration at the lower dose had not exceeded 1 year at the time of data extraction. No difference in disease activity at the time of dose reduction was observed between those who maintained the new dose and those who did not (mean DAS28-CRP: 1.48 ± 0.26 vs. 1.89 ± 0.62).
Conclusion: Past use of JAKis may contribute to decreased response and continuation rates for JAKi treatment. In this study, conducted in Japan, development of herpes zoster was found to the most frequent adverse event among the priority survey items.
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Disclosure of Interests: None declared
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POS0676 EFFICACY AND SAFETY OF FILGOTINIB IN PATIENTS AGED ≥75 YEARS: A POST HOC SUBGROUP ANALYSIS OF THE FINCH 4 LONG-TERM EXTENSION (LTE) STUDY

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Background: Filgotinib (FIL) is a Janus kinase 1 preferential inhibitor for the treatment of moderate to severe rheumatoid arthritis (RA)[1]. The recommended dose for adults with RA is 200 mg (FIL200); however, a starting dose of 100 mg (FIL100) is recommended for those aged ≥75 years (y) in view of limited clinical experience[1]. An important consideration is the generally higher incidence of adverse events (AEs) in the elderly due to comorbidities.
Objectives: To evaluate the efficacy and safety of FIL100 and FIL200 in patients with RA aged ≥75 y.
Methods: FINCH 4 (NCT03025308) is an ongoing phase 3 open-label LTE study of FIL100 and FIL200 for RA. Eligible patients completed a prior phase 3 randomized double-blind study of FIL lasting 52 weeks (FINCH 1 or 3) or 24 weeks (FINCH 2). In this *post hoc* analysis, safety and efficacy were assessed in patients aged <75 and ≥75 y in FINCH 4. Efficacy measures were American College of Rheumatology (ACR)20/50/70 responses, clinical disease activity index (CDAI) ≤10/≤2.8, disease activity score (DAS)28 <2.6/≤3.2 and health assessment questionnaire-disability index (HAQ-DI).
Results: At LTE Week 48, 52% and 44% of patients aged <75 and ≥75 y, respectively, were on methotrexate. In both age groups, response rates for key efficacy measures at LTE Week 48 were generally maintained from LTE baseline (Figure 1) in patients with and without prior FIL exposure in FINCH 1–3, and were numerically higher with FIL200 vs FIL100. Mean change from baseline in

HAQ-DI with FIL200 and FIL100 was 0.61 and 0.74 in those aged <75 y and 1.04 and 0.98 in those aged ≥75 y, respectively.

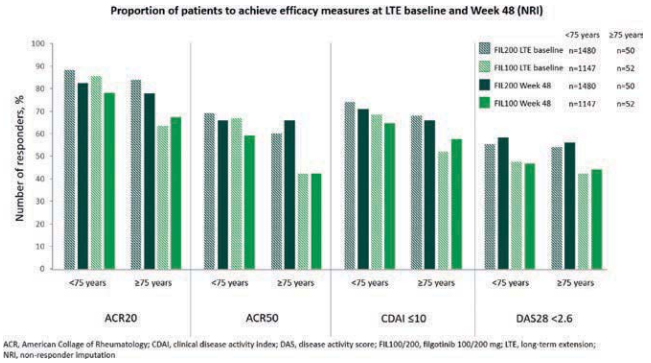

Figure 1.

The exposure-adjusted incidence rate (EAIR) of serious AEs and AEs of special interest (AESI) was generally higher in patients aged ≥75 y than <75 y. In those aged ≥75 y, the EAIR of AEs leading to premature study discontinuation, treatment-emergent AEs (TEAEs), and serious TEAEs was higher with FIL200 vs FIL100; the incidence of major adverse cardiovascular events, venous thrombotic and embolic events, serious infections, herpes zoster and malignancies was low in both dose groups (Table 1). Three patients died, all from the FIL200 group; each had a medical history relevant to the cause of death.

Table 1. Exposure-adjusted incidence rate (95% CI) of AEs at Week 48 as events per 100 years of exposure

	FIL200		FIL100	
Age, years	<75	≥75	<75	≥75
	n=1469	n=61	n=1136	n=63
	(PYE 2253.9)	(PYE 92.2)	(PYE 1753.7)	(PYE 98.4)
With prior FIL exposure, n (%)	1142 (77.7)	53 (86.9)	830 (73.1)	33 (52.4)
TEAE	48.3 (45.5, 51.3)	55.3 (42.1, 72.8)	48.7 (45.5, 52.1)	42.7 (31.6, 57.8)
Serious TEAE	6.8 (5.8, 8.0)	17.4 (10.6, 28.3)	7.4 (6.2, 8.7)	14.2 (8.4, 24.0)
AE leading to premature study discontinuation	2.9 (2.3, 3.7)	9.8 (5.1, 18.8)	3.9 (3.1, 5.0)	4.1 (1.5, 10.8)
AE leading to death	0.5 (0.3, 0.9)	3.3 (0.7, 9.5)*	0.3 (0.2, 0.8)	0.0 (0.0, 3.8)
Infections	28.8 (26.6, 31.1)	29.3 (20.1, 42.7)	27.4 (25.0, 29.9)	26.4 (18.0, 38.8)
Serious infections	1.6 (1.2, 2.2)	2.2 (0.5, 8.7)	1.7 (1.1, 2.4)	3.1 (1.0, 9.5)
Herpes zoster	1.6 (1.2, 2.3)	2.2 (0.5, 8.7)	1.0 (0.6, 1.6)	3.1 (1.0, 9.5)
Adjudicated major adverse cardiovascular event	0.4 (0.2, 0.7)	2.2 (0.5, 8.7)	0.5 (0.2, 0.9)	1.0 (0.1, 7.2)
Venous thrombotic and embolic events	0.3 (0.1, 0.6)	2.2 (0.5, 8.7)	0.2 (0.1, 0.5)	1.0 (0.1, 7.2)
Malignancy excluding NMSC	0.7 (0.4, 1.2)	4.3 (1.6, 11.6)	0.7 (0.4, 1.2)	3.1 (1.0, 9.5)
NMSC	0.4 (0.2, 0.8)	1.1 (0.0, 6.0)	0.2 (0.1, 0.6)	0.0 (0.0, 3.8)

*Cause of death: esophageal carcinoma; cardiovascular; unknown. FIL(100/200), filgotinib (100/200 mg); NMSC, nonmelanoma skin cancer; PYE, patient years of exposure; (TE)AE, (treatment-emergent) adverse event

Conclusion: In the ≥75 y group, response rates for key efficacy measures remained stable to Week 48 and were generally higher with FIL200 vs FIL100. The incidence of serious AEs and AESI was higher in those aged ≥75 than <75 y. Patient numbers/exposure time may have been insufficient to show potential between-group differences in safety/efficacy outcomes.

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[1] Filgotinib SmPC

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POS0677 CONSISTENCY IN TIME TO RESPONSE WITH UPADACITINIB AS MONOTHERAPY OR COMBINATION THERAPY AND ACROSS PATIENT POPULATIONS WITH RHEUMATOID ARTHRITIS

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Background: Upadacitinib (UPA) has demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) across various patient populations.[1–4]

Objectives: This post hoc analysis aimed to evaluate the consistency in time to achieving meaningful clinical response with UPA 15 mg + conventional synthetic (cs) DMARDs in biologic (b) DMARD-inadequate responder (IR) versus csDMARD-IR patients with RA as well as with UPA 15 mg monotherapy versus UPA 15 mg + csDMARDs in csDMARD-IR patients.

Methods: Patients originally randomized to UPA 15 mg once daily from four Phase 3 trials were included in this analysis: SELECT-BEYOND[1] and SELECT-CHOICE[2] (UPA 15 mg + csDMARDs in bDMARD-IR patients), SELECT-NEXT[3] (UPA 15 mg + csDMARDs in csDMARD-IR patients), and SELECT-MONOTHERAPY[4] (UPA 15 mg monotherapy in methotrexate-IR patients). Time to response was estimated using the Kaplan–Meier method for clinical outcomes over 24 weeks (26 weeks in SELECT-MONOTHERAPY). Clinical outcomes included achievement of 28-joint Disease Activity Score with C-reactive protein (DAS28[CRP]) ≤3.2; low disease activity (LDA) defined as Clinical Disease Activity Index (CDAI) ≤10 and Simple Disease Activity Index (SDAI) ≤11; and 50% improvement in American College of Rheumatology (ACR) core components and morning stiffness (MS) duration/severity. Data presented were as observed.

Results: Overall, 905 patients were included (SELECT-BEYOND: n=164; SELECT-CHOICE: n=303; SELECT-NEXT: n=221; SELECT-MONOTHERAPY: n=217). csDMARD-IR patients had a mean disease duration of 7.3 (SELECT-NEXT) or 7.5 years (SELECT-MONOTHERAPY); bDMARD-IR patients had a mean disease duration of 12.4 years, with a more refractory population (≥3 prior bDMARDs) in SELECT-BEYOND (23%) than SELECT-CHOICE (10%). In general, the median time to DAS28(CRP) ≤3.2, CDAI LDA, 50% improvement in ACR core components, and 50% improvement in MS duration/severity were consistent across the studies in bDMARD-IR and csDMARD-IR patients. For SELECT-BEYOND, SELECT-CHOICE, SELECT-NEXT, and SELECT-MONOTHERAPY, the median (95% CI) time to achieve DAS28(CRP) ≤3.2 was 12 (12, 16), 12 (8, 12), 12 (8, 12), and 14 (8, 14) weeks, respectively (Figure 1), and the median time to achieve CDAI LDA was 20 (12, 24), 16 (12, 16), 16 (12, 16), and 20 (14, 20) weeks, respectively (Figure 2). A longer median (95% CI) time to achieve SDAI LDA was observed with UPA monotherapy (20 [14, 20] weeks) versus UPA + csDMARDs (12 [12, 16] weeks) in csDMARD-IR patients. Among bDMARD-IR patients, the median (95% CI) time to 50% improvement in pain was longer in SELECT-BEYOND versus SELECT-CHOICE (16 [12, 20] versus 8 [8, 12] weeks).

Conclusion: In diverse patient populations with RA, patients treated with UPA 15 mg, as monotherapy or with csDMARDs, generally demonstrated consistent

time to achieving DAS28(CRP) ≤3.2, CDAI LDA, and 50% improvement in clinical outcomes.

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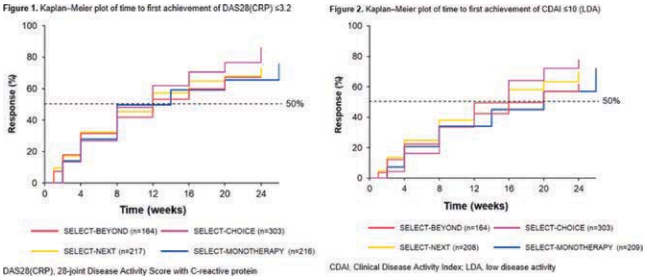

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POS0678

CLINICAL OUTCOMES OF METHOTREXATE (MTX)-NAIVE RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) ON FILGOTINIB (FIL) LONG-TERM EXTENSION (LTE) TRIAL INITIALLY ON FIL OR MTX DURING THE PHASE 3 PARENT STUDY (PS)

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Background: The preferential Janus kinase-1 inhibitor FIL is approved for treatment of moderate to severe active RA in Europe and Japan.

Objectives: In this post hoc, exploratory analysis, efficacy and safety of long-term treatment with FIL (± MTX) were assessed in MTX-naïve pts treated with FIL or MTX in the Phase 3 PS (NCT02886728).[1]

Methods: Pts received FIL 200 mg (FIL200)+MTX, FIL 100 mg (FIL100)+MTX, FIL200 alone, or MTX alone up to 52W in PS.[1] Those completing PS on study drug could enter LTE (NCT03025308; data cutoff: June 1, 2020). MTX completers were rerandomized, blinded, to FIL200 or FIL100; pts on FIL in PS remained on the same dose in LTE. MTX was washed out for 4W at LTE baseline (BL); pts could (re)start MTX and/or other conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) ≥4W after LTE first dosing.[1] Efficacy data to LTE W48 and safety data are reported.

Results: As of June 1, 2020, 439/492 (89%) and 144/169 (85%) pts who entered LTE from PS FIL200 and PS FIL100 groups, respectively, remained on LTE study treatment; of those rerandomized from MTX, 131/148 (89%) FIL200 and 133/151 (88%) FIL100 pts remained on study treatment. LTE BL characteristics were similar between FIL200 and FIL100 groups. After MTX washout, 17% of FIL200 and 23% of FIL100 pts (re)started MTX (at clinical judgment). ACR20/50/70 response rates among pts from PS FIL arms decreased modestly from LTE BL to W12 then stabilized. Among pts who switched from PS MTX to LTE FIL, response rates remained stable or improved to approach those of PS FIL pts by W48 (Figure 1). Similar trends were seen in DAS28(CRP) and CDAI. Treatment-emergent adverse events (TEAEs), Grade ≥3 AEs, serious AEs, and infections were largely comparable across groups and did not increase after MTX to FIL switch. There were 6 deaths, all among PS FIL200 pts (Table 1).

Table 1. EAIRs of TEAEs through June 2020

EAIR (95% CI)	FIL200+MTX → FIL200 LTE	FIL200 → FIL200 LTE	FIL100+MTX → FIL100 LTE	MTX → FIL200 LTE	MTX → FIL100 LTE
	n=325	n=167	n=169	n=148	n=151
	PYE=474.4	PYE=232.5	PYE=236.4	PYE=213.4	PYE=215.4
TEAE	49.7 (43.8, 56.5)	46.9 (38.9, 56.6)	49.9 (41.7, 59.8)	50.6 (41.9, 61.1)	46.4 (38.2, 56.5)
TEAE Grade ≥3	7.2 (5.1, 10.0)	6.5 (3.9, 10.7)	10.2 (6.8, 15.1)	7.0 (4.2, 11.7)	7.0 (4.2, 11.6)
TE serious AE	5.9 (4.1, 8.5)	6.0 (3.6, 10.2)	8.9 (5.8, 13.6)	6.6 (3.9, 11.1)	6.5 (3.9, 11.0)
Death	1.1 (0.3, 2.5)	0.4 (0.1, 3.1)	0 (0, 1.6)	0 (0, 1.7)	0 (0, 1.7)
Infections	28.5 (24.0, 33.7)	29.7 (23.4, 37.6)	27.5 (21.6, 35.1)	28.6 (22.2, 36.7)	27.4 (21.2, 35.4)
Serious infections	1.1 (0.4, 2.5)	3.0 (1.4, 6.3)	2.5 (1.1, 5.7)	1.9 (0.7, 5.0)	1.9 (0.7, 4.9)
Opportunistic infections	0.2 (0, 1.5)	0 (0, 1.6)	0.8 (0.2, 3.4)	0 (0, 1.7)	0 (0, 1.7)
Herpes zoster	0.8 (0.3, 2.2)	1.7 (0.6, 4.6)	0.8 (0.2, 3.4)	1.9 (0.7, 5.0)	0.9 (0.2, 3.7)
MACE (adjudicated)	0.6 (0.1, 1.8)	0.9 (0.2, 3.4)	0 (0, 1.6)	0 (0, 1.7)	0 (0, 1.7)
VTE (adjudicated for DVT/PE)	0.2 (0, 1.2)	0.4 (0.1, 3.1)	0 (0, 1.6)	0 (0, 1.7)	0 (0, 1.7)
Malignancies (excluding NMSC)	0.6 (0.2, 2.0)	0 (0, 1.6)	1.7 (0.6, 4.5)	0.5 (0, 2.6)	0 (0, 1.7)
NMSC	0.6 (0.2, 2.0)	0.4 (0.1, 3.1)	0.8 (0.2, 3.4)	0.5 (0, 2.6)	0 (0, 1.7)

DVT, deep vein thrombosis; EAIRs, exposure-adjusted incidence rates (per 100 patient-years of exposure); MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PE, pulmonary embolism; VTE, venous thromboembolism

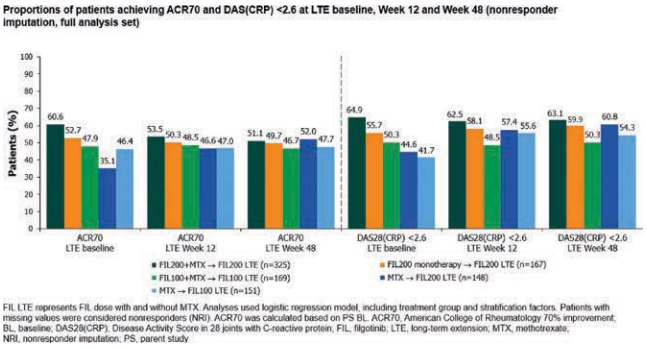

Figure 1.

Conclusion: Overall, response rates improved from LTE BL to W48 for pts switched from PS MTX to FIL and decreased modestly for PS FIL pts. Rates of AEs of special interest were generally low and tended to be higher in pts maintained on FIL from PS. Safety findings in this subpopulation were comparable with the PS through W52[1] and with a 7-trial integrated safety analysis.[2] Limitations: the LTE was not formally randomized at BL, the groups were of unequal size, and the switch from MTX to FIL for LTE was by design rather than based on disease activity.

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POS0679

CLINICAL OUTCOMES UP TO WEEK (W) 48 IN THE ONGOING FILGOTINIB (FIL) LONG-TERM EXTENSION (LTE) TRIAL OF RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) WITH INADEQUATE RESPONSE (IR) TO METHOTREXATE (MTX) INITIALLY TREATED WITH FIL OR ADALIMUMAB (ADA) DURING THE PHASE 3 PARENT STUDY (PS)

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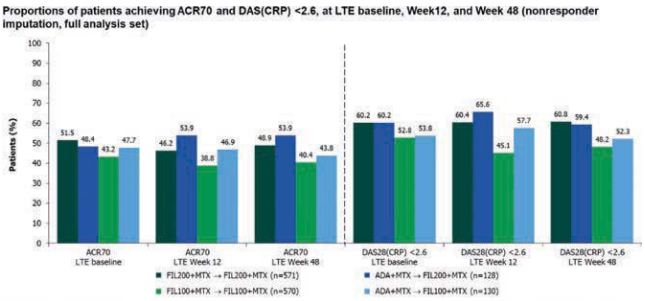
Background: The preferential Janus kinase-1 inhibitor FIL is approved for treatment of moderate to severe active RA in Europe and Japan.

Objectives: Efficacy and safety of FIL were assessed in pts with IR to MTX who completed a Phase 3 trial (NCT02889796)[1] and enrolled in an LTE (NCT03025308).

Methods: Pts completing the PS[1] on study drug were eligible to enter the LTE (data cutoff: June 1, 2020). Median exposure: 2.2 years (y). Efficacy data to W48 are reported for 4 treatment groups (all with background MTX): pts receiving FIL 200 mg (FIL200) or FIL 100 mg (FIL100) in the PS and continuing their dose in LTE (FIL200/FIL200, FIL100/FIL100) and ADA pts rerandomized, double blind, to FIL200 or FIL100 for LTE (ADA/FIL200, ADA/FIL100); safety data are reported.

Results: As of June 1, 2020, 522/571 (91%) FIL200/FIL200, 502/570 (88%) FIL100/FIL100, 118/128 (92%) ADA/FIL200, and 115/130 (89%) ADA/FIL100 pts remained on study drug. LTE baseline disease characteristics were similar between groups: mean duration of RA approximately 8.7 y; DAS28(CRP) 2.55, and mean concurrent MTX dosage was 15.0 mg/week. Proportions of pts achieving ACR20/50/70, DAS28(CRP) ≤3.2, <2.6, and CDAI ≤10, ≤2.8 were generally maintained in all LTE groups through W48 (Figure 1). Numerically greater proportions of pts met response criteria at W48 in the FIL200 groups vs FIL100, regardless of PS treatment. Treatment-emergent AEs (TEAE), serious AEs, and AEs Grade ≥3 were largely comparable between groups and lowest in ADA/FIL100. There were 10 deaths (Table 1). Exposure-adjusted incidence rates (EAIRs)/100 pt-y of exposure for deaths were lower for FIL/FIL vs ADA/FIL.



FIL200+MTX and FIL100+MTX groups included patients who were initially on placebo but later were rerandomized at W24 to FIL200+MTX or FIL100+MTX to W52. Analyses used the logistic regression model, including treatment group and stratification factors; no formal comparison of efficacy outcomes was performed. ACR70 was calculated based on PS BL. ACR70, American College of Rheumatology 70% improvement; ADA, adalimumab; BL, baseline; DAS28(CRP), Disease Activity Score in 28 joints with C-reactive protein; FIL, filgotinib; MTX, methotrexate; PS, parent study; W, week

Figure 1.

Conclusion: During the LTE through W48, response rates generally were maintained for FIL/FIL and ADA/FIL pts. Though there were differences between LTE groups, safety was largely comparable and consistent with PS observations[1] and previously reported results from 7 trials[2]: rates of AEs of special interest were low; all confidence intervals were overlapping. Limitation: the LTE was not formally randomized for comparison between FIL/FIL and ADA/FIL treatment groups, the groups were of unequal size, and the switch from ADA to FIL for LTE was by design, rather than based on disease activity.

Table 1. EAIRs of TEAEs in LTE, as of June 1, 2020

1TEAE, n (%)	3FIL200+MTX → FIL200+MTX	6ADA+MTX → FIL200+MTX	9FIL100+MTX → FIL100+MTX	12ADA+MTX → FIL100+MTX
2EAIR (95% CI)	4n=571	7n=128	10n=570	13n=130
	5PYE=859.4	8PYE=197.8	11PYE=852.3	14PYE=192.6
TEAE	429 (75.1)	91 (71.1)	443 (77.7)	88 (67.7)
	49.9 (45.4, 54.9)	46.0 (37.5, 56.5)	52.0 (47.4, 57.0)	45.7 (37.1, 56.3)
TEAE Grade ≥3	64 (11.2)	15 (11.7)	72 (12.6)	7 (5.4)
	7.4 (5.8, 9.5)	7.6 (4.6, 12.6)	8.4 (6.7, 10.6)	3.6 (1.7, 7.6)
TE serious AE	52 (9.1)	13 (10.2)	60 (10.5)	9 (6.9)
	6.1 (4.6, 7.9)	6.6 (3.8, 11.3)	7.0 (5.5, 9.1)	4.7 (2.4, 9.0)
Death	3 (0.5)	2 (1.6)	3 (0.5)	2 (1.5)
	0.3 (0.1, 1.1)	1.0 (0.3, 4.0)	0.4 (0.1, 1.1)	1.0 (0.3, 4.2)
TE infections	243 (42.6)	52 (40.6)	249 (43.7)	43 (33.1)
	28.3 (24.9, 32.1)	26.3 (20.0, 34.5)	29.2 (25.8, 33.1)	22.3 (16.6, 30.1)
TE serious infections	7 (1.2)	2 (1.6)	13 (2.3)	1 (0.8)
	0.8 (0.4, 1.7)	1.0 (0.3, 4.0)	1.5 (0.9, 2.6)	0.5 (0.1, 3.7)
Opportunistic infections	2 (0.4)	0	2 (0.4)	0
	0.2 (0, 0.8)	0 (0, 1.9)	0.2 (0, 0.8)	0 (0, 1.9)
TE herpes zoster	16 (2.8)	5 (3.9)	13 (2.3)	1 (0.8)
	1.9 (1.1, 3.0)	2.5 (1.1,6.1)	1.5 (0.9, 2.6)	0.5 (0.1, 3.7)
TE MACE (adjudicated)	1 (0.2)	0	3 (0.5)	3 (2.3)
	01 (0, 0.6)	0 (0, 1.9)	0.4 (0.1, 1.1)	1.6 (0.5, 4.8)
TE DVT/PE (adjudicated)	3 (0.5)	0	3 (0.5)	0
	0.3 (0.1, 1.0)	0 (0, 1.9)	0.4 (0.1, 1.0)	0 (0, 1.9)
Malignancies (excluding NMSC)	5 (0.9)	3 (2.3)	4 (0.7)	0
	0.6 (0.2, 1.4)	1.5 (0.5, 4.7)	0.5 (0.1, 1.2)	0 (0, 1.9)
NMSC	3 (0.5)	0	2 (0.4)	0
	0.3 (0.1, 1.0)	0 (0, 1.9)	0.2 (0, 0.8)	0 (0, 1.9)

DVT, deep vein thrombosis; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PE, pulmonary embolism; TE, treatment-emergent

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POS0680

PHYSICIANS' REASONS FOR PRESCRIBING JANUS KINASE INHIBITORS (JAKI) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), AND ASSOCIATED ALIGNMENT BETWEEN PHYSICIANS AND PATIENTS IN A REAL-WORLD CLINICAL SETTING

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Background: Shared decision making, a cornerstone of RA management[1], allows physicians and their patients to make informed decisions about their treatment goals and choice of care. As new treatments become available, it is important to understand rheumatologists' reasons for choosing JAKi.
Objectives: This survey evaluated rheumatologists' clinical and patient centric reasons for choosing JAKi, in addition to exploring alignment between rheumatologists and RA patients in terms of treatment choice and satisfaction.
Methods: The Adelphi RA Disease Specific Programme™[2] is a large, multinational, point-in-time survey conducted amongst rheumatologists and their consulting patients with RA in Europe (Belgium, France, Germany, Italy, Spain, UK) between January and October 2020. Physicians completed record forms for up to 10 consecutive RA patients, collecting demographic, clinical and treatment data, and reasons for current treatment choice. Patients were invited to complete a patient questionnaire to assess their satisfaction with ongoing treatment (5-point scale), and perceptions of shared decision making for the current treatment.
Results: 316 rheumatologists provided data for 3121 patients, of whom 1130 (36.2%) completed patient reported questionnaires. Overall, 67% were female, mean age was 53 years (SD 14), 23% had moderate-high disease activity score (DAS28: >3.2). 68% of patients were currently receiving either a biologic or targeted synthetic disease-modifying antirheumatic drug (DMARD; defined here as advanced therapy, AT), 72% were on first line AT. Overall, physicians and their patients were aligned that a conversation took place about a treatment decision (n=855, 79% net alignment), and this was a shared treatment decision (n=814, 75% net alignment). 15% of patients not taking an AT were reported to have a clinical condition warranting one; reasons for not taking AT included patients' concerns about infection (24%), conventional synthetic DMARDs were tolerable and safe in the patient (18%), and patient dislike of infusions/injections (17%). Of 2143 patients receiving AT, 19% were prescribed JAKi; 57% as monotherapy, 43% as combination therapy. For physician stated reasons for choice of JAKi, factors were driven by both perceptions of clinical efficacy and onset of action, as well as factors relating to patient acceptability such as method of delivery and ease of use (Table 1). With respect to JAKi treatment (n=135 patient-physician pairs), 62% of physicians and their patients were aligned on satisfaction, however 30% of patients reported less satisfaction than their consulting physician (Figure 1).

Table 1. Physician stated clinical and patient centric reasons for prescribing a JAKi in their patients with RA (data are percentage of patients; n=397)

Reasons for prescribing JAKi	Patients (%)
Top 5 clinical reasons	
Strong overall efficacy	74
Fast onset of action	49
Inhibition of disease progression	42
Strong efficacy as monotherapy	39
Achievement of clinical remission	37
Top 5 patient centric reasons	
Acceptability of method of delivery for the patient	39
Enabling patient to perform everyday tasks/activities	36
Ease of product use (for the patient)	33
Improvement or maintenance of quality of life	30
Improving patient's mood/state of mind	14

Conclusion: Communicating the choice of pharmacological therapy to patients with RA has become increasingly complex for physicians with expansion of approved treatments. In this subgroup of patients on JAKi, the drug attributes considered as reasons for prescribing were driven by clinical factors as well as by patient centric attributes. Although communications between patients and physicians were largely aligned, better understanding of patient expectations might serve to improve messaging about treatment options and resulting satisfaction.
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Figure. Level of alignment between physician and patient-reported satisfaction with JAKi

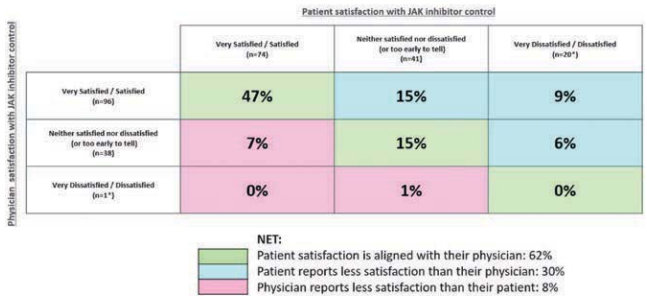

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Table 1. Baseline characteristics of RA patients

	1st group (n=62)	2nd group (n=57)	non-D2TRA group (n=25)	D2TRA group (n=76)
Age (years)	64.9 ± 14.8	66.1 ± 11.5	64.6 ± 16.1	63.0 ± 15.0
Female (%)	75.8	79.0	96.0	80.3
Disease durations (years)	10.4 ± 11.7	17.6 ± 17.6	22.6 ± 22.4	16.3 ± 15.7
RF (IU/ml)	296.3 ± 1153.8	314.9 ± 1037.7	262.4 ± 375.9	305.9 ± 819.6
RF positive ratio (%)	81.8	78.4	79.2	75.7
Anti CCP antibody (U/ml)	221.8 ± 327.2	157.8 ± 258.7	95.9 ± 101.6	191.8 ± 250.6
Anti CCP antibody positive ratio (%)	79.6	79.6	72.2	83.3
CRP (U/ml)	1.5 ± 2.1	1.1 ± 2.0	1.6 ± 1.6	1.8 ± 2.9
MMP-3 (ng/ml)	185.7 ± 167.6	146.7 ± 122.1	190.1 ± 152.6	268.0 ± 451.2
DAS28-CRP	4.3 ± 1.2	4.1 ± 1.3	3.9 ± 1.4	4.4 ± 1.3
SDAI	21.8 ± 12.2	21.7 ± 13.1	18.4 ± 13.0	23.9 ± 12.8
CDAI	20.3 ± 11.3	20.7 ± 12.7	17.6 ± 12.8	22.1 ± 12.2
HAQ	1.1 ± 0.8	1.2 ± 1.0	0.9 ± 0.8	1.4 ± 1.1
MTX use (%)	69.4	63.2	56	47.4
MTX (mg/day)	10.7 ± 3.4	10.4 ± 3.5	8.8 ± 3.5	9.0 ± 4.3
Glucocorticoid use (%)	29.1	36.8	16	46.1
Glucocorticoid dose (mg/day)	3.3 ± 2.1	3.0 ± 1.5	3.5 ± 1.9	5.1 ± 2.8

Galapagos NV, Katrien Van Beneden Shareholder of: Galapagos NV, Employee of: Galapagos NV, Roberto Caporali Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Fresenius Kabi, Galapagos, Gilead, Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB, Consultant of: Galapagos, Gilead, Janssen, Lilly, and MSD, Rieke Alten Consultant of: AbbVie, Amgen, Biogen, BMS, Celltrion, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and Roche
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POS0681 DRUG RETENTION RATE AND EFFECTIVENESS OF JAK INHIBITOR IN PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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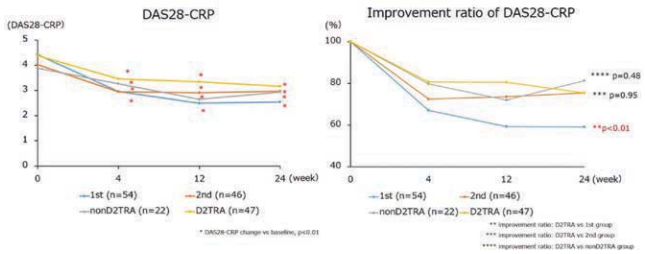
Background: Recently, the disease activity of rheumatoid arthritis (RA) was improved due to the 'treat-to-target' strategy. However, some patients remain various symptoms despite recommended treatment was performed. Then, the term of 'difficult-to-treat RA (D2TRA)' is widely recognized. Janus kinase inhibitor (JAKi) might be effective for D2TRA patients, because JAKi can simultaneously block the function of multiple cytokines.
Objectives: The aim of this study was to evaluate drug retention rate and effectiveness of JAKi in patients with D2TRA.
Methods: This study included 220 RA patients (tofacitinib 101, baricitinib 83, upadacitinib 20, peficitinib 14, filgotinib 2) treated with JAKi. Sixty-two patients were treated as first line bDMARDs/JAKi (1st group), 57 patients were treated as second line bDMARDs/ JAKi (2nd group), 101 patients were treated as third and more bDMARDs/ JAKi. In these 101 patients, 25 patients did not met D2TRA criteria (non-D2TRA group) and 76 patients met D2TRA criteria (D2TRA group). Drug retention rate and effectiveness of JAKi were evaluated during 24 weeks in each group.
Results: Usage rate of methotrexate was lower and dosage of glucocorticoid was higher in D2TRA group than in other groups (Table 1). Drug retention rate at 24 weeks was 87.1% (54/62) in 1st group, 80.1% (46/57) in 2nd group, 88% (22/25) in non-D2TRA group, 61.8% (47/76) in D2TRA group. Drug retention rate was lower in D2TRA group compared to 1st group, 2nd group and non-DT2RA group (p<0.01, p=0.03, p=0.01). DAS28-CRP was 4.4, 4.0, 3.9, 4.4 at baseline, 3.0, 3.0, 3.3, 3.5 at 4 weeks, 2.5, 2.9, 2.7, 3.3 at 12 weeks, 2.5, 3.0, 2.9, 3.2 at 24 weeks in 1st group, 2nd group, non-D2TRA group and D2TRA group, respectively. Improvement ratio of DAS28-CRP was 32.9, 27.6, 20.4, 19.3 % at 4 weeks, 40.8, 26.5, 28.1, 19.5 % at 12 weeks, 40.8, 24.6, 18.7, 24.7 % at 24 weeks. DAS28-CRP was improved in all groups. Altough 1st group showed higher improvement ratio of DAS28-CRP at 24 weeks compared to 2nd group, non-DT2RA group and D2TRA group (p<0.01, p<0.01, p<0.01), there was no differences between DT2RA group and 2nd group or non-D2TRA group (p=0.95, p=0.48). SDAI was 22.9, 19.9, 18.3, 23.9 at baseline, 11.8, 11.9, 13.3, 14.4 at 4 weeks, 7.9, 11.3, 8.4, 13.3 at 12 weeks, 8.5, 11.5, 9.7, 12.6 at 24 weeks. CDAI was 21.3, 18.8, 17.6, 21.8 at baseline, 11.3, 11.2, 12.5, 13.9 at 4 weeks, 7.5, 10.9, 8.0, 12.3 at 12 weeks, 8.1, 10.7, 8.6, 12.1 at 24 weeks. HAQ was 1.15, 0.99, 0.89, 1.39 at baseline, 0.84, 0.76, 0.93, 1.22 at 4 weeks, 0.79, 0.84, 0.77, 1.17 at 12 weeks, 0.76, 0.79, 0.76, 1.14 at 24 weeks. Improvement rate of HAQ at 24 weeks were 44.3%, 23.9%, 21.2%, 8.1%.

figure



Conclusion: Drug retention rate of JAKi in treatment of D2TRA group were lower than that of 1st group, 2nd group, and non-D2TRA group. Clinical efficacy of JAKi in D2TRA group were not significantly different to 2nd group and non-D2TRA group. However, HAQ improvement was weak in D2TRA group.
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POS0682 LONG-TERM EFFICACY OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO BDMARDS: RESULTS FROM RA-BEYOND FOLLOWING 6.9 YEARS OF TREATMENT

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Background: Baricitinib (BARI), an oral selective Janus kinase 1/2 inhibitor, is approved for treatment of adults with moderately-to-severely active rheumatoid arthritis (RA). BARI demonstrated efficacy in patients (pts) with RA who have inadequate response to biologic disease-modifying antirheumatic drugs (bDMARD-IR) in a 24-week (wk) phase 3 study, RA-BEACON.[1] BARI efficacy was evaluated up to 3 years (yrs) of treatment in a long-term extension (LTE) study, RA-BEYOND.[2]
Objectives: Disclose long-term efficacy of BARI 4 mg and 2 mg in bDMARD-IR pts in the completed study RA-BEYOND.
Methods: In RA-BEACON, pts were randomized 1:1:1 to BARI 4 mg, 2 mg, or PBO; pts with no response could be rescued after wk 16. Completers to wk 24 could enter with BARI 4 or 2mg RA-BEYOND for up to 360 wks (6.9 yrs). LTE data were analysed by treatment assigned at baseline in RA-BEACON as observed up to time of stepdown (if applicable), study discontinuation, or study completion, whichever occurred earlier. Efficacy response rates (RR) were assessed as proportions of pts with observed data up to wk 360 for low-disease activity (LDA) (SDAI ≤ 11, DAS28-hsCRP ≤ 3.2, CDAI ≤ 10), remission (REM) (SDAI ≤ 3.3, DAS28-hsCRP < 2.6, CDAI ≤ 2.8, Boolean), and physical functioning (HAQ-DI ≤ 0.5). No formal statistical comparisons were conducted.
Results: 156, 152, and 140 pts entered the LTE (4 mg, 2 mg, and PBO, respectively). Pts in BARI 4 and 2 mg arms had higher LDA and REM RR vs PBO at LTE

Table 1. Efficacy outcomes in RA-BEYOND

		LDA			REM				
Time[a]	N/n (%)	SDAI	CDAI	DAS-28 CRP	SDAI	CDAI	DAS-28 CRP	Boolean	HAQ-DI ≤0.5
Wk 24	PBO[b]	135/31 (23.0)	138/32 (23.2)	135/31 (23.0)	135/6 (4.4)	138/8 (5.8)	135/14 (10.4)	135/3 (2.2)	139/6 (4.3)
	BARI 2 mg	148/42 (28.4)	152/43 (28.3)	148/38 (25.7)	148/10 (6.8)	152/10 (6.6)	148/22 (14.9)	148/9 (6.1)	152/17 (11.2)
	BARI 4 mg	150/57 (38.0)	156/60 (38.5)	150/60 (40.0)	150/14 (9.3)	156/17 (10.9)	150/37 (24.7)	150/11 (7.3)	156/17 (10.9)
Wk 48	PBO	128/59 (46.1)	129/58 (45.0)	128/58 (45.3)	128/14 (10.9)	129/15 (11.6)	128/31 (24.2)	128/5 (3.9)	130/6 (4.6)
	BARI 2 mg	139/54 (38.8)	140/56 (40.0)	139/53 (38.1)	139/13 (9.4)	140/14 (10.0)	139/30 (21.6)	139/11 (7.9)	140/16 (11.4)
	BARI 4 mg	147/70 (47.6)	149/71 (47.7)	147/68 (46.3)	147/22 (15.0)	149/19 (12.8)	147/49 (33.3)	147/14 (9.5)	149/19 (12.8)
Wk 156	PBO	84/47 (56.0)	85/47 (55.3)	84/45 (53.6)	84/15 (17.9)	85/14 (16.5)	84/33 (39.3)	84/9 (10.7)	85/8 (9.4)
	BARI 2 mg	98/60 (61.2)	99/60 (60.6)	98/58 (59.2)	98/25 (25.5)	99/27 (27.3)	98/43 (43.9)	98/13 (13.3)	99/21 (21.2)
	BARI 4 mg	76/36 (47.4)	78/35 (44.9)	76/37 (48.7)	76/11 (14.5)	78/13 (16.7)	76/25 (32.9)	76/9 (11.8)	78/12 (15.4)
Wk 360	PBO	33/26 (78.8)	35/25 (71.4)	34/27 (79.4)	33/8 (24.2)	35/9 (25.7)	34/17 (50.0)	34/6 (17.6)	36/1 (2.8)
	BARI 2 mg	38/28 (73.7)	38/28 (73.7)	38/27 (71.1)	38/10 (26.3)	38/8 (21.1)	38/20 (52.6)	38/5 (13.2)	39/6 (15.4)
	BARI 4 mg	27/19 (70.4)	27/20 (74.1)	27/20 (74.1)	27/7 (25.9)	27/7 (25.9)	27/15 (55.6)	27/4 (14.8)	27/7 (25.9)

N: Number of pts with observed data; n: Number of pts with response. [a]Number of wks from randomisation. [b]Treatment groups as assigned at randomisation.

entry (wk 24) (Table 1). PBO-treated pts achieved comparable RR to pts in the BARI 4 mg arm by wk 48 (24 wks after switch to BARI 4 mg) and up to wk 360. Of pts enrolled to RA-BEYOND, approx. 50% in BARI 4 mg, 65% in 2 mg and 61% in PBO remained active at wk 156; 17%, 26% and 26% at wk 360, respectively. SDAI LDA RR were 47%/70% and 61%/74% for pts treated with BARI 4 mg and 2 mg, at wk 156 (yr 3)/ 360 (yr 6.9), respectively; SDAI REM RR were 15%/26% and 26%/26% for BARI 4 mg and 2 mg, at wk 156/360, respectively (Table 1). SDAI and CDAI had comparable RR. DAS-28CRP LDA RR were similar to SDAI and CDAI, while REM RR were about twice those of SDAI and CDAI. HAQ-DI ≤ 0.5 RR was 15%/26% (BARI 4 mg), 21%/15% (BARI 2mg), and 9%/3% (PBO) at 3/6.9 yrs.

Conclusion: In observed data, BARI maintained efficacy and normative physical function bDMARD-IR population up to 6.9 yrs (360 wks).

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POS0683

EFFICACY AND SAFETY OF UPADACITINIB IN TNFI-IR PATIENTS WITH RHEUMATOID ARTHRITIS FROM THREE PHASE 3 CLINICAL TRIALS

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Background: For patients with RA who are refractory to biologic DMARDs (bDMARDs), such as tumor necrosis factor inhibitors (TNFis), optimal disease control is less likely to be achieved with subsequent therapy.[1] In line with recommendations from EULAR and ACR, switching to a treatment with a different mechanism of action is appropriate for these patients.

Objectives: To describe the efficacy and safety of upadacitinib (UPA) 15 mg once daily in patients with RA and an inadequate response or intolerance to TNFis (TNFi-IR).

Methods: A post hoc subgroup analysis was conducted in TNFi-IR patients who were treated with UPA 15 mg once daily in three Phase 3 clinical trials: SELECT-BEYOND,[2] -CHOICE,[3] and -COMPARE.[4] For COMPARE, only patients treated with adalimumab and switched to UPA as rescue therapy were included. ≥20/50/70% improvement in ACR criteria, DAS28(CRP), CDAI, and SDAI, as well as change from baseline in HAQ-DI and other patient-reported outcomes (PROs) were reported through 24 weeks. Non-responder imputation was used for all missing categorical outcomes; as observed (COMPARE) or multiple imputation (CHOICE, BEYOND) were used for missing continuous outcomes. Pooled safety results were presented as exposure-adjusted event rates (EAERs) with a cut-off of June 30, 2021.

Results: 568 TNFi-IR patients were included: 146 from BEYOND, 263 from CHOICE, and 159 from COMPARE. Mean duration since RA diagnosis was longer for BEYOND and CHOICE versus COMPARE; cardiovascular (CV) risk factors were common among this refractory population (Table 1). ACR20/50/70 and disease activity outcomes observed in the TNFi-IR population were generally consistent with the overall BEYOND[2] and CHOICE[3] bDMARD-IR populations, and consistent across the three studies in the TNFi-IR subgroups (Figure 1). Improvements in PROs including HAQ-DI, fatigue, pain, and morning stiffness over 24 weeks were observed (data not shown). Pooled safety results reporting 1574.8 patient-years (PY) of exposure in the TNFi-IR subgroup showed similar results to the overall BEYOND[2] and CHOICE[3] bDMARD-IR study populations, with EAERs of 3.1 events/100 PY for herpes zoster and 0.8 events/100 PY for adjudicated major adverse CV events, adjudicated venous thromboembolism (VTE), and malignancy excluding non-melanoma skin cancer. The EAER of any AE leading to death was 1.4 events/100 PY.

Table 1. Baseline characteristics of TNFi-IR patients treated with UPA 15 mg

n (%), unless specified	SELECT-BEYOND (n=146)	SELECT-CHOICE (n=263)	SELECT-COMPARE (ADA → UPA) (n=159)
Female	122 (83.6)	219 (83.3)	133 (83.6)
Mean (SD) age, years	56.6 (11.0)	55.5 (11.1)	53.9 (10.6)
Mean (SD) duration of RA diagnosis, years	13.2 (9.5)	12.5 (9.4)	8.2 (8.5)
Concomitant csDMARDs			
MTX alone	100 (70.4)	195 (74.1)	159 (100.0)
MTX and other csDMARDs	20 (14.1)	25 (9.5)	0
csDMARDs other than MTX	22 (15.5)	38 (14.4)	0
Concomitant oral steroids	73 (50.0)	140 (53.2)	98 (61.6)
1 prior bDMARD	68 (46.6)	172 (65.4)	142 (89.3)
2 prior bDMARDs	40 (27.4)	62 (23.6)	17 (10.7)[a]
≥3 prior bDMARDs	38 (26.0)	29 (11.0)	0
Failed ≥1 prior TNFi due to lack of efficacy[b]	131 (89.7)	223 (84.8)	159 (100.0)
History of VTE / CV event	3 (2.1) / 28 (19.2)	6 (2.3) / 20 (7.6)	4 (2.5) / 14 (8.8)
CV risk factors			
Hypertension	72 (49.3)	109 (41.4)	68 (42.8)
Diabetes mellitus	22 (15.1)	34 (12.9)	17 (10.7)
Smoking (current former past)	68 (46.6)	109 (41.5)	55 (34.6)
Elevated LDL-C (≥3.36 mmol/L)	38 (26.0)	52 (20.0)	48 (30.2)
Low HDL-C (≤1.55 mmol/L)	80 (54.8)	171 (65.0)	88 (55.3)

[a]These patients received one bDMARD before entry into SELECT-COMPARE.[b]Remaining patients were intolerant to ≥1 prior TNFi.

Conclusion: In this post hoc subgroup analysis, TNFi-IR patients treated with UPA 15 mg achieved clinically meaningful efficacy responses over 24 weeks, with safety consistent with the overall bDMARD-IR patient population in the Phase 3 program.

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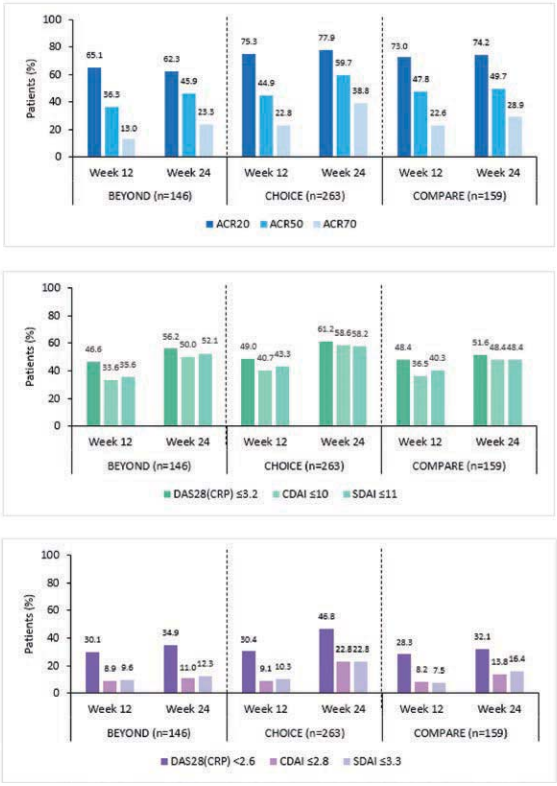
Figure. ACR20/50/70 and disease activity outcomes of UPA 15 mg in TNFi-IR patients with RA



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IS UPADACITINIB CAPABLE OF IMPROVING PATIENT-REPORTED OUTCOMES OF RHEUMATOID ARTHRITIS IN A REAL-WORLD SETTING? RESULTS FROM THE POST-MARKETING OBSERVATIONAL UPWARDS STUDY

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Background: The efficacy of Upadacitinib (UPA), a selective Janus kinase inhibitor, has been evaluated in the SELECT clinical program [1-6]. In addition, recent results from the non-interventional UPwArds study further confirmed UPAs clinical effectiveness regarding standard disease activity scores for rheumatoid arthritis (RA) in a real-world setting [7]. However, patient-reported outcomes (PROs) as another cornerstone of clinical decision making yet remain to be addressed in the context of a post-marketing setting. This interim analysis, conducted after 250 patients had completed the 6-month follow-up visit, aims to fill this gap.

Objectives: To evaluate the change of selected PROs over 6 months in patients treated with UPA in a real-world data environment.

Methods: UPwArds is a prospective, open-label, multicenter, non-interventional, post-marketing study including adult patients with moderate-to-severe RA (swollen joint count [SJC28] ≥ 3 and inadequate response or intolerance to at least one previous disease-modifying antirheumatic drug). According to the German label, patients were treated with UPA 15 mg once daily, as monotherapy or in combination with methotrexate. For this analysis, the following PROs were included: 0-10 numerical rating scales (NRS) for pain and fatigue, the Health Assessment Questionnaire Disability Index (HAQ-DI), the duration and severity of morning stiffness, the Patient Health Questionnaire 9 (PHQ-9), and the Rheumatoid Arthritis Impact of Disease Questionnaire (RAID). Changes from baseline were evaluated for follow-up periods of 1 month, 3 months, and 6 months. Results are presented for the total sample using descriptive measures reflecting sample size (N), average values (standard deviation) for each assessment and average change scores (standard deviation) for follow-up visits. All data were analyzed as observed, with no imputation of missing data.

Results: 483 patients (369 female, 114 male) were included in the study, with available baseline PRO information for 481 patients. 6-months follow-up data were yet available from 279 patients The baseline average age and disease duration were 58.0 (12.3) years and 9.0 (8.0) years, respectively, whereas the mean initial DAS28-CRP was 4.6 (1.0). At baseline, 60.8% of enrolled patients had previously been treated with biologic or targeted synthetic disease-modifying antirheumatic drugs. Overall, PRO scores improved from baseline throughout month 6 with a considerable amelioration at month 3, which was maintained at month 6. Responses were rapid, with improvement already evident at month 1 (Table 1). The NRS pain as a crucial PRO in RA confirmed the previously described pattern of results seen for most of the other PROs (Figure 1).

Table 1. Baseline scores and average changes from baseline scores

	N	Baseline scores (SD)	N	Change from baseline - month 1 (SD)	N	Change from baseline - month 3 (SD)	N	Change from baseline - month 6 (SD)
Pain (NRS)	481	6.2 (2.2)	393	-2.2 (2.3)	392	-2.5 (2.5)	258	-2.4 (2.4)
Fatigue (NRS)	481	5.5 (2.6)	393	-1.4 (2.3)	393	-1.6 (2.4)	259	-1.5 (2.3)
HAQ-DI	471	1.3 (0.6)	380	-0.2 (0.3)	376	-0.2 (0.4)	253	-0.2 (0.4)
Morning stiffness (duration, minutes)	439	68.9 (63.9)	313	-25.0 (55.3)	296	-29.6 (54.9)	179	-31.6 (51.7)
Morning stiffness (severity)	478	5.2 (2.7)	386	-1.8 (2.3)	393	-2.2 (2.6)	258	-2.2 (2.9)
PHQ-9	477	8.7 (5.2)	383	-1.9 (3.9)	381	-2.3 (4.0)	255	-2.2 (3.8)
RAID	481	5.6 (2.0)	393	-1.7 (1.8)	392	-2.0 (2.0)	258	-1.9 (1.9)

Conclusion: This interim analysis confirmed a meaningful improvement regarding included PROs that cover various RA-related symptoms, depressiveness and the impact of symptoms of RA on daily life.

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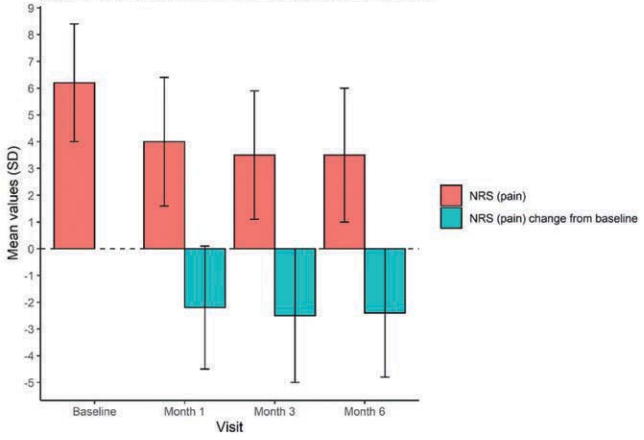
Figure. NRS pain scores and changes from baseline



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POS0685 LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: FINAL RESULTS FROM THE BALANCE-EXTEND OPEN-LABEL EXTENSION STUDY

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Background: Upadacitinib (UPA) was previously evaluated in two Phase 2, randomized, controlled trials (RCTs) in patients (pts) with rheumatoid arthritis (RA) and inadequate response to tumor necrosis factor inhibitors (BALANCE-1) or methotrexate (BALANCE-2).

Objectives: To assess the final safety and efficacy of UPA in BALANCE-EXTEND, a 312-week open-label extension (OLE) enrolling pts who completed either BALANCE-1 or BALANCE-2.

Methods: All pts initially received UPA 6 mg twice daily (BID). Increase to 12 mg BID was required for pts with <20% improvement in swollen or tender joint counts (S/TJC) at Week 6 or 12, and permitted for those not achieving Clinical Disease Activity Index (CDAI) low disease activity (LDA). Pts with <20% improvement in SJC or TJC 6 weeks after escalation, or at any two consecutive visits, discontinued. Return to 6 mg BID was permitted for safety or tolerability reasons. After January 2017, the 6 and 12 mg BID doses were replaced by 15 and 30 mg once-daily (QD) extended-release equivalents. As-observed efficacy data are shown at Week 312 for three subgroups: pts who received 6 mg BID/15 mg QD throughout ("Never titrated"), those titrated up to 12 mg BID/30 mg QD for efficacy ("Titrated up"), and those titrated up to 12 BID/30 mg QD and then back to 6 mg BID/15 mg QD due to safety concerns ("Titrated up and down"). Exposure-adjusted adverse events (EAERs) per 100 patient-years (PY) of exposure were summarized from OLE Day 1 in all pts who received UPA (Any UPA).

Results: Overall, 493 pts entered the OLE, receiving UPA for ≤6.2 years (Never titrated, n=306; Titrated up, n=149; Titrated up and down, n=38), and 270 pts (54.8%) discontinued, mostly due to withdrawal of consent (16.8%; n=83) or AEs (14.6%; n=72). Mean (standard deviation) duration of UPA exposure was 3.8 (2.4) years (range <1–6.2 years); cumulative exposure was 1863 PY. The AE profile in pts receiving UPA 15 mg was generally similar to the Any UPA population, and to that observed in the Phase 3 UPA 15 mg clinical trial population (Table 1). Efficacy was maintained to Week 312, with 84.5% and 86.6% of pts in the Never titrated group achieving DAS28-CRP ≤3.2 and CDAI LDA, respectively (Figure 1).

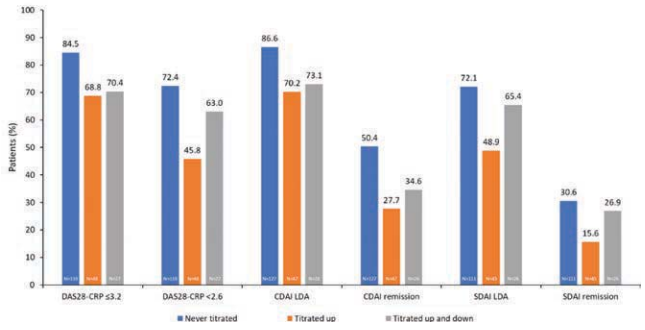
Table 1. Summary of AEs in pts who received UPA 6 mg BID/15 mg QD in the OLE and in the UPA 15 mg Phase 3 study program

	BALANCE-EXTEND (UPA 6 mg BID/15 mg QD)	UPA 15 mg – Phase 3 program[b]
	Events/100 PY (95 CI)[a]	Events/100 PY (95% CI)[a]
	N=493, PY=1277	N=3209, PY=9079
Any AE	138.4 (132.0, 145.0)	205.5 (202.5, 208.5)
Any SAE	7.9 (6.4, 9.6)	12.4 (11.7, 13.2)
AE leading to discontinuation	4.2 (3.2, 5.5)	4.9 (4.4, 5.3)
Death	0.4 (0.1, 0.9)	0.5 (0.4, 0.7)[c]
Infection	49.2 (45.5, 53.2)	63.9 (62.3, 65.6)
Serious infection	1.4 (0.8, 2.2)	2.8 (2.4, 3.1)
Opportunistic infection	0.2 (0.0, 0.6)	0.3 (0.2, 0.4)
Herpes zoster	2.0 (1.3, 3.0)	3.0 (2.6, 3.3)
Anemia	1.1 (0.6, 1.8)	3.0 (2.7, 3.4)
Neutropenia	1.3 (0.8, 2.1)	2.1 (1.8, 2.5)
Lymphopenia	1.7 (1.1, 2.6)	1.7 (1.4, 1.9)
Gastrointestinal perforation	0	<0.1 (0.0, 0.1)
Any malignancy	1.2 (0.7, 1.9)	1.1 (0.9, 1.4)
Non-melanoma skin cancer (NMSC)	0.4 (0.1, 0.9)	0.4 (0.3, 0.5)
Excluding NMSC	0.8 (0.4, 1.4)	0.7 (0.6, 0.9)
Creatinine phosphokinase elevation	3.4 (2.5, 4.6)	4.4 (4.0, 4.9)
Hepatic disorder	4.1 (3.0, 5.3)	10.2 (9.5, 10.8)
Venous thromboembolism	0.5 (0.2, 1.0)	0.4 (0.3, 0.6)
Major adverse cardiovascular event	0.5 (0.2, 1.0)	0.4 (0.3, 0.5)

[a]Multiple events occurring in the same pts are counted in the calculation of events/100 PY. [b]Cut-off, June 30, 2021. [c]Based on 9080 PY.

Conclusion: In this OLE, UPA treatment over ~312 weeks showed sustained long-term efficacy in pts with RA who had completed Phase 2 RCTs. Overall safety results showed that UPA was well tolerated over time; the types and frequencies of AEs were consistent with those in pts with similar populations of moderately to severely active RA receiving Janus kinase inhibitors.

Figure. Summary of disease activity measures at Week 312 in pts who entered the OLE (observed data)



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POS0686

EFFECTIVENESS OF UPADACITINIB IN THE TREATMENT OF RHEUMATOID ARTHRITIS: ANALYSIS OF 6-MONTH REAL-WORLD DATA FROM THE UNITED RHEUMATOLOGY NORMALIZED INTEGRATED COMMUNITY EVIDENCE (UR-NICETM) DATABASE

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Background: The efficacy of upadacitinib (UPA), an oral Janus kinase inhibitor (JAKi), in the treatment of rheumatoid arthritis (RA) has been demonstrated in the phase 3 SELECT clinical trial program.[1–6] However, few real-world data have been reported to date.

Objectives: To assess the 6-month effectiveness of UPA in patients (pts) with RA initiating UPA treatment in clinical practice.

Methods: This observational study included US-based pts from the United Rheumatology Normalized Integrated Community Evidence (UR-NICE) database who initiated UPA 15 mg once daily from Aug 2019 to the data cut-off in Nov 2021. Pts with ≥6 months of baseline (BL) data before UPA initiation, and with Clinical Disease Activity Index (CDAI) score recorded at BL and 6 months (±45 days) after initiation, were included in the analysis. Effectiveness measures included CDAI score, Routine Assessment of Patient Index Data 3 (RAPID3), and Disease Activity Score in 28 joints based on C-reactive protein (DAS28-CRP); patient-reported outcomes (PROs) including Health Assessment Questionnaire-Disability Index (HAQ-DI), Pain, and Patient's Global Assessment of Disease Activity (PtGA); and Physician's Global Assessment of Disease Activity (PhGA). Subgroup analyses were conducted by prior tumor necrosis factor inhibitor (TNFi) and tofacitinib (TOFA) treatment history.

Results: 363 pts were included in the analysis and most were female (80.2%) (Table 1). 140 (39%) received UPA monotherapy and 223 (61%) received UPA plus conventional synthetic (cs) disease-modifying antirheumatic drugs (DMARDs). 83% of pts received prior csDMARDs, 72% prior biologics (TNFi 55%), and 41% JAKis (TOFA 39%). Overall, 46% (166/363), 23% (57/245), and 55% (95/173) of pts achieved LDA by CDAI, RAPID3, and DAS28-CRP, respectively, and 14% (51/363), 16% (39/245), and 36% (62/173) of pts achieved remission (REM) by CDAI, RAPID3, and DAS28-CRP, respectively. Results were similar regardless of prior TNFi or TOFA exposure (Figure 1). Improvements from BL were seen in PhGA and all PROs in the total population and all subgroups.

Table 1. Demographic and baseline characteristics

Parameter, n (%)	Full analysis set		Prior TNFi		Prior TOFA	
	(N=363)		(n=199)		(n=143)	
Female	291 (80.2)		156 (78.4)		119 (83.2)	
Age, years						
<40	22 (6.1)		11 (5.5)		8 (5.6)	
40–<65	240 (66.1)		132 (66.3)		94 (65.7)	
≥65	101 (27.8)		56 (28.1)		41 (28.7)	
Oral steroid use	185 (51.0)		103 (51.8)		83 (58.0)	
Parameter, mean (SD)	**N**	**Mean (SD)**	**n**	**Mean (SD)**	**n**	**Mean (SD)**
Duration of RA, years	276	4.5 (3.1)	162	5.1 (3.0)	113	5.1 (2.9)
Body mass index, kg/m^2	321	30.0 (6.9)	175	29.9 (6.6)	125	29.2 (6.7)
Oral steroid dose (prednisone equivalent), mg/day	154	7.9 (6.9)	87	7.8 (6.5)	70	7.6 (6.1)
Methotrexate dose, mg/week	119	18.3 (4.9)	74	17.8 (5.2)	37	18.2 (4.7)
C-reactive protein, mg/L	228	9.6 (16.2)	132	9.4 (15.0)	90	11.3 (17.9)
CDAI	363	21.2 (12.8)	199	22.1 (13.0)	143	21.7 (13.3)
RAPID3	268	4.7 (2.1)	141	4.7 (2.2)	100	4.9 (2.1)
DAS28-CRP	228	3.9 (1.3)	132	4.0 (1.4)	90	4.2 (1.3)
HAQ-DI[a]	273	2.6 (2.1)	148	2.8 (2.2)	106	3.0 (2.2)
Pain[b]	338	59.6 (26.6)	186	58.4 (27.2)	131	61.3 (25.1)
PtGA[b]	363	54.1 (25.6)	199	54.7 (26.9)	143	55.9 (25.2)
PhGA[b]	363	41.3 (26.0)	199	41.2 (24.8)	143	40.7 (26.8)

[a]0–10 visual analog scale. [b]0–100 visual analog scale. SD, standard deviation.

Conclusion: In this study, almost half (46%) of pts treated with UPA achieved CDAI LDA at 6 months and 14% achieved CDAI REM. Improvements in all PROs and PhGA were observed. Effectiveness of UPA was not impacted by prior TNFi or TOFA exposure, supporting UPA as an effective treatment option in clinical practice, including in pts with prior exposure to advanced therapy.

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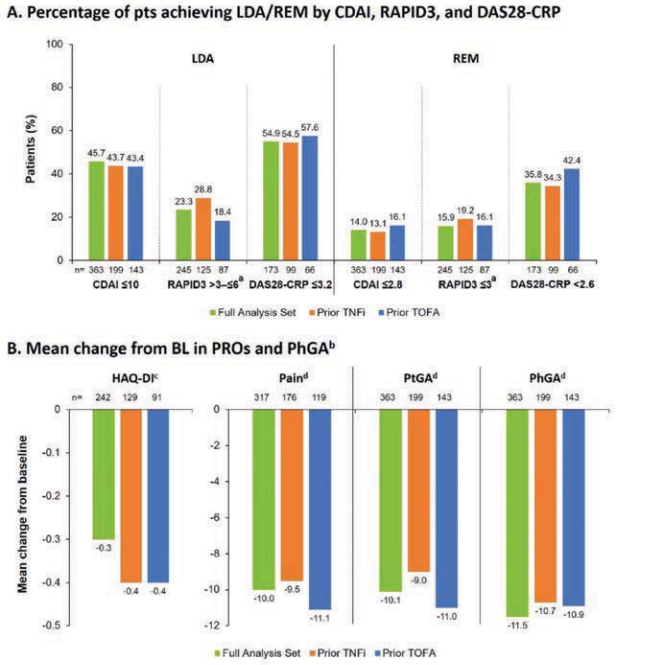
Figure. Effectiveness of UPA 15 mg at Month 6



[a]RAPID3 was measured on a scale of 0–10 and the cut-off values are based on conversion to a 0–30 scale. [b]Increasing negative values indicate increasing improvement. [c]0–10 visual analog scale. [d]0–100 visual analog scale.
BL, baseline; CDAI, Clinical Disease Activity Index; DAS28-CRP, Disease Activity Score in 28 joints based on C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; PhGA, Physician's Global Assessment of Disease Activity; PRO, patient-reported outcome; PtGA, Patient's Global Assessment of Disease Activity; Pts, patients; RAPID3, Routine Assessment of Patient Index Data 3; REM, remission; TNFi, tumor necrosis factor inhibitor; TOFA, tofacitinib; UPA, upadacitinib.

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Disclosure of Interests: Allan Gibofsky Shareholder of: AbbVie, Amgen, Johnson & Johnson, and Pfizer (stocks), Consultant of: AbbVie, Celgene, Eli Lilly, Flexion, Pfizer, Relburn Pharma, and Samumed (consulting fees); and Gerson Lehrman Group (paid consultant with investment analysts), Mark E. Pearson Shareholder of: AbbVie (may own stock or options), Andrew Concoff Speakers bureau: Flexion Therapeutics and Exagen, Consultant of: Flexion Therapeutics and Exagen, Anna Shmagel Shareholder of: AbbVie (may own stock or options), Employee of: AbbVie, Patrick Zueger Shareholder of: AbbVie (may own stock or options), Employee of: AbbVie, Yanna Song Shareholder of: AbbVie (may own stock or options), Employee of: AbbVie, Lauren Smith Shareholder of: AbbVie (may own stock or options), Employee of: AbbVie, Grace C. Wright Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Exagen, Myriad Autoimmune, Novartis, Sanofi/Regeneron, UCB, and Vindico, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Exagen, Gilead, Janssen, Myriad Autoimmune, Novartis, Pfizer, Sanofi/Regeneron, and UCB, Employee of: Association of Women in Rheumatology (President and Founder)
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POS0687

INHIBITION OF BONE EROSION, DETERMINED BY HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (HR-PQCT), IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING A CONVENTIONAL SYNTHETIC DMARD (CSDMARD) PLUS DENOSUMAB VS CSDMARD THERAPY ALONE: RESULTS OF AN OPEN-LABEL, RANDOMIZED, PARALLEL-GROUP STUDY

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Background: Denosumab, a human IgG2 monoclonal antibody with high affinity for RANKL, is approved for treatment of bone erosion (ER) in patients with RA, based on the results of clinical trials. However, its effectiveness in combination with conventional therapy in RA patients has not been fully investigated in clinical practice.
Objectives: This exploratory study aimed to compare, in patients receiving conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) for treatment of RA, the effectiveness of combined use of csDMARD and denosumab vs csDMARD alone, in terms of inhibition of ER determined by HR-pQCT.
Methods: Detail protocol of this open-label, randomized, parallel-group study has been published previously.[1] RA patients with moderate or low disease activity and progressive ER were eligible, and were randomly assigned to receive denosumab in addition to the csDMARD (denosumab) group or to continued use of the csDMARD alone (csDMARD) group. Denosumab was administered every 6 months during the 12-month study period. The primary endpoint was change in ER-depth at the second and third metacarpal bones, determined by HR-pQCT at month 6. For the primary endpoint, a linear mixed effect model analysis was performed using treatment group, sex, anti-cyclic citrullinated peptide (CCP) antibody (positive vs negative), and baseline disease activity (DAS28-ESR) as fixed effects, patients as random effects, and baseline values as covariates. For extension data, measurement time-point and the interaction between treatment group and measurement time-point was further added as fixed effects. The adverse events (AEs) were recorded.
Results: A total of 46 patients were randomized to denosumab and csDMARD groups (both N=23), and baseline characteristics were similar between both groups. Although the difference was not significant, the estimate mean (95%CI) change of ER-depth at month 6 from baseline as the primary endpoint was –0.57 (–1.52, 0.39) in the denosumab group vs –0.22 (–0.97, 0.53) in the csDMARD group, respectively. At months 6 and 12, ER-depth, -width, and -volume (extension data) were numerically lower in the denosumab group than in the csDMARD group (Table 1). Compared with patients in the csDMARD group, those in the denosumab group had significantly higher volumetric bone mineral density (vBMD) at month 12. AEs were reported in 12 (52.2%) and 13 (56.5%) of patients in the denosumab and csDMARD groups, respectively. The most common AEs of denosumab groups was hypocalcemia (reported in 4), and all the events were causally related with denosumab. Serious AEs were reported in 1 (4.3%) and 2 (8.7%) of patients in the denosumab and csDMARD groups, and which were not related to treatment drug.

Table 1. ER and microstructure in denosumab group vs csDMARD group

	Month	Denosumab group (n=21)		csDMARDs group (n=22)		Difference (Denosumab- csDMARDs)
		n1	Estimate Means [95%CI]	n1	Estimate Means [95%CI]	Estimate Means [95%CI]
ER-depth	6	17	–0.46 [–1.31, 0.39]	25	–0.20 [–0.89, 0.49]	–0.27 [–0.86, 0.32]
	12	17	–0.56 [–1.41, 0.29]	22	–0.20 [–0.90, 0.49]	–0.35 [–0.95, 0.24]
ER-width	6	17	–0.26 [–1.10, 0.57]	25	–0.06 [–0.73, 0.61]	–0.20 [–0.81, 0.40]
	12	17	–0.27 [–1.10, 0.56]	22	–0.03 [–0.70, 0.64]	–0.24 [–0.85, 0.38]
ER-volume	6	16	–6.21 [–23.89, 11.46]	24	–1.71 [–16.07, 12.66]	–4.51 [–16.67, 7.65]
	12	17	–6.25 [–23.94, 11.44]	21	–3.18 [–17.56, 11.20]	–3.07 [–15.32, 9.17]
vBMD	6	42	6.41 [2.78, 10.03]	44	2.46 [–1.33, 6.24]	3.95 [–0.05, 7.94]
	12	38	9.20 [5.46, 12.95]	42	3.66 [–0.15, 7.46]	5.55 [1.46, 9.63]*

These were extension data.This is the efficacy analysis set which excluded 3 patients from the full analysis set.*; p<0.01n, number of patients; n1, number of measurement points

Conclusion: Our results suggest that adding denosumab to csDMARD therapy may help prevent ER, promote ER repair, and improve bone microstructure.
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Shiraishi: None declared, Konosuke Watanabe: None declared, Nozomi Ohki: None declared, Akitomo Okada: None declared, Tomohiro Koga: None declared, Makiko Kobayashi Employee of: Daiichi Sankyo Co., Ltd. (retired at submission), Kengo Saito Employee of: Daiichi Sankyo Co., Ltd., Naoki Okubo Employee of: Daiichi Sankyo Co., Ltd., Atsushi Kawakami Speakers bureau: Daiichi Sankyo Co., Ltd., Grant/research support from: Daiichi Sankyo Co., Ltd.
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POS0688 PHASE 2A STUDY IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO MTX AND/OR ANTI-TNFA THERAPEUTICS SHOWS THAT ORAL ABX464 50 MG ONCE DAILY IS SAFE, WELL TOLERATED AND SHOWS PROMISING EFFICACY RESULTS

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Background: ABX464 upregulates the expression of the anti-inflammatory microRNA miR-124 and is a first-in-class drug candidate as an oral treatment for moderate-to-severe Rheumatoid Arthritis (RA).
Objectives: This phase 2a randomized, double blind, placebo controlled, parallel group 12-week study evaluated the safety and preliminary efficacy of ABX464 (50 and 100 mg q.d.), in combination with methotrexate (MTX) in 60 patients (1:1:1 ratio) with moderate-to-severe active RA who have inadequate response to MTX or/and to an anti-TNFα therapy. Patients who completed the 12-week induction phase could roll over into a 52-week open-label maintenance study to evaluate the long-term safety and efficacy of 50 mg q.d oral ABX464 in RA.
Methods: The primary end point was the safety of ABX464; efficacy endpoints included the proportion of patients achieving ACR20/50/70 responses, disease activity scores (DAS28, SDAI, CDAI), EULAR response, DAS28 low disease activity (DAS28-CRP ≤ 3.2) or remission. Blood samples from patients were used to measure the expression of miR-124 and the relative concentrations of cytokines (baseline and week 8).
Results: Patients baseline characteristics were well balanced in terms of disease severity and demographics (mean ± SD DAS28-CRP: 5.43 ± 0.78; RA duration: 6.43 ± 7.43 years). ABX464 50 mg was safe and well tolerated. Two serious adverse events (SAEs) were reported (one on placebo group and one on ABX464 100 mg). Eleven patients were withdrawn for AEs (9 patients on 100 mg, 1 on 50 mg and 1 on placebo). An increased incidence of largely mild-to-moderate gastrointestinal AEs in the 100 mg treatment group led to a higher drop-out rate of patients. The nature of these AEs was consistent with what has been observed in more than 1023 subjects who have so far been treated in other clinical trials with ABX464 across different indications. No cases of opportunistic infection, no malignancies and no death were reported. Although the sample size of this proof-of-concept study was not powered to show efficacy, multiple early efficacy endpoints showed signs of promise with the ABX464 50 mg daily dose. Compared to placebo, ABX464 50 mg showed significantly higher proportions of patients achieving ACR20 and ACR50 responses at week 12 in the per protocol population (PP). DAS28-CRP and DAS28-ESR decreased significantly (Intent-to-Treat Population, ITT) and rates of categorical DAS28-CRP response (PP) or CDAI remission (ITT) increased significantly on ABX464 at week 12 (Table 1). Compared to placebo, a significant upregulation of miR-124 expression and a decrease in IL-6 blood levels were observed for every patient dosed with ABX464. 40 patients enrolled in the ongoing open-label maintenance study with ABX464 50 mg q.d. At week 52, the drop-out rate of patients was 44 % (17/39), including 7 drop-outs due to AE (18 %). Preliminary maintenance efficacy data, defined as Low Disease Activity, were obtained from 22 patients who reached 52 weeks of treatment: 44 % patients achieved LDA according to ITT.
Conclusion: Efficacy and safety findings of the first-in-class drug candidate ABX464 warrant further exploration at 50 mg q.d. or less as an oral treatment for RA patients.
Disclosure of Interests: Claire Daien Speakers bureau: Abivax, Consultant of: Abivax, Abbvie, Amgen, BMS, Fresenius-Kabi, MSD, Novartis, Pfizer, Sandoz, Sanofi, Roche-Chugai, UCB, Grant/research support from: punctual links or research grant from Abbvie, Amgen, BMS, Fresenius-Kabi, MSD, Novartis, Pfizer, Sandoz, Sanofi, Roche-Chugai, UCB, Marek Krogulec: None declared, Paul Gineste Employee of: Abivax, Jean-Marc Steens Employee of: Abivax, Laurence Desroys Du Roure Employee of: Abivax, Sophie Biguenet Employee of: Abivax, Didier Scherrer Employee of: Abivax, Julien Santo Employee of: Abivax, Hartmut Ehrlich Employee of: Abivax, Patrick Durez: None declared
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POS0689 GENICULAR NERVE BLOCK IN JUVENILE IDIOPATHIC ARTHRITIS: A RANDOMIZED CLINICAL TRIAL

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Background: Genicular nerve block (GNB) showed promising results in improving pain, function, and inflammation in adults with rheumatoid arthritis suffering from persistent knee arthritis (1).
Objectives: This study aimed at testing the effect of GNB in juvenile idiopathic arthritis (JIA) patients with unilateral persistent knee arthritis on pain, function, range of motion, and inflammation parameters.
Methods: N=104 JIA patients diagnosed according to the ILAR criteria with persistent unilateral knee arthritis. They were assigned randomly into two groups; group I received nerve block, group II received intra-articular triamcinolone. Visual analogue scale, SOLAR scoring system, and Lysholm scores were assessed at 0, 2, and 12 weeks intervals. Tenderness and swelling were evaluated by a semi-quantitative score at the same intervals.
Results: VAS, tenderness, swelling, and SLOAR scores were significantly decreased after 2 weeks of interventions in both groups, but this reduction was greater in GNB group regarding VAS and tenderness, while was greater in steroid group regarding SOLAR and swelling. At 12 weeks, all these outcome measures revealed better values in GNB group in comparison to steroid group, but this was significant only for VAS. Moreover, Lysholm score was significantly increased in both groups at 2 and 12 weeks intervals with higher values in steroid group versus GNB group at 2 weeks.
Conclusion: Nerve block was able to control pain, improve function and inflammation outcome measures of the knee joint in JIA patients. Although steroid achieved better results after 2 weeks, GNB achieved a better long-term improvement after 12 weeks.

Table 1. Efficacy endpoints.

	Placebo		50 mg		100 mg	
	PP	ITT	PP	ITT	PP	ITT
	(n=19)	(n=20)	(n=16)	(n=21)	(n=7)	(n=19)
Early discontinuations due to AE	1		1		9	
ACR20 n (%)	4 (21%)	4 (20%)	**9 (56%)** *	9 (43%)	3 (43%)	3 (16%)
ACR50 n (%)	1 (5%)	1 (5%)	**5 (31%)** *	5 (24%)	2 (29%)	2 (11%)
ACR70 n (%)	1 (5%)	1 (5%)	4 (25%)	4 (19%)	1 (14%)	1 (5%)
DAS28-CRP Mean change from baseline	-0.63	-0.60	**-1.79** *	**-1.41** *	**-1.94** *	-0,72
DAS28-ESR Mean change from baseline	-0.65	-0.59	**-1.86** *	**-1.43** *	**-2.0** **	-0.74
Low Disease Activity (DAS28-CRP ≤ 3.2) n (%)	2 (11%)	2 (10%)	4 (25%)	4 (19%)	3 (43%)	3 (16%)
Categorical DAS28-CRP response n (%)	8 (42%)	8 (40%)	**14 (88%)** **	14 (67%)	**6 (86%)** *	6 (32%)
CDAI ≤ 10 n (%)	2 (11%)	2 (10%)	5 (31%)	5 (24%)	3 (43%)	3 (16%)
CDAI Remission n (%)	0	0	**3 (19%)** *	**3 (14%)** *	0	0

* P < 0.05, ** P < 0.01 Chi-squared test ABX-464 *versus* placebo

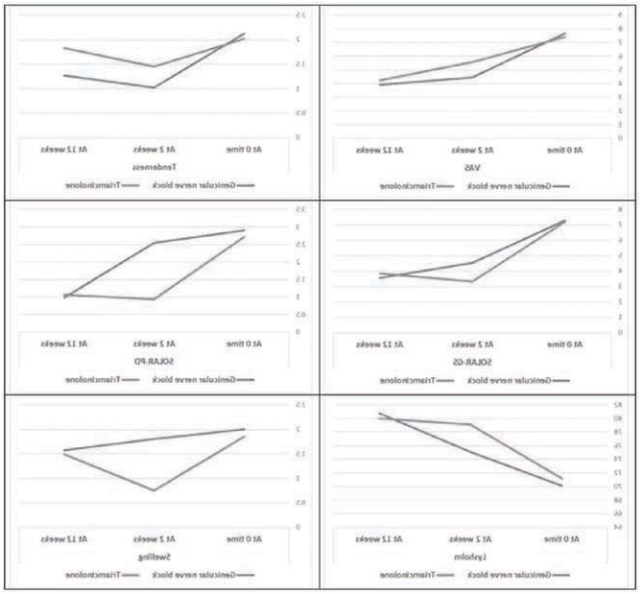

Figure 1.

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POS0690 SYSTEMATIC LITERATURE REVIEW: WHICH ROUTE AND DOSE OF CORTICOSTEROID IS MOST EFFECTIVE IN INDUCING REMISSION IN EARLY RHEUMATOID ARTHRITIS?

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Background: Current NICE guidance for rheumatoid arthritis (RA) states that glucocorticoids may be used for bridging therapy and to rapidly decrease inflammation in acute flares[1]. However, a recommended route and dosage is not specified, and variation has been observed between individual departments as to whether or not steroids are administered[2]. Glucocorticoids are associated with adverse events that can be severe, leading to a strong recommendation by the American College of Rheumatology to avoid long term use[3]. It is therefore important to ascertain the efficacy of available routes and dosages of glucocorticoids to weigh against these risks.
Objectives: This review aimed to ascertain the optimum route and dose of corticosteroid for adults with early RA.
Methods: Papers included were full text, English language, randomised controlled trials that fulfilled the PICO criteria. The population was defined as adults with early RA with onset <2 years, the intervention corticosteroids of any route or dose, the comparator conventional DMARDs or placebo, and the primary outcome remission. Functional improvement and X ray progression were considered as secondary outcomes. MEDLINE, Embase, Web of Science and Cochrane Central were searched. Screening of results and extracted data was carried out by both reviewers. During data extraction, outcomes were rounded to timepoints of 3, 6 and 12 months, and steroid doses were stratified into low (up to 10mg/day prednisolone or equivalent), medium (15-30mg) and high (>30mg). Meta-analyses were carried out in RevMan 5.4 when 3 or more studies measured the same outcome at the same dose and route. A funnel plot was generated to check for publication bias.
Results: Three papers measured DAS28 remission rate at 1 year, comparing DMARDs only to DMARDs plus low dose oral steroids. The Forest plot for this meta-analysis is shown in Figure 1. As I^2 = 0%, a fixed effect method was used. This shows an odds ratio (OR) of 1.73 (95% CI 1.25, 2.39) favouring low dose steroids in addition to DMARDs. Meta-analyses were also possible for HAQ at 1 year, and mean DAS28 at 1 year, comparing DMARDs alone to DMARDs plus low dose steroids. Both analyses favoured steroids; for HAQ scores the standardised mean difference (SMD) was -0.69 (95% CI -1.66, 0.29), and for DAS28 the SMD was -0.36 (95% CI -0.58, -0.15). At 3 and 6 months there was a lack of available data for meta-analyses.

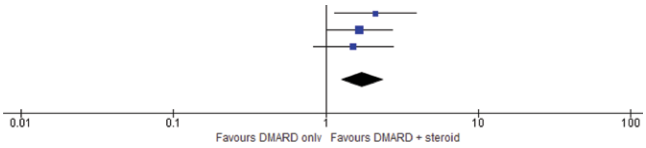

Figure 1. Forest plot showing the OR of DAS28 remission with low dose steroids and conventional DMARDs vs DMARDs only

Conclusion: At 1 year, remission and improvement in function appear more likely if low dose steroids are used. Due to a lack of available data, non-oral routes, higher doses and X ray progression could not be analysed. Studies were not designed to detect differences in adverse events. This highlights the need for further clinical research into steroid efficacy in early RA, as the meta-analyses suggest that glucocorticoids may be more effective in inducing remission in early disease than conventional DMARDs alone.

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POS0691 EMULATING A TARGET TRIAL OF ADALIMUMAB VERSUS TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: A COMPARATIVE EFFECTIVENESS ANALYSIS USING THE OPAL REAL-WORLD DATASET

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Background: There is increasing recognition of the complementary role for real-world evidence (RWE) in health care and regulatory decision-making (1). However, careful analysis is required when drugs are compared using observational data to account for differences between treatment groups. Electronic medical records (EMR) are an important source of real-world data (RWD), but outcomes are often recorded incompletely. We emulated a target trial of adalimumab (ADA) versus tofacitinib (TOF) in patients with rheumatoid arthritis (RA) using the OPAL dataset to illustrate the application of methodologies to address the challenges of non-random treatment assignment and incomplete data. The OPAL dataset is derived from EMR of 112 community-based rheumatologists around Australia, where practitioners have discretion to prescribe whichever b/tsDMARD they consider most clinically appropriate.
Objectives: To estimate the average treatment effect (ATE) of TOF compared to ADA at 3 and 9 months, defined as the difference in mean disease activity score (DAS28CRP), in patients with RA who are new users of a b/tsDMARD. This is equivalent to aiming to estimate the intention-to-treat effect in a randomised controlled trial.
Methods: OPAL patients diagnosed with RA were included if they initiated ADA or TOF between 1 October 2015 and 1 April 2021, were new b/tsDMARD users (no prior recorded b/tsDMARD, at least 6 months of prior csDMARD treatment), and had at least 1 component of DAS28CRP recorded at baseline or during follow-up. Data were also extracted on baseline characteristics. Baseline characteristics were DAS28CRP, patient demographics, regional location, disease duration, prescriber characteristics (including gender, experience), prior recorded comorbidities, and prior and concomitant treatment with csDMARDs and oral corticosteroids. We used random forest multiple imputation to impute missing baseline and follow-up DAS28CRP components (2). Stable balancing weights (SBW) were then used to balance the treatment groups in terms of their

baseline characteristics, including DAS28CRP (3). For each imputed dataset, the ATE at 3 months was estimated as the difference between the mean outcome in the two treatment groups after balancing (i.e. weighting) the sample, and then these estimates were averaged across the 10 imputed datasets. The ATE at 9 months was estimated similarly. The whole procedure was subsequently performed in 1000 bootstrap samples to estimate a 95% confidence interval (CI) for the ATEs using the percentile method (4).

Results: 842 patients were identified including n=569 treated with ADA and n=273 treated with TOF. After applying the SBW, the maximum difference between the mean of each baseline characteristic in the ADA and TOF groups was less than 0.03% of the corresponding standard deviation in the whole sample, indicating reasonable balance was achieved in this complex dataset. After weighting, mean DAS28CRP reduced from 5.3 at baseline (both ADA and TOF groups) to 2.6 and 2.3 at 3 and 9 months for ADA, and 2.4 and 2.3 at 3 and 9 months for TOF. The estimated ATE was -0.22 (95% CI -0.36, -0.03; p=0.02) at 3 months, indicating a modest but significant reduction in disease activity for patients on TOF. The estimated ATE was -0.03 (95% CI -0.19, 0.1; p=0.56) at 9 months, indicating no difference between groups.

Conclusion: DAS28CRP was significantly lower at 3 months for patients treated with TOF compared to ADA. However, 3 months of treatment with either drug led to substantive average reductions in mean DAS28CRP, consistent with remission. There was no difference between drugs at 9 months. Future work will estimate a per-protocol effect.

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POS0692

RHEUMATOID ARTHRITIS PATIENTS WHO SWITCHED TREATMENT FROM ADALIMUMAB TO UPADACITINIB DEMONSTRATE A ROBUST REDUCTION OF INFLAMMATION-RELATED BIOMARKERS: PROTEOMICS ANALYSIS FROM THE SELECT-COMPARE PHASE 3 STUDY

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Background: Upadacitinib 15 mg QD (UPA), an oral JAK inhibitor, showed greater efficacy compared to adalimumab (ADA) in patients (pts) with active rheumatoid arthritis (RA) on background MTX at wk 12 of the SELECT-COMPARE phase 3 study[1]. A subset of pts switched treatment (ADA to UPA [23.5%] and UPA to ADA [19.2%]) due to non-response (NR) to the initial therapy. A higher proportion of pts rescued from ADA to UPA achieved CDAI ≤10 (LDA) post-switch (47%) vs pts rescued from UPA to ADA through 24 wks (36%)[2].

Objectives: To explore the biological mechanisms associated with the differential clinical response in RA pts who switched treatment due to NR to initial ADA or UPA therapy in comparison to pts who continued treatment based on response (R) to the initial therapy.

Methods: We included a random subset of pts (100 pts each from the originally randomized treatment groups [UPA, n=651; ADA, n=327]). NR was defined as <20% improvement in TJC or SJC at wks 14–24 compared to baseline (BL) and R as achieving these improvements. The levels of 181 inflammation-related protein biomarkers (BM) were analyzed using the Olink platform at BL, wks 2, 8, and 26. Contrasts between relative BM levels were assessed using a repeated measure mixed linear model, and correlations between BM levels and DAS28-CRP were computed using Pearson's method.

Results: In this patient subset, 40% of ADA NR who switched to UPA achieved CDAI LDA at wk 26 vs 17% of UPA NR who switched to ADA. Proteomics analysis identified 42 BMs that showed significant differential modulation between R and NR prior to switch (BL to wk 8) or after switch (wks 8–26) (Table 1). Ten BMs (CCL7, CCL8, CHI3L1, CSF1, IL6, MMP1, SLAMF1, TNFRSF9, TNFSF14, and VEGFA) were differentially modulated between ADA R and NR and were significantly decreased after switching to UPA (wk 26). The levels of these 10 BMs were similar between UPA R and NR through wk 8, except for CHI3L1, and MMP1, SLAMF1, and TNFSF14 increased after switching to ADA (wk 26). Another group of 13 BMs (CCL13, CCL19, CCL23, FGF21, IL18, IL10RA, IL18BP, IL1R1, IL2RA, MMP3, TNFSF11, TNFSF13B, TNFRSF1A) had similar levels between ADA R and NR through wk 8 and were significantly decreased after switching to UPA (wk 26). The levels of these 13 BMs were similar between UPA R and NR, except for FGF21, and the levels of CCL13, CCL19, CCL23, IL10RA, IL1R1, IL2RA, and TNFSF11 increased after switching to ADA (wk 26). Notably, the BL levels of CCL7, CCL23, CHI3L1, CSF1, IL2RA, IL6, MMP1, MMP3, and VEGFA were correlated with DAS28-CRP at BL, suggesting a potential relationship of these BMs in the pathobiology of RA. Among the remaining BMs, the levels of CCL3, CCL4, CX3CL1, EPCAM, and FLT3LG were similar between UPA R and NR and decreased after switching to ADA (wk 26).

Conclusion: We propose that switching to UPA from ADA NR leads to more favorable clinical improvement that is paralleled by a more profound immune modulation than switching to ADA from UPA NR, consistent with the broader mechanistic inhibition achieved by JAK-associated signaling pathway inhibition compared with discrete TNF-signaling inhibition.

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Table 1. Classification of Selected Protein BMs

		BL to Week 14: ADA				BL to Week 14: UPA		
		R / NR (n = 79 / 21)				R / NR (n = 84 / 16)		
		BM Wk 8				BM Wk 8		
		NR>R	NR=R	NR<R		NR>R	NR=R	NR <R
ADA → UPA WEEK 8 - 26	BM ↓	**CCL7**, CCL8, **CHI3L1**, **CSF1**, **IL6**, **MMP1**, SLAMF1, TNFRSF9, TNFSF14, VEGFA	CCL13, CCL19, **CCL23**, FGF21, IL18, IL10RA, IL18BP, IL1R1, **IL2RA**, **MMP3**, TNFSF11, TNFSF13B, TNFRSF1A		UPA → ADA WEEK 8 - 26		CCL3, CCL4, CX3CL1, EPCAM, FLT3LG	
	BM ↔	CCL3, CCL4, CXCL8, CXCL9, **CXCL10**, CXCL16, IL17A	CCL11, CCL25, **CDCP1**, CX3CL1, FABP4, FLT3LG, IL12B, KITLG, MMP10, **SPP1**			**CDCP1**, **CHI3L1**	**CCL7**, CCL8, **CSF1**, CXCL8, CXCL9, **CXCL10**, **IL6**, IL17A, IL18BP, **MMP3**, TNFRSF9, TNFSF13B, TNFRSF1A, VEGFA	CCL11, CXCL16, FABP4, FGF21, KITLG, MMP10, PON3
	BM ↑	EPCAM		PON3		IL12B	CCL13, CCL19, CCL23, IL10RA, IL1R1, **IL2RA**, **MMP1**, SLAMF1, **SPP1**, TNFSF11, TNFSF14	

POS0693

IMPACT OF UPADACITINIB VERSUS ABATACEPT ON INDIVIDUAL DISEASE OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSES TO BIOLOGIC DMARDS

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Background: The phase 3 SELECT-CHOICE trial of patients with rheumatoid arthritis (RA) and prior inadequate response to biologic DMARD(s) (bDMARD-IR) demonstrated superiority of the JAK inhibitor upadacitinib (UPA) vs abatacept (ABA) in the mean change from baseline (BL) in DAS28(CRP) and in the proportion achieving DAS28(CRP) <2.6 at week (wk) 12, with higher incidence of serious adverse events reported in the UPA treatment group.

Objectives: To evaluate the impact of UPA vs ABA on individual components of composite measures of disease activity in SELECT-CHOICE.

Methods: In SELECT-CHOICE, a double-blind phase 3 trial, bDMARD-IR patients were randomly assigned to UPA 15 mg once daily or ABA, each with background conventional synthetic DMARDs, for 24 wks. For this post hoc analysis, the proportions of patients achieving improvement from BL through wk 24 in ACR core variables (including SJC, TJC, Patient Global Assessment [PtGA], Physician Global Assessment [PhGA], pain, HAQ-DI, and hsCRP) and Boolean remission criteria were evaluated. Differences in the cumulative distributions of CDAI, DAS28(hsCRP), SDAI, and ACR-n (the lowest of percent change in TJC, percent change in SJC, or median of the other 5 ACR components) were determined using the Kolmogorov-Smirnov test and are reported as observed. For all other variables, non-responder imputation was applied for missing data. Nominal *P* values are provided throughout.

Results: A total of 616 bDMARD-IR patients with moderate to severe RA were randomized in SELECT-CHOICE (UPA 15 mg, n=303; ABA, n=309). BL demographic and disease characteristics were generally comparable between treatment groups, with a mean disease duration of approximately 12 years and mean CDAI of 39.6. At wk 12, more patients receiving UPA vs ABA achieved ≥50% improvements from BL in TJC68, PtGA, and hsCRP, with comparable proportions observed between UPA and ABA for the remaining ACR components (Figure 1). At wk 24, similar proportions of patients receiving UPA and ABA achieved ≥50% improvements in all but the hsCRP component. Overall, 15% and 26% of patients on UPA compared with 6% and 15% on ABA demonstrated ≥50% improvements across all ACR components at wks 12 and 24, respectively. At wks 12 and 24, Boolean remission was achieved by 6% and 14% of patients on UPA vs 2% and 10% of patients on ABA, respectively; the proportion of patients in both treatment groups achieving the individual Boolean components were also reported (Table 1). While comparable at BL, cumulative distributions of CDAI, SDAI, DAS28(hsCRP), and ACR-n were improved on UPA vs ABA at wk 12 (all nominal *P* <0.05); differences persisted for most measures at wk 24.

Table 1. Proportions of Patients Achieving Boolean Remission and Its Components at Week 12 and 24 (NRI)

	Week 12		Week 24	
	UPA 15 mg	ABA	UPA 15 mg	ABA
n (%)	(N=303)	(N=309)	(N=303)	(N=309)
Boolean Remission	19 (6)***	5 (2)	42 (14)*	30 (10)
PtGA ≤10	54 (18)***	29 (9)	80 (26)*	66 (21)
TJC ≤1	89 (29)***	64 (21)	134 (44)*	115 (37)
SJC ≤1	127 (42)**	106 (34)	169 (56)*	152 (49)
hsCRP ≤1 mg/dL	257 (85)***	209 (68)	244 (81)***	199 (64)

Nominal ***P <.001, **P <.01, *P <.05 for UPA vs ABA. ABA, abatacept; PtGA, Patient's Global Assessment of disease severity; UPA, upadacitinib.

Conclusion: In this post hoc analysis of bDMARD-IR RA patients, improvements in components of disease measures were reported for both UPA and ABA through 24 weeks, with numeric differences noted for several components. Nominally higher attainment of Boolean remission and its components were observed for UPA over ABA.

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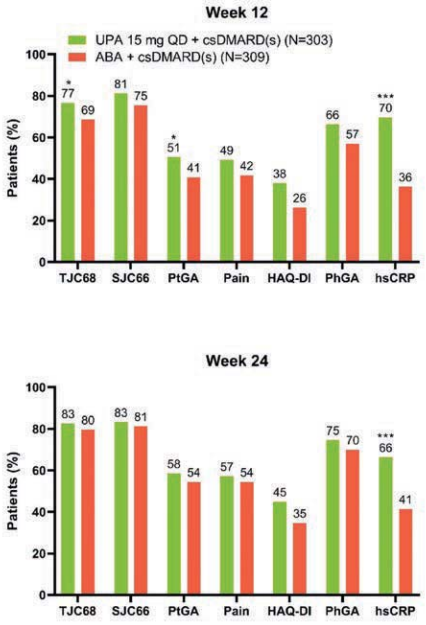
Figure. Proportions of Patients Receiving UPA vs ABA Who Achieved at Least 50% Improvement From Baseline in Each of the ACR Components at Week 12 and 24 (NRI)



Nominal ***P <.001, **P <.01, *P <.05 for UPA vs ABA. *P* values were calculated using the Cochran-Mantel-Haenszel test, with adjustment for the main stratification factor of previous failed biologic DMARD. ABA, abatacept; ACR, American College of Rheumatology; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire–Disability Index; hsCRP, high sensitivity C-reactive protein; NRI, non-responder imputation; PhGA, Physician's Global Assessment of disease severity; PtGA, Patient's Global Assessment of disease severity; QD, daily; SJC66, Swollen Joint Count based on 66 joints; TJC68, Tender Joint Count based on 68 joints; UPA, upadacitinib.

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POS0694

WHAT TREATMENT GIVES THE BEST CLINICAL RESPONSE AFTER CESSATION OF JAKI THERAPY IN PATIENTS WITH RA? DATA OF THE TARDIS-RA REGISTRY, A NATIONWIDE BELGIAN BIOLOGIC REGISTRY

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Background: JAKi represent a new important class in Rheumatoid Arthritis (RA) treatment options. It is unknown which specific bDMARD or mode of action should be selected after stopping a JAKi.

Objectives: To study if clinical response differs between advanced therapies that are initiated after stopping a JAKi.
Methods: Patients were included from the electronic platform "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS). Data from all Belgian RA patients on biologic and targeted therapy are collected here for drug reimbursement. Patients were selected for this analysis if they had stopped JAKi therapy and initiated a subsequent therapy. Patients were grouped by TNFi, T/B cell therapy, IL6i or JAKi therapy. The DAS28 response and proportion of patients in remission at the first follow-up (between 3 and 6 months) were compared between groups. Remission was defined as DAS28<2.6. Analyses were repeated in patients who were prescribed the stopped JAKi as first-line or as subsequent line therapy. Data were compared via χ^2, Anova and t-tests.
Results: In total, 1238 patients who had stopped JAKi therapy were included. TNFi, T/B cell therapy, IL6i or JAKi therapy was initiated in 36% (441/1238), 19% (233/1238), 18% (227/1238) and 27% (337/1238) respectively. Most baseline demographic and clinical characteristics differed between groups (Table 1).

Table 1.

	TNFi	B/T cell	IL6i	JAKi	p-value
Number	441 (36%)	233 (19%)	227 (18%)	337 (27%)	
Age (years)	**55 ± 14**	**57 ± 13**	**55 ± 14**	**59 ± 12**	**<0.001**
Gender (women)	323 (73%)	177 (76%)	186 (82%)	257 (76%)	0.100
Weight (kg)	74 ± 15	79 ± 17	75 ± 15	75 ± 15	0.111
Disease duration (years)	**9 ± 8**	**10 ± 9**	**11 ± 9**	**11 ± 9**	**0.002**
HAQ (0-3)	1.6 ± 0.7	1.8 ± 0.6	1.5 ± 0.7	1.5 ± 0.8	0.353
PGA (0-100)	**65 ± 20**	**68 ± 21**	**67 ± 21**	**57 ± 24**	**<0.001**
CRP (mg/l)	**10 ± 16**	**14 ± 20**	**16 ± 28**	**11 ± 17**	**0.003**
ESR (mm/h)	22 ± 21	24 ± 19	27 ± 21	25 ± 22	0.117
TJC28	**8 ± 6**	**8 ± 6**	**9 ± 6**	**7 ± 6**	**0.001**
SJC28	**5 ± 4**	**6 ± 5**	**6 ± 4**	**5 ± 5**	**0.006**
DAS28	**4.7 ± 1.1**	**4.8 ± 1.1**	**4.9 ± 1.2**	**4.4 ± 1.3**	**<0.001**
2nd line of therapy after initial JAKi therapy	**211 (48%)**	**56 (24%)**	**52 (23%)**	**112 (33%)**	**<0.001**

Numbers given are mean ± SD or number, proportion. TNFi = tumour necrosis factor inhibitor, ts= targeted synthetic, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints

The clinical response could be studied in 577 patients. Patients on rituximab were excluded as these were retreated on flare, following Belgian reimbursement criteria. TNFi, Tcell therapy, IL6i or JAKi therapy was initiated in 37% (211/577), 13% (76/577), 18% (102/577) and 33% (188/577) of these patients respectively. DAS28 decreased on average with 1.7 ± 1.5, 1.6 ± 1.4, 2.4 ± 1.6* and 1.3 ± 1.6 for patients on TNFi, T cell therapy, IL6i or JAKi therapy respectively (*p<0.001). Remission was reached in 42%, 41%, 56%* and 39% for patients on TNFi, T cell therapy, IL6i or JAKi therapy respectively (*p=0.045).
Before switching, JAKi therapy was the first advanced therapy in 35% (204/577). In this "naïve" subgroup, DAS28 decreased on average with 1.9 ± 1.5, 1.9 ± 1.3, 2.4 ± 1.8 and 1.0 ± 1.7* for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (*p=0.001). Remission was reached in 44%, 48%, 58% and 35% for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (p=0.279).
In the "experienced" subgroup, who started JAKi therapy as subsequent line therapy in 65% (373/577), DAS28 decreased on average with 1.5 ± 1.6, 1.5 ± 1.4, 2.3 ± 1.6* and 1.4 ± 1.6 for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (*p<0.001). Remission was reached in 40%, 38%, 55% and 41% for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (p=0.118).
Conclusion: Our results show clearly that IL6 inhibitors have a better clinical response after JAKi cessation compared to other mode of actions, including other JAKi. However, considerable baseline differences existed, that could influence our results.
Disclosure of Interests: None declared
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POS0695 EFFECT OF METHOTREXATE AND FOLIC ACID CO-ADMINISTRATION IN ARTHRITIS

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Background: Methotrexate (MTX) is the recommended first-line treatment for rheumatoid arthritis. Adjuvant-induced arthritis (AIA) rat is a robust model with a high prevalence of arthritis used to investigate arthritis. MTX reduces inflammation, but associated with adverse events, such as gastrointestinal, hepatic, and hematology toxicity (1). To reduce these side effects, folic acid (FA) is administrated at distance to MTX with no defined recommendation for its dosing (5-25mg/week) or time point of administration (2) (1-3 days after MTX application). Whether the complicated therapeutic regimen with MTX once a week and FA at another time point affects compliance is an open question. MTX is metabolized in polyglutamates derivates (MTX-PG), which is a biomarker of MTX efficacy as its half-life (1-4 weeks) is longer than MTX (4h) (3).
Objectives: The aim of this study was to assess efficacy and tolerance of co-administration of MTX and FA compared to MTX with FA applied one day after MTX in the AIA.
Methods: Female Lewis rat were randomly divided in three groups and received an injection of Mycobacterium butyricum defining day (D) 0 to induce arthritis. An historic AIA group was used as control. Treatment began on D9, one day before arthritis onset in this model. The first group rats were treated with MTX only (n=13), the second group received MTX and FA at the same day (n=14), and the third group received FA one day after MTX administration (n=14). MTX was administrated intraperitoneally (IP) at 1 mg/kg every 3 days (4) and FA was delivered IP at 0.17 mg/kg. Arthritic index (AI) and ankle circumference (AC) were monitored to assess arthritis. Microcomputed tomography of the ankle was performed to assess bone loss. Moreover, complete blood count, transaminases, and MTX-PG were assessed.
Results: Arthritis developed at D10 in all groups. AI and AC were similar in MTX groups at the various time points. At D17, arthritis severity was lower in MTX groups (AI (mean and standard deviation): 1.4 ± 1.6; AC: 35 ± 7 mm) compared to AIA historical group (AI: 3.3 ± 0.6; AC: 42 ± 4 mm). Bone erosion and bone loss parameters were similar in all groups. Cortical porosity was around 0.40% ± 0.15 and bone volume / total volume was around 0.22% ± 0.13. MTX-PG1 was found at similar levels in MTX groups and correlated negatively with AI in MTX alone or MTX and FA at the same day groups ($p<0.05$ and $p<0.01$, respectively). Finally, white and red blood cells, platelets, hemoglobin, mean corpuscular volume, transaminases, and creatinine were found at a similar level in MTX groups.
Conclusion: Co-administration of MTX with FA on the same day is effective compared to FA application one day after MTX. MTX metabolism was not affected, as demonstrated by the MTX-PG concentrations. The biological tolerance between the protocols was comparable. Thus, co-administration of MTX and FA seems to be possible and may be more convenient to the patients and improve compliance at the end.
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POS0696 DOES PREDNISONE USE DURING PREGNANCY IN WOMEN WITH RHEUMATOID ARTHRITIS INDUCE INSULIN RESISTANCE IN THE OFFSPRING?

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Background: The use of long-term corticosteroids during pregnancy has been growing over the past decades[1]. Corticosteroids can be given when an auto-inflammatory disease like rheumatoid arthritis (RA) is too active. Several studies have shown that long-term corticosteroids use in pregnancy is associated with maternal and fetal adverse outcomes, like preeclampsia, shorter gestational age, lower birth weight and rapid catch-up growth [1-3]. These last two outcomes could influence the insulin resistance later in life[4].

Objectives: Does prednisone use in pregnant women with RA induces insulin resistance in the offspring?
Methods: 103 children were included after their mother had participated in a prospective cohort study on RA and pregnancy. 42 children were *in utero* exposed to prednisone and 61 were non-exposed. To assess insulin resistance, we measured Homeostasis Model of Assessment Insulin Resistance (HOMA-IR), serum adiponectin and lipid levels, corrected for body fat distribution.
Results: There was no difference in mean HOMA-IR (SD) between the children who were prednisone-exposed *in utero* (1.10 (0.84)) and those non-exposed (1.09 (0.49)). No difference was found in mean adiponectin (SD) level, 16.45 (4.06) µg/mL and 15.40 (3.59) µg/mL, respectively. Also no difference was found in body fat distribution or lipids such as total cholesterol, fasting triglyceride or high-density lipoprotein.
Conclusion: Children who are prednisone-exposed *in utero* have no increased risk for insulin resistance at the age of approximately 7-years. This findings are reassuring, but further research has to be performed to evaluate if prednisone-exposure *in utero* has no other negative effects on the long-term and if insulin resistance remains absent in the future.
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POS0697 OPHTHALMOLOGICAL ADVERSE EVENTS UNDER JAK: CASE ANALYSIS OF THE EUROPEAN PHARMACOVIGILANCE DATABASE

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Background: Ophthalmological manifestations in rheumatic diseases include dry syndrome, scleritis, episcleritis, uveitis and peripheral ulcerative keratitis (PUK). Among the target therapies, JAK inhibitors (JAKinhib) are the most recent to have been approved in rheumatic diseases, rheumatoid arthritis (RA) and spondyloarthritis (SpA), but also in other indications such as inflammatory bowel disease.
Objectives: The aim of this work is to describe and characterise ophthalmological events in patients exposed to JAKinhib based on European pharmacovigilance (PV) data.
Methods: The ophthalmological manifestations that appeared under JAK inhib were extracted from the European PV database (April 2020), EUDRAVIGILANCE following a request addressed to the National Drug Safety Agency carried out according to the following MedDRA classification "SOC eye disorders and BARICITINIB" and "SOC eye disorders and TOFACITINIB".
Results: A total of 1411 patients with ophthalmological adverse events (AEs) were identified with JAKinhib. 103 with BARICITINIB (81 women, mean age 59.7 years), 1308 with TOFACITINIB (1116 women, mean age 64.7 years). Among these AEs, 58% were reported by medical and paramedical staff and 42% were reported by patients. JAKinhib was initiated mainly in patients with RA (1070 patients), SpA (26 patients) and ulcerative colitis (UC) (27 patients). Of the reported AEs, 10% were inflammatory disorders of the anterior or posterior segments of the eye [51 uveitis (40 RA, 1 SpA, 1 RCUH, 1AJI, 8 undetermined (n.d.)), 49 corneal ulcerations (38 RA, 2 RCHU, 9 n.d.), 28 scleritis (20 RA, 8 n.d.), 13 keratitis (8 RA, 1 SpA, 1 Crohn's, 3 n.d.)]. Visual loss and complete loss of vision were also reported in 200 patients. Finally, retinal detachment, retinal vascular thrombosis, cataracts and unspecified ophthalmological AEs were observed in 27, 25, 329 and 185 patients respectively. The mean time to onset of inflammatory ophthalmological events was 258 days after initiation of treatment (Table 1).

Table 1. Ophthalmological adverse events with JAK inhibitors

	BARICITINIB	TOFACITINIB	
	n=103	n=1308	Mean delay (in days)
Inflammatory involvement	2 (2)	26 (2)	190±197
Scléritis, n (%)	8 (8)	41 (3)	321±405
Corneal ulcération, n (%)	1 (1)	50 (4)	292±296
Uvéitis, n (%)	2 (2)	11 (1)	172±244
Kératitis			
Decreased visual acuity, n (%)	10 (10)	118 (9)	165±193
Visual loss, n (%)	0	72 (5)	74±83
Red eyes, n (%)	14 (14)	51 (4)	80±149
Dry eyes, n (%)	15 (15)	136 (10)	166±454
Photophobia, n (%)	3 (3)	14 (1)	272±519
Retinal detachment, n (%)	1 (1)	26 (2)	461±360
Retinal vascular thrombosis, n (%)	3 (3)	22 (2)	367±490
Retinal haemorrhage, n (%)	2 (2)	19 (1)	168±199
Cataract, n (%)	9 (9)	320 (24)	
Glaucoma, n (%)	0	77 (6)	432±360
Age related macular degeneration (%)	0	34 (3)	351±549
Unspecified ophthalmological AEs	8 (8)	177 (14)	126±184

Conclusion: Ophthalmological manifestations under JAK inhib seem rare but not exceptional. The rheumatologist must be made aware of them in order to discuss the potential imputability of the treatment and to report these manifestations to the pharmacovigilance structures. A detailed history, exclusion of infections and histopathological evaluation of the lesions are recommended to ensure that a differential diagnosis is not ignored. Topical treatments, and if necessary, discontinuation of the drug and switching to another targeted therapy may be considered. Discontinuation of JAKinhib appears to be warranted pending ophthalmologic advice.
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POS0698 CHANGES IN RA PATIENT PROFILE AT INITIATION OF FIRST TARGETED THERAPY OVER A FIVE-YEAR PERIOD: ANALYSIS OF THE STRATEGE 1 AND STRATEGE 2 STUDIES.

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Background: The objective of the STRATEGE2 study (inclusion period: Feb. 2019-Dec. 2020) is to describe the therapeutic strategy in rheumatoid arthritis (RA) patients treated with methotrexate (MTX) for at least 3 months, not having received targeted biological (bDMARD) or synthetic (tsDMARD) therapy and who are candidates for initiation of first b/tsDMARD therapy due to RA activity.
The STRATEGE1 study [1] (conducted between 2014 and 2015) described the therapeutic strategies introduced for RA patients with an inadequate response to MTX monotherapy.
Objectives: We aim to compare the profiles of patients included in these two studies at first prescription of b/tsDMARD therapy, in order to evaluate changes in rheumatologist practices over this five-year period.
Methods: STRATEGE1 and 2 are two French multicentre, prospective, longitudinal, observational studies including patients with confirmed RA (ACR 1987 or ACR/EULAR 2010). Our aim is to compare baseline data. Only data from the sub-group of patients initiating b/tsDMARD therapy are presented for STRATEGE1. Qualitative variables are compared by Fisher's exact test and quantitative variables by t-test.
Results: In STRATEGE1 (2014-2015), 117 out of 854 patients initiated a b/tsDMARD therapy. In STRATEGE2 (2019-2020), 230 patients were included, with 180 in the analysis population.

Table 1.

At baseline (before b/tsDMARD initiation)	STRATEGE1 (N=117)	STRATEGE2 (N=180)	p
Mean age (years)	52.6 ±12.5	56.4 ±13.6	0.0158
RA duration (years)	6.5 ±7.1	5.6 ±7.2	NS
Radiological signs	50.0%	48.0%	NS
Average MTX initiation (years)	4.6 ±4.3	4.3 ±5.3	NS
MTX per os	44.0%	28.9%	0.0088
→ mean dosage (mg/week)	16.2 ±3.6	16.0 ±4.1	NS
MTX subcutaneous	52.6%	70.6%	0.003
→ mean dosage (mg/week)	18.5 ±3.2	19.9 ±3.9	NS
→ Patients self-administration	53.8%	75.8%	0.0001
Corticosteroid therapy	53%	50.6%	NS
→ mean dosage (mg/day)	8.1 ±4.1	9.5 ±5.8	NS
Mean DAS28	4.6 ± .1	4.3 ±1.2	0.0074
Mean HAQ	1.4 ±0.9	1.0 ±0.7	<0.0001

The baseline visits involved initiation of b/tsDMARD therapy with 100% *vs.* 88.9% bDMARD (anti-TNF: 78.8% *vs.* 58.3%; anti-IL6: 6.7% *vs.* 12.8%; CTLA4 Ig: 11.5% *vs.* 16.7%; anti-CD20: 2.9% *vs.* 1.1%) and 0% *vs.* 11.1% tsDMARD. Therapeutic decisions concerning MTX were (STRATEGE 1 vs STRATEGE 2): identical regimen maintained (pharmaceutical form + dosage): 69.2% *vs.* 76.1%; discontinuation: 4.3% *vs.* 2.2%; adjustment: 26.7% *vs.* 21.7% [with dose reduction: 18.2% *vs.* 93.5% and/or change in pharmaceutical form (p.o. to SC): 54.5% *vs.* 0%].
Main reasons for adjusting treatment were (STRATEGE 1 vs STRATEGE 2): active RA: 86.1% *vs.* 77.8%; RA not in remission: 3.5% *vs.* 21.1%; exacerbation based on clinical/laboratory parameters: 42.6% *vs.* 10%.
Conclusion: Over the five-year period, these results suggest a change in practices for RA patients with an inadequate response to MTX and initiating their first targeted therapy: now with earlier recourse to first targeted therapy, for less active RA, and more pronounced investigation of remission.
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POS0699

SIMILAR EFFICACY AND DRUG SURVIVAL RATES OF BARICITINIB MONOTHERAPY AND BARICITINIB/METHOTREXATE COMBINATION THERAPY IN REAL-LIFE TREATMENT OF RHEUMATOID ARTHRITIS - RESULTS FROM A PROSPECTIVE COHORT OF BARICITINIB-TREATED PATIENTS

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Background: In clinical trials, baricitinib (BARI), in combination with methotrexate (MTX), demonstrated efficacy in patients with rheumatoid arthritis (RA) who have not responded adequately to conventional (cs)or biologic (b) DMARDs [1]. Since MTX is often not tolerated very well [2], BARI monotherapy may be preferable over BARI/MTX combination in some patients with RA. Therefore, real-life data on BARI mono- vs. combination therapy are needed to support such decisions.
Objectives: The aim of our study was to evaluate the efficacy of BARI as mono- or combination therapy in a prospective, open label cohort of RA patients failing previous cs/bDMARD therapy.
Methods: Patients with active RA (DAS28-ESR >3.2), fulfilling the ACR/EULAR 2010 classification criteria and failing previous cs/bDMARD therapy were included. All patients received BARI either as monotherapy or in combination with MTX based on the judgement of the treating physician. Demographics, medical history, disease activity parameters such as 66/68 TJC/SJC, composite scores such as DAS28-ESR, HAQ-DI, as well as medication were prospectively recorded every 3 months according to a pre-defined protocol. Informed consent and ethics approval (19_18 B) were obtained. To evaluate clinical efficacy, DA28 ESR responses was recorded at respective visit dates (until week 96). We estimated least-square mean DAS-28 scores over time using linear mixed effects models including time-group interactions. Kaplan-Meier method was used to estimate baricitinib survival and probability of remission over time.
Results: 139 patients (98 women/41 men; aged 58.4 (12.8) years; mean disease duration of 9.7 years) were included between 4/2017-10/2021. Of these, 46 patients received a combination of BARI with MTX (BARI/MTX) and 93 patients BARI monotherapy. Baseline demographic and disease-specific characteristic were comparable between BARI/MTX and BARI patients (Table 1). Median follow up was 53.1 weeks (IQR 23.0-109.3). Decrease in DAS28-ESR showed a similar dynamics in BARI/MTX (baseline DAS28-ESR: 4.2+/-1.3; 48 weeks: 2.9 (95%CI 2.6 to 3.2)) and BARI (4.3+/-1.3; 48 weeks: 3.0 (95%CI 2.8 to 3.3)) with numerical but no significant differences (Figure 1a). 62% (95%CI 40 to 76%) patients in the BARI/MTX group and 51% (95%CI: 37 to 61%) patients in the BARI attained DAS28ESR remission after 48 weeks. Drug survival was comparable among BARI/MTX and BARI patients. (69 vs.67% at 1 year and 62 vs 56% at 2 years) (Figure 1b).
Conclusion: These data show that BARI monotherapy is efficacious in real life treatment in RA patients with insufficient response to MTX. Clinical efficacy and drug survival is comparable between BARI monotherapy and BARI/MTX combo in a real-life setting.
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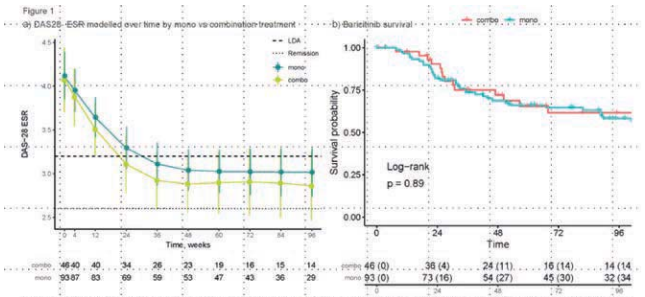

Figure 1a) shows DAS28 ESR values (SD) over time for each group including the number of patients. For example, at week 48, 47 patients in the combination group and 26 patients in the monotherapy group were still on baricitinib. At week 48 mean DAS28 ESR values for monotherapy were: 3.17 (2.95 to 3.40) compared to 2.73 (2.42 to 3.94) for combination therapy with no statistic difference. This was maintained until week 96. Figure 1b displays survival probability curve for baricitinib treatment in this cohort with respect to mono vs combination therapy

Table 1			All	combo	mono
N			139	46	93
Age		Mean (SD)	58.4 (12.8)	56.2 (14.1)	59.5 (12.0)
Sex	Female	N(%)	98 (70.5)	28 (60.9)	70 (75.3)
	Male	N(%)	41 (29.5)	18 (39.1)	23 (24.7)
CCP-AB Status	negativ	N(%)	45 (32.4)	17 (37.0)	28 (30.1)
	positiv	N(%)	94 (67.6)	29 (63.0)	65 (69.9)
Disease duration (y)		Mean (SD)	9.7 (8.5)	9.7 (7.5)	9.6 (9.1)
		Median (IQR)	6.9 (3.5-13.8)	7.5 (4.4-13.8)	6.2 (3.0-13.8)
Follow up (y)		Mean (SD)	68.9 (53.6)	61.5 (48.9)	72.5 (55.6)
		Median (IQR)	53.1 (23.0-109.3)	47.6 (21.0-112.4)	62.3 (23.1-105.0)
DAS-28 ESR		Mean (SD)	4.3 (1.3)	4.2 (1.3)	4.3 (1.3)
HAQ		Mean (SD)	1.1 (0.7)	1.1 (0.6)	1.2 (0.7)

Table1: Demographics, DAS28 ESR, Antibody Status, Follow up time, HAQ are shown for all patients as well as for the monotherapy and combination therapy arm: statistically no significant difference between the groups.

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POS0700

IMPACT OF DELAYING INITIATION OF METHOTREXATE BY 1 MONTH ON THE OUTCOME OF RHEUMATOID ARTHRITIS AT 1 YEAR

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Background: It is recommended that vaccinations should be performed prior to start methotrexate (MTX) knowing that delaying initiation of background therapy may have an impact on the progression of RA.
Objectives: To access the impact of delaying initiation of MTX by 1 month on the outcome of RA at 1 year.
Methods: The VACIMRA study is a prospective, randomized, parallel-group, multicenter trial comparing the vaccine protection obtained in patients with rheumatoid arthritis according to the 1-month delay between anti-pneumococcal vaccine PCV13

Table 1. Baseline characteristics

Variable	Modality	Total population	GROUP IMMEDIATE	GROUPE DELAY	p
Gender, n(%)		N=261	n=131	n=130	0.97
	Man	74 (28.35)	37 (28.24)	37 (28.46)	
	Woman	187 (71.65)	94 (71.76)	93 (71.54)	
Age (years)	Mean (± SD)	55.74 (± 14.68)	55.31 (± 15.27)	56.16 (± 14.11)	0.76
MTX true naive (n(% col))	No	13 (4.98)	8 (6.11)	5 (3.85)	0.40
	yes	248 (95.02)	123 (93.89)	125 (96.15)	
Age at diagnosis (years)	Mean (± SD)	N=205 55.86 (± 15.16)	n=98 55.31 (± 16.07)	n=107 56.37 (± 14.34)	0.80
Positive rheumatoid factor	n(% col)	166 (64.59)	84 (65.12)	82 (64.06)	0.86
Positive ACPA	n(% col)	174 (68.24)	89 (68.99)	85 (67.46)	0.79
CRP (mg/L)	Mean (± SD)	N=260 17.62 (± 24.87)	n=131 15.36 (± 17.95)	n=129 19.91 (± 30.23)	0.65
DAS28-ESR	Mean (± SD)	N=249 5.01 (± 1.11)	n=125 5.03 (± 1.13)	n=12 4.98 (± 1.10)	0.54
Sharp modified VdH total radiographic score	Mean (± SD)	N=93 1.53 (± 3.62)	n=47 1.57 (± 3.68)	n=46 1.48 (± 3.60)	0.88

DAS 28-ESR evolution during 1 year of follow-up

and methotrexate initiation in one arm, versus immediate introduction of MTX following vaccination in the other arm. We analyzed disease activity based on DAS28-ESR at baseline (M0), 1, 2, 3, 6 and 12 months between the 2 groups. For structural progression, we performed a radiographic analysis of 79 RA patients included in the Montpellier center at baseline, 6 and 12 months. This analysis was performed by the same physician two times, blinded to the patient's group. Structural damage progression at 6 months and 1 year was assessed according to van-der-Heijde-modified Sharp score (vSHS) on radiographs performed at inclusion, at 6 and 12 months of follow-up. Comparisons of the means of activity scores and radiographic scores were made with the non-parametric Wilcoxon-Mann-Whitney test.

Results: Of the 276 patients randomized, 261 could be analyzed (131 in the IMMEDIATE group and 130 in the DELAY group). At inclusion, there were no significant differences in demographic, disease activity (DAS28-ESR), biological and radiographic characteristics between the 2 groups (Table 1).

There was a significant difference in the means of DAS28-ESR at 1 month between the DELAY and IMMEDIAT groups (3.96 ± 1.46 vs 3.41 ± 1.33; p<0.001, respectively). There was no significant difference in the means of DAS28-ESR between the 2 groups at 3 months (3.19± 1.46 in the 2 groups p<0.91), at 6 months (3.11 ± 1.42 vs 3.24 ± 1.43; p=0.46, respectively) and at 12 months (2.96 ± 1.34 vs 2.98 ± 1.26p=0.89) (Graphic). Similarly, there was no significant difference in mean radiographic scores at 6 months (2.00 ± 4.41 vs. 1.80 ± 4.03 p=0.81) or at 12 months (2.23 ± 4.86 vs. 2.00 ± 4.07 p=0.93).

There was no significant variation between radiographic scores at 6 months compared to baseline in either group (mean difference 0.21 ± 0.52 vs. 0.36 ± 1.01, p=0.90) nor at 12 months compared to baseline (mean difference 0.40 ± 1.06 vs. 0.62 ± 1.58, p=0.85).

Conclusion: In patients with rheumatoid arthritis, initiation of methotrexate 1 month after PCV13 vaccination has no significant impact on RA activity and structural outcome at 1 year. Performing vaccinations 1 month before starting MTX can be proposed without significant impact on RA outcome at 1 year.

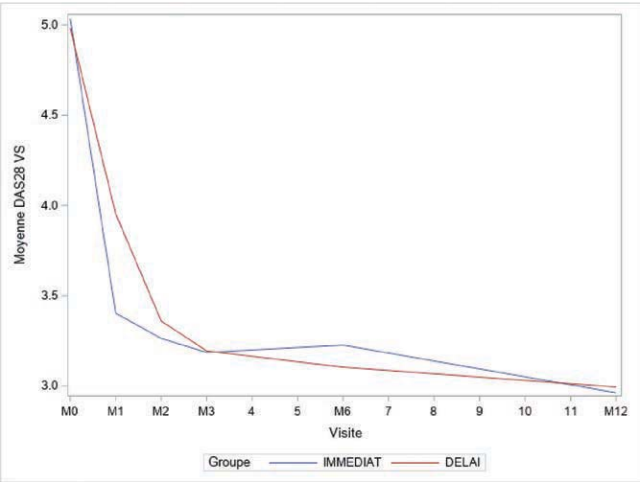

Figure 1.

Disclosure of Interests: None declared

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POS0701

LONG-TERM EFFICACY OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAVE HAD INADEQUATE RESPONSE TO CSDMARDS: RESULTS FROM RA-BEYOND UP TO 7 YEARS OF TREATMENT

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Background: Baricitinib (BARI), an oral selective Janus kinase 1/2 inhibitor, has demonstrated efficacy in patients (pts) with rheumatoid arthritis (RA) for up to 3 years (yrs) in a long-term extension (LTE) study RA-BEYOND.[1]

Objectives: Disclose efficacy of BARI in csDMARD-IR pts in the completed LTE study (up to 7 yrs).

Methods: In RA-BUILD, csDMARD-IR pts were randomized 1:1:1 to BARI 4 mg, 2 mg, or placebo (PBO). Completers to week (wk) 24 could enter the LTE and received BARI 4 or 2 mg. In RA-BEAM, MTX-IR pts were randomized 1:1:1 to BARI 4 mg, adalimumab (ADA) 40 mg, or PBO. Completers to wk 52 received BARI 4 mg in the LTE. Pts with no response could be rescued after wk 16 in both studies. Data were analysed by treatment assigned at baseline in originating studies as observed up to time of stepdown (if applicable), study discontinuation or completion, whichever occurred earlier. Efficacy response rates (RR) were assessed as proportions of pts with observed data up to yr 7 (wk 364) for low-disease activity (LDA) (SDAI ≤ 11, DAS28-hsCRP ≤ 3.2, CDAI ≤ 10), remission (REM) (SDAI ≤ 3.3, DAS28-hsCRP < 2.6, CDAI ≤ 2.8, Boolean), and physical function (HAQ-DI ≤ 0.5). No formal statistical comparisons were conducted.

Results: Approximately 56%/25% of pts in BARI 4 mg, 80%/31% in BARI 2 mg, and 60%/25% in PBO from RA-BUILD remained active at yr 3/7; 59%/17% of pts in ADA, 54%/16% in BARI 4 mg, and 67%/14% in PBO from RA-BEAM remained active at year 3/7. SDAI and CDAI had comparable RR for LDA and REM (Table 1). DAS-28CRP LDA RR were similar to SDAI and CDAI, while REM RR were about twice those of SDAI and CDAI (Table 1). HAQ-DI ≤ 0.5 RR was achieved by 25-30% of BARI-treated pts from both trials and maintained to the end of LTE.

Conclusion: In observed data, BARI demonstrated maintained efficacy in treatment and maintenance of physical function of a csDMARDs-IR RA pt population up to 7 yrs.

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Disclosure of Interests: Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Eli Lilly and Company, Galapagos, Pfizer, Fresenius-Kabi, MSD, UCB, Roche,Janssen, Novartis, Sandoz, Consultant of: Abbvie, Amgen, BMS, Celltrion, Eli Lilly and Company, Galapagos, Pfizer, MSD, UCB, Janssen, Novartis, Sandoz, Daniel Aletaha Speakers bureau: Abbvie, Amgen, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Grant/research support from: Abbvie, Amgen, Eli Lilly and Company, Novartis, Roche, SoBi, Sanofi, Raimón Sanmartí Speakers bureau: Eli Lilly and Company, Grant/research support from: Eli Lilly and Company, Tsutomu Takeuchi Speakers bureau: AbbVie Japan GK, Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co, Ltd. Daiichi Sankyo Co., Ltd. Eisai Co., Ltd. Eli Lilly Japan K.K.; Gilead Sciences, Inc. Janssen Pharmaceutical K.K.; Mitsubishi-Tanabe Pharma Co.; Novartis Pharma Co.; Pfizer Japan Inc.; Sanofi K.K.; UCB Japan Co., Ltd., Consultant of: AbbVie Japan GK, Astellas Pharma, Inc.; Chugai Pharmaceutical Co, Ltd.; Eli Lilly Japan K.K.; Eisai Co., Ltd.; Gilead Sciences, Inc.; Janssen Pharmaceutical K.K.; Mitsubishi-Tanabe Pharma Corp., Pfizer Japan Inc., Grant/research support from: AbbVie Japan GK, Asahikasei Pharma Corp., Chugai Pharmaceutical Co, Ltd., DNA Chip Research Inc.; Eisai Co., Ltd., Eli Lilly Japan K.K.; Mitsubishi-Tanabe Pharma Corp., UCB Japan Co., Ltd., Daojun Mo Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Ewa Haladyj Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Liliana Zaremba-Pechmann: None declared, Peter C. Taylor Consultant of: AbbVie, Biogen, Eli Lilly and Company, Fresenius, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Nordic Pharma, Pfizer Inc, Roche, and Sanofi, Grant/research support from: Celgene, and Galapagos

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Table 1. Efficacy outcomes in RA-BEYOND

		LDA			REM				
Time[a]	N/n (%)	SDAI	CDAI	DAS-28 CRP	SDAI	CDAI	DAS-28 CRP	Boolean	HAQ-DI ≤0.5
RA-BEYOND entry	BARI 2 mg (BUILD)	197/109 (55.3)	197/103 (52.3)	200/108 (54.0)	197/38 (19.3)	197/35 (17.8)	200/72 (36.0)	200/29 (14.5)	200/50 (25.0)
	BARI 4 mg (BUILD)	188/113 (60.1)	191/116 (60.7)	189/112 (59.3)	188/33 (17.6)	191/35 (18.3)	189/75 (39.7)	189/26 (13.8)	193/44 (22.8)
	BARI 4 mg (BEAM)	412/288 (69.9)	414/290 (70.0)	412/280 (68.0)	412/112 (27.2)	414/108 (26.1)	412/199 (48.3)	412/78 (18.9)	414/133 (27.3)
Yr 3	BARI 2 mg (BUILD)	156/120 (76.9)	158/116 (73.4)	156/112 (71.8)	156/41 (26.3)	158/44 (27.8)	156/81 (51.9)	156/34 (21.8)	159/38 (23.9)
	BARI 4 mg (BUILD)	107/76 (71.0)	107/76 (71.0)	107/74 (69.2)	107/24 (22.4)	107/26 (24.3)	107/56 (52.3)	107/17 (15.9)	108/26 (24.1)
	BARI 4 mg (BEAM)	222/166 (74.8)	224/166 (74.1)	222/164 (73.9)	222/72 (32.4)	224/71 (31.7)	222/119 (53.6)	222/48 (21.6)	224/54 (24.1)
Yr 7	BARI 2 mg (BUILD)	61/50 (82.0)	61/49 (80.3)	61/51 (83.6)	61/17 (27.9)	61/18 (29.5)	61/40 (65.6)	61/12 (19.7)	62/16 (25.8)
	BARI 4 mg (BUILD)	45/37 (82.2)	48/37 (77.1)	45/34 (75.6)	45/13 (28.9)	48/16 (33.3)	45/25 (55.6)	45/8 (17.8)	48/14 (29.2)
	BARI 4 mg (BEAM)	60/53 (88.3)	64/57 (89.1)	60/53 (88.3)	60/18 (30.0)	64/22 (34.4)	60/38 (63.3)	60/13 (21.7)	64/14 (21.9)

N: Number of pts with observed data; n: Number of pts with response. [a]Time from randomization in originating studies. Entry to RA-BEYOND=wk 24 and wk 52; Yr 3=wk 156 and wk 160; and Yr 7=wk 360 and wk 364 of RA-BUILD and RA-BEAM, respectively.

POS0702

ANTI-RHEUMATIC TREATMENT ALTERS PFKFB3 EXPRESSION, KEY OF GLYCOLYSIS, IN CD14+ MONOCYTES OF RA PATIENTS, WHICH CONTRIBUTES TO DISSIMILARITIES OF THE IFNG-SIGNATURE

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Background: Interferon-gamma (IFNαnterferon-gamma (IFNRheumatology clinic, Gothenburg, Swedenh, Göteborg, Swedenmonocytes of RA patients, which contributes to dissimilarities of the IFNg-signature Peter C. Taylor Consultant of: AbbVie, Biogen, Eli Lilly and Company, Fresenius, Galapagos, mulation is energy consuming and often demands metabolic adaptation of a cell by switching glucose metabolism from the tricarboxylic acid cycle (TCA) to the pentose phosphate pathway (PPP) alternative of glycolysis that dramatically increases glucose intake. Fructose-2,6-biphosphatase 3 (coded by *PFKFB3*) has been identified as the rate-limiting regulator of glucose metabolism suppressed in leukocytes of RA patients (2).

Objectives: To study effect of anti-rheumatic treatment on the cellular energy metabolism of $CD14^+$ mononuclear cells and its connection to the phenotype and IFNαmononuclear.

Methods: $CD14^+$ cells were sorted from the peripheral blood of the randomly recruited 60 RA patients (mean age 59.6y, DD 13.8y). The cells were LPS activated for 2h and submitted to RNA sequencing (RNAseq, IluminaNextseq). The patients were divided by actual DMARD treatment into those who had no DMARDs (n=8), methotrexate (MTX) only (n=15), biologics (MTX+aTNF n=12, MTX+RTX n=4) and JAK-inhibitors (JAKi, n=24). Differentially expressed gene (DEG) analysis between the groups was performed in R-studio, Bioconductor package, DESeq2. Reported IFN signatures (1) were combined in a set of 51 IFN signature genes (ISG) and analyzed in relation to the transcriptomic profile behind the cellular energy metabolism and DMARD treatment.

Results: MTX and JAKi but not biologics make a significant and opposing contribution of the transcriptomic of energy metabolism in $CD14^+$ cells. MTX-treated patients had significantly higher levels of the rate-limiting enzyme of glycolysis *PFKFB3* and *PGAM1* compared to those with no DMARDS, which normalized aerobic glycolysis by increasing expression of the pyruvate dehydrogenase complex proteins *PDHA1*, *PHDX* and *PDK3* linking glycolysis with TCA and decreasing PPP enzymes *PGLS*, *RPIA* and *TKT*. In contrast, *PFKFB3* was suppressed in patients treated with JAK-inhibitors compared to those treated with MTX (cor. p=1.32e-8), which significantly activated glycolysis downstream of PFKFB3 and shunting metabolism to PPP inducing expression of *G6PD* (cor.p=5.0e-92) and *PGLS* (cor.p=3.1e-46) and increased the major glucose transporter *SLC2A1* (cor. p=1.11e-24). These differences in glucose metabolism were linked to divergent phenotype of $CD14^+$ cells being short-lived $CD14^{int}CD11c^{hi}$ cells and IL6 producing in MTX-treated patients and long-lived mature $CD14^{hi}CD11b^{hi}CX3CR1^{hi}$ cells and IFNαcells and IFN producing in MTX-treated pa^+ cells of JAKi-treated patients expressed low levels of *STAT1* and ISGs compared to MTX-treated patients.

Conclusion: DMARD treatment har divergent effect on glycolysis of $CD14^+$ cells, acting through PFKFB3. This has significant impact on the phenotype of $CD14^+$ cells and inflammatory ability.

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POS0703

BIOLOGIC-DMARDS AND TARGETED SYNTHETIC-DMARDS EFFECT ON RAPID WITHDRAWAL OF STEROID IN 6 MONTHS OBSERVATIONAL PERIOD IN RHEUMATOID ARTHRITIS PATIENT'S COHORT: REAL LIFE DATA EXTRACTED FROM BIOPURE REGISTRY.

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Background: Considering the highest adverse events risk (predominantly infectious disease and osteoporosis) of glucocorticoids (GCs), EULAR recommended a short-term use of GCs with rapid tapering as soon as clinically feasible in rheumatoid arthritis (RA) patients. Although a prednisone dose less than or equal to 7,5 mg/die is considered more safety, the complete discontinuation of the GCs would be desirable. Few data are available on real tapering or withdrawal of GCs in RA patients treated with DMARDs both in clinical trial and registry study.

Objectives: To evaluate the steroid tapering rate and the discontinuation of GCs in RA patients treated with biological-DMARDs (b-DMARDs) or target synthetic DMARDs (ts-DMARDs) in different treatment lines.

Methods: We revised retrospectively 1616 clinical records of RA patients who started b/ts-DMARDs between December 2017 and June 2021. We recruited 420 RA patients who were stably treated for at least 6 months with b/ts-DMARDs with or without cs-DMARDs and were taken GCs at baseline visit. The evaluations of GCs discontinuation time were realized by Kaplan-Meier estimate, followed by log-rank (Mentel-Cox) test for the comparison among different b/ts-DMARDs groups. Statistical significance was set at $p \leqslant 0.05$.

Results: RA patients treated with different b/ts-DMARDs were comparable for disease duration (anti TNF-alpha: 76 weeks ± 64; JAK-I: 121 weeks ± 122; anti-IL6: 78 weeks ± 70; abatacept: 111 weeks ± 121), disease activity (DAS 28 ESR: anti TNF alpha: 3,9 ± 1,3; JAK-I: 4,1 ± 1; anti IL-6: 4 ± 1,3; abatacept: 4 ± 1,2; p=0,958), and GCs dose (anti TNF alpha: 5,7 mg ± 7,5; JAK-I 5,5 mg ± 2,5; anti IL-6 5,7 mg ± 4,1; abatacept 5,6 mg ± 2,5; p=0,879) at baseline visit. 158 RA patients started for the first-time b/ts-DMARDs, 83 patients started 2^{nd} line of b/ts-DMARDs, 66 patients started 3^{rd} line b/ts-DMARDs and 113 patients were failure to more than 3 b/ts-DMARDs.

Considering RA patients who started b/ts-DMARDs for the first time, the groups treated with anti-IL6 or JAK-I showed a shorter discontinuation time than those treated with anti TNF-alpha or Abatacept (respectively 22 weeks ± 0,7, 22,6 weeks ± 0,7, 23,8 weeks ± 0,1, 23,1 weeks ± 0,4; p=0,046). As regards the steroid sparing in 6^{th} month of follow-up, the rates of GCs dose spared than the staring GCs dose were higher in JAK-I (44%) and anti-IL 6 (42%) compared to abatacept (30%) and anti-TNF alpha (33%).

Considering the group of RA patients treated in 2^{nd} or other lines of b/ts-DMARDs, no differences were found among various treatments in GCs discontinuation time.

Conclusion: In clinical practice GCs are useful therapeutic tools to reach as rapidly as possible low disease activity in RA patients; but the possible adverse effects of long-term GCs treatment limit their use. The introduction of biotechnological drugs has significantly improved clinical management of RA patients, achieving the aim of

rapid GCs discontinuation or their dose reduction. In particular, the mechanisms of action of anti-IL6 and JAK-I seems perform more quickly on steroid discontinuation than anti TNF alpha or abatacept, above all in 1st line of b/ts-DMARDs in RA patients.
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POS0704

EFFICACY AND SAFETY OF FILGOTINIB IN PATIENTS WITH INADEQUATE RESPONSE TO METHOTREXATE, WITH 4 OR <4 POOR PROGNOSTIC FACTORS: A POST HOC ANALYSIS OF THE FINCH 1 STUDY

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Background: Patients (pts) with rheumatoid arthritis (RA) and poor prognostic factors[1] (PPF) are at risk for progression without adequate treatment. Filgotinib (FIL) is a once daily Janus kinase 1 preferential inhibitor. In FINCH 1 (NCT02889796), FIL 200 mg (FIL200) was effective vs placebo (PBO) and non-inferior to adalimumab (ADA) in pts with RA and inadequate response to methotrexate (MTX-IR); FIL200 and FIL 100 mg (FIL100) were well tolerated.[2]
Objectives: This post hoc, exploratory analysis examined efficacy and safety of FIL in MTX-IR pts with 4 or <4 PPF.
Methods: The FINCH 1 52-week (W), double-blind trial randomised MTX-IR pts with moderate–severe RA to FIL200 or FIL100, ADA, or PBO; all received background MTX. PBO pts were rerandomised, blinded, at W24 to FIL200 or FIL100. We examined pts with 4 PPF at baseline (BL): erosions on X-ray, seropositivity for rheumatoid factor or anticyclic citrullinated peptide, high-sensitivity C-reactive protein (hsCRP) ≥6 mg/L, and disease activity score in 28 joints with CRP (DAS28[CRP]) >5.1, along with those with <4 PPF. Efficacy included DAS28(CRP) <2.6 and modified Total Sharp Score (mTSS) change from baseline (CFB). Fisher's exact test was used for DAS28(CRP); the mixed-effects model was used to generate least squares mean mTSS CFB. *P* values were nominal, not adjusted for multiplicity.
Results: At BL, of 1755 randomized, treated pts, 687 had 4 PPF, and 1068 had <4 PPF. Among pts with <4PPF, 804 [75%] had erosions, 810 [76%] were seropositive, 377 [35%] had hsCRP ≥6 mg/L, 638 [60%] had DAS28[CRP] >5.1). Pts with 4 vs <4 PPF were aged 53 vs 52 years, had RA duration 8.3 vs 7.4 years, DAS28(CRP) 6.3 vs 5.4, and SDAI 45.6 vs 37.7. In pts with 4 or <4 PPF, higher proportions receiving FIL200 or FIL100 achieved DAS28(CRP) <2.6 at W12 vs PBO (nominal *P* <.001); proportions with DAS28(CRP) <2.6 increased with FIL200, FIL100, or ADA at W52 (Figure 1). DAS28(CRP) responses for FIL200 at W52 were similar in 4 vs <4 PPF pts; FIL100 and ADA responses were numerically higher in <4 vs 4 PPF pts. At W24, mTSS CFB in pts with 4 PPF was 0.21, 0.23, 0.30, and 0.66 for FIL200, FIL100, ADA, and PBO (*P* <.05 for FIL200 and FIL100 vs PBO); corresponding changes in <4 PPF pts were 0.08, 0.10, 0.11, and 0.24 (*P* >.05). At W52, mTSS CFB in 4 PPF pts was 0.29, 0.84, and 0.80 for FIL200, FIL100, and ADA, respectively, and 0.14, 0.25, and 0.53 in <4 PPF pts. Rates of adverse events (AEs), including AEs of interest, were comparable for pts with 4 PPF and <4 PPF for all treatment arms (Table 1).
Conclusion: In high-risk (4 PPF) pts with MTX-IR RA, FIL200 and FIL100 showed similar reductions in disease activity vs PBO at W12 as in pts with <4 PPF; mTSS in FIL200 pts changed little from W24 to W52. Tolerability was comparable across treatment arms, regardless of presence of 4 or <4 PPF.

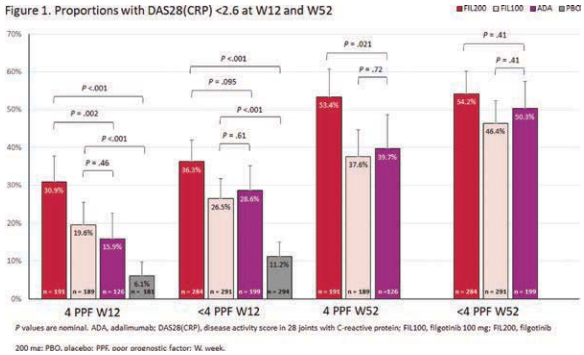

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Table 1. AEs and AEs of interest in BL 4 PPF and <4 PPF subgroups

	4 PPF				<4 PPF			
	FIL200	FIL100	ADA	PBO before	FIL200	FIL100	ADA	PBO
	(n = 191)	(n = 189)	(n = 126)	W24 switch (n = 181)	(n = 284)	(n = 291)	(n = 199)	before W24 switch (n = 294)
All AEs	146 (76.4)	136 (72.0)	85 (67.5)	90 (49.7)	206 (72.5)	214 (73.5)	154 (77.4)	164 (55.8)
AEs of interest								
Serious infectious AE	5 (2.6)	4 (2.1)	6 (4.8)	2 (1.1)	8 (2.8)	9 (3.1)	4 (2.0)	2 (0.7)
Opportunistic infections	0	0	1 (0.8)	0	0	0	1 (0.5)	0
Active tuberculosis	0	0	0	0	0	0	1 (0.5)	0
Herpes zoster	1 (0.5)	1 (0.5)	1 (0.8)	0	5 (1.8)	3 (1.0)	1 (0.5)	2 (0.7)
Hepatitis B or C	0	1 (0.5)	0	0	1 (0.5)	0	1 (0.5)	0
MACE	0	1 (0.5)	0	1 (0.6)	0	1 (0.3)	1 (0.5)	1 (0.3)
VTE	0	0	1 (0.8)	1 (0.6)	1 (0.4)	0	0	1 (0.3)
DVT	0	0	1 (0.8)	1 (0.6)	0	0	0	1 (0.3)
PE	0	0	0	0	1 (0.4)	0	0	0
Malignancy (non-NMSC)	0	0	0	3 (1.7)	2 (0.7)	2 (0.7)	2 (1.0)	0
GI perforation	0	0	0	0	1 (0.4)	0	0	0

Values are n (%). ADA, adalimumab; AE, adverse event; BL, baseline; DVT, deep vein thrombosis; FIL100, filgotinib 100 mg; FIL200; filgotinib 200 mg; GI, gastrointestinal; MACE, major adverse cardiac event; NMSC, nonmelanoma skin cancer; PBO, placebo; PE, pulmonary embolism; PPF, poor prognostic factor; VTE, venous thromboembolism; W, week.

SLE, Sjögren's and APS – treatment

POS0705 DILEMMA OF BELIMUMAB THERAPY (DIS) CONTINUATION DURING PREGNANCY: RESULTS OF A RETROSPECTIVE STUDY IN EUDRAVIGILANCE

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Background: Active systemic lupus erythematosus (SLE) and nephritis due to SLE contribute to poor pregnancy outcomes. (1, 2) A meta-analysis has shown a relative risk of 1.51 for miscarriage in SLE patients compared to women without SLE. (3) The risk is even higher if the disease is active during pregnancy (around 3-fold increase in pregnancy loss). (4) Corticosteroids, azathioprine, hydroxychloroquine, ciclosporine and tacrolimus are considered safe treatments. (5) However, these treatment options may still not be sufficient in patients poorly responsive to conventional therapies or patients who suffer from nephritis. (6) The only biologic authorized for SLE up to this date, belimumab, is currently not recommended for use during pregnancy due to lack of data. Provided that the health of the child begins with the health of the mother, pregnant patients, face the dilemma of cessation or continuation of belimumab. If belimumab is stopped there will be a risk of SLE flare and its consequences for mother and foetus. Continuation is also not optimal because the lack of knowledge on safety for use during pregnancy.

Objectives: To compare the reported foetal outcomes in SLE patients who stopped scheduled belimumab within the first trimester (group A) and who continued scheduled belimumab during the first trimester or thereafter (group B).

Methods: All belimumab-exposed pregnancy-related reports, were extracted from the EudraVigilance (EV) database until March 11th 2021. After case review, repeated cases, uninformative reports, non-medical elective abortions and foetal chromosomal abnormalities were excluded. Included pregnancies were divided into two groups (group A and B, as described above). Foetal outcomes were divided into live birth or foetal death (due to miscarriage or still birth) and were compared between both groups. Furthermore, neonatal outcomes, such as reporting rates of pre-term birth, low birth weight and major congenital malformations (CMs) were compared.

Results: No statistical difference in foetal death was observed between group A and B (reporting rates: 46.4% and 52.4%, respectively; p-value>0.05). Occurrence of major CMs, pre-term birth and low birth weight was higher - though not statistically different- in group A (Table 1).

Table 1. Neonatal characteristics of live born children (including twin pregnancies)

Live births	Stopped (group A); (n=37)	Continued (group B); (n =10)	Total; (n=47)
Gestational age at birth, median (IQR), weeks	37.1 (35.5, 40.0)	38.2 (36.4, 39.1)	**37.6 (36.0, 39.4)**
Weight, median (IQR), grams	2749 (2268, 3200)	2975 (2700, 3175)	**2835 (2406-3175)**
Preterm birth*; n (%)	16 (43.2)	4 (40.0)	**20 (42.5)**
Low birth weight*; n (%)	9 (24.3)	0 (0.0)	**9 (19.4)**

Conclusion: Based on our data belimumab continuation during first trimester or thereafter does not result in higher reporting of foetal death. Therefore, continuation might be even preferable if the pregnancy is already exposed to belimumab. Since the analysis is based on spontaneous reports / retrospective data, additional studies are needed to confirm the results.

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POS0706 LONG-TERM HYDROXYCHLOROQUINE TREATMENT IMPROVES ESSPRI AND ESSDAI IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a chronic, systemic autoimmune disease typically affecting the salivary and lacrimal glands and producing symptoms of dry mouth, dry eyes, fatigue and pain. Hydroxychloroquine (HCQ) have been shown to have various immunomodulatory and immunosuppressive effects, and currently have established roles in the management of rheumatoid arthritis and systemic lupus erythematosus (SLE). However, the use of HCQ in pSS is based in expert recommendations and in few studies with a low level of evidence. There are very few publications assessing HCQ use in a double-blind, randomized, and placebo-controlled studies. In Japan, HCQ is indicated for patients with SLE and cutaneous lupus erythematosus (CLE) and is off-label use for pSS patients without CLE. Recently, ESSPRI and ESSDAI have been developed by the European League Against Rheumatism (EULAR) SS study group as standardized outcome tools for measuring patients' reported symptoms and disease-specific activity. ESSDAI and ESSPRI have been proven to be valid and reliable, they have been used to select patients or as the primary or secondary outcome measures in clinical trials.

Objectives: The aim of this study was to examine the efficacy of HCQ in pSS at 8 and 52 weeks after treatment evaluated by ESSPRI and ESSDAI.

Methods: Twenty-six pSS patients (26 female, mean age 51.6 ± 13.6 years) with CLE who fulfilled the ACR/EULAR classification criteria for SS and/or the Japanese Ministry of Health and Welfare criteria for SS were studied. The clinical indexes were evaluated by ESSDAI, ESSPRI, IgG and CH50 before and after HCQ treatment at 8 and 52weeks. ESSPRI components were calculated individually and as a single factor composed of the mean of the three components (pain, fatigue, and dryness: VAS 0-10). ESSDAI (0–123) proposes the evaluation of 12 domains or organ systems (constitutional, lymphadenopathy, glandular, articular, cutaneous, pulmonary, renal, peripheral nervous system, central nervous system, muscular, hematological and biology).

Results: ESSPRI and component of fatigue and pain were significantly lower at 8 and 52 weeks after treatment than HCQ pre-treatment (ESSPRI: 4.14±1.45 vs 3.38±1.57, 3.34±1.56, p=0.005, p=0.045, fatigue: 4.68±2.12 vs 3.68±1.96, 3.58±1.87, p=0.010, p=0.036, pain: 3.32±1.94 vs 2.09±1.60, 1.79±1.51, p=0.0043, p=0.0014). However, there was no significant difference in dryness component between HCQ pre-treatment and 8 and 52 weeks after treatment (4.41 ± 2.09 vs 4.32 ± 2.06, 4.21 ± 2.39, p = 0.71, p = 0.94), and the amount of saliva produced by the gum test also showed no significant difference between pre-HCQ treatment and 52 weeks after treatment (8.21 ± 6.72 vs 8.24 ± 6.79 mL / 10 minutes, p = 0.45). There was also a significant decrease in ESSDAI and constitutional, articular, cutaneous and biological domain at 52 weeks after treatment compared to HCQ pre-treatment (ESSDAI: 9.68±6.14 vs 4.74±6.43, p=0.0004; constitutional: 1.41±1.50 vs 0.63±1.26, p=0.034, articular: 1.00±1.02 vs 0.21±0.63, p=0.0027, cutaneous: 2.86±3.27 vs 1.11±2.49, p=0.010, biological: 1.14±0.83 vs 0.79±0.86, p=0.014). An improvement of at least 1 point or 15% in ESSPRI and at least 3 points in ESSDAI compared to HCQ pr-treatment were observed in 63.6% and 31.8% at 8 weeks and 73.7% and 68.4% at 52 weeks after treatment. In addition, IgG was significantly decreased at 52 weeks after treatment compared to HCQ pre-treatment (1934 ± 613 vs 1714 ± 564 mg / dL, p=0.0005).

Conclusion: HCQ treatment improved pain such as arthritis, fatigue, constitutional and cutaneous manifestations, but was not effective for salivary function and dryness. HCQ treatment was useful in improving ESSPRI and ESSDAI, and long-term treatment increased the number of effective cases from 8 weeks to 52 weeks.

Disclosure of Interests: None declared

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POS0707 POTENTIAL USE OF BELIMUMAB IN LUPUS PATIENTS FROM ARGENTINE COHORT ACCORDING DISEASE ACTIVITY STATE

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Background: The goal of targeted treatment in patients with Systemic Lupus Erythematosus (SLE) is to achieve clinical remission or low disease activity, with the best quality of life, low damage rates and better survival [1-4]. RELESSAR is a multicenter, cross-sectional study registry of ≥18 years SLE (ACR 97) patients [5].
Objectives: To describe demographic, clinical characteristics and treatments in SLE patients according to disease activity state. To evaluate the proportion of SLE and refractory SLE patients that are potentially candidates for Belimumab treatment (Active SLE despite standard treatment including increased acDNA autoantibodies and low complement).
Methods: We evaluated demographic and clinical data, treatments, score of damage (SLICC), activity (SLEDAI) and comorbidity (Charlson), hospital admissions and severe infections. The patients were compared according to disease activity: remission (SLEDAI = 0 and without corticosteroids), low disease activity (LDA, SLEDAI> 0 and ≤4 and without corticosteroids) and non-optimal control (SLEDAI> 4 and any dose of corticosteroids). Refractory SLE was defined according to Rituximab (RTX) use, non-response to cyclophosphamide or two or more immunosuppressant or splenectomized patients. Potential use of Belimumab according approved prescription in Argentina was analyzed.
Results: Overall, 1277 patients were analyzed: 299 (23.4%) were in remission, 162 (12.7%) in LDA and 816 (63.9%) with non-optimal control of the disease. Patients in non-optimal control group were younger, less frequently female and they showed less time of disease and lower socioeconomic status (p < 0.001). They were also more prevalent mestizos (p= 0.004), had higher SLEDAI and SLICC indexes (p <0.001) and higher use of immunosuppressant therapy (p <0.001). There was no difference regarding biologic treatment (RTX p= 0.547 and Belimumab p= 0.08). This group had higher proportion of hospital admissions and severe infections (p<0.001, respectively). Two hundred and one SLE patients fulfilled the use of Belimumab prescription criteria but only 45/201 patients (22,3%) received it in the last visit. Malar rash was the only clinical variable associated with the use of Belimumab (72.7% vs 29.8% p= 0.005). Seventy-six patients classified as refractory SLE (15.7%) and 56/76 (75.7%) never received Belimumab. Patients on Belimumab therapy were associated to treatment with lower doses of corticoids (p= 0.018) and lower rate of hospital admission caused by SLE flare (p= 0.027).
Conclusion: A high percentage of patients had uncontrolled disease upon entry into the registry and were potential candidates for treatment with Belimumab. The patients who received biologic treatment showed the benefit of requiring fewer doses of corticosteroids and having a lower rate of hospitalizations.

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POS0708 EVALUATING THE HYPERSENSITIVITY PROFILE OF ANIFROLUMAB AND THE NEED FOR PREINFUSION PROPHYLACTIC TREATMENT IN PATIENTS WITH SLE

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Background: Anifrolumab, a human monoclonal antibody (mAb), is approved in Canada, Japan, and the United States for the treatment of patients with systemic lupus erythematosus (SLE) based on results from the phase 2b MUSE and the phase 3 TULIP-1/-2 trials.[1–3] Anaphylactic reactions (ARs), hypersensitivity reactions (HSRs), and infusion-related reactions (IRRs) are risks of mAb infusions, so physicians prescribing anifrolumab may wish to understand the hypersensitivity profile and whether prophylactic pretreatments are required to mitigate HSR/IRRs.
Objectives: To evaluate the hypersensitivity profile of anifrolumab and the need for pretreatment.
Methods: Pooled data were analyzed from patients with moderate to severe SLE despite standard therapy who received intravenous infusions (every 4 weeks, 48 weeks) of anifrolumab or placebo in the randomized, 52-week MUSE (NCT01438489),[1] TULIP-1 (NCT02446912),[2] and TULIP-2 (NCT02446899)[3] trials. An AR (analyzed in the anifrolumab 150/300/1000 mg and placebo groups) was defined as acute illness onset within minutes to several hours of infusion with involvement of skin and/or mucosal tissue, and/or respiratory compromise, and/or reduced blood pressure, and/or persistent gastrointestinal symptoms. HSRs and IRRs were analyzed in the anifrolumab 300 mg group (as this is the approved dose) and the placebo group. An HSR was defined as acute illness onset with involvement of skin and/or mucosal tissue during infusion (not meeting the AR definition); IRR was defined as any other reaction occurring during/within 24 hours of infusion. Patients did not receive pretreatment unless they had experienced a previous IRR/HSR in the program. Pretreatment was assumed if a patient received prophylactic antihistamine, corticosteroid, non-steroidal anti-inflammatory drug, and/or dopamine antagonist 1 day before/on the day of infusion.
Results: Of patients who received anifrolumab 300 mg (n=459), anifrolumab 1000 mg (n=105), or placebo (n=466), none experienced ARs; 1 patient who received anifrolumab 150 mg (n=93) experienced an AR. HSRs occurred in 3% (n=12) of anifrolumab 300 mg-treated patients (of whom 4 had a history of

HSRs) vs 1% (n=3) in the placebo group. IRRs occurred in 9% (n=43) of anifrolumab-treated patients vs 7% (n=33) in the placebo group. All HSRs and IRRs were mild/moderate in intensity. There were no discontinuations due to HSRs or IRRs in the anifrolumab group, while there were 2 in the placebo group (HSR: n=1; IRR: n=1). In the anifrolumab 300 mg and placebo groups, more patients experienced HSR/IRRs with the initial (1–6) vs later infusions (Figure 1). In the anifrolumab group, the median (median absolute deviation) time to first HSR or IRR was 30.5 (29.5) days or 27.0 (26.0) days, respectively. Of the 12 anifrolumab-treated patients with ≥1 HSR, 3 received subsequent pretreatment, and none had any HSR after the use of pretreatment. Of the 43 anifrolumab-treated patients with ≥1 IRR, 2 received pretreatment, of whom 1 had an IRR after pretreatment and anifrolumab dosage remained unchanged.

Conclusion: Following anifrolumab infusion, ARs were uncommon, and few (3%) patients experienced HSRs. HSRs and IRRs with the approved anifrolumab 300 mg dose were mild to moderate, occurred early in treatment, did not lead to discontinuation, and only rarely required pretreatment. Our data support a safe and manageable hypersensitivity profile for anifrolumab.

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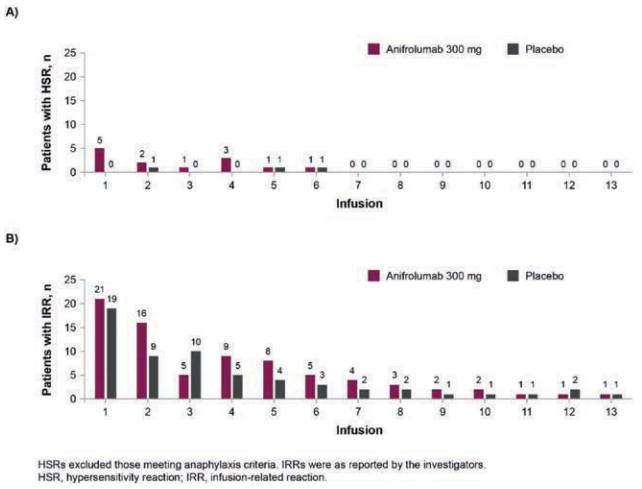
Figure. Number of Patients With **A)** Any Hypersensitivity Reaction or **B)** Any Infusion-related Reaction in the Anifrolumab 300 mg (n=459) and Placebo (n=466) Groups (Data Pooled From the MUSE, TULIP-1, and TULIP-2 Trials)



HSRs excluded those meeting anaphylaxis criteria. IRRs were as reported by the investigators.
HSR, hypersensitivity reaction; IRR, infusion-related reaction.

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POS0709

SUSTAINED BICLA AND BILAG ORGAN DOMAIN RESPONSES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) RECEIVING ANIFROLUMAB IN TWO PHASE 3 TRIALS

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Background: Incomplete SLE disease control is associated with progressive organ damage, poor quality of life, and increased mortality.[1–3] Sustained reduction in overall disease activity is therefore an important treatment goal.

Objectives: To investigate sustained British Isles Lupus Assessment Group 2004–based Composite Lupus Assessment (BICLA) response and British Isles Lupus Assessment Group (BILAG) responses by organ domain in pooled data from the TULIP-1 and TULIP-2 trials of the type I interferon receptor monoclonal antibody, anifrolumab, in patients with SLE.[4,5]

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were phase 3, randomized, placebo-controlled, 52-week trials of intravenous anifrolumab administered every 4 weeks for 48 weeks in eligible patients with moderate to severe SLE who were receiving standard therapy.[4,5] Sustained BICLA and BILAG response rates, measured as the number of consecutive patient visits with BICLA or BILAG domain responses, respectively, from Week 4 to Week 52 were compared between the anifrolumab vs placebo groups. BILAG-2004 response was defined as a reduction from A (severe disease) at baseline to B (moderate), C (mild), or D (no current disease) or reduction from B at baseline to C or D.[6]

Results: In total, 360 patients received anifrolumab 300 mg and 366 patients received placebo in the TULIP-1 and TULIP-2 trials. Analysis of pooled TULIP data revealed that more patients who received anifrolumab had sustained BICLA responses compared with placebo (Table 1). The proportions of patients who had BICLA responses sustained for ≥3, ≥6, ≥9, and 12 months inclusive of Week 52 were 33.6%, 27.2%, 16.4%, and 9.2% in the anifrolumab group, and 20.5%, 15.0%, 8.5%, and 1.9% in the placebo group, respectively. The most commonly affected organ domains were musculoskeletal (645/726 patients) and mucocutaneous (627/726 patients) (Figure 1). More patients receiving anifrolumab had BILAG responses for 12 months compared with placebo in these two domains (musculoskeletal: 19.9% vs 13.1%; mucocutaneous: 17.1% vs 7.1%); analyses of all other organ domains were limited by small sample sizes.

Table 1. Number of Patients With Consecutive Visits of Sustained BICLA Response Up to and Including Week 52 in Pooled TULIP-1 and TULIP-2 Trials

n (%)	Anifrolumab 300 mg (n=360)	Placebo (n=366)
≥3 months (≥5 visits, Week 36–52)	121 (33.6)	75 (20.5)
≥6 months (≥8 visits, Week 24–52)	98 (27.2)	55 (15.0)
≥9 months (11 visits, Week 12–52)	59 (16.4)	31 (8.5)
12 months (13 visits, Week 4–52)	33 (9.2)	7 (1.9)

BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment.

Conclusion: In two phase 3 studies, more anifrolumab-treated patients achieved sustained BICLA and BILAG responses compared with placebo. In the frequently affected musculoskeletal and mucocutaneous domains, sustained treatment benefit of anifrolumab over placebo was observed. These data support the durable clinical benefit of anifrolumab treatment in patients with moderate to severe SLE who are receiving standard therapy.

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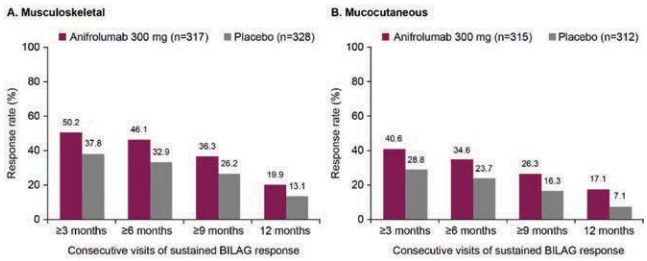
Figure. BILAG Response in the (A.) Musculoskeletal and (B.) Mucocutaneous Domains in Pooled TULIP-1 and TULIP-2 Trials on Consecutive Study Visits Up to and Including Week 52



Organ domains with few patients that had organ involvement at baseline were excluded from these data: cardiorespiratory, constitutional, gastrointestinal, hematological, neuropsychiatric, ophthalmic, and renal.
BILAG, British Isles Lupus Assessment Group.

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POS0710 INTERSTITIAL LUNG DISEASE IN PRIMARY SJÖGREN'S SYNDROME: CLINICAL AND LABORATORY FEATURES, EFFECTIVENESS OF RITUXIMAB THERAPY.

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Background: Interstitial lung disease (ILD) often occurs in primary Sjogren's syndrome (pSS) and reduces the survival of patients [1, 2]. Diagnosis and therapy in pSS-ILD are not standardized.
Objectives: To evaluate clinical characteristics of pSS-ILD and efficacy of rituximab therapy in this group of patients.
Methods: We conducted retrospective study which included 19 pSS-ILD patients. pSS was diagnosed based on the ACR 2012 or ACR/EULAR 2016 criteria. Diagnosis and dynamic assessment of ILD was carried out on the basis of high-resolution computed tomography (HRCT) and pulmonary function tests (PFT). The median age of pSS debut was 49 years (7-72 years), the median age of ILD debut – 57 years (29-75 years). All 19 patients received rituximab: 10 as a monotherapy, 6 in combination with cyclophosphamide, 3 in combination with mycophenolate mofetil. The median follow-up duration was 24 months (3-108 months).
Results: In 5 of 19 patients (26%), ILD was the first manifestation of pSS, while 14 patients (74%) developed ILD after an average of 9 years of disease course in the absence of therapy or taking low doses of glucocorticoids and hydroxychloroquine. The most common patterns of ILD were nonspecific interstitial pneumonia (52,6%) and lymphocytic interstitial pneumonia (26,3%), while organizing pneumonia and usual interstitial pneumonia were significantly less common (10,5% respectively). Both patients with organizing pneumonia were diagnosed with pulmonary lymphoma (also they had persistent salivary gland enlargement, lymphadenopathy and paraproteinemia). When analyzing clinical and laboratory features, we did not identify any predictors of ILD in pSS (Table 1). Rituximab therapy was effective in 16 of 19 patients (84,2%) based on stabilization or improvement in HRCT and PFT. The therapy was ineffective in 3 patients (15,8%), one of whom (patient with pulmonary lymphoma) died from an acute exacerbation of ILD.

Table 1. Clinical and laboratory features of pSS-ILD patients (N=19).

Sign	Frequency, %
Asymptomatic course of ILD	36,8
ANA+	100
AntiRo+	73,7
AntiLa+	47,4
RF IgM +	55
High CRP	28
High ESR	33
Hypocomplementemia	37,5
Hypergammaglobulinemia	44
High IgG	39
mIg	36
Cryoglobulinemia	18
Severe xerostomia, xerophthalmia	44
Focus score>4	44
Vasculitis	26
Lymphoma	31,6

Conclusion: Considering asymptomatic cases and the absence of pSS-ILD predictors, all patients with pSS at the onset of the disease and in the dynamics should undergo HRCT and PFT for the purpose of ILD early diagnosis. In the present study, rituximab therapy was highly effective in pSS-ILD, further prospective studies are needed to confirm these data. In patients with pSS-ILD, vigilance for pulmonary lymphoma is necessary, especially in the presence of persistent salivary gland enlargement, lymphadenopathy, paraproteinemia, pattern of organizing pneumonia and a lack of response to rituximab and cyclophosphamide therapy.
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POS0711 TOLERANCE AND EFFICACY OF TARGETED THERAPIES PRESCRIBED FOR OFF-LABEL INDICATIONS IN REFRACTORY SYSTEMIC AUTOIMMUNE DISEASES: DATA OF THE FIRST 100 PATIENTS ENROLLED IN THE TATA REGISTRY (TARGETED THERAPY IN AUTOIMMUNE DISEASES)

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Background: The low prevalence of systemic autoimmune diseases and the diversity of their clinical manifestations make complex to conduct randomised clinical trials to assess the potential efficacy of targeted treatments.
Objectives: To assess the tolerance and efficacy of targeted therapies prescribed off-label in refractory autoimmune diseases.
Methods: The TATA registry (*TArgeted Therapy in Autoimmune Diseases)* is a prospective, observational, national and independent cohort follow-up. The inclusion criteria in the registry are as follows: age > 18 years; rare systemic autoimmune disease (systemic lupus erythematosus, Sjögren's syndrome, systemic scleroderma, inflammatory myopathy, vasculitis) or other refractory rheumatism treated with off-label drugs started after 1st January 2019.
Results: Hundred (100) patients (79 females) were enrolled. The median age was 52.5 years [49;56], the median disease duration before enrolment was 5

years [3;7]. The targeted therapies at enrolment were as follows: JAK/STAT inhibitors (44%), anti-IL6R (22%), anti-IL12/23, anti-IL23 and anti-IL17 (9%), anti-BAFF (5%), abatacept (5%), other targeted treatments (9%), and combination of targeted treatments (6%). 73% of patients were receiving corticosteroid therapy at enrolment (median dose 10 mg/day). The current median follow-up time is 9 months [8;10]. Safety: 11 serious infections (incidence rate of 14.8 /100 patient-years) and 1 cancer (1.3 cancers/100 patient-years) were observed. Two patients died from severe COVID-19 (2.7 deaths/100 patient-years). Efficacy: The targeted treatment was considered effective by the clinician in 56% of patients and allowed in responders a median reduction of oral corticosteroids of 15 [9-21] mg/day.

Conclusion: These initial results of the TATA registry confirm the diversity of targeted treatments prescribed off-label in refractory autoimmune diseases and their corticosteroid-sparing effect when effective. Tolerance was acceptable in these refractory patients with a long history of treatment with immunosuppressive drugs.

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POS0712

YEAR-4 OBSERVATIONAL FOLLOW-UP OF BELIMUMAB SAFETY (MORTALITY AND MALIGNANCIES) IN PATIENTS WITH SLE WHO COMPLETED A PHASE 4, 52-WEEK, RANDOMISED, DOUBLE-BLIND PLACEBO-CONTROLLED SAFETY STUDY

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Table 1. Yr 1 plus Yrs 2–4 post-treatment* follow-up mortality and new primary malignancy rates by Yr-1 study treatment

	Pts with events per yr, n (%)			Pt incidence rate per 100 pt-yrs (Cumulative rate, %)		
	BEL	**PBO**	**Total**	**BEL**	**PBO**	**Total**
Yr-1 (as-treated) population	**N=2002**	**N=2001**	**N=4003**			
Deaths	13 (0.65)	22 (1.10)	35 (0.87)	0.66 (0.65)	1.11 (1.10)	0.87
New primary malignancies†	9 (0.45)	10 (0.50)	19 (0.47)	0.45	0.50	0.47
Yr-2 (as-treated in Yr-1) population	**N=1695**	**N=1670**	**N=3365**			
Deaths	9 (0.53)	21 (1.26)	30 (0.89)	0.60 (1.10)	1.18 (2.15)	0.89 (1.62)
New primary malignancies	3 (0.18)	7 (0.42)	10 (0.30)	0.34 (0.60)	0.48 (0.85)	0.41 (0.72)
Yr-3 (as-treated in Yr-1) population	**N=1659**	**N=1630**	**N=3289**			
Deaths	9 (0.54)	17 (1.04)	26 (0.79)	0.58 (1.55)	1.14 (3.00)	0.86 (2.27)
New primary malignancies, n (%)	7 (0.42)	9 (0.55)	16 (0.49)	0.37 (0.95)	0.49 (1.25)	0.43 (1.10)
Yr-4 (as-treated in Yr-1) population	**N=1622**	**N=1582**	**N=3204**			
Deaths by MedDRA SOC	14 (0.86)	13 (0.82)	27 (0.84)	0.65 (2.25)	1.07 (3.65)	0.86 (2.95)
Infections/infestations	4 (0.25)	5 (0.32)	9 (0.28)			
Cardiac disorders	2 (0.12)	1 (0.06)	3 (0.09)			
General disorders/ administration site conditions	2 (0.12)	2 (0.13)	4 (0.12)			
Respiratory/thoracic/ mediastinal disorders	2 (0.12)	1 (0.06)	3 (0.09)			
Nervous system disorders	2 (0.12)	1 (0.06)	3 (0.09)			
Other‡	2 (0.12)	3 (0.18)	5 (0.15)			
New primary malignancies	10 (0.62)	5 (0.32)	15 (0.47)	0.43 (1.45)	0.44 (1.45)	0.43 (1.45)

*Pts in the post-treatment follow-up period are no longer receiving study treatment. †Includes nonmelanoma skin cancer.‡Contains 1 event for 5 distinct pts of each of renal/urinary disorders, and neoplasms (BEL); musculoskeletal/connective tissue disorders, injury/poisoning/procedural complications, and vascular disorders (PBO).MedDRA, Medical Dictionary for Regulatory Activities; SOC, system organ class

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Background: Belimumab (BEL) is an approved systemic lupus erythematosus (SLE) treatment. Despite BEL clinical studies demonstrating a favourable benefit–risk profile, varying incidence rates of mortality and adverse events of special interest, including malignancies, require further evaluation.
Objectives: To assess long-term safety following BEL therapy.
Methods: This was a Year (Yr)-4 post-treatment follow-up of the Phase 4, double-blind, placebo (PBO)-controlled Belimumab Assessment of Safety in SLE (BASE) study (GSK Study BEL115467; NCT01705977).[1] Overall, 4003 adults with active, autoantibody-positive SLE received BEL (10 mg/kg IV) or PBO, plus standard therapy (ST), for 48 weeks. Patients (pts) then entered a Yr 2–5 follow-up period in which they received physician-directed ST. All pts were contacted annually by telephone, including pts who discontinued treatment. Mortality and new malignancies (including nonmelanoma skin cancer) were the endpoints collected, and rates summarised. We present Yr-4 follow-up data by Yr-1 treatment received.
Results: Baseline characteristics for the Yr-4 follow-up population (N=3204) were similar to the Yr-1 double-blind study population (N=4003). By the Yr-4 follow-up, cumulatively 12.7% and 11.0% of pts in the BEL and PBO Yr-1 groups had received BEL as part of physician-directed care, respectively (data not shown). As shown in the Table 1, cumulative follow-up adjusted mortality rates were lower in the BEL vs PBO Yr-1 treatment group for Yrs 2 to 4. Cumulative follow-up adjusted new primary malignancy rates were lower in the BEL vs PBO Yr-1 treatment group for Yrs 2 and 3, but similar in Yr 4.
Conclusion: Post-treatment Yr-4 follow-up results in BASE, the largest double-blind trial in pts with SLE to date, support the safety of BEL therapy, with no new BEL safety concerns identified in this analysis.
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POS0713 BIIB059 EFFICACY IN PARTICIPANTS WITH ACTIVE CUTANEOUS LUPUS ERYTHEMATOSUS (CLE): SUBGROUP ANALYSIS OF PARTICIPANTS ACHIEVING CLEAR/ALMOST CLEAR DISEASE ACTIVITY FROM PART B OF THE TWO-PART PHASE 2 LILAC STUDY

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Background: CLE is an autoimmune disease that occurs with or without systemic manifestations. The chronic manifestations of CLE often have a lasting negative impact on a patient's quality of life.[1,2] Clearance of skin activity is the most desirable outcome for a targeted treatment in patients with CLE; however, it is a challenging target to achieve. Activation of both the innate and adaptive immune systems leads to the typical inflammatory histopathological characteristics of CLE and its clinical manifestations.[3] BIIB059 is a humanized monoclonal antibody that engages blood dendritic cell antigen 2 (BDCA2), a receptor on plasmacytoid dendritic cells, inhibiting production of Type I interferons and other chemokines/cytokines.[4] The randomized Phase 2 LILAC study (NCT02847598) met its primary endpoint in CLE (Part B), demonstrating a dose response in the percent change in Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity (CLASI-A) from baseline (BL) to Week 16 for BIIB059 vs placebo (PBO).[5]
Objectives: To determine the proportions of participants achieving a clear or almost clear skin status as defined by the attainment of CLASI-A scores of 0–1 or 0–3 at Week 16.
Methods: In Part B, adults with histologically confirmed active CLE with or without systemic manifestations and adjudicated BL CLASI-A ≥8 received BIIB059 (50, 150, or 450 mg) or PBO subcutaneously Q4W through Week 12, with an additional loading dose at Week 2. CLASI-A was assessed at each dosing visit and at Week 16. The proportions of participants achieving CLASI-A scores of 0–1 (prespecified analysis) or 0–3 (ad-hoc analysis) and mean absolute CLASI-A score changes at Week 16 were determined.
Results: At BL, mean (standard deviation [SD]) CLASI-A scores were 16.6 (8.8) and 16.5 (8.5) for the pooled BIIB059 and PBO groups, respectively. At Week 16, more participants in the BIIB059 50, 150, and 450 mg treatment groups achieved CLASI-A scores of 0–1 and 0–3 vs those in the PBO group (Table 1). In participants achieving CLASI-A scores of 0–1, mean (SD) absolute CLASI-A scores decreased by 11.0 (SD not applicable), 19.6 (11.1), and 16.4 (11.5) points from BL at Week 16 in the 50, 150, and 450 mg treatment groups, respectively; in participants achieving CLASI-A scores of 0–3, CLASI-A scores decreased by 8.8 (2.7), 15.4 (10.3), and 13.2 (9.5) points from BL at Week 16 in the 50, 150, and 450 mg treatment groups, respectively, vs 8.3 (2.5) points in the PBO group. Among the 11 participants who achieved CLASI-A scores of 0–1, six had CLASI-A scores of 0 (representing a 100% resolution of skin disease) with a decrease in CLASI-A score ranging from 11 to 30 points.

Table 1. Proportion of pts who achieved CLASI-A scores of 0–1 and 0–3

		BIIB059		
	PBO	50 mg	150 mg	450 mg
	(n=33)	(n=26)	(n=25)	(n=48)
Number of pts achieving CLASI-A score of 0–1 at Week 16 (%)	0/32 (0)	1/26 (3.9)	5/25 (20.0)	5/43 (11.6)
Number of pts achieving CLASI-A score of 0–3 at Week 16 (%)	3/32 (9.4)	5/26 (19.2)	8/25 (32.0)	9/43 (20.9)

Pts considered as treatment failures or who discontinued treatment were classified as non-responders at visits post treatment failure or treatment discontinuation. Pts who completed treatment but had a missing score at any primary timepoint are classified as non-responders for that timepoint.

Conclusion: After 16 weeks of treatment, greater proportions of participants with active CLE treated with BIIB059 vs PBO achieved a clear or almost clear skin status, defined as CLASI-A score of 0–1 or 0–3, further supporting the efficacy of BIIB059 in CLE.
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POS0714

POOLED SAFETY ANALYSIS OF BARICITINIB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THREE RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CLINICAL TRIALS

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Background: Baricitinib (BARI), an oral selective inhibitor of Janus kinase 1 and 2 approved for the treatment of rheumatoid arthritis and atopic dermatitis, has been evaluated in clinical studies in patients with systemic lupus erythematosus (SLE).
Objectives: To assess the safety profile of BARI in patients with SLE.
Methods: Patients with SLE receiving stable background therapy were randomised 1:1:1 to BARI 2-mg, 4-mg, or placebo (PBO) once daily in one 24-week, phase 2 (NCT02708095) and two 52-week, phase 3, PBO controlled studies (NCT03616912 and NCT03616964).
Results: A total of 1,849 patients were included in this pooled analysis, representing 1,463.5 patient years of exposure (PYE). The incidence rates per 100 PYR at risk (IR/100 PYR) for serious adverse events (SAEs) were 9.5, 14.7, and 14.1 respectively for PBO, BARI 2-mg, and BARI 4-mg. There were no clinically meaningful differences between treatment groups for discontinuations due to AEs or death (Table 1).

Table 1. Overview of safety measures of baricitinib in patients with SLE

	PBO	BARI 2-mg	BARI 4-mg	Pooled-BARI
	N=614	N=621	N=614	N=1235
	PYE=488.1	PYE=494.0	PYE=481.4	PYE=975.4
	n(%)	n(%)	n(%)	n(%)
	PYR	PYR	PYR	PYR
Safety measure	**[IR; 95%CI]**	**[IR; 95%CI]**	**[IR; 95%CI]**	**[IR; 95%CI]**
SAEs	45 (7.3)	70 (11.3)*	65 (10.6)*	135 (10.9)*
	473.2	476.6	461.9	938.5
	[9.5; 6.9, 12.7]	[14.7; 11.5, 18.6]	[14.1; 10.9, 17.9]	[14.4; 12.1, 17.0]
Discontinuation of study drug due to AE	48 (7.8)	58 (9.3)	57 (9.3)	115 (9.3)
	485.3	492.3	480.6	973.0
	[9.9; 7.3, 13.1]	[11.8; 8.9, 15.2]	[11.9; 9.0, 15.4]	[11.8; 9.8, 14.2]
Death	4 (0.7)	1 (0.2)	4 (0.7)	5 (0.4)
	488.2	494.0	481.5	975.5
	[0.8; 0.2, 2.1]	[0.2; 0.0, 1.1]	[0.8; 0.2, 2.1]	[0.5; 0.2, 1.2]
Serious infections	12 (2.0)	22 (3.5)	28 (4.6)*	50 (4.0)*
	484.3	487.2	472.5	959.7
	[2.5; 1.3, 4.3]	[4.5; 2.8, 6.8]	[5.9; 3.9, 8.6]	[5.2; 3.9, 6.9]
Herpes Zoster	18 (2.9)	17 (2.7)	29 (4.7)	46 (3.7)
	481.1	486.5	468.6	955.1
	[3.7; 2.2, 5.9]	[3.5; 2.0, 5.6]	[6.2; 4.1, 8.9]	[4.8; 3.5, 6.4]
VTEs#	6 (1.2)	3 (0.6)	1 (0.2)	4 (0.4)
	444.0	450.2	438.1	888.3
	[1.4; 0.5, 2.9]	[0.7; 0.1, 1.9]	[0.2; 0.0, 1.3]	[0.5; 0.1, 1.2]
MACE#	0	1 (0.2)	3 (0.6)	4 (0.4)
	443.9	450.1	438.1	888.3
	[0.0; NA, 0.8]	[0.2; 0.0, 1.2]	[0.7; 0.1, 2.0]	[0.5; 0.1, 1.2]
Malignancy excluding NMSC	2 (0.3)	3 (0.5)	2 (0.3)	5 (0.4)
	488.0	494.1	481.4	975.5
	[0.4; 0.0, 1.5]	[0.6; 0.1, 1.8]	[0.4; 0.1, 1.5]	[0.5; 0.2, 1.2]
NMSC	2 (0.3)	0	0	0*
	486.7	494.0	481.4	975.4
	[0.4; 0.0, 1.5]	[0.0; NA, 0.7]	[0.0; NA, 0.8]	[0.0; NA, 0.4]

Data are n (%) patients PYR [IR; 95% CI]. #Phase 2 study data not included. AE=adverse event; CI=confidence interval; MACE=major adverse cardiac event; NMSC=non-melanoma skin cancers; VTE=venous thrombotic event (includes deep vein thrombosis and pulmonary embolism); IR=incidence rate (100 times the number of patients reporting an adverse event divided by the event-specific exposure to treatment); N=number of patients in the analysis population; n=number of patients in the specified category; PYE=patient-year of exposure; PYR=patient years at risk; SAE=serious adverse event. *p≤0.05 vs placebo.

The IR/100 PYR for serious infections were 2.5, 4.5, and 5.9 respectively for PBO, BARI 2-mg, and BARI 4-mg. The risk of Herpes Zoster was higher in BARI 4-mg (4.7%) vs PBO (2.9%) (Table 1).
The IR/100 PYR for positively adjudicated venous thrombotic events (VTEs) were 1.4, 0.7, and 0.2 respectively for PBO, BARI 2-mg, and BARI 4-mg. The IR/100 PYR for positively adjudicated major adverse cardiac event (MACE) was numerically higher in BARI 2-mg (0.2) and BARI 4-mg (0.7) vs PBO (0.0), however the pooled-BARI IR/PYR (0.5) was within the range of background disease (1). No increased risk for malignancies was observed.
Conclusion: The safety profile of BARI in SLE patients was consistent with the known BARI safety profile. There was no increased risk of VTE in BARI treatment groups.
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POS0715

TREATMENT OF SLE PATIENTS WITH ZETOMIPZOMIB (KZR-616), A SELECTIVE INHIBITOR OF THE IMMUNOPROTEASOME, RESULTS IN CIRCULATING GENE EXPRESSION, PROTEIN LEVEL, AND IMMUNE CELL PHENOTYPIC CHANGES WITH POTENTIAL CORRELATIONS TO CLINICAL RESPONSE

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Background: Systemic lupus erythematosus (SLE), a severe multiorgan autoimmune disease, involves dysfunction of multiple immune system components. In preclinical studies, KZR-616, a first-in-class small molecule selective inhibitor of the immunoproteasome, demonstrated pleiotropic immunomodulatory functions encompassing both innate and adaptive immune pathways[1,2]. In the recently completed MISSION Phase 1b trial in SLE patients (pts), KZR-616 exhibited encouraging safety, tolerability, and clinical improvements[3]. Preliminary biomarker analysis of the first two cohorts was previously reported[4]. Here, we present complete biomarker results from all cohorts in this study.
Objectives: 1) To characterize biomarker changes (gene expression, circulating protein levels and immune cell phenotypes) following KZR-616 treatment. 2) To evaluate correlations between biomarker changes and treatment response to KZR-616.
Methods: The open-label Phase 1b MISSION Trial (NCT 03393013) was a 25-week trial of KZR- 616 administered subcutaneously once weekly at doses ranging from 30-75 mg for 13 weeks (W) with a 12 W follow-up. Forty-seven SLE pts with and without nephritis were enrolled with 35 completing all 25 W of study. Clinical response definitions at W13 or later were defined as either a >4 reduction of SLEDAI-2K or >50% drop in swollen joint counts (SJC) (baseline SJC>2). Biomarker samples included whole

blood in RNA tubes (31 pts), cryopreserved PBMCs (15 pts), plasma (35 pts) and urine (2 pts). Whole blood RNA sequencing was performed using Illumina TruSeq. Differential expression was modelled using DESeq2. Fast pre-ranked gene set enrichment analysis (GSEA) was performed with gene sets derived from published literature. Cryopreserved PBMCs were analysed by flow cytometry to profile immune cell subtypes. Plasma protein was measured by Meso Scale Discovery (MSD) kits. Healthy volunteer (HV, N=12) samples were used to establish potential disease-related biomarker changes in patients at baseline (BL).

Results: Many gene modules were found to be altered at BL in SLE pts, relative to HV, including those representing interferon (IFN) response and B/plasma cells and changes were consistent with our prior report[4]. Comparisons of SLEDAI-2K responders (R) versus non-responders (NR) revealed enrichment of 193 gene modules (57 down and 136 up-regulated, p_{adj}<0.1) at BL and 190 modules (105 down and 85 up) 4 weeks after treatment (W17). Expression of a 4-gene IFN module was enriched in SLEDAI-2K R vs NR at BL; expression of this module trended downward at W17 in R, whereas it increased over time in NR at W 5. Reduced numbers of circulating class-switched memory B cells and IgG-producing plasma cells were observed at W17 and/or W25. Plasma levels of BAFF were consistently increased at W5 but returned to BL levels by W17. Plasma levels of CD169/ SIGLEC-1, a monocyte activation marker, were higher at BL in SJC R vs. NR and were reduced after treatment in both groups. Two pts with active proliferative nephritis were enrolled into this study and both showed a reduction in levels of urine CD163 (uCD163), while plasma levels of this marker were stable.

Conclusion: Our integrative analysis indicates that KZR-616 elicits a potent effect on multiple immune pathways in SLE patients. Potential new biomarkers (gene, gene module, circulating protein) that may be useful for prediction of patient response were identified. Future biomarker studies in placebo-controlled trials may further our understanding of KZR-616 mechanism of action, patient selection and prediction of patient responses.

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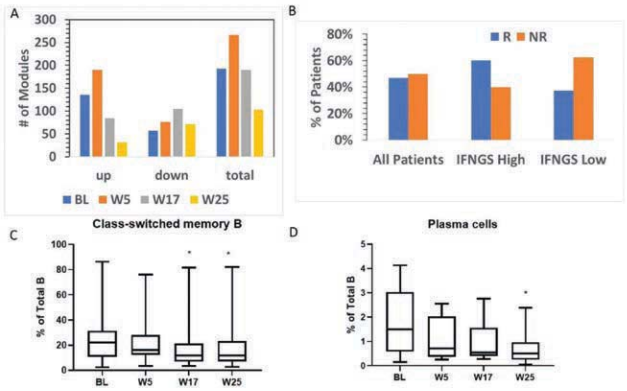
Figure: Gene expression analysis and plasma cell signature change after KZR-616 treatment. A. Gene module comparisons of SLEDAI-2K responders versus non-responders (p_{adj}<0.1) B. Patients were stratified as type I IFN high or low groups and assessed clinically from W13-W25 for response based on SLEDAI-2K C, D. Class-switched memory B cells(C) and plasma cells (D) changes in patients after treatment (*significant change over BL, p<0.05).



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POS0716 EFFICACY AND SAFETY OF LOW-DOSE IL-2 IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by disturbances of regulatory and effector $CD4^+$T cells, which were regulated by interleukin (IL)-2[1,2].

Objectives: The aim of this study was to systematically evaluate the efficacy and safety of low-dose IL-2 therapy in SLE treatment.

Methods: Systematic searches of PubMed, EMBASE, Web of Science, the Cochrane Library and Medline, CNKI, CBM and Technology Journal Database were performed. Original case reports, case series, observational studies and clinical trials reporting the efficacy or safety data on SLE patients treated with IL-2 were included. A random-effects meta-analysis was performed to calculate the pooled efficacy. Inconsistency was evaluated by using the I^2 and Egger tests were used for the evaluation of potential publication bias (STATA v.12.0).

Results: A total of 7 studies comprising 327 patients were identified (Table 1). After the low-dose IL-2 treatment, 54.8% Lupus nephritis patient had distinct clinical remission. The SRI-4 response rates were 0.816 (95%CI 0.730-0.901) and the SELENA-SLEDAI scores were significantly decreased [SMD=-2.504, 95%CI (-4.089,-0.919), P=0.002]. Injection site reaction and fever, which were common side effects for IL-2, occurred in 33.1% and 14.4% of patients, None serious adverse events were reported among all these studies. Besides, the proportions of $CD4^+$T cells and Tregs were significantly increased after IL-2 injection [SMD=0.600, 95%CI (0.108,1.093), P=0.017; SMD=1.168, 95%CI (0.429,1.908), P=0.002], while there were no statistical differences in the proportions of $CD8^+$T cells, Th17 cells, Th1 cells and Th2 cells between before and after IL-2 treatment (P>0.05)(Figure 1).

Conclusion: Low-dose IL-2 was promising and well-tolerated in the treatment of SLE, which could promotes the proliferation and functional recovery of Tregs.

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Table 1. Available evidence including patients with SLE treated with low-dose IL-2.

Study. Year. (design)	Patients (include in analysis)	Gender (female %)	Dosage	SRI-4,n(%)	SELENA–SLEDAI	Remission (%)
Jing He. 2019. (PCT)	60(30)	90.00	1 million IU every other day	16 (55.17)	0 w: 12.00±4.75 12 w: 6.00±4.00	53.85
Jing He. 2016. (PCT)	40(23)	92.50	1 million IU every other day	34 (89.50)	0 w: 11.14±3.79 12 w: 3.92±2.23	NA
Miao Shao. 2019. (PCT)	30(18)	88.89	1 million IU every other day	NA	NA	55.56
Chunmiao Zhao. 2019. (PCT)	50(50)	94.00	1 million IU, 3-5d/month	NA	0 w: 5.92±0.36 12 w: 4.05±0.31	NA
Shengxiao Zhang. 2019. (PCT)	495(54)	NA	0.5 million IU per day for 5 days	NA	NA	NA
Kai Fan. 2018. (PCT)	106(76)	NA	0.5 million IU per day for 5 days	NA	NA	NA
Jing Wang. 2017. (PCT)	76(76)	93.42	0.5 million IU per day for 5 days	NA	0 d: 10.87±6.48 5 d: 5.83±4.18	NA

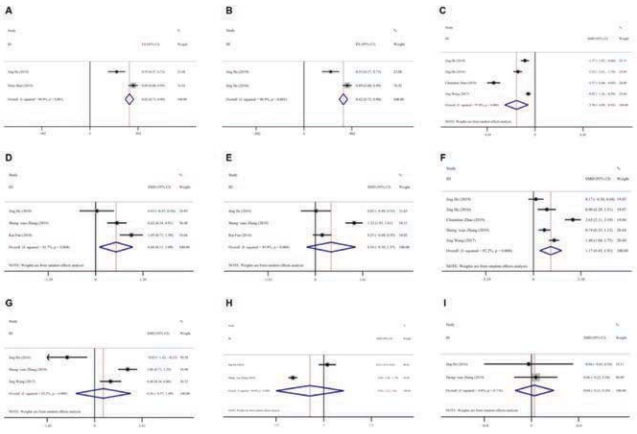

Figure 1: Efficacy and safety of IL-2 in patients with systemic lupus erythematosus. (A) Remission. (B) SRI-4 response rates. (C) SELENA-SLEDAI scores. (D-I) the proportions of $CD4^+T$, $CD8^+T$, Tregs, Th17, Th1 and Th2 cells before and after low-dose IL-2 treatment.

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POS0717

ASSOCIATION BETWEEN CUMULATED HYDROXYCHLOROQUINE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND DEVELOPMENT OF CARDIAC CONDUCTION ALTERATIONS: A MULTIPLE LOGISTIC REGRESSION ANALYSIS

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Background: Hydroxychloroquine (HCQ) is a widely used drug in Systemic Lupus Erythematosus (SLE). It may cause cardiac alterations which includes short term arrhythmic events (via QT interval prolongation) and medium-late term dose dependent cardiomyopathy[1]. The few research articles published on the medium-late term effects of HCQ in cardiac conduction disorder do not show relevant alterations[2-3].
Objectives: To assess the effect of HCQ in cardiac conduction in a consecutive SLE population.
Methods: Observational, single University hospital study of all consecutive SLE patients with an electrocardiogram (EKG) at HCQ onset and at least one EKG in follow-up, with a period of at least 3 months on HCQ treatment was performed. We assessed conduction alteration (CA) by EKG, defined as atrio-ventricular block, bundle branch block or QT interval prolongation. The EKGs were gathered from the clinical history and interpreted at the beginning of the treatment and during the 15.2 years (CI95% 13.24-17.16) follow-up period. We defined cumulated HCQ (cHCQ) as the multiple of the mean annual dose of the sample. A Multiple logistic regression model, adjusted by different variables according to statistical significance and clinical relevance, was performed.
Results: We studied 109 (96 women/13 men) SLE patients with a mean (±SD) age of 61 ±. 2.78 years. A statistically significant association was observed between the cHCQ, and the development of CA [OR 1.1 CI95% 1.02-1.9; p = 0.011] (Table 1 **&** Figure 1). A total of 8 covariates were included. Among them, those that had the greatest influence on the development of the primary event were previous CA [OR 4.15 CI95% 6.39-624.54; p <0.01]; valvular heart disease [OR 7.15 CI95% 1.31-38.91; p = 0.023] and age [OR 1.07 95% CI 1.0-1.14; p = 0.04].

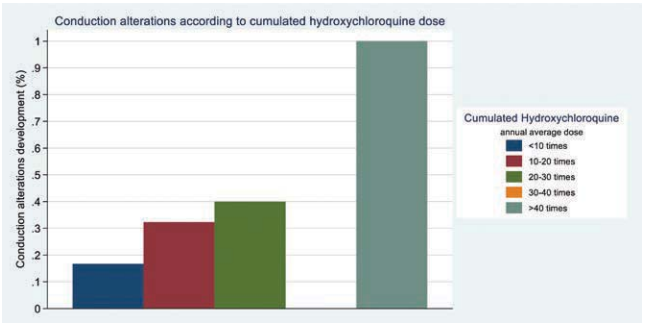

Figure 1. Cardiac conduction alterations development according to cumulated Hydroxychloroquine dose.

Conclusion: According to our study, it seems to be an association between the cHCQ and development of CA regardless of other variables evaluated. Wider longitudinal studies are required with a protocolized EKG performance in successive visits to further analyze this association.

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POS0718

SIROLIMUS MONOTHERAPY FOR THROMBOCYTOPENIA IN PRIMARY ANTIPHOSPHOLIPID SYNDROME: A PILOT STUDY FROM A TERTIARY REFERRAL CENTER

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Background: Thrombocytopenia (TP) is considered as a warning sign of high-risk antiphospholipid syndrome (APS) and sometimes a paradoxical sign of

Table 1. Results of univariable and multivariable logistic regressions evaluating the association between cumulated hydroxychloroquine and the development of cardiac conduction alterations.

Variable	Unadjusted OR	95%CI		P-value	Adjusted OR	95%CI		P-value
Cumulated hydroxychloroquine	1.07	1.02	1.12	0.01	1.10	1.02	1.19	0.01
Covariates								
Previous cardiac conduction alterations	28.23	5.67	140.54	0.00	63.21	6.40	624.54	0.00
Cardiac valve disease	4.71	1.66	13.37	0.00	7.15	1.31	38.91	0.02
Age	1.06	1.02	1.10	0.00	1.07	1.00	1.14	0.04
Diabetes mellitus	3.79	1.26	11.41	0.02	3.44	0.59	20.11	0.17
Cerebrovascular disease	2.95	1.02	8.50	0.05	0.10	0.01	1.03	0.05
Chronic renal disease	6.65	1.77	24.98	0.05	4.88	0.65	36.91	0.13
Pulmonary Hypertension	6.40	0.56	73.58	0.14	3.84	0.13	114.96	0.44
Alcohol consumption	6.40	0.56	73.58	0.14	10.59	0.58	194.87	0.11
Gender	0.33	0.10	0.11	0.07				
Hypertension	2.32	0.91	5.90	0.08				
Dyslipemia	1.46	0.61	3.50	0.40				
Obesity	1.85	0.41	8.32	0.42				
Smoking	1.67	0.69	4.02	0.26				
Cardiac ischaemic disease	2.08	0.33	13.16	0.44				
Heart Failure	5.91	1.31	26.68	0.02				
Pericarditis	2.08	0.33	13.16	0.44				

OR: Odds Ratio; CI: Confidence

anti-thrombosis treatment. Currently there is an extreme paucity of effective and safe drugs for long-term management of TP in primary APS patients.
Objectives: We aimed to explore the efficacy and safety of sirolimus monotherapy.
Methods: In this real-world study, we included 7 consecutive patients with primary APS who received sirolimus monotherapy for TP. Oral sirolimus was initiated at a dose of 1-2 mg once daily and then adjusted primarily based on clinical efficacy and tolerance, with consideration of sirolimus trough concentration of ≤15 ng/ml.
Results: Of included patients, the median age was 58 years with median disease course of 1.5 years and 4 patients were treatment-naïve. All patients completed 6 months of sirolimus therapy with median follow-up of 6 months (range: 6-15). All patients received sirolimus monotherapy for TP during entire follow-up, without adding any additional agents. Overall, platelet count exhibited substantially increasing trend after sirolimus administration during the first six months ($p<0.001$) and being stable later. Specifically, median platelet count was significantly increased from 59×10^9/L before sirolimus to 90×10^9/L at month 1 ($p=0.028$), 131×10^9/L at 3 months ($p=0.028$) and 178×10^9/L at 6 months ($P=0.018$). Overall and complete response were respectively achieved in 6 (85.7%) and 5 (71.4%) patients at month 6. Importantly, overall response was achieved in all 4 treatment-naïve patients. Additionally, there was different extents of decline in the titers of antiphospholipid antibodies after sirolimus treatment. Regrading safety, only one patient experienced elevated cholesterol level with recovery after atorvastatin treatment.
Conclusion: Sirolimus monotherapy confers good efficacy and tolerance for TP in primary APS patients, and therefore may be considered as a first-line therapy.

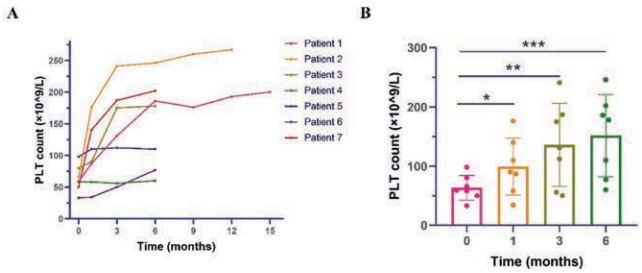

Figure 1. Changes in platelets levels after sirolimus therapy in primary antiphospholipid syndrome patients with thrombocytopenia, (A) platelet count of individual patient during the whole follow-up, (B) Median platelet count of included patients during the first six months.

Disclosure of Interests: None declared
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POS0719 **RAPID EFFICACY OF ANIFROLUMAB IN MULTIPLE SUBTYPES OF RECALCITRANT CUTANEOUS LUPUS PARALLELS DISCRETE CHANGES IN TRANSCRIPTOMIC AND CELLULAR BIOMARKERS.**

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Background: Cutaneous lupus eyrthematosus (CLE) is frequently refractory to immunosuppressive therapies including B-cell depletion, but this varies by morphology with the chronic discoid (DLE) subtype being particularly resistant. Local production and response to type-I interferon (IFN-I) is implicated in all subtypes of CLE. Therapeutic blockade of the IFN-I receptor with anifrolumab has direct effects on IFN-I signaling, and subsequent more widespread effects on other immune functions regulated by IFN-I[1]. Response to anifrolumab by lesion subtype have not been described, and it is unclear which effects of IFN-blockade are responsible for cutaneous response. We hypothesise that the efficacy of anifrolumab will differ dependent on the relative contribution of direct IFN-I effects vs. the downstream immunostimulatory effects of IFN-I on other immune functions.
Objectives: To evaluate the effect of anifrolumab on (i) rituximab-refractory CLE; (ii) on DLE; (iii) to compare clinical responses with IFN-specific biomarkers and transcriptomic evaluation of broader immune responses; (iv) to compare early and late immunophenotypic and clinical responses.
Methods: SLE patients with active recalcitrant CLE were treated with anifrolumab 300 mg IV every 4 weeks and evaluated using the cutaneous lupus erythematosus disease area and severity index (CLASI) and dermatology life quality index (DLQI). Fluorescence intensity of tetherin (CD317), a cell surface interferon biomarker, was evaluated on major cell subsets by multiparameter flow cytometry of peripheral blood mononuclear cells (PBMCs). Previously validated IFN-Scores-A and B [2], in addition to gene expression scores annotated to inflammation, myeloid lineage and plasmablasts modules [3], were measured in PBMCs using customised Taqman array at baseline, 1 month and 3 months into treatment.
Results: 8 patients (DLE n=5, chillblain / nodular vasculitis n=2, subacute CLE n=1) have enrolled to date. One month clinical and biomarker data are now available for 5. Median number of previously failed standard therapies is 6, including rituximab in 6/8 patients, belimumab in 3/8 and thalidomide in 4/8. Four patients required long-term oral prednisolone >10 mg daily. Median baseline CLASI activity score was 16 and DLQI was 16/30. Rapid clinical responses were evident at 1 month in 4/5 patients, being greatest in magnitude in patients with SCLE and DLE compared with chillblain lesions. Median fall in CLASI activity score at 1 month was 6 points with a median percentage change from baseline of 31%. In all patients, a rapid and marked suppression of IFN-Score-A (mean difference 2.92, $p<0.01$) and plasmablast tetherin ($p=0.01$), was evident by 1 month. Small and variable downward trends were observed in inflammation- and IFN-Score-B ($p=0.06$), myeloid ($p=0.27$) and plasmablast ($p=0.15$) -annotated gene expression scores. Major cell population numbers were proportionally unaltered in flow cytometry.
Conclusion: These preliminary results suggest that anifrolumab: (i) may be effective in rituximab-resistant CLE, (ii) is effective in DLE; (iii) rapidly suppresses IFN-I response, but with lesser effects on non-IFN immune biomarkers and (iv) early direct effects on IFN-I are associated with rapid clinical response.
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Disclosure of Interests: Lucy Marie Carter: None declared, Zoe Wigston: None declared, Philip Laws Speakers bureau: AbbVie, Actelion, BMS, Consultant of: Amgen, Celgene, Janssen, Leo, Lilly, Sanofi, Grant/research support from: UCB, Almirall, and Novartis, Edward Vital Consultant of: AstraZeneca, Genentech, Aurinia, Lilly, ILTOO and Modus Therapeutics., Grant/research support from: AstraZeneca and Sandoz
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POS0720 **LOW-DOSE GLUCOCORTICOIDS WITHDRAWN IN SYSTEMIC LUPUS ERYTHEMATOSUS: A DESIRABLE AND ATTAINABLE GOAL**

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Background: Prolonged use of GC may cause irreversible organ damage, leading to impaired quality of life and even increased mortality. However, many physicians are worried about severe flares after GC withdrawal in daily practice.
Objectives: To assess the risk of flare in systemic lupus erythematosus (SLE) patients after low dose glucocorticoids (GC) discontinuation and evaluate the risk factors of flare.
Methods: SLE patients who ever discontinued GC were identified from PKUFHS cohort. The disease flare profile after GC discontinuation were analyzed. Flare rate was analyzed using Kaplan-Meier analysis. COX regression was used to determine the effect of variables on SLE flare. A prognostic nomogram using Cox proportional hazards regression modeling were developed.
Results: 132 SLE patients were eligible for the final analysis. They were followed up for a median (IQR) period of 21.8 (9.01, 36.7) months. The cumulative probability of flare after GC discontinuation was 8.3 % at 6 months, 16.8% at year 1 and 27.5% at year 2 (Figure 1A). In multivariate COX analysis, hypocomplementemia and serologically active clinically quiescent (SACQ) were independent risk factors of flare [HR 2.53, 95% CI (1.32, 4.88); HR 3.17, 95% CI (1.44, 6.97), respectively]. Age ≥ 40y at GC withdrawal and hydroxychloroquine usage were independent protective factors of flare [HR 0.53, 95% CI (0.29, 0.99); HR 0.32, 95% CI (0.17, 0.62), respectively] (Table 1). The protective effect of hydroxychloroquine was dosage related. From the prospective of different tapering strategies embodied as duration from prednisone 5mg/d to complete discontinuation, slower tapering strategy (12-24 months) significantly reduced the risk of flare compared to faster tapering strategy (< 3 months) [HR 0.30, 95% CI (0.11, 0.82), p=0.019]. The prognostic nomogram including aforementioned factors effectively predicted 1- and 2-year probability of flare-free (Figure 1B).

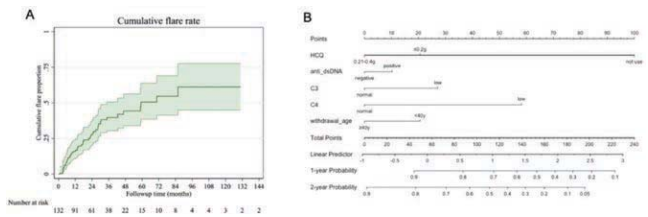

Figure 1.

Conclusion: Low-dose GC is feasibly discontinued with infrequent flare in real-life setting. SACQ and younger age are potential risk factors of SLE flare,

Table 1. Predictors of flare by univariate and multivariate COX analysis.

			Multivariate		Multivariate	
	Univariate	**p**	**Model 1**	**p**	**Model 2**	**p**
age≥40y at GC withdrawal	0.59 (0.33,1.07)	0.084	0.53 (0.29, 0.99)	0.049	0.63 (0.33, 1.18)	0.147
Age at onset ≥18y	2.03 (0.62, 6.66)	0.244	2.75 (0.77, 9.85)	0.121	2.88 (0.81, 10.2)	0.103
Remission duration≥60 months since the last flare	0.66 (0.35, 1.27)	0.217	0.81 (0.41, 1.57)	0.526	0.73 (0.38, 1.41)	0.346
history of thrombocytopenia	1.73 (0.94, 3.18)	0.077	1.36 (0.70, 2.65)	0.359	1.45 (0.74, 2.83)	0.278
history of lupus nephritis	0.86 (0.47, 1.55)	0.610	/	/	/	/
Hypocomplementemia	1.97 (1.06, 3.66)	0.031	2.53 (1.32, 4.88)	0.005	/	/
anti-dsDNA positive	1.25 (0.70, 2.23)	0.456	/	/	/	/
SACQ (both)	2.91 (1.38, 6.15)	0.005	/	/	3.17 (1.44, 6.97)	0.004
SACQ (or)	1.29 (0.73, 2.30)	0.380	/	/	/	/
Hydroxychloroquine or not	0.29 (0.16, 0.53)	<0.001	0.29 (0.15, 0.56)	<0.001	0.32 (0.17, 0.62)	0.001
Immunosuppressant or not	0.77 (0.40, 1.48)	0.426	/	/	/	/

There was strong collinearity between hypocomplementemia and SACQ, so the two parameters were separated into two models. SACQ (both): anti-dsDNA positive and hypocomplementemia; SACQ (or): anti-dsDNA positive or hypocomplementemia; GC: glucocorticoids. Data were shown as HR (95% CI).

while hydroxychloroquine usage and slow GC tapering to withdrawal can reduce relapse. The visualized model we developed may help to predict risk of flare among SLE patients who discontinued GC.

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POS0721

ASSOCIATION BETWEEN PRECONCEPTION COMPLEMENT LEVELS AND USE OF HYDROXYCHLOROQUINE WITH PREGNANCY OUTCOME IN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME AND CARRIERS OF ANTIPHOSPHOLIPID ANTIBODIES: AN INTERNATIONAL MULTICENTER STUDY

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Background: Antiphospholipid Syndrome (APS) is a rare autoimmune disease characterized by thrombotic events and/or pregnancy morbidities in the presence of confirmed positivity for antiphospholipid antibodies (aPL). Complement was demonstrated to be involved in aPL-related pregnancy loss in animal models and several groups investigated the significance of complement levels in human disease. C3 and C4 serum levels were assessed in several cohorts of pregnant patients with APS and/or aPL positivity in order to relate complement consumption with adverse pregnancy outcome (APO). According to some authors, hydroxychloroquine (HCQ) can control the activation of the complement system, improve pregnancy outcome and reduce aPL title.
Objectives: This study was designed to verify the effect of HCQ in addition to low dose aspirin (LDA) + low molecular weight heparin (LMWH) treatment in a multicenter cohort of primary APS (PAPS) and aPL carriers pregnant women and the possible correlation with preconception serum C3/C4 levels.
Methods: Medical records of pregnant women with confirmed positivity for aPL antibodies attending twelve referral centers from January 2010 to December 2020 were retrospectively evaluated. We considered as aPL-related APO: spontaneous abortions (<10 weeks of gestation), fetal loss (≥10 weeks of gestation), neonatal death (death of a formed fetus alive at birth in the first 28 days of life), preterm delivery before 37 weeks of gestation, preeclampsia, eclampsia or HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet).
Results: We have analyzed 164 singleton PAPS/aPL carrier pregnancies (22 aPL carriers - 13%) in 128 patients: all were treated with combination therapy (LDA+LMWH), and in 30 HCQ was added. 58 pregnancies (43%) had low levels of preconception C3/C4. A triple aPL positivity was observed in 54 pregnancies, 14 of them were treated with combination therapy + HCQ. When considering the whole cohort, the addition of HCQ had not significantly improved the gestational outcome. Further stratification was performed on the basis of complement consumption. In the group of patients with preconception low C3/C4 levels the addition of HCQ had not significantly improved pregnancy outcome. We have lastly evaluated 40 pregnancies with a high-risk profile (triple aPL positivity and complement consumption), in which we have found that HCQ significantly improved gestational outcome (p=0.018, Table 1).
This observation could not be confirmed in patients with single or double aPL positivity.
Conclusion: The study shows that administering HCQ in addition to combination therapy can improve gestational outcome in aPL/PAPS high-risk patients. This observation confirms that HCQ exerts a beneficial effect on aPL pregnancies by complement inhibition as it was shown in animal models. In addition, our results provide the clinicians a useful tool to implement conventional treatment in patients at high risk of pregnancy complication or loss.

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Table 1. Relationship between APO, therapy during pregnancy and risk profile.

	All pregnancies (n=164)			**Reduced C3/C4 (n=58)**			**Triple aPL+ and reduced C3/C4 (n=40)**		
					LDA+LMWH+HCQ		**LDA+LMWH**	**LDA+LMWH+HCQ**	
	LDA+LMWH (n, %)	**LDA+LMWH+HCQ (n, %)**	**p**	**LDA+LMWH (n, %)**	**(n, %)**	**p**	**(n, %)**	**(n, %)**	**p**
APO	62 (46%)	16 (53%)	ns	32 (68%)	4 (36%)	ns	23 (77%)	3 (30%)	0.018
No APO	72 (54%)	14 (47%)		15 (32%)	7 (64%)		7 (23%)	7 (70%)	
Total	134	30		47	11		30	10	

SLE, Sjögren's and APS - clinical aspects (other than treatment)

POS0722 CLONAL HEMATOPOIESIS OF INDETERMINATE POTENTIAL AND ACCELERATED ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS (HEMATOPLUS STUDY)

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Background: The detection of somatic mutations in genes of myeloid cells in asymptomatic patients - defining clonal hematopoiesis of indeterminate potential (CHIP) - predisposes to cardiovascular events (CVE) in the general population.
Objectives: We aimed to determine whether CHIP was associated with CVE in SLE patients.
Methods: The study is an ancillary study of the randomized, double-blind, placebo-controlled, multicenter trial PLUS study conducted from June 2007 through August 2010 at 37 centers in France involving 573 SLE patients. The search for somatic mutations by high-throughput sequencing of 53 genes involved in clonal hematopoiesis was performed on genomic DNA collected at PLUS inclusion. The CHIP prevalence was assessed in SLE and in a retrospective cohort of 479 patients free of hematological malignancy. The primary outcome was the incident CVE in SLE.
Results: Screening for CHIP was performed in 438 SLE patients (38 [29-47] years, 91·8% female). Overall, 63 somatic mutations were identified in 47 patients defining a CHIP prevalence of 10·7% in SLE. Most SLE patients (78·7%) carried a single mutation. Most variants (62·5%) were located in the *DNMT3A* gene. CHIP was associated with age, age at SLE diagnosis and a lower frequency of antiphospholipid antibodies. CHIP occurred more than 20-years earlier (p<0·00001) in SLE than in controls. The detection of CHIP at inclusion was not associated with the occurrence of CVE during follow up (HR= 0·42 (0·06 – 3·21), p=0·406).
Conclusion: The prevalence of CHIP is high in SLE with respect to age but was not associated with incident CVE.
Disclosure of Interests: None declared
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POS0723 DIETARY HABITS AND THE IMPACT ON CLINICAL FEATURES IN PRIMARY SJOGREN'S SYNDROME

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Background: In recent years, increasing evidence on the role of diet on chronic conditions, including cardiovascular diseases (CV) and rheumatic and musculoskeletal diseases (RMDs) has accrued. Most studies exploring the possible role of nutrients and dietary patterns on both the risk to develop RMDs in the general population and the natural history of the disease in patients with established RMDs pertain to rheumatoid arthritis. Data in patients with established primary Sjogren's syndrome (pSS) is lacking.
Objectives: To explore dietary habits and their relationship with metabolic and inflammatory features in a cohort of patients with established pSS.
Methods: Consecutive patients with pSS were recruited and dietary habits over the previous 12 months were explored. Adherence to the Mediterranean Diet was assessed with the 14-item PREvencion con DIeta MEDiterranea' (PREDIMED) tool and the 28-item Mediterranean Lifestyle (MEDLIFE) index. Adherence to the Dietary Approaches to Stop Hypertension (DASH) was estimated using a score based on 8 food items. Tea/herbal tea and coffee intake were also explored and clinical/serological records were retrospectively collected.
Results: We enrolled 105 patients with pSS (95% females) with a mean age of 59 years. According to the PREDIMED score 32 (31%) patients had a good adherence to the Mediterranean Diet, 64 (61%) a medium adherence and only 9 (8%) a poor adherence. According to the DASH score, 74 (71%) patients had low adherence and 31 (29%) had high adherence. When dividing patients according to the extent of adherence to either of the dietary patterns and correlating the diet adherence scores to disease specific variables some associations emerged. The PREDIMED score was inversely correlated with disease activity, as measured by the EULAR Sjögren's syndrome disease activity index (ESSDAI) (Spearman's rho=-0.27, p= 0.009) and ClinESSDAI (Spearman's rho=-0.26, p=0.01) revealing that a higher adherence to the Mediterranean Diet was associated with lower disease activity. With regard to the MEDLIFE, the total of blocks 1 and 2, that are related to Mediterranean foods and dietary habits, did not correlate with the total of block 3 (related to other healthy habits such as physical activity), meaning that the patients adhering the most to the Mediterranean Diet not necessarily had an overall healthy lifestyle. Adherence to DASH was not associated with disease activity. With regard to individual nutrients, fish consumption was associated with a lower prevalence of hypertension as observed in the general population. Higher intake of red meat was associated with higher values of self-reported pain (Spearman's rho=-0.3; p=0.01) while high wholegrain intake was associated with a lower number of coexisting CV risk factors (OR=0.7; 95% CI=0.52-0.97; p=0.03).
Conclusion: Adherence to the Mediterranean Diet, with particular attention to high intake of fish and wholegrains and low intake of red meat, may be beneficial on various domains in pSS, such as the CV system and the inflammatory environment, and as such should be recommended to patients with this disease.
Disclosure of Interests: None declared
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POS0724 RISK FACTORS FOR CORONARY ARTERY DISEASE IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTI-CENTER, RETROSPECTIVE, COHORT STUDY

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Background: Coronary artery disease (CAD) not only has an increased prevalence but also is a major cause of premature mortality in systemic lupus erythematosus (SLE) [1, 2]. However, information is limited regarding the risk factors for CAD in Chinese patients with SLE.
Objectives: To assess the risk factors for CAD in Chinese patients with SLE.
Methods: This multi-center, retrospective, cohort study included 3778 consecutive SLE patients, with CAD (CAD group) or without a medical history of CAD (control group). CAD was defined as a coronary stenosis ≥50% in any major epicardial coronary vessel detected by coronary angiography or a history of myocardial infarction confirmed by medical records. General parameters, clinical features, laboratory tests and medical therapies were compared between groups, and the risk factors for CAD in SLE were analyzed by logistic regression analysis.
Results: The age at baseline was older, male ratio was higher and body mass index was greater in CAD group (all *P*<0.001). Traditional CAD risk factors including diabetes mellitus, hypertension, dyslipidemia, family history of CAD and smoking were more common in CAD group (all *P*<0.001) (Figure 1). SLE Disease Activity Index 2000 was greater (*P*=0.012), hyperuricemia and elevated C-reactive protein (CRP) were more prevalent (both *P*<0.001), and an increased corticosteroids' usage (*P*=0.018) was detected in CAD group (Table 1). Binary logistic regression analysis showed hyperuricemia (odds ratio: 3.082, 95% confidence interval: 1.283-7.403; *P*=0.012) and CRP (odds ratio: 7.248, 95% confidence interval: 2.931-17.925; *P*<0.001) were independent risk factors for CAD in SLE patients.

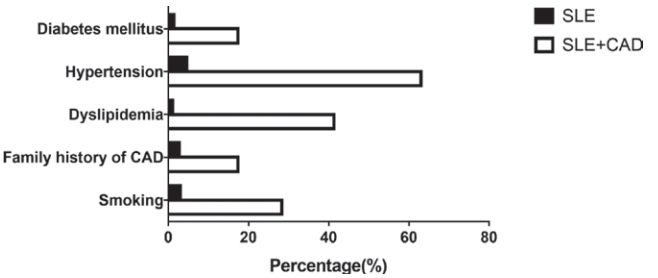

Figure 1. Comparison of traditional risk factors in SLE patients between CAD group and control group. Abbreviations: CAD, coronary artery disease; SLE, systemic lupus erythematosus. All *P*<0.001.

Table 1. Comparison of clinical features in SLE patients between CAD group and control group.

Parameters	Control group (n=3732)	CAD group (n=46)	*P*
Age at baseline [years, median (P25, P75)]	35.00 (29.00, 45.00)	59.50 (50.25, 67.75)	***<0.001***
Male, n (%)	296 (7.94)	11 (23.91)	***<0.001***
Disease duration [years, median (P25, P75)]	8.00 (4.00, 12.00)	10.00 (4.00, 19.00)	0.173
Body mass index [kg/m^2, median (P25, P75)]	21.77 (19.63, 24.16)	23.50 (22.09, 25.36)	***<0.001***
Renal disorder, n (%)	1737 (46.57)	9 (19.57)	***<0.001***
Neurologic disorder, n (%)	595 (15.95)	3 (6.52)	0.082
Thrombocytopenia, n (%)	859 (23.03)	8 (17.39)	0.366
SLEDAI-2K [median (P25, P75)]	3.00 (0.00, 8.00)	5.50 (1.50, 14.00)	***0.012***
Elevated creatinine, n (%)	295 (7.91)	10 (21.74)	***0.002***
Hyperuricemia, n (%)	209 (5.60)	16 (34.78)	***<0.001***
Elevated ESR, n (%)	951 (25.5)	22 (47.83)	***0.001***
Elevated CRP, n (%)	210 (5.63)	15 (32.61)	***<0.001***
Positive aPL, n (%)	734 (19.68)	11 (23.91)	0.474
Corticosteroids, n (%)	2752 (73.78)	41 (89.13)	***0.018***
Immunosuppressants, n (%)	2950(79.09)	37 (80.43)	0.823

Abbreviations: aPL, antiphospholipid antibody; CAD, coronary artery disease; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000. *P* <0.05 are shown as italics and bold.

Conclusion: Hyperuricemia and CRP are independent risk factors for CAD in SLE patients. This study highlights the association between hyperuricemia, CRP and CAD burden in SLE, and might provide a modifiable perspective on improving SLE outcomes.

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POS0725 VALIDATION OF SJÖGREN'S SYNDROME SCREENING QUESTIONNAIRE (SSSQ) IN A COHORT OF PATIENTS WITH SICCA SYMPTOMS

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Background: ACR/EULAR 2016 classification criteria for Sjögren disease (SS) [1] use 5 standard questions on ocular and oral sicca symptoms as an entrance criteria. However, these questions do not differentiate between SS and non-SS sicca etiology. Recently, a new 5-item Sjögren's Syndrome Screening Questionnaire based on SICCA study data was designed for the use in clinical practice, better differentiating SS from non-SS sicca patienents.[2]

Objectives: We aimed to validate the SSSQ in our population with sicca symptoms.

Methods: Our study cohort represented 535 patients referred to UMC Ljubljana during the 3-year period Jan/2016 to Dec/2019 with suspected SS. All subjects underwent at that time a standardized SS diagnostic procedure, including 5 standard sicca questions, Schirmer test, Rose Bengal test, unstimulated salivary flow test, salivary gland ultrasound, immunoserological and lip biopsy. In Sep - Oct 2021 all subjects were contacted by phone to fulfil the new SSSQ (5 questions resulting in 0-11 points: cut-off for SS ≥7 points). The performance of SSSQ recognizing SS was assessed using ACR/EULAR 2016 classification criteria as gold standard test for SS diagnosis.

Results: 415 out of 525 subjects agreed to participate in the study (384 (92.5%) females, mean (SD) age 57.6(13.8)), the rests either declined (21), died (2) or could not be reached (97). Based on the ACR/EULAR 2016 criteria SS was diagnosed in 127 (30.6%) and excluded in 288 subjects. 376/415 (90.6%) subjects responded positively on 5 standard sicca questions (110 with and 266 without SS). In the new SSSQ 129 (31.1%) subjects (54 with and 75 without SS) responded positively (reached ≥7 points). The performance of SSSQ recognizing SS is presented in Table 1.

Table 1. Diagnostic accuracy of SSSQ (Sjögren's Syndrome Screening Questionnaire) and ACR/EULAR 2016 sicca questions in our cohort. PLR Positive Likelihood Ratio; NLR Negative Likelihood Ratio; PPV Positive Predictive Value; NPV Negative Predictive Value;

Statistics	SSSQ	Standard sicca questionairre
	Value (95% CI)	Value (95%CI)
Sensitivity	42.5% (33.8 to 51.6%)	86.6% (79.4 to 92.0%)
Specificity	73.7% (68.5 to 78.9%)	7.6% (4.9 to 11.3%)
PLR	1.4 (1.2 to 2.2)	0.9 (0.9 to 1.0)
NLR	0.8 (0.7 to 0.9)	1.8 (1.0 to 3.2)
PPV	41.9% (35.2 to 48.8%)	29.3% (27.7 to 30.9%)
NPV	74.5% (71.2 to 77.5%)	56.4% (41.6 to 70.2%)
Accuracy	64.3% (59.5 to 69.0%)	31.8% (27.4 to 36.5%)
AUC	0.58 (0.52-0.64)	0.52 (0.46-0.57)

Conclusion: SSSQ showed higher specificity and better diagnostic accuracy compared to current standard questionnaire in a cohort of sicca patients.

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POS0726 HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA AND POTENTIAL APPLICATIONS OF THE MEXICAN REGISTER OF LUPUS.

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Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease, characterized by a wide variety of clinical manifestations, as well as continuous relapses and exacerbation of symptoms. This complex panorama complicates an early and proper diagnosis, treatment, and follow-up of the people with SLE and therefore has a significant impact on their health-related quality of life (HRQoL). Although the importance of assessing HRQoL in SLE has become evident in recent years, in Mexico there is no epidemiological surveillance system nor national registry that conveys this information.

Objectives: To evaluate health related quality of life (HRQoL) in Mexican individuals with SLE using the data from the Mexican Register of Lupus (Lupus RGMX).

Methods: The Mexican Lupus Registry (Lupus RGMX) is an ongoing online register. This cohort includes sociodemographic and clinical data of Mexican individuals with SLE. In this study we assessed and compared HRQoL in patients with SLE and a matched control group of Mexican individuals without SLE diagnosis. We estimated QoL using the World Health Organization Quality of Life (WHOQOL-bref) and Short Form-36 (SF36) questionnaires. For both WHOQOL-bref and SF36, higher scores mean better HRQoL. Statistical analysis was performed using R 4.1.2 (R Core Team, 2021).

Results: A total of 631 SLE and 272 control registers were analyzed (Table 1). Significant lower scores on HRQoL were observed on participants with SLE for both SF36 and WHOQOL-bref questionnaires, compared with the matched control group. All score components were lower in SLE individuals. Physical role functioning, bodily pain and general health exhibited the lowest scores among

the SF36 factors, whereas physical factor was the lowest for WHOQOL-bref (Table 1).

Table 1. SF36 and WHOQOL-bref median scores (25-75 IQR) of SLE participants and controls.

	Controls	SLE	*p-value*
	(n=272)	(n=631)	
Female sex n (%)#	211 (77.6%)	596 (94.4%)	<0.001
Age*	28 (24-35)	35 (28-43)	<0.001
*SF36 (max 100 points per function) **			
Physical functioning	100 (95-100)	65 (45-85)	<0.001
Physical role functioning	100 (100-100)	25 (0-100)	<0.001
Bodily pain	84 (61-100)	31 (22-52)	<0.001
General health	77 (62-100)	35 (20-47)	<0.001
Vitality	65 (50-100)	40 (25-55)	<0.001
Social functioning	100 (62.5-100)	50 (37.5-75)	<0.001
Emotional role functioning	100 (66.7-100)	66.7 (0-100)	<0.001
Mental health	76 (60-100)	56 (42-74)	<0.001
*WHOQOL-bref (max 20 points per function) **			
Physical	16.6 (14.8-17.7)	11.4 (9.1-13.1)	<0.001
Psychological	15.3 (13.3-19.3)	12.7 (10.7-14.7)	<0.001
Social relations	14.7 (12-16)	12 (9.3-14.7)	<0.001
Environmental	15.5 (14-17)	13 (11-15)	<0.001

Chi-square test, *U Mann-Whitney test

Conclusion: In Mexican people with SLE, a significant decrease in HRQoL was detected compared with controls. The implementation of a national register in Mexico (Lupus RGMX) will provide additional psychosocial and clinical information to deepen our knowledge of this disease.

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POS0727 IMPACT OF AIR POLLUTANTS ON DISEASE ACTIVITY AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN MALAYSIA

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Background: Systemic Lupus erythematous (SLE) is an autoimmune disease with a wide spectrum of clinical manifestations and characterized by remission and flares. Recent epidemiological studies postulated that air pollution confers an increased risk of flare in various autoimmune diseases. Haze is a common phenomenon afflicting Southeast Asia (SEA), including Malaysia, and has occurred almost every year within the last few decades.

Objectives: This study was aimed to determine the correlation and association between SLE disease activity with exposure to inhaled Particulate Matter (PM_{10}) and Nitrogen Dioxide ($NO_{2)}$.

Methods: SLE patients who attended rheumatology and nephrology clinic in University Kebangsaan Malaysia Medical Centre (UKMMC) from June 2019 until March 2020 were recruited. Their medical records were reviewed for retrospective assessments of the disease activity using the Modified-SLE Disease Activity Index (M-SLEDAI) and The British Isles Lupus Assessment Group (BILAG 2004) index from January 2015 until September 2019. Clinic visits with presence of infection or recent change of immunosuppressive treatment of ≤ 3 months were excluded. The average of daily concentrations of inhaled PM_{10} ($\mu g/m^3$), and NO_2 (ppb) were evaluated within 30 days preceding the clinic visits, and the data was obtained from Department of Environment (DOE) Malaysia. Comparison of the means was performed by Student's t-test; and the correlations between PM_{10}, and NO_2 were determined by Pearson's correlation coefficient. The associations between the effect of daily pollutant concentrations on M-SLEDAI and BILAG 2004 scores were analyzed using the generalized estimating equation (GEE) model, while considering fixed effects for repeated measures.

Results: A total of 46 patients were recruited with 603 clinic visits were recorded. A significantly higher NO_2 level was found in active disease patients with M-SLEDAI score of ≥ 4 (33.09 ± 9.15 vs 31.09 ± 9.79, p=0.32), and presence of BILAG B and/or A (score ≥ 8), 35.03± 2.97 vs 31.1 ± 9.8, p= 0.003). There were positive correlations between M-SLEDAI scores (r_s 0.128, p=0.002) and BILAG scores with NO_2, (r_s 0.142, p<0.001). In the GEE analysis, significant correlations were found between M-SLEDAI score [OR 1.27 (95% C.I: 1.06-1.53), p=0.01] and BILAG score with NO_2 [OR 1.47 (95% C.I: 1.15-2.1.88), p=0.002].

Conclusion: Our study suggests that air pollutant NO_2 exposure 30 days prior to clinic visit is associated with high disease activity among patients with SLE in Malaysia. Further prospective study is warranted to confirm this finding.

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POS0728 ASSOCIATION BETWEEN TREATMENT GOAL ACHIEVEMENT AND GRIT PERSONALITY CHARACTERISTICS OF ATTENDING PHYSICIAN IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTICENTER CROSS-SECTIONAL STUDY

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Background: In clinical practice for systemic lupus erythematosus (SLE), the concept of "treat to target" has been introduced with an established goal of reducing glucocorticoid dose as much as possible while controlling disease activity. Although it has been shown that various personality characteristics of patients with SLE affect their disease activity and damage, it is not clear whether the personality characteristics of attending physicians affect the outcomes of patients with SLE. Grit is a personality trait characterized by perseverance and passion for achieving long-term goals.

Objectives: This study aims to evaluate the relationship between attending physicians' grit personality characteristics and treatment goal achievements in patients with SLE.

Methods: A cross-sectional study was conducted on 386 patients with SLE in five referral hospitals in Japan. The main exposure was the "perseverance" and "consistency" (scores 1-5) of the attending physicians, as measured by the Short Grit Scale, and the primary outcome was the achievement of the Lupus Low Disease Activity Score (LLDAS). Considering the clustering of achievement of LLDAS by each attending physician, the association between attending physician's personality and LLDAS was analyzed by logistic regression with cluster robust variance estimation. Odds ratios to assess the relationship between perseverance and consistency and LLDAS were estimated with adjustment for confounders (age, sex, disease duration, hydroxychloroquine use, immunosuppressant use, and Systemic Lupus International Collaborating Clinics-Damage Index). We used multiple imputation to handle the uncertainty caused by missing values of potential confounders on the assumption of missing at random.

Results: The median age of the patients was 45 years (interquartile range[IQR],36-56), 88% were female, and the median disease duration was 152 months(IQR, 80-240). Thirty-seven doctors were in charge of the patients (1-79 patients/each doctor). The median age of the attending physicians was 40 years (IQR, 35-43), and 19% were female. The median perseverance and consistency scores of attending physicians were 3.1 (IQR, 3.0-3.5) and 3.3 (IQR, 2.8-3.8), respectively. Of the enrolled patients, 154 (40%) had achieved LLDAS. The attending physicians with a lower consistency score of <3 were more frequent in the patients who achieved LLDAS (40% vs. 29%, p=0.026). The lower consistency score of attending physicians was still related to LLDAS independently (adjusted odds ratio 1.63, 95% confidential interval 1.17-2.27). There was no association between the achievement of LLDAS and perseverance.
Conclusion: The grit personality characteristics of the attending physician may affect the achievement of treatment goals in patients with SLE.
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POS0729 FOOT DISORDERS ASSOCIATED WITH JACCOUD'S ARTHROPATHY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A DESCRIPTIVE STUDY.

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Background: Systemic lupus erythematosus (SLE) is a chronic disease of autoimmune origin mediated by autoantibodies, affecting various organs[12]. 95% of patients with SLE develop musculoskeletal involvement[1], most of the time as arthralgia or non-erosive arthritis, mainly affecting the hands and knees. A subgroup of patients with lupus that is seen with increasing frequency, late develops a deforming arthropathy as a result of the laxity of ligaments and peritendinous apparatus that produces a joint subluxation. The foot is a highly affected structure that may initially go unnoticed, but it leads to significant disability.
Objectives: To know the prevalence of foot problems in a sample of patients with SLE.
Methods: A cross-sectional study design. Forty-seven subjects with a diagnosis of SLE were consecutively recruited in a Rheumatology Unit between March and May 2021. The inclusion criteria were: patients with a diagnosis of SLE according to the EULAR / ACR 2019 criteria, with at least one year of evolution and age equal to or greater than 18 years. A Rheumatology nurse collected information on socio-demographic data and the characteristics of the feet regarding the musculoskeletal system, skin, appendages, circulatory system and nervous system using a pre-designed questionnaire. The study was approved by the Ethics Committee, following the recommendations of the Declaration of Helsinki and the legal regulations in force in our country regarding clinical research and the current Good Clinical Practice standards. All participants were informed of the objectives and methods of the study and signed the informed consent. Descriptive statistical analysis.
Results: 47 subjects participated (93.6% women) with a mean age (SD) of 49.2 (10.8) years (range 23-66 years). Thirty-five (74.5%) patients presented a low internal longitudinal arch in one or both feet, 19 (40%) Hallux Abductus Valgus (HAV) and 30 (63.8%) presented alterations in the other toes. Seventeen (36.2%) patients had pain in the hindfoot, 16 (34.0%) in the midfoot, 17 (36.2%) in the forefoot, and 14 (29.8%) in the toes. Stiffness in the feet appeared in 8 (17%) while joint swelling appeared in only one (2.1%). On the skin and appendages: 10 (21.3%) showed nail lesions and 39 (80.3%) presented some dermal lesion of the hyperkeratosis type due to friction or poor support. In the circulatory system there were no findings. Two (4.3%) patients had less bilateral sensitivity in the examination of the nervous system in the feet.
Conclusion: The most prevalent foot problems affect the musculoskeletal system and are related to Jaccoud arthropathy, especially the sinking of the internal longitudinal arch. Hyperkeratosis associated with poor foot support were also very prevalent.

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POS0730 A BETTER SELF-EFFICACY IS PREDICTIVE OF BETTER HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS. DATA FROM A LATIN AMERICAN MESTIZO COHORT

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Background: Systemic lupus erythematosus (SLE) patients have a worse health-related quality of life (HRQoL) than the general population. This seems to be related to patients characteristics like age, poverty, behavioral issues rather than to disease activity or damage. Self-efficacy is defined as individual's confidence on performing a task and could impact on patient-reported outcomes.
Objectives: To determine the possible predictive value of self-efficacy on HRQoL in SLE patients.
Methods: SLE patients from a single-center prevalent cohort were included. Self-efficacy was ascertained with six instruments of the Patient-Reported Outcomes Measurement Information System (PROMIS) Self-efficacy for Managing Chronic Conditions. Instruments included were general self-efficacy, and self-efficacy for managing emotions, managing symptoms, managing daily activities, managing social interactions and managing medications and treatments. For PROMIS instruments, a score of 50 is the average for a clinical population (people with a chronic condition), a higher score indicates that the respondent has greater self-efficacy. HRQoL was ascertained with the physical and mental component summary (PCS and MCS) measures of the Short-Form 36 (SF-36). Generalized estimating equations were performed, using as outcome the PCS or MCS in the subsequent visit, and the self-efficacy instrument in the previous visit; multivariable models were adjusted for possible confounders (age at diagnosis, gender, socioeconomic status, SLEDAI-2K, SLICC/ACR damage index, disease duration at baseline, prednisone daily dose, antimalarial and immunosuppressive drugs use and PCS or MCS in the previous visit). All the confounders were measured in the same visit than the self-efficacy instrument.
Results: Two-hundred and nine patients for a total of 564 visits were included; 194 (92.8%) patients were women, mean age at diagnosis was 36.4 (14.0) years and disease duration at baseline was 6.5 (6.0) years. At baseline, PCS was 55.0 (22.3) and MCS was 53.9 (20.4). At baseline, mean general self-efficacy was 47.2 (10.4), self-efficacy for managing emotions was 44.6 (8.0), for managing symptoms was 47.7 (8.2), for managing daily activities was 45.5 (7.5) for managing social interactions was 42.9 (7.9) and for managing medications and treatment was 43.9 (7.0). In the multivariable models a better PCS was predicted by a better general self-efficacy, and self-efficacy for managing symptoms, managing social interactions and managing medications and treatments and a better MCS was predicted by a better self-efficacy for managing symptoms, managing daily activities, managing social interactions and managing medications and treatments. These data are depicted in Table 1.
Conclusion: A better self-efficacy is predictive of a subsequent better HRQoL, even after adjustment for possible confounders. These results should encourage clinicians to develop strategies to improve self-efficacy in SLE patients.
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Table 1. The predictive value of self-efficacy on HRQoL in SLE patients

	PCS				MCS			
	Univariable model		Multivariable model		Univariable model		Multivariable model	
	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value
General	**0.98 (0.11)**	**<0.001**	**0.18 (0.08)**	**0.037**	**0.92 (0.11)**	**<0.001**	0.20 (0.10)	0.051
Managing emotions	**0.99 (0.16)**	**<0.001**	0.12 (0.11)	0.257	1.05 (0.15)	<0.001	0.17 (0.11)	0.161
Managing symptoms	**1.26 (0.14)**	**<0.001**	**0.25 (0.11)**	**0.021**	**1.19 (0.13)**	**<0.001**	**0.32 (0.12)**	**0.006**
Managing daily activities	**1.59 (0.13)**	**<0.001**	0.22 (0.13)	0.091	**1.44 (0.13)**	**<0.001**	**0.39 (0.13)**	**0.002**
Managing social interactions	**0.77 (0.15)**	**<0.001**	**0.27 (0.09)**	**0.002**	**0.86 (0.14)**	**<0.001**	**0.37 (0.10)**	**<0.001**
Managing medications and treatment#	**0.71 (0.17)**	**<0.001**	**0.20 (0.10)**	**0.046**	**0.65 (0.16)**	**<0.001**	**0.24 (0.10)**	**0.016**

PCS: Physical component summary. MCS: Mental component summary. SE: Standard error. * Adjusted for age at diagnosis, gender, socioeconomic status, SLEDAI-2K, SLICC/ACR damage index, disease duration at baseline, prednisone daily dose, antimalarial and immunosuppressive drugs use and PCS or MCS in the previous visit. #Only patients taking at least one medication were included in these analyses.

POS0731

ASSOCIATION OF PATIENT-REPORTED OUTCOMES WITH TYPE I INTERFERON GENE SIGNATURE FROM THE INTERNATIONAL SYSTEMIC LUPUS ERYTHEMATOSUS PROSPECTIVE OBSERVATIONAL COHORT STUDY (SPOCS)

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Background: The aim of the Systemic Lupus Erythematosus Prospective Observational Cohort Study (SPOCS) is to examine the disease course of patients with systemic lupus erythematosus (SLE) in relation to their type I interferon gene signature (IFNGS) status.[1] IFNGS has been associated with SLE disease activity.[2]
Objectives: To identify associations between IFNGS status and patient-reported outcomes (PROs) among patients receiving clinical care while enrolled in SPOCS.
Methods: This noninterventional, international, prospective, observational cohort study included adult patients (≥18 years) with moderate to severe SLE receiving standard therapy. Short Form 36 Health Survey version 2 (SF-36; 0–100), Lupus Quality of Life (LupusQoL; 0–100) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F; 0–52) were assessed at baseline, 6 months, and 12 months. Higher scores indicate better outcomes. Analyses were stratified by high or low IFNGS status (4-gene test) at baseline.
Results: Of 827 patients, mean (standard deviation [SD]) age was 45.1 (14.0) years, 771 (93%) were female, 525 (63%) were IFNGS high, and 219 (26%) were IFNGS low. IFNGS-high patients were younger than IFNGS-low (mean [SD] 43.0 [13.7] vs 50.7 [12.9] years), had fewer comorbidities (83% vs 91%) and similar baseline disease activity (mean [SD]: SLE Disease Activity Index 2000, 9.8 [4.3] vs 9.2 [5.2]; Physician's Global Assessment, both 1.5 [0.6]). At baseline, there were some differences in PROs between IFNGS-high and -low patients. At Month 12, changes in most domains did not meet the minimal clinically important difference (MCID). Slight improvement was observed only in selected domains in the IFNGS-high group. This group was younger and had fewer comorbidities at baseline. (Table 1, Figure 1).
Conclusion: In this cohort study, patients with moderate to severe SLE had poor health status, health-related quality of life, and fatigue. A clinically meaningful change was not met in most PROs, suggesting patients continue to have a high need for improved treatment options.
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Figure. Spydergram of SF-36 Domain Scores at Baseline and Year 1 by IFNGS status (High and Low)

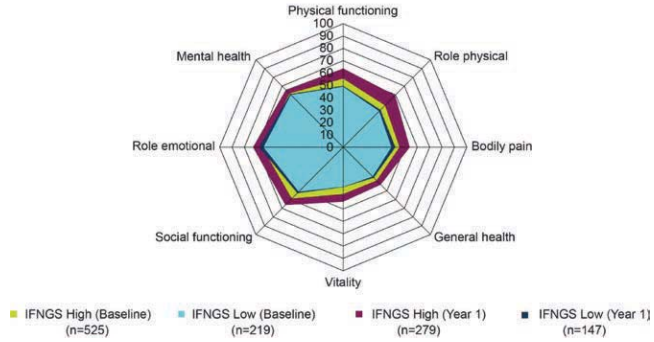

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Table 1. PRO Scores at Baseline and Month 12 by IFNGS Status

	Baseline			Month 12			Change From Baseline			
		IFNGS High	IFNGS Low		IFNGS High	IFNGS Low				
PRO	Total (n=810)	(n=525)	(n=219)	Total (n=431)	(n=279)	(n=147)	Total	IFNGS High	IFNGS Low	MCID (≥)
SF-36										
Physical Component Summary	37.4 (10.5)	38.3 (10.5)+	35.2 (10.6)1	39.8 (10.8)	41.7 (10.4)+	35.7 (10.8)	2.3 (7.6)	3.0 (8.1)*	0.6 (6.4)	2.5
Mental Component Summary	43.2 (11.6)	43.6 (11.7)	42.7 (11.6)	44.9 (11.2)	45.9 (10.6)	43.4 (11.5)	0.9 (9.2)	1.4 (9.6)	-0.3 (8.4)	2.5
LupusQoL										
Physical health	56.4 (27.4)	58.1 (27.0)+	52.1 (27.7)	60.5 (26.9)	65.0 (25.3)+	52.5 (27.7)	2.6 (18.1)	5.0 (19.2)*	-1.4 (16.4)	3.4
Pain	54.3 (30.3)	55.7 (29.8)	50.2 (30.8)	61.4 (28.5)	66.0 (26.5)+	52.6 (29.1)	5.4 (23.8)	8.1 (25.2)	0.7 (21.3)	8.5
Planning	61.4 (32.2)	63.7 (31.8)+	57.0 (32.2)	66.3 (29.6)	70.8 (27.8)+	58.5 (30.8)	2.9 (24.4)	4.2 (24.7)	-1.0 (22.9)	6.5
Intimate relationships	58.0 (34.8)	61.2 (34.1)+	50.9 (34.8)	59.8 (33.9)	65.6 (32.3)+	50.6 (34.7)	-0.6 (24.5)	-0.7 (25.9)	-0.8 (22.3)	9.2
Burden to others	50.7 (32.6)	50.7 (32.6)	50.4 (33.5)	56.4 (30.7)	59.7 (29.5)	51.8 (31.7)	3.1 (25.4)	5.6 (26.0)*	0.1 (23.9)	5.3
Emotional health	66.3 (25.6)	66.1 (26.0)	67.8 (24.8)	71.1 (24.7)	72.9 (23.8)	69.2 (24.7)	1.8 (19.4)	3.1 (20.3)	-0.5 (18.1)	3.4
Body image	62.6 (29.4)	61.0 (30.1)	66.4 (28.3)	68.2 (27.6)	70.3 (27.4)	65.1 (27.0)	2.0 (23.9)*	4.1 (24.3)*	-0.4 (22.1)	1.1
Fatigue	48.6 (27.8)	49.9 (27.6)	45.5 (28.2)	53.7 (26.9)	57.4 (26.2)+	46.9 (25.7)	2.1 (19.3)	3.5 (20.0)	-0.9 (18.7)	3.9
FACIT-F	25.8 (13.4)	26.9 (13.4)+	23.4 (12.9)	28.7 (13.2)	31.1 (12.7)+	24.6 (12.9)	2.3 (9.6)	3.2 (10.2)	0.6 (8.5)	4.0

Data are mean (SD). Asterisks (*) indicate changes from baseline ≥ MCID. +Comparison between high and low IFNGS status by Mann-Whitney U test (nominal p-value<0.01). Data for n are patients per subgroup and do not reflect responses per PRO assessment.

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POS0732 CLINICAL, HISTOLOGICAL, AND SEROLOGICAL FEATURES ASSOCIATED WITH SALIVARY GLAND ULTRASOUND IN PRIMARY SJÖGREN'S SYNDROME

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Background: Salivary gland ultrasound (SGUS) is a simple and non-invasive procedure that is readily available and supplies important information on the major salivary glands. Several recent studies have assessed SGUS as a tool for diagnosing primary Sjögren's syndrome (pSS), and have reported its association with different features in pSS.

Objectives: To investigate the association of SGUS findings with clinical, histological, and serologic features of pSS in our cohort. In addition, we include monospecific antibody determination to Ro60 or Ro52.

Methods: Patients with pSS were determined according to the American-European Consensus Group (AECG) criteria for pSS. A total of 53 of these pSS patients underwent SGUS evaluation. We considered SGUS score based on parenchymal homogeneity, presence of hypoechogenic areas, and clearness of posterior glandular border of salivary glands. The score of the highest graded gland was considered and a score ≥2 was defined as a positive SGUS, according to OMERACT US-SG scoring [1]. Patients were classified into two groups according to positive vs. negative SGUS. Demographic, clinical, histopathological, and laboratorial data were collected and compared between the groups. Categorical variables were compared using the Chi-square test or Fisher's exact test when the conditions for Chi-square test were not met, and continuous variables were compared using Student's t-test with Welch's correction. p-values <0.05 were considered significant.

Results: Study participants were predominantly women (98%) and had a mean age of 60.2 years. SGUS was positive in 32 (63%) pSS patients, they were all women and had a mean age of 59 years. Positive SGUS was associated with objective evidence of ocular involvement (defined as a positive result for at least one of the ocular tests, p<0.001), time of evolution of xerophthalmia at diagnosis (mean 5.8 years vs. 2.2 years, p=0.037), pathological result of the labial salivary gland biopsy when it was performed (p<0.001), and the presence in the serum of both antiRo60 and antiRo52 antibodies (p=0.004), antiLa antibody (p=0.008) and ANA titer ≥1:320 (p<0.001). No significant differences were found between positive SGUS and negative SGUS patients regarding the presence of xerophthalmia nor xerostomia, time of evolution of xerostomia at diagnosis, episodes of parotid inflammation, abnormal salivary scintigraphy, nor the presence in the serum of monospecific antiRo52 nor antiRo60 in the absence of each other, nor positive rheumatoid factor.

Conclusion: Positive SGUS was associated in pSS patients with objective evidence of pathological ocular function, histopathology of minor salivary glands, and serology of pSS, specifically the presence of both antiRo52 and antiRo60 antibodies. In our cohort, no significant association was found regarding xerostomia, episodes of parotid inflammation, nor objective evidence of oral involvement. Thus, SGUS could be a useful tool to establish objective salivary gland involvement, independently of oral symptoms and other oral tests.

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POS0733 DISCORDANCE BETWEEN PATIENT GLOBAL ASSESSMENT AND PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN THE MODERATE TO SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS PROSPECTIVE OBSERVATIONAL COHORT STUDY (SPOCS)

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Background: Emphasis in clinical research and care has been placed on the need to include evaluations that reflect the perspectives of both patients and physicians.

Objectives: The goal of this study was to analyze patient and physician assessments and to determine characteristics associated with concordance and discordance of these assessments.

Methods: Baseline data of patients with moderate to severe SLE enrolled in the Systemic Lupus Erythematosus Prospective Observational Cohort Study (SPOCS)[1] were analyzed. Physician's Global Assessment (PGA) representing disease activity during the 4-week interval prior to baseline and Patient Global Assessment (PtGA) representing the impact of disease during a 1-month interval prior to baseline were independently scored on visual analogue scales (PGA 0-3; PtGA 0-100). Spearman's rank (rho) was calculated to assess their correlation. A difference between PGA and PtGA scores ≥25 points defined discordance (after rescaling PGA to 0–100).[2] Baseline characteristics associated with concordance and discordance were assessed.

Results: 827 patients were included in this analysis. At baseline, the mean PGA score was 1.5 (SD 0.6, n=824), and the mean PtGA score was 51.1 (SD 25.5, n=790). The correlation between PGA and PtGA was low (rho=0.19, *P*<0.001, n=787) (Figure 1). PGA and PtGA scores were discordant in 301 (38%) of patients. Among those patients exceeding the threshold defining discordance, 152 (19%) had higher PGA scores than PtGA scores, and 149 (19%) had higher PtGA scores than PGA scores. The subgroup of PGA-higher discordant patients had higher mean SLEDAI-2K scores, greater serological activity, and more frequent type 1 interferon gene signature positivity, whereas PtGA-higher discordant patients were more likely to be using analgesics and/or anti-depressants, had higher mean BMI and were less likely to be employed (Table 1).

Table 1. Characteristics associated with PGA and PtGA scores*a*

	Concordant (N=486)	PGA higher (N=152)	PtGA higher (N=149)	P-value-1[b]	P-value-2[b]
Age, years	45.5 (13.7)	42.7 (14.4)	46.4 (14.0)	0.022	0.043
Race, White	326 (71%)	96 (66%)	94 (69%)	0.192	0.360
BMI, kg/m²	27.6 (7.2)	25.6 (5.4)	27.2 (6.4)	0.032	0.011
Employed	249 (51%)	80 (53%)	51 (34%)	0.001	0.001
SLEDAI-2K total score	10.0 (4.8)	10.8 (5.1)	8.2 (3.0)	<0.001	<0.001
Positive ANA/anti-dsDNA	436 (90%)	143 (94%)	127 (85%)	0.012	0.041
Low Complement (C3 or C4)	132 (46%)	58 (60%)	41 (43%)	0.014	0.026
High IFNGS	313 (71%)	101 (78%)	89 (64%)	0.014	0.049
≥1 mild flare	115 (24%)	20 (13%)	45 (30%)	<0.001	0.001
≥1 moderate flare	88 (18%)	37 (24%)	23 (16%)	0.057	0.120
≥1 severe flare	39 (8%)	11 (7%)	15 (10%)	0.372	0.628
OCS daily dose				0.052	0.129
No OCS	214 (44%)	57 (38%)	62 (42%)		
>0–7.5 mg	139 (29%)	38 (25%)	52 (35%)		
>7.5–15 mg	75 (15%)	37 (25%)	18 (12%)		
>15 mg	57 (12%)	19 (13%)	17 (11%)		
Immunosuppressants	271 (56%)	80 (53%)	75 (50%)	0.690	0.467
Biologics	106 (22%)	25 (16%)	19 (13%)	0.364	0.032
Analgesics	152 (31%)	22 (14%)	46 (31%)	<0.001	<0.001
Antidepressants	123 (25%)	31 (20%)	52 (35%)	0.005	0.013

[a]Mean (SD) for continuous, n (%) for nominal variables. Missing data was <10% of patients for the variables displayed. Denominators exclude missing data. [b]*P*-value-1 compares PGA higher vs PtGA higher. *P*-value-2 compares all 3 groups. Based on the chi-squared test for categorical variables and t-test or ANOVA for continuous variables.IFNGS, type 1 interferon gene signature; OCS, oral corticosteroid; PGA, physician global assessment; PtGA, patient global assessment

Conclusion: Low correlation between PGA and PtGA suggests both should be used to acquire a broad perspective of the impact of disease on the overall health of patients. Different baseline characteristics were associated with the PGA-higher compared to the PtGA-higher discordant subgroups.

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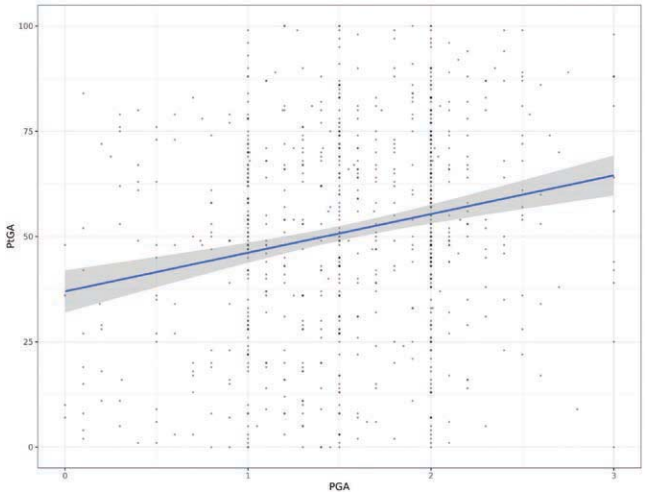
Figure. Physician (PGA) vs Patient (PtGA) Global Assessment Scores (n=787)



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POS0734 THE CLINICAL JUDGMENT FOR THE ACCEPTABILITY OF PREGNANCY IN PATIENTS WITH SEROLOGICALLY ACTIVE SLE IN JAPAN: A NATIONWIDE ONLINE SURVEY FROM THE VIGNETTE STUDY

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Background: The risk of pregnancy complications, such as gestational hypertension is high in pregnancies with SLE. In addition, the risk of flare is elevated if pregnancy occurs during the high disease activity. The EULAR recommendation provides a checklist for preconception counseling, in which patients with SLE desiring pregnancy were required the condition that the disease activity prior to pregnancy should be stable for 6-12 months in terms of serological activity (1). However, it does not provide specific criteria for serological activity so that physicians should evaluate the risk of pregnancy in each case by their clinical intuitions.

Objectives: In order to uncover the present clinical situation for the acceptability of pregnancy in patients with SLE, we performed questionnaire survey to physicians regarding to the degree of serological activity.

Methods: This cross-sectional study was performed to physicians registered with the Japanese College of Rheumatology from December 2020 to January 2021 using the online survey. The questionnaire asked about the characteristics of physicians, facilities and the permission of pregnancies with SLE using vignette scenarios. In this study, data from vignettes of women visiting a regular outpatient clinic were used. The vignettes varied in age (28 or 35 years), duration of stable disease and serological activity. Analysis methods were descriptive statistics, chi-square test. generalized estimating equations (GEE) was performed to investigate the relationship between the determining permission for pregnancy and the scenario patient's characteristics (age, period of stable disease, titer of anti ds-DNA antibody)

Results: The questionnaire was distributed to 4946 physicians, and 463 responded. Completion rate (ratio agreed to participate/finished survey) of survey was 91.1%. The median age of physicians was 46 (interquartile range (IQR) 2-10). The specialty was rheumatology (84.9%), other internal medicine (8%), and pediatrics (5.6%). There were no significant differences in patient's age about the acceptability of pregnancy (coeffficianet -0.02, 95% CI -0.17 -0.01, p=0.42). Case who had been stable for 6 months were more tolerant of pregnancy than case who had been stable for 3 months (coeffficianet 0.12, 95% CI 0.09-0.15, P<0.001) Pregnancy was not allowed in case with mild or high serological activity (mild: coefficient -0.49, 95% CI -0.29- -0.22, p <0.001, high: -0.64, 95% CI -0.65 - -0.61, p <0.001). In contrast, as many as 92 (19.2%) physicians tolerated pregnancy even in the presence of residual high anti ds-DNA antibody titers. Female physicians are significantly more cautious about pregnancy than male when patients have a serologically high activity (12% vs 37.5%, p<0.001). There were no significant differences in specialty status or clinical experience.

Conclusion: We found that even mild serological activity alone had a significant negative effect on the physician's decision to allow pregnancy. We conclude that current physicians make cautious decisions about pregnancies of patients with SLE following the recommendation. On the other hand, an additional investigation should be performed about the results of pregnancies in patients with serological abnormalities, since there are some physicians who thought that pregnancy may be acceptable for patients with only serological abnormalities if the clinical symptoms are stable.

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POS0735

EFFECT OF OSTEOPOROSIS ON MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACES) AND MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL STUDY

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Objectives: To study the effect of osteoporosis on major adverse cardiovascular events (MACEs) and mortality in a longitudinal cohort of patients with systemic lupus erythematosus (SLE).
Methods: Patients who fulfilled ≥4 1997 ACR criteria for SLE and participated in a cross-sectional study on osteoporosis in the year 2011 were studied. All patients had a dual energy x-ray absorptiometry (DXA) scan (Delphi densitometer; Hologic, Bedford, USA) performed between the years 2004-2008 and were followed in the rheumatology clinics by the same team of physicians. The incidence of new MACEs, which were defined as ischemic vascular events (acute coronary syndrome, stroke, peripheral vascular disease) documented by imaging and angiographic studies, was evaluated. Patients were stratified into 2 groups according to the presence of osteoporosis at baseline, which was defined as a DXA T score of <-2.5 or Z score <-2.0 at the hip, femoral neck or lumbar spine, or having a past history of fragility fractures. The effect of osteoporosis on the development of MACEs and mortality was studied by Cox regression analysis, adjusted for demographic characteristics, traditional cardiovascular risk factors, antiphospholipid antibodies and the use of medications.
Results: 383 SLE patients were studied (age at DXA scan 40.5±13 years; 94% women; SLE duration 8.0±7.4 years). Osteoporosis at the hip, femoral neck or spine at baseline was present in 105 patients (13 with old fragility fractures) and 8 patients had osteopenia and past fragility fractures. The demographic characteristics, prevalence of traditional atherosclerotic risk factors and antiphospholipid (aPL) antibodies (lupus anticoagulant or moderate/high titers of IgG-anticardiolipin antibodies) were not significantly different between those with osteoporosis/fracture (N=113) and without (N=270). Patients with osteoporosis/fracture were more likely to be using glucocorticoids (79% vs 62%; p=0.002) and mycophenolate mofetil/azathioprine/calcineurin inhibitors (58% vs 48%; p=0.08) but less likely to be treated with hydroxychloroquine (40% vs 51%; p=0.051) at baseline. Over a follow-up of 153±41 months, 44 new MACEs (acute coronary syndrome [n=19]; ischemic stroke [n=19]; peripheral vascular disease with digital gangrene/amputation [n=6]) developed in 42 patients. The incidence of MACEs was significantly higher in patients with osteoporosis/fracture than those without (1.59 vs 0.63/100 patient-years; p=0.001). The cumulative risk of MACEs at 3, 5 and 10 years was 6.3%, 11.7%, 14.7%, and 0.4%, 1.9%, 4.7%, respectively, in the osteoporosis and non-osteoporosis groups (log rank test; p=0.002; univariate hazard ratio 2.58[1.40-4.74]; p=0.002). In a Cox regression model, osteoporosis/fracture remained an independent risk factor for the development of MACEs after adjustment for age, sex, LDL level, atherogenic index, diabetes mellitus, hypertension, past MACE, aPL antibodies, smoking, obesity and the use medications that included immunosuppressive drugs, aspirin/warfarin, statins, vitamin D and bisphosphonates (HR 2.41[1.25-4.67]; p=0.009). At last follow-up, 62(16%) patients succumbed (MACEs in 8 patients [vascular mortality], infective complications in 27 patients, cancer in 10 patients). Osteoporosis/fracture was associated with vascular mortality (HR 11.1[1.02-120]; p=0.048) but not with all-cause mortality (HR 1.55[0.89-2.68]; p=0.12) after adjustment for the same covariates in separate multivariate models.
Conclusion: Osteoporosis increases the risk of MACEs and vascular mortality in patients with SLE, which is not accounted by traditional vascular risk factors. Elevation of inflammatory cytokines in SLE that are common to bone metabolism and atherosclerotic vascular disease may be responsible.
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POS0736

PREVALENCE AND RISK FACTORS OF FRAGILITY FRACTURES IN SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL STUDY OVER 12 YEARS

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Objectives: To study the prevalence and risk factors of fragility fractures in a longitudinal cohort of patients with systemic lupus erythematosus (SLE).
Methods: All patients who fulfilled ≥4 1997 ACR criteria for SLE and have been registered in our cohort database since 1990 were included. Symptomatic fragility fractures, defined as those that occurred with no preceding injury or after a low-energy impact, were identified from the SLE organ damage index (SDI) data and verified by record review. A longitudinal cohort of 383 SLE patients who participated in a cross-sectional study in 2011 and had a baseline dual energy x-ray absorptiometry (DEXA) scan performed was further analyzed for factors predicting new fragility fractures over time. These patients were stratified into 2 groups according to the presence of previous fragility fracture or osteoporosis at baseline, defined as a DEXA T score <-2.5 or Z score <-2.0 at the hip, femoral neck or lumbar spine. The cumulative incidence of new fractures was studied by Kaplan-Meier's analysis and risk factors were studied by Cox regression, adjusted for demographic characteristics, medications and other confounding factors.
Results: 1140 SLE patients were included (age of onset 34.7±14.4 years; 91.5% women). 102 fractures (hip [n=15]; vertebral [n=54]; limbs (non-hip) [n=14]; digital/rib [n=19]) developed in 91(8.0%) patients over a mean of 13.1 years. The prevalence of major osteoporotic and hip fractures was 0.56 and 0.10 per 100 patient-years, respectively. A cohort of 383 SLE patients were further analyzed (age at DEXA scan 40.5±13 years; 94% women). Osteoporosis was present in 105 patients (13 with past fractures) at baseline and 8 other patients had osteopenia but a history of fragility fractures. Patients with osteoporosis/previous fractures (N=113), compared to those without (N=270), were more likely to have SLE onset during childhood (<18 years), longer SLE duration and a higher prevalence of thrombocytopenia, hemolytic anemia or neuropsychiatric manifestations that required immunosuppressive therapies. Use of glucocorticoids (79% vs 62%; p=0.002) and mycophenolate mofetil (MMF)/azathioprine (AZA) (55% vs 42%; p=0.02), body mass index (BMI) ≤18kg/m2 (14% vs 7%; p=0.04) or menopause before the age of 45 years (14% vs 4%; p=0.001) were also more frequent in the osteoporosis/fracture group. However, no difference in the SLEDAI scores at time of DEXA scan was observed between the 2 groups (3.7±3.8 vs 4.1±3.3; p=0.26). Over a follow-up of 153±41 months, new symptomatic fragility fractures developed in 34(8.9%) patients (vertebral [n=19], hip [n=2], limbs (non-hip) [n=6], digital/rib [n=7]; incidence 0.69 per 100 patient-years). The cumulative risk of new fragility fractures at 3,5,10 and 15 years was 1.8%, 3.7%, 14.7%, 22.2%; and 1.5%, 1.9%, 3.9%, 6.7%, respectively, in the osteoporosis/previous fracture and non-osteoporosis groups (log rank test; p<0.001). Cox regression showed that older age (HR1.08[1.03-1.12]; p=0.001), osteoporosis/previous fracture (HR3.47[1.59-7.59]; p=0.002) and a family history of fracture (HR4.31[1.41-13.2]; p=0.01) at baseline were independently associated with the development of new fractures after adjustment for confounding factors. SLE duration, childhood onset disease, low BMI, chronic smoking, premature menopause, use of glucocorticoids, MMF, AZA or hydroxychloroquine, anti-Ro positivity, history of thrombocytopenia, hemolytic anemia and neuropsychiatric manifestations were not significant risk factors for new fractures. In those patients using glucocorticoids at baseline, there was no significant relationship between the daily dosage of prednisolone and new fractures.
Conclusion: In a longitudinal cohort of SLE followed for over 12 years, new fragility fracture developed in 8.9% of patients. Increasing age, osteoporosis, a personal or family history of fractures were major risk factors.
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POS0737

SICCA SYNDROME: A MULTIMODAL ASSESSEMENT TO CHARACTERIZE PATIENT COHORTS BEYOND SJÖGREN'S SYNDROME CLASSIFICATION CRITERIA

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Background: Sicca syndrome represents a heterogeneous group of conditions, including Sjögren syndrome, causing xerophthalmia and xerostomia.
Objectives: This study characterizes in depth patients with Sicca syndrome and evaluates salivary gland ultrasound (SGUS) in this cohort.
Methods: Principal component analysis and hierarchical clustering of clinical parameters, including ESSPRI, ESSDAI and laboratory data were performed on all referrals for assessment of Sicca symptoms between October 2018 and March 2021. SGUS and labial gland biopsies were compared across groups.
Results: 583 patients were assessed. Objective dryness was confirmed in 73% of patients. Cluster analysis identified 3 groups with *post-hoc* analysis confirming distinct phenotypes: *Somatic Group* (283/583; 49%) with higher reported symptoms but limited objective dryness; *Dry Without Autoimmune Features* (DAF_{neg}, 206/532; 35%) and *Dry With Autoimmune Features* (DAF_{pos}, 94/532; 16%). DAF_{pos} patients had highest autoantibody titres (SSA 240 vs 3.6 vs 3.8; p<0.001), most extra-glandular manifestations (p<0.001) and highest median SGUS Score (DAF_{pos}: 8 [IQR 4-10] vs SG: 2 [1-4] vs DAF_{neg} 4 [2-5]; p< 0.001). No tangible correlation primary Sjögren syndrome criteria was observed.
Conclusion: SGUS score correlated with a subset of Sjögren syndrome patients, identified in the DAF_{pos} cluster. This study highlights heterogeneity within Sicca and indeed Sjögren syndrome, highlighting the need for further studies.

Table 1. Comparing and contrasting the clinical demographics and attributes of the entire cohort subdivided into the three groups identified through principal component analysis and subsequent hierarchical clustering. Results are shown as mean and interquartile range unless otherwise stated.

	Somatic		DAF_{neg}		DAF_{pos}		*p*
N (%)	283	(49)	206	(35)	94	(16)	
Female, n (%)	239	(84)	142	(69)	81	(86%)	<0.001
Age at Onset, yrs	47.3	[36.6-55.9]	60.2	[51.1-67.3]	50.1	[35.5-59.4]	<0.001
BMI, kgm^{-2}	26.1	[23.0-31.0]	24.7	[21.7-27.7]	24.6	[22.4-28.0]	0.003
Smoker, n (%)	50	(18)	15	(7)	4	(4)	0.06
ESSPRI Scores							
- Dryness	6	[3-7]	2	[1-3]	4	[2-7]	<0.001
- Limb Pain	7	[5-8]	5	[2-6]	6	[4-8]	
- Fatigue	8	[6-9]	3	[2-5]	5	[3-8]	
Reported Symptoms							
Raynaud, n (%)	86	(30)	51	(25)	44	(47)	0.006
Arthralgia, n (%)	222	(78)	118	(57)	61	(65)	0.002
Myalgia, n (%)	197	(70)	87	(42)	40	(43)	0.003
Stiffness, n (%)	98	(35)	37	(18)	23	(25)	0.001
Parotitis, n (%)	62	(22)	24	(12)	33	(35)	0.001
Sand corn, n (%)	168	(59)	62	(30)	44	(47)	0.001
Ocular Inf, n (%)	120	(42)	45	(22)	26	(27)	0.005
ESSDAI							
- Score	5	[2-12]	5	[0-11]	11	[4-17]	<0.001
Antibody Titres							
- ANA ≥ 1:160	178	(63)	152	(74)	44	(47)	<0.001
- RhF U/ml	10.0	[10.0-10.9]	10.0	[10.0-11.3]	23.3	[11.7-71.0]	<0.001
- Alpha-Fodrin U/ml	9	[5-22]	9	[6-19]	12	[6-25]	0.05
- anti-SSA(Ro) U/ml	3.6	[0.3-101.3]	3.8	[0.3-102.3]	240.0	[192.8-240.0]	<0.001
- anti-SSB(La) U/ml	0.4	[0.3-3.4]	0.3	[0.3-1.9]	73.1	[3.8-312.5]	<0.001
Measurable Dryness							
Saxon, g	3.5	[2.4-4.9]	4.2	[3.3-5.3]	2.3	[0.6-3.7]	<0.001
Schirmer, mm	7.0	[2.0-17.9]	3.0	[0.5-12.0]	2.5	[0.0-7.1]	<0.001
Labial Gland Biopsy, n (%)							
- Biopsy performed	150	(53)	120	(58)	18	(19)	
- Chisholm Score ≥3	66	(44)	64	(53)	9	(50)	
- Median Score	2	[1-3]	3	[2-3]	3	[3-4]	
Salivary Gland Ultrasound, n (%)							
- SGUS = 0	39	(14)	39	(19)	1	(1)	
- SGUS ≥6	73	(26)	55	(27)	38	(41)	
SGUS Score	2	[1-4]	4	[2-5]	8	[4-10]	<0.001

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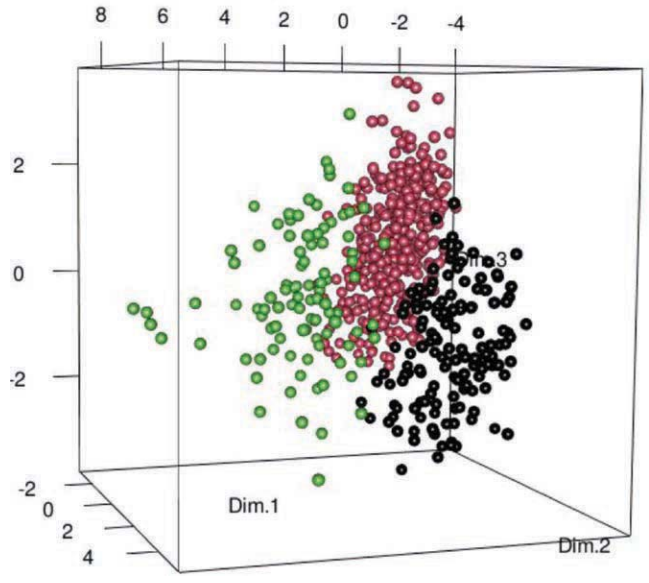

Figure 1. A 3D scatterplot composed of the first 3 dimensions of the principal component analysis, identified as providing greatest inertia gain on hierarchical clustering. The Somatic Group (SG) are represented by the black points. Patients in the Dryness without autoimmune features (DAF_{neg}) are represented by pink points and Dryness with autoimmune features (DAF_{pos}) patients with green dots.

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POS0738

IMMUNOGENICITY AND SAFETY OF COVID-19 VACCINATION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Patients with primary Sjögren's syndrome (pSS) worry about the effectiveness and safety of COVID-19 vaccination. pSS is characterized by B-cell hyperactivity, and previous influenza vaccination studies showed that pSS patients generate higher influenza-specific antibodies than healthy controls (HC).[1,2] Furthermore, influenza vaccination resulted in elevated auto-antibody levels.[1,2] Therefore, it is hypothesized that COVID-19 vaccination may also lead to a higher spike-specific antibody response.

Objectives: To evaluate humoral and cellular immune response and adverse events (AEs) after COVID-19 vaccination in pSS patients compared to HC, and disease activity following vaccination in pSS patients. Furthermore, to evaluate change in spike-specific antibody levels in saliva and anti-SSA levels in serum following vaccination.

Methods: In this prospective, longitudinal cohort study, pSS patients and HC were included in a 2:1 ratio. Participants received COVID-19 vaccinations following the Dutch vaccination programme. pSS patients did not use

immunomodulatory drugs, except hydroxychloroquine (HCQ). Anti-spike 1 (S1) receptor binding domain (RBD) IgG serum antibody levels were measured 28 days after complete vaccination. AEs were collected 7 days after vaccination. Change in disease activity following vaccination was measured with EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) and EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). In a subgroup of participants, spike-specific T-cell response was measured 7 days after complete vaccination with IFN-γ ELIspot. Definition of a T-cell responder was ≥2-fold increase in spot-forming cell (SFC) counts from pre- to post-vaccination and SFC counts of ≥50/10^6 cells in the post-vaccination sample. Salivary anti-S1 and anti-RBD antibodies and serological anti-SSA antibodies were also measured in this subgroup in pre- and post-vaccination samples (28 days after complete vaccination).

Results: In total, 67 pSS patients and 33 HC were included. Of these, 47 (70%) and 14 (42%) received BNT162b2 (Pfizer-BioNtech), 13 (19%) and 5 (15%) received ChAdOx1 nCoV-19 (AstraZeneca), 6 (9%) and 8 (24%) received mRNA-1273 (Moderna), and 1 (1%) and 6 (18%) received Ad.26.COV2.S (Janssen), respectively. Overall, pSS patients were significantly older than HC, which was mainly due to the younger age in the Moderna and Janssen groups. All participants had positive anti-SARS-CoV-2 antibody levels (>2500 AU/ml) post-vaccination. No differences in anti-SARS-CoV-2 antibody levels were observed between pSS patients and HC, for any of the vaccine types (Figure 1). Percentage of spike-specific T-cell responders was comparable between pSS patients (20/24, 83%) and HC (4/5, 80%). Salivary anti-SARS-CoV-2 IgG antibodies, but not IgA, increased post-vaccination in pSS patients (n=26) and HC (n=9). Salivary anti-RBD IgG antibodies were significantly correlated with serum anti-RBD antibodies (r= 0.597, p<0.001).

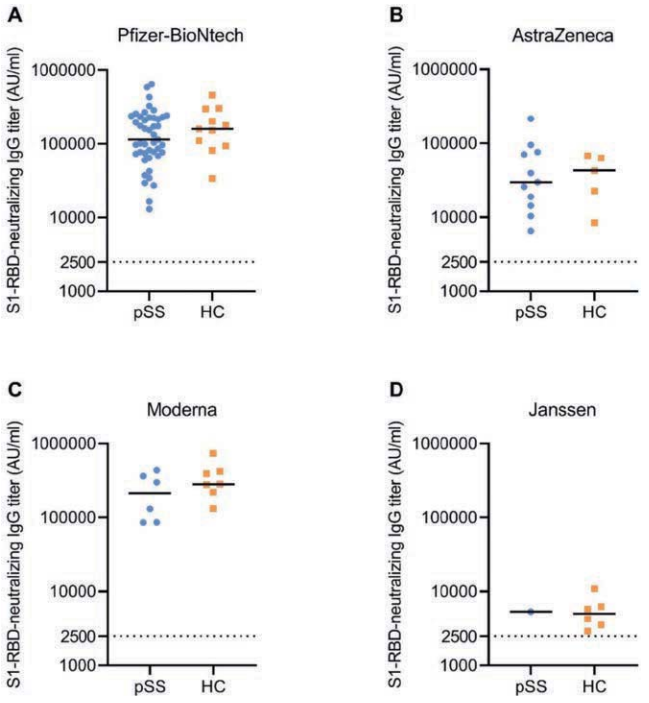

Figure 1. Anti-S1 RBD IgG antibody levels of participants who received **A)** Pfizer-BioNtech **B)** AstraZeneca **C)** Moderna or **D)** Janssen. Dashed line indicates positive level.

No serious AEs occurred. Frequencies of systemic AEs were comparable between pSS patients and HC (first vaccination: 34/67 (51%) vs. 16/33 (48%), p=0.83; second: 41/66 (62%) vs. 14/25 (56%), p=0.59). No significant worsening was observed in median ESSPRI (baseline: 6 (IQR 5-7), post-vaccination: 6 (4-7), p=0.16, n=64) and ESSDAI (baseline: 3 (IQR 1-4), post-vaccination: 2 (0-5), p=0.88, n=36). Furthermore, no increase in anti-Ro52 and anti-Ro60 antibody levels was seen (p=0.65 and p=0.58, respectively).

Conclusion: pSS patients had similar humoral and cellular immune responses as HC, providing evidence that COVID-19 vaccination is effective in pSS patients. AEs were also comparable, and no increase in disease activity was seen in pSS patients, indicating COVID-19 vaccination is safe in pSS patients.

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POS0739

THE RENAL ACTIVITY INDEX FOR LUPUS (RAIL) DIFFERENTIATES ACTIVE AND INACTIVE NEPHRITIS IN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Lupus nephritis (LN) confers a poor prognosis, with lack of effective laboratory tests to diagnose and evaluate therapies. We have demonstrated that the RAIL score, based on a set of six urinary biomarkers (*NGAL, KIM-1, MCP-1,* adiponectin, hemopexin, ceruloplasmin) is sensitive and specific in adult patients with active LN, using renal biopsy as reference.[1,2] RAIL has been shown in the pediatric population to be effective in distinguishing inactive vs active LN with no effect from mycophenolate mofetil (MMF) treatment. A comparable study has not been conducted in an adult population.

Objectives: To assess the ability of RAIL to discriminate patients with active LN vs active non-renal SLE and to evaluate if RAIL performance varies by MMF treatment using urine samples from adult LN patients.

Methods: Urine samples were obtained at baseline in two clinical trials: a phase 2 study in adult patients with biopsy-proven active Class III and IV LN (NCT02547922) and a subset of patients from the phase 3 trial in adults with active non-renal SLE (NCT02446912) who had baseline renal BILAG scores C, D, or E. RAIL biomarkers were assayed using single-plex assays. Patient demographics and clinical characteristics were compared between studies. Wilcoxon rank sum test was performed comparing the urinary biomarkers between the two studies and RAIL score was then calculated. Receiver operating characteristic (ROC) analyses were conducted assessing the ability for RAIL scores to distinguish patients with renal activity and involvement.

Results: Comparison of the patient demographic, clinical characteristics, and biomarkers is in the Table 1. Wilcoxon rank sum test showed the six urinary biomarkers were significantly different between two groups of patients as demonstrated (Table 1). Each of the RAIL biomarker concentrations and the creatinine-adjusted median score were higher in the active LN group than the SLE group (P<0.001). ROC analyses including RAIL score showed an area under the ROC curve of 0.8 (Figure 1), with odds ratio of log-transformed RAIL 2.027 (95% CI [1.587, 2.589]). There were no significant interactions between RAIL and MMF. RAIL remained significant after adjusting for estimated glomerular filtration rate (eGFR), which was not statistically significant.

Table 1. Study Demographics and Biomarkers

	Variables	LN study (N=131)		SLE study (N=59)	
		Observed N	Observed Median (IQR) or %	Observed N	Observed Median (IQR) or %
Demographics	Age	131	34 (25, 42)	59	36 (28, 44)
	Sex, Female	109	83.21%	55	93.22%
	Race, White	56	42.75%	45	76.27%
	Ethnicity, Hispanic or Latino	61	46.56%	9	15.25%
	OCS use, yes	127	97.69%	57	96.61%
	MMF use, yes	95	72.52%	21	35.59%
	Spot UPCR (mg/mg)	128	2.13 (1.22, 4.04)	59	1.11 (0.55, 2.61)
	eGFR	130	91.8 (63.1, 125)	59	98.06 (81.91, 116.54)
	Non-renal SLEDAI-2K score	130	4 (4, 6)	59	12 (9, 13)
	Renal SLEDAI-2K score	130	4 (4, 8)	59	0 (0, 0)
Biomarkers	NGAL (ng/mL)	128	33.33 (17.55, 56.7)	58	19.47 (11.37, 42.05)
	MCP-1 (pg/mL)	128	658.24 (271.58, 1049.95)	58	275.62 (106.09, 481.99)
	Ceruloplasmin (ng/mL)	128	93.55 (44.5, 311.25)	58	47.2 (13.05, 231.25)
	Adiponectin (ng/mL)	128	42.45 (16.71, 139.64)	58	9.33 (3.35, 25.51)
	Hemopexin (ng/mL)	128	1876.8 (745.07, 4743.4)	58	513.4 (236.36, 1388.74)
	KIM-1 (pg/mL)	128	1673.5 (772.5, 2767)	58	864 (394, 1480)
	Creatinine (mg/mL)	128	0.7 (0.46, 1.3)	58	0.99 (0.46, 1.74)
	Adult RAIL score (creatinine adjusted)	**128**	**5.59 (4.31, 6.47)**	**58**	**3.57 (2.78, 4.47)**

eGFR, estimated glomerular filtration rate; IQR, interquartile range; KIM, kidney injury molecule; LN, lupus nephritis; MCP, monocyte chemotactic protein; MMF, mycophenolate mofetil; NGAL, neutrophil gelatinase-associated lipocalin; OCS, oral corticosteroid; SLEDAI-2K, SLE Disease Activity Index 2000; UPCR, urine protein/creatinine ratio.

Conclusion: The analyses performed suggest that creatinine-corrected RAIL discriminates between active LN and non-renal adult SLE, with RAIL scores not influenced by MMF use.

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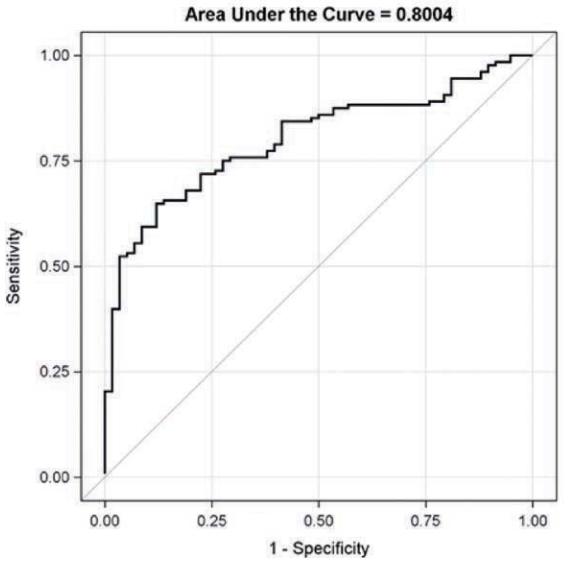
Figure 1: ROC of creatinine adjusted RAIL Scores



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Disclosure of Interests: Ellen Cody: None declared, Hermine Brunner Speakers bureau: Novartis, Pfizer, GSK, Consultant of: AbbVie, Astra Zeneca-Medimmune, Biogen, Boehringer, Bristol Myers Squibb, Celgene, Lilly,EMD Serono, Idorsia, Cerocor, Janssen, GSK, F. Hoffmann-La Roche, Merck, Novartis, R-Pharm, Sanofi, Grant/research support from: Pfizer, Bin Huang: None declared, Tingting Qiu: None declared, Prasad Devarajan Speakers bureau: Reata, Alnylam, Dicerna, Consultant of: BioPorto Inc, Madhu Ramaswamy Shareholder of: AstraZeneca, Employee of: AstraZeneca, Dominic Sinibaldi Shareholder of: AstraZeneca, Employee of: AstraZeneca, Philip Z Brohawn Shareholder of: AstraZeneca, Employee of: AstraZeneca, Jacob Knagenhjelm Shareholder of: AstraZeneca, Employee of: AstraZeneca, Frederick Jones Shareholder of: AstraZeneca, Employee of: AstraZeneca, Raj Tummala Shareholder of: AstraZeneca, Employee of: AstraZeneca, Catharina Lindholm Employee of: AstraZeneca, Wendy White Shareholder of: AstraZeneca, Employee of: AstraZeneca

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POS0740

IMPACT OF TIME TO REMISSION, FLARES AND EXPOSURE TO IMMUNOSUPPRESSIVES ON THE DEVELOPMENT OF ADVANCED CHRONIC KIDNEY DISEASE (STAGE IV OR WORSE) IN LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) affects up to 40% of patients with SLE and leads to end stage kidney disease (ESKD) in 17-33% after 10 years. The prevalence of chronic kidney disease stage IV (estimated glomerular filtration rate, eGFR=15-29ml/min/1.73m^2) is not known; however, approximately two thirds of such patients will progress to ESKD after 6 years on average.[1]

Objectives: To determine the impact of time to remission and flares on the development of advanced CKD (stage IV or worse) in LN.

Methods: Patients with LN based on biopsy or abnormal proteinuria (>0.5g/day) with or without hematuria/pyuria/casts for two consecutive visits in the absence of other plausible explanation were retrieved from the Toronto Lupus Clinic database. Individuals with advanced CKD at baseline were excluded. All patients were followed for at least 5 years. The primary outcome was the development of advanced CKD (eGFR≦29ml/min/1.73m^2). Remission was defined as proteinuria<0.5g/24h, no active urinary sediment and serum creatinine of ≤120% of baseline. Flare was defined as any abnormal proteinuria (>0.5g/day) after remission. Death was treated as competing risk in survival analysis. Statistical analysis with SAS 9.4; $p<0.05$ was considered significant.

Results: Out of 418 eligible patients, 209 (50%) achieved remission within the first year from LN diagnosis, 102 (24.4%) within the 2nd and 3rd years, 70 (16.7%) after 3 years and 37 (8.9%) never achieved remission. Sixty-six patients (15.8%) developed advanced CKD after 9.5 years on average (37 with ESKD). At baseline, these patients had a higher SLICC/Damage Index (0.6±1.2 vs. 0.3±0.7, $p=0.003$), lower eGFR (73±38 vs. 94±33ml/min/1.73m^2, $p<0.001$), higher prevalence of hypertension (85% vs. 73%, $p=0.046$), proliferative nephritis (combined class III and IV, 66% vs. 47.8%, $p=0.017$) and more often treated with ACE inhibitors or angiotensin receptor blockers (35% vs. 22%, $p=0.02$). The other variables did not differ significantly. Remission rates, flares and exposure to immunosuppressives after remission are shown in Table 1.

Table 1. A. Time to remission, exposure to immunosuppressives and flares in all patients

VARIABLE	Advanced CKD (n=66)	No advanced CKD (n=352)	*p*
Years from LN to complete remission	3.0 ± 3.4	1.6 ± 2.1	<0.001
Years on Immunosuppressives from complete remission to outcome/last date (median)	2 (0-7)	4 (0-8)	0.008
Number of flares in first five years after LN			
0	12 (18.2%)	156 (44.3%)	<0.001
1	14 (21.2%)	79 (22.4%)	
2 or more	40 (60.6%)	117 (33.2%)	
B. Multivariate analysis for the outcome of advanced CKD (stage IV or worse)			
	HR	**95%CI**	***p***
Serum creatinine at baseline	1.02	1.01-1.02	<0.0001
Complete remission between 1-3 years (compared to remission within 1 year)	2.48	1.14-5.37	0.022
Complete remission after 3 years or no remission (compared to remission within 1 year)	2.99	1.41-6.34	0.004
Years on Immunosuppressives from complete remission to outcome/last date	0.89	0.83-0.95	<0.0001
One flare (compared to no flares)	2.68	1.05-6.86	0.04
Two or more flares (compared to no flares)	3.55	1.51-8.34	0.004

Patients who achieved remission within one year from diagnosis demonstrated better outcomes compared to all other groups ($p<0.0001$), Figure 1. Patients with complete remission between one and three years had similar outcomes for the first 10 years from diagnosis and deteriorated during the second decade of follow-up.

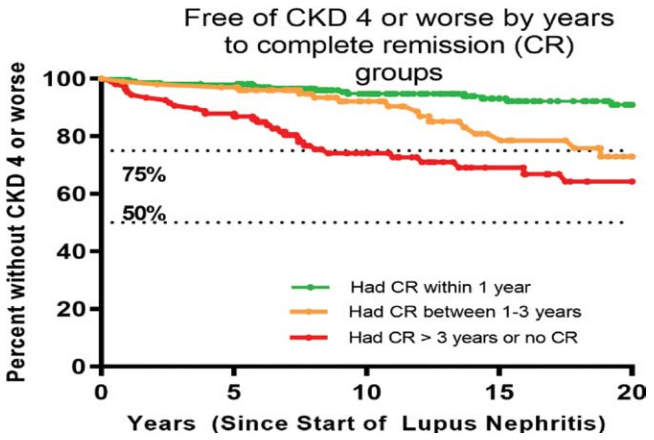

Figure 1.

Conclusion: Complete remission within the 1st year from LN diagnosis strongly protects against advanced CKD. Flares significantly affect prognosis. One flare was associated with 2.7-fold increased risk for advanced CKD (3.6-fold for 2 or more flares). Longer time on immunosuppressives after remission is associated with decreased risk for advanced CKD. Our findings emphasize the importance of early remission as well as flare prevention with prolonged immunosuppressive use to maximize renal survival in LN.

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POS0741 REPORT FROM THE APS STUDY GROUP OF THE ITALIAN SOCIETY FOR RHEUMATOLOGY (SIR-APS) ON APL NEGATIVIZATION

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Background: The rate of antiphospholipid antibodies (aPL)negativization in antiphospholipid syndrome (APS) patients is uncertain, but it is estimated to be as high as 8%. aPL disappearance seems to be more frequent in patients positive for one single aPL test and appears to be related with the immunosuppressant/immunomodulatory treatment undertaken by the patient. Currently, a consensus definition of aPL negativization is lacking, as well as international recommendations on how to approach treatment in patients with a persistent aPL negative seroconversion.

Objectives: The aim of our work was to evaluate the clinical approach and the level of consensus among experts from the APS Study Group of the Italian Society for Rheumatology (SIR-APS) in different clinical scenario addressing aPL negativization and its definition.

Methods: Experts of SIR-APS were contacted using a survey methodology.

Results: A structured survey was circulated among 30 experts.Up to 90% of the interviewed experts agreed on defining aPL negativization as the presence of two negative determinations, one year apart (90%).Almost ful lconsensus exist among experts in some clinical settings, including: a) the role of aPL negativitation in the management of a thrombotic event determined by concomitant presence of cardiovascular risk factors, both modifiable and not modifiable (90%): b) approach to young patients with triple aPL positivity who experienced pulmonary arterial thrombotic event and tested negative for aPL detection after five year of vitamin K antagonist (VKA) treatment (90%); c)the use of "*extra criteria*" aPL antibodies testing before pondering VKA suspension (93%).

Conclusion: Consensus is needed to support the management of patients with APS in areas where controlled data are missing. A substantial agreement exists among expert in defying aPL negativization as the presence of two negative determinations, one year apart. On the contrary, VKA suspension should be embraced with extreme caution when it comes to APS patients, particularly if they experienced arterial thrombotic events and/or tested positive for triple aPL. Nevertheless, VKA cessation might be considered when risk factors are carefully monitored/treated and the presence for "*extra criteria"* aPL is ruled out.

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POS0742 DISCRIMINATIVE POWER OF SALIVARY GLAND ULTRASOUND IN RELATION TO ENDOTYPES IN SUSPECTED AND DEFINITE PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's Syndrome (pSS) is an auto-immune disease with characteristic complaints of oral and ocular dryness, typically affecting adult women. In addition, up to 30-40% of patients suffers from systemic manifestations and lymphoma risk is increased 15-20 fold. pSS is thus highly heterogenous both in presentation and pathophysiology. In an attempt to address this issue Tarn et al. applied cluster analysis based on patient reported outcomes assessing dryness, fatigue, pain and features of anxiety and depression, on a population of pSS patients. This resulted in four groups: low symptom burden (LSB), pain dominant with fatigue (PDF), dryness dominant with fatigue (DDF) and high symptom burden (HSB). These groups, referred to as endotypes, also seemed to have different biological profiles.(1)

Objectives: The aim of this study was to explore salivary gland ultrasound (SGUS) in relation to symptom-based endotypes in a cohort of patients with definite and suspected pSS.

Methods: Data from the Belgian Sjögren's Syndrome Transition Trial (BeSSTT) were used in which patients positive for at least one of the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria, were enrolled. Patients were considered 'definite pSS' when fulfilling these criteria and 'suspected pSS' otherwise.

The Newcastle Sjögren's Stratification Tool, developed and provided by J. Tarn and colleagues, was applied to stratify the cohort into endotypes. Hocevar score (0-48) was used to assess SGUS abnormalities. Scores of at least 17 were considered positive.

Results: Stratification of the BeSSTT (n=241) cohort resulted in 4 endotypes, both in definite (n=141) and suspected pSS (n=100). The proportion of anti-SSA positive patients was high in definite pSS in all endotypes (91.9%; p=0.239). This proportion was significantly lower in suspected pSS patients in all endotypes

(27.6%; p=0.064) albeit that the difference was less pronounced in LSB (50.0%) and, to a lesser degree, in PDF (32.7%) endotypes.
SGUS scores were higher in definite than suspected pSS (22 (12-37) vs 10 (2-16); p<0.001) in all endotypes (Figure 1). In definite pSS, Hocevar scores were highest in DDF compared to other endotypes (35 (24-43); p<0.001) and SGUS had a very strong discriminating power in this endotype (PPV=94.1%, NPV=76.2%). Salivary gland function was poorest in the definite pSS DDF endotype.

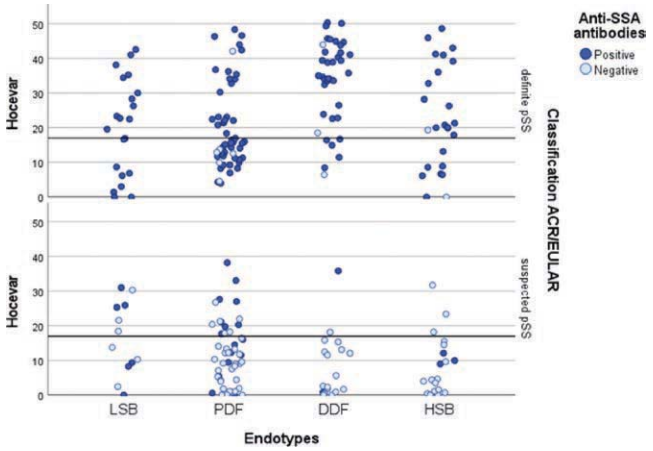

Figure 1. Scatter plot of Hocevar score (0-48) by endotype. The upper plot represents patients with definite and the lower with suspected pSS. The colour of the dots indicates presence or absence of anti-SSA antibodies. The horizontal line is drawn at a Hocevar score of 17 and represents cut-off for positive SGUS.

In the suspected pSS subgroup, Hocevar scores tended to be higher in the LSB endotype (17 (6-26); p=0.053) and were significantly higher in anti-SSA positive than negative patients (12 (6-26) vs 8 (1-14); p=0.017) (Figure 1). Of the 24 suspected pSS patients (24.0%) with a positive SGUS, 12 (50.0%) were anti-SSA positive. Anti-SSA positive suspected pSS patients with an aberrant SGUS were markedly younger than the rest of the BeSSTT cohort (mean±SD age of 36 ±15 years vs 52 ±14 years) suggesting they may represent an early at-risk population.
Conclusion: These results show prominent SGUS differences between endotypes in pSS, supporting its potential as biomarker. Hocevar scores are highest in patients with DDF endotypes, further suggesting a different biological profile. SGUS is a powerful tool to identify definite pSS patients from a group of patients with DDF endotypes who fulfil at least one of the ACR/EULAR classification criteria. In addition, a subset of young anti-SSA positive patients without overt dryness (LSB and PDF endotype) reveals high SGUS scores. We would thus propose SGUS in all anti-SSA positive patients, regardless of symptoms, to reveal this glandular involvement.
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POS0743 CLINICAL CHARACTERISTICS AND BURDEN AMONG PATIENTS WITH SLE AND MUSCULOSKELETAL ORGAN INVOLVEMENT: RESULTS FROM A REAL-WORLD STUDY IN THE US

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Background: Limited information exists concerning the clinical burden and unmet need of musculoskeletal (MSK) organ involvement among patients with SLE in clinical practice.
Objectives: To examine demographics, clinical status, treatment patterns, and patient-reported outcomes (PROs) among patients with SLE in clinical practices and assess the impact of MSK organ involvement.
Methods: Data were drawn from the Adelphi Real World Lupus IV (2021) Disease Specific Programme™, a point-in-time survey of 79 US physicians and their patients with SLE. Physicians completed questionnaires regarding patient demographics, clinical status, and treatment. The same patients were invited to complete questionnaires containing the EuroQoL 5-Dimensions (EQ-5D), Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-Fatigue) and Work Productivity & Activity Impairment questionnaire (WPAI) PRO tools. Physicians stated their patients' organ involvement at the time of data collection (current), in the categories of musculoskeletal, mucocutaneous, renal, cardiorespiratory, constitutional, haematologic, ophthalmologic, gastrointestinal, respiratory, or other. Two mutually exclusive patient groups were analysed: A.MSK – Current physician assessed musculoskeletal organ involvement (+/- other organ/tissue involvement). B.Non-MSK – No current musculoskeletal organ involvement as assessed by the physician Bivariate analysis was conducted for numeric variables using t-tests; binary categorical variables using a Fisher's exact test; ordinal categorical variables using a Mann-Whitney test; and other categorical variables were compared using a chi-squared test.
Results: A total of 595 patients were included in this analysis: 64.7% MSK and 35.3% non-MSK. Mean[SD] patient age was 45.2[14.3] years, 83.2% were female, 53.3% were White/Caucasian, 27.9% were African American, and mean[SD] time diagnosed with any SLE was 5.3[6.2] years. Point-in-time assessment of clinical status, treatment patterns and patient-reported outcomes, revealed that those with MSK organ involvement assessed by their rheumatologist had higher overall SLE disease severity, more flares in the last 12 months, and slightly worse quality of life scores and work impairment.

Table 1. Point-in-time clinical status, treatment patterns and PROs among patients with SLE MSK organ involvement

		Total	MSK	Non-MSK	
		(n=595)	(n=385)	(n=210)	p value
Physician-Reported Patient Clinical Status & Treatment History					
Current SLE severity, n(%)	Mild	405 (68.1)	243 (63.1)	162 (77.1)	<0.001
	Moderate	169 (28.4)	128 (33.3)	41 (19.2)	
	Severe	21 (3.5)	14 (3.6)	7 (3.3)	
Current joint symptoms, n(%)	Joint tenderness	251 (42.2)	210 (54.6)	41 (19.5)	<0.001
	Joint stiffness	255 (42.9)	212 (55.1)	43 (20.5)	<0.001
	Joint swelling	135 (22.7)	111 (28.8)	24 (11.4)	<0.001
Mean [SD] Flares in the last 12 months		1.6 [1.7]	1.7 [1.8]	1.2 [1.3]	0.015
Currently prescribed, n(%)	Belimumab	113 (19.0)	79 (20.5)	34 (16.2)	0.198
	Immunosuppressant	164 (27.6)	105 (27.3)	59 (28.1)	0.830
	Corticosteroids	333 (56.0)	228 (59.2)	105 (50.0)	0.030
	Antimalarials	429 (72.1)	268 (69.6)	161 (76.7))	0.067
Mean [SD] years on current treatment		2.9 [3.6]	2.5 [3.0]	3.6 [4.4]	<0.001
Patient-Reported Outcomes					
Mean [SD] EQ5D-5L Utility score (0= death to 1= full health)		0.79 [0.20]	0.76 [0.22]	0.85 [0.16]	0.002
Mean [SD] FACIT-Fatigue score (0 worst fatigue to-52= no fatigue)		32.4 [12.0]	31.0 [11.5]	35.4 [12.6]	0.005
Mean [SD] WPAI, overall work impairment score(0= no impact to 100= completely impacted)		29.0 [21.0]	30.5 [18.6]	25.9 [25.2]	0.223

Conclusion: In this large sample of patients with SLE followed in clinical practices in the U.S., compared to those with little or no rheumatologist assessed MSK involvement, those with MSK involvement, had lower quality of life, with higher impact on their work productivity. These results highlight the heterogeneity of SLE and the impact of major MSK manifestations on quality of life in SLE.
REFERENCES: N/A
Disclosure of Interests: Aisha Vadhariya Employee of: Eli Lilly and Company, Julie Birt Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jianmin Wu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Kirstin Griffing Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Fiona Bailey: None declared, James Hetherington: None declared, Elke Rottier: None declared, Sophie Barlow: None declared, Karen Costenbader Consultant of: Lilly, Astra Zeneca, Janssen, Amgen, Glaxo Smith Kline, Grant/research support from: Exagen, Gilead, Merck
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POS0744 SYSTEMIC LUPUS ERYTHEMATOSUS WITH ACTIVE MUSCULOSKELETAL SYMPTOMS: PATIENT REPORTED SYMPTOM IMPACT, TREATMENT PATTERNS AND SATISFACTION WITH CURRENT THERAPY OPTIONS

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Background: Musculoskeletal (MSK) symptoms affect 50-95% of patients with SLE over their disease course negatively impacting functioning, and quality of life (QoL).1 In SLE-UPDATE, a US, cross-sectional, non-interventional online survey of adults with SLE, over half of the participants reported active MSK symptoms, including pain or swelling in the joints (53%) and stiffness (57%).2 The present study evaluated the sub-group of participants with 'currently active' MSK symptoms.

Objectives: To describe the self-reported disease burden, treatment patterns, and satisfaction with therapies in patients with SLE, comparing those with versus without active MSK symptoms.

Methods: This secondary analysis of SLE-UPDATE survey data stratified participants into active or non-active MSK group. Participants currently experiencing pain or swelling and/or stiffness in their joints and had a Joint Pain NRS > 4 were in the "active MSK group". All remaining participants were in the "non-active MSK group". Analysis comprised descriptive statistics, mean (standard deviation [SD]) for continuous variables, and frequency (percentage [%]) for categorical variables. Two-sample t-test to compare mean scores and chi-squared testing to compare proportions were used.

Results: Of the survey participants, 285 were in the active MSK group and 215 in the non-active MSK group. The active MSK group was older (44.3 vs. 40.2 years, <0.001) and had a longer time since diagnosis (12.6 vs. 9.2 years, <0.001). More people in the MSK group had fibromyalgia (FM) (45 vs 12%, <0.0001), worse pain, fatigue, and QoL (Table 1) suggestive of Type 2 non-inflammatory SLE symptoms. Fewer in the MSK group were employed full-time (36.5 vs. 62.8%) and more were on permanent disability (27.0 vs. 6.5%). More participants in the active MSK group negatively assessed their general health (fair or poor) over the last month (53.4 vs. 20.4%). The active MSK group self-reported more "flares" over the prior 3 months; with 44.9 vs 41.9% reporting 1-3 flares, 15.1 vs 5.1% reporting 4-6 flares, and 8.1 vs 2.3% reporting > 7 flares.

Table 1. Patient Reported Outcomes

	Active MSK		Non-Active MSK	
	FM	Non-FM	FM	Non-FM
	N=129	N=156	N=26	N=189
Worst Pain NRS, Mean (SD)	6.5 (1.7)*		4.8 (2.6)	
	6.9 (1.6)*	6.2 (1.8)	4.0 (2.2)	4.9 (2.6)~
Worst Joint Pain NRS, Mean (SD)	6.7 (1.7)*		4.5 (2.6)	
	7.1 (1.6)*	6.5 (1.6)	3.5 (2.0)	4.6 (2.6)*
FACIT Fatigue Score, Mean (SD)	19.1 (10.8)*		28.1 (11.6)	
	15.4 (9.5)*	22.1 (10.9)	25.7 (13.8)	28.4 (11.3)~
LupusPRO HRQoL Score (SD)	48.9 (20.2)*		64.1 (23.0)	
	45.5 (18.1)*	51.7 (21.4)	63.0 (23.9)	64.3 (22.9)~

NRS: 0 (none)-10 (worst imaginable); FACIT Fatigue: 0-52, higher= less fatigue; LupusPRO: 0-100, higher= better QoL; *p < 0.05; ~ Not significant

The active MSK group used more anti-malarials (50.9 vs. 30.7%), immunosuppressants (37.2 vs. 26.5%), including methotrexate (12.6 vs 3.3%), narcotic analgesics (18.6 vs. 10.2%), and topicals for joint pain (30.5 vs. 10.2%). Interestingly, treatment goals of greatest importance in both groups were reduction in fatigue and pain, but pain reduction had higher importance in active MSK group (rated very important by 26.7 vs. 18.1%). Lower proportions in the active MSK group were satisfied with steroids (58.0 vs. 77.8% <0.01), immunosuppressants (65.1 vs. 80.7% <0.05), methotrexate (47.2 vs. 85.7% =0.061), and belimumab (80 vs. 95.5%=0.102).

Conclusion: Reduction of pain and fatigue was the main treatment goal of patients with SLE whether they had active or non-active MSK symptoms. Patients with active MSK symptoms had higher pain and fatigue, lower QoL, and less satisfaction with current therapies compared to SLE patients without active MSK symptoms, driven only in part by co-morbid FM. Findings from these analyses suggest there are unmet needs to better understand MSK manifestations, their overlap with Type 2 SLE symptoms, align patient/physician priorities, and improve therapies for MSK symptoms for patients with SLE.

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POS0745 GUT DYSBIOSIS ASSOCIATED WITH PERIPHERAL LYMPHOCYTES AND CYTOKINES IN PATIENTS WITH SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by disorders of lymphocyte subpopulations with various cytokines and auto-antibodies[1]. Growing evidences suggest that gut microbiome dysbiosis may contribute to the development of pSS[2].

Objectives: To investigate the alterations to the gut microbiome and the correlation with peripheral lymphocytes and serum cytokines as well as inflammatory factors in pSS patients.

Methods: A total of 101 pSS patients and 101 age- and sex- matched healthy controls (HCs) were enrolled in this study from The Second Hospital of Shanxi Medical University (Taiyuan, Shanxi, China). Patients fulfilled the 2019 ACR/EULAR classification criteria. We conducted 16S rRNA gene sequencing using fecal microbiota samples and analyzed the peripheral lymphocyte subsets by flow cytometry. Serum cytokines, erythrocyte sedimentation rate (ESR), C-reaction protein (CRP), unstimulated and stimulated whole saliva (UWS and SWS) secretion rate was also collected, respectively. Sequence data were compiled and processed using Qiime2 and OTU-profiling tables were constructed. Correlations between different taxa and gut microbiome, as well as clinical variables, were calculated by Spearman's rank test.

Results: Patients with pSS exhibited a significant reduction in the richness and diversity of gut microbiota compared with those of HCs (Figure 1A-B, $p < 0.05$). Detailly, at the phylum level, pSS patients had a lower frequency of Firmicutes while higher Proteobacteria (Figure 1C, $p < 0.05$). Compared with HCs, 11 species of flora were discovered to be distinctly different at the genus level ($p < 0.05$). Patients presented fewer Faecalibacterium and Roseburia but more Lactobacillus (Figure 1D, $p < 0.05$). Lactobacillus negatively correlated with T cells (r=-0.407), CD8+T (r=-0.417) and Th2 (r=-0.323). There was a significant positive correlation between Faecalibacterium and IL-2(r=0.312), IFN-γ(r=0.338), TNF-α levels(r=0.322) (Figure 1E, $p < 0.05$). As for clinical disease measures, IL-6 increases were in line with ESR and CRP, while IL-2 levels inversely related to CRP. Additional UWS secretion rate and SWS secretion rate had negative correlation with ESR (Figure 1F, $p < 0.05$).

Conclusion: The structural disorder of gut microbiota was distinct in pSS which were associated with peripheral lymphocyte subsets and cytokines. Disorders of gut microbiota and immune systems may contribute to the occurrence and development of pSS.

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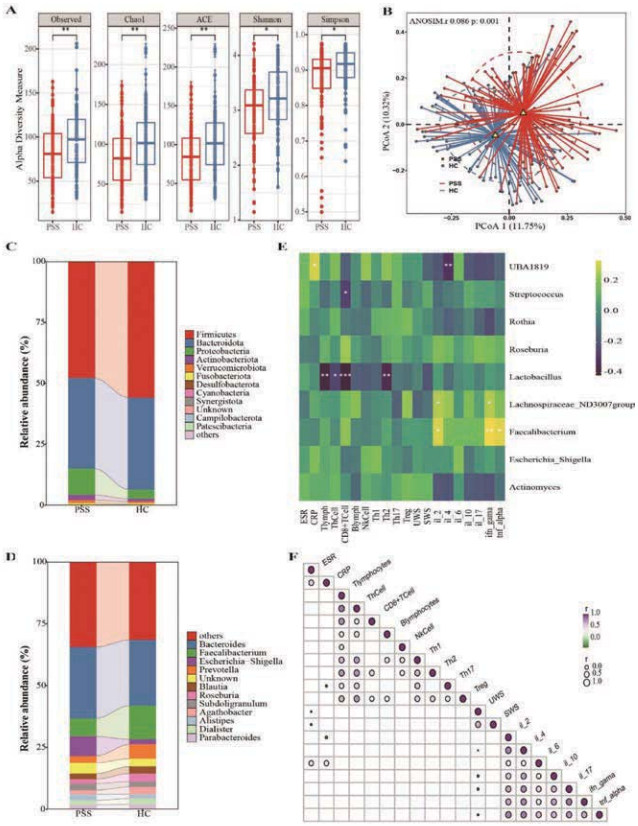

Figure1: (A) Comparison of alpha-diversity indices between pSS and HC groups. **(B)** With regard to beta diversity, Bray-Curtis analysis indicated that PCoA could discriminate the HC samples from pSS. **(C-D)**The most abundant bacterial groups depicted for pSS and HC at phylum and genus levels, respectively. **(E)** Correlations between the relative abundance of significantly different bacteria and clinical parameters. Correlations with p<0.05 are shown. **(F)** The relationship among various clinical index. the purple points represent the positive correlation and green points represent negative correlation, and the size of points represent the size of correlation by spearman.

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POS0746

MEASUREMENT OF ANTI-SUPRABASIN ANTIBODIES, MULTIPLE CYTOKINES AND CHEMOKINES AS POTENTIAL PREDICTIVE BIOMARKERS FOR NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE) is multifactorial and involves diverse cytokines, autoantibodies and immune complexes inducing blood-brain barrier (BBB) dysfunction, neuroendocrine-immune imbalance, vascular occlusion, tissue, and neuronal damage. Several pro-inflammatory cytokines have been implicated in the pathogenesis of NPSLE [1]. Previously we have shown that the titer of anti-suprabasin (SBSN) antibodies in cerebrospinal fluid (CSF) of NPSLE patients was significantly higher than in SLE, MS and NPH groups [2]. However, distinguishing NPSLE from other neuropsychiatric conditions with different etiologies is challenging.
Objectives: This study determined the most critical serum biomarkers for the development of NPSLE as they may have clinical utility prior to the onset of neuropsychiatric symptoms.
Methods: We retrospectively analyzed 35 NPSLE patients, 34 SLE patients, 20 viral meningitis (VM) patients, and 16 relapsing-remitting multiple sclerosis (MS) patients. We measured anti-SBSN antibodies concentrations in serum by using Luciferase immunoprecipitation system (LIPS) assay. The serum concentrations of cytokines/chemokines were measured by using multiplex bead-based assay. All the clinical information and laboratory tests were collected at the time of admission.
Results: The Bayesian posterior mean and 95% HPDI of the cut-off of AI and its PPV and 1-NPV values were 5.26 (3.68;7.17), 0.87, (0.72; 1.0) and 0.44, (0.36; 0.5), respectively (Figure 1).

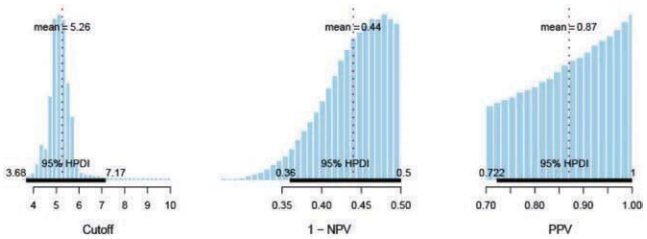

Figure 1. Summary of the posterior distribution of the cutoff of AI and its predictive value (1-NPV and PPV). The 95% HPDI is shown as the thick black horizontal line with the boundaries written above the line

Among analyzed biomarkers, VEGF had the highest sparsity-oriented important learning (SOIL) importance, followed by AI, sCD40L, IL-10, GRO, MDC, IL-8, IL-9, TNFα, MIP-1α (Figure 2).

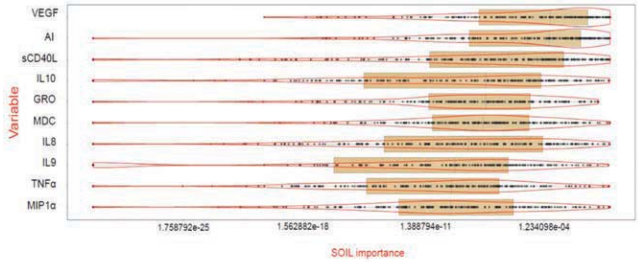

Figure 2. Top 10 biomarkers having highest SOIL importance in prediction of NPSLE. Abbreviations• AI: anti-SBSN antibody index• PPV: positive predictive• NPV: negative predictive value• SOIL: sparsity-oriented important learning• IL: interleukin•MIP: macrophage inflammatory protein• sCD40L: soluble CD40 ligand• MDC: macrophage-derived chemokine• VEGF: vascular endothelial growth factor• MDC: macrophage-derived chemokine• TNF: Tumor necrosis factor

Conclusion: Our data demonstrated the ranking of serum biomarkers for the prediction of NPSLE. The most essential biomarkers are VEGF, anti-SBSN antibodies, sCD40L, IL-10, GRO, MDC, IL-8, IL-9, TNFα, MIP-1α.
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POS0747

ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN ANTIBODIES AND VASCULAR EVENTS ASSOCIATE POSITIVELY WITH HLA-DRB1*13 AND NEGATIVELY WITH HLA-DRB1*03 IN SLE

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Background: Anti-phosphatidylserine/prothrombin antibodies (anti-PS/PT) associate with thrombotic events (1). *HLA-DRB1* alleles contribute to the occurrence of conventional antiphospholipid antibodies (aPL), including anti-beta2glycoprotein-I (beta2GPI) and anti-cardiolipin (CL) (2).
Objectives: We investigated associations between anti-PS/PT and *HLA-DRB1* alleles and thrombosis in patients with SLE. Conventional aPL were included for comparison.
Methods: We included 341 consecutive Swedish SLE patients, with information on general cardiovascular risk factors, including blood lipids, lupus anticoagulant (LAC) and thrombotic events. Anti-PS/PT, anti-beta2GPI and anti-CL of IgA/G/M isotypes were quantified in parallel using particle-based multi-analyte technology. The 99th percentiles among 162 age- and sex-matched populations controls were used as cutoffs. *HLA-DRB1* typing was performed using sequence-specific primer PCR.

Results: Anti-PS/PT antibodies associated positively with *HLA-DRB1*13* (odds ratio [OR] 2.7, P=0.002), whereas anti-beta2GPI and anti-CL antibodies associated primarily with *HLA-DRB1*04* (OR 2.5, P=0.0005; Table 1). These associations remained after adjustment for other significant *HLA-DRB1* alleles identified in Table 1 (Figure 1a and b) also for LAC (Figure 1c), and also after adjustment for age and gender (not shown). *HLA-DRB1*13*, but not *DRB1*04*, remained as an independent risk factor for thrombosis after adjustment for significant HLA alleles (Figure 1d), and also after adjustment for cardiovascular risk factors in stepwise regression (not shown). Mediation analysis showed that 31.3% of the *HLA-DRB1*13*-related risk for thrombosis was mediated by anti-PS/PT positivity. *HLA-DRB1*03*, on the other hand, associated negatively with thrombotic events (Figure 1d) as well as with all aPL (Figure 1a-c). *HLA-DRB1*03* had thrombo-protective effect in aPL positive patients (Figure 1d). Additionally, *HLA-DRB1*03* positivity was associated with a favourable lipid profile regarding high-density lipoprotein (median 1.4 vs. 1.2 mmol/L, p=0.02) and triglycerides (median 0.9 vs 1.1 mmol/L, p=0.04); whereas no other *HLA-DRB1* alleles showed any associations to lipid levels.

Table 1. Frequency of individual HLA DRB1 and associations with antibody phenotypes. Odds ratios (OR) and confidence intervals (CI) for being antibody positive given a specific HLA allele and corresponding p values were calculated using Chi2 tests, with significant associations underlined.

HLA DRB1	*HLA-DRB1* n (%) total patients	Anti-PS/PT positive (any isotype) n=48	OR (95%CI); P	Anti-β_2GPI or anti-CL positive (any isotype) n=96	OR (95%CI); P
*01	41 (12.9%)	4 (8.3%)	0.6 (0.2-1.7); 0.3	11 (11.4%)	0.8 (0.4-1.7); 0.6
*03	147 (46.5%)	13 (27.1%)	0.4 (0.2-0.7); 0.004	33 (34.4%)	0.5 (0.3-0.8); 0.006
*04	94 (29.7%)	18 (37.5%)	1.6 (0.8-2.9); 0.2	41 (42.7%)	2.5 (1.5-4.1); 0.0005
*07	28 (8.9%)	6 (12.5%)	1.5 (0.6-4); 0.4	9 (9.4%)	1 (0.4-2.4); 0.9
*08	28 (8.9%)	6 (12.5%)	1.6 (0.6-4.3); 0.3	9 (9.4%)	1.2 (0.5-2.7); 0.7
*09	9 (2.8%)	1 (2.1%)	0.7 (0.1-5.5); 0.7	2 (2.1%)	0.6 (0.1-3.0); 0.5
*10	7 (2.2%)	0 (0)	NA	2 (2.1%)	0.9 (0.2-4.6); 0.9
*11	27 (8.5%)	6 (12.5%)	1.6 (0.6-4.3); 0.3	8 (8.3%)	0.9 (0.4-2.2); 0.8
*12	7 (2.2%)	0 (0)	NA	1 (1%)	0.4 (0.05-3.7); 0.4
*13	79 (25%)	21 (43.7%)	2.7 (1.4-5.2); 0.002	33 (34.3%)	2 (1.2-3.4%); 0.01
*14	6 (1.9%)	2 (4.2%)	3.7 (0.6-23); 0.1	2 (2.1%)	1.4 (0.2-8.9); 0.8
*15	118 (37.3%)	12 (48%)	0.5 (0.2-0.9); 0.045	27 (28.1%)	0.5 (0.3-0.9); 0.01
*16	8 (2.5%)	1 (2.1%)	0.8 (0.09-6.4); 0.8	4 (4.2%)	2.2 (0.5-9.2); 0.2

Conclusion: *HLA-DRB1*13* confers risk for both anti-PS/PT and thrombotic events in SLE. The association between *HLA-DRB1*13* and thrombosis is largely, but not entirely, mediated through anti-PS/PT. Due to the negative association of *HLA-DRB1*03* with aPL and the positive association with favourable lipid levels, *HLA-DRB1*03* seems to identify a subgroup of SLE patients with reduced vascular risk.

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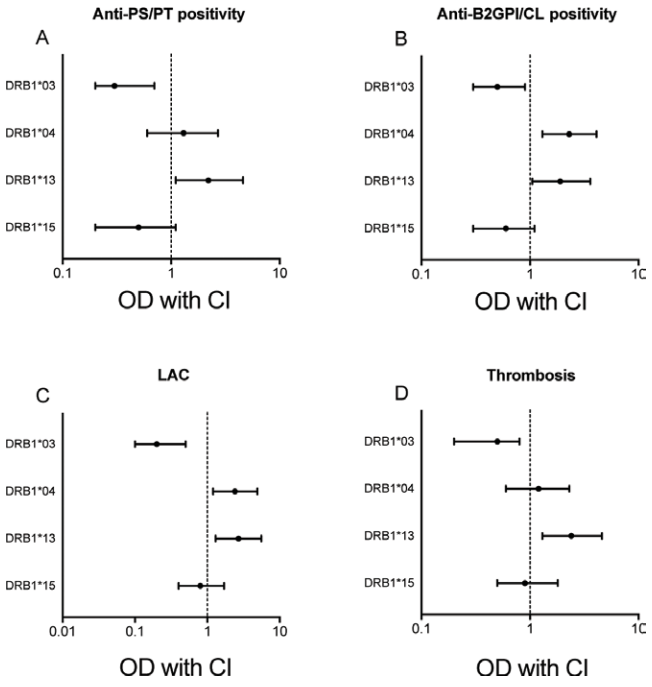

Disclosure of Interests: Sahwa Elbagir: None declared, Lina M. Diaz-Gallo: None declared, Giorgia Grosso: None declared, Agneta Zickert: None declared, Iva Gunnarsson: None declared, Michael Mahler Employee of: Dr Mahler is employee of Werfen., Elisabet Svenungsson Speakers bureau: Dr Svennungson has obtained speaker's fees from Janssen., Grant/research support from: Dr Svennungson has obtained research grant from Merck., Johan Rönnelid Speakers bureau: Dr Rönnelid has given paid lectures for Thermo Fisher Scientific., Consultant of: Dr Rönnelid has been a member of the Scientific Advisory Board for Thermo Fisher Scientific.

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POS0748 COMPARISON BETWEEN PRIMARY SJÖGREN'S SYNDROME PATIENTS WITH AND WITHOUT DRYNESS

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Background: To date, no study has clinically focused on primary Sjögren's Syndrome (pSS) patients presenting without or with low level of dryness features.

Objectives: To describe pSS patients presenting no dryness or with low level of dryness and to compare them with pSS patients with dryness features to determine whether a specific clinical presentation can be identified in these patients.

Methods: All patients diagnosed with pSS according to AECG or ACR/EULAR criteria in our tertiary reference center were included. All patients were recruited between 1999 and 2020. Patient were considered without subjective dryness if the VAS for dry eyes or dry mouth was ≤ 30/100 and/or without objective dryness if having both normal Schirmer and salivary flow rate.

Results: Overall, 509 patients were included in the subjective dryness comparison group and 434 in the objective one (Table 1). Compared to patients with subjective dryness (n=456), patients without subjective dryness (n=53) were significantly younger (p=0,0025), were diagnosed earlier (p=0,0056), were more frequently anti-SSA positive (p=0,008), had lower levels of fatigue (p=0,0005). But no difference was observed regarding the level of disease activity or frequency of organ involvement. By contrast, patients reporting subjective dryness had more frequently chronic cough (p=0,022), with no more frequent objective lung involvement. Thus, the higher prevalence of chronic cough might be explained by dryness of the upper airways.

Table 1. Comparison of pSS patients with or without dryness

	No Subjective dryness n=53	Subjective dryness n=456	P value
Age, median (IQR)	49 (39-62)	58 (47-67)	0,0025**
Diagnostic delay, mean, years	4,32	6,27	0,0056**
ESSDAI, mean (SD)	3,55 (3,38)	3,22 (3,28)	0,52
MSGB# Chisolm score of 3 or 4, n (%)	36 (68)	362 (79)	0,08
Anti Ro/SSA, n (%)	44 (83)	292 (64)	0,008**
Chronic cough, n (%)	5 (9)	110 (24)	0,022*
VAS pain, median (IQR)	40 (4-70)	53 (23-77)	0,06
VAS fatigue, median (IQR)	47 (13-71)	65 (44-82)	0,0005***
	No Objective dryness n=108	Objective dryness n=326	
Age, median (IQR)	52 (41-60)	59 (47-67)	0,0026**
Diagnostic delay, mean, years	5,9	6,1	0,75
ESSDAI, mean (SD)	3,46	2,96	0,056
MSGB# Chisolm score of 3 or 4, n (%)	81 (75)	255 (78)	0,49
Anti Ro/SSA, n (%)	84 (78)	204 (62)	0,0042**
Arthralgia, n (%)	81 (75)	210 (64)	0,04*
VAS pain, median (IQR)	59,5 (32,5-80)	50 (20-73)	0,03*
VAS fatigue, median (IQR)	66 (44-83)	61 (39-80)	0,27
VAS eye dryness, median (IQR)	49 (17-71)	57 (25-80)	0,019*
VAS mouth dryness, median (IQR)	58 (34-75)	70 (48-88)	0,001**

MSGB: minor salivary gland biopsy

The patients without objective dryness (n=108) were also younger (p=0,0026), and had more frequently anti-SSA positive (p=0,0042). They also had a higher disease activity (mean ESSDAI: 3,46 versus 2,96, p=0,056). In this group of patients, the higher frequency of anti-SSA might be explained by the need of other criteria to fulfil diagnostic criteria, in the absence of abnormal Schirmer and salivary flow. Patients with objective dryness had more frequently arthralgia (p=0,04), a higher level of pain VAS (p=0,03) and subjective dryness VAS (p=0,019 for ocular and p=0,01 for oral) than patients without objective dryness.
Among the 108 patients with no objective dryness, only 17 had also had no subjective dryness (VAS <30mm).
P value corresponds to the comparison of the two strata with Student's t or Mann Whitney-U test
Conclusion: Among the patients with pSS, those without subjective or objective dryness features had a younger profile, shorter diagnosis delay which may result from a more acute onset, were more frequently anti-SSA positive. Those having no objective dryness also had more systemic disease, arthralgias and pain than patients with dryness features. Subjective dryness was associated with higher level of fatigue.
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[1] Characters from table content including title and footnotes:
Disclosure of Interests: None declared
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POS0749 ANTI-Β2GPI-DOMAIN 1 ANTIBODIES STRATIFY HIGH RISK OF EXTRA-CRITERIA MANIFESTATIONS IN A LARGE PROSPECTIVE CHINESE COHORT OF ANTIPHOSPHOLIPID SYNDROME

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Background: Anti-β2GPI-Domain 1 (β2GPI-D1) antibodies are potentially pathogenic in patients with antiphospholipid syndrome (APS), but their clinical associations and diagnostic value were unclear.
Objectives: To evaluate the clinical characteristics of APS patients with anti-β2GPI-D1 positivity, and its utility in diagnosing APS among SLE patients.
Methods: A total of 338 patients were included, of which 169 patients diagnosed with primary APS (PAPS group), 50 with APS secondary to SLE (SAPS group), 209 with SLE (SLE group). Serum anti-β2GPI-D1 IgG was measured using chemiluminescent immunoassay (Inova Company). Extra-criteria manifestations were analyzed, including thrombocytopenia, autoimmune hemolytic anemia, valvular lesions, APS nephropathy, and non-vascular neurological manifestations.
Results: Similar presence of anti-β2GPI-D1 IgG was seen among PAPS (32.80%) and SAPS (32.0%) patients, and 96.4% of those with positive anti-β2GPI-D1 IgG showed triple aPLs positivity. Anti-β2GPI-D1 IgG was significantly associated with recurrent thrombosis before APS diagnosis, microscopic thrombosis (p<0.05), but not with adverse pregnancy events (Figure 1). Notably, patients with extra-criteria manifestations, especially thrombocytopenia and APS nephropathy, showed significantly higher titers in anti-β2GPI-D1 IgG (p<0.05). After a median follow-up of twenty-five months, patients with anti-β2GPI-D1 IgG also showed a tendency of more extra-criteria events (3/55 vs 1/114, p=0.095), but not thrombotic events or adverse pregnancy events. Anti-β2GPI-D1 was positive among 8.13% of the SLE controls, and showed higher specificity (91.9%) in diagnosing SAPS among SLE patients as compared to classic aPLs.

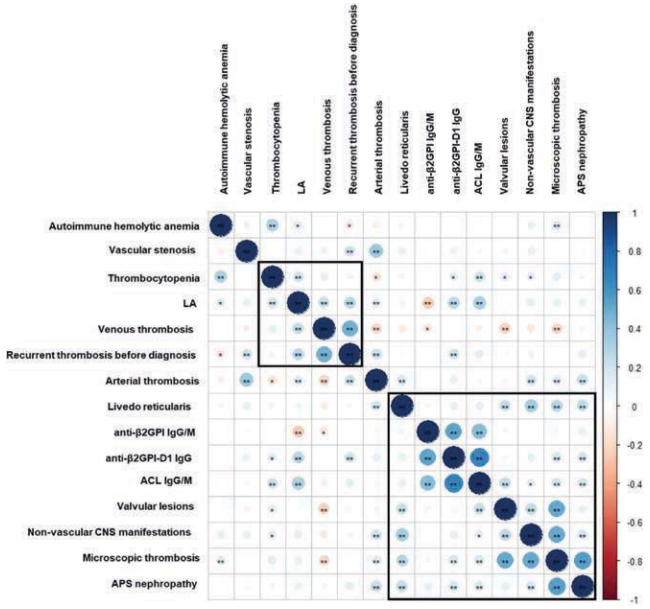

Figure 1.

Conclusion: Anti-β2GPI-D1 IgG had a stronger association with extra-criteria manifestations in APS patients compared to three classic APLs, which properly indicated its pathogenic role of microangiopathy.
Disclosure of Interests: None declared
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POS0750 THE STATUS OF BREGS AND BREG-RELATED CYTOKINES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Table 1. Characteristics of the individual studies included in the meta-analysis.

				Case Numbers				
Author	Publish Year	EI[a]	Q[b]	SLE	HC	Breg's definition	Mean % of Breg (mean(or median)±SD)	% of Breg among PBMC/CD19$^+$T cells
Blair,P.A	2010	4	6	25	14	CD19$^+$CD24^{hi}CD38^{hi}	SLE: 13.9±5.21 HC: 9.02±2.71	PBMC
Wang,T.	2017	4	7	56	35	CD19$^+$CD24^{hi}CD38^{hi}	SLE: 39.83±21.39 HC: 8.74±3.97	PBMC
Wang,H.	2019	4	6	36	30	CD19$^+$CD24^{hi}CD38^{hi}	SLE: 12.94±5.45 HC: 5.64±3.13	PBMC
Simon,Q	2016	4	6	16	33	CD19$^+$CD24^{hi}CD38^{hi}	SLE: 17.9±7.2 HC: 11.65±4.01	PBMC
Zhuo-long Wang	2018	4	6	28	30	CD19$^+$CD24^{hi}CD38^{hi}	SLE: 3.62±1.25 HC: 4.07±1.48	PBMC
Heinemann,K.	2016	4	6	33	21	CD19$^+$CD24^{hi}CD38^{hi}	SLE: 1.6±2.6 HC: 1.5±1.1	PBMC
Chu,M.	2015	4	7	43	32	CD19$^+$CD24^{high}CD27$^+$	SLE: 8.39±7.22 HC: 26.58±8.96	PBMC
Vadasz,Z.	2015	4	6	21	20	CD19$^+$CD25^{hi}FoxP3^{hi}	SLE: 18.5±3.05 HC: 11±1.65	PBMC
Cai,X.	2015	4	7	60	20	CD19$^+$CD5$^+$	SLE: 1.86±0.8 HC: 4.35±1	PBMC
Yang,X.	2014	4	7	30	15	CD19$^+$CD5$^+$CD1d^{hi}	SLE: 4±1.57 HC: 1.63±0.99	PBMC
Shan-feng Liu	2015	4	6	10	10	CD19$^+$CD5$^+$CD1d^{hi}	SLE: 0.83±0.28 HC: 0.2±0.21	CD19$^+$B cell
Zhong-wei Huang	2014	4	5	34	30	CD19$^+$CD5$^+$CD1d^{hi}	SLE: 7.86±4.1 HC: 22.71±9.17	PBMC
Ye, Z.	2019	4	6	47	20	CD19$^+$IL-10$^+$	SLE: 0.1±2.78 HC: 4.85±4.54	CD19$^+$B cell
Rong-wei Zhang	2016	4	6	50	20	CD19$^+$IL-35$^+$	SLE: 1.77±0.79 HC: 4.24±1.11	PBMC

SLE: systemic lupus erythematosus. [a]Evidence level (EL) of each study was based on Oxford Center for Evidence-Based Medicine 2011. [b]Quality (Q) of each study was based on the Newcastle-Ottawa Quality Assessment Scale case.

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Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease which involves in multiple tissue and organ injury. Regulatory B cells (Bregs) are unique subpopulations of B cells with immune-regulating properties. Interestingly, different subsets of Bregs have distinct markers and phenotypes and participate in self immune regulation by different ways. However, the level of Bregs in SLE remains debated.
Objectives: This study aims to clarify the proportions of Bregs with special controversial cellular markers and Breg-related cytokines in SLE patients.
Methods: We explored the proportion of Bregs and Breg-related cytokines (IL-10) in SLE patients by searching literature through November 2021 from CBM, CNKI, China Science and Technology Journal Database, Wan Fang Data, PubMed, Embase, Web of Science, Cochrane Library and Medline. Random effects model was used to pool data. Heterogeneity and risk of bias was examined with I-squared index (I^2) statistic. Inconsistency was evaluated by using the I^2 and Egger tests were used for the evaluation of potential publication bias (STATA v.12.0).
Results: Total 14 case-control studies involving 489 PsA patients and 330 healthy controls (HCs) were included in this study (Table 1). No significant difference in the proportions of Bregs was evident between SLE patients and HCs [SMD=0.067, 95%CI (-0.924,1.059), P=0.894]. Because of a significant statistical heterogeneity observed [I^2=97.1%, p<0.001], we conducted sub-analyses based on individual definitions of Bregs. We found the proportions of $CD19^+CD24^{hi}CD38^{hi}$ Breg cells was significantly increased in SLE [SMD=0.902, 95%CI (0.157,1.647), P<0.001](Figure 1A). The level of serum IL-10 was increased in SLE compared to that of HCs [SMD=1.062, 95%CI (0.754,1.370), P<0.001] with no publication bias based on the Egger tests (t=0.91, P=0.366)(Figure 1B).

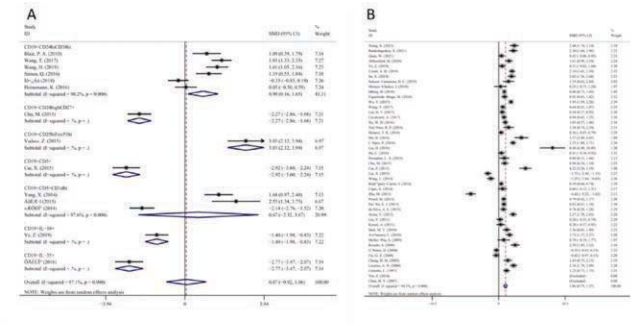

Figure 1: (A)Forest plot of the subgroup meta-analysis of individual definitions of peripheral Bregs proportions, between SLE and HCs. (B) Forrest plot of the levels of serum IL-10 between SLE and HCs.SLE, systemic lupus erythematosus; HCs, healthy controls.

Figure 1.

Conclusion: The levels of $CD19^+CD24^{hi}CD38^{hi}$ Bregs and IL-10 were significantly increased in SLE patients, suggesting that the abnormalities of Bregs numbers and function are the critical causes in the development of SLE.
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Disclosure of Interests: None declared
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POS0751 TEMPORAL TREND IN HOSPITALISATION FOR OPPORTUNISTIC INFECTIONS IN PATIENTS WITH CONNECTIVE TISSUE DISEASES.

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Background: Patients with autoimmune connective tissue disease (CTD) and systemic vasculitis (SV) often require aggressive immune-modulating therapy to prevent organ damage. This however increases the risk for common and uncommon infections.
Objectives: To compare the temporal rates and associated mortality of hospitalisation with opportunistic infections (OI) for CTD and SV patients in Western Australia between 1985 and 2015.
Methods: All patients hospitalized in Western Australia in the period 1985-2015 with ≥ 2 ICD based diagnostic codes for SLE (n=1432), other CTD (o-CTD; incl DM/PM, systemic sclerosis, Sjogren's syndrome; n=2161) and Systemic vasculitis (SV; n=1599) and a microbiologically confirmed OI (Mycobacterial, Fungal and viral infections) were included. Descriptive data are given as median (IQR) and frequency (%). Incidence rates per 1000 person years (IR) were calculated during 100.410 person years.
Results: OI occurred in 12.4 % of lupus, 11.5% of SV and 10.4% of o-CTD patients (p=0.72), but overall IR rates for OI were higher for lupus patients (9.87, CI 5 .49-15.76) than for SV (5.94, CI-2.81-10.24) and o-CTD patients (3.40, CI 1.62-7.23). However, whereas the IR for OI in lupus decreased over time, the IR increased for SV and o-CTD patients (Figure 1). Viral infections were the most frequent specific OI followed by tuberculosis and mycotic infections. Cryptococcal infections were observed in lupus patients only and the limited cases of pneumocystis occurred predominantly in SV patients with no cases observed after 2000 (Figure 2). In hospital mortality during OI admission was 11.5% for SV, 5.6 % for lupus and 3.5% for o-CTD patients (p=0.004).

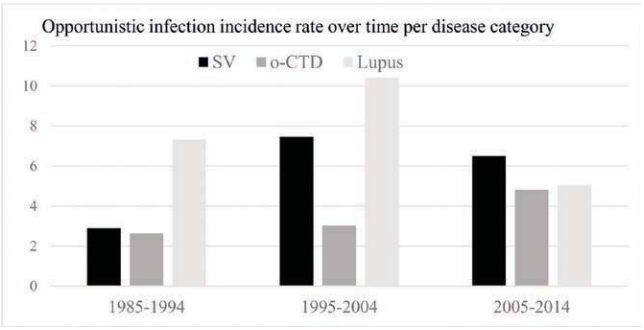

Figure 1.

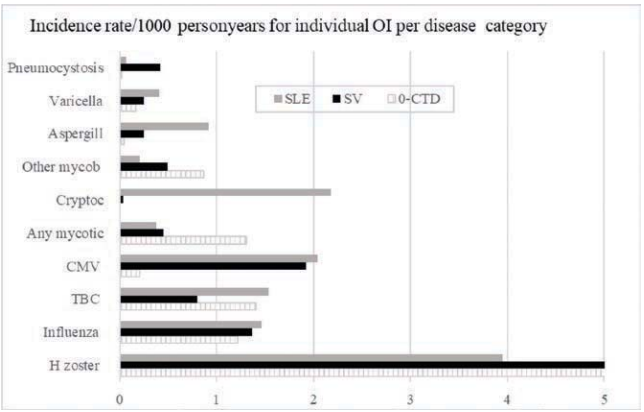

Figure 2.

Conclusion: Hospitalization rates for OI have decreased for lupus patients especially since 2005, whereas viral and mycotic OI rates have increased for both SV and o-CTD patients. Hospitalization for OI associated with significant case fatality in especially SV patients, indicating a need for increased prevention of OI.
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Disclosure of Interests: None declared
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POS0752 DISEASE FEATURES AT DIAGNOSIS AND CHANGES IN DISEASE COURSE SEVERITY AMONG PATIENTS WITH CHILDHOOD-ONSET COMPARED TO ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is characterised by a heterogeneous clinical presentation with alternating periods of remission and relapse. Disease severity is determined by the type and level of involvement of different organ systems. SLE can occur in childhood or later in life, and patients may present with differing levels of disease severity according to the age of onset. Changes in disease severity following treatment may also differ depending on age of onset. There are limited data that document these differences.
Objectives: To compare demographic and clinical characteristics including baseline disease severity and changes in severity over time between patients with childhood-onset and adult-onset SLE in the United States.
Methods: We identified patients aged 0–64 years and diagnosed with SLE during 2015–2019 using the IBM MarketScan claims databases. SLE severity was determined using a published algorithm, which combines elements of organ involvement and the use of SLE-related medications to assign patients to mild, moderate, and severe disease states.[1] Baseline disease severity was determined using a 90-day period following the initial SLE diagnosis. The index date was the day after this initial 90-day period. Baseline comoribidities were assessed during the 12 months prior to the index date. Disease severity was evaluated at 0 to <6 months, ≥6 to <12 months, and ≥12 to <24 months post-index. Patients were categorised according to the highest severity level identified during each period. Changes in severity vs. baseline were also measured during each evaluation period. For example, worsening severity was defined as a transition from a lower to higher disease severity state (e.g., moderate to severe). Analyses were conducted separately for cohorts with Commercial Health Insurance (CHI) and Medicaid. Within each cohort, patients with childhood-onset (≤17 years) were descriptively compared to those with adult-onset (≥18 years) SLE.
Results: Most enrolees were female (CHI: 90%, Medicaid: 92%). Mean age at index date was 14.0 vs. 43.4 years for childhood- and adult-onset groups, respectively. Baseline infections were more prevalent among children vs. adults in both CHI (41.4% vs. 30.1%) and Medicaid (45.3% vs. 39.3%) cohorts (Table 1). A higher proportion of children vs. adults had severe disease at baseline in the CHI (38.3% vs. 10.7%) and Medicaid (48.0% vs. 14.2%) cohorts. Overall, the largest decreases in SLE severity compared to baseline were observed during ≥6 to <12 months of follow-up. Children were more likely to experience a decrease in severity than adults. During ≥12 to <24 months, 19.9% of children in the Medicaid cohort had an increase in severity compared to baseline vs. only 12.3% of children in the CHI cohort.

Table 1. Profiles of patients with SLE

Characteristic %	Commercial Health Plan		Medicaid	
	0–17 years	18–64 years	0–17 years	18–64 years
	(N=290)	(N=10,622)	(N=298)	(N=3,143)
Age in years at index date, mean (SD)	14.2 (2.7)	44.6 (12.0)	13.7 (3.1)	39.2 (11.9)
Median (range)	15.0 (1–17)	48.0 (18–64)	15.0 (2–17)	39.0 (18–64)
Female	86.7%	90.1%	83.9%	93.1%
Baseline treatment				
Corticosteroids	77.6%	69.3%	84.6%	69.7%
Immunomodulators	42.4%	23.2%	55.0%	19.4%
Antimalarials	71.7%	60.5%	80.2%	49.1%
SLE severity change from baseline				
0–<6 months follow-up				
Increase	10.9%	20%	7.5%	21.7%
Decrease	20.9%	17.2%	25.9%	18.8%
≥6–<12 months follow-up				
Increase	11.6%	20.4%	9.2%	22.8%
Decrease	36.7%	19.9%	39.5%	22.7%
≥12–<24 months follow-up				
Increase	12.3%	30.1%	19.9%	33.2%
Decrease	33.3%	15.6%	38.0%	17.8%

SD, standard deviation.

Conclusion: Children with SLE present with greater severity of symptoms compared to adults and are more likely to experience an improvement following the initial treatment period.
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Disclosure of Interests: Andrea Phillips-Beyer Consultant of: Idorsia Pharmaceuticals, Qian Li Consultant of: Idorsia Pharmaceuticals, Michael E. Stokes Consultant of: Idorsia Pharmaceuticals, Marilia Pozzobon da Silva Employee of: Idorsia Pharmaceuticals
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POS0753 PROSPECTIVE EVALUATION OF HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN A MONOCENTRIC COHORT OF PATIENTS WITH LONGSTANDING SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: The optimization of HRQoL in SLE patients is defined as one of the treatment goals in the 2019 EULAR recommendations[1] for the management of SLE. Most studies have examined HRQoL at one point in time, while the few longitudinal studies do not report a clear variation in Patient Reported Outcomes (PROs) with respect to changes in disease activity. It would be important to understand if, even in a real-life setting, the improvement of patients' HRQoL may represent an achievable target.
Objectives: the aim of this study was to analyze HRQoL over time in a monocentric cohort of patients with SLE and investigate which disease-related factors determine short-term variation of HRQoL in a real-life setting.
Methods: this is a longitudinal, prospective monocentric study which included consecutive adult outpatients with SLE (1997 ACR classification criteria), regularly followed at the Rheumatology Unit of Pisa. Patients were enrolled over a period of 2 years, before the pandemic outbreak, and had at least 2 assessments per year. For each patient, demographics, comorbidities, treatment, clinical and laboratory data were collected. Disease activity was evaluated with the SELENA-SLEDAI and organ damage with the SLICC/DI. We defined as a significant variation of disease activity, a difference of clinical SELENA-SLEDAI ≥ 4 points between 2 subsequent evaluations. At each visit, patients completed the following PROs: SF-36, FACIT-Fatigue and LIT.
Results: we enrolled 210 consecutive SLE patients, mainly female (93.8%) and of Caucasian ethnicity (97.1%), with a mean age at enrollment of 45.1±12.7 years and a median disease duration of 13 years (IQR 5-21). At baseline, the median SLEDAI of the cohort was 2 (IQR 0-4). The most frequent active disease manifestations were: articular (17.1%) and hematological (15.2%); 6.7% of patients had active renal disease. 47.14% had a SLICC-DI > 0 with a median SLICC-DI among them of 2 (IQR 1-3). 11.43% of patients had a concomitant fibromyalgia. Most patients were on Hydroxychloroquine (78.1%) and low dose glucocorticoid (55.2%), with a median daily dose of 2 mg (IQR 0-4) of prednisone equivalent; 41.4% were on conventional immunosuppressants and 11.9% on biologics, mainly belimumab. The median scores of PROs at enrollment are reported in Table 1. At baseline, fibromyalgia confirmed to have a significant negative impact on all PROs after adjustment for confounding factors (p<0.05). Each patient underwent two consecutive evaluations, with a median interval between them of 11.4 months. We observed a significant variation of disease activity in 36/210 patients (17.14%). Then, we compared the subgroup of patients with unchanged disease activity with that of patients who showed a significant variation of disease activity. We found that FACIT and LIT scores didn't change over time in both subgroups, whereas PCS (p<0.001) and MCS (p<0.01) scores of the SF-36 showed a significant variation in both groups, between the first and the second clinical assessment. However, in the subgroup of patients with a significant change of disease activity, the variation of PCS and MCS was not correlated with the variation of disease activity or ongoing treatment. In particular, patients with a significant improvement of HRQoL over time didn't have a corresponding significant reduction of the SLEDAI score or of the daily glucocorticoid dose.

Table 1. PROs scores at baseline.

PROs	Median scores at baseline
SF-36 PCS	58 (IQR 49.09- 68)
SF-36 MCS	57 (IQR 46.42-67)
FACIT	42 (IQR 32-46)
LIT	20 (IQR 7.5-40)

Conclusion: our findings seem to suggest that HRQoL over time in outpatients with longstanding SLE tends to be stable (maybe because patients are able to adapt to their illness) or varies unpredictably, maybe influenced by not disease-related factors. Further studies are needed to better understand which factors influence HRQoL over time and which questionnaires are more sensitive to catch its variation.
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POS0754 PATIENT ACCEPTABLE SYMPTOM STATE (PASS) IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME IN DAILY CLINICAL PRACTICE

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Background: Primary Sjögren's syndrome (pSS) has great impact on all aspects of patients' lives, not only physically, but also mentally, socially and financially.[1] Sicca symptoms are mainly treated with local treatment, but no systemic immunosuppressive treatment is registered yet for pSS, which may have significant consequences on whether patients find their symptom state acceptable (PASS). In a previous study, a cut-off for acceptable symptom state based on the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI, score <5) was developed for inclusion of patients with an unacceptable symptom state in clinical trials.[2]

Objectives: To explore the presence of PASS in a standard of care cohort of pSS patients and to compare patient characteristics and disease activity including ESSPRI between patients with and without PASS.

Methods: Consecutive outpatients with pSS from the REgistry of Sjögren Syndrome LongiTudinal (RESULT) cohort, who fulfilled the ACR/EULAR classification criteria and had available PASS data at baseline were included. Patient-reported outcomes were reported through questionnaires, which included the PASS ("Considering all the different ways your disease is affecting you, if you were to stay in this state for the next few months, do you consider your current state satisfactory?"; yes/no) and ESSPRI ("How severe has your dryness, fatigue and pain been during the last two weeks?"; scale 0-10). An acceptable ESSPRI symptom state has been defined as <5.[2] Systemic disease activity was assessed with EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). Independent samples t-test, Mann-Whitney U test or Chi Square test were used to analyse differences between patients with or without PASS.

Results: Of 277 included pSS patients, 248 (90%) were female, median age was 54 years (IQR 43-64) and disease duration 5 years (2-11). 198 (71%) patients scored their symptom state as acceptable according to PASS. Patients with PASS were significantly older and had a longer disease duration compared to patients without PASS. Furthermore, patients with PASS had more often a low disease activity according to ESSDAI, and less often moderate disease activity (Table 1). The difference in ESSDAI activity was mainly observed in the articular and constitutional domains. ESSPRI was significantly lower in patients with PASS (median 5 vs. 7). No differences were seen in functional or laboratory parameters (Table 1). Of all included patients, only 86 (31%) patients had an acceptable symptom state according to the pre-defined cut-off point for ESSPRI (score <5). Sensitivity and specificity of this ESSPRI cut-off point for reaching PASS was 40% and 92%, respectively.

Table 1. Baseline characteristics of pSS patients with and without PASS

	PASS (n=198)	Without PASS (n=79)
Gender (female)	177 (89)	71 (90)
Age (years)	57 (44-65)*	49 (41-60)*
Disease duration (years)	6 (2-12)*	5 (2-8)*
ESSDAI (total)	4 (2-6) (n=191)	4 (2-9) (n=75)
<5	127 (66)*	38 (51)*
5-14	52 (27)*	32 (43)*
≥14	12 (6)	5 (7)
ESSPRI (total)	5 (4-7)**	7 (6-8)**
<5	80 (40)**	6 (8)**
Schirmer's test (mm)	4 (1-10) (n=179)	4 (1-10) (n=72)
Ocular staining score	2 (1-4) (n=190)	2 (0-4) (n=77)
Unstimulated whole salivary flow (ml/min)	0.05 (0.01-0.14) (n=187)	0.08 (0.01-0.19) (n=76)
Stimulated whole salivary flow (ml/min)	0.54 (0.15-0.99) (n=189)	0.58 (0.21-0.97) (n=76)
SSA positive	172/197 (87)	66/79 (84)
IgG (g/L)	14 (11-19) (n=196)	14 (10-19) (n=79)
Rheumatoid factor (IU/ml)	12 (3-39) (n=196)	16 (2-47) (n=78)

Data presented as median (IQR) or n (%)*Significant difference p<0.05***Significant difference p<0.001

Conclusion: The majority (71%) of pSS patients reported being in an acceptable symptom state according to the PASS question in our standard of care cohort in daily clinical practice, despite high ESSPRI scores (60% with score ≥5). Further analyses of influences of treatment in these patients will be conducted.

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POS0755 SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF A SINGLE ORALLY ADMINISTERED DOSE OF ENPATORAN IN A PHASE I STUDY OF HEALTHY JAPANESE AND CAUCASIAN PARTICIPANTS

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Background: Enpatoran, a novel, highly selective and potent dual toll-like receptor (TLR) 7 and TLR8 inhibitor, is in development for the treatment of autoimmune disorders including systemic and cutaneous lupus erythematosus. A first-in-human study in healthy participants has shown that enpatoran is well-tolerated and has a linear pharmacokinetic (PK) profile.

Objectives: To compare the PK parameters, safety, and tolerability of single ascending oral doses of enpatoran in a Phase I study in Japanese and Caucasian participants, and to explore a potential PK/pharmacodynamic (PD) relationship.

Methods: A single-centre, open-label, sequential dose group study enrolled healthy Japanese and Caucasian participants into three dose cohorts. Each Caucasian participant was matched by body weight (± 20%), height (± 15%) and sex to a Japanese participant. Participants received a single orally administered enpatoran dose of 100 mg, 200 mg, or 300 mg as a film-coated tablet under fasting conditions. PK parameters, (maximum plasma concentration [C_{max}]; area under the plasma concentration–time curve (AUC) from time 0 to infinity [$AUC_{0\text{-inf}}$]; AUC from time 0 to the last sampling time [$AUC_{0\text{-tlast}}$]) determined using noncompartmental analysis, were estimated post-dose from Day 1–3. Safety was assessed from Day -1 to 8. PK (exposure) between the two ethnic groups was compared using an analysis of covariance (ANCOVA) model including ethnic group, natural log-transformed dose, and ethnic group by natural log dose interaction. *Ex vivo* secretion of cytokines (PD) under stimulated (using the TLR7/8 agonist, R848) and unstimulated conditions, was assessed pre- and post-dose. A panel of cytokines was analysed by multiplex immunoassay; IL-6 was considered the primary PD biomarker.

Results: The study included 36 male participants (18 Japanese and 18 Caucasian) with a mean (± SD) age of 35.1 (± 10.8) years and mean (± SD) body mass index of 23.1 (± 2.1) kg/m^2. Each dose group included six Japanese and six Caucasian participants. The geometric mean enpatoran plasma exposure parameters (C_{max}, $AUC_{0\text{-inf}}$, and $AUC_{0\text{-tlast}}$) were consistent between the two ethnic groups for each dose level (Table 1) and indicated dose proportionality. ANCOVA modeling demonstrated comparable exposure between the two groups (geometric least square mean ratio [Japanese/Caucasian;90% CI] of C_{max}: 0.9409 [0.7855–1.1270]; $AUC_{0\text{-inf}}$: 0.8959 [0.7497–1.0704] and $AUC_{0\text{-tlast}}$: 0.8963 [0.7511–1.0695]). Treatment-emergent adverse events (TEAEs) were observed in six Japanese (n = 0, 100 mg; n = 3, 200 mg; n = 3, 300 mg) and four Caucasian (n = 1, 100 mg; n = 0, 200 mg; n = 3, 300 mg) participants. There we no serious TEAEs; most were mild and not dose dependent. Treatment-related TEAEs were mild diarrhoea, mild flatulence, and moderate headache. There were no deaths, withdrawals, or early terminations due to TEAEs. Administering enpatoran effectively reduced *ex vivo* stimulated cytokine

release, with maximal inhibition observed at 2 hours post-dose (IL-6: mean ≥99%). High inhibition levels were sustained through 24 hours in a dose-dependent manner (IL-6: mean ~76–97%). The pattern of cytokine release inhibition was consistent across doses and ethnic groups.

Table 1. PK parameters in Japanese and Caucasian participants at the three enpatoran dose levels

Parameter	100 mg		200 mg		300 mg	
	Japanese	Caucasian	Japanese	Caucasian	Japanese	Caucasian
	N = 6	N = 6	N = 6	N = 6	N = 6	N = 6
C_{max} (ng/mL)	139	175	260	245	486	490
$AUC_{0\text{-inf}}$ (h*ng/mL)	774	948	1910	1850	2840	3330
$AUC_{0\text{-tlast}}$ (h*ng/mL)	758	931	1880	1830	2810	3270

All values are Geometric mean.C_{max}, maximum plasma concentration $AUC_{0\text{-inf}}$, area under the plasma concentration–time curve (AUC) from time 0 to infinity; $AUC_{0\text{-tlast}}$, AUC from time 0 to the last sampling time.

Conclusion: There were no relevant ethnic differences in PK, PD, and safety between healthy Japanese and Caucasian participants across a range of single oral enpatoran doses, thus supporting the inclusion of Asian participants in future global Phase II studies.

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POS0756 DETERMINANTS OF HEALTH-RELATED QUALITY OF LIFE (HR-QOL) ACROSS THE SPECTRUM OF SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES: RESULTS FROM THE LEAP COHORT

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Background: Poor health-related quality of life (HR-QoL) is recognised in patients with established connective tissue diseases (CTDs), however it is not clear how it affects patients with undifferentiated CTD (UCTD) which has traditionally been associated with a mild or more benign profile.

Objectives: To investigate HR-QoL in patients affected with a variety of CTDs (including UCTD) using the SF-36 questionnaire; and secondly, to review demographic and clinical factors predictive of a poor HR-QoL

Methods: The Lupus Extended Autoimmune Phenotype (LEAP) cohort is a multicentre prospective study of patients with a CTD. Rheumatologist diagnosis was used to classify patients into four groups: systemic lupus erythematosus (SLE), primary Sjögren's syndrome (pSS), UCTD, and (combined because of low numbers) those with an idiopathic inflammatory myopathy (IIM), systemic sclerosis (SSc) or overlap syndrome. The SF-36 quality of life questionnaire was completed at enrolment and includes eight domains: physical function (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH) which range from 0 to 100, with higher scores reflecting better HR-QoL. Physical (PCS) and mental component score (MCS) were calculated for each group, with a score below 50 representing a worse HR-QoL compared to the general UK population. Predictors for poor HR-QoL was chosen a priori, then tested using linear regression adjusted for age, gender and ethnicity. All statistical analysis was performed using STATA v14, with results expressed as beta coefficients with 95% confidence intervals (95%CI).

Results: Data were collected from 309 patients (280 [90.6%] women, with a mean [SD] age of 48.9 [12.9] years) from three UK rheumatology centres. The majority of patients were Caucasian (n=235, 76.1%). By rheumatologist diagnosis, 115 (37.2%) had SLE, 56 (18.1%) pSS, 72 (23.3%) UCTD and 66 (21.4%) SSc, IIM or an overlap syndrome. Patients with UCTD, pSS and SSc/IIM spectrum disorders had a shorter median disease duration (3.8, 3.7 and 6.1 years respectively) compared with patients with those with SLE (11.0 years), p<0.001. Previous steroid and immunosuppressant use was highest in patients with SLE and SSc/IIM spectrum disorders (p<0.001). The most affected domains include VT, GH and BP (Figure 1), and the PCS is more impaired compared with the MCS, with similar scores across disease groups. Agnostic of disease group, factors associated with a lower PCS include increasing age (beta -0.15 [95%CI -0.26, -0.06], p=0.008), prednisolone use (-3.1 [-6.05, -0.19], p=0.037), c-reactive protein (-0.09 [-0.62, -0.10], p=0.007), fatigue (-2.00 [-3.79, -0.22], p=0.028), and sicca syndrome (-4.70 [-7.66, -1.74] p=0.002), and these remained significant in a multivariate model.

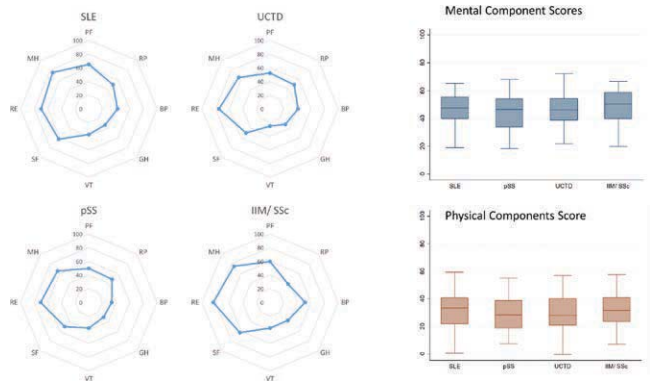

Figure 1. radar diagrams of eight SF-36 domains, and MCS and PCS boxplots. SLE; systemic lupus erythematosus; UCTD, undifferentiated CTD; pSS, primary Sjögren's syndrome; IIM, idiopathic inflammatory myopathy; SSc, systemic sclerosis; PF, physical function; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health

Conclusion: Patients with UCTD exhibit similar impairment in physical components of HR-QoL compared with other established CTDs, despite perceived differences in disease severity. This study highlights sicca syndrome, fatigue, and steroid burden as key targets for improving HR-QoL in patients across the spectrum of CTDs.

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POS0757

COVID-19 INFECTION AND RECOVERY AMONGST PATIENTS WITH MODERATE-TO-SEVERE LUPUS DURING THE PANDEMIC: RESULTS FROM THE BILAG-BIOLOGICS REGISTER (BILAG-BR)

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Background: Patients with systemic lupus erythematosus (SLE) are thought to be at greater risk of severe COVID-19 illness and associated complications due to a combination of inherent aberrant immune responses, immunosuppressive medications and co-morbidities.
Objectives: To review COVID-19 infections, hospitalisation and recovery in a real-world cohort of patients with moderate to severe SLE and high immunosuppressant use.
Methods: The British Isles Lupus Assessment Group Biologics Registry (BILAG-BR) is a national prospective registry of lupus patients from the UK (2010-21) requiring significant immunosuppressive therapies. Patients from the BILAG-BR were invited to complete a paper or online questionnaire which consisted of 17 questions to assess prior COVID-19 infection and their recovery during the COVID-19 pandemic. Questionnaires were completed between 9th Oct 2021 and 7th Jan 2022. Responses were linked with data collected in the BILAG-BR. Mortality data were collected from study centres and the Office of National Statistics from Dec 2019-Jan 2022.
Results: Data were collected from the first 202/1268 patients to respond. Patients were predominately female (186, 92.1%), had a median age of 51 (IQR 38-61) years and were from 37 UK centres. Previous therapy included rituximab (165, 81.7%), belimumab (33, 16.3%) and cyclophosphamide (54, 26.7%). In the past 12 months, over two thirds of patients (138, 68.3%) had received oral prednisolone (current median dose 5mg [IQR 5-8mg] daily), and almost a third had received parental steroids (60, 29.7%). Self-reported COVID-19 diagnosis occurred in 48 (23.8%) patients, of whom 20 reported a positive test. Eleven (55%) patients reported testing positive for COVID-19 after being vaccinated. Median reported recovery was 80% (IQR 60-100%), with subjective full recovery reported in 30% of patients (6/20) who had received a positive test. Of the 20 patients who tested positive for COVID-19, 5 were receiving belimumab, 1 tocilizumab, and in the prior 12 months, 2 had received cyclophosphamide and 4 rituximab. Of all respondents, three individuals were hospitalised with COVID-19, and one required an ICU admission. Of those hospitalised, two patients were unvaccinated prior to COVID-19 infection, and the other patient had received rituximab and cyclophosphamide prior to vaccination. Four/1387 patients registered in the BILAG-BR were confirmed to have died from COVID-19 since the beginning of the pandemic.
Conclusion: In this cohort of moderate-to-severe SLE patients there was a low incidence of COVID-19 infection. Despite this, full recovery from PCR or lateral flow test proven COVID-19 infection was seen in only a third of patients. This raises concerns over the potential risk of long COVID in patients with SLE and warrants further investigation.
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POS0758

REDUCED CENTRAL NERVOUS SYSTEM DRIVE IN PRIMARY SJÖGREN'S SYNDROME IS ASSOCIATED WITH OBJECTIVE DECLINE IN MOTOR PERFORMANCE AND SELF-REPORTED FATIGUE

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Background: Fatigue is a major complaint in primary Sjögren's syndrome (pSS). The importance of fatigue in pSS is demonstrated by its inclusion as one of the three domains of the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) as well as being the primary outcome measure of a large clinical trial.[1] To date, there is no effective treatment for fatigue and more fundamental studies are needed to identify potential targets for therapy. In a conceptual framework, fatigue is defined as a self-reported symptom derived from two attributes: performance fatigability and perceived fatigability (Figure 1).

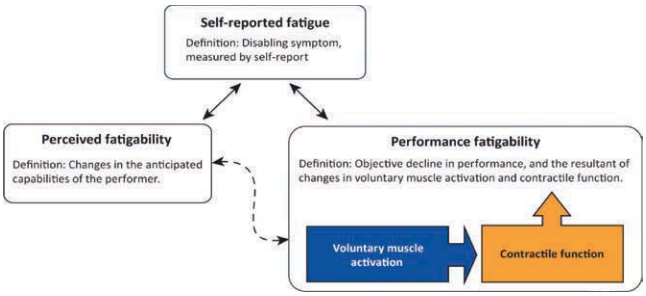

Figure 1. Conceptual framework (adapted from Enoka)[2]

Objectives: To acquire a better understanding of fatigue in pSS, we investigated objective measures of performance decline and evaluated the relation of self-reported fatigue with performance fatigability and factors modulating perceptions of fatigability.
Methods: 39 pSS patients and 27 healthy controls were included. To assess performance fatigability, force decline was measured during a sustained (124s) maximal voluntary contraction (MVC) with the index finger abductor muscle, and voluntary muscle activation was indexed using peripheral nerve stimulation superimposed on maximal voluntary contractions. Self-reported fatigue was quantified using the Fatigue Severity Scale (FSS) and Modified Fatigue Impact Scale (MFIS). Pain, depression, and anxiety were assessed using questionnaires and serological inflammatory markers were measured in serum as factors relating to perceived fatigability.
Results: Self-reported fatigue was significantly higher in pSS than controls (FSS: 4.8 vs. 2.3, $p<0.001$); 67% of patients and no controls reported significant fatigue (FSS>4). Mean voluntary muscle activation was reduced in pSS compared to controls (81.5% vs. 87.8%, $p=0.030$). Force decline during the sustained MVC did not differ between groups (60.6% vs. 63.1%, $p=0.246$). MFIS physical was positively associated with symptoms (ESSPRI pain: $\rho=0.51$, HADS depression: $\rho=0.45$ and HADS anxiety: $\rho=0.29$) and negatively associated with serological inflammatory markers (MxA: $\rho=-0.49$ and CXCL10: $\rho=-0.37$). Multivariable linear regression showed that force decline, pain and depression were associated with the MFIS physical domain in pSS (total explained variance of 47%). The inclusion of serological inflammatory markers did not help to explain more variance in this model.
Conclusion: This study demonstrates that performance fatigability in pSS was compromised by a reduced capacity of the central nervous system to drive the muscle. Furthermore, self-reported fatigue is a multifactorial symptom associated with both performance fatigability and perceived fatigability in patients with pSS.
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Disclosure of Interests: Roeland Prak: None declared, Suzanne Arends: None declared, Gwenny M. Verstappen: None declared, Greetje S. van Zuiden: None declared, Frans G.M. Kroese: None declared, Hendrika Bootsma Speakers bureau: Bristol Myers Squibb, Novartis, Consultant of: Bristol Myers Squibb, Roche, Novartis, Medimmune, Union Chimique Belge, Grant/research support from: Bristol Myers Squibb, Roche, Inge Zijdewind: None declared
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POS0759

DOES LLDAS DEFINITION MATCH THE RHEUMATOLOGIST OPINION? THE FIRST VISIT EVALUATION OF A LONGITUDINAL SPANISH MULTICENTER STUDY TO ASSESS REASONS OF DISAGREEMENT.

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Background: Treat to Target strategies are necessary in Systemic Lupus Erythematosus (SLE). They are difficult to establish due to the heterogeneity of the disease. The current definitions of Lupus Low Disease Activity State (LLDAS) according to the Asia Pacific Lupus Collaboration (APLC) and remission according to Definition of Remission in SLE (DORIS) 2021 are difficult to achieve and maintain over time.
Objectives: To evaluate the concordance between the LLDAS and the clinical status according to the rheumatologist opinion and reasons of disagreement. To explore modifications in LLDAS definition that best fit with the expert´s opinion.
Methods: Prospective multicenter study of SLE patients (ACR 1997 Classification Criteria or clinical diagnosis by the physician) from seven Spanish Rheumatology Departments. Statistical analysis: descriptive cross-sectional (at the time of recruitment) analysis of the demographic and clinical characteristics, treatments; remission and LLDAS and the subjective evaluations of SLE activity by the rheumatologist. Analysis of the level of agreement between expert opinion and the definition of LLDAS and its modification were evaluated using Cohen's kappa.
Results: DEMOGRAPHIC, DISEASE CHARACTERISTICS AND TREATMENTS. Five hundred and eight were included (92% women; mean age (±SD): 50.4 years (±13.7)). Mean SLEDAI-2K (±SD) was 2.84 (±3.31). A total of 406 (79.9%) patients presented SLEDAI-2K≤4. A total of 317 (74.1%) patients were on antimalarial treatment. Two hundred and twenty-two (43.7%) patients were on some type of immunosuppressive or biological therapy. More than half of patients were not taking glucocorticoids (n=310, 61%). A total of 38 patients (7.5%) were taking doses of prednisone higher than 7.5mg/day.
REMISSION/LLDAS 267 (54.4%) patients were in remission and 304 (62.7%) patients were in LLDAS. According to the expert opinion of the rheumatologist, remission was the most frequent state considered (n=206, 41.6%); followed by low activity (n=153, 30.9%); serologically active (n=71, 14.3%); moderate activity (n=55, 11.1%) and high activity (n=10, 2%).
AGREEMENT Overall agreement between expert opinion and the definition of LLDAS was 71.4 % with a Cohen's kappa of 0.3. The majority of the cases (96.1%) that fulfilled the definition of LLDAS, were classified by the expert as remission, serologically active or low activity. Only 12 (3,9%) patients were classified by the expert as moderate or high activity. Of the patients that did not fulfill the definition of LLDAS, 126 out of 179 (70.4%) patients were classified by the expert as remission/low disease activity (Figure 1). The main reasons for discordance in the group that did not fulfill the definition of LLDAS were the presence of new clinical features compared to previous visit and a SLEDAI 2-K >4, in 74 (58.7%) and 59 (46.8%) patients, respectively. The LLDAS adjustment that meant a significant increase in the agreement was the exclusion of the comparative features with the previous visit, with an increase in the agreement to 82.6% (95% CI: 81.61-83.96%). The modification of prednisone to 5mg/daily dose, did not represent a significant change in agreement from the original definition.

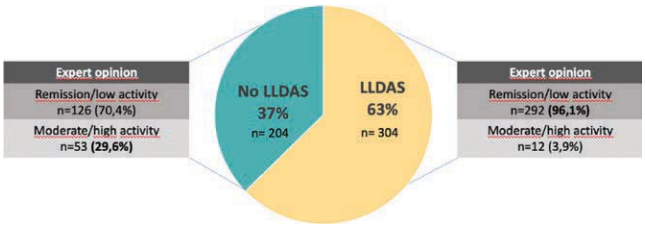

Figure 1. Comparison of LLDAS and expert opinion

Conclusion: At a given point in time, almost two thirds of SLE patients were in remission or in LLDAS. There is a good correlation between LLDAS and the physician's opinion, particularly for those patients who fulfill LLDAS definition. However, the agreement is not so good for patients who don't, these being excessively classified by the physician as remission or low activity. The main LLDAS items causing this disagreement were a SLEDAI-2K >4 and the appearance of different clinical manifestations from the previous evaluation. On the contrary, physician assessment by the PGA adequately fits the LLDAS definition. The modification of the LLDAS definition excluding the comparison with previous assessment increases the agreement with the expert opinion to 82.6%.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3044

POS0760 HIGH LEVELS OF PROTEINS, CELL COUNTS, AND IL-6 IN CEREBROSPINAL FLUID IN PATIENTS WITH NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS ARE ASSOCIATED WITH DAMAGE ACCRUAL OF NON-NEUROPSYCHIATRIC DOMAINS AS WELL AS THAT OF NEUROPSYCHIATRIC DOMAINS

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Background: Neuropsychiatric systemic lupus erythematosus (NPSLE) is one of severe organ manifestations and directly associated with neuropsychiatric damages, such as cerebral vascular accident, cognitive impairment, or seizures. However, factors associated with damage accrual of neuropsychiatric and non-neuropsychiatric domains in NPSLE patients remain unknown.
Objectives: The aim of this study was to identify factors associated with damage accrual in patients with NPSLE.
Methods: We reviewed all patients with SLE who had attended our hospital between January 2010 to December 2020 retrospectively and identified those with NPSLE. We analyzed clinical characteristics and laboratory data including cerebrospinal fluid (CSF) in association with the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index (SDI) progression after the onset of NPSLE.
Results: 461 patients with SLE were reviewed. Among them, 37 (8.0%) were diagnosed with NPSLE. Thirty-six patients were included in the analysis after excluding one patient with insufficient information. Seventeen (47.2%) patients were diagnosed with NPSLE at the same time with SLE diagnosis and 19 patients were diagnosed at relapse. At NPSLE onset, the mean age was 33.7 years, 35 were female, and the mean SLEDAI-2K was 21.8. Eighteen (50.0%) patients had active lupus nephritis simultaneously at the onset of NPSLE. The most frequent NPSLE types according to the 1999 ACR classification were lupus headache in 10 patients, followed by cerebrovascular disease in 7, seizure disorders in 6, acute confusional state, psychosis and mononeuropathy in 3, and aseptic meningitis in 2. All patients were treated with glucocorticoids, and the mean initial dose of prednisolone was 52.3 mg/day with steroid pulse therapy in 19 patients. Thirty (83.3%) patients were treated with concomitant immunosuppressive treatments. During the observation period with the mean of 10.0 years, 17 (47.2%) patients developed at least one point of SDI. Among them, 9 patients (25.0%) had neuropsychiatric damage progression including cerebrovascular accident in 6, seizures requiring drug treatment for more than 6 months in 2, and cognitive impairment in 1. Non-neuropsychiatric damage was also increased such musculoskeletal in 5, ocular in 3, cardiovascular in 2, renal, gastrointestinal, premature gonadal failure, diabetes, and malignancy in each one case. Neither neuropsychiatric nor overall damage progression were associated with SLEDAI-2K, anti-cardiolipin antibodies positivity, abnormal electroencephalogram, abnormal single photon-emission computed tomography at NPSLE onset or kinds of immunosuppressive treatments. In 21 patients who underwent CSF examination, the high level of CSF IL-6 was associated with neuropsychiatric damage progression (p=0.032). Also, high levels of CSF protein (p=0.030), cell counts (p=0.007), and IL-6 (p=0.032) were associated with overall SDI progression.
Conclusion: CSF IL-6 concentrations are associated with neuropsychiatric damage progression, and high CSF protein, cell counts and IL-6 at onset in patients with NPSLE can predict overall damage accrual.
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POS0761 TIME-DEPENDENT ANALYSES OF CLINICAL MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IDENTIFY PATIENTS AT HIGH RISK OF INCIDENT PROTEINURIA

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Background: Nephritis (LN) in systemic lupus erythematosus (SLE) is still a major determinant of poor prognosis[1]. The vast majority of LN occurs in proximity to the SLE diagnosis[2]. Identification of individuals at high risk, especially early onset SLE, is therefore warranted. Inclusion of risk factors prior to the SLE diagnosis may thus be of importance to enable sufficient risk factor profiling. SLE-patients seem to cluster according to clinical and serological phenotypes suggesting distinct disease trajectories[3-5].
Objectives: To determine if incident proteinuria associated with the debut age of non-renal SLE characteristics.
Methods: Data of SLE patients from six Danish centers were obtained from the Danbio-database from 2017 – 2020. The occurrence and timing of proteinuria was compared with first time onset of any non-renal manifestations as defined by the 1997 American College of Rheumatology Classification Criteria. Cox-regression models were used to identify risk factors for incident proteinuria. Time from first occurring non-renal manifestation to incident proteinuria or censoring defined time at risk. Covariates were eliminated if p >0.01 in a 'backwards' manner. After the model reduction process p-values <0.05 were considered statistically significant.
Results: 586 SLE patients, mainly white (94%) women (88%), mean age at inclusion of 34.6 years (standard deviation, SD = 0.6 years) and observed for a mean of 14.9 years (SD =0.5 years), were recruited. The cumulative prevalence of proteinuria was 40%. Male gender hazard ratio, HR = 1.35 (range 0.77-2.35), p=0.009, lymphopenia HR = 1.77 (range 1.24-2.52), p=0.005 were associated with incident proteinuria. In contrast, patients with discoid rash had lower risk of incident proteinuria HR 0.42 (range 0.21-0.83), p=0.01. Male patients with lymphopenia had the highest risk of proteinuria with a one-, 5- and 10-year risk of proteinuria ranging from 9-27%, 34-75% and 51-89 %, depending on the age at presentation (debut at 20, 30, 40 or 50 years). The corresponding risk-profiles for women with lymphopenia were 3-9%, 8-34% and 12-58%, respectively, as illustrated in Figure 1.
Conclusion: The occurrences of lymphopenia and discoid rash were oppositely associated with risk of incident proteinuria and the risk effects varied according to gender and patient age at onset of these manifestations. Thus, the risk of proteinuria may not be constant but could vary according to presentation of non-renal manifestations that may call for a differentiated clinical follow-up. Based on these findings, we suggest that the debut age of known prognostic factors, even prior to the SLE diagnosis should be considered when designing prognostic statistical models.
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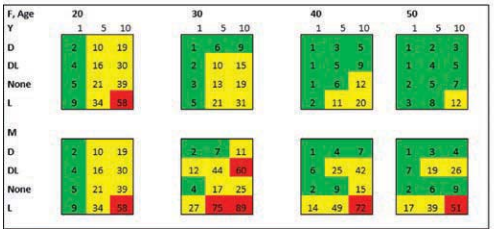
Fig. 1. One-, 5- and 10-year (Y) risk of incident proteinuria in 586 patients with SLE by gender (M,F) and age at onset of discoid rash (D) and/or lymphopenia (L) that all emerged as predictors of incident proteinuria in a time-dependent Cox regression model. Abbreviations: Age = age at debut; F = female; M= Male, None = absence of Discoid rash and Lymphopenia.



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POS0762 LONG-TERM RENAL OUTCOMES OF PATIENTS WITH NON-PROLIFERATIVE LUPUS NEPHRITIS

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Background: Although proliferative (class III or IV) lupus nephritis (LN) is the most common finding in the classification of LN, pure membranous (class V) or mesangial (class I or II) LN can occur as a form of LN. Even though non-proliferative LN (class I, II, or V) is a less severe form with good outcomes, data on long-term renal prognosis are limited.
Objectives: This study investigated the long-term outcomes and prognostic factors in non-proliferative LN.

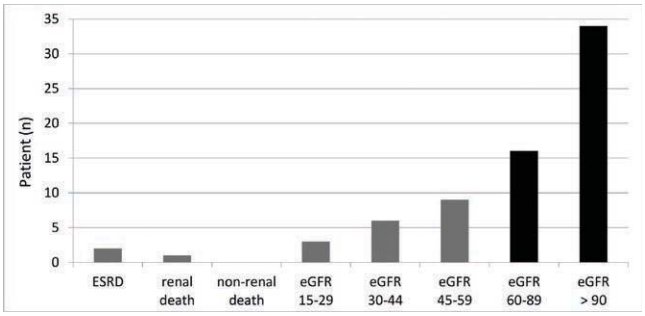

Figure 1. Renal outcomes at last follow upeGFR, estimated glomerular filtration rate (ml/min/1.73m^2)

Table 1. Univariate and multivariate Cox proportional hazard regression analyses of the factor associated with poor renal outcomes

	Univariate analysis			Multivariate analysis		
Parameter	HR	95% CI	p value	HR	95% CI	p value
Clinical features						
Age	1.046	1.003-1.091	0.036	1.002	0.960-1.047	0.921
Sex	1.654	0.375-7.298	0.506			
SLEDAI	1.036	0.965-1.112	0.327			
Extra renal SLEDAI	1.038	0.971-1.11	0.272			
Renal profiles						
eGFR at LN diagnosis	0.993	0.976-1.011	0.456			
Proteinuria at LN diagnosis	1.000	1.000-1.000	0.444			
> 1g/24 hours	0.669	0.243-1.841	0.437			
> 3g/24 hours	0.624	0.229-1.699	0.356			
eGFR at 6M	0.967	0.948-0.986	0.001	0.968	0.948-0.988	0.002
eGFR at 12M	0.964	0.947-0.981	0.000			
Complete remission at 6M	0.332	0.119-0.924	0.035	0.553	0.179-1.707	0.303
Complete remission at 12M	0.667	0.232-1.914	0.451			
Transformation	1.246	0.423-0.701	0.692			
Laboratory data						
Anti-dsDNA	1.001	0.999-1.003	0.196			
C3	1.020	1.000-1.041	0.051			
C4	1.027	0.969-1.089	0.367			
Albumin	1.180	0.661-2.109	0.576			
Classification[a]						
Class I	0.802	0.102-6.303	0.834			
Class II	1.298	0.412-4.088	0.656			
Class V	0.887	0.308-2.557	0.824			
Class II+V	0.048	0.000-1685	0.837			
Medications[b]						
ACEi/ARB	1.652	0.603-4.528	0.329			
Hydroxychloroquine	1.326	0.414-4.242	0.635			
Corticosteroid	1.186	0.154-9.108	0.870			
CNI	2.439	0.464-12.824	0.292			
MMF	3.788	0.959-14.965	0.057			
AZA	0.589	0.133-2.611	0.486			

[a] LN classifications were based on the International Society of Pathology/Renal Pathology Society (ISN/RPS) classification.[b] Medications maintained at least one year since Lupus Nephritis diagnosis.HR, hazard ratio; 95% CI, 95% confidence interval; SLEDAI, systemic lupus erythematosus disease activity index; eGFR, estimated glomerular filtration rate; LN, lupus nephritis; anti-dsDNA, anti-double strand DNA; C3/C4; complement 3/4; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CNI, carcineurin inhibitor; MMF, mycophenolate mofetil; AZA, azathioprine.

Methods: We retrospectively reviewed the medical records of patients with systemic lupus erythematosus who were diagnosed with LN class I, II, V or II+IV by kidney biopsy between 1997 and 2021 at a tertiary referral center. Clinical and laboratory data were compared between patients with and without poor renal outcomes. Poor renal outcome was defined as an estimated glomerular filtration rate (eGFR) of < 60 mL/min/1.73 m2 or death due to renal cause. Univariate and multivariate analyses were performed with the Cox proportional hazard model to identify the factors associated with poor renal outcomes.

Results: We included 71 patients with non-proliferative LN (4: class I; 17: class II; 48: class V, 17; 2: class II+V). Median follow-up duration was 103 months (interquartile range 27–185) and the overall rate of poor renal outcomes at last follow-up was 29% (21/71), including end-stage renal disease (n=2) and renal death (n=1). Univariate analysis indicated that older age (HR 1.05; 95% CI: 1.00–1.09), low eGFR (HR 0.97; 95% CI: 0.95–0.99) and failure to reach complete remission at 6 months (HR 0.332; 95% CI: 0.12–0.92) were significantly associated with poor renal outcomes. Multivariate analysis revealed that low eGFR at 6 months (HR 0.97; 95% CI: 0.95–0.99) was significantly associated with poor renal outcomes.

Conclusion: Poor renal outcomes occurred in approximately 30% of patients with non-proliferative LN (class I, II or V) after long-term follow-up. Our findings suggest that more active management may be needed for non-proliferative LN, particularly in patients with low eGFR at 6 months.

Disclosure of Interests: None declared

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POS0763

A MULTIMODAL MAGNETIC RESONANCE IMAGING STUDY OF COGNITIVE FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: A MACHINE LEARNING APPROACH

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder that can affect the central nervous system. Cognitive dysfuncion is the most common neuropsyhiatric event in SLE patients, yet it is also one of the hardest to diagnose.

Objectives: To investigate if multimodal imaging to assess anatomical magnetic resonance imaging (MRI) abnormalities in the brains of SLE patients can predict cognitive function.

Methods: Subjects underwent voxel-based morphometry (VBM), magnetization transfer imaging (MTI), and dynamic contrast-enhanced (DCE) MRI. Automated Neuropsychological Assessment Metrics (ANAM) was used to assess cognitive function in this cross-sectional study and the primary measure was the total throughput score (TTS). TTS is the total of the throughput scores for each of the 8 ANAM subtests: (i) code substitution learning (CSL); (ii) code substitution immediate (CSI); (iii) code substitution delayed (CSD); (iv) spatial processing (SP); (v) matching to sample (MSP); (vi) running memory continuous performance test (CPT); (vii) mathematical processing (MTH) and (viii) memory search (MS). Olfactory assessment was done using the University of Pennsylvania Smell Identification Test. We used a machine learning-based model (i.e. GLMnet) to predict TTS. Subjects with active SLE disease or above 40 years old were excluded.

Results: Thirty SLE patients [26 female, 32.0 (26.8-37.0) years] without clinically overt neuropsychiatric manifestations and 10 healthy controls (HCs) [9 females, 27.0 (23.0-31.5) years] were enrolled in this study. Both groups had comparable cognitive and olfactory functions. No significant differences were observed in VBM, MTR, olfactory blub and tract (OBT) volume in SLE patients compared to HCs. We observed increased blood-brain barrier (BBB) permeability parameters (Ktrans and PS) in several regions of SLE patients. DCE-MRI perfusion parameters such as perfusion (F) and vp but not permeability measures were associated with TTS. In particular, F right amygdala correlated with TTS in SLE patients (r = 0.636, FDR p < 0.05) (Table 1). Using GLMnet, we trained a multimodal MRI model comprising of VBM, MTR, DCE-MRI and OBT volume parameters to predict TTS in SLE patients (r = 0.998, p < 0.0005) (Figure 1).

Figure 1

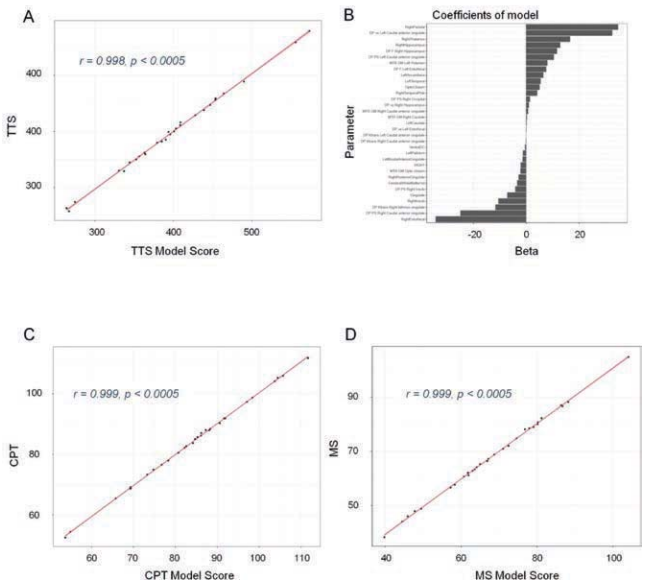

Figure 1. Machine learning-based models to predict cognitive function.

Table 1. Correlation between ANAM tests with perfusion (F) in SLE patients, ranked in descending order of statistical significance for TTS.

Variable	TTS	CSL	CSI	CSD	SP	MSP	CPT	MTH	MS
F right amygdala	0.636‡*	0.520‡	0.337	0.437†	0.559‡	0.323	0.633‡	0.412†	0.598‡
F left entorhinal	0.504‡	0.422†	0.366	0.416†	0.305	0.185	0.530‡	0.186	0.416†
F left amygdale	0.495‡	0.400†	0.189	0.378†	0.330	0.237	0.491‡	0.376†	0.449†
F choroid plexus	0.469†	0.384†	0.216	0.413†	0.458†	0.202	0.456†	0.340	0.406†
F right rostal anterior cingulate	0.453†	0.301	0.118	0.296	0.393†	0.214	0.547‡	0.420†	0.383†
F right entorhinal	0.448†	0.368†	0.232	0.312	0.376†	0.156	0.438†	0.271	0.407†
F cerebellum white matter	0.427†	0.358	0.201	0.370†	0.273	0.078	0.449†	0.290	0.297
F left hippocampus	0.427†	0.355	0.134	0.390†	0.356	0.203	0.511‡	0.336	0.332
F brain stem	0.407†	0.298	0.138	0.275	0.294	0.153	0.478‡	0.308	0.369†
F right insula	0.407†	0.308	0.074	0.300	0.324	0.176	0.437†	0.323	0.347
F left parietal	0.400†	0.263	0.092	0.254	0.294	0.224	0.487‡	0.274	0.332
F ventricles	0.396†	0.303	0.083	0.321	0.370†	0.192	0.477‡	0.286	0.361
F right temporal	0.395†	0.280	0.113	0.281	0.288	0.167	0.477‡	0.322	0.331
F right hippocampus	0.395†	0.307	0.077	0.325	0.356	0.190	0.486‡	0.357	0.339
F right parietal	0.376†	0.249	0.082	0.274	0.283	0.139	0.460†	0.255	0.311
F right parahippocampal gyrus	0.375†	0.353	0.119	0.302	0.341	0.241	0.353	0.208	0.273

† p < 0.05, ‡ p < 0.01, *FDR p < 0.05

Conclusion: These findings suggest that the BBB may be affected early in the course of cognitive dysfunction, even preceding detectable changes in other MRI sequences and machine learning algorithms can be used to predict TTS measures, even in asymptomatic SLE patients.

REFERENCES: Nil.

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POS0764

CLINICAL AND LABORATORY FINDINGS IN PRIMARY SJOGREN'S SYNDROME PATIENTS WITHOUT SUBJECTIVE SICCA SYMPTOMS

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Background: Sjogren's syndrome (SS) is a systemic autoimmune rheumatic disease characterized by symptoms of dryness. In fact, subjective manifestations of dry eyes or dry mouth are part of the inclusion criteria of the 2016 ACR-EULAR Classification Criteria for primary SS (pSS). However, some patients with SS diagnosis may present without subjective dryness, meeting the inclusion criteria based on the EULAR SS disease activity index (ESSDAI) questionnaire (1). Studies on non-dryness SS patients are missing.
Objectives: To describe the clinical phenotype of pSS patients who lack subjective dryness symptoms.
Methods: From 1738 consecutive pSS patients who fulfill the 2016 ACR-EULAR Classification Criteria for primary SS and were followed up in 4 centers from Greece and Italy (Universities of Athens, Pisa, Harokopio and Ioannina) (PAHI group), those without sicca symptoms were identified (non-Dryness Group) (1). Cumulative, clinical, laboratory, immunologic and histologic data were collected and compared with age, gender and disease duration-matched SS patients with both oral and eye dryness in 1:2 ratio (Dryness Group) (Table 1). Statistical analysis for categorical data was performed by Fisher exact test or $\chi 2$ square test accordingly and numerical data with Mann-Whitney test or t test.

Table 1. Comparison of clinical and laboratory features of pSS patients with (Dryness Group) and without sicca manifestations (Non-dryness Group)

Clinical and Laboratory features	Non-Dryness Group, %, n=38	Dryness Group, %, n=76	p-value
ANA positivity %	100	95.9	0.55
RF positivity %	58.3	64.3	0.7
Anti-Ro positivity %	100	90.8	0.09
Anti-La positivity %	54.1	50.7	0.89
Salivary gland biopsy positivity %	93.9	89.8	0.71
Focus score	2.12	2.19	0.97
Ocular tests positivity %	55.6	93.9	**<0.001**
Salivary gland enlargement %	26.3	30.3	0.83
Arthralgias %	52.6	56.6	0.84
Arthritis %	25.7	17.6	0.48
Raynaud's phenomenon %	23.7	27.6	0.82
Palpable purpura %	7.9	18.4	0.17
Lymphadenopathy %	22.6	20.3	0.99
Leukopenia %	20.7	26.1	0.76
Lymphopenia %	0	17.3	**0.049**
Neutropenia %	20.8	5.8	0.1
Thrombocytopenia %	13.8	3.1	0.07
Low C4 %	23.3	30.3	0.65
Cryoglobulinemia %	10.5	3.9	0.3
Lymphoma %	10.8	6.7	0.47

Results: Thirty-eight SS patients were found without sicca manifestations (2.19%). The most common presenting clinical manifestation of non-dryness pSS patients were arthralgias (47.4%), followed by parotid gland enlargement (23.6%), Raynaud's phenomenon (10.5%), generalized lymphadenopathy (10.5%), fatigue (10.5%), palpable purpura (5.3%) and pulmonary symptomatology of dry cough or exertional dyspnea (5.3%). Despite the lack of ocular dryness, non-dryness group had positive ocular tests but statistically lower compared to those with sicca symptoms (55.6% vs 93.9%, p<0.001), and displayed lymphopenia less frequently (0 vs 17.3%, p=0.049). No statistical differences were found in terms of salivary gland enlargement (SGE), focus score (FS), cryoglobulinemia and autoantibody profile between the 2 groups.
Conclusion: SS patients without subjective dryness are characterized by similar underlying immunopathologic processes as typical SS sicca patients.
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POS0765 IS THERE ANY DIFFERENCE IN THE CLINICAL FEATURES AND OUTCOMES OF PROLIFERATIVE AND NON-PROLIFERATIVE FORMS OF LUPUS NEPHRITIS PROVEN BY BIOPSY?

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Background: Lupus nephritis (LN), which occurs in 60-70% of patients with systemic lupus erythematosus, is a major determinant of morbidity and mortality. There still are many uncertain aspects in clinical, pathological, and prognostic characteristics about LN.
Objectives: We aimed to compare clinical features, outcomes, and to define the predictive factors of complete renal response (CRR) in patients with proliferative and non-proliferative LN.
Methods: Patients with SLE followed between 2014 and 2020 at Hacettepe University Hospitals and who had a kidney biopsy were the subject of the study. One hundred and sixteen patients whose kidney biopsy reported as LN were evaluated retrospectively. Clinical features, laboratory values at the time of kidney biopsy, histopathological forms of LN, and renal response (complete or partial) were recorded. The predictive factors for CRR during the two-year follow-up after induction therapy were analyzed.
Results: Of 116 (93 females, 23 males) patients, 95 (81.9%) were in the proliferative (class III and IV) and 21 (18.1%) were in the non-proliferative group (class II and V). In the proliferative group, elevated basal creatinine, median daily proteinuria, anti-dsDNA positivity, low C3 and C4, the presence of active urinary sediment, and median renal SLE Disease Activity Index (SLEDAI) scores at the time of kidney biopsy were significantly higher than non-proliferative group. During the two-year follow-up after LN diagnosis, 70 patients achieved CRR and time-to-CRR was similar for the groups (p=0.64, log-rank). The Cox proportional hazards model showed that achieving CRR was associated with female gender [HR: 2.15 (1.19-3.89 95% CI), p=0.011], newly diagnosed SLE with renal biopsy [2.15 (1.26-3.67), p=0.005], hypertension [0.40 (0.27-0.94), p=0.032], eGFR increase [1.01 (1.00-1.01), p=0.046], and presence of active urinary sediment [0.46 (0.22-0.96), p=0.039].
Conclusion: Achieving CRR was similar in both the proliferative and non-proliferative LN patients although certain laboratory parameters differed at onset. Our results indicated the importance of kidney biopsy in the decision-making of treatment of SLE patients with renal involvement and that the defined factors associated with CRR achievement help to predict good renal response.

Table 1. Demographic, clinical characteristics, and outcomes of the patients with LN

Variables*	All patients n=116	Proliferative LN n=95	Non-Proliferative LN n=21	p
Age at SLE diagnosis, years	18.3 (16)	19.2 (15)	16 (16)	0.32
Sex, female	93 (80.2)	75 (78.9)	18 (85.7)	0.48
Age at kidney biopsy, years	21 (17.7)	22 (17)	18 (15)	0.19
Patients newly diagnosed SLE with renal biopsy	65 (56)	53 (55.8)	12 (57.1)	0.91
Follow-up time for LN, years	5.5 (8)	5.1 (8.2)	6.2 (5.1)	0.80
SLE disease duration	8 (8.7)	8.1 (9.6)	7.9 (7.3)	0.53
Hypertension	31 (26.7)	26 (27.4)	5 (23.8)	0.74
Laboratory values on the kidney biopsy				
Creatinine level (mg/dL)	0.7 (0.5)	0.8 (0.5)	0.56 (0.1)	**0.006**
Creatinine > UNL	37 (32.5)	34 (36.6)	3 (14.3)	**0.04**
eGFR (mL/min/1.73m^2)	113 (54)	107 (54)	129 (45)	**0.04**
Albumin (g/dL)	3.3 (1.1)	3.1 (1.2)	3.5 (1)	0.09
24-hour urine protein, gr/day	2.3 (3.3)	2.4 (3.6)	0.9 (1.8)	**0.03**
Anti-dsDNA positivity	94 (81)	80 (87.9)	14 (70)	**0.04**
Low C3 and C4 levels	93 (80.2)	81 (88)	12 (57.1)	**0.001**
Active urinary sediment	91 (83.5)	78 (89.8)	12 (57.1)	**<0.001**
Renal SLEDAI	12 (8)	12 (8)	4 (4)	**<0.001**
During the two-year follow-up after LN diagnosis				
Complete renal response	70 (70.7)	56 (70.9)	14 (70)	0.99
Partial renal response	23 (23.2)	17 (21.5)	6 (30)	0.64
No response	6 (6.1)	6 (7.6)	0	NA
Relapse	20 (21.5)	15 (20.5)	5 (25)	0.84
ESRD	4(4)	4 (4.2)	0	NA
Death	3 (3)	3 (3.2)	0	NA

* n (%), if otherwise specified; median (IQR) for numeric valuesESRD: End-stage renal disease, GFR: Glomerular filtration rate, LN: Lupus nephritis, SLE: Systemic lupus erythematosus, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; UNL: Upper normal limit

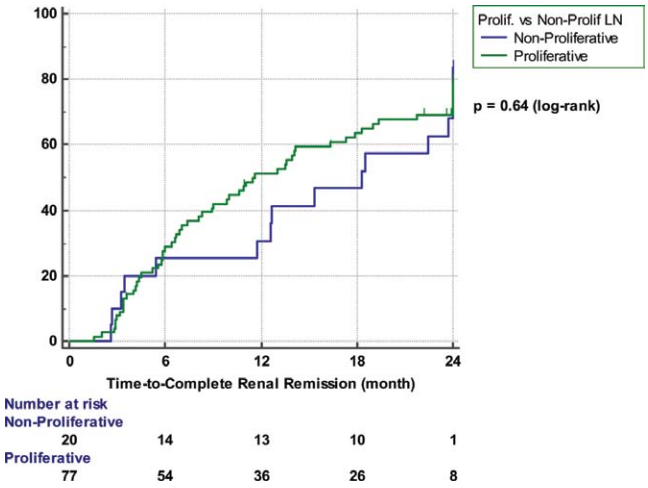

Figure 1. Kaplan-Meier survival curve for complete renal response (CRR) achievement during the two-year follow-up according to the kidney biopsy results

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POS0766 THE ROLE OF ANTIBODIES TO THE PHOSPHATIDYLSERINE/PROTHROMBIN COMPLEX IN THE DIAGNOSIS OF ANTIPHOSPHOLIPID SYNDROME

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Background: The study of other non-criteria antiphospholipid antibodies (aPL) may improve the stratification of patients with antiphospholipid syndrome (APS) and assist in the interpretation of conflicting results on aPL testing.
Objectives: To determine the significance of antibodies to the phosphatidylserine/prothrombin complex (anti-PS/PT) in patients with systemic lupus erythematosus (SLE) and APS.
Methods: The study included 190 patients who signed informed consent, aged 37,0 [29,0-44,0] years and disease duration 7,0 [2,0-15,0] years. Male/female ratio was 44 (23)/146 (77). 123 (64,7%) of 190 patients had reliable SLE and 55 (29%) had PAPS. The control group was left with 100 relatively healthy, age-matched individuals. Classical aPL (IgG/IgM-aCL, IgG/IgM-$\alpha\beta$2-GP1, LA) were meassured at two time points separated by at least 12 weeks in all patients included in this study. IgG/IgM anti-PS/PT was determined by enzyme immunoassay (ELISA) using a Tecan sunrise absorbance microplate spectrophotometer (Austria) with an AESKULISA Serin-Prothrombin-GM antibody reagent kit. IgG/IgM anti-PS/PT were measured in U/ml. Values >18 U/ml were considered positive. The range of measurements was: 1 to 300 U/ml.
Results: In 144 (76%) of 190 patients were revealed IgG anti-PS/PT, 55 (29%) - IgM anti-PS/PT, a combination of IgG anti-PS/PT and IgM anti-PS/PT was found in 53 (28%). IgG anti-PS/PT and IgM anti-PS were detected in 39 of the 70 (56%) remaining patients who were negative for criterion aPL. The median IgG anti-PS/PT was 101.2 U/ml [31,0-180,5] in patients with APS and was significantly higher than 23,7 [14,1-49,8] U/ml in patients without APS and controls. IgM anti-PS/PT levels in patients with and without APS were comparable. Thrombosis was significantly more common in patients with IgG anti-PS/PT: 95 (81,2%) of 117 patients with thrombosis compared with patients negative for IgG anti-PS/PT (22 (18,8%) of 46 patients) (χ2=4,85; P=0,03). Arterial, but not venous thrombosis, was associated with IgG anti-PS/PT positivity. IgG anti-PS/PT was detected in 53 (88,3%) of 60 patients with arterial thromboses, and in 7 (11,7%) of 46 patients of IgG anti-PS/PT negative. The incidence of thrombocytopenia in the SLE+APS patient group was associated with the presence of IgG anti-PS/PT, which was detected in 18 of 19 patients, versus 6 of 12 in SLE without aPL (P<0,007). In the other patient groups, the frequency of thrombocytopenia and IgG anti-PS/PT positivity was not statistically significant. The frequency of anti-PS/PT detection was independent of LA positivity. IgG and/or IgM anti-PS/PT were detected in 26 (87%) of 30 patients positive for LA and in 21 (78%) of 27 patients LA negative. (P<0,05). The sensitivity of anti-PS/PT IgG for APS was 85%, specificity - 64%, the sensitivity of anti-PS/PT IgM was lower - 35%, but higher specificity - 88%.
Conclusion: The frequency of anti-PS/PT detection in the examined patients was high: 76% had IgG anti-PS/PT, 29% - IgM anti-PS/PT and 28% - a combination of them. The levels of IgG anti-PS/PT were significantly higher in patients with APS compared to patients without APS and controls. IgM anti-PS/PT values in patients with and without APS were comparable but higher compared to controls. Thrombosis was associated with IgG anti-PS/PT positivity. Arterial thrombosis was significantly more frequent in patients with IgG anti-PS/PT (χ2=4,85; P=0,006). The sensitivity of IgG anti-PS/PT for APS was 85%, and specificity was 64%; IgM anti-PS/PT had a lower sensitivity of 35%, but a higher specificity of 88%.
The study was performed at the V.A. Nasonova Research Institute of Rheumatology within the framework of the fundamental topic FURS-2022-003.
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POS0767 GLANDULAR INVOLVEMENT IN PRIMARY SJÖGREN SYNDROME PATIENTS WITH INTERSTITIAL LUNG DISEASE (ILD) ONSET: A SINGLE CENTER CROSS-SECTIONAL STUDY

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Background: Primary Sjögren Syndrome (pSS) is an autoimmune exocrinopathy classically presenting with sicca symptoms. Nonetheless, disease onset with extraglandular manifestations, particularly interstitial lung disease (ILD), is increasingly reported and probably underestimated. However, studies investigating pSS patients presenting with ILD (pSS-ILD) are limited.
Objectives: Aim of this study was to better characterize the phenotype of pSS patients presenting with ILD in comparison to pSS patients with classical sicca-onset. We especially investigated whether the two groups differed in glandular involvement comparing functional, imaging and histologic findings, as well as patient reported outcome (PRO).
Methods: Consecutive newly diagnosed pSS patients, all fulfilling the ACR/EULAR 2016 criteria, were included in this cross-sectional study from September 2016 to October 2021. Clinical, serological and histological initial features where compared in pSS-ILD patients and in pSS patients without ILD involvement, diagnosed during the same time period. Presence of ILD at pSS diagnosis was defined based on clinical findings, imaging assessment and pulmonary function tests. In addition to functional tests, a minor salivary gland biopsy was performed in all cases, recording number of foci and GC-like structures and focus score (FS). Salivary glands ultrasonography (SGUS) was graded using the OMERACT semiquantitative scoring system (0-3) based on parenchyma inhomogeneity. PRO including ESSPRI, OHIP and OSSDI were collected. Extraglandular clinical features and biological abnormalities included in the ESSDAI were recorded. Data were presented as mean±SD, or percent frequency as appropriate. Intergroup comparisons were made using the t-test/Mann–Whitney test for continuous variables and Fisher's exact test for categorical variables.
Results: We included 178 newly diagnosed pSS patients (F:M=158:20). ILD was the first pSS manifestation in 11 (6%) cases, 8 F and 3 M, with a median time from ILD onset to pSS diagnosis of 2 ± 2 years. At HRCT, the following patterns were observed: NSIP (4/11), UIP (4/11), NSIP+OP (2/11) and LIP (1/11). Dyspnea on exertion or chronic cough were reported by 7/11 (63.6%) patients. In comparison to sicca-onset patients, pSS-ILD patients presented an older age at diagnosis (55±13 vs 70±7, p= 0.001) and a higher ESSDAI (3.9±4.7 vs 12.3±4.3, p=0.001) driven by the pulmonary domain. Regarding glandular involvement, pSS-ILD patients reported milder xeropthalmia (VAS 5.8±3.1 vs 2.8±3.5, p=0.002), and significative lower scores in OSDI (35.6±24.9 vs 15.3±22.9, p=0.04) and OHIP (4.8±4.4 vs 1.4±3.8, p=0.04), despite no significant differences observed between the two groups in ocular tests and unstimulated salivary flow rate. With respect to histology, no significant differences were found in number of foci and GC-like structures, and FS. Notably, there was a trend towards a different distribution of the SGUS OMERACT score in the two groups. Particularly, none of pSS-ILD patients presented OMERACT score 3 in parotid and submandibular glands, in contrast to 26/167 (15.5%) and 18/167 (10.8%) of classic sicca-onset pSS patients respectively. Finally, no significant differences were observed between the two groups with respect to non-pulmonary extraglandular manifestations, serologic features and other biological parameters.
Conclusion: ILD-onset pSS patients represent an atypical phenotypic subset, with less pronounced sialadenitis sonographic changes in salivary glands, and with sicca symptoms probably overshadowed by the respiratory disease.
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POS0768

PRESENCE OF ANTI-RO/SSA AUTOANTIBODIES, HYPOCOMPLEMENTEMIA AND PHOTOSENSITIVITY INDICATE INDIVIDUALS WITH CONNECTIVE TISSUE DISEASE FEATURES WHO ARE AT INCREASED RISK FOR TRANSITION TO SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Early or pre-clinical forms of lupus encompass a broad range of presentations, spanning from asymptomatic individuals with immunological abnormalities to individuals with autoantibodies and some features suggestive of SLE who do not yet meet the classification criteria. Research on this topic could reveal predictive and diagnostic biomarkers for individuals at-risk for progression to SLE.
Objectives: To examine the rate of transition from at-risk to classified (ACR 1997 criteria) SLE, and identify demographic and clinical predictors. To prospectively evaluate the sensitivity and accuracy of the newer classification criteria (SLICC 2012, EULAR/ACR 2019) and the SLE Risk Predictive Index (SLERPI)[1] in patients at-risk who progress or not to classified SLE.
Methods: This is a single-centre analysis of individuals at-risk for SLE as part of an ongoing multicentric inception cohort study aiming to identify clinical, environmental and molecular prognostic factors for SLE onset. Enrolled individuals: a) were 18–55 years old; b) had clinical and/or serological features suggestive of SLE; c) had no clinical diagnosis of SLE or other autoimmune rheumatic disease; and d) did not fulfill the ACR 1997 classification criteria. Prospective monitoring at 6-month intervals was performed to determine accrual of classification and non-classification features, and ascertain the disease status (at-risk/undifferentiated connective tissue disease, SLE, other connective tissue disease).
Results: A total 124 subjects were included, all Whites, 94.4% women, with an average (standard deviation) age 36 (11) years. At first assessment, individuals fulfilled 2.25 (0.72) ACR 1997 criteria with ANA being the most prevalent feature (75.8%) followed by low complement (43.5%), arthritis (37.9%), photosensitivity (28.2%), malar rash (23.4%), and non-scarring alopecia (18.5%). After a median follow-up of 16 months, 27 participants (21.8%) fulfilled the ACR 1997 criteria, of whom 8 (6.5%) developed moderate or severe SLE. Multivariable-adjusted logistic regression identified anti-Ro/SSA (odds ratio [OR] 6.93; 95% confidence interval [95% CI] 1.75–27.5, p=0.006), combined low C3 and low C4 (OR 4.82; 95% CI 1.42–16.3, p=0.012) and photosensitivity (OR 3.25; 95% CI 1.17–8.99, p=0.023) as independent predictors for transition to classified SLE. The sensitivity of SLICC 2012, EULAR/ACR 2019 and SLERPI (>7) at baseline for detecting individuals who progressed to SLE (ACR 1997) was 40.7%, 25.9% and 40.7%, respectively, with corresponding specificities of 83.5%, 88.7% and 79.4%.
Conclusion: Among individuals at-risk for SLE, about 20% may evolve into classified disease after a medium follow up of 16 months which is predominantly of mild severity. Presence of anti-Ro/SSA, hypocomplementemia, and photosensitivity indicate subjects who at increased risk for transition to SLE. Newer classification systems may capture as many as 40% of progressors with acceptable specificity.
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POS0769

CANCER DEVELOPMENT IN PATIENTS HOSPITALISED WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL, POPULATION-LEVEL DATA LINKAGE STUDY

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Background: The association between systemic lupus erythematosus (SLE) and cancer risk is unclear.
Objectives: Describe the association between systemic lupus erythematosus (SLE) and the risk of cancer development and subsequent 5-year mortality in Western Australia (WA).
Methods: Population-level cohort study of SLE patients (n=2,111) and general population comparators (n=21,110) hospitalised between 1980–2014. SLE patients (identified by ICD-9-CM: 695.4, 710.0, and ICD-10-AM: L93.0, M32.0) were nearest matched (10:1) for age, sex, Aboriginality, and temporality. Follow-up was from timezero (index SLE hospitalisation) to cancer development, death or 31/12/2014. Using longitudinal linked health data, we determined the risk of cancer development and subsequent 5-year mortality between SLE patients and comparators with Cox proportional hazards regression models.
Results: SLE patients had similar multivariate-adjusted risk (aHR 1.03, 95%CI 0.93, 1.15; P=0.583) of cancer development. Cancer development risk was higher in SLE patients <40 years old (aHR 1.51), and from 1980-1999 (aHR 1.28). SLE patients had higher risk of developing cancer of the oropharynx (aHR 2.13); vulvo-vagina (aHR 3.22); skin (aHR 1.20), and, lymphatic and haematopoietic tissues (aHR 1.78), all P<0.05. SLE patients had reduced risk of breast cancer (aHR 0.64). After cancer development, SLE patients had increased risk of 5-year mortality (aHR 1.16, 95%CI 1.01, 1.33); highest in 40-49 years old (aHR 1.89), and in those with skin (aHR 1.65) or prostate cancer (aHR 4.74).
Conclusion: Hospitalised SLE patients had increased risk of multiple cancers, but a reduced risk of breast cancer. Following cancer development, SLE patients had increased risk of 5-year mortality. Together there is scope to improve cancer prevention and surveillance in SLE patients.
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POS0770

INCREASED RISK OF FRACTURE, RECURRENT FRACTURE AND POST-FRACTURE MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A POPULATION-LEVEL, LINKED DATA STUDY

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Background: Systemic lupus erythematosus (SLE) patients have higher fracture risk, driven by primary (chronic inflammation) and secondary (glucocorticoids treatment) osteoporosis. However, there is limited data on fracture recurrence and post-fracture mortality in this vulnerable population.
Objectives: To describe the association between systemic lupus erythematosus (SLE) and the risk of fracture(s), 5- and 10-year recurrent fracture(s), and 5-year post-fracture mortality, compared to hospital-based controls in Western Australia (WA) from 1980 - 2014.
Methods: Population-level cohort study of SLE patients (n=2,440, 28,002 person-years) and general population comparators (controls) (n=10,220; 161,392 person-years) identified within the Western Australia (WA) Rheumatic Disease Epidemiological Registry (WARDER). SLE patients 18-80 years old (identified by ICD-9-CM: 695.4, 710.0, ICD-10-AM: L93.0, M32.0) and controls were nearest matched (5:1) for age, sex, Aboriginality, and temporality. Follow-up was from timezero (index SLE hospitalisation) to fracture-related hospitalisation, death or 31/12/2014. Using longitudinal linked health data we determined the relative risk of (low impact) fracture-related hospitalisations (after excluding for traumatic and external factors, such as, falls from more than standing height and transport accidents), 5- and 10-year recurrent fractures, and 5-year post-fracture mortality between SLE patients and controls with multivariate Cox proportional hazards regression models from 1980-2014.
Results: Compared to general population controls, SLE patients had higher multivariate-adjusted risk (aHR 2.44, 95%CI 2.08, 2.87; P<0.01) of fractures during follow-up. SLE patients had higher fracture risk regardless of sex, Aboriginality, age group (highest in those <50 years of age), or study period (2000-2014: aHR 1.83, 95%CI 1.32, 2.55; P<0.01). SLE patients had higher risk of hand, wrist and forearm fractures (aHR 1.95), vertebral fractures (aHR 5.73), hip fractures (aHR 1.83), and lower limb, ankle and foot fractures (aHR 2.14). Similarly, SLE patients had higher risk of both 5- (aHR 2.89) and 10-year (aHR 3.00) fracture recurrence, which held across sub-group analyses and remained high in the most recent 2000-2014 period (aHR 2.84 and aHR 3.04, respectively). SLE patients had higher (aHR 1.56, 95%CI 1.16, 2.09; P<0.01) risk of 5-year post-fracture mortality, which held for female SLE patients (aHR 1.45), those ≥70 years-old (aHR 1.72), and remained in the 2000-2014 period (aHR 1.57).

Conclusion: SLE patients have an increased risk of fractures, 5- and 10-year recurrent fractures, and 5-year mortality post-fracture compared to controls from the general population. After adjustment for conventional risk factors, these associations remained unchanged in the most recent period (2000-2014). This study highlights the need for improved primary prevention of a first fracture event in SLE patients.

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POS0771 ULTRA HIGH-FREQUENCY ULTRASOUND (UHFUS) OF MINOR LABIAL SALIVARY GLANDS (MLSGS): DIAGNOSTIC ACCURACY IN ANTI-RO/SSA POSITIVE AND ANTI-RO/SSA NEGATIVE PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME (PSS)

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Background: Last-generation Ultra High-frequency ultrasound (UHFUS) transducers are highly sensitive tools for the study of tiny superficial structures such as minor labial salivary glands (MLSGs). Compared to conventional ultrasound, UHFUS operates with higher frequencies allowing for outstanding image resolution, up to 30 µm.

Objectives: To determine the diagnostic accuracy of MLSG UHFUS in primary Sjogren's syndrome (pSS) and to assess its contribution in anti-Ro/SSA positive and anti-Ro/SSA negative patients

Methods: Consecutive patients undergoing a MLSG biopsy for clinically suspected pSS were included in this cross-sectional study from January 2018 to October 2021. MLSG UHFUS was performed by using a 70 MHz probe, evaluating parenchymal inhomogeneity (score 0-3, similar to major salivary glands four-grade OMERACT scoring system). Patients' clinical, biological, and histological features were collected. Anti-Ro/SSA antibody specificity was determined by immunoblotting. Receiver operating characteristic (ROC) curves, optimal cut-off point, AUC (area under curve), sensitivity (SE), specificity (SP), positive (PPV) and negative predictive values (NPV) were identified.

Results: A total of 194 patients were enrolled. Out of them, 88 patients fulfilled the ACR/EULAR 2016 criteria for pSS and 74 were anti-Ro/SSA+ (69 pSS and 5 no-SS). The distribution of UHFUS grades was significantly different in patients with pSS than in no-SS subjects: grade 0: 0/88 (0) vs 17/106 (16%); grade 1: 28/88 (31.8%) vs 55/106 (51.9%); grade 2: 46/88 (52.3%) vs 31/106 (29.2%); grade 3: 14 (15.9%) vs 3(2.8%); p<0.0001. ROC curve analysis indicated that at the optimal cut-off value of 2, UHFUS identified pSS and no-SS patients with a SE=68.2%, a SP=67.9%, a PPV= 63.8%, and a NPV= 72% (AUC=0.722, 95%CI: 0.651-0.793) and can predict a FS≥1 at the MLSG biopsy with a SE =73%, a SP=63.4%, a PPV= 48.9% and a NPV = 83% (AUC= 0.732, 95% CI: 0.657-0.806). Subgroup analyses highlighted significant differences in UHFUS diagnostic accuracy between anti-Ro/SSA+ and anti-Ro/SSA- patients. Particularly, in the latter group UHFUS showed a higher diagnostic accuracy (AUC= 0.754, 95% CI: 0.641-0.867) with a NPV increased up to 93.3%; similarly, UHFUS showed a higher accuracy (AUC= 0.755, 95% CI: 0.650-0.860) in predicting a MLSG FS≥1 with a NPV raised up to 90.7%.

Conclusion: MLSG UHFUS score system presents a good SE and SP in distinguishing pSS from no-SS subjects. The diagnostic accuracy of MLSG UHFUS may be significantly enhanced when combined with anti-Ro/SSA antibodies status. If anti-SSA antibodies are negative and UHFUS grade is 0 or 1, the diagnosis of pSS is very improbable and MLSG biopsy could be avoided. Further studies are in progress to define the added value of UHFUS with respect to major salivary gland ultrasonography.

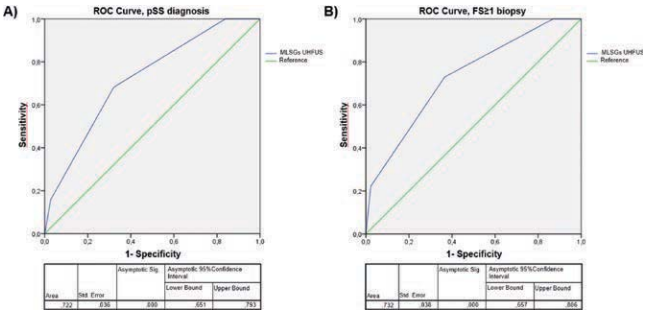

Figure 1. ROC curves showing UHFUS diagnostic accuracy in pSS (A) and for predicting a MLSG FS≥1

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POS0772 HEPATIC STEATOSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: PREVALENCE AND ASSOCIATION WITH DISEASE FEATURES

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Background: The spectrum of hepatic involvement in patients with systemic lupus erythematosus (SLE) is broad and multifactorial. Steatosis is a common finding in liver biopsies performed on these patients; however, there is no further evidence of its prevalence in this population. Early detection of steatosis is important to consider ideal management options, and transient elastography (Fibroscan) offers a non-invasive, fast, and easy tool that provides reliable diagnoses.

Objectives: To determine the prevalence of hepatic steatosis in patients with SLE by using the controlled attenuation parameter (CAP). We also aimed to describe factors associated with steatosis in lupus, such as metabolic syndrome criteria, treatment, and disease activity.

Methods: Between July and December 2021, we measured the degree of hepatic steatosis in patients who fulfilled the 2019 EULAR/ACR SLE classification criteria from a rheumatology outpatient clinic in a tertiary referral center in Mexico City, using the CAP obtained with Fibroscan. The cut-off value for considering hepatic steatosis was 275 dB/m. Fibroscan results, metabolic syndrome criteria, treatment, and SLE-associated variables were recorded. Variables were analyzed using Chi-squared, Fisher's exact, and Mann-Whitney U tests. We used logistic regression to compare variables associated with lupus activity and steatosis. A p value <0.05 was considered statistically significant.

Results: A total of 102 patients (83% female, mean age 39±14 years) with SLE were included. We identified 23 patients (22.5%) with hepatic steatosis. Patients with steatosis had a higher mean waist-to-hip ratio (WHR; 0.92 vs 0.85 cm p<0.001), and prevalence of overweight/obesity (82% vs 49% p=0.004) compared with patients without steatosis. Univariate analyses showed that steatosis was significantly associated with higher body mass index (BMI; OR 1.24 [95%CI 1.11-1.39], p<0.001), WHR (OR 1.13 [95%CI 1.03-1.23], p=0.006), serum glucose (OR 1.04, [95%CI 1.00-1.07], p=0.04), and paradoxically, higher C3 complement levels (OR 1.03 [95%CI 1.01-1.05], p=0.002). Additionally, hydroxychloroquine was found to be a protective factor (OR 0.34 [95%CI 0.12-0.98], p=0.047). There were no differences between patients with and without steatosis in terms of disease duration and types of activity. Also, no differences were found in the activity (SLEDAI-2K) and chronic damage (SLICC-DI) indices between groups. In the multivariate analysis, the only variables that remained significantly associated with steatosis were BMI (OR=1.23 [95%CI 1.05-1.43], p=0.007), and WHR (OR 1.15 [95%CI 1.03-1.28], p=0.01).

Table 1. UHFUS diagnostic accuracy in pSS (A) and for predicting a MLSG FS≥1 in all the cases and in anti-Ro/SSA negative patients. OCP, optimal cut-off value.

	SE	SP	PPV	NPV	AUC (95%CI)	OCP
pSS diagnosis (all pts)	60/88 (68.2%)	72/106 (67.9%)	60/94 (63.8%)	72/100 (72%)	0.722 (0.651-0.793)	2
FS≥1 prediction (all pts)	46/63 (73%)	83/131 (63.4%)	46/94 (48.9%)	83/100 (83%)	0.732 (0.657-0.806)	2
pSS diagnosis (SSA- pts)	14/19 (73.7%)	70/101 (63.9%)	14/45 (31.1%)	*70/75 (93.3%)*	0.754 (0.641-0.867)	2
FS≥1 prediction (SSA- pts)	17/24 (70.8%)	68/96 (70.8%)	17/45 (37.9%)	*68/75 (90.7%)*	0.755 (0.650-0.860)	2

Although it did not reach statistical significance, current use of hydroxychloroquine tended to be a protective factor for steatosis (OR=0.18 [95%CI 0.03-1.10], p=0.06).

Conclusion: The prevalence of hepatic steatosis in patients with SLE is similar to that of the general population. Metabolic risk factors were associated with a higher prevalence of steatosis in patients with lupus, contrary to other SLE disease features such as activity, treatment, and chronic damage. Interestingly, hydroxychloroquine use tended to be a protective factor for steatosis in these patients.

Table 1. Characteristics of SLE patients according to the presence of steatosis.

	All patients	Patients without steatosis	Patients with steatosis	
	(n=102)	(n=79)	(n=23)	P value
Age	37 (29-51)	38 (29-51)	34 (30-55)	0.8
Weight (kg)	66.5 (58-76.7)	63 (57-73)	77 (68-89)	**<0.001**
Body mass index (kg/m^2)	26.3 (22.9-29.9)	25 (22-29)	31 (26-33)	**<0.001**
Obesity	25 (24%)	13 (16%)	12 (52%)	**<0.001**
Waist-to-hip ratio	87.2 (81.3-92.2)	85.6 (80.2- 91.7)	92.2 (87.4-94.6)	**0.003**
Current use of hydroxychloroquine	85 (80%)	70 (84%)	15 (65%)	**0.04**
SLEDAI score	4 (2-6)	4 (2-6)	2 (1-6)	0.4
SLICC-DI score	1 (0-1)	1 (0-1)	1 (0-1)	0.8
Glucose (mg/dl)	84 (79-92)	83.5 (78-90)	88 (82-93)	**0.03**
C3	102 (81-124)	99 (78-121)	123 (100-137)	**0.003**
C4	17 (12-25)	16 (12-25)	20 (14-25)	0.3

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POS0773 AUTOANTIBODIES IN A MULTI-INSTITUTIONAL INDIAN COHORT (INSPIRE) OF SLE PATIENTS: PREVALENCE, CLUSTER ANALYSIS AND PHENOTYPE ASSOCIATION

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Background: Systemic Lupus Erythematosus (SLE) is characterized by an array of autoantibodies. Different autoantibodies have been associated with different clinical features like anti-dsDNA antibodies with nephritis and anti-phospholipid antibodies with pregnancy loss. However, the prevalence of autoantibodies has been variable across different ethnic groups. Data on the Indian population is limited.

Objectives: To assess the prevalence of different autoantibodies in a multi-institutional cohort (INSPIRE) of Indian SLE patients and to test their association with various clinical features using cluster analysis

Methods: The patients (n=1053) enrolled in a multi-institutional cohort of Indian patients (Indian SLE inception cohort for Research [INSPIRE]) were included.[1] Antibodies were assayed using Immunoline (Euroimmune, Germany) 17 antigen kit. Anti-phospholipid antibodies (IgG and IgM anti-cardiolipin antibodies (ACLs), IgG anti-Beta 2 GpI antibodies) were measured using ELISA (Euroimmune). Lupus anticoagulant was available in a subset of patients. The prevalence data for autoantibodies were analyzed using an intensity of only ++ and above on Immunoline assay as significant. Univariate analysis by Chi-square test was done to identify associations between individual autoantibodies and their clusters with clinical manifestations.

Results: The clinical features were fever in 702, alopecia in 813, oral ulcers in 628, acute cutaneous lupus (ACLE) in 520, proteinuria in 400, pleural effusion in 181, thrombocytopenia in 250 and autoimmune hemolytic anemia in 137 patients. The prevalence of various autoantibodies by ELISA was anti-dsDNA antibodies in 70.2% (551/784), IgG Anti- beta-2 GpI in 4.47% (42/938), IgG ACL in 6.14% (61/992) and IgM ACL in 7.1% (54/760). Lupus anticoagulant was present in 13.9% (112/ 805). By Immunoline assay, the prevalence for anti-Ro 52, anti-Ro 60, anti-La and anti-Ribosomal P was 28.49%, 33.14%, 10.07% and 24.03% respectively (Table 1).

Table 1. Prevalence of different autoantibodies in the INSPIRE lupus cohort

S. No.	Autoantibody	Prevalence (%) (n=1053)
1.	dsDNA	28.11
2.	Nucleosomes	27.83
3.	Histones	24.88
4.	Ro_52_SSA	28.49
5.	Ro_60_SSA	33.14
6.	SSB-La	10.07
7.	Ribosomal P	24.03
8.	nRNP	36.75
9.	Sm	33.14
10.	Scl-70	3.23
11.	PM-Scl	0.38
12.	Jo-1	0.09
13.	CENP-B	0.38
14.	PCNA	1.33
15.	AMA-M2	2.28

Cluster analysis (Figure 1) revealed association (Odds ratio with 95% confidence interval) of Cluster 1 (antibodies against dsDNA, histones and nucleosomes) with arthritis (1.51 [1.18-1.94]), proliferative nephritis (3.05[2.08-4.48]) and pleural effusion (1.49[1.08-2.05]), cluster 2 (antibodies against Sm, nRNP, Ro52, Ro60 and Ribosomal P) with ACLE (1.3[1.02-1.65]) and non-proliferative nephritis (1.64[1.09-2.46]) and cluster 3 (antiphospholipid antibodies) with thrombocytopenia (3.34[1.57-7.11]).

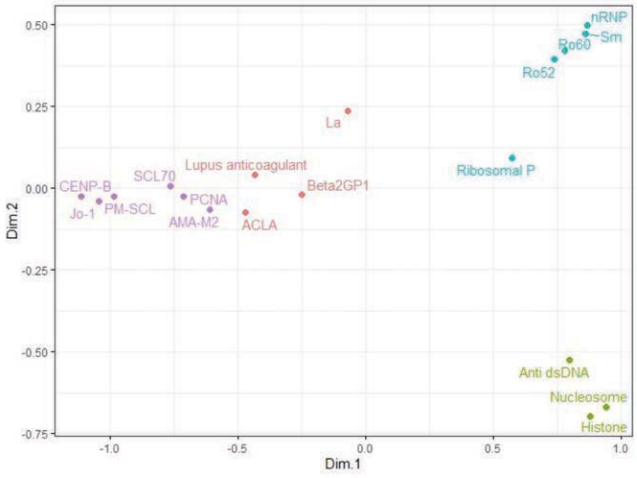

Figure 1. Cluster analysis of autoantibodies (Cluster 1: dsDNA, histone and nucleosome; cluster 2: Sm, nRNP, Ro52, Ro60 and Ribosomal P; cluster 3: cardiolipin, β2GP1 and La and lupus anticoagulant; cluster 4: Scl-70, Jo-1, PCNA, AMA-M2, PM-SCL and CENP-B)

Conclusion: The prevalence of anti-Sm antibody and Anti-Ribosomal P antibody is higher whereas that of anti-La antibody is lesser in the Indian SLE patients as compared to other cohorts of SLE patients with different ethnicities.[2] Cluster analysis reveals co-occurrence of different autoantibodies in our patients and their significant association with various clinical manifestations which suggests a possible pathogenic role of autoantibodies or a common genetic basis for it.

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POS0774

ANTI-SM AUTOANTIBODIES IDENTIFY A PHENOTYPE OF SEVERE SLE WITH AN ASSOCIATED SERUM BIOMARKER PROFILE

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Background: Antibodies to Smith (Sm) have been described as one of the most specific autoantibodies for systemic lupus erythematosus (SLE). Other than its association with lupus nephritis, there is, however, limited understanding of its clinical significance[1,2].

Objectives: To describe clinical associations and serum protein profiles of anti-Sm positivity in SLE.

Methods: Patients fulfilling SLE classification criteria who were followed longitudinally in a prospective multicentre cohort were studied according to their baseline anti-Sm antibody status. Comparison between Sm+ and Sm- patients was made using descriptive statistics. Clinical associations of Sm positivity with patient disease characteristics were studied using logistic regression. In a subset, 211 serum analytes were measured using Quantibody, Luminex and ELISA assays. Associations between serum proteins and Sm positivity were studied using Least Absolute Shrinkage and Selection Operator (LASSO) penalised regression, adjusting for demographics (age, sex, ethnicity) and medication use

Results: 383 patients were studied with median (IQR) follow-up of 4.9 (2,9) years; 65 (17%) had positive anti-Sm antibodies. Sm+ patients were significantly more likely to be of non-European ancestry (OR 2.73, 95% CI 1.55-4.82, p<0.001), and to be positive for anti-dsDNA antibodies (OR 2.8, 95% CI 2.3-3.4, p<0.001), anti-RNP antibodies (OR 15.7, 95% CI 13.9-17.8, p<0.001), direct anti-globulin test (OR 2.36, 95% CI 2.07-2.7, p<0.001) and hypocomplementemia (OR 7.73, 95% CI 5.1-11.7, p<0.001). Sm+ patients were significantly more likely to have active disease during the observation period in a range of organ domains, including mucocutaneous, renal, vasculitis and fever. More Sm+ patients had episodes of High Disease Activity Status (HDAS, SLEDAI-2K ≧10)[3] (OR 3.07, 95% CI 1.70-5.54, p<0.001) and persistent active disease (time-adjusted mean SLEDAI-2K > 4) (OR 3.23. 95% CI 1.84-5.70, p<0.001). Conversely, fewer Sm+ patients attained LLDAS for ≥50% observed time (19.7% vs 41.8%, p=0.002). Sm+ patients were more likely to be treated with glucocorticoids, immunosuppressants, and rituximab. There was no significant difference in damage accrual between Sm + and Sm - patients. In serum protein analysis (n=197, 29 Sm+), LASSO modelling retained 3 proteins associated with Sm+ status, CXCL13, IL1RL1 and FLT1, along with Asian ethnicity and age. In analysis including pairwise interaction between predictors, 28 Sm+ associated proteins were identified, including CCL4, VCAM1, IL1RL1, Fcg R IIB/C, TDGF1, CEACAM1, TIMP1, BMP5, GDF15, and TNFRSF17.

Conclusion: Anti-Sm autoantibodies, present in 17% of SLE patients, were strongly associated with classical disease manifestations, more severe disease activity, and a specific serological and proteomic profile. These findings suggest anti-Sm+ SLE as a specific disease subset.

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POS0775

COMBINED MODEL OF RENAL HISTOPATHOLOGY AND CLINICAL PARAMETERS BETTER PREDICT ONE YEAR RENAL OUTCOMES IN LUPUS NEPHRITIS: ANALYSIS OF 334 KIDNEY BIOPSIES

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Background: Diagnosis of Lupus Nephritis (LN) is currently based on laboratory tests and renal histopathology. Role of histopathological features in determining long term outcomes is unclear.

Objectives: 1. To assess if clinical and biochemical parameters at baseline can identify renal histopathological class. 2. To assess the clinico-histopathological predictors of renal response.

Methods: This is a single centre retrospective study comprising 334 LN renal biopsies. Clinical and biochemical parameters at the time of biopsy were noted and their association with histopathological class, activity and chronicity scores (AS/CS) (ISN/RPS classification) were evaluated. Complete, partial or no response (CR, PR, NR) for renal outcome (EULAR/EDTA) at 1 year were assessed for 293 patients. Binary logistic regression was done to look for the predictors of NR.

Results: Class III/IV LN was seen in 240(71.8%). Hypertension was seen in (52.1%) of class III/IV and <25% each with class II, V and combined class(p<0.001). Class III/IV had lower eGFR [87.6(62.75-118.8)] (p<0.001) than the other classes. Nephrotic range proteinuria was seen in 32% of class V and 21% in class III/IV (p=0.004). Among class-III/IV, AS had weak correlation with baseline UPCR (r=0.31) and eGFR (r=-0.172) (p<0.01). CS had weak negative correlation with eGFR (r=-0.212, p<0.01). NR at 1 year was higher in males (OR-4.6,95%CI-1.9-10.8, p<0.001), those with abnormal serum creatinine (OR-3.3,95%:CI1.6-7.02, p-0.001), higher renal SLEDAI (p<0.05), higher AS, CS (p<0.001), interstitial inflammation and tubular atrophy(p<0.005) (Table 1). On binary logistic regression a combined clinico-histopathological model comprising of serum creatinine, UPCR, male sex and CS performed best in predicting NR (Figure 1).

Table 1. Comparison of baseline characteristics among those who attained any response (CR/PR) versus others at 1 year

Parameter	Any response Complete Response CR/PR (n=233)	Others (No response/rescue) (n=60)	OR (95% CI)	P value
Female/male, n (%)	221(94.8)/12(5.2)	48(80)/12(20)	**4.6(1.9-10.8)**	**0.001**
Median age at nephritis onset	28(11-65)	25(13-67)		0.079
Median SLE duration	12(0-232)	18(0-144)		0.770
Hypertension, n (%)	100(42.9)	34(56.7)		0.061
Creatinine>1.3mg/dL (median, IQR)	21(9.0)	15(25)	**3.3(1.6-7.02)**	**0.001**
eGFR categories, n (%)	137(58.8)	27(45)	**1.7(0.96-3.03)**	**0.003**
>90	57(24.5)	15(25)		
61-90	34(14.6)	9(15)		
30-60	4(1.7)	8(13.3)		
<30				
Active urinary sediments, n (%)	132(56.7)	44(73.3)		**0.019**
uPCR g/day (median with IQR)	1.38(0.8-2.67)	1.95(1.18-4.19)		0.098
Class III/IV, n (%)	167(71.7)	49(81.7)		0.117
Class V, n (%)	17(7.3)	5(8.3)		0.788
Combined class, n (%)	7(3.0)	3(5.0)		0.469
Activity score, median with IQR	3(1-6)	6(3-9)		**0.001**
Chronicity score, median with IQR	0(0-1)	1(0-2)	**5.06(1.49-17.21)**	**0.001**
Presence of Crescents, no (%)	43(18.5)	17(28.3)		0.104
Fibrinoid necrosis, n (%)	28(12.0)	7(11.7)		0.791
Interstitial inflammation, n (%)	86(36.9)	33(55)	**2.08(1.17-3.70)**	**0.003**
Interstitial fibrosis, n (%)	23(10.7)	9(15)		0.273
Tubular atrophy, n (%)	64(27.5)	27(45)		**0.003**
Blood vessel changes, n (%)	2(0.9)	1(1.7)		0.606
Fibrinoid necrosis	206(88.4)	50(83.3)		0.339
Other changes*				

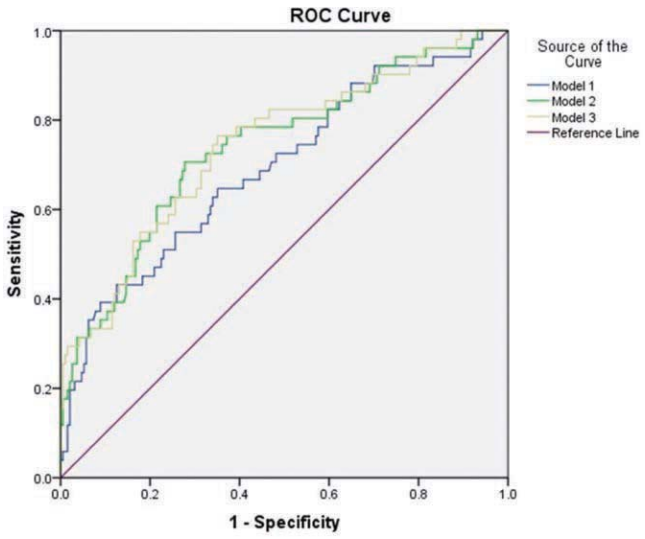

Figure 1. ROC curve and AUC for the three different modelsModel 1: Baseline serum creatinine, urine PCR, male sex; AUC – 0.694(0.609-0.779), p <0.001Model 2: Baseline serum creatinine, urine PCR, male sex, chronicity score; AUC – 0.740(0.660-0.820), p<0.001Model 3: Baseline serum creatinine, urine PCR, male sex, chronicity score, crescents, interstitial inflammation; AUC – 0.744(0.664-0.824), p<0.001

Conclusion: Clinical and biochemical parameters can predict the renal histological class to a fair extent but has limited value in predicting the activity and chronicity parameters. Since a combination of clinical and histopathology parameters are better in predicting renal outcomes, performing renal biopsies should be encouraged in LN.

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POS0776 IMMUNOGENICITY AND SAFETY OF INACTIVATED AND MRNA COVID-19 VACCINES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Vaccination against SAR-CoV-2 is a new campaign and believed to be the key to end the pandemic. Currently, there are two COVID-19 vaccines with different mechanism of action available in Hong Kong - they are the inactivated virus vaccine and the mRNA-based vaccine. Both vaccines have obtained approval for emergency use by the World Health Organization (WHO) and were widely deployed globally (1). A mass voluntary vaccination program for all Hong Kong residents has started in late February, 2021 (2). However, the efficacy and safety of COVID-19 vaccines in patients with SLE is uncertain due to a complex interplay of underlying autoimmunity and immunosuppressive therapies used.

Objectives: This study was to investigate the effects of both inactivated and mRNA COVID-19 vaccines in patients with SLE.

Methods: This was a prospective, single-centre, case-control study. Patients with SLE planning to receive COVID-19 vaccines were recruited and matched 1:1 with healthy controls. The immunogenicity of the COVID-19 vaccines was assessed by a surrogate neutralization assay at 28 days after the second dose. The main outcomes included the antibody response and adverse effects comparing SLE patients and controls. Predictors of responses in SLE patients were analyzed. The change of SLE disease activity was evaluated.

Results: Sixty-five SLE patients received 2 doses of COVID-19 vaccines (Comirnaty: 38; CoronaVac: 27) were recruited. Many of them were on systemic glucocorticoids (75.8%) and immunosuppressants (54.5%). At day 28 after the second dose of vaccines, 92.3% (Comirnaty: 100%; CoronaVac: 81.5%, p=0.01) had positive neutralizing antibody. However, compared to the age, gender, vaccine type matched controls, the level of neutralizing antibody was significantly lower (p<0.001) in patients with SLE (Figure 1). The self-reported side effects of the vaccines in lupus patients were common but mild, and were more frequent in the Comirnaty group. There was no significant change in lupus disease activity up to 28 days after vaccination. The independent predictors of neutralizing antibody level included the dosage of systemic glucocorticoids, use of mycophenolate and type of vaccines (Table 1).

Table 1. Multivariate linear regression analysis for neutralizing antibody activity

	Beta	95% confidence interval	P value
Age	-0.022	-0.425 – 0.381	0.914
Gender	8.16	25 (92.6)	0.296
SLEDAI-2k	-1.96	-4.22 – 0.31	0.088
Prednisolone dosage	-2.01	-3.66 - -0.37	**0.018**
Mycophenolate mofetil	-15.2	-24.4 - -6.0	**0.002**
Type of vaccines: Comirnaty	28.8	20.1 – 37.5	**<0.001**

Conclusion: COVID-19 vaccines produced satisfactory but impaired serological response in SLE patients compared to controls which was dependent on the immunosuppressive medications use and type of vaccines received. There was no new short-term safety signal noted. Booster dose is recommended.

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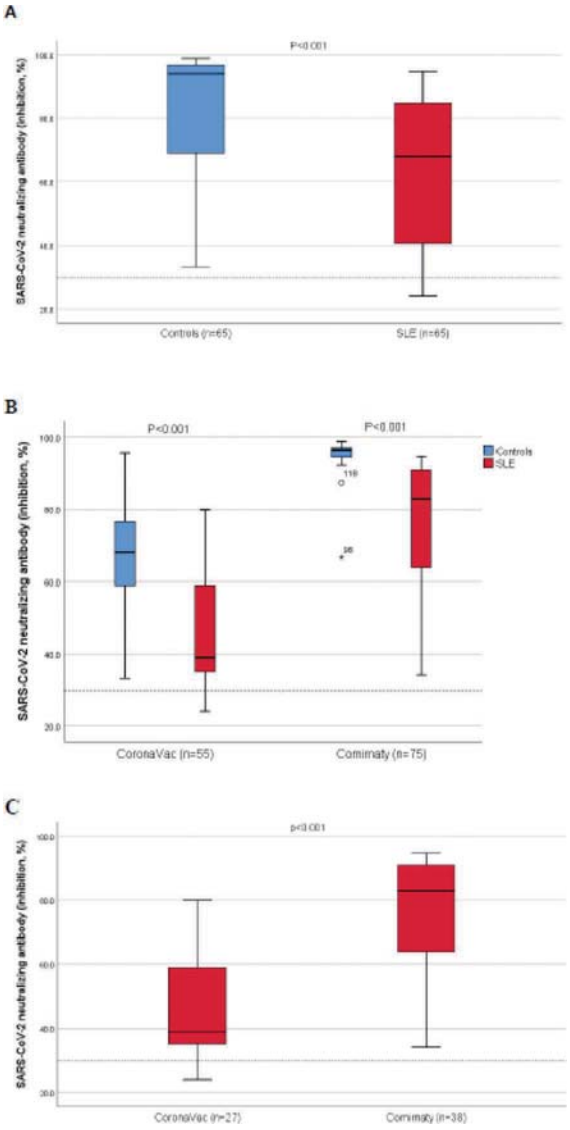

Figure 1. Distribution of neutralizing antibody levels after COVID-19 vaccines comparing (A) SLE patients and matched controls, (B) SLE patients and matched controls in two vaccine subgroups, and (C) two vaccine types in SLE patients. Data for each group are presented as box plots: central values within boxes correspond to median; the range between the lower (Q1) and upper (Q3) bounds of the boxes is the IQR. Whiskers represent scores outside IQR and ends in maximum (higher "calculated value" = Q3 + 1.5 x IQR) and minimum (lower "calculated value" = Q1 – 1.5 x IQR). Spots are outliers above the maximum or under the minimum values. Data regarding were analyzed using Mann-Whitney-U test. Dotted line denotes the cut-off level for positivity (30%).

POS0777 STUDY OF PERIPHERAL BLOOD B CELL IMMUNOPHENOTYPING IN PATIENTS WITH LUPUS NEPHRITIS: PARAMETERS OF DISEASE ACTIVITY, REMISSION AND FLARE

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Background: B cells play a central role in systemic lupus erythematosus (SLE) pathogenesis connecting innate with adaptative immunity.

Objectives: To investigate the peripheral blood B cell phenotype in a cohort of SLE patients with renal involvement (LN-SLE) in relation to disease activity and renal histological lesions compared to healthy controls.
Methods: One hundred LN-SLE patients with active renal involvement, 40 at disease onset (Early) and 60 in whom LN occurred after the disease onset (Long) were enrolled. Thirty-seven healthy controls were included. Clinical, laboratory and demographic data were collected at baseline and at 6 and 12 month of follow-up. Disease activity was recorded using SLEDAI-2K. Ultrasound-guided renal biopsy has been performed for the definition of the nephritic class according to the ISN/RPS classification. The memory B cells immunophenotyping (IgD/CD27 classification) was analyzed in peripheral blood through flow cytometry. To clarify the role of key molecules in the B cells activation, IL-6 and BAFF serum levels were assayed by Enzyme-linked immunosorbent assay (ELISA).
Results: According to the onset of renal symptoms, there were no differences in the distribution of the renal classes and in activity and chronicity indices in the two groups. A direct correlation was observed between chronicity index score and creatinine in the whole cohort (R=0.342;*p<0.01*) and in LN-SLE Early (R=0.528;*p=0.01*) and Long (R=0.337;*p=0.02*). The disease activity index was found to be significantly higher in anti-dsDNA positive than in negative ones (6.6±4.8 *vs* 2.8±3.5;*p=0.01*), and in patients with at least one antiphospholipid antibody-APL positivity (6.8±4.8 *vs* 5.1±4.8;*p=0.05*). Considering predictive biomarkers of the remission within 12 months, the presence of histological lesions (glomerulosclerosis and fibrocellular crescents) and the positivity for at least one of the APL antibodies were associated to the failure in achieving clinical remission, while baseline 24h-UP levels ≤2750mg were associated to remission achievement [OR:2.6(95%CIs:1.1-5.8)]. Studying the B cells subset, a lower percentage of $CD19^{pos}$ and unswitched memory ($IgD^{pos}CD27^{pos}$) in LN-SLE compared to controls (6.8±5.5% *vs* 10.5±3.5%;*p<0.01* and 11.1±12.0% *vs* 15.3±8.0%;*p<0.01,*respectively) was observed. In addition, we found higher levels of double-negative memory B cells ($IgD^{neg}CD27^{neg}$) and plasmablasts ($CD27^{pos}CD38^{pos}$) in LN-SLE than in controls [($CD27^{neg}IgD^{neg}$ 10.0±8.7% *vs* 4.1±1.9%;*p<0.01*)($CD27^{pos}CD38^{pos}$ 4.4±5.3% *vs* 1.0±0.5%;*p<0.01*)]. Furthermore, $CD19^{pos}$ and $IgD^{pos}CD27^{pos}$ negatively correlated with BAFF [(R=-0.327;*p=0.03* and R=-0.305;*p=0.04*) respectively] while a direct correlation was observed between $IgD^{neg}CD27^{neg}$ B cells and IL-6 serum levels (R=0.302;*p*<0.01). No correlation was found between B cells subsets and the disease activity parameters. Considering the remission status achievement within 12 months both LN-SLE groups had significantly lower frequencies of $IgD^{pos}CD27^{pos}$ than controls [(Remission:10.7±12.4% *vs* 15.3±8.0%;*p<0.01*) (No-Remission:9.8±9.5% *vs* 15.3±8.0%;*p<0.01*)] conversely had a significantly higher rate of $IgD^{neg}CD27^{neg}$ than controls [(Remission:11.5±10.0% *vs* 4.1±1.9%;*p<0.01*;NoRemission:9.6±6.7% *vs* 4.1±1.9%;*p<0.01*] and plasmablasts [(Remission 5.2±6.7% *vs* 1.0±0.5;*p=0.05;*NoRemission:4.1±3.4 *vs* 1.0±0.5;*p<0.01*)]
Conclusion: This study suggests that the active injury and chronic damage histological features of LN do not depend on the SLE duration *per se*, but could be associated to the failure in achieving clinical remission within 12 months. Furthermore, data on memory B cells immunophenotyping reveals a distinct B cells subset of SLE patients when compared to healthy controls, confirming an alteration of B cells subsets in SLE patients and strengthening the hypothesis of the pathogenetic role played by B lymphocytes in the course of LN.
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POS0778 THE USEFULNESS OF ULTRASOUND-GUIDED CORE NEEDLE BIOPSY OF THE PAROTID GLAND FOR THE DIAGNOSIS OF PRIMARY SJÖGREN'S SYNDROME

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Background: Ultrasound-guided Core Needle Biopsy (US-guided CNB) of the parotid gland has proved to be a novel and safe technique for the diagnosis of lymphoma in Sjögren's Syndrome (pSS) patients with salivary gland enlargement.[1] The potential role of US-guided CNB for the diagnosis of pSS has been never reported, while only one group uses open surgical parotid biopsy to this end in pSS[2].
Objectives: To explore the value of US-guided CNB of the parotid gland as a diagnostic tool for pSS.
Methods: From September 2019 to June 2021, 22 patients with a clinical diagnosis of pSS underwent US-guided CNB of the parotid gland due to persistent (≥2 months) parotid swelling and suspected glandular lymphoma. In 21/22 (95.4%) patients, the tissue sampling was adequate for the histopathological diagnosis. No persistent complications were reported. For the aim of this study, 2/21 (9.5%) patients were excluded for a different final diagnosis (i.e., IgG4-RD and sarcoidosis), and 13/21 (61.9%) patients for a diagnosis of parotid gland lymphoma. Six out of 21 (28.5%) were finally included for the evaluation of US-guided CNB in the histopathological diagnosis of pSS. The following histopathological features related to pSS were studied: focus score (FS); presence of germinal centres (GCs); presence of lymphoepithelial lesions (LELs); and presence of Myo-/Lympho-epithelial sialadenitis (MESA/LESA).
Results: All 6 patients already satisfied the ACR/EULAR classification criteria for pSS and were females, with a mean age of 47.6 years (SD ±17.0) and a mean disease duration of 8.3 years (SD ±8.0). In all of them, specific findings of pSS were observed (Table 1). The FS could be calculated in 3/6 cases and was ≥1 in 2/3 cases, while in 3/6 cases it could be not calculated due to the evidence of MESA/LESA. GCs were found in 4/7 cases, while LELs were present in 3/7 cases (Table 1).

Table 1. Histopathological features in the parotid gland biopsy.

#Patient	Focus score	LELs	GCs	MESA/LESA
#1 NI	Not applicable	✗	✗	✓
#2 BM	≥1	✓	✓	✗
#3 CM	Not applicable	✓	✓	✓
#4 RC	<1	0	✓	✗
#5 FR	Not applicable	✓	✓	✓
#6 RV	≥1	✗	✗	✗

Conclusion: US-guided CNB of the parotid gland could represent a potential novel tool for the diagnosis of pSS patients. When parotid swelling is present, it may be more convenient than lip biopsy. In addition, CNB can be ultrasound-guided in specific glandular areas showing different sonographic appearances, consistent with different histopathology, leading the way for the role as diagnostic tool for pSS, and not only as improved lymphoma detection tool.
The next step is to evaluate US-guided CNB in pSS patients without glandular swelling, and to compare the results with labial biopsy.
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POS0779 STANDARDIZED MORTALITY RATIO AND RISK FACTORS FOR DEATH IN SOUTHERN CHINESE PATIENTS WITH THE ANTIPHOSPHOLIPID SYNDROME (APS)

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Objectives: To report the mortality rate and risk factors for death in southern Chinese patients with the antiphospholipid syndrome (APS)

Methods: The HKAPS registry was established in early 2020 by the Hong Kong Society of Rheumatology to study the outcomes of Chinese patients with APS treated in public hospitals in Hong Kong. Patients aged ≥18 years were identified by the Hospital Authority Clinical Data retrieval system using the ICD-10 diagnostic code of APS. The medical history and APS diagnosis was verified by sub-investigators in different hospitals using the 2006 modified consensus criteria for the APS. Eligible patients were classified into definite APS or probable APS, which was further categorized into primary (without underlying rheumatic diseases) and secondary types. The treatment and outcome (recurrence and mortality) of the patients was studied by Kaplan-Meier analysis and risk factors for recurrence of thrombosis and mortality were studied by Cox regression.

Results: 428 APS patients were studied - 282 fulfilled the 2006 criteria for APS while 146 patients had probable APS (anti-phospholipid [aPL] antibodies positive once or with non-criteria manifestations). All were ethnic Chinese. The mean age at diagnosis was 44.1±15.6 years and the female to male ratio was 3.4:1. APS was primary in 211 patients and secondary to concomitant rheumatic diseases in 217 patients (SLE in 89.9%). 369(86.4%) patients had thromboembolic manifestations, 85(19.9%) had obstetric morbidities and 20(4.7%) had both. In patients with secondary APS, 23% thrombotic or obstetric manifestations occurred before diagnosis of the rheumatic diseases. Lupus anticoagulant (LAC), moderate/high titers of IgG anticardiolipin and anti-β2glycoprotein-1 antibodies was present in 326(76.1%), 242(56.5%) and 29(6.7%) patients, respectively. 137(32%) patients were double positive while 19(4.4%) patient was triple positive for these aPL antibodies. Among the thromboembolic manifestations, arterial thrombosis (n=201) was more common than venous thrombosis (n=186). The following treatment regimens were used: warfarin (63.6%), aspirin plus subcutaneous heparin (6.8%), aspirin plus warfarin (3%), aspirin alone (17.8%) and direct oral anticoagulant (DOAC) (2.8%). Bleeding complications developed in 77(18%) patients. After a mean follow-up of 8.0±14.1 years, recurrence of thromboembolic or obstetric complications occurred in 83(19.4%) and 14(3.3%) patients, respectively (1 patient had recurrence of both thrombosis and obstetric complications). Cox regression did not reveal any factors significantly associated with recurrence of thrombosis. A total of 67(15.7%) patients succumbed (median time to death 7.3 years). The causes of death were vascular in 29.9% (intracranial haemorrhage [35%], myocardial infarction [30%], limb ischemia [10%], ischemic stroke[10%], bowel ischemia[5%]) and non-vascular in 70.1% of patients (infection [59.6%], malignancy [10.6%], SLE activity [6.4%], pulmonary arterial hypertension [2.1%], organ failure [6.4%] and others). The cumulative risk of mortality over time was 6.4% at 5 years and 11.9% at 10 years. The age and sex adjusted standardized mortality ratio (SMR) of our APS patients relative to the general population was 18.2(14.2-23.0). In patients with thrombotic APS, mortality was associated with older age (≥60 years) (HR 2.57[1.34-4.95]) and the presence of LAC (HR 2.01[1.07-3.75]), adjusted for age, sex and vascular risk factors that included hypertension, diabetes mellitus, dyslipidaemia, smoking and atrial fibrillation.

Conclusion: APS in southern Chinese is relatively uncommon and most cases were associated with SLE. In contrast to the Caucasians, venous thrombosis related to APS is less frequent. Over 8 years, recurrence of thrombotic events is uncommon. The mortality of APS in our Chinese patients was increased, with older age and the presence of LAC being independent risk factors.

Disclosure of Interests: None declared

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POS0780 MONOGENIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN NORTHERN ISRAEL

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Background: Systemic Lupus erythematous (SLE) is a heterogenic clinical syndrome with a multifactorial etiology including diverse environmental, immunological and genetic causes and modifiers. Increasingly, utilizing next generation sequencing tools, monogenic forms of SLE have been identified.

Objectives: The aim of our study was to identify monogenic causes of SLE in the unique pediatric population of Northern Israel.

Methods: A retrospective and prospective study was carried out between 2010-2021 in a single tertiary pediatric medical center. Genetic testing including Whole exome sequencing (WES) was performed for select patients including family history of SLE, consanguinity and\or clinical findings suggestive of specific disorder.

Results: 75 children were diagnosed with SLE. 13/75 had one or more relatives with SLE, including a pedigree with 4 affected members. Mean age at presentation was 10.1±4.7. A monogenic disorder was identified in total of 7/75 of pedigrees. Four patients were diagnosed with Prolidase deficiency, one patient with *ADAR1* mutation related to Aicardi–Goutières syndrome and one pedegree with APC5 mutations. Candidate variants in genes related to immune system were identified in one proband and her father requiring further study. Additional WES results are pending

Conclusion: We detected monogenic causes of SLE in a select cohort of patient in Northern Israel. Identification of a genetic basis for disease has direct clinical implication for patients and families and can also enhance our understanding of the pathogenesis and disease mechanisms involved in the more common sporadic forms of SLE.

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POS0781 RESIDUAL DISEASE ACTIVITY IN SLE: A REAL-LIFE CROSS-SECTIONAL STUDY IN THREE TERTIARY CENTRES TO EXPLORE THE ROOM FOR NOVEL THERAPIES

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Background: According to updated EULAR recommendations, the goal of treatment in systemic lupus erythematosus (SLE) should be remission or low disease activity in all organ systems, achieved with the least possible dose of glucocorticoids.[1] The proportion of patients achieving these two activity states under conventional therapies may vary between different patient cohorts and clinical settings.

Objectives: To assess the current disease activity state of SLE patients during their most recent visit in three tertiary centres experienced in the management of SLE.

Methods: In a cross-sectional study, patients were categorized as: 1) *Remission off-therapy*: SLE Disease Activity Index (SLEDAI)=0 without glucocorticoids (GC) or immunosuppressive drugs (IS), 2) *Remission on-therapy:* SLEDAI=0, GC ≤5mg/day prednisone (Pz) and/or IS (conventional and biologic, maintenance phase), 3) *Low disease activity (LDA)*: SLEDAI ≤4, Pz ≤7.5mg/day and/or IS (maintenance phase), 4) Active/Non-optimally controlled: SLEDAI >4 and/or Pz >7.5mg/day and/or IS (induction phase).[2] Hydroxychloroquine (HCQ) was allowed in all groups.

Results: A total of 332 patients were included [93.1% female, mean (SD) age 48.5 (14.7) years, median (IQR) disease duration 6.5 (12.4) years]. 81% (n=269) of patients were on HCQ and 69.6% (n=231) were receiving an additional IS at last visit. Regarding glucocorticoids (GC), almost half of our patients (48.2%, n=160) were not receiving any GC and of those receiving, only 7.8% (n=26) were receiving a Pz dose > 7.5 mg/day. Mean (SD) total and clinical SLEDAI were 3.7 (3.0) and 3.0 (2.9), respectively. At their most recent visit, 33.7% (n=112) of patients had no clinical activity (clinical SLEDAI=0) and 24.4% (n=81) had neither clinical nor serological activity (total SLEDAI=0). 31.6% and 49.1% of patients had a total SLEDAI-2K ≥6 and a clinical SLEDAI-2K ≥4, respectively (Table 1). Regarding disease activity states, 23.2% (n=77) of patients were in remission (off or on therapy), 36.7% (n=122) were in LDA, while 40.1% (n=133) were categorized as non-optimally controlled. In the latter group, a total SLEDAI > 4 was present in most of patients (79.2% vs. 21.9% for prednisone > 7.5 mg/day and 19.8% for IS at induction regimen). In patients with LDA or non-optimally controlled disease, activity was mainly driven by the mucocutaneous and musculoskeletal components of SLEDAI, along with serologic activity (Figure 1).

The latter was more common in LN patients. Overall, 83 patients (25.0%) in our cohort had evidence of serologic activity, of whom 31 (9.3% of total) had a clinical SLEDAI of 0.

Table 1. Distribution of patients based on total and clinical SLEDAI-2K score at most recent visit

Total SLEDAI		Clinical SLEDAI	
Score	Patients, n(%)	Score	Patients, n(%)
0	81(24.4)	0	112(33.7)
1-5	146(44)	1-3	57(17.2)
6-10	101(30.4)	4-8	154(46.5)
>10	4(1.2)	>8	9(2.7)

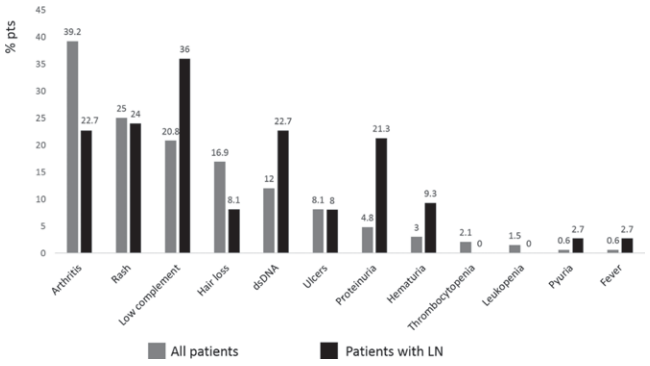

Figure 1. Components of SLEDAI-2K at most recent visit (total cohort of patients and patients with LN)

Conclusion: Although a significant proportion of our patients were on HCQ and additional IS, about 40% of them were not in optimal control. Yet, residual disease activity, based on SLEDAI-2K, was moderate, compared to relatively high mean baseline SLEDAI-2K of lupus trials. These data provide a pragmatic view of lupus patients, who could be potential candidates for novel treatments or inclusion in clinical trials.

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POS0782 ULTRASONOGRAPHIC EVALUATION OF MAJOR SALIVARY GLANDS IN PRIMARY SJOGREN'S SYNDROME: COMPARISON OF THREE SCORING SYSTEMS AND ASSOCIATION WITH BIOPSY RESULTS.

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Background: Salivary glands ultrasound is an imaging technique useful for primary Sjogren's syndrome (pSS) diagnosis. Nowadays, the use of ultrasound in diagnostic criteria is not clear. Different scoring systems have been published in recent years.

Objectives: This study aims to compare the reliability between three salivary glands ultrasound (SGUS) scores in a series of patients with pSS. Furthermore, we assessed the association of the three SGUS scores with minor salivary gland biopsy.

Methods: A cross-sectional study including 98 subjects fulfilling the ACR-EULAR 2017 classification criteria for pSS. All patients underwent an ultrasound of the salivary glands and a minor salivary gland biopsy requested as per clinical practice. An experienced Rheumatologist in SGUS evaluated systematically the previously acquired images. This Rheumatologist classified the images using three different scoring systems obtained from the grades of bilateral parotid and submandibular glands: De Vita (0-3), Salaffi (0-4) and Omeract (0-3). These three scores were performed in different days and blinded for the previous scores results. SGUS grade ≥ 2 was considered positive. Positive biopsy was deemed when focus score ≥1. We evaluated the agreement between the three scores and the individual scores with respect to the biopsy.

Results: This study included 98 patients with pSS. The distribution of the different grades according to the score system and the percentage of a positive SGUS are shown in Table 1. The reliability for a positive score for the three evaluated systems was almost perfect, with a Light's kappa of 0.95 [0.9-1] for the De Vita-Salaffi, 0.87 [0.77-0.97] for De Vita- Omeract and 0.83 [0.71-0.94] for Salaffi-Omeract. We observed a same degree of concordance when the individual parotid and submandibular scores were evaluated. There was only a fair agreement for positivity of SGUS and a positivebiopsy in all scoring systems, specifically De Vita (kappa = 0.27 [0.09-0.45]), Salaffi (kappa = 0.26 [0.06-0.45]) and Omeract (kappa = 0.22 [0.03-0.42]). This associations with a positive biopsy did not change in magnitude when individually evaluated parotid and submandibular glands.

Table 1. Distribution of the ultrasound grades and the percentage of positive biopsy in the different scoring systems evaluated.

	0	1	2	3	4	Positive score
Vita	23 (23.5%)	31 (31.6%)	26 (26.5%)	18 (18.4%)	0	44 (44.9%)
Salaffi	23 (23.5%)	29 (29.6%)	16 (16.3%)	23 (23.5%)	7 (7.1%)	46 (46.69%)
Omeract	27 (28.4%)	29 (30.5%)	23 (24.2%)	16 (16.8%)	0	39 (41.1%)

Conclusion: The three SGUS scores are reliable for the evaluation of the main salivary glands in pSS. There was only weak agreement for SGUS and biopsy, so these two techniques provides complementary information and currently, SGUS cannot replace the biopsy for diagnosis purposes.

Disclosure of Interests: None declared

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POS0783 ASSOCIATION BETWEEN ENVIRONMENTAL FACTORS AND SALIVARY GLAND ULTRASOUND FINDINGS IN PATIENTS WITH SUSPECTED PRIMARY SJÖGREN SYNDROME

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Background: The influence of environmental factors in primary Sjögren's syndrome (pSS) and their relationship with serological, histological and ultrasound findings remains still poorly understood. A possible protective effect of female sex hormones and smoking has been related to a lower focal lymphocytic sialadenitis on the minor salivary gland biopsy (MSGB), but the relationship between histological findings and other chemical, toxic or dietary factors remains scarce or controversial, and even more so the relationship between these factors with salivary gland ultrasound (SGUS) findings, an emerging tool in the diagnostic and management of pSS.

Objectives: To analyze the relationship between sociodemographic, clinical and environmental factors with pathologic SGUS findings in patients with suspected pSS.

Methods: 72 patients with clinical and/or analytical suspicion of pSS were consecutively recruited. SGUS was performed: pathological (grade ≥2 according to *Cornec et al* system) vs non-pathological. Final diagnosis of pSS was made according to AECG, ACR/EULAR criteria and MSGB. Sociodemographic, clinical, analytical, activity indexes (ESSPRI and ESSDAI), environmental factors, toxic and dietary habits were collected. Chi-square and Fisher tests were used to compare qualitative variables and T-student and U-Mann Whitney tests, for quantitative variables (statistical significance $p<0.05$). Defining pathologic vs non-pathologic US as the outcome variable, binomial logistic regression was performed for bivariate analysis, with calculation of Odds Ratio (OR) and 95% confidence interval (CI).

Results: 70.8% presented pathological SGUS, this percentage was significantly higher in patients with a definitive diagnosis of pSS (56.6% vs 26.6%; p=0.02). 97.2% were women with a mean age 57.3±11.8 years. Patients with pathological SGUS had in lower frequency a varied diet (64.2 vs 89.5; p=0.03), higher exposure to environmental toxics (71.1 vs 61.1; p=0.05), lower percentage of smokers (26.4 vs 52.6; p=0.03) and a lower mean age at menopause than patients with non-pathologic SGUS (47.3±3.9 vs 50.2±4.2; p=0.03). Significant differences were found in antiRo52 positivity and hypergammaglobulinemia. Bivariate analysis showed that menopause at younger age confers higher probability

of presenting pathologic SGUS (OR=1.2 CI95% 1.02-1.41) and smoking was protective against pathologic SGUS (OR=0.32 CI95% 0.11-0.95). Hypergammaglobulinemia (OR=8.80 CI95% 2.27-34.02) and antiRo52 (OR=3.89 CI95% 1.14-13.20) imply an increased risk of pathological findings on SGUS.

Conclusion: Pathologic SGUS was more frequent in patients with definitive diagnosis of pSS, antiRo52 antibodies and hypergammaglobulinemia. Late menopause and smoking were protective factors against pathologic SGUS, and a tendency for a varied diet and absence of exposure to environmental chemicals. SGUS could be the initial diagnostic test in patients with suspected pSS and positive antiRo who have less exposure to estrogens, tobacco and mediterranean diet and greater exposure to chemicals. For this reason, SGUS could be useful in identifying modifiable environmental risk factors to decrease the incidence and severity of this disease, for which effective therapy is still lacking.

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POS0784 LOW COMPLEMENT LEVELS ARE ASSOCIATED WITH HIGHER MORTALITY IN HOSPITALIZED PATIENTS WITH POSITIVE ANTIPHOSPHOLIPID ANTIBODIES

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Background: Antiphospholipid Syndrome is an autoimmune disease characterized by increased risk for vascular thrombosis (arterial and/or venous) thrombosis and/or pregnancy morbidity in the presence of antiphospholipid antibodies. The mechanisms by which aPLs induce thrombosis are unclear; several have been suggested, among them complement activation.(1-2) The complement system is a system of enzymes and regulatory proteins of the innate immune system that play a crucial role in the inflammatory response to various pathogenic stimuli. The complement and coagulation pathways are interconnected, and expanding evidence indicates that complement may be activated in patients with antiphospholipid syndrome (3-5).

Objectives: Our study was intended to better characterize the complicated relations between antiphospholipid antibodies and complement activation among hospitalized patients with antiphospholipid syndrome and its impact on short- and long-term prognosis

Methods: A retrospective cohort studies. Clinical and prognostic data of hospitalized patients with antiphospholipid syndrome and a measurement of complement levels (C3 or C4) were obtained. Rates of long-term mortality, one-year mortality, deep vein thrombosis (DVT), and pulmonary emboli (PE) were compared between patients with low complement levels and patients with normal complement levels. Low complement was defined as C3 < 90 mg/dl or C4 < 10 mg/dl. A multivariate analysis was performed to control for Anticardiolipin levels, β_2 macroglobulin levels and RVVT ratio.

Results: Complete data was available for 6,599 patients, of which 712 (11%) had low complement levels. The median age of the cohort was 47.7, and most of the patients were females (56%). Patients with low complement levels had significantly higher mortality rates 30% vs. 18%, p < 0.001 for long-term mortality (Figure 1) and 15% vs. 5%, p < 0.001 for 1 year mortality when compared to patients with normal complement levels. DVT and PE rates were similar (4% vs 3.8%, P = 0.78 and 4% vs 2.4%, P = 0.13 respectively). Results of the multivariate analysis (Table 1) were consistent and showed that patients with low complement levels had 111% higher mortality rates (CI 1.52-2.90, P < 0.001).

Table 1. Multivariate Analysis for long term mortality

Multivariate Analysis		
	OR (CI)	p
Low Complement	2.11 [1.52, 2.90]	<0.001
Anticardiolipin IGG	1.00 [1.00, 1.01]	0.243
Anticardiolipin IGM	0.99 [0.98, 1.00]	0.084
β_2 IGM	1.01 [1.00, 1.01]	0.017
β_2 IGG	1.00 [0.99, 1.00]	0.663
RVVT Ratio	0.99 [0.63, 1.52]	0.954

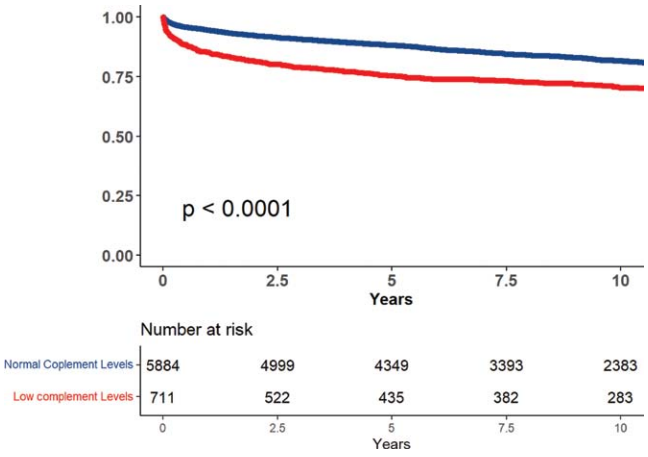

Figure 1. Cumulative 10-Year survival

Conclusion: In hospitalized patients with high aPLs, low complement levels are associated with significantly higher mortality rates. This finding is in correlation with recent literature, suggesting an important role for complement activation in APS.

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Disclosure of Interests: None declared

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POS0785 EXPRESSION OF MYXOVIRUS RESISTANCE PROTEIN A IN LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is regarded as one of the most severe organ manifestations of systemic lupus erythematosus (SLE) [1]. It has been shown that type I interferons (IFN) are important cytokines in the pathogenesis of SLE and LN and could possibly serve as a histological marker for kidney lesions in LN [2]. However, the direct measurement of type I IFN protein in tissues has remained elusive. Myxovirus resistance protein A (MxA) which is upregulated by IFN-1, can easily be measured, and could be used as a potential biomarker. In addition, dendritic cells are main producers of IFN-1.

Objectives: To investigate the expression of MxA and CD303 which is a plasmacytoid dendritic cells (pDCs) specific marker [3] by immunohistochemical analysis of renal specimens obtained from LN patients and from patients with other types of nephritis.

Methods: LN was diagnosed based on the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification. In total, 41 renal tissue samples were collected from lupus nephritis including all classes (I-V according to ISN/RPS classification), and compared to 70 biopsies from other forms of nephritis. MxA was detected by immunohistochemistry staining. Scoring of MxA staining was done semi-quantitative for separate structures in nephritis tissues with a range from 0 to 3+. Scoring was based on the intensity of the staining, in which '0' meant no expression; '1': weak expression; '2': moderate expression; and '3+': strong expression. The expression of CD303 was measured by counting the number of CD303 positive cells in the glomerulus or in the tubular interstitium.

Results: The MxA average scores of the total LN group were higher than control specimens especially in distal tubules (Figure 1). The MxA expression in LN

classes I, II, and V biopsies was mainly increased compared to tissues of patients with minimal change disease, mesangioproliferative nephritis, and membranous nephropathy (Figure 2a,2b,2d). However, MxA staining was comparable in LN classes III/IV compared to control groups (Figure 2c). The staining of CD303 showed that pDC are more present in tubular interstitium than in glomeruli. Furthermore, CD303-positive cells were highest in LN class IV, but overall numbers of pDCs were higher in controls groups compared to LN groups (Figure 3).

Conclusion: Our data indicate that MxA expression is higher in LN vs. other types of nephritis. These results suggest that MxA could be a potential additional histological marker to establish the diagnosis of lupus nephritis on the kidney biopsy. In contrast to the increased expression of MxA in LN, we found decreased numbers of pDCs. Therefore, it is important to investigate which other cells are the main producers of IFN-1 in further studies.

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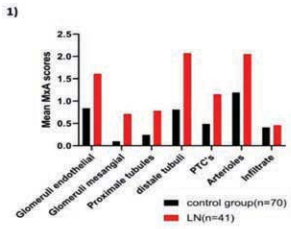

Figure 1.Bar graphs showing Mean MxA scores in lupus nephritis and control groups.

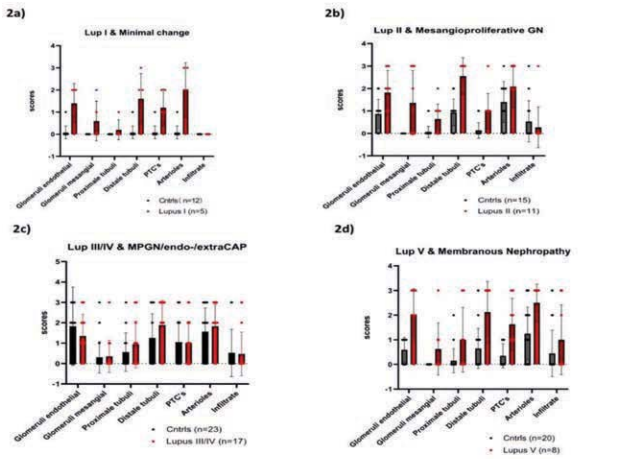

Figure 2.Bar graphs with dot plots of subgroups showing MxA scores by biopsy specimen. Error bar represents mean with SD. (2a) Comparison between type I lupus (n=5) and minimal change disease (n=12). (2b) Comparison between type II lupus (n=11) and mesangioproliferative nephritis (n=15). (2c) Comparison between type III/IV lupus(n=17) and extracapillary glomerulonephritis/endocapillary glomerulonephritis/membranoproliferative glomerulonephritis (MPGN) (n=23). (3d) Comparison between type V lupus (n=8) and membranous nephropathy (n=20).

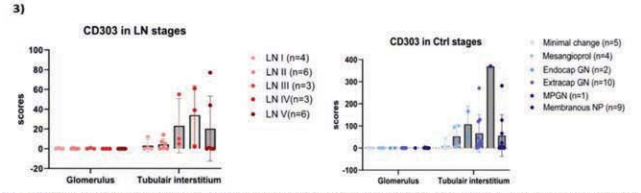

Figure 3.Bar graph showing CD303-positive pDCs in different lupus nephritis stages and control groups stages of glomerulus and tubular interstitium. Error bar represents mean with SD.

Disclosure of Interests: None declared

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POS0786

IDENTIFYING INDIVIDUALS AT RISK FOR SJÖGREN'S SYNDROME – THE PRE-SJÖGREN SYNDROME TARGETED IMMUNOLOGY EVALUATION (PRESTIGE) STUDY

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Background: Primary Sjögren's Syndrome (pSS) is a chronic autoimmune disease. Symptoms range from sicca to systemic, potentially life-threatening organ damage. Little is known about the onset of the disease. Anti-Ro antibodies are described to develop years before the first symptoms. In addition, first degree relatives of pSS patients have an 11- to 19- fold increased risk of developing pSS themselves.

Objectives: To identify and follow-up individuals at risk for pSS in order to study symptoms and immune pathology before and at development of pSS.

Methods: In this ongoing long-term study individuals at risk for developing pSS but not fulfilling the ACR-EULAR classification criteria of pSS were included, defined as: 1.) Anti-SSA positive individuals (Anti-SSA$^+$) without any sicca symptoms or diagnosis of an underlying systemic autoimmune disease; 2.) First degree relatives of patients (relatives) with an established diagnosis of pSS and typical autoantibodies (ANA ≥ 1:160 and/or anti-SSA$^+$ and/or rheumatoid factor$^+$); 3.) Individuals with at least one feature of the ACR-EULAR classification criteria for pSS, but not fulfilling the criteria (incomplete). At baseline and at annual visits, demographic data, blood, saliva and urine samples were collected and stored. Salivary and lacrimal flow, salivary gland ultrasonography (SGUS), and patient-related outcome measures were analysed. A lip salivary gland biopsy was performed at baseline and upon development of symptoms suggestive of pSS. The primary endpoint was the development of definite pSS according to the ACR-EULAR classification criteria.

Results: After the first year of recruitment, 50 individuals (Anti-SSA$^+$ n=27, relatives n=21, incomplete n=2) were screened at baseline, of whom 28 were identified as individuals at risk for pSS and were included in the study. Twenty-two individuals were excluded from the study, most of whom were "relatives" with negative autoantibodies. Of these 28 individuals at risk, 89% were female (n=25), they had a median age of 53 years (IQR: 19) and 57% (n=16) had positive antinuclear antibodies. 86 percent were positive for anti-SSA and 14% were positive for anti-SSB. Decreased complement C3 and C4 were found in 18% and 4%, respectively. Serum IgG concentration was elevated in 29% of individuals. A reduction of lacrimal flow was found in 29% and stimulated whole salivary flow was reduced in 29%. The median of the ESSPRI was 1.6 (3.0). Eight-teen percent of the investigated individuals had a pathological ultrasound [Hocevar score median 4,5 (9,0)] and in 9% a focus score ≥ 1 [median 0.15 (0.57)] was found in the lip salivary gland biopsies. Four patients (14%) met the primary endpoint and were diagnosed with pSS within the first year.

Conclusion: The design of the PRESTIGE study allows us to follow individuals at risk for pSS and will help to unveil symptoms and immune pathology as pSS develops. We suggest to establish a larger international pre-pSS cohort to increase statistical power.

Disclosure of Interests: None declared

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POS0787

THE EFFECT OF ANTI-RIBOSOMAL-P AND ANTI-NR2 ANTIBODIES ON FUNCTIONAL BRAIN MRI NETWORKS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH DEPRESSION AND BEHAVIORAL COGNITIVE DISORDERS.

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Background: Cognitive dysfunction (CD) and mood disorders (MD) are among the most frequent neuropsychiatric (NP) events in Systemic Lupus Erythematosus (SLE), but their pathogenesis has not been clarified yet. Until now, an unquestionable correlation between the presence of specific autoantibodies, brain alterations and the presence of CDs and MDs in SLE is lacking.

Objectives: The primary aim of the study was to explore the effects of anti-NR2 (anti-DWEYS) and anti-ribosomal-P (anti-P) antibodies on CDs and MDs and their relation with functional brain connectivity in patients affected by SLE.

Methods: A cross-sectional study was conducted, between April 2019 and February 2020, including adult patients who fulfilled the ACR/EULAR 2019 SLE criteria. Demographics, ongoing medications, SLEDAI and SLICC/Damage Index were recorded. Serum level quantification for anti-P (normal values <18 U/ml) and anti-NR2 (normal values <0.5 OD) antibodies were performed using an ELISA. A battery of neuropsychological testing was interpreted by a neuropsychologist, exploring cognitive domains, depression and quality of life. A resting-state functional connectivity (rs-fc) MRI analysis was performed within 2 weeks since the neuropsychological status assessments. Two region

of interest to region of interest (ROI-to-ROI) analyses with the graph theory was performed.

Results: Thirty-three SLE patients (9% male) were enrolled, mean age 43.5 (+-14) years, and median disease duration of 10.4 years (IQR 2.9-25.4) (Table 1). Anti-P were positive (range 0-255 U/ml) in 6 patients (18.2%) and anti-DWEYS (range 0-1.8 OD) in 14 (42.4%). Nineteen out of 33 patients (57.6%) showed at least a cognitive test alteration, but no significant association with antibodies was found. Depression was found in 14 (42.4%) patients using the Center for Epidemiologic Studies Depression Scale (CES-D) as screening instrument. In multiple regression backward models, after correction for age, disease duration, SLEDAI and SDI, the CES-D showed an independent association with anti-P titre (β= 0.32 per U/ml; p=0.049) and prednisone daily dose (β=0.38 per mg/day; p=0.023). The rs-fc MRI analysis revealed a statistically significant association between the titre of anti-P and many altered properties of the brain ROIs (Figure 1), but no effects of PDN daily dose on specific cerebral networks.

Table 1. Demographic and clinical characteristics of the patients in total, Legend: PDN: Prednisone; LLDAS: Lupus Low Disease Activity State; OD: Optical density

Demographic and clinical characteristics of the participants	(N=33)
Age, years mean (DS)	43.5 (14.0)
Gender (M, %)	3 (9%)
Disease duration, months median (IQR)	124.4 (34.7-305)
SLEDAI-2k mediane (IQR)	4 (0-14)
Dose PDN mg/daily median (IQR)	6.4 (3.8-13.5)
LLDAS N, %	12 (36,4%)
SLICC-DI mediane (IQR)	0 (0-1)
Ongoing treatment	25 (75.8%)
Hydroxychloroquine	30 (90.9%)
Immunosuppressive	9 (27.3%)
Biologics	
Education less than 8 years	13 (39.4%)
Anti-Rib-P N, %	6 (18.2%)
Anti-Rib-P (U/ml) mean (DS)	10.9 (5.7-13.3)
Anti-DWEYS N, %	14 (42.4%)
Anti-DWEYS (OD) mean (DS)	0.4 (0.25-0.67)
Anti-phospholipids N, %	11 (33.3%)
anti-dsDNA N, %	18 (54.5%)
anti-dsDNA Titre mediane (IQR)	22.5 (2.9-74.5)

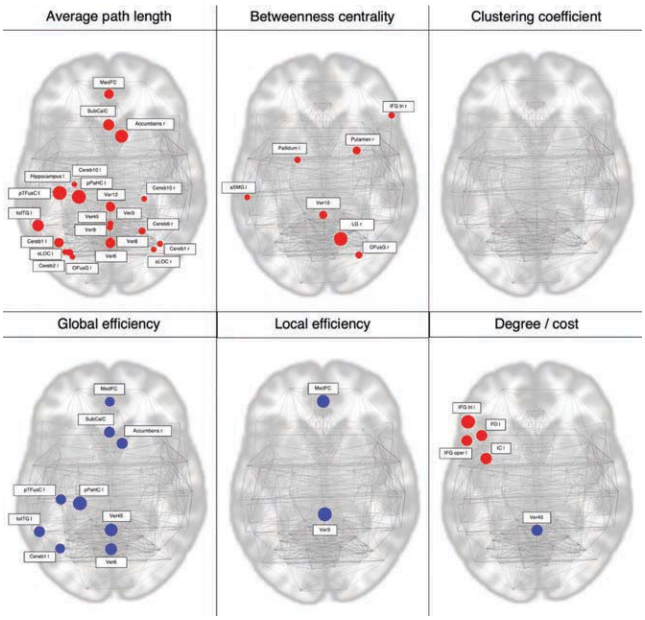

Figure 1. Results of rs-fc MR Analysis 1 (effects of Anti-rib-P titre) on cerebral networks. The regions with decreased and increased property are shown in blue and red nodes, respectively (p< 0.01). The node size represents the significance of the between-group differences in the nodal degree.

Conclusion: Anti-P antibodies are associated with depressive symptoms and changes of brain network properties in SLE patients, which add knowledge on their pathogenetic effect.

Disclosure of Interests: None declared

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POS0788

DISTINCT CYTOKINE/CHEMOKINE PROFILE IN SJÖGREN'S SYNDROME IS ASSOCIATED WITH DISEASE ACTIVITY AND CLINICAL MANIFESTIONS

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Background: Sjögren's syndrome (SjS) is an autoimmune disease of unknown aetiology. Several cytokines, chemokines and collagenases have been implicated in the pathogenesis of the disease. Nonetheless, biomarkers of diagnosis, outcome and response to treatment are still lacking.

Objectives: We aimed at evaluating potentially pathogenic cytokines/chemokines in a monocentric cohort of SjS patients.

Methods: Sera were drawn from SjS patients classified according to 2016 ACR/EULAR criteria and 23 cytokines/chemokines (CCL2/MCP-1, IP-10/CXCL10, Flt3 Ligand, IFNa2, IL6, IL7, IL12, IL13, IL15, IL17A, TNFa, IL-1Ra, CXCL13, IL21, IL23, IL33, TSLP, IL-2RA, IL1RII, TNFRII, BAFF, CCL19/MIP-3B 66, MMP-8) were quantified using Luminex multiplex immunoassay (BioRad- BioPlex 200 System-Luminex-Map technology R&D Systems, USA) following the manufacturer's instructions and customized procedures. Data were acquired using Bioplex manager v 6.1. P value ≤ 0.05 was considered significant. Data were analyzed using GraphPad Prism V.8 (GraphPad Software, Inc.) software.

Results: Clinical and demographic features of 21 SjS patients are reported in Table 1. Our main findings were that several cytokines positively correlated with indexes of disease activity. Particularly, we observed a correlation between IL-2RA and ESSDAI (r=0.602, P=0.005) and between IL-12p40 and ESSPRI (r=0.674, P=0.016) (Figure 1). Levels of IL-17A seem to be influenced by age (r=0.622, P=0.039) and showed a trend towards a positive correlation with labial salivary gland biopsy focus score (r=0.942, P=0.058). The only patient with cryoglobulins was the male who showed levels of BAFF/BLyS >20x higher than the remaining 20 females (43.4 ng/ml vs 1.8±1.6 ng/ml).

Table 1.

	N	%
Sex	1M/20F	4.8/95.2
Age (years, mean±SD)	53.43±12.27	
disease duration (months, mean±SD)	30.29±10.47	
ESSDAI (mean±SD)	2.20±2.40	
ESSPRI (mean±SD)	4.18±2.12	
Global dryness VAS (0-10) (mean±SD)	5.00±2.32	
VAS fatigue (0-10) mean±SD)	4.00±2.39	
VAS pain (0-10) (mean± SD)	3.48±3.28	
Dry mouth	15	71.40
Dry eyes	17	81
Parotid Gland Swelling	4	19
Articular involvement	6	28 .6
Skin Involvement	1	4.7
Raynaud's Phenomenon	5	23.8
Other Organs	3	14.3
Lymphoma	1	4.7
Low Complement (C3 Or C4)	3	14.3
Low C3	3	14.3
Low C4	1	4.7
Leukopenia	7	33.3
Hypergammaglobulinemia	7	61.9
Monoclonal Gammopathy	2	10
Ana	19	90.5
Anti-SSA	19	90.5
Anti-SSB	10	47.6
Rheumatoid Factor	9	42.9
Cryoglobulins	1	4.7
Salivary Gland Biopsy Focus Score (Mean±SD)	1.99±1.45	
Hydroxychloroquine	5	23.8
Immunosuppressant	1	4.7

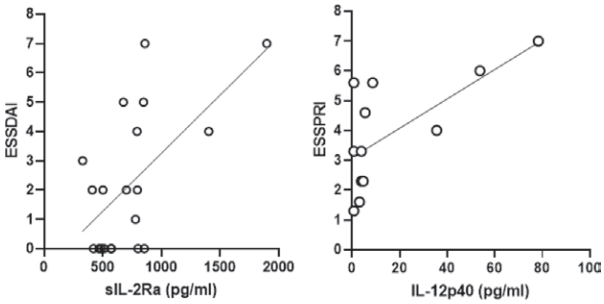

Figure 1.

Conclusion: For the first time we suggest the potential usefulness of IL-2RA as a marker of disease activity in SjS. Notably, IL2RA has been used as a marker to identify CD4+FoxP3+ regulatory T cells. So far, it is known that T follicular helper (Tfh) cell differentiation is inhibited by IL-2 while regulatory T cell differentiation and survival depend on it. Nonetheless, Wing et al. (1) described a CD25- subpopulation within human PD1+CXCR5+Foxp3+ Tfh cells preferentially located in germinal centers which is reduced by the presence of IL-2, possibly explaining the association with disease activity. IL-12p40 is known to have a pathogenic role in SjS (2) and we suggest that it may represent a complementary tool in the evaluation of patients' symptoms. The presence of high levels of IL-15 in SjS is not novel and associated with T cell migration and proliferation in germinal centers. Finally, the observation of very high BAFF/BLyS levels in the male with cryoglobulins will require further analysis.

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POS0789 CLINICAL FEATURES OF SJÖGREN'S SYNDROME WITH AND WITHOUT NEUROLOGICAL INVOLVEMENT (NEURO-SJÖGREN)

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Background: Sjögren's Syndrome is well known for its characteristic sicca symptoms due to autoinflammatory destruction of the salivary and lacrymal glands, but neurological involvement is also common in this entity. Nevertheless, previously published smaller studies suggested distinct clinical features for Sjögren's syndrome with and without neurological involvement, such as a more balanced gender distribution and lower IgG levels in patients with Sjögren' syndrome and neurological involvement[1,2].

Objectives: We therefore aimed to systematically assess clinical features of patients with Sjögren's syndrome with and without neurological involvement, find relevant in-between group differences and hereby aid early detection of both patient groups in the clinical routine to facilitate further studies, potentially with new therapeutic approaches.

Methods: We retrospectively assessed patients with Sjögren's syndrome treated at the neurological and rheumatological/ immunological departement of our university hospital between 05/2014 and 09/2021 for available laboratory and clinical data. The displayed data represent preliminary results of this ongoing study.

Results: 405 patients, who fulfilled the current ACR/EULAR classification criteria for Sjögren's syndrome[3] were currently included in the study (median age 59years [IQR 50-70 years], median ESSDAI 10 [IQR 3-16]). 228 patients (56%) showed neurological involvement. They were significantly more often male (32% vs. 14%; p<0.001) and showed lower IgG serum levels (median 11 g/l [IQR 9-13 g/l] vs 12 g/l [IQR 10-16 g/l], p<0.01) in comparison to patients with Sjögren's syndrome but without neurological involvement. However, presence of objective xerostomia, objective xerophthalmia, SSA(Ro)-antibody-positivity or sialadenits grade 3 or 4 (Chisholm and Mason) on salivary gland biopsy did not differ between the two groups.

Conclusion: Preliminary analysis of this ongoing study supports the hypothesis, that patients with Sjögren's syndrome and neurological impairment might express a distinct clinical phenotype in comparison to patients with Sjögren's syndrome but without neurological involvement.

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POS0790 18F-FLUORODEOXYGLUCOSE (FDG) PET-CT IMAGING OF SALIVARY GLANDS IN PRIMARY SJÖGREN'S SYNDROME AND ITS CORRELATION WITH ULTRASONOGRAPHIC SCORES AND SALIVARY FLOW RATE COMPARED TO HEALTHY CONTROLS

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Background: The use of salivary gland imaging modalities in patients with primary Sjögren's syndrome (pSS) has been increasing recently. The contribution of each imaging method in terms of diagnosis or disease activity differs from each other. Although ultrasound and MRI are the most commonly used imaging modalities, the role of PET-CT for diagnosing pSS and determining glandular and extraglandular involvement has largely been neglected.

Objectives: This study aimed to compare the sizes and metabolic activities of the major salivary glands in patients with pSS and healthy controls (HC). Correlation of the ^{18}F-FDG PET-CT uptake characteristics with ultrasound scores and salivary flow rates of the patients and HC was also determined.

Methods: 22 patients with pSS and 10 age/sex-matched HC were included in the study. The sizes and FDG uptakes of the parotid and submandibular glands of pSS patients and HC were assessed by PET-CT. The maximum standardized uptake value (SUVmax) was evaluated for FDG uptakes, and each patient's liver uptake and salivary gland uptake ratio were calculated. In addition, correlations of gland sizes and FDG uptakes in PET-CT with OMERACT and Hocevar ultrasound scores, stimulated and unstimulated SFR, ESSPRI dryness scores and disease durations of pSS patients were calculated by Spearman test.

Results: The mean age (SD) of the patients was 58.6 years (10.5) versus 58.6 years (19.1) of HC; the mean (SD) disease duration was 8.96 (8.77) years. ANA was positive in all patients, anti-SSA positivity was present in 82.6%, and 30.4% of patients experienced ≥1 parotid swelling episode. Compared to HCs, the mean size of both submandibular glands (p=0.006 for left and p=0.032 for right) and SUVmax of the left submandibular gland (p=0.044) were significantly smaller in patients with pSS. In pSS patients, both right and left parotid sizes were smaller and SUVmax uptake was greater than in HC; these differences however did not reach statistical significance. When the PET-CT involvement characteristics of the patients were compared with the salivary gland ultrasonography scores, there was a statistically significant negative correlation between the left parotid gland size in PET-CT and the ultrasonographic inhomogeneity of Hocevar score and OMERACT score. There was a statistically significant negative correlation between right parotid gland size measured on PET-CT with ultrasonographic inhomogeneity, hyperechoic foci, parenchymal echogenicity, Hocevar total score, and OMERACT score. No statistically significant correlation was found between SUVmax scores detected by PET-CT and ultrasound scores in both parotid glands and submandibular glands. A statistically significant positive correlation was found between the total gland size measured in PET-CT and the unstimulated salivary flow rate (p=0.038, r=0.604). There was a negative correlation between total gland size and ESSPRI dryness scores and symptom duration, which did not reach statistical significance.

Conclusion: PET-CT SUVmax measurements do not provide sufficient information for pSS-related involvement of the major salivary glands. Secondly, size measurement of the parotid glands by PET-CT is associated with OMERACT ultrasound scores, and also the sizes of both submandibular and parotid glands are smaller than HC.

Table 1. Correlations of gland sizes and ultrasonographic scores

Gland			Parenchymal			Hiperechoic			
							Visibility		
Size		OMERACT			Hypoechoic		of Gland	Parenchymal	
(PET/CT)		Score	Echogenity	Homogeneity	Areas	Foci	Border	Inhomogenicity	Total
R-Parotis	**r**	-.699*	-.717*	-.704*	-0,598	-.656*	-0,368	-.758**	-.645*
	p	0,017	0,013	0,016	0,052	0,028	0,266	0,007	0,032
L-Parotis	**r**	-.699*	-.717*	-.704*	-0,598	-.656*	-0,368	-.758**	-0,482
	p	0,017	0,013	0,016	0,052	0,028	0,266	0,007	0,134
R-Subm	**r**	-0,011	0.118	-0,011	-0,270	0,203	-0,006	0,247	0.024
	p	0,972	0.714	0,972	0,397	0,526	0,986	0,439	0.942
L-Subm	**r**	0,245	0,306	0,245	0,071	0,327	0,118	0,306	0,435
	p	0,443	0,333	0,443	0,826	0,300	0,714	0,333	0,158

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Vasculitis — large vessel vasculitis

POS0791 A NATIONWIDE STUDY OF OCULAR MANIFESTATIONS AMONG HOSPITALIZED PATIENTS WITH GIANT CELL ARTERITIS

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Background: Ocular manifestations are common among patients with giant cell arteritis (GCA). Most feared is a permanent visual impairment reported in up to 15-20% of GCA patients[1]. Estimates of ocular manifestations vary significantly between studies, and large, nationwide studies are currently lacking. In GCA, visual impairment has been associated with high and low inflammatory markers[2]. Also, low-dose aspirin treatment has been associated with a reduced risk of visual impairment in patients with GCA[3], but the evidence remains sparse.
Objectives: To investigate the risk of ocular manifestations among hospitalized patients with GCA. Furthermore, to investigate the association between inflammatory marker levels and low-dose aspirin treatment with the risk of ocular manifestations.
Methods: A Danish, nationwide, register-based cohort study including 14,574 incident GCA patients diagnosed between 1996 and 2018, and 145,740 general population referents, matched on age, sex, and calendar time. Ocular manifestations were defined as retinal vascular occlusions, disorders of opticus, visual impairment, diplopia, and amaurosis fugax. We tabulated characteristics of the GCA and reference cohort at the time of diagnosis including ocular manifestations recorded within one year of the GCA diagnosis. Regression analyses for incident ocular manifestations were performed using a pseudo-observational approach with the index date defined as the date of the GCA diagnosis. Cumulative incidence proportions (CIPs) and relative risks (RRs) of incident ocular manifestations with 95% confidence intervals (CIs) were calculated with death as a competing risk.
Results: Within one year of the diagnosis, 1,026/14,574 (7%) of GCA patients were registered with ocular manifestations with 392/1,026 (38%) being prior to and 634/1,026 (62%) after the GCA diagnosis, and 744/1,026 (73%) were registered within one month of the diagnosis. A total of 336/1,026 (33%) were retinal vascular occlusions, 300/1,026 (29%) disorders of the opticus nerve, 177/1,026 (17%) visual impairment, 90/1,026 (9%) diplopia, and 123/1,026 (12%) amaurosis fugax. The CIP of ocular manifestations among GCA patients was 4.0% (95% CI: 3.6-4.3), 4.2% (95% CI: 3.9-4.6), and 4.6% (95% CI: 4.2-4.9) after 3, 6, and 12 months following the diagnosis with a 1-year RR of 28.0 (95% CI: 24.0-32.7) compared to the general population. Age above 70 years, male sex, and a positive temporal artery biopsy were associated with an increased 1-year RR of incident ocular manifestations. Neither treatment with low-dose aspirin nor baseline CRP nor ESR levels was related to the risk of ocular manifestations.
Conclusion: In GCA, most cases of ocular manifestations occur at the time of diagnosis with over one-third of cases occurring prior to the diagnosis, emphasizing the need for early recognition and treatment. Low-dose aspirin treatment was not associated with a reduced risk of ocular manifestations among patients with GCA.
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POS0792 PULMONARY ARTERY INVOLVEMENT IN BEHCET'S DISEASE: SINGLE CENTER RESULTS

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Background: Behcet's disease (BD) is a multisystem inflammatory vasculitis. Skin, mucosa, eye, vascular area, joint, gastrointestinal system and central nervous system involvement is observed.
Objectives: In this study, we aimed to present the data of patients with pulmonary artery involvement (PAI) followed up with the diagnosis of BD.
Methods: The clinical, demographic and laboratory data of 394 patients with the diagnosis of BD, who were followed up in our rheumatology outpatient clinic between 2000 and 2020, were evaluated retrospectively.
Results: Of the patients followed up with the diagnosis of BD, 44% were female and 56% were male. Oral aphthous ulcers were found in 96%, genital ulcers in 65%, papulopustular lesions in 33%, erythema nodosum in 38%, and pathergy positivity in 47% of the patients. PAI was detected in 3% (n:13) of the patients who were followed up with a diagnosis of BD. 69% of the patients who had PAI were male, and their mean diagnosis age was 27±9, disease duration was 10±4.7 years. Pulmonary artery aneurysm was observed in 62%, pulmonary artery thrombosis (PAT) was observed in 85%, and both conditions were observed in 46% of the patients. Oral aphthous ulcer were found in all patients, genital ulcers in 70%, papulopustular lesions in 23%, pathergy positivity in 39%, and erythema nodosum in 23%. One of the patients with PAI had hereditary thrombophilia and also lower extremity deep vein thrombosis (DVT). Cardiac involvement was in the form of intracardiac thrombus in patients with PAI. Patients with and without PAI were compared in terms of clinical findings. A significant difference was observed in terms of DVT in the lower extremity, venous and cardiac involvement. The relationship between PAI and these involvements was also shown in the regression analysis (Table 1).

Table 1. Comparison of data of patients with and without pulmonary artery involvement

	Pulmonary Artery Involvement (+)	Pulmonary Artery Involvement (-)		
N (%)	N=13	N=381	P	OR (%95 CI)*
Gender Female	4(30)	168(44)	0.341	
Male	13(70)	213(56)		
Family History	2(15)	46(12)	0.664	
Oral Aphthous Ulcer	13(100)	366(96)	1	
Genital Ulcer	9(70)	247(65)	1	
Papulopustular lesion	3(23)	126(33)	0.559	
Erythema Nodosum	3(23)	147(39)	0.385	
Pathergy positivity	5(39)	180(47)	0.738	
Uveitis	-	138(36)	NA	
Retinal Vasculitis	-	11(3)	NA	
Arthritis	1(8)	97(26)	0.200	
Venous Involvement	8(62)	68(18)	***0.001***	7.365(2.33-23.20)
Lower Extremity Deep Venous Thrombosis	6(46)	46(12)	***0.003***	6.24(2.01-19.38)
Peripheral Artery Aneurysm	-	5(1)	NA	
GIS involvement	-	17(5)	NA	
Cardiac involvement	3(23)	4(1)	***0.001***	38.27(5.57-143.25)
Cranial Involvement	-	24(6)	NA	

*Significant data in logistic regression analysis were presented, GIS: Gastrointestinal system

Cranial involvement was not detected in any of our patients with PAI. In subgroup analysis, a significant relationship was observed between PAT and intracardiac thrombus (p=0.001 OR:21.05 95%CI 3.4-130) and lower extremity DVT (p=0.001 OR: 8.79 95%CI 2.58-29.96).
Conclusion: PAI is rare but the most important involvement affecting mortality in BD patients. Recently, there has been an increase in the incidence of isolated PAT with the contribution of the developments in imaging methods.[1] PAI is associated with lower extremity DVT, cerebral venous thrombosis and intracardiac thrombus.[2] In our study, a significant correlation was found between PAI and the presence of venous involvement, lower extremity DVT and intracardiac thrombus.
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POS0793 IMPROVED RELAPSE-FREE SURVIVAL WITH THE NORWICH PREDNISOLONE REGIMEN FOR GIANT CELL ARTERITIS

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Background: Glucocorticoid therapy is the mainstay treatment for GCA. There is no consensus on the dose of prednisolone to be used. Prednisolone regimens used in clinical trials have reported relapse rates of 66 to 92%. The long-term follow-up of Tocilizumab and prednisolone for 1-year showed a relapse rate of 74% at 2 years. The Norwich Regimen is a bespoke prednisolone plan with an initial dose of 1mg/kg of lean body mass. It delivers 164.64 mg/kg of lean body mass in a logarithmic taper over 100 weeks. It was devised to reduce the risk of relapse and allow patients to be in control of their prednisolone reduction.
Objectives: To document drug-free survival at 150 weeks of people with GCA treated with a bespoke prednisolone taper
Methods: All patients were diagnosed by biopsy, ultrasonography or PET scan and provided with a printed prednisolone plan at diagnosis. All individuals were assessed at approximately 3-6 monthly intervals in addition to suspected relapse, toxicity or other need for course correction. Relapses were confirmed objectively using a modification of the Kerr criteria. Relapse free survival was recorded at 100 weeks. Patients were given an open invite to contact us in the event of a suspected relapse after coming off prednisolone. A notes review was done to record events at 150 weeks.
Results: 150 consecutive people with objectively diagnosed GCA (mean age 74) since 10/01/2012 have completed 150 weeks since starting prednisolone. Drug-free, relapse-free survival at 100 weeks was met by 133/150 (89%). 7 individuals died and 20 relapsed. A further 5 died and 15 relapsed by week 150; 103/150 (69%) survivors were in prednisolone-free remission. Of the 12 deaths – 6 died of cancer, 1 subdural haemorrhage, 1 ischaemic bowel, 1 septicaemia, 1 general decline (aged 93). The cause of death was not available for 2 individuals who died in the community. The median time to relapse for the 35 individuals was 80 weeks (IQR 64,109).
Conclusion: We report the first results of a bespoke prednisolone taper to be used in real life. The Norwich Regimen for the treatment of GCA results in drug-free relapse-free survival of 89% at 100 weeks and 69% at 150 weeks, which is superior to all other reports published so far.
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POS0794

PREGNANCY AND CHILDBIRTH IN TAKAYASU ARTERITIS IN JAPAN – A NATIONWIDE RETROSPECTIVE STUDY

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Background: Takayasu arteritis (TAK), a granulomatous large vessel vasculitis, mainly involves the aorta and its proximal branches and commonly occurs in young females. However, studies of pregnancy in women with TAK are sparse and limited, probably due to the rarity of the disease.
Objectives: The purpose of this study was to understand the status quo of medical treatments of the primary disease and outcomes of pregnancy in patients with TAK, and birth outcomes of the children in Japan.
Methods: Patients with TAK who conceived after the onset of the disease and were managed at medical facilities participating in the Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS) were retrospectively enrolled in this study. The following information was collected from patients who had a live-born baby: age at diagnosis of TAK, disease classification, age at delivery, treatments before and during pregnancy, complications during pregnancy, birth outcomes of the children, and changes in disease activity during pregnancy and after delivery.
Results: Fifty-one cases and 69 pregnancies from 19 ethics committee-approved centers were enrolled during the study period 2019–2021. Of these, 49 cases and 66 pregnancies (95.7%) resulted in delivery and live-born babies. The Numano classification of the 49 cases was as follows: type I, 11; type IIa, 15; type IIb,12; type III, 1; type IV, 1; type V, 9; with type IIa being the most common. The age of diagnosis was 22 years (13–37 years, year of diagnosis 1965–2017), the median age of the delivery of 66 pregnancies was 31 years (year of delivery 1969-2021), and the median duration of illness at delivery was nine years. There were 34 planned pregnancies (51.5%, including four pregnancies by artificial insemination/ovulation induction). Preconception therapy included prednisolone (PSL) in 51 pregnancies (77.3%, median dose 7.5 mg (range 4–30 mg)/day), immunosuppressive drugs in 18 pregnancies (27.3%, azathioprine 8, tacrolimus 7, methotrexate 4, cyclosporin A 1, and colchicine 1), biologics in 12 pregnancies (18.1%, infliximab 6, tocilizumab 5, and adalimumab 1), antihypertensive drugs in 5 pregnancies (7.6%). Surgical treatment had been performed before pregnancy in 6 cases (aortic root replacement 2, subclavian artery dilatation 1, subclavian artery bypass 1, subclavian artery stenting 1, and ascending aorta semicircular artery replacement 1). Medications used during the course of pregnancy included PSL in 48 pregnancies (72.7%, median dose 8 mg (range 4–30 mg)/day, increased in 13 pregnancies, decreased in 1 pregnancy), immunosuppressants in 13 pregnancies (19.7%, azathioprine 6, tacrolimus 6, and cyclosporin A 1), biologics 9 pregnancies (13.6%, infliximab 4, tocilizumab 4, and adalimumab 1). Immunosuppressants and biologics were discontinued in five and four pregnancies after conception. Complications during pregnancy were observed in 20 pregnancies (30.3%), with hypertension being the most common. Complications related to TAK or its treatment were severe infections in two pregnancies and aneurysm enlargement due to increased circulating plasma volume in one pregnancy. Aortic arch replacement was performed after delivery for the latter case. Relapse of TAK was observed in 4 pregnancies (6.1%) during pregnancy and in 8 pregnancies (12.1%) after delivery. One pregnancy resulted in restenosis of subclavian artery for which dilatation procedure was performed prior to the pregnancy. There were 13/66 (19.7%)

preterm infants and 17/59 (28.8%) low birth weight infants; all but one had a birth weight of more than 2,000 g and no had serious postnatal abnormalities. Forty-three (82.7%) of the 52 confirmed infants were breastfeed fully or mixed.
Conclusion: Most of the pregnancies in patients with TAK were successfully delivered while they had low disease activity at a dose of less than 10 mg/day of PSL. Relapse occurred during pregnancy and after delivery in some cases. The babies tended to have low birth weight, but 82.7% of them were breastfed without serious complications.
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POS0795 EPIDEMIOLOGY, DIAGNOSIS AND CLINICAL CHARACTERISTICS OF GIANT CELL ARTERITIS IN PATIENTS INCLUDED IN THE ARTESER MULTICENTER STUDY

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Background: Epidemiological information on Giant Cell Arteritis (GCA) comes mainly from the Scandinavian countries of northern Europe, which show a higher incidence than the countries of southern Europe. GCA clinical manifestations can be divided into cranial, extracranial, and general syndrome.
Objectives: In a large series of GCA from Spain, we studied **a)** the incidence of GCA, **b)** clinical manifestations, and **c)** comorbidities at the time of disease diagnosis.
Methods: ARTESER is a retrospective epidemiological observational study of GCA promoted by the Spanish Society of Rheumatology in which 26 hospitals participate. The inclusion criteria were: all new patients diagnosed with GCA by a) ACR criteria, b) positive diagnostic test (temporal artery biopsy, temporal artery ultrasound or other relevant imaging techniques) and/or c) investigator's clinical judgment. The patient recruitment period ranged from June 1, 2013 to March 29, 2019. The overall incidence of GCA per 100,000 people ≥50 years for the whole period and the mean annual incidence were evaluated. The clinical variables were collected by reviewing the patient's medical history.
Results: 1675 patients were included. The average annual incidence rate was 7.42 (95% CI: 6.57-8.27). All the cases were older than 50 years, and the age group with the highest annual incidence was that of 80 to 84 years, where it reached a value of 22.63 (95% CI: 22.04 -23.22). The mean annual incidence is higher in women than in men 10.07 (95% CI: 8.74-11.55) vs 4.81 (95% CI 3.84-5.93) (Table 1).

Table 1. General characteristics, comorbidities and clinical manifestations

Epidemiologic, demographic and diagnosis	Men	Women	Total
Gender, n (%)	497 (29.7)	1178 (70.3)	1675
Incidence annual rate (95% CI)	4.81 (3.84-5.93)	10.07 (8.74-11.55)	7.42 (6.57-8.27)
Age at diagnosis, years, mean (SD)	76.9 (8.3)	76.9 (8.0)	76.9 (8.1)
Diagnosis only by ACR Criteria	89 (17.91)	266 (22.58)	355 (21.19)
Diagnosis only with objective tests	73 (14.69)	140 (11.88)	213 (12.72)
Diagnosis ACR criteria + diagnosis objective tests	311 (62.58)	734 (62.31)	1045 (62.39)
Diagnosis by clinical judgment	24 (4.8)	38 (3.2)	62 (3.7)
Comorbidities at diagnosis			
Arterial hypertension, n (%)	330 (66.8)	749 (63.7)	1079 (64.6)
Dyslipidemia, n (%)	238 (48.3)	563 (47.9)	801 (48.0)
Cranial clinical manifestations			
New-onset headache, n (%)	382 (76.9)	955 (81.1)	1337 (79.9)
Visual Clinic, n (%)	194 (39.0)	411 (34.9)	605 (36.1)
Extracranial manifestations and general syndrome			
Polymyalgia rheumatica, n (%)	178 (35.8)	521 (44.3)	699 (41.8)
Asthenia, n (%)	239 (48.1)	634 (53.9)	873 (52.2)
Analysis at diagnosis			
Erythrocyte sedimentation rate mm/h, mean (SD)	72.3 (34.7)	77.4 (33.0)	75.9 (33.6)

The principal clinical characteristics of the population is shown in Table 1, the mean age at diagnosis was 76.9±8.1 years, 1178 (70.3%) were women. 1045 patients (62.39%) had ACR criteria and some positive objective test, 355 patients (21.9%) presented only ACR criteria and 213 (12.72%) only had a positive diagnostic test; 62 (3.7%) of the patients underwent diagnosis based on clinical judgment. The more frequent comorbidity was arterial hypertension (n=1079; 64.6%),

followed by dyslipidemia (n=801, 48%). The predominant cranial manifestation was headache (n= 1337; 79.9%) and 605 patients experienced visual symptoms (36.1%). Polymyalgia rheumatica (n=699; 41.8%) and asthenia (n=837; 52.2%) were the most frequent extracranial and general syndrome manifestation, respectively. Regarding laboratory parameters, the most characteristic data was the increase of ESR (75.9±33.6 mm/1st h).

Conclusion: The mean annual incidence of GCA in Spain, 7.42 (95% CI: 6.57-8.27), is lower than that of the Scandinavian countries. It is higher in people older than 80 years. More than 60% of the patients met the ACR criteria and had a positive diagnostic test. Cranial manifestations constituted the most clinical features. The most frequent clinical manifestations are cranial. Up to a third of patients had visual manifestations.

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POS0796 TREATMENT, ADVERSE EVENTS AND FOLLOW UP IN PATIENTS WITH GIANT CELL ARTERITIS IN THE ARTESER MULTICENTER STUDY

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Background: Glucocorticoids (GC) are the mainstay therapy in Giant Cell Arteritis (GCA), initially at high doses (40-60 mg/day) followed by gradual glucocorticoid tapering. This treatment, especially in older patients, is associated with numerous adverse effects (AE). In addition, there are frequent relapses. Therefore, conventional synthetic immunosuppressants such as methotrexate (MTX), leflunomide, azathioprine, cyclophosphamide or mycophenolate, have been used with controversial results. Studies with biological immunosuppressants, such as TNFi have been ineffective; in contrast, tocilizumab (TCZ) has obtained positive results and was approved for the treatment of GCA.

Objectives: In the ARTESER study we describe **a)** treatment with GC, synthetic or biological immunosuppressants; **b)** AE of CG; and **c)** evolution.

Methods: ARTESER is a retrospective observational study sponsored by the Spanish Society of Rheumatology. 26 Spanish centers participated and all new patients diagnosed with GCA from June 1, 2013 to March 29, 2019 were included. Data on GC and immunosuppressants were collected at the beginning and during the follow-up of GCA patients. For the calculation of the cumulative dose of GC, an application was developed that, by including the periods of time, dose and type of GC received during follow-up, performs the automatic calculation in mg of prednisone.

Results: Of the 1675 patients included, GC treatment was adequately recorded in 1650 patients (Table 1). All received oral treatment, being prednisone the most frequently drug used (N=1602, 97.09%). In addition, 426 (25.82%) patients received at least one iv pulse of methylprednisolone, being the 1000 mg regimen the most frequent (n=217; 50.9%). The total mean duration of GC treatment was 22.65 months. The mean cumulative dose per patient at the end of follow-up was 8514.98 mg of prednisone.

Table 1. Corticosteroid treatment and immunosuppressive treatment

Patients taking oral corticosteroid	1650
Prednisone, n (%)	1602 (97.09)
Methylprednisolone, n (%)	164 (9.94)
Deflazacort, n (%)	64 (3.88)
Patients receiving intravenous corticosteroid, n (%)	426 (25.82)
Mean duration of steroid treatment, mean (SD)	22.65 (17.36)
Mean cumulative dose at the end of follow-up per patient, mg of prednisone, mean (SD)	8514.98 (6570.21)
Methotrexate at diagnosis*, n (%)	165 (9.9)
Leflunomide at diagnosis*, n (%)	2 (0.1)
Azathioprine at diagnosis*, n (%)	3 (0.2)
Cyclophosphamide at diagnosis*, n (%)	7 (0.4)
Mycophenolate at diagnosis*, n (%)	1 (0.1)
Tocilizumab at diagnosis*, n (%)	22 (1.3)
Methotrexate during follow-up, n (%)	532 (31.8)
Leflunomide during follow-up, n (%)	19 (1.2)
Azathioprine during follow-up, n (%)	26 (1.5)
Cyclophosphamide during follow-up, n (%)	10 (0.6)
Mycophenolate during follow-up, n (%)	10 (0.6)
Tocilizumab during follow-up, n (%)	153 (9.1)

The most widely used immunosuppressant was MTX both at diagnosis (n=165; 9.9%) and during follow-up (n=532; 31.8%), followed by TCZ, at diagnosis (22; 1.3%) and at follow-up (153; 9.1%). AE with GC were described in 393 patients (23.8%), highlighting serious infections (n=67; 10.03%) followed by diabetes mellitus (n=63; 9.43%), steroid myopathy (n=53; 7.9%), vertebral fractures (n=47; 7.04%), non-vertebral fractures (n=36; 5.39%), heart failure (n=36; 5.39%), arterial hypertension (n=34; 5.09%) and neuropsychiatric alterations (n=27; 4.04%). During the follow-up, 334 (19.9%) patients had relapses, 532 (31.8%) were hospitalized on some occasion, and 142 patients (8.48%) died. The main cause of death were infections (n=44; 30.99%), neoplasms (n=23; 16.2%), cardiovascular (n=15; 10.56%), and cerebrovascular (n=10; 7.04%).

Conclusion: The main treatment for GCA was oral GC, which were required for almost two years on average, in a quarter of patients associated with IV pulses. The cumulative steroid dose was high as well as the side effects. MTX was the most widely used immunosuppressant and TCZ was prescribed in 10%. Relapses and admissions at the hospital were relatively frequent.

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POS0797 EFFICACY AND SAFETY OF TOFACITINIB VERSUS LEFLUNOMIDE TREATMENT IN TAKAYASU ARTERITIS: A PROSPECTIVE STUDY

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Background: Takayasu arteritis (TAK) is a rare large-vessel vasculitis characterized by vascular granulomatous inflammation. TA is more prevalent in young women aged less than 40 years old. It mainly involves aorta and its major branches. Those involved arteries can progress into stenosis and occlusion, which can lead to further ischaemia of the corresponding tissue and life-threatening events. Thus, effective treatment is in need to improve patients' prognosis. To date, glucocorticoids (GCs) and immunosuppressants remain as the first-line therapy for TAK patients. According to 2021 American College of Rheumatology/Vasculitis Foundation guideline, GCs and immunosuppressants such as methotrexate and azathioprine were recommended as initial therapy [1]. LEF functions as an inhibitor of pyrimidine synthesis. It has been widely used in a variety of autoimmune disease. In TAK treatment, by comparing LEF with methotrexate or cyclophosphamide, LEF showed its superiorities in remission induction, relapse prevention and good tolerance. Tofacitinib (TOF) is a JAK1/JAK3 signaling pathway inhibitor. In TAK, increasing evidence has suggested that JAK/STAT signaling pathway played an essential role in the pathogenesis of TAK [2]. More importantly, according to our recent study, TOF is superior to MTX for complete remission (CR) induction, relapse prevention and GC tapering. However, its efficacy needs further confirmation.

Objectives: Thus, this study aimed to compare the effectiveness and safety of TOF with another effective agent, LEF in patients with TAK.
Methods: A total of 67 active patients with TAK were recruited from an ongoing observational TAK cohort. Thirty-five patients were treated with GCs and LEF, and 32 patients were treated with GCs and TOF. The study period was 12 months. The primary endpoint was effectiveness rate (ER) at 6 months. The other aspects were also evaluated at 6 or 12 months, including remission rate and relapse rate, inflammatory parameters reduction, vascular imaging changes, GCs tapering, and side effects. The treatment effect was also evaluated separately among naive or refractory patients between two groups.
Results: After 6 months' treatment, no difference was observed in ER between two groups (LEF group: 31/35 (88.57%) vs. TOF group: 28/32 (87.50%), p=1.00). During 12 months' treatment, the relapse rate was also comparable between two groups (LEF group: 6 (17.14%) vs. TOF group 7 (21.88%), p=0.76,). ESR and CRP were decreased significantly at 6 (ESR: LEF group: p<0.0001; TOF group: p=0.15; CRP: LEF group: p=0.06; TOF group: p=0.007) and 12 months (ESR: LEF group: p<0.0001; TOF group: p=0.06; CRP: LEF group: p=0.006; TOF group: p=0.14) in both groups compared with their corresponding baseline levels. The proportion of patients with imaging improvement after 12 months' treatment were low in both groups (LEF group: 1 (2.86%) vs. TOF group: 3 (9.38%) p=0.17). After treatment, the doses of GCs were significantly reduced in both groups from the third month onwards compared with their corresponding baseline dose (p<0.05). Among patients with initial GCs dose ≥ 30mg/day, patients in TOF group gained a much lower daily GCs dose than that of LEF group at 9 months and 12 months (p<0.05). Furthermore, the frequency of side effects was higher in LEF group than that of TOF group (12/35, 34.29%, vs 3/32, 9.38%; p=0.02).
Conclusion: LEF and TOF have comparable treatment effects for patients with TAK. However, TOF is superior to LEF in GCs tapering and safety profile.
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POS0798 NUMANO TYPE IIB, INFLAMMATORY PROGRESSION OF DISEASE AND DILATION OF ASCENDING AORTA AND AORTIC ROOT ARE IMPORTANT RISK FACTORS CAUSING AORTIC VALVE INVOLVEMENT IN TA PATIENTS.

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Background: Takayasu arteritis (TA) can involve cardiac valves. In Chinese patients with TA, valvular abnormalities were found in 48.9% (201/411) patients[1,2]. Another research showed that cardiac valvular involvements were found in 34.9% (373/1069) TA patients in China[3], and in a recent study, they also found that 64.08% (66/103) of TA patients had valvular damage[4]. In addition, the most common valve involved in TA is the aortic valve, and the most common valvular lesion caused by TA is valvular insufficiency. The incidence of aortic regurgitation in patients with TA has been reported as 33.2% (455/1372) in Japan[5], 21.7% (13/60) in Italy[6], 18.1% (29/160) in Korea[7], and 20.4% (84/411)[1] to 39.8% (41/103)[4] in China. AR can further induce congestive heart failure or arrhythmia, both of which are considered one of the main causes of death in TA patients[8].
Objectives: Aortic valve involvement is not uncommon in patients with Takayasu arteritis (TA). The aim of our study was to evaluate the clinical characteristics of aortic valve involvement in TA patients, and to explore the risk factors of aortic valve involvement in TA.
Methods: In this retrospective study, 174 patients with TA were divided into groups with or without aortic valve involvement. We compared the clinical manifestations, laboratory parameters, and imaging results between the two groups. The logistic regression analysis was used to identify the risk factors of aortic valve involvement in TA patients.
Results: In our study, a total of 94 TA patients (54.02%) had aortic valvular lesion. The proportion of elevated ESR and elevated high-sensitivity CRP, and ITAS-A score in the aortic valve involvement group were significantly higher than in the non-aortic valve involvement group. 2 patients were found to have the infiltration of Inflammatory cells in surgical specimens of the aortic valve. The Numano type IIb and elevated hs-CRP level were found to be statistically related to aortic valvular lesion in TA patients (6.853 [1.685-27.875], p=0.007; 4.896 [1.646-14.561], p=0.004). Dilation of the ascending aorta and aortic root were significantly associated with aortic valvular involvement in TA patients (4.509 [1.517-13.403], p=0.007; 9.340 [2.188-39.875], p=0.003).
Conclusion: The Numano type IIb, elevated hs-CRP level, dilation of the ascending aorta and aortic root are risk factors for aortic valve involvement in TA patients.
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POS0799 BIOMARKER CHANGES IN TAKAYASU ARTERITIS AFTER TOFACITINIB TREATMENT AND THE MOLECULAR SIGNATURE ASSOCIATED WITH DISEASE CHARACTERISTICS

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Background: Takayasu's arteritis (TAK) is a chronic, non-specific, granulomatous macrovasculitis and its pathogenesis is still unclear. The increasing evidence indicated that multiple pathological process involved in the development of TAK. According to previous reports, multiple biomarkers representative different pathological process (1-3), However, which biomarker can closely reflect disease activity or vascular changes and whether these abnormal processes can be prevented by current therapies remained unknown.
Objectives: To analyze changes of serum cytokine, chemokine, and growth factor profiles in patients with Takayasu arteritis (TAK) after tofacitinib treatment and explore potential molecular signatures related with various disease characteristics
Methods: Seventeen patients from a TAK cohort treated with tofacitinib and 12 healthy controls were recruited in this study. Potential biomarkers with TAK including cytokines, MMPs, chemokines and growth factors were detected in these patients (0, 6, 12 months) and healthy controls. Molecular changes, disease activity, disease remission, and vascular imaging changes were analyzed in these patients after treatment. Furthermore, molecule signatures associated with these clinical features/outcomes were explored via radar plot and correlation analysis.
Results: At baseline, all the patients were in active status. Meanwhile, patients' cytokines (PTX3, IL-6, IFN-γ), chemokines (IL-16, CCL22, CCL2), growth factor (VEGF) and MMP9 were significantly higher than those of healthy controls (all p<0.05), while FGF-2 was significantly lower in patients with TAK (p=0.02). After treatment, 94.12% of patients achieved complete remission at 6 and 12 months; patients' ESR and CRP levels were significantly reduced at 6 months (p=0.02, p=0.046 respectively); vascular improvement were observed in 6 (35.29%) patients at 12 months. With regards to these molecules, IL-10 was increased at 6 months compared with its baseline level (p=0.007). No changes were observed in other cytokines, chemokines, or growth factors. Besides, the radar plot demonstrated that PTX3 was closely correlated with disease activity. In addition, patients with vascular imaging improvement had relatively higher baseline levels of TNFα, ESR, and CRP (p=0.04, p=0.056, p=0.07, respectively), lower CCL22, FGF, and PDGF-AB levels (p=0.056, p=0.06 and p=0.08 respectively) compared with patients without it.
Conclusion: Multiple molecules representative different pathological mechanism participated in the pathogenesis of TAK. PTX3 was a prominent marker for disease activity, and CCL22 may have a predictive value for vascular imaging changes.
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POS0800 THE JOINT VASCULITIS REGISTRY IN GERMAN-SPEAKING COUNTRIES (GEVAS) – SUBGROUP ANALYSIS OF 131 GCA-PATIENTS REFERENCES:

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Background: The most frequent form of vasculitis in elderly people is giant cell arteritis (GCA) with an annual incidence rate less than 10 per 100,000 persons over the age of 50. Like most vasculitides, GCA is characterized by chronicity and relapses, leading to significant overall morbidity and higher mortality in a subset of patients with aortic involvement and dissection. Most studies carried out so far have been retrospective, used monocentric study designs and small patient cohorts. Therefore, the Joint Vasculitis Registry in German-speaking countries (GeVas) has been established to record patients, who have been recently diagnosed with vasculitis or who have changed their treatment due to a relapse (inception cohort). The GeVas-Registry allows a long-term follow-up of a substantial cohort of vasculitis patients in a prospective and multicenter manner.
Objectives: To describe the subgroup of GCA and its characteristics within the GeVas registry.
Methods: GeVas is a prospective, web-based, multicenter, clinician-driven registry for the documentation of organ manifestations, damage, long-term outcomes, and therapy regimens in various types of vasculitis. Recruitment started in June 2019. By January 2022, 17 centers in Germany were initiated and have begun enrolling patients. Meanwhile, more than 350 patients have been documented in the registry. Sites in Austria and the German-speaking cantons of Switzerland will be integrated soon (1).
Results: By mid-October 2021, the participating centers recruited 131 GCA patients into the registry. 21.7% of patients (n=28) were enrolled in the registry due to relapse, and 78.3% (n=101) due to a first-time diagnosis. In accordance with long-standing epidemiology data, the majority of patients (67,2%), were female (n=88), and 32.8% (n=43) were male. Mean age was 74 years (max. 92y, min. 52y). The most frequently recorded organ manifestations in GCA patients addressed cranial and ophthalmic symptoms, and the cardiovascular system. However, vascular lung/chest involvement was also observed in 3% of cases (n=4). Out of the 131 patients, 97.7% (n=128) received immunosuppressive therapy, three refused to take any medication. An equal number of patients were treated with glucocorticoid (GC) therapy. While about two equal parts were treated by stable long term oral GC therapy (47,7%, n=62) or by i.v. pulse therapy followed by tapering (49,2%, n=64), only about 2.3% (n=3) were treated by oral GC therapy with intermittent i.v. pulses. 48.5% (n=63) of patients received tocilizumab as additional immunosuppressive therapy, 19.2% (n=25) methotrexate, and 18.5% (n=24) cyclophosphamide i.v. pulses.
Conclusion: In June 2019, we successfully established the prospective multicenter vasculitis registry GeVAS. It describes the first systematically recorded prospective GCA cohort in German-speaking countries. Its characteristics correspond to those that can be expected from the literature, with some unexpected finding e.g. the high proportion of patients treated with cyclosphosphamid, probably reflecting a sicker patient population with e.g. aortic or central nervous involvement. After 2.5 years of follow-up documentation, the first long-term results will be systematically evaluated and interpreted. The newly acquired data on disease manifestation, diagnostics and therapy regimens will provide important insights into the treatment of GCA patients in Germany and may generate further research goals.
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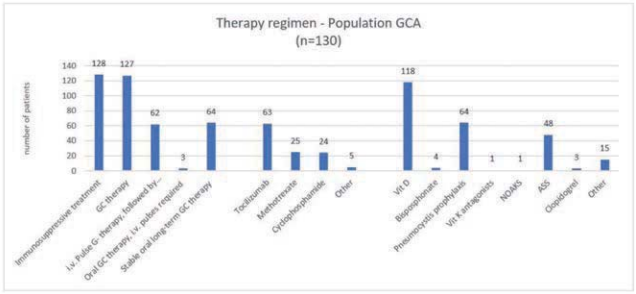

Figure 2 Immunosuppressive Treatment of GCA patients (n=131), 19.10.2021

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POS0801 VISUAL INVOLVEMENT AND PERMANENT VISUAL LOSS IN GIANT CELL ARTERITIS: PREDICTIVE FACTORS

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Background: Visual involvement is the most feared complication of Giant Cell Arteritis (GCA) **(1-5)**. Permanent visual loss (PVL) may be preceded by transient visual loss. Once blindness is established, the prognosis is poor. Most of the series of predictive factors of visual involvement in GCA are old and with a small number of patients.

Objectives: To assess the predictive factors of visual involvement and PVL in GCA.

Methods: Multicenter observational study of 471 patients with GCA. The diagnosis of GCA was performed between 2016 and 2021 according to: **a)** ACR criteria, and/or **b)** temporal artery biopsy, and/or **c)** imaging techniques.

From the 471 patients, we selected patients who developed **a)** visual involvement at any time during GCA and **b)** PVL. PVL was defined as partial or complete visual loss of >24 hours. Predictive factors were identified by multivariate analysis.

Results: Visual involvement was observed in 122 cases and PVL in 60 (Table 1). The ischemic and systemic manifestations set of variables associated with visual involvement were headache, and jaw claudication, whereas large-vessel involvement was a protective variable (Figure 1). The area under the curve (AUC) for the model was 0.72 (95%CI 0.67-0.77; p<0.0001).

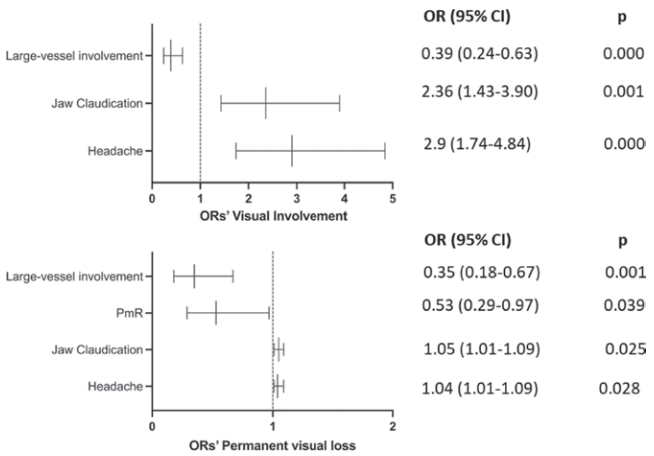

Figure 1. Forest plot of multivariate analysis.

In the same line, the set of variables associated with PVL were headache, and jaw claudication. By contrast, polymyalgia rheumatica (PmR), and large-vessel involvement were protective factors (Figure 1). The AUC for this model was 0.77 (95%CI 0.71-0.83; p<0.0001).

Conclusion: Headache, and jaw claudication seem to be associated with visual involvement in GCA, while large vessel involvement seems to be a protective factor. PmR also appears to be a protective factor for the development of PVL.

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POS0802 INVOLVEMENT OF THE AORTA AND/OR ITS MAIN BRANCHES IN GIANT CELL ARTERITIS. TREATMENT WITH TOCILIZUMAB

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Table 1. Main features of the patients

	Overall (n= 471)	GCA without visual involvement (n=349)	GCA with visual involvement (n= 122)	GCA with PVL (n=60)	P visual vs non visual involvement	P PVL vs non visual involvement
Age at diagnosis of GCA (mean±SD)	72±9	71±9	75±8	75±9	**0.001**	**0.001**
Female/Male (% of female)	342/129 (73)	265/84 (76)	77/45 (63)	41/19 (68)	**0.006**	0.21
Positive TAB, n (%)	201 (43)	146 (42)	55 (45)	33 (55)	0.53	0.34
Cardiovascular risk factors						
High blood pressure, n (%)	272 (58)	189 (54)	83 (68)	40 (67)	**0.013**	0.058
Dyslipidemia, n (%)	241 (51)	175 (50)	66 (54)	32 (53)	0.61	0.63
Diabetes, n (%)	81 (17)	50 (14)	31 (25)	16 (27)	**0.007**	**0.016**
Previous or current smoking history, n (%)	47 (10)	31 (9)	16 (13)	8 (13)	0.21	0.27
CHADS2 score, median [IQR]	1 [1-2]	1 [0-2]	2 [1-2]	2 [1-2]	**0.001**	**0.004**
Ischemic manifestations						
Headache, n (%)	259 (55)	167 (48)	92 (75)	42 (70)	**0.000**	**0.002**
Jaw claudication, n (%)	112 (24)	63 (18)	49 (40)	26 (43)	**0.000**	**0.000**
Systemic manifestations						
Fever, n (%)	57 (12)	47 (13)	10 (8)	4 (7)	0.12	0.20
Constitutional syndrome, n (%)	175 (37)	132 (38)	43 (35)	20 (33)	0.55	0.47
PmR, n (%)	284 (60)	218 (62)	66 (54)	29 (48)	0.094	**0.022**
Large-vessel involvement, n (%)	254 (54)	211 (60)	43 (35)	20 (33)	**0.000**	**0.000**
ESR, mm/1st hour, median [IQR]	32 [12-57]	30 [11-54]	34 [15-67]	42 [12-67]	0.22	0.28
CRP (mg/dL), median [IQR]	1.5 [0.5-3.4]	1.4 [0.5-3.0]	1.5 [0.4-4.7]	1.5 [0.4-3.6]	0.042	0.30

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Background: Large vessel involvement in Giant Cell Arteritis (GCA), especially the aorta and/or its main branches, is frequent. Tocilizumab (TCZ) has shown efficacy and safety in GCA and other large-vessel vasculitis **(1-4)**.
Objectives: To assess the efficacy and safety of TCZ in GCA patients with involvement of the aorta and/or its main branches.
Methods: Multicenter observational study of 196 patients with GCA and involvement of the aorta and/or its major branches treated with TCZ. GCA was diagnosed by: **a)** ACR criteria, and/or **b)** temporal artery biopsy, and/or **c)** imaging techniques. The presence of aortitis was performed by imaging techniques, mainly PET, and A-MRI.
Maintained remission was considered according to EULAR definitions **(5)**.
Results: The main features of the 196 patients are showed in Table 1. Polymyalgia rheumatica, constitutional syndrome and headache were the most frequent clinical manifestations at TCZ onset. At 6 months after starting TCZ, 20% of the patients reached a sustained remission, that was progressively increasing. (Figure 1**).** A corticosteroid-sparing effect was observed from month 1 of TCZ onset (Figure 1). Relevant adverse events were observed in 12 per 100 patients-year, documenting serious infections in 4.8 per 100 patients-year (Table 1).

Table 1. Main features of 196 GCA patients with involvement of the aorta and/or its main branches treated with TCZ.

	GCA (n=196)
Features at TCZ onset	
Age(years), mean±SD	71.3±9.5
Sex, female/male (% female)	148/48 (75)
Time from GCA diagnosis to TCZ onset (months), median [IQR]	7 [2-18.25]
Systemic manifestations, n (%)	
Fever, n (%)	24 (12)
Constitutional syndrome, n (%)	87 (44)
PmR, n (%)	131 (67)
Ischaemic manifestations, n (%)	
Visual involvement, n (%)	16 (8)
Headache, n (%)	74 (38)
Jaw claudication, n (%)	27 (14)
Laboratory data	
ESR, mm 1st hour, median [IQR]	32 [14-54]
CRP, mg/dL, median [IQR]	1.5 [0.6-3.2]
Prednisone dose, mg/day, median [IQR]	15 [10-30]
Safety after TCZ onset	
Relevant adverse events, per 100 patients-year	12
Serious infections, per 100 patients-year	4.8

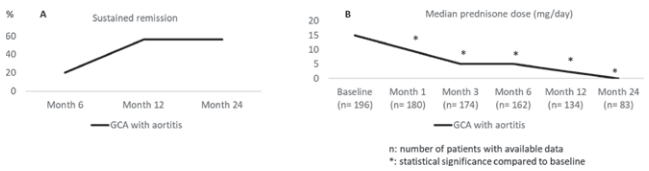

Figure 1. A) Sustained remission, and **B)** median prednisone dose required in GCA patients with aortitis treated with tocilizumab

Conclusion: TCZ seems to be effective and relatively safe in GCA patients with involvement of the aorta and/or its main branches.
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Disclosure of Interests: Lara Sanchez-Bilbao: None declared, Javier Loricera Speakers bureau: from Roche, Novartis, UCB Pharma, Celgene, and Grünenthal., Rafael Melero: None declared, Santos Castañeda Speakers bureau: UAM-Roche, EPID- Future chair, Department of Medicine, Universidad Autónoma de Madrid, Madrid, Spain., Clara Moriano: None declared, Iván Ferraz-Amaro: None declared, J. Narváez: None declared, Vicente Aldasoro: None declared, Olga Maiz: None declared, Ignacio Villa-Blanco: None declared, Paloma Vela-Casasempere: None declared, Susana Romero-Yuste: None declared, Jose Luis Callejas-Rubio: None declared, Eugenio de Miguel: None declared, E. Galíndez-Agirregoikoa: None declared, Francisca Sivera: None declared, Carlos Fernández-López: None declared, Carles Galisteo: None declared, Julio Sanchez-Martin: None declared, Monica Calderón-Goercke: None declared, J. Luis Hernández: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene, and MSD., Grant/research support from: AbbVie, MSD, Jansen, and Roche,, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Lilly, Janssen, and MSD., Grant/research support from: Abbvie, MSD, and Roche
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POS0803 INCREASED RISK OF MALIGNANCY IN PATIENTS WITH TAKAYASU'S ARTERITIS: A POPULATION-BASED COHORT STUDY IN KOREA

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Background: Recent studies have identified neoplasms as the second most common cause of death in patients with Takayasu's arteritis (TAK) [1,2]. Various autoimmune diseases are related to the increased rates of malignancies. Despite conflicting data, most studies concluded that there is no increase in the risk of malignancies in giant cell arteritis [3]. In the case of TAK, there have been few reports of malignancies [4]. However, only one study compared the risk of malignancies in TAK to that of the general population [5]. Because the previous study only included 180 patients with TAK from single center, no definite conclusion could be drawn. Here, we evaluated the relative risk of malignancies in patients with TAK and compared them with the general population using the medical insurance data of South Korea.
Objectives: This study aimed to evaluate the relative risk of malignancy in patients with TAK compared to that in the general population.
Methods: This retrospective nationwide cohort study used data from the Korean Health Insurance Review and Assessment Service database. All newly diagnosed patients with Takayasu's arteritis were identified between January 2009 and December 2019. They were observed until the diagnosis of malignancy, death, or end of the observational period, December 2020. The occurrence of malignancy was regarded as the first claim under ICD-10 codes, including C00–97, D46, and D47.1, according to the incidence of malignancy classification published by the National Cancer Registry (NCR). The incidence of malignancy in the general population was retrieved from the 2014 NCR, which collects the annual incidence of malignancies in the entire population of South Korea. The standardized incidence ratios (SIRs) of the overall and site-specific malignancies were estimated and compared with the incidence of cancer in the general population.
Results: We identified 1,449 newly diagnosed patients with Takayasu's arteritis during the observational period (9,196 person-years). A total of 74, 66, and 8 patients had overall, solid, and hematologic malignancies, respectively. The risks of overall (SIR, 1.62; 95% confidence interval [CI], 1.27–2.03), solid (SIR, 2.04; 95% CI, 1.56–2.61), and hematologic (SIR, 4.05; 95% CI, 3.72–7.98) malignancies were increased compared to those in the general population. In solid malignancies, breast (SIR, 2.07; 95% CI, 1.16–3.42), ovarian (SIR, 4.45; 95% CI, 1.21–11.39), and major salivary gland (SIR, 19.04; 95% CI, 2.31–68.76) cancers had an increased risk. In hematologic malignancies, the risk of myelodysplasia increased (SIR, 18.02; 95% CI, 3.72–52.66). Immunosuppressive agent use was not associated with malignancy. There was no specific period when cancer more frequently occurred.
Conclusion: An increased risk of malignancy was observed in patients with Takayasu's arteritis compared to that in the general population in this large-scale nationwide population study of Korean health insurance data.
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POS0804

TOCILIZUMAB IN LARGE-VESSEL GIANT CELL ARTERITIS AND TAKAYASU ARTERITIS: MULTICENTRIC OBSERVATIONAL COMPARATIVE STUDY

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Background: Tocilizumab (TCZ) has shown to be effective for large vessel vasculitis including giant cell arteritis (GCA) and Takayasu arteritis (TAK) **(1-5)**. However, LVV-GCA and TAK show different demographic and clinical features that may influence on TCZ therapeutic response.
Objectives: To compare the effectiveness of TCZ in patients with LVV-GCA and patients with TAK.

Methods: Observational multicenter study of patients with LVV-GCA and TAK who received TCZ. Outcome variables were: **a)** proportion of patients who achieved complete clinical improvement along with normalization of laboratory markers (CRP ≤0.5mg/dL and/or ESR ≤ 20 mm/1st hour) at 12 months **b)** complete improvement in imaging techniques. A comparative study between patients with LVV-GCA and TAK was performed.
Results: We evaluated 70 LVV-GCA and 57 TAK patients who received TCZ. Main clinical and demographic characteristic are described in Table 1. Patients with TAK were younger, had longer disease duration, had received more commonly previous biologic therapy and were receiving higher doses of prednisone at baseline. TCZ intravenous administration was more common in TAK patients (80.7% vs 48.6%; p<0.01). Follow-up time after TCZ onset was similar in both groups. At 12 months, about 75% of patients achieved complete clinical improvement and ESR/CRP normalization in both groups. A follow-up imaging technique was performed in 37 LVV-GCA patients after a mean time of 12.9±6.0 months and 38 TAK patients after 9.5±5.0 months. Complete improvement in imaging techniques was only observed in 18.9% and 21.1% of patients with LVV-GCA and TAK, respectively (Figure 1).

Table 1.

	LVV-GCA (n=70)	TAK (n=57)	p
General features			
Age (years), mean ± SD	67.2 ± 10.5	40.5 ± 16.3	**< 0.01**
Sex (female), n (%)	51 (72.9)	49 (86)	0.07
Disease evolution before TCZ onset (months), median [IQR]	5 [2-15]	12 [3-37]	**<0.01**
Baseline laboratory parameters			
ESR (mm/1st hour), median [IQR]	32 [12.5-54.7]	31 [10-52]	0.82
CRP (mg/dL), median [IQR]	1.4 [0.5-2.4]	1.4 [0.5-3.5]	0.41
Baseline prednisone dose (mg/day), median [IQR]	15 [10-20]	30 [15-50]	**< 0.01**
Previous therapy			
Conventional DMARDs, n(%)	45 (64.3)	44(77.2)	0.51
Biologic therapy, n (%)	0(0)	12 (21.1)	**<0.01**
TCZ therapy			
Intravenous, n (%)	34 (48.6)	46 (80.7)	**< 0.01**
Combined with MTX, n(%)	24 (34.3)	24 (42.1)	0.37
Follow-up time after TCZ onset, median [IQR]	20 [10-36]	18 [7-41]	0.73
Complete clinical improvement and ESR/CRP normalization at 12 months, n/N (%)	35/47 (74.4)	30/39 (76.9)	0.79
Complete improvement in imaging techniques, n/N(%)	7/37 (18.9)	8/38 (21.1)	0.85

CRP: C-reactive protein; DMARDs: Disease-modifying anti-rheumatic drugs ESR: erythrocyte sedimentation rate; GCA: giant cell arteritis; IQR: interquartile range; LVV: large vessel; MTX: methotrexate; n: Number of patients; N: total number of patients: TCZ: tocilizumab; TAK:takayasu

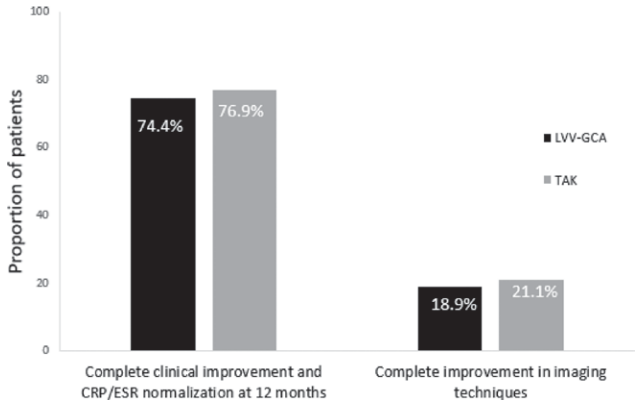

Figure 1.

Conclusion: The effectiveness of TCZ was similar in patients with LVV-GCA and TAK, despite a more refractory disease in TAK patients. A discordance between clinical and imaging activity improvement was observed in both LVV-GCA and TAK, as reported in previous studies **(3)**.

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POS0805

GLUCOCORTICOID-RELATED ADVERSE EVENTS IN GIANT CELL ARTERITIS: APPLICATION OF THE GLUCOCORTICOID TOXICITY INDEX IN A MONOCENTRIC COHORT OF 140 PATIENTS

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Background: Oral glucocorticoids (GC) are the mainstay of treatment for giant cell arteritis (GCA) but chronic exposure to GC is associated with serious comorbidities.
Objectives: The objective of this study was to determine the GC exposure and risk of GC-related adverse events (AEs) in GCA, validating the Glucocorticoid Toxicity Index (GTI) (1,2) in a cohort of real-world patients.
Methods: 140 consecutive patients with GCA were enrolled in this retrospective monocentric study. All patients were older than 50 years of age, met the 1990 ACR criteria for GCA and/or had the evidence of a large vessel vasculitis at FDG-PET/CT scan. Patients' clinical data were collected from clinical charts, calculating GC cumulative dose and GTI at baseline and in the following 5 years.
Results: 140 patients were enrolled in the study: median (IQR) age at diagnosis 74 (67-79), Female: 97 (69%), Male: 43 (31%). According to vascular involvement patients were classified in cranial-GCA (C-GCA, n:91), large vessel-GCA (LV-GCA, n:21) and cranial and large vessel-GCA (LV-C-GCA, n:28). Furthermore, 50 (36%) patients were treated with only GC, 44 (31%) with GC+methotrexate (MTX), 46 (33%) with GC+tocilizumab (in 20 cases TCZ was started in the first 3 months after diagnosis: early-TCZ, in 26 cases after 3 months for relapses or AEs: late-TCZ).
During the follow up, 57 (41%) patients presented at least one relapse. In the GC group 22 relapses in 18 patients were reported, in MTX group 33 relapses in 25 patients (with 15 relapses before and 18 after MTX start), in early-TCZ group no relapses were reported, in late-TCZ group 21 relapses in 14 patients (with 17 relapses before and 4 after TCZ start) were reported.
Median cumulative GC doses after 1 and 5 years were respectively 7.9 (6.3-9.8) gr and 16.5 (13.8-18.9) gr in GC group, 8.7 (5.9-10.0) gr and 16.5 (13.2-20.7) gr in MTX group, 7.1 (5.5-8.0) gr and 13.3 (12.8-13.7) gr in early-TCZ and 7.7 (6.2-11.1) gr and 19.7 (12.2-23.8) gr in late-TCZ. Eighty-eight percent of patients developed at least one GC-AE, with infections and hypertension being the most common reported AEs (42% e 44%, respectively). Median GTI-CWS (Cumulative Worsening Score) after 1 year was 65 (20-137) in GC, 63 (10-95) in MTX, 51 (33-116) in TCZ-early, 44 (0-91) in TCZ-late. Median GTI-CWS after 5 years was 219 (118-240) in GC, 137 (65-206) in MTX, 147 (146-147) in TCZ-early, 200 (121-231) in TCZ-late. A correlation between GTI-CWS and the GC cumulative dose was found (after 5 years r: 0.295, p: 0.026).
Conclusion: Chronic GC treatment is associated with a high risk of developing comorbidities. GTI score demonstrated to be an effective tool to assess GC-related AEs and proved to correlate with GC cumulative dose. TCZ confirmed its efficacy in reducing relapse rate, both in early and late-TCZ groups (3). TCZ showed for the first time in a real-life cohort a GC sparing effect, with a 19% reduction in GC cumulative dose and a 33% reduction in GTI-CWS in 5 years (comparing GC group *vs* early-TCZ group).
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POS0806

OPTIMIZATION OF TOCILIZUMAB THERAPY IN GIANT CELL ARTERITIS. A MULTICENTER REAL-LIFE STUDY OF 471 PATIENTS.

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Background: Tocilizumab (TCZ) has shown to be useful in the treatment of large-vessel vasculitis, including giant cell arteritis (GCA) **(1-4)**. There is general agreement on the initial and the standard maintenance dose of TCZ. However, information on duration and optimization of TCZ in GCA is really scarce.
Objectives: Our aim was to assess the effectiveness and safety of TCZ therapy optimization in an unselected wide series of GCA in real-world clinical practice.
Methods: Multicenter study on 471 patients with GCA who received TCZ therapy. Once complete remission was reached (n=231) TCZ was optimized in 125 patients. We compared patients in whom TCZ was optimized (TCZ_{OPT} group) or not ($TCZ_{NON-OPT}$ group). Complete remission was defined as normalization of clinical and analytical (CRP and ESR) data. Optimization was done by decreasing the dose and/or prolonging the TCZ dosing interval progressively. We performed a comparison in effectiveness and safety parameters between optimized and non-optimized patients.
Results: We evaluated 231 GCA patients treated with TCZ with complete remission. No demographic or laboratory data differences was observed at TCZ onset between both groups (Table 1). The mean prednisone dose was higher in the $TCZ_{NON-OPT}$ group at TCZ onset. The first TCZ optimization was performed after a median [25-75th] follow-up of 12 [6-17] months.

Table 1. Main general features at TCZ onset of 231 GCA patients with prolonged remission.

	OPTIMIZED-TCZ GROUP (n=125)	NON-OPTIMIZED TCZ GROUP (n=106)	p
GENERAL FEATURES			
Age, years, mean± SD	72.7±8.6	74±8.7	0.197
Sex, female/male n (% female)	91/34 (72.8)	74/32 (69.8)	0.616
Time from GCA diagnosis to TCZ onset (months), median [IQR]	8 [2-21.5]	5 [2-21]	0.384
SYSTEMIC MANIFESTATIONS			
Fever, n (%)	14 (11.2)	15 (14.2)	0.500
Constitutional syndrome, n (%)	54 (43.2)	39 (36.8)	0.322
PMR, n (%)	75 (60)	69 (65.1)	0.426
ISCHEMIC MANIFESTATIONS			
Visual involvement, n (%)	14 (11.2)	16 (15.1)	0.380
Headache, n (%)	66 (52.8)	62 (58.5)	0.386
Jaw claudication, n (%)	24 (19.2)	25 (23.6)	0.417
AORTITIS (large-vessel involvement), n (%)	65 (52)	42 (39.6)	0.060
ANALYTICAL FINDINGS			
ESR, mm/1st hour, mean (SD)	39.1±29.3	37.5±33.5	0.334
CRP, mg/dL mean (SD)	2.6± 3.4	2.7± 4	0.305
Hemoglobin, g/dL, mean (SD)	13.5±9.6	12.9±1.5	0.153
GLUCOCORTICOIDS			
Prednisone dose, mg/d mean (SD)	20.3±16.4	27±17.8	**0.001**

Abbreviations: CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GCA: giant cell arteritis; IQR: interquartile range; IV: intravenous; PMR: polymyalgia rheumatica; SC: subcutaneous; SD: standard deviation; TCZ: tocilizumab.

The median prednisone dose at first TCZ optimization was 2.5 [0-5] mg/day. At the end of follow-up prolonged remission was observed in 78.2% of TCZ_{OPT} group compared with 66.7% in the $TCZ_{NON-OPT}$ group (p= 0.001) (Figure 1). Seven (5.6%) of the 125 optimized cases relapsed. Serious adverse events were similar in both groups, while serious infections were more frequent in the $TCZ_{NON-OPT}$ group (p=0.009).
Conclusion: Once complete remission is reached in GCA patients under TCZ treatment, optimization of biologic may be performed. Based on our experience it could be performed by reducing the dose or by prolonging dosing interval of TCZ. It seems to be an effective and safe practice.

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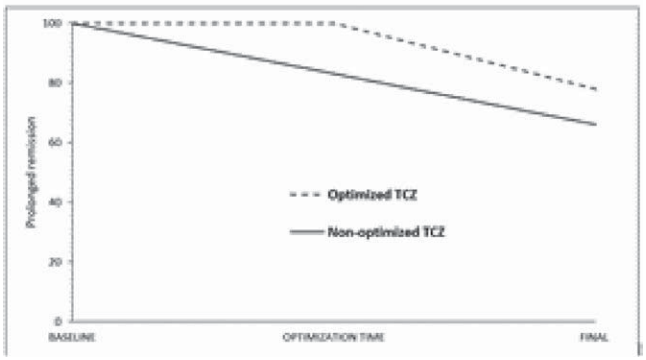
FIGURE. Mean prolonged remission.



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POS0807 EVALUATION OF DISEASE MANIFESTATIONS AND ADVERSE PREGNANCY OUTCOMES IN PREGNANCIES OF PATIENTS WITH BEHÇET'S SYNDROME

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Background: Behçet's Syndrome (BS) is a chronic, multisystemic inflammatory vasculitis with unknown etiology, generally diagnosed at reproductive age. Data related to disease manifestations and pregnancy outcomes are limited.
Objectives: To investigate disease manifestations during pregnancy and adverse pregnancy outcomes (APOs) in female patients with BS.
Methods: In this single centre study, 110 voluntary women who had long-term follow-ups in Ankara University Multidiciplinary Behçet outpatient clinic and their 323 pregnancies were evaluated. Patients were interviewed about their previous pregnancies. As 238 of 323 (73.6%) pregnancies were before BS diagnosis and additional 13 pregnancies were terminated due to family planning, we evaluated disease manifestations and APOs of 72 pregnancies. APOs were defined as spontaneus abortion, intrauterine exitus, stillbirth, premature rupture of membranes (PROM), intrauterine growth restriction/small for gestational age (IUGR/SGA), gestational diabetes mellitus (GDM), macrosomia, preeclampsia and eclampsia, arteriovenous thrombosis, congenital malformations and Rh incompatibility.
Results: A total of 30 APOs in 72 (41.7%) pregnancies was stated by participants (Table 1). There were not any statistical differences between groups in terms of gestational age and BS disease duration (p= 0.85 and p= 0.21). In 24 (33.3%) pregnancies, BS manifestations were exacerbated, genital ulcer being the most common (20.8%) followed by oral ulcers (15.3%), skin manifestations (8.3%), and both articular and skin manifestations (8.3%). Ocular flares did not occur during pregnancies whereas *de novo* venous thromboses and parenchymal neurological involvement were detected in 2 (2.8%) and 1 (1.4%).

Table 1. The characteristics of pregnancies with and without APOs

		Pregnancy without APOs (n=42, 58.3%)	Pregnancy with APOs (n= 30, 41.7%)	P value
Maternal characteristics	Gestational age, years mean (SD)	24.4 (5.6)	24.5 (5.9)	0.85
	Disease duration, years mean (SD)	6.5 (10.4)	7.9 (10.3)	0.21
APOs and other complications	Spontaneous abortion, n(%)		4 (13.3%)	
	Stilbirth, n(%)		1 (3.3%)	
	IUGR-SGA, n(%)		8 (26.7%)	
	Preeclampsia, n(%)		3 (10.0%)	
	PROM, n(%)		5 (16.7%)	
	Termination due to teratogens, n(%)		4 (13.3%)	
	Trombosis, n(%)		2 (6.7%)	
	GDM, n(%)		3 (10.0%)	
	Macrosomia, n(%)		4 (13.3%)	
	Rh incompatibility, n(%)		3 (10.0%)	
Drug use in pregnancy	Colchicine, n(%)	11 (26.1%)	8 (26.6%)	0.96
	Azathioprine n(%)		2 (6.7%)	
	Corticosteroids, n(%)		1 (3.3%)	
Neonatal outcomes	Median birth week, median (Q1-Q3)*	39.0 (38.0-40.0)	38.0 (33.5-39.0)	0.001
	Median birth weight, grams, median (Q1-Q3)**	3445.0 (3123.8-3600.0)	2850.0 (2500.0-3700.0)	0.038

SD=Standart Deviation*Calculations were done in 42 pregnancies of the group without APOs and in 26 pregnancies of the group with APOs**Calculations were done in 40 pregnancies of the group without APOs and in 21 pregnancies of the group with APOs

The effects of medications during pregnancies were also examined. There were 19 pregnancies, in which colchicine was continued. When the pregnancies were compared between continued and cessation groups, median birth weights at continued and cessation groups were 3450 (Q1-Q3: 3125-3450) grams and 3300 (Q1-Q3: 2900-3820) grams (p=0.42), respectively. There was not any statistical difference between median birth weeks of continued and cessation groups 38.0 (Q1-Q3: 38.0-39.0) weeks at continued group and 39.0 (Q1-Q3: 38.0-40.0) weeks at cessation group (p=0.18)).There were not any significant differences between two groups in terms of exacerbated manifestations of BS and APOs (p values were 0.90 and 0.96, respectively). Azathioprine was used in 2 (2.7%) pregnancies, which resulted in termination and spontaneous abortion.
Conclusion: In this study, we found that APOs occurred in almost half of BS patients and colchicine use seemed to be safe throughout pregnancy. Some BS manifestations exacerbated and even occurred *de novo* during pregnancies. Prospective studies are needed to reveal the effects of BS and drugs on pregnancy.
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POS0808 CHARACTERISTICS AND PROGNOSIS OF BINOCULAR DIPLOPIA IN PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a large vessel vasculitis associated with a risk of permanent ophthalmologic complications. Diplopia is an uncommon feature at GCA diagnosis and data about diplopia in GCA are scarce, especially regarding its prognosis.
Objectives: This study was designed to better characterize diplopia in newly diagnosed GCA patients.
Methods: All consecutive patients diagnosed with GCA between January 2015 and April 2021 in a French tertiary ophthalmologic center were retrospectively reviewed. GCA diagnosis relied on 1990 ACR criteria and either a positive temporal artery biopsy or high-definition MRI.
Results: Among 111 patients diagnosed with GCA in our tertiary eye-care center, 80 patients (72%) had visual signs, including 30 patients (27%) with binocular diplopia. Characteristics of patients with diplopia were similar to other GCA patients. Twenty-eight patients (93%) had cephalic symptoms (Headaches n = 25, scalp tenderness n = 14, jaw claudication n = 17) and 7 patients (23%) had associated polymyalgia rheumatica. All patients with diplopia had an elevated C-reactive protein compared with 91% of patients without diplopia (p = 0.06). Large vessel involvement was found in 4 patients (16%) with diplopia. Diplopia was attributed to cranial nerve palsy in 21/24 (88%) patients, especially third (50%) and sixth cranial nerve (48%) palsies. Median duration of diplopia before GCA diagnosis was 10 days (Inter-quartile

range [IQR]: 4-19). Eleven patients (37%) were diagnosed with ocular ischemic lesions, including 5 patients (17%) with bilateral visual impairment, resulting in a severe loss of vision in 9 patients and a resolution of binocular diplopia in all these patients due to unilateral or bilateral vision loss. Acute ischemic optic neuropathy (AION) was diagnosed in 11 eyes, central retinal artery occlusion (CRAO) in 4 eyes and paracentral acute middle maculopathy in 2 eyes. Diplopia resolved spontaneously in 6 patients (20%). In the remaining 13 patients, diplopia resolved after the initiation of corticosteroids in 12 patients (92%) with a median delay of 10 days (IQR: 5-24). IV corticosteroids seemed to be associated with a quicker improvement than oral corticosteroids (6 days [IQR 4-28] vs 11 days [IQR 6-13], p = 0.81) but with a similar resolution rate of diplopia at one month (66% vs 78 %, p = 1). Two patients had visual impairment after the initiation of corticosteroids and two patients had diplopia relapse during the course of GCA.

Conclusion: Diplopia is a rare but not exceptional feature at GCA diagnosis and should raise clinician suspicion for GCA when associated with cephalic symptoms and elevated inflammatory biomarkers. We confirmed in this study that patients with diplopia were also at risk of ischemic ocular lesions, particularly AION and CRAO, with a subsequent risk of severe loss of vision. In patients without visual impairment, the prognosis of diplopia is good after initiation of treatment with a complete resolution in most patients at one month but with a potential risk of diplopia recurrence in case of GCA relapse.

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POS0809 CHARACTERIZATION OF RELAPSES IN PATIENTS WITH GIANT CELL ARTERITIS (GCA) PATIENTS- DATA FROM THE REAL-LIFE TREATMENT AND SAFETY (REATS)-GCA COHORT

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Background: Giant cell arteritis (GCA) has the tendency to relapse once treatment is tapered or stopped. Such relapses represent a potential threat to GCA patients as they can lead to severe symptoms and organ damage.

Objectives: To assess the frequency and type of relapses in patients with GCA

Methods: The Real-Life Treatment and Safety (REATS)-GCA cohort has been established by extracting the data on clinical presentation, inflammatory markers, imaging, comorbidities, treatments and serious adverse events of GCA patients from 6 specialized centres in Germany. We undertook descriptive and survival analyses (Kaplan-Meier), and compared baseline characteristics of participants with vs. without relapse. Ethical approval for the cohort was obtained.

Results: We included 395 patients with a mean age of 71 years, including 264 (66.8 %) females and 129 (32.7%) males. Diagnosis of GCA was supported by temporal artery ultrasound in 37%, ^{18}F-FDG-PET/CT in 29%, temporal artery biopsy in 14% of patients and by MRI or clinically in the remaining patients. 31% of patients presented with an isolated cranial manifestation and 18% with isolated extracranial manifestations. Most common presenting symptoms were headache (57%), fatigue (55%), weight loss (42%) and polymyalgia (38%) (Table 1). The most common comorbidities at the time of study inclusion were arterial hypertension (68%), followed by osteoporosis (26%). Within a median total follow-up duration of 22.2 (11.7-40.6) months, 97 of the 395 patients relapsed including 15 patients who relapsed more than once. The median (IQR) time to first relapse was 12.5 (7.1-21.8) months. Median relapse-free survival was 7.8 years with a relapse risk of 12% (CI, 9 to 15%) at 1 year and 38% (CI, 30 to 45%) at 5 years (Figure 1). Most common symptoms at relapse were headache (35%), polymyalgia (23%), fatigue (19%) and night sweats (12%) (Table 1). Three patients relapsed with sudden loss of vision. Among the 114 relapses observed, 94 (83%) occurred under prednisolone treatment with a median dose of 7.0 mg/day (IQR 4.0-12.5). 26 (23%) occurred under methotrexate and 14 (12%) under tocilizumab treatment. Comparing the baseline characteristics that were documented in this study, we did not find a statistically significant difference in relapsing versus non-relapsing GCA patients.

Table 1.

Symptom at disease onset	N=395 (%)	Symptom at relapse	N=97 (%)
Headache	216 (54.7)	Headache	35 (30.7)
Fatigue	208 (52.7)	Polymyalgia (PMR)	23 (20.2)
Weight loss	159 (40.3)	Fatigue	19 (16.7)
Polymyalgia (PMR)	144 (36.5)	Vision impairment	13 (11.4)
Night sweats	140 (35.4)	Night sweats	12 (10.5)
Headache in the temple area	125 (31.6)	Headache in the temple area	12 (10.5)
Jaw pain	121 (30.6)	Jaw pain	11 (9.6)
Vision impairment	118 (29.9)	Morning stiffness	7 (6.1)
Morning stiffness	89 (22.5)	Weight loss	7 (6.1)
Fever	80 (20.3)	Claudication upper limb	6 (5.3)
Swelling temporal arteries	77 (19.5)	Arthralgia	6 (5.3)
Vision loss	57 (14.4)	Claudication lower limb	5 (4.4)
Scalp tenderness	38 (9.6)	Vision loss	3 (2.6)
Claudication upper limb	38 (9.6)	Arthritis	3 (2.6)
Claudication lower limb	34 (8.6)	Scalp tenderness	2 (1.8)
Arthralgia	28 (7.1)	Fever	2 (1.8)
Arthritis	3 (0.8)	Swelling temporal arteries	2 (1.8)

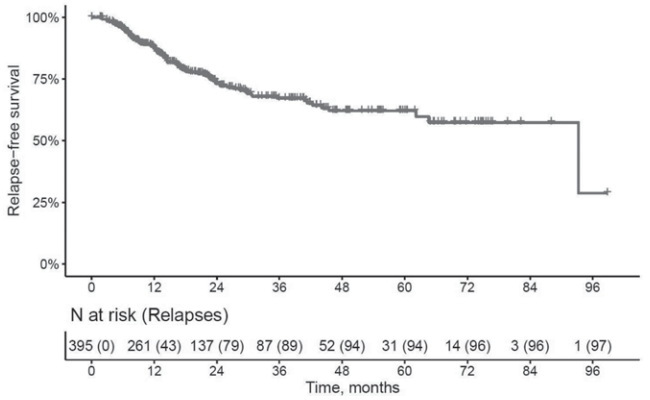

Figure 1.

Conclusion: About one fourth of GCA patients relapsed and the overwhelming majority of relapses occurred before patients were able to stop glucocorticoids. The leading symptoms at relapse are headache and fatigue, while loss of vision is rare (0.76%). Baseline characteristics seem to be poorly informative about the risk of relapse, therefore regular monitoring of GCA patients is necessary.

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POS0810 FREQUENCY OF VISUAL MANIFESTATIONS IN GIANT CELL ARTERITIS IN NORFOLK

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Background: The ophthalmic features of giant cell arteritis (GCA) involve a spectrum of severity from transient symptoms to bilateral visual loss from anterior ischaemic optic neuropathy or less commonly central retinal or cilioretinal artery occlusion. Reported ocular involvement varies between 10-70%.[1,2]. At the Norfolk and Norwich University Hospital an interdisciplinary fast track service is provided for potential GCA patients. This report aims provides a complete picture of the frequency and nature of ocular involvement in GCA.

Objectives: 350 records of consecutive patients diagnosed objectively with GCA based on biopsy or imaging were reviewed. In our centre, the hospital pathway mandates all suspected GCA cases to have a formal ophthalmology assessment

including visual acuity, pupil exam and full-dilated fundus assessment. Systemic and Ophthalmic symptoms and signs were recorded.

Methods: From January 2012 to September 2021, 350 individuals were diagnosed with GCA by biopsy, ultrasonography or positron emission tomography. The mean age was 74 ± 7.7 years. 235 (67%) of patients were females. 101 (29%) presenting with GCA had visual symptoms and/or signs. 42 of them had mono-ocular and 5 had binocular loss of vision. A summary of the key visual symptoms and signs are shown in Table 1. Only 6 patients with visual symptoms did not have any symptoms commonly associated with GCA.

Table 1. Visual Symptoms and Signs (N=350 patients)

Visual Symptoms	101
Blurred Vision	36
Loss of vision	47
Double Vision	27
Ocular Signs	
Right CRAO[1]	1
Left CRAO[1]	10
Right AION[2]	19
Left AION[2]	23
Right extraocular muscle weakness	6
Left extraocular muscle weakness	4

[1] Central retinal artery occlusion [2] Anterior ischaemic optic neuropathy

Results: From January 2012 to September 2021, 350 individuals were diagnosed with GCA by biopsy, ultrasonography or positron emission tomography. The mean age was 74 ± 7.7 years. 235 (67%) of patients were females. 101 (29%) presenting with GCA had visual symptoms and/or signs. 42 of them had mono-ocular and 5 had binocular loss of vision. A summary of the key visual symptoms and signs are shown in Table 1. Only 6 patients with visual symptoms did not have any extra-ocular symptoms commonly associated with GCA.

Conclusion: We report the frequency of visual involvement in one of the largest cohorts of individuals with GCA. 29% have ocular symptoms. Partial or total field loss occurred in 13% of cases. 2% of patients presented with visual manifestations as the only feature of GCA. Rarely, permanent visual loss may occur without any other manifestation of GCA.

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POS0811 CHARACTERISTICS OF INTESTINAL MICROBIOTA AND ITS RELATIONSHIP WITH LYMPHOCYTE SUBSETS AND CYTOKINES IN PATIENTS WITH VASCULITIS

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Background: Vasculitis include a group of autoimmune inflammatory diseases with clinical heterogeneous characterized by inflammation of vascular wall, inflammation of perivascular tissues, and cell-like necrosis[1]. Disorder of gut microbiota, which plays a crucial role in regulating immune cells such as Th1, Th17 and Treg, is associated with other autoimmune diseases[2], and may also be involved in the pathogenesis of vasculitis.

Objectives: To investigate the changes of intestinal microbiota and its correlation with peripheral lymphocyte subsets and inflammatory factors levels in patients with vasculitis.

Methods: Combined with clinical manifestations and laboratory examination, 33 patients with vasculitis who met the 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides[3] and 33 of age- and gender- matched healthy controls (HCs) were selected from the Second Hospital of Shanxi Medical University. The demographic characteristics, general laboratory indicators such as erythrocyte sedimentation rate (ESR), C-reaction protein (CRP), levels of peripheral lymphocyte subpopulations and serum cytokines detected by modified flow cytometry. Fecal microbiota detected by 16S rRNA gene sequencing and compiled and processed using Qiime2 and OTU-profiling tables were collected and analyzed in this study.

Results: Compared with HCs, the richness and diversity of intestinal flora in patients with vasculitis tended to decrease with a statistically significant difference in β diversity (P = 0.025, Figure 1 A and B). More specifically, vasculitis patients had a lower frequency of Firmicutes while higher Proteobacteria and Bacteroidota at the phylum level (P < 0.001, Figure 1C). In vasculitis patients, the relative abundances of 23 bacteria differed from HCs at the genus level was all decreased, including Gemella, Anaeroglobus, Campylobacter, Fournierella, et al (P < 0.001, Figure 1D and E). More importantly, the relative abundance of Muribaculaceae were positively correlated with the absolute count of Th2 and the proportions of Th1 and $CD4^+$T cells and negatively correlated with CRP and ESR, while relative abundance of [Eubacterium]_ventriosum were positively associated with the absolute number of Treg cells and negatively correlated with the percentages of Th2 and $CD8^+$T cells (Figure 1F).

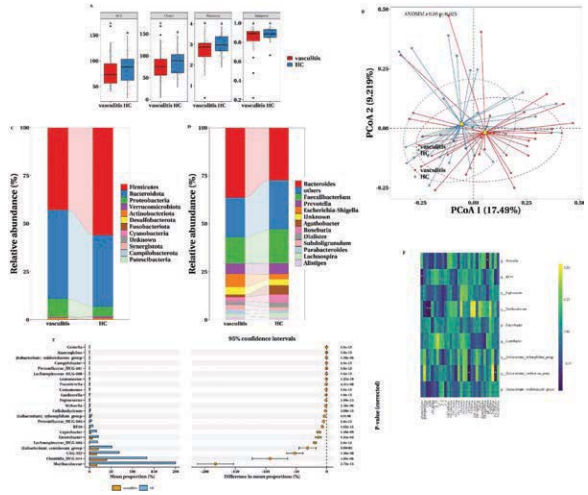

Figure 1. Differences in α diversity (A), β diversity (B), phylum (C), genus (D), and microbial composition (E) between vasculitis patients and HC and correlation analysis between differential microflora and clinical data in patients with vasculitis (F).

Conclusion: Disturbance of intestinal flora, mainly manifested by decreased diversity and richness, may be involved in the occurrence and development of vasculitis by inducing disroders in lymphocyte subsets and cytokines. Consequently, further studies on the immune mechanisms and influencing factors of intestinal flora may provide new ideas for the diagnosis and treatment of the disease for vasculitis patients.

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POS0812 CAROTID INTIMA-MEDIA THICKNESS/DIAMETER RATIO AND PEAK SYSTOLIC VELOCITY AS RISK FACTORS FOR NEUROLOGICAL SEVERE ISCHEMIC EVENTS IN TAKAYASU'S ARTERITIS

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Background: Takayasu's arteritis (TAK) is an idiopathic systemic vasculitis characterized by the involvement of the aorta and its major branches [1]. The supra-aortic arteries are often involved in TAK, with the reported prevalence ranging from 40% to 84% [2-3]. Importantly, patients with supra-aortic involvement carry a higher risk of neurological severe ischemic events (SIE) [4-5]. The common carotid artery (CCA) is the most affected artery and is more closely associated with neurologic symptoms than other supra-aortic arteries [6]. Ultrasonography (US) has been regarded as the most popular, user-friendly, and repeatable tool for the diagnosis and follow-up of CCA injuries.

Objectives: Our aim was to characterize TAK with supra-aortic involvement and determine the associations between clinical features, carotid US parameters, and neurological SIE.

Methods: Patients with supra-aortic involvement including brachiocephalic trunk, bilateral common carotid artery and internal carotid artery, and bilateral subclavian

and vertebral artery and baseline carotid US examination were enrolled. Bilateral carotid diameter, intima-media thickness (IMT), and peak systolic velocity (PSV) were measured by US. Then, IMT/diameter ratio (IDR) was calculated. Risk factors associated with neurological SIE were analyzed by multivariate logistic regression.
Results: Totally, 295 patients were included, of whom 93 (31.5%) experienced neurological SIE, with common carotid artery involved (81.7%). Involved supra-aortic artery distribution (p=0.04) and number (p<0.01) differed between neurologic and non-neurologic SIE subjects, showing higher prevalence of common carotid and vertebral artery involvement in cases with neurological SIE and 57.1% neurological SIE patients having more than four involved arteries. The left carotid IMT (p=0.03) and IDR (p<0.01) differed between patients with and without neurological SIE. The left carotid IDR (cut-off value ≥0.55, odds ratio [OR] 4.46; 95% confidence interval [CI] 2.05-9.71; p<0.01) and PSV (≤76 cm/s, OR 3.38; 95% CI 1.62-7.04; p<0.01) and involved supra-aortic artery number (≥4, OR 3.16; 95% CI 1.54-6.47; p<0.01) were independently associated with neurological SIE.
Conclusion: The left carotid IDR, PSV and involved supra-aortic artery number would perform as valuable markers for recognizing neurological SIE in TAK patients with supra-aortic lesions.
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POS0813 GLUCOCORTICOIDS, CONVENTIONAL DMARDS AND TOCILIZUMAB DIFFERENTLY AFFECT 18F-FDG PET METABOLIC ACTIVITY IN GIANT CELL ARTERITIS PATIENTS.

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Background: Imaging role in large vessel vasculitis (LVV) patients is tremendously increased in recent years. However, the role of ^{18}F-FDG PET in evaluating treatment response is still an unmet need.
Objectives: The aim of the present study is to evaluate the effect of different treatment regimens, namely glucocorticoids (GC), conventional disease modifying anti-rheumatic drugs (cDMARDs) and tocilizumab (TCZ), on clinical and metabolic activity of giant cell arteritis (GCA) with extra-cranial involvement.
Methods: Consecutive LVV inpatients and outpatients, classified as GCA, were prospectively enrolled. We included all patients who underwent to at least 2 consecutive ^{18}F-FDG PET-CT or MR scan between October 2010 and October 2021. Demographic and clinical data as well as disease activity were assessed before every PET scan. Remission was defined absence of signs and symptoms attributable to GCA and normalization of ESR (<30 mm/Hr) and CRP (<1 mg/dL) [1]. GCA patients were compared according to current treatment regimen: GC monotherapy versus cDMARDs (methotrexate, azathiopirine) and versus TCZ (administered both subcutaneous and intravenous). For each PET scan the vessel's metabolic activity was evaluated using the Meller's grading [2] and the PETVAS score [3].
Results: The study included 47 patients (age 66 [60-70], 72.3% female) exposed to a total of 77 treatment regimens (n=37 GC monotherapy, n=26 cDMARDs, n=14 TCZ). A total of 181 PET scan were conducted (min 2 – max 6). Overall clinical remission rate during the follow-up was 75.7% in GC-treated patients, 69.2% in cDMARDs-treated and 85.7% in TCZ-treated (p=0.513).
Persistence was comparable among the different treatment regimens (GC 19±10 months vs cDMARDs 22±16 months vs TCZ 23±11 months, p=0.445).
All the treatment led to significant reduction of acute phase reactants (GC-treated: ESR 50vs20 mmh, p<0.001, ΔESR= -43.3%, CRP 13.6vs5.3 mg/L, p=0.001, ΔCRP= -87.7%; cDMARDs-treated: ESR 36vs27 mmh, p=0.134, ΔESR= -152%, CRP 13.6vs5.3 mg/L, p=0.038, ΔCRP= -66.3% and TCZ-treated: ESR 27vs3 mmh, p=0.017, ΔESR= -86.7%, CRP 11.4vs2.7 mg/L, p=0.023, ΔCRP= -80.2%).
Significant improvement in PETVAS was observed only in TCZ-treated patients (12vs4, p=0.002, ΔPETVAS -66.7%), while the other treatment approaches resulted not significant (GC treated 12vs5, p=0.052, ΔPETVAS= -50%; cDMARDs 11vs4, p=0.124, ΔPETVAS -52.4%).
Daily prednisone dose at last examination was 4.5 [0-5] mg/d in the cDMARDs group vs 1.25 [0-5] mg/d in the TCZ group (p=0.057). Interestingly, at last PET examination low-grade inflammation (Meller 1-2) was observed in 56.8% of GC-treated patients, 57.7% of cDMARDs-treated patients and 64.3% of TCZ-treated patients (p=0.884).
Conclusion: ^{18}F-FDG PET may be useful in assessing disease activity and monitoring response to therapy. Tocilizumab treatment significantly reduce vessel's metabolic activity over time, when compared to conventional treatment. A persistent low-grade uptake during remission is common features in LVV patients, irrespectively of treatment regimens.
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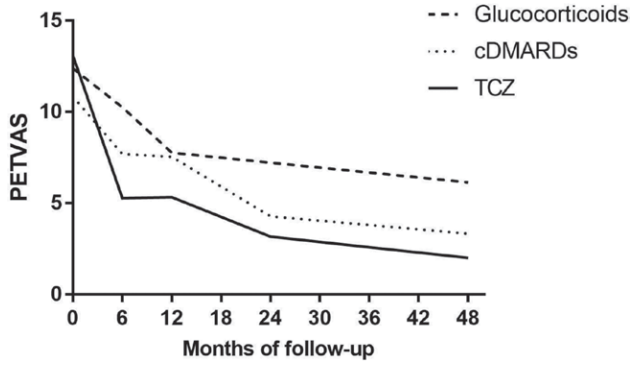

Figure 1.

Disclosure of Interests: None declared
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POS0814 OUTCOME OF VASCULAR INVOLVEMENT OF BEHÇET'S SYNDROME TREATED WITH INFLIXIMAB: A RETROSPECTIVE COHORT STUDY

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Background: Vascular involvement is the most common cause of mortality and an important cause of disability in patients with Behçet's syndrome (BS). Cyclophosphamide has been the treatment choice for severe vascular involvement, but high frequency of adverse events such as infertility and infections cause concern. TNF inhibitors can be an alternative for BS patients with vascular involvement.
Objectives: To survey the efficacy and safety of infliximab (IFX) in BS patients with arterial and venous vascular involvement.
Methods: We reviewed the charts of BS patients who used IFX for vascular involvement. We extracted data on demographic and clinical features, type of vascular involvement, laboratory tests, imaging modalities, concomitant immunosuppressives, duration of IFX use, and outcome. The primary endpoint was remission, defined as the presence of all of the following 3 parameters: 1) lack of new clinical symptoms/findings associated with the vascular lesion 2)

normalization of CRP level defined as <10 mg/dl) 3) lack of worsening of the primary vascular lesion or a new lesion vascular at another site on imaging. Remission was assessed at month 6 and month 12. Secondary endpoints were relapse, overall disease activity assessed with BDCAF at baseline and at the final visit, development of new organ involvement other than vascular involvement during IFX treatment, severe adverse events leading to discontinuation of IFX therapy, hospitalization or death, and death.

Results: Among the 371 patients who used IFX between 2004 and June 2021, 127 patients (102 men, 25 women, mean age 40 ± 8.7 years) had used it for vascular involvement. The types of vascular involvement that required IFX were venous thrombosis in 61 patients (48%), pulmonary artery involvement in 37 (29%), non-pulmonary artery involvement in 16 (13%), and venous ulcer in 13 (10%). Remission rate was 72% (92/127) at month 6 and 61% (71/117) at month 12. 17/99 (17%) patients experienced 22 relapses during a mean follow-up of 28.4±21 months of IFX therapy. Among the 22 relapses, 12 were the progression of the pre-existing vascular lesion and 10 were new vascular lesions. Overall disease activity improved with a decrease in mean BDCAF score from 1.76 ± 1.27 to 0.6 ± 0.8 at the final visit (p<0.001). Remission and relapse rates according to type of vascular involvement and causes of IFX discontinuation are presented in the Table 1. Adverse events leading to IFX discontinuation were infusion reactions in 5, tuberculosis, disseminated zona, lung adenocarcinoma, fibromyxoid sarcoma, heart failure, SLE, palmoplantar pustulosis, auricular chondritis, and aortic stent graft infection in 1 patient each.

Table 1. The frequency of concomitant immunosuppressive use, duration of infliximab use and outcomes of BS patients with vascular involvement treated with IFX

	Venous thrombosis (n=61)	Pulmonary artery involvement (n=37)	Non-pulmonary arterial involvement (n=16)	Venous ulcers (n=13)	Overall (n=127)
Number of patients who used concomitant immunosuppressives	48 (79)	24 (65)	14 (87)	7 (54)	93 (73)
Duration of IFX use (mean ± SD months)	24 ± 19.7	25 ± 19.3	35 ± 29.6	26 ± 24	25 ± 21
Remission rate at month 6	50 (82)	31 (84)	10 (63)	1 (8)	92 (72)
Remission rate at month 12[a]	40 (70)	21 (64)	8 (53)	2 (17)	71 (60)
Relapse rate	4 (7)	4 (11)	9 (60)	0	17 (13)
Number of patients who discontinued IFX	31 (51)	23 (62)	5 (31)	9 (69)	68 (54)
Due to remission	15	6	0	1	22
Due to inefficacy	3	1	3	4	11
Due to relapse	1	0	1	0	2
Due to adverse event	7	4	1	1	13
Due to noncompliance	3	4	0	3	10
Due to new organ development	1	0	0	0	1
Due to other reasons[b]	1	8	0	0	9
Death	2	2	0	0	4

[a] Since 10 patients did not reach the 12th month yet, the percentages were calculated on 117 patients. [b] Other reasons were preparation for surgical operation (n=2), not wanting to come to the infusion frequently during the pandemic (n=2), pregnancy (n=1), willing to get pregnant (n=1), lack of health insurance (n=1), due to prison sentence (n=1), and death (n=1).

Conclusion: Infliximab may be beneficial in BS patients with vascular involvement, even in those who are refractory to immunosuppressives and corticosteroids.

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POS0815 DIFFERENCES IN GIANT CELL ARTERITIS MANIFESTATIONS ACCORDING TO THE ULTRASOUND PATTERN OF DISEASE INVOLVEMENT

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Background: Giant cell arteritis (GCA) is the most common form of primary systemic vasculitis in patients aged >50 years. It predominantly affects the cranial arteries; however, extra-cranial disease involving the aorta and its major branches, known as large-vessel GCA (LV-GCA), can be present in 20-80% of cases, depending on the imaging modality used for screening the disease.

Objectives: We aim to compare the clinical features and outcomes of GCA patients with exclusive cranial, exclusive LV and combined cranial and LV involvement.

Methods: Single centre retrospective study, using data from patients diagnosed with GCA registered at the Rheumatic Diseases Portuguese Registry (Reuma.pt). All patients underwent ultrasound of both temporal (TA) and axillary (AX) arteries ± facial (FA), occipital (OC), subclavian (SC) or common carotid (CC) arteries at the time of diagnosis. Only patients with the presence of "halo sign" in at least one of these arterial segments were included. Three groups of patients were established according to their ultrasound results: i) exclusive cranial-GCA in cases of TA, FA, or OC involvement; ii) exclusive LV-GCA in cases of AX, SC, or CC involvement; and iii) cranial- and LV-GCA in cases of both cranial and LV involvement. Univariate analysis was performed using T-test, Chi-square and ANOVA, as appropriate. Multivariate analysis was performed using logistic regression modelling.

Results: We included 81 patients with GCA, 55 (67.9%) females, with a mean ± SD age of 75.8 ± 8.6 years. Halo sign was found in the TAs of 66/81 (81.5%) patients, AXs of 38/81 (46.9%) patients, FAs of 37/71 (52.1%) patients, OCs of 15/58 (25.9%) patients, SCs of 27/46 (58.7%) patients and CCs of 12/57 (21.1%) patients. A total of 37 (45.7%) cases had exclusive cranial-GCA, 14 (17.3%) had exclusive LV-GCA and 30 (37.0%) had cranial- and LV-GCA. Regarding clinical manifestations, temporal headache was more frequently found in cases of exclusive cranial-GCA than in the other groups (67.6% vs 7.1% vs 56.7%, p=0.001). By contrast, patients with exclusive LV-GCA were less likely to experience temporal and frontal headache (67.6% vs 7.1% vs 56.7%, p=0.001; 48.6% vs 0% vs 40.0%, p=0.007; respectively), jaw claudication (67.6% vs 14.3% vs 60.0%, p=0.004), scalp tenderness (32.4% vs 0% vs 23.3% p=0.037) or a cranial ischemic event (54.1% vs 21.4% vs 66.7%, p=0.020). Concerning physical examination, exclusive LV-GCA was associated with abnormalities of the upper limb arteries (0% vs 15.4% vs 3.3%, p=0.042) and lack of TA changes (37.8% vs 0% vs 30.0%, p= 0.023). No significant differences were found between groups regarding demographics, comorbidities and occurrence of relapses or mortality in the first two years of disease (p>0.05). Multivariate analysis, adjusted for jaw claudication, scalp tenderness, frontal and temporal headache, cranial ischemic events, abnormalities of the TA and upper limb arteries on examination, was performed to assess the association between these variables and the three GCA groups. The occurrence of a cranial ischemic event was independently associated with a lower probability of exclusive LV-GCA [OR: 0.069 95%CI: 0.009-0.526, p=0.010]. No other independent predictors were found.

Conclusion: GCA can encompass various patterns of vascular disease on ultrasound. LV involvement was frequently found in these patients, including in cases without evidence of cranial disease, highlighting the need to incorporate LV assessment in the diagnosis of GCA. Patients with exclusive LV-GCA had fewer cranial manifestations and more abnormalities on upper limb arteries on examination than the other groups. The occurrence of a cranial ischemic event was an independent negative predictor for exclusive LV-GCA. No differences were found between groups regarding the clinical outcomes at two years. Further studies with longer time of follow-up are needed.

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Disclosure of Interests: None declared

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POS0816 DRUG SURVIVAL OF INFLIXIMAB IN BEHÇET'S SYNDROME PATIENTS WITH DIFFERENT TYPES OF INVOLVEMENT

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Table 1. Drug survival of infliximab and reasons for infliximab discontinuation

	Mucocutaneous involvement (n=10)	Uveitis (n=164)	Vascular (n=114)	CNS (n=55)	Arthritis (n=19)	GIS (n=15)	Venous ulcer (n=13)
Male (n, %)	3 (30)	127 (77)	89 (78)	49 (89)	14 (74)	9 (60)	12 (92)
Age at infliximab initiation (mean ± SD years)	35.8 ± 9.3	34 ± 9.9	36 ± 9.1	36.2 ± 10.4	39.6 ± 10.7	43 ± 14.1	37.4 ± 8.2
Number of patients who used concomitant immunosuppressives (n, %)	5 (50)	108 (66)	86 (75)	38 (69)	5 (26)	11 (73)	7 (54)
Duration of infliximab use (mean ± SD months)	33 ± 38	45 ± 38	28 ± 23	37 ± 28	37 ± 35	26 ± 26	25 ± 25
Number of patients who discontinued infliximab (n, %)	5 (50)	93 (57)	58 (51)	23 (42)	12 (63)	7 (47)	9 (69)
Due to remission	-	30	21	2	1	2	1
Due to primary inefficacy	1	5	7	-	-	-	5
Due to secondary inefficacy	2	12	5	4	5	-	-
Due to adverse event	1	23	12	11	5	4	1
Due to noncompliance	1	11	1	3	-	-	2
Due to other reasons	-	12	12	3	1	1	-

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Background: Infliximab (IFX) is an effective therapeutic option in the management of severe and refractory manifestations of Behçet's syndrome (BS).
Objectives: We aimed to evaluate long term drug survival of IFX in a large cohort of BS patients.
Methods: We reviewed the charts of BS patients who received IFX between 2004 and June 2021 and noted demographic features, reasons for IFX use, IFX duration, and reasons for discontinuation.
Results: 371 patients (290 men, mean age at IFX initiation: 35.5 ± 10 years) received IFX for uveitis (n=164), vascular involvement (n=114), central nervous system (CNS) involvement (n=55), arthritis (n=19), gastrointestinal (GI) involvement (n=15), mucocutaneous involvement (n=10), venous ulcers (n=13), and secondary amyloidosis (n=1). Twenty patients had more than one type of involvement requiring IFX. During a median follow-up of 30 months (IQR: 13-52), 175 (47%) patients were still receiving IFX for a median period of 40 months (IQR: 22-66) while 196 (53%) patients had discontinued IFX after a median follow-up of 19 months (IQR: 8-34). IFX retention rate was 50% for mucocutaneous involvement, 43% for uveitis, 49% for vascular involvement, 58% for CNS involvement, 37% for arthritis, 53% for GI involvement, and 31% for venous ulcer (Table 1). Reasons for discontinuation were adverse events in 56 (15%), remission in 54 (15%) patients, inefficacy in 45 (12%) (secondary inefficacy in 26 (7%), primary inefficacy in 19 (5%)), and lack of patient compliance in 18 (5%). Other reasons were preparation for surgical operation (n=4), pregnancy (n=4), lack of health insurance (n=4), preferring subcutaneous administration during the pandemic (n=3), due to prison sentence (n=3), willing to get pregnant (n=1), rejecting the treatment (n=1), and death (n=3). Adverse events (n=56) leading to the cessation of IFX were infusion reactions (n=22), infections (n=7), tuberculosis (n=6), malignancy (n=6), palmoplantar psoriasis (n=5), hepatotoxicity (n=4), lichen planus (n=1), drug induced lupus (n=1), auricular chondritis (n=1), macrophage activation syndrome (n=1), splenic infarction (n=1) and a decrease in left ventricular ejection fraction (n=1). At the end of the follow-up, 2 patients had died due to lung adenocarcinoma, 1 patient had died due to pneumosepsis, 1 due to severe parenchymal neurologic involvement and 1 with pulmonary artery involvement due to massive hemorrhage during IFX treatment. Additionally, 7 patients had died 9, 10 months, 3, 3, 4, 7 and 9 years after IFX discontinuation. The causes of death were severe nervous system involvement in 2 patients, right heart failure due to pulmonary hypertension, laryngeal adenocarcinoma, lung adenocarcinoma, sepsis and gastrointestinal bleeding in 1 patient each.
Conclusion: IFX seems to be effective for the treatment of organ and life-threatening manifestations in the majority of the patients. However, drug retention rate was not optimal, mainly due to adverse events, inefficacy and patient non-compliance.
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POS0817 TOCILIZUMAB IN NEWLY DIAGNOSED GIANT CELL ARTERITIS VERSUS REFRACTORY/RECURRENT GIANT CELL ARTERITIS; MULTICENTER STUDY OF 471 PATIENTS OF CLINICAL PRACTICE

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Background: Tocilizumab (TCZ) is the only biologic drug approved in giant cell arteritis (GCA), based in two clinical trials (CT) **(1,2)**. CT included selected patients who may differ from those of clinical practice (CP). A high proportion of GCA patients treated with TCZ in CT had a newly diagnosed GCA, whereas in CP, most of them are refractory/recurrent GCA **(3,4)**. Although in CT the efficacy of TCZ seems to be similar in patients with newly diagnosed GCA and in patients with refractory/recurrent GCA, in CP it is not documented.
Objectives: To compare in CP, the effectiveness and safety of TCZ in newly diagnosed vs refractory/recurrent GCA.

Methods: Multicentre observational study on 471 GCA patients treated with TCZ. GCA was diagnosed by: **a)** ACR criteria, and/or **b)** temporal artery biopsy, and/or **c)** imaging techniques. A comparative study between patients with newly diagnosed GCA (<6 weeks) and those with refractory/recurrent GCA (>6 weeks) (according to GiACTA study definitions) **(2).** Sustained remission was based on EULAR definitions **(5)**.
Results: The 471 GCA patients were divided into 2 subgroups: **a)** newly diagnosed GCA (n=91) and **b)** refractory/recurrent GCA (n=380) (Table 1).

Table 1. Main features of patients with newly diagnosed GCA and refractory/recurrent GCA treated with tocilizumab.

	Newly diagnosed GCA (n=91)	Refractory/recurrent GCA (n=380)	p
Baseline characteristics at TCZ onset			
Age(years), mean±SD	74.3±8.5	73.3±9.1	0.35
Sex, female/male (% female)	60/31 (66)	282/98 (74)	0.11
Time from GCA diagnosis to TCZ onset (months), median [IQR]	1 [0.5-1]	10 [4-24]	**0.0001**
ESR, mm 1st hour, median [IQR]	46 [17.5-80.5]	27 [10-50]	0.02
CRP, mg/dL, median [IQR]	2.1 [0.7-8.5]	1.3 [0.4-2.8]	0.13
Haemoglobin, g/dL, mean±SD	12.3±1.5	12.7±1.5	**0.03**
Prednisone dose, mg/day, median [IQR]	40 [21.2-50]	15 [10-30]	**<0.001**
Effectiveness and Safety after TCZ onset			
Follow-up, (months), median [IQR]	15 [6-27.5]	22 [11-37]	**0.004**
Relevant adverse events, n (%)	23 (25)	102 (27)	0.54
Relevant adverse events per 100 patients-year	20	15	NS
Serious infections, n (%)	13 (14)	53 (14)	0.49
Serious infections per 100 patients-year	11.2	8	NS
MACES, n (%)	0 (0)	1 (0.3)	-
MACES per 100 patients-year	0	0.2	-
Malignancies n (%)	2 (2)	3 (0.8)	0.99
Malignancies per 100 patients-year	1.6	0.5	NS

Abbreviations: CRP: C-reactive protein;ESR: erythrocyte sedimentation rate;GCA: giant cell arteritis; IQR: interquartile range; IV: intravenous; MACEs: major adverse cardiovascular events; NS: non significant; SC: subcutaneous; SD: standard deviation

No significant differences were observed between both groups in sustained remission, although a greater tendency towards sustained remission is observed in newly diagnosed than in refractory/recurrent GCA patients (Figure 1**).** The decrease in glucocorticoids dose was faster in the first three months in the newly diagnosed GCA group, but thereafter, was similar in both groups, as well as the appearance of relevant adverse events and serious infections.

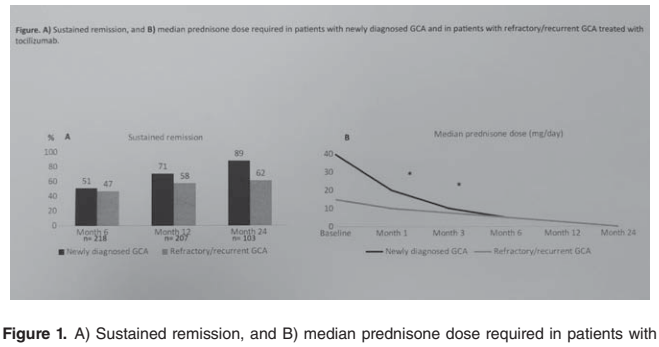

Figure 1. A) Sustained remission, and B) median prednisone dose required in patients with newly diagnosed GCA and in patients with refractory/recurrent GCA treated with tocilizumab.

Conclusion: The effectiveness and safety of TCZ seems to be similar in patients with newly diagnosed GCA and in patients with refractory/recurrent GCA.

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POS0818 SOUTHEND PRE-TEST PROBABILITY SCORE AND HALO SCORE AS MARKERS FOR DIAGNOSIS AND MONITORING OF GCA: EARLY RESULTS FROM THE PROSPECTIVE HAS-GCA STUDY

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Background: Ultrasound (US) is recommended as the first line imaging test in patients with suspected Giant Cell Arteritis (GCA). Traditionally, the US halo sign has been used for diagnosis. We have recently described a composite Halo Score that allows to quantify vascular inflammation on US. Prospective studies on response and disease monitoring are lacking.
Objectives: To prospectively assess the role of US in diagnosing and monitoring GCA patients. We report early baseline and 12-month data on our current recruitment in a study that has suffered disruption from the pandemic.
Methods: HAS GCA (IRAS#264294) is an ongoing, prospective, multicentre study recruiting from referrals of suspected GCA to fast-track clinics. Based on the Southend GCA clinical pre-test probability score (SPTPS)1, patients were stratified in to low, intermediate and high risk categories2. Temporal and axillary US Halo Scores were calculated from the halo thickness and extent in bilateral temporal arteries, parietal and frontal branches (TAHS) and axillary arteries (AAHS). These scores were summed (TAHS x1 plus; AAHS x3) to generate a Total Halo Score (THS)3.
Mann Whitney U test was used to compare baseline features between GCA and controls. Wilcoxon signed rank test was used to evaluate disease features at baseline and at 12 months in GCA patients. Sensitivity (Sn), Specificity (Sp) and ROC curve were calculated, where applicable. P value <0.05 is statistically significant
Results: 202 patients (71 GCA, 131 controls) have been recruited thus far: 23 completed 12-month follow up assessment; 6 were lost to follow up (4 died, 2 withdrew consent due to pandemic). Demographics, clinical features, and US results are shown (Table 1).

Table 1. Baseline features of GCA patients and controls

	GCA (n=71)	Controls (n=131)	P-value
Age, median (IQR)	75 (70-81)	68 (62-76)	0.001
Female, n (%)	38 (54)	89 (68)	0.05
SPTPS category, n (%)			
Low risk	0 (0)	59 (45)	<0.001
Intermediate risk	16 (23)	49 (37)	0.04
High risk	55 (77)	23 (18)	<0.001
Halo score (HS), median (range)			
Temporal artery HS	12 (0-22)	2 (0-17)	<0.0001
Axillary artery HS	12 (0-21)	6 (0-18)	<0.0001
Total HS	21 (2-40)	8 (0-29)	<0.0001
Clinical features, n (%)			
Temporal headache	53 (75)	93 (71)	0.62
Scalp tenderness	36 (51)	40 (31)	0.006
Jaw claudication	38 (54)	9 (7)	<0.001
PMR symptoms	29 (41)	35 (27)	0.06
Constitutional symptoms	42 (59)	29 (22)	<0.001
Visual disturbance	40 (56)	58 (44)	0.11
Vision loss	21 (30)	9 (7)	<0.001

AA, axillary artery; GCA, Giant cell arteritis; TA, Temporal artery

Among GCA patients, 50 had cranial, 5 large-vessel and 16 mixed phenotypes. Diseases were diagnosed by US and additional tests such as PET CT.

Jaw claudication (54%) and constitutional symptoms (59%) were the dominant features in GCA patients. Median age was 75 years in GCA (54% females) and 68 years in controls (68% females). GCA and controls were stratified by SPTPS to Low risk (0% vs 45%; Sn-undefined, Sp-98), Intermediate risk (23% vs 37%; Sn-81, Sp-98) and High risk (77% vs 18%; Sn-98, Sp-91). Optimal SPTPS cut-off point was ≥12 (Sn-89, Sp-76).

Median THS was 21 in GCA and 8 in controls. Optimal cut-off Halo Score in diagnosis was TAHS ≥5 (Sn-89, Sp-86), AAHS ≥11 (Sn-55, Sp-75), THS ≥15 (Sn-79%, Sp-86%). Baseline Halo Score and CRP levels showed positive correlation (spearman rank correlation). Among the 23 patients who completed 12-months follow up, median TAHS, AAHS and THS reduced from 12 to 2, 12 to 6 and 21 to 10, respectively (Figure 1).

Conclusion: Along with SPTPS, Halo Score successfully discriminates GCA from non GCA mimics and. HS is effective in showing 12-month response. This score may be a useful marker to monitor GCA disease activity

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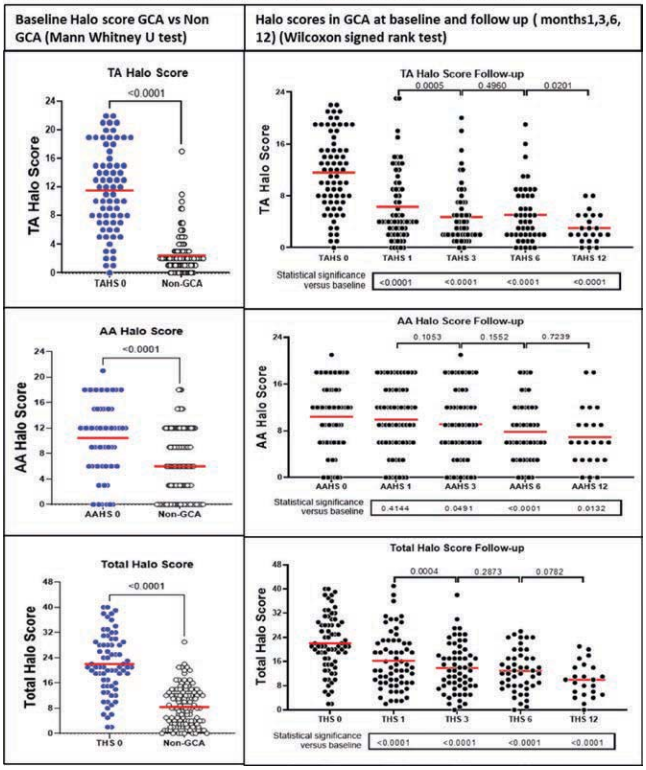
Figure: Halo score comparing GCA vs non GCA and baseline halo score vs follow up (in months)



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POS0819 RACIAL DIFFERENCES IN CARDIOVASCULAR AND INFECTIOUS MORBIDITY AMONG PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is the most common primary vasculitis in adults. It presents with signs of vascular insufficiency of the extracranial arteries of the head, but may also affect the aorta and its primary and secondary branches. GCA is more prevalent in Caucasians of Scandinavian and Northern European descent, and is considered to be less common in African, Asian, Arab and Latin American populations.[1,2] However, this may reflect a lack of formal epidemiological data in these populations rather than a true lower incidence. This is evidenced by extensive studies in white populations and a significant paucity of data in other ethnic groups. The most frequent causes of death in GCA are cardiovascular disease (CVD) (39%) followed by cerebrovascular disease (CVA) (14%), infection (13%), and malignancy (12%).[3] Overall, the mortality rate is increased in the first two years and is associated with the disease severity, extent, ischemic, and treatment complications, particularly from glucocorticoids.[4,5]

Objectives: The aim of this study was to compare the rate of cardiovascular and infectious complications in GCA patients among different ethnicities.

Methods: In this retrospective cohort study, we identified patients with biopsy proven GCA based on ICD-10 codes, using the Nationwide Inpatient Sample database (NIS) from 2016 to 2019. We included acute coronary syndrome (ACS), CVA, thoracic ascending aneurysm rupture (TAA), and infection (composite of UTI, sepsis and pneumonia) as our outcomes of interest and compared them between Caucasian, African American (AA), and Hispanic ethnicities. We implemented logistic regression analysis in the univariable and multivariable models. In the multivariable model, we adjusted all outcomes for potential confounders, including age, sex, obesity, hyperlipidemia, congestive heart failure, peripheral vascular diseases, diabetes, hypertension, renal failure, history of smoking or alcohol abuse, history of other drug abuse, prior history of MI, primary coronary intervention, or coronary artery bypass grafting, coagulopathy, liver disease, chronic pulmonary disease, ischemic cardiomyopathy, Elixhauser comorbidity index, type of insurance, bed size of hospital, history of defibrillator or pacemaker, and long-term use of steroids. The analysis was done using the STATA software, version 17.0 (MP2).

Results: We identified 7,750 patients with GCA, of whom 5,710 (74%) were Caucasian, 1,335 (17%) were AA, and 705 (9%) were Hispanic. Our results showed that Hispanics had both a higher prevalence (16.30% vs 9.80% vs 7.50%, p-value = 0.017) and risk for infections (OR: 2.74; 95%-CI 1.4-5.5; p-value = 0.004) when compared to the other racial groups. There was no difference in the risk of ACS among Caucasians (OR: 2.72; 95%-CI 0.6-12.4; p-value = 0.2) and Hispanics (OR: 2.72; 95%-CI 0.4-17.4; p-value = 0.004) when compared to AA population. Similarly, risk of CVA was not different between racial groups (Caucasians: OR: 1.04; 95%-CI 0.6-1.7; p-value = 0.87; Hispanics: OR: 0.8; 95%-CI 0.4-1.7; p-value = 0.567). The prevalence for TAA was only reported in the Caucasian group (0.50%).

Conclusion: ACS and CVA are known complications of GCA. There does not appear to be a difference in the risks of these common cardiovascular complications among racial groups. However, there was a significantly higher rate of infections in the Hispanic population. This may be explained by biologic differences in susceptibility and racial disparities in insurance coverage and access to care.

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Table 1. Multivariable logistic regression comparing clinical outcomes across races*

	Caucasian			Hispanic		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
ACS	2.72	0.6-12.4	0.2	2.72	0.4-17.4	0.291
CVA	1.04	0.6-1.7	0.87	0.8	0.4-1.7	0.567
TAA	NA			NA		
Infection	1.55	0.9-2.6	0.11	2.74	1.4-5.5	0.004

*AA are taken as reference

Disclosure of Interests: None declared
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POS0820 PREDICTIVE VALUE OF OBJECTIVE EXAMINATION OF TA ON POSITIVITY OF TAB IN GIANT CELL ARTERITIS

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Background: Previous studies have reported the utility of temporal artery examination for the diagnosis of GCA but no data are available on the correlation between clinical examination and the subsequent temporal artery biopsy (TAB) results of the biopsied vessel.
Objectives: Evaluate the predictive value of temporal artery (TA) examination in patients with suspected GCA on the results of TAB of the same vessel.
Methods: 97 pts consecutively seen at our center because of suspected cranial arteritis between 01.01.2015 to 31.12.2021 were enrolled in the study. All patients had complete clinical examination, laboratory investigations (included ESR and CRP determination), clinical examination of the temporal arteries and their frontal and parietal branches for tenderness (P), reduced or absent pulse (R) and thickening (T). All patients underwent arterial ultrasound (US) followed by a TAB of the most US involved frontal branches. The presence of inflammatory infiltrate of the vessel wall or the inflammation of the periadventitial blood vessel were considered positive for the presence of arteritis. The clinical features of the biopsied vessel were compared with the histological results by chi square test and the correspondent OR with 95%CI. Sensitivity, specificity, negative and positive PV, negative and positive LR were calculated for every singular objective abnormalities.
Results: 97 pts entered the study (F 56 (58%), mean age 73 ± 8, biopsy positive 56 (57%). At clinical examination of the biopsied vessel P was reported in 26 cases (27%) of TAB + and 10 (24.4%) in TAB- group (p=0.646, OR 1.24), R in 15 (15.5%) vs 2 (4.9%) (p=0.021, OR 5.69) and T in 16 (28.6%) vs 2 (4.9%) (p=0.003, OR 7.80), anyone (T or P or R) 30 (54.5% vs 11 (26.8%) (p=0.007, OR 3.27), presence of T or R 23 (41.8%) vs 4 (9.8%) (p=0.001, OR 6.65). Sensitivity, specificity, PPV, NPV, PLR, and NLR of any singular objective data and of US examination are reported in Table 1

Table 1. SENS, SPEC, PPV, NPV. PLR, NLR, PRETEST probability, POST TEST probability of clinical objective examination and US results FOR TAB POSITIVITY

	SENS	**SPEC**	**PPV**	**NPV**	**PLR**	**NLR**	**PRE**	**POST**
TA EXAMINATION								
TENDERNESS (P)	0.286	0.756	0.615	0.437	1.17	0.94	0.57	0.61
REDUCED/ ABSENT PULSE (R)	0.232	0.951	0.867	0.476	4.76	0,80	0.58	0.87
THICKENING (T)	0.286	0.951	0.889	0.494	5.86	0.75	0.57	0.89
ANYONE (P or R or T)	0.545	0.732	0.732	0.545	2.03	0.55	0.57	0.73
R or T	0.418	0.902	0.851	0.536	4.28	0.65	0.57	0.85
US								
HALO	0.875	0.643	0.636	0.878	2.45	0.19	0.42	0.64
CT+	0.878	0.654	0.654	0.878	2.54	0.19	0.43	0.65

Conclusion: Clinical examination (in particular reduced pulse and arterial thickening) of the temporal arteries is predictive of histological positivity of the TAB.
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POS0821 CORONARY ARTERIAL INVOLVEMENT CAN BE OBSERVED IN A SIGNIFICANT SUBSET OF TAKAYASU'S ARTERITIS PATIENTS BY CORONARY CT-ANGIOGRAPHY

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Background: Besides the aorta and its main branches, coronary arterial involvement is also seen at a substantial rate in patients with Takayasu's arteritis (TAK). Computerized tomography (CT)-angiography, as a non-invasive assessment tool, has started to be used instead of conventional angiography in the evaluation of coronary arteries. However limited data is available for its role in TAK patients.
Objectives: In this study, we aimed to assess the coronary arterial involvement by coronary CT-angiography in TAK patients with or without symptoms and to compare clinical characteristics of patients with or without coronary arterial involvement.
Methods: Patients with TAK (n=49, F/M: 40/9, mean age: 42.61±9.95 years) followed in Marmara University Vasculitis Clinic and underwent coronary CT-angiography with or without cardiac symptoms were evaluated retrospectively. Data of four patients who were not suitable for coronary CT-angiography but underwent conventional angiography were also included. CT angiography findings in the coronary arteries were defined as osteal stenosis, stenosis, calcific plaque and aneurysm and patients were categorized into two groups as those with or without coronary artery pathology. Demographic data, cardiac symptoms, clinical findings, BMIs, angiographic Hata and Goel classifications, treatments received for TAK, acute phase reactants and lipid levels were compared.
Results: Coronary artery pathology was detected in 14 patients (28.7%). Only 9 patients had a history of angina and 6 had cardiac symptoms in this group. Calcific plaque was present in 11 (22.5%), coronary artery stenosis in eight (16.3%) and aneurysm, osteal stenosis and occlusion in one patient each (2.0%). RCA was involved in 20.4%, LAD in 28.6%, LMCA in 22.4%, CX in 26.6% and more than one coronary arterial involvement in 26.5% of patients. In patients with coronary artery involvement, age (p=0.02), age at TAK diagnosis (p=0.004) and number of anti-hypertensive drugs (p=0.011) were significantly higher than those without coronary artery involvement. History of angina (p=0.004) and statin use (p=0.001) were also significantly higher in patients with coronary artery abnormalities, whereas HDL levels were significantly lower (p=0.037). No significant differences were observed between the groups when gender, smoking history, diabetes, BMI, ITAS2010 scores, biological therapy use, angiographic classifications, aortic involvement, presence of cardiac symptoms, CRP, ESR, total cholesterol and LDL levels were compared (Table 1).

Table 1. Comparison of patient groups with and without coronary artery involvement (BMI: Body Mass Index, SD: Standard Deviation, ITAS: Indian Takayasu Activity Score, LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein)

	Presence of Coronary Arterial Involvement (n=14)	**Absence of Coronary Arterial Involvement (n=35)**	**p value**
Age	49.29 (8.23)	39.94 (9.39)	***p=0.02***
Gender (F/M)	10/4	30/5	p=0.254
Disease duration, years	7.43 (6.42)	8.46 (6.25)	p=0.608
Age at TAK diagnosis	41.21 (12.58)	31.37 (9.18)	***p=0.004***
Diabetes mellitus	3/14	1/35	p=0.065
Family history	4/14	7/35	p=0.706
Smoking history	8/14	25/35	p=0.122
BMI (kg/m^2)	25.08 (2.53)	25.17 (4.68)	p=0.930
Biological therapy	4/14	15/34	p=0.317
CRP (mg/L) mean (SD)	4.45 (3.4)	8.68 (24.08)	p=0.642
ITAS2010 mean (SD)	0.57 (0.94)	0.51 (1.15)	p=0.869
LDL (mg/dL) mean (SD)	102 (41.96)	112.44 (35.79)	p=0.398
HDL (mg/dL) mean (SD)	46.23 (12.78)	55.12 (12.62)	***p=0.037***
Cardiac Symptom	6/14	2/35	p=0.159
Aorta involvement	8/14	18/35	p=0.717
Statin use	10/14	6/34	***p=0.001***
Number of antihypertensives	1.79 (0.89)	0.85 (1.18)	***p=0.011***
Acetylsalicylic acid use	10/14	24/34	p=1
Angina history	9/14	6/35	***p=0.004***

Conclusion: Coronary artery involvement which is an important cause of morbidity and mortality can be detected non-invasively by coronary CT-angiography in up to 1/3 of patients with Takayasu's arteritis, also in patients without angina and cardiac symptoms. Traditional cardiac risk factors are present more commonly in this group.

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Vasculitis — small vessel vasculitis

POS0822 HYPERTROPHIC PACHYMENINGITIS IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS: A MULTICENTER SURVEY IN JAPAN

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Background: Hypertrophic pachymeningitis (HP), characterized by an inflammatory disorder indicating intracranial or spinal thickening of dura mater, is found to develop as a neurological involvement in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Meanwhile, the previous studies focusing on HP in AAV have been reported as a single-institution study, and the analyses were performed in a small number of patients because HP is a rare neurological disorder. Therefore, neither etiological nor clinical characteristics of HP in AAV have been adequately elucidated.

Objectives: This study clarified the characteristics of HP in AAV by analyzing the information of multicenter study in Japan (Japan collaborative registry of ANCA-associated vasculitis: J-CANVAS).

Methods: We analyzed the clinical information from 541 Asian patients with AAV enrolled in J-CANVAS. Of them, newly diagnosed and relapsed AAV were included in 448 and 93, respectively. The epidemiological and clinical findings were compared between patients with and without HP. Clinical manifestations related to AAV were evaluated based on the Birmingham Vasculitis Activity Score version 3. To elucidate independent factors in HP development, logistic regression analyses were additionally performed.

Results: Of the total 541 patients (mean age: 71±14 years, M:F = 1:1.2), HP was demonstrated in 28 (5.17%), including 17 (3.79%) in newly diagnosed AAV and 11 (11.8%) in relapsed AAV. The classification of granulomatosis with polyangiitis (GPA) was significantly higher in patients with HP than those without HP (50% vs. 21%, p = 0.0007). In newly diagnosed AAV, patients with HP significantly had higher GPA classification and higher positivity for PR3-ANCA than those without HP (53% vs. 17%, p = 0.001; 29% vs. 9%, p = 0.015, respectively). Conversely, positivity for MPO-ANCA was significantly higher in patients with HP than those without HP in relapsed AAV (91% vs. 55%, p = 0.025), despite not significantly different in the classification of AAV. Headache and cranial neuropathies were significant neurological symptoms in patients with HP compared to those without HP (82% vs. 6.6%, p < 0.0001; 32% vs. 2.9%, p < 0.0001, respectively). Besides, ear, nose and throat (ENT) and mucous membranes/eyes were significantly higher involvements in patients with HP than in those without HP (54% vs. 26%, p = 0.003; 29% vs. 9%, p = 0.003, respectively). Moreover, higher complications of "conjunctive hearing loss" and "sudden visual loss", which are included in the categories of ENT and mucous membranes/eyes involvement, respectively, were significantly indicated in patients with HP than those without HP (39% vs. 7.2%, p < 0.0001; 21% vs. 1.2%, p < 0.0001, respectively). Multivariable logistic regression analysis identified that ENT (odds ratio [OR] 1.28, 95% confident interval [CI] 1.09 to 1.49, p = 0.002) and mucous membranes/eyes involvement (OR 1.37, CI 1.14 to 1.65, p = 0.0006), as well as conjunctive hearing loss (OR 4.52, CI 1.56 to 13.05, p = 0.005) and sudden visual loss (OR 1.84, CI 1.12 to 3.00, p = 0.015), were independent related factors in patients with HP.

Conclusion: GPA could be significantly classified in patients with HP. Notably, patients with HP significantly showed higher positivity for PR3-ANCA than those without HP in newly diagnosed AAV. Furthermore, sudden visual loss and conjunctive hearing loss might be implicated in HP development.

Disclosure of Interests: None declared

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POS0823 KL-6 IN ANCA-ASSOCIATED VASCULITIS PATIENTS WITH AND WITHOUT ILD: A MACHINE LEARNING APPROACH

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Background: ANCA-associated vasculitis (AAV) are small vessel vasculitis which may variously affect upper and lower respiratory tract. Patients with microscopic polyangiitis (MPA) and, less commonly, granulomatosis with polyangiitis (GPA), especially those who are ANCA-MPO-positive, may suffer from interstitial lung disease (ILD), which is associated with high morbidity and mortality as it is often underdiagnosed and responds poorly to conventional treatments

Objectives: In this study, we aimed to assess whether Krebs von den Lungen-6 (KL-6), a marker of fibrotic ILD, may be useful for distinguishing AAV patients with ILD from those without ILD, and whether its changes over time are correlated with disease activity.

Methods: We enrolled all consecutive patients evaluated in the period December 2020 - November 2021. Inclusion criteria were a diagnosis of GPA or MPA, active disease, and eligibility for Rituximab treatment according to EULAR recommendations. All patients underwent concomitant rheumatological and pneumological evaluation, lung function tests, routine blood tests, autoimmunity evaluation and KL-6 assay. Current and previous treatments, Birmingham vasculitis score (BVAS) and vasculitis damage index were also recorded.

Results: A total of 13 patients (Table 1) were enrolled. One was excluded due to a concomitant diagnosis of lung cancer. Higher serum KL-6 were in AAV-ILD compared with those without ILD (972.8±398.5 vs 305.4±93.9, p=0.0040). Area under the Receiver Operating Characteristics curve showed 100% of the diagnostic performance of KL-6 for identifying the ILD involvement (accuracy 91.7%) and the best cutoff value of 368 U/mL (Sensitivity 100% and specificity 87.5%). The decision-tree model showed a 33% improvement in class purity using a cut-off value of 513 U/mL to distinguish AAV patients with and without ILD (Figure 1). Stratifying AAV patients as MPA and GPA with and without ILD considering T0 and T1 KL-6, the model obtained an improvement of 40% for classifying GPA non-ILD with a T0 serum KL-6 cut-off value of 513 U/mL and a T1 KL-6 cut-off of 301 U/mL. A direct correlation was found between serum T0 KL-6 and T0 BVAS (r=0.578, p=0.044).

Table 1. Patients' features

Sex/age	Diagnosis	Length of disease * (months)	Organs involved	Type of lung involvement	T0 KL6 levels	T0 BVAS	T0 VDI	T1 KL6 levels	T1 BVAS	T1 VDI
F/83	MPA	28	Lung, kidney, PNS	ILD, alveolar hemorrhage	625	8	7	325	0	7
M/48	GPA	1	Lung, kidney, nose, eye	Nodules	352	18	0	279	2	0
F/55	GPA	252	Lung, skin	Nodules	401	15	3	602	3	3
F/38	MPA	1	Skin	-	347	6	0	-	-	-
F/74	MPA	180	Kidney, PNS	-	368	11	5	414	0	5
M/77	MPA	8	Lung, kidney, PNS, skin	ILD, alveolar hemorrhage	982	24	1	-	-	-
F/49	GPA	60	Nose, eye	-	122	6	2	116	0	2
M/60	MPA	40	Skin, PNS	-	205	9	1	-	-	-
F/39	GPA	4	Nose	-	310	6	3	-	-	-
M/71	GPA	24	Lung, eye, joints	Nodules, ILD	1528	9	3	-	-	-
F/64	MPA	24	Lung	ILD	756	4	-	1003	0	-
F/59	GPA	72	Lung	Nodules	338	4	-	-	0	-

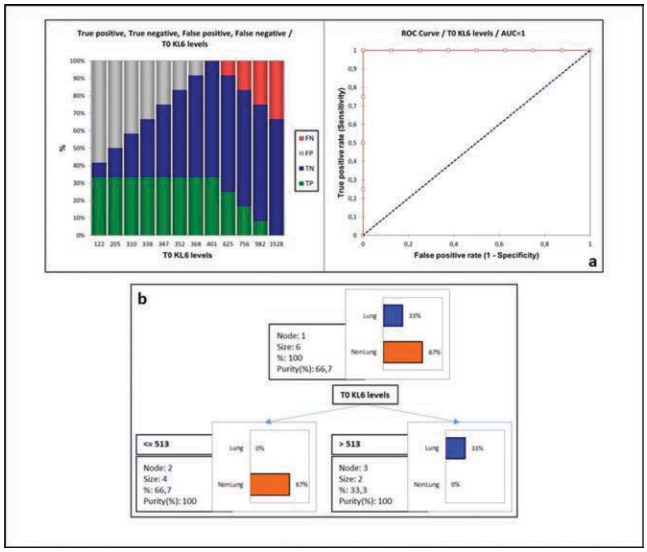

Figure 1. ROC curve and decision tree model

Conclusion: Our multicentre study demonstrated KL-6 as a reliable, non-invasive and easy-to-perform marker of ILD in AAV patients and its helpfulness for disease activity assessment. Changes in serum concentrations of KL-6 over time could be useful for monitoring AAV patients. Further study of KL-6 as a marker of response to therapy during long-term follow-up would also be worthwhile.
Disclosure of Interests: None declared
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POS0824 SAFETY AND EFFICACY OF THE INTENSIFIED B CELL DEPLETION INDUCTION THERAPY FOR PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND SEVERE RENAL INJURY: A CONTROLLED STUDY

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Background: Rituximab (RTX), an anti-CD20 monoclonal antibody, has shown to be an effective induction treatment for small-vessel vasculitides associated with antineutrophil cytoplasm antibodies (AAV) in both newly diagnosed and relapsing patients. However, the role of RTX in the management of the most severe cases of AAV remains to be fully elucidated.
Objectives: to assess both safety and efficacy of an intensified B-cell depletion therapy (IBCDT) protocol, including RTX, cyclophosphamide (CYC), and methylprednisolone pulses without additional maintenance immunosuppressive therapy compared to conventional therapy regimen based on oral CYC and steroids and prolonged maintenance therapy with azathioprine (AZA) in patients with AAV and severe renal injury.
Methods: A cohort of 15 AAV patients with the most severe features of AVV renal involvement (as <15 ml/min GFR and histological findings of paucimmune necrotizing glomerulonephritis with more than 50% crescents of non-sclerotic glomeruli at the renal biopsy) was treated IBCDT and compared to compared toa control group of 10 patients with AAV treated with a conventional therapy regimen based on oral CYC and steroids and prolonged maintenance therapy with azathioprine (AZA). Independently on the pharmacologic regimen, plasma exchange (7 procedures with 1-1.5 plasma volume replacement) was performed in the presence of 1. alveolar haemorrhage, and 2. more than 50% florid crescents in the nonsclerotic glomeruli, or 3. dialysis dependence.
Results: Complete clinical remission (BVAS 0) was observed at 6 months in 14 of 15 patients (93%). All cases treated with IBCDT who achieved a complete clinical remission experienced a depletion of peripheral blood B cells at the end of therapy. Of the 10 dialysis dependent patients at onset, 6 subjects (60%) experienced a functional recovery allowing the suspension of dialysis treatment. When compared to the control group, no statistically significant difference was observed in patients treated with IBCDT in terms of overall survival, 6-month therapeutic response rate, and 6-, and 12-month functional renal recovery. The cumulative total dose of CYC in the case group was on average 1 g/patient while in the control group on average 8.5 g / patient (p = 0.00008). Plasmapheresis sessions were performed at part of the induction therapy among 13 patients (87%) in the case group and 8 (80%) in the control group.
Conclusion: The results of this study showed that IBCDT appeared to be safe and has the same efficacy profile when compared to conventional therapy with CYC plus AZA in the management of the most severe patients with AAV. Additionally, this avoids the need of prolonged maintenance therapy for long, and limits the exposure to CYC with consequent reduced toxicity and drug-related side effect rates.
Disclosure of Interests: None declared
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POS0825 CLINICAL CHARACTERISTICS AND TREATMENT MANAGEMENT OF NON-INFECTIOUS SCLERITIS WITH CORTICOSTEROID-SPARING THERAPY. A RETROSPECTIVE STUDY FROM A TERTIARY EYE CARE CENTER.

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Background: Non-infectious scleritis refers to a rare and sight-threatening scleral inflammation. An association with an underlying systemic disease is noted in 30% to 40% of cases. Their management may require the use of nonsteroidal anti-inflammatory drugs, oral corticosteroids, and sometimes steroid-sparing immunosuppressive agents. Because of the low incidence and prevalence of scleritis, treatment guidelines are currently not available.
Objectives: We analyzed in a retrospective observational study patients with scleritis referred to the Foundation Rothschild Hospital (Paris) from March 2011 to June 2021.
Methods: Characteristics, visual outcomes, ocular complications, associations with systemic diseases and efficacy of treatment were assessed in patients with non-infectious scleritis who needed steroid-sparing immunosuppressive agents.
Results: Among 731 patients diagnosed with scleritis, 54 patients (71 eyes, 7%) were treated by steroid-sparing immunosuppressive agents. Mean follow up was 111.9 ± 84.5 weeks. Mean age was 48.4 years ± 18.3, and 31 patients (57%) were female. Scleritis was anterior in 51 eyes (72 %), including 25 (35%) with diffuse scleritis, 24 (34%) with nodular scleritis and 2 (3%) with necrotizing scleritis. Scleritis was posterior in 20 eyes (28%). Bilateral involvement was noted in 17 patients (32 %). Ocular complications were observed in 52 eyes (73 %): scleral thinning in 25 eyes (35%), anterior uveitis in 24 eyes (34 %), loss of vision in 20 eyes (28%), posterior segment ocular complications in 18 eyes (25%), ocular hypertension in 17 eyes (24%) and corneal involvement in 16 eyes (23%). An underlying systemic disease was identified in 28 patients (52 %), and scleritis was the first manifestation of the systemic disease in 17 out of 28 patients. Rheumatoid arthritis was the most frequently identified disease (n=12), followed by granulomatosis with polyangiitis (n=8) and relapsing polychondritis (n=4). All patients received at least

one immunosuppressive agent. Corticosteroid sparing with a daily dose ≤ 5 mg of prednisone was achieved in 85% of patients. Conventional immunosuppressive agents were used as the first steroid-sparing agent in 38 patients (70%) (methotrexate n=33, azathioprine n=4, mycofenolate mofetil (MMF) n=1) and as second steroid-sparing agent in 1 patient (MMF). This treatment led to control scleral inflammation in 23 (59%) patients after a mean delay of 10.0 ± 6.0 weeks. Biologic therapy was used in 33 (61%) patients (TNF alpha inhibitor n=17, IL6-R inhibitor n=7, anti-CD20 n=9), and as the first steroid-sparing agent in 16 (30%) (TNF alpha inhibitor n=4, IL6-R inhibitor n=4, anti-CD20 n=8). This treatment led to control scleral inflammation after a mean delay of 4,9 ± 3,7 weeks in 29 patients (87.9%).

Conclusion: Scleritis is a severe ocular inflammatory disease that requires repeated and thorough ophthalmologic and general examinations given the high frequency of complications and the possibility of an underlying systemic disease. This study reports real-life experience in management of non-infectious scleritis. Biological therapies seemed to be associated with a better outcome and a quicker reponse than conventional immunosuppressive agents. Further studies are warranted to develop specific guidelines

Disclosure of Interests: None declared

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POS0826 CIRCULAR RNA EXPRESSION PROFILES AND IDENTIFICATION OF HSA_CIRC_0028381 AS A POTENTIAL BIOMARKER OF ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

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Background: Growing evidence indicated that dysregulated circRNAs play a vital role in autoimmune diseases. However, their role in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) has never been illustrated.

Objectives: This study aims to determine the expression profiles of circRNA in plasma of AAV patients and explore the potential of circRNA as biomarker of AAV.

Methods: RNA-sequencing (RNA-seq) was performed to identify the circRNAs and mRNAs expression profiles in plasma from 5 AAV patients and 5 healthy controls (HCs). Hsa_circ_0028381, one of the four candidate circRNAs were validated by quantitative reverse-transcription (qRT)-PCR in a validation cohort of 51 AAV patients and 30 HCs and was confirmed to be significantly upregulated. And it was further verified in other connective tissue diseases (CTDs) by qRT-PCR. The receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic value.

Results: RNA expression profiles revealed that 143 circRNAs and 304 mRNAs were aberrantly expressed, among which, 62 circRNAs were upregulated and 81 circRNAs were downregulated in AAV patients compared to HCs. The result of qRT-PCR verification suggested that hsa_circ_0028381 was significantly increased in plasma from AAV patients compared to that in HCs and CTDs. The receiver operating characteristic (ROC) curves analysis showed has_circ_0028381 had a good diagnostic value to distinguish AAV patients from controls (HCs and other CTDs) with area under the curve (AUC) of 0.81. In addition, has_circ_0028381 was associated with renal involvement. Most importantly, increased baseline level of has_circ_0028381 had a predictive value for renal progression to end-stage renal disease (ESRD).

Conclusion: RNA-seq revealed that circRNAs were aberrantly expressed in plasma of AAV patients. Has_circ_0028381 might function as a potential biomarker for AAV diagnosis and renal prognosis.

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POS0827 VASCULITIDES AS MEDICATION-INDUCED ADVERSE EVENTS BASED ON A NATIONAL DATABASE REPORTING SYSTEM

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Background: Vasculitides have been reported as adverse events (AEs) related to a wide variety of medications.

Objectives: For the present study, we aimed to analyze the vasculitides reported to a national AEs spontaneous reporting system from October 2012 through September 2021.

Methods: All spontaneous reports of vasculitis related to any medications from October 1st, 2012, to September 30th, 2021, were retrieved from the Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) database. We performed a descriptive analysis of demographics, medications, and type of vasculitis based on 25 Medical Dictionary for Regulatory Activities (MedDRA) preferred term (PT) codes. Medications identified as the primary suspect in individual case safety reports (ICSRs) were retrieved by their product active ingredient. RStudio v1.4.1717 was used for general data analysis and the R package openEBGM v0.8.3 was used for the calculation of the Empirical Bayes Geometric Mean (EBGM) as the disproportionality score with its 90% two-sided credibility interval, frequently used in safety signal detection models. Drug-event combinations with an EBGM 5% lower limit credibility interval ≥ 2 were considered significant. An EBGM score of 2 indicates that the drug had at least 2 times as many reports for the AE as expected.

Results: During the study period, we retrieved 10,404 ICSRs reporting 10,931 AEs of vasculitis associated with a medicinal product as the primary suspect for that AE. The patient's mean age was 56.5 years, and 61% of them were female. Of the 25 PTs selected, the generic term "Vasculitis" was the most frequently reported AE (29.1%), followed by "Hypersensitivity vasculitis" (14.9%), "Polymyalgia rheumatica" (7.7%), "Anti-neutrophil cytoplasmic antibody-positive vasculitis" (ANCA-associated vasculitis) (6.2%), and "Cutaneous vasculitis" (5.4%). Of the total ICSRs with vasculitis AEs, 90% were expedited because they reported serious, unexpected AEs. Eighty drug-event combinations were disproportionately reported. Of those, the strongest association was observed for alemtuzumab and Goodpasture's syndrome (anti-glomerular basement membrane disease), followed by minocycline and polyarteritis nodosa, palivizumab and Kawasaki's disease (KD), then ribavirin and cryoglobulinemia, ezetimibe and microscopic polyangiitis, and so on. Some medications were associated with more than one AE, such as infliximab with Takayasu's arteritis (TAK), Behcet's syndrome (BS) and Henoch-Schönlein purpura (IgA vasculitis); adalimumab with BS and TAK; hydralazine with ANCA-associated vasculitis and renal vasculitis; and rituximab with granulomatosis with polyangiitis (GPA) and cryoglobulinemia.

Conclusion: Many different vasculitides were reported as AEs in the national database. Some of the medications were associated with the diseases they treat, which raises concern for possible confounding by indication. In other cases, the events were already known as adverse reactions, as for example alemtuzumab and Goodpasture's syndrome or montelukast and eosinophilic granulomatosis with polyangiitis. In other cases, no label or publication references were found, as for palivizumab and KD. These latter cases may raise a concern for potential safety signals that should be investigated. The improved understanding of the mechanism of action of drugs associated with some of these AEs may help to elucidate the pathogenesis of vasculitides.

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POS0828 BIOLOGIC THERAPY IN REFRACTORY PARENCHYMAL AND NON-PARENCHYMAL NEUROBEHÇET DISEASE: NATIONAL MULTICENTER STUDY

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Background: Ocular and Neurobehçet's Disease (NBD) are the most severe manifestations of Behcet's disease **(1-4)**. NBD can be classified as **a)** primary neural parenchymal lesions, also known as parenchymal NBD (p-NBD) or **b)** secondary to vascular involvement or non-parenchymal NBD (np-NBD) **(4)**. Response to biologic therapy (BT) in these two refractory subtypes of NBD is unknown.
Objectives: To assess efficacy and safety of BT in refractory subtypes of NBD.
Methods: Open-label multicenter study of refractory NBD from 21 different referral National Hospitals. NBD diagnosis was based on the International Consensus Recommendation criteria **(4)**. Efficacy was determined by complete or partial response and no-response. Complete, partial or no response was defined according to the resolution of the neurological syndrome (signs and/or symptoms) after the BT onset.
Results: We studied 41 patients (21 women/20 men; mean age: 40.6±10.8 years). NBD was classified as p-NBD (n= 33, 80.5%) and np-NBD (n=17, 41.5%). There were no significant differences in baseline general features and in neurological clinical response in both subgroups (Table 1 and Figure 1). The first BT used in p-NBD were Infliximab (IFX) (n=15), Adalimumab (ADA) (n=11), Golimumab (GLM) (n=3), Tocilizumab (TCZ) (n=2) and Etanercept (ETN) (n=2) and in np-NBD were IFX (n=9), ADA (n=6), TCZ (n=1) and ETN (n=1).

Table 1. Main features of p-NBD and np-NBD

	Total	p-NBD	np-NBD	*P* p-NBD vs np-NBD
Age at biological therapy initiation, years (mean±SD)	44±13.9	41.4±9.6	39.4±10.6	0.412
Gender, n (m/f) (%)	21/20 (48.8/52.2)	18/15 (54.5/45.5)	5/12 (29.4/70.6)	0.091
HLAB51 +/ patients tested, n (%)	15/31 (57.7)	14/25 (58.3)	4/10 (40)	0.391
Oral aphthae, n (%)	40 (97.6)	32 (97)	15 (88.2)	0.323
Cutaneous involvement, n (%)	28 (63.4)	23 (69.7)	10 (58.8)	0.603
Ocular involvement, n (%)	21 (48.8)	15 (45.5)	9 (52.9)	0.616
Vascular involvement, n (%)	9 (22)	10 (30.3)	7 (41.2)	0.442
Articular involvement, n (%)	9 (22)	7 (21.2)	3 (17.6)	0.765
Previous conventional Immunosuppressive drugs to BT				
Azathioprine	24 (58.5)	20 (60.6)	10 (58.8)	-
Methotrexate	16 (39.0)	12 (36.4)	3 (17.6)	-
Cyclophosphamide	13 (31.7)	13 (39.4)	5 (29.4)	-
Cyclosporine A	9 (22.0)	8 (24.2)	3 (17.6)	-
Mycophenolate Mofetil	2 (4.9)	2 (6.1)	0	-

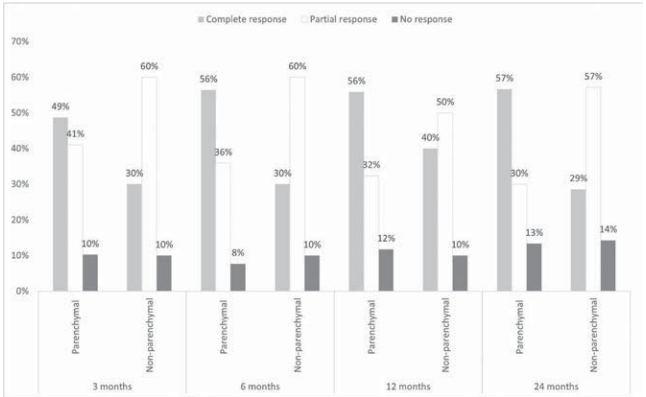

Figure 1. Response to biological therapy according to NBD subtypes.

After an overall mean follow-up of 57.5±50.9 months BT was switched in 22 patients due to inefficacy (n=16) or Adverse Effects (AE) (n=6) and in 4 cases was definitively discontinued because of complete prolonged remission (n=3) or AE (n=1). AE were observed in 7 (17.1%) patients. Severe AE were observed in 2 cases, one due to demyelinating disease and the other due to pulmonary tuberculosis, both in patients undergoing IFX therapy. The other 6 AE were infusion reaction to IFX (n=1), IFX-induced psoriasis (n=1), IFX-induced acneiform eruption (n=1), infusion reaction to TCZ (n=1), intolerance to IFX and recurrent mild infections (n=1) and erosive lichen planus and bullous impetigo (n=1).
Conclusion: In our series, BT seems equally effective and safe in both refractory p-NBD and np-NBD.

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POS0829

SPECTRUM OF ANCA-SPECIFICITIES IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS IN A RETROSPECTIVE MULTICENTER STUDY

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Background: Anti-neutrophil cytoplasmic autoantibodies specific for myeloperoxidase (MPO-ANCA) are found in 10-70% of the patients with eosinophilic granulomatosis with polyangiitis (EGPA) depending on disease activity, methodological aspects and cohort examined [1-3]. Recently, a higher prevalence of anti-pentraxin 3 (PTX3)-ANCA has been reported in EGPA compared to granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) [4].
Objectives: To investigate the spectrum of ANCA specificities in a multicenter cohort of patients with EGPA and identify novel ANCA antigens.
Methods: We conducted a retrospective analysis of 73 patients with EGPA treated between 2015 and 2020 in 3 tertiary referral centers. In addition to in-house ANCA testing with indirect immunofluorescence (IFT) on fixed human granulocytes and antigen-specific enzyme-linked immunosorbent assays (ELISA), ANCA specificities were determined using a cell-based assay (CBA; Euroimmun, Lübeck, Germany). Diagnosis was based on Chapel Hill consensus conference definitions, ACR- and MIRRA-criteria for EGPA. Patient characteristics and clinical manifestations were evaluated and compared based on ANCA status. Fisher`s exact test was employed for comparison of patient groups.
Results: ANCA findings are summarized in Table 1. MPO- and proteinase 3 (PR3)-ANCA positive patients (13.7%) had a higher prevalence of peripheral neuropathy (70% *vs.* 44.4%, p = 0.0003) and glomerulonephritis (20% *vs.* 14.3%, not significant). MPO- and PR3-ANCA-negative patients (86.3%) had a higher prevalence of heart (10% *vs.* 46%, p <0.0001), central nervous system (CNS) (0% *vs.* 14.3%, p <0.0001) and gastrointestinal (10% *vs.* 22.2%, p = 0.0327) involvement. PTX3-ANCA were associated with a higher prevalence of ear-nose-throat (ENT) (100% *vs.* 85.3%, p <0.0001), lung (100% *vs.* 89.7%, p = 0.0015), gastrointestinal involvement (60% *vs.* 17.6%, p <0.0001) and peripheral neuropathy (100% *vs.* 48.5%, p <0.0001). Kidney (0% *vs.* 16.2%, p <0.0001) and CNS involvement (0% *vs.* 13.2%, p = 0.0002) occurred less frequently in PTX3-ANCA positive patients. The 2 olfactomedin 4 (OLM4)-ANCA positive patients presented with ENT, lung and kidney involvement, and polyneuropathy, respectively.

Table 1. ANCA in EGPA cohort (n = 73). BPI = bactericidal permeability-increasing protein.

IFT / ELISA	No. of patients (%)
P-ANCA	11 (15.1)
C-ANCA	5 (6.8)
MPO-ANCA	8 (10.9)
PR3-ANCA	2 (2.7)
BPI-ANCA	1 (1.4)
PTX3-ANCA	5 (6.8)
OLM4-ANCA	2 (2.7)

Conclusion: We report on the detection of PTX3-, BPI- and OLM4-ANCA in addition to MPO- and PR3-ANCA in EGPA. OLM4-ANCA has been reported in 2 patients with non-vasculitic inflammatory symptoms previously [5]. Herein, detection of OLM4-ANCA in EGPA is reported for the first time. Our study shows that the presence of ANCA with various specificities other than MPO and PR3 contribute to a higher prevalence of ANCA in EGPA. Moreover, clinical manifestations differ between ANCA-negative EGPA and ANCA-positive EGPA, and between patients with different ANCA-specificities.

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POS0830 SYSTEMATIC LITERATURE REVIEW INFORMING THE 2022 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF ANCA-ASSOCIATED VASCULITIS: FOCUS ON TREATMENT STRATEGIES

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Background: The 2008 and 2016 European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of ANCA-associated vasculitis (AAV)[1,2] have supported clinicians with comprehensive recommendations for the treatment of patients with AAV in daily practice. During the past 5 years, the publication of several high-impact randomized-controlled studies have further improved the standard of care of AAV.

Objectives: The aim of this systematic review was to collect evidence supporting the 2022 update the AAV management recommendations.

Methods: The recommendations were developed based on an evidence-based approach as outlined in the 2014 EULAR standardized operating procedures (SOP)[3]. Areas of interest were adopted from the 2016 recommendations and updated by identifying additional topics through a Delphi process. Key questions were framed in the PICO (Population, Intervention, Comparator, Outcome) format and a search strategy consisting of keywords identifying treatment-related topics of interest was created based on the PICO questions. Aspects of drug treatment and other therapeutic interventions in AAV were included in the search, with a focus on remission induction, maintenance treatment and steroid sparing protocols. Outcomes such as survival, remission/relapses, infectious complications and malignancies were also covered. PubMed (Medline), Embase and the Cochrane Library databases were searched for articles providing data on the search questions. Abstracts of the annual meetings of EULAR, ACR, ERA-EDTA, ASN and the Vasculitis and ANCA Workshops were also screened, but restricted to randomized controlled clinical trials (RCTs). After deduplication publications were sorted by title and abstract first. There was full text review for articles eligible after title/abstract screening. The data were extracted from included articles and grouped according to the PICO questions. Data extraction results were collected in evidence tables.

The Cochrane revised tool for assessing risk of bias for RCTs (RoB2), ROBINS-1 for observational studies and AMSTAR II for meta-analyses were used for bias assessment. Evidence was categorized based on the GRADE system as per EULAR SOP[3].

Results: Based on the results of the Delphi, 11 topics related to therapeutic interventions were identified that were transformed into PICO questions (Table 1). Other items that received lower scores were added in the format of subquestions. Based on these research questions, search strings for the SLR were created.

Table 1. Key topics of interest for treatment strategies identified in the Delphi exercise grouped according to the PICO format

Patients	Intervention & Comparators	Outcome
Diagnosis	Cyclophosphamide	Disease-related outcomes
Granulomatosis with Polyangiitis	Rituximab	Treatment-related adverse events
Microscopic Polyangiitis	Mycophenolate	
Eosinophilic Granulomatosis with Polyangiitis	Methotrexate	
Disease severity	Azathioprine	
New-onset disease	Glucocorticoids	
Relapsing disease	Avacopan	
Organ- or life-threatening disease	Mepolizumab	
Not organ- or life-threatening disease	Plasma exchange	

The SLR was still ongoing at the time this abstract has been written and results of the SLR will be presented at the meeting.

Conclusion: This SLR identified recent developments affecting key areas of AAV treatment, that provide systematic evidence to inform the 2022 update of the EULAR recommendations for the management of AAV, which will also be presented at this meeting.

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POS0831 IGA VASCULITIS IN ADULTS, PEDIATRICS AND NON-VASCULITIC IGA NEPHROPATHY

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Background: IgA vasculitis (IgAV) has been extensively studied in children, while its natural history remains poorly studied in adults. Sparse data comparing childhood and adult-onset disease has shown significant differences in their clinical presentation, especially in the severity of renal involvement, which accounts for the major long-term morbidity. IgAV shares similar renal histologic features with IgA nephropathy (IgAN), while clinically IgAN is a chronic kidney disease which may lead to end stage renal disease and dialysis. The extent of kidney injury among adults with IgAV is still a matter of uncertainty.

Objectives: We aimed to evaluate clinical manifestations, laboratory data, treatment patterns and long-term outcomes of pediatric and adult-onset IgAV in comparison to IgAN.

Methods: This retrospective collaborative study examined medical records of adults and children with IgAV and IgAN adult patients admitted to rheumatology clinic and in hospital pediatric departments in a 13-year period (2007-2019). Diagnosis of adults with IgAV relied on the Ankara criteria and was confirmed by a consistent skin biopsy with positive IgA staining by immunofluorescence. Children with IgAV were included in our study on a clinical basis. All IgAN patients had a kidney biopsy proven disease. We analyzed and compared frequencies of clinical manifestations, laboratory findings, treatment regimens and long-term outcomes at one year follow-up. Finally, we assessed long term outcomes, such as time to dialysis and all-cause mortality, till the end of the follow-up time.

Results: A total of 60 adult IgAV, 60 pediatric IgAV and 45 IgAN patients were included in our study. There were significantly more males in the IgAN group compared to the adult and pediatric IgAV groups (77.8%, 41.7% and 55% respectively, p=0.01). Adult IgAV patients were significantly older than IgAN patients (53.1±17.4 years vs. 45.1±15.7 years, p=0.02) and had significantly higher rates of diabetes (43.3% vs. 24.4%, p=0.05) and ischemic heart disease (18.3% vs. 4.4%, p=0.03). The pediatric IgAV group had a statistically higher rate of previous infection compared to the adult IgAV group (44.8% vs. 20%, p=0.02). At one year follow-up, IgAN patients had higher levels of serum creatinine compared to the adult IgAV group (2.002 vs. 1.100, p<0.01). Data observed until the end of the follow-up time showed no difference in time to dialysis (IgAV adults: 9.8-12.4 years, IgAN: 5.0-6.6 years, p>.41). Nevertheless, IgAV adult patients had significantly shorter survival time (5.5 years, 95% CI: 4.8-6.2 years) than IgAN patients (7.0 years, 95% CI: 6.6-7.5 years, p<.01).

Conclusion: This retrospective study demonstrates that IgAV in adults presents substantial clinical manifestations, including high risk of progression to persistent renal impairment and possesses higher mortality rate in comparison with pediatric-onset disease and IgAN.

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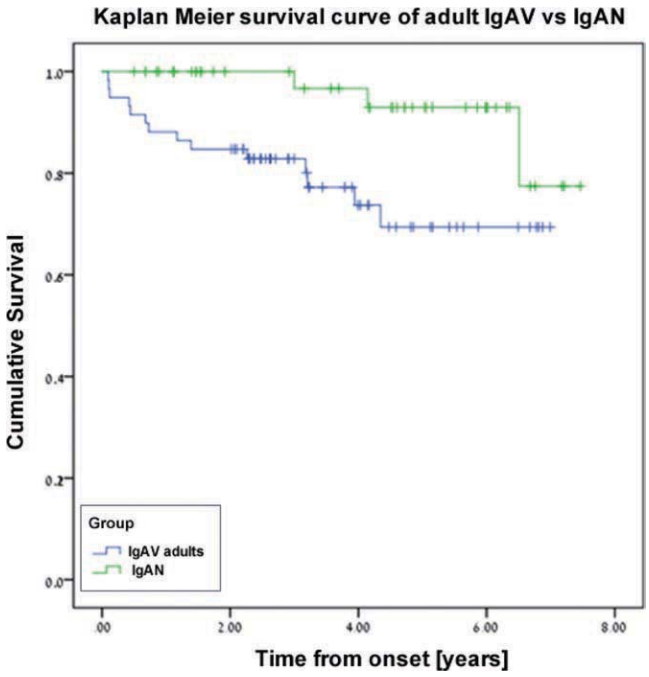

Figure 1.

Disclosure of Interests: None declared

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POS0832 MORTALITY TRENDS IN ANCA-ASSOCIATED VASCULITIDES (AAVS): DATA FROM A CONTEMPORARY, MULTICENTER ANCA REGISTRY

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Background: AAVs are a group of rheumatic diseases with excess morbidity and mortality (~3-fold higher compared to the general population). Long-term studies looking at mortality trends in contemporary patient cohorts are limited.

Objectives: To investigate the overall long-term survival and all-cause mortality in a contemporary AAV patient cohort.

Methods: Multicenter cohort study of patients registered and prospectively followed in the Greek ANCA Registry.

Results: Data for 165 patients (989.38 patient-years of follow up) with a diagnosis of AAV (GPA n=95, 58%, MPA n=54, 33%, EGPA n=16, 9%) were analyzed (January 1, 1998 - January 10, 2022). 53% of patients were female, with a mean age of 65 (±16.4) years; the majority (97%) had generalized disease and were ANCA positive (76%). The mean follow-up since diagnosis was 5.9 (±5.1) years. At the end of follow-up, the overall mortality rate was 20% (33/165), whereas the cumulative mortality rates at 5 and 10 years were 24% and 26% respectively. Overall cumulative survival at 5 years was worse in patients with MPA (57%) compared to GPA (81%) and EGPA (92%), (p<0.001). There was no difference in long-term survival among those treated with different induction regimens including cyclophosphamide (CYC, n of deaths=24/83, 28.9%), rituximab (RTX, n=4/40, 10%) or the CYC+RTX combination (n=3/16, 18.7%). Furthermore, there was no difference in survival between relapsing (≥1 relapses) and non-relapsing (n=76) patients (Figure 1). Cumulative survival was worse in patients who initially presented with lung (66% *vs.* 90% at 5 years, p=0.007), kidney (56% *vs.* 96% at 5 years, p<0.001) and simultaneous lung and kidney (39% *vs.* 93% at 5 years, p<0.001) involvement. Among the 33 registered deaths, the most frequent causes were infections (52%), followed by cardiovascular events (24%), disease flares (14%) and malignancies (10%).

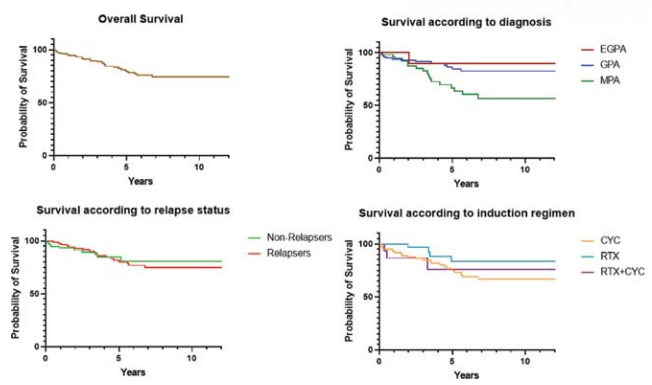

Figure 1.

Conclusion: In a contemporary multi-center AAV cohort, the cumulative mortality rates at 5 and 10 years were 24% and 26% respectively. Overall survival was worse in patients with MPA as well as those with combined lung and kidney involvement at baseline while there were no survival differences according to the initial induction regimen. Infection was the most common cause of death. These findings emphasize the unmet needs for better, less toxic therapies.

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POS0833 DIFFERENCES BETWEEN AVACOPAN AND PREDNISONE FOR THE TREATMENT OF ANCA-ASSOCIATED VASCULITIS AT DIFFERENT THRESHOLDS OF GLUCOCORTICOID TOXICITY

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Background: Treatment with glucocorticoids (GCs) for ANCA-associated vasculitis (AAV) is associated with substantial toxicity. The Glucocorticoid Toxicity Index (GTI) was developed to measure change in GC toxicity over time.[1] Data from the composite GTI domains provide both an Aggregate Improvement Score (AIS) and a Cumulative Worsening Score (CWS) of GC toxicity, permitting the

instrument to compare both improvement and worsening of GC toxicity across treatment groups. The GTI was a pre-specified secondary outcome in ADVOCATE, a randomized, double-blind, placebo-controlled trial in patients with AAV that aimed to replace a GC taper with avacopan, a complement C5a receptor inhibitor. Patients were randomized to either avacopan or a prednisone taper on a background of either cyclophosphamide or rituximab.[2] In ADVOCATE, the median GC exposure was 400 mg vs. 2939 mg in the avacopan and prednisone groups, respectively, which is an 86% median reduction in GC exposure from all sources. Remission rates were comparable in the two groups at 26 weeks (72.3% vs. 70.1%, respectively), and avacopan was superior at 52 weeks (sustained remission in 65.7% vs. 54.9%).[2]

Objectives: To compare GC toxicity between the treatment groups at three different thresholds of GC toxicity, beginning with the minimum detectable difference (MDD) of the GTI.

Methods: The MDD for the GTI (10 points) was calculated in the initial validation phase of the instrument. Thus, any GTI score > 10 points may be considered to represent a true change in GC toxicity. We compared the two groups at GTI thresholds of 10, 20, and 30 points for both the CWS and AIS. The CWS comprises a total of all GC-related toxicities that have occurred in the GTI between baseline and 26 weeks (time of primary outcome). The AIS, in contrast, allows toxicities to be added if they are new or subtracted if they improve. Higher CWS and AIS values indicate greater severity of GC toxicity. The two scores together capture the nuances of longitudinal GC toxicity across multiple domains. We compared the percentages of those in the two treatment groups who exceeded GTI threshold values of 10, 20, and 30 points in the CWS or AIS.

Results: The percentages of patients exceeding the specified AIS thresholds differentiated the avacopan group from the prednisone group (48.2% vs. 60.4%, respectively, at the 10-point threshold, p=0.02; 29.5% vs. 45.1% at the 20-point threshold, p=0.003; and 18.1% vs. 33.5% at the 30-point threshold, p=0.001) (Table 1). The CWS differentiated avacopan from prednisone at the 20- and 30-point thresholds (57.8% vs 73.2%, respectively, at 20 points, p=0.002; 41.0% vs 55.5% at 30 points, p=0.007).

Table 1. Percentages of Patients in ADVOCATE Exceeding Selected GTI Thresholds at Week 26

GTI threshold/study group	n (%) exceeding CWS threshold	p-value	n (%) exceeding AIS threshold	p-value
GTI worsening > 10 points				
Avacopan (N = 164)	138 (83.1%)	0.147	80 (48.2%)	0.022
Prednisone (N = 166)	144 (87.8%)		99 (60.4%)	
GTI worsening > 20 points				
Avacopan (N = 164)	96 (57.8%)	0.002	49 (29.5%)	0.003
Prednisone (N = 166)	120 (73.2%)		74 (45.1%)	
GTI worsening > 30 points				
Avacopan (N = 164)	68 (41.0%)	0.007	30 (18.1%)	0.001
Prednisone (N = 166)	91 (55.5%)		55 (33.5%)	

AIS, Aggregate Improvement Score; CWS, Cumulative Worsening Score; GTI, Glucocorticoid Toxicity Index

Conclusion: Among patients with AAV, treatment with avacopan was associated with lower GC toxicity across multiple GTI thresholds compared to treatment with prednisone, consistent with the substantial reduction in total GC exposure associated with avacopan. The GTI scores differentiated the two treatment groups effectively through a composite of GC toxicity domains.

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POS0834 COMPARISON OF NOVEL INFLAMMATORY MARKERS IN IDIOPATHIC AND SECONDARY LEUKOCYTOCLASTIC VASCULITIS

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Background: Positive diagnosis of Leukocytoclastic vasculitis (LV) is easy to establish via cutaneous biopsy, while etiologic diagnosis can be quiet challenging which leads to a still concerning high rate of idiopathic LV (ILV). Novel inflammatory Ratios such as platelet to lymphocyte ratio (PLR), neutrophil to lymphocyte ratio (NLR), C-reactive protein (CRP) to albumin ratio (CAR) and Fibrinogen to albumin ratio (FAR) have been recently described in multiple inflammatory pathologies, but their description and role in distinguishing idiopathic and secondary LV (SLV) is yet to be explored.

Objectives: We conducted a study aiming to compare new inflammatory markers and their potential role in distinguishing both LV subtypes.

Methods: Cross sectional study in which LV diagnosis was retained on cutaneous biopsy examination from January 2001 to November 2020. Patient's clinical assessment and laboratory data measured for each patient included age and sex, aspect and extent of the LV cutaneous lesions, neutrophil (N) count, lymphocyte (L) count, platelet (PLT) count, CRP, albumin (ALB), gammaglobulin (GG). PLR, NLR, CAR and FAR were calculated according to the results of individual items. We have also defined the number of positive aetiological examination (NPE) as the sum in a unique patient of the positive para clinical examinations involved in the etiological assessment of LV. Categorical variables were compared with the $\chi 2$ -test. Comparisons of the differences of continuous variables were performed by the Mann–Whitney U test or Student's t-test. Pearson correlation ratio was used for linear correlation analysis.

Results: A total of 77 patients were included in this study with 52 patients in the SLV group and 25 patients in the ILV group, demographic and clinical characteristics of both groups were distributed respectively as followed: mean age at diagnosis was 44+/-18 vs 49+/-21, gender ratio was at 29/23 vs 11/14, petechial aspect (89% vs 92%), ecchymotic aspect (64% vs 52%), necrotic aspect (46% vs 28%), extent to the trunk (31% vs 46%) and extend to upper limbs (50% vs 55%), none of these differences were statistically significant (p>0.05). Aetiologies of SLV were distributed as followed: IGA vasculitis 16 cases, Sjogren's syndrome 6 cases, Systemic lupus erythematous and cryoglobulinemia 5 cases each, Viral hepatitis and infectious endocarditis 3 cases each, rheumatoid arthritis, granulomotosis with polyangeitis, post streptococcal and chlamydia infection 2 cases each, Castleman's disease, tuberculosis, lymphoma, primary APS, periarteritis nodosa and parvovirus B19 infection 1 case each. Comparison of PLR, NLR, CAR and FAR showed statistically significant difference in means between SLV and ILV groups with 199 (177-309) vs 127 (79-193) (p=0.01) for PLR, 3.6 (1.9-5.1) vs 2.3 (1.7-3.4) (p=0.048) for NLR, 1.9mg.g-1 (0.4-3.6) vs 0.6mg.g-1 (0.2-1.9) (p=0.043) for CAR, 156mg.g-1 (91-192) vs 108mg.g-1 (82-148) (p=0.034) for FAR. PLR, CAR and FAR were significantly positively correlated to NPE (r=0.463, P<0.001; r=0.434, P<0.001 and r=0.411, P<0.001 respectively), there was no significant correlation between NLR and NPE (r=0.165, P=0.151).

Conclusion: In conclusion, this is the first study to explore the role of PLR, NLR, CAR and FAR in LV, it demonstrates that elevation of these ratios is a good predictor of SLV and that PLR, CAR and FAR were correlated with NPE in LV, which leads us to suggest to exhaustively explore patients with elevated ratios in order to make sure not to miss any underlying aetiology and provide more specific management for LV patients.

Disclosure of Interests: None declared

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POS0835 RELAPSE RATES IN NEWLY DIAGNOSED AND ESTABLISHED PATIENTS WITH ANTI-NEUTROPHIL CYTOPLASMIC AUTOANTIBODY (ANCA)-ASSOCIATED VASCULITIS

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Background: Anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis is a life- or organ-threatening condition in which patients experience severe inflammation of small- to medium-sized blood vessels. Clinical relapses are common in ANCA-associated vasculitis and previously reported rates vary between 21-89% at 5 years depending on the regimens used for induction and maintenance (1). Relapses require repeated treatment with immunosuppressive therapy and increase the risks of adverse events.

Objectives: Identify the incidence of relapse in newly diagnosed and established granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) patients in commercially insured and Medicare fee-for-service (FFS) populations.

Methods: Using the 2016-2019 Milliman proprietary commercial claims data and Medicare 100% FFS Innovator Research data, newly diagnosed and established GPA and MPA patients were identified in index years 2017 and 2018. Newly diagnosed

patients were identified as those with at least two qualifying claims on different dates of service, coded with a GPA or MPA ICD-10-CM code, and no claim coded with GPA or MPA in the 12 months prior to their first claim. Established patients required 12-months continuous enrollment in the year of their established status and 12-months continuous enrollment in the year prior to their established status. Relapses for incident patients were identified during the 7 to 12 months after the index date for newly diagnosed patients to avoid mischaracterizing claims around the time of the initial diagnosis as relapses and over a 12-month period for the established patients. Relapse was defined based on specific inpatient and outpatient claims with a GPA or MPA diagnosis code or claims coded with one major or at least three minor vasculitis signs or symptoms followed by a claim within 30 days for plasmapheresis or cyclophosphamide or glucocorticoids (> 20 mg prednisolone equivalent) or 2+ rituximab claims within 30 days of each other. Relapse had to occur 30 days after the previous event and 6 months after index date for incident patients.

Results: 542 (GPA) and 83 (MPA) commercially insured newly diagnosed patients with 12 months eligibility following their index date and 1,748 (GPA) and 184 (MPA) commercially insured established patients were identified. 15.5% (GPA) and 15.7% (MPA) newly diagnosed patients relapsed during months 7-12 after diagnosis and 27.9% (GPA) and 29.3% (MPA) established patients relapsed over a 12-month period. 2,397 (GPA) and 655 (MPA) Medicare FFS newly diagnosed patients with 12 months of eligibility following their index date and 5,955 (GPA) and 833 (MPA) Medicare FFS established patients were identified. 19.3% (GPA) and 27.2% (MPA) newly diagnosed patients relapsed during months 7-12 after diagnosis and 33.5% (GPA) and 40.2% (MPA) established patients relapsed over a 12-month period.

Conclusion: Using administrative healthcare claims, we observed relapse rates after GPA and MPA diagnosis ranging between 15.5-27.2% in months 7-12 after diagnosis for newly diagnosed patients and between 27.9-40.2% over a 12-month period for established patients. There is an unmet need for new therapies that sustain remission and decrease relapse rates in patients with ANCA-associated vasculitis. This is an important clinical strategy to reduce the risks of adverse events from long-term immunosuppression therapy and decrease end-organ damage.

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Disclosure of Interests: Kate Fitch Consultant of: ChemoCentryx, Carol Bazell Consultant of: ChemoCentryx, Steven Metz Consultant of: ChemoCentryx, Irene von Hennigs Shareholder of: ChemoCentryx, Consultant of: ChemoCentryx, Employee of: ChemoCentryx

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POS0836 EFFICACY OF MEPOLIZUMAB IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS AND A VASCULITIC PHENOTYPE

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Background: Patients with eosinophilic granulomatosis with polyangiitis (EGPA) can present with vasculitic or eosinophilic phenotypes.[1] The Phase III MIRRA study demonstrated that patients with EGPA spent more time in remission and had reduced oral corticosteroid (OCS) use with mepolizumab versus placebo.[2]

Objectives: To evaluate the efficacy of mepolizumab in patients with a vasculitic EGPA phenotype enrolled in the MIRRA study.

Methods: MIRRA was a Phase III, multicentre, double-blind, parallel-group trial in adult patients with relapsing/refractory EGPA and ≥4 weeks stable OCS treatment. Patients were randomised to receive standard of care plus mepolizumab (300 mg subcutaneously every 4 weeks) or placebo for 52 weeks. Primary endpoints were: accrued weeks of remission (defined as Birmingham Vasculitis Activity Score [BVAS] of 0 and OCS dose ≤4 mg/day prednisolone or equivalent) over the 52-week study period categorised in weeks (0, >0 to <12, 12 to <24, 24 to <36 and ≥36 weeks), and the proportion of patients in remission at both Weeks 36 and 48. This post hoc analysis used data from the MIRRA study to evaluate these endpoints according to patients' antineutrophil cytoplasmic antibody (ANCA) history (current or previous positive test for myeloperoxidase[MPO]/proteinase 3[PR3]-ANCA at study baseline versus no history of a positive MPO/PR3-ANCA test at baseline), baseline BVAS (=0 vs >0) and Vasculitis Damage Index (VDI) score (<5 vs ≥5). Types of disease relapse (vasculitis [BVAS >0], asthma [active asthma symptoms and/or signs with a worsening in Asthma Control Questionnaire-6 score] and sinonasal [active nasal and/or sinus disease with a worsening in ≥1 sinonasal symptom questions]) reported during the treatment period were also described. EGPA disease characteristics focusing on vasculitic components were assessed in patients who did and did not achieve remission at any point during the study.

Results: Of the 136 patients in the study, 26 (19%) had a history of a positive ANCA test at study baseline and 110 (81%) did not. In addition, 51 (38%) had a BVAS =0 at baseline while 85 (63%) had a BVAS >0; 74 (54%) had a VDI <5 at baseline and 62 (46%) had a VDI ≥5. Accrued remission duration was greater with mepolizumab versus placebo, irrespective of ANCA positive status, baseline BVAS or baseline VDI score (Figure 1). Across all the subgroups, a larger proportion of patients achieved remission at both Weeks 36 and 48 with mepolizumab versus placebo (Figure 1). Among patients receiving mepolizumab, the numbers (proportion) of patients achieving remission at both Weeks 36 and 48 were: 7 (54%) for patients with a history of an ANCA-positive test and 15 (27%) for patients without a history of an ANCA-positive test; 14 (45%) in the BVAS =0 and 8 (22%) in the BVAS >0 groups; 11 (29%) in the VDI score <5 and 11 (37%) in the VDI score ≥5 groups. Mepolizumab reduced all types of disease relapse assessed during the treatment period, including vasculitis, asthma and sinonasal relapses, compared with placebo. Vasculitic characteristics including neuropathy, glomerulonephritis, alveolar haemorrhage, palpable purpura and ANCA positivity were generally similar among patients who did and did not achieve remission during the study.

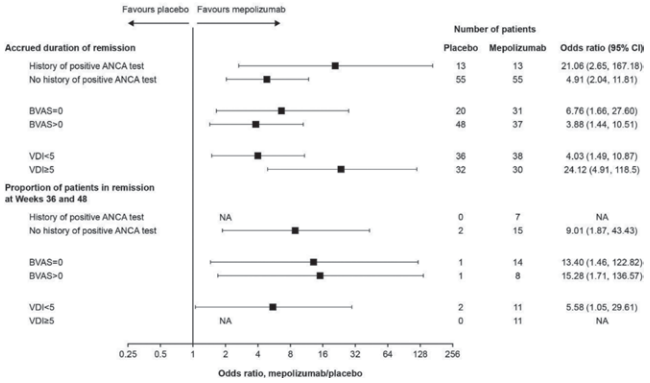

Figure 1. Mepolizumab efficacy by patient baseline characteristicsANCA, antineutrophil cytoplasmic antibody; BVAS, Birmingham Vasculitis Activity Score; CI, confidence interval; NA, data not available – estimate could not be calculated owing to a lack of patients in the placebo group achieving remission at Weeks 36 and 48; VDI, Vasculitis Damage Index.

Conclusion: Mepolizumab is associated with clinical benefits in patients with EGPA, including those with and without a vasculitic phenotype.

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POS0837

EFFICACY OF ULTRA-LOW DOSE RITUXIMAB FOR REMISSION MAINTENANCE THERAPY IN ANCA-ASSOCIATED VASCULITIS

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Background: Rituximab (RTX) achieved high remission-induction and sustained maintenance rates for patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) [1], [2]. However, RTX is an expensive medication, which may potentially lead to serious side effects. Defining the best dose regimen for maintenance in AAV is still an unmet need.
Objectives: The aim of the present study is to compare the effects of ultra-low dose RTX (500 mg or 1000 mg once per year) to standard low dose RTX (500 or 1000 mg twice per year) as remission-maintenance therapy in AAV patients.
Methods: We included consecutive AAV patients (classified as GPA and MPA [3]) referring to four different Rheumatology centers in Italy. We assessed all AAV patients who successfully achieved disease remission (BVASv3=0) with conventional RTX or cyclophosphamide regimens and have been subsequently treated with RTX for maintenance of remission. All included patients received at least three maintenance infusions with either 1000 mg or 500 mg, twice per year (standard low dose) or once per year (ultra-low dose). After a period of 18 months, we assessed the remission rate, damage (VDI), glucocorticoids intake, ANCA status, B-cells depletion and serum IgG levels.
Results: From January 2011 to December 2021, 83 AAV patients (mean age 51±16, 49.4% female, 95.2% ANCA positive, 65.8% anti PR3, 34.2% anti MPO), 61 classified as GPA and 22 MPA, achieved complete disease remission with conventional RTX induction regimen. After 7 [6-9] months, 29.9% patients started maintenance treatment with ultra-low dose RTX (once per year), while 70.1% patients with standard low dose (twice per year), for 18 months. No significant differences at baseline were noted between patients receiving ultra-low dose when compared to those treated with conventional low-dose.
At the end of observation period, a disease flare was observed in 22.7% of the low-dose group, and 21.2% in those treated with the standard dose (p=0.881). Relapse-free survival was comparable between the two group (log-rank p=0.818, Figure 1).

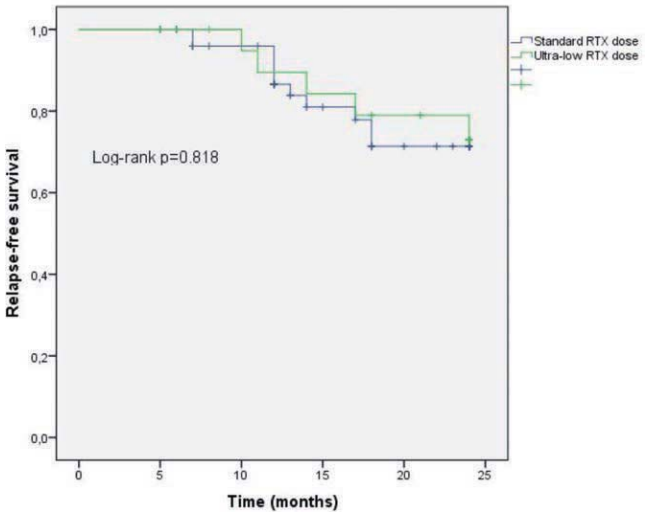

Figure 1.

When comparing AAV patients treated with ultra-low dose regimen to those treated with low-dose, no differences were noted in negative ANCA rate (72.2% vs 67.1%, p=0.262), ANCA titer (0 [0-7.8] vs 0 [0-50] UI/mL, p=0.232), B-cells depletion rate (70.6% vs 75%, p=0.725), mean serum IgG (811 [146-922] vs 680 [429-861] mg/dL, p=0.367), mean daily glucocorticoid dosage (2.5 [0-5] vs 3.75 [0-5] mg/d, p=0.647), VDI (4 [1-5] vs 2 [1-4], p=0.098), hypogammaglobulinaemia rate (31.8% vs 36.5%, p=0.697) and deaths (4.5% vs 5.8%, p=0.831).
Although not significant, patients treated with ultra-low dose had lower severe infection rate (10.5% vs 26.8%, p=0.154). Notably, in the all cohort 5 deaths were related to COVID19 pneumonia.
Conclusion: Reduced exposure to RTX was not associated with an impaired efficacy of maintenance therapy in patients with AAV. Remission maintenance with ultra-low dose RTX is a safe and more cost-effective option.
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Disclosure of Interests: None declared
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POS0838

INCIDENCE OF CANCER IS SIGNIFICANTLY INCREASED IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS PATIENTS: RESULTS FROM A MULTICENTRE STUDY.

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Background: No large assessment of the general cancer occurrence in eosinophilic granulomatosis with polyangiitis (EGPA) has been reported.
Objectives: The aim is to investigate the incidence of malignancies in EGPA patients and to examine the effect of immunosuppressive therapy on malignancy risk in these patients.
Methods: The occurrence of cancers was assessed in a cohort of 303 incident EGPA patients (54.8% female, 44% MPO-ANCA positive, 53 [41-61] years old at diagnosis), diagnosed between 1987 and 2019. Demographic, clinical and laboratory data, and the use of immunosuppressive drugs were assessed. Through linkage with Regional Italian Cancer Registries, information about any malignancy occurring before and after EGPA diagnosis was collected. For each patient, the person-years (PY) of follow-up was calculated till the first event: cancer occurrence, last follow-up or death. The PY was stratified by sex, age (in 5-year groups) and calendar-decades (2000-2009 and 2010-2019). Standardized incidence ratios (SIR) between observed and expected numbers (retrieved from the AIRTUM-AIOM database) of cancers were calculated with exact Poisson regression analysis and used as a measure of risk difference.
Results: Thirty patients developed a total of 42 malignancies during a median follow-up of 4.4 [2.1-8.5] years. After excluding patients with a diagnosis of cancer before EGPA onset, 20 first malignancies were observed in 1276 PY observation period. The SIR (95% Poisson CI) malignancy risk was 1.99 (1.22-3.08; p=0.007) for all cancers at all sites, and 1.86 (0.98-2.75; p= 0.025) for all cancers excluding non-melanoma skin cancers. Incidence rates were significantly higher in ANCA positive patients (SIR 2.43 [1.30-4.16]; p=0.007) when compared to ANCA negative, and in those treated with cyclophosphamide (SIR 2.42 [1.11-4.60]; p=0.030) when compared to other immunosuppressive agents. Median latency from EGPA onset and first cancer diagnosis was 5 (2-11) years, with 63.3% of patients developing cancer within 1 and 5 years. Malignancy-free survival at 2, 5, and 10 years of follow-up was 96%, 91%, and 70%, respectively. Of these malignancies, 30% were skin cancers, 25% prostate cancers and 20% breast cancers. Comparing patients who developed malignancies with those who did not, any significant difference was noted regarding sex, ANCA status, age at diagnosis, clinical manifestations, BVAS, FFS, environmental exposure, smoking habit and cancer familiarity. Type of treatment and cumulative doses of cyclophosphamide were not associated with higher incidence of cancers.
Conclusion: EGPA patients have a two-fold risk of overall malignancy than the general population. This cancer excess might be driven by a combination of already known treatment-associated factors and other unknown disease-associated factors, which should be further investigated
REFERENCES: NA

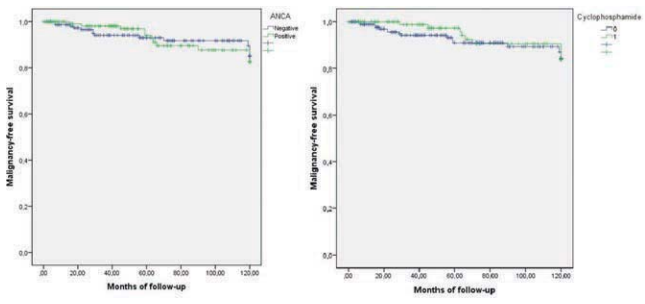

Figure 1.

Disclosure of Interests: None declared
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Scleroderma, myositis and related syndromes

POS0839

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO EVALUATE EFFICACY AND SAFETY OF SC ABATACEPT IN ADULTS WITH ACTIVE IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Limited therapies are available for patients with idiopathic inflammatory myopathy (IIM), a heterogenous group of chronic, systemic, autoimmune inflammatory diseases characterized by progressive muscle weakness and/or distinct skin rashes.[1] Abatacept, a selective co-stimulation modulator, may be a useful treatment option.[2]

Objectives: To evaluate efficacy, safety, and tolerability of abatacept + standard of care (SOC) in patients with IIM compared with SOC alone (placebo).

Methods: A 24-week, randomized, double-blind, placebo-controlled phase 3 trial of SC abatacept (125 mg weekly) + SOC (corticosteroids and immunosuppressants alone or combined; NCT02971683) in patients with active, treatment-refractory IIM (Manual Muscle Testing-8 [MMT-8] ≤ 135) was performed. Primary endpoint was proportion of patients meeting International Myositis Assessment and Clinical Studies definition of improvement (IMACS DOI) at week 24. Change from baseline in myositis Functional Index-2 (FI-2), HAQ-DI, Myositis Disease Activity Assessment Tool (MDAAT), and Myositis Response Criteria (MRC) were secondary endpoints with safety. Post hoc analyses by disease subtype were performed.

Results: Overall, 148 patients were randomized (75 abatacept; 73 placebo); IIM subtypes were dermatomyositis (DM; 53.3% vs 57.5%), polymyositis (PM; 25.3% vs 34.2%), and autoimmune necrotizing myopathy (ANM; 21.3% vs 8.2%). Mean baseline MMT-8 and HAQ-DI scores were 112.7 and 1.5, respectively. Approximately 90% of patients completed week 24. Week 24 IMACS DOI rates were abatacept 56.0% vs placebo 42.5% (adjusted odds ratio, 1.8 [95% CI, 0.9–3.5]; $P = 0.083$). Pre-specified IMACS DOI analysis showed no differences for patients with DM but notable benefit for those with non-DM subtypes, PM and ANM (Table 1). Secondary endpoints showed similar differences (Table 1). MRC at day 169 by category is shown in Figure 1. Proportion of AEs (69.3% and 75.3%) and serious AEs (5.3% and 5.5%) were similar in the abatacept and placebo arms.

Table 1. Primary and secondary (mean change from baseline at week 24) endpoints

Outcome	IIM	Abatacept	Placebo	Nominal *P* value (abatacept vs placebo) or adjusted mean difference from placebo (95% CI)
IMACS DOI,[a] n/N (%)	All	42/75 (56.0)	31/73 (42.5)	$P = 0.083$
	DM	22/40 (55.0)	21/42 (50.0)	$P = 0.679$
	Non-DM	20/35 (57.1)	10/31 (32.3)	$P = 0.040$
FI-2	All	4.1 (1.3)	1.2 (1.4)	2.9 (0 to 5.8)
	DM	2.3 (1.6)	0.3 (1.4)	1.9 (–2.3 to 6.2)
	Non-DM	3.2 (1.4)	–0.6 (1.5)	3.7 (–0.3 to 7.8)
HAQ-DI	All	–0.31 (0.07)	0.20 (0.07)	–0.12 (–0.28 to 0.04)
	DM	–0.31 (0.08)	–0.19 (0.07)	–0.11 (–0.32 to 0.10)
	Non-DM	–0.25 (0.09)	–0.07 (0.09)	–0.18 (–0.44 to 0.07)
MDAAT, Extramuscular Global Activity, (95% CI)[b]	All	–1.56 (–1.96 to –1.16)	–1.40 (–1.81 to –0.99)	–0.16 (–0.63 to 0.30)
	DM	–1.90 (–2.43 to –1.37)	–1.85 (–2.35 to 1.36)	–0.05 (–0.77 to 0.68)
	Non-DM	–1.09 (–1.46 to –0.72)	–0.85 (–1.27 to –0.43)	–0.24 (–0.80 to 0.32)
MMT-8	All	12.9 (1.9)	11.0 (2.0)	1.8 (–2.7 to 6.4)
	DM	14.4 (2.2)	14.0 (2.2)	0.4 (–5.7 to 6.4)
	Non-DM	12.1 (2.5)	7.8 (2.7)	4.3 (–3.0 to 11.7)
Physician Global Assessment[b]	All	–2.89 (0.30)	–2.69 (0.30)	–0.20 (–0.92 to 0.52)
	DM	–2.78 (0.29)	–2.43 (0.28)	–0.35 (–1.15 to 0.46)
	Non-DM	–2.35 (0.43)	–2.21 (0.48)	–0.14 (–1.43 to 1.15)
Patient Global Assessment[b]	All	–1.4 (0.31)	–0.98 (0.32)	–0.38 (–1.11 to 0.35)
	DM	–1.4 (0.33)	–1.4 (0.31)	–0.00 (–0.91 to 0.90)
	Non-DM	–1.2 (0.41)	–0.3 (0.44)	–0.93 (–2.14 to 0.29)

Data are adjusted mean change from baseline score (SE) unless stated. [a]Defined as improvement of ≥ 20% in 3 IMACS core measures, worsening by ≥ 25% in ≤ 2 IMACS core measure scores, and a reduction of < 25% in MMT-8; [b]100 mm visual analog scale.

Conclusion: In this double-blind trial of SC abatacept vs placebo, abatacept failed to meet primary or secondary endpoints. Post hoc analyses suggest a treatment benefit in patients with PM and ANM (not DM) when treated with abatacept. Abatacept use was well tolerated.

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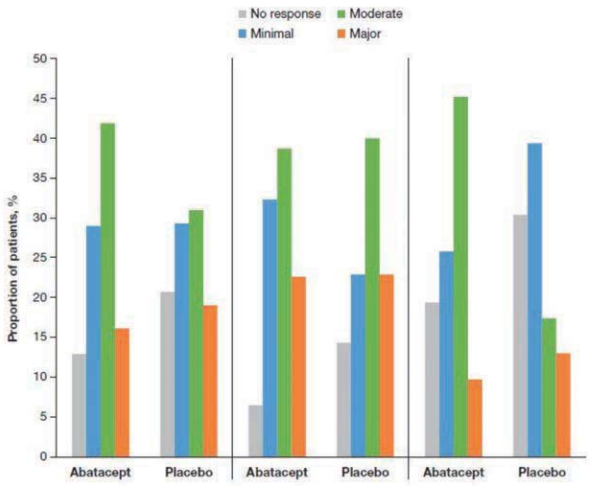
Figure 1. Myositis Response Criteria at day 169 by category



Response at day 169, n/m (%)	All		DM		Non-DM	
No response	8/62 (12.9)	12/58 (20.7)	2/31(6.5)	5/35 (14.3)	6/31 (19.4)	7/23 (30.4)
Minimal (≥ 20)	18/62 (29.0)	17/58 (29.3)	10/31 (32.3)	8/35 (22.9)	8/31 (25.8)	9/23 (39.1)
Moderate (≥ 40)	26/62 (41.9)	18/58 (31.0)	12/31 (38.7)	14/35 (40.0)	14/31 (45.2)	4/23 (17.4)
Major (≥ 60)	10/62 (16.1)	11/58 (19.0)	7/31 (22.6)	8/35 (22.9)	3/31 (9.7)	3/23 (13.0)
Adjusted mean MRC total improvement score	41.5 (n = 47[a])	38.7 (n = 45[a])	46.0 (n = 31[a])	43.6 (n = 35[a])	38.4 (n = 31[a])	31.7 (n = 23[a])

[a]Number of patients with measurements (intention-to-treat analysis population).
n/m, number of patients achieving response/number of patients in the analysis.

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POS0840

MELANOMA DIFFERENTIATION-ASSOCIATED GENE 5 ANTIBODY (ANTI-MDA5) DERMATOMYOSITIS: CLINICAL FEATURES AND OUTCOME IN A RACIALLY DIVERSE PATIENT COHORT

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Background: Melanoma differentiation associated gene 5 antibody (anti-MDA5) dermatomyositis, is an idiopathic inflammatory musculoskeletal disorder with specific phenotypic manifestations of rapidly progressing interstitial lung disease (RP-ILD) and ulcerative skin lesions, with or without muscle involvement. [1] There is currently a lack of consensus and guidelines on early diagnosis and timely escalation of therapy to avoid untoward outcomes.
Objectives: To identify distinguishing clinical and laboratory features to assess disease progression amongst individuals with anti- MDA5 dermatomyositis based on the serologic, histopathologic, and radiographic status. We identified and compared the disease phenotype in a racially diverse juvenile and adult population with anti-MDA5 dermatomyositis.
Methods: After Institutional review board approval, we queried the electronic health record at the Montefiore Medical Center, NY, and identified a total of 194 dermatomyositis patients. We included 21 dermatomyositis patients with MDA5 antibody. We performed a retrospective chart review to extract clinical data and analyzed data using Fischer's exact test.
Results: Of the 21 dermatomyositis patients with anti-MDA5, 12 adult patients represented 8% of all adult dermatomyositis cases (12/148) and 9 patients represented 19 % of the pediatric dermatomyositis cases (9/46). There was a 2:1 female to male predominance in both groups. In adults, the mean age of disease onset was 45.2 years (SD 14.4 years). Nine ILD cases were noted, of which 2 were RP-ILD. The presence of the Ro52 antibody was associated with rapid disease progression. In children, the mean age of onset was 6.6 years (SD 4.9 years). All children had muscle weakness, with only 5 having ILD. Myositis was noted to be more prevalent in the pediatric population, compared to adults (9/9 Vs 4/12 cases; P=0.005). In this patient cohort, ILD was statistically significant between the African American population (9/10 cases) and non-African American population (5/11 cases), p=0.03, of these 3 African American cases had RP-ILD with mortality. The combined mortality rate of 14.2% was superior to 40-60% reported in the literature. [2]
Conclusion: Anti MDA5 dermatomyositis is relatively rare and difficult to diagnose. In this study, the general disease characteristics of our cohort were similar in both adult and pediatric patients except for myositis, which was more common in the pediatric population. The incidence of ILD by contrast was higher in the adults, especially in the African American population who had worse outcomes. The rapid escalation of therapy and use of rituximab may have improved our outcomes over historic controls. Controlled studies are needed to evaluate patients with anti-MDA5 dermatomyositis for appropriate treatment interventions and to avoid untoward outcomes.

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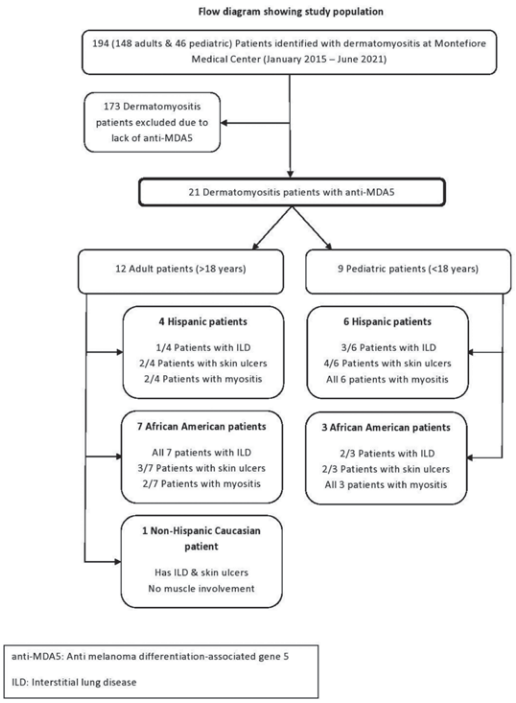

Figure 1.

Disclosure of Interests: None declared
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POS0841

HIGH-INTENSITY INDUCTION THERAPY COMBINING TOFACITINIB, RITUXIMAB, AND PLASMAPHERESIS IN RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE ASSOCIATED WITH ANTI-MDA5 ANTIBODY POSITIVE DERMATOMYOSITIS

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Background: Rapidly progressive interstitial lung disease (RP-ILD) associated with anti-melanoma differentiation-associated protein 5 (MDA5) autoantibody (Ab) -positive dermatomyositis (DM) is one of the most life-threatening autoimmune conditions. The clinical course is very rapid, leading to death within three months after the onset of symptoms. Although triple therapy which consists of corticosteroids, cyclophosphamide, and tacrolimus has been considered as standard therapy and additional treatments including plasma exchange (PE) and rituximab (RTX) have been reported, the survival rate of patients with poor prognostic factors is still poor even if all of these treatments were applied. Recently, there exist increasing evidences regarding the efficacy of tofacitinib (TOF) in refractory DM. We have treated anti-MDA5Ab-positive RP-ILD with multiple poor prognostic factors with high-intensity induction therapy which combined triple therapy, PE, RTX, and TOF.
Objectives: This study aimed to investigate the therapeutic efficacy of high-intensity induction therapy for patients with anti-MDA5Ab-positive RP-ILD with multiple poor prognostic factors.
Methods: 31 patients who were diagnosed with anti-MDA5Ab-positive DM during 2014 to 2021 in our institution were included in this study. The clinical characteristics for poor prognosis were retrospectively analyzed, and the outcomes of high-intensity induction therapy were analyzed for the survival and adverse events.
Results: 17 cases were treated before the introduction of TOF. Although triple therapy with RTX, PE, or intravenous immunoglobulin (IVIG) were used, eight out of 10 RP-ILD cases with a ferritin level >400 ng/mL (range, 402.5-5,831; mean, 2,342 ± 2,069) died in median 2.5 months. Poor prognosis was predicted by followings; elevated levels of serum ferritin, lactate dehydrogenase, transaminases, creatinine phosphokinase, and C-reactive protein; decrease in platelets, serum albumin, and oxygen saturation; use of oxygen; higher age; shorter disease duration to admission. The addition of RTX and PE was not enough to control RP-ILD in anti-MDA5Ab positive DM, and prevention of the initial exacerbation of ILD following induction therapy was considered to be important. Based on these observations, high-intensity induction therapy was consisted as follows; triple therapy with decreasing the dose of methylprednisolone by half from 1g to 1 mg/kg, liposteroid to suppress macrophage activity, TOF, PE, and RTX. High-intensity induction therapy was applied in eight patients (ferritin levels; range, 412.2-7,095 ng/mL; mean, 3,558±3,152 ng/mL) with multiple poor prognostic factors described above. Although deaths at two months and eight months due to ILD were observed, significant improvement of survival was documented (Figure 1). Two patients in whom RTX was not initially administered, exacerbation of ILD was observed one month later, which prompted the use of RTX. Several adverse events were observed in high-intensity induction therapy. The most common events were reactivation of cytomegalovirus, meanwhile herpes zoster was not documented. Sustained leukocytopenia and thrombocytopenia were observed in three patients, and two patients developed thrombotic microangiopathy which led to the discontinuation of tacrolimus. Fungal infections in lung were also documented. These adverse events were controllable.

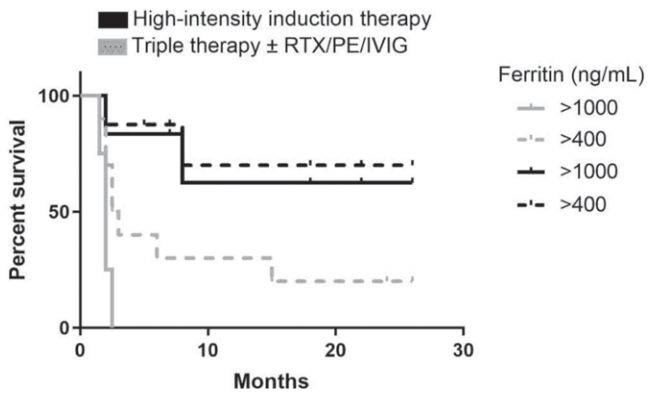

Figure 1.

Conclusion: Significant improvement of survival was observed in patients treated with high-intensity induction therapy. Meanwhile, stratification of patients for poor prognosis would be important.

REFERENCES: None

Disclosure of Interests: None declared
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POS0842 NON-INVASIVE COHERENT RAMAN IMAGING OF INVOLVED FOREARM SKIN REVEALS ALIGNED COLLAGEN IN DERMIS OF SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is an immune-mediated connective tissue disease with clinical hallmark of inflammation, vasculopathy and fibrosis resulting in abnormal collagen and intercellular matrix formation in the dermis and internal organ. Skin severity correlates with systemic complications and mortality in SSc. Many skin assessment tools studied do not fulfilled all standards set by OMERACT which include criterion validity, construct validity, discrimination, responsiveness, reliability and feasibility. Modified Rodnan skin score (mRSS) is commonly used as outcome measure in clinical trials of SSc. It is however, limited by inter-rater variability. Studies also showed that skin biopsy samples from body part of SSc patients with clinically normal mRSS had demonstrable pathological deposition of collagen. While repeat skin biopsy to track longitudinally, may be unacceptable to patients. Hence, ongoing research for non-invasive tools are encouraged.
Objectives: We follow through our previous work studying commercially available non-invasive imaging tools in SSc skin assessment by using Coherent-Raman scattering microscopy (CRS).
Methods: Skin biopsies of 4mm were obtained from SSc (n=3) and HC (n=1). Skin samples were collected at anterior surface of forearm from newly diagnosed diffuse SSc which were treatment naïve. Samples were frozen at -80c prior to analysis under CRS at skin depth of 150-200um. The laser setting was 3% pump (802nm) and 6% stokes (1045nm) to avoid tissue burn. 3 contrast methods used are Coherent anti-Stokes Raman scattering (CARS) for imaging of lipids, Second Harmonic Generation (SHG) for collagen and Two-Photon Fluorescence (TPF) for elastin fibers. We analysed collagen and elastin fibers in the skin samples which is disease relevant end products of fibroblast activation in SSc. Descriptive study of the skin CRS characteristics is reported.
Results: The SHG analysis revealed denser collagen fibers in dermal layer of diseased skin. It also appears that the collagen deposition occurs in more superficial layers of the skin. Peak of collagen curve were at depth of 110-130um HC vs 75-90um in SSc. Collagen fibres were more aligned in the SSc (Figure 1).

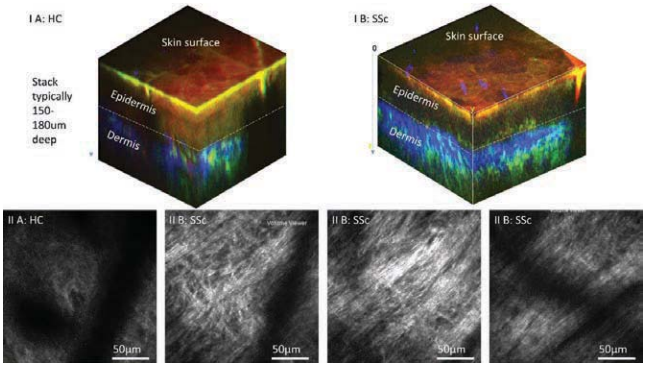

Figure 1. Microscopy analysis of SSc (B) vs HC (A) skin. I: 3D image of biopsy samples with three contrasts. Red is CARS for lipid, blue is SHG for collagen and green is TPF for elastin fibers. II. SHG. Imaging revealed denser and more aligned collagen fibers in SSc.

Furthermore, TPF revealed larger number of disordered elastin fibres in the dermal layer of SSc than HC.
Conclusion: Nailfold capillaroscopy is used to define and stage micro-vasculopathy in SSc. Inflammatory pro-fibrotic processes on the other hand cause abnormal collagen and intercellular matrix formation in the dermis and internal organ. With the demand of better tools in diagnosis of early SSc and therapeutic research, our work with CRS prove better in objective evaluation of skin changes at the molecular level. Here, we demonstrate that the SHG is altered in the early diffuse SSc skin with increased and aligned collagen in the SSc dermis compatible with mRSS score. Others have observed this alignment of the collagen, and we have published that SSc fibroblasts migrate/invade along aligned collagen and modify the underlying extracellular matrix, adding collagens I and III, cross-linking enzymes and other factors including TSP-1.
Our future work include:
1.Generating a computer module in defining pathological collagen level
2.Analysis of metabolites and pathological pathways in SSc
3.In-vivo trials with novel therapeutic peptides.
4.Lastly, manufacturing of non-invasive handheld device that is capable of diagnosis subclinical SSc and for outcome measure in clinical-therapeutic research

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POS0843 PREDICTORS OF INTERSTITIAL LUNG INVOLVEMENT AND TIMING OF ONSET IN SYSTEMIC SCLEROSIS: OUR EXPERIENCE AT A THIRD-LEVEL HOSPITAL

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Background: Interstitial lung disease (SSc-ILD) and pulmonary hypertension are the leading causes of death in patients with systemic sclerosis (SSc). Identifying SSc-ILD development and initiating treatment is essential to optimize therapeutic benefit.
Objectives: We aimed to identify predictors of SSc-ILD and compared early (<5 years from diagnosis) versus late (>5 years from diagnosis) onset.
Methods: We conducted a retrospective cohort study by including patients diagnosed with SSc from 1980 to 2020 followed in our unit and compared the clinical profile of patients with SSc-ILD to control SSc-non-ILD patients. Demographic features, clinical and immunological characteristics, baseline pulmonary function and capillaroscopy data were retrieved. Logistic regression modelling was run to identify factors associated with SSc-ILD development. Factors associated with ILD were then determined as factors associated with early or late onset using multivariate analysis. Bonferroni correction was used to limit Type I errors.
Results: We have included 103 patients from our patient registry from 1980 to 2021 (42% with SSc-ILD). Logistic regression identified risk factors associated with increased or decreased odds ratio for developing ILD is summarized in Table 1. Smoking history, male sex, the presence of myositis, anti-Scl70 and anti-Ro52 positivity, baseline pulmonary function including FVC and DLCO, mMRC (Modified Medical Research Council) dyspnea scale>2, mMSS (Modified Rodnan Skin Score), and late pattern in capillaroscopy were identified as SSc-ILD predictors. Older age at SSc diagnosis, the presence of telangiectasias and smoking status were correlated with of SSc-ILD onset before 5 years, while male gender, the presence of myositis and antiphospholid antibodies were correlated with late-onset SSc-ILD.

Table 1. Significant logistic regressions for predictors for SSc-ILD

Predictor	OR (95% CI)	P value
Male	2.8 (1.16-6.8)	0.02
Smoking history	2.15 (1.33-3.46)	0.001
Diffuse cutaneous involvement	10.4 (2.2-48.3)	0.003
Raynaud duration	0.89 (0.79-1.0)	0.04
Myositis	3.45 (1.09-10.9)	0.03
Anti-Scl70	5.45 (2.02-14.7)	0.001
Anti-Ro52	3.37 (1.49-9.45)	0.002
FVC	0.97 (0.91-0.98)	0.03
DLCO	0.96 (0.93-0.98)	0.003
mMSS	3.73 (1.64-8.5)	0.01
mMRC>2	2.01 (1.52-4.2)	0.04
Late capilaroscopy pattern	2.3 (1.02-5.27)	0.04
Early onset SSc-ILD	**β value**	**P value**
Older age at onset	0.47	0.0017
Telangiectasias	0.29	0.04
Smoking stauts	0.37	0.02
Late onset SSc-ILD	**β value**	**P value**
Male gender	0.57	0.001
Myositis	0.34	0.02
Antiphospholipid antibodies	0.31	0.04

Conclusion: We identified 10 factors significantly associated with risk of developing SSc-ILD: smoking, male sex, diffuse cutaneous involvement, the presence of myositis, shorter Raynaud duration to SSc diagnosis, anti-Scl70 and anti-Ro52 positivity and baseline pulmonary function (lower baseline DLCO and FVC increasing risk) and late capillaroscopy pattern and identified predictors for early and late-onset SSc-ILD.

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POS0844 LONG-TERM AND SHORT-TERM RISK OF MALIGNANCY IN IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Idiopathic inflammatory myopathy (IIM) is associated with a high prevalence of malignancy, in which anti-transcriptional intermediary factor 1-γ(TIF1-γ) antibody is at a high risk of malignancy compared to the other myositis-specific antibodies, including anti-aminoacyl-tRNA synthetase (ARS), melanoma differentiation-associated gene 5 (MDA5), and Mi-2 antibody [1]. Although some subgroups of IIM have a high risk of malignancy up to 10 years after diagnosis [2], long-term relationships between malignancy and each antibody are not elucidated so far.

Objectives: To clarify the risk of malignancy in IIM in each antibody type with standard incidence ratios (SIR) of malignancy and the long-term occurrence of malignancy.

Methods: From our IIM cohort at the University of Tokyo hospital, we enrolled patients who fulfilled with Bohan and Peter criteria for dermatomyositis/polymyositis or 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for IIMs and with positivity for anti-ARS, MDA5, Mi-2, or TIF1-γ antibody. We retrospectively collected the data and calculated SIRs by using the database of Cancer Statistics, Cancer Information Service, National Cancer Center, Japan. Fisher exact test and Wilcoxon test were used to compare the clinical features in each group. Cumulative incidence of cancer occurrence was estimated by Kaplan-Meier methods, and Log-rank test was used to compare the cancer-free survival.

Results: The study included 111 patients, including 16 patients being diagnosed with a malignancy within a three-year before and after the occurrence of IIM. Patients with malignancy were significantly older age at the onset of IIM (median age (interquartile range) 67.5 (62.3-70.8) vs. 52.0 (41.5-61.5). p<0.001) and more frequently with anti-TIF1-γ antibody (25.0% vs. 4.2%, p=0.015). After adjustment for age, the proportion of anti-TIF1-γ antibody remains significantly higher in the malignancy group (p=0.01). SIRs (95% confidence interval) in each type of antibody were anti-ARS of 2.21 (1.03-4.55), anti-MDA5 of 1.89 (0.49-6.02), anti-Mi-2 of 2.75 (0.14-17.84), and anti-TIF1-γ of 14.73 (4.72-40.50) (Table 1). Types of malignancy included four gastric cancers, two bladder cancers, breast cancers, cervical cancers, ovarian cancers, and lung cancer, one pancreatic cancer, rectal cancer, and renal cancer. Kaplan-Meier estimated cancer-free survival was significantly lower in patients with anti-TIF1-γ antibody than patients with anti-ARS antibody (p<0.01) (Figure 1). The frequencies of malignancy of IIM patients with anti-ARS, MDA5, Mi-2, or TIF1-γ antibody through the follow-up period were 15.6%, 20.0%, 11.1%, 50.0%, respectively.

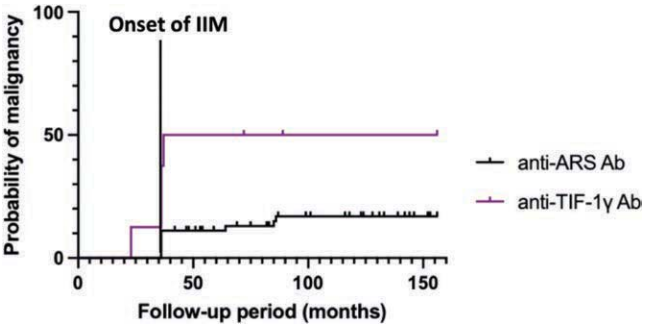

Figure 1. Comparison of malignancy rate of idiopathic inflammatory myopathy with anti-ARS, and TIF1-γ antibodies in 10 years.

Table 1. Standard incident ratio (SIR) of malignancy in idiopathic inflammatory myopathy according to myositis-specific antibodies.

	Total (Person-years)	Observed	Expected	SIR (95% CI)
Anti-ARS antibody	510	8	3.62	2.21 (1.03-4.55)
Anti-MDA5 antibody	210	3	1.59	1.89 (0.49-6.02)
Anti-Mi-2 antibody	56	1	0.36	2.75 (0.14-17.84)
Anti-TIF1-γ antibody	39	4	0.27	14.73 (4.72-40.50)
Total	815	16	5.84	2.74 (1.62-4.56)

Conclusion: IIM patients with anti-TIF1-γ antibody and with anti-ARS antibody had a higher prevalence of malignancy than the general population. In addition, anti-TIF1-γ antibody are more associated with malignancy rather than anti-ARS antibody in 10 years as well. Malignancy associated with anti-TIF1-γ positive IIM occurred exclusively within the one year before and after the IIM diagnosis, and cancer should be particularly investigated at the IIM diagnosis.

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POS0845 ASSESSING FRAILTY IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY COMPARING FRAIL AND EDMONTON FRAILTY SCALES WITH PHYSICAL FRAILTY PHENOTYPE

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Background: Systemic sclerosis (SSc) is a chronic disease characterized by autoimmunity, vasculopathy and fibrosis. During the disease course, patients with SSc are prone to accumulate multiple organ damage, increasing their vulnerability to adverse outcomes in comparison with individuals of the same age: a phenomenon called frailty. One of the most used definitions of frailty is the physical frailty phenotype (PFP) by Fried, *et al*. The PFP consists of 5 components: unintentional weight loss, exhaustion, muscle weakness, slow walking speed, and low physical activity. There is scarce data about frailty in patients with SSc.

Objectives: To study the prevalence and clinical aspects of PFP in a sample of patients with SSc. Also, we aim to investigate the diagnostic accuracy of the Fatigue, Resistance, Ambulation, Illness and Loss of weight (FRAIL) scale and the Edmonton frailty scale (EFS) using the PFP as the reference standard.

Methods: Cross-sectional study, including patients with SSc according to the 2013 ACR-EULAR classification criteria or the criteria suggested by Le Roy and Medsger for early disease. PFP assessment was according to the original definition, except for physical activity domain, assessed with the International Physical Activity Questionnaire (IPAQ). Patients were classified according to Fried's criteria in robust (0), pre-frail (1-2), and frail (≥3). FRAIL scale and EFS were also applied to the same individuals. The FRAIL score ranges from 0 to 5 and patients were classified as robust (0), pre-frail (1-2), or frail (≥3). The EFS score ranges from 0–17 and categorizes patients as not frail (0–4), vulnerable (5–6), mild frailty (7–8), moderate frailty (9–10), and severe frailty (≥11). For the diagnostic assessment of FRAIL scale and EFS, we estimated the area under the receiver operating characteristic curve (AUC), considering PFP as the reference standard and dichotomizing the results in frail vs. non-frail.

Results: Between March and December 2019, 82 SSc patients were consecutively included. The mean age and disease duration were 60.4 (±10.6) and 13.4 (±8.2) years, respectively; 91.5% were women, and 19.5% with diffuse cutaneous SSc. The PFP distribution was: 8 (9.8%) robust, 47 (57.3%) pre-frail and 27 (32.9%) frail patients. The PFP domains´ frequencies were: low physical activity in 57 (69.5%), muscle weakness in 41 (50%), exhaustion in 34 (41.5%), unintentional weight loss in 15 (18.3%) and slow walking speed in 8 (9.8%) patients.

Using the FRAIL scale, 44 (53.7%) patients were considered pre-frail and 25 (30.5%) frail. According to the EFS, 26 patients (31.7%) were classified as vulnerable and 12 (14.6%) as frail: mild in 6 (7.3%), moderate in 4 (4.9%) and severe in 2 (2.4%). The AUC against PFP was: 0.871 (95% CI 0.789-0.954, p<0.001) for FRAIL scale and 0.870 (95% CI 0.791-0.948, p<0.001) for EFS (Figure 1).

Conclusion: Frailty is prevalent in patients with long-standing SSc, and most of them are considered pre-frail or vulnerable. Low physical activity, muscle weakness and exhaustion are among the most frequent clinical aspects of the frailty phenotype. Both FRAIL scale and EFS showed overlapping diagnostic accuracy against PFP as the reference standard, and FRAIL scale seems to be more feasible than EFS.

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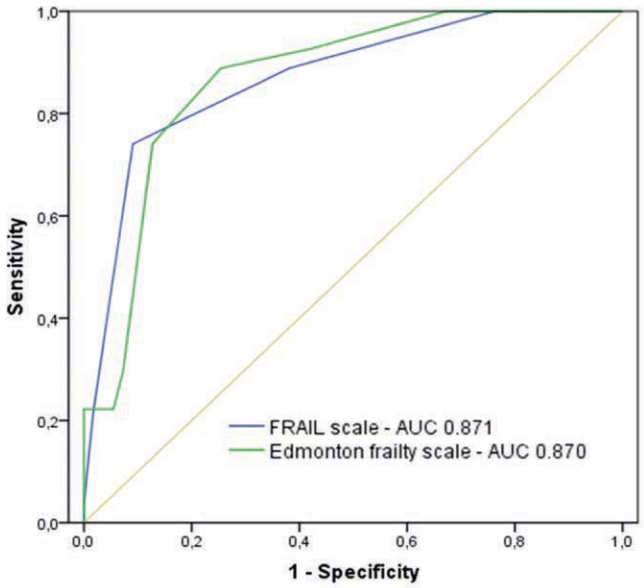

Figure 1. Receiver operating characteristic (ROC) curve analysis of two scales in relation to frailty defined according to physical phenotype: FRAIL and Edmonton frailty scales.

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POS0846

MORTALITY OUTCOME OF ACUTE MYOCARDIAL INFRACTION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES, A QUALITATIVE APPROACH ANALYSIS OF THE NATIONAL INPATIENT SAMPLE FROM 2016-2019

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Background: The pathophysiology of cardiovascular damage in myositis is a multi-factorial process. Myositis can cause inflammation of the myocardium with accelerated coronary atherosclerosis,the risk of cardiovascular disease in hospitalized patients with idiopathic dermatomyositis was 15% from 2016-17.[1]

Objectives: To investigate the quality of care of acute myocardial infarctions (AMI) events in myositis compared to non-myositis patients across the United States categorized by the types of hospitals, probability of myocardial events, and mortality outcome from the NIS from 2016-19.

Methods: We used SAS statistical software to perform analyses on the NIS database (2016-19) in the US. Adults with AMI and myositis at the time of discharge were identified by International Statistical Classification of Disease 10 (ICD-10) codes. Latent class analysis was used to empirically identify hospital groups across different regions in the U.S where myositis patients received their cardiac care. Once hospital groups were determined, patients were compared with and without myositis in each hospital group. Probabilities of AMI event and mortality among myositis patients were compared using logistic regression analysis.

Results: The NIS sample included 38,363 myositis patients and 24,179,176 non-myositis patients. Three hospital groups were identified, the first two represented inner-city hospitals, with the second group of hospitals tending to be larger and serving lower income patients (Table 1). The third hospital group represented rural hospitals, though they also tended to perform fewer cardiac procedures. Importantly, this third group was about half as likely to identify myositis patients and more likely to identify the unrelated confounder conditions. (myositis=0.10%, confounder=41.0%) This provides evidence that rural hospitals may lack the training and resources to properly care for myositis patients, as hypothesized. Overall, the odd ratio (OR) for myositis patients to have AMI event was 0.83 ($p < 0.0001$); among those who had AMI events, OR for mortality was 0.60 ($p < 0.0001$). Patients who received care at more rural hospitals (group 3) were at heightened mortality risk (OR=1.12, $p < 0.0001$). Opposite to the patient experiences in urban hospitals, the unique risk of mortality to myositis patients in rural hospitals was heightened (OR = 1.88, $p < 0.0001$).

Conclusion: Myositis was not associated with higher AMI events and mortality outcomes in this nationwide hospitalization cohort. Hospitals in rural locations had fewer diagnosed cases of myositis, catheter procedure and transfer out rate may have contributed to higher AMI mortality outcome in group 3. Further studies should examine if catheter procedure mortality outcome of AMI event in myositis differ in the three hospital groups.

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POS0847

MYOSITIS AUTOANTIBODIES DETECTED BY LINE BLOT IMMUNOASSAY: CLINICAL ASSOCIATIONS AND CORRELATION WITH ANTIBODY TITERS

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Background: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune diseases (AID) characterized by muscle inflammation and weakness, often accompanied with other organ involvement, such as skin rash or interstitial lung disease (ILD). Myositis specific (MSA) and myositis associated

Table 1. Hospital Characteristics and Patient Outcomes

Trait	Group 1	Group 2	Group 3		Group 1	Group 2	Group 3	Overall
Patient Diagnoses (%)				**MI Event (%)**				
Myositis ^	0.22	0.18	0.10	**Myositis patients**	19.02	11.31	9.89	
Myocardial infarction ±	8.97	7.02	10.85	**Non-myositis patients**	22.13	12.05	12.59	
Unrelated confounder *	34.64	35.87	41.60	**OR**	0.86	0.94	0.79	0.83
Catheter procedures	2.52	2.39	0.84	***p***	0.0026	< 0.0001	< 0.0001	<0.0001
Hospital Characteristics				**Mortality (%)**				
Bedsize (1 = small to 3 = large)	1.31	1.36	1.86	**Myositis patients**	6.12	5.15	10.02	
Rural setting (%)	7.08	0.64	37.00	**Non-myositis patients**	9.77	6.82	8.95	
Transfers out (%)	20.03	20.61	17.12	**OR**	0.63	0.76	1.12	0.60
Patient income quartiles (M)	2.10	1.75	2.12	***p***	0.0001	< 0.0001	< 0.0001	< 0.0001

^ Based on ICD 10 codes under M33, M60 and G72 groups± Based on ICD 10 codes under I21group* Confounder diagnoses: hypertension, hyperlipidemia, diabetes mellitus, tobacco/alcohol/substance abuses, obesity, rheumatoid arthritis, systemic lupus erythematosus and gout.

antibodies (MAA) can be detected in approximately 60% of patients with IIM. Besides, antibody titers have been suggested to be related with diagnostic accuracy, although it has not been widely studied. MSA are considered to be exclusive of patients with IIM, whilst MAA can occur in IIM and other systemic autoimmune diseases, nevertheless, most of the studies are focused exclusively on IIM patients.

Objectives: The aim of this study is to assess the relationship between MSA/MAA and diagnosis (including IIM and other AID), and to explore the impact of antibody titers in diagnostic accuracy.

Methods: We retrospectively reviewed all the serum samples obtained from patients tested for MSA/MAA between 01/01/2018 and 31/12/2020 in the Immunology department of Ramón y Cajal University Hospital (Spain). These antibodies were tested by line blot immunoassay (LIA) (EUROLINE Autoimmune Inflammatory Myopathies 16 Ag, Euroimmun, Lübeck, Germany). Positivity was stablished according to absorbance titer and adjusted by positive control of each test (arbitrary units, AU). True positive (TP) MSA and MAA were defined as those patients with IIM or AID with phenotypes expected of that MSA/MAA, according to the available information. The patients that did not have a phenotype compatible with that antibody were regarded as false positive (FP). Statistical analysis was carried out using IBM SPSS statistics version 22.

Results: We analyzed 130 positive samples which corresponded to 130 patients, 85 were women and mean age was 55.08 years. 44 patients (33.8%) were classified as IIM, 43 (33.1%) as AID, and 43 (33.1%) as non-IIM/AID. Among these 130 patients, 164 MSA/MAA were detected. 83 (50.6%) positive MSA/MAA were regarded as TP, and 81 (49.4%) as FP (positive predictive value [PPV] 50.6%). Antibodies regarded as TP had a higher antibody titer compared to FP (49,19 AU vs 26,96 AU, p<0.001). This difference was statistically significant for MSA and MAA when analysed separately (Figure 1). FP antibodies were associated with negative ANA and low titer ANA (p<0.001). Multiple positive antibodies (antibodies included in samples that were positive for > 1 MSA/MAA) were more frequently FP in comparison with isolated positive MSA/MAA (p<0.001).

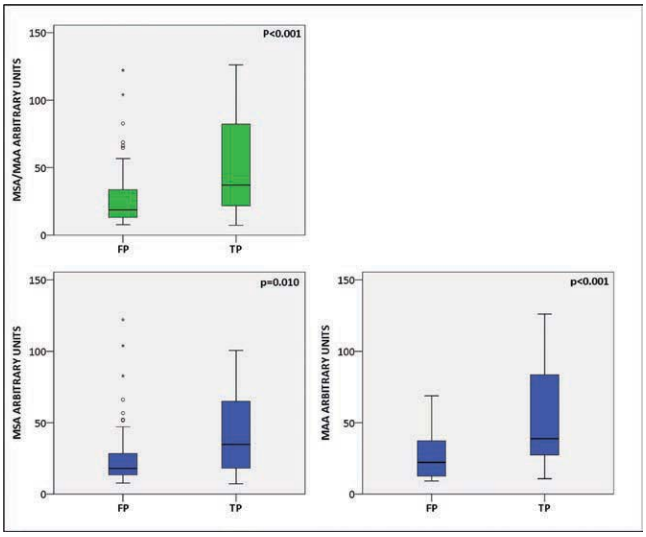

Figure 1. Autoantibody titers comparison between false positives and true positives. MSA=myositis specific antibody, MAA=myositis associated antibody, FP=false positive, TP=true positive

Conclusion: In this study we confirm that FP results using LIA are relatively frequent, and are associated with lower titer MSA/MAA, negative ANA, lower titer ANA, and with multiple positive MSA/MAA within one sample.

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POS0848 HEALTHCARE RESOURCE UTILIZATION AND COST BURDEN OF DERMATOMYOSITIS

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Background: Dermatomyositis (DM) is a rare chronic systemic autoimmune disease characterized by muscle weakness and skin rashes. DM is also frequently associated with other clinical manifestations including interstitial lung disease, calcinosis, dysphagia, cardiac involvement, and malignancy. With few approved treatment options, DM has high morbidity and mortality. Limited information is available on the economic impact imposed by DM on the healthcare system.

Objectives: To estimate the economic burden associated with DM in a prevalence cohort, including healthcare resource utilization and costs from both the health insurance plan and patient perspectives.

Methods: A retrospective cohort study was conducted using a large, integrated administrative database of employer-sponsored commercial and public health plans in the United States (PharMetrics Plus, Jan 2014 - June 2020). Patients (age ≥18 years) were selected if they were diagnosed with dermatomyositis (≥1 inpatient claim or ≥2 outpatient claims ≥30 days apart with International Classification of Diseases, 10th Revision, Clinical Modification: M33.0x, M33.1x, or M33.9x) and continuously enrolled in the health plan during the 6 months before (baseline) and 1 year after (follow-up) a randomly selected DM diagnosis date (index date). Patients were matched 1:3 to a control group without DM or related myositis conditions based on birth year, gender, census region, insurance plan type, and index year. Healthcare resource use (HCRU) and costs over the 1-year follow-up period were compared between patients with DM versus matched controls to assess the incremental economic burden of DM. Statistical comparisons were conducted using generalized estimating equation models with binomial, negative binomial, or Tweedie distributions for binary, count, and cost outcomes, respectively. The models used robustly clustered standard errors to account for correlation between the matched samples.

Results: Patients with DM (N=3,207) and matched controls (N=9,621) were 49.4 years old on average and 76.8% were female. HCRU was significantly higher among patients with DM than controls in terms of outpatient, inpatient, emergency room, and other medical visits (all p<0.001; Table 1). Medical service and pharmacy costs to the plan were also significantly higher for patients with DM (p<0.001 vs. controls for all cost categories; Figure 1). Total annual costs to the healthcare plan were 5.4-fold higher among patients with DM (mean ± standard deviation: $39,508 ± 83,093) relative to controls without DM ($7,349 ± 32,816) (Δ=$32,159; p<0.001). Outpatient visit costs ($28,131) comprised 71.2% of the total for patients with DM; costs of outpatient-administered DM-related treatments ($15,855) accounted for the majority of outpatient visit costs. Patients with DM incurred 2-fold higher out-of-pocket costs (coinsurance, copayments, or deductibles) than controls ($4,803 ± 13,181 vs. $2,456 ± 10,708; Δ=$2,346; p<0.001).

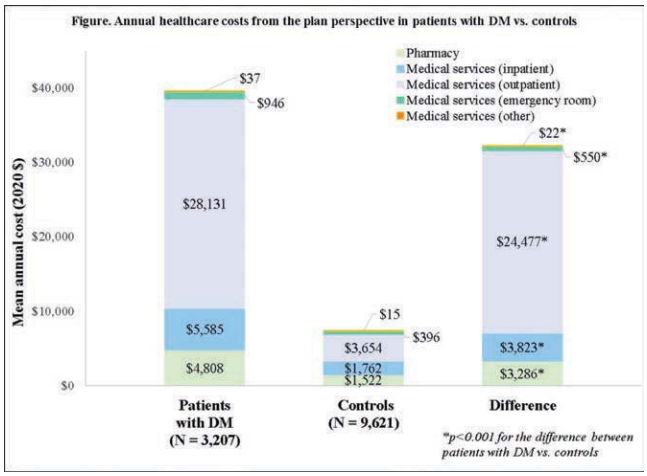
Table 1. Annual resource use in patients with DM vs. controls

	Patients with DM N = 3,207	Controls N = 9,621	IRR or OR	95% confidence interval	P-value
Inpatient admissions, mean ± SD	0.2 ± 0.7	0.1 ± 0.4	3.1	(2.6 - 3.7)	< 0.001
Any inpatient admission, %	12.1%	4.9%	2.7	(2.3 - 3.1)	< 0.001
Outpatient visits, mean ± SD	27.7 ± 31.7	10.8 ± 18.9	2.6	(2.4 - 2.7)	< 0.001
Emergency room visits, mean ± SD	0.7 ± 1.6	0.4 ± 1.2	1.8	(1.6 - 2.0)	< 0.001
Any emergency room visit, %	30.4%	20.7%	1.7	(1.5 - 1.8)	< 0.001
Other visits, mean ± SD	0.3 ± 0.8	0.2 ± 0.7	1.8	(1.6 - 2.1)	< 0.001
Any other visit, %	20.0%	11.2%	2.0	(1.8 - 2.2)	< 0.001

IRR: incidence rate ratio; OP, outpatient; OR: odds ratio, SD: standard deviation.*Notes:* IRRs are reported for count outcomes; ORs are reported for binary outcomes. Other visits include durable medical equipment and dental or vision care.

Conclusion: DM is associated with substantial HCRU and costs per patient, with average incremental costs of $32,159 to the health plan and $2,346 to the patient

annually as compared to controls. This study is among the first to document the clinical burden leading to high economic impacts of DM.



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POS0849 DEVELOPMENT AND VALIDATION OF A MACHINE LEARNING FOR MORTALITY IN THAI SYSTEMIC SCLEROSIS

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Background: Clinical predictors of mortality in systemic sclerosis (SSc) are diversely reported due to different healthcare conditions and populations. A universal and simplified predictive model for SSc mortality is needed so that practitioners can be used for managing their patients appropriately.
Objectives: We aimed to develop and validate a simple predictive model for predicting mortality among patients with SSc.
Methods: Prognostic research with a historical cohort study design was conducted between January 1, 2013, and December 31, 2019, **in** adult SSc patients and attending the Scleroderma Clinic at a university hospital in Thailand. The data were extracted from the Scleroderma Registry Database. A deep learning algorithm with Adam optimizer and different machine learning algorithms (including Decision tree, AdaBoost, Random Forest, Gradient Boosting, and XGBoost) was used to classify SSc mortality. In addition, the model's performance was evaluated using the area under the receiver operating characteristic curve (auROC) and its 95% confidence interval (CI) and values in the confusion matrix.
Results: The analysis and predictive model development included 658 SSc patients, 416 (63.2%) females, 452 (69.1%) had dcSSc, and 218 died. The final model included the modified Rodnan skin score (mRSS) and the WHO functional class (WHO-FC) ≥II (model 1). The final model provided the highest predictive performance, followed by model 2 (mRSS and WHO-FC ≥III). After internal validation, the accuracy and auROC were good, and the specificity was high in models 1 and 2 (81.1%, 0.84, and 95.5% in model 1 vs. 82.7%, 0.82, and 87.1% in model 2).
Conclusion: This simplified machine learning model for predicting mortality among patients with SSc could guide early referrals to specialists and help rheumatologists with close monitoring and management planning. External validation across multi-SSc clinics should be considered for further study.
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POS0850 A PHASE II RANDOMISED CONTROLLED TRIAL OF ORAL PREDNISOLONE IN EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (PREDSS)

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Background: A highly controversial question is whether or not corticosteroids should be prescribed for patients with early diffuse cutaneous systemic sclerosis (dcSSc). Although the painful and disabling features of early dcSSc (including tight itchy skin, contractures, fatigue) have an inflammatory basis and are likely to respond to corticosteroids, corticosteroids are a risk factor for potentially life-threatening scleroderma renal crisis.
Objectives: Our aim was to examine safety and efficacy of moderate dose prednisolone in patients with early dcSSc. Specific objectives were to evaluate whether moderate dose prednisolone reduced pain and disability, and improved

Table 1. Generalizability of selected model(s) presented as accuracy, area under ROC, positive predictive value, positive likelihood ratio, specificity, and sensitivity

Selected Model	Accuracy	AUC (95%)	PPV (95%)	+LR (95%CI)	Specificity (95%)	Sensitivity (95%)
Model 1 mRSS and WHO FC ≥ II	81.1	83.6 (77.5 – 89.6)	84.6 (69.5 - 94.1)	11.3 (5.0-25.7)	95.5 (90.4 - 98.3)	51.6 (38.7 - 64.2)
Model 2 mRSS and WHO FC ≥ III	82.7	82.4 (75.8 - 88.9)	73.4 (60.9 - 83.7)	5.7 (3.6-9.1	87.1 (87.2 - 92.3)	73.4 (60.9 - 83.7)

95%CI 95% confidence interval, AUC Area Under the receiver operating characteristics (ROC), mRSS modified Rodnan skin score

skin score, and whether prednisolone was safe with particular reference to renal function

Methods: PRedSS set out as a Phase II, multicentre, double-blind randomised controlled trial, converted to open-label because of the Covid-19 pandemic. Patients were randomised to receive either moderate dose prednisolone (approximately 0.3 mg/kg) or matching placebo (or no treatment during open-label) for 6 months. The co-primary endpoints were the Health Assessment Questionnaire Disability Index (HAQ-DI) and modified Rodnan skin core (mRSS) at 3 months. Over 20 secondary endpoints included patient reported outcome measures reflecting pain, itch, anxiety and depression, fatigue and helplessness. 72 participants randomised 1:1 were planned and anticipated to yield 60 evaluable, giving over 80% power for each co-primary outcome in ANCOVA analyses [assumptions; HAQ-DI ($\alpha = 0.025$, $\delta = -0.6$, $\sigma = 0.9$, $\rho = 0.6$), mRSS ($\alpha = 0.025$, $\delta = -5.5$, $\sigma = 8.2$, $\rho = 0.6$)]. Mixed Models for Repeated Measures (week 6, month 3, month 6) were fitted with covariates trial arm, baseline score, anti-Scl-70 and their interactions with time point. An unstructured covariance matrix was assumed with the primary focus being the trial arm effect at 3 months.

Results: The study terminated early due to the Covid-19 pandemic and consequently did not meet the recruitment target of 72 patients. Thirty-five patients (Table 1) were randomised (17 to prednisolone and 18 to placebo/control, 25 during the double-blind phase), of whom 34 completed the 3 month assessment. The adjusted mean difference between treatment groups at 3 months in HAQ-DI score was -0.10 (97.5% CI -0.29 to 0.10), p=0.25, and in mRSS -3.90 (97.5% CI -8.83 to 1.03), p=0.070, both favouring prednisolone but not significantly. Patients in the prednisolone group experienced less pain, helplessness and anxiety than control patients at 3 months: mean difference in pain scores -0.49, 95%CI (-0.93 to -0.06), p=0.027, in Hospital Anxiety and Depression (HADS) anxiety scores -2.05, 95%CI (-3.73 to -0.37), p=0.018, and in helplessness scores -1.54, 95%CI (-3.01 to -0.07), p=0.040. There were no renal crises.

Table 1. Baseline characteristics of patients by treatment allocation

Characteristic	Prednisolone (n=17)	Control (n=18)
Age (years)	52.7 (14.0)	55.3 (12.7)
Female n (%)	10 (59)	9 (50)
Duration of skin thickening (years)	1.6 (0.8)	1.7 (0.8)
Anti-topoisomerase-1 n (%)	5 (29)	6 (33)
Anti-RNA polymerase III n (%)	6 (35)	8 (44)
HAQ-DI	1.6 (0.8)	1.7 (0.7)
mRSS	18.8 (7.9)	23.5 (8.6)

Values are mean (standard deviation) unless stated otherwise

Conclusion: PRedSS exemplified the challenges of running a clinical trial of an investigational medicinal product potentially associated with increased infection risk during the Covid-19 pandemic. Because PRedSS was terminated prior to target recruitment, it was underpowered, and any conclusions have to be extremely cautious. Although PRedSS suggested some benefit from moderate dose prednisolone, the small sample indicates the need for a further randomised trial.

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POS0851 FREQUENCY OF METABOLIC SYNDROME AND ITS RELATIONSHIP WITH DISEASE CHARACTERISTICS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Although the frequency of metabolic syndrome (MetS) has been found to increase in many rheumatological diseases such as rheumatoid arthritis, systemic lupus erythematosus, few studies have been conducted on the frequency of MetS in systemic sclerosis (SSc), and the results are inconsistent.

Objectives: In our study, we aimed to investigate the frequency of MetS in patients with SSc and its relationship with disease characteristics including organ involvement.

Methods: In a cross-sectional, single-center study, 76 patients who applied to our outpatient clinic between July and September 2021 were included in the study. MetS diagnoses were determined according to anthropometric measurements, lipid parameters, blood pressures, and NCEP ATP 3 criteria, and its relationship with SSc end-organ involvement and disease characteristics was examined.

Results: MetS was detected in 37 (48.7%) of 76 patients. Systolic and diastolic blood pressure, waist circumference, height, body mass index, LDL, triglyceride, and fasting blood glucose mean were found to be statistically significantly higher in patients with MetS ($p<0.05$). In addition, HDL was found to be significantly lower in patients with MetS diagnosis than in patients without MetS ($p<0.05$). While no significant relationship was found between MetS and SSc end-organ involvement, SSc disease activities (RAI, SCTC-DI), disease duration, a significant statistical relationship was found between MetS and modified Rodnan skin score (mRSS). It was found that patients with MetS had lower mRSS (p:0.019). According to ROC analysis, the mRSS cut-off point that predicting the presence of MetS was mRSS ≤11 (specificity: 84%, sensitivity: 45.95%, AUC: 0.656, p: 0.014). No statistically significant correlation was found in the comparison with MetS risk factors for mRSS ≤11.

Conclusion: In our study, the frequency of MetS in patients with SSc was found to be lower than in the same age group in Turkey MetS prevalence studies. The frequency of Mets in our study is thought to be due to age and gender dominance rather than SSc itself. Although mRSS was found to be significantly lower in patients with MetS, its sensitivity to predict MetS was found to be low. MetS is less common in patients with high mRSS; It is thought that cachexia due to inflammation, loss of appetite, and malnutrition due to GI involvement may have been effective.

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POS0852 SYMPTOMS OF GASTROESOPHAGEAL REFLUX ARE A BETTER PREDICTOR OF SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE PROGRESSION THAN QUANTITATIVE RADIOGRAPHIC ASSESSMENT OF ESOPHAGEAL PARAMETERS

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Background: Esophageal dysfunction affects the majority of patients with systemic sclerosis (SSc). Gastroesophageal reflux (GERD)-associated microaspiration may serve as an inciting and/or exacerbating factor in the pathogenesis of interstitial lung disease (ILD) in SSc. Few studies have investigated the relationship between objective measures of esophageal involvement in SSc and the progression of SSc-ILD.

Objectives: (1) To investigate whether patient-reported symptoms of GERD predict SSc-ILD severity and progression; (2) To explore whether quantitative radiographic measurements of esophageal parameters predict SSc-ILD severity and progression.

Methods: Participants of Scleroderma Lung Study (SLS) II (24 months of mycophenolate versus 12 months cyclophosphamide followed by 12 months of placebo in patients with active SSc-ILD) were included.[1] The UCLA SCTC GIT 2.0 was used to assess the severity of reflux at baseline. Quantitative image analysis was used to calculate the diameter and area of the esophagus in the area of maximum dilation. Univariate and multivariable linear regression analyses were used to evaluate the relationship between baseline reflux scores/esophageal parameters and the severity and progression of SSc-ILD based on the

quantitative radiographic extent of ILD (QILD) and fibrosis (QLF) in the lobe of maximum involvement (LM). All multivariable models controlled for treatment arm and baseline ILD severity, as well as proton pump inhibitor (PPI) use.

Results: Among the 141 of 142 SLS II participants with patient-reported reflux scores at baseline, the mean score was 0.57, indicating moderate reflux. The mean maximal esophageal diameter and area at baseline were 22 mm and 242 mm^2, respectively. There were no significant correlations between reflux scores, esophageal diameter, esophageal area and QILD-LM and QLF-LM at baseline. However, in the 96 participants with HRCT scans available at 24 months, increased reflux scores were significantly associated with worsening of QLF-LM and QILD-LM (Figure 1). Even after controlling for disease severity at baseline, treatment arm and PPI use, reflux scores remained significantly associated with change in QLF-LM (P-value 0.05) and QILD-LM (P-value 0.003). Neither the maximum esophageal area, nor the maximum esophageal diameter was associated with the change in QILD-LM or QLF-LM in univariate or multivariate analyses.

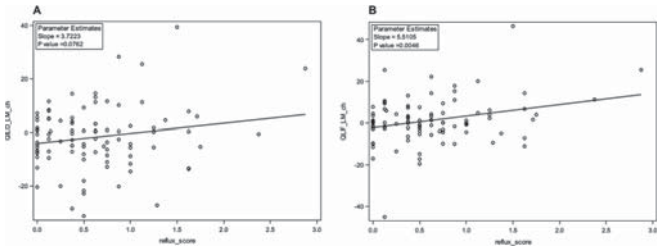

Figure 1. Increased reflux scores at baseline are associated with increased progression (worsening) of QILD (A) and QLF (B) in the lobe of maximum involvement in patients with SSc-ILD.

Conclusion: Increased self-reported reflux was independently associated with worsening radiographic fibrosis and ILD in patients receiving treatment for SSc-ILD. The maximum esophageal diameter and esophageal area did not correlate with reflux scores and did not predict severity or progression of SSc-ILD. These findings illustrate the importance of eliciting a careful patient history of reflux symptoms in patients with ILD and further highlight the need for improved objective measures of esophageal dysfunction in SSc.

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POS0853

EFFECTS OF NINTEDANIB ON CIRCULATING BIOMARKERS IN SUBJECTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD)

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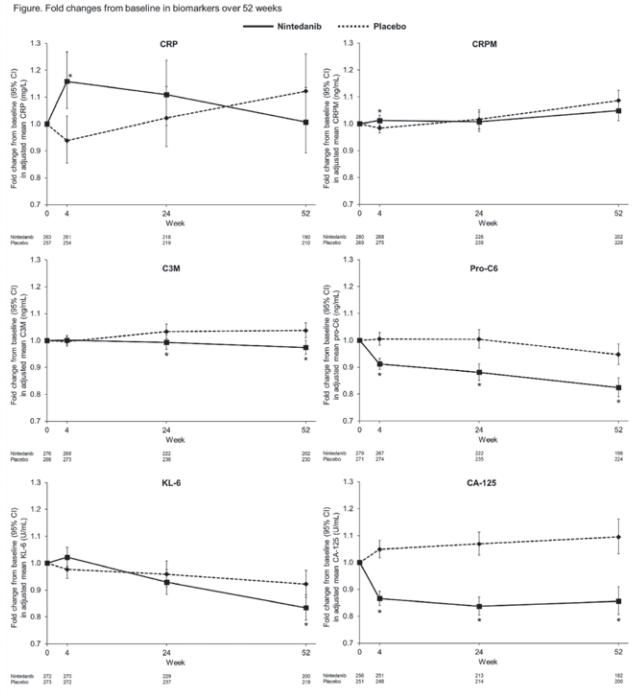
Background: In the SENSCIS trial in subjects with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) over 52 weeks by 44% compared with placebo.

Objectives: To investigate the effects of nintedanib on circulating biomarkers of extracellular matrix (ECM) turnover, epithelial injury and inflammation in the SENSCIS trial.

Methods: Subjects had SSc with first non-Raynaud symptom in the prior ≤7 years, extent of fibrotic ILD on high-resolution computed tomography (HRCT) ≥10% and FVC ≥40% predicted. Patients were randomised to receive nintedanib or placebo stratified by anti-topoisomerase I antibody (ATA). Blood samples were taken at baseline and at weeks 4, 24 and 52. Fold changes in adjusted mean levels of circulating biomarkers were analyzed using a linear mixed model for repeated measures. Data were log_{10} transformed before analysis and estimates of change from baseline were back-transformed.

Results: A total of 576 subjects received trial drug (288 nintedanib, 288 placebo). A transient increase in fold change from baseline in C-reactive protein (CRP) (a marker of inflammation) was observed in subjects who received nintedanib versus placebo at week 4. After an initial increase at week 4 in the fold change from baseline in CRP degraded by MMP-1/8 (CRPM) (a marker of ECM turnover), a trend to decreasing levels was observed in subjects who received nintedanib compared with placebo at week 52. Decreases in the fold change from baseline in collagen 3 degraded by MMP-9 (C3M) and N-terminal propeptide of type VI collagen (pro-C6) (markers of ECM turnover) were observed in subjects who received nintedanib compared with placebo from week 24 and week 4, respectively. A decrease in fold change from baseline in Krebs von den Lungen-6 (KL-6) (a marker of epithelial injury) was observed in subjects who received nintedanib versus placebo at week 52. A decrease in fold change from baseline in cancer antigen 125 (CA-125) (a marker of epithelial injury) was observed in subjects who received nintedanib versus placebo from week 4 (Figure 1).

Conclusion: Data from the SENSCIS trial suggest that nintedanib reduced circulating levels of markers of ECM turnover and epithelial injury in subjects with SSc-ILD.



*p<0.05 for difference versus placebo in fold change from baseline.
For CRP, KL-6 and CA-125: Based on linear mixed model for repeated measures for absolute change from baseline in log-transformed biomarker values, with fixed categorical effects of treatment at each visit, sex, ATA status, SSc subtype (limited cutaneous SSc, diffuse cutaneous SSc), mycophenolate use at baseline, methotrexate use at baseline, and fixed continuous effects of the baseline value of the protein biomarker at each visit, BMI and age.
For Pro-C6, C3M, CRPM: Based on linear mixed model for repeated measures for log-transformed biomarker values (including baseline timepoint), with fixed categorical effects of treatment at each visit, sex, ATA, SSc subtype (limited cutaneous SSc, diffuse cutaneous SSc), mycophenolate use at baseline, methotrexate use at baseline, and batch, and the fixed continuous effects of BMI and age.

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of Boehringer Ingelheim, Oliver Distler Speakers bureau: OD has/had relationships with the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three calendar years:
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POS0854 BASELINE CHARACTERISTICS OF PATIENTS WITH IMPROVEMENT OR PROGRESSION OF SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) DURING THE SENSCIS TRIAL

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Background: The course of SSc-ILD is variable, and may include periods of stability or even improvement in forced vital capacity (FVC) as well as periods of decline.
Objectives: To investigate the baseline characteristics of patients with SSc-ILD in the placebo group of the SENSCIS trial whose ILD improved or progressed over 52 weeks.
Methods: The SENSCIS trial enrolled patients with SSc with first non-Raynaud symptom in the prior ≤7 years, extent of fibrotic ILD on high-resolution computed tomography (HRCT) ≥10% and FVC ≥40% predicted. Patients who had been taking a stable dose of mycophenolate for ≥6 months were allowed to participate. We investigated the baseline characteristics of patients in the placebo group whose ILD showed improvement (absolute increase in FVC ≥5% predicted), stability (absolute decline or increase in FVC <5% predicted), progression (absolute decline in FVC ≥5% predicted), or significant progression (absolute decline in FVC ≥10% predicted) over 52 weeks. P-values based on ANOVA or Chi-squared tests were used to compare the baseline characteristics of the patients who showed improvement, stability and progression.
Results: Of 288 patients, 21 (7.3%) showed improvement, 166 (57.6%) stability, and 101 (35.1%) ILD progression, of whom 37 (12.8% of all patients) had significant ILD progression over 52 weeks. Most baseline characteristics were similar across the groups based on progression, but there were differences in DL_{CO} % predicted (p=0.02) and in the proportion of patients taking mycophenolate (p=0.09) among patients who showed improvement, stability and progression (Table 1).
Conclusion: These findings suggest that in the SENSCIS trial, patients who had higher DL_{CO} % predicted or who were taking mycophenolate at baseline were less likely to show progression of SSc-ILD over 52 weeks.
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POS0855 IMPAIRED PROMIS PHYSICAL FUNCTION IN IDIOPATHIC INFLAMMATORY MYOPATHY PATIENTS: RESULTS FROM THE MULTICENTER COVAD PATIENT REPORTED E-SURVEY

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Table 1. Baseline characteristics of patients in the placebo group of the SENSCIS trial in subgroups based on course of SSc-ILD over 52 weeks.

	Improvement (n=21)	Stability (n=166)	Progression (n=101)	Significant progression (n=37) (subset of Progression)	P-value for comparison of Improvement, Stability, Progression
Age, years	55.9 ± 12.0	53.2 ± 12.6	53.1 ± 12.8	55.3 ± 11.8	0.64
Female	71.4	75.9	70.3	73.0	0.59
Years since first non-Raynaud symptom	3.7 ± 1.7	3.5 ± 1.7	3.5 ± 1.9	3.6 ± 1.9	0.81
Diffuse cutaneous SSc	47.6	49.4	53.5	56.8	0.78
Anti-topoisomerase I antibody positive	61.9	58.4	66.3	56.8	0.44
High sensitivity C-reactive protein, mg/L	5.1 ± 8.9	7.8 ± 23.0	5.6 ± 9.9	4.2 ± 4.4	0.62
Modified Rodnan skin score	9.3 ± 7.3	10.5 ± 8.4	11.9 ± 9.7	12.7 ± 11.3	0.29
History of gastroesophageal reflux disease (GERD)	76.2	72.9	78.2	78.4	0.62
Extent (%) of fibrotic ILD on HRCT*	26.4 ± 16.2	35.5 ± 20.4	36.6 ± 21.8	40.8 ± 23.5	0.12
Presence of honeycombing on HRCT	14.3	16.8	15.5	26.5	0.94
Presence of ground glass opacities on HRCT	81.0	86.6	89.7	84.8	0.51
FVC % predicted	77.1 ± 18.0	71.7 ± 17.2	73.3 ± 15.2	74.2 ± 14.8	0.33
DLco % predicted	61.5 ± 14.9	53.4 ± 14.8	51.1 ± 15.1	47.3 ± 14.5	0.02
Taking mycophenolate	71.4	48.2	45.5	35.1	0.09

Data are mean ± SD or % at baseline. Missing data were excluded. *Assessed visually in whole lung to nearest 5%. The assessment did not include pure (non-fibrotic) ground glass opacities.

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Background: Evaluation of physical function is fundamental in the management of idiopathic inflammatory myopathies (IIMs). Patient-Reported Outcome Measurement Information System (PROMIS) is a National Institute of Health initiative established in 2004 to develop patient-reported outcome measures (PROMs) with improved validity and efficacy. PROMIS Physical Function (PF) short forms have been validated for use in IIMs [1].

Objectives: To investigate the physical function status of IIM patients compared to those with non-IIM autoimmune diseases (AIDs) and healthy controls (HCs) utilizing PROMIS PF data obtained in the coronavirus disease-2019 (COVID-19) Vaccination in Autoimmune Diseases (COVAD) study, a large-scale, international self-reported e-survey assessing the safety of COVID-19 vaccines in AID patients [2].

Methods: The survey data regarding demographics, IIM and AID diagnosis, disease activity, and PROMIS PF short form-10a scores were extracted from the COVAD study database. The disease activity (active vs inactive) of each patient was assessed in 3 different ways: (1) physician's assessment (active if there was an increased immunosuppression), (2) patient's assessment (active vs inactive as per patient), and (3) current steroid use. These 3 definitions of disease activity were applied independently to each patient. PROMIS PF-10a scores were compared between each disease category (IIMs vs non-IIM AIDs vs HCs), stratified by disease activity based on the 3 definitions stated above, employing negative binominal regression model. Multivariable regression analysis adjusted for age, gender, and ethnicity was performed clustering countries, and the predicted PROMIS PF-10a score was calculated based on the regression result. Factors affecting PROMIS PF-10a scores other than disease activity were identified by another multivariable regression analysis in the patients with inactive disease (IIMs or non-IIM AIDs).

Results: 1057 IIM patients, 3635 non-IIM AID patients, and 3981 HCs responded to the COVAD survey until August 2021. The median age of the respondents was 43 [IQR 30-56] years old, and 74.8% were female. Among IIM patients, dermatomyositis was the most prevalent diagnosis (34.8%), followed by inclusion body myositis (IBM) (23.6%), polymyositis (PM) (16.2%), anti-synthetase syndrome (11.8%), overlap myositis (7.9%), and immune-mediated necrotizing myopathy (IMNM) (4.6%). The predicted mean of PROMIS PF-10a scores was significantly lower in IIMs compared to non-IIM AIDs or HCs (36.3 [95% (CI) 35.5-37.1] vs 41.3 [95% CI 40.2-42.5] vs 46.2 [95% CI 45.8-46.6], $P < 0.001$), irrespective of disease activity or the definitions of disease activity used (physician's assessment, patient's assessment, or steroid use) (Figure 1). The largest difference between active IIMs and non-IIM AIDs was observed when the disease activity was defined by patient's assessment (35.0 [95% CI 34.1-35.9] vs 40.1 [95% CI 38.7-41.5]). Considering the subgroups of IIMs, the scores were significantly lower in IBM in comparison with non-IBM IIMs ($P < 0.001$). The independent factors associated with low PROMIS PF-10a scores in the patients with inactive disease were older age, female gender, and the disease category being IBM, PM, or IMNM.

Conclusion: Physical function is significantly impaired in IIMs compared to non-IIM AIDs or HCs, even in patients with inactive disease. The elderly, women, and IBM groups are the worst affected, suggesting that developing targeted strategies to minimize functional disability in certain groups may improve patient reported physical function and disease outcomes.

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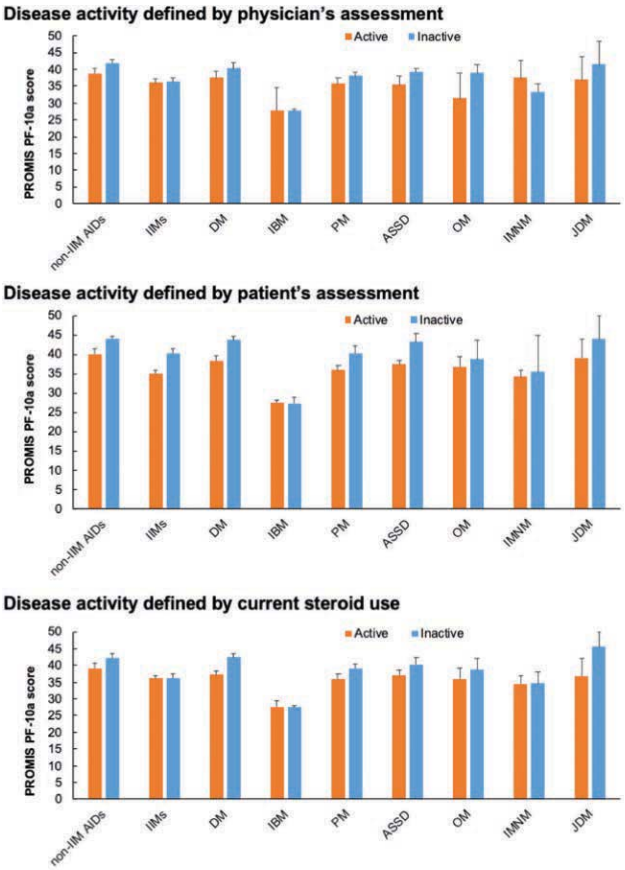

Figure 1. PROMIS PF-10a scores in each disease category stratified by disease activity assessed with 3 different definitions.
Data are shown as the predicted mean with 95% confidence interval. AIDs, autoimmune inflammatory diseases; ASSD, anti-synthetase syndrome; DM, dermatomyositis; HCs, healthy controls; IIMs, idiopathic inflammatory myopathies; IBM; inclusion body myositis; IMNM, immune-mediated necrotizing myopathies; JDM, juvenile dermatomyositis; OM, overlap myositis; PF, physical function; PM, polymyositis; PROMIS, Patient-Reported Outcome Information System.

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POS0856 DEFINING THE CLINICAL UTILITY OF PET OR PET/CT IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A SYSTEMATIC LITERATURE REVIEW

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Background: Positron emission tomography (PET), now often combined with computed tomography (CT), is a well-established tool for evaluating malignancy and inflammatory disease. The idiopathic inflammatory myopathies (IIM) are chronic, multi-system diseases characterised by skeletal muscle inflammation, the potential for extramuscular manifestations such as interstitial lung disease (ILD) and an increased risk of malignancy. PET or PET/CT thus has appeal as an imaging modality that may permit simultaneous assessment of multiple features of IIM, however its role in evaluation of these diseases remains poorly defined.
Objectives: This systematic review seeks to evaluate and describe the utility of PET or PET/CT in IIM, specifically for the detection of inflammatory muscle pathology, associated malignancy and extramuscular manifestations (e.g. ILD).
Methods: We performed a search of Medline and EMBASE from 1990-2021 using keywords related to IIM and PET. We included English language studies of adults with IIM who had PET or PET/CT as part of their diagnostic workup.
Results: Our search identified 910 potentially relevant abstracts, 18 of which were included. The majority of studies used fluorodeoxyglucose (FDG) PET or PET/CT scans, while the remainder used other radiotracers including [18F] florbetapir and [^{11}C] Pittsburgh compound B ([^{11}C] PIB). 1. Malignancy – PET vs. conventional screening Six studies investigated the ability of 18F-FDG PET or 18F-FDG PET/CT to detect malignancy in people with IIM. When reported, the sensitivity and specificity of PET or PET/CT for diagnosing malignancy compared with standard detection methods was 66.7-94% and 88.9-97.8%, respectively. 2.ILD Using high-resolution CT (HRCT) as the gold standard for detection of ILD, three studies reported the ability of PET or PET/CT to detect ILD. The sensitivity of 18F-FDG PET alone for ILD was 39%, while the sensitivity of 18F-FDG PET/CT for ILD was 93-100%. FDG lung uptake was significantly increased in people with rapidly progressive-ILD (RP-ILD) in comparison to those with non-RP-ILD in two studies. 3.Muscle disease activity Ten studies evaluated either 18F-FDG PET or 18F-FDG PET/CT for its ability to detect muscle inflammation in IIM. In the nine studies where controls were used, PET or PET/CT appeared to accurately detect the presence of muscle inflammation, although correlations with clinical measures of myositis disease activity such as strength and serum creatine kinase were mixed. 4.A word on amyloid Skeletal muscle amyloid deposition was evaluated using [11C]PIB-PET in two studies and [18F] florbetapir PET/CT in one study. In all three studies, PET or PET/CT was able to differentiate sporadic inclusion body myositis (IBM) from non-IBM myositis.
Conclusion: PET or PET/CT performs relatively well as a malignancy screening tool for people with IIM in comparison to standard screening methods. While false positives for malignancy on PET can lead to unnecessary invasive investigations, this also occurs with conventional screening. PET/CT also appears to be a beneficial tool for detecting ILD in those with IIM and may predict its severity. While PET/CT may detect skeletal muscle inflammation in IIM, its utility beyond the standard and readily available diagnostic tests for measuring muscle disease activity remains unclear. Early evidence indicates PET-amyloid may be able to subtype IBM from non-IBM myopathic disease, although more data are needed. More research is needed to evaluate whether PET could be used as a tool for detecting cardiac involvement in IIM, or if extending the PET scan field of view might increase the cancer detection yield and permit a more accurate assessment of extramuscular manifestations in IIM. PET/CT holds promise as a single tool that can simultaneously evaluate multiple aspects of IIM early in the diagnostic process. These include screening for associated malignancy in high-risk patients, stratifying higher risk ILD, and providing information on muscle inflammation.
Disclosure of Interests: None declared
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POS0857 PHARMACOKINETICS, SAFETY, AND EFFICACY OF SUBCUTANEOUS BRODALUMAB FOR SYSTEMIC SCLEROSIS WITH MODERATE-TO-SEVERE SKIN THICKENING: A SINGLE-ARM, OPEN-LABEL, MULTI-DOSE, PHASE 1 TRIAL

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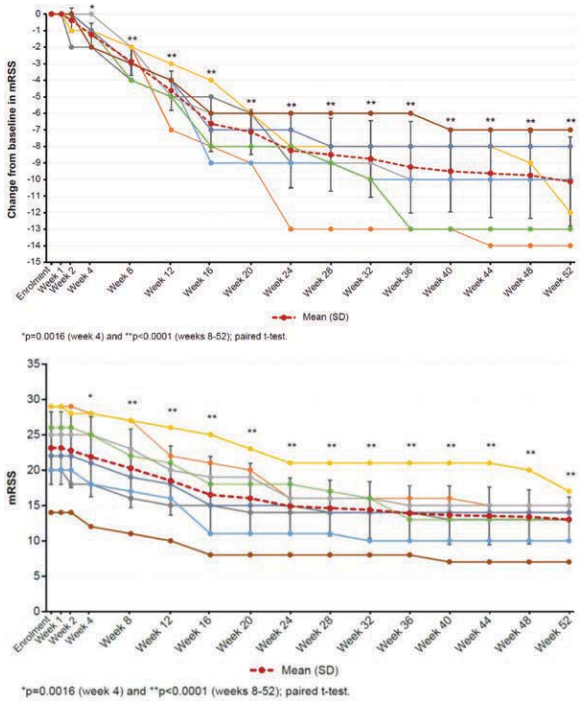
Background: Systemic sclerosis (SSc) is a rare autoimmune disease that causes fibrosis of the skin and internal organs. The mechanism of SSc pathogenesis and progression is not clear yet and SSc is therefore a disease with high unmet medical need. Though recent evidence reveals that interleukin-17 (IL-17) may play an essential role in the pathogenesis of multiple autoimmune inflammatory diseases, the role of IL-17 in SSc has not been established.
Objectives: This trial assessed the pharmacokinetics (PK), safety, and efficacy of multiple subcutaneous doses of brodalumab, a fully human anti–IL-17RA monoclonal antibody that inhibits the activity of IL-17A, IL-17C, IL-17F, IL-17A/F, and IL-17E (also called IL 25), in Japanese SSc patients with moderate-to-severe skin thickening.
Methods: In this trial, eligible patients (the modified Rodnan skin score (mRSS):10-29, present with the first symptoms of SSc other than Raynaud's phenomenon within 60 months at enrolment) were enrolled and received subcutaneous brodalumab 210 mg every 2 weeks (Q2W) during the 52-week period. Primary endpoints were PK and safety. Secondary endpoints included change from baseline in mRSS and Composite Response Index in SSc (CRISS) score. Exploratory endpoints included lymphocyte subset testing.
Results: Eligible 8 patients were enrolled. Mean (SD) age was 53.6 (10.6) years. All patients had diffuse cutaneous SSc, total mRSS was 23.1 (5.1) and disease duration was 2.2 (1.9) years. Mean (SD) serum brodalumab trough concentration increased to 21.8 (16.7) μg/mL at week 2 and remained almost constant at week 52. Drug-related treatment-emergent adverse events were observed in three patients: oral candidiasis (n=3), vulvovaginal candidiasis (n=1), and arthralgia (n=1). A rapid decrease in mRSS was observed as early as week 4 (-1.3 vs baseline, $p<0.005$), which continued until week 52 (-10.125 vs baseline, $p<0.0001$). Brodalumab reduced dermal thickness of the lesional skin consistent with the decrease in mRSS. All patients achieved a CRISS score ≥0.6 at week 24, which continued until week 52. Brodalumab induced Th17/Treg balance to Treg dominance over 52 weeks (vs baseline, $p<0.05$). The rapid decrease in the number of immunoglobulin G class-switched memory B cells and plasmablasts (vs baseline, $p<0.01$) was accompanied by an increase in the number of transitional B cells (vs baseline, $p<0.05$) by week 52.
Conclusion: Brodalumab demonstrated a rapid and sustained decrease in mRSS over 52 weeks in Japanese SSc patients with moderate-to-severe skin thickening, which could be attributed to its direct effects on fibroblasts and indirect effects via impacts on B and T cell subsets.
REFERENCES: None.



cMean Change from Baseline in mRSS and Mean mRSS over the 52-week follow up. (Mean +/- SD)

Table 1. Other efficacy endpoints

		Baseline	Week 12	Week 24	Week 52
Number of finger digital ulcers	mean	1.9	1.6	1	0.3
	SD	2.3	2.3	1.6	0.7
	P value	NA	0.17	0.04	0.04
Percent predicted FVC, %	mean	86.7	87.1	85.9	85.3
	SD	13.1	14.4	14	14.1
	P value	NA	0.7	0.45	0.3
Percent predicted DLCO, %	mean	92.6	89.3	88.9	89.1
	SD	22.5	22.9	19.4	22.2
	P value	NA	0.06	0.09	0.18
PGA, mm	mean	48.6	47.9	43.4	45.8
	SD	23.9	25.7	26	24.6
	P value	NA	0.66	0.04	0.71
CGA, mm	mean	68.9	53.5	39.5	30.3
	SD	23.9	19	16.7	13.9
	P value	NA	<.001	<.001	<.001
J-HAQ-DI score	mean	0.22	0.17	0.13	0.19
	SD	0.49	0.44	0.35	0.35
	P value	NA	0.4	0.17	0.7

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POS0858 NAILFOLD VIDEOCAPILLAROSCOPY FINDINGS AND ASSOCIATIONS WITH ORGAN INVOLVEMENT IN MIXED CONNECTIVE TISSUE DISEASE

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Background: Mixed connective tissue disease (MCTD) is a rare autoimmune condition characterized by Raynaud's phenomenon, positivity of antibodies targeting the U1 small nuclear ribonucleoprotein particle (U1 snRNP), various clinical features and potential risk of severe cardio-pulmonary involvement (interstitial lung disease, ILD, and pulmonary hypertension, PH) (1), (2). Nailfold videocapillaroscopy (NVC) is a simple, non-invasive and inexpensive imaging technique that allows a detailed assessment of skin microcirculation. NVC abnormalities have been barely described in MCTD and associations between NVC features and MCTD disease characteristics have only been partially investigated.

Objectives: To describe the NVC patterns observed in MCTD and assess their potential association with disease characteristics.

Methods: Cross-sectional study based on the retrospective analysis of patients hospitalized in the department of Rheumatology, Cochin Hospital, Paris France. To be included, patients were required to fulfil at least one classification criteria used in MCTD (3). The following data were collected: demographics, clinical features, para-clinical and laboratory data, treatment, and NVC findings.

Results: 51 patients met the inclusion criteria. Mean age was 51±12 years, 44 (86%) were women, mean disease duration was 13.8±11.1 years and 16 patients (31%) had ILD. Three different NVC patterns have been identified in our cohort (Figure 1): A) normal findings in 6 patients (11,7 %); B) non-specific organic microangiopathy in 16 patients (31,4%) and C) scleroderma pattern in 18 patients (35.3%), defined by the presence of at least 3 of the 4 following features: at least 1 giant capillary, decreased capillary density (<7/mm), avascular areas and disorganization of capillary bed architecture (4). Scleroderma pattern was associated with clinical features of systemic sclerosis: skin sclerosis (9/18 vs. 5/33; p=0.008) and digital ulcers (6/18 vs. 2/31; p=0.017). Conversely, no association was observed between the normal or the non-specific NVC pattern and disease specific characteristics.

Interestingly, we observed, a significant reduction in the number of capillaries in patients with ILD (4.80±1.87 vs. 6.03±1.47; p=0.039), and patients with severe reduction of capillary density (≤4/mm) were more likely to have ILD (5/7 vs. 5/33; p=0.002). Neoangiogenesis was also more frequent in patients with ILD (6/13 vs. 4/27; p=0.034). Multivariate logistic regression analysis showed that the association between severe reduction of capillary density and ILD was observed independently of the presence of a scleroderma NVC pattern and skin fibrosis.

Figure 1.

Conclusion: We identified three main NVC patterns in MCTD patients. The scleroderma NVC pattern was associated with clinical scleroderma characteristics whereas non-specific microangiopathy and normal NVC were not associated with a specific phenotype. Moreover, severe capillary loss was independently associated with the presence of ILD. These data suggest that NVC may be helpful for disease risk stratification in MCTD, and that NVC findings, and particularly severe capillary loss, may be a warning for the presence of ILD.

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POS0859 C-REACTIVE PROTEIN AND INTERLEUKIN-6: POTENTIAL BIOMARKERS OF DISEASE ACTIVITY AND TREATMENT RESPONSE IN SYSTEMIC SCLEROSIS-INTERSTITIAL LUNG DISEASE

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Background: Clinically feasible and valid biomarkers of systemic sclerosis-interstitial lung disease (SSc-ILD) are needed. While promising candidate biomarkers are under investigation (e.g., KL-6, CCL-8), clinical assays for these proteins are not currently available. C-reactive protein (CRP) measurements are feasible, cost-effective, and have been shown to predict mortality in SSc.[1] Measuring interleukin (IL)-6, a proinflammatory cytokine implicated in SSc-ILD pathogenesis, is also feasible in most clinical settings.

Objectives: (1) To investigate whether CRP and IL-6 levels change in response to treatment with immunosuppression in SSc-ILD; (2) To explore whether the change in CRP and IL-6 predict the future course of forced vital capacity (FVC).

Methods: CRP and IL-6 levels were measured in serum at baseline and after 12 months in participants of Scleroderma Lung Study (SLS) II (patients with active SSc-ILD receiving 24 months of mycophenolate or 12 months cyclophosphamide followed by 12 months of placebo[2]). Measured values were log-transformed to remove skewness. The FVC%-predicted was measured every 3 months over the course of 24 months. Spearman's correlations evaluated the relationship between baseline CRP or IL-6 measurements and other patient parameters. Paired t-tests were used to compare the change in individual CRP and IL-6 measurements from baseline to 12 months. Linear mixed effects models were used to examine the relationship between the change in CRP and IL-6 (baseline to 12 months) and the subsequent course of the FVC (12 to 24 months). All analysis were performed for the entire cohort and separately by treatment arm.

Results: Of the 142 participants of SLS II, 101 had CRP and IL-6 measurements at baseline and 12 months. Baseline CRP and IL-6 levels correlated significantly with higher modified Rodnan skin score (CRP: r=0.3, P=0.005; IL-6: r=0.2, P=0.01) and shorter disease duration (CRP: r=-0.3, P=0.005; IL-6: r=-0.2, P=0.01) and were higher in patients with diffuse SSc (CRP: P=0.007; IL-6: P=0.01). Relationships to baseline FVC and DLCO were not observed. CRP decreased significantly from baseline to 12 months in the whole group (P=0.01), but the decrease was slightly greater in patients randomized to mycophenolate versus cyclophosphamide (-0.47 vs. -0.33 ug/mL). IL-6 also decreased from baseline to 12 months in the whole group with a trend towards significance (P=0.10) (Figure 1). The mean decrease in IL-6 was again slightly greater in patients randomized to mycophenolate versus cyclophosphamide (-0.31 vs. -0.10 pg/mL). After controlling for baseline FVC and treatment arm in the mixed effects model, there was a relationship between the decrease in CRP from baseline to 12 months and an improved course of FVC 12 to 24 months (Estimate -0.64), but this did not reach significance (P=0.14). However, after controlling for baseline FVC and treatment arm, a greater decrease in IL-6 from baseline to 12

months was significantly associated with a greater improvement in FVC from 12 to 24 months (Estimate -1.28; P=0.01).

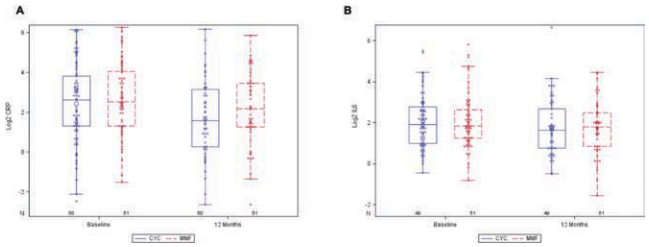

Figure 1. Change in CRP (A) and IL-6 (B) from baseline to 12 months by treatment arm in SLS II. CYC=cyclophosphamide (Blue), MMF=mycophenolate (red)

Conclusion: Patients with active SSc-ILD receiving one year of immunosuppressive therapy in the SLS II study experienced reductions in their CRP and IL-6 levels over this interval. The magnitude of the decrease in CRP and IL-6 over the first year also correlated with the course of FVC over the ensuing 12 months. These findings suggest a dynamic relationship between CRP and IL-6 measurements and the course of SSc-ILD in patients on immunosuppressive therapy. Further investigation of these findings is warranted.

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POS0860 ULTRA-HIGH FREQUENCY ULTRASOUND FOR DIGITAL ARTERIES: COMPLETING THE CHARACTERIZATION OF VASCULOPATHY IN SYSTEMIC SCLEROSIS

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Background: Despite microangiopathy is the hallmark of systemic sclerosis (SSc), macrovascular involvement is arousing interest. In particular, proper palmar digital arteries (PPDA) play an important role in Raynaud's phenomenon and can contribute to the exacerbation of vascular damage. However, PPDA full characterization is still an unmet need.

Objectives: To assess the state of PPDA in a cohort of patients with SSc using ultra-high frequency ultrasound (UHFUS), comparing the results with those obtained in healthy controls (HC) and looking for any association with SSc-specific characteristics. Correlations between UHFUS features of PPDA and microvascular bed were also investigated.

Methods: Consecutive SSc patients without active digital ulcers and HC were enrolled. Epidemiological and SSc-specific data were collected. Each subject underwent UHFUS (70 MHz) evaluation of PPDA (2 per finger, from II to V finger bilaterally), searching for occluded or not viewable vessels and measuring the thickness of the three arterial layers, as well as the systo-diastolic excursion range. Finally, microvascular bed was investigated by capillaroscopy and laser speckle contrast analysis (LASCA).

Results: Forty-six SSc patients (87% female, mean age 55.5 years, mean disease duration 8.2 years) and 15 HC matched for age and sex were enrolled. UHFUS in SSc revealed 123 (16.7%) PPDA occluded or not viewable, whereas in HC they were all patent. Considering the finger with at least one of the two PPDA occluded or not viewable as ultrasonographically pathological, 30 (65.2%) patients presented at least one pathological finger (Figure 1). All three arterial layers were significantly thicker in SSc than in HC ($p<0.001$ for all), as well as systo-diastolic excursion range was significantly reduced in SSc ($p<0.001$). On 63 fingers previously affected by digital ulcers, 73% were ultrasonographically pathological. A direct correlation emerged between disease duration and the thickness of all three arterial layers (intima $p<0.001$; $\rho=0.527$; intima-media $p<0.001$; $\rho=0.502$; intima-media-adventitia $p=0.001$; $\rho=0.491$). No significant correlations emerged between capillaroscopy or LASCA findings and UHFUS features.

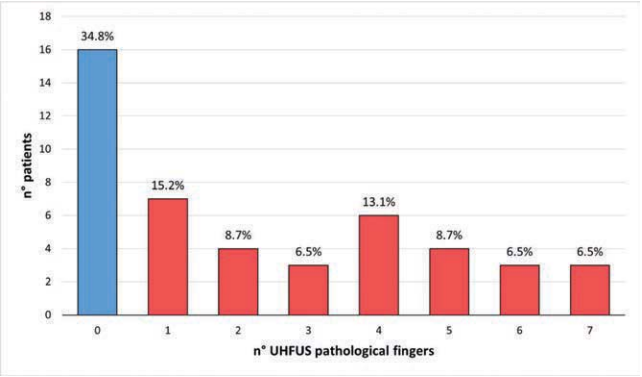

Figure 1. Representation of the number of ultrasonographically pathological fingers per patient.

Conclusion: SSc presents a vasculopathic involvement of PPDA well characterized by UHFUS, a useful diagnostic tool able to show also subclinical vascular impairment. The lack of correlations between UHFUS and capillaroscopy or LASCA reflects the existence of vasculopathic processes that are not exactly the same. Thus, UHFUS evaluation of PPDA emerges as complementary to microcirculation assessment, in order to obtain a more accurate and complete characterization of the vasculopathy in SSc.

Disclosure of Interests: None declared

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POS0861 ANTI-KU ANTIBODY SYNDROME: IS IT A DISTINCT CLINICAL ENTITY? A CLUSTER ANALYSIS OF 75 PATIENTS.

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Background: Anti-Ku antibodies are rare among patients with Connective Tissue Diseases (CTD) (1). Their potential role as a disease biomarker is not well established.

Objectives: To identify subgroups of anti-Ku positive patients according to their spectrum of anti-nuclear antibody (ANA) specificities and analyze their clinical and analytical features.

Methods: Multicenter, cross-sectional study of anti-Ku positive patients, irrespective of their diagnosis, followed at eight Rheumatology outpatient clinics. Patients were spontaneously identified according to the local work-out for suspected autoimmune diseases. Anti-Ku and other ANA specificities were determined at each hospital's Immunology lab according to the local methodology and strategy to decide on which auto-antibodies to check when faced with a positive ANA immunofluorescence. Clinical, analytical and treatment cumulative features were identified following a dedicated structured questionnaire. Hierarchical cluster analysis (method: between-groups linkage, squared Euclidian distance) for ANA specificity variables was performed to identify subgroups.

Results: Seventy-five anti-Ku positive patients were included (female: 73.3%, mean age at diagnosis: 50.5±17.9 years, mean disease duration: 4.7±5.4 years). Their clinical diagnosis were undifferentiated connective tissue disease (UCTD) (21.3%), systemic lupus erythematosus (17.3%), Sjögren's syndrome (16.0%), inflammatory myositis (14.7%), systemic sclerosis (10.7%), overlap CTD syndrome (8.0%), other connective tissue diseases (17.3%), healthy anti-Ku carrier (17.3%). Six autoantibody clusters were identified and included most patients (Figure 1): Cluster 1 - anti-Ku without any other ANA specificities (36.0%); cluster 2 - Anti-nor90 and anti-fibrillarin (8.0%); cluster 3 - anti-Jo1, PL-7, PL-12, and PM-Scl100 (9.3%); cluster 4 - anti-Scl70 (4.0%); cluster 5 - anti-Sm, anti-ribosome, and anti-dsDNA (13.3%); cluster 6 - anti-centromere, Th/To, PM-Scl75 (8.0%). The remaining patients were outliers (21.3%) not fitting in any cluster.

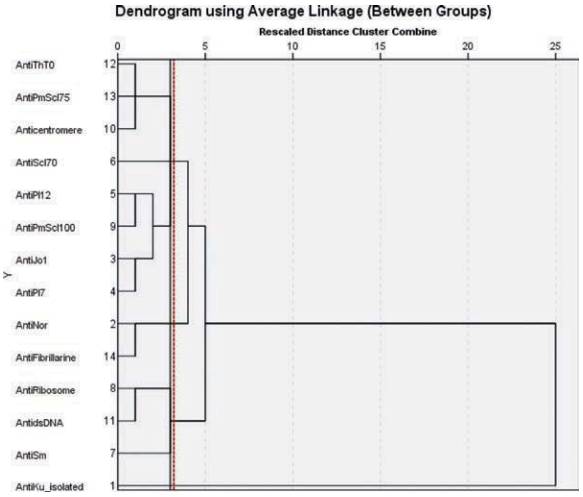

Figure 1. Hierarchical cluster analysis of ANA specificities in anti-Ku+ patients

Detailed clinical analysis of patients in cluster 1, the most numerous, presenting anti-Ku antibodies without any other ANA specificities, the most frequent clinical manifestations were: Raynaud's phenomenon (40.7%), arthritis (25.9%), sicca syndrome (25.9%), myositis (14.8%), and interstitial lung disease (ILD) (14.8%); 25.9% were healthy anti-Ku carriers. Patients from cluster 1 were most frequently treated with low dose glucocorticoids (51.9%), hydroxychloroquine (37.0%), or methotrexate (18.5%). Among the whole study population (n=75), major organ involvement was present in 18.7%, with ILD in 10.7% and renal involvement in 8.0%. None of the patients in cluster 1 presented nephritis.

Conclusion: Anti-Ku positive patients without any other ANA specificities is the largest subset and may represent a distinct entity among the differentiated CTD (2). Patients with this anti-Ku syndrome may develop ILD. In addition, anti-Ku antibodies can be found in patients with a diversity of other ANA specificities and heterogeneous CTD diagnosis.

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POS0862 INAUGURAL DROPPED HEAD SYNDROME AND CAMPTOCORMIA IN INFLAMMATORY MYOPATHIES

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Background: The idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of diseases that can affect the muscles, skin, lungs, heart, and joints. Increase knowledge about histopathological findings, clinical manifestations and auto-antibodies have allowed further novel classification of IIMs. Today, the main IMs subgroups are: dermatomyositis (DM), inclusion body myositis (IBM), immune-mediated necrotizing myopathies (IMNM), overlap myositis (OM) and immune-checkpoint inhibitor-related myositis (ICIrm). Axial muscle involvement results either in a "Dropped Head Syndrome (DHS)," with a marked weakness of the neck extensors, or in a camptocormia (CC), with a weakness of the thoracolumbar paraspinal muscles. This atypical presentation is poorly described in the course of IMs while it may results in a major disability, and may lead to myositis diagnosis delay.

Objectives: This study aimed to describe IMs revealed by DHS and/or CC. Secondary outcomes were to define subgroups of patients according to clinical, biological and histopathological characteristics. Then, the effects of treatments used were analyzed.

Methods: A historical cohort was designed using the register MYOLYON which includes all IMs followed at the University Hospital of Lyon (France) between 2000 and 2021. All patients with IM revealed by DHS and/or CC and having an histologically proven IMs were included, after exclusion of alternative (e.g., myasthenia gravis, motoneuron disease). Clinical, biological, immunological, histopathological data as well as outcome and care were collected through a standardized form. Agreement for the study was obtained from the French Ministry of the Research and the study was approved by the Local Research Ethics Committee.

Results: Twenty-two patients were fully characterized: DM (n=4), IBM (n=7), OM (n=8), ICIrm (n=2) and one myositis with anti-Hu antibodies. Two groups of patients were identified according to the age at first symptoms and to the type of muscle axial involvement (e.g, DHS and/or CC). Before the age of 70 (n=13/22), the two most common diagnoses (n=11/13) were DM (n=4/4) and OM (n=7/8). Axial muscle involvement was diffuse (DHS and CC) in 10/13 patients. After 70 years old (n=9/22), there were a majority of IBM (n=6/9) and all cases of ICIrm (n=2). Axial involvement was restricted to one group of muscles (DHS or CC) in 5/9 patients. Finally, 77% (17/22) of patients had refractory disease and required a second line treatment (e.g, immunoglobulins). All of these results are summarized in the Figure 1.

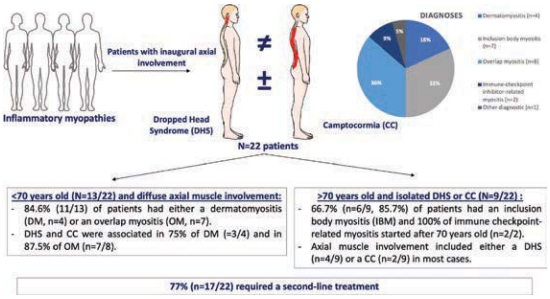

Figure 1.

Conclusion: While IM diagnosis is challenging in the presence of inaugural axial involvement, these results highlight the subset of IM to be considered according to the age at first symptoms and the type of axial involvement (e.g., DHS and/or CC).

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POS0863 ANTI-NOR90 ANTIBODIES IN THE SETTING OF CONNECTIVE TISSUE DISEASE: CLINICAL SIGNIFICANCE AND COMPARISON WITH A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Anti-NOR90 antibodies are directed against a 90-kD nucleolar protein located in the nucleolus organizing regions (NORs), mainly described in systemic sclerosis (SSc) [1, 2, 3] but reported also in other rheumatologic and oncologic diseases [4, 5, 6]. The clinical correlates of anti-NOR90 antibodies are still to be defined because the cohorts described thus far include a low number of patients.
Objectives: To describe the characteristics of a large cohort of anti-NOR90 antibodies positive patients and compare them with a matched cohort of SSc patients negative for anti-NOR90 antibodies.
Methods: A retrospective analysis was performed on patients positive for anti-NOR90 antibodies referring to participating centres. The concomitant positivity for anti-RNA polymerase III, Th/To, PM-Scl, Ku, and PDGFR antibodies was an exclusion criterion. In all cases the diagnoses, the different organ involvement and related clinical, instrumental and laboratory characteristics were evaluated. The EUROLINE SystemicSclerosisProfile kit from Euroimmun (Lübeck, Germany) was used to detect anti-NOR90 antibodies.
Results: We included 101 patients positive for anti-NOR90 (M/F=13/88, mean age 52.5 years). They were mainly classified as SSc (n=38), undifferentiated connective tissue disease (UCTD) (n=21), interstitial pneumonia with autoimmune features (IPAF) (n=11) (graph 1). The most frequent clinical manifestations were arthralgias (n=72), Raynaud's phenomenon (RP) (n=58), sicca syndrome (n=49), ILD (n=40), puffy fingers (n=32), arthritis (n=30), and limited skin sclerosis (n=24). Anti-NOR90 antibodies were associated with anti-Ro52 antibodies in the 16% of cases, with anticentromere antibodies in the 7% of cases, and with anti-Scl70 in the 5% of cases. After excluding these patients, and considering the isolated anti-NOR90 positivity, 12 patients had SSc, 35 UCTD, and 11 IPAF. The most frequent clinical manifestations were arthralgias (n=40), RP (n=37), and sicca syndrome (n=21). Compared to 242 matched SSc without anti-NOR90 antibodies, patients with anti-NOR90 had more frequently joint manifestations and sicca syndrome and less frequently all vasculopathic manifestations (RP, telangiectasias, pitting scars, acral ulcers), dysphagia and fibromyalgia.
Conclusion: Our study shows that anti-NOR90 antibodies are more commonly observed in females, and clinically associated with the occurrence of arthritis/arthralgias, sicca syndrome and RP. In more than the 50% of cases they may be found with other autoantibodies, such as the anti-Ro52, the anticentromere, and the anti-Scl70 antibodies. Anti-NOR90 seems to play an accompanying role in the context of CTDs, without strong influence on the clinical phenotype expression of the underlying CTD.
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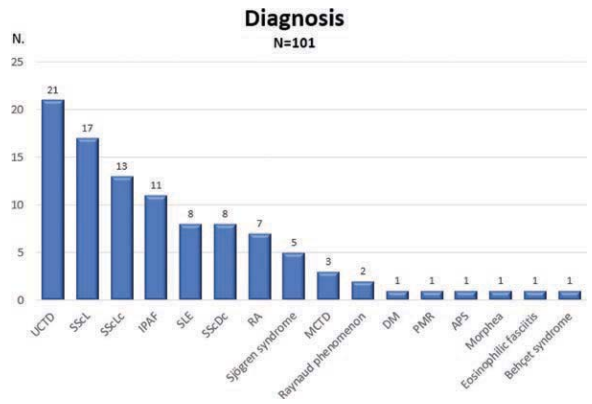

Figure 1.

Disclosure of Interests: None declared
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POS0864 ASSESSMENT OF SYSTEMIC SCLEROSIS RELATED MYOCARDIAL FIBROSIS BY 68GA-FAPI-04 PET/CT

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Background: Myocardial fibrosis is a poor prognostic factor and a relevant cause of SSc-related mortality. Current non-invasive screening methods for myocardial fibrosis (MF) include echocardiography, electrocardiography and serum Nt-pro-BNP, which are not specific for MF and not sensitive for early changes. Cardiac MRI predominately visualizes extracellular space changes as consequence of long-standing fibroblast activation. Direct visualization of the remodeling fibrotic remodeling process has not been feasible so far.
Objectives: Here, we use a tracer labeled probe directed against Fibroblast-Activation-Protein (FAP) to visualize activated fibroblasts in the myocardium of SSc patients and healthy individuals to test the hypothesis that FAPI-based PET imaging might enable the assessment of disease activity in SSc-related MF.
Methods: In this exploratory trial, 7 patients with SSc-related myocardial fibrosis (MF) confirmed by cardic MRI and 8 SSc patients without myocardial involvement were enrolled. All participants underwent ^{68}Ga-FAPI-04 PET/CT imaging and cardiac MRI as well as echocardiography, electrocardiogram, and serum NT-pro-BNP. Patients were followed for at least 6 months including a follow-up cardiac MRI. Regional mapping of ^{68}Ga-FAPI-04-uptake, late gadolinium enhancement (LGE) and T1-relaxation times were performed according to the American Heart Association 17 regions model. Myocardial tissue was analysed by immunofluorescence- (aSMA and FAP) and Sirius-Red staining.
Results: Myocardial FAPI-04-accumulation was significantly increased in SSc patients with myocardial fibrosis as defined by LGE in MRI compared to SSc patients without LGE. Consistent with the previously reported widespread remodeling in SSc-associated myocardial disease, the distribution of FAPI uptake was observed across multiple areas and did not correspond to the supply areas of the coronary arteries. Histological analyses of myocardial tissue biopsied from a LGE and ^{68}Ga-FAPI-04-positive region revealed the accumulation of FAP+; SMA+ myofibroblasts in regions of pronounced collagen deposition. Slightly increased ^{68}Ga-FAPI-04 -uptake values were observed in SSc patients without LGE, but with cardiovascular risk factors. Comparing ^{68}Ga-FAPI-04-uptake with cardiac MRI based mapping techniques, we observed a partial overlap for certain regions and differences in others. These observations suggest, that ^{68}Ga-FAPI-PET/CT and cMRI could visualize different aspects of the disease process. To confirm that ^{68}Ga-FAPI-04-uptake assesses current molecular fibroblast activity rather than accumulating disease damage, we analyzed associations of ^{68}Ga-FAPI-04-uptake with changes of clinical parameters of SSc-MF on follow-up: Here we observed different dynamics of change of ^{68}Ga-FAPI-04-uptake and cardiac MRI-based, e.g. in response to start of immunosuppressive therapy.
Conclusion: Our study presents first in human evidence on a limited number of patients that FAPI-04-uptake correlates with fibrotic activity in SSc-associated myocardial fibrosis and that ^{68}Ga-FAPI-04-PET/CT may thus improve risk stratification in this population.
Disclosure of Interests: None declared
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POS0865 THE EFFECT OF SILVER FIBER GLOVES ON RAYNAUD'S PHENOMENON IN PATIENTS WITH SYSTEMIC SCLEROSIS: A DOUBLE-BLIND RANDOMIZED CROSS-OVER TRIAL.

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Background: Over 90% of patients with systemic sclerosis (SSc) experience Raynaud's phenomenon (RP), which strongly influences quality of life. Therapeutic options of RP include drug treatment and general lifestyle measures such as smoking cessation and avoiding cold by wearing warm clothes and gloves including electrically heated gloves or silver fiber gloves. Clinical observations suggest an additional benefit of silver fiber gloves compared to normal gloves. Silver is thought to help by reflecting heat back into the hands allowing less heat to escape and has an antimicrobial effect. Despite its generalized use among SSc patients, no objective evidence regarding its superiority for RP over normal gloves exists.
Objectives: To evaluate the added value of 8% silver fiber gloves compared to normal gloves in the treatment of patients with RP secondary to SSc.
Methods: This was a multicenter double-blind randomized cross-over trial in which 85 SSc patients were randomized in two sequences: 8% silver fiber gloves in period 1 and normal gloves in period 2 or vice versa; each period lasted six weeks. To

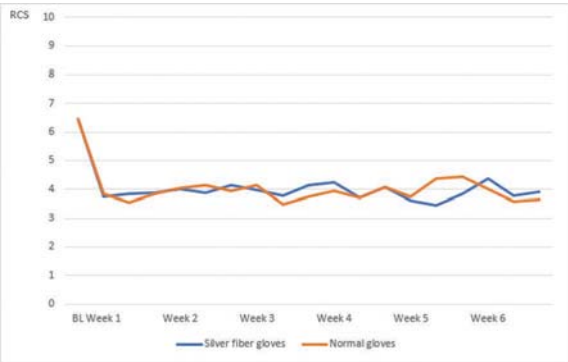
reduce bias of interindividual differences and external factors (e.g. temperature), a cross-over design was performed in the Netherlands during the winter months. The primary outcome was the triweekly Raynaud Condition Score (RCS), a scale from 1 (no symptoms) to 10 (extreme symptoms). A linear mixed model was used with RCS as dependent and type of gloves as independent variable, adjusted for baseline RCS. Secondary outcome measures included number of RP attacks, RP attack duration, Health Assessment Questionnaire (HAQ-DI) and vascular complications. Secondary outcomes were also analyzed with linear mixed models. All analyses were performed and interpreted before unblinding.

Results: The 85 included SSc patients had a mean age of 60 (SD:12), 80% were female, 60% had limited cutaneous SSc and 67% used vasoactive medication. Ten patients prematurely ended the study due to various reasons, most notable: allergic reaction to gloves (n=2). At baseline, mean RCS was 6.43 (SD 1.6), with silver fiber gloves the mean RCS decreased to 3.91 (SD 2.3) and with normal gloves to 3.90 (SD 2.3) (Figure 1). No statistically significant difference in RCS during follow-up was observed between the silver fiber gloves and normal gloves (β 0.067, 95% CI -0.006 to 0.19), meaning that on the 1-10 scale, silver fibre gloves gave only a 0.067 higher RCS compared to normal gloves (Table 1). For all other secondary outcome measures, we did not find a statistically significant difference between silver fiber gloves and normal gloves, except for the HAQ (β 0.036, 95% CI 0.026 to 0.046; Table 1), which is not clinically relevant. One vascular complication occurred in the silver fiber gloves, compared to three vascular in the normal gloves, which was not statistically significant different (OR:3.2, 95% CI 0.32 to 31.1).

Table 1. Primary and secondary efficacy outcomes

	β	95% confidence interval
Primary outcome		
Raynaud Condition Score	0.067	-0.0059; 0.194
Secondary outcomes		
Raynaud attacks frequency	-0.480	-1.215; 0.255
Raynaud attacks duration	39.80	-36.051; 115.654
VAS warmth hands	-0.086	-0.212; 0.041
Impact Raynaud	0.088	-0.035; 0.211
HAQ_DI	0.036	0.026; 0.046

VAS: visual analogue scale; HAQ: Health Assessment QuestionnaireThe reference category was Normal gloves.Linear mixed models were performed with the primary and secondary outcomes as dependent variables, the type of gloves as independent variable, adjusted for baseline Raynaud Condition Score.



RCS: Raynaud Condition Score; BL: Baseline.

Figure 1. Raynaud Condition Score during the study period

Conclusion: This trial shows that wearing any type of glove decreases the RP burden in SSc patients, but no additional benefit from gloves containing 8% silver fibers compared to normal gloves could be demonstrated. Potentially, less vascular complications may arise in SSc patients wearing silver fiber gloves. Further confirmation of this potential benefit is necessary.

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POS0866 THE PARAMETERS RELATED TO DECLINE OF LUNG FUNCTION ON RITUXIMAB THERAPY IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS

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Background: Rituximab (RTX) is considered as one of the effective options for the treatment of interstitial lung disease associated with systemic sclerosis (ILD-SSc) [1]. Factors that affect the effect of RTX therapy are not well investigated.
Objectives: To evaluate associations of clinical parameters of the disease with response to RTX therapy in patients with ILD-SSc.
Methods: This prospective study included 102 patients with ILD- SSc, 86 (84%) of them were women. The mean age was 47.6±12.9 years, mean disease duration 6.2±5.5 years. The mean follow-up period was 12.9±2.1 months. The diffuse cutaneous subset of the disease had 55 pts (54%). 69 (68%) pts were positive for antitopoisomerase-1 antibody (anti-Topo-1). All pts received prednisolone at a dose of 11.3±4.5 mg/day. 49 (68%) subjects were exposed to immunosupressants (IS) at baseline. Subjects were categorized as having improvement if baseline forced vital capacity (FVC % predicted) increased by > 5% [2]. Stabilization was defined as a change in FVC of < 5 % and a decrease of > 5% in FVC as worsened ILD-SSc. Out of the 102 patients who started treatment with RTM, 46 pts (45%, group I) fulfilled the improvement criteria during follow-up. A total of 34 patients (33%) stabilized and 21 (20%,, group 2) worsened during follow-up. We compared patients of groups 1 and 2 and performed the statistical analysis, including the linear regression analysis.
Results: For the age, baseline diffusing capacity for carbon monoxide (DLCO % of predicted), anti-Topo-1 level, activity index (EScSG-AI) and mean dose of prednisolone there were no differences (all p > 0.05) between the two groups. There was a significant differences between the different response groups in a higher percentage of men (13% in group 1 vs 27% in group 2), patients with a limited form of the disease (40 vs 55%), an initially lower Rodnan skin score (median 10 (4;16) and 6 (4;9) and with ΔmRss of 0 (-1; 2) and 2 (0; 8), p=0,02), lower frequency of anti-Topo-1 (50 vs. 74%) and a higher frequency of prescribing IS before inclusion in the study (68 vs. 38%). Worsened pts initially had a higher FVC (88.8±18.1 vs 74.1±19.8, p=0.01) and DLCO (53.6±19.3 vs. 46.8±17.2, p>0.05), but received the lowest cumulative mean dose of RTX (1.2±0.5 vs 1.9±0.6, p=0.001). The linear regression analysis revealed a number of parameters associated with worsening of FVC (with a sensitivity of 75% and a specificity of 91%). These parameters included a limited subset of the disease (odds ratio (OR) 6.374, 0.83-48.8, p=0.068), increased activity index (OR 2.04, 0.19-4.18, p=0.046) and the presence of arthritis (OR 1.39, 0.08-23.19, p=0.82) at the end of the study. The risk of worsening of FVC was associated with an initially elevated level of creatine phosphokinase (OR 1.02, 0.1-0.84, p=0.054) and a decrease of glomerular filtration rate according to EPI (OR = 1.075,1.0-1.14, p=0.022). In patients initially receiving IS, the OR was 9.85, 1.154-84.066, p=0.033). The highest OR =19.6 (2.4; 156, p=0.005)] was associated with the cumulative mean dose of RTX.
Conclusion: In this study 45% of the pts improved, one third stabilized, and one fifth worsened over a one-year period. On multivariate analysis, limited scleroderma subsets (dcSSc vs lcSSc), increased activity index, the presence of arthritis at the end of the study, cumulative mean dose of RTX (<2 g per year) were found to be independently associated with the decline of FVC. Identification of this parameters could improve monitoring of rituximab effects

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POS0867 COMORBIDITY AND COMPLICATIONS PRIOR TO SYSTEMIC SCLEROSIS DIAGNOSIS: A RETROSPECTIVE COHORT ANALYSIS

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Background: Systemic sclerosis (SSc) is a rare autoimmune disease characterized by progressive microvascular damage, collagen deposition and subsequent

fibrosis of the skin and internal organs which contributes to substantial morbidity and premature death.[1-2]

Objectives: The objective was to evaluate the disease burden of SSc patients prior to their SSc diagnosis.

Methods: Patients with SSc were identified in a claims dataset (IBM MarketScan Commercial Database, 2015-2019) using ICD 10 diagnosis codes for SSc. Eligible subjects were required to have > 1 inpatient or >2 outpatient/office claims with a scleroderma diagnosis code on separate days and > 24 months of continuous health plan enrollment without a SSc diagnosis before the first SSc claim ('index date') and > 12 months of enrollment after the index date. Overall comorbid disease burden was assessed via the Charlson Comorbidity Index (CCI) 13-24 and 12 months before and 12 months after index date. The prevalence of SSc-related complications for atherosclerosis, pulmonary arterial hypertension (PAH), pulmonary fibrosis (PF), Raynaud's Phenomenon (RP), and gastrointestinal (GI) complications (e.g., GERD, dysphagia, etc.) were identified using ICD codes and reported as percentages for the aforementioned time intervals relative to patients' index dates.

Results: 902 eligible SSc patients were identified for analysis. The mean age at index SSc diagnosis was 54.3 years and 84.7% of patients were female. Mean CCI scores 13-24 months before, 12 months before, and 12 months after index SSc diagnosis were 0.84, 1.13 and 1.30, respectively. From the time points 13-24 months before, 12 months before, and 12 months after index SSc diagnosis, increasing rates were also observed of atherosclerosis, PAH, PF, RP, and GI complications (Table 1).

Table 1. Charlson Comorbidity Index (CCI) and systemic sclerosis-related complications by time-interval

Clinical characteristic	13-24 months before Index	12 months before Index	12 months after Index
Mean CCI (std dev)	0.84 (1.58)	1.13 (1.71)	1.30 (1.75)
Systemic sclerosis-related complications			
Atherosclerosis	7%	9%	14%
Pulmonary arterial hypertension (PAH)	1%	4%	12%
Pulmonary fibrosis (PF)	5%	8%	16%
Raynaud's Phenomenon (RP)	13%	29%	43%
GI complications	23%	32%	46%

Conclusion: Results from this analysis suggests that SSc-related sequalae are present at least two years prior to SSc diagnosis and rates of these complications increased markedly over time. Patients' overall comorbid disease burden also worsened substantially over this period, likely because of these complications. The internal organ involvement is likely under reported due to requirements to link each diagnosis with an ICD-10 code. These data indicate the significant burden of SSc, prior to and after diagnosis, highlighting the need for awareness, prompt diagnosis, and effective therapies for SSc and its related complications.

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POS0868

THE DEVELOPMENT OF THE LINEAR CRISS; A CLINICAL AND PATIENT MEANINGFUL ANCHOR TO THE ACR-CRISS IN SCLERODERMA.

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Background: The ACR Composite Response Index in Systemic Sclerosis (ACR-CRISS) is one of the first composite outcome measures in diffuse cutaneous Systemic sclerosis (dcSSc).[1] It relies on validated clinical domains selected through a data-driven methodology; however, it only provides a probability of response and is unable to differentiate between patients who do not improve and who worsen respectively.

Objectives: To improve the clinical interpretation of the ACR-CRISS by creating a continuous ranked score of clinically and patient meaningful changes of its individual measures.

Methods: Following OmerACT guidelines for outcome measurement development, relevant stakeholders were identified from 5 continents, including 100 physicians with proven experience in managing patients with dcSSc and 100 patients with dcSSc who have participated in at least one clinical trial. An adaptive conjoint analysis survey based on the PAPRIKA method[2] and implemented using 1000minds software was administered. Patients and doctors were asked to choose which of two hypothetical patients had a better or worse outcome according to Minimally Clinical Important Differences (MCID) in two domains at a time from FVC, HAQ-DI and mRSS and the presence of organ failure. These pairwise choices were analysed to rank and weight the MCIDs against each other. With patient and public involvement, utilising a 'think aloud' approach, a video tutorial was produced explaining the objectives and process of the adaptive survey to the participants.

Results: Eighty rheumatologists and 80 patients with dcSSc completed the survey, which ran from June 2020 to January 2021. From the survey, relative weights for the 4 domains, reflecting their relative importance with respect to improving and worsening outcomes, were determined. A continuous composite ranked score reflecting the relative weighting of the individual outcome measures (Ranked Composite Important Difference, RCID) was developed accordingly (Table 1). The score ranges from -1 (worst possible outcome) to 1 (best possible outcome), in patients who experience no organ failure and do not meet any MCID in any of the 3 domains scoring 0.

Table 1. The relative median weights of each of the core set measures within the better and worse outcome models, expressed as a score from -1 to 1

	Worsening weights			Improvement weights		
	Doctors	Patients	Combined	Doctors	Patients	Combined
Organ failure	-0.355	-0.333	**-0.326**	N/A	N/A	N/A
FVC	-0.324	-0.306	**-0.316**	0.463	0.452	**0.451**
mRSS	-0.205	-0.229	**-0.217**	0.320	0.320	**0.324**
HAQ-DI	-0.114	-0.115	**-0.141**	0.200	0.227	**0.224**

Conclusion: This collaborative process using a novel, robust methodology and involving both rheumatologists and patients has created a clinically and patient meaningful composite score that can be used as an anchor to the ACR-CRISS, or other clinical outcomes. Performance against the ACR-CRISS and revised CRISS in randomised controlled trials and in observational cohorts will determine the clinical value of the RCID.

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POS0869

CYTOKINES IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE AND IDIOPATHIC PULMONARY FIBROSIS

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Background: Immune pathways have been implicated in both systemic sclerosis (SSc)-related interstitial lung disease (ILD) and idiopathic pulmonary fibrosis (IPF). Determination of blood cytokine differences in these two disorders need to be elucidated to better understand potential biological processes and common pathogenic pathways.

Objectives: This study compared 87 circulating cytokine levels amongst healthy controls and both SSc-ILD and IPF. There was also exploration of the association between cytokine levels and disease progression based on the annualized rate of decline of forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO).

Methods: Levels of 87 plasma cytokines were measured using commercial panels for consecutive SSc-ILD, IPF, and healthy individuals recruited at a Canadian tertiary-care center. Pulmonary function tests were performed as clinically indicated every 3-12 months. Cytokine levels are compared using the Wilcoxon rank sum test for two samples pairwise. The association between differentially expressed cytokines with both percent predicted annualized FVC and DLCO change was assessed within each disease group using multiple linear models adjusted for age, sex, baseline FVC, and immunosuppressive or anti-fibrotic treatment at sampling. Correction for multiplicity of testing was by Holm's method.

Results: There were 19 healthy controls, 40 SSc-ILD, and 17 IPF participants with clinical features shown in Table 1. Eotaxin-1 and interleukin 6 (IL-6) were significantly elevated in both SSc-ILD and IPF compared to healthy controls (Figure 1). SSc-ILD had significantly lower soluble epidermal growth factor receptor (sEGFR) and higher levels of both soluble tumor necrosis factor receptor type II (sTNFRII) and soluble vascular endothelial growth factor receptor-1 (sVEGFR1) compared to healthy controls. IPF cases were distinguished from healthy controls by significantly higher monocyte chemoattractant protein-1 (MCP-1) and monokine induced by gamma interferon (MIG, also known as CXCL9) levels. No significant association was found for any of the cytokines with ILD progression based on annualized rates of either FVC or DLCO change.

Table 1. Baseline patient characteristics stratified by disease groups

	Healthy control (n = 19)	SSc-ILD (n = 40)	IPF (n = 17)
Age, year	51 ± 19	56 ± 12	73 ± 7
Male, count (%)	6 (32)	12 (30)	12 (71)
Disease duration, year	NA	6.41 (7.81)	1.76 (2.14)
Ever smoker, count (%)	2 (11)	19 (48)	14 (82)
• 4 (82)oker	0.4 [0, 1]	11 [4, 29]	19 [11, 35]
Treatment presence, count (%)	NA	16 (40)	7 (41)
Baseline FVC %	NA	80 ± 22	85 ± 21
Baseline DLCO %	NA	51 ± 17	49 ± 11
Annualized FVC % change	NA	-1.7 ± 8.2	-6.2 ± 13.6
Annualized DLCO % change	NA	-0.5 ± 6.2	-7.8 ± 18.6

The number (%), mean ± standard deviation, and median [interquartile range] are shown. Disease duration is defined as time of ILD first seen on HRCT in IPF and time from first non-Raynaud's phenomenon in SSc-ILD. Treatment includes presence of ILD therapies: nintedanib, pirfenidone, mycophenolate mofetil, azathioprine, rituximab. FVC = forced vital capacity, DLCO = diffusing capacity for carbon monoxide

Conclusion: Differences in seven circulating cytokines between healthy controls with both SSc-ILD and IPF show evidence of systemic cytokine activation. All seven cytokines have a role in immune cell extravasation and pro-fibrotic signaling, which provides further evidence of immune pathways involved in pulmonary fibrosis. Further studies will be pursued of longitudinal change of these biomarkers for halting or slowing disease progression and improving response to treatment.

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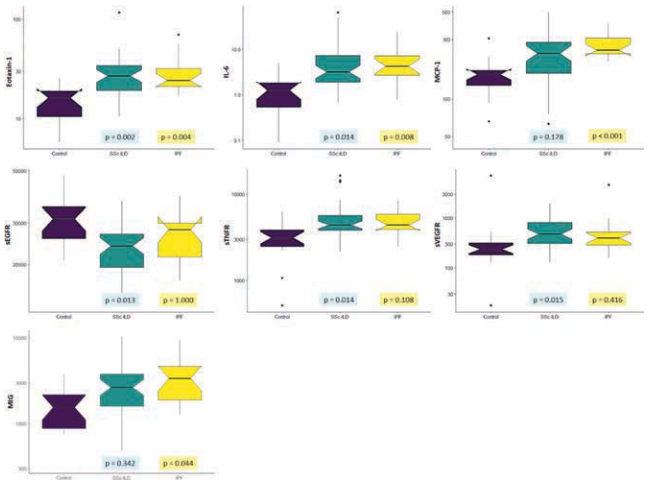

Figure 1. Notched box plots of cytokine differences between disease groups. All cytokine levels are shown on a log scale. Overlap of notches indicates lack of a statistically significant difference in medians in a pairwise comparison. P-values are for SSc-ILD or IPF compared to healthy controls using Wilcoxon rank sum two-sample test corrected for multiple testing using Holms method.

POS0870

PATIENTS WITH SYSTEMIC SCLEROSIS HAVE IMPAIRED FORCED VITAL CAPACITY, EVEN IN THE ABSENCE OF INTERSTITIAL LUNG DISEASE

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Background: Spirometry, in particular forced vital capacity (FVC), is a widely implemented tool in the initial diagnostic workup and monitoring of systemic sclerosis-related interstitial lung disease (SSc-ILD). In addition to ILD, several other extra-pulmonary complications can affect pulmonary function. There is currently limited data on lung function in SSc patients with and without ILD compared to a healthy reference population.

Objectives: To compare forced vital capacity (FVC) of a well-defined SSc patient cohort with and without ILD to multi-ethnic reference values provided by the European Respiratory Society (ERS) global lung function initiative (1).

Methods: SSc patients from the Oslo University hospital SSc cohort with at least one PFT were included. We registered each patient's first available FVC value and a follow-up FVC at 12 +/- 3 months if available. We registered clinical characteristics including sex, age, height, the extent of skin changes, and presence of ILD assessed on HRCT. Predicted FVC values from the reference population were calculated using the GLI 2012 equation (1), including age, height and ethnicity. Descriptive statistics were applied.

Results: In total, 404 SSc patients were included; of these 58 (14%) patients were anti-Scl 70-antibody positive, 61 (15%) were male, 155 (38%) had ILD and 93 (23%) had diffuse cutaneous SSc (dcSSc). At baseline, mean age was 55.8 (SD 14.0) years, and mean time from first non-Raynaud symptom was 35 (53.2) months. A follow-up spirometry at 12 +/-3 months was available in 164 (41%) patients. Mean FVC was 0.48 L lower at baseline compared to the reference population. At 12 +/-3 months the SSc cohorts mean FVC was 0.39 L lower compared to the reference group (Table 1). The low FVC values at baseline were most pronounced in patients with ILD (0.87L), in male patients (0.86L) and in anti—Scl 70 positive patients (0.67L). But SSc patients with no ILD showed also impaired FVC compared to the reference population (0.24L), even more pronounced when they had dcSSc (0.34L) (Table 1).

Conclusion: Mean FVC at baseline was significantly lower in SSc patients compared to the reference population. As expected, SSc patients with ILD had impaired FVC, but also patients without ILD and in patients with limited skin

Table 1.

	The Oslo SSc cohort	Matched controls	Difference in L (95% CI)	P-value
Baseline				
FVC (n=404), L (SD)	3.14 (0.86)	3.62 (1.13)	-0.48 (-0.59, -0.37)	<0.001
FVC (male, n=61), L (SD)	3.89 (1.14)	4.75 (0.58)	-0.86 (-1.10, -0.66)	<0.001
FVC (anti-Scl-70-antibody, n=58), L (SD)	2.98 (0.90)	3.65 (0.75)	-0.67 (-0.83, -0.50)	<0.001
FVC (dcSSc, n=93), L (SD)	3.06 (0.91)	3.7 (1.00)	-0.64 (-0.81, -0.51)	<0.001
FVC (ILD, n=155), L (SD)	2.83 (0.78)	3.70 (1.57)	-0.87 (-1.13, -0.60)	<0.001
FVC (no ILD, n=241), L (SD)	3.32 (0.85)	3.56 (0.74)	-0.24 (-0.31, -0.18)	<0.001
FVC (no ILD and no skin changes or lcSSc, n=196), L (SD)	3.31 (0.84)	3.53 (0.71)	-0.22 (-0.29, -0.15)	<0.001
FVC (dcSSc and no ILD, n=43), L (SD)	3.36 (0.89)	3.70 (0.84)	-0.34 (-0.52, -0.16)	<0.001
12 months follow up				
FVC (n=164), L (SD)	3.20 (0.86)	3.60 (0.69)	-0.39 (-0.49, -0.30)	<0.001
FVC (dcSSc, n=39), L (SD)	3.29 (1.00)	3.92 (0.88)	-0.63 (-0.87, -0.40)	<0.001
FVC (ILD, n=63), L (SD)	2.96 (0.73)	3.66 (0.72)	-0.69 (-0.87, 0.52)	<0.001
FVC (no ILD, n=97), L (SD)	3.34 (0.90)	3.56 (0.67)	-0.21 (-0.31, -0.12)	<0.001

changes. This highlights the importance of other factors than ILD on lung function in SSc patients.

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POS0871 DIAGNOSTIC ACCURACY OF POWER DOPPLER ULTRASONOGRAPHY FOR THE DIAGNOSIS OF IDIOPATHIC INFLAMMATORY MYOPATHIES.

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Background: No clear-cut guidelines exist about the use of imaging procedures for the diagnosis of idiopathic inflammatory myopathies (IIM). Similarly, conflicting, and scanty data exist about Power Doppler Ultrasonography (PDUS) in this subset of patients. In this regard, we recently proposed (1) a 0-3 grey scale (GS) and Power Doppler (PD) score in a cohort of patients affected by IIM, evidencing a positive, statistically significant, correlation for PD and oedema and disease activity.

Objectives: The aim of this study was to assess the diagnostic accuracy of our score in IIM patients compared to a control group.

Methods: We prospectively collected, since July 2020 to December 2021, all patients evaluated in Vasculitis and Myositis clinic, Rheumatology Unit, University of Siena, with a recent diagnosis of IIM, as well as patients with a previous, definite diagnosis of IIM and evaluated during follow-up or referred from other centres for a second opinion. As control group, we collected all patients affected by amyopathic dermatomyositis (DM) or who underwent myositis immunoblot or muscle biopsy for proximal limbs weakness but eventually received a diagnosis other than IIM. All patients underwent US examination of both thighs in axial and longitudinal scans.

Results: Forty-five IIM patients (11 anti-synthetase syndrome, 20 DM, 12 PM, 2 scleromyositis) and twenty-six controls were included. During the observational period, 7, 8, 1 and 1 patients underwent PDUS twice, three, four and five times, respectively

Assessing area under the receiver operating characteristic (AUROC) curve analysis, IIM patients and control group were distinguished according to PD sum, Oedema sum, atrophy sum and CRP values (Figure 1a). The best cut-off value for PD sum values was 0.5 (70.2% SE and 83.3% SP), for Oedema sum 1.5 (74.5% SE and 79.2% SP), atrophy sum 0.5 (63.4% SE and 65.4% SP) and CRP was 0.22 mg/dL (61.5% SE and 75% SP).

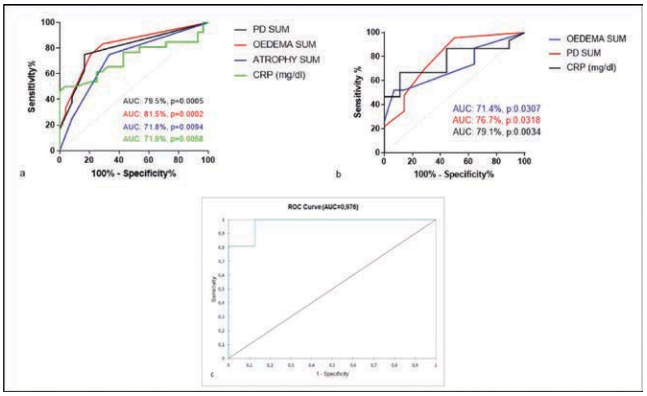

Figure 1.

Stratifying IIM population into two groups according to disease activity (PhGA≥2), AUROC curve analysis allow to distinguish these groups according to PD and oedema sum and CRP values (Figure 1b) and the best cut-off values was 1.5 (69.6% SE and 76.9% SP), 2.5 (52.2% SE and 92.3% SP) and 0.55 mg/dL (66.7% SE and 88.9% SP), respectively.

Testing the IIM group versus control as dependent variable by logistic regression, with PD sum, oedema sum, atrophy sum, CRP, CPK and myoglobin as independent variables, the AUROC was 0.976. From the probability associated with the Chi-square tests, the Type II analysis showed the variable that most influences the IIM diagnosis was PD sum and oedema sum (p=0.017 and p=0.013, respectively) (Figure 1c).

Conclusion: GS and PDUS have proven an overall good diagnostic accuracy in distinguishing between IIM and myositis mimicker. In particular, even low values of PD (sum 1.5) display a good sensitivity and specificity and, together with oedema, elevated CRP values and myositis-specific and associated antibodies, may be considered a reliable tool for a definite diagnosis of IIM.

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Disclosure of Interests: None declared

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POS0872 SERUM LEVEL OF SOLUBLE INTERLEUKIN-2 RECEPTOR IS LINKED TO BETA2-MICROGLOBULINE, NT-PRO BNP AND HIGH-SENSITIVITY TROPONIN T AND MAY HELP TO IDENTIFY PATIENTS WITH EARLY CLINICAL PROGRESS IN SSC.

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Background: Systemic sclerosis (SSc) is characterized by chronic inflammation that leads to damage of the vascular endothelium and excessive collagen deposition in several target organs (1). The interaction of interleukin 2 (IL-2) with the corresponding receptor (IL-2R) is involved in the regulation of autoimmune processes (2). The shedding product of the IL-2R alpha chain, soluble IL-2 receptor (sIL-2R, CD25), is able to either reduce or enhance immune responses (2). Previously, elevated serum levels of sIL-2R were found in the bronchoalveolar lavage of SSc patients with interstitial lung disease (SSc-ILD) as well as serologically in patients with early SSc, and thus suggested to be a biomarker for clinical development of SSc (3,4).
Objectives: To examine concentrations of sIL-2 in patients with SSc and analyse their association with clinical and serological parameters.
Methods: To determine if serological levels of sIL-2R serve as predictor of clinical complications in SSc, sera were analysed [limited cutaneous SSc (lcSSc) n=160; diffuse cutaneous SSc (dSSc), n=137] using a sandwich ELISA. Clinical data (pulmonary fibrosis, PAH, mRSS, therapy) and serological markers (hs-CRP, NT-pro BNP, neutrophil counts, creatinine, hs-troponin T, creatinine kinase, beta2-microglobuline) were assessed at the time of serum sampling and up to 48 months after baseline. Clinical progress was defined by the need to change therapies.
Results: Patients with dSSc presented elevated levels of sIL-2R compared to SSc (dSSc: 673±428 U/ml vs. 646±473 U/ml, p=0.0001). In SSc general, sIL-2R levels correlated with beta2-microglobuline (r=0.6161, p<0.0001, ROC-AUC:0.8428), hs-CRP (r=0.4091, p<0.0001, ROC-AUC:0.7110), NT-proBNP (r=0.2610, p<0.0001, ROC-AUC:0.6793), neutrophil count (r=0.2749, p<0.0001) and hs-troponin T (r=0.4548, p<0.0001, ROC-AUC:0.8729). Further, sIL-2R levels discriminated normal from pathological levels of hs-troponin T (sensitivity 80.0%, specificity 80.1%). Using Log-rank test and Mantel-Cox proportional hazard models, we found that sIL-2R levels above 745.5 U/ml predicted early clinical progress in SSc (HR: 3.45, p=0.0070, Figure 1) within 12 months.

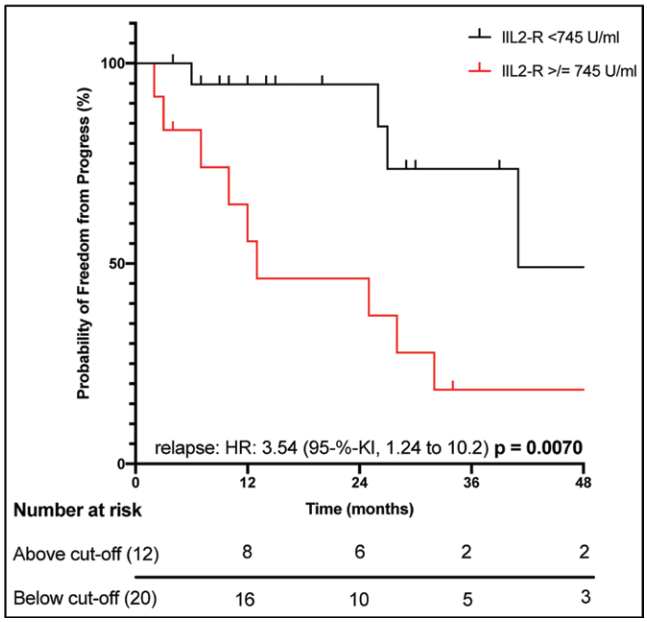

Figure 1. Kaplan-Meier survival analysis for the complete group of patients with SSc. Soluble Il-2R levels above 745U/ml were associated with early progress in SSc.

Conclusion: In SSc, serum levels of sIL-2R could be of diagnostic value by identifying clinical progress. Its role in pathophysiology, especially with regard to disease manifestations such as cardiac involvement needs to be investigated in more detail.
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POS0873

PERSISTENT INFLAMMATION IN SYSTEMIC SCLEROSIS IS STRONGLY ASSOCIATED WITH SEVERE DISEASE AND MORTALITY: AN ANALYSIS FROM THE EUSTAR DATABASE

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Background: Systemic sclerosis (SSc) is a heterogeneous autoimmune disease, with a high disease-related mortality and morbidity. A subset of patients show elevated CRP levels (20-35%), which has been reported as inflammatory SSc. Preliminary data suggest that this subset is characterized by a severe phenotype.
Objectives: To analyse the phenotype and the survival of inflammatory compared with non-inflammatory SSc patient subsets.
Methods: Data from 8571 SSc patients with available CRP measurement from the EUSTAR cohort were analysed. Exclusion criteria included acute infection, missing follow-up and tocilizumab treatment. Patients with a CRP ≥5mg/l at ≥80% of visits were stratified as persistent inflammatory and as non-inflammatory if CRP was ≥5 mg/l at <20% of visits (as described previously (1)). As a sensitivity analysis, patients were defined as inflammatory and non-inflammatory based on a single CRP measurement at baseline only (CRP ≥5 or <5mg/l, respectively). We compared baseline characteristics using Chi-square and non-parametric Kruskal–Wallis tests as appropriate. Kaplan Meier curves with log-rank tests were used to estimate time from baseline to death or censoring, and Cox regression to compare mortality risks adjusted for time from diagnosis to baseline.
Results: Out of 2883 patients with more than two visits, 404 (14%) showed persistent inflammation and 1032 (36%) a non-inflammatory phenotype. Out of 5619 patients with more than one visit, 1830 (33%) were stratified as inflammatory as defined by as single CRP measurement at baseline and 3789 (67%) as non-inflammatory. With both definitions, the inflammatory subset revealed a more severe phenotype than non-inflammatory patients, including more frequent diffuse-cutaneous disease, anti-Scl-70 autoantibodies, pulmonary fibrosis, pulmonary hypertension, higher modified Rodnan skin score, and lower forced vital capacity and diffusing capacity for carbon monoxide. Patients with persistent inflammation had a strongly increased risk of all-cause mortality (HR 7.1 [95%CI 3.7 to 13.5], p<0.001) compared to non-inflammatory patients, whereas this association was weaker when based on a single CRP measurement (HR 2.6 [95%CI 2.1 to 3.2], p<0.001).
Conclusion: The severe phenotype and decreased survival of the inflammatory SSc subset, which was most prominent in patients with persistently elevated CRP levels, suggest a distinct disease subset. Therefore both, the need for more regular monitoring of inflammatory parameters and implications for immune-modulating treatment, needs to be carefully analysed.
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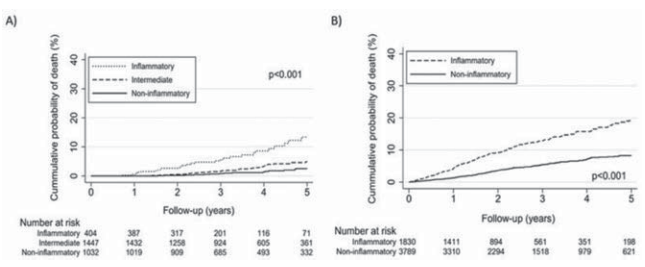

Figure 1. Overall mortality from baseline onward a. by persistent inflammatory phenotype, b. by inflammatory phenotype at baseline

Disclosure of Interests: Adela-Cristina Sarbu: None declared, Sabina Guler: None declared, Odile Stadler: None declared, Yannick Allanore: None declared, Vera Bernardino: None declared, Jörg H.W. Distler: None declared, Armando Gabrielli: None declared, Anna-Maria Hoffmann-Vold: None declared, Marco Matucci-Cerinic: None declared, Ulf Müller-Ladner: None declared, Vera Ortiz-Santamaria: None declared, Simona Rednic: None declared, Valeria Riccieri: None declared, Vanessa Smith: None declared, Susanne Ullman: None declared, Ulrich Walker: None declared, Thomas Geiser: None declared, Oliver Distler: None declared, Britta Maurer Speakers bureau: Boehringer-Ingelheim, Consultant of: Novartis, Boehringer Ingelheim, Janssen-Cilag, Grant/research support from: AbbVie, Protagen, Novartis Biomedical Research, Florian Kollert Shareholder of: Roche, Consultant of: BMS, Actelion, Boehringer-Ingelheim, Pfizer, Grant/research support from: Roche, Gilead, Pfizer, Employee of: Roche
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POS0874 GLUCOCORTICOIDS PRESCRIBING PRACTICES IN SYSTEMIC SCLEROSIS: AN ANALYSIS OF THE EUSTAR DATABASE.

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Background: The use of glucocorticoids (GC) in systemic sclerosis (SSc) is controversial (1). Despite the lack of solid evidence about their efficacy in SSc, GC are prescribed to control musculoskeletal symptoms, or in combination with immunosuppressive drugs (1). The extent of GC use over the disease course has been poorly investigated in SSc. As long-term GC exposure is detrimental even at low doses, estimating the use of GC and identifying patients at high risk for long-term utilization is crucial to plan better management of SSc patients.
Objectives: To estimate the prevalence of GC use in a large sample of SSc patients, identify patient characteristics associated with time spent on GC, and describe the variations in GC utilization over time and across main recruiting countries.
Methods: We included SSc patients with at least one visit in the EUSTAR database from January 2013 (defined as baseline visit) to November 2019. We analyzed the prevalence and the main features of patients using GC at baseline, and the exposure to GC over time. Multivariable linear regression analysis identified patient characteristics associated with the proportion of follow-up time spent on GC. Time trends and variations in GC utilization across main recruiting countries were explored. Missing data were imputed using multiple imputation with chained equations.
Results: The 9819 patients included were mostly females (85%), with limited cutaneous (lc) SSc (73%), and median age of 58 years. At baseline, 2769 (34%) patients (48% diffuse cutaneous (dc) SSc vs. 29% lcSSc) were on GC, at a median dose 7.5 mg/day [IQR 5-9 mg]. Only 2% of patients (n = 162) received >15 mg/day prednisone equivalent. GC were mostly used in combination with an immunosuppressive drug, mainly methotrexate (29%), cyclophosphamide (21%), and mycophenolate mofetil (21%). Compared to patients not receiving GC at baseline, GC users were more frequently males (18% vs. 14%), anti-Scl70 positive (42% vs. 27%), had more synovitis (21% vs. 8%), pericardial effusion (9% vs. 5%), C-reactive protein elevation (33% vs. 19%), increased CK (12% vs. 8%), and significantly lower respiratory volumes. In the subgroup of patients with an early disease duration (< 3 years from first non-Raynaud's onset) (n = 1896), the prevalence of GC users was similar to that observed in the entire sample, but more dcSSc patients were receiving GC in combination with immunosuppressors. On average, GC users spent 25% of their follow-up time (median 33.2 months) on GC, with no significant difference between lcSSc and dcSSc patients. Notably, 971 (33%) and 647 (22%) patients followed-up for >1 year received GC for >6 or >12 months, respectively. In multivariable analysis, patient characteristics poorly explained the variability of GC exposure (adjusted-R^2 = 0.062, P < 0.001). The yearly proportion of glucocorticoids users (2013 - 2018) gradually decreased over time (36% in 2013 vs. 23% in 2018). The rate of GC users and the median proportion of follow-up time spent on GC was highly heterogeneous within and across countries.
Conclusion: GC are widely and long-term used in SSc, mainly to patients with dcSSc, with significant between- and within-country(ies) differences. A gradual decrease in their utilization over time is observed.
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POS0875 LATENT TRAJECTORY MODELING OF PULMONARY ARTERY PRESSURE IN SYSTEMIC SCLEROSIS: A RETROSPECTIVE COHORT STUDY

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Background: Systemic sclerosis (SSc) is an autoimmune disease that is characterized by systemic vasculopathy and fibrosis. Pulmonary hypertension (PH), defined as elevated pulmonary arterial pressure (PAP), is one of the leading causes of death of SSc[1]. In recent years, various therapies have been developed to target each of the pathogenesis of SSc – autoimmunity, vasculopathy, and fibrosis. Accordingly, treatment strategies based on risk stratification for PH progression are aspired; however, prediction of changes in PAP in diverse patients with SSc has not been established[2].

Objectives: To visualize the patterns of PAP elevation in SSc and to identify the clinical characteristics of each trajectory, by applying latent trajectory modeling for PAP measured repeatedly by echocardiography.

Methods: This was a multicenter, retrospective cohort study conducted at four referral hospitals in Kyoto, Japan. Patients with SSc who visited the study site between April 2008 and March 2021 and had at least three echocardiographic measurements of systolic pulmonary arterial pressure (sPAP) were included in this study. Follow-up concluded in March 2021. A group-based trajectory model[3] was applied to the change in sPAP over time, and individual patients were classified into distinct subgroups that followed similar trajectories. The number and shape of the trajectories were estimated based on adequacy, goodness of fit, parsimony, and interpretability of the model. Clinical plausibility was assessed by comparing PH-free survival, i.e., time to either PH or death, for each trajectory. Multinomial logistic regression analysis was performed for baseline clinical characteristics associated with trajectory assignment.

Results: A total of 236 patients with a total of 1097 sPAP measurements were included. We identified five trajectories following the quadratic function as "rapid progression (n=9, 3.8%)", "early elevation (n=30, 12.7%)", "mid elevation (n=54, 22.9%)", "late elevation (n=24, 10.2%)", and "low stable (n=119, 50.4%)". Each trajectory, in this order, showed earlier elevation of sPAP and shorter PH-free survival (Figure 1). In the multinomial logistic regression (with the "low stable" as reference), cardiac involvement was associated with the "rapid progression" (adjusted odds ratio [OR] 28.9, 95% confidence interval [CI] 3.21–259.5), diffuse cutaneous SSc was associated with the "early elevation" (OR 4.08, 95% CI 1.27–13.1), anti-centromere antibody positive was associated with the "mid elevation" (OR 4.50, 95% CI 1.11–18.2), and older age of onset was associated with the above three trajectories.

Conclusion: The pattern of changes in pulmonary artery pressure over time in SSc can be classified into five distinct trajectories. Each trajectory differed in baseline clinical characteristics and outcomes.

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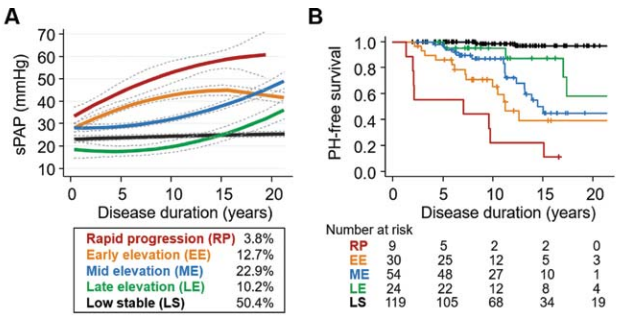

Figure 1. Trajectories of pulmonary arterial pressure and clinical outcomes in patients with systemic sclerosis

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POS0876 SERUM INTERFERON SCORE PREDICTS SEVERITY OF PATIENT REPORTED HAND DISABILITY IN SYSTEMIC SCLEROSIS

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Background: Hand involvement is a major cause of disability in systemic sclerosis (SSc) patients. Loss of hand function is the result of a complex and overlapping series of manifestations including Raynaud's, cutaneous ulcerations as well as skin fibrosis, joint inflammation, and contractures. The natural history of hand involvement in SSc and potential biomarkers to predict its outcome are still poorly defined. Type 1 Interferon (IFN) activation has been extensively correlated with skin fibrosis, joint disease activity, vascular manifestations, and poor prognosis in SSc patients.

Objectives: To characterize hand disability burden in SSc and explore its relationship with IFN activation in a national, multicenter, longitudinal, observational cohort of patients with SSc.

Methods: The Cochin Hand Function Scale (CHFS) was assessed in consecutively enrolled SSc patients at baseline and after 12 months. CHFS values above the patient acceptable symptom state (PASS)(CHFS>25)[1] were considered as clinically meaningful hand impairment (CMHI). Minimal clinically important difference (MCID) in CHFS for improvement (reduction of 13.1%) and worsening (increase >24.6%) were assessed in longitudinal analysis. Serum IFN score was evaluated as previously described[2].

Results: A total of 397 SSc patients from 10 centers (female 85.3%, aged 54.9±11.5 years, white Caucasian 88.2%) were available for longitudinal (12m) analysis. The median disease duration was 9 (IQR 3-16) years, 37.1% of patients had a diffuse cutaneous variant, while anticentromere (ACA) and anti-Scl70 antibody positivity was reported in 41.2% and 33.5% of cases, respectively. Hand digital ulcers, forearm-hand-finger skin score ≥6, and tenosynovitis/arthritis were clinically reported in 24.0%, 15.3%, and 17.9% of patients, respectively. 37.3% of patients reported a CHFS > PASS at baseline. CMHI was associated with male gender (p<.001), diffuse cutaneous variant (p<.001), anti Scl70 positivity (p<.001), ACA negativity (p=.002), and digital ulcers (p=.001). Patients with CMHI had greater serum IFN score than patients with CHFS < PASS (p=.002). In multivariate logistic regression analysis, high serum IFN score remained associated with CHFS>PASS when adjusted for male gender, ACA positivity, anti-Scl70 positive, diffuse subset, and current digital ulcers (OR 2.67, p=.005). Over the 12-month follow-up, vasoactive and immunosuppressive treatment were escalated or introduced in 7.2 and 7.8% of patients, respectively. Median CHFS worsened over time (from 18 (IQR 5-37) to 21 (IQR 6-37), p=.002)) with 32.5% of patients having a clinically meaningful worsening and 32.0% improving their hand function. Functional hand worsening was associated with lower baseline CHFS (p=.001) and ACA negativity (p=.002), while improving with female gender (p=.047), limited cutaneous subset (p=.029), higher baseline CHFS (p=.001), and active baseline tenosynovitis (p=.014).

Conclusion: One third of the patients within our cohort complain of a significant hand impairment. This is associated with higher IFN activation and worsens at group level in patients despite standard of care treatment.

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POS0877 INTERSTITIAL LUNG DISEASE IN ANTI-U1RNP SYSTEMIC SCLEROSIS PATIENTS: A EUROPEAN SCLERODERMA TRIALS AND RESEARCH (EUSTAR) ANALYSIS

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Background: Interstitial lung disease (ILD) has become the leading cause of mortality in systemic sclerosis (SSc) patients (1). The presence of anti-U1RNP antibodies is primarily associated with mixed connective tissue disease (MCTD), however these autoantibodies may be found in up to 10% of SSc patients (2). A recent large multicenter study showed that the presence of anti-U1RNP antibodies was independently associated with more severe disease in SSc patients. However, so far, little is known about the influence of anti-U1RNP antibodies specifically on lung outcomes in SSc-ILD patients.
Objectives: To describe the clinical features, outcomes and prognosis of anti-U1RNP SSc-ILD patients.
Methods: SSc patients with available data on their autoantibody profile were identified from the EUSTAR database. Those with ILD identified by high-resolution chest tomography (HRCT) were included for analysis. Baseline demographic and disease features were compared between anti-U1RNP positive and anti-U1RNP negative patients. For the longitudinal part in patients with repeated lung function tests, the mean annual decline in %predicted forced vital capacity (%pFVC) was compared between the two groups. Predictors associated with death of any cause or severe ILD progression, defined as a drop >10% in %pFVC/year, were evaluated in SSc-ILD patients with or without U1RNP. Mild progression was defined as a loss of 5-10% in %pFVC/year. Demographic and clinical parameters were compared between patients positive and negative for anti-U1RNP antibodies in univariate analysis. Associations between anti-U1RNP status and lung involvement were tested in multivariate logistic regression models.
Results: A total of 5676 SSc-ILD patients were included for the analysis, among which 320 (5.6%) were positive for anti-U1RNP antibodies. Mean age was 56.4±13.5 years and 4645 (81.8%) were women. Anti-U1RNP+ SSc-ILD patients had more frequently limited cutaneous SSc (52.5% vs 39.8%, p<0.001), higher frequency of joint synovitis (20.0% vs 12.9%, p<0.001) and myositis (22.2% vs 18.2%, p<0.03) and lower incidence of scleroderma renal crisis (0.3% vs 2.0%, p=0.02). Anti-U1RNP+ patients had a baseline lower mean %pFVC (81.1% vs 85.3%, p=0.002) and lower mean %predicted diffusing capacity for carbon monoxide (%pDLCO) (58.9% vs 60.2%, p=0.004) than anti-U1RNP- SSc-ILD patients. No significant differences were found at baseline HRCT, including lung involvement >20% (4.4 vs 4.2%%, p=0.39), or the presence of ground glass opacities (38.1% vs 33.6%, p=0.14).A total of 2697 (50.3%) patients with SSc-ILD had at least one FVC measurement available during a mean follow-up of 20.8±20.5 months. Mean expected decline in %FVC per year was not different between U1RNP positive and negative patients (-0.21% vs -0.68%, p=0.70). Mortality or severe ILD progression was not statistically different between the two groups (35 (21.6%) vs 677 deaths (26.7%), p=0.43, and 23 (14.0%) vs 283 severe progressors (11.0%), p=0.25, respectively). Mild ILD progression was also not statistically different between the two groups (11.0% vs 10.0%, p=0.20). The proportion of patients with FVC<80% at last follow-up was similar between U1RNP positive and negative patients (50.6% vs 44.3%, p=0.13).
Conclusion: Our results from the EUSTAR database show that SSc patients positive for anti-U1RNP antibodies have more impaired baseline lung function but similar rate of progression during follow-up. This suggests that early stages might be important in RNP+ SSc-ILD patients who may require specific management and follow-up.
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POS0878 ASSOCIATION OF A LOWER BODY-MASS INDEX WITH THE PRESENCE OF ILD IN SSC PATIENTS – A DERIVATION PREDICTION STUDY USING DECISION TREE-BASED ALGORITHMS

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Background: Upper-gastrointestinal involvement (GI) is associated with more severe interstitial lung disease in patients with systemic sclerosis (SSc-ILD). However, there are many unexplored GI risk factors for the presence of SSc-ILD which could be potentially revealed by machine learning algorithms.
Objectives: The aim of our study was to identify GI related risk factors for the presence of SSc-ILD using machine learning algorithms based on decision trees (DT).
Methods: Data of the last follow-up visit from consecutive patients fulfilling the 2013 ACR/EULAR SSc classification criteria recorded in our local EUSTAR registry were used for this study. The study outcome was the *presence of SSc-ILD* on high-resolution computed tomography. Two sets of predictors were identified based on their potential association with GI. The first set contains the following variables available in the EUSTAR registry: *esophageal symptoms (dysphagia and reflux)*, *stomach symptoms (early satiety, vomiting)*, *intestinal symptoms (diarrhea, bloating and constipation)*, *malabsorption syndrome*, *body-mass-index (BMI)* and *proton pump inhibitor therapy, calcium channel blocker therapy and immunosuppressive therapy*. In the second set, we replaced the first three EUSTAR variables of the first set with the scales of the UCLA Gastrointestinal Tract Questionnaire 2.0 (UCLA-GIT). Of these two sets, the most important variable was selected using three different DT-based algorithms: *(1) recursive partitioning and regression trees (RPART)* –which uses trees to build decision rules, *(2) random forest (RF)* - an ensemble of DT built in parallel, and *(3) gradient boosting machines (GBM)* - an ensemble of DT built sequentially. The selected variables were eventually integrated with established predictors for presence of SSc-ILD (*diffuse cutaneous subset*, *anti-Scl-70 positivity*, *male gender*, *forced vital capacity [FVC]* and *diffusion capacity of the lung for carbon monoxide-single breath [DLCO-SB]*) into final prediction models for SSc-ILD presence using RPART, RF and GBM respectively. Their performance was evaluated by C-statistics. The importance of the newly detected predictor was assessed by variable importance plots (VIPs).
Results: We included in our study 334 patients. The median age was 61 [IQR: 50-69] years, 59 (17.7%) were males and 266 (79.6%) had limited cutaneous SSc. Median BMI was 23 [IQR: 21-26] kg/m2, 133 (39.8%) of the patients had SSc-ILD, median FVC% 93 [IQR: 81-105], DLCO 72.5 [56-84] and. Of the

UCLA-GIT scales the highest score was for the distension/bloating with a value of 0.50 [IQR: 0-1.24]. Regarding medications, 167 (50%) patients were exposed to PPI, 39 (11.7%) to CCB and 105 (31.4%) to immunosuppressive therapy.
The BMI was deemed by all three algorithms as the most important predictor of SSc-ILD among both sets of GI related variables (Figure 1A-F). The final model, which included established risk factors for presence of ILD and the BMI, supported the importance of BMI in predicting the SSc-ILD. The VIPs obtained by GBM also ranked the BMI as the most important predictor.

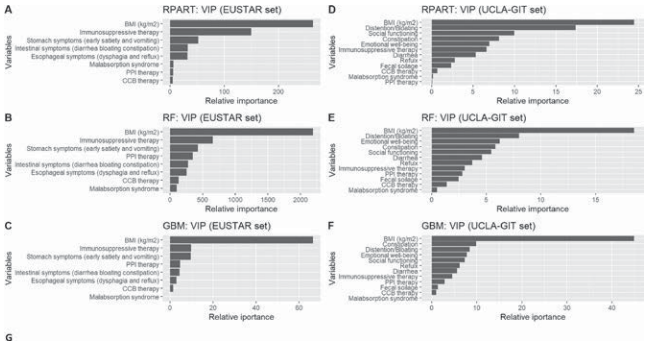

Figure 1. Tree-based algorithms revealing the importance of BMI for prediction of SSc-ILD. Panels A, B and C are variable importance plots (VIPs), which reveals the most important GI-predictor for occurrence of SSc-ILD in the EUSTAR set– the predictor with the highest relative importance is the most important predictor. Panels D, E and F are VIPs reveals the most important GI-predictor for occurrence of SSc-ILD in the UCLA-GIT set.

A lower BMI was associated with presence of SSc-ILD (C-statistics for the RPART, RF and GBM models were 0.79, 0.70 and 0.76, respectively, corresponding to a fair accuracy). As expected, also a lower FVC, and DLCO-SB, and a positivity for Scl-70 ab were associated with presence of ILD.
Conclusion: Lower BMI is a novel promising predictor for the presence of ILD, which should be confirmed in additional analyses.
Disclosure of Interests: Alexandru Garaiman: None declared, Carina Mihai Speakers bureau: MEDtalks Switzerland, Mepha, Rucsandra Dobrota Consultant of: Actelion and Boehringer-Ingelheim, Grant/research support from: Articulum Fellowship, Pfizer, Actelion, Cosimo Bruni Speakers bureau: Eli-Lilly, Actelion, Boehringer-Ingelheim, Grant/research support from: Gruppo Italiano Lotta alla Sclerodermia (GILS), European,, Scleroderma Trials and Research Group (EUSTAR), Scleroderma Clinical Trials Consortium (SCTC), AbbVie, Muriel Elhai: None declared, Suzana Jordan: None declared, Lea Stamm: None declared, Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Jansen, Roche, Merck Sharp & Dohme, ARXX Therapeutics, Lilly and Medscape, Consultant of: Actelion, Boehringer Ingelheim, Jansen, Roche, Merck Sharp & Dohme, ARXX Therapeutics, Lilly and Medscape, Grant/research support from: Boehringer Ingelheim, Bayer, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche, Pfizer, Roche, Sanofi, Consultant of: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos, Glenmark, GSK, Horizon, Inventiva, iQvia, Kymera, Lupin, Medac, Medscape, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Prometheus Biosences, Roche, Roivant, Topadur and UBC, Lilly, Pfizer, Grant/research support from: Kymera, Mitsubishi Tanabe, Mike O. Becker Speakers bureau: Mepha, MSD, Novartis, GSK, Bayer and Vifor
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POS0879 LUNG ULTRASOUND FOR INTERSTITIAL LUNG DISEASE DETECTION IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS: ROLE OF B-LINE AND PLEURAL LINE MODIFICATIONS

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Background: Lung ultrasound (LUS) is a technique that showed a high diagnostic accuracy for interstitial lung disease (ILD) detection in systemic sclerosis (SSc) patients and currently in progress of standardization. Traditionally, B-lines represented the finding of ILD, with the ≥10 total cut-off reported by Tardella et al. resulting to be closely related to moderate ILD detected on high resolution chest computed tomography (HRCT). Recently, Fairchild et al. proposed novel LUS criteria for the evaluation of pleural line, disclosing high accuracy and reproducibility.
Objectives: To compare B lines cut-off with novel pleural line criteria and the respectively associated variables.
Methods: We enrolled 55 consecutive patients affected by SSc according to ACR/EULAR 2013 criteria who underwent respiratory functional tests (RFTs) during 2021, excluding smokers and those with arterial pulmonary hypertension. Twenty-four of them carried out a HRCT during a ± 6-months' time. In the same day of RFTs, two certified blinded operators performed LUS for each patient applying the 14-areas technique proposed by Gutierrez et al., looking for the presence of total ≥10 cumulative B lines and the fulfilling of Fairchild's criteria for pleural line. A 3-13 MHz operating linear probe was used. Clinical-demographic data and ongoing therapies were collected.
Results: Among 55 total SSc patients, the agreement between the two operators for Fairchild's criteria was almost perfect (Cohen's kappa (k) =0.81) and substantial for ≥10 cumulative B-lines count (k=0.74). Fairchild's criteria showed a higher diagnostic accuracy compared with ILD detected on HRCT, with an overall specificity (SP) and a positive predicted value (PPV) of 100% (Table 1). A negative correlation emerged between total lung capacity values (TLC%) and both B lines cut-off [first operator (IO): p 0.04, r -0.27; second operator (IIO): p 0.042, r-0.28] and pleural line criteria (IO: p 0.009, r -0.35; IIO: p 0.08, r – 0.36), but only the latter negatively correlated also with forced vital capacity values (FVC%) (IO: p 0.04, r – 0.27; IIO p 0.03, r -0.28). The ≥10 total B lines amount correlated positively with concurrent mycophenolate therapy (IO: p 0.09, r 0.28; IIO: p 0.005, r 0.37) and negatively with anti-centromere antibodies (IO: p 0.002, r -0.3; IIO p 0.009, r -0.34). The presence of digital ulcers showed a positive correlation with pleural line criteria (IO: p 0.03, r 0.29; IIO: p 0.005, r 0.37), with a significant association on multivariate analysis (IO: p 0.03, IIO: p 0.01).

Table 1. Overall sensitivity, specificity, positive predictive value, negative predictive value of LUS compared to ILD detected on HRCT. C.I. 95% confidence interval.

	SE (C.I.)	SP (C.I.)	PPV (C.I.)	NPV (C.I.)
Fairchild's criteria fulfilling	0.91 (0.76 - 0,97)	1 (0.78 – 1.000)	1 (0.88 -1.00)	0.82 (0,59 – 0.94)
≥10 cumulative B-lines count	0.73 (0.56 – 0.85)	0.8 (0.55 – 0.93)	0.89 (0.72 – 0.96)	0.57 (0.36 – 0.75)

Conclusion: We confirmed the feasibility and reliability of Fairchild's recently proposed pleural line LUS criteria, that showed a higher diagnostic accuracy versus ≥10 cumulative B-lines count for ILD detected on HRCT, presenting SP and PPV values of 100% in SSc. Furthermore, these LUS features seem to differently associate with other aspects of the disease such as autoantibody specificity and vascular lesions, thus deserving future deeper evaluations. For the first time, we found that Fairchild's criteria were associated with a clinical variable such as digital ulcers. Our results highlight the relevance of pleural line evaluation for ILD detection in SSc on LUS and its possible role towards a standardization of this diagnostic technique.
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POS0880 CHARACTERISTICS AND DISEASE COURSE OF UNTREATED PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease (ILD) is the leading cause of death in systemic sclerosis (SSc). European consensus guidelines consider that some patients with mild disease might not need pharmacological treatment (1). Up to now, the disease characteristics and the disease course of non-treated SSc-ILD patients remain unknown.
Objectives: To describe disease characteristics and the disease course of non-treated SSc patients with ILD.
Methods: We included patients from our local EUSTAR center registered since 2008, who had a diagnosis of ILD on high-resolution computed

tomography (HRCT) and available data on pulmonary function tests and treatment. Longitudinal study included patients with at least one follow-up visit. Patients were classified as treated if they received a potential ILD modifying drug (immunosuppressive therapy or nintedanib). Treated and untreated patients were compared at baseline. Progression in the untreated group was defined as (i) forced vital capacity (FVC) decline from baseline of ≥10% or (ii) an FVC decline of 5-9% in association with a decline in diffusing capacity for carbon monoxide (DLCO) of ≥15%, or (iii) start of a ILD modifying treatment during follow-up. In the untreated group, patients who progressed at any time were compared with patients with stable disease during follow-up. Multivariable logistic regression was performed to identify (i) factors associated with non-prescription of a treatment in ILD patients at baseline and (ii) factors associated with progression in the untreated patients. Covariates were selected according to clinical experience and literature evidence.

Results: Among 496 patients included in our cohort, 209 (42%) patients had ILD on baseline HRCT: 48/209 (23%) were males, median disease duration 8 [IQR: 4-12] years, 67/209 (32%) of diffuse cutaneous subset and 86/209 (41%) had anti-Scl70 antibodies. Among them, 142/209 (68%) did not receive any potentially ILD modifying treatments at baseline. Untreated patients were older (59 vs. 54 years), had a longer disease duration, were less frequently smokers, had more frequently anticentromere antibodies and lower levels of CRP. They had more frequently a limited extent (<20%) of lung fibrosis on HRCT, higher FVC (97.02 (±19.76) % vs. 78.29 (±19.23) %) and DLCO (72.10 (±18.97) % vs. 57.57 (±20.81) %), better performances in the 6 minute walking test and were less frequently treated with low dose of glucocorticoids. In multivariable logistic regression, older age (OR: 1.04 [1.01-1.08], p=0.021), a less extensive disease on HRCT (OR: 0.29 [0.09-0.90], p=0.037) and less frequent prescription of glucocorticoids (OR: 0.036 [0.12-0.92], p=0.037) were independently associated with absence of ILD modifying treatment prescription in our cohort. From the 142 untreated patients, 96 were followed-up for 64 [39-96] months. Of these, 56 (58%) patients showed progression of ILD, of whom 43 progressed by lung function parameters. Of these 56 patients, 31 (56%) progressed in the first 18 months. Diffuse cutaneous subtype (OR: 5.26 [1.26-27.62], p=0.031), shorter disease duration (OR: 0.95 [0.90-0.99], p=0.035) and oesophageal symptoms (reflux, dysphagia) (OR: 3.51 [1.12-12.18], p=0.036) at baseline were independent predictors of progression during follow-up in untreated patients.

Conclusion: A considerable number of SSc patients with ILD are not treated in clinical practice, in particular patients with limited cutaneous SSc, older age and an overall less extensive ILD. However, during a follow-up of 5 years, contrary to the common belief, about 60% of the untreated patients showed ILD-progression. The diffuse cutaneous subtype, shorter disease duration and oesophageal symptoms at baseline characterized these patients. With the development of effective and safe therapies for SSc-ILD, our results support a change in practice for selecting patients for treatment.

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POS0881

EFFICACY AND SAFETY OF SUBCUTANEOUS BRODALUMAB, A FULLY HUMAN ANTI–IL-17RA MONOCLONAL ANTIBODY, FOR SYSTEMIC SCLEROSIS WITH MODERATE-TO-SEVERE SKIN THICKENING: A MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND PHASE 3 STUDY

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Background: Systemic sclerosis (SSc) is a rare chronic connective tissue disease of unknown cause characterized by autoimmunity, vasculopathy, and fibrosis of the skin and various internal organs. It is considered to constitute an area of high unmet medical needed due to limited treatment options and no sufficiently effective treatments. Our previous study (the single-arm, open-label, phase 1 study) indicated that brodalumab, a fully human anti-IL-17RA monoclonal antibody, had a potential to improve skin sclerosis in SSc patients, which could be attributed to its direct effects on fibroblasts and indirect effects via impacts on both B cell and T cell subsets (NCT04368403).

Objectives: To evaluate the efficacy and safety of brodalumab for SSc patients with moderate-to-severe skin thickening in a phase 3, multicenter, randomized, placebo-controlled, double-blind study.

Methods: Eligible patients (modified Rodnan skin score (mRSS):10-29, present with the first symptoms of SSc other than Raynaud's phenomenon within 60 months at enrolment) were randomized (1:1) to receive subcutaneous brodalumab 210 mg every 2 weeks (Q2W) or placebo during the 52-week placebo-controlled period. Primary endpoint was change from baseline of mRSS at week 24. Patients with an increase in mRSS of ≥5 points and ≥20% from baseline at or after week 24 were permitted to receive open-label treatment with brodalumab.

Results: A total of 100 patients was randomized to the brodalumab group (n=50) or the placebo group (n=50). Forty-six and 45 patients had diffuse cutaneous SSc in the brodalumab and placebo groups, respectively. In both groups, 47 patients completed the 24-week follow-up. Forty-four and 43 patients in the brodalumab and placebo groups completed the 52-week follow-up, respectively. At or after week 24, 38 patients (placebo, n=37; brodalumab, n=1) were switched to the active drug. Brodalumab achieved the primary endpoint (treatment difference of least square mean: –21.2 [95% CI -23.9, 18.5]; P<0.0001), and demonstrated a rapid, sustained reduction in mRSS over 52 weeks. Brodalumab also elevated the composite response index in SSc (CRISS) score, suppressed new development of digital ulcers, deterioration of respiratory function, and progression of lung lesions. Moreover, treatment of brodalumab improved the frequency scale for the symptoms of gastroesophageal reflux disease (FSSG) score, global assessment by physician (CGA) and patient (PGA), the Japanese version of the health assessment questionnaire-disability index (J-HAQ-DI) score, and the functional assessment of chronic illness therapy-fatigue (FACIT-Fatigue) score. The safety profile did not differ from that previously observed in other diseases such as psoriasis and ankylosing spondylitis and non-radiographic axial spondyloarthritis.

Conclusion: Brodalumab demonstrated a rapid, sustained, and significant decrease in skin sclerosis. Moreover, the outcome of brodalumab treatment suggested its therapeutic effects on lung/respiratory functions, digital ulcers, the symptoms of gastroesophageal reflux disease, and QOL without any noteworthy safety concerns.

REFERENCES: None.

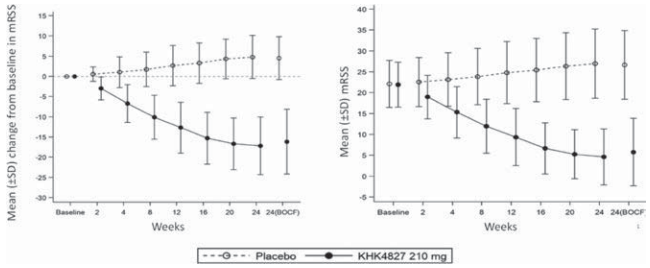

Figure 1. mRSS over the 24-week follow up. (Mean +/- SD)

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Table 1. Secondary endpoints at week 24

	Brodalumab		Placebo				
	mean	SD	mean	SD	Difference	95% CI	P value
Median CRISS score	1	NA	0	NA	NA	NA	<0.0001
Cumulative new digital ulcer count	0.1	0.28	5.0	6.5	-4.9	[-6.8, -3.0]	<0.0001
Percent predicted FVC*, %	0.19	4.43	-5.04	7.39	5.23	[2.73, 7.72]	<0.0001
Percent predicted DLCO*, %	-0.59	6.808	-5.96	6.773	5.38	[2.60, 8.16]	0.00022
FSSG score*	-2.3	5.99	10.1	11.16	-12.4	[-16.1, -8.7]	<0.0001
PGA*, mm	-6.8	21.94	26.1	24.17	-32.9	[-42.3, -23.4]	<0.0001
CGA*, mm	-34.0	14.69	13.8	23.05	-63.4	[-71.9, -54.9]	<0.0001
J-HAQ-DI*	-0.045	0.234	0.698	0.7065	-0.743	[-0.958, -0.527]	<0.0001
FACIT-Fatigue subscale score*	2.234	6.869	-9.404	14.7658	11.638	[6.920, 16.356]	<0.0001

*Change from baseline

POS0882

HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY FOR THE ASSESSMENT OF CALCINOSIS, ACROOSTEOLYSIS, AND PERIPHERAL BONE MINERAL DENSITY IN PATIENTS WITH SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL PILOT STUDY

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Background: Systemic Sclerosis (SSc) is a rare disorder associated with hand radiological damage, typically acro-osteolysis (AO) and calcinosis, and increased risk of osteoporosis [1, 2]. Recently, high resolution peripheral quantitative computed tomography (HR-pQCT) has contributed to advances in noninvasive imaging in patients with osteoporosis, inflammatory arthritis, and osteoarthritis. Due to its three-dimensional, high resolution (82 μm^3) imaging of calcified structures, HR-pQCT might be beneficial in detecting and describing early AO changes, calcifications or bone mineral density (BMD) loss and in studying potential treatment effects on progression/resolution of pathological manifestations.
Objectives: To study the association between different types of hand radiological damage assessed by HR-pQCT, and to evaluate volumetric BMD and microarchitecture at distal radius among SSc patients with and without AO.
Methods: This single-centre, cross-sectional study included patients with SSc according to ACR/EULAR 2013 recruited from the outpatient clinic at the Department of Rheumatology, Aarhus University Hospital, between 1st of October and 21st of December 2021. All patients underwent HR-pQCT (Xtreme CT, Scanco Medical AG) scan of the dominant hand's distal radius and both hand's distal phalanges (DP) on the 2nd to 4th finger. A semiquantitative scale of 0-3 was composed to quantify the degree of soft tissue calcifications identified in the 2nd to 4th finger (Figure 1). Lengths of the DPs and soft tissue extending distally from the most distal part of DPs (ST) were measured in a three-dimensional multiplanar reconstruction. Volumetric BMD and bone microarchitecture were analyzed using HR-pQCT scanner specific software at the distal radius.
Results: We included 40 patients with SSc of whom 13 had AO according to hand radiographs. The two groups had a similar distribution regarding age, sex, and BMI. Patients with AO had longer disease duration compared to patients without AO (med. 17 yrs. (IQR 7-20 yrs.) vs 3 yrs. (IQR 2-7 yrs.) (P<0.001)). One patient was excluded from the BMD analysis, and 21 (9%) DP and 20 (8%) soft tissue measurements were excluded due to motion-induced image degradation. A higher prevalence of calcinosis was observed in patients with AO (n=11/13) compared to patients without AO (n=11/27) (P<0.05). Patients with AO had more or larger calcifications according to our grading system (med. 2 (IQR 1-3) vs 0 (IQR 0-1)) (P<0.001). Grade 3 changes were observed in patients with AO (n=6/13, 46%) but not in patients without AO. Furthermore, the patients with AO had shorter DPs on the 2nd finger on both hands (right P<0.001; left P<0.01) and less ST on the right 2nd, 3rd, and 4th (P<0.01; P<0.001; P<0.01) as well as the left 3rd (P<0.05). We observed no differences between bone volume ratio (med. 0.101 (IQR 0.068-0.143) vs 0.126 (IQR 0.104-0.141) (P=0.38)), cortical BMD (med. 828 (IQR 774-853) vs 842 (IQR 762-882) (P=0.60)), or trabecular BMD (med. 121 (IQR 82-172) vs 151.6 (IQR 125-170) (P=0.36)). Yet, the patients with AO had a lower number of trabeculae (P<0.05) and a lower homogeneity of spacing between trabeculae (P<0.05) at distal radius.
Conclusion: Patients with AO had larger and a higher number of calcifications and had significantly shortened DPs and ST on several fingers assessed by HR-pQCT. A potential superiority compared with hand radiographs is yet to be established. Still, the modality could eventually prove useful in detecting and monitoring small hand lesions and facilitate earlier diagnosis and proper treatment among patients with SSc.

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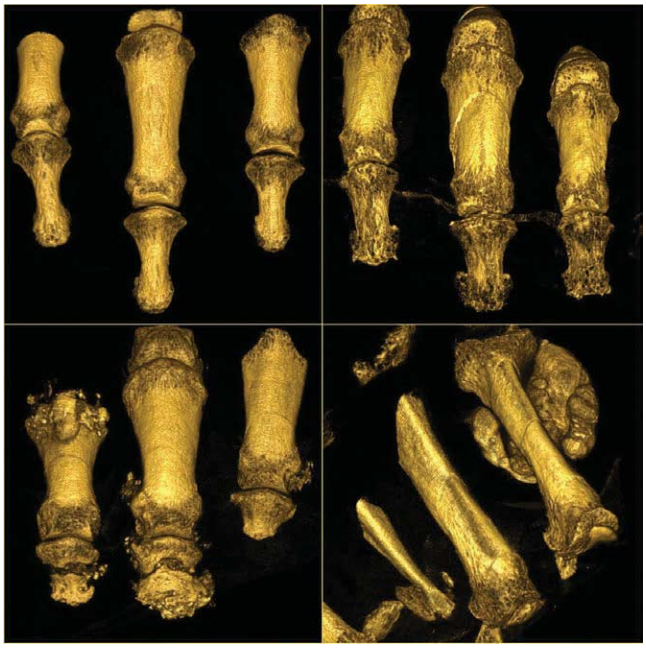

Figure 1.

POS0883

BIOPHYSICAL PROPERTIES OF MONOCYTES INDICATE DISEASE ACTIVITY, SEVERITY OF FIBROTIC OR MICROVASCULAR MANIFESTATIONS AND THE RISK FOR PROGRESSION IN SYSTEMIC SCLEROSIS

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Background: Dysregulated immune responses are major pathogenic players in systemic sclerosis (SSc). The biophysical properties (such as cell deformation, Young's modulus (a measure of cell stiffness) and area) of circulating immune cells reflect their states and functions, as well as their pathological activation (1-3). Thus, biophysical phenotyping can provide access to a novel, mostly unexplored layer of information that is currently not accessible with standard techniques of cellular and molecular biology. Real-time fluorescence and deformability cytometry (RT-FDC) is a novel technique that enables biophysical phenotyping of individual immune cells at a high throughput, which allows its use in a clinical setting (3-5).
Objectives: Here, we hypothesized that biophysical properties of circulating immune cells in SSc and rheumatoid arthritis (RA) might specifically reflect their distinct pathophysiological activation in the respective disease, and might indicate clinical outcomes such as disease activity or severity. We thus performed

RT-FDC-based biophysical phenotyping of circulating immune cells in SSc, RA and healthy controls.

Methods: 63 SSc patients, 59 RA patients fulfilling the respective ACR/EULAR classification criteria and 18 age- and sex-matched healthy controls were included in the study between 05.2019 and 09.2021. Peripheral blood mononuclear cells (PBMC) were isolated and immunolabelled. PBMC subpopulations were identified in RT-FDC by standard gating strategies based on their marker expression and their deformation, Young's modulus and area were determined.

Results: We identified SSc-specific changes (changes in SSc, but not in RA compared to healthy controls) in the biophysical properties of NK, NKT-like cells and monocyte subpopulations in SSc. Monocytes subpopulations had a higher deformation and cross-sectional area and/or more compact intra-donor distributions of these parameters in patients with active disease and with extensive skin or lung fibrosis in comparison with patients with stable disease and limited skin or lung fibrosis, respectively. All monocytes subsets were stiffer in patients with progression of skin of lung fibrosis at the time of measurement in comparison with a previous visit. The deformation and area of intermediate monocytes could also identify patients at risk for future progression of lung fibrosis. Changes in biophysical properties of monocytes can indicate, beyond fibrotic burden, clinical manifestations of microvascular damage such as active digital ulcers and pulmonary arterial hypertension.

Conclusion: We demonstrated that changes in the biophysical properties of monocytes subsets are associated with multiple clinical outcomes in SSc such as disease activity, severity of fibrotic or microvascular manifestations and risk of progression and might thus directly reflect SSc-specific pathologic immune cell activation. Our results thus provide first evidence that RT-FDC-based biophysical phenotyping of circulating immune cells may be a useful tool for clinical evaluation of SSc patients.

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POS0884 DESCRIPTIVE EPIDEMIOLOGY OF SEVERE CARDIAC INVOLVEMENT IN SYSTEMIC SCLEROSIS: A BICENTRIC RETROSPECTIVE STUDY ON 459 PATIENTS

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Background: The prevalence of cardiac involvement in systemic sclerosis (SSc) varies in the literature between 3% and 44% and represents a leading cause of mortality in this disease. The incidence of severe cardiac involvement and the factors associated with the occurrence of severe cardiac involvement are not known in the literature.

Objectives: The objective of this study was to evaluate the incidence, prognosis and factors associated with the occurrence of severe cardiac involvement during SSc course.

Methods: We conducted a retrospective, bi-centric study from January 1, 1966 to December 31, 2018. The patients included had a diagnosis of SS according to the ACR/EULAR 2013 criteria. The primary endpoint was the occurrence of severe cardiac involvement. Cardiac involvement was defined by the presence of at least one of the following elements: death of cardiovascular origin, left ventricular ejection fraction less than or equal to 50%, abnormality of at least 3 measurement parameters of diastolic function, global longitudinal strain less than or equal to 18 in absolute value, ventricular tachycardia, ventricular extrasystoles requiring intervention or elevated troponin. Patients with associated myositis and whose only criterion for cardiac involvement was elevated troponin were not included in the group with cardiac involvement. Severe cardiac involvement was defined by the occurrence of hospitalization for cardiovascular reasons or by death of cardiovascular origin. Univariable and multivariable Cox proportional hazards models were used to determine variables associated with severe cardiac involvement occurrence. Survival analysis was performed using the Kaplan-Meier method with comparisons performed using the log rank test.

Results: Four hundred and fifty-nine patients with SSc were included and were followed for a median of 7.1 years [3.1; 13.3]. The median age of our population was 54 years old. There were 81% of women, 77% of patients had limited cutaneous SSc, 15% diffuse cutaneous SSc and 8% SSc sine scleroderma. Of the 459 patients, 105 (23%) had cardiac involvement and 56 (12%) severe cardiac involvement. The incidence of severe cardiac involvement was 2.42 per 100 patient years. Ninety-six hospitalizations were recorded, including 40 (42%) for acute heart failure, 19 (20%) for arrhythmia, 5 (5%) for acute pericarditis, 6 (6%) for acute myocarditis and 14 (15 %) for coronary artery disease (acute coronary syndrome, myocardial infarction or coronary revascularization). The independent factors associated with severe cardiac involvement in SSc were age over 54 years at SSc-diagnosis (OR = 3.21 95% CI [1.73; 5.95], p < 0.001), the presence of myositis (OR = 5.01 95% CI [1.89; 13.28], p = 0.001), pericardial involvement (OR = 3.79 95% CI [2.05; 7.03]; p < 0.001) or scleroderma renal crisis (OR = 4.72 95% CI [2.05; 10.92], p < 0.001). The survival rate of patients with severe cardiac involvement was 70% at 5 years and 53% at 10 years. Patients with severe cardiac involvement had a mortality risk three times greater than patients without severe cardiac involvement, HR = 3.1 (95% CI [1.7; 5.7], p<0.0001) (Figure 1). Pericardial involvement was an independent risk factor for mortality, HR = 2.0 (95% CI [1.02; 4.0], p=0.04).

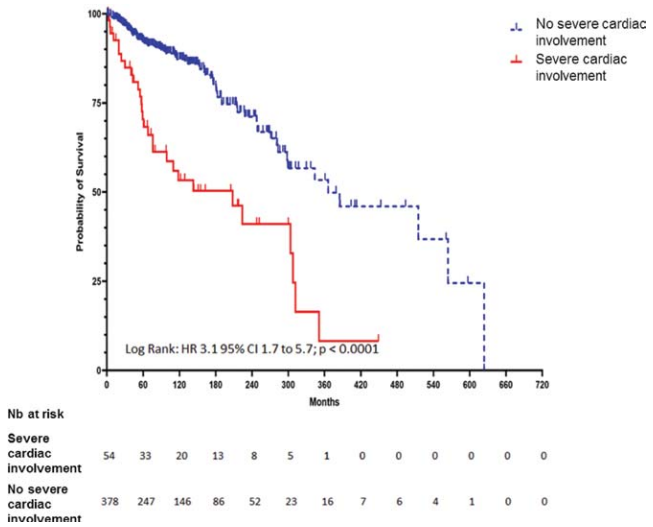

Figure 1. Survival of patients with severe cardiac involvement of systemic scleroderma. HR: Hazard ratio; 95% CI: 95% Confidence interval; Nb at risk: Number at risk

Conclusion: We need to focus our clinical attention on diagnosing and manage cardiac involvement in SSc, as severe cardiac involvement is not uncommon and is responsible for a poor prognosis.

Disclosure of Interests: None declared

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POS0885 HYPOCHROMIC ERYTHROCYTES AS PROGNOSTIC INDICATOR OF SURVIVAL AMONG PATIENTS WITH SYSTEMIC SCLEROSIS SCREENED FOR PULMONARY HYPERTENSION

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Background: Iron deficiency is frequent among patients with systemic sclerosis (SSc), particularly among those with pulmonary hypertension (PH). First data indicate prognostic importance of hypochromic erythrocytes (HRC) >2% among patients with PH[1]. Hence, the aim of this study was to investigate the predictive value of HRC in SSc patients screened for PH.

Objectives: The objective of this study was to investigate the predictive value of HRC in SSc patients screened for PH.

Methods: In this retrospective, single-center cohort study SSc patients screened for PH were included. Clinical characteristics, laboratory and pulmonary functional parameters associated with the prognosis of SSc were analysed using uni- and multivariable analysis.

Results: A total of 280 SSc patients were screened, 171 were included in the analysis having complete data of iron metabolism (79% female, 61.0±12.9 years of age, 73.2% limited cutaneous SSc, 56 manifest PH and 112 pulmonary fibrosis). The patients were followed for 2.4±1.8 (median 2.4) years. HRC >2% at baseline was significantly associated with worse survival in the uni- (p=0.018) and multivariable analysis (p<0.0001). Overall 34.5% of the patients suffered from iron deficiency and 22% received iron substitution during follow-up. HRC >2% was identified as independent predictor of mortality, for patients with and without pulmonary manifestations of SSc.

Conclusion: This study detected for the first time that HRC >2% is an independent prognostic predictor and can possibly be used as a biomarker among SSc-patients. Further studies are needed to confirm these results.

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POS0886 EFFICACY AND SAFETY OF RITUXIMAB IN AUTOIMMUNE DISEASE–ASSOCIATED INTERSTITIAL LUNG DISEASE: A PROSPECTIVE COHORT STUDY.

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Background: Interstitial lung disease (ILD) is a common condition in patients with connective tissue disease (CTD). It is associated with increased morbidity and mortality. Rituximab (RTX) has been approved for treatment of RA and some recent retrospective studies suggest that it could be an alternative treatment for patients with CTD-ILD, even in cases that prove refractory to conventional immunosuppressants.

Objectives: To analyze the efficacy and safety of RTX in connective tissue disease associated with interstitial lung disease (CTD-ILD).

Methods: We performed a multicenter, prospective, observational study of patients with CTD-ILD receiving RTX between 2015 and 2020. Patients who had worsening of respiratory symptoms or decline in the pulmonary function tests (PFT) compared to the time of ILD diagnosis were treated with rituximab. The patients were assessed using high-resolution computed tomography and PFT baseline, at 12 months, and at the end of follow-up. The main outcome measure at the end of follow-up was forced vital capacity (FVC)>10% or diffusing capacity of the lungs for carbon monoxide (DLCO)>15% and radiological progression or death. We recorded clinical characteristics, time to initiation of RTX, concomitant treatment, infections, and hospitalization. A Cox regression analysis was performed to identify factors associated with worsening of ILD.

Results: We included 37 patients with CTD-ILD treated with RTX for a median (IQR) of 38.2 (17.7-69.0) months (Table 1). At the end of the follow-up, disease had improved or stabilized in 23 patients (62.1%) and worsened in 7 (18.9%); 7 patients (18.9%) died. Mean PFT values decreased significantly at the start of RTX compared to the date of ILD diagnosis in FVC (72.2[21.3]vs 73.5 [16.9] mg/l;p=0.040) and DLCO-SB (55.9 [15.7] vs 58.3 [16.1] mg/l; p=0.041). No

Table 1. Baseline demographic and clinical characteristics of 37 patients with CTD-ILD receiving rituximab.

Variable	Total n=37	RA n=19	SS n=14	IM n=4	p Value
Female sex, n (%)	27 (73.0)	13 (68.4)	11 (78.6)	3 (75.0)	0.806
Age in years, mean (SD)	62.8 (9.9)	67.7 (9.7)	57.9 (7.9)	56.6 (5.5)	0.001
Smoking					0.147
Never smoked, n (%)	20 (54.1)	9 (47.4)	7 (50.0)	4 (100.0)	
Smoked at some time, n (%)	17 (45.9)	10 (52.6)	7 (50.0)	0 (0.0)	
Duration of CTD, months, median (IQR)	107.8 (49.5-188.8)	151.0 (8.,0-240.5)	89.6 (51.3-184.4)	35.1 (25.1-49.0)	0.017
Duration of ILD, months, median (IQR)	65.4 (31.1-110.3)	82.2 (37.4-120.1)	64.5 (35.5-107.1)	25.9 (25.0-36.0)	0.136
Time to initiation of RTX, median (IRQ)	12.0 (6.5-48.2)	25.1 (7.0-57.6)	11.4 (3.9-43.6)	7.4 (7.0-10.4)	0.455
Duration of treatment with RTX, median (IQR)	38.2 (23.4-69.9)	45.3 (22.2-79.9)	52.5 (24.7-63.3)	22.8 (17.7-36.2)	0.291
Combined with csDMARDs, n (%)	15 (40.5)	9 (47.4)	5 (35.7)	1 (25.0)	0.637
Methotrexate, n (%)	5 (13.5)	2 (10.5)	3 (21.4)	0 (0.0)	0.468
Leflunomide, n (%)	2 (5.4)	2 (10.5)	0 (0.0)	0 (0.0)	0.367
Sulfasalazine, n (%)	1 (2.7)	1 (5.3)	0 (0.0)	0 (0.0)	0.615
Hydroxychloroquine, n (%)	7 (18.9)	4 (21.1)	2 (14.3)	1 (25.0)	0.840
Combination with immunosuppressants, n (%)	20 (54.1)	7 (36.8)	9 (64.3)	4 (100.0)	0.044
Mycophenolate, n (%)	19 (51.4)	6 (31.6)	9 (64.3)	4 (100.0)	0.021
Azathioprine, n (%)	1 (2.7)	1 (5.3)	0 (0.0)	0 (0.0)	0.615
Corticosteroids, n (%)	25 (67.6)	14 (73.7)	7 (50.0)	4 (100.0)	0.121
Doses of corticosteroids, median (IQR)	5.0 (0.0-10.0)	5.0 (0.0-10.0)	2.5 (0.0-7.5)	10.0 (8.1-10.5)	0.519

significant decline was observed in median FVC (72.2 vs 70.8; p=0.530) or DLCO (55.9 vs 52.2; p=0.100). The multivariate analysis showed the independent predictors for worsening of CTD-ILD to be baseline DLCO (OR [95% CI], 0.904 [0.8-0.9]; p=0.015), time to initiation of RTX (1.01 [1.001-1.02]; p=0.029), and mycophenolate (0.202 [0.04-0.8]; p=0.034). The infection incidence rate was 0.21 patient-years.

Conclusion: Lung function improved or stabilized in more than half of patients with CTD-ILD treated with RTX. No significant increase in infection rates was observed. Early treatment and combination with mycophenolate could reduce the risk of progression of ILD.

Disclosure of Interests: None declared

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POS0887 CHORIORETINAL MICROVASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: The optical coherence tomography angiography (OCTA) is a new non-invasive imaging technique that can detect flow and provide information about the vessel density (VD) at different layers in the eye. The ocular microvascular network has been only occasionally addressed as disease target in scleroderma (SSc) considering the relatively low prevalence of ocular symptoms in these patients.

Objectives: The study aims to evaluate retinal and choriocapillaris microvasculature in a group of SSc patients compared to matched controls (HC)and according to disease characteristics, capillaroscopy findings and pulmonary function tests.

Methods: VD was assessed through OCTA at the retinal superficial (SCP) and deep (DCP) capillary plexus, at the foveal avascular zone perimeter (FAZP) and at the choriocapillaris (CC) of 30 SSc patients compared to 30 sex- and age-matched subjects without any retinal disease.

Results: The SSc patients (age 57.3±10.0, female 86.7%) had diffuse cutaneous skin disease in 30.0% of the cases, an average disease duration of 10.4±7.2 yy, and anti-centromere and anti-Scl70 antibody positivity in 40.0%and in 30.0% of the cases, respectively. Compared to the HC, SSc showed an impaired VD at SCP (47.7±3.6 vs59.1±3.5%, p=0.009), DCP (50.0±6.7 vs 54.3±6.4%, p=0.015), FAZP (48.7±4.55 vs 51.0±3.55%, p=0.034) and CC(67.1±2.2 vs 68.6±1.7, p=.005). Moreover, in the SSc group, the presence of digital ulcers (46.7%),telangiectasias (43.3%) and interstitial lung disease (46.7%) was related to reduced VD at FAZP (46.8±4.1 vs50.3±4.3%, p=0.033), CC (66.1±1.4 vs 67.9±2.4%, p=0.004), and DCP (47.2±8.8 vs 51.9±4.3, p=0.004),respectively. Lastly, the average capillary density on capillaroscopy showed a positive correlation with VD at FAZP (r=0.474, p=0.008), DCP (r=0.414, p=0.023), and foveal CC (r=0.482, p=0.007) and there was also a correlation between CC and both DLco (r=0.467, p=0.009) and FVC/DLco (r=-0.436, p=0.004).

Conclusion: The SSc patients in our cohort showed lower ocular vessel density at different levels compared to HC. Furthermore, impaired VD at different levels of the eye correlates with the organ involvement and the degree of digital and pulmonary microvascular impairment. According to those data, the OCTA could be proposed as a biomarker tool to investigate the microvascular abnormalities in SSc.

Disclosure of Interests: None declared

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POS0888 NON-SURGICAL LOCAL TREATMENTS FOR DIGITAL ULCERS IN SYSTEMIC SCLEROSIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Digital ulcers(DUs) in systemic sclerosis(SSc) represent a major clinical challenge. There are no recommendations for the local management of SSc-DUs. Systemic therapy is considered the standard of care. However, there is a strong rationale for local approaches to DU by avoiding side effects from systemic therapies. The World Scleroderma Foundation DU Working Group intends to develop evidence-based recommendations for DU management including local, non-surgical treatment(ln-sT).

Objectives: To summarise the literature on the safety and efficacy of ln-sT for SSc-DUs.

Methods: A systematic literature review(SLR) of papers describing the use of ln-sT for DU in SSc was performed up to May 2021 according to the PICO framework. References were independently screened by two reviewers who independently assessed the full text of eligible articles and extracted data.

Results: Among 790 retrieved references, 12 were included. Median(range) number of patients per study was 9(7–84), mean age ranging from 37 to 62.5 years. In 5(41%) studies a control group was included. Background systemic therapies are summarized in Table 1. The most studied treatment was botulin toxin A(BTA). It was used as hand injection in 3 studies (median dose ranging from 90 to 150 U) and as 50 U single finger injection in 1 study. Healing rate after a median time of 8-49 weeks ranged from 71% to 100%. In 2 studies a reduction in VAS pain was observed from 20% to 100%. Transient muscle weakness was the most common side effect in 10% of patients. Amniotic(Am) and hydrocolloid membranes(HyM) were used in 1 study each. They were associated with a good healing rate, statistically significant for the HyM. Tadalafil 2% cream was studied in 1 study and was associated with a reduction in the median DU number from 1.6 to 1 per patient after a median time of 4 weeks and a reduction by 1.4 point in the 10-mm VAS scale. Vitamin E gel was shown to be associated with a statistically significant reduction in the healing time compared to SoC alone in 1 RCT(13.2 ± 2.7 versus 20.9 ± 3.6 weeks, P=<0.001). Low-level light therapy, hydrodissection and corticosteroid injection and extracorporeal shock wave(ESW) were evaluated in 1 study each. They were all associated with positive outcomes which was statistically significant only for the ESW. The only negative trial examined dimethyl sulfoxide and was associated with local toxicity.

Conclusion: Our SLR supports interest to develop ln-sTs for SSc-DUs. The number of studies is limited and mainly case reports and small single studies are present. Treatments were well tolerated and there was evidence of efficacy for BTA, vitamin E, ESW and HyM in refractory DUs. The evidence is not robust and confounding factors (vasodilators background therapies) could impact on the findings. Future research is indicated to conduct larger, well-designed studies.

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Table 1. Characteristics of the studies.

Treatment	Type of study	Patients	Baseline DU	Background therapy (%) ETA	CCB	APA	PG	ARB	ACE-I	PDE-5i	IS	Follow-up (weeks)	Healing rate(%)*	Pain Reduction (VAS/10)	Comparator
Hydrodissection and corticosteroid injection	P	12				0						2	33	4.4	Rheumatoid Arthritis
Tadalafil 2%	R	15	1.6(1)	0	46	27	0	13	0	7	0	4	1(1)	1.4	SoC
Vitamin E gel	RCT	13	3.5±2.3				0					24	Reduced time to heal**		
Am	R	6	3	0	100	0	0	0	28	17	33	3	100		SoC
HyM	P	7	10	0	28		0			0	14	8	90**		
BTA	R	7	31	71	71	85	85	14		71		8	77	20%	Untreated CH
Median 90 U per hand	R	7	4	14	85	5	14	14				49	71	100%	
High-concentration hand	P	20	5	0	5	100	20					8	75		
100 U non-dominant hand	P	10					100					12	100		
Single finger 50 U															
Low-level light therapy	P	8	10	25	37	0	25			37		8	100		
ESW	P	9	49	33		55	66			11	44	4	41**	1.31	
Dimethyl sulfoxide	DBRCT	84	No change, skin toxicity with 70% formulation												

*Unless otherwise stated. **Statistically significant. ARB= angiotensin receptor antagonist. ACEi= ACE inhibitors. APA= anti-platelet agents. CCB= calcium channel blockers. CH= contralateral hand. DBRCT= double blind randomized-controlled trial. ETA = endothelin antagonist. IS= immunosuppression. PG= prostaglandins. PDE-5i= Phosphodiesterase type-5 inhibitors. P = prospective. R = retrospective. SoC= standard of care (as per local protocol).

POS0889

CASE SERIES OF PATIENTS WITH EOSINOPHILIC FASCIITIS SECONDARY TO IMMUNE CHECKPOINT INHIBITORS THERAPY

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Background: Eosinophilic fasciitis (EF), a fibrotic disease that causes inflammatory infiltration in the subcutaneous fascia is clinically characterized by edema and subsequent induration and tightening of the skin and subcutaneous tissue. EF is a rare immune-related adverse event of immune checkpoint inhibitors (ICI).
Objectives: This article aims to investigate the clinical features of ICI-related EF and to improve the understanding of the disease among rheumatologists.
Methods: Searching relevant articles in the electronic databases Medline, PubMed, Science Citation Index, China Biomedical Literature Database (CBM), China Journal Full Text Database (CNKI), and WANFANG Data with the key words of "eosinophilic fasciitis" or "Shulman syndrome" and "checkpoint inhibitor", "CTLA-4", "PD-1" or "PD-L1". Only articles or case reports with detailed medical records of ICI-related EF patients were included. ICI-related EF patients in our department were also included.
Results: A 58-year-old male patient with angioimmunoblastic T cell lymphoma presented with skin edema, subsequent induration, tightening of the skin, and subcutaneous tissue (Figure 1 A&B). The eosinophils elevated in peripheral blood after 6-month treatment of PD-1 inhibitor (Camrelizumab). The patient was diagnosed as ICI-related EF and then was referred to our rheumatology department. Other seventeen EF patients from the above databases were also included for analysis. Among these 18 patients, 50% (9/18) were male and the mean age was 57±14 years. The most commonly used ICI was PD-1 inhibitor such as nivolumab and pembrolizumab, accounting for 72% (13/18), next was PD-L1 inhibitor (17%, 3/18), and 3 patients used PD-L1 inhibitor combined with CTLA-4 inhibitor. Of all cases, 50% (9/18) was metastatic melanoma and 17% (3/18) was lung cancer. After ICI treatment, the median onset time of EF was 12 months. The most common involved organ was skin and 94% (17/18) of patients presenting with symmetrical skin edema and sclerosis. For other skin manifestations, 44% (8/18) of patients had typical "groove sign", and one case showed unilateral skin involvement of skin tension and erythema from pubis to left anterior iliac crest. When the affected limb raised, there is a visible sulcus due to the decrease of venous dilation pressure, namely "sulcus sign". The second common involved organ was the joints which were presented with limited function in 56% (10/18) of patients. Additionally, 39% (7/18) showed muscle involvement such as myalgia and myasthenia. Increased eosinophils in peripheral blood was observed in 72% (13/18) of patients. Twelve patients (63%) received MRI examinations which showed the signal in the subcutaneous and deep fascia increased in both fat-suppressed T2 images(Figure 1 C&E) and post-enhancement T1 images(Figure 1 D&F). Fifteen patients underwent full-thickness skin biopsy at the lesion site, the pathological changes in all patients supported the diagnosis of EF. The ICI was discontinued in 94% of patients. Meanwhile, 83% received glucocorticoids and 56% of patients were treated with methotrexate. After these treatment, the clinical symptoms of EF improved in 89% of patients (n=16), while eosinophils returned to normal after a median treatment time of 2.5 months. EF progressed even through the combined treatment of prednisone, MTX, and abatacept in one patient. Another one case died after 6 months due to metastasis of bladder cancer (stageIV).
Conclusion: Although EF is a rare adverse effect of ICI treatment, individuals receiving these drugs should be monitored closely for symptoms of EF. Discontinuation of ICI and administration of immunosuppressants may prevent the progression of EF.

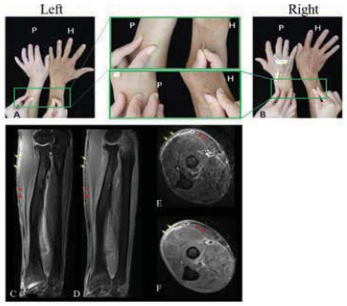

Figure1 Skin signs and MRI images of a 58-year-old male patient with eosinophilic fasciitis secondary to immune checkpoint inhibitors therapy. A&B: Skin signs of the representative patient (P) and a 58-year-old male healthy volunteer (H). The skin of the patient's left (A) and right forearm (B) was tight and difficult to lift. The fat-suppressed T2 images (C&E) and the fat-suppressed post-enhancement T1 images (D&F) showed the signal in the subcutaneous and deep muscle fascia of the right forearm increased and was enhanced obviously after enhancement (red arrows). There was a little long T2 signal of effusion shadow between myofascial and subcutaneous fatty layer (yellow arrows).

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POS0890

NINTEDANIB REAL-LIFE EFFICACY AND SAFETY IN SYSTEMIC SCLEROSIS (SSC)-INTERTISTIAL LUNG DISEASE (ILD): AN ITALIAN MULTICENTRE PRELIMINARY STUDY.

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Background: Nintedanib (NTD) has been approved for Systemic Sclerosis (SSc)-Interstitial Lung Disease (ILD) following the positive results of the SENSCIS trial.
Objectives: to describe the efficacy and safety of NTD in SSc-ILD in a real-life setting.

Methods: The clinical data of SSc-ILD patients treated with NTD from 10 Italian SSc centres were retrospectively evaluated at baseline, 6 and 12 months: SSc clinical features, NTD tolerability, pulmonary function tests (PFTs) and modified Rodnan skin score (mRSS) were recorded.
Results: 69 SSc-ILD patients (22 males [32%], mean age 60±12 years, disease onset 50±13 years, 4 [6%] anti-centromere, 53 [77%] anti-topoisomerase I, 3 [4%] anti-RNA-polimerase III) were identified. The vast majority (84%) was previously treated with immunosuppressants: 27 (39%) cyclophosphamide, 45 (65%) mycophenolate mofetil, 6 (9%) methotrexate, 9 (13%) azathioprine, 6 (9%) tocilizumab and 22 (32%) rituximab. In 11 (16%) patients, NTD was the first treatment for SSc-ILD. At baseline, 57 patients (83%) were on corticosteroids (mean daily prednisone dose 6±5 mg), 58 (84%) on immunosuppressants, 47 (68%) on mycophenolate mofetil, 14 (20%) on rituximab, 3 (4%) on tocilizumab, 2 on methotrexate (3%) and 1 (1%) on azathioprine. At baseline HRCT showed UIP pattern in 27 (39%) and NSIP pattern in 42 (61%) patients. The modifications of PFTs and mRSS over time are shown in Table 1. Since NTD introduction, gastro-intestinal (GI) side effects were recorded in 34 (49%) patients, with diarrhoea being the most common complaint (35%), followed by nausea/vomiting (23%) and weight loss (16%). In 21 (30%) patients, after a mean time of 2.6±3.4 months, NTD was maintained after dose adjustment. In 5 (7%) patients NTD was stopped after a median time of 5 (1-6) months due to subocclusion and persistent diarrhoea in 3 patients, untreatable nausea and vomiting in one patient and liver toxicity in 1 patient. During the follow-up after a median time of 10 (6 – 33) months, 4 patients died.

Table 1. Pulmonary function tests and mRSS at baseline, 6 and 12 months in SSc-ILD on NTD.

	Baseline	6 months	P value	Baseline	12 months	P value
FVC (% predicted)	64 ± 18	65 ± 18 (33 pts)	0.638	70 ± 19	69 ± 18 (20 pts)	0.586
TLC (% predicted)	64 ± 15	61 ± 14 (27 pts)	0.154	64 ± 14	65 ± 18 (16 pts)	0.944
DLCO (% predicted)	40 ± 17	41 ± 18 (29 pts)	0.660	40 ± 18	38 ± 18 (20 pts)	0.304
mRSS	9 ± 6	8 ± 6 (26 pts)	0.002	7 ± 4	8 ± 6 (15 pts)	0.334

pts= patients

Conclusion: Our preliminary data confirm that in a real-life clinical scenario NTD, in combination with immunosuppressants, may stabilize PFT. However, despite the fact that GI side effects are frequent, they may be controlled with NTD dose adjustment thus retaining the drug in SSc-ILD patients. The NTD efficacy on skin involvement needs to be thoroughly evaluated on a larger SSc population.
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POS0891 **REUMA.PT/MYOSITIS – THE PORTUGUESE REGISTRY OF INFLAMMATORY MYOPATHIES**

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Background: The idiopathic inflammatory myopathies (IMM) module of the Rheumatic Diseases Portuguese Register (Reuma.pt/Myositis) is a tool used to systematically evaluate IIM patients.
Objectives: To clinically characterise the Reuma.pt/Myositis cohort.
Methods: Multicentre open cohort study, including IIM patients registered in Reuma.pt up to January 2022. Data collected included demographic, clinical, and treatment data and patient-reported outcomes. Data were presented as frequencies and median (interquartile range) for categorical and continuous variables, respectively.
Results: 280 patients were included, 71.4% female, 89.4% Caucasian, with a median age at diagnosis and disease duration of 48.9 (33.6-59.3) and 5.3 (3.0-9.8) years, respectively. Patients were classified as having definite (N=57/118, 48.3%; N=35/224, 15.6%), likely (N=23/118, 19.5%; N=50/224, 22.3%), or possible (N=2/118, 1.7%; N=46/224, 20.5%) IIM by 2017 EULAR/ACR and Bohan-Peter criteria, respectively. Disease subtypes included dermatomyositis (DM, N=122/280, 43.6%), polymyositis (N=59/280, 21.1%), myositis in overlap syndromes (N=41/280, 14.6%), clinically amyopathic DM (N=17/280, 6.1%), nonspecific myositis (N=13/280, 4.6%), mixed connective tissue disease (N=12/280, 4.3%), immune-mediated necrotizing myositis (N=9/280, 3.2%), and inclusion bodies myopathy (N=7/280, 2.5%). Over the course of the disease, the most common symptoms were proximal muscle weakness (N=180/215, 83.7%), arthralgia (N=127/249, 52.9%), erythema (N=63/166, 38.0%), fatigue (N=47/127, 37.0%), Raynaud's phenomenon (N=76/234, 32.5%), and dysphagia (N=33/121, 27.3%), and the most common clinical signs were Gottron's sign (N=75/184, 40.8%), heliotrope rash (N=101/252, 40.1%), Gottron's papules (N=93/237, 39.2%), and arthritis (N=38/98, 38.8%). Organ involvement included lung (N=78/230, 33.9%), oesophageal (N=40/221, 18.1%), and heart (N=11/229, 4.8%) involvements. Most patients expressed myositis-specific (MSA, N=158/242, 65.3%) and/or myositis-associated (MAA, 112/242, 46.3%) antibodies. The most frequent antibodies were anti-SSA/SSB (N=70/231, 30.3%), anti-Jo1 (N=56/236, 23.7%), and anti-Mi2 (N=31/212, 14.6%). Most patients had a myopathic pattern on electromyogram (N=101/138, 73.2%), muscle oedema in magnetic resonance (N=33/62, 53.2%), and high CK (N=154/200, 55.0%) and aldolase levels (N=74/135, 54.8%) at diagnosis, with median highest CK levels of 1308 (518-3172) and aldolase of 42 (12-121) mg/dL. Neoplasia was found in 11/127 patients (8.7%), most commonly breast (N=3/11, 27.3%), non-melanoma skin (N=2/11, 18.2%), and colorectal (N=2/11, 18.2%) cancer (Table 1). Most patients with cancer-associated myositis had DM (N=8/11, 72.7%) and expressed MSA (N=6/11) and/or MAA (N=3/11). The most used drugs over the course of disease were glucocorticoids (N=201/280, 71.8%), methotrexate (N=117/280, 41.8%), hydroxychloroquine (N=87/280, 31.1%), azathioprine (N=85/280, 30.4%), mycophenolate mofetil (N=56/280, 20.0%), intravenous immunoglobulin (N=55/280, 19.6%), and rituximab (N=45/280, 16.1%). At the last follow-up, there was a median MMT8 of 150 (142-150), modified DAS skin of 0 (0-1), global VAS of 10 (0-50) mm, and HAQ of 0.125 (0.000-1.125).

Table 1. Autoantibodies in cancer-associated myositis

Cancer	IIM	Autoantibodies
Breast	DM (3)	Mi2, SRP (+ SSA/SSB), Pm/Scl
Skin (non-melanoma)	Clinically amyopathic DM, PM	Jo1, SAE1 (+SSA/SSB)
Colorectal	DM (2)	Mi2 (2)
Kidney	DM	-
Lung	DM	-
Lymphoma	Inclusion bodies myopathy	-
Unknown	DM	-

Conclusion: Reuma.pt/Myositis adequately captures the main features of inflammatory myopathies' patients, depicting in this first report a heterogeneous population, with frequent muscle, joint, skin and lung involvements. Of interest, most patients reached low disease activity at the last follow-up appointment.
Disclosure of Interests: None declared
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POS0892

IDENTIFICATION OF DEFINED MICROANGIOPATHIC CHANGES IN NAILFOLD CAPILLAROSCOPY IMAGES OF PATIENTS WITH SYSTEMIC SCLEROSIS USING A VISION TRANSFORMER MODEL – A MONOCENTRIC IMPLEMENTATION AND VALIDATION COHORT STUDY

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Background: An accurate assessment of nailfold capillaroscopy (NFC) images has great importance in the diagnosis and prognosis of systemic sclerosis (SSc). To overcome some of the inherent problems with NFC image analysis (operator/observer bias, time requirements), there is an interest to automate and standardize NFC image assessment using computer vision algorithms, such as the Vision Transformer (ViT), which are based on recent advances in deep learning.
Objectives: Our aims were (1) to implement and assess the performance and the reliability of ViT in detecting changes on NFC images, and (2) to compare the performance of ViT to that of practicing rheumatologists.
Methods: For this study, we used NFC images of patients with SSc enrolled in our European Scleroderma Trials and Research group (EUSTAR) and Very Early Diagnosis of Systemic Sclerosis (VEDOSS) local registries. Concretely, we included routine NFC images (all NFC images available – digit II to V of both hands-, irrespective of any image artefacts) of patients aged ≥ 18 years with visits between 2012 and 2021, who fulfilled either the 2013 American College of Rheumatology / European League Against Rheumatism classification criteria for SSc (established disease) or the preliminary criteria for VEDOSS (mild/early disease). ViT was trained to identify the following NFC signs of microangiopathy: enlarged capillaries (apex diameter of the capillary > 20 µm, and < 50µm), giant capillaries (> 50 µm), loss of capillaries (< 7 capillaries/mm), and microhaemorrhages. Absence of any of these signs was considered as being a "normal NFC", while presence of any of these signs was seen as an abnormal NFC image. Its performance was evaluated in a cross-fold (k = 5) validation setting, and the gold standard was the treating physician. Area under the ROC curve (AUC) was used as indicator of the performance. Considered cut-offs for AUC were 90-100% - excellent, 80-89.9% - good, 70-79.9% - fair, 60-69.9% - poor, 50-59.9% - fail. From the first cross-fold, a randomly sampled reliability set was created which was used to compare the NFC assessment performance of four rheumatologists (three invited and trained annotators and the treating physician) with that of of ViT.

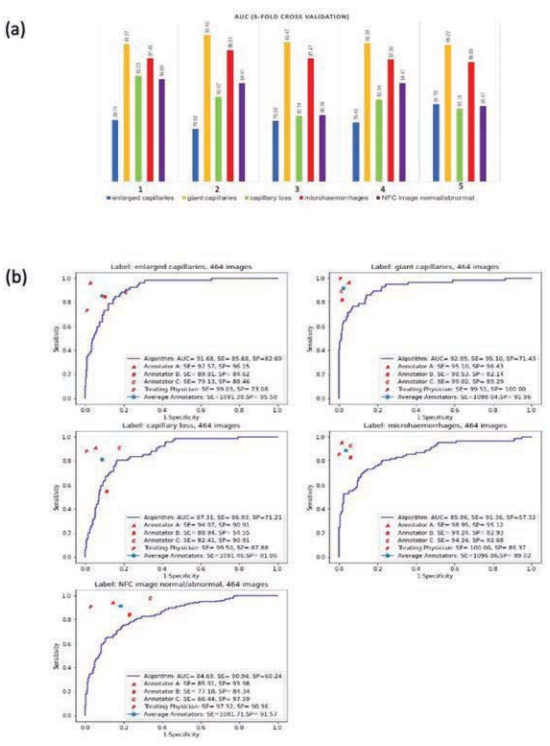

Figure 1. Performance of the ViT: (a) AUCs values for ViT in diagnosing the respective feature on NFC image. (b) Sensitivity / specificity trade-off across the images in the reliability set. The blue lines show the ROC curves corresponding to the ViT predictions, with ViT's AUC, "optimal" sensitivity and specificity shown in the box. Also shown are the point performances of each of the four annotators, with performances below the blue line indicating lower performance than ViT.

Results: We analysed 17,126 NFC images of 234 EUSTAR patients (14.6% males, 67.8% limited cutaneous SSc, median age 57 years, median disease duration 9 years) and 55 VEDOSS patients (92.7% females, median age 44 years, median time elapsed since first Raynaud's phenomenon 5 years). ViT had fair to excellent performance in identifying the different NFC changes across all five folds (of 3443 NFC images each), with an area under the ROC curve ranging from 78.59% to 90.4% (Figure 1a).
In the reliability set (see Figure 1b), we observed highest performance for diagnosing giant capillaries (AUC =92.89%) followed by identification of enlarged capillaries (AUC = 91.7%). Good AUCs were seen in depicting capillary loss (AUC = 87.3%), microhemorrhages (AUC = 85.9%) and the abnormal/normal NFC classification (AUC = 84.7%). The rheumatologists had generally higher performance in assessing NFC images. However, ViT outperformed two rheumatologists with different experience in classifying capillary loss and enlarged capillaries, respectively.
Conclusion: ViT is a modern, well performing and readily available AI model to assess signs of microangiopathy on NFC images acquired during routine practice.
Disclosure of Interests: Alexandru Garaiman: None declared, Farhad Nooralahzadeh: None declared, Carina Mihai Speakers bureau: MEDtalks Switzerland, Mepha, Nikitas Gkikopoulos: None declared, Nicolas Perez Gonzalez: None declared, Mike O. Becker Speakers bureau: Mepha, MSD, Novartis, GSK, Bayer and Vifor, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche, Pfizer, Roche, Sanofi, Consultant of: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos, Glenmark, GSK, Horizon, Inventiva, iQvia, Kymera, Lupin, Medac, Medscape, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Prometheus Biosences, Roche, Roivant, Topadur and UBC, Lilly, Pfizer, Grant/research support from: Kymera, Mitsubishi Tanabe, Michael Krauthammer Speakers bureau: Oncobit, Britta Maurer Speakers bureau: Boehringer-Ingelheim, Medtalk, Pfizer, Roche, Actelion, Mepha, and MSD, Consultant of: Novartis, Boehringer Ingelheim, Janssen-Cilag, Grant/research support from: AbbVie, Protagen, Novartis Biomedical Research
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POS0893

FACTORS TO CONSIDER FOR MEASURING THE EFFECT OF LUNG FUNCTION ON PATIENT REPORTED OUTCOMES IN SYSTEMIC SCLEROSIS PATIENTS: ANALYSIS OF THE EUSTAR DATABASE.

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Background: Patient Reported Outcomes (PROs) are central to measure how patients feel and function especially when determining the effect of disease modifying agents. In patients with Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD), dyspnea is the main driver of HAQ decline but the effect of reduced lung function on both generic and specific measures of functional impairment is not well defined, and there are many potential confounding biases that could distort the apparent extent and direction of this relationship. Moreover, collider biases potentially induced by selection into the cohort and in clinical trials can also play a role.
Objectives: To define within the EUSTAR database, the correlation of Forced Vital Capacity (FVC) and functional impairment PROs and identify potential confounders to be considered in casual inference studies.
Methods: A cross-sectional analysis included for each patient with SSc-ILD (by X-ray and/or HRCT) in the EUSTAR registry the last visit with at least one PRO (Health Assessment Questionnaire Disability Index [HAQ-DI], Cochin hand function scale [CHFS] and/or dyspnoea visual analogue scale [VAS]) and % predicted FVC (%pFVC), if available. Patients with LVEF≤50% or pulmonary arterial hypertension at RHC were excluded. SSc-ILD with restricted lung volume was defined as %pFVC≤70 [1]. Spearman's correlation analysis was performed. Results of this analysis and literature review were integrated to design a directed acyclic graph (DAG) and identify the appropriate confounder adjustment set for the total causal effect of FVC on functional impairment PROs.
Results: Among 17.338 SSc patients in the EUSTAR registry (extracted in November 2019), 727 SSc-ILD patients fulfilled the inclusion criteria (median %pFVC 90 (IQR 74-104), median %pDLCO 60 (IQR 47-52)). Patients with %pFVC<70 (n=149), as compared to those with %pFVC≥70 (n=578) had worse HAQ-DI, CHFS and VAS-dyspnoea scores (Table 1). In unadjusted analysis, %pFVC showed a weak correlation with HAQ-DI (r=-0.21) and CHFS (r=-0.17), but a stronger correlation with VAS dyspnoea (r=-0.33).

Table 1. Results are reported as number/number available (%) for dichotomic variables, or as median (IQR) (n available) for continuous variables.

	%pFVC≥70 (n=578)	%pFVC<70 (n=149)
Age at disease onset (years)	60.6 (52.3-69.3) (546)	52.5 (45.6-63-7) (137)
Disease duration (months)	134.4 (77.5-212.2) (546)	110.3 (66.3-199.7) (137)
Male sex	84/578 (14.5)	32/149 (21.5)
Anti-Scl70+	231/468 (40.7)	81/122 (66.4)
Smoker ever	52/389 (13.4)	17/107 (15.9)
Caucasian ethnicity	545/569 (95.8)	131/145 (90.3)
dcSSc	167/559 (29.9)	74/147 (50.3)
Oesophageal symptoms	319/571 (55.9)	93/147 (63.3)
Muscle weakness	78/565 (13.8)	37/149 (24.8)
CRP elevation	141/540 (26.1)	53/134 (39.6)
Elevated sPAP (ECHO)	45/456 (9.9)	21/121 (17.2)
Pericardial effusion	2/448 (0.4)	4/110 (3.6)
Diastolic function abnormality	151/431 (35.0)	31/102 (30.4)
Conduction blocks	78/480 (16.3)	35/120 (29.2)
%pDLCO	62 (52-74) (527)	42 (35-53) (118)
CHFS	7 (1-23) (493)	16 (2-34.8) (114)
HAQ-DI	0.63 (0.13-1.13) (578)	1.25 (0.38-2) (139)
VAS dyspnoea (0-100)	15 (10-45) (391)	40 (20-70) (109)
NYHA stage 3/4	47/561 (8.4)	37/143 (25.9)

Subsequently, we created a DAG showing the proposed causal pathway considered relevant to the relationship between FVC and HAQ (Figure 1).

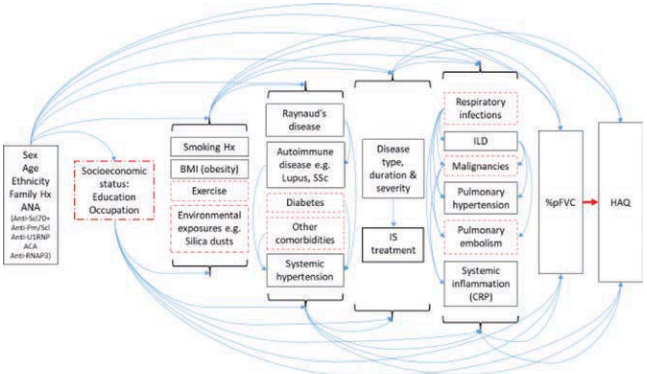

Figure 1. Directed Acyclic Graph (DAG) of factors to consider for direct casual inference of FVC on HAQ.
Variables in red dotted lines are those not systematically recorded in the EUSTAR registry.

Conclusion: Lung function as measured by FVC appears to correlate with worse patient-reported function in our unadjusted analysis of the large multicentre EUSTAR dataset. However, to estimate the total causal effect we must consider a multitude of potentially confounding factors, which need to be integrated and analysed in a causal inference framework. The proposed DAG will inform the development of simulations of the potential impact of bias (confounding, collider and omitted variable) on effect estimates we could obtain from EUSTAR cohort.

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POS0894 COMPARISON OF PULMONARY AND SMALL AIRWAYS FUNCTION BETWEEN IDIOPATHIC INFLAMMATORY MYOPATHIES PATIENTS WITH AND WITHOUT INTERSTITIAL LUNG DISEASE

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Background: Pulmonary manifestations of idiopathic inflammatory myopathies (IIM) include interstitial lung disease (ILD) and respiratory muscle weakness, but function of small airways has not been studied in these patients (1). Spirometry, impulse oscillometry and measurement of respiratory resistance by the interrupter technique (Rocc) are tools to evaluate function of small airways. In addition, body plethysmography is the gold standard for measuring lung volumes, whereas nitrogen washout seems impaired, "underestimating" lung volumes in patients with small airways obstruction due to gas trapping (2). Thus, discrepancies between lung volumes measured by those two techniques may be an indication of early small airways dysfunction.

Table 1. Comparison of pulmonary and small airways function variables between IIM patients with and without ILD.

Pulmonary function variables	IIM-ILD patients (n=13)	IIM patients without ILD (n=13)	p value
FVC%	88.2	104.1	0.09
FEV1%	85.8	101.9	0.07
FEV1/FVC	82.7	80.9	0.57
FEF_{25-75}%	85.7	90.4	0.74
TLC_{pleth}%	82.6	89.9	0.32
RV_{pleth}%	83.9	76.1	0.40
TLC_{N2WO}%	111.1	153.4	0.03
RV_{N2WO}%	171	210	0.039
TLC_{N2WO}/TLC_{pleth}	1.28	1.45	0.039
DLco%	56.3	78.2	0.005
MEP%	69	62.4	0.57
MIP%	93.4	72.5	0.06
ΔN2(%)	2.8	5.4	0.013
Rocc Exp %	100.5	76.6	0.053
R(20)%	99.4	123.4	0.09

Objectives: To compare pulmonary and small airways function between IIM patients with and without ILD.

Methods: This prospective observational study included 13 IIM patients with ILD (8 patients with dermatomyositis and 5 with polymyositis) and 13 IIM patients without ILD (9 patients with dermatomyositis and 4 with polymyositis) who were diagnosed and followed up in the outpatient rheumatology clinic of the Department of Pathophysiology between June and December 2021. All IIM patients fulfilled the 2017 EULAR/ACR classification criteria (3). The presence of ILD was determined by high resolution computed tomography of the lungs that was performed as baseline standard of care at the time of diagnosis and was evaluated by a special radiologist blindly, according to Fleischner Society definitions for ILD (4). Clinical, laboratory and immunological data were recorded at the time of diagnosis and pulmonary function was assessed by spirometry, body plethysmography, single and multiple breath nitrogen washout, impulse oscillometry and measurement of Rocc, diffusing capacity for carbon monoxide (DLco) and maximal inspiratory and expiratory pressures. Statistical analysis for categorical data was performed by Fisher exact test or $\chi 2$ square test accordingly and numerical data with Man-Whitney test or t test.

Results: IIM-ILD patients presented more frequently with dyspnea (53.8% vs 0%, p<0.01), fever (61.5% vs 7.7%, p<0.05) and arthralgias (76.9% vs 23%, p<0.05), compared to IIM patients without ILD. Inflammatory markers, serum muscle enzymes, myositis specific autoantibodies and classic spirometric parameters did not differ between the two groups. IIM-ILD patients had markedly lower predicted DLco compared to those without (mean: 56.3% vs 78.2%, p<0.01). Predicted total lung capacity and residual volume (TLC_{N2WO}%, RV_{N2WO}%) measured by nitrogen washout and the TLC nitrogen washout: TLC body plethysmography ratio (TLC_{N2WO}/TLC_{pleth}) were significantly lower in IIM-ILD patients compared to those without ILD (mean: 111.1% vs 153.4%, p<0.05, median: 171% vs 210%, p<0.05 and median: 1.28 vs 1.45, p<0.05, respectively). Similarly, ΔN2(%) was found significantly higher among non-ILD than ILD-IIM patients [5.4 vs 2.8%, p=0.013]. Predicted normal value of Rocc tended to be higher in IIM-ILD patients, although not statistically significantly.

Conclusion: Abnormal single breath nitrogen washout and discrepancies between lung volumes measured by body plethysmography and nitrogen washout in IIM-ILD patients, indicate an early small airways dysfunction in these patients.

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POS0895 THE ROLE OF SURGERY IN THE ESOPHAGEAL INVOLVEMENT IN SYSTEMIC SCLEROSIS: A SYSTEMATIC LITERATURE REVIEW

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Table 1. GERD ASSESSMENT AND SURGICAL OUTCOMES

Domain assessed/outcome	Instrument/Measurement
N° of studies	
Reflux severity	Dysphagia: 20 Number of antireflux medications: 10 High dose PPI: 9 pH monitoring (pre-procedure): 11 Oesophagitis/Barret 4
Reflux improvement (post-procedure)	Symptom resolution/reduction 24 pH monitoring 12 Repeat EGDS 8
N° of patients	
N° of surgical procedures	Tot_{SSc} 257 Collis-Nissen FP 54 Nissen FP 39 Dor FP 37 Collis-Belsey FP 20 Toupet FP 18 RYGB 23 Others 30 Undefined 36
Post-operative surgical complications	73 (2,5%)*
Mortality (n° deaths)	8 (0,27%)*

*rate in total population (2919)

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Background: Among gastrointestinal (GI) manifestations in Systemic Sclerosis (SSc) one of the predominant and challenging problems is gastroesophageal reflux disease (GERD), which occurs in ~75% of patients. Although proton pump inhibitors are useful, they are ineffective in 40% of cases with chronic use at high doses, against the background of long-term risks (e.g., cardiovascular disease and infections) which have been identified in the general population. Surgery might be an option following failure of medical therapy but currently, there is no consensus regarding the optimal surgical procedure for refractory GERD in SSc.
Objectives: To evaluate, among the surgical approaches to GERD, the feasibility of fundoplication (FP) with regards to its safety, efficacy, indications, and timing.
Methods: Four research questions based on the PICO framework were developed to guide the systematic literature review that was conducted up to 22 December 2021. The search and performed across different databases including PubMed, MEDLINE (OVID), EMBASE, Cochrane Library, Web of Science, Google Scholar, Emcare and Academic Search Premier. References were independently screened by two reviewers (PMC and AA) who also independently assessed the full text of eligible articles, and extracted data. Due to heterogeneity of retrieved studies, narrative summaries are used to present the data.

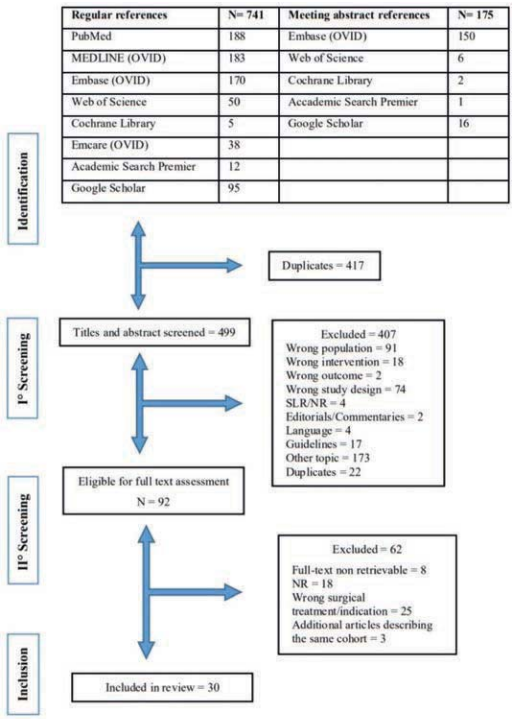

Figure 1. Flow chart of the search

Results: The search yielded 916 papers of which 30 were eligible for full text review. In these studies, out of 2919 clinically heterogeneous patients, 348 SSc patients were identified (mostly female, mean age 52.7 years). Out of these 348, only 257 underwent anti-reflux surgical procedure and were included in the analysis. Most of the studies were conducted in surgical settings and relevant rheumatological data were largely missing. Refractory GERD symptoms, were the commonest indication for surgery, with post-operative dysphagia being the most frequent complication. In 18 studies, FP was effective, whereas 4 studies had equivocal findings and in 5 a lack of efficacy was reported. The Collis-Nissen FP was the most popular procedure overall as well as in earlier studies, followed by Nissen FP, and Dor FP in relatively more recent studies, reflecting the change in surgical strategy over time. The data extracted shows also an acceptable rate of mortality and morbidity related to surgery, and heterogeneous outcome measures were used hampering any comparison of the studies (Table 1). Due to the heterogeneity of the data, it was not possible to separate the mortality and morbidity rate of SSc patients from the rest of the population.
Conclusion: Our SLR has highlighted that the surgical management of GERD in SSc patients is still highly challenging since the available evidence is scarce and of poor quality. Among the surgical approaches to the problem of GERD, overall FP seems a safe and effective procedure in SSc. Transient post-operative dysphagia was noted in many studies, particularly related with the posterior FP. In the future, it will be necessary to develop minimal requirement to conduct surgical studies in SSc as well as to design studies aimed at defining the clinical criteria for referral to surgery. Indeed, the right timing for surgery and the best surgical procedure in SSc still remains an unmet need.
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POS0896 CRYOFIBRINOGEN-ASSOCIATED SYSTEMIC SCLEROSIS: POSSIBLE CORRELATIONS WITH SCLERODERMA DIGITAL ULCERS AND PULMONARY ARTERIAL HYPERTENSION

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Background: Cryofibrinogenemia (CF) is a rare disorder characterized by the presence of an abnormal protein in the plasma that precipitates when cooled and redissolves at room temperature (1). CF is rarely symptomatic, therefore it is often underestimated. Nevertheless, the cryoprecipitation of native fibrinogen could induce thrombotic occlusion of small and medium sized vessels; as a consequence, this condition could become potentially lethal without the proper treatments. CF is classified into an essential and secondary form. The association of CF with Systemic Sclerosis (SSc) is described in literature (2-4); however, the role of this phenomenon it is not completely clarified, especially because some clinical aspects could be similar in both conditions.
Objectives: The aim of our study was to analyze the clinical, laboratory, instrumental and therapeutic features of SSc patients with cryofibrinogenemia, with particular attention to the possible prevention strategy and appropriate therapy of SSc digital ulcers.
Methods: 101 SSc patients (M:F 1:13) referring to the SSc Unit-Rheumatology Unit of our University Hospital have been tested both for cryofibrinogen and cryoglobulins from February 2020 to January 2022. Clinical, laboratory, instrumental features and ongoing therapies were collected.
Results: Patients with diffuse cutaneous form, limited cutaneous form, and sine-scleroderma subsets were 20 (19,8%), 79 (78,2%), and 2 (2,0%), respectively. The overall positivity for CF was 69,3%, of which 90,7% as isolated CF and 9,3% in addition to cryoglobulins. No correlation between CF positivity and positivity for rheumatoid factor, Scl-70, CENP B, anti-fibrillarin, anti-U1RNP, anti-Th/To, anti-Ku, anti-MDA5, anti-mitochondrial, anti-SSA, anti-SSB, anti-citrullinated peptide, anti-phospholipids, anti-CORE, and anti-HCV antibodies was observed. An inverse correlation trend between CF positivity and anti-RNAP3 antibodies positivity (OR=0.0577, 95% CI 0.0029-1.1537, p=0.0620) was noted. No significant correlation between CF positivity and interstitial lung disease, pulmonary arterial hypertension (PAH), history of digital ulcers, and amputation was recorded; however, considering cryocrit sample ≥1%, a correlation between the presence of an estimated pulmonary arterial systolic pressure (ePASP) higher than 30 mmHg and the positivity of CF was obtained (OR = 2.71, 95% CI 1.01-7.28, p=0.0482). The same association was achieved if we considered patients without endothelin receptor antagonist therapy (n=47) and CF positivity (OR=6.19, 95% CI 1.19-32.2, p=0.0304).

Furthermore, no correlation between CF positivity and the presence of digital ulcers at the moment of the blood sampling was verified; however, if we stratified patients according to their ongoing treatments (absence of an endothelin receptor antagonists therapy plus PDE5 inhibitors), a significant correlation between digital ulcers and CF positivity emerged (OR=8.14, 95% CI 1.03-64,5, p=0.0470, n=91).

Conclusion: Our preliminary results on this issue are extremely interesting as they can open new perspectives on the identification of cryofibrinogen as possible prognostic marker that could be involved in the pathogenesis of scleroderma digital ulcers and PAH. Moreover, therapies which are currently used for the treatment of PAH and the management of digital ulcers, could determine circulating cryofibrinogen disappearance, with possible challenging future impact on SSc therapeutic approaches.

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POS0897 A SYSTEMATIC REVIEW AND META-ANALYSIS OF DIAGNOSTIC ACCURACY OF WHOLE-BODY 18F-FDG PET AND 18F-FDG PET/CT IN DETECTING OCCULT MALIGNANCY IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Idiopathic inflammatory myopathies (IIMs) are chronic, systemic autoimmune diseases that can cause muscle inflammation, weakness, and skin manifestations. Several studies have confirmed the association between IIMs and malignancy in adult population with varied frequency (4-42%), highest in patients with dermatomyositis. Detecting occult malignancy is a diagnostic challenge involving cost- and time-consuming methods. The (18)F] fluorodeoxyglucose positron emission tomography ([(18)F] FDG-PET) role in this context has been studied in multiple studies.

Objectives: The purpose of this study is to assess the diagnostic performance of whole-body ^{18}F-FDG PET or ^{18}F-FDG PET/CT for detection of occult malignancy in patients with IIMs.

Methods: A systematic search was performed in PubMed (Medline), Embase, and Scopus, Cochrane and clinicaltrial.gov to identify relevant published studies reporting the performance of ^{18}F-FDG PET or ^{18}F-FDG PET/CT in detecting occult malignancy in IIMs. Histopathologic confirmation and/or clinical follow-up was considered as the gold standard for diagnosis. Studies were eligible if all patients were 18 years or older, does not have history or current diagnosis of cancer and classified as IIMs according to Bohan and Peter classification criteria or have confirmed tissue diagnosis. The screening, full text review, quality assessment with QUADAS-2 tool and data extraction were performed by two investigators. Pooled estimates, with 95% confidence intervals (CIs), of sensitivity, specificity, and diagnostic odds ratio were calculated. A summary receiver-operating-characteristic curve (SROC) was constructed, and the area under the curve (AUC) was determined along with the Q* index.

Results: Out of 499 studies collected, six studies including a total of 293 patients with IIMs and who underwent ^{18}F-FDG PET or ^{18}F-FDG PET/CT examinations met our inclusion criteria. In two studies (87 participants), there was no clear data about the age and gender of the participants. The other four studies (total of 206 patients) 131/206 were females and 75/206 were males. Information about the type of IIMs was available in 5/6 studies with total of 283 participants; Dermatomyositis (194/283), Overlap polymyositis (41/283), Immune mediated necrotizing myositis (14/283), Polymyositis (11/283), non-specific (4/283), and orbital myositis (1/283). A total of 47 cancers were detected with lung (9/47), Breast (8/47) and nasopharyngeal (6/47) cancers were the most reported malignancies. Interestingly, all the breast cancers were reported as false negative. The pooled sensitivity, specificity, and diagnostic odds ratio of ^{18}F-FDG PET or ^{18}F-FDG PET/CT for the detection of underlying malignancy were 0.81 (95% CI, 0.67–0.91), 0.89 (95% CI, 0.84–0.92), and 38.19 (95% CI, 7.6-190.60), respectively. The heterogeneity of the studies was moderate with Chi-square, and I^2 index of 15.6 (P <0.05) and 68% respectively. The AUC and the Q* index was 0.95(SE, 0.033) and 0.89, indicating excellent diagnostic accuracy (Figure 1).

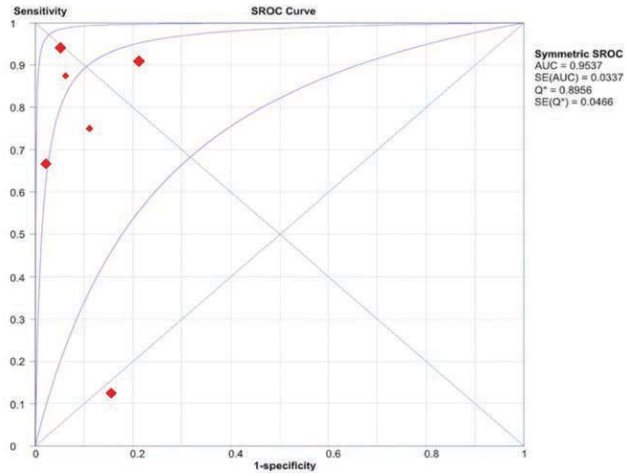

Figure 1. Summary Receiver Operating Characterestic curve of PET scan in detecting occult malignancy in IIMs

Conclusion: This meta-analysis demonstrates that whole-body ^{18}F-FDG PET or ^{18}F-FDG PET/CT has high diagnostic accuracy and moderate to high sensitivity and specificity for detection of underlying malignancy in patients diagnosed with IIMs.

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POS0898 SURGICAL MANAGEMENT OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS: A SYSTEMATIC LITERATURE REVIEW.

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Table 1. Characteristics of the extracted studies.

	Study design	Patients (n)	Baseline DU (n)	Background therapy (%)	Follow-up	Outcome Healed ulcers(%)
Adipose tissue graft	p	9	.15	PG, CCB—100 ETA 26 PDE-5i 13	8-12 wks	66
Autologous fat graft Adipose tissue grafting	RCT	25 case 13- Ctr	25-case 13- Ctr	PG- 100 CCB 100	8 wks	92-case 7-Ctr
Adipose tissue implant	p	15	15	no therapy	7 wks	100
Adipose tissue graft	p	12	9	PG,CCB-100 ETA	6 month	88
adipose derived SVF	p	12	15	PDE-5i, ccb, PG allowed	22m	6
Adipose derived SVF	p	12	15	CCB 50 ETA16	6 m	63
Adipose derived SVF	p	18	19	CCB 50 PG 27 ETA 5 IS 71	24 wks	32
Sympathectomy Sympathectomy	R	6	11	CCB-100	20 m	81
Sympathectomy	R	13	35	PG CCB APA		35
Sympathectomy, vascular bypass (+vein graft	R	17	26	Ccb 35 APA 47 PDE-i5 58	9 m	100
Bone marrow derived cells transplantation)	p	8	8	PG-62	36 m	87
Direct microsurgical revascularization	R	4			4m	100
Limited microsurgical arteriolysis	R	6	17		12 m	100

SVF =stromal vascular fraction P = prospective. R = retrospective. RCT= double blind randomized-controlled trial. ETA = endothelin antagonist. CCB= calcium channel blockers. APA= anti-platelet agents. PG= prostaglandins. ARB= angiotensin receptor antagonist. ACEi= ACE inhibitors. PDE-5i= PDE-5 inhibitors. IS= immunosuppression. M=median. SoC= standard of care. HR= healing rate

Background: Management of digital ulcers (DUs) in systemic sclerosis (SSc) is a major clinical challenge. To date, systemic therapy is generally considered as the 'standard of care' for significant SSc-DUs. However, there is a strong rationale to develop local approaches to DUs, to avoid side effects from systemic therapies. World Scleroderma Foundation DU Working Group intends to develop practical, evidence-based recommendations for DU management including local, Surgical Treatment (L-ST).

Objectives: To summarize the literature on the safety and efficacy of L-ST for SSc-DUs.

Methods: A systematic literature review (SLR) was conducted up to May 2021. According to the PICO framework, eligibility criteria were defined and original research articles about surgical treatment of SSc DUs in adult patients were included. References were independently screened by 2 reviewers who assessed the full text of eligible articles and extracted data.

Results: Thirteen eligible articles out of 790 total publications were identified (Table 1). Due to the paucity of randomized controlled trials of surgical treatments for SSc-DU, we included retrospective studies and case series with at least 4 patients. Autologous fat (adipose tissue AT) grafting was the surgical modality mostly identified (7 studies of which 1 RCT and 6 prospective open label single arm). The healing rate (HR) with autologous fat grafting (4 studies) ranged from 66-100 %. In the RCT, two age and sex matched groups were included, adipose tissue (AT) group (n=25 pts) and sham procedure (SP) group (n=13), DU healing was reported in 23/25 in AT group versus 1/13 in the SP group in 8 wks, ($p<0.0001$), 12 pts in the SP group, received rescue AT injection, all of them healed after 8 wks. Three studies reported autologous adipose-derived stromal vascular fraction(SVF) grafting and the HR ranged from 32-60%, followed up to 12 months. Transient edema and paresthesia were reported in 2 studies, and amputation in 2 ulcers in 1 study, and no complications were reported in other studies. Surgical sympathectomy was reported in 3 studies, with a median healing rate of 81%. Bone marrow derived cell transplantation in a single study showed 87% healing rate over (4-24 wks). Two surgical studies (of direct microsurgical revascularization N=4, and microsurgical arteriolysis, N=6), showed 100% healing of ulcers, no complications reported.

Conclusion: Our SLR has identified several surgical modalities for SSc-DUs. L-STseemed generally effective and safe for DU healing, thus Significant methodological issues emerged including small numbers of pts, lack of comparator, failure to report confounders such as background therapies and variable follow up. Future research is warranted to rigorously investigate surgical interventions for Dus.

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POS0899

HIGH FATIGUE SCORES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: A MULTIGROUP COMPARATIVE STUDY FROM THE COVAD E-SURVEY.

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Background: Idiopathic inflammatory myopathies (IIM) are a rare, multisystem, heterogeneous diseases, and contribute to high psychological burden. The patients' perception of physical health, deteriorating independence and social and environmental relationships may not always be a direct function of disease activity. To face with these aspects, several worldwide specialized organization have recommended the use of patient reported outcome measures (PROMs) both in clinical trials and observational studies to highlight patient's perception of the disease (1). Unfortunately, data on fatigue scores in IIM is limited.

Objectives: We compared fatigue VAS scores in patients with IIM, autoimmune diseases (AIDs) and healthy controls (HCs) and triangulated them with PROMIS physical function in a large international cohort made up of answers from the e-survey regarding the COVID-19 Vaccination in Autoimmune Diseases (COVAD) study.

Methods: Data of 16327 respondents was extracted from the COVAD database on August 31th 2021. VAS fatigue scores were compared between AID, HC and IIM using univariate followed by multivariate analysis after adjusting for baseline differences. We further performed a propensity score matched analysis on 1827 subjects after adjusting for age, gender and ethnicity. The Kruskal-Wallis test was used for continuous variables and chi-square test for categorical variables, and Bonferroni's correction was applied for the post hoc analyses considering IIMs as a reference group.

Results: We analyzed answers from 6988 patients, with a mean age of 43.8 years (SD 16.2). The overall percentage of female was 72% and the population ethnicity was mainly composed of White (55.1%), followed by Asian (24.6%), and Hispanic (13.8%). The overall fatigue VAS was 3.6 mm (SD 2.7). IIMs VAS was 4.8 mm (SD 2.6), AIDs 4.5 mm (SD 2.6), and HC 2.8 mm (SD 2.6) (P <0,001). VAS fatigue scores of IIMs were comparable with AIDs (P 0.084), albeit significantly higher than the HCs (P <0,001). Notably, fatigue VAS was lower in IIMs than AIDs in two distinct subsets: inactive disease as defined by the patient's perception and the "excellent" general health condition group, where IIMs had worse scores (P <0,05). Interestingly, fatigue VAS was comparable in active disease defined by physician assessment, patient perception, based on general functional status, or when defined by steroid dose being prescribed. Notably, after propensity matched analysis of patients adjusting for gender, age and ethnicity (1.827 answers, i.e. 609 subjects per group, P =1) the differences disappeared and IIMs and AIDs had comparable fatigue levels across all levels of disease activity, although the fatigue discrepancies with HCs were substantially confirmed. After application of a multivariate linear regression analysis we found that lower fatigue VAS scores were related to HC (P <0,001), male gender (P <0,001), Asian and Hispanic ethnicities (P <0,001 and 0,003).

Conclusion: Our study confirms that there is a higher prevalence of fatigue in all the AIDs patients, with comparable VAS scores between IIMs and other AIDs. We can also read our data commenting that females and/or Caucasians patients suffer a higher impact of this manifestation of chronic autoimmune diseases upon their lives. This is why these subjects, to our judgement, should be carefully evaluated during outpatients visits and to whom we should spend some extra time to discuss health related issues and how to improve them.

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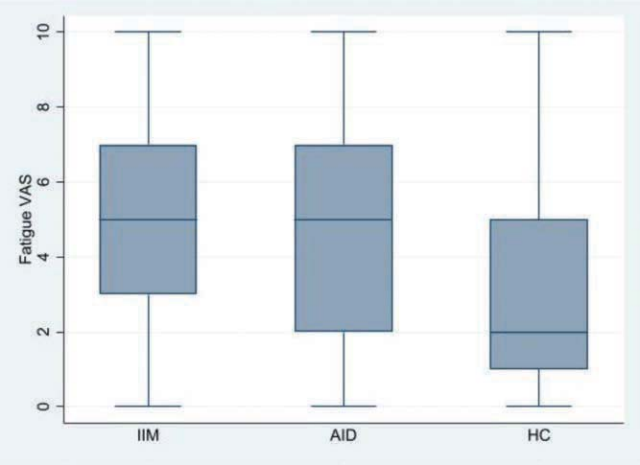

Figure 1. distribution of Fatigue VAS scores in the three population evaluated. IIM idiopathic inflammatory myositis; AID autoimmune diseases; HC healthy controls; * P < 0,05.

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POS0900

SYSTEMIC PHARMACOLOGICAL TREATMENT OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Digital ulcers (DU) are common in systemic sclerosis (SSc) and associated with reduced survival, high morbidity and poor quality of life. Recommendations have previously been proposed for DU management yet there remains significant unmet patient need. Therefore the World Scleroderma Foundation DU Working Group intends to develop practical evidence based recommendations for DU management.

Objectives: To summarise data on efficacy and safety of systemic treatments for SSc DU.

Methods: A systematic literature review to May 2021 was performed. PubMed, MEDLINE, Embase, Web of Science, Cochrane Library, Emcare (OVID) and Academic Search Premier databases were searched for original studies on adult patients with SSc DU treated with systemic pharmacological treatment. Based on the PICO framework, eligibility criteria were defined and references were independently screened by two reviewers. Reviewers independently assessed the full text of eligible articles. Owing to interstudy heterogeneity narrative summaries were used to present data.

Results: The search strategy identified 1271 references of which 45 eligible articles were included. Seventeen studies were randomised placebo controlled trials (RCT) pertaining to PDE5 antagonists (PDE5i) (n=3), endothelin receptor antagonists (ERA) (n=3), prostanoids (n=7), antiplatelet agents (n=1) and other (n=3) (Table 1). No head to head RCT was retrieved. All other studies were observational studies (OBS). Studies were highly heterogeneous with application of differing definition of DU, variable study eligibility criteria, clinical endpoints and follow up periods. This limited the calculation of effect size and comparison across studies.

Table 1. Characteristics of placebo controlled randomised controlled trials

Author Year	Intervention	n	Follow up	Outcome	Favours intervention
Hachulla 2016	Sildenafil	83	12 weeks	Time to DU healing	-
Andrigueti 2017	Sildenafil	41	12 weeks	DU healing	+
Shenoy 2010	Tadalafil	24	6 weeks	New DU	+
Khanna 2016	Macitentan	554	16 weeks	New DU	-
Matucci-Cerinic 2011	Bosentan	188	32 weeks	New DU Time to healing of DU	+-
Korn 2004	Bosentan	122	12 weeks	New DU	+
Kawald 2008	IV iloprost	50	12 months	DU healing	-
Wigley 1992	IV iloprost	35	10 weeks	DU healing	+
Wigley 1994	IV iloprost	73	9 weeks	50% reduction in DU-score	-
Seibold 2017	Treprostinil	148	20 weeks	Net DU burden	-
Vayssairat 1999	Beraprost	107	25 weeks	% patients with new DU	-
Denton 2017	Selexipag	74	12 weeks	Number of new DU DU healing	-
Lau 1993	Cicaprost	33	4 weeks	Number of DU	-
Abou-Raya 2008	Atorvastatin	84	4 months	Number of DU	+
Au 2010	Cyclophosphamide	158	12 months	Number of patients with DU	-
Beckett 1984	Dipyridamole / aspirin	41	2 years	Change in general SSc	-
Nagaraja 2019	Riociguat	17	32 weeks	Net DU burden	-

+ significantly superior to comparator- non significantly different from comparatorDU: digital ulcers IV: intravenous SSc: systemic sclerosis

Several RCT found improved DU healing with treatment: two with PDE5i, one with iloprost and one showed improved DU healing and prevention with atorvastatin. Two RCT demonstrated effective prevention of new DU with bosentan. OBS studies with a total of 621 patients showed variable improvements in the healing of DU with CCB, PDE5i, ERA, statins, N-acetylcysteine, prostanoids and ketanserin and prevention of new DU with ERA. Regarding safety, all treatments were generally tolerated with few serious adverse events. Treatment was ceased in 6.25-17.5% of patients in RCT due to treatment related side effects.

Conclusion: Despite several studies assessing the efficacy and safety of systemic pharmacological treatment of SSc DU, it is not possible to draw solid conclusions due to study heterogeneity. Small RCT have shown treatment benefit with PDE5i, iloprost and atorvastatin. Large studies demonstrated effective prevention of new DU with bosentan. Our results highlight the urgent need for improved clinical trial design to generate more robust evidence and novel therapies to guide the management SSc DU.

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POS0901 INTERSTITIAL LUNG DISEASE IN MIXED CONNECTIVE TISSUE DISEASE: CLINICAL AND SEROLOGICAL ASSOCIATIONS

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Background: Mixed connective tissue disease (MCTD) is a rare systemic rheumatic disease characterized by the expression of autoantibodies targeting the U1-ribonucleoprotein and overlapping clinical features of systemic sclerosis, systemic lupus erythematosus, and inflammatory myopathies. Interstitial lung disease (ILD) is present in 47% to 78% of patients and has been associated with higher mortality rates. Associations of ILD with Raynaud's phenomenon, dysphagia, anti-Ro52 antibodies, and a scleroderma pattern on nailfold capillaroscopy have been reported in MCTD patients.
Objectives: This study aims to identify clinical and serological associations and independent predictors of ILD for patients with MCTD.
Methods: Multicenter retrospective study using data collected from clinical records. Adult patients who underwent lung computed tomography (CT) and met at least one of four MCTD diagnostic criteria (Sharp, Alarcón-Segovia, Kasukawa, or Kahn criteria) were included. Univariate analysis was performed using Chi-Square, Fischer's Exact, and Mann-Whitney tests, as appropriate. Multivariate analysis was performed using binary logistic regression modelling. The linearity of the continuous variables concerning the logit of the dependent variable was assessed via the Box-Tidwell procedure. Cases with missing information and outliers were excluded from the multivariate analysis to fulfil all assumptions necessary to assure the validity of the regression.
Results: Fifty-seven patients, of whom 37 were Caucasian (64.9%) and 48 were females (84.2%), with a mean age of 39.4±14.0 years, were included. Twenty-seven patients had ILD (47.4%), of whom 22 had nonspecific interstitial pneumonia (81.5%), 4 had usual interstitial pneumonia (14.8%), and 1 had lymphoid interstitial pneumonia (3.7%) pattern on CT. Among patients with ILD, 13 were asymptomatic (48.1%), while 14 had respiratory symptoms (51.9%), including dyspnea (N=13, 48.1%), cough (N=7, 25.9%), and pleuritic chest pain (N=1, 3.7%). Pulmonary function tests were performed in 22 patients (81.5%), 20 of whom had a restrictive pattern (90.9%).
In the univariate analysis, lymphadenopathy at disease onset (22.2% vs 3.3%, p=0.045) and esophageal involvement at any time point (40.7% vs 16.7%, p=0.043), were associated with ILD.
The binary logistic regression model predicting ILD included 56 patients, and the model explained 36.5% (Nagelkerke R2) of the variance in ILD and correctly classified 75% of all cases. Older age at diagnosis (OR 1.10/year, 95%CI: 1.00-1.12, p=0.046) and lymphadenopathy at disease onset (OR 19.65, 95%CI: 1.91-201.75, p=0.012) were identified as predictors of ILD in MCTD patients, irrespective of sex and esophageal involvement.
Conclusion: Older age at diagnosis and lymphadenopathy at disease onset were independent predictors of ILD in MCTD. Therefore, these factors should be considered when evaluating MCTD patients, especially at the time of diagnosis. To the best of our knowledge, this is the largest study ever describing predictors of ILD for MCTD patients.
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POS0902 RISK FACTORS FOR LUNG FUNCTION DECLINE IN SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE IN A LARGE SINGLE-CENTER COHORT

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Background: Systemic sclerosis associated interstitial lung disease (SSc-ILD) is the leading cause of scleroderma-related mortality.
Objectives: This work identifies factors associated with SSc-ILD decline on pulmonary function testing (PFT).
Methods: This single center cohort identified 312 patients with ILD as determined by high resolution chest. 184 patients (59% of 312) completed baseline and serial PFTs (with at least two follow-up PFTs) and were included in this analysis. Mixed linear models were fit to assess the decline in the percent predicted forced vital capacity (ppFVC) over time. Demographics, disease factors, autoantibodies, and ILD features were included in the univariate mixed linear model; those achieving a p-value <0.20 were included in the multivariable mixed linear model. Patients were followed longitudinally, with survival as an endpoint identified using the National Death Registry Index, reviewing death certificates, and hospital records.
Results: The 184 patients were an average of 53.2 [12.1] years old; the median [IQR] disease duration from the first non-Raynaud's phenomenon symptom was 1.8 [0.7, 4.8] years. SSc subtype was diffuse in 55.4% (n=102), limited in 32.6% (n=60), overlap syndrome in 8.2% (n=15), and SSc sine scleroderma in 3.87% (n=7). Serologies were positive for anti-topoisomerase I (ATA), anti-centromere and anti-RNA polymerase III in 31.4% (n=53/169), 10.4% (16/154) and 22.9% (25/109) respectively. Mean ppFVC was 70.8 (18.9) and ppDLco 57.2 (20.8). Whole lung involvement (WLI%) of ≥20% on visual read was found in 49.3% of subjects (74/150 (49.3%)) where quantification was available. Over a median of 4.9 (2.4, 6.8) years, 21 patients (11.4%) died. The ppFVC declined a mean of 0.28/year in the overall group. There were differences in terms of ppFVC decline/year between patients who died in the first 2 years (n=10, -8.28%), 2-8 years (n=5, -3.89%), after 8 years (n=6, -1.00%), or who were still alive (n=163, -0.13%). The primary cause of death was ILD (6/21, 28.6%); those who died in the first 2 years most often died from progressive ILD (4/6, 67%). Factors significantly associated with decline in ppFVC on univariate analyses, included longer disease duration (ref. < median, P=0.0048), ATA positivity (ref. negative, P=0.0081), and WLI ≥20% (ref. 0-20%, P=0.0484). In multivariate analysis the only statistically significant variable associated with decline in ppFVC/ year was ATA positivity.
Conclusion: In a large single center cohort of SSc-ILD, ATA positivity is a risk factor for developing progressive SSc-ILD, consistent with other SSc-ILD cohorts. Stratifying patients by survival demonstrates that lung function declines dramatically in those who died within 2 years, whose main cause of death was progressive ILD. These data support the growing need to identify risk factors for disease severity and risk for progression, and to target intervention in patients most likely to develop progressive SSc-ILD[1,2].
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POS0903 ASSOCIATION STUDY BETWEEN ANTI-TIF 1Γ ANTIBODY AND DEVELOPMENT OF NEOPLASIA IN THREE TERTIARY HOSPITALS.

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Background: Anti-transcriptional intermediary factor 1γ (anti-TIF 1γ) antibody is robustly linked with cancer-associated dermatomyositis (DM) in adults, but its specificity varies widely between series. TIF 1γ can act either as a tumor promoter or suppressor and may behave as an autoantigen.
Objectives: Investigate the association between anti-TIF 1γ antibody positivity and development of neoplasia.
Methods: A retrospective chart review was conducted among patients with positive anti-TIF 1γ antibodies detected by immunoblot from March 2019 to December 2021 in three tertiary hospitals. Demographic variables, creatine kinase (CK) values, other autoantibodies, associated autoimmune diseases (AIDs) and existence or not of a cancer diagnosis were analyzed. To rule out malignancy, patients had to present a PET-CT scan without pathological findings or a chest CT scan, a gynecological study and a digestive study without alterations. A descriptive statistical analysis was performed.

Results: 29 patients with anti-TIF 1γ antibodies were analyzed, 82.7% women, with a mean age of 61 years (31-96 years).
The reason for requesting this antibody was: clinical features suggestive of DM in 10 patients (34.5%), muscle weakness in 9 (31%), interstitial lung disease (ILD) in 5 (17.2%), persistent CK elevation in 3 (10.3%), constitutional syndrome in 1 (3.5%) and antiphospholipid syndrome in 1 patient (3.5%). The mean time from symptoms onset to the detection of anti-TIF 1γ was 14 months (0-60 months).
10 patients (34.5%) had a diagnosis of DM; 4 patients (13.8%) systemic lupus erythematosus (SLE); one (3.5%) had a SLE/DM overlap syndrome; one patient (3.5%) subacute cutaneous lupus; one (3.5%) was diagnosed with diffuse systemic sclerosis; one patient (3.5%) limited systemic sclerosis; one patient (3.5%) antiphospholipid syndrome; one patient (3.5%) HLA-B27+ spondyloarthritis and 9 patients (31%) had no associated AIS. 5 patients (17.2%) showed ILD with different patterns: UIP (n=2), NSIP (n=2) and COP (n=1). Only 9 patients (31%) had elevated CK levels at the time of antibody determination. 10 patients (34.5%) were diagnosed with cancer: lung adenocarcinoma (n=2), small cell lung carcinoma (n=2), breast carcinoma (n=2), hepatocarcinoma (n=1), cervical cancer (n=1), ovarian carcinoma (n=1) and gallbladder adenocarcinoma (n=1). Of those, 7 patients (70%) had elevated CK levels and 6 (60%) had a diagnosis of DM. None of the patients diagnosed with cancer had ILD. In 4 patients (40%), the diagnosis of cancer was simultaneous with the diagnosis of anti-TIF 1γ antibodies; in 4 (40%), the diagnosis of the tumor preceded the finding of the antibodies; in the other 2 (20%), the finding of the antibodies preceded that of the tumor. 30-month survival after cancer diagnosis was 10%.
In 17 patients (58.6%) no malignancy has been found so far in the annual cancer screening. In two patients (6.9%) no cancer screening was performed.
Conclusion: In our study, 60% of patients with DM and anti-TIF 1γ presented neoplasia, a prevalence similar to that established in other series (60-80%). Furthermore, 21% of patients with antibodies and without DM were diagnosed with cancer, suggesting that anti-TIF 1γ antibodies could also be associated with neoplasia in patients without DM. Patients with ILD did not present cancer, supporting the observation of previous studies in which the presence of ILD is a marker of low risk for neoplasia in patients with DM. HyperCKemia might predict the association with neoplasia in patients with anti-TIF 1γ antibodies.
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POS0904 CHANGES OF PULMONARY ARTERY SYSTOLIC PRESSURE IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS ON RITUXIMAB TREATMENT

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Background: Nowadays, there is already published a lot of data on the treatment of systemic sclerosis (SSc) with rituximab (RTX). Recent studies reported about improvement of skin fibrosis and interstitial lung disease associated with SSc (ILD-SSc) on RTX treatment. However, there is not enough data on changes of pulmonary artery systolic pressure (PASP) in SSc patients (pts) on RTX therapy.
Objectives: To evaluate changes of PASP in ILD-SSc pts on RTX therapy.
Methods: 30 pts with initially elevated PASP (detected as ≥35mmHg by echocardiography) were retrospectively selected from a group of 103 SSc pts who received RTX as a therapy for ILD. The mean follow-up period was 25.3±2.4 months. The mean age was 52.6 years (30-65), female-26 pts (87%), the diffuse cutaneous subset of the disease had 13 pts (43%). The mean disease duration was 7.2±6.3 years. The cumulative mean dose of RTX was 2.3±1.1 grams. All pts received prednisolone at a dose of 11.3±3.7mg/day, immunosuppressants received 47% of them. All pts were positive for ANA. An assessment of basic parameters was obtained at baseline (Point 0), after 13.6±2.7 months (Point 1) and at the end of follow-up (25.3±2.4 months - Point 2). The results at baseline and at the end of the follow-up are presented in the form of mean values.
Results: There was already an improvement of all main parameters at the point 1 and further - by the end of follow-up (Table 1). There was a significant decrease in PASP, which was accompanied by the improvement of lung function - increase in forced vital capacity % predicted (FVC), stabilization of diffusion capacity for carbon monoxide % predicted (DLCO). A moderate negative statistically significant correlation was found between the PASP and FVC (r=-0,522; p=0,003). There was a significant increase in 6-minute walk distance (6-mwd), ejection fraction of left ventricular (ER), activity index (EScSG-AI) and a decrease of Rodnan skin score.

Table 1. Changes of the main parameters on RTX treatment.

Parameters	Point 0 (baseline)	Point 1 (13.6±2.7 month)	Point 2 (25.6±2.4 month)	P Point 0-1	P Point 0-2
FVC, %, M±σ	75.6±20.1	82.5±19.2	88.2±22.5	0.01	0.002
PASP, mmHg, M±σ	48.2±13.8	44.4±12.3	39.5±11.8	0.008	0.004
DLCO, %, M±σ	42.7±16.2	42.6±15.2	44.9±15.6	NS	NS
ER, %, M±σ	61.6±5.5	63.5±6.2	65.8±5.7	0.02	0.01
Rodnan skin score, M±σ	11.1±12.4	7.2±8.1	6.1±7.6	0.003	0.0001
6-mwd, m, M±σ	419.6±103	453.8±85	458.8±78.4	0.02	0.02
Activity index (EScSG-AI), M±σ	3.3±1.5	1.5±1.3	1.4±1.1	0.001	0.001
Cumulative mean dose of RTX, g, M±σ	-	1.65±0.69	2.3±1.1	-	-

Conclusion: In our study, the PASP significantly decreased already in a year after initiation of RTX therapy and further there was an improvement of this parameter at the end of the observation. Decrease of PASP correlated with an increase of FVC and was accompanied by an increase of 6-minute walk distance, ejection fraction of left ventricular, improvement of Rodnan skin score and disease activity index. RTX could be considered as a potentially effective in combined treatment of ILD-SSc, complicated with pulmonary hypertension.
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POS0905 CHARACTERISATION OF SWEDISH MYOSITIS PATIENTS WITH ANTI-MDA5 AUTOANTIBODIES AND CORRELATION OF CLINICAL FEATURES WITH AUTOANTIBODY LEVELS

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Background: The association between anti-melanoma differentiation association protein 5 autoantibodies (aMDA5) and rapidly progressive interstitial lung disease (RP-ILD) in clinically amyopathic dermatomyositis is well established in Asian population cohorts. In western cohorts, ILD has been strongly associated with aMDA5 but data regarding RP-ILD have been more conflicting. It is also suggested that western cohorts have more pronounced myopathic features than Asian.
Objectives: To characterise the disease manifestations of a Swedish aMDA5 positive idiopathic inflammatory myositis (IIM) cohort and to explore antigen reactivity of the MDA5 protein.
Methods: First available serum samples collected from 28 consecutive patients with IIM and positive aMDA5 ever tested by ELISA, Line Blot (LB) or Immunoprecipitation, attending Karolinska University Hospital between 1999 and 2021, were included. Clinical data including presence of anti-SSA autoantibodies by ELISA or LB was retrieved retrospectively. An in-house ELISA was used to screen serum samples for reactivity against a recombinant MDA5 protein (rMDA5, aa A110-D1025, UniProt ID Q9BYX4) and seven MDA5-derived constructs containing different domains. Correlations between aMDA5 reactivity levels and clinical data were explored.
Results: Nine patients showed no reactivity to any of the rMDA5 constructs by ELISA and were excluded from further analysis.
Reactivity against rMDA5 was confirmed by ELISA in 19 patients (median 184.7 µg/mL (interquartile range (IQR) 277.07). The cohort included 13 male and 6 female patients, 94% Caucasian, with mean age at diagnosis of 41.05 years (standard deviation (SD) 10.5). Median disease duration at time of sampling was 0 months (IQR 1). All patients except one had signs of muscle involvement (muscle weakness, elevated muscle enzymes, muscle oedema or muscle biopsy consistent with myositis). At diagnosis 63.2% of patients reported muscle weakness (21.1 % had a manual muscle test 8 score <75). Dermatological findings were observed in 17/19 (89.7 %). During disease course nine patients (47.4%) had confirmed arthritis. ILD was diagnosed in 16/19 patients (84.2%), four of these (25%) developed a RP-ILD. One patient passed away due to RP-ILD and one required a lung transplant. Patients with ILD had a statistically significant higher mean age at diagnosis than those without (42.8.5 (SD 10.3) vs 31.3 (SD

4.7) years, p=0.02). Patients developing RP-ILD were not significantly older than patients with chronic ILD. Respiratory symptoms were reported by 75% of patients with ILD at time of diagnosis. The mean total lung capacity (TLC) of the ILD cohort was 68% (SD 17), mean diffusion capacity of carbon monoxide (DLCO) was 59% (SD 15) and mean forced vital capacity (FVC) was 62% (SD 19). There was a higher proportion of patients with CRP ≥ 3 times the reference range at diagnosis amongst patients with FVC <70 % than patients with FVC >70 % (88.9 % vs 16.7 %, p= 0.01).

Ten patients (52.6%) had anti-SSA autoantibodies, all had ILD. Anti-SSA positive patients had a statistically significant lower TLC than those without (62% vs 79% respectively, p=0.04) and a lower FVC (57% vs 76% respectively, p=0.05).

We found a weak non-statistically significant negative correlation between titres of aMDA5 and TLC, DLCO and FVC (Pearson coefficients -0.187, -0.289, -0.130 respectively). Frequency of ILD was higher in patients with aMDA5 titres >100 µg/mL than those with titers <100, but not statistically significant (81.3% vs 18.8%, respectively).

Conclusion: In this Caucasian cohort of aMDA5 positive IIM patients, ILD was present in over 80% of patients, of these, one quarter had RP-ILD. Older patients were more likely to present with ILD. Anti-SSA positivity and higher CRP levels were associated with worse lung function. We found a weak negative correlation between aMDA5 titres and lung function tests, as well as a trend of higher frequency of ILD in patients with higher aMDA5 titres. Muscle and skin involvement were found in a high proportion of patients.

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POS0906 PREVALENCE OF SPECIFIC AND ASSOCIATED MYOSITIS ANTIBODIES IN A COHORT OF PNEUMOLOGICAL PATIENTS: FROM THE DIAGNOSIS OF INTERSTITIAL LUNG DISEASE TO A POSSIBLE DIAGNOSIS OF CONNECTIVE TISSUE DISEASE

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Background: Interstitial lung disease (ILD) could be the first and only manifestation of idiopathic inflammatory myopathies (IIMs). Myositis-associated (MAA) or myositis-specific autoantibodies (MSA) are found in 60%-65% of cases [1, 2], but only anti-Jo1 have been included in EULAR 2017 criteria [3].

Objectives: Aim of this work is to evaluate the presence of MSA/MAA in patients with ILD on serum analyzed by line blot (LB) immunoassay, the associated clinical diagnoses and the consistency of these diagnoses with antibody specificity.

Methods: Between march 2017 and march 2021, 267 sera were analyzed for MSA/MAA, 84 (31.4%) of which requested after a pneumological evaluation. The search was performed by LB (EUROLINE, Autoimmune Inflammatory Myopathies 16 Ag Profile). Medical records were analyzed for patients with at least one MSA/MAA and diagnosis divided in: connective tissue disease (CTD), interstitial pneumonia with autoimmune features (IPAF) or only pneumological diagnosis.

Results: A positivity for at least one MSA/MAA was found in 37/84 (44%) patients that had the following pneumological diagnosis: 13 non-specific interstitial pneumonia (NSIP, 35.1%), 10 organizing pneumonia (OP, 27%), 10 usual interstitial pneumonia (UIP, 27%), 1 acute interstitial pneumonia (AIP, 2.7%), 1 lymphoid interstitial pneumonia (LIP, 2.7%), 1 iatrogenic ILD for amiodarone (2.7%) and 1 idiopathic pulmonary artery hypertension (IPAH, 2.7%). Distribution of antibodies is reported in Table 1. The most frequent autoantibody was anti-Ro52 (13 sera, 35.2%), while anti-Mi2 was the most frequent MSA (10 sera, 32.4%) followed by anti-Jo1 and anti-SRP with 5 (13.5%) positive sera each. In Figure 1 the heatmap represents the frequency of MSA/MAA and their mutual associations. Multiple autoantibodies were found in 17 (46%) sera. More than one MSA was found in 8 (21.6%) sera of patients with the following diagnosis: 4 only pneumological diseases, 3 ASS and 1 IPAF.

Table 1. Distribution of MSA/MAA and associated autoimmune diseases

Autoantibodies distribution N (%)	Sera with a single MSA/MAA (N/positive; %)	CTD* (N/positive; %)	IPAF (N/positive; %)
MSA			
Jo-1 = 5 (13.5)	2/5 (40)	3/5 (60)	0
PL7 = 4 (10.8)	0	2/4 (50)	1/4 (25)
PL12 = 6 (16.2)	3/6 (50)	3/6 (50)	0
OJ = 3 (8.1)	2/3 (66.6)	1/3 (33.3)	2/3 (66.6)
EJ = 1 (2.7)	1/1 (100)	1/1 (100)	0
Mi-2 = 10 (32.4)	3/10 (30)	2/10 (20)	0
NXP2 = 1 (2.7)	0	0	1/1 (100)
SRP = 5 (13.5)	2/5 (40)	2/5 (40)	0
TIF1gamma = 2 (5.4)	0	1/2 (50)	0
MAA			
Ro-52 = 13 (35.2)	3/13 (23)	9/13 (69.2)	1/13 (7.6)
PM/Scl = 6 (18.9)	4/6 (66.6)	0	1/6 (16.6)

For some patients there are multiple positive antibodies.*The following diagnosis were included: antisynthetase syndrome, dermatomyositis, polymyositis and systemic sclerosis.

During the diagnostic work-up, at least one MSA/MAA were detected in 13 patients diagnosed with a CTD (35%), 5 with a IPAF (13%), 19 (51%) only a pneumological diagnosis. Of these 19 patients, 11 (57.9%) had a single autoantibody positivity (8 for a MSA, 3 for a MAA) while 8 (42.1%) had multiple positivity (4 with a MSA plus MAA and 4 with multiple MSA positivity).

The most frequently diagnosed CTD was ASS with 9 patients (24.3%), followed by 2 polymyositis (5.4%), 1 dermatomyositis (2.7%) and 1 systemic sclerosis (2.7%). Pulmonary involvement in patients with CTD was represented by 9 cases of NSIP (69,3%) and 4 UIP (30,7%).

Conclusion: During the last 4 years about 1/3 of research for MSA/MAA requests to our laboratory had a pneumological indication and MSA/MAA were found in 44% of these patients. In patients with pulmonary involvement and MSA/MAA positivity 35% developed a CTD. Interstitial lung disease could be the first manifestation of a systemic autoimmune disease: research for MSA/MAA and a collaboration between rheumatologist and pneumologist allows a correct diagnostic work-up and therapeutic approach.

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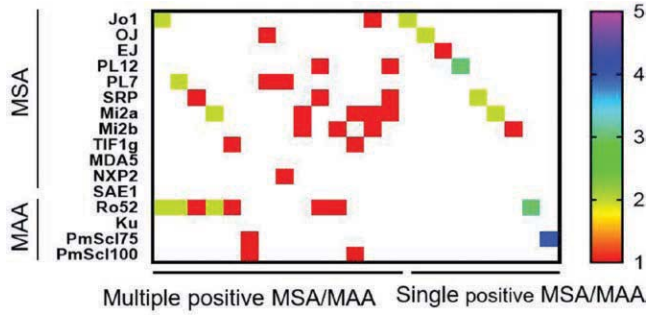

Figure 1. Heat-map represents the frequency of MSA and MAA and their mutual associations.

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POS0907 ASSOCIATION BETWEEN DISEASE ACTIVITY AND DAMAGE IN IDIOPATHIC INFLAMMATORY MYOPATHIES. DIFFERENCES BETWEEN INCIDENT AND PREVALENT CASES

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Background: There are different measures and tools validated to evaluate disease activity and damage in idiopathic inflammatory myopathies (IIM). Disease activity and damage in patients with early diagnosis is not still well defined.
Objectives: To analyze disease activity outcomes and their association with damage in IIM differentiating between incident and prevalent cases.
Methods: Multicenter cross-sectional study of a cohort of patients included in the Spanish Registry of patients with IIM (Myo-Spain)(1). Patients were classified as incident cohort (time between diagnosis and study initiation ≤ 12 months) or prevalent cohort (> 12 months). Activity and damage data were collected at the initial visit. Differences between both groups were tested by Chi-square, Student's t and Mann-Whitney tests. Spearman's correlation coefficients (Rho) were used to analyze correlations between disease activity and damage measures (weak ≥ 0.2 - <0.3; moderate ≥ 0.3 <0.7; strong ≥ 0.7).
Results: We included 139 (67.63% women) and 417 patients (74.34% women) with a mean age at diagnosis of 54 and 48 years in the incident and prevalent cohort, respectively. Patients in the incident cohort had significantly higher disease activity measures: myositis disease activity assessment visual analogue scale (MYOACT) total, extramuscular activity of MYOACT, physician global activity (PhGA), patient global activity (PGA), manual muscle testing (MMT)8, CK, and HAQ ($p < 0.001$).The organ systems with the bigger differences between the incident and the prevalent cohort were skin and constitutional ($p<0.001$). No significant differences were found respect to physician global damage (PhGD), patient global damage (PGD) and myositis damage index (MDI), between both cohorts ($p > 0.2$). Correlations between disease activity and damage measures are showed in the Table 1. The main differences found between both cohorts were the correlations of PhGA, CK, PGD and MDI with other measures of disease activity.
Conclusion: Incident cases had higher disease activity. In those in whom damage was detected, no differences were found in damage measures with prevalent cases. The correlation between the different measures of activity and damage was slightly better in prevalent patients.

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POS0908 AUDIOLOGICAL DISTURBANCES IN PATIENTS WITH SYSTEMIC SCLEROSIS: ASSOCIATION WITH CLINICAL MANIFESTATIONS AND NAILFOLD CAPILLARY MICROSCOPIC ABNORMALITIES

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Background: Systemic Sclerosis (SSc) is a rare connective tissue disease with several systemic and organ specific manifestations, characterized by immune dysfunction, vascular abnormalities, and fibrosis. The microvascular damage is a prominent feature of SSc, being easily assessed by nailfold video-capillaroscopy (NVC). These vascular changes may result in the involvement of the inner ear as the cochlea is highly sensitive to these changes. Blood changes and hypoxia seem to culminate with necrosis of the cochlear tissue, which is clinically expressed as hypoacusis and tinnitus. Hearing loss and auditory symptoms have been reported in 20 to 40% of SSc patients. The prominence of other symptoms may be a reason for audiovestibular symptoms being neglected in these patients, but this can negatively affect patient's quality of life (QoL) and social interaction.
Objectives: The aim of this study is to assess the prevalence of audiological disturbances in patients with SSc and to evaluate its relationship with the duration, characteristics, and severity of the disease.
Methods: Cross-sectional study included 24 patients with SSc, who fulfilled ACR/EULAR criteria followed at outpatient rheumatology clinic between 2012 and 2020 and 20 healthy controls. Socio-demographic, clinical data and pattern of NVC were collected. Both groups underwent a complete ear-nose-throat physical examination, pure-tone audiometry, speech audiometry and impedance. QoL was assessed by the European Quality of Life–5 Dimensions (EQ-5D) questionnaire. Descriptive analysis was performed, p-value <0.05 was statistically significant.
Results: Clinical characteristics and audiometric findings of all patients are listed in Table 1. 13% of patients with SSc reported hearing loss and 38% reported tinnitus and vertigo. Similar values were reported in control group with exception to vertigo symptoms (20%). 37.5% patients presented abnormal hearing loss in the pure-tone audiometry compared with 5% of the controls (p=0.02). Sensorineural hearing loss and abnormal speech reception threshold were more common in SSc patients compared to controls (p=0.03; p=0.04). Auditory recruitment was found in 1 SSc patient. There was no correlation between objective hearing loss and type of scleroderma, duration of disease, type of antibodies, skin score, NVC

Table 1. Correlations between disease activity and damage measures

		Incident cohort				Prevalent cohort			
		MYOACT total	Extramuscular activity of MYOACT	PhGA	MMT- 8	MYOACT total	Extramuscular activity of MYOACT	PhGA	MMT- 8
Extramuscular activity of MYOACT	Rho	0.76	1	**0.673**	**-0.166**	0.777	1	**0.764**	**-0.214**
	P-value	<0.001	<0.001	**<0.001**	**0.065**	<0.001	<0.001	**<0.001**	**<0.001**
PhGA	Rho	0.823	0.673	1	-0.5	0.779	0.764	1	-0.301
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
PGA	Rho	0.667	0.544	0.679	-0.434	0.585	0.528	0.623	-0.345
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
MMT-8	Rho	-0.471	**-0.166**	-0.5	1	-0.383	**-0.214**	-0.301	1
	P-value	<0.001	**0.065**	<0.001	<0.001	<0.001	**<0.001**	<0.001	<0.001
CK	Rho	0.221	**-0.086**	0.234	-0.438	**0.07**	**-0.024**	0.112	-0.11
	P-value	0.014	**0.351**	0.008	<0.001	**0.178**	**0.648**	0.029	0.034
HAQ	Rho	0.486	0.338	0.528	-0.49	0.386	0.248	0.384	-0.505
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
PhGD	Rho	0.367	0.31	0.448	-0.305	0.573	0.492	0.598	-0.334
	P-value	<0.001	0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001
PGD	Rho	**0.293**	**0.163**	0.354	**-0.295**	**0.468**	**0.408**	0.476	**-0.347**
	P-value	**0.003**	**0.102**	<0.001	**0.002**	**<0.001**	**<0.001**	<0.001	**<0.001**
MDI	Rho	0.398	**0.279**	0.388	**-0.232**	0.579	**0.477**	0.545	**-0.343**
	P-value	<0.001	**0.006**	<0.001	**0.026**	<0.001	**<0.001**	<0.001	**<0.001**

Myositis disease activity assessment visual analogue scale (MYOACT), physician global activity (PhGA), patient globalactivity (PGA), manual muscle testing (MMT)8, health assessment questionnaire (HAQ), physician global damage(PhGD), patient global damage (PGD), myositis damage index (MDI).

patterns and organ involvement but there were statistically significant differences with history of digital ulcers. We also found middle ear dysfunction: absence of stapedius reflex (20.8%) and abnormal tympanometry (45.8%) in patients with SSc versus control group (p=0.001). The mean value of EQ-VAS was lower in SSc group (63.8±13.1) compared to controls (71.1±11.0) (p=0.04), but without significant differences with the changes in the pure-tone or speech audiometry.

Table 1. Clinical characteristics and audiometric findings of all patients

	SSc n=24	Controls n=20	*p*
Age, years (mean±SD)	58.4±11.4	55.3±10.3	0.63
Sex (M/F), n	5/19	6/14	0.49
Duration disease (mean±SD)	50.3±41.2	-	
Diffuse cutaneous, n (%)	7 (29.2)	-	
Anti-Scl70 antibody, n (%)	6 (25.0)	-	
Anticentromere antibody, n (%)	14 (58.3)	-	
Anti-RNA polymerase III antibody, n (%)	3 (12.5)	-	
Pulmonary involvement, n (%)	7 (29.2)	-	
Gastrointestinal involvement, n (%)	8 (33.3)	-	
Articular involvement, n (%)	2 (8.3)	-	
Nailfold video-capillaroscopy pattern		-	-
Nonspecific	1 (4.2)		
Early	11 (45.8)		
Active	8 (33.3)		
Late	4 (16.7)		
Subjective hearing loss, n (%)	3 (12.5)	3 (15)	0.58
Tinnitus, n (%)	9 (37.5)	4 (20)	0.41
Objective hearing loss, n (%)	9 (37.5)	1 (5)	**0.02**
Sensorineural hearing loss (%)	7 (29.2)	1 (5)	**0.03**
EQ-VAS (mean±SD)	63.8±13.1	71.1±11.0	**0.04**

Conclusion: Our study found higher prevalence of inner and middle ear pathologies in SSc patients. It is also important to emphasize the relationship found with history of digital ulcer. In these patients, this type of involvement should be considered both during diagnostic and therapeutic procedures. Further investigation is needed for a better understanding of ear damage in these patients.

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POS0909 THE ROLE OF IMACS CORE SET MEASURES TO ROUTINELY EVALUATE THE QUALITY OF LIFE OF IDIOPATHIC INFLAMMATORY MYOPATHIES PATIENTS IN CLINICAL PRACTICE

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Background: Idiopathic Inflammatory Myopathies (IIMs) are rare, multisystemic and complex diseases, often impacting on patients' quality of life (QoL). Patient Reported Outcomes (PROs) assess the overall health status of patients, particularly for emotional and functional domains. In clinical practice the administration of PROs might have some limitations, because they tend to be time-consuming and sometimes difficult to be filled in by patients. The International Myositis Assessment & Clinical Studies Group Disease Activity Core Set Measures (IMACS-CSM) are a tool created to specifically assess disease activity and QoL in IIMs.
Objectives: To evaluate the ability of IMACS-CSM in assessing IIMs patients' QoL in comparison with both generic and IIMs specific PROs.
Methods: Consecutive adult patients with an established diagnosis of IIM (2017 EULAR/ACR criteria) followed at our Myositis Clinic were enrolled and evaluated during scheduled follow-up visits. Demographic and clinical data (age, sex, disease subset and duration, organ involvement) were collected. IMACS-CSM [Physician Global Activity (PhGA), Patient Global Activity (PGA), 8-items Manual Muscle Testing (MMT8), Health Assessment Questionnaire (HAQ), CPK values, Myositis Disease Activity Assessment Tool (MDAAT)] were used to evaluate both disease activity and QoL. Patients' perspective was evaluated also by administration of PROs not included in the IMACS-CSM: Short-Form 36 Items Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-F), Myositis Activity Profile (MAP), MD Anderson Dysphagia Inventory (MDADI). Results were expressed as mean±SD for continuous variables and as percentage for categorical variables. Intergroup comparisons were assessed by using Chi-square, t-test and ANOVA. Pearson coefficient was used to analyse the correlations between IMACS-CSM variables and the other PROs. P values <0.05 were considered significant.
Results: Sixty patients (65% female, mean age 59.9±13.5 years, mean disease duration 7.7±6.1 years), 37 (61.7%) with polymyositis, 20 (33.3%) with dermatomyositis and 3 (5%) with inclusion body myositis, were enrolled. Among IMACS-CSM, the mean HAQ and PGA scores were significantly worse in case of muscle (p=0.017) and oesophageal involvement (p=0.017), respectively; as expected, MMT8 score was associated with muscle involvement (p=0.017); MDAAT score was instead associated with oesophageal dysfunction (p<0.001). No associations were found between IMACS-CSM and others clinical and demographic parameters. FACIT-F correlated positively with MMT8 (r 0.432, p=0.001) and negatively with PhGA, PGA, HAQ and MDAAT (all r <-0.404 and p≤0.002 except for PhGA with r=-0.338 and p=0.016). SF-36 domains correlated positively with MMT8 (all r >0.259, p≤0.05) and negatively with PGA (all r <-0.393, p≤0.001), HAQ (all r <-0.422, p≤0.001) and MDAAT (all r <-0.276, p≤0.05). Opposite correlations were found for MAP domains: MMT8 all r <-0.297, p≤0.05; PGA all r >0.326, p≤0.05; HAQ all r >0.483, p≤0.001; MDAAT all r >0.268, p≤0.05. Similarly, MDADI scores correlated negatively with MMT8 (r <-0.363, p=0.005) and positively with PGA, HAQ and MDAAT (all r >0.318, p≤0.015). Notably, no correlations emerged between these PROs and CPK values.
Conclusion: Even if IMACS-CSM offer a partial evaluation of patients' perspective, our data show how not only HAQ and PGA, but also PhGA, MMT8 and MDAAT (expressing rheumatologist's point of view) seem to adequately reflect overall health status of IIMs patients, thus giving to clinicians a reliable assessment of their QoL. Therefore, the core set should be routinely used in clinical practice during every outpatient visit, while more accurate and complex PROs might be administered at larger time intervals or during disease flares, to optimize IMACS-CSM's analysis.

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POS0910 PSYCHIATRIC COMORBIDITIES ASSESSMENT: AN UNMET NEED IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES?

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Background: Idiopathic Inflammatory Myopathies (IIMs) are rare and complex chronic diseases, with a strong impact on patients' Quality of Life (QoL) in terms of both physical and emotional functioning. Despite its key role in daily life, patients' emotional status could be difficult to be investigated by physicians. As known, patients with chronic conditions are at higher risk of anxiety and depression, but data about their prevalence in IIMs are still limited. The Hospital Anxiety and Depression *Scale* (*HADS*) is a validated questionnaire to evaluate the presence and severity of both anxiety (HADS-A) and depression (HADS-D) in patients.
Objectives: To determine the prevalence of anxiety and depression in a monocentric cohort of IIMs patients and to evaluate possible correlations with clinical features, disease activity and parameters of QoL.
Methods: Consecutive adult patients with a diagnosis of IIM (2017 EULAR/ACR criteria) were recruited during a scheduled follow-up visit. Demographic and clinical features were recorded (sex, age, disease subset and duration, organ involvement, comorbidities). IIM disease activity was evaluated following International Myositis Assessment & Clinical Studies Group Disease Activity Core Set Measures. To detect anxiety and depression status, HADS was administered to patients, who were also asked to fill in Short-Form 36 Items Health Survey (SF-36). For both HADS-A and -D subscales, patients were classified as at risk for scores ≥8 (borderline for scores 8-10, high risk if ≥11). Results were reported as mean±SD for continuous variables and as percentage for categorical variables. Intergroup comparisons were assessed by using Chi-square, t-test and ANOVA. Pearson coefficient was used to analyse the correlations between variables. P values <0.05 were considered significant.
Results: Fifty-three patients (72% female; mean age 64.8±12.0 years; mean disease duration 7.4±6.2 years) were enrolled. Twenty (37.7%) showed increased anxiety scores (mean 11.35, min. 8 – max. 17): 10 (50%) borderline and 10 (50%) high risk. Twenty (37.7%) had an increased depression score (mean 11.75, min. 8 – max. 19): 6 (30%) borderline and 14 (70%) high risk. If abnormal scores of both HADS-A and -D were found in 15 patients (28.3%), 17 patients (32.1%) were at high risk of at least one of the conditions. Sex, age, disease subset and duration did not seem to influence patients' emotional status. Apart from an association between Raynaud's Phenomenon occurrence and higher HADS-A scores (p=0.045), no significant correlations with organ involvements emerged. A strong association was found between fibromyalgia and higher HADS-A and -D scores (p=0.006 both). Patients with elevated anxiety levels presented significantly higher scores of Patient Global Assessment (PGA, p=0.002) and Health Assessment Questionnaire (HAQ, p=0.007) and significantly lower scores of Manual Muscle Testing (MMT8, p=0.004). HADS-D scores were similarly associated with PGA (p=0.001), HAQ (p<0.0001) and MMT8 (p=0.001). The presence of anxiety and depression was associated with lower scores in all SF-36 domains (all p≤0.016 for HADS-A and all p≤0.006 for HADS-D). Moreover, a correlation was found among SF-36 scores and PGA (all r <-0.516, p<0.01), HAQ (all r <-0.541, p<0.01) and MMT8 values (all r >0.299, p<0.05).
Conclusion: These results show nearly 40% of our cohort was at risk of anxiety or depression; almost 30% were at risk of developing both conditions together and quite one third was at high risk to develop at least one of them. As expected, these conditions were favoured from a concomitant fibromyalgia. Moreover, a compromised QoL and a functional limitation, as evaluated by PGA, HAQ and MMT8, in agreement with SF-36

domains, were significant risk factors for their occurrence. Therefore, our data, although preliminary, underline the need of a more comprehensive evaluation of IIMs patients, who should be screened for psychiatric comorbidities and, in case of high risk, referred to a specialist evaluation, in the perspective of improving their quality of care.

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POS0911 DIAGNOSTIC VALUE AND CLINICAL RELEVANCE OF MUSCLE BIOPSY IN PATIENTS WITH SUSPECTED MYOSITIS

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Background: Diagnosis of idiopathic inflammatory myopathies (IIM) represents a clinical challenge and muscle biopsy itself is regarded as the cornerstone for confirming diagnosis of IIM. However, the significance of muscle biopsy as diagnostical tool remains inconclusive

Objectives: To determine the diagnostic accuracy and clinical relevance of muscle biopsy in patients with suspected myositis.

Methods: In this retrospective cohort study, histopathological findings of muscle biopsy specimens of adult (≥ 18 years of age) patients with clinically suspected or differential diagnosis of myositis referred from all over Austria to the Medical University of Vienna through the period of 01.01.2007-31.10.2021 were analyzed. Following information were extracted from handwritten assignment sheets: referral department, suspected diagnosis (inflammatory and/or non-inflammatory myopathy), sampling location, demographic, clinical, laboratory and serologic data, and imaging results. Histological findings were grouped in: 1) inflammatory, 2) non-inflammatory (neurogenic, metabolic etc.), 3) inflammatory and non-inflammatory mixed, and 4) normal. Clinical information on start of immunosuppressive treatment after muscle biopsy could be partly retrieved form electronical medical records (EMR). Sensitivity, specificity, positive (PPV) and negative predictive values (NPV) of histological results were calculated using clinical diagnosis (defined as initiation of immunosuppressive therapy) as gold standard.

Results: 778 muscle biopsy specimens of 762 patients with suspected myositis (49.6% female, mean age of 56 years) were analyzed. Cohort descriptives are displayed in Table 1. Overall, 373/778 (47.9%) muscle biopsies revealed inflammatory features only or had mixed results with non-inflammatory characteristics. Out of 541 samples with suspected diagnosis of myositis, diagnosis was confirmed histologically in 300 (55.5%) cases; 46 (8.5%) specimens additionally showed co-features of non-inflammatory myopathy, whereas 221 (40.3%) were non-inflammatory at all and 15 (2.8%) were normal. Proportion of myositis was more pronounced, when CK was elevated at time of biopsy (Figure 1).

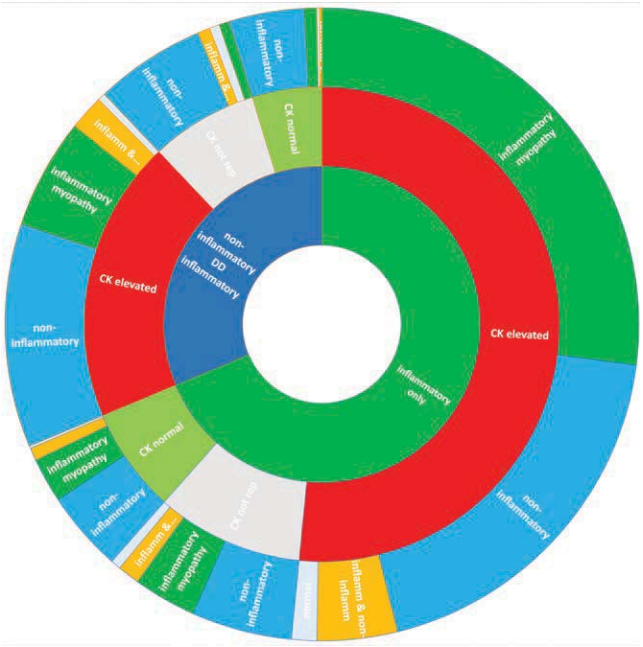

Figure 1. From suspicion to histological verification depending on CK-levels

Out of 237 samples with differential diagnosis of non-inflammatory myopathy in addition to myositis, 53 (22.4%) were histology. confirmed as inflammatory only and 20 (8.4%) showed mixed features. 153 (64.6%) biopsies were non-inflammatory only and 8 (3.4%) normal. Samples with no pathological features were observed in 24/778 (2.3%) of the cases, with 0.8% sampling error (no muscle tissue). Of 421/778 (54.1%) patients, clinical data could be extracted from EMR of which 209/421 (49.6%) had histological features of inflammation. In 287/421 (68%) cases, information regarding initiation of immunosuppressive treatment were available on EMR. 224/287 (78%) patients received immunosuppression (steroids and/or disease-modifying anti-rheumatic drug [DMARD]), thus fulfilled clinical diagnosis of myositis. In 155/224 (69.2%) cases, muscle biopsy confirmed histology. features of inflammation. Tests on diagnostic accuracy of muscle biopsy using initiation of any immunosuppressive treatment as gold standard were performed. The sensitivity of the test (biopsy) for diagnosing IIM was 71.4% with a specificity of 79.6%. PPV was high (92.8%), whereas NPV low (43.1%).

Conclusion: Less than 50% of biopsy samples with suspected diagnosis of myositis histologically revealed an inflammatory myopathy. The percentage increased when CK levels were elevated. Sensitivity and specificity of muscle biopsy was moderate, when using start of immunosuppressive therapy as gold standard for IIM diagnosis.

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Table 1: Patients characteristics.

No. of biopsy specimens (n)	778
No. of patients (n)	762
Gender (female) (n,%)	385 (49.6%)
Mean age in years (mean±SD)	56.08 ± 15.89
Referral department (n,%)	
• Neurology	392 (50.5%)
• Rheumatology	137 (17.7%)
• Dermatology	52 (6.7%)
Sampling location (n,%)	
• Proximal upper extremity	177 (22.8%)
• Proximal lower extremity	434 (55.8%)
Clinical symptoms:	
• Muscle weakness	51.6%
• Muscle pain	36.5%
• Atrophy	8.9%
• Skin affection	7.0%
Creatine kinase (CK) levels reported n(%)	641 (82.4%)
• CK elevated	86.9%
Manual Muscle Testing (MMT) reported n(%)	48 (6.2%)
• MMT score (maximum score of 80), mean±SD	65 ± 11

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POS0912 THE EFFECT OF A 24-WEEK TRAINING ON METABOLIC PARAMETERS OF SKELETAL MUSCLE CELLS DERIVED FROM PATIENTS WITH ESTABLISHED IDIOPATHIC INFLAMMATORY MYOPATHIES.

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Background: Persistent muscle weakness after reduction of inflammation and resistance to immunosuppressive therapy in some patients with idiopathic inflammatory myopathies (IIM) suggest that not only immune but also non-immune

mechanisms, such as mitochondrial abnormalities and metabolic disturbance, contribute to the pathogenesis of myositis. Exercise improves muscle function in IIM patients.

Objectives: To evaluate the effect of activities-of-daily-living, resistance and stability training on metabolic parameters of primary tissue culture myotubes established from muscle biopsies obtained from patients with established IIM.

Methods: Seven patients with established IIM underwent a 24-week supervised training focused on activities of daily living, muscle-strengthening and stability. Muscle biopsy was performed before and after the 24-week program in patients, and in healthy controls (n=9). Isolated skeletal muscle cells were grown and differentiated into myotubes for 6 days. After differentiation, the myotubes were cultured for another 24 hours in fresh medium, and then the conditioned media were collected, and the cells were harvested in TRIzol. A relative number of mitochondria was quantified by the ratio between mitochondrial gene (NADH dehydrogenase subunit 1) and reference nuclear gene (lipoprotein lipase) and determined by qPCR. Glucose, pyruvate, lactate, citrate, and fumarate were assessed in a conditioned medium using the comprehensive two-dimensional gas chromatography coupled to time of flight mass spectrometer.

Results: Patients significantly improved their muscle strength and endurance during the 24-week training [1]. There was no difference in the relative number of mitochondria in muscle tissue and myotubes between IIM patients and controls. A significant increase in the number of muscle tissue mitochondria was found in IIM patients after 24 weeks of training ($p = 0.004$), on average twofold. A similar effect was observed in cultured myotubes, with at least 4 of 7 IIM patients showing a twofold increase in mitochondria number. Compared with myotubes from HC, myotubes derived from IIM patients consumed non-significantly more glucose and pyruvate from the culture medium; however, their glucose and pyruvate utilization were significantly reduced as a result of the 24-week training ($p = 0.016$ and $p = 0.030$, respectively). Skeletal muscle cells from IIM patients before training intervention did not differ from HC cells in the amount of released lactate; however, the lactate concentration in the conditioned medium from myotubes obtained from patients after the 24-week training was significantly lower ($p = 0.016$). When measuring citrate cycle products released into the culture medium, no difference in citrate and fumarate secretion was observed between myotubes of myositis patients and myotubes of healthy controls. In contrast, their release was significantly ($p < 0.05$) lower in myotubes from IIM patients after 24 weeks of training compared to muscle cells isolated prior to intervention.

Conclusion: In conclusion, 24 weeks of rehabilitation training in patients with IIM significantly increases the number of mitochondria in muscle tissue. Lower release of lactate and citrate cycle intermediates (citrate and fumarate) by myotubes obtained from patients after training intervention indicates an increase in mitochondrial functional capacity and confirms a positive response to exercise in muscles previously affected by the inflammatory process in IIM.

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POS0913 INCREASED HEALTH CARE UTILIZATION IN SYSTEMIC SCLEROSIS PATIENTS WHO HAVE DIGITAL ULCERS

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Background: Systemic sclerosis is a multi-system autoimmune disease characterized by fibrosis of the skin and internal organs, and vasculopathy which manifests as pulmonary arterial hypertension and digital ulcers. Digital ulcers are debilitating and painful lesions most commonly present in the digit tips or extensor surfaces of the hands leading to significant morbidity and decreased quality of life. SSc patients with digital ulcers may require increased support and therefore may have greater healthcare resource utilization compared to those patients without digital ulcers.

Objectives: We assessed the impact of DUs on resource utilization including hospitalizations, outpatient visits and procedures within a large SSc Canadian registry.

Methods: A cohort of patients with SSc and digitals ulcers was derived from the Canadian Scleroderma Research Group registry and matched to controls individually based on sex, age (±3 years), SSc subtype, and disease duration (±2 years). Eligible patients met the 2013 ACR/EULAR criteria (confirmed by an experienced rheumatologist), were 18 years of age, had completed the Resource Utilization Questionnaire (RUQ), and had active digital ulcers at two consecutive annual visits (baseline study visit and at 1st year). The Medgser Disease Severity Scale was used to assess ulcer disease severity. Unadjusted and adjusted regression analyses compared the association between DUs and resource utilization.

Results: RUQs in 104 SSc patients with active DUs at two consecutive annual visits were compared with 104 patients without DUs matched 1:1 for age, sex, disease subtype and duration. Over one year, DUs were associated with a higher number of tests ($p<0.05$) and visits to health professionals, especially to a rheumatologist ($p<0.0001$) and internist ($p=0.003$), a greater need for an accompanying person ($p<0.05$) and aids purchased/received ($p<0.05$). Having DUs was associated with more severe disease, even after excluding the peripheral vascular domain from a total DSS (9.7±4.5 vs 5.6±2.7, $p<0.0001$). After adjustment for disease severity in other organs, the presence of DUs remained a significant predictor of more frequent physician visits and more tests (all<0.05) by linear regression analysis.

Conclusion: SSc patients with DUs utilized significantly more healthcare resources per annum even after adjustment for disease severity in other organ systems.

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POS0914 LATE SKIN FIBROSIS IN SYSTEMIC SCLEROSIS: A STUDY FROM THE EUSTAR COHORT

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Background: Skin fibrosis is a cardinal feature of systemic sclerosis (SSc) and associated with significant disability. The early trajectory of skin fibrosis provides

insights into the course of the disease including mortality; however, little is known about late skin fibrosis in SSc.

Objectives: The aims of our study were to ascertain the prevalence and characteristics of late skin fibrosis in SSc.

Methods: We developed and tested three conceptual scenarios of late (>5 years after 1st non-RP sign or symptom) skin fibrosis (Figure 1):

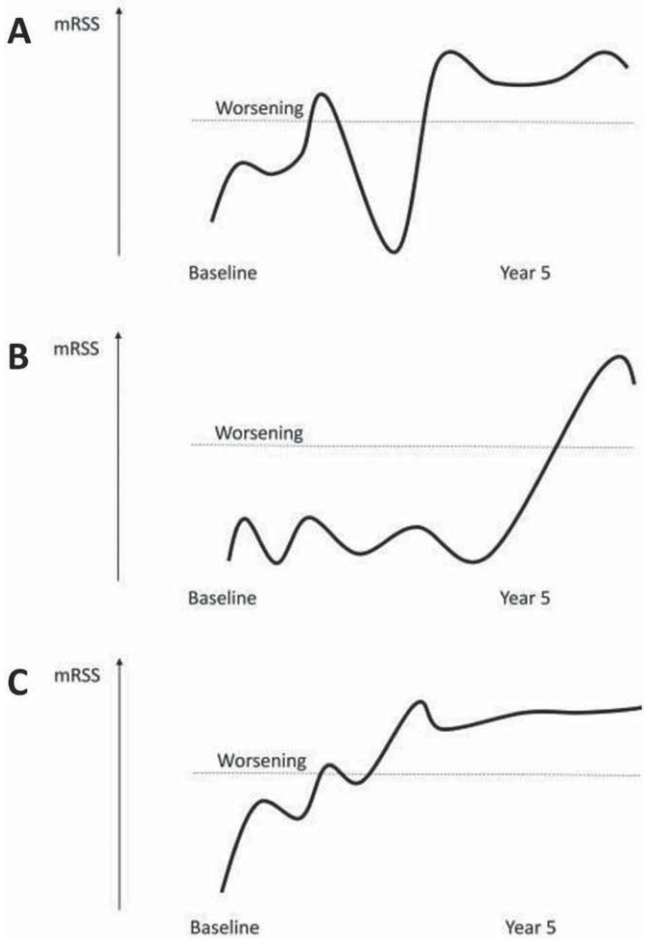

Figure 1. Conceptual models/scenarios of late skin fibrosis in SSc. A: worsening and then improvement (>3 mRSS) during the first 5 years, and then worsened again after 5 years. B: worsening for the first time after 5 years. C: worsening in the first 5 years and stayed high after 5 years (i.e., failure to improve).

A. Worsening and then improvement (>3 mRSS) during the first 5 years, and then worsened again after 5 years.
B. Worsening for the first time after 5 years.
C. Worsening in the first 5 years and stayed high after 5 years (i.e., failure to improve).
We defined skin worsening as modified Rodnan skin score (mRSS) ≥ 5 units or ≥ 25%. Using strict inclusion criteria including complete mRSS, we identified 1,043 (out of 19,115) patients within the EUSTAR database for our analysis. We further restricted analysis within 887 (out of 1,043) patients who had limited (lcSSc) or diffuse cutaneous SSc (dcSSc) at baseline.

Results: One-fifth of patients among the whole cohort (n=208/1043, 19.9%) including in patients with lcSSc or dcSSc at baseline (n=193/887, 21.8%) developed late skin fibrosis. This was largely due to new skin worsening or failure to improve. Patients with lower baseline mRSS and lcSSc were more likely to develop late skin fibrosis. Anti-Scl-70 antibodies (Table 1) were associated with progression from baseline lcSSc to dcSSc, and anticentromere antibodies were protective.

Conclusion: Late skin fibrosis affects approximately 20% of SSc patients >5 years after onset of disease. We have identified different patterns relevant to clinical practice and trial design. Late skin fibrosis is usually due to new worsening or failure of skin to improve. Progression from baseline limited to diffuse cutaneous SSc was associated with anti-Scl-70 antibodies, and anticentromere antibodies were protective. Late skin fibrosis is a neglected manifestation of SSc and warrants further investigation including to determine clinical outcomes and optimal therapeutic strategy.

Acknowledgements: On behalf of EUSTAR collaborators.

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POS0915

MYOSITIS-SPECIFIC AND ASSOCIETED ANTIBODIES, ESPECIALLY ANTI-ARS ANTIBODIES AND ANTI-RO52 ANTIBODY MAY PREDICT THE CHARACTERISTICS AND FIBROSING PROGRESS OF INTERSTITIAL LUNG DISEASE WITH DERMATOMYOSITIS / POLYMYOSITIS

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Background: Myositis-associated antibodies (MAA) and myositis-specific antibodies (MSA) have been associated with clinical manifestations of dermatomyositis and polyneuropathy, including interstitial lung disease (ILD), myopathy, malignancy, arthritis, and skin rashes. Among them, anti-ARS and anti-MDA5 antibodies are strongly associated with complications of ILD that are associated with life expectancy. It has been reported that anti-Ro52 antibody affects severity of myositis and ILD. (1) Based on these findings, it is possible that autoantibodies possessing features of ILD associated with dermatomyositis and polymyositis may be predictive.

Table 1. Impact of autoantibody status on progression from baseline limited to diffuse cutaneous SSc (dcSSc).

		Skin worsening after 5 years (Scenario B) (n=70)			Skin worsening within 5 years and failed to improve after 5-year window (Scenario C) (n=61)		
		Progressed to dcSSc (n=23)	*Not progressed to dcSSc (n=47)*	*P-value*	*Progressed to dcSSc (n=37)*	*Not progressed to dcSSc (n=24)*	*P-value*
Anticentromere	***+ve***	2/22 (9.1%)	19/42 (45.2%)	0.0034	6/34 (17.6%)	14/21 (66.7%)	0.0002
	-ve	20/22 (90.9%)	23/42 (54.8%)		28/34 (82.4%)	7/21 (33.3%)	
Anti-Scl-70	***+ve***	15/23 (65.2%)	14/44 (31.8%)	0.0088	22/36 (61.1%)	8/23 (34.8%)	0.0485
	-ve	8/23 (34.8%)	30/44 (68.2%)		14/36 (38.9%)	15/23 (65.2%)	
Anti-RNA-Polymerase-III	***+ve***	0/12 (0.0%)	1/22 (4.5%)	1.0000	0/6 (0.0%)	0/14 (0.0%)	--
	-ve	12/12 (100%)	21/22 (95.5%)		6/6 (100%)	14/14 (100%)	

Objectives: The purpose of this study is to clarify the relationship between MSA/MAA and clinical features of ILD complicated by dermatomyositis and polymyositis.
Methods: We retrospectively analyzed IIMs patients diagnosed according to Peter & Bohan's diagnostic criteria in our hospital from 2011 to 2018. The presence of 14 MSA / MAA (Jo1, PL12, PL7, EJ, OJ, KS, Mi2, MDA5, TIF1γ, SRP, PM-Scl70, 100, Ku, Ro52) was measured using ELISA (MESACUP, MBL, Japan) and line blot (EUROLINE myositis profile3, EUROimmun, Germany). Clinical characteristics, including HRCT imaging findings, were extracted from medical records. HRCT imaging findings were analyzed by multiple radiologists. The association between the extracted clinical features and the MSA / MAA held was analyzed.
Results: Seventy-eight cases of IIM were included in the analysis. The frequency of ILD complications was 53/78 (68%), and 60% of ILD complications were ARS antibody positive. The complication rate of ILD in MDA5- and ARS-positive cases was 100% (3/3 cases) and 94% (32/34 cases), respectively. These MDA5- and ARS-positive patients with ILD had rapidly progressive ILD. One of the three MDA5 antibody-positive RPILD cases died, but none of the four ARS antibody-positive RPILD cases died. However, in patients with multiple MSA or MAA including ARS, three case had rapidly progressive ILD, and none died. n the analysis of the presence of Ro52 antibody, it was detected in 46% (36 cases) of all cases, but in 74% of anti-ARS antibody positive cases.
In the analysis of ILD patterns by radiologists using HRCT, fibrosing NSIP (fNSIP), fibrosing OP (fOP), and UIP were the most frequent in that order. analysis of the association between ILD patterns and MSA / MAA showed that there was no MSA / MAA associated with each ILD pattern. No MSA/MAA was found to be associated with each ILD pattern. ARS antibody-associated ILD, the most common type of ILD, had a worse prognosis than other MSA / MAA positive ILD. Death due to ILD was observed in 5 patients (PL7: 3cases, PL12: 1case, PM-Scl75: 1case). Oxygen was required for ILD progression in 3 Jo1-positive patients, 1 PL7-positive patients, and 1 PL12-positive patient, respectively. The frequency of UIP, which is considered to have a poor prognosis in other rheumatic diseases, was higher in patients with anti-ARS and anti-Ro52 antibodies.
Conclusion: The prognosis of anti-ARS antibody-positive ILD associated with dermatomyositis and polymyositis was associated with fibrosis by analysis of HRCT patterns, and the prognosis was confirmed to be poor.In addition, the UIP pattern, which is strongly associated with fibrosis, was found to be associated with anti-Ro52 antibody. In the treatment of ILD, which is strongly associated with the prognosis of dermatomyositis and polymyositis, it may be necessary to consider antifibrotic treatment for patients with anti-ARS antibody and anti-Ro52 antibody positivity.
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POS0916 A 10-YEAR JOURNEY OF CARING FOR PATIENTS WITH SYSTEMIC SCLEROSIS: FOLLOW-UP DATA ON DISEASE DURATION OF THE LEIDEN CCISS COHORT.

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Background: Combined Care in Systemic Sclerosis (CCISS) is a prospective cohort of patients referred to Leiden University Medical Center for Raynaud's Phenomenon (RP), a suspicion of systemic sclerosis (SSc) or a connective tissue disease. This cohort is characterized by its standardized and extensive annual follow-up. Since initiation of the cohort in 2009, diagnostic criteria for SSc have been updated leading to a higher sensitivity for early SSc (ACR 2013 criteria). A recent Dutch study showed that there is a gap to time of diagnosis between men and women, despite of overall increase of SSc awareness (PMID: 31539063).
Objectives: To determine whether 1. time between first disease symptoms and diagnosis has changed over time, and 2. disease characteristics of SSc at first presentation in an expert clinic have changed over time for the total cohort, and between male and female patients.
Methods: Patients included in the CCISS cohort undergo annual evaluation and clinical, laboratory, and imaging variables are systematically recorded. For this study, patients fulfilling the ACR/EULAR 2013 SSc criteria were included, and categorized into three groups based on the cohort entrance year: 1) 2010 – 2013, 2) 2014 – 2017, and 3) 2018 – 2021. SSc patients with a baseline visit in 2009 (n=65) were excluded as these patients were often not newly referred. Disease duration was defined by months since first RP, since first non-RP symptom and months between first date of diagnosis by a physician and first non-RP symptom. Disease characteristics included presence of interstitial lung disease (ILD), pulmonary arterial hypertension, digital ulcers (DU), diffuse cutaneous SSc, anti-topoisomerase and anticentromere antibodies. At baseline, disease duration and disease characteristics were compared between the three groups using appropriate tests. In addition, disease duration was compared between males and females in the three groups.
Results: In total, 643 SSc patients were included of whom 229 (36%) had their baseline visit from 2010 until 2013, 207 (32%) from 2014 until 2017, and 207 (32%) from 2018 until 2021. The proportion of female patients was significantly higher in the 2010 – 2013 group compared to the 2014 – 2017 and 2018 – 2021 group (Table 1). Over time, disease duration defined by RP duration and non-RP duration decreased as well as time between diagnosis and first non-RP symptom (Table 1). The proportion of patients presenting with ILD and DU was highest in the first group (Table 1).

Table 1.

	2010 - 2013 N=229	2014- 2017 N=207	2018 – 2021 N=207	P-value
BASELINE				
Age, mean (SD)	53 (15)	57 (14)	55 (14)	0.003
Female, %	86	76	75	0.010
RP duration, months (IQR)	122 (46 – 240)	93 (20 – 202)	67 (20 – 210)	0.003
Non RP duration, months (IQR)	43 (16 – 227)	20 (5 – 112)	17 (6 – 54)	<0.001
Diagnosis duration, months (IQR)	116 (80 - 177)	65 (45 – 105)	25 (5 – 45)	<0.001
ΔRP and Non-RP, months (IQR)	24 (0 – 99)	18 (0 – 118)	22 (0 – 120)	0.337
Anti-centromere antibodies, %	38	43	49	0.092
Anti-topoisomerase antibodies, %	24	24	18	0.259
Diffuse cutaneous SSc, %	19	23	16	0.073
Interstitial lung disease, %	43	31	31	<0.001
Pulmonary arterial hypertension, %	3	2	4	0.746
Digital ulcers, %	20	13	11	0.041

In both male and female SSc patients, disease duration and time between diagnosis and first non-RP decreased over time with a longer time in females for all durations which was significantly different for time between first RP and non-RP in 2014-2017 and 2018-2021 (Figure 1). For the 2018 – 2021 group, duration since diagnosis for female was 26 (4 - 46) and male 17 months (7 – 39; p=0.355), and time between RP and non-RP for female 24 (0 - 168) and male 12 months (0 – 48; p=0.029).

Figure 1.

Conclusion: Over time, we observe a decrease in disease duration and in SSc patients presenting with ILD or DU at cohort entrance. Our results indicate increased awareness of early SSc and identification of SSc patients before severe complications have occurred. At the same time our results show the urge for specific attention to improve timely diagnosis in female SSc patients.
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POS0917 TRANSTHORACIC LUNG SONOGRAPHY (LUS) – USEFUL SURVEILLANCE TOOL IN SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE?

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Background: The Interstitial lung disease (ILD) represent a major cause of mortality in Systemic sclerosis (SSc). Validated methods for screening and therapy monitoring of SSc-ILD are needed. In the recent literatur, the transthoracic lung sonography (LUS) emerges as a reliable tool for the early detection of lung alterations. It was recently reported that SSc-ILD-patients have thicker artefacts reflecting the pleuraline compared with SSc-patients without ILD, but it still remains unknown if the thickness of the pleuraline changes with a proper therapy response.

Objectives: The aim of the study was to compare the thickness of the pleuraline of SSc-ILD-patients without biological Disease Modifying Anti-Rheumatic Drugs (bDMARDS) with those successfully treated with bDMARDs in order to establish if LUS can be a reliable surveillance tool in SSc-ILD. Additionally, since our Grazer-Schema (Mycofenolat mofetil (MMF)+ rituximab (RTX) 500 mg i.v. in week 0 and 2 every 3 months) is succesfully used in our clinic since more than 10 years in patients nonresponding to methotrexate (MTX) or cyclophosphamide, we report 10 years follow-up data of 5 Patients before and after receiving that schema.
Methods: 29 prospectively enrolled SSc-patients were assessed according to the European League Against Rheumatism Scleroderma Trial and Research standards. Written informed consent was obtained from all patients and the study was approved by the Ethics Committee of Graz. Validated clinical scores, such as the scleroderma disease activity (SScAS) and the scleroderma disease severity scale (SScSS) were assessed. The thickness of the pleuraline was detected with LUS. The presence of ILD was assessed by high-resolution computed tomography. Twenty-five SSc-patients enrolled between 2008 and 2009, who underwent LUS with the same technical instruments and some of the same operators, were taken as a control group since they were untreated yet or were not assuming bDMARDs(1).
Results: Of the 29 SSc-patients (27 females/2 males) enrolled between 2019 and 2020, seventeen patients had radiographic signs of ILD (SSc-ILD+/2019-20, n=17). Until the LUS was performed, all SSc-ILD+/2019-20 showed a good clinical response to the therapy with RTX in combination with MMF. Of the 25 SSc-patients enrolled in our previous study, (n=25; 23 females/ 2 males), twelve of these patients had radiographic signs of ILD (SScILD+/2009-10, n=12); 7 were under MTX or Cyclosporin and 5 were untreated. Additionally, data collected from 5 SSc-ILD+/2009-2010 at baseline were analysed in a 10- years- follow up. As expected, SSc-ILD+ patients had a thicker pleuraline than SSc-ILD- patients. The pleura was significantly thinner in patients under MMF und RTX compared to the pleuraline of patients without bDMARDs (1,8 mm ± 0,7 Vs 0,95 ± 0,31; p < 0,00). Interestingly those patients reported less frequently dry cough or dyspnoea, showing that the lower pleura thickness could be associated with a better clinical outcome. In a 10 Year follow-up after continued treatment with MMF and RTX, a significant reduction of the thickness of the pleura could be found (Mean 0,68 ± 0,2 VS 1,5 ± 0,4; p < 0,00). Interestingly, such significant improvement could be found in all of these 5 patients receiving our Grazer Schema. Remarkably, the pleuraline-thickness was comparable to the thickness of the pleura of SSc-ILD-patients. This finding shows that the increase in thickness of the pleuraline can be totally reversible under treatment.
Conclusion: Due to the encouraging validity, reliability and simplicity of LUS, it has been increasingly considered as an excellent screening tool for SSc-ILD. Its sensitivity to reveal parenchyma and pleura changes over time in treated patients, make it also a helpful and safe methodology to follow up SSc-ILD patients.
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POS0918 TARGET-CONTROLLED INFUSION (TCI) WITH PROPOFOL AND REMIFENTANIL FOR PROCEDURAL SEDATION AND ANALGESIA (PSA) IN PATIENTS WITH SYSTEMIC SCLEROSIS (SSC) UNDERGOING AUTOLOGOUS FAT GRAFTING PROCEDURES

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Background: Systemic sclerosis-SSc is an autoimmune disease characterized by vascular alterations and fibrosis. Difficult airway management, peripheral venous access and systemic comorbidities are often concomitant. Therefore, performing general anesthesia or moderate to deep sedation in these patients can be challenging. A high psychiatric burden is also common. These conditions, in association with a history of chronic pain, make even the local anesthesia procedure less effective than usual. Oral/digital autologous fat grafting approaches may improve aesthetic/functional aspects in SSc but the surgical procedure itself is painful and requires proper sedation. Target-Controlled Infusion with propofol (hypnotic) and remifentanil (opioid) is a well consolidated anesthesia technique and could be the best Procedure Sedation and Analgesia strategy to tolerate these interventions.
Objectives: Developing a new Procedural Sedation and Analgesia-PSA protocol to obtain moderate to deep sedation in Day Surgery environment to allow complete analgesia, amnesia and safe discharge in SSc patients undergoing autologous fat grafting procedures.
Methods: Eighteen-18 SSc patients referring to the Scleroderma Unit of our University Hospital were recruited for oral/digital autologous fat grafting procedures between July and December 2021. A proper anaesthesiology schedule was assessed by an expert anesthesiologist of the team. After informed consent acquisition, patients were monitored with ECG/SpO2/Non Invasive Blood Pressure-NIBP. A peripheral intra-venous line with an ultrasound probe was placed if needed and TCI was started. Patients were maintained in spontaneous breathing and supplementary oxygen (4lt/min) with a rhinopharyngeal cannula. The use of TCI pumps for the delivery of propofol and remifentanil allowed trained anesthesiologists to control and adjust the level of sedation and analgesia. The synergy between both propofol and remifentanil is well known, main risk for such technique is to oversedate patients resulting in respiratory depression and hypotension. Bispectral Index-BIS was used to monitor sedation level starting from 60-80, then tailoring the infusion according to surgical needs. TCI was stopped at the end of surgery. Vital parameters were registered every 5 minutes and potential complications were monitored (hypotension=PAS<30% of basal line, hypoxia=SpO2<92%). Paracetamol 1g/ketorolac 15mg were administered for postoperative analgesia. A simplified satisfaction questionnaire based on LPPSq was also administered before discharge.
Results: All subjects have successfully undergone surgery and no hospitalization after the procedures was needed. A peripheral blood desaturation (SpO2<90%) was registered as main complication in 4 subjects, promptly relieved through nasal cannula replacement. One patient registered transient hypotension (decrease in systolic blood pressure>30% below baseline) without vasoactive drugs need. Mean time to recovery of consciousness was 6.3 minutes (range 3-11). Two patients experienced transient pain and nausea, 1 itchiness, and 1 subjective difficulties in breathing/talking some minutes after the surgery with spontaneous resolution. All patients gave their consent to perform the same approach in the future.
Conclusion: TCI of propofol and remifentanil might be successfully used to ensure procedural sedation and analgesia in SSc surgical settings in presence of a skilled anesthesiologist. Further data are required to assess the incidence of possible major complications and patients' satisfaction.
Disclosure of Interests: None declared
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POS0919 MOLECULAR AND BIOLOGICAL PATHWAYS OF BREAST CANCER IN PATIENTS WITH SYSTEMIC SCLEROSIS: IMMUNOHISTOCHEMICAL INVESTIGATIONS FROM THE SCLERO-BREAST STUDY

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Background: Systemic Sclerosis (SSc) is a life-threatening connective tissue disease characterized by endothelial dysfunction, autoimmune abnormalities and aberrant fibrosis. Several reports showed an increased risk of cancer in SSc compared to general population, including breast cancer (BC). The relationship between BC and SSc has long been discussed with contradictory results. In our recent Sclero-Breast study we analyzed clinical-pathological features of BC in SSc; we finally observed the development of BC with early stages and good prognosis among these patients.
Objectives: The aim of this project was to explore the immunohistochemical (IHC) expression of potential biomarkers involved in the molecular pathways at the basis of SSc and BC etiophatogenesis as update analysis from the Sclero-Breast study.
Methods: Our observational multicenter retrospective study, performed at Modena University Hospital and Reggio Emilia Hospital in northern Italy, enrolled 33 SSc women with a personal history of BC between January 2017 and December 2019. Clinical and pathological characteristics of BC and SSc were collected. For 22 patients, BC tissues were available and IHC analysis was performed using specific antibodies to evaluate biomarkers and pathways potentially involved. The antibodies used included: PI3K/mTOR/TGFβ/PDGFRα/PDGFRβ/VEGF/EGFR/IL-6/CTLA-4/PDL1. We also reported TILs percentage (stromal tumor-infiltrating

lymphocytes) of each sample. The following scores were assigned for general IHC analysis: (-) negative, (1+) positive tumor cells <20%, (2+) positive tumor cells 20-50%, (3+) positive tumor cells >50%. For PDL1 we considered a positivity in case of PD-L1 expression ≥1% in infiltrating inflammatory cells. For TILs quantification we applied the score: 0 (negative), ≤ 50% (low-median expression), >50% (high expression).

Results: The first IHC analysis was performed on the samples of invasive BC patients (20 pts) and showed a prevalence of high PI3K expression (score of 3+ in 55% of cases) with mTOR overexpression in 45%. A PDL1 positivity was detected in 30%, with high TILs expression in 30%. Biopsies from the 2 pts with ductal carcinoma in situ were characterized by a negativity of almost all parameters, except for a medium-high TILs expression reported (40%/90% respectively). See Figure 1. IHC analysis was also performed according to BC subtypes. The group of HR+/HER2 negative showed high PI3K expression (score 3+) in most of cases (59%) with mTOR overexpression in 50%. CTLA-4 and PDL1 were positive in 25%, with high TILs expression in 25%. HER2 positive patients showed a high PI3K positivity in 50% of cases with mTOR positivity (score 3+) in 25% and high TGFβ expression (score 3+) in 25%. PDL1 was positive in 50% with high TILs expression in 25%. In Triple Negative group, PI3K overexpression was found in 75% of pts with half of cases represented by mTOR score 3+. PDL1 was positive in 50% with high TILs representation (80% of total cell count) in 50% of pts.

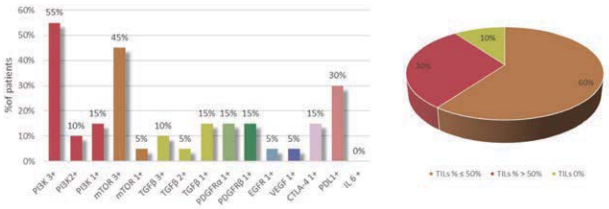

Figure 1. IHC analysis and TILs% expression in histological samples of SSc patients with invasive BC.

Conclusion: According to our results, SSc patients with BC showed high positivity for PDL1 and high TILs representations in all subtypes. Furthermore, the high expression of PI3K, did not always correlate with mTOR overexpression. Further investigations on larger numbers are needed; however, these aspects seem to confirm that SSc subjects might develop BC at good prognosis, suggesting again a de-escalation strategy of cancer therapies. Finally, the possibility to personalize oncological targeted treatments in this subset of fragile patients could be promising.

Disclosure of Interests: None declared

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POS0920 THE EFFECT OF COVID-19 PANDEMIC ON IDIOPATHIC INFLAMMATORY MYOSITIS PATIENTS – A SINGLE CENTRE'S EXPERIENCES

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Background: Pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-Cov2/COVID19) determines the life of clinicians and patients since 2 years. Limited information is available on the nature, prognosis, and complications of SARS-Cov2 virus infection in patients with idiopathic inflammatory myopathies (IIM). There are also few data on triggered humoral response, side effects and disease course after COVID19 infection or vaccination in IIM.

Objectives: The primary goals of the current research were to assess frequency and outcome of COVID-19 disease and to determine the vaccination rate and effect in our IIM cohort. Secondary objectives were to search for risk factors of infection, predictive factors of hospitalization and to assess incidence of vaccination adverse events, complications and post vaccination breakthrough infections.

Methods: We retrospectively identified the confirmed COVID19 positive patients and assessed the symptoms, disease course and outcome on 01/06/2021 then patients were prospectively followed. Incidence and complications of vaccination were determined by questionnaires. Anti-SARS-CoV-2 S enzyme electrochemiluminescent immunoassay has been used to assess seroconversion, which measures total antibody (IgM and IgG) to the SARS-CoV2 S protein and SARS-CoV2 N protein. Disease activity was determined by physician global activity.

Results: A total of 176 patients were screened and 101 participated in the study. By 01/06/2021, the COVID infection rate was 34,7% (mean age: 49.54 years, 72.72% women), which was significantly higher than the national prevalence at that time (8.2%). A third of these infections occurred asymptomatically or mild but 20% of the infected patients were hospitalized, one patient died. Longer disease duration (8.67 vs. 17.87 years; p=0.003) and higher incidence of anti-Jo-1 antibody (57% vs. 10% p=0.018) were significantly associated with hospitalization. All of COVID infected patients became seropositive regardless of immunosuppressive therapy or symptoms severity. 53,4 % of the patients received anti-COVID19 vaccine, 75,9 % choose the mRNA type. The titer of antibodies against the spike protein induced by vaccines showed high variance, but 72,3% of patients became seropositive after vaccination. Higher antibody titer against spike protein was detected after Pfizer-BioNTech vaccination compared to others (177,1 U / ml vs. 81.1 U / ml; p <001). Patients receiving steroid therapy had decreased post-vaccination antibody response compared to those without steroid treatment (94,03 U/ml vs. 165.6 U/ml; p = 0.008). With the follow-up of vaccinated patients, we did not found short term vaccine related major adverse events, but long term data revealed 7,4 % post vaccination disease relapse. Breakthrough infection was detected in 9.25 % of the vaccinated patients, one cancer associated patient without post vaccination seroconversion died due to COVID pneumonia. All the fatal COVID infections occurred in patients with seronegativity to anti- SARS-CoV2 S protein.

Conclusion: Based on our results, myositis may be associated with an increased risk of infection with SARS-CoV-2. Independent risk factor for hospitalization is anti-Jo1 positivity and longer disease duration. Anti-SARS-CoV2 vaccines are safe, tolerable and strongly recommended for IIM population, but further investigation is required to assess clinical significance of post-vaccination disease flare.

Disclosure of Interests: None declared

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POS0921 DIGITAL GANGRENE IN SYSTEMIC SCLEROSIS: AUTOLOGOUS FAT GRAFTING AND BONE SHAVING TO AVOID AMPUTATION

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Background: Systemic Sclerosis (SSc) is a connective tissue disease characterized by microvascular dysfunction, abnormal fibroblast activation and antibodies production, with cutaneous and visceral involvement. Hand-related manifestations include sclerosis, loss of elasticity, sclerodactyly, painful digital ulcers, atrophy, and gangrene. Autologous fat grafting is based on the implantation of adipose-derived stem cell (ADSCs) which have demonstrated to have pro-angiogenic, anti-inflammatory, regenerative, and immunosuppressive properties. This technique, combined with bone shaving, is believed to be effective in avoiding finger amputation in SSc-patients affected by digital gangrene.

Objectives: Evaluate our experience with the use of autologous fat grafting and bone shaving for the treatment of digital necrosis in patients affected by SSc.

Methods: According to our schedule, we treated 7 female SSc patients with digital gangrene and exposed bone at the fingertips, enrolled in our University Hospital from March 2018 to January 2020. Digital gangrene was treated by a combination of bone shaving and autologous fat grafting in order to avoid amputation. During the bone shaving, necrotic tissue was removed until bone bleeding was obtained. This procedure could be repeated by trained rheumatologists every 2 weeks in our Clinic. The aim of this repeated debridement was to promote the progression of the granulation tissue inside the dead tissue of the finger. Autologous fat grafting consists of a surgical procedure of ADSCs implantation at the base of the finger. It is performed in order to empower the neurovascular bundle and improve tissue healing. This treatment could be performed every 3 months by trained plastic surgeons. The combination of these two techniques allows the maximum finger length preservation.

Results: Complete healing of all fingers was achieved in 6-12 months by performing bone shaving every 2 weeks and 2 treatments of autologous fat grafting. Results have proved to be long-lasting. At 1-year follow-up, patients did not present any recurrence. Every procedure was performed under local anaesthesia and appropriate analgesic therapy. A high degree of compliance and satisfaction of all patients was noted.

Conclusion: Finger amputation in Systemic Sclerosis should be avoided. This traumatic surgical procedure is responsible for microvascular damages worsening SSc-related vasculopathy. Stump ulcers often occurs and wound healing usually takes place by secondary intention. In our experience, the combination of bone shaving and autologous fat grafting has proven to be effective and safe in preserving the maximum amount of viable tissue and obtaining a long-lasting result in treated SSc patients.

Disclosure of Interests: None declared

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POS0922

RECOMBINANT HUMAN HYALURONIDASE-FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN FOR IDIOPATHIC INFLAMMATORY MYOSITIS: A MULTICENTER OBSERVATIONAL STUDY

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Background: The spectrum of idiopathic inflammatory myositis (IIM) includes a heterogeneous group of diseases characterized by chronic inflammation of skeletal muscle, often associated with skin, joints, lungs, esophageal, gastrointestinal and cardiac involvement. Conventional treatment for IIM is based on glucocorticoids and immunosuppressants. Moreover, intravenous immunoglobulin (IVIg) has emerged as a promising steroid- and DMARD-sparing treatment for myositis [1]. However, the long-term use of IVIg is complicated by the fact that the intravenous route requires in-hospital drug administration, which not only influences patients' quality of life, but is also associated with an increased risk of systemic adverse effects, difficulties in venous access over time, and high costs [2]. On these bases, administration of subcutaneous Ig (SCIg) by a programmable pump has been considered as a possible alternative to IVIg. Recombinant human hyaluronidase-facilitated (hf)-SCIg is currently approved for the use in patients with primary immunodeficiency disorders, while its efficacy and safety in myositis disorders is limited [3].
Objectives: This multicenter retrospective observational study is sought to evaluate the effectiveness and safety of recombinant human hf-SCIg in patients with IIM treated at different referral centers.
Methods: A multicenter, retrospective, cohort study was conducted on adult patients diagnosed with IIM according to the EULAR/ACR classification criteria [4] treated with recombinant human hf-SCIg according to routine clinical practice. The effectiveness of this treatment was assessed in terms of variations in the Medical Research Council (MRC) score, creatine kinase values, inflammatory parameters, and daily prednisolone dosage. Safety data were also collected.
Results: Twenty-three patients with IIM treated with hf-SCIg were included (16/23 females, 70%; median age at diagnosis of 61 years (IQR 43-65)).
In most patients (22/23, 96%), IIM had been initially treated with high-dose corticosteroids (+/- synthetic or biologic DMARDs), and 20/23 patients (87%) had received previous IVIg treatment (in 12 for remission induction and in 8 for maintenance).
Hf-SCIg were introduced after a median time of 2 years (1-4) from the diagnosis of IIM, mostly for remission maintenance (18/23). Hf-SCIg was started in combination with oral corticosteroids in 19/23 [83%, at a median dose of 5 mg/day (4-12.5)] and/or with traditional or biologic DMARDs (18/23, 78%).
At time of hf-SCIg introduction, the median MRC score was 4 (3-4) and the median creatine kinase level was of 134 U/L (44-243). After 6 months of treatment, the median MRC score was 4 (3-5); no patient discontinued hf-SCIg, and only one experience a mild adverse event.
Conclusion: Hf-SCIg seems effective to maintain remission in a high proportion of IIM patients, while showing a good safety profile in the first 6 months of treatment.
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Table 1. Effectiveness and safety of hf-ScIG treatment in a cohort of patients with IIM

	hf-Sclg beginning	3 months	6 months
N patients with available follow-up data	23	20 *	19*
MRC score §	4 (3-4)	4 (4-5)	4 (3-5)
Creatine kinase, U/L §	134 (44-243)	118 (77-308)	130 (84-222)
ESR, mm/h §	21 (15-28)	30 (25-43)	31 (23-39)
CRP, mg/dl §	0.2 (0.1-0.5)	0.3 (0.1-0.5)	0.3 (0.1-0.3)
Prednisolone dosage, mg/day §	5 (4-12.5)	7.5 (5-10)	5 (5-7.5)
Adverse events	-	NA	1 **

*none discontinued**One infusion site reaction§ median value (IQR)CRP=C reactive protein; ESR=erythrocyte sedimentation rate

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POS0923

EXTRACELLULAR VESICLES AS POTENTIAL BIOMARKERS OF EARLY DISEASE STAGE IN SYSTEMIC SCLEROSIS

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Background: Extracellular vesicles (EVs) are membrane-coated vesicles most often generated from the vasculature and circulating blood cells upon cell activation and during the early phase of apoptosis (1).
Objectives: To evaluate the concentration of different subpopulations of EVs in plasma from patients with SSc in relation to the disease duration and to the markers of endothelial injury.
Methods: Our study included 59 SSc patients (36 limited (lSSc) and 23 diffuse cutaneous subset (dSSc)) and 46 healthy age and gender matched controls subjects. Disease duration less than 3 years in patients with dSSc and less than 5 years in those with lSSc was considered as early disease stage. Clinical evaluation of patients was performed. EVs were analysed with flow cytometry after staining platelet poor plasma with fluorescent cell-specific monoclonal antibodies. The concentration of following phosphatidylserine-positive EVs (PS+ EVs) were analyzed: total EVs, endothelial EVs (EEVs; CD144+), platelet EVs (PEVs; CD42b+), monocytes EVs (LEVs; CD14+), EVs expressing ICAM1 (CD54+), VCAM1 (CD106+) and P selectin (CD62p+). Serum levels of ICAM1, VCAM1 and P selectin were determined with ELISA.
Results: Median disease duration of our cohort was 4 (0-29) years (early lSSc [20/36]: 2.5 (0-4.5) years; early dSSc [11/23]: 10 (1-30) months). All types of investigated EVs were significantly elevated in SSc patients compared to controls ($p<0.05$). Patients with early disease stage had significantly increased levels of all PS+EVs compared to HC ($p<0.05$). Moreover, the levels of EVs expressing ICAM1 and VCAM1 showed good validity in identifying patients with early disease stage (AUC 0.7, $p<0.01$). PEVs were increased in early dSSc compared to early lSSc, but the difference did not reach statistical significance ($p=0.07$). There was a correlation between serum levels and the levels of EVs expressing specific adhesion molecules (ICAM1: $r=0.7$, $p<0.01$; VCAM1: $r=0.7$, $p<0.01$; P selectin: $r=-0.7$, $p<0.01$), only within the group with early dSSc subtype of the disease. Further correlations were detected between ICAM1+EVs with either mRSS ($r=0.07$, $p< 0.01$) or EUSTAR activity index ($r=0.07$, $p= 0.02$) among patients with early dSSc.
Conclusion: Increased levels of circulating EVs of different cell origin were present in patients with early SSc. EVs expressing either ICAM1 or VCAM1 could be novel biomarkers of early disease. EVs expressing ICAM1 showed association with severity of skin involvement and disease activity in patients with early dSSc giving insight into their role in the pathogenesis of SSc.
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POS0924

THE ROLE OF RAYNAUD'S PHENOMENON ON MATERNAL AND FETAL OBSTETRICAL OUTCOMES

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Background: It is established that Raynaud's phenomenon (RP) may influence pregnancy outcomes when secondary to rheumatic conditions (1,2). Data on the impact of primary RP (pRP) on pregnancy are very limited.
Objectives: To retrospectively evaluate the impact of pRP on pregnancy outcomes.
Methods: Women with pRP were included in the study. They were compared with a group of women affected by UCTD with RP, and by UCTD without RP. These women were assessed and followed at our outpatient clinic from January 2011 to October 2020 and they did not exhibit an evolution to a UCTD or to a definite CTD during at least one-year follow-up. Antiphospholipid antibody positivity, twin pregnancies and voluntary termination of pregnancy were exclusion criteria. Women with pRP were also compared with a group of healthy pregnant women

enrolled by our gynaecologist during the first trimester of pregnancy. Maternal and foetal outcomes were retrospectively recorded. ANOVA or the Kruskal-Wallis test for continuous variables, and the Chi2 test or the Fischer exact test for categorical were performed (level of significance. P<0.050). In the post-hoc analysis we used the Mann-Whitney test (quantitative variables) or with the Chi2 test/ Fischer exact test (qualitative variables), applying the Bonferroni correction with pRP women as a reference group (level of significance: p<0.0167).

Results: The analysis included 188 women with a total of 375 pregnancies divided in 4 groups:

-Group "pRP": 46 women with RP without secondary causes, and a total of 106 pregnancies (reference group),

-Group "RP-UCTD": 48 UCTD women with RP and a total of 88 pregnancies,

-Group "UCTD": 37 UCTD women without RP and a total of 88 pregnancies,

-Group "HC": 57 healthy women with a total of 93 pregnancies.

The reference group did not differ from the others regarding age at conception. Prophylactic acetylsalicylic acid was administered during pregnancy to 9% of patients with pRP compared to 1% in HC (p=0.010). In contrast, in the RP-UCTD this percentage was significantly higher (32%, p<0,001) than in pRP.

pRP group showed an increased rate of 1st trimester miscarriages (33% vs 16%, p=0.006, OR 2.05 and 95%CI 1.05-3.98), a lower median birth weights (3038 g vs 3358 g, p=0.002), a higher rate of infants with a birth weight <10th percentile (21% vs 3%, p=<0.001, OR 8.36 and 95% CI 1.85 - 37.84) with respect to HC. There was no statistically significant difference between the reference and the UCTD groups.

No statistically significant differences were observed when considering obstetrical outcomes (eg: mode of delivery, median gestation duration, gestational diabetes mellitus, hypertensive disorder of pregnancy, premature rupture of membranes, oligo-anhydramnios).

Conclusion: Our study shows that pRP in a retrospective cohort has an impact on pregnancy outcomes, with significantly more miscarriages and lower birth weight infants compared to HC. Importantly, pregnancy outcome in pRP women did not differ with respect to UCTD with and without RP, conditions generally associated to maternal morbidity, but in the RP-UCTD group prophylactic acetylsalicylic acid was more commonly prescribed. Further prospective studies aiming at evaluating these differences and at identifying the appropriate follow-up and the possible benefit from the use of prophylactic acetylsalicylic acid during pregnancy in RP are necessary.

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Table 1. Analysis of obstetrical outcomes

	Primary RP (pRP)	RP-UCTD	UCTD	HC	p-value
Miscarriages *N. (%)*	35 (33%)	17 (19%)	30 (31%)	15 (16%)	**p=0,017**
vs pRP	*reference*	p=0,051	p=0,750	**p=0,006**	
Median weight at birth *(IQR), gr*	3038 (2710-3500)	3180 (2935 - 3465)	3157 (2910 - 3610)	3358 (3195 - 3583)	**p=0,02**
vs pRP	*reference*	p=0,3473	p=0,1542	**p=0,0002**	
Birthweight < 10th percentile *N. (%)*	15 (21%)	7 (10%)	5 (8%)	2 (3%)	**p=0,002**
vs pRP	*reference*	p=0,087	p=0,03	**p=<0,001**	

Disclosure of Interests: None declared

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POS0925 HIGH LEVELS OF BOTH CCL2 AND CCL17 WERE ASSOCIATED WITH MORE SEVERE SSC-ILD

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Background: Systemic sclerosis (SSc) carries a high risk for progressive interstitial lung disease (ILD). Several anti-inflammatory therapies have been used to treat SSc-ILD and recently the first antifibrotic therapy has been approved. Personalized treatment strategies are largely missing to date. The two chemokines, CCL2 (MCP-1) and CCL17 (TARC), have been shown to be markers of inflammation and fibrosis, respectively.

Objectives: To examine associations between ILD severity and serum levels of CCL2 and CCL17 in two different but complementary sources of biomaterial.

Methods: Sera from the prospective Oslo University Hospital SSc cohort (n=371) and healthy blood donor controls (HC; n=100) and lung tissue at the time of lung transplantation from UCLA SSc-ILD patients (n = 12) and healthy donors (n = 12) were analyzed for CCL2 and CCL17 by multiplex assays. CCL2 and CCL17 levels were defined in serum as high or low using 95% CI in HC sera as cut-off values. Paired pulmonary function tests and HRCT images were obtained at baseline and follow-up. ILD was diagnosed on HRCT and categorized by the extent of lung fibrosis as limited (<10%) or extensive (>10%) ILD. Cellular sources of CCL-2 and CCL-17 in lung tissues were determined by immunohistochemistry. Descriptive statistics were applied.

Results: CCL2 and CCL17 were increased in SSc in sera and in lung tissue compared to HC (Figure 1). High levels of CCL17 (>700 pg/ml) and CCL2 (>1000pg/ml) in sera were identified in 43/254 (17%) and 84/471(18%) of the SSc patients (Table 1 and Figure 1). High levels of both CCL17 and CCL2 were associated with lower FVC at baseline and higher extent of lung fibrosis on HRCT (Table 1). Of those with high CCL2 and CCL17, 67% had extensive lung fibrosis. Categorization of ILD into no ILD, limited or extensive ILD showed an association between high CCL17 levels and the extent of fibrosis (Table 1). Reactive epithelium and macrophages and plasma cells expressed TARC, while more AM and infiltrating mononuclear cells expressed CCL-2.

Conclusion: High levels of both CCL17 and CCL2 were associated with more severe ILD and expressed in end-stage kung tissue and may reflect an ongoing inflammatory and fibrotic processes in SSc-ILD. This may have an implication on treatment choices for SSc-ILD.

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POS0926 HOW GOOD ARE WE AT CAPTURING THE GI SYMPTOMS IN OUR PATIENTS WITH SCLERODERMA?

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Background: Scleroderma is a rare autoimmune condition affecting around 1 in 10,000 individuals causing multisystem inflammation and fibrosis. The gastrointestinal (GI) system is the most commonly affected system, with nearly 90% of patients experiencing GI manifestations. The disease can affect any part of the GI tract with symptoms ranging in severity. Complications include oesophagitis and oesophageal strictures, vascular lesions in the stomach, reduced movement and absorption within the intestines and anorectal involvement. Recent guidance by the BSR highlight the importance of GI complications.

Objectives: To conduct a quality improvement project to improve the care provided to our scleroderma patients, focusing on GI symptom burden and identifying any unmet need when comparing local care to BSR guidelines and consensus best practice guidelines.

Methods: A proforma was developed for assessing and treating GI symptoms based on BSR and consensus best practice guidelines. This proforma was trialled on an initial cohort of 32 scleroderma patients from the Royal Glamorgan Hospital in Wales. The last clinical assessment was assessed for the following - regurgitation, nausea, vomiting, heartburn, dysphagia, abdominal pain, bloating, diarrhoea, faecal incontinence, constipation and weight loss. The symptoms were recorded as present, not present or not documented. The management of symptoms were evaluated against the guidelines. The cohort were then contacted regarding their last clinical assessment and asked if they were experiencing these symptoms at the time of their last assessment. The results from the documented assessment were compared to the additional patient information to address unmet needs.

Results: The results show that there is limited documentation of the presence of GI symptoms amongst scleroderma patients at clinic appointments. The initial assessment results were compared with the subsequent patient telephone reported symptoms in order to identify unmet need. The following refer to unidentified symptoms at assessment - regurgitation 9%, nausea 6%, vomiting 3%, heartburn 31%, dysphagia 31%, abdominal pain 9%, bloating 25%, diarrhoea 6%, faecal incontinence 9%, constipation 15% and weight loss 19%. Many patients stated they were unaware that their condition could cause GI symptoms and would not routinely mention these symptoms in a rheumatology assessment. The proforma proves to be an effective way to document and guide management of these patients. The clinical proforma that has now been created will help us improve patient care which can be reassessed in the future.

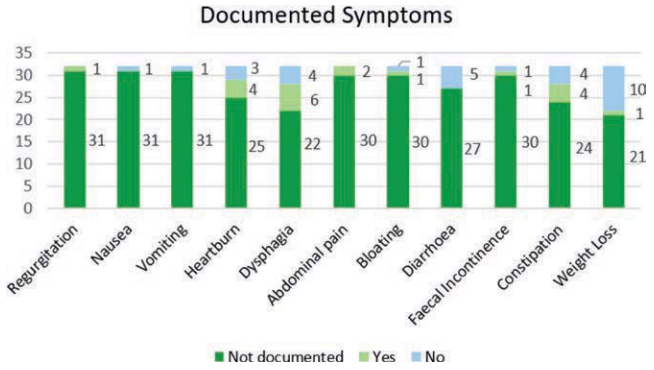

Table 1.

Symptoms	Management
Regurgitation	1 case - not investigated due to pre-existing dysmotility
Nausea	0 cases
Vomiting	0 cases
Heartburn	4 cases – 3 on PPIs, 1 gastroscopy arranged
Dysphagia	6 cases – 2 of known dysmotility, 3 not investigated
Abdominal pain	2 cases – not investigated
Bloating	1 case – not investigated
Diarrhoea	0 cases
Faecal incontinence	1 case – MRI arranged for query small bowel obstruction
Constipation	4 cases – 1 longstanding issue, 1 MRI arranged, 2 not investigated
Weight loss	1 case – not investigated

Conclusion: The piloting of our proforma of the GI assessment of patients with scleroderma has identified that the documentation of GI symptoms was poor. We don't know whether GI symptomology was discussed during assessment however it's evident that it was not often documented. Patients don't always report symptoms unless targeted questions are asked. A clinic proforma would be invaluable, leading to an increased awareness amongst both practitioners and patients of the potential clinical manifestations. Having presented this data locally we have now introduced such a proforma and will re-evaluate clinical practice in the future. Sharing this information will hopefully help improve patient care elsewhere.

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POS0927 CORONARY ARTERY CALCIFCATION IN SYSTEMIC SCLEROSIS: EVALUATION OF CARDIOVASCULAR RISK AND CLINICAL OUTCOME

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Background: The primary prevention of cardiovascular disease (CVD) is a priority element of the worldwide health care agenda. An increased risk of CVD and CV mortality has been shown in lots of studies conducted on patients affected by inflammatory and autoimmune diseases. A routine evaluation of CV risk in these patients should be encouraged and in particular cases is recommended.
Objectives: The aim of this study is to evaluate the presence of subclinical atheromatosis, the CV risk and its performance in a cohort of patients affected by Systemic Sclerosis (SSc) from a single reference tertiary care hospital.
Methods: Sixty-seven patients with SSc according to the ACR/EULAR 2013 criteria were included. Traditional CV risk factors and SSc related factors were analyzed. Thoracic high resolution computed tomography (CT) was performed, using the quantification of coronary calcium for the study. Furthermore, a doppler ultrasonography of the carotids and the lower extremity arteries was conducted for the detection of subclinical atheromatosis. The CV risk has been calculated through different CV risk scales including the MESA CAC, the Italian Progetto Cuore, the Framingham score, the Score2 and the QRISK3. After conducting a 5-year follow up, CV outcome and electrocardiography abnormalities were examined.
Results: Calcium artery coronary score > 0 was reported in twenty-eight SSc patients (41,8%). Considering traditional CV risk factors, the multivariate regression analysis showed a correlation with age (OR 1.151 [95% CI 1.06–1.25], P = 0.001) and systemic arterial hypertension (OR 5 [95% CI 1.148–22.357], P = 0.032). Instead, the presence of anti-CENP-B (OR 3.47 [95% CI 1.09–11.06], P = 0.035) and late-onset disease (OR 1.062 [95% CI 1.007–1.119], P = 0.026) were identified as potential specific disease risk factors. The prevalence of ultrasonography atherosclerosis was high: peripheral artery disease (PAD) and carotid plaque were respectively 43% and 41%, and the presence of coronary calcifications was a risk factor for their detection with a OR respectively of 20.39 and 20.49 (p=0.0001). All CV risk scores considered SSc patients in a low risk, except for the QRISK3, whose values were higher in patients with coronary calcifications (18.4±12.6 vs 5.1±4.9, p=0.0001). In 5-years follow up only 1 patient died for CVD and 2 CV events occurred. Electrocardiography anomalies were found in 28.35% of patients, and in particular in 43% of patients with coronary calcifications (OR 3.321 [95% CI 1.094-10.08], P = 0.03).
Conclusion: Subclinical coronary atherosclerosis seems to be largely observed in SSc patients and may represent an additional risk factor for electrocardiography anomalies and subclinical atheromatosis in other anatomical districts, with no impact on CVD mortality. In our study coronary calcifications well correlated with CV risk score, especially the novel QRISK3 by classifying these patients between low and moderate CV risk. Other studies are needed to support the hypothesis that subclinical coronary atherosclerosis, occasionally detected in thoracic CT, may represent a clinical alert to establish timing and weight of diagnostic and specific treatment protocols for the CV prevention in SSc patients.

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POS0928 THE IDENTIFICATION OF PENTRAXIN 3 AS BIOMARKER OF DISEASE ACTIVITY IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Muscle involvement is only one feature of idiopathic inflammatory myopathies (IIM). Muscle enzymes do not always represent the best marker of disease activity and other inflammation markers such as ESR and CRP may be normal even with an active disease. Pentraxin-3 (PTX3) is an inflammatory marker produced in many inflammatory and non-inflammatory cells and serum level has been related to higher risk of major cardiovascular events and atherosclerosis[1]. PTX3 levels have been examined in various rheumatic and autoimmune diseases[2], but data of PTX3 levels in patients affected with IIM have not been reported.
Objectives: The aim of the current study was to identify whether serum PTX3 level could be a marker of disease activity in patients affected with IIM.
Methods: Twenty patients affected with IIM (13 Dermatomyositis and 7 Polymyositis), 10 rheumatoid arthritis patients and 10 healthy controls (HC) aged, sex and BMI matched were evaluated. PTX3 levels was assessed using a commercially available enzyme-linked immunosorbent assay (Human Pentraxin3 ELISA Kit, Abcam) kit. Three different cardiovascular risk scores were used to estimate the 10-years CV risk. Carotid intima media thickness (cIMT) was measured with a My Lab XPro80 (Esaote SpA, Genova, Italy) using a linear array ultrasound probe small parts broadband transducer (5–15 MHz) both in right and left carotid. Myositis disease activity was evaluated by using myositis disease activity assessment visual analog scales (MYOACT) [19] established by the International Myositis Assessment and Clinical Studies (IMACS) group. Manual muscle test (MMT8) was used to assess muscle impairment. Exclusion criteria were a diagnosis of diabetes or a history of previous major CV events.
Results: Demographic and disease characteristics of our cohort are showed in Table 1. IIM patients showed higher levels of PTX3 compared to HCs (518±260 pg/ml vs 275±114 pg/ml, p<0.05), while no difference was observed compared to RA patients (383±260 pg/ml). PTX3 levels do not correlate with lipid levels, QIMT and cardiovascular risk scores both in IIM, RA and HC. No correlation was found between DAS28-ESR and PTX3 levels in RA patients. Of note, a direct correlation

was found between PTX3 levels and MYOACT-GLOBAL DISEASE ACTIVITY (r=0.675, p=0.002), PTX3 levels and MYOACT- GLOBAL-EXTRA-SKELETAL MUSCLE DISEASE ACTIVITY (r=0.542, p=0.013), while an inverse correlation was found between PTX3 levels and MMT8 (r=-0.510, p=0.02).

Table 1.

	IIM 20pz (13 DM, 7 PM)	RA 10pz	Healthy Control 10pz
Female, n. (%)	18 (90%)	9 (90%)	9 (90%)
Age	55,3 (7,8)	58,3 (5,9)	54,6 (6,5)
BMI	25,5 (4,1)	23,9 (3,1)	24,6 (3,5)
Duration of disease, median (IQR)	7,3 (4 – 12,8)	13,5 (10,5 – 18,5)*	
Physician Global Assessment	2,1 (2,1)	2 (2,2)	
Patient Global Assessment	4 (3,6)	2,7 (2,3)	
Health Assessment Questionnaire	0,7 (0,8)	0,9 (0,9)	
Manual Muscle Testing 8	76,2 (6,6)		
DAS28		2,6 (1,1)	
Skin involvement, n. (%)	13 (65)		
Lung involvement, n. (%)	7 (35)		
Dysphagia, n. (%)	11 (55)		
Arthritis, n. (%)	4 (20)		
Malignancies, n. (%)	0 (0)	0 (0)	0 (0)
Arterial hypertension, n. (%)	6 (30)	2 (20)	1 (10)
Current steroid therapy	2,5 (0 – 5)	0 (0 – 3,8)	
Smoking, n. (%)	6 (30)	2 (20)	3 (30)
Total cholesterol, mg/dl	203,3 (28,6)	215,0 (29,5)	216,2 (27,3)
HDL cholesterol, mg/dl	62,7 (14,7)	62,6 (14,2)	65,1 (18,2)
ESR, mm/h	16,7 (12,2)	19 (11,7)	
PCR, mg/l	2,9 (2,1)	4,1 (5)	
SCORE median (IQR)	0,5 (0 – 2)	1 (0 – 3)	1 (0,8 – 1,3)
CUORE median (IQR)	1,9 (0,6 – 3,5)	1,6 (1 – 4)	1,7 (1,2 – 2,8)
QRISK3 median (IQR)	4,7 (2,1 – 11,3)	7,5 (3,2 – 13,6)	4,2 (3,1 – 5,5)
QIMT Max, median (IQR)	742,5 (636,8 – 804)	833 (685,3 – 961) *	756 (711 – 820)
Mean QIMT, median (IQR)	679 (613,1 – 736,3)	764,3 (664,5 – 854,1) *	703,3 (697,3 – 742,8)
Pentraxin 3, pg/ml	518 (260)	383 (146)	275 (114)*

Data are expressed as "mean (SD)" where not otherwise specified.*p<0.05, **p<0.01, ***p<0.001 vs IIM

Conclusion: In IIM patients, PTX3 levels are higher than HC and correlate with disease activity, both for muscular and extra-muscular manifestations, being a possible biomarkers of disease activity.

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POS0929

MICRO VASCULAR IMAGING AS A NOVEL TOOL TO QUANTIFY BLOOD FLOW IN THE FINGERTIPS IN PATIENTS WITH SYSTEMIC SCLEROSIS VS. HEALTHY CONTROLS: A SINGLE-CENTER FEASIBILITY STUDY

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Background: Systemic sclerosis (SSc) is characterized by tissue fibrosis and vasculopathy. Raynaud's phenomenon is present in almost all patients (1). Nailfold video capillaroscopy is an established imaging tool for a morphologic assessment but is not able to quantify blood flow (2). Micro Vascular Imaging (MVI) is a novel ultrasound technique for blood flow quantification, especially of small vessels with low flow (3). The technique has not been used in SSc to quantify blood flow.

Objectives: To evaluate Micro Vascular Imaging (MVI) as a novel ultrasound tool for flow quantification of small fingertip vessels in healthy controls (HC) compared to SSc patients.

Methods: In this single-center prospective cohort study MVI scans of the second to fifth fingertip were performed in 20 healthy controls vs. SSc patients. Demographic data were analyzed using descriptive statistics. For flow velocity analysis, MVI peak systolic (PS) and end-diastolic (ED) flow values were used. Receiver operator characteristics (ROC) curves were generated to detect an optimal cut-off value for each parameter to discriminate between HCs vs. SSc patients. Sensitivity and specificity were reported with 95% CI based on Youden's J.

Results: The median age of the 20 HCs was 26 years (19-56), and 13 (65%) were female. 19 (95%) participants were right-handed. Twenty female SSc patients were included. The median age was 60 years (24-79). All SSc patients were right-handed (100%). SSc patients were older than HCs (p<0.0001) and included more female participants (p=0.0083). Some of the recruited SSc patients were past (n=4, 20%) or current (n=2, 10%) smokers, while all HCs were non-smokers (p=0.0293). No differences were found regarding dexterity (p>0.9999). 13 SSc patients had limited cutaneous SSc, five had diffuse cutaneous SSc, one patient was diagnosed with Very Early Diagnosis of Systemic Sclerosis, and one patient had no skin involvement (*sine* scleroderma). Eighteen patients (90%) reported the presence of RP. It was shown that PS flow velocity and ED flow velocity were significantly higher in HCs (Figure 1). For all fingers measured, the difference of the medians (D) for PS velocity was 4.675 cm/s (95% CI 3.3-5.25, p<0.0001), for ED velocity 1.375 cm/s (95% CI 0.85-1.65, p<0.0001). No correlation with age was found, neither in HCs (r2=0.03 for PS flow, r2=0.18 for ED flow), nor in SSc patients (r2=0.08 for PS flow, r2=0.01 for ED flow).

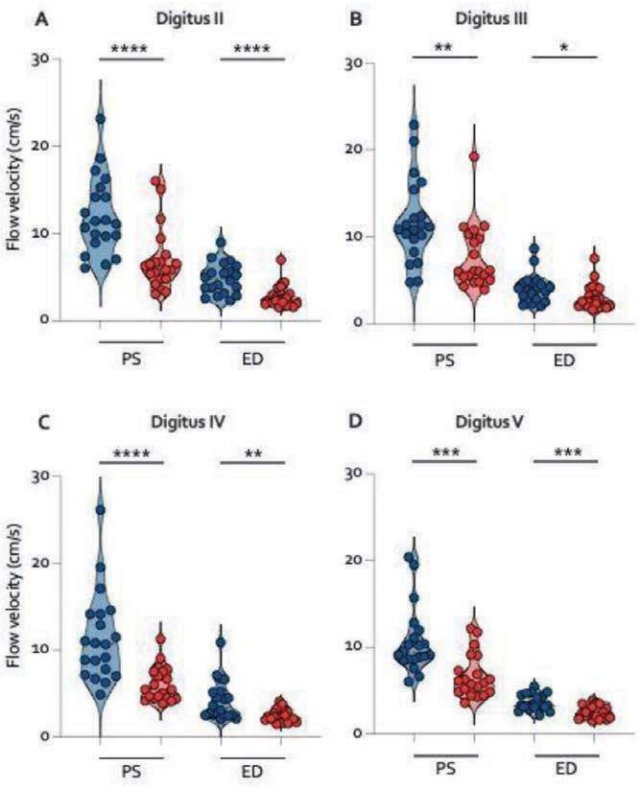

Figure 1. Comparison of peak systolic (PS) and end-diastolic (ED) blood flow of Digitus II-V in healthy controls (blue) vs. systemic sclerosis patients (red).

The highest PS velocity was measured on Digitus II with 5.225 cm/s (95% CI 2.95-7.5, p<0.0001), and 2.325 (95% CI 1.1-3.1, p<0.0001) for ED flow velocitiy, while lowest values were observed at Digitus V with PS = 3.325 cm/s (95% CI 2.2-5, p<0.001), and ED = 0.875 cm/s (95% CI 0.6-1.6, p<0.001). For PS flow velocity, an optimal cut-off point of <6.13 cm/s showed excellent sensitivity (0.90, 95% CI 0.70-0.98) and specificity (0.85, 95% CI 0.64-0.95), corresponding to a LR+ of 6.0. For ED flow velocity, the optimal cut-off point was calculated at <2.13 cm/s, sensitivity was 0.85 (95% CI 0.64-0.95), specificity was 0.80 (95% CI 0.58-0.92), corresponding to a LR+ of 4.25.

Conclusion: We present the first study of MVI as a novel imaging technique to measure blood flow velocity in patients with SSc. We report the method's feasibility and discriminative cut-off points between HCs and SSc. In an extenstion of this study, we aim to longitudinally assess the results with organ manifestations or vascular complications of SSc in a larger cohort.

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Spondyloarthritis - treatment

POS0930 SAFETY AND EFFICACY OF IXEKIZUMAB TREATMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: 3-YEAR CLINICAL TRIAL RESULTS FROM THE COAST PROGRAMME

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Background: Ixekizumab (IXE) has demonstrated efficacy at week (wk) 16 which was maintained through 2 years (yrs) and was associated with a consistent safety profile in patients (pts) with r- and nr-axSpA, who are bDMARD-naïve and TNFi-experienced.[1-3]

Objectives: To report safety and efficacy from the COAST programme at 3 yrs: 1 yr of the originating studies (COAST-V/W/X) and 2 yrs of COAST-Y.

Methods: COAST-Y (NCT03129100) is the phase 3, long-term extension study of the 3 originating studies COAST-V/W/X. Pts continued with the dose received at the end of the originating trial at week (wk) 52: either with 80 mg IXE every 4 wks (Q4W) or every 2 wks (Q2W). Pts assigned to adalimumab (ADA) or placebo (PBO) were re-randomised to IXE Q4W or Q2W at wk 16 in COAST-V and -W. Pts who received PBO for 52 wks in COAST-X were switched to IXE Q4W to continue in COAST-Y. Starting at wk 116 (wk 64 of COAST-Y), pts receiving IXE Q4W could have their dose escalated to Q2W. This analysis focused on pts receiving ≥1 dose of IXE Q4W, observed data while on IXE Q2W dose escalation are excluded. Continuous data are summarised as observed. Safety data while on IXE were analysed for pts who received ≥1 dose of IXE; observed data while on PBO or ADA are excluded.

Results: A total of 932 pts received ≥1 dose of IXE, 414 received ≥1 dose of IXE Q4W, and 562/932 (60%) pts completed 3 yrs of follow-up (PBO→IXE Q4W, 63/119 (53%); ADA→IXE Q4W, 29/44 (66%); and IXE Q4W→IXE Q4W, 114/251(45%)). Through 3 yrs, the most frequently reported treatment-emergent adverse events were infections [incidence rate (IR) 25.7/100 patient years (PY)] and injection site reactions [IR 7.4/100 PY]; the majority of which were mild/moderate in severity. Serious adverse events were reported at an IR of 4.8/100 PY, of which osteoarthritis was the most frequent at 0.4/100 PY. A total of 3 deaths were reported among all pts who received ≥1 dose of IXE [IR 0.1/100 PY]. For all pts, baseline disease activity (Ankylosing Spondylitis Disease Activity Score; ASDAS) was high (see Table 1). The 3 yr mean (SD) change from baseline (observed) in ASDAS among bDMARD-naïve pts with r-axSpA, TNFi-experienced pts with r-axSpA, and bDMARD-naïve pts with nr-axSpA is presented in the Table 1. A consistent disease control through 3 yrs was confirmed across additional efficacy endpoints (Table 1).

Conclusion: This analysis of a subset of pts in COAST-Y demonstrated that the safety profile is consistent with the established safety profile, with no new safety signals observed. IXE Q4W was efficacious (observed data) in all patients studied who remained on the treatment through 3 yrs.

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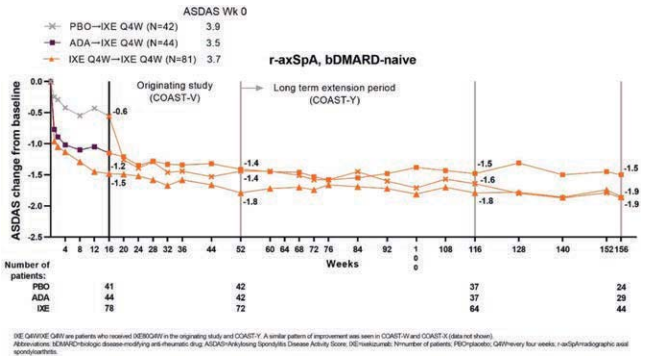

Figure 1. Observed mean CFB in ASDAS for pts treated with IXE Q4W in COAST-V. At wk 16, PBO pts received IXE Q4W.

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POS0931 EFFICACY AND IMPROVEMENT IN PATIENT-REPORTED OUTCOMES AT WEEKS 16 AND 52 IN IXEKIZUMAB TREATED BIOLOGICAL NAÏVE PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS ACHIEVING CLINICALLY IMPORTANT PAIN AT NIGHT REDUCTION AT WEEK 16: RESULTS FROM COAST-V TRIAL

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Table 1. Baseline demographics and disease activity characteristics through 3 yrs. Data presented as mean (SD) unless otherwise specified.

	COAST-V			COAST-W		COAST-X	
	PBO (N=87)	ADA (N=90)	IXE Q4W (N=81)	PBO (N=104)	IXE Q4W (N=114)	PBO (N=105)	IXE Q4W (N=96)
Age	43 (12)	42 (11)	41 (12)	47 (13)	47 (13)	40 (12)	41 (15)
Male, n (%)	71 (83)	73 (81)	68 (84)	87 (84)	91 (80)	44 (42)	50 (52)
Symptom duration (years)	16.6 (10.1)	15.6 (9.3)	15.8 (11.2)	19.9 (11.6)	18.8 (11.6)	10.1 (8.3)	11.3 (10.7)
HLA-B27, n (%)	76 (89)	82 (91)	75 (93)	86 (83)	91 (80)	77 (74)	71 (75)
ASDAS	3.9 (0.7)	3.7 (0.8)	3.7 (0.7)	4.1 (0.8)	4.2 (0.9)	3.8 (0.9)	3.8 (0.8)
BASDAI	6.8 (1.2)	6.7 (1.5)	6.8 (1.3)	7.3 (1.3)	7.5 (1.3)	7.2 (1.5)	7.0 (1.5)
3 years (observed)							
	PBO→ IXE Q4W N=42	**ADA→ IXE Q4W** N=44	**IXE Q4W→ IXE Q4W** N=81	**PBO→ IXE Q4W** N=46	**IXE Q4W→ IXE Q4W** N=114	**PBO→ IXE Q4W** N=31	**IXE Q4W→ IXE Q4W** N=56
ASDAS CFB	-1.9 (0.9)	-1.5 (0.9)	-1.9 (0.9)	-1.6 (1.0)	-1.7 (1.0)	1.8 (1.0)	-1.7 (1.4)
ASDAS LDA, n (%)	13/24 (54)	21/29 (72)	33/44 (75)	7/20 (35)	16/41 (39)	13/19 (68)	19/29 (66)
BASDAI CFB	-3.9 (1.9)	-3.5 (2.3)	-4.0 (2.2)	-3.7 (1.7)	-3.4 (2.2)	-4.4 (2.1)	-3.4 (2.7)
BASDAI50, n (%)	15/24 (63)	18/29 (62)	31/44 (71)	9/20 (45)	20/41 (49)	12/19 (63)	16/29 (55)
ASAS40, n (%)	13/24 (54)	18/29 (62)	30/44 (68)	10/20 (50)	23/41 (56)	15/19 (79)	17/29 (59)

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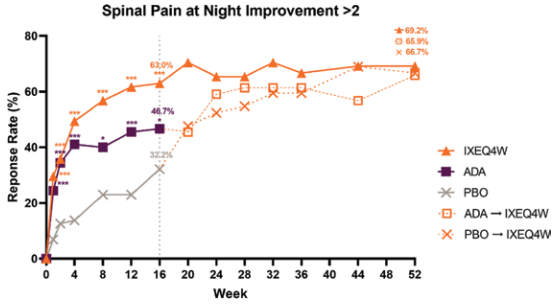
Background: Ixekizumab (IXE), a monoclonal antibody that selectively targets interleukin IL-17A, has shown efficacy in patients with radiographic axial spondyloarthritis (r-axSpA). Spinal pain, in particular spinal pain at night (SP-N), is a major contributor to the patient burden of r-axSpA.
Objectives: To assess SP-N improvement in patients up to week (W) 52 and to determine the association of SP-N improvement in patients treated with IXE with other patient-reported outcomes (PROs) at W16 and with reaching ASDAS LDA at W52.
Methods: The Phase III COAST-V (NCT02696785) trial investigated the efficacy of IXE in 341 patients with r-axSpA and were biological disease-modifying anti-rheumatic drug (bDMARD)-naïve. Patients were randomised to IXE every 2W (IXEQ2W), IXE every 4W (IXEQ4W), adalimumab (ADA) or placebo (PBO) up to W16. Only approved dose IXEQ4W data are presented here. SP-N was measured at each visit using a numeric rating scale (NRS) (0-10). A clinically relevant improvement in SP-N was defined as >2 point improvement from baseline. Differences in baseline variables between those achieving versus not achieving >2 improvement in SP-N were tested using Fisher's exact test (binary variables) and analysis of variance (ANOVA; continuous variables). Associations of SP-N improvement with PROs (BASFI, Fatigue Severity NRS, Jenkins Sleep Evaluation Questionnaire (JSEQ), SF-36 PCS) at W16, and ASDAS LDA at W52 were tested using analysis of covariance (ANCOVA; continuous variables) and logistic regression (binary variables). Missing values were imputed using non-responder imputation, and modified baseline observation carried forward.
Results: A greater proportion of patients achieved >2 improvement in SP-N with IXE treatment compared to PBO at W16 (63.0% vs. 32.2%, p <0.001) and improvement was sustained up to W52 (Figure 1). Of the 81 patients originally randomised to IXE, those achieving >2 improvement in SP-N (63%) at W16 were younger, more frequently positive for HLA-B27 and had higher disease activity at baseline compared to those that did not achieve >2 improvement (Table 1). Achieving >2 improvement in SP-N was associated with improvement in PROs including BASFI, Fatigue Severity, JSEQ and SF-36 PCS at W16 and with achieving ASDAS<2.1 at W52 compared to those not achieving >2 improvement in SP-N (Table 1).

Table 1. Baseline demographics, clinical characteristics, and PROs of IXE treated patients achieving vs. not achieving >2 improvement in SP-N at W16.

Achieved >2 Improvement in SP-N at W16	Yes (n=51)		No (n=30)	
Baseline Characteristics				
Age, yrs	38.6 (11.4)*		44.9 (12.4)	
Positive for HLA-B27, n (%)	50.0 (98.0)*		25.0 (83.3)	
CRP (mg/L)	14.9 (14.9)*		7.6 (8.4)	
ASDAS	3.9 (0.8)*		3.5 (0.6)	
Spinal Pain at Night	7.4 (1.3)*		6.4 (1.4)	
PROs	**Baseline**	**W16 CFB**	**Baseline**	**W16 CFB**
BASFI	6.1 (1.9)	-3.4 (2.2)***	6.0 (1.6)	-0.7 (1.5)
Fatigue Severity NRS	6.9 (1.7)	-3.5 (2.6)***	6.3 (1.6)	-0.7 (2.0)
JSEQ	7.1 (5.4)	-3.2 (4.2)***	7.2 (5.2)	-0.1 (2.7)
SF-36 PCS	32.8 (7.7)	10.9 (7.7)***	36.1 (6.7)	2.0 (6.5)
ASDAS <2.1 at W52 Response, n (%)	34 (66.7)**		9 (33.3)	

Values represent mean (SD) unless otherwise stated. *p<0.05, **p<0.01, ***p<0.001 versus those not achieving >2 improvement in SP-N.HLA-B27; Human Leukocyte antigen-B27, CRP; C-reactive protein, ASDAS; Ankylosing Spondylitis Disease Activity Score, CFB; change from baseline, BASFI; Bath Ankylosing Spondylitis Functional Index, NRS; Numeric Rating Score, JSEQ; Jenkins Sleep Evaluation Questionnaire, SF-36 PCS; Short-Form 36 physical component score.



Footnote: ADA; Adalimumab (reference arm), PBO; Placebo, IXE; Ixekizumab

W0-16; IXEQ4W: N=81, ADA: N=90, PBO: N=87,

Pts initially randomised to IXE remained on the same regimen up to W52. Pts on PBO or ADA were re-randomised to IXEQ2W or IXEQ4W at W16. Only approved dose IXEQ4W data are presented here.

W16-52; IXEQ4W: N=78, ADA→IXEQ4W: N=44, PBO→IXEQ4W: N=42.

**p <0.05, ***p<0.001 versus PBO (Logistic regression analysis with treatment, geographic region, and baseline CRP status as factors).*

Figure 1. Patients achieving meaningful spinal pain at night improvement through W52.

Conclusion: IXE improved SP-N for patients with r-axSpA not previously treated with bDMARDs. Improvements in SP-N were associated with improvements in disease activity, function, fatigue and quality of life.
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POS0932 UPTAKE OF NEWER BIOLOGIC AND TARGETED SYNTHETIC DMARDS IN PSORIATIC ARTHRITIS, RESULTS FROM FOUR NORDIC BIOLOGIC REGISTRIES

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Background: The treatment landscape in psoriatic arthritis (PsA) is changing, including newer biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) with different modes of action becoming available. However, the most effective treatment strategy in routine care remains to be established.
Objectives: To explore the uptake and treatment patterns of newer b/tsDMARDs, namely JAK-inhibitors (JAKi; baricitinib, tofacitinib, upadacitinib), IL-17-inhibitors (ixekizumab, secukinumab), abatacept, apremilast, and ustekinumab in PsA patients from the Nordic countries. Furthermore, to describe patient characteristics and extra-musculoskeletal manifestations at treatment start (=baseline).
Methods: Observational cohort study, using prospectively collected routine care data from 4 Nordic rheumatology registries. Treatments (newer b/tsDMARDs with tumor-necrosis-factor inhibitors (TNFi) as the reference) initiated from January 2009 until December 2020 and corresponding baseline patient characteristics were identified. Linkage to national patient registries was used to identify previous extra-musculoskeletal manifestations (0-5 years). Country-level data were pooled for analyses. Uptake of each drug was explored as the cumulative number of treatment starts (a) overall, irrespective of previous b/tsDMARD experience, and (b) in b/tsDMARD-naïve patients. Each patient could contribute >1 treatment course.
Results: Overall, 13,364 unique patients contributing 24,325 treatment courses with either a newer b/tsDMARD (4,855, 20%) or a TNFi (19,470, 80%, whereof 10,897 were started year 2015-20) were identified. For the sub-group of 11,892 first b/tsDMARD treatment courses, 1,009 (8%) were a newer b/tsDMARD (10,883 were a TNFi, whereof 5,956 were started year 2015-20). Secukinumab dominated the newer b/tsDMARD uptake (1,848 new-starts, Figure 1). Ustekinumab-uptake increased over time both overall and in b/tsDMARD-naïve patients. In b/tsDMARD-naïve patients, apremilast had the fastest uptake (490 new-starts) (Figure 1). Use of JAKi was limited, especially in b/tsDMARD-naïve patients.

Table 1. Baseline characteristics upon treatment start

		Abata-cept	Apre-milast	Bari-citinib	Ixe-kizumab	Secuki-numab	Tofa-citinib	Upada-citinib	Uste-kinumab	Any TNFi
Cumulative uptake, n		362	935	106	342	1848	494	6	691	19470
Male gender, %		33	42	27	38	40	33	33	37	44
Age		54 (12)	53 (12)	55 (13)	52 (13)	51 (13)	54 (13)	52 (10)	50 (12)	49 (13)
b/tsDMARD treatment	1	9	52	9	11	14	9	0	20	56
number, %	2	19	15	12	26	25	18	17	19	25
	≥3	72	33	78	74	61	73	83	62	19
Disease duration, yrs		9 (8)	8 (8)	10 (8)	10 (8)	9 (9)	11 (10)	8 (8)	8 (9)	7 (8)
Pain, VAS (0-100)		63 (21)	61 (23)	64 (23)	64 (25)	63 (24)	66 (23)	75 (17)	64 (23)	59 (24)
DAS28		4.73 (1.34)	4.04 (1.35)	3.95 (1.36)	4.24 (1.19)	4.13 (1.36)	4.49 (1.33)	4.74 (0.88)	4.19 (1.32)	4.07 (1.29)
Uveitis, %*		3	2	3	1	2	3	0	2	2
IBD, %*		1	1	3	1	1	1	-	3	1

Numbers are mean (SD) unless otherwise statedIBD: inflammatory bowel disease, bDMARD: biologic DMARD, ts: targeted synthetic*0-5 years previously, available all study period for Iceland, Sweden, Finland until 31Dec2018, not available for Denmark

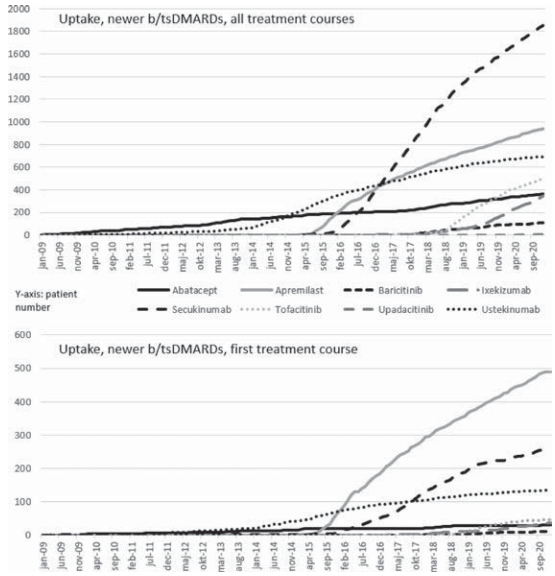

Figure 1.

Patients starting a newer b/tsDMARD tended to have longer disease duration and slightly higher disease activity at baseline (DAS28, patient-reported outcomes) than TNFi initiators (Table 1). Previous extra-musculoskeletal manifestations (uveitis, IBD) were rare, and with similar distributions across treatments (Table 1).

Conclusion: In this cross-country collaboration we were able to explore uptake of newer b/tsDMARDs. TNFi still dominates compared to newer b/tsDMARDs in routine care treatment of PsA. Newer b/tsDMARDs are mainly used in patients with several previous treatment failures, i.e. with longer disease duration and higher disease activity, indicating difficult to treat disease. Further studies are planned to explore real-world treatment patterns and outcomes.

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POS0933

IMPACT OF SACROILIAC JOINT STEROID INJECTION IN AXIAL SPA PATIENTS WITH BONE MARROW EDEMA ON DIFFERENT DISEASE OUTCOME MEASURES: A RANDOMIZED CONTROLLED TRIAL

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Background: Sacroiliac joint injection in axial spondyloarthritis (SpA) patients with steroid was controversial. A well designed randomized clinical trial testing its effect on different disease outcome measures particularly bone marrow edema was missing [1].

Objectives: To test the effect of steroid injection in the sacroiliac joint of axial SpA patients on different disease outcome measures.

Methods: N = 43 were registered. They were randomly assigned into 2 groups; Group I (23 cases) received sacroiliac joint injection lidocaine hydrochloride mixed with triamcinolone, whereas Group II (22 cases) received subcutaneous saline injections. All participants fulfilled the ASAS criteria for axial SPA and they all had bone marrow edema at baseline. Outcomes measures were: Visual Analogue Scale (VAS), ASDAS, BASFI, and SPARCC scores. Participants were assessed at baseline (before and after sacroiliac joint injection) and after 3 months.

Results: There was a significant difference between both groups regarding pain, spine mobility, SPARCC and ASDAS scores in favor of group I. Spine mobility showed the earliest improvement, followed by pain whilst SPARCC and ASDAS scores showed improvement after 3 months. Higher disease activity, younger age, and shorter disease duration all were associated with better outcomes. Bilateral hip involvement was a predictor of poor response

Conclusion: Sacroiliac joint injection of lidocaine and triamcinolone in axial SpA patients is effective in controlling pain, improving function, disease activity scores, and bone marrow edema with acceptable complications and relatively sustained effect.

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Table 1. Comparison between the two study groups

		Group I (N=24)	Group II (N=23)	P value*
Age		35.4±6.2	33.5±6.7	0.354
Sex	Male	17(77.3%)	16(76.2%)	1.000
	Female	5(22.7%)	5(23.8%)	
VAS	Before injection (0)	7.95±0.84	7.86±0.73	0.688
	After injection (1)	3.55±1.44	6.95±1.02	**<0.001**
	12 weeks later (2)	4.82±1.37	7.19±0.81	**<0.001**
	P value 0 vs 1**	**<0.001**	**0.003**	-
	P value 0 vs 2**	**<0.001**	**0.001**	-
	P value 1 vs 2**	**<0.001**	0.397	-
ASDAS	Before injection	2.69±0.44	2.60±0.37	0.451
	12 weeks later	1.51±0.44	2.40±0.46	**<0.001**
	P value **	**<0.001**	**0.022**	
BASFI	Before injection	61.91±9.70	62.95±11.71	0.752
	12 weeks later	57.50±8.13	61.24±0.53	0.199
	P value **	**<0.001**	0.081	-
SPARCC	Before injection	34.73±9.14	33.48±8.93	0.652
	12 weeks later	15.68±6.60	30.95±7.85	**<0.001**
	P value **	**<0.001**	**0.024**	-
Finger to floor	Before injection (0)	27.68±9.94	26.90±11.62	0.815
	After injection (1)	17.09±7.00	25.48±11.23	**0.005**
	12 weeks later (2)	19.64±7.83	26.76±11.79	**0.024**
	P value 0 vs 1**	**<0.001**	**0.001**	-
	P value 0 vs 2**	**<0.001**	0.791	-
	P value 1 vs 2**	**0.001**	0.072	-
Lateral bending	Before injection (0)	21.64±5.91	22.29±4.51	0.688
	After injection (1)	25.50±6.13	22.57±3.43	0.060
	12 weeks later (2)	24.55±4.95	22.24±2.95	0.071
	P value 0 vs 1**	**<0.001**	0.649	-
	P value 0 vs 2**	**0.003**	0.947	-
	P value 1 vs 2**	0.087	0.426	-

* p values were calculated using Independent t test, except for the sex, where Fisher Exact test was used.** p values for paired data was calculated using paired t test, to compare the baseline values (0) with either immediate post-injection (1) or 12 weeks later (2) values.

Disclosure of Interests: None declared
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POS0934

EFFICACY OF UPADACITINIB ON PSORIATIC ARTHRITIS WITH AXIAL INVOLVEMENT DEFINED BY INVESTIGATOR ASSESSMENT AND PRO-BASED CRITERIA: RESULTS FROM TWO PHASE 3 STUDIES

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Background: Patients with PsA and axial involvement have higher disease activity and greater reductions in quality of life;[1] however, there are no accepted criteria for identifying axial involvement in PsA.

Objectives: The objective of this post-hoc analysis is to assess the efficacy of upadacitinib (UPA), a Janus kinase inhibitor, on axial symptoms in patients with active PsA and axial involvement defined by investigator assessment and PRO-based criteria from two phase 3 SELECT trials.[2,3]

Methods: Patients with active PsA (≥3 swollen joints and ≥3 tender joints) and prior inadequate response or intolerance to ≥1 non-biologic (SELECT-PsA 1) or ≥1 biologic (SELECT-PsA 2) DMARD were randomly assigned to once daily oral UPA 15 mg or 30 mg, placebo (PBO), or every other week subcutaneous adalimumab (ADA) 40 mg (SELECT-PsA 1 only).[2,3] At baseline, axial involvement in PsA was determined by investigator assessment based on the totality of clinical information, such as duration and character of back pain, age of onset, and previous imaging. In addition to investigator assessment, PRO-based criteria for axial involvement (BASDAI ≥4 and BASDAI Question 2 ≥4 at baseline) were applied for this analysis to identify patients with active disease. Efficacy in the sub-group of patients defined using both investigator assessment and PRO-based criteria was evaluated at week 24 for UPA 15 mg vs PBO and ADA (SELECT-PsA 1 only). Data were analyzed using mixed-effect model repeated measures (MMRM) or non-responder imputation (NRI), with nominal *P*-values shown.

Results: Based on investigator assessment alone, 31.3% (n=534/1704) of patients in SELECT-PsA 1 and 34.2% (n=219/641) in SELECT-PsA 2 were defined as having axial involvement. When both investigator assessment and PRO-based criteria were applied, 23.1% (n=393/1704) of patients in SELECT-PsA 1, or 73.6% (n=393/534) of those defined using investigator assessment alone, and 27.5% (n=176/641) in SELECT-PsA 2, or 80.4% (n=176/219) using investigator assessment alone, met the combined criteria for axial involvement. In both studies, UPA 15 mg showed significantly greater clinical responses vs PBO at week 24 across all endpoints assessed (Figure 1). In SELECT-PsA 1, UPA showed numerically greater responses than ADA at week 24 across all BASDAI and Ankylosing Spondylitis Disease Activity Score (ASDAS) endpoints. The proportion of patients achieving ASDAS clinically important improvement (CII) at week 24 was significantly greater with UPA vs ADA based on nominal *P*-value.

Conclusion: Patients with active PsA and axial involvement defined by both investigator assessment and PRO-based criteria demonstrated statistically greater clinical responses related to their axial involvement with UPA 15 mg compared to PBO, and consistently numerically higher responses compared to ADA, at week 24 in the SELECT-PsA trials. Findings from this post-hoc analysis are consistent with previous data based on investigator assessment alone.[4]

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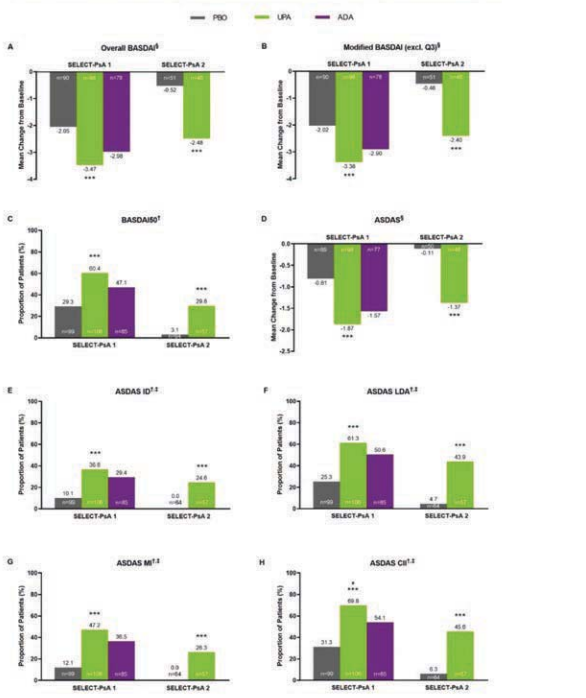
Figure: Clinical Responses in Patients with Axial Involvement Defined by Investigator Assessment and PRO-Based Criteria at Week 24 from SELECT-PsA 1 and SELECT-PsA 2



ADA, adalimumab; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CII, clinically important improvement; EOW, every other week; ID, inactive disease; LDA, low disease activity; MI, major improvement; MMRM, mixed-effect model repeated measures; NRI, non-responder imputation; PBO, placebo; QD, once daily; UPA, upadacitinib

***P<0.001, UPA 15 mg vs. PBO; *P<0.05, UPA 15mg vs. ADA; nominal *P*-values are presented and were not adjusted for multiple comparisons
[†]NRI analysis constructed using Cochran-Mantel-Haenszel test adjusting for the main stratification factor of current DMARD use (yes/no) was used for binary endpoints
[‡]ASDAS thresholds: ID <1.3; LDA <2.1; MI change from baseline ≥2; CII change from baseline ≥1.1
[§]MMRM analysis with unstructured variance-covariance matrix, including treatment, visit, treatment-by-visit interaction, the stratification factor current DMARD use (yes/no) as fixed factors and the continuous fixed covariate of baseline measurement was used for continuous endpoints

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Table 1. Efficacy data (BASDAI and ASDAS-CRP values)

		First line			Second or subsequent lines			All lines		
Index		**Baseline**	**1 year**	**2 or more**	**Baseline**	**1 year**	**2 or more**	**Baseline**	**1 year**	**2 or more**
Anti-TNF										
Female <45 n=240	BASDAI	5.6 (2.3)	3.3 (2.1)	3.2 (2.0)	5.4 (2.5)	3.7 (2.3)	3.5 (2.2)	5.5(2.4)	3.5 (2.2)	3.3 (2.1)
	ASDAS-CRP	3.7 (1.2)	2.0 (0.9)	2.1 (0.9)	3.2 (2.0)	1.9 (1.0)	1.9 (1.1)	3.4 (1.7)	1.9 (1.0)	2.0 (1.0)
Female >45 n=367	BASDAI	6.0 (1.9)	-	4.2 (2.6)	5.7 (2.3)	-	-	5.8 (2.2)	-	4.2 (2.6)
	ASDAS-CRP	3.9 (0.9)	-	1.8 (0.7)	3.3 (1.2)	-	-	3.6 (1.1)	-	1.8 (0.7)
Male n=1252	BASDAI	5.4 (2.1)	3.1 (2.1)	2.9 (1.9)	5.2 (2.4)	3.8 (2.5)	3.3 (2.3)	5.3 (2.3)	3.4 (2.3)	3.1 (2.1)
	ASDAS-CRP	3.3 (1.3)	1.9 (0.9)	1.8 (0.9)	3.0 (1.3)	2.0 (1.1)	2.2 (1.1)	3.2 (1.3)	1.9 (1.0)	1.9 (1.0)
CZP										
Female <45 n=35	BASDAI	5.5 (1.6)	3.0 (1.7)	1.3 (1.0)	5.2 (2.6)	3.9 (3.1)	2.9 (2.2)	5.3 (2.2)	3.5 (2.6)	2.2 (1.9)
	ASDAS-CRP	3.3 (0.5)	1.2 (0.5)	1.3 (1.1)	2.6 (1.1)	2.2 (1.2)	1.9 (0.7)	2.9 (0.9)	1.8 (1.1)	1.7 (0.8)
Female >45 n=25	BASDAI	6.7 (1.6)	-	-	6.4 (1.8)	-	-	6.4 (1.8)	-	
	ASDAS-CRP	-	-	-	3.5 (1.1)	-	-	3.5 (1.1)	-	
Male n=86	BASDAI	5.6 (2.3)	3.3 (2.0)	1.9 (2.0)	5.3 (2.4)	5.8 (1.8)	3.1 (2.7)	5.4 (2.3)	4.5 (2.3)	1.4 (2.3)
	ASDAS-CRP	2.4 (1.4)	2.2 (2.0)	1.5 (0.6)	3.1 (0.8)	2.8 (1.4)	2.1 (1.8)	2.8 (1.1)	2.4 (1.8)	1.7 (1.2)
Anti-IL17A										
Female <45 n=36	BASDAI	6.0 (1.4)	4.2 (2.0)	3.8 (1.7)	6.8 (2.2)	4.8 (2.3)	4.9 (2.6)	6.5 (1.9)	4.5 (2.1)	4.4 (2.2)
	ASDAS-CRP	3.6 (0.89)	1.8 (0.7)	1.6 (0.7)	3.3 (0.8)	2.0 (1.1)	1.8 (0.8)	3.4 (0.8)	1.9 (0.9)	1.7 (0.7)
Female >45 n=57	BASDAI	6.2 (1.8)	-	-	6.3 (1.8)	-	-	6.3 (1.8)		
	ASDAS-CRP	3.7 (1.2)	-	-	3.8 (2.0)	-	-	3.8 (1.8)		
Male n=205	BASDAI	5.5 (2.2)	2.9 (2.3)	3.7 (2.5)	5.8 (2.3)	4.3 (2.2)	3.6 (2.4)	5.7 (2.3)	3.8 (2.3)	3.6 (2.4)
	ASDAS-CRP	3.2 (0.9)	1.6 (1.0)	1.9 (0.8)	3.4 (1.2)	2.5 (1.0)	2.5 (1.0)	3.4 (1.1)	2.1 (1.1)	2.3 (1.0)

POS0935

HIGHER 5-YEAR SURVIVAL OF CERTOLIZUMAB PEGOL IN YOUNG WOMEN WITH AXIAL SPONDYLOARTHRITIS. BIOBADASER DATA

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Background: Certolizumab pegol (CZP) in women of childbearing age with rheumatoid arthritis has a more favorable response, suggesting a possible distinctive effect in this group[1,2].
Objectives: To evaluate the retention rate of CZP compared to other anti-TNFs and anti-IL17A in patients affected by axSpA, grouped according to gender and age
Methods: Cross-sectional study within the BIOBADASER registry. Patients older than 17 years old, with axSpA receiving anti-TNFs or anti-IL-17A were selected. Mean and standard deviations of ASDAS-CRP and BASDAI were performed at baseline, 1st and 2nd year of treatment. Patients were classified according to treatment into groups 1) CZP, 2) anti-TNF, and 3) anti-IL17A, and according to sex and age in the following groups: 1) women between 18 and 45 years old (young), 2) women over 45 years old (old), 3) men.
Results: Groups and gender distribution, treatment prescription, ASDAS-CRP and BASDAI values according to therapeutic line and demographical characteristics are shown in Table 1. Overall, young women treated with CZP showed remission or low activity during follow-up, compared to low activity for the rest of the molecules. A greater survival of CZP compared to other treatment groups was observed in young women. This difference was observed since the first year of treatment (71,4 (64.2-77.4) all antiTNF, 84.4 (66.4-93.2) CZP, 72.2 (53.2-84.5) antiIL17) and the magnitude was maintained during the first 5 years of follow-up (Figure 1). In older women, a higher retention rate was observed for both CZP and anti-IL17A compared to anti-TNFs (71.6 (65.4-76.8) in all antiTNF, 78.1 (54.9-90.3) in CZP, 75.3 (61.3-84.9) in antiIL17). In males there were no long-term differences (79.2(76.3-81.8) all antiTNF, 73.0 (62.0-81.4) CZP, 64.6 (57.3-71.0) antiIL17)

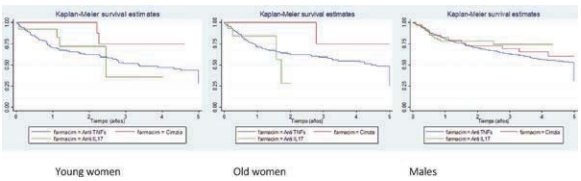

Figure 1. Five years retention rate (first line treatment)

Focussed on first line treatment, the differences were greater in young women. The second and subsequent lines showed the same trends with a lesser extend. Globally, we do not observe these differences in men.
Conclusion: These data suggest a possible specific effect of Certolizumab Pegol in women with axial spondyloarthritis, especially in young women and when used as first line treatment.

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POS0936

DISEASE TRAJECTORIES OF AXIAL SPONDYLOARTHRITIS PATIENTS INITIATED ON BIOLOGIC DMARDS: PRELIMINARY ANALYSIS FROM A REAL-WORLD COHORT

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Background: The number of biologic/targeted synthetic (b/ts) disease-modifying anti-rheumatic drugs (DMARDs) available for the treatment of axial spondyloarthritis (axSpA) are increasing. However, 1 in 4 axSpA patients may discontinue their first bDMARD within the first 12-months (1). A greater understanding of real-world axSpA disease/treatment trajectories pre- and post-bDMARD initiation is needed to inform optimal treatment for patients.
Objectives: To explore the use of biologic therapies in patients living with axSpA, and estimate the natural progression of disease and patient reported measures pre- and post- initiation of first bDMARD.
Methods: Data was extracted from the Bath SpA Research Biobank for all bio-naïve axSpA patients initiated on bDMARDs between 7th March 2000 and 1st February 2021. Patients were grouped based on first bDMARD. Linear regression models were used to explore changes in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and Bath Ankylosing Spondylitis Functional Index (BASFI) over time; from 36-months before first bDMARD initiation, to 36-months after initiation. Changes in BASDAI/BASFI were estimated using piecewise mixed-effects linear regression. Models included fixed terms for age, sex, HLA-B27 status and disease duration. Switches to a second bDMARD and reasons for switching were captured.
Results: In total, 282 axSpA patients were included, and grouped into 3 cohorts based on first bDMARD: adalimumab (46.1%), etanercept (30.9%), other (23.1%; 6.4% certolizumab pegol, 5.0% golimumab, 5.3% infliximab, 0.7% rituximab, 5.7% secukinumab). Mean age at diagnosis was 30.7 (SD 11.3), 69.9% of patients were male, 11.0% diagnosed with non-radiographic axSpA and 85.3% HLA-B27 positive. In the 36-month period before bDMARD initiation, patients on average had a BASDAI score of 4.50 (95% CI 4.21-4.79) and BASFI of 4.02 (95% CI 3.68-4.38), with a linear and statistically significant worsening of 0.56 (95% CI 0.43-0.68) per year for the BASDAI and 0.55 (95% CI 0.41-0.69) for the BASFI (minimally clinically important difference defined as 1.1 and 0.6 for BASDAI and BASFI, respectively (2)). Following bDMARD initiation, patients indicated a statistically significant reduction in BASDAI to 3.13 (95% CI 2.82-3.45), 3.23 (95% CI 2.83-3.63) and 3.46 (95% CI 3.04-3.88) and reductions in the BASFI to 3.22 (95% CI 2.86-3.60), 3.06 (95% CI 2.61-3.53) and 3.64 (95% CI 3.16-4.12) for those treated with adalimumab, etanercept or other biologics respectively. Reduced scores were maintained over 36-months post initiation (Figure 1). Details of first and second bDMARD are outlined in Table 1. Reasons for switching were switch to biosimilar (32.4%), intolerance (25.1%), inefficacy (22.2%), malignancy (1.9%) or other (18.4%).

Table 1. ***First and second bDMARD***

	Second bDMARD		
First bDMARD	**Adalimumab**	**Etanercept**	**Other**
Adalimumab	59 (57.3%)	22 (21.4%)	22 (21.4%)
Etanercept	28 (40.6%)	37 (53.6%)	4 (5.8%)
Other	15 (48.4%)	8 (25.8%)	8 (25.8%)

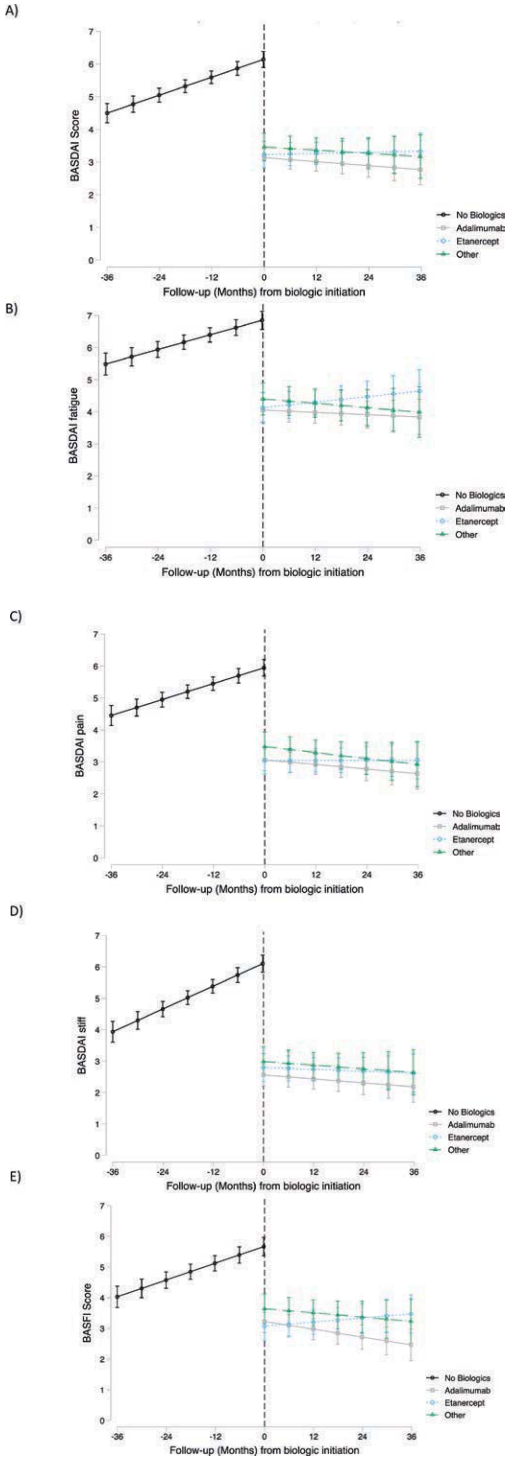

Figure 1. Predictive margins of BASDAI and BASFI 36-months pre- and post- bDMARD initiation*A-E, Predictive margins of the BASDAI score (overall – all components, A); BASDAI Q1 fatigue (B); BASDAI average of Q2-Q4 spinal pain, joint pain, enthesitis (C); BASDAI average of Q5-Q6 morning stiffness (D); and BASFI (E).*

Conclusion: In our study population, there was clinically meaningful worsening of disease activity over 36-months prior to initiation of first bDMARD, despite baseline (36-months prior to first bDMARD initiation) BASDAI exceeding the current threshold for bDMARD treatment (BASDAI≥4). A clinically meaningful and maintained improvement in disease activity was reported across all cohorts in the 36-months following first bDMARD initiation.

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POS0937

MEASURE 2: SECUKINUMAB PROVIDES RAPID AND SUSTAINED RELIEF FROM KEY CLINICAL SYMPTOMS OF ACTIVE ANKYLOSING SPONDYLITIS IN TNFI-NAÏVE PATIENTS THROUGH 5 YEARS

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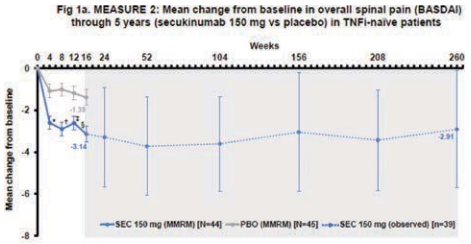
Background: Ankylosing spondylitis (AS) is a chronic, inflammatory disease resulting in debilitating clinical symptoms such as pain (70–83%), stiffness (54–90%) and fatigue (53–62%).[1-3] Secukinumab (SEC 150 mg) has demonstrated long-term efficacy across multiple indications and is approved for the treatment of active AS in adults who have had an inadequate response to NSAIDs.[4,5]

Objectives: The Phase 3 MEASURE 2 trial (NCT01649375) assessed long-term efficacy, safety and tolerability of SEC in patients (pts) with active AS. This post-hoc analysis was conducted specifically to evaluate long-term efficacy of SEC 150 mg on key clinical symptoms of pain, morning stiffness, physical function and fatigue in TNFi-naïve pts over 5 years.

Methods: The MEASURE 2 study design has been reported previously.[5] This post-hoc analysis evaluated key clinical symptoms at baseline through Wk 260. Assessments included total and nocturnal back pain (visual analogue scale [0–100 mm]), overall spinal pain (neck, back, or hip) from BASDAI, and morning stiffness (average BASDAI). Physical function (SF-36 PCS, BASFI), fatigue (BASDAI, FACIT) and disease activity (ASDAS-CRP) are also reported. Data are presented as LS mean change (± SE) using mixed model repeated measures from Wks 4–16 and observed data (mean ± SD) from Wks 24–260.

Results: Of TNFi-naïve pts randomised to SEC 150 mg, 89 were included (SEC, n=44, placebo [PBO], n=45) in this analysis. Of these pts randomised to SEC 150 mg, 84% completed 5 years of treatment. Significantly greater improvements were observed in pts treated with SEC 150 mg vs PBO at Wk 16 and were sustained through 5 years (Figure 1; Table 1).



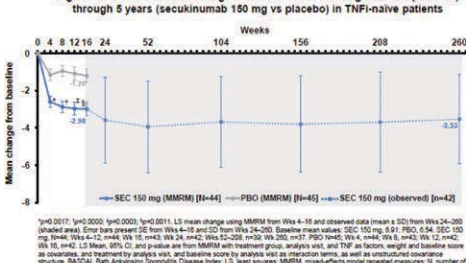


Table 1. Pain, physical function and fatigue scores

Endpoint	Treatment	BL mean ± SD*	Wk 16 LS mean, SE (*p*-value)	Wk 52 ± SD	Wk 104 ± SD	Wk 156 ± SD	Wk 208 ± SD	Wk 260 ± SD
BACK PAIN								
Total back pain	SEC	66.86 ± 15.42	-33.99, 3.42 (*p*=0.0000)	-40.56 ± 24.35	-37.74 ± 26.09	-39.03 ± 26.65	-37.77 ± 28.40	-36.78 ± 29.76
	PBO	67.69 ± 17.71	-12.75, 3.46	NA	NA	NA	NA	NA
Nocturnal back pain	SEC	66.84 ± 14.17	-36.25, 3.50 (*p*=0.0000)	-45.13 ± 23.92	-40.54 ± 25.23	-43.92 ± 25.10	-41.13 ± 24.87	-38.95 ± 28.91
	PBO	63.87 ± 18.78	-14.41, 3.54	NA	NA	NA	NA	NA
PHYSICAL FUNCTION								
SF-36 PCS	SEC	34.87 ± 6.58	7.90, 0.98 (*p*=0.0012)	8.44 ± 7.48	8.95 ± 7.87	8.98 ± 8.17	9.39 ± 8.39	8.55 ± 9.32
	PBO	35.45 ± 6.51	3.23, 0.98	NA	NA	NA	NA	NA
BASFI	SEC	6.42 ± 1.95	-2.89, 0.31 (*p*=0.0002)	-3.38 ± 2.38	-3.23 ± 2.39	-3.10 ± 2.49	-3.10 ± 2.47	-2.86 ± 2.61
	PBO	6.34 ± 1.99	-1.18, 0.32	NA	NA	NA	NA	NA
FATIGUE								
Overall level (BASDAI)	SEC	7.00 ± 1.26	-2.39, 0.34 (*p*=0.0095)	-3.44 ± 2.32	-3.30 ± 2.45	-3.16 ± 2.61	-3.12 ± 2.34	-2.92 ± 2.71
	PBO	7.18 ± 1.49	-1.12, 0.34	NA	NA	NA	NA	NA
FACIT	SEC	22.27 ± 8.02	10.62, 1.26 (*p*=0.0052)	12.14 ± 9.76	11.00 ± 9.37	10.79 ± 8.91	12.39 ± 9.09	10.64 ± 10.66
	PBO	23.22 ± 7.94	5.48, 1.26	NA	NA	NA	NA	NA
DISEASE ACTIVITY								
ASDAS-CRP	SEC	3.73 ± 0.82	-1.47, 0.14 (*p*=0.0000)	-1.80 ± 1.16	-1.66 ± 1.21	-1.63 ± 1.35	-1.69 ± 1.24	-1.58 ± 1.36
	PBO	3.89 ± 0.76	-0.51, 0.14	NA	NA	NA	NA	NA

*Baseline refers to mean ± SD of observed values. LS mean change using MMRM for Wk 16 and observed data (mean ± SD) from Wks 24–260. SEC 150 mg, N=44 and PBO, N=45. ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score - C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BL, baseline; FACIT, Functional Assessment of Chronic Illness Therapy; LS, least square; MMRM, mixed-effects model repeated measures; NA, not available; PBO, placebo; SD, standard deviation; SEC, secukinumab; SF-36 PCS, Short Form-36 Physical Component Summary; Wk, week.

Conclusion: TNFi-naïve pts with active AS treated with SEC 150 mg experienced rapid improvements across a range of key clinical symptoms including pain, physical function and fatigue measures, that were sustained through 5 years.

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POS0938

MAINTENANCE OF RESPONSE TO BIMEKIZUMAB OVER 3 YEARS OF TREATMENT IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: POST HOC ANALYSES FROM THE BE AGILE STUDY AND ITS OPEN-LABEL EXTENSION

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Background: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL17A, has demonstrated significant and rapid efficacy in patients (pts) with active ankylosing spondylitis (AS) treated for up to 48 weeks (wks) in the phase 2b BE AGILE study.[1] Maintaining stringent disease control is an internationally recognised treatment target in spondyloarthritis and a relevant goal in clinical research.[2]

Objectives: To report on the maintenance of clinical response, including the achievement of sustained remission or low disease activity (LDA), to support and extend previous findings on the long-term efficacy of BKZ in pts with active AS treated for up to 3 years (yrs) in BE AGILE and its open-label extension (OLE).[3]

Methods: Study design of the 48-wk BE AGILE study (NCT02963506) and its ongoing 4-yr OLE (NCT03355573) have been reported previously.[1,3] During the OLE, pts received BKZ 160 mg every 4 wks (Q4W) regardless of prior dosing. In this post hoc study, maintenance of response analyses through 156 wks were conducted for Ankylosing Spondylitis Disease Activity Score (ASDAS) <2.1 and Assessment in SpondyloArthritis international Society 40 (ASAS40) response. ASDAS <2.1 includes both ASDAS-LDA (1.3–<2.1) and ASDAS inactive disease (ID; <1.3). Data from pts randomised at baseline to BKZ 160 mg and 320 mg Q4W were used for these analyses. ASDAS and the ASAS components were assessed at every study visit to Wk 24, then every 12 wks. All reported analyses are observed case.

Results: At baseline, 121/303 pts were randomised to BKZ 160 mg (n=60) or 320 mg (n=61). Overall, 36/121 (29.8%) had ASDAS high disease (HD) and 84/121 (69.4%) had very high disease (VHD) activity. At Wk 12, 48/119 (40.3%) had achieved ASDAS <2.1, increasing further to 66/111 (59.5%) at Wk 48 and 63/93 (67.7%) at Wk 156, of which 32 pts (32/63; 50.8%) had ID. Improvement in ASDAS was consistent across both BKZ 160 mg and 320 mg groups, with treatment response levels maintained following dose reduction to 160 mg at Wk 48 in the 320 mg group (Figure 1). Of those pts who achieved ASDAS <2.1 at Wk 12 across both groups, 33/37 (89.2%) maintained ASDAS <2.1 at Wk 156. In the most stringent maintenance of response analysis, 24/37 (64.9%) pts who achieved ASDAS <2.1 at Wk 12 maintained this state at every ASDAS assessment during Wks 12–156. Efficacy measured by ASAS40 response was also sustained over 3 years, with 56/119 (47.1%) pts having achieved ASAS40 at Wk 12, 72/111 (64.9%) at Wk 48 and 69/96 (71.9%) at Wk 156. In line with ASDAS <2.1, of those pts who achieved ASAS40 at Wk 12, 44/47 (93.6%) maintained ASAS40 at Wk 156, and 36/47 (76.6%) had maintained ASAS40 at every assessment during Wks 12–156.

Conclusion: BKZ 160 mg Q4W provided a robust maintenance of disease control over 3 yrs in pts with active AS who initially responded at Wk 12, irrespective of the initial dosing regimen (BKZ 160 mg or 320 mg Q4W).

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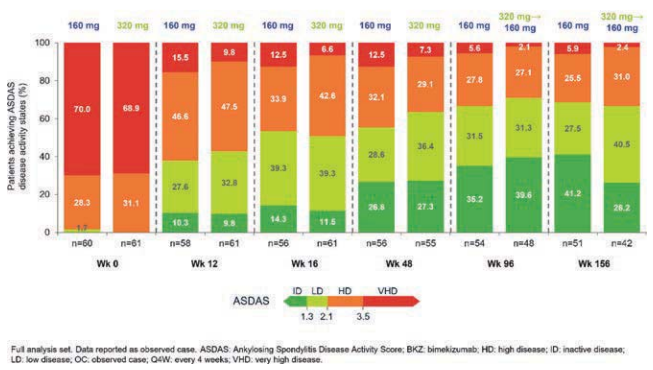
[1] van der Heijde D. Ann Rheum Dis 2020;79:595–604; 2. Smolen J. Ann Rheum Dis 2018;77:3–17; 3. Gensler L. Arthritis Rheumatol 2021;73(suppl 10):0491.

Figure. ASDAS disease activity states across Wks 0–156 for pts randomised to BKZ 160 mg and 320 mg Q4W at baseline



Full analysis set. Data reported as observed case. ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; HD: high disease; ID: inactive disease; LD: low disease; OC: observed case; Q4W: every 4 weeks; VHD: very high disease.

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Disclosure of Interests: Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie and Novartis, Martin Rudwaleit Speakers bureau: AbbVie, BMS, Boehringer Ingelheim, Chugai, Eli Lilly, Janssen, Novartis, Pfizer, UCB Pharma, Paid instructor for: Janssen, Novartis, UCB Pharma, Consultant of: AbbVie, Novartis, UCB Pharma, Natasha de Peyrecave Employee of: UCB Pharma, Carmen Fleurinck Employee of: UCB Pharma, Marga Oortgiesen Employee of: UCB Pharma, Vanessa Taieb Employee of: UCB Pharma, Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Paid instructor for: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma
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POS0939

BIMEKIZUMAB IN PATIENTS WITH ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 24-WEEK EFFICACY & SAFETY FROM BE MOBILE 1, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED STUDY

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Background: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. BKZ has shown rapid and sustained efficacy and was well tolerated up to 156 weeks (wks) in a phase 2b study in patients (pts) with active ankylosing spondylitis.[1,2]
Objectives: To assess efficacy and safety of BKZ vs placebo (PBO) in pts with active non-radiographic axial spondyloarthritis (nr-axSpA) up to Wk 24 in the ongoing pivotal phase 3 study, BE MOBILE 1.
Methods: BE MOBILE 1 (NCT03928704) comprises a 16-wk double-blind, PBO-controlled period and 36-wk maintenance period. Pts were aged ≥18 yrs, had BASDAI ≥4 and spinal pain ≥4 at BL, and sacroiliitis on MRI and/or elevated CRP at screening. Pts were randomised 1:1, BKZ 160 mg Q4W:PBO. From Wk 16, all pts received BKZ 160 mg Q4W. Primary and secondary efficacy endpoints were assessed at Wk 16.
Results: Of 254 randomised pts (BKZ: 128; PBO: 126), 244 (96.1%) completed Wk 16, 240 (94.5%) Wk 24. BL characteristics were comparable between groups: mean age 39.4 yrs, symptom duration 9.0 yrs; 54.3% pts male, 77.6% HLA-B27+, 10.6% TNFi-experienced. At Wk 16, the primary (ASAS40: 47.7% BKZ vs 21.4% PBO; p<0.001) and all ranked secondary endpoints were met (Table 1). Responses were rapid with BKZ, including in PBO pts who switched to BKZ at Wk 16, and increased to Wk 24 (Figure 1; Table 1). Substantial reductions of hs-CRP by Wk 2 and MRI SIJ inflammation by Wk 16 were achieved with BKZ vs PBO (Table 1). At Wk 24, >50% of pts initially randomised to BKZ had achieved ASDAS <2.1 (Figure 1).
Over 16 wks, 80/128 (62.5%) pts had ≥1 TEAE on BKZ vs 71/126 (56.3%) on PBO; most frequent were nasopharyngitis (BKZ: 9.4%; PBO: 4.8%), upper respiratory tract infection (BKZ: 7.0%; PBO: 7.1%) and oral candidiasis (BKZ: 3.1%; PBO: 0%). No systemic candidiasis was observed. Up to 16 wks, incidence of SAEs was low (BKZ: 0.0%; PBO: 0.8%); no MACE or deaths were reported; 0 IBD cases occurred in pts on BKZ vs 1 (0.8%) in a pt on PBO.
Conclusion: Dual inhibition of IL-17A and IL-17F with BKZ in pts with active nr-axSpA resulted in rapid, clinically relevant improvements in efficacy outcomes vs PBO. No new safety signals were observed.[1,2]

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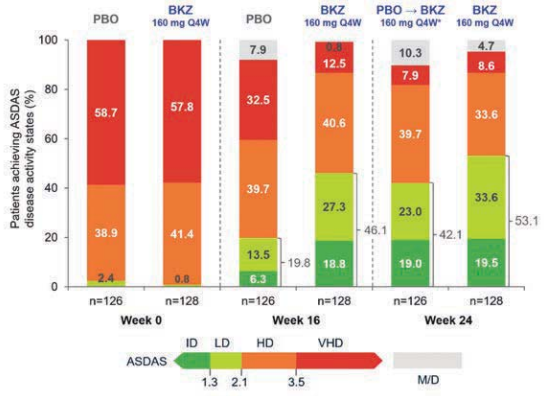
[1]van der Heijde D. Ann Rheum Dis 2020;79:595–604;
[2] Gensler L. Arthritis Rheumatol 2021;73(suppl 10):0491.

Figure. ASDAS states over time



Randomised set. Data reported as observed case. *At Wk 16, pts on PBO switched to BKZ.

Abbreviations: ASAS20/40: Assessment of SpondyloArthritis international Society 20/40 response; ASAS PR: ASAS partial remission; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS-MI: ASDAS major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; CRP: C-reactive protein; HD: high disease; HLA-B27: human leukocyte antigen B27; hs-CRP: high sensitivity-CRP; IBD: inflammatory bowel disease; ID: inactive disease; IL: interleukin; LD: low disease; M/D: missing data; MACE: major adverse cardiovascular event; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MI: multiple imputation; MRI: magnetic resonance imaging; n: number; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; OC: observed case; PBO: placebo; Pts: patients; Q4W: every four weeks; SAE: serious adverse event; SD: standard deviation; SE: standard error; SPARRC: Spondyloarthritis Research Consortium of Canada; SIJ: Sacroiliac Joints; SF-36 PCS: Short Form-36 Physical Component Summary; TNFi: tumour necrosis factor inhibitor; VHD: very high disease; Wks: weeks; yr: year.

Table 1. Efficacy at Wks 16 and 24

		BL		Wk 16			Wk 24	
		PBO N=126	BKZ 160 mg Q4W N=128	PBO N=126	BKZ 160 mg Q4W N=128	p value	PBO→BKZ 160 mg Q4W N=126	BKZ 160 mg Q4W N=128
Ranked endpoints in hierarchical order	**ASAS40*** [NRI] n (%)	-	-	27 (21.4)	61 (47.7)	<0.001	59 (46.8)	67 (52.3)
	BASDAI CfB† [MI] mean (SE)	6.7 (0.1)	6.9 (0.1)	–1.5 (0.2)	–3.1 (0.2)	<0.001	–3.2 (0.2)	–3.4 (0.2)
	ASAS20† [NRI] n (%)	-	-	48 (38.1)	88 (68.8)	<0.001	87 (69.0)	96 (75.0)
	ASAS PR† [NRI] n (%)	-	-	9 (7.1)	33 (25.8)	<0.001	35 (27.8)	37 (28.9)
	ASDAS-MI† [NRI] n (%)	-	-	9 (7.1)	35 (27.3)	<0.001	37 (29.4)	41 (32.0)
	ASAS 5/6† [NRI] n (%)	-	-	21 (16.7)	49 (38.3)	<0.001	51 (40.5)	57 (44.5)
	BASFI CfB† [MI] mean (SE)	5.3 (0.2)	5.5 (0.2)	–1.0 (0.2)	–2.5 (0.2)	<0.001	–2.3 (0.2)	–2.8 (0.2)
	Nocturnal spinal pain CfB† [MI] mean (SE)	6.7 (0.2)	6.9 (0.2)	–1.7 (0.2)	–3.6 (0.3)	<0.001	–3.5 (0.2)	–4.0 (0.3)
	ASQoL CfB† [MI] mean (SE)	9.4 (0.4)	9.5 (0.4)	–2.5 (0.4)	–5.2 (0.4)	<0.001	–4.8 (0.4)	–5.7 (0.4)
	SF-36 PCS CfB† [MI] mean (SE)	33.6 (0.8)	33.3 (0.7)	5.5 (0.7)	9.5 (0.7)	<0.001	10.1 (0.8)	10.6 (0.8)
Other endpoints[d]	**Enthesitis-free state†[a]** [NRI] n (%)	-	-	22 (23.9)[b]	48 (51.1)[c]	-	40 (43.5)[b]	45 (47.9)[c]
	ASAS40 in TNFi-experienced [NRI] n (%)	-	-	2 (11.8)[e]	6 (60.0)[f]	-	-	-
	ASDAS-CRP CfB [MI] mean (SE)	3.7 (0.1)	3.8 (0.1)	–0.6 (0.1)	–1.5 (0.1)	-	–1.5 (0.1)	–1.6 (0.1)
	hs-CRP, mg/L [MI] geometric mean (median)	5.0 (6.5)	4.6 (6.1)	3.8 (4.1)	2.0 (1.8)	-	2.3 (2.6)	1.9 (1.8)
	MRI spine Berlin CfB[g] [OC] mean (SD)	1.9 (3.2)[h]	1.6 (2.9)[i]	–0.1 (1.7)[j]	–0.7 (2.2)[k]	-	-	-
	SPARCC MRI SIJ score CfB[g] [OC] mean (SD)	10.5 (13.8)[l]	8.5 (10.3)[m]	–1.5 (9.2)[n]	–6.3 (10.0)[o]	-	-	-

Randomised set. *Primary endpoint; †Secondary endpoint; [a]MASES=0 in pts with BL MASES >0; [b]n=92; [c]n=94; [d]Nominal p values not shown; [e]n=17; [f]n=10; [g]In pts in MRI sub-study; [h]n=65; [i]n=75; [j]n=58; [k]n=73; [l]n=68; [m]n=79; [n]n=60; [o]n=77.

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POS0940

FACTORS ASSOCIATED WITH LONG-TERM RETENTION OF TREATMENT WITH GOLIMUMAB IN A LARGE COHORT OF PATIENTS WITH RHEUMATIC DISEASES, WITH UP TO 8 YEARS OF FOLLOW-UP

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Background: The long-term retention rate of a biological drug is a surrogate marker of its effectiveness and tolerability.

Objectives: We assessed the probability of golimumab retention (persistence or drug survival) and the associated factors in a large cohort of patients with rheumatic diseases, with up to 8 years of follow-up.

Methods: This was an analysis of the BIOBADASER database (Spanish registry of biological drugs of the Spanish Society of Rheumatology and the Spanish Medicines Agency) on all adult patients who had initiated golimumab for treating rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (SpA). The probability of golimumab retention was assessed with the Kaplan-Meier method, differences between groups with the log-rank test, and factors related to retention with a Cox-regression model. Patients were right-censored if they were still treated with golimumab at the last observation for data analysis.

Results: A total of 885 patients were included, of whom 59 had received golimumab in 2 separate cycles (with a grace period of 3 months), totaling 944 cycles of treatment (286 RA, 396 axial SpA and 262 PsA). At golimumab initiation, mean (SD) age was 52 (13) years, 54% were women and median duration of disease was 7.6 (2.8-14.4) years. Golimumab was prescribed as first, second and third/subsequent biological drug in 313 (33%), 303 (32%) and 328 (35%) treatments. Concomitant medications at golimumab initiation included methotrexate (MTX) (32%), steroids (29%), leflunomide (13%) and sulphasalazine (6%). The probability of retention of golimumab since treatment initiation was 71% (95% confidence interval [CI]: 68 – 74) at year 1, 60% (95% CI: 57-63) at year 2, 54% (95% CI: 51-58) at year 3, 48% (95% CI: 44-51) at year 4, 44% (95% CI: 40-48) at year 5, 41% (95% CI: 37-45) at year 6 and 38% (95% CI: 33-42) at year 7 and at year 8. In bivariate analysis, the retention rate was higher when golimumab was used as first biological agent (p log-rank <0.001), in patients with axial SpA or PsA compared to RA (p <0.001, Figure 1) in men (p<0.001) and in those not using steroids (p<0.001). As first biological drug the probability of retention was 82% at year 1 and 50% at year 7. As second, it was 70% at year 1 and 35% at year 8, and at third/further, 62% (year 1) and 28% (year 8). Cox-regression analysis (Table 1) showed that golimumab retention was positively associated to use as first vs second or third biological, to axial SpA or PsA compared to RA and to use of methotrexate, and inversely to corticosteroid use and to disease activity over the median at golimumab initiation.

Table 1. Cox-regression analysis. Hazard Ratio for discontinuation of golimumab

	Hazard Ratio	95% Confidence interval	p
Age at golimumab initiation	1.01	1.00-1.02	0.063
Gender (women vs men)	1.23	0.98-1.55	0.079
Axial SpA vs RA	0.59	0.44-0.80	<0.001
PsA vs RA	0.67	0.51-0.89	0.005
Second vs first biological drug	1.52	1.17-1.97	0.002
Third or further vs first biological drug	1.79	1.38-2.32	<0.001
Corticosteroids	1.46	1.16-1.85	0.001
Methotrexate	0.79	0.63-0.99	0.041
Disease activity over the median*	1.29	1.05-1.59	0.015

*DAS28 > 4.3 (RA, PsA) or BASDAI > 5.6 (axial SpA) at golimumab initiation

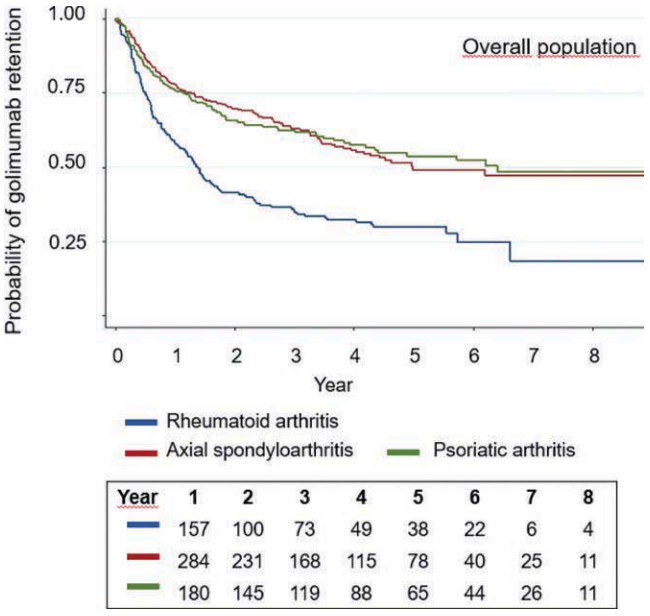

Figure 1.

Conclusion: This study provides new information on long-term golimumab effectiveness for the treatment or rheumatic diseases, with retention rates of 71% at year 1, 44% at year 5 and 38% at year 8. The probability of golimumab retention was higher as first biological drug, in patients with PsA or axial SpA and in those treated with methotrexate, and lower in those treated with steroids or with higher disease activity at golimumab initiation.

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POS0941

LONG-TERM CLINICAL OUTCOMES OF CERTOLIZUMAB PEGOL TREATMENT IN PATIENTS WITH ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS STRATIFIED BY BASELINE MRI AND C-REACTIVE PROTEIN STATUS

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Background: Certolizumab pegol (CZP) has demonstrated clinical efficacy in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) and objective signs of inflammation during the 52-week (wk) placebo (PBO)-controlled period and 104 wk open-label (OL) safety follow-up extension (SFE) of the C-axSpAnd study.[1] There is, however, a paucity of data on the long-term efficacy of biologics in nr-axSpA according to patients' baseline MRI and C-reactive protein (CRP) status.

Objectives: This post hoc analysis from C-axSpAnd aimed to evaluate whether patients' baseline MRI and CRP status impacted long-term (3-year) clinical responses to CZP.

Methods: C-axSpAnd (NCT02552212) was a 3-year, phase 3, multicentre study. Adults (N=317) with nr-axSpA fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria and objective signs of inflammation (CRP ≥ upper limit of normal (10 mg/L) [CRP+] and/or evidence of sacroiliitis on MRI [MRI+])[2] were randomised 1:1 to PBO or CZP (400 mg at Wks 0, 2 and 4, then 200 mg every 2 wks [Q2W]) for 52 wks.[3] Those enrolled into the SFE received OL CZP (200 mg Q2W) for an additional 104 wks. Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) alongside the percentage of patients achieving ASDAS major improvement (ASDAS-MI, C-axSpAnd primary outcome) and ASAS 40% response (ASAS40) at Wks 52 and 156 were assessed according to prespecified subgroups based on MRI/CRP status (MRI+/CRP+, MRI–/CRP+, MRI+/CRP–). All data are reported as observed case.

Results: 243/317 (76.7%) patients entered the SFE, 120 from the group initially randomised to CZP (36 MRI+/CRP+, 32 MRI–/CRP+ and 52 MRI+/CRP–) and 123 from the initial PBO group (30 MRI+/CRP+, 34 MRI–/CRP+ and 59 MRI+/CRP–; 75/123 had switched to OL treatment in the 52 wk double-blind phase). 206/243 completed the SFE; 102/120 (85.0%) from the group initially randomised to CZP, 104/123 (84.6%) from the initial PBO group. Among CZP-randomised patients, mean ASDAS was similar between timepoints (MRI+/CRP+: 1.6 at Wk 52 vs 1.6 at Wk 156; MRI–/CRP+: 2.1 vs 2.2; MRI+/CRP–: 1.7 vs 1.6), the percentage achieving ASDAS-MI was lower at Wk 156 compared to Wk 52 across all subgroups (Figure 1 **A**). Patients initially randomised to PBO showed improvements in mean ASDAS over time (MRI+/CRP+: 2.1 Wk 52 vs 1.8 Wk 156; MRI–/CRP+: 2.2 vs 1.9; MRI+/CRP–: 2.0 vs 1.7) and a sustained proportion of patients achieved ASDAS-MI. Similar results were shown for BASDAI, with mean scores for CZP-randomised patients sustained from Wk 52 to Wk 156 across all subgroups (Figure 1 **B**). Mean BASDAI decreased (indicative of clinical improvements) from Wk 52 to Wk 156 in patients initially randomised to PBO, at which point the values aligned with those reported for the CZP-randomised group. In CZP-randomised patients, ASAS40 responses were sustained at Wk 156 compared to Wk 52. An increased percentage of patients achieved ASAS40 in all MRI/CRP subgroups initially randomised to PBO at Wk 156 compared to Wk 52 (Figure 1 **C**).

Conclusion: In this analysis of patients with nr-axSpA and objective signs of inflammation, long-term clinical outcomes achieved after 1 year were generally sustained at 3 years across MRI+/CRP+, MRI–/CRP+ and MRI+/CRP– subgroups; ASDAS-MI was numerically highest in the MRI+/CRP+ subgroup.

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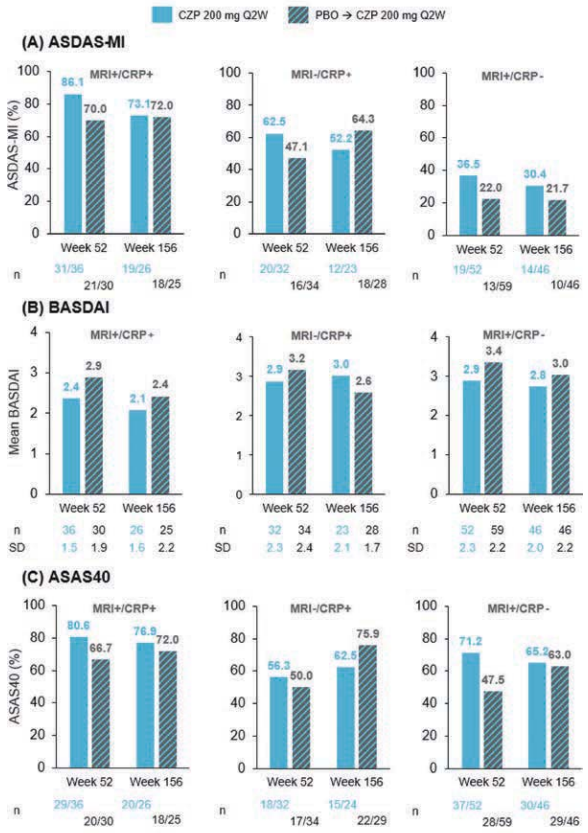
Figure. Clinical outcomes by MRI/CRP subgroup



Data reported as observed case. ASAS40: Assessment of SpondyloArthritis international Society ≥40% improvement; ASDAS -MI: Ankylosing Spondylitis Disease Activity Score Major Improvement (reduction of ≥2 units from baseline); ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; CZP: certolizumab pegol; Q2W: every 2 weeks.

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Pharma, Employee of: Employee of UCB Pharma, Lars Bauer Shareholder of: Stockholder of UCB Pharma, Employee of: Employee of UCB Pharma, Thomas Kumke Shareholder of: Stockholder of UCB Pharma, Employee of: Employee of UCB Pharma, Mindy Kim Shareholder of: Stockholder of UCB Pharma, Employee of: Employee of UCB Pharma, Atul Deodhar Speakers bureau: Speaker for Janssen, Novartis and Pfizer, Consultant of: Consulting fees from AbbVie, Amgen, Aurinia, Bristol Myers Squibb, Celgene, Eli Lilly, GSK, Janssen, MoonLake, Novartis, Pfizer and UCB Pharma, Grant/research support from: Research grants from AbbVie, Eli Lilly, GSK, Novartis, Pfizer and UCB Pharma

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POS0942 DEVELOPMENT OF PREDICTION MODEL FOR FLARE AFTER TAPERING OF TNF INHIBITORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Tumor necrosis factor inhibitors (TNFi) have become a mainstay of management for axial spondyloarthritis (axSpA). However, it remains unclear whether patients with axSpA should continue the standard-dose TNFi after achieving stable disease activity. Although complete discontinuation of TNFi is followed by early relapse in most cases, several studies documented that reduced doses of TNFi in patients with prolonged low disease activity showed similar effects on disease control and drug survival compared to standard dose of TNFi. One of the main problem in the dose-tapering strategies for TNFi is a selection of the appropriate patient. However, there has been a lack of robust evidence regarding clinical factors predicting the flare after tapering of TNFi in patients with axSpA.

Objectives: This study aims to develop and validate the prediction model to select the patients in whom tapering of TNFi does not lead to flare.

Methods: We used the data from Korean College of Rheumatology Biologics registry, which included a total of 1,730 patients receiving biologic DMARD from 2017 to 2019 in South Korea. In this study, a total of 526 patients who were initially treated with the standard-dose TNFi and tapered the dose after at least 1 year of the treatment were analyzed. Dose quotient (DQ, 0-1) was applied to quantified TNFi used during interval. The main outcome was an occurrence of flare defined as ASDAS-CRP score of ≥2.1 after 1 year of tapering TNFi. To develop the prediction model, clinical factors having relevant association ($p < 0.1$) with the outcome were first selected as candidate predictors. Logistic regression using a stepwise approach through backward elimination was used for the final model.

Results: Patients' mean (SD) age was 37.5 (11.9) years, 418 (79.5%) were men, and 474 (90.1%) were HLA-B27 positive. Mean disease duration was 5.0 (6.1) years and 433 (82.3%) were TNF naïve. The mean BASFI and ASDAS-CRP at baseline were 3.4 (2.6) and 3.7 (1.0), respectively. Approximately two-thirds of the patients (65.8%) were initiated TNFi tapering at the first 1 or 2 years from baseline. At the time of TNFi tapering, the mean DQ was 0.67 (0.15) and 381 (72.4%) were prescribed concurrently with NSAIDs, and the mean BASFI and ASDAS-CRP were 1.3 (1.8) and 1.6 (0.9), respectively. During 12 months of follow up starting from the TNFi tapering, 127 (24.1%) experienced the flare. The multivariable analysis revealed that HLA-B27 positivity (OR 0.337; 95% CI 0.161-0.705; p=0.004), inflammatory back pain (OR 2.920; 95% CI 1.283-6.648; p=0.011), ASDAS-CRP at tapering (OR 2.798; 95% CI 2.030-3.856; p<0.001), and BASFI at tapering (OR 1.214; 95% CI 1.051-1.402; p=0.008) were significantly associated with flare. Based on the results of the logistic regression analysis, the predicted probability was calculated by the following formula: P=1/[1+ exp{-(1.088 x HLA-B27 negativity + 1.072 x inflammatory back pain + 1.567 x psoriasis + 0.623 x family history of axSpA + 1.092 x diabetes mellitus + 0.435 x DQ at TNFi tapering + 1.029 x ASDAS-CRP at TNFi tapering + 0.194 x BASFI at TNFi tapering)}]. The best cut-off value of the model to define the flare was 0.2416 (95% CI 0.176, 0.301) with sensitivity 74.0% and with specificity 81.0%. AUC was 0.828 (95% CI 0.786-0.869) indicating a good predication (Figure 1). The internal validation with bootstrapping showed minimal overfitting (estimated AUC 0.794) and good calibration between observed and predicted values (calibration slope 1.110, 95% CI 0.903, 1.317; intercept 0.026, 95% CI -0.091, 0.039).

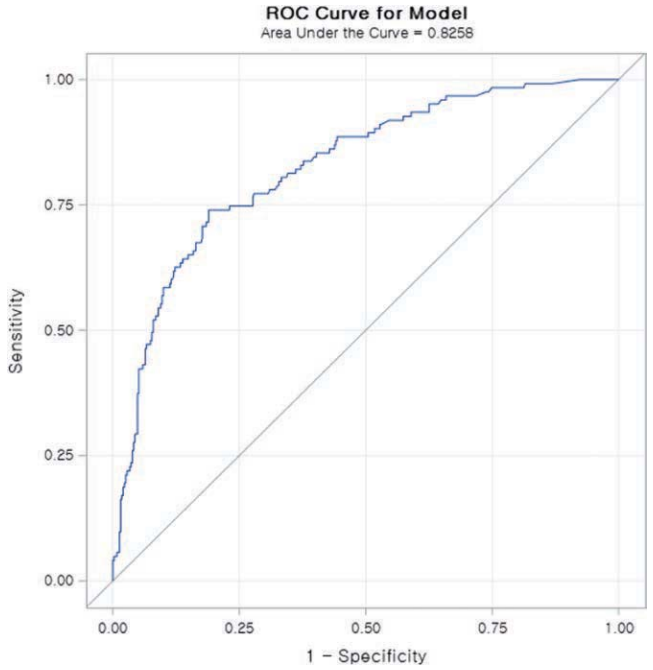

Figure 1. Apparent performance of developed model for prediction of flare after 12 months of tumor necrosis factor inhibitors tapering.

Conclusion: We developed the prediction model for the flare after 12 months of TNFi tapering in patients with axSpA. It might be applicable in real world setting, although external validation will be required in the future investigation.

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POS0943 EFFECT OF NERIDRONATE ON AXIAL SPONDYLOARTHRITIS WHEN BDMARDS ARE NOT AN OPTION: RESULTS FROM A RESTROSPECTIVE STUDY

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended as first-line treatment of axial Spondyloarthritis (axSpA) and biological disease-modifying antirheumatic drugs (bDMARDs) are effective in the management of patients refractory to NSAIDs. However, in some cases the introduction of bDMARDs is limited by absolute contraindications or patient opposition. Beyond the well-known anti-osteoclastic properties, bisphosphonates (BPs) can exert their benefits through other mechanisms, including reduction of proinflammatory cytokines (such as IL6 and TNFα), and modulation of macrophage and osteoblast activity.

Objectives: To examine the potential therapeutic properties of a BP, IV neridronate (IVNer), in patients with axSpA refractory to NSAIDs and not eligible for a second-line therapy with bDMARDs.

Methods: We retrospectively collected data of patients affected by axSpA according to ASAS classification criteria, treated with IVNer, referred to a tertiary Rheumatology Centre between Sept 2015 and Dec 2021. Patients with active disease, as defined by a BASDAI score ≥4, with active sacroileitis (SI) on MRI (according to ASAS MRI definition of active SI), who had failed/were intolerant to NSAIDs and not eligible for bDMARDs, were recruited. IVNer (100 mg) was given intravenously on Days 1, 4, 7, and 10, over 3 h in 500 ml of 0.9% saline. Response to IVNer was evaluated after 60 days from the last infusion as the mean change from baseline of BASDAI and visual analogue scale (VAS) pain score, and the improvement of MRI imaging.

Results: We included 30 patients (77% females, mean age±SD 39.0±16.8 yrs, and mean disease duration of 24±14.4 months (range 1.0-298). Fourteen had ankylosing spondylitis (AS), six had undifferentiated SpA, two had enteropathic arthritis, one had non-radiographic axSpA, and seven had axial psoriatic arthritis. 50% had axial involvement, 30% axial and peripheral arthritis, and 20% had axial and enthesis involvement. Eleven were HLA-B27 positive. On MRI evaluation, 43% had

monolateral SI, 57% bilateral SI and 7% had erosions. Among the reasons of ineligibility to bDMARDs, 6 patients have concurrent solid tumor, 11 had comorbidities contraindicating bDMARDs, and 12 preferred not to undergo to bDMARDs. Mean BASDAI significantly decrease after IVNer (5.86±1.98 vs 3.52±2.39, p=0.0002, Figure 1a), as well as VAS pain score (6.14±1.92 vs 3.18±2.62, p<0.05, Figure 1b). MRI showed a complete resolution of SI in 47%, partial resolution in 33%, and persistent active SI in 40% of patients, without correlation with the previous presence of erosions.

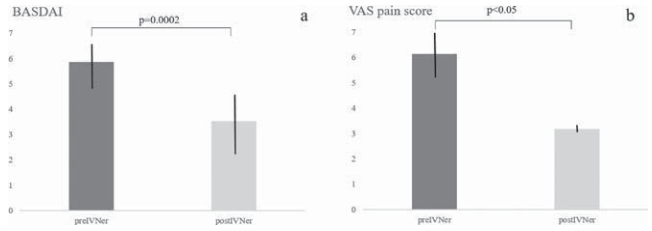

Figure 1.

Conclusion: IVNer was effective in reducing disease activity measured by BASDAI and VAS pain score in patients with axSpA refractory to NSAIDs and not eligible for bDMARDs. When recommended second-line treatments are contraindicated or according to patients' preference, IVNer can be considered as a potential alternative therapeutic option. Further evaluations in controlled trials are needed to confirm these results.

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Disclosure of Interests: None declared

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POS0944 PREDICTORS OF SUSTAINED REMISSION IN PEOPLE WITH AXIAL SPONDYLOARTHRITIS TREATED WITH BIOLOGIC DRUGS

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Background: The ultimate goal of treatment in axial spondyloarthritis (axSpA) is sustained remission. Data on predictors of sustained remission are scarce in axSpA.

Objectives: To determine predictors of sustained remission in people with axSpA after treatment with their first biological disease-modifying anti-rheumatic drug (bDMARD).

Methods: Hacettepe University Rheumatology Biologic Registry (HUR-BIO) is a prospective, single center registry of rheumatic disease patients treated with bDMARDs. Patients with axSpA were selected and sustained remission defined as attainment of Assessment of SpondyloArthritis International Society partial remission (ASAS-PR) and/or Ankylosing Spondylitis (AS) Disease Activity Score C-reactive protein Inactive Disease (ASDAS-ID) for two or more consecutive visits spanning ≥6 months during follow-up. Patients achieving and not achieving sustained remission were compared using the independent t-test. Multivariable logistic regression analysis was performed to determine independent factors predictive of sustained remission. Variables with a p-value<0.1 were re-tested in multivariable models. Forward selection was performed until the best-fit model was obtained, taking possible confounders into account. Two separate multivariable models were built, one with and one without the covariate "achievement of remission at 3-6 months", to assess consistency of findings and to account for missing information regarding remission status between 3 and 6 months.

Results: Data on 990 patients with sustained remission data were available. Of these, 299 (30%) were in sustained remission, while 691 (70%) were not. Patients in sustained remission were younger, had earlier disease onset, were more frequently male, had lower BMI and were more frequently HLA-B27 positive, compared to patients not in sustained remission. Furthermore, at the start of bDMARD treatment, Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), and patient global assessment (PGA, 0-10 scale) were lower, while acute phase reactants (ESR and CRP) were higher, in the sustained remission group. In multivariable analysis, male gender (OR 2.2, 95% CI 1.21-3.95), concomitant conventional synthetic DMARD (csDMARD) use (OR 3.63, 95% CI 1.29-10.19), PGA (OR 0.96, 95% CI 0.95-0.98), and early achievement (between 3-6 months) of remission (OR 13.1, 95% CI 7.13-24.02) were independently associated with sustained remission (Table 1, model 1). In the model without the variable early achievement of remission (Table 1, model 2), similar and a few additional associations were described: age at diagnosis (OR 0.97, 95% CI 0.96-0.99), male gender (OR 2.31, 95% CI 1.60-3.35), concomitant csDMARD use (OR 1.88 95% CI 1.23-2.86), PGA (OR 0.98, 95% CI 0.97-0.99), BASDAI (OR 0.87, 95% CI 0.78-0.96), and baseline symptom duration (OR 0.97, 95% CI 0.94-0.99).

Table 1. Multivariable analysis (best-fit model) of predictors of sustained remission

	Model 1		Model 2	
	Multivariable Analysis (n= 541)		Multivariable Analysis (n=739)	
Covariates	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Age at diagnosis	NS	NS	0.97 (0.96-0.99)	0.006
Male sex	2.84 (1.71-4.70)	<0.001	2.31 (1.60-3.35)	<0.001
Concomitant csDMARD use (at baseline or follow-up)	2.94 (1.57-5.51)	0.001	1.88 (1.23-2.86)	0.003
Baseline PGA	0.97 (0.96-0.98)	<0.001	0.98 (0.97-0.99)	0.002
Baseline BASDAI	NS	NS	0.87 (0.78-0.96)	0.009
Baseline symptom duration	NS	NS	0.97 (0.94-0.99)	0.021
Achievement of remission at 3-6 months after baseline	11.70 (7.11-19.23)	<0.001	NA	NA

NA: not applicable; NS: not selected (not contributing to the model). Baseline refers to start of bDMARD treatment.

Conclusion: This study demonstrates that patients in sustained remission after starting bDMARD treatment have distinctive characteristics compared to patients not in sustained remission. These data can be used to aid clinical and personalized management of axSpA, and to facilitate better communicate between health care professionals and patients regarding the course and prognosis of their condition.

Disclosure of Interests: Bayram Farisogullari: None declared, Gözde Kübra Yardımcı: None declared, Emre Bilgin: None declared, Ertugrul Cagri Bolek: None declared, Emine Duran: None declared, Gizem Ayan: None declared, Zehra Özsoy: None declared, Gullu Sandal Uzun: None declared, Mustafa Ekici: None declared, Erdinc Unaldi: None declared, Levent Kılıç: None declared, Ali Akdoğan: None declared, Omer Karadag: None declared, Şule Apraş Bilgen: None declared, Sedat Kiraz: None declared, Ali İhsan Ertenli: None declared, Umut Kalyoncu: None declared, Pedro M Machado Speakers bureau: Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, Consultant of: Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB

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POS0945 IMPROVEMENT OF ENDOTHELIAL DYSFUNCTION AND INFLAMMATION IN ANKYLOSING SPONDYLITIS: IMPROVE-AS STUDY

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Background: Cardiovascular (CV) disease is the leading cause of death in Ankylosing Spondylitis (AS)[1]. The chronic inflammatory-driven endothelial dysfunction and accelerated atherosclerosis contribute to the enhanced CV risk in AS. However, the therapeutic options to treat the enhanced CV risk are limited.

Objectives: To investigate the impact of Olmesartan and Rosuvastatin on endothelial dysfunction and inflammation in AS.

Methods: 60 consequtive AS patients were randomized to receive 24-weeks of treatment with Olmesartan (OLME) (10 mg/day, n=20), Rosuvastatin (Rvs) (10 mg/day, n=20), or placebo (PL) (n=20) as an adjunct to existing stable csDMARDs. Endothelial function was assesed by brachial artery flow-mediated dilatation (FMD) using AngioDefender. EPCs ($CD34^+/CD133^+$) were estimated by flow cytometry. Serum nitrite, TBARS, ICAM-1, VCAM-1 and lipids levels estimated at baseline and after treatment. Inflammatory measures included: ASDAS, BASDAI, BASFI, ESR and CRP, pro-inflammatory cytokines. Quality of life and CV 10-year risk (SCORE high risk charts) were estimated using standard tools.

Results: Baseline levels of FMD and EPC population were impaired indicating endothelial dysfunction. Basal concentrations of inflammatory markers, pro-inflammatory cytokines and markers of endothelial dysfunction were elevated among three

groups. After 24-weeks of treatment, FMD improved significantly in the rosuvastatin and olmesartan group as compared to placebo from their baseline levels: {OLME vs. PL (p≤0.01), Rvs vs. PL (p<0.01), Rvs vs. OLME (p=0.10) (Figure 1A). EPCs and nitrite (Figure 1B) levels improved significantly in both rosuvastatin and olmesartan groups. A significant reduction found in ICAM-1 after rosuvastatin treatment (p<0.01) where as olmesartan significantly decreased VCAM-1 (p=0.04) levels. Both rosuvastatin and olmesartan resulted in significant reductions of ASDAS, BASDAI, BASFI, ESR, CRP, IL-6 (Figure 1C) and TNF-α (Figure 1D) as compared to placebo. A significant reduction found in TBARS concentration after olmesartan treatment (p<0.01) as compared with rosuvastatin and placebo. There was a significant reduction in SCORE, HAQ-DI & SF-36 (PH) after treatment with rosuvastatin and olmesartan.

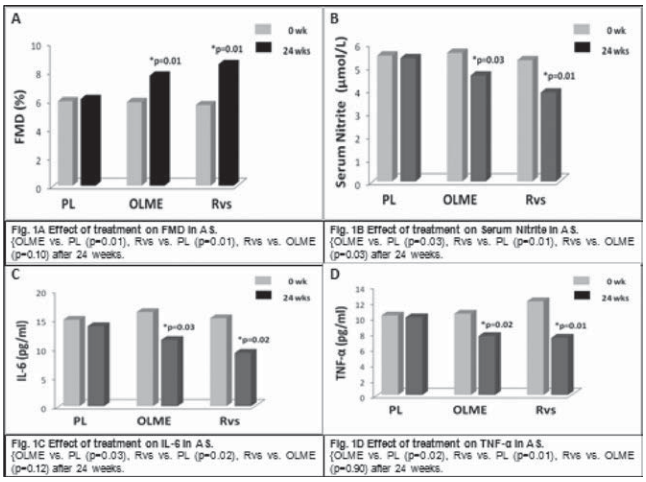

Fig. 1A Effect of treatment on FMD in AS. {OLME vs. PL (p=0.01), Rvs vs. PL (p=0.01), Rvs vs. OLME (p=0.10) after 24 weeks.

Fig. 1B Effect of treatment on Serum Nitrite in AS. {OLME vs. PL (p=0.03), Rvs vs. PL (p=0.01), Rvs vs. OLME (p=0.03) after 24 weeks.

Fig. 1C Effect of treatment on IL-6 in AS. {OLME vs. PL (p=0.03), Rvs vs. PL (p=0.02), Rvs vs. OLME (p=0.12) after 24 weeks.

Fig. 1D Effect of treatment on TNF-α in AS. {OLME vs. PL (p=0.02), Rvs vs. PL (p=0.01), Rvs vs. OLME (p=0.90) after 24 weeks.

Conclusion: Olmesartan and rosuvastatin improve endothelial dysfunction and vascular inflammation and QoL in AS patients. Olmesartan and Rosuvastatin lower the proinflammatory cytokines, especially TNF-α, that upregulate eNOS and downregulates the production of adhesion molecules, CRP and nitric oxide which, in turn, improves endothelial dysfunction. Both drugs also decrease nitrite concentration and improve the EPC population in AS patients. The augmentation of EPCs by olmesartan and rosuvastatin represents a fascinating new approach for the management of AS. However, Rosuvastatin in addition also favorably impacted ICAM-1 and lipid abnormalities. In contrast, olmesartan has beneficial effect on blood pressure. Thus, both rosuvastatin and olmesartan have anti-inflammatory, immunomodulatory, vasculoprotective and cardioprotective effects in AS mediated through anti-proinflammatory cytokine action. These findings suggests that both drugs could mediate modest but clinically apparent anti-inflammatory effects with modification of CV risk in the context of high-grade autoimmune inflammation of AS and may provide a novel strategy to prevent cardiovascular events in these patients.

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Disclosure of Interests: None declared

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POS0946 THE COURSE OF BONE MINERAL DENSITY DURING 8 YEARS OF TREATMENT WITH TNF-α INHIBITORS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Bone loss reflected by lower bone mineral density (BMD) compared to age and gender matched healthy controls is a common feature of ankylosing spondylitis (AS) and can already be observed at early stages of the disease[1]. AS patients starting TNF-α inhibitors (TNFi) show overall a rapid increase in BMD[2]. However, the course of BMD during long-term TNFi in these patients is not known.

Objectives: To assess the course of BMD of the lumbar spine (LS) and hip in AS patients treated with TNFi during 8 years.

Methods: Patients from the GLAS cohort who received TNFi for at least 8 years were included. Patients were excluded when they used bisphosphonates. BMD of the LS (AP projection L1-L4) and hip (total proximal femur) was measured at baseline, 1 year, 2 years and then bi-annually using DEXA. Low BMD was defined as LS and/or hip BMD Z-score ≤1. Generalized estimating equations were used to analyze BMD Z-scores over time within subjects.

Results: 131 AS patients were included; 73% were male, mean ± SD age was 41.3 ± 10.8 years, median (IQR) symptom duration was 14 (7-24) years, 83% were HLA-B27+, mean ASDAScrp was 3.8 ± 0.8, median CRP level was 13 (6-22) mg/L, and median vitamin 25(OH)D3 was 61 (46-80) nmol/L at baseline. Disease activity showed rapid and sustained during TNFi treatment, with mean ASDAScrp of 2.1 ± 0.9 and median CRP of 2 (2-5) at 8 years. Serum levels of vitamin D remained stable, with median vitamin 25(OH)D3 of 60 (47-81) at 8 years. At baseline, mean LS and hip BMD Z-scores were -0.37 ± 1.08 and -0.05 ± 1.04, respectively. Low BMD at the LS and hip (Z-score ≤1) was present in 34% and 19% of patients, respectively. Overall, both LS and hip BMD Z-scores improved significantly during TNFi at all follow-up visits compared to baseline. Significant improvement of BMD Z-scores compared to the previous time point was found up to and including 4 years for LS and up to and including 2 years for hip. Thereafter, deflection of improvement was observed. Median percentage of improvement in absolute BMD after 8 years of TNFi compared to baseline was 7.1% (IQR 0.8-13.5) for LS and 1.6% (IQR -3.5-5.5) for hip (Figure 1). At 8 years, low BMD at the LS and hip (Z-score ≤1) was present in 23% and 19% of patients, respectively.

Conclusion: In AS patients treated long-term with TNFi, both hip and LS BMD significantly increased especially during the first 2-4 year of treatment and stabilized thereafter. This effect was most pronounced in the LS and small in the hip.

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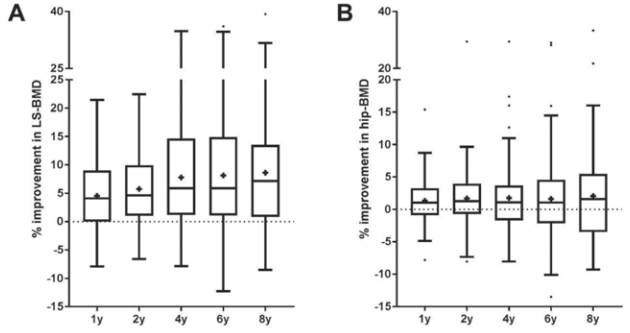

Figure 1. Percentage improvement during 8 years of TNF-α blocking therapy on LS-BMD (A) and hip-BMD (B) in patients with AS (n=131). Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers.

Disclosure of Interests: Mark Siderius: None declared, Anneke Spoorenberg Consultant of: AbbVie, Novartis Pharma, Pfizer, UCB Pharma, Lilly, Grant/ research support from: Novartis Pharma, Pfizer, Employee of: AbbVie, Novartis Pharma, Pfizer, UCB Pharma, Lilly, Freke Wink: None declared, Suzanne Arends: None declared

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POS0947 LONG-TERM GOLIMUMAB PERSISTENCE: 5-YEAR TREATMENT RETENTION DATA POOLED FROM FIVE PHASE III CLINICAL TRIALS IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND ANKYLOSING SPONDYLITIS

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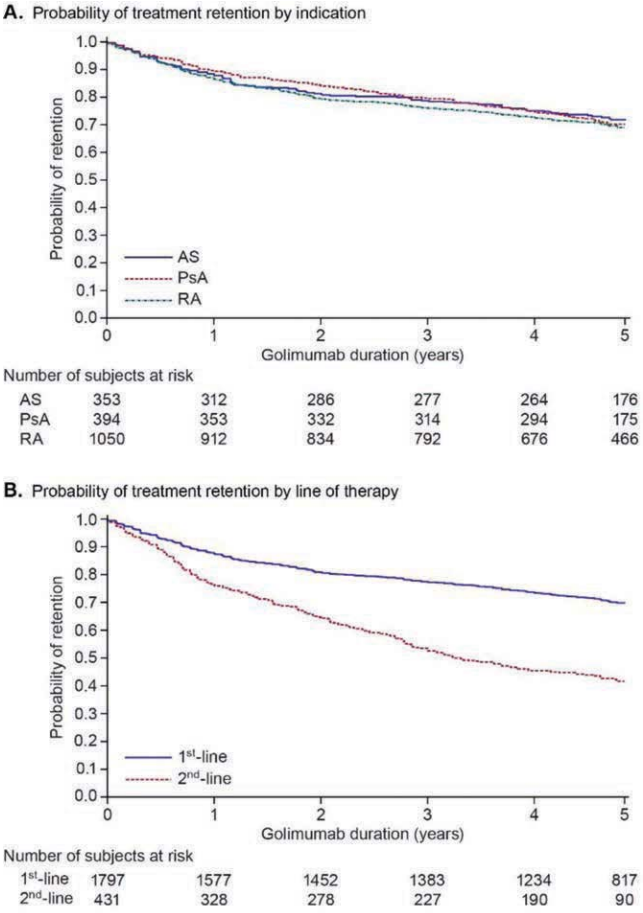
Background: Tumor necrosis factor-alpha inhibitors (TNFi), such as golimumab (GLM), are widely prescribed for treatment of chronic immune-mediated rheumatic diseases, such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Long-term persistence of GLM response in these diseases has previously been described from individual randomized controlled trials.[1-5] While treatment retention is considered an important factor for disease progression, health care utilization, and overall quality of life, and has previously been described, the probability of retention on GLM treatment in these trials has not been evaluated.

Objectives: To evaluate probability of GLM treatment retention over a 5-year period in adult patients with immune-mediated rheumatic diseases, by indication and line of therapy, using pooled data from five Phase III randomized controlled clinical trials.

Methods: Using data prospectively collected from five Phase III studies, this post-hoc analysis evaluated subcutaneous (SC) GLM (50 mg or 100 mg every 4 weeks) for up to 5 years in participants with RA (GO-BEFORE,[1,6] GO-AFTER[2,7] and GO-FORWARD[3,8]), PsA (GO-REVEAL[4,9]), and AS (GO-RAISE[5,10]). Four of the five studies (GO-BEFORE, GO-FORWARD, GO-REVEAL and GO-RAISE) were pooled to examine 1st-line GLM therapy, while the remaining

study (GO-AFTER) was used to examine 2nd-line (i.e., ≥ 1 line) GLM therapy in participants who had previously received and discontinued at least one other TNFi (etanercept, adalimumab, or infliximab) for any reason. Log-rank tests were performed to estimate retention rates by indication and line of therapy. Similarly, Kaplan-Meier analysis was used to estimate the probability of GLM retention over time.

Results: Among the 2228 participants enrolled in the 5 trials, 1797 participants had received GLM as1st-line treatment (RA = 1050; PsA = 394; AS = 353) and 431 participants had received GLM as 2nd-line treatment. Compared to the pooled 1st-line GLM analysis cohort, more participants receiving 2nd-line GLM were female (78.7% vs 62.2%), were > 50 years (61.5% vs 41.2%), and had a longer disease duration (median of 9.2 years vs 3.7 years). In the pooled 1st-line studies, GLM treatment retention remained high over five years, with an overall probability of retention of 87.8% (95% confidence interval [CI], 86.2–89.2) at Year 1 (Week 52), 80.9% (79.0–82.6) at Year 2 (Week 104), 77.3% (75.3–79.2) at Year 3 (Week 156), 73.5% (71.4–75.5) at Year 4 (Week 208) and 69.8% (67.6–71.9) at Year 5 (Week 252). GLM retention rates were similar across the four 1st-line GLM studies with no notable differences observed by indication over time (Figure 1, panel A). Treatment retention was better in participants using GLM as a 1st-line therapy compared to 2nd-line therapy (Figure 1, panel B), with a probability of retention at 5 years (Week 252) with 2nd-line therapy of 41.6% (95% CI: 36.8-46.3).



2nd-line refers to any participant receiving GLM after ≥1 line of another TNFi therapy. In the 2nd-line study, 115 (25%) participants had received two and 43 (9%) had received three TNFi therapies before enrollment.

Figure 1.

Conclusion: In this post-hoc analysis of prospectively collected clinical trial data, the probability of 1st-line GLM treatment retention at 5-years was consistently high across all rheumatic indications (RA, PsA and AS). Probability of long-term GLM treatment retention with 2nd-line therapy, while lower than 1st-line therapy, also remained favorable. Collectively, these data support the value of GLM as a 1st- or 2nd-line therapy in these chronic immune-mediated rheumatic diseases.

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Disclosure of Interests: Cindy Weinstein Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USQA, Employee of: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, Marinella Govoni Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: MSD Italy, a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, Jianxin Lin Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, Alan Meehan Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, Zaina Qureshi Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA
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POS0948

SIX YEARS TREATMENT WITH TNF-α INHIBITORS DOES NOT LEAD TO LONG-TERM CONTINUOUS HYPERMINERALIZATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: In a previous study, we showed that the bone turnover balance favored bone formation, especially mineralization, during the first years of treatment with TNF-α inhibitors (TNFi)[1] in patients with ankylosing spondylitis (AS).

Objectives: To explore if this effect continues during more long-term TNFi treatment. Therefore our goal was to investigate the prolonged course of serum levels of bone turnover markers (BTM) during 6 years of TNFi treatment in patients with AS.

Methods: Included were consecutive AS outpatients from the UMCG GLAS cohort who were treated with TNFi for at least 6 years. Patients were excluded when they used bisphosphonates. Data for a specific visit was coded as missing when patients either had experienced a fracture or received systemic corticosteroids within 1 year from that particular visit regarding the possible effect on BTM. Standardized follow-up visits were performed at baseline (before start of TNFi), 3 and 6 months, 1, 2, 4 and 6 years. Serum markers of collagen resorption sCTX, bone regulation OC, collagen formation PINP, and bone mineralization BALP were measured. Z-scores were calculated to correct for the normal influence of age and gender using a healthy reference population. Generalized estimating equations were performed to analyze BTM Z-scores over time within patients.

Results: 53 AS patients were eligible for analyses: 66% were male, mean (SD) age was 38.5 ± 11.3 years, median (IQR) symptom duration was 16 (9-25) years, 87% were HLA-B27+, mean ASDAS was 3.8 ± 1.0, and median CRP 14 (7-27) mg/L. Etanercept, infliximab or adalimumab was prescribed as first TNFi in 60%, 2% and 38% of patients, respectively. 26% (n=14) of patients switched to a second TNF-α inhibitor during follow-up. Disease activity showed rapid and sustained improvement after start of TNFi (Figure 1). At group level, collagen resorption marker sCTX Z-score did not significantly change during treatment. Bone regulation marker OC Z-score was only significantly increased at 3 months compared to baseline. Collagen formation marker PINP Z-score showed significantly increased levels at 3 and 6 months and 2 years. Bone mineralization marker BALP Z-score was significantly increased at all time points up to and including 2 years and decreased thereafter. Only a few patients still had higher BTM values above the normal range (+2 SD) (Figure 2). The net effect of collagen metabolism corrected for the normal influence of age and gender (PINP Z-score – sCTX Z-score) confirmed that the initial balance was in favor of collagen formation; this increase was only significant at 6 months compared to baseline.

Conclusion: In AS patients receiving long-term TNFi, the bone turnover balance favored bone formation during the first 2 years of treatment. Thereafter, at group level, serum levels of BTM returned to levels not significantly different from baseline. Therefore, 6 years of treatment with TNF-α inhibitors did not seem to lead to long-term continuous hypermineralization in patients with AS.

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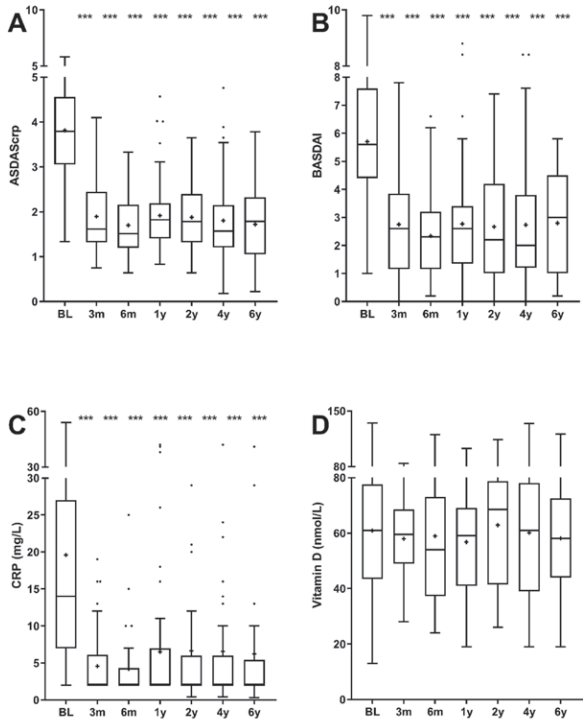

Figure 1 Disease activity index score ASDAScrp (A), BASDAI (B), levels of acute phase reactant CRP (C) and levels of vitamin D (D) during 6 years of treatment with TNFi in patients with AS (n=53). Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers.

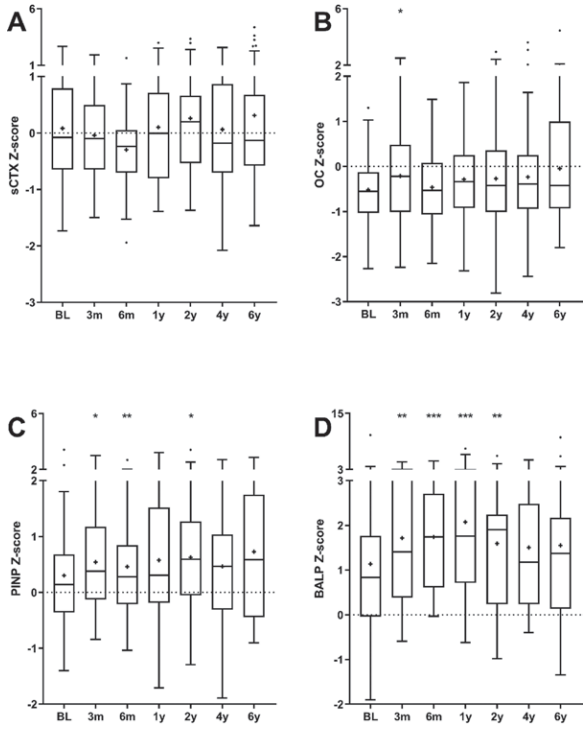

Figure 2 Z-scores of collagen degradation marker sCTX (A), bone regulation marker OC (B), collagen formation marker PINP (C) and bone mineralization marker BALP (D) during 6 years of treatment with TNFi in patients with AS (n=53). Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers.

Disclosure of Interests: Mark Siderius: None declared, Anneke Spoorenberg Consultant of: AbbVie, Novartis Pharma, Pfizer, UCB Pharma, Lilly, Grant/research support from: Novartis Pharma, Pfizer, Eveline Van der Veer: None declared, Frans G.M. Kroese: None declared, Suzanne Arends: None declared

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POS0949

NO CHANGE IN SERUM LEVELS OF BONE TURNOVER MARKERS CORRECTED FOR AGE AND GENDER DURING THE FIRST YEAR OF SECUKINUMAB TREATMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: In patients with ankylosing spondylitis (AS), TNF-α inhibitors influence the course of serum bone turnover markers (BTM), favoring an increase in mineralization during the first years[1]. Little is known about the effect of IL-17 inhibitors on these serum BTM levels.

Objectives: To evaluate serum markers of bone resorption, formation, and mineralization during 1 year of secukinumab treatment in AS patients in daily clinical practice.

Methods: Included were consecutive outpatients from the GLAS cohort with a clinical diagnosis of AS who started treatment with secukinumab between April 2016 and June 2020, and had available serum samples at ≥1 visit. Standardized follow-up visits were performed at baseline (before start of secukinumab) and after 3 or 6 months and 1 year of treatment. BTM were measured in serum: osteocalcin (OC; regulation marker), serum type 1 collagen C-telopeptide (sCTX; collagen resorption marker), procollagen type 1 N-terminal peptide (PINP; collagen formation marker) and bone-specific alkaline phosphatase (BALP; bone mineralization marker). BTM Z-scores were calculated using a healthy reference population to correct for the normal influence of age and gender. Patients using bisphosphonates were excluded from analyses. Data was coded missing if patients experienced a fracture or received systemic corticosteroids within 1 year of a study visit. Generalized estimating equations were used to analyze BTM Z-scores over time within patients.

Results: In total, data of 26 AS patients were eligible for analyses; 50% were male, mean age was 46.0±14.6 years, 81% were HLA-B27 positive, mean ASDAS at baseline was 3.7±1.0, and 50% was TNFi naïve. Before secukinumab treatment, median PINP and BALP Z-scores were +0.6 and +0.7 SD, respectively, compared to age and gender matched healthy controls, however, the large majority remained within the normal range of ±2 SD. Overall, BTM Z-scores of OC, sCTX, PINP and BALP did not change significantly compared to baseline during the 1st year of secukinumab treatment (Figure 1).

Conclusion: In daily clinical practice, serum BTM levels including mineralization corrected for the normal influence of age and gender did not change during the 1st year of secukinumab treatment in patients with AS. Our data confirm recent findings of stable BTM levels at group level during 2 years of secukinumab treatment in posthoc analysis of MEASURE 1[2].

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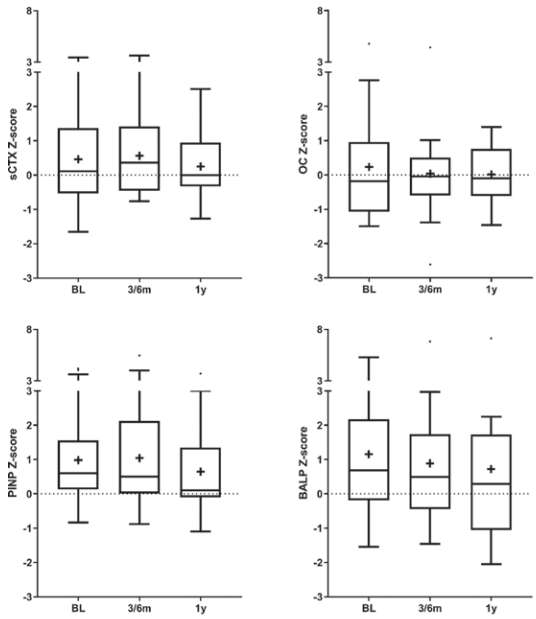

Figure 1. Z-scores of collagen degradation marker sCTX, bone regulation marker OC, collagen formation marker PINP and bone mineralization marker BALP in AS patients during 1 year of secukinumab treatment. Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances.

Acknowledgements: This study was supported by an investigator initiated research grant from Novartis.
Disclosure of Interests: Mark Siderius: None declared, Suzanne Arends: None declared, Freke Wink: None declared, Anneke Spoorenberg Consultant of: AbbVie, Novartis Pharma, Pfizer, UCB Pharma, Lilly, Grant/research support from: Novartis Pharma, Pfizer
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POS0950 LONG-TERM FOLLOW-UP OF STARTING AND SWITCHING FROM ORIGINAL ADALIMUMAB TO ADALIMUMAB BIOSIMILAR: REAL-WORLD DATA IN AXIAL SPONDYLOARTHRITIS

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Background: Biological drugs have revolutionized the treatment of rheumatic diseases, and the recent expiry of the patents for many biological agents has led to the marketing of highly similar, low-cost versions known as biosimilars. However, questions regarding its efficacy compared to bio-originator drugs, in a real-life setting, have been raised. National Institute for Health and Care Excellence (NICE) guidelines state that the response to biologic disease-modifying anti-rheumatic drugs (bDMARDs) should be assessed 12 weeks after the beginning of the drug. Treatment should only be continued if there is clear evidence of response, defined as a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and a reduction in the 10-cm spinal pain visual analogue scale (VAS) by 2 cm or more.
Objectives: To compare the response to adalimumab (ADA) originator and biosimilar in bDMARD-naïve patients with axial spondyloarthritis (axSpA) and in patients who switched from originator to biosimilar drug, accordingly to NICE guidelines; to compare the effectiveness and safety of the originator and biosimilar drugs in patients with axSpA, measured by persistence rates (PR) over three years.
Methods: A retrospective observational single-centre UK study was performed in bDMARD-naïve patients with a clinical diagnosis of axSpA who initiated treatment with ADA (original or biosimilar) and in patients who switched from originator to biosimilar drug. Descriptive statistics were used. Disease activity at baseline and follow-up data at 3 and 6 months of treatment was compared using the chi-square test. The Kaplan-Meier method was used to calculate persistence rates in biologic treatment over time. Reasons for discontinuing therapy were summarized using descriptive statistics and stratified by treatment.
Results: A total of 153 patients were included: 83 patients started on original ADA, 31 started on biosimilar ADA and 40 switched from original to biosimilar drug. The population's baseline characteristics are similar in the three groups. However, some differences were found, namely disease duration was longer in the group that did switch and the disease activity is similar in patients who started original and biosimilar ADA and was lower in the group of patients who switched from original to the biosimilar. The 3-year PR was not significantly different between originator and biosimilar ADA in bDMARD naïve patients and in the group of patients that switched from original drug to biosimilar drug (p=0.080), as shown in Figure 1. In the original ADA group, 3-years PR was 67.5% with a median time-on-drug (TOD) of 29.5 months; for biosimilar drug, 3-years PR was 64.5%, with a median TOD of 24.2 months. In patients who switched from original to biosimilar drug, 3-years PR was 77.5% with a median TOD of 30.3 months. Response to treatment according to NICE guidelines was similar between original and biosimilar drugs (p>0.05). Overall, 47 (30.7%) patients stopped adalimumab (27 patients on original drug and 20 on biosimilar drug). Discontinuations due to adverse events and inefficacy were the most frequent, and there were no significant differences between original and biosimilar drugs. Other reasons for discontinuation were less frequent, such as patient choice, loss of follow-up and death, and again without differences between original and biosimilar drugs.

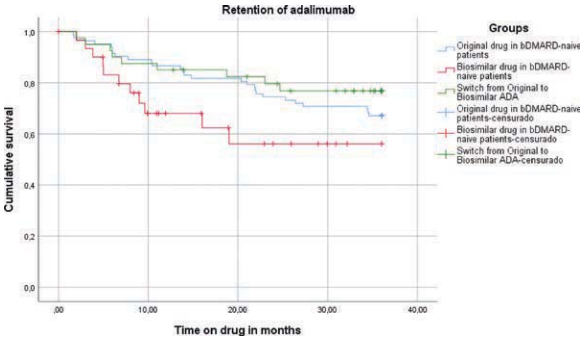

Figure 1. Drug survival in the three adalimumab groups (original adalimumab – blue line, biosimilar adalimumab – red line, and switch from original to biosimilar adalimumab – green line)

Conclusion: Adalimumab original and biosimilar used as a first-line biological treatment showed similar effectiveness and safety in our long-term cohort of patients with axSpA. Switch from original to biosimilar drug showed to have a good persistence on drug after three years of follow-up (77.5%).
Disclosure of Interests: Ana Sofia Pinto: None declared, Kalveer Flora: None declared, Dilpreet Matharu: None declared, Anthony Isaacs: None declared, Pedro Machado Speakers bureau: Received consulting/speaker's fees from Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript, Consultant of: Received consulting/speaker's fees from Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript
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POS0951 SERUM PROTEIN RESPONSE TO A SINGLE HIGH-INTENSITY INTERVAL TRAINING BOUT – COMPARISON BETWEEN INDIVIDUALS WITH SPONDYLOARTHRITIS AND HEALTHY CONTROLS

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease affecting mainly the axial skeleton. To decrease the risk of cardiovascular comorbidity, aerobic training is recommended as a part of disease management in patients with axSpA. High-intensity interval training (HIIT) interventions are, in addition to other recommended treatments, believed to positively affect the disease activity (1). However, the knowledge about the acute effects of HIIT on the inflammatory process at the molecular level is less studied. Understanding the acute HIIT effects on cytokines and additional serum proteins in axSpA is important for further long-term HIIT interventions and recording of the effect of HIIT on the axSpA disease profile.
Objectives: To study the acute effects on serum proteins, such as cytokines, myokines, and inflammatory- and bone-related proteins, in response to a single bout of HIIT, and to compare the levels between baseline and post-HIIT in patients with axSpA and healthy controls (HC).
Methods: The pilot study included twenty-one participants (10 female, 11 male), mean (SD) age 40 (7) years, ten with axSpA, and eleven age and sex matched HC, who performed a single HIIT on a cycle ergometer consisting of 4x4 minutes interval (90% heart rate, HR-max) with three minutes active rest in between (70% of HR-max). Disease activity (BASDAI, 0-10) in patients with axSpA was 1.6 (0.8). Health status EuroQol (EQ5D, 0-1) were 0.87 (0.11) for axSpA, and 0.93 (0.10) for HC. The groups were well matched with no difference in baseline data for weight, BMI, EQ5D, blood pressure or aerobic capacity.
Blood samples were taken before (baseline) and one hour after the single HIIT. The following serum proteins were analyzed on a Luminex MAGPIX

System (Luminex corporation, Austin, TX USA): Interleukin (IL)-6, IL-17, IL-18, TNFαAGPIX System (Luminex corporatiosteoprotegerin, osteocalcin, osteopontin, and FGF-23. A three-way analysis of variance (ANOVA) was used to detect differences between groups, between sexes, and before and after a HIIT bout in a 2(group)*2(sex)*2(time) design. For main effects or interactions significant at p≤0.05, simple effect t-tests were used to determine the specific effects.

Results: A group main effect (p=0.048) showed that the serum level of IL-6 was increased one hour after the HIIT session primarily in the HC, 0.4 pg/ml (SD±0.4) at baseline vs. post-HIIT 1.8 (2.0). The concentration of the cytokines/chemokine IL-17, IL-18, TNFα group main effect (p=0.048) showed that the serum level of IL-6 was increased one hour after the HIIT session primarily in30) in VEGF-A showed that the axSpA group had significantly lower VEGF-A at baseline, 159 pg/ml (138) vs 326 (184) in the control group (which might be due to anti-inflammatory medication). A sex main effect (p=0.029) was observed from baseline to post-HIIT for the bone hormone osteocalcin, with a more pronounced decrease of serum osteocalcin in women with axSpA, 14.0 ng/ml (8.3) vs. post HIIT 13.2 (6.9). Moreover, the level of the multifunctional protein osteopontin was significantly lower (sex main effect, p=0.021) in women, 10.7 ng/ml (7.0) vs. men 20.4 (10.1), post-HIIT.

Conclusion: This pilot study shows that one bout of HIIT influences the expression of proteins involved in inflammation and metabolism, and that sex is an important factor in the response to HIIT. The results should be followed up in longer intervention studies including higher numbers of participants.

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POS0952 THE IMPACT OF DIET ON DISEASE ACTIVITY IN SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Diet is thought to have a role in inflammatory diseases development and course. However, at present, no recommendations can be given to spondyloarthritis (SpA) patients regarding a specific type of diet/dietary supplement, as evidence on the topic is sparse.

Objectives: To review the evidence about the effect of diet/dietary supplements on SpA disease activity

Methods: A systematic literature review (SLR) was conducted in MEDLINE and SCOPUS according to the "PEO" format (Population: SpA, axial or peripheral, including Psoriatic Arthritis-PsA; Exposure: any kind of diet/dietary supplement; Outcome: any available disease activity measurement). Inclusion criteria were: adult patients, Randomized Controlled Trials (RCTs) and longitudinal studies (so that a pre-and post-intervention assessment were available), papers in English. Risk of bias (RoB) was independently judged by 2 authors (AO, MF) and conducted with different tools according to the study design: Newcastle Ottawa Scale (NOS) for observational studies, the ROBINS-1 tool for non-randomized studies, and the Cochrane risk of Bias tool 2.0 for RCTs.

Results: Literature search yielded 286 publications. After exclusion of 59 duplicates, 171 titles/abstract, and 44 full-texts, we included 8 interventional and 3 observational studies (Table 1). Among the former, 2 RCTs, one at unclear and one at low RoB, failed to show benefit of probiotics in SpA. One RCT at unclear RoB showed that weight loss, but not hypocaloric diet, was associated to MDA achievement in PsA. The other RCT, as well as the 4 quasi-interventional studies, were at high/serious RoB respectively. Among the observational studies, one study on Mediterranean diet demonstrated an association of diet adherence and a>=20% decrease of ASDAS in axSpA. Two other studies were judged of poor quality.

Conclusion: weight loss seems to be able to impact disease activity in SpA, while probiotics were not effective in the available RCTs so far. Adherence to Mediterranean diet might play a role in reducing disease activity. Evidence for effectiveness of dietary behaviors in SpA is quite heterogeneous and high quality studies are warranted to better understand the role of diet in SpA.

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POS0953 IMPACT OF A WEARABLE ACTIVITY TRACKER ON DISEASE ACTIVITY IN SPONDYLOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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Table 1. Characteristics of the included studies

Author year	Popula- tion	Interven tion	Study design	Rando- mized	Controlled	Sample size	Follow-up (weeks)	Primary outcome	Male Sex (%)	Mean Age (years)	Concomitant medications besides symptomatics
Experimental design											
Lassus 1990	PsA	PU ethyl ester lipids supplementation	Quasi-exp	No	No	80	8	NR	50	49	stable csDMARDs
Appelboom 1994	AS	Milk product deprivation	Quasi-exp	No	Yes (AS vs RA)	25/10	6	NR	NR	NR	28% on stable csDMARDs
Sundström 2006	AS	Omega 3 fatty acids	RCT	Yes	Yes (high vs low dose)	24	21	NR	61	NR	No csDMARDs
Di Minno 2014	Obese/ overweight PsA	Hypocaloric diet	RCT	Yes	Yes (hypocaloric vs free diet)	138	24	MDA (+)	36	45	All patients started anti-TNF; concomitant MTX in 29%
Klinberg 2019	Obese PsA	Hypocaloric diet	Quasi-exp	No	No	46	12-16	MDA (+)	36	56	100% on stable cs/bDMARDs
Klinberg 2020	Obese PsA	Hypocaloric diet	Quasi-exp	No	Yes (PsA vs controls)	74	20	NR	36	56	100% on stable cs/bDMARDs
Brophy 2008	SpA	Probiotics	Internet- based RCT	Yes	Yes (probiotics vs placebo)	147	12	Satisfaction of CONSORT statement (+)	64	44	10% on stable b/csDMARDs
Jenks K 2010	SpA	Probiotics	RCT	Yes	Yes (probiotics vs placebo)	63	12	BASFI (-)	63	43	28.5% on csDMARDs
Observational Design											
Adawi 2018	PsA	Intermittent fasting	cohort	-	No	37	4	NR	37	43	100% on stable cs/bDMARDs
Ben Nessib 2020	SpA	Fasting-refeeding	cohort	-	No	12	28	NR	45	47	40% on stable cs/ bDMARDs
Ometto 2021	axSpA	Mediterra-nean diet	cohort	-	Yes (Mediterra-nean vs free diet)	161	24	NR	65	51	100% on stable cs/bDMARDs

PsA: Psoriatic arthritis, AS ankylosing spondylitis, SpA spondyloarthritis, ax: axial; RA Rheumatoid Arthritis, PU polyunsaturated; RCT Randomized Controlled Trial; exp=experimemntal; MDA Minimal Disease Activity; CONSORT CONsolidated Standards of Reporting Trials; BASFI Bath Ankylosing Spondylitis Functional Index; (+) or (-) indicate whether the primary outcome of the study was met or not

Background: Other studies have shown the ability of a wearable activity tracker (TAP) to improve physical activity (PA) in different rheumatic diseases. Given the importance of PA in spondyloarthritis, our hypothesis is that the use of a TAP could improve physical activity and thus disease activity.
Objectives: The purpose of this study is to evaluate the impact of a TAP used to encourage PA on disease activity in patients with spondyloarthritis.
Methods: In this randomized controlled trial consisting of three 12-week stages (Figure 1). Patients with spondyloarthritis were randomized to a group with TAP (GT), or a group without TAP (GST). For the first stage, both groups received physical activity counseling. In the second 12-week stage, no patients received TAP. In the third 12-week stage, all patients received supervised PA combined with TAP for GT only. Disease activity, performance (assessed by the TM6 6-minute walk test), and quality of life (assessed by the Short Form 36 Health Survey Questionnaire [SF-36]) were assessed at 12, 24, and 36 weeks. The primary endpoint was the progression of relapses between baseline and 12 weeks.

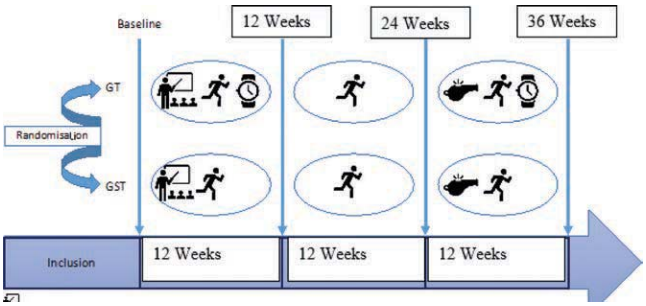

Figure 1.

Results: A total of 108 patients were included in the study. At 12 weeks, both groups showed a non-significant improvement in the number of relapses: mean change (Δ), -0.32 [95% CI-0.68;60.09] in GT and Δ, -0.38 [95% CI-0.68;60.09] in GST. But, differences in outcome between groups were not significant (p=0.87). The TM6 was improved in the GT and GST groups at 12, 24, and 36 weeks ($p < 0.01$, and $p < 0.001$, respectively). We observed improvement in different dimensions of the SF36, mainly in physical function, emotional role, general health, and physical pain at 12 weeks ($p < 0.01$). Multivariate analysis showed improvement over time in performance ($p < 0.01$) and moderate flare-ups ($p < 0.01$) without the influence of a PAR ($p = 0.29$, and $p = 0.66$, respectively).
Conclusion: To our knowledge, our study is the first to explore the impact of TAP use on disease activity in spondyloarthritis. We observed an improvement in disease activity, physical performance and quality of life without significant difference between the two groups. The lack of difference could be explained by the encouragement of physical activity to both groups. But also by the fact that our patients presented a significant number of severe relapses. Indeed, authors have shown the limits of the use of TAP in severe diseases, particularly in pulmonary pathologies [1]. Our study did not show any effect of the use of a connected object on disease activity. However, this study confirmed the benefits of physical activity on disease activity, quality of life and physical performance in patients with spondyloarthritis.
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Disclosure of Interests: Guillaume Labat: None declared, Meggy Hayotte: None declared, Olilvier Brocq: None declared, laurent bailly: None declared, Roxane fabre: None declared, manuella Fournier: None declared, Véronique Breuil: None declared, fabienne d'arripe longueville: None declared, Christian Roux Speakers bureau: Pfizer, BMS, Novartis, Lilly, Grant/research support from: Novartis and Lilly
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POS0954

WHAT DOES IT MEAN – A GOOD RESPONSE TO NSAIDS? A SYSTEMATIC COMPARISON OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND CONTROLS WITH CHRONIC BACK PAIN

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Background: A fast response to non-steroidal anti-inflammatory drugs (NSAIDs) is an important finding in the evaluation of clinical findings within the items comprising the ASAS classification criteria but also for the treatment decision for escalation to a bDMARD in patients with axial spondyloarthritis (axSpA). However, the differentiation of NSAID responses between patients with axSpA and degenerative or unspecific back pain is still unclear.
Objectives: To study the differences in the velocity and magnitude of NSAID response velocity in patients with established bDMARD naïve axSpA vs. patients with other, non-inflammatory reasons of back pain.
Methods: Patients with axSpA without degenerative reasons for back pain or patients with degenerative or unspecific back pain presenting due to high levels of back pain (NRS≥4/10) were consecutively recruited. Assessments included clinical examination, laboratory tests and MRI of the lumbar spine.
Previous NSAID intake was allowed only if it was taken in low doses without showing a clinical response, otherwise patients were NSAID naïve. Upon study inclusion, patients were treated with the maximum possible dose of an NSAID that they have reported to tolerate in lower doses in the past, independent of whether this was a Cox-2 inhibitor or a non-coxib. Assessment of response was performed using a standardized questionnaire after 2, 6, 12, 24, 36, 48 hours and after 1, 2 and 4 weeks. Any NSAID response was defined as improvement of pain >2/10 points and a good response to NSAIDs as an improvement >50% from the initial status.
Results: A total of 68 patients with axSpA, 107 patients with degenerative back pain and 58 patients with unspecific back pain were included.
The mean age was 42.7±10.7, 51.2±11.3, and 45.8±10.0 years, the main symptom duration 15.1±11.1, 16.1±12.6, and 11.9 ±10.1 years and the proportion of males was 57.4%, 19.6%, and 19.0% respectively. Inflammatory back pain was reported by 42 (75%), 48 (57.8%), and 29 (60.4%) patients, respectively and the mean pain score was 6.2±2.3,6.7±1.8, and 6.2±1.8, respectively.
In axSpA, the mean BASDAI and BASFI scores were 5.5±1.8 and 4.5±2.5, respectively. There was no difference in the cumulative response to NSAIDs between all three diagnoses, with an overall proportion of 27%-30% of patients showing improvement. However, better but not faster responses were found for the subgroups of patients with nr-axSpA (Figure 1) and for the male patients in the entire axSpA group, while axSpA patients with systemic inflammatory activity defined by increased CRP showed lower rates of response as compared to non-inflammatory reasons of back pain diagnoses. All other subanalyses did not reveal any differences between axSpA patients and other non-inflammatory reasons of back pain.

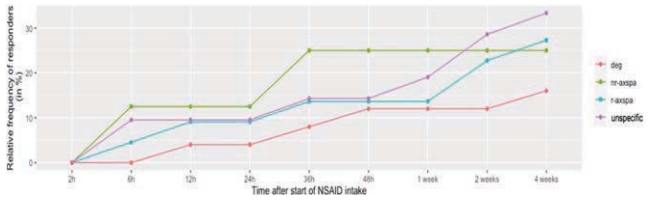

Figure 1.

Conclusion: In this prospective evaluation, the generally proposed better response of axSpA patients to treatment with high doses of NSAIDs as compared with non-inflammatory back pain was not confirmed, although the overall rate of responders was similar to previously reported rates. On the other hand, better responses were found in patients treated in the early (nr-axSpA) stage and in male patients. axSpA patients with increased CRP values showed lower rates of response.
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Spondyloarthritis - clinical aspects (other than treatment)

POS0955

PATIENTS' PERSPECTIVES ON DISEASE- AND TREATMENT-RELATED ISSUES ARE ESSENTIAL FOR TREATMENT SUCCESS IN PATIENTS WITH SPONDYLOARTHRITIS AND ASSOCIATED DISEASES: A QUALITATIVE CLINICAL CONCEPT MAPPING STUDY

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Background: Each patient's way of living with and relating to their chronic disease is unique. However, patients with chronic diseases may have some mutual concerns and challenges. They must not only handle the disease itself, but also the consequences that the disease has for their everyday and emotional lives[1]. Exploring the patient's perspectives for significant factors of relevance for patients living with a chronic disease is important in order to discover unmet needs and challenges for complying with a comprehensive lifelong treatment strategy and ensuring high-quality lives. Increasing awareness about the possible discrepancy between doctor experienced quality in care and patient experienced quality in care is of high relevance when aiming to ensure optimal disease management.
Objectives: The objective of this study was to explore disease- and treatment-related issues and concerns experienced by adult patients with spondyloarhtritis (SpA) and associated diseases; psoriatic arthritis (PsA), psoriasis (PsO), axial spondyloarthritis (axSpA), and inflammatory bowel disease (IBD; Crohn's disease (CD) and ulcerative colitis (UC)), and whether these factors were generic or disease dependent.
Methods: Concept Mapping were used to identify and organize disease- and treatment-related issues and concerns[2]. Concept Mapping is a formal group process with a structured approach to identify ideas on a topic of interest and organize them into cogent domains. Participants were asked to respond to an initial task: 'Thinking as broadly as you can, please list your thoughts (issues and concerns) related to your disease", PsA, PsO, axSpA, CD or UC, respectively. Data were obtained through a nominal group technique and then organized using participants' themes, multidimensional scaling, cluster analysis, participant validation, and thematic analyses to generate a conceptual model of disease- and treatment related issues and concerns experienced by patients with PsA, PsO, axSpA, CD, and UC.
Results: Seven AxSpA patients, 8 PsA patients, 9 PsO patients, 13 CD patients, and 13 UC patients contributed to generating the conceptual models. Seven AxSpA clusters, 7 PsA clusters, 7 PsO clusters, 10 CD clusters, and 11 UC clusters with each cluster having sub-clusters, emerged from the workshops producing 137 AxSpA statements, 160 PsA statements, 187 PsO statements, 335 CD statements, and 408 UC statements. Some clusters were generic: 'Concerns about the disease and the future', 'Consequences of the disease', 'Acceptance of the disease', 'Medication and treatment', and 'At the doctor' (Figure 1). Specific clusters were: for AxSpA: 'Use of public services, for PsA: 'Difficult to have an invisible disease', for PsO: 'Ashamed (about appearance)', for CD: 'Speculations and thoughts; life now and in the future - can I expect more surgeries in the future?', and for UC: 'The influence and importance of the diet' and (Figure 1).

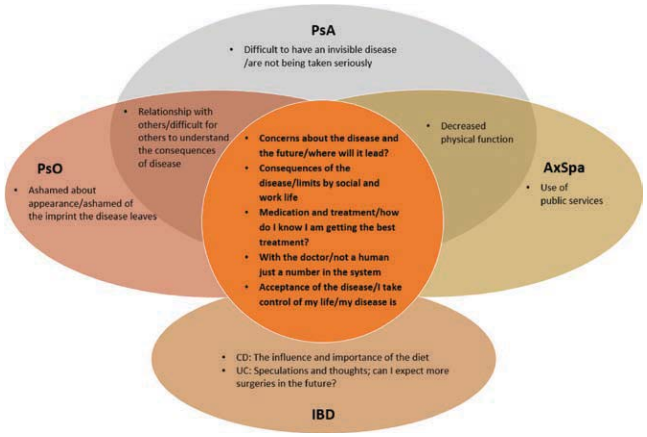

Figure 1.

Conclusion: Patients with SpA and associated diseases largely agree on which concepts describe their disease- and treatment-related issues and concerns with a few of them being disease-dependent.
Living a good life with a chronic disease is much more than having clinical control of the disease. This study gives insight to patients' perspectives on themes that are essential when living with a chronic disease. Considering the patients' perspectives, it is necessary to promote patient empowerment and adherence to treatment, and thereby optimize disease management and quality of life.

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POS0956

HIGH INFLAMMATORY BURDEN PREDICTS CARDIOVASCULAR EVENTS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A LONG-TERM FOLLOW-UP STUDY

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Background: Axial spondyloarthritis (axSpA) patients had a higher risk of cardiovascular disease (CVD) than the general population (1). It is also suggested that inflammation, rather than a particular disease, drives the increased risk of CVD (2). But the relationship between inflammation in axSpA and CVD is unknown.
Objectives: To examine whether inflammatory burden over time can predict cardiovascular events (CVE) independent of baseline CV risk factors in axial spondyloarthritis (axSpA) patients.
Methods: A cohort analysis was performed in patients who had been recruited since January 2001. The primary outcome was a first CVE occurring between January 2001 and December 2020. Three CVD risk scores were computed at baseline. The performance of the original and modified (x 1.5 multiplication factor) CV risk algorithms were assessed. Time-varying Cox proportional hazard models and Kaplan-Meier survival analysis were used to assess whether inflammatory burden (Bath ankylosing spondylitis disease activity index [BASDAI] and inflammatory markers), non-steroidal anti-inflammatory drugs (NSAIDs) and disease modifying anti-rheumatic drugs (DMARDs) can predict the development of first CVE.
Results: 463 patients [35(26-45) years, male: 360(77.8%)] were recruited. After a median follow up of 12 (7-19) years, 61 patients (13.2%) experienced a first CVE. Traditional/modified CV risk scores underestimated CV risk. Erythrocyte sedimentation rate (ESR)≥20 mm/hr was associated with a significantly higher risk of CVE during follow-up [HR: 2.07, 95%CI (1.10, 3.98), p=0.008]. Active disease as indicated by a rising BASDAI also showed positive trend towards a higher risk of developing CVE over time. After adjusting for CV risk scores in the multivariable models, high ESR level (ESR≥20 mm/hr) over time remained significantly associated with a higher risk of developing CV events (Table 1a and 1b). A significant difference in the CV event-free survival between patients with ESR≥20 mm/hr and ESR<20 mm/hr was demonstrated in Figure 1.

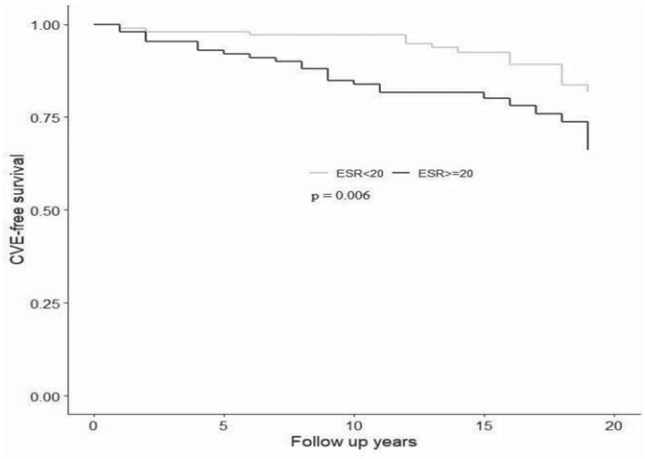

Figure 1. Kaplan-Meier survival analysis between time-varying ESR level and CVE. P=0.006 for difference in CVE-free survival rate between patients with ESR≥20mm/hr and ESR<20mm/hr during their follow-up intervals. ESR: Erythrocyte Sedimentation Rate.

Table 1. Multivariable analysis with time-dependent Cox proportional hazard regression for the predictors of cardiovascular events.

Table 1a.

	Model 1		Model 2		Model 3	
	Time-dependent HR (95%CI)	p-value	Time-dependent HR (95%CI)	P-value	Time-dependent HR (95%CI)	P-value
ESR≥20	2.75 (1.23, 6.14)	0.014*	2.74 (1.21, 6.21)	0.016*	2.93 (1.31, 6.57)	0.009*
BASDAI	1.07 (0.90, 1.28)	0.455	1.06 (0.88, 1.28)	0.519	1.07 (0.89, 1.28)	0.442
FRS	1.06 (1.03, 1.09)	<0.001*				
QRISK3			1.05 (0.99, 1.11)	0.132		
SCORE					1.25 (1.09, 1.42)	0.001*

Table 1b.

	Model 1		Model 2		Model 3	
	Time-dependent HR (95%CI)	P-value	Time-dependent HR (95%CI)	P-value	Time-dependent HR (95%CI)	P-value
ESR≥20	2.77 (1.24, 6.18)	0.013*	2.78 (1.23, 6.28)	0.014*	2.95 (1.32, 6.59)	0.008*
BASDAI≥4	1.37 (0.62, 2.99)	0.434	1.26 (0.58, 2.78)	0.559	1.42 (0.65, 3.09)	0.376
FRS	1.06 (1.03, 1.09)	<0.001*				
QRISK3			1.05 (0.99, 1.11)	0.138		
SCORE					1.24 (1.09, 1.42)	0.001*

*Statistically significant at p≤0.05.HR, hazard ratio; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; FRS: Framingham Risk Score; SCORE: Systematic Coronary Risk Evaluation.

Conclusion: Increased inflammatory burden as reflected by elevated ESR levels (ESR≥20) was associated with increased risk of CVE, while the use of NSAIDs and DMARDs were not.

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POS0957 EXTERNAL VALIDATION OF THE ALTERNATIVE ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE IN THREE PHASE-3 RCTS

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Background: In axial spondyloarthritis (axSpA), an alternative ASDAS (altASDAS) was developed to be used when Patient Global Assessment (PGA) is unavailable. AltASDAS replaces PGA with BASDAI total score and has so far only been internally validated [1].

Objectives: To test the psychometric properties of altASDAS in an external cohort, according to the OMERACT filter 2.0 (truth, discrimination; feasibility was evaluated in our previous work).

Methods: Cohorts from the COAST trial programme of ixekizumab (COAST-V,-W,-X;primary endpoint: 16-week), enrolling radiographic/non-radiographic axSpA (r-/nr-axSpA) patients, were pooled. AltASDAS was calculated for all evaluations. ***Truth*** was assessed by: 1) agreement with original-ASDAS, as a continuous score and as a categorical variable (disease activity-DA-states), with intraclass correlation coefficients (ICC) and weighted Kappa respectively; 2) Bland & Altman plots with mean difference (MD) and 95% limits of agreement (LoA) 3) comparison of Pearson correlations of altASDAS and original-ASDAS with other constructs. ***Discrimination*** was tested by 1) the ability of altASDAS to distinguish high/low DA states according to an external anchor (nocturnal pain>6 indicating high DA) 2) agreement (kappa) with original-ASDAS in major/clinically important-improvement (MI/CII) achievement at 16-weeks 3) comparison of number of patients reaching MI/CII in the treatment versus placebo arm at 16-weeks, according to original and altASDAS (higher Chi-square=better discrimination).

Results: 958 patients were included, 70% males, mean age 42.7 years, 68% r-axSpA. ***Truth:*** 1) agreement with original-ASDAS: ICC=0.97 (95%CI:0.93-0.99), kappa=0.84 (0.83-0.85) 2) MD with original-ASDAS: 0.14; 95% LoA -0.56 to 0.28 3) correlation coefficients of altASDAS with related constructs were within a pre-specified 0.3-wide band around those between original-ASDAS and the same construct (Table 1 *a*). ***Discrimination*** altASDAS discriminated between DA states (Table 1 *b*) and in sensitivity to change (Kappa with original-ASDAS for MI=0.87 95%CI:0.83-0.91; for CII=0.93; 95%CI:0.90-0.95) and Table 1 *e c*

Table 1. Psychometric properties of alternative Ankylosing Spondylitis Disease Activity Score (altASDAS)

a) Truth: correlations with constructs related to disease activity

Data expressed as correlation coefficient r

	Function (BASFI)	Quality of Life (MCS)	Quality of life (PCS)	Overall functioning and health (ASAS HI)
Original-ASDAS	0.58	-0.11	-0.48	0.35
altASDAS	0.57	-0.11	-0.47	0.35
b) Discrimination: disease activity states				
Anchor to define disease activity: Nocturnal pain (NRS 0-10)	**NRS >6 Mean ASDAS (SD)**	**NRS ≤ 6 Mean ASDAS (SD)**		**SMD**
Original-ASDAS	3.99 (0.76)	2.61 (0.86)		-1.68
altASDAS	3.87 (0.83)	2.46 (0.96)		-1.57
c) Discrimination: sensitivity to change				
	Treatment N (%)	**Placebo N (%)**		**Chi-square**
N° of patients	628	272		-
Original-ASDAS MI	151 (24)	12 (4)		49.3
altASDAS-MI	167 (26)	13 (5)		56.4
Original-ASDAS CII	342 (54)	62 (23)		76.9
altASDAS-CII	350 (56)	64 (23)		79.2

BASFI: Bath Ankylosing Spondylitis Functional Index, MCS and PCS: mental and physical component summary of Short-Form 36; ASAS HI: ASAS Health Index; NRS: Numerical rating scale; SD: standard deviation; SMD: standardised mean differences; MI and CII: Major and Clinically Important Improvement

Conclusion: AltASDAS was shown to be truthful and discriminative in an external cohort and as such has been fully validated and can be used in cases when PGA is unavailable.

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POS0958

PROGRESSIVE IMPROVEMENT IN TIME TO DIAGNOSIS IN AXIAL SPONDYLOARTHRITIS THROUGH AN INTEGRATED REFERRAL AND EDUCATION SYSTEM

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Background: Despite the advances in the treatment and management of axial spondyloarthritis (axSpA), there remains a significant delay in the diagnosis of the condition. The diagnostic delay is 8-10 years in Europe and 8.5 years on average in the United Kingdom. This is contributed by the lack of awareness of axSpA, limited access to diagnostic tests and unstructured referral pathways. The delayed diagnosis leads to higher morbidity from the condition.

Objectives: To assess the delay in the diagnosis of axSpA over time in a real world axSpA cohort diagnosed over a 7 year period from 2015 and to evaluate factors associated with this delay. During this time, we evaluated the effectiveness of the interventions to reduce the delay to diagnosis.

Methods: A cohort of axSpA patients newly diagnosed between 2015 to 2021, were studied. This was a cross-sectional study on patients with axSpA who visited a specialist rheumatology clinic at a single centre. The demographic, clinical and diagnostic variables were recorded. Diagnostic delay was defined as the time interval between the year of first symptom and year of diagnosis. The mean and median diagnostic delay were calculated. An integrated educational and referral system were implemented from 2015[1]. This included education to the main referrers in to the system including general practitioners (GPs) and community musculoskeletal (MSK) triage physiotherapists. The electronic referral systems were updated annually according to best practice guidelines[2]. An impact analysis was performed evaluating diagnostic delay for axSpA during this period.

Results: Of the 110 axSpA patients studied, 60 (54.4%) were male and 50 (45.5%) female. The mean (range) age was 37 (18-52) years. All patients met the ASAS classification criteria for axSpA. Radiographic axSpA (Ankylosing spondylitis) fulfilling New York criteria, was diagnosed in (62%) of the patients. There were more patients with radiographic axSpA in the earlier years of diagnosis (100% in 2015) and more of non-radiographic axSpA in the later years (83% in 2021). HLA-B*27 positivity was found in 79 (71.8%) of patients. The majority of referrals were from general practitioners 63 (57.2%), physiotherapists 19 (17.3%), orthopaedics 18 (16.4%) and other specialties 10 (9.1%). There was no significant difference in the mean (years) delay to diagnosis from the source of the clinic referral. The mean and median delay to diagnosis by year of diagnosis were 9.9, 9.5 (±3.1) years in 2015, 7.1, 7(±1) in 2016, 5.3,5 (±2.7) in 2017, 4.9, 4 (±3) in 2018, 4.4, 2.5 (±4.8) in 2019, 3.6, 2 (±3.2) in 2020, 2.2, 1 (±2.6) in 2021. The majority of the patients were diagnosed between 31-40 years (41%), 22% between 18-30 years, 31% between 41-50 years and 4% after the age of 50 years. Higher age at diagnosis was associated with a longer diagnostic delay. Diagnosis of disease at 18-30 years of age was associated with shorter mean delay to diagnosis (2.9 years), age 31-40 (4.6), age 41-50 (5.9), and age > 51 (6.5).

Conclusion: Delay in axSpA diagnosis has significantly improved in this real-world cohort during the last seven years. The mean diagnostic delay was 2 years indicating diagnostic delay may be for most patients shorter than previously reported. The factors associated with a faster diagnosis were a) more recent year of first rheumatology consult b) earlier age at presentation. Increased educational and awareness campaigns in primary care and musculoskeletal triage has led to the early recognition of axSpA. Early referral to a rheumatology service using electronic referral symptom can improve the diagnostic delay of axSpA. With continuous improvement cycles, our aim is to get reduce delays to diagnosis to under 1 year with line with the Gold Standard to Diagnosis in axSpA.

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Disclosure of Interests: Antoni Chan Speakers bureau: Janssen, Novartis, Amgen, Abbvie, Celgene, UCB, Consultant of: Novartis, Lilly, Abbvie, Grant/research support from: Novartis, UCB, Kathryn Rigler: None declared, Nadia Ahmad: None declared, Tanguy Lafont: None declared

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POS0959

RISK FACTORS FOR NON-VERTEBRAL FRACTURES IN ANKYLOSING SPONDYLITIS

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Background: Osteoporosis is common in patients with ankylosing spondylitis (AS) and a risk factor for fragility fractures. Additional established risk factors for fractures in the general population include higher age, female sex, previous fracture, fall tendency, glucocorticoid treatment, insulin dependent diabetes, smoking and high alcohol consumption.

Objectives: To estimate the influence of established risk factors for fragility fractures on the development of non-vertebral fractures in AS and population controls.

Methods: Through linkage of national population and health care registers 2001-2016, patients with AS (n=11611, 65.5% men, mean age 48 years) and age-, sex- and geography-matched population controls (n=58050) were identified and from 1 January 2007 (or 3 months after the first registered AS diagnosis if this occurred later) followed prospectively until the time of a non-vertebral fracture, death, emigration or end of study (30 December 2016). Occurrence of established risk factors for a fracture and AS related characteristics at start of follow-up were identified in the National Patient and Prescribed Drug Registers using ICD-10 and ATC codes. Smoking status and anthropometric measurements are not available in these registers. Chi-square, Fischer's exact test and T tests were used to compare between subjects with and without a non-vertebral fracture during follow-up, separately for AS and controls. Multivariable Poisson regression

Table 1.

	AS			Controls		
	No fracture (n=10637)	Fracture (n=974)	P-value	No fracture (n=53944)	Fracture (n=4106)	P-value
Male sex	7002 (65.8)	603 (61.9)	0.014	35448 (65.7)	2572 (62.6)	<0.001
Mean age (SD)	47.6 (14.7)	53.8 (14.8)	<0.001	47.8 (14.7)	53.0 (15.0)	<0.001
Prior fracture	667 (6.3)	140 (14.4)	<0.001	2715 (5.0)	486 (11.8)	<0.001
Osteoporosis*	359 (3.4)	83 (8.5)	<0.001	367 (0.7)	85 (2.1)	<0.001
Fall injury without fracture	714 (6.7)	97 (10.0)	<0.001	3205 (5.9)	350 (8.5)	<0.001
Harmful use of alcohol	158 (1.5)	26 (2.7)	0.005	889 (1.6)	171 (4.2)	<0.001
Hyperthyroidism	39 (0.4)	7 (0.7)	0.105	180 (0.3)	19 (0.5)	0.173
Diabetes type 1	178 (1.7)	30 (3.1)	0.002	651 (1.2)	80 (1.9)	<0.001
Liver disease	66 (0.6)	10 (1.0)	0.132	197 (0.4)	32 (0.8)	<0.001
Malnutrition	8 (0.1)	3 (0.3)	0.058	16 (0.0)	2 (0.0)	0.367
Hypogonadism or premature menopause	11 (0.1)	1 (0.1)	1.000	33 (0.1)	0 (0.0)	0.169
Use of oral glucocorticoids[#]	1531 (14.4)	152 (15.6)	0.304	839 (1.6)	97 (2.4)	<0.001
Anterior uveitis	2168 (20.4)	204 (20.9)	0.677	317 (0.6)	32 (0.8)	0.126
Psoriasis	316 (3.0)	34 (3.5)	0.364	605 (1.1)	58 (1.4)	0.091
Inflammatory bowel disease	675 (6.3)	64 (6.6)	0.783	441 (0.8)	35 (0.9)	0.811
Use of any DMARD[¤]	3411 (32.1)	266 (27.3)	0.002	465 (0.9)	52 (1.3)	0.008
Use of TNF inhibitor[¤]	1539 (14.5)	109 (11.2)	0.005	43 (0.1)	4 (0.1)	0.573

The data is presented as number (%) if not stated otherwise. *Diagnosed osteoporosis and/or use of osteoporosis medication. [#]Prednisolone equivalent cumulative dose of ≥450 mg within the last year before start of follow-up. [¤]Use within the last year before start of follow-up.

was used to estimate the influence of each established risk factor in AS and controls. Risk factors for which there were ≤20 observed events in the AS cohort were not included. Results are presented as incidence rate ratios (IRR) with 95% confidence intervals.

Results: In total 974 (8.4%) patients with AS and 4106 (7.1%) of their controls were registered with a non-vertebral fracture during the study period. The characteristics of the patients and controls at start of follow-up are presented in Table 1 stratified by fracture status during follow-up. Figure 1 displays the results from the Poisson regression.

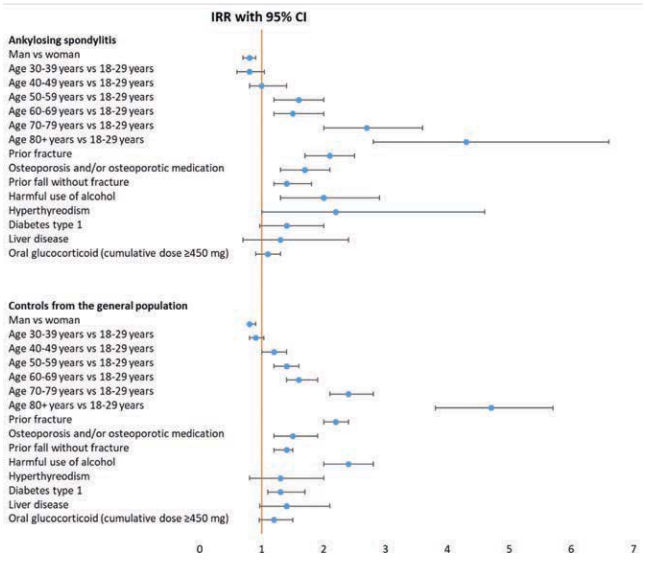

Figure 1. Multivariable Poisson regression analyses for a non-vertebral fracture during follow-up, with results presented for each included baseline variable as IRR with 95% CI, separately for AS and controls.

Conclusion: The influence of established risk factors for fragility fractures in AS is similar to that in the general population; in both populations with advanced age, prior fracture and harmful use of alcohol being the strongest risk factors.

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POS0960 INCIDENCE AND RISK OF OVERALL INFECTIONS IN PATIENTS WITH ANKYLOSING SPONDYLITIS RECEIVING BIOLOGIC THERAPIES: A REAL-WORLD PROSPECTIVE OBSERVATIONAL STUDY USING KOBIO REGISTRY

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Background: Infection is a perpetual concern in patients treated with biological therapy. However, long-term real-world data on infectious profile of AS patients are lacking.

Objectives: The aim of this study was to characterize infection events in a longitudinal cohort of patients with ankylosing spondylitis (AS) and to identify the risk factors associated with the development of infections receiving biologics therapies in a real-world setting.

Methods: This was a prospective observational cohort study including AS patients in the KOBIO registry starting a biologics from December 2012 to April 2020. Infections were evaluated by types or organ during the follow-up period. Infection rates (IR) per 1,000 person-years were calculated with 95% CI based on Poisson distribution method. Cox proportional hazard regression models with adjustment of confounding factors was used to estimate hazard ratios (HRs) with 95% CIs for occurrence of infection. Confounders included demographics, comorbidities and disease severity index.

Results: A total of 1610 AS patients were included in the analysis. Most (76.8%) were men and the median age was 37 years with 5.73 median AS duration. 129 infection events occurred during 5020.5 person-years of follow-up. The most frequent infections were upper and lower respiratory tract (39.8%), followed by herpes zoster (23.7%), skin and soft tissue (except herpes infection), gastrointestinal tract, and genitourinary tract. The overall incidence of any infection was 25.7/1000 patient-years (PY) of follow-up (95% confidence interval [CI] 21.5 - 30.5): 29.5/1000 PY (95% CI 20.6 – 41.1) among those treated with infliximab and biosimilar; 26.8/1000 PY (95% CI 20.1 – 34.9) among those treated with adalimumab; 21.5/1000 PY (95% CI 14.1 -31.6) among those treated with golimumab; 17.8/1000 PY (95% CI 9.5 -30.5) among those treated with etanercept and biosimilar.; 81.1/1000 PY (95% CI 2.1 – 451.9) among those treated with secukinumab. Significant univariate risk factors for infection were age, ischemic heart disease, complicated diabetes, solid tumor, abnormal chest x-ray, anemia, and biologics user. In multivariate Cox regression model, ischemic heart disease, very high disease activity (ASDAS-ESR>3.5), complicated diabetes, abnormal chest x-ray and current biologics users remained significant.

Conclusion: In the KOBIO-AS registry, the total incidence rate of infections was 26 events/1000 PY of follow-up, with respiratory infection being the most common, followed by herpes zoster infection. In this large cohort of AS patients, ischemic heart disease, very high disease activity (ASDAS-ESR>3.5), complicated diabetes, abnormal chest x-ray and current biologics user were risk factors for any infection in this large cohort of patients with AS, whereas male gender was protective factor for developing infection.

Disclosure of Interests: None declared

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POS0961 CLINICAL PROFILE AND TREATMENT UTILIZATION IN HLA-B27 POSITIVE VERSUS HLA-B27 NEGATIVE PATIENTS: RESULTS FROM ASAS-PERSPA STUDY

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Background: HLA-B27 is a genetic marker strongly associated with axial spondyloarthritis (axSpA). However, the strength of this association varies worldwide. Although some regional studies have assessed the effect on HLA-B27 status on clinical features of axSpA, no worldwide study has been performed.

Objectives: To characterize differences in the clinical features, extra-articular manifestations, and treatment utilizations in a global axSpA cohort based on their HLA-B27 status.

Methods: We performed a post-hoc analysis of the ASAS-PerSpA study (Peripheral involvement in Spondyloarthritis) dataset that includes patients with axial (axSpA) and peripheral SpA(pSpA), psoriatic arthritis (PsA), juvenile SpA, SpA associated with inflammatory bowel disease (IBD) and reactive arthritis based on their rheumatologist's diagnosis. We identified patients that had been diagnosed with axSpA meeting the 2009 ASAS classification criteria and been typed for HLA-B27. The patient characteristics were compared between the HLA-B27(+) and HLA-B27(–) subgroups using Student's t-test and the Mann-Whitney U test. Multivariable logistic regression with backward stepwise selection was conducted to identify predictors of HLA-B27 positivity. Variables with p-value <0.15 on univariate analysis were included in the multivariable model. All tests were two-tailed with p-value <0.05 considered significant.

Results: A total of 4465 patients with axSpA from 24 countries were identified. We observed that 2910 patients fulfilled the 2009 ASAS classification criteria. Of these patients, 2269 were tested for HLA-B27 (HLA-B27+: 1753 and HLA-B27-: 516). Significant differences were observed between these two groups in age of symptom onset and manifestations of the disease as shown in Table 1. The HLA-B27(-) patients had a significantly later age of symptom onset and disease diagnosis, more often had concomitant IBD, psoriasis, peripheral arthritis, enthesitis and were more often treated with csDMARDS. On multivariable logistic regression factors significantly associated with HLA-B27 positivity included male sex (OR: 1.99), family history of axSpA (OR: 2.26), and occurrence of anterior uveitis (OR: 2.72).

Conclusion: In a large heterogeneous cohort of AxSpA patients from 24 countries, we found that male sex, family history, and occurrence of anterior uveitis are significant predictors of HLA-B27 positivity. In contrast, the HLA-B27(-) have a significantly later age of onset and longer delay in diagnosis, more often have concomitant IBD, psoriasis, peripheral arthritis and enthesitis, and also more often receive treatment with csDMARDs.

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Table 1. Patient Characteristics Based on HLA-B27 Status

	Total N = 2269	HLA-B27 (+) N = 1753	HLA-B27 (-) N = 516	p-value	Multvariate Logistic Regression Analysis using variables <0.15 OR (95%CI)
Mean age (SD)	41.3 (12.8)	40.6 (12.8)	43.4 (12.6)	<0.001	1.04 (1.03 – 1.06)
Gender (male %)	1554 (68.0)	1264 (72.1)	280 (54.3)	<0.001	1.99 (1.60 – 2.49)
University studies (%)	1056/2267 (46.6)	837/1751 (47.8)	219 (42.4)	0.032	
Family history of axSpA (%)	601 (26.5)	522 (29.8)	79 (15.3)	<0.001	2.26 (1.72 – 3.01)
Mean age of symptoms onset (%)	26.8 (10.0)	25.9 (9.4)	30.0 (11.1)	<0.001	
Mean age of diagnosis in yrs (%)	33.0 (11.5)	31.6 (10.9)	37.7 (12.1)	<0.001	0.93 (0.91 – 0.94)
BMI (%)	25.9 (5.1)	25.7 (4.9)	26.5 (5.6)	0.001	0.98 (0.96 – 0.99)
Past or current peripheral arthritis (%)	981/2266 (43.3)	736/1750 (42.1)	245 (47.5)	0.029	
Past or current enthesitis (%)	1165/2268 (51.4)	873/1752 (49.8)	292 (56.6)	0.007	0.79 (0.54 – 0.98)
Past or current dactylitis (%)	205 (9.0%)	153 (8.7)	52 (10.1)	0.347	
Past or current uveitis (%)	520 (22.9)	461 (26.3)	59 (11.4)	<0.001	2.72 (2.00 – 3.76)
Past or current psoriasis (%)	279/2268 (12.3)	179/1752 (10.2)	100 (19.4)	<0.001	0.54 (0.40 – 0.74)
Past or current IBD (%)	125 (5.5)	59 (3.4)	66 (12.8)	<0.001	0.21 (0.14 – 0.31)
NSAIDs ever (%)	1606 (70.8)	1240 (70.7)	366 (70.9)	0.932	
csDMARDs ever (%)	1281 (56.5)	965 (55.0)	316 (61.2)	0.013	
bDMARDs ever (%)	1377 (60.7)	1070 (61.0)	307 (59.5)	0.529	

POS0962

CAN RADIOMICS REPLACE SPARCC SCORING SYSTEM IN EVALUATING BONE MARROW OEDEMA OF THE SACROILIAC JOINTS IN AXIAL SPONDYLOARTHRITIS?

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Background: Bone marrow oedema (BMO) of the sacroiliac joints (SIJs) is evaluated to diagnose, classify and monitor disease activity in patients with axial spondyloarthritis (axSpA). Available quantitative methodologies rely on human visual assessment, and errors can't be completely avoided. Radiomics can extract and select discriminative and quantified features from regions of interest (ROIs), making a more accurate and objective description of BMO.
Objectives: To develop a more objective and efficient method based on radiomics to evaluate BMO of the SIJs by magnetic resonance imaging (MRI) in patients with axSpA in comparison with Spondyloarthritis Research Consortium of Canada (SPARCC) scoring system.
Methods: From September 2013 to July 2021, 523 patients with axSpA underwent 3.0T SIJ-MRI were included, who were randomly classified as training cohort(n=367) and validation cohort(n=156). The optimal radiomics features, selected from the 3.0T SIJ-MRI in the training cohort, were included to build the radiomics model. Four clinical risk predictors were adopted to build the clinical model. The performance of the clinical and radiomics models was evaluated by ROC analysis and decision curve analysis (DCA). Rad-scores were calculated by the radiomics model and SPARCC scores were performed to quantify the BMO of SIJs. We also assessed the correlation between Rad-score and SPARCC score.
Results: The radiomics model, built by 15 optimal features, showed favorable discrimination about SPARCC score <2 or ≥2 both in the training (AUC, 0.91; 95% CI: 0.88-0.94) and the validation cohort (AUC, 0.89; 95% CI, 0.84-0.94). DCA confirmed that the radiomics model was clinically useful. Furthermore, Rad-score has significant correlation with SPARCC score for scoring the status of BMO (r_s=0.78, P< 0.001), and moderation correlation for scoring the change (r=0.40, P=0.005).
Conclusion: The radiomics can accurately assess the BMO of the SIJs in axSpA, providing an alternative to SPARCC scoring system. There was a positive correlation between Rad-score and SPARCC score.
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Table 1. Rad-scores corresponding to different SPARCC score intervals about the status of SIJ-BMO.

SPARCC score	n	Rad-score		
		Mean(sd)	Median (iqr)	Range
0-1	170	-1.31(1.64)	-1.39(2.16)	-6.46, 2.35
2-6	125	0.73(1.86)	0.62(2.12)	-3.08, 8.48
7-11	55	2.25(1.80)	2.36(1.79)	-1.17, 8.36
12-16	43	2.65(2.14)	2.66(3.21)	-0.76, 7.39
17-21	38	3.31(2.05)	3.25(2.88)	-0.88, 7.55
22-26	26	3.08(1.55)	3.38(2.12)	-1.00, 5.38
27-31	25	3.77(1.36)	3.77(1.59)	0.40, 6.27
>31	41	4.10(1.51)	4.32(2.28)	1.00, 6.96

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POS0963

HOW IS EARLY SPONDYLOARTHRITIS DEFINED IN THE LITERATURE? RESULTS FROM A SYSTEMATIC REVIEW

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Background: The term "early spondyloarthritis (SpA)" has been frequently used to refer to the first phase of the disease, however, no standardized definition on "early" has been established. The ASAS-SPEAR (SPondyloarthritis EARly definition) project aims at developing a consensual definition on what is meant by "early SpA". In order to inform the ASAS-SPEAR working group, it is highly relevant to assess the current meaning of "early SpA" in the literature.
Objectives: To identify all possible definitions of "early SpA" employed in the literature, including "early axial SpA (axSpA)" and "early peripheral SpA (pSpA)".
Methods: A systematic literature review was conducted in Medline, EMBASE and the Cochrane Library (through April 28th, 2021). The eligibility criteria were studies with any design, in adults that included any mention of "early SpA" or its subtypes in the title or abstract. Two reviewers independently identified eligible studies and extracted data, including the literal definition of early SpA used in each of them. The proportion of studies reporting a definition was calculated, and the different definitions were assessed, including the core of the definition: whether they were based on symptom duration, disease duration, radiographic damage, a combination of them or any other aspects, and their boundaries.
Results: Out of 9,651 titles identified, 355 publications reporting data from 186 studies were included (291 full papers, 64 conference abstracts). Among them, 217 (61%) were cohort studies, 72 (20%) were reviews and 46 (13%) were

clinical trials. Over time, an increasing number of publications on early SpA were identified: <2005 (n=34), 2005-2010 (n=48), 2011-2015 (n=109) and 2016-2020 (n=164). Overall, 63 studies (34%) included the term "early axSpA", 60 (32%) "early ankylosing spondylitis (AS)", 58 (31%) "early SpA", 4 (2%) "early non-radiographic axSpA (nr-axSpA)" and 1 (1%) "early pSpA". In total, 116 (62%) studies reported a specific definition: 40 (34%) based it on symptom duration, 35 (30%) on radiographic damage, 32 (28%) on disease duration, 6 (5%) on both symptom/disease duration and radiographic damage, and 3 (3%) on other aspects. Symptom duration was defined as the time since the onset of low back pain in 21/40 (53%) studies, whereas in 14/40 (35%) the symptom of onset was not specified. Thirty-five of 116 studies (30%) included a definition referred to "early SpA", 38 (33%) to "early axSpA", 38 (33%) to "early AS", 4 (3%) to "early nr-axSpA", and 1 (1%) to "early pSpA". Figure 1 shows the 18 distinct definitions that were identified (after combining some similar categories). The three most used definitions per subtype of disease are shown in Table 1. Regarding the studies that referred to "early axSpA", the most used definition was symptom/disease duration <5 years, whereas for "early AS" was symptom/disease duration <10 years. After 2010, the definition of "early axSpA" based on the absence of radiographic sacroiliitis was less used compared to before 2010 (5/30, 17% vs 3/8, 38%).

Table 1. Top 3 candidate definitions for "early SpA" and subtypes

	Core of the definition	Number of studies, n (%)
SpA (n= 35)	nr-axSpA	10 (29%)
	< 2 years duration	10 (29%)
	< 1 year duration	6 (17%)
AxSpA (n=38)	< 5 years duration	12 (34%)
	< 3 years duration	9 (24%)
	nr-axSpA duration	8 (21%)
AS/r-axSpA (n=38)	<10 years duration	9 (24%)
	nr-axSpA	7 (18%)
	< 2 years duration	6 (16%)
nr-axSpA (n=4)	nr-axSpA	2 (50%)
	< 1 year & nr-axSpA	1 (25%)
	< 5 years & nr-axSpA	1 (25%)
pSpA (n=1)	< 12 weeks duration	1 (100%)

"Duration" refers to symptom duration or disease duration.

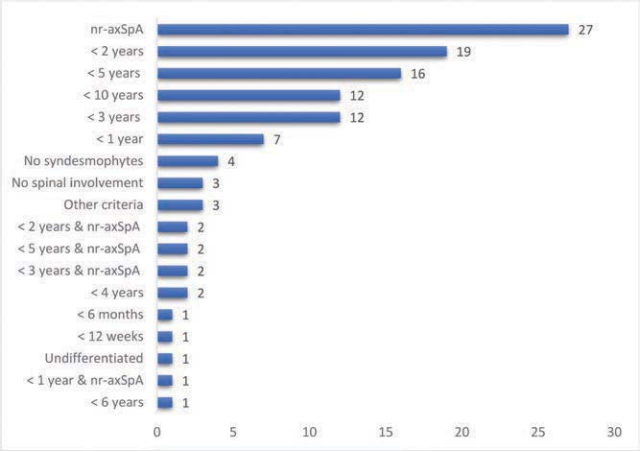

Figure 1. Number of studies stratified by the core of the definition.

Conclusion: Over time, the term "early SpA" and its subtypes are increasingly used. Despite addressing early SpA, more than one third of the studies did not include a clear definition of the term. The studies reporting a definition of early SpA showed a large heterogeneity, with two out of three of them based on the duration of symptoms or disease. These results emphasize the need for a standardised definition of early SpA.

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POS0964

IS LOW VERTEBRAL BONE DENSITY ASSOCIATED WITH SUBSEQUENT BONE FORMATION AT THE SAME VERTEBRA IN AXIAL SPONDYLOARTHRITIS? – A MULTILEVEL ANALYSIS FROM THE SIAS COHORT

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Background: In radiographic axial spondyloarthritis (r-axSpA) it has been hypothesized that inflammation-driven bone loss triggers bone repair at anatomically distinct sites of the same vertebra: bone loss occurring in the trabecular bone and ectopic bone formation in the periosteum[1].

Objectives: To investigate whether inflammation is associated with lower bone density (surrogate of bone loss) and subsequently, if lower bone density is associated with 2-year bone formation in r-axSpA at the same vertebra.

Methods: Data from the Sensitive Imaging in Ankylosing Spondylitis (SIAS), a multicentre 2-year cohort, was used. Baseline vertebral bone density was assessed by Hounsfield Units (HU) on low dose Computed Tomography (ldCT) by two independent readers (Figure 1). Baseline magnetic resonance imaging (MRI) bone marrow edema (BME) status scores, and 2-year ldCT syndesmophyte formation or growth change scores were assessed by three and two readers respectively. Inter-reader reliability was assessed for each imaging scoring by vertebra. Average of readers´ continuous scores (bone density HU) or readers´ agreement in binary scores (MRI-BME and bone formation) were used at the same vertebra (1-present in ≥1 quadrant/0-absent in all quadrants). The hypothesised associations were tested in multilevel generalised estimating equations models adjusted for confounders, the unit of analysis being the vertebra.

Results: We analysed 1,100 vertebrae in 50 patients with r-axSpA. Intraclass correlation coefficients for HU measurements varied from 0.89 to 0.97, Fleiss Kappa values for MRI-BME were between 0.41-0.78 and Cohen´s kappa for syndesmophyte formation/growth change scores varied from 0.36 to 0.74. Bone density HU decreased from cranial to caudal vertebrae. Baseline MRI-BME was present in 300/985 (30%) and syndesmophytes in 588/910 (65%) vertebrae, both most prevalent at the thoracolumbar region. Syndesmophyte formation or growth was observed in 18% of at-risk vertebrae (124/691). A significant association was found between inflammation (MRI-BME) and lower bone density (regression coefficient=-51; 95% CI:-63;-39) (Table 1***A***). Bone density was not associated with 2-year syndesmophyte formation or growth (adjOR 1.00; 95% CI:0.99;1.00) (Table 1***B***).

Table 1. Relationships between (A) baseline MRI detected spinal inflammation (MRI-BME) and bone density, and (B) baseline bone density and ldCT bone formation after two years, at the same vertebra.

A.	**Independent variables**	**Bone density (Hounsfield Units)**	
		Univariable analysis Reg coeff. (95% CI) N = 910 to 985	Multivariable analysis Adj Reg coeff. (95% CI) N = 985
	MRI-BME (presence)	**-51 (-63 to -39)**	**-51 (-63 to -39)**
	Age (years)	-1 (-2 to 1)	-1 (-2 to 1)
	Gender (male)	21 (-20 to 63)	16 (-24 to 57)
	TNFi treatment (yes)	26 (-7 to 59)	27 (-6 to 61)
	Baseline syndesmophytes (presence)*	**-42 (-54 to -30)**	-
B.	**Independent variables**	**Syndesmophyte formation or growth§**	
		Univariable analysis OR (95% CI) N = 672 to 691	Multivariable analysis AdjOR (95% CI) N = 672
	Bone density (HU)	1.00 (0.99 to 1.00)	1.00 (0.99 to 1.00)
	Age (years)	1.02 (0.99 to 1.06)	1.02 (0.98 to 1.05)
	Gender (male)	0.44 (0.13 to 1.52)	0.56 (0.15 to 2.06)
	Smoking (current)	0.89 (0.40 to 1.97)	1.02 (0.42 to 2.44)
	Treatment with TNFi (yes)	1.34 (0.56 to 3.21)	1.30 (0.43 to 3.90)
	MRI-BME (presence)	**2.03 (1.23 to 3.71)**	**1.73 (1.06 to 3.34)**
	Baseline syndesmophytes (presence)*	**2.84 (1.83 to 4.41)**	-

*Multicollinearity with MRI-BME. § Absolute agreement of readers. **adjOR -** adjusted odds ratio; **CI-**confidence interval; **BME -** bone marrow edema; **HU -** Hounsfield units; **ldCT -** low dose computed tomography; **MRI -** magnetic resonance imaging; **TNFi –** Tumour necrosis factor inhibitors. Statistical significance highlighted in bold.

Conclusion: While in r-axSpA vertebral inflammation associates with low vertebral bone density, lower vertebral bone density itself does not increase the risk for ectopic bone formation at the same vertebra.

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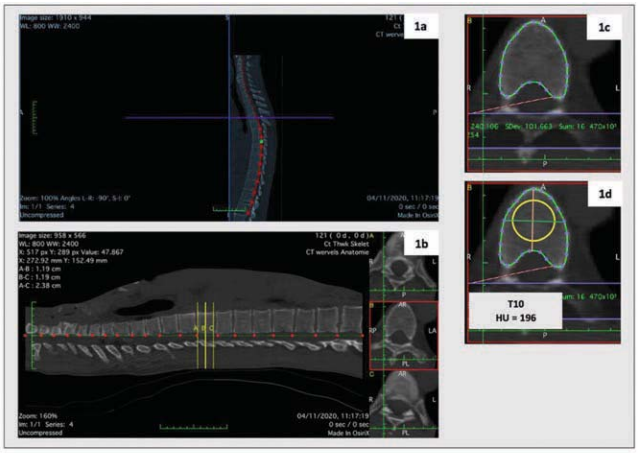

Figure 1. **Methodology of Hounsfield Units (HU) measurement.** Using a three-dimensional curved-multiplanar reconstruction the curve of the spine was identified from the spinal canal (**1a**). On the obtained sagittal image, the vertebrae could be identified. At each vertebra, two lines of reference were positioned at the superior (yellow line A) and inferior (yellow line C) limits of the vertebra. Equidistant to A and C, the yellow line B was positioned at the center of the vertebral body (**1b**). In the reconstructed cross-sectional slice, the vertebral body was delimited (**1c**). A centered region of interest (ROI) was manually selected, having a diameter equal to 75% of the average of anteroposterior and transverse diameters, and the density of the vertebra was calculated as the average image density within the sample region, reported in HU. (**1d**).

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POS0965

MAGNETIC RESONANCE ENTEROGRAPHY AS A SCREENING TOOL FOR AXIAL SPONDYLOARTHRITIS IN CROHN'S DISEASE: A PROSPECTIVE SINGLE-CENTER CROSS-SECTIONAL OBSERVATIONAL STUDY USING MRE SCREENING FOLLOWED BY CLINICAL ASSESSMENT (PROSPA-CD)

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Background: Patients with inflammatory bowel disease (IBD) have an excess burden of axial spondyloarthritis (axSpA) (1), but currently there are no reliable screening tools available. Magnetic resonance enterography (MRE) is an oral contrast MRI of the small bowel used to aid the diagnosis of Crohn's disease (CD) (2). MRE also captures the sacroiliac joints (SIJs) but the radiological assessment of this is often overlooked. MRE scans therefore contain potentially valuable unreported data, which could be used to screen for axSpA in CD patients.

Objectives: To determine: (i) the validity, sensitivity, specificity and area under the receiver operating characteristic (ROC) curve (AUC) of MRE as a screening tool for axSpA in CD, using dedicated axial MRI scans with clinical assessment as the gold standard; (ii) the proportion of patients with evidence of axSpA on MRE who fulfill the 2009 Assessment of Spondyloarthritis International Society (ASAS) criteria for axSpA; (iii) whether the presence of extra-intestinal manifestations (EIMs) or CD location can predict the occurrence of axSpA in CD.

Methods: ProSpA-CD was a pair of linked prospective observational studies conducted at a large secondary care university hospital in the UK. In ProSpA-CD-Screen, patients who had undergone MRE between 2015-2019 were assessed for eligibility. The consenting participants' MRE images were evaluated by a rheumatologist and a radiologist, using a scoring system for evidence of axSpA. Participants with evidence of axSpA and a control group of participants without evidence of axSpA were invited to participate in ProSpA-CD-Assess, in which the performance of MRE as a screening test was assessed against a gold standard of clinical assessment, serological testing and dedicated MRI of the spine and pelvis of each participant. ROC curve and logistic regression analyses were performed.

Results: A total of 1344 MRE scans were performed between 2015-2019, of which 501 eligible patients were identified. For ProSpA-CD-Screen, 259 participants were recruited. MRE SIJ abnormalities were identified in 94/259 participants and from these, 90 cases were recruited to ProSpA-CD-Assess. For the control group, 71/165 participants with normal SIJs were recruited to ProSpA-CD-Assess (total cases + controls = 161). A clinical diagnosis of axSpA was made in 41/161 (25.47%) participants, of which 25/161 (15.53%) fulfilled ASAS criteria. We constructed a ROC curve to assess test performance using different thresholds on the MRE scoring system. The optimum threshold corresponded to a sensitivity of 0.60 (95%CI 0.39, 0.79) and specificity of 0.85 (95%CI 0.78, 0.91) for MRE as a screening tool for axSpA (ASAS criteria) with an AUC value of 0.78 (95%CI 0.65, 0.86, p<0.05). We did not find a significant association between axSpA and CD location. Multivariable logistic regression demonstrated significant associations between axSpA (ASAS criteria) and inflammatory back pain (OR 11.03; 95%CI 2.53, 48.10; p<0.05), *HLA B27* (OR 9.94; 95%CI 1.84, 53.87; p<0.05), history of dactylitis (OR 51.01; 95%CI 1.07, 2423.90; p<0.05) and plantar fasciitis (OR 9.08; 95%CI 1.30, 63.55; p<0.05).

Conclusion: We have shown that MRE as a screening tool for axSpA in a cohort of CD patients has good specificity, but poor sensitivity, suggesting that its use as a screening tool is limited. There was no significant association between axSpA and CD location or CD EIMs.

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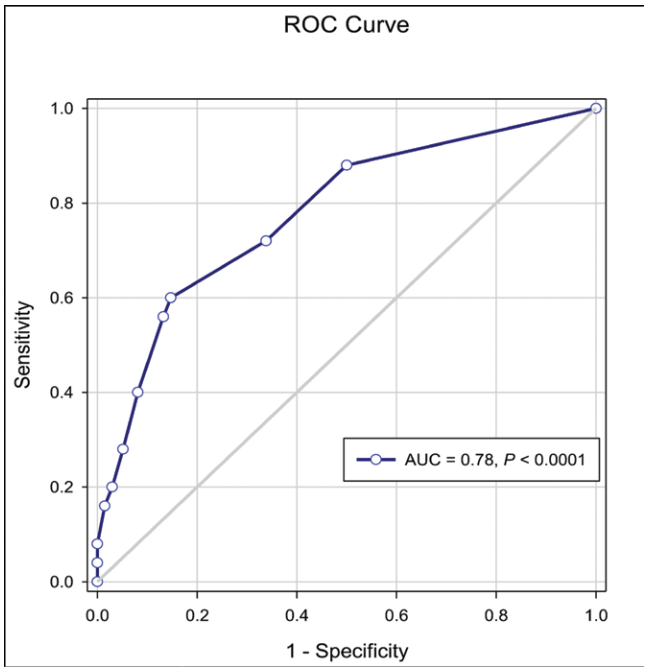

Figure 1. MRE score ROC curve for participants fulfilling ASAS criteria for axial spondyloarthritis.

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POS0966 DEVELOPMENT AND VALIDATION OF AN ANKYLOSING SPONDYLITIS RISK PREDICTION MODEL USING LONGITUDINAL REAL-WORLD DATA FROM A LARGE INTEGRATED HEALTHCARE DELIVERY SYSTEM

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Background: Early detection and diagnosis of Ankylosing spondylitis (AS) is challenging due to heterogeneity in disease presentation, lack of specific biomarkers and high prevalence of mechanical back-pain that is difficult to distinguish from inflammatory back-pain. However, if diagnosed and treated early, the risk of AS complications and disease progression can be slowed.
Objectives: To develop and validate a risk prediction model for early identification of patients at high risk of AS, using a large longitudinal real-world clinical data in the US.
Methods: This retrospective study included all members aged ≥ 21 years with back pain symptoms who were enrolled in the Kaiser Permanente Southern California health plan between 01/2009-12/2013. Patients who presented with back pain symptoms at a physician visit were followed until 12/2020 to see if they subsequently developed AS. The cohort was randomly divided into a training (60%) and a validation (40%) sample. A proportional odds model was specified to create a risk score for AS in the training sample. Best fit model was determined based on Area Under the Curve (AUC) and Akaike Information Criterion (AIC). The cut off threshold of "high-risk" was based on Youden's (1950) index.[1] We assessed the model performance for internal validity using split-samples. The model was further validated using manual chart review of 900 patient records. These 900 records were selected such that 70% (N=630) met the high-risk cut-off and the remainder had scores below the cut-off. We also derived the probability of AS in each chart reviewed case using the method proposed by Feldtkeller et al. (2013) and Rudwaleit et al. (2006).[2,3]
Results: The cohort comprised 527,509 members with mean age 54 years and majority female (58%). Sixty-six percent were White race and 33% were Hispanic ethnicity. The crude incidence of AS was 1% and increased steadily during the follow-up period (Figure 1). The final risk prediction model included 15 risk factors and had an AUC of 0.72 (Table 1). Using Youden's index, a cut-off value of 11 or higher was identified as the threshold to define high-risk. No evidence of overfitting to our training sample was observed based on the split-sample analysis. The model validation based on manual chart review of 900 records showed sufficient ability to discriminate between those at high-risk vs those not identified to be high-risk. When a concrete rule out or rule in determination could be made using Feldtkeller et al. approach, our model correctly classified 75% of such records.

Table 1. Final Model Coefficients and Derived Risk Score

	Model Coefficient	Pr(>|z|)	Risk Score
Age above 45 years	0.146	0.011	1.46
Male Sex	-0.292	<0.001	-2.92
White Race	0.259	<0.001	2.59
Non-Hispanic Ethnicity	0.177	<0.001	1.77
Corticosteroid Use (Yes/No)	0.235	<0.001	2.35
*NSAID User (Yes/No)	0.202	<0.001	2.02
Opioid Analgesic User (Yes/No)	0.416	<0.001	4.16
Had Enthesitis (Yes/No)	0.298	<0.001	2.98
Had Disorders of the Back (Yes/No)	0.973	<0.001	9.73
Had Fatigue and/or Malaise (Yes/No)	0.155	0.056	1.55
Had Psoriasis (Yes/No)	0.288	0.008	2.88
Had Spondylosis (Yes/No)	0.838	<0.001	8.38
Had Synovitis (Yes/No)	0.143	0.066	1.43
Had Uveitis (Yes/No)	0.621	0.007	6.21
Depression Diagnosis (Yes/No)	0.099	0.017	0.99

*** NSAID: Non-steroidal anti-inflammatory drugs**

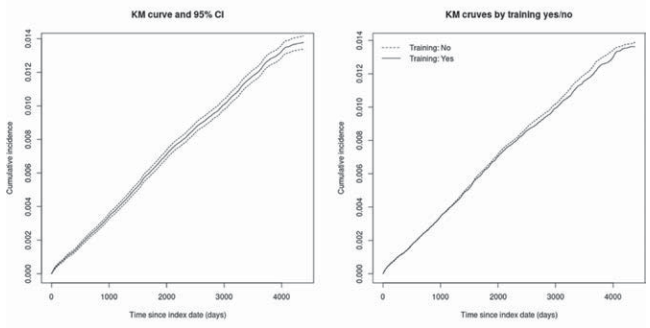

Figure 1. Cumulative Incidence Over Time (in Days)

Conclusion: To aid early detection, we have developed and validated an AS risk prediction model with an easy to implement scoring system using demographics, medication use and diagnosis data that is routinely collected in clinical practice.
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POS0967 THE IMPACT OF PSORIASIS ON THE CLINICAL CHARACTERISTICS, DISEASE BURDEN AND TREATMENT PATTERNS OF PERIPHERAL SPONDYLOARTHRITIS: AN ANCILLARY ANALYSIS OF THE ASAS-PERSPA STUDY

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Background: Psoriasis (PsO) is one of the common extramusculoskeletal manifestations of spondyloarthritis (SpA). There is a natural overlap between peripheral SpA (pSpA) and psoriatic arthritis. However, there are several unmet needs in patients with pSpA who cannot be classified otherwise (i.e., patients without PsO and without axial involvement) due to a lack of formally approved treatment options and lack of evidence of efficacy of different drug classes in this specific population.
Objectives: To evaluate the clinical characteristics, disease burden, and treatment patterns of pSpA patients with and without PsO using data from the cross-sectional ASAS-perSpA study.
Methods: We analysed 433 patients who had a diagnosis of pSpA according to the rheumatologist's diagnosis from the ASAS-perSpA cohort. A personal history of PsO was defined as the presence of signs of PsO on physical examination, psoriatic nail dystrophy, including onycholysis, pitting, and hyperkeratosis, or a personal history of PsO diagnosed by a dermatologist. Clinical characteristics, patient-reported outcomes and treatment patterns were compared between subgroups with and without PsO.
Results: A total of 83 patients (19.2%) had a personal history of PsO. Patients with PsO were older (48.4 vs. 43.2 years), had a longer diagnostic delay (7.4 vs. 3.5 years), a higher frequency of dactylitis (36.1 vs. 20.0%), and enthesitis (65.1 vs. 55.4%) than patients without PsO (Table 1). A longer diagnostic delay (odds ratio – OR=1.06 [95% CI 1.01-1.11]), lower HLA-B27 positivity (OR=0.31 [95% CI 0.15-0.65]), and higher frequency of enthesitis (OR=2.39 [95% CI 1.16-4.93])

were associated with the presence of PsO in the multivariable logistic regression analysis (Figure 1). Higher patient global assessment scores and lower use of bDMARD treatments were observed in patients without PsO as compared to patients with PsO.

Table 1. Demographics and clinical characteristics of patients with pSpA according to the presence or absence of personal history of PsO

	Total N=433	Patients without personal history of PsO N=350	Patients with personal history of PsO N=83	p-value
Age, mean (SD)	44.2 (14.4)	43.2 (14.2)	48.4 (14.5)	0.005
Sex (male)	203/433 (46.9)	167/350 (47.7)	36/83 (43.4)	0.541
Symptom duration of SpA (years), mean (SD)	10.1 (9.5)	9.0 (8.8)	14.4 (10.8)	**<0.001**
Diagnostic delay of SpA (years), mean (SD)	4.3 (6.6)	3.5 (5.9)	7.4 (8.4)	**<0.001**
First- or second-degree relatives with SpA (except psoriasis)	74/433 (17.1)	61/350 (17.4)	13/83 (15.7)	0.871
First- or second-degree relatives with psoriasis	63/391 (16.1)	29/308 (9.4)	34/83 (41.0)	**<0.001**
Patients who fulfilled peripheral ASAS critieria	95/433 (21.9)	74/350 (21.1)	21/83 (25.3)	0.461
Patients who fulfilled CASPAR critieria	81/433 (18.7)	12/350 (3.4)	69/83 (83.1)	<0.001
Peripheral articular disease ever	410/433 (94.7)	335/350 (95.7)	75/83 (90.4)	0.059
Any enthesitis in the past confirmed by specific investigations	112/433 (25.9)	81/350 (23.1)	31/83 (37.3)	**0.045**
Current SPARCC Enthesitis Index score, mean (SD)	0.4 (1.1)	0.3 (0.9)	0.6 (1.6)	**0.013**
Dactylitis ever	100/433 (23.1)	70/350 (20.0)	30/83 (36.1)	**0.003**
HLA-B27 positive	197/316 (62.3)	179/269 (66.5)	18/47 (38.3)	**<0.001**
CRP mg/L, mean (SD)	13.9 (25.4)	15.2 (26.9)	8.5 (16.5)	**0.019**
PGA, mean (SD)	4.5 (2.7)	4.7 (2.7)	3.9 (2.5)	**0.018**
Local injection of glucocorticoids for peripheral musculoskeletal involvement ever	183/193 (94.8)	156/159 (98.1)	27/34 (79.4)	**<0.001**
csDMARDs ever	384/433 (88.7)	310/350 (88.6)	74/83 (89.2)	>0.999
bDMARDs ever	223/433 (51.5)	164/350 (46.9)	59/83 (71.1)	**<0.001**
bDMARDs current	160/433 (37.0)	119/350 (34.0)	41/83 (49.4)	**0.011**

Categorical variables were given as n/N (%)

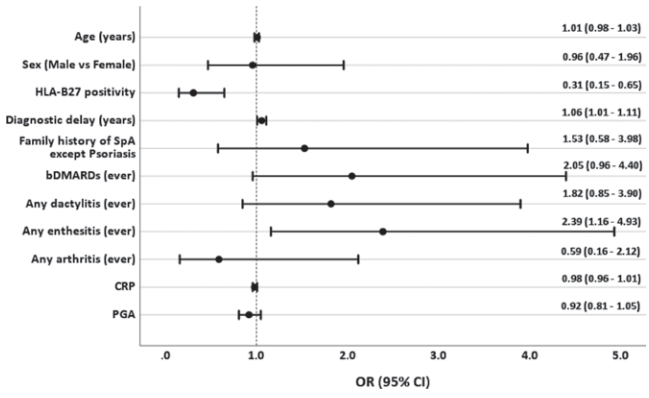

Figure 1. Association of demographic and clinical characteristics of pSpA with the presence of a personal history of PsO

Conclusion: The presence of skin PsO has an impact on clinical characteristics of pSpA. pSpA patients without PsO were less frequently treated with bDMARDs despite an comparable or even higher burden of the disease.

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POS0968 CESAREAN SECTION IN WOMEN WITH SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

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Background: There is sparse documentation on pregnancy outcomes in women with spondyloarthritis (SpA) and psoriatic arthritis (PsA). Data on disease activity is often lacking, preventing the direct investigation of the effect of inflammation on pregnancy outcomes. A cesarean section (CS) implies a higher risk for the mother than vaginal delivery. It delays mobilization after birth necessary to counteract inflammatory pain and stiffness as well as the (re)start of disease modifying medication.
Objectives: To explore the possible association of disease activity (inflammation) and occurrence of cesarean section in women with SpA and PsA.
Methods: Data from the Medical Birth Registry of Norway (MBRN) were linked with data from RevNatus, a nationwide observational register recruiting women with inflammatory rheumatic diseases. Singleton births in women with SpA and PsA included in RevNatus 2010 to 2019 were cases. All other singleton births registered in MBRN during this time served as population controls.
Results: CS occurred more frequently in both SpA (21.9%) and PsA (29.4%) compared to population controls (15.6%), with even higher frequencies in active SpA (23.5%) and active PsA (30.1%). Women with SpA had higher risk for elective CS (risk difference 4.1%, 95% CI 1.4% to 7.9%, p=0.002), while women with PsA had higher risk for emergency CS (risk difference 9.8%, 95% CI 3.8% to 17.6%, p<0.001) as compared to population controls.
Conclusion: Women with SpA and PsA had increased odds for elective and emergency CS, respectively. Further analysis will explore the role of active inflammation.

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Table 1. Characteristics of population controls, total patient groups and patient active disease groups, reported as n (%) unless specified as mean (SD)

Characteristic	Population controls	Spondyloarthritis SpA	SpA active BASDAI≥4	Psoriatic Arthritis PsA	PsA active DAS28>2.6
Number singleton births 2010 - 2019	575 798	319	115	126	29
Maternal age (years), mean (SD)	30.6 (5.1)	31.7(4.3)[1]	31.8 (4.3)	32.0 (4.7)[4]	31.8 (4.4)
<35	460 720 (80.0)	242 (77.6)	89 (78.1)	87 (71.9)	20 (74.1)
≥35	115 077(20.0)	70 (22.4)	25 (21.9)	34 (28.1)	7 (25.9)
Parity					
No children	244 354 (42.4)	141 (45.2)	43 (37.7)	48 (39.7)	10 (37.0)
≥ 1 child	331 444 (57.6)	171 (54.8)	71 (62.3)	73 (60.3)	17 (63.0)
Smoking in pregnancy	34 237 (6.7)	19 (6.3)	10 (9.3)	9 (7.1)	5 (20.0)
BMI first trimester, mean (SD)	24.4 (4.8)	25.1 (5.0)	26.5 (5.8)	26.9 (5.6)[5]	28.8 (4.9)
Cesarean section, CS	89 840 (15.6)	70 (21.9)[2]	27 (23.5)	37 (29.4)[6]	9 (31.0)
Elective	32 114 (5.6)	31 (9.7)[3]	15 (13.0)	12 (9.5)	2 (6.9)
Emergency	57 691 (10.0)	39 (12.2)	12 (10.5)	25 (19.9)[7]	7 (24.1)
Earlier caesarean section	55 992 (9.7)	32 (10.0)	16 (13.9)	15 (11.9)	3 (10.3)
Disease activity					
Inactive 3rd trim	na	134 (53.8)	na	67 (69.8)	na
Active 3rd trim	na	115 (46.2)	115	29 (30.2)	29

[1-7] Group compared to population controls [1]p<0.001 [2] p=0.002 [3] p=0.002 [4] p=0.001 [5] p<0.001 [6] p<0.001 [7] p<0.001

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POS0969 GENETIC AND MOLECULAR DISTINCTIONS BETWEEN AXIAL PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

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Background: Psoriatic arthritis (PsA) and ankylosing spondylitis (AS) represent the prototypical spondyloarthritides. PsA patients may also suffer from axial disease (axPsA). Despite overlapping symptoms, axPsA and AS may be distinct disorders with differing clinical manifestations, genetic associations, and radiographic findings.[1] These disorders also respond differently to immunomodulatory therapies such as anti-interleukin (IL)-23 inhibitors. While guselkumab, a human monoclonal antibody targeting the IL-23p19 subunit, improved symptoms of axPsA,[2] risankizumab, a humanized monoclonal antibody targeting the IL-23p19 subunit, did not show improvement in the primary endpoint of proportion of AS patients achieving an Assessment of SpondyloArthritis International Society 40% (ASAS40) response at week (W) 12.[3]

Objectives: To understand molecular distinctions between axPsA and AS to differentiate these diseases and guide treatment choice.

Methods: Whole blood and serum samples were collected from consenting patients in the NCT03162796/NCT0315828 studies of guselkumab in PsA and the NCT02437162/NCT02438787 studies of ustekinumab in AS. axPsA patients were investigator-verified as having magnetic resonance imaging- or pelvic x-ray-confirmed sacroiliitis at screening (locally read). Human leukocyte antigen (HLA) genotypes were determined by RNA sequencing, limited to Caucasian patients to reduce genetic variability,[4] and select serum cytokine levels were analyzed alongside samples from healthy individuals. Differential prevalence of HLA alleles in axPsA versus AS was determined using a Fisher's Exact test. Statistical significance of differential baseline serum cytokine expression among axPsA versus non-axPsA versus AS patients, and of guselkumab effect on serum cytokine reduction versus placebo among axPsA and non-axPsA patients, were determined with a generalized linear model performed on log2-transformed data. Biomarker data from guselkumab every-4-weeks and every-8-weeks treatment arms were pooled.

Results: Among the 186/234 Caucasian axPsA/AS patients with available data, 34%/15% were female, 70%/14% used methotrexate at baseline, mean serum C-reactive protein (CRP) levels were 2.8/2.4 mg/dL and mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores were 6.4/7.5, respectively. Aside from race, baseline demographics and disease characteristics were representative of the overall population. The prevalence of class I HLA allele -B27, -C01, and -C02 carriers was significantly lower in axPsA than AS patients (30.7% versus 92.3%, p<0.001; 5.9% versus 31.6%, p<0.001; and 28.0% versus 62.0%, p<0.001, respectively), while the prevalence of HLA-C06 was significantly higher in axPsA than AS populations (36.0% versus 8.6%, p<0.001). Baseline serum levels of IL-17A and IL-17F were significantly higher in axPsA (N=71) than in AS (N=58) patients (p<0.01 and p<0.001, respectively). Comparable IL-17A/F expression was seen for axPsA and non-axPsA (N=229) patients (both p=not significant). Significant and comparable reductions from baseline in serum IL-17A/F in axPsA and non-axPsA patients were seen with guselkumab treatment (axPsA N=41, non-axPsA N=160) versus placebo (axPsA N=30, non-axPsA N=69) at W4/24 (all p<0.05).

Conclusion: Adults with axPsA and AS exhibit different genetic risk factors and serum IL-17 levels, supporting the concept of distinct disorders. Guselkumab demonstrated significant pharmacodynamic effects in axPsA patients that aligned with such effects in non-axPsA patients, consistent with observed clinical improvement.[2]

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POS0970

SAME OR DIFFERENT? ANALYSIS OF SIMILARITIES AND DIFFERENCES OF CROHN'S DISEASE AND ULCERATIVE COLITIS IN SPONDYLOARTHRITIS: AN ANCILLARY ANALYSIS FROM THE WORLDWIDE ASAS-PERSPA STUDY.

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Background: Crohn's disease (CD) and ulcerative colitis (UC) are grouped as inflammatory bowel disease (IBD), and both are frequently found as extra-musculoskeletal manifestations in spondyloarthritis (SpA). Several studies have described the connection between SpA and IBD in both directions. Still until today, no studies have investigated possible differences in the musculoskeletal manifestations between the two main entities of inflammatory bowel disease: CD and UC.

Objectives: To evaluate the clinical characteristics associated with the presence of CD or UC in patients with spondyloarthritis from the international cross-sectional ASAS-perSpA study.

Methods: We analyzed 3152 patients from the ASAS per-SpA cohort who had a diagnosis of axial SpA or peripheral SpA according to the treating rheumatologist. Patients with IBD - confirmed by endoscopy - were identified and stratified by CD or UC. Patients in which their IBD disease was not specified, were excluded. Demographics, clinical characteristics, treatments and patient-reported outcomes were compared between both subgroups.

Results: Among the 146 patients diagnosed with IBD from the 3152 patients included in the analysis, 87 (59.6%) presented with CD (75 patients with axial SpA and 12 with peripheral SpA) and 39 (26.7%) with UC (34 patients with axial SpA and 5 with peripheral SpA) - Figure 1. A total of 20 (13.7%) patients with IBD were excluded, due to an inconclusive diagnosis of IBD. Patients with CD and UC had similar age (44.9 vs 44.0 years old) and sex distribution, although a slightly higher frequency of males was observed in CD than UC (63.2% vs 51.3%). The diagnostic delay for SpA was 7.0 years for CD and 8.1 years for UC. We did not find differences between both groups related to any musculoskeletal manifestations such as chronic back pain, uveitis, arthritis, enthesitis or dactylitis (Table 1). The only parameter showing a significant difference between CD and UC was the Bath Ankylosing Spondylitis Functional Index (BASFI) with a mean score of 3.3 vs 2.2 respectively (p=0.02) (Table 1). CD patients showed a higher tendency to be HLA-B27 positive (51.9% in CD vs. 39.4% in UC), but this did not reach statistical significance. No differences were observed regarding treatment patterns between both groups.

Table 1. Demographics and clinical characteristics related to spondyloarthritis of patients with concomitant Crohn's disease or ulcerative colitis (n=146).

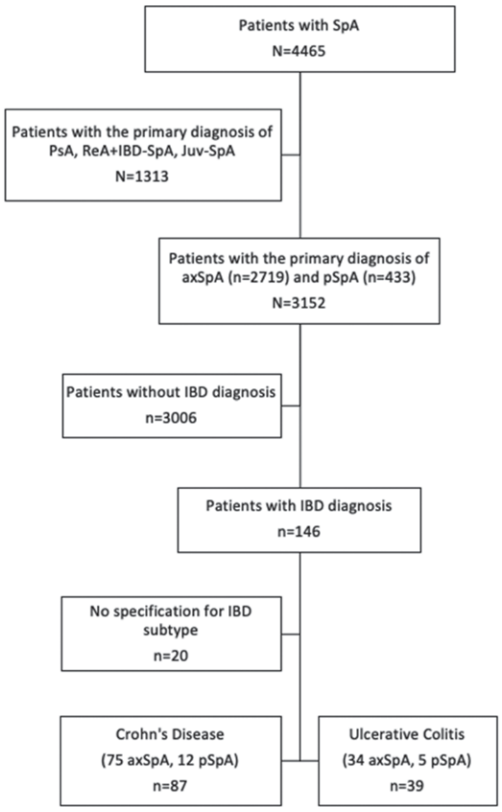
	Crohn's Disease N=87	Ulcerative Colitis N=39	P
Age, mean (SD)	44.9 (13.5)	44.0 (13.0)	0.68
Sex, n/N (%) male	55/87 (63.2)	20/39 (51.3)	0.21
Smoker ever, n/N (%)	36/87 (41.4)	19/39 (48.7)	0.44
Diagnostic delay of SpA (years), mean (SD)	7.0 (6.9)	8.8 (8.1)	0.38
Psoriasis ever, n/N (%)	9/87 (10.3)	6/39 (15.4)	0.47
Uveitis ever, n/N (%)	17/87 (19.5)	11/39 (28.2)	0.28
Synovitis ever, n/N (%)	42/87 (48.3)	18/39 (46.2)	0.83
Enthesitis ever, n/N (%)	26/87 (29.9)	14/39 (35.9)	0.50
Dactylitis ever, n/N (%)	3/87 (3.4)	1/39 (2.6)	0.79
Axial involvement ever (according to the rheumatologist), n/N (%)	79/87 (90.8)	37/39 (94.9)	0.44
Sacroiliitis on X-ray, n/N (%)	64/87 (73.6)	26/39 (66.7)	0.19
HLA-B27 positive, n/N (%)	28/54 (51.9)	13/33 (39.4)	0.26
CRP mg/L, mean (SD)	11.1 (33.8)	15.3 (30.1)	0.13
ASDAS-CRP, mean (SD)	2.4 (1.0)	2.4 (1.1)	0.84
BASFI, mean (SD) 0-10	3.3 (2.6)	2.2 (2.1)	**0.02**
csDMARDs ever, n/N (%)	71/87 (81.6)	35/39 (89.7)	0.25
bDMARDs ever, n/N (%)	72/87 (82.8)	33/39 (84.6)	0.80

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARD, biological disease-modifying antirheumatic drugs; CRP, c-reactive protein; csDMARD, conventional synthetic disease-modifying antirheumatic drugs; SD, standard deviation; SpA, spondyloarthritis.

Conclusion: In our ancillary analysis of the ASAS-perSpA study in patients with SpA and concomitant CD or UC, no differences in the clinical presentation or

demographic characteristics between the two subgroups were observed, except for the BASFI.

Figure 1. Flow-chart showing the selection of patients included in the analysis



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POS0971

THE RELATIONSHIP OF AXIAL [18F]FLUORIDE UPTAKE ON PET-CT TO ANATOMICAL CHANGES ON MRI AND X-RAY IN CLINICALLY ACTIVE ANKYLOSING SPONDYLITIS PATIENTS

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Background: Bone formation is a histopathologic feature of ankylosing spondylitis (AS), causing structural changes through the formation of syndesmophytes and spinal ankyloses (1, 2) Recent studies with [^{18}F]Fluoride Positron emission tomography (PET) demonstrated that disease activity of AS is best reflected by bone formation rather than inflammation and is sensitive to change during therapy (2, 3). [^{18}F]Fluoride PET(/CT) identifies more lesions in active AS than bone marrow edema on MRI, so may provide complementary information about the disease activity (3). A direct comparison between [^{18}F]Fluoride PET(/CT) and MRI and X-rays will allow better understanding of PET-CT positive lesions and will support further positioning of the technique for diagnostics and monitoring of AS.
Objectives: To relate uptake of [^{18}F]Fluoride on PET-CT to abnormalities on MRI and conventional radiography in patients with clinically active AS.
Methods: Ten patients (female 6/10, age 38±11 years) with AS based on modified New York criteria, a BASDAI of ≥ 4 and naïve to biologicals were included. All patients received a [^{18}F]Fluoride PET(/CT) scan, MRI scan and x-rays of the spine and SI-joints. Experienced readers blinded to clinical data and findings on other modalities scored the respective scans. PET scans were dichotomously scored for PET-positivity. MRI scans were scored in the spine for fatty lesions, erosions, ankylosis and bone marrow edema (BME) and erosions, ankylosis and BME in the SI-joints. X-rays were scored for erosions, syndesmophytes and ankylosis. Lesions on all modalities were compared with Cohen's kappa, linear regression, and univariate and multivariate analysis with a generalized mixed model.
Results: In total, 69 lesions with enhanced [^{18}F]Fluoride uptake compared to local background, 257 MRI lesions and 88 x-ray lesions were observed in the spine (Table 1). Most lesions were found in the thoracic spine. PET lesions were frequently located outside the field of view (FOV) of the MRI and X-ray in respectively costovertebral and facet joints (31/69; 45%). Univariate analysis PET positivity had the strongest association with the presence of MRI BME and x-ray bridges (OR 6.6, 95% C.I. 2.0 – 21.1, p = 0.002 and OR 34, 95% C.I. 6.0 – 183, p <0.001 respectively). Multivariate analysis confirmed these findings (OR 39, 95% C.I. 7 – 223, p < 0.01 and OR 6.4, 95% 1.7 – 23.5, p < 0.01 respectively) (Figure 1). However, of all PET-positive lesions only 7/24; 29% within the FOV of the MRI showed BME and 13/23; 56% of the PET lesions within the FOV of the X-ray showed bridges on X-ray. In the SI-joints, a total of 15 lesions (15/20; 75%) with PET enhancement were found. Erosions, ankylosis and BME lesions on MRI were observed in respectively 13/15; 87%, 4/15; 27% and 13/15; 87% of the lesions with PET enhancement.

Table 1. ***Distribution of lesions throughout the spine on different modalities.***

Number of lesions	Cervical spine	Thoracic spine	Lumbar spine	Total
PET	4	42	23	69
PET, within FOV MRI	1	11	12	24
PET, within FOV x-ray	1	10	12	23
MRI – fatty lesions	15	30	15	60
MRI – erosions	0	0	1	1
MRI – ankylosis	2	121	27	150
MRI – BME	1	35	10	46
X-ray erosions	14	25	0	39
x-ray syndesmophytes	1	0	1	2
X-ray bridges	4	31	12	47

FOV: field of view

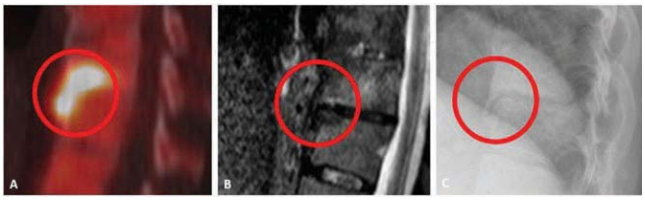

Figure 1. Example of Fluoride uptake on PET (A), corresponding BME on MRI (B) and bridges on X-ray (C).

Conclusion: Lesions with [^{18}F]Fluoride on PET showed significant correlation to MRI BME and x-ray bridge lesions. It showed partial agreement with BME of MRI and bridges on X-ray. This suggests that [^{18}F]Fluoride PET visualizes different mechanisms central to AS disease activity compared to MRI and X-ray, thereby providing novel and additional information.
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POS0972

MOST DISEASE OUTCOME MEASURES BUT NOT ASDAS ARE INFLUENCED BY GENDER IN PATIENTS WITH AXIAL SPA: RESULTS FROM ASAS-PERSPA

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Background: There is growing evidence revealing that females report worse patient-reported outcomes compared to males in axial spondyloarthritis (axSpA). However, in which precise outcomes there is a meaningful difference across gender and whether this also occurs in patients with peripheral spondyloarthritis (pSpA) and psoriatic arthritis (PsA) is not fully understood.
Objectives: To investigate the influence of gender on disease outcomes in patients with SpA, including axSpA, pSpA and PsA, in a worldwide setting.
Methods: Data from 4185 patients with axSpA, pSpA or PsA from the ASAS-PerSpA study were analysed. The ASAS-PerSpA is a cross-sectional study that recruited consecutive patients with SpA (according to their rheumatologist) from 24 countries. Associations between gender and disease activity [Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Score (BASDAI), C-reactive protein (CRP)], function [Bath Ankylosing Spondylitis Functional Index (BASFI)], and overall health [ASAS-Health Index (ASAS HI), European Quality of Life Five Dimension (EQ-5D)] were investigated. Multilevel (country) univariable and multivariable linear mixed models were used. Interactions between gender and disease phenotype (SpA, pSpA and PsA) were analysed, and if relevant, models were stratified by disease subtype. Models were adjusted for relevant confounders (Table 1).

Table 1. Multivariable multilevel model by disease phenotype

		Disease phenotype		
Outcome	Determinant of interest	**AxSpA**	**pSpA**	**PsA**
ASDAS $^{+}$	Gender (female vs male)	0.02 (-0.07, 0.11)	**0.36 (0.15, 0.58)**	**0.25 (0.12, 0.38)**
BASDAI *		**0.39 (0.20, 0.58)**	**1.22 (0.77, 1.69)**	**0.88 (0.59, 1.16)**
BASFI $^{-}$		0.01 (-0.14, 0.17)	0.30 (-0.12, 0.71)	**0.46 (0.20, 0.72)**
CRP^		-1.36 (-3.17, 0.44)		
ASAS-HI$^{\#}$		**0.90 (0.70, 1.10)**		
EQ-5D°		**-0.02(-0.03, -0.01)**		

All models are adjusted by age, gender and education. $^{+}$Also adjusted for marital status, BMI, smoking, axial involvement, peripheral arthritis, enthesitis, fibromyalgia, NSAIDs, steroids, csDMARDs, bDMARDs* Also adjusted for marital status, BMI, smoking, axial involvement, peripheral arthritis, enthesitis, psoriasis, fibromyalgia, NSAIDs, bDMARDs^{-} Also adjusted for marital status, BMI, ASDAS, radiographic damage, fibromyalgia, NSAIDs, bDMARDs^ Also adjusted for marital status, BMI, radiographic damage, concomitant NSAIDs, steroids, csDMARDs$^{\#}$ Also adjusted for smoking, ASDAS, BASFI, peripheral arthritis, enthesitis, fibromyalgia° Also adjusted for BMI, smoking, ASDAS, BASFI, radiographic damage, HLA-B27, enthesitis, fibromyalgiaResults are expressed in β (95% CI). Estimates with p<0.05 are highlighted in bold

Results: In total, 4185 patients were included, of which 2719, 1033 and 433 had a diagnosis of axSpA (mean age 42 years, 32% female), PsA (mean age 52 years, 52% female) and pSpA (mean age 44 years, 53% female), respectively. A significant interaction between gender and disease phenotype was found for ASDAS, BASDAI and BASFI. Multivariable models for each outcome are shown in Table 1 (stratified by disease phenotype). While being female independently contributed to higher BASDAI across the three disease phenotypes (though with varying magnitude), female gender was only associated with higher ASDAS in pSpA [β (95% CI): 0.36 (0.15, 0.58)] and PsA [0.25 (0.12, 0.38)] but not in axSpA [0.016 (-0.07, 0.11)]. Female gender was associated with higher BASFI in PsA [0.46 (0.20, 0.72)]. No associations were observed between gender and CRP levels. Female gender was associated with higher ASAS-HI [0.90 (0.70, 1.10)] and EQ5D [-0.02 (-0.03, -0.01)], without significant differences across disease phenotype.
Conclusion: Female gender was associated with less favorable outcomes across the SpA spectrum, except for CRP in which there were no differences between gender. While female gender influenced BASDAI across disease phenotypes, ASDAS was not associated with gender in axSpA. These results suggests that ASDAS should be the preferred instrument in clinical practice both for females and males with axSpA.
Acknowledgements: We would like to thank all ASAS-perSpA investigators and members of the scientific committee.
Disclosure of Interests: Diego Benavent Speakers bureau: Janssen, Roche, Grant/research support from: Novartis, Dafne Capelusnik Speakers bureau: Bristol Myers Squibb, Pfizer, Grant/research support from: Pfizer, Sofia Ramiro Speakers bureau: Eli Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB, Sanofi, Grant/research support from: AbbVie, Galapagos, Novartis, Pfizer, UCB, Anna Moltó Consultant of: Abbvie, UCB, Novartis, Gilead, Pfizer, Lilly y Janssen, Grant/research support from: UCB, Clementina López-Medina Speakers bureau: Lilly, Novartis, Janssen, UCB and Abbvie, Maxime Dougados: None declared, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie and Novartis
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POS0973 INFLUENCE OF ANATOMICAL VARIATION OF THE SACROILIAC JOINTS ON INFLAMMATORY LESIONS ON MAGNETIC RESONANCE IMAGING

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Background: Anatomical variation of the sacroiliac (SI) joints is more common among patients with LBP than healthy controls; increased biomechanical strain to the joint may play a role in axial spondyloarthritis (axSpA).
Objectives: To assess the association of lesions joint shape variation on inflammatory lesions on SI joint magnetic resonance imaging (MRI) in patients with axSpA.
Methods: In this post-hoc analysis a total of 684 patients from four different prospective cohorts were evaluated (379 axSpA). Two readers independently scored all patients for joint form, erosion, sclerosis, fat metaplasia and bone marrow edema (BME). Logistic regression analyses were used to assess the association of lesions on imaging joint form; this analysis was performed separately for axSpA patients and controls.
Results: Typical joints were observed in 56.5% of axSpA patients (200/354) and 55.7% of control patients (169/303); in axSpA patients exhibited a significantly higher proportion of intra-articular variants (18.4% vs. 11.6%; p<0.001) and crescent joint shapes (11.0% vs. 5.3.%; p<0.001) than controls. AxSpA patients with intraarticular joint form variants had increased odds for erosions (OR 2.09; 95%CI 1.18-3.69) and BME (OR 1.79; 95%CI 1.13-2.82); this association was not seen in controls. Accessory joints increased the odds for sclerosis in axSpA patients (OR 2.54;95%CI 1.10-5.84) and for BME (2.05; 95%CI 1.03-4.07) and sclerosis (OR 17.91; 95%CI 6.92-46.37) in controls.
Conclusion: Joint form variations are associated with inflammatory lesions on SI joint MRI of axSpA patients but not controls; this indicates a role for atypical joint forms in sacroiliitis.
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POS0974 LOW DOSE COMPUTED TOMOGRAPHY HOUNSFIELD UNITS: A RELIABLE METHODOLOGY FOR ASSESSING CHANGES IN VERTEBRAL BONE DENSITY IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Background: Assessing local vertebral bone loss in radiographic axial spondyloarthritis (r-axSpA) poses challenges, namely because Dual-energy X-ray absorptiometry (DXA) only allows assessment of lumbar vertebrae. The measurement of Computed Tomography (CT) vertebral Hounsfield Units (HU) has been shown to correlate with vertebral bone density as measured by DXA in trauma patients. We have recently reported the excellent reliability of low dose CT (ldCT) HU measurements from C3 to L5 in patients with r-axSpA[1]; however, HU change scores have never been studied.
Objectives: To describe ldCT HU change scores and their inter-reader reliability per vertebra in patients with r-axSpA over 2 years.
Methods: We used spine ldCT scans of r-axSpA patients included in the multicenter 2-year Sensitive Imaging in Ankylosing Spondylitis (SIAS) study. A standardized protocol and automatic exposure control calibration in ldCT imaging acquisition were used. Baseline and 2-year ldCT scans were independently assessed by two trained readers. The HU measurements were performed as described in Figure 1. Mean (standard deviation, SD) for the change-from-baseline

Table 1. Change scores for both readers, mean differences and intraclass correlation coefficients (ICC) from C3 to L5

Vertebra§	Mean change (SD) Reader 1	Mean change (SD) Reader 2	Mean Difference (SD)	Change > 5 #	Change < -5 #	Change >|5| #	ICC
C3	18 (56)	17 (56)	0.2 (5.0)	55	32	87	0.97
C4	18 (53)	17 (52)	0.3 (5.5)	59	32	91	0.98
C5	28 (70)	29 (70)	-0.7 (5.0)	61	32	93	0.99
C6	23 (62)	23 (62)	0.4 (5.8)	50	39	89	0.99
C7	-3 (60)	-2 (59)	-0.7 (6.9)	40	49	89	0.98
T1	-6 (87)	-6 (88)	0.6 (5.0)	47	49	96	0.98
T2	3 (45)	3 (45)	0.7 (4.0)	41	45	86	0.97
T3	1 (43)	2 (43)	0.6 (4.4)	29	35	64	0.95
T4	-2 (48)	-1 (47)	0.2 (5.3)	39	45	84	0.94
T5	0.02 (48)	-0.3 (48)	0.3 (5.1)	39	45	84	0.91
T6	-3 (44)	-3 (45)	-0.1 (4.6)	35	45	80	0.95
T7	-4 (43)	-4 (43)	-0.1 (4.5)	29	51	80	0.99
T8	-1 (38)	-1 (40)	0.1 (4.6)	35	45	80	0.98
T9	-9 (50)	-9 (50)	0.02 (5.4)	22	59	81	0.99
T10	0.2 (59)	1 (59)	-0.4 (5.2)	33	39	72	0.96
T11	-8 (53)	-7 (53)	-0.6 (4.3)	35	43	78	0.94
T12	-23 (59)	-23 (60)	-0.3 (4.4)	35	53	88	0.99
L1	-9 (33)	-7 (33)	-1.9 (6.3)	27	41	68	0.97
L2	1 (46)	2 (45)	-1.1 (4.6)	29	41	70	0.98
L3	-4 (35)	-2 (34)	-1.2 (6.3)	24	39	63	0.92
L4	-2 (24)	1 (22)	-1.5 (5.4)	31	37	68	0.91
L5	8 (43)	9 (43)	-1.0 (6.0)	47	33	80	0.97

§ C3-C7: n=44; T1-L5: n=49 **#** % of vertebrae in which both readers agreed on a change score > smallest detectable change.

scores were provided by reader, together with the respective mean differences (SD). Inter-reader reliability for the change scores was assessed using intraclass correlation coefficients (ICC) absolute agreement, applying two-way random effect models. Agreement was assessed using the smallest detectable change ($SDC = 1.96 \times SD_{difference} / (\sqrt{2} * \sqrt{k})$; $SD_{difference}$ is the SD of the differences in change scores between the two readers, and k=2 readers) and Bland-Altman plots. The percentage of vertebrae in which readers agreed on the direction of the change (positive vs negative) and on change scores > |SDC|were also computed.

Results: Whole spine ldCT scans from 49 r-axSpA patients (mean age of 49 (SD 10) years; 88% male and 84% HLA-B27 positive) were included. In total, 1,053 vertebrae were assessed by both readers. The HU mean change values varied from -23 to 28 and -23 to 29 for reader 1 and 2, respectively – Table 1. More vertebrae showed a positive change in the cervical spine compared with the thoracic and lumbar spine. Inter-reader reliability was excellent (ICC: 0.91 to 0.99). SDC varied from 4 to 7, mean and median of 5. Bland-Altman plots showed homoscedasticity throughout the whole spine, with negligible systematic error between the readers. The two readers agreed on the direction of the change score in 88-96% of vertebrae, and agreement on change scores > |SDC| was obtained in 64-96% of the vertebrae.

Conclusion: LdCT measurement of HU is a reliable method to assess changes in bone density at each vertebra from C3 to L5. This methodology can aid the study of bone loss in r-axSpA, a disease affecting the whole spine.

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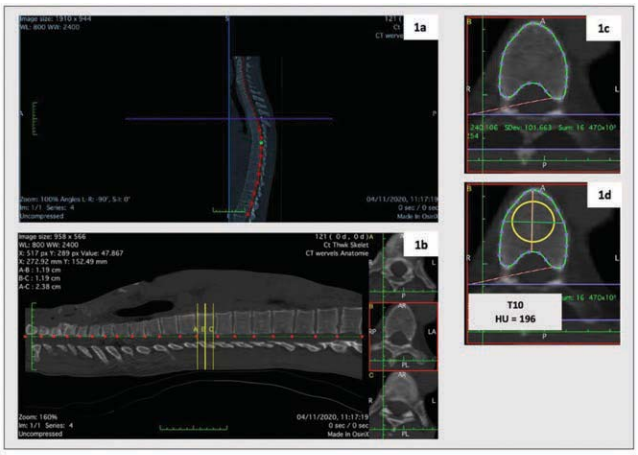

Figure 1. **Methodology of Hounsfield Units (HU) measurement.** Using a three-dimensional curved-multiplanar reconstruction the curve of the spine was identified from the spinal canal (**1a**). On the obtained sagittal image, the vertebrae could be identified. At each vertebra, two lines of reference were positioned at the superior (yellow line A) and inferior (yellow line C) limits of the vertebra. Equidistant to A and C, the yellow line B was positioned at the center of the vertebral body (**1b**). In the reconstructed cross-sectional slice, the vertebral body was delimited (**1c**). A centered region of interest (ROI) was manually selected, having a diameter equal to 75% of the average of anteroposterior and transverse diameters, and the density of the vertebra was calculated as the average image density within the sample region, reported in HU. (**1d**).

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POS0975 COMPARISON OF CLINICAL AND DEMOGRAPHIC FINDINGS OF PATIENTS DIAGNOSED AS WITH FULL SPINAL FUSION AND WITHOUT ANY SPINE DAMAGE

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Background: Erosions and sclerosis are early manifestations of radiographic progression, which can form syndesmophytes that bridge between the vertebrae and eventually lead to spinal fusion or the characteristic bamboo spine appearance in some patients.Bridging syndesmophytes in the spinal column plays a key role in the progression of AS.[1] The development of ankylosis in the axial skeleton is considered to be the most important long-term outcome parameter for axial pondyloarthritis (axSpA).[2]

Objectives: In this study, we aimed to evaluate patients with ankylosing spondylitis (AS) diagnosed with grade 4 sacroiliitis followed in our rheumatology clinic, without spinal column involvement and with complete spinal ankylosis (bamboo vertebra), together with their clinical, demographic and laboratory findings.

Methods: A total of 202 patients with unilateral/bilateral grade 4 sacroiliitis, who were registered in the Dokuz Eylul University Hospital data system, diagnosed with AS according to the modified New York criteria, were included in the study. Cervical, dorsal and lumbar radiographs of all patients were evaluated for structural damage, in addition to lateral and anteroposterior aspects, as well as posterior and facet joint involvement. In the study, all radiographs were evaluated twice at separate times.

Results: It was found that 19 (9.5%) patients had no involvement of the spinal column and 19 (9.5%) had spinal fusion appearance. It was determined that patients with spinal fusion were older (p<0.001) and the frequency of male gender was higher (p=0.042) than patients without any spinal involvement.(Table 1) In multivariate analysis; ≥45 years old [OR: 10.5, CI: 95%, 2.8-39.2; (p<0.001)] and male patients [OR: 10.5, CI: 95%, 1.14-96.56; (p=0.042)] was found to have an increased risk for the development of spinal fusion. TNFi retention rates (78.9% vs. 52.6%), TNF switch rates (53.3% vs. 45.5%) and TNF type distributions were similar in both groups (p>0.05). There was no significant difference between the patients with complete spinal fusion and no spinal involvement in terms of right and left hip BASRI scores (p>0.05).

Table 1. Demographics

	Spinal Involvement (-) (n=19)	Full Spinal Involvement (+) (n=19)	p
	n (%)	n (%)	
Age			**<0.001**
≤45	17 (89.5)	0 (0)	**AUC (SH.): 0.945 (0.040)**
>45	2 (10.5)	19 (100)	**10.5 (2.8-39.2)** oo
Sex (Erkek)	12 (63.1)	**18 (94.7)**	**0.042**
			10.5 (1.14-96.56) oo
CRP	11 (57.9)	12 (63.2)	0.999
HLA-B27	10 (64.3)	9 (60.0)	0.831
Psoriasis	1 (5.2)	1 (5.3)	-
Family History	4 (21)	0 (0)	-
Alcohol	1 (5.2)	2 (10.5)	-
Cigarette	7 (36.8)	4 (21.1)	0.475
Dactylitis	1 (5.2)	0 (0)	-
Enthesitis	0 (0)	1 (5.3)	-
Uveitis	3 (15.7)	4 (21.1)	0.234
IBD	3 (15.7)	0 (0)	-
HT	1 (5.2)	7 (36.8)	0.044
DM	1 (5.2)	5 (26.3)	0.182
CHD	0 (0)	2 (10.5)	-
Aortic Failure	1 (5.2)	0 (0)	-

Mann-Whitney U Test (Monte Carlo), ROC (Receiver Operating Curve) Analysis (Honley&Mc Nell - Youden index J); **AUC:**Area under the ROC curve; **OR:** Odds Ratio; **RC:** ROC Curve Analyze, **IBD:** Inflammatory Bowel Disease, **HT: H**ypertension, **DM:** Diabetes Mellitus, **CHD:** Coronary Heart Disease, **CRP:** C-Reaktif Protein, **n:**Number, **%:** Percent

Conclusion: In our study, we reached four important clinical results: (1) Spinal fusion was observed in 9.5% of the patients with bilateral Grade 4 sacroiliitis diagnosed with AS, 9.5% had no spinal involvement and 81% had varying degrees of spinal injury. (2) Anti-TNF treatment responses were similar in patients with spinal fusion and no spinal involvement. (3) Except for being >45 years old and having a male gender, no other factor was found to predict the development of spinal fusion. (4) There was no difference in the degree of hip involvement between patients with complete spinal fusion and no spinal involvement.

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POS0976

IMPACT OF PATIENT AND DISEASE CHARACTERISTICS ON GLOBAL FUNCTIONING AND HEALTH IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A BAYESIAN NETWORK ANALYSIS OF DATA FROM AN EARLY AXSPA COHORT

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Background: Current knowledge on the health status of patients (pts.) with axial spondyloarthritis (axSpA) mainly focusses on physical function and disease activity. Using a generic measure for physical- or mental health (SF36), a hierarchical relationship between disease activity, spinal damage, spinal mobility, physical function and overall health has been demonstrated in pts. with radiographic axSpA (r-axSpA) [1]. Disease-specific global functioning and health can be assessed in pts. with axSpA using the ASAS Health Index (ASAS HI), which encompasses physical function, as well as aspects of emotional and social functioning and aspects of activity and participation.

Objectives: To build a structural model that visualizes interrelationships of different patient- and disease characteristics with global functioning and health in pts. with early axSpA.

Methods: Data of pts. with axSpA from the DESIR cohort was analyzed, which included information on socio-demographics (age, BMI), disease activity (ASDAS), physical function (BASFI), spinal mobility (BASMI), structural damage (mSASSS), disease-specific global functioning (ASAS HI), and comorbidity count. Information on patient- and disease characteristics was retrieved from the visit performed 72 months after inclusion, which was the first time point of ASAS HI collection. A Bayesian network (BN) was used to obtain insight of the underlying structural model. BNs are probabilistic graphical models consisting of "nodes" (representing specific variables) joined by "edges" (lines representing directions of effects). They are capable of capturing complex relationships between variables and allow the incorporation of existing (prior) knowledge from previous studies.

Results: The DESIR cohort contained data from 582 pts. at month 72, of whom 398 had data for ASAS HI. Descriptive information of these pts. is shown in Table 1. The mean ASAS HI was 5.7 (range: 0 - 16). Applying existing cut-offs for ASAS HI, 51% had 'good' global functioning (ASAS HI ≥5), 40% had 'moderate' global functioning (5< ASAS HI <12) and 9% had 'bad' global functioning (ASAS HI ≥12). The structural model that was constructed from combining data and prior expert knowledge is visualized in Figure 1. It suggests that ASDAS and BASFI have a direct impact on ASAS HI and that ASDAS has an indirect impact via BASFI. The model also suggests that ASDAS has an impact on the number of co-morbidities via BMI and that BASFI determines BASMI, which is in turn also influenced by age and mSASSS. In addition, it suggests a direct effect of age, BMI and ASAS HI on the comorbidity count. The model denies a relationship between BASMI or mSASSS and ASAS HI.

Table 1. Patient and disease characteristics at month 72

	N = 398
Gender (male), N (%)	181 (45%)
Age (years)	40.7 (8.7)
Symptom duration (years)	7.5 (0.9)
BMI (kg/m^2)	25.0 (4.6)
ASDAS	2.0 (1.0)
BASFI (0–10)	2.3 (2.1)
BASMI (0–10)	2.5 (1.0)
mSASSS (0-72)	1.0 (3.6)
ASAS HI (0-17)	5.7 (3.9)
good global functioning: ASAS HI ≤5, N (%)	201 (51%)
moderate global functioning: 5< ASAS HI <12, N (%)	160 (40%)
bad global functioning: ASAS HI ≥12, N (%)	37 (9%)
Comorbidity count	1.4 (0.7)

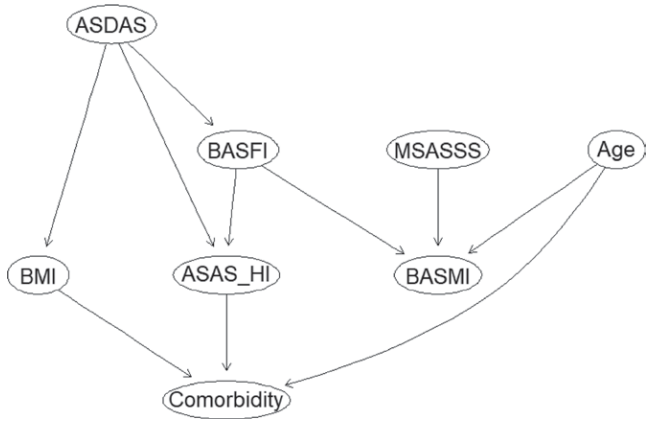

Figure 1. Structural model on interrelationships of different patient- and disease characteristics with global functioning and health (ASAS HI) in patients with early axSpA

Conclusion: The BN-analysis approach, that combines prior knowledge and measured data, serves to better understand the construct of global functioning and health in pts. with early axSpA. Our model shows that global functioning (ASAS-HI) is determined both by patient-reported physical function (BASFI) and by disease activity (ASDAS), which confirms the hierarchical model once proposed by Machado et al. The observed directional relationship between ASAS HI and comorbidity count is counterintuitive and requires further investigation.

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Table 1.

Features	M694V (+) (n=91)	M694V (-) (n=22)	P1	M694V Homozygous (n=45)	M694V Nonhomozygous (n=68)	P2
Age at FMF symptom onset [years, med (25-75)]	11 (5-18)	21 (8-30)	**0,005**	7 (1-42)	18 (3-53)	**<0,001**
Age at FMF diagnosis [years, med (25-75)]	18 (10-27)	33 (27-38)	**<0,001**	12 (1-42)	28 (3-59)	**<0,001**
Age at AxSpA symptom onset [years, med (25-75)]	20 (15-25)	29 (24-38)	**<0,001**	20 (5-50)	22 (5-58)	0,43
Age at AxSpA diagnosis [years, med (25-75)]	24 (19-33)	37 (28-44)	**<0,001**	23 (11-51)	29 (7-59)	**0,039**
Fever n (%)	84 (92,3)	21 (95,5)	0,60	44 (97,8)	61 (89,7)	0,10
Abdominal pain n (%)	80 (87,9)	20 (90,9)	0,70	43 (95,6)	57 (83,8)	0,056
Peripheral arthritis n (%)	45 (49,5)	7 (31,8)	0,13	24 (53,3)	28 (41,2)	0,20
Erysipelas n (%)	19 (20,9)	2 (9,1)	20,2	13 (28.9)	8 (11,8)	**0,02**
Enthesitis n (%)	21 (23,1)	4 (18,2)	0,62	11 (24,4)	14 (20,6)	0,63
Uveitis n (%)	11 (12,1)	4 (18,2)	0,45	4 (8,9)	11 (16,2)	0,26
Psoriasis n (%)	6 (6,6)	1 (4,5)	0,72	2 (4,4)	5 (7,4)	0,82
HLA-B27 (+) n (%)	25 (27,3)	4 (18,2)	0,54	2/15 (13,3)	12/40 (30)	0,30
Syndesmophyte n (%)	20/82 (24,4)	6/19 (31,6)	0,52	7/43 (16,3)	19/59 (32,2)	0,07
Total ankylosis n (%)	4/83 (4,8)	1/19 (5,3)	0,94	1/43 (2,3)	4/59 (6,8)	0,39
Moderate to severe hip disease * n (%)	22 (24,2)	2 (9,1)	0,12	12/45 (26,7)	12 (17,6)	0,25
Total hip replacement n (%)	10 (11,0)	1 (4,5)	0,36	4 (8,9)	7 (10,3)	0,80

* BASRI-hip score ≥3 on any side

BMS, Boehringer, Celltrion, Chugai, Fresenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Novartis, Pfizer und UCB, Consultant of: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, Fresenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Novartis, Pfizer und UCB, Grant/research support from: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, Fresenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Novartis, Pfizer und UCB, Uta Kiltz Speakers bureau: AbbVie, Biocad, Biogen, Chugai, Eli Lilly, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, Biocad, Biogen, Chugai, Eli Lilly, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Biogen, Fresenius, Amgen, Hexal, Novartis, Pfizer

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POS0977 ASSOCIATION OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER AND AXIAL SPONDYLOARTHRITIS WITH THE M694V MUTATION

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Background: The incidence of co-occurrence of FMF and axial spondyloarthritis (axSpA) in adults is reported to be 0.5-7.5%. M694V mutation is the most frequent variant in patients with FMF+AxSpA (1).
Objectives: To evaluate the association of demographic and clinical characteristics of patients with FMF+axSpA with the M694V mutation.
Methods: A total of 9630 FMF patients were identified according to the ICD-10 code (E85.0) in the electronic database of Hacettepe University Hospital. 7525 patients aged <18 years old and no hospital admissions after 2014 were excluded. 2105 adult FMF patients screened for accompanying axSpA according to ICD-10 code (M45) and 241 patients detected as FMF+axSpA. FMF diagnosis was confirmed with Tel-Hashomer criteria. The diagnosis of axSpA was confirmed by the presence of sacroiliitis on sacroiliac radiography according to the Modified New York (mNY) criteria or the presence of active sacroiliitis on sacroiliac magnetic resonance imaging according to the ASAS criteria. According to these criterias, the diagnosis of FMF+AxSpA association was confirmed in 136 patients. MEFV gene result was present in 113 (83%) of 136 patients and were included in the study. Patients were divided into two groups as M694V (+) and M694V (-) according to the M694V mutation, and the demographic and clinical characteristics of the patients were compared. p<0.05 was considered statistically significant.
Results: Of 113 patients with known MEFV gene result, 91 (80.5%) were M694V (+), 22 (19.5%) were M694V (-), 45 (39.8%) were homozygous for M694V. In the M694V (+) group, symptom onset and diagnosis of both FMF and axSpA were at an earlier age compared to M694V (-) patients (p<0.05). The frequency of radiographically proven moderate to severe hip involvement (24.2% vs. 9.1%) and total hip replacement (11% vs. 4.5%) was higher in M694V (+) patients. However, these differences were not statistically significant (p=0.12; p=0.36). In the homozygous M694V (+) group, symptom onset and diagnosis of both FMF and axSpA were significiantly at an earlier age than in the group homozygous M694V (-) (p<0.001). Although erysipelas-like skin rash was more common in homozygous M694V (+) group (28.9% vs. 11.8% p=0.02), other symptoms and findings were similar in both groups (Table 1).
Conclusion: FMF and SpA symptoms appear at an earlier age in M694V positive patients. The M694V mutation is associated with severe disease and early disease onset.

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POS0978 LUMBAR FACET JOINTS ARTHRITIS RELATES TO ITS ADJACENT MRI INFLAMMATORY LESIONS IN AXIAL SPONDYLOARTHRITIS

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Background: Facet joints are frequently impaired in patients with axial spondyloarthritis (axSpA), which raises high disease activity and poor physical function. However, insufficient attention is paid to the relationship between the feature of disease and facet joint arthritis (FJA) in magnetic resonance imaging (MRI) examination, because of lacking an ideal assessment tool. The Canada-Denmark (CANDEN) MRI scoring system is adopted in our study because it is a comprehensive method to assess the alteration of spine [1].
Objectives: We aimed to find relevant factors for lumbar FJA in axSpA patients.
Methods: This was a cross-sectional study that analyzed the lumbar MRI of axSpA patients using the CANDEN system. Demographic and clinical information was recorded. Univariate and multivariate linear mixed model (LMM) was used to screen related factors for lumbar FJA in MRI examinations.
Results: (1) Totally 108 axSpA patients were investigated in our study, while ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) accounted for half respectively. Sixty-five (60.19%) participants were male and their median age was 35 years. (2) Twenty (37.10%) and 1 (1.80%) AS and nr-axSpA suffered lumbar FJA (P<0.05). (3) Univariate LMM found gender, vertebral body corner inflammation subscore (VBCIS), spondylodiscitis subscore (SDS), posterolateral elements inflammation subscore (PLEIS), fat posterior elements subscore (FPES), fat vertebral body subscore (FVBS), and AS disease activity score with C-reactive protein (ASDAS) related to lumbar FJA in AS patients. Besides, gender, the duration of symptom, peripheral arthritis, enthesitis, non-steroidal anti-inflammatory drugs, VCBIS, SDS, PLEIS, FPES, the ankylosis of sacroiliac joints, and bony erosion of hips were involved in the univariate LMM for nr-axSpA. (4) Multivariate LMM displayed that odd ratio (OR) and 95% confidence intervals (CI) of PLEIS, FPES, and ASDAS were 0.66 (0.40, 0.91), 0.45 (0.20, 0.71), and 0.23 (0.01, 0.44) (P<0.05). OR (95%CI) for VBCIS and PLEIS were 0.02 (0.00, 0.04) and 0.23 (0.16, 0.30) in nr-axSpA patients (P<0.05).
Conclusion: Prevalence of lumbar FJA is higher in AS patients than nr-axSpA. This lesion is mainly related to MRI changes of its neighborhood structure, especially inflammatory alterations, rather than demographic and clinical characteristics.

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POS0979

IMPROVING THE VALIDITY OF DIAGNOSTIC CODES AND POINT PREVALENCE ESTIMATION OF SPONDYLOARTHRITIS IN A LARGE POPULATION-BASED DATABASE

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Background: Large population-based databases provide an opportunity to study the epidemiology of spondyloarthritis (SpA), however, strict validation procedures for case ascertainment are required (1).
Objectives: To examine the validity of the ICD-9 codes of SpA in a large population-based database and to assess whether applying a specific algorithm would improve the case ascertainment. Finally, the point prevalence of SpA in the database was estimated using the validated algorithm.
Methods: A Database of a large public health fund, which serves approximately 3.17 million enrollees older than 18 years old, was used. The database includes real-time input from pharmaceutical, medical and administrative operating systems. At first, the database was searched for all individuals who received an ICD-9 code of SpA, 720.0: 7200, 7201, 7202, 7208, 72081 and 72089. All medical records of a random sample of 169 patients were thoroughly reviewed by a rheumatologist. Based on the information available in the database, a decision was made whether SpA diagnosis was: 1) definite/probable SpA; 2) not SpA/; not enough data to verify the diagnosis of SpA. The positive predicted value (PPV) and 95% confidence interval (CI) were calculated. In order to improve the case ascertainment, a second validation process was performed using a specific algorithm. The algorithm applied was: a permanent ICD-9 code of SpA assigned by the family physician plus at least one of the following criteria: 1. At least one visit at a rheumatology clinic either in the community or at a hospital outpatient clinic; 2. A diagnosis of SpA given during a hospital admission; 3. A prescription fulfilled of an anti-Tumor Necrosis Factor agent or anti IL-17 agent. This algorithm was validated by two rheumatologists in a random sample of 182 cases. Finally, the point prevalence of SpA was estimated applying the validated algorithm.
Results: The PPV of the ICD-9 codes of SpA was 44% (95%CI 36%-52%). The specific algorithm improved the PPV to 90% (95%CI 85%-94%). The concordance between the two rheumatologists was 91.3 95%CI (85.7-94.8). On the 31/12/2021, the validated algorithm identified 2892 live SpA patients older than 18 among a population of 3,167,329 enrollees in the database, reflecting a point prevalence of 0.09%, 94 patients per 100,000. Fifty one percent of the patients were male, 49% females. The point prevalence of males was 0.096%, and females - 0.087%. On the 31/12/2021, 6% of the patients were 18-29 years old, 34% 30-44 years old and 60% older than 45.
Conclusion: A specific algorithm can accurately identify patients with SpA in this large population-based database. The estimated prevalence of SpA is 0.09%. This figure is consistent with other population-based estimates (2).
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POS0980

ADAPTING TO LIVING WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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Background: Axial spondyloarthritis (axSpA) is associated with a high disease burden which may require patients to make functional adaptations in response to the disease
Objectives: The aim is to identify factors associated with implementing functional adaptations due to axSpA.
Methods: Data from 2,846 unselected patients participating in EMAS, an online survey (2017-2018) across 13 European countries, were analysed. Adaptations were assessed by: "Please indicate any steps you have taken since you have been affected by Spondylitis/ Spondyloarthritis?" with possible answers: purchasing customized or comfortable shoes, workplace or home or car adaptations. BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and mental health via the General Health Questionnaire GHQ-12 (0-12) were collected. Univariable and multivariable logistic regression models were used to identify variables associated with life adaptations, including sociodemographic factors, PROs, employment status, health behaviours, and comorbidities (n= 2,754).
Results: Mean age was 43.8 years, 61.5% female, 48.9% had a university degree, and 67.6% married. 76.9% (n=2,118) patients had made at least one adaptation: 72.0% (n=1,525) purchased customised or comfortable shoes, 54.9% (n=1,163) adapted their workplace, 40.7% (n=861) their home, and 29.0% (n= 614) their car. Compared to those who did not require adaptations, those who made adaptations were typically female (78.9% vs. 73.7% male, p=0.002), separated/divorced/widowed (82.0% and 80.0% vs. 71.5% singles, p=0.002), had retired early, or were on sick leave (temporary or permanent) (85.0%, 84.0%, 84.3% vs. 74.5% of employed), members of a patient organisation (81.5% vs. 74.0% of non-member, p<0.001), physically active (78.9% vs. 66.5% vs. not physically active, p<0.001), and overweight/obese (78.6% vs. 75.1% of underweight/normal weight). Those requiring functional adaptations reported greater BASDAI (5.7 vs. 4.9), functional limitations (21.4 vs. 16.5), poorer mental health (5.2 vs. 4.3), and longer diagnostic delay (7.9 vs. 6.0), all p<0.001. The variables independently associated with functional adaptations were being physically active (OR=1.98), patient organisation membership (OR=1.39), female gender (OR=1.31), being overweight or obese (OR=1.26), separated, divorced or widow status (OR= 1.20), higher BASDAI (OR= 1.14) and functional limitation (OR= 1.01; Table 1).

Table 1. Regression analysis for variables associated with the presence of at least one functional adaptations (n= 2,162)

	Univariable logistic analysis		Multivariable logistic analysis	
	OR	**95%CI**	**OR**	**95%CI**
Gender. Female[1]	1.34	**1.12, 1.60**	1.31	**1.06, 1.63**
Marital Status. Separated/ divorced/widow[2]	1.33	**1.14, 1.55**	1.20	**1.00, 1.44**
Employment status. Sick leave/ early retirement[3]	1.83	**1.45, 2.32**	1.17	0.89, 1.53
Patient organization. Member[4]	1.55	**1.29, 1.88**	1.39	**1.12, 1.74**
Physical activity	1.88	**1.51, 2.35**	1.98	**1.52, 2.59**
Body Mass Index. Overweight/ obesity[5]	1.22	**1.02, 1.46**	1.26	**1.02, 1.55**
BASDAI (0-10)	1.21	**1.16, 1.27**	1.14	**1.07, 1.22**
GHQ-12 (0-12)	1.06	**1.03, 1.08**	1.01	0.98, 1.04
Functional Limitation (0-54)	1.02	**1.01, 1.03**	1.01	**1.00, 1.02**
Spinal Stiffness (3-12)	1.10	**1.06, 1.14**	0.99	0.94, 1.03
Diagnostic delay	1.03	**1.02, 1.04**	1.01	0.99, 1.03
Anxiety	1.26	**1.03, 1.54**	0.87	0.65, 1.18
Depression	1.56	**1.25, 1.95**	1.31	0.95, 1.79
Sleep disorders	1.54	**1.27, 1.86**	1.17	0.91, 1.51

[1]Male vs. Female; [2]Separated/divorced/widow vs. married/single; [3]Sick leave/early retirement vs. other employment status; [4]Member vs. non-member; [5]Overweight/obesity vs. underweight/normal weight

Conclusion: Three out of four axSpA patients made at least one functional adaptation due to their axSpA, which were often implemented by those with higher body weight, disease activity, engaging in physical activity, and patient organization membership. This is most likely explained by need as those with high disease burden or weight may face limitations, which can be alleviated through functional adaptations, enabling them to engage in physical activity.
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POS0981

RELATIONSHIP BETWEEN CLINICAL MANIFESTATIONS OF AXIAL SPONDYLOARTHRITIS AND PROGRESSION OF COXITIS.

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Background: Almost half of the patients with axial spondyloarthritis (axSpA) in Russia diagnosed hip joint lesions (HJ), but the causes and rates of progression

are not studied. Until now, it remains unclear whether synovitis detected on MRI and ultrasound of hip joint is a predictor of radiological progression of coxitis.
Objectives: To determine the factors influencing the progression of coxitis in axSpA.
Methods: 77 patients (mean age 28 ± 5.92 years) with a diagnosed with axSpA (ASAS criteria 2009), which were observed for at least 2 years. Among them, AS according to the modified New York criteria (1984) - 66 (86%) patients, and 11 (14%) were diagnosed with nr-axSpA. The median duration of the disease was 30 [3–60] months, BASDAI 4.5 [3.2; 5.9], BASFI 2.4 [0.9; 4.8]. All patients underwent clinical, X-ray, ultrasound and MRI examination of the hip joint during the entire observation period. For ultrasound, coxitis was considered an increase in the cervical-capsular distance (CCD) of more than 7mm. For MRI inflammatory changes were taken as osteitis of the acetabulum and / or femoral head and synovitis in STIR mode. The sum of stages of radiographic coxitis (ssrC) was used to assess HJ injury progression. During the study, a formula was developed to assess the progression rate of radiographic coxitis (R-rpC).
Results: Cluster analysis of the main parameters was performed to detect the relationship between the clinical manifestations of axSpA and radiological progression of coxitis (Figure 1). During the analysis, it was found that the most closely related group of clinical parameters, such as the presence of the HLA B 27 gene and the sex of patients, the rate of radiographic progression of coxitis and srsc (Euclidean distance < 20). The second group of related measures included the BASDAI and ASDAS-CRP disease activity indices, as well as their associated functional impairment (BASFI index) (Euclidean distance < 30). These two groups of signs are also related to each other — Euclidean distance < 30. It should be noted that laboratory indicators of inflammation (ESR and CRP), the age of patients, and especially the duration of the disease, turned out to be weakly related to each other (Euclidean distance > 100). It should also be noted that the relationship between laboratory indicators of inflammation and disease activity indices is relatively weak, as well as with structural damage in axSpA.

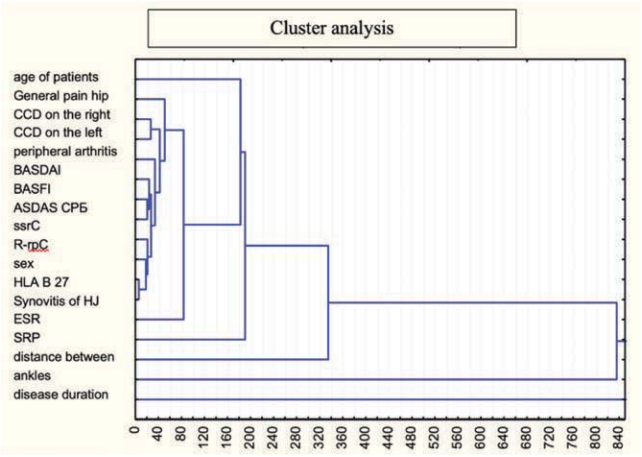

Figure 1.

Conclusion: Factors influencing the development and progression of coxitis in axSpA are a combination of such features as high clinical activity of the disease, the presence of peripheral arthritis, HLA B27 positivity and male sex.
Disclosure of Interests: None declared
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POS0982 ANTIBODIES TO TWO NOVEL PEPTIDES IN NEW ONSET AXIAL SPONDYLOARTHRITIS

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Background: Diagnosis of axial spondyloarthritis (axSpA) is challenging since clinical manifestations often overlap with other disorders and a specific laboratory test for diagnosis is lacking. Previously, we identified antibodies to 3 Hasselt University (UH)-axSpA peptides which could provide a novel tool for diagnosis of a subset of axSpA patients. Validation of antibody reactivity in plasma samples of early axSpA patients (disease duration < 5 years) from the UH and the Leuven Spondyloarthritis (Biologics) Cohort ((Bio)SPAR) cohorts revealed antibody reactivity against at least one of these 3 peptide targets in 14.2% of early axSpA patients (22/155)[1].
Objectives: We aim to validate the diagnostic potential of the antibodies to these 3 peptides in a third independent cohort of new onset axSpA patients and controls.
Methods: Using enzyme-linked immunosorbent assays (ELISA), presence of antibodies to the 3 peptides was determined in 188 serum samples of the Belgian Inflammatory Arthritis and Spondylitis (Be-Giant) cohort, 74 controls with non-specific chronic low back pain (CLBP) and 112 age and gender-matched healthy controls from the UH cohort. Patients were classified as having axSpA according to the ASAS classification criteria and had a mean age of 32.7 years. We further investigated whether clinical and disease characteristics were correlated with antibody reactivity.
Results: The presence of antibodies against 2 of the 3 UH-axSpA peptides was confirmed in the Be-Giant cohort. Antibody reactivity against 1 of the 2 UH-axSpA peptides was found in 11.2 % of newly diagnosed axSpA patients (21/188) compared to 3.6% (4/112, *p=0.0290*) in HC and 6.8% (5/74, *p=0.3619*) in CLBP. We did not detect a significant difference in age, sex, HLA–B27 status, enthesitis, symptom duration, treatment, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), BathAnkylosing Spondylitis Functional Index (BASFI), erythrocyte sedimentation rate (ESR), or C-reactive protein (CRP) levels between axSpA patients with and those without antibody reactivity against these 2 UH-axSpA peptides.
Conclusion: The presence of antibodies to 2 UH-axSpA peptides was confirmed in an independent cohort of newly diagnosed axSpA patients and could be of added value for discriminating axSpA patients from HC in the Be-Giant cohort.
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POS0983 LIFESTYLE IN AXIAL SPONDYLOARTHRITIS - COMPARISONS BETWEEN PATIENTS AND CONTROLS, AXIAL SPONDYLOARTHRITIS SUBTYPES, MALE AND FEMALE PATIENTS, AND ITS ASSOCIATION WITH DISEASE AND HEALTH OUTCOMES. RESULTS FROM THE SPARTAKUS COHORT

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Background: Healthy lifestyle behaviours are associated with better health outcomes and quality of life in the general population (1, 2). In patients with axial spondyloarthritis (axSpA), however, little is known regarding multiple lifestyle behaviours and their associations with disease and health outcomes.
Objectives: To study lifestyle behaviours in patients with axSpA in relation to healthy controls, between axSpA subtypes and male and female patients, respectively, and to assess how the presence of two or more unhealthy lifestyle factors associate with disease and health outcomes.
Methods: We performed a cross-sectional study of 250 well-characterized axSpA patients (167 with radiographic axSpA [r-axSpA; ASAS and/or modified New York criteria], 83 with non-radiographic axSpA [nr-axSpA; ASAS criteria]) and 48 controls (frequency-matched to the patients for age and sex), participating in the population-based SPARTAKUS study in southern Sweden. Self-reported data on smoking, alcohol use, physical activity, dietary habits, and objectively measured body mass index (BMI), respectively, for all subjects was categorized as fulfilling national recommendations or not (healthy/unhealthy), and summarized in an index (0-5, indicating the number of unhealthy lifestyle factors). The index was also dichotomized into 0-1 vs. 2-5 unhealthy lifestyle factors. Comparisons between patients and controls, axSpA subtypes (r-axSpA vs. nr-axSpA), and between male and female patients were performed by Student's t-test/Chi-square test, as appropriate. Linear regression analyses were used to explore associations between having ≥2 unhealthy lifestyle factors (yes/no) and disease and health outcomes.
Results: Characteristics and lifestyle factors for axSpA patients and controls are presented in the Table 1. Reporting ≥2 unhealthy lifestyle factors was more common in axSpA patients than controls (35% vs. 19%, p=0.029), while no difference was found between the axSpA subtypes (Figure 1 a and b). Male patients more often reported several unhealthy lifestyle factors than female patients (Figure 1 c), with more frequent unhealthy alcohol use (19% vs. 9%, p=0.023) and overweight/obesity; BMI ≥25 (63% vs. 50%, p=0.043), while smoking, physical activity, and dietary habits were similar. In addition, older patients displayed more unhealthy lifestyle factors (Figure 1 d). Having ≥2 unhealthy lifestyle factors was associated with worse disease activity (ASDAS-CRP) (β-est [95% CI]) (0.34 [0.11: 0.58]), physical function (BASFI) (0.73 [0.18; 1.28]), pain (1.03 [0.39; 1.67]), fatigue (0.95 [0.24; 1.66]), and quality of life (EQ-5D) (-0.09 [-0.15; -0.02]) in axSpA patients, adjusted for age, sex, and axSpA subtype (all p≤0.010)

Table 1. Characteristics and lifestyle factors

	r-axSpA/nr-axSpA combined n = 250	Controls n =48
Female sex	116 (46%)	24 (48%)
Age, years	51 (13)	51 (14)
Symptom duration, years	7.7 (7.6)	N/A
ASDAS-CRP	1.8 (0.9)	N/A
BASFI	2.0 (2.2)	N/A
BASMI	3.0 (1.6)	N/A
NRS patients' global health	3.1 (2.5)	1.1 (1.1)*
NRS pain	3.1 (2.5)	1.5 (1.6)*
NRS fatigue	3.5 (2.8)	2.2 (2.0)*
EQ-5D utility	0.72 (0.24)	0.90 (0.12)*
Ongoing csDMARD	54 (22%)	N/A
Ongoing bDMARD	103 (41%)	N/A
Ongoing glucocorticoids	18 (7%)	N/A
Smoking, not fulfil rec.	31 (12%)	2 (4%)
Alcohol, not fulfil rec.	35 (14%)	5 (10%)
Physical activity, not fulfil rec.	72 (29%)	8 (17%)
Dietary habits, not fulfil rec.	35 (14%)	5 (10%)
BMI, not fulfil rec.	142 (57%)	15 (31%)*

Mean (SD) or n (%). * p<0.05 by Chi^2-test or Student t-test, as appropriate. Missing data: ≤ 2%.

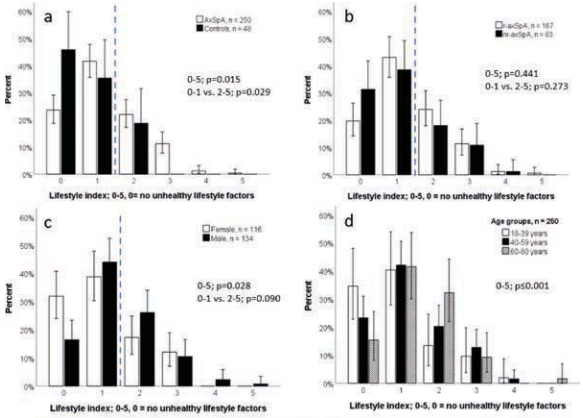

Figure. Percental distribution of lifestyle index; 0-5 and dicotomized; 0-1 vs. 2-5 for a) axSpA patients versus healthy controls, b) r-axSpA versus nr-axSpA, c) female versus male axSpA patients, d) axSpA patients in different age groups. Comparisons by Chi-square test.

Conclusion: Unhealthy lifestyle behaviours were more common in axSpA patients than controls, and in male axSpA patients compared to females. Having two or more unhealthy lifestyle factors was associated with worse disease activity, physical function, pain, fatigue, and quality of life in the axSpA patients.

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POS0984

PREVALENCE OF AXSPA IN PATIENTS TREATED FOR CHRONIC BACK PAIN IN CHIROPRACTIC CLINICS: THE OREGON CHIROPRACTIC AXIAL SPONDYLOARTHRITIS STUDY (ORCAS) – AN INTERIM ANALYSIS

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Background: Non-rheumatology settings such as chiropractor clinics, where chronic back pain (CBP; including chronic back, buttock, or hip pain) patients are first seen, lack consistency in referral of patients to rheumatologists where the underlying cause may be axial spondyloarthritis (axSpA).

Objectives: Primary objective was to estimate the prevalence of axSpA in CBP patients attending four chiropractic clinics in Portland, Oregon, referred to a rheumatology clinic using a referral strategy identifying features of spondyloarthritis (SpA).

Methods: Adults attending one of four chiropractor clinics between Nov 2020 and Nov 2021 for CBP starting before age of 45, without prior diagnosis of SpA were eligible for inclusion. Patients were referred to rheumatologist for diagnostic assessment via phone consultation, if they had inflammatory back pain (IBP) and/or ≥1 of the following features: a family history of SpA, inflammatory bowel disease (IBD), psoriasis, good response to non-steroidal anti-inflammatory drugs, history of heel pain, uveitis, or joint swelling. The subsequent rheumatology assessment included history, C-reactive protein, HLA-B27, x-ray and MRI of the sacroiliac joints. Based on the assessment, patients were categorized as radiographic axSpA, non-radiographic axSpA, peripheral SpA, or no SpA. Endpoints were summarized using descriptive statistics.

Table 1. Demographic and clinical characteristics stratified by diagnosis as confirmed by Rheumatologist

	Radiographic axSpA (N = 1)	Non-radiographic axSpA (N = 5)	Peripheral SpA Including PsA (N= 2)	No SpA (N = 55)
Age, years (Mean; SD)	73 (-)	36.8 (6.4)	46 (1.4)	45.1 (12.1)
Sex, Female – n (%)	0	4 (80.0)	2 (100)	32 (58.2)
Family history of spondyloarthritis, Yes – n (%)	0	1 (20.0)	1 (50.0)	9 (16.4)
Chronic back pain duration, years (Mean; SD)	49 (-)	12.4 (6.0)	11 (7.0)	15 (10.8)
Confirmed during rheumatology visit – n (%)				
IBP* (4 out of 5 criteria as checked by patient)	1 (100)	3 (60.0)	1 (50.0)	27 (49.1)
IBP* (4 out of 5 criteria per rheumatologist's opinion)	0	2 (40.0)	0	22 (40.0)
History of plantar fasciitis or Achilles tendinitis	0	4 (80.0)	2 (100)	14 (25.5)
History of peripheral joint swelling	0	0	1 (50.0)	8 (14.6)
Positive response to NSAIDs	1 (100)	1 (20.0)	2 (100)	21 (38.2)
Psoriasis	1 (100)	0	1 (50.0)	2 (3.6)
Inflammatory bowel disease	0	0	0	1 (1.9)
Uveitis	0	0	0	1 (1.8)
HLA-B27 positive	0	2 (40.0)	1 (50.0)	4 (7.3)
CRP, Above 10.0 mg/L	0	2 (40.0)	1 (50.0)	1 (1.8)
SI Joints X-ray positive for sacroiliitis (modified New York criteria)	1 (100)	0	0	1 (1.8)
SI Joints MRI positive for active inflammation	1 (100)	3 (60.0)	0	0

*According to the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA

Results: A total of 3,103 visits were recorded at four chiropractic offices between Nov 2020 and Nov 2021. Top ten chief complaints are presented in Figure 1. In total, 115 patients were referred by the chiropractors and 84 patients were confirmed to be eligible. Of the 74 patients who provided consent, 59 (79.7%) had IBP, and 66 (89.2%) had at least one clinical SpA feature. At interim data lock, 63 patients were fully assessed by a rheumatologist, of which 7 (11.1%) were HLA-B27 positive and 24 (38.1%) had rheumatologist-evaluated IBP. Eight (12.7%) patients had SpA, 6 (9.5%) were diagnosed as axSpA and fulfilled Assessment of Spondyloarthritis International Society (ASAS) classification criteria, 1 (1.6%) patient was diagnosed as psoriatic arthritis without imaging evidence of axial involvement and fulfilled Classification Criteria for Psoriatic Arthritis, and 1 (1.6%) had undifferentiated peripheral SpA and fulfilled ASAS Classification Criteria.

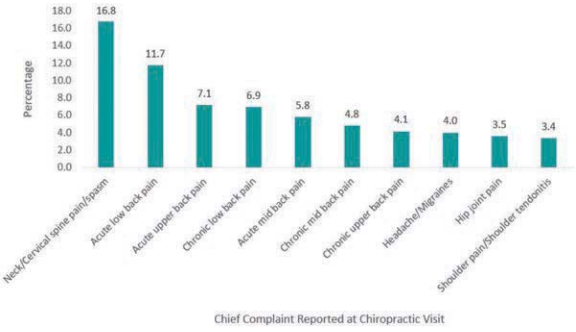

Figure 1. Chief complaints reported by patients at chiropractor visits (n=3103)

Conclusion: More than 10% of patients attending chiropractic clinics for musculoskeletal complaints had undiagnosed SpA conditions, with axSpA being the most common. Educational efforts targeted at chiropractors to suspect and refer appropriate cases to rheumatologists are needed.

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POS0985

MILD PSORIASIS SEEMS OFTEN UNDERDIAGNOSED IN PATIENT WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is known to be associated with several extra-skeletal manifestations, including the inflammatory skin disease psoriasis. It is important to recognize and diagnose psoriasis timely in axSpA to provide the most optimal treatment and outcome for both axSpA and psoriasis. Furthermore, in patients suspected of axSpA, it may add to making the axSpA diagnosis.

Objectives: To explore the self-reported prevalence of psoriasis in axSpA patients using a questionnaire with prototypical color pictures, and to compare this with the prevalence of a verified diagnosis. Secondly, to explore if there are differences in disease and patient characteristics between axSpA patients with and without self-reported psoriasis.

Methods: All patients from the Dutch Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort included before June 2016, were sent a questionnaire with self-screening psoriasis questions. The applied self-diagnostic psoriasis question "Do you have psoriasis?" was supported with the following brief elucidation: "Psoriasis is a skin disease in which red and scaly patches develop on the body, especially on the elbows, knees and hairy head. The nails can also be affected, and sometimes there are joint complaints." In addition, to enable patients to self-assess the presence of psoriasis more accurately, prototypical color pictures of psoriasis lesions were added. Patients could reply with "no", "yes, in the past" or "yes, currently". In patients who indicated having psoriasis symptoms, a medical record check was done to verify previously diagnosed psoriasis. The diagnosis of psoriasis was considered valid if it was described in the medical record by a dermatologist or rheumatologist.

Results: Of the 592 questionnaires sent, 471 (79.6%) were returned, of which 448 (75.7%) were eligible for analysis. Of these 448 included patients, 79% were diagnosed with AS and 21% with nr-axSpA, mean (±SD) age was 50.1±12.7 years, 64% were male, median (IQR) SpA symptom duration was 21.0 (12.0-32.0) years, 79% were HLA-B27 positive and mean $ASDAS_{CRP}$ was 2.2±1.0. History of peripheral arthritis, enthesitis and dactylitis was present in 39%, 20% and 7% of patients, respectively. The male-female ratio between the 448 included and 144 excluded patients was similar. Excluded patients were significantly younger (43.3 ± 13.6, p<0.001). Of the 448 respondents, 58 (13%) had a positive self-screening for psoriasis symptoms, currently or in the past. In 28 (48%) of these 58 patients, psoriasis diagnosis could be verified by medical records, resulting in a confirmed psoriasis prevalence rate of 6.3%. AxSpA patients reporting psoriasis symptoms without a verified diagnosis mentioned more often mild than moderate or severe psoriasis symptoms (25% vs. 3%, p=0.02) and their psoriasis lesions were less often located on the torso area (3% vs. 18%, p=0.04), intergluteal cleft (0% vs. 25%, p=0.02) and legs (7% vs. 43%, p<0.01) compared to axSpA patients with a confirmed diagnosis. Of the 31 axSpA patients who reported currently active psoriasis (irrespective of confirmed diagnosis), 23 (74%) had only mild psoriasis symptoms.

Conclusion: Especially mild psoriasis seems often underdiagnosed in patient with axSpA according to a patient questionnaire with prototypical pictures of psoriasis lesions. This questionnaire could be beneficial in tracing patients with undiagnosed psoriasis in daily clinical practice, however further validation of this questionnaire is needed in daily clinical practice.

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POS0986

SELF-REPORTED PHYSICAL ACTIVITY IN PATIENTS WITH AXSPA: ADHERENCE TO PUBLIC HEALTH RECOMMENDATIONS AND ASSOCIATION WITH HEALTH STATUS IN TWO DUTCH COHORTS

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Background: In general, regular physical activity (PA) is associated with a reduced risk of cardiovascular disease and all-cause mortality. In people with axial spondyloarthritis (axSpA) specifically, regular PA has shown beneficial effects on function, spinal mobility and pain. The World Health Organization (WHO) developed public health recommendations for the frequency, intensity and duration of PA in adults required to offer significant health benefits and mitigate health risks.

Objectives: To assess the proportion of axSpA patients fulfilling the WHO PA recommendations and to investigate the association of the amount of PA with health status and quality of life (QoL).

Methods: Patients from two Dutch cohorts were included; one in the Northern (GLAS cohort, n=148) and one in the Western (LUMC cohort, n=193) part of the Netherlands. The (m)SQUASH was used to assess the type, intensity and time spent on PA during a normal week in the past month. Fulfillment of the WHO PA recommendations was defined as aerobic PA of least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity (or an equivalent combination), and muscle-strengthening activities twice a week. Univariate linear regression analysis was used to explore the association of (m)SQUASH total score with health status (ASAS-HI) and quality of life (ASQoL). Multivariate regression analysis was used to correct these associations for age, gender, BMI and ASDAS as potential confounders.

Results: In the GLAS cohort, 59% were male, mean age (± SD) was 48.5 ± 13.2 years, median (IQR) ASAS-HI was 4.4 (1.9-8.1) and median ASQoL was 4 (1-9). In the LUMC cohort, 69% were male, mean age was 55.7 ± 14.1 years, and median ASAS-HI was 5.3 (2.1-8.0). Of these GLAS and LUMC patients, 57 (40%) and 62 (35%) fulfilled the WHO PA recommendations, respectively. Total (m)SQUASH score was significantly associated with ASAS-HI (GLAS cohort: R^2 0.16, B (95%CI) -0.4 (-4.3;-1.6); LUMC cohort: R^2 0.13, B (95%CI) -0.3 (-4.3;-2.0)) and ASQoL (GLAS cohort: R^2 0.18, B (95%CI) -4.4 (-3.5;-1.4). These associations remained significant after correcting for age, gender, BMI and ASDAS (Table 1).

Conclusion: In both Dutch cohorts, only 35-40% of axSpA patients fulfilled the WHO PA recommendations, which seems less compared to the average 48% in the Dutch adult population[1]. AxSpA patient reporting a higher level of PA had better health status and QoL. Therefore, in daily clinical practice, greater awareness and focus on moderate-to-high intensity and muscle strengthening activity is desirable for axSpA patients.

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Table 1. Association between total (m)SQUASH score and health status or quality of life in axSpA patients.

	ASAS-HI			ASQoL		
	R^2	B (95% CI)	P-value	R^2	B (95% CI)	P-value
GLAS cohort						
mSQUASH total score	0.16	-0.4 (-4.3;-1.6)	<0.001	0.18	-4.4 (-3.5;-1.4)	<0.001
mSQUASH corrected for age, gender	0.19	-0.4 (-0.1;-1.5)	<0.001	0.21	-4.2 (-0.9;-1.3)	<0.001
mSQUASH corrected for age, gender, BMI, ASDAS	0.30	-4.4 (-6.3;.2.6)	<0.001	0.31	-3.4 (-5.1;-1.9)	<0.001
LUMC cohort						
SQUASH total score	0.13	-0.3 (-4.3;-2.0)	<0.001			
SQUASH corrected for age, gender	0.23	-2.7 (-3.9;-1.6)	<0.001			

POS0987

DETERMINANTS OF CLINICALLY IMPORTANT WORSENING IN EARLY AXIAL SPA: ANALYSIS OF THE DESIR COHORT OVER 5 YEARS

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Background: A definition for clinically important worsening (CIW) of axSpA has been proposed by ASAS: i.e. an increase of ≥0.9 points of ASDAS. However, it is unknown how this definition performs in an early axSpA cohort.
Objectives: To determine the prevalence of CIW in a population of early axSpA, as well as the association between the occurrence of CIW and the presence of concomitant signs of inflammation; finally, to determine whether MRI inflammation was predictive of a future CIW.
Methods: 708 patients with early axSpA from the French DESIR cohort were included in the analysis. Patients were followed every 6 months for the first 2 years and annually thereafter. All patients had an MRI of spine and sacroiliac joints at baseline, but only patients from the APHP centers performed those at 2 and 5 years. Prevalence of CIW was calculated during the 5 years of follow-up in the cohort. The association between CIW and concomitant objective signs of inflammation (such as swollen joint count) was assessed over time using mixed models adjusted for sociodemographic and other clinical covariates. CIW predictive factors including the predictive capacity of MRI inflammation (measured by SPARCC at SIJ and spine) and MRI structural damage (defined by presence of ≥5 structural lesions of SI joints or spine) on the occurrence of a future CIW (time-lagged models) were evaluated.
Results: Total number of CIW was 378 in 5 years with 42.8% (303/708) of patients presenting at least one CIW during the follow-up. There were no significant sociodemographic or clinical differences at inclusion between patients with at least one episode of CIW and those without CIW during follow-up.
In the association models, concomitant tender joint count (OR 1.02, CI95%[1.00; 1.03]) and ASAS-NSAID score last week (OR 1.00, CI95%[1.00; 1.01]) were significantly associated with CIW over time. Presence of MRI-SIJ inflammation (OR (per SPARCC point) 1.02, CI95%[1.01; 1.04]) and MRI-SIJ structural damage (OR 2.74, CI95%[1.27; 5.93]) were predictive of future (next visit) occurrence of CIW.
Conclusion: Patients with CIW according to the ASAS definition had significantly more objective signs of inflammation concomitantly but also over time. These data support the construct validity of this definition of CIW in an early axSpA population. MRI-SIJ inflammation and structural damage may have a predictive role in the subsequent occurrence of CIW.
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Table 1. Effect of MRI lesions on the future development of CIW

Variables	OR [95%CI]
Visit	**1.01** [0.98; 1.04]
Sex (Women)	**1.55** [0.71; 3.36]
Age	**0.99** [0.95; 1.04]
Marital status (Single)	**0.64** [0.30; 1.37]
Education (University or equivalent)	**0.89** [0.41; 1.94]
White collar workers vs blue collars	**0.52** [0.19; 1.46]
HLA B27 status	**1.15** [0.57; 2.32]
Symptoms duration	**1.43 [1.00; 2.05]**
Enthesitis score	**1.00** [0.92; 1.08]
Tender joint count	**1.02** [0.98; 1.06]
Swollen joint count	**0.81** [0.39; 1.70]
ASAS NSAID score last week	**1.01 [1.00; 1.01]**
csDMARD intake last 6 months	**0.76** [0.20; 2.80]
TNF last 6 months	**0.78** [0.37; 1.63]
Lag SPARCC-SIJ	**1.02 [1.00; 1.04]**
Lag SPARCC-spine	**0.98** [0.95; 1.02]

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POS0988

ANKYLOSING SPONDYLITIS (AS) ACTIVITY DURING THE YEAR AFTER CHILDBIRTH.

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Background: Currently, data on the course of AS during pregnancy are being accumulated. However, information about the activity of AS in the postpartum period including against the background of lactation, remains scanty and contradictory.
Objectives: To assess the dynamics of activity of AS during the year after childbirth, to identify predictors of high activity.
Methods: 44 women with confirmed AS (modified New York criteria, 1984) were followed within 1 year after childbirth. The visits were carried out in 1, 6 and 12 months after delivery. The average age of the patients was 32,5 ± 5,8 years, the duration of the disease was 149,0 ± 96,3 months. The activity according to the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in the 1st, 2nd and 3rd trimesters of pregnancy was 2,8 ± 1,9; 2,9 ± 1,9 and 2,7 ± 1,8, respectively. The Ankylosing Spondylitis Disease Activity Score CRP (ASDAS-CRP) was 1,8 [1,6; 2,5]; 2,1 [1,5; 2,9] and 2 [1; 3,5], respectively. Delivery period was 39,0 ± 1,2 weeks. Lactation was established in 40 women and the duration was 10 [4; 12] months.
Results: Subjective deterioration of well-being was noted by 36 (81,8%) women after 8 [4; 17] weeks after delivery, while 29 (65,9%) patients associated deterioration of well-being with increased activity of AS, including recurrence of uveitis and arthritis, and 7 cases of increased severity of back pain of mechanical rhythm was revealed. 1 month after delivery, 39 patients (88,6%) reported back pain with NRS intensity of 3,0 [2,0; 6,0]; night pain – 29 women with intensity of 3,0 [2,0; 6,0]. 6 months after delivery, back pain was observed in 38 (86,4%) patients, its intensity was 4,0 [3,0; 5,0]; nocturnal pain – in 32 women with intensity of 3,0 [2,0; 5,0]. 12 months after delivery, 33 (75%) women experienced back pain with NRS intensity of 4,0 [3,0; 6,0]; Night pain – 27 women with intensity of 2,0 [1,0; 4,0]. The BASDAI at 1, 6 and 12 months after giving birth was: 2,4 [1,4; 4,2]; 2,6 [1,4; 4,4]; 2,7 [1,5; 4,1], respectively (p > 0,05). ASDAS-CRP was 2,0 [1,2; 2,7]; 1,9 [1,4; 2,5]; 1,7 [1,3; 2,3], respectively (p > 0,05). CRP level – 3,4 [2,0; 8,6], 3,5 [1,0; 7,8] and 2,6 [0,8; 8,2] mg/l, respectively (p >0,05). There were no differences between activity during 1 year after childbirth and during pregnancy. There were no differences between the values of BASDAI, ASDAS-CRP, CRP, and the severity of night pain between women with and without lactation. Predictors of high AS activity (BASDAI ≥ 4) 1 month after delivery were: BASDAI ≥ 4 in the 1st trimester (OR 8,1; 95% CI 1,8 – 37,0; p = 0,006) and 2nd trimesters of pregnancy (OR 5,1; 95% CI 1,2 – 20,6; p = 0,02); NRS back pain > 4 in the 2nd trimester (OR 4,3; 95% CI 1,1 – 17,2; p = 0,04); cancellation of bDMARD therapy in the 1st trimester of pregnancy (OR 21,0; 95% CI 1,0 – 440,9; p = 0,05). Predictors of high AS activity in 6 months after delivery were: BASDAI ≥ 4 in the 1st trimester (OR 6,5; 95% CI 1,5 – 28,7; p = 0,01), in the 2nd (OR 6,7; 95% CI 1,6 – 27,8; p = 0,009) and in the 3rd trimesters of pregnancy (OR 8,7; 95% CI 1,9 – 38,6; p = 0,005); high activity in 1 month after delivery (OR 4,0; 95% CI 1,0 – 15,9; p < 0,05). The predictor of high activity in 12 months after delivery was high activity 6 months after delivery (OR 8,3; 95% CI 1,9 – 37,2; p = 0,005).
Conclusion: There was no increase in AS activity according to BASDAI and ASDASCRP within 1 year after childbirth, while 66% of women noted a subjective deterioration of well-being associated with AS symptoms intensification. High AS activity during pregnancy was a risk factor for high activity within 6 months after delivery. Given the generally accepted opinion that AS activity at the time of conception is a predictor of activity during gestation, we can talk about the importance of pregnancy planning from the point of view of the postpartum period. Further studies on large groups of patients are required to clarify the dynamics of AS activity after childbirth.
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POS0989

DEVELOPMENT OF INTERNATIONAL CONSENSUS ON A STANDARDIZED IMAGE ACQUISITION PROTOCOL FOR DIAGNOSTIC EVALUATION OF THE SACROILIAC JOINTS BY MRI – AN ASAS-SPARTAN COLLABORATION.

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Background: In 2009, ASAS published a 'Definition of active sacroiliitis on MRI for classification of axial spondyloarthritis (axSpA)'. This definition relied on two MRI sequences to make this determination – semicoronal T1 and STIR. Since then, this approach has frequently been used for diagnosis, even though that was never the intent of the definition. In 2015, the European Society of Skeletal Radiology (ESSR) published its recommendations for an SIJ MRI image acquisition protocol (IAP) for diagnostic purposes that required 4 MRI sequences but there is still no IAP that has been widely accepted as a minimum standard worldwide. In 2020, an informal survey of 24 academic sites (12 Europe, 12 North America) confirmed that 24/24 sites performed a minimum of 3 MRI sequences for diagnosis (19 performed 4-8 sequences) because the 2-sequence protocol was considered inadequate.
Objectives: To develop the minimum requirements for a standardized IAP for MRI of the sacroiliac joints for diagnostic ascertainment of sacroiliitis.
Methods: All radiologist members of the ASAS and SPARTAN Classification in axSpA (CLASSIC) project, along with one European and one North American rheumatologist with extensive MRI experience in SpA clinical practice and research, were invited to participate in a consensus exercise. A draft IAP was circulated to all participants along with background information and justification for the draft proposal. Feedback on all issues was received by email, tabulated and recirculated. Participants were broadly in favour of the proposal and two months later a teleconference meeting took place and remaining points of contention were resolved. Examples of the proposed IAP performed on new, 10 and 22 years' old MRI scanners were made available for review in DICOM format. Next the revised draft of the IAP was presented at the ASAS annual meeting to the entire membership on 14 January 2022, and voted on.
Results: A 4-sequence IAP, 3-semicoronal and 1-semiaxial, is recommended for diagnostic ascertainment of sacroiliitis and its differential diagnoses (Table 1). It must meet the following requirements: Semicoronal sequences should be parallel to the dorsal cortex of the S2 vertebral body, and include: 1) a sequence sensitive for the detection of active inflammation being T2-weighted with suppression of fat signal; 2) a sequence sensitive for the detection of structural damage in bone and bone marrow with T1-weighting; 3) a sequence that is designed to optimally depict the bone-cartilage interface of the articular surface and be sensitive for detection of bone erosion; plus 4) a semiaxial sequence sensitive for inflammation detection. The IAP was approved at the ASAS annual meeting by a vote of the entire membership with 91% in favour.

Table 1. A standardized SIJ MRI Acquisition Protocol for diagnostic ascertainment of sacroiliitis

Orientation	Sequence	Target Lesion(s)
Semicoronal Parallel to the dorsal cortex of the S2 vertebral body	T1-weighted Spin Echo	Structural: Fat lesions, erosion, sclerosis, backfill, ankylosis.
	T2-weighted with suppressed fat signal (STIR, T2FS or equivalent)	Inflammatory: Bone marrow edema (BME)
	T1-weighted with suppressed fat signal (2D or 3D T1FS)	Structural: Erosion of the articular surface
Semiaxial Perpendicular to semicoronal	T2-weighted with suppressed fat signal (STIR, T2FS or equivalent)	Inflammatory: Bone marrow edema (BME)

Conclusion: A standardized IAP for MRI of the sacroiliac joints for diagnostic ascertainment of sacroiliitis is recommended and should be comprised of a minimum of 4 sequences, in 2-planes, that will optimally visualize inflammation, structural damage, and the bone-cartilage interface.
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POS0990 DEEP LEARNING ALGORITHMS FOR MAGNETIC RESONANCE IMAGING OF INFLAMMATORY SACROILIITIS IN AXIAL SPONDYLOARTHRITIS.

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Background: Magnetic resonance imaging (MRI) of the sacroiliac (SI) joints is increasingly important in the management of axial spondyloarthritis (SpA). Artificial intelligence (AI) may be the next crucial step in enabling the widespread application of MRI.
Objectives: To develop a deep learning algorithm for detection of active inflammatory sacroiliitis in short tau inversion recovery (STIR) sequence MRI.
Methods: A total of 326 participants with axial spondyloarthritis (SpA), and 63 participants with non-specific back pain (NSBP) were recruited. STIR MRI of the SI joints was performed and clinical data were collected. Region of interests (ROIs) were drawn outlining bone marrow edema, a reliable marker of active inflammation, which formed the ground truth masks from which "fake-colour" images were derived. Both the original and "fake-colour" images were randomly allocated into either the training and validation dataset or the testing dataset. Attention U-net was used for the development of deep learning algorithms. As comparison, an independent radiologist and rheumatologist blinded to the ground truth masks, were tasked with identifying bone marrow edema in the MR images.
Results: Inflammatory sacroiliitis were identified in 1398 MR images from 228 participants. No inflammation was found in 3944 MR images from 161 participants. The mean sensitivity of algorithms derived from the original dataset and "fake-colour" image dataset were 0.86±0.02, and 0.90±0.01 respectively. The mean specificity of algorithms derived from the original and "fake-colour" image dataset were 0.92±0.02, and 0.93±0.01 respectively. The mean testing dice coefficients were 0.48± 0.27 for the original dataset and 0.51±0.25 for the "fake-colour" image dataset. The area under the curve of the receiver operating characteristic (AUC-ROC) curve of the algorithms using original dataset and "fake-colour" image dataset were 0.92 and 0.96 respectively. Sensitivity and specificity of algorithms were comparable to interpretation by a radiologist, but outperformed the rheumatologist.
Conclusion: An MRI deep learning algorithm was developed for detection of inflammatory sacroiliitis in axial SpA.
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POS0991 PREDICTORS OF DEVELOPMENT OF ADVANCED SPINAL ANKYLOSIS/BAMBOO SPINE IN AXIAL SPONDYLOARTHRITIS: RESULTS FROM REAL-LIFE DATA

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Background: In axial spondyloarthritis (axSpA), intervertebral ossification bridges of consecutive vertebrae may progress to advanced spinal ankylosis and bamboo spine over the years [1].
Objectives: To identify demographic, clinical, disease activity and treatment factors associated with development of bamboo spine / advanced spinal ankylosis and bamboo spine-only in the Hacettepe University Rheumatology Biologic Registry (HUR-BIO) cohort.
Methods: HUR-BIO is a prospective, single center database of biological disease-modifying antirheumatic drug (bDMARD) treatments. 770 patients on bDMARDs treatment had both lumbar and cervical lateral radiographies at the time of the data collection, and were included in the study. Bamboo spine was defined Bath Ankylosing Spondylitis Radiologic Index (BASRI)-spine grade 4 with a complete fusion of lumbar and cervical spines. Advanced spinal ankylosis was defined as the presence of at least two intervertebral adjacent bridges and/or

Table 1. Predictors of Bamboo Spine and Advanced Spinal Ankyloses, and Bamboo Spine-only

Multivariable Model

	Bamboo Spine and Advanced Spinal Ankylosis		Bamboo Spine	
Covariates	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Age	1.12 (1.07-1.17)	**<0.001***	1.17 (1.09-1.3)	**<0.001***
Male (vs female)	4.26 (1.75-10.41)	**0.001***	8.31 (2.09-33.1)	**0.003***
Delay Diagnosis (≥ 24 months vs <24 months)	2.7 (1.27-5.74)	**0.01***	2.39 (0.85-6.71)	0.09
BMI		**0.019***		0.074
- 25 to < 30 (vs <25)	2.05 (0.77-5.46)	0.15	3.37 (0.84-13.6)	0.087
- ≥ 30 (vs <25)	4.03 (1.53-10.64)	**0.005***	5.15 (1.25-21.27)	**0.024***
Hip involvement (present vs absent)	4.94 (1.94-12.6)	**0.001***	4.74 (1.32-16.96)	**0.017**
Smoking (≥ 10 package/year vs <10 package/year)	2.28 (1.003-5.2)	**0.049***	3.19 (1.03-9.89)	**0.044***
Family History of SpA (First-degree; present vs absent)	1.67 (0.61-4.57)	0.32	2.82 (0.79-10.06)	0.11
Uveitis History (present vs absent)	1.04 (0.39-2.74)	0.94	1.19 (0.33-4.29)	0.79
Use SSZ (present vs absent)	0.6 (0.17-2.07)	0.42	2.09 (0.39-11.28)	0.39
Use Corticosteroids (present vs absent)	0.69 (0.27-1.75)	0.43	0.73 (0.18-2.97)	0.66

*p <0.05

BMI: Body mass index; SpA: Spondyloarthritis; SSZ: Sulfasalazine

fusion at the lumbar and/or cervical spine without bamboo spine. We analyzed the ensemble of variables by multivariable logistic regression to identify predictors associated with bamboo spine / advanced spinal disease, and bamboo spine-only.
Results: In the study, there were 99 patients with advanced spinal ankylosis and 78 patients with bamboo spine. Older age (OR 1.12, 95% CI 1.07-1.17), male gender (OR 4.26, 95% CI 1.75-10.41), delay diagnosis ≥ 24 months (OR 2.7, 95% CI 1.27-5.74), obesity (OR 4.03, 95% CI 1.53-10.64), hip involvement (OR 4.94, 95% CI 1.94-12.6), smoking ≥ 10 package/year (OR 2.28, 95% CI 1.003-5.2) were significantly associated factors with bamboo spine / advanced spinal ankylosis. Similarly, older age (OR 1.17, 95% CI 1.09-1.3), male gender (OR 8.31, 95% CI 2.09-33.1), obesity (OR 5.15, 95% CI 1.25-21.27), hip involvement (OR 4.74, 95% CI 1.32-16.96) and smoking ≥ 10 package/year (OR 3.19, 95% CI 1.03-9.89) were showed statistical significance with bamboo spine (**Table 1**).
Conclusion: Data on the predictors of development of advanced spinal ankylosis and bamboo spine are scarce. In this study, we showed that older age, male gender, delay in diagnosis, obesity, hip involvement and smoking are factors that predict the development of advanced spinal involvement in axSpA.
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POS0992 CLINICAL AND IMAGING FEATURES IN SPONDYLOARTHRITIS PATIENTS WITH AND WITHOUT HLA-B27 AND HLA-B51: A VALIDATION COHORT

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Background: Despite being commonly expressed in the general population, the human leucocyte antigen (HLA)-B27 allele strongly increases the susceptibility to develop spondyloarthritis (SpA). Likewise, the association between the HLA-B51 allele and the development of Behçet's disease is well documented. In a previous pilot study, we identified similarities and differences in patients with axial or peripheral SpA according to the presence of HLA-B51 only, HLA-B27 only or neither of the two.
Objectives: To investigate the clinical and imaging findings of SpA patients according to the absence or presence of HLA-B27 or HLA-B51 in an independent validation cohort.
Methods: We retrospectively analyzed patients with axial or peripheral SpA, according to the ASAS criteria, referring to our institution between 2020 and 2021. All patients had been tested for HLA-B alleles. Patients with HLA-B51 haplotype and fulfilling the criteria for Behçet's disease were excluded.
Results: The independent validation cohort included 185 patients and was comparable to the original cohort of 236 patients with regard to age, gender, age at diagnosis and symptom duration. In line with the findings in the original cohort we observed that aphtous lesions were more prevalent in patients with HLA-B51 (p< 0.001) while inflammatory bowel disease was more prevalent in the double negative group (p=0.0006). Unlike the original cohort, patients of the validation cohort did not show a different prevalence of inflammatory back pain (IBP) at disease onset or in the disease course based on the HLA status. A sub-analysis by gender demonstrated a comparable prevalence of IBP in males and females within the 3 groups. As novel finding, we observed that enthesitis and psoriasis were significantly more prevalent in the double negative group compared to the B27 and B51 groups (p=0.004) and their prevalence did not differ when comparing B27 and B51 groups. With regard to imaging in patients with axial manifestations, in the original cohort we observed that sacroiliitis, assessed by X-ray or magnetic resonance imaging (MRI), were more prevalent in double negative and HLA-B27 patients, compared to HLA-B51 patients and the latter showed a significant negative association with sacroiliitis on imaging (OR 0.342 CI 0.189-0.619 p<0.0005). In this validation cohort we observed that the prevalence of sacroiliitis on X-ray was similar in the 3 groups while sacroiliitis on MRI scan was significantly more prevalent in the B27 group (81%) compared to the double negative (63%) and the B51 group (51%). A negative association between sacroiliitis on MRI and HLA-B51 but not double negative status was observed in the validation cohort (OR=0.23, 95% CI=0.07-0.8, p=0.02).
Conclusion: Our findings underscore the clinical and radiological heterogeneity of patients with SpA and HLA-B51 alone or neither HLA-B27 nor HLA-B51 compared to those with HLA-B27 only and underline the need to explore further this area by means of registry data with large real-life cohorts.
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POS0993 RADIOLOGICAL CERVICAL INVOLVMENT IN ANKYLOSING SPONDYLITIS

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Background: Cervical involvement in ankylosing spondylitis (AS) is particularly disabling and has been poorly studied yet. Actual radiologic scoring design to assess disease progression does not provide a comprehensive picture of the cervical involvement in AS. [1] Association with clinical features such as psoriasis are discussed.
Objectives: We aimed to assess radiographic features of cervical involvement in AS and clinico-biological parameters associated with this specific radiographic location.
Methods: Cross-sectional study based on radiographic analysis of a subgroup of patients included in the French BambooSpine cohort, originally designed to study the genetic risk factors of AS structural severity. The analysis was based on patients included in Parisian hospitals to have access to images of the entire spine on the Picture Archiving and Communication System (PACS) shared by all University Hospitals in Paris. A double reading of the images was performed by a rheumatologist/radiologist pair until consensus was reached, to identify syndesmophytes, zygapophyseal joint (ZJ) involvement and posterior ligament structures (PLS) at each cervical level, syndesmophytes in the thoracic region, and ZJ and PLS involvement in the lumbar region.
Results: Of the 113 assessed patients, 101 were men, mean age 53 years (+/- 11 years) with 27 years (+/- 13 years) of disease duration (Table 1). Of those whose HLA B27 status was known, 85% (70/82) were carriers. Among 86 patients with radiological cervical involvement, 83% had syndesmophytes, 86% had ZJ involvement and 24% had PLS involvement. In the cervical region, 13 patients (15%) had zygapophyseal fusion without syndesmophytes. 26/113 patients were completely free of any cervical involvement while 30/113 had a maximal cervical involvement (anterior and posterior). In univariate analyses, HLA-B27 was

significantly associated with ZJ involvement at the cervical and lumbar level (p=0.016). Cervical involvement of any type was not associated with psoriasis. Low educational level (not beyond secondary school) was significantly associated with syndesmophytic involvement (p=0.035). There was a non-significant trend for an association between arthritis and ZJ involvement.

Table 1. Clinical features

Men (n,%)	101/113	89,4%
Age at diagnosis (mean, SD)	31,2	11,68
Duration of evolution (mean, SD)	27,0	13,0
Smoking ever (n,%)	65/112	58,0 %
Chronic Back Pain (for > 3 months) (n,%)	109/113	96,5%
Chest pain	45/110	40,9%
Buttock pain	78/109	71,6%
Arthritis	36/111	32,4%
Enthesitis	38/112	33,9%
Dactylitis	6/111	5,4%
HLA B27	70/82	85,4%
CRP	87/103	84,5%
X ray sacro-iliitis	112/112	100%
Personnal history		
-Uveitis	41/113	36,3%
-Inflammatory bowel disease	13/113	11,5%
-Reactive arthritis	2/112	1,8%
-Psoriasis	19/111	17,1%

Conclusion: Cervical involvement was very frequent (76% of this severe AS population) but not associated with psoriasis, as usually thought. Zygapophyseal involvement was present in 86 % of cases and exclusive in 15 % of cases. This latter radiological form of the disease, i.e. without syndesmophytes, is usually more difficult to diagnose, and should be systematically assessed among AS patients with cervical pain and/or patients with reduced cervical mobility.

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POS0994 DEVELOPMENT OF AN AUTOMATED ALGORITHM BASED ON METHODS OF ARTIFICIAL INTELLIGENCE TO ASSIST IN THE PREDICTION OF CORRECT REFERRALS OF PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS BY USING PATIENT HISTORY TEXTS

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Background: Diagnosis and treatment of PsA and axSpA is often delayed due to missing clear diagnostic criteria and limitations in resources for referral to rheumatologist including high numbers of incorrect referrals. Primary care is usually provided by either general practitioner, dermatologists, or orthopedics. Clinical discriminators with a high specificity for rheumatic conditions include morning stiffness (MST; peripheral or axial, >30min). Artificial intelligence (AI) and natural language processing (NLP) methods offer algorithms for learning systems to recognize disease associated terms and classify clinical phenotypes using large data sets that may support early identification of patients with suspected diagnosis of PsA or axSpA.

Objectives: AI and NLP methods are used to identify patients with typical attributes for inflammation by using morning stiffness as one potential discriminating pattern, which can be detected automatically and might help to prioritize referral for rheumatologist appointments.

Methods: Within a multicentre observational study, patients with visits at the rheumatologist with a suspected diagnosis of PsA or axSpA from the referral primary care provider were recruited. All data on clinical examinations and findings were collected and evaluated by rheumatologists in focus on criteria for diagnosis of PsA/axSpA (gold standard for evaluation). Unstructured text from the patient history was used to extract diagnosis-relevant characteristics. The information extraction algorithms used NLP models to detect expert curated "morning stiffness" (MST) keywords and puts them into a contextualized framework that allows to capture possible negations.

Results: A total of 116 patients were recruited (73 female, 63%) with a median age of 42 (IQR: 34-54). 51 patients were referred as axSpA (44%) and 60 as PsA (52%) by primary care providers. After preselection for PsA and axSpA patients, we observed a 23% rate of referrals without rheumatic diagnosis. Only 7.1% of patients were admitted without signs of MST, 29% with axial MST, 35% with peripheral MST and 28% with both MST types. Average morning stiffness duration was recorded as 35 minutes; patients with a finally confirmed rheumatic diagnosis had a higher average MST duration reported (36 minutes) compared to patients without a confirmed diagnosis. Our AI assisted extraction of MST identified MST in 82.7% of patient history texts. In 75% NLP methods correctly identified the negation of MST symptoms (6 of 8), and 94% of MST was detected when both axial and peripheral joints were affected (30 of 32). Manual inspection of 20 patient history reports where MST was not detected by our automated algorithm revealed that 17 reports did not contain information about MST and three mention unspecific early morning discomfort, without mention of MST.

Conclusion: The high rate of correct detection of MST from patient history text using NLP methods allowed us to assess the potential for NLP models to support automated analysis of patient reports to facilitate intelligent patient referral.

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POS0995 VALIDATION OF THE SPARCC MRI-RETIC E-TOOL FOR INCREASING SCORING PROFICIENCY OF MRI LESIONS IN AXIAL SPONDYLOARTHRITIS

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Background: The web-based Spondyloarthritis Research Consortium of Canada (SPARCC) real-time iterative calibration (RETIC) modules for scoring MRI lesions in axial spondyloarthritis (axSpA) have been created by SPARCC developers to enable remote training of readers to appropriately use the SPARCC MRI inflammation and structural damage instruments and to attain adequate scoring proficiency.

Objectives: We aimed to test the performance of these modules in enhancing scoring proficiency in comparison to SPARCC developers.

Methods: The $SPARCC_{RETIC}$ SIJ inflammation and structural damage modules are each comprised of 50 DICOM axSpA cases with baseline and follow up scans and an online scoring interface based on SIJ quadrants. Continuous visual real-time feedback regarding concordance/discordance of scoring per SIJ quadrant with expert readers is provided by a color-coding scheme. Reliability is assessed in real-time by intra-class correlation coefficient (ICC), ICC data being provided every 10 cases, which are scored until proficiency targets for ICC are attained. In the present exercise, participants (n=15) from the EuroSpA Imaging project were randomized, stratified by reader expertise in scoring with SPARCC, to one of two reader training strategies (groups A and B) that each comprised 3 stages (25 patients per stage, 2 timepoints, blinded to chronology; independent assessment of Inflammatory and structural lesions): Group A. 1. Review of original SPARCC manuscript describing scoring method. 2. Review of PowerPoint summary of SPARCC method plus completion of $SPARCC_{RETIC}$ module. 3. Re-review of PowerPoint summary. Group B. Same 3-step strategy as A except $SPARCC_{RETIC}$ module completed at stage 3. The reliability of scoring was compared to an expert radiologist (SPARCC developer).

Results: Very good scoring proficiency for status and change scores was evident for SPARCC BME even by non-experienced readers with similar levels of reliability irrespective of prior expertise. The beneficial impact of the $SPARCC_{RETIC}$ module on scoring proficiency was most consistently evident for the scoring of structural lesions and for Strategy B, where the impact was evident for all structural lesions, level of reader expertise, and status as well as change scores (Table 1). Scoring proficiency improved the most for the least experienced readers (Figure 1).

Table 1. Inter-rater reliability (Status/Change ICC) compared to radiologist SPARCC developer

		Strategy A			Strategy B		
MRI Lesion	**Reader expertise**	**Stage 1 cases (n=25)**	**Stage 2 cases (n=25)**	**Stage 3 cases (n=25)**	**Stage 1 cases (n=25)**	**Stage 2 cases (n=25)**	**Stage 3 cases (n=25)**
BME	**None (n=4)**	0.91 / 0.94	0.83/0.82	0.77/0.78	0.82/0.88	0.65/0.82	0.88/0.90
	Intermediate (n=6)	0.88/0.88	0.90/0.90	0.85/0.90	0.93/0.94	0.78/0.80	0.83/0.80
	Experienced (n=5)	0.92/0.94	0.90/0.88	0.92/0.93	0.83/0.88	0.84/0.90	0.89/0.89
ANKYLOSIS	**None (n=4)**	0.86/0.66	0.83/0.28	0.86/0.78	0.66/0.41	0.69/0.34	0.88/0.80
	Intermediate (n=6)	0.89/0.57	0.83/0.37	0.92/0.81	0.82/0.68	0.74/0.47	0.93/0.84
	Experienced (n=5)	0.96/0.76	0.93/0.64	0.94/0.86	0.97/0.24	0.83/0.41	0.91/0.79
BACKFILL	**None (n=4)**	-0.08/-0.05	0.38/0.22	0.59/0.38	0.64/0.13	0.05/-0.09	0.47/0.27
	Intermediate (n=6)	0.41/0.13	0.44/0.42	0.69/0.39	0.50/0.22	0.30/0.30	0.70/0.42
	Experienced (n=5)	0.82/0.38	0.55/0.40	0.91/0.64	0.65/0.24	0.21/0.26	0.71/0.30
EROSION	**None (n=4)**	0.13/-0.08	0.67/0.42	0.51/0.33	0.34/0.33	0.23/0.08	0.38/0.37
	Intermediate (n=6)	0.42/0.18	0.56/0.12	0.51/0.44	0.33/0.27	0.45/0.18	0.53/0.39
	Experienced (n=5)	0.61/0.33	0.64/0.34	0.64/0.42	0.51/0.27	0.58/0.11	0.62/0.31
FAT METAPLASIA	**None (n=4)**	0.62/0.54	0.30/0.17	0.57/0.29	0.43/0.53	0.38/0.07	0.83/0.63
	Intermediate (n=6)	0.49/0.38	0.59/0.30	0.79/0.51	0.57/0.78	0.50/0.42	0.81/0.47
	Experienced (n=5)	0.75/0.62	0.81/0.34	0.91/0.70	0.84/0.90	0.56/0.13	0.78/0.37

Conclusion: Attaining scoring proficiency for MRI structural lesions in axSpA is difficult but can be consistently improved by using the $SPARCC_{RETIC}$ module, even for experienced readers.

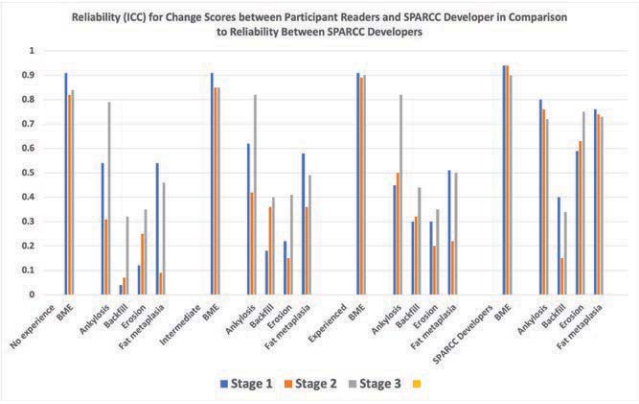

Figure 1.

Disclosure of Interests: Walter P Maksymowych Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, Boehringer Ingelheim, Celgene, Eli-Lilly, Galapagos, Novartis, Pfizer, UCB, Grant/research support from: Abbvie, Novartis, Pfizer, UCB, Anna Enevold Fløistrup Hadsbjerg Grant/research support from: Novartis, Mikkel Østergaard Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly and Company, Galapagos, Gilead, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB, Grant/research support from: AbbVie, BMS, Merck, Celgene, Novartis, Raphael Micheroli: None declared, Susanne Juhl Pedersen Grant/research support from: Novartis, Adrian Ciurea: None declared, Nora Vladimirova Grant/research support from: Novartis, Michael J Nissen Speakers bureau: Eli-Lilly, Janssen, Novartis, Consultant of: Abbvie, Celgene, Eli-Lilly, Janssen, Novartis, Pfizer, Kristyna Bubova: None declared, Stephanie Wichuk: None declared, Manouk de Hooge: None declared, Ashish Jacob Mathew Grant/research support from: Novartis, Karlo Pintaric: None declared, Monika Gregová: None declared, Ziga Snoj: None declared, Marie Wetterslev: None declared, Karel Gorican: None declared, Joel Paschke: None declared, Iris Eshed: None declared, Robert G Lambert Paid instructor for: Novartis

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POS0996

EFFECTS OF DISEASE MODIFYING ANTI RHEUMATIC DRUGS ON SACROILIAC MRI SCORE IN AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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Background: Sacroiliac bone marrow edema is an important factor in the diagnosis and management of axial spondyloarthritis (axSpA).

Objectives: The aim of this meta-analysis is to assess the effect of the different bDMARDs and tsDMARDs on the SPARCC score at 12-16 and 48-52 weeks.

Methods: A systematic review, performed on Pubmed, Embase and Cochrane databases, included randomized controlled studies evaluating the sacroiliac joint (SIJ) SPARCC score at 12-16 or 48-52 weeks in patients with axSpA meeting the ASAS 2009 criteria or the modified New York criteria. We included studies evaluating the effects of the different treatments on the SPARCC score of SIJ in axial spondyloarthritis in comparison to a control group.

Results: Fifteen studies were included in the meta-analysis. Nine studies evaluated the effect of TNF inhibitors (TNFi), two for ixekizumab, one for filgotinib and one for tofacitinib. At 12 and 16 weeks, SIJ SPARCC score was significantly improved by TNFi (WMD: - 3.29 [95% CI -4.25; -2, 34]), IL-17 inhibitors (WMD: -3.98 [95% CI –5.76; -2.20]) and by JAK inhibitors (JAKi) (WMD: - 3.02 [95% CI -4.54; -1.51]). There was no difference between the molecule subgroups. At 48-52 weeks, TNFα inhibitors, introduced at baseline, reduced more SIJ SPARCC, but not significantly (WMD: -2.26 [95% CI -4.94; 0.42]), than placebo groups who began a TNFi treatment with delay.

Conclusion: Our meta-analysis shows a comparable improvement of the SIJ SPARCC score regarding TNFi, JAKi and IL-17 inhibitors at three months and suggests the presence of an opportunity window.

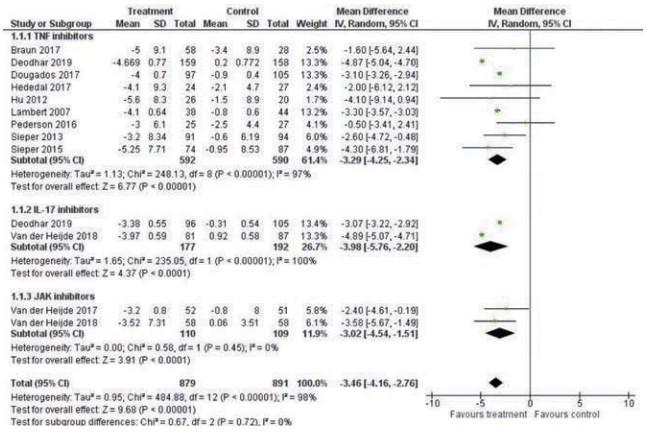

Figure 1. Forest plot of SPARCC SIJ score for all therapeutic agents versus controls at week 12-16.

Disclosure of Interests: None declared

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POS0997

CLINICAL FEATURES OF UVEITIS ASSOCIATED TO SPONDYLOARTHRITIS. SINGLE CENTER UNIVERSITY STUDY.

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Background: Uveitis is a frequent extraarticular manifestation of spondyloarthritis (SpAs). It has been classically reported that whereas uveitis in axial spondyloarthritis (ax-SpA) is predominantly anterior, unilateral, acute, and non-recurrent; in psoriatic arthritis (PsA) and in inflammatory bowel disease (IBD) it has been described as posterior, bilateral, insidious, and continuous [1,2].
Objectives: In a large unselected series of SpAs, our aim was to assess the epidemiology and clinical features of SpAs-associated uveitis.
Methods: Study of consecutive patients from a single University Hospital with **a)** ax-SpA, **b)** PsA, and **c)** IBD (Crohn's disease and Ulcerative colitis). We have selected patients with uveitis that were classified according to Standarization Uveitis Nomenclature (SUN) Working Group. Main general features, and uveitis pattern, location and onset were recorded.
Results: We studied 2156 (1038 women/118 men) patients with SpAs: IBD (n= 1449; 67.2%); PsA (n= 406; 18.8%); and ax-SpA (n= 301; 14%).
Uveitis was present in 87 (4%) (102 eyes) of 2156 patients with SpAs. However, uveitis occurs with varying frequency according to the SpAs subtype:14.6% of axSpA (n=44), 4.9% of PsA (n=20), and 1.6% of IBD (n=23) (**Table 1**).
In the global SpAs, the most common pattern of uveitis was typically anterior (n=78; 89.7%), unilateral (n=72; 82.8%), acute (n=19; 82.6%), and non-recurrent (n=83; 95.4%).
The comparative study between these three groups of SpAs showed a significant greater frequency of HLA-B27 positive, anterior location and acute onset in ax-SpA-related uveitis (**Table 1**).

Table 1. Main clinical features and uveitis pattern.

	Ax-SpA (n=44)	PsA(n=20)	IBD(n=23)	p
Main general features				
Age, years, mean ±SD	45.6 ± 10.3	43.1 ± 14.5	49.1 ± 14.6	0.472
Sex, w/m, n, (% of women)	25/19 (56.8)	12/8 (60)	17/6 (73.9)	0.382
Disease Duration, years, mean±SD	18.6 ± 10.5	9.9 ± 8.2	17.4 ± 10.2	0.067
HLA-B27 positive, n (%)	37 (84.1)	9 (45)	5 (2.8)	**0.001***
Uveitis location				
Anterior, n (%)	44 (100)	16 (80)	18 (78.3)	**0.006***
Posterior, n (%)	0 (0)	0 (0)	4 (17.4)	-
Panuveitis, n (%)	0 (0)	0 (0)	1 (4.5)	-
Uveitis pattern				
Unilateral, n (%)	37 (84.1)	16 (80)	19 (82.6)	0.922
Uveitis onset				
Acute, n (%)	44 (100)	20 (100)	19 (82.6)	**0.003***

Conclusion: Although SpAs associated uveitis have different frequencies depending on the underlying disease, they share the same clinical pattern: anterior, unilateral, acute, and non-recurrent, in contrast with published data from selected series.

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POS0998 DEPRESSION IN SPONDYLOARTHRITIS: THE CHOICE OF MEASUREMENT INSTRUMENT MATTERS

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Background: The prevalence of depression is increased in spondyloarthritis (SpA). Research on this topic in SpA is challenging for several reasons, one of them being the wide variety of different instruments used to assess depressive symptoms. It is unknown whether these instruments are comparable in measuring the construct 'depression' and can be considered interchangeable. If these instruments actually differ in what they measure, this should be taken into account when designing and interpreting studies, and in clinical practice when monitoring patients with SpA.
Objectives: To compare the constructs of several instruments used to assess depressive symptoms in patients with SpA.
Methods: Data from the international ASAS Health Index Validation Study were used. Included patients had a diagnosis of SpA and fulfilled the ASAS classification criteria for axial/peripheral SpA. Data on demographics and disease characteristics were collected. The following instruments that have been used to assess depressive symptoms in SpA were available: the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D), the Short Form 36 (SF-36) and item 5 of the 5-level EuroQoL 5D (EQ-5Di5). The HADS-D ranges 0-21 (best-worst), with scores ≥8 and ≥11 indicating possible (HADS-possible) and probable depression (HADS-probable), respectively. The SF-36 was summarized using all 36 items in a Mental Component Summary (SF-36MCS, score ≤40 indicating depression), or using only 5 items in the Mental Health subscale (SF-36MH, score ≤56 indicating depression). For the EQ-5Di5, a score of at least "moderately" (level ≥3 on 1-5 scale) or "severely" depressed (level ≥4) indicated depression. Spearman correlations between instrument scores, agreement (kappa) between depressed states, and test characteristics (sensitivity [SE], specificity [SP], positive and negative predictive value [PPV, NPV]) were calculated with HADS-D as external standard, as it was specifically designed to detect depression and considered to have highest content validity.
Results: In total, 1548 patients were included, of which 1281 (83%) had axial SpA, mean age was 41.6 (SD 13.5) years, 1005 were male (65%), mean symptom duration 14.5 (11.4) years, mean ASDAS 2.6 (1.2) and BASDAI 4.1 (2.5). The prevalence of depression varied around 1 in 3 patients for the lower thresholds of depression (32% for HADS-possible, 45% for SF-36MH, 33% for SF-36MCS and 24% for EQ-5Di5-moderately) and was lower for the more stringent thresholds of HADS-probable (15%) and EQ-5Di5-severely (6%); 192 patients (24% of those who scored positive for depression on ≥1 instrument) scored positive on all instruments (Figure 1). Correlations between instruments were moderate (rho = 0.59-0.66), except between SF-36MH and MCS (rho = 0.85). Agreement between instruments was moderate for lower thresholds for depression (pairwise kappa = 0.47-0.58 for HADS-possible, SF-36MCS, SF-36MH, EQ-5Di5-moderately) and substantial for higher thresholds (pairwise kappa = 0.75 for HADS-probable/EQ-5Di5-severely). Using HADS-D as external standard, EQ-5Di5 was very specific but less sensitive, while SF-36MCS/MH were more sensitive but less specific (Table 1).

Table 1. Test characteristics of instruments

	External standard: HADS-D≥8 (possible)			
Definition of 'depression'	**SE**	**SP**	**PPV**	**NPV**
EQ-5Di5 ≥3 (moderate)	51	89	69	80
EQ-5Di5 ≥4 (severe)	17	99	85	72
SF-36MCS ≤40	68	83	66	85
SF-36MH ≤56	78	71	56	87
	External standard: HADS-D≥11 (probable)			
Definition of 'depression'	**SE**	**SP**	**PPV**	**NPV**
EQ-5Di5 ≥3 (moderate)	67	84	41	94
EQ-5Di5 ≥4 (severe)	30	98	68	89
SF-36MCS ≤40	83	75	37	96
SF-36MH ≤56	88	63	29	97

All values are percentages.

Conclusion: Instruments used to assess depression in SpA are not interchangeable. The choice of instrument should be taken into account when interpreting studies on depression in SpA. SF-36MCS and SF-36MH are sensitive and could be considered for screening while EQ-5Di5 is useful when high specificity is required. In situations where assessment of depression is the primary objective, depression-oriented instruments such as the HADS are recommended.

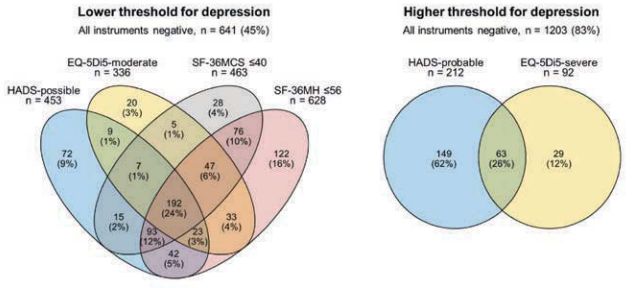

Figure. Venn diagram of instruments used to assess depression
Number of patients that scored positive for depression on the instrument(s). The percentages in the diagrams are based on the population of patients that scored positive on at least one of the assessed instruments (n=784 for lower threshold and n=241 for higher threshold for depression).

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POS0999

HIGHER CARDIOVASCULAR MORBIDITY SEEN IN MEN WITH LONGER DELAY TO THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS

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Background: Diagnostic delay in axial spondyloarthritis (axSpA) is a well-defined feature of the disease, despite increased awareness. Morbidity and mortality are higher in axSpA than the general population[1]. Much of this excess burden is due to increased comorbidity. However, the association between delayed diagnosis and increased comorbidity in this population is unknown.

Objectives: (1)Examine the relationship between delayed diagnosis and comorbidity in a large cohort of well characterised individuals with axSpA
(2)Assess the impact of sex on the relationship between diagnostic delay and comorbidity.

Methods: The Ankylosing Spondylitis Registry of Ireland (ASRI), a descriptive epidemiological study of the Irish axSpA population, provided the cohort for this study. A standardised clinical assessment was performed on each patient. Delay to diagnosis was calculated as age at diagnosis minus age at symptom onset. Comorbidities were considered as any condition present in addition to axial SpA, excluding extra-musculoskeletal manifestations (EMM). SPSS was used for statistical analysis, with appropriate tests used for normally and non-normally distributed data.

Results: Of the 913 included patients, 659 (72%) were male and mean age was 46 years (SD 13). Detailed baseline clinical and demographic characteristics are outlined in Table 1. Median delay to diagnosis was 5 (2, 12) years. Comorbidity was present in 37% (n=341) of the cohort, with hypertension the most prevalent (see Figure 1).

Table 1. Baseline demographic and clinical characteristics

Variable	
Age, mean (SD)	45.8 (12.6)
Female, n (%)	254 (27.8)
Caucasian, n (%)	819 (96.5)
Ever Smoker, n (%)*	527 (57.7)
HLA-B27 positive, n (%)	631 (89.9)
Disease duration, median (25^{th},75^{th})	17.1 (9.5, 27.8)
Delay to diagnosis, median (25^{th}, 75^{th})	5.0 (2.0, 12.0)
AAU, n (%)	308 (34.4)
PsO, n (%)	150 (16.7)
IBD, n (%)	96 (10.7)
Biologic use, n (%)	628 (68.5)
BASMI, mean (SD)	3.6 (2.1)
BASFI, mean (SD)	3.4 (2.9)
BASDAI, mean (SD)	3.9 (2.4)
HAQ, median (25^{th}, 75^{th})	0.38 (0.0, 0.9)

The median delay to diagnosis was significantly longer in those with ≥1 comorbidity compared to those with none (7 v 5 years, p<0.01). Hypertension (6 v 5 years, p=0.1) and cerebrovascular disease (10 v 5 years, p=0.03) were associated with a significantly longer delay to diagnosis, with a similar trend seen in those with hyperlipidaemia (7 v 5 years, p=0.09) and ischaemic heart disease (10 v 5 years, p=0.07). The delay to diagnosis was also longer in those that currently (7 v 5 years, p=0.03) or ever smoked (6 v 5 years, p<0.01). The delay to diagnosis was significantly longer in those with depression (9 v 5, p<0.05). The presence of EMM did not contribute to a delay to diagnosis, and there was no association with any categories of medication.

There was no significant difference in the median delay to diagnosis between females (5 v 6 years) for males. However, there were differences in the relationship between delay to diagnosis and the pattern of comorbidities between sexes. There was a significantly (p<0.05) longer delay to diagnosis in men with cerebrovascular disease (12 v 6 years), ischaemic heart disease (10 v 6 years) and diabetes (10 v 6 years), which wasn't evident in females. Depression was associated with a longer delay to diagnosis in males (10 v 6 years, p<0.05), but not females (6 v 5 years, p=0.5).

Conclusion: Delay to diagnosis of axSpA was associated with a higher prevalence of comorbidities. This was particularly evident in men, with higher cardiovascular morbidity in those with a longer delay to diagnosis. Further research is needed to determine if shortening the delay to diagnosis would reduce the burden of cardiovascular morbidity.

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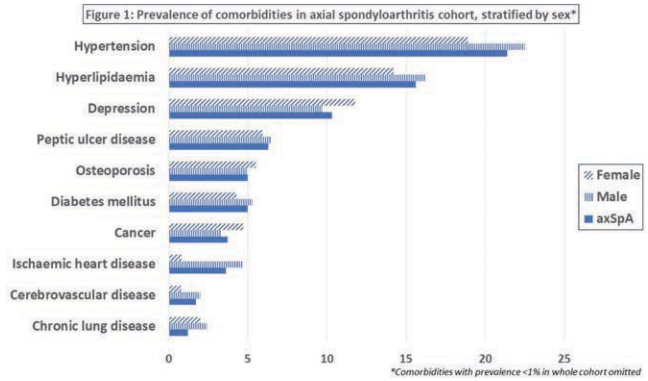

Disclosure of Interests: None declared
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POS1000

MORE THAN 30 % OF WOMEN WITH SPONDYLOARTHRITIS HAVE AN UNFAVORABLE PREGNANCY OUTCOME MOST FREQUENTLY DUE TO SMALL FOR GESTATIONAL AGE: ANALYSIS OF THE PROSPECTIVE GR2 COHORT

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Background: Spondyloarthritis (SpA) is one of the most common chronic inflammatory diseases and regularly affects women of childbearing age[1]. However, there is limited knowledge about the impact of the disease and its treatment on pregnancy.

Objectives: The aim of the study was to determine the factors associated with adverse pregnancy outcome in women with SpA.

Methods: All SpA patients (diagnosis according to the Rheumatologist) included in the national multicenter GR2 cohort from 2015 to June 2021 were included in the analysis. Patients could be included either with a pregnancy wish (i.e., preconceptional period) or because of a clinical pregnancy (<12 weeks of gestation). The main endpoint was favorable pregnancy outcome, a composite outcome defined as a live birth at term ≥ 37 gestation weeks of a healthy newborn with a weight greater than the 10th percentile. We performed a multilevel logistic regression model, in which we considered patient and center random effects (patient random effect for some women included in the cohort two times). Disease activity was defined by a BASDAI score ≥ 4 at least once during pregnancy. We used a multiple imputation to address missing data among the explanatory variables. Results are presented as an odds ratio (OR) with confidence interval (CI).

Results: Among the 207 pregnancies in women with SpA included in the GR2 cohort, 126 were retained for analysis of obstetrical outcome. Of these, 29 (23.0%), 14 (11.1%), 69 (54.8%) were exposed to corticosteroid, NSAID and biologics at least once during pregnancy, respectively. An active disease at least once during pregnancy was found in 47 (37.3%) pregnancies. A live birth was found in 116 (92.1%) women, including 110 (87.3%) full-term births. Early miscarriages and stillbirths were observed in 7 (0.06%) and 3 (0.02%) women, respectively. A caesarean section was performed in 20 (17.2%) cases.

A favorable pregnancy outcome was found in 80 (63.5%) of the women. Unfavorable pregnancy outcome was most frequently due to small for gestational age,

observed in 22 (19%) pregnancies. The multivariate model adjusted for age, BMI, nulliparity, active disease during pregnancy, smoking, and exposure to NSAIDs and corticosteroids during pregnancy found an association between unfavorable pregnancy outcome with nulliparity (OR 2.63 95% CI [1.01-6.81] p = 0.05).

Conclusion: This study provides original results on pregnancy in women with SpA. It found a favorable pregnancy outcome in 63.5% of women. Unfavorable pregnancy outcome was most frequently due to small for gestational age, which should lead to a coordinated management with obstetricians for the follow-up of pregnancy in women with SpA.

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Table 1. ***Multilevel logistic regression model: factors associated with unfavorable pregnancy outcome in women with SpA.***

	Univariate analyses		Multivariate analyses	
	Crude OR 95% CI	**p**	**Adjusted OR 95% CI**	**p**
Age	1.01 [0.92-1.10]	0.859	1.05 [0.95-1.17]	0.297
BMI	0.99 [0.91-1.07]	0.796	0.99 [0.90-1.08]	0.747
Nulliparity	2.16 [0.94-4.94]	0.071	**2.63 [1.01-6.81]**	**0.049**
Smoking	0.84 [0.23-3.03]	0.805	0.84 [0.22-3.21]	0.805
Disease activity*	0.98 [0.40-2.43]	0.964	1.15 [0.43-3.07]	0.778
Corticosteroids**	1.09 [0.45-2.65]	0.876	1.15 [0.51-2.71]	0.902
NSAIDs**	0.65 [0.18-2.33]	0.196	0.67 [0.18-2.56]	0.565

* BASDAI score ≥ 4 at least once during pregnancy. ** Use at least once during pregnancy

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POS1001 CURRENT SMOKING IS ASSOCIATED WITH LOWER RISK OF UVEITIS AND PERIPHERAL ARTHRITIS IN MALES WITH AXIAL SPONDYLOARTHRITIS

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Background: The associations between smoking and extra-axial manifestations of axial spondyloarthritis (axSpA) are inadequately described. Previous observational studies have demonstrated smoking as protective against some but not other manifestations. However, the impact of sex on these associations is unknown.

Objectives: Using a large descriptive epidemiological dataset, we performed a sex-stratified analysis of the association between smoking status and extra-axial manifestations in axSpA.

Methods: This study was carried out within the framework of ASRI (Ankylosing Spondylitis Registry of Ireland), a descriptive epidemiological study of the axSpA population of Ireland. A standardised clinical assessment was performed on each patient, collecting demographic and clinical data. Smoking status was characterised as current, previous or never. The number of cigarettes per day, plus number of years smoking was also collected. Data on the following extra-axial manifestations was collected: arthritis, enthesitis, dactylitis, acute anterior uveitis (AAU), psoriasis (PsO), inflammatory bowel disease (IBD). Standardised measures of disease severity were also collected. Separate logistic regression models were used to define the association between extra-axial manifestations and smoking, controlling for potential confounders. SPSS was used for statistical analysis.

Results: Smoking data was available for 913 out of the 917 axSpA individuals with data in ASRI (mean age 46 (SD 13) years, disease duration 19 (SD 12) years, 72% male, 97% Caucasian). Twenty eight percent (n=259) were current smokers, 29% (n=268) were past smokers and 42% (n=386) were never smokers. Of the current smokers, the mean number of cigarettes per day was 12 (SD 7) and number of years smoking was 22 (SD 12). Thirty one percent had peripheral arthritis, 7% had dactylitis, 18% had enthesitis, 34% had AAU, 17% had psoriasis and 11% had IBD. Current smokers had a significantly lower prevalence of arthritis and uveitis than past or non-smokers (see Table 1). A sex-stratified analysis was performed. There was no association between smoking status and any extra-axial manifestation in females. However, current smoking was associated with lower prevalence of arthritis in males compared to past or non-smokers (22% v 36% v 42%, p=0.002). A similar pattern was seen for uveitis, where male current smokers had a lower prevalence than non-smokers (24% v 38%, p=0.01). In contrast, psoriasis was more prevalent in men who were current smokers compared to non-smokers (18% v 12%, p=0.01), with no difference seen in females. There was no association with number of cigarettes smoked or number of years smoking.

Table 1. Association between smoking status and extra-axial manifestations in axSpA.

	AxSpA cohort	Current smoker	Past smoker	Non-smoker
Arthritis	30.9%	**22.4%[a]**	**35.5%[b]**	**33.3%[b]**
Dactylitis	6.7%	5.5%[a]	6.7%[a]	7.4%[a]
Enthesitis	18.1%	17.4%[a]	16.2%[a]	19.9%[a]
Uveitis	34.3%	**27.4%[a]**	**35.0%[b]**	**38.6%[b]**
Psoriasis	16.7%	18.5%[a]	19.3%[a]	13.8%[a]
Inflammatory bowel disease	10.7%	9.9%[a]	13.2%[a]	9.5%[a]

Different subscript letters denote significant (p<0.05) differences between groups. Significant values highlighted in bold.

There was no association between smoking status and disease severity by subjective or objective measures, either for the cohort as a whole or by sex.

When compared to non- or ex-smokers and controlled for potential confounders including sex, age, biologic use, the association remained only between current smokers and lower risk of uveitis (OR 0.68, 95% CI 0.49 to 0.96) and arthritis (OR 0.62, 95% CI 0.43 to 0.88), in separate logistic regression models. The association between current smoking and increased prevalence of psoriasis in males did not remain significant once controlled for confounders (OR 1.10, 96% CI 0.73 to 1.65).

Conclusion: We demonstrated that current smoking is independently associated with a lower risk of uveitis and arthritis in males with axSpA, but not females. More research is needed to further investigate this paradoxical finding.

Disclosure of Interests: None declared

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POS1002 DIAGNOSTIC DELAY AND ITS ASSOCIATED FACTORS IN CHINESE AXIAL SPONDYLOARTHRITIS: A RETROSPECTIVE STUDY

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Background: Few data on the prolonged diagnosis and its associated factors in Chinese axial spondyloarthritis (axSpA) is available.

Objectives: To delineate the landscape of diagnostic delay in Chinese axSpA, investigate its associated factors and explore its potential impact on medication modalities.

Methods: A total of 1,295 patients fulfilling the ASAS classification criteria were obtained. Demographic and clinical data were collected through predesigned questionnaires and available medical records. Logistic regression analyses in univariate and multivariable model were performed, using the median of diagnostic delay as cut-off point for group classification. Differences between early and late diagnosed group were subsequently compared by the Pearson chi-square test or Mann-Whitney U test.

Results: The median (IQR) diagnostic delay in Chinese axSpA was 3.0 (1.0~7.0) years and 24.8% of them reported a history of misdiagnosis. Older age at onset (OR=0.97, *P*<0.001) and higher education attainment (*P*=0.001) were correlated with early diagnosis of axSpA, whereas coming from less developed areas (*P*=0.002), a history of peripheral arthritis at the time of diagnosis (OR=1.58, *P*=0.002) and history of misdiagnosis (OR=1.98, *P*<0.001) increased the risk of diagnostic delay. Medication modalities were similar between two groups, but the proportion with no medication ever and percentage without regular medication in recent 3 months were higher in the late diagnosed group than early group (26.5% vs. 20.7%, *P*=0.02; 34.7% vs. 28.6%, *P*=0.02).

Conclusion: Our findings depicted a detailed spectrum of diagnostic delay in Chinese axSpA, verified five associated factors and pinpointed a remarkable treatment delay even after diagnosis, especially in late diagnosis group.

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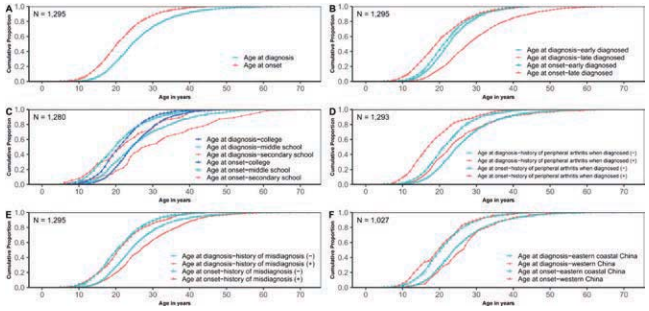

Figure 1. Cumulative distribution of age at onset and age at diagnosis in Chinese axSpA

(A) the entire group. (B) stratified by early and late diagnosed group. (C) stratified by education level (college, middle school, secondary school). (D) stratified by history of peripheral arthritis when diagnosed. (E) stratified by history of misdiagnoses when diagnosed. (F) stratified by native place, as statistical significance was found between eastern coastal and western China, only these two groups were presented.

Disclosure of Interests: None declared

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POS1003 IMPACT OF ELECTRONIC MEDICAL RECORD MANAGEMENT SYSTEM ON DISEASE ACTIVITY AND FREQUENCY OF OUTPATIENT VISITS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: We developed an electronic medical record management system (EMRMS) at the Taichung Veterans General Hospital (TCVGH) to assess ASDAS by integrating patient reported outcomes (assessed by an independent nurse) and ESR/CRP for AS patients. We aimed to investigate the impact of the EMRMS on frequency and time of outpatient visits.

Objectives: To investigate the impact of the EMRMS on frequency and time of outpatient visits.

Methods: We identified 652 AS patients who were followed up for at least one year before and after the first ASDAS assessment. We compared the number of outpatient visit and average visit time within one year before and after the initial ASDAS assessment. We identified 201 AS patients who received ≥ 3 continuous ASDAS assessment with an interval of 3 months and compared the 2nd and 3rd ASDAS with the first ASDAS.

Results: The annual number of outpatient visits was increased after starting ASDAS assessment (5.8±3.5 vs. 5.4±3.4, p<0.001), in particular among those whose initial ASDAS-CRP was > 3.5 (8.7±4.0 vs. 5.7±3.4, p<0.001). The average visit time was shortened within one year after ASDAS assessment (8.7±3.8 vs. 9.2±4.4 minutes, p = 0.030), especially among patients whose ASDAS-CRP was <1.3 (8.5±3.3 vs. 9.2±4.2 minutes, p=0.022). Among patients who received at least 3 ASDAS assessments, the 3rd ASDAS-CRP was significantly lower than the 1st ASDAS-CRP (1.5±0.8 vs. 1.6±0.8, p=0.040).

Conclusion: EMRMS may increase the frequency of ambulatory visits for AS patiets with very high disease activity and decrease the visit time for AS patients with inactive disease. Continual ASDAS assessment may help control disease activity of AS patients.

Disclosure of Interests: None declared

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POS1004 THE IMPACT OF MRI SLICE THICKNESS ON THE DETECTION OF SPINAL SYNDESMOPHYTES IN AXIAL SPONDYLOARTHRITIS

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Background: Conventional radiographs (CR) are the gold standard for detecting syndesmophytes in axial Spondyloarthritis (axSpA), mainly because magnetic resonance imaging (MRI) is not able to detect thin bony structures due to its slicing technique.

Objectives: To assess the ability and performance of detection of syndesmophytes using different slice thicknesses on MRI and compare them with findings on CR.

Methods: MRI with T1W and STIR images with slice thicknesses of 1-6mm and CR of the lower thoracic and lumbar spine performed on the same day were prospectively performed in 43 axSpA patients. Clinical and laboratory characteristics of the patients from the same timepoint were available. Each vertebral corner (VC) (anterior superior and posterior, inferior anterior and posterior) from the thoracic (Th11) to the lumbar (L5) vertebral body were assessed for the presence/absence of syndesmophytes but also fat lesion (FL) on MRI by two experienced readers (one radiologist and one rheumatologist) independently. Disagreements were solved in consensus.

Results: A total of 1.204 VCs was assessed from all patients. The mean time needed for scoring the MRIs varied between 2:27 and 4:12min for the MRI thicknesses of 1-6mm, respectively.

Syndesmophytes were detected in 19.3% VCs on CR and in 38.3%, 37.5%, 34.8%, 33.7%, 31.4%, 28.7% VCs on MRI slice thicknesses of 1-6mm, respectively (p≤0.001 for all MRI vs. CR evaluations and within MRI slice thicknesses). The anterior superior VC of L1 was the most affected site among all vertebral corners in all MRI slice thicknesses and CRs. In thoracic spine, the anterior superior corner of T12 was the most frequently affected site in both MRI (all slice thicknesses) and CR. Although MRI could detect more syndesmophytes in both lumbar and thoracic vertebrae than CR, MRI at any slice thickness could not detect 15.4%-23.2% of syndesmophytes detected in CR (Table 1).

Table 1. Agreement and disagreement of CR and MRI for syndesmophyte detection per MRI slice thickness

		CR		Agreement CR/MRI	False positive MR based on CR as gold standard
MRI		yes	no		
1mm	yes	182	279	72,6%	23,2%
	no	51	692		
2mm	yes	184	267	73,8%	22,2%
	no	49	704		
3mm	yes	181	238	75,9%	19,8%
	no	52	733		
4mm	yes	175	231	76,0%	19,2%
	no	58	740		
5mm	yes	169	209	77,3%	17,4%
	no	64	762		
6mm	yes	160	186	78,5%	15,4%
	no	73	785		

Fat lesions were detected in 38.3%, 37.5%, 34.8%, 33.7%, 31.4%, 28.7% of VC with MRI slice thicknesses of 1-6mm, respectively. MRI slice thickness had no role in detecting fat lesions (p>0.05 within MRI slice thicknesses).

Conclusion: MRI of the lower thoracic and the lumbar spine at any slice thickness detected more syndesmophytes than CR, but the best agreement and least false-positive findings on MRI based on CR as gold standard was found in the thicker slice thicknesses. The presence of fat lesions did not influence syndesmophyte detection on MRI. These results may influence the performance of spinal MRI in identification of SpA-specific spinal lesions in daily practice.

Disclosure of Interests: None declared

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POS1005 ACTIVE INFLAMMATORY LESIONS OF THE SPINE IN SACROILIAC JOINTS MRI (SIJS-MRI): AN OVERLOOKED FINDING BY RADIOLOGISTS.

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Background: Establishing a diagnosis for axial spondylarthritis (axSpA) is based on the combined presence of several clinical and laboratory features in association with imaging: the presence of active inflammatory lesions (bone marrow edema, BME) in sacroiliac joints (SIJs), also associated with structural lesions, is the main element in favor of a diagnosis of axSpA and SIJ MRI is currently the main recommended technique for detecting inflammation, enabling early diagnosis in patients with normal radiographic findings. MRI of the spine is generally not recommended for axSpA diagnosis, since spine involvement is considered less sensitive and specific. Several studies explored the incremental value of spine MRI for diagnosing patients with axSpA, especially when the findings of SI are equivocal, and "predicting" clinical disease activity.

Objectives: To evaluate the effectiveness of the MRI study dedicated to SIJs to identify the inflammatory involvement of the lumbar spine in patients with active sacroiliitis and clinical diagnosis of axSpA.

Methods: MRI of 96 patients (26 M, 70 F, mean age 48 years) with SIJs-MRI positive for inflammatory involvement according to ASAS criteria, were evaluated retrospectively. The presence of signs of inflammation of posterior spinal elements and vertebral bodies included in the field of vision (FOV) was therefore researched
Results: Of 96 patients with active sacroiliitis, 88 had concomitant inflammatory lesions of the lumbar spine. Facet capsulitis (87.6 %) and posterior enthesitis (42.2 %) were the most common lesions and these lesions frequently coexisted (39.3%). Twelve patients with facet capsulitis presented also facet arthritis. Only 20 out of 96 patients (22%) had vertebral bodies inflammatory lesions: 15 corner inflammatory lesions and 5 aseptical spondylodiscitis.
Conclusion: On the basis of current working consensus MRI examination of the spine is not recommended for axSpA diagnosis, because it is considered less sensitive and specific. However the high prevalence (91.7%) of spinal inflammatory changes in patients with active sacroiliitis suggests that these features can be used as an additional element in favor of diagnosis, especially in doubtful cases. This evaluation takes little reporting time, without any increase in MRI execution time.

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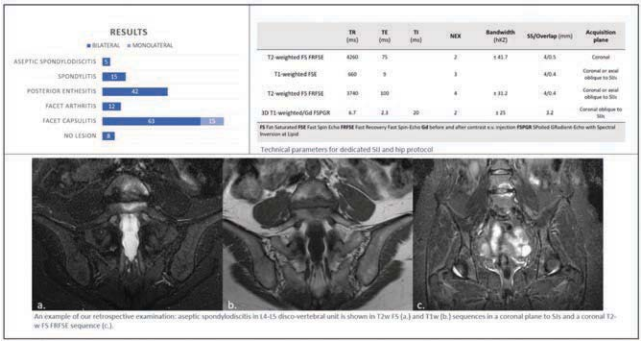

Figure 1.

Disclosure of Interests: None declared

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POS1006 DIAGNOSIS OF AXIAL SPA AND ADDITIONAL FEATURES IN HLA-B27 POSITIVE INDIVIDUALS REPORTING CHRONIC INFLAMMATORY BACK PAIN: DATA FROM A LARGE DUTCH POPULATION-BASED COHORT

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Background: Chronic low back pain (CLBP; back pain >3 months with age of onset <45) and inflammatory back pain (IBP) are regarded as early and key features of axSpA. HLA-B27 is the most important genetic risk factor. Despite improved diagnostics, especially the use of MRI in demonstrating active sacroiliitis, the substantial delay in axSpA diagnosis has not improved[1].
Objectives: To explore the presence of CLBP and IBP in combination with HLA-B27 and the presence of other axSpA associated features in the general population.
Methods: Participants of the Lifelines cohort, a large population-based cohort which is representative of the mostly Caucasian Northern region of the Netherlands[2], responded to a survey with questions concerning the presence of CLBP and the European Spondyloarthropathy Study Group (ESSG) criteria for IBP. HLA-B haplotypes were imputed from genome-wide SNPs genotyped with the Illumina GSA beadchip-24 v1.0, using the R-package HIBAG with published parameter estimates. Analyses were performed on participants with available HLA-B haplotype and CLBP/IBP data. Prevalence rates were calculated and logistic regression was performed to identify whether participant characteristics and other available SpA features were independently associated with the presence of the key axSpA features HLA-B27, CLBP and IBP.
Results: 20,619 participants had data available on CLBP, IBP and HLA-B haplotype. Of these participants, 1,610 (7.8%) were HLA-B27+, 3,717 (18.0%) reported CLBP, 2,670 (13.0%) fulfilled the IBP criteria, and 47 (0.23%) reported a previous SpA diagnosis, of which 37 (0.18%) reported axSpA. In total, 226 (1.1%) participants had the combination of CLBP/IBP/HLA-B27. Only 11 (4.9%) of these 226 participants reported a previous SpA diagnosis, all of which were axSpA. Participant characteristics and the presence of other available SpA related features are presented in Table 1.
In multivariable logistic regression analysis, current NSAID use and a reported history of peripheral arthritis were independently associated with the axSpA key features CLBP, IBP, and IBP+HLA-B27.
Conclusion: In this large Dutch population-based cohort only 4,9% of participants presenting the combined axSpA key features IBP and HLA-B27 reported a previous axSpA diagnosis, indicating possible axSpA underdiagnosis. Although not all SpA features were available in Lifelines, current NSAID use and a history of peripheral arthritis in combination with the axSpA key features may have additional value in identifying patients with axSpA in primary care.

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Table 1. Characteristics and features associated with SpA in the different subgroups of Lifelines participants. Data presented as mean ± SD or n (%). [1]Participants already reporting a previous SpA diagnosis excluded from this group.

	Available data in Lifelines of CLBP/IBP & HLA-B (n=20,619)	Self-reported SpA diagnosis (n=47)	CLBP$^+$ (n=3,698[1])	CLBP$^+$/IBP$^+$ (n=2,653[1])	HLA-B27$^+$ (n=1,585[1])	CLBP$^+$/IBP$^+$/ HLA-B27$^+$ (n=226[1])
General characteristics						
Male	8173 (39.6%)	24 (51.1%)	1443 (39.0%)	1058 (39.9%)	630 (39.7%)	89 (41.4%)
Age	44.2 ± 14.2	48.1 ± 12.6	42.5 ± 13.2	44.0 ± 12.8	44.1 ± 14.1	41.7 ± 12.5
BMI	25.7 ± 4.1	26.7 ± 4.3	26.2 ± 4.5	26.3 ± 4.3	25.7 ± 4.4	25.9 ± 4.6
Features associated with SpA						
Reported diagnosis of:						
- Uveitis	11 (0.1%)	1 (2.1%)	1 (0.0%)	0 (0%)	2 (0.1%)	0 (0%)
- IBD	179 (0.9%)	3 (6.4%)	31 (0.8%)	22 (0.8%)	14 (0.9%)	2 (0.9%)
- Psoriasis	588 (2.9%)	8 (17%)	491 (2.8%)	79 (3.0%)	52 (3.3%)	7 (3.3%)
Current NSAID use	766 (3.7%)	20 (42.6%)	252 (6.8%)	189 (7.1%)	82 (5.2%)	22 (10.2%)
History of peripheral arthritis	609 (3.0%)	7 (14.9%)	229 (6.2%)	196 (7.4%)	43 (2.7%)	17 (7.9%)
Reported rheumatism in FDR	3572 (17.3%)	12 (25.5%)	724 (19.6%)	535 (20.2%)	315 (19.9%)	47 (21.9%)
At least 1 of above features	4803 (23.3%)	30 (63.8%)	1013 (27.4%)	744 (28.0%)	418 (26.4%)	69 (32.1%)
At least 2 of above features	302 (1.5%)	7 (14.9%)	85 (2.2%)	66 (2.5%)	34 (2.1%)	7 (3.3%)

POS1007

MRI CHANGE SCORE BUT NOT THE STATUS SCORE IS RELATED TO DISEASE ACTIVITY AND CLINICAL RESPONSE OVER TIME IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM ESTHER STUDY.

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Background: Magnetic resonance imaging (MRI) of the spine and sacroiliac joints (SIJ) are important tools for the diagnosis of axial SpA. However, there is very little data investigating how clinical symptoms and response to treatment relate to the degree of MRI inflammation and to its change over time.

Objectives: To evaluate the relationship between clinical response in axial SpA patients and inflammation in MRI of spine and SIJ after 6 months of treatment.

Methods: In the ESTHER study[1], a total of 76 patients with early axial SpA with a symptom duration less than 5 years, and with active inflammation on MRI in the spine and/or SIJ at baseline were randomized to be treated with etanercept (n=40) or sulfasalazine (n=36) for one year.

Clinical and laboratory outcome assessments included C-reactive protein (CRP), Bath ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI) and ankylosing spondylitis disease activity score (ASDAS). The following efficacy parameters were calculated: change in CRP, BASDAI, BASFI and ASDAS between baseline and Week 24; response of the ASAS response criteria for 20 and 40% improvement in disease activity (ASAS20 and ASAS40); and ASAS criteria for partial remission at Week 24.

MRI of spine and SIJ were performed at weeks 0, 24, and 48; and were scored by two radiologists, who were blinded for all clinical data, treatment arm and time point, according to the Berlin scoring system. The final osteitis score for the SIJ and for the spine was calculated as the mean score of both readers. Residual inflammation in MRI at Week 24 was defined as an osteitis score of ≥5 for SIJ and >0 for the spine (median values at Week 24).

To understand the relationship between MRI and clinical outcomes, two types of models were performed: 1) a model with status scores at baseline and Week 24 for MRI and clinical outcome parameters; and 2) a model with change scores between baseline and Week 24 for MRI and clinical outcome parameters.

Results: A total of 67 patients with axial SpA were included in this analysis due to availability of MRIs at baseline and Week 24. The characteristics of patients included for this analysis were similar to the whole group of the ESTHER study. SIJ and spine osteitis score on MRI at baseline (mean±SD) was 6.9±6.1 and 1.5±2.5, respectively. The status scores showed no association at baseline, neither at Week 24, with the only exception of ASAS20 at Week 24 (Figure 1). However, changes in osteitis score of SIJ and spine were associated to clinical response outcomes between baseline and Week 24 (Figure 1). Further, we compared patients with and without residual inflammation on MRI of the spine and SIJ as defined above. There were no differences between the groups regarding clinical response and disease activity at week 24.

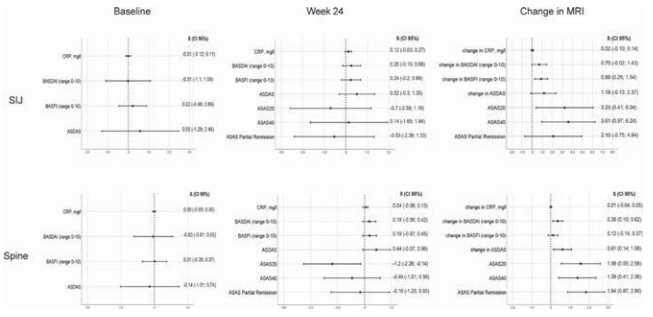

Figure 1. Association between disease activity parameters and MRI osteitis score in spine and SIJ in patients with axial spondyloarthritis over 6 months of treatment. Each line in the figure refers to an outcome (dependent variable) in the multivariable regression analysis, which were adjusted for age, sex, symptom duration and HLA-B27 positivity. MRI, magnetic resonance imaging; SIJ, sacroiliac joints.

Conclusion: Change of score for osteitis in MRI of spine and SIJ was associated to disease activity in patients with axial SpA during 6 months of treatment. Presence of residual inflammation on MRI after 6 months of treatment seems to be irrelevant regarding clinical response and clinical disease activity.

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POS1008

FACTORS ASSOCIATED WITH HIP INVOLVEMENT AND ITS IMPACT ON TREATMENT DECISION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS; TREASURE EXPERIENCE

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease affecting sacroiliac joints, spine and peripheral joints. In addition to spinal and peripheral manifestations, root joints (hip or sholder) involvement may also develop. Hip involvement is reported 24-36% in patients with Ankylosing Spondylitis (AS) by clinical evaluation of the rheumatologists. However, there is limited data regarding the factors related with the presence of hip involvement and treatment preference in patients with axSpA.

Objectives: The aim of this study was to evaluate the factors/covariates associated with the hip involvement and its impact on the treatment preferences in patients with axSpA patients who initiated their first biologic therapy.

Methods: In total, 1600 axSpA patients who initiated his/her first biologic were included in the study. The data for the current study was obtained from the TReasure web-based registry. Baseline demographics and disease related characteristics were collected. Characteristics and treatment preference of patients with and without hip involvement were compared. The factors/covariates associated with the presence of hip involvement were evaluated by regression analysis.

Results: Hip involvement was reported in 375 patients (23.4%). Patients with hip involvement were more common male patients in addition they had lower education level, lower BMI and more frequent HLA-B27 positivity as well as longer disease duration. Hip involvement was more frequent in patients with r-axSpA than patients with nr-axSpA. We found lower percentages of peripheral arthritis, enthesitis and dactylitis, higher BASFI or ASDAS-CRP scores, higher serum CRP levels and ESR values in patients with hip involvement. Moreover, patients with hip involvement had less frequently SpA-related family history (Table 1). When we analyzed patients according to age at diagnosis (≥ 16 years, <16 years) we found that patients with hip involvement were more common in juvenile onset axSpA group. In multivariate analysis, we found that lower education level (OR:2.029, 95%CI:[1.461-2.817]; p<0.001), diagnosis (r-axSpA) (OR:0.532, 95%CI:[0.337-0.839]; p=0.007) longer disease duration (OR:1.002, 95%CI:[1.001-1.004]; p=0.002), lower percentages of enthesitis (OR:0.405, 95%CI:[0.283-0.579]; p<0.001), higher BASFI scores (OR:1.086, 95%CI:[1.025-1.151]; p=0.005) and serum CRP levels (OR:1.005, 95%CI:[1.001-1.010]; p=0.019) absence of SpA family history (OR:0.713, 95%CI:[0.528]; p=0.027) were associated with hip involvement.

Table 1. Characteristics of patients with axSpA

	All patients (n=1600)	Hip involvement (+) (n=375)	Hip involvement (-) (n=1225)	P*
Juvenile (<16 years) onset, n(%)	30 (1.9)	12 (3.2)	18 (1.5)	0.031
Male sex, n(%)	940 (58.8)	255 (68)	685 (55.9)	<0.001
HLA-B27 positivity, n(%)	605 (55)	178 (62.7)	427 (52.3)	0.002
BMI, kg/m^{2}mean (SD)	27.2 (5.2)	26.7 (5.0)	27.4 (5.2)	0.023
Education duration (≤12 years), n (%)	1014 (65.9)	263 (71.3)	751 (64.2)	0.013
mNY positivity, n(%)	1276 (79.8)	338 (90.1)	938 (76.6)	<0.001
Disease duration (month) median (IQR 25-75)	82 (36-151)	111 (52-200)	74.5 (32-139)	<0.001
SPA-related family history, n (%)	544 (34)	110 (29.3)	434 (35.4)	0.029
BASFI, mean (SD)	3.9 (2.5)	4.3 (2.1)	3.8 (2.7)	0.007
ASDAS-CRP, mean (SD)	3.1 (1.5)	3.7 (1.4)	2.9 (1.5)	<0.001
CRP (mg/dl), median (IQR 25-75)	8.6 (3-21)	12.0 (4.0-27.9)	7.6 (2.5-19)	<0.001

When we compared the treatment patterns of axSpA patients with and without hip involvement, we found that the percentages of NSAID as well as csDMARD use were similar in groups. However, the percentages of patients who were prescribed etanercept were higher in axSpA patients with hip involvement (p<0.001).
Conclusion: In addition to inflammation and function, hip involvement seems to be related with diagnosis (r-axSpA), education level and absence of SpA family history. Moreover, enthesitis may not accompany hip involvement.
Disclosure of Interests: None declared
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POS1009 COMPARING OF DISEASE ACTIVITY, FUNCTION AND QUALITY OF LIFE IN PATIENTS FROM THE CLINICAL AND IMAGING ARM OF NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Background: The concept of axial spondyloarthritis (axSpA) and non-radiographic axSpA (nr-axSpA), a subgroup of axSpA, has recently emerged. There are several studies proving the similar levels in disease activity and quality of life in patients with or without structural damage in spondyloarthritis.
Objectives: The aim of this study is to compare disease activity, functional status and quality of life in patients from the clinical and imaging arm of nonradiographic axial spondyloarthritis in Bulgaria.
Methods: A cross-sectional survey was conducted with rheumatologists and their consulting patients in Bulgaria from February 2012 through April 2019. Patients who had a rheumatologist confirmed diagnosis of nr-axSpA were eligible to participate. An information about patient demographics and symptoms duration were collected. Acute- phase reactants, patients' reported data for disease activity (BASDAI), functional status (BASFI) and quality of life (ASQoL) were compared between the patients with or without MRI data for sacroiliitis. The level of significance was set to 0.05.
Results: A total of 98 patients from the imaging arm of nonradiographic arm and 62 patients from the clinical arm of nr-axSpA patients were included in this analysis. A higher proportion of patients from the imaging arm were male patients (51% vs 37%). The mean age was 33.8±7.71 in the imaging arm and 34.12±6.95 in the clinical arm (p>0.05), with mean symptoms duration in both groups- respectively 0.76±0.26 and 0.48±0.13 years (p>0.05). The mean value of C-reactive protein in the imaging arm was 14.81±28.59 and 7.05 ± 10.04, p=0.02 in both groups. The disease activity determined using patients reported data from BASDAI was 4.1±0.67 vs 4.01±0.78 (p>0.05) and using ASDAS-CRP 2.31±0.87 vs 2.05±0.52 (p>0.05) in the imaging and clinical arm. The evaluation of the function BASFI was 5.06±1.28vs 4.48±1.18, p>0.05 in both groups of patients with nr-ax SpA. The QoL, determined by ASQoL revealed non statistical significant values between the groups – 4.79±3.27 and 5.18±3.03, p>0.05.
Conclusion: Patients from the imaging and clinical arm of nr-axSpA share the same clinical features. The burden of the disease, as assessed by ASQoL measurement, is also similar in the investigated subgroups of Bulgarian nr-axSpA patients.
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POS1010 SPINAL RADIOGRAPHIC PROGRESSION AND ITS ASSOCIATION WITH PROGRESSION TO ANKYLOSING SPONDYLITIS IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS.

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Background: Prevention of structural damage of the axial skeleton is an important goal of treatment in axial spondyloarthritis (axSpA)[1]. Most studies concerning spinal radiographic progression focused on ankylosing spondylitis (AS). Data on spinal radiographic progression in patients with non-radiographic (nr)-axSpA is limited and data on the relation between spinal and sacroiliac radiographic progression in this population is lacking.
Objectives: To assess long-term spinal radiographic progression in patients with nr-axSpA. Secondly, to explore the association between radiographic progression to AS and spinal radiographic progression in these patients.
Methods: Patients enrolled in the ongoing Groningen Leeuwarden Axial SpA (GLAS) cohort, classified as nr-axSpA at baseline, with pelvic and spinal (lumbar and cervical) radiographs available at baseline and at least one follow-up visit at 2, 4 or 6 years were selected for analyses. Progression from nr-axSpA to AS was defined as progression to modified New York (mNY) sacroiliitis score ≥2 bilaterally or ≥3 unilaterally. Radiographs of nr-axSpA patients were randomized with radiographs of AS patients and scored in known time sequence by two trained readers blinded for patient characteristics. SK and RW scored the SI joints and in case of disagreement in axSpA classification, the score of a third independent reader (AS) was used. SK and MS scored the spinal radiographs according to the modified stoke ankylosing spondylitis spinal score (mSASSS; 0-72), and the mean of both total scores was calculated. In case of >5 points discrepancy between both readers, the mSASSS of a third independent reader (FM) together with the closest of the scores of the primary readers was used. The mSASSS change of nr-axSpA patients who did en did not progress to AS was compared with Mann-Whitney U tests.
Results: Included were 60 patients with a clinical diagnosis of nr-axSpA, confirmed by their sacroiliac radiographic score at baseline. Mean age was 37±10 years, 53% were male, median symptom duration was 9 (IQR 2-17) years, 75% were HLA-B27$^+$, and mean ASDAS was 2.6±1.1.
In total 15 patients progressed to AS. Median mSASSS at baseline was 1.5 (IQR 0.5 – 4.4). Median change in mSASSS from baseline was 0.0 (IQR 0.0 – 1.0) vs. 1.0 (IQR 0.0 – 1.5) at 2 years; 1.2 (IQR 0.3 – 3.5) vs. 2.0 (0.5 – 2.7) at 4 years; and 1.8 (1.0 – 3.8) vs. 2.5 (0.5 – 3.5) at 6 years for non-AS progressors and AS progressors, respectively (Figure 1). These mSASSS changes weres were not significantly different at any timepoint (p = 0.456, p=0.814, p=0.929 for 2-, 4-, and 6-year follow-up, respectively).

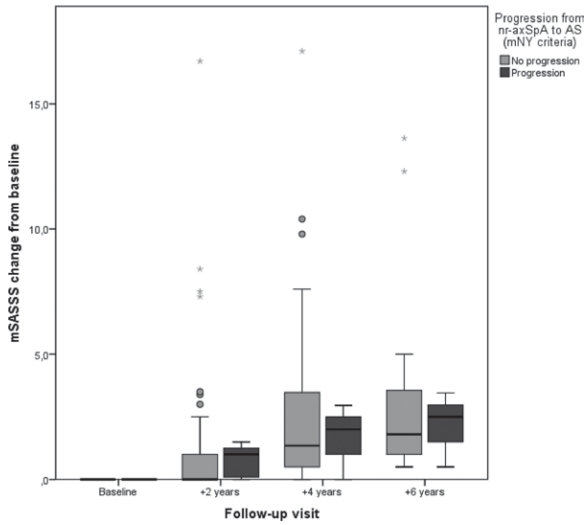

Figure 1. Comparison of mSASSS progression between patients with and without progression to AS during the first 6 years of follow-up.

Conclusion: In our observational cohort of patients with nr-axSpA with up to 6 years of follow-up, mSASSS progression was low (< 1 mSASSS unit/year) and was not different between patients who did and did not progress to AS.
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POS1011 THE STUDY OF DETECTION OF FECAL CALPROTECTIN AS A MARKER OF EARLY DIAGNOSIS OF THE DEVELOPMENT OF INFLAMMATORY BOWEL DISEASES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) can be characterized not only by the detection of the musculoskeletal system, but by the probable contribution of extraskeletal manifestations (ESMs), which can aggravate the course of the disease, and may occur in the first place in terms of the activity of the process. At the same time, according to the findings, in 3.5-10% of patients with AS, a diagnosis of IBD was detected, and in 70% of patients with AS, subclinical symptoms of intestinal disorders were detected. AS and IBD have common links of pathogenesis: microbiota and intestinal wall condition. Currently, highly sensitive fecal laboratory tests are used to monitor inflammation activity in IBD prior to ileocolonoscopy. Fecal calprotectin (FCP) is a marker of neutrophilic inflammation in gastrointestinal diseases and an indicator of the intensity of the inflammatory process in the intestine. The concentration of FCP is statistically significantly higher in IBD patients with signs of clinical activity and, as a rule, does not go beyond the normal range in patients with irritable bowel syndrome. These data make it possible to consider fecal calprotectin as a promising marker of the onset and latent course of inflammatory bowel disease in patients with ankylosing spondylitis.
Objectives: To reveal the peculiarities of fecal calprotectin concentration in patients with ankylosing spondylitis in case of occurrence and recurrence of inflammatory bowel diseases as extraskeletal manifestations.
Methods: The study included 80 patients with ankylosing spondylitis: women - 28 (35%), men - 52 (65%). The average age of patients was 45.12±12.4 years, the average age of onset symptoms - 28.43±13.18 years, mean duration of AS - 18.7±11.75 years. Patients already diagnosed with AS were asked to complete a questionnaire using the Universal Questionnaire to identify signs of immunoinflammatory diseases - psoriasis, psoriatic arthritis, IBD (Crohn's disease, ulcerative colitis) to identify clinical signs of intestinal damage. With a positive answer to one main and one additional questions, the patient was asked to conduct a qualitative determination of fecal calprotectin. Before the study, patients were stopped taking non-steroidal anti-inflammatory drugs for two weeks. Patients in whom the presence of calprotectin in the feces was detected, at the next stage, a semi-quantitative determination of calprotectin in the feces was carried out by immunochromatographic method. Patients who had an increase in the concentration of fecal calprotectin above 200 μg/g were recommended to perform a diagnostic colonoscopy on an outpatient basis to clarify the diagnosis. The next step was the determination of fecal calprotectin in patients with a positive survey result. In 26 patients (32.5%) a positive result was revealed.
Results: In 71 (88.7%), according to the results of the questionnaire, subclinical signs of intestinal damage were identified. At the next stage, patients with a positive result in the determination of FCP underwent an immunochromatographic test to detect the concentration of calprotectin in the feces. Of these, 22 patients (84.6%) had a concentration of 50-200 μg/g, which indicates the need for dynamic monitoring of this group of patients. In 4 patients (15.38%), the concentration of PCP was found to be higher than 200 μg/g.
Conclusion: Among patients with ankylosing spondylitis, 88.7% have subclinical signs of intestinal damage. Of these, calprotectin is determined in feces in 32.5%, which may indicate a latent course or debut of inflammatory bowel disease. Determination of the presence of fecal calprotectin in patients with ankylosing spondylitis contributes to the early diagnosis of inflammatory bowel disease.
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POS1012 PATIENT CHARACTERISTICS AND CLINICAL ASSESSMENTS ASSOCIATED WITH PROGRESSION FROM NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TO ANKYLOSING SPONDYLITIS

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Background: Part of the patients with non-radiographic spondyloarthritis (nr-axSpA) will progress to ankylosing spondylitis (AS). Varying factors are reported to be predictive of this progression of which the presence of elevated CRP and active sacroiliitis on MRI are most often found[1].
Objectives: To explore patient characteristics and clinical assessments associated with progression from nr-axSpA to AS up to 6 years follow-up in daily clinical practice.
Methods: Patients from the ongoing Groningen Leeuwarden axial SpA (GLAS) cohort classified as nr-axSpA enrolled into the cohort (baseline) between 2009 and 2018 were included in the analyses. Nr-axSpA was defined as sacroiliitis of ≥ 2 grade bilaterally or ≥ 3 unilaterally on the AP view of pelvic radiographs, according to the modified New-York (mNY) criteria. Baseline and available radiographs at 2 (n=85), 4 (n=53) and 6 years (n=30) of follow-up were randomized with radiographs of patients with AS and scored with known time sequence according to the mNY criteria by 2 trained readers (SK and RW). In case of disagreement in classification, the score of a third independent reader (AS) was used. Progression to AS was defined as progression in mNY sacroiliitis score to a score of ≥2 bilaterally or ≥3 unilaterally at any time during the 6-year follow-up period. Patient characteristics and clinical assessments at baseline were compared between patients who did and did not progress from nr-axSpA to AS, using chi-squared tests, Mann-whitney U tests or independent t-tests when appropriate.
Results: 85 patients were classified as nr-axSpA at baseline. Mean age was 39±11 years, 52% was male, median symptom duration was 6 (IQR 3-17) years, 75% was HLA-B27$^+$, and mean ASDAS was 2.7±1.1.
After 2, 4 and 6 years, 9/85 (10.6%), 4/47 (8.5%) and 2/24 (8.3%) of nr-axSpA patients progressed to AS. In total, 15 patients progressed to AS and 31 and 19 patients did not yet reach follow-up at 4 and 6 years, respectively.
Patients with nr-axSpA progressing to AS were significantly more often current smokers (62% vs. 21%, p=0.003) and had more often a history of uveitis (47 vs. 11%, p=0.001). Furthermore, patients with nr-axSpA progressing to AS tended to have higher CRP (and therefore ASDAS), more entheseal involvement, and worse lumbar spinal mobility then non-progressors; however, due to the relatively low number of progressors during the analyzed follow-up period, significance could not be reached (Table 1).
Conclusion: In our cohort, active smoking and a history of uveitis were independently associated with the progression of nr-axSpA to AS. Combining data of different cohorts will help to assess a more robust picture of axSpA features and patient characteristics associated with progression to AS.
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Table 1. Comparison of baseline characteristics between patients with nr-axSpA who did and did not progress to AS. Values presented as mean ± SD, median (IQR) and n (%) for normally distributed, non-normally distributed and categorical variables, respectively. *p<0.05.

Baseline characteristics	All patients (n=85)	No progression (n=70)	Progression (n=15)	p
Male sex	44 (52%)	39 (56%)	5 (33%)	0.115
Age	38.6 ± 10.8	38.4 ± 10.2	39.5 ± 13.8	0.774
Symptom duration	6 (3 – 17)	7 (3 – 16)	4 (2 – 20)	0.663
HLA-B27$^+$	62 (75%)	52 (74%)	10 (67%)	0.758
Currently smoking	22 (28%)	14 (21%)	8 (53%)	0.003*
BMI	26.1 ± 4.4	26.2 ± 4.5	25.8 ± 4.2	0.750
History of uveitis	15 (18%)	8 (11%)	7 (47%)	0.001*
History of IBD	7 (8%)	6 (9%)	1 (8%)	0.808
History of psoriasis	12 (14%)	10 (15%)	2 (13%)	0.923
ASDAS	2.7 ± 1.1	2.6 ± 1.1	3.2 ± 1.0	0.107
- ASDAS >2.1	51 (72%)	41 (68%)	10 (91%)	0.126
BASDAI	5.3 (3.4 – 6.7)	5.4 (3.2 – 6.8)	4.7 (3.6 – 6.7)	0.538
CRP ≥5.0	21 (27%)	16 (25%)	5 (39%)	0.320
Start TNFi (during first 2 years of follow-up)	27 (32%)	23 (33%)	4 (27%)	0.640
Chest expansion (cm)	5.2 ± 2.1	5.3 ± 2.1	4.7 ± 2.1	0.367
Lateral spinal flexion (cm)	14.4 (10.5 – 17.5)	14.5 (10.7 – 17.7)	11.3 (9.0 – 17.5)	0.163
mSchober (cm)	14.1 ± 1.3	14.1 ± 1.3	13.7 ± 1.3	0.308

Psoriatic arthritis - treatment

POS1013 HOW DOES BODY MASS INDEX AFFECT SECUKINUMAB TREATMENT OUTCOMES AND SAFETY IN PATIENTS WITH PSORIATIC ARTHRITIS? – REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

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Background: There is a higher prevalence of obesity in patients (pts) with psoriatic disease[1]. The German non-interventional study AQUILA provides real-world data on the influence of body mass index (BMI) of pts with psoriatic arthritis (PsA) on therapeutic effectiveness and safety under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits IL-17A.

Objectives: The aims of this interim analysis are to describe selected baseline (BL) demographics and to evaluate secukinumab treatment outcomes on disease activity and impact of disease on health and to report safety profile depending on the BMI of PsA pts.

Methods: AQUILA is an ongoing, multi-center study including up to 3000 pts with active PsA or ankylosing spondylitis. Pts were observed from BL up to week (w) 52. Real-world data were assessed prospectively and analyzed as observed. Data were collected on Psoriatic Arthritis Impact of Disease-12 items (PsAID-12 score) and Patient's Global Assessment (PGA). For calculation of proportion of pts that experienced (serious) adverse events ((S)AEs), all PsA pts were included that received at least one dose of secukinumab. This interim analysis focuses on BMI subgroups *≤25* kg/m^2 (normal weight), *>25 to ≤30* kg/m^2 (overweight) and *>30* kg/m^2 (obese) in PsA pts.

Results: At BL, BMI data were available for 1228 PsA pts: 26.5% (n=325) normal weight, 35.0% (n=430) overweight and 38.5% (n=473) obese PsA pts. Proportion of men was lower in normal weight and obese PsA pts. As BMI increased, so did age and comorbidities/extraarticular manifestations (EAMs; Table 1); e.g. percentage of PsA pts with heart-related disease increased from 5.2% in normal weight to 9.3% in obese PsA pts.

Table 1. Overview of baseline characteristics in PsA pts depending on BMI

Demographics	BMI ≤25 kg/m^2 (N=325)	BMI >25 to ≤30 kg/m^2 (N=430)	BMI >30 kg/m^2 (N=473)
Male*	105 (32.3)	219 (50.9)	188 (39.7)
Age, years**	49.5 (±12.7)	53.2 (±11.0)	54.1 (±10.6)
PsAID**	4.7 (2.4)	4.9 (2.2)	5.4 (2.0)
PGA**	4.8 (2.6)	5.4 (2.4)	5.5 (2.4)
Comorbidities/EAMs*			
Heart-related disease	17 (5.2)	29 (6.7)	44 (9.3)
Coronary heart disease	10 (3.1)	25 (5.8)	35 (7.4)
Stroke	1 (0.3)	9 (2.1)	11 (2.3)
Heart insufficiency	9 (2.8)	15 (3.5)	15 (3.2)
Uveitis	5 (1.5)	6 (1.4)	10 (2.1)
Depression	137 (53.5)	190 (55.2)	231 (58.5)

*variables are given as n (%); **variables given as mean (SD)

Mean PsAID at BL was similar for all BMI subgroups (*≤25*: 4.7; *>25-≤30*: 4.9; *>30*: 5.4; Figure 1A). Mean improvement from BL to w52 was 1.9 (40.4%) for normal weight, 1.8 (36.7%) for overweight, and 1.7 (31.5%) for obese PsA pts.

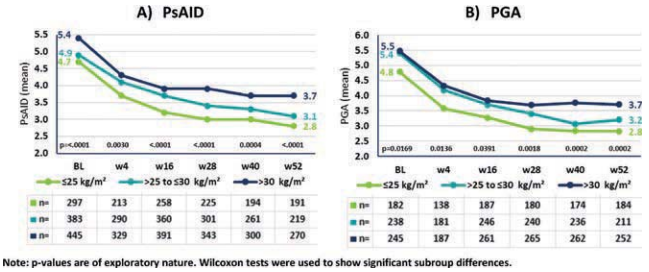

Figure 1. Impact of disease and PGA in PsA pts stratified by BMI. Note: p-values are of exploratory nature. Wilcoxon tests were used to show significant subroup differences.

Mean PGA developed in a similar way over time with lowest scores for normal weight and highest scores for obese PsA pts (Figure 1B). Mean improvement from BL to w52 was 2.0 (41.6%) for normal weight, 2.2 (40.7%) for overweight, and 1.8 (32.7%) for obese PsA pts.

The occurrence of AEs/SAEs with or without suspected relationship to secukinumab was most frequent in overweight and obese PsA pts. For example, the percentage of SAEs in normal weight PsA pts was 21.6%, in overweight 26.3% and in obese 25.9%. There were no unexpected safety signals in either subgroup. One male obese PsA patient died. Cause of death was not reported, however, treating physician did not suspect a causal relationship to secukinumab.

Conclusion: In a real-world setting, secukinumab improved impact of disease and patient´s global assessment of disease activity in all BMI subgroups of PsA pts. However, normal weight PsA pts had numerically better PsAID and PGA scores than obese PsA pts. Altogether, real-world data of this interim analysis show that secukinumab is an effective treatment with a favorable safety profile up to 52 weeks in PsA pts in all BMI subgroups.

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POS1014 IMPACT OF SERUM INTERLEUKIN 22 AS A BIOMARKER FOR THE DIFFERENTIAL USE OF MOLECULAR TARGETED DRUGS FOR PSORIATIC ARTHRITIS

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Background: Although each bDMARD target different molecules, no optimal drug selection method has been established. Because studies directly comparing TNF-i and IL-17-i have shown that these drugs are equally effective, the establishment of an optimal selection method for these drugs can contribute to better patient outcomes. We reported the possibility of stratification of patients by peripheral blood lymphocytes phenotyping and precision medicine based on the selective use of bDMARDs in psoriatic arthritis (PsA). However, since peripheral blood lymphocytes phenotyping is complex, the development of simple methods using biomarkers to stratify patients and simple treatment strategies based on such methods is needed to promote precision medicine in a real-world clinical setting.

Objectives: We explored whether serum cytokines could be used as biomarkers for optimal use TNF-i and IL-17-i in patients with PsA.

Methods: In cohort 1 (IL-17-i [n=23] or TNF-i [n=24] for ≥1 year), we identified serum cytokines that predicted the achievement of DAPSA remission (REM), PASI 90 and Minimal Disease Activity after 1 year of TNF-i or IL-17-i therapy. Subsequently, we developed treatment strategies based on the identified cytokines. In cohort 2, treatment responses were compared between the strategic treatment group (n=17), which was treated based on the treatment strategies, and the mismatched treatment group (n=17) to verify the validity of the treatment strategies developed using serum cytokines as biomarkers.

Results: In cohort 1, serum IL-22 concentrations were statistically identified as a predictor of DAPSA remission after 1 year of IL-17-i therapy. However, no baseline serum cytokines were identified as factors contributing to achievement of DAPSA-REM in the TNF-i-treated group or achievement of PASI90 and Minimal Disease Activity in either group. Using a cut-off value of 0.61376 (sensitivity, 81.8%; specificity, 91.7%; area under the curve, 0.848) determined by a ROC analysis, we stratified 47 patients into the IL-22 high group (n=25) (0.61376<) and the IL-22 low group (n=22) (< 0.61376). Serum IL-17 concentrations were significantly higher in both the IL-22 high and IL-22 low groups than in the healthy control (HC), whereas no significant difference was observed between the IL-22 high and IL-22 low groups. The serum TNF-α concentrations did not significantly differ between the IL-22 low and HC; however, they were significantly higher in the IL-22 high group than in the HC and IL-22 low groups. Based on these results, we created treatment strategies using TNF-i and IL-17-i based on serum IL-22 concentrations, that is, initiation of IL-17-i therapy in patients with low IL-22 concentrations and TNF-i therapy in patients with high IL-22 concentrations. To

validate the efficacy of the treatment strategies, we retrospectively compared the efficacy of the bDMARDs at 1 year between the following groups in cohort 2. The strategic treatment group (n=17) included patients with low IL-22 concentrations who were treated with IL-17-i and those with high IL-22 concentrations who were treated with TNF-i. The mismatched treatment group (n=17) included patients with low IL-22 concentrations who were treated with TNF-i and those with high IL-22 concentrations who were treated with IL-17-i. No statistically significant differences were observed between the two groups in baseline characteristics at the initiation of bDMARD. After initiation of bDMARD, tender joint counts, swollen joint counts, CRP, DAPSA, and PASI were significantly improved in both groups. When the treatment responses over 1 year were compared between the two groups, the rate of achieving DAPSA-REM (58.8% vs. 25.3%, P=0.0399) and Minimal Disease Activity (82.3% vs. 41.2%, P=0.0162) at M12 was significantly higher in the strategic treatment group. There were no statistically significant differences in the rates of achieving PASI75 or PASI90 at M 6 or 12.

Conclusion: We verified that serum IL-22 can be used as a simple biomarker for the proper selection of TNF-i and IL-17-i.

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POS1015

SAFETY OF GUSELKUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS WHO ARE BIO-NAÏVE OR TNFI-EXPERIENCED: POOLED RESULTS FROM 4 RANDOMIZED CLINICAL TRIALS THROUGH 2 YEARS

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Background: Guselkumab (GUS), a selective IL-23p19 subunit inhibitor, demonstrated efficacy and a favorable safety profile in active psoriatic arthritis (PsA) in the Phase (Ph)2[1], Ph3 (DISCOVER [D]-1&2)[2,3], and Ph3b COSMOS[4] randomized controlled trials (RCTs).

Objectives: Assess GUS safety through 2 years (Y) in biologic (bio)-naïve and tumor necrosis factor inhibitor (TNFi)-experienced (exp) active PsA patients (pts) pooled across 4 RCTs (Week [W] 56: Ph2 and COSMOS; W60: D1; W112: D2).

Methods: Eligible pts in COSMOS had inadequate response to 1 or 2 prior TNFi; 9% of Ph2 pts and 30% of D1 pts had 1 or 2 prior TNFi; D2 pts were bio-naïve. Incidence rates of adverse events (AEs) are summarized among all treated pts for the placebo (PBO)-controlled (W0-24) and active treatment periods through 2Y (max duration of exposure 100W) according to actual treatment received, calculated as the number of events per 100 pt-Y of follow-up (PY), along with 95% confidence intervals (CI). Gastrointestinal (GI)-related serious AEs (SAEs) were identified using the Medical Dictionary for Regulatory Activities (MedDRA) system-organ class; major adverse cardiovascular events (MACE; predefined as MI, Stroke, or CV death) and opportunistic infections (OIs) were identified through medical review.

Results: Across the 4 RCTs, 1508 pts with active PsA received GUS 100 mg every 4 weeks (Q4W) or Q8W and were followed for a median of 1.2 Y, representing 2125 PY. In the overall population (N=1554), which includes PBO-treated pts that discontinued study agent prior to W24, 1138 pts were bio-naïve and 416 pts were TNFi-exp. Among all treated pts, the overall GUS safety profile was generally consistent with that of PBO through W24; rates remained low through 2Y of GUS (Table 1). The GUS safety profile was similar to that observed with PBO within the bio-naïve and TNFi-exp cohorts through W24. Incidence rates of AEs were generally consistent between cohorts in GUS-treated pts; whereas, TNFi-exp PBO-treated pts had more SAEs, study agent d/c due to AEs, and serious infections than bio-naïve PBO pts (Figure).

Conclusion: The favorable GUS safety profile demonstrated through W24 persisted through 2Y across bio-naïve and TNFi-exp pts.

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Table 1. Overall Treatment-emergent AEs

	PBO-controlled (W0-24)[a]				Through up to 2Y		
	PBO[b] (N=517)	GUS Q8W (N=664)	GUS Q4W (N=373)	Combined GUS (N=1037)	GUS Q8W (N=664)	GUS Q4W (N=373)	Combined GUS[c] (N=1508)
Total (median) PY	230 (0.5)	305 (0.5)	172 (0.5)	478 (0.5)	941 (1.1)	645 (2.1)	2125 (1.2)
Events/100 PY (95% CI)							
AEs	223	233	223	229	164	139	146
	(204, 243)	(216, 250)	(201, 246)	(216, 243)	(156, 172)	(130, 148)	(141, 151)
SAEs	8.7	4.9	5.2	5.0	6.4	4.7	5.7
	(5.3, 13)	(2.8, 8.1)	(2.4, 9.9)	(3.2, 7.5)	(4.9, 8.2)	(3.1, 6.6)	(4.7, 6.8)
AEs leading to study agent d/c	4.4	3.6	7.0	4.8	2.6	2.9	2.7
	(2.1, 8.0)	(1.8, 6.5)	(3.6, 12.2)	(3.1, 7.2)	(1.6, 3.8)	(1.8, 4.6)	(2.1, 3.5)
Infections	59	56	57	57	43	37	39
	(50, 70)	(48, 65)	(47, 70)	(50, 64)	(38, 47)	(33, 42)	(36, 42)
Serious Infections	2.2	0.33	1.7	0.84	1.7	0.77	1.5
	(0.71, 5.1)	(0.01, 1.8)	(0.36, 5.1)	(0.23, 2.1)	(0.97, 2.8)	(0.25, 1.8)	(1.0, 2.1)
Malignancy	0.44	0.98	0.00	0.63	0.42	0.00	0.28
	(0.01, 2.4)	(0.20, 2.9)	(0.00, 1.7)	(0.13, 1.8)	(0.12, 1.1)	(0.00, 0.46)	(0.10, 0.61)
MACE	0.44	0.33	0.58	0.42	0.21	0.46	0.24
	(0.01, 2.4)	(0.01, 1.8)	(0.01, 3.2)	(0.05, 1.5)	(0.03, 0.77)	(0.10, 1.4)	(0.08, 0.55)
GI-related SAEs	1.3	0.33	0.00	0.21	0.32	0.46	0.28
	(0.27, 3.8)	(0.01, 1.8)	(0.00, 1.7)	(0.01, 1.2)	(0.07, 0.93)	(0.10, 1.4)	(0.10, 0.61)
OIs	0.00	0.00	0.00	0.00	0.21	0.00	0.14
	(0.00, 1.3)	(0.00, 0.98)	(0.00, 1.7)	(0.00, 0.63)	(0.03, 0.77)	(0.00, 0.46)	(0.03, 0.41)

MedDRA Version 23.1. [a] Includes safety follow-up data through 2Y for pts who d/c study agent prior to W24 and did not receive any study agent at or after W24. [b] Includes data prior to GUS in PBO pts who switched from PBO to GUS. [c] Includes PBO to GUS cross-over at W24.

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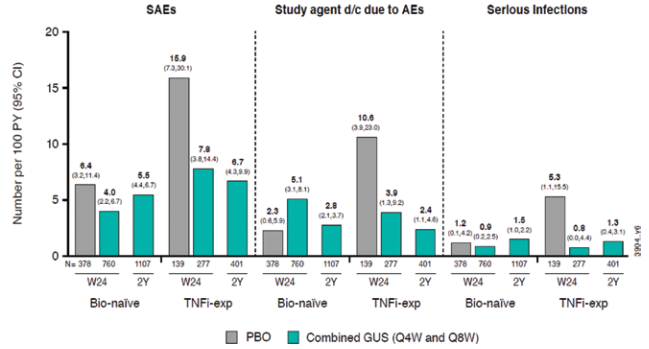
Figure. Summary of Select Treatment-emergent AEs Through 2Y: Bio-naïve vs. TNFi-exp at Baseline



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POS1016

RELATIONSHIPS BETWEEN DISEASE DURATION AND RADIOGRAPHIC PROGRESSION AMONG PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB IN FUTURE 5

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Background: For patients with psoriatic arthritis (PsA), delays in diagnosis and treatment can lead to permanent radiographic damage, even early in the course of disease.[1] In the phase 3 FUTURE 5 study (NCT02404350), treatment with secukinumab (SEC) was shown to inhibit progression of structural damage through Week 104 in patients with PsA.[2] However, the effect of disease duration on inhibition of radiographic progression by SEC has not been characterized.
Objectives: This post hoc analysis explored relationships between time since diagnosis (TSD) of ≤1 year vs >1 year and radiographic progression among patients with PsA receiving SEC over 2 years in FUTURE 5.
Methods: Patient data from FUTURE 5 were stratified by TSD ≤1 year vs >1 year and analyzed by treatment arm. Through Week 24, patients received SEC 300 or 150 mg with subcutaneous loading dose (LD), SEC 150 mg without LD, or placebo (PBO) (period 1). After Week 24, patients receiving PBO were switched to SEC 300 or 150 mg (period 2), and a protocol amendment allowed those with suboptimal clinical response to SEC 150 mg to escalate to SEC 300 mg after Week 52 per investigator judgment.[2] The proportion of patients with no radiographic progression, defined as change from baseline in van der Heijde total modified Sharp score ≤0.0, was analyzed at Weeks 24, 52, and 104. Mean total Sharp score was evaluated at baseline, and mean change from baseline was determined at Weeks 24, 52, and 104.
Results: Of 996 patients with PsA included here, 217 (21.8%) had a TSD ≤1 year and 779 (78.2%) had a TSD >1 year. At baseline, patients with TSD >1 year had greater radiographic damage than patients with TSD ≤1 year as determined by mean total Sharp score (Table 1). As early as Week 24, patients receiving SEC had less radiographic progression than those receiving PBO, regardless of TSD. From Week 24 to Week 104, radiographic progression remained low among all patients receiving SEC, with a trend of least progression among patients randomized to SEC 300 mg at baseline. Regardless of treatment, patients with TSD >1 year had numerically greater radiographic progression than those patients with TSD ≤1 year. Overall, the proportion of patients receiving SEC who did not have any radiographic progression was higher than that of placebo at Week 24 irrespective of TSD, with a trend towards a higher number of non-progressors among those treated with SEC 300 mg (Figure). Patients randomized to SEC 300 mg were the least likely to experience radiographic progression through 52 weeks.
Conclusion: SEC resulted in low rates of radiographic progression through 2 years of treatment among patients in FUTURE 5, regardless of time since PsA diagnosis.

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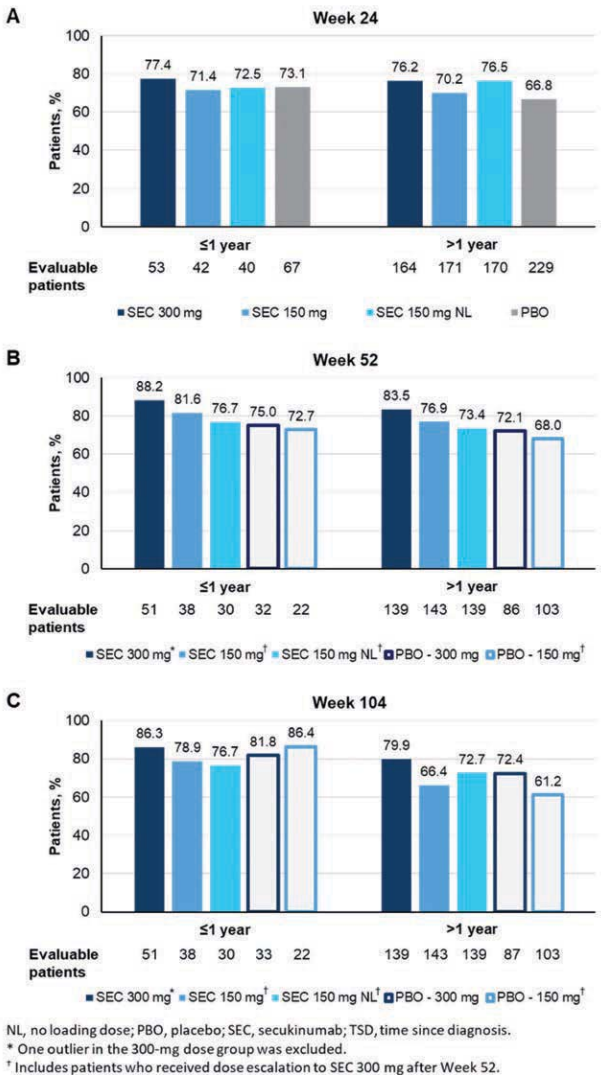
Table 1. Baseline Total Sharp Score and Change From Baseline at Weeks 24, 52, and 104 by TSD

Total Sharp score	TSD ≤1 year					TSD >1 year				
Period 1	**SEC 300 mg n = 54**	**SEC 150 mg n = 46**	**SEC 150 mg NL n = 43**	**PBO n = 74**		**SEC 300 mg n = 168**	**SEC 150 mg n = 174**	**SEC 150 mg NL n = 179**	**PBO n = 258**	
Baseline, mean (SD)	8.02 (20.77)	8.82 (12.06)	12.74 (33.67)	8.84 (20.42)		14.37 (24.17)	14.67 (28.01)	15.56 (37.52)	17.34 (41.21)	
Week 24 change from baseline, mean (SD)	0.05 (0.72)	−0.08 (1.40)	−0.61 (5.25)	0.76 (2.05)		0.09 (1.37)	0.23 (1.24)	0.03 (2.05)	0.42 (1.56)	
Period 2	**SEC 300 mg* n = 54**	**SEC 150 mg† n = 46**	**SEC 150 mg NL† n = 43**	**PBO – 300 mg n = 40**	**PBO – 150 mg† n = 30**	**SEC 300 mg* n = 168**	**SEC 150 mg† n = 174**	**SEC 150 mg NL† n = 179**	**PBO – 300 mg n = 113**	**PBO – 150 mg† n = 123**
Week 52 change from baseline, mean (SD)	0.05 (0.48)	−0.03 (1.22)	0.35 (2.25)	0.22 (0.70)	0.18 (0.75)	−0.07 (1.16)	0.26 (1.96)	0.26 (1.05)	0.16 (0.94)	0.40 (2.00)
Week 104 change from baseline, mean (SD)	0.06 (0.63)	0.11 (0.99)	0.20 (2.71)	0.11 (0.68)	−0.07 (0.50)	0.11 (2.00)	0.62 (2.94)	0.46 (2.08)	0.12 (0.90)	0.81 (2.66)

NL, no loading dose; PBO, placebo; SEC, secukinumab; TSD, time since diagnosis. * One outlier in the 300-mg dose group was excluded. † Includes patients who received dose escalation to SEC 300 mg after Week 52.

Figure. Proportion of Patients Without Radiographic Progression at **(A)** Week 24, **(B)** Week 52, and **(C)** Week 104 Grouped by TSD



NL, no loading dose; PBO, placebo; SEC, secukinumab; TSD, time since diagnosis.
* One outlier in the 300-mg dose group was excluded.
† Includes patients who received dose escalation to SEC 300 mg after Week 52.

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POS1017

GUSELKUMAB PROVIDES CONTINUED IMPROVEMENT IN KEY DOMAINS OF PSORIATIC ARTHRITIS THROUGH 2 YEARS

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Background: Recent guidelines from the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommend that psoriatic arthritis (PsA) therapy achieve lowest possible disease activity across 6 key domains and related conditions.[1] In the DISCOVER-1&2 trials, guselkumab (GUS) significantly improved signs and symptoms of PsA at Week (W) 24.
Objectives: Evaluate GUS efficacy through W100 of DISCOVER-2 by GRAPPA-recommended PsA domains (peripheral arthritis, skin, dactylitis, enthesitis, axial disease [nails not evaluated]) and related conditions of inflammatory bowel disease (IBD) and uveitis.
Methods: Enrolled adults had active PsA, were naïve to biologics/JAK inhibitors, and had ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL. Randomized (1:1:1) patients (pts) received GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then every 8 weeks (Q8W); or placebo (PBO) with crossover to GUS 100 mg Q4W at W24. Outcomes selected aligned with GRAPPA-recommended domains/conditions: overall disease activity (Psoriatic Arthritis Disease Activity Score [PASDAS], Minimal Disease Activity [MDA]), peripheral arthritis (changes

Table 1. Number (%) of GUS-randomized Pts (N=493) Achieving Therapeutic Endpoints Over Time (NRI)*

	Q4W					Q8W				
Week	8	16	24	52	100	8	16	24	52	100
MDA*	8 (3)	33 (14)	47 (19)	83 (34)	93 (38)	9 (4)	42 (17)	63 (25)	77 (31)	100 (40)
DAPSA ≤14';	43 (18)	61 (25)	88 (36)	125 (51)	151 (62)	43 (17)	79 (32)	97 (39)	130 (52)	147 (59)
≤4	5 (2)	12 (5)	21 (9)	39 (16)	52 (21)	3 (1)	15 (6)	23 (9)	46 (19)	60 (24)
cDAPSA ≤13'	41 (17)	58 (24)	89 (36)	125 (51)	150 (61)	44 (18)	75 (30)	95 (38)	131 (53)	147 (60)
≤3	5 (2)	13 (5)	29 (12)	44 (18)	59 (24)	4 (2)	19 (8)	25 (10)	53 (21)	65 (26)
PASDAS										
≤3.2	25 (10)	44 (18)	58 (24)	105 (43)	126 (51)	28 (11)	56 (23)	76 (31)	106 (43)	122 (49)
≤1.9	4 (2)	11 (4)	22 (9)	36 (15)	51 (21)	2 (1)	16 (6)	23 (9)	52 (21)	58 (23)
Skin										
PASI75†	-	137 (74)	146 (79)	160 (87)	152 (83)	-	129 (73)	139 (79)	151 (86)	144 (82)
PASI90†	-	100 (54)	114 (62)	142 (77)	136 (74)	-	97 (55)	121 (69)	131 (74)	123 (70)
PASI100†	-	62 (34)	83 (45)	106 (58)	109 (59)	-	48 (27)	80 (46)	93 (53)	94 (53)
IGA 0/1 Response‡	-	122 (66)	127 (69)	147 (80)	140 (76)	-	110 (62)	124 (70)	131 (74)	126 (72)
Enthesitis resolution§	45 (27)	66 (40)	71 (43)	93 (56)	102 (61)	50 (32)	75 (48)	87 (55)	97 (62)	110 (70)
Dactylitis resolution§	39 (32)	64 (53)	80 (66)	90 (74)	87 (72)	34 (31)	51 (46)	66 (60)	86 (77)	92 (83)

*Repeated Measures Generalized Linear Mixed Effects Models; excludes pts who achieved endpoint at BL. †Pts with BL IGA≥2 and BSA≥3%. ‡IGA skin response = score of 0 or 1 and ≥2grade improvement from BL. §Among pts with domain at BL.

in Disease Activity Index for Psoriatic Arthritis [DAPSA] and clinical DAPSA [cDAPSA]), skin (Psoriasis Area and Severity Index [PASI], Investigator's Global Assessment of psoriasis [IGA]), dactylitis (Dactylitis Severity Score [DSS]), enthesitis (Leeds Enthesitis Index [LEI]), axial disease (spinal pain) and IBD/uveitis (adverse events [AEs]). Among 493 GUS-randomized pts, change from baseline (BL) through W100 in continuous outcomes were analyzed by Repeated Measures Generalized Linear Mixed Effects Models adjusting for respective BL score and GUS regimen. Achievement of therapeutic endpoints was summarized by descriptive statistics using nonresponder imputation (NRI) for missing categorical data.

Results: ~90% of GUS-randomized pts completed treatment at W100. For continuous outcomes, improvements over time in key PsA domains extended through W100 of GUS (Figure 1). Therapeutic endpoint response rates also increased incrementally through W100 (Table 1). Mean improvements and response rates were consistent across key domains with no significant difference between GUS regimens. For related conditions, 1 GUS pt had IBD and 4 had uveitis at BL and none had AE of exacerbation through W100. No pt developed IBD through W100 (vs 1 PBO pt through W24); 1 GUS pt had AE of iridocyclitis through W100 (vs 1 PBO pt through W24).

Conclusion: In DISCOVER-2 bio-naïve PsA pts, both GUS regimens provided continued improvements in key GRAPPA-recommended domains of PsA through up to 2 years of treatment.

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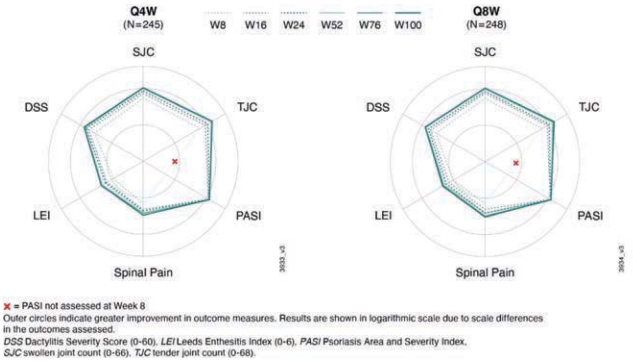
Figure. Change/Improvement (Δ) from Baseline Over Time in Continuous Outcomes Assessing Key PsA Domains Among GUS-Randomized Pts



× = PASI not assessed at Week 8
Outer circles indicate greater improvement in outcome measures. Results are shown in logarithmic scale due to scale differences in the outcomes assessed.
DSS Dactylitis Severity Score (0-60), *LEI* Leeds Enthesitis Index (0-6), *PASI* Psoriasis Area and Severity Index, *SJC* swollen joint count (0-66), *TJC* tender joint count (0-68).

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POS1018

DRUG SURVIVAL AND TREATMENT RESPONSE RATES IN PSORIATIC ARTHRITIS PATIENTS SWITCHING TO FIRST- OR SECOND-LINE IL-17 INHIBITOR TREATMENT: A DANISH POPULATION-BASED COHORT STUDY

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Background: Psoriatic arthritis (PsA) is a seronegative spondyloarthropathy associated with psoriasis [1]. It is defined as a multifaceted chronic inflammatory disease with chronic peripheral and/or axial arthritis, enthesopathy and dactylitis. PsA patients also experience fatigue, decreased physical functions and sleep disturbances, which may result in impaired social activity and decreased work productivity [2, 3]. All of these disease associated symptoms can cause substantial functional and mental impairment and thereby result in decreased quality of life [4-5]. Patient impacting factors are important when trying to further understand the disease and when choosing a treatment option to properly manage the symptoms of PsA [2].

Objectives: The objective of this study was to assess the effectiveness of switching to a first- or second-line IL-17 inhibitor treatment in patients with PsA from 2014 to 2021, using data from the Danish Rheumatology registry (DANBIO) by investigating drug survival and treatment response rates.

Methods: PsA patients recorded in DANBIO who switched to a first- or second-line IL-17 inhibitor treatment from a previous biologic disease-modifying antirheumatic drugs (bDMARD) between 2014 and 2021 were included in this study. Baseline characteristics were analyzed in subgroups: first-line IL-17 inhibitor treatment and second-line IL-17 inhibitor treatment and presented as median and interquartile ranges or number and percentage. Visual analog scale (VAS) fatigue 50% improvement and VAS pain 50% improvement, Disease Activity Scores-28 C-reactive protein (DAS-28-CRP) remission and ΔDAS28 scores at 6- and 12-months follow-up was reported. Drug survival of first- or second-line IL-17 inhibitor treatment was reported as a Kaplan Meier plot.

Results: 583 patients were identified and included in the study. Baseline characteristics (Table 1) showed that the age, percentage of females, CRP, HAQ, VAS patient pain, VAS global and DAS28CRP in both first- and second-line IL-17 inhibitor treatment was comparable. First- and second-line IL-17 inhibitor treatment had almost identical drug survival (Figure 1).

Table 1.

	First-line IL-17 inhibitor n= 434	Second-line IL-17 inhibitor n= 97
Age, years	51.0 (49.6-52.3)	51.9 (46.4-54.7)
Female, % (n)	59.0 (256)	53.6 (52)
Disease duration, years	6.8 (6.1-7.8)	8.2 (6.5-12.6)
CRP, mg/dl	4.0 (4.0-5.2)	3.0 (2.9-5.3)
HAQ	1.1 (1.1-1.3)	1.0 (0.9-1.3)
VAS pain, 100 mm	68 (65-72)	73 (66-76)
VAS global, 100 mm	75 (73-78)	80 (75-88)
DAS28-CRP	4.0 (3.8-4.1)	4.2 (3.7-4.6)
Previous bDMARD	2.0 (1.0-3.0)	4.0 (2.0-5.5)

CRP: C-reactive protein, HAQ: Health Assessment Questionnaire, VAS: Visual analog scale, DAS28: 28-joint Disease Activity Score, DMARD: disease-modifying antirheumatic drug.

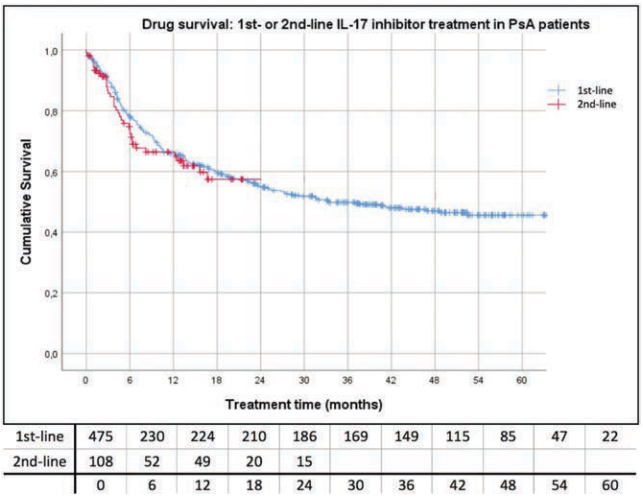

Figure 1.

Conclusion: PsA patients switching to a first- or second-line IL-17 inhibitor showed comparable baseline characteristics and an almost identical drug

survival. Thus, treatment failure of a first-line IL-17 inhibitor treatment, should not block for a second-line IL-17 inhibitor treatment.

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POS1019 REAL-WORLD EVALUATION OF TREATMENT PATTERNS AND PERSISTENCE OF TOFACITINIB IN TREATMENT OF PSORIATIC ARTHRITIS IN AUSTRALIA: AN ANALYSIS OF THE OPAL DATASET.

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Background: Tofacitinib (TOF), a potent selective inhibitor of Janus kinase (JAK), is an approved treatment of psoriatic arthritis (PsA). In Australia, patients with active PsA despite six months of therapy with a pre-specified combination of csDMARDs are eligible to receive subsidised b/tsDMARDs. The clinician can prescribe the b/tsDMARD they deem to be the most clinically appropriate for the patient. Limited data exist to describe the real-world treatment patterns, characteristics and clinical outcomes of patients with PsA who receive TOF in the real-world setting.
Objectives: To describe real-world treatment patterns and treatment persistence among patients with PsA treated with TOF in the Australian post-approval setting using the OPAL dataset.
Methods: The OPAL dataset is a collection of deidentified clinical data derived from the electronic medical records of 112 rheumatologists at 43 sites around Australia. Adult patients with a diagnosis of PsA who received at least one prescription of TOF, a tumour necrosis factor inhibitor (TNFi) or an interleukin 17 inhibitor (IL-17Ai) between May 2019 and Sept 2020 were eligible, with data up to Sept 2021 included in the analysis. Results were summarised descriptively. Treatment persistence was summarised using Kaplan-Meier methods.
Results: Of 16,692 patients with PsA identified in the OPAL dataset, 1,486 (TOF n=406, IL-17Ai n=416, and TNFi n=664) were eligible for inclusion in this study. At the time of treatment initiation, the mean (SD) age of TOF, IL-17Ai and TNFi treated patients was 55.56 (12.68), 52.65 (12.72) and 50.32 (14.57) years, respectively. 19.2% of patients receiving TOF were first line compared with 41.8% of IL-17Ai and 62.8% of TNFi treated patients. The mean (SD) time from symptom onset to treatment initiation was longest for patients receiving TOF in first line (153.29 (127.50) months) compared to first line IL-17Ai (116.83 (113.97) months) and TNFi treated patients (92.37 (89.01) months). Overall, 34.2% of TOF, 32.9% of IL-17Ai and 26.4% of TNFi treated patients initiated therapy without concomitant cDMARDs being recorded.
Overall median persistence was 16.54 months (95% CI 13.84, 19.53) for TOF treated patients, 17.65 months (95% CI, 15.75, 19.56) for IL-17Ai treated patients and 17.16 months (95% CI 14.86, 20.48) for TNFi treated patients. As expected, persistence was generally longer in patients treated as first line (Figure 1) with patients receiving TOF observed to have slightly higher persistence in the first 15 months of treatment.

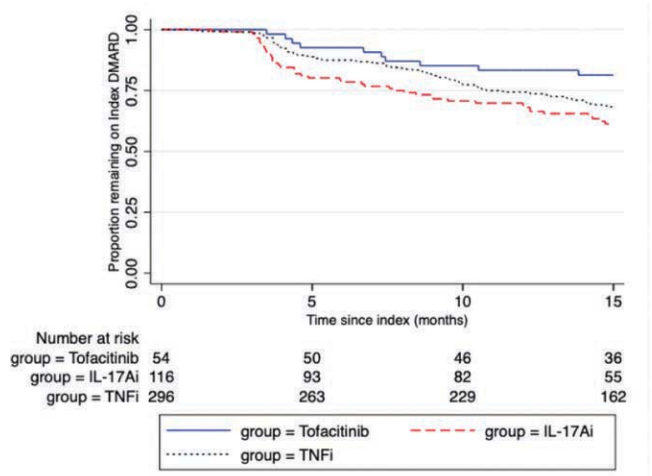

Figure 1. Treatment persistence of patients receiving TOF, IL-17Ai and TNFi as first line therapy. Plot curtailed at 15 months as relatively few patients have information past this point. Where no stop date was recorded, censoring occurs at last recorded visit

Conclusion: In this analysis of a large Australian real-world dataset, TOF was more commonly utilised as a later line therapy for patients with PsA. Patients receiving TOF were observed to have slightly higher persistence within the first 15 months of starting first line therapy in this preliminary analysis.
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Disclosure of Interests: Geoff Littlejohn Consultant of: Abbvie, Janssen, Bristol Myers Squibb, Gilead, Eli Lilly, and MSD, Jo Leadbetter: None declared, Belinda Butcher: None declared, Marie Feletar: None declared, Catherine OSullivan: None declared, Tegan Smith: None declared, David Witcombe Employee of: Pfizer Australia, Ho Yin Employee of: Pfizer Australia, Peter Youssef Speakers bureau: AbbVie, Novartis, Janssen and Eli Lilly
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POS1020 BIOLOGICAL DMARD TREATMENT IN PSORIATIC ARTHRITIS IS LIKEWISE EFFECTIVE IN PATIENTS WITH HIGH AND WITH LOW JOINT COUNTS – RESULTS FROM THE SWISS CLINICAL QUALITY MANAGEMENT (SCQM) FOR RHEUMATIC DISEASES COHORT STUDY

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Background: Biological and targeted synthetic (b/tsDMARDs) may be used in absent remission in psoriatic arthritis (PsA) independent of a defined number of affected joints. However, minimum three swollen and three tender joints are a common inclusion criterion in trials of b/tsDMARDs, and less is currently known about their effectiveness in PsA patients with low joint counts.
Objectives: To characterize PsA patients with low or high joint counts (LJC/HJC), analyze their drug treatment in routine care, and estimate the effectiveness of a first bDMARD in LJC and HJC patients.
Methods: We defined patients with less than three tender *or* swollen joints as LJC, and those with at least three tender *and* swollen joints as HJC patients. Patients were twice categorized according to their joint counts at registration in

the registry, and at start of a first bDMARD (Table 1). We compared HJC and LJC at registration for current and future DMARD therapies, and at start of a first bDMARD for treatment effectiveness, using drug retention in univariate and in multivariable Cox regression models.

Table 1. Selected characteristics of bDMARD naïve PsA patients with a low and with a high number of affected joints at start of their first bDMARD.

Variable	Levels	HJC	% high	LJC	% low	N all	p
bDMARD type	TNFi	176	92.6	175	88.8	351	=0.22
	OMA	14	7.4	22	11.2	36	
csDMARD cotherapy	yes	117	61.6	90	45.7	207	<0.01
csDMARD history	naive	23	12.1	55	27.9	78	<0.01
tsDMARD_history	naive	175	92.1	177	89.8	352	=0.47
Dactylitis history	yes	115	60.5	60	30.5	175	<0.01
HLA B27	yes	12	11.5	28	23.3	40	=0.02
MDA	Yes	0	0.0	17	8.6	17	<0.01
DAPSA remission		0	0.0	12	6.1	12	<0.01
Dactylitis	Yes	93	49.0	33	16.8	126	<0.01
Enthesitis	Yes	63	61.8	55	47.0	118	=0.03
BMI	mean (SD)	27.65	(5.05)	26.58	(4.72)	333	=0.046
MASES	mean (SD)	2.86	(3.93)	1.61	(2.47)	219	=0.005
HAQ-DI	mean (SD)	0.77	(0.58)	0.60	(0.50)	292	=0.010
EQ-5d	mean (SD)	62.22	(20.63)	67.22	(16.27)	294	=0.022
Patient global	mean (SD)	5.93	(2.41)	4.83	(2.58)	288	<0.001
Tender joint count	mean (SD)	10.15	(8.93)	4.92	(8.17)	387	<0.001
Swollen joint count	mean (SD)	7.16	(4.91)	1.37	(2.15)	387	<0.001
Patient pain	mean (SD)	5.96	(2.47)	4.85	(2.51)	290	<0.001

Abbreviations: DAPSA: Disease activity of PsA. BMI: Body mass index, EQ-5d: European Quality of Life Measurement in five dimensions. HAQ-DI. Health assessment questionnaire disability index. HJC: High joint count, LJC: Low joint count, MASES: Maastricht ankylosing spondylitis enthesitis score, MDA: minimal disease activity, OMA: other mode of action than TNFi.

Results: We followed DMARD therapies for median (IQR) 3.2 (1.6, 5.0) in 675 LJC patients and for 3.4 (1.8, 5.2) years in 334 HJC patients. LJC patients at registration as well as at start of a first bDMARD were less often female, with less severe skin, enthesitis, dactylitis and nail involvement. Furthermore, LJC patients had lower disability indices and a more favorable health related quality of life. When defined at registration, LJC were as frequent as HJC patients on csDMARDs, but less often on bDMARDs. During their follow-up, a csDMARD, a first and a second bDMARD were less often and on average later commenced in LJC than in HJC patients. However, when defined at start of a first bDMARD, drug retention did not significantly differ between LJC and HJC patients (Figure 1).

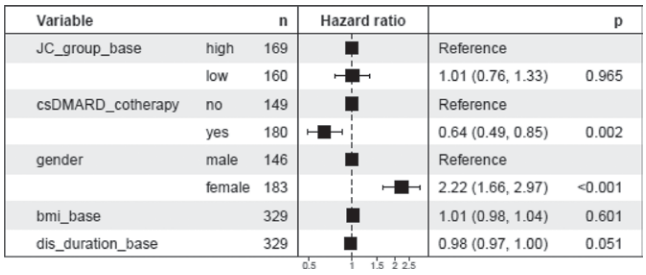

Figure 1. Multivariable adjusted Cox regression model for discontinuation of a first bDMARD. Abbreviation: JC_group_base: Low and high joint count groups at baseline.

Conclusion: The majority of Swiss PsA patients is in LJC status, which also means a better status in most PsA domains than in HJC patients. LJC status was associated with established bDMARD therapy and with slower treatment escalation. However, bDMARDs were likewise effective in bDMARD-naïve LJC and HJC patients, and should not withhold only for reasons of a low joint count.

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POS1021

THE EFFECT OF CANNABIDIOL ON QUANTITATIVE SENSORY TESTING PARAMETERS IN PATIENTS WITH HAND OSTEOARTHRITIS AND PSORIATIC ARTHRITIS: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Background: Cannabidiol (CBD) has been proposed as an analgesic/anti-inflammatory treatment modality for joint pain. This study is based on a randomised, placebo controlled, double blind study (NORDCAN), investigating the effect of CBD in patients with painful hand osteoarthritis or psoriatic arthritis [1].

Objectives: The aim of the present study was to investigate the effect of CBD on quantitative sensory testing (QST) parameters.

Methods: The present randomised, placebo controlled, double blind study included 128 patients with hand osteoarthritis or psoriatic arthritis with chronic pain of moderate intensity. The trial compared 12 weeks of 20-30 mg CBD treatment with placebo. The QST parameters were assessed at baseline and after treatment. Pressure pain thresholds was measured at the most painful finger joint (local site) and the shin of the right leg (distal non-painful site). Temporal summation of pain and conditioned pain modulation were assessed using computer-controlled cuff algometry with the tourniquets on lower leg at the level of the upper portion of the gastrocnemius.

Results: Baseline characteristics (demographics and pain) for the CBD treated group and placebo group were comparable. No significant differences were observed in QST variables between baseline and end of treatment when comparing CBD and placebo.

Conclusion: No differences in modulation in QST parameters were demonstrated in patients in treatment with 20-30 mg CBD compared to placebo. Further studies of patients with rheumatic diseases treated with different dosage of CBD are needed to clarify the effect of CBD on pain in this patient group.

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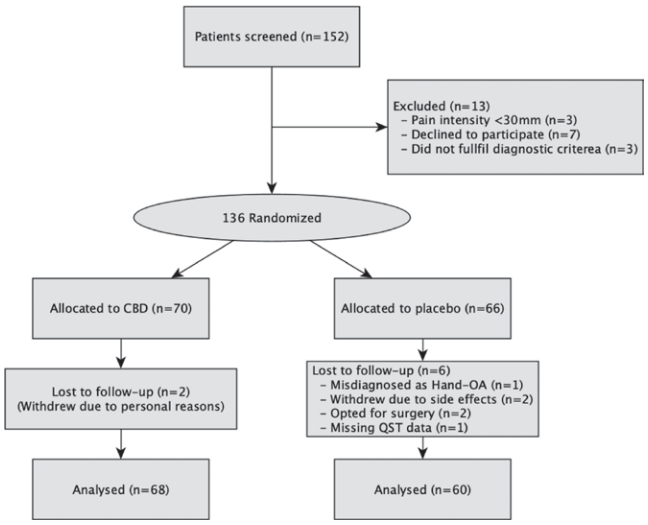

Figure 1. Flow-diagram of participant in the NORDCAN study

Table 1. Difference in QST outcomes after 12 weeks of treatment with CBD or placebo.

	Placebo group			CBD group		
	Difference	**95% CI**	**p**	**Difference**	**95% CI**	**p**
PPT Joint, kPa*	18.62	-19 to 56.76	0.32	42.56	1.95 to 86.31	0.03
PPT Shin, kPa*	35.02	-8.72 to 78.76	0.11	5.88	-30.12 to 41.89	0.75
CPM, kPa	3.23	-2.11 to 8.58	0.17	3.92	-1.75 to 9.59	0.17
TSP	0.18	-0.58 to 0.94	0.64	0.12	-0.41 to 0.65	0.63

* Assessed using handheld algometer. Abbreviations: CPM, Conditioned pain modulation; PPT, Pressure pain threshold; TSP, Temporal summation of pain

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POS1022

RELATIONSHIPS BETWEEN INHIBITION OF RADIOGRAPHIC PROGRESSION AND ACHIEVEMENT OF LOW DISEASE ACTIVITY OR REMISSION AND THEIR CORE COMPONENTS IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB IN FUTURE 5 DURING THE FIRST 24 WEEKS

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Background: Patients with active psoriatic arthritis (PsA) experience inflammation that may result in structural damage and disability. In the phase 3 FUTURE 5 study, treatment with secukinumab (SEC) inhibited radiographic progression and led to sustained remission and low disease activity (LDA) through Week 104.[1,2]
Objectives: This post hoc analysis of FUTURE 5 explored relationships between radiographic progression status and achievement of LDA or remission in patients treated with SEC.
Methods: Patients were randomized 2:2:2:3 to receive SEC 300 mg with loading dose (LD), 150 mg LD, SEC 150 mg without LD, or placebo (PBO) at Baseline, Weeks 1, 2, 3, 4, and every 4 weeks thereafter until Week 24. In this post hoc analysis, patients were grouped by radiographic progression status at Week 24 (non-radiographic progressors: change from baseline in modified total Sharp score [mTSS] ≤0.0; radiographic progressors: change from baseline in mTSS >0.0). Efficacy (achievement of Minimal Disease Activity [MDA] or Very Low Disease Activity [VLDA] and their individual components, and Disease Activity Index for Psoriatic Arthritis [DAPSA] LDA or remission) was assessed at Week 24.
Results: Of 933 patients with available data, 675 (72.3%) were classified as non-radiographic progressors and 258 (27.7%) were radiographic progressors at Week 24. Non-progressors at Week 24 were more likely than progressors to achieve DAPSA LDA and remission at Week 24 across all treatment arms (Figure 1A). In addition, non-progressors were more likely to achieve MDA and VLDA at Week 24 than progressors across all treatment arms (Figure 1B). Similar trends were observed for all of the individual MDA/VLDA criteria at Week 24 among patients treated with SEC 300 mg or SEC 150 mg LD (Table 1). Notably, non-progressors were more likely to achieve improvements in physical function, pain, and patient global assessment of disease activity than progressors across all treatment arms.
Conclusion: Patients who did not have radiographic progression over 6 months of SEC treatment were more likely to achieve LDA or remission and improvement in physical function at Week 24. Additional analyses will explore relationships between radiographic progression and additional clinical and patient-reported outcomes over longer time periods.
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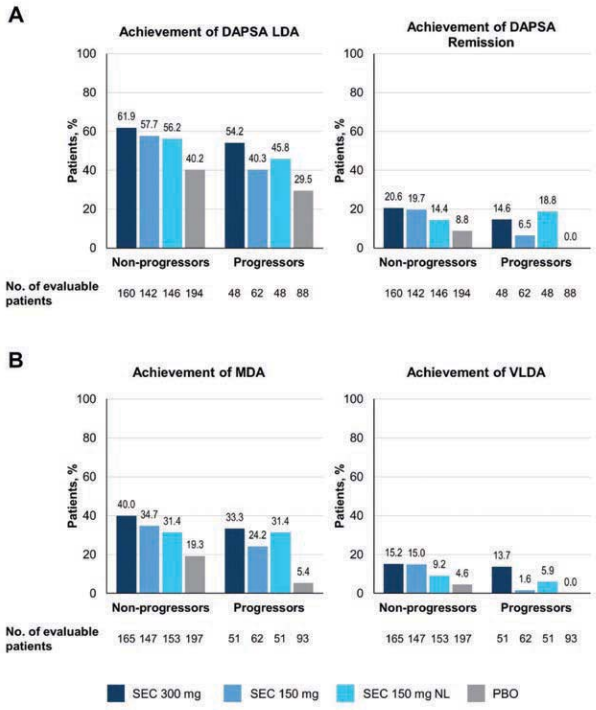
Figure 1. Proportion of Patients Who Achieved **(A)** DAPSA LDA and DAPSA Remission* and **(B)** MDA and VLDA† at Week 24 Grouped by Radiographic Progression Status at Week 24



DAPSA, Disease Activity Index for Psoriatic Arthritis; LDA, low disease activity; MDA, Minimal Disease Activity; NL, no loading dose; PBO, placebo; SEC, secukinumab; VAS, visual analog scale; VLDA, Very Low Disease Activity.
* DAPSA LDA defined as DAPSA ≤14; DAPSA remission defined as DAPSA ≤4.
† MDA is defined as achievement of 5 of the following 7 criteria: tender joint count ≤1; swollen joint count ≤1; Psoriasis Area and Severity Index ≤1 or body surface area ≤3%; patient pain VAS ≤15; patient global disease activity VAS ≤20; Health Assessment Questionnaire Disability Index ≤0.5; tender entheseal points ≤1. VLDA is defined as achievement of all 7 criteria.

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Table 1. Proportion of Patients Achieving MDA/VLDA Components at Week 24 Grouped by Radiographic Progression Status at Week 24

	Week 24 non-progressors				Week 24 progressors			
Outcome, n/N (%)	SEC 300 mg n = 166	SEC 150 mg n = 150	SEC 150 mg NL n = 159	PBO n = 200	SEC 300 mg n = 51	SEC 150 mg n = 63	SEC 150 mg NL n = 51	PBO n = 93
TJC78 ≤1	52/161 (32.3)	46/146 (31.5)	37/150 (24.7)	38/196 (19.4)	15/50 (30.0)	13/62 (21.0)	13/49 (26.5)	11/90 (12.2)
SJC76 ≤1	105/160 (65.6)	85/146 (58.2)	83/150 (55.3)	88/196 (44.9)	32/50 (64.0)	28/62 (45.2)	20/49 (40.8)	30/90 (33.3)
PASI ≤1 or BSA ≤3%	99/128 (77.3)	90/128 (70.3)	69/109 (63.3)	64/153 (41.8)	29/38 (76.3)	27/47 (57.4)	28/40 (70.0)	26/70 (37.1)
Patient pain VAS ≤15	57/144 (39.6)	50/133 (37.6)	50/141 (35.5)	33/179 (18.4)	14/42 (33.3)	15/60 (25.0)	13/43 (30.2)	7/82 (8.5)
PtGA VAS ≤20	63/145 (43.4)	47/125 (37.6)	50/135 (37.0)	39/173 (22.5)	13/41 (31.7)	14/61 (23.0)	13/41 (31.7)	7/81 (8.6)
HAQ-DI ≤0.5	72/135 (53.3)	55/118 (46.6)	54/122 (44.3)	47/158 (29.7)	13/39 (33.3)	18/58 (31.0)	17/39 (43.6)	19/77 (24.7)
Tender entheseal points ≤1	70/87 (80.5)	44/63 (69.8)	42/76 (55.3)	45/88 (51.1)	13/18 (72.2)	17/31 (54.8)	11/19 (57.9)	23/38 (60.5)

BSA, body surface area; HAQ-DI, Health Assessment Questionnaire Disability Index; MDA, Minimal Disease Activity; NL, no loading dose; PASI, Psoriasis Area and Severity Index; PBO, placebo; PtGA, patient global assessment of disease activity; SEC, secukinumab; SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale; VLDA, Very Low Disease Activity.

POS1023

LONG-TERM SAFETY OF RISANKIZUMAB IN PATIENTS WITH PSORIATIC DISEASE: FINDINGS FROM INTEGRATED ANALYSES OF 17 CLINICAL TRIALS IN PSORIASIS AND 4 IN PSORIATIC ARTHRITIS

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Background: Risankizumab, an interleukin-23 inhibitor, was efficacious and well tolerated in phase 2 and 3 clinical studies in patients with psoriatic disease.
Objectives: To report long-term risankizumab safety in patients with psoriatic disease.
Methods: Risankizumab safety data to March 25, 2021 were pooled from 17 phase 1–3 clinical trials in plaque psoriasis (PsO) and 4 phase 2/3 trials in psoriatic arthritis (PsA). Adverse events (AEs) of safety interest were reported for patients receiving ≥1 dose risankizumab.
Results: Among 3197 patients with PsO (9982.6 patient years' [PY] exposure; median (range) treatment duration, 3.7 years [1 day–6.9 years]) and 1542 patients with PsA (1594.9 PY; 1.0 year [84 days–2.0 years]), rates of treatment-emergent AEs (158.3 and 160.8 events (E)/100PY), serious AEs (7.6 and 8.4 E/100PY) and AEs leading to discontinuation (1.9 and 2.3 E/100PY) were similar. Nasopharyngitis (PsO 14.5 E/100PY, PsA 7.9 E/100PY) and upper respiratory infection (PsO 7.8 E/100PY, PsA 5.6 E/100PY) were the most common infections; sepsis and pneumonia for PsO (0.1 E/100PY each) and COVID-19 for PsA (0.4 E/100PY) were the most common serious infections. Rates of opportunistic fungal infections were <0.1 and 0.1 E/100PY in PsO/PsA patients. Rates of non-melanoma skin cancer (NMSC) were 0.7 and 0.4 E/100PY, and malignant tumors excluding NMSC were 0.6 and 0.3 E/100PY in PsO/PsA patients. Rates of major adverse cardiovascular events were 0.5 and 0.4 E/100PY in PsO/PsA patients.
Conclusion: Rates of AEs of safety interest remained low in this largest and longest safety reporting for risankizumab to date, supporting the safety of risankizumab for the long-term treatment of patients with psoriatic disease.
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POS1024

EFFICACY AND SAFETY OF RISANKIZUMAB (RZB) FOR ACTIVE PSORIATIC ARTHRITIS (PSA): 52-WEEK RESULTS FROM KEEPSAKE 1

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Background: RZB, a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits the p19 subunit of the human cytokine IL-23, is being investigated as a treatment for PsA.
Objectives: To compare efficacy and safety of RZB vs. placebo (PBO) in patients with PsA who had an inadequate response or intolerance to conventional synthetic disease modifying antirheumatic drug (csDMARD-IR).
Methods: KEEPsAKE 1 (NCT03675308) is an ongoing, phase 3 study that includes a screening period; a 24-week double-blinded, placebo-controlled, parallel-group period (period 1); and an open-label extension period (period 2). Eligible patients aged ≥18 years with active PsA (symptom onset ≥6 months prior to screening, meeting the Classification Criteria for PsA [CASPAR], and ≥5 swollen and ≥5 tender joints) and who had an inadequate response or intolerance to ≥1 csDMARD-IR, were randomized 1:1 to receive RZB 150 mg or placebo (PBO) at weeks 0, 4, and 16. The primary endpoint was the proportion of patients achieving ≥20% improvement in American College of Rheumatology (ACR20) response at week 24. Period 2 started at week 24, and patients were switched to receive open-label RZB 150 mg every 12 weeks through week 208. Mixed-effect model repeated measures and nonresponder imputation methods were used to assess continuous and binary variables, respectively. Efficacy and safety were analyzed in all patients who received ≥1 dose of study drug through week 52. Treatment-emergent adverse events (TEAE) were summarized using exposure-adjusted event rates (EAERs, events/100 patient-years [PY]).
Results: At week 24, a greater proportion of RZB-treated (N=483) vs PBO-treated (N=481) patients achieved ACR20 (55.3% and 32.8%, respectively). At week 52, 70% of patients who were randomized to receive RZB and 63% of patients who were randomized to receive PBO and switch to RZB at week 24 achieved ACR20. In patients with ≥3% of body surface area affected at baseline, 52.7% of RZB-treated patients (N=273) and 9.9% of PBO-treated patients (N=272) achieved ≥90% improvement in Psoriasis Area and Severity Index (PASI 90) at week 24; 67.8% who were randomized to receive RZB and 59.9% who were randomized to receive PBO and switch to RZB at week 24 achieved PASI 90 at week 52. Similar results were observed for other efficacy measures. RZB was well tolerated through 52 weeks of treatment. EAERs of adverse events were stable between weeks 24 and 52. At the week 52 data cut-off (19 April 2021), the total EAER of any TEAE in patients receiving RZB was 143.1/100 PY.
Conclusion: Continuous RZB treatment provided durable efficacy and a consistent safety profile through 52 weeks of treatment in patients with active PsA who were csDMARD-IR.
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POS1025 COMPARISON OF COMPOSITE INDICES FOR DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH UPADACITINIB: A POST-HOC ANALYSIS FROM SELECT-PSA 1

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Background: Achieving low disease activity (LDA) or remission is a main treatment target in PsA. Composite indices used to assess disease activity include Disease Activity index for PsA (DAPSA) and PsA Disease Activity Score (PASDAS), which both have cut points for the states of remission and LDA. In addition, LDA and remission can be assessed by the pure state instrument Minimal Disease Activity (MDA)/Very Low Disease Activity (VLDA).

Objectives: These analyses aim to identify overlap and differences between these composite indices in PsA patients treated with upadacitinib (UPA), a Janus kinase inhibitor, or adalimumab (ADA) in the phase 3 SELECT-PsA 1 trial.

Methods: In SELECT-PsA 1 (phase 3, randomized controlled trial, with long-term extension up to 5 years), patients with moderate to severely active PsA with prior inadequate response or intolerance to ≥1 non-biologic DMARD were randomized to oral UPA at doses of 15 mg or 30 mg (once daily), subcutaneous ADA 40 mg (every other week), or placebo.[1] LDA was assessed using MDA (threshold: 5/7 criteria), DAPSA (≤14), PASDAS (≤3.2), and Patient Global Assessment of Disease Activity (PtGA; ≤3).[2,3] These post-hoc descriptive analyses include 1-year (cut off: week 56) *as observed* data from UPA 15 mg and ADA.

Results: In total, 858 patients (UPA 15 mg: n=429; ADA: n=429) were included in these analyses. Patients receiving UPA and ADA were on average 52 years of age, 54% were female, with an average disease duration of approximately 6 years.[1] With both UPA and ADA, there was a high degree of overlap in the proportion of patients achieving LDA thresholds in MDA, DAPSA, and PASDAS (Figure 1), with reported PtGA improvements showing a similar trend. Defining LDA according to MDA or respective cut points for DAPSA, PASDAS, or PtGA, the proportion of "non-responders" (ie, patients who did not reach such states) is shown in Figure 2. Of the individual components included in these indices, fewer patients reported low levels of SF-36 Physical Component Summary (SF36-PCS), Patient Assessment of Pain Numeric Rating Scale (Pain NRS), and Health Assessment Questionnaire - Disability Index (HAQ-DI) scores, as well as Tender Joint Count 68 (TJC68), with similar responses observed across all indices.

Conclusion: In this post-hoc analysis from the SELECT-PsA 1 trial, there was a high degree of overlap between patients in LDA across the composite indices, including MDA, DAPSA, and PASDAS, irrespective of treatment with UPA 15 mg or ADA and despite variability in inclusion of certain components in some indices but not others. Across all indices, fewer patients reported low levels of SF36-PCS, Pain NRS, and HAQ-DI scores, and TJC68. These data show that improvements in (subjective) "patient-driven" components were the most challenging to achieve. These data indicate a similar pattern of residual disease activity, or influence by residual damage or external factors, regardless of composite endpoint utilized.

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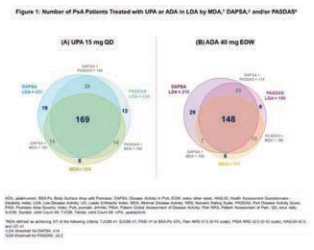

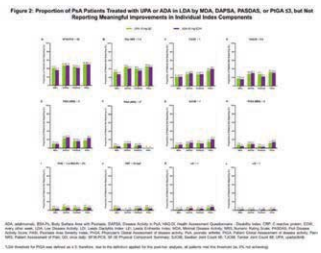

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POS1026 PREDICTORS FOR ACHIEVEMENT OF LOW DISEASE ACTIVITY AT WEEK 56 IN PATIENTS WITH PSORIATIC ARTHRITIS WHO RECEIVED UPADACITINIB 15 MG ONCE DAILY: POOLED ANALYSIS OF TWO PHASE 3 STUDIES

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Background: Upadacitinib (UPA) 15 mg once daily (QD) has demonstrated efficacy and safety in patients with psoriatic arthritis (PsA) for up to 56 weeks in the Phase 3 SELECT-PsA 1 and 2 trials.[1,2]

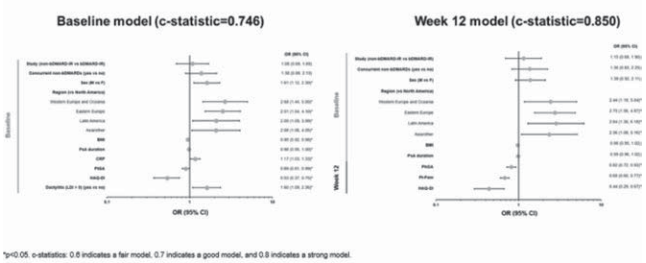
Objectives: This post hoc analysis of these studies explored the association of baseline characteristics and short-term responses with achievement of minimal disease activity (MDA) and Disease Activity Index for Psoriatic Arthritis (DAPSA) low disease activity (LDA).

Methods: Data were pooled from patients with prior inadequate response or intolerance to ≥1 non-biologic (b) DMARDs (SELECT-PsA 1) or ≥1 bDMARDs (SELECT-PsA 2) originally randomized to UPA 15 mg QD. Logistic regression models were used to assess the association between baseline characteristics and short-term (Week 12) responses with achieving MDA or DAPSA LDA at 56 weeks, sustained MDA (MDA at Weeks 36 and 56), or sustained DAPSA LDA (DAPSA LDA at Weeks 36, 44, and 56). Each predictor was evaluated separately in an initial model that included effects for study and concurrent non-bDMARD use. Odds ratios and concordance (c-)statistics were used to determine the predictive accuracy. Statistically significant predictors were then evaluated simultaneously using stepwise logistic regression with the Akaike Information Criterion for model-building.

Results: Of 640 patients included in the analysis, 40% and 47% achieved MDA and DAPSA LDA, respectively, at 56 weeks. Evaluated separately, younger age, sex (male), geographic region, lower weight, lower body mass index, the presence of dactylitis or enthesitis, and lower scores of Patient's Assessment of Pain (Pt-Pain), Patient's Global Assessment (PtGA), tender joint count in 68 joints, and Health Assessment Questionnaire-Disability Index (HAQ-DI) were significant baseline predictors for achieving MDA and DAPSA LDA at Week 56. Lower Pt-Pain (Weeks 12–24) and PtGA (Weeks 16–24) scores were strongly predictive (c-statistics >0.8) of achieving MDA at Week 56, and both measures (from Week 8) were moderately predictive (c-statistics >0.7) of achieving DAPSA LDA. Evaluated simultaneously with several baseline characteristics, lower Pt-Pain and HAQ-DI scores at Week 12 were included in models strongly predictive of achieving MDA (c-statistic=0.850; Figure 1) and DAPSA LDA (c-statistic=0.840; Figure 2) at Week 56. For each 1-point increase in Pt-Pain or HAQ-DI scores at Week 12 (after adjusting for other effects in the model), patients were less likely to achieve MDA (by 32% or 56%, respectively) or DAPSA LDA (by 23% or 31%, respectively) at Week 56. Predictors for achieving sustained MDA and sustained DAPSA LDA were generally similar to those identified for achieving MDA and DAPSA LDA, respectively.

Conclusion: In patients with PsA receiving UPA 15 mg, baseline characteristics and early responses strongly predicted achievement of MDA or DAPSA LDA at Week 56. This may guide considerations of treatment targets in clinical trials and encourage physicians to further optimize treatment of their patients in clinical practice.

Figure 1. Predictors of Achievement of MDA at Week 56 with Upadacitinib 15 mg – Evaluated Simultaneously

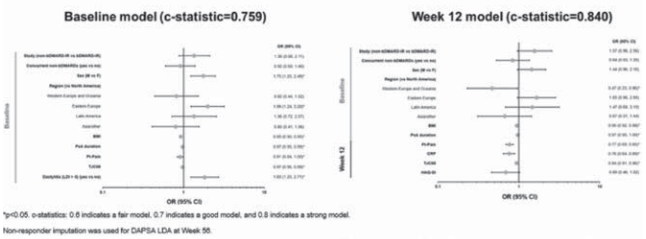


*p<0.05. c-statistics: 0.8 indicates a fair model, 0.7 indicates a good model, and 0.8 indicates a strong model.

Non-responder imputation was used for MDA at Week 56.

bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; F, female; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate responder; LDI, Leeds Dactylitis Index; M, male; MDA, minimal disease activity; OR, odds ratio; PhGA, Physician's Global Assessment; PsA, psoriatic arthritis; PtGA, Patient's Global Assessment; Pt-Pain, Patient's Assessment of Pain.

Figure 2. Predictors of Achievement of DAPSA LDA at Week 56 with Upadacitinib 15 mg – Evaluated Simultaneously



*p<0.05. c-statistics: 0.8 indicates a fair model, 0.7 indicates a good model, and 0.8 indicates a strong model.

Non-responder imputation was used for DAPSA LDA at Week 56.

bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; DAPSA, Disease Activity Index for Psoriatic Arthritis; F, female; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate responder; LDA, low disease activity; LDI, Leeds Dactylitis Index; M, male; OR, odds ratio; PsA, psoriatic arthritis; Pt-Pain, Patient's Assessment of Pain; TJC68, tender joint count in 68 joints.

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POS1027

APREMILAST EFFICACY IN REAL WORLD SETTINGS: RESULTS FROM AN ITALIAN MULTI-CENTER OBSERVATIONAL STUDY.

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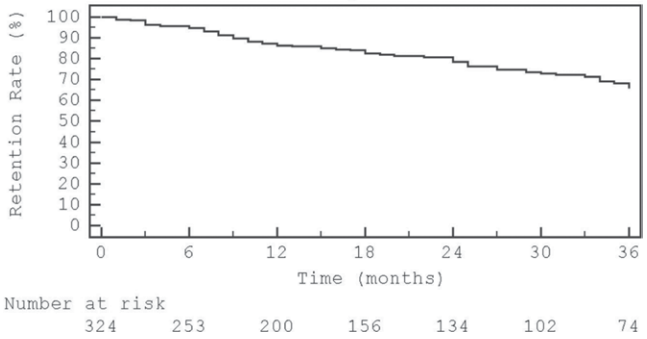
Background: Apremilast, an inhibitor of the phosphodiesterase 4, is indicated for Psoriatic Arthritis (PsA) treatment. The 3 years retention rate, an outcome indirectly related to efficacy, observed in clinical trials [1] is 55,5%. A single subsequent real world setting study [2] suggested a lower efficacy as it reported that the six months retention rate was about 57%.
Objectives: The main aim of this retrospective observational study is the assessment of apremilast 3 years retention rate in a real world PsA patients' cohort. Moreover, the secondary objective is reporting the reasons of apremilast suspension and the most relevant factor related to treatment persistence.
Methods: In thirteen Italian rheumatological referral centers, all PsA consecutive patients who received apremilast were enrolled. Anamnestic data, treatment history and PsA disease activity (DAPSA) at baseline and after 6 and 12 months were recorded. The Kaplan-Meier curve and the Cox analysis computed the apremilast retention rate and treatment persistence-related risk factors. A p-value < 0.05 was considered statistically significant.
Results: The three-hundred-twenty-four enrolled patients (median age 60 [Inter-Quartile Range IQR 52-67] yrs; female prevalence 57,0%) median observation period was 17 [IQR 7-36] months (6848 patients-months). The apremilast retention rate at 6, 12 and 36 months was, respectively, 95%, 86% and 66% (Figure 1). The main discontinuation reasons were: primary inefficacy (40% of interruptions), secondary inefficacy (18%) and gastro-intestinal intolerance (17%%). The oligo-articular onset was the only factor associated to apremilast persistence (Hazard ratio 0.57 IQR 0.34-0.96). Sex, age, and sever comorbidities (cancer, chronic infections etc) were not related to treatment discontinuation. The basal DAPSA (24.1, IQR 18.5-32.0) decreased after 6 and 12 months (respectively 14.5, IQR 10.1-22.6 and 10.5, IQR 8,0-15.2). Remission or minimal disease activity (DAPSA < 15) was achieved after 12 months in 38.0% of patients.

Figure 1



Conclusion: Almost two third of PsA patients receiving apremilast were still in treatment after 3 years. The study's data, confirmed its efficacy and safety profile. Apremilast appear a good treatment choice in patients with oligo articular PsA or burdened by severe comorbidities.
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[2] Favalli et al Clin Exp Rheum (2020)
Disclosure of Interests: Alarico Ariani Speakers bureau: Zentiva, Consultant of: Boeringher, Amgen, Bristol-Meyers-Squibb, Novartis, Sanofi, Novo Nordisk, Lilly, Janssen, Bruno Farmaceutici, Simone Parisi: None declared, Patrizia Del Medico: None declared, antonella farina: None declared, elisa visalli: None declared, Aldo Molica Colella: None declared, Federica Lumetti Consultant of: Amgen, rosalba caccavale: None declared, Palma Scolieri: None declared, Romina Andracco: None declared, Francesco Girelli: None declared, Elena Bravi: None declared, Matteo Colina: None declared, Veronica Franchina: None declared, Ilaria Platé: None declared, eleonora Di Donato Consultant of: Novartis, Giorgio Amato: None declared, Carlo Salvarani: None declared, Francesco De Lucia: None declared, Daniele Santilli Consultant of: Novartis, eugenio arrigoni: None declared, Flavio Mozzani Consultant of: Novartis, Abbvie, Rosario Foti: None declared, Gilda Sandri: None declared, Vincenzo Bruzzese: None declared, Marino Paroli: None declared, Enrico Fusaro: None declared, Andrea Becciolini: None declared
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POS1028

GUSELKUMAB MAINTAINS RESOLUTION OF DACTYLITIS AND ENTHESITIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS THROUGH 2 YEARS FROM A PHASE 3 STUDY

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Background: Guselkumab (GUS), a selective inhibitor of IL-23, significantly improved the diverse manifestations of active psoriatic arthritis (PsA), including dactylitis and enthesitis, in DISCOVER (D)-1 & 2 trials of patients (pts) with active PsA[1,2], with maintenance of response rates through 1 year (yr).[3,4] Dactylitis and enthesitis, extra-articular manifestations of PsA, can be difficult to treat and cause significant disease burden.[5,6]
Objectives: To evaluate the ability of GUS to provide long-term resolution of dactylitis and enthesitis in pts with PsA through 2 yrs of D-2.
Methods: D-2 biologic naïve pts with active PsA were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo (PBO). At W24, PBO pts crossed over to GUS Q4W. Independent assessors evaluated dactylitis (total score: 0-60) and enthesitis (Leeds Enthesitis Index [LEI]; total score 0-6). These post hoc analyses assessed baseline (BL) frequency and severity of enthesitis in pts with dactylitis and dactylitis frequency in pts with enthesitis. Post BL, changes in dactylitis and LEI scores over time (least squares [LS] mean changes; analysis of covariance [ANCOVA]) and rates of resolution of dactylitis and enthesitis (Chi square correlation test) were determined in pts with these manifestations at BL (missing data imputed as no change/response).
Results: At BL, more D-2 pts had enthesitis (68%) than dactylitis (45%). At BL, 78% of pts with dactylitis vs 61% without (w/o) dactylitis had enthesitis and 51% of pts with enthesitis vs 32% w/o enthesitis had dactylitis. Among pts with enthesitis at BL, a higher percentage of pts with dactylitis (52%) had severe enthesitis (LEI score ≥3) vs pts w/o dactylitis (44%). Among those with the condition at BL, resolution rates of dactylitis (57%, Q4W; 64%, Q8W) and enthesitis (44%, Q4W; 54%, Q8W) at W24 increased through W52 (dactylitis: 74%, Q4W; 78%, Q8W; enthesitis: 57%, Q4W; 61%, Q8W) and were maintained at W100 (dactylitis: 72%, Q4W; 83%, Q8W; enthesitis: 62%, Q4W; 70%, Q8W). Consistent results were observed when evaluating mean changes in dactylitis and LEI scores and in pts who crossed over from PBO to GUS Q4W at W24 (Table 1). In pts with dactylitis and enthesitis at BL, GUS-treated pts showed significant correlations between resolution of enthesitis and dactylitis at W24 (p=0.004), W52 (p<0.001) and W100 (p=0.039), with nearly 90% of pts with enthesitis resolution also achieving dactylitis resolution at W52 and W100 (Figure).

Table 1. LS mean change from baseline over time in dactylitis and LEI scores in pts with manifestation at baseline

	GUS 100 mg Q4W	GUS 100 mg Q8W	PBO → GUS 100 mg Q4W
Dactylitis score (0-60)			
Pts, N	121	111	99
W24[a]	-5.9 (-6.7, -5.0)	-6.0 (-6.8, -5.1)	-4.0 (-5.0, -3.1)
W52[a]	-6.5 (-7.2, -5.8)	-7.2 (-7.9, -6.5)	-6.9 (-7.6, -6.2)
W100[a]	-6.5 (-7.1, -5.8)	-7.5 (-8.1, -6.8)	-6.9 (-7.6, -6.2)
LEI score (1-6)			
Pts, N	170	158	178
W24[a]	-1.5 (-1.8, -1.3)	-1.6 (-1.8, -1.4)	-1.0 (-1.3, -0.8)
W52[a]	-1.8 (-2.0, -1.6)	-1.9 (-2.1, -1.7)	-2.0 (-2.2, -1.8)
W100[a]	-1.9 (-2.1, -1.7)	-2.1 (-2.3, -1.8)	-2.1 (-2.3, -1.9)

[a]Results are LS mean change (95% confidence interval [CI]); LS mean change determined by ANCOVA; missing data was imputed as no change for pts who discontinued treatment and using multiple imputation for remaining missing data GUS, guselkumab; LEI, Leeds Enthesitis Index; LS, least squares; PBO, placebo; pts, patients; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week

Conclusion: Pts with PsA often present with concurrent enthesitis and dactylitis, both of which can be recalcitrant to treatment. GUS resolved enthesitis and dactylitis in substantial proportions of pts through W100. GUS-treated pts who achieved enthesitis resolution were more likely to achieve dactylitis resolution and vice versa.
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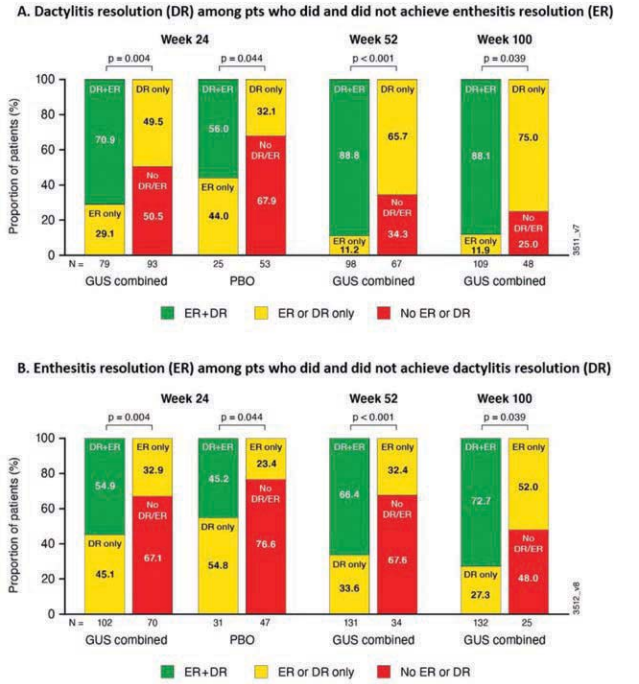
Figure. Correlation analysis between resolution of enthesitis & dactylitis over time among pts with enthesitis & dactylitis at baseline



P-value was calculated using Chi square test; ER=enthesitis resolution; DR=dactylitis resolution

Disclosure of Interests: Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis, Iain McInnes Consultant of: AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Gilead, Janssen, Novartis, and UCB, Grant/research support from: AstraZeneca, Bristol Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, Atul Deodhar Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, and UCB, Georg Schett Speakers bureau: Abbvie, Janssen, and Novartis, Philip J Mease Speakers bureau: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Consultant of: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Grant/research support from: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, May Shawi Shareholder of: Janssen Global Services, LLC, Employee of: Janssen Global Services, LLC, Daniel Cua Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, Jonathan Sherlock Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, Alexa Kollmeier Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, Yusang Jiang Consultant of: Janssen, Employee of: Cytel Inc, Shihong Sheng Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, and UCB Pharma, Grant/research support from: AbbVie, Amgen, and UCB Pharma, Dennis McGonagle Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB

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POS1029

EFFECTS OF TREATMENT WITH RISANKIZUMAB ON MINIMAL DISEASE ACTIVITY (MDA) AND DISEASE ACTIVITY IN PSORIATIC ARTHRITIS (DAPSA): AN ANALYSIS OF THE KEEPSAKE-1 AND -2 TRIALS

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Background: Risankizumab (RZB) is a monoclonal antibody that specifically inhibits interleukin 23.

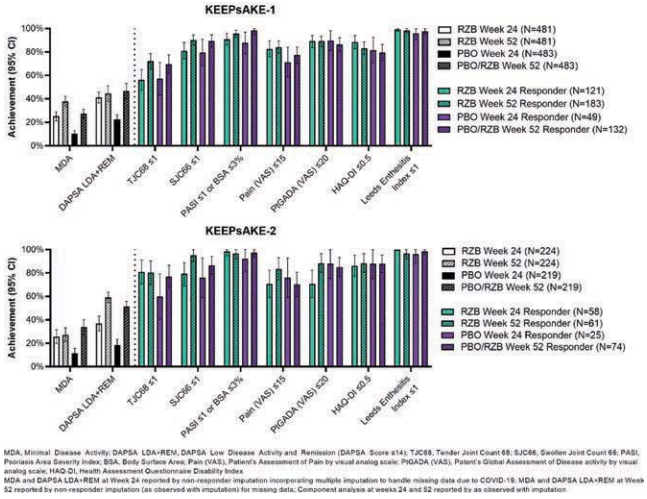
Objectives: To evaluate the achievement of Minimal Disease Activity (MDA), its components, and achievement of Disease Activity in PsA Low Disease Activity and Remission (DAPSA LDA+REM, [DAPSA score ≤14]) in patients receiving RZB or placebo (PBO) in the KEEPsAKE 1 and 2 clinical trials.

Methods: KEEPsAKE-1 and -2, double-blind, phase 3 trials, evaluated the efficacy of RZB versus PBO for the treatment of adult patients with active psoriatic arthritis (PsA). Patients were randomized (1:1) to receive subcutaneous RZB 150mg or PBO at weeks 0, 4, and 16. The open label extension began at Week 24 with all patients receiving RZB 150mg every 12 weeks thereafter. Achievement of MDA, its components, and achievement of DAPSA LDA+REM are reported using non-responder imputation.

Results: MDA achievement at Week 52 in KEEPsAKE-1 was 37.9% for patients originally randomized to RZB and 27.4% for patients originally randomized to PBO. In KEEPsAKE-2, MDA achievement was 27.2% and 33.8% for patients originally randomized to RZB and PBO, respectively. Achievement of MDA and its components are presented in Figure 1. In KEEPsAKE-1, at Week 52 59.2% of patients originally randomized to RZB and 51.4% of patients originally randomized to PBO achieved DAPSA LDA+REM. At Week 52 in KEEPsAKE-2, DAPSA LDA+REM was achieved by 44.6% of patients originally randomized to RZB and 46.6% of patients originally randomized to PBO (Figure 1).

Conclusion: Patients treated with RZB demonstrate achievement of MDA, its components, and DAPSA LDA+REM at Weeks 24 and 52.

Figure 1



MDA, Minimal Disease Activity; DAPSA LDA+REM, DAPSA Low Disease Activity and Remission (DAPSA Score ≤14); TJC68, Tender Joint Count 68; SJC66, Swollen Joint Count 66; PASI, Psoriasis Area Severity Index; BSA, Body Surface Area; Pain (VAS), Patient's Assessment of Pain by visual analog scale; PtGADA (VAS), Patient's Global Assessment of Disease activity by visual analog scale; HAQ-DI, Health Assessment Questionnaire Disability Index
MDA and DAPSA LDA+REM at Week 24 reported by non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; MDA and DAPSA LDA+REM at Week 52 reported by non-responder imputation (as observed with imputation) for missing data; Component analysis at weeks 24 and 52 reported by as observed with imputation

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POS1030

PAIN RESPONSE IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH GUSELKUMAB IS DRIVEN PREDOMINANTLY BY INFLAMMATION-INDEPENDENT EFFECTS

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Background: Although reducing inflammation has been associated with pain improvement, the two do not always correlate. Recent studies have suggested that, in addition to its role in inflammation pathogenesis, IL-23 may be involved in pain regulation in a lymphocyte-independent manner[1]. Guselkumab (GUS), a fully human monoclonal antibody that selectively inhibits IL-23, has demonstrated safety and efficacy in treating multiple domains of active PsA in the DISCOVER-1&2 (D1&D2) trials[2,3].
Objectives: To quantify the role of reducing inflammation on the observed relationship between GUS and pain response in PsA patients (pts) using mediation modelling.
Methods: Pooled data from the D1&D2 studies were analyzed. Pts in D1 had ≥3 swollen and ≥3 tender joints (SJC/TJC) and C-reactive protein (CRP)≥0.3 mg/dL; in D2, pts had ≥5 SJC and ≥5 TJC and CRP≥0.6 mg/dL. 31% of D1 pts received 1-2 prior tumor necrosis factor inhibitors (TNFi); D2 pts were bio-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then every 8 weeks (Q8W); or placebo (PBO); PBO pts crossed over to GUS 100 mg Q4W at W24. Pts with history of fibromyalgia were excluded from the analysis. Least square mean changes in pt-reported pain (0-100 VAS) through W52 were estimated with a repeated measures linear mixed model adjusting for known pain determinants. Mediation modelling was performed separately for Q4W & Q8W, W4 & W24, and TNFi-naïve & -experienced (exp) pts. In each model, change in pt-reported pain was the dependent variable; treatment regimen was the independent variable; inflammation, measured by change in SJC or CRP, was the designated mediator; covariates were: age; sex; and baseline (BL) pain score, BMI, SF-36 MCS score, and NSAID use.
Results: Mean (SD) BL pain levels in the GUS Q4W, GUS Q8W, and PBO groups were 60.4 (19.8), 62.0 (20.2), and 61.1 (19.6), respectively. Treatment with GUS was associated with significantly greater pain improvement compared with PBO as early as W4 ($\Delta_{Q4W\text{-}PBO}$ [95%CI]: -4.9 [-7.6, -2.2]; $\Delta_{Q8W\text{-}PBO}$ [95%CI]: -5.2 [-7.9, -2.5] (Figure 1). These between-group differences were further enhanced by W24 ($\Delta_{Q4W\text{-}PBO}$ [95%CI]: -14.6 [-17.6, -11.5]; $\Delta_{Q8W\text{-}PBO}$ [95%CI]: -14.3 [-17.3, -11.2]); by W52, GUS-randomized pts exhibited an approximate 30-point (-50%) decrease in pain. Similar results were observed for TNFi-naïve and TNFi-exp pts.

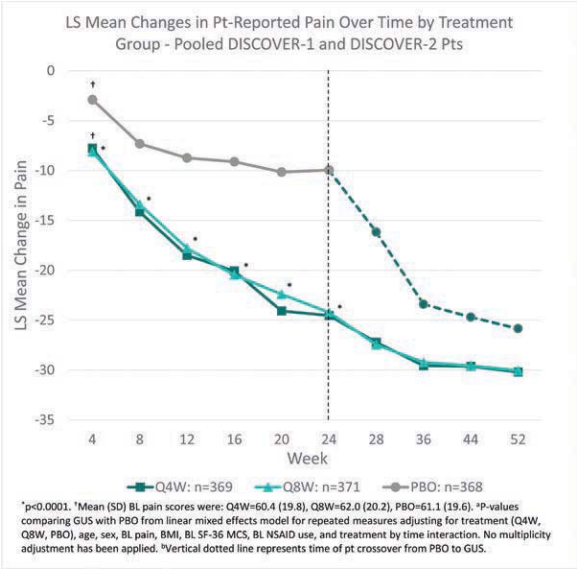

Figure 1.

Mediation analyses demonstrated that the majority of GUS effect on pain at W4 was not attributable to SJC (direct effect), specifically ≤6% was mediated by inflammation as assessed by changes in SJC (indirect effect; Table 1). Similarly, at W24, the indirect effect via SJC improvement represented ≤10% of the GUS treatment effect. No differences were observed between TNFi-naïve and -exp pts at either timepoint.
Consistent results were obtained when using CRP as the mediator variable instead of SJC, whereby ≤2-9%% of GUS effect on pan was mediated by inflammation and 91-98% was direct (Table 1).

Table 1. Direct (D) Treatment Effect vs. Indirect (IND) Effect via Inflammation Markers on Pain Improvement

Mediator	Week	Pt Group	Effect	GUS Q4W	GUS Q8W
SJC	4	All	D	96.7%*	97.0%*
			IND†	3.3%	3%
		TNFi-Naive	D	93.7%*	98.5%*
			IND†	6.3%	1.5%
		TNFi-Exp	D	100%*	100%*
			IND†	0%	0%
	24	All	D	94.8%*	92.0%*
			IND†	5.2%*	8.0%*
		TNFi-Naive	D	89.6%*	90.1%*
			IND†	10.4%*	9.9%*
		TNFi-Exp	D	99.8%*	95.7%*
			IND†	0.2%	4.3%
CRP	4	All	D	97.6%*	95.0%*
			IND‡	2.4%	5.0%
		TNFi-Naive	D	98.2%*	95.4%*
			IND‡	1.8%	4.6%
		TNFi-Exp	D	97.6%*	95.3%*
			IND‡	2.4%	4.7%
	24	All	D	97.2%*	94.2%*
			IND‡	2.8%	5.8%*
		TNFi-Naive	D	98.1%*	95.9%*
			IND‡	1.9%	4.1%
		TNFi-Exp	D	96.5%*	91.4%*
			IND‡	3.5%	8.6%

*p<0.05; †via SJC; ‡via CRP

Conclusion: GUS induced significant improvement in pt-reported pain as early as W4 of treatment, which was continuously enhanced through W52. While the known mediation effect of SJC and CRP, as markers of inflammation, on pain was confirmed, the majority of GUS's effect on pain reduction was independent of its effect on these markers, regardless of dosing regimen or prior TNFi experience.
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[1] Arthritis Res Ther. 2020;22:123
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[3] Lancet. 2020;395:1126
Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, Consultant of: AbbVie, Aclaris, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, Enrique Soriano Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Janssen, Novartis, and Roche, Grant/research support from: AbbVie, Janssen, Novartis, Pfizer, Roche, and UCB, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC and Drexel University College of Medicine, Emmanouil Rampakakis Consultant of: Janssen, Employee of: JSS Medical Research, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Pharmaceutical Companies of Johnson & Johnson, Peter Nash Speakers bureau: Janssen, Abbvie, Pfizer, Novartis, Lilly, Gilead, Roche, Sandoz, Celgene, Sun, Boehringer, and Bristol Myers Squibb, Consultant of: Janssen, Abbvie, Pfizer, Novartis, Lilly, Gilead, Roche, Sandoz, Celgene, Sun, Boehringer, and Bristol Myers Squibb, Grant/research support from: Janssen, Abbvie, Pfizer, Novartis, Lilly, Gilead, Roche, Sandoz, Celgene, Sun, Boehringer, and Bristol Myers Squibb, Proton Rahman Speakers bureau: Janssen, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, and UCB, Grant/research support from: Janssen and Novartis
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POS1031

EARLIER CLINICAL RESPONSE PREDICT LOW RATES OF RADIOGRAPHIC PROGRESSION IN BIO-NAIVE ACTIVE PSORIATIC ARTHRITIS PATIENTS RECEIVING GUSELKUMAB TREATMENT

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Background: Guselkumab (GUS), an IL-23p19-subunit inhibitor, demonstrated efficacy and a favorable safety profile in patients (pts) with psoriasis (PsO) and psoriatic arthritis (PsA). In the Phase 3, double-blind, placebo (PBO)-controlled DISCOVER-2 study, GUS 100 mg every 4 or 8 weeks (Q4W or Q8W) significantly improved joint and skin symptoms; GUS-treated pts had smaller mean changes in radiographic progression vs. PBO at W24.[1] Low rates of radiographic progression were observed through 2 years among GUS-treated pts, regardless of dosing regimen.[2,3]
Objectives: Determine whether earlier clinical improvement predicts long-term radiographic progression through 2 years in DISCOVER-2.
Methods: DISCOVER-2 included biologic-naïve pts with active PsA (≥5 swollen and ≥5 tender joint counts [SJC/TJC]; CRP ≥0.6 mg/dL) randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W (PBO→Q4W) at W24. For pts randomized to GUS Q4W or Q8W, predictive models (mixed linear) were developed post-hoc to assess the associations of earlier (at W16) improvement in disease activity (DAPSA remission, DAPSA Improvement, DAPSA Improvement more than the median of 20.7 [>20.7]) or skin improvement (PASI90, PASI≤1) with changes in total PsAmodified van der Heijde-Sharp [vdH-S] score through W100, after adjusting for known baseline (BL) determinants of radiographic progression (vdH-S score, age, gender, and CRP).
Results: PsA duration, CRP, and SJC at BL weakly correlated with BL vdH-S score. No correlation was seen between BL PASI and BL vdH-S score (Table 1). Greater improvement in DAPSA score (β [95%CI]: -0.03 [-0.04, -0.01]) and improvement >20.7 in DAPSA from BL to W16 was associated with significantly less radiographic progression through W100 after adjusting for BL DAPSA score, vdH-S score, age, gender, and CRP level. Achievement of PASI90, PASI≤1, and DAPSA remission at W16 was associated with numerically less radiographic progression through W100 after adjusting for BL PASI, vdH-S score, age, gender, and CRP (Figure).

Table 1. Correlation of Select BL Disease Characteristics with BL vdH-S Score Among GUS Randomized Pts

BL Determinants	Spearman's correlation coefficient	p-value
Age	0.27335	<.0001
CRP	0.28181	<.0001
PASI Score	0.03078	0.5153
PsA Duration	0.37070	<.0001
PsO Duration	0.20509	<.0001
SJC (66)	0.26321	<.0001

Conclusion: In GUS-treated biologic-naïve pts with active PsA, following adjustment for known BL determinants of radiographic progression, earlier (W16) DAPSA improvement was a significant predictor of less radiographic progression through W100; DAPSA remission and skin improvement at W16 each showed a numerical trend toward less radiographic progression through W100.
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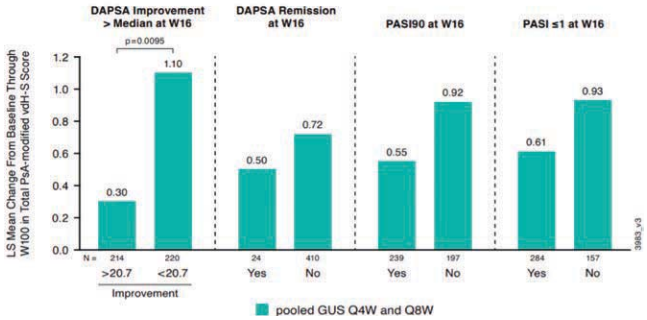
Figure. LS Mean Change in Total PsA-modified vdH-S Scores from BL at W100 by Achievement of Earlier DAPSA Improvement/Remission or Skin Improvement



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POS1032

RISANKIZUMAB FOR ACTIVE PSORIATIC ARTHRITIS: INTEGRATED SUBGROUP ANALYSIS FROM 2 DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 3 STUDIES (KEEPSAKE 1 AND KEEPSAKE 2)

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Background: Risankizumab (RZB), a monoclonal antibody that specifically inhibits interleukin 23, is being investigated as a treatment for adults with psoriatic arthritis (PsA).
Objectives: We report the proportion of patients with active PsA treated with RZB vs placebo who achieved ≥20% improvement in American College of Rheumatology criteria (ACR20) by baseline demographics and by concomitant or prior medication use subgroups.
Methods: KEEPsAKE 1 (NCT03675308) and KEEPsAKE 2 (NCT03671148) are ongoing, multicenter, randomized, double-blind, placebo-controlled, phase 3 studies. Patients with active PsA with an inadequate response or intolerance to conventional synthetic disease-modifying, anti-rheumatic drug (csDMARD; KEEPsAKE 1 and 2) and/or biologic therapy (KEEPsAKE 2) received RZB 150 mg or placebo (1:1). The primary endpoint was the proportion of patients achieving ≥20% improvement in ACR criteria (ACR20) at week 24.
Results: In KEEPsAKE 1 (RZB, n=483; placebo, n=481) and KEEPsAKE 2 (RZB, n=224; placebo, n=219), baseline demographics and characteristics were generally balanced between treatment groups. In this integrated analysis, a greater proportion of patients receiving RZB vs placebo achieved ACR20 at week 24, regardless of age (<65 years, ≥65 years, ≥65 to <75 years, ≥75 years), sex, body mass index (<25 kg/m^2, ≥25 to <30 kg/m^2, ≥30 kg/m^2), race (White, non-White), PsA duration (≤5 years, >5 to ≤10 years, >10 years), baseline hs-CRP (<3 mg/L, ≥3 mg/L), concomitant csDMARD at baseline (any csDMARD, any methotrexate, none), or prior biologics use (yes, no). The proportion of RZB-treated patients who achieved ACR20 was generally similar across most assessed demographic or prior treatment subgroups. No new safety concerns were observed with RZB.

Conclusion: RZB demonstrates efficacy vs placebo for active PsA as shown by greater proportions of patients achieving ACR20 at week 24, regardless of baseline demographics, concomitant csDMARD use at baseline, or prior biologic use.
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POS1033

DYNAMICS OF NAIL PSORIASIS WITH GUSELKUMAB TREATMENT AND WITHDRAWAL IN ASSOCIATION WITH SKIN RESPONSE AND PATIENT-REPORTED OUTCOMES: A POST HOC ANALYSIS OF THE VOYAGE 2 PHASE 3 TRIAL

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Background: Nail psoriasis can be difficult to treat, affects ~50% of patients with psoriasis and can involve the nail matrix (pitting, leukonychia) and/or nail bed (onycholysis, splinter haemorrhages). Evidence suggests nail psoriasis may be associated with risk of developing psoriatic arthritis, in particular distal interphalangeal joint erosion.[1–3] Data to Week (Wk) 24 from VOYAGE 1 and 2, two Phase 3 clinical trials, indicate that the anti-interleukin-23 monoclonal antibody guselkumab (GUS) is more effective than placebo and as effective as adalimumab in treating nail psoriasis.[4] Furthermore, GUS is also associated with maintained Psoriasis Area and Severity Index (PASI) following treatment withdrawal in VOYAGE 2; however, nail response is not as well understood in this context.[5]
Objectives: This VOYAGE 2 *post hoc* analysis evaluated nail response and its association with skin response and patient-reported outcomes (PROs) in two groups, one experiencing GUS withdrawal and the other receiving continuous GUS.
Methods: Patients had moderate-to-severe plaque psoriasis and nail psoriasis, were initially randomised to GUS, and achieved PASI 90 at Wk 28. Patients were then re-randomised to placebo (GUS withdrawal) or GUS every 8 wks (GUS continuation). Nail Psoriasis Severity Index (NAPSI; grading the most affected nail), fingernail Physician's Global Assessment (f-PGA), PASI and Dermatology Life Quality Index (DLQI) are reported as observed at Wk 0, 16, 24 and 48.
Results: Among 209 patients, NAPSI, f-PGA, PASI and DLQI showed similar trends in both groups until Wk 24. All endpoints improved from baseline; and at Wk 24, patients in the GUS withdrawal and GUS continuation groups achieved a mean NAPSI of 1.7 and 1.8 (nail matrix 1.0 and 1.0; nail bed 0.7 and 0.8); f-PGA 0.9 and 0.9; PASI 0.6 and 0.6; and DLQI 2.2 and 2.3, respectively (Table 1). Nail changes continued to follow skin trends through Wk 48 (Figure 1); with GUS withdrawal, worsening of PASI and DLQI was proportionally greater than that of NAPSI and f-PGA; with GUS continuation, PASI and DLQI remained fairly stable, and NAPSI and f-PGA continued to improve. Nails were numerically slower to respond to GUS initiation and withdrawal than skin, with a more pronounced delay for nail matrix vs nail bed. In patients who sustained a PASI 90 response at Wk 48, despite GUS withdrawal, a high level of nail response was also maintained.

Table 1. NAPSI, f-PGA, PASI and DLQI through Wk 48 in GUS withdrawal and GUS continuation groups

	Wk 0	Wk 16	Wk 24	Wk 28	Wk 48
GUS withdrawal*	**GUS**			**R**	**Placebo**
n	97	96	96		96
NAPSI	5.0 (2.1)	2.5 (1.9)	1.7 (1.9)		1.9 (2.1)
Nail matrix	2.7 (1.3)	1.5 (1.3)	1.0 (1.2)		0.9 (1.3)
Nail bed	2.2 (1.2)	0.9 (1.0)	0.7 (1.0)		1.0 (1.1)
n	98	97	97		97
f-PGA	2.5 (0.8)	1.3 (0.9)	0.9 (0.8)		1.1 (1.0)
n	101	101	100		100
PASI	23.1 (9.0)	1.3 (2.7)	0.6 (1.4)		5.2 (6.1)
n	101	101	100		100
DLQI	14.5 (6.1)	2.8 (4.1)	2.2 (3.6)		7.0 (7.4)
GUS continuation	**GUS**			R	**GUS**
n	108	106	107		105
NAPSI	4.4 (1.8)	2.4 (2.2)	1.8 (2.0)		1.2 (1.6)
Nail matrix	2.5 (1.2)†	1.4 (1.3)	1.0 (1.2)		0.7 (1.0)
Nail bed	1.9 (1.2)	1.0 (1.1)	0.8 (1.0)		0.5 (0.8)
n	108	106	107		105
f-PGA	2.4 (0.9)	1.1 (0.9)	0.9 (0.9)		0.7 (0.8)
n	108	108	108		106
PASI	22.6 (8.8)	1.2 (2.1)	0.6 (1.1)		1.3 (3.5)
n	107	108	108		104
DLQI	14.3 (6.4)	2.9 (4.2)	2.3 (4.0)		1.8 (3.4)

Data are mean (standard deviation). *n=10 reinitiated GUS upon loss of 50% of Wk 28 PASI 90 (at n=1 Wk 36, n=2 Wk 40, n=7 Wk 44); †n=107; R, re-randomisation of PASI 90 responders.

Conclusion: GUS treatment through Wk 48 improved nail psoriasis, skin psoriasis and PROs. When GUS was withdrawn, loss of response was slower in nails vs skin. These findings support that nail outcomes follow skin outcome trends with GUS treatment and that nail outcomes should contribute to evaluation of treatment efficacy and disease progression.[2,3,6]
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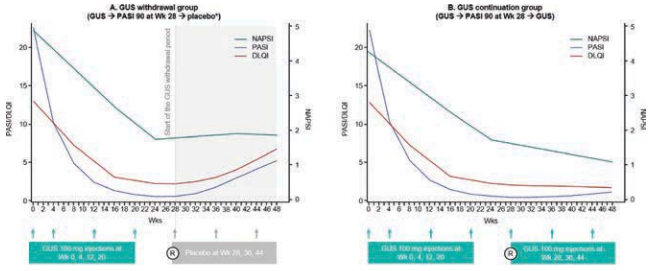

Figure. NAPSI, PASI and DLQI through Wk 48 in (A) GUS withdrawal and (B) GUS continuation groups. Curves are based on locally estimated scatterplot smoothing from data at all available timepoints. *Included n=10 reinitiated on GUS upon loss of 50% of Wk 28 PASI 90 response (n=1 at Wk 36, n=2 at Wk 40, n=7 at Wk 44). DLQI, Dermatology Life Quality Index; GUS, guselkumab; NAPSI, Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; R, re-randomisation of PASI 90 responders; Wk, week.

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POS1034

EVOLVING MECHANISM OF ACTION PREFERENCE FOR THE TREATMENT OF PSORIATIC ARTHRITIS IN AUSTRALIA: AN ANALYSIS OF THE OPAL DATASET

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Background: There are currently ten biologic and targeted synthetic (b/ts)DMARDs acting via five different modes of action (MOA) available for the treatment of psoriatic arthritis (PsA) in Australia. b/tsDMARDs are government-subsidised, and once the patient reaches the eligibility requirements, the clinician can prescribe the agent deemed most appropriate. Available agents include TNF inhibitors (TNFi, adalimumab, etanercept, infliximab, golimumab, certolizumab pegol), IL-17A inhibitors (IL-17Ai, secukinumab, ixekizumab), and IL-12/23 inhibitor (IL-12/23i, ustekinumab). Two new MOAs were recently added to the rheumatologist's armamentarium: the first JAK inhibitor (JAKi, tofacitinib) was subsidized from May 2019 followed by upadacitinib from Oct 2021, and an IL-23 inhibitor (IL-23i, guselkumab) was subsidized from July 2021.
Objectives: The aim of this analysis was to describe the changing patterns of b/tsDMARD use for the treatment of PsA in real-world practice in Australia.
Methods: Deidentified clinical data were sourced from the OPAL dataset, which is collected in a custom-built electronic medical record during the routine consultation1. Data from patients >18 years with a physician diagnosis of PsA who were prescribed a b/tsDMARD between Jan-2007 and Sept-2021 were included in the analysis. The software program Tableau was used to display the data.
Results: At Sept 2021, 6,150 (38% of the total) patients with PsA in the OPAL dataset were prescribed b/tsDMARDs. Of these patients, 3741 (61%) were currently prescribed a TNFi, 1503 (24%) an IL-17Ai, 556 (9%) a JAKi, 222 (4%) an IL-12/23i and 134 patients (2%) an IL-23i. Over time, the 1st line TNFi initiations have decreased from 79.5% in 2018 to 65.2% in 2021. Conversely, 1st line IL-17Ai initiations have increased from 14.4% in 2018 to 22.2% in 2021. In 2021, TNFi accounted for 53.4% of 2nd line initiations and 38.2% of 3rd line initiations. IL-17Ai accounted for 30.4% of 2nd and 37.0% of 3rd line initiations and JAKi accounted for 10.5% of 2nd line and 14.2% of 3rd line initiations. In the 3 months that IL-23i has been subsidised, this MOA was the most initiated agent for patients who had been treated with more than two prior b/tsDMARDs. In 2021, 52.1% of patients switching from a 1st line TNFi switched to an alternative TNFi, 33.3% switched to an IL-17Ai and 11.3% switched to a JAKi in 2nd line. Of those switching from a 1st line IL-17Ai, 59.6% initiated a TNFi, 21.2% switched to an alternative IL-17Ai and 11.5% switched to a JAKi.
Conclusion: The patterns of b/tsDMARD utilisation for the treatment of PsA, when the choice of agent is at the discretion of the rheumatologist, remains dynamic and is evolving as new MOAs become available. TNFi remains the most prescribed b/tsDMARD for first line therapy. However an increase in first line use of alternative MOAs has been observed. TNFi cycling remains a commonly utilised real world treatment strategy but appears to be declining as new MOAs become available.

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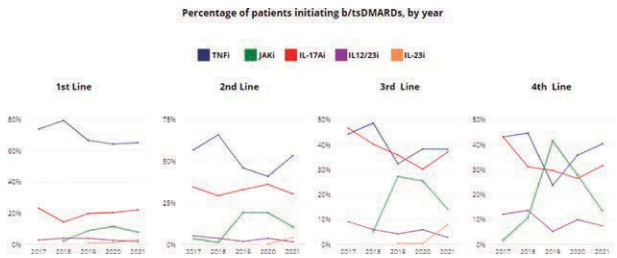

Figure 1. Percentage of patients initiating b/tsDMARDs by year and line of therapy.

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POS1035

LOW RATES OF RADIOGRAPHIC PROGRESSION WITH 2 YEARS OF GUSELKUMAB, A SELECTIVE INHIBITOR OF THE INTERLEUKIN-23P19 SUBUNIT: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: In the phase 3 DISCOVER-2 (D2) study, guselkumab (GUS) 100 mg every 4/8 weeks (Q4W/Q8W) significantly improved joint and skin symptoms in patients (pts) with active psoriatic arthritis (PsA); GUS-treated pts had smaller mean changes in radiographic progression vs placebo (PBO) at W24.[1] Clinical response rates and favorable safety profile were durable through W100.[2, 3]
Objectives: To report details of radiographic assessments comprising Reading Session 3 through W100 of D2, including relationships between radiographic changes and measures of clinical outcomes.
Methods: Biologic-naïve adults with active PsA (≥5 swollen + ≥5 tender joint count; CRP ≥0.6 mg/dL) were randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W (PBO→Q4W) at W24, all through W100. Radiographic Reading Session 3 included assessments at W0/24/52/100 (or at discontinuation after W52) from pts ontinuing study treatment at W52; readers were blinded to treatment group and timepoint. Observed mean changes in total PsA-modified van der Heijde-Sharp (vdH-S), joint space narrowing (JSN), and erosion scores were reported. Changes in total vdH-S scores from W0-100 were determined in pts who did and did not achieve clinical response at W100, assessed by ACR20/50/70, low disease activity (LDA) based on Disease Activity in Psoriatic Arthritis score (DAPSA; ≤14) or Psoriatic Arthritis Disease Activity Score (PASDAS; ≤3.2), minimal disease activity (MDA), and normalized Health-Assessment Questionnaire-Disability Index (HAQ-DI) score (<0.5).
Results: Of 739 randomized pts, 664 had evaluable data from Reading Session 3; 629 had evaluable data from W52-100. Mean total baseline vdH-S scores were: Q4W, 28.0; Q8W, 23.9; PBO→Q4W, 25.6. Mean progression of joint damage from W0-24 was numerically lower in GUS- than PBO-treated pts for erosion, JSN, and total vdH-S scores (Table 1), consistent with the results from Reading Session 1.[1] Mean changes in radiographic scores from W52-100 indicated low rates of radiographic progression across GUS groups. Among GUS-randomized pts, mean changes in vdH-S score from W0-100 were numerically lower for pts achieving clinical response assessed using ACR20/50/70, DAPSA LDA, PASDAS LDA, MDA, and HAQ-DI vs pts not achieving response at W100 (Figure 1).
Conclusion: In biologic-naïve pts with active PsA enriched for greater risk of radiographic progression, GUS 100 mg (Q4W or Q8W) was associated with low rates of radiographic progression through 2 years. Pts achieving clinical response across several global measures of disease activity or normalized physical function at W100 had lower mean changes in total PsA-modified vdH-S scores compared with nonresponders.

Table 1. Observed erosion, joint space narrowing, and total PsA-modified vdH-S scores through W100 of DISCOVER-2

	GUS Q4W			GUS Q8W			PBO→GUS Q4W		
Baseline PsA-modified vdH-S score, n	221			228			215		
Erosion	14.2 (23.3)			12.0 (21.9)			12.1 (21.9)		
Joint space narrowing	13.8 (21.8)			11.9 (19.5)			13.5 (21.6)		
Total	28.0 (43.6)			23.9 (40.4)			25.6 (42.4)		
Mean (SD) change in PsA-	**W0-24**	**W24-52**	**W52-100**	**W0-24**	**W24-52**	**W52-100**	**W0-24**	**W24-52**	**W52-100**
modified vdH-S score	**N=221**	**N=221**	**N=211**	**N=228**	**N=228**	**N=216**	**N=215**	**N=213**	**N=202**
Erosion	0.27 (1.91)	0.36 (1.77)	0.45 (2.90)	0.51 (1.96)	0.20 (1.24)	0.26 (1.75)	0.73 (2.20)	0.25 (1.85)	0.09 (1.98)
Joint space narrowing	0.21 (1.17)	0.21 (1.11)	0.30 (1.32)	0.17 (0.69)	0.12 (0.66)	0.20 (0.92)	0.39 (1.72)	0.09 (1.11)	0.04 (1.90)
Total	0.48 (2.70)	0.57 (2.66)	0.75 (4.02)	0.68 (2.36)	0.31 (1.57)	0.46 (2.42)	1.12 (3.80)	0.34 (2.79)	0.13 (3.74)

Data presented as mean (SD).GUS, guselkumab; PBO, placebo; PsA, Psoriatic Arthritis; Q4W, every 4 weeks; Q8W, every 8 weeks; SD, standard deviation; vdH-S, van der Heijde-Sharp; W, week

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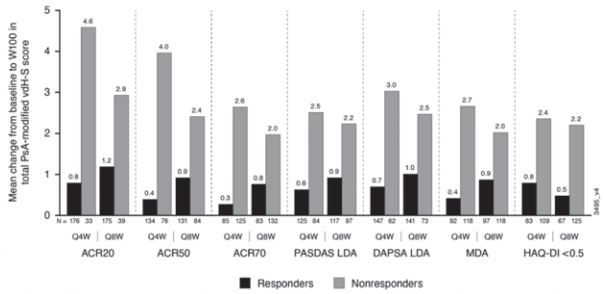
Figure. Mean changes in PsA-modified total vdH-S score from W0-100 for patients who did and did not achieve select clinical responses at W100



ACR20/50/70=American College of Rheumatology 20/50/70 improvement; HAQ-DI=Health Assessment Questionnaire Disability Index; DAPSA= Disease Activity in Psoriatic Arthritis score; LDA=Low Disease Activity; MDA=Minimal Disease Activity; PASDAS= Psoriatic Arthritis Disease Activity Score; PsA=Psoriatic Arthritis; Q4W= every 4 weeks; Q8W=every 8 weeks; vdH-S= van der Heijde-Sharp; W=week

Disclosure of Interests: Philip J Mease Consultant of: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Grant/research support from: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Alice B Gottlieb Shareholder of: Xbiotech (stock options only), Consultant of: Anaptyps Bio, Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Incyte, Janssen, LEO Pharma, Novartis, Pfizer, Sun Pharmaceuticals, UCB, Grant/research support from: Boehringer Ingelheim, Janssen, Novartis, Sun Pharmaceuticals, UCB, and Xbiotech, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Yusang Jiang Employee of: Cytel, Inc., Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Frederic Lavie Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma, Employee of: Director of Imaging and Rheumatology BV
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POS1036 EFFICACY AND SAFETY OF RISANKIZUMAB (RZB) FOR ACTIVE PSORIATIC ARTHRITIS (PSA): 52-WEEK RESULTS FROM KEEPSAKE 2

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Background: RZB, a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits the p19 subunit of the human cytokine interleukin-23, is being investigated as a treatment for PsA.
Objectives: Evaluate longer-term safety and efficacy of RZB in patients with active PsA who experienced inadequate response or intolerance to 1 or 2 biologic therapies and/or to at least 1 csDMARD therapy.
Methods: KEEPsAKE 2 (NCT03671148) is an ongoing, phase 3, multicenter study that includes a screening period; a 24-week double-blinded, randomized, placebo-controlled, parallel-group period (period 1); and an open-label extension period (period 2). Eligible patients were ≥18 years of age with active PsA (symptom onset ≥6 months before screening, meeting Classification Criteria for PsA [CASPAR], and ≥5 tender and ≥5 swollen joints) and had inadequate response or intolerance to 1 or 2 biologic therapies (Bio-IR) and/or ≥1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR). Patients received RZB 150 mg or placebo (PBO) at weeks 0, 4, and 16 (1:1). The primary endpoint was the proportion of patients achieving ACR20 response at week 24. Period 2 started at week 24, and patients were switched to receive open-label RZB 150 mg every 12 weeks through week 208. Efficacy and safety were analyzed in patients who received ≥1 dose of study drug through week 52. Mixed-effect model with repeated measures and nonresponder imputation methods were used to assess continuous and binary variables, respectively. Treatment-emergent adverse events (TEAEs) were summarized using exposure-adjusted event rates (EAERs, events/100 patient-years [PY]).
Results: At week 24, 51,3% of RZB-treated (N=224) and 26.5% of PBO-treated (N=219) patients achieved ACR20. At week 52, 58.5% of patients who were randomized to RZB and 55.7% of patients who were randomized to PBO and then switched to RZB at week 24 achieved ACR20. In patients with ≥3% of body surface area affected at baseline, 55.0% of RZB-treated patients (N=123) and 10.2% of PBO-treated patients (N=119) achieved PASI 90 at week 24. At week 52, 64.2% of patients randomized to RZB and 59.7% of patients who were randomized to PBO and then switched to RZB at week 24 achieved PASI 90. For other efficacy measures, similar trends were observed. RZB was well tolerated through 52 weeks of treatment, and EAERs of adverse events were stable between weeks 24 and 52. At the week 52 data cutoff (19 April 2021), the total EAER of any TEAE in patients receiving RZB was 184.2/100 PY.
Conclusion: Continuous RZB treatment resulted in maintained efficacy responses with a consistent safety profile through 52 weeks of treatment in patients with active PsA who were Bio-IR and/or csDMARD-IR.
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POS1037 EFFECT OF GUSELKUMAB, A SELECTIVE IL-23P19 INHIBITOR, ON AXIAL-RELATED ENDPOINTS IN PATIENTS WITH ACTIVE PSA: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY THROUGH 2 YEARS

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Background: Guselkumab (GUS), a selective IL-23p19 inhibitor, showed greater mean improvements in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores vs placebo (PBO) at Week (W) 24 in patients (pts) with active PsA and investigator-confirmed sacroiliitis in pooled post hoc analyses of data from phase 3 DISCOVER (D)-1&2 trials. Improvements in symptoms of axial involvement were maintained through 1 year.[1]

Objectives: To assess maintenance of GUS effect on symptoms of axial involvement in biologic-naïve PsA pts with investigator-confirmed sacroiliitis through 2 years of D-2.

Methods: In D-2, 739 bio-naïve pts with active PsA (≥5 swollen + ≥5 tender joints, CRP ≥0.6 mg/dL despite standard therapies) were randomized 1:1:1 to GUS 100 mg every 4W (Q4W; n=245), GUS 100 mg at W0, W4, then Q8W (n=248), or PBO (n=246) with PBO→GUS 100 mg Q4W at W24. Pts with investigator-identified axial symptoms and sacroiliitis (prior X-ray or MRI, or pelvic X-ray at screening) were evaluated. Efficacy was assessed by changes in BASDAI, modified BASDAI (mBASDAI, excluding Q3 [peripheral joint pain]), and BASDAI Q2 (Spinal Pain) scores, and proportions of pts achieving BASDAI 50, Spinal Pain score ≤2, and AS Disease Activity Score (ASDAS) responses through W100. Through W24, pts who met treatment failure criteria or had missing data were considered nonresponders. After W24, missing data were imputed as nonresponse for binary endpoints or no change from baseline for continuous endpoints (nonresponder imputation [NRI]). Axial-related outcomes were also summarized by HLA-B27 status (+/-).

Results: 246 pts had investigator-confirmed sacroiliitis. Baseline characteristics were similar across treatment groups (62% male; mean age 44.4 years; mean BASDAI scores 6.5-6.6). At W24, LS mean/mean changes in BASDAI (-2.4/-2.6) and ASDAS (-1.3/-1.5) scores were greater in GUS- vs PBO-treated pts. Improvements were maintained through W100 in GUS-treated pts: BASDAI, -3.1; Spinal Pain, -3.1; mBASDAI, -3.1; ASDAS, -1.7. Response patterns were similar for BASDAI 50 response rates in GUS-treated pts (W24 38-40%; W100 49-54%). At W24, GUS-treated pts had higher response rates for achievement of ASDAS inactive disease, major improvement, and clinically important improvement vs PBO; response rates (NRI) were maintained, or in some cases further increased, at 2 years. Results were consistent for achievement of ASDAS LDA and Spinal Pain score ≤2 (data not shown). GUS-related improvements in axial symptoms through W100 were generally consistent in HLA-B27+/- pts (data not shown).

Conclusion: In bio-naïve pts with active PsA and investigator-confirmed sacroiliitis, GUS provided durable improvements in axial symptoms through W100, with substantial proportions of pts achieving and maintaining clinically meaningful improvements.

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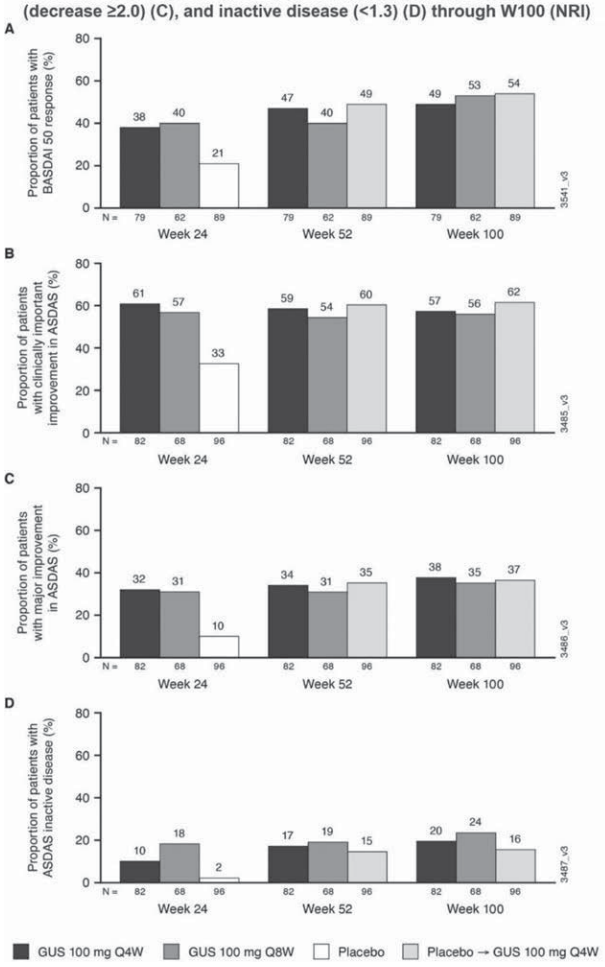
Table 1. Axial symptom assessments through W100 in PsA pts with investigator-confirmed sacroiliitis in DISCOVER-2 (NRI)

	GUS Q4W N=82	GUS Q8W N=68	PBO→GUS Q4W N=96
Change in BASDAI score			
W24, LS mean (95% CI)	-2.5 (-2.9, -2.0)	-2.4 (-3.0, -1.8)	-1.2 (-1.7, -0.7)
Mean (SD)	-2.5 (2.0)	-2.6 (2.4)	-1.4 (2.4)
W52, mean (SD)	-2.9 (2.3)	-2.7 (2.5)	-2.9 (2.6)
W100, mean (SD)	-3.0 (2.3)	-3.1 (2.6)	-3.3 (2.6)
Change in mBASDAI (excludes Q3) score			
W24, LS mean (95% CI)	-2.4 (-2.9, -1.9)	-2.4 (-2.9, -1.8)	-1.2 (-1.7, -0.7)
Mean (SD)	-2.5 (2.1)	-2.6 (2.5)	-1.3 (2.3)
W52, mean (SD)	-2.7 (2.6)	-2.6 (2.5)	-2.9 (2.4)
W100, mean (SD)	-3.3 (2.6)	-3.1 (2.6)	-3.0 (2.4)
Change in Spinal Pain (BASDAI Q2) score			
W24, LS mean (95% CI)	-2.2 (-2.7, -1.7)	-2.3 (-2.9, -1.7)	-0.9 (-1.5, -0.4)
Mean (SD)	-2.3 (2.6)	-2.5 (2.8)	-1.1 (2.5)
W52, mean (SD)	-2.6 (2.7)	-2.5 (2.7)	-2.5 (2.7)
W100, mean (SD)	-2.8 (2.7)	-3.1 (2.8)	-3.0 (2.8)
Change in ASDAS score			
W24, LS mean (95% CI)	-1.3 (-1.6, -1.1)	-1.3 (-1.6, -1.1)	-0.6 (-0.8, -0.4)
Mean (SD)	-1.4 (1.0)	-1.5 (1.2)	-0.7 (1.1)
W52, mean (SD)	-1.5 (1.1)	-1.5 (1.3)	-1.5 (1.3)
W100, mean (SD)	-1.6 (1.2)	-1.7 (1.2)	-1.6 (1.2)

Figure. Proportion of PsA patients with investigator confirmed sacroiliitis achieving BASDAI 50 response (A), and ASDAS clinically important improvement (decrease ≥1.1) (B), major improvement (decrease ≥2.0) (C), and inactive disease (<1.3) (D) through W100 (NRI)



Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Aclaris, Amgen, BMS, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Consultant of: AbbVie, Aclaris, Amgen, BMS, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Grant/research support from: AbbVie, Aclaris, Amgen, BMS, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Inmagene, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Philip Helliwell Speakers bureau: AbbVie, Janssen, and Novartis, Consultant of: Eli Lilly, Janssen, and Pfizer, Dafna D Gladman Consultant of: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Denis Poddubnyy Consultant of: AbbVie, Eli Lilly, GlaxoSmithKline, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, MDS, Novartis, and Pfizer, Xenofon Baraliakos Speakers bureau: AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Stephen Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma, Employee of: Imaging Rheumatology BV, Atul Deodhar Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, Glaxo Smith & Kline, Novartis, Pfizer, and UCB

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POS1038

GUSELKUMAB EFFICACY IN PSORIATIC ARTHRITIS ASSESSED BY MULTI-DOMAIN COMPOSITE INDICES: DATA FROM THE PHASE 3B COSMOS TRIAL IN A TNFI-IR POPULATION

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Background: The Phase 3b COSMOS study (NCT03796858) demonstrated the efficacy and safety of guselkumab (GUS), an IL-23 p19 subunit inhibitor, in patients (pts) with psoriatic arthritis (PsA) who had inadequate response (IR; insufficient efficacy or intolerance) to 1–2 tumour necrosis factor inhibitors (TNFi).[1]

Objectives: Assess the efficacy of GUS 100 mg Q8W in TNFi-IR pts through 1 year by using and comparing 6 multi-domain composite indices validated in PsA.

Methods: In total, 285 pts (189 GUS, 96 placebo [PBO]) were enrolled in COSMOS; mean age was 49 years and mean disease duration was 8.4 years.[1] Pts who received PBO crossed over to GUS at either Week (W) 16 (early escape, n=45/96) or W24 (planned, n=51/96). PsA Disease Activity Score (PASDAS), GRAppa Composite scorE (GRACE), Disease Activity Index for PsA (DAPSA), modified Composite Psoriatic Disease Activity Index (mCPDAI, excludes BASDAI), PsA Response Criteria (PsARC), and Minimal Disease Activity (MDA) were analysed (thresholds as published[2,3]). As-observed data are presented at baseline (BL), W24 and W48, without imputation of missing data.

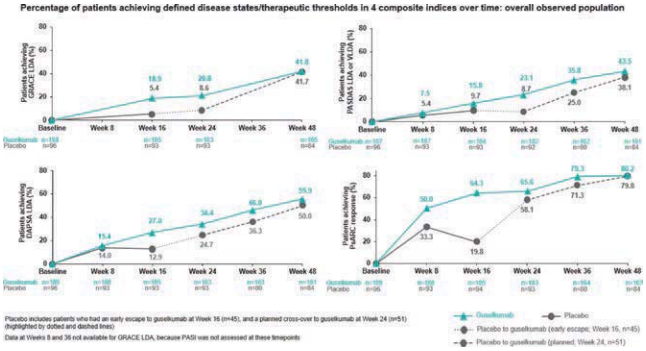

Figure 1.

Results: Overall, 167/189 (88%) GUS and 83/96 (86%) PBO→GUS pts completed the study through W44. Pts had active disease, with similar BL mean values for PASDAS, GRACE, DAPSA and mCPDAI between GUS and PBO groups (Table 1). Across these indices, GUS pts demonstrated robust improvements (45–62%) in mean scores from BL to W48 (Table 1). PBO pts who crossed over to GUS at W16 or W24 also showed rapid improvement in their index scores, with mean values and % improvement at W48 consistent with those observed in pts randomized to GUS at BL (Table 1).

Conclusion: GUS provided robust and substantial benefits to pts with active TNFi-IR PsA across multiple domains. Importantly, rates of achieving low levels of disease activity continued to increase through the duration of the study without an observable plateau at W48. Thresholds for DAPSA and PsARC response were easier to achieve than comprehensive indices with more domains that are required to improve simultaneously (eg GRACE, PASDAS, MDA). GUS performed well regardless of the focus of the composite indices (joints, skin, enthesitis, dactylitis, or patient-reported outcomes). Together, these findings support the role of GUS as an effective treatment option for the diverse domains of PsA.

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Table 1. As observed mean values (± standard deviation) for composite indices

	PASDAS		GRACE		DAPSA		mCPDAI	
	GUS Q8W	PBO→ GUS	GUS Q8W	PBO→ GUS	GUS Q8W	PBO→ GUS	GUS Q8W	PBO→ GUS
BL	6.4	6.2	6.0	5.6	45.5	40.6	7.3	7.1
N	±1.0	±0.9	±1.1	±1.0		±15.8	±2.2	±2.2
	187	*96*	*188*	*96*	±19.9	*96*	*187*	*96*
					189			
W24	4.3	4.8	3.7	4.3	23.7	26.9	4.6	5.3
N	±1.5	±1.3	±1.6	±1.4		±17.5	±2.3	±2.0
	182	*92*	*183*	*93*	±17.9	*93*	*182*	*92*
					183			
W48	3.5	3.6	2.8	2.9	17.5	16.3	3.7	3.8
N	±1.5	±1.4	±1.7	±1.6		±11.9	±2.4	±1.9
	161	*84*	*165*	*84*	±16.7	*84*	*165*	*84*
					161			
% improvement from BL at W48	45.3	41.9	53.3	48.2	61.5	59.9	49.3	46.5

Among the 4 indices with defined disease states/therapeutic thresholds for low disease activity (LDA) (Figure 1), those focusing on joints (PsARC [4 components] and DAPSA [5 components]) resulted in the highest response rates (range, 50–80%); LDA according to GRACE (8 items, including skin) and PASDAS (8 items, focus on musculoskeletal with no skin assessment) was attained less frequently (range, 38–44%). Using the PsARC, 50% of GUS pts responded as early as W8. Response rates among GUS-treated pts generally did not plateau by W48 (Figure 1). At W48, 33% and 30% of GUS and PBO→GUS pts, respectively, achieved a status of MDA.

POS1039 DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 INHIBITOR, IN A PHASE 2 TRIAL IN PSORIATIC ARTHRITIS: ACHIEVEMENT OF MINIMAL DISEASE ACTIVITY AND ITS COMPONENTS

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Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase in the Janus kinase (JAK) family that mediates the signalling of multiple cytokines, including those central to the immunopathogenesis of psoriatic arthritis (PsA), such as IL-23. Deucravacitinib (DEUC) is a novel, oral, selective, allosteric inhibitor of TYK2 that acts by binding to the unique regulatory domain on the enzyme. In a Phase 2 trial in patients with active PsA, DEUC was significantly more efficacious than placebo (PBO) after 16 weeks of treatment and was well tolerated.[1]
Objectives: This analysis further evaluated the effect of DEUC in this trial on achievement of individual components of minimal disease activity (MDA).
Methods: This double-blind, multicenter Phase 2 trial (NCT03881059) enrolled patients (n=203) with a PsA diagnosis ≥6 months who fulfilled Classification Criteria for Psoriatic Arthritis at screening and had active joint disease (≥3 tender and ≥3 swollen joints), high-sensitivity C-reactive protein ≥3mg/L, and ≥1 plaque psoriasis lesion (≥2cm). Eligible patients had failed or were intolerant to ≥1 nonsteroidal anti-inflammatory, conventional synthetic DMARD, and/or 1 tumour necrosis factor inhibitor (≤30%). Patients were randomized 1:1:1 to receive PBO, DEUC 6mg once daily (QD), or 12mg QD. The percentage of patients achieving MDA (5/7: tender joint count [TJC] ≤1, swollen joint count [SJC] ≤1, tender entheseal points [TEP] ≤1, Patient Global Assessment of disease activity [PtGA] ≤20, Patient Global Assessment of pain [Pain] ≤15, Health Assessment Questionnaire-Disability Index [HAQ-DI] ≤0.5, and Psoriasis Area and Severity Index [PASI] ≤1 or body surface area [BSA] ≤3%) as well as proportions of patients achieving each of the MDA components in all patients, MDA responders, and nonresponders were assessed through Week 16.
Results: Of 203 patients randomized, 180 (89%) completed 16 weeks of treatment (PBO, 58/66 [88%]; DEUC 6mg QD, 63/70 [90%]; DEUC 12mg QD, 59/67 [88%]). Demographic and baseline disease characteristics were generally similar across groups. Although no patient had met 5 of 7 criteria required for achieving MDA at baseline, several individual components of MDA were met at baseline, most frequently TEP ≤1 (PBO, 57.6%; DEUC 6mg QD, 64.3%; DEUC 12mg QD, 65.7%). After 16 weeks of treatment, 7.6%, 22.9%, and 23.9% of patients in the PBO, DEUC 6mg QD, and DEUC 12mg QD groups, respectively, achieved MDA response. Treatment with DEUC was associated with a numerically greater mean reduction from baseline in all MDA components versus PBO over 16 weeks of treatment in all patients. At Week 16, more patients receiving DEUC versus PBO achieved the threshold for each of the MDA components (Figure 1).
Conclusion: In this study, patients treated with DEUC achieved a higher rate of MDA response compared with patients treated with PBO after 16 weeks of treatment. More patients receiving DEUC treatment achieved each of the MDA components compared with patients receiving PBO.

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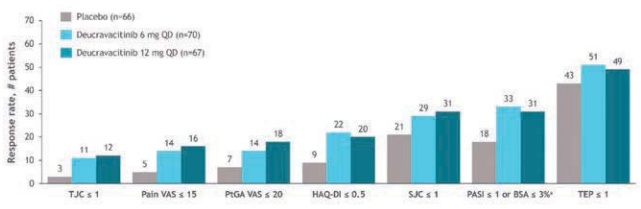
[1] Mease PJ et al. Efficacy and Safety of Selective TYK2 Inhibitor, Deucravacitinib, in a Phase 2 Trial in Psoriatic Arthritis. *Ann Rheum Dis.* (In Press).

Figure. Achievement of MDA components at Week 16



*Patients who had PASI ≤ 1 or BSA ≤ 3% at baseline did not have PASI assessments done and were imputed as nonresponders at Week 16, therefore the actual numbers of patients achieving the PASI component of MDA are likely underrepresented.
BSA, body surface area; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; Pain, Patient Global Assessment of pain; PASI, Psoriasis Area Severity Index; PtGA, Patient Global Assessment of disease activity; QD, once daily; SJC, swollen joint count; TEP, tender entheseal point; TJC, tender joint count; VAS, visual analogue scale.

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Disclosure of Interests: Arthur Kavanaugh Grant/research support from: Clinical research sponsored by Abbott, Amgen, Janssen, and UCB, Laura Coates Speakers bureau: Has been paid as a speaker for AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB., Consultant of: Worked as a paid consultant for AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB., Grant/ research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis, Joseph F. Merola Consultant of: Consultant and/or investigator: Amgen, AbbVie, Biogen, Bristol-Myers Squibb, Dermavant, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB., Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB., Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Miroslawa Nowak Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Subhashis Banerjee Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Lauren Hippeli Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Thomas Lehman Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb
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POS1040 SAFETY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 INHIBITOR: AS ASSESSED BY LABORATORY PARAMETERS – RESULTS FROM A PHASE 2 TRIAL IN PSORIATIC ARTHRITIS AND 2 PHASE 3 TRIALS IN PSORIASIS

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Background: Deucravacitinib (DEUC) is a novel, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor with a unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibitors. DEUC mediates signalling of key cytokines in psoriatic arthritis (PsA) and psoriasis (PsO). DEUC was well tolerated and efficacious vs placebo (PBO) in a Phase 2 trial in patients (pts) with PsA,[1] and vs PBO or apremilast in 2 Phase 3 PsO trials.[2]
Objectives: To assess the effects of DEUC on multiple laboratory parameters through the first 16 weeks of treatment (PBO-controlled) in these trials.
Methods: The Phase 2 double-blind PsA trial randomised pts (n=203) 1:1:1 to PBO, DEUC 6mg once daily (QD), or 12mg QD. The Phase 3 double-blind PsO trials, POETYK PSO-1 and POETYK PSO-2, randomised pts (n=666 and 1020, respectively) 1:2:1 to PBO, DEUC 6mg QD, or apremilast 30mg twice daily. Changes from baseline in haematologic (neutrophils, lymphocytes, platelets, haemoglobin) and chemistry (cholesterol, triglycerides, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and creatine phosphokinase [CPK]) parameters were evaluated. Shifts in Common Terminology Criteria for Adverse Events (CTCAE; version 5.0) severity grade ≥3 of laboratory abnormalities were assessed.
Results: In the PsA trial, 65% of pts were on concomitant conventional synthetic DMARDs (csDMARDs) and 54.7% of pts were on methotrexate. The vast majority of pts continued to have laboratory parameters within normal range throughout the 3 trials in PsO and PsA. No clinically meaningful changes from baseline were observed in laboratory parameters in pts treated with DEUC, PBO, or apremilast. Rates of CTCAE grade 3 and 4 were rare (≤1 pt) and similar across DEUC-, PBO-, and apremilast-treated pts for the following parameters: lymphocytes, neutrophils, platelets, haemoglobin, AST, ALT, and cholesterol (Table 1). Shifts to CTCAE grades ≥3 in triglycerides and CPK were infrequent and generally comparable across treatment arms.
Conclusion: DEUC treatment did not result in clinically meaningful laboratory changes, abnormalities often seen with JAK 1/2/3 inhibition, through 16 weeks of treatment in a Phase 2 trial in PsA, despite two-thirds of pts being on concomitant csDMARDs, and in 2 large Phase 3 trials in PsO.

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[1] Mease PJ et al. Efficacy and Safety of Selective TYK2 Inhibitor, Deucravacitinib, in a Phase 2 Trial in Psoriatic Arthritis. *Ann Rheum Dis*. (In Press).
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Table 1. Maximal shifts to Grades ≥3 in laboratory parameters, Weeks 0-16

		PsA Phase 2						PsO Phase 3[a]					
CTCAE Term	**Grade**	**Placebo (n=66) n (%)**		**DEUC 6 mg QD (n=70) n (%)**		**DEUC 12 mg QD (n=67) n (%)**		**Placebo (n=419) n (%)**		**DEUC 6 mg QD (n=842) n (%)**		**Apremilast 30 mg BID (n=422) n (%)**	
		BL	**Wk 1-16**	**BL**	**Wk 1-16**	**BL**	**Wk 1-16**	**BL**	**Wk 1-16**	**BL**	**Wk 1-16**	**BL**	**Wk 1-16**
Lymphocyte count decreased	3	0	0	0	1 (1.4)	0	0	0	1 (0.2)	0	1 (0.1)	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0
Neutrophil count decreased	3	0	0	0	0	0	0	0	1 (0.2)	1 (0.1)	1 (0.1)	0	0
	4	0	0	0	0	0	0	0	0		0	0	0
										0			
Platelet count decreased	3	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0
Anaemia	3	0	0	0	0	0	0	0	0	0	0	0	1 (0.2)
	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Alanine aminotransferase increased	3	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0
Aspartate aminotransferase increased	3	0	0	0	0	0	1 (1.6)	00	0	0	1 (0.1)	0	1 (0.2)
	4	0	0	0	0	0	0		0	0	0	0	0
CPK increased	3	0	1 (1.5)	0	0	0	0	1 (0.2)	3 (0.7)	1 (0.1)	5 (0.6)	1 (0.2)	2 (0.5)
	4	0	0	0	0	0	1 (1.6)	0	1 (0.2)	0	6 (0.7)	0	1 (0.2)
Cholesterol high	3	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0
Hypertriglyceridemia	3	0	0	1 (1.4)	2 (2.9)	1 (1.6)	4 (6.0)	2 (0.5)	6 (1.5)	4 (0.5)	12 (1.5)	3 (0.7)	8 (2.0)
	4	0	0	1 (1.4)	1 (1.4)	0	0	1 (0.2)	0	1 (0.1)	2 (0.2)	0	0

[a]POETYK PSO-1 and PSO-2 pooled data.BID, twice daily; BL, baseline; CPK, creatine phosphokinase; CTCAE, Common Terminology Criteria for Adverse Events; DEUC, deucravacitinib; N/A, not applicable because there is no haemoglobin value for CTCAE Grade 4 (life-threatening consequences; urgent intervention indicated); PsA, psoriatic arthritis; PsO, psoriasis; QD, once daily; Wk, week.

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Disclosure of Interests: Roy M. Fleischmann Consultant of: Abbvie, Acea, Akros, Amgen, Bristol Myers Squibb, Celtrion, Eli Lilly & Co., Galvani, Gilead Sciences, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Sandoz, Sanofi Aventis, Taiho, and UCB., Grant/research support from: AbbVie, Acea, Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly & Co., Gilead Sciences, GlaxoSmithKline, Janssen, Merck, Pfizer, Roche/Genentech, Samumed, Sanofi Aventis, and UCB, Diamant Thaçi Consultant of: Advisory board, principal investigator, and lecture fees: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DS-Pharma, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche-Posay, Samsung, Sandoz-Hexal, Sanofi, and UCB., Melinda Gooderham Consultant of: Investigator, speaker, advisory board member or consultant for: AbbVie, Akros, Amgen, Anaptys Bio, Arcutis, Aslan, Bausch, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermira, Dermavant, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Janssen, Kyowa Kirin, Leo Pharma, Medimmune, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, SUN Pharma, and UCB., Bruce Strober Consultant of: Honoraria or consultation fees: AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Immunic Therapeutics, Bristol Myers Squibb, Connect Biopharma, Dermavant, Equillium, Janssen, Leo Pharma, Eli Lilly, Maruho, Meiji Seika Pharma, Mindera, Novartis, Pfizer, GlaxoSmithKline, UCB Pharma, Sun Pharma, Ortho Dermatologics, Regeneron, Sanofi-Genzyme, and Ventyxbio; Speaker: AbbVie, Janssen, Lilly, and Sanofi-Genzyme; Scientific co-director (consulting fee): CorEvitas Psoriasis Registry; Investigator: AbbVie, Cara, CorEvitas Psoriasis Registry, Dermavant, Eli Lilly/Dermira, and Novartis., Neil J Korman Consultant of: Advisory board, consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Principia, Regeneron, Sanofi-Genzyme, Sun Pharma, and UCB, Grant/research support from: Grant support/principal investigator: AbbVie, Amgen, Argenx, Bristol Myers Squibb, Celgene, Chemocentryx, Eli Lilly, Galderma, Kyowa Hakko Kirin, Leo Pharma, Menlo, Principia, Prothena, Rhizen, Syntimmune, Trevi, and Xbiotech. Speaker: AbbVie, Eli Lilly, Janssen, Novartis, Regeneron, and Sanofi-Genzyme., Subhashis Banerjee Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Thomas Lehman Shareholder of: Employees and shareholders of Bristol Myers Squibb, Employee of: Employees and shareholders of Bristol Myers Squibb, Miroslawa Nowak Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Antoine Sreih Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Akimichi Morita Consultant of: Research grants, consulting fees, and/or speaker's fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Eisai, Janssen, Kyowa Hakko Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe, Nichi-Iko, Nippon Kayaku, Novartis, Pfizer, Sun Pharmaceutical Industries, Taiho Pharmaceutical, Torii Pharmaceutical, Ushio, and UCB Pharma., Grant/research support from: Research grants, consulting fees, and/or speaker's fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Eisai, Janssen, Kyowa Hakko Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe, Nichi-Iko, Nippon Kayaku, Novartis, Pfizer, Sun Pharmaceutical Industries, Taiho Pharmaceutical, Torii Pharmaceutical, Ushio, and UCB Pharma., Philip J Mease Consultant of: Consulting and/or speaker fees: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, and UCB., Grant/research support from: Research grants: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, and UCB;

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POS1041

LONG-TERM EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS REFRACTORY TO BIOLOGIC THERAPIES: 2-YEAR RESULTS FROM THE PHASE 3 SELECT-PSA 2 STUDY

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Background: Upadacitinib (UPA), an oral Janus kinase (JAK) inhibitor, demonstrated efficacy and safety in patients (pts) with psoriatic arthritis (PsA) and prior inadequate response or intolerance to ≥1 biologic disease-modifying antirheumatic drug (bDMARD) at week (wk) 56 in the phase 3 SELECT-PsA 2 study.[1]

Objectives: To evaluate the efficacy and safety of UPA at wk 104 from the ongoing long-term extension of SELECT-PsA 2.

Methods: Pts were randomized to UPA 15 mg (UPA15), UPA 30 mg (UPA30), or placebo (PBO) for 24 wks; PBO pts were then switched to UPA15 or UPA30. For continuous UPA treatment groups, efficacy endpoints at wk 104 were analyzed using non-responder imputation (NRI) and as observed (AO) (binary endpoints) or mixed-effect model repeated measures (MMRM) and AO (continuous endpoints). Treatment-emergent adverse events (TEAEs) were summarized for pts who received ≥1 dose of study drug using visit-based cut-off at wk 104.

Results: A total of 641 pts received ≥1 dose of study drug. At wk 104, 38.4% of all patients had discontinued study drug, with the highest discontinuation observed

in patients randomized to PBO at baseline (all PBO: 46.7%). The most common reasons for discontinuation were lack of efficacy (UPA15: 12.3%, UPA30: 8.7%, all PBO: 21.7%) and adverse event (UPA15: 10.9%, UPA30: 13.3%, all PBO: 12.7%). The proportion of UPA pts that achieved ACR20/50/70, MDA, PASI75/90/100, and resolution of dactylitis and enthesitis were generally similar, or further improved, with 104 wks of treatment vs 56 wks[1] (Table 1). Similarly, mean change from baseline in HAQ-DI, patient's assessment of pain, BASDAI, and ASDAS was improved with UPA treatment. At 104 wks of therapy, clinical responses were largely similar with UPA15 and UPA30. Generally, safety data at wk 104 (Figure 1) were consistent with that reported at wk 56.[1] Rates of serious infection, herpes zoster, hepatic disorder, anemia, neutropenia, lymphopenia, and CPK elevation remained numerically higher with UPA30 vs UPA15, while rates of malignancies, MACE, and VTE were similar for both UPA groups. One death was reported with UPA15 (unexplained due to lack of information; however, the patient had recently been diagnosed with ovarian cancer) and 2 with UPA30 (pancytopenia and COVID-19 pneumonia).

Table 1. Efficacy Endpoints at Week 104

Endpoint	UPA15 (n=211)		UPA30 (n=218)	
Proportion of Pts (%)[a]	**NRI**	**AO**	**NRI**	**AO**
ACR20	55.5	80.3	54.6	81.8
ACR50	44.5	62.9	39.9	59.4
ACR70	23.2	32.2	21.6	31.5
Minimal Disease Activity (MDA)	29.4	41.3	33.9	49.3
PASI75[b]	47.7	69.8	52.7	81.1
PASI90[b]	37.7	55.2	44.3	67.8
PASI100[b]	23.1	35.4	35.9	55.6
Resolution of enthesitis by LEI[c]	39.8	67.8	37.5	68.4
Resolution of dactylitis by LDI[d]	54.5	97.4	52.0	96.9
Change from BL[e]	**MMRM**	**AO**	**MMRM**	**AO**
Health Assessment Questionnaire - Disability Index (HAQ-DI)	-0.36	-0.39	-0.50	-0.53
Patient's assessment of pain (numeric rating scale)	-2.7	-3.0	-2.9	-3.1
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[f]	-2.6	-3.0	-2.6	-2.9
Ankylosing Spondylitis Disease Activity Score (ASDAS)[f]	-1.4	-1.7	-1.3	-1.5

ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology criteria; AO, as observed; BL, baseline; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MMRM, mixed effect model repeated measurement; NRI, non-responder imputation; PASI75/90/100, ≥75%/90%/100% improvement in Psoriasis Area and Severity Index; pts, patients; UPA, upadacitinib.[a]Data shown as NRI and AO for binary endpoints.[b]For pts with psoriasis affecting ≥3% of body surface area at BL. [c]For pts with LEI >0 at BL; resolution LEI=0.[d]For pts with LDI >0 at BL; resolution LDI=0. [e]Data shown as MMRM (LS mean) and AO (mean) for continuous endpoints.[f]For pts with psoriatic spondylitis at BL.

Conclusion: In PsA pts with prior inadequate response or intolerance to ≥1 bDMARD, clinical responses were maintained with UPA15 and UPA30 up to 2 years of treatment. No new safety signals were identified in this long-term extension.

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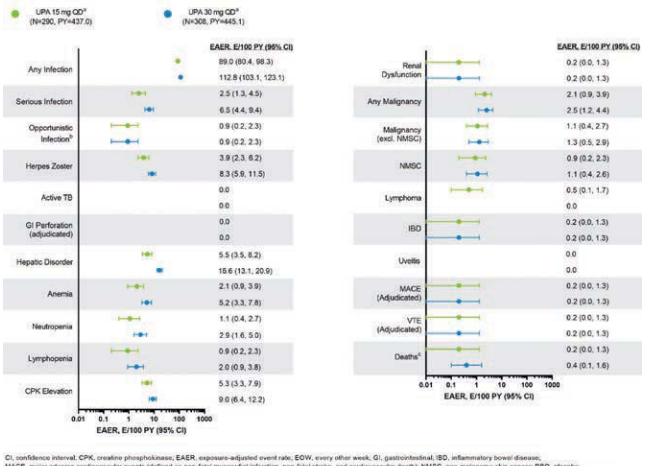
[1] Mease PJ, et al. *Rheumatol Ther*. 2021;8:903-19.

Figure: Exposure-Adjusted Event Rates of Treatment-Emergent Adverse Events at Week 104



CI, confidence interval; CPK, creatine phosphokinase; EAER, exposure-adjusted event rate; EOW, every other week; GI, gastrointestinal; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular events (defined as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death); NMSC, non-melanoma skin cancer; PBO, placebo; PY, patient years; QD, once daily; TB, tuberculosis; UPA, upadacitinib; VTE, venous thromboembolism (includes deep vein thrombosis [DVT] and pulmonary embolism [PE] [fatal and non-fatal]).
[a]Includes PBO patients that switched to UPA.
[b]Opportunistic infections excluding tuberculosis and herpes zoster.
[c]Deaths: UPA15: 1 unexplained; UPA30: 1 due to pancytopenia and 1 due to COVID-19 pneumonia.

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POS1042

IMPACT OF RISANKIZUMAB ON IMPROVING HEALTH-RELATED QUALITY OF LIFE, WORK PRODUCTIVITY, AND REDUCING FATIGUE AMONG PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: A POOLED ANALYSIS OF TWO PHASE 3 CLINICAL TRIALS

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Background: Risankizumab (RZB) has been approved in the UK and Europe for the treatment of adults with active PsA. Patient-reported outcomes (PROs) are important tools for understanding a therapy's efficacy from the patient's perspective.

Objectives: This study evaluated the impact of RZB versus placebo on health-related quality of life (HRQoL), fatigue, and work productivity in patients with psoriatic arthritis (PsA) and inadequate response to 1 or 2 biologics and/or ≥1 conventional synthetic DMARDs in two Phase 3 trials (KEEPsAKE 1&2).

Methods: Eligible patients with active PsA (n=1402) were randomized (1:1) to receive risankizumab 150 mg (n=706) or placebo (n=696). Patient-reported

outcomes assessed were 36-Item Short-Form Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-Fatigue), EQ-5D-5L, and Work Productivity and Activity Impairment–PsA questionnaire. Least squares (LS) mean changes from baseline at Week 24 were compared between risankizumab versus placebo by mixed-effects repeated regression modeling.

Results: At Week 24, risankizumab- versus placebo-treated patients reported greater improvements in LS mean changes with between-group differences (all nominal $P<0.001$) in SF-36 physical component score (mean difference=3.5, 95% confidence interval [CI] 2.7, 4.2) and mental component score (mean difference=1.8, 95% CI 0.9, 2.6), FACIT-Fatigue (mean difference=2.5, 95% CI 1.5, 3.4), EQ-5D-5L index score (mean=0.07, 95% CI 0.05, 0.09), and EQ-5D-5L visual analogue scale score (mean difference=5.8, 95% CI 3.6, 8.0). In addition, risankizumab- versus placebo-treated patients reported greater reductions with between-group differences (all nominal $P<0.001$) in overall work impairment (mean difference= –8.9%, 95% CI –13.1, –4.7), activity impairment (mean difference= –7.7%, 95% CI –10.3, –5.2), and presenteeism (mean difference= –9.8%, 95% CI –13.3, –6.3).

Conclusion: Compared to placebo, risankizumab resulted in greater improvements in HRQoL, fatigue, and work productivity among patients with PsA.

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POS1043

STRONG CORRELATION BETWEEN SHORT- VS LONG-FORM COMPOSITE MEASURES OF PSORIATIC ARTHRITIS DISEASE ACTIVITY IN A TNFI-IR POPULATION TREATED WITH GUSELKUMAB: DATA FROM THE PHASE 3B COSMOS TRIAL

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Background: Accurate assessment of psoriatic arthritis (PsA) disease activity in clinical practice requires a feasible, continuous, multidimensional composite instrument to assess key domains of this heterogeneous disease. While currently available composite tools used in PsA, including the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis Composite Exercise (GRACE) and the PsA Disease Activity Score (PASDAS), are useful in clinical trials, their complexity and time required to complete limit their use in clinical practice.[1] Abbreviated instruments, known as 3 visual analogue scale (VAS) and 4VAS, have demonstrated good performance in an observational study, but further testing was recommended.[2]

Objectives: Explore the correlation between 3VAS or 4VAS and GRACE, PASDAS and measures of quality of life using data from COSMOS.

Methods: The Phase 3b COSMOS study assessed guselkumab (GUS) 100mg Q8W versus placebo (PBO) in tumour necrosis factor inhibitor (TNFi) inadequate response (IR, inadequate efficacy or intolerance) pts with active PsA.[3] Pts who received PBO crossed over to GUS at either Week (W) 16 (early escape [EE], n=45/96) or W24 (planned, n=51/96). Each domain of the 3VAS (physician global, pt global, pt skin) and 4VAS (physician global, pt pain, pt joint, pt skin) was evaluated using a 0–10 VAS (higher score=more active disease), and calculated mean scores were plotted over time in a pt-continuer population (those with W0 *and* W48 data). Pearson correlation assessed relationships between observed values over time for 3VAS/4VAS versus GRACE, PASDAS, the Health Assessment Questionnaire-Disability Index (HAQ-DI), and the 36-item Short Form Health Survey Physical Component Summary (SF-36 PCS) score.

Results: Data from 285 pts were examined (GUS, n=189; PBO, n=96). Substantial improvements (>45%) were seen in GRACE, PASDAS, 3VAS and 4VAS scores through W48 in GUS-treated pts (Table 1), with separation from PBO as early as W8 (Figure 1). Strong correlations between 3VAS/4VAS and GRACE (r=0.83–0.92)/PASDAS (r=0.72–0.85) were observed in GUS-randomized pts at each visit (Table 1). 3VAS/4VAS showed moderate correlation with HAQ-DI (r=0.45–0.63) and SF-36 PCS (r=–0.40 to –0.65). Consistent results were observed in PBO→GUS pts.

Table 1. Observed composite index scores and Pearson correlation coefficients by visit

	Mean (SD)				Correlation of 3VAS with		Correlation of 4VAS with	
Visit	**GRACE**	**PASDAS**	**3VAS**	**4VAS**	**GRACE**	**PASDAS**	**GRACE**	**PASDAS**
GUS								
BL	6.0 (1.1)	6.4 (1.0)	6.6 (1.5)	6.6 (1.5)	0.85	0.72	0.83	0.72
N	*188*	*187*	*188*	*188*				
W8	–	5.2 (1.3)	4.5 (1.8)	4.7 (1.8)	–	0.80	–	0.81
N		*187*	*188*	*188*				
W16	4.0 (1.7)	4.7 (1.6)	4.1 (2.0)	4.2 (2.1)	0.91	0.85	0.92	0.85
N	*185*	*184*	*185*	*185*				
W24	3.7 (1.6)	4.3 (1.5)	3.7 (1.9)	3.9 (2.0)	0.88	0.84	0.89	0.84
N	*183*	*182*	*183*	*183*				
W48	2.8 (1.7)	3.5 (1.5)	2.7 (1.9)	2.8 (2.0)	0.90	0.83	0.90	0.83
N	*165*	*161*	*168*	*168*				
PBO→GUS (at W16 [n=45] or W24 [n=51])								
BL	5.7 (1.0)	6.2 (0.9)	6.1 (1.5)	6.1 (1.5)	0.81	0.63	0.83	0.66
N	*96*	*96*	*96*	*96*				
W8	–	5.5 (1.3)	5.3 (1.9)	5.3 (1.9)	–	0.78	–	0.80
N		*93*	*94*	*94*				
W16	5.1 (1.6)	5.5 (1.5)	5.3 (2.1)	5.4 (2.1)	0.91	0.87	0.92	0.88
N	*93*	*93*	*94*	*94*				
W24	4.4 (1.4)	4.8 (1.3)	4.4 (1.9)	4.5 (1.9)	0.91	0.82	0.90	0.81
N	*93*	*92*	*93*	*93*				
W48	2.9 (1.6)	3.6 (1.4)	2.8 (2.0)	3.0 (2.1)	0.91	0.86	0.92	0.85
N	*84*	*84*	*85*	*85*				

BL, baseline; SD, standard deviation

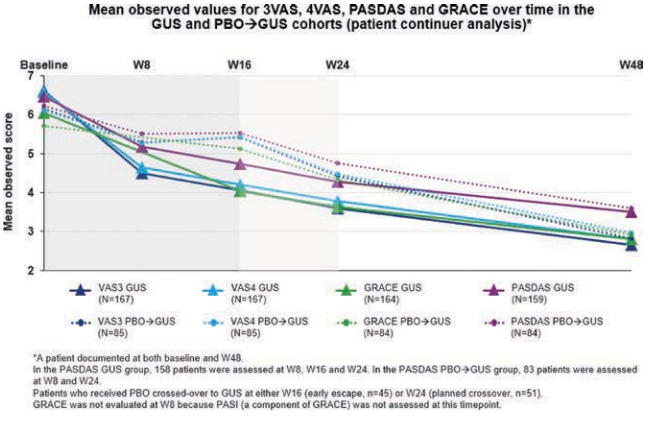

Figure 1.

Conclusion: In these TNFi-IR pts, GUS treatment led to substantial improvements in PsA disease activity through 1 year using several composite indices. All indices, including the 3VAS/4VAS, allowed early discrimination between the GUS and PBO cohorts. The strong correlation between 3VAS/4VAS and GRACE/PASDAS in this pt population is promising and highlights that abbreviated composite indices can provide an accurate assessment of disease activity that may, because of better feasibility, lead to a wider use of such instruments and thus improve pt care. As a next step, thresholds for disease states should be further evaluated.

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[3] Coates LC *et al. Ann Rheum Dis* 2021 (epub)

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POS1044

GUSELKUMAB PROVIDES CONSISTENT AND DURABLE PAIN IMPROVEMENT IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS OF 2 PHASE 3, RANDOMIZED, CONTROLLED CLINICAL TRIALS

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Background: Guselkumab (GUS), an anti-IL23p19-subunit mAb, demonstrated significant efficacy vs placebo (PBO) in achieving ACR20 response at week (W) 24 in patients (pts) with active PsA in phase 3 trials, DISCOVER-1&2 (D1&2).[1,2] Pts with PsA report pain relief as a treatment priority.[3]

Objectives: To assess GUS treatment effect through 2 years on pt-reported pain across outcome measures.

Methods: Pts with active PsA in D1 (n=381; 31% received 1-2 prior TNFi) and D2 (n=739; biologic-naïve) were randomized (1:1:1) to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W at W24 (PBO→Q4W). Pts rated pain using visual analog scale (VAS; 0-10; Pt Pain) and reported Bodily Pain intensity over past 4 W via 36-Item Short-Form Health Survey question 21 (0-5). Pts with spondylitis and peripheral arthritis at baseline (BL) rated Spinal and Joint Pain (0-10). Observed mean change, % improvement from BL in tender (TJC; 0-68) and swollen joint counts (SJC; 0-66), and proportion of pts achieving ≥20/≥50% improvement in Pt Pain (nonresponder imputation [NRI]) were evaluated.

Results: In D2, mean BL for Bodily Pain (range: 4.4-4.5), Pt Pain (6.2-6.3), Spinal Pain (6.5-6.7), Joint Pain (6.3-6.8), SJC (11.7-12.9) and TJC (19.8-22.4) indicated moderate pain and disease activity at study outset. GUS-treated pts reported ~2x improvement in Pt Pain, Spinal Pain, Joint Pain, and Bodily Pain intensity at W24 vs PBO, which were maintained or increased at W52 and W100. PBO→Q4W pts had similar improvements. Pt-reported pain appeared more sensitive to treatment effect, with larger differences in % improvement vs PBO than physician-reported TJC/SJC at W24. D1 showed consistent results through 1 year. In 748 GUS-treated pts across D1&2, substantial proportions achieved meaningful improvement in Pt Pain at early time points: 32% (W4) and 48% (W8) achieved ≥20% improvement; 28% (W12) and 33% (W16) achieved ≥50% improvement. At W24, 63%/39% reported ≥20%/≥50% improvement in pain.

Conclusion: GUS provided consistent and durable improvements in pt-reported pain across several outcome measures. Pt-reported pain as an early and sensitive indicator of treatment effect in pts with active PsA and additional factors merits further evaluation.

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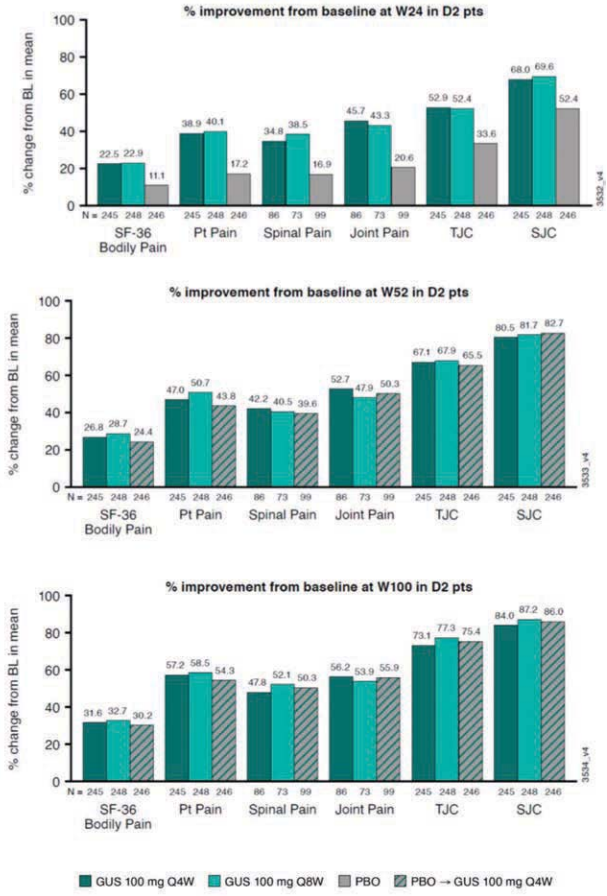
Table 1. Observed Mean (SD) Change from Baseline in Pain Scores, TJC, and SJC at W24, W52, and W100 in DISCOVER-2

	W24			W52			W100		
	GUS Q4W	**GUS Q8W**	**PBO**	**GUS Q4W**	**GUS Q8W**	**PBO→Q4W**	**GUS Q4W**	**GUS Q8W**	**PBO→Q4W**
Pt Pain (0-10)**,* N**	240	243	243	229	234	231	220	224	215
	-2.39 (2.35)	-2.53 (2.47)	-1.08 (2.42)	-2.89 (2.68)	-3.20 (2.56)	-2.75 (2.66)	-3.52 (2.62)	-3.69 (2.63)	-3.41 (2.58)
Spinal Pain (0-10), **+ N**	80	65	92	79	64	88	76	61	82
	-2.26 (2.57)	-2.54 (2.70)	-1.13 (2.48)	-2.74 (2.63)	-2.67 (2.71)	-2.65 (2.69)	-3.11 (2.67)	-3.44 (2.71)	-3.37 (2.66)
Joint Pain (0-10),**+ N**	80	65	92	79	64	88	76	61	82
	-2.88 (2.17)	-2.90 (2.68)	-1.40 (2.91)	-3.32 (2.27)	-3.21 (2.76)	-3.42 (2.92)	-3.54 (2.35)	-3.61 (2.77)	-3.80 (2.95)
SF-36 (Q21; 0-5)**, N**	240	243	242	229	234	230	220	224	214
	-0.99 (1.03)	-1.03 (1.12)	-0.50 (1.11)	-1.18 (1.33)	-1.29 (1.17)	-1.10 (1.16)	-1.39 (1.25)	-1.47 (1.38)	-1.36 (1.27)
TJC (0-68)**, N**	240	243	243	228	234	231	220	224	213
	-11.85(9.88)	-10.37(9.49)	-7.26(11.15)	-15.04(10.51)	-13.44(10.03)	-14.15(11.39)	-16.37(10.70)	-15.27(11.10)	-16.29(11.27)
SJC (0-66)**, N**	240	243	243	228	234	231	220	224	213
	-8.77(5.46)	-8.14(6.07)	-6.44(7.20)	-10.38(6.17)	-9.56(6.28)	-10.17(6.79)	-10.83(6.66)	-10.20(6.88)	-10.58(6.15)

*ACR, DAPSA, MDA: VAS 0-10; +BASDAI: VAS 0-10ACR=American College of Rheumatology; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; DAPSA=Disease Activity in Psoriatic Arthritis; GUS=guselkumab; MDA=minimal disease activity; PBO=placebo; pt=patient; Q=question; QxW=every x week; SD=standard deviation; SF-36=36-Item Short-Form Survey; SJC=swollen joint count; TJC=tender joint count; VAS=visual analog scale; W=week

Figure: Percent Improvement from Baseline in Pt-Reported Pain Scores and Physician-Reported TJC and SJC in DISCOVER-2 Pts



BL=Baseline, D2=DISCOVER-2; GUS=guselkumab; PBO=Placebo; pt=patient; QxW=every x weeks; SJC=swollen joint count; TJC=tender joint count; W=week

Disclosure of Interests: Peter Nash Consultant of: AbbVie, Bristol Myers Squibb, Boehringer, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Roche, Sandoz, and Sun Pharma, Grant/research support from: AbbVie, Bristol Myers Squibb, Boehringer, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Roche, Sandoz, and Sun Pharma, Lai-Shan Tam Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly, Janssen, Pfizer, and Sanofi, Grant/research support from: Amgen, Boehringer Ingelheim, GSK, Janssen, Novartis, and Pfizer, Wen-Chan Tsai Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer, and Janssen, Ying Ying Leung Consultant of: AbbVie, Eli Lilly, Janssen, and Novartis and on advisory board for Janssen, Daniel Furtner Shareholder of: Johnson & Johnson, Employee of: Janssen, a division of Johnson & Johnson Pte. Ltd, Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Yanli Wang Consultant of: Janssen, Employee of: Cytel, Inc., May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Jonathan Sherlock Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Daniel Cua Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC

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POS1045

MASS SPECTROMETRY-BASED PROTEOMICS FOR THE IDENTIFICATION OF CANDIDATE SERUM PROTEIN BIOMARKERS THAT MAY PREDICT TREATMENT RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) has identified a need for biomarkers to predict which patients (pts) with psoriatic arthritis (PsA) are most likely to respond to a specific therapy. Failure to identify effective treatments early on results in sub-optimal PsA disease management. Tofacitinib is an oral JAK inhibitor for the treatment of PsA. The efficacy and safety of tofacitinib 5 and 10 mg twice daily (BID) in pts with PsA have been demonstrated.[1,2]

Objectives: To identify protein biomarker candidates, which may identify responders (R) vs non-responders (NR) to treatment of PsA, using mass spectrometry-based proteomics.

Methods: Baseline (BL) serum samples from pts with PsA receiving tofacitinib 5 or 10 mg BID, adalimumab or placebo in OPAL Broaden (NCT01877668)[1] were analysed. Pts were identified as R and NR based on the Psoriatic Arthritis Disease Activity Score (PASDAS) at Month 3; pts with lowest PASDAS ≤3.2 were defined as R, those with highest PASDAS >3.2 as NR. Two proteomic strategies were employed for analysis of BL serum samples: (1) targeted mass spectrometric multiple reaction monitoring analysis of an in-house panel ('PAPRICA') comprising of 206 proteins, originally developed to distinguish between different arthropathies, and (2) unbiased discovery liquid chromatography-tandem mass spectrometry (LC-MS/MS). PAPRICA data were normalised using two methods: normalisation to stable isotopically labelled peptide spike-ins (SIL; corrects for fluctuations in sample injections/mass spectrometry loading amounts), and normalisation to an endogenous peptide panel representing total serum protein abundance (TSPA; corrects for different amounts of total serum protein across samples). Univariate analyses (Student's t-test) and multivariate machine learning Random Forest (RF) modelling[3] were performed. Univariate analysis of the PAPRICA panel of proteins was performed on R vs NR, and within each treatment arm, with no adjustment for multiplicity.

Results: 96 pts were identified as 47 R and 49 NR based on PASDAS scores. Of pts receiving tofacitinib 5 or 10 mg BID (data pooled), adalimumab or placebo, there were 26 R vs 26 NR, 13 R vs 13 NR and 8 R vs 10 NR, respectively. Results from univariate analysis identified 110 differentially expressed PAPRICA peptides between R vs NR ($p \leq 0.05$). RF multivariate analysis of all data (n=96) revealed a set of PAPRICA peptide signatures with the ability to differentiate between R and NR. Two RF models generated from the PAPRICA peptide data had training area under curves (AUCs) 0.956 [95% CI 0.93, 0.99] (TSPA) and 0.959 [95% CI 0.94, 0.98] (SIL). In total, 115 PAPRICA peptides representing 87 proteins were identified as potential biomarkers for predicting treatment response. Using unbiased discovery LC-MS/MS, univariate analysis of all data revealed one candidate peptide biomarker ($p \leq 0.05$). RF modelling revealed peptides that contributed to two prediction models with training AUCs of 0.903 [95% CI 0.86, 0.96] and 0.928 [95% CI 0.89, 0.96]. In total, from unbiased discovery LC-MS/MS, 66 peptides representing 39 proteins that may act as potential peptide biomarkers were identified in univariate and multivariate analyses.

Conclusion: Using two complementary proteomic approaches and a combination of univariate and machine learning models, a total of 181 candidate biomarker peptides corresponding to 106 proteins have been identified that may act as potential biomarkers for predicting response to treatment of PsA. Further study is required to verify and evaluate these candidate biomarkers, and we will report how these proteins map to biological processes, pathways and networks.

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POS1046 DEUCRAVACITINIB LONG-TERM EFFICACY AND SAFETY IN PLAQUE PSORIASIS: 2-YEAR RESULTS FROM THE PHASE 3 POETYK PSO PROGRAM

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Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signalling of key cytokines (eg, interleukin [IL]-23 and Type I interferons) involved in the pathogenesis of immune-mediated diseases including plaque psoriasis and psoriatic arthritis (PsA). Deucravacitinib is a novel, oral, selective TYK2 inhibitor that achieves high selectivity by uniquely binding to the regulatory domain of the enzyme, rather than to the more conserved active domain. Deucravacitinib showed superior efficacy compared with placebo at 16 weeks in a Phase 2 trial in patients with PsA.[1] The efficacy and tolerability of deucravacitinib in patients with moderate to severe psoriasis were previously demonstrated in 2 pivotal, Phase 3, double-blind trials, POETYK PSO-1 and PSO-2.[2]

Objectives: To assess the long-term efficacy and safety of deucravacitinib in patients with psoriasis in a Phase 3, open-label, long-term extension (LTE) trial.

Methods: The 52-week PSO-1 and PSO-2 trials randomised patients with moderate to severe plaque psoriasis 2:1:1 to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily. Patients could then enrol in the LTE trial and receive open-label deucravacitinib 6 mg once daily.

Results: 1221 patients enrolled in the LTE trial and received ≥1 dose of deucravacitinib. Demographic and baseline disease characteristics were balanced across treatment groups; mean age at disease onset was 28.6 years, mean disease duration was 18.9 years, and 18.0% of patients had PsA at baseline. Cumulative exposures in person-years from randomisation in PSO-1 or PSO-2 and the LTE trial were 2166.9 and 2482.0 for efficacy and safety analyses, respectively. At enrolment in the LTE trial, PASI 75 and sPGA 0/1 response rates were 65.1% and 50.9%, respectively, and were maintained for up to 2 years after initial randomisation (Week 48 of LTE; PASI 75: 75.7%; sPGA 0/1: 56.4% [as observed]). Exposure-adjusted incidence rates per 100 person-years for adverse events were similar in the controlled period (Weeks 0–52) of PSO-1 and PSO-2 and during the cumulative PSO-1, PSO-2, and LTE trial period (229.2 [controlled period] vs 154.4 [cumulative period]), serious adverse events (5.7 vs 6.1), discontinuations (4.4 vs 2.8), deaths (0.2 vs 0.4), herpes zoster (0.9 vs 0.7), malignancies (1.0 vs 0.9), major adverse cardiovascular events (0.3 vs 0.4), and venous thromboembolism (0.1 vs 0.1).

Conclusion: Deucravacitinib demonstrated persistent efficacy and consistent safety profiles in patients with psoriasis for up to 2 years after initial randomisation in the POETYK PSO-1, PSO-2, and LTE trials.

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POS1047 TRAF3IP2, HCP5 AND IL10 GENES POLYMORPHISMS INFLUENCE THE RESPONSE TO TNF-I IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic Arthritis (PsA) is a chronic inflammatory disease, characterized by both articular and periarticular manifestations, usually associated with psoriasis. The identification of the correct therapy for patients is still a critical issue, but the use of biological drugs, such as TNFi (Tumor Necrosis Factor Inhibitors), modified the outcome of PsA patients even if there is great variability in the clinical efficacy. Since the response to drugs is a complex trait, the identification of genetic factors could help to define new genomic biomarkers for more effective and personalized therapy.

Objectives: The aim of this study was to evaluate the potential role of polymorphisms in genes already known to be involved in PsA susceptibility (ERAP1, HCP5, IL10, MIR146, PSORS1C1, STAT4, TNFAIP3 and TRAF3IP2) as predictors of efficacy of treatment, in a cohort of Italian PsA patients, treated with first-line TNF-i, in particular with Etanercept (ETN) and Adalimumab (ADA).

Methods: Polymorphisms were analyzed in a cohort of 163 patients with peripheral PsA. For each patient was estimated the Disease Activity in Psoriatic Arthritis (DAPsA) score. Genotyping was performed by allelic discrimination by TaqMan assay. The possible association between the selected SNPs and mean values of DAPsA differences, at 22 (ΔT22) and 54 (ΔT54) weeks from the beginning of the TNF-i treatment, were evaluated by T-test. A multivariate logistic regression analysis was used to evaluate the contribution of each genetic variant investigated in the TNF-i treatment response.

Results: We have observed that TRAF3IP2 SNP was associated with TNF-i treatment response in PsA patients. In particular, the patients carrying variant alleles seem to respond better to treatment, both at 22 ($P = 0.032$) and 54 weeks ($P = 0.019$). Moreover, the variant allele of TRAF3IP2 SNP resulted associated with a better response of joints involvement. Indeed, the number of tender and swollen joints decrease more in patients carrying variant allele ($P = 0.006$ and $P = 0.024$, respectively). We also observed that PsA patients carrying IL10 variant allele decrease their mean DAPsA value less than patients with wild-type genotype only at 54 weeks of treatment ($P = 0.031$). Also, HCP5 polymorphism showed a difference of mean difference of DAPsA values between genotypes for both follow up, even if these difference does not reach a statistical significance (

P = 0.068 and P = 0.086). The multivariate regression analysis was performed with a stepwise method and it confirmed the involvement of TRAF3IP2 (P = 0.016) and HCP5 (P = 0.035) polymorphisms in the TNF-i response after 22 weeks and of TRAF3IP2 (P = 0.007), IL10 (P = 0.022) and HCP5 (P = 0.036) polymorphisms after 54 weeks. The two final models explain about 6% and 11% of the variability in TNF-i treatment response at 22 and 54 weeks respectively.
Conclusion: Our results suggest that some polymorphisms in genes associated to PsA susceptibility could also play a role in TNFi treatment response and could give a contribution in the definition of a genetic profile associated with the response to anti-TNF drugs.

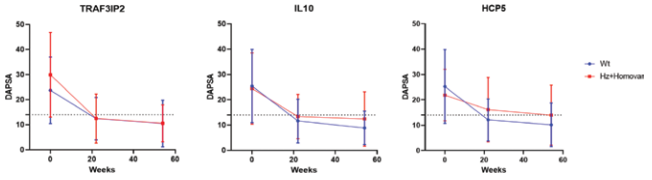

Figure 1. Mean differences of DAPsA values in the genotypic classes for TRAF3IP2, IL10 and HCP5 SNPs. DAPsA = Disease Activity Index for PsA; Wt = wild-type genotype; Hz = heterozygous genotype; Homo var = homozygous variant genotype.

Disclosure of Interests: None declared
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POS1048

SAFETY AND EFFICACY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 INHIBITOR, IN PATIENTS WITH PSORIATIC ARTHRITIS: 52-WEEK RESULTS FROM A RANDOMISED PHASE 2 TRIAL

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Background: Deucravacitinib (DEUC) is a novel, oral, selective, allosteric inhibitor of tyrosine kinase 2 (TYK2) that acts by binding to the unique TYK2 regulatory domain, thereby suppressing signalling of key cytokines (eg, IL-23) involved in skin psoriasis and psoriatic arthritis (PsA) pathogenesis. Results from the initial 16-week (wk), placebo (PBO)-controlled period (Part A) of a 52-wk, blinded Phase 2 trial in PsA showed that DEUC was significantly more efficacious than PBO.[1] The Psoriatic Arthritis Disease Activity Score (PASDAS), a validated comprehensive measure assessing a variety of PsA clinical domains, was used to assess efficacy of DEUC up to 52 wks.
Objectives: Evaluate the safety and efficacy of DEUC in Part B (Wks 16-52) in the Phase 2 PsA trial.
Methods: Patients (pts) with PsA were randomised 1:1:1 to PBO, DEUC 6 mg once daily (QD), or 12 mg QD. After Wk 16 (Part A), pts could enrol in an optional, double-blind period until Wk 52 (Part B). In Part B, pts receiving DEUC who had achieved minimal disease activity (MDA) at Wk 16 continued DEUC treatment and those who had not achieved MDA were switched to ustekinumab (UST) at the approved PsA dose. All pts treated with PBO in Part A switched to UST in Part B. Pts were assessed up to 52 wks for adverse events (AEs) and exploratory efficacy endpoints including change in PASDAS. Analyses were descriptive using data as observed.
Results: Of 203 pts randomised in Part A, 180 (89%) completed 16 wks of treatment and 173 (96%) of these pts chose to enrol in Part B. Of 118 pts initially randomised to DEUC, 25% (29/118; 6 mg QD, 22% [13/60]; 12 mg QD, 28% [16/58]) achieved MDA at Wk 16 and continued at the same dose. All other pts switched to UST in Part B: PBO, 100% (55/55; including 5 pts who had achieved MDA at Wk 16); DEUC 6 mg QD, 78% (47/60); DEUC 12 mg QD, 72% (42/58). The safety profile of DEUC in Part B (Table 1) was consistent with that in Part A, and all AEs were mild or moderate except 2 AEs in 1 pt with severe cataract/macular fibrosis. There were no opportunistic infections, herpes zoster, malignancy, thrombotic events, or treatment-related serious AEs reported in pts who remained on DEUC. Decreases in mean PASDAS score observed at Wk 16 were maintained at Wk 52 in pts who continued on DEUC (Figure 1). Improvements in other outcomes, including ACR components, PASI, and FACIT-Fatigue, were also sustained at Wk 52 in pts who continued DEUC treatment. Pts who had not achieved MDA on DEUC at Wk 16 showed a decrease in mean PASDAS score at Wk 52 after switching to UST.

Table 1. Overall summary of safety in Part B (Weeks 16 to 52)

AE, n (%)[a]	DEUC 6 mg QD n = 13	DEUC 12 mg QD n = 16	DEUC 6 mg QD →UST n = 47	DEUC 12 mg QD → UST n = 42	PBO → UST n = 55
Total AEs	11 (84.6)	8 (50.0)	26 (55.3)	26 (61.9)	30 (54.5)
Deaths	0	0	1 (2.1)[d]	1 (2.4)[d]	0
SAE	1 (7.7)[b]	0	3 (6.4)	4 (9.5)	0
Treatment-related SAE	0	0	0	0	0
Discontinued due to AE	0	1 (6.3)[c]	0	2 (4.8)[c,e]	0

Includes all treated patients in Part B. Medical Dictionary for Regulatory Activities version 23.0 was used. [a]n is the number of patients who experienced an event. [b]One patient had SAEs of psoriatic arthropathy in 1 joint and peripheral neuropathy. [c]Patient had an AE of COVID-19 infection leading to discontinuation. [d]Deaths in UST arms were due to car accident and sudden death in a 71-year-old patient with hypertension. [e]Patient had an AE of urinary tract infection leading to discontinuation. AE, adverse event; DEUC, deucravacitinib; PBO, placebo; QD, once daily; SAE, serious adverse event; UST, ustekinumab.

Conclusion: In the 16- to 52-wk blinded Part B of a Phase 2 study in pts with PsA, no new safety signals were observed with continuous DEUC treatment vs the earlier Part A period. Efficacy in PASDAS, as well as other key efficacy measures, was maintained with continued DEUC treatment through Wk 52.
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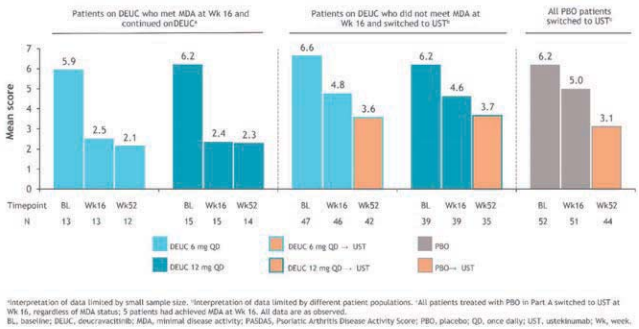
Figure. Mean PASDAS score through Week 52



[a]Interpretation of data limited by small sample size. [b]Interpretation of data limited by different patient populations. [c]All patients treated with PBO in Part A switched to UST at Wk 16, regardless of MDA status; 5 patients had achieved MDA at Wk 16. All data are as observed.
BL, baseline; DEUC, deucravacitinib; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; QD, once daily; UST, ustekinumab; Wk, week.

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POS1049 ASSESSING TREATMENT PATTERNS WITH DISEASE-MODIFYING ANTIRHEUMATIC DRUGS AND PREDNISONE FOR PSORIATIC ARTHRITIS BY RACE/ETHNICITY

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Background: Psoriatic arthritis (PsA) is a comorbidity commonly associated with psoriasis. Studies have demonstrated delays in the diagnosis and treatment of PsA[1] that may disproportionately affect racial/ethnic minority patients as indicated by one study that found Black Medicaid patients with PsA to be less likely to receive disease-modifying antirheumatic drugs [DMARDs] than White Medicaid patients with PsA [2]. Yet much remains unknown about potential racial/ethnic disparities in PsA management.

Objectives: The objective of our study was to evaluate treatment patterns for PsA by race/ethnicity.

Methods: We performed a cross-sectional study of adult (≥18 years old) patients with PsA who had at least one outpatient visit within the University of Pennsylvania health system between 2010 and 2019. Patients with PsA were identified by the presence of at least two International Classification of Diseases (ICD)-9 or ICD-10 codes for PsA associated with two different healthcare encounters. The primary outcomes were receipt of a prescription for: (i) an oral DMARD, (ii) a biologic DMARD, and (iii) prednisone. Oral DMARDs included apremilast, methotrexate, sulfasalazine, leflunomide, azathioprine, cyclosporine, tofacitinib, hydroxychloroquine, and upadacitnib. Biologic DMARDs included abatacept, adalimumab, brodalumab, certolizumab, etanercept, golimumab, guselkumab, infliximab, ixekixumab, secukinumab, ustekinumab, and risankizumab. The primary independent variable was race/ethnicity categorized as White (reference), Black, Asian, Hispanic, or other race. Multivariable logistic regression was used to assess the relationship between race/ethnicity and each treatment outcome.

Results: The study population included 1781 patients with PsA who were a mean age of 50.7 (SD 14.3), 54.6% female, and 72.5% commercially insured. The racial/ethnic distribution was 81.9% White, 5.6% Black, 4.0% Asian, 3.0% Hispanic, 2.5% other race, and 3.1% missing race/ethnicity. Of these patients, 64.3% were prescribed an oral DMARD, 55.6% were prescribed a biologic, and 44.1% were prescribed prednisone. There were no statistically significant differences across race/ethnicity for prescription of either oral or biologic DMARDs. However, prescription of prednisone did differ by race/ethnicity (p<.005) with Black (54.6%) and Hispanic (56.6%) patients being more likely to receive prednisone prescriptions and Asian (32.4%) patients being less likely to receive prednisone prescriptions than White (44.2%) patients. In adjusted logistic regression models controlling for sociodemographic and other factors, Hispanic patients were more likely to receive a prednisone prescription (OR 1.79, 95% CI 1.01 – 3.20, p=0.05) while Asian (OR 0.58, 95% CI 0.34 – 0.97, p=0.04) patients were less likely to receive a prednisone prescription compared to White patients.

Conclusion: We found Hispanic patients with PsA to be more likely to receive prednisone prescriptions than White patients with PsA but did not identify any racial/ethnic differences in prescription patterns for oral or biologic DMARDs for PsA. Greater use of prednisone among Hispanic patients may reflect different diseases trajectories (e.g., more disease flares or greater disease severity) or other factors that affect prescription patterns that require further study.

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POS1050 UPADACITINIB VERSUS ADALIMUMAB ON ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3 (RAPID3) IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: RAPID3 (Routine Assessment of Patient Index Data 3) is a disease activity index that is calculated from 3 patient-reported measures: physical function, pain, and patient global assessment. A fast and convenient tool, RAPID3 can be easily used in clinical practice and is applicable to multiple rheumatic diseases, including psoriatic arthritis (PsA), and was shown to correlate with other clinical composite measures of disease activity[1]. Here, we assessed the long-term effect of upadacitinib (UPA), an oral JAK inhibitor, and adalimumab (ADA) on RAPID3 scores in patients with PsA via a post hoc analysis from the SELECT-PsA 1 phase 3 trial[2,3].

Objectives: To evaluate the impact of treatment with UPA vs ADA on RAPID3 through 56 weeks in SELECT-PsA 1, as well as the association of RAPID3 with other disease measures used in PsA.

Methods: Data are from the double-blind SELECT-PsA 1 trial, in which patients with PsA and an inadequate response or intolerance to ≥1 non-biologic DMARD received UPA 15 mg or 30 mg once daily, ADA 40 mg every other week (wk), or placebo (PBO; switched at wk 24 to either UPA 15 mg or 30 mg). This analysis included data from the UPA 15 mg, ADA, and PBO treatment arms. RAPID3 endpoints were calculated using pain scores, patient's global assessment of disease activity, and HAQ-DI (each rescaled to 0–10 in this analysis); summed together, RAPID3 scores range from 0 (no disease activity) to 30 (severe activity). Mean change from baseline (BL) in RAPID3 as well as the proportions of patients reporting minimal clinically important differences (MCID) in RAPID3 and RAPID3 remission (≤3), low (LDA, >3 to ≤6), moderate (MDA, >6 to ≤12), and high disease activity (HDA, >12) were assessed through wk 56. Associations between RAPID3 scores and disease activity in psoriatic arthritis (DAPSA) and Minimal Disease Activity (MDA)/Very Low Disease Activity (VLDA) were determined by Mantel-Haenszel chi-square test. All data are as observed.

Results: A total of 1,274 patients (PBO: n=421; UPA 15 mg: n=425; ADA: n=428) were included from SELECT-PsA 1. RAPID3 scores at BL were comparable across all treatment arms, and most patients were in HDA. Patients receiving UPA showed a greater improvement from BL in RAPID3 vs ADA at all visits from wk 16 to wk 56 as well as better responses compared with PBO at all assessments (**Figure 1**). Similarly, a higher proportion of patients treated with UPA achieved MCID in RAPID3 scores than those on ADA from wk 24 to wk 56. By wk 56, approximately half of patients on either therapy were in RAPID3 remission or LDA, with UPA showing a slight numerical improvement relative to ADA (30/21/31/18% of patients were in remission/LDA/MDA/HDA on UPA vs 28/17/30/25% on ADA). RAPID3 disease categories were strongly associated with DAPSA and MDA/VLDA status at wk 56 across all treatment arms pooled together (**Table 1**) and for the UPA 15 mg arm alone (nominal *P* <0.0001 for all associations).

Table 1. Association of RAPID3 With DAPSA and MDA/VLDA Across All Treatment Arms at Week 56[a]

	RAPID3		
n (%)	**Moderate-High [>6]**	**Low [3 - ≤6]**	**Remission [≤3]**
DAPSA (n=879)			
Moderate-High [>14]	292 (33)	33 (4)	14 (2)
Low [4 - ≤14]	154 (18)	122 (14)	87 (10)
Remission [≤4]	6 (1)	21 (2)	150 (17)
MDA/VLDA (n=907)			
Not in MDA	410 (45)	39 (4)	5 (1)
MDA but not VLDA	63 (7)	129 (14)	80 (9)
VLDA	0	13 (1)	168 (19)

[a]DAPSA vs RAPID3 and MDA/VLDA vs RAPID3 were nominally significant at P <0.0001. Data were pooled across UPA 15 mg, ADA, and PBO to UPA 15 mg groups.

Conclusion: UPA 15 mg treatment led to greater improvements over PBO in RAPID3 scores over 56 wks in patients with PsA, and greater improvements over ADA from wk 16 to 56. The majority of patients achieved MCID in RAPID3 after 12 wks of UPA or ADA, with higher proportions achieving MCID on UPA vs ADA by wk 24. RAPID3 was strongly associated with other joint-focused (DAPSA) or multiple manifestation (MDA/VLDA) composite measures, further supporting the utility of RAPID3 in assessing disease activity in PsA.

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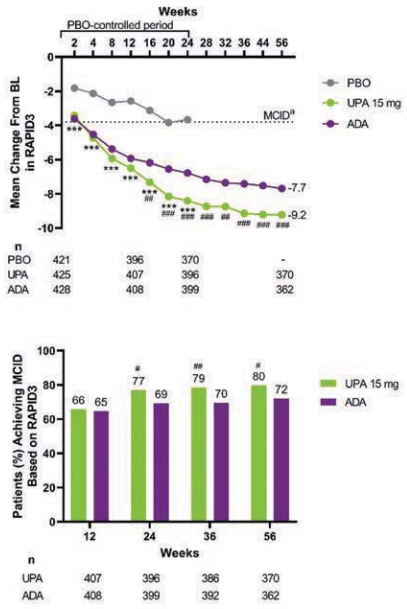
Figure: Change from Baseline in RAPID3 Scores and Achievement of MCID Through 56 Weeks (As Observed)



Nominal ***P <.001 for UPA vs PBO and ###P <.001, ##P <.01, and #P <.05 for UPA vs ADA. Negative RAPID3 values indicate improvement from BL. [a]MCID equals a decrease of at least 3.8 points from BL. ADA, adalimumab; BL, baseline; DAPSA, disease activity in psoriatic arthritis; MCID, minimal clinically important difference; PBO, placebo; RAPID3, Routine Assessment of Patient Index Data 3; UPA, upadacitinib.

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POS1051

TO WHAT EXTENT ARE BASELINE CHARACTERISTICS IN BIOLOGIC-EXPERIENCED PATIENTS WITH PSORIATIC ARTHRITIS ASSOCIATED WITH ACHIEVEMENT OF MINIMAL DISEASE ACTIVITY AT WEEK 24 OF GUSELKUMAB TREATMENT: A POST HOC ANALYSIS OF THE PHASE IIIB COSMOS CLINICAL TRIAL

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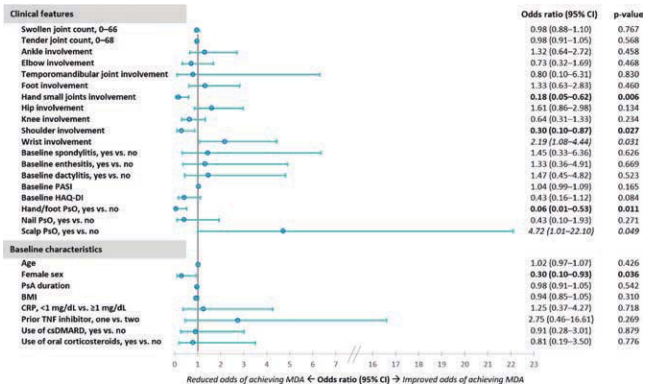
Background: Guselkumab (GUS) is a human monoclonal antibody targeting the interleukin-23p19-subunit. It has demonstrated efficacy at Week 24 in the Phase IIIb COSMOS clinical trial of patients with active psoriatic arthritis (PsA) and inadequate response or intolerance to one or two tumour necrosis factor inhibitors (TNFis).[1]

Objectives: The aim of this *post hoc* analysis was to identify predictors of minimal disease activity (MDA) with GUS at Week 24 in patients with active PsA and inadequate response or intolerance to one or two TNFis.

Methods: A multiple logistic regression analysis was performed to identify potential predictors of MDA with GUS at Week 24 in TNFi-refractory patients with PsA. Odds ratios, 95% confidence intervals and p-values were calculated. Baseline characteristics assessed as predictors included age, sex, body mass index (BMI), C-reactive protein (CRP), other medication use and disease duration. Clinical features included tender and swollen joint counts (TJC/SJC), affected joint location, dactylitis, enthesitis, spondylitis, Psoriasis Area and Severity Index (PASI) score and psoriasis (PsO) localisation (Figure 1). Missing data for MDA at Week 24 were imputed as non-response; missing baseline values were imputed for two patients.

Figure 1. Odds ratios and 95% CIs for potential predictors of minimal disease activity response to guselkumab 100 mg every 8 weeks at Week 24 in patients with PsA and an inadequate response or intolerance to one or two prior TNF inhibitors.



BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; csDMARD, conventional systemic disease-modifying anti-rheumatic drug; HAQ-DI, Health Assessment Questionnaire - Disability Index; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; TNF, tumour necrosis factor.N=187 for all clinical features and baseline characteristics. Negative predictors are indicated by bold text and positive predictors by italicisation (p<0.05).

Results: Of the 187 patients in this study, 54.6% were women and the mean disease duration was 8.3 years. The patients had a mean TJC 0–68 of 21.0, a mean SJC 0–66 of 10.3, a mean PASI score of 11.6 and a mean BMI of 28.9. Furthermore, 67.9% had enthesitis and 35.8% had dactylitis at baseline. One prior TNFi had been received by 88.2% of patients, and two received by 11.8%. At

Week 24, 17.1% of patients (32/187) achieved MDA. Wrist involvement (p=0.031) and scalp PsO (p=0.049) were positive predictors of MDA. Women were significantly less likely to achieve MDA (p=0.036) than men; other negative predictors included involvement of shoulder or small joints of the hand, and hand/foot PsO (all p<0.05). Age, BMI, CRP, TJC/SJC, HAQ-DI, PASI, spondylitis, enthesitis, dactylitis, other medication use and number of prior TNFis were not predictive of MDA (Figure 1).

Conclusion: Baseline characteristics and clinical features may be positively (wrist involvement, scalp PsO) or negatively (female sex, involvement of shoulder or small joints of the hand, hand/foot PsO) associated with achieving MDA with GUS at Week 24 in a TNFi-refractory population. Though the low patient number limits the generalisability of this analysis, assessment of Week 48 data may further elucidate potential predictors of MDA after longer-term treatment.

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[1] Coates C et al. *Ann Rheum Dis* 2021; 0: 1–11.

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POS1052

DEVELOPING EVIDENCE-BASED PATIENT FOCUSED LEARNING MATERIALS TO SUPPORT HEALTH BEHAVIOUR CHANGE FOR PEOPLE LIVING WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a complex condition that requires high levels of self-management from those living with the condition. It is associated with many comorbidities, including depression, metabolic syndrome, and increased cardiovascular disease risk and can adversely affect quality of life. There is growing evidence that people living with psoriatic arthritis (PsA) are more likely to be overweight, consume alcohol above recommended levels, smoke, be affected by poor sleep, fatigue, anxiety, and take insufficient exercise for healthy living. These modifiable health behaviours further increase the already known risk of cardiovascular morbidity and mortality. These issues are not systematically addressed in routine clinical care due to low confidence in effective delivery and time constraints.

Objectives: To co-develop evidence-based patient-focused learning materials to support healthy lifestyle changes for people living with PsA.

Methods: The development of the materials was overseen by a steering group of people living with PsA, psychologists, rheumatologists, and researchers. The COM-B model was used in the development of the materials, and they are designed around motivational interviewing principles. Firstly, a systematic literature review was performed to establish the evidence for the current burden and potential interventions aimed at these issues in PsA. These included diet, weight, alcohol, smoking, exercise, anxiety, depression, and stress. An initial focus group of people living with PsA was used to identify priority behaviours and ideas for content. The steering group developed draft materials, and we partnered with a design agency to create engaging materials. They developed a website and downloadable postcards. A second focus made up of people living with PsA was held for people to give their views on the draft content for the materials and initial design ideas. A third focus group was held with people living with PsA and a fourth with clinicians to refine the design materials and ensure they were accessible, interesting, and helpful to initiate and maintain change. A final evaluation survey was performed to review the draft website before launching the final materials. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) approved the final materials.

Results: Following the steering and focus groups' input, 15 candidate topics were prioritised (Table 1). A website and downloadable postcards summarising each of the topics were developed by the design team and refined following feedback from the patient focus groups. An example of the postcard for 'keeping active' can be found in Figure 1. The resources are free to use and can be accessed at https://www.informatree.org.

Table 1.

Topics	
1	Pain
2	Fatigue
3	Healthcare appointments
4	Tobacco
5	Different treatments
6	Alcohol
7	Work
8	Social support
9	Food and weight
10	Sleep
11	Keeping active
12	Mood
13	Intimacy
14	Travel
15	Using treatments

Figure 1.

During the development of the website and downloadable postcards, particular attention was paid to making the material as accessible and as friendly as possible for patients.

Conclusion: This project created patient-focused information to support behaviour change in clinical practice. It addresses common concerns of people living with PsA about how they may optimise their health by providing practical and

brief interventions to challenge and support them to make personal changes. Future research is needed to test the impact of the resource.

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POS1053

LONG-TERM RETENTION, EFFECTIVENESS AND SAFETY OF SECUKINUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS OR ANKYLOSING SPONDYLITIS: RESULTS FROM THE OBSERVATIONAL SERENA STUDY

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Background: SERENA is an ongoing, longitudinal, observational study of more than 2900 patients (pts) with moderate to severe psoriasis, active psoriatic arthritis (PsA), and ankylosing spondylitis (AS) conducted at 438 sites across Europe with an expected duration of up to 5 years.[1,2]

Objectives: We report long-term results (at least 3 years follow up) on secukinumab (SEC) retention, effectiveness and safety in pts with active PsA or AS from the SERENA study.

Methods: This analysis includes data of 524 PsA and 473 AS pts enrolled in the study and followed up for at least 3 years. Pts (aged ≥18 years) with active PsA or AS were required to have received at least 16 weeks of SEC treatment before enrolment in the study. Retention rate was defined as the percentage of pts who have not discontinued SEC treatment. Effectiveness assessments included swollen and tender joint counts (SJC and TJC) in pts with PsA, and BASDAI score in pts with AS. Safety assessments included the number of pts with any adverse events (AEs) and serious AEs, treatment-emergent AEs, AEs of special interest and their incidence rates.

Results: The mean (SD) treatment duration prior to enrolment in the study for PsA and AS pts was 1.0 (0.5) years and 0.9 (0.5) years, while time since diagnosis was 8.7 (7.4) and 9.8 (9.5) years, respectively. Prior to SEC initiation, 67.4% of pts with PsA and 63.0% of pts with AS received a biologic therapy, with lack of efficacy reported as major reason for discontinuation (PsA: 89.5%; AS: 87.6%). SEC retention rates after at least 3 years since enrolment in the study were 67.3% for pts with PsA and 72.1% for pts with AS. Survival probabilities for individual indications are presented in Figure 1. Over 3 years of observation, SEC showed sustained effectiveness in pts with PsA [SJC, mean (SD): baseline, 3.2 (5.6); Year 3, 1.7 (2.7) and TJC: baseline, 6.4 (9.4); Year 3, 4.9 (6.4)] and AS [BASDAI, mean (SD): baseline, 3.2 (2.3); Year 3, 2.7 (2.2)]. No new or unexpected safety signals were reported; 11.0% of pts with PsA (N=574) and 12.9% of pts with AS (N=505) reported serious AEs (Table 1).

Conclusion: After more than 3 years of observation in the SERENA study, SEC showed sustained retention rates, indicating high persistence in a real-world setting. Responses across effectiveness assessments in both PsA and AS cohorts were maintained or improved during the 3 years of follow up in the study. SEC showed a favourable safety profile, consistent with previous reports.

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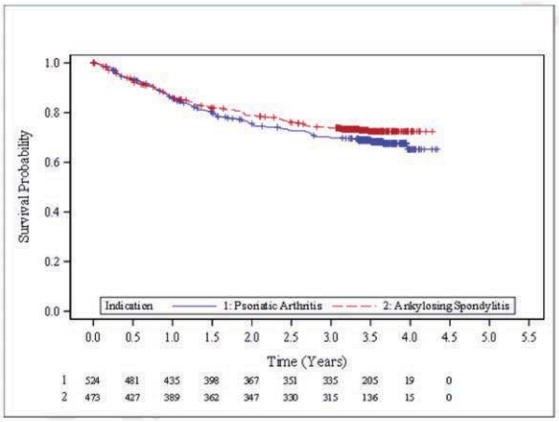
Figure 1. Time to treatment discontinuation of SEC in pts with PsA and AS



AS, ankylosing spondylitis; PsA, psoriatic arthritis; pts, patients; SEC, secukinumab

Table 1. Overall safety profile within the study period (Safety set)

Variable, n (%) unless otherwise specified	PsA (N=574)		AS (N=505)	
Pts with AE (≥1)	327 (57.0)		291 (57.6)	
Pts with SAE (≥1)	63 (11.0)		65 (12.9)	
AE leading to death	3 (0.5)		3 (0.6)	
AE leading to discontinuation	119 (20.7)		81 (16.0)	
Treatment emergent AE leading to discontinuation (in >1% pts in any group)	**n (%)**	**IR**	**n (%)**	**IR**
General disorders and administration site conditions	74 (12.9)	4.90	50 (9.9)	3.75
Skin and subcutaneous tissue disorders	13 (2.3)	0.86	3 (0.6)	0.22
Musculoskeletal and connective tissue disorders	26 (4.5)	1.72	9 (1.8)	0.67
Infections and infestations	2 (0.3)	0.13	7 (1.4)	0.52
Gastrointestinal disorders	2 (0.3)	0.13	3 (0.6)	0.22
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	4 (0.7)	0.26	3 (0.6)	0.22
Injury, poisoning and procedural complications	0	0	2 (0.4)	0.15
Treatment emergent AE of special interest (PT)	**n (%)**	**IR**	**n (%)**	**IR**
Candida infections	2 (0.3)	0.13	4 (0.8)	0.30
Malignancy	8 (1.4)	0.53	5 (1.0)	0.37
MACE	3 (0.5)	0.20	4 (0.8)	0.30
Injection site reaction	0	0	2 (0.4)	0.15
Inflammatory bowel disease	1 (0.2)	0.07	2 (0.4)	0.15

Safety set consisted of pts who received at least one dose of SEC treatment after signing the informed consentAE, adverse event; AS, ankylosing spondylitis; IR, incidence rate; MACE, major adverse cardiac events; N, total number of pts; n, number of pts; PsA, psoriatic arthritis; pts, patients; PT, preferred term; SAE, serious adverse event; SEC, secukinumab

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POS1054 PAIN AND DEPRESSION ARE ASSOCIATED WITH NON-RESPONSE TO METHOTREXATE IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a heterogeneous, immune-mediated inflammatory arthritis. Methotrexate (MTX) is the first-line treatment in PsA patients, despite diverse clinical phenotypes and highly varied responses(1). As yet, it is not possible to predict MTX treatment response. The identification of demographic, clinical and psychosocial factors associated with MTX non-response, would facilitate a paradigm shift from a 'one-size-fits-all' approach to a more personalized medicine strategy, based on individual patient characteristics.
Objectives: The aim of this study was to identify demographic, clinical and psychosocial factors associated with MTX non-response 3 months after MTX initiation in adult patients with PsA.
Methods: Newly diagnosed, adult PsA patients were recruited to the DEPAR (Dutch southwest Early Psoriatic Arthritis cohort) study. MTX non-response was defined as patients achieving <5/7 point of the Minimal Disease Activity (MDA) criteria after 3 months of MTX therapy. A logistic regression analysis was performed to identify demographic, clinical and psychosocial factors associated with MTX non-response. Demographic characteristics included age, sex, alcohol use, smoking (pack years) and body mass index (BMI). Clinical characteristics included duration of PsA symptoms, swollen and tender joint counts (66/68), Psoriasis Area and Severity Index (PASI) scores, presence of dactylitis and enthesitis scores (Leeds Enthesitis Index/Maastricht Ankylosing Spondylitis. [LEI_MASES]). Psychosocial variables included both subscales of the Hospital and Anxiety Depression Scale (HADS).
Results: Complete data of the variables of interest were available for 174/332 (52%) patients starting MTX monotherapy within the first year of diagnosis. Mean (SD) age was 53 (14) years and 88 patients (51%) were male. A total of 39 patients (22%) achieved MDA after 3 months of MTX therapy. Correlations between the variables and regression statistics are shown in Table 1. A significant correlation was seen between MTX non-response and enthesitis (OR 0.66, CI 0.47-0.94) and depression (OR 0.41, CI 0.25-0.66). Furthermore, the interaction of BMI with tender joint count (OR 0.95, CI 0.91-1.00) was found to be significantly correlated, whereas the independent variables were not.

Table 1. Final model of the logistic regression analysis of methotrexate non-response 3 months after methotrexate initiation.

Independent variables	Odds Ratio	95% CI
Demographic variables		
BMI	1.26	0.61-2.60
BMI[3]	1.00	1.00-1.00
Clinical characteristics		
Tender joint count (68)	3.16	0.94-10.57
Enthesitis (LEI/MASES)	**0.66**	**0.47-0.94**
Psoriasis (PASI)	1.11	0.99-1.25
BMI*Tender joint count (68)	**0.95**	**0.91-1.00**
Patient reported outcomes		
Depression (HADS)[†]	**0.41**	**0.25-0.66**

FootnotesSignificant values in bold face[†] Root transformed

Conclusion: Our results indicate that enthesitis, depression and the combination of a higher BMI with a tender joint count are all associated with MTX non-response 3 months after MTX initiation. Pain may be the common denominator preventing patients from achieving MDA.

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POS1055 IDENTIFICATION OF PSA PHENOTYPES WITH MACHINE LEARNING ANALYTICS USING DATA FROM A PHASE 3 CLINICAL TRIAL PROGRAMME OF GUSELKUMAB IN A BIO-NAÏVE PATIENT POPULATION

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Background: Psoriatic arthritis (PsA) is typically described by its individual domains or clinical components.[1,2]
Objectives: This *post hoc* analysis aimed to identify hypothesis-free phenotype clusters according to patients' clinical features and baseline (BL) characteristics with data from the Phase 3 DISCOVER-1 and -2 guselkumab (GUS) clinical trials.
Methods: Data from bio-naïve patients with PsA treated with GUS 100 mg every 4 or 8 weeks in DISCOVER-1 and -2 were retrospectively analysed. Non-negative matrix factorisation was used as an unsupervised machine learning technique to identify clusters of PsA phenotypes, with BL characteristics and clinical observations as input features, according to which clusters were described.
Results: Data from 661 patients were pooled and 8 distinct clusters of PsA phenotypes identified (Table 1). Cluster 1 was characterised by lower limb involvement and the lowest rates of severe skin involvement (Figure 1); Cluster 2 by high skin involvement, the lowest proportion of women and highest proportion of overweight patients (body mass index [BMI] 25–<30, 70%); and Cluster 3 by high burden of disease in the hand/wrist. In Cluster 4 all patients had dactylitis and ≥3% body surface area (BSA) psoriasis involvement and the second highest proportion of men. Cluster 5 had the highest BL enthesitis rate; large joint involvement was also common. Cluster 6 had a high level of small joint involvement in the hands/feet, but low mean dactylitis score; nail involvement and BL enthesitis were also common. In Cluster 7, all patients had axial involvement at BL, 49.4% had dactylitis, 69.9% had enthesitis and most had BSA ≥3% (Figure 1). Cluster 8 had limited joint involvement, extensive skin involvement and the highest proportion of obese patients (BMI >30, 67%). Minimal disease activity (MDA) response rates at Week (W)24 and W52 were

Table 1. Baseline characteristics of PsA phenotype clusters.

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Cluster 8
	Feet dominant	**Male, overweight, psoriasis burden**	**Hand dominant**	**Dactylitis dominant**	**Enthesitis and large joints**	**Enthesitis and small joints**	**Axial dominant**	**Female, obese, large joints**
Randomised and treated patients, n	79	125	95	38	57	60	83	124
Age, years	45.8 (10.4)	45.8 (13.2)	48.9 (11.8)	44.8 (12.3)	43.6 (13.3)	45.8 (11.6)	43.8 (10.4)	47.5 (11.1)
Female %	54.4	**20.0**	60.0	**26.3**	64.9	41.7	36.1	61.3
BMI, kg/m^2	29.3 (5.4)	27.4 (3.6)	29.3 (6.1)	26.9 (4.6)	28.6 (7.5)	29.0 (6.2)	28.4 (6.9)	**32.1 (6.5)**
CRP, mg/dL	1.7 (1.8)	1.7 (2.0)	1.4 (2.3)	**2.5 (2.8)**	1.7 (1.9)	1.7 (1.8)	2.2 (3.1)	1.5 (1.8)
Disease duration, years	5.0 (5.3)	5.1 (4.8)	5.8 (6.5)	6.1 (5.5)	6.8 (7.6)	6.1 (5.6)	4.7 (4.6)	5.2 (6.7)
SJC, 0–66	13.2 (7.1)	8.2 (3.8)	15.0 (8.0)	**18.0 (10.1)**	10.1 (5.1)	**17.5 (11.8)**	9.0 (4.2)	8.8 (3.9)
TJC, 0–68	23.4 (10.1)	12.8 (5.9)	26.0 (12.0)	**30.6 (15.3)**	23.2 (12.6)	**37.5 (18.6)**	14.6 (6.5)	12.7 (5.2)
BSA, %	12.6 (19.4)	20.7 (19.8)	14.8 (19.5)	29.7 (26.4)	14.6 (21.6)	14.5 (18.4)	15.2 (19.4)	14.4 (15.7)
Dactylitis %	48.1	30.4	42.1	**100.0**	36.8	53.3	**49.4**	31.5
Dactylitis score	3.0 (4.8)	1.4 (3.2)	2.7 (4.8)	**27.5 (12.3)**	2.3 (5.2)	3.9 (6.8)	**2.2 (2.9)**	1.3 (2.5)
Enthesitis %	70.9	49.6	58.9	**81.6**	**96.5**	73.3	**69.9**	45.2
LEI score	2.0 (1.7)	1.0 (1.3)	1.7 (1.8)	2.9 (1.9)	**4.2 (1.6)**	**2.7 (2.3)**	1.3 (1.2)	1.0 (1.3)

Data shown are mean (standard deviation) or %. Bold font indicates differentiating features of individual clusters. BMI, body mass index; BSA, body surface area; CRP, C-reactive protein; LEI, Leeds Enthesitis Index; PsA, psoriatic arthritis; SJC, swollen joint count; TJC, tender joint count.

highest in Cluster 2 and lowest in Cluster 5. Clusters 3 and 4 had low MDA response rates at W24, increasing at W52.

Conclusion: Unsupervised machine learning identified 8 clusters of PsA phenotypes with significant differences in demographic and clinical features, including patterns of domain involvement and MDA responses. These clusters differ in their initial vs. later responses to GUS.

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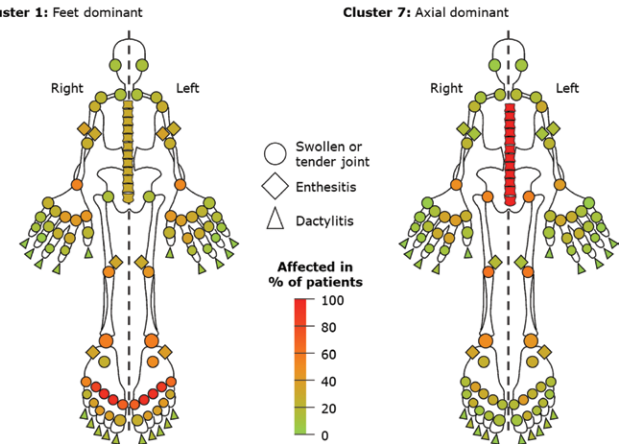
Figure 1. Examples of unsupervised machine learning-identified Clusters, 1 and 7.



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POS1056

PREDICTORS OF RISK OF ANTI-TNF TREATMENT WITHDRAWAL IN PATIENTS WITH PSORIATIC ARTHRITIS – DATA FROM MOSCOW UNIFIED ARTHRITIS REGISTRY (MUAR)

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Background: Retention on therapy is the most important integrative indicator of the success of the drug, reflecting both the effectiveness and tolerability and general acceptability of treatment. This indicator can be evaluated with high accuracy in observational trials.

Objectives: to identify predictors of TNF inhibitors withdrawal risk in patients with PSA.

Methods: Patients with (PSA) from Moscow Unified Arthritis Registry (MUAR) treated with TNF inhibitors were analyzed. All treatment episodes interrupted due to non-medical reasons were excluded from the study. Breaks in biologic therapy up to 4 months were allowed (for infliximab a break in therapy up to 6 month was considered possible) The search for predictors of treatment withdrawal risk was carried out in two steps. At the first step possible predictors of the risk of TNF inhibitors therapy discontinuation were selected in univariate correlations. At the second step significant predictors of retention on TNF inhibitors therapy were selected by forward stepwise variable selection within multivariate Cox regression. The relationship between the line of anti-TNF treatment and the risk of therapy discontinuation was analyzed separately.

Results: We analyzed 371 treatment episodes in 239 patients with PSA enrolled in MUAR, 97 male (40.6%), 50.2±12.1 years old. The age of disease onset was 36.8 ± 12.7 years. The patients received adalimumab (ADA) (101 treatment episodes), golimumab (GOL) (n=32), infliximab (INF) (n=55), certolizumab pegol (CER) (n=31), etanercept (ETA) (n=152). There were 187 (50.4%) completed treatment episodes. The relationship between risk of TNF inhibitors discontinuation and the drug line was analyzed. We found that the withdrawal risk on the second TNF inhibitor didn't significantly differ from the withdrawal risk on the first line anti-TNF drug (p=0,201). The third and subsequent lines of TNF inhibitors where associated with the significantly higher risk of withdrawal. Direct step-by-step selection of variables made possible to identify the following significant predictors of retention on therapy – social status, the presence of HLA B-27, fever during the disease, pain in sacral zone at the onset of the disease, coccidinia during the disease, patient reports on the association of the onset of the disease with a genital infection (uretritis, adnexitis, prostatitis, endometritis) (Table 1)

Table 1. Independent predictors of anti-TNF treatment discontinuation

Predictors	Direction of association with the dicontinuitation risk	p
Social status	Working patients had a lower risk	0.038
The presence of HLA-B27	HLA-B27 positive patients had lower risk	0.005
Temperature elevation during the disease	Patients WHO reported an increase in body temperature during the disease had an increased risk	< 0.001
Sacral pain at the onset of the disease	Patients who reported sacral pain at the onset of the disease had an increased risk	0.037
Coccygeal pain during the disease	Patients who reported pain in the coccyx during the disease had an increased risk	0.026
Presence of genital infections	Patients who reported a link between the onset of the disease and a history of urethritis or endometritis had a high risk	0.011

After adjusting for the line of therapy and the identified predictors of the risk of drug withdrawal it was found that retention on all analyzed TNF inhibitors in patients with PSA didn't differ significantly (Figure 1)

Conclusion: The identified significant mutually independent predictors of the risk of discontinuation of treatment may be useful when choosing biological therapy in patients with PSA. Discontinuation therapy risk of various TNF inhibitors does not differ significant.

The risk of withdrawal therapy with the second TNF inhibitor is not significantly differ from the first one. Thus, in case of failure of the first attempt of treatment with an TNF inhibitor, a second attempt can be made The probability of success of subsequent attempts seems to be very low

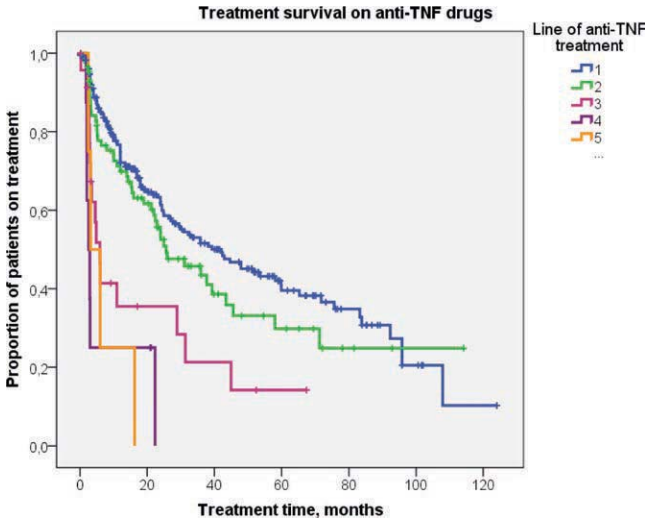

Figure 1. Adjusted analysis of treatment survival on TNF inhibitors

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POS1057

IMPACT OF RISANKIZUMAB ON ENTHESITIS AND ASSOCIATED PAIN: POOLED RESULTS FROM THE PHASE 3, RANDOMIZED, DOUBLE-BLIND KEEPSAKE 1 AND 2 TRIALS

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Background: Controlling or improving musculoskeletal disease activity of psoriatic arthritis (PsA) (eg, enthesitis and associated pain) is a treatment priority for patients, rheumatologists, and dermatologists.[1] Enthesitis is the cardinal lesion in PsA and is immunogenetically and experimentally linked to the interleukin-23 (IL-23) pathway.[2] Risankizumab (RZB), a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits IL-23 by binding to its p19 subunit, was studied in a phase 3 adult PsA program (KEEPsAKE clinical trials).[3,4] Pooled analyses from the program demonstrated the efficacy of RZB to treat enthesitis and pain associated with PsA, and increase the proportion of patients whose enthesitis resolved compared with placebo (PBO) in those patients who had an inadequate response or intolerance to ≥1 conventional synthetic disease-modifying antirheumatic drugs (KEEPsAKE 1 and 2) and/or ≤ 2 biological therapies (KEEPsAKE 2).

Objectives: To investigate whether patients without enthesitis at baseline (BL) (Leeds Enthesitis Index [LEI] = 0 at BL) remained enthesitis-free through week (W) 52, patients with enthesitis at BL (LEI > 0 at BL) had resolution of enthesitis through W52, and if greater pain relief was achieved with RZB 150 mg in patients with enthesitis at BL vs PBO up to W24.

Methods: The study design and primary results of KEEPsAKE 1 (NCT03675308) and KEEPsAKE 2 (NCT03671148) have been previously reported.[3,4] Briefly, patients were randomized to receive RZB 150 mg or PBO subcutaneously at weeks 0, 4, and 16 during a 24-week, double-blind treatment period; at W28 all patients received open label RZB 150 mg. For this post hoc analysis, the RZB 150 mg and PBO groups were pooled across the 2 studies. Pain reductions (as measured by change from BL in visual analogue scale [VAS] scores) were assessed at each time point through W24 among patients with enthesitis at BL (LEI > 0 at BL) using mixed-effect model repeated measurement analysis. Additional enthesitis analyses were calculated on the data as observed.

Results: Across the pooled population, over 60% of patients in each treatment group had enthesitis at BL (RZB=444/707 [63%]; PBO=448/700 [64%]). Conversely, 37% (263/707) and 36% (252/700) had no enthesitis (LEI=0) at BL among those randomized to RZB and PBO, respectively. Among enthesitis-free patients at BL (LEI=0 at BL), 84.7% on PBO and 90% on RZB remained free of enthesitis through W24; by W52, approximately 93% of patients in both groups (RZB and PBO to RZB) remained enthesitis free. A numerically higher proportion of patients with enthesitis at BL (LEI > 0 at BL) treated with RZB (52.1%) achieved an enthesitis-free state at W24 vs PBO (41.8%); similar proportions achieved an enthesitis-free state at W36 and W52 during open label treatment (Figure 1). Among patients with enthesitis at BL, a significantly greater improvement in VAS pain scores was observed in patients treated with RZB 150 mg vs PBO, as early as W4 ($P < .01$) and increased through W24 (Figure 1; $P < .001$).

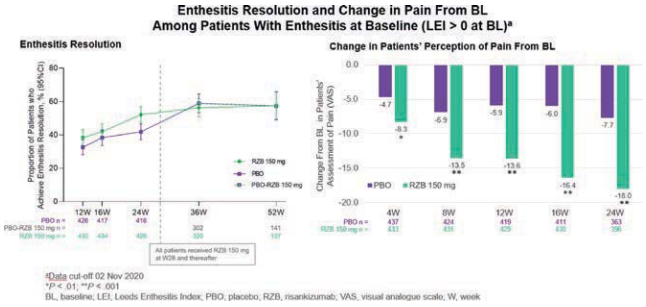

Figure 1.

Conclusion: Long-term maintenance of an enthesitis-free state (LEI = 0) was similar between the RZB 150 mg and PBO groups, with approximately 93% of patients remaining free of enthesitis at W52. For LEI > 0 patients, the RZB 150-mg group had numerically more patients whose enthesitis resolved at W24, and similar proportions were observed at W52 after the open label switch. Patients with enthesitis at BL treated with RZB 150 mg had statistically greater improvements in pain compared with patients taking PBO starting at W4 through to W24.

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POS1058 BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PSORIATIC ARTHRITIS: PREDICTORS OF TREATMENT SURVIVAL IN A REAL-LIFE SETTING

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Background: Psoriatic arthritis (PsA) is a chronic, immune-mediated, inflammatory arthropathy, distinctively involving joints and enthesis. The improved understanding of PsA pathogenesis has enabled the development of biological disease-modifying anti-rheumatic drugs (bDMARDS) targeting specific cytokines and signalling pathways. The availability of these drugs deeply modified PsA history, by preventing disease progression and by improving quality of life. Nevertheless, bDMARDS are not effective in all the patients who may experience primary or secondary inefficacy or adverse events development.

Objectives: In a real-life scenario, we evaluated the bDMARDs retention rate in a large PsA cohort. In detail, we compared drug survival of the first and second biological drug and we investigated the presence of factors associated with the bDMARDs treatment withdrawal.

Methods: We longitudinally evaluated adult PsA patients (2016 CASPAR criteria) treated with at least one bDMARD during disease history. For each PsA patient, the clinical and laboratory data, including demographics, past medical history with the date of diagnosis and treatments, clinical disease phenotypes, were collected in a standardized, computerized and electronically filled form. The retention rate was estimated by using the Kaplan-Meier method. Predictors for bDMARDs withdrawal were investigated in univariate and multivariate Cox proportional hazards analysis, adjusted for relevant variables.

Results: The present analysis included 223 PsA patients [M/F 91/132; median age 57 years (IQR 17); median disease duration 120 months (IQR 132)]. Adalimumab and Etanercept were the most frequently prescribed bDMARDs (41.5% and 41.0%, respectively). The retention rate of the first prescribed bDMARD as reported in Figure 1A: in detail, we found a 12-months retention rate of 79.8%. The comparison between etanercept and adalimumab showed a similar 12-months retention rate, but significantly higher for etanercept at 24 months (82.4% versus 69.5%, p=0.0034, Figure 1B). Out of 223 enrolled PsA patients, 109 (48.9%) received only one bDMARDs, while the remaining 114 (51.1%) received at least 2 drugs. When comparing these two groups of patients, drug survival at 24 months was significantly higher in patients treated with one bDMARD in comparison with those treated with at least two drugs (67.7% versus 52.2%, p=0.03, Figure 1C). Finally, female sex and anxiety-depressive disorders were significantly associated with the treatment with at least two dDMARDs (p=0.005 and p=0.01, respectively).

Conclusion: The results of the present study demonstrated a higher retention rate in the first-line bDMARDs treatment in comparison with second-line. Female sex and anxiety-depressive disorders may negatively affect drug retention rate.

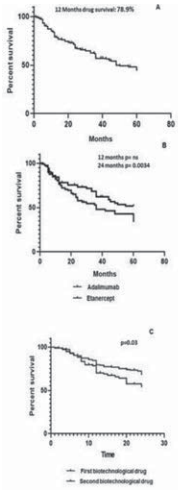

Figure 1
A. 12 Months first drug survival
B. Comparison of adalimumab and etanercept survival at 12 and 24 months.
C. Comparison of first biological drug and second biological drug survival at 24 months.

Disclosure of Interests: None declared

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POS1059 EFFICACY OF UST IN ACTIVE PSA IS INDEPENDENT FROM CONCOMITANT MTX USE, EVEN IN PATIENTS WITH MORE SEVERE SKIN PSORIASIS: SUBGROUP ANALYSIS FROM A RANDOMIZED PLACEBO-CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL

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Background: The use of bDMARDs treatments in patients with psoriatic arthritis (PsA) usually requires treatment failure or intolerance of csDMARD/MTX before initiation. The value of MTX in combination with bDMARDs is still unclear. We designed an investigator-initiated, randomized, placebo-controlled trial (IIT) in active PsA to examine if outcomes of treatment with ustekinumab (UST) in combination with MTX (either newly initiated or ongoing) were different from UST only (+Placebo; PBO). With known efficacy of MTX on skin psoriasis outcomes may differ in patients with or without significant skin involvement of their psoriatic disease.

Objectives: To compare efficacy outcomes in UST+PBO vs UST+MTX in dependency of skin involvement (Body Surface Area [BSA]) at baseline.

Methods: A total of 186 patients with active PsA (defined as TJC≥4, SJC≥4 [68/66 joint count] and DAS28≥3.2) were screened for eligibility. 173 patients were randomized to UST+MTX (new or ongoing) or UST+PBO. With this post hoc subgroup analysis outcome parameters were compared between patients with or without skin psoriasis > 3 % BSA. Demographic data and disease activity status of arthritis (joint count [TJC/SJC], DAPSA, DAS28), skin (PASI, BSA), HR-QoL (EQ5D, DLQI) and physical function (HAQ) were compared between groups.

Table 1. Outcomes at Week 24 (LOCF)

	UST+MTX		UST+PBO	
	BSA ≤3%	**BSA >3%**	**BSA ≤3%**	**BSA >3%**
	n=46	**n=40**	**n=51**	**n=23**
TJC68 change from BL	-7.83 (SD 10.3)	-9.5 (SD 10.3)	-8.9 (SD 9.5)	-7.3 (SD 7.4)
SJC66 change from BL	-6.0 (SD 5.4)	-7.1 (SD 3.5)	-6.5 (SD 6.2)	-6.4 (SD 3.8)
PASI change from BL+	-1.3 (SD 1.9)	-8.5 (SD 9.6)	-1.5 (SD 2.4)	-9.0 (SD 10.7)
DAS-28 ESR [mm/hr] change from BL	-1.6 (SD 1.1)	-1.8 (SD 1.2)	-1.7 (SD 1.4)	-1.8 (SD 1.1)
DAS-28 CRP [mg/l] change to BL	-1.5 (SD 1.2)	-1.5 (SD 1.3)	-1.6 (SD 1.2)	- 1.7 (SD 1.1)
DAPSA change from BL	-17.4 (SD 16.8)	-20.8 (SD 13.2)	-20.5 (SD 16.6)	-20.4 (SD 15.3)
HAQ change from BL	-0.1 (SD 0.4)	-0.2 (SD 0.5)	-0.3 (SD 0.3)	-0.3 (SD 0.5)
DLQI change from BL	-3.1 (SD 5.5)	-5.5 (SD 8.2)	-2.3 (SD 3.3)	-6.4 (SD 7.9)
EQ5D VAS Health State change from BL	6.7 (SD 24.7)	11.7 (SD 23.6)	8.0 (SD 24.2)	21.3 (SD 25.3)

Results: BL data were well-balanced between main treatment groups (UST+MTX, n=86; UST+PBO, n=74) including gender (42.5% vs 40.5% female) and mean values for age (49.2 vs 47.2 years), BMI (29.4 vs 28.9 kg/m2), SJC (8 vs 8), TJC (12 vs 12), DAS28-CRP (4.6 vs 4.4), DAPSA (36.7 vs 34.9) and PASI (2.8 vs 2.4. Disease activity remained well-balanced even after dividing groups according to skin involvement ((a) BSA ≤3% and (b) BSA >3%) with a trend of more severe joint involvement (SJC, TJC) in BSA >3% for UST+MTX compared to UST+PBO. At week 24, relative changes in TJC (-62% vs -62%), change in DAS28 and DAPSA were equal in all treatment groups independent from skin involvement (Table 1). Differences between the groups according to skin involvement were seen for relative changes in SJC (BSA >3%: -74.8% UST+MTX vs -84.3% UST+PBO), subject global assessment (SGA), physician global assessment (PGA), DLQI and EQ5D. Highest levels for changes were detected in the UST+PBO group with high skin involvement (BSA >3%).

Conclusion: IL12/23 inhibition with UST is an effective treatment for active PsA independent of MTX use. Data from this IIT indicate that additional MTX has no positive impact on UST efficacy for arthritis, skin, HR-QoL and physical function. This independency of UST effect from MTX can also be demonstrated in patients with active skin involvement despite known efficacy of MTX for skin psoriasis.

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POS1060

CHANGES IN DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH IXEKIZUMAB IN A REAL-WORLD US COHORT

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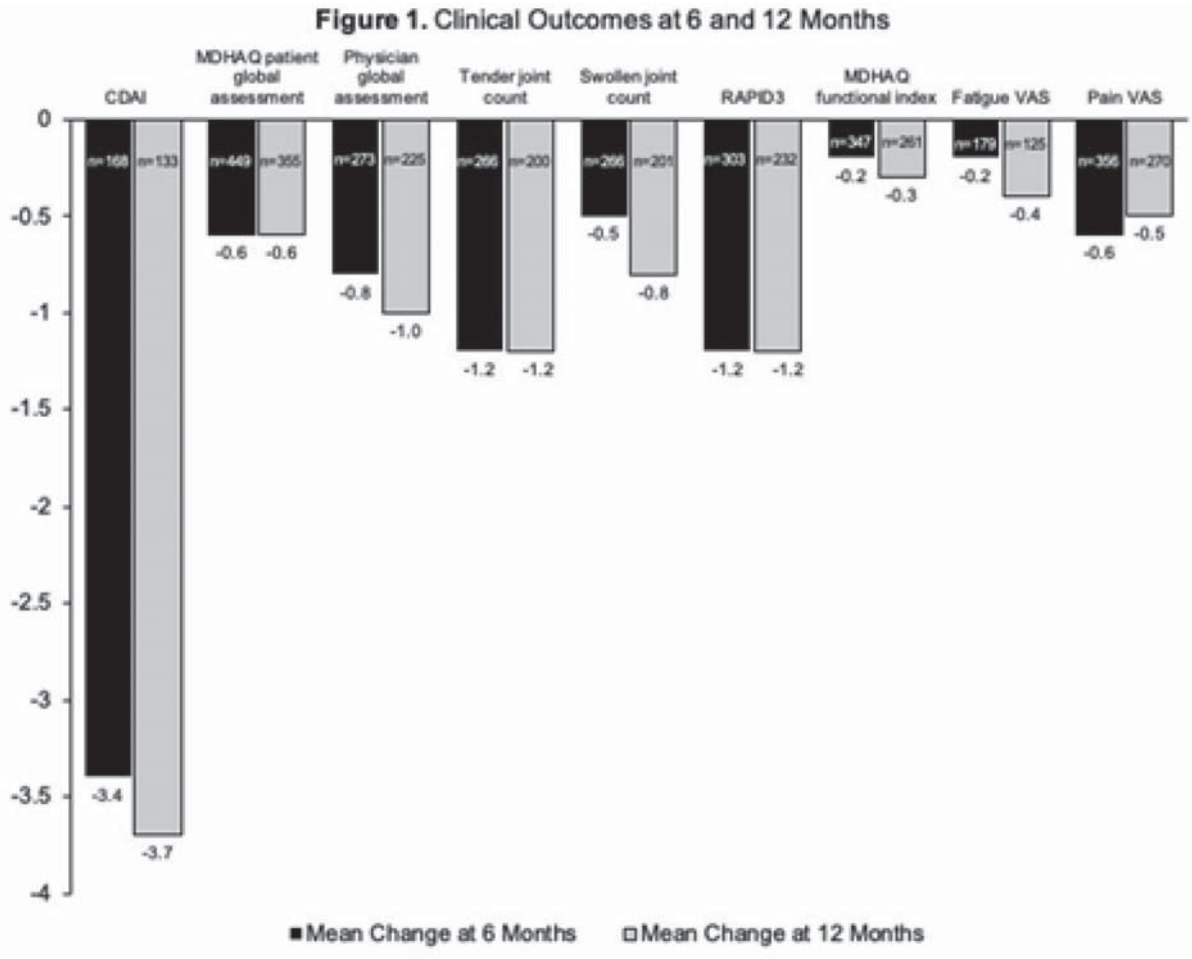
Background: Ixekizumab (IXE), an IL-17A inhibitor, has demonstrated efficacy in clinical trials[1-3] but real-world effectiveness (RWE) data are limited.[4]

Objectives: To describe changes in disease activity and patient-reported outcomes (PROs) at 6 and 12 months follow-up among psoriatic arthritis (PsA) patients initiating IXE in a routine clinical setting.

Methods: This retrospective cohort study included patients from the OM1 PsA Registry (OM1, Boston, MA), a linked electronic medical record and administrative claims dataset with over 50,000 patients. Eligible patients had ≥1 prescription for IXE (first = index), were ≥18 years old at index, had ≥1 diagnosis code for PsA in the 12 months before or on index, and had ≥12 months of baseline and ≥6 months of follow-up data as of June 2021. For patients with baseline and follow-up measures available, changes in Clinical Disease Activity Index (CDAI), PROs, and other clinical outcomes from baseline to 6 and 12 months were described. For patients on IXE monotherapy, change in CDAI score from

Table 1. Demographic and Clinical Characteristics by Therapy Status

		All Patients (N=1,812)	*Monotherapy (N=1,485)*	*Combination Therapy (N=327)*
Age (years)	Mean (s.d.)	53.7 (12.2)	53.9 (12.3)	52.9 (11.7)
	Median (Q1-Q3)	55 (46-62)	55 (46-62)	54 (45-61)
Sex	Female	1,108 (61.1%)	909 (61.2%)	199 (60.9%)
	Male	704 (38.9%)	576 (38.8%)	128 (39.1%)
Charlson Comorbidity Index	Mean (s.d.)	1.3 (1.6)	1.3 (1.6)	1.5 (1.7)
	Median (Q1-Q3)	1 (0-2)	1 (0-2)	1 (0-2)
BMI	Underweight: <18.5	10 (0.6%)	10 (0.7%)	0 (0.0%)
	Normal weight: 18.5-24.9	210 (12.2%)	172 (12.2%)	38 (12.1%)
	Overweight: 25-29.9	455 (26.5%)	379 (27.0%)	76 (24.2%)
	Obese: >= 30	1,045 (60.8%)	845 (60.1%)	200 (63.7%)
	Missing	92	79	13
Domains of PsA: Psoriasis	Yes	1,490 (82.2%)	1,222 (82.3%)	268 (82.0%)
	No	322 (17.8%)	263 (17.7%)	59 (18.0%)
Domains of PsA: Enthesitis	Yes	510 (28.1%)	409 (27.5%)	101 (30.9%)
	No	1,302 (71.9%)	1,076 (72.5%)	226 (69.1%)



baseline to 6 and 12 months was assessed using mixed effects linear models adjusted for age, sex, and baseline CDAI score.

Results: The study population included 1,812 patients with a mean age of 53.7 years (Table 1). Psoriasis was present in 82% and enthesitis in 28%. Over 60% of patients were obese, and the mean CharIson Comorbidity Index was 1.3. Most patients (84%) had prior treatment with a biologic disease-modifying antirheumatic drug (bDMARD) and 40% with a targeted synthetic DMARD (tsDMARD). The mean number of bDMARDs and tsDMARDs used during all available prior history was 2.3 and 1.1, respectively. The most common prior bDMARDs were secukinumab (n=428, 24%) and adalimumab (n=245, 14%). Of patients with a baseline CDAI score, 61% had moderate or severe disease activity. For all patients, CDAI scores improved (decreased) by an average of 3.4 and 3.7 points at 6 and 12 months, respectively, from a baseline mean of 15.4. All disease activity measures and PROs improved from baseline to 6 and 12 months (Figure 1). In patients persistent with IXE, 35.3% and 33.7% were in CDAI remission or low disease activity at 6 and 12 months after initiation, respectively. For IXE monotherapy users (82% of patients), at baseline, patients had a mean CDAI of 14.3 (n=131) and 15.1 (n=105) for the 6 and 12 month analyses, respectively. Adjusted mean changes in CDAI from baseline to 6 months (-3.6 points, $p < 0.0001$) and 12 months (-4.9 points, $p < 0.0001$) were statistically significant.

Conclusion: In this cohort of PsA patients with multiple prior b/tsDMARD failures, improvements in disease activity and PROs were observed at 6 and 12 months after initiating treatment with IXE. Improvements were observed in patients overall and in the monotherapy subgroup. More real-world research on IXE and other bDMARDs are important to understand the effect of treatment choices on clinical and PROs in both bDMARD-naive and experienced PsA patients.

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POS1061

HYPOVITAMINOSIS D IN PSORIATIC ARTHRITIS PATIENTS: PREDICTIVE ROLE ON DRUG SURVIVAL OF METHOTREXATE MONOTHERAPY AND FIRST LINE OF B-DMARDS.

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Background: The immunomodulatory role of vitamin D is extensively studied enough to hypothesize a pathogenetic role in chronic arthritis and psoriasis. Few data has been published on possible interference of hypovitaminosis D on drug response in rheumatoid arthritis patients, but data in psoriatic arthritis (PsA) patients is completely lacking.

Objectives: To compare drug survival and retention rate of methotrexate (MTX) and the first line of biotechnological drugs (b-DMARDs) in PsA patients with hypovitaminosis D and those with normal level of vitamin D.
Methods: We conducted a retrospective study on 250 PsA patients (age 57,3 years ± 13,2). All patients were required to fulfill the CASPAR criteria for PsA and were tested for vitamin D levels at baseline visit. Clinical characteristics, MTX and first line of b-DMARDs treatment duration and comorbidities information were recorded for each patient. The evaluations of drug survivals were realized by Kaplan-Meier estimate, followed by log-rank (Mentel-Cox) test for the comparison between the groups of patients in study. Statistical significance was set at $p \leqslant 0.05$.
Results: Sixty-four percent of PsA patients presented hypovitaminosis D (22,2ng/ml ± 8,8). PsA patients with hypovitaminosis D and those with normal levels were comparable for age (56,8 years ± 13 vs 58,5 years ± 12), and disease activity at baseline visit (DAS 28 VES: 4 ± 0,8 vs 3,8 ± 0,8). MTX monotherapy survival was shorter in hypovitaminosis D group (90 ± 19 weeks vs 166,8 ± 28 weeks, p=0,041), with discontinuation risk hazard ratio = 1,4 (95% CI: 1,005 – 2,014; p=0,046). The drug survival of first line of b-DMARDs was significantly shorter in patients with hypovitaminosis D (246,1 ± 40 weeks vs 302,1 ± 35 weeks; p=0,048), with discontinuation risk hazard ratio = 1,5 (95% CI: 1,1-2,4; p=0,05).
Conclusion: Vitamin D seems play an important role not only in the regulation of immune system but also in the modulation on immune response induced by drugs, as MTX or b-DMARDs. The evaluation of sera levels of vitamin D at the begging of immunomodulatory therapy could have a predictive role on treatment management in PsA patients. Further studies should be useful to detect if supplementation of vitamin D could improve the performance of immunomodulatory drugs.
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POS1062 HARNESSING THE POWER OF MACHINE LEARNING TO PREDICT REMISSION IN PATIENTS WITH PSORIATIC ARTHRITIS ON SECUKINUMAB: IMPLEMENTATION AND VALIDATION OF A CANDIDATE ALGORITHM ON 121 PATIENTS

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Background: Although novel therapies with biotechnological agents and small molecules may lead to the complete clearing of psoriasis in the vast majority of patients, the latter drugs only allow Psoriatic Arthritis (PsA) disease control in up to 50% of patients (1). In an increasing number of clinical scenarios, machine learning (ML) is emerging as a tool for the implementation of multi-parametric decision algorithms. ML allows to handle complex non-linear relationships between patient attributes that are hard to model with traditional statistical methods, merging them to output a forecast or a probability for a given outcome, enabling personalized medicine (2).
Objectives: We aimed to develop a ML algorithm capable of predicting the probability of remission in PsA patients on Secukinumab to support clinicians in choosing the optimal treatment strategy.
Methods: Patients with classified PsA according to CASPAR criteria undergoing Secukinumab treatment between September 2017 and September 2020 at our tertiary Centre were retrospectively observed.Either at treatment baseline and at 12-month follow up, we retrieved demographic and clinical characteristics, including Body Mass Index (BMI), disease phenotypes, Disease Activity in PsA (DAPSA), Leeds Enthesitis Index (LEI) and Ankylosing Spondylitis Disease Activity Score (ASDAS, on C-Reactive Protein). After a ML variable selection method, based on an eXtreme Gradient Boosting (XGBoost) wrapper, an attribute core set with the least number of predictors was used for implementing n.3 ML algorithms, namely Logistic Regression (LR), Decision Trees (DT) and XGBoost. Each algorithm was trained and validated with 10-fold cross-validation. The performance of each algorithm in both phases was assessed in terms of of accuracy and area under receiver operating characteristic curve (AUROC).
Results: The dataset consisted of n.121 PsA patients (62/121 female, 51.2%), with mean age (±SD) 52.9±10.1 years and mean disease duration of 5.9 ±10.4 years. Twenty-five of them (20.7%) had axial involvement whereas 88/121 (72.7%) had polyarticular involvement. Psoriasis was present in 84/121 patients (69.4%). At baseline, mean DAPSA was 14.9 ± 9.2, mean HAQ-DI 1.1 ± 0.7, mean LEI 0.6 ± 1, mean ASDAS 2.5 ± 0.8, mean PASI 2 ± 2.9, mean BMI 28.4 ± 4.9 . Secukinumab at 300 mg dose was administered to 79/121 patients (65.3%). At 12 months DAPSA remission was achieved by 24/121 patients (19.8%). Accuracy of LR, DT and XGBoost was of 0.70 ± 0.11, 0.81 ± 0.07 and 0.89 ± 0.05, respectively. Consistently AUROC (Figure 1 Panels ABC) were 0.63 ± 0.2, 0.79 ± 0.2 and 0.93 ± 0.1, respectively. A sample decision tree explaining XGBoost algorithm function has been provided (Figure 1 Panel D). LEI and DAPSA at baseline were shown as the most important attributes for such algorithm (Figure 1 Panel E).

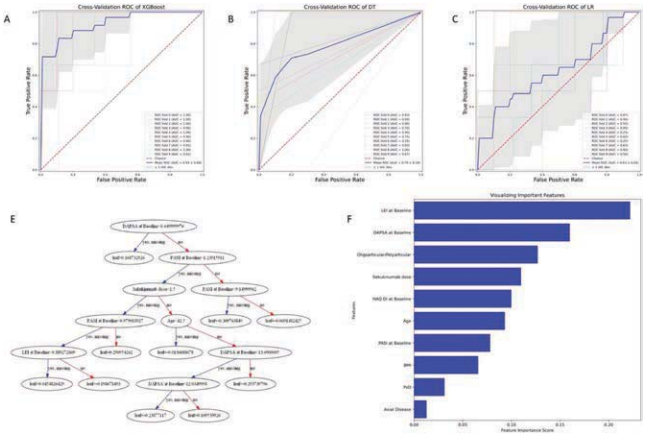

Figure 1.

Conclusion: ML can support Rheumatologists in profiling those patients more likely to respond to Secukinumab.
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Psoriatic arthritis - clinical aspects (other than treatment)

POS1063 STAT PHOSPHORYLATION AS A MARKER FOR DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS: AN EXPLORATIVE ANALYSIS

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Background: Numerous cytokines that influence disease activity in psoriatic arthritis (PsA) are modulators of the Janus Kinases/Signal Transducers and Activators of Transcription (JAK/STAT) pathway. The JAK1/STAT1/STAT3/STAT5 network can drive the expansion of Th17 and regulatory T cells via proinflammatory cytokines in PsA joints,[1], [2] while hyperphosphorylation of STAT3 in immune cells has previously been shown to promote PsA pathogenesis through the Interleukin (IL)-23/IL-17/IL-22 axis.[3] Therefore, the phosphorylation status of STAT molecules in leucocytes of PsA patients may indicate active disease and could potentially guide treatment with JAK inhibitors.
Objectives: To analyse phosphorylated STAT (pSTAT) levels of circulating leucocyte subsets in PsA patients with active and inactive disease
Methods: Whole blood was drawn on consecutive PsA patients fulfilling the CASPAR criteria[4] to perform flow cytometry analysis using the BD FACS-Lyric platform. Disease activity was assessed using the Disease activity for psoriasis arthritis (DAPSA) score.[5] All steps from storage of drawn blood to cell fixation were performed at 4°C to prevent auto-activation of leucocytes. The geometric mean fluorescence intensities (gMFI) of pSTATs in granulocytes, monocytes, B cells and CD4+/- naïve/memory T cells were compared between patients with moderate to high (MoDA/HDA) and remission to low disease activity (REM/LDA). Correlation analysis between gMFIs and DAPSA scores were performed.
Results: Forty-two patients (female ratio: 0.48) with established PsA (median ± standard deviation, age: 56 ± 12.54 years, disease duration: 8.50 ± 7.10 years) were included in this study. Twenty-one percent of patients were in MoDA/HDA, while the remaining 79% were in REM/LDA. Patients in MoDA/HDA showed significantly higher pSTAT3 levels in CD4+ naïve (gMFI median ± standard deviation: 284.5 ± 79.9 vs 238 ± 92.9, p = 0.011), CD4- naïve (297 ± 107.5 vs 238 ± 98.4, p = 0.04), CD4+ memory (227 ± 62.9 vs 190.5 ± 72.2, p = 0.009) and CD4- memory T cells (209 ± 66.8 vs 167.0 ± 64.9, p = 0.036). On the other hand, PsA patients in remission or low disease activity displayed higher pSTAT1 levels in granulocytes (2509 ± 1887 vs 1330.5 ± 784.1, p = 0.040) and monocytes (255 ± 230 vs 144 ± 62.5, p = 0.049). Positive correlations were found between DAPSA scores and pSTAT3 in CD4+ naïve and memory T cells (Spearman's correlation coefficient rho (ρ) = 0.5, p = 0.0012 and ρ = 0.47, p = 0.0025 resp.) whereas pSTAT1 in granulocytes and monocytes were negatively correlated with the DAPSA scores (ρ = -0.45, p = 0.0074 and ρ = -0.34, p = 0.05).
Conclusion: Differential phosphorylation of STAT3 and STAT1 molecules in circulating leucocyte subsets indicates PsA disease activity. Further studies to examine the value of STAT phosphorylation patterns guiding JAK inhibitor therapy are underway.
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POS1064 CLINICAL AND ECONOMIC BURDEN OF PATIENTS WITH PSORIATIC ARTHRITIS WITH AND WITHOUT AXIAL INVOLVEMENT

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Background: Axial involvement affects about 12% to 50% of patients (pts) with psoriatic arthritis (PsA),[1,2] and these pts report worse pain and function than pts without axial involvement.[3] Limited evidence exists quantifying the clinical and economic impact of axial involvement and pain in pts with PsA.
Objectives: To examine the clinical and economic burden of pts with PsA with and without axial involvement and assess the relationship between pain and frequency/costs of healthcare resource utilization (HCRU).
Methods: This cross-sectional study was conducted using de-identified linked electronic medical record and administrative claims data from the OM1 PsA Registry, a subset of the OM1 Real-World Data Cloud (OM1, Inc, Boston, MA, US). Adults aged ≥18 years with PsA (ICD-10 codes: L40.5x except for L40.53) were divided into two cohorts based on the presence or absence of the diagnosis code for axial involvement (ICD-10: L40.53) during 2019. Demographic and clinical characteristics between pts with and without axial involvement were compared with t-tests or Chi-square tests. Poisson regression models were used to assess the association of pain with HCRU. Mean costs per HCRU encounter (inpatient and emergency department [ED] visits) in 2019 were obtained from Optum's de-identified Clinformatics Data Mart Database (2007-2019) and multiplied by the mean annual rate of HCRU encounters to generate per patient per year (PPPY) costs.
Results: Of 11,531 pts with PsA, 1,118 (10%) were diagnosed as having axial involvement. The two cohorts were similar in age, Charlson comorbidity score, and biologic disease-modifying antirheumatic drug (DMARD) use (Table 1). More pts with vs without axial involvement were commercially insured, had higher pain, and used opioids. Higher mean annual rates of inpatient (9 vs 5 per 100 pts) and ED (19 vs 14 per 100 pts) visits were seen in pts with vs without axial involvement, respectively, which translated to higher mean annual inpatient ($1,899 vs $1,055) and ED ($222 vs $164) visit costs PPPY (Figure 1). A 1-point higher pain score was associated with a higher likelihood of inpatient (52% vs 11%) and ED (20% vs 10%) visits (Table 1) and additional mean annual inpatient ($987 vs $116) and ED ($44 vs $16) visit costs PPPY (Figure 1) in pts with and without axial involvement, respectively.

Table 1. Demographics, treatment utilization, and healthcare resource utilization

Mean (SD), unless otherwise specified	PsA pts without axial involvement n=10,413	PsA pts with axial involvement n=1,118	p-values
Age, years	56.7 (13.0)	56.8 (14.0)	0.8948
Female, n (%)	6,401 (61%)	653 (58%)	0.0494
Insurance, n (%)			<0.0001
Commercial	3,285 (62%)	414 (73%)	
Medicaid	110 (2%)	18 (3%)	
Medicare	1,618 (30%)	103 (18%)	
Charlson comorbidity score	0.4 (1.0)	0.4 (1.0)	0.9900
Pain, VAS (0–10)	4.2 (2.6)[a]	4.5 (2.6)[b]	0.0422
bDMARD use, n (%)	6,871 (66%)	753 (67%)	0.3762
tsDMARD use, n (%)	1,117 (11%)	91 (8%)	0.0072
Opioid use, n (%)	1,722 (17%)	224 (20%)	0.0034
Inpatient visits/100 pts	5 (32)	9 (35)	0.0021
ED visits/100 pts	14 (63)	19 (72)	0.0168
Association of pain and HCRU, IRR (95% CI)[c]			
Inpatient visits	1.11 (1.08–1.15)*	1.52 (1.13–2.03)**	
ED visits	1.10 (1.07–1.13)*	1.20 (1.05–1.38)**	

bDMARD, biologic DMARD; CI, confidence interval; IRR, incidence rate ratio; MTX, methotrexate; NSAIDs, non-steroidal anti-inflammatory drugs; SD, standard deviation; tsDMARD, targeted synthetic DMARD; VAS, visual analog scale. *p<0.0001 and **p<0.01 for association between 1-point increase in pain and HCRU. [a]n=9,981 [b]n=320 [c]Based on Poisson regression model adjusted for age, sex, race, insurance type, Charlson comorbidity score, and PsA treatments (b/tsDMARDs, MTX, and NSAIDs).

Conclusion: Axial involvement in PsA was associated with an increased clinical and economic burden. Higher pain was associated with higher HCRU and costs in pts with vs without axial involvement.

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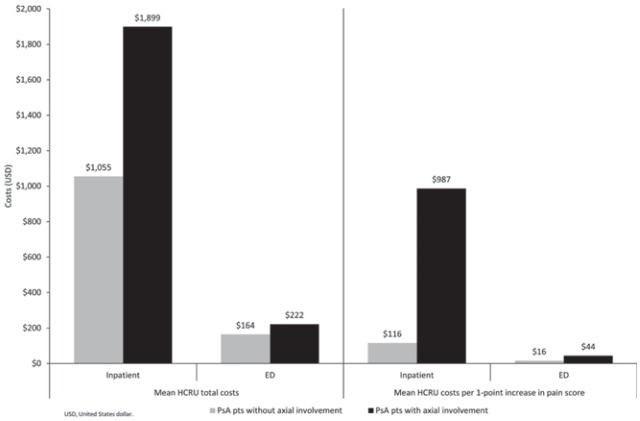
Figure. Mean annual HCRU total costs and costs per 1-point increase in pain score (PPPY)



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POS1065

IMPACT OF HYPERURICEMIA ON CLINICAL PHENOTYPE, COMORBIDITIES, AND RESPONSE TO SECUKINUMAB IN PSORIATIC ARTHRITIS: POST HOC ANALYSIS OF FUTURE AND MAXIMISE STUDIES

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Background: Hyperuricemia (HU) is a metabolic abnormality associated with psoriasis (PsO) and psoriatic arthritis (PsA)[1]. The prevalence of HU is 2–13% in general population, 19–20% in PsO patients (pts), and 27–32% in PsA pts[1,2]. Pts with PsO/PsA are at significantly increased risk of HU and development of gout[1]. The pathogenic role of chronic HU in the development and maintenance of PsA is based on epidemiological, clinical, and fundamental arguments and hence does not appear fortuitous. These processes can influence each other[3]. Moreover, PsA with HU has been shown to be more peripheral, destructive, and challenging to treat[4].
Objectives: To evaluate the impact of HU on PsA in terms of clinical presentation, severity, comorbidities, and response to secukinumab (SEC) over 1-year.
Methods: This *post hoc* analysis included pooled data from PsA pts enrolled in the FUTURE 2–5 and MAXIMISE phase 3 trials. Pts were stratified into 2 groups based on baseline (BL) serum uric acid (SUA) level (HU: ≥360 µmol/L; without HU: <360 µmol/L and no history of gout and/or uric acid lowering therapies [ULT]). Demographic and disease characteristics, PsA and therapeutic history, and comorbidities data, were collected at BL. Evaluations included ACR20/50/70 responses, Psoriasis Area and Severity Index (PASI) 90 response, resolution of enthesitis and dactylitis, Health Assessment Questionnaire Disability Index (HAQ-DI), and mean change in SUA level, up to Week 52. All analyses were performed at a descriptive level and data presented as observed.

Results: Overall, 2504 PsA pts were included in the analysis, of which 822 (32.8%) had HU (62 [2.5%] with gout; 49 [2.0%] treated with ULT). At BL, pts with HU were mostly male (76.0% vs 34.2%) and had a higher body mass index (30.9 vs 28.3 kg/m^2) with more comorbidities, such as hypertension (43.8% vs 31.3%), compared to pts without HU. A higher proportion of pts with HU had dactylitis (34.5% vs 25.9%), and PsO (48.3% vs 36.3%) with a greater mean PASI score (13.6 vs 10.2), compared to pts without HU (Table 1). The proportion of pts achieving ACR50, resolution of enthesitis/dactylitis, and mean change in HAQ-DI score were comparable up to Week 52 irrespective of BL HU status. The PASI90 response rate was higher in pts without HU with SEC 150 mg (with and without load) and similar in SEC 300 mg group irrespective of BL HU status (Figure 1).

Table 1. Demographics and baseline characteristics

Parameters, mean ± SD unless specified	With hyperuricemia (N=822)	Without hyperuricemia (N=1682)
Age (Years)	48.5 ± 12.41	48.3 ± 12.19
Gender (Male), n (%)	625 (76.0)	576 (34.2)
Weight (kg)	92.71 ± 18.62	79.59 ± 17.55
BMI (kg/m^2)	30.90 ± 5.86	28.33 ± 5.91
History of hypertension, n (%)	360 (43.8)	526 (31.3)
History of diabetes mellitus, n (%)	85 (10.3)	144 (8.6)
TJC	20.6 ± 15.52	21.3 ± 16.25
SJC	10.9 ± 9.31	10.8 ± 9.13
Enthesitis, n (%)	412 (50.1)	852 (50.7)
Dactylitis, n (%)	284 (34.5)	436 (25.9)
Evidence of current psoriasis; n (%)	397 (48.3)	611 (36.3)
Mean PASI score*	13.61 ± 11.03	10.16 ± 9.13
TNFi naïve, n (%)	477 (58.0)	938 (55.8)
MTX use at randomization, n (%)	321 (39.1)	685 (40.7)
Serum uric acid (µmol/L)	420.7 ± 57.11	274.9 ± 51.98
CRP (mg/L)	11.6 ± 18.66	10.7 ± 23.36

*not collected in MAXMISE BMI, body mass index; CRP, C-reactive protein; MTX, methotrexate; SJC, swollen joint count; TJC, tender joint count; TNFi, tumor necrosis factor inhibitor

Conclusion: In this pooled analysis of SEC PsA studies, pts with HU reported a higher prevalence of hypertension, with more clinical dactylitis, and more PsO, with higher PASI score compared to pts without HU. Efficacy across all musculoskeletal manifestations was similar with SEC 150 and 300 mg; while PASI90 response rate was slightly better in patients without HU with SEC 150 mg, and similar with SEC 300 mg irrespective of HU status, at 1-year.

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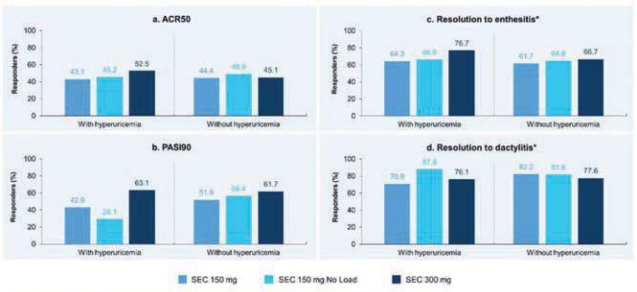
Figure : Efficacy endpoints at Week 52



*Resolution to enthesitis/dactylitis were evaluated in patients with enthesitis/dactylitis at baseline.
ACR, American College of Rheumatology; PASI, Psoriasis Area and Severity Index; SEC, secukinumab

Disclosure of Interests: Renaud FELTEN Consultant of: Novartis (Advisory board), Laura Widawski: None declared, Lionel Spielmann: None declared, Corine Gaillez Shareholder of: Novartis, Employee of: Novartis, Weibin Bao Shareholder of: Novartis, Employee of: Novartis, Jacques-Eric Gottenberg Consultant of: Novartis (Advisory board), Pierre-Marie Duret: None declared, Laurent Messer: None declared

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POS1066

DEVELOPMENT OF PHYSICAL AND MENTAL COMPONENT SUMMARY SCORES FROM PROMIS-29 INSTRUMENT IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Patients (pts) with psoriatic arthritis (PsA) experience pain, fatigue, anxiety, depression, sleep disturbance, and impaired physical function that can negatively affect health-related quality of life (HRQoL).[1] As the Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) Profile is a generic instrument assessing 7 health outcome domains, composite scores to summarize these domains into generalized concepts of mental and physical health using physical component summary (PCS) and mental component summary (MCS) scores[2,3] will be useful to evaluate overall HRQoL in pts with PsA.
Objectives: Calculate and validate PCS and MCS scores, using PROMIS-29 data from the DISCOVER-1 Phase 3 study, and compare the scores for guselkumab (GUS) vs placebo (PBO).
Methods: The DISCOVER-1 study evaluated 381 pts with active PsA (≥3 swollen & ≥3 tender joints; C-reactive protein ≥0.3 mg/dL; 31% with prior tumor necrosis factor inhibitor exposure) and inadequate response to standard therapies.[4] The PROMIS-29 Profile contains 4 items for each of 7 domains (physical function, anxiety, depression, fatigue, sleep disturbance, social participation, pain interference; 28 items scored on 5-point Likert scale) and 1 pain intensity item (0-10 visual analog scale). Using standardized scoring coefficients,[3] PROMIS-29 PCS/MCS at baseline and Week 24 were calculated based on the 7 domains and pain intensity item. The validity of scores was assessed by Spearman correlation between PROMIS-29 PCS/MCS and 36-item Short-Form (SF-36) PCS/MCS, Health Assessment Questionnaire-Disability Index (HAQ-DI), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores. To evaluate the ability of derived PROMIS-29 PCS/MCS scores to distinguish between treatments, responder analyses (employing an improvement of ≥1/2 standard deviation [SD] of baseline scores) by treatment group (GUS 100 mg Q4W, GUS 100 mg Q8W, PBO) were conducted and compared with SF-36 PCS/MCS scores.
Results: As construct validity analysis, PROMIS-29 PCS/MCS strongly/very strongly correlated with SF-36 PCS/MCS scores at baseline and Week 24 (coefficients 0.66-0.86; Table 1). PROMIS-29 and SF-36 PCS scores showed strong/very strong correlations with HAQ-DI scores, a key component of physical health (coefficients 0.66-0.83), while PROMIS-29 MCS and SF-36 MCS scores showed strong/very strong correlations with FACIT-F scores, a key component of mental health (coefficients 0.63-0.91). The proportions of pts achieving improved PROMIS-29 PCS/MCS scores (≥1/2 SD at baseline) were similar to a comparable degree of improvement in SF-36 PCS/MCS scores (≥1/2 SD at baseline). For both PROMIS-29 PCS/MCS and SF-36 PCS/MCS scores, significantly higher proportions of GUS Q4W/Q8W- vs PBO-treated pts achieved these response thresholds (all p<0.05; Figure 1) with the deltas between both GUS groups vs PBO for PROMIS-29 PCS/MCS responses numerically greater than for SF-36 PCS/MCS responses.

Table 1. Mean (SD) PCS and MCS Scores: Construct Validity

	Instruments Assessing Physical Aspects of HRQoL		Instruments Assessing Mental Aspects of HRQoL	
	SF-36 PCS	**PROMIS-29 PCS**	**SF-36 MCS**	**PROMIS-29 MCS**
Baseline, N	381	381	381	381
Mean (SD)	34.6 (8.2)	39.4 (7.2)	47.4 (10.2)	45.3 (7.7)
Median	34.4	38.2	47.8	45.1
Spearman's correlation PROMIS-29 vs SF-36	0.76		0.66	
Week 24, N	380	381	380	381
Mean (SD)	39.6 (9.3)	43.3 (8.3)	50.3 (9.7)	49.3 (8.5)
Median	39.3	42.2	52.3	50.0
Spearman's correlation PROMIS-29 vs SF-36	0.86		0.71	

Conclusion: PROMIS-29 PCS/MCS scores calculated in DISCOVER-1 showed evidence of validity as summary scores with the ability to efficiently evaluate pt-reported HRQoL outcome in PsA. PROMIS-29 PCS/MCS scores, similar to the commonly employed and validated SF-36 PCS/MCS scores, may reliably be used to assess physical and mental health in pts with PsA.

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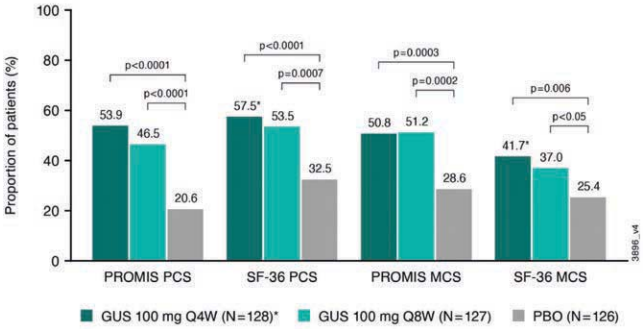
Figure. Responder analysis: PROMIS-29 vs SF-36 PCS/MCS Scores



* SF-36 PCS and SF-36 MCS, N=127

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POS1067

DOMAINS CONTRIBUTING TO MINIMAL DISEASE ACTIVITY ACHIEVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS RECEIVING GUSELKUMAB

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Background: Despite effective treatments, a minority of psoriatic arthritis (PsA) patients (pts) realize sustained minimal disease activity (MDA).[1] Pt-driven domains of MDA are less frequently achieved, potentially arising from comorbid conditions.[1]
Objectives: Identify domains contributing to and factors influencing MDA achievement in the 2-year Phase 3 DISCOVER-2 trial.
Methods: Randomized and treated adults (N=739) had active PsA, were biologic/JAK inhibitor-naive, and had swollen and tender joint counts (SJC/TJC) each ≥5 and C-reactive protein ≥0.6 mg/dL. Pts with medical history of fibromyalgia (FM) were not excluded. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then every 8 weeks (Q8W); or placebo (PBO); PBO pts crossed over to GUS 100 mg Q4W at W24. MDA requires fulfillment of ≥5/7 criteria: TJC ≤1, SJC ≤1, Psoriasis Area and Severity Index (PASI) score ≤1, Pt Pain score ≤15, Pt global disease activity (PtGA) score ≤20, Health Assessment Questionnaire – Disability Index (HAQ-DI) score ≤0.5, and ≤1 tender entheses. A longitudinal trajectory of achieving each MDA

criterion through W100 was derived (nonresponder imputation [NRI]). Time to achieve was estimated via Kaplan-Meier survival curve for scores deriving from native scales and those normalized to a 0-66 scale (corresponding to SJC). Multivariate regression models for time to achievement (cox proportional hazard) and achievement (logistic regression) of MDA at W100 identified predictors of response.

Results: Among 492 GUS pts, continuous improvement across all MDA domains was shown through proportions of pts achieving criteria at W24 & W100 (NRI): SJC (45% & 65%), TJC (16% & 34%), PASI (71% & 72%), Pt Pain (23% & 37%), PtGA (29% & 45%), HAQ-DI (34% & 44%), entheseal points (75% & 80%). Times to achieve minimal SJC, PASI, and enthesitis with GUS were significantly faster than for PtGA, Pt Pain, TJC, and HAQ-DI for native-scale scores; when normalized, PtGA, Pt Pain, and HAQ-DI were achieved less often (Figure 1). Higher baseline (BL) Pt Pain score and lower BL Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score (worse fatigue) were significant predictors of longer time; lower BMI was associated with shorter time to achieve Pt Pain ≤15. Results for achieving Pt Pain ≤15 at W100 were similar. Worse baseline fatigue and PtGA were significant predictors of longer time to PtGA ≤20; worse fatigue also predicted non-achievement of PtGA ≤20 at W100. For time to achieve HAQ-DI ≤0.5, significant BL negative predictors were higher age and BL HAQ-DI score, which were also significant predictors of HAQ-DI ≤0.5 non-achievement at W100. Although seen in only a small number of pts, a significant impact of FM history and suicidal ideation/behavior on Pt Pain ≤15 and HAQ-DI ≤0.5, respectively, was observed (Table 1).

Table 1. Predictors of Time to Achievement and Achievement of Recalcitrant MDA Domains at Week 100 in GUS-randomized Pts (N=492)

Time to achievement	Independent BL Variables	Pt Pain ≤15	PtGA ≤20	HAQ-DI ≤0.5
		HR (95% CI)	HR (95% CI)	HR (95% CI)
	Age	-		0.98 (0.97-0.99)†
	HAQ-DI	-		0.26 (0.19-0.36)‡
	PtGA VAS	-	0.99 (0.98-1.00)*	-
	Pain VAS	0.99 (0.98-1.00)†		-
	FACIT-Fatigue§	1.02 (1.00-1.03)*	1.02 (1.01-1.04)‡	-
	BMI	0.98 (0.96-1.00)*		
	FM (N=8)	0.70 (0.55-0.90)†	-	-
Achievement at W100		OR (95% CL)‖	OR (95% CL)‖	OR (95% CL)‖
	Age	-	-	0.98 (0.96: 1.00)*
	HAQ-DI	-	-	0.13 (0.08: 0.20)‡
	Pain VAS	0.98 (0.97: 1.00)†	-	-
	FACIT-Fatigue§	1.02 (1.00: 1.05)*	1.05 (1.03: 1.07)‡	-
	BMI	0.97 (0.94: 1.00)*	-	-
	Suicidal Ideation/ Behaviour (N=9)	-	-	0.16 (0.03: 0.86)*
	FM (N=8)	0.59 (0.40: 0.86)†	-	-

HR Hazard Ratio *CI* Confidence Interval *OR* Odds Ratio *CL* Confidence Limits
*p <0.05; †p <0.01; ‡p ≤0.0001
§Higher score indicates less fatigue
‖Wald CL

Conclusion: GUS provided continuous improvement in each MDA domain through W100. BL domain score, as well as age, fatigue, and BMI, were significant determinants of MDA achievement in recalcitrant pt-driven domains (Pt Pain, PtGA, HAQ-DI). The impact of FM and mental health status merits further evaluation.

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POS1068 DISCOVERY OF ARTHRITIS IN PSORIATIC PATIENTS FOR EARLY RHEUMATOLOGICAL REFERRAL (DAPPER): DEVELOPMENT OF A SCREENING TOOL FOR ACTIVE PSORIATIC ARTHRITIS IN PSORIASIS PATIENTS

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Background: One in three patients with psoriasis (Pso) will develop psoriatic arthritis (PsA). Active PsA can lead to disability and joint damage. Current screening methods are targeted at finding all PsA patients in a Pso population. However, PsA patients with inactive disease are unlikely to benefit from rheumatological referral.

Objectives: To develop a screening tool for dermatologists to identify patients with a high risk for active PsA in their Pso population, who would benefit from rheumatological referral.

Methods: This observational study consisted of Pso patients, stratified 1:1:1 for current therapy (topical, conventional systemic, biologic). Patients were screened by a rheumatologist for PsA, adjacent to a regular scheduled dermatologist visit. Active PsA was defined as a diagnosis of PsA, with at least 1 inflamed joint or entheses, or evidence of active spondyloarthritis. Inactive PsA was defined as a diagnosis of PsA, with no active (spondylo)arthritis at moment of screening. Univariable logistic regression was used to determine variables indicative of the presence of active PsA versus Pso only. Parameters with a P < 0.1 were entered into a multivariable model. A P-value of < 0.05 was considered significant. Sensitivity, specificity, positive and negative likelihood of the model were calculated using a 2x2-grid.

Results: The DAPPER cohort consisted of 304 patients: 225 (74%) Pso only, 48 (16%) Pso and inactive PsA, 30 (10%) Pso and active PsA. One patient could not be classified. Mean age was 54 ± 16.1 years (Pso 53 ± 16.6; inactive PsA 55 ± 15.7; active PsA 52 ± 13.5). Thirty six percent of patients were female (Pso 30/225 – 36%; inactive PsA 19/48 – 40%, active PsA 10/30 – 33%). Univariable logistic regression showed significant differences between Pso only and Pso with active PsA for: treatment history with methotrexate (OR 3.03; 95% CI 1.12, 8.23), treatment history with biologics (OR 4.96, 95% CI 2.17, 11.37), current use of biologics (OR 3.37; 95% CI 1.55, 7.33), patient-reported history of nail Pso (OR 3.01; 95% CI 1.28, 7.04), patient-reported history of swollen joints (OR 7.95; 95% CI 3.12, 20.28), patient-reported history of swollen digits (OR 4.82, 95% CI 2.19, 10.62), previous diagnosis of arthritis by physician (OR 15.09; 95% CI 6.32, 36.03), current joint pain (OR 5.81; 95% CI 1.35, 25.098); current back pain (OR 2.74; 1.23, 6.12); prolonged morning stiffness (OR 4.43; 95% CI 1.90, 10.34), and a higher VAS joint pain (OR 1.02; 95% CI 1.00, 1.03). Two backward selection models were made: model 1 using 4 variables with the highest significance, model 2 using 4 variables with the highest effect size. Both methods resulted in 2 predictors: patient-reported history of swollen joints (OR 3.95; 95% CI 1.43, 10.95), and previous diagnosis of arthritis by physician (OR 9.53; 95% CI 3.80, 28.88). A forward selection model using all parameters with a P-value <0.1 resulted in a model with 3 variables: age at start Pso (OR 0.96; 95% CI 0.93-0.99), patient-reported history of swollen joints (OR 3.68; 95% CI 1.30, 10.12), and previous diagnosis of arthritis by physician (OR 11.22; 95% CI 4.21, 29.92). Based on these models, we developed a screening tool using two questions: 1. Did you ever have a swollen joint? 2. Did a doctor ever tell you that you had arthritis? A positive answer to either question would indicate a positive test. This screening method results in a sensitivity for active PsA of 84%, a specificity of 52%, with a positive likelihood ratio of 1.74 and a negative likelihood ratio of 0.31.

Conclusion: This dermatology-based Pso cohort showed that ten percent of Pso patients had active PsA. We showed that the best predictors for the presence of active PsA were a patient-reported history of swollen joints, and a previous diagnosis of arthritis by physician. With these predictors, we could detect 84% of patients with active PsA.

	Pso + not-active PsA	Active PsA	Total
Negative Test	141	5	146
Positive Test	131	26	157
Total	272	31	303
	Specificity: 52%	Sensitivity: 84%	

Figure 1.

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POS1069

COVERAGE OF THE SWEDISH RHEUMATOLOGY QUALITY REGISTER: TO WHAT DEGREE ARE B/TSDMARD TREATMENTS FOR PSORIATIC ARTHRITIS RECORDED?

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Background: In a national context, the Swedish Rheumatology Quality register (SRQ) is a major source of information on clinical data for patients treated with biological and targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) for rheumatic diseases. Data from SRQ are fundamental for research on drug effectiveness and safety.
Objectives: To understand to what degree patients with psoriatic arthritis (PsA) and their dispensed b/tsDMARD treatments are recorded in the SRQ.
Methods: We identified all dispensed oral or subcutaneously administered b/tsDMARDs, approved for use in PsA, from the Swedish Prescribed Drug register (PDR, with 100% coverage) in 2018-2019. We required the patients who received the dispensation to have at least one ICD code for PsA (L405, M070, M071, M072, M073) as main diagnosis from a visit to a rheumatology or internal medicine (IM) unit in the National Patient Register (NPR) before dispensation, but no main diagnosis of rheumatoid arthritis (ICD code: M05, M06 (excluding M06.1 and M06.4), M12.3). Furthermore, to limit the assessment to patients with contemporary contact with the specialized rheumatology care, we also required at least one visit with a PsA main diagnosis from rheumatology/IM during 2017-2019. We then checked if the patients and their treatments were registered in SRQ. In a sensitivity analysis, we excluded patients with a visit in dermatology within 6 weeks prior to the first prescription of each b/tsDMARD, in order to exclude patients being prescribed the drug for cutaneous psoriasis.
Results: In 2018-2019, a total of 7922 unique b/tsDMARD prescriptions had been dispensed to 6311 patients with PsA, having contemporary contact with the specialized rheumatology care. Of them, 5687 patients were registered in SRQ (90.1%), of which 94.4% with a PsA diagnosis and 95.5% with at least one registration of a b/tsDMARD. The coverage of the single drugs in SRQ, as compared to dispensations in PDR, ranged between 53.5% to 93.3% (69.3% to 95.8% considering only patients also in SRQ), with the tumor necrosis factor inhibitors (TNFi) having the best coverage (79.4-93.3%) (Table 1). In a sensitivity analysis, among the 5290 patients without a main diagnosis of psoriasis before start of treatment, 4919 (93%) were registered in SRQ, of which 94% with a PsA diagnosis and 96% with at least one registration of a b/tsDMARD.

Table 1. coverage of the single b/tsDMARD approved for use in PsA patients in the SRQ as compared to the prescribed drug register, 2018-2019

ATC	Drug*	Total patients in PDR	Patients with the same drug in SRQ	Percentage	Percentage only considering patients included in SRQ
L04AB01	Etanercept	2753	2348	85.3%	92.5%
L04AB04	Adalimumab	2436	1933	79.4%	88.8%
L04AB05	Certolizumab pegol	243	213	87.7%	89.9%
L04AB06	Golimumab	418	390	93.3%	95.8%
L04AA24	Abatacept	94	73	77.7%	83.9%
L04AA32	Apremilast	547	294	53.7%	69.3%
L04AC10	Secukinumab	833	656	78.8%	84.8%
L04AC13	Ixekizumab	118	71	60.2%	74%
L04AC05	Ustekinumab	219	138	63%	76.2%
L04AA29	Tofacitinib	261	194	74.3%	77%

* In Sweden intravenously administered drugs are not prescribed and therefore not included in the PDR. Also, some hospitals administer ustekinumab in hospital, due to its high cost. However, all b/tsDMARDs, irrespectively of administration route, can be registered in SRQ.

Conclusion: The coverage of b/tsDMARD-treated PsA patients in SRQ as compared to the PDR in Sweden is ranging between 90 and 93%, and SRQ is performing well in the registration of the single drugs, especially for TNFi. These results suggest that research studies based on data from the SRQ are representative of the Swedish b/tsDMARD-treated PsA population.
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POS1070

BASELINE DETERMINANTS OF PAIN RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS RECEIVING GUSELKUMAB

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Background: Pain in patients (pts) with psoriatic arthritis (PsA) has multifaceted origins; sustained improvement is difficult to achieve.[1] Guselkumab (GUS), a fully human monoclonal antibody that selectively inhibits IL-23, is effective in treating multiple domains of PsA including joint, skin, and entheseal symptoms, and also elicits long-lasting improvements in pt-reported pain in the DISCOVER-1&2 trials of pts with active PsA.[2]
Objectives: These post hoc analyses were conducted to identify determinants of changes in pt-reported pain in PsA pts using pooled data through 1 year of DISCOVER-1&2.
Methods: Enrolled adult pts had active PsA despite standard therapies. DISCOVER-1 pts had ≥3 swollen and ≥3 tender joints and C-reactive protein (CRP) ≥0.3 mg/dL; DISCOVER-2 pts had ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL. 31% of DISCOVER-1 pts received 1-2 prior tumor necrosis factor inhibitors; DISCOVER-2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (wks) (Q4W); GUS 100 mg at W0, W4, then every

8 wks (Q8W); or placebo (PBO); PBO pts crossed over to GUS 100 mg Q4W at W24. Determinants with a statistically important effect ($p<0.15$) on pain (0-100 mm Visual Analogue Scale) in univariate Repeated Measures Generalized Linear Mixed Effects Models were included in a multivariate model employing backward stepwise selection ($P_{out}=0.1$) to identify independent determinants of pain improvement over 24 wks; the model was then tested separately in pts treated with PBO (through W24) and with GUS (through W24 and through W52).
Results: GUS was associated with significantly greater improvement in pain compared to PBO as early as 2 wks post-treatment; there was a significant interaction between treatment group and time, with effect of GUS on pain continuously enhanced through W24. Higher baseline (BL) pain score, worse mental health (assessed with the Short-Form-36 Mental Component Summary [SF-36 MCS] score), and lower fatigue level and lower tender joint count [TJC] were also associated with significantly greater pain improvements at W24, while background use of NSAIDs was a negative predictor of pain improvement (Table 1). Treatment effect on pain was independent of PsA duration, gender, PsA subtype, prior TNFi exposure, BL skin disease, and BL swollen joint count (SJC). Continuous significant improvement from BL in pain with GUS extended through W52 even after adjustment for the identified determinants of pain improvement through W24 (Figure 1). At W52, predictors of change in pain remained significant with the exception of SF-36 MCS score (Table 1). Results did not exclude a small number of enrolled pts with fibromyalgia (FM: $n_{GUS}=8$; $n_{PBO}=4$). According to these exploratory findings, medical history of FM was associated with lower pain improvement through W24 ($p=0.066$); in the models run separately in pts with GUS and PBO, pts with FM treated with GUS had a mean (95% CI) pain improvement (-9.1 [-19.5, 1.2]) while pts treated with PBO had a mean worsening (0.7 [-12.5, 13.9]). Pain improvement through 52 wks was significant regardless of FM: pts with FM had a mean (95% CI) improvement of -14.7 (-25.9, -3.6) comparable to non-FM pts at W24, while pain improvement in pts with no FM was -22.2 (-24.0, -20.4).

Table 1. Significant Predictors of Change in Pain (W24 and W52)

BL Determinant	W24	W52
	Estimate (95% CL)	Estimate (95% CL)
Pain score	-0.62 (-0.69:-0.55) ‡	-0.75 (-0.83:-0.67) ‡
Fatigue	-0.38 (-0.50:-0.27) ‡	-0.37 (-0.53:-0.22) ‡
SF-36 MCS	0.20 (0.11:0.30)‡	0.11 (-0.02:0.24)
TJC	0.13 (0.06:0.19) †	0.12 (0.04:0.21) †
NSAID use (Y vs N)	2.29 (0.62:3.96) †	2.76 (0.55:4.98) *

* $p<0.05$; †$p<0.01$; ‡$p\leq0.0001$

Conclusion: Early significant effects of GUS on pain were enhanced through 1 year. Significant predictors of change in pain were consistent at W24 and W52, with the exception of mental health measures. The impact of mental status on pt-reported pain and the potential for GUS to improve pain in pts with FM warrant further consideration.

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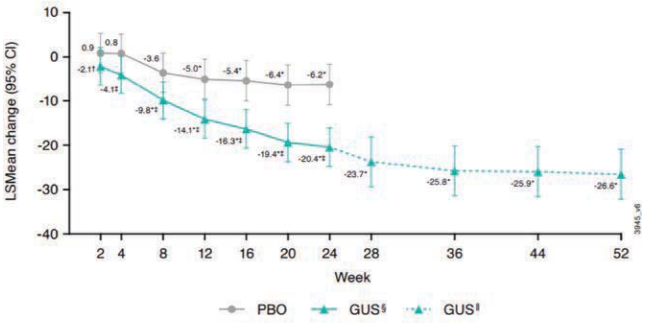
Figure. Change in Pain Over 52 Weeks



* Significant change from BL, $p<0.05$; †GUS vs PBO, $p=0.0059$; ‡GUS vs PBO, $p<0.0001$
§ Least square mean (LSMean) changes from a repeated measures generalized linear mixed model adjusting for baseline pain score, treatment type (GUS vs. PBO), baseline TJC, baseline fatigue, medical history of fibromyalgia, baseline SF-36 MCS, baseline use of NSAIDs, treatment by time interaction, baseline pain score by time interaction.
‖ LSMean changes from a repeated measures generalized linear mixed model adjusting for baseline pain score, baseline TJC, baseline fatigue, medical history of fibromyalgia, baseline SF-36 MCS, baseline use of NSAIDs, and time. GUS treatment only. Multivariate models through 24 weeks (PBO + GUS) and 52 weeks (GUS only)

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POS1071 [18F]FLUORIDE PET-CT SCANS VISUALIZE BOTH AXIAL AND PERIPHERAL BONE FORMATION IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) can present with peripheral (i.e. arthritis, enthesitis, dactylitis) and/or axial (spondyloarthritis) manifestations. Positron Emission Tomography (PET) may be a promising imaging technique for detection of whole body disease activity since it combines quantification and picomolar sensitivity for accurate depiction of pathologic processes with anatomical low dose CT imaging as a reference (3, 4). It was recently demonstrated that [^{18}F]Fluoride PET-CT scans can successfully visualize and monitor ankylosing spondylitis disease activity by imaging of bone formation in the axial skeleton (5). Since bone formation is associated with enthesitis and synovitis in PsA, [^{18}F]Fluoride may enable sensitive, whole body detection of disease activity in PsA.
Objectives: To investigate the feasibility of [^{18}F]Fluoride PET-CT to visualize disease activity of PsA by imaging of bone formation at axial and peripheral sites in PsA patients.
Methods: Sixteen patients (female 10/16, age 50.6 ±8.9 years) with PsA fulfilling CASPAR criteria and clinically active disease including ≥1 clinically active enthesitis site were included. Clinical disease activity was assessed by swollen joint count/tender joint count 44, MASES and SPARCC. Of each patient, a whole body [^{18}F]Fluoride PET-CT scan at 45 minutes post injection was performed. All scans were dichotomously scored by two board certified readers (blinded for clinical data) for PET-positive lesions in the joints, peripheral enthesis sites and spine. Low dose CT was used for anatomical reference.
Results: Out of 1088 evaluated joints, 109 joints showed PET enhancement, most frequently in the interphalangeal- and metatarsal joints of the feet (14/109, 12,9%) (Figure 1A) and the distal interphalangeal joints of the hands (14/109, 12,9%). Out of 416 evaluated entheseal sites, PET positivity was found at 44 sites, mainly located at the patella tendon insertion (11/44, 25%) (Figure 1B) and the quadriceps tendon insertion (10/44, 22.7%). Of the PET positive joints and entheses sites, respectively 81.1% and 70.5% were not associated with tender or swollen joints and clinical enthesitis, respectively. In 11 out of the 16 patients ≥1 axial PET positive lesion was observed (Figure 1C), most frequently located in the cervical spine (19/49 observed axial lesions, 38.8%). Two patients showed PET enhancement in one sacro-iliac joint (SIJ) without any inflammatory back pain (IBP). Only four out of 15 patients reported IBP and missing data for 1 patient. In two patients clinical dactylitis was observed which was also depicted on PET-CT.

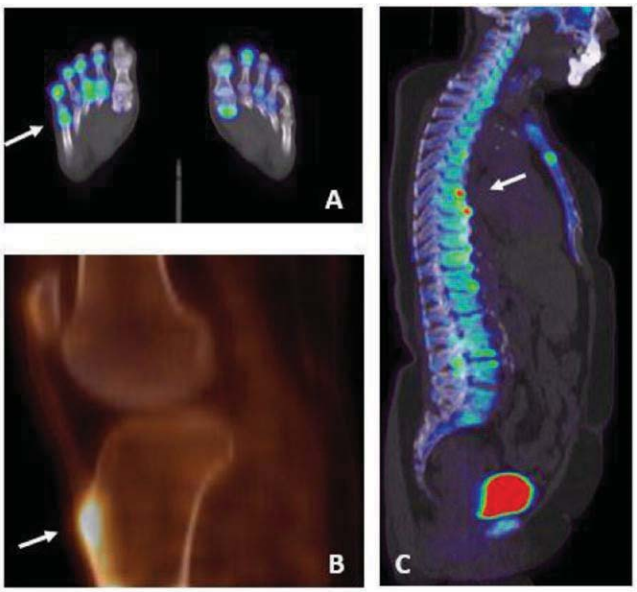

Figure 1. [^{18}F]Fluoride uptake in the metatarsal and IP-joints of the feet (A), in the patella tendon (B) and in the spine (C)

Conclusion: [^{18}F]Fluoride PET-CT scans can visualize disease activity at whole body musculoskeletal manifestations of PsA by demonstrating local bone formation in joints, entheses and the axial skeleton. By sensitive imaging of bone formation at active sites, [^{18}F]Fluoride PET-CT adds information to clinical disease activity, reflected by a high number of clinically negative, PET positive sites on top of concordant findings.

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POS1072 OBESITY AND LOWER LIKELIHOOD OF ACHIEVING MINIMAL DISEASE ACTIVITY AND REMISSION IN PSORIATIC ARTHRITIS PATIENTS

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Background: Among patients with psoriatic arthritis (PsA), obesity is a common comorbidity, and it is associated with difficulted disease management. This may be explained by the understanding of obesity as a low-grade inflammatory disease, which shares pathological pathway with PsA.

Objectives: We aimed to assess the impact of elevated body mass index (BMI) on the achievement of successful clinical outcomes in PsA patients within one-year after starting their first biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD).

Methods: This observational cohort study was performed using data from the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry (from 1997 to July 31st 2019), and it included adult PsA patients starting their first b/tsDMARD. Patients were classified according to their BMI as normal weight (BMI <25), overweight (BMI 25.0-29.9), and obese (BMI ≥30). Overweight and obese patients were compared to the normal weight group (reference group). Logistic regression (crude and adjusted by confounders) was used to assess the impact of elevated BMI category on the achievement of clinical outcomes at ≤12-months after start of the patient's first b/tsDMARD. These clinical outcomes included Minimal Disease Activity (MDA), as well as remission defined by Disease Activity for Psoriatic Arthritis (DAPSA), clinical DAPSA, and 28-joint disease activity score (DAS28). Similarly, the likelihood of treatment persistence at one year was compared between the overweight and obese groups *vs* the normal weight group. Additionally, the overlapping or accordance across the study outcomes was investigated.

Results: The study included 306 (39.53%) normal weight, 285 (36.82%) overweight, and 183 (23.64%) obese patients. Compared to the normal weight group, obese patients had lower odds of achieving MDA at ≤12-months (Adjusted odds ratio [ORadj] 0.45, 95% confidence interval [CI] 0.24-0.82). This was consistent with the observed reduced odds of achieving DAPSA remission (ORadj 0.42, 95%CI 0.21-0.85), clinical DAPSA remission (ORadj 0.51, 95%CI 0.27-0.96), and DAS28 remission (ORadj 0.51, 95%CI 0.32-0.81) in obese *vs* normal weight patients. No differences were observed in treatment persistence across the BMI strata. And there was high overlap between achievement of MDA and clinical DAPSA remission.

Conclusion: Among PsA patients starting b/tsDMARDs, obesity was associated with ca. 50% reduced odds of achieving MDA and remission in comparison to normal weight patients, while it did not impact treatment persistence.

Acknowledgements: We thank all patients and rheumatologists contributing to the SCQM registry, as well as the entire SCQM staff. A list of rheumatology offices and hospitals which contribute to the SCQM registry can be found at http://www.scqm.ch/institutions. A list of financial supporters of SCQM can be found at http://www.scqm.ch/sponsors. We would like to add a personal thank you to Axel Finckh (University Hospitals of Geneva) for his input regarding the database. AMB acknowledges that her professorship is partly endowed by the Swiss National Pharmacy Association (PharmaSuisse) and the ETH Foundation.

Disclosure of Interests: None declared

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POS1073 INCREASED NUMBER OF COMORBIDITIES AND CARDIOVASCULAR RISK FACTORS IN EARLY PSORIATIC ARTHRITIS PATIENTS SUGGESTS AN INTRINSIC DISEASE IMPACT.

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Background: Metabolic and cardiovascular comorbidities in psoriatic arthritis (PsA) are seen as a consequence of long-lasting inflammation. Patients with Pso and PsA develop metabolic and cardiovascular comorbidities over the course of time[1]. PsA patients have a higher burden of comorbidities and cardiovascular risk factors (CV RF) as compared to those with other forms of arthritis[2,3]. Despite a lower grade of systemic inflammation as measured by CRP, the nature of this increased prevalence in PsA is not fully understood. We hypothesize that the risks may be intrinsic to the disease, and be already present in early stages.

Objectives: The aim of this study was to investigate the presence of comorbidities and CV RF in treatment naïve Early PsA (EPsA) as compared to sex- and age-matched healthy volunteers and to study factors contributing to the metabolic burden of the patients.

Methods: Clinical, demographic characteristics, cardiovascular risk factors and comorbidities of newly diagnosed treatment-naïve adult patients with PsA compared to sex- and age-matched controls were studied in an observational prospective longitudinal multicentre study.

Results: Sixty-seven EPsA patients were matched to 61 healthy volunteers. At diagnosis, 73% of EPsA had oligoarticular and 22% polyarticular disease. Majority had mild PASI scores (median PASI 1.2). The median duration of skin psoriasis before the onset of PsA was 11.4 years. Symptom duration at onset of PsA was 0.6 years.

Table 1.

	early PsA, baseline (n=67)	healthy controls, baseline (n=61)	p value
male sex, n (%)	47 (70.1)	35 (57.4)	0.144
age, mean (±SD)	47.9 (±14.3)	45 (±14.2)	0.25
BMI, mean (±SD)	28.2 (±4.5)	25.7 (±(5.2)	0.006*
Obesity (BMI ≥30), n patients (%)	27 (40.3)	11 (18.3)	0.011*
Abdominal obesity#	34 (50.7)	18 (29.5)	0.019*
number (%) of patients with ≥2 comorbidities	35 (52.2)	17 (27.9)	0.007*
presence of cardiovascular risk factors ≥1, n patients (%)	55 (82.1)	23 (37.7)	0.017*
number (%) of patients with ≥2 CV RF	38 (56.7)	16 (26.2)	<0.001*
cardiovascular morbidity, n patients (%)	14 (20.7%)	4 (6.6)	0.07
Charlson comorbidity index, n patients (%)	21 (31.3)	4 (6.6)	<0.001*
median (IQL)	0 (0-1)	0 (0)	0.005*§
metabolic syndrome, n patients (%)	15 (22.4)	5 (8.2)	0.03*
diabetes mellitus t2, n patients (%)	8 (11.9)	1 (1.6)	0.034*
dyslipidemia, n patients (%)	43 (64.2)	24 (39.3)	0.008*

EPsA showed a significantly higher rate of obesity (40.3% vs 18.3% in controls, p=0.011). PsA patients had significantly higher rates of dyslipidemia and metabolic syndrome than controls. Rate of insulin resistance, arterial hypertension, depression, COPD, gout were similar in EPsA and in controls. The overall number of comorbidities was comparable in EPsA and healthy controls, but strikingly 82% of EPsA patients had CV RF already present at baseline as compared to 38% of the controls (p=0.017). More than half of PsA patients had multiple (≥2) comorbidities and CV RF at baseline as compared to controls(33%) (Figure 1*)*. Overall rate of cardiovascular morbidity and Charlson comorbidity index were low, but were significantly higher in the PsA group (p=0.007 and <0.001 accordingly). Duration of skin psoriasis had no effect on comorbidities or CV RF in EPsA.

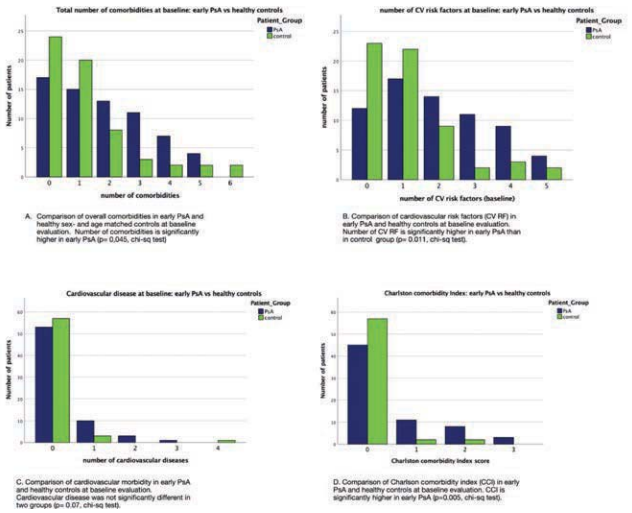

Figure 1. Comparison of comorbidities, CV RF, cardiovascular disease and Charlson comorbidity index in early PsA and healthy controls.

In multiple regression analysis diagnosis of PsA was the strongly associated with the number of comorbidities and CV RF after adjusting for age, sex and BMI.

Conclusion: Our data imply that PsA patients have higher comorbidities and cardiovascular burden at early stages of the disease. Rates of dyslipidemia, metabolic syndrome and obesity are significantly higher in the early PsA population. Presence of metabolic and lipid disturbances at early stages of the disease might suggest a bidirectional relationship and potentially playing role as initial triggers of PsA.

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POS1074

MINIMAL DISEASE ACTIVITY (MDA) IN PATIENTS WITH RECENT-ONSET PSORIATIC ARTHRITIS. PREDICTIVE MODEL BASED ON MACHINE LEARNING

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Background: Very few data are available on predictors of minimal disease activity (MDA) in patients with recent-onset psoriatic arthritis (PsA). Such data are crucial, since the therapeutic measures used to change the adverse course of PsA are more likely to succeed if we intervene early.

Objectives: To detect patient and disease variables associated with achieving MDA in patients with recent-onset PsA.

Methods: We performed a multicenter observational prospective study (2-year follow-up, regular annual visits), promoted by the Spanish Society of Rheumatology. Patients aged ≥18 years who fulfilled the CASPAR criteria, with less than 2 years since the onset of symptoms, were included. The intention at the baseline visit was to reflect the patient's situation before disease progress was modified by the treatments prescribed by the rheumatologist. All patients gave their informed consent. The study was approved by the Clinical Research Ethics Committee of the Principality of Asturias. MDA was defined as fulfillment of at least 5 of the following: ≤1 tender joint; ≤1 swollen joint; PASI ≤1 or BSA ≤3%; score on the visual analog scale (VAS) for pain provided by the patient ≤1.5; overall score for disease activity provided by the patient ≤2; HAQ score ≤0.5; ≤1 painful enthesis [1]. The dataset contained data for the independent variables from the baseline visit and from follow-up visit number 1. These were matched with the outcome measures from follow-up visits 1 and 2, respectively. We trained a random forest–type machine learning algorithm to analyze the association between the outcome measure and the variables selected in the bivariate analysis. In order to understand how the model uses the variables to make its predictions, we applied the SHAP technique. This approach assigns a SHAP value to each value of each variable according to the extent to which it affects the prediction of the model (the higher the absolute SHAP value, the greater the influence of this data item on prediction) and to how it affects the prediction (if the SHAP value is positive, the data item positively affects the prediction, that is, it confers a higher value on the prediction). The SHAP summary graphs order the predictors by their importance in the predictions of the model. This importance is calculated with the mean of the SHAP values assigned to each data item of a variable; mean values <0.01 indicate the low importance of the variable in the model. We used a confusion matrix to visualize the performance of the model. This matrix shows the real class of the data items, together with the predicted class, and records the number of hits and misses.

Results: The sample comprised 158 patients. 14.6% were lost to follow-up. 55.5% and 58.3% of the patients had MDA at the first and second follow-up visit, respectively. The importance of the variables in the model according to the mean of the SHAP values is shown in Table 1. The variables with the greatest predictive ability were global pain, impact of the disease (PsAID), patient global assessment of disease and physical function (HAQ-Disability Index). The SHAP values for each value of each variable are shown in Figure 1. The percentage of hits in the confusion matrix was 85.94%.

Table 1. Variables in the predictions of the random forest for MDA according to the SHAP method.

Variable	Importance according to SHAP[1]
Global pain	0.069
PsAID	0.064
Patient global assessment of disease	0.047
HAQ	0.044
Articular pattern at diagnosis	0.029
Physician global assessment of disease	0.023
Tender joint count	0.014
Sex	0.009
Weekly alcohol consumption	0.009

[1]Mean of the SHAP values for each value of the variable. MDA: minimal disease activity.

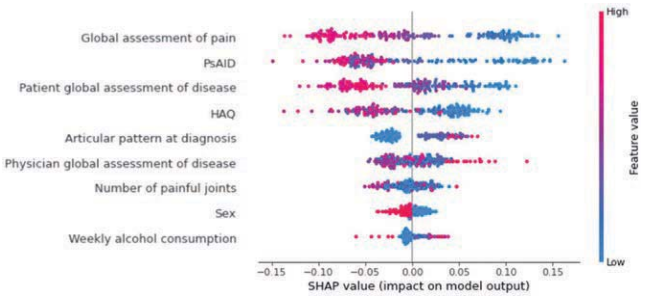

Figure 1. SHAP summary graph.

Conclusion: A key objective in the management of PsA should be control of pain, which is not always associated with inflammatory burden, and the establishment of measures to better control the various domains of PsA.

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POS1075

CROSS-SECTIONAL OBSERVATIONAL AND MULTICENTER STUDY FOR THE VALIDATION OF THE SPANISH VERSION OF THE PURE-4 QUESTIONNAIRE

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Background: The Psoriatic arthritis UnclutteRed screening Evaluation (PURE-4) has been culturally adapted to Spanish language recently following the standardized methodology.[1] A group of experts in psoriasis and psoriatic arthritis (PsA) has recently recommended the use of the Spanish version of PURE-4 due to the reduced number of items, its high sensitivity and specificity and the feasibility to implement in the clinical practice.

Objectives: To validate the Spanish version of the PURE-4 questionnaire.

Methods: Cross-sectional, observational and multicenter study conducted with primary data collection under conditions of routine clinical practice in Spain. The study included adult patients with diagnosis of psoriasis of any time of evolution and any type of severity, that voluntarily accepted to participate. Primary endpoint: validation of PURE-4 questionnaire in terms of sensitivity, specificity, feasibility, reliability (internal consistency) and construct validity. The study consists in two cross-sectional evaluations: assessment I (a visit performed by a dermatologist, followed by an independent visit to the rheumatologist within the following 4 weeks after to the dermatologist's visit and scheduled according to routine clinical practice) and assessment II (patients without PsA in assessment I will be evaluated by the rheumatologist one year ±2 months later and the rheumatologist will perform the PsA diagnostic confirmation according to the rheumatologist criteria and will collect clinical characteristics). Since data from assessment II are not yet available, data from assessment I are presented.

Results: 268 evaluable patients included, 57.1% male, with a mean (SD) age of 47.1 (12.6) years, a mean (SD) time from diagnosis of 18.6 (12.9) years and mostly receiving psoriasis treatment (88.8%), biological treatment being the most common (43.3%). Mean (SD) PURE-4 score for all patients was 1.4 (1.3), being 2.3 (1.1) for patients with PsA and 1.3 (1.3) for patients without PsA diagnosis (Table 1). 268 (100.0%) patients answered the full PURE-4 questionnaire. Area under the receiver-operating characteristic (ROC) curve was 0.7185 (95% CI: 0.6391, 0.7978), showing good quality of fit or quality of the questionnaire (Figure 1). Using the Youden index, which determines the optimal cut-off point for the classification of patients, it was identified that a score ≥2 indicated a diagnosis of PsA. PURE-4 questionnaire showed a sensitivity of 77.1% and a specificity of 61.1%.

Table 1. Sociodemographic and clinical baseline characteristics (assessment I)

Characteristics	With PsA diagnosis (n=35)	Without PsA diagnosis (n=226)	Not assesable (n=7)	Total (n=268)
Age, mean (SD)	50.5 (10.0)	46.5 (12.9)	49.9 (11.2)	47.1 (12.6)
Female, n (%)	14 (40.0%)	97 (42.9%)	4 (57.1%)	115 (42.9%)
Years since diagnosis, mean (SD)	19.7 (14.2)	18.3 (12.8)	22.4 (9.0)	18.6 (12.9)
Current treatment for psoriasis, n (%)	32 (91.4%)	199 (88.1%)	7 (100.0%)	238 (88.8%)
Phototherapy, n (%)	5 (15.6%)	16 (8.0%)	0 (0.0%)	21 (8.8%)
Topic treatment, n (%)	20 (62.5%)	66 (33.2%)	3 (42.9%)	89 (37.4%)
Conventional systemic no biological treatment, n (%)	7 (21.9%)	40 (20.1%)	2 (28.6%)	49 (20.6%)
Biological treatment, n (%)	8 (25.0%)	91 (45.7%)	4 (57.1%)	103 (43.3%)
Phosphodiesterase-4 inhibitors, n (%)	0 (0.0%)	8 (4.0%)	0 (0.0%)	8 (3.4%)
Others, n (%)	0 (0.0%)	3 (1.5%)	0 (0.0%)	3 (1.3%)
PASI, mean (SD)	8.7 (5.5)	7.0 (5.0)	4.2 (3.1)	7.2 (5.1)
Mild (PASI<7), n (%)	11 (31.4%)	95 (42.0%)	5 (71.4%)	111 (41.4%)
Moderate/severe (PASI≥7), n (%)	24 (68.6%)	131 (58.0%)	2 (28.6%)	157 (58.6%)

APs, psoriatic arthritis; PASI, *Psoriasis Area and Severity Index*; SD, standard deviation.

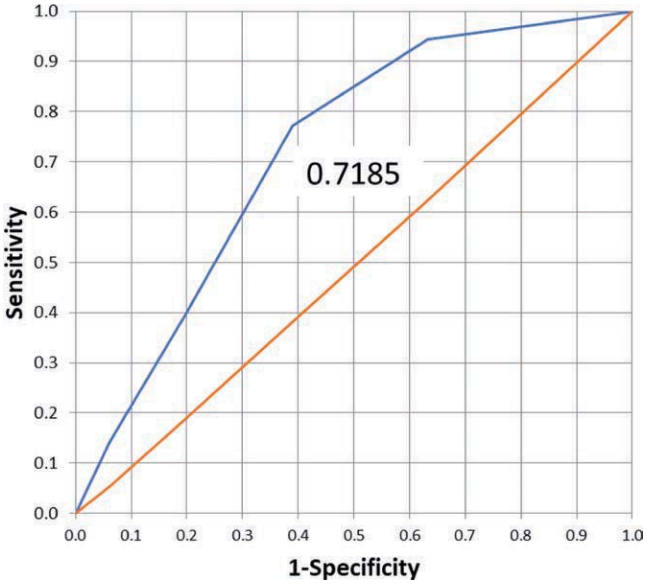

Figure 1. Area under the ROC curve (assessment I)

Conclusion: PURE-4 is a valid and compliant questionnaire with clinical practice in dermatology. It could be answered by patients in the waiting room and reviewed by dermatologists during the visit to support decision-making. PURE-4 could also help rheumatologists to early diagnose PsA patients in clinical practice.

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POS1076 OBESITY IS ASSOCIATED WITH LESS LIKELIHOOD OF REMISSION/ LOW DISEASE IN PSORIATIC ARTHRITIS, A CROSS-SECTIONAL STUDY OF 414 PATIENTS

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Background: Obesity is a risk factor for psoriatic arthritis (PsA) and is associated with higher disease activity [1].
Objectives: We aimed to evaluate whether obese patients with PsA were less likely to achieve remission/low disease in a real-life multi-centre cohort.
Methods: We used data from the ReFlap study (NCT03119805)[2], which recruited consecutive adult patient with definite PsA for more than 2 years of disease duration from 14 countries. We collected demographic characteristics, self-reported weight and height, clinical data and patient reported outcomes. Remission/low disease was defined as Disease Activity in PSoriatic Arthritis (DAPSA) ≤ 4, or Minimal disease activity (MDA). Obesity was defined as body mass index (BMI) ≥ 30kg/m^2. We compared patient characteristics, disease activity parameters and impact scores between patients with obesity versus non-obese. A multivariable regression model was performed for demographic variables associated with reaching each definition of remission/low disease, adjusted on age, sex, level of education, disease duration, current use of conventional (c-) and biological (b-) disease modifying anti-rheumatic drugs (DMARDs).
Results: Among 414 patients (49.3% women, mean disease duration 11.0 ±8.2 years), 119 (28.7%) had BMI ≥ 30kg/m^2 (obese). Obese patients were more likely to be female, had higher swollen joint and enthesitis counts, higher self-reported pain, poorer physical function, more fatigue and poorer mental health (Table 1). Obese patients were half as likely to achieve MDA or DAPSA remission in multivariable analysis with odd ratios of 0.6 (95% confidence interval, CI: 0.3, 0.8, p=0.049) and 0.4 (95% CI: 0.2, 0.8, p=0.012), respectively for obese compared to non-obese patients (Figure 1).

Table 1. Patient characteristics and remission achievement between obese and non-obese patients with psoriatic arthritis

	Non-obese (n=295)	BMI ≥30 (n=119)	p
Female, %	44.3	61.5	0.002
Number of comorbidities	1.61 (0.93)	2.83 (2.01)	<0.001
Tender joints, 0-68	3.56 (7.81)	5.75 (10.0)	0.018
Swollen joints, 0-66	2.19 (7.29)	1.46 (2.39)	0.285
Leeds enthesitis index, 0-6	0.48 (1.23)	0.86 (1.70)	0.012
PGA disease activity, 0-10	3.90 (2.73)	4.76 (2.67)	0.004
DAPSA	14.9 (15.5)	18.3 (16.1)	0.045
HAQ-DI, 0-3	0.56 (0.65)	0.89 (0.70)	<0.001
PsAID-12, 0-10	3.11 (2.36)	3.96 (2.50)	0.001
pain, 0-10	3.80 (2.81)	4.54 (2.83)	0.017
fatigue, 0-10	3.93 (3.01)	4.68 (3.17)	0.025
work or leisure activities, 0-10	3.39 (3.01)	4.75 (3.11)	<0.001
functional capacity, 0-10	3.36 (2.97)	4.40 (3.16)	0.002
depression, 0-10	1.88 (2.70)	2.75 (3.26)	0.006

Mean (SD) shown unless specified otherwise. HAQ-DI: Health Assessment Questionnaire – Disability Index; PsA: psoriatic arthritis; PGA: patient global assessment of disease activity; DAPSA: Disease Activity in PSoriatic Arthritis; PsAID: Psoriatic Arthritis Impact of Disease.

Conclusion: In this real-life data from 14 countries, obesity was frequent and PsA patients with BMI ≥ 30kg/m^2 were more likely to be female, and had higher subjectively reported disease activity and illness impact compared to those with lower BMI. Obese patients had a two-fold lower likelihood of achieving remission/low disease defined by both MDA and DAPSA compared to non-obese patients. PsA patients with comorbid obesity may have different disease profiles from non-obese patients, and require specific management.
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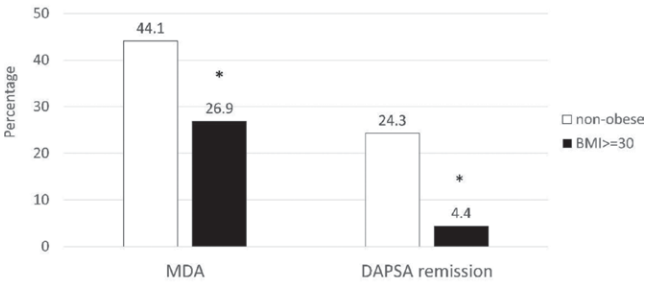
Figure 1. Rates of remission for patients with BMI ≥30 kg/m² versus non-obese



*p<0.01; BMI: body mass index; DAPSA: Disease Activity in PSoriatic Arthritis; MDA: Minimal Disease Activity.

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POS1077 LARGE JOINT INVOLVEMENT AND SUBSTANTIAL DISEASE BURDEN IN PATIENTS WITH OLIGOARTICULAR AND POLYARTICULAR PSORIATIC ARTHRITIS IN THE MULTINATIONAL UPLIFT SURVEY

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Background: Patients (pts) with oligoarticular psoriatic arthritis (PsA) report quality-of-life impairment similar to polyarticular PsA pts despite less joint involvement. In the 2020 Understanding Psoriatic Disease Leveraging Insights for Treatment (UPLIFT) survey, we evaluated other aspects of disease burden in pts with oligoarticular (≤4 joints) and polyarticular (>4 joints) PsA.

Objectives: To explore joint involvement distribution and relative disease burden in pts with self-reported healthcare provider (HCP)–diagnosed PsA who self-identified with oligoarticular vs polyarticular joint involvement.

Methods: UPLIFT was a multinational Web-based survey in adults who reported an HCP diagnosis of PsA and/or psoriasis. This analysis evaluated demographics, disease characteristics, joint distribution, and quality-of-life measures in pts with PsA with or without psoriasis with self-identified oligoarticular vs polyarticular joint involvement. Small joint classification includes foot/toes, hands/fingers, and thumbs; intermediate joints includes wrists, elbows, and ankles; and large joints includes shoulders, hips, and knees.

Results: Of the 1256 pts with PsA completing the survey, 44% had oligoarticular PsA and 56% polyarticular PsA. The polyarticular PsA group had higher mean age, fewer males, and more pts with body mass index ≥25 kg/m^2 (Table 1). Prevalence of depression, hypertension, and diabetes was generally similar between groups (Table 1). In pts with oligoarticular and polyarticular PsA, respectively, involvement of large joints was most prevalent (63%, 91%), followed by intermediate (46%, 87%) and small (20%, 76%) joints. Axial involvement was less prevalent in pts with oligoarticular (30%) vs polyarticular (67%) PsA. Common areas of joint involvement were the knees, elbows, and shoulders for oligoarticular PsA pts and the knees, hands, and elbows for polyarticular PsA pts (Figure 1). Involvement in the hands, wrists, thumbs, feet, and ankles was proportionately greater in polyarticular pts vs oligoarticular pts. Dactylitis, enthesitis, and nail disease, respectively, were each present in approximately one third of oligoarticular PsA pts and more than half of polyarticular PsA pts. Mean Patient Assessment of PsA Severity, Health Assessment Questionnaire (HAQ)-8, and Psoriatic Arthritis Impact of Disease 12-item (PSAID-12) scores indicated similar disease burden between the two groups (Table 1). In both groups, >70% reported an unacceptable PsA symptom state (PSAID >4), and >60% had Patient Health Questionnaire 2-item (PHQ-2) score ≥3, consistent with positive screening for depression (Table 1).

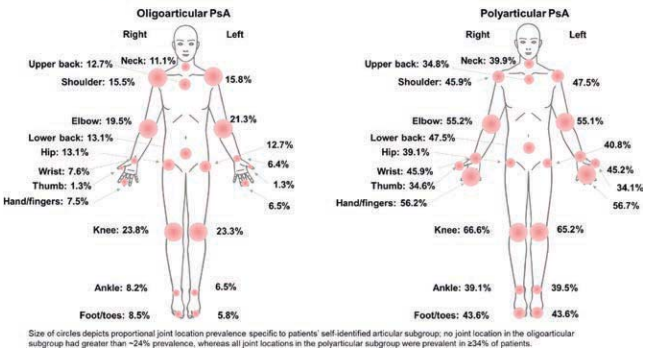
Table 1. Demographics and Patient Characteristics

	Oligoarticular PsA (n=550)	Polyarticular PsA (n=706)
Age, mean (SD), y	39.5 (15.23)	45.6 (14.89)
Male sex, n (%)	327 (60)	347 (49)
Body mass index ≥25 kg/m^2 (overweight/obese), n (%)	164 (30)	292 (41)
PsA duration, mean (SD), y	11.1 (10.44)	13.8 (11.40)
PsA treatment use, n (%)*		
Prior oral prescription	231 (44)	217 (31)
Prior injectable/intravenous	177 (34)	169 (24)
Current oral prescription	185 (35)	364 (53)
Current injectable/ intravenous	154 (29)	246 (36)
Comorbidities, n (%)		
Hypertension	230 (42)	302 (43)
Depression	214 (39)	291 (41)
Diabetes	201 (37)	236 (33)
Skin or non-skin cancer	200 (36)	168 (24)
Heart disease	149 (27)	123 (17)
Inflammatory bowel disease	156 (28)	142 (20)
Liver disease	149 (27)	98 (14)
Patient Assessment of PsA Severity, mean, (SD)	5.0 (2.92)	5.7 (2.53)
HAQ-8, mean, (SD)	0.9 (0.65)	0.8 (0.64)
PSAID-12, mean, (SD)	5.3 (2.54)	5.6 (2.42)
PSAID >4, n (%)	389 (71)	533 (76)
PHQ-2 ≥3, n (%)	383 (70)	452 (64)

*n=525 with oligoarticular PsA; n=691 with polyarticular PsA.

Conclusion: In the UPLIFT survey, almost half of pts with PsA self-identified with oligoarticular PsA. Both oligoarticular and polyarticular PsA groups experienced similar levels of disease burden, including a high prevalence of an unacceptable PsA symptom state and a PHQ-2 score ≥3, indicative of a positive screen for depression.

Figure. Distribution of Joint Involvement



Size of circles depicts proportional joint location prevalence specific to patients' self-identified articular subgroup; no joint location in the oligoarticular subgroup had greater than ~24% prevalence, whereas all joint locations in the polyarticular subgroup were prevalent in ≥34% of patients.

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POS1078 COMPARISON OF PATIENTS WITH AXIAL PSA AND PATIENTS WITH AXSPA AND CONCOMITANT PSORIASIS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease affecting the peripheral and axial musculoskeletal system as well as skin and nails. Diagnostic criteria of axial PsA (axPsA) are not well defined. Treatment strategy is mostly based on evidence generated for axial spondyloarthritis (axSpA), as only rare clinical trial data for axPsA exist. However, it is still unclear whether axSpA with concomitant psoriasis (axSpA/pso) is the same as axPsA.

Objectives: To compare PsA patients with axial manifestations with axSpA patients with concomitant psoriasis.

Methods: RABBIT-SpA is a prospective longitudinal cohort study including PsA and axSpA patients enrolled at start of a new conventional treatment or b/tsDMARD treatment. Two definitions of axPsA were used:

Clinical definition: documentation of axial manifestation as diagnosed by a rheumatologist

Radiographic definition: presence of sacroiliitis according to modified NY criteria (mNYc).

axSpA patients were stratified into axPsA/pso (with psoriasis either in patient history or present) and axSpA.

Results: Psoriasis was documented in 182/1407 axSpA patients (13%). Of 1355 PsA patients, 295 (22%) fulfilled the clinical definition of axPsA. Using the radiographic definition, 127 (9%) PsA patients fulfilled mNYc, 230 (17%) did not fulfil mNYc and 998 (74%) did not undergo radiographic evaluation.
AxSpA/pso patients differed from axPsA regardless of the definition (Table 1). axPsA patients were older, less often HLA-B27 positive, and peripheral manifestations were much more often present in axPsA than in axSpA/pso. Uveitis and inflammatory bowel disease were more common in axSpA/pso.

Table 1. Baseline characteristics of axSpA/pso patients and clinical resp. radiographic defined axPsA.

	axSpA/pso	axPsA/clin	axPsA/rad
N	182	295	127
female gender, n (%)	80 (44)	178 (60.3)	80 (63)
age, mean (SD)	47 (12.8)	51.1 (11.3)	51.6 (11.4)
HLA-B27 positive, n (%)	106 (67.1)	44 (22.7)	28 (32.9)
CRP mg/l, mean (SD)	8.7 (14.6)	7.1 (11.8)	6.9 (11.5)
CRP ≥5 mg/l, n (%)	70 (42.4)	106 (40)	50 (45.9)
uveitis ever, n (%)	26 (14.3)	10 (3.4)	7 (5.5)
IBD ever, n (%)	13 (7.1)	14 (4.7)	7 (5.5)
≥3 comorbidities, n (%)	48 (26.4)	117 (39.7)	48 (37.8)
peripheral manifestations, n (%)	65 (36.3)	251 (85.1)	109 (85.8)
enthesitis, n (%)	29 (16.2)	77 (26.4)	32 (25.4)
number of sites with enthesitis, mean (SD)	0.5 (1.6)	0.9 (2.2)	0.9 (1.9)
affected joints, n (%)	53 (29.6)	234 (80.1)	102 (80.3)
number of affected joints, mean (SD)	1.4 (3.7)	6.8 (8.4)	5 (5.9)
physician global disease activity, mean (SD)	5.6 (2.1)	5.6 (1.9)	5.6 (2)
patient global disease activity, mean (SD)	5.4 (2.6)	5.9 (2.3)	5.8 (2.2)
patient pain, mean (SD)	5.5 (2.6)	5.7 (2.3)	5.7 (2.2)
sakroiliitis, n (%)	124 (84.4)	97 (56.1)	127 (100)
clinical axial definition, n (%)	n.d.	295 (100)	97 (76.4)

In contrast, disease activity measured by physician global as well as patient global, and patient pain were similar in axSpA/pso and axPsA.
Conclusion: Regardless whether clinical or radiographic definitions of axPsA were used, differences to axSpA/pso patients were identified. These data indicate a need for a specific diagnostic, and a potentially more targeted treatment approach for axPsA.
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POS1079 CLINICAL CHARACTERIZATION OF PRODROMAL AND VERY EARLY PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW FOR THE DEFINITION OF CLINICAL AND IMAGING SUSPICIOUS FEATURES FOR PROGRESSION TO PSORIATIC ARTHRITIS

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Background: The transition from psoriasis (PsO) to psoriatic arthritis (PsA) is a focus of considerable scientific interest: is it possible to target pre-PsA and very early PsA, in particular for physiopathology and drug studies? Recently, a EULAR taskforce has been set up in this area (1).
Objectives: To characterize the prodromal and the very early PsA through a systematic literature review (SLR).
Methods: A SLR explored MEDLINE, EMBASE and CENTRAL, up to 22 October 2021. The objective was to identify the symptoms, objective signs, lab tests, imaging features and other characteristics of patients later diagnosed as "new onset" PsA in two key populations: 1) patients with PsO and 2) patients with early undifferentiated arthritis (UA). Studies of adult patients published in English were included, if they reported characteristics of pre-PsA or new onset PsA patients, and data were extracted by 2 readers. Meta-analysis was not done due to data heterogeneity (PsA classification criteria, outcome measures and length of observation). Results are reported semi-quantitatively.
Results: Of 31449 references, 22 studies were included of which 12 were prospective; 7 retrospective and 3 cross-sectional. Eighteen studies reported on patients with PsO (n=95828) later diagnosed as PsA (n=2136) with a mean duration of follow up of 5.2 (±3.9) years. Seven out of 18 (38.8%) studies were informative regarding the clinical features of the new onset PsA. Four studies on early UA patients (n=492) later diagnosed as PsA (n=49) were included. Progression to PsA was associated with the presence of musculoskeletal (MSK) complaints (mainly joint tenderness) and the presence of subclinical MSK inflammation detected by imaging. Peripheral oligo-arthritis was the prevalent clinical presentation of new onset PsA.
Conclusion: As expected, joint pain and imaging evidence of MSK inflammation were associated with PsA development in PsO patients. The SLR highlights the lack of robust evidence regarding data associated with the development of PsA. More prospective studies focusing on transition from PsO to PsA are needed.

Table 1.

Features		Transition from PsO to PsA (n = 18 studies)	Transition from UA to PsA (n = 4 studies)	Clinical characterization of New Onset PsA (n = 5 studies)
Patient reported symptoms	VAS pain	+++		NA
	Entheseal pain	+		NA
	Morning stiffness	+		NA
	Fatigue	+		NA
	HAQ more compromised	++		NA
	Arthralgia	+++		NA
Clinical examination	Joint tenderness	+++	+	+++
	Swelling joints		+	+++
	Entheseal tenderness			
Major domain of pattern presentation	Peripheral arthritis (more frequent)			+++
	Polyarthritis			
	Mono-oligoarthritis		+	+
Inflammatory marker(s)	CRP	+		+
Imaging	MSK inflammation detected by imaging	+++		+
	Radiographic evidence of specific damage		+	+

Legend:PsO = psoriasis (affecting skin); PsA = psoriatic arthritis; UA = undifferentiated inflammatory arthritis; VAS = visual-analogue scale; NA = not applicable; HAQ = health assessment questionnaire; CRP = C-reactive protein; MSK = musculoskeletal+ = 1 study for positive association; ++ = 2 studies for positive association; +++ >= 3 studies for positive association

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[1] *https://www.eular.org/ongoing_initiatives.cfm*
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POS1080 CHARACTERIZATION OF JOINT DISTRIBUTION AND DISEASE BURDEN IN PATIENTS WITH EARLY OLIGOARTICULAR PSORIATIC ARTHRITIS: RESULTS FROM THE ONGOING FOREMOST STUDY

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Background: Oligoarticular psoriatic arthritis (PsA) is commonly reported in early disease. Although fewer joints are involved, there may be significant impact on patients' (pts) quality of life. The ongoing FOREMOST study (NCT03747939) is investigating the efficacy of apremilast vs placebo for treatment of early oligoarticular PsA (>1 but ≤4 tender and swollen joints involved).
Objectives: To characterize disease burden in pts with early oligoarticular PsA and disease phenotype including location and size of involved joints and presence of certain baseline clinical PsA manifestations in FOREMOST pts.
Methods: Baseline swollen and tender joint distribution was analyzed. Baseline disease burden was assessed in the overall group and a subgroup with small joint involvement only (for context) using clinical disease activity measures, pt-reported outcomes, and additional PsA manifestations.
Results: At data cut-off for analysis, 220 pts of 285 planned were enrolled. In the overall group, disease duration was <1 year and joint distribution for swollen or tender joints involved predominantly small joints, with ~48% of joint involvement observed in finger proximal interphalangeal (PIP) joints and <2% in temporomandibular and clavicular joints across swollen or tender joints (Figure 1). Mean Physician's and Patient Global Assessment of Disease Activity (PhGA and PtGA, respectively) scores were 43.9 and 51.3; mean pt pain assessment score was 50.7. Mean Health Assessment Questionnaire Disability Index (HAQ-DI) functional assessment score was 1.0; 25.5% of pts had HAQ-DI ≤0.5. Pts reported an average PsA Impact of Disease (PsAID-12) domain score of 4.7. Additional manifestations of PsA at baseline included dactylitis (14.5%), enthesitis (32.7%), nail involvement (67.3%), and skin disease (47.7% with body surface area [BSA] ≥3%). Within the overall group, 59% had >1 joint size involved (small [metacarpophalangeal, metatarsophalangeal, distal interphalangeal, PIP, hand carpometacarpal and mid-tarsal]; intermediate [wrist, elbow, ankle, temporomandibular, acromioclavicular, sternoclavicular]; large [shoulder, hip, knee]). Of those with only 1 joint size involved (41% of pts), the majority had small joint involvement predominantly in PIPs (n=84 for small joints; n=1 for intermediate joints; n=5 for large joints). The overall pattern of clinical and disease presentation indicated elevated burden for pts with early oligoarticular PsA, including those pts with only small joints involved (Table 1).

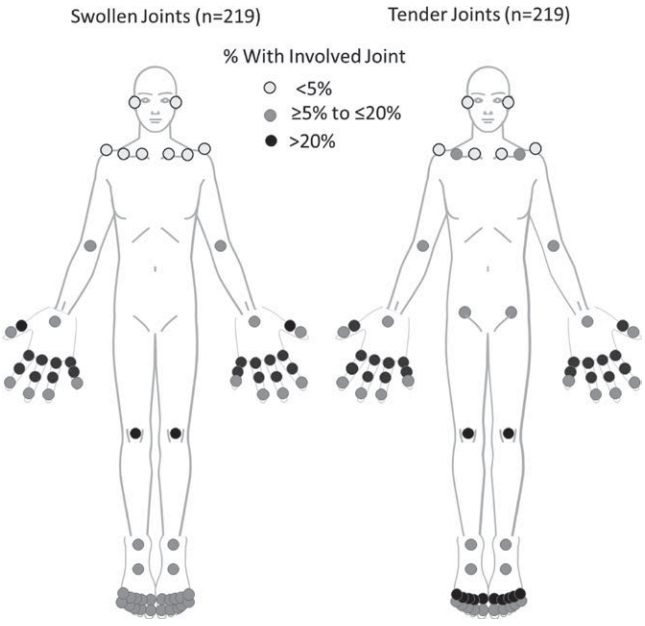

Figure 1. FOREMOST population: baseline demographics and disease burden in the overall population and pts with involvement in small joints only

Conclusion: In FOREMOST, despite few joints involved, pts with early oligoarticular PsA experienced high disease burden and impaired quality of life. Small joint involvement, although less commonly expected in oligoarticular PsA, was the most frequently observed pattern.

Table 1.

Characteristics	Overall Population (PBO + APR), N=220	Small Joints Only (PBO + APR), N=84
Age, mean, y	49.6	51.3
Men, n (%)	98 (44.5)	40 (47.6)
Europe/Russia, n (%)	47 (21.4)/66 (30.0)	22 (26.2)/11 (13.1)
Canada/United States, n (%)	8 (3.6)/99 (45.0)	1 (1.2)/50 (59.5)
Body mass index, mean, kg/m^2	30.4	29.3
Duration of disease, mean, y	0.69	0.71
Previous cDMARD use, n (%)	143 (65.0)	48 (57.0)
Tender joint count (0–68), mean	3.2	3.1
Swollen joint count (0–66), mean	2.6	2.8
PhGA (VAS 0–100)[a], mean	43.9	39.0
PtGA (VAS 0–100)[a], mean	51.3	45.6
Patient's Assessment of Pain (VAS 0–100)[a], mean	50.7	46.3
Dactylitis present, n (%)	32 (14.5)	14 (16.7)
Enthesitis present, n (%)	72 (32.7)	21 (25.0)
BSA ≥3%, n (%)	105 (47.7)	34 (40.5)
Nail involvement present, n (%)	148 (67.3)	53 (63.1)
HAQ-DI (0–3)[a], mean	1.02	0.84
HAQ-DI ≤0.5, n (%)	56 (25.5)	31 (36.9)
PsAID-12 (0–10)[a], mean	4.73	3.98

cDMARD, conventional disease-modifying antirheumatic drugs; VAS, visual analog scale.[a]Higher scores indicate greater burden/worse status. Early oligoarticular = ≤2 years in the initial protocol; ≤5 years in the current protocol for inclusion.

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POS1081 SERUM MPO-DNA COMPLEX LEVEL CORRELATES WITH DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

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Background: NETosis has been found to participate in the pathogenesis of many autoimmune diseases, however rarely reported in psoriatic arthritis (PsA).
Objectives: We aimed to explore the involvement of NETosis in the inflammation of PsA.

Methods: Serum MPO-DNA complex was detected by a modified enzyme-linked immunosorbent assay (ELISA) and compared among 74 patients with PsA, 58 patients with psoriasis (PsO) and 20 healthy controls. The association of MPO-DNA level with disease activity index at baseline and follow-up was analyzed in PsA patients. Receiver operating characteristic curve was used to evaluate the predictive value of MPO-DNA for treatment response.
Results: MPO-DNA complex level in serum was significantly increased in PsA/PsO patients compared to healthy controls (p<0.001). The level of MPO-DNA was positively associated with DAPSA score and its components (including TJC, SJC, PGA, EGA, VAS-pain and CRP, r=0.25-0.409, all p-value<0.05). Serum MPO-DNA level was downregualted at 12-week after treatment compared to baseline (p=0.022). The decrease of MPO-DNA level was more dramatic in PsA patients who achieved both ACR50 and PASI50 response than those achieving neither of them at 12 weeks (p=0.023). ROC analysis revealed that the serum MPO-DNA level predicted both ACR50 and PASI50 achievement at week 12 (p=0.04, 95% CIs 0.56-0.94). Moreover, the baseline MPO-DNA level (p=0.009, 95% CIs 0.748-1) and change of MPO-DNA at week 12 from baseline (p=0.004, 95% CIs 0.802-1) were associated with the achievement of both ACR70 and PASI75 response.
Conclusion: NETosis plays an important role in psoriatic diseases. The level of MPO-DNA complex in serum reflects disease activity. Serum MPO-DNA complex may be a useful biomarker to predict the therapeutic response in PsA.

Table 1. Treatment response and changes of serum MPO-DNA of 29 PsA patients.

Items	Baseline	12 weeks	24weeks
TJC, median (IQR)	3(7)	3(4)	2(3.5)
SJC, median (IQR)	2(5)	2(2)	1(3)
ESR, median (IQR) mm/h	13(15)	8(10)	10(14)
CRP, median (IQR) mg/L	3(10.2)†	2.6(3.72)	2.3(3.8)
PGA, median (IQR)	40(30)*†	20(30)††	10(17.5)
EGA, median (IQR)	30(20)††	20(10)††	10(20.4)
VAS-pain, median (IQR)	30(30)*††	20(20)††	10(10)
PASI, median (IQR)	2.8(6.2)*†	0.7(1.5)	0.35(1.55)
DAPSA, median (IQR)	15(15.1)†	8.4(8.4)	6.15(10.3)
MPO-DNA, median (IQR)	0.416(0.615)*	0.231(0.321)	-
Minimal disease activity, n (%)	4(13.7%)	6(20.6%)	12(41.3%)
ACR50, n (%)	-	13(44.8%)	15(51.7%)
PASI50, n (%)	-	14(48.2%)	17(58.6%)
ACR70, n (%)	-	4(13.7%)	7(24.1%)
PASI75, n (%)	-	11(37.9%)	14(48.2%)
Both ACR50PASI50, n (%)	-	8(27.5%)	13(44.8%)
Both ACR70PASI75, n (%)	-	3(10.3%)	5(17.2%)

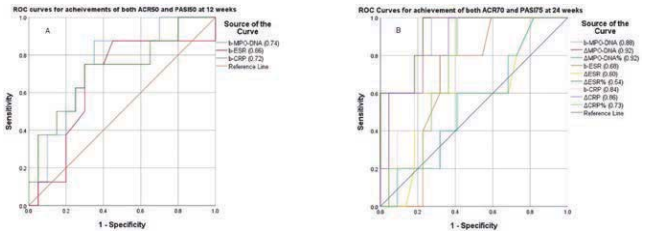

Figure 1. ROC curves for predictions of treatment achievements at 12 and 24weeks.

Disclosure of Interests: None declared

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POS1082 **CHARACTERISTICS OF PSORIATIC ARTHRITIS (PSA) PATIENTS WITH ENTHESITIS. DATA FROM RUSSIAN PSA REGISTRY (RU-PSART).**

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Background: Psoriatic arthritis (PsA) is a disease with multidomain clinical presentation such as arthritis, enthesitis, dactylitis, spondylitis and psoriasis (PsO). [1]. Enthesitis is a key clinical feature of PsA with significant impact on function, quality of life and choice of treatment [2]. There are limited real-world studies on the characteristics of patients (pts) with PsA and enthesitits.
Objectives: To compare clinical characteristics of PsA pts with and without enthesitis.
Methods: 603 pts (M/F=278/326) with PsA according to CASPAR criteria were examined. Data was collected from 6 rheumatology clinics of the Russian Federation. Pts' mean age 46.6±12.5 years (yrs.), PsA duration 9.7±7.1 yrs, PsO duration 20.45±13.0 yrs. Median (Me) DAPSA 25.5 [15.2; 41.8], body mass index (BMI) 27.5 [24.3; 31.2]. At baseline (BL) PsA activity by tender/swelling joint count (TJC)/68, (SJC)/66, enthesitis by LEI and plantar fascia, BSA (%), PASI, HAQ, DAPSA were evaluated. DAPSA>28 indicate high disease activity (HDA). The one-factor model of logistic regression was used to identify a group of features that are associated with presence of enthesitis. M±SD, Me [Q25; Q75], Min-Max, %, t-test, Pearson-χ^2, Manna-Whitney tests, ORs with 95% CI were performed. All p<0.05, were considered to indicate statistical significance.
Results: Enthesitis was found in 295 out of 603 pts (49%). Comparative analysis in both groups with and without enthesitis and one-factor model of logistic regression showed the following features at BL were associated with enthesitis: TJC>5 (p=0.001), SJC>3 (p=0.001), dactylitis (p=0.001), high disease activity by DAPSA (p=0.001), HAQ≥0.5 (p=0.001), BSA>10% (p=0.001), nail PsO (p=0.003), CRP>10 mg/l (p=0.018), BMI>30 kg/m^2 (p=0.02). Pts with enthesitis had significantly more often depression (p=0.026), metabolic syndrome (p=0.047), fatty hepatosis (p=0.017), OR analysis with CI 95% for all parameters are shown on Figure 1.

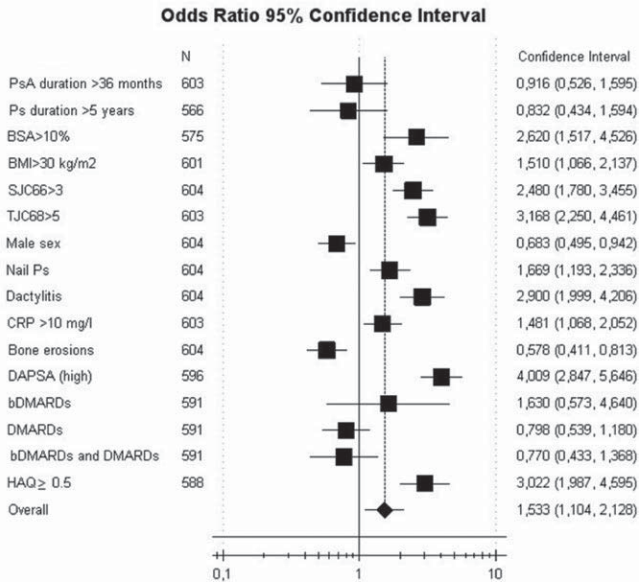

Figure 1. Factors associated with enthesitis in PsA pts.

Conclusion: In real clinical practice enthesitis was found in half of PsA pts. Enthesitis are associated with more severe peripheral arthritis, dactylitis, skin and nail PsO, higher PsA activity by DAPSA, worse quality of life and more likely to have depression, metabolic syndrome and fatty hepatosis. This should be considered for optimizing disease management strategy.
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POS1083

INCREASED INTESTINAL PERMEABILITY IN PATIENTS WITH PSORIATIC ARTHRITIS CLASSIFIED AS TREATMENT FAILURES DURING THE 26-WEEK FLORA TRIAL

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Background: Changes in the integrity of the intestinal wall may be implicated in the gut-joint axis of inflammatory arthritis.[1] Yet, the gut barrier is only poorly evaluated in psoriatic arthritis (PsA).[2]

Objectives: In this exploratory study, we evaluated intestinal permeability before and 26 weeks after one faecal microbiota transplantation (FMT) or sham intervention in adults with PsA.

Methods: We have previously reported the clinical results of a 26-week, double-blind, parallel-group, 1:1 randomised, sham-controlled, superiority trial of gastroscopic-guided FMT as an add-on treatment to methotrexate in 31 adults with active peripheral PsA (FLORA trial, NCT03058900).[3] The primary efficacy endpoint was the proportion of participants who experienced treatment failure through 26 weeks, defined as need for more than one intra-articular glucocorticoid injection and/or anti-TNFα inhibition. We encouraged patients not to take nonsteroidal anti-inflammatory drugs during the trial. The FMT material was obtained from one of four healthy blood donors. As part of the trial, we performed a lactulose and mannitol test (L:M test) at baseline (n=31) and at the final 26-week visit (n=26) to assess the permeability of the intestinal wall (higher L:M ratios indicate higher permeability). After an overnight fasting, patients provided a urine sample before ingesting 10 g of lactulose and 5 g of D-mannitol. Samples were collected after 3 hours and stored at –80°C until analysis. No food or drinking (except for water) was allowed during the test. We measured the lactulose-to-mannitol ratio in the urine samples using a Waters Acquity UPLC system coupled to a high-resolution mass spectrometer Waters Xevo G2 QToF (Waters Corp., Milford, MA, USA). MassLynx software (Waters Corporation) was used for data acquisition and visual inspection. We used StataSE-64 to perform the Wilcoxon rank sum and the matched-pairs signed-rank test. Data is presented as median and range. The level of significance was set to 0.05.

Results: At baseline, no significant difference was observed in the L:M ratio between donors (n=4) and patients (n=31) (0.0065 [0–0.063] vs 0.014 [0–0.28]; p=0.50). The L:M ratio increased from baseline to week 26 in both the FMT (0.0020 [-0.27 – 0.32] and the sham group (0.0046 [-0.012 – 0.088]), but only in the sham group differed the baseline L:M ratio significantly from the one measured at week 26 (p=0.92 [FMT] and p=0.032 [sham]). The patients who were classified as treatment failures during the trial (n=7) had a significantly higher L:M ratio at week 26 compared to the patients who were non-failures (n=19) (0.027 [0.017 – 0.33]) vs 0.012 [0 – 0.064], p=0.01), please see Figure 1.

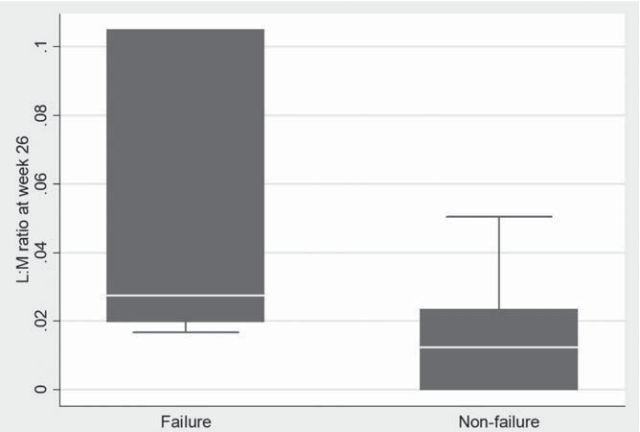

Figure 1. L:M ratios at week 26 in treatment failures (n=7) and non-failures (n=19), respectively. Higher L:M ratios indicate higher intestinal permeability.

Conclusion: In the FLORA trial, intestinal permeability evaluated by the L:M test did not differ significantly between donors and patients at baseline. Whether the higher intestinal permeability observed in patients classified as treatment failures compared to non-failures at week 26 can be attributed to differences in disease activity and/or the instigation of additional immunosuppression in the failure group during the trial needs further investigation.

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POS1084

IMPACT OF PSORIASIS REMAINS IMPORTANT IN PSORIATIC ARTHRITIS PATIENTS WITH LOW MUSCULOSKELETAL DISEASE ACTIVITY

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Background: Psoriatic arthritis (PsA) is a complex, chronic auto-immune disease that affects health-related Quality of Life (HRQoL). Earlier research showed that general HRQoL in PsA patients is mainly affected by musculoskeletal pain.[1] However, psoriasis has also shown to impact HRQoL.[2] Therefore, it is of value to know if HRQoL of PsA patients who reached musculoskeletal low disease activity can be further improved by additionally achieving remission of their psoriasis.

Objectives: The aim of this study was to assess HRQoL in patients with active psoriasis who reached musculoskeletal low disease activity one year after their diagnosis.

Methods: Data were collected from the Dutch south west Psoriatic Arthritis cohort. Musculoskeletal low disease activity (LDA) was defined as Disease Activity in Psoriatic Arthritis Low disease activity (DAPSA) ≤14 and active skin at baseline as Psoriasis Area and Severity Index (PASI) >0. Patients who reached DAPSA-LDA after one year were divided based on reaching psoriasis remission (PASI ≤1). General HRQoL, and dermatology-specific HRQoL were compared between both groups.

Results: We included 624 patients, of which 106 (17%) patients had no psoriasis and 518 (83%) had active psoriasis. After one year, 230 (44%) patients with active psoriasis at baseline reached DAPSA-LDA, of which 108 (47%) patients also achieved psoriasis remission. The group of patients with active psoriasis (n=122, 53%) contained significantly more men (63% vs. 48%) and scored lower on the 12-item Psoriatic Arthritis Impact of Disease questionnaire (p=0.012). This group also had significantly lower median (IQR) scores of the psychosocial subscale (1 [0-5]) and symptoms subscale (4 [2-5]) of the dermatology-specific Skindex-17 questionnaire. Clinically, this implies little impairment psychosocially and a few physical symptoms. Evaluation of the absolute scores of the Skindex-17 subscales in this group showed that 31% of patients experienced moderate to high psychosocial impairment and 28% experienced a lot of symptoms (Figure 1).

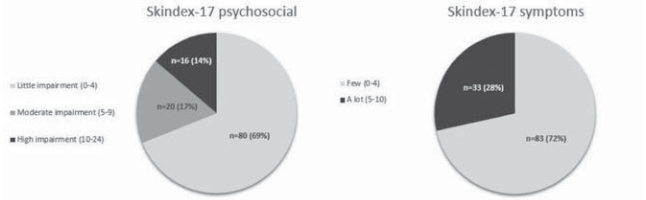

Figure 1. Clinical categories of Skindex-17 psychosocial and symptoms scores of patients with DAPSA-LDA and active psoriasis (PASI>1) one year after diagnosis (n=116)

Conclusion: In daily clinical practice approximately half of PsA patients who reached musculoskeletal low disease activity (DAPSA-LDA) one year after their diagnosis has not reached psoriasis remission. The majority of these patients has a good HRQoL. However, a proportion of them still experiences considerable skin burden. We therefore recommend rheumatologists to always assess and treat psoriasis in order to reduce skin burden, even in PsA patients who achieved musculoskeletal low disease activity.

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Disclosure of Interests: None declared

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POS1085 FREQUENCY OF DYSLIPIDEMIA AND COMPLIANCE WITH THE TREATMENT IN PSA PATIENTS USING BDMARDS

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Background: Dyslipidemia is the leading treatable-modifiable factor among comorbidities in Psoriatic arthritis (PsA) patients. International treatment recommendations have left the management of dyslipidemia to national guidelines and especially to the rheumatologists.
Objectives: In this study, we aimed to determine the frequency of dyslipidemia and the rates of initiation of treatment within the indication in PsA patients using bDMARDs.
Methods: The Hacettepe University biological database (HUR-BIO), was established in 2005 and data of 520 PsA patients included until 2021 were analyzed. In all included patients, the diagnosis of PsA was made by therheumatologist. Lipid profiles of PsA patients were evaluated at diagnosis, during the first bDMARD initiation, and at the last visit. Total cholesterol (TC), Triglyserides (TG), HDL-C and LDL-C values were grouped as optimal, borderline, high and severely high according to the Turkish Endocrine and Metabolism society criteria (1).
Results: Lipid profile values of PsA patients were known at diagnosis (n=159, 30.6%), in the initial bDMARD baseline (n=161, 30.9%), and at the last visit (n=203, 39.0%). The time to diagnosis of PsA and first bDMARD use was 2.8 years, and the time between the start of bDMARD and the last visit was 3.7 years. Accordingly, the rates of high TC, borderline TG, and high LDL increased over time. Rates at the time of PsA diagnosis, first bDMARD onset and at the last visit are as follows; high TC (14.3%, 17.1% and 28.0%), borderline TG (20.4%, 27.7% and 40.5%) and high LDL (17.0, 24.0% and 27.9%). On the other hand, low HDL-C slightly improved in men (33.3%, 29.4% and 23.1%), but did not show a significant change in women. While LDL-C level was >160 in 24.0% of patients who were started on bDMARD, anti-hyperlipidemic drug was started in only 6.2% of them. A similar situation persisted at the last visit (27.9% had LDL-C levels >160, but 10.8% received anti-hyperlipidemic therapy) (Table 1).

Table 1. Lipid levels and changes over time

Lipid levels	At the time of diagnosis n= 159	At the time of bDMARD initiation n=161	bDMARD last visit n= 203
Total Cholesterol (TC) mean (SD)	195 (42)	201 (43)	214 (47)
- TC < 200 (optimal) (%)	56.5	52.8	45.3
- TC 200-239 (borderline) (%)	27.2	30.1	25.7
-- TC > 240 (high) (%)	14.3	17.1	28.0
Triglyceride (TG) mean (SD)	115 (52)	132 (90)	158 (103)
- TG < 150 (optimal) (%)	79.6	71.7	58.0
- TG 150-499 (borderline) (%)	20.4	27.7	40.5
- TG 500-880 (high) (%)	0	0	1.0
-- TG ≥ 880 (severely high) (%)	0	0.6	0.5
HDL-C mean (SD)	51.8 (13.1)	50.6 (13.0)	53.2 (12.5)
- ≥60 (optimal) (%)	20.6	20.4	25.6
- 40-59 (borderline) in men (%)	54.6	60.8	52.3
- 50-59 (borderline) in women (%)	32.3	24.5	30.3
- Male < 40 (low) (%)	33.3	29.4	23.1
-- Women < 50 (low) (%)	32.3	39.6	33.8
LDL-C mean (SD)	126 (33)	132 (37)	139 (36)
- LDL-C < 100 (optimal) (%)	21.4	21.1	14.2
- LDL 130-159 (borderline) (%)	22.5	25.1	27.0
- LDL 160-190 (high) (%)	17.0	24.0	27.9
-- LDL > 190 (very high) (%)	4.4	6.3	8.4
Anti-hyperlipidemic drug n (%)	5 (3.1)	10 (6.2)	22 (10.8)

Conclusion: Among the modifiable risk factors for cardiovascular comorbidities in PsA patients, the leading risk factor is dyslipidemia. On the other hand, dyslipidemic drug use rates in daily practice are significantly lower. Although attention is paid to the management of comorbidities in all recommendations, there is still work to be done in real life.
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POS1086 HIGH CARDIOVASCULAR RISK IN PATIENTS WITH PSORIATIC ARTHRITIS: EVALUATION OF MACROANGIOPATHY AND ITS PREDICTORS BY AORTIC PULSE WAVE VELOCITY.

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Background: Systemic inflammatory rheumatic diseases are associated with macroangiopathy and increased cardiovascular (CV) risk [1, 2]. Psoriatic arthritis (PsA) has also been associated with an increased risk of CV events. However, data on diagnostic CV markers in PsA are scarce. Carotid-femoral pulse wave velocity (cfPWV; oscillometric diagnostic method) is considered to be the gold standard evaluation method of aortic stiffness and is used in the general population to assess CV risk (Figure 1). Moreover, EULAR and the European Society of Cardiology (ESC) recommend the use of Systematic Coronary Risk Evaluation (ESC-SCORE) in order to screen and classify patients regarding CV risk.

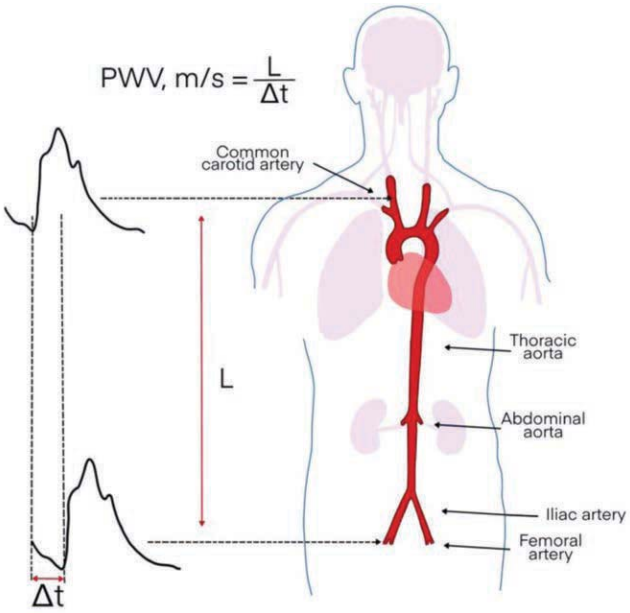

Figure 1. Measurement of aortal pulse wave velocity: pulse waves of carotid and femoral artery (Δt: time, L: distance between the two arteries, m/s: meters/second), modified after [3].

Objectives: Aim of this study was to evaluate aortic stiffness and CV risk in patients with PsA based on measurements of cfPWV and ESC-SCORE. Moreover, we sought to investigate associations of cfPWV with patient- and disease-associated characteristics, as well as with traditional CV risk factors.
Methods: cfPWV measurements were performed in patients with PsA from two large rheumatological medical departments in Germany, according to the classification criteria for psoriatic arthritis (CASPAR), and in healthy control subjects. In addition to assessing cfPWV, clinical and laboratory parameters were evaluated, traditional CV risk factors were documented, and the ESC-SCORE was determined. Differences in cfPWV measurements between the two groups and associations between cfPWV and patient- or disease-associated characteristics were

examined statistically (correlation analyses, Mann-Whitney-U-Tests, ANOVA and multivariate regression analyses).
Results: 112 patients with PsA [55.45%♀, median age: 55 years, IQR 47-63] and 88 healthy control subjects [81%♀, median age: 51 years, IQR 36.5-58] were recruited. cfPWV was significantly higher in PsA patients compared to the healthy control subjects ($p < 0.001$), even after the adjustment for the effect of confounding factors. In both the patient and the control group, cfPWV correlated with age ($r = 0.560$, $p < 0.01$ and $r = 0.638$, $p < 0.01$, respectively). In addition, cfPWV showed a moderate significant correlation with the ESC-SCORE ($r = 0.280$, $p = 0.22$) and a weak significant association with mean arterial pressure (rho =0.19, $p = 0.043$) in the patient group. No statistical associations could be found between cfPWV and lipid levels, CRP levels or DAS28 (all; $p>0.05$). Moreover, no significant differences regarding cfPWV measurements could be observed between patients with and without active disease.
Conclusion: This is one of the largest CV surrogate marker studies in patients with PsA. We were able to show that PsA patients had significantly higher aortic stiffness values, and thus, a higher CV risk compared to healthy individuals. Therefore, cfPWV could be a useful tool for the identification of PsA patients at high-risk. The fact that aortic stiffness can be predicted by mean arterial pressure and ESC-SCORE could assist forming therapeutic strategies that would promote artery de-stiffening and thus CV risk lowering.
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POS1087 THE RELATIONSHIP BETWEEN CHANGES IN PSORIATIC ARTHRITIS DISEASE ACTIVITY AND COMORBIDITIES IN PATIENTS TREATED WITH BDMARDS

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Background: Comorbidities are common in psoriatic disease, needed to be recognized and managed to effectively when treating psoriatic arthritis (PsA) patients. However, the data on the impact of particular comorbidities on the disease activity in patients requiring bDMARDs are very small.
Objectives: Our aim was to understand the relationship between the disease activity and comorbidities in PsA patients under bDMARDs.
Methods: The Hacettepe University biological database (HUR-BIO), was established in 2005 and data of 520 PsA patients included until 2021 were analyzed. In all included patients, the diagnosis of PsA was made by the rheumatologist. DAS-28 score (at the last visit) and all comorbidities were documented after bDMARD initiation. Multivariate analysis was performed to understand comorbidities that have impact on DAS-28 remission.
Results: There were 469 patients with a known DAS-28 score median (IQR) 28 (61) months after bDMARD initiation. It was detected in 214/469 (45.6%) patients with a DAS-28 score below 2.6. Patients in remission of DAS-28 were younger, remission was less frequent in women, and comorbidities, mainly BMI, Diabetes Mellitus (DM) and hypertension, were also found less frequent (Table 1). In the multivariate analysis, no determining factor was found in male gender. On the other hand, in females, smoking, presence of comorbidity, Body mass index (BMI) at the start of bDMARDs, age at onset of bDMARDs, DM at the start of bDMARDs, HT at the start of bDMARDs, coronary artery disease, and cardiovascular risk factors were included in the analysis and revealed, bDMARD baseline BMI [OR 1.06 (95% CI 1.02-1.11), p= 0.004] and presence of bDMARD baseline DM [OR 3.08 (95% CI 1.14-8.30), p=0.026] had significant impact on DAS-28 remission.

Table 1. Relationship between remission according to DAS-28 score and comorbidities

Parameters	DAS-28 ≤ 2.6 (n=214)	DAS-28 > 2.6 (n=255)	p
Age, mean (SD), years	43.8 (11.7)	47.5 (12.5)	**0.001**
Age at PsA diagnosis, mean (SD), years	36.8 (11.5)	41.6 (11.7)	**<0.001**
Gender, female, n(%)	115 (53.7)	211 (82.7)	**<0.001**
Comorbidity count	1.54 (0.98)	1.98 (1.31)	**<0.001**
Comorbidity (yes/no)	67 (31.9)	118 (47.6)	**0.001**
Comorbidity distribution			**0.001**
-No	143 (68.1)	130 (52.4)	
-1 Comorbidity	38 (18.1)	47 (19.0)	
-≥ 2 Comorbidity	17 (8.1)	36 (14.5)	
-≥ 3 Comorbidity	12 (5.7)	35 (14.1)	
Body Mass Index (BMI)	28.1 (5.4)	30.3 (5.9)	**<0.001**
BMI > 30, n(%)	70 (32.9)	123 (48.4)	**0.001**
Diabetes Mellitus, n(%)	10 (4.7)	35 (13.7)	**0.001**
Hypertension, n(%)	29 (13.6)	71 (27.8)	**<0.001**
Total cholesterol > 240, n(%)	8 (10.5)	22 (28.6)	**0.019**
Thyroid Disease	20 (9,8)	43 (17,3)	0,02

Conclusion: Previous data showed that obesity, hypertension and at least 1 point from charlson comorbidity index are poor prognositc factors for treatment outcomes (1). Our data showed that BMI and presence of DM were determined as factors affecting bDMARD treatment response in female PsA patients.
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Disclosure of Interests: None declared

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POS1088 CHALLENGES IN THE MANAGEMENT OF PSORIATIC ARTHRITIS IN LATIN AMERICA: A SYSTEMATIC REVIEW

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Background: In 2020, the International League of Associations for Rheumatology (ILAR) recommendations for management of psoriatic arthritis (PsA) were published. This aimed to adapt GRAPPA and EULAR recommendations to resource-poor settings. At that time, the paucity or absence of clinical studies endorsing the management of PsA patients in Latin America was remarked on by the international working group. Despite several challenges faced by patients and physicians in resource-poor countries, the literature on this theme is scarce.
Objectives: To recognize the main challenges on the management of PsA in Latin America described in recent publications.
Methods: A systematic literature review of clinical trials reporting at least one challenge/difficulty on the management of PsA in Latin America was conducted following PRISMA statements. References published in English, Spanish, French and Portuguese language and published in PubMed, Embase, and LILACS between 1980 and 2020 were included. The selection of references was conducted independently by two researchers in Rayyan QCRI program. Data were independently extracted by two reviewers. The Cochrane tool was used to assess the quality of studies. All challenges were noted and categorized into domains. Data analysis was descriptive.
Results: The search strategy resulted in 1505 references. Sixteen studies (15,145 PsA patients) were included in the final analysis: most were performed in Brazil (81.2%, N=13), recruited patients on biological therapy (75.0%, N=12) and were observational studies (87.5%, N=14). Difficulties faced by PsA patients and physicians in Latin America were the high incidence of opportunistic infections (described in 43.7% of publications, N=7), non-adherence to therapy (18.7%, N=3), discordance between patients and physicians regarding remission rates (18.7%, N=3), limited access to DMARDs (12.5%, N=2), issues related to the storage of biological drugs (12.5%, N=2), high impact of PsA on work and productivity (12.5%, N=2), elevated cost of biological drugs (12.5%, N=2), low drug persistence (6.2%, N=1), limited access to medical care (6.2%, N=1) and diagnostic delay (6.2%, N=1).
Conclusion: The challenges in the management of PsA in Latin America go beyond the care of opportunistic infections: special attention should be paid to logistical questions (e.g., correct medication storage, access to drugs and

medical care) and educational problems (e.g., importance of adherence, patients understanding of disease and therapy)

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POS1089 HLA-CW6 ALLELE AND BIOLOGICAL TREATMENTS ARE PROTECTIVE FACTORS AGAINST LIVER FIBROSIS IN PSORIATIC ARTHRITIS PATIENTS

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Background: Non-alcoholic fatty liver disease can be expressed from an indolent steatosis, evolve to steatohepatitis and eventually evolve to liver fibrosis. This spectrum of non-alcoholic inflammatory liver disease is increased in psoriasis and psoriatic arthritis (PsA). To date, the relationship between non-alcoholic liver fibrosis and genetics in PsA has not been studied.

Objectives: The objective of our study is to evaluate the association between the HLA-Cw6 allele and the FIB-4 (fibrosis-4) index in patients with PsA.

Methods: Retrospective longitudinal study in patients older than 18 years with PsA according to CASPAR criteria with determination of the HLA-Cw6 allele. To estimate liver fibrosis, the FIB-4 index was obtained, calculating it at the onset of PsA and at the last available visit. A descriptive analysis of the variables was carried out using mean and standard deviation (SD) for those with symmetric distribution, and median and interquartile range (IR) for the asymmetric ones. Qualitative variables were described using absolute values and percentages. A bivariate analysis was carried out using parametric and non-parametric hypothesis contrast tests to determine the association between the main variable (current FIB-4) and the secondary variables. Bivariate correlations were analyzed using Pearson's coefficient. A multivariate model was developed to assess the association between HLA-Cw6 and liver fibrosis adjusted for potential confounding factors, and results were presented as Odds Ratio (OR) with 95% confidence interval (CI) and level of statistical significance p-value=0.05. The statistical program SPSS version 20 was used. The study was approved by the local committee.

Results: 209 patients with PsA were included (56.9% men, mean age 42.72±14.24 years), 84.7% with psoriasis, and median (IR) ESR (mm/h) of 16.9(9-28) and CRP (mg/l) 5.0(2.52-12.25). 74.3% of patients were HLA-Cw6 negative. 79.4% of patients were receiving treatment with MTX, and 59.8% biological therapy. Regarding comorbidities, 29.6% had hypertension, 24% dyslipidemia, 10.1% diabetes, and 4.2% acute myocardial infarction. FIB-4 could be calculated in 154 patients at the onset of PsA, with a mean of 1.53±9.05 points, being 58.9% of patients at FIB-4 F0-1 (non advanced fibrosis, <1, 30 points). At the last available visit, FIB-4 could be calculated in 180 patients, mean of 1.35±0.85 points, 86.4% of the patients at FIB-4 F0-1. Table 1 shows bivariate analysis and Table 2 the multivariate one.

Table 1. Bivariate analysis of the main variable (current FIB-4) categorized into normal (result F0-1, non advanced fibrosis, <1.30 points) and altered (result F2-3-4, intermediate zone and significant fibrosis, >1.3 points). [1]Median (IR) [2]Mean±SD. * p-value < 0.05. AMI acute myocardial infarction.

	Normal current FIB-4 (N = 106)	Altered current FIB-4 (N = 74)	p value
HLA-Cw6 (%)	18.54	6.74	0.024 *
ESR (mm/h)[1]	16 (9-32)	10 (6-19)	0.362
CRP (mg/l)[1]	5.31 (2.41-12.97)	3.30 (2.11-9.00)	0.348
PsA age onset (years)[2]	37.33±11.71	51.53±12.33	0.630
Male sex (%)	60.4	39.6	0.627
Biologic (%)	64.3	35.7	0.059
Methotrexate (%)	56.8	43.3	0.211
Leflunomide (%)	60	40	0.915
Psoriasis (%)	58.9	41.1	0.648
Hypertension (%)	42.2	57.8	0.002 *
Diabetes (%)	40	60	0.079
AMI (%)	16.7	83.3	0.023 *
Dyslipidemia (%)	45.9	54.1	0.030 *

Table 2. Multivariate analysis. * p-value < 0.05.

Variable	OR (IC 95%)	p value
HLA-Cw6	0.210 (0.062-0.707)	0.012 *
Male sex	1.553 (0.624-3.864)	0.344
Hypertension	2.973 (1.125-7.858)	0.028 *
Diabetes	1.478 (0.395-5.530)	0.561
Dyslipidemia	1.429 (0.541-3.773)	0.471
Methotrexate	1.113 (0.357-3.466)	0.854
ESR at onset (mm/h)	0.993 (0.967-1.019)	0.605
AMI	6.302 (0.495-80.246)	0.156
Biologic	0.397 (0.166-0.949)	0.038 *

Conclusion: In our study, having the HLA-Cw6 allele and receiving biological treatment behaved as a protective factor for liver fibrosis in PsA, while arterial hypertension was an independent risk factor. The presence of psoriasis was not related to hepatic fibrosis measured by FIB-4.

Disclosure of Interests: None declared

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POS1090 THE IMPACT OF NUMBER OF COMORBIDITIES ON ACHIEVEMENT REMISSION OR LOW DISEASE ACTIVITY BY DAPSA IN PSORIATIC ARTHRITIS. DATA FROM THE RUSSIAN OBSERVATIONAL COHORT

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Background: The goal of psoriatic arthritis (PsA) treatment is achievement remission (REM) or Low Disease Activity (LDA) by DAPSA. The impact of comorbidities, especially obesity, metabolic syndrome on PsA activity and on biological treatment response are shown in some registry [1]. Obesity, hypertension and Charlson Comorbidity Index ≥1 are prognostic factors for poorer treatment outcome rates in PsA [2]. But influence of number of comorbidities on treatment response has not been fully studied in real practice

Objectives: To evaluate the impact of number of comorbidities on achievement remission by DAPSA in PsA pts

Methods: 528 pts (M/F=256 (48.5%)/272 (51.5%) with PsA according to CASPAR criteria were included in the Russian observational cohort. Mean age 48.7±12.33 years (yrs.), PsA duration 122.6±81.85 months (mo.), psoriasis (Ps) duration 239.0±155.45 mo. Pts who completed ≥2 visits were analyzed. Mean observational period 73.6±83.47 mo. All pts underwent standard clinical examination: tender joint count (TJC)/68, swollen joint count (SJC)/66, Pain (VAS), Patient global assessment of disease activity (PtGA, VAS), CRP mg/l, BSA (%), BMI, HAQ, comorbidities by ICD-10, X-ray of hands and foods. DAPSA>28 indicates as high disease activity (HDA), >14-28 - moderate activity (MoDA), >4-14 – LDA, ≤4 – REM. Analyses were performed based on number of comorbidities: 1st group (gr) - without comorbidities, 2nd gr – pts with 1 comorbidity, and 3rd gr – pts with ≥ 2 comorbidities. M±SD, %, t-test, Pearson-χ^2, ORs with 95% CI were calculated. All p<0.05 were considered to indicate statistical significance

Results: In 236 out of 528 (44.7%) pts no comorbidity found, in 145 out of 528 (27.5%) found 1 comorbidity and 147 out of 528 (27.8%) pts had ≥ 2 comorbidities. Comparative analysis in groups showed the following features: pts of 3rd gr were significantly more often females, had longer Ps and PsA duration, they were older, had worse HAQ, higher BMI, TJC (p<0.05). Joint erosions were found significantly more often in the 2nd gr compared to the 1st gr (p=0.02). No significant differences were in the frequency of axial PsA (p=0.906), Ps severity (BSA>10%) (p=0.237), the number of pts receiving bDMARDs (p=0.078). REM/LDA achievement according to DAPSA was significantly lower in the 3rd gr (15 (10,2%)/69(46.9%) comparing to the 1st gr (62 (26,3%)/94 (39.8%), and to the 2nd gr (32 (22,1%)/69 (47.6%) (p=0.007). The probability of achieving REM/LDA is 1.6 times lower in the gr of pts with ≥2 comorbidities compared to the gr of pts without comorbidities (OR 0.608, 95% CI 0.394 to 0.936) and 1.3 times lower compared to gr of pts with 1 comorbidity (OR 0.789, 95% CI 0.489 to 1.243) (Figure 1)

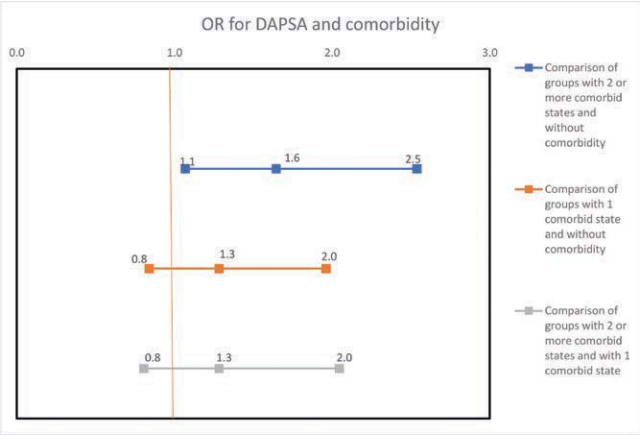

Figure 1. Chances of REM/LDA achievement in pts with ≥2 comorbidities compared to pts with 1 comorbidity and pts without comorbidities

Conclusion: In real clinical practice comorbidities were seen in more than half PsA pts. Third of PsA pts had number of comorbidities. PsA pts with number of comorbidities are associated with high disease activity, reduced quality of life and are 1,6 times more likely to have no chance to attain REM/LDA by DAPSA. It should be considered for personalized treatment

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POS1091 LESS RADIOGRAPHIC SPINAL DAMAGE IN PSORIATIC ARTHRITIS PATIENTS COMPARED TO SPA PATIENTS

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

Objectives: A step towards fathoming this issue is to report on baseline radiographic spinal damage in PsA and SpA patients (pts) from 2 prospective multicentre cohort studies in private and academic rheumatology practices.

Methods: Data on PsA pts were from the Belgian Epidemiological Psoriatic Arthritis Study (BEPAS); prospective multicentre cohort in 17 Belgian rheumatology practices. Recruitment was Dec2012-Jul2014. Pts were included when fulfilling the Classification criteria for Psoriatic Arthritis (CASPAR). SpA pts were from a Belgian observational cohort (Be-Giant) of SpA pts fulfilling the ASAS SpA classification criteria. Radiographs of the spine were obtained at baseline and after 2 years. Two calibrated readers evaluated radiographic damage by assessing modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Readers were blinded for time sequence, clinical data and information from other obtained images (radiographs of hands, feet, sacroiliac joints). Consensus scores are described.

Results: In total 461 pts were included in BEPAS. Mean age was 52.79±12.29 years and 43.0% (n=198) were female; average disease duration was 8.5 ± 9.3 years and approximately 34% of the pts reported inflammatory axial pain. From 312 pts spinal radiographs were obtained. At baseline, the vast majority of PsA pts had an mSASSS of 0 (n=273, 87.5%), according to both readers. In 33 PsA pts (10.6%) mSASSS was 2 or more. For the SpA pts percentages were lower but the trend was similar (see Figure 1). Though lesser pts showed abnormalities, the SpA pts with spinal damage show a higher mSASSS, therefore indicating more spinal damage then the PsA pts ($p<0.05$). Both patient groups show some outliers with high mSASSS, increasing the average mSASSS especially in the SpA cohort (mean mSASSS = 9.1±14.11) compared to the median of 3 (IQR 2-6) in both cohorts Syndesmophytes are seen in 10.6% and 6.2% of the PsA and SpA pts, respectively. Similar to the mSASSS, SpA pts had more syndesmophytes (mean: 4.4±5.50) compared to PsA pts (mean 2.0±1.45); $p<0.05$. PsA pts had more often syndesmophytes located in the cervical spine (24/35, 68.6%) compared to the SpA patient group (9/21, 42.9%); $p<0.05$. Erosions and especially sclerosis and squaring are uncommon in both patient groups.

Conclusion: Spinal damage is seen in approximately 10% or less of both PsA and SpA pts in these cohorts. SpA pts show higher mSASSS values and more syndesmophytes as compared to the PsA pts. Syndesmophytes in PsA pts are more often located in the cervical spine while the location is more equally distributed in SpA pts.

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POS1092 THE IMPACT OF A STRUCTURED WEIGHT LOSS PROGRAM ON PHYSICAL FITNESS IN PATIENTS WITH PSORIATIC ARTHRITIS AND OBESITY COMPARED TO MATCHED CONTROLS: A PROSPECTIVE INTERVENTIONAL STUDY

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Table 1. Spinal damage at baseline of patients from the BEPAS (PsA patients) and Be-Giant (SpA patients) cohorts

	PsA patients (n=312)	SpA patients (n=260)		PsA patients (n=312)	SpA patients (n=260)
mSASSS ≥2, no of patients	33 (10.6%)	19 (7.3%)	**Syndesmophytes (total spine)**	33 (10.6%)	16 (6.2%)
mSASSS ≥1, no of patients	39 (12.5%)	22 (8.5%)	mean, (SD)	2.0 (1.45)	4.4 (5.50)
mean, (SD)	4.5 (4.24)	9.1 (14.11)	min, 0.25, median, 0.75, max	1.0 1.0 **2.0** 2.0 8.0	1.0 1.0 **2.5** 5.0 22.0
min, 0.25, median, 0.75, max	1.0 2.0 **3.0** 6.0 21.0	1.0 2.0 **3.0** 10.0 64.0	**Syndesmophytes (cervical spine)**	24 (7.7%)	9 (3.5%)
Erosions ≥1, no of patients	13 (4.2%)	5 (1.9%)	mean, (SD)	1.8 (1.32)	2.9 (2.89)
mean, (SD)	1.5 (1.39)	1 (0.0)	min, 0.25, median, 0.75, max	1.0 1.0 **1.0** 2.0 7.0	1.0 1.0 **2. 0** 3.0 10.0
min, 0.25, median, 0.75, max	1.0 1.0 **1.0** 1.0 6.0	1.0 1.0 **1.0** 1.0 1.0	**Syndesmophytes (lumbar spine)**	11 (3.5%)	12 (4.6%)
Squaring ≥1, no of patients	No obs.	4 (1.5%)	mean, (SD)	1.9 (0.70)	3.7 (4.21)
mean, (SD)	No obs	1.8 (0.96)	min, 0.25, median, 0.75, max	1.0 1.0 **2.0** 2.0 3.0	1.0 1.0 **1.0** 5.0 12.0
min, 0.25, median, 0.75, max	No obs	1.0 1.0 **1.5** 2.5 3.0			
Sclerosis ≥1, no of patients	2 (0.6%)	6 (2.3%)			
mean, (SD)	1.5 (0.71)	1.8 (1.33)			
min, 0.25, median, 0.75, max	1.0 1.0 **1.5** 2.0 2.0	1.0 1.0 **1.0** 3.0 4.0			

Background: Obesity is over-represented in patients with psoriatic arthritis (PsA) and associated with increased disease activity. We have previously shown that weight loss treatment with Very Low Energy Diet (VLED) in patients with PsA and obesity was associated with a sustained weight reduction and significant improvement of the disease activity in joints, entheses and skin during 24 months follow-up. A side effect with a large weight loss is however a concomitant reduction of muscle mass, which can negatively affect physical fitness.
Objectives: This study aimed to evaluate the effects of weight loss treatment on physical fitness i.e., muscle strength, cardiorespiratory fitness, body composition and self-reported physical functioning, in patients with PsA and obesity compared to matched controls undergoing the same treatment.
Methods: In total, 46 patients with PsA (Caspar criteria) and obesity and 52 controls (matched for age, sex, body weight and height) were included. VLED (640 kcal/day) was provided to all participants for 12-16 weeks depending on baseline BMI (<40 or ≥40 kg/m^2), followed by reintroduction of energy restricted diet. Brief support for physical activity was given. Primary outcome was muscle strength, assessed in hand-grip with a dynamometer (Grippit) and in leg muscle by measuring the time (seconds) needed to stand up ten times from a standard chair (Timed Stand Test: TST). Secondary outcomes were cardiorespiratory fitness (O_2 l/ min), measured with the Åstrand's submaximal bicycle test, body composition analyzed with dual energy x-ray absorptiometry and physical functioning, assessed with the Short Form 36 Health Survey Physical Component Score (SF-36PCS). Outcomes were evaluated at baseline (BL), six (M6) and 12 months (M12).
Results: In total, 41 PsA patients (median age 54; 63% women) and 42 controls (median age 54; 74% women) completed the treatment. At M6 the median weight loss since baseline in patients and controls was 18.9 kg and 23.0 kg respectively (p=0.546), and at M12 16.1 kg and 16.6 kg (p=0.885). Significant changes (all p<0.001) were seen at M12 in the body composition of both patients and controls, with decreases in total fat mass (-30.1% vs. -27.4%), total lean mass (-7.0 % vs -8.3 %), lean arm mass (-13.7% vs -2.4%) and lean leg mass (-6.0% vs -8.6%). Leg muscle strength did however improve in both patients and controls at M6 (p<0.001) and remained improved at M12 (p=0.001 and p<0.001), while hand-grip strength was unchanged in both groups. Cardiorespiratory fitness increased in controls at M6 (p=0.018) and M12 (p=0.028), but not in the patients. Physical functioning improved in both groups at M6 and remained improved at M12.
Conclusion: Patients with PsA and obesity can benefit from weight loss treatment without risk of deterioration in muscle strength. However, muscle strength and cardiorespiratory fitness were below suggested normative values for the majority of the patients at all timepoints, implying that more structured exercise strategies might be warranted to counteract physical fitness deficiencies in patients with PsA undergoing weight loss treatment.

Table 1.

	PsA patients n=41			Controls n=42		
	BL	**M12**	**p-value**	**BL**	**M12**	**p-value**
BMI, kg/m^2	35.2 (34.1–38.1)	30.5 (28.0–32.9)	**<0.001**	38.5 (36.9–41.7)	32.6 (30.3–34.8)	**<0.001**
Hand-grip strength, N	268 (196–326)	244 (180–352)	0.457	304 (280–348)	300 (244–384)	0.573
Leg strength TST, sec	26.9 (22.1–35.4)	23.2 (19.4–30.4)	**0.001**	23.7 (21.0–32.8)	20.1 (16.8–25.9)	**<0.001**
Cardiorespiratory fitness, O_2 l/ min	2.0 (1.8–2.2)	2.1 (1.8–2.6)	0.098	2.0 (1.6–2.3)	2.1 (1.7–2.4)	**0.028**
Tot fat mass, kg	48.5 (41.7–56.7)	33.9 (25.9–40.5)	**<0.001**	50.7 (46.2–59.2)	36.8 (27.8–39.5)	**<0.001**
Tot lean mass, kg	51.9 (45.9–61.8)	48.3 (43.6–58.3)	**<0.001**	49.7 (46.9–58.6)	45.6 (44.5–57.9)	**<0.001**
Lean mass arm, kg	2.79 (2.48–3.85)	2.43 (2.10–3.45)	**<0.001**	2.63 (2.39–3.34)	2.57 (2.22–3.36)	**<0.001**
Lean mass leg, kg	8.9 (8.0–10.9)	8.4 (7.2–9.8)	**<0.001**	9.1 (8.5–10.4)	8.1 (7.7–9.8)	**<0.001**
SF-36 PCS, score 0-100	35.8 (24.9–46.3)	46.1 (34.5–49.8)	**0.008**	45.7 (32.9–50.9)	51.6 (43.8–55.4)	**<0.001**

Figures are Median IQR

Disclosure of Interests: None declared

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POS1093

EFFECT OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS ON DEPRESSION IN PATIENTS WITH PSORIATIC ARTHRITIS IN A LONGITUDINAL COHORT

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Background: Depression, and its improvement with disease modifying anti-rheumatic drugs (DMARDs) is understudied in psoriatic arthritis (PsA).
Objectives: To determine the effectiveness of DMARDs on depression in PsA patients.
Methods: Patients enrolled from January 2000 to May 2020 in a large PsA cohort were included. Depression was defined as medical outcomes study short form-36 (SF-36) mental component summary score (MCS) ≤ 40 or mental health (MH) subscale score ≤ 56. Primary outcome was resolution of depression within 1 year of DMARDs, defined by two definitions: 1) MCS > 40 and/or MH subscale score of > 56; 2) Increase in MCS by 2.5 and MH subscale score by 5, the minimal clinically important difference (MCID). Baseline medications [non-steroidal anti-inflammatory drugs (NSAIDs) and/or conventional or targeted (c/t) DMARDs] were recorded for all patients and stratified into 3 mutually exclusive ordinal categories: I-No treatment/NSAIDs; II-cDMARDs±NSAIDs without tDMARDs; III-tDMARDs±cDMARDs/NSAIDs. Univariable and multivariable logistic regression models were created to determine the association between medications and resolution of depression, after controlling for age, sex, disease duration and baseline MCS/MH subscale score.
Results: Based on the MCS and MH subscale score definitions, 608 (48%) and 655 (52%) of the 1270 patients, respectively were depressed at baseline. 374 (50.8% males) and 399 (52.4% males) patients were followed up in the groups defined by MCS and MH subscales, respectively for 1 year. Patients in both groups had comparable body mass indices, baseline psoriasis area and severity index and active joint count. Mean MCS and MH subscale scores (standard deviation) were 33.2 (5.2) and 46.0 (10.2). A mean of 11.9 and 11.7 months was noted for resolution of depression in the MCS based analysis and MH subscale-based analysis groups, respectively. More patients achieved resolution of depression based on definition 2 (MCS, 64.7%; MH, 62.2%) as compared to definition 1 (MCS, 54.5%; MH, 53.9). The proportion of patients on each category of medications in both models is shown in the Figure 1. Table 1 depicts the univariate and multivariable regression results by both the definitions of primary outcome in the MH subscales model. The global p-value for medication categories showed a trend towards significance in both models using definition 2. There was a trend towards higher likelihood of response when comparing patients in treatment category III vs category I. A significant response was noted when comparing patients in category III with category II as reference (OR 1.71; 95% CI 1.05-2.76; p 0.03). No significant effect of treatment category on depression was noted using definition 1.

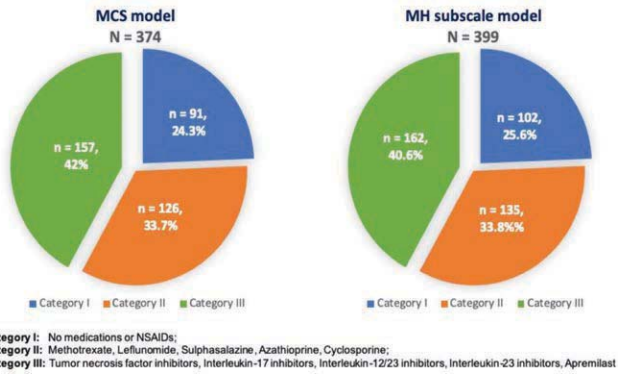

Figure 1. Patients in each drug category.

Conclusion: In an observational setting, resolution of depression occurs in majority of patients with PsA within 1 year. Patients on t-DMARDs may experience better improvement in depression compared to other treatments. Future effectiveness studies warrant better definitions of depression and treatment response.
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Table 1. Association between treatment and resolution of depression in the MH Subscale model (n = 399)

	Resolution by MCID				Resolution by MH subscale reduction			
	Univariable model		Multivariable model		Univariate model		Multivariate model	
Variable	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Male vs. Female	0.81 (0.54–1.22)	0.31	0.83 (0.5–1.26)	0.39	1.02 (0.68–1.51)	0.94	0.94 (0.63 –1.42)	0.79
Baseline age	1.01 (1.00 –1.03)	0.09	1.01 (1.00 –1.03)	0.16	1.02 (1.00–1.03)	0.05	1.01 (0.99 –1.03)	0.30
Baseline PsA duration	1.02 (1.00 –1.04)	0.12	1.01 (0.99 –1.03)	0.37	1.02 (1.00– 1.04)	0.07	1.01 (0.99 –1.03)	0.22
Baseline MH subscale score	0.98 (0.96 –1.00)	**0.03**	0.98 (0.95 –1.00)	**0.02**	1.04 (1.02– 1.06)	**<0.0001**	1.04 (1.02 –1.06)	**<0.0001**
Medication category		**0.07***		**0.09***		0.20*		0.20*
I	Reference							
II	0.81 (0.48 –1.36)	0.42	0.83 (0.48 –1.41)	0.48	1.09 (0.65– 1.82)	0.75	1.12 (0.66 –1.91)	0.67
III	1.40 (0.84 –2.36)	0.20	1.41 (0.83 –2.38)	0.20	1.51 (0.92– 2.49)	0.10	1.55 (0.92 –2.59)	0.10

*global p value

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POS1094 CORRELATION OF FLUORESCENCE-OPTICAL IMAGING AND PHYSICIAN TJC/SJC ASSESSMENT AND ULTRASOUND IN PSORIASIS PATIENTS WITHOUT ARTHRITIS BUT MUSCULOSKELETAL COMPLAINTS WITHIN THE LAST 6 MONTHS

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Background: Psoriasis (PsO) is one of the most common chronic inflammatory skin diseases in Europe. Psoriatic arthritis (PsA) is closely associated to PsO; up to 40% of PsO patients develop PsA. The transition from PsO to PsA includes different stages with unspecific clinical symptoms such as fatigue or musculoskeletal (MSK) symptoms as well as changes in synovial vascularization combined with increased expression of proangiogenic factors [1]. Fluorescence-optical imaging (FOI, [Xiralite]) is an easy-to-use method to detect changes in microvascularisation of the hands.

Objectives: To compare findings from FOI assessment to clinical examination (SJC/TJC) and musculoskeletal ultrasound in patients (MSUS) with non-specific MSK-symptoms and changes in microvascularisation without evidence of clinical active PsA.

Methods: The German multicentre observational XCITING study recruited patients with dermatological confirmed PsO at risk for development of PsA (either nail psoriasis or MSK symptoms such as joint pain or swelling within the last 6 months). Clinical examination (CE; swollen (66) and tender (68) joint count, enthesitis, dactylitis assessment), standardized MSUS and FOI assessment were performed by a qualified rheumatologist at one time point with focus on the question of presence of PsA. Data were analyzed in focus on increased vascularization of MSK structures of both hands as marker of inflammation. The patients at-risk for PsA development but without clinically active PsA (CE negative, FOI positive) were analyzed. Results from CE of joints, MSUS and FOI were compared.

Results: 391 PsO patients were recruited for the XCITING study in total. 108 patients (27.6%) were identified as at-risk population (CE negative, FOI positive). Baseline characteristics included a mean age of 51.4 years (SD 11.3), 61.1% female, mean BMI 27.8 kg/m2 (SD 5.2), mean age of onset PsO 30.4 years (SD 17), mean duration of PsO of 16.9 years (SD 14.4), mean PASI 4.3 (SD 5.8) and mean patient's global disease activity for PsO of 24.4mm (SD 21.1). In 24.1% psoriasis plaques on the hand were documented. Pattern for frequency of scores in FOI, CE and MSUS in the dominant hand were compared (Figure 1). Frequency of swollen joints and synovitis with power Doppler activity (PD Mode) was very low in these patients whereas TJC, detection of synovitis in MSUS and FOI signals were detected in overlapping regions at the hands, showing high correlation. The highest correlation is found between TJC and FOI (Figure 1).

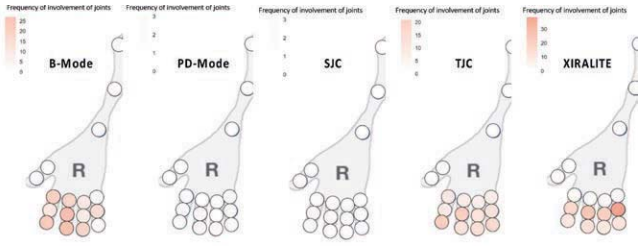

Figure 1. Overview of frequency of involvement in joints for the different assessments (MSUS, SJC/TJC and FOI)

Conclusion: FOI signals in the hands correlate to the findings of TJC (and B-Mode US) in the clinical examination indicating early stages of MSK inflammation that may result in active PsA development. FOI as standardized and easy-to-use technique might be a suitable tool for early detection of PsA in Psoriasis population. A follow up in these patients will reveal prediction values of the method.

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POS1095 RELATIONSHIP BETWEEN PLASMA IL-12, IL-23 LEVELS AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a heterogeneous, chronic, inflammatory spondyloarthropathy associated with psoriasis. PsA is accompanied by many comorbidities, especially hypertension, metabolic syndrome, obesity, hyperlipidemia and cardiovascular diseases (CVD) (1). Mediators that cause chronic inflammation such as IL-23R, IL-17, IL-12B are thought to play an important role in the pathogenesis of both PsA and its comorbidities (2,3).

Objectives: The aim of our study was to compare plasma levels of IL-12 and IL-23 with endothelium-dependent (FMD) and independent dilatation (NMD) measurements in psoriatic arthritis (PsA), ankylosing spondylitis (AS) patients and healthy controls and to look for the relationship of IL-12, IL-23 with FMD, NMD, clinical findings, laboratory parameters and disease activity scores of patients.

Methods: A total of 136 subjects (49 patients with PsA, 46 patients with AS and 41 healthy controls) were included in the study. Subjects were evaluated with detailed anamnesis and physical examination. The routine biochemical parameters, CRP, ESR of all subjects and disease activity scores of all patients were noted. IL-12 and IL-23 were measured using ELISA method. Endothelial-dependent and independent dilatations were measured by Doppler USG on the brachial artery.

Results: Though IL-12 levels were higher in the PsA group when compared with the healthy group, this difference was not statistically significant. IL-23 levels were significantly higher in PsA patients when compared with the healthy control group (Table 1). IL-12 and IL-23 levels were found to be significantly higher in the AS group compared with the healthy group. A statistically significant difference in endothelial dependent measures were found between PsA patients and healthy controls. No statistically significant correlation was found between IL-12, IL-23 levels and brachial artery basal diameter, FMD, NMD values in PsA patients. Fasting blood glucose and triglyceride levels were higher in PSA patients, while CRP and ESR were higher in AS patients. HDL levels of healthy controls were higher than those of PSA and AS patients. There was no significant correlation between IL-12, IL-23 and BASDAI, BASFI, DAPSA, DAS 28, PsAQoL, HAQ, HAD-A, VAS scores in PSA group; hospital anxiety and depression scale (HAD) and BASMI were positively correlated with IL-23. In the AS group, IL-23 was correlated with VAS and BASMI and IL-12 was correlated with HAQ score.

Table 1. The average of the interleukin levels according to the diagnoses of the participants

			p
IL 12	PSA AS	**0,007**	**0,027**
	PSA Healthy Control	0,995	
	AS Healthy Control	**0,009**	
IL 23	PSA AS	0,706	**<0,001**
	PSA Healthy Control	**0,006**	
	AS Healthy Control	**0,010**	

Conclusion: In the PsA group, IL-23 levels and FMD values were higher than the healthy group in our study. The risk of metabolic syndrome and CVD increases due to high insidence of glucose dysregulation, dyslipidemia and obesity in these patients. PsA patients should be monitored for the development of these comorbidities and preventive measures should be taken. More studies are necessary to examine the relationship between IL-12, IL-23 levels and endothelial dysfunction, which is an early indicator of CVD and atherosclerosis in PsA patients.

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Disclosure of Interests: None declared

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POS1096 **CHARACTERIZATION OF A PSA COHORT IN CLINICAL ROUTINE CARE USING THE DAPSA AND ITS CORE-SET PARAMETERS.**

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Background: A large number of therapeutics have become available to treat Psoriatic Arthritis (PSA). Still, the level of disease activity in contemporary PSA patients in clinical practice may span broadly across the range.

Objectives: To investigate disease activity in PsA patients at their last clinical visit in a tertiary academic European centre using treat-to-target as management principle, and with access to all contemporary treatments, by Disease Activity in PSA (DAPSA) index and its components.

Methods: Disease characteristics of 138 PSA patients at an academic referral centre was assessed at their last clinical visit, including DAPSA scores, DAPSA states, and DAPSA components (swollen joint count 66, tender joint count 68, patient global assessment, patients' assessment of pain and C-reactive protein), as well as ongoing DMARD therapy. Cumulative frequencies of DAPSA core-set parameters and Health-Assessment Questionnaire Disability Indices were calculated and tabulated. All patients provided their written informed consent to participate, and this study was approved by the local ethics committee.

Results: Of 138 PsA patients included, 68 were female (49%), the mean disease duration was 11.8 years and patients had 2.4 mean swollen joints and 6.4 tender joints. Most patients received conventional synthetic DMARDs as monotherapy (73/138 53%), but about the half of patients (53%) were not at treatment target of DAPSA low disease activity or remission (Table 1). When investigating the composition of disease activity by components, about 50% of patients had ≤1 swollen joint (0-66), ≤3 tender joints (0-68), ≤4.0cm of patient global assessment (0-10) and ≤4.0cm of pain (0-10) as well as a HAQ ≤0.5 and normal CRP values.

Table 1. Demographics and clinical characteristics of 138 patients at their last visit in a tertiary academic European centre (shown as numbers and percent or mean and standard deviation).

N	138
Female	68 (49%)
Age (years)	48.8±17.5
Disease duration (years)	11.9±10.2
Swollen Joint Count (0-66)	2.4±3.2
Tender Joint Count (0-68)	6.4±9.4
Patient Global Assessment (VAS 0-10cm)	4.0±2.9
Patients Assessment of Pain (VAS 0-10cm)	3.6±2.6
C-reactive Protein (mg/dL)	1.1±2.6
Health Assessment Questionnaire (0-3)	0.7±0.8
DAPSA	18.7±16.5
Treatment	
Any csDMARD	91 (66%)
Methotrexate	78 (57%)
Leflunomide	10 (7%)
Sulfasalazine	6 (4%)
Any bDMARD	35 (25%)
TNF inhibition	30 (22%)
IL17 inhibition	1 (1%)
IL12/23 inhibition	4 (3%)
csDMARD monotherapy	73 (53%)
bDMARD monotherapy	17 (12%)
bDMARD + csDMARD combination	18 (13%)
DAPSA disease activity state	
Remission	26 (19%)
Low Disease Activity	40 (29%)
Moderate Disease Activity	45 (33%)
High Disease Activity	27 (20%)

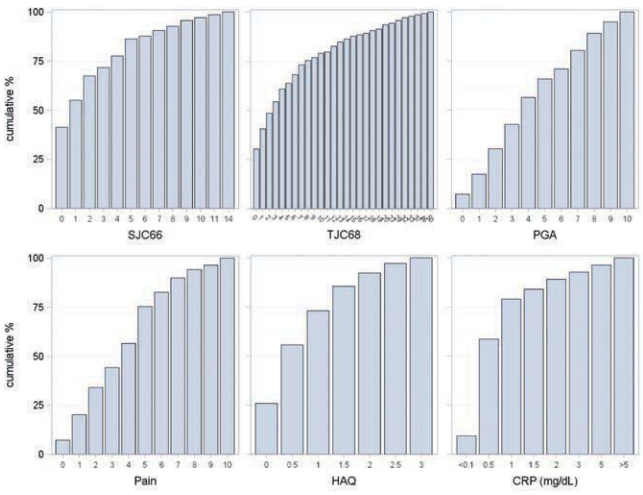

Figure 1. Cumulative probability plots of swollen and tender joint assessments, patient global assessment (PGA), patients assessment of pain, Health Assessment Questionnaire (HAQ) Disability Index and C-reactive protein (CRP).

Conclusion: This analysis of PsA patients in routine care at a European tertiary academic center showed that many patients are not on treatment target. Their presentation is oligoarticular, with moderate levels of pain and patient global assessments, but mostly normal or slightly elevated CRP levels. Despite the treat-to-target strategy and a large number of therapeutics, and overall good control of objective measures of disease activity, many patients in real life may potentially benefit from more intensive treatment escalation.

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POS1097 BIOMARKERS OF INFLAMMATION AND JOINT TISSUE TURNOVER CAN HELP IMPROVING THE DIFFERENTIATION BETWEEN OSTEOARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS

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Background: Osteoarthritis (OA) is a slow progressive disease characterized by degeneration within the joint cartilage, leading to destruction and dysfunction of the involved joints. Psoriatic arthritis (PsA) is a chronic inflammatory disease manifesting itself in skin lesions and progressive inflammatory changes within the musculoskeletal system, leading to joint damage and functional limitation. Although OA and PsA are considered to be distinct diseases, they share overlapping clinical and inflammatory features that can cause diagnostic challenges. Throughout these inflammatory and degenerative processes in the joint tissues, proteases hold a major role in remodelling of the extracellular matrix (ECM) which results in protein breakdown products released into the synovial fluid (SF). These protein fragments can be quantified in SF as biomarkers of tissue remodelling and may be helpful in characterizing disease-specific or overlapping pathologies between OA and PsA.

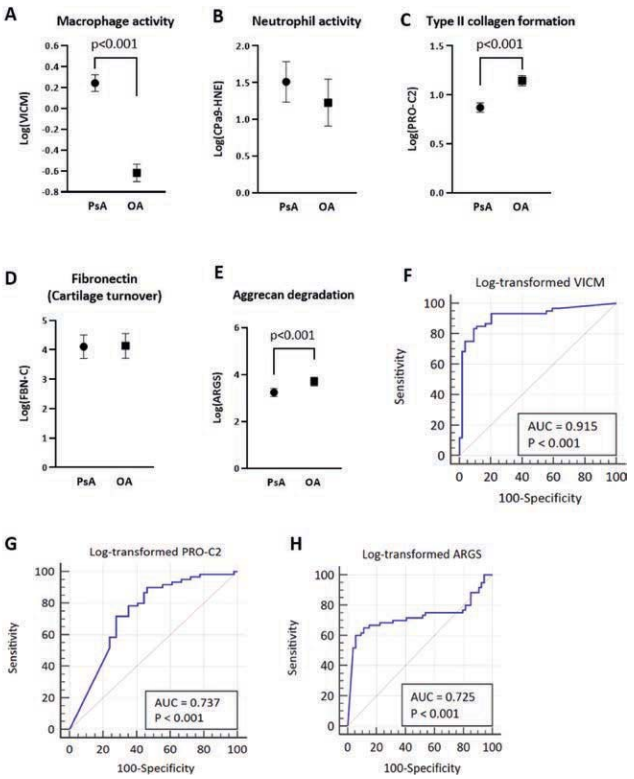
Objectives: Our aim of this study is to measure biomarkers of inflammation and joint tissue turnover in SF to explore the distinct and overlapping pathologies between OA and PsA.

Methods: SF samples were collected from patients with OA (n=54, mean ±SD age 62.1 ±11.9, 48% female) and patients with PsA (n=59, mean ±SD age 47.8±13.3, 37% female) recruited through Toronto Western Hospital, Canada. Study was approved by the local ethics committee. Biomarkers of inflammation reflecting macrophage activity (VICM) and neutrophil activity (CPa9-HNE) were measured in the SF samples. Moreover, ECM remodelling was assessed in the SF samples by biomarkers quantifying type II collagen formation (PRO-C2), fibronectin turnover (FBN-C), and aggrecan degradation (ARGS). Data were log-transformed and presented as mean ± standard deviation (SD). An ANCOVA corrected for age was applied to test the difference between biomarker levels across the two patient groups and a p-value below 0.05 was considered significant. Area under the receiver operating characteristic (ROC) curve (AUC) analysis was performed to describe the discrimination accuracy of each biomarker between the two patient groups.

Results: PsA patients presented significantly higher levels of macrophage; VICM, activity compared to OA (p<0.001, Figure 1A). On the other hand, OA patients demonstrated increased type II collagen formation and aggrecan degradation compared to PsA (p<0.001, Figure 1C, E). Interestingly, no significant difference in biomarkers levels of neutrophil activity and fibronectin remodelling was observed between the two disease groups. Moreover, VICM, PRO-C2, and ARGS showed high distributional difference between OA and PsA patients with an AUROC=0.915 (p<0.001, Figure 1F), AUROC=0.737 (p<0.001, Figure 1G), and AUROC=0.725 (p<0.001, Figure 1H), respectively.

Conclusion: PsA patients demonstrated higher macrophage activity in the SF compared to the OA patients, while higher levels of cartilage formation and degradation were observed in OA patients compared to PsA. No differences between OA and PsA were observed in neutrophil activity and fibronectin turnover, which may mirror the clinical difficulty in telling the two arthritides apart. Identifying the unique characteristics of the pathological processes underlying the two diseases may improve diagnosis and allow for the precise management of both OA and PsA patients.

Fig. 1



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POS1098 DO THE CHANGES DETECTED BY ULTRASOUND AFFECT THE QUALITY OF LIFE OF YOUNG AND MIDDLE-AGED PATIENTS WITH PSORIATIC ARTHRITIS?

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Background: The quality of life (QoL) is included in the main domain for psoriatic arthritis (PsA) course assessment.[1] In the last years, the role of imaging has grown up. The European League Against Rheumatism recognized that ultrasound (US) has higher sensitivity than clinical examination to detect inflammatory disease activity. The data showing the association between (b/w) QoL and US changes in PsA is limited.

Objectives: To study relationship b/w US articular and entheseal involvement and QoL in PsA.

Methods: 18-60-aged patients (n=92) were enrolled to study with fulfilled PsA criteria (CASPAR, 2006). Clinical and demographical data was fixed. All patients completed questionnaires (Health Assessment Questionnaire-Disability Index (HAQ-DI), FACIT-Fatigue, Dermatology Life Quality Index (DLQI), Short Form – 36 (SF-36). US was done by 2 US rheumatologists - 1288 large joints and 4968 entheses at the projection of these joints (total number - 54) were examined. The following was evaluated: synovitis count (by Grey Scale), Power Doppler(PD)+

synovitis), thickening and hypoechogenicity at enthesis, PD+ enthesitis, entheses with structural components. Entheseal findings were fixed according to consensus-based US definition and scoring for enthesitis in spondyloarthritis and PsA (OMERACT US).[2]

Results: In all 92 patients: male - 42 (45.7%), mean age was 42.9±9.6 (SD) years (y), PsA duration was 7 (2; 11.8) y, Disease Activity in PsA score was 15.2 (10.2; 21.4). Thus, the impact of psoriasis on the quality of life of patients with PsA was revealed. DLQI scores correlated with skin psoriasis activity and nail onychodystrophy, as well as clinical enthesitis (p<0,01). Minimal (67.4%) and moderate (29.3%) disability levels were found. HAQ-DI scores were associated with higher PsA activity and duration, age and clinical enthesitis (p<0,01). Physical and mental health (SF-36) correlated with Disease Activity in PsA and clinical enthesitis (p<0,05). Fatigue was found in 50% of patients and increased with PsA activity and duration, and clinical enthesitis (p<0,01). US data showed no association with QoL in PsA (p>0.05).

Conclusion: QoL scores of this study were related to clinical data, particularly to clinical enthesitis. US articular and entheseal inflammation were not correlated with QoL scores. This is probably due to the subclinical course of US changes. This allows us to conclude that QoL is associated with clinical than with US characteristics in PsA.

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POS1099

QUALITY OF LIFE, WORK IMPAIRMENT, AND DAILY ACTIVITY IMPAIRMENT OF PATIENTS WITH PSORIASIS VERSUS PSORIATIC ARTHRITIS: A REAL-WORLD SURVEY IN US AND EUROPE

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Background: Psoriasis (PsO) and psoriatic arthritis (PsA) and are chronic immune-mediated diseases characterised by joint inflammation and skin lesions which negatively impact patients' health-related quality of life (HRQoL). Several previous comparative studies have focused on PsA patients with or without skin involvement. Better understanding of the impact of both PsO and PsA on HRQoL and work / activity impairment will improve understanding of the incremental burden of PsA compared to PsO, and may lead to more personalised treatment options.

Objectives: To compare HRQoL, work impairment, and daily activity impairment of patients with a PsO diagnosis (dx) only, PsO dx with musculoskeletal (MSK) symptoms (sx), PsA dx with active skin sx, and PsA dx without active skin sx.

Methods: Data were drawn from the Adelphi PsO & PsA Disease Specific Programmes™ (DSP), real-world point-in-time surveys of rheumatologists, dermatologists and their consulting patients in the United States and Europe (France, Germany, Italy, Spain and UK); conducted in 2018/19. Patients were grouped according to their symptoms and confirmed diagnoses, comprising four groups:

1. Patients with PsO dx only,
2. Patients with PsO dx and with MSK sx,
3. Patients with PsA dx and with active skin sx,
4. Patients with PsA dx with no active skin sx,

Multivariate linear regression analyses with marginal mean predictions examined differences in patient-reported outcome measures (PROMs) between the four groups. Measures included HRQoL (EuroQol 5-Dimension 5-Level [EQ-5D Utility] and EuroQoL Visual Analogue Scale [EQ-VAS]), work impairment, and daily activity impairment (Work Productivity and Activity Impairment Questionnaire [WPAI]). Analyses controlled for demographics (age, sex, BMI), comorbidities present in >10% of patients and current treatment class (biologics, csDMARDs, steroids & other).

Results: 4491 patients were included: Group 1 (n=1833), Group 2 (n=91), Group 3 (n=2451), and Group 4 (n=116). 54% of patients were male, 89% of patients were white, with a mean age of 46.6 years. Demographics were consistent across all patient groups.

The model-predicted EQ-5D-Utility was lower in Groups 2, 3 and 4, compared with Group 1 (p=0.003, p<0.001 and p=0.004 respectively). Similarly, predicted EQ-VAS was lower in Group 3 compared with Group 1 (p=0.006), Table 1.

Table 1. Predictions of PROMs for PsO-PsA patient groups

PRO tool	Group [n]*	Predicted PRO value	Population norm (MCID)	Regression model p-value (vs. reference group)
EQ-5D Utility score (n=1839)	1 (ref) [743]	0.922	0.88 (0.07)	
	2 [32]	0.816		**0.003**
	3 [1023]	0.810		**<0.001**
	4 [41]	0.850		**0.004**
EQ-VAS (n=1882)	1 (ref) [763]	78.78	78.2 (n/a)	
	2 [36]	70.56		0.057
	3 [1040]	73.89		**0.006**
	4 [43]	75.23		0.248
WPAI % overall work impairment (n=1015)	1 (ref) [422]	15.36	n/a (15.0)	
	2 [14]	17.86		0.560
	3 [558]	22.16		**<0.001**
	4 [21]	26.09		**0.014**
WPAI % work time missed (n=1028)	1 (ref) [424]	0.91	n/a (n/a)	
	2 [14]	3.57		0.486
	3 [569]	4.46		**0.002**
	4 [21]	10.43		**0.003**
WPAI % impairment while working (n=1153)	1 (ref) [486]	14.90	n/a (20.0)	
	2 [18]	13.89		0.846
	3 [626]	19.63		**<0.001**
	4 [23]	17.39		0.435
WPAI % activity impairment (n=1818)	1 (ref) [732]	18.02	n/a (20.0)	
	2 [32]	26.25		0.122
	3 [1012]	26.14		**<0.001**
	4 [42]	25.24		**0.044**

*n values provided for reference, but margins are predictions as a result of the model and not for the specific number of patients in each subgroup.
(1) patients with PsO dx only
(2) Patients with PsO dx and MSK sx
(3) Patients with PsA dx and with active skin sx
(4) Patients with PsA dx with no active skin sx

Overall work impairment increased in Groups 3 and 4, compared with Group 1 (p<0.001 and p=0.014 respectively). Furthermore, Groups 3 and 4 missed more work compared with Group 1 (p=0.002 and p=0.003 respectively). Group 3 patients exhibited an increase in presenteeism and activity impairment compared with Group 1 (p<0.001), Table 1.

Conclusion: Patients experiencing PsA dx or MSK sx experienced an additional disease burden compared to patients with PsO sx alone, as measured by worse HRQoL and work impairment.

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POS1100 PSYCHOMETRIC PROPERTIES OF PATIENT GLOBAL ASSESSMENT IN THE EVALUATION OF PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Recommendations emphasize the need for the physician to work in partnership with the patient and a shared decision-making process is nowadays fundamental to manage properly Psoriatic Arthritis (PsA). Patient Global Assessment (PtGA) is a score that reflects the patient's judgment about the disease activity and is getting more used in clinical routine and research.
Objectives: The objective of this systematic literature review (SLR) is to analyze the role of PtGA in PsA and to describe its psychometric properties.
Methods: This SLR was conducted by two independent reviewers in accordance with the PRISMA statement, searching for articles reporting on the use of PtGA in PsA. All articles published until February 2021 in Pubmed were screened with no limitation about years of publication, language or patients' age. Articles reporting data of PtGA of skin assessment were excluded. Psychometric properties data were analysed according to the OMERACT (Outcome Measures in Rheumatology) Filter methodology version 2.1. Measurement properties of the PtGA were analysed according to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) terminology.
Results: The literature search identified 45 studies, accounting for 8516 patients in 20 longitudinal cohort studies, 15 cross-sectional studies, 5 randomized controlled trials, 2 post-hoc analyses, 1 retrospective study and one review. Ten articles were excluded because PtGA was referred to the assessment of cutaneous psoriasis. Content validity was reported in 32 studies. Different definitions, acronyms, scales and questions to assess PtGA were retrieved through the literature (see Table 1).

Table 1. Different questions, definitions, acronyms, scales and scores used to assess Patient Global Assessment retrieved. STD: studies

QUESTIONS
"How would you rate the patient's joint disease activity?"
"In all the ways in which your PSORIASIS and ARTHRITIS, as a whole, affect you, how would you rate the way you felt over the past week?"
"How active was your rheumatic disease on average during the last week?"
"Considering all the ways PsA has affected you during the last week, circle the number that best describes how you have been doing"
"How do you estimate your disease activity today?"
"How active do you feel your joint disease is today?"
DEFINITIONS
Pt visual analogue scale (VAS) for pain and global assessment
Pt general disease assessment
Pt global activity
Pt global assessment
Pt global disease activity
Pt opinion on the level of disease activity
Pt global evaluations
Pt perception of disease
Pt disease severity
ACRONYMS
PtGA; PGA; PaGA
SCALES
VAS (23 std); NRS (12 std)
SCORES
0-100 (23 std); 0-10 (11 std); 0-5 (5 std)

Face validity was reported in all the articles retrieved. PtGA was always used together with other instruments, alone or as part of composite indices: supporting its face validity, in 2 studies it was considered the instrument of reference to assess the outcome. A good correlation with PhGA, DAS28, BASDAI, ASDAS and DAPSA was found (see Figure 1). One study showed that the correlation became better (ES 1.81, 95%CI 1.42 2.19) during the follow up assessment. Three studies analyzed the discordance between patient and physician global assessment and in 25.0-49.0% found a positive discordance (PtGA higher than PhGA). Criterion validity was assessed exploring the PtGA correlation with quality of life measurements, demographic characteristics, biomarkers levels, treatment changes and damage assessments in 11 studies. The intrarater reliability was calculated only in 1 study, with an optimal correlation (ICC=0.87; 95%CI 0.83–0.90). PtGA responsiveness was used to evaluate response to treatment in 14 studies.

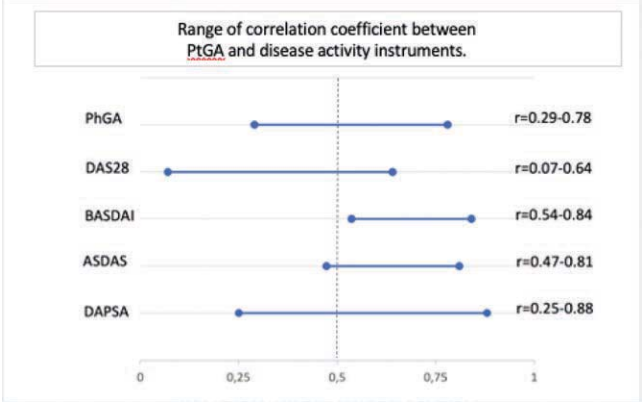

Figure 1. Forest plot showing correlation between PtGA and other instruments

Conclusion: PtGA demonstrated to be valid and feasible, but more studies are necessary to confirm its reliability and to evaluate its sensitivity to change. In addition, a clear definition of what PtGA refers to, what time and what kind of scale to adopt should be standardized.
Disclosure of Interests: None declared

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POS1101 DAPSA CORRECTED FOR PSAID12 IMPROVES ITS CONCORDANCE WITH MINIMAL DISEASE ACTIVITY.

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease of highly variable presentation, which determines a physical and psychological deterioration, with a negative impact on the quality of life of patients and knowing the patient's perception of their health status is very important for a good management of PsA.
Objectives: To assess an adjustment of the DAPSA according to the status of the PsAID-12 (Impact of the disease in psoriatic arthritis) and to analyze its relation in clinical practice with the minimal activity of the disease (Minimal Disease Activity or MDA) in psoriatic arthritis.
Methods: Multicenter cross-sectional study, which recruited 200 patients, who met the criteria for Classification of Psoriatic Arthritis (CASPAR), in six Spanish rheumatology centers. At the time of the visit, demographic, clinical, laboratory data, HAQ (0-3) and PsAID12 (0-10) self-questionnaires were collected. Disease activity was measured using DAPSA (with its cut-off points), MDA status was obtained, and the PsAID12 index was calculated. When a PsAID≤4 was not reached, the DAPSA was scaled to a higher interval (DAPSA corrected) obtaining a new index, DAPSA-PsAID. All analyzes were performed using SPSS23 software. Differences were considered statistically significant if $p < 0.05$.
Results: Of the total number of patients, 55% were men, with an age of 55.2 ± 11.6 years; 75% had only peripheral involvement and 25% had pure or mixed axial involvement. 43% were on biological treatment (18% join to csDMARDs). The patients who reached the MDA were 102 (51%), 62.7% in men vs 37.3% in women (p 0.025). With the PsAID-corrected DAPSA, the proportion of patients in low activity-remission who did not reach the MDA was lower than with the standard DAPSA (see Table 1), 16.3% vs 27.6% (Kappa 0.750 vs 0.688). In the binary regression analysis for MDA status, adjusted for sex, an OR (95% CI) for DAPSA and DAPSA corrected for PsAID of 8.12 (1.88-35.04) and 12.31 (3.74-40.50), respectively, was obtained.

Table 1.

	MDA N=102	No MDA N= 98	p
HAQ≤0.5, n (%)	82 (92.0)	**31 (36.5)**	<0.0001
DAPSA REM/LDA, n (%)	98 (96.1)	**27 (27.6)**	<0.0001
PsAID≤4, n (%)	92 (90.2)	**45 (45.9)**	<0.0001
DAPSA-PsAID REM/LDA, n (%)	93 (91.2)	**16 (16.3)**	<0.0001

Conclusion: A PsAID-corrected DAPSA could be a more reliable alternative to MDA than conventional DAPSA and facilitate clinician decisions in daily practice.

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POS1102 THE PREVALENCE OF INFLAMMATORY BACK PAIN IN PATIENTS WITH SKIN PSORIASIS WITHOUT PSORIATIC ARTHRITIS. DATA FROM DERMATOLOGICAL REAL-WORLD SETTING.

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Background: Psoriasis (PsO) is an inflammatory disease associated with psoriatic arthritis (PsA). PsA affects peripheral and axial joints[1,2]. Psoriasis can precede the onset of PsA by approximately 3 to 8 years, axial involvement often undiagnosed[3]. There are limited data about the prevalence of inflammatory back pain (IBP) in PsO patients (pts) without clinical symptoms of PsA[4].

Objectives: To study the prevalence of IBP in PsO pts without PsA symptoms

Methods: 108 PsO pts without PsA over a 10-month period (March 2021 to December 2021) were incluided. Participants filled out a questionnaire on IBP. Additionaly the prevalence of stiffness in the back and neck was estimated. IBP was defined as an affirmative answer to the question 'Did you suffer from low back pain for ≥3 months?' and IBP criteria was based on criteria ASAS (the ASsessment in Ankylosing Spondylitis) and was confirmed if at least 3 out of the following 4 criteria were present: (a) onset before age 40, (b) insidious onset, (c) improvement with exercise, (d) associated with morning stiffness

Results: It was found that more than 40% of patients complained of pain or stiffness in the back. Stiffness and pain in the neck were observed in every fourth patient on average. Of those patients who complained of pain in the back or neck, 37% noted that they had pain at rest (when they get up in the morning or lie down for a long time), and 21.3% had inflammatory pain at night (when patients are forced to woke up, they needed to do exercises) (Table 1). It was found that the risks of developing spondylitis with neck pain, neck stiffness, back pain, back stiffness were higher in 4,549 times (95% CI [1,720; 12,031]), in 19,444 times (95% CI [6,480; 58,343]) 15 times (95% CI [4.646; 48.427]) and 34.857 times (95% CI [7.583; 160.230]), respectively.

Conclusion: IBP was found in more than 40% PsO patients. Every fourth PsO patients complained of stiffness and pain in the neck. The presence of these symptoms significantly increased the risk of developing PsA with spondylitis. The presence of IBP should be taken into account for early diagnosis of PsA in the dermatological practice.

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POS1103 "WHAT MATTERS": PATIENT AND CLINICIAN PERSPECTIVES IN PSORIATIC ARTHRITIS CARE

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Background: Recent psoriatic arthritis (PsA) treatment recommendations (1) highlight the importance of shared decision making; this ideally requires the clinician understands "what matters" to each patient regarding their disease. Concurrently, patient research partners have been incorporated into projects for the OMERACT core domain set (2) and measures of physical function and (health related) quality of life (3). Currently, less is known about the similarities and differences between patient and clinician perspectives.

Objectives: To interrogate and deliniate commonalities and discrepancies in "what matters" to patients and to physicians in routine clinical care.

Methods: A comprehensive list of items describing the PsA patient experience was generated in medical anthropologist-designed (CH) peer-to-peer discussions in 4 patient focus groups across the United States (Seattle, Cleveland, Washington, DC). These items were combined with those from the GRAPPA-OMERACT PsA Outcomes patient-physician consensus project (2). A PsA physician and patient steering committee reviewed and revised the list with additional topics considered to be of importance. The final list of 51 items went through a 3 round Delphi process starting with 53 PsA patients and a 2 round Delphi with 13 PsA expert rheumatologists. In each round, participants rated each item for level of importance out of 100 total points.

Results: Top priority items for each group are depicted in Figure 1. Both patients and physicians rated 'Arthritis -Joint pain and swelling' in the top two. Five additional items were included for both groups but with different scores; all related to disease manifestations or physical consequences. Several items received disparate priority between groups. In this set, patients included two unique items: access to care and future health uncertainty. Other items affecting everyday function were noted. Physician priorities included specific disease manifestations and physical/functional outcomes, and the topic of "disease management goals", focusing on patient-physician communication regarding a treatment plan.

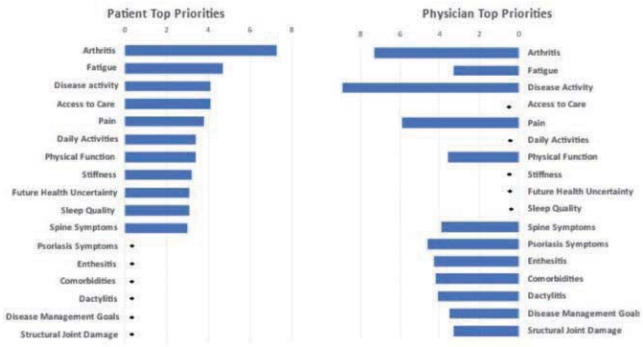

Figure 1. Top Patient and Physician Priorities *Not in set of highest ranked items for that group

Conclusion: Patients and physicians were in consensus that arthritis disease activity, pain and fatigue are key features of the patient's experience of PsA. Differences appeared in other domains; physicians ranked clinical domains such

as enthesitis, dactylitis, and skin disease more highly, patients considered items such as access to care, future health uncertainty and sleep quality to be most important. This study highlights the need for physicians to ask and address "what matters" with patients and to educate patients about potential differences in physicians' areas of concern to optimize shared decision making.

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POS1104

PHYSIOLOGIC ADAPTIVE CHANGE OF THE PATELLAR AND ACHILLES TENDONS: SENSITIVITY TO CHANGE DETECTED BY COMPUTER ANALYSIS OF SEQUENTIAL STATIC IMAGES

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Background: Sensitivity to change is the ability of a tool to detect changes in the measurement of a variable when this measurement is made on the same target over time. In the follow-up of patients with immune-mediated diseases, it is required that the instruments used to evaluate changes over time demonstrate enough precision. However, ultrasound studies stratify the results of the evaluations in ordinal degrees of intensity of findings dependent on the evaluator's opinion. Computer analysis of static images has recently been introduced in the study of patients with rheumatic diseases. Nonetheless, its application in musculoskeletal ultrasound is still very limited.

Objectives: -To determine if this type of image analysis is sensitive to structural adaptive change of the patellar and Achilles tendons in healthy subjects.

Methods: We recruited young volunteers with a declared sedentary habit and with a normal BMI. They carried out a supervised physical exercise routine for 6 months.

Two ultrasound measurements of the patellar and the Achilles long axis were performed. Also, two elastographies of the same tendons and two anthropometric measurements of the thigh and calf were made at the beginning and end of the training period. To demonstrate sensitivity to change, a correlation was made between the ultrasound, elastrographic and anthropometric morphological changes, and the result of the computer analysis of the image in terms of gray scale mean and mode.

Results: 19 volunteers were evaluated (mean age 24 ±2 years, 12 women).
After the exercise routine, we found statistically significant differences between calf perimeter (mean -3,70 ±1,803; p .000), Achilles elastography (-,347 ±,294; p .000), Achilles and patellar MGI (4,229 ±4,849; p .001 and 2,331 ±3,115; p,004). Regarding the non-normal distributed variables, we met statistically significant differences between patellar elastography (average range 11,45, sum of the ranks 126,00; Z -2,343; p,019), Achilles and patellar grey intensity modes (average 12,92, sum 168,00; Z -2,938; p,003 and average 11,77, sum 176,50; Z -3,28; p,001). The correlations study is shown in Table 1.

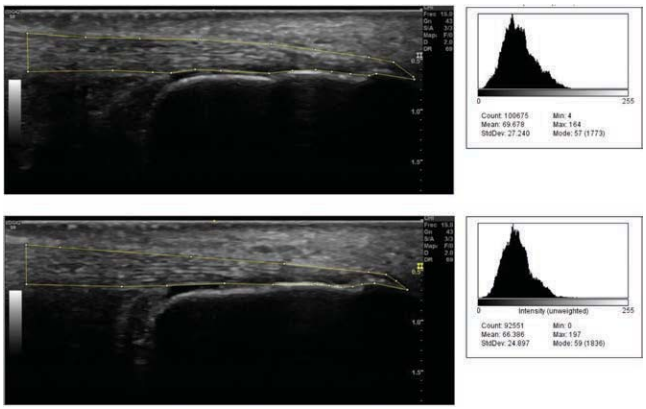

Figure 1. Before (upper) and after (lower) evaluation.

Conclusion: Computer analysis of static images of the Achilles and patellar tendons is sensitive to the change induced by exercise in young and healthy subjects. The mean gray intensity correlates better with elastography. This shows that the predominance of the fibrillar pattern induced by exercise produces a higher speed of sound conduction. The gray intensity mode correlates better with the anthropometric changes experienced by the subjects. The concentration of shades in white extremes translates into greater anthropometric changes. This demonstrates that the stiffness or elasticity of a tendon correlates with the global distribution of gray. The response to mechanical stimuli correlates with the concentration of more intense white tones that are not necessarily scattered (endophytes or pre-enthesophytes).

Disclosure of Interests: Carlos Guillén-Astete Speakers bureau: Novartis, Janssen, Abbvie, Grunenthal, UCB, Gebro, Paid instructor for: Roche, Novartis, Janssen, Esteve, Menarini, Consultant of: Janssen, Novartis, Roche, Grant/research support from: Pfizer, Grunenthal, Gebro, Novartis, África Andreu-Suárez: None declared, Marina Tortosa-Cabañas: None declared, Cristina Pijoan Moratalla: None declared, Paula Barrio Rufino: None declared, Esther Muñoz Rodriguez: None declared, Jorge Mollá Cuadrillero: None declared

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Table 1. ***Results of the Pearson correlation tests of changes experienced over time.***

Variables of change (Final-Baseline)		Achilles tendon elasticity change	Patellar tendon elasticity change	Achilles mean grey intensity changes	Patellar mean grey intensity changes	Achilles mode grey intensity changes	Patellar mode grey intensity changes
Calf circumference change	Pearson correlation	,050	,470*	,094	,530*	,935**	,029
	Sig. (bilateral)	,840	,042	,701	,020	,000	,907
Thigh circumference change	Pearson correlation	,014	-,069	,120	-,160	,022	,904**
	Sig. (bilateral)	,956	,780	,624	,514	,928	,000
Body Fat % Change	Pearson correlation	-,237	,098	-,033	,119	-,091	,011
	Sig. (bilateral)	,330	,689	,893	,626	,712	,963
Achilles tendon elasticity change	Pearson correlation	1	,221	,779**	,090	,147	-,032
	Sig. (bilateral)		,362	,000	,715	,548	,896
Patellar tendon elasticity change	Pearson correlation	,221	1	,353	,899**	,416	-,154
	Sig. (bilateral)	,362		,139	,000	,076	,529

Osteoarthritis

POS1105

EFFICACY AND SAFETY OF COLCHICINE FOR THE TREATMENT OF OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF INTERVENTION TRIALS

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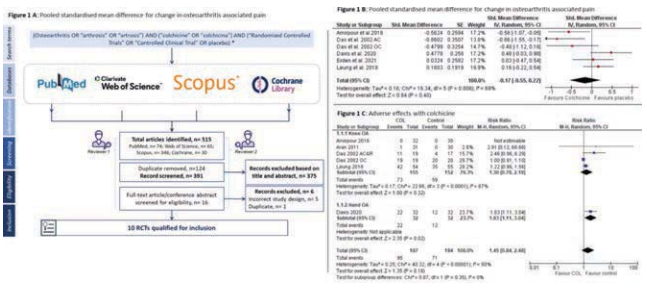
Background: Colchicine, an approved treatment for gout, has been trialled in many diseases, including osteoarthritis (OA), due to its anti-inflammatory effects. However, its efficacy and safety remain unclear in OA.
Objectives: This systematic review and meta-analysis evaluated the efficacy and safety of colchicine for the treatment of OA.[1]
Methods: PubMed, Web of Science, Scopus, and Cochrane Central were searched from inception through November 2020. Two reviewers independently screened for randomised controlled trials (RCTs) comparing colchicine with placebo or other active-comparators for the treatment of OA (knee, hand, or hip OA), extracted data, and performed Cochrane risk of bias assessments.
Results: The search retrieved 391 articles after removing duplicates, and 16 full-text articles were reviewed for eligibility (Figure 1**A**). Ten RCTs, nine in knee OA, one in hand OA, consisting of 847 patients (429 in colchicine arm, 409 in control arm) were included. RCTs were conducted between 2002 and 2021; three in India, two in Iran and Turkey, and one each in Australia, Singapore, and Iraq; follow-up period ranged 2 to 12 months. Moderate-quality evidence showed no clinically important pain reduction with colchicine compared to placebo in knee/hand OA patients (standardised mean difference [SMD], -0.17; 95% confidence interval [CI], -0.55 to 0.22) (Figure 1**B**). Moderate-quality evidence showed no improvement in dysfunction with colchicine compared to placebo in knee OA patients (SMD, -0.37; 95% CI, -0.87 to 0.13). Colchicine showed an acceptable safety profile with AEs/SAEs comparable to placebo (Figure 1**C**)



Conclusion: Current evidence does not conclusively suggest a benefit of colchicine in reducing pain and improving physical function in hand/knee OA patients. Future trials should focus on the sub-groups of OA patients with local or systemic evidence of inflammation and/or mineralisation who may benefit from colchicine.
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POS1106

MEDIATORS OF THE EFFECT OF THERAPEUTIC EXERCISE ON PAIN AND FUNCTION IN PATIENTS WITH KNEE AND HIP OSTEOARTHRITIS; AN INDIVIDUAL PATIENT DATA MEDIATION STUDY FROM THE OA TRIAL BANK.

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Background: Currently, there is no cure for osteoarthritis (OA). Therapeutic exercise is recommended in all international guidelines to improve pain and function (1). However, randomised controlled trials (RCTs) investigating therapeutic exercise showed that, on average, effect sizes are small to moderate compared to non-exercise controls (2-3). Better knowledge about how therapeutic exercise works to improve pain and function could help improve the design and delivery of future therapeutic exercise interventions and potentially improve patient outcomes.
Objectives: To evaluate the mediating effects of 1) muscle strength, proprioception, and range of motion (ROM) among patients with knee OA, and 2) muscle strength among patients with hip OA, using the procedures established for Individual Participant Data (IPD) analyses by the OA Trial Bank.
Methods: Relevant IPD were sought from all published RCTs comparing therapeutic exercise to a non-exercise control group among people with knee and/or hip OA, using previously published methods (4). For each potential mediator separately, the effect of exercise on the absolute change in pain/function directly after the intervention was determined, controlling for the relative change in mediator under investigation and potential mediator-outcome confounders, using the 'counterfactual framework' (5). Next, the effect of exercise on the relative change in the mediator was determined. The percentage mediated was calculated by dividing the natural indirect effect by the total effect.
Results: We obtained IPD from 12 RCTs and 1407 participants (knee OA = 1113; hip OA n=294) that were eligible for inclusion in one or more mediation analyses. Therapeutic exercise showed a significant effect on the relative change in muscle strength in knee OA, but not for proprioception or ROM in knee OA, nor for muscle strength in hip OA. Of all mediators, only the change in muscle strength had a significant effect on the change in pain in knee OA, and on function in knee OA and in hip OA. The percentage mediated for each mediator and each outcome was small (5.3% or less, see Table 1).

Table 1. Percentage mediated for all potential mediators, by outcome and joint.

	Knee OA Pain	Knee OA Function	Hip OA Pain	Hip OA Function
Muscle strength	2.4%	2.3%	absent	absent
Proprioception	absent	0.2%	-	-
Range of motion	1.8%	5.3%	-	-

'absent': no percentage mediated calculated, since direct and indirect effect had opposite directions;'-': factors not considered a potential mediator for therapeutic exercise in hip OA.

Conclusion: In the first IPD mediation analysis to our knowledge of this scale, muscle strength, proprioception and ROM did mediate the effect of therapeutic exercise for pain and function in knee OA, but only to a very small degree. We observed no such mediating effect of muscle strength for therapeutic exercise in patients with hip OA. The challenge remains to better understand the key mechanisms of action of therapeutic exercise for knee and hip OA, so that exercise interventions can be designed and delivered to target these and therewith optimise the effects for patients.
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Disclosure of Interests: Jos Runhaar Grant/research support from: Fellowship from the Foundation for Research in Rheumatology (FOREUM), Melanie Holden Grant/research support from: Grant from the Chartered Society of Physiotherapy Charitable Trust (grant no PRF/16/A07), and the National Institute for Health Research (NIHR) School of Primary Care Research (grant no 531), Miriam Hattle: None declared, Johny Quicke Grant/research support from: JQ is part-funded by an NIHR CRN West Midlands Research Scholarship and part funded by the Haywood Foundation, Richard Riley: None declared, Emma Healey Grant/research support from: part funded by the National Institute for Health Research (NIHR) Applied Research Collaboration (ARC) West Midlands., Danielle van der Windt: None declared, Krysia Dziedzic: None declared, Marienke Van Middelkoop: None declared, S.M.A. Bierma-Zeinstra Grant/research support from: OA Trial Bank received long-term funding by the Dutch Arthritis Association, Nadine Foster: None declared

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POS1107 CHANGE IN ULTRASOUND-BASED KNEE JOINT INFLAMMATORY MARKERS AFTER WEIGHT LOSS IN PATIENTS WITH OSTEOARTHRITIS: A PROSPECTIVE COHORT STUDY.

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Background: Pain and impaired function due to knee OA (KOA) can be reduced with weight loss in obese patients. The role of synovitis in symptom improvement after weight loss is not fully understood. MRI and ultrasound (US) can be used in assessment of inflammation in the KOA. Knee joint synovitis assessed by MRI does not seem to change with weight loss, however, the typical MRI score is semiquantitative, which might be less sensitive to change than a quantitative score. US has a higher resolution than MRI and borders between synovium and surrounding tissues might be clearer allowing for a quantitative score. Changes in US-based synovitis following a weight has not been assessed.
Objectives: To assess changes in US synovitis in the knee joint after 8 weeks low-calorie weight loss intervention in overweight persons with KOA.
Methods: prospective cohort study (NCT02931370) including overweight persons (BMI ≥ 27 kg/m^2) with KOA. Weight loss was induced by an intensive 8-week diet (1200 kcal/day), participants had symptomatic and radiographically confirmed KOA (KL grade 1-3). At week 0 and 8 all participants filled in the KOOS questionnaire assessing pain, physical function, symptoms, quality of life, and sport/recreation in relation to KOA (0= worst; 100=best). Furthermore, an US examination of the most affected knee was performed assessing the amount of synovial hypertrophy (SH) and effusion in medial and lateral recesses. The US examination was performed in a strictly standardized manner on a high-end US machine. The subsequent image evaluation was done both according to a semiquantitative score from 0 to 3 (0=no SH/effusion and 3=pronounced SH/effusion) and a quantitative scoring system using specific anatomic landmarks to measure the synovial hypertrophy/effusion in millimeter. Statistical analyses were performed on the per protocol population (participants completing diet intervention).
Results: 135 patients with KOA with a mean age of 60y (SD 9.8), a body weight of 106.0 kg (SD18.5) and mean BMI of 36.4 (SD5.4) completed the weight loss intervention. After the diet intervention mean weight change was -12.8 kg (95%CI -13.3 to -12.4) and the reductions in SH were -0.3mm (95%CI -0.5 to -0.1) (medial recess) and -0.4mm (95%CI -0.6 to -0.1) (lateral recess), and -0.03 (-0.13 to 0.07) (medial recess) and -0.07 (-0.20 to 0.05) using the semi-quantitative system. The mean change in the KOOS subscales range from 15.8 (sport/recreation) to 7.4 (QoL). See Table 1.

Table 1.

n=135	Baseline	Change	
	Mean (SD)	Mean (95%CI)	P
Age	60.0 (9.8)	-	-
Females, n (%)	87 (64.4%)	-	-
BMI	36.4 (5.4)	-4.4 (-4.5 to -4.3)	<.0001
KL-scores; 1	22 (16.3%)	-	-
KL-scores; 2	56 (41.5%)	-	-
KL-scores; 3	57 (42.2%)	-	-
KL-scores; 4	0 (0%)	-	-
Synovial Hypertrophy			
Medial, mm	3.8 (1.8)	-0.3 (-0.5 to -0.1)	0.0198
Lateral, mm	5.3 (2.3)	-0.4 (-0.6 to -0.1)	0.0210
Medial, 0-3	1.2 (0.6)	-0.03 (-0.13 to 0.07)	0.5584
Lateral, 0-3	1.8 (0.8)	-0.07 (-0.20 to 0.05)	0.2311
KOOS, 0-100			
Pain	64.1 (16.0)	12 (10.2 to 13.8)	<.0001
Function	68.4 (17.3)	14 (12.4 to 15.6)	<.0001
Symptoms	68.9 (16.4)	9 (7.2 to 10.8)	<.0001
Sports/Recreation	35.9 (24.0)	15.8 (13.2 to 18.3)	<.0001
QoL	43.8 (17.5)	7.4 (5.7 to 9.2)	<.0001

SD = Standard Deviation; CI = Confidence Interval; BMI = Body Mass Index; KOOS = Knee injury and Osteoarthritis Outcome Score; QoL = Knee-related Quality of Life

Conclusion: Quantitative measures of SH assessed by US decreased after a significant weight loss over 8-weeks; however, no linear association with weight loss magnitude was seen. A weak correlation between changes in SH in the lateral recess and change in pain was seen. This indicates changes in SH assessed by US examination is associated with a low-calorie diet but seems uncoupled with weight loss magnitude. The weight loss induced changes in synovitis and KOA symptoms seem vaguely related.

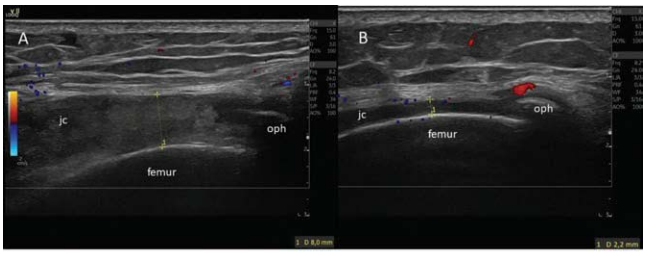

Fig.1**Fig 1** A: medial reces; B: lateralt reces.
Yellow line shows the point measured
Jc=joint cavity; oph=osteophyt

Disclosure of Interests: None declared

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POS1108 USE OF MACHINE LEARNING IN OSTEOARTHRITIS RESEARCH: A SYSTEMATIC LITERATURE REVIEW

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Background: Artificial intelligence techniques, in particular machine learning (ML), are increasingly used in rheumatology and especially in osteoarthritis (OA). ML studies in OA are very heterogeneous, hence the need to have an overview of their field of application.
Objectives: The aim of this systematic literature review is to provide a comprehensive and exhaustive landscape of the use of ML in the clinical care of OA.
Methods: A systematic review of the literature was performed in July 2021 using the Medline database with key words and MeSH terms referring to ML methods in OA. Only original articles in English were considered. Articles related to replacement surgery, theorical imaging, rehabilitation, molecular biology, and spinal or temporomandibular OA were excluded. For each selected article, the

number of patients, the ML algorithms used, the type of data analyzed, the validation methods, and the data availability were collected.
Results: From 1,148 screened articles, 46 were selected and analyzed, most of which were published after 2017 (Figure 1). Twelve articles were related to diagnosis, 7 to prediction, 4 to phenotyping, 12 to severity and 11 to progression. The number of patients included ranged from 18 to 5,749. Deep learning (DL) was used in 35% of the cases. Imaging analyses represented 74% of the studies. Knee OA was studied in 85% of these articles while 15% investigated hip OA. None were on hand OA. Most of the studies were done on the same cohort with data from the Osteoarthritis Initiative (OAI) used in 46% of the articles whereas the Multi-Center Osteoarthritis Study (MOST) and the Cohort Hip and Cohort Knee Study (CHECK) cohort were respectively used in 11 % and 7 % of the articles. Data and source code were publicly available in 54% and 22% of the articles. External validation was provided in only 7 % of the articles.

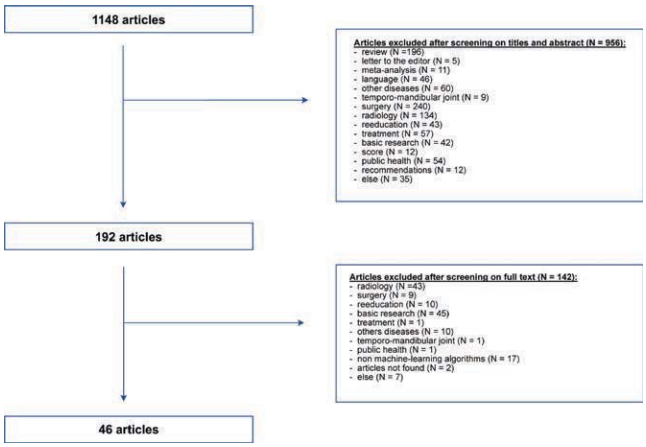

Figure 1. Article selection flow chart

Conclusion: This review provides a comprehensive update of ML in OA research. The number of ML articles in OA has increased exponentially over the last 5 years with applications across all major research themes. However, there is methodological heterogeneity, with articles based mainly on radiological data, but also on knee OA. To date, there is no ML article on digital osteoarthritis. This work also shows the need to develop clinical cohorts to bring more diversity in ML work and to allow external validation This article is the first systemic review of the literature in OA and provides an overview of ML in OA, its applications, limitations and perspectives.
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POS1109 GENETIC MARKERS PREDICT THE DEVELOPMENT OF POSTOPERATIVE PAIN

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Background: Postoperative pain (POP) is a serious complication that affects the outcome of total arthroplasty (TA) of the knee (CJ) and hip (HJ) joints in patients with osteoarthritis (OA). The search for the genetic characteristics of POP is an urgent direction in the study of this problem.
Objectives: To determine the relationship between the polymorphisms of the KCNS1, COMT, and OPRM1 genes and the development of postoperative pain in patients with osteoarthritis of the knee joint and hip joint who underwent total arthroplasty.
Methods: The study group consisted of 95 patients with knee osteoarthritis and / or hip joint osteoarthritis (64.6% of women; mean age - 65.4 ± 9.0 years) who underwent TA CJ (47.8%) or TA HJ (52.2 %). The presence of POP was determined when it persisted or appeared after 3 and 6 months. After surgery, pain in the area of the operated joint ≥40 mm by 100 mm visual analogue scale. All patients underwent genotyping of KCNS1 (rs734784), COMT (rs6269, rs4633), and OPRM1 (rs1799971) gene polymorphisms by real-time polymerase chain reaction using original sequence-specific primers and probes labeled with various fluorescent labels. Registration and interpretation of the obtained results were carried out on a DT-96 amplifier (DNA-Technology LLC, Russia).
Results: POP was observed in 32.6% of patients who underwent TA CJ or TA HJ. The incidence of POP after TA CJ and TA HJ was 30.2% and 34.0%, respectively (p = 0.882). There were no differences in the frequencies of genotypes of the studied genes (p>0.05). The presence of the homozygous GG genotype of the KCNS1 gene polymorphism (rs734784) was associated with the presence of POP in accordance with the recessive genetic model (GG vs AA + AG; odds ratio (OR) - 3.96 [95% confidence interval (CI): 1, 51; 10.37]; p = 0.005). The presence in the genotype of the mutant allele T (TT + CT) of the COMT polymorphism (rs4633) reduced the risk of developing POP compared with the carriage of the CC genotype (OR = 0.32 [95% CI: 0.12; 0.83]; p = 0, 02) according to the dominant genetic model. There was no statistically significant correlation between the development of POP and the carriage of various genotypes and alleles of the COMT (rs6269) and OPRM1 (rs1799971) genes.
Conclusion: There is a statistically significant association between the polymorphism of the KCNS1 (rs734784) and COMT (rs4633) genes and the development of chronic POP in patients who underwent TA CJ and TA HJ. Further studies of the genetic predisposition to POP are required using more clinical material.
Disclosure of Interests: None declared
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POS1110 WHAT FACTORS ARE ASSOCIATED WITH THE DEVELOPMENT OF PAIN AFTER TOTAL JOINT REPLACEMENT?

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Background: Chronic postoperative pain (CPP) is one of the most common complications of total hip (HJ) and knee (CJ) arthroplasty (TA). The search for the factors that determine this pathology is an urgent scientific and practical task.
Objectives: To determine the factors associated with the development of CPP in patients who underwent TA, CJ or HJ.
Methods: The study group consisted of 124 patients with osteoarthritis of the knee or hip joint, mean age 63.6 + 9.9 years, 63% of women and 37% of men, who in 2019-2020 year done out by TA KJ or HJ. The development of CPP was assessed after 3 and 6 months. telephone survey of patients. This complication was diagnosed in the presence of moderate to severe pain (≥40 mm on a visual analogue scale, VAS), persisting for at least 3 months, causing concern in patients and / or requiring regular use of analgesics. A comparison was made between the groups of patients with CPP and the absence of CPP for a number of factors determined in the preoperative period.
Results: The incidence of CPP was 27.4%. There were no differences in the incidence of CPP in patients who underwent TA CJ and TA HJ: 28.1% and 26.9%, respectively (p = 0.88). The presence of CPP was significantly associated with such preoperative indicators as a higher body mass index (BMI), a higher intensity of pain at rest, higher values of the WOMAC pain index, WOMAC and WOMAC stiffness in general, and the severity of symptoms of neuropathic pain. (PainDetect questionnaire), signs of depression and anxiety (HADS questionnaire). The risk of developing CPP was significantly higher (p <0.05) in patients

with BMI> 30 kg / m2 - odds ratio (OR) 2.755 (95% confidence interval, CI 1.053-7.206), for pain at rest ≥40 mm VAS - OR 1.349 (95% CI 0.478-3.803), Pain Detect score ≥13 - OR 3.598 (95% CI 1.048-12.36), depression score HADS ≥8 - OR 2.193 (95% CI 0.745-6.454), number of pain sources ≥ 2 - OR 6.996 (95% CI 2.358-20.756).

Conclusion: The risk of CPP after TA CJ and HJ is higher in patients with overweight, high preoperative pain, signs of neuropathic pain and depression, and in the presence of several sources of musculoskeletal pain (except for the affected joint planned for TA).

Disclosure of Interests: None declared

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POS1111 WHAT DOES GRIP STRENGTH REFLECT IN HAND OSTEOARTHRITIS? RESULTS FROM THE DIGICOD COHORT

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Background: Among the general population over 60 years-old, the decrease in grip strength is a marker of morbidity and mortality: its measurement during follow-up consultations is considered as a predictive marker of good health status or the patient's overall fragility (1). However, hand osteoarthritis (HOA), which can modulate grip strength and is also associated with comorbidities is never taken into account, while it is a very common disease.

Objectives: The objectives of this study are to describe grip strength in a symptomatic HOA population, to investigate painful osteoarthritic joints associated with decreased grip strength, and to determine whether decreased grip strength is independently associated with comorbidities in this population.

Methods: DIGICOD is a hospital-based observational cohort including patients with radiographic features of HOA of at least 2 joints or radiographic thumb base OA. Inflammatory rheumatism or crystal arthropathy were excluded. The data at baseline were used for the analysis. Grip strength was the higher score of 3 repeated measures using a Jamar dynamometer. Baseline grip strength of the dominant hand was compared in the cohort between men and women (Student's T test) and was described by age (by 10-year age groups using Kruskal-Wallis test). In this cross-sectional study, factors associated with a decreased grip strength were investigated using univariate and then multivariate linear regression analysis (with adjustment on age, BMI and variables with $p \leq 0.2$ in univariate analysis) with stratification by sex. Results were presented by beta coefficients and their 95% confidence intervals. A first analysis focused on the association of grip strength with local factors: painful locations in the dominant hand by row and radiographic severity according to the total Kellgren-Lawrence (KL) score. The second analysis assessed the patient-level association between decreased grip strength and general characteristics, including cumulative comorbidities and markers of radio-clinical severity of hand OA, namely the AUSCAN pain score and total KL score. A sensitivity analysis was performed to look for association between grip strength and each comorbidity.

Results: 394 patients were analyzed, including 329 women (mean ± SD of the dominant hand's grip strength of 21.6 ± 6.9 kg) and 65 men (34.9 ± 9.8 kg) with a mean age of 66.9 ± 7.3 years. Grip strength decreased with age ($p<0.001$) and was lower for women ($p<0.0001$). Among women, locally, decreased grip strength was independently associated with painful involvement of at least 2 metacarpophalangeal joints (MCPs) (estimated coefficient [95% CI] -3.6 [-6.2; -1.0] kg versus no painful MCPs) but not with proximal and distal interphalangeal joints, and with a high KL total sum score (-0.06 [-0.10; -0.01] kg per additional point). At the patient-level, decreased grip strength was not associated with comorbidities but with radio-clinical severity ($p<0.05$), i.e. a higher KL total sum score and AUSCAN pain score. Among men, neither radiographic severity nor painful locations were independently associated with a decrease of grip strength. Conversely, decreased grip strength was associated with at least 3 comorbidities (-8.5 [-15.5; -1.43] kg versus a single comorbidity being OA), independently of radiographic severity. The study of comorbidities individually did not show any particular association with grip strength.

Conclusion: In this cohort of symptomatic HOA, the decrease of grip strength reflects the radio-clinical severity of hand OA among women, whereas among men, it is independently associated with the accumulation of comorbidities. The presence of hand OA should be considered for further studies investigation the relationship between grip strength and morbi-mortality.

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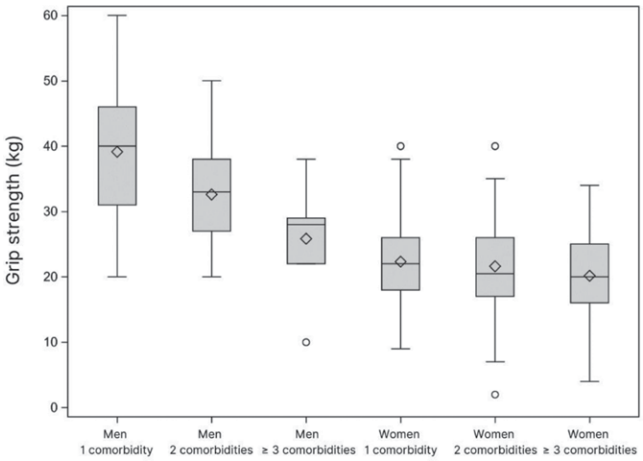

Graph 1. Grip strength according to the number of comorbidities among men and women

Disclosure of Interests: None declared

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POS1112 A RANDOMIZED, CROSS-OVER STUDY TO INVESTIGATE THE EFFECT OF WEIGHT-BEARING VS NON-WEIGHT-BEARING EXERCISE AND CARDIOVASCULAR STRESS ON TYPE II COLLAGEN TURNOVER IN KNEE OSTEOARTHRITIS PATIENTS – BIOMARKER DATA FROM THE EFEX-OA-02 STUDY

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Background: Biomechanical stress is a prerequisite for OA development and studies have shown a difference in the effect of impact- and shear stress[2], although studies of the direct impact of exercise on cartilage turnover have not demonstrated clear trends[1].

Objectives: Exploring how weight-bearing (WB), non-weight-bearing (NWB) exercise and cardiovascular stress influence circulating biomarkers of cartilage extracellular matrix turnover in OA.

Methods: EFEX-OA-02 was a randomized, cross-over, clinical study investigating the direct effect of exercise on joint biomarkers in knee OA. Subjects were randomized to an order of cycling and running followed by adrenaline infusion and finally resting one week apart. Exercise and infusion sessions were multiphasic, consisting of 4x5-minute intervals. Peak cardiorespiratory stress (PCS) per interval was set to ≥80% of the heart rate reserve during exercise. Blood samples were obtained before, during, at five time points after and 24 h post exercise/infusion. For adrenaline infusion, 0.06 mg/kg of adrenaline was prepared in a 50 mL saline solution and administered intravenously. At rest, samples were collected at corresponding time points, except for the 24 h sample, which was omitted. Levels of serum C2M, T2CM (type II collagen degradation) and PRO-C2 (type II collagen formation) were measured using ELISA-assays (Nordic Bioscience). Coll2-1 and Coll2-1NO2 (type II collagen degradation) were measured using ELISA (Artialis).Changes in biomarker concentrations after activity were compared to baseline (BL) and the corresponding resting samples. We used ANCOVA and Dunnett's test with geometric means of change from BL up to 240 min as the dependent variable and subject and activity as covariates. Paired t-test was used to compare values at 24-hour to BL.

Results: Forty subjects were included. Mean age was 60.4 years (SD: 8.7), 24 (60%) were females, mean BMI was 27.0 kg/m^2 (SD: 3.5), 18 had cumulated KL grade of 2 or 3 (45%) and 22 (55%) had KL 4, 5 or 6. and mean KOOS pain at BL was 67.5 (SD: 15.2) corresponding to mild-moderate pain. All subjects

reached minimum PCS during exercise, but only an average of 70% (SD: 8.7) of that during infusion. Cycling induced a small reduction in C2M (peak: -5.3%, 95%CI: -7.8 to -2.7%). PRO-C2 increased rapidly in response to cycling (peak: 11.7%, 95%CI: 4.3 to 19.1%) and running (peak: 12.9%, 95%CI: 3.54 to 22.2%). T2CM decreased up to one hour after cycling (peak: -10.8%, 95%CI: -15.1 to -6.5%) and running (peak: -9.5%, 95%CI: -15.5 to -3.6%), similar to adrenaline, then increased. Coll2-1NO2 increased rapidly following cycling (peak: 12.5%, 95%CI: 2.8 to 22.2%) and running (peak: 9.8%, 95%CI: 0.26 to 19.6%). Trends of increase was found in Coll2-1 (21.3%, 95%CI: 2.9 to 39.6) and Coll2-1NO2 (11.6%, 95%CI: -7.9 to 31.1%) in response to running at 240 min (Figure 1 – Error bars: SE, *Change to resting, †Change from BL, */†: P < 0.05, **/††: P < 0.01 ***/†††: P<0.001).

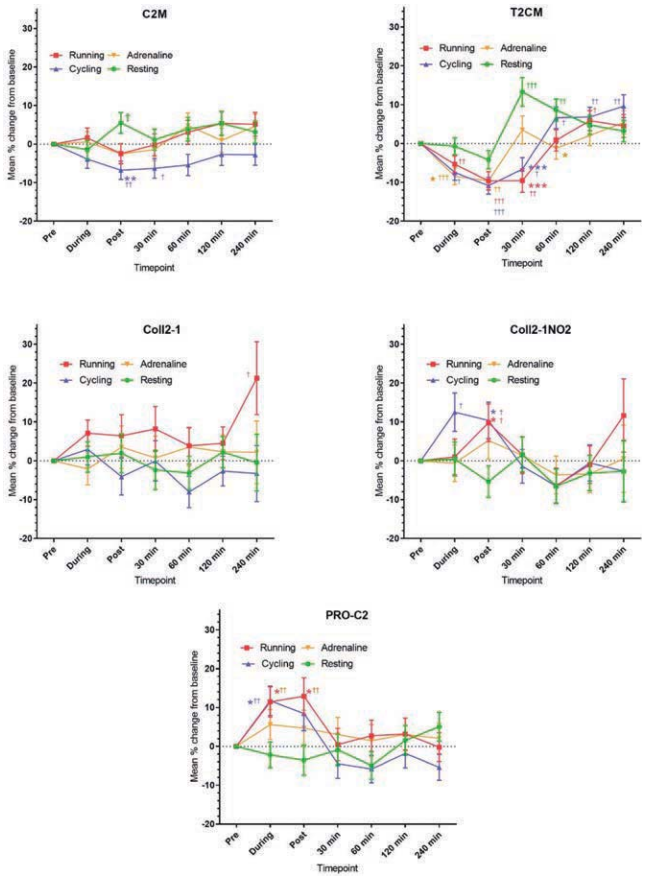

Figure 1.

At 24h PRO-C2 reduced -9.4% (95%CI: -18.2 to -0.5%) after cycling, Coll2-1NO2 reduced -8.33% (95%CI: -17.0 to 0.3%) after running and T2CM elevated by 6.0% (95%CI: -0.8 to 12.8%) after running and 7.1% (95%CI: 0.5 to 13.7%) after cycling.
Conclusion: Running, cycling and adrenaline infusion induced rapid small-to-moderate changes in circulating biomarkers reflecting type II collagen turnover. Changes after adrenaline-infusion suggests a cardiovascular contribution to exercise-induced changes. This model could potentially be used to evaluate treatment effects on collagen turnover.

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POS1113

CONSTRUCT VALIDITY, RELIABILITY, RESPONSIVENESS AND INTERVAL SCALE TRANSFORMATION OF THE WESTERN ONTARIO AND MCMASTER UNIVERSITIES OSTEOARTHRITIS INDEX (WOMAC) IN PATIENTS UNDERGOING KNEE ARTHROPLASTY

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Background: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is commonly used in research studies of knee osteoarthritis (OA). It is commonly reported as ordinal raw scores. Previous validation studies using Rasch models requires item deletion. Conversion table to Interval scale for meaningful measurement is not available.
Objectives: We aim to evaluate the fit of WOMAC to the Rasch model in a large sample of patients with knee OA who have undergone knee arthroplasty (KA) to derive the transformation table for interval scale measurement.
Methods: We used data collected from knee OA patients undergoing KA before surgery and at 6-months after KA. We collected demographics, WOMAC, Short-form-36 (SF-36) and Oxford Knee Score (OKS) with the latter two as comparison. WOMAC was calibrated for fit to Rasch model for monotonicity, homogeneity, local item independence and absence of differential item functioning (DIF) in a randomly selected sample of 300 patients from each time point. Parameter estimates were then imported into the full data set to provide the necessary estimates of all the scales. We report responsiveness through Standard Error of Measurement (SEM); Smallest Detectable Difference (SDD), %SDD and effect sizes (ES) between pre-operative and 6-months. Transformation tables of the ordinal to interval values for WOMAC was performed.
Results: Data was analysed for 1136 patients (mean age 65.9 years, 69% female) who underwent KA. WOMAC pain, function and total scores had adequate fit to unidimensional Rasch model with good reliability (Person Separation Index: 0.76, 0.80 and 0.79). No item deletion was required. The SEM, SDD and %SDD of WOMAC total were 4.4, 6.9, 10.1, and ES was 1.97 between pre-operative and 6-months. No significant DIF was seen for age, sex, body mass index, education level or uni-compartmental versus total KA. WOMAC pain, function and total scales were transformed to interval scales.
Conclusion: The WOMAC total, pain and function scales had adequate fit to the Rasch model, providing unidimensional measure with good reliability and responsiveness. Transformation of WOMAC to interval scale measurement is feasible and applicable to wide ranges of studies.

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Disclosure of Interests: Ying Ying Leung Speakers bureau: Received speaker fee from AbbVie, DKSH, Janssen, Novartis and Pfizer., Julian Thumboo: None

Table 1. Fit of Scales of WOMAC to the Rasch Model

WOMAC/ subscale	Residuals		Conditional Chi-Square		Reliability		Unidimens-ionality	ECV	Responsiveness (Interval Scale)		
	Item	Person	Value(df)	P	PSI	A	% Significant t-tests		SEM	SDD	ES (6m-baseline)
Pain	2.499	0.779	18.7(10)	0.044	0.76	0.87	3.03	1.0	2.9	1.04	2.11
Stiffness	1.215	0.462	57.0(9)	<0.001	0.60	0.82	2.53	-	-	-	-
Functioning	2.496	0.702	47.0(42)	0.274	0.80	0.94	1.16	0.93	10.2	2.49	1.91
Total	4.193	0.699	43.3(58)	0.925	0.80	0.80	2.03	0.90	9.9	4.4	1.97

declared, Seng Jin Yeo: None declared, Vikki Wylde: None declared, Alan Tennant: None declared
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POS1114 LABORATORY BIOMARKERS OF JOINT REMODELING AND INFLAMMATION IN PATIENTS WITH EARLY KNEE OSTEOARTHRITIS

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Background: Record prevalence of osteoarthritis (OA) around the world is aggravated by the fact that doctor most often meets it on advanced stage, so that therapeutic interventions can no longer provide significant success [1]. It is advisable to study early joint remodeling, when gross irreversible changes have not yet occurred, and laboratory markers appear to be valuable diagnostic and prognostic tool, potentially able to identify patients-responders to particular treatment method [2].
Objectives: To verify joint tissue remodeling and synovitis in patients with early knee OA Kellgren-Lawrence (K-L) Grades 0-2 using laboratory biomarkers.
Methods: The study included 90 patients with knee OA K-L Grades 0-2 (3 groups of 30 people each) and 30 healthy volunteers; to clarify early OA, Luyten FP criteria (2018) were used [3]. Among persons with knee OA, there were 57 women (63.3%) and 33 men (36.7%), mean age 32 [27; 35] years; participants without OA were presented by 18 (60%) men and 12 (40%) women, mean age 29,5 [25; 34] years. Knee radiography, ultrasonography, laboratory biomarkers assessment including interleukin-1beta (IL-1b), N-Terminal Propeptide of Type 1 Procollagen (P1NP), Beta-Cross laps, cartilage oligomeric matrix protein (COMP) were carried out.
Results: All groups with knee OA was characterised by women predominance (Table 1). Laboratory study revealed slight increase in IL-1β and both bone markers in K-L Grade 0. Grade 1 was characterized by elevation of COMP and Beta-Cross Laps on background of IL-1β increased. In Grade 2 the highest level of COMP, slight decrease in Beta-Cross Laps and IL-1β, weak increase in P1NP were found. Correlation analysis have detected positive significant relationships between COMP and IL-1β (r=0.37), as well as Beta-Cross Laps and P1NP (r=0.43). The analysis of laboratory and instrumental relationships demonstrated significant correlation between COMP and medial condyle cartilage thickness (r=-0.18), COMP and bursa suprapatellar square (r=0.26), Beta-Cross Laps and osteophytes size (r=0.79), IL-1β and synovial membrane thickness (r=0.24).
Conclusion: Early knee OA of K-L Grade 0 is characterized by bone metabolism activation and synovial inflammation before articular cartilage involvement. On Grade 1, cartilage destruction appears and bone resorption is enhanced. Grade 2 is characterized by significant intensification of cartilage destruction, weakening of bone resorption on the background of synovial inflammation. In addition to cartilage damage, COMP is associated with joint inflammation, which requires further research to take in account it as also synovial biomarker.
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POS1115 EFFICACY AND SAFETY OF THE COMBINATION OF PRP + NON-CROSSLINKED HYALURONIC ACID VERSUS HYALURONIC ACID, IN MONO-INJECTION, IN SYMPTOMATIC KNEE OSTEOARTHRITIS. RANDOMIZED CONTROLLED PHASE III TRIAL, SINGLE BLIND

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Background: Despite the recent results of meta-analyses of randomized controlled trials (RCTs), the place of PRP and hyaluronic acid in the symptomatic treatment of knee osteoarthritis (KOA) remains uncertain in the latest international recommendations. Very few studies are available on the potential synergistic effect of their combination in mild to moderate forms of KOA(1).
Objectives: Randomized, controlled, multicenter, non-inferiority trial (*clinical trial NCT03328728*), single-blinded (investigator) to compare the efficacy and safety of the combination of PRP and non-crosslinked hyaluronic acid (PRP-HA, *Cellular Matrix A-CP-HA, Regen Lab*) as a single injection versus Hylan G-F 20 (HA), with follow-up at 1, 3 and 6 months, on an intention-to-treat (ITT) basis.
Methods: Patients aged 40-80 years with symptomatic femorotibial KOA (WOMAC A1 (pain on walking) or WOMAC Function > 50/100) and a Kellgren and Lawrence (KL) radiographic stage II or III were randomized into two groups: PRP-HA vs. HA, as a radio- or ultrasound-guided single injection at M0. Patients should not have received injectable treatments (corticosteroids, HA or PRP) for 3 months, nor per os NSAIDs for at least 1 month. A 6-month follow-up of the impact of the KOA was performed at M1, M3 and M6. The primary endpoint was the difference in the WOMAC score for pain on walking between M0 and M6 between the 2 groups. Secondary endpoints were collected and compared at M1, M3, and M6 (WOMAC Pain, Function, and Total; SF-36 score) as well as the percentage of patients responding at M6 according to the OMERACT-OARSI criteria, according to the Patient Acceptable Symptomatic State (PASS), and the Minimal Clinical Important Improvement (MCII) of the WOMAC pain. The factors of good response (PASS and MCII responders) at M6 were investigated in univariate and multivariate analysis. Tolerance was assessed by comparing adverse events over 6 months in both groups.
Results: 156 patients were included in three French teaching hospitals between 2018 and 2021 with the following characteristics: age 59.6±9.2 years, BMI 28.1±5.8 kg/m^2, 37.8% grade II KL and 62.2% grade III KL. The two groups were homogeneous at inclusion except in terms of analgesic consumption (PRP-HA vs. HA, 30% vs. 45%, p=0.042) and KL III radiographic stage (70% vs. 53%, p=0.04). The symptomatic improvement (WOMAC pain, function and WOMAC Total) was significant in both groups at M1, M3 and M6. The difference in WOMAC pain on walking at M6 was significant for the non-inferiority test (-6.34 [-12.51; -0.18], p=0.044) and for the superiority

Table 1. ***Comparative analysis of clinical and laboratory parameters in patients of different knee OA Grades and volunteers***

Parameter	Volunteer group	Knee OA groups			Significan-cy, p-value
		K-L Grade 0	K-L Grade I	K-L Grade II	
0	1	2	3	4	5
Gender	M-18 (60%) F-12 (40%)	M-13 (43,3%) F- 17 (56,7%)	M-10 (33,3%) F -20 (66,7%)	M-10 (33,3%) F -20 (66,7%)	1-3: 0,038 1-4: 0,038
Mean age, years	29,5 [25; 34]	26 [20; 32]	39 [36; 44,5]	45 [43,5; 48]	1-4: 0,049 2-4: 0,038
COMP, ng/ml	527,3 [355,1;576,5]	495,7 [421,9;737,2]	737,5 [660,2; 1033]	1683,5 [1288,4; 2260,1]	1-3: 0,044 1-4: 0,002 2-4: 0,011 3-4: 0,058
P1NP, ng/ml	58 [51,3; 64,3]	98,2 [72,4; 126,1]	101,3 [85,0; 123,4]	117,1 [105,1; 142,7]	1-2: 0,042 1-3: 0,039 1-4: 0,024
Beta-Cross Laps, ng/ml	0,545 [0,466;0,645]	0,697 [0,656; 0,861]	0,939 [0,823; 1,497]	0,793 [0,697; 1,032]	1-3: 0,032 1-4: 0,044 2-4: 0,092
IL-1β, pg/ml	3,7 [2,5; 6,0]	7,3 [5,0; 16,3]	19,1 [15,4; 29,5]	10,4 [8,6; 20,2]	1-3: 0,012 1-4: 0,028

test (-6.34 [-12.45; -0.22], p=0.042) in favor of PRP-HA. At M6, there was a non-significant difference in terms of OMERACT-OARSI responders in favor of the PRP-HA combination (58% vs. 48%, p=0.261) but significant in terms of MCII responders (78.8% vs. 61.3%, p=0.036) and PASS responders (50.6% vs. 33.3%, p=0.035).PASS response was associated in univariate analysis with pain and total WOMAC at inclusion (p<0.001) as well as with allocated treatment (p=0.03). In multivariate analysis, only allocated treatment was associated with a good response at M6 for both PASS (PRP+HA, OR=2.05 [1.02-3.92]; p=0.05) and MCII (PRP+HA, OR=2.21 [1.09-4.44]; p=0.02). There was no difference in patient satisfaction at M1, M3 and M6, nor in the occurrence of adverse events.

Conclusion: In this non-inferiority RCT in symptomatic knee osteoarthritis, the combination of PRP-non-crosslinked HA in mono-injection was at least equivalent to Hylan G-F 20 for symptomatic benefit (WOMAC) at 6 months, with a good safety profile. The proportion of patients achieving PASS and MCII of WOMAC pain was higher in the PRP-HA group.

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POS1116 DIETARY INFLAMMATORY INDEX AND KNEE STRUCTURES ON MRI AND PAIN: A PROSPECTIVE COHORT STUDY

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Background: While some individual dietary nutrients/components have been shown to be associated with knee osteoarthritis (OA) progression, the associations of the dietary inflammatory index (DII), which reflects the overall inflammatory potential of a diet, with MRI-detected structural changes and pain have not been investigated.

Objectives: This longitudinal study aimed to determine whether DII scores are associated with knee structural changes and pain over a 10.7-year follow-up in community-dwelling older adults.

Methods: This study utilised the data from a prospective population-based cohort study (mean age 63 years, 51% women) in which 1,099, 875, 768 and 563 participants completed assessments at baseline, 2.6, 5.1 and 10.7 years, respectively. T1-weighted or T2-weighted MRI of the right knee was performed to measure cartilage volume (CV) and bone marrow lesions (BMLs) at baseline and 10.7 years. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain questionnaire was used to measure knee pain at all assessments. Baseline energy-adjusted DII (E-DII) scores were calculated using a validated Food Frequency Questionnaire. X-ray was performed to assess radiographic knee osteoarthritis (ROA). Linear, log-binomial regression and linear mixed-effects modelling with adjustments for covariates were used to examine the associations of E-DII with CV loss, BML size increase and knee pain, respectively. Pain trajectories (i.e., 'Minimal Pain', 'Mild Pain', and 'Moderate Pain') were previously identified in this cohort using group-based trajectory modelling [1]. Multi-nominal logistic regression was used to examine the association between E-DII and pain trajectory groups.

Results: The mean E-DII at baseline was -0.48±1.39. In multivariable analyses, E-DII score was not associated with tibial CV loss and BML size increase [CV loss: β=0.03% per annum, 95%CI -0.01–0.06; BML size increase: relative risk (RR)=0.94, 95%CI 0.84–1.05;]. Higher E-DII was associated with greater pain score over 10.7 years (β=0.21, 95%CI 0.004-0.43) and an increased risk of belonging to 'Moderate pain' as compared to 'Minimal Pain' trajectory group [relative risk ratio (RRR): 1.19, 95%CI 1.02-1.39] after adjustment for age, body mass index, physical activity, education level, employment, emotional problems, comorbidities, and ROA.

Conclusion: Higher DII was associated with greater pain score and higher risk of more severe pain trajectory, but not structural changes, suggesting discordance between effects of diet on structural damage and pain, and that targeting pro-inflammatory diets may be beneficial to reduce pain.

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POS1117 SAFETY AND EFFICACY OF ADIPOSE-DERIVED MESENCHYMAL STEM CELLS FOR OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Osteoarthritis (OA) is a debilitating joint disorder affecting articular cartilages and subchondral bones, prompting synovial membrane irritation and inflammation (1). Nowadays, knee OA can be treated either by surgical or non-surgical approaches, while the Osteoarthritis Research Society International (OARSI) suggested pharmacological medications joined with other functional approaches such as exercise, joint inflammation instructions, and weight reduction (2), yet most of them exhibit modest safety and efficacy (3). Mesenchymal stem cells (MSCs) have been well-known in regenerative medicine for their wide differentiation capacity. Moreover, MSCs can be derived from various sources (4); however, Adipose-derived mesenchymal stem cells (ADMSCs) are easiest to assemble for clinical use with higher isolation yields (4).

Objectives: This study investigated the potential and regenerative capacity of adipose-derived mesenchymal stem cells (ADMSCs) for osteoarthritis (OA).

Methods: We created a search strategy and applied it to six databases. After screening the records for eligibility, we identified and evaluated the risk of bias in both the randomized and non-randomized research studies. Then, data were extracted and implemented into single-arm and double-arm analyses

Results: 16 studies with 469 patients were included. We found a significant improvement in the quality of life (QOL) among the three doses subgroups (high, medium, and low doses) which was estimated by the SF-36 scores after a year of follow up (low dose: Mean (M) -23.991; p = 0.000; medium dose: M -15.96; p = 0.000; high dose: M -19.306, p = 0.000). Furthermore, we noticed a significant decrease in pain as estimated by the numeric pain rating scale (NPRS) after three months of follow-up with no significant difference between the low and medium doses (low dose: M -3.119; p = 0.002; medium dose; M -2.17; p = 0.000). Our double-arm analyses illustrated significant pain reduction in the ADMSCs group over the control after 12 months as estimated by WOMAC pain subscore (Mean difference (MD) -1.85, p =0.03); moreover, The knee functions and activity levels improved significantly among the low dose group as measured by the WOMAC physical function and stiffness subscales after six months (M -23.797; p = 0.001; M -10.249; p = 0.009, respectively) and the KOOS scores after 12 months ($p \leq 0.007$ for all KOOS subscales). No significant adverse events were observed in the ADMSCs injections group (Event rate (ER) p = 0.001).

Conclusion: Although ADMSCs were associated with significant reductions in pain scores, improvements in QOL score and knee functions, and achieving disease modification in patients with OA, they did not significantly differ from the control. Therefore, implementing ADMSCs in routine clinical practice needs more studies with large sample sizes, longer follow-up periods.

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POS1118

METFORMIN AS A POTENTIAL DISEASE-MODIFYING DRUG IN OSTEOARTHRITIS: A SYSTEMATIC REVIEW OF PRE-CLINICAL AND HUMAN STUDIES

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Background: Osteoarthritis causes significant pain and disability with no approved disease-modifying drugs. There is evidence emerging from pre-clinical and human studies suggesting metformin may have disease-modifying properties in osteoarthritis[1-5]. Given its pleiotropic effects and safety profile, metformin has the potential to be a novel therapy for osteoarthritis.

Objectives: We systematically reviewed the evidence from both pre-clinical and human studies for the potential disease-modifying effect of metformin in osteoarthritis.

Methods: Ovid Medline, Embase and CINAHL were searched between inception and June 2021 using MeSH terms and key words to identify studies examining the association between metformin use and outcome measures related to osteoarthritis. Two reviewers performed the risk of bias assessment and 3 reviewers extracted data independently. Qualitative evidence synthesis was performed. This systematic review is registered on PROSPERO (CRD42021261052 and CRD42021261060).

Results: Fifteen (10 pre-clinical and 5 human) studies were included. Most studies (10 pre-clinical and 3 human) assessed the effect of metformin using knee osteoarthritis models. In pre-clinical studies, metformin was assessed for the effect on structural outcomes (n=10); immunomodulation (n=5); pain (n=4); and molecular pathways of its effect in osteoarthritis (n=7). For human studies, metformin was evaluated for the effect on structural progression (n=3); pain (n=1); and immunomodulation (n=1). Overall, pre-clinical studies consistently showed metformin having a chondroprotective, immunomodulatory and analgesic effect in osteoarthritis, predominantly mediated by adenosine monophosphate-activated protein kinase activation. Evidence from human studies, although limited, was consistent with findings in pre-clinical studies.

Conclusion: We found consistent evidence across pre-clinical and human studies to support a favourable effect of metformin on chondroprotection, immunomodulation and pain reduction in knee osteoarthritis. Further high-quality clinical trials are needed to confirm these findings as metformin could be a novel therapeutic drug for the treatment of osteoarthritis.

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POS1119

EFFICACY OF CORTICOSTEROIDS FOR HAND OSTEOARTHRITIS - A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Hand osteoarthritis (OA) is a prevalent joint condition, causing disabling pain, reduced mobility, impaired daily functioning and quality of life [(1-2)]. Corticosteroids are anti-inflammatory medications frequently used in musculoskeletal diseases. There is some evidence that corticosteroids may have a beneficial effect in hand osteoarthritis [(3-4)].

Objectives: To examine the efficacy of corticosteroids on symptoms and structural outcomes in hand osteoarthritis.

Methods: Ovid MEDLINE, Embase and Cochrane Central Register of Controlled Trials were searched from inception to October 2021 for randomized controlled trials investigating the efficacy of corticosteroids in hand osteoarthritis. Two authors independently screened records, extracted data, and assessed risk of bias using the RoB 2 tool. Standardized mean difference (SMD) or mean difference was calculated, and random-effects meta-analyses were performed.

Results: Of 13 included trials, three examined oral and ten examined intra-articular injection of corticosteroids on clinical outcomes. In meta-analysis, oral corticosteroids reduced pain (SMD=-0.53, 95%CI -0.79 to -0.28) and improved function (SMD=-0.37, 95%CI -0.63 to -0.12) at 4-6 weeks, and intra-articular corticosteroid injection improved function (SMD=-0.48, 95%CI -0.90 to -0.06) at 4-6 weeks. Corticosteroids had no significant effects on pain and function over 3 months and 6-12 months. Two trials evaluated joint structure at 4-6 weeks: one study showed oral corticosteroids reduced synovial thickening, neither showed an effect on synovitis.

Conclusion: There was low-certainty evidence for a medium effect of oral corticosteroids on pain relief and small-to-medium effect on functional improvement at 4-6 weeks. Intra-articular corticosteroids showed low-certainty evidence for a medium effect on functional improvement at 4-6 weeks. Corticosteroids had no significant effect on any outcomes over longer term. No trials examined the effect of corticosteroids on disease progression. The role of corticosteroids in hand osteoarthritis is limited.

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POS1120

ASSOCIATION OF ADIPOKINES WITH SEVERITY OF KNEE OSTEOARTHRITIS ASSESSED CLINICALLY AND ON MAGNETIC RESONANCE IMAGING

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Background: Adipokines secreted by adipose tissue create a low grade systemic inflammatory state that could contribute to the pathogenesis of knee OA (KOA). Previous studies of association between adipokines and radiographic KOA represented late-stage disease shown as bony changes. Magnetic Resonance Imaging (MRI) has the advantage of showing early changes of KOA in all joint structures.

Objectives: We aimed to evaluate the association between the adipokines: Leptin, Adiponectin, Resistin, and hs-CRP with clinical, radiographical and MRI assessment of KOA severity.

Methods: We performed a cross-sectional study in participants with early KOA. Demographics, clinical (WOMAC), and MRI (BLOKS scoring) KOA severity were assessed. Serum leptin, adipokines, resistin and hs-CRP were measured. Association of adipokines with clinical and MRI severity outcomes were evaluated using regression models with adjustment with age, sex, and body mass index (BMI).

Results: 139 participants with early KOA (82% women, mean ± SD age: 55.5 ± 7.8 years) were included. Participants had moderate KOA symptoms, mean WOMAC pain and function were 31.1 ± 18.4, and 32.0 ± 19.9 respectively. Mean BMI was 26.0 ± 5.9 kg/m^2. After adjustment with age, sex and BMI, Leptin (p=0.001) and hs-CRP (p=0.03) were positively associated, while adiponectin (p=0.02) and resistin (p=0.03) were negatively associated with osteophyte size

(Table 1). In addition, leptin was statistically significantly associated with cartilage loss, synovitis, and effusion, while hs-CRP was associated with meniscus extrusion. As for WOMAC assessed severity, only adiponectin was statistical significantly associated with WOMAC function.

Table 1. Association of adipokines with MRI features and clinical symptoms, adjusted with age, sex and BMI

KOA severity	β (95% confidence intervals)			
	leptin	Adiponectin	Resistin	hs-CRP
OST Size	**1.11 (0.5, 1.7)****	**-1.86 (-3.53, -0.18)***	**-2.12 (-3.95, -0.30)***	**0.17 (0.02, 0.31)***
% Cart Loss	**0.37 (0.04, 0.71)***	-0.45 (-1.32, 0.42)	-0.72 (-1.67, 0.23)	0.02 (-0.06, 0.10)
BML Size	0.24 (-0.02,0.50)	-0.03 (-0.70,0.65)	-0.15 (-0.92,0.56)	0.02 (-0.04, 0.08)
Synovitis	**0.24 (0.08, 0.40)****	-0.21 (-0.63, 0.22)	-0.33 (-0.79, 0.13)	0.03 (-0.01, 0.07)
Effusion	**0.21 (0.07, 0.35)****	-0.25 (-0.62, 0.12)	-0.09 (-0.49, 0.32)	0.02 (-0.02, 0.05)
Meniscus Extrusion	0.09 (-0.06, 0.24)	0.01 (-0.39, 0.40)	-0.08 (-0.51, 0.35)	**0.04 (0.00, 0.07)***
WOMAC pain	1.72 (-1.45, 4.89)	7.07 (-0.98, 15.1)	-2.61 (-11.4, 6.14)	0.04 (-0.68, 0.76)
WOMAC function	0.01 (-3.34,3.35)	**13.2 (5.0, 21.5)****	-0.07 (-9.26, 9.12)	-0.22 (-0.97, 0.54)

**p<0.05, **p<0.01, Bold: statistically significant.*

Conclusion: Adipokines, particularly leptin was associated with severity of various structural defects of the knee joint beyond age, sex and BMI in early KOA.
MRI: Magnetic Resonance Imaging; %: percentage; BML: Bone Marrow Lesion; Cart: Cartilage; OST: Osteophyte; KL: Kellgren and Lawrence grading; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.
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POS1121 HAND OSTEOARTHRITIS IS ASSOCIATED WITH LIMITATIONS IN PAID AN UNPAID WORK PARTICIPATION AND RELATED SOCIETAL COSTS: THE HOSTAS COHORT

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Background: Rheumatic musculoskeletal diseases (RMDs) can cause impairment in paid and unpaid work which can contribute to societal burden and costs. However, data on this topic concerning hand osteoarthritis (OA) is scarce, while this is crucial for assessing the societal impact of this disease.
Objectives: To investigate the association of hand OA with paid and unpaid work limitations, productivity loss and costs of productivity loss.
Methods: We used data of the Dutch Hand OSTeoArthritis in Secondary care (HOSTAS) cohort, a primary hand OA cohort from a general rheumatology outpatient clinic. The treating rheumatologist defined hand OA presence. We assessed patient and OA characteristics using validated questionnaires and tests. We investigated work impairment due to hand OA with the Health and Labour Questionnaire (HLQ) which assesses the last two weeks on hand-OA related limitations, hours of sick leave and unproductiveness during paid work, and limitations and hours of the necessity of being replaced by others for unpaid work tasks. We estimated societal costs of paid work by multiplying unproductive and sick leave hours due to hand OA by the average Dutch hourly societal costs of paid work for persons of the same age category and sex. We estimated societal costs of unpaid work by multiplying the hours of unpaid work replaced by others by the Dutch gross average hourly salary of a household help (€12.50).
Results: HLQ data was available for 382 patients (mean age 61 years, 86% women, 26% having a university degree, 41% having any comorbidity). Of these persons, 181 (47%) had paid work, 16 (4%) had full work disability due to hand OA and 117 (30%) were retired. Thirteen employed persons (7%) reported sick leave due to hand OA in the last two weeks, for whom a median of 42 working hours (interquartile range (IQR) 24 to 54) was lost. Unproductive paid work hours were present for 28 (15%) patients, with a median of 4 hours in the last two weeks (IQR 2 to 6). Hinder at work in the last two weeks was reported by 120 out of 181 working patients (66%), for whom median hinder score (score range 6-24) was 7 (IQR 6 to 8). Work production loss in the last two weeks due to hand OA (the sum of sick leave hours and unproductive hours) was present for 36 patients (19%). Patients with paid work productivity loss (n = 35, 19%) did not differ statically significantly in patient and disease characteristics from those without productivity loss (n = 146, 19%). Unpaid work replacement in the last two weeks was reported by 171 patients (45%), with a median of three hours replaced (IQR 2 to 7). Any unpaid work hinder was reported by 297 (78%). Median unpaid work hinder score (score range: 4-16) was 8 (IQR 7 to 10) . Patients with unpaid work replacement by others due to hand OA (n=171, 45%) were statically significantly more often female and had a higher BMI than with those without any replacement (n=210, 55%). We estimated total societal costs of hand OA related to paid work production loss at €61 (95% confidence interval (CI) 27 to 96) per two weeks, and societal costs for unpaid work at €33 (CI 27 to 40). Total estimated work-related societal costs per patient with hand OA were €94 (CI 59 to 130), translating to €2452 (CI 1528 to 3377) per year.
Conclusion: Hand OA is associated with impairment in paid and unpaid work, which translates into substantial societal costs. This highlights the social and economic importance of adequate hand OA treatment. It also highlights the importance of investigating work impairment experienced by hand OA patients visiting the outpatient clinic, for potentially more tailored treatment.
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POS1122 ULTRASOUND GUIDED INJECTIONS OF HYADD4 FOR KNEE OSTEOARTHRITIS IMPROVES PAIN AND FUNCTIONAL OUTCOMES AT 3 AND 6 MONTHS WITHOUT CHANGES IN SYNOVIAL FLUID VOLUMES.

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Background: Prior studies have demonstrated improved accuracy and efficacy when Intra-articular (IA) therapeutics are injected using ultrasound (US) guidance. There is also growing evidence that many patients with knee osteoarthritis (OA) exhibit a pro-inflammatory catabolic synovial fluid (SF) profile. However, it is not known if temporary clinical improvement in pain and function after IA Hyaluronic acid (HA) injections is associated with changes in SF volumes.
Objectives: The purpose of this study was to determine if IA HA injections delivered using US directed needle visualization with an external pneumatic compression device would result in improved clinical outcomes for knee OA at 3 and 6 months, and if this was associated with a reduction in the amount of knee synovial fluid (SF) measured on US.
Methods: 49 eligible subjects with symptomatic Knee OA, BMI < 40 and KL radiographic rating of II or III OA were consented for this open label prospective IRB approved Investigator Initiated SF OA biomarker study (HS 3179, NCT 04093232). All standing radiographs were reviewed by a fellowship-trained MSK radiologist. 36 subjects had adequate aspirated SF volumes of > 500 mcl for biomarker analysis and therefore were eligible to receive two IA injections of HYADD4, 24 mg/3ml (Fidia Farmaceutici S.p.A. Italy) 7 days apart by a MSK US certified Rheumatologist. An external pneumatic compression device and US visualized needle insertion ensured injections were delivered into the intra-synovial space. Despite COVID-19 restrictions, 34 patients (17 women and 17 men) between 35 and 78 years of age returned for 3 month evaluations and 30 had evaluations at 6 months. The following clinical variables were measured: Western Ontario and McMaster Universities Index (WOMAC) total scores, Visual Analog Pain Scale (VAS, 0-10), PCS scores on the SF-36 health survey questionnaires (physical function/bodily pain and general health), 6-minute walking distance in meters (6 MWD), and measured SF depth before and after an external pneumatic compression device was inflated to 100 mmHg to facilitate aspiration by increasing available SF volumes under positive presure. The SF depth was measured on the recorded US image (GE logiq e) as the largest anechoic region selected for aspiration on either the lateral (n= 30) or medial (n=4) compartment. SF and simultaneous peripheral blood samples were centrifuged and cryopreserved at -80 ^{o} C within 45 minutes of aspiration for future analysis. Statistical differences between baseline values compared to those levels at 3 and 6 months were determined using a paired ANOVA test with $p < 0.05$ significance.
Results: Improvements over baseline values were observed at 3 and 6 months respectively, after IA HA injections in WOMAC (40%, 40%), VAS (45%, 51%) and PCS (15%, 18%) all $p < 0.0001$. The 6 WWD improved by 7 % at 3 months ($p < 0.007$) but was not statistically improved at 6 months. US measured SF depth at baseline was 3.2 ± 2.2 mm before inflation and 6.4 + 3.7 mm after inflation of the

pneumatic external compressioin device but statistical differences in SF depth were not observed at 3 and 6 months.

Conclusion: Despite improvements in WOMAC, VAS scores, and PCS scores on the SF 36 at 3 and 6 months after US guided knee injections with an HA product, a statistically significant reduction in the amount of US measured SF was not observed. The 6 MWD improved at 3 months but was not statistically different from the baseline distance by 6 months. IA injections using US needle visualization confirmed that the product was delivered into the synovial space with 100 % accuracy which might have resulted in improved efficacy results in this study compared to prior IA HA studies injected without US or using different HA products. In the future, we hope SF biomarkers may identify which individual OA patients will likely achieve the greatest benefit with IA HA injections and to determine if this is associated with a reduction in catabolic pro-inflammatory proteins.

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POS1123 WEAK OPIOIDS AND TREATMENTS WITH ANTICHOLINERGIC PROPERTIES INCREASE BUT ANTIHYPERTENSIVE TREATMENTS DECREASE THE NUMBER OF FALLS IN PATIENTS FOLLOWED FOR KNEE AND/OR HIP OA: ANALYSES OF THE KHOALA COHORT

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Background: The risk of falling is increased in people with knee osteoarthritis (OA) but the risk factors may not be the same as in the general population. The level of evidence for the associations between the different risk factors and falls in OA is moderate, the number of studies for each factor being small.

Objectives: The main objective of the study was to identify factors associated with the number of falls in patients with symptomatic knee and/or hip OA during five years of follow-up, in particular the drug-related risk factors that are modifiable factors.

Methods: This study was based on data from the KHOALA (Knee and Hip OsteoArthritis long term Assessment) cohort, consisting of 878 patients aged 40 to 75 years, with symptomatic knee and/or hip OA, recruited between 2007 and 2009 in the general population. Patients were followed up annually for 10 years. This study is a longitudinal analysis using data from years 5 to 10, with falls data collected from year 5.

The primary endpoint was the number of falls reported by the patient. The potential risk factors studied were: medications grouped into ATC classes, a score of treatments with anticholinergic properties*, demographic (age, sex, education, socio-professional category), clinical (comorbidities), perceived health (WOMAC-pain, WOMAC-function, quality of life by the SF-36), and radiological (Kellgren stage) data. Statistical analyses used generalized linear mixed models.

Results: 661 patients were included in the analyses. The majority of the sample was female (69%); the mean age was 62 years at year 5, and 153 patients (23.15%) had reported one or more falls in the previous 12 months.

In multivariate analyses, and thus independent of pain and functional abilities, a significantly higher number of falls was found in women (OR [CI95%] 1.70 [1.12-2.57]), patients living alone (0.65, [0.47-0.95], P=0.02), retired people (1.92, [1.094-3.37]), patients with more comorbidities (OR 1.10, [.01-1.21]), using fewer antihypertensive drugs (OR 0.61, [.42-0.90]), more weak opioids (OR 1.44, [.05-1.96]) and more treatments with anticholinergic properties (OR 1.31, [.00-1.73])

Conclusion: Weak opioids and the score of treatments with anticholinergic properties increased, but antihypertensive treatments decreased the number of falls in patients followed for knee and/or hip OA. The risk factors found in this study are identical to those of the general population, whose pain and functional capacities are less impaired.

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POS1124 EVALUATION OF COMORBIDITY PATTERNS AND IDENTIFICATION OF SUB-GROUPS IN PATIENTS DIAGNOSED WITH HIP OSTEOARTHRITIS IN 94,720 PATIENTS FROM SPAIN

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Background: Osteoarthritis (OA) patients are more likely to have other comorbidities (Swain, Sarmanova et al. 2020). Improving the understanding of comorbidity profiles of OA patients may lead to improvement in their clinical care.

Objectives: To identify sub-groups in patients diagnosed with hip OA using patterns of comorbidity.

Methods: Routinely-collected data of individuals ≥18 years with an incident diagnosis of hip OA (baseline/time of diagnosis), with at least 1 year of follow-up in SIDIAP (Information System for Research in Primary Care, a primary case database from Spain) were collected from January 1st 2006 to June 31st 2020. Those with soft-tissue disorders or other bone/cartilage diseases at the same joint in the year prior/after baseline were excluded. Comorbidities associated with OA in the literature and

present in ≥1% of the study population were included. Clusters of comorbidities were identified at baseline using latent class analysis (LCA), a soft clustering method that classifies individuals according to the distribution of their measured items. The number of clusters or sub-groups within the study population was decided by comparing goodness of fit parameters (CAIC, BIC, ABIC) and log-likelihood changes of models from 2 to 8 clusters. The selected model was externally evaluated by a survival analysis assessing 10 years mortality within each cluster, where the weight of the posterior probability was used as a probability of sampling weight.

Results: We identified 94,720 individuals with an incident diagnosis of hip OA, 56.3% women and 43.7% men, with a mean age (SD) of 67.2 (13.1) years. We selected the LCA model with 5 clusters that could be described as: healthier (lower prevalence of all comorbidities than average in the cohort), multimorbidity (higher prevalence of all comorbidities, multiple comorbidities), back/neck pain plus mental health (B/N-mental), cardiovascular disease (CVD), and metabolic syndrome (MetS) (Figure 1). Cox regression (HR [95CI%]) showed higher mortality risk for multimorbidity (3.76 [3.70-3.83]), CVD (1.56 [1.53-1.59]) and MetS (4.56 [4.35-4.78]), compared to healthy. No difference was observed for B/N-mental cluster.

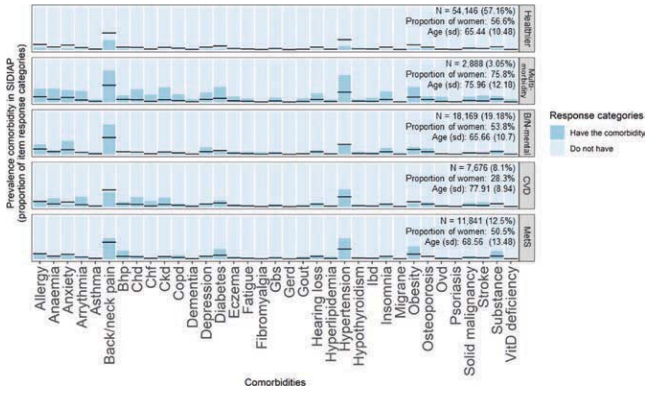

Figure 1. Distribution of comorbidities within each cluster using latent class analysis. Clusters were described as Healthier, Multimorbidity, B/N-mental, CVD and MetS. Black horizontal lines represent the prevalence of the comorbidity before the clusterization. Abbreviations: Healthier, lower prevalence of all comorbidities; Multimorbidity, higher prevalence of all comorbidities; B/N-mental, back/neck pain plus mental health disorders; CVD, cardiovascular disease; Met, metabolic syndrome; Bhp, benign prostate hypertrophy; Chd, chronic heart disease; Chf, chronic heart failure; Ckd, chronic kidney disease; Copd, chronic obstructive pulmonary disease; Gbs, gall bladder stone; Gerd, gastroesophageal reflux disease; Ibd, inflammatory bowel disease; Ovd, other vessel diseases; Substance, substance abuse.

Conclusion: Clustering of co-morbidities in hip OA patients at the time of diagnosis has the potential to detect sub-groups of hip OA patients who might require additional care.

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Disclosure of Interests: None declared
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POS1125

EFFICACY OF TUMOR NECROSIS FACTOR INHIBITORS IN HAND OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Hand osteoarthritis (OA) is a leading cause of functional impairment associated with chronic pain and stiffness in hand joints[(1)]. It is well documented that inflammation plays an important role in the pathogenesis of hand [(2)]. Therefore, therapies targeting inflammation may offer a novel approach for the management of hand OA. Tumor necrosis factor (TNF) inhibitors are a class of anti-inflammatory drugs that have been used in musculoskeletal conditions [(3-5)].

Objectives: To examine the efficacy of tumor necrosis factor (TNF) inhibitors on symptoms and structural outcomes in hand osteoarthritis.

Methods: The study was carried out according to PRISMA protocol. Ovid Medline, Embase and Cochrane Central Registry of Controlled Trials were searched from inception to October 2021 for randomized controlled trials examining the efficacy of TNF inhibitors in hand osteoarthritis. We performed quantitative extraction of data and risk of bias assessment for the eligible studies. Where data were available, mean difference was calculated and random effect meta-analysis was performed. Quality of the evidence was assessed using GRADE criteria.

Results: Four studies were identified involving 276 participants in total. There studies had low risk of bias and one study had some concerns. Meta-analysis showed that TNF inhibitors had no effect on pain at 4-6 weeks and 24-26 weeks and no effect on grip strength at 1 year (Table 1). There was no effect of TNF inhibitors on most of the clinical and structural outcomes. There was conflicting evidence for the effect of TNF inhibitors on radiographic progression, bone marrow lesion or erosive evolution at 12 months. Quality of evidence was low for the effect of TNF inhibitor on pain and moderate for grip strength.

Conclusion: Our systematic review found no effect of TNF inhibitors on clinical outcomes and the effect of TNF inhibitors on structural outcome over longer term is inconclusive. More clinical trials are needed to clarify the role of TNF inhibitors in the management of hand OA.

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Table 1. Effect of TNF inhibitor versus control on pain and grip strength

Study	scale	range	Mean (SD)	Mean (SD), extracted	Mean Difference (95% CI)	Number	Number	Meta-analysis result
			TNF[1] inhibitor	control		TNF[1] inhibitor	control	
Short term/pain								
Aitkin 2018	VAS[2]	0-100	-6.1 (22.7)	-4.1 (23)	-2.5 (-14 to 9)	40	41	-0.93 (-7.41, 5.55)
Chevalier 2014	VAS[2]	0-100	-19.3 (4.20	-16.8 (4.3)	-0.2 (-8.1 to 7.6)	38	35	
Long term/pain								
Kloppenburg 2018	VAS[2]	0-100	39.2 (24.7)	46.5 (23.4)	-5.7 (-15.9 to 4.5)	38	41	-3.82 (-11.46 to 3.83)
Chevalier 2014	VAS[2]	0-100			-1.4 (-13 to 10.1)	36	33	
Long term/grip strength								
Kloppenburg 2018	Dynamometer				0 (-2.2, 2.1)		41	-0.35 (-1.08, 0.37)
Verbruggen 2012	Dynamometer		0.8 (1.2)	1.2 (1.8)		30	30	

[1]Tumor necrosis Factor, [2]Visual Analogue Scale

POS1126

CLINICAL EFFICACY AND SAFETY OF MONOCLONAL ANTIBODY AGAINST NERVE GROWTH FACTOR AND FIBROBLAST GROWTH FACTOR-18 THERAPY OF OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is the most common chronic progressive musculoskeletal system disease affecting more than 500 million people globally, which represents the formidable public health challenge. Currently osteoarthritis treatment includes acetaminophen, NSAIDs and/or opioids, intra-articular corticosteroid injections. Some guidelines also recommended chondroitin and glucosamine sulfate, suggested that they may be effective and reduce functional impairment. However, despite of the huge amount of data on the problem of OA, there is still no effective treatment that slows down the progression of the disease. Recently appeared monoclonal antibodies against nerve growth factor (NGF) as well as fibroblast growth factor (FGF)-18 may be the promising tool for clinical improvement of OA

Objectives: To evaluate the safety and efficacy of anti-NGF and FGF-18 on patients with osteoarthritis by a systematic review.

Methods: In the current study the search process was conducted in PubMed using the following strategy: "FGF-18" or "anti-NGF" and "OA", "monoclonal antibody" + "osteoarthritis". All articles published in the format of Case Reports, Clinical Study, Clinical Trial Protocol, Clinical Trial, Multicenter Study were reviewed. Clinical outcomes were assessed using clinical scores, included the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Pain and Physical Function score, Patient's Global Assessment of OA (PGA-OA), adverse events (AEs); cartilage repair and total femorotibial joint cartilage thickness were assessed using magnetic resonance imaging.

Results: Based on our search 23 publication were included in the study after omitting repetitions. Among 23 studies, 16 used anti-NGF monoclonal antibodies (Tanezumab, Fasinumab, Fulranumab), and **7** used recombinant human FGF-18 (Sprifermin). The total of 6679 patients were analysed in these articles. In the pooled analysis NGF inhibitors demonstrated statistically significant improvements compared with placebo in WOMAC Pain and Physical Function score (all studies revealed significantly better clinical outcomes in the anti-NGF group). After treatment with FGF-18 (Sprifermin) there was also improvement in WOMAC scores though not statistically significant. However, FGF-18 therapy was associated with the reductions in loss of total and lateral femorotibial cartilage thickness. Moreover, it does not only significantly reduce cartilage loss but also increase cartilage thickness. In terms of cartilage repair, 5 of 7 studies reported improvement in total femorotibial joint cartilage thickness. The AEs of FGF-18 or anti-NGF therapies were not serious, however they may affect the compliance and satisfaction of patients and clinicians. The proportion of patients with adverse events in anti-NGF treatment group was higher than that in FGF-18. The following conditions were reported in anti-NGF: abnormal peripheral sensation such as hypoesthesia (7.43%), paraesthesia (9.15%), hyperesthesia (0.36%), peripheral neuropathy and sensory disturbance (0.35%); arthralgia (15%), back pain (15.06%), pain in extremity (10%), headache (9.11%), upper respiratory tract infection (10.65%), diarrhoea (11.95%), sinusitis or nasopharyngitis (10.13%). The difference in AEs between sprifermin and placebo groups was found insignificant, most frequently reported event was arthralgia.

Conclusion: In recent years significant progress has been achieved in search for pathogenetic therapy of OA. Based on the results of current research findings, NGF inhibitors relieved pain and enhance joint function and may be considered as the most effective for functional improvement. FGF-18 decrease the cartilage loss and may improve cartilage thickness. However, further clinical longitudinal studies characterised the risk-benefit are needed to establish their safety and efficacy.

Disclosure of Interests: None declared

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POS1127

USE OF ARTIFICIAL INTELLIGENCE AND CLOUD-BASED INFRASTRUCTURE TO IMPROVE THE SPEED AND ACCURACY OF ELIGIBILITY READS IN OSTEOARTHRITIS TRIALS.

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Background: The Kellgren-Lawrence grading (KLG) system is used in clinical trials of osteoarthritis (OA) to define the structural severity of the disease as part of patient eligibility assessment. However, the use of KLG system has proven to be challenging due to considerable inter-reader variability[1], [2], which may result in recruitment of sub-optimal patient cohort or delays in patient recruitment.

Objectives: The objective of this study was to determine the impact of an AI-assisted, cloud-based data management system on the rate of adjudication and the speed of OA patient recruitment.

Methods: A total of 3855 bilateral fixed-flexion posteroanterior radiographs of the tibiofemoral joints from global multi-centre trials were included in this study. Two experienced readers performed an initial KLG assessment of both knees; the adjudication was performed by a third experienced reader. A cloud-based imaging data management system was deployed, the readers could access the data simultaneously and adjudication was automatically triggered. We quantified the adjudication rate and the distribution of disagreements in KLG scores provided by the initial readers. Furthermore, the delay in delivery time of the KLG reports to the recruiting site was recorded.

Results: 48% (1836) of the initial reads required adjudication. Approximately 70% of the disagreements affected the conventional KLG 2-3 inclusion range of OA clinical trials. Use of the cloud-based data management allowed 41% of the reports to be delivered within 24 hours, if no adjudication was required vs an average of 5 days as estimated based on the readers' prior experience. Table 1 provides details on the distribution of disagreements resulting in adjudication reads. Figure 1 shows the delivery time for KLG with and without adjudication.

Table 1. Distribution of disagreements of initial reads resulting in an adjudication read being triggered.

Disagreement triggering Adjudication	Number of Cases	Percentage
KLG 0 – 1	713	27.8%
KLG 1 – 2	820	31.9%
KLG 2 – 3	482	18.7%
KLG 3 – 4	446	17.4%
Other	110	4.3%
Total	2569	100%

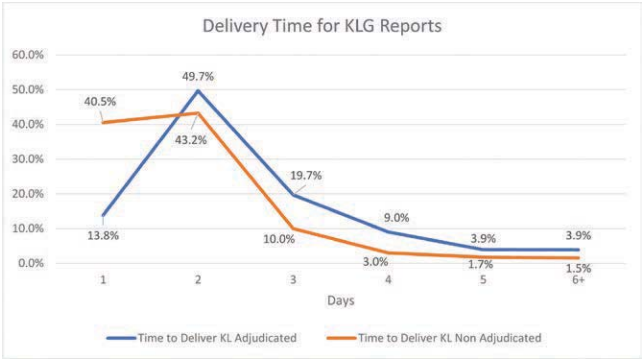

Figure 1. Time to deliver eligibility report

Nehrer *et al.* showed that assisting the readers with AI generated KLG scoring reports, the agreement rate between readers for KLG assessment increased by 21% [2]. Adding to this, 30% of the adjudications (stemming from KLG 0 –1 disagreements between readers) could be avoided when using AI generated reports.

Conclusion: We assess the rate of adjudication and speed of reporting of KLG of data from multi-centre OA clinical trials. Future work is planned to assess the effect of AI-assisted OA grading systems within our cloud-based data management system on reader agreement and recruitment speed in global clinical trials.

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POS1128

SERUM MARKERS OF GUT PERMEABILITY AND ENDOTOXEMIA IN PATIENTS WITH METABOLIC SYNDROME-ASSOCIATED KNEE OSTEOARTHRITIS: AN EXPLORATORY STUDY

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Background: Metabolic syndrome (MetS)-related osteoarthritis (OA) has been proposed as a distinct phenotype of OA (1). One of the many putative pathways linking MetS with OA is increased gut permeability resulting in endotoxemia, systemic inflammation, and cartilage damage. There is a lack of studies evaluating markers of gut permeability and endotoxemia in patients with MetS-associated OA.
Objectives: In this exploratory study we aimed to: a. compare serum markers of gut permeability and endotoxemia in patients with knee OA and concomitant MetS vs patients with knee OA b. evaluate possible associations between the studied biomarkers, knee pain, function and body mass index (BMI) in patients with MetS plus OA.
Methods: In this cross-sectional study, we evaluated consecutive patients diagnosed with knee OA according to ACR criteria and willing to participate in the study. MetS was defined in accordance with NCEP ATP III criteria. Knee pain and function were assessed using the WOMAC scale. Serum concentrations of gut permeability marker zonulin, lipopolysaccharide (LPS), and soluble LPS receptor (sCD14) were measured using commercial ELISA kits.
Results: Forty patients (19 with OA plus MetS, 21 with OA), all women, mean age 65.5 years, were included in the study. The participants in the compared groups were of similar age. Patients with MetS had significantly higher BMI, increased knee pain, impaired knee function, and elevated serum C-reactive protein levels. Serum LPS, sCD14, and zonulin concentrations were significantly higher (1.5 fold, 2 fold, and 3.5 fold, respectively) in patients with OA+MetS. In the latter group, serum zonulin, sCD14, and LPS concentrations were moderately positively correlated with BMI. There were no correlations between the studied serum biomarkers and WOMAC knee pain, only zonulin was moderately positively associated with WOMAC knee function (Figure 1)

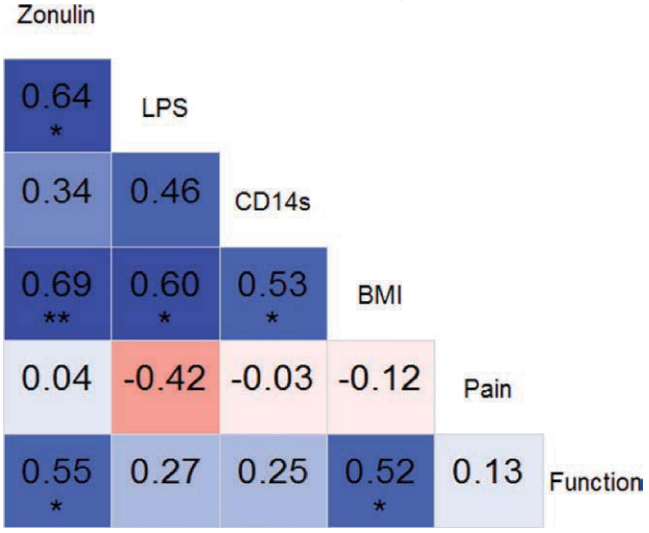

Figure 1. Spearman correlation between serum gut permeability markers, BMI, knee pain and function. * - p<0.95, ** - p<0.01

Conclusion: These findings suggest that while associated with MetS, increased gut permeability may not play a significant role in OA clinical manifestations.
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Disclosure of Interests: None declared
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POS1129

MAIN PREDICTORS OF STRUCTURAL PROGRESSION IN PATIENTS WITH METABOLIC PHENOTYPE OF OSTEOARTHRITIS

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Objectives: to determine the main predictors of structural progression in patients with metabolic phenotype of knee osteoarthritis (OA).
Methods: 82 female patients with metabolic phenotype of knee OA (diagnosis of OA according to the ACR criteria, radiologic stages varying I-III Kellgren & Lawrence) aged 40-75 were included in this prospective study. Mean age was 59.1 ± 8.5 years (42-74), BMI was 32.5 ± 3.48 kg/m^2, disease duration was 13 (7-19) years. Individual case report forms, which included history of the disease, physical assessment data, VAS knee pain, WOMAC, joint status, comorbidities and previous medications, were filled out for each patient. All patients performed plain knee radiography, ultrasound and MRI (WORMS).
Results: 13 patients (15.9%) showed structural progression at two years of follow-up. When comparing groups with (n=13, group 1) and without (n=69, group 2) structural progression, there were no differences in terms of age, age of disease onset and disease duration. However, in the progression group patients had higher bodyweight: 99 ± 12.9 vs 82.5 ± 8.1 kg (p = 0.0003), they also had higher VAS knee pain (69 (66-73) vs 54 (34-66) mm (p=0.0009), and WOMAC (359 (339-381) vs 255 (200-316) mm (p=0.003)). More patients from the progression group had hypertension (92.3% vs 79.7%) and type 2 diabetes (100% vs 4.3%). MRI showed significant intergroup differences in terms of both frequency and severity of cartilage damage. Cartilage defects (via WORMS) were more frequent in the medial tibial compartment of group 1: 50% vs 4.9%, RR=10.2, 95% CI 2.9-35.1, p=0.0004. Identical trend was found when evaluating bone marrow lesions (BMLs) in the medial (75% vs 27.9%, RR=2.7, 95% CI 1.6-4.5, p=0.003) and lateral (50% vs 16.4%, RR=3.05, 95% CI 1.4-6.8, p=0.02) tibial compartments. Synovitis was verified via MRI in 100% of group 1 patients vs 56.5% (RR=1.8, 95% CI 1.4-2.2, p=0.007).
Correlation analysis confirmed the relationship (p<0.05 for all) between metabolic phenotype structural progression and the following parameters: bodyweight (r=0.39), WOMAC pain (r=0.37), type 2 diabetes (r=0.27), synovium thickness via ultrasound (r=0.32), medial (r=0.44) and lateral (r=0.32) tibial compartment subchondral BMLs, medial tibial cartilage defects (r=0.42), presence of subchondral bone cysts in the medial tibial compartment (r=0.38) and femur (r=0.37); lateral tibial (r=0.28) compartment and femur (r=0.28) and also synovitis (r=0.32).
Discriminant analysis has shown that the most significant risk factors for structural progression of the metabolic phenotype of knee OA were high WOMAC pain, synovitis, type 2 diabetes and medial tibial compartment BMLs. Based on the selected factors and their coefficients, we have created a formula that allows to predict the risk of structural progression of metabolic OA.
Conclusion: this prospective trial has shown that the main predictors for metabolic knee OA phenotype progression are high WOMAC pain, type 2 diabetes, MRI-detected synovitis and BMLs in the medial tibial compartment. These risk factors may serve as a basis for further personalized therapeutic and preventive approaches.
Disclosure of Interests: None declared
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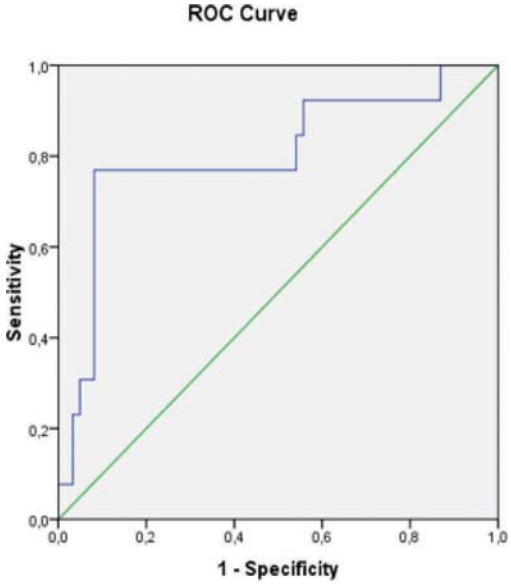
Table 1. Discriminant function coefficients to create a model of structural progression of metabolic knee osteoarthritis

Factors	Discriminant function coefficients	ROC-curve
WOMAC pain	0.00608	XXXX
Type 2 diabetes	2.11052	
BMLs in the medial tibial comparment	1.3734	
Synovitis	1.19864	
Constant	6.34279	AUC=0.802 (0.650-0.954)

Model accuracy – 89%



POS1130

A RANDOMISED CONTROLLED STUDY OF POLYACRYLAMIDE HYDROGEL VS. HYALURONIC ACID IN KNEE OSTEOARTHRITIS: RESULTS AT 12-MONTHS

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Background: Polyacrylamide hydrogel (iPAAG), manufactured by Contura International, is CE marked for the symptomatic treatment of patients with knee osteoarthritis (OA). iPAAG fulfils an unmet clinical need for an effective, long-acting, safe and minimally invasive treatment that may postpone and potentially prevent knee surgery for those with OA.

Objectives: To compare the effectiveness of single intra-articular injections of iPAAG and hyaluronic acid (HA) in participants with moderate to severe knee OA. To compare the effectiveness of iPAAG and HA in subgroups based on age, BMI or Kellgren-Lawrence (KL) grade at baseline by assessing changes from baseline in transformed WOMAC pain subscale scores.

Methods: This prospective, double-blind study (NCT04045431) randomized 239 participants to receive a single intra-articular injection of either 6 mL iPAAG (n=119) or 6 mL HA (n=120). The study was approved by the Capital Region's Committee on Health Research Ethics. All participants provided informed consent prior to study activities. Outcomes included changes in the WOMAC pain, stiffness and function subscales and Patient Global Assessment of disease impact (PGA) at 52 weeks. All statistical analyses were based on the ITT principle using a mixed model for repeated measurement with a restricted maximum likelihood-based approach. The estimated mean treatment difference based on this model was reported with 95 % CI and p-value.

Results: Demographic and baseline characteristics were similar between treatment groups with an average age at treatment of approximately 67 years (range 31 – 90 years) and slightly more females (53%) than males. There was a clinically relevant decrease in WOMAC pain subscale score from baseline to 52 weeks in both groups (Figure 1). There were also clinically relevant decreases in the WOMAC stiffness subscale and physical function subscale and PGA in both groups. Treatment differences in favor of iPAAG compared to HA, were measured for the 3 WOMAC subscales and PGA. However, none of these differences reached statistical significance.

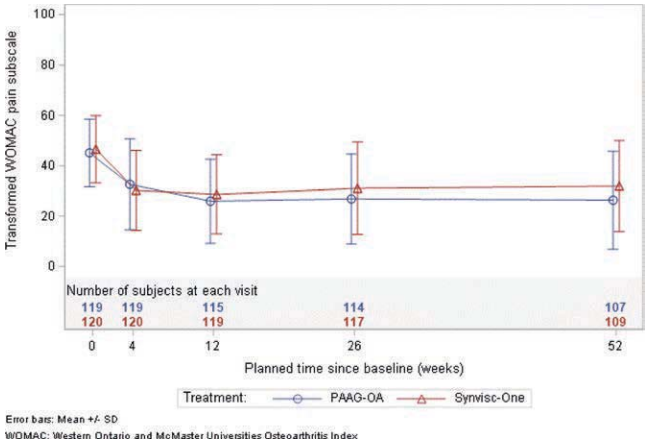

Figure 1. Mean plot of transformed WOMAC pain subscale (0-100) – ITT analysis set

The treatment difference in favor of iPAAG compared to HA for the WOMAC pain subscale score was statistically significant in the subgroup with age at baseline <70 years but did not reach statistical significance in the subgroup with age at baseline ≥70 years. The treatment difference in favor of IPAAG compared to HA for the WOMAC pain subscale score was statistically significant in the subgroup with normal BMI but did not reach statistical significance in the subgroups with overweight or obese BMI. The treatment difference in favor of IPAAG compared to HA for the WOMAC pain subscale score was statistically significant in the subgroup with KL grade 2 or 3. In the subgroup with KL grade 4, a treatment difference in favor of HA was not statistically significant.

Table 1. Change from baseline in transformed (0-100) WOMAC pain subscale at week 52

	LSMean (95% CI)	Treatment difference (95% CI)	p-value
Overall			
HA	-13.3 (-16.7; -10.0)		
iPAAG	-17.9 (-21.3; -14.6)	4.6 (-0.1; 9.4)	0.0572
Age <70 years			
HA	-14.0 (-18.3; -9.6)		0.0195
iPAAG	-21.3 (-25.5; -17.0)	7.3 (1.2; 13.4)	
Age ≥ 70 years			
HA	-12.5 (-17.6; -7.4)		0.7970
iPAAG	-13.4 (-18.7; -8.2)	1.0 (-6.3; 8.2)	
BMI normal			
HA	-13.5 (-18.1; -8.9)		0.0110
iPAAG	-17.5 (-22.2; -12.9)	10.9 (2.6; 19.1)	
BMI overweight			
HA	-14.3 (-19.5; -9.2)		0.6114
iPAAG	-16.1 (-21.0; -11.3)	1.8 (-5.3; 8.9)	
BMI obese			
HA	-14.5 (-22.7; -6.2)		0.5565
iPAAG	-17.8 (-25.6; -10.0)	3.3 (-8.0; 14.7)	
KL grade 2 or 3			
HA	-13.4 (-17.0; -9.7)		0.0332
iPAAG	-18.9 (-22.5; -15.4)	5.6 (0.5; 10.7)	
KL grade 4)			
HA	-13.1 (-21.9; -4.3)		0.6757
iPAAG	-10.3 (-20.6; 0.0)	-2.8 (-16.4; 10.8)	

Conclusion: At 52 weeks after treatment, the effectiveness of iPAAG was numerically superior to HA but not statistically significantly different.
In subgroups of participants with normal BMI, participants <70 years old or participants with KL grade 2 or 3 iPAAG performed statistically significantly better than HA at 52 weeks after treatment.

Disclosure of Interests: None declared
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POS1131

ASSOCIATION BETWEEN ANTIBIOTIC USE AND RADIOGRAPHIC PROGRESSION OF OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: Gut dysbiosis has been proposed as one risk factor for osteoarthritis (OA) (1).To date, there have been no studies assessing association between the use of antibiotics and structural progression of knee OA.

Objectives: To evaluate association between the use of antibiotics and radiographic progression of knee OA.

Methods: For the current study we used 9-year longitudinal data obtained from the Osteoarthritis Initiative (OAI) progression (n= 1390) and incidence (n = 3284) subcohorts, which are publically available at https://oai.nih.gov. For the assessment of antibiotic influence on knee OA progression we analyzed all knees having baseline JSN<3 from both subcohorts. The main outcome was knee OA progression (defined as increase in semiquantitative JSN or a new knee replacement). To acquire information about the use of antibiotics, a medication inventory method was used. We excluded participants who used antibiotics at or 30 days prior to baseline (a "new-user" design). Antibiotic users were defined as those with at least one recorded use during first four years of the study. Other participants who did not use antibiotics prior to baseline and throughout the observation period were classified as non-users. Logistic regression models were used to evaluate the relationship between the outcome and antibiotic use. Generalized estimating equations (GEE) were used to adjust for the correlation between knees.

Results: A total of 8415 of knees (7404 non-user knees and 1011 user knees) were included in the analysis. No association between the use of antibiotic and radiographic progression of knee OA was found (odds ratio 1.23, 95% confidence interval 0.59-2.56, p = 0.59). No associations were also observed in multiple stratified analyses based on different duration of antibiotic use, particular classes of antibiotics, or different baseline KL grades.

Conclusion: These findings do not support the effects of antibiotics on knee OA progression.

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POS1132

PATTERNS OF JOINT SURGERY IN THE TEN YEARS PRIOR TO PRIMARY KNEE REPLACEMENT IN ENGLAND AND SWEDEN – A POPULATION-BASED CASE-CONTROL STUDY

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Background: Primary knee replacement (KR) is an effective intervention for end-stage knee osteoarthritis (OA). However, there are no definitive recommendations for the timing at which patients should receive this surgery, potentially resulting in differences in referral patterns depending on geographical area or the clinicians' preferences.
Objectives: To investigate the prevalence of meniscus, knee ligament and knee synovial surgeries as well as knee osteotomy and hip replacement (HR) across the ten years preceding a KR in cases and controls in England and Sweden.
Methods: This was a multi-national, population-based, case-control study within England and Sweden. Cases underwent primary TKR and controls, matched using risk-set sampling by age, sex and practice/region, did not. Electronic healthcare databases were used; the Clinical Practice Research Datalink (CPRD) in England, and the Health Register of Skåne (Sweden's southernmost region) in Sweden.
ICD-10 codes and KVÅ codes in Sweden and Medcodes (SNOMED CT (UK edition) and Read codes) in England were used to identify subjects aged ≥45 years who underwent primary KR between 1st January 2015 and 31st December 2019. Eligible cases had to be registered for ≥10 years prior to the primary KR (index date), and have no record of prior KR in that period. Office of Population Censuses and Surveys (OPCS) codes in England and ICD-10 codes in Sweden were used to identify selected orthopaedic surgeries. Meniscal (e.g. excision, resection, repair) and ligament surgery (e.g. ligament reconstruction, replacement, suture) were included, as well as osteotomy (e.g. angle, rotational or displacement osteotomy of the knee or lower leg). Hip replacement (HR) (any primary HR) was also included, to evaluate the rate at which patients undergoing KR also undergo further major arthroplasty in the years preceding this – The annual prevalence of having at least one recorded surgery for each type in each of the 10 years preceding KR was estimated using Poisson regression models and expressed per 1,000 people.
Results: We identified 6,337 and 47,010 subjects who underwent a knee replacement between 2015 and 2019 in southern Sweden and England, respectively (Table 1). Overall, the prevalence of all analysed surgeries was consistently lower in the controls with minimal trends detectable throughout follow-up in both England and Sweden (Figure 1).

Table 1. demographic

	Sweden		England	
	Cases (n=6,337)	Controls (n=6,337)	Cases (n=47,010)	Controls (n=47,010)
Age, mean (SD)	69.0 (8.9)	68.9 (9.1)	69.6 (9.6)	69.6 (9.6)
Female Sex, n (%)	3,585 (56.6%)	3,585 (56.6%)	26,154 (55.6%)	26,154 (55.6%)
Surgeries, n				
Hip replacement	562	324	3,933	1,889
Meniscus	384	44	8,659	833
Ligaments	16	5	90	11
Synovial	164	15	369	30
Osteotomy	98	3	107	5

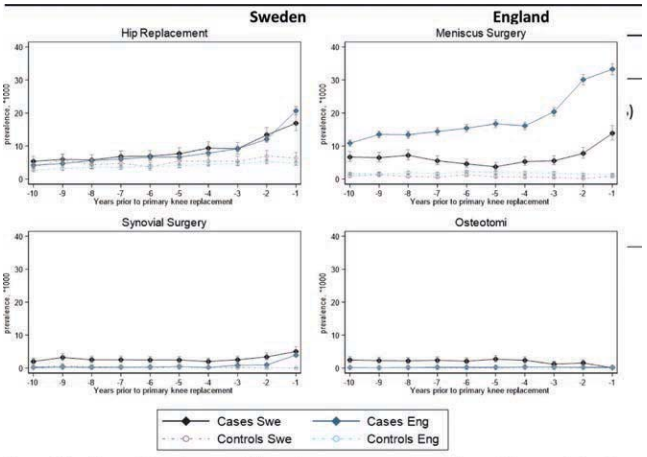

Figure 1: Prevalence of hip replacement (HR), meniscus surgery, osteotomy and synovial surgery in the 10 years leading to a joint replacement

On the other hand, an increasing trend among the cases, signifying a higher prevalence of surgeries when nearing KR, was observed for HR and meniscal surgeries in both nations. The prevalence of HR was similar in England and southern Sweden at all-time points showing an increase most noticeable in the 3 years before KR. The prevalence of meniscus surgery in England was higher than the one observed in Sweden throughout the follow-up. Prevalence in England increased most noticeably in the four years prior to KR reaching 33.2 (95%CI 31.6, 34.9) surgeries per 1,000 people in the year preceding KR. In Sweden, the prevalence of meniscus surgery remained between four and eight surgeries per 1,000 people until the last year prior to KR when the prevalence increased to 13.8 (95%CI 11.9, 16.2) surgeries per 1,000 people.
Conclusion: HR and meniscal surgeries are common procedures that a person is likely to have experienced in the ten years prior to a KR. Comparing England and southern Sweden, we noticed similar prevalence and trends for what concerns HR suggesting similar practice in the two healthcare systems. Meniscus surgeries were more frequently utilised in England. Nevertheless, in both countries, a marked increase in the prevalence of this surgery was observed in the last years prior to the KR.
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POS1133

IRISIN LEVELS IN KNEE OSTEOARTHRITIS ARE RELATED TO GENDER, OBESITY AND LOCAL INFLAMMATION

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Background: Irisin is a myokine synthesized mainly in skeletal muscle with exercise, although its secretion has also been observed in other tissues such as adipose and has been related to obesity and other metabolic alterations. Although obesity and other metabolic factors are risk factors for knee osteoarthritis and patients with this condition often do less exercise and have poor muscular state, irisin has been poorly studied.
Objectives: To measure irisin levels in synovial fluid and plasma and evaluate their relationship with clinical severity and inflammation parameters in patients with knee osteoarthritis.
Methods: Patients with symptomatic and radiographical osteoarthritis were studied. Demographic and anthropometric variables, Kellgren-Lawrence scale radiographic stage, the presence of synovial fluid and hypertrophy on ultrasound (at medial patellar line), clinical severity by Lequesne algofunctional index and physical exercise level were recorded. Levels of irisin, IL-6, TNF and hs-PCR were determined using ELISA.
Results: We included 168 women (age 69 ±1.5 y, symptoms duration 48 ±3 m) and 31 men (age 66.5 ±4 y, symptoms duration 36 ±12 m). Significantly higher levels of irisin in synovial fluid were observed in women who did not perform any physical exercise compared to those who did exercise sporadically or regularly (p.0.05), while in plasma a non-significant trend was observed. A weakly positive correlation between intraarticular levels (r= 0.17, p .0.05) and plasma levels (r= 0.16, p. 0.05) of irisin and Lequesne index in women was also evidenced. Regarding inflammatory parameters, in female patients the synovial levels of irisin presented a weak positive correlation with the synovial levels of IL-6 (r= 0.18, p< 0.05) but not in plasma; an association was also found in women between synovial levels of irisin and synovial fluid >8mm and severe synovial hypertrophy (p<0.05) in women, but not with plasma levels. All significant associations disappeared when adjusting by IMC except in the case of synovial hypertrophy. No statistically significant results were obtained in men.
Conclusion: Levels of irisin are related to gender and obesity in patients with knee osteoarthritis. However, the association with the intraarticular levels of IL-6 and the synovial hypertrophy could point to a possible local inflammatory effect at intraarticular level.
Disclosure of Interests: None declared
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POS1134

THE EFFECT OF ETORICOXIB ON PAIN AND SIGNS OF CENTRAL SENSITIZATION IN PATIENTS WITH OSTEOARTHRITIS

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Background: Central sensitization (CS) plays an important role in the development of chronic pain in osteoarthritis (OA).
Objectives: to evaluate the effect of etoricoxib on pain and signs of CS in patients with OA.
Methods: 790 patients with OA (knee or hip) were included in an open observational study. Most of them (71.6%) were female, mean age 54.5 ± 13.0 years. All patients received etoricoxib 60 mg/day for 2 weeks. The dynamics of pain was assessed on a numerical rating scale (NRS 0-10), the dynamics of the sign of CS was assessed using the Central Sensitization Inventory (CSI). CSI ≥ 40 was observed in 35.3% of patients.

Results: After 2 weeks of treatment with etoricoxib, the intensity of pain at movement, at rest and at night decreased by 58.8±24.1%, 69.7±32.6% and 70.1±32.8. There was a decrease in CSI values by 33.1±14.5% (p<0.001), as well as a decrease in the number of patients with CSI ≥40: from 35.3% to 10.3% (p<0.001). There were no serious complications during the treatment. The total number of adverse events was 5.9%, mainly dyspepsia and arterial hypertension.
Conclusion: Etoricoxib improved pain in OA patients and reduces the severity of signs of CS, supporting the central mode-of-action of the drug.
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POS1135 METABOLIC OSTEOARTHRITIS: THE ROLE OF THE NUMBER OF COMPONENTS OF METABOLIC SYNDROME AND EXPRESSION OF CARTILAGE TISSUE DESTRUCTION GENES.

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Background: Osteoarthritis (OA) associated with metabolic syndrome (MS) or its components is considered as the metabolic phenotype of OA. It is well known that obesity and other components of MS affect the clinical picture, course and progression of OA. The cumulative effect of metabolic disorders has an effect on the course and outcomes of OA. The study of molecular genetic relationships between the expression of cartilage tissue destruction genes and metabolic OA is one of the little-studied and relevant directions in rheumatology.
Objectives: To determine the role of MS component count and gene expression associated with cartilage tissue destruction in metabolic OA.
Methods: The study included women (n = 117) 45-75 y.o with knee OA (according by ACR criteria) I-III X-ray stage by Kellgren-Lawrence with different numbers of MS components. The duration of the study was 2 years. The clinic conducted visits 1 times a year. At each visit, anthropometric patient scores, articular status, VAS for knee pain, WOMAC and comorbidities were recorded. Patients underwent a laboratory examination (biochemical blood examination: glucose, total cholesterol, LDL, HDL, TG, isolation of blood RNA to determine the level of expression of cell proliferation genes - m-TOR and cartilage destruction - cathepsin K), instrumental examination (X-ray of knee joints) 1 once a year.
Results: All patients with knee OA included in the study (n = 117) showed an abdominal type of obesity (waist circumference > 80 cm in women), which is the main criterion for MS. With frequency analysis in 5.5% of patients, 1 component of MS was detected, in 13.5% - 2 components of MS, in 70.2% - 3 components of MS, in 10.8% - 4 components of MS. Median (Me, 25%; 75% percentile) duration of knee OA disease was greater in patients with 2 or more MS components and was 7.3 years (6.0-8.0) compared to patients with 1 MS component, in whom the duration of OA was 5.4 years (2.0-11.0), p < 0.05. Spearman correlation analysis showed significant relationships between MS component count and OA duration, age, BMI, VAS for knee pain, WOMAC (Table 1).

Table 1. Analysis of the relationship between the number of MS components and OA by Spearman.

Parameters	Number of MS components	p
Age	r=0,57	<0,05
Duration of knee OA	r=0,56	<0,05
X-ray stage by Kellgren-Lawrence of knee OA	r=0,24	<0,05
BMI	r=0,48	<0,05
VAS for knee pain	r=0,36	<0,05
WOMAC pain	r=0,47	<0,05
WOMAC stiffness	r=0,42	<0,05
WOMAC functional insufficiency	r=0,47	<0,05
Total WOMAC	r=0,46	<0,05

Patients showed high expression rates of m-TOR cell proliferation regulator (11.08 (4.27-15.5)) and cathepsin K articular cartilage destruction (9.34 (3.66-12.5)). In analysis of Spearman correlations of cell metabolism gene expression with clinical manifestations of OA and MS components, direct positive correlations with VAS for knee pain were found (p < 0.001, r = 0.95), body weight (p < 0.001, r = 0.92), the number of MS components (p < 0.001, r = 0.78) and WOMAC pain (p < 0.001, r = 0.76).
Conclusion: In our work, it has been demonstrated that 3 or more components of MS in patients with knee OA are observed at pronounced X-ray stages of OA with longer disease duration and a long history of obesity. There are positive correlations between the number of MS components and the clinical course of OA, X-ray severity of OA, hyperexpression of cell proliferation and cartilage destruction genes.
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POS1136 OSTEOARTHRITIS AND METHOTREXATE: EFFICACY AND SAFETY.

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Background: One of the common phenotypes of osteoarthritis (OA) is the "inflammatory phenotype," which is characterized by persistent synovitis of knee joints, small joints of the hands, the development of the erosive hand OA (EOA), and insufficient effectiveness of standard OA therapy. In the inflammatory OA phenotype, changes observed in the synovial sheath have similar features to rheumatoid arthritis, so baseline anti-inflammatory drugs used in RA may be considered as possible treatments for OA. The literature presents few studies with mixed results on the use of methotrexate (MTX) in patients with OA.
Objectives: To examine the efficacy and safety of MTX use in patients with inflammatory knee OA and hand EOA.
Methods: The study included 40 patients (women) with OA (according by ACR criteria) and insufficient effectiveness of previous OA standard therapy: with knee OA (47.5%), hand EOA (25%) and a combination of these 2 localizations (27.5%). The clinical characteristics are shown in Table 1. For 24 weeks, patients received MTX subcutaneously with a dose escalation of 10mg to 15mg per week combined with folic acid 5mg per week and meloxicam 15mg "on demand." The efficacy of MTX therapy was assessed by WOMAC and AUSCAN, by the OMERACT-OARSI criteria. During the study, laboratory indicators were monitored (clinical, biochemical, immunological blood tests, general urine test).
Results: As a result of 24 weeks of MTX therapy, there was a statistically significant decrease in pain, stiffness and functional insufficiency in the small joints of the hand on the AUSCAN index and in the knee joints on the WOMAC index (Figure 1). In hand EOA, there was a decrease in pain by 40.21%, stiffness by 48.21%, functional insufficiency by 23.72%. In knee OA, there was a reduction in pain by 50.45%, stiffness by 49%, and functional failure by 42.7%. 85.5% of patients with knee OA and 72.5% of patients with hand EOA became responders to therapy according to the OMERACT-OARSI criteria. The best clinical effect was achieved in knee OA (89.9% of patients). As a result of MTX therapy, the need for non-steroidal anti-inflammatory drugs (NSAID) decreased: initially, 85% of patients took NSAID daily or more than 3 times a week, and after 6 months of MTX therapy, only 15% of patients took NSAID daily. In general, the tolerability of MTX was satisfactory. The study of 7 patients was stopped: 4 (10%) due to nausea, 3 (8%) due to a moderate increase

Table 1. Clinical characteristic of patients.

Parameters	Values
Age, y.o., Me [25%; 75% percentiles]	62.5 [58;69]
Age of OA onset, y.o., Me [25%; 75% percentiles]	51.0 [46;58]
Duration of disease, years, Me [25%; 75% percentiles]	9.53 [5;15]
Kellgren-Lawrence grades of knee OA	
II grade, %	73.3%
III grade, %	26.7%
BMI, kg/m^2 (M ± δ)	30.68±6.48
WOMAC pain, mm, Me [25%; 75% percentiles]	328 [236; 360]
WOMAC stiffness, mm, Me [25%; 75% percentiles]	100 [87;121]
WOMAC functional insufficiency, mm, Me [25%; 75% percentiles]	776 [610; 1019]
Total WOMAC, mm, Me [25%; 75% percentiles]	1220 [819; 1640]
AUSCAN pain, mm, Me [25%; 75% percentiles]	235 [191;313]
AUSCAN stiffness, mm, Me [25%; 75% percentiles]	56 [35;66]
AUSCAN functional insufficiency, mm, Me [25%; 75% percentiles]	430 [334;580]
Total AUSCAN, mm, Me [25%; 75% percentiles]	671 [392;912]
ESR, mm/h, Me [25%; 75% percentiles]	11 [7;13]
CRP, mg/l, Me [25%; 75% percentiles]	1.3 [0.8;2.5]

Graph 1. Dynamics of the total AUSCAN and total WOMAC as a result of MTX therapy

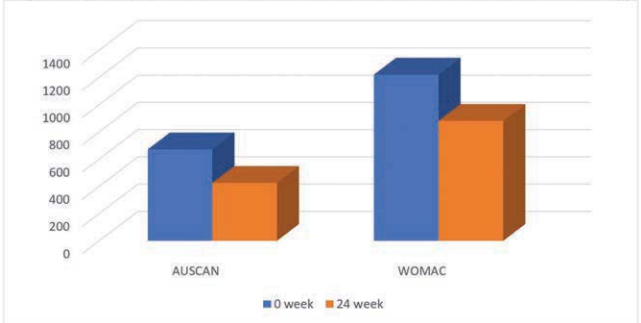

Figure 1.

in transaminases, one of these patients (3%) had one episode of neutropenia up to 1.82x10*9/l (norm 2.04 - 5.80 x10*9/l). There were no serious adverse events.
Conclusion: The results demonstrated a good symptomatic effect of MTX in patients with knee OA and hand EOA. There was a statistically significant decrease in pain, stiffness and functional insufficiency in knee joints and small joints of the hands, a decrease in the need for NSAID throughout MTX therapy. The best clinical effect was achieved in patients with knee OA. Thus, the study showed that MTX has a good clinical effect in OA and a satisfactory safety profile.
Disclosure of Interests: None declared
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POS1137 CORRELATIONS BETWEEN CLINICAL PARAMETERS AND SERUM CYTOKINE LEVELS IN OSTEOARTHRITIS PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Type 2 diabetes mellitus (T2DM) is one of frequent factor that can influence on development and progression of osteoarthritis (OA) and has similar mechanisms of immunopathogenesis.
Objectives: To explore the symptoms and the proinflammatory serum cytokine levels in OA (hand, knee, and hip) patients with T2DM and to estimate relationships between clinical and immunological features.
Methods: Patients who participated in this study (n=137) were divided in two groups: patients with bilateral hand, knee and hip OA (n=56) and T2DM and control group (n=81) which had only hand, knee and hip OA without such comorbidity. All patients were comparable in age, sex and duration of OA. We assessed serum cytokine levels (IL-1b, IL-6, IL-10, IL-18), NO including adipokines such as adiponectin, leptin and C-reactive protein (CRP), erythrocyte sedimentation rate (ESR). Various symptoms of OA and mental health were measured using visual analog scale (VAS), Functional Index for Hand Osteoarthritis (FIHOA), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC Knee/Hip), Knee injury and Osteoarthritis Outcome Score – (KOOS), Hip injury and Osteoarthritis Outcome Score – (HOOS) and with short form 36 (SF-36), Psychological Health Questionnaire (PHQ9), Coping Pain Strategy Questionnaire (CSQ). We used U-Mann-Whitney test to detect differences between groups. Correlation was assessed using Spearman correlation coefficient (r_s).
Results: Patients with OA and T2DM are characterized by the prevalence of KOOS symptoms (median (Me) 58,3; interquartile range (IQR) 50–71,5; p<0.001), WOMAC Knee Total (Me 1327; IQR 930,8–1546; p<0.001) and low values of mental health (SF-MH) (Me 48; IQR 33–56; p<0.001). We found increase of IL 6 (p = 0.0018), IL18 (p = 0.0006), NO (p < 0.0001) levels in the blood serum of patients with OA and comorbidity. Patients with OA and T2DM had high ESR level (p < 0.0001) and leptin level (p = 0,0002) also. Correlation analysis identified the relationships between clinical parameters and such cytokines as IL-1b, IL-6, IL-10 and leptin, CRP in OA patients with T2DM. Some data are presented (Table 1).

Table. Relationships between clinical parameters and serum cytokine levels in studied groups.

Cytokines	OA patients with T2DM (n=56)							
	Pain (VAS)	General Health (VAS)	Knee Symptoms (KOOS)	Hip Pain (HOOS)	Hand OA Index (FIHOA)	Social Functioning (SF-36-SF)	General Physical Health (SF-36-PH)	Coping Pain Strategy (CSQ)
IL-1b (pg/ml)	0,07	0,01	**–0,28***	0,09	0,13	0,08	–0,16	–0,15
IL-6 (pg/ml)	**0,3***	0,21	–0,15	**0,42***	**0,31***	**–0,27***	**–0,27***	–0,03
IL-10 (pg/ml)	0,07	**0,36***	–0,11	0,07	–0,08	–0,09	–0,21	**–0,41***
NO (pg/ml)	0,05	–0,06	–0,11	0,14	0,13	0,14	–0,15	0,11

Table legend: * r- $p < 0,05$

Conclusion: Such comorbidity as OA and T2DM has clinical and laboratory features of progression of OA. Such immunological factors as serum cytokines concentrations, adipokines, CRP are linked with the severity of T2DM-associated OA. A different variation of correlations may suppose role of this proinflammatory factors in the pathogenesis of this OA phenotype. These data should be verified by larger studies.
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POS1138 PERSISTENCY OF DEPRESSIVE SYMPTOMS AND PHYSICAL PERFORMANCE IN KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis (OA) is the most prevalent arthritic disorder, characterized by joint paint, which is exacerbated by chronic depressive episodes. Depression in knee OA is also associated with declines in physical activity level and greater disability; however, the impact of persistent depressive symptoms on physical performance remains unclear.
Objectives: To determine how the persistence of depressive symptoms affects functional capacity in knee OA.
Methods: Participants (n=2,212) were from the Osteoarthritis Initiative cohort and included individuals with radiographic disease (Kellgren-Lawrence grade ≥ 2) and complete data on study measures at baseline. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D; range 0-60) at baseline and the first three follow-up visits. Physical Performance was measured using 20-meter gait speed (meters per second) during follow-up at the first four annual visits. Persistency of depressive symptoms was operationalized as a cumulative exposure using average severity over time. Gait speed was standardized so that outcome estimates could be interpreted in standard deviations. Time-invariant confounders measured at study enrollment included demographic, socioeconomic, and lifestyle factors. Time-varying confounders assessed concurrent to CES-D scores were body mass index, analgesic medications, pain, and other knee OA signs and symptoms. Marginal structural models accounting for time-dependent confounding and selective attrition were the primary method of analysis. The outcome model included all potential statistical interactions between depressive symptoms and follow-up time indicators. Post-estimation linear combinations estimated time-specific effects of time-averaged CES-D scores on standardized gait speed and differences in physical performance between participants with (i.e., CES-D=16) and without (i.e., CES-D=0) depressive symptoms satisfying screening criteria for major depression.
Results: The interaction between depressive symptoms and time was statistically significant (P=<0.001). Time-specific associations indicated that the largest negative impact of depressive symptoms on physical performance was from baseline through year one (β = -0.0077; 95% CI: -0.0125, 0.0030). However, the effect of persistent depressive symptoms decreased over time and reversed in magnitude and directionality, evidenced by the time-specific associations between time-averaged CES-D scores from baseline through year one and year two and gait speed at year two (β = -0.0033; 95% CI: -0.0084, 0.0019) and year three (β = 0.0014; 95% CI: -0.0046, 0.0074), respectively. Consequently, the strongest negative affect of depressive symptoms on gait speed (β = -0.1232; 95% CI: -0.1998, -0.0473) between participants with and without depressive symptoms satisfying screening criteria for major depression was when depressive symptoms were first measured closest to the initial gait speed assessment.
Conclusion: In the contrast to the dose-dependent relationship between chronic depressive episodes and pain in knee OA, study findings imply that the negative effect of depressive symptoms on physical performance decreases over time with increasing depression persistency. These results may reflect diminishing marginal effects, where the largest impact on physical performance in knee OA is during the first depressive episode closest to initial gait speed assessment, especially when averaged against improvement in symptoms over the same duration.
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Disclosure of Interests: Rhea Mehta: None declared, Michelle Shardell: None declared, Alice Ryan: None declared, Yu Dong: None declared, Brock Beamer: None declared, Joseph Gallo: None declared, Elizabeth Stuart: None declared, Megan Schuler: None declared, Marc Hochberg Shareholder of: Dr. Marc C. Hochberg is the President of Rheumcon Corporation., Consultant of: Dr. Marc C. Hochberg receives consulting fees from Bioiberica SA, Bristol-Myers Squibb, Eli Lilly, EMD Serono, Galapagos, IBSA Biotechniq SA, Novartis Pharma AG, Pfizer, Plexxikon, Samumed LLC, Theralogix LLC, and TissueGene Inc., Alan Rathbun: None declared
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Osteoporosis

POS1139 GLUCOCORTICOIDS AND BONE DENSITY IN POLYMYALGIA RHEUMATICA, GIANT CELL ARTERITIS, AND OTHER VASCULITIDES – A CROSS-SECTIONAL ANALYSIS OF THE RH-GIOP COHORT

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Background: There are only few, inconclusive investigations on bone density and the effects of glucocorticoids (GCs) in polymyalgia rheumatica (PMR) and vasculitides.
Objectives: To determine whether GCs are associated with bone density in patients with PMR and other vasculitides after adjustment for confounders.
Methods: The Rh-GIOP cohort study started in 2015 and investigates bone health in patients with rheumatic diseases. In this cross-sectional analysis of baseline visits, we included patients with PMR and vasculitides. Multiple regression was used to model the effect of current and cumulative GC intake on the minimum T-score (mTs; lumbar spine or hip) with adjustment for several confounders such as age, sex, body mass index (BMI), or inflammation (measured by c-reactive protein (CRP)). GCs were modelled both as continuous and as categorical predictors in separate models. Several sensitivity analyses were performed. Patients with early disease (<3 months) were excluded from inferential analyses as were patients with very high GC dosages (>100mg/d prednisolone equivalent). Multiple imputation by chained equations was used for missing data (about 5%).
Results: 198 patients (mean age 68 ± 11 years; 68% females) with a mean disease duration of 5.3 ± 6.3 years were included. The most common rheumatic disease was PMR (36%), followed by giant cell arteritis (26%) and granulomatosis with polyangiitis (17%). 87% were currently taking GCs, 88% received vitamin D supplements, 7% had a deficiency. Osteoporosis (OP) diagnosed by DXA (T-score ≤ -2.5) was present in 20% of patients. Mean CRP was 13.2 ± 26.1 mg/l. Scatter- and boxplots of mTs and GC intake are presented in Figure 1 **A-D**. GC dose was not associated with mTs in any model (current intake: β(continuous model) = -0.01, 97.5% CI -0.02 to 0.01; *p*(all models) ≥ 0.49; cumulative intake: β(continuous model) = 0.01, 97.5% CI -0.04 to 0.07; *p*(all models) ≥ 0.35). Inflammation (measured by CRP) was also not associated with mTs (*p*(all models) ≥ 0.56), and no significant interaction between CRP and GC intake was found (*p* for interaction(all models) ≥ 0.32). Lower body mass index (*p*(all models) ≤ 0.01), history of vertebral fractures (*p*(all models) ≤ 0.02), and proton-pump inhibitor intake (*p*(all models) ≤ 0.04) were associated with bone loss in all models. The results were similar with femoral neck and lumbar spine T-scores as dependent variables, and after excluding patients with PMR.

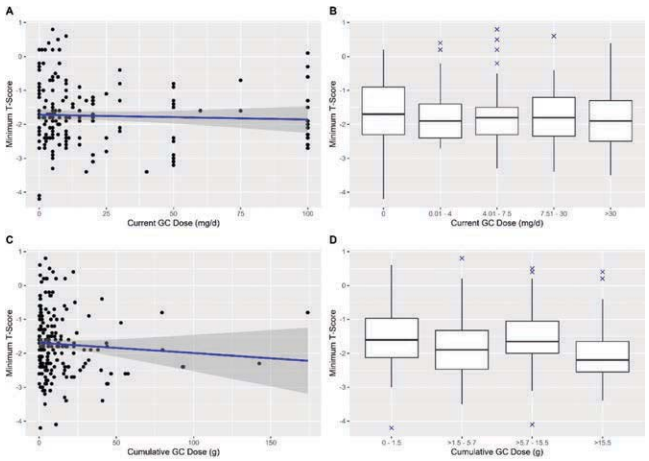

Figure 1.

Conclusion: In this cohort of PMR and vasculitides, the prevalence of OP was similar to the overall elderly German population.[1] Vitamin D supplementation was common while deficiencies were surprisingly rare – In population-based studies, about 32% of Germans are estimated to have a vitamin D deficit.[2] We found no association between current or cumulative GC intake, inflammation, and bone density. Proton-pump inhibitor intake and BMI as modifiable risk factors were associated with mTs. These findings need confirmation from longitudinal analyses of our and other cohorts.

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POS1140 SHORT-TERM EXPOSURE TO FINE PARTICULATE MATTER AND RISK OF FRAGILITY HIP FRACTURES, A CASE-CROSSOVER STUDY ON 1,042 HIP FRACTURES

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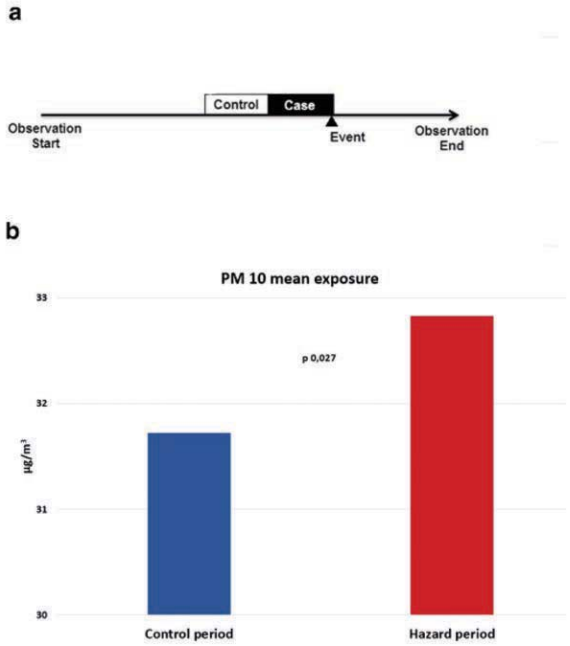
Background: Fragility femoral fracture is a common, world-spread, medical condition, that has a relevant impact both clinically and economically. Chronic exposure to environmental air pollution has been linked with a higher risk of developing osteoporosis. However, little is known regarding the relationship between short-term exposure to air pollution and bone fractures.
Objectives: Our study aims to investigate the link between short-term exposure to fine particulate matters and fragility hip fractures
Methods: We retrieved data of patients suffering of hip fractures admitted to the Orthopedic Unit of the University of Verona Hospital from 2015 to 2020. We retrieved data on the monitoring of PM10 concentrations from the Italian institute of environment protection and research (ISPRA). We designed a case-crossover study to compare the exposure to particulate matters (PM10) in the 30-day period immediately before the fracture (hazard period) referent to a 30-day control period (from day -30 to -60 from the fracture). Exposure to PM10 was evaluated as mean value and AUC. Case-crossover is a peculiar study design applied to longitudinal datasets that controls for within-person time-invariant and between-patient confounders such as indoor air pollution, chronic comorbidities or concomitant medications and have been used extensively to study the effects of transient, short-term exposures on the risk of acute events (Figure 1**A**)
Results: 1042 patients (73.7% female n=768), with a hip fracture admitted to the hospital were included in the study. Mean age of the cohort was 82.6 years (±9.55). Average exposure to PM 10 in the control period was 33,84 ug/mm3, cumulative exposure (AUC) was 952,42 ug/mm3 compared 31,72 ug/mm3 and AUC of 920,24 ug/mm3 in the hazard period (Figure 1**B**) The difference between levels of PM10 in the two periods was statistically significant as levels of PM10 was higher in the hazard period compared to control period, with a p-value = 0,027 (α <0,05) when comparing average concentrations in the two groups and a p-value = 0,024 (α <0,05), when comparing AUCs.
Conclusion: Our study suggests that the short-term exposure to environmental air pollution might increase the risk of femoral fragility fractures. Further studies should be taken to further investigate the biological mechanisms underlining this finding.

Figure 1. A. Case-crossover study design B. Mean exposure to PM10 before a hip fracture compared to the control period (-30 to -60 days).



Disclosure of Interests: Giovanni Adami Shareholder of: Theramex, Galapagos, Marco Pontalti: None declared, Angelo Fassio: None declared, Camilla Benini: None declared, Davide Gatti: None declared, Stefano Negri: None declared, Pietro Olivi: None declared, Maurizio Rossini Shareholder of: Abbvie, Amgen, Bms, Eli Lilly, Galapagos, Novartis, Pfizer, Sandoz, Theramex, Ucb.
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POS1141 FACTOR ANALYSIS OF FRAGILITY FRACTURES BY SITE IN PATIENTS REFERRED FOR DUAL-ENERGY X-RAY ABSORPTIOMETRY SCAN

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Background: Fragility fractures are defined as fractures which occur secondary to low energy trauma (1). Fractures lead to substantial pain, reduced quality of life and significant burden to society, with 3.5 million fragility fractures occurring in the EU in 2010 costing €37 billion (2). It is predicted that by 2025 this cost will have increased by 25% (2). Studying fractures is in the interest of our ageing society in order to aid management of patients at risk. To our knowledge, no other studies have grouped fractures based on site by factor analysis.
Objectives: 1.Determine which fractures are most common in patients who present for dual-energy X-ray absorptiometry (DEXA) scan
2.Apply a factor analysis to establish any patterns in the incidence of fractures based on site
Methods: Between 1996 and 2017, 31546 patients presented to a district general hospital in the North West of England for bone mineral density estimation by DEXA scan. Demographic details, risk factors, incidence of fractures and site of fractures were recorded at time of scan. These data were retrospectively studied to identify patients who had sustained at least one fracture. *STATA* was used to conduct a factor analysis using the principal component factors (PCF) method. Ethical approval was granted by the Northwest Regional Ethics Committee.
Results: 11839 patients were identified to have had at least one fracture (14756 total fractures). Mean age was 67.96, with 9993 females and 1846 males. Mean height was 161.21 cm, mean weight was 70.41 kg and mean BMI was 27.04 kg/m2. Mean T-scores at femoral neck, total femur and lumbar spine were -1.55, -1.38 and -1.30 respectively. The most common fracture site was at the wrist/forearm with 5421 (36.74%) cases. Further, there were 2795 tibia/fibula (18.94%), 2530 spine (17.15%), 1363 femur (9.24%), 1224 humerus (8.29%), 1063 rib (7.20%), 315 pelvis (2.13%), 43 elbow (0.29%) and 2 ankle (0.01%) fractures. 9390 patients had 1 fracture and 2449 patients had more than 1, with 9 patients sustaining 5 fractures. Factor analysis on fracture sites revealed 6 factors with an eigenvalue > 1. Fracture sites were grouped together based on those fractures which loaded most heavily on each factor. Loading was as follows: spine and ribs on Factor 1; spine, pelvis and wrist/forearm on Factor 2; humerus and femur on Factor 3; elbow and ankle on Factor 4; ribs and humerus on Factor 5; ribs and femur on Factor 6 (Table 1).

Table 1. Factor analysis on sites of fractures using the PCF method.

Variable	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Uniqueness
Tibia/fibula	0.0862	-0.9485	-0.0530	0.1182	0.0325	-0.0896	0.0671
Spine	0.6906	0.3263	-0.4535	-0.1501	-0.2681	-0.1837	0.0829
Ribs	0.2128	0.1089	-0.0689	-0.0957	0.7535	0.6074	0.0193
Pelvis	0.0810	0.2050	0.1185	-0.0158	0.2113	-0.3663	0.7368
Humerus	0.0386	0.1433	0.5578	0.0892	0.3832	-0.5101	0.2518
Femur	0.1227	0.0946	0.7052	0.0071	-0.4814	0.4532	0.0416
Elbow	0.0397	0.1300	-0.0740	0.7306	0.0305	0.0363	0.4401
Ankle	0.0547	0.1082	-0.1084	0.7189	-0.0365	0.0716	0.4503
Wrist/forearm	-0.8856	0.2389	-0.2461	-0.0479	-0.0608	0.0071	0.0920

Conclusion: In-keeping with published data, the most common site for fracture was forearm (3). Factor analysis grouped together sites of fractures into 6 factors, suggesting that these fractures are more likely to co-exist. Moving forward it would be beneficial to ascertain differences between the groups in terms of demographics, risk factors and any bone protection measures taken. This may highlight clinically relevant data in order to make evidence based decisions in the identification and management of patients at risk of fragility fractures.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.662

POS1142 A CONCORDANCE STUDY OF CT DENSITOMETRY WITH DXA DENSITOMETRY

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Background: Osteoporosis is a skeletal disorder characterised by compromised bone strength resulting in an increased risk of fracture. Although DXA is the only technology that can be used for diagnostic classification of osteoporosis according to WHO, computed tomography imaging (CT) densitometry of the spine has equal or superior ability to predict vertebral fractures in postmenopausal women. Therefore the continued use of DXA as the primary modality of calculating BMD may lead to inaccurate exclusion of osteoporosis and prognostication.
Objectives: To assess the concordance of spinal CT densitometry with current standard of assessment through DXA-derived densitometry.
Methods: 50 patients who had had both a DXA scan of the lumbar spine and CT lumbar spine/thorax/abdomen performed within 18 months of each other were included. The CT images were analysed to attain a mean Hounsfield score of the lumbar vertebrae and this was compared to DXA derived T-scores. A Hounsfield score of 131 was used as the threshold for diagnosing osteoporosis akin to a DXA-derived T score of -2.5. The final data was analysed to find correlation values of Hounsfield score with T-score using Pearson correlation coefficient.
Results: The mean Hounsfield score was 108.4 (osteoporotic) compared to a mean T-score of -1.22 (osteopenic) with a statistically significant correlation coefficient of 0.447, ($p<0.01$).Using T score ≤ -2.5, 15 (30%) of the patients included on our study would have a diagnosis of osteoporosis whereas this would be 36 patients (72%) if using the threshold of Hounsfield score <131. Out of the 50 patients included, 15 had vertebral fragility fractures. The mean T-score for these patients was -1.2 (indicating osteopenia) and mean Hounsfield score was 108 (indicating osteoporosis).
Conclusion: Our study showed a moderate positive correlation between the DXA-derived T-scores and CT Hounsfield scores. This further validates previous studies that suggest CT scans can be used to identify patients with osteoporosis. 93% of patients with vertebral fragility were identified as having osteoporosis using CT densitometry whereas only 40% were identified via DXA. These findings highlight the limitations of DXA, particularly in terms of overestimation of bone mineral density related to degenerative changes. CT images of the thorax, abdomen or lumbar spine that have already been performed for other indications can be used to opportunistically screen

for osteoporosis without additional radiation exposure, waiting time or cost. This may allow for more accurate diagnosis and subsequent treatment and fracture risk reduction.

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Disclosure of Interests: None declared

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POS1143 FIVE-YEAR TREATMENT OUTCOME OF DENOSUMAB ON OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS, IN CLINICAL PRACTICE

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Background: Osteoporosis (OP) is a frequent complication identified in patients with rheumatoid arthritis (RA). Effective treatment must be provided to treat OP in RA (RAOP). Denosumab (DMB) is a promising drug, currently being used for the treatment of RAOP. Although DMB was determined to be effective in a long-term FREEDOM extension trial [1] for treating postmenopausal OP, its efficacy in the treatment of RAOP in real-world is not be fully evaluated.

Objectives: This retrospective study assessed the five-year treatment outcome of DMB in Japanese patients with RAOP.

Methods: Data from the Toyohashi RA Database (TRAD) was used, which is a collection of single-center retrospective data. Our study included 65 female patients with RAOP for whom DMB treatment was initiated between October 2013 and May 2016. The following information was collected: 1) baseline characteristics, 2) DMB continuation rates using the Kaplan–Meier method and reasons for stopping DMB, 3) fracture occurrence during DMB treatment, and 4) time-course of bone mineral density (BMD) [lumbar spine (LS) and total hip (TH)] and bone turnover markers (BTM) [bone-specific alkaline phosphatase (BAP), type I procollagen-N-propeptide (P1NP), type I procollagen-N-propeptide (NTX), and tartrate-resistant acid phosphatase-5b (TRACP-5b)] in 38 patients who underwent DMB treatment over a period of five years.

Results: 1) The mean age and RA duration were 69.4 years (46–86) and 17.2 years (1–49), respectively. Prednisolone and biologics were administered in 21 (32.3%) and 20 (30.8%) patients, respectively. Twenty-seven patients (41.5%) had a history of fragility fractures, and 24 patients (36.9%) had a history of vertebral fractures. Pretreatment drugs for OP were as follows: bisphosphonate in 22 patients; teriparatide, 17; none, 16; activated vitamin D, 7; and selective estrogen receptor modulator, 3.

2) Continuation rates of DMB were 96.9% at one year, 95.4% at two years, 85.8% at three years, 79.4% at four years, and 71.1% at five years. DMB treatment was terminated in 24 patients due to lack of efficacy in nine patients, death in seven patients (unknown reason in four, pneumonia in two, and senile decay in one), adverse events except death in five patients (worsening of dementia in two, brain hemorrhage in one, necrosis of jaw in one, and pneumonia in one), and other reasons in three patients.

3) Nine patients (13.8%) experienced fractures during DMB treatment; vertebral and non-vertebral fractures occurred in three and four patients, respectively. Two cases of fractures remained undefined.

4) Both mean LS-BMD and TH-BMD significantly increased in 38 patients for whom DMB administration was continued for five years. Average percent changes of LS-BMD and TH-BMD were 3.9% and 3.0% at six months, 5.5% and 3.8% at one year, 7.6% and 4.1% at two years, 9.8% and 5.7% at three years, 10.8% and 6.5% at four years, and 12.9% and 6.8% at five years (Figure 1). Four BTMs, BAP, P1NP, NTX, and TRACP-5b, significantly decreased from six months to five years when compared to baseline values, with average changes at 5 years equaling –38.4%, –37.8%, –23.8%, and –24.6%, respectively.

Conclusion: DMB treatment of RAOP proved effective and reasonably safe, and it increased BMD by a percentage similar to that observed in the FREEDOM extension trial. However, DMB administration was ceased in 13.8% of cases due to fractures and lack of efficacy. Although DMB is recommended for the treatment of RAOP, future evaluations should be conducted to predict its efficacy and determine alternative treatment strategies.

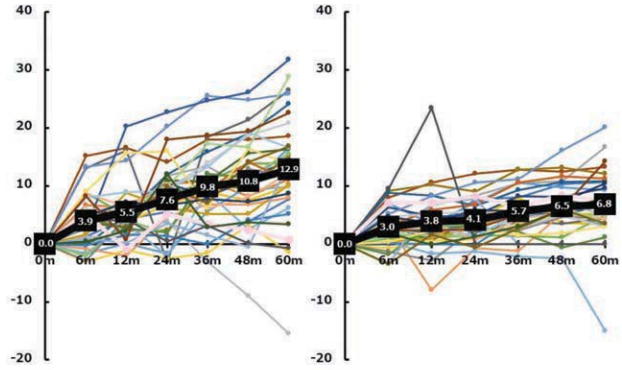

Figure: Time-course of % Change of Bone Mineral Density (Left: lumbar spine, Right: total hip)

Bold lines indicated averaged values. Thin lines indicated individual values of each patient.

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Disclosure of Interests: None declared

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POS1144 INCREASED EXPRESSION OF RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS IN SARCOPENIC PATIENT SKELETAL MUSCLE

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Background: Animal studies suggest that advanced glycation end-products (AGEs) and their interaction with receptor for AGEs (RAGE) are involved in sarcopenia, but their relationship in human skeletal muscles has yet to be elucidated.

Objectives: We aimed to determine whether RAGE expression in human skeletal muscle is associated with serum AGE levels and sarcopenia-related changes.

Methods: We reviewed 33 consecutive women (mean age, 65 years) with distal radius fracture who had consented to donate a sample of forearm flexor muscle for research purposes, which was taken during surgical fracture repair. The muscle RAGE expression was measured with immunohistochemistry staining and serum AGE levels using ELISA method. We compared RAGE expression and AGE levels in patients with and without sarcopenia. We also correlated RAGE expression with such clinical parameters as age, body mass index, bone mineral density (BMD), as well as sarcopenia-related changes, including grip strength, appendicular skeletal muscle mass, and muscle cross-sectional area (CSA) ratios.

Results: Twelve patients (36%) were diagnosed with sarcopenia according to the Asian Working Group for Sarcopenia. They had a significantly higher RAGE expression ($p = 0.044$) and AGE level ($p < 0.001$) than those without sarcopenia. The RAGE expression correlated significantly with a high serum AGE level ($r = 0.510$, $p = 0.011$) and correlated inversely with a muscle CSA ratio ($r = -0.696$, $p < 0.001$).

Conclusion: This study shows that RAGE expression increases in sarcopenic patient skeletal muscles. This expression also correlates positively with serum AGE levels and inversely with muscle CSA ratios. Further studies are necessary to determine whether targeting RAGEs can be a therapeutic option for sarcopenia.

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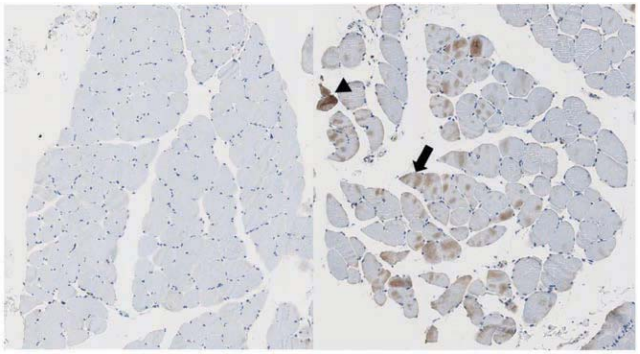

Figure 1. Skeletal muscle tissue (x 7.0) obtained from (a) a 76-year-old female with receptor for advanced glycation end-products (RAGE) expression scoring 14, and (b) a 75-year-old female with RAGE expression scoring 50. Disparity between the percentage of fibers with signal intensity of 1+ (arrow) and those with signal intensity of 2+ (arrowhead) is obvious. Difference in the diameter and homogeneity of the muscle fibers imply the role of RAGE hyper-expression in sarcopenia.

Disclosure of Interests: None declared
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POS1145 PREDICTORS OF FRACTURE IN PATIENTS WITH NORMAL BONE DENSITY, AN OBSERVATIONAL STUDY

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Background: Although most fragility fractures occur in osteoporotic patients, fractures of the lumbar spine and the femora are also common in patients with normal bone mineral density (BMD). A number of risk factors are known to be associated with fractures in patients with reduced BMD. However, risk factors for fractures in patients with normal BMD remain relatively unexplored.
Objectives: Evaluate the risk factors associated with fractures in patients with a normal BMD (T-score ≥ -1.00) in the lumbar spine and right and left femur in an observational cohort
Methods: Data was collected from patients attending a District General Hospital in the Northwest of England for a DEXA scan between 2004 to 2019. Patients with a T-score ≥-1.00 in L1-4 and the right and left femur were included. Chi-squared test and Student's t-test were used to compare risk factors in patients with and without fractures. A series of logistic regression models that adjusted for age and sex were then fitted to determine risk factors associated with a fracture. Area under the ROC curve was calculated for each model. Ethical approval was obtained from the Northwest Regional Ethics Committee.
Results: 6,504 patients were included in analysis, 1,491 (22.9%) of whom had a fracture. Mean age (SD) at scan was 58.64 (12.98) years and 5,347 (82.2%) were female. Risk factors and their association with fracture occurrence after adjusting for age and sex are shown in Table 1. Weight, BMI, and current alcohol use were statistically significantly (p <0.05) associated with increased risk of fracture. History of Rheumatoid Arthritis, steroid use, and increased T-score in L1-4 or the right or left femur were statistically significantly (p <0.05) associated with decreased risk of fracture.

Table 1. Logistic regression with adjustment for age and sex

Characteristic	Odds ratio (95% confidence interval)	P-value	AUC
Height, cm	1.006 (0.997, 1.016)	0.176	0.5666
Weight, kg	1.010 (1.007, 1.014)	0.000	0.5804
BMI	1.027 (1.016, 1.037)	0.000	0.5773
Current smoker	1.164 (0.975, 1.389)	0.094	0.5664
Previous smoker	1.120 (0.976, 1.284)	0.106	0.5672
Current excess alcohol use	1.299 (1.033, 1.634)	0.025	0.5668
Pervious excess alcohol use	1.441 (0.943, 2.202)	0.091	0.5664
History of Rheumatoid Arthritis	0.674 (0.520, 0.874)	0.003	0.5708
Current steroid use	0.498 (0.406, 0.611)	0.000	0.5911
Previous steroid use	0.796 (0.669, 0.946)	0.010	0.5682
Mean T-score L1	0.929 (0.880, 0.980)	0.007	0.5698
Mean T-score L2	0.917 (0.874, 0.961)	0.000	0.5734
Mean T-score L3	0.906 (0.868, 0.947)	0.000	0.5758
Mean T-score L4	0.925 (0.889, 0.962)	0.000	0.5734
Mean T-score left neck of femur	0.866 (0.803, 0.933)	0.000	0.5662
Mean T-score total left femur	0.839 (0.780, 0.902)	0.000	0.5710
Mean T-score right neck of femur	0.847 (0.785, 0.914)	0.000	0.5672
Mean T-score total right femur	0.839 (0.779, 0.904)	0.000	0.5723

Conclusion: In the FRAX tool, increased weight is considered protective against fractures, and steroid use and Rheumatoid Arthritis are thought to increase fracture risk. In our cohort of patients with normal BMD, patients with increased weight had a higher risk of fracture, and patients with Rheumatoid Arthritis and steroid use had a decreased fracture risk.
While there is overlap in the risk factors associated with fractures in patients with reduced BMD and normal BMD, our study suggests that some characteristics protective of fractures in osteoporotic patients may increase the risk of fracture in patients with a normal BMD.
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www.sheffield.ac.uk/FRAX/
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POS1146 ROMOSOZUMAB INCREASE BONE MINERAL DENSITY AT LUMBAR AND FEMORAL IRRESPECTIVE OF PREOSTEOPOROSIS TREATMENT, HISTORY OF FRAGILITY FRACTURE AND COMBINATION OF VITAMIN D

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Background: Romosozumab, a monoclonal antibody that binds sclerostin, increases bone formation and decreases bone resorption. Romosozumab has an excellent therapeutic effect on patients with osteoporosis. However, there are few reports investigated the efficacy and the effect of various factors relative to osteoporosis in real-world.
Objectives: We evaluated bone mineral density (BMD) and bone metabolism marker (BMM) change in osteoporosis patients treated with romosozumab, and assessed the effect of various factors, such as preosteoporosis treatment, history of fragility fracture and combination of vitamin D.
Methods: This study included 141 osteoporosis patients (132 female, mean age: 78.8 ± 7.5 years, mean hight: 151.1 ± 7.5 cm, mean weight: 50.9 ± 8.9 kg) treated with romosozumab. BMD measurements using dual energy X-ray absorptiometry (DXA) and BMM measurements using N-terminal propeptide of type 1 collagen (P1NP) were evaluated at 0, 4, 6, and 12 months after treatment. DXA were performed at the lumbar spine (n=92), at proximal femoral and femoral neck (n=92), and at distal third radius (n=49). We evaluated the influence of preosteoporosis treatment, history of fragility fracture and combination of vitamin D for BMD change.
Results: BMD at lumbar spine (5.2%: p<0.01, 9.2%: p<0.01, 10.8%: p<0.01), proximal femoral (1.3%: p=0.02, 2.8%: p<0.01, 4.5%: p<0.01) and femoral neck (2.0%: p=0.03, 2.7%: p=0.06, 5.0%: p=0.01) were significantly increased at 4, 8, 12 months after treatment. BMD at distal third radius (-1.5%: p<0.01, -0.8%: p=0.17, -1.0%: p=0.13) were not increased at 4, 8, 12 months after treatment. P1NP chane were 63% (p<0.01), 6.4% (p=0.55), -2.3% (p=0.2) at 4, 8, 12 months after treatment. There were no significant differences in 1 year improvement ratio of BMD at lumbar spine, proximal femoral and femoral neck between 38 patients with pretreatment of osteoporosis and 54 patients without pretreatment of osteoporpsis (13.5 vs 9.5%: p=0.1, 4.9 vs 4.4%: p=0.7, 6.1 vs 4.6%: p=0.67), between 33 patients with a history of fragility fracture and 59 patients without a history of fragility fracture (7.3 vs 11.7%: p=0.42, 0.8 vs 5.5%: p=0.08, -0.7 vs 6.6%: p=0.14), between 50 patients with romosozumab alone and 42 patients with romosozumab plus vitamin D (11.3 vs 10.0%: p=0.93, 4.1 vs 5.3%: p=0.59, 6.8 vs 2.3%: p=0.47). There were no significant differences in 1 year improvement ratio of BMD at distal third radius between 33 patients with pretreatment of osteoporosis and 16 patients without pretreatment of osteoporpsis (-1.1 vs -0.9%: p=0.63), between 31 patients with a history of fragility fracture and 18 patients without a history of fragility fracture (-1.5 vs -0.5%: p=0.3).
Conclusion: Romosozumab improved BMD at lumbar and femoral independently regardless of preosteoporosis treatment, history of fragility fracture and combination of vitamin D.
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POS1147

CHALLENGES IN CONDUCTING PRAGMATIC CARE STRATEGY STUDIES IN OSTEOPOROSIS: PATIENT PERCEPTIONS

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Background: Large pragmatic osteoporosis studies to improve outcomes are needed. Direct-to-patient studies have highest generalizability but achieving sufficient sample size is difficult; recruitment challenges represent an important consideration given limited participant eligibility and interest. The Fracture Liaison Service (FLS), a team approach to post-fracture care, is a secondary fracture prevention method that has significantly improved outcomes internationally.
Objectives: Our goal was to evaluate the interest, barriers, and lessons learned in recruiting participants for a future trial assessing remote FLS approaches for post-fracture care.
Methods: We used ICD10 fracture codes to identify patients > 50 years of age with a documented hip/pelvis, spine, humerus, or wrist fracture in the previous 1 year. We excluded patients with i) prescriptions for osteoporosis medications (e.g., bisphosphonates, parathyroid hormone analogs, denosumab, romosozumab, raloxifene) in the prior 1 year; ii) an ICD10 code for end-stage renal disease, non-osteoporotic metabolic bone disease, malignant neoplasm, or motor vehicle accident. In December 2021, research assistants reviewed electronic health records (EHR) of potentially eligible patients for evidence of additional serious illness limiting life expectancy to < 1 year or non-ambulatory status prior to fracture. Research assistants called preliminary eligible patients that met inclusion and exclusion criteria and asked them to complete a survey by phone. Interest in a FLS future clinical trial was evaluated using a Likert scale (1="Definitely would not volunteer," to 5="Definitely would volunteer"). We used descriptive statistics to analyze baseline demographic, clinical characteristics, and interest. This pilot was approved by the UAB Institutional Review Board (IRB-300008310-005).
Results: We identified 1,577 patients > 50 years of age with a fracture. After applying exclusion criteria, we identified 869 preliminary eligible patients. Over 3 weeks, we screened the medical records of a random sample of half of the preliminary eligible patient cohort (n=414), of whom we contacted 271 patients determined potentially eligible, and successfully reached 141 (52% of those contacted) by phone. A total of 108 (77% of those reached) persons, mean (SD) age 69.5 (11.5) years, 40% men, 21% Black or non-white Hispanics completed the survey. Among those contacted, 68 (63%, interest rate) said they would be very or highly interested in participating in a future clinical trial evaluating FLS approaches. Among the 40 (37%) people who said they were not sure, unlikely or very unlikely to volunteer the most common reasons cited were "I don't want to participate in a study" (33%); "I don't feel well enough to participate" (10%); "I don't understand what the study is for" (3%). From this pilot, we calculated a refined eligibility/interest rate of 9.1% among those patients preliminarily identified as eligible using administrative data alone.
Conclusion: Based on our pilot, we estimate that approximately 9% of eligible patients with fractures will be interested in enrolling in a future comparative effectiveness study to prevent recurrent fragility fractures. We identified several potential modifiable barriers to clinical trial recruitment. Patient perceptions collected from this pilot will inform enrollment strategies, which can be incorporated early when planning direct-to-patient pragmatic osteoporosis studies to achieve recruitment goals.
Disclosure of Interests: Lesley Jackson: None declared, Ellen McNeeley: None declared, Norma C. Techarukpong: None declared, Faith Mugeta: None declared, Kiara Aaron: None declared, Amy Mudano: None declared, Jeanne Merchant: None declared, Kellie Warren: None declared, Jeff Foster: None declared, Kenneth Saag Grant/research support from: Amgen, Horizon, LG Chem, Radius, SOBI, Maria Danila Grant/research support from: Pfizer, Horizon
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POS1148

SONOGRAPHIC VARIATION OF SYNOVITIS IN RHEUMATOID ARTHRITIS IS SUGGESTIVE OF BONE MINERAL DENSITY CHANGE.

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder initiated from local synovium inflammation and consequently bone/cartilage destruction. Active disease status brings persistent inflammation, which stimulates the activation of osteoclasts, accelerating systemic bone loss and decreasing bone mineral density (BMD)(1). Ultrasound (US), a powerful tool for clinical practice, was reported to be beneficial for the prediction of new bone erosion and disease activity (2, 3), based on the synovitis grading recommendation by the European League against rheumatism- Outcome Measures in Rheumatology Clinical Trial (EULAR-OMERACT) Taskforce. The severity of RA synovitis is associated with local bone destruction; however, the impact on systemic bone loss is still unknown.
Objectives: This pilot study aims to investigate if the US-detected synovitis change is associated with systemic bone loss.
Methods: A registry was conducted in Chang Gung Memorial Hospital, Kaohsiung, from September 2014 till April 2021 to monitor BMD changes in patients with rheumatic diseases. In RA patients, we regularly assessed synovium change of bilateral wrist by ultrasound at enrollment and one year later, based on EULAR-OMERACT system(4), which is a semiquantitative grading tool incorporating both gray-scale synovial hypertrophy (SH) and power Doppler (PD) signal. These ultrasound scans were performed by an independent and well-trained rheumatologist, using MyLab 70 system (Esaote, Firenze, Italy) and B-mode frequency at 12–18 MHz. We performed a longitudinal scan of volar and dorsal wrists, observing GS and PD signals. All participants who underwent standard care for RA were followed at least three years to monitor BMD change, and those who underwent anti-osteoporosis therapy at index day were excluded. We defined improvement of US-detected synovitis (US+) as a change from high to low grade by EULAR-OMERACT score. Conversely, patients who failed improvement were recorded as "US- ", defined as change from low to high grade. Patients who improved one or more grades, such as from Grade 3 to 2 (or from Grade 2 to 0), were registered as US+1 (or US+2) and vice versa. If there is no change of synovitis grade, we registered as US+0.
Results: A total of 212 participants were enrolled in the current study, with a mean age of 56.0 ± 10.1 years and a mean RA disease duration of 13.6 ±9.1 years. In patients with US+, the mean change of hip BMD [defined as (final BMD-baseline BMD)/baseline BMD, in percentage] was 0.73 ±6.8%, while US- was -2.2 ±7.7% and US+0 -1.9 ±6.6% (p=0.047). in post-hoc analysis, US+ demonstrated borderline significance compared to US-(p=0.059) and US+0 (p=0.087) by Bonferroni method. Subsequent analysis (Figure 1 A) revealed that patients with US+2 presented preservation of hip bone mass (3.1 ±6.8%), followed by US+1 (0.1 ±6.8%) and then US+0. US-1 and US-2 showed rapid bone loss on the hip (-2.1 ±7.9% and -2.3 ±6.7%, respectively).

(A). Variations of ultrasound-detected synovitis grading are associated with hip BMD change.

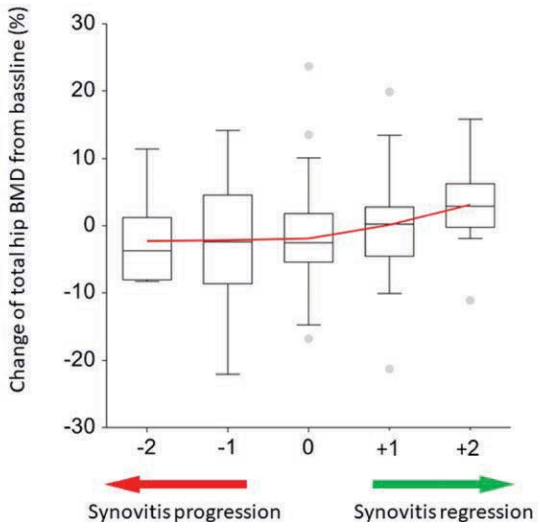

Figure 1.

Conclusion: Persistent synovitis is associated with total hip bone loss, and detection of synovitis change by ultrasound with EULAR-OMERACT scoring system is helpful to predict hip BMD change.
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POS1149 BONE MANIFESTATIONS IN SYSTEMIC MASTOCYTOSIS AND RELATED RISK FACTORS

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Background: Clinical characteristics in Systemic Mastocytosis (SM) range from asymptomatic (indolent) to aggressive forms. Up to 28-34% of patients with SM have symptoms related to bone involvement at diagnosis and 16% have fractures (1). Skeletal manifestations include bone pain, osteoporosis (OP), osteosclerosis, focal osteolytic and osteoblastic lesions. OP is frequently related to indolent SM but not the aggressive forms (2).
Objectives: To describe bone involvement in patients with SM and analyze related risk factors.
Methods: Retrospective cohort study comprising patients with SM that attended the Rheumatology Department from 2010 to 2021. Sociodemographic variables, SM classification, OP risk factors, bone lesions, fracture presence and analytical parameters were collected, and we analyzed whether they were associated with the presence of fractures (Table 1). Densitometry data were registered at diagnosis and up to 8 years of follow-up.

Table 1. Clinical features and differences between fractured and not fractured patients

	ALL	Fractures	No fractures	
	(N=22)	(N=3)	(N=19)	*p*
Age (y), mean (SD)	47.05(12.4)	44.3 (13.3)	47.5 (2.5)	0.69
Sex W/M, N(%)	15(68.2)/7 (31.8)	1(33.3)/2(66.7)	14 (73.7)/5(26.3)	0.23
Mastocytosis classification N(%)				0.37
Indolent	19(86.4)	2(66.7)	17 (89.5)	
Aggressive forms*	3(13.6)	1(33.7)	2(10.5)	
Menopause, N(%)	8 (36.4)	1 (100%)	7(83.6)	0.66
Low calcium intake, N(%)	16(72.7)	2 (66.7%)	14 (73.7)	0.63
Low BMI, N(%)	5 (22.7)/17(77.3)	0	5(26.3)	0.44
Smoking, N(%)	2 (9.1)	0	2 (10.5)	0.74
Alcoholism, N(%)	2(9.1)	0	2 (10.5)	0.74
Hypovitaminosis D, N(%)	5(22.7)	0	5(41.7)	-
Hyperparathyroidism, N(%)	5(22.7)	0	5(45.5)	-
Tryptase, mean (SD)	34.4(26.1)	20(-)	35.3(26.7)	0.58
BMD at diagnosis, mean (SD)				
Lumbar spine (g/cm^2)	0.976 (0.2)	0.509	1.012(0.1)	**<0.01**
Femoral neck (g/cm^2)	0.860 (0.1)	0.704	0.872(0.1)	0.17

*Aggressive forms include smoldering, hematologic malignancy, and mast cell leukemia

Results: 22 patients were included, 19 SM were indolent, 1 smoldering, 1 hematologic malignancy and 1 mast cell leukemia. Radiologically, 17 patients did not present lesions, 4 presented sclerotic lesions and 1 lytic lesions. Vertebral fractures were observed in 3 patients and 2 of them were before SM diagnosis. 10 patients received anti-osteoporotic treatment, 3 of them with teriparatide. At diagnosis, 2 patients (9.1%) had osteoporosis and 11 (50%) osteopenia. None of the analyzed risk factors were associated with OP presence. Of note, during follow-up significant changes were observed between those with indolent SM and aggressive forms at lumbar spine (LS) and femoral neck (FN) at 2 years (change in LS in indolent form -2.9% vs 29.6% in aggressive forms, p <0.001 and change at FN of 1% vs 20.5%, respectively, p=0.003). At 4 years change at LS was -4.1% vs 25.8%, p=0.034 between indolent and aggressive forms but there were no differences regarding the presence of fractures (2 fractures in indolent group and 1 in aggressive, p=0.371).
Conclusion: Bone involvement was present in more than 50% of patients at diagnosis and the presence of fractures was not uncommon (14%), especially at lumbar spine (LS). Aggressive forms were associated with an increase in aBMD. The presence of fractures was associated with lower LS aBMD at diagnosis.
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POS1150 BONE MINERAL DENSITY AND TRABECULAR BONE SCORE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) have an increased risk of osteoporosis and low trauma fractures due to several important factors: the inflammatory disease itself, low vitamin D level, use of some disease-modifying anti-rheumatic drugs, glucocorticoids, etc. [1]. Bone mineral density (BMD) and trabecular bone score (TBS) measured by DXA are the important parameters of bone strength that evaluate the different aspects of bone architecture [1, 2].
Objectives: The aim of the research was to determine BMD and TBS in women with SLE.
Methods: We have examined 150 females from 20 to 75 years old (average age – 51.1±11.6 years) which were divided into 2 groups: patients with SLE (n=50) and healthy women (n=100). The females did not differ in terms of age (51.4±10.8 and 50.4±13.2 years, respectively; p=0.60), height (163.8±15.4 and 163.6±6.6 cm, p=0.86), body mass (73.6±15.9 and 68.8±14.8 kg, p=0.09), and the duration of the postmenopausal period (8.9±6.9 and 9.6±8.1 years, p=0.81), but the age of menopause was significantly lower in patients with SLE (47.9±4.7 and 42.1±15.3 years, respectively, p<0.05). The BMD was measured at the lumbar spine, femoral neck, proximal femur, and total body, by means of the "Prodigy" unit (CE Medical systems, model 8743, 2005). The TBS was evaluated using the installed TBS iNsight software for an X-ray densitometer (Med-Imaps, Pessac, France).
Results: The parameters of BMD were significantly lower in patients with SLE compared to the healthy women in all measured areas: in the total body (0.95±0.05 and 1.06±0.12 g/cm^2, respectively; p=0.03), in the lumbar spine (0.87±0.13 and 0.96±0.17 g/cm^2, p=0.02), femoral neck (0.68±0.11 and 0.75±0.14 g/cm^2, p=0.03), proximal femur (0.83±0.10 and 0.92±0.16 g/cm^2, p=0.02). In the patients with SLE TBS was significantly lower compared to the index in healthy women (1.28±0.11 and 1.33±0.12 un., p=0.02).
Conclusion: The parameters of BMD and TBS in women with SLE are significantly lower than in the healthy population. Our results emphasize the importance of combined BMD and TBS measurement in the evaluation of the different aspects of bone architecture for dynamic monitoring of bone health and risk of fracture in patients with SLE and timely start of osteoporosis treatment.
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POS1151 OPPORTUNISTIC BONE MINERAL DENSITY SCREENING IN PATIENTS UNDERGOING CARDIAC CT SCANS: EFFECT OF USING IMAGES CONTAINING INTRAVENOUS CONTRAST

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Background: Osteoporosis is under-diagnosed worldwide causing increased risk of fractures and death (*1*). Computed tomography (CT) scans performed on other indications such as coronary artery disease harbor the potential for automatic detection of low volumetric bone mineral density (vBMD) of the vertebrae using quantitative CT (QCT); hence allowing estimation of future fracture risk (*2*). CT is often performed with intravenous (iv) contrast administration. In 2015, the International Society of Clinical Densitometry stated: "*There is insufficient evidence to judge the effect of contrast agents on a classification of low BMD*" (*3*); this position remains. Thus, it is important to assess the effect of contrast enhancement in order to broaden the potential of vBMD screening using routine CT scans.
Objectives: We aimed to compare thoracic vBMD measurements from CT scans with and without iv contrast enhancement.
Methods: This cross-sectional multicenter sub-study is based on a larger clinical trial, Dan-NICAD-1, from which we randomly selected a cohort of 136 participants. First, a non-contrast scan was performed followed by a contrast-enhanced scan during which 60-90mL of iv contrast was administered (Iomeron, 350 mgI/

mL). Mindways QCT Pro software was used to measure BMD values (mg/cm^3) and the mean estimate was calculated for each participant (*4*). American College of Radiology quantitative CT cut-off values for lumbar spine were used to categorize patients into very low (<80mg/cm^3), low (80-120mg/cm^3), or normal BMD (>120mg/cm^3).

Results: In 136 participants undergoing cardiac CT (Table 1), we found a different mean vBMD before vs. after contrast; 117.5 mg/cm^3 [95%CI: 111.6–123.4] vs. 132.1 mg/cm^3 [95%CI: 125.1–139.1], *p<.0001*. The absolute difference was 14.7mg/cm^3 [95%CI: 12.3–17.0]; the relative difference, was 12.5% [95% CI: 10.5–14.5]. In total, 8/15 (53%) participants changed from very low BMD to low BMD after contrast administration, and 21 participants (21/63, 33%) changed from low to normal BMD (Figure 1). No participants changed from very low BMD to normal BMD.

Table 1. Demographics by vBMD*

Characteristics	All (n=136)	Very low BMD (n=15)	Low BMD (n=63)	Normal BMD (n=58)
Gender M:F	89:47	8:7	49:14	32:26
Age, yrs (range)	57±9 (40-73)	64±6 (48-72)	59±8 (44-73)	54±8 (40-72)
Mean vBMD before contrast, mg/cm	92.2±16.1	68.0±10.5	98.0±10.1	151.5±21.9
Mean vBMD after contrast, mg/cm	95.2±16.0	68.6±10.5	100.8±10.3	159.6±31.6
Risk factors				
Diabetes mellitus**	16	0	7	9
Smoking status**				
Never	65	4	17	44
Former	18	1	7	10
Active	52	5	24	23
Bone data				
DXA performed previously**	7	2	3	2
Osteoporosis diagnosed previously**	1	0	1	0
Family history of osteoporosis**	22	5	8	9
Anti-osteoporotic medication**	15	2	3	10

* Classifications defined by American College of Radiology and grouped using the non-enhanced CT. Data: number of participants, (range) and mean with standard deviations. ** Self-reported

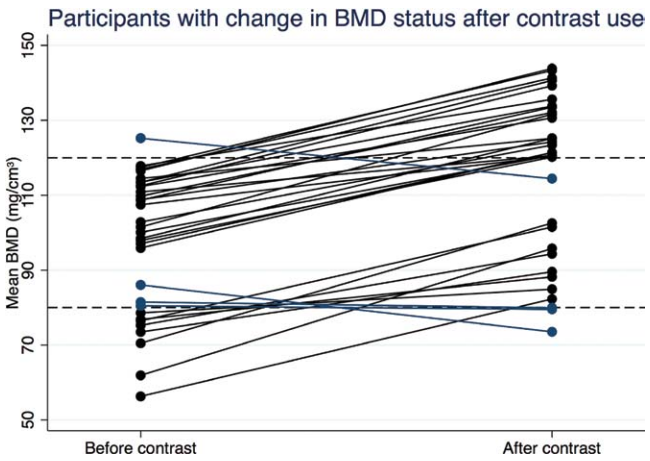

Figure 1. Participants with change in BMD category after contrast administration Figure 1. vBMD measurements before and after contrast administration. 33/136 participants changed BMD category illustrated by the dotted lines (80 mg/cm^3; 120 mg/cm^3). Black lines: increase in vBMD after contrast (n=29); blue lines: decrease in vBMD after contrast (n=4).

Conclusion: Our data suggest a significant effect of contrast on clinical vBMD measurements; thus, this should be adjusted for before using contrast-enhanced cardiac CT for opportunistic vBMD screening. This urges further studies on the effect of scan protocols on the contrast-enhanced increase in BMD.

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POS1152

BONE AND MUSCLE IMPAIRMENT AND HIGHER VISCERAL ADIPOSE TISSUE MASS IN WOMEN WITH LONG-TERM POLYARTICULAR JUVENIL IDIOPATHIC ARTHRITIS

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Background: Some studies suggest that patients with juvenile idiopathic arthritis (JIA) may have reduced bone parameters and muscle mass. Despite those considerations, there is no validated consensus about this topic in the literature as the population and the methods for bone and muscle evaluation are often heterogeneous and not standardized.

Objectives: To assess bone parameters and body composition of women with long-term polyarticular JIA and compare them to healthy controls.

Methods: Twenty-seven women with long-term polyarticular JIA were compared with twenty-seven healthy controls, matched by sex, age, and body mass index (BMI). Dual-energy X-ray absorptiometry (DXA) was performed to evaluate the lean mass, body fat percentage (% Fat), and visceral adipose tissue mass (VATm). High resolution peripheral quantitative computed tomography (HR-pQCT) at the distal radius and tibia was performed to assess trabecular (Tb.) and cortical (Ct.) volumetric bone mineral density (v.BMD) and strength bone parameters (stiffness - S; estimated fail load - FL). Group means were compared using Student's t-test.

Results: Polyarticular JIA patients have a lower trabecular and cortical volumetric bone density, a lower bone strength, and a lower lean mass compared to healthy controls. Moreover, long-term JIA patients have a higher visceral adipose tissue mass (Table 1).

Table 1. Bone parameters using high resolution peripheral quantitative computed tomography (HR-pQCT) and body composition in long-term polyarticular patients and healthy controls.

	Polyarticular JIA n=27	Healthy controls n=27	*p-value*
Age, years	31.8 ± 7.6	33 ± 8.2	0.597
BMI, Kg/m^2	24 ± 4.8	24.6 ± 4.7	0.931
Disease duration, years	22 ± 10	-----	
Remission or low activity, n (%)	16 (59)	-----	
Use of prednisone, n (%)	5 (18)	-----	
Rheumatoid factor	9 (33)	0 (0)	
Lean mass, kg	35.7 ± 4.7	39 ± 7.2	**<0.001**
%Fat, %	39 ± 8	37 ± 7	0.364
VATm, kg	588 ± 538	212 ± 209	**0.001**
HR-pQCT at the distal radius			
Tb.v.BMD, mg HA/cm^3	125 ± 32	159 ± 38	**<0.001**
Ct.v.BMD, mg HA/cm^3	994 ± 46	1035 ± 43	**<0.001**
S, kN/mm	64 ± 11	78 ± 18	**0.001**
FL, N	3174 ± 879	3710 ± 827	**<0.001**
HR-pQCT at the distal tibia			
Tb.vBMD, mg HA/cm^3	128 ± 48	162 ± 32	**0.003**
Ct.vBMD, mg HA/cm^3	990 ± 57	993 ± 52	0.811
S, kN/mm	179 ± 39	212 ± 40	**<0.001**
FL, N	8519 ± 1773	9675 ± 2525	**0.004**

Data expressed as mean ± standard deviation or frequency (percentage). Tb.vBMD – trabecular volumetric bone mineral density, Ct.vBMD – cortical volumetric bone mineral density; S - stiffness; FL - estimated fail load

Conclusion: Pre-menopausal women with long-term polyarticular JIA have an impairment of bone mineral density at peripheral sites in addition to lower muscle mass and higher visceral adipose tissue. These findings may contribute to the increasing osteoporosis/fractures and cardiovascular risk in this population, suggesting that measures should be considered to prevent these damages.

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POS1153

CHARACTERISTICS OF GUT MICROBIOME AND THEIR ASSOCIATIONS WITH PERIPHERAL LYMPHOCYTE SUBPOPULATIONS AND CYTOKINES IN RHEUMATOID ARTHRITIS PATIENTS COMPLICATED WITH OSTEOPOROSIS

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Background: Osteoporosis(OP) is one of the major comorbidities of rheumatoid arthritis(RA) which is associated with immune disorders[1]. The gut microbiota has been highlighted to be an important environmental factor to influence immune system in maintaining bone health and regulating bone remodeling[2]. However, the alterations of intestinal flora and its relationship with immune system in RA patients with OP are unclear.
Objectives: To investigate the characteristics of gut microbiome as well as the associations between flora and peripheral lymphocyte subpopulations and cytokines in rheumatoid arthritis patients complicated with osteoporosis.
Methods: Total 28 RA patients were divided into 14 RA-non-OP and 14 gender- and age-matched RA-OP groups according to their bone mineral density (BMD) and the history of fragility fracture. Gut microbiota of participants were investigated by 16s rRNA and peripheral lymphocyte subsets and cytokines were assessed via flow cytometry. Indicators like erythrocyte sedimentation rate (ESR), C-reaction protein (CRP), anti-cyclic citrullinated peptide antibody (ACPA) and anti-mutated citrullinated vimentin (MCV) antibody were recorded meanwhile. Alpha diversity (ACE, Chao1, Simpson, Shannon) and beta diversity indices were analyzed using QIIME2. Biomarker species were recognized based on STEMP. Spearman analysis was adopted for correlation of two variables. All *P*-values reported herein were two-tailed and *P*-value<0.05 was taken as statistically significant.
Results: The alpha-diversity have no significant difference between RA-non-OP and RA-OP groups (*P* >0.05, Figure 1A). The community structure of microflora differed between two groups (*P* <0.05, Figure 1B). As for the composition of intestinal flora at genus level, Faecalibacterium, Proteus, Catenibacterium, Enterobacter and Erysipelatoclostridium in RA-OP group as well as Lachnospiraceae_ND3007_group, Parasutterella, Megasphaera, Tyzzerella, UCG-005, Clostridium_sensu_stricto_1, UCG-002, Lachnospiraceae_NK4A136_group, Christensenellaceae_R-7_group, Prevotella, Parabacteroides in RA-non-OP group were significantly increased (Figure 1C). There were positive correlations between Lachnospiraceae_NK4A136_group and the level of T, Th1 and Th17 cells, but negative relevance with ESR, CRP and IL-10 (*P* <0.05). The relative abundance of Faecalibacterium was negatively correlated with IL-2, IL-4, TNF-α and positively with MCV (*P* <0.05). Clostridium_sensu_stricto_1 and Lachnospiraceae_ND3007_group were negatively correlated with ACPA and MCV respectively as well as IL-2 (*P* <0.05, Figure 1D-E).
Conclusion: Abnormality of immune system may contribute directly or indirectly to OP in RA, which may be related to the disturbance of gut microbiota.

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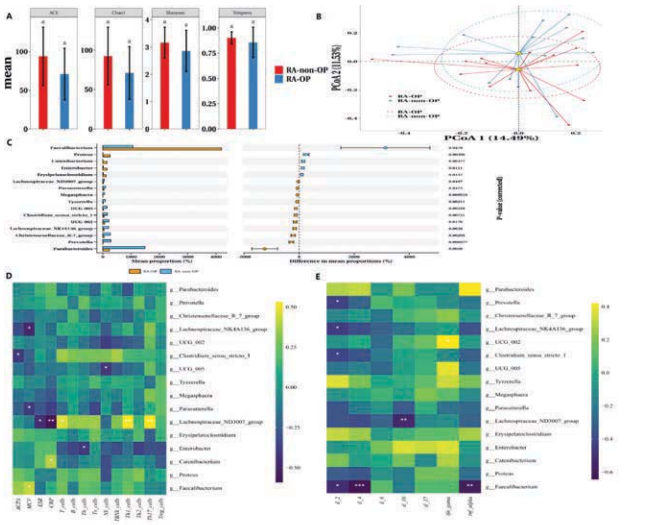

Figure 1 (A) Alpha-diversity indexs between RA-non-OP and RA-OP groups was shown using boxplot. (B) Beta diversity of the gut microbiome between RA-non-OP and RA-OP patients was revealed by Bray-Curtis distances. (C) STEMP was adopted to detect biomarker species. (D-E) Relationship between gut microbiota and lymphocyte subsets as well as cytokines. **P*<0.05, ***P*<0.01.

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Crystal diseases, metabolic bone diseases other than osteoporosis

POS1154

OUTCOMES AND RESOURCE UTILIZATION AFTER TOTAL HIP ARTHROPLASTY IN PATIENTS WITH CALCIUM PYROPHOSPHATE DEPOSITION DISEASE

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Background: Total hip arthroplasty (THA) is a safe and effective treatment option in patients with advanced degenerative joint disease who have failed conservative management. Calcium pyrophosphate deposition disease (CPPD) is a common crystal-induced arthritis in older adults characterized by the deposition of calcium pyrophosphate crystals in the articular and periarticular tissues[1]. CPPD might manifested with acute and chronic arthritis that can lead to joint damage and the need for joint replacement. To our knowledge, no previous studies investigated the outcomes of CPPD patients who underwent THA.
Objectives: We aim to examine the mortality, in-hospital complications, and resource utilization following THA in patients with and without CPPD.
Methods: We queried the US National Inpatient Sample (NIS) database to identify patients who underwent THA between 2006 and 2014. The ICD-9 code 81.51 was used to identify the patients who underwent THA and of those, we classified 2 groups of patients: (i) those with ICD-9 codes defining CPPD (275.49 and 712.1–712.39) and (ii) those without any CPPD code. Data collection included patient demographics and comorbidities. Outcomes post-THA were in-hospital mortality, hospital length of stay, hospital charges, and discharge disposition. Associations between CPPD and specific morbidity were evaluated with chi-square tests. T tests were used for continuous variables.
Results: Among the 4,111,808 (adjusted for sampling weight) patients who underwent THA between 2006 and 2014, 6198 (0.15%) had CPPD, with a mean age of 77 years and 65.2% were females (Table 1). CPPD patients were more likely to be older (mean age 77 vs 72.7; p<0.001) than non-CPPD patients. Comorbidities more frequently observed among CPPD patients included chronic kidney disease, osteoarthritis, rheumatoid arthritis, gout, hyperparathyroidism and hypomagnesemia. Further, Charlson Comorbidity Index scores ≥ 2 was more frequent seen in CPPD (96.1% vs 89.1%, p <0.001). The in-hospital mortality post-THA was lower in the CPPD patients (0.76% vs 1.72%, p <0.001). THA in CPPD patients was associated with a longer mean length of stay than those

without CPPD (6 vs 5.1 days; p <0.001) while mean total charges were not statistically different between the 2 groups (p=0.344). CPPD patients were more likely to be discharged to rehabilitation or other nursing facilities (p<0.001).

Table 1. Demographics, clinical characteristics, outcomes and resource utilization of patients with and without CPPD who underwent hip arthroplasty between 2006-2014.

	No CPDD, n (%) (N=4105610)	CPPD, n (%) (N=6198)	P-value*
Age in years at admission, median (mean ± SD)	75 (72.7 ± 31.5)	80 (77.0 ± 24.2)	<0.001†
Female	2507971 (61.1)	3979 (64.2)	<0.001
Chronic kidney disease	516688 (12.5)	1154 (18.6)	<0.001
Osteoarthritis	684171 (16.6)	1280(20.6)	< 0.001
Gout	139648 (3.4)	330 (5.3)	<0.001
Rheumatoid arthritis	199175 (4.8)	478(7.7)	<0.001
Hyperparathyroidism	7959 (0.1)	24(0.3)	<0.001
Hypomagnesemia	100390 (2.45)	239 (3.86)	<0.001
Charlson Comorbidity Index score ≥ 2	3659906 (89.1)	5961(96.1)	<0.001
Outcomes/Resource utilization			
Length of stay, (mean ± SD)	5.15 ± 11.72	6.04 ± 13.91	<0.001†
Total hospital charges, (mean ± SD)	$ 41284 ± 108238	($ 42757 ± 124894)	0.344†
Death during hospitalization	70706 (1.7)	47 (0.7)	<0.001†
Discharge Disposition			
Home (including home health care)	2653860 (64.7)	3558 (57.4)	<0.001
All others§	1447312 (35.3)	2635 (42.5)	<0.001

*Chi-square P except †t-test §All others include transfer to nursing or rehabilitation facility.

Conclusion: CPPD patients who underwent THA were more likely to be older, with a higher comorbidity burden, longer length of stay, and discharged to a non-home setting, than non-CPPD patients.

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POS1155 THE INTERNATIONAL X-LINKED HYPOPHOSPHATAEMIA (XLH) REGISTRY: OVERVIEW OF THE DATA SET

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Background: X-Linked Hypophosphataemia (XLH) is a rare, progressive, lifelong, hereditary renal tubule phosphate-wasting disorder characterised by a pathological increase in fibroblast growth factor 23 concentration/activity.[1] Despite XLH being increasingly recognised as a chronic progressive disease, there are few data documenting its natural history or the impact of treatment on patient outcomes.[2] The International XLH Registry was established to address this lack of information on XLH to help inform future clinical management. The Registry will collect data to characterise the treatment, burden of disease, disease progression and long-term outcomes of XLH.

Objectives: To provide an overview and status update of the International XLH Registry as of 31 December 2021.

Methods: The International XLH Registry (NCT03193476) was initiated in August 2017, aims to recruit 1,200 children and adults with XLH, and will run for 10 years. This Registry is an international, multicentre, non-interventional data collection programme and will provide the largest single dataset representing children and adults with XLH. To be eligible for inclusion in the registry, patients must meet all the following criteria:1) Male or female subjects of all ages; 2) Diagnosis of XLH with clinical, radiological, biochemical and/or genetic findings consistent with XLH. The Registry captures any treatment details and clinical outcome variables in patients with XLH and patients are followed for as long as informed consent (and assent, where applicable) and regulatory permissions are maintained. Only data collected during standard routine examinations are recorded within the Registry, and no specific examinations/data entries are mandated. Parameters collected at baseline included demographics, medical and treatment history, and clinical presentation data. The conduct of the International XLH Registry is overseen by 17 Steering Committee physician members representing the region.

Results: As of 31 December 2021, 1,043 subjects diagnosed with XLH were enrolled from 88 hospital sites in 19 countries. The geographic distribution of subjects is as follows: Belgium n=29, Bulgaria n=7, Czech Republic n=8, Denmark n=23, France n=267, Germany n=79, Hungary n=11, Ireland n=5, Israel n=21, Italy n=88, The Netherlands n=26, Norway n=23, Portugal n=9, Slovakia n=5, Slovenia n=3, Spain n=55, Sweden n=43, Switzerland n=17, and the UK n=324. A further 30 sites are yet to enrol (including sites in Austria and Latvia). Overall, 400 adults (18–29y, n=116; 30–39y, n=81; 40–49y, n=95; 50–59y, n=58; ≥60y, n=50) and 620 paediatric subjects (<5y, n=138; 5–12y, n=321; 13–17y, n=161) have been enrolled (date of birth not reported, n=23). The majority of enrolled subjects are female (648 (62.1%), with 372 male (35.7%) and 23 for whom sex was not reported (2.2%). The quantity of data from the patients included in this Registry will enable ongoing snapshot and prospective analyses to be conducted over the coming years to answer research questions and inform clinical practice.

Conclusion: This International XLH Registry forms the largest dataset of subjects with XLH collected to date. Patients have been recruited from a wide geographical region and baseline demographics are consistent with a hereditary X-linked dominant disease. Information collected during the 10-year Registry duration will generate real-world evidence to help inform clinical practice throughout the region, with the aim of improving the care and quality of life of adults and children living with this debilitating disease.

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POS1156 PHASE 1 TRIALS OF NOVEL ORAL ENZYME THERAPY (ALLN-346) FOR HYPERURICEMIA & GOUT: SAFETY, PHARMACODYNAMICS, AND LACK OF SYSTEMIC ABSORPTION OF SINGLE AND MULTIPLE ASCENDING DOSES IN HEALTHY VOLUNTEERS

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Background: Currently available therapies for gout in patients with advanced chronic kidney disease (CKD) are either dose-limited or contraindicated due to safety and tolerability concerns. In gout patients with advanced CKD, the intestinal tract becomes the major route of urate elimination, in contrast to healthy people with normal kidney function whose kidneys are the primary route of uric acid excretion.[1.] Considering some of the limitations of present urate lowering therapies (ULTs) in gout & CKD and the extra-renal pathway of urate secretion, a new oral therapy with ALLN-346 (engineered urate oxidase) is under development as a non-absorbed, urate specific enzyme, designed to enhance degradation and secretion of urate in the intestinal tract. [2]

Objectives: To assess safety and tolerability and evidence for the lack of systemic absorption at various dose levels of ALLN-346 in normal healthy volunteers (NHV) up to 7 days.

Methods: Two randomized, double-blind Phase 1 studies of ALLN-346 or placebo were conducted in adult NHV in a domicile setting; a single-ascending dose (SAD) study of 3 doses on a single day of dosing, and a multiple ascending dose (MAD) study of 2 doses during 7 days (NCT04236219 and NCT04829435, respectively). In the SAD study, subjects received 3 ascending doses of ALLN-346 (3 capsules,6 capsules, and 6 capsules administered twice, or placebo) and were randomized 3:1 (ALLN-346:placebo, n=24). In the MAD study, subjects received 3 (Cohort A) or 5 (Cohort B) of ALLN-346 capsules or placebo (2:1 randomization, n=18) administered orally 3 times daily for 7 days. To assess possible ALLN-346 absorption, a specific ELISA and uricase potency assay were used on PK serum samples collected from all subjects in both studies pre-dose and at intervals post dose.

Results: In both studies, all randomized subjects completed treatment with 100% compliance. ALLN-346 was well-tolerated, with no serious adverse

events (AE) and with no clinically significant safety signals across all cumulative doses. Clinical and laboratory parameters revealed no clinically significant safety signals among all cumulative dosing cohorts across hematology, serum biochemistry, vital signs, or ECGs. The majority of reported AEs were mild with no pattern of differences between ALLN-346 and placebo. No evidence of systemic absorption of ALLN-346 was seen, as confirmed by both ELISA and by uricase potency assay of all PK serum samples from all subjects from SAD (n=240) and MAD (n=324).

Conclusion: ALLN-346, a new oral enzyme therapy in development for the treatment of hyperuricemia and gout in advanced CKD was well tolerated. Consistent with its mechanism of action, no evidence of systemic absorption was demonstrated. Furtherstudies in hyperuricemia patients with gout and CKD are underway.

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POS1157 SAFETY AND EFFICACY OF ALLN-346 ORAL ENZYME THERAPY IN PATIENTS WITH HYPERURICEMIA AND CHRONIC KIDNEY DISEASE (CKD): RESULTS OF THE PHASE 2A STUDY 201

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Background: Currently available urate lowering therapies (ULTs) are limited in their use for gout patients with advanced CKD based on dosing restrictions, tolerability, safety concerns, and reduced effectiveness, compared to options for the broader gout population. In gout patients with advanced CKD, the intestinal tract becomes the major route of urate elimination, as opposed to in healthy people with normal kidney function where kidneys are the primary route of uric acid excretion.[1] Considering some of the limitations of present urate-lowering therapies (ULTs) in gout & CKD and the extra-renal pathway of urate secretion, a new oral therapy, ALLN-346 (engineered urate oxidase), is under development as a non-absorbed, urate specific enzyme, designed to enhance degradation and secretion of urate in the intestinal tract.[2]

Objectives: To assess the safety, tolerability, and initial bioactivity data of ALLN-346 in adults with hyperuricemia and CKD.

Methods: This one-week inpatient Phase 2a study (NCT04987242) was conducted at a clinical pharmacology unit. Eleven otherwise healthy adult patients with hyperuricemia (sUA ≥ 6.8 mg/dL) and normal to Stage 2 CKD (eGFR ≥60), not on concurrent ULTs, were randomized (2:1) to receive either 5 capsules of ALLN-346 or matching placebo, three times daily for 7 days. Serum urate was measured daily, and urine uric acid was assessed on days -2, -1, 1, 4, and 7. Safety was monitored throughout the study. To assess possible ALLN-346 systemic absorption, a specific ELISA was used on serum samples collected pre- and post-dose over 7 days.

Results: Of the 11 patients 7 received ALLN-346 and 4 received placebo. Most patients had Stage 2 CKD, including 5 of the 7 subjects treated with ALLN-346. A statistically significant reduction in mean sUA was recorded with ALLN-346 compared to placebo [Figure 1]. The largest mean % reduction in sUA was observed among patients with stage 2 CKD; sUA reduction was correlated with eGFR in the ALLN-346 group (r=0.95; *P*=0.003), but not the placebo group (r=-0.2; *P*=0.91). No serious adverse events were reported, and clinical and laboratory parameters revealed no significant safety signals. Lack of systemic absorption of ALLN-346 was confirmed by ELISA assays.

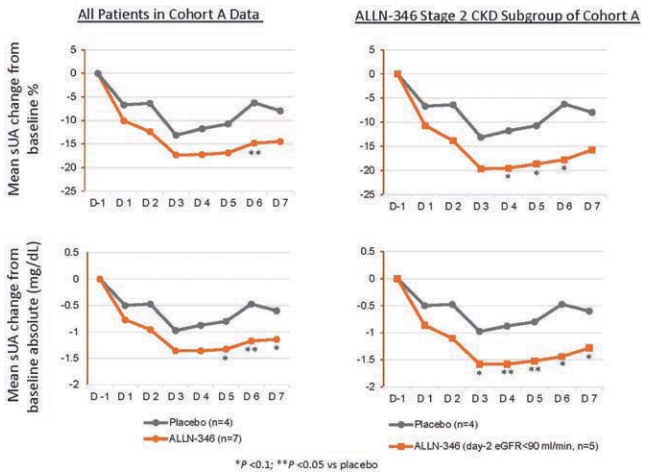

Figure 1. Absolute and Percent Change from Baseline in Serum Urate over 7 -days of Treatment

Conclusion: In this study, oral therapy with ALLN-346 for 7 days was well tolerated and resulted in a significant reduction in sUA. Consistent with the known pathophysiologic adaptation of increased intestinal elimination of uric acid in patients with impaired kidney function and the intestinal-based mechanism of action of ALLN-346, there was a strong correlation between the effect of ALLN-346 on sUA reduction and the level of kidney function. The generated data support proof of pharmacology for the intestinal mechanism of action of ALLN-346 to degrade urate either formed or secreted in the gut. Future studies in the larger gout population with CKD are underway.

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POS1158 CHARACTERIZATION OF GOUT IN US PATIENTS UNDERGOING HEMODIALYSIS (HD) AND PERITONEAL DIALYSIS (PD)

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Background: Gout is the most common inflammatory arthritis and occurs frequently in patients with renal disease often leading to a significant burden on quality of life and functional status.[1,2] Despite the established connection of renal disease with gout, little has been reported on the prevalence, patient characteristics, and associations of gout with other outcomes in the US hemodialysis (HD) and peritoneal dialysis (PD) population.

Objectives: This project used a large end-stage renal disease (ESRD) focused-database, Dialysis Outcomes and Practice Patterns Study (DOPPS), to examine gout in dialysis-dependent patients.

Methods: Gout patients were identified by active prescription (Rx) of (1) colchicine, (2) febuxostat, or (3) allopurinol; or by (4) prior diagnosis of gout from US cohorts of 70,297 HD (DOPPS, 2012-2020) patients and 5117 PD (Peritoneal DOPPS, 2014-2020) patients. Outcomes of HD and PD patients with and without a history of gout were compared with propensity score matching. Outcomes included erythropoietin resistance index (ERI = ESA dose/(hemoglobin*weight),

cardiovascular death, all-cause mortality/hospitalization, and baseline patient-reported outcomes (PROs).

Results: Gout prevalence was 13% in HD and 21% in PD and was highest among incident dialysis patients. Of the gout patients identified, the most-commonly used gout-related medications were allopurinol (9-12%), followed by colchicine (2-3%), and then febuxostat (1%, Figure 1). Both HD and PD patients with gout (vs. no gout) were older and more likely male. Gout HD and PD patients had higher BMI and higher prevalence of cardiovascular comorbidities than HD and PD patients without gout. After propensity score matching, mean ERI was 4% higher for gout vs. non-gout patients, while there was minimal evidence of association with clinical outcomes (mortality and hospitalization) or PROs.

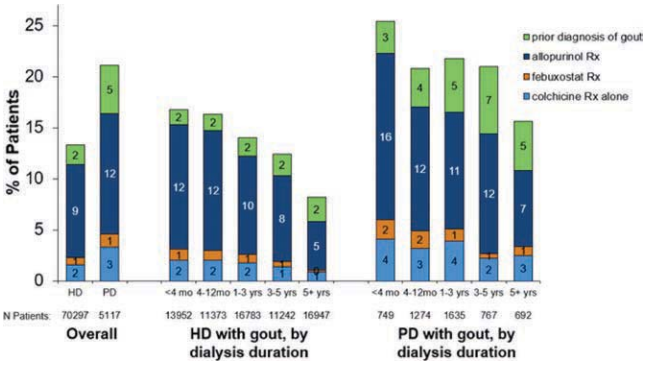

Figure 1. Gout prevalence by dialysis duration in patients undergoing HD and PD. Criteria for gout included gout diagnosis and use of a urate-lowering therapy. HD, hemodialysis; PD, peritoneal dialysis; mo, months; Rx, prescription; yrs, years. Some patients were included in multiple gout categories.

Conclusion: Gout was common in US HD and PD patients, with a large proportion of these patients treated with drugs indicated for hyperuricemia (allopurinol and febuxostat) and gout flares (colchicine). The true prevalence of gout was likely higher than observed when considering potential under-ascertainment of gout diagnosis history in nephrology/dialysis-focused clinical settings.[3] This report provides a snapshot of gout in the US dialysis population and offers opportunities to expand on research to improve awareness and care for patients with gout and ESRD.

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POS1159 SUBCLINICAL ATHEROSCLEROSIS IN GOUTY ARTHRITIS PATIENTS: A CROSS SECTIONAL STUDY BY ULTRASONOGRAPHY

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Background: Hyperuricemia is closely associated with cardiovascular disease (CVD). However, it has not been definitively established whether this association is independent of traditional cardiovascular risk factors in gout patients.

Objectives: To clarify the incidence of subclinical atherosclerosis and associated factors in gouty arthritis patients by ultrasonography.

Methods: We conducted this cross-sectional study to investigate the frequency and clinical factors correlated with carotid changes in patients with gout by ultrasonography.

Results: 200 consecutive patients with gout were recruited. Carotid ultrasound was performed in all patients in First hospital of Peking University from 2014 to 2020, finding atheroma plaques in 33.0% patients. None of these patients received urate-lowering drugs. On univariate analysis, the pattern was significantly associated with age, estimated gout duration, clinical tophi, double contour sign at the scanned joint and decreased estimated glomerular filtration rate; While arterial hypertension, hyperuricemia were not associated with carotid plaques. On multivariable analysis, the atheroma plaques were associated with estimated disease duration, clinical tophi, double contour sign and decreased estimated glomerular filtration rate. Thus, carotid plaque was frequently demonstrated in gout patients with tophaceous gout and associated with features of tubulointerstitial nephritis. This finding reveals the hypothesis of crystal-led inflammation and comorbidities relates to gout associated cardiovascular disease, predominantly seen in high uric acid burden patients, which could be an important treatment target for gout therapy.

Conclusion: Ultrasonography can detect crystal deposits in joints and connective tissues. We investigated the frequency and clinical correlates of plaques in carotid by ultrasound in consecutive gout patients.

The pattern was significantly associated with age, estimated gout duration, clinical tophi, double contour sign and decreased estimated glomerular filtration rate.

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POS1160 PROTECT: PEGLOTICASE TREATMENT FOR UNCONTROLLED GOUT IN KIDNEY TRANSPLANTED PATIENTS; RESULTS FROM A PHASE 4 TRIAL

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Background: A phase 4 trial (NCT04087720) of kidney transplant (KT) recipients on stable immunosuppressants with uncontrolled gout previously reported that pegloticase produced a sustained decrease in serum uric acid (sUA) levels and was associated with clinically meaningful improvements in pain and disability without worsening of key kidney function markers. Pegloticase treatment was well tolerated overall with no infusion reactions or anaphylaxis. Here we report additional exploratory and secondary endpoints.

Objectives: To evaluate the results of clinically important efficacy endpoints as supportive evidence for the efficacy of pegloticase in kidney transplant patients on immunosuppression.

Methods: PROTECT a multicenter, open-label, efficacy and safety study of pegloticase in included kidney transplant recipients (KT>1 year prior) with uncontrolled gout (sUA ≥7 mg/dL, oral urate lowering therapy contraindication/inefficacy, and with either visible tophi, chronic gouty arthritis, or ≥2 flares in past year), who had a functioning graft (estimated glomerular filtration rate [eGFR] ≥15 ml/min/1.73m^2), and were on a stable immunosuppressant regimen. Pegloticase (8 mg infusion) was administered biweekly for 24 weeks (12 infusions) followed by a final follow up visit 3 months post-treatment. The global health component of the Health Assessment Questionnaire (HAQ-Health), and the physician global assessment of gout (PGA) were assessed at baseline, weeks 6, 14, 20, 24, and the end of pegloticase infusions (EOI) visit (if applicable, when the final infusion occurred prior to week 22). Both were visual analog scales (VAS), where HAQ-health ranged from 0 (very well) to 100 (very poor) and PGA ranged from 0 (excellent) to 10 (very poor). Heart rate and blood pressure measurements were recorded at baseline, weeks 6, 12, 18, 24 and the EOI visit.

Results: 20 patients received at least 1 dose of pegloticase and were included in the analysis with the majority (90.0%) 40 to 81 years of age. Most were male (85.0%), 45.0% white, and 35.0% black or African American. Median body weight (88.46 kg) and body mass index (29.68 kg/m^2) were high. Median baseline eGFR and baseline Urine Albumin-Creatinine Ratio (UACR) were 41.70 mL/min/1.73m^2 and 312.00 mg/g, respectively. An improvement from baseline to weeks 14

(n=18), and 24 (n=15 [PGA], n=14 [HAQ]) in mean PGA and HAQ-Health was observed. Change from baseline (Mean [SD]) at 14 and 24 weeks for PGA was -2.3 (1.94) and -2.3 (2.19), and for HAQ-Health was -32.74 (21.26) and -21.52 (27.47) respectively. Improvement was sustained at the 3-month post-treatment follow-up visit. Mean decreases from baseline in sitting systolic blood pressure, diastolic blood pressure, and mean arterial pressure were observed at weeks 6, 12, 18 and 24. Change from baseline values at 24 weeks (n=15) for systolic, diastolic and mean arterial pressures were (Mean [SD]) -11.01 (14.04), -4.37 (9.18), and -6.58 (9.675) mmHg respectively. Heart rate showed no clinically meaningful trends from baseline at any of the post-baseline timepoints.

Conclusion: Clinically important improvements in both HAQ and PGA were demonstrated for pegloticase treated kidney transplant patients. Improvements were also observed in systolic, diastolic, and mean arterial blood pressure. These data support the benefits of pegloticase treatment for uncontrolled gout in kidney transplant recipients using immunosuppression.

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POS1161 CAN DOCTORS TREAT GOUT WELL? INSIGHT ON GOUT MANAGEMENT IN REFERRAL CENTRES

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Background: Recent studies have shown a lack of implementation of gout recommendations in primary care. In this context of therapeutic inertia, the French Society of Rheumatology (SFR) published its first recommendations on gout (RECO) in 2020 [1,2], which were deliberately simple and concise.

Objectives: To determine the profile of patients referred to French gout expert centres, and to examine the results of their management.

Methods: Three hundred patients attending a first visit for gout management in three French referral centres were retrospectively included. Visits were performed at baseline (M0) and scheduled for month 6 (M6), month 12 (M12), and month 24 (M24). Data collected included: patient profile; disease activity and treatments; serum urate (SU) level; estimated glomerular filtration rate (eGFR).

Results: Patients were 81% male, mean age 62.2 ± 15.2 years, 42.7% prevalence of eGFR <60ml/min/1.73m^2, 28.1% diabetes mellitus, and 25.4% had a history of major cardiovascular event. Management followed French recommendations after the baseline visit in 94.9% of cases. Overall, 50 patients (16.7%) received off-label anakinra for flare treatment or flare prophylaxis. SU levels were below 6.0mg/dL in 59.4% of patients at M6, 67.9% at M12, and 78.6% at M24. At M24, 50% of patients were treated with allopurinol (313 ± 105 mg/d), which exceeded renal restrictions of doses in 61.5% of them, and 48.2% received febuxostat (84 ± 36mg/d). At inclusion, 94% of patients had experienced at least one flare in the previous six months, versus 23.6% at M12, and 13.1% at M24 (of which 8/12 (66.7%) had SU>6.0mg/dL).

Conclusion: Simple application of gout management guidelines is feasible in clinical practice, and is efficient with a majority of patients achieving SU targets and clinical improvement. A minority of patients in referral centres have 'difficult-to-treat' gout requiring specific management.

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POS1162 PREVALENCE AND IMPACT OF DERMATOLOGIC CONDITIONS IN PATIENTS WITH GOUT

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Background: Gout is the most common inflammatory arthritis in adults and affects approximately 3-5% of the population in Europe and the United States.[1] Chronic hyperuricemia leads to monosodium urate (MSU) crystal deposition in both joints and soft tissues, including the heart, eyes, kidney, skin, and liver.[2] Systemic manifestations of gout have been well-characterized, with dermatologic involvement typically described as subcutaneous tophi, miliary gout, gouty panniculitis, and gout nodulosis.[2] Other dermatologic conditions may occur more often in gout patients and provide better understanding of a patient's overall condition.

Objectives: This claims-based study examined the prevalence of dermatological conditions in a large US population of gout patients. Patients with and without dermatologic conditions (identified by diagnosis codes) were compared to assess comorbidity burden, review healthcare utilization, and better understand the underlying consequences of dermatological manifestations of gout.

Methods: The Symphony 2012-2017 claims database was searched to identify patients with ≥1 ICD-9 or -10 gout code (ICD-9: 274.xx, ICD-10: M1*) using Bellweather software (PearlDiver Technologies™). All patients were in the database ≥1 year before and ≥2 years after first gout code (index). Patients were said to have a dermatologic condition if they had ≥1 diagnosis code for atopic dermatitis (ICD-9: 6918, ICD-10: L2*), psoriasis (ICD-9: 6961, ICD-10:L4*), osteomyelitis (ICD-9:73008, ICD-10: M86*), melanoma (ICD-9:1729, ICD-10: C43*), peripheral ulcers (ICD-9: 70710), varied cutaneous abscesses (ICD-9: 9829, ICD-10: L022*), or cellulitis (ICD-9:6826, ICD-10: L03*). Diagnosis code prevalence and healthcare utilization were examined and compared between those with/without a dermatological diagnosis code.

Results: Of the nearly 1.7 million identified gout patients, 29% had ≥1 dermatology diagnosis code. Patients with and without ≥1 dermatology code were of similar age at index (62.72 vs. 61.84 years) but those with ≥1 code were less often male (62% vs. 65%). The most common dermatological codes identified included cellulitis (10.7%), dermatitis (4.8%), psoriasis (2.2%), and osteomyelitis (2.1%, Table 1). Overall, comorbidity diagnosis codes were more prevalent in patients with ≥1 dermatology code, including hypertension, chronic kidney disease, cardiovascular disease, and type 2 diabetes (Table 1). Additionally, healthcare utilization and pain medication use were higher in gout patients with dermatological conditions despite similar ULT use.

Table 1. Incidence of select dermatologic conditions in gout vs general US populations and comorbidity prevalence among gout patients with/without ≥1 dermatological diagnosis code.

Dermatologic conditions	Gout population	General US population	p-value
Cellulitis, incidence, cases/100,000 person-yrs	1094	199[3]	<0.001
Osteomyelitis, incidence, cases/100,000 person-yrs	219	22[4]	<0.001
	Gout pts with ≥1 dermatology code (N=488,356)	**Gout pts without a dermatology code** (N=1,201,082)	
Age, years, mean ± SD	62.72 ± 12.35	61.84 ± 12.67	----
Male, n (%)	305,012 (63%)	779,103 (65%)	<0.001
Comorbidity, n (%)			
Hypertension	446,577 (91%)	1,040,381 (87%)	<0.001
Chronic kidney disease	215,670 (44%)	408,826 (34%)	<0.001
Cardiovascular disease	358,930 (73%)	749,577 (62%)	<0.001
Type 2 diabetes	254,914 (52%)	435,911 (36%)	<0.001

Conclusion: These claims-based analyses suggest the prevalence of dermatologic conditions other than those historically associated with gout. Additionally, gout patients with dermatologic conditions had higher comorbidity burden than those without. Therefore, as with other conditions, the skin may provide clues of a larger, systemic disease burden.

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POS1163 PHARMACOKINETICS OF PEGLOTICASE AND METHOTREXATE POLYGLUTAMATE(S) IN PATIENTS WITH UNCONTROLLED GOUT RECEIVING PEGLOTICASE AND CO-TREATMENT WITH METHOTREXATE

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Background: In a prior open-label, single-arm trial in adults with uncontrolled gout (MIRROR open-label [OL] trial), methotrexate (MTX) co-treatment with pegloticase suggested improved efficacy of pegloticase by reducing its immunogenicity.[1,2] The current randomized, controlled trial (MIRROR RCT) confirmed that pegloticase-MTX co-therapy markedly increased pegloticase response rate (response defined as serum uric acid <6 mg/dL during ≥80% of Month 6) compared to pegloticase-placebo (PBO) co-therapy (71.0% vs. 38.5%) with a decreased infusion reaction rate and no new safety signals reported.
Objectives: To evaluate systemic exposures of pegloticase and its immunogenicity in uncontrolled gout patients receiving pegloticase with and without MTX as part of the MIRROR RCT; and to determine exposure of methotrexate polyglutamate(s) (MTX-PGs) in uncontrolled gout patients through Month 6 of treatment.
Methods: In MIRROR RCT, MTX (15 mg/wk) or matching PBO was given orally 4 weeks prior to the first pegloticase dose and continued weekly, in combination with pegloticase 8 mg given intravenously every 2 weeks, over a 52-week treatment period. Pre-infusion blood samples were collected to measure MTX polyglutamates (MTX-PGs, including MTX-PG_{1-5}) in red blood cells and pre- and post-infusion serum samples were obtained to measure trough (Cmin) and peak (Cmax) concentrations of pegloticase, respectively, at multiple visits. MTX-PG and pegloticase concentrations were summarized by visit and by treatment group. Pre-infusion serum samples for anti-polyethylene glycol (PEG) antibody (Ab) measurement were also collected at multiple pre-defined time points. Anti-PEG Ab incidence and titer were summarized by visit and by treatment group.
Results: Overall, higher Cmax and Cmin of pegloticase were observed in the pegloticase + MTX group than in the pegloticase + PBO group (Figure 1). At Week 14, median (first quartile [Q1], third quartile [Q3]) Cmin was 1.32 (0.73, 1.74) µg/mL and 0.63 (0.30, 1.28) µg/mL for the pegloticase + MTX and pegloticase + PBO groups, respectively. Median (Q1, Q3) Cmax was 3.01 (1.94, 3.94) µg/mL and 2.66 (1.45, 3.20) µg/mL for the pegloticase + MTX and pegloticase + PBO groups, respectively. Improved pegloticase response was associated with higher pegloticase concentrations. At Week 14, Cmin was below the quantitation limit (0.6 µg/mL) for 8 of 10 non-responders and 1.26 (0.72, 1.71) µg/mL for responders. MTX co-administration reduced the incidence of new anti-PEG antibody formation. The proportion of subjects with an increase from baseline in anti-PEG Ab titers or who were negative at baseline and developed an anti-PEG Ab response at ≥1 post-dose time point during pegloticase treatment was 29.5% and 51.0%, for the pegloticase + MTX and pegloticase + PBO groups, respectively. The pegloticase + MTX group had overall lower titer levels than those in the pegloticase + PBO group. Positive anti-PEG Ab status was associated with a lower pegloticase Cmin. Concentrations of MTX-PGs were maintained during the treatment course in the pegloticase + MTX group, suggesting compliance with MTX administration. There was no apparent difference in concentrations of MTX-PGs (including MTX-PG_3, the predominant form of MTX-PGs[4]) between responders and non-responders. MTX-PG concentrations were in the same range as those reported for low-dose oral MTX use in patients with rheumatoid arthritis,[3] suggesting no impact of pegloticase on MTX PK.

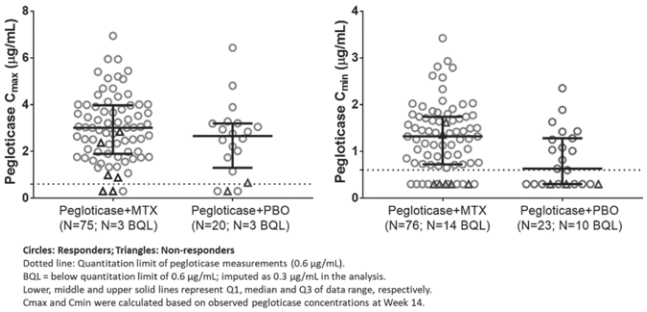

Figure. Comparison of pegloticase exposures (Cmax and Cmin) with and without MTX co-treatment

Conclusion: Pegloticase 8 mg IV every 2 weeks with MTX co-treatment (oral 15 mg weekly) reduced anti-PEG Ab incidence and resulted in higher pegloticase exposures compared to pegloticase administered with PBO, consistent with the increased clinical efficacy observed with pegloticase + MTX co-administration.
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POS1164 COMPARISON OF PATIENTS WITH EARLY-ONSET GOUT AND COMMON GOUT: A CLAIMS-BASED ANALYSIS

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Background: Data from the United States indicate that 8% of gout patients have disease onset before 40 years of age (early-onset gout [EOG]),[1,2] with similar age stratification in the United Kingdom, The Netherlands, and New Zealand.[3] At diagnosis, EOG patients have lower rates of renal and cardiometabolic comorbidities than their counterparts who developed gout at a later age.[4-6] Published reports also indicate that patients with EOG are less responsive to urate-lowering therapy[4] and more often have severe gout, with higher flare rate[4-6] and polyarticular disease occurrence.[4,5] At present, the literature is limited in comparisons between EOG and common gout (CG) patients.
Objectives: These claims-based analyses on a very large population examined and compared characteristics and comorbidity profile of patients with EOG and CG.
Methods: Patients with ≥1 ICD-9 or -10 gout code were identified in the Symphony claims database using Bellweather software (PearlDiver Technologies™). All patients were in the database ≥2 years before and ≥3 years after first gout code. Patients were said to have EOG if their first gout code occurred before 40 years of age. Patient demographics and comorbidities were compared to those with CG, defined here as first gout code at ≥50 years of age.
Results: 68,709 and 933,375 patients were classified as having EOG (mean age: 33.2±5.0 years) and CG (66.3±8.3 years), respectively. The EOG group had a higher proportion of men (72% vs. 62%). EOG and CG patients were in plan for a mean of 5.74±1.57 and 5.72±1.61 years, respectively after first gout diagnosis code. Prior to first gout code, comorbidity rates were lower in EOG than CG patients, including hypertension, cardiovascular disease, diabetes, stroke/transient ischemic attack, and renal disease. Additionally, the proportion of EOG and CG patients with hypertension, type 2 diabetes, and chronic kidney disease codes increased following the first gout code at a faster rate than in the general US population of a similar age (Figure 1).[7-9] As a result comorbidity rates were markedly higher in both EOG and CG groups in the years following gout diagnosis.
Conclusion: In agreement with prior studies,[4-6] these claims-based analyses suggest that patients with EOG have a lower comorbidity burden than patients with CG, though still higher than the general US population. Importantly, our

data suggest that, in the years following gout diagnosis, EOG patients develop comorbidities at a faster rate than their peers without gout. Further study of how gout influences comorbidity development in EOG patients is warranted to better understand and verify these claims-based findings.

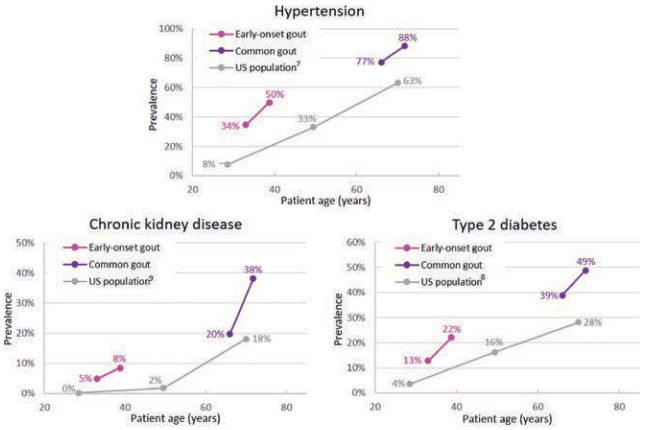

Figure. Key comorbidity prevalence and change with age in the early-onset gout (EOG), common gout (CG), and the general US populations.[7-9] First gout code occurred at mean age of 33 years in the EOG group and 66 years in the CG group. Mean time in plan following first gout code averaged 5.7 years in both groups.

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POS1165 ASSOCIATION OF LDHD RARE VARIANTS WITH EARLY-ONSET GOUT IN TWO FAMILIES WITH AN ADDITIONAL ASSOCIATION OF RHBG VARIANT IN ONE.

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Background: Elevated lactate is known to favor urine urate reabsorption by the URAT1 urate/anion exchanger. Autosomal recessive gout caused by pathogenic variant in the *LDHD* gene encoding for D-lactate deshydrogenase has been recently identified in a large consanguineous Bedouin-Israeli kindred (1).
Objectives: We report here on two families in whom early-onset gout was linked to other variants leading to deficient D-LDH enzymes.
Methods: Studies of the two families were approved by appropriate Ethics committees. Whole exome sequencing (WES) was used to identify the genetic cause of familial gout. Dosages of D-lactate were performed on immediately frozen serum and urine samples by ELISA, using a D-lactate colorimetric assay kit (Abcam ab83429).
Results: Family 1 was Melanesian, living in the Lifou island of New Caledonia. The two index patients were two sisters who developed gout at the age of 13 and 16 years respectively. When seen at the ages of 25 and 27 years, they both had severe gout with frequent polyarticular flares, and multiple tophi and destructive arthropathies in the earliest age of onset one. WES, performed on the 2 affected sisters, their non-consanguine parents, and an unaffected brother, showed that the 2 affected sisters carried homozygous rare variant in *DLDH* gene (NM_153486.3: c.206 C>T; rs1035398551). This variant was at heterozygote level in both parents and absent in the unaffected brother. It was considered as probably damaging according to in silico prediction software. No association with any other gene was found. The c.206C>T variant in *LDHD* was searched by Sanger sequencing method in 13 other extended family members. One 23 year-old brother of the two diseased sisters with atypical MTP flares, high uricemia and double contours at US examination of his MTPs, carried the c.206 C>T variant at the homozygous level. Three other heterozygous patients were found; two of whom were male with late-onset gout, the third one being a non-menopausal female with no gout. No variant carrier was found in the other 9 genotyped family members. The 3 homozygous patients for the c.206 C>T variant had very high hyperuricemia (range 738-834 was searched by Sanger sequencing method in 13 other extended family members. One 23 year-old brother of the two diseased sisters with atypical MTP flares, high uricemia and double contours at US examination of had very low or no D-lactate in plasma and urine. L-lactate blood and urine levels were normal in all subjects. Family 2 was Vietnamese, living in a remote area of central Vietnam. The two affected children suffered from an extremely severe, destructive gout, which started at the age of 21 years in a daughter and at the age of 9 in her youngest brother, who had developed for the last 3 years, dysarthria, night shakes, memory loss, urine incontinence and an inability to read and count and died at the age of 34, a few months after being seen by us. WES was performed in the two probands, their father and mother (who denied consanguinity), and an unaffected brother. An undescribed variant in *LDHD* (NM_153486.3: c.1363dupG) was identified in homozygous level in the 2 juvenile gout patients and at the heterozygous level in their 2 parents and unaffected brother. This variant led to a frameshift followed by a stop codon p.(AlaGly432fsTer58). In addition, the two juvenile gout patients were homozygous for an undescribed frameshift (NR_046115.1: c.1064dup) variant of the *RHBG* gene encoding for a Rhesus Blood Group family ammonium transporter. The two parents carried the heterozygous variant which was not identified in the non-gout brother.
Conclusion: We report on 2 families in whom autosomal recessive juvenile gout was due to rare or undescribed, damaging *LDHD* gene variants. In addition, we observed in the Vietnamese family, an additional non-described frameshift homozygous variant in *RHBG*, the pathophysiological role of which deserves to be investigated.

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POS1166 GOUT AND SERIOUS KIDNEY DISEASE IN THE US: A NATIONAL PERSPECTIVE

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Background: There is a strong association between gout and kidney disease due to the kidney's key role in uric acid excretion.[1-4] Several studies have also demonstrated that serum uric acid is an independent risk factor for decline in renal function[1,2]. There are little national data available regarding the clinical burden of kidney disease in gout patients in the US.
Objectives: To estimate the percentage of US hospitalizations with a concomitant diagnosis of gout and either acute or chronic kidney disease compared with percentage of hospitalizations with kidney disease in the general population.
Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. Detailed information including clinical and nonclinical data elements on each hospital stay including International Classification of Diseases (ICD) 10 diagnosis, age, gender, length of stay, payer, charges, and comorbidities etc. is available. We examined all hospitalizations with acute renal failure (ICD10 codes N170-179), chronic kidney disease stages 3-5 (ICD10 codes N183-185), N19 (unspecified kidney failure), and end-stage renal disease (ICD10 code N186) in persons with gout (ICD 10 codes M10.* and M1A.*) and compared these with hospitalizations with kidney disease in the general US population.

Results: In 2019, there were 35.4 million all-cause hospitalizations in the US. Of these, 7.9 million had a diagnosis of serious kidney disease (22.3%). There were 915,070 hospitalizations with primary or secondary diagnosis of gout in the US (mean age 70.8 years, 68.4% men and 31.6% women). Of these 533,365 hospitalizations (mean age 72.6 years, 65.9% men) also had a concomitant diagnosis of serious kidney disease (58.3%, p<0.0001 compared to general population). Concomitant diagnosis of serious kidney disease increased with age, reaching 38.3% of all hospitalizations in 65 years and older in the general population compared to 62.5% in persons with gout (p<0.001).

Table 1. Kidney disease-related hospitalization in the US general and gout populations.

	GENERAL US HOSPITALIZATIONS		US HOSPITALIZATIONS WITH COMORBID GOUT	
Patient Age	Overall Hospitalizations N	Hospitalizations with Serious Kidney Disease n (%)	Overall Hospitalizations N	Hospitalizations with Serious Kidney Disease n (%)
18-44 years	8,356,284	622,170 (7.4%)	32,445	13,480 (41.5%)
45-64 years	8,440,831	2,160,220 (25.6%)	232,695	116,490 (50.1%)
≥65 years	13,421,154	5,257,220 (39.2%)	649,865	414,620 (83.8%)
Total in 2019	**35,419,023**	**7,907,730 (22.3%)**	**915,070**	**533,365 (58.3%)**

Note: Total numbers include patients 0-17 years old.

Conclusion: Acute and chronic kidney disease are highly prevalent comorbid conditions in overall US hospitalizations. Among patients admitted with a diagnosis of gout, the proportion of kidney dysfunction is significantly higher affecting 58% of these hospitalizations. The high prevalence of kidney dysfunction in hospitalized gout patients in the US may represent an impactful component to the duration, complexity, and costs of hospital care.

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POS1167 EFFICACY AND SAFETY OF FEBUXOSTAT IN PATIENTS WITH STAGE 4-5 CHRONIC KIDNEY DISEASE NOT YET ON DIALYSIS: A META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: The efficacy and safety of febuxostat in patients with stage 4-5 chronic kidney disease (CKD) are still unclear, even though it's commonly used in clinical practice [1]. However, clinical trials are lacking to determine them due to ethical problems about enrollment of advanced CKD patients.

Objectives: We aimed to evaluate the efficacy and safety of febuxostat in patients with stage 4-5 CKD not yet on dialysis through a meta-analysis of observational studies.

Methods: We performed a systematic search in PubMed, Ovid MEDLINE, Embase, and the Cochrane Library to find articles reporting on advanced CKD patients from observational cohorts who start or take febuxostat at baseline in September 2021. Articles had to describe change from baseline in serum urate levels and renal function as assessed by estimated glomerular filtration rate (eGFR). The articles were screened by two independent reviewers (YP, HJ). Meta-analysis using a random-effects model was performed. R software was used for statistical analyses.

Results: Among 148 retrieved studies, 5 relevant observational studies were included in the meta-analysis. The febuxostat dose was administered at 10-120 mg per day, and the treatment period was 3 to 12 months. Five studies were included with a total of 327 patients to analyze urate-lowering efficacy. The urate-lowering effect after use of febuxostat medication showed statistical significance (weighted mean difference, -1.85; 95% CI, -2.04 to -1.67; I^2; 0%, Figure 1A). Three studies with 145 patients were available for assessment of eGFR. Renal function as assessed by eGFR did not decrease even after use of febuxostat (weighted mean difference, 0.11; 95% CI, -0.25 to 0.47; I^2; 45%, Figure 1B).

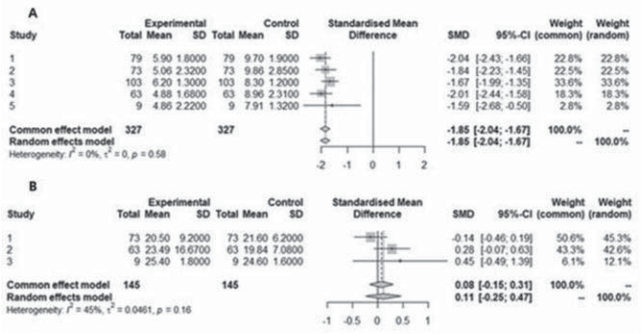

Figure 1. Meta-analyses of serum urate levels and estimated glomerular filtration rate at baseline and follow-up.

Conclusion: Our meta-analysis showed that febuxostat had good urate-lowering efficacy and renal safety in hyperuricemia patients with stage 4-5 CKD, who are not yet on dialysis. More studies with larger sample sizes and higher quality are required to clarify the efficacy and safety of febuxostat in advanced CKD.

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POS1168 TREAT TO TARGET OF GOUT: AN EVIDENCE-BASED CONSENSUS ON CLINICAL PRACTICE GUIDELINES

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Background: New therapies, management approaches and evidence regarding the management of gout have become available over the past years. This triggered the need for updated recommendations for the management of gout.

Objectives: to develop an up-to-date consensus evidence-based clinical practice guideline for the management of gout including recommendations for management of acute gout flares, optimum usage of urate lowering therapy for chronic gout as well as patient education and lifestyle guidance.

Methods: An extensive systematic literature review was performed, and evidence-based recommendations were extrapolated, based on 16-key questions identified according to population, intervention, comparator, and outcomes (PICO) approach. For each item, the level of evidence was determined using the Oxford Centre for Evidence-based Medicine (CEBM) system. These were evaluated by a panel of 17-experts via online surveys over a 2-round Delphi process.

Results: At the end of round 2, a total of 30-recommendation items, categorized into 10 domains to were obtained. Agreement with the recommendations (rank 7-9) ranged from 90-100%. Consensus was reached (i.e.≥75%of respondents strongly agreed or agreed) on the wording, the grade of recommendation and level of evidence of all the 30 clinical standards identified by the scientific committee. The guideline emphasized that all gouty patients should be screened for comorbidities. Based on this, an algorithm for treat to target management approach tailored to the individual patient's needs and associated comorbidities has been outlined.

Conclusion: This work provides updated evidence-based recommendations for the prevention and treatment of acute as well as chronic gouty arthritis. It provides an approach for physicians and patients making decisions on the management of gout. It will also facilitate improvement and uniformity of care.

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POS1169

THE INFLAMMATION INDUCED BY MONOSODIUM URATE AND CALCIUM PYROPHOSPHATE CRYSTALS DEPENDS ON OSMOLARITY AND AQUAPORIN CHANNELS.

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Background: The inflammation induced by monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals is driven by interleukin (IL)-1β production. This later relies on NLRP3 inflammasome which can be activated by variation of ion concentration.
Objectives: To assess the role of osmolarity and water flux in MSU and CPP crystal-induced inflammation.
Methods: In vitro, THP1 monocytes were stimulated by pyrogen-free synthetic MSU and CPP crystals in iso-, hypo- or hyperosmotic media. Cytokine production was quantified by ELISA in cell culture supernatants. Cell size was measured using video microscopy. The role of aquaporin channels was assessed by pharmacological inhibitor (mercury chloride, HgCl2). In vivo, murine air pouch model was used. MSU and CPP crystals were injected in air pouch of mice treated or not with HgCl2 or mannitol. Osmolarity of mouse sera and patient synovial fluids (SF) were measured using freezing point osmometer. The size of cells collected from SF was assessed with imageJ software.
Results: MSU and CPP crystal-induced IL-1β production was substantially reduced by HgCl2 treatment (MSU 4900 vs 880 pg/ml; CPP 10500 vs 980, p<0.0001) or when cells were cultured in hyperosmotic medium. MSU and CPP crystals induced a transient increase in cell size which was 1.6 and 1.5 bigger after 30 and 100 min of stimulation by MSU and CPP crystals, respectively. After 150 min of stimulation, cell size decreased to their baseline size. Cell size increase was abolished by HgCl2 or hyperosmotic medium. In vivo, MSU and CPP crystal-induced inflammation (assessed by cell infiltration, IL-1β and CXCL2 production in air pouch lavage) was drastically reduced by HgCl2 or mannitol treatment. The serum osmolarity was higher in mannitol-treated mice than untreated mice (320 vs 300 mmosm/L). In patients, cells collected from SF during CPP or MSU crystal-induced flares had a bigger size than cells collected from osteoarthitic SF. The osmolarity of MSU or CPP crystal-containing SF was lower than the osmolarity of osteoarthritic SF (270 vs 310 mmosm/L). Finally, the IL-1β concentration in SF was strongly correlated with cell size and SF osmolarity.
Conclusion: These results suggest that the variation of osmolarity plays central role in MSU and CPP crystal-induced inflammation. Deciphering how crystals modulate osmolarity will identify new therapeutic targets.
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POS1170

ASYMPTOMATIC URATE-CRYSTALS DEPOSITS IN PATIENTS WITH STAGES 3-5 CHRONIC KIDNEY DISEASE DETECTED BY ULTRASOUND

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Background: One in ten patients with hyperuricemia may develop gout over time, with urate deposition sometimes asymptomatic. Recent reviews support ultrasound (US) to assess asymptomatic hyperuricemic (AH) patients to detect gout lesions, showing double contour (DC) and tophus the highest specificities and positive predictive values. Hyperuricemia and gout are common in chronic kidney disease (CKD), especially with glomerular filtration rate (GFR) <60, and are associated with worse prognosis. US gout lesions have been found more frequently in AH (up to 35%) than in normouricemic (NU) patients, but evidence is scarce in CKD.
Objectives: To assess the prevalence of urate deposit in stages 3-5 CKD detected by US, and to investigate if there are differences between AH and NU patients.
Methods: Case-control study, recruiting patients aged ≥18 years with AH and stages 3-5 CKD in 4 hospitals from January 2020 to December 2021. Controls were patients with stages 3-5 CKD and NU. Exclusion criteria: previous diagnosis of gout, tophi. Hyperuricemia was defined as serum uric acid (sUA) >6.8 mg/dl, documented at least twice during the last 12 months. A standardized US exam of the knees and bilateral first metatarsophalangeal joints was performed to assess patients for DC/tophus as defined by OMERACT. Demographic, clinical and laboratory data were recorded. A descriptive analysis was performed using SPSS. Pre-clinical gout (PCG: DC and/or tophus) was considered as outcome variable. Chi-square and Fisher's exact test were used for qualitative variables, and Mann-Whitney U test for quantitative variables; significant threshold p<0.05.
Results: Forty-four patients with stages 3-5 CKD (59.6% stage 3, 19.1% stage 4, 21.3% 5) were recruited, 35 AH and 9 NU. Hyperuricemia was associated with a higher prevalence of US findings, with significant differences between cases (AH) and controls (NU): PCG 19 vs 1 (p=0.023), DC 13 vs 1, and tophus 11 vs 0. No significant differences were found in demographic variables, comorbidities and treatments. sUA levels, were higher in patients with PCG (8.3±1.4 vs 7.6±2.2; p=0.36), and these patients also showed lower GFR (31.4±14.1 vs 33.7±16.9; p=0.62). Patients with PCG also showed a non-significant trend towards shorter duration of CKD [6.3±5.7 vs 8.3±4.9 years; p=0.1] and younger age (66.4±15.1 vs 70.0 ±11.0; p=0.30).
Conclusion: We found an outstanding prevalence of asymptomatic urate deposits in our cohort of patients with stages 3-5 CKD, that is higher in hyperuricemic than in normouricemic patients. The prevalence of DC and tophus in our cohort of AH patients with stages 3-5 CKD was higher than that reported in AH patients in studies conducted in general population (37% vs 16-31% and 31% vs 16%, respectively). Early diagnosis of pre-clinical gout by ultrasound might change therapeutic approach in CKD.
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POS1171

TRIPLE THE RATE OF EMERGENCY ROOM VISITS AND HOSPITALIZATIONS FOR GOUT AMONG US BLACKS VS WHITES – 2019 NATIONWIDE ANALYSIS

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Background: Gout is a highly prevalent inflammatory arthritis with increasing global disease burden in recent years.[1,2] Gout prevalence has been reported to be higher among Blacks compared to Whites,[3] and that they are less likely to receive allopurinol in outpatient care.[4] The potential nationwide impact of these racial disparities on emergency department (ED) visits and hospitalizations is unknown.

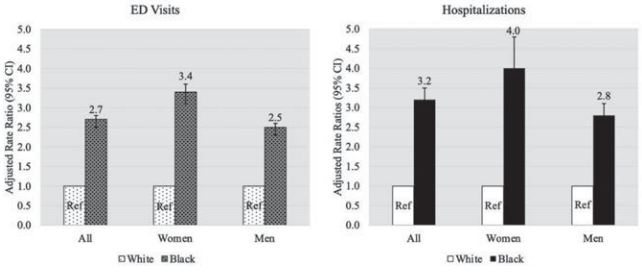
Objectives: To examine the contemporary racial disparities in ED visits and hospitalizations with a primary discharge diagnosis of gout in the US (2019).
Methods: We compared ED visits and hospitalizations between Blacks and Whites in the latest data (2019) from the US National Emergency Department Sample (NEDS) and National Inpatient Sample (NIS). We focused on encounters for which the primary diagnosis was gout based on ICD codes (M1A.xx, M10.xx). We calculated annual population rates of ED visits and hospitalizations for gout (per 100,000 US adults) using the 2019 US census adult population (>18 years) according to race.
Results: There were a total of 160,759 ED visits and 9,560 hospitalizations among White and Blacks with a gout diagnosis in the US in 2019. The mean age (58.2 years vs. 56.5 years) and male proportion (78.0% vs. 74.8%) tended to be higher among Whites, while more Blacks tended to live in the South (40.7% vs. 66.5%) and reported a median household income of < $50,000 (30.7% vs. 57.1%). Compared to Whites, Blacks had 2.7- and 3.2-fold higher rates of gout ED visits and hospitalizations, respectively, after adjusting for age, sex, payer, region, and household income (Table 1 & Figure 1). Black women, in particular, had 3.4- and 4.0-fold higher rates of ED visits and hospitalizations compared to White women, while the corresponding rate ratios for men were 2.5 and 2.8, respectively. The mean costs per gout ED visit were similar for Blacks compared to Whites (adjusted difference, -$7.6 [95% CI, -25.4 to 1.0]), while hospitalizations were more costly (adjusted difference, $1,055.3 [95% CI, 553.1 to 1557.5]). The duration of ED visits and hospitalizations was also higher among Blacks than Whites (adjusted difference of 0.41 days [95% CI, 0.19 to 0.63] and 0.59 days [95% CI, 0.25 to 0.94], respectively).

Table 1. Racial Disparities in Emergency Department Visits and Hospitalizations with Primary Diagnosis of Gout in 2019

	Emergency Department Visits		Hospitalizations	
Race	White	Black	White	Black
All	68011965	24521330	19851043	4519150
Visits, N	88810	71949	6200	3360
Rate per 100,000	130.6	293.4	31.2	74.4
Rate Ratio (95% CI)*	1.0 (ref)	**2.81 (2.63, 3.00)**	1.0 (ref)	**3.08 (2.79, 3.40)**
Rate Ratio (95% CI)**	1.0 (ref)	**2.66 (2.50, 2.82)**	1.0 (ref)	**3.17 (2.86, 3.50)**
Women	37851369	14363031	11039093	2647105
Visits, N	19567	18163	1770	1145
Rate per 100,000	51.7	126.5	16.0	43.3
Rate Ratio (95% CI)*	1.0 (ref)	**3.68 (3.39, 3.99)**	1.0 (ref)	**4.01 (3.40, 4.73)**
Rate Ratio (95% CI)**	1.0 (ref)	**3.36 (3.11, 3.62)**	1.0 (ref)	**4.02 (3.39, 4.78)**
Men	30156101	10156573	8809815	1871620
Visits, N	69228	53783	4430	2215
Rate per 100,000	229.6	529.5	50.3	118.3
Rate Ratio (95% CI)*	1.0 (ref)	**2.59 (2.42, 2.78)**	1.0 (ref)	**2.66 (2.36, 3.00)**
Rate Ratio (95% CI)**	1.0 (ref)	**2.47 (2.32, 2.64)**	1.0 (ref)	**2.77 (2.45, 3.14)**

*Adjusted for age and sex for all, adjusted for age for sex-specific rate ratios**Adjusted for age, sex, payment, region, and household income

Figure 1. Racial Disparities in Emergency Department Visits and Hospitalizations with Primary Diagnosis of Gout in 2019



Conclusion: These latest national data indicate that ED visits and hospitalization due to gout are both 3 times higher among Blacks than Whites; this disparity was particularly prominent among women with gout. Higher risk of developing gout[3] and suboptimal care[4] both translate to these avoidable costly healthcare utilizations, calling for improved primary prevention and gout care.

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POS1172 RISK OF VENOUS THROMBOEMBOLISM AFTER GOUT FLARES

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Background: Several population-based cohort studies have reported an increased risk of venous thromboembolism (VTE) in gout patients. However, none of these studies has investigated the temporal relationship between gout flares and VTE.
Objectives: To explore whether gout flares increase the risk of VTE in the short-term using the self-controlled case series (SCCS) method.
Methods: We identified participants with incident gout from the Clinical Practice Research Datalink (CPRD). Participants having less than one year of registration in CPRD and patients with a history of VTE or anticoagulant prescription more than one year before the first gout consultation were excluded. Participants with at least one gout flare and a diagnosis of VTE were selected. VTEs and gout flares were ascertained using primary care data, hospitalisation and mortality records, using previously validated algorithms (positive predictive value of 94% for VTE [1] and 68-95% for gout flares [2,3]). SCCS method involves fitting a Poisson model conditioned on the number of VTEs, and it calculates the adjusted incidence risk ratio (aIRR) and its 95% confidence interval (95%CI) for each stratum of the "at-risk" period as compared with the "baseline" period (Figure 1). The analysis was adjusted for age and calendar season.

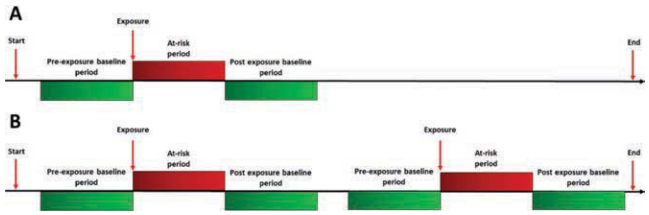

Figure 1. Schematic description of the observation period ("at-risk" and baseline periods).

The "at-risk" period (in red) was defined as the period following the exposure (the gout flare), and it was subdivided as follows: days 0-30, 31-60 and 61-120 after each gout flare. The baseline period (in green) consisted of a pre-exposure and a post-exposure period of 365 days each. The length of each period varied according to the occurrence of the next flare and its timing. Panel A and panel B provide a schematic representation of patients with a single observation period and with multiple "non-overlapping" observation periods, respectively. In such cases, the length of the "at risk" period was 120 days, while the length of the pre-exposure and post-exposure period was 365 days each.
Results: Among the 104,962 patients with an incident diagnosis of gout in CPRD between 1997 and 2020, we identified 2,678 VTE (4.0 events/1,000 person-years). There were 53 VTE (13.3 events/month) during the "at-risk" period and 143 (6.0 events/month) during the "baseline" period (crude incidence rate ratio, 1.75; 95%CI: 1.27-2.42). The rates were highest in the first month after gout flares and then fell progressively (Table 1). Sensitivity analyses were consistent with the main analysis (Table 1).

Table 1.

Gout flare	Number of events per month	aIRR (95%CI)	p_{trend}
Main analysis			
0-30 days	17.0	2.11 (1.27-3.50)	0.01
31-60 days	14.0	1.86 (1.07-3.24)	
61-90 days	11.0	1.50 (0.95-2.37)	
Baseline period	6.0	Reference	
Sensitivity analysis (excluding participants with risk factors for VTE) [4]			
0-30 days	14.0	3.13 (1.77-5.53)	0.01
31-60 days	7.0	1.66 (0.76-3.61)	
61-90 days	8.0	1.75 (0.94-3.37)	
Baseline period	3.4	Reference	

Conclusion: A transitory increase in the risk of VTE was observed after gout flares.

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POS1173

CLINICAL PRESENTATION AND TREATMENT OF STERNOCOSTOCLAVICULAR HYPEROSTOSIS (SCCH): A SYSTEMATIC REVIEW AND META-ANALYSIS OF SCATTERED EVIDENCE

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Background: Sternocostoclavicular hyperostosis (SCCH) is an inflammatory bone disorder within the spectrum of chronic non-bacterial osteomyelitis. SCCH can be a manifestation of SAPHO syndrome, standing acronym for synovitis, acne, pustulosis, hyperostosis and osteitis, but also appears as an isolated clinical entity without joint and skin involvement[1,2]. Consensus on nomenclature, diagnostic classification, and therapy for SCCH is currently lacking[3]. Literature is diffuse, and spreads over a wide range of medical disciplines, calling for a first systematic overview.
Objectives: We critically appraised literature with the aim to i) gain overview on the clinical presentation of SCCH and features leading to diagnosis and to ii) evaluate different treatment modalities and treatment response. We focused on the clinical entity of SCCH in adults, either isolated or as a part of SAPHO syndrome.
Methods: We conducted a systematic review and meta-analysis according to the PRISMA guidelines on the clinical presentation and therapeutic modalities applied in adult SCCH patients. Studies covering these respective domains were selected. Risk of bias was assessed using validated tools according to study type. Untransformed numerical data and double-arcsine transformed proportional data were analyzed in a random effects model in R-4.0.5; pooled proportions were reported with 95% confidence intervals (95%CI). Treatment response was categorized as good, partial, or none.
Results: 28(i) and 12(ii) studies were included, containing heterogeneous data on 1818 patients. A female predisposition (67%, 95%CI 60-73) and major diagnostic delay (5 years 95%CI 3-7) were noted. Clinical presentation was marked by anterior chest pain (89%, 95%CI 79-96), and swelling (79%, 95%CI 62-91). Pustulosis palmoplantaris was present in 53%, 95%CI37-68, whereas acne (8%, 95%CI4-13) and peripheral arthritis (24%, 95%CI 11-39) were less prevalent. Inflammatory markers were inconsistently elevated and autoantibodies and HLA-B27 prevalence normal. Histopathology was unspecific, and cultures almost exclusively negative. Increased isotope uptake (99%, 95%CI96-100) was the most consistent imaging finding. Amongst manifold treatments (see Figure 1), NSAIDs were mainly partially effective. Pamidronate and biologicals (mainly TNF-α inhibitors) yielded good, though heterogeneous, response in 83%, 95%CI 60-98 and 56%, 95%CI 26-85 respectively.

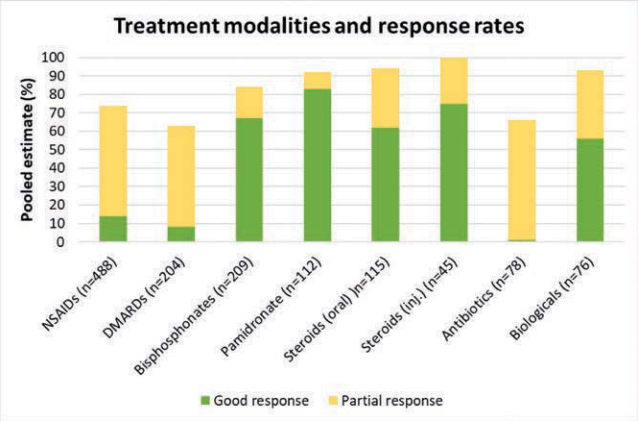

Figure 1. Treatment modalities applied in SCCH and their effects on bone pain (data from trials and several cohort studies combined)

Conclusion: Literature on SCCH is extremely heterogeneous. Timely diagnosis proves challenging and mainly follows from the increased isotope uptake on nuclear examination. Biopsies, autoantibodies and HLA-status are non-contributory, and inflammatory biochemical profiles only variably detected. Pamidronate and TNF-α inhibitors emerged as promising therapies, but powered, placebo-controlled research with standardized measures of response is warranted. Inherently, international consensus on SCCH's diagnostic classification and name appears critical to improve scientific collaboration on this rare disease, and to advance the development of clinical guidelines.

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POS1174

COLCHICINE TREATMENT IN GOUT PATIENTS – IMPACT ON CARDIOVASCULAR EVENTS AND ON MORTALITY

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Background: Gout and hyperuricemia are independent risk factors for cardiovascular events and increased mortality. A significant proportion of gout patients receive colchicine, additionally to urate-lowering therapy.
Recently, colchicine treatment was found to reduce the risk of cardiovascular events in patients with chronic cardiac disease.
Objectives: To assess the incidence of cardiovascular events and the mortality rate among gout patients who received colchicine treatment.
Methods: This retrospective cohort study was conducted using data from the Maccabi Healthcare Services (MHS) central computerized database. MHS is the second largest state-mandated health care provider in Israel, covering >2.5 million members (25% of the population) and is a representative sample of the Israeli population. The study included gout patients from the MHS registry aged ≥40 years who received colchicine for at least 3 months and a control group matched by age, gender and socioeconomic status. The data extracted included smoking status, body mass index (BMI), co-morbidities (diabetes, hypertension, chronic renal disease, hyperlipidemia, malignancy), antiplatelet and anticoagulant treatment, cardiovascular events and mortality rate. The statistical analysis included univariate and cox regression analysis.

Results: 3671 individuals were included in each group (mean(SD) age 56(12.5), 87% males, mean(SD) follow-up 2744.7(1616.2) days). The gout group had a statistically significant higher incidence (p<0.001) of cardiovascular events (14.7% vs 10.8%), high BMI (35.1% vs 15%), diabetes (17% vs 12.7%), hypertension (52% vs 32.4%), chronic renal disease (35% vs 15%), hyperlipidemia (65% vs 46%). The mortality rate was similar (8.9% vs 7.9%, p=0.11) for both groups. The mortality hazard ratio (95% CI) for gout patients was 1.18 (1-1.39, p=0.05), for diabetes 1.6 (1.3-1.9, p<0.0001), for hypertension 1.38 (1.1-1.67, p=0.002).
Conclusion: Although the gout patients had a higher incidence of co-morbidities and cardiovascular events, the mortality rate was not significantly different compared to the matched group. Chronic colchicine treatment might have a protective effect. Further long-term studies are required.
Disclosure of Interests: None declared
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POS1175 IMPACT OF COVID-19 ON THE CLINICAL COURSE OF GOUT AND THE OVERALL USAGE OF MEDICATION IN PATIENTS WITH GOUT

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Background: Data on the course and outcomes of the coronavirus disease 2019 (COVID-19) in patients with gout are scarce, as gout is underrepresented in leading COVID-19 and rheumatological scientific publications [1].
Objectives: To describe clinical changes, quality of life, therapy of gout before and after COVID-19, and the clinical course of severe acute respiratory syndrome-related coronavirus 2 (SARS-Cov-2) infection in the cohort of patients with gout.
Methods: In total, 84 males with gout were examined before the pandemic, during COVID-19 (March 2020 to December 2021) and 6 months after SARS-Cov-2 infection. The severity of COVID-19 in our cohort was determined. We conducted a comparative analysis of clinical and laboratory data, Gout Activity Score (GAS), urate-lowering (UST) and symptomatic therapy, Physical Component Summary (PCS) and Mental Component Summary (MCS) of the Short Form 36 (SF-36) Health Survey Questionnaire. Statistical difference of qualitative indicators was carried out using the Pearson Chi-square test ($\chi 2$), quantitative indicators using the Student's or the Wilcoxon test between groups.
Results: The mean age (mean±SD) of the study patients was 51.07±7.45 years and the disease duration was 9.84±6.02 years. Most SARS-CoV-2 infected patients with gout exhibited a moderate illness (40.48%), almost every third (28.57%) had mild, 21.43% had severe and 9.52% had critical illness. Comparison of pre-COVID-19 vs 6-month post-COVID-19 data demonstrated an increase of gout flares in preceding 6 months (0.7±0.59 vs 4.35±2.25, p<0.001), serum uric acid level (5.9±1.54 vs 7.62±1.99, p<0.01), GAS (3.83±0.4 vs 6.1±1.63, p<0.01), non-steroidal anti-inflammatory drug intake (19.05% vs 72.62%, p<0.001), colchicine (27.38% vs 53.6%, p<0.001), and corticosteroid use (5.95% vs 34.52%, p<0.001), but decreased intake of ULT (88.09% vs 77.38%, p>0.05), SF-36 PCS (43.7 ± 6.19 vs 36.08±6.54, p<0.01) and SF-36 MCS (48.35±5.89 vs 40.13±6.84, p<0.01).
Conclusion: The current study identified the majority of patients with gout had a moderate course, every fifth had a severe course and 9.52% had a critical course of COVID-19. In the post-COVID-19 period, we found a six-fold increase in gout flares, rising gout activity by 59.3%, more frequent medication use for symptomatic therapy of gout, decreased physical and mental health in the cohort of patients with gout.
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POS1176 EFFECT OF LIFESTYLE CHANGE ON INCIDENT GOUT: A NATIONWIDE POPULATION-BASED COHORT OF YOUNG MEN

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Background: Although gout in young people is increasing, studies on the risk factors for gout in these people are lacking.
Objectives: In this study, we explored the risk factors of gout and effect of lifestyle change on the development of gout in large nationwide population-based cohort of young men.
Methods: Between 2009–2012, men aged 20–39 years who participated in two national health examinations at 2-year intervals were included in the study. The outcome was occurrence of gout, which was defined using the diagnosis code of gout (ICD-10 code M10) in the claims database. Cox proportional hazard model was used to evaluate the association between incident gout and baseline factors or lifestyle change.
Results: A total of 1,977,849 subjects were included in the study, and the mean follow-up period was 5.5 ± 4.3 years. Gout occurred in 38,839 subjects (incidence rate = 3.59/1,000 person-years). A high body mass index, alcohol drinking, and comorbidities such as hypertension, diabetes mellitus, and hyperlipidemia were associated with an increased risk of gout. Among lifestyle factors, change in obesity had the greatest impact on gout, followed by drinking. Development of obesity increased the risk of gout by 1.75 times (95% CI 1.68–1.81), and recovery from obesity decreased the risk of gout by 40% (aHR 0.60, 95% CI 0.57–0.64). Heavy drinking increased the risk of gout by 38% (aHR 1.38, 95% CI 1.33–1.43), and stopping heavy drinking decreased the risk of gout by 11% (aHR 0.89, 95% CI 0.85–0.94). The effect of obesity on gout was evident in the younger age group, and the effect of heavy drinking on gout was weak in the severely obese group.
Conclusion: Obesity and heavy drinking in young men are important modifiable risk factors for gout. Therefore, the management of these risk factors in young men should be emphasized.
Disclosure of Interests: None declared
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POS1177 TREATMENT OF GOUTY ARTHRITIS IS ASSOCIATED WITH RESTORING GUT MICROBIOTA AND PROMOTING PRODUCTION OF SHORT CHAIN FATTY ACIDS

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Background: Although factors initiating the inflammatory response to monosodium urate crystals have been identified, the role of the gut microbiota and their metabolites on gout remain unknown.
Objectives: This study aimed to investigate changes in both gut microbiota and short chain fatty acids (SCFAs) according to inflammatory states of gout in the same patients.
Methods: This study enrolled 20 patients with gout in the acute state who had active joints and were followed-up until the recovery state with no active joints. Blood and fecal samples were simultaneously collected within 3 days for each disease state. The stool microbiome was analyzed using 16S rRNA sequencing, and serum SCFAs were measured by gas chromatography-mass spectrometry. Differences in gut microbiome and serum SCFAs were compared between the acute and recovery states.
Results: Beta diversity of the microbiome was significantly different between the acute and recovery states in terms of weighted UniFrac distance. In the recovery state, Prevotellaceae (p = 0.006) and the genus *Prevotella* (p = 0.009) were significantly enriched, whereas Enterobacteriaceae (p = 0.019) and its derivative genus *Shigella* (p = 0.023) were significantly decreased compared to the acute state. Similarly, the levels of acetate was dramatically increased in the recovery state compared to the acute state (p < 0.010). Levels of propionate and butyrate tended to increase but without statistical significance.
Conclusion: Substantial alterations of bacterial composition with promotion of SCFA formation (especially acetate) were found after treatment in patients with gouty arthritis.
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Infection-related rheumatic diseases

POS1178 PRESCRIBING RITUXIMAB IN PATIENTS WITH AUTO-IMMUNE DISEASES AND ACQUIRED HYPOGAMMAGLOBULINEMIA: DESCRIPTION OF THE RISK OF SEVERE INFECTION IN 121 PATIENTS BEFORE THE SARS-COV2 ERA

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Background: Rituximab (RTX) induces rapid, usually complete and prolonged depletion of circulating B cells, and also hypogammaglobulinemia in some patients. There are limited data regarding the risk of severe infection events (SIE) when initiating or continuing rituximab in patients with acquired hypogammaglobulinemia, especially in patients suffering from autoimmune diseases (ADs) other than rheumatoid arthritis (RA) (1).
Objectives: To describe the risk of severe infectious events (SIE) following initiation (rituximab-naïve patients [RNP]) or continuation of RTX therapy (rituximab-continuing patients [RCP]) in patients suffering from severe ADs other than RA and acquired hypogammaglobulinemia.
Methods: We conducted a single-center retrospective cohort study at the University Hospital of Toulouse (France) between 2010 and 2018. Patients were included if they had received at least one dose of RTX in the year following the evidence of hypogammaglobulinemia (defined as gammaglobulins [GG]≤ 6g/L on serum protein electrophoresis) in the setting of ADs other than RA. The primary outcome was the occurrence of a SIE within 2 years after the date of first RTX infusion (T0) prescribed after the evidence of hypogammaglobulinemia. SIE were infections either fatal or requiring hospitalization.
Results: We included 121 patients (37 RNP and 84 RCP): 48 had ANCA-associated vasculitis (AAV), 48 multiple sclerosis (MS, n=41) or neuromyelitis optica (NMO, n=7), and 21 another severe AD. RTX was prescribed as induction therapy in 39 patients and as maintenance therapy in 82; 112/121 patients were followed for 2 years. Mean GG level were 5.5 g/L (IQ_{25-75} 4.6-5.7) at T0, 5.5 g/L (IQ_{25-75} 5-6.4) at one year, 5.7g/L (IQ_{25-75} 4.8-6.1) at two years and 8 patients had a decrease of their GG level below 4g/L. Ten patients received immunoglobulin replacement therapy (IGRT) mostly after infection (n=6). Twenty-six patients (23.2%) had at least one SIE during follow-up: 12.8 % in the MS/NMO group with a 2-year incidence at 6.9 (3.1-15.3) per 100 person-years, 29.5 % in the AAV group with a 2-year incidence at 18.3 (9.3-20.1) per 100 person-years, 33.3 % in the 'other ADs' group with a 2-year incidence at 22.2 (10.6-46.5) per 100 person-years. Infection was opportunistic in 8 patients (33.3%) and 4 died from SIE. Risk factors of SIE at T0 were male gender (61.5% vs. 39.5% p<0.05), lung disease (65.4% vs. 37.2% p=0.01), renal failure (59.1% vs. 28.6% p=0.01), a higher Charlson comorbidity index (p=0.001), a previous treatment by cyclophosphamide (53.8% vs. 30.2%; p=0.03), ≥ 5 mg/d prednisone (69.2% vs. 33.7%, p=0.003), lack of pneumococcal vaccination (61.5% vs 31.4%, p=0.01). GG level was 5.3 g/l [4.1-5.6] in the 'SIE' group vs 5.6 g/l [4.8-5.8] in the 'no SIE' group (p=0.04). Incidence of SIE was 46% and 20.2% among patients with GG< 4 g/L or GG≥ 4 g/L, respectively (p=0.07). No multivariable analysis provided reliable results.
Conclusion: Our study provides useful information for clinicians considering initiating or continuing rituximab therapy in patients with acquired hypogammaglobulinemia before Sars-Cov2 era. Prospective studies are necessary to improve the knowledge on outcome of patients treated by rituximab despite low immunoglobulins levels. Prophylactic IGRT may be appropriate in higher risk patients, especially if the GG level is below 4 G/L.

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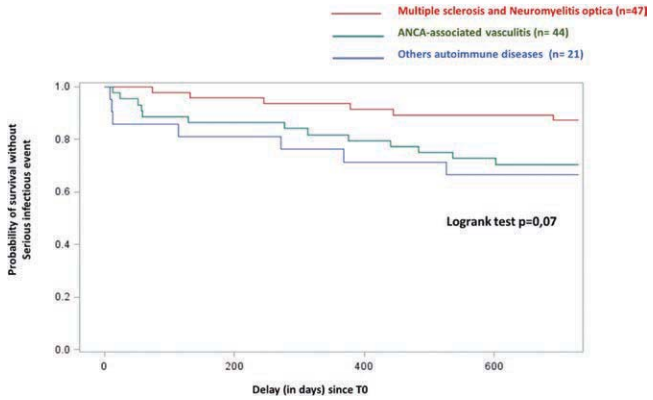

Figure 1. Two years probability of survival without serious infectious event according to pathology group (112 patients included)

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POS1179 SYSTEMATIC LITERATURE REVIEW ON THE SCREENING AND PROPHYLAXIS OF CHRONIC AND OPPORTUNISTIC INFECTIONS

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Background: Opportunistic and chronic infections can arise in the context of treatment used for Autoimmune Rheumatic Diseases (ARDs). Although it is recognized that screening procedures and prophylactic measures must be followed, clinical practice is largely heterogeneous, with relevant recommendations not currently developed or disparately located across the literature.
Objectives: To conduct a systematic literature review (SLR) focusing on the screening and prophylaxis of opportunistic and chronic infections in ARDs. This is preparatory work done by members of the respective EULAR task force (TF).
Methods: Following the EULAR standardised operating procedures, we conducted an SLR with the following 5 search domains; **1) Infection:** infectious agents identifed by a scoping review and expert opinion (TF members), **2) Rheumatic Diseases**: all ARDs, **3) Immunosuppression:** all immunosuppressives/immunomodulators used in rheumatology, **4) Screening:** general and specific (e.g mantoux test) terms, **5) Prophylaxis:** general and specific (e.g trimethoprim) terms. Articles were retrieved having the terms from domains 1 AND 2 AND 3, plus terms from domains 4 OR 5. Databases searched: Pubmed, Embase, Cochrane. Exclusion criteria: post-operative infections, pediatric ARDs, not ARDs (e.g septic arthritis), not concerning screening or prophylaxis, Covid-19 studies, articles concerning vaccinations and non-English literature. Quality of studies included was assessed as follows: Newcastle Ottawa scale for non-randomized controlled trials (RCTs), RoB-Cochrane tool for RCTs, AMSTAR2 for SLRs.
Results: 5641 studies were initially retrieved (Figure 1). After title and abstract screening and removal of duplicates, 568 full-text articles were assessed for eligibility. Finally, 293 articles were included in the SLR. Most studies were of medium quality. Reasons for exclusion are shown in Figure 1. Results categorized as per type of microbe, are as follows: For *Tuberculosis*; evidence suggests that tuberculin skin test (TST) is affected by treatment with glucocorticoids and conventional synthetic DMARDs (csDMARDs) and its performance is inferior to interferon gamma release assay (IGRA). Agreement between TST and IGRA is moderate to low. Conversion of TST/IGRA occurs in about 10-15% of patients treated with biologic DMARDs (bDMARDs). Various prophylactic schemes have been used for latent TB, including isoniazide for 9 months, rifampicin for

4 months, isoniazide/rifampicin for 3-4 months. For *hepatitis B (HBV)*: there is evidence that risk of reactivation is increased in patients positive for hepatitis B surface antigen. These patients should be referred for HBV treatment. Patients who are positive for anti-HBcore antibodies, are at low risk for reactivation when treated with glucocorticoids, cDMARDs and bDMARDs but should be monitored periodically with liver function tests and HBV-viral load. Patients treated with rituximab display higher risk for HBV reactivation especially when anti-HBs titers are low. Risk for reactivation in *hepatitis C* RNA positive patients, treated with bDMARDs is low. However, all patients should be referred for antiviral treatment and monitored periodically. For *pneumocystis jirovecii*: prophylaxis with trimethoprim/sulfamethoxazole (alternatively with atovaquone or pentamidine) should be considered in patients treated with prednisolone: 15-30mg/day for more than 4 weeks. Few data exist for screening and prophylaxis from viruses like *EBV, CMV and Varicella Zoster Virus*. Expert opinion supports the screening of rare bugs like *histoplasma* and *trypanosoma* in patients considered to be at high risk (e.g living in endemic areas).

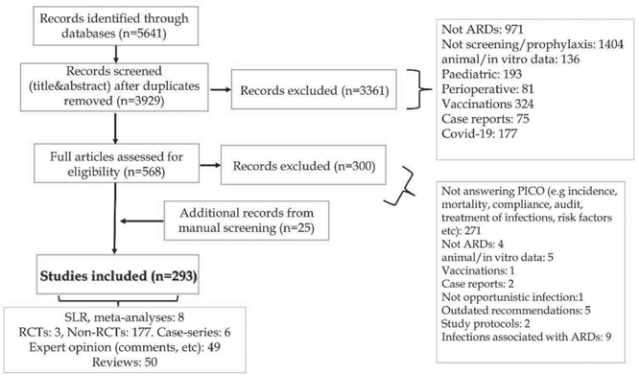

Figure 1. SLR flowchart

Conclusion: The risk of chronic and opportunistic infections should be considered in all patients prior to treatment with immunosuppressives/immunomodulators. Different screening and prophylaxis approaches are described in the literature, partly determined by individual patient and disease characteristics. Collaboration between different disciplines is important.

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POS1180 AUTOIMMUNE SYNDROMES WITH CHRONIC HEPATITIS C VIRUS INFECTION AND DIRECT-ACTING ANTIVIRAL TREATMENT.

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Background: Chronic hepatitis C virus (HCV) infection is a multifaceted disease that has been associated with systemic as well as organ-specific, autoimmune manifestations with increasing virologic, and clinical evidence supporting the association. The development of direct-acting antivirals (DAAs) is considered an advent that might aid the clearance of extrahepatic immune manifestations of HCV.[1,2,3]

Objectives: Investigate the effect of directly acting antiviral drugs (DAA) on the different autoimmune manifestation and serologic changes associating chronic HCV infection.

Methods: Inclusion criteria: This is a cohort study that included adult patients aged ≥18 years, of either sex, having CHCV with detectable HCV ribonucleic acids (RNA) by Polymerase Chain Reaction (PCR) and eligible for the DAAs treatment. Exclusion criteria: Patients with established rheumatological disease prior to the onset of HCV diagnosis. Patients with decompensated cirrhosis**.** Patients with platelet count less than 50000/ mm^3.Patients with HCC (except after 6 months of curative intervention). All patients were subjected to full history taking, clinical and laboratory investigations.

Results: The study enrolled 130 chronic HCV patient (90 patients completed follow up). 66.7 % females and 33.3% males (ratio 2:1), the mean age was 49.2±12.3 years. The study found 77/ 90 (85.55%) patients to have immune mediated manifestations and associated serological changes prior to DAA. The most prevalent were musculoskeletal manifestations in 56 patients (72.7%), arthralgia (66.2%), fatigue (54.5%) and myalgia (50.6%), xerophthalmia (24.7%), neuritis (28.6%) (P-value > 0.01), and a positive RF in 33.8% (P-value 0.013). HCV Among patients who achieved sustained viral response, autoimmune manifestations persisted in 66 out of 71 patients (92.9%) who were positive at baseline. The most prevalent autoimmune manifestations after therapy were musculoskeletal manifestations 53 patients (68.8%). Responders with persistent autoimmune manifestations had an observable rise in inflammatory biomarkers posttreatment erythrocyte sedimentation rate was (46.22±19.62) became (56.05±25.45),C reactive protein titer was (8.46±12.76) became (20.01±25.92), P >0.01. Predictors for persistence of autoimmune manifestation were older age ≥ 49 years P-value 0.009, female sex P= 0.026, tobacco consumers P= 0.043.

Conclusion: The introduction of directly acting antiviral drugs wasn't associated with a significant change in the prevalence of autoimmune manifestations in our population of Egyptian patients with chronic HCV who attained a sustained viral response.

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POS1181 INFECTIOUS COMPLICATIONS OF BIOLOGIC THERAPY IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM

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Background: The appearance of biological disease-modifying drugs (bDMARDs) has revolutionized the treatment of rheumatic diseases. However, their functions in modulating pro-inflammatory cytokines and acquired immunity largely increase the risk of infections.

Objectives: The aim of this work is to study the epidemiological, clinical and biological characteristics of infections occurring under biotherapies, and to identify the factors associated with its occurrence.

Methods: It is a retrospective descriptive study including patients with chronic inflammatory rheumatism between 2006 and 2021 and who were placed during their follow-up under a biotherapy. Statistical data analysis was performed using SPSS version 20 software. The bivariate study was performed by Chi-square test.

Results: Of the 106 cases reported, 68 infectious episodes were counted in 46 patients (43.4%) who had at least one infection with biotherapy: 56.5% women and 43.5% men with an average age of 50.9 ± 14.29 years. These included rheumatoid arthritis in 16 patients (34.8%), spondylarthritis in 29 patients (63%) and one case of psoriatic arthritis. All patients were on conventional treatments before switching to biotherapy. The infections occurred under Rituximab in 43.8% of the cases, under Infliximab in 33.3% of the cases, under Etanercept in 25% of the cases (a total of 60.9% of the cases were under anti-Tumor Necrosis Factor) and tocilizumab in 12.5% of cases. The infection was of bacterial origin in 40.7% of cases: 27.3% urinary tract infections, 20.5% bronchial infections, 11.4% skin infections, 6.8% septic arthritis. Fungal infections were found in 33.3% of cases in relation to dermatophyte infections and intertrigo. A viral origin was noted in 25.9% of the cases: 5 cases of labial herpes and only one case on herpes zoster. C-reactive protein was increased in 47.2% of cases with a mean value of 36 ± 29.6 mg /L, the hemogram showed hyperleukocytosis in 50% of cases with neutrophil predominance. The treatment was medical in the majority of cases (94.9%), it was both medical and surgical in one case. The favorable outcome in all patients was marked by a temporary interruption of 3.27 ± 1.84 weeks of biotherapy. In multivariate analysis, an association was found between bacterial infection and both female gender (p=0.033), low socioeconomic level (p=0.033), Methotrexate + bDMARDs intake (p=0.027), corticosteroids + bDMARs intake (p=0.014) and Between fungal infection and bDMARs +corticosteroids intake (p=0.044).

Conclusion: The risk of infection is higher in patients with chronic inflammatory rheumatism, especially if they are under biotherapy. It turns out that bacterial and fungal infections are the most common in this study. Patients taking Rituximab or Infliximab are the most affected by these infectious episodes.

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POS1182 EPIDEMIOLOGICAL, CLINICAL AND THERAPEUTIC ASPECTS OF TABETIC ARTHROPATHY IN A POPULATION OF SOUTHERN MOROCCO

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Background: Tabetic arthropathies (TA) are a destructive neurogenic disease complicating 10% of syphilis at the tertiary stage. Although they have become exceptional due to early and appropriate treatment of syphilis, they are still relevant in undeveloped countries and remain difficult to manage due to the severity of the handicap and the absence of a specific treatment.
Objectives: We described épidemiological, clinical, biological, radiographic, and therapeutic characteristics of TA.
Methods: Retrospective study, from 2004 to 2021 includind patients with tabetic arthropathy, whose diagnosis was retained on clinical criteria (discordance between the importance of joint deformities and indolence), radiological (lesions destructive and constructive), biological (positive syphilitic serology in joint fluid, blood and/or cerebrospinal fluid).
Results: A total of 21 cases were collected, 15 men and 6 women, the mean age was 52.14 years. The history of syphilitic chancre was found in 9 patients, sexual risk behavior was noted in 8 patients, no other STI was found. Joint swelling with painless deformation was the main mode revealing the disease (76.1%), followed by pathological fracture in 3 cases and then mechanical arthralgia with neuropathic pain in 2 patients. The delay diagnosis was 6.8 years. TA concerned lower limb in 81,5%. The knee was the most affected site in 15 cases (71.4%),followed by the hip,ankles, MTP, in respectively 4(19%), 3(14%), 2(9,5%) cases. The upper limb was involved in 4 cases, with MCP involvement in one patient. TA was bilateral in 29% and multifocal in 19%. Joint instability was found in 16 patients. Involvement of the thoracolumbar spine was noted in one case. Tabetic neurological involvement was found in 16 patients (76.1%) with an Argyll Robertson sign noted in 6 cases (28.6%), a radiculocordonal posterior syndrome in 10 cases (47.6%). TPHA and VDRL were positive in blood in 21 patients, in cerebrospinal fluid in 11 patients and in synovial fluid in 9 cases. Radiological exams showed destructive and constructive lesions with the presence of intraosseous and periarticular fragments, damage to small joints was noted in two patients, bilateral talocrural involvement in one patient, a fracture with dislocation and calcification of the soft tissues was noted in two cases. Axial tabetic involvement made of vertebral compression D12, L1 L2 L3 was found in one case (4.8%). Nineteen patients (90.4%) were treated with Penicillin G and two patients with C3G. Orthopedic immobilization with weight-bearing was prescribed to all patients, the surgical indication was posed in 11 patients, 4 of whom benefited from surgery: total hip prosthesis in 3 cases, knee arthrodesis in one case. The serological evolution at the end of treatment showed a decrease in the VRDL titer in the blood, CSF, synovial fluid in 10 patients and negativity in 4 patients.
Conclusion: Tabetic arthropathy, one of the exceptional complications of neurosyphilis, is still relevant. Its diagnosis must reffered to any destructive and painless joint damage. Given the difficulty of treating this articular form, prevention based on the management of syphilis at an early stage before the occurrence of joint and neurological complications is essential.
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POS1183 RISK FACTORS FOR CYTOMEGALOVIRUS INFECTION IN PATIENTS WITH RHEUMATIC DISEASE; SINGLE-CENTER PROSPECTIVE COHORT STUDY.

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Background: Cytomegalovirus (CMV) infection is one of serious opportunistic infections for immunosuppressed patients, therefore, identifying patients at risk for CMV infection is of importance. However, no prospective study about CMV infection in systemic rheumatic disease has been reported.
Objectives: To identify risk factors relevant with CMV infection in patients with systemic rheumatic disease during intensive remission induction therapy.
Methods: Consecutive systemic rheumatic disease cases who started intensive immunosuppressive therapy from February 2017 until February 2019 were enrolled. Serum CMV-IgG was measured before the induction therapy, and subsequently, CMV pp65 antigen was monitored weekly. Patients were divided into 2 groups according to the presence or absence of CMV infection, and risk factors for CMV infection were analyzed.
Results: 157 patients consisting of 136 CMV-IgG positive and 21 CMV-IgG negative patients were enrolled in the study. Mean age was 60.8 ± 17.4 y/o, and female was 70.7%. The underlying diseases were following; vasculitides 54, systemic lupus erythematosus 27, polymyositis/dermatomyositis 25, rheumatoid arthritis 14, IgG4-related disease 13, mixed connected tissue disease 6, Behçet disease 5, adult-onset Still's disease 4, and others 9. The initial dose of glucocorticoid (GC) was 48.4 ± 11.5 mg/day (0.91 ± 0.16 mg/kg/day) as prednisolone (PSL) with additional methylprednisolone (mPSL) pulse therapy being conducted in 44 (28.0%). Concomitant immunosuppressive therapies were intravenous cyclophosphamide (IVCY) in 55, calcineurin inhibitor 27, mycophenolate mofetil 16, hydroxychloroquine 5, and methotrexate 4. Concomitant biological agents were rituximab 12, tocilizumab 6, infliximab 2, golimumab 1, and abatacept 1. CMV infection occurred in 52 patients (33.1%), and all of them were CMV-IgG positive before induction therapy (38.2% in the CMV-IgG positive patients). Univariable analysis revealed initial PSL dose >0.91 mg/kg/day (odds ratio [OR] 5.2, p<0.01), IVCY (OR 3.4, p<0.01), diabetes mellitus (OR 5.2, p<0.01), and a history of malignancy (OR 2.9, p=0.02) were independent risk factors for CMV infection. CMV antiviral drugs were administered in 22 patients (42.3%). At the first detection of CMV pp65 antigen, PSL dose ≥37.5 mg/day (OR 5294.8, p<0.01), CMV pp65 antigen-positive cells ≥2 cells/2 slides (OR 16.0, p = 0.04), and serum albumin levels <3.0 g/dL (OR 26.3, p=0.01) were associated with subsequent CMV antiviral drug administration.
Conclusion: CMV infection occurred only in CMV-IgG positive patients with systemic rheumatic diseases who were undergoing intensive remission induction therapy. CMV infection was related with treatment regimen and comorbidities, and the necessity of CMV antiviral treatment was predicted with prednisolone dose, the number of CMV pp65 antigen positive cells, and albumin levels at the first detection of CMV pp65 antigen.
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POS1184 EPIDEMIOLOGICAL CHARACTERISTICS OF VIRAL HEPATITIS IN PATIENTS WITH RHEUMATIC DISEASES – IMPLICATIONS FROM TREASURE DATABASE

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Background: Recent epidemiological data on HBV and HCV in Turkey revealed that the seroprevalence rates of hepatitis B surface antigen and antibody against HCV were 4% and 1%, respectively, and seropositivity rates for hepatitis B surface antibody and hepatitis B core antibody were 31.9% and 30.6%, respectively. A previous multicenter nationwide study conducted in Turkey reported that the HBsAg positivity was determined in 2.3% of patients with rheumatoid arthritis (RA) and 3% of patients with ankylosing spondylitis (AS), and the anti-HCV positivity was detected in 1.1% of patients in each group. Given these rates, viral hepatitis is still considered a potential threat to patients with rheumatic diseases, specifically for the treatment-related viral reactivation.
Objectives: This study aimed to evaluate the serologic HBV and HCV frequency and clinical characteristics among our patients with RA or SpA and receive biological treatments based on this background.
Methods: The prospective TReasure database, which observationally collects data of patients with rheumatic diseases from fifteen centers across Turkey, was analyzed for viral hepatitis, patient characteristics, and treatments used. TReasure registry study protocol, and the data collection was started on December 2017. At the time of the analysis for this study was performed, the registry database included 3147 patients with RA and 6071 patients with SpA. For hepatitis B; Hepatitis B surface antigen (HBsAg), anti-HBV core antibody (anti-HBc) and anti-HBV surface antibody (Anti-HBs) tests were evaluated. HBV-DNA was studied in HBsAg positive patients. Anti-HCV antibody has been studied for HCV. The clinical and serological HBV reactivation in the follow-up of the patients was evaluated by looking at the HBV-DNA viral loads.
Results: A total of 9218 patients (3147 RA and 6071 patients with SpA) were included in the analyses. The screening rate for HBV was 97% in RA and 94.2% in SpA groups. HBsAg positivity rates were 2.6% and 2%, anti-HBs positivity rates were 32.3% and 34%, anti-HBc positivity rates were 20.3% and 12.5%, HBV DNA positivity rates were 3.5% and 12.5%, and anti-HCV positivity rates were 0.8% and 0.3% in these groups, respectively (Table 1).

Table 1. Serological analyses in the study group

	RA		SpA		
	N	n (%)	N	n (%)	p
Hepatitis testing	2896	2809 (97.0)	5444	5130 (94.2)	<0.001
HBsAg positivity	2750	71 (2.6)	5017	99 (2)	0.080
Anti-HBs positivity	2708	876 (32.3)	4893	1663 (34)	0.147
Anti-HBc positivity	2362	480 (20.3)	4194	524 (12.5)	<0.001
HBV-DNA positivity	454	16 (3.5)	637	35 (5.5)	0.129
Anti-HCV positivity	2602	22 (0.8)	4627	16 (0.3)	0.005

The HBsAg (+) patients were older and had higher comorbidities, including hypertension, diabetes, and coronary artery disease. In addition, RF positivity was more in HBsAg(+) cases. The most frequently prescribed bDMARDS were adalimumab (28.5%), etanercept (27%), tofacitinib (23.4%), and tocilizumab (21.5%) in the RA group, whereas adalimumab (48.1%), etanercept (31.4%), infliximab (22.6%), and certolizumab (21.1%) in the SpA group. HBV reactivation was observed in one patient with during RA treatment, who received rituximab and prophylaxis with tenofovir.

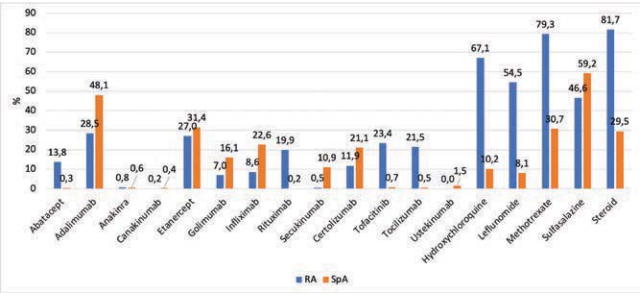

Figure 1. Prescription proportions of medications in the rheumatoid arthritis (RA) and spondyloarthritis (SpA) groups

Conclusion: The epidemiological characteristics of patients with rheumatic diseases and viral hepatitis are essential for effective patient management. This study provided the most recent epidemiological characteristics from the prospective TReasure database, one of the most comprehensive registries in rheumatology practice. According to the results of our study; It can be thought that there is no risk in the choice of treatment by the rheumatologist in patients who receive appropriate prophylaxis.
Disclosure of Interests: None declared
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POS1185 PERFORMANCE OF ADENOSIN DEAMINASE ACTIVITY IN SYNOVIAL FLUID FOR THE EARLY DIAGNOSIS OF TUBERCULOUS ARTHRITIS: A META-ANALYSIS

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Background: Adenosin deaminase activity (ADA) has shown good performance in diagnosing pleural, peritoneal and meningeal tuberculosis. Still, the performance of ADA activity in synovial fluid for the diagnosis of tuberculous arthritis has received less attention.
Objectives: To analyze the performance of ADA in synovial fluid to diagnosis tuberculous artrhritis.
Methods: We research Medline and EMBASE from the inception to October 2021 and the American College of Rheumatology and European League Against Rheumatism for conference abstracts (2012-2021) to assess the accuracy of ADA activity in synovial fluid compared to a composite reference standard (necrotizing granulomas in a synovial biopsy; acid-fast stain, Mycobacterium culture or RT-PCR assay for tuberculosis and/or clinical response to tuberculosis treatment) to early diagnosis tuberculous arthritis. We performed meta-analysis using a random-effects model and evaluated the sources of heterogeneity via subgroup analysis and meta-regression.
Results: Seven independent studies (N= 307 subjects) that compared ADA activity in synovial fluid with the composite reference standard were included. The pooled sensitivity and specificity of ADA activity was 0.939 (95% confidence Interval [CI], 0,873-0,977; heterogeneity p=0.297; I2=17.4%) and 0.885 (95% confidence Interval [CI], 0.833-0.925; heterogeneity p=0.002; I2=85.3%) compared to the composite reference standard, respectively. The random-effects model for pooled diagnostic Odds Ratio was 74.582 (95% CI, 19.826-280.57; heterogeneity p=0.133; I2=38.8%). The receiver operating characteristic curve area was 0.9617 (95% CI, 0.925-1.000). Meta-regression did not identify the type of study (prospective or retrospective), country of publication, type de assay, or cut-off value as sources of heterogeneity.
Conclusion: Measuring adenosine deaminase activity in synovial fluid demonstrates good performance for the early diagnosis joint tuberculosis.
Acknowledgements: El estudio fue apoyado con una beca de investigación de la Asociación para la Investigación en Reumatología de la Marina Baixa (AIRE-MB)
Disclosure of Interests: None declared
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POS1186 STUDY OF SPONDYLODISCITIS WITHOUT BACTERIOLOGICAL DOCUMENTATION FROM A COHORT OF 142 PATIENTS WITH SUSPECTED INFECTIOUS SPONDYLODISCITIS ON IMAGING

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Background: The incidence of infectious spondylodiscitis was estimated at 2.4/100,000 people in 2002. When faced with an image of spondylodiscitis on imaging, infectious spondylodiscitis is the most feared etiology. In recent years, several non-infectious spondylodiscitis etiologies have been described: Andersson lesion, crystal-induced discopathy, degenerative changes, etc (2). The identification of the germ by blood cultures or disc-vertebral puncture-biopsy allows the treatment to be best adapted antibiotic. Bacteriological investigation is inconclusive in about 30% (1). More and more undocumented spondylodiscitis are described.
Objectives: The aim of this study is to describe a cohort of spondylodiscitis without bacteriological documentation and to compare it to spondylodiscitis with bacteriological documentation.

Methods: Using a "clinical data warehouse", we searched for the key word "spondylodiscitis" in the documents associated with hospitalisations in the Rheumatology department of the Rouen University Hospital between 2010 and 2020. Four hundred and twenty-two records were analysed: 196 were excluded because they were not hospitalizedn in Rheumatology, among the 226 suspected spondylodiscitis, imaging allowed us to exclude 84 records for which there was no infectious spondylodiscitis and to retain 142 records. We collected demographic data, history, clinical symptoms, results of imaging, biological and bacteriological examinations. Statistical analysis was performed by Fisher's exact test for qualitative data and by Mann-Whitney test for quantitative data.

Results: Four hundred and twenty-two patients were collected, 142 were analyzed. The average age was 65.5 +/- 14 years, 64.1% were male. Spinal pain was present in 96.5% of the cases without any difference between the two groups. One hundred and nine cases of spondylodiscitis were documented, of which 72 were confirmed by blood cultures and 36 by spinal disc biopsy. Thirty-three were not documented. Documented spondylodiscitis was more often febrile (41.3% vs 15.21% in undocumented cases, p = 0.006), had a greater biological inflammatory syndrome (mean CRP 152.4 +/- 112.6 mg/L versus 73 +/- 73.1 mg/L, p < 0.0001), and had been evolving for a shorter period of time than undocumented spondylodiscitis (54.1% vs 24.2% less than one month). *Staphylococcus aureus* was the most frequently retrieved bacteria 27.5%, followed by coagulase-negative staphylococci and streptococci (18.3% and 19.3% respectively). One hundred and twenty-one patients (85%) had an MRI at diagnosis; one hundred and two (71.8%) had a CT scan; and 81 patients (57%) had both examinations. The imaging analysis showed that there was no difference in soft tissue infiltration, erosions and abscesses. Probabilistic antibiotic therapy was proposed in 28/33 (84.5%) of cases. After collegial discussion, the alternative diagnoses retained were degenerative disc disease (4 cases), spinal gout (1 case), spondyloarthritis (1 case).

Conclusion: Undocumented spondylodiscitis is a recurrent problem in hospital practice. Alternative diagnoses are increasingly reported, their diagnosis is based on a collegial discussion.

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Disclosure of Interests: None declared

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POS1187 DO IMMUNOSUPPRESSIVE AGENTS AFFECT IGRA TESTS IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: Tuberculin skin test (PPD) or interferon gamma release assays (IGRAs) are used to detect latent tuberculosis infection. Induration of 15 mm or more is considered positive in any person whereas this cut-off is ≥5 mm for immunosuppressed individuals such as Rheumatoid arthritis. Since IGRAs are dependent on normal T-cell function, it may result in false-negatives for among RA patients due to disease itself and immunosuppressive drugs.

Objectives: We aimed to compare IGRA results of RA patients using high dose DMARDS vs. not using any of them.

Methods: Totally 534 RA patients among Hacettepe University Rheumatology Biologic Registry Database (HURBIO) database was enrolled into this study. QFT-Plus test of patients with rheumatoid arthritis (RA) between January 2018 and March 2021 during work up before biologic/targeted therapy were analysed, retrospectively. The patient group was divided into two according to the drugs have been using at the time of IGRA test. Patients using methotrexate ≥ 10 mg or leflunomide (any dose) or steroids (≥7.5 mg prednisolone) or any combination thereof were classified as the "High Dose" group. The other group consisted of patients who did not take these drug doses. Demographic characteristics, comorbidities, drugs and doses used, and hemogram, sedimentation, and CRP values of the patients were recorded. QuantiFERON test was recorded as positive, negative, indeterminate.

Results: 353(66.1%) RA patients were in the high dose patient group and also 287(81.3%) of these patients were female, the median age was 55 years (min:19- max:82). The high dose group was older than the other group. When the two groups were compared, no statistically significant difference was found between comorbidity, and smoking (Table 1). While QFT positivity was detected in 37 (10.5%) patients in the high-dose group, it was found to be positive in 37 (20.4%) patients in the other group (p<0.001). However, there was no significant difference regarding acute phase reactants, hemogram including lymphocyte counts and IFN-gamma levels in the tubes between these two groups.

Table 1. Comparison of RA patients' groups using high-dose immunosuppressives and not using any of them

		High Dose Methotrexate or Leflunomide or Steroid (+), (%) 66.1	High Dose Methotrexate or Leflunomide or Steroid (-), (%) 33.9	P Value
Female		81.3	75.1	0.09
Age, med (min-max)		55 (19-82)	52 (19-81)	0.01
Diabetes Mellitus		11	10.5	0.84
Hypertension		30.6	24.9	0.16
Chronic Renal Failure		0.3	0	0.66
Chronic Obstructive Pulmonary Disease		4.2	3.3	0.59
Coronary Artery Disease		3.7	6.1	0.20
History of malignancy		0.8	1.7	0.40
Smoking	**Never**	49	52.5	0.19
	Ever	24.1	27.6	
	Quit	26.3	18.8	
Leukocyte,*10^3/ml	Median	7.6 (2.8-28.8)	7.9 (3.5 – 20.8)	0.26
Neutrophil,*10^3/ml	(min-max)	4.8 (0.2-23.0)	5.0 (1.5-19.1)	0.18
Lymphocyte,*10^3/ml		1.9 (0.4-5.9)	1.8 (0.5-5.3)	0.67
Thrombocyte,*10^3/ml		285 (117-669)	285.5 (60-724)	0.79
Hemoglobine,g/dL		12.8 (7.7-17.9)	12.8 (9.3-16.6)	0.41
Sedimentation,mm/saat		30 (2-294)	28 (2-104)	0.27
C Reactive Protein,mg/dl		1.1 (0.1-62.8)	1.1 (0-20.7)	0.96
QuantiFERON-TB Gold-Plus (QFT-Plus)		10.5	20.4	0.00
Nil med (min-max)		0.07 (0-2.7)	0.05 (0-0.85)	0.48
QFT-Plus TB-1 med (min-max)		1 (0->10)	0.99 (0->10)	0.25
QFT-Plus TB-2 med (min-max)		1 (0->10)	1.1 (0->10)	0.42
Mitogen med (min-max)		10 (0->10)	9.5 (0->10)	0.27
Methotrexate	Not Taking	31.4	33.7	
	Less than 10 mg	44.2	66.3	
	10 mg and more	24.4	0	
Leflunomide	Not Taking	25.8	100	
	Taking	74.2	0	
Hydroxychloroquine	Not Taking	25.2	40.9	
	Taking	74.8	59.1	
Sulfasalazine	Not Taking	62.6	61.9	
	Taking	37.4	38.1	
Steroids	Not Taking	4.2	19.9	
	Less than 7.5 mg	66.3	80.1	
	7.5 mg and more	29.5	0	

Conclusion: Our results confirmed a significantly lower QFT-Plus positivity in patients with RA taking methotrexate ≥ 10 mg or leflunomide (any dose) or steroids (≥7.5 mg prednisolone). Physicians should be careful in interpretation of QFT-Plus in patients with rheumatoid arthritis. Further analysis including flow cytometry analysis is required to better identifying cut-offs for immunosuppressive individuals and patients with inflammatory rheumatic diseases.

Disclosure of Interests: None declared

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POS1188 INCIDENCE AND MANIFESTATIONS OF LYME DISEASE: A SINGLE-CENTER RETROSPECTIVE ANALYSIS.

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Background: Lyme disease is widespread throughout the world, including Latvia. On average period 2009 to 2018, there have been 613 cases of Lyme disease registered in Latvia every year according to data from the Center for Disease Prevention and Control. Mainly early skin manifestations such as erythema migrans and neurological manifestations such as meningitis, cranial neuropathy and motor or sensor radiculoneuropathy of this disease are being discussed and emphasized. Therefore, undiagnosed and unexamined often remain articular manifestations of Lyme disease, leading to prolonged treatment and reduced patient quality of life.
Objectives: To investigate clinical presentation, immunological changes, and response to therapy in patients with Lyme disease.
Methods: A retrospective single center study was performed in the outpatient clinic Orto (Riga, Latvia) in the period from January 2018 until December 2021. Medical records from patients with diagnosed Lyme disease and articular symptoms, based on epidemiological, clinical and immunological findings, were analyzed. Patients who had other types of arthropathies were excluded.
Results: In total 76 patients were included in the study (54 females, 22 males, age range 19-84 years, median age 48.5 years), of whom 48 patients had arthritis and 28 arthralgias. Out of all patients with arthritis - 25 had monoarthritis, 16 - had oligoarthritis and 7 had polyarthritis. At the first visit patients with arthralgia had a median IgM 28.2 Au/ml (IQR 15.27- 47.35) and IgG 25.00 Au/ml (IQR 5.00 – 142.30) and patients with arthritis had a median IgM 14.7 Au/ml (IQR 5.50 - 28.80) and IgG 142.7 Au/ml (IQR 82.32-237). After the treatment with Doxycycline 200 mg QD for 30 days, 52 patients came to the 2nd visit, of them 41 patients with improvement of symptoms and 11 without. More improvement was seen in the arthritis group. After treatment the median IgM in arthralgia/ arthritis groups was 22.5 Au/ml (IQR 8.72-38.82) / 13.8 Au/ml (IQR 6.03-24.15) and IgG was 42.4 Au/ml (IQR 8.15 – 90.60) / 106.7 Au/ml (IQR 23.57-203.95). In both groups with arthralgias or arthritis, patients who had a positive clinical response after treatment had a significantly lower post-treatment IgG than before treatment ($p < 0.05$, Wilcoxson signed rank test). At the same time patients who did not respond to the treatment had no significant difference between pre- and post-treatment IgG antibodies ($p > 0.05$, Wilcoxson signed rank test).
Conclusion: In all patients with musculoskeletal complaints the possibility of Lyme disease should be evaluated. The decrease of antibody titers may indicate a positive prognosis in patients with musculoskeletal manifestations of Lyme disease.
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POS1189 RHEUMATIC FEVER AND CUTANEOUS STREPTOCOCCAL INFECTION: A CASE-CONTROL STUDY IN THE LOYALTY ISLANDS, NEW CALEDONIA

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Background: Acute Rheumatic Fever (ARF) and Rheumatic Heart Disease (RHD) remain major public health problems in the South Pacific. Triggering by group A beta hemolytic streptococcal (GAS) skin infection has been suspected but little documented[1]. Very high incidences of ARF (106/100 000) and cutaneous infections have been reported in the Loyalty islands (New Caledonia), where health care of the 20,000 Melanesian inhabitants is centralized in a few locations and provides an extensive electronic database since 1998, and systematic screening for RHD is regularly performed.
Objectives: To explore the link between ARF, RHD and skin infections by a retrospective case-control study.
Methods: The study was approved by the New Caledonian committee of Ethics and dealt with patients aged 6 to 26 years, seen from 1998 to 2018. Cases were ARF and/or RHD. Definite ARF was diagnosed according to the Jones criteria[2]; additional cases with strong clinical suspicion were also included as probable cases. RHD was diagnosed by cardiac ultrasound scan allowing definite and borderline diagnosis[2]. Sore throat and presumed streptococcal cutaneous infections were diagnosed by an algorithm, previously validated on a sample of 3000 events by an experimented clinician, which identified specific medical terms and ICD-10 codes in the electronic medical records. Each case was matched with 3 controls (without ARF and RHD) of same age, sex and living location. Infections were retrieved from the electronic medical records during the month, 6 months, one year, 5 years preceding the date of the first ARF/RHD diagnosis, for each case with the same index date for its matched control, and since birth. Numbers of infections per these time intervals were compared between cases and controls by univariate and multivariate conditional regression analysis in the total study population and its various subcategories (definite or probable ARF, definite or borderline RHD).
Results: 311 cases of ARF and RHD including 206 definite cases were identified. Polyarthralgias (48%) were the main clinical presentation. Marginal erythema was not seen and Sydenham chorea was rare (6.8%). Mean age of diagnosis was 10.6 ±3.8 years. Skin infection episodes were 3 to 4 times more frequent than sore throats in all studied time-intervals. Multivariate analysis showed an increased exposure to skin infections and sore throats in the year preceding ARF/RHD diagnosis in the whole population of cases as compared to controls (OR 2.18, 95% CI 1.46, 3.26) and 1.54, 95% CI 1.01, 2.36] respectively); skin infections (but not sore throat) were also increased the 206 definite cases (OR 1.34, 95% CI 1.01, 1.80) and in the 220 definite and probable ARF (OR 1.47, 95% CI 1.11, 1.94). In addition we observed a correlation between the seasonality of ARF and skin infections, which were both more frequent during the rainy season, and an overlap of areas with high incidence of ARF and areas with high incidence of skin infections.
Conclusion: Our results support the hypothesis that GAS skin infections play a role in the pathophysiology of ARF/RHD. In view of these results, there is an urgent need to implement preventive measures to reduce the incidence of skin infections in the Loyalty Islands.
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COVID-19

POS1190 IMPACT OF COVID-19 PANDEMIC ON PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: DISRUPTIONS IN CARE AND SELF-REPORTED OUTCOMES

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Background: The COVID-19 pandemic represents a challenge to the care of patients with rheumatic and musculoskeletal diseases (RMDs).
Objectives: This study aimed to evaluate the impact of the pandemic on the care of RMD patients, their health and wellbeing.
Methods: This cross-sectional study involved 120 RMDs patients at the rheumatology department at Suez Canal University Hospital in Ismailia, Egypt. Patients were interviewed for sociodemographic and disease-related history. Further assessments were performed using Kessler 6-items (1), Fear of COVID-19 scale (2), and COVID-19–Impact on Quality-of-Life scale (3).
Results: Patients with rheumatoid arthritis and systemic lupus erythematosus made up most of our sample (72.5%, 19.2% respectively). About 50% of patients were experiencing limitation in the access to rheumatologic care, and a similar percentage had changed or discontinued their medications. DMARDs shortage and concerns about the increased risk of COVID-19 infection because of immunosuppressive drugs were the most frequently reported reasons for non-adherence to medication. The percentage of patients with uncontrolled disease had significantly increased from 8.3% prior to the COVID-19 pandemic to 20% during the pandemic. Patients perceived their overall quality of life as average (4.93 on a rating scale from 0 to 10). The Fear of COVID-19 score ranged from 7 to 35 with a mean of 26 (±7.6), while the COV19–Impact on Quality of Life score ranged from 6 to 30 points with a mean of 22.6 (±6.7). About 60% of patients reported a high level of psychological distress.
Conclusion: The pandemic negatively influenced the mental health, quality of life, adherence to medications, access to rheumatology care, and disease control of RMDs patients.
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POS1191 IMMUNE RESPONSES TO MRNA VACCINES AGAINST SARS-COV2 IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY RHEUMATIC DISEASES

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Background: Patients with immune-mediated rheumatic diseases (IMRD) are commonly treated with immunosuppressors and prone to infections. Recently introduced mRNA SARS-Cov2 vaccines have demonstrated extraordinary efficacy across all ages. Immunosuppressed patients were excluded from phase III trials with SARS-Cov2 mRNA vaccines.
Objectives: To fully characterize B and T cell immune responses elicited by mRNA SARS-Cov2 vaccines in patients with rheumatic diseases under immunotherapies, and to identify which drugs reduce vaccine´s immunogenicity.
Methods: Humoral, CD4 and CD8 immune-responses were investigated in 100 SARS-Cov2-naïve patients with selected rheumatic diseases under immunosuppression after a two-dose regimen of SARS-Cov2 mRNA vaccine. Responses were compared with age, gender, and disease-matched IMRD patients not receiving immunosuppressors and with healthy controls.
Results: IMRD patients showed decreased seroconversion rates (80% vs 100%, p= 0.03) and cellular immune responses (75% vs 100%, p= 0.02). Patients on methotrexate achieved seroconversion in 62% of cases and cellular responses in 80% of cases. Abatacept decreased humoral and cellular responses. Rituximab (31% responders) and belimumab (50% responders) showed impaired humoral responses, but cellular responses were often preserved. Antibody titers were reduced with mycophenolate and azathioprine but preserved with leflunomide and anticytokines.
Conclusion: IMRD patients exhibit impaired SARS-CoV-2 vaccine-immunogenicity, variably reduced with immunosuppressors. Among commonly used therapies, abatacept and B-cell depleting therapies show deleterious effects, while anticytokines preserved immunogenicity. The effects of cumulative methotrexate and glucocorticoid doses on immunogenicity should be considered. Humoral and cellular responses are weakly correlated, but CD4 and CD8 tightly correlate. Seroconversion alone might not reflect the vaccine's immunogenicity.
Graph 1: Multivariate analysis
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POS1192 INCIDENCE AND RISK FACTORS OF COVID-19 IN PATIENTS WITH VASCULITIS: A DANISH NATIONWIDE COHORT STUDY

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Background: Patients with small vessel vasculitis (SVV) and large vessel vasculitis (LVV, including giant cell arteritis (GCA)) are considered at higher risk of infections compared to the general population, owing to their underlying condition and the use of immunosuppressive drugs. Thus, the risk of COVID-19 infection and related outcomes during the global pandemic is of immediate concern to rheumatologists worldwide.
Objectives: To estimate the incidence of COVID-19 hospitalisation in patients with vasculitis, and to evaluate the impact of glucocorticoid treatment on the outcome between March 2020 and February 2021.

	Abatacept	HCQ	Cumulative glucocorticoid dose	Cumulative methotrexate dose	Age > 65 years	Disease duration >10 years
Seronversion	β - 0.1 p= 0.04	β 0.22 p= 0.01	β - 0.26 p= 0.44	β - 0.19 p= 0.03	β - 0.27 p= 0.002	β - 0.10 p= 0.22
IgG anti-spike levels	β - 0.13 p= 0.001	β 0.27 p= 0.01	β - 0.25 p= 0.004	β - 0.29 p= 0.001	β - 0.19 p= 0.02	β - 0.14 p= 0.04
CD4 T-cell response	β - 0.1 p= 0.03	β 0.10 p= 0.24	β - 0.04 p= 0.61	β - 0.03 p= 0.64	β - 0.05 p= 0.56	β - 0.14 p= 0.11
CD8 T -cell response	β - 0.08 p= 0.02	β 0.20 p= 0.12	β - 0.1 p= 0.43	β - 0.02 p= 0.24	β - 0.1 p= 0.56	β - 0.1 p= 0.15

Methods: With use of the Danish nationwide registers, a cohort of patients with LVV and SVV, respectively, and general population controls (GPCs) matched on age and gender was established. Hazard ratios (HR) for COVID-19 hospitalisation was estimated. National COVID-19 surveillance data was used to calculate the odds ratio (OR) of having had a positive SARS-CoV2 PCR test. Lastly, a nested case-control design and conditional logistic regression was used to estimate the impact of glucocorticoids on the risk of hospitalisation.
Results: Patients with SVV (n=1090) had an increased incidence of COVID-19 hospitalisation compared with GPCs (comorbidity-adjusted HR 2·73; 95% CI 1·64-4·55), whereas no increased risk was seen in patients with LVV. Patients with vasculitis had similar likelihoods of having had a positive PCR test as GPCs. Glucocorticoids did not increase the HR of hospitalisation among patients with LVV or SVV.
Conclusion: Patients with SVV were more likely to be admitted with COVID-19 than the GPCs. The impact of glucocorticoid treatment on the risk of hospitalisation needs further investigation.
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POS1193 COVID-19 IN PATIENTS WITH GIANT CELL ARTERITIS

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Background: Patients with giant cell arteritis (GCA) represent a fragile population with an increased infection risk. In a recent study[1] older age, a higher number of comorbidities, higher disease activity, and prednisolone ≥10 mg qd were associated with worse COVID-19 outcomes.
Objectives: We aimed to evaluate the frequency and severity of COVID-19 in a well-defined GCA cohort.
Methods: We reviewed medical records of histologically and/or by imaging proven GCA patients diagnosed between September 2011 and February 2020 at our secondary/tertiary center and followed during the COVID-19 pandemic between March 2020 and December 2021 (22 months). Descriptive statistics was used to analyze the studied population.
Results: Of 314 GCA patients diagnosed for the first time during a 102-month period, 49 patients died before March 2020. Of the remaining 265 patients (69.4% females), SARS-CoV-2 infection was proven by PCR test in 39 (14.7%) patients (74.2% females, mean (SD) age at infection 76.2 (±9.6 years), 13 (33.3%) with large vessel GCA and 16 with cranial limited GCA). At the time of SARS-Cov-2 infection GCA was in a stable remission in 38 patients (13 without therapy, 10 on steroids alone, 9 on leflunomide monotherapy, 6 on steroids plus leflunomide (10 or 20 mg qd), 1 on ustekinumab; mean prednisolone equivalent dose of 4.6 mg qd) and relapsed in one patient 6 weeks earlier (prednisolone 30 mg plus leflunomide). Data on clinical manifestations of COVID-19 were available for 33 (84.6%) patients and are presented in Table 1, part A. Twenty-nine/39 (74.4%) patients had mild COVID-19 and were symptomatically treated at home, while 10 patients had severe infection (defined as a need of hospitalization and/or death), and one of those patients died due to COVID-19. One patient developed a transient neurologic ischemic attack related to COVID-19. Table 1, part B shows differences in GCA demographic and treatment at the time of mild vs. severe infection. We found no differences in gender, age, GCA type and GCA treatment between those with mild vs. severe COVID. Three patients developed COVID-19 after receiving two doses of anti-COVID vaccine (1.4% breakthrough rate). Overall, of 257 GCA patients eligible for vaccination, 210 (81.7%) were vaccinated by the end of December 2021.

PART A

Characteristics of COVID (33 GCA patients)	%		%
Symptom duration (d)	12±10	Respiratory insufficiency	27.3%
Fever	48.5%	Chest pain	21.2%
Headache	24.2%	Abdominal pain	18.2%
Rhinitis	27.3%	Nausea/vomiting	0%
Smell loss	39.4%	Diarrhoea	18.%
Taste loss	33.3%	Malaise/fatigue	66.7%
Cough	48.5%	Myalgia	42.4%
Dyspnoea	30.3%	Arthralgia	36.4%

PART B

Characteristics of GCA (39 GCA with COVID)	Mild COVID (29 pts.)	Severe COVID (10 pts.)	P value
Gender	22 (75.9%)	6 (60.0%)	0.423
Age (years)	75.2±9.8	78.9±9.0	0.865
LVV	10 (34.5%)	3 (30.0%)	1.0
No treatment	8 (27.6%)	5 (50.0%)	0.254
Steroids	12 (41.4%)	4 (40.0%)	1.0
Leflunomide	10 (34.5%)	5 (50.0%)	0.463
Ustekinumab	1	0	1.0

Conclusion: A quarter of our GCA patients had severe COVID-19. Low doses of glucocorticoids and treatment with leflunomide were not associated with severe COVID-19 course in our cohort.
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POS1194 COVID-19 IN PATIENTS WITH INFLAMMATORY MYOPATHY

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Background: Older age, male sex, multimorbidity and glucocorticoids emerged in rheumatic patients as risk factors for severe COVID-19.
Objectives: We aimed to evaluate the frequency and severity of COVID-19 in a well-defined cohort of patients with idiopathic inflammatory myopathy (IIM).
Methods: We analyzed medical records of IIM patients diagnosed and followed at our secondary/tertiary center between January 2005 and December 2021.
Results: During the 204-month period IIM was newly diagnosed in 191 patients, of whom 52 died before COVID-19 pandemic. Of the remaining 139 patients (69.8% females; 9 polymyositis, 47 dermatomyositis; 38 antisynthetase syndrome, 26 overlap syndrome; 17 immune mediated necrotizing myopathy; 2 inclusion body myositis), SARS-CoV-2 infection was proven in 13 (9.4%) patients (61.5% females, mean (SD) age at infection 62.9 (±16.8 years)). Seven/13 COVID-19 patients (53.8%) had a diagnosis of antisynthetase syndrome. At the time of infection IIM was in a remission in 12/13 patients and relapsed 5 weeks earlier in one patient. Seven patients were without immunomodulatory therapy, 1 patient was on steroids alone, 2 on DMARD alone, 3 on steroids and DMARD; a mean daily prednisolone equivalent dose was 5 mg). Eleven/13 (84.6%) patients had mild COVID-19 (one had an asymptomatic infection) and were treated symptomatically, while 2 patients were hospitalized due to severe infection (respiratory insufficiency). Table 1 shows clinical characteristics and duration of COVID-19 symptoms. During pandemic overall 9/139 (6.5%) patients with IIM died, including one patient due to COVID-19.

Table 1. Characteristics of COVID-19 in IIM patients

Characteristics (13 patients)	No.	Characteristics (13 patients)	No.	Characteristics (13 patients)	No.
PM/DM/ASyS/OS/IMNM	1/1/7/1/3	COVID duration (days)	14 (±5)	Respiratory insufficiency	2
F / M gender	8 / 5	Fever	9	Nausea	1
Age (years)	62 (±16)	Headache	4	Diarrhoea	1
IIM therapy		Rhinitis	1	Malaise/fatigue	7
Steroids	1	Smell loss	3	Vertigo	1
DMARD	2	Taste loss	3	Myalgia	2
Steroids+DMARD	3	Cough	4	Arthralgia	2
No treatment	7	Dyspnea	5		

Legend: IIM idiopathic inflammatory myopathy; PM polymyositis, DM dermatomyositis; ASyS antisynthetase syndrome, OS overlap syndrome; IMNM immune mediated necrotizing myopathy; F female; M male; DMARD immunomodulatory drug.

Conclusion: In our IIM cohort, antisynthetase syndrome represented a higher relative risk for COVID-19 compared to other IIIM subtypes.
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POS1195 CAN PRE-TREATMENT INFLAMMATORY BIOMARKER LEVELS GUIDE TO DETERMINE APPROPRIATE TIME OF TOCILIZUMAB THERAPY IN COVID-19

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Background: Due to the pleiotropic cytokine interleukin-6 (IL-6) plays a pivotal role in the pathogenesis of COVID- 19, tocilizumab, an inhibitor of the IL-6 receptors, was considered as an attractive therapeutic option. When the inflammation cascade is excessive and therapy is delayed, the efforts for suppression of inflammation does not necessarily reduce mortality in all cases. Besides, early using anti-cytokine therapy may lead to both increased cost and risks including iatrogenic immunosuppression (1). Defining of patients who will benefit from tocilizumab and determining optimal timing of tocilizumab will prevent drug-related side effects and increased costs due to unnecessary drug use.
Objectives: To investigate the reliability of pre-treatment levels of prognostic nutritional index (PNI), C-reactive protein/albumin ratio (CAR), systemic immune-inflammatory index (SII), IL-6, lactate dehydrogenase (LDH) as a treatment response biomarker in hospitalized COVID-19 patients who administered tocilizumab.
Methods: One hundred thirty three COVID-19 patients received tocilizumab were included. The end-points of treatment effectiveness were evaluated with the rate of death and emerging need for mechanical ventilation at 28 days of hospitalization. To determine independent mortality risk factors, multivariate logistic regression analyzes were performed for statistically different variables among groups that were statistically different in univariate analysis. The capacity of IL-6, CAR, PNI, SII and LDH values in predicting of tocilizumab response in COVID-19 patients were analyzed using receiver operating characteristic (ROC) curve analysis.
Results: 34 (25.56%) patients died after tocilizumab therapy. Patients who improved after tocilizumab were significantly younger and had significantly lower IL-6, LDH, SII, CAR and higher PNI than patients who died. In univariate analyses, mortality was significantly associated with age, IL-6, LDH, PNI, SII, CAR and CRP. In multivariate analysis, age (OR:1.070, 95%CI:1.019-1.124, p:0.007) and LDH (OR:1.006, 95CI%:1.003- 1.010, p<0.001) were found to be independent predictors of mortality after tocilizumab therapy. To identify of tocilizumab response in COVID-19 patients, IL6 had the highest area under curve (AUC) value (AUC:0.782, 95%CI:0694-0.870), followed by LDH (AUC:0.761, 95%CI:0.661-0.861), PNI (AUC:0.696, 95%CI:0.584-807), SII (AUC:0.671, 95%CI:0.551–0.790), CAR (AUC:0.682, 95%CI:0.578– 0.786) and CRP (AUC:0.643, 95%CI:0.535–0.751). Predictive performance of inflammatory biomarkers in the prediction of mortality after tocilizumab therapy was presented in Table 1.

Table 1. Predictive performance of inflammatory biomarkers in the prediction of mortality after tocilizumab therapy

	Sensitivity	Specificity	PLR	NLR	PPV	NPV	Accuracy	DOR
IL-6 (pg/mL) >143.12	64.71%	84.85%	4.27	0.42	59.46%	87.50%	79.70%	10.27
LDH (U/L)	73.53%	71.72%	2.60	0.37	47.17%	88.75 %	72.18%	7.04
>460								
PNI<31.35	55.88%	79.80%	2.77	0.55	48.72%	84.04%	73.68%	5.00
SII>3895.92	47.06%	90.91%	5.18	0.58	64.00%	83.33%	79.70%	8.89
CAR>61.15	61.76%	67.68%	1.91	0.56	39.62%	83.75%	66.17%	3.38

CAR: C-reactive protein/albumin ratio; DOR: diagnostic odds ratio; IL-6: interleukin-6; LDH: lactate dehydrogenase; NLR: negative likelihood ratio; NPV: negative predictive value; PLR: positive likelihood ratio; PNI: prognostic nutritional index; PPV: positive predictive value; SII: systemic immune-inflammatory index.

Conclusion: Although the patients with significantly lower IL-6, LDH, SII, CAR and higher PNI levels improved after tocilizumab therapy, only serum LDH levels and age were found to be as independent predictors of mortality. To specify the optimal time interval and the patients who will benefit from tocilizumab, these biomarkers may be used.

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POS1196

SARS-COV-2 VACCINE ACCEPTANCE AND ASSOCIATED PSYCHOLOGICAL FACTORS IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: The mortality rate of coronavirus disease 2019 (COVID-19) in patients with rheumatic and musculoskeletal disease (RMD) is as high as approximately 10% [1]. Therefore, vaccination promotion is a critical issue. However, there are few reports on the psychological aspects of patient vaccine acceptance.
Objectives: To investigate the intention of patients with RMD to receive the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine and explore the psychological factors related to vaccine acceptance.
Methods: We conducted a questionnaire-based survey of 406 outpatients with RMD at Shiga General Hospital from July to October 2021. The questionnaire included the following sections: (1) vaccination status; (2) expectation of susceptibility to severe COVID-19; (3) expectation of vaccine efficacy; and (4) anxiety about the vaccine, which included concerns on I) the diminishing effect of the vaccine due to current treatment and II) the influence of vaccination on: i) primary disease status, ii) treatment, and iii) adverse reaction.
Results: There were 305 vaccinated and 101 unvaccinated individuals. Unvaccinated individuals were classified into the acceptance group (n=60) and hesitancy group (n=41) according to their vaccination status (Figure 1).

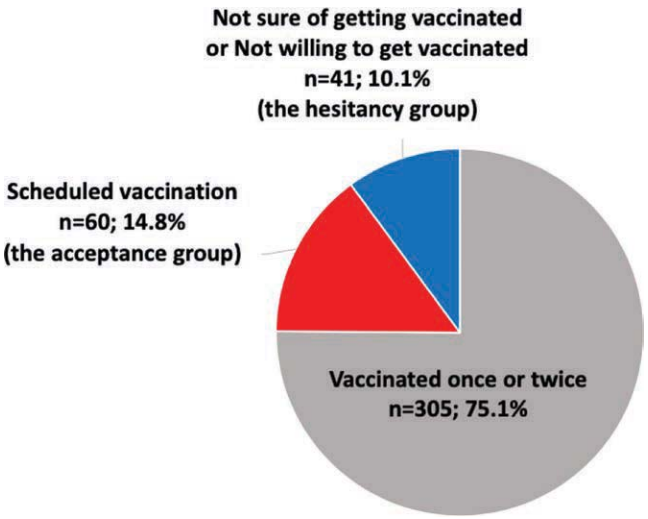

Figure 1. SARS-CoV-2 vaccination status (n=406)

We compared the backgrounds and awareness of the patients on vaccination between the two groups. Univariate analysis did not show any difference in the backgrounds. The expectation of susceptibility to severe COVID-19 was similar

Table 1. Awareness towards COVID-19 and SARS-CoV-2 vaccine associated with vaccination intention

Awareness towards COVID-19 and SARS-CoV-2 vaccine	Acceptance (N=60)		Hesitancy (N=41)		Univariate Analysis§	Multivariate Analysis‖
	Median	[IQR]	Median	[IQR]	*p*-value	*p*-value
Expectation of susceptibility to severe COVID-19 *	2.0	[1.0-3.0]	2.0	[1.5-2.5]	0.8472	0.3440
Expectation of vaccine efficacy†	3.0	[3.0-3.0]	2.0	[1.0-3.0]	<0.0001¶	<0.0001**
Concerns about the diminishing effect of the vaccine due to current treatment‡	2.0	[1.0-3.0]	3.0	[2.0-3.0]	0.0475	0.3600
Concerns about the effect of vaccination on treatment‡	3.0	[1.0-3.0]	3.0	[2.0-4.0]	0.0128	0.6232
Concern about the effect of vaccination on primary disease status‡	3.0	[1.0-3.0]	3.0	[2.0-3.0]	0.0576	0.7134
Concern about the effect of vaccination on adverse reaction‡	3.0	[3.0-3.0]	3.0	[3.0-4.0]	0.0093	0.8335

*0: Less likely to become severe~3: Very likely to become severe, †0: Not expected at all~4: Highly expected, ‡0: Not concerned at all ~4:Very concerned§Pearson's chi-square test or Wilcoxon test, ‖Nominal logistic regression analysis, ¶ $p<0.008$ (after Bonferroni correction), ** $p<0.05$.

in both groups. There were also no significant differences in the vaccine-related anxiety levels. However, the expectation of vaccine efficacy was higher in the acceptance group and significantly influenced vaccination intention as revealed by multivariate analyses (Table 1).

Conclusion: The perception of vaccine efficacy is strongly correlated with vaccine acceptance. In order to promote vaccination in patients with RMDs, this study suggests that emphasizing the efficacy of the vaccine may be more effective than alleviating anxiety about the adverse effects of the vaccine.

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POS1197

REMOTE AND PHYSICAL CONSULTATIONS DURING THE FIRST 15 MONTHS OF THE COVID-19 PANDEMIC: USE AND PATIENT-SATISFACTION IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES FOLLOWED IN THE DANBIO REGISTRY

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Background: During COVID-19 related lockdowns, physical attendance may be replaced by remote (by telephone, email, video consultations in patients with inflammatory rheumatic diseases (IRD). During re-opening of society, reallocation of health-care resources could potentially cause persistent changes in access to physical consultations.

Objectives: To explore use of remote consultations in patients with IRD followed in the nationwide DANBIO registry at three time points (lockdown from spring 2020 followed by gradual reopening of society) during the COVID-19 pandemic. Furthermore, to explore satisfaction with treatment access, and preferred mode of consultation including potentially associated clinical factors.

Methods: We performed a nationwide survey where three times, an online questionnaire (Q) "*You and your arthritis in times of COVID-19"* with questions regarding use of and access to remote and physical consultations was sent to all patients in DANBIO (Q1: March-April 2020, Q2: November 2020, Q3: May 2021). (ref)

Patient characteristics were captured in DANBIO (gender/age/diagnosis/biological therapy) and from the questionnaire (work status/comorbidities/EQ-5D). Use of physical and/or remote consultations 0-3 months before surveys and satisfaction with access was identified. Clinical factors associated with a preference for physical consultations at time of Q3 (versus remote contact (telephone/e-mail/video)) were explored with multivariable logistic regression analysis.

Results: Totally, 12,789/14,755/13,921 patients responded to Q1/Q2/Q3, respectively, with 23,311 unique patients participating in at least one survey. Characteristics of patients responding to Q3 are shown in Table 1.

Table 1. Respondents to questionnaire 3, n=13,921.

Gender	Female	63%
Median age, IQR, years		64 (54-72)
Diagnosis	Rheumatoid arthritis	64%
	Psoriatic arthritis	16%
	Axial spondyloarthritis (AxSpA)	12%
	Other	8%
Current occupational status	Working	41%
No. of self-reported comorbidities	≥1	65%
Current biologic use	yes	27%*
EQ-5D, median (IQR)		0.8 (0.7-0.9)

EQ-5D: EuroQol quality of life (5-dimension)*By March 2020

During the preceding 3 months, proportions of patients with physical/remote consultations were 22%/45%, 41%/38%, 40%/39% for Q1, Q2, Q3, respectively. Remote consultations were mainly by telephone, whereas email (<5%) and video (<1%) were rarely used. In all three surveys, only 7% of respondents found that access to counseling with their rheumatologist had deteriorated during the pandemic (Figure 1A) whereas the majority found it to be unchanged or did not know. The preferred contact form was physical consultations (68-74%, Figure 1B, not available for Q1). Factors associated with preference for physical consultation were female gender, higher age (>60 years), biological treatment, low EQ-5D and not having axial spondyloarthritis, whereas work status and comorbidities were without significance (logistic regression analyses, details not shown).

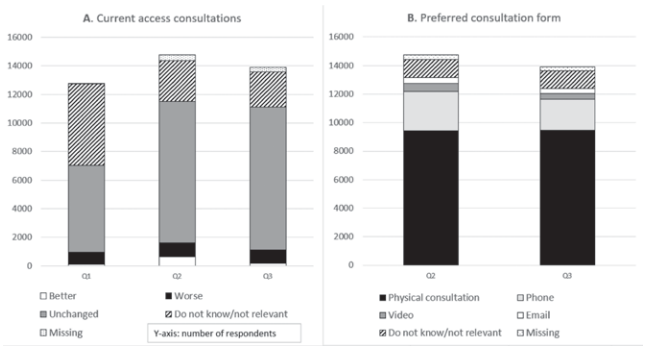

Figure 1.

Conclusion: Despite a widespread use of remote consultations during the pandemic, nationwide questionnaire surveys performed at three time-points during the COVID-19 pandemic showed that most patients were satisfied with access to rheumatic counseling. Nevertheless, in-person contacts were preferred by most patients, mainly women and elderly.

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POS1198

VACCINATION AGAINST COVID-19 SHOULD BE ENCOURAGED IN PATIENTS WITH RHEUMATIC DISEASE, AS MOST PATIENTS DEVELOP A SEROLOGICAL RESPONSE AGAINST THE VACCINE AND VACCINATION REDUCES SELF-IMPOSED ISOLATION AND SHIELDING BEHAVIOR

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Background: Vaccine trials of the SARS-CoV-2 mRNA vaccines were encouraging but excluded most patients with rheumatic diseases (RD) and patients treated with immunosuppressive therapy. However, reports of a more severe COVID-19 disease course in patients with RDs prompted strategies for expediting vaccination of RD patients in most countries. In addition to the impact experienced by most people of the pandemic, patients with RDs were adversely impacted by the potential risk of severe COVID-19 due to their disease and immunosuppressive treatment. Fear of COVID-19 led to disproportionate anxiety, self-isolation, and shielding behavior for many RD patients at the beginning of the pandemic.

Objectives: We investigated antibody levels in serum against SARS-CoV-2 after a two-dose vaccination with an mRNA vaccine in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Further, we examined the association between reactogenicity and immunogenicity and how vaccination influenced patient behavior concerning fear of COVID-19 and shielding.

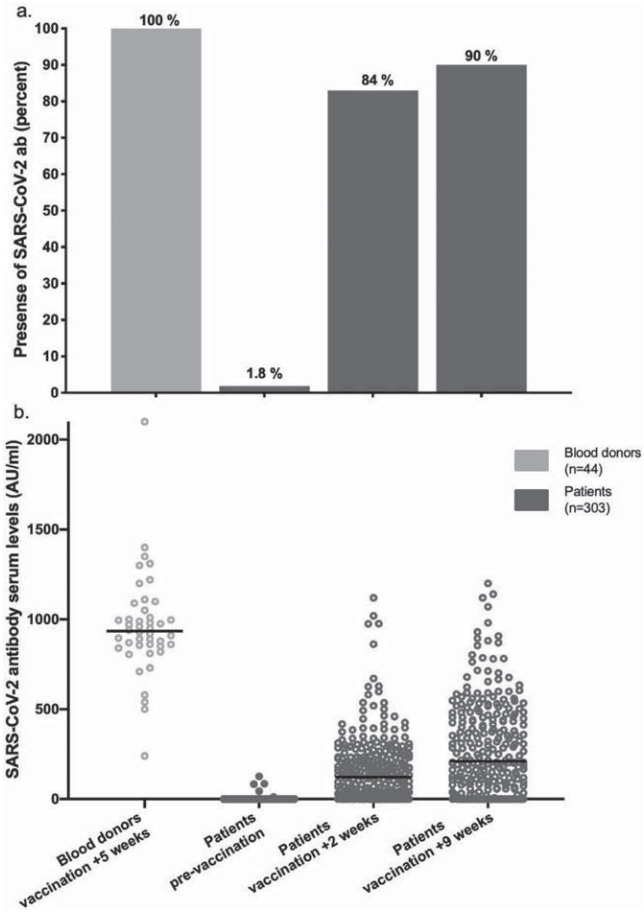

Figure 1. Total antibody response against SARS-CoV-2 after two mRNA vaccines. Antibody response against mRNA COVID-19 vaccine pre-vaccination, 1 and 9 weeks after in patients with rheumatic diseases and 5-6 weeks after vaccination in blood donors. (A) Percentage with measurable SARS-CoV-2 antibody results after vaccination. (B) Levels of SARS-CoV-2 antibodies in serum.

Methods: Patients with SLE or RA from the COPANARD (Corona PANdemic Autoimmune Rheumatic Disease)[1] cohort received two doses of an mRNA vaccine between January and August 2021 and had total antibodies against SARS-CoV-2 measured before vaccination and 2 and 9 weeks after the second vaccination. In addition, patients answered an electronic questionnaire before and eight weeks after vaccination concerning behavior, anxiety, and symptoms of depression (PHQ-9).

Results: Three-hundred-and-three patients and 44 blood donors (healthy controls) were included. Significantly fewer patients (90%) had measurable antibodies against SARS-CoV-2 compared to blood donors (100%) after the second vaccination (p<0.001) (Figure 1). Treatment with Rituximab was the strongest predictor of unfavorable vaccine response, as only 27% were seropositive after vaccination. We found a negative effect of prednisone and methotrexate but no effect of age, comorbidity, or pausing medication on seroconversion. Patients experienced significant improvement after vaccination in 10 out of 12 questions regarding behavior and fear of COVID-19, but no change was observed in symptoms of depression (p=0.62) or anxiety (p=0.46).

Conclusion: The majority of patients with SLE or RA had a measurable serological response to the COVID-19 mRNA vaccine after two doses. Treatment with Rituximab was the strongest predictor of no seroconversion. Our findings warrant encouragement of vaccination against COVID-19 for patients with RD, as most patients benefits with both a serological immune response and reduced isolation and shielding behavior.

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POS1199

IS PSORIATIC ARTHRITIS A RISK FACTOR FOR SEVERE COVID -19 INFECTION? DATA FROM THE ARGENTINIAN REGISTRY SAR-COVID

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Background: Comorbidities, particularly cardio-metabolic disorders, are highly prevalent in patients with psoriatic arthritis (PsA) and they were associated with an increased risk of atherosclerotic cardiovascular disease, which have been associated with higher morbidity and mortality. Whether PsA enhances the risk of SARS-CoV-2 infection or affects the disease outcome remains to be ascertained.

Objectives: To describe the sociodemographic, clinical and treatment characteristics of patients with PsA with confirmed SARS-CoV-2 infection from the SAR-COVID registry and to identify the variables associated with poor COVID-19 outcomes, comparing them with those with rheumatoid arthritis (RA).

Methods: Cross-sectional observational study including patients ≥18 years old, with diagnosis of PsA (CASPAR criteria) and RA (ACR / EULAR 2010 criteria), who had confirmed SARS-CoV-2 infection (RT-PCR or serology) from the SAR-COVID registry. Recruitment period was between August 13, 2020 and July 31, 2021. Sociodemographic variables, comorbidities, and treatments were analyzed. To assess the severity of the infection, the ordinal scale of the National Institute of Allergy and Infectious Diseases (NIAID)1 was used, and it was considered that a patient met the primary outcome, if they presented criteria of categories 5 or higher on the severity scale. For this analysis, Chi2 test, Fisher's test, Student's test or Wilcoxon test, and binomial logistic regression using NIAID>=5 as dependent variable were performed.

Results: A total of 129 PsA patients and 808 with RA were included. Clinical characteristics are shown in Table 1. Regarding PsA treatment, 12.4% of PsA were receiving IL-17 inhibitors, 5.4% IL12-23 inhibitors, one patient apremilast and one abatacept. The frequency of NIAID≥5 was comparable between groups (PsA 19.5% vs RA 20.1%; p=0.976). (Figure 1).

Table 1. Characteristics of patients with PsA and RA who presented COVID-19 in the SAR-COVID registry.

	Psoriatic arthritis (n=129)	Rheumatoid arthritis (n=808)	P value	Total (n=937)
Age (years), mean (SD)	51.7 (12.7)	53.1 (12.9)	0.239	52.9 (12.9)
Female	72 (55.8)	684 (84.7)	<0.001	756 (80.7)
Comorbidities	65 (50.4)	355 (43.9)	0.203	420 (44.8)
Obesity (BMI ≥30)	19 (15.2)	102 (13.4)	0.692	121 (13.7)
Morbid obesity (BMI ≥40)	1 (0.8)	10 (1.3)	1	11 (1.25)
Hypertension	35 (28.5)	205 (26.8)	0.783	240 (27.0)
Diabetes	16 (13.0)	67 (8.8)	0.188	83 (9.39)
Dyslipidemia	24 (19.5)	102 (13.5)	0.106	126 (14.4)
Cardiovascular or cerebrovascular disease	5 (11.4)	32 (3.9)	0.033	37 (4.2)
Two or more comorbidities	55 (42.6)	219 (27.1)	<0.001	274 (29.2)
Current smoking	4 (3.6)	60 (8.4)	0.79	64 (7.7)
High disease activity	0 (0)	29 (3.8)	0.027	29 (3.23)
Glucocorticoids treatment	5 (20.0)	95 (60.1)	<0.001	100 (54.6)
Conventional DMARDs	47 (36.4)	443 (54.8)	<0.001	490 (52.3)
Biologic DMARDs	60 (46.5)	193 (23.9)	<0.001	253 (27.0)
JAK inhibitors	4 (3.10)	72 (8.9)	0.038	76 (8.1)
Full recovery of COVID-19	105 (84.0)	644 (81.7)	0.127	749 (82.0)
COVID-19 complications	16 (12.5)	68 (8.7)	0.227	84 (9.2)
Death due to COVID-19	1 (0.8)	34 (4.3)	0.074	35 (3.8)

Notes=values n (%) unless otherwise indicated; BMI: Body Mass Index; DMARDs: disease-modifying antirheumatic drugs; JAK inhibitors: Janus kinase inhibitors.

PsA patients with NIAID≥5 in comparison with NIAID<5 were older (58.6±11.4 vs 50±12.5; p=0.002), had more frequently hypertension (52.2% vs 23%; p=0.011) and dyslipidemia (39.1% vs 15%; p=0.017). In the multivariate analysis, age (OR 1.06; 95% CI 1.02–1.11) was associated with a worse outcome of the COVID-19 (NIAID≥5) in patients with PsA, while those who received methotrexate (OR 0.34; 95% CI 0.11–0.92) and biological DMARDs (OR 0.28; 95% CI 0.09–0.78) had a better outcome.

Graphic 1. COVID -19 severity according to the ordinal scale of the National Institute of Allergy and Infectious Diseases (NIAID) in PsA and RA patients.

Conclusion: Although PsA patients have a higher frequency of cardiovascular and metabolic comorbidities than those with RA, the COVID-19 severity was similar. Most of the patients had mild SARS-CoV-2 infection and a low death rate.

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POS1200

DIFFERENCES BETWEEN THE FIRST AND THE SECOND WAVE OF SARS-COV-2 INFECTION IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES IN ARGENTINA: DATA FROM THE SAR-COVID REGISTRY

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Background: In Argentina we have witnessed two COVID 19 waves between 2020 and 2021. The first wave occurred during the spring of 2020 and it was related to the wild type of the virus, the second occurred during the fall/winter of 2021 when the gamma variant showed a clear predominance. During the first wave, patient with rheumatic diseases showed a higher frequency of hospitalization and mortality (4% vs 0.26%) when compared to the general population[1]; at that time, however, vaccination was not yet available.

Objectives: To compare sociodemographic and disease characteristics, course and outcomes of SARS-CoV-2 infection in patients with immune-mediated/auto-inflammatory diseases (IMADs) during the first and second waves in Argentina.

Methods: SAR-COVID is a national, multicenter, longitudinal and observational registry, in which patients ≥18 years of age, with a diagnosis of a rheumatic disease who had confirmed SARS-CoV-2 infection (RT-PCR or positive serology) were consecutively included since August 2020. For the purpose of this report, only patients with IMADs who had SARS-CoV-2 infection during the first wave (defined as cases occurred between March 2020 and March 2021) and the second wave (cases occurred between April and August 2021) were examined. Sociodemographic characteristics, disease diagnosis and activity, comorbidities, immunosuppressive treatment and COVID 19 clinical characteristics, complications and outcomes: hospitalization, intensive care unit (ICU) admission, use of mechanical ventilation and death were compared among groups. Descriptive statistical analysis was performed. Variables were compared with Chi squared test and Student T test or Mann Whitney test. Multivariable logistic regression models with forward and backward selection method, using hospitalization, ICU admission and death as dependent variables were carried out.

Results: A total of 1777 patients were included, 1342 from the first wave and 435 of the second one. Patients had a mean (SD) age of 50.7 (14.2) years and 81% were female. Both groups of patients were similar in terms of socio-demographic features, disease diagnosis, disease activity, the use of glucocorticoids ≥ 10 mg/day and the immunosuppressive drugs (Table 1 below). Patients infected during the first wave have higher frequency of comorbidities (49% vs 41%; p= 0.004). Hospitalizations due to COVID 19 (31% vs 20%; p <0.001) and ICU admissions (9% vs 5%; p= 0.009) were higher during the first wave. No differences in the use of mechanical ventilation (16% vs 16%; p= 0.97) nor in the mortality rate (5% vs 4%; p= 0.41) were observed. In the multivariable analysis, after adjusting for demographics, clinical features and immunosuppressive treatment, patients infected during the second wave were 40% less likely to be hospitalized (OR= 0.6, IC95% 0.4-0.8) and to be admitted to the ICU (OR= 0.6, IC95% 0.3-0.9).

Table 1.

Variable (% or Mean – SD)	First wave (n=1342)	Second wave (n=435)	p Value
Female gender	81	80	0.7
Age (years)	51.0 (14.5)	50.0 (13.3)	0.2
Disease diagnosis			
Rheumatoid arthritis	46	46	1
Ankylosing spondylitis	10	11	0.8
Systemic lupus erythematosus	17	185	0.9
Systemic Scleroderma	5	5	1
Sjögren´s syndrome	6	5	0.7
Inflammatory myopathies	3	3	0.5
Vasculitis	4	3	0.4
Disease activity			
High	4	3	0.5
Use of immune modulators			
DMARDcs	53	56	0.2
DMARDts	4	6	0.1
DMARDb	82	82	1
Use of glucocorticoids ≥10 mg	12	12	0.9
Comorbidities	49	41	**0.004**

Conclusion: The impact of COVID 19 in Argentina, in terms of mortality in patients with IMADs was still higher compared to the general population during the second wave. However, the frequency of hospitalizations and ICU admissions was lower. These findings could be explained by the introduction of the SARS COV 2 vaccination and, probably, by the cumulative knowledge and management improvement of this infection among physicians.

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POS1201

SAFETY OF SARS-COV-2 VACCINES IN PATIENTS WITH RHEUMATIC DISEASES: DATA FROM THE NATIONAL REGISTRY SAR-COVAC FROM ARGENTINA

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Background: Patients with rheumatic diseases (RD) have been excluded from SARS-CoV-2 vaccine trials, though data appear to show safety and efficacy, mostly evidence remains in mRNA vaccines. In our country, adenovirus-vector, inactivated and heterologous scheme vaccines are frequently used.

Objectives: To describe the safety of SARS-CoV-2 vaccines in patients with RD from the national registry SAR-CoVAC and to assess sociodemographic and clinical factors associated to AE and disease flares after vaccination.

Methods: Adult patients with RD who have been vaccinated for SARS-CoV-2 from de Argentine Society of Rheumatology Vaccine Registry (SAR-CoVAC) were consecutively included between June 1st and December 21st, 2021, This is a national multicentric observational registry that includes patients that have received at least one dose of any SARS-CoV-2 available vaccines in Argentina. Data is voluntarily collected by the treating physician. Naranjo scale was use to assess the association between the AE and vaccination. Homologous and heterologous schedules were defined according to whether both vaccines received were the same or different, respectively. Descriptive statics, Chi2 test, Fischer test, T test, ANOVA and multivariate regression logistic model were used.

Results: A total of 1679 patients, with 2795 SARS-CoV-2 vaccine doses were included. Vaccines more frequently used were: Gam-COVID-Vac (1227 doses, 44%), ChAdOx1 nCov-19 (872 doses, 31%), BBIBP-CorV (482 doses, 17%) and mRAN-1273 (172 doses, 6%). Altogether, 510 EA were experienced by 449 (27%) patients. Pseudo-flu syndrome was the most frequent (11%), followed by injection site reaction (7%). They were significantly more frequent after the first dose in comparison to the second one (13% vs 7% and 9% vs 5%, respectively, p<0.001 in both cases). All were mild or moderate and no patient was hospitalized due to an AE. One case of moderate anaphylaxis was reported by a patient who received Gam-COVID-Vac. No cases of vaccine-induced thrombotic thrombocytopenia were observed. There were 25 disease flares reported, 17 (68%) cases of arthritis. Among patients with two doses, those with heterologous schedule presented AE more frequent after the second dose (39% vs 17%).Total incidence of EA was 182.5 events/10 00 doses, it was significantly lower for BBIBP-CorV (105.9 events/1000 dosis, p<0.002 for all cases). The higher incidence of AE was observed for mRAN-1273 (261.6 events/1000 doses) and ChAdOx1 nCov-19 (232.8 events/1000 doses). Patients with AE were younger [mean 55 years (SD 14) vs 59 years (SD 14), p <0.010], not Caucasian ethnicity [48% vs 35%, p<0.001], had higher education level [mean 13.8 years (SD 4) vs 11.9 years (SD 5), p<0.001], were more frequently employed [54% vs 44%, p<0.001], lived mostly in urban area [99% vs 95% p <0.001, had more frequently dyslipidemia [38% vs 28% p 0.012], and less frequently arterial hypertension [49% vs 65%, p<0.001]. Systemic lupus erythematosus [11% vs 7%, p=0.039] and Sjögren syndrome [6% vs 1.8%, p<0.001] were more frequent among them, while non inflammatory diseases were less prevalent [19% vs 31%, p<0.001]. They were taking steroids [24 vs 18%, p=0.007], antimalarials [17% vs 10%, p<0.001] and methotrexate [41% vs 31%, p <0.001] more frequently. In the multivariable analysis, mRAN-1273 and ChAdOx1 nCov-19 were associated with AE, while BBIBP-CorV with lower probability of having one. (Figure 1)

Conclusion: The incidence of AE was 1825 events/1000 doses, were significantly higher for mRAN-1273 and ChAdOx1 nCov-19 and lower for BBIBP-CorV. Most common AE was pseudo-flu syndrome. Female sex, being younger, higher education level, ChAdOx1 nCov-19 and mRAN-1273 vaccines, the use of methotrexate and antimalarials were related of EA in patients with RD.

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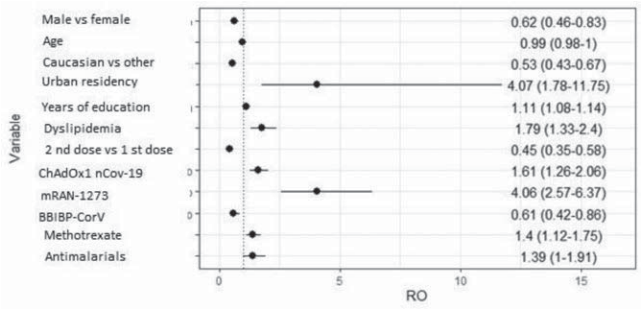

Figure 1. Variables associated with the development of AE. Multivariate logistic regression model

POS1202

B-CELL RECONSTITUTION IS STRONGLY ASSOCIATED WITH A POSITIVE SEROLOGIC RESPONSE TO THE COVID-19 BOOSTER VACCINE IN PREVIOUSLY SEROLOGICALLY UNRESPONSIVE RITUXIMAB TREATED RHEUMATIC DISEASE PATIENTS

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Background: Booster doses of SARS-CoV-2 vaccines have emerged as an important strategy for containing the pandemic and may be especially important to rituximab treated patients. B-cell depletion has been associated with worse outcomes from COVID-19 infection, and many rituximab treated patients demonstrate an inadequate serologic response to the initial vaccine series (1). Strategies to optimize serologic response to COVID-19 vaccine boosters in previously serologically unresponsive patients is, therefore, of particular relevance.

Objectives: To assess factors associated with serologic response to COVID-19 booster vaccines in rituximab treated patients previously serologically unresponsive to the initial vaccine series.

Methods: A retrospective chart review of rituximab treated patients who failed to demonstrate a serologic response to the first SARS-CoV-2 vaccination series and subsequently received an mRNA vaccine booster was performed. Serologic response four weeks or more after the booster was the primary outcome. T-tests, Fisher's exact tests, and Wilcoxon rank sum tests were used for comparisons. Box and whisker plots were constructed to visualize differences between serologic response.

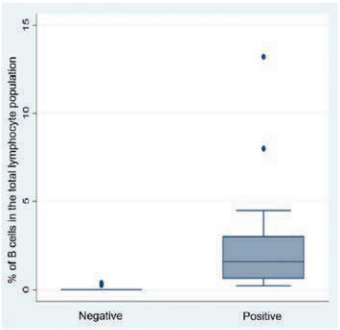
Results: In 31 rituximab treated patients who were seronegative following the initial vaccine series, demographic characteristics, concurrent therapies, rheumatologic diagnosis, and vaccine type were not associated with serologic positivity to the booster vaccine (Table 1). B-cell reconstitution was significantly different between those with positive (median, IQR 1.785 (0.65, 3)) and negative (median, IQR 0 (0,0)) serologic responses to the booster (p-value<0.001) as was time from last rituximab exposure (p-value = 0.030) (Figure 1). Positive predictive value of B-cell presence was 90.9% (95% CI: 70.8%, 98.9%) and negative predictive

Table 1. Bivariate comparisons between seronegative and seropositive patients to the COVID-19 booster vaccine by patient characteristics and demographics

Factor	Value	Negative	Positive	p-value[a]
N	31	10	21	
Age, median (IQR)	64 (51, 72)	63 (51, 69)	65 (51, 73)	0.75
Sex				1.00
Female	23 (74%)	7 (70%)	16 (76%)	
Male	8 (26%)	3 (30%)	5 (24%)	
Any immunosuppressant[b]	9 (29%)	3 (30%)	6 (29%)	1.00
Corticosteroid	5 (16%)	1 (10%)	4 (19%)	1.00
3rd Vaccine dose type				0.24
Pfizer	19 (61%)	8 (80%)	11 (52%)	
Moderna	12 (39%)	2 (20%)	10 (48%)	
Dichotomous B-cell status around booster dose				<0.001
No detectable B-cells	7 (23%)	7 (70%)	0 (0%)	
Detectable B-cells	22 (71%)	2 (20%)	20 (95%)	
Missing	2 (6%)	1 (10%)	1 (5%)	
Time from last RTX infusion to booster, median (IQR)	260 (216, 379)	188 (169, 245)	301 (251, 368)	0.030
Time from last RTX infusion to booster dose				0.10
<6months	8 (25.81%)	5 (50%)	3 (14%)	
6-12 months	15 (48.39%)	3 (30%)	12 (57%)	
>12 months	8 (25.81%)	2 (20%)	6 (29%)	

[a]P-values are from Fisher's exact test, Student's T-test and Wilcoxon rank sum tests[b]Immunosuppressants included Leflunomide, Azathioprine, Methotrexate, Mycophenolate Mofetil, and Tocilizumab IQR= Interquartile range

Figure 1: COVID-19 booster vaccine response in rituximab treated patients by B-cell status



Among N=29 people with % B-cells available, 9 were serologically negative and 20 were serologically positive. The percentage of B-cells among the negative serologic response median IQR was 0 (0, 0). Among the positive serologic vaccine response group, the median IQR was 1.785 (0.65, 3). The p-value is from the Wilcoxon rank sum test. The Y-axis is the percentage of B-cells in the total lymphocyte population as measured by flow cytometry.

value was 100% (95% CI: 59%, 100%) for serologic response to the mRNA booster. Positive predictive value of time >6 months from last rituximab to the booster was 78.3% (95% CI 56.3%, 92.5%) and the negative predictive value was 62.5% (95% CI 24.5%, 91.5%).

Conclusion: Presence of detectable B-cells and longer time from last rituximab were associated with the development of SARS-CoV-2 spike protein antibodies following the booster vaccine. These factors should be considered in timing of administration of booster vaccine doses in previously unresponsive rituximab treated patients.

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POS1203 INCREASED PROTEASE-ACTIVATED RECEPTOR 1 AUTOANTIBODIES ARE ASSOCIATED WITH SEVERE COVID-19

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Background: In acute COVID-19 infection, growing evidence hints towards a broad activation of plasma cells and the presence of pathologic autoantibodies (abs). A systematic screening for abs confirmed induction of diverse functional abs by SARS-CoV-2 infection (1, 2). Immune-mediated thrombosis, involving platelet activation, has been identified as one of the key pathogenic mechanisms in COVID-19 and is linked to morbidity and mortality (3). As natural abs against G protein-coupled receptors, functional abs against the thrombin receptor type-1 (PAR-1) might predispose for increased activation of the coagulation system present in COVID-19 infection.

Objectives: The aim of this study is to identify the diagnostic value of anti-PAR1 antibodies and their capacity to predict the outcome of COVID-19 infection.

Methods: 82 serum samples from 55 individuals with COVID-19 derived from three different hospitals in Schleswig-Holstein, Germany, and 88 single time point samples from healthy controls were subjected to ELISA-based quantification of anti-PAR-1 abs (CellTrend GmbH Luckenwalde, Germany). The levels of anti-AT1R abs were compared with clinical and laboratory parameters.

Results: COVID-19 patients revealed markedly increased levels of circulating anti-PAR1 abs in hospitalized patients particularly in those required intensive care treatment in comparison to controls ($p < 0.0001$, Figure 1a). Anti-PAR1 ab levels were highest in patients with fatal outcome ($p = 0.006$, Figure 1a). Receiver operating characteristic (ROC) analysis of PAR1 abs levels in COVID-19 patients revealed a sensitivity of 84.00% and a specificity 79.25% for patients requiring intensive care unit (ICU) treatment and a sensitivity of 87.50 % and a specificity 84.51 % to distinguish fatal vs. non-fatal disease outcome (Figure 1b). We found correlation of circulating anti-PAR1 abs with D dimers.

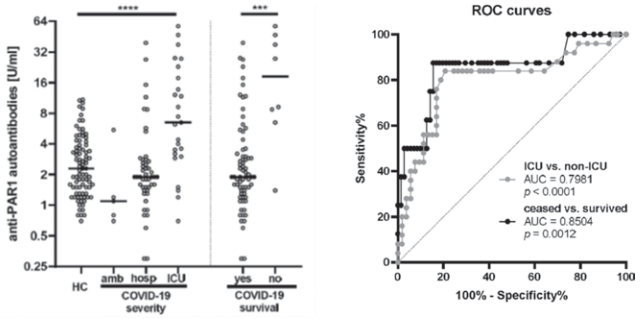

Figure 1. Levels of anti-PAR-1 abs in healthy controls (HC) versus COVID-19 positive patients with different disease severity and in non survivors (left). ROC curves are shown to discriminate patients requiring intensive care unit (ICU) or survivors in COVID-19 infection.

Conclusion: The increased anti-PAR1 abs, their prediction to identify patients requiring ICU and fatal outcome, and the correlation with markers for blood clotting suggest a role for antibodies against PAR1 in the disease development of blood clotting in COVID-19.

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POS1204 SARS-COV-2 INFECTION AFTER VACCINATION IN PATIENTS WITH RHEUMATIC DISEASES FROM ARGENTINA

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Background: Patients with rheumatic diseases (RD) have been excluded from SARS-CoV-2 vaccine trials. Though data appear to show safety and efficacy, mostly evidence remains in mRNA vaccines. However in our country, adenovirus and inactivated vaccines, as well as heterologous schemes are frequently used.

Objectives: To describe clinical characteristics and outcomes of SARS-CoV-2 infection after vaccination in patients with RD from de the SAR-CoVAC registry and to compare them with patients who got infected before vaccination. Additionally, factors associated with COVID-19 unfavorable outcome were assessed.

Methods: Adult patients with RD who have been vaccinated for SARS-CoV-2 were consecutively included between June 1st and December 21st, 2021. Confirmed SARS-CoV-2 infection (RT-PCR o serology) was reported by the treated physician. Infection after an incomplete scheme was defined when the event was diagnosed at least 14 days after first dose; and after a complete scheme when it occurred > 14 days after second dose. Homologous scheme is defined by two same doses of vaccine and heterologous by two different doses. Patients with previous SARS-CoV-2 infection were excluded. To compare SARS-CoV-2

infection characteristics in not vaccinated patients, subjects from the SAR-COVID registry, which includes patients with RD and SARS-CoV-2 infection, were matched 2:1 by gender, age and RD.
WHO-Ordinal Scale ≥5 was used to define unfavorable infection outcome. Descriptive statics, Chi2 test, Fischer test, T test and ANOVA were used.
Results: A total of 1350 patients from the SAR COVAC registry were included, 67 (5%) presented SARS-CoV-2 infection after vaccination. The later were mostly (72%) females with a mean age of 57 (SD 15) years old. The most frequent RD were rheumatoid arthritis (41%), psoriatic arthritis (12%) and systemic lupus erythematosus (10%). At vaccination, most of them (75%) had low disease activity or remission, 19% were taking steroids, 39% methotrexate, 27% bDMARDs and 6% JAK inhibitors. A total of 11 (16%) patients had SARS-CoV-2 infection <14 days after the first vaccine dose, 39 (58%) after an incomplete scheme and 17 (25 %) following a complete one. In the incomplete scheme group, 59% received Gam-COVID-Vac, 31% ChAdOx1 nCov-19 and 10% BBIBP-CorV; and in patients with complete scheme 47%, 24% and 29%, respectively. No event was reported after a complete heterologous scheme. No significant differences regarding sociodemoghraphic characteristics, RD, disease treatment, type of vaccine and regimen was found between in those with infection and those without it. After vaccination only 8 (12%) of the patients who got infected had an unfavorable course, 88% of them following an incomplete scheme (5 received Gam-COVID-Vac, 1 ChAdOx1 nCov-19 and 1 BBIBP-CorV) and one subject after a complete homologous Gam-COVID-Vac scheme. Having an unfavorable outcome of SARS-CoV-2 infection was associated to: male gender [63% vs 24%, p=0.036], older age [mean 70 years (SD 7) vs 55 years (SD 15), p=0.005], being Caucasian [100% vs 54%, p=0.018], higher education [mean 17 years (SD 4) vs 12 years (SD 4), p=0.010], the presence of comorbidities [100% vs 39%, p=0.001, having pulmonary disease [37% vs 5%, p=0.019], dyslipidemia [63% vs 17%, p=0.011] and arterial hypertension [63% vs 24%, p=0.036], RD, treatments, disease activity and types of vaccines received were comparable between groups. When comparing patients with and without vaccination prior SARS-CoV-2 infection, those who received at least one dose of vaccine had less frequently severe COVID-19 (12% vs 24%, p=0.067) and presented lower mortality due to COVID-19 (3% vs 6%, p=0.498). However these differences did not reach statistical significance.
Conclusion: In the SAR-CoVAC registry 5% of the patients had SARS-CoV-2 infection after vaccination, most of them mild and 25% after a complete scheme. Any vaccine was associated with severe COVID-19. When comparing with non-vaccinated patients, those with at least one dose, had less frequently severe disease and died due COVID-19.
Disclosure of Interests: None declared
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POS1205 COVID-19 IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES - DATA FROM THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES

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Background: Registries are providing real-life, long-term data relevant to safety, efficacy and long-term outcomes in patients with various rheumatic diseases. The Romanian Registry of Rheumatic Diseases (RRBR) collects efficacy and safety data, for patients with inflammatory rheumatic conditions treated with biologics and targeted synthetic DMARDs in the country. Infections are the most frequently adverse events associated with biologics exposure.
Objectives: To analyze the distribution, severity class and outcome of infection with SARS-CoV-2 in inflammatory arthritides during the last 2 years of COVID-19 pandemic.
Methods: We collected data for the past 2 years (2020 and 2021) from the RRBR, for the three main inflammatory rheumatic diseases (Rheumatoid Arthritis - RA, Spondyloarthritis - SpA and Psoriatic Arthritis - PsA): treatment exposure (drug class) at the time of COVID-19 diagnosis, severity class (mild, moderate, severe), the disease outcome (recovered, disabled, death). Finally, we compared those data to reported numbers of COVID - 19 infections in the general population, aiming to observe if there is a significant difference between the two groups.
Results: The study included 9469 patients with inflammatory rheumatic disease, in 298 (3.14%) patients a history of COVID-19 infection was recorded: 160 (53.69%) were diagnosed with RA, 116 (38.92%) with SpA and 22 (7.28%) with PsA. At the moment of COVID-19 infection, 200 patients were receiving anti-TNF inhibitors (67.11%), 27 JAK inhibitors (9.06%), 24 tocilizumab (8.05%), 23 rituximab (7.71%), 9 anti-IL17A monoclonal antibodies (3.02%) and 4 abatacept (1.34%). More than half of the cases were mild - 59.39% (177), whereas moderate forms were noted in 26.17% (78) and severe in 14.09% (42) of the total infected patients. Out of the 42 severe COVID-19 cases, 11 (26.19%) were treated with rituximab, 18 (42.85%) with TNF inhibitors, 7 (16.66%) with JAK inhibitors, 4 (9.52%) with tocilizumab, 1 (2,38%) with secukinumab and 1 (2.38%) with abatacept. Almost all cases recovered: 286 (95.97%) patients, while 12 (4.02%) deaths were recorded. The patients who died were on treatment with rituximab (5), tofacitinib (3), etanercept (2), secukinumab (1) and tocilizumab (1). Data from the National Public Health Institute showed a rate of COVID-19 infection in the general population of 9.36%, out of which 96.7% had a favorable outcome, while 3.26% deaths were reported.
Conclusion: This study confirms that patients receiving treatment with rituximab are at risk for a worse COVID-19 outcome. The increased number of severe cases and deaths related to COVID19 in patients receiving TNF inhibitors may be explained by the large use of this therapeutic option. Surprisingly, we noted 4 severe cases and one death related to COVID19, in patients treated with tocilizumab. We observed no significant differences in death rates and the outcomes of COVID-19 in patients with rheumatic diseases treated with biological therapies and the general population. The low rate of SARS-CoV-2 reported infections in the registry, compared to the general population, is most probably due to the commonly found underreporting of adverse events in registries.
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Disclosure of Interests: None declared
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POS1206 UNDERSTANDING THE LANDSCAPE OF RHEUMATOID ARTHRITIS (RA) PATIENTS TREATED WITH IL-6 INHIBITORS DURING THE COVID-19 PANDEMIC

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Background: Rheumatoid Arthritis (RA) is a complex autoimmune disease which affects the joints and various organs[1] and patients may experience frequent and painful flare ups. Besides conventional therapies, multiple bDMARDS are approved to treat RA, including tocilizumab and sarilumab. With IL-6 inhibitors being approved for emergency use to treat critically ill COVID-19 patients, this may influence the treatment paradigms of some RA patient cohorts.
Objectives: The objective of this study is to observe the landscape of RA patients treated with IL-6 inhibitors during the COVID-19 pandemic period, compared to the pre COVID-19 period.
Methods: A multi-centre online medical chart review study of patients with RA was conducted between January 2019 – March 2020 ("pre-COVID") and April 2020 – June 2021 ("during-COVID") among UK, FR, DE, IT & ES rheumatologists practicing across hospital and private practices. Recruited from a large access panel, physicians were screened for duration of practice in their specialty (3-30 years) and caseload (2 or more RA patients seen in an average week). Participants were asked to complete a 3-part survey online: (1) a doctor demographic questionnaire, (2) a perceptual questionnaire, and (3) patient charts for the next 5 biologic/JAKi receiving RA patients seen following receipt of the survey, which captures patient demographics and treatment history. Descriptive statistics were used to analyse the data.
Results: For the pre-COVID cohort, 1283 physicians were recruited and collectively reported 6250 RA patients, 754 of which were treated with IL-6 inhibitors for their RA. For the during-COVID cohort, 1279 physicians were recruited and collectively reported 6188 RA patients, 760 of which were treated with IL-6 inhibitors for their RA. 96% of sampled physicians cited access to IL-6 inhibitors in hospital or practice in the during-COVID period, compared to 77% in the pre-COVID period ($p<0.01$) - this may be linked to the approval of emergency use of IL-6 inhibitors to treat critically ill COVID-19 patients, hence making it more widely available during this period. A larger proportion of reported IL-6 inhibitor patients in the during-COVID cohort had stayed on this drug class for more than 6 months, compared to the pre-COVID cohort (67% vs 62%, $p<0.05$). Association with high-risk comorbidities, severity of RA at diagnosis and previous therapies received were key areas of differentiation between the two reported patient groups. For the during COVID cohort, IL-6 patients were significantly more likely to be recorded as having concomitant metabolic conditions vs the pre-COVID cohort (72% vs 48%, respectively; $p<0.01$) and respiratory conditions (4% vs 1%, respectively; $p<0.01$). Furthermore, reported IL-6 patients from the during COVID cohort were significantly more likely to have their RA classified as 'severe' (physician-defined) at the time of diagnosis vs pre-COVID reported IL-6 patients (41% vs 33%, respectively; $p<0.01$) and were significantly more likely to have switched from previous TNFi/CD20 biosimilar therapy compared to the pre-COVID cohort (16% vs 7%, respectively; $p<0.01$).

Conclusion: From the sample surveyed, it appears that high risk comorbidities, severity of RA at diagnosis and type of previous therapy are key differentiating points behind IL-6 usage in RA patients pre vs during the COVID-19 pandemic. With the increasing risk that RA patients may experience severe side effects if infected with COVID-19[2] and guidance to use IL-6 inhibitors in certain patient cohorts during this time, this may explain the patterns seen in our dataset. Further investigation using comparator cohort is warranted.

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Disclosure of Interests: None declared

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POS1207 SEROCONVERSION AFTER A THIRD COVID-19 VACCINATION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH (ULTRA-)LOW DOSE RITUXIMAB WITH A PREVIOUS INSUFFICIENT HUMORAL RESPONSE IS DEPENDENT ON RITUXIMAB DOSAGE

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Background: Around 60% of rheumatoid arthritis (RA) patients treated with ≥1000 mg rituximab (RTX) has an insufficient deemed humoral response after two COVID-19 vaccinations.[1] Recent research shows that a third COVID-19 vaccine may actually lead to a humoral response in 27% of patients with a previous non-response.[2] After two-dose vaccination, both ultra-low dose (ULD) 200 mg RTX and a longer time between latest RTX and vaccination were positively associated with sufficient response.[3] Yet, no data is available on the effect of those variables after a third vaccination in these ULD patients with an insufficient response after two vaccinations.

Objectives: To investigate the role of dosage and relative timing of RTX and vaccination on humoral response after a third COVID-19 vaccine in RA patients treated with RTX with insufficient humoral response after two COVID-19 vaccinations.

Methods: We included RA patients treated with ≥1 RTX dose in the year previous to the first vaccine from the COVAC cohort (Netherlands Trial Register, NL9342), who had an insufficient humoral response after two COVID-19 vaccines. Humoral response was measured 2-6 weeks after the third vaccine. As there is still a lot of uncertainty about a serological correlate of protection, we dichotomized between 'sufficient' and 'insufficient' response based on the cut-off of the specific assay used. Univariable logistic regression was used to investigate the association between dosing and timing, and sufficient response.

Results: Eighty-nine patients had an antibody measurement performed within the right time-frame and could be included (Table 1). Overall, 17 patients (19%) had a sufficient antibody response. Proportion of patients with sufficient humoral response was higher when the latest dose was 200 mg compared to 500 and 1000 mg (38% versus 21% versus 13% (Figure 1); odds ratio 200 versus 1000 mg (OR) 4.25; 95% confidence interval (CI) 0.99 to 18.29 (p=0.052), and especially when the dose was already 200 mg before the first vaccination (OR 4.63; 95% CI 1.08-19.84 (p=0.039)). Time since latest RTX infusion was not significantly associated with sufficient response after third vaccination (OR 1.00; 95% CI 1.00-1.01 (p=0.15)).

Table 1. Characteristics and outcomes sorted by rituximab dose before first vaccination

	200 mg (n=13)	500 mg (n=34)	1000 mg (n=42)
Age (years)‡	66 ± 11	67 ± 11	65 ± 13
Female sex	7 (54%)	29 (85%)	29 (69%)
Disease duration (years)†	21 (16-26)	18 (8-26)	14 (5-23)
RF and/or ACPA positive	13 (100%)	27 (80%)	31 (74%)
Concomitant csDMARD use at baseline	7 (54%)	21 (62%)	29 (69%)
Duration of RTX use (years)‡	5.8 ± 3.1	4.9 ± 3.1	4.5 ± 3.2
Days between latest RTX and 3rd vaccine†	127 (100-160)	117 (99-153)	126 (91-150)
Latest RTX dose before 3rd vaccine			
200 mg	12 (92%)	1 (3%)	0 (0%)
500 mg	1 (8%)	31 (91%)	5 (12%)
1000 mg	0 (0%)	2 (6%)	37 (88%)
Sufficient humoral response after 3rd vaccine	5 (38%)	7 (21%)	5 (12%)

Either displayed as number (percentage), median (interquartile range)† or mean ± standard deviation‡.

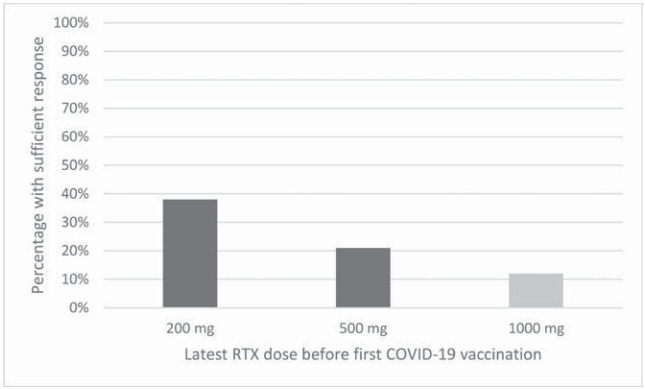

Figure 1. Humoral response rate after third COVID-19 vaccination sorted by baseline rituximab dose

Conclusion: Our study shows that a third COVID-19 vaccine can induce sufficient humoral response in a relevant proportion of (ultra-)low dose RTX treated RA patients who did not respond to the first two vaccinations, and that lower RTX dosing is associated with significant higher proportion of patients with sufficient humoral response. In contrast to the analysis after two vaccine doses, time since latest infusion was not significantly associated with response.

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POS1208 EQUITY CONSIDERATIONS IN COVID-19 VACCINATION STUDIES OF INDIVIDUALS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES

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Background: Individuals with autoimmune inflammatory rheumatic diseases (AIRDs) have an increased baseline risk of severe COVID-19 infection. Intersection of inequity factors may result in more severe adverse effects through influencing opportunities for health. We sought to examine the extent to which populations experiencing inequities were considered in studies of COVID-19 vaccination in individuals with AIRDs.

Objectives: The objective of this study is to assess how health equity is considered in studies of COVID-19 vaccination studies in individuals with AIRDs.

Methods: All studies (*N*=19) from an ongoing Cochrane living systematic review on the effects of COVID-19 vaccination in people with AIRDs were included. We identified inequity factors using the PROGRESS-Plus framework which stands for Place of residence, Race/ethnicity, Occupation, Gender/sex, Religion, Education, Socioeconomic status, and Social capital. Age, multimorbidity, and

health literacy were also assessed as "Plus" factors. We applied the framework to assess equity considerations in relation to differences in COVID-19 baseline risk, description of participant characteristics, controlling for confounding factors, subgroup analysis and applicability of study findings.

RESULTS:

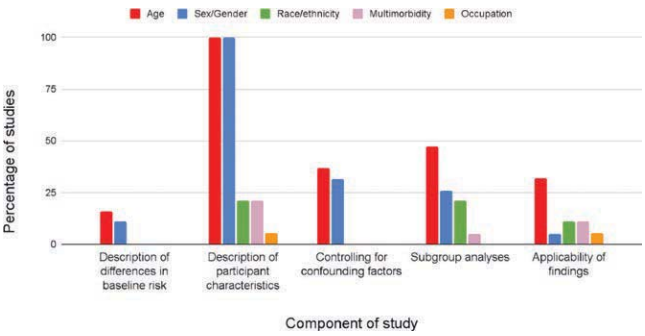

Figure 1.

All nineteen studies are cohort studies that followed individuals with AIRDs after COVID-19 vaccination. Two articles (11%) described differences in baseline risk for COVID-19 across age. All nineteen studies described participant age and sex, with race/ethnicity and multimorbidity described in four (21%) and occupation in one (5%). Seven studies (37%) controlled for age and/or sex as confounding factors. Eleven studies (58%) conducted subgroup analysis across at least one PROGRESS-Plus factor, most commonly age. Eight studies (42%) discussed at least one PROGRESS-Plus factor in interpreting the applicability of results, most commonly age (32%), then race/ethnicity and multimorbidity (11%).

Conclusion: It is unknown whether COVID-19 vaccine studies on individuals with AIRDs are applicable to populations experiencing inequities, as key inequity factors beyond age and sex have little to no reporting or analysis. Future COVID-19 vaccine studies should report social characteristics of participants consistently, facilitating informed decisions about the applicability of study results to the population of interest.

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POS1209 THE IMPACT OF THE COVID-19 PANDEMIC ON WORK PRODUCTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS: RESULTS FROM THE DUTCH SPA-NET REGISTRY

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Background: Since early 2020, governments have initiated local and nationwide measures to contain the spread of the coronavirus disease 2019 (COVID-19). In the Netherlands, people were strongly recommended to work from home, and several work sectors were shut down. In addition, hospitals had to reduce regular care. These changes, together with the risk of contracting COVID-19 and becoming ill, could have affected people's employment perspectives and work productivity. It is unknown to what degree this affected persons with chronic disorders, such as spondyloarthritis (SpA).

Objectives: To investigate whether work productivity in patients with SpA changed following the onset of the pandemic and the associated government-initiated containment measures in the Netherlands.

Methods: Data from the Dutch eHealth monitoring system SpA-Net were used. Since 2016, patients in SpA-Net completed outcome measurements when they attended outpatient rheumatology visits. Employment and work productivity were assessed with the Work Productivity and Activity Impairment questionnaire (WPAI, work productivity loss range 0-100%), capturing both sick leave and reduced at-work productivity. Covariables of interest were age, gender, education (high vs. low) and disease activity (ASDAS, BASDAI, patient global). The proportions of patients employed and their work productivity losses were compared during a 1-year period before and after the onset of the pandemic (March 2020). Generalized Estimating Equations (GEE) analysis of all assessments over time explored if work productivity in employed patients had changed with the onset of the pandemic, adjusting for potential confounders. Similar analyses with disease activity as outcome were used to facilitate interpretation of work productivity results.

Results: Of 238 patients, data were available during the 1-year period both before and after onset of the pandemic. Pre-pandemic, 128 (54%) patients were employed. These employed patients had a mean age of 49.0 (SD 10.2) years, 66 (54%) were male and the mean ASDAS was 2.1 (0.9). After the onset of the pandemic, 7 (5.5%) were no longer employed. In addition, 8 out of 110 (7.3%) originally unemployed patients had become employed by this time. Work productivity loss (0-100%) was worse after the onset of the pandemic (37.0) compared to the pre-pandemic year (27.0) (p<0.01). In multivariable GEEs with work productivity loss as outcome (and stratified by education due to interaction), patients with low education had work productivity losses that were almost 10% (absolute) higher after onset of the pandemic compared to pre-pandemic (B = 9.57, 95%CI 5.63-13.51) (Table 1). This was independent of ASDAS and other confounders. In patients with high education, however, no such association between pandemic onset and work productivity was seen. Analyses adjusting for other measures of disease activity (BASDAI, patient global) showed similar results. In GEEs with disease activity as outcome, disease activity before and after pandemic onset did not differ (B = -0.05, 95%CI -0.15 to 0.06 for ASDAS, model not shown).

Conclusion: Work productivity has worsened in patients with SpA since the onset of the pandemic, especially in patients with lower educational attainment, while disease activity remained stable. Care should be taken to support patients in their work role during the pandemic, and thereafter.

Table 1. GEE of work productivity loss (0-100, higher = worse)

	Univariable		Multivariable			
			Low education		High education	
Variable	B	95%CI	B	95%CI	B	95%CI
Age, years	0.26	-0.02 to 0.53	0.02	-0.40 to 0.45	0.17	-0.26 to 0.60
Male gender	**-6.78**	**-13.18 to -0.39**	-0.93	-10.39 to 8.53	-2.68	-12.41 to 7.06
High education	**-7.91**	**-14.24 to -1.58**	n/a		n/a	
ASDAS	**12.46**	**9.66 to 15.26**	**13.08**	**11.05 to 15.11**	**10.51**	**7.10 to 13.91**
Time, after vs. before onset pandemic*	**5.32**	**1.17 to 9.47**	**9.57**	**5.63 to 13.51**	1.49	-5.39 to 8.36

Associations in bold are significant (p<0.05)*Binary variable, indicating whether assessment took place after onset of pandemic vs. pre-pandemic (primary variable of interest)

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POS1210 SAFETY AND IMMUNOGENICITY OF COVID-19 VACCINES IN PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASE

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Background: COVID-19 vaccination strategies have evolved with increasing vaccine availability and emerging vaccine safety data. While data on immunogenicity and safety of COVID vaccination strategies exists, there is limited data

for people with immune mediated inflammatory diseases (IMIDs) such as inflammatory arthritis (IA), systemic autoimmune rheumatic disease (SARD), inflammatory bowel disease (IBD) and multiple sclerosis (MS).

Objectives: In IMID patients treated with homologous or heterogeneous COVID vaccines, to compare post vaccine IMID disease activity and COVID antibody responses.

Methods: Between March 2021 and Dec 2021, patients with IA (n= 70; 77% rheumatoid arthritis), SARD (n=82; 70% lupus), IBD (n= 92; 40% crohn's), and MS (n= 71; 77% RRMS) self-reported COVID illness and exposure risks, and disease activity prior to and 1 month post both COVID-19 vaccinations (V1 and V2). Disease activity was assessed by the Systemic Lupus Activity Questionnaire (SLAQ) for SARDs, the RAPID-3 and RA flate index for IA, the IBD Symptoms Inventory-short form (IBDSI) and IBD flare index for IBD and the 25 meter walk and 9 hole peg test and Expanded Disability Status Scale (EDSS) for MS. Patient reported flare state was assessed using the relevant questions these indices (SLAQ "Have you had a flare?"; RA Flare index "Are you in a flare?"; IBD flare "My IBD is sometimes to continously active"). Disease activity and serum anti-spike, anti-receptor binding domain (RBD) and anti-nucleocapsid (NC) IgG antibody titers at 30 days post V2 were compared across vaccine courses and to age-sex matched vaccinated blood donor controls (CNTS).

Table 1.

	All IMIDs	IA	SARD	IBD	MS
Age (mean (sd) years)	**56(15)**	**63(12)**	**56(14)**	**54(16)**	**51(17)**
Female (%)	**80**	**84**	**90**	**64**	**83**
COVID risk exposure (%)					
Any	**44**	**39**	**46**	**50**	**44**
Contact	**14**	**12**	**14**	**12**	**21**
Travel	**6**	**6**	**6**	**6**	**6**
HCW/hospitalized	**15**	**15**	**16**	**20**	**9**
Other risk	**9**	**6**	**10**	**12**	**8**
V1 mRNA (%)	**74**	**80**	**68**	**82**	**64**
V2 mRNA (%)	**97**	**98**	**96**	**96**	**99**
Homologous V1 V2 (%)	**71**	**79**	**67**	**74**	**64**
Flare status post V2 (%)	**10**	**15**	**6**	**0**	**-**
Seroconversion (%)					
Anti-Spike	**89**	**90**	**86**	**93**	**84**
Anti-RBD	**91**	**92**	**86**	**96**	**88**

Results: Patients were predominantly female (79.7%), with a mean (standard deviation-sd) age of 56 (15) years; 8% had suspected or diagnosed COVID-19 illness; 1.2% positive anti-NC (Table 1). For all IMIDS, the majority received mRNA vaccines-BNT162b2 (BNT) or mRNA1273 (V1 74%; V2 97%;) the rest received ChAdOx1 viral vector vaccines; 71% received homologogous vaccines (ChAdOx1-ChAdOx n=6; BNT-BNT n=174; mRNA1271-mRNA1273 n=21; ChAdOx1-BNT n=36; ChAdOx1- mRNA1273 n=30; BNT-mRNA1273 n=15; mRNA1273-BNT n=3; other n=4). For most IMIDs, disease activity was similar before and after each vaccination. Post V2 disease activity did not differ between homologous versus heterologous vaccines nor by vaccine type (RAPID3; SLAQ, 25 meter walk and 9 hole peg test and EDSS overall and subscales, IBDSI overall and subscales all p=NS). In 254 IMIDs, most seroconverted (anti-spike 86%; anti-RBD 96%). Seroconversion rates for CNTS were 98.1% for anti-Spike and 3.5% for anti-NC. Antibody titers were higher following homologous mRNA (BNT or mRNA12723) than homologous vector vaccine (Figure 1). For IMIDs primed with ChAdOx vector vaccine, boosting with BNT or mRNA1273 generated similarly increased anti-Spike and anti-RBD titers.

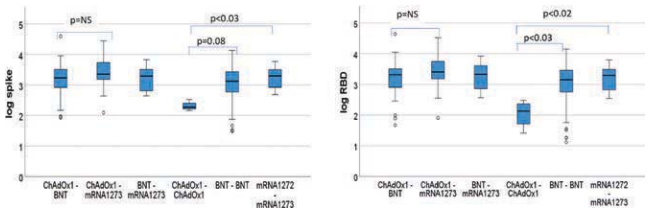

Figure 1. Post vaccine antibody titers

Conclusion: Heterologous COVID vaccination improves seroconversion rates following a viral vector vaccine and does not lead to disease flare in most IMID patients. While data is needed to assess vaccine effectiveness, duration of immunogenicity and effects of subsequent vaccination, this work supports mixing COVID vaccines for IMID patients.

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POS1211 SEROLOGICAL RESPONSE TO BNT162B2 MRNA ANTI-SARS-COV-2 VACCINATION IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: RESULTS FROM THE RHEUVAX COHORT

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Background: To date, globally considered, the literature suggests that AIRD may be at higher risk of infection and death due to COVID19 compared to the general population. Vaccination against SARS-CoV-2 reduces the risk of hospitalization and mortality. However, immunological alteration associated with Autoimmune Inflammatory Rheumatic Diseases (AIRD) and immunosuppressive medications may impair the response to vaccination. Emerging data suggest that immunosuppressive treatment may negatively impact the response to anti-SARS-CoV-2 vaccines in the AIRD population; data are robust for some treatments, more controversial for others. Identifying patients at higher risk of lack of protection is essential for shielding them and for adapting therapeutic protocol and vaccination timing.

Objectives: In the light of the current COVID19 epidemic and the availability of effective vaccines, this study aims to identify predictors of non-response to anti-SARS-CoV-2 vaccines in patients affected by AIRD.

Methods: An observational cross-sectional study was conducted evaluating the serological response and the persistence of antibodies at eight weeks in IRD patient cohort and non-IRD control. IRD and age and sex-matched controls volunteer among the health professionals (CTRL) who underwent vaccination with two doses of BNT162b2 were recruited for this study. Anti-Trimeric Spike protein antibodies were assayed eight ± one week after the second vaccine dose. Univariate and logistic regression analyses were performed to identify predictors of non-response and low antibody titers.

Results: Samples were obtained from 237 IRD patients (m/f 73/164, mean age 57, CI 95% [56-59]): 4 autoinflammatory diseases (AI), 62 connective tissue diseases (CTD), 86 rheumatoid arthritis (RA), 71 spondylarthritis (SpA) and 14 vasculitis (Vsc). 232 CTRL were recruited (m/f 71/161, mean age 57, CI 95% [56-58]). Globally, IRD had a lower seroconversion rate (88.6% vs 99.6%, CI 95% OR [1.61-5.73], p<0.0001) and lower antibody titer compared to controls (median (IQR) 403 (131.5-1012) vs 1160 (702.5-1675), p<0.0001). After logistic regression, age, corticosteroid (CCS), Abatacept (ABA), and Mycophenolate Mofetil (MMF) use were predictors of non-response. The antibody titers eight weeks after the second dose of vaccine were lower in AIRD compared to controls, median (IQR) 403 (131.5-1012) vs 1160 (702.5-1675), p<0.0001 with no difference between sexes and age groups. CTD, RA and SpA had lower antibodies levels. However, the logistic regression model identified treatment with MMF, ABA, CCS, Methotrexate (MTX), Rituximab (RTX), Janus Kinase inhibitors (JAKi) and TNF inhibitors (TNFi) as independent predictors of serum titer. ABA, RTX, MMF, and MTX had the strongest effect size.

Conclusion: The response to anti-SARS-CoV-2 vaccines is often impaired in AIRD patients under treatment and may pose them at higher risk of severe COVID-19. Although this work focused on serological response, most of the treatment the impaired vaccine response are known to act on T cells, possibly also influencing the cellular response. Evidence-based protocols are required to time vaccination and treatment to improve immunization of AIRD patients.

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POS1212 SARS-COV-2 VACCINE SAFETY IN ADOLESCENTS WITH INFLAMMATORY RHEUMATIC AND MUSCULOSKELETAL DISEASES AND ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: There is a lack of data on Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) vaccination safety in children and young people (CYP) with rheumatic and musculoskeletal diseases (RMDs). Current vaccination guidance is based on data from adults with RMDs or CYP without RMDs.

Objectives: To describe the characteristics and outcomes of adolescents with inflammatory RMDs and adults with juvenile idiopathic arthritis (JIA) vaccinated against SARS-CoV-2.

Methods: We described patient characteristics, flares, and adverse events in adolescent cases under 18 with inflammatory RMDs and adult cases aged 18 or above with JIA submitted to the European Alliance of Associations for Rheumatology (EULAR) COVAX registry.

Results: Thirty-six adolescent cases were reported from 4 countries, the most frequent diagnosis was JIA (42%). Over half (56%) reported early reactogenic-like adverse events (AEs) experienced within 7 days of vaccination. One mild polyarthralgia flare and one serious AE (malaise) were reported. No CYP reported SARS-CoV-2 infection post-vaccination. In addition to the adolescent cases, eleven countries reported 74 adult JIA cases. Among these, 62% reported early reactogenic-like AEs and two flares were reported (mild polyarthralgia and moderate uveitis). No serious AEs of special interest were reported among adults with JIA. Three 20-30 year old females were diagnosed with SARS-CoV-2 post-vaccination; all fully recovered.

Conclusion: In this observational registry dataset, SARS-CoV-2 vaccines appeared safe in adolescents with RMDs and adults with JIA, with a low frequency of disease flares, serious AEs, and SARS-CoV-2 re-infection seen in both populations.

Table 1. Characteristics of adolescents with RMDs and adults with JIA reported to the EULAR COVAX registry

		Adolescents with RMDs (N=36)	Adults with JIA (N=74)
Sex	Female	21 (58)	54 (73)
	Male	15 (42)	20 (27)
Age (median [IQR])		15 [14.5, 17]	26 [23, 31]
Primary RMD diagnosis	Non-systemic JIA	10 (28)	63 (85)
	Systemic JIA	5 (14)	11 (15)
	Systemic lupus erythematosus	5 (14)	
	Spondyloarthritis/psoriatic arthritis	5 (14)	
	Vasculitis/other RMD #	11 (30)	
RMD disease activity	Remission	23 (64)	33 (45)
	Minimal	8 (22)	21 (28)
	Moderate	2 (6)	12 (16)
	Severe	1 (3)	1 (1)
	Not applicable/missing	2 (6)	7 (10)
RMD medication	None	9 (25)	3 (4)
	b-DMARD	9 (25)	50 (68)
	cs-DMARD	21 (58)	25 (34)
	ts-DMARD	5 (14)	2 (3)
	Systemic glucocorticoids	5 (14)	1 (1)
	Colchicine		7 (10)
	Other immunosuppressant *		
COVAX type	Pfizer/BioNTech	33 (92)	50 (68)
	Moderna	2 (6)	10 (14)
	AstraZeneca/Oxford	1 (3)	10 (14)
	Janssen		1 (1)
	CoronaVac		2 (3)
	UNK		1 (1)
COVAX doses	1	11 (31)	8 (11)
	2	2 (24)	61 (82)
	3	1 (3)	5 (7)
RMD flare	Yes	1 (3)	2 (3)
AE	Yes	20 (56)	46 (62)
Early AE	Injection site pain	8 (22)	16 (22)
	Redness	6 (17)	2 (3)
	Muscle pain	1 (3)	9 (12)
	Joint pain	4 (11)	3 (4)
	Headache	9 (25)	10 (14)
	Fever	1 (3)	26 (35)
	Chills	2 (6)	5 (7)
	Fatigue	1 (3)	13 (18)
	Vomiting		
AE of special interest	Non-serious	1 (3)	1 (1)
	Serious – important medical event	1 (3)	

All data are N(%) of the column unless stated otherwise.# Other RMD includes Sjogren's syndrome, systemic sclerosis, undifferentiated connective tissue disease, non-monogenic auto-inflammatory syndrome, chronic recurrent multifocal osteomyelitis, and other inflammatory arthritis* Other immunosuppressant includes ciclosporin, mycophenolate mofetil/mycophenolic acid.RMD, rheumatic and musculoskeletal disease; JIA, juvenile idiopathic arthritis; EULAR, European Alliance of Associations for Rheumatology; ANCA-associated vasculitis, anti-neutrophil cytoplasmic antibody-associated vasculitis; cs-, conventional synthetic; b-, biological; ts-, targeted synthetic; DMARD, disease-modifying anti-rheumatic drug; COVAX, Coronavirus vaccine; AE, adverse event.

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POS1213 SAFETY AND EFFICACY ASSESSMENT OF COVID-19 IMMUNIZATIONS / VACCINATIONS IN PATIENTS OF A GERMAN GENERAL RHEUMATOLOGICAL PRACTICE

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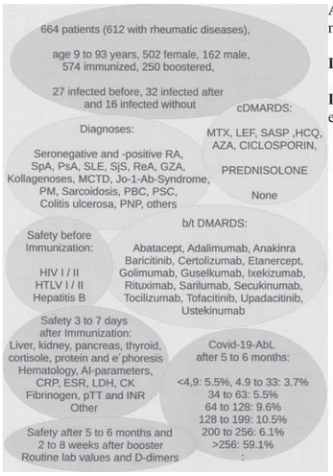
Background: German Covid-19 pandemic immunization program started Dec 26th, 2020 without population representative standardized real world data efficacy study protocols(1). Safety assessment: side effect panel of the Paul-Ehrlich Institute reporting system of suspected side effects (analogue and digital): Comparison of reported side effects against 100000 immunization doses vs historical known medical events against 100000 patient years. Not much is known how long side effect reporting periode after MRNA / Vector immunization is appropiate for the different immunization drugs (Biontech/Pfizer-Comirnaty(2), AstraZeneca-Vaxzevria, Moderna-Spikevax, Johnson&Johnson–Covid-19 vaccine Janssen) because for these no pharmacokinetic and –dynamic data (2,3) are available on spike protein biodistribution and how long it lasts in the human body. EMA / WHO guidelines declare these data not as essential for approval of vaccines, only for drugs (4).

Objectives: Real world safety and efficacy of Covid-19 immunizations.

Methods: In 664 patients (612 patients with rheumatic diseases) planned standardized assessment: Safety parameters before and 3-7 days after immunization (organ, hematology, myositis, thrombosis, inflammatory, autoimmunity parameters), after 5-6 months (before booster decision) d-dimer-levels, routine lab assessment (routine surveillance of rheumatic patients under therapy) and Covid-19-antibody levels (AbL).

Results: Most patients (94.5%) developed Covid19-AbL (except a few under Abatacept and Rituximab). After 5-6 months most patients (77%) still had Covid19 sufficient AbL above 128 BAU/ml (87% above 64 BAU/ml) (1). 37% of all patients developed relevant elevated d-dimers (still 5-6 months after immunization). In most of these patients the suspicion of inflammation of the microvascular system was a reasonable explanation (large vessel or pulmonary thromboembolism was ruled out in 98 %).



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Conclusion: Inflammation of the microvascular system as an underestimated side effect of MRNA / Vector immunization should be taken into account if (booster)-immunization decisions in patients with rheumatic diseases (maybe general) are to be made. Most patients with rheumatic diseases under (DMARD) therapy developed Covid-19 AbL (94.5%) (1) 5-6 months after MRNA / Vector immunization. All immunization decisions should also made dependent on AbL, because in case 5.5 % of immunized people do not react with AbL response, high numbers of breakthrough infection rates and hospitalization of immunized patients could be explained. Microvascular inflammation after MRNA / Vector immunization as a side effect in 37 % of rheumatologic patients could cause medical problems later on. Therefore also for safety reasons MRNA / Vector (booster) immunizations should also depend on the amount of already existing humoral response reflected by AbL.

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POS1214 COVID-19 VACCINATION RATE AND SAFETY PROFILE IN PATIENTS AFFECTED BY MIXED CRYOGLOBULINEMIC VASCULITIS.

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Background: Mixed cryoglobulinaemic vasculitis (MCV) is an immune-complex-mediated systemic vasculitis characterized by heterogeneous clinical manifestations mainly involving skin, kidney and peripheral nervous system. Despite reassuring safety data from EULAR Coronavirus Vaccine (COVAX) physician-reported registry, a significant proportion of patients with autoimmune diseases reported unwillingness to get vaccinated against SARS-CoV-2 infection in the preliminary results of the COVAD study, due to concerns about the lack of long-term safety data, and fear of associated side effects and disease flare.

Objectives: Aims of this multicentre Italian study were to investigate the prevalence of vaccination against SARS-CoV-2 in Italian population of MCV patients, to explore the reason for the missed vaccination, and to investigate short and long-term side effects of the vaccine, including vasculitis flare.

Methods: All MCV patients referring to 12 Italian centres were investigated about vaccination and possible both short- (within 48 hours) and long-term (within 30 days) adverse events (AE), classified according to FDA Toxicity Grading Scale for preventive vaccine clinical trials, and possible disease flares. Patients with MCV related to lymphoproliferative disorders or connective tissue diseases were excluded from the study. The baseline variables were expressed as percentages or mean±standard deviation. The differences between continuous variables were analysed using the Mann–Whitney nonparametric test. The chi-squared test, or Fischer's exact when appropriate, were used for categorical variables (absolute numbers and percentages) regarding baseline characteristics.

Results: A total of 416 patients, 69.2% females and 30.8% males, with a mean age of 70.4±11.7 years, were included in the study. Only 7.7% of patients were not vaccinated, mainly for fear of adverse events (50%) or for medical decision (18.8%). Corminaty was the vaccine most frequently used (80.5%). Interestingly, 6 patients (1.44%) were with a heterologous vaccination (usually AstraZeneca-Corminaty). Considering ongoing treatment, not vaccinated subjects were more frequently treated with chronic glucocorticoid therapy and/or Rituximab (p=0.049 and p=0.043 respectively). AE were recorded in 31.7% of cases, mainly mild and self-limiting (grade 1). More severe adverse events, such as flare of vasculitis, were observed in 5.3% of cases. AE were not associated with the kind of vaccine used and with the clinical manifestations of vasculitis. Patients with active MCV showed a lower frequency of short-term (within 48 hours) adverse events, but patients affected by peripheral neuropathies or skin vasculitis frequently showed a flare of their symptoms, recorded in 40% and 25% of cases, respectively. Finally, patients under glucocorticoid treatment were more prone to develop a vasculitis flare within a month after vaccination.

Conclusion: Vaccination in MCV patients has been performed in a high percentage of patients showing a good safety. Other than patients' fear, treatments with rituximab and glucocorticoids are the main reasons for delaying vaccination, and it should be considered by the physician before starting therapy. Vasculitis flares were observed in about 5% of cases, in line with that observed in other autoimmune diseases. Specific attention should be reserved to people with purpura or peripheral neuropathy, for the increased risk of exacerbation of their symptoms.

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POS1215

IMMUNE CORRELATES AND CLINICAL COURSE OF PATIENTS WITH RHEUMATOID ARTHRITIS FOLLOWING VACCINATION WITH ANTI SARS-COV-2 MRNA BASED VACCINES: RESULTS FROM A PROSPECTIVE, OBSERVATIONAL AND CONTROLLED STUDY

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Background: Vaccines are highly effective in preventing COVID-19 associated hospitalization and deaths. Strong and persistent immune responses are critical to provide protection for patients with immunomodulatory therapies.
Objectives: To assess humoral and cellular immune responses following 2 doses of an anti-SARS-CoV-2 mRNA based vaccine in rheumatoid arthritis (RA). Immune responses in patients treated with csDMARDs, bDMARDs (with the exception of rituximab) and JAK inhibitors were compared to healthy controls (HC) over 24 weeks. In addition, disease activity by CDAI and vaccine-induced side effects were prospectively monitored.
Methods: The RECOVER trial (**R**heumatoid **C**ovid-19 **V**accin**e** Immune **R**esponse) is a non-randomised, prospective observational control group trial and enrolled 77 RA patients on DMARD therapy and 21 HC. Clinical assessment and blood sampling was performed at baseline, 3 weeks after the 1st and 2 weeks after the 2nd vaccine dose and at week 12 and 24 after the 1st. Antibody response to the receptor binding domain (RBD) within the SARS-CoV-2 S1 protein was measured with the Elecsys Anti-SARS-CoV-2-S (Roche Diagnostics GmbH) test. The seroprofiling assay ABCORA, which has been suggested as a surrogate for neutralization,[1] was used to determine IgG, IgA and IgM responses to RBD, S1, S2 and N. The neutralizing activity NT50 at week 12 was assessed against Wuhan-Hu-1 pseudoviruses (HIV-based). IFN-γ ELISpots were applied to detect spike-reactive T cell responses after in vitro stimulation with a spike peptide mix.
Results: Baseline characteristics of participants are detailed in Table 1. Vaccination was well tolerated with no differences between RA patients and HC. At baseline, the majority of RA patients were in remission/LDA (57/77, 74%), this proportion decreased to 51% (39/77) after the second vaccine dose ($p = 0.005$). Treatment adjustments were required in 11/77 patients. The immunogenicity analyses were based on 73 RA patients after exclusion of 4 patients with previously unnoticed SARS-CoV-2 infection (positive for anti-nucleoprotein). In contrast to HC, anti-S titers were lower at all timepoints with significantly reduced titers observed in patients on abatacept and JAK inhibitors (Figure 1). Potent neutralizing activity (NT50 ≥ 250)) was detected in all HC at week 12, in contrast to 62% RA patients. NT50 correlated to the results based on the ABCORA assay. Peak anti-S titers (2 weeks after 2nd vaccine) were predictive of NT50 ≥ 250 at week 12 ($p < 0.0001$). In contrast to marked differences in the humoral immune responses, spike-protein specific IFN-α secreting T cells were largely unaltered by different DMARD regimen.

Table 1. Baseline characteristics

	RA patients (n = 77)	HC (n = 21)	p-value
Age (yrs), mean (± SD)	64 (13)	44 (14)	< 0.0001
Female, n (%)	46 (60)	15 (71)	NS
Vaccination type			
mRNA-1273, n (%)	12 (16)	0 (0)	0.06
BNT162b2, n (%)	65 (84)	21 (100)	
Disease activity (CDAI)			
Remission (≤ 2.8), n (%)	17/77 (22)		
Low (2.9 - 10), n (%)	40/77 (52)		
Moderate (10.1 - 22.0), n (%)	15/77 (20)		
High (22.1 - 76.0), n (%)	5/77 (7)		
DMARD therapy			
Mono csDMARDs, n (%)	22/77 (29)		
bDMARDs, n (%)	35/77 (46)		
Mono bDMARDs, n (%)	14/35 (40)		
JAKi, n (%)	20/77 (26)		
Mono JAKi, n (%)	8/20 (40)		
Prednisone, n (%)	25/77 (33)		
Mean daily dose (mg ± SD)	5.6 ± 3.6		

Conclusion: RA patients, in comparison with HC, revealed a slower kinetic and lower magnitude of humoral immune responses depending on the treatment regimen while T cell responses were largely maintained. Peak anti-S responses two weeks after the second vaccine were able to predict the development of potent neutralizing activity and should therefore be considered to individually tailor vaccination strategies.
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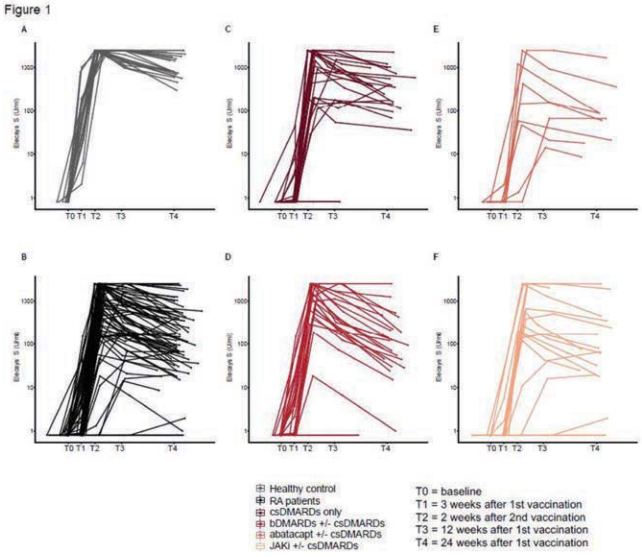
Figure 1



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POS1216

POTENTIAL PREDICTORS OF OUTCOME FOR ANAKINRA TREATMENT IN COVID-19 PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME

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Background: A hyperinflammatory response compatible with features of macrophage activation syndrome (MAS) contributes to this worse outcome in patients with Coronavirus Disease 2019 (COVID-19). Glucocorticoids have become the standard of care for those requiring oxygen support or mechanical ventilation. More targeted anti-inflammatory treatments with tocilizumab and anakinra have also been shown to be effective.
Objectives: More studies are being awaited to clarify the features of patients who would benefit more, and we investigated the characteristics of the surviving and dead patients who received anakinra.
Methods: The records of hospitalized adult patients between March 2020 and May 2021 in a tertiary referral center were evaluated. Diagnosis of COVID-19-related MAS was based on the expert opinion and preliminary criteria developed by our group that patients with a score of ≥45 were accepted COVID-19-related MAS.[1] Patients who received anakinra constituted the study group. Anakinra dose was determined according to the clinical and inflammatory parameters; and doses varied between daily 100-300 mg SC to 400-800 mg IV. Laboratory data of surviving and died patients were comparatively analyzed by using the ANCOVA method on the relevant days (baseline, anakinra-onset day, first response to anakinra treatment, and discharge or death). The temporal variation (drug onset day-first response day, drug onset day-discharge, or death day) was evaluated

using the ANOVA method. A 50% reduction of CRP compared to the anakinra start day was accepted as the first response to the treatment.
Results: Out of 1080 hospitalized patients, 218 (151 male, 67 female, mean age 60.0±14.1) who received anakinra were identified. Among them, 125 (57.3%) patients were followed in the ward, 21 (9.6%) did not need oxygen treatment during the hospitalization; 69 (31.6%) patients were followed at ICU, 40 of them were intubated, 30 (13.7%) died in ICU. Anakinra had been started in a mean of 4.8 days of hospitalization. Twenty had tocilizumab initially and then received anakinra because of ongoing inflammatory parameters. The majority (83.5%) received steroid treatment (79.5% methylprednisolone, 5% of dexamethasone), and 6 received one IV pulse 250 mg of methylprednisolone; 36 (16.5%) were followed before September 2020 and received anakinra without steroids because of the standard of care at that period. Only CRP was different between the alive and dead patients for the baseline parameters (p=0.05). On the first day of drug treatment, CRP and procalcitonin values were significantly higher in dead patients (Table 1). A 50% decrease in CRP level was achieved in 3.1 days in survivors and 4.7 days in dead patients. D-dimer (p=0.018), CRP (p=0.006), LDH (p=0.003), procalcitonin (p=0.005), creatinine kinase (p=0.001), and fibrinogen levels (p=0.05) were significantly different between the surviving and dead patients when the measurements between the first drug administration day and response day were compared. Neutrophil, lymphocyte count, ferritin, D-dimer, CRP, LDH, AST, procalcitonin, creatinine kinase, and fibrinogen levels were significantly different between the patients when the parameters between the first drug administration day and discharge/death day were compared. Dead patients had higher CRP values and they did not show a continuing CRP decrease with the steroids and anakinra (Figure 1).
Conclusion: Retrospective analysis of 218 patients suggests that starting anakinra earlier in hospitalized patients may provide better results, and a decrease in CRP, ferritin, D-dimer values, as well as an increase in lymphocyte count, are associated with favorable outcomes. Increasing values of D-dimer and troponin during treatment are associated with worse outcomes, possibly indicating cardiovascular and thrombotic pathologies not responding to anakinra. Changes in the CRP values are found to help monitor the response to anakinra. Other inflammatory pathways could be targeted in those who are not responding to appropriate doses of anakinra within 5 days.

Figure 1: Mean CRP changes in healthy and dead patients

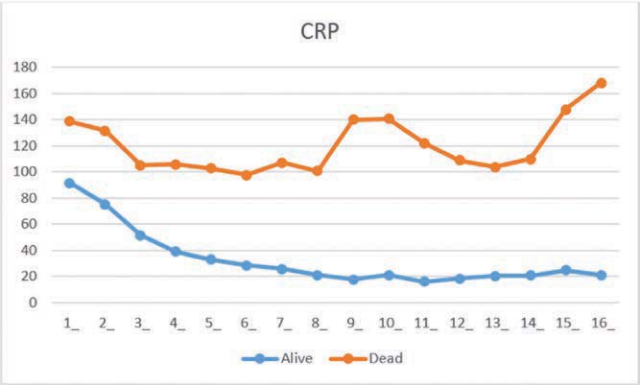

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Table 1: Characteristics of patients with baseline, anakinra first day, first response day, and exit day

	Baseline			Anakinra: first day			Anakinra: first response				Discharge			
	Survivors	Died	P-value	Survivors	Died	P-value	Survivors	Died	P-value	Drug Dose	Survivors	Died	P-value	Total dose
Neutrophil	6.9±0.31	6.7±0.8	0.79	7.7±0.3	8.8±0.8	0.24	7.2±0.27	9.1±0.81	0.02	1400	6.5±0.3	10±0.7	0.005	3300
Lymphocyte	1.06±0.22	0.62±0.57	0.47	1.1±0.3	0.46±0.9	0.48	1.2±0.3	0.78±0.9	0.64	1400	1.4±0.06	1.0±0.1	0.03	3300
Monocyte	0.44±0.02	0.42±0.06	0.78	0.45±0.02	0.40±0.05	0.50	0.52±0.02	0.53±0.06	0.98	1400	0.59±0.03	0.64±0.09	0.65	3300
Platelet	237.5±7.9	225±20.3	0.57	286.0±9.6	246.2±24.0	0.12	346.5±10.5	300±31.0	0.16	1400	332.9±11	229.8±26.4	0.005	3300
Ferritin	1249.6±80.3	1066.7±204.4	0.40	1530.7±141	1701±353.2	0.62	1270±104	1363.9±306	0.77	1400	773.4±221.6	3034±548.9	0.005	3300
D-dimer	2208.6±302.5	2001.4±764	0.80	1806.3±210	2732±528	0.10	1598.8±179.2	2889.2±525.7	0.02	1400	979.8±192	5343±464	0.005	3300
CRP	114.3±6	147.9±15.8	0.05	91.4±5.5	138.2±13.9	0.002	36±2.4	52.2±7.1	0.03	1400	7.4±4.1	155.8±10	0.005	3300
LDH	395.9±12.9	411±32	0.66	403.8±12	464.3±31	0.07	357.5±11.9	480±34.9	0.003	1400	268.8±18.8	601.3±45.4	0.005	3300
ALT	44.4±2.6	40±6.6	0.54	58.3±4.5	50.2±11.9	0.52	76.4±7.1	61.4±21.1	0.50	1400	80.7±7.7	124.9±18.7	0.03	3300
AST	48.8±3.3	43.6±8	0.56	49.9±3.2	51.8±8.2	0.83	52.5±5.5	45.9±16.4	0.70	1400	34.7±14	226.9±35	0.005	3300
Procalcitonin	0.92±0.5	0.81±1.3	0.94	0.26±0.03	0.57±0.09	0.003	0.15±0.09	1.2±0.26	0.005	1400	0.2±0.1	3.8±0.4	0.005	3300
Troponin	27.5±5.5	30.8±14	0.84	67.0±38	20.7±94.8	0.65	65±38.4	24.8±111.8	0.73	1400	27.5±7	127±17.4	0.005	3300
Creatinine kinase	283.4±70.3	229±202.8	0.80	214.5±67.6	330.9±175	0.53	95.6±19.6	293±57.7	0.002	1400	43.4±20.6	595.3±70.6	0.005	3300
Fibrinogen	612±12.5	669.7±32	0.09	631.5±12.7	646.8±32.6	0.31	547.7±10.8	566.9±32.9	0.58	1400	385.4±10	532±25.4	0.005	3300
Creatinin	1.2±0.07	1.3±0.1	0.60	1.1±0.05	1.2±0.1	0.44	1.1±0.08	1.5±0.2	0.09	1400	1.1±0.08	1.2±0.2	0.66	3300

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POS1217

ANTI-TNF THERAPY FOR IMMUNE MEDIATED INFLAMMATORY DISEASES MAY BE ASSOCIATED WITH LOWER ANTIBODY LEVELS AND VIRUS NEUTRALIZATION EFFICACY FOLLOWING SARS-COV-2 MRNA VACCINATION

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Background: The impact of immunosuppressants on COVID-19 vaccination response and durability in patients with immune-mediated inflammatory diseases (IMID) is yet to be fully characterized. Humoral response may be attenuated in these patients especially those on B cell depleting therapy and higher doses of corticosteroids, but data regarding other immunosuppressants are scarce.
Objectives: We aimed to investigate antibody and T cell responses and durability to SARS-CoV-2 mRNA vaccines (BNT162b and/or mRNA 1273) in IMID patients on immunomodulatory maintenance therapy other than B-cell depleting therapy and corticosteroids.
Methods: This prospective observational cohort study examined the immunogenicity of SARS-CoV-2 mRNA vaccines in adult patients with IMIDs (psoriatic arthritis, psoriasis, inflammatory bowel disease and rheumatoid arthritis) with or without maintenance immunosuppressive therapies (anti-TNF, methotrexate/azathioprine [MTX/AZA], anti-TNF + MTX/AZA, anti IL12/23, anti-IL-17, anti-IL23) compared to healthy controls. Automated ELISA for IgGs to spike trimer, spike receptor binding domain (RBD) and the nucleocapsid (NP) and T-cell release of 9 cytokines (IFNg, IL2, IL4, IL17A, TNF) and cytotoxic molecules (sFasL, GzmA, GzmB, Perforinin) in cell culture supernatants following stimulation with spike or NP peptide arrays were conducted at 4 time points: T1=pre vaccination, T2=median 26 days after dose 1, T3=median 16 days after dose 2 and T4=median 106 days after dose 2. Neutralization assays against four SARS-CoV-2 variants (wild type, delta, beta and gamma) were conducted at T3.
Results: We followed 150 subjects: 26 healthy controls and 124 IMID patients: 9 untreated, 44 on anti-TNF, 16 on anti-TNF with MTX/AZA, 10 on anti-IL23, 28 on anti-IL12/23, 9 on anti-IL17, 8 on MTX/AZA (Table 1). Most patients mounted antibody and T cell responses with increases from dose 1 to dose 2 (100% seroconversion at T3) and some decline by T4, with variability within groups. Antibody levels and neutralization efficacy was lower in anti-TNFgroups (anti-TNF, anti-TNF + MTX/AZA) compared to controls and waned by T4 (Figure 1). T cell responses were not consistently different between groups. Pooled data showed a higher antibody response to mRNA-1273 compared to BNT162b.
Conclusion: Following 2 doses of mRNA vaccination there is 100% seroconversion in IMID patients on maintenance therapy. Antibody levels and neutralization efficacy in anti-TNF group are lower than controls, and wane substantially by 3 months after dose 2. These findings highlight the need for third dose in patients undergoing treatment with anti-TNF therapy and continued monitoring of immunity in these patient groups, taking into consideration newer variants and additional vaccine doses.
Acknowledgements: This work was funded by a donation from Juan and Stefania Speck and by grants VR-1 172711, VS1-175545, FDN-143250, GA1- 177703 and GA2- 177716, from Canadian Institutes of Health Research and COVID Immunity task force and by Sinai Health Foundation
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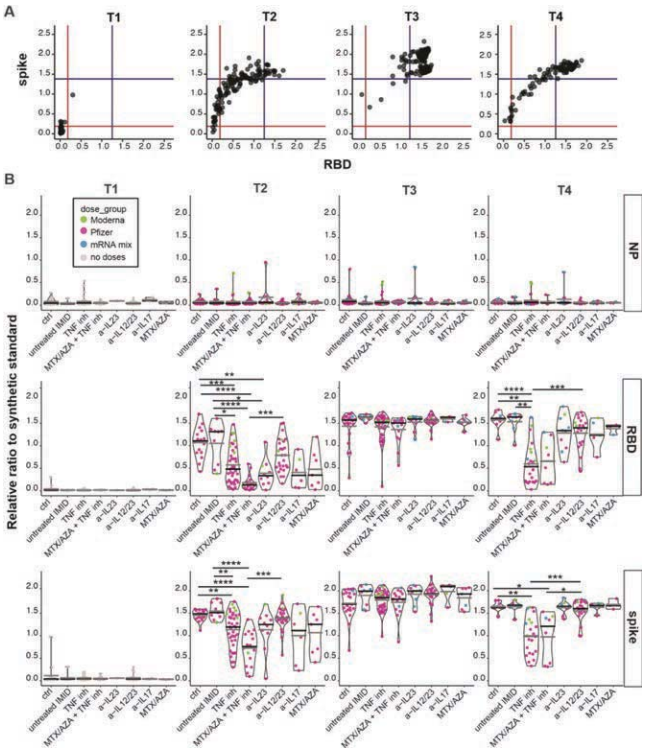

Figure 1. Antibody responses (A) Anti spike and anti RBD IgG levels at indicated time points. Blue line represents median ratio in convalescent patients. The red line is the seropositivity threshold: the median antibody level of those that pass both a 1% false positive rate and show ≥3SD from the log means of the negative controls. (B) Relative ratio of RBD, spike and NP across time. Black and gray lines indicate median and mean values, respectively. *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001

Table 1. Baseline characteristics of study participants

	Control	untreated IMID	Anti-TNF	Anti- TNF +MTX/ AZA	Anti-IL-23	Anti -IL-12/23	Anti -IL-17	MTX/ AZA	
	n=26	n=9	n=44	n=16	n=10	n=28	n=9	n=8	p-value
IMID*	N/A								
IBD		9	30	10	0	27	0	4	
Psoriasis		1	3	1	8	1	2	2	
PA		0	7	3	2	1	7	2	
AS		0	8	3	0	0	1	0	
RA		1	1	0	0	0	1	1	
Age									
median years [IQR]	36 [26-46]	33 [27-41]	38 [30-51]	53 [44-59]	48 [45-61]	34 [28-47]	49 [46-61]	42 [31-55]	<0.001^
Sex									
male (%)	16 (62)	5 (56)	18 (41)	8 (50)	5 (50)	13 (46)	6 (67)	4 (50)	0.772~
BMI									
median kg/m2 [IQR]	25 [23-28]	26 [22-27]	22 [24-26]	26 [24-28]	27 [24-35]	22 [21-24]	32 [26-34]	26[25-33]	0.001^
Vaccine interval									
median days [IQR]	74 [35-84]	54 [31-64]	60 [45-69]	64 [50-72]	74 [35-84]	62 [49-69]	65 [52-75]	58 [21-97]	0.372^

*multiple IMIDs per patient possible

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POS1218

RELAPSES OF IDIOPATHIC INFLAMMATORY MYOPATHIES AFTER VACCINATION AGAINST COVID19: A REAL-LIFE ITALIAN STUDY

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Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination plays a crucial role as pivotal strategies to curb the coronavirus disease-19 (COVID-19) pandemic. Despite the mass-scale vaccination, literature data about the incidence of disease flares in IIM patients are still not reported as well as the immunological condition.
Objectives: The present study aimed to describe the clinical status of patients affected by IIM after vaccination against COVID19 in order to assess the number of relapses or immune-mediated reactions in a cohort of Italian patients with such disease.
Methods: We included all patients affected by IIM and followed by Myositis Clinic, Rheumatology and Respiratory Diseases Units, Siena University Hospital, Bari University Hospital, Policlinico Umberto I, Sapienza University, Rome, and Policlinico Paolo Giaccone, Palermo. Inclusion criteria were a recent (<3 months) clinical and serological assessment before the survey and a definite diagnosis of dermatomyositis, polymyositis and anti-synthetase syndrome. All patients underwent a telephone survey in order to establish their clinical status and potential relapses after vaccination.
Results: A total of 119 IIM patients (median, IQR 58 (47-66) years; 32 males) were consecutively enrolled. Fifty had a diagnosis of DM, 39 had PM and 30 had ASS. The median months of disease duration was 79.62±83.98. According to number of organs involvement, forty-two had only one, 45 had two organs involvement, 20 had three, 11 had four and one had five. The majority of them received two doses of COVID-19 vaccine, except four patients who refused the vaccination: 94 (78.9%) Cominarty, 16 (13.4%) Moderna, 5 (0.04%) AZ. Seven (0.06%) patients had flare after vaccination, the majority of them were mild except one major with three organs involved and one life-threatening with systemic involvement. In order to understand or predict the effect of demographic and clinical features on the flare development after vaccination, a logistic regression analysis was performed. The goodness-of-fit statistics showed a Chi^2 associated with the Log ratio (L.R.) of 0.045. From the probability associated with the Chi-square tests, the Type II analysis showed the variable that most influences the development of flare was the number of organs involved (p=0.047). Sixty-eight patients received the third dose of COVID-19 vaccination: 51 (75%) Cominarty and 17 (25%) Moderna. Only one (0.01%) patient (the same who had life-threatening flare with systemic involvement after two doses) had flare after third dose and eventually died.
Conclusion: Vaccines against SARS-CoV2 have provided, both in registratory studies and in preliminary real-life evidence, an overall good efficacy and safety. Nevertheless, only scanty data are available for rheumatic patients in general and the ones affected by IIM in particular. To the best of our knowledge, ours represent the largest cohort of IIM patients in which immunogenicity of anti-SARS-CoV2 vaccine was assessed. In line with real-life data from other diseases, we found a non-statistically significant risk of relapse in our patients, which occurred seldom, usually mild and in patients with a more severe and aggressive course of disease.
Disclosure of Interests: None declared
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Parameters	Flare after two doses (n=7)	No-flare after two doses (n=108)	P value
Age (years)	55 (51-68)	59 (47-67)	NS
Gender (M/F)	2/5	30/82	NS
Diagnosis (DM/PM/ASS)	2/2/3	48/36/28	NS
Antibodies			
Jo1	2	25	
PL7	-	3	
PL12	-	1	
Ku	-	2	
Mi2	1	7	
PM/Scl	1	5	
Ro52	1	7	
TIG1g	-	5	
MDA5	-	6	
SRP	-	1	
SAE	-	2	
cN1a	-	-	
NPX	-	1	
SSA	-	12	
Ds-DNA	-	1	
ANA (only positivity)	-	3	
negative	2	27	
Length of disease (months)	50 (19-200)	60 (24-108)	NS
Number of organs involved:			
One	0	36	0.0004
Two	2	43	
Three	3	19	
Four	1	10	
Five	1	0	
Type of vaccination:			
Cominarty	6	88	NS
Moderna	1	15	
AZ	0	5	
Disease activity (PhGA≥2/PhGA<2)	3/4	27/81	NS
MDI	3 (1-6.5)	2 (1-4)	NS
CRP (mg/dL)	0.1 (0.01-0.3)	0.99 (0.3-2.9)	0.0041
ESR	32 (14-39)	15.5 (8-27.5)	NS
CPK	111 (63-905)	97.5 (63-158)	NS
Treatment at time of vaccination:			
GCs	0	10	NS
Immunosuppressive	3	19	
Biologic	1	2	
Combination	3	65	
no-treatment	-	12	

POS1219

SARS-COV-2 COURSE AND OUTCOME IN PATIENTS WITH SYSTEMIC AUTOINFLAMMATORY DISEASES (SAID) TREATED WITH IL-1 INHIBITORS AND COLCHICINE

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Background: The spread of COVID-19 had a strong impact in north-east Italy especially during 2020 and in the first months of 2021. Patients affected by rheumatological disorders are at high risk of infections due to immunosuppressant therapies and a clear immunological imbalance. However, some anti-cytokines such as IL-1 inhibitors proved to be effective in curbing the cytokine storm, frequent feature of severe COVID-19.

Objectives: We assessed the SARS-CoV-2 clinical course in 28 patients affected by autoinflammatory diseases, referring to the Autoinflammatory Outpatient Clinic of Padova University; in particular we observed if patients undertaking IL-1 inhibitors (group-1) had a diverse outcome compared to those not on anti-IL-1 drugs (group-2).

Methods: Through telephone or e-mail consultancy, 28 patients (18 females, mean age 39.5±15), confirmed to have contracted COVID-19 between March 2020 and January 2022. Twelve patients (42.8%) were affected by periodic fevers (FMF/TRAPS), 10/28 (35.7%) had Adult-Onset Still's Disease, 3/28 (10.7%) had Undifferentiated Autoinflammatory Diseases, while 2/28 (7.1%) were affected by Behçet Disease and one patient had Schnitzler Syndrome. 12 out of 28 patients (42.8%) were undertaking IL-1 inhibitors; 8/28 (28.5%) were in therapy with colchicine; 2 patients were in therapy with methotrexate and abatacept respectively, and 6/28 (21.4%) received no therapy. All were diagnosed with COVID-19 after molecular nasopharyngeal swab performed either for the presence of symptoms or close contact with a positive subject. 5/28 patients had the infection after receiving the second vaccine shot, two after the booster dose. All the others had COVID-19 before the vaccine injection. *GraphPad5* was used for statistical analysis and Fisher's test was applied.

Results: COVID-19 clinical course was benign in 27 out of 28 patients (96.4%); a total of 29 infections were counted due to a case of re-infection; 2 patients discontinued the therapy; all the others continued their medications (92.8%). Two patients (7.1%) of the entire cohort were hospitalized, one died. Regarding the major symptoms (fever ≥ 38 C°, cough/respiratory or gastro-intestinal symptoms) no difference was noticed between group-1 and group-2 (p=0.449); despite group-1 required less symptomatic therapy than group-2, the difference was not significant (p=0.471). Table 1 summarizes the clinical features exhibited by the patients and the therapies undertaken during the infection.

Table 1. Clinical features and therapies of the examined cohort

	Total COVID-19 infections (%) 29 (100)	Group-1 (anti IL-1 drugs) 12 (41.3)	Group-2 (no anti IL-1 drugs) 17 (58.6)
COVID-19 symptomatic therapy			
Acetaminophen	4 (13.7)	0	4 (23.5)
NSAIDs	8 (27.5)	3 (25)	5 (29.4)
Other (corticosteroids, mAb°)	5 (17.2)	3 (25)	2 (11.7)
Total	17 (58.6)	6 (50)	11 (58.8)
No therapy for COVID-19	12 (41.3)	6 (50)	6 (35.2)
COVID-19 major symptoms *	10 (34.4)	3 (25)	7 (41.1)
COVID-19 minor symptoms **	16 (48.7)	8 (66.6)	8 (47)
COVID-19 asymptomatic	3 (10.3)	1 (8.3)	2 (11.7)
Discontinuation of therapy	2 (6.8)	0	2 (11.7)
Outcome			
Home	27 (93.1)	11 (91.6)	16 (94.1)
Hospitalization (and fully recovered)	1 (3.44)	1 (8.33)	0
Death	1 (3.44)	0	1 (5.8)
Infection after receiving vaccine (at least II doses)	7 (24.13)	5 (41.6)	2 (11.7)

Legend: *(Fever ≥ 38 C°, cough/pneumonia, important gastro-intestinal symptoms); **(Fever < 38 C°, anosmia, ageusia, asthenia, arthralgias); °Monoclonal antibodies

Conclusion: Despite the low sample size, our study is of interest since it proves that the inhibition of IL-1 with both anakinra or canakinumab and the employment of colchicine, an important inflammasome regulator, may curb the hyperinflammation typical of COVID-19. Given the promising results obtained with anti-IL-1 and colchicine in treating severe COVID-19, it is conceivable a "protective" role of these drugs in preventing a massive cytokine release. Unsurprisingly, none of our patients but one, had a severe course or fatal outcome after SARS-CoV-2 infection.

Disclosure of Interests: None declared

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POS1220

HUMORAL IMMUNE RESPONSE AGAINST BNT162B2 MRNA COVID-19 VACCINE IN JAPANESE RHEUMATIC DISEASE PATIENTS RECEIVING IMMUNOSUPPRESSIVE THERAPY: A MONOCENTRIC STUDY

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Background: Patients with immune-mediated inflammatory diseases are inherently susceptible to infections and are at high risk of developing COVID-19. COVID-19 vaccination in patients with rheumatoid and musculoskeletal disease (RMD) is strongly recommended [1]. BNT162b2 is the most used COVID-19 vaccine in Japan. The safety and efficacy of this vaccine has been demonstrated in the general population [2], but patients receiving immunosuppressive therapy were excluded from the study. Although data on the immunogenicity of COVID-19 vaccine in the immunocompromised adult population is rapidly increasing, the immunogenicity of mRNA COVID-19 vaccine in RMD patients receiving medication has been reported in various and still inadequate ways. Furthermore, the immunogenicity of mRNA COVID-19 vaccine may vary depending on the medication. In addition, most of these data were reported from Western countries, and data on Japanese patients with RMD are limited.

Objectives: To investigate serum antibody titre against SARS-CoV-2 spike protein following BNT162b2 vaccination in Japanese RMD patients on various immunomodulatory treatment.

Methods: Two hundred and twelve RMD outpatients undergoing treatment at Kagawa University Hospital and 43 healthy volunteers, who had received two doses of BNT162b2, were included in the study. Serum sample was collected at least 14 days after the second dose. Antibody titer against SARS-CoV-2 spike protein in serum was measured by ELISA (Elecsys Anti-SARS-CoV-2 S RUO). We analyzed the relationship between clinical characteristics, including the type of disease and treatment of RMD, and antibody titer against SARS-CoV-2 spike protein.

Results: The antibody titer against SARS-CoV-2 spike protein in RMD patients was significantly lower than that in healthy subjects. In the analysis with therapeutic agents, the mean antibody titer in RMD patients treated with rituximab (RTX) was much lower than that in healthy controls. Patients treated with baricitinib, azathioprine, mycophenolate mofetil, abatacept, TNF inhibitors, cyclosporine, IL-6 inhibitors, methotrexate (MTX), or glucocorticoids (GC) had only moderately lower antibody titers. Patients treated with tacrolimus, an immunosuppressive drug commonly used for treatment in Japan, showed a slight decrease in antibody titer, but the difference was not significant compared with healthy subjects. IL-17 and IL-23 inhibitors did not impair the humoral response. In addition, the combination of MTX with various immunosuppressive agents reduced titers, although this was not statistically significant.

Conclusion: Many of the immunosuppressants impaired the immunogenicity to BNT162b2 in Japanese RMD patients. The degree of decline of antibody titers differed according to immunosuppressant. MTX potentially impairs the immunogenicity of BNT162b2 also in the case of concomitant use with other immunosuppressant.

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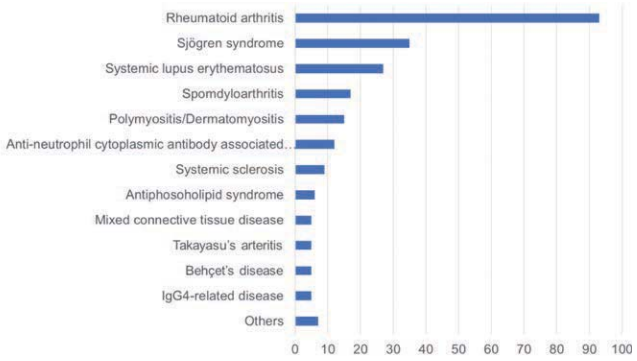

Figure 1. RMD diagnosis of study patients, n

Table 1. Serum antibody titre against SARS-CoV-2 spike protein according to the use of immunosuppressive treatments in comparison with controls

Immunosuppressive treatments, n	Serum antibody titre, mean±SD, U/mL	P value
Control, n=43	939 ± 973	-
Patients with RMD, n=212	572 ± 950	0.023
Without immunosuppressant, n=27	1074 ± 758	0.485
IL-17 or IL-23 inhibitors, n=7	1653 ± 2471	0.035
Tacrolimus, n=32	614 ± 920	0.095
GC, n=103	481 ± 927	0.009
MTX, n=78	310 ± 493	<0.001
IL-6 inhibitors, n=10	303 ± 201	0.030
Cyclosporine, n=8	261 ± 228	0.035
TNF inhibitors, n=26	201 ± 252	<0.001
Abatacept, n=10	186 ± 320	0.010
Mycophenolate mofetil, n=11	183 ± 357	0.007
Azathioprine, n=13	150 ± 159	0.003
Baricitinib, n=6	101 ± 97	0.021
RTX, n=6	20 ± 32	0.012

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POS1221

EFFECT OF COVID-19 ON CHILDREN WITH RHEUMATIC DISEASE

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Background: Pediatric patients with a diagnosis of rheumatic disease are at increased risk for infectious diseases due to immune dysregulation arising fromthe disease itself, as well as immunoregulatory or immunosuppressive drugs they use. However, there are studies reporting that COVID-19 disease has a moderate course in children with rheumatic disease.

Objectives: This study aims to determine the seroprevalence of SARS-CoV-2 in children with rheumatic disease during the COVID-19 pandemic, to evaluate the effects of immunosuppressive drugs and biological agents on seroprevalence of COVID.

Methods: Between September 2020 and September 2021, patients aged 2-18 years with a diagnosis of and with a follow-up period of more than 6 months were included in the study. Patients were selected by "simple random sampling" method.

Anti-SARS-CoV-2 antibodies (IgG and IgA) against the S1 domain of the SARS-CoV-2 spike protein were investigated with a micro ELISA kit.

Results: 170 patients, 92 (54.1%) girls, with a mean age of 12.16±4.18 years, were included. The median age at diagnosis was 7.59 (IQR 4.33-11.30) years, and the median follow-up time after diagnosis was 3.24 (IQR 1.87-5.99) years. Primary disease distribution was presented on Figure 1. The co-morbid diseases as obesity, hypertension and chronic kidney disease was present in 4.7%, 9.4% and 5.3% of patients, respectively. The distribution of medications was as follows; colchicine 101 patients (59.4%), Disease Modifying Anti-Rheumatism Drugs 49 (28.8%), steroid 25 (14.7%), and biological agents 28 (16.5%).

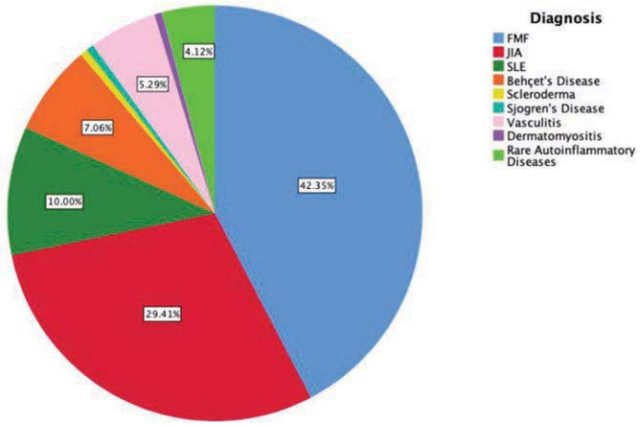

Figure 1. Distribution of patients according to primary rheumatologic diagnosis

Anti-SARS-CoV-2 Ig G antibody was positive in 40 (23.5%) of the patients. Demographic characteristics and treatment-related variables were similar between SARS-CoV-2 IgG seropositive and seronegative patients (Table 1).

Table 1. Characteristics of patients who are seropositive and seronegative for anti-SARS-CoV-2 Ig G

Variable	Anti-SARS-CoV-2 IgG negative patients (n=130)	Anti-SARS-CoV-2 IgG positive patients (n=40)	p
Age (years)	11.96±4.19	12.80±4.14	0.528
Sex (%) Female	67 (%72.8)	25 (%27.2)	0.150
Median age at diagnosis (years)	7.56±4.03	8.69±4.75	0.195
Median follow-up time after diagnosis (years)	4.39±3.27	4.11±3.19	0.891
Diagnosis (%)			
FMF and other autoinflammatory disease	62 (%78.5)	17 (%21.5)	0.166
Juvenile idiopathic arthritis	39 (%78.0)	11 (%22.0)	
SLE ve other autoantibody related diseases	16 (%80.0)	4 (%20.0)	
Behçet's disease	8 (%66.7)	4 (%33.3)	
Vasculitis	5 (%55.6)	4 (%44.4)	
MEFV mutation			
Homozygous	30 (%75.0)	10 (%25.0)	0.991
Heterozygous	33 (%76.7)	10 (%23.3)	
No mutation	36 (%75.0)	12 (%25.0)	
Presence of colchicine usage			
Yes	76 (%75.2)	25 (%24.8)	0.396
No	54 (%78.2)	15 (%21.7)	
Median colchicine dose (mg/day)	1.09±0.44	1.13±0.42	0.842
Presence of DMARD usage			
Yes	37 (%75.5)	12 (%24.5)	0.499
No	93 (%76.9)	28 (%23.1)	
Presence of steroid usage			
Yes	17 (%68.0)	8 (%32.0)	0.202
No	113 (%77.9)	32 (%22.1)	
Median steroid dose (mg/day)	10.50±8.91	14.71±11.95	0.333
Presence of biological agent usage			
Yes	21 (%75.0)	7(%25.0)	0.505
No	109 (%76.8)	33(%23.2)	

Thirty-eight (22.4%) of the patients had close contact with an individual diagnosed with COVID-19. Thirty two (18.9%) patients underwent PCR testing for SARS-CoV-2; only 4 (2.4%) had positive. Of these 32 patients, 28.1% were positive for IgG. IgG seropositivity was observed in 3 (75.0%) of 4 patients with PCR positivity.

Conclusion: We found the SARS-CoV-2 seroprevalence of 23.5% in children with a diagnosis of rheumatic disease. It seems that primary rheumatological diagnosis does not affect COVID seropositivity in children.

Disclosure of Interests: None declared

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POS1222 FOLIC ACID AND METHOTREXATE USE AND THEIR ASSOCIATION WITH COVID-19 DIAGNOSIS AND MORTALITY: AN ANALYSIS FROM THE UK BIOBANK

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Background: Folate metabolism is implicated in SARS-CoV-2 infectivity (Ref).

Objectives: To determine if methotrexate (an antifolate) or folic acid prescription were associated with a lowered and increased risk, respectively, for COVID-19 diagnosis or mortality in a large population-based cohort (UK Biobank).

Methods: Data from 380,380 UK Biobank participants with general practice prescription data were used. Criteria for COVID-19 diagnosis were 1) a positive SARS-CoV-2 test and / or 2) ICD-10 code for confirmed COVID-19 (U07.1) or probable COVID-19 (U07.2) in hospital records, or death records. This definition identified 26,003 individuals diagnosed with COVID-19 of whom 820 were known to have died from COVID-19. Logistic regression statistical models were adjusted for age group (4 categories), sex, ethnicity, Townsend deprivation index, BMI, smoking status, presence of rheumatoid arthritis, sickle cell disease, use of anticonvulsants, statins and iron supplements.

Results: Compared with people prescribed neither folic acid nor methotrexate, people prescribed folic acid supplementation had increased risk of diagnosis of COVID-19 (OR 1.51 [1.42; 1.61]). The prescription of methotrexate with or without folic acid was not associated with COVID-19 diagnosis (P≥0.18). Compared with people prescribed neither folic acid nor methotrexate, people prescribed folic acid supplementation had an increased risk of death after a diagnosis of COVID-19 (OR 2.64 [2.15; 3.24]) in a fully adjusted model. The prescription of methotrexate in combination with folic acid was not associated with an increased risk for death after a diagnosis of COVID-19 (1.07 [0.57; 1.98]). (Table 1)

Table 1. COVID-19 diagnosis and associated death in people prescribed methotrexate and / or folic acid in the UKBB, compared to people not prescribed methotrexate or folic acid. Model 1 adjusted for age group, sex, ethnicity, Townsend deprivation index, BMI, smoking status Model 2 is model 1 plus adjustment by the presence of rheumatoid arthritis, sickle cell disease, use of statins, anticonvulsants and iron supplementation.

	Unadjusted		Model 1		Model 2	
	OR [95% CI]	*P*	OR [95% CI]	*P*	OR [95% CI]	*P*
Neither Folic acid nor Methotrexate	1.0	-	1.0	-	1.0	-
COVID-19 diagnosis						
Folic acid only	1.58 [1.49; 1.68]	<0.001	1.60 [1.50; 1.70]	<0.001	1.51 [1.42; 1.61]	<0.001
Methotrexate and Folic acid	1.09 [0.96; 1.23]	0.18	1.15 [1.02; 1.30]	0.021	1.09 [0.96; 1.23]	0.18
COVID-19 associated death						
Folic acid only	5.14 [4.23; 6.24]	<0.001	2.91 [2.38; 3.55]	<0.001	2.64 [2.15; 3.24]	<0.001
Methotrexate and folic acid	1.47 [0.81; 2.67]	0.21	1.26 [0.70; 2.30]	0.44	1.07 [0.57; 1.98]	0.84

Conclusion: We report increased risk for COVID-19 diagnosis and COVID-19-related death for people prescribed folic acid supplementation. The prescription and use of supplemental folic acid may confer risk of infection with the SARS-CoV-2 virus as well as the risk of death resulting from COVID-19. Our results also suggest that methotrexate might attenuate an increased risk for COVID-19 diagnosis and death conferred by folic acid.

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POS1223 DIFFERENT ANTI-SARS-COV-2 VACCINE RESPONSE UNDER B- AND T-CELL TARGETED THERAPIES VERSUS ANTI-CYTOKINE THERAPIES IN PATIENTS WITH INFLAMMATORY ARTHRITIDES

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Background: Vaccination against SARS-CoV-2 is effective in preventing severe forms of COVID-19, but there remain concerns about a reduced vaccine response in patients suffering from inflammatory arthritides who are treated by immunosuppressive therapies.

Objectives: We analysed the impact of bDMARDs on the humoral anti-SARS-CoV-2 vaccine response of patients followed in day hospitals.

Methods: We studied the vaccine response after a complete vaccine regimen followed in day hospital in 5 French hospitals and treated with an intravenous bDMARD between September 2019 and August 2021. After obtaining their informed consent, we included patients with an anti-SARS-CoV-2 serology. They were considered non-responders if the antibody level detected was inferior to the threshold of positivity of the kit used.

Results: 205 patients were included (148 females/57 males). The median age was 64 years (Interquartile Range [IQR] 56-71). 25 were treated with tocilizumab (TCZ), 36 with abatacept (ABA), 53 with infliximab (IFX) and 91 with rituximab (RTX). When considering both patients after a complete vaccination schema (2 doses,

or 1 dose in case of prior COVID-19) and those with 1 booster dose, 34 patients (16.6%) were non-responders (2 [5.9%] treated by IFX, none treated by TCZ, 9 [26.5%] treated by ABA and 23 [67.7%] treated by RTX). In multivariate analysis, the only characteristics that significantly and independently differed between responders and non-responders were last bDMARD and corticosteroid therapy at the time of 1st vaccination (Table 1). In RTX-treated patients, the delay from last infusion to 1st vaccine dose was significantly shorter in non-responders (median 4.3 IQR [2.9-6.1] months in non-responders versus 8.4 IQR [5.7-14.5] in responders, p=0.0007). Median survival, i.e. achieving a vaccine response in 50% of RTX-treated subjects, was achieved after 277 days (95CI [209-310]) in patients vaccinated with 2 or 3 doses (Figure 1). In ABA-treated patients, the delay from last infusion to 1st vaccine dose was not different between non-responders and responders.

Table 1. Patients' characteristics and comparisons between responders and non-responders.

	All patients (n=205)	Responders (n=171)	Non responders (n=34)	Univariate p value	Multivariate p value
Age (median [IQR]), in years	64 [56-71]	64 [54-70]	69 [57-75.5]	0.07	0.40
Female sex, n (%)	148 (72.2)	125 (73.1)	23 (67.7)	0.53	
Inflammatory arthritides, n (%)				0.16**	0.24
Rheumatoid Arthritis	156 (78.0)	128 (74.9)	28 (82.4)	0.51	
Spondyloarthritis	33 (16.1)	31 (18.1)	2 (5.9)	0.12	
Others*	16 (7.8)	12 (5.9)	4 (1.9)	0.31	
Last bDMARDs at time of 1st vaccination, n (%)				0.0004 ABA/RTX versus IFX/TCZ	0.00024
Infliximab	53 (25.9)	51 (29.8)	2 (5.9)		
Tocilizumab	25 (12.2)	25 (14.6)	0		
Abatacept	36 (17.6)	27 (15.8)	9 (26.5)	< 0.0001	
Rituximab	91 (44.4)	68 (39.8)	23 (67.7)		
Associated treatments at time of 1st vaccination					
CsDMARDs, n (%)	126 (61.5)	107 (62.6)	19(55.9)	0.56	
Methotrexate	91 (44.4)	78 (45.6)	13 (38.2)	0.46	
Median dose in users (mg /week) [IQR]	15 [10-17.5]	13.8 [10-15.6]	15 [13.8-20]	0.07	
Corticosteroids, n (%)	25 (12.2)	19 (11.1)	6 (17.6)	0.29	
Median dose (mg /day) [IQR]	0 [0-0]	0 [0-0]	0 [0-2]	0.035	0.016
Previous COVID-19 infection, n (%)	23 (11.2)	21 (12.3)	2 (5.9)	0.38	
Type of vaccine, n (%)				0.62	
Pfizer	169 (82.4)	142 (83.0)	27 (79.4)	0.62	
Moderna	14 (68.3)	11 (6.4)	3 (8.8)	0.71	
Astra-Zeneca	17 (8.3)	15 (8.8)	2 (5.9)	0.74	
Janssen	5 (2.4)	3 (1.8)	2 (5.9)	0.19	
Vaccination, n (%)					
Complete	167 (81.5)	141 (82.5)	28 (16.8)	0.47	
Complete + 1 booster dose	56 (27.3)	43 (25.1)	13 (38.2)	0.14	

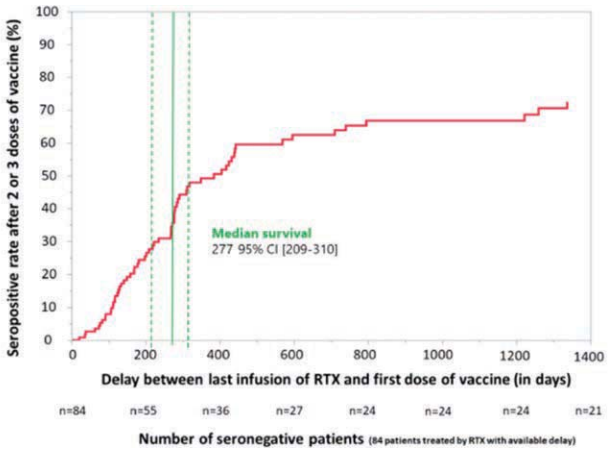

Figure 1. Cumulative seropositive rate according to the interval (days) between the last course of rituximab administration and vaccination

Conclusion: ABA and RTX alter the anti-SARS-CoV-2 vaccine response and were associated with nearly all vaccine non-responses in the present study. Corticosteroid therapy was associated with a lower vaccine response regardless of its indication or the concomitant use of bMARD.

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POS1224

RHEUMATOID ARTHRITIS DISEASE ACTIVITY ASSESSED BY PATIENT-REPORTED OUTCOMES AND FLOW CYTOMETRY BEFORE AND AFTER AN ADDITIONAL DOSE OF COVID-19 VACCINE

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Background: The Centers for Disease Control and Prevention recommends an additional dose (AddDose) of COVID-19 vaccine for moderately/severely immunosuppressed individuals following an initial vaccine series. The American College of Rheumatology suggests that patients interrupt use (hold) certain DMARDs around the time of COVID-19 vaccination to improve immunogenicity. Whether holding DMARDs around an AddDose of COVID-19 vaccine affects RA disease activity or affects frequencies of lymphocyte populations that may be associated with RA disease activity remains unknown.

Objectives: To test whether RA disease activity and frequencies of lymphocyte populations change pre- vs. post-AddDose of COVID-19 vaccine, overall and stratified by holding vs. continuation of DMARDs around the AddDose.

Methods: Prospective observational cohort study of patients with RA who had completed an initial COVID-19 vaccine series (2 doses of mRNA vaccine or 1 dose of adenovirus vector vaccine). Subjects enrolled July-November 2021, prior to receiving an AddDose. Subjects held or continued DMARDs around the AddDose based on discussion with their rheumatologist and/or personal decision-making. RA disease activity was assessed weekly using the validated patient-reported RA Disease Activity Index-5 (RADAI-5) from enrollment through 4 weeks post-AddDose. We compared mean RADAI-5 pre- vs. post-AddDose using generalized estimating equations to account for correlated data among individual subjects. We aimed to enroll 60 subjects to achieve 91% power to detect a 15% non-inferiority margin in mean RADAI-5 post- vs. pre-AddDose. A subset of subjects with seropositive RA provided blood for flow cytometry at enrollment and week 4 post-AddDose. Frequencies of lymphocyte populations (T peripheral helper [Tph] cells, T follicular helper [Tfh] cells, age-associated B cells [ABC], and plasmablasts) were compared pre- vs. post-AddDose using Wilcoxon paired tests with Bonferroni correction.

Results: Among 71 subjects, mean age was 62 (SD 12) years, 85% were female, and 87% had seropositive RA. Methotrexate (42%) and TNF inhibitors (38%) were the most common DMARDs; 21% were taking prednisone. One subject reported COVID-19 infection prior to the AddDose. The mean RADAI-5 was 3.20 (SD 0.23) pre-AddDose compared to 3.25 (SD 0.23) after (difference of 1.6%, p=0.51). Figure 1 displays mean RADAI-5 in 35 (49%) subjects that held at least 1 DMARD and 36 (51%) subjects that continued all DMARDs around the AddDose. Mean change in RADAI-5 between pre- vs. post-AddDose did not significantly differ based on whether subjects held vs. continued DMARDs (p for interaction = 0.16). Frequencies of Tph, Tfh, ABC, and plasmablast populations did not significantly differ between the pre- and post-AddDose timepoints in subjects that held at least 1 DMARD (n=16) or subjects that continued all DMARD (n=11) (Figure 1).

Conclusion: RA disease activity, measured weekly with a validated patient-reported outcome, is stable around the time of an AddDose of COVID-19 vaccine. Lymphocyte subsets of interest in RA were also similar before and after the AddDose, supporting the observation of stable patient-reported RA disease activity. Holding DMARDs was not associated with greater RA disease activity following the AddDose.

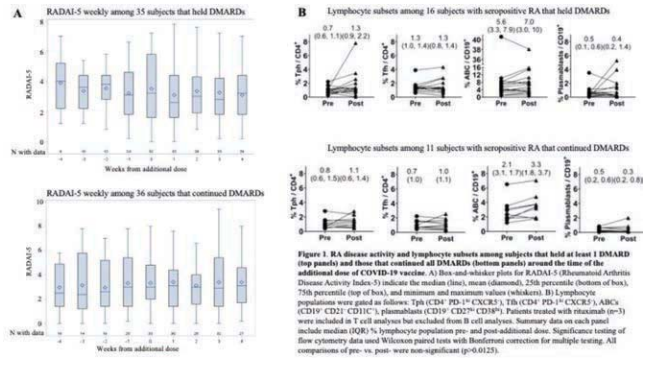

Figure 1. RA disease activity and lymphocyte subsets among subjects that held at least 1 DMARD (top panels) and those that continued all DMARDs (bottom panels) around the time of the additional dose of COVID-19 vaccine. A) Box-and-whisker plots for RADAI-5 (Rheumatoid Arthritis Disease Activity Index-5) indicate the median (line), mean (diamond), 25th percentile (bottom of box), 75th percentile (top of box), and minimum and maximum values (whiskers). B) Lymphocyte populations were gated as follows: Tph (CD4+ PD-1hi CXCR5+), Tfh (CD4+ PD-1hi CXCR5+), ABCs (CD19+ CD21- CD11C+), plasmablasts (CD19+ CD27hi CD38hi). Patients treated with rituximab (n=3) were included in T cell analyses but excluded from B cell analyses. Summary data on each panel include median (IQR) % lymphocyte population pre- and post-additional dose. Significance testing of flow cytometry data used Wilcoxon paired tests with Bonferroni correction for multiple testing. All comparisons of pre- vs. post- were non-significant (p>0.0125).

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Bristol Myers Squibb: participation on scientific advisory board with compensation paid to Dr. Rao, Grant/research support from: Moderna: research funding paid to institution
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POS1225 PREDICTORS OF WEAK ANTIBODY RESPONSE POST-COVID-19 MRNA VACCINATION IN SLE

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Background: Throughout the COVID-19 pandemic, the BNT162b2 (manufactured by Pfizer—BioNTech) and mRNA-1273 (manufactured by Moderna Inc) vaccines have demonstrated an acceptable safety profile and a high degree of effectiveness in preventing severe COVID-19 outcomes in healthy individuals. However, it remains to be determined if similar benefits can be replicated in immunocompromised patients, who were largely excluded from Phase III clinical trials. Preliminary data on vaccine immunogenicity among lupus patients reveal blunted humoral responses, particularly in those using prednisone and/or mycophenolate (1-2).
Objectives: This study sought to measure the antibody responses following SARS-CoV-2 vaccination in patients with SLE and to identify clinical and laboratory parameters associated with low antibody responses.
Methods: We prospectively enrolled SLE patients from the Beth Israel Deaconess Medical Center Systemic Lupus Erythematosus Cohort (BIDLC). The patients received two doses of either BNT162b2 or mRNA-1273 and were tested for the SARS-CoV-2 IgG spike antibody at least 4 weeks after the second vaccine dose. Patients with evidence of prior COVID-19 infection were excluded. The primary goal of this study was to measure the prevalence of a weak IgG spike antibody response and identify predictive clinical-laboratory factors. We first measured the antibody responses in a healthy control group and defined a low antibody titer as values that fell below the 25% percentile of this reference group (<6). We then used simple logistic regression to assess for associations between different predictive variables and our predefined dichotomous outcome: <6 vs ≥6 IgG spike antibody titer. To account for potential cofounders, a multiple logistic regression model was performed. Risk ratios were calculated with the Log Binomial regression. Significance level was set at p <0.05.
Results: A total of 71 patients were included in the study. At the time of vaccination, patients were on various immune modulator and suppressive medications, including: Hydroxychloroquine 87%, Prednisone 38%, Mycophenolate 38%, Azathioprine 18% and Belimumab 7%. The proportion of patients who received BNT162b2 and mRNA-1273 were 58% and 42%, respectively. Overall, 63% of patients had a high IgG spike antibody titer (≥ 6) and 37% of patients had a low IgG spike antibody titer (<6). Univariate logistic regression demonstrated that a SLEDAI ≥6 (OR: 4.55, *p = 0.02*), the use of azathioprine (OR: 3.55, *p = 0.04*) and receiving the BNT162b2 vaccine vs. mRNA-1273 (OR: 3.80, *P = 0.01*) were independent predictors of antibody titers <6. After controlling for age, sex, race, time to spike testing and use of immunosuppressive drugs, the association between a high SLEDAI score or receiving the BNT162b2 vaccine and a weak antibody response remained significant (Figure 1). Using the Log Binomial regression, the BNT162b2 and the high SLEDAI group were found to have 2.1- and 2.4-times, respectively, higher likelihood of developing weak antibody responses.

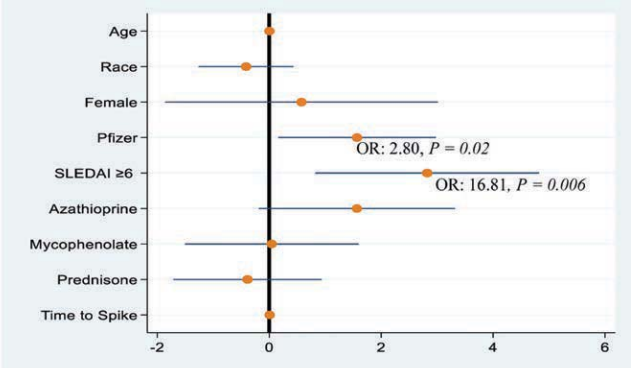

Figure 1. Logistic regression plot

Conclusion: In patients with SLE, Azathioprine use independently predicts reduced antibody titers. More importantly, we demonstrated that a pre-vaccine high disease activity score or receiving BNT162b2 (Pfizer—BioNTech) increases the risk of impaired immune response to the COVID-19 vaccine.
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POS1226 CLINICAL FACTORS ASSOCIATED WITH A POSITIVE SARS-COV-19 TEST AND WITH FREQUENT TESTING DURING THE COVID-19 PANDEMIC IN >10.000 PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES. RESULTS FROM A NATIONWIDE SURVEY FROM THE DANISH DANBIO REGISTRY

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Background: Patients with inflammatory rheumatic diseases (IRD) have used self-isolation and social distancing during the pandemic to avoid SARS-CoV-19 infection (reference). In countries with unlimited and free access to SARS-CoV-19 testing, anxiety or other patient related factors might potentially increase test-frequency.
Objectives: In patients with IRD followed in the nationwide DANBIO registry we aimed to explore clinical factors including self-isolation associated with a) a positive SARS-CoV-19 test result ('infection'), b) higher frequency of SARS-CoV-19 testing during the first 1½ year of the pandemic.
Methods: In May-June 2020, IRD patients followed in the quality registry, DANBIO (n=36,152), were invited to participate in the voluntary online questionnaire survey 'You and your rheumatic disease during times with corona-virus'. Patient characteristics, treatment and patient reported outcomes were captured in DANBIO and from the questionnaire. Patients were considered as self-isolating if they agreed to the question: I stay at home and avoid others as much as possible.
After written consent, information on dates and SARS-CoV-19 test results (by PCR, polymerase chain reaction) during follow-up (until Nov 2021 and thus before entry of the Omicron variant) was obtained through linkage to the nationwide laboratory system.
Time to first positive PCR and associated characteristics were explored by multivariable Cox regression analyses with hazard ratios, HR, adjusted for: gender/age-group/ diagnosis/biologic therapy/working/ self-isolation/HAQ/EQ-5D. Day 0 was defined as the date of first positive test in cohort (May-07-2020).
Number of SARS-CoV-19 tests (median (IQR)), and characteristics associated with higher test frequency (upper quartile) was explored with multivariable logistic regression analyses (odds ratios, OR, adjustment like above).
Results: In 10,098 included patients, 2.8% were infected during follow-up (Table 1). Age and HAQ seemed lower in infected (Table 1, Figure 1). In multivariable Cox

regression analyses, male gender was associated with higher infection risk (HR 1.38 (1.05;1.80) whereas risk was lower in the age-group 61-80 years (0.60 (0.39;0.92) vs. below 40 years). Other factors were statistically insignificant.

Table 1.

		Total population	SARS-CoV-19 tests		Number of tests	
			POSITIVE*	NEGATIVE	<9	≥9
Patient number		**10,098**	**282**	**9816**	**7406**	**2692**
Patient %		**100**	**3**	**97**	**74**	**26**
Female, %		6654	3	97	72	28
Male, %		3444	3	97	77	23
Age, yrs, median (IQR)		61 (51-70)	56 (47-55)	61 (51-70)	55 (47-61)	64 (54-72)
Age, strata, yrs	< 40	969	4	96	62	38
	40-60	3898	4	96	59	41
	61-80	4984	2	98	85	15
	>80	247	1	99	97	3
Diagnosis	AxSpA	1464	4	96	66	34
	RA	6345	2	98	76	24
	PsA	1689	3	97	70	30
	Other	600	4	96	79	31
Biologic treatment, yes**		3831	3	97	72	28
HAQ, median**		0.5	0.375	0.5	0.375	0.5
EQ-5D, median		0.8	0.8	0.8	0.8	0.8
Self-isolating, yes		8474	3	97	74	26
Working		4616	4	96	58	42

Row percentage unless otherwise shown* At least one positive PCR before Nov 2021**May 2020AxSpA: Axial spondyloarthritis, EQ-5D: EuroQol quality of life (5D), HAQ: health assessment questionnaire, IQR: interquartile range, PsA: psoriatic arthritis, RA: rheumatoid arthritis

Median number of PCR tests was 4 (IQR 1-9). In patients with <9 tests, 2.6% were infected whereas for patients with ≥9 tests, 3.2% were infected. Patients with ≥9 tests were younger, more frequently female and working in univariate (Table 1) and adjusted analyses, whereas other characteristics were statistically insignificant (details not shown).

Conclusion: Few patients with IRD were infected during the first 1½ years of the pandemic. Gender and age were associated with infection risk and frequency of testing. Self-isolation and a range of other clinical characteristics had no impact, which to some extent may be due to behavioral differences across age-groups.

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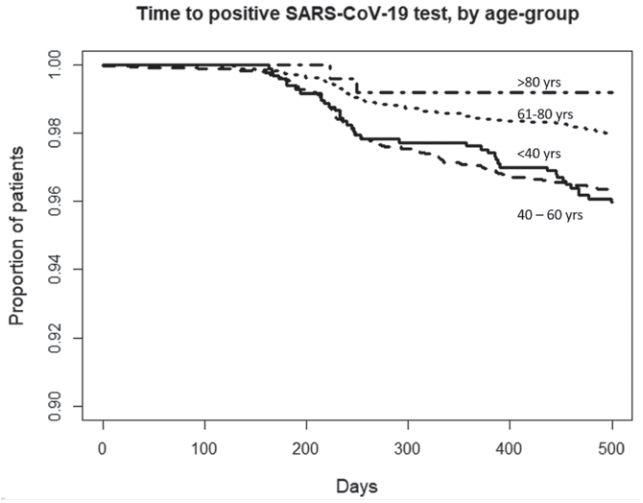

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POS1227 TIME BETWEEN SECOND AND THIRD DOSES INFLUENCES RESPONSE TO COVID-19 VACCINE IN AUTO-IMMUNE DISEASE PATIENTS TREATED WITH RITUXIMAB WITHOUT RESPONSE TO TWO DOSES.

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Background: It is now well established that patients treated with rituximab (RTX) for auto-immune disease (AID) have a diminished antibody response to COVID-19 vaccines after two doses. Optimizing antibody response is a key objective in this population. To achieve this goal, a 3rd booster dose may be considered.

Objectives: Focusing on the population of AID patients treated with RTX without any antibody response after two doses we sought to explore how these patients could respond to a 3rd dose and identify factors of response.

Methods: We performed a French retrospective bicentric observational trial which is a follow up of previously published work (1). We included consecutive patients treated with RTX that were non-responders regarding their anti-Spike antibody (anti-S) status at least one month after the second dose of COVID-19 vaccination. Patients were included between March and October 2021. All patients then received a third dose according to local guidelines and had an anti-S measurement at least one month after the third dose. Some patients without response to a third dose had a fourth dose. Anti-S were measured in serum with various kits, but all results were in BAU/mL with upper quantification limit at 243. Patients with anti-S above 49 BAU/mL, which has been demonstrated to be the threshold associated with detectable neutralizing response were considered as responders (1).

Results: 60 patients treated with RTX without response to 2 doses (Anti-S Ab < 49 BAU/mL) were included in the study. 9/60 (15%) patients responded to the 3rd vaccine dose with anti-S > 49BAU/ml. Responders and non-responders had similar demographic characteristics (Table 1). There was a positive correlation between anti-S Ab levels after dose 3 and time between 2nd and 3rd doses (r=0,41 p=0,001) (Figure 1). Nevertheless, the median time between 2nd and 3rd doses was numerically but not significantly higher in responders than in non-responders (129 vs 80 days, p=0.30). There was no correlation between anti-S levels after the third dose and the time between the last RTX infusion and the third vaccine dose. There was a trend towards more patients with methotrexate co-medication in the non-responder group 31/51 (61%) vs 3/9 (33%) in the responder group (p=0,15). Seven non-responder patients after the 3rd dose received a 4th dose and 4 (57%) responded.

Table 1. Characteristics of patients without response after the second dose of vaccine treated with Rituximab for auto-immune diseases according to their seroconversion status after the third dose.

	Non responders (n=51)	Responders (n=9)	p
Age, median (min-max)	61 (17-85)	58 (36-78)	0,33
Female sex n (%)	42 (82)	6 (67)	0,36
Underlying disease n (%)			
Rheumatoid Arthritis	36 (69)	5 (56)	0,46
Other auto-immune disease	16 (31)	4 (44)	
Rituximab treatment			
Received a RTX infusion between dose 2 and 3 n (%)	14(27)	3(33)	0,70
Time between the last RTX infusion and the 3rd dose of vaccine in days median (min-max)	162 (1-687)	187 (79-959)	0,16
Previous number of RTX injections, median (min-max)	7 (0-34)	6 (1-22)	0,58
Vaccination scheme			
Interval between 2nd and 3rd vaccine dose in days, median (min-max)	80 (23-287)	129 (24-220)	0,30
Less than 3 months between 2nd and 3rd vaccine dose n (%)	27(53)	2(22)	0,14
Co-medications			
Patients on steroids n (%)	20(40)	5 (37,5)	0,99
Prednisone equivalent dose per day in mg median (min-max)	5(2-25)	5(5-10)	0,48

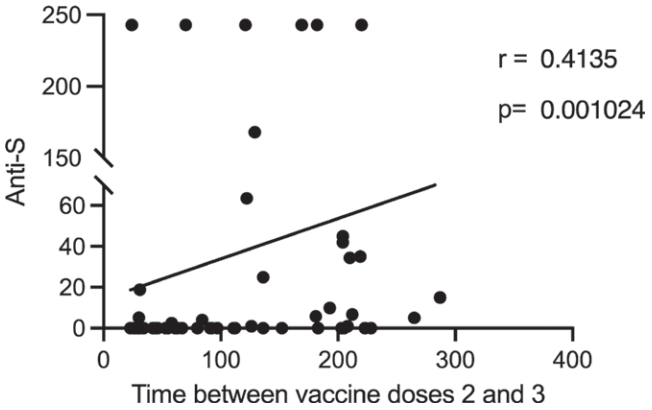

Figure 1. Correlation between anti- spike Ab levels after the third dose and time in days between doses 2 and 3.

Conclusion: A third vaccine dose of COVID-19 vaccine leads to only 15% of response in previously non-responding RTX treated AID patients. A longer time between 2nd and 3rd doses might positively influences response to a 3rd COVID-19 vaccine. Finally exploratory findings show that a fourth dose could be useful to obtain response non-responders.

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POS1228 IMPACT OF COVID-19 ON THE PRESCRIPTION OF BIOLOGIC DMARDS: A POPULATION-LEVEL STUDY IN ENGLAND

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Background: There has been considerable uncertainty about the impact of biologic DMARDs (bDMARDs) on COVID-19 morbidity and vaccine efficacy, which may have influenced prescribing during the pandemic.

Objectives: To assess trends in the prescription of three commonly used bDMARDs with different modes of action - adalimumab (ADA), rituximab (RTX) and tocilizumab (TOC) - in England before and during the COVID-19 pandemic.

Methods: The National Health Service (NHS) Secondary Care Medicines dataset was utilised to analyse temporal trends in bDMARD prescriptions issued by all NHS hospital pharmacies in England. Monthly averages of prescriptions issued for ADA, RTX and TOC for combined indications, standardised using WHO Defined Daily Doses (DDD), were described from January 2019 to November 2021. Interrupted time-series analyses (ITSA) were used to estimate the effect of the pandemic on prescription trends for ADA, RTX and TOC; Newey-West standard errors with lags were used to account for autocorrelation between observation periods in these models.

Results: Temporal trends in ADA, RTX and TOC prescriptions are shown in Figure 1. A 46% decrease in RTX prescriptions was observed between March and April 2020, from 1,338,300 DDD to 718,900 DDD, respectively, coinciding with the worsening COVID-19 pandemic in England. RTX prescriptions increased after May 2020, reflected in the positive prescription trend observed in ITSA models (Table 1); however, RTX prescriptions remained below pre-pandemic levels, before decreasing again between November 2020 and February 2021. This coincided with increasing COVID-19 case numbers in England.

Table 1. Trends in prescriptions issued for ADA, RTX and TOC in England before and after the onset of the COVID-19 pandemic, assessed using interrupted time-series analyses. The absolute change in prescriptions issued in March 2020, relative to April 2020, is shown.

	Rituximab	Adalimumab	Tocilizumab
Prescription trend before March 2020	-0.23% per year (95% CI -0.97 to 0.52)	+2.94% per year (95% CI 2.14 to 3.73)	+0.04% per year (95% CI -0.07 to 1.53)
Absolute change in prescriptions in March 2020	-46.3%	+15.5%	+10.7%
Prescription trend after March 2020	+2.11% per year (95% CI 0.52 to 3.70)	+3.24% per year (95% CI 2.02 to 4.46)	+0.64% per year (95% CI 0.38 to 0.90)
Difference in trends post vs. pre-March 2020	+2.33% per year (95% CI 0.51 to 4.17) P=0.014	+0.30% per year (95% CI -1.03 to 1.63) P=0.65	+0.60% per year (95% CI 0.31 to 0.90) P<0.001

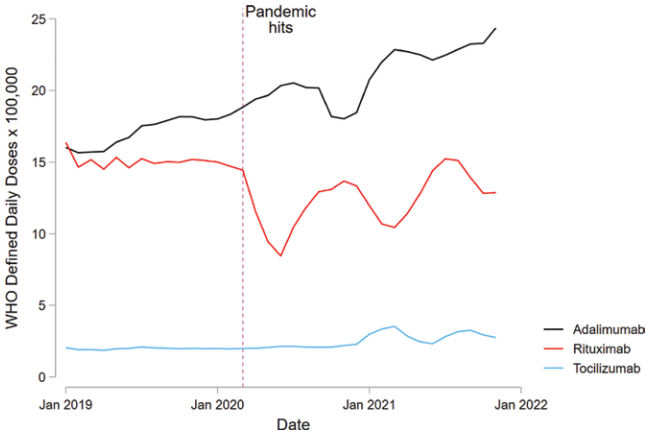

Figure 1. Temporal trends in prescriptions for ADA, RTX and TOC in England between January 2019 and November 2021. Monthly averages of prescriptions for combined disease indications are shown, standardised using WHO Defined Daily Doses.

For ADA, the pre-pandemic trend of increasing prescriptions continued during the pandemic, with no differences in prescription trends seen in ITSA models (Table 1). A 22% decrease in ADA prescriptions was observed between September and October 2020, from 2,037,800 DDD to 1,587,500 DDD, respectively, before rebounding to above pre-pandemic levels. Prescriptions for TOC increased during the pandemic, driven primarily by a 76% increase in prescriptions between December 2020 and January 2021, from 241,800 DDD to 425,000 DDD, respectively.

Conclusion: Prescriptions for RTX in England halved during the early COVID-19 pandemic, and remain below pre-pandemic levels as of November 2021. This likely reflects concerns about RTX use and increased COVID-19 mortality and reduced vaccine efficacy.[1,2] In contrast, prescriptions for ADA have continued to increase during the pandemic, while prescriptions for TOC surged in December 2020, coinciding with the more widespread use of TOC for the treatment of severe COVID-19.

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POS1229 THE IMPACT OF COVID-19 ON MEDICATION NON-ADHERENCE IN A RHEUMATOID AND PSORIATIC ARTHRITIS UK COHORT

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Background: In March 2020, as part of the UK's COVID-19 prevention strategy, those identified as 'clinically extremely vulnerable,' were advised to shield. This included a number of patients prescribed anti-rheumatic drugs, who were asked to continue their current treatment unless they developed symptoms of infection. Suboptimal treatment adherence (16.0%-81.0%) has been reported in patients with arthritic diseases, and is associated with psychological factors, including anxiety (1). Previous literature in

non-UK cohorts has highlighted suboptimal adherence levels in immunosuppressed patients during the pandemic, although many were single centre studies (2,3).

Objectives: The aim of this multi-centre study is to investigate the impact of the COVID-19 pandemic on adherence to anti-rheumatic medications in patients with established rheumatoid (RA) and psoriatic (PsA) arthritis in the UK who had recently commenced a biologic or targeted synthetic DMARD.

Methods: Between September 2020 and May 2021, RA and PsA patients prescribed biologic or targeted synthetic anti-rheumatic drugs from two multi-centre observational studies (BRAGGSS and OUTPASS) were sent a questionnaire on medication usage, adherence, and perceptions to establish the impact of COVID-19 on these parameters. Patients were asked about compliance during the COVID-19 pandemic using a 5-point Likert scale (always, often, sometimes, rarely, and never) and the reason for non-adherence. Adherence was defined as never missing or delaying a dose, unless medically advised. Descriptive summary statistics were calculated, and logistic regression and Pearson's chi-squared tests were employed to investigate variables associated with self-reported non-adherence.

Results: In total 159 questionnaires were returned (81.1% RA and 18.9% PsA). Methotrexate (53.5%) was the most frequently prescribed agent, followed by etanercept (25.2%), sulfasalazine (22.6%), hydroxychloroquine (21.4%) and adalimumab (19.5%). Furthermore, 68.6% of patients were prescribed ≥2 drugs. During the pandemic, 42.1% of patients reported missing or delaying a treatment dose for any reason. Adherence information was available for 97.5% of patients with 25.8% reporting non-adherence which was not medically advised. Methotrexate non-adherence was 27.1%, with similar levels reported for etanercept (20.0%), sulfasalazine (27.8%), hydroxychloroquine (35.3%) and adalimumab (29.0%). No drugs had significantly different adherence compared to methotrexate. Furthermore, there was no association between disease type or perception of disease control and adherence. Of non-adherent patients, 17.5% reported increased anxiety, fear, and increased risk due to the COVID-19 pandemic as an influencing factor. Meanwhile, 37.5% of non-adherent patients listed non-COVID-19 intentional reasons and 45.0% reported non-intentional reasons, with forgetting and running out of treatment listed most frequently.

Conclusion: In a UK cohort self-reported non-adherence was reported in 25.8% of patients during the COVID-19 pandemic, despite medical advice, with reasons including increased anxiety due to COVID-19.

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POS1230

INCREASED ANTIBODY RESPONSE AFTER SARS-COV-2 MRNA-BASED VACCINATION IN RITUXIMAB-TREATED PATIENTS WITH PREVIOUS COVID-19 INFECTION

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Background: Rituximab (RTX) is associated with reduced humoral response to SARS-CoV-2 mRNA-based vaccine (1, 2). A recent study has shown that, despite their immunosuppression burden, kidney transplant recipients with previous exposure to SARS-CoV-2 showed a marked increase in antibody titer, even after a single dose of vaccine (3).

Objectives: To describe the results of immunization after 1 to 3 doses of mRNA SARS-CoV-2 vaccine in RTX-treated patients with previous symptomatic COVID-19 infection.

Methods: Observational prospective usual care study including consecutive patients with inflammatory rheumatic diseases in maintenance therapy with RTX. All patients received a 1 to 3-dose regimen of mRNA-based COVID-19 vaccination (BNT162b2 Pfizer/BioNTech or mRNA-1273, Moderna). Serum IgG antibody levels against SARS-CoV-2 spike proteins were measured at the time of the new RTX infusion. The SARS-CoV-2 S1/S2 IgG immunoassay (DiaSorin) was used for the quantitative determination of antibodies to the receptor-binding domain of the viral spike (S) protein. Seropositivity was defined by anti-S antibodies >15 UA/mL.

Results: We included 69 patients (60 females, mean age 60±13 years) on maintenance therapy with RTX including 13 with previous symptomatic COVID-19, all proven by RT-PCR (10 females, mean age 58±12 years) (Table 1). SymptomaticCOVID-19 occurred between March 2020 and May 2021. The mean interval between the infection and vaccination was 8±3 months and the serological response was assessed after a mean of 74±58 days from the last dose of vaccination (3rd dose for 3 patients, 2nd dose for 6 patients and 1st dose for 4 patients). The 56 patients with no history of symptomatic COVID-19 infection all received 3 doses of vaccine and the serological response was assessed after a mean of 63±27 days from the 3rd dose of vaccination. The seropositivity rate was significantly higher in RTX-treated patients with previous symptomatic COVID-19 infection (11/13, 85% vs.15/56, 27%, p<0.001). Anti-S antibody titles were also markedly increased in patients with previous symptomatic COVID-19 infection (median 119 AU/mL, 95% CI 16-400 AU/mL vs. 3.80 AU/mL, 95% CI 3.80-4.81 AU/mL p<0.0001) (Figure 1). Antibody titles were not different according to the severity of previous COVID-19, the number of doses of vaccine, the underlying disease, and B-cell counts.

Table 1. Study population

	Patients with previous symptomatic COVID-19 (n=13)	Patients without symptomatic COVID-19 (n=56)
Age (years), mean ± SD	58±12	60±11
Females, n (%)	10 (77)	50 (89)
Underlying disease:		
Rheumatoid arthritis	10 (77)	45 (80)
Systemic sclerosis	2 (15)	5 (9)
Systemic lupus erythematosus	1 (8)	1 (2)
Sjögren syndrome	0 (0)	3 (5)
Mixed connective tissue disease	0 (0)	2 (4)
Disease duration (years), mean ± SD	17±9	20±10
Associated Methotrexate, n (%)	9 (69)	36 (64)
Current treatment with corticosteroids, n (%)	5 (38)	21 (38)
Corticosteroid dose >10 mg/day, n (%)	0 (0)	0 (0)
CD19+ (/µL) (100-600), mean ± SD	65±106	45±51
CD19 <18/µL, n (%)	7 (54)	33 (58)

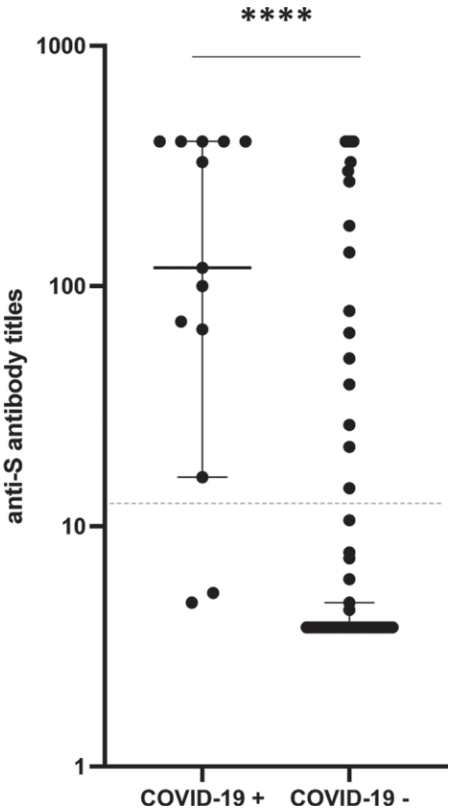

Figure 1. Distribution of SARS-CoV-2 spike antibody levels according to the history of proven symptomatic COVID-19. **** p<0.0001 by Mann Whitney test. Dotted red line corresponds to the seropositivity threshold

Conclusion: RTX-treated patients with previous proven COVID-19 showed increased seropositivity and antibody titers after SARS-CoV-2 vaccination, even after a single-dose of vaccine. This response is strikingly different from that observed for SARS-CoV-2-naïve RTX treated patients who received 3 doses of SARS-CoV-2 mRNA-based vaccination. An "antigen dose phenomenon" may account for these discrepancies. A potential clinical implication might be to increase antibody response with an additional dose of vaccine following an exposure to SARS-CoV-2 in RTX-treated patients with absent or insufficient post-vaccination antibody response.

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POS1231 PREDICTORS OF MORTALITY IN SEVERE AND CRITICAL COVID-19 PATIENTS WHO RECEIVED ANAKINRA

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Background: Several predictive factors were described in COVID-19 during the pandemic, however there is limited data in severe/critically ill patients (pts) with COVID-19 who received biologic therapies including anakinra.

Objectives: We aimed to evaluate the predictive factors of mortality in pts with severe and critically ill COVID-19 who received anakinra.

Methods: Diagnosis of COVID-19 was confirmed by PCR and/or typical CT findings. Severe and critically ill pts according to NIH severity scale who received anakinra in the ward were evaluated retrospectively (1). Laboratory values at admission, highest levels and the last day of hospitalization were recorded. COVID hyperinflammatory syndrome score (cHIS) was calculated according to the highest levels of laboratory results (2). All pts received background steroid therapy with 80 mg methylprednisolone (or its equivalent). Anakinra was started in pts who did not respond to steroid therapy at least two days or concomitantly with steroids in pts with higher risk and/or critical illness at admission. Average starting dose of anakinra was 600 mg/day intravenously and increased gradually to 1600 mg/day if necessary.

Results: Data of 148 pts (53 % male) were analyzed. Of those 57 pts (38.5 %) severe, 91 pts (61.5 %) had critical disease. Overall, 56 pts (37.8 %) died during the follow-up and intensive care unit admission was in 60 pts (40.5 %) and intubation in 54 pts (54.5 %). Diabetes mellitus was in 28 %, hypertension in 59 %, coronary heart disease in 19 %, heart failure in 12.6 %, chronic kidney failure in 21 %, chronic obstructive pulmonary disease in 16 %, dementia in 12.8 %, malignancy in 11 % and rheumatic disease in 5.6 % of pts. Only dementia significantly differed between pts had mortality and had not (p=0.005 OR:9.8).

In univariable analysis; patient age, neutrophil to lymphocyte ratio (NLR), mean cHIS scores were higher in pts had mortality. Higher baseline, maximum and last values of CRP, LDH, ferritin, D-dimer levels were observed in pts had mortality. Mortality was also higher in pts with critically ill compared to severe disease

In multivariate analysis; higher age (p=0.01 OR:1.05 CI: 1.01-1.09), cHIS score (p=0.002 OR:2.6 CI:1.4-4.9), critical illness compared to severe disease (p=0.02 OR:14 CI:1.6-122) were associated with mortality.

In ROC analysis; cut-of values for cHIS score (3.5), NLR (7.1), CRP (160.5 mg/L), LDH (581 U/L), ferritin (771 ng/mL), D-dimer (7.56 mcg/mL) with 72/72, 69/70, 70/69, 72/75, 70/72, 70/73.4 sensitivity/specificity were calculated, respectively.

Table 1.

Variables	mortality -	mortality +	p value	ROC [AUC (95 % CI)]
Age, years*	63.4±18	72.3±14	*0.001*	
Gender, male$^{\kappa}$	44 (48)	34 (61)	0.1	
Duration of hospitalization (days)‡	10.5 (12)	12 (14)	0.8	
COVID severity (critical vs severe)$^{\kappa}$	36 (40)	55 (60)	*<0.001 (OR:51)*	
cHIS*	3±1	4.1±1.1	*<0.001*	0.77 (0.69-0.86)**
NLR‡	5.6 (5)	10 (9)	*<0.001*	0.72 (0.6-0.82)**
Platelets*	215±77	192±82	*0.01*	
CRP (mg/L)‡				
1th	107 (110)	136 (126)	*0.004*	
2nd	137 (100)	194 (134)	*<0.001*	0.73 (0.63-0.82)**
3rd	6.8 (8)	103 (132)	*<0.001*	
Ferritin (ng/mL)‡				
1th	326 (531)	557 (767)	*0.06*	
2nd	555 (606)	1212 (2336)	*<0.001*	0.76 (0.68-0.85)**
3rd	296 (270)	814 (1590)	*<0.001*	
D-dimer(mcg/mL)‡				
1th	1 (1)	1.5 (1.7)	*0.016*	
2nd	2.8 (7)	12.4 (24)	*<0.001*	0.74 (0.65-0.83)**
3rd	1.2 (1.2)	7.4 (18)	*<0.001*	
LDH (U/L)‡				
1th	399 (193)	391 (245)	0.9	
2nd	513 (200)	676 (528)	*<0.001*	0.78 (0.69-0.86)**
3rd	319 (104)	641 (439)	*<0.001*	

*mean±std dev ‡median (IQR) $^{\kappa}$n, (%) ** p<0.001 1th at admission 2nd maximum level 3rd last level

In ROC analysis; cut-of values for cHIS score (3.5), NLR (7.1), CRP (160.5 mg/L), LDH (581 U/L), ferritin (771 ng/mL), D-dimer (7.56 mcg/mL) with 72/72, 69/70, 70/69, 72/75, 70/72, 70/73.4 sensitivity/specificity were calculated, respectively.

Conclusion: In our study mortality was developed in third of anakinra receiving pts. Mortality was independently associated with advanced age, critical illness and higher cHIS score reflecting higher inflammatory burden. Furthermore, highest levels of CRP, LDH, ferritin, D-dimer and higher cHIS score predict higher mortality in pts receiving anakinra. It is important to identify the pts with higher mortality risk to improve outcome.

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POS1232 LONG-TERM OUTCOMES OF COVID-19 VACCINATION IN PATIENTS WITH RARE AND COMPLEX CONNECTIVE TISSUE DISEASES: AN AD-INTERIM ANALYSIS OF ERN-RECONNET VACCINATE STUDY

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Background: Since the COVID-19 vaccination campaign was launched all over Europe, there has been general agreement on how benefits of SARS-CoV2 vaccines outweigh the risks in patients with rare connective tissue diseases (rCTDs). Yet, there is still limited evidence regarding safety and efficacy of such vaccines in these patients, especially in the long-term. For this reason, in the framework of ERN-ReCONNET, an observational long-term study (VACCINATE) was designed in order to explore the long-term outcome of COVID-19 vaccination in rCTDs patients. The consent form was developed thanks to the involvement of the ERN ReCONNET ePAG Advocates (European Patients Advocacy Group).

Objectives: To evaluate the safety profile of COVID-19 vaccination in rCTDs patients and the potential impact on disease activity. Primary endpoints were the prevalence of adverse events (AEs) and of disease exacerbations post-vaccination. Secondary endpoints were the proportion of serious adverse events (SAEs)

and adverse events of special interest for COVID-19 (adapted from https://bright-oncollaboration.us/wp-content/uploads/2021/01/SO2_D2.1.2_V1.2_COVID-19_AESI-update-23Dec2020-review_final.pdf)

Methods: The first ad-interim analysis of the VACCINATE study involved 9 ERN-ReCONNET Network centres. Patients over 18 years of age with a known rCTD and who received vaccine against COVID-19 were eligible for recruitment. Demographic data and diagnoses were collected at the time of enrolment, while the appearance of AEs and potential disease exacerbations were monitored after one week from each vaccination dose, and then after 4, 12 and 24 weeks from the second dose. A disease exacerbation was defined as at least one of the following: new manifestations attributable to disease activity, hospitalization, increase in PGA from previous evaluation, addition of corticosteroids or immunosuppressants.

Results: A cohort of 300 patients (261 females, mean age 52, range 18-85) was recruited. Systemic lupus erythematosus (44%) and systemic sclerosis (16%) were the most frequent diagnoses, followed by Sjogren's syndrome (SS,12%), idiopathic inflammatory myositis (IMM,10%), undifferentiated connective tissue disease (UCTD,8%), mixed connective tissue disease (MCTD,4%), Ehlers-Danlos's syndrome (EDS,4%), antiphospholipid syndrome (APS,2%). AEs appearing 7 days after the first and second doses were reported in 93 (31%) and 96 (32%) patients respectively, mainly represented by fatigue, injection site reaction, headache, fever and myalgia. Otitis, urticaria, Herpes Simplex-related rash, stomatitis, migraine with aura, vertigo, tinnitus and sleepiness were reported with very low frequency. Less than 2% of patients experienced AEs within 24 weeks from the second dose. No SAEs or AEs of special interest were observed in the study period. There were 25 disease exacerbations (8%), 7 of which severe. The highest number of exacerbations was observed after 4 weeks from the second dose (12 within week 4, 6 within week 12 and 7 within week 24). Disease exacerbation was most frequent in patients with EDS (33%) and MCTD (25%).

Conclusion: This preliminary analysis shows that COVID-19 vaccination is safe in rCTDs patients. AEs appear most often early after vaccination and are usually mild. Disease exacerbations are not frequent, but can be potentially severe and tend to occur most frequently within the first month after vaccination. Exacerbations can also occur 3-6 months after vaccination, although a causal relationship with the vaccination remains to be established. Our present data underline the importance of long-term observational studies.

Table 1. AEs and disease exacerbations per disease

Diagnosis	Patients enrolled (%) (n=300)	EAs after 1st and 2nd dose (%)	Exacerbations (%)
APS	2	57	14
EDS	4	50	33
IIM	10	52	7
MCTD	4	42	25
SS	12	59	8
SLE	44	69	8
SSC	16	49	2
UCTD	8	50	-

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POS1233 DIFFICULTIES AND MENTAL IMPACT OF THE SARS-COV- 2 PANDEMIC IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE PATIENT ASSOCIATION STUDY

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Background: The COVID-19 pandemic has taken a toll on the mental health of the general population. Patients with systemic lupus erythematosus (SLE) were particularly exposed due to many uncertainties linked to the virus and their immunosuppression as well as difficulties to access medical care and their treatment (eg, hydroxychloroquine) during the early pandemic.

Objectives: To evaluate the difficulties encountered by SLE patients during the early COVID-19 pandemic, and evaluate their impact on patient mental health.

Methods: We conducted a nationwide survey including SLE patients from France metropolitan and overseas territories, recruited by their treating specialist or through a patient association (AFL+). The survey was administered online or in paper form between November 2020 and April 2021, and included questions aiming at evaluating the difficulties encountered during the early COVID-19 pandemic (March to August 2020). The impact on mental health was evaluated using Hospital Anxiety and depression scale (HADS) and post-traumatic stress disorder (PTSD) Checklist for DSM-5 (PCL-5).

Results: 536 SLE patients (91.9% women) of mean age 50 (±14.1) years responded to the survey. The main reported difficulties were issues to access medical care (n = 136, 25.4%) or to obtain hydroxychloroquine treatment (n = 98/389, 25.2%), the loss of employment (n = 85/349, 24.4%) and financial difficulties (n = 75/536, 11%). Hydroxychloroquine shortage was responsible for difficulties in obtaining the drug for 25.2% (98/389) of HCQ-treated patients, and 57 had to interrupt HCQ treatment for a median of 7 days (IQR: 3-17). In the 342 patients with complete assessment, 161 (47.2%) screened positive for anxiety, 141 (41.2%) for depressive syndrome and 128 (38.7%) for PTSD. Multivariate analysis showed that female sex (OR=4.29 [95%CI: 1.39-13.24]), financial issues (OR=2.57 [1.27-5.22]), difficulties to access medical care (OR=2.15 [1.26-3.69]), or to obtain hydroxychloroquine treatment (OR=1.90 [1.06-3.40]) were independently associated with a positive screening for PTSD.

Conclusion: The COVID-19 pandemic resulted in a severe burden in SLE patients, including difficulties in access to care and treatment along with high psychological distress. Better understanding these difficulties will allow better prevention and care in times of crisis.

Table 1. Factors associated with the development of anxiety, depression or PTSD. Odds ratio (CI95%) using multivariate logistic regression are shown.

Patient and pandemic-associated factors	Odds ratio (95%CI) for anxiety	Odds ratio (95%CI) for depression	Odds ratio (95%CI) for PTSD
Female sex	2.25 (0.97-5.25), p = 0.058	ns	**4.29 (1.39-13.24) p = 0.01**
Financial difficulties	ns	**2.59 (1.31-5.11) p = 0.006**	**2.57 (1.27-5.22) p = 0.009**
Difficulties to obtain HCQ	**1.70 (0.97-2.98) p = 0.065**	**ns**	**1.90 (1.06-3.40) p = 0.03**
Difficulties to access medical care	**1.94 (1.15 3.25) p = 0.012**	**2.57 (1.53-4.33) p < 0.0001**	**2.15 (1.26-3.69) p = 0.005**

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POS1234 DMARD DISRUPTION, INCREASED DISEASE ACTIVITY, AND PROLONGED SYMPTOM DURATION AFTER ACUTE COVID-19 AMONG PATIENTS WITH RHEUMATIC DISEASE: A PROSPECTIVE STUDY

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Background: Systemic autoimmune rheumatic disease (SARD) patients may be at risk for disease flare and prolonged symptom duration after COVID-19, perhaps related to DMARD disruption and immune activation.

Objectives: To describe DMARD disruption and identify differences in SARD activity among patients with and without prolonged COVID-19 symptom duration.

Methods: We identified all SARD patients with confirmed COVID-19 at the Mass General Brigham healthcare system in Boston, USA; prospective recruitment is ongoing. Surveys were used to collect demographics, clinical characteristics, DMARD disruption, COVID-19 course, and SARD disease activity before and after COVID-19. The survey included validated instruments measuring disease activity, pain, fatigue, functional status, and respiratory quality of life. Prolonged symptom duration was defined as COVID-19 symptoms lasting ≥28 days. We compared differences in patient-reported measures between those with and without prolonged symptoms.

Results: We analyzed survey responses from 174 COVID-19 survivors with SARDs (mean age 52±16 years, 81% female, 80% White). The most common SARDs were RA (40%) and SLE (14%). Fifty-one percent of the 127 respondents on any DMARD reported a disruption to their regimen at COVID-19 onset (Figure 1). Among individual DMARDs, 56-77% were reported to have any change, except for hydroxychloroquine (23%) and rituximab (46%). SARD flare after COVID-19 was reported by 41% of respondents (Table 1). Patient global assessment of SARD activity was worse after COVID-19 (mean 7.6±2.3 before vs. 6.6±2.9 after COVID-19, p<0.001). Prolonged symptom duration was reported by 45% of participants. Those with prolonged symptoms had a higher initial COVID-19 symptom count (median 7 vs. 4, p<0.001) and were more likely to be hospitalized for COVID-19 (28% vs. 17%, p=0.001). Respondents experiencing prolonged symptom duration had higher disease activity on RAPID3 (p=0.007) as well as more pain (p<0.001) and fatigue (p=0.03) compared to those without prolonged symptoms.

Table 1. Acute COVID-19 course, SARD flare/activity, and patient-reported outcomes among COVID-19 survivors with SARDs.

	All COVID-19 survivors with SARDs (n=174)	Prolonged symptom duration ≥28 days (n=78)	No prolonged symptom duration/ (n=96)	p-value (prolonged vs. not)
Acute COVID-19 course				
COVID-19 symptom duration, days, median [IQR]	14 [9, 29]	46 [30, 65]	11 [7, 14]	<0.0001
Initial symptom count, median [IQR]	6 [3, 8]	7 [6, 9]	4 [2, 7]	<0.001
Hospitalized, n (%)	38 (22)	22 (28)	16 (17)	0.001
SARD flare/activity				
Self-reported SARD flare after COVID-19, n (%)	71 (41)	38 (49)	33 (34)	0.15
Disease activity by RAPID3, median [IQR]	9 [4, 14]	11.2 [6, 16]	7 [3, 13]	0.0067
RAPID3 categorical score, n (%)				0.13
Remission (0)	11 (7)	4 (5)	7 (7)	
Near remission (0.3-1.0)	23 (14)	5 (7)	18 (19)	
Low severity (1.3-2.0)	26 (15)	10 (14)	16 (17)	
Moderate severity (2.3-4.0)	55 (33)	27 (36)	28 (29)	
High severity (4.3-10.0)	54 (32)	28 (38)	26 (27)	
Patient-reported outcomes				
Pain by SF-MPQ, median [IQR]	2 [1, 2]	2 [1, 2]	1 [0, 2]	0.0008
Fatigue by FSI, median [IQR]	53 [27, 84]	66 [31, 91.5]	43 [26, 76]	0.031
mHAQ, median [IQR]	0.125 [0, 0.38]	0.25 [0, 0.75]	0.125 [0, 0.38]	0.11
Respiratory quality of life by SGRQ, global [IQR]	15 [4, 29]	16 [4, 36]	10 [4, 26]	0.49

RAPID3, Routine Assessment of Patient Index Data 3; SF-MPQ, Short-form McGill Pain Questionnaire; FSI, Fatigue Symptom Inventory; mHAQ, modified Health Assessment Questionnaire; SGRQ, Saint George's Respiratory Questionnaire.

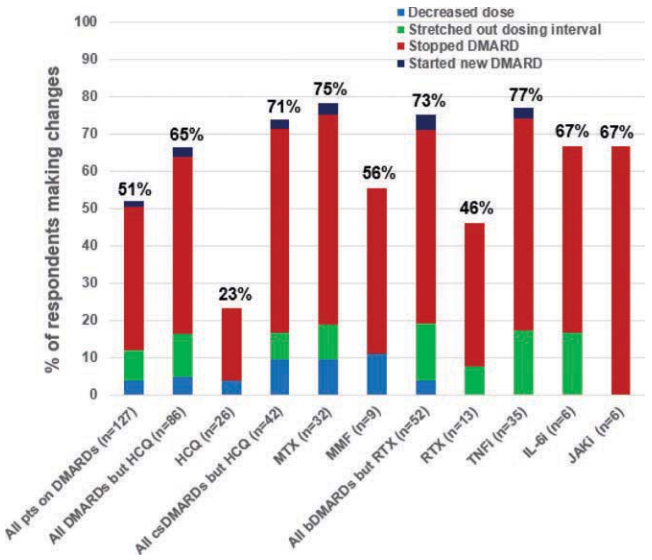

Figure 1. Frequency of baseline DMARD use and proportion with any disruption at COVID-19 onset.

Conclusion: DMARD disruption, SARD flare, and prolonged symptoms were common in this prospective study of COVID-19 survivors with SARDs. Those with prolonged COVID-19 symptom duration, defined as ≥28 days, had higher SARD activity, more pain, and more fatigue compared to those without prolonged symptoms. These findings suggest that post-acute sequelae of COVID-19 may have a large impact on underlying SARD activity and quality of life.

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POS1235 WORKING FROM HOME IN PATIENTS WITH RMDS DURING THE COVID-19 PANDEMIC IN EUROPE. RESULTS FROM THE REUMAVID STUDY (PHASE 1 AND 2)

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Background: The COVID-19 pandemic has introduced significant changes in the workplace, implementing teleworking as an effective solution to reduce contagion

Objectives: We sought to explore the impact of working from home on people with rheumatic and musculoskeletal diseases (RMDs) in Europe during the COVID-19 pandemic.

Methods: REUMAVID is an international cross-sectional study collecting data through an online survey in seven European countries led by the Health & Territory Research group of the University of Seville, together with a multidisciplinary team including patient representatives, rheumatologists, and health researchers. Data were collected in two phases, the first (P1) between April-July 2020 and the second (P2) between February-April 2021. Demographics, health behaviors, employment status, access to healthcare services, disease characteristics, WHO-5 Well-Being Index and Hospital Anxiety and Depression Scale (HADS) were collected. Workplace conditions including internet connection, computer, workstation, webcam, telephone, light, noise, calmness, and temperature were assessed (on a scale of 0 to 5, being 5 the best condition). Pearson's Chi-square test, Kruskal-Wallis and Mann-Whitney test were used to explore association with working from home.

Results: There were a total of 3,802 participants across both phases (mean age 52.6 (P1) vs. 55.0 years (P2); 80.2% female (P1) vs 83.7% (P2); 69.6% married (P1) vs 68.3% (P2), 48.6% university educated (P1) vs 47.8% (P2), 34.7% employed (P1) vs 38.1 (P2)). Most prevalent RMD was axial spondyloarthritis in P1 (37.2%), and rheumatoid arthritis in P2 (53.1%). Rates of working from home were consistent (P1: 39.8% vs P2: 39.9%).

In P2, 37.4% of those working from home had a home office, while 38.5% worked from their living room or kitchen. Work-related aspects at home were assessed, with the worst rated being the workplace (3.2) and the best being the computer (4.0). Compared to patients with good well-being and without anxiety and depression, patients with poorer well-being and at higher risk of anxiety or depression reported more frequently poorer rating of work from home issues, such as workplace (3.0 vs. 3.5; 2.9 vs. 3.6; 2.9 vs. 3.4; p<0.001), light (3.6 vs. 4.0; 3.6 vs. 4.0; 3.5 vs. 4.0; p<0.001), noise (3.3 vs. 3.8; 3.2 vs. 3.9; 3.2 vs. 3.8; p<0.001) and calmness (3.3 vs. 4.0; 3.2 vs. 3.9; 3.1 vs. 3.9; p<0.001; Table 1).

Conclusion: Patients with poorer well-being, at higher risk of anxiety or depression reported poorer ratings of workspace-related aspects. Therefore, although work from home has helped to reduce the spread of the COVID-19 pandemic, the conditions under which RMD patients work from home must be considered, as these may affect the well-being and mental health of an already vulnerable group. It is necessary to assess the conditions of home-based workspaces - especially for workers with chronic diseases such as RMD patients - to ensure that it is feasible to work from home and that employers provide the necessary equipment for healthy work.

Table 1. Bivariate analysis of aspect related to work from home and well-being, anxiety and depression in the second REUMAVID phase

	Mean ± SD or n (%)								
	Poor well-being	Good well-being	P-value	Risk of anxiety	No risk of anxiety	P-value	Risk of depression	No risk of depression	P-value
WIFI N: 354	3.8 ± 1.1	3.9 ± 1.1	0.534	3.8 ± 1.2	3.9 ± 1.0	0.193	3.8 ± 1.1	3.9 ± 1.1	0.264
Computer or laptop N: 352	3.9 ± 1.1	4.1 ± 1.0	**0.031**	3.8 ± 1.2	4.2 ± 0.9	**0.002**	3.9 ± 1.1	4.1 ± 1.1	**0.049**
Workstation N: 347	3.0 ± 1.4	3.5 ± 1.3	**<0.001**	2.9 ± 1.4	3.6 ± 1.2	**<0.001**	2.9 ± 1.4	3.4 ± 1.3	**<0.001**
Webcam N: 342	3.4 ± 1.5	3.7 ± 1.4	0.069	3.4 ± 1.5	3.7 ± 1.4	**0.043**	3.4 ± 1.3	3.6 ± 1.5	0.055
Telephone[2] N: 350	3.9 ± 1.2	4.0 ± 1.3	0.289	3.9 ± 1.3	4.0 ± 1.2	0.484	3.8 ± 1.2	4.0 ± 1.3	**0.034**
Light N: 354	3.6 ± 1.2	4.0 ± 1.1	**<0.001**	3.6 ± 1.2	4.0 ± 1.1	**0.001**	3.5 ± 1.2	4.0 ± 1.1	**<0.001**
Noise N: 353	3.3 ± 1.3	3.8 ± 1.4	**<0.001**	3.2 ± 1.4	3.9 ± 1.2	**<0.001**	3.2 ± 1.4	3.8 ± 1.3	**<0.001**
Calmness N: 353	3.3 ± 1.4	4.0 ± 1.2	**<0.001**	3.2 ± 1.4	4.0 ± 1.1	**<0.001**	3.1 ± 1.4	3.9 ± 1.3	**<0.001**
Temperature N: 353	3.6 ± 1.2	3.8 ± 1.2	0.053	3.5 ± 1.3	3.9 ± 1.1	**0.008**	3.5 ± 1.2	3.8 ± 1.2	**0.039**

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POS1236

THE IMPACT OF ANTI-SARS-COV-2 VACCINES IN A MULTICENTER COHORT STUDY OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Vulnerable subjects, including systemic lupus erythematosus (SLE) patients have been prioritised to receive anti-SARS-CoV-2 vaccine. Questions have been raised about the effect of vaccines on immunity and their potential role as trigger for flare. Few data about the safety of these vaccines in SLE are available

Objectives: To investigate the safety of different anti-SARS-CoV-2 vaccines in SLE

Methods: Data on SLE patients who have received anti-SARS-CoV-2 vaccine (from 12/2020 to 10/2021) were collected. Patients referred to 7 SLE tertiary centres (Lupus Clinic, ASST Pini-CTO, Milan; Nephrology Unit of Ospedale Giovanni Bosco, Turin; IRCCS Humanitas Research Hospital; Renal and Rheumatology Units, San Gerardo Hospital, Monza; ASST Spedali Civili Brescia; Lupus Clinic IRCCS Ospedale S. Raffaele, Milan, Italy; IRCCS Policlinico, Milan)

Results: 452 SLE patients who had received anti-SARS-CoV-2 vaccines were included (91% BNT162b2 mRNA, 8% mRNA-1273, 1% ChAdOx1-S). 12 (3%) were off therapy, 71% were on low-medium dose prednisone, 83% on anti-malarials, 50% were treated with an immunosuppressant. 9 patients transiently discontinued therapy. 119 (26%) reported adverse symptoms after the first/second shot (12% and 21%) The most frequent were fever, local reaction, fatigue and

Table 1. distribution of demographic and SLE characteristics according to sides effects and disease flares after vaccination

	Side effects (n=119)	No side effects (n=333)	p-value (<0.05)	Disease flare (n=19)	No disease flare (n=430)	p-value (<0.05)
Age, years, median (IQR)	46 (33.5-54)	48 (35.7-57)	0.18	52 (39.5-56.0)	48 (35.0-56.9)	0.849
Disease duration, months, median (IQR)	138 (76-262)	126 (73-193)	0.30	144 (122-242)	127 (73-195)	0.249
MSK, %	84.9	84.4	1.00	78.9	84.8	0.514
Mucocutaneus, %	71.4	62.8	0.094	57.9	64.5	0.624
Renal, %	42.0	52.3	0.069	52.6	49.4	0.819
NPSLE, %	13.4	9	0.215	5.3	10.4	0.708
Cardiopulmonary %	22.7	19.8	0.510	26.3	20.3	0.562
Hematological, %	32.8	33	1.00	42.1	32.6	0.455
Constitutional symptoms %	48.7	30	**0.0003***	26.3	35.3	0.473
Gastrointestinal %	4.2	3.3	0.772	5.3	3.5	0.503
Ophthalmic %	0.8	3.3	0.197	0	2.8	1.00
Secondary APS %	10.9	10.5	0.864	5.3	10.9	0.708
aPL positivity %	26.2	33.6	0.137	26.3	31.9	0.802
Anti-dsDNA positivity %	30.7	27.4	0.545	55.6	27.1	**0.0142***
ESR, mm/h, median (IQR)	14 (7-19)	13 (7-22)	0.730	19 (10-24)	13 (7-21)	0.125
CRP, mg/dL, median (IQR)	0.5 (0.1-0.5)	0.5 (0.3-0.6)	0.312	0.42 (0.13-0.50)	0.50 (0.30-0.5)	0.464
Urinary abnormalities, %	9.2	21.9	0.0023	21.1	18.5	0.764
Moderate or high DAS before vaccine, %	16	9.3	0.060	26.3	10.4	**0.0474***
No therapy before vaccine, %	0	3.6	**0.0419***	0	2.8	1.00
At least 1 immunosuppressant, %	63	46.8	**0.0027***	73.7	50.1	0.059
Mycophenolate, %	31.9	23.1	0.066	42.1	24.7	0.106
Methotrexate, %	5.9	6.6	1.00	5.3	6.5	1.00
Belimumab, %	21.8	13.5	**0.0396***	36.8	14.8	**0.0184***
Rituximab ever, %	11.8	13.5	0.751	5.3	13.4	0.490
Prednisone, %	74.8	70	0.347	78.9	70.9	0.607

arthralgias. Nineteen (4%) patients flared up after immunisation with a 7 days median time to relapse. Baseline demographics, SLE characteristics and therapy stratified by adverse events and disease flare are reported in Table 1. Anti-dsDNA positivity, moderate/high DAS before vaccine and use of Belimumab were significantly more frequent in the group of patients flared. These patients displayed a significantly higher rate of adverse events after vaccination. Flares consisted mainly musculoskeletal and constitutional manifestations (32%), involvement of renal (21%), cardio-respiratory (16%), hematological (16%) or mucocutaneous domains (10%) was less frequent

Conclusion: our reassuring data confirm that anti-SARS-CoV-2 vaccine is safe in SLE patients and should be recommended in this clinical setting, as potential benefits widely outweigh the risk of adverse events. Treatment adjustment might be considered with the aim of minimizing the risk of side effects and/or flare, while ensuring a satisfying protection against infection

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Disclosure of Interests: None declared

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POS1237 SARS-COV-2 MRNA VACCINE IMMUNOGENICITY IN CHRONIC INFLAMMATORY ARTHRITIS ON DMARD THERAPY

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Background: Patients with chronic inflammatory arthritis (CIA) are at increased risk for the development and mortality from COVID-19[1]. Vaccinations are integral to the management of these conditions. Disease-modifying antirheumatic drugs (DMARDs) used to treat CIA have the potential to blunt the immune response and efficacy of vaccinations[2]. There is little data on the effect of DMARDS used for CIA on the response to novel mRNA vaccines, limiting guidelines to direct therapy.

Objectives: Assess the antibody response (ABR) to the SARS-CoV-2 mRNA vaccines in patients with CIA on treatment with either methotrexate (MTX), tumor necrosis factor inhibitors (TNFi), or both with healthy controls. Determine the effect of interrupting therapy after vaccination in patients with CIA on the ABR to the vaccine.

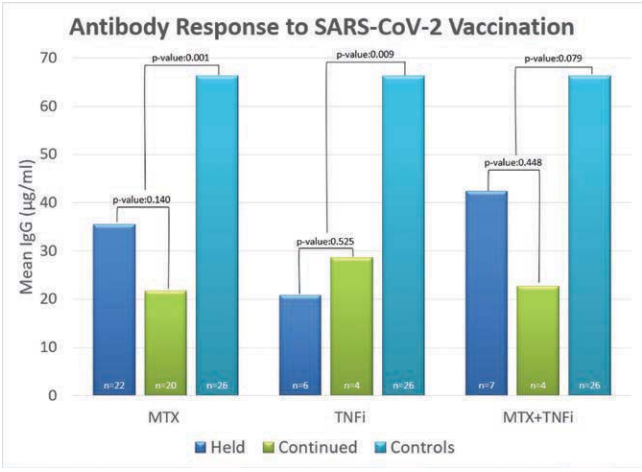
Methods: 63 patients with rheumatoid or psoriatic arthritis on MTX, TNFi or both were recruited from a community-based rheumatology practice. All subjects received two doses of a mRNA COVID vaccine. Use of hydroxychloroquine (HCQ), NSAID's, and prednisone (Pred) ≤10mg daily were allowed. Those with prior COVID infection were excluded, as determined by SARS-CoV-2 nucleocapsid assay. 26 healthy age-matched controls were obtained from banked blood from Labcorp. IRB approval was obtained, and patients were consented to participate in the study. SARS anti-receptor binding domain IgG antibodies were measured by electro chemiluminescent immunoassay 90-120 days post initial vaccine dose. Patients were divided into 3 groups based on therapy:

1. MTX monotherapy
2. TNFi with eternacept (ETN) or adalimumab (ADA)
3. A combination of MTX with either ETN or ADA

Each of the groups were subdivided into two categories:

1. Continued treatment uninterrupted at the time of each of the two vaccines.
2. Held treatment for two weeks after each vaccine. Statistical significance (p<.005) determined using one way ANOVA with Scheffe procedure and Student's T-test.

Results: The 63 patients with CIA had a significantly lower ABR to vaccine compared with healthy controls (p=0.001). Further analysis was limited by sample size: The MTX held group had a higher ABR than the MTX continued group (mean IgG=35.5 vs 21.74; p=0.14), demonstrating a trend toward increased immunogenicity. There was a similar ABR to vaccine between those on TNFi who held vs continued therapy (mean IgG 20.83 vs 28.65; p=0.525). Combination MTX +TNFi held vs continued groups demonstrated a trend toward increased immunogenicity when holding therapy post vaccine (mean IgG 42.4 vs 22.7; p=0.44). All treatment groups were comparable in Pred, HCQ, NSAID use, age, Rapid 3 score, and time between vaccination and blood draw for antibody levels (VI).



Conclusion: The ABR in patients with CIA to the mRNA vaccine appeared to be blunted by ongoing therapy with MTX. This effect was attenuated by holding MTX post-vaccine. There was no significant difference in the ABR to vaccine in patients on TNFi who held vs continued these agents after vaccine, due to small sample size. Patients with CIA on DMARD therapy had a significantly lower ABR to the vaccine compared to healthy controls. Our findings need further validation in a larger cohort. Clinicians may consider holding MTX for two weeks post vaccination to optimize the immune response to the vaccine.

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Table 1. Antibody response to Vaccination

	MTX		TNF		MTX + TNFi		Controls			
Variable	M	SD	M	SD	M	SD	M	SD	p value	Test
IgG	28.95	30.01	23.96	14.77	35.27	38.81	66.31	38.06	0.001	ANOVA
Drug	**Variable**		**Held**			**Continued**			**p value**	
		n	**M**	**SD**	**n**	**M**	**SD**			
MTX	Age	22	67.95	7.33	20	71.3	11.07		0.251	T-test
	IgG	22	35.5	29.92	20	21.74	29.13		0.14	
	VI	22	97.27	13.71	20	98.15	10.19		0.817	
TNFi	Age	6	64.5	10.19	4	70.25	13.77		0.467	
	IgG	6	20.83	10.07	4	28.65	20.9		0.525	
	VI	6	98.67	22.24	4	93.75	12.29		0.701	
MTX + TNFi	Age	7	63.86	6.36	4	62.75	11.53		0.839	
	IgG	7	42.43	45.11	4	22.75	24.92		0.448	
	VI	7	100	19.09	4	97.75	22.59		0.864	
Variable		**CIA**			**Controls**				**p value**	
	n	**M**	**SD**	**n**	**M**	**SD**				
Age	63	63.05	9.61	26	52.31	8.84			0.001	T-test
VI	63	97.79	14.31	26	88.65	5.43			0.002	

M: Mean; VI: Vaccine Interval in days

POS1238

GLUCOCORTICOIDS, RITUXIMAB AND THE PRESENCE OF INTERSTITIAL LUNG DISEASE ARE ASSOCIATED WITH POOR OUTCOMES OF THE SARS-COV-2 INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE NATIONAL REGISTRY SAR-COVID.

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Background: High disease activity, treatment with glucocorticoids (GC) and rituximab (RTX), have been related to worse outcomes of COVID-19.
Objectives: To assess the clinical characteristics and severity of the SARS-CoV-2 infection in patients with rheumatoid arthritis (RA) included in the SAR-COVID registry and to identify factors associated with poor outcomes.
Methods: SAR-COVID is a national, longitudinal and observational registry. Patients of ≥18 years old, with diagnosis of RA (ACR-EULAR criteria 2010) who had confirmed SARS-CoV-2 infection (RT-PCR or positive serology) were included between 13-8-20 and 31-7-21. Sociodemographic and clinical data, comorbidities, disease activity and treatment at the moment of the SARS-CoV-2 infection were collected. Additionally, infection symptoms, complications, medical interventions and treatments for COVID-19 were registered. Infection severity was assessed using the WHO-ordinal scale (WHO-OS)[1]. A cut-off value of ≥5 identified patients with severe COVID-19 and those who died.
Statistical analysis: Descriptive statistics. Chi^2 or Fischer test, Student T test or Mann-Whitney and Kruskal Wallis or ANOVA, as appropriate. Multiple logistic regression model.
Results: A total of 801 patients were included, with a mean age of 53.1 ± 12.9 years, most of them were female (84.5%) and the median (*m*) disease duration was 8 years (IQR 4-14). One third were in remission and 46.4% had comorbidities, being the most frequent, hypertension (26.9 %), dyslipidemia (13.5 %), obesity (13.4 %) and diabetes (8.9%). Moreover, 3.2% had interstitial lung disease (ILD) associated with RA. At SARS-CoV-2 diagnosis, 42.5% were receiving glucocorticoids (GC), 73.9% conventional (c) disease modifying antirheumatic drugs (DMARD), 24% biologic (b) DMARD and 9.1% targeted synthetic (ts) DMARD. Among bDMARD, the most frequently used were TNF inhibitors (17%), followed by abatacept (2.8%), IL-6 inhibitors (2.4%) and rituximab (RTX) (2.1%). During the SARS-CoV-2 infection, 95.8% had symptoms, 27% required hospitalization, 7.9% presented complications and 4.4% died due to COVID-19. Severe disease and death (WHO-OS≥5) was present in 7.5% of the patients. They were older (62.9±12.5 vs 52.2±12.7, p<0.001), and they had more frequently ILD (18.5% vs 2%, p<0.001), comorbidities (82.5% vs 43.7%, p<0.001), ≥2 comorbidities (60.3% vs 25.8%, p<0.001), treatment with GC (61% vs 40.7%, p=0.04) and RTX (8.3% vs 1.6%, p=0.007). Conversely, the use of cDMARD and TNF inhibitors was more frequent in patients with WHO-OS<5, nevertheless this difference was not significant. Disease activity was comparable between groups.

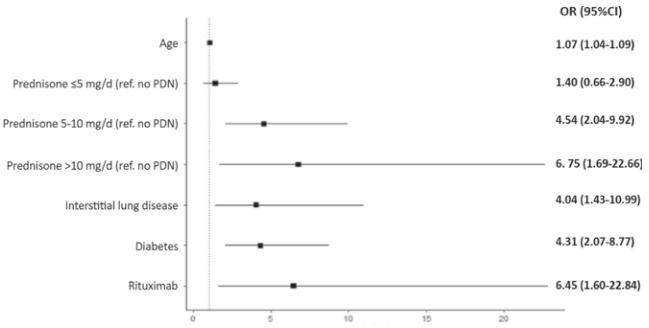

Figure 1. Factors associated with severe disease and death due to COVID-19 (WHO-OS≥5) in patients with rheumatoid arthritis. Multivariable analysis. (ref.: reference; PDN: prednisone; OR: odds ratio; CI: confidence interval)

In multivariable analysis, older age, the presence of diabetes, ILD, the use of GC and RTX were significantly associated with WHO-OS≥5 (Figure 1). Furthermore, older age (65.7±10.8 vs 52.4±12.8, p<0.001), the presence of comorbidities (87.9% vs 44.7%, p<0.001), chronic obstructive pulmonary disease (21.9% vs 5.2%, p=0.002), diabetes (30.3% vs 7.9%, p<0.001), hypertension (57.6% vs 25.6%, p<0.001), cardiovascular disease (15.6% vs 3.2%, p=0.005), cancer (9.1% vs 1.3%, p=0.001), ILD (23.3% vs 2.4%, p<0.001) and the use of GC (61.8% vs 41.4%, p=0.02) were associated with mortality. Older age [OR 1.1 IC95% 1.06-1.13] and the use of GC 5-10 mg/day [OR 4.6 IC95% 1.8-11.6] remained significantly associated with death due to COVID-19.
Conclusion: Treatment with RTX and GC, as well as older age, the presence of diabetes and ILD were associated with poor COVID-19 outcomes in this national cohort of patients with RA. Older patients and those taking GC had a higher mortality rate.

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POS1239

RISK FACTORS FOR SEVERE DISEASE COURSE IN MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) – A MULTICENTER, RETROSPECTIVE STUDY

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Background: Multisystem Inflammatory Syndrome in Children (MIS- C) associated with COVID-19, presents as a cytokine storm with features of Kawasaki disease. Many cases present with shock and require intensive care admission.
Objectives: We aimed to identify predictors for severe clinical course of MIS-C as defined by the need for ionotropic support during admission
Methods: A retrospective multinational cohort study was conducted. Patients with a diagnosis of MIS-C from 9 Israeli medical centers and one US medical center (Chicago, IL) were included. Demographic, clinical, laboratory and imaging variables during admission and hospitalization were retrieved. Univariate and multivariate regression models were used to assess odds ratio (OR) of ionotropic support need during hospitalization.
Results: Overall 100 MIS-C patients were included in the study. Sixty-five patients (65%) were hypotensive, 44% required ionotropic support, and 37% had finding of Left ventricular dysfunction. Univariate model showed that LVD was associated with the need for ionotropic support (OR 4.178 [95%CI 1.760-9.917], while conjunctivitis (OR 0.403 [95%CI 0.173-0.938]) and mucosal changes (OR 0.333 [95%CI 0.119-0.931]) were protective. Laboratory markers for severe disease course were low hemoglobin levels, leukocyte count, thrombocyte count, lymphocyte count, neutrophils count, albumin and potassium, as well as high troponin and BNP.

Table 1. and laboratory characteristics on admission of patients diagnosed with MIS-C

	w/o Hemodynamic support N=56 (56.0%)	with Hemodynamic support N=44 (44.0%)	p-value
Gastrointestinal symptoms	46 (82.1%)	41 (93.2%)	0.103
Mucosal changes	18 (32.1%)	6 (13.6%)	0.031
Rash	34 (60.7%)	20 (45.5%)	0.129
Conjunctivitis	27 (48.2%)	12 (27.3%)	0.033
Extremity changes	4 (7.1%)	6 (13.6%)	0.280
Lymphadenopathy	11 (19.6%)	11 (25.0%)	0.521
No. of days of fever at admission	4 [3-5]	5 [3-5]	0.646
Systolic BP	99 [90-108]	97 [85-102]	0.263
Diastolic BP	60 [53-67]	53 [45-59]	0.006
HR	124 [114-143]	126 [108-144]	0.957
hemoglobin admission (g/dL)	11.65 [10.83-12.67]	11.25 [10.22-12.58]	0.220
White cells admission (K/μL)	9.02 [6.63-12.01]	9.03 [5.75-16.99]	0.742
platelets admission (K/μL)	174.0 [134.50-250.0]	147.50 [121.25-146.25]	0.126
lymphocytes admission (K/μL)	0.90 [0.64-1.70]	0.70 [0.48-1.11]	0.015
ESR admission (mm/hr)	43.00 [35.5-74.50]	44.00 [28.50-66.00]	0.575
C-reactive protein admission (mg/dL)	14.05 [10.32-22.28]	19.50 [10.90-27.30]	0.117
Creatinine admission (mg/dL)	0.55 [0.40-0.70]	0.69 [0.50-0.81]	0.008

Conclusion: Patients with MIS-c that present with a Kawasaki-like phenotype are less likely to require ionotropic support, while other clinical and laboratory parameters were found as risk factors and should be monitored during MIS-C hospitalization.

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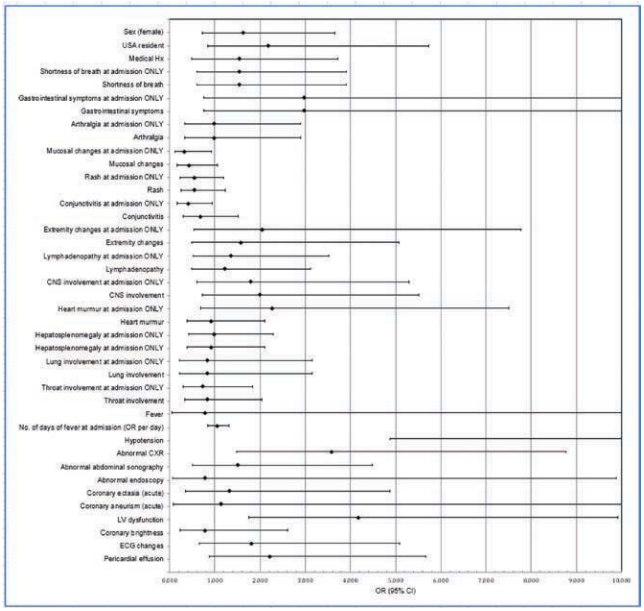

Figure 1. - forest plot - clinical risk factors for need of hemodynamic support in MIS-C patients; Odds Ratio [95% CI] (univariate analysis)

Disclosure of Interests: None declared
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POS1240 HIGH PREVALENCE OF SERUM AUTOANTIBODIES IN SEVERELY ILL COVID-19 PATIENTS HOSPITALIZED IN THE INTENSIVE CARE UNIT.

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Background: Coronavirus Disease-19 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is characterized by a wide range of clinical manifestations [1]. Although COVID-19 was initially considered a respiratory infection, it was shortly recognized as a multisystemic disorder associated with heightened inflammatory responses, including autoimmune phenomena [1]. The presence of autoantibodies (AAbs) has been described in COVID-19 patients, highlighting the state of immune dysregulation in COVID-19 [1]. The clinical significance of AAbs, however, is still elusive.
Objectives: To assess the prevalence of AAbs in critically ill, mechanically ventilated COVID-19 patients admitted to the intensive care unit (ICU) and investigate whether AAbs influence the clinical outcome of these patients.
Methods: The current study evaluated prospectively from March 8th, 2021 to May 10th, 2021 the presence of AAbs against nuclear antigens (ANA), extractable nuclear antigens (ENA), neutrophil cytoplasmic antigens (ANCA), cyclic citrullinated peptides (anti-CCP), double stranded-DNA (anti-dsDNA), cardiolipin (anti-CL), β2-glycoprotein-I (anti-β2-GPI), thyroid peroxidase (anti-TPO), and thyroglobulin (anti-TG) in critically ill COVID-19 patients upon admission in the ICU (n=217). Samples from 60 COVID-19 patients that were available 15 days after ICU admission were further analyzed for the evaluation of de novo AAbs production. Serum samples of age and sex matched healthy individuals before the COVID-19 pandemic were used as a control group (n=117).
Results: COVID-19 patients treated in ICU had more commonly at least one AAb compared to age and sex matched controls (174/217, 80.2% vs 73/217, 62,4%, p< 0,001). More specifically, COVID-19 patients expressed more frequently ANAs (48.4% vs 21.4%, p<0.001), anti-dsDNA (5.1% vs 0%, p=0.01), anti-CCP (8.3% vs 1.7%, p=0.014) and anti-CL IgM AAbs (21.7% vs 9.4%, p=0.005) than controls. The majority of critical COVID-19 patients who were positive for AAbs (144, 82.8%) expressed reactivity in up to three autoantigens with the most prominent being ANA, anti-phospholipid, ANCA and anti-TPO AAbs. AAbs-positive patients demonstrated more robust anti-SARS-CoV-2 humoral responses compared to AAbs-negative patients [detectable anti-SARS-CoV-2 S1-protein IgG antibodies: 150 (86.2%) vs 28 (65.1%), p=0.001; adequate neutralizing activity: 159 (91.4%) vs. 33 (76.7%), p=0.007]. The two groups, however, did not differ in terms of clinicoepidemiologic characteristics or the incidence of death in the ICU. Convalescent COVID-19 patients (n=111) compared to those who died (n=106), did not differ in the prevalence of serum AAbs or antibody responses against SARS-CoV-2. Differences were only shown in clinicolaboratory parameters including patients' age, comorbidities, O2 saturation, inflammatory markers, and in-hospital prognostic scores as expected. Paired samples testing (n=60) revealed that 45 patients had at least one newly induced AAb, 28 patients lost at least one reactivity and only 6 patients didn't show any seroconversion. The most common new-onset AAb reactivity was against anti-CL (IgG isotype) (n=21) followed by ANA (n=20), anti-β2-GPI (IgG isotype) (n=11), myositis-related antigens (n=13) and ENAs (n=9); nevertheless, no associations with clinicoepidemiologic features or COVID-19 outcome were revealed.
Conclusion: Patients with severe COVID-19 express AAbs more commonly than age and sex matched controls, suggesting that SARS-COV-2 infection may induce a hitherto unknown B-cell autoreactivity. The presence of autoantibodies does not play a role in the outcome of SARS-COV-2 infection. However, further studies are needed to define their role in future development of systemic autoimmune disorders or the long-COVID syndrome.
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POS1241 THE IMPACT OF TELEMEDICINE CONSULTATIONS FOR RHEUMATOID ARTHRITIS, GIANT CELL ARTERITIS, OSTEOARTHRITIS AND CRYSTAL ARTHRITIS DURING COVID19 PANDEMIC

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Background: Rheumatology departments across the UK have adapted to the COVID-19 pandemic, implementing novel methods of working via remote consultations.
Objectives: We wanted to explore the rates of telemedicine consultations for patients with Rheumatoid Arthritis (RA), Giant cell arteritis (GCA), Osteoarthritis (OA), and Crystal arthritis (CA). We also wanted to check how effective the telemedicine consultations had been in terms of avoiding the need for a face-to-face appointment.
Methods: No telemedicine consultations took place before the COVID-19 pandemic in patients diagnosed with GCA, RA, CA and OA. We assessed the number of telemedicine consultations (telephone or videocall) using data from the departmental database covering September 2020 to December 2021. We analysed the rates of face-to-face versus telemedicine appointments for both new referrals and follow-up consultations. The statistical analysis was conducted using chi-square test.
Results: There were 20,648 patients assessed in our department from September 2020 to December 2021. In total 1786 face-to-face and 2079 telemedicine consultations were conducted for GCA (18%), RA (66%), OA (13%) and CA (3%). The highest percentage of telemedicine consultations versus face-to-face for new referrals were observed for OA (30% Vs 70%) followed by RA (14% Vs 86%), CA (12% Vs 88%) and GCA (2% Vs 98%) (Table 1). Combining all these conditions, 68% of clinicians felt the telemedicine appointment avoided a face-to-face appointment. However, 33% of clinicians seeing new patients with RA did not feel the telemedicine appointment avoided a face-to-face appointment.

Table 1.

Diagnoses	New referrals		Follow-up	
	Telemedicine	Face-to-face	Telemedicine	Face-to-face
RA	36 (14%)	227 (86%)	1480 (65%)	783 (35%)
CA	7 (12%)	50 (88%)	41 (61%)	26 (39%)
OA	82 (30%)	187 (70%)	115 (51%)	109 (49%)
GCA	3 (2%)	21 (98%)	315 (53%)	283 (47%)

In contrast, follow-up appointments were mainly conducted by telemedicine when compared with face-to-face; RA (65% Vs 35%), GCA (53%Vs 47%), OA (51% Vs 49%) and CA (61% Vs 39%). For the follow-ups, an overall majority of 90% of telemedicine consultations avoided the need for a face-to-face appointment, particularly observed for patients with CA and GCA (98% and 93% respectively). We noted that patients with RA were more likely than GCA to have a telemedicine follow-up (p value<0.00001).

Conclusion: Telemedicine appointments for new referrals and follow-up patients with Rheumatological diagnoses has been a new development because of COVID-19 pandemic. Our analysis shows that most of our new RA, GCA, OA, and CA referrals are still being seen face-to-face but most follow-up appointments are telemedicine consultations. In most cases, clinicians felt that telemedicine consultations avoided the need for a face-to-face appointment.

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POS1242 BARICITINIB AND PULSE STEROIDS COMBINED TREATMENT IN SEVERE COVID-19 PNEUMONIA: PRELIMINARY DATA FROM A RHEUMATOLOGIC EXPERIENCE IN INTENSIVE CARE UNIT

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Background: Growing evidence from in vitro and clinical studies have highlighted important similarities between severe COVID-19 and rapidly progressive interstitial lung diseases (ILD) occurring in systemic autoimmune disorders. These data supported the use of anti-rheumatic drugs, baricitinib and glucocorticoids, for the treatment of COVID-19 pneumonia.

Objectives: To compare mortality rate and inflammatory response in critically ill COVID-19 patients treated with either a "rheumatologic approach" based on baricitinib plus pulse steroids (BPS) or with a "conventional approach" (Standard of Care, SoC).

Methods: In this retrospective study, we enrolled patients admitted to the Intensive Care Unit (ICU) with CT-proven SARS-CoV2 pneumonia, from September 2020 to April 2021. Demographic, laboratory, and clinical data were collected at the admission to ICU and after one week of treatment. SoC included dexamethasone 6 to 8 mg daily plus remdesivir (+/- antibiotics and hydroxychloroquine); BPS approach was based on baricitinib 4 mg daily for 10-14 days plus 6-methylprednisolone pulses (250-500 mg) for three consecutive days followed by rapid tapering. The primary endpoint was the intra-ICU mortality rate; the secondary endpoint was the change in inflammatory biomarkers at week 1 after treatment.

Results: We enrolled a total of 210 consecutive patients with SARS-CoV2 pneumonia (male 61.4%, mean age 66.6 ± 10.9 years); 137/210 (male 59.8%, mean age 66.3 ± 11.9 years) were treated with SoC and 73/210 (male 64.3%, mean age 67.3 ± 8.8 years) with BPS.

At admission in ICU, all patients presented lag time from the first symptom of SARS-CoV2 infection ≤ 10 days, laboratory biomarkers' alterations suggestive of hyper-inflammatory response (CRP 10.8 ± 11.9 mg/dL, ferritin 1238 ± 1005 µg/L, fibrinogen 575 ± 173 mg/dL, LDH 385 ± 152 U/L) and severe respiratory failure, requiring non-invasive or invasive ventilatory support. Lung-CT pattern showed multiple and diffuse areas of ground glass opacities, septal thickening, and/or consolidation.

No statistically significant differences were found between SoC and BPS groups in terms of demographic, laboratory, and clinical features at enrolment.

59/210 (28.1%) patients died during ICU hospitalization (mean ICU length of stay 14.6 ± 9.6 days). Mortality rate in the BPS group (13/73, 17.8%) resulted significantly lower compared to that in the SoC group (46/137, 33.6%) (p= 0.016). Furthermore, patients in the BPS group had significantly lower levels of CRP (BPS=1.9 ± 2.8 vs SoC 6.1 ± 7.3, p<0.001) and fibrinogen (BPS=335 ± 108 vs SoC 453 ± 172, p<0.001) at one week after the start of treatment.

Conclusion: Our real-life experience, in an ICU setting, showed that baricitinib and pulse steroids combination was associated with a lower mortality rate paralleled by a prompt reduction of inflammatory biomarkers. These results shed new light on the possible usefulness of baricitinib for the treatment of rapidly progressive ILD in patients with systemic autoimmunity and hyper-inflammation.

Disclosure of Interests: None declared

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POS1243 ACCELERATED WANING OF PROTECTIVE IMMUNITY AFTER SARS-COV-2 MRNA VACCINATION IN PATIENTS TREATED WITH BIOLOGICAL AND TARGETED SYNTHETIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS

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Background: Little is known about the duration of humoral antibody levels after two SARS-CoV-2 mRNA vaccinations in patients with immunosuppression. During this ongoing global epidemic, it is of essential interest to gather information about the time of protection after initial immunization in the vulnerable patients receiving either conventional synthetic disease modifying antirheumatic drugs (csDMARD) or biological/ targeted drugs (b/tsDMARDs).

Objectives: In this study we compared the antibody level development after vaccination and after six months in patients with inflammatory arthritis, inflammatory bowel disease (IBD) and healthy controls. Furthermore, we assessed factors affecting the quality and quantity of the humoral response.

Methods: We enrolled 85 healthy controls (HC), 75 patients with rheumatoid arthritis and spondyloarthritis and 41 patients suffering from IBD. Patients treated with B-cell depleting therapies were excluded from this study. Binding antibody units were measured after vaccination and 6 or more months. Neutralizing antibodies were measured after 6 months. Multivariate regression analyses analyzing factors associated with low titers after 6 months was performed.

Results: We found that patients with inflammatory arthritis or IBD showed reduced anti-SARS-CoV-2 S titers compared to HC. When we stratified for therapies, we found that patients receiving conventional synthetic disease modifying antirheumatic dugs (csDMARDs) had comparable anti-SARS-CoV-2 S titers to HC. In contrast, patients receiving biological or targeted synthetic (b/tsDMARDs) showed reduced anti-SARS-CoV-2 Igs as well as neutralizing antibody titers compared with healthy controls (HC) or patients receiving conventional synthetic (cs)DMARDs. We further show that anti-SARS-CoV-2 titers declined more rapidly in patients receiving b/tsDMARDs compared to HC, leading to a 50 percent reduction in vaccination-associated protection time in patients receiving b/tsDMARDs when compared to those receiving csDMARDs or even HC. In multivariate regression analyses, we found that in addition to the type of treatment, also age as well as corticosteroid use were associated with reduced anti-SARS-CoV-2 S titers.

Conclusion: Patients under ongoing b/tsDMARDs therapy exposed an accelerated waning of anti-SARS-CoV-2 S titers and therefore decreased immunity and protection against severe Covid-19 infections over time. These results may lead to more personalized approaches for further vaccination strategies in this group of immunosuppressed patients.

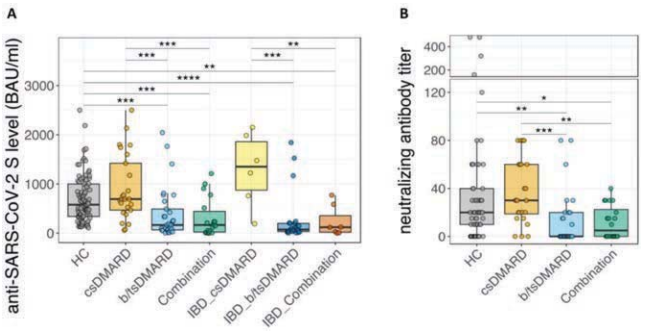

Figure 1. A, Analysis of anti-SARS-CoV-2 S titers 6 months after the second vaccination in patients with inflammatory arthritis, inflammatory bowel disease and HC (** p ≤ 0.01; *** p ≤ 0.005, **** p ≤ 0.001). **B**, Determination of neutralizing antibody activity in sera of HC and patients with inflammatory arthritis receiving the indicated therapies.

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POS1244 THE EFFECT OF SECUKINUMAB ON THE HUMORAL RESPONSE FOLLOWING TWO AND THREE DOSES OF THE BNT162B2 MRNA VACCINE IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Data on the effect of secukinumab on the humoral response to the BNT162b2 mRNA vaccine are limited.
Objectives: We aimed to assess prospectively the humoral response to the BNT162b2 mRNA vaccine in patients with spondyloarthritis (SpA) treated with secukinumab in comparison to immunocompetent controls.
Methods: Patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS) treated with secukinumab for at least 3 months and immunocompetent controls were vaccinated with two-dose regimen of the BNT162b2 mRNA vaccine. Clinical and laboratory assessments were performed at 2-8 weeks [SpA: 37 on secukinumab, (median age 53% female), 122 controls (median age 53, 51% female)], and 6 months [SpA: 27 on secukinumab, 116 controls] after the second vaccine dose. A subgroup of patients (22 SpA on secukinumab, 45 controls) were evaluated after the third vaccine dose. The seropositive response was defined as a detectable S1/S2 IgG ≥15 binding antibody units (BAU)/ml.
Results: The two-dose vaccine regimen induced a similar immunogenic response in patients and controls reflected by the seropositivity rates of 100% in both groups. After six months, the rate of seropositivity remained as high as 96% in both secukinumab-treated patients and immunocompetent controls. The decline of S1/S2 IgG titer within six months was similar in controls and secukinumab-treated patients, -66.4 (95% CI {-70.9, -39.9}) and -55 BAU/ml (95% CI {-95.42, -36.87}). Following the third vaccine, the seropositivity rate increased to 100 % in both groups. At all-time points, S1/S2 IgG titers were similar in secukinumab treated patients and immunocompetent controls (Figure 1).

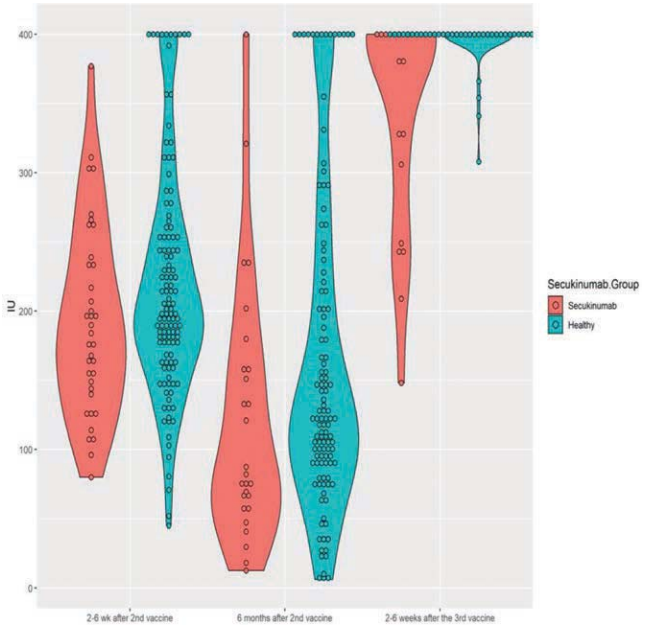

Figure 1. Kinetics of an immunogenic response (S1/S2 IgG titer) to two and three doses of the BNT162b2 mRNA vaccine in SpA patients treated with secukinumab and immunocompetent controls.

Conclusion: SpA patients treated with secukinumab consistently demonstrated an adequate humoral response to the BNT162b2 mRNA vaccination similar to immunocompetent controls, both short-term and within six months after two vaccine doses and after the third vaccine dose.
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POS1245 REVERSAL OF DECLINE IN HUMORAL RESPONSE TO BNT162B2 MRNA COVID-19 VACCINE AFTER BOOSTER ADMINISTRATION IN AUTOIMMUNE INFLAMMATORY RHEUMATOID DISEASES (AIRD) PATIENTS

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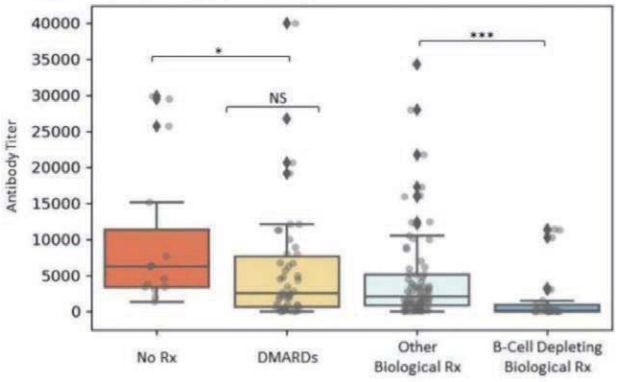
Background: Previous studies proved that mRNA vaccinations against SARS CoV2 induced significant humoral responses in AIRD patients (pts). However, the humoral response was blunted in pts treated with CD20 depleting antibodies. There are limited data regarding the long-term outcome of the humoral response and the contribution of the booster vaccine, in immunosuppressed AIRD pts.

Objectives: To assess the long-term outcome of the humoral response to mRNA vaccine against SARS CoV2, in AIRD pts treated with immunomodulating drugs, and the contribution of the booster vaccination.
Methods: Consecutive pts treated at the Rheumatology Institute at Rambam Hospital who received their first SARS-CoV-2 (Pfizer) vaccine were recruited to the study, at their routine visit. The visit included AIRD activity assessment and questioning regarding vaccine side effects. We performed serology test 4-6 weeks and 24 weeks after receiving the second dose of vaccine. Pts who received the booster (3rd vaccine) were invited for serology tests 4-8 weeks afterwards. The immunomodulating treatment was not modified, either before or after the vaccination. IgG Antibodies (Ab) against SARS COV2 virus were detected using the SARS-Cov-2 IgG II Quant (Abbott) assay based on a chemiluminescent microparticle immunoassay (CMIA) on the ARCHITECT ci8200system from Abbott. This assay is measuring IgG antibodies against the spike receptor-binding domain (S-RBD) of the virus. The test was considered positive above 50 AU/ml.
Results: 262 pts (mean age(SD) 57(13), disease duration 11.2(7.4), were recruited. The cohort included 152 pts with inflammatory joint disease, 26 pts with systemic lupus erythematosus, 62 pts with other connective tissue disease and 22 pts with vasculitis; 27 % received csDMARDs only, 35% - b/tsDMARDs only, 30% - combined therapy (csDMARDs+b/tsDMARDs) and 26% received steroids. 225 pts (86%) were seropositive for IgG Ab against SARS CoV2 virus (median 2832.5 AU/ml, IQR 58-29499). 37 (14%) pts had negative tests, 23 (62.2%) of them were rituximab treated.
The IgG levels correlated with the medication used to treat the AIRD, the patients' age but not with the type of the AIRD (Figure 1). 24 weeks afterwards, the median IgG level dropped to 282 AU/ml and 15% of the pts with previous seropositive tests became negative. The booster administration (Pfizer) significantly augmented the humoral response (median 8328 AU/ml, IQR 375-40000). De novo serologic response was observed in 10 out of 37 pts (4/23 rituximab treated pts).

Figure 1: Serology per drug



	No Rx (N=21)	DMARDs (N=71)	Other Biological Rx ± DMARDs (N=119)	B-Cell Depleting Biological Rx (N=51)
Antibody Titer	9891±2615	4947±883	4524±733	1769±719
Age (yr)	61.2	57.17	59.57	60.36

Plus–minus values are means ±SE; ***, p-value<0.005; *, p-value<0.05; NS, not significant

Figure 1.

The reported side effects of the vaccine were minor (muscle sore, headache, low grade fever). The AIRD remained stable in all pts following all three vaccinations.
Conclusion: Although the vast majority of AIRD pts developed a substantial humoral response following the administration of the second dose of the Pfizer mRNA vaccine against SARS CoV2 virus, the humoral response significantly declined 24 weeks afterwards. An enhanced response was obtained after the third booster vaccination. Only minor side effects were reported and no apparent impact on AIRD activity was noted. Notably, 62% of the non-responders were treated with B cell depleting agents.
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POS1246 COVID-19 IN RITUXIMAB TREATED PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: At the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) pandemic, the influence of anti-inflammatory therapy on the course of SARS-CoV-2 infection in patients with inflammatory rheumatic diseases (IRD) was unknown. In the meantime, several data indicate an association of severe courses of COVID-19 with the use of rituximab (RTX).
Objectives: To gather further knowledge about SARS-CoV-2 infections in RTX-treated IRD patients, data from the German COVID-19-IRD-registry were analysed.
Methods: Hospitalisation was used as a surrogate of COVID-19 severity. Baseline characteristics, disease features, medication and outcome of COVID-19 were compared in RTX-treated inpatients and outpatients.
Results: In total, 3592 cases were reported in the registry, which included 130 RTX patients (3.6%) for our analysis. RTX-treated inpatients were older than RTX-treated outpatients (median age 63 y vs 56 y, p=0.007). Patients with granulomatosis with polyangiitis treated with RTX (n=32) showed a significant higher COVID-19 related hospitalisation rate (33% vs 11%, p=0.005), which was not the case for patients with rheumatoid arthritis (49% vs 50%). Cardiovascular comorbidities were reported more frequently in hospitalised RTX-treated patients (20% vs. 6%, p=0.032). More than 50% of the RTX-treated inpatients developed COVID-19 related complications, e.g. acute respiratory distress syndrome. The median time period between the last RTX treatment and SARS-CoV-2 infection was shorter in inpatients than in non-hospitalised patients (3 (range 0-17) vs. 4 months (range -29), p=0.039). The COVID-19 related mortality rate was 14% (n=19) in RTX-treated IRD patients. In RTX-treated inpatients and outpatients, there were no relevant differences with respect to the use of concomitant glucocorticoids or other disease modifying anti-rheumatic drugs, disease activity, median last RTX dose or median number of immunomodulatory drugs prior to RTX treatment.
Conclusion: In addition to general risk factors, such as age and comorbidities, it is already known that IRD patients treated with RTX show a higher rate of severe COVID-19. In our registry, RTX-treated patients with granulomatosis with polyangiitis appear to be at even higher risk to develop severe COVID-19 compared to other IRD. Moreover, the shorter the time since the last RTX treatment, the higher seems to be the risk of developing severe COVID-19. This might be explained by a more profound B-cell depletion in the first weeks after RTX treatment warranting further studies.
Disclosure of Interests: None declared
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POS1247 THE EFFECT OF IMMUNOSUPPRESSIVE AGENTS ON ANTIBODY FORMATION AFTER COVID-19 VACCINATION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: There is still controversy about the efficacy of COVID-19 vaccination and its extent in lowering immunogenicity of Rheumatoid Arthritis (RA) patients. The guideline in whether immunosuppressive agents need to be discontinued before the vaccination is continuously updated because it is considered to lower immunogenicity. Furthermore, there is great discussion on the effectiveness of the COVID-19 booster vaccine and interest in antibody generation in different types of vaccine, as in South Korea there are many patients who were prescribed the mRNA booster vaccine after two doses of ChAdOx1-S nCoV-19 vaccine.

Objectives: Thus, we investigated the differences of antibody production between patients who received only two doses of ChAdOx1-S nCoV-19 and those who received the mRNA booster vaccine. Also, antibody production under different types of immunosuppressive agents was analyzed.

Methods: From October 14, 2021 to January 21, 2022 at a tertiary referral center, two patient groups diagnosed with RA were studied prospectively; one group that completed 1st and 2nd doses of ChAdOx1-S nCoV-19 vaccine, second group that completed mRNA booster vaccine as well as two doses of ChAdOx1-S nCoV-19 vaccine. SARS-CoV-2 antibody testing on the semiquantitative anti-SARS-CoV-2 S enzyme immunoassay was done, and differences in antibody titers were analyzed in patients who received different immunosuppressive agents such as csDMARD, TNF inhibitor, JAK inhibitor, Tocilizumab, Abatacept and Corticosteroid. Statistical analysis with a multivariate logistic regression model was performed.

Results: In a total of 261 patients, 153 patients had completed two doses of ChAdOx1-S nCoV-19, 108 patients had completed third mRNA booster vaccine. Anti-SARS-CoV-2 RBD antibody positive rate (titer>0.8U/mL) was 97%(149/153) and 99%(107/108) respectively, and only 5 patients showed negative result. In the aspect of high antibody titer(>250U/mL), which is the upper limit of the RBD antibody immunoassay, the result showed rate of 31% (47/153) in the non-booster group and 94%(102/108) in the booster group respectively.

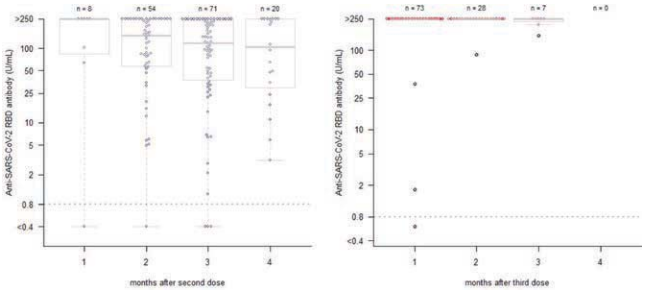

Figure 1. Anti-SARS-CoV RBD antibody titer of two groups

Among the different immunosuppressive agents and other clinical aspects, multivariate analysis revealed that corticosteroid use (OR 0.91; 95% CI: 0.86-0.98), older age(OR 4.33; 95% CI: 1.34-13.91), and male gender(OR 0.35; 95% CI 0.16-0.75) were significantly associated with low rate of high antibody titer. Furthermore, out of 14 patients who underwent antibody test twice before and after the mRNA booster vaccine, other than four patients who already showed high titer of >250U/mL before the mRNA booster vaccine, 10 patients showed an increase in titer after the booster vaccine and 7 patients were acquired high titer of >250U/mL.

Conclusion: Anti-SARS-CoV-2 RBD antibody positive rate was 97% or more regardless of the mRNA booster vaccination. However, patients who received the mRNA booster vaccine after two doses of ChAdOx1-S nCoV-19 vaccine showed high antibody titer (>250U/mL) three times more than those who did not receive the booster shot. Our findings also showed that corticosteroid use, old age, and male gender is significantly associated with low rate of acquiring high antibody titer.

Disclosure of Interests: None declared

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POS1248 URIC ACID AND COVID-19: PATTERN OF CHANGES AND ASSOCIATION WITH PROGNOSIS

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Background: Coronavirus disease causes a proximal tubule dysfunction of kidneys, inducing uric acid loss [1]. It has been established that several changes in laboratory markers (C-reactive protein (CRP), ferritin, interleukin-6 (IL-6)) can predict the severity of Covid-19 [2]. The purpose of this retrospective study was to analyze whether uric acid could act as another predictor of severe Covid-19.

Objectives: To evaluate the relationship between the severity of Covid-19 and uric acid levels on admission to the hospital.

Methods: This retrospective study included 150 hospitalized patients with confirmed Covid-19 (mean age 60.3±14.6 years; 52% were men), the severity of which was determined by the presence and type of oxygen support: (1) without O2, (2) O2 by mask or nasal cannula, (3) continuous positive airway pressure, (4) positive bi-pressure in the airways or high-flow oxygen, (5) invasive ventilation. Among them, 90 subjects required oxygen support, and 60 people didn't. The mortality rate in our study was 9.3%. The average uric acid level was compared with patients without Covid-19 (40 subjects). The study included patients who didn't receive urate-lowering therapy. Levels of CRP, ferritin, IL-6, D-dimer were also determined on admission. The Spearman's rank coefficient was used for measuring correlation.

Results: The mean uric acid level in patients with coronavirus disease was 251.5±104.1 μmol/L; without Covid-19 it was significantly higher — 328.6±96.9 μmol/L (p<0.001). Approximately one in four (24.6%) Covid-19 patients had uric

Table 1. Analysis of immunosuppressive agents and other clinical aspects for high antibody titer(>250U/mL) after two doses of ChAdOx1-S nCoV-19

	Univariate analysis			Multivariate analysis		
Parameter	OR	95% CI	p value	OR	95% CI	p value
Clinical features						
Age	0.917	0.860-0.978	0.008	0.917	0.857-0.981	0.012
Sex	3.674	1.206-11.191	0.022	4.330	1.348-13.912	0.014
DAS 28	1.144	0.670-1.950	0.622			
Duration	0.930	0.830-1.043	0.214			
Medications						
csDMARD	1.273	0.639-2.533	1.273			
TNF inhibitor	2.211	0.795-6.145	0.128			
JAK inhibitor	0.665	0.275-1.607	0.365			
Abatacept	0.368	0.038-3.602	0.391			
Tocilizumab	1.264	0.438-3.648	0.665			
Corticosteroid	0.472	0.235-0.949	0.035	0.349	0.163-0.748	0.007
Medication dose						
Methotrexate	0.993	0.919-1.072	0.855			
Corticosteroid	0.849	0.719-1.003	0.054			

acid levels below the lower limit of normal (208 µmol/L for men, 155 µmol/L for women). A decrease in serum uric acid levels was also observed in patients suffering from asymptomatic hyperuricemia or gout. However, there was no correlation between uric acid levels and disease severity (r=0.01, p=0.88). Also, uric acid levels did not correlate with other laboratory markers of severe Covid-19 (CRP: r=0.07, p=0.73; ferritin: r=0.15, p=0,07; IL-6: r=0.11, p=0,22; D-dimer: r=0.02, p=0,79).

Conclusion: Low uric acid levels are common in patients with Covid-19, but are not predictive of a more severe course of this disease. A correlation between uric acid and the level of other laboratory markers of severe Covid-19 was not found.

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POS1249 EFFICACY AND SAFETY OF CHADOX1 NCOV-19/AZD1222 AND MRNA-1273 VACCINES: A COMPARATIVE STUDY IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES

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Background: Several studies have demonstrated immunogenicity after COVID-19 vaccination in patients with autoimmune rheumatic diseases (AIRD) [1], but the differences between mRNA-based and vector vaccines and the cellular responses to COVID-19 vaccines according to distinct immunogenicity in AIRD patients are still unclear.

Objectives: To investigate the differences in efficacy and safety between the vector vaccine ChAdOx1 nCoV-19/AZD1222 (Oxford-AstraZeneca) and mRNA-based vaccine mRNA-1273 (Moderna) in patients with AIRD, and to explore the cell-cell interactions between high and low anti-SARS-CoV-2 IgG levels in patients with rheumatic arthritis (RA) by single-cell RNA sequencing (scRNA-seq).

Methods: From September 16 to November 15, 2021, we consecutively enrolled 243 participants aged ≥20 years with AIRD who received COVID-19 vaccination, of whom 113 were immunized with AZD1222 and 130 with mRNA-1273. The level of serum IgG antibodies to the SARS-CoV-2 receptor-binding domain on the spike protein S1 subunit was quantified by electrochemiluminescence immunoassay at 4-6 weeks after vaccination. Moreover, peripheral blood mononuclear cells were isolated from two RA patient with high anti-SARS-CoV-2 IgG level and four RA patients with low level for scRNA-seq and cell-cell communication signal was analyzed by CellChat.

Results: The anti-SARS-CoV-2 IgG seropositivity rate was 78.8% (89/113) for AZD1222 and 83.1% (108/130) for mRNA-1273. The level of anti-SARS-CoV-2 IgG was higher in patients who received mRNA-1273 than in those who received AZD1222 (β: 30.15, 95% CI: 11.67-48.63, p=0.002) (Table 1). Prednisolone-equivalent dose >5 mg/day and methotrexate (MTX) use in AIRD patients, and non-anti-tumor necrosis factor (TNF)-α biologics and Janus kinase (JAK) inhibitor use in RA patients were associated with inferior immunogenicity. ScRNA-seq revealed CD16⁻monocytes were predominant in RA patients with high anti-SARS-CoV2-IgG antibody level, and enriched pathways related to antigen presentation via major histocompatibility complex class II (MHC class II) were found (Figure 1). HLA-DRA and CD4 interaction was vigorous among all identified MHC-II pathway and was enhanced in high anti-SARS-CoV2-IgG antibody group.

Table 1. Multivariate analysis of anti-SARS-CoV-2 IgG level in patients with rheumatic diseases following COVID-19 vaccines

	Multivariate analysis			
	β	95% CI		*p* value
Medications				
Glucocorticoids				
Not used	Reference			
≤5 mg/day	−22.48	(−56.33,	11.37)	0.192
>5 mg/day	−23.45	(−43.54,	-3.36)	**0.022**
Methotrexate	−24.89	(−45.70,	-4.08)	**0.019**
Targeted therapies				
Targeted therapies group				
Not used	Reference			
TNF inhibitor	−15.78	(−41.33,	9.76)	0.224
Non-TNF bDMARD	−25.27	(−55.47,	4.93)	0.100
JAK inhibitor	−17.08	(−47.23,	13.07)	0.265
Vaccine				
ChAdOx1 nCoV-19/AZD1222	Reference			
mRNA-1273	30.15	(11.67,	48.63)	**0.002**

TNF: tumor necrosis factor, bDMARDs: biologic disease-modifying antirheumatic drugs, JAK: Janus kinase.

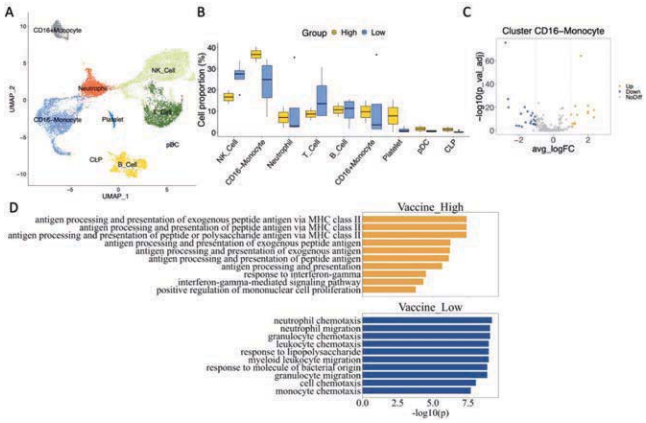

Figure 1. The comprehensive cell atlas of PBMC of RA patients with high and low anti-SARS-CoV2-IgG antibodies. A) UMAP visualization of PBMC cells from RA patients. B) The proportion of cell types between high and low antibody groups. C) Volcano plot of CD16-monocyte showed differential expressed genes. D) Pathway analysis between high and low antibody groups; PRBC: peripheral blood mononuclear cell, RA: rheumatoid arthritis, NK cell: natural killer cell, pDC: plasmacytoid dendritic cell, CLP: common lymphoid progenitor.

Conclusion: mRNA-1273 and AZD1222 vaccines exhibited differential immunogenicity in patients with AIRD. Enriched pathways related to antigen presentation via MHC class II in CD16⁻monocytes might be associated with higher anti-SARS-CoV2-IgG level in RA patients and further study is warranted.

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POS1250 EVALUATION AFTER COVID-19 VACCINATION IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: A RETROSPECTIVE COHORT STUDY.

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Background: Anti-phospholipid syndrome (APS) is an autoimmune disorder characterized by presence of anti-phospholipid antibodies (aPL) comprising lupus anticoagulant, anti-β2-glycoprotein I and/or anti-cardiolipin antibodies together with recurrent thrombosis and/or obstetric morbidity. In the course of COVID-19, thromboembolism may ocur due to endothelial dysfunction directly related to the viral factor and systemic inflammatory response. Concerns about COVID-19 vaccines began to arise after unexpected thromboembolic events were launched with the launch of vaccine campaigns around the world to prevent the disease.

Objectives: The purpose of the study is to contribute to the literature on this subject by evaluating the development of any side effects or activation of the disease after the COVID-19 vaccine in our APS patients.

Methods: This study was designed as a cross-sectional, retrospective cohort study. The patients who meet the Sapporo Criteria for APS which are followed up in Ankara City Hospital Rheumatology Clinic, 18 years and over and vaccinated with any of the COVID-19 vaccines, were included into the study. The files of the patients were examined in order to evaluate the side effects and APS disease activation (thrombosis, embolism or pregnancy complications) in the 3-month period after the last dose of the COVID-19 vaccines (CoronaVac and BNT162b2). Also, information of the patients was collected via telephone or reviewed at regular follow-up visits.

Results: A total of 35 patients were included into the study (Table 1). In our patients, we did not observe any new thrombotic events or pregnancy complications during the 3-months observation period after COVID-19 vaccinations. The most common side effects after vaccinations were as follows; myalgia (30%), weakness (16.7%) and fever (10%) (Table 2). No patient became pregnant or gave birth during the follow-up.

Table 1. Demographic and clinical characteristics of patients with Antiphospholipid antibody syndrome who received Covid-19 vaccine

	N=35
Age, years, meadian (min-max)	43 (28-63)
Gender, female, number (%)	33 (94.3)
Active smokers, number (%)	2 (5.7)
Comorbidities, number (%)	
Hypertension	6 (17.1)
Chronic kidney disease	2 (5.7)
Sjogren syndrome	2 (5.7)
Diabetes mellitus	0
Coronary artery disease	0
Other	4 (11.4)
Time from diagnosis, years, median (min – max)	7.0 (1.0 – 27.0)
APS characteristics, number (%)	
Thrombotic APS	22 (62.9)
Cerebrovascular event	11 (52.4)
Deep vein thrombosis	10 (47.7)
Pulmonary thromboembolism	2 (9.6)
Obstetric APS	21 (63.6)
Treatment agents, number (%)	
Hydroxychloroquine	28 (82.4)
Acetylsalicylic acid	16 (59.3)
Varfarin	16 (48.5)
Corticosteroids	15 (50)
Adherence to APS drugs during vaccination	32 (97)

Conclusion: According to our results, no thrombotic events or pregnancy complications were observed after CoronaVac and BNT162b2 vaccines in APS patients. Apart from this, minor side effects related to COVID-19 vaccines were clinically acceptable level.

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Table 2. Adverse events in vaccine recipients

	BNT162b2	CoronaVac
Patients ever vaccinated with BNT162b2 or CoronaVac, n	17	15
Dose per patient, median (min-max)	2 (1-2)	2 (1-3)
Patients vaccinated with BNT162b2 or CoronaVac alone, n(%)	17 (48.6)	15 (42.9)
Patients with an adverse effect after a dose of BNT162b2 or CoronaVac, n (%)	6 (40)	6 (50)
Fever	3 (18.7)	0 (0)
Malaise	2 (12.5)	4 (30.7)
Local pain/arm pain	2 (12.5)	2 (15.3)
Myalgia	4 (25)	4 (30.7)
Patients with an adverse effect after 1st dose of BNT162b2 or CoronaVac, n (%)		
Fever	0	0
Malaise	0	0
Local pain/arm pain	1 (16.6)	0
Myalgia	0	0
Patients with an adverse effect after 2nd dose of BNT162b2 or CoronaVac, n (%)		
Fever	3 (20)	0
Malaise	2 (13.3)	1 (14.2)
Local pain/arm pain	0	0
Myalgia	4 (26.6)	1 (14.2)
Patients with an adverse effect after 3rd dose of BNT162b2 or CoronaVac, n (%)		
Fever	0	0
Malaise	0	3 (50)
Local pain/arm pain	0	0
Myalgia	0	3 (50)

POS1251 INCIDENCE AND OUTCOMES OF SARS-COV-2 INFECTION IN PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES: A POPULATION-BASED STUDY OF MORE THAN FOUR MILLION INHABITANTS IN THE LAZIO ITALIAN REGION

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Background: The impact of the severe acute respiratory syndrome Coronavirus 2 disease (COVID-19) pandemic on people with systemic autoimmune rheumatic diseases (SARDs) remains to be fully established. It is unclear whether SARDs are an independent risk factor for COVID-19 infection and poor outcome.

Objectives: The aim of our study is to assess the incidence and prognosis of test-proven SARS-CoV-2 infection during the first COVID-19 wave in a large population of SARD patients of the Lazio Italian region.

Methods: We retrospectively evaluated in a cohort of 4.716.119 subjects aged over 18 years and affiliated to the health system of the Lazio Italian Region, the incidence and 30-day outcomes of COVID-19 infection in 40.490 SARD pts and compared to the affiliated population as incidence rate ratio adjusted for demographics and comorbidities (adjIRR). SARD diagnosis and comorbidities were derived from medical administrative records using the Chronic Related Group classification system. Data on COVID-19 infection were derived from a dedicated regional digital network.

Results: The risk of COVID-19 infection was increased in patients with Psoriatic Arthritis (adjIRR=1.21, 95% CI 1.10-1.33) and Undifferentiated Connective Tissue Disease (adjIRR=1.26, 95% CI 1.03-1.54). The risk of hospitalisation was higher in patients with Axial Spondylarthritis (adjIRR=2.16, 95% CI 1.45-3.22), and Systemic Vasculitis (adjIRR=1.81, 95% CI 1.07-3.06) while the risk of Intensive care unit admission was higher in Systemic Erythematous Lupus (adjIRR=3.67, 95% CI 1.52-8.83) and primary Sjögren Syndrome (adjIRR=4.13, 95% CI 1.71-9.96) patients. An increased COVID-19 mortality was reported in patients with Rheumatoid Arthritis (adjIRR=1.50, 95% CI 1.04-2.17), Systemic Erythematous Lupus (adjIRR=2.67, 95% CI 1.10-6.44), primary Sjögren Syndrome (adjIRR=2.51, 95% CI 1.12-5.62), and Scleroderma (adjIRR=4.60, 95% CI 2.06-10.29).

Conclusion: The incidence of severe COVID-19 is not increased in the same percentage in SARDs. Each SARD presents a peculiar pattern in terms of increased risk of COVID-19 incidence, hospitalisation, intensive care unit admission and death, that is not linked to the immunosuppressive behaviour of the disease.
Disclosure of Interests: None declared
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POS1252 DURABILITY OF THE HUMORAL RESPONSE TO M-RNA BASED ANTI-SARS-COV-2 VACCINES IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASE, A COMPARATIVE STUDY

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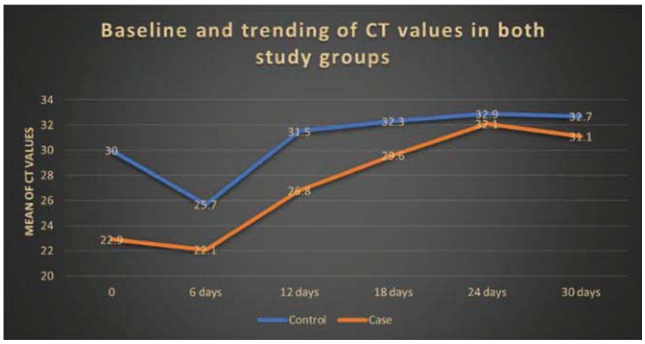
Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral load and its impact on disease outcome in patients with autoimmune rheumatic disease (ARD) are lacking. Also, whether patients with ARD receiving immunomodulators have different viral loads compared to the general population is unknown.
Objectives: To compare the viral load of SARS-CoV-2 and its trending between patients without and with ARD.
Methods: Retrospectively, patients with ARD infected with SARS-CoV-2 were matched by age and sex at a ratio of 1:2 to patients without ARD and not receiving immunosuppression or immunomodulator drugs. Viral load was determined by the cycle threshold (CT) value measured by a number of platforms: (a) Automated Platforms - the Roche Cobas 6800 system using the Cobas SARS-CoV-2 Test targeting the E and orf1a/b genes (Roche, Switzerland) and the Xpert Xpress SARS-CoV-2 targeting the E and N genes (Cepheid, USA); (b) Manual platforms - EZ1 (QIAGEN, USA), QIAsymphony (QIAGEN, USA), and Bioneer ExiPrepTM 96 Virus DNA/RNA kits Catalogue No K4614 (Bioneer, South Korea) extraction with thermal cycling using TaqPath™ PCR COVID-19 Combo Kit targeting the N, S and orf1a/b genes (Thermo Fisher Scientific, USA) on ABI 7500 thermal cyclers. Independent samples t-test was used to compare the mean CT values of the study groups at baseline and at 5 subsequent intervals (1 – 5.9, 6 – 11.9, 12 – 17.9, 18 – 23.9 and 24 – 30 days).
Results: Mean age (SD) of 197 cases and 420 controls were 45.2 (11.8) and 44.1 (12.3) years, respectively. Females were predominant in both groups 60% vs. 52%, P=0.053. The most common ARD was rheumatoid arthritis in 82 cases (41.6%), followed by spondyloarthropathy in 33 (16.8%) and systemic lupus erythematosus in 31 (15.7%). Of the cases, 67% were on conventional synthetic disease modifying anti-rheumatic drugs (DMARDs), 15.2% on biological DMARDs and 4.6% patients were on rituximab. The mean CT values was significantly lower in the ARD group at baseline and persisted till day 24.

Table 1. Demographic characteristics and comparison of the mean CT values in the study groups at baseline and at different intervals with the corresponding OR (95% CI)

	Case (N=197)	Control (N=420)	OR (95% CI)
Mean (SD) age, years	45.2 (11.8)	44.1 (12.3)	1.008 (0.994–1.022)
Sex, female N (%)	120 (60.9%)	221 (52.6)	0.713 (0.505–1.006)
Mean (SD) CT values at			
Baseline	22.9 (5.5)	30 (5.2)	**0.799 (0.745–0.858)**
1 – 5.9 days	22.1 (4.6)	25.7 (6.3)	**0.901 (0.842–0.963)**
6 – 11.9 days	26.9 (4.9)	31.5 (3.9)	**0.802 (0.724–0.888)**
12 – 17.9 days	29.6 (4.1)	32.3 (3.2)	**0.827 (0.743–0.921)**
18 – 23.9 days	32.1 (4)	32.9 (2.5)	0.903 (0.728–1.119)
24 – 30 days	31.2 (1.2)	32.7 (2.6)	0.824 (0.589–1.151)



Conclusion: Compared to patients without ARD, the viral load of SARS-CoV-2 in patients with ARD is significantly higher at baseline testing and persists till day 24. This finding may indicate that patients with ARD are at higher risk of severe SARS-CoV-2 infection and prolonged potential transmission. Clinical outcome correlation is needed.
REFERENCES: None
Disclosure of Interests: None declared
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POS1253 THE COURSE OF COVID-19 IN A COHORT OF SPONDYLOARTHRITIS PATIENTS: A CASE-CONTROL PROSPECTIVE STUDY

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Background: With the outbreak of the SARS-CoV-2 pandemic, the rheumatologists' attention was directed at understanding whether infected patients could have a less favorable outcome. Available data seem to indicate that the course in rheumatic patients is not dissimilar from that in the general population. However, data on the outcome of COVID-19 in patients with spondyloarthritis (SpA) are scant.
Objectives: To describe the outcome of COVID-19 in patients with SpA in terms of hospitalization, need of oxygen therapy, and symptoms compared to a control group. The variation in disease activity before and after COVID-19 was also assessed.
Methods: We enrolled adult patients with psoriatic arthritis (PsA) and ankylosing spondylitis (AS) classified according to standard criteria, that received a diagnosis of COVID-19 through molecular or rapid antigen swab tests between September 2020 and January 2022. Demographic and clinical data, including age, body mass index (BMI), smoking habit, comorbidities, rheumatic treatment at diagnosis of COVID-19, date of COVID-19 diagnosis, symptoms and additional therapy during the infection and vaccination status were collected through a questionnaire and recorded on an electronic database. Disease activity, assessed by DAPSA in PsA patients and by BASDAI and ASDAS in AS patients, was evaluated before and at the first visit after the infection. As controls, individuals with COVID-19 but with no known diagnosis of rheumatic/autoimmune disease were recruited using the "best friend" system.
Results: Sixty-two patients were enrolled [43 with PsA and 19 with AS; F:M=40:22; median age 51 years, 25th-75th percentile 39.5-61; median BMI 25.5, 25th-75th percentile 21.75-28; median disease duration 90 months, 25th-75th percentile 36-192; 6 (9.7%) smokers, 37 (59.7%) non-smokers, 19 (30.6%) past smokers; 15 (24.2%) only treated with one conventional DMARD, 27 (43.5%) with bDMARDs and 20 (32.3%) with both; 44 (71%) had received no vaccine, 18 (29%) one or more doses of vaccine]. Forty-eight controls were also recruited [F:M=29:19; median age 48 years, 25th-75th percentile 41.5-57; median BMI 23.86, 25th-75th percentile 20.69-28.03; 10 (20.83%) smokers, 28 (58.33%) non-smokers, 10 (20.83%) past smokers; 43 (89.6%) had received no vaccine, 5 (10.4%) one or more doses of vaccine]. Among patients, 10 (16.1%) were hospitalized, of whom 8 (80%) required noninvasive oxygen therapy. Among controls, 7 (14.5%) were hospitalized, of whom 5 (71.4%) required noninvasive oxygen therapy. No differences were observed compared to the control group in terms of hospitalization and need for oxygen support. Likewise, the two groups did not bear any statistically significant difference in terms of symptoms (fever, dysgeusia, dyspnoea) and cardiovascular and respiratory comorbidities. BMI and smoking habit did not influence the outcome of COVID-19 in SpA patients, while a BMI of 25 or above was associated with hospitalization in the control group (p=0.0004, RR 3.417). Baseline treatment with immunosuppressants did not influence the disease outcome. DAPSA, ASDAS, and BASDAI did not significantly change after the infection (Table 1). We did not record any COVID-19-related death in either group.

Table 1. Disease activity before and after COVID-19

	Last visit before COVID-19		**First visit after COVID-19***	
	PsA (n=43)	**AS (n=19)**	**PsA (n=43)**	**AS (n=19)**
Remission/low disease activity, n (%)	19 (44.2%)	17 (89.5%)	23 (53.5%)	14 (73.7%)
Moderate/high disease activity, n (%)	11 (25.6%)	0 (0%)	7 (16.3%)	1 (5.3%)
	NA 13 (30.2%)	NA 2 (10.5%)	NA 13 (30.2%)	NA 4 (21%)

* Reassessment of patients was performed 2 months (median) after COVID-19, 25th-75th percentile 1-4 monthsPsA, psoriatic arthritis; AS, ankylosing spondylitis; NA, not available

Conclusion: Our data show that patients with SpA do not face a worse prognosis of COVID-19 than subjects without rheumatic/autoimmune diseases and that demographic and clinical features did not influence the course of the disease.
Disclosure of Interests: None declared
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POS1254 RISK FACTORS FOR SEVERE COVID-19 INFECTION AMONG PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIRD) AND THE IMPACT OF VACCINATIONS - AN ISRAELI, MULTI-CENTER EXPERIENCE

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Background: AIRD patients (pts) may be more susceptible to severe COVID19.
Objectives: To determine the risk factors for severe COVID19 and the effect of vaccinations among AIRD pts followed at dedicated rheumatology clinics.
Methods: At the onset of the pandemic, we established a national registry of AIRD pts, diagnosed with COVID19, based on voluntary reporting by the treating rheumatologist. 12 centers from Israel participated in the study. COVID19 was confirmed by a positive SARS CoV2 PCR. The indications for PCR testing were clinical symptoms or close contact with an infected person. Severe illness was defined by SpO_2 <94% in room air, respiratory rate of >30 breaths/min, PaO_2/FiO_2 <300 mm Hg, or lung infiltrates >50% on imaging. The registry included demographic data, AIRD diagnosis and duration, visceral involvement, co-morbidities, immunomodulatory treatment, date of diagnosis and severity of COVID19 disease, management, complications, duration of hospitalization, the dates of the mRNA vaccinations, lab results and outcome. We analyzed data from 1.3.2020 to 30.11.2021
Results: During the study period we experienced 4 outbreaks of COVID19 infection. Initially social distancing, followed by a lockdown were imposed. The low number of cases led to relaxation of the measures. Two more severe outbreaks followed, which triggered 2 new lockdowns. The 3rd outbreak ended almost 2 months after vaccination started (BNT162b2 mRNA COVID19 vaccine). From March 1st 2020 to April 30, 2021, 298 AIRD pts (70.8% females, mean (SD) age 53.3(15.3)) with confirmed COVID19 infection were included. 43.3%(129) had visceral involvement due to the AIRD. 58.7%(175 pts) were on conventional synthetic disease modifying drugs (csDMARDs), 44.6% (133) on biologic/targeted DMARDs and 40% (120) on prednisone. Almost 2/3 of pts had at least one comorbidity.
In a multivariate logistic regression analysis age, AIRD with pulmonary involvement, diabetes and treatment with prednisone, mycophenolate mofetil or JAK inhibitors were associated with hospitalization. Older age, renal and vascular involvement due to the AIRD, and congestive heart failure were associated with higher mortality.
The 4th outbreak occurred 6 months after the introduction of vaccines, with spreading of the delta variant: 110 AIRD pts with COVID19 were recorded. Demographic data, clinical AIRD's characteristics, immunomodulatory treatment and comorbidities were similar to the previous outbreaks. However, during the 4th outbreak, the proportion of pts with severe COVID19, the hospitalization and mortality rate were significantly lower as compared to the first 3 outbreaks (15% vs 24%, 27% vs 53%, 6.7% vs 9.1%, respectively). Among COVID19 pts, 25% received a 3rd vaccine dose (booster), 56% contracted infection more than 5 months after the 2nd vaccine dose and 24% were unvaccinated. Most of the pts who received the booster contracted the disease within a week of vaccination. The odds ratio for hospitalization in vaccinated pts compared to unvaccinated was 0.11 (0.01 – 0.63 95% CI, p=0.041) in those vaccinated within the previous 1-5 months, and 0.38 (0.21-0.67 95% CI, p=0.001) in those vaccinated more than 6 months ago. 9 pts died, 5 were more than 6 months after the 2nd mRNA vaccine, 2 were unvaccinated and 1 patient received the booster on the same day of COVID19 diagnosis.
Conclusion: Before the vaccination campaign, the hospitalization and mortality rate in our cohort were similar to the data reported by other registries. COVID19 tends to be more severe, with increased mortality in patients with active AIIRD and visceral involvement (pulmonary, cardiac, renal), advanced age and co-morbidities. The delta outbreak occured 6 months after the implementation of vaccinations and was associated with significantly lower hospitalization and mortality rates, despite the increased aggressiveness of the variant. Vaccination of AIIRD pts with 3 doses of mRNA vaccines protects from severe COVID19 disease, hospitalization, and death.
Acknowledgements: Fadi Kharouf and Tali Eviatar had equal contribution
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POS1255 SAFETY OF THE PFIZER/BIONTECH AND SINOVAC/CORONAVAC VACCINES AMONG PATIENTS WITH BEHCET'S SYNDROME AND FAMILIAL MEDITERRANEAN FEVER

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Background: Since first emerged in December 2019, the COVID-19 pandemic has resulted in a death toll surpassing 5.5 million worldwide and had severe consequences on the global economy, environment, public health and social life [1, 2]. Multiple potential vaccines against COVID-19 have been developed swiftly and as shown in several phase 3 clinical trials, they demonstrated considerable efficacy without an unusual safety signal in healthy individuals.
Objectives: In this study, we aimed to evaluate vaccine reactivity and disease flare following vaccination with either Sinovac/CoronaVac or Pfizer/BioNTech among BS and FMF patients compared with patients with various diagnosis of RD and healthy controls.
Methods: Only those patients and healthy controls who rece,ved at least one single shot of either CoronoVac or BioNTech against COVID-19 were included in the study. We tried to contact all of these patients and controls consecutively by telephone and attempted to make interviews with the eligible ones.
Results: We studied the efficacy, side effects and disease flares after COVID-19 vaccination in 256 patients with Behcet's syndrome (BS), 247 with familial Mediterranean fever (FMF), 601 with rheumatic diseases (RD) and 612 healthy controls (HC). Study participants were vaccinated either with CoronaVac (BS:109, FMF: 90, RD: 343, and HC: 334) or BioNTech (BS: 147, FMF:157, RD: 258 and HC: 278). BioNTech ensured a significantly better efficacy than CoronaVac against COVID-19 in all patient groups (BS: 1.4% vs 10.1%; FMF: 3.2% vs 12.2%, RD:2.7% vs 6.4%). Those with at least one adverse event (AE) were significantly more frequent among those vaccinated with BioNTech than those with CoronaVac (BS: 86.4% vs 45%; FMF: 83.4% vs 53.3%; RD: 83.3% vs 45.5% and HC: 86.3% vs 52.1%). The majority of AEs were mild to moderate and transient and this was true for either vaccine. There were also AEs that required medical attention in all study groups following CoronaVac (BS:5.5%, FMF:3.3%, RD:2.9% and HC:3.3%) or BioNTech (BS:5.4%, FMF:1.9%, RD:4.7% and HC:4.7%). The main causes for medical assistance were disease flare, and cardiovascular events. Disease flares after vaccination were significantly more frequent among BS (41/256; 16.0%) and FMF (43/247; 17.4%) patients compared to patients with RD (36/601; 6.0%). This was true for both CoronaVac (BS: 11.0%, FMF: 24.4% and RD: 5.2%, p<0.001) and BioNTech (BS: 19.7%, FMF: 13.4% and RD: 7.0%, p=0.001)(Table 1).

Table 1. Flares among patients with Behçet's syndrome, familial Mediterranean fever, rheumatic diseases after vaccination with CoronaVac and BioNTech

CoronaVac		
Behçet's syndrome, n=109	Familial Mediterranean Fever, n=90	Rheumatic diseases, n=343
Flares, n (%)	Flares, n (%)	Flares, n (%)
12 (11.0)	22 (24.4)	18 (5.2)
BioNTech		
Behçet's syndrome, n=147	Familial Mediterranean Fever, n=157	Rheumatic diseases, n=258
Flares, n (%)	Flares, n (%)	Flares, n (%)
29 (19.7)	21 (13.4)	18 (7.0)

RA, Rheumatoid Arthritis; BS, Behçet's syndrome; FMF, Familial Mediterranean Fever

Conclusion: Our study demonstrates that BS and FMF patients vaccinated with either CoronaVac or BioNTech demonstrated almost similar AE profile and frequency compared to RD patients and HC. AEs that required physician consultation or hospitalization occurred in all study groups after either CoronaVac or BioNTech. Caution should be required when monitoring these patients after vaccination. Increased frequency of flares in BS and FMF compared to that seen in RD might reflect defects in innate immunity and deserves further investigation.

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POS1256

RISK FACTORS FOR SHORT-TERM ADVERSE EVENT IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Background: Many countries are promoting booster SARS-CoV-2 vaccination campaigns as the COVID-19 pandemic continues. Incremental short-term adverse events after two SARS-CoV-2 vaccinations have been reported in healthy individuals.[1,2] However, data on incremental short-term adverse events in patients with various immune-mediated inflammatory diseases (IMIDs) after repeated SARS-CoV-2 vaccination is scarce.

Objectives: We report risk factors for short-term adverse events in IMID patients after SARS-CoV-2 vaccination.

Methods: Self-reported daily questionnaires on adverse events in the first seven days after SARS-CoV-2 vaccination were obtained from individuals participating in an ongoing prospective multi-arm multicenter cohort study on SARS-CoV-2 vaccination in patients with various IMIDs in the Netherlands (T2B! immunity after SARS-CoV-2). Clinically relevant adverse events were defined as systemic adverse advents lasting longer than two days or hindering daily activities. Adjusted relative risks for developing clinically relevant adverse events were calculated using a logistic mixed-effects model.

Results: Data of 2081 patients and 178 healthy controls were obtained. Inflammatory bowel disease (N:480), Multiple sclerosis (N:343) and Rheumatoid arthritis (N:266) were the largest disease groups. Adjusted relative risks for relevant adverse events are presented in Figure 1. Third vaccination was not associated with increased risk on adverse events when compared to a second vaccination (aRR: 0.93 95% CI: 0.84-1.02). Patients with IMIDs were at increased risk for developing adverse events after vaccination when compared to controls (aRR: 1.16 95% CI: 1.01-1.34). Female sex (aRR 1.43 95% CI: 1.32-1.56), age below 50 (aRR 1.14 95% CI: 1.06-1.23) and a preceding SARS-CoV-2 infection (aRR: 1.14 95% CI: 1.01-1.29) were also associated with increased risk of adverse events following vaccination. Allergic reactions and hospital admission were uncommon (0.67% and 0.19% respectively); 7.4% and 6.8% of patients reported adverse events impacting daily life on day seven after second and third vaccination, respectively. Data on increase in disease activity of the IMID following vaccination are currently being investigated.

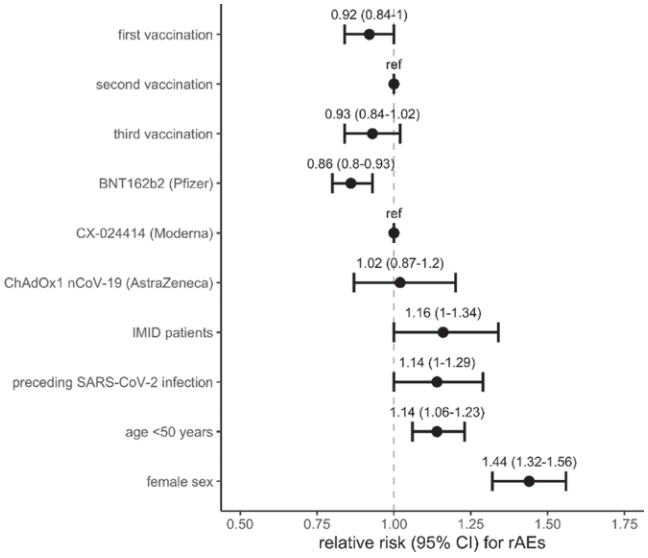

Figure 1. Risk factors for adverse events after SARS-CoV-2 vaccination in patients with immune-mediated inflammatory disease

Conclusion: A third SARS-CoV-2 vaccination was not associated with an increased risk on short-term clinically relevant adverse events when compared to a second vaccination. Although patients with IMIDs may be slightly more at risk to develop adverse events after SARS-CoV-2 vaccination, most adverse events were transient and disappeared within seven days. This message should reassure IMID patients who are hesitant on booster vaccination. Data on potential IMID flare-ups after vaccination will follow.

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POS1257

READING THE WAVES: IDENTIFYING DISTINCT PHENOTYPES OF MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN IN A SINGLE CANADIAN CENTER DURING THE 2020-2021 COVID-19 PANDEMIC

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Background: The COVID-19-associated multisystem inflammatory syndrome in children (MIS-C) is characterized by Kawasaki disease (KD)-like features and circulatory shock [1]. The genesis of SARS-CoV-2 variants triggered successive waves of mass infections followed by MIS-C outbreaks.
Objectives: To compare MIS-C phenotypes across the waves of the COVID-19 pandemic. To identify predictors of pediatric intensive care unit (PICU) admission and treatment with biologic agents.
Methods: Youth aged 0-18 years, fulfilling the WHO case definition of MIS-C, and admitted to the Alberta Children's Hospital during the COVID-19 pandemic (May 2020-December 2021) were included. Clinical, laboratory, imaging, and treatment data were captured (KD-like manifestations, signs of shock and/or hypotension, peak C-reactive protein (CRP) and ferritin, platelet count nadir, peak NT-proBNP and troponin, liver enzyme abnormalities, sodium and albumin nadir, echocardiogram findings, biologic agents).
Results: 57 consecutive MIS-C patients (median age 6 years, IQR 4-6; 72% males) were included. 31 patients (54%) required PICU admission. All received immunoglobulins, 44 (77%) received corticosteroids, 8 patients (14%) were treated with biologic agents. Patients presenting during the third (mainly driven by Alpha variant) or fourth wave (mainly driven by Delta variant) presented with higher ferritin and NT-proBNP levels, and more liver enzyme abnormalities, hypoalbuminemia and thrombocytopenia compared to those presenting during the first or second wave (Table 1, Figure 1). PICU admission was associated with the presence of shock/hypotension, higher CRP, ferritin, and NT-proBNP levels, lower albumin levels, and the presence of ventricular dysfunction on echocardiogram (Table 1). A logistic regression model combining peak NT-proBNP, troponin and ferritin levels explained 70% (Nagelkerke R^2) of the variance in PICU admission and correctly classified 91% of the cases. NT-proBNP was the sole significant contributor (p=0.017). Treatment with biologic agents was associated with higher CRP (mean 148.8 mg/l versus 251.7 mg/l; p=0.024) and ferritin (797 µg/l versus 1280 µg/l; p=0.049) levels.

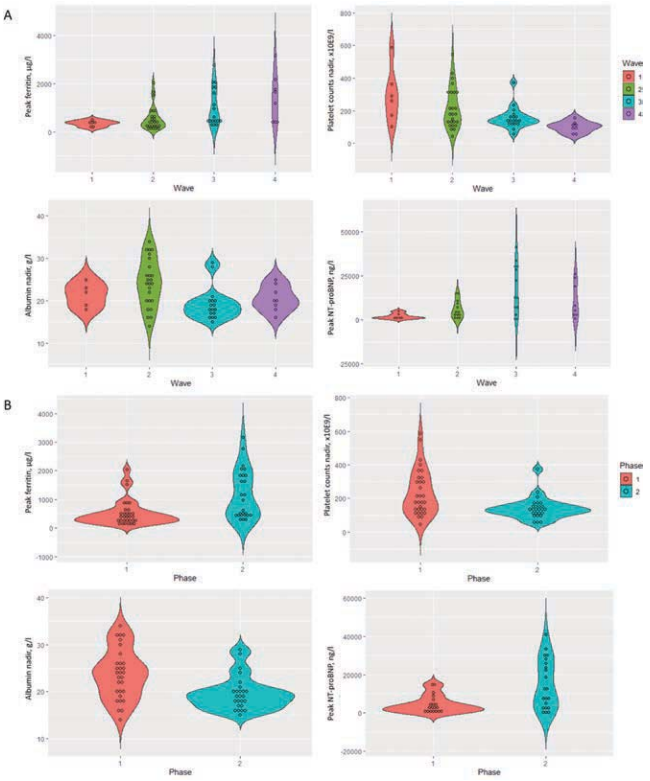

Figure 1. Violin plots depicting differences in key laboratory MIS-C features between the waves (A) and both phases (phase 1 = wave 1+2, phase 2 = wave 3+4; B) of the COVID-19 pandemic.

Table 1. Upper panel: Differences in MIS-C features of patients presenting during the first phase of the COVID-19 pandemic (first + second wave) compared to those presenting during the second phase (third + fourth wave) (*one missing value). Lower panel: Differences regarding MIS-C features between patients admitted to PICU compared to those managed on the general ward.

	Phase 1 (n = 31)	Phase 2 (n = 26)	P-value
Peak ferritin, µg/l (mean, SD)	548 (529)	1129 (724)	<0.001
Liver enzyme abnormalities (n, %)	10 (32)	18 (69)	0.008
Peak NT-proBNP, ng/l (mean, SD)	5250 (4721)	13366 (11211)	0.012
Hypoalbuminemia (n, %)	24 (80)*	25 (100)*	0.027
Thrombocytopenia (n, %)	11 (35)	18 (69)	0.017
		PICU	
	No (n = 26)	**Yes** (n = 31)	**P-value**
Shock/hypotension (n, %)	19 (73)	31 (100)	0.002
Peak CRP, mg/l (mean, SD)	140.7 (92)	203.8 (84)	0.008
Peak ferritin, µg/l (mean, SD)	612 (676)	1183 (627)	0.002
Peak NT-proBNP, ng/l (mean, SD)	3772 (5074)	15584 (9662)	<0.001
Albumin nadir, g/l (mean, SD)	24 (4)	19 (3)	0.014
Ventricular dysfunction (n, %)	2 (8)	18 (58)	<0.001

Conclusion: A shift in MIS-C phenotype was identified across the successive COVID-19 waves, including the predominance of features associated with macrophage activation syndrome in later stages. These findings may reflect the impact of distinct SARS-CoV-2 variants. NT-proBNP emerged as the most important MIS-C feature predicting PICU admission, underscoring the importance of monitoring.

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POS1258

LESS THAN EXPECTED IMPACT OF RHEUMATOID ARTHRITIS AND AXIAL SPONDYLOARTHRITIS DISEASE ON COVID SEVERITY

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Background: Throughout the pandemic, there has been ongoing concern that people with autoimmune diseases such as rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) will have more severe COVID-19 disease due to immune dysfunction associated with autoimmune diseases and their treatment.
Objectives: We aimed to compare the severity of COVID-19 in patients with RA versus axSpA and characterize the predictors of COVID-19 severity during the pre-Omicron pandemic phases.
Methods: The IMPACT (**IMP**act of inflammatory **A**rthritis on **C**OVID Outcomes S**T**udy) study is a monthly survey of two established northern Alberta, Canada prospective cohorts of RA and axSpA patients from November 2020-2021 who answered Redcap surveys through de-identified email link surveying patient demographics, disease characteristics, COVID-19 symptoms, treatment of RA and axSpA, health care utilization, vaccination status and vaccine adverse events. Descriptive and univariate analyses (dependent variable = severe COVID-19) were performed followed by multivariate analyses of all significant and clinically relevant independent variables from the univariate analysis. Infection severity was defined as any patient with COVID-19 symptoms who visited a doctor, ER or required hospital admission.
Results: 773 of 2167 (36%) patients (RA n=574, axSpA n=197) registered in both cohorts answered at least one baseline survey, 28 (4%) reporting positive COVID-19 tests (24 positive once). Of 442 reporting COVID-19 symptoms during the survey, 11 (3%) were admitted for a mean of 4 days, 2 requiring ICU or blood clot treatment and 1 requiring advanced therapy. 116 (26%) visited a physician for Covid symptoms. Univariate analysis showed that the use of steroids, NSAIDs and increased disease activity were associated with having less severe infection but these associations were not significant in the multivariate analysis (Table 1). There were no significant impacts of RA vs axSpA, age, gender, treatment, disease activity, or smoking.

Table 1. Multivariate Level Mixed-Effect Logistic Regression Model: IMPACT of RA and axSpA Disease Characteristics on COVID Infection Severity Defined as Patients with COVID Symptoms Requiring Visit to Doctor, Emergency Room and/or Hospital Admission.

Variable		Coefficient (S.E)	Odds Ratio (95 % Confidence Interval)	P-value
Gender	Male	0.17 (0.34)	1.18 (0.61 – 2.31)	0.6193
	Female	Reference		
Age		-0.01 (0.01)	0.99 (0.97 – 1.01)	0.2543
Rheumatic Disease Type	RA	0.18 (0.40)	1.20 (0.58 – 2.48)	0.6213
	SpA	Reference		
Steroids	Yes	-0.40 (0.56)	0.67 (0.23 – 2.01)	0.4757
	No	Reference		
NSAIDS	Yes	-0.20 (0.26)	0.82 (0.49 – 1.37)	0.4508
	No	Reference		
Current Disease Activity		-0.04 (0.06)	0.96 (0.85 – 1.09)	0.5275
HAQ		-0.03 (0.29)	0.97 (0.55 – 1.70)	0.9041
Nicotine products	Yes	-0.67 (0.37)	0.51 (0.25 – 1.06)	0.0714
	No	Reference		
Cannabis products	Yes	-0.45 (0.31)	0.64 (0.35 – 1.18)	0.1510
	No	Reference		
DMARDs	Yes	0.26 (0.30)	1.30 (0.72 – 2.35)	0.3860
	No	Reference		
Biologic DMARD	Yes	-0.46 (0.43)	0.63 (0.27 – 1.46)	0.2813
	No	Reference		

Conclusion: Possible disease related risk factors for increased COVID-19 severity in RA and axSpA patients preceding the onset of the Omicron variant including use of steroids or DMARDs were not associated with severe infection. These findings are consistent with other international studies whereby other non-rheumatic disease comorbidities played a greater role in infection severity.

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POS1259

AXIAL SPONDYLOARTHRITIS, AGE AND MALE GENDER IMPACT COVID VACCINATION AES MORE THAN RHEUMATOID ARTHRITIS

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Background: Rheumatologists recommend vaccination in rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) patients, but there are few studies on the occurrence of adverse events (AEs), particularly worsening disease related activity and unrelated immune reactions in these groups.

Objectives: To evaluate the uptake of COVID vaccination in RA and axSpA patients, compare the frequency of AEs, and identify risk factors associated with vaccine AEs in two prospective cohorts comprised of these patients.

Methods: The IMPACT study is a monthly survey of two prospective cohorts of established RA and axSpA patients in northern Alberta, Canada from November 2020-2021 who answered at least one or more Redcap surveys through de-identified email link surveying demographics, disease characteristics, COVID symptoms, treatment of RA and axSpA, health care utilization, vaccination status, vaccine AEs and use of cannabis. Univariate analyses evaluated independent variables associated with the dependent variables of (1) any AE, (2) any severe

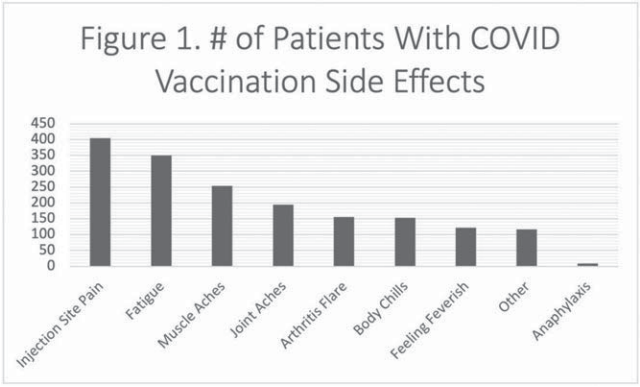

Table 1. Summary of Multivariate Level Mixed-Effect Logistic Regression Models Evaluating the IMPACT of RA and axSpA Disease Characteristics on Vaccine AEs

Variable		Any Adverse Event OR (95 % CI) p value	Severe Adverse Event* OR 95 % CI) p value	Any Arthritis Flare or Joint Ache Adverse Event OR (95 % CI) p value	Any Severe Arthritis Flare or Joint Ache* OR (95 % CI) p value
Gender	Male	1.47 (0.89 – 2.43)	**2.10 (1.30-3.41)**	**2.05 (1.20 – 3.50) p=0.01**	**3.97 (1.84 – 8.57)**
	Female	p=0.13	**p=0.003**		**p=0.0004**
Age		**1.06 (1.04 – 1.08)**	**1.05 (1.03 – 1.06)**	**1.03 (1.01 – 1.04)**	**1.03 (1.01 – 1.06)**
		p<0.01	**p<0.01**	**p=0.003**	**p=0.004**
Rheumatic Disease Type	RA	**0.42 (0.23 – 0.76)**	**0.55 (0.31 – 0.98)**	**0.52 (0.28 – 0.98)**	0.78 (0.34 – 1.78)
	axSpA	**p=0.05**	**p=0.04**	**p=0.04**	p=0.55
Steroids	Yes	0.85 (0.40 – 1.83)	0.66 (0.32 – 1.35)	0.84 (0.36 – 1.95)	**0.38 (0.15 – 0.97)**
	No	P=0.68	p=0.25	p=0.69	**p=0.04**
NSAIDS	Yes	1.11 (0.81 – 1.52)	1.03 (0.75 – 1.41)	1.05 (0.74 – 1.48)	1.17 (0.73 – 1.89)
	No	p=0.51	p=0.86	p=0.80	p=0.52
Current Disease Activity		0.95 (0.88 – 1.03)	0.90 (0.83 – 0.97)	0.92 (0.85 – 1.00)	**0.82 (0.74 – 0.92)**
		p=0.23	p=0.19	p=0.06	**p=0.001**
HAQ		1.08 (0.73 – 1.61)	**0.77 (0.52 – 1.14)**	0.74 (0.48 – 1.13)	0.65 (0.38 – 1.11)
		p=0.70	**p=0.01**	p=0.17	p=0.12
Nicotine products	Yes	1.33 (0.75 – 2.37)	1.42 (0.80 – 2.52)	1.15 (0.60 – 2.01)	0.97 (0.43 – 2.17)
	No	p=0.34	p=0.24	p=0.76	p=0.94
Cannabis products	Yes	0.78 (0.49 – 1.25)	0.87 (0.55 – 1.38)	**0.51 (0.31 – 0.83)**	0.66 (0.35 – 1.26)
	No	p=0.30	p=0.55	**p=0.07**	p=0.21
DMARDs	Yes	**1.98 (1.28 – 3.06)**	**1.52 (1.01 – 2.28)**	1.43 (0.91 – 2.23)	**1.86 (1.03 – 3.36)**
	No	**p=0.002**	**p=0.05**	p=0.12	**p=0.04**
Biologic DMARD	Yes	0.72 (0.42 – 1.25)	0.79 (0.45 – 1.41)	1.20 (0.66 – 2.18	1.39 (0.63 – 3.08)
	No	p=0.24	p=0.43	p=0.54	p=0.42

*Severe = Any of the following: ranked moderate to severe and/or lasting more than 7 days and/or saw physician

AE, (3) any arthritis flare, and (4) any severe arthritis flare, followed by multivariate analyses of these four dependant variables using all clinically relevant variables from the univariate analysis.

Results: 773/2167 patients (RA 574, axSpA 197) responded to at least one survey. 32/663 (5%) were single vaccinated, 631 (95%) double vaccinated and 230 (54%) triple vaccinated with 80% receiving Pfizer, 24% Moderna, 28% AstraZeneca and 30% "other". 456 (69%) reported at least one AE (Figure 1) with 21 (3%) patients seeing a physician for their AE. Increased age was associated with all AEs. RA patients had lower reported AEs versus axSpA patients for all AE definitions except for severe arthritis flares. Generally, males reported worse AEs (Table 1). "Any arthritis flare" was lower in patients reporting cannabis use.

Conclusion: RA and axSpA patients showed high uptake of COVID vaccination with largely minor AEs. Older age and male gender were associated with more general and arthritis specific AEs. The association of any AE and/or arthritis-specific AEs in SpA versus RA patients is a novel finding which may correlate with the male predominance of SpA. The association of cannabis with fewer arthritis AEs may reflect the nociceptive properties of cannabis.

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POS1260

COVID-19 VACCINATION-RELATED ADVERSE EVENTS AMONG AUTOIMMUNE DISEASE PATIENTS: RESULTS FROM THE COVID-19 VACCINATION IN AUTOIMMUNE DISEASES (COVAD) STUDY

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Background: COVID-19 vaccines have been proven to be safe and effective in the healthy population at large. However, significant gaps remain in the evidence of their safety in patients with systemic autoimmune and inflammatory disorders (SAIDs). Patients and rheumatologists have expressed concerns regarding vaccination triggered allergic reactions, thrombogenic events, and other adverse events (ADEs) contributing to vaccine hesitancy (1)

Objectives: This study aimed to assess and compare short term COVID-19 vaccination associated ADEs in patients with SAIDs and healthy controls (HC) seven days post-vaccination, as well as between patients with SAIDs receiving different vaccines.

Methods: We developed an comprehensive, patient self-reporting electronic-survey to collect respondent demographics, SAID details, COVID-19 infection history, COVID-19 vaccination details, 7-day post vaccination adverse events and patient reported outcome measures using the PROMIS tool. After pilot testing, validation, translation into 18 languages on the online platform surveymonkey.com, and vetting by international experts, the survey was circulated in early 2021 by a multicenter study group of >110 collaborators in 94 countries. ADEs were categorized as injection site pain, minor ADEs, major ADEs, and hospitalizations. We analyzed data from the baseline survey for descriptive and intergroup comparative statistics based on data distribution and variable type (data as median, IQR).

Results: 10900 respondents [42 (30-55) years, 74% females and 45% Caucasians] were analyzed. 5,867 patients (54%) with SAIDs were compared with 5033 HCs. All respondents included in the final analysis had received a single dose of the vaccine and 69% had received 2 primary doses. Pfizer (39.8%) was the most common vaccine received, followed by Oxford/AstraZeneca (13.4%), and Covishield (10.9%). Baseline demographics differed by an older SAID population (mean age 42 vs. 33 years) and a greater female predominance (M:F= 1:4.7 vs. 1:1.8) compared to HCs.

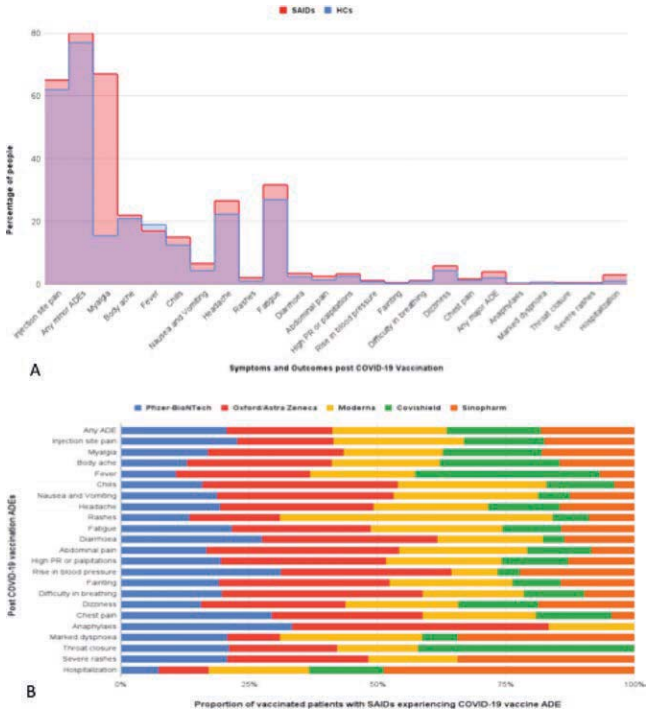

Figure 1. A. Post Vaccination ADEs in SAIDs compared to HCs. B. Proportions of post COVID-19 vaccination ADEs in SAIDs by vaccine type.

79% had minor and only 3% had major vaccine ADEs requiring urgent medical attention overall. In adjusted analysis, among minor ADEs, abdominal pain [multivariate OR 1.6 (1.14-2.3)], dizziness [multivariate OR 1.3 (1.2-1.5)], and headache [multivariate OR 1.67 (1.3-2.2)], were more frequent in SAIDs than HCs. Overall major ADEs [multivariate OR 1.9 (1.6-2.2)], and throat closure [multivariate OR 5.7 (2.9-11.3)] were more frequent in SAIDs though absolute risk was small (0-4%) and rates of hospitalization were similarly small in both groups, with a small absolute risk (0-4%). Specific minor ADEs frequencies were different among different vaccine types, however, major ADEs and hospitalizations overall were rare (0-4%) and comparable across vaccine types in patients with SAIDs (Figure 1).

Conclusion: Vaccination against COVID-19 is relatively safe and tolerable in patients with SAIDs. Certain minor vaccine ADEs are more frequent in SAIDs than HCs in this study, though are not severe and do not require urgent medical attention. SAIDs were at a higher risk of major ADEs than HCs, though absolute risk was small, and did not lead to increased hospitalizations. There are small differences in minor ADEs between vaccine types in patients with SAIDs.

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Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Consultant of: OD has/had consultancy relationship with and/or has received research funding from or has served as a speaker for the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three years: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, Baecon, Blade, Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos, Glenmark, GSK, Horizon (Curzion), Inventiva, iQvia, Kymera, Lupin, Medac, Medscape, Mitsubishi Tanabe, Novartis, Roche, Roivant, Sanofi, Serodapharm, Topadur and UCB. 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Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Hector Chinoy Speakers bureau: HC has served as a speaker for UCB, Biogen., Consultant of: HC has received consulting fees from Novartis, Eli Lilly, Orphazyme, Astra Zeneca, Grant/research support from: HC has received grant support from Eli Lilly and UCB, Vikas Agarwal: None declared, Rohit Aggarwal Consultant of: RA has/had a consultancy relationship with and/or has received research funding from for the following companies-Bristol Myers-Squibb, Pfizer, Genentech, Octapharma, CSL Behring, Mallinckrodt, AstraZeneca, Corbus, Kezar, Kyverna, Janssen, Roivant, Boehringer Ingelheim, Argenx, Q32, Alexion, EMD Serono, Jubliant, Abbvie, Janssen, Alexion, Argenx, Q32, EMD-Serono, Boehringer Ingelheim, Roivant., Grant/research support from: RA has/had a consultancy relationship with and/or has received research funding from for the following companies-Bristol Myers-Squibb, Pfizer, Genentech, Octapharma, CSL Behring, Mallinckrodt, AstraZeneca, Corbus, Kezar, Kyverna, Janssen, Roivant, Boehringer Ingelheim, Argenx, Q32, Alexion, EMD Serono, Jubliant, Abbvie, Janssen, Alexion, Argenx, Q32, EMD-Serono, Boehringer Ingelheim, Roivant., Latika Gupta: None declared

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POS1261 CLINICAL RESPONSE PREDICTORS OF TOCILIZUMAB THERAPY IN PATIENTS WITH SEVERE COVID-19

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Background: Aberrant immune response is hallmark of severe COVID-19, irrespectively from viral replication. Immunomodulatory therapies such as interleukin-6 (IL-6) receptor inhibitors were proven to be beneficial in reducing in-hospital mortality[1]. Yet, it remains unclear which patients can benefit most from such therapy.

Objectives: To identify predictors of clinical response to tocilizumab (TCZ) added to dexamethasone in patients hospitalized with severe COVID-19.

Methods: We prospectively assessed clinical and laboratory details of 120 patients hospitalized due to severe COVID-19 treated with TCZ (two doses of 8 mg/kg 24h apart) in our ward between 1st Feb 2021 and 31st Dec 2021. Severe COVID-19 was defined as SpO_2 <94% on room air with ground glass opacities in chest computed tomography (CT). Clinical response was defined as respiratory improvement on day 5 after TCZ infusion compared to day of treatment initiation, no further deterioration and survival. Decision of adding TCZ to dexamethasone as emergency therapy was made collectively by rheumatologists experienced in COVID-19 treatment. Laboratory and clinical parameters from hospital admission day and from TCZ institution day were analyzed. Statistical analysis was conducted with PQStat v.1.8.2 and predictors were identified in univariate logistic regression.

Results: We identified 86 (71.7%) clinical responders and 34 (28.3%) non-responders. 20 (58.8%) of the second group needed ICU admission, 18 (52.9%) died on ICU and 2 patients (5.9%) died on the ward. Responders were significantly younger (mean age 56.1 vs. 63.5 years, p=0.006), had lesser comorbidity burden (median Charleson Comorbidity Index 2 vs. 3, p=0.005), lower median lung involvement (50 vs. 70%, p<0.001), higher median baseline PaO2/FiO2 index (203 vs. 106, p<0.001) and less of them needed high-flow oxygen therapy on TCZ initiation day (12.7% vs 32.4%, p=0.025). Identified predictors of clinical response are shown in Table 1.

Conclusion: Administration of TCZ early in severe disease, with moderate IL-6 concentration and low organ damage indices is most beneficial in patients with severe COVID-19, especially in younger patients without respiratory and cardiac comorbidities.

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Table 1. Predictors of good response to TCZ therapy in severe COVID-19. Apart from PaO2/FiO2 all parameters identified as predictors were measured on TCZ initiation day.

Predictor	OR	95%CI	*p* value
LDH <447 U/l	12.67	4.42-36.31	<0.001
<70% of lungs involved in CT	6.76	2.63-17.36	<0.001
9-12 days from symptoms onset	6.43	1.82-22.73	0.004
RR <20/min	5.40	2.29-12.75	<0.001
hs-TnI <26 ng/l	4.80	1.55-14.81	0.006
BUN <22.2 mg/dl	4.71	2.02-10.99	<0.001
SpO2/FiO2 >122	4.47	1.92-10.40	<0.001
fibrinogen ≥490 mg/dl	4.46	1.86-10.72	<0.001
no history of asthma/COPD	4.39	1.55-16.71	0.030
no history of atrial fibrillation	4.20	1.23-14.33	0.022
baseline PaO2/FiO2 >200 mmHg	4.04	1.59-10.27	0.003
$25(OH)D_3$ ≥30 ng/ml	3.98	1.40-11.28	0.009
age <65 years	3.69	1.60-8.46	0.002
no history of ischaemic heart disease	3.56	1.29-9.79	0.014
procalcitonin 0.06-0.12 ng/ml	3.20	1.20-8.54	0.020
D-Dimer ≤1.28 µg/ml	3.12	1.37-7.09	0.006
IL-6 47.4-137.0 pg/ml	3.07	1.90-4.98	<0.001

OR – odds ratio, 95%CI – 95% confidence interval, LDH – lactate dehydrogenase, RR – respiratory rate, hs-TnI – high sensitivity troponin I, BUN – blood urea nitrogen, COPD – chronic obstructive pulmonary disease, $25(OH)D_3$ – 25-hydroxycholecalciferol, IL-6 – interleukin 6

POS1262 COVID-19 VACCINATION IN PATIENTS WITH RHEUMATIC DISEASES –RESULTS OF 2,134 CASES ANALYSIS

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Background: Decrease of COVID-19-associated morbidity and mortality among patients with rheumatic diseases (RD) is one of the main goals of current rheumatology. Vaccination may be one way to limit the incidence of COVID-19 in population of patients with RD.

Objectives: The goal of this work was to evaluate the results of vaccination in patients with RD against the new coronavirus infection COVID-19 bases on the data from real clinical practice.

Methods: We analyzed data from the St. Petersburg register of patients with RD till September 1, 2021 (totally 16,263 patients, vaccinated 2,134 patients). The data from the register were compared with population data of morbidity and mortality associated with new coronavirus infection in Russia (data from Russian Federations' Ministry of Health). Statistics was performed with SPSS2022.

Results: The rates of COVID-19 associated morbidity and mortality in rheumatological patients were comparable with morbidity and mortality in total Russian population (morbidity 26.2% and 28.5%, mortality 3.47% and 2.8%, respectively, p≥0.05).

Patients with RD demonstrate three times less frequency of vaccination against COVID-19 (13.2% of patients versus 31.8% in the population, respectively). Vaccination was prescribed by rheumatologists in 8.2% of cases, 75% of patients are self-vaccinated or were vaccinated by their general practicians.

An analysis of data from 2,134 rheumatological patients vaccinated in 2021 with Gam-COVID-Vac (Sputnik V™) showed a decrease in the incidence of new coronavirus infection from 26.2% to 0.25% in the absence of deaths among the vaccinated (mortality rate from COVID-19 in non-vaccinated patients was 2,8%, p<0.0000). From 2,134 vaccinated patients 42 had manifestation of COVID-19 in 6 months after vaccination, 39 persons of them demonstrated symptoms of COVID-19 during the first month after receiving the first dose of vaccine.

There were no serious adverse reactions to vaccination among vaccinated rheumatological patients; in 12 % of cases, slight pyrogenic post-vaccination reactions, arthralgias and myalgias were established. 11 patients showed a prolonged slight pyrogenic reaction, myalgias, arthralgias, hypercreatinophosphataemia, which resolved within 3-6 months. Relapses of the underlying RD after vaccination were recorded by patients in 12% of cases, but rheumatologists classified the presented clinical symptoms as the RD worsening in 1.57% of cases, another reports of RD relapse were classified as postvaccination reactions, as they were resolved in 1-2 weeks with the use of standard tactics recommended by Association of Russian Rheumatologists.

Conclusion: The analysis of the data from 2,134 rheumatological patients vaccinated Gam-COVID-Vac (Sputnik V™) demonstrated the efficacy and safety of vaccination against COVID-19 in middle-time perspective. No serious post-vaccination reactions or severe worsening of rheumatic diseases were recorded.

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POS1263 PRE-EXPOSURE PROPHYLAXIS FOR SARS-COV-2 INFECTION WITH SUBCUTANEOUS CASIRIVIMAB/IMDEVIMAB IN PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASES.

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Background: Patients with immune-mediated inflammatory diseases (IMID), particularly if treated with B-cell depleting therapies, show reduced humoral responses to SARS-CoV-2 vaccines and increased risk of severe COVID-19 (1,2). Since pre-exposure prophylaxis (PrEP) with monoclonal antibodies against SARS-CoV-2 proved effective in preventing infection and COVID-19 (3) in the general population, PrEP could be used for passive immunization of vaccine-refractory patients with IMIDs.

Objectives: To evaluate the persistence of serum and salivary anti-SARS-CoV-2 IgG antibodies in vaccine-refractory patients with IMID after PrEP with casirivimab/imdevimab. Secondary outcomes were safety, SARS-CoV-2 infection, and adverse COVID-19 outcomes.

Methods: We performed a longitudinal analysis on anti-SARS-CoV-2 IgG titers in IMID patients who received a PrEP with 1200 mg of subcutaneous casirivimab/imdevimab due to high infection risk, as they had not developed an adequate humoral response at least 21 days after three COVID-19 vaccinations (Table 1). Serum and salivary anti-SARS-CoV-2 Spike IgG were quantified by ELISA (EUROIMMUN, Lübeck, Germany) before PrEP and after 1, 14, and 30 days. IgG levels are given as antibody ratios by dividing the optical density of the sample by that of the calibrator. A cutoff of ≥1.1 was considered positive. Safety as well as polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection and adverse COVID-19 outcomes (hospitalization, mechanical ventilation, death) after PrEP were recorded.

Table 1. Baseline characteristics.

N		26
Age, mean (SD)		54 (14)
Sex, n (%)	Female	15 (57.7)
	Male	39 (42.3)
Diagnosis, n (%)	ANCA-associated vasculitis	10 (38.5)
	Rheumatoid arthritis	6 (23.1)
	Immunoglobulin deficiency	4 (15.4)
	Systemic sclerosis	2 (7.7)
	Psoriatic arthritis	1 (3.8)
	Systemic Lupus Erythematosus	1 (3.8)
	Non-infectious Uveitis	1 (3.8)
	Multiple sclerosis	1 (3.8)
	IgG4-related disease	1 (3.8)
	Autoinflammatory syndrome	1 (3.8)
CD20-depletion	Rituximab, n (%)	22 (84.6)
Other therapies, n (%)	Methotrexate	6 (23.1)
	Immunoglobulins	4 (15.4)
	Mycophenolate	1 (3.8)
	Infliximab	1 (3.8)
CD19+ lymphocytes/mm^3, median (IQR)		0 (0-9)
Serum total IgG, median (IQR)		894 (745-987)

SD, standard deviation; IQR, interquartile range; ANCA, anti-neutrophil cytoplasmic antibodies.

Results: We obtained 92 serum and 75 saliva samples from 26 participants at four consecutive timepoints (Figure 1). Anti-SARS-CoV-2 IgG titers were observed in serum and saliva samples of all participants from day 1 and throughout 30 days after PrEP independently of diagnosis, therapy, total IgG, and peripheral CD19+ B-cells. Serum IgG increased rapidly at day 1 and plateaued from day 14 to 30 (Figure 1A), reaching similar levels as seen in healthy subjects after full vaccination (1), while saliva IgG increased steadily from administration up to day 14 and plateaued at day 30 (Figure 1B). No side effects were reported. Five patients (19.2%) had a close contact with a SARS-CoV-2-infected person, after which all but one remained asymptomatic and with a negative PCR test. The patient who tested positive developed mild COVID-19 with fever and cough.

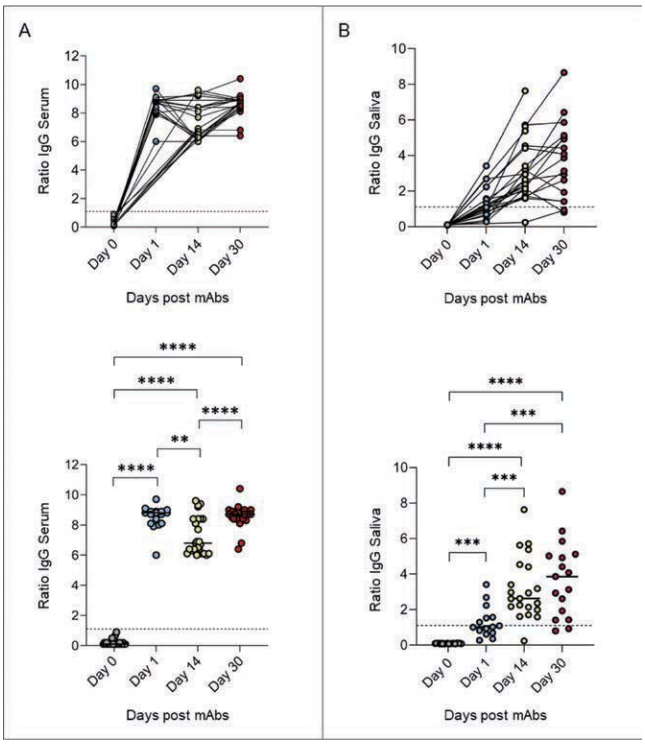

Figure 1. Temporal pattern and distribution of serum (A) and salivary (B) anti-SARS-CoV-2 IgG levels. Results from individual participants are represented as line (top) and scatter plots (bottom). Horizontal lines represent median values, the dotted horizontal line represents the positivity cutoff of 1.1. ** p =0.0082; *** p <0.001; **** p <0.0001. mAbs: monoclonal antibodies.

Conclusion: SARS-CoV-2 PrEP induces stable serum and salivary antibody levels in IMID patients who did not respond to COVID-19 vaccination, regardless of pre-existing clinical and serological features. In IMID, PrEP with casirivimab/imdevimab is safe and has the potential to prevent infection and severe COVID-19.

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POS1264 LONGITUDINAL FOLLOW-UP OF HUMORAL RESPONSE AGAINST SARS-COV-2 AND VIRAL PERSISTENCE IN 96 DMARDS-TREATED PATIENTS WITH PREVIOUS COVID-19 INFECTION

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Background: Although it prevents severe forms of the disease, vaccination does not completely protect against the occurrence of COVID19 disease. If, DMARDs used have been associated with variable humoral response to SARS-CoV-2 vaccination, the impact of their use after SARS-CoV-2 natural infection have been poorly studied.

Objectives: To characterize humoral response after SARS-CoV-2 infection and viral persistence in the nasopharyngeal sphere (NP), stools and blood of patients with rheumatic disease under DMARDs, and compared to healthy controls.

Methods: Prospective monocentric longitudinal study including patients with rheumatoid arthritis or spondyloarthritis under DMARDs and with a confirmed SARS-CoV-2 infection (positive NP PCR and/or positive serology and/or pathognomonic thoracic tomography (CT)) during the first or second wave of the COVID pandemic. Patients were followed up until one year after infection and humoral response was assessed before vaccination. Serum IgG and IgA antibodies against spike (S) and nucleocapsid (N) proteins were measured at every visit. Viral persistence was assessed at the early visit in the NP and stools using conventional RT-PCR and in the blood using a high sensitive technique (droplet digital PCR).

Results: Between June 2020 and July 2021, we include 96 patients (50 SpA and 46 RA) with a mean age of 53 +/- 14 years and 20 healthy controls (mean age 49 ± 16 years) corresponding to relatives of patients (spouses, children) living together and infected at the same time. The immune responses were analyzed according to 6 treatment groups: methotrexate (MTX)/salazopyrine (SLZ) monotherapy (n=17/2); anti-TNF monotherapy (n=24), anti-TNF + MTX (n=23); rituximab (RTX) (n=11); anti-IL17 or -23 (n=8); others (n=11). Visits were made at 1 month (29 ±13 days; n=18), 3 months (110 ±23 days; n=67), 6 months (231 ±35 days; n=48) and 12 months (368 ± 19 days; n=19) after infection. The anti-S and anti-N IgG Ab titers were not significantly different in the 6 treatment groups and the control population at 3 months. A significant decrease in anti-S IgA Ab titers was noted in the group treated with RTX (p=0.007) and with molecules targeting the IL17/23 pathway (p=0.007). A similar but non-significant trend was observed in these same treatment groups for anti-N IgA Ab (p=0.07). The titers of anti-SARS-CoV-2 antibodies at M3, was not associated with a severe COVID disease. Detection of SARS-Cov-2 RNA in stools and serum was negative for all samples taken at 1 month or 3 months. 4 patients (2 RA treated with abatacept/RTX and 2 SpA treated with anti-TNF/secukinumab) had a positive RT-PCR NP with low to very low viral load at the 1-month visit (mean Ct 36). None of these 4 patients had had a severe form of COVID19 infection.

Conclusion: DMARDs - treated patients with previous proven COVID-19 did not seem to alter IgG Ab response but RTX and anti-IL17/-IL-23 might alter IgA humoral response. This lower immune response was not associated with a more severe disease. In these patients, new infection may not be considered as a full boost for the immune system. DMARDs did not induce viral persistence in the serum, the NP or in the stool.

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POS1265 DISTURBED CELLULAR IMMUNITY FOLLOWING MRNA VACCINATION AGAINST COVID-19 IN PATIENTS WITH B-CELL DEPLETING THERAPY

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Background: Immunocompromised patients are considered high-risk and prioritized for vaccination against COVID-19 (1). Furthermore, vaccination-induced CD4 and CD8 T-cell responses have been suggested to have a protective role in COVID-19 (2). If T-cell responses are diminished after vaccination in immunocompromised individuals is not known to date.

Objectives: To investigate cellular immunity following mRNA vaccination against COVID-19 in healthy individuals and patients undergoing B-cell depletion therapy.

Methods: In this interim analysis of the CoVVac study (NCT04858607), we analyzed T-cell responses in autoimmune patients treated with B-cell depleting therapy (BD, n=41) and age-matched healthy controls (HCs, n=50) 3-4 weeks after the second dose of mRNA vaccination against COVID-19. Therefore, we isolated PBMCs and stimulated them with a peptide pool covering the spike protein *in vitro*. Reactive CD4 and CD8 T-cells were determined by staining for IFNg, TNFa, IL-2 and GzmB by flow cytometry. Anti-SARS-CoV-2 antibody assays targeting the receptor-binding domain (RBD) or trimeric S protein (TSP) were performed to elucidate concomitant B-cell responses.

Results: We observed significant alterations in anti-SARS-CoV-2 antibody responses in our cohort, the frequency of IFNg+ and IL-2+ CD4 and CD8 T-cells was similar in BD patients and controls. On the other hand, TNFa+ CD4 T-cells were significantly enriched in healthy controls versus BD patients (p=0.017) and correlated significantly with antibody titres (p=0.003). Similarly, GzmB+ CD8 T-cells were significantly diminished in our patient cohort (p<0.001) and also showed a significant correlation with antibody titres (p<0.001). Overall, the frequency of GzmB+ CD8 T-cells correlated very well with reactivity of T-cell subsets for other cytokines. This effect, however, is lost in the BD cohort. No difference was observed in the frequency of TNFa+ CD8 T-cells between the groups.

Only 21 (42%) healthy individuals and 14 (34%) patients showed reactive T-cells for all the cytokines tested. This observation is mainly explained by a lack of cytokine production of CD8 T-cells in 26 (52%) HCs and 27 (66%) BD patients. In turn, 22 (44%) HCs and 17 (42%) patients didn't show any IL-2 producing CD8 cells. Of note, only 2 (4%) of HCs showed no GzmB+ CD8 T-cells whereas the number increased to 15 (37%) of BD individuals (p<0.001). In contrast, 42 (84%)

HCs as well as 32 (78%) of patients showed production of all IFNg, TNFa and IL-2 in CD4 T-cells.

Conclusion: Our data suggest that most patients with B-cell depleting therapy are able to mount T-cell responses similar to those of healthy individuals while a minority of these patients did not show complete immunity against SARS CoV-2. Further analyses are needed to better understand a possible link of B-cell depletion therapy and CD8 T-cell responses.

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POS1266 MULTICENTER RETROSPECTIVE STUDY EVALUATING THE SAFETY OF ANTI-SARS-COV-2 VACCINE IN A COHORT OF PATIENTS WITH SYSTEMIC VASCULITIS

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Background: Vaccinations against SARS-CoV-2 represent a fundamental tool in controlling the pandemic. To date, data on the safety of anti-SARS-CoV-2 vaccines in patients with rare rheumatic diseases, such as systemic vasculitis, are limited.

Objectives: In this study we aimed at evaluating the safety of anti-SARS-CoV-2 vaccines in a multicentric cohort of patients with systemic vasculitis.

Methods: Patients with systemic vasculitis from two Rheumatology centres who had received anti-SARS-CoV-2 vaccine were retrospectively examined. The primary outcome was to evaluate, in this multi-centric cohort, the occurence of a disease flare after the administration of the vaccine, defined as development of clinical manifestations related to vasculitis with a concomitant increase in serum inflammatory markers. As a secondary outcome we aimed at evaluating, in a monocentric cohort of patients with vasculitis, the occurrence of adverse events (AEs) following vaccine administration compared to healthy controls (HC).

Results: We examined 111 patients with systemic vasculitis (n=69 female, n=42 male), with a mean age of 64.3 (± 13) years. Sixty had ANCA-associated vasculitis (AAV), fourty-two had Giant-Cell Arterities (GCA), five had Periarteritis Nodosa, four had Takayasu's arteritis. One-hundred and five patients received a mRNA vaccine and six a viral vector one. A disease flare occurred in only 2 patients (1.8%) after the first dose of a mRNA vaccine: both had AAV (microscopic poliangioitis) and developed a pulmunary disease flare (respiratory failure requiring hospitalization and treatment with high-dose glucocorticoids). Of note, one of these patients had multiple previous comorbidities, including a severe COPD. Multivaried analysis, adjusted for age and sex, performed in a single monocentric cohort of patients with systemic vasculitis [n=60 (39 AAV, 21 GCA), 37 female, 23 male, mean age 71 (± 12.5) years] demonstrated a statistically significant higher frequency of AEs in vasculitis patients compared to HC (p=0.015) after the first dose of vaccination. No significant differences in the frequency of AEs in vasculitis patients compared to HC after the second dose were detected. All the AEs were mild in both groups (malaise was the most frequently reported); no serious AEs were reported.

Conclusion: Our data show a very low incidence of disease flares after the administration of anti-SARS-CoV-2 vaccines in patients with systemic vasculitis. Patients with systemic vasculitis seem more prone to develop mild AEs after the first dose of the vaccine. Taken together, this data suggest a good risk profile for anti-SARS-CoV-2 vaccine in patients with systemic vasculitis.

Disclosure of Interests: None declared

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POS1267 LONG-TERM SURVEY STUDY OF THE IMPACT OF COVID-19 ON SYSTEMIC AUTOIMMUNE DISEASES. LOW DEATH RATE DESPITE THE INCREASED PREVALENCE OF SYMPTOMATIC INFECTION. ROLE OF PRE-EXISTING INTERSTITIAL LUNG DISEASE AND ONGOING TREATMENTS.

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Background: Patients with autoimmune systemic diseases (ASDs) can be counted among frail populations as regards the predisposition to COVID-19 due to the frequent visceral organ involvement and comorbidities, as well as the ongoing immunomodulating treatments.
Objectives: Our long-term multicenter telephone survey prospectively investigated the prevalence, prognostic factors, and outcomes of COVID-19 in Italian ASD patients during the first 3 pandemic waves.
Methods: A large series of 3,918 ASD patients (815 M, 3103 F; mean age 59±12SD years) was consecutively recruited at the 36 referral centers of COVID-19 & ASD Italian Study Group. In particular, ASD series encompassed the following conditions: rheumatoid arthritis (n: 981), psoriatic arthritis (n: 471), ankylosing spondylitis (n: 159), systemic sclerosis (n: 1,738), systemic lupus (172), systemic vasculitis (n: 219), and a miscellany of other ASDs (n: 178). The development of COVID-19 was recorded by means of telephone survey using standardized symptom-assessment questionnaire (1).
Results: A significantly increased prevalence of COVID-19 (8.37% vs 6.49%; p<0.0001) was observed in our ASD patients, while the cumulative death rate revealed statistically comparable to the Italian general population (3.65% vs 2.95%; p: ns). In particular, among the 328 ASD patients complicated by COVID-19, 57 (17%) needed hospitalization, while mild-moderate manifestations were observed in the large majority of individuals (83%). In addition, 12/57 hospitalized patients died due to severe interstitial pneumonia and/or cardiovascular manifestations.
Interestingly, a significantly higher COVID-19-related death rate was observed in systemic sclerosis patients compared to the Italian general population (6.29% vs 2.95%; p=0.018). Other adverse prognostic factors to develop COVID-19 were the patients' older age, male gender, pre-existing ASD-related interstitial lung involvement, and chronic steroid treatment. Conversely, patients treated with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) showed a significantly lower prevalence of COVID-19 compared to those without (3.58% vs 46.99%; p=0.000), as well as the chronic administration of low dose aspirin in a subgroup of SSc patients (with 5.57% vs without 27.84%; p=0.000).
Conclusion: The cumulative impact of COVID-19 on ASD patients after the first 3 pandemic waves revealed less severe than that observed during the first phase of pandemic (1), especially with regards to the death rate that was comparable to the Italian general population in spite of the increased prevalence of complicating COVID-19 in the same ASD series.
Ongoing long-term treatments, mainly csDMARDs, might usefully contribute to generally positive outcomes of in this frail patients' population.
Of note, a significantly increased COVID-19-related mortality was recorded in only SSc patients' subgroup, possibly favored by pre-existing lung fibrosis. Among different ASD, SSc deserves special attention, since it shares the main pathological alterations with COVID-19, namely the interstitial lung involvement and the endothelial injury responsible for diffuse microangiopathy.
Besides SSc, the patients' subgroups characterized by older age, chronic steroid treatment, pre-existing interstitial lung disease, and/or impaired COVID-19 vaccine response (1-3), may deserve well-designed prevention and management strategies.

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POS1268 PHASE II TRIAL OF ENPATORAN IN PATIENTS HOSPITALIZED WITH COVID-19 PNEUMONIA

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Background: Enpatoran is a selective and potent dual toll-like receptor (TLR) 7/8 inhibitor in development for the treatment of cutaneous and systemic lupus erythematosus (CLE/SLE). Enpatoran inhibits TLR7/8 activation *in vitro* and suppresses disease activity in lupus mouse models.[1] Enpatoran was well tolerated and had linear pharmacokinetic (PK) parameters in healthy volunteers.[2] As TLR7/8 mediate immune responses to single-stranded RNA viruses, including SARS-CoV-2, it was postulated that enpatoran may prevent hyperinflammation and cytokine storm in COVID-19.
Objectives: In response to the COVID-19 pandemic, we conducted an exploratory Phase II trial to assess safety and determine whether enpatoran prevents clinical deterioration in patients (pts) hospitalized with COVID-19 pneumonia. PK and pharmacodynamics (PD) of enpatoran were also evaluated.
Methods: ANEMONE was a randomized, double-blind, placebo (PBO)-controlled study conducted in Brazil, the Philippines, and the USA (NCT04448756). Pts aged 18–75 years, hospitalized with COVID-19 pneumonia (WHO 9-point scale score =4) but not mechanically ventilated, with SpO_2 <94% and PaO_2/FiO_2 ≥150 (FiO_2 maximum 0.4) were eligible. Those with a history of uncontrolled illness, active/unstable cardiovascular disease and SARS-CoV-2 vaccination were excluded. Pts received PBO or enpatoran (50 or 100 mg twice daily [BID]) for 14 days, with monitoring to Day 28 and safety follow-up to Day 60. Primary outcomes were safety and time to recovery (WHO 9-point scale ≤3). Clinical deterioration (time to clinical status >4, WHO 9-point scale) was a secondary outcome. Exploratory endpoints were enpatoran and biomarker concentrations (cytokines, C-reactive protein [CRP], D-dimer and interferon gene signature [IFN-GS] scores) assessed over time.
Results: 149 pts received either PBO (n=49), or enpatoran 50 mg (n=54) or 100 mg (n=46) BID; 88% completed treatment and 86% received concomitant steroids. Median age was 50 years (77% <60 years old), 66% were male, and 50% had ≥1 comorbidity (40% hypertension, 24% diabetes). Overall, 59% pts reported a treatment-emergent adverse event (TEAE) with three non-treatment-related deaths; 11% reported a treatment-related TEAE. The proportion of pts in the enpatoran group reporting serious TEAEs was low (50 mg BID 9%; 100 mg BID 2%) vs PBO (18%). Gastrointestinal disorders were most common (PBO 8%; 50 mg BID 28%; 100 mg BID 9%). The primary outcome of time to recovery with enpatoran vs PBO was not met; medians were 3.4–3.9 days. A positive signal in time to clinical deterioration from Day 1 through Day 28 was observed; hazard ratios [95% CI] for enpatoran vs PBO were 0.39 [0.13, 1.15] (50 mg BID) and 0.30 [0.08, 1.08] (100 mg BID). Mean enpatoran exposure was dose-proportional, and PK properties were within expectations. The median (quartile [Q]1– Q3) interleukin 6 (IL-6), CRP and D-dimer baseline concentration across the groups were 5.7 (4.0–13.5) pg/mL, 30.04 (11.40–98.02) and 0.62 (0.39–1.01) mg/L, respectively. Baseline IFN-GS scores were similar across groups.
Conclusion: The ANEMONE trial was the first to evaluate the safety and efficacy of a TLR7/8 inhibitor in an infectious disease for preventing cytokine storm. Enpatoran up to 100 mg BID for 14 days was well tolerated by patients acutely ill with COVID-19 pneumonia. Time to recovery was not improved with enpatoran, perhaps due to the younger age of patients who had fewer comorbidities compared to those in similar COVID-19 trials. However, there was less likelihood for clinical deterioration with enpatoran than placebo. This trial provides important safety, tolerability, PK and PD data supporting continued development of enpatoran in SLE and CLE (NCT04647708, NCT05162586).

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POS1269 CLINICAL COURSE AND OUTCOMES OF COVID-19 INFECTION IN PATIENTS WITH SJOGREN'S SYNDROME TREATED WITH RITUXIMAB.

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Background: Data from multiple rheumatological cohorts have shown that treatment with rituximab (RTM) is associated with higher COVID-19 morbidity and mortality. Information about the course of COVID-19 in patients (pts) with Sjogren's syndrome (SjS) is still lacking.
Objectives: To compare clinical course of COVID-19 in pts with SjS treated with anti-CD20 monoclonal antibody (RTM) and treated with synthetic disease-modifying antirheumatic drugs and low doses of glucocorticoids.
Methods: Single center observational study. Pts with SjS were screened for SARS-CoV-2 infection anamnesis via telephone interview. Diagnosis of SjS was based on ECR/EULAR 2016 criteria. COVID-19 diagnosis was based on positive PCR test and typical clinical features (CT signs, fever and anosmia). RTM was administered as two infusions of 1000 mg each 2 weeks apart, and then 500 mg every 6 months.
Results: 387 pts with SjS were interviewed, 142 of them with confirmed SARS-CoV-2 were included in the study and divided into 2 groups. The first group (gr) consisted of 86 pts (79 women and 7 men) receiving RTM (gr R), median age was 56 years (33-66,5 years), and median rituximab treatment duration was 36 months (12-42 months). Pts in the control gr (gr C), 56 pts did not receive RTM (55 women and 1 man), their median age was 50 years (35-69 years). Median time from last RTM administration to COVID-19 symptoms onset was 4 months (2-6 months). Ten pts had concomitant RA, 4 pts - SLE, 5 pts - Systemic sclerosis. Fifteen pts had MALT-lymphoma anamnesis. Additionally, 15 pts (10.5%) had pulmonary involvement secondary to rheumatic disease. In total 37 pts had chronic ischemic heart disease and/or severe arterial hypertension, diabetes mellitus type 2.
In gr R 31 pts (36%), and in gr C 13 (23%) required hospitalization due to marked shortness of breath and long febrile period (p=0,1). Anti-IL6 treatment or/and Jak inhibitors were prescribed to 17 of 31 pts (54.8%) in gr R and to 5 of 13 (38%) in gr C (p=0,1). The risk of hospitalization was slightly higher in pts with comorbidity (p=0.06) and with a history of lymphoma (p=0.056) and didn't correlate with the following parameters: age, the duration of RTM therapy, lung damage. A high rate of hospitalization correlated with a shorter period between the administration of the RTM and the development of COVID-19 (R=0,387, Spearman`s Rank Correlation). Anti-SARS-CoV-2 IgG were measured in 66 pts, 47 (71%) of them were positive. Positive Anti-SARS-CoV-2 IgG were significantly more often detected in gr C (84% vs. 57,6%). No correlation was found between the formation of antibodies and the duration of RTM therapy or the time from the last RTM administration.
Conclusion: According to our data anti-CD20 therapy doesn't predispose SjS pts to severe course of COVID-19. Lymphoma anamnesis, cardiovascular diseases and diabetes have greater impact on COVID-19 severity. Obviously, anti-CD20 therapy negatively affected the formation of specific anti-SARS-CoV-2 humoral immunity.
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POS1270 COVID19 VACCINATION IN PATIENTS WITH AXIAL AND PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: ADVERSE EVENTS AND IMPACT ON DISEASE ACTIVITY

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Background: There is scarce evidence on the rate of adverse events and the consequences on disease activity after vaccination against covid19
Objectives: To evaluate adverse events to vaccination and disease flares after vaccination in patients with axial spondyloarthritis (axSpA), peripheral spondyloarthritis (pSpA) and psoriatic arthritis (PsA) and to evaluate factors associated with adverse event.
Methods: Cross-sectional, observational, descriptive study. Consecutive patients with diagnosis of ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) according to ASAS 2009 criteria; pSpA according to ASAS 2011 criteria and PsA according to CASPAR criteria were included. Demographic data, disease clinimetry, treatments, vaccination received and post-vaccination adverse events were recorded. We evaluated, according to medical criteria, whether the patient presented a flare disease after vaccination and whether it was mild, moderate or severe. We also evaluated the factors associated with the presence of at least one mild adverse event. Statistical analysis: descriptive statistics were performed, qualitative variables were expressed as frequency and percentage (%), numerical variables as mean and standard deviation (SD) or median and percentile25-75. Binary logistic regression was performed using the presence of at least one mild adverse event to vaccination as the dependent variable.
Results: 210 patients were included with a mean age of 45 (SD 15) years. The diagnoses were: AS 50 (23.8%), nr-axSpA 10 (4.8), pSpA 9 (4.3%), PsA 141 (67%) and time of disease evolution in months 109 (SD 96). Regarding comorbidities, the following frequencies were reported: arterial hypertension 60 (30%), diabetes mellitus 25 (12%), heart failure 4 (2%), asthma/EPOC 15 (7%), inflammatory bowel disease 2 (1%), acute anterior uveitis 20 (9.5%), psoriasis 128 (61%). Sixteen percent (n=33) of the patients had SARS-CoV-2 infection prior to vaccination. Regarding treatments, those used were: antiTNF 88 (42%), Tofacitinib 6 (2.9%), Ustekinumab 2 (1%), Secukinumab 35 (17%), Ixekizumab 2 (1%), methotrexate 98 (47%), leflunomide 7 (3. 3), sulfasalazine 7 (3.3), apremilast 1 (0.5%), continuous NSAIDs 26 (12.4%) and NSAIDs on demand 103 (49%). Vaccines received were: Sputnik V 109 (51.9%), Oxford Vaccine, AstraZeneca 63 (30%), Janssen 1 (0.5%), BioNTech Vaccine, Pfizer 1 (0.5%), Sinopharm 33 (15.7%), Moderna 0%, Novavax 0% and others; 3 (1.4%). Thirty-eight percent (n=80) of patients reported having mild post-vaccination symptoms, of which 3.75% did not resolve, 41% resolved with medication and 39% resolved ad integrum without medication. The presence of mild adverse event to the vaccine was associated with lower use of methotrexate (31% vs 56 %, p<0.001), and lower age (54 (SD 14) vs 47 (SD 12), p<0.001), and lower BMI (25 (24-30.5) vs 28 (25-31), p<0.001); while no association was found with sex, diagnosis, comorbidities, treatments, desease activity or vaccines. In the logistic regression analysis all the variables remained independently associated with a lower probability of presenting a mild adverse event: methotrexate: OR: 0.30, 95%CI 0.15-0.58, p<0.001, age: OR: 0.97, 95%CI 0.95-0.99, p: 0.03, BMI: OR: 0.92, 95%CI 0.95-0.99, p: 0.02. Sixty-one percent (n=129) of patients received the 2nd dose of vaccination, which 27% (n=35) presented mild adverse event and only 1 (0.8%) patient suffered post vaccination disease flare.
Conclusion: Vaccination against COVID19 appears to be safe in this population, with only mild adverse events and low frequency of flare disease. Mild adverse events were associated with less use of methotrexate, younger age and lower BMI.
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POS1271 THE COURSE AND OUTCOMES OF COVID-19 IN PATIENTS WITH TAKAYASU ARTERITIS: CASE SERIES OF 15 PATIENTS FROM A TERTIARY SINGLE CENTER

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Background: The Coronavirus disease 2019 (COVID-19) has affected more than two hundred million individuals and many risk factors for increased mortality and morbidity in COVID-19 have defined. There are many studies evaluating the effect of immunosuppressants used in inflammatory rheumatic diseases in the course of COVID-19. (1,2) However, fewer data are available on the course of COVID-19 in patients with Takayasu arteritis (TAK).
Objectives: In this study, we aimed to evaluate the characteristics and outcomes of TAK patients with COVID-19.
Methods: A phone survey was conducted among TAK patients that are followed up in our clinic between February 2021 and March 2021. All patients were asked whether they were diagnosed as COVID-19 during the pandemic. The patients who had a history of confirmed COVID-19 were asked about the symptoms, hospitalization status and the treatment received for COVID-19. Information about their chronic diseases were obtained from the patient files.
Results: Among 118 TAK patients, 15 had COVID-19 infection during the first year of pandemic, 13 of them were female and mean age was 42,5 ± 12,0 years. None of the patients had been vaccinated before the diagnosis of COVID-19. Nine of the patients were taking prednisone therapy and 3 of them were taking moderate to high doses of glucocorticoids during the infection period. Twelve patients were taking conventionally synthetic disease-modifying antirheumatic drugs (csDMARDs), 7 patients were taking biological disease-modifying antirheumatic drugs (bDMARDs), and 5 patients were taking a combination of csDMARD and bDMARD therapy when they were diagnosed with COVID-19. Two patients were hospitalized; one of them required nasal oxygen support and discharged after 5 days. The other patient was 61 years old and had multipl comorbidities and had admitted to intensive care unit for 5 days. One patient who had a mild COVID-19 disease had pulmonary thromboembolism 2 weeks after the infection and his symptoms resolved after starting anticoagulation therapy. All of the patients fully recovered and had no mortality related to COVID-19.

Conclusion: To our knowledge, this is the largest cohort reporting the course of COVID-19 in TAK patients. Our data suggest that there is no increased risk for morbidity or mortality related to COVID-19 in TAK patients.

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POS1272 EVALUATION OF DIAGNOSIS, TREATMENT AND OUTCOME RESULTS OF MIS-C PATIENTS

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Background: SARS-COV-2 infection, which has become a pandemic worldwide, has led to various results, from mild clinical findings to severe respiratory failure. Multisystem inflammatory syndrome (MIS-C) in children is a rare but severe condition characterized by fever, inflammation, and multi-organ failure, caused by an overreaction of the immune system after SARS-CoV-2 infection.

Objectives: This study aims to report the clinical and laboratory findings, diagnostic methods, treatment regimens, and short-term follow-up results of patients diagnosed with MIS-C.

Methods: This is a retrospective observational study from a tertiary pediatric rheumatology center including patients (aged 1 month to 21 years) diagnosed with MIS-C between April 2020-December 2021. Demographic, clinical, laboratory results, and follow-up data were collected through the electronic patient record system and analyzed.

Results: Of the 110 patients included in the study, 67.2% (n=74) were male. Fever was a common finding in all. Macrophage activation syndrome (MAS) was dominant in 28.2% (n=31), while Kawasaki-like disease was observed in 40% of the patients. Gastrointestinal symptoms were found in 64.5% of the cases, rash in 40%, conjunctivitis in 35.5%, lymphadenopathy in 30%, hypotension in 27.3%, cardiac decompensation in 16.4%, bradycardia in 8.2%, neurological findings in 4.5%, and/or coronary artery pathology in 3.6% respectively. Included in the study, 63.6% had lymphopenia, 48.2% had hypoalbuminemia, and 39.1% had hyponatremia. Thirty-eight patients (34.5%) were followed up in the intensive care unit; 19 of them had MAS. Concomitant chronic disease was present in 21.8% of the patients. The mean hospital stay was 12±7.8 days. Hypotension and MAS were the most common indications for admission to the intensive care unit. Intravenous immunoglobulin treatment was applied to 87.2% of the cases, the steroid was given to 70.9%, and anakinra treatment was given to 27.3%, respectively. In the outpatient follow-up, it was determined that the coronary abnormalities had regressed entirely. While 97.3% of the cases recovered without sequelae, three died. Three patients who died had the comorbid disease. While there was no significant difference in terms of Kawasaki-like disease and gender in those followed up in the intensive care unit (p=0.25, p=0.81), D-dimer was higher, and the mean age was greater (p=0.08, p=0.02). No statistical correlation was found between those with Kawasaki-like disease regarding age and gender (p=0.058 p=0.068).

Conclusion: Multisystem inflammatory syndrome in children may lead to severe cardiac findings and intensive care requirements at admission and hospital follow-up. The majority of MIS-C-related findings resolve completely until discharge or in short-term follow-up. Although the pathogenesis and treatment plan of the disease has been largely clarified, follow-up studies are needed in terms of long-term prognosis and relapse probabilities.

Disclosure of Interests: None declared

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POS1273 EVALUATION OF THE SAFETY PROFILE OF COVID-19 VACCINES IN CHILD PATIENTS USING BIOLOGICAL THERAPY

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Background: Coronavirus vaccines have been widely applied all over the world after the coronavirus pandemic. There are inactivated vaccines and mRNA vaccines in our country. There is no clear guideline for the vaccination programs of patients receiving immunosuppressive therapy, especially childhood.

Objectives: For this reason, we wanted to evaluate the frequency of side effects developed after covid-19 vaccine in pediatric patients diagnosed with rheumatic disease using biological therapy and nonbiologic disease modifiying drugs

Methods: A total of 226 patients over the age of 12, who were followed up in the pediatric rheumatology clinic of the University of Health Sciences, Umraniye Training and Research Hospital, using biological therapy and were vaccinated against Covid-19, were included in the study. The standard questionnaire forms were filled in face-to-face after each administration for both vaccines. The patient, who had any serious side effects, was followed up in the hospital.

Results: Of the 226 patients included in the study, 97 were male and 128 were female. Their mean age was 16.4+2.4. It was determined that 88.4% (n=200) of the patients had mRNA vaccine and 11.6% (n=26) had inactivated vaccine. 105 of the patients were using biologic drugs during vaccination. Of these, 63 (27.9%) patients were treated with anti-TNF drugs (46 adalimumab, 10 etanercept, 6 infliximab), 32 patients were anti-il-1 (30 canakinumab, 2 anakirna), 4 patients were anti-il-6, 3 patients were anti-il-17, 3 patient was receiving abatacept and 1 patient was receiving rituximab. 121 patients were using DMARDs. Of these, 61 were using colchicine. 26.5% (n=60) of the patients had covid infection before vaccination. Side effects were observed in 180 of our patients. No side effects were observed in 46 patients. Pain at the injection site was the most common among them, 72.6% (n=164). Headache was seen in 16.8% (n=38) of the patients, myalgia in 18.1% (n=41), fever in 16.4% (n=37) and arthralgia in 6.6% (n=15). The frequency of serious adverse events was determined as 0.9%(n=2). Both patients were followed up in the ward. When the patients were compared in terms of covid infection and gender, there was no significant difference in the frequency of side effects. When the vaccines were compared, the incidence of side effects in the mRNA vaccine was statistically significantly higher (p=0.001). Pain at the injection site was significantly less frequent in the inactivated vaccine (p=0.004). In terms of drug distribution, there was no significant difference in the frequency of side effects between patients using biologic drugs and DMARDs. p=0.004) There was no statistically significant difference in the frequency of side effects when the patients using dmard were compared as colcicine and other dmards.

Conclusion: In our study, we have shown that the use of vaccines in individuals with adolescent rheumatological diseases is safe and that the biological treatments used by the patients do not cause an increase in the risk of vaccine side effects. In addition; We have shown in our study that the side-effect profile of the inactivated vaccine used in our country is milder than the mRNA vaccine, and that it affects daily life less. Another result of our study was that anti-TNF drugs could cause a decrease in pain sensation due to the relationship of anti-TNF with pain pathways.

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POS1274 A SINGLE CENTER COVID-19 VACCINE EXPERIENCE IN FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Background: To prevent COVID-19 disease SARS-CoV 2 vaccines put into use worldwide with emergency use authorizations despite ongoing safety concerns. Since pyrin mediated inflammasome response is dysregulated in FMF, exposure to SARS-CoV 2 proteins via vaccination may potentially trigger inflammation, leading to attacks and/or increased rate of adverse events (AE).

Objectives: Aim of this study to investigate frequency of adverse events and attacks related to vaccination in recipients of CoronaVac and BNT162b2 comparatively in our FMF patients.

Methods: Data regarding, number of vaccine doses, types of vaccines (CoronaVac or BNT162b2), presence of AEs and/or FMF attacks after any vaccine dose within a month, history of COVID-19 infection before or after vaccination, adherence to FMF treatment during vaccination were collected from hospital database or via telephone.

Results: A total of 161 vaccinated FMF patients were included. Mean ± SD age was 40.5 ± 11.7 years. 57.1% was female. 10.6% of the patients had chronic kidney disease and 9.3% had amyloidosis. Most common MEFV mutations were M694V heterozygous (27%) and M694V homozygous (21.6%). 93.2% of the patients were under colchicine, 21.8% under anti-interleukin 1 agents, 2.5% under TNF-a inhibitors. 96.3% of the patients adhered to FMF treatment during vaccination. Vaccination properties and data regarding adverse events are presented in Table 1. 57.8% of patients reported to suffer from an AE/attack after a vaccine dose. Number of patients with AE after BNT162b2 was significantly higher (p<0.001). None of the patients had severe AEs. 39 patients had COVID-19 infection prior to primary vaccination. 61.5% of these suffered from an adverse reaction/attack after vaccination, in comparison to 56.6% of the patients without

prior COVID-19 infection (p=0.584). When patients with and without AEs/attacks were compared, no significant differences were observed regarding age, gender, body mass index, comorbidities, FMF treatments and total vaccine doses.

Table 1. Adverse events and FMF attacks in a total of 161 vaccine recipients

	BNT162b2	CoronaVac	p
Total vaccine doses, n	213	140	
Patients ever vaccinated with BNT162b2 and CoronaVac, n (%)	117 (72.7)	67 (41.6)	
Dose per patient, median (min-max)	2 (1-4)	2 (1-4)	
Patients with primary vaccination completed with BNT162b2 or CoronaVac, n (%)*	88 (54.7)	57 (35.4)	
Patients with a booster with BNT162b2 or CoronaVac, n (%)	23 (14.2)	14 (8.6)	
Patients vaccinated with BNT162b2 or CoronaVac alone, n(%)	94 (58.4)	44 (27.3)	
Patients with an adverse event after any vaccine dose of n (%)¶	64/117 (54.7)	20/67 (29.9)	**<0.001**
Adverse events, n (%)¶			
Fever	13 (11.1)	6 (9.0)	0.644
Malaise	21 (17.9)	4 (6.0)	**0.023**
Local pain/arm pain	17 (14.5)	4 (6.0)	0.079
Arthralgia	19 (16.2)	4 (6.0)	**0.043**
Myalgia	6 (5.1)	0 (0.0)	0.059
Headache	11 (9.4)	0 (0.0)	**0.010**
Nausea	6 (5.1)	1 (1.5)	0.215
Vomiting	4 (3.4)	1 (1.5)	0.439
Others	22 (18.9)	7 (10.4)	
Patients with FMF attack within one month after any vaccine dose, n (%)¶	26 (22.2)	13 (19.4)	0.653
Time from vaccine dose to FMF attack, days, median (IQR)	7.0 (12.5)	10.0 (13.5)	0.758

*9.9 % of the patients had only single dose of either vaccine, ¶Over 117 ever vaccinated with BNT162b2 and 67 ever with CoronaVac

Conclusion: We observed considerable number of FMF patients suffered from vaccine related AEs/attacks, particularly with BNT162b2. However, no serious AE was detected. Demographics, clinical characteristics and prior history of vaccination did not significantly affect AE/attack occurrence.

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POS1275 A RETROSPECTIVE STUDY ON UVEITIS FLARES FOLLOWING COVID19 VACCINATION: SHARING EXPERIENCE FROM A TEACHING HOSPITAL COMBINED RHEUMATOLOGY AND UVEITIS CLINIC

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Background: Uveitis is a sight threatening disease caused by inflammation of the uveal tract of the eye. Uveitis is a manifestation of many autoimmune conditions and is associated with seronegative axial spondyloarthritis, reactive arthritis, Behçet's disease, inflammatory bowel disease, and psoriatic arthritis. Acute anterior uveitis is the most common presentation and is most commonly idiopathic or associated with the HLA-B27 gene (around 20% of cases). Studies have shown that anterior uveitis frequently recurs in patients after it has previously remitted. (1) Patients suffering from autoimmune conditions are frequently prescribed immunosuppressant drugs to control their illness, thus leaving them more susceptible to bacterial and viral illnesses including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Previous studies have shown that some patients suffer exacerbation of their autoimmune condition after coronavirus vaccination, including uveitis(2). We aim to evaluate our cohort of patients suffering from autoimmune conditions treated at Leicester Uveitis Service at Leicester Royal Infirmary and explore any proposed link.

Objectives: To assess if COVID19 vaccination is associated with uveitis flares in immunosuppressed patients.

Methods: A retrospective study, to determine if patients diagnosed with autoimmune conditions suffered from uveitis following COVID-19 vaccination. A data collection sheet was used to document demographic and clinical data: age, sex, ethnicity, autoimmune condition, dates of COVID-19 vaccination(s), type of vaccine, medication at the time of vaccine, symptoms of autoimmune recurrence, date of uveitis onset and number of days between uveitis onset and latest vaccine. We used an already existing uveitis database with an active register of 2346 patients, of which 246 were on immunomodulation.

Results: After reviewing the first 50 patients on immunosuppression for uveitis, we found a total of 4 patients had a uveitis flare despite tight control previously; 3 are female and 1 male, their median age was 39.5 years. They experienced a recurrence of uveitis in the last 6 months. Of these 4 patients 3 were on synthetic DMARDS (2 mycophenolate mofetil, 1 azathioprine), 1 was on steroids and 1 was on a biological DMARD (adalimumab). 2 of the patients suffered from posterior uveitis and 2 from anterior uveitis. All the 50 patients had been vaccinated against COVID19 however there was no clear record of booster dose.

Conclusion: Our study showed that of 50 immunosuppressed patients, 4 had a uveitis flare following vaccination. Clinicians need to be aware of uvetis flares in rheumatology patients following vaccination. This is a small retrospective analysis of our cohort however a large observational study on flare of uveitis following COVID-19 primary vaccination and booster vaccination would be useful to get meaningful data.

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POS1276 HUMORAL IMMUNE RESPONSE TO SARS-COV-2 VACCINE IN RITUXIMAB-TREATED PATIENTS

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Background: Vaccination against SARS-CoV-2 has shown efficacy and safety in patients with chronic inflammatory rheumatic disease, similar to the general population. However, in patients treated with rituximab (RTX) it is known that usually have a lower vaccination response rate (1-2), and recent studies suggest that it also happens with the new SARS-CoV 2 vaccine (3), which entails an increased risk of hospitalization and mortality in this specific group of patients.

Objectives: To describe humoral immune response to SARS-CoV-2 vaccine in rituximab-treated patients after one and six months from the vaccination, and study if there is any other factor associated with a lower response rate.

Methods: Prospective analysis of a cohort of patients treated with RTX who received the SARS-CoV-2 vaccine between the months of April and October 2021. Demographic and medical data were collected through electronic medical records. Blood tests and serologies with levels of antibodies against SARS-CoV-2 were performed one and six months after having received the vaccine against SARS-CoV-2. The administration of a booster dose of the vaccine was recorded. A descriptive and statistical analysis of the data was carried out using the SPSS program.

Results: From a cohort of 41 patients, of whom 81,4% were women with a mean age of 56 (13,4 SD) years, vaccine response rate was only 36,7% after a 6-month follow-up. The 88,4% of them received a booster dose of the vaccine, but this failed to produce a vaccine response in any of the patients who had not developed it with the previous ones. One patient became infected after receiving one dose of the vaccine and failed to develop a serological response either.

Hypogammaglobulinemia was associated with a statistically significant lower probability of vaccine response (p=0,04). A trend of lower vaccination response rate was observed in patients who had received the last cycle of RTX in the 6 months prior to vaccination (p=0,058). In addition, the antibody levels developed one month after vaccination were statistically significantly correlated with the time between the last RTX cycle and vaccination (p=0,014) and also with CD19 B cells levels prior to vaccination (p<0,001); however, there was no correlation with the antibody levels detected at the 6-months serology. No statistically significant differences were found in relation to the number of previous cycles of RTX, concomitant treatment with synthetic disease-modifying drugs (DMARDs) or corticosteroids.

Conclusion: In our sample, after a 6-month follow-up only 36,9% achieved a vaccine response against SARS-CoV-2, which did not improve despite the administration of a booster dose. Hypogammaglobulinemia, the time between the last RTX cycle and vaccination (at least 6 months), and previous CD19 B cells levels significantly influenced in the development of a humoral response to the vaccine.

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POS1277 LONGTERM IMMUNOGENICITY AND TOLERABILITY OF A 3RD DOSE OF AN MRNA ANTI-SARS-COV-2 VACCINE IN RA PATIENTS WITH AN INADEQUATE RESPONSE TO A PREVIOUS STANDARD TWO DOSE REGIMEN

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Background: Lower seroconversion rates have been reported in patients with rheumatic diseases receiving immunomodulatory therapies following a standard mRNA-based vaccine regimen. Data with regard to immunogenicity and safety of a 3rd vaccine dose in this patient population is limited[1].
Objectives: We aim to study immunogenicity, vaccine associated side effects and the occurrence of flares in RA patients unresponsive to a standard vaccine regimen eligible for a 3rd vaccine dose.
Methods: RA patients who had a low or absent anti-S1 response after 12 (Cohort A) or 24 weeks (Cohort B) following a standard vaccination regimen received a 3rd vaccine dose. Temporary discontinuation of DMARD therapy was recommended. Serum samples were collected before, 2, 12, and 24 weeks after the 3rd vaccine dose. Quantitative measurement of anti-S was performed using the Roche Elecsys Anti-SARS-CoV-2 spike subunit assay. Neutralizing activity (NT50) against Wuhan WT and αasβ-, γ-, and δ- variants was assessed by using a HIV-based pseudovirus system.
Results: Baseline characteristics are shown in Table 1. 45/47 patients temporarily discontinued DMARD therapy: Mtx and JAKi were paused one 1 week before/restarted 2 weeks after the 3rd vaccine dose, bDMARDs were paused 2 weeks before/restarted 2 weeks after the 3rd dose. Local pain and/or systemic vaccine associated side effects following the 3rd vaccine dose were reported in 12/17 (71%) in Cohort A, and 10/29 (35%) patients in Cohort B (p = 0.018). Flares were defined as loss of low disease activity (LDA), subsequent to the 3rd vaccine dose and occurred in 17/47 (36%) patients (p = 0.0332) with comparable frequencies in both cohorts (41% Cohort A, 33% Cohort B (NS)).

Table 1. Baseline characteristics of RA patients in Cohort A and Cohort B

	RA patients (n = 17) Cohort A	RA patients (n = 30) Cohort B	p-value
Age (yrs), mean (± SD)	69 (8)	63.9 (8)	NS
Female sex, n (%)	9 (53)	13 (43)	NS
Vaccination type/schedule			
mRNA-1273/BNT162b2, n=	3/14	5/25	NS
RA disease characteristics			
ACPA ± RF, n (%)	13 (77)	12 (40)	0.02*
Disease activity (CDAI)			
Remission (≤ 2.8), n (%)	3 (18)	6 (20)	NS
LDA (2.9 - 10), n (%)	11 (64)	18 (60)	NS
Moderate CDAI (10.1 - 22.0), n (%)	2 (12)	3 (10)	NS
High CDAI (22.1 - 76.0), n (%)	1 (6)	3 (10)	NS
DMARD therapy			NS
Monotherapy of csDMARDs, n (%)	2/17 (12)	10/30 (33)	NS
bDMARDs ± csDMARDs, n (%)	8/17 (47)	14/30 (47)	NS
JAKi ± csDMARDs, n (%)	7/17 (41)	6/30 (20)	NS
Prednisone, n (%)	5/17 (29)	11/30 (37)	NS
Mean daily dose prednisone (mg ± SD)	4.1 ± 1.6	4.1 ± 1.5	NS

Low or absent anti-S titers were confirmed before the third vaccination (Cohort A: median 19.5 U/ml, IQR 0.47-57; cohort B: median 65.9 U/ml, IQR 22-154) (p = 0.0018). Two weeks after the 3rd dose, a rapid and significant increase in anti-S were observed in 12/17 (82%) and 25/28 (89%) patients (Cohort A: median 2500 U/ml, IQR 798-2500; Cohort B: median 2500 U/ml, IQR 2500-2500) (NS). High levels of anti-S were maintained in the majority of patients 55% (11/20) until week 12 in both cohorts (Figure 1). NT50 against Wuhan-WT and other variants was assessed in 21 patients 2 weeks after the 3rd vaccine dose revealing a low or absent NT50 against delta in 38% of patients despite a median anti-S response of 2500 U/ml (IQR 798-2500). 14/21 patients had peak anti-S titres of 2500 U/ml, of those 12/14 developed a strong NT50 response against the delta variant.

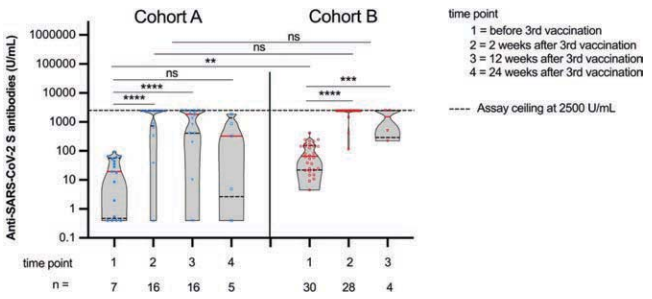

Figure 1.

Conclusion: Our data demonstrate that a 3rd vaccine dose, maybe complimented by temporary discontinuation of DMARD therapy, may lead to a rapid increase in anti-S antibodies when using a homologous vaccine and profound neutralizing activity in the majority of RA patients previously unresponsive to a standard two dose regimen. This seems to be independent of the interval to the previous standard vaccine regimen. As flares occurred in 36% of all patients, the necessity and length of DMARD discontinuation should be explored in more detail to balance between sustained control of disease activity and optimized vaccine induced immune responses.
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POS1278 EXCELLENT PROGNOSIS OF RHEUMATIC MANIFESTATIONS FOLLOWING COVID-19 VACCINATION: 7 MONTHS FOLLOW-UP DATA

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Background: It is well established that severe forms of SARS-CoV2 infection can induce a massive cytokine storm, which may disrupt the immune system stability and conceivably stimulate the development of reactive manifestations through a molecular mimicry process. Likewise, anti-COVID-19 vaccines, which have so far proved an excellent tolerability and safety profile, are able boost the immune response via different biologic technologies and adjuvant combinations possibly facilitating, in predisposed subjects, the onset of inflammatory or even autoimmune manifestations.
Objectives: We report a case series of suspected rheumatic adverse events following immunization (AEFI) associated with anti-COVID-19 vaccine. We focused our attention on the prognosis of these patients by analysing their available follow-up data.
Methods: We included patients evaluated at first-aid rheumatologic consultancy and at rheumatologic outpatient and inpatient clinic at Padua University Hospital between May and September 2021 presenting with new-onset rheumatic manifestation or a flare of an underlying rheumatic disease within 30 days after receiving an anti-COVID-19 vaccine dose. Inclusion and exclusion criteria were in accordance with the World Health Organization guidelines for AEFI surveillance. All patients were re-evaluated in January 2022: telemedicine or face-to-face visit. Response to therapy was classified as complete, good or absent according to the clinician's judgment based on clinical examination, patient's reporting and analysis of laboratory data.
Results: We identified 30 cases of suspected rheumatic AEFI reported in Table 1. Comprehensively the most common manifestations were inflammatory arthritis (40.0%), rheumatic polymyalgia (26.7%) and adult-onset Still disease (13.3%). Among patients with an underlying rheumatic disease we recorded an AOSD flare, a rheumatoid arthritis flare with involvement of hands proximal interphalangeal joints, one case of wrist arthritis in a patient with psoriatic arthritis, one of aortitis in a patient with large vessels vasculitis, one case of polyarthritis in undifferentiated connective tissue disease and a nephritis flare in a patient with systemic lupus erythematosus.
Treatment for the suspected AEFI was based on systemic glucocorticoids (GC) alone (63.3%), systemic GC plus IL-1R antagonists (13.3%), non-steroidal

autoinflammatory drugs (13.3%), intra-articular GC (6.6%), colchicine (3.3%) and non-steroidal anti-inflammatory drugs (13.3%).

At last follow-up contact (7.8±1.5 months) 26 patients (89.6%) were classified as complete responders. Eleven of them (42.3%) withdrew therapy without experiencing recurrence of disease manifestation. One patient with lupus nephritis had a proteinuric flare after the first BNT162b dose; he showed an initial good response to increased glucocorticoid therapy but had a new 24h proteinuria increase at second follow-up visit three months later requiring implementation of immunosuppressive therapy. Another patient with AOSD was in remission at last FU visit in December 2021 but required hospitalization in January 2022 for disease relapse due to a suspected gastrointestinal infection. Finally, one patient hospitalized for a seronegative polyarthritis after the first BNT162b dose achieved complete remission at last available contact (one month after hospital discharge) but was then lost in follow-up.

Conclusion: After a mean follow-up of 7.8±1.5 months nearly all of patients showed a complete/good response to standard therapy and about half of them withdrew the treatment without losing the remission status

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Table 1 Summary of patient's characteristics and follow-up data

New onset RD	Number of pts	Vaccine received	Dose	Time to disease onset (days)	Therapy	Clinical response at last-FU (January 2022)	Therapy withdrawal	Notes
AOSD	3 (10%)	BNT162b2: 2 pts (66.7%) ChAdOx1: 1 pts (33.3%)	1st dose: 3 pts (100%) 2nd dose: 0 pts (0%)	13 ± 9	Oral/iv GC + anti-IL1	**Complete**: 3 pts (100%) Mean FU: 7.6 ± 12 months	Yes: 0 pts (0%) No: 3 pts (100%)	• One patient was hospitalized two times during FU: the first time for MAS during GC tapering and then for disease relapse due to GI infection • One patient was hospitalized for pachymeningitis during GC tapering, then remission
RPm	8 (26.7%)	BNT162b2: 5 pts (62.5%) ChAdOx1: 3 pts (37.5%)	1st dose: 2 pts (25%) 2nd dose: 6 pts (75%)	5 ± 5	Oral GC	**Complete**: 8 pts (100%) Mean FU: 8.3 ± 0.6 months	Yes: 2 pts (25%) No: 6 pts (75%)	• One patient required second line therapy with MTX for GC resistant disease • One patient required GC intra-articular injection besides oral GC
Inflammatory arthritis Microcrystalline arthritis Seronegative polyarthritis Seronegative enthesopathia Seronegative RPm-like arthritis	11 (36.7%) 2 (6.7%) 4 (13.3%) 3 (10%) 2 (6.7%)	BNT162b2: 7 pts (63.4%) ChAdOx1: 5 pts (36.6%)	1st dose: 3 (27.3%) 2nd dose: 8 (72.7%)	15 ± 9	Intra-articular GC: 1 pts (9.1%) Colchicine: 1 pts (9.1%) Oral GC: 5 pts (45.5%) Oral NSAID: 4 pts (36.4%)	**Complete** 10* (100%) Mean FU: 7.4 ± 1.3 months	Yes: 7 pts (70%) No: 3 pts (30%)	*One patient was lost in FU
Cutaneous purpura	1 (3.3%)	BNT162b2	1st dose	2	Oral GC	**Complete** FU duration: 10 months	Yes	-
Ocular myositis	1 (3.3%)	BNT162b2	1st dose	7	Oral GC	**Good** FU duration: 13 months	No	-
RD flare	**Number of pts**	**Vaccine received**	**Dose**	**Time to disease onset (days)**	**Therapy**	**Clinical response at last-FU (January 2022)**	**Therapy withdrawal**	**Notes**
AOSD	1 (3.3%)	BNT162b2	1st dose	15	Oral GC+ anti-IL1	**Complete** FU duration: 7 months	Oral GC withdrawal	-
LVV	1 (3.3%)	BNT162b2	2nd dose	15	Iv and oral GC	**Complete** FU duration: 7 months	No	-
Psoriatic arthritis	1 (3.3%)	BNT162b2	1st dose	2	Intra-articular GC injection	**Good** FU duration: 8 months	No	-
RA	1 (3.3%)	BNT162b2	1st dose	10	Oral GC	**Complete** FU duration: 8 months	No	-
Lupus nephritis	1 (3.3%)	BNT162b2	1st dose	30	Oral GC	**Active disease** FU duration: 7 months	No, belimumab was added	Initial good response to increased glucocorticoid therapy. New 24h proteinuria increase at second follow-up visit three months later
UCTD	1 (3.3%)	BNT162b2	2nd dose	2	Oral GC	**Complete** FU duration: 6 months	Yes	-

Pts, patients; RD, Rheumatic disease; FU, follow-up; GC, glucocorticoid; NSAID, non-steroidal anti-inflammatory drug; AOSD, adult onset Still disease; MAS, macrophage activation syndrome; RPm, rheumatic polymyalgia; RA, rheumatoid arthritis; LVV, large vessel vasculitis; UCTD, undifferentiated connective tissue disease; MTX, metothrexate

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POS1279 FAVOURABLE COURSE OF COVID-19 IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER USING BIOLOGIC AGENTS

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Background: Serious infections are more frequently seen in patients with inflammatory rheumatic diseases, being treated with immunosuppressive or biologic disease-modifying antirheumatic drugs (b-DMARDs). Potential harmful effects of immunosuppressive drugs as well as b-DMARDs were a major concern during the early phases of the Coronavirus disease 2019 (COVID-19) pandemic, and preliminary data documented the worse outcome of COVID-19 associated with B cell depleting treatments (1). On the other hand, limited information has been shared about the course of COVID-19 in patients with monogenic autoinflammatory disorders using IL-1 inhibitors.

Objectives: We herein aimed to evaluate the course of COVID-19 in adult patients with the most common form of inflammasomopathy, Familial Mediterranean Fever (FMF), who were on biologic agents.

Methods: In this cross-sectionally study, FMF patients were evaluated by screening their clinical and electronic records in our database in October 2021. The FMF patients with a record of PCR-confirmed COVID-19 were investigated in more detail in our hospital. Characteristics of FMF findings as well as clinical and laboratory findings associated with COVID-19 were recorded from the outpatient follow-up cards.

Results: We identified 184 FMF patients using biologic agents, and their baseline characteristics are summarized in Table 1. Among them, 36 had PCR-confirmed COVID-19; 32 of them were currently on b-DMARD along with colchicine (31 anti-IL-1, 1 anti-TNF), and 4 of them had a previous history of b-DMARD treatment. Data about the course of COVID-19 could be reached in 34 patients. Four (11%) patients had an asymptomatic course. Remaining patients with symptomatic COVID-19 had the following symptoms: cough (50%), headache (47.2%), fever (44.4%), loss of taste and smell (41.6%), myalgia (0.6%), dyspnoea (27.8%), diarrhea (25%) abdominal pain (5.6%). Thorax computed tomography was performed in 10 patients, and findings of pneumonia were documented in 6 (16.7%). The mean values of the laboratory parameters were as follows: C-reactive protein 99.48 ± 112.66 mg/L; ferritin 316 ± 208.3; D-Dimer 2445 ± 3917, Lactate Dehydrogenase 253 ± 61, troponin T 26 ± 20, procalcitonin 0.348 ± 0.53. Lymphopenia

Table 1: Baseline clinical, laboratory, and treatment characteristics of FMF patients

Features	
Female/Male [n (%)]	21 (58.3%) /15(41.7%)
Age, years, mean (SD)	40.0 (11.5)
MEFV gene mutation [n (%)]	
- **M694V homozygous**	20 (55.6%)
- **M680I homozygous**	1 (2.8%)
- **M694V heterozygous**	1 (2.8%)
- **M694V/M680I heterozygous**	4 (11.1%)
- **M694V/V726A heterozygous**	2 (5.6%)
- **NA**	8 (22.2%)
Attack properties [n (%)]	
- **Fever**	30 (83.3%)
- **Peritonitis**	30 (83.3%)
- **Pleuritis**	14 (38.9%)
- **Arthritis**	26 (72.2%)
- **NA**	2 (5.6%)
Amyloidosis [n (%)]	16 (44.4%)
- **Renal**	14 (38.9%)
- **Gastrointestinal system**	5 (13.9%)
Renal Transplantation history [n (%)]	8 (22.2%)
Colchicine use	36 (100%)
Patients on biologic treatment [n (%)]	32 (88.9 %)
- **Anakinra**	22 (61.1%)

was detected in 5 (13.9%) patients; mean lymphocyte count was 1080 ± 363. Data about the treatment could be reached in 34 patients. Antiviral therapy was prescribed in 25 (69.4%) patients (favipiravir, n=22; and oseltamivir, n=3). Antibiotics were given to 6 (16.7%) patients, and 6 (16.7%) received hydroxychloroquine. Parenteral steroids were administered to 2 patients during the hospitalization. Six (16.7%) patients required hospitalization, and 2 (5.6%) required oxygen support, non-invasive mechanical ventilation, and one of them followed in the intensive care unit. Twenty-two patients were on anakinra treatment, and none of them required additional dose. Only 1 patient, a 61-year-old male patient with a history of lung lobectomy and renal transplantation, received tocilizumab due to macrophage activation syndrome, and he later died of sepsis. This patient was on anakinra until 2 years before, and it was discontinued due to an allergic reaction. Only 4 patients had a history of vaccination before COVID-19, and none of them developed pneumonia and required hospitalization. Six patients had FMF attacks after recovering from COVID-19. None of the patients developed thromboembolism and secondary bacterial infections.

Conclusion: This survey identified 36 biologic b-DMARD receiving FMF patients, who had COVID-19. All but 1 patient had complete recovery, and b-DMARD usage did not negatively affect the COVID-19 course. None of the patients currently on anti-IL-1 or anti-TNF had a worse outcome. Based on these observations, it can be suggested that refractory FMF patients can continue their b-DMARD treatments when they had COVID-19.

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POS1280

EFFECTS OF ANTI-SARS-COV-2 VACCINATION ON SAFETY AND DISEASE EXACERBATION IN BEHCET'S DISEASE PATIENTS: A SINGLE CENTRE STUDY

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Background: Pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome – coronavirus 2 (SARS-CoV-2), has become a major global health issue since December 2019. Patients affected by systemic rheumatic disorders represent a high-risk group for severe COVID-19. During the COVID-19 pandemic, vaccination has become one of the cornerstones of the fight against this disease. The EULAR and the ACR recommend vaccination in all patients with rheumatological diseases. There is a paucity of data regarding the safety of COVID-19 vaccines in patients with rheumatic and musculoskeletal diseases such as Behçet's disease (BD).

Objectives: In this study, we evaluated the safety and tolerance of COVID-19 vaccines, post-vaccine BD exacerbation and discontinuation of BD therapy in BD patients by retrospectively examining our BD cohort, from the patients' perspective.

Methods: We retrospectively evaluated 450 BD patients followed in our clinic using hospital records and formed a retrospective cohort of patients who met the International Study Group (ISG) criteria. COVID-19 vaccination status, vaccine type (inactivated or mRNA), post-vaccine side effects and exacerbations, drug compliance, change in treatment after exacerbation, and post-vaccine COVID-19 occurrence were evaluated by interviewing patients over the phone or face to face. Patient demographics, comorbid diseases, and active BD treatments were collected from our hospital records. Disease activity was measured using the BSAS and the BDCAF form.

Results: Our cohort consisted of a total of 450 BD patients. Two hundred and eighty seven patients had at least 1 dose of the COVID-19 vaccine. Of the total number of COVID-19 vaccines (n= 639), 379 (59%) were Pfizer-BionTech vaccines and 257 (41%) were Sinovac vaccines. The side-effects after first, second, third and fourth vaccine dose were 151 (52.6%), 135 (47%), 29 (10.1%) and 3 (1%), respectively. Behçet flare after first, second, third and fourth vaccine dose were 151 (52.6%), 135 (47%), 16 (22.9%) and 3 (33.3%), respectively. The most common side effects were arm pain, joint pains or arthritis, malaise, while the most common BD exacerbations were arthralgia or arthritis, oral aphthae, papulopustular eruption Pfizer-BionTech and Sinovac vaccines were compared in terms of side effects, there was a significant difference after the 1st (p<0.001) and 2nd doses (p<0.001), but no significant difference was found at the 3rd dose (p= 0.353) (Table 1). When Pfizer-BionTech and Sinovac vaccines were compared in terms of BD exacerbations, no significant difference was found after the 1st (p= 0.417), 2nd (p= 0.465) and 3rd doses (p= 0.565). Only 4 patients (1.3%) developed exacerbation with organ involvement after COVID-19 vaccine. Anterior uveitis developed in 2 patients, panuveitis in 1 patient, panuveitis and deep vein thrombosis in one patient.

Table 1. Side effects and Behçet's flare according to COVID vaccines

Side effects according to COVID vaccines

COVID vaccine, n/ N	Side effects after first dose of vaccine	p	Side effects after second dose of vaccine	p	Side effects after third dose of vaccine	p	Side effects after fourth dose of vaccine	p
Sinovac Biontech	**47 (39.5)** **104 (61.9)**	**<0.001**	**34 (30.1)** **101 (63.1)**	**<0.001**	**9 (36)** **20 (47.6)**	**0.353**	**None** 3 (33.3)	-
Behçet flare according to COVID vaccines								
COVID vaccine, n/N	Flare after first dose of vaccine	p	Flare after second dose of vaccine	p	Flare after third dose of vaccine	p	Flare after fourth dose of vaccine	p
Sinovac Biontech	**13 (11.0%)** **24 (14.3%)**	**0.417**	**18 (15.9%)** **31 (19.4%)**	**0.465**	**5 (20.0%)** **11 (26.2 %)**	**0.565**	**None** 3 (33.3)	-

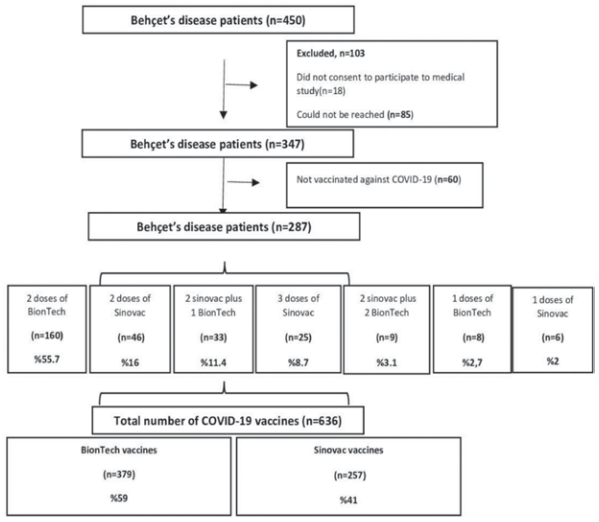

Figure 1. Flow chart of the study

Conclusion: In conclusion, our study shows that the COVID-19 vaccine is well tolerated in BD patients, and that post-vaccine Behçet's exacerbation predominantly includes mucocutaneous and articuler findings, and exacerbations with organ involvement are rare. According to the COVID-19 vaccines, although the side effects were more in the Pfizer-BioNTech group compared to the Sinovac group, there was no difference between Behçet's flare compared to the COVID-19 vaccines.

Disclosure of Interests: None declared

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POS1281 DIFFERENT HUMORAL BUT SIMILAR CELLULAR RESPONSES OF PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES UNDER DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS AFTER COVID-19 VACCINATION

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Background: The interplay between humoral and cellular response after vaccination against SARS-CoV-2 in patients (pts.) with autoimmune inflammatory rheumatic diseases (AIRD) remains unknown.
Objectives: To investigate the impact of different immunosuppressive therapies on the development of humoral and cellular immune responses to full 2-dose SARS-CoV-2 vaccination in AIRD pts. with stable low disease activity.
Methods: The immune reactivity to COVID-19 vaccination was investigated in a prospectively recruited AIRD cohort with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis which received a therapy with IL-17i, TNFi, JAKi or MTX (alone or in combination). Almost all patients received mRNA-based vaccine, only 4 patients had a heterologous scheme. Anti-spike(S) antibodies(ab.) and sera neutralizing capacity (neutralization dilution 50; ND50) were measured 4 weeks after the first (prime+4w) and 4 weeks after the second vaccination (boost+4w). Vaccine-specific cellular immunity was evaluated by quantifying expression of activation markers on T cells as well as their production of key cytokines, at prime+4w and boost+4w.
Results: Overall, a total of 92 pts. were included in the final cohort. 31 (33.7%) pts. were on TNFi, 24 (26.1%) on IL-17i, 24 (26.1%) on JAKi, each group encompassing pts. receiving drug inhibitors alone or in combination with MTX.13 (14.1%) were treated with MTX alone. The median time between the vaccination and blood sampling was 31 [IQR: 28-34] days after prime+4w and 28 [IRQ: 28-28] days after boost+4w. Although at prime+4w only 34/90 (37.8%) of pts. presented neutralizing ab., the majority (86/91, 94.5%), developed them at boost+4w. The highest neutralization titer developed the pts. on IL-17i both at prime+4w (74 [IQR: 13-91]) and boost+4w (798 [IQR: 511-1344]), while no statistically significant differences were found in the neutralization titer at boost+4w for the TNFi, JAKi, and MTX groups: 207 ND50 [IQR: 120-576], 319 [IQR: 133-461] and 749 [IQR: 264-1920], respectively. 81/90 (90.0%) pts. developed IgG ab. against SARS-CoV-2 S-protein at prime+4w and 91/92 (98.9%) at boost+4w. Pts. receiving IL-17i developed higher ab. titers (8295 U/mL [IQR: 4586-11,237]) compared to the other three groups: JAKi (4405 U/mL [IQR: 1436-7265], TNFi (2313 [IQR: 1156-3630] U/mL) and MTX (2010 U/mL [IQR: 693-9254]). Neutralization capacity correlated well with the titer of anti-S ab. at both timepoints. Co-administration of biologic/tsDMARDs and MTX led to lower titers compared to biologic/tsDMARDs monotherapy. All therapies left frequencies of $CD154^+CD137^+$ $CD4^+$ T cells and $CD137^+$ $CD8^+$ T cells at prime+4w and boost+4w unchanged. Polyfunctionality and T cell cytokine profiles across therapies did not significantly vary at boost+4w.
Conclusion: Even after insufficient seroconversion for neutralizing capacity and ab. response against SARS-CoV-2 S-proteins between pts. of different mod of action agents, particularly for MTX and JAKi after first vaccination, a second vaccination covered almost all pts. regardless of DMARDs therapy, with better outcomes in those on IL-17i. T cell immunity revealed similar frequencies of activated T cells in all modes of action after the second vaccination.

Table 1. Demographics and therapy

	All	IL-17i	IL-17i+MTX	TNFi	TNFi+MTX	JAKi	JAKi+MTX	MTX
Patients (n)	92	19	5	27	4	18	6	13
Age (years)	50 [39-56]	42 [36-53]	37 [32-38]	51 [42-56]	58 [54-61]	50 [43-56]	55 [49-59]	54 [37-64]
Female sex	46 (50.0%)	6 (31.6%)	3 (60.0%)	10 (37.0%)	3 (75.0%)	13 (72.2%)	3 (50.0%)	8 (61.5%)
Patients with concomitant glucocorticoids (n)	13 (14.1%)	1 (5.3%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	5 (27.8%)	3 (50.0%)	3 (23.1%)
Prednisolone dosage (mg)	5.0 [2.5-5.0]	5.0 [5.0-5.0]	3.0 [3.0-3.0]			5.0 [2.5-5.0]	2.0 [2.0-4.0]	5.0 [4.0-5.0]

IL interleukin, i inhibitor, MTX methotrexate: TNF tumor necrosis factor, JAK janus kinase. For quantitative variables, data are provided as median [IQR], for categorical variables the count (% frequency)

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POS1282 PEDIATRIC INFLAMMATORY MULTISYSTEM SYNDROME TEMPORALLY-ASSOCIATED WITH SARS-COV-2 – A PORTUGUESE SINGLE CENTRE CASE SERIES

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Background: Across the globe, coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 appears to affect paediatric population in a milder and non-threatening way, when compared to adults. However, since April 2020 case reports of previously healthy children presenting with unremitting fever, biologic inflammatory syndrome and cardiac dysfunction have been emerging. This syndrome, which has been termed Pediatric Inflammatory Multisystem Syndrome Temporally Associated with SARS-CoV-2 infection (PIMS-TS), represents a rare complication of COVID-19 in children[1].
Objectives: To describe the clinical, laboratory and imaging characteristics, course, management and outcomes of hospitalized children diagnosed with PIMS-TS in a Portuguese tertiary care hospital.
Methods: A retrospective study including children (< 18 years) that attended our hospital from April 2020 to December 2021 was performed. All the children included fulfilled the case definition of PIMS-TS published by the Centre for Disease Control and Prevention. Sociodemographic and clinical data, laboratory markers and imaging findings were collected.
Results: A total of 19 children met the criteria for PIMS-TS, 68% male with a mean age at diagnosis of 8 years old (IQR 5.8-15). They were all caucasian, except for a mixed-race patient, and all previously healthy, except one patient who was obese. Twelve had recent infection by SARS-CoV-2 detected by reverse transcriptase (RT) PCR and 18 had positive IgG serology.
All had fever at diagnosis, with a median duration of 6 days (IQR 5-6) and 89.5% had mucocutaneous, gastrointestinal and hematological attainment,

respectively. Other affected systems were respiratory (73.7%), cardiovascular (63%), lymphoid organs (52.6%), musculoskeletal (47%), genito-urinary (31.6%) and neurological (26.3%). Laboratory findings can be found in Table 1. Thirty-six percent were admitted in intensive care unit for a median duration of 8 days (IQR 4-9). 42.1% needed respiratory support, 87.5% with supplemental oxygen therapy, 62.5% with mechanical ventilation and 12.5% with non-invasive ventilation. All patients received intravenous (IV) immunoglobulin, 52.6% IV corticosteroid (CS) pulses and 78.9% IV and oral CS. Other treatments included acetylsalicylic acid (n=18), heparin (n=8) and antibiotic therapy (n=19) - Table 3. Seventeen fully recovered and 2 had sequalae: one of them with coronary artery aneurysms and other exertional dyspnea.

Table 1 – Laboratory results at presentation.

Hematology [a]		
	Reference range	
Total white blood cells count, x10⁹/L	4.0-11.0	10.19 (7.37-14.85)
Neutrophil count, x10⁹/L	1.5-7	10.38 (5.71-11.79)
Lymphocyte count, x10⁹/L	1.5-4	0.94 (0.67-1.45)
Hemoglobin, g/dL	12-16	11 (9.4-12.1)
Platelet count, x10⁹/L	150-400	156 (104-248)
Inflammatory markers [a]		
	Reference range	
C-reactive protein, mg/L	0-3	218.5 (132-262)
Procalcitonin, ng/mL	0-0.05	2.72 (0.00-8.18)
Ferritin, ug/L	6-140	598 (226-769)
Cardiac markers [a]		
Troponin, ng/L	0-34	118 (34-1021)
CK-MB, ng/mL	0.00-6.4	0.7 (0.3-8.1)
Pro-BNP, pg/mL	0-100	238.4 (67.5-525)

Abbreviations: PIMS-TS, pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2.
[a] Data showed as median and inter Quartile Range (P25, P75)
[b] Data showed as frequency and percentage

Conclusion: In this case series, there was a broad spectrum of clinical symptoms and disease severity, ranging from fever and systemic inflammation to critical care admission with myocardial injury, shock, and development of coronary artery aneurysms.

Despite short-term morbidity, there were no mortality cases, with most of them recovering without sequelae. All physicians providing clinical care to children should consider this rare but severe delayed syndrome in paediatric population.

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POS1283 THE COURSE OF NOVEL CORONAVIRUS DISEASE 2019 (COVID-19) IN PATIENTS WITH IGG4-RELATED DISEASE TREATED WITH RITUXIMAB

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Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) raised many questions and concerns about the safety of different immunosuppressive agents in patients (pts) with rheumatic diseases during the pandemic. There is some data that anti-B-cell depletion strategies could lead to more severe disease course. Rituximab (RTM) is one of the most effective, safe and well tolerated agents in IgG4-related disease (IgG4-RD) treatment. Information about the course of COVID-19 in pts with IgG4-RD is lacking.

Objectives: To examine clinical course of COVID-19 in pts with IgG4-RD treated with anti-CD20 monoclonal antibody (RTM).

Methods: Single center observational study. We searched in our clinical base from 2019 to 2021 years for pts with IgG4-RD, treated with RTM within this period. Diagnosis of IgG4-RD was based on comprehensive diagnostic criteria (H. Umehara, 2011). COVID-19 infection was registered when PCR test results were positive. RTM was administered in two 1000 mg infusions 14 days apart for the 1st course, then 500 mg every 6 months. We used mean ± standard deviation and median values with interquartile range of 25 - 75 percentile to characterize quantitative data.

Results: Fifteen pts, 6 women and 9 men, mean age 53.2 ± 12 years, receiving RTM monotherapy were included. The majority of patients (80%) had multiple organ involvement, mean number 2,3 (from 1 to 5): dacryadenitis – 11 pts, sialadenitis – 10 pts, AIP 1 – 4 pts, lung disease – 3 pts, sclerosing cholangiris – 2 pts, kidney disease – 2 pts, retroperitoneal fibrosis – 1 pt, aortitis – 1 pt, prostatitis – 1 pt. Median duration of IgG4-RD before COVID-19 onset was 48 [27;72] months, median duration of RTM treatment was 22 [11,5;30,5] months and median time from the last dose of RTM was 2 [1;4,5] months. Three pts had arterial hypertension or coronary heart disease anamnesis, 4 pts had asthma, 2 pts were overweight and 1 had class 3 obesity. No pts were vaccinated against SARS-CoV-2. Six patients (40%) required hospitalization and 4 of them received IL-6 inhibitors, only 1 required mechanical lung ventilation, 6 patients (40%) had only minor symptoms and didn't require any specific treatment, glucocorticoids were administered to 8 patients. All patients, except one, were older than 50, but they didn't have severe comorbidities. One patient, a 46 year-old man with a long anamnesis of IgG4-related dacryo- and sialadenitis, bronchial asthma, arterial hypertension class 3 and class 3 obesity, died. Due to small number of studied pts no statistical correlations could be established.

Conclusion: The proportion of hospitalized pts with IgG4-RD and RTM treatment was surprisingly high. The worst course was in patient with severe comorbidity. It appears that RTM can have negative impact on susceptibility to COVID-19 and its disease course.

Disclosure of Interests: None declared

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POS1284 PAINFUL CERVICAL INVOLVEMENT AND FEBRILE TORTICOLLIS: A FREQUENT SYMPTOM OF PIMS

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Background: Pediatric Inflammatory Multisystemic Syndrome associated to SARS-CoV2 (PIMS) happens 4 to 6 weeks after SARS-CoV2 infection[1-2]. Its early diagnostic recognition as well as its early management is important to avoid cardiac complications related to this pathology.

Objectives: To highlight a frequent symptom in PIMS and improve its therapeutic care.

Methods: The JIR Cohort database, an international registry collecting data on patients with pediatric inflammatory diseases, was consulted to include patients between 03/15/20 and 12/31/2021.

Results: Of the 140 patients in whom a diagnosis of PIMS was retained, we present a series of 38 patients (27%) who presented at diagnosis or during evolution, febrile torticollis or painful cervical involvement. These patients were on average 8.2 years old (0.6-15.2). The proportion of boys was 14 out of 38 (37%). Twenty-four patients out of 33 (73%) were hospitalized in intensive care. Ten patients out of 38 (26%) underwent cervical imaging, 5 (50%) had abnormalities such as collection or infiltration of the soft tissues. At the therapeutic level, 27/38 patients (71%) received corticosteroid therapy, 33/38 (87%) immunoglobulins, and 26/38 (68%) antibiotic therapy.

Conclusion: PIMS is a pathology with significant clinical heterogeneity and severe consequences in case of delay in therapeutic management. In this epidemic context, it is important to consider PIMS in any patient with febrile torticollis, especially if he does not respond to antibiotics.

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POS1285 IMMUNOGENICITY AND SAFETY OF THE CHADOX 1 COVID-19 VACCINE IN PATIENTS WITH AUTOIMMUNE DISEASES AND HEALTHY CONTROLS: DATA FROM SAFER STUDY

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Background: Patients with autoimmune inflammatory diseases (AID) have been prioritized for urgent vaccination to mitigate COVID-19 risk. However, few studies in the literature assessed the immunogenicity and safety of the COVID-19 vaccine in patients with AID.

Objectives: In this context, the present study aims to evaluate the immunogenicity and safety of the vaccine against COVID-19 in patients with AID.

Methods: These data are from "Safety and efficacy on COVID-19 Vaccine in Rheumatic Disease" - SAFER study, a Brazilian multicentric prospective phase IV study to evaluate COVID-19 Vaccine in AID, in the real-life, in Brazil. Immunogenicity and adverse events (AE) from a single center were assessed, after 2 doses of ChAdOx1 (Oxford/AstraZeneca), 8 weeks of interval, in patients with AID and healthy controls (HC). Inclusion criteria were age ≥ 18 years and fulfilling criteria according to international classification for AID. Exclusion criteria: pregnancy, previous severe AE to any vaccine, other immunosuppression causes. Stratification of post-vaccination AE was performed using a diary, filled out daily and returned at the end of 28 days for each dose. Participants were followed up through blood collection for measurement of IgG antibodies against SARS-CoV-2 spike receptor-binding domain by chemiluminescence (SARS-CoV-2 IgG II Quant assay, Abbott Laboratories, Abbott Park, IL, USA) at baseline and 28 days after the second dose. The seropositivity was defined for titers ≥50 AU/mL. Quantitative analyses were presented as observed frequency, percentage, central tendency, and variability measurements. The sample's normal distribution was verified through the Shapiro-Wilk test. The Kruskal-Wallis test and the post-hoc Dwass-Steel-Critchlow-Fligner pairwise comparisons test were used to compare the IgG-S titers between the groups through the evaluation period. Categorical data were addressed using the Fisher´s exact or Chi-squared (χ^2) test. An alpha level of 5% significance was used in all analyses.

Results: A total of 377 volunteers with AID and 50 HC were included in the study. Patients with spondyloarthritis (N=64), systemic lupus erythematosus (N=63), rheumatoid arthritis (N=61), primary Sjögren's syndrome (N=61), vasculitis (N=31), systemic sclerosis (N=14), inflammatory myopathy (N=9), Crohn´s disease (N=49), ulcerative colitis (N=11) and other systemics AID (N=12) were evaluated. Both groups had female predominance (73.5% vs. 74.0%, p=0.937) and were homogeneous for age (43.5 vs. 41.7,p=0.308). The seroconversion among those not reactive (IgG-S negative at baseline) (46 HC and 191 AID), 28 days after second dose was 97.1% for spondyloarthritis (p=0.425), systemic lupus erythematosus 88.2% (0.006), rheumatoid arthritis 93.5% (0.158), primary Sjögren's syndrome 92.6% (0.133), systemic sclerosis or inflammatory myopathy 47.1% (0.001), inflammatory bowel disease 100% (0.999) and vasculitis 80% (0.006), while in healthy control was 100%. In comparison with HC, there was a statistically significant difference in IgG-S titles only in systemic sclerosis or inflammatory myopathy (1.694 AU/ml vs. 3.719 AU/ml; p=0.006). Both groups only presented mild AE. Pain at the injection (85.7% vs. 78.4%, p=0.239), headache (67.3% vs. 53.8, p=0.074) and fatigue (59.2% Vs. 46.2%, p=0.089) were more common in HC than AID. Overall, reactions like arthralgia (52.6 vs. 22.4%, p<0.001), hematoma (14.1 vs. 4.1%, p=0.05), cutaneous rash (9.5 vs. 0%, p=0.024) were more frequent in AID. Most participants related that they felt safer after receiving a COVID-19 vaccination, and 52.4% did not reported a worse patient global assessment (PGA) index.

Conclusion: In conclusion, our data indicated that ChAdOx1 vaccine is safe and induced high titers and seroconversion rate in AID. More severe AID, such as vasculitis, systemic lupus erythematosous, and systemic sclerosis and myositis showed a lower seroconversion rate. Further analysis will explore the association between immunossupressant and reactivity, and booster dose.

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POS1286 SEVERITY OF COVID-19 IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING BIOLOGICAL DMARDS

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Background: The safety of biological DMARDs for rheumatic diseases in the context of the covid 19 pandemic is one of the key aspects of modern rheumatology

Objectives: assess the severity of the course of COVID-19 infection in patients with rheumatoid arthritis receiving various biological disease-modifying antirheumatic drugs.

Methods: to assess the severity of the course of SARS-CoV-2, discharged epicrisis from hospitals or the conclusion of computed tomography were used.

Since March 2020 to November 2021, among the 1389 patients with rheumatic diseases observed at the of the anticytokine therapy center of the North-Western State Medical University Named after I.I. Mechnikov 105 cases of COVID-19 infection of patients with rheumatoid arthritis were registered, of which 53 patients received outpatient treatment, and 52 patients received inpatient treatment. In 76% of cases, patients received biological DMARDs in combination with synthetic DMARDs.

Results: In patients treated on an outpatient basis, only 17% (9 patients) underwent chest X-ray examination, according to which grade 2 CT was observed in three patients. Among hospitalized patients, multispiral computed tomography was performed in all cases (n=8; 15.3%) of this group of interstitial lung lesions consistent with CT-1. At the same time, CT-2 was determined in 25 (48,1%), CT-3 - in 16 (30.8%), CT-4 - in 3 (5.8%) (2 lethal cases) patients. The most severe cases of COVID-19 (CT-3 and CT-4) were observed most often in patients (12 and 3, respectively) treated with rituximab (Table 1).

Table 1. The volume of lung damage in patients with RA with COVID-19 who received biological DMARDs before infection

	CT-1 (<25%)	CT-2 (25-50%)	CT-3 (50-75)	CT-4
TNF-alpha inhibitors (n=4)	2	2		
Abatacept (n=5)	1	2	2	
Rituximab (n=37)	3	19	12	3
Tocilizumab (n=1)			1	
Tofacitinib (n=5)	2	2	1	
Total	8 (15,3%)	25 (48,1%)	16 (30,8%)	3 (5,8%)

Conclusion: Previous rituximab therapy in patients with rheumatoid arthritis is the most unfavorable prognostic factor during COVID-19 infection.

Disclosure of Interests: None declared

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Pain in rheumatic diseases, including fibromyalgia_

POS1287 INFLUENCES ON FIBROMYALGIA AND AUTOANTIBODIES DIRECTED TO NEURO- AND VASOREGULATORY MOLECULES NEED TO BE CONSIDERED IN BIOMARKER RESEARCH

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Background: Fibromyalgia syndrome (FMS) is often present in autoimmune diseases but can also occur in its primary form. Biomarkers for FMS are currently missing. Systemic chronic inflammation, dysautonomia and metabolic dysfunction have been suggested to contribute to the disease. Recent studies indicate that FMS involves autoantibodies (abs), which bind to neurons, macrophages and endothelial cells.

Objectives: In the present study, we aimed to delineate changes in natural abs directed to neuro- and vasoregulatory molecules and potentially confounding factors, which could influence these abs and disease state.

Methods: Sera from 91 patients with primary FMS (pFMS), 24 patients with secondary FMS (sFMS) and 31 healthy controls (HC) were analysed for the presence of 27 different natural abs directed to e.g., cholinergic, opioid, cannabinoid, endothelin or complement receptors or angiotensin system molecules by individual ELISAs (CellTrend GmbH, Luckenwalde, Germany). All participants were characterized by several questionnaires to obtain demographic data and measures of disease state (using the Widespread Pain Index (WPI) and Symptom Severity Score (SSS)). Linear regression on log-transformed ab levels adjusted for potential confounders was used to compare ab levels between groups. Random forest analysis was applied to differentiate between pFMS and HC by measuring the Area Under the Curve Receiver operating characteristics (AUC-ROC).

Results: Compared to HC, patients with pFMS showed increased levels of abs directed to ACE II, the angiotensin receptor type-2 (AT2R), the cannabinoid receptor type 1 and 2 (Can1-R, Can2-R), the endothelin receptor type-B (ETBR), the opioid receptor κ (Op-k-R) and lower levels against the complement receptor 5a (C5a-R) and the muscarinergic acetylcholine receptor type 3 (M3)(Figure 1). After adjustment for age (linear and squared) and sex, differences in the ab levels remain significant for abs against ACE II, AT2R, ETBR and the Op-k-R. However, none of which remained significant after further adjustment for Body Mass Index (BMI). Random forest analysis of unadjusted ab levels revealed an AUC-ROC of 0.94 for pFMS compared to HC with an average accuracy of 0.85 and a kappa of 0.55. Again, after adjusting the ab levels for age, sex and the BMI, AUC-ROC to discriminate HC from pFMS patients decreased to 0.73 (accuracy = 0.79, kappa = 0.33).

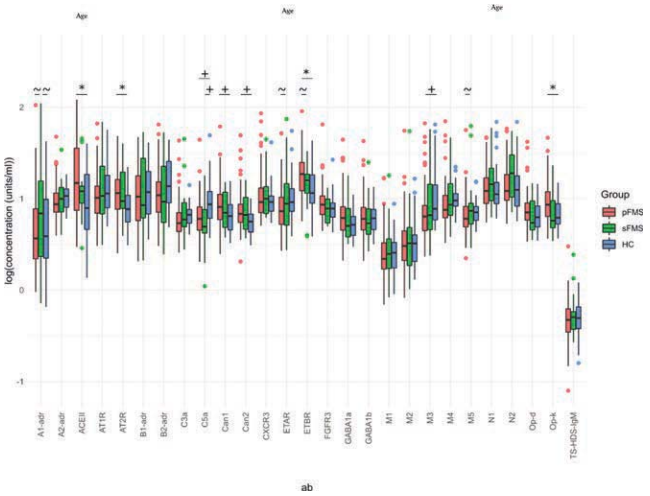

Figure 1. Boxplots of logarithmized abs levels between groups. *: p < .05 in unadjusted analysis and after adjusting for age and sex, ~: p < .05 only significant after adjusting for age and sex, +: p < .05 only in unadjusted analysis (all FDR-corrected within group comparisons across abs). Unadjusted Adjusted for age, sex and BMI

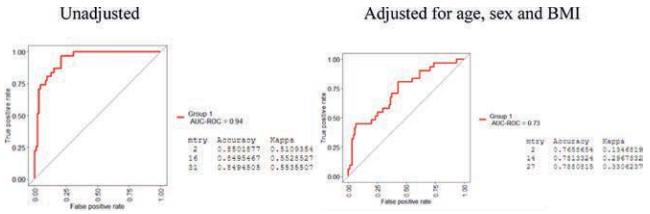

Figure 2. AUC ROC as detected by random forest analysis in pFMS patients versus HC for unadjusted ab levels as well as for ab levels adjusted for age, sex, and BMI.

Conclusion: Abs might be potential biomarkers for pFMS. However, these results highlight the important role of correct covariate adjustment for research on biomarkers supposed to classify FMS or other diseases. In FMS, increase in BMI might be a cause or a consequence of FMS and it is also unknown how BMI and abs influence each other. Thus, BMI might or might not be a confounder so that adjusting for BMI might be correct or incorrect. However, these abs could provide a link to understand how acquired conditions interact with the immune system.

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POS1288 TREAT TO TARGET MANAGEMENT OF FIBROMYALGIA: EVIDENCE-BASED CONSENSUS ON CLINICAL PRACTICE GUIDELINES

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Background: Because of the subjective character of symptoms, absence of a diagnostic test, modest response to treatments, and at times, patient reports of important functional disability, fibromyalgia remains a challenge for the treating health care professionals in the standard clinical practice.

Objectives: To develop an up to date consensus, evidence-based clinical practice guidelines for treat to target management of fibromyalgia.

Methods: 15 key clinical questions were identified by a scientific committee according to the Patient/ Population, Intervention, Comparison, and Outcomes (PICO) approach. A literature review team performed a systematic review to summarize evidence advocating the benefits and harms of available pharmacologic and nonpharmacologic therapies for fibromyalgia. Subsequently, recommendations were formulated. The level of evidence was determined for each section using the Oxford Centre for Evidence-based Medicine (CEBM) system. A 3-round Delphi process was conducted with 16 experts. All rounds were conducted online. A consensus was achieved on the direction and the strength of the recommendations.

Results: An online questionnaire were sent to expert panel who participated in the three rounds (response rate 100%). At the end of round 3, a total of fifteen recommendation items, categorized into 10 sections to address the main fibromyalgia categories, were obtained. Agreement with the recommendations (rank 7-9) ranged from 85-100%. Consensus was reached (i.e.≥80%of respondents strongly agreed or agreed) on the wording of all the 15 clinical standards identified by the scientific committee. Algorithm for the management of fibromyalgia have been suggested.

Conclusion: These recommendations provide an updated consensus on both the non-pharmacological as well as the pharmacological treatment of fibromyalgia. The provide strategies to reach optimal treat to target outcomes in common clinical scenarios, based on a combination of evidence and expert opinion. Best treatment decisions should be tailored to each individual patient situation.

Disclosure of Interests: None declared

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Spine, mechanical musculoskeletal problems, local soft tissue disorders

POS1289 ANALYSIS OF INFECTIOUS SPONDYLODISCITIS: FIVE-YEARS DATA

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Background: Spondylodiscitis (SD) is an infection of the vertebral body or disc and may also extend to the epidural space, posterior elements, and paraspinal soft tissues. It is a cause of morbidity and mortality. However, the diagnosis is often delayed because of the non-specific clinical features.
Objectives: In this study, we aimed to describe the clinical and diagnostic features of infectious SD
Methods: We conducted a retrospective study including 40 cases of infectious SD, performed over a period of five years (2014-2019). Epidemiological, clinical characteristics, laboratory results and imaging findings were uniformly collected.
Results: : Of the 40 patients, 37.3% were male. The mean age was 53.3 ± 13.9 years [28-83] and the median Charlson Comorbidity Index was 1. Advanced age, tuberculosis and brucellar contagion were the predominant risk factors. The median duration from onset to diagnosis was 41 days [8-300]. Low back pain (LBP) was the most common symptom (98%). Lumbar spine was the most frequent location (71%). Seven patients had contiguous multiple levels (>2 vertebral bodies). Neurologic symptoms (radicular pain, spinal chord compression, neurologic loss) were observed in 15 patients. The median erythrocyte sedimentation rate was 54 mm/1st h [13-223], the median CRP was 26.3 mg/L [7-387]. Leukopenia (<4000 WBCs/mm3) was found in three patients (9.8%). Magnetic resonance imaging confirmed the diagnosis in all cases, and revealed spinal epiduritis in 17 patients (34.8%), paravertebral abscesses in 11 (20.3%) and spinal cord compression in 4 (7.8%). Pathogens were isolated in 19 cases. Computed tomography-guided percutaneous disc biopsy (PDB) was performed in 16 (53.5%) and was conclusive in (11/15) cases (66.8%). Mycobacterium tuberculosis (MT) was the most common pathogene (46.4%) followed by Brucella (21.4%), Pyogenes (17.8%) and Gram-negative bacteria (14.2%). One patient had both MT and Staphylococcus haemolyticus.Paravertebral abscess formation (19.6%) occurred most frequently in patients with tuberculous SD (P= 0.02). Leucocytosis (>10,000 WBCs/mm3) was significantly higher in patients with Pyogenes SD (p=0.002) than in patients with other types of SD. All patients were treated with antibiotics and only one patient underwent surgical act. The outcome was favourable in 27 cases (86.8%).
Conclusion: Spondylodiscitis should be considered for all patients presenting with chronic backpain especially when associated with laboratory examination abnormalities. In our study, tuberculous spondylodiscitis was the most frequent, which highlights the fact that osteoarticular tuberculosis remains endemic in developing countries, where it still constitutes a major public health problem
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.2892

POS1290 EFFICACY AND SAFETY OF SODIUM THIOSULFATE IN CALCIFIC TENDINITIS OF THE ROTATOR CUFF – AN INTERIM ANALYSIS OF A RANDOMIZED CLINICAL TRIAL

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Background: Calcific tendinitis of the rotator cuff is one of the most common causes of shoulder pain. (1) Ultrasound guided percutaneous lavage (UGPL) is indicated when conservative treatments have failed. (2) Recent reports have shown the interest of topical sodium thiosulfate (STS) in the treatment of other diseases characterizes by ectopic calcifications (3, 4, 5).
Objectives: To assess the efficacy and safety of UGPL with STS versus with saline solution (standard of care - SOC) in calcific tendinitis.
Methods: Double-blinded randomized clinical trial including adult patients with calcific tendinitis, shoulder pain for more than 3 months and at least one positive shoulder impingement test. Only dense type A calcifications (according to the Molé Classification) > 5 mm in diameter were included. Patients were randomized in two groups: STS and saline solution lavage. Informed consents were collected. Both groups were reevaluated at week 1, month 1 and month 3 after UGPL. Pain Visual Analogue Scale (VAS) at rest and during activities, shoulder range of motion and strength, impingement tests, Disabilities of the Arm, Shoulder and Hand (DASH), DASH-Work, EuroQol five-dimensional (EQ5D) and University of California at Los Angeles (UCLA) scores, ultrasound (US) and radiographic evaluations were performed on all follow up visits.
SPSS was used for statistical analysis and significance level was defined as 2-sided p<0.05.
Results: Twenty-six patients were included, where 76.9% (20) were women, with a mean age of 51.2 (SD=9.0) years old. The mean duration of pain before the procedure was 12.7 months (SD=11.3) (minimum of 3 months and a maximum of 48 months).
Fifteen patients (57.7%) were randomized to the control group (SOC) and performed a saline UGPL; the other 11 patients (42.3%) were randomized to the treatment group (STS). Demographic and baseline clinical characteristics are shown in Table 1. Since patient inclusion is dynamic, our sample met 23 patients at week 1 (SOC group = 13 and STS group = 10), 19 patients at month 1 (SOC group = 10 and STS group = 9) and 16 patients at month 3 (SOC group = 8 and STS group = 8).

Table 1. Demographic and baseline clinical characteristics.

	STS lavage (n=11)	Saline solution lavage (n=15)	p-value
Age (years), M (SD)	52.3 (10.6)	50.3 (8.0)	NS
Sex, female % (n/N)	72.7% (8/11)	80% (12/15)	NS
Dominant side, right % (n/N)	100% (11/11)	93.3% (14/15)	NS
Nocturnal pain, yes % (n/N)	100% (11/11)	100% (15/15)	NS
VAS at rest (0–10), M (SD)	5.7 (2.0)	5.9 (2.1)	NS
VAS during activities (0–10), M (SD)	7.1 (1.8)	6.0 (2.5)	NS
DASH Score, M (SD)	60.2 (14.0)	52.6 (13.8)	NS
DASH-Work Score, M (SD	73.4 (11.0)	63.4 (22.6)	NS
EQ5D, M (SD)	0.2897 (0.3)	0.4070 (0.2)	NS
VAS EQ5D (0–100), M (SD)	54 (15.9)	58 (20.0)	NS
UCLA score, M (SD)	18.7 (4.1)	14.7 (3.3)	0.014
Bursitis, yes % (n/N)	72.7% (8/11)	66.7% (10/15)	NS
Calcification morphology, % (n/N)			
Acr-shaped	18.2% (2/11)	40% (6/15)	0.039
Fragmented	18.2% (2/11)	26.7% (4/15)	
Nodular and dense, well-defined	63.6% (7/11)	33.3% (5/15)	
Calcification size, median (IQR)	12.6 (5.7)	10.5 (6.3)	NS

SD: Standard deviation; M: Mean; NS: non-significant; IQR: interquartile range

Overall, there were no differences between control (SOC) and treatment group (STS). Both procedures were effective improving pain at rest (p=0.024), EQ5D (p=0.019), DASH-Work (p=0.032) and UCLA scores (p=0.009) and calcification size measured by US (p=0.031) at month 3.
No adverse effects or complications were reported on both groups.
Conclusion: Although well tolerated with no side effects, STS UGPL has failed to show increased benefit for calcific tendinopathy local treatment. Further studies using STS will be needed to ascertain its interest in this disease. This on-going work will be reevaluated with a larger sample.
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POS1291 DEGENERATIVE DISC DISEASE IN YOUNG: IMMUNOHISTOCHEMICAL EXPRESSION OF INFLAMMATORY BIOMARKERS AND ANGIOGENIC FACTORS

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Background: Low back pain (BP), associated with the degenerative disc disease (DDD), poses a heavy social and economic burden, emerging among young adults. The pathophysiological basis of accelerated degeneration of the intervertebral disc (IVD) and its contribution to the formation of spine osteoarthritis are at the active study stage.

Objectives: To assess infammation and angiogenesis biomarkers in IVD among young patients with chronic LBP, associated with DDD.
Methods: Human IVD tissue from 25 patients was obtained from discectomy surgery to relieve LBP (men – 13, women – 12, age: 36,7 ±3,77) and from autopsy in healthy control group (n=5, age: 37,8±2,52). The grade of DDD was verified by magnetic resonance (MRI) by the classification of C.W. Pfirrmann. Four-micron serial sections of the tissue blocks were stained with hematoxylin and eosin (H-E), than examined by immunohistochemistry staining on the automated VENTANA BenchMark ULTRA platform. Anti-IL-1β, anti-IL-6, and anti-IL-17 were used to study the expression of inflammatory cytokines; anti-VEGF-A and anti-CD31 were used as markers of angiogenesis. All slides were visualized using a Axio Imager.Z2 microscope with EC Plan-Neofluar 40X objective.
Results: In 64% of patients IVD hernias were localized at the level of L5-S1, in 36% - L4-L5. The average Pfirrmann DD stage at the operated level was 4.43±0.57. 72% of patients had Modic changes (MC). 52% of patients had a combination of hernia with endplate erosion (EP) and MC. There were identified evidence of DD on H-E-stained sections, including clusters of cells of the nucleus pulposus (NP), inflammatory cell infiltration and blood vessels in the absence of them in the fissures of the NP and annulus fibrosus (AF). Immunostaining was mainly limited to the cytoplasm of native NP chondrocyte-like cells and AF fibroblast-like cells. IL-1β expression was considerably higher in degenerate samples than in controls for both NP ($p < 0,05$) and AF ($p < 0,01$). Staining for IL-17 was more pronounced in the cytoplasm of chondrocyte-like cells of degenerative NP compared to the control ($p < 0,01$), and statistically lower in AF cells ($p < 0,05$). The number of IL-6 immunopositive cells was similar in NP and AF degenerate tissue, but a greater proportion of IL-6 immunopositive cells was seen in NP tissue ($p<0,05$). The percentage of cells immunopositive for VEGF-A and CD-31 was significantly increased in NP DD cell clusters compared to controls ($p < 0,001$) (88% and 36%, respectively) and was weakly expressed in the extracellular matrix ($p < 0,05$). This suggests that the PU cells trigger angiogenesis. Blood vessels in native sections were confirmed by CD31 detection in 64% of patient specimens versus 10% of control cartilage specimens ($p < 0,001$). The number of CD31 immunopositive cells had a tendency for decrease in severe DD ($p=0,05$), which indicates the extinction of vascularization in the terminal stage of DD. Fissures in the disc did not stained for CD31, which excludes the ingrowth of vessels directly in the area of mechanical damage and proves the immunogenic cause of vascularization. This is confirmed by the synergistic high level of expression of IL-1 and -17 in perivascular, endotheliocytes and intravascular pathological samples versus weak expression in the disc matrix ($p<0.01$).The high level of expression of all interleukins was in the hyaline cartilage of EP patients versus the absence in the controls ($p<0.001$). It indicates their association with aseptic inflammation of EP with the formation of EP erosions and reactive spondylitis (MC) development, detected by MRI in young adults with DD.
Conclusion: Local immune inflammation is a component of the degenerative cascade in IVD, it initiates angiogenesis in cartilage and EP, as well as the development of reactive osteitis of adjacent vertebrae with the formation of inflammatory-erosive lesions of the vertebral-motor segment in chronic back pain. The results obtained will help to identify molecular targets and form a new direction of anti-inflammatory therapy of LBP among young people.
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POS1292 ULTRASONOGRAPHIC GUIDED INTRA ARTICULAR STEROID AND HYALURONIC ACID IN ADHESIVE CAPSULITIS WITH AND WITHOUT SUPRASCAPULAR NERVE BLOCK

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Background: Adhesive capsulitis (AC), often known as frozen shoulder, is a common musculoskeletal condition characterised by shoulder pain and reduced active and passive mobility. Intra-articular injections is an effective treatment option and provide faster pain relief in patients with AC
Objectives: Compare the effictiveness of intra articular injection (IAI) of steroid and HA with or without Suprascapular nerve block (SSNB) in the management of AC.
Methods: Randomized control trial involved 80 patients (62 women and 18 men) clinically diagnosed as having adhesive capsulitis divided into 2 main groups; intra articular injection with SSNB (40 cases) and without SSNB (40 cases), each group divided into 2 subgroups; Twenty patients were treated with ultrasound guided intra articular injection of steroid (4ml of 2% lidocaine and 2ml of 40mg/ml triamcinolone) and another twenty patients were treated with ultrasound guided intra articular injection of hyaluronic acid (4ml of 2% lidocaine and 2ml hyaluronic acid).
Results: Intra articular shoulder injection with SSNB has higher significant visual analogue scale (VAS) score at baseline and lower significant VAS score at 1st and 3rd week ($p < 0.001$). However, there was no significance between both groups regarding disability score at 3rd weak ($p=0.316$). In contrast, there was a high significance between them considering disability score at baseline, 1st, 6th weak ($p<0.001$ and 0.008, respectively).
Conclusion: In patients with adhesive capsulitis, both a combination an IAI alone or with SSNB dramatically improved pain and functional results. The use of an SSNB in conjunction with an IAI especially with steroid enhanced therapeutic effectiveness.
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Paediatric rheumatology

POS1293 TEN-YEAR EFFICACY DATA FROM THE CLIPPER STUDIES: OPEN-LABEL, LONG-TERM ETANERCEPT TREATMENT IN CHILDREN AND YOUNG ADULTS WITH EXTENDED OLIGOARTICULAR, ENTHESITIS-RELATED, OR PSORIATIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: CLIPPER2 was an 8-year, open-label extension of the phase 3b, 2-year CLIPPER study of the safety and efficacy of etanercept (ETN) in patients (pts) with juvenile idiopathic arthritis (JIA), categorized as extended oligoarticular JIA (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA).
Objectives: Evaluation of the efficacy of ETN and its effect on health outcomes over 10 years of follow-up were secondary objectives and are reported here.
Methods: Pts (n=127) with eoJIA (n=60; 2-17 years of age), ERA (n=38; 12-17), or PsA (n=29; 12-17) who received ≥1 ETN dose (0.8mg/kg once weekly [max, 50 mg]) in CLIPPER were eligible to enter CLIPPER2. The study design has been reported previously.[1] Efficacy endpoints included proportions of pts achieving JIA American College of Rheumatology (ACR) 30/50/70/90/100 criteria, Juvenile Arthritis Disease Activity Score (JADAS) inactive disease and clinical remission criteria, and sustained clinical remission (ACR criteria) or JADAS ≤1 for 12 continuous months (mths). Exploratory efficacy endpoints included time to flare following ETN withdrawal (based on ≥30% worsening in ≥3/6 ACR Pedi components, with ≥30% improvement in <2/6 remaining components and ≥2 active joints), and time to re-treatment with ETN.
Observed Cases were used (i.e., there was no imputation for missing data) for pts who were in the Active Treatment Period.
Results: A total of 109/127 (86%) CLIPPER participants entered CLIPPER2 (n=55 eoJIA, n=31 ERA, n=23 PsA), with 99 (78%) pts continuing in the Active Treatment Period. Overall, 84 (66%) pts completed 120 mths of follow-up; 27 (21%) while actively taking ETN. Thirty (24%) pts entered the Withdrawal Period from the Active Treatment Period (i.e., they discontinued ETN, either by meeting the Wallace definition for clinically inactive disease for at least 6 months on ETN, or by having had a good clinical response and being deemed to benefit from withdrawal in the investigator's judgment). Of the pts in the Active Treatment Period, over 90% achieved JIA ACR 50 response at all study time points. Sustained JADAS and ACR remission was achieved by 42 (33%) pts and 17 (13%) pts, respectively. The mean improvements from baseline in JADAS disease activity at mth 24 of CLIPPER were largely maintained through CLIPPER2 A total of 109/127 (86%) CLIPPER participants entered CLIPPER2 (n=55 eoJIA, n=31 ERA, n=23 PsA), with 99 (78%) pts continuing in the Active Treatment Period. Overall, 84 (66%) pts completed 120 mths of follow-up; 27 (21%) while actively taking ETN. Thirty (24%) pts entered the Withdrawal Period from the Active

Treatment Period (i.e., they discontinued ETN, either by meeting the Wallace definition for clinically inactive disease for at least 6 months on ETN, or by having had a good clinical response and being deemed to benefit from withdrawal in the investigator's judgment). Of the pts in the Active Treatment Period, over 90% achieved JIA ACR 50 response at all study time points. Sustained JADAS and ACR remission was achieved by 42 (33%) pts and 17 (13%) pts, respectively. The mean improvements from baseline in JADAS disease activity at mth 24 of CLIPPER were largely maintained through CLIPPER2.

Conclusion: The low numbers of evaluable pts notwithstanding, efficacy results were consistent with the profile of ETN, and treatment responses were considered clinically meaningful and durable with long-term treatment.

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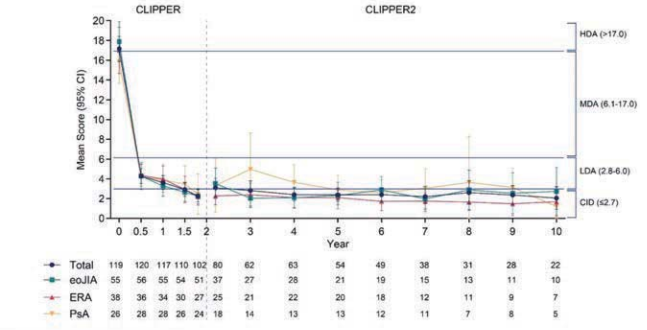
Trial Registration: NCT00962741/NCT01421069

Figure. JADAS 73 Score by Visit (Observed Cases).*



*Disease activity based cut-off values of the JADAS.[1]
CI, confidence interval; CID, clinically inactive disease; eoJIA, extended oligoarticular juvenile idiopathic arthritis; ERA, enthesitis-related arthritis; HDA, high disease activity; JADAS, Juvenile Arthritis Disease Activity Score; LDA, low disease activity; MDA, moderate disease activity; PsA, psoriatic arthritis.

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POS1294 SAFETY AND EFFICACY OF ADALIMUMAB BIOSIMILAR (AMGEVITA) IN PAEDIATRIC RHEUMATOLOGY PATIENTS

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Background: The approval of biosimilars requires pharmacokinetic studies to prove that there are no clinically significant differences to the originator molecule. These studies are also used to extrapolate additional indications and for different populations including paediatrics. Literature is lacking for the efficacy and safety of biosimilars for paediatric rheumatology conditions. Amgevita, a biosimilar of adalimumab, was approved for use in Singapore on 31 July 2019. It was used in KK Women's and Children's hospital (KKH), Singapore from 1 September 2020.

Objectives: To report the safety and efficacy of adalimumab biosimilar in children at our centre.

Methods: This is an ongoing prospective, IRB-approved, observation study in a paediatric rheumatology clinic sited within KKH, a tertiary children's hospital. Patients were reviewed in clinic to determine the need to initiate adalimumab (Amgevita), and completed pre-biologic screening to assess suitability to start. Patients were included if they received minimum 1 dose of adalimumab biosimilar. Safety parameters tracked: allergy, including urticaria, anaphylaxis, severe injection site reactions, rate of new onset infections requiring hospitalization and reactivation of latent infections (e.g., tuberculosis or herpes zoster). Adverse reactions were graded according to CTCAE v5.0. Efficacy parameters were tracked for patients with juvenile idiopathic arthritis (JIA) included JADAS27, JADAS71 and JSpADA.

Results: From 1 September 2020 to 31 October 2021, a total of 187 of 20mg syringes and 1403 pre-filled 40mg pens were dispensed to 117 paediatric rheumatology patients. Mean age was 14.9 years, 53.9% were male, 70.9% were Chinese and ethesitis-related arthritis (46.1%) was the most common indication. There were 68 (58.1%) biologic naïve patients. Two patients experienced injection-site urticaria which prompted discontinuation (grade 2). One patient reported initial injection site soreness which resolved spontaneously (grade 1). One patient developed latent tuberculosis requiring inpatient management and temporary interruption in adalimumab therapy (grade 3). No other adverse events were reported. Efficacy data was available for 96 patients. Median scores at baseline and at 3-months and 6-months are presented in Table 1.

Table 1. Summary of paediatric patients initiated on adalimumab biosimilar (Amgevita)

Diagnosis, n (%)						
Enthesitis related arthritis			54 (46.1)			
Of which HLA-B27 positive			44 (81.5)			
Polyarthritis			21 (17.9)			
Extended or persistent oligoarthritis			15 (12.8)			
Undifferentiated JIA			6 (5.1)			
Psoriatic arthritis			1 (0.8)			
Other indications			21 (17.9)			
Concomitant DMARDs, n (%)	Methotrexate			50 (42.7)		
	Sulfasalazine			37 (31.6)		
*Efficacy, Median (range)	Biologic naïve			Not biologic naïve		
Month number	**0**	**3**	**6**	**0**	**3**	**6**
JADAS27	2 (0-21.6)	0 (0-8.5)	0 (0-6.05)	2 (0-10.6)	0 (0-8.4)	0 (0-12.2)
JADAS71	2 (0-27.8)	0 (0-12.0)	0 (0-6.08)	2 (0-10.6)	0 (0-8.4)	0 (0-12.2)
JSpADA	0.25 (0-3.5)	0 (0-1.0)	0 (0-1.0)	0.5 (0-1.5)	0 (0-0.5)	0 (0-2.0)

DMARDs: Disease modifying anti-rheumatic drugs; JADAS: Juvenile Arthritis Disease Activity Score; JSpADA: Juvenile spondyloarthritis disease activity. *Efficacy data only for patients with juvenile idiopathic arthritis

Conclusion: We report our 14-month experience of using adalimumab biosimilar in a pediatric rheumatology population. Majority of the patients did not report major adverse reactions. Majority of JIA patients responded well when initiated on adalimumab (Amgevita). Rheumatologists should continually monitor patients for latent infections after prescribing biologics including biosimilars.

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Disclosure of Interests: None declared

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POS1295 SYSTEMIC AND AUTO-INFLAMMATORY DISEASES OF PEDIATRIC ONSET: THE EXPERIENCE OF THE FRENCH OVERSEAS DEPARTMENTS OF AMERICA

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Background: Systemic diseases of pediatric onset are more frequent in Afro-Caribbean population, especially Pediatric systemic lupus (pSLE).

Objectives: Our work is a retrospective study of patients followed in French overseas departments of America for systemic disease or auto-inflammatory syndrome of pediatric onset. It describes their clinical and biological specificities at diagnosis, during childhood and early adulthood.

Methods: Our retrospective study was conducted between 01/01/2000 and 01/09/2021. Listings of adult patients with pediatric onset and pediatric patients were obtained in each center through computerized hospital archives, list of patients followed by referent pediatricians and adult specialists in internal medicine and the French National Registry for rare disease. Data were then gathered by going through their medical files. The spectrum of diseases studied included pSLE, Sjogren syndrome, antiphospholipid syndrome (APS), connectivitis, systemic scleroderma, dermatomyositis, Systemic juvenile idiopathic arthritis (sJIA), unclassified auto-inflammatory syndrome.

Results: 2148 patients were identified on a 21 year-period, and 135 patients were included. Most patients diagnosed with a systemic pathology (102) suffered from pSLE (53%), followed by dermatomyositis (17%). Average follow up was 8.3 years (0.3 - 25 years), median age at last follow up was 21.2 (14 - 36.7). We found an increase in the number of new diagnoses throughout the years. For pSLE, sex repartition was 4/1 girl/boy and did not vary according to age (p= 0,31). At onset, patients had 10 Sclicc criteria (4-12) and median EULAR/ACR 2019 score was 38 (12 - 54). The combination of typical skin involvement, arthritis and fever was found for 87%. At onset, a third of patients had renal involvement, 15% had Neurolupus and 41% cardiac involvement. All patients had a positive ANA and Anti-DNA antibodies, followed by anti-Ssa/Ssb antibodies (78%), Anti-Sm (78%) and anti RNP (52%). During childhood, 54% had renal involvement and 26% suffered from Neurolupus. Patients suffered in median from 3 flares and 26% suffered from more than 5 flares during childhood. Pre-pubertal patients (26%) had worst outcomes, 93% had renal and / or neurological involvement, they had more flares (median at 5 p = 0,02) and needed an average of 4 background therapies (p = 0,04). Boys seemed to have better disease control at transition to adult care but gender was not an independent predictor of severity during childhood (p = 0,21). 17 patients had dermatomyositis, 29% of them had respiratory involvement during childhood. 33 patients had auto-inflammatory syndromes mostly sJIA (67%), 50% of them had hemophagocytic syndrome during childhood and their disease was controlled by steroids for 64%, 36% needed biotherapy. The overall mortality was 3%.

Conclusion: This is a large cohort of patients of Afro-Caribbean origin with a higher frequency of pSLE. Although the outcomes for these patients were similar to western countries, they had loud symptoms at onset, not corelated to delay at diagnosis. Compared to ethnic studies of North America or Africa, the French health care system being universal and free, the bias related to socio-economic status was lower. This work will continue with the exploration by transcriptomic and genetic tests for early and severe forms to identify the extra-environmental causes. The environmental factors specific to these regions should be explored in additional prospective studies.

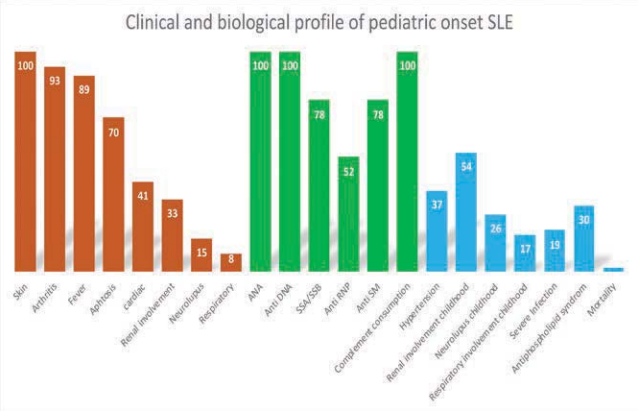

Figure 1. Clinical and biological characteristics of patients with pediatric onset systemic lupus. Orange: clinical signs at onset, Green: immunological profile, Blue: evolutive profile and proportion of organ involvement during childhood. ANA: anti-nuclear antibody.

Disclosure of Interests: None declared
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POS1296 T-CELL RESPONSE MEASURED BY INTERFERON-Γ RELEASE ASSAY AS A NOVEL TOOL FOR BETTER UNDERSTANDING OF SARS-COV-2 IMMUNITY: THE PRELIMINARY RESULTS OF A PROSPECTIVE STUDY IN PEDIATRIC PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS.

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Background: While serological assays detecting antibodies in blood serum remain the standard exam for evaluating immunity against SARS-CoV-2 infection, the latest publications reveal certain limitations to this broadly used method. Recent studies showing the decline of antibodies titers in time, together with scientific reports which detect SARS-CoV-2-specific T-cells in seronegative individuals, evoke questions with regard to the reliability of the sole assessment of the humoral response to SARS-CoV-2. A novel T-cell-based Interferon-γ Release Assay (IGRA) is proposed to adapt our approach to the individual immunity to the new coronavirus.

Objectives: The objectives of this study were to assess T-cells and antibodies responses to the SARS-CoV-2 virus among pediatric patients at different stages of juvenile idiopathic arthritis (JIA) undergoing diverse treatment regimes. In addition, the authors aimed to evaluate humoral and cellular responses to the Covid-19 mRNA vaccine in the cohort of immunocompromised patients.

Methods: This prospective study included 30 pediatric patients between the ages 2-16 at different stages of JIA. The cohort group consisted of vaccinated and unvaccinated individuals and children with both positive and negative history of past Covid-19 infection. SARS-CoV-2 T-cell response was measured using a specific quantitative IGRA in whole blood, followed by anti-SARS-CoV-2 ELISA test measuring the presence and quantity of IgG, IgM and IgA antibodies in serum.

Results: The magnitude of the SARS-CoV-2 specific T-cell response measured by the IGRA test correlated significantly with the levels of IgG ($p<0.00005$, $R=0.653$) and IgA antibodies ($p<0.00001$, $R=0.675$) in serum, while no correlation with IgM antibodies level in serum was found. All vaccinated patients developed a cellular response to the vaccine ($p=0.0108$), regardless of the number of administered doses. The T-cells response in children undergoing biological treatment (specifically: etanercept, adalimumab or tocilizumab) was recognizably weaker compared to the group not receiving such treatment. Nevertheless, the difference did not reach statistical significance ($p=0.0715$). Similar dependencies were found in children treated with hydroxychloroquine (n=6), however, due to the small study group, a statistical significance could not have been reached.

Conclusion: Suppression of cellular response observed in different drug protocols may prove to become a protective factor against SARS-CoV-2 infection. Additionally, the authors postulate that the strong correlation found between T-cell response and IgA antibodies titer can be related to SARS-CoV-2 strong affinity with mucosal membranes. Thus, the sole testing of IgG and IgM antibodies levels in serum with regard to Covid-19 may not be the most precise diagnostic method. The presented study group needs to be expanded with more patients, mainly children receiving biological agents or hydroxychloroquine to validate the demonstrated preliminary results.

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POS1297 SACROILIITIS AT DIAGNOSIS ASSOCIATED WITH LESS DISEASE FLARE AFTER STOPPING MEDICATION - OUTCOMES AND PREDICTORS OF A SOUTHEAST ASIAN ENTHESITIS RELATED ARTHRITIS (ERA) LONGITUDINAL COHORT

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Background: ERA is a subtype of Juvenile Idiopathic Arthritis (JIA) characterized by involvement of entheses and axial skeleton. Outcomes have been shown to be poorer compared with oligoarticular and polyarticular JIA[1].

Objectives: To assess short-and long-term outcomes and predictors of ERA in a large monocentric cohort in Singapore.

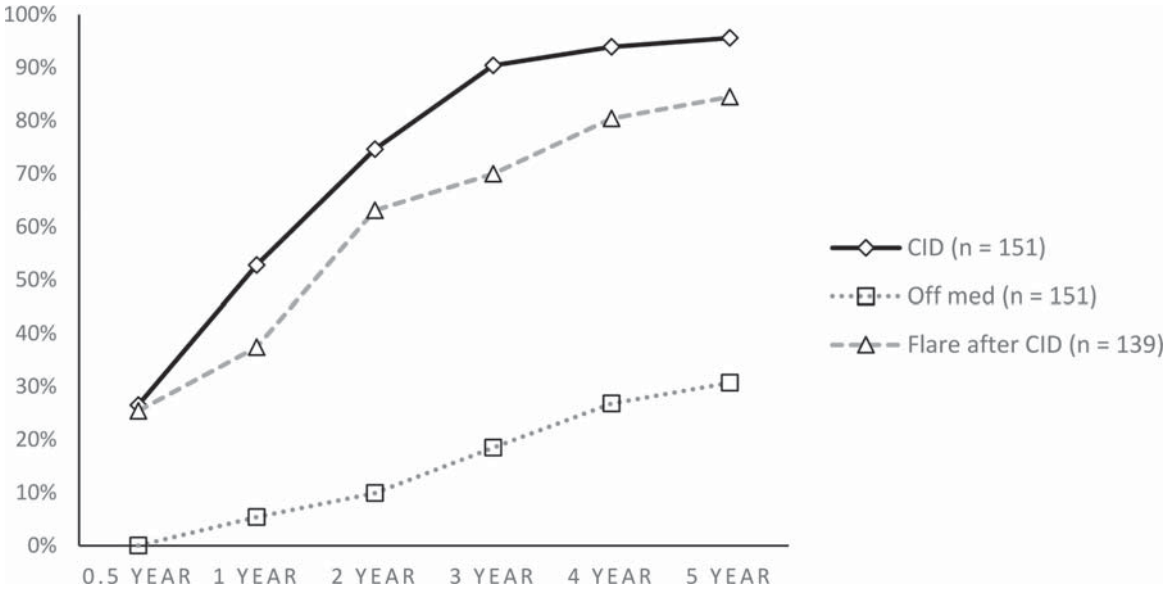

Figure 1. Probability of attaining outcomes over time

Methods: Children diagnosed with ERA according to ILAR criteria from 2002 to 2021 at KK Women's and Children's Hospital, Singapore, were recruited. Outcome statuses were defined according to the criteria for clinical inactive disease (CID) and complete remission (CR) proposed by Wallace et al.[2], with additional criteria of no enthesitis and no active sacroiliitis on MRI. Nonparametric descriptive statistics were used. Univariate and multivariate analysis were performed using logistic regression analyses. The significant level was set at < 0.05.

Results: A cohort of 151 ERA patients (male 86%; Chinese 81%) were included. Median age at onset was 11.9 years (IQR 9.4-13.9) and disease duration was 5.3 years (IQR 2.9-8.4). HLA-B27 was positive in 83% of the patients. At diagnosis, 39% of the patients had sacroiliitis, 46% had hip arthritis, 36% had knee arthritis and 25% had enthesitis. Methotrexate was used in 77% of the patients, while biologics was started in 72% of the patients.

CID was achieved in 92% of the patients, of which 27% achieved CID in 6 months or less. Sacroiliitis at diagnosis is an unfavourable predictor of CID at 6 months but not a significant predictor of ever achieving CID. Older age at diagnosis is also an unfavourable predictor of CID ever.

Medication was totally discontinued in one third of the patients. Half of them went on to have complete remission (CR) off medication. Favourable predictor includes male gender, while positive HLA-B27 and ANA were unfavourable predictors.

Two thirds of the patients with CID had at least one disease flare (23% flared after off medication, 13% flared after CR). Both intra-articular joint injection and anti-TNF use were associated with flare after CID, while anti-TNF use was associated with flare after off medication. Sacroiliitis at diagnosis is a protective predictor of flare after stopping medication.

Conclusion: Despite a high proportion of ERA patients achieving CID, only one third could stop medication completely with high rates of disease flare even after attaining CR. Unfavourable predictors include older age at onset as well as HLA-B27 and ANA positivity. While sacroiliitis at diagnosis is a negative predictor of CID at 6 months, it is protective predictor of flare after discontinuing medication.

Table 1. Predictors of outcomes

Clinical parameters	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
CID at 6 months						
Sacroiliitis at diagnosis	0.187	0.048-0.724	0.015	0.023	0.003-0.177	<0.001
CID ever						
Age at onset	0.790	0.626-0.998	0.048	0.777	0.605-0.997	0.047
Off medication ever						
Male	5.029	1.121-22.566	0.035	7.703	1.622-36.575	0.010
HLA-B27	0.374	0.158-0.886	0.025	0.290	0.110-0.764	0.012
ANA	0.104	0.013-0.803	0.030	0.077	0.010-0.613	0.015
Flare after CID						
Intra-articular injection	2.585	1.116-5.988	0.027	3.205	1.299-7.909	0.011
Anti-TNF	3.683	1.697-7.993	0.001	4.328	1.905-9.832	<0.001
Flare after discontinue medication						
Sacroiliitis at diagnosis	0.222	0.060-0.821	0.024	0.079	0.009-0.722	0.025
Anti-TNF	17.333	3.696-81.300	<0.001	37.942	4.151-346.841	0.001

CID – Clinical Inactive Disease, TNF – Tumor Necrosis Factor, HLA-B27 – Human Leukocyte Antigen-B27, ANA – Antinuclear Antibodies

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POS1298

RELATIONSHIP BETWEEN DISEASE ACTIVITY BY JADAS-27, SDAI, AND DAS-28 AND SUBSEQUENT CHANGES IN PHYSICAL FUNCTION IN ADULT PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Arthritis Disease Activity Score (JADAS) has been developed as a composite disease activity score specific to Juvenile idiopathic arthritis (JIA). Evaluation of disease activity with a composite measure associated with subsequent changes in structural damage of joints and physical function is necessary for the proper management of Rheumatoid Arthritis (RA) with treat-to-target strategy, and this concept should be considered for patients with JIA in transition and adulthood as well. However, the usefulness of JADAS-27 and other composite measures for RA in these patients has been scarecely investigated. Additionally, JADAS-27 is unfamiliar to non-pediatric rheumatologists.

Objectives: We aimed to investigate an optimal composite score for disease activity in adult JIA from the viewpoint of the subsequent changes in physical function.

Methods: Patients diagnosed with JIA with the following conditions were enrolled: 1) disease onset at age < 18 years; 2) registered in the IORRA database for the first time between 2000 and 2020; and 3) ≥18 years old at the time of IORRA registration. The baseline of each patient was their initial entry into the IORRA database. The Simplified Disease Activity Index (SDAI), Disease Activity Score using 28 joints (DAS28), and JADAS-27 were compared. The patients were stratified into four disease activity categories: remission/inactive disease, low disease activity, moderate disease activity, and high disease activity according to mean disease activity scores in each index during the first year from baseline, and mean changes in J-HAQ (mean ΔJ-HAQ) during 2 years from baseline in each disease activity group were estimated using the linear mixed effect model

to account for correlations of repeated measures without filling in the missing data after adjusting for sex, age, and disease duration.

Results: We included 294 eligible individuals (median age at onset, 14.0 years; rheumatoid factor positive in 64.7%). The median age at baseline and disease duration was 33.8 (24.1–47.7) years and 21.0 (11.0–34.0) years, respectively. The J-HAQ was completed in all 294 patients, and 171 (58.1%) had a score of less than 0.5 at baseline, which is defined as functional remission. During the 2-year observation period, the median J-HAQ of all patients remained unchanged. There was a trend toward improvement in disease activity over time in all three composite scores. Some differeces were obsered across the three indeces: a higher proportion of patients with high disease activity and a lower proportion of patients in remission/inactive disease were observed with JADAS-27 versus SDAI and DAS28. A significant increasing trend of the estimated mean ΔJ-HAQ at 2 years after baseline was observed along with an increase in the mean disease activity during the first year measured using DAS28 (p = 0.01) and SDAI (p = 0.018), but not using JADAS-27 as shown in Table 1.

Table 1. Association of the mean disease activity categories during the first year after baseline and mean changes in J-HAQ during the two years after baseline

(n = 294)	SDAI	DAS28	JADAS-27
Remission/inactive disease	0.019 [–0.190, 0.228]	0.053 [0.024, 0.130]	0.081 [–0.072, 0.234]
LDA	0.091 [–0.150, 0.332]	0.102 [–0.013, 0.217]	0.054 [–0.102, 0.210]
MDA or HDA	0.155 [–0.286, 0.596]	0.136 [0.030, 0.242]	0.087 [0.022, 0.152]
p-value for trend	0.019	0.010	0.115

(Data are expressed as J-HAQ [95% confidence interval]. P-value less than 0.05 indicate a significant trend of the mean ΔJ-HAQ during the two years after baseline. LDA low disease activity; MDA moderate disease activity; HDA high disease activity)

Conclusion: Disease activity measured using SDAI and DAS28, but not using JADAS27, was significantly associated with subsequent changes in physical function in transitional and adult patients with JIA. This study support the use of SDAI and DAS28, but not JADAS27, in assessing disease activity in these patients to adjust treatments for preventing future deterioration of physical function.

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POS1299 JUVENILE SYSTEMIC SCLEROSIS TREATMENT PRACTICES IN AN INTERNATIONAL COHORT AND COMPARISON TO RECENT SHARE CONSENSUS GUIDELINES.

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Background: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 in 1,000,000 children. Currently no medications are licensed for the treatment of jSSc. Due to its rarity, only recently have the first management and treatment guidelines been published, the jSSc SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) recommendations, reflecting consensus opinion upon pediatric rheumatologists (1).

Objectives: To better understand treatment practices internationally for jSSc, both at baseline and over 24 months observation period and to compare if real world therapies are congruent with the recent SHARE recommendations.

Methods: The juvenile systemic sclerosis inceptions cohort (jSScC) is a multinational cohort that prospectively collects clinical data, including medications at baseline and subsequent visits. The jSScC enrollment criteria include age of onset of the first non-Raynaud symptom younger than 16 years and age younger than 18 years at cohort entrance. The frequency of medications (general category and specific medication) was calculated across the cohort at timepoint 0 (enrollment), 12 months and 24 months.

Results: We extracted data from the jSScC of patients who were followed for 12 or 24 months. 109 patients were followed at time point 0 (T0) and 12 months (T12), and data was available for 77 of them up at 24 months (T24). The mean age of the patients was 13.2 years at the timepoint 0. 77% were female and 75% had diffuse subtype. Disease duration at baseline visit was 3.1 years. The medications the patients were on recorded by the physician were captured at T0, T12 and T24 listed in Table 1.

Table 1.

MEDICATIONS	Time point 0 N=109	T12 months N=109	T24 months N=77
Any Medication	92% (100)	97% (106)	97% (75)
Vascular medications			
Endothelial receptor antagonist	16% (17)	24% (26)	21% (16)
PDE-5-Blocker	5% (5)	8% (9)	9% (7)
Immunomodulators			
Corticosteroids	52% (57)	44% (48)	44% (21)
All csDMARDs:	81% (88)	93% (101)	92% (71)
csDMARDs monotherapy	61% (67)	66% (72)	60% (46)
csDMARDs combination therapy	17% (18)	15% (16)	14% (11)
Methotrexate	51% (56)	50% (55)	39% (30)
Mycophenolate Mofetil	26% (28)	44% (48)	47% (36)
Hydroxychloriquine	11% (12)	15% (16)	21% (16)
Cyclophosphamide	12% (13)	2% (2)	1% (1)
Azathioprine	2% (2)	2% (2)	3% (2)
All bDMARDs:	5% (5)	14% (15)	18% (14)
bDMARDs monotherapy	2%(2)	2%(2)	1% (1)
bDMARDs combined with csDMARDs	3% (3)	12% (13)	17% (13)
Tocilizumab	2% (2)	10% (11)	14% (11)
Rituximab	2% (2)	4% (4)	4% (3)
Adalimumab	1% (1)	0% (0)	0% (0)
Autologous Stem cell transplantation	0% (0)	1% (1)	0% (0)

csDMARDs: Conventional synthetic disease-modifying antirheumatic drugs b DMARDs: Biological disease-modifying antirheumatic drugs

Conclusion: At baseline half of the patients were on corticosteroids. This is more frequent than typical adult SSc practice but coincides with jSSc SHARE treatment recommendations (#1). After 12 months observation in the cohort over 90% of patients received a DMARD therapy. Methotrexate and mycophenolate mofetil were the most commonly prescribed DMARDs, which also reflects the SHARE treatment recommendations (#2, #3). At 12 months the use of glucocorticoid decreased and the use of bDMARDs increased. In general, biological DMARDs are typically considered in severe or refractory (SHARE recommendation #7), reflecting the lower percentage compared to csDMARDs. Autologous stem cell transplantation was observed in one patient at 12 months, reflecting an option in jSSc with progressive and refractory disease (SHARE recommendation #8). Endothelial receptor antagonists, such as bosentan, were used over time in approximately 20% of the patients, reflecting SHARE recommendation #6 for pulmonary hypertension and/or digital tip ulcers. This is the first evaluation looking at clinical medication practice pattern in jSSc, and its comparison to recently published consensus guidelines.

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POS1300

PAIN AND ITS ASSOCIATION WITH HEALTH-RELATED QUALITY OF LIFE, SLEEP, PHYSICAL ACTIVITY, AND SEDENTARY BEHAVIOR IN 10-YEAR-OLD CHILDREN FROM A SWEDISH BIRTH COHORT

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Background: Pain in children may be underreported and undertreated today, but due to methodological variations, pain prevalence is difficult to determine. Moreover, it is unclear to what extent pediatric pain is associated with health-related quality of life (HRQoL) and other lifestyle habits. There is a need for an increased understanding of pain in children.
Objectives: To study pain prevalence and cross-sectional associations between pain, HRQoL, sleep, physical activity, and sedentary behavior in 10-year-old children from a Swedish birth cohort.
Methods: The Swedish birth cohort the "Halland Health and Growth Study" (H^2GS) recruited 2860 children at birth (2007–2009). At 10 years of age the children answered questionnaires regarding pain (mannequin with 20 regions, frequency never–daily for each region) and HRQoL (Kidscreen-27, 27 questions, 5 domains scored worst–best). Parents estimated their child's sleep (6–8, 9, or 10–12 hours/night), physical activity time, and sedentary time (hours/weekdays and hours/weekends respectively). Children were categorized into the groups of "infrequent pain" (never–monthly pain) or "frequent pain" (weekly–almost daily pain) from the highest reported pain frequency from at least one body region. Differences in pain prevalence between boys and girls were analyzed with chi^2-test. Logistic regression analyses were performed to study associations between frequent pain (dependent variable) and HRQoL, sleep, physical activity, and sedentary behavior (independent variables). Each variable was adjusted for sex.
Results: 733 children (351 boys and 382 girls) answered pain and HRQoL questions at 10 years of age. Frequent pain was reported by 37% (boys 35% vs. girls 39%, p=0.267). The number of frequent pain regions ranged from 1–13 in boys and 1–20 in girls. Higher HRQoL in the domains physical wellbeing (OR 0.965; 95%CI 0.948–0.983; p<0.001), psychological wellbeing (OR 0.971; 95%CI 0.955–0.987; p<0.001), autonomy and parents (OR 0.971; 95%CI 0.954–0.988; p=0.001), peers and social support (OR 0.977; 95%CI 0.961–0.994; p=0.007), and school environment (OR 0.972; 95%CI 0.956–0.989; p=0.002) was associated with less risk of belonging to the frequent pain group. More sedentary time in weekdays (OR 1.107; 95%CI 1.028–1.192; p=0.007) and weekends (OR 1.122; 95%CI 1.037–1.215; p=0.004) was associated with having frequent pain, but no associations were found between frequent pain and the amount of physical activity or sleep.
Conclusion: The high prevalence of frequent pain in 10-year-old children must receive attention by the school and health-care services. The association between frequent pain and low HRQoL is troublesome. Improving HRQoL and reducing sedentary time is beneficial for children's health, but further studies are needed to follow associations over time.
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POS1301

OCCURRENCE OF ARTHRITIS IS IN 37% OF THE PATIENTS WITHOUT OVERLYING SKIN INVOLVEMENT IN JUVENILE LOCALIZED SCLERODERMA. SUMMARY OF THE EXTRACUTANEOUS INVOLVEMENT IN A MONOCENTRIC COHORT.

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Background: Localized scleroderma in childhood (locSSc) occurs with a prevalence of 3.2 to 3.6 per 10 000 children[1]. There are not many publications assessing in detail the extracutaneous manifestations (EM) of locSSc. It is very important to assess the EM too, because the EM can lead to significant damage and morbidity too.
Objectives: To assess the occurrence of extracutaneous manifestations in locSSc in our cohort and the correlation of the occurring EM to the subtype of locSSc and the localisation of the skin involvement.
Methods: Retrospective chart review of all consecutive patients, who were followed at our centre from January 2000 to July 2020 with the diagnosis of locSSc. The subtype was classified according Laxer et al[2]. The patients were under the age of 18 years at the time point of the first visit. Demographic and clinical data were extracted.
Results: 73 patients could be identified, 71% of them were female. Mean age at disease onset was 8 years (4-14 years). The mean time of follow up was 5 years. The subtype distribution was 42 (57%) linear, 24 (33%) mixed, 6 (8%) circumscribed morphea and 1 (1%) pansclerotic morphea. 9 (21%) of the 42 patients with linear subtype had coup de sabre and 4 (10%) of them had Parry Romberg. Fifty six (76%) patients had EM, 40 (53%) of them had 1 form of EM, 10 (13%) of them 2 forms of EM and 6 (8%) patients 3 forms of EM. 53(73%) of the 76 patients had arthritis. Twenty (37%) of the 53 arthritis involvement occurred on a localisation without overlaying skin involvement. Most frequent localisation of arthritis without overlaying skin involvement was in the hip joints (18%). Of the 53 patients with articular involvement had 31 (58%) linear, 17 (32%) mixed, 4 (7.5) circumscribed morphea and 1 (2%) pansclerotic subtype. 14 (19%) of the 73 had length discrepancy of the extremities and 13 (93%) of them had linear subtype. Neurologic symptoms presenting as headache occurred in 8 (11%) patients, 6 (75%) of them had Parry Romberg subtype and 2 (25%) of them coup de sabre. "White" anterior uveitis was screened according to published recommendations[3,4] and it occurred in 3 patients, only one of them had coup the sabre the other two linear and mixed subtype without involvement of the face.
Conclusion: EM is very common and it occurs in 76% of the patients. Thirty seven percent of the articular involvement occurred in joints without overlaying skin involvement, which suggest the importance of the whole body joint count as in juvenile idiopathic arthritis. Only 1 of 3 patients with uveitis had skin involvement in the face, which emphasize the recommended uveitis screening.
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POS1302

PATIENT AND PHYSICIAN REPORTED OUTCOMES OF JUVENILE SYSTEMIC SCLEROSIS PATIENTS SIGNIFICANTLY IMPROVE OVER 12 MONTHS OBSERVATION PERIOD IN THE JUVENILE SYSTEMIC SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children (1). The Juvenile Systemic Scleroderma Inception cohort (jSScC) is the largest cohort of jSSc patients in the world. The jSScC collects longitudinal data prospectively in jSSc, allowing the evaluation of the development of organ involvement and patients and physician reported outcomes in jSSc over time.
Objectives: To review the changes in the clinical characteristics and patient and physician reported outcomes over 12 months observation period from the time of inclusion into the cohort.
Methods: The jSScC cohort enrolls jSSc patients who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion (2, 3). We reviewed jSScC patient clinical data and patient and physician reported outcomes, who had 12 months follow up from the time of inclusion until 1st of December 2021.
Results: We could extract data of 113 patients. The female/male ratio was 3.5:1. Median age of onset of Raynaud´s was 10.1 years and the median age of onset of non-Raynaud´s was 10.8 years. Eighty-eight percent of the patients were treated with disease modifying anti-rheumatic drugs (DMARDs) at time of inclusion in the cohort (T0) and 93% after 12 months (T12). Median disease

duration was 2.5 years at T0. Antibody profile stayed unchanged. Only 3 clinical parameters changed and improved significantly, the median modified Rodnan skin score improved from 13 to 8 (p=0.002), the number of patients with swollen joints decreased from 17% to 8% (p=0.043) and number of patients with joints with pain on motion decreased from 20% to 12% (p=0.048). All other organ involvement did not show any statistically significant change from T0 to T12.

All collected patient reported outcomes improved significantly from T0 to T12: the patient reported disease activity (VAS 0 – 100) from 40 to 20 (p=0.011), the patient reported disease damage (VAS 0 – 100) from 40 to 20 (p=0.001), patient reported ulceration activity (VAS 0 – 100) from 10 to 0 (p=0.02) and the CHAQ score from 0.3 to 0.1 (p=0.002). Two of the three physician reported outcomes improved significantly, the physician global disease activity (VAS 0 – 100) from 30 to 20 (p=0.011) and physician reported global disease damage (VAS 0 – 100) from 30 to 25 (p=0.028).

Conclusion: Skin and musculoskeletal clinical features improved over 12 months, with almost all patients on DMARDs, supporting likely response of these features to therapy. It was promising that internal organ involvement, like cardiac and lung, although potentially stable, did not significantly worsen or increase. The most striking observation in the positive direction is improvement across several patient and physician reported outcome measures over the 12 month time period in this large international cohort.

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POS1303 METHOTREXATE RESPONSE IN PEDIATRIC NON-INFECTIOUS UVEITIS

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Background: Children with chronic non-infectious uveitis (NIU) are at risk for sight-threatening complications. Methotrexate (MTX) is the preferred first-line systemic treatment. Initial therapeutic response takes 3-6 months to achieve NIU control, leading to prolonged glucocorticoid use. Moreover, at least 50-70% of children fail to fully respond and may accrue ocular damage while awaiting MTX response.

Objectives: To identify features of children with NIU that are associated with MTX failure.

Methods: We included children who started MTX monotherapy for NIU. We collected demographics, NIU features (type, location, & complications), ANA status, and clinical examination. We characterized children as MTX responders or non-responders. MTX responders are those whose NIU was controlled, defined by: 1) inactive graded by SUN criteria, 2) absence of new or worsening complications, and 3) requirement for ≤2 drops of prednisolone acetate and no oral glucocorticoids.

Results: Of 47 NIU children, 68% were MTX non-responders (Table 1), having a longer duration of NIU (Odds Ratio [OR]=1.28, [CI=1.03-1.8], p =0.023) and developing more ocular complications (OR=1.95 [CI=1.23-3.38], p=0.017), (ROC Area Under the Curve = 0.85). MTX non-responders were more likely to have anterior and/or posterior synechiae (p = 0.001), cataracts (p=0.015), and ocular hypertension (p=0.039). Treatment included adalimumab: 27, infliximab: 14, tocilizumab: 5, golimumab: 4, etanercept: 3, and abatacept: 2.

Table 1. Comparison of children with NIU based on MTX response.

	Responders n=15	Non-responders n=32
Caucasian	14 (93)	27 (84)
Hispanic or Latino	0 (0)	3 (9)
Female	12 (80)	23 (72)
Age of NIU onset, yrs, median (IQR)	4.3 (2.9 – 12.3)	4.6 (2.8 - 7.0)
Duration of NIU, yrs, median, (IQR)	4.1 (2.6 – 5.3)	8.2 (4.7 - 11.3)
JIA-NIU	10 (67)	25 (78)
Idiopathic CAU	2 (13)	3 (9)
Other	3 (20)	4 (12)
Bilateral disease	12 (80)	23 (72)
Anterior	12 (86)	29 (91)
Presenting BCVA (LogMAR) worst eye, median (IQR)	0.2 (0.1 – 0.3)	0.1 (0.0 - 0.2)
Average # of total complications/person, median (IQR)	1 (0 – 2)	2.5 (1.0 – 5.5)
ANA positive	10 (67)	26 (81)
Earliest ESR	8 (6– 18)	12 (8 - 18)
Earliest Vitamin D	32 (26 – 35)	31 (23 - 35)
Time on MTX, months, median (IQR)	35 (19 - 64)	19 (7 - 74)
Time from systemic or NIU onset to MTX, yrs, median (IQR)	0.3 (0.1 – 0.5)	0.2 (0.0 - 0.8)
MTX PO	6 (40)	19 (59)
MTX SC	13 (87)	31 (97)

We performed a sub analysis of children with idiopathic chronic anterior NIU (CAU) and JIA-associated NIU that included children who failed MTX due to intolerance/toxicity (Figure 1). Using Cox proportional hazard regression, 8 idiopathic CAU failed MTX earlier than 38 JIA-associated NIU (HR 2.77, [CI-=1.06-7.27], p=0.039). Results were similar with the inclusion of other types of NIU (p=0.088) (e.g., HLA-B27, non-anterior idiopathic or with systemic disease).

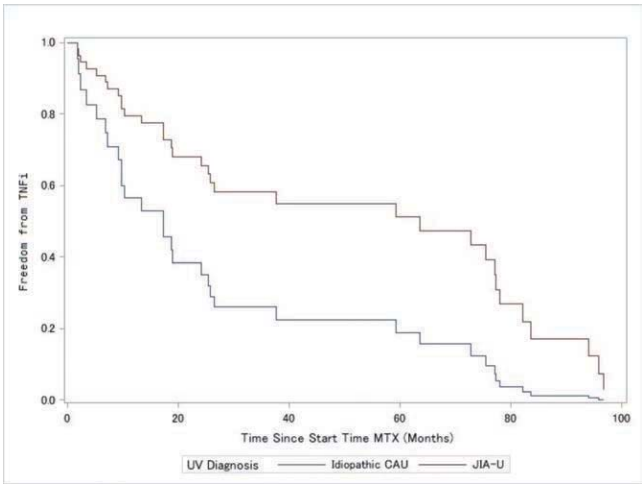

Figure 1. Kaplan-Meier curve showing freedom from TNFi (mos) stratified by diagnosis

Conclusion: Two out of three children with NIU fail initial MTX monotherapy, exposing them to increased accrual of ocular complications prior to biologic starts. The risk for delay in starting tumor necrosis factor α inhibitors (TNFi) seems higher with CAU. Future studies will examine risk factors that predict MTX response in NIU.

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POS1304 CORRELATION OF SKIN SCORES (LOSCAT) WITH PATIENT REPORTED OUTCOMES IN JUVENILE LOCALISED SCLERODERMA

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Background: Juvenile localised scleroderma (JLS) or morphea is a rare condition, causing inflammation and fibrosis in skin and underlying tissues. A validated skin score (Localized Scleroderma Cutaneous Assessment Tool, LoSCAT) has been developed [1]. This tool has both activity (mLoSSi) and damage indices (LoSDI). Several patient-reported outcomes (PRO) have been studied in JLS including visual analogue scales (VAS), functional and health-related quality of life measures.
Objectives: To assess the associations between different PROs and the activity and damage indices of the LoSCAT.
Methods: Participants aged 4 to 17 were recruited from 3 tertiary paediatric rheumatology centres in the UK and attended 4 visits at 3 monthly intervals as part of a program of research on JLS. Patient-reported VAS (6 different scales), the Children's Dermatology Life Quality Index (CDLQI) and Childhood Health Assessment Questionnaires (CHAQ) were completed at each visit. LoSCAT was completed by the two same clinicians throughout the study (both trained in skin score techniques). Pearson correlation coefficients were calculated between each PRO and each component of the LoSCAT.
Results: 24 participants completed all 4 visits and 1 attended 3 visits. 20 participants were female (80%) and 5 were male (20%). Mean age at diagnosis was 7.6 years with mean disease duration of 4.9 years. Subtype of disease was linear head in 5/25 (20%), linear limb 12/25 (48%), generalised morphoea 1/25 (4%), mixed 5/25 (20%) and superficial plaque in 2/25 (8%). Table 1 shows the correlations with figures in bold highlighting positive correlations which were statistically significant ($p<0.05$) and medium-sized ($r>0.3$).

Table 1. Correlation between patient reported outcomes and LoSCAT

PRO	Total skin activity (mLoSSi)		Total skin damage (LoSDI)	
	r (95% CI)	p-value	r (95% CI)	p-value
CDLQI	**0.61 (0.02, 1.20)**	**0.044**	**0.42 (0.01, 0.83)**	**0.044**
CHAQ	**0.30 (0.03, 0.57)**	**0.027**	**0.20 (-0.14, 0.54)**	**0.244**
VAS 1: How much IMPACT has your disease had on your life in the PAST MONTH?	**0.49 (0.00, 0.98)**	**0.050**	**0.38 (0.06, 0.71)**	**0.021**
VAS 2: How much has your condition (localized scleroderma) affected you OVERALL in the PAST MONTH?	**0.59 (0.09, 1.09)**	**0.022**	**0.42 (0.13, 0.72)**	**0.005**
VAS 3: Have your lesions felt itchy and/or scratchy in PAST MONTH?	0.40 (-0.01, 0.81)	0.056	0.31 (0.03, 0.59)	0.028
VAS 4: Have you felt numbness, tingling, and/or other "funny" feeling in or around your lesion in PAST MONTH?	**0.55 (0.04, 1.05)**	0.033	0.33 (-0.04, 0.71)	0.084
VAS 5: How much WORRY do you have about LONG--TERM problems from your disease?	0.40 (-0.01, 0.81)	0.053	**0.32 (0.00, 0.63)**	**0.047**
VAS 6: How much WORRY do you have about problems from MEDICATIONS used to treat your condition?	**0.41 (0.00, 0.82)**	0.050	0.29 (-0.09, 0.66)	0.131

The VAS of symptoms of numbness/tingling showed a strong positive correlation with mLoSSi but a weak and/or non-significant correlation with LoSDI. VAS itchy/scratchy did not show a strong correlation with mLoSSi but showed a moderate correlation with LoSDI. Patient global VAS correlated with both mLoSSi and LoSDI, as did CDLQI. CHAQ correlated with activity only.
Conclusion: Symptoms within lesions are often interpreted as indicating disease activity. A previous study in adults and children showed itch positively correlated with mLoSSi suggesting it may be a marker of active disease [2]. However, in our study numbness/tingling correlated with disease activity whereas itch did not. Further work is required to understand whether itch correlates to both activity and damage and whether numbness/tingling is a better indicator of activity than itch. Limitations of our study include a heterogenous group of participants with longstanding high-burden disease.

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POS1305 PEDIATRIC SAPHO SYNDROME: SINGLE ENTITY OR COMBINATION OF DIFFERENT DISEASES?

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Background: SAPHO is a heterogeneous autoinflammatory disease, characterized by bone and joint involvement and by a wide variety of dermatologic manifestations, including palmo-plantar pustulosis (PPP), acne, hidradenitis suppurativa (HS), pyoderma gangrenosum (PG), psoriasis, Snedd-Wilkinson disease and Sweet syndrome. In children, the osteo-articular manifestations are characterized by chronic recurrent multifocal osteomyelitis (CRMO), involving the metaepiphysis of the long bones and the axial skeleton, as in the adult form. The SAPHO treatment still today is a challenge, and no therapeutic guidelines are available in children: NSAIDs are frequently used as first line treatment for CRMO lesions, followed by bisphosphonates, methotrexate and biologic therapies. In the literature there are many case reports but only a few case series[1-3], of which this is the largest in Europe (29 cases reported in China[4]).
Objectives: to report the clinical and radiological features and the response to therapy of SAPHO children.
Methods: the clinical data (serological, imaging and therapy) of 13 SAPHO patients, followed between 2001 and 2021 at the Unit for Autoinflammatory diseases at the Gaslini Hospital were reviewed.
Results: 7/13 patients were male. At disease onset, acne-HS was present as the only manifestation in 8/13 patients while PPP was concomitant or subsequent to bone manifestations. The skin involvement was characterised by acne (comedonic in 3 cases, nodulo-cystic in 4 cases), PPP (5), HS (3), PG (1). Multifocal inflammatory bone lesions with axial or long bone involvement were both present in 92% of patients, whereas sternoclavicolar involvement was observed in 85% of patients.
At disease onset all patients were treated with NSAIDS but only 4, with also PPP, achieved remission. In 7/13 patients, Methotrexate or salazopirin were used, and in 2/13 with severe painful bone lesions bisphosphonates were successfully employed. In the 5 PPP patients, the cutaneous involvement was mild and did not need treatment. In 9/13 patients, the skin manifestations required a therapeutic upgrade with biologics: Etanercept in 5 with partial result, Adalimumab in 6 had an optimal response, in 1 a partial response, even if requiring an increased dose (80mg per week) and 1 was swapped to dapsone. Anakinra (3), ustekinumab and secukinumab (2) were not efficacious. It is to note that the 3 patients with comedonic acne were refractory to all treatments and needed multiple therapy cycling to achieve a partial remission only.
Conclusion: Our patients were characterised by well known SAPHO clinical manifestations. Despite the optimal therapeutic response of CRMO, comedonic acne was refractory to any treatment while PPP and nodulo-cystic acne achieved remission. This may suggest that the skin involvement in SAPHO may identify clinical phenotypes with a different response to treatments.

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POS1306 EXTREME PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS AND CERVICAL ADENITIS (PFAPA) ARE A SUBSET OF PFAPA PATIENTS WITH FLARES THAT OCCUR MORE THAN TWICE A MONTH.

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Background: The febrile episodes of periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome occur, by definition, every 2 to 8 weeks. However, a subset of our patients appears to experience attacks at an even higher rate of more than twice a month, and was therefore named extreme PFAPA, or ePFAPA group.
Objectives: To characterize this group both demographically and clinically in order to compare them to the non-extreme PFAPA (nPFAPA) group.
Methods: We retrospectively reviewed the medical records of patients with PFAPA that were treated in the Schneider Children's Medical Center of Israel from 3/2014 to 4/2021. Patients with concomitant familial Mediterranean fever were excluded. Thereafter the ePFAPA and nPFAPA groups were compared using Wilcoxon rank sum, Pearson's chi-squared and Fisher's exact tests.
Results: 47 patients (12.9%) out a total of 365 PFAPA patients were included in the ePFAPA group. Compared to the nPFAPA group, ePFAPA patients had earlier disease onset (age 1.7 vs 2.96 years, P<0.001) and diagnosis (age 2.94 vs 5.02 years, P<0.001). Moreover, after initiation of an abortive treatment with corticosteroids, ePFAPA patients had higher increased flares frequency (72% vs 40%, P<0.001) and were treated with colchicine prophylaxis more often (67% vs 26%, P<0.001). Other clinical and demographic aspects were not significantly different between the two groups.
Conclusion: EPFAPA patients are a subset of patients who have earlier onset and diagnosis of PFAPA, and also increased flares frequently after abortive therapy with steroids. Current study is underway to describe the long-term outcome of this group.
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POS1307 **HEMATOLOGICAL MANIFESTATIONS IN THE PRESENCE OF ANTIPHOSPHOLIPID ANTIBODIES IN A PEDIATRIC COHORT**

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Background: Antiphospholipid syndrome (APS) is an autoimmune disease characterized by thrombotic events (TEs) and/or pregnancy morbidity, in association with two consecutive positive determinations (at least 12 weeks apart) of antiphospholipid antibodies (aPLs). Several manifestations which are not considered clinical criteria of APS have been identified, including hematologic disorders. [1]
Objectives: To identify the different variables associated with the development of hematological manifestations in the presence of aPLs in a pediatric cohort.
Methods: Multicentric historical cohort of children ≤ 18 years from three Spanish and one Italian tertiary referral hospitals with at least 2 positive determinations (≥12 weeks apart) of IgG/IgM anticardiolipin (aCL), IgG/IgM anti β2-glycoprotein I (aβ2GP) and/or LA. Demographic, clinical and analytical data were collected. A bivariate and multivariate analysis were carried out. Multicollinearity was also explored to build the model.
Results: 131 children were included. Demographic, clinical, analytical data; and results of bivariant analysis are shown in Table 1.

Table 1. ***Demographic characteristics; non-thrombotic clinical manifestations; immunologic laboratory findings; and bivariate analysis according to each specific entity and the occurrence of "hematological" manifestations. Categorical variables expressed as number (n) and percentage (%); Numerical variables with normal distribution expressed as mean and SD (standard deviation). * p<0.05.***

Variables	Total n= 131	Hematological manifestations n= 55	Absence of hematological manifestations n= 76	P-value
Sex, female, n (%)	85 (64.9)	39 (70.9)	46 (60.5)	0.219
Age, years, mean (SD)	10.9 (5.1)	10.8 (5.03)	10.9 (5.2)	0.974
Rage, n (%)				
Caucasian	105 (81.4)	43 (79.6)	62 (82.7)	
Maghreb	9 (7)	2 (3.7)	7 (9.3)	0.126
Latinoamerican	8 (6.2)	6 (11.1)	2 (2.7)	
Asian	5 (3.9)	3 (5.6)	2 (2.7)	
Family history of AIDs, n (%)	33 (25.2)	17 (33.3)	16 (21.1)	0.122
SLE diagnosis, n (%)	34 (26)	20 (36.4)	14 (18.4)	0.021*
Thrombotic events, n (%)	16 (12.2)	7 (12.7)	9 (11.8)	0.879
Hematological, n (%)	55 (42)	-	-	-
Thrombocytopenia	30 (22.9)			
Leucopenia	16 (8.4)			
Hemolytic anemia	7 (5.3)			
Evans syndrome	2 (1.2)			
Neurological, n (%)	26 (20)	10 (18.2)	16 (21.3)	0.657
Chorea	8 (6.1)			
Epilepsy	5 (3.8)			
Migraine	4 (3)			
Cutaneous, n (%)	23 (17.6)	6 (10.9)	17 (22.4)	0.089
Raynaud	17 (13)			
Livedo	5 (3.1)			
Cardiac, n (%)	22 (16.8)	12 (21.8)	10 (13.2)	0.191
Renal, n (%)	2 (1.5)	0 (0)	2 (2.6)	0.225
aCL, n (%)				
IgG	54 (41.2)	24 (43.6)	30 (39.5)	0.633
IgM	31 (23.7)	20 (36.4)	11 (14.5)	0.004*
aB2GP, n (%)				
IgG	59 (45)	29 (52.7)	30 (39.5)	0.132
IgM	24 (18.3)	16 (29.1)	8 (10.5)	0.007*
LA, n (%)	76 (58.5)	37 (67.3)	39 (52)	0.081
aPL profile, n (%)				
Simple	76 (58)	25 (45.5)	51 (67.1)	0.008*
Double	30 (22.9)	13 (23.6)	17 (22.4)	
Triple	25 (19.1)	17 (30.9)	8 (10.5)	
ANA +, n (%)	72 (59.5)	33 (66)	39 (54.9)	0.222

The multivariate analysis identified as independent risk factors to develop a hematological manifestation, children with: SLE diagnosis [OR 1.2, 95 CI (0.5-5.8), p= 0.015], cutaneous manifestations [OR 1.01, 95 CI (0.6 -2.8), p= 0.091], LA + [OR 0.8, 95 CI (0.4 -3.6), p= 0.058], and IgG aβ2GP + [OR 0.9, 95 CI (0.4 - 3.9), p= 0.048]. Sex, age, familiar history of AIDs or IgM B2GP+ did not show a higher risk.

Conclusion: Non-criteria manifestations, specially hematologic disorders, are the most frequent events in the presence of aPLs in our cohort. Cutaneous manifestations, a positive personal history of SLE, LA positivity and IgG aβ2GP positivity were associated with a higher risk of developing hematological manifestations. Therefore, their inclusion as APS classification criteria should be considered.

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POS1308 SINGLE CENTER REAL-LIFE PRACTICE OF BIOLOGICAL THERAPY IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH JUVENILE ONSET

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Background: In recent years the use of Biologics (B) at the management of systemic lupus erythematosus including with juvenile onset (jSLE) has increased. Belimumab (BEL) became the first approved B for SLE. The use of rituximab (RTM), despite the status "of label," remains relevant in a number of patients (pts) with poor response to standard therapy and the presence of life-threatening conditions. However, use of B in real clinical practice has increase slowly, in part, due to uncertainty over which pts should be treated with B and in what stage of the disease, in part, due to uncertainty over safety.

Objectives: To analyze in retrospective study the efficacy and safety of B in pts with jSLE.

Methods: The study included all pts with jSLE in our pediatric rheumatologic department, who received B.

Results: Among 160 pts with jSLE, 52 (32.5%) received B: 43 – RTM, 12 – BEL, 1 – abatacept (ABA). 4 pts received 2B in sequence (2 – RTM-BEL; 1 - BEL-RTM; 1 – RTM-ABA). The proportion of pts with jSLE was 47% among all those who received RTM in our center. The median age at onset – 12.2 y.o. [IQR 9.9; 14.6], median disease duration at start of RTM – 2.5 years [IQR 0.9; 4.5]. The girls and boys ratio = 6.2:1. The median of activity by SLEDAI at start of RTM was – 16 [12; 22]. 58% of pts underwent more than one course of RTM, with a maximum of 6 courses. The median time between each course was 182 [96–315] days. RTM was effective in 40 (93%) pts with the achievement of the inactive status of the disease and reduction of GC-therapy. Various adverse events (AE) were observed in 46.5% of pts as recurrent uncomplicated upper respiratory tract infections being the most common (23.2%). RTM was discontinued in 9 pts: 1 - the flare of Ro-associated vasculitis, 1 - inefficiency, 7 - serious AEs. Serious AEs included: pneumonia – in 1 (2.3%), serious infusion reaction – 1 (2.3%), toxic epidermolysis – 1 (2.3%), MAS – 2 (4.6%), death (inefficiency for treatment of MAS in SLE) – 2 (4.6%). Among pts receiving BEL the median age at onset was 12.7 y.o. [IQR 10.0; 15.0], median disease duration at start of BEL – 1.5 years [IQR 1.0; 2.1]. The girls and boys ratio = 1.4:1. The median of activity by SLEDAI at start of BEL was – 10 [9; 14]. 6 pts receive BEL more than 1 year with the achievement of the inactive status of the disease and reduction of GC-therapy. AEs were registrated in 3 pts (25%): neutropenia (III degree) – in 1, SAEs – in 2 pts (toxic epidermolysis after 1st infusion, flare of SLE after 6 months of therapy, with discontinuation of BEL in both pts). One patient, boy, 4 y.o. at onset, received ABA (RTM was discontinue after MAS). Disease duration at start of ABA – 7.5 years, the activity by SLEDAI – 10. Treatment with ABA allowed to decrease the activity of jSLE (now SLEDAI=2). Now boy receives ABA during 51 months with good safety, continues GC 5 mg per day, hydroxychloroquine 100 mg per day, MMF 750 mg per day.

Conclusion: Our study has shown that B is effective in jSLE and has an acceptable safety profile if possible adverse reactions are carefully monitored. In the presence of severe organ lesions, to improve the long-term prognosis, the appointment of B at an early stage of the disease can be discussed. The overall picture that emerges is one of optimism that advances in therapy of jSLE will be realised through the targeted use of an increasing different B.

Disclosure of Interests: None declared

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POS1309 THE IMPACT OF PSORIASIS ON PATIENT-REPORTED OUTCOMES IN JUVENILE PSORIATIC ARTHRITIS

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Background: Children with juvenile psoriatic arthritis (JPsA) are treated similarly to patients in other categories of juvenile idiopathic arthritis (JIA) despite distinctive clinical features, including either a personal or family history of psoriasis. It remains unknown whether the unique features in JPsA lead patients to experience the impact of disease differently from other JIA patients, and how the presence of psoriasis within JPsA affects patient outcomes. These gaps in our knowledge suggest there may be unmet treatment needs in these children and young people.

Objectives: To compare patient-reported outcomes in patients with JPsA and other JIA categories. Additionally, this study explores whether the presence or absence of psoriasis in patients with JPsA is associated with different outcomes.

Methods: Children and young people with JIA were selected if recruited to the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort of JIA, between January 2001 and March 2018. Detailed demographic information, clinical data and patient-reported outcomes were collected at initial presentation to paediatric rheumatology. Patient-reported outcomes included well-being as measured on the parental global evaluation (10cm), functional ability (Childhood Health Assessment Questionnaire: CHAQ), pain (10cm), health-related quality of life (Child Health Questionnaire, CHQ psychosocial score), depressive symptoms (Mood and Feelings Questionnaire, MFQ) and parent psychosocial health (General Health Questionnaire: GHQ). The CHQ and MFQ questionnaires were completed in a subset of children recruited until 2015 and aged above 5 and 7 years old, respectively.

Patient-reported outcomes in patients with JPsA versus other JIA categories, and in patients with and without psoriasis within JPsA, were tested via multivariable linear regression, adjusted for age at first presentation, gender, disease duration, ethnicity, and number of active joints.

Results: A total of 1653 patients had JIA; the majority (64.7%) were female and median age at onset was 6.5 years (IQR 2.7 - 10.8). A total of 111 (6.7%) were categorised with JPsA, of which 62 (55.9%) were female with median age at onset of 10.2 (IQR 4.3 - 12.5). In those with JPsA, 35% had psoriasis at diagnosis. There were no significant differences between JPsA and non-JPsA in terms of parental global evaluation of wellbeing (p=0.21), CHAQ (p=0.19), pain (p=0.38), CHQ psychosocial (p=0.18), GHQ (p=0.31) or MFQ (p=0.34).

Within JPsA, depressive symptom score on the MFQ was higher in patients with psoriasis compared to those without (coefficient=9.8, 95% CI=0.5 to 19.0, p-value=0.04). However, there were no significant differences in parental global evaluation (p=0.4), CHAQ (p=0.3), pain (p=0. 3), CHQ psychosocial score (p=0.5) or GHQ (p=0.7) between those with and without psoriasis in JPsA (Table 1).

Table 1. Patient-reported outcomes in children and young people with JPsA with and without psoriasis

Patient-reported outcome at JPsA diagnosis	Outcome	Coefficient	95% confidence interval	p-value
	Reference – JPsA without psoriasis	Reference	Reference	Reference
	JPsA with psoriasis			
Wellbeing: Parent global (0-10cm)		0.5	-0.8, 1.8	0.45
Function: CHAQ (0-3)		0.2	-0.2, 0.6	0.28
Pain (0-10cm)		0.8	-0.8, 2.4	0.34
Psychosocial health: CHQ (0-100)		-2.4	-10.1, 5.3	0.52
Parent psychosocial: GHQ (0-84)		-1.3	-8.7, 6.1	0.72
Depressive symptoms: MFQ (0-66)		9.8	0.5, 19.0	0.04

Conclusion: Despite the differences in clinical features present in JPsA compared to the other JIA subtypes, there were no statistically significant differences in patient-reported outcomes overall at diagnosis. However, within the JPsA group, even when adjusting for age, children with psoriasis at time of arthritis diagnosis reported higher depressive symptom scores compared to those without psoriasis. When treating children with JPsA, attention to diagnosing and treating both arthritis and psoriasis may help mood. If poor mood persists in this subtype, then further allied health care may be required.

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POS1310 LONG - TERM OUTCOMES IN ADULT PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Systemic juvenile idiopathic arthritis (sJIA) debuts in childhood and persists throughout the patient's lifetime. Currently there is not enough information about the course and therapeutic approaches in patients who have reached the age of 18 and moved from pediatric service to adult healthcare system.
Objectives: Evaluate long - term outcomes in patients with sJIA over 18 years of age.
Methods: Thirty - two patients with sJIA have been analyzed after their transition to adult rheumatological chain. The following parameters have been estimated: clinical manifestations, disease duration, radiological changes, medication intake, disease activity, number of arthroplasties, pregnancy, level of education. Disease activity has been assessed using a standardized DAS28 index (remission - less than 2.6, low activity - from 2.6 to 3.2, moderate activity - from 3.2 inclusive to 5.1, high activity - more than 5.1) and counting systemic manifestations.
Results: Among patients included in the study, there were 11 men (34.38%) and 21 women (65.62%); the average age at the time of inclusion was 23.68 (±5.93). In 13 (40.63%) patients the onset of the disease occurred before the age of 5, in 7 (21.87%) - from 6 to 10 years and in 12 (37.50%) - after 11 years. In 9 (28.13%) patients the duration of the disease was less than 10 years, in 23 (71.87%) patients – more than 11 years. The onset of the disease was accompanied by the following symptoms: fever - 28 (87.50%) patients, arthritis - 21 (65.63%), rash - 17 (53.13), arthralgia - 6 (18.75%), pericarditis - 4 (12.50%), sore throat - 4 (12.50%), lymphadenopathy - 3 (9.38%), hepatomegaly - 2 (6.25%). Among patients with arthritis 11 (52.38%) had oligoarthritis, 10 (47.62%) had polyarthritis. 2 patients (6.25%) were diagnosed with uveitis. According to the X-ray examination (Steinbrocker's classification of radiographic changes): 5 (15.63%) patients had the I stage, 13 (40.62%) - the II stage, 4 (12.50%) - the III stage, 6 (18. 75%) - the IV stage and 4 (12.50%) had no radiological changes. Three (9.38%) were diagnosed with aseptic necrosis and these patients underwent arthroplasty. Four (12,50%) patients had pregnancy.
Education: 17 (53.13%) people study at higher educational institutions. Two (6.25%) have a higher educational level.
Disease activity: 24 (75%) patients are currently in low activity or disease remission, 8 (25%) are in moderate activity. Twenty (62.50%) patients receive therapy with disease - modifying antirheumatic drugs (DMARDs), 14 of them take methotrexate at an average dose of 12.68 (±3.98) mg. 6 (18.75%) patients take glucocorticoids at a dose of 1 to 8 mg per day. Non - steroidal anti - inflammatory drugs (NSAIDs) are received by 2 (6.25%) patients. Biological disease - modifying antirheumatic drugs (bDMARDs) are used by 27 (84.38%) patients, 18 (66.67%) of whom are on therapy with tocilizumab.
Among the patients with low activity and disease remission: 15 out of 24 (62.50%) are treated with tocilizumab, 3 (12.50%) – with canakinumab, 3 (12.50%) – with etanercept, and 1 (4.17%) – with adalimumab; 2 (8.33%) patients don't take bDMARDs.
Conclusion: The use of bDMARDs helps successfully control the disease in patients with sJIA, maintain long - term remission and improve long - term outcomes in adult patients with sJIA.
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POS1311 HETEROZYGOUS IFIH-1 AND DDX58 VARIANTS DETECTED IN CHILDREN WITH IMMUNO-MEDIATED DISEASES

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Background: IFIH1 gene codes for the MDA5 protein participating in interferon I signaling pathway, which is important in the innate immune response [1]. IFIH1 polymorphisms are associated with a spectrum of autoimmune disease [2]. Rare IFIH1 gene defects have been found in patients with Aicardi- Goutières syndrome-7, Singleton-Merten syndrome, and MDA-5 immunodeficiency. All these conditions are characterized by upregulation of interferon signaling [3]. DDX58 encodes RIG-I receptor that is responsible for the recognizing of single- and double-stranded viral RNA. Mutation of DDX58 was described in Singleton-Merten syndrome [4].
Objectives: to describe clinical characteristics of patients with rare IFIH1 and DDX58 variants detected by clinical exome sequencing.
Methods: 8 patients (5 girls and 3 boys) having rare IFIH1 and DDX58 variants (MAF less than 0.005) were found in heterozygous state among the patients who underwent genetic testing in our hospital in 2019-2021. Clinical manifestations, laboratory parameters, IFN I score values and treatment options were analyzed.
Results: 3 patients (#3, #6, #7) had undifferentiated systemic autoinflammatory syndromes, while others were presented with SLE, SLE-like disease, JDM and PFAPA syndrome. All of them had elevated IFN-I score and skin rash. IFIH-1 variants were in 5 patients (#1-5); 3 patients carried the same c.1879G>T polymorphic variant. Patient #6-8 have VUS DDX58 variants. All the alleles were in heterozygous state. Detailed information is presented in Table 1.

Table 1.

#	Genetic variants	MAF	IFN-score	Diagnosis	Manifestation	Treatment
1	IFIH1 c.1879G>T (p.E627X)	0.003	11.3	SLE	Fever, photosensitivity, pancytopenia, thrombosis	CS, RTX, MMF
2	IFIH1 c.1879G>T (p.E627X)	0.003	2.95	PFAPA	Fever, pharyngitis, stomatitis, adenitis	CS in flares
3	IFIH1 c.1558A>G p.T520A	0.00009	5.52	uSAID	Fever, pancytopenia, petechias, panniculitis, hepatomegaly, inflammation	CS, CsA, TOC, TOF
4	IFIH1: c.1784G>A (p.R595H)	0.0001	29.0	JDM	Gottron's papules, periorbital erythema, muscle weakness, osteoarthritis	CS, CYC, IVIG, MTX
5	IFIH1 c.1879G>T (p.E627X)	0.003	20.2	SLE-like disease	Face erythema, skin thickening	topical tacrolimus
6	DDX58 c1061A>G (p.N354S)	0.00007	2.13	uSAID	Recurrent pericarditis	CS
7	DDX58 c109G>A (p.E37K)	0.000008	n/a	uSAID	Fever, livedo racemose, inflammation	NSAIDS
8	DDX58 c.2587_2590dup (p.Cys864fs)	0.0006	21.0	SLE	Skin, mucous, joints, kidney involvement, pancytopenia	CS, RTX

Abbreviations: MAF- minor allele frequency; SLE- systemic lupus erythematosus; uSAID- undifferentiated systemic autoinflammatory syndrome; JDM- juvenile dermatomyositis; CS- corticosteroids; RTX- rituximab; CYC- cyclophosphamide; MTX- methotrexate; IVIG- intravenous immunoglobulin; MMF- mycophenolate mofetil; CsA- cyclosporine A; TOF- tofacitinib.

Conclusion: while rare IFIH1 and DDX58 variants have been repeatedly detected in children with clinically heterogeneous immune-mediated diseases, it is unclear whether these alleles have casual role. Functional testing and collection of patients with the same gene variants are required.
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POS1312 ANALYSIS OF INTERFERON TYPE I SIGNATURE IN JUVENILE DERMATOMYOSITIS

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Background: the crucial role of hyperactivation IFN I signaling pathway has been proved in the pathogenesis of dermatomyositis. IFN I genes and chemokines activity vary according to subtype of inflammatory myopathies. IFN type 1 signature could be measured using different genes in the blood, skin and muscle tissue [1].
Objectives: to evaluate IFN-score in children with dermatomyositis and compare with disease activity
Methods: 15 patients (5 boys and 10 girls) were enrolled in the study. Clinical and laboratory parameters, disease activity (CMAS-childhood myositis assessment tool, aCAT- abbreviated cutaneous assessment tool) and treatment were assessed. Patients were compared accordingly to IFN-score elevation. IFN I-score was assessed by RT-PCR quantitation of 5 IFN I-regulated transcripts (IFI44L, IFI44, IFIT3, LY6E, MXA1); median relative expression of ≥ 2 was considered as a cut-off. IFN I-score was evaluated in dynamics in 9 patients.
Results: median age of patients was 6.2 (3.6; 7.6) years. Skin and muscle involvement were in all patients, arthritis in 5 (33%) patients, calcinosis in 3 (20%), lipodystrophy in 2 (13%) and lung involvement in 5 patients (33%), and 9 patients (60%) had positive myositis-related antibodies. Ten patients (67%) had an active disease, while elevated IFN-signature was detected in 12 (80%) patients.
Cumulative IFN I-score and its' five components were higher in active patients, compare to inactive (13.6 vs 1.4, p=0.006).
Patients with increased IFN I-score had lower CMAS score and higher aCAT score compare to patients with normal levels of IFN I-score. IFN-I score correlated with aCAT, arthritis and lung involvement.
Conclusion: IFN-I score may be considered as disease activity biomarker in juvenile dermatomyositis with predominantly skin activity process.
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POS1313 HIP INVOLVEMENT IS A MORE FREQUENT COMPLICATION IN ENTHESITIS-RELATED ARTHRITIS COMPARING TO THE ADULT SPONDYLARTHRITIS

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Background: The hip disease develops in 30% to 50% of children with juvenile idiopathic arthritis (JIA) and is associated with poor outcomes and functional impairment. The coxitis in enthesitis-related arthritis (ERA or juvenile-onset spondyloarthritis) patients was frequent but weakly studied.
Objectives: To assess the occurrence of coxitis in patients with ERA and compare it to that of older patients with spondyloarthritis (SpA).
Methods: We conducted a retrospective comparative study including patients with ERA and adult spondyloarthritis patients.
The first group included patients under 16 years old fulfilling the International League of Associations for Rheumatology (ILAR). The second group of patients fulfilled the Assessment of SpondyloArthritis International Society (ASAS) 2009 criteria.
We studied the socio-demographic characteristics of both groups, the hip involvement occurrence, and the treatment modalities.
Quality of life was appraised by the Study 36-item Short-Form Health Survey (SF-36) and the Ankylosing spondylitis quality of life test (ASQOL).
Results: Forty ERA (mean age= 25,3 ± 10,15) patients and 134 SpA (mean age=37,96±11,77) patients were enrolled. Seventeen ERA patients (42,5%) had coxitis at recruitment compared to 28 SpA patients (20,9%), p=0,06. More than half of the ERA patients were positive to HLAb27, compared to the SpA group (44,7%) without reaching a significant threshold, p=0,07. The mean delay of coxitis onset in ERA patients was 4,66 ± 8,46 years, and was 5,65 ± 6,85 years in SpA patients, with no significant difference between the two groups (p=0,527). There was no difference between the two groups for the coxitis being unilateral or bilateral (p=0,272 and 0,169 respectively). Regarding the treatment approach, local therapy was proposed to 11 patients in the ERA group and 13 patients in the SpA group (p=0,07), with synoviorthesis being the most common therapy. Total hip replacement was done in 8 ERA patients (of which seven were bilateral) and in 17 SpA patients (of which ten were bilateral), without reaching the significant threshold (p=0,858). There was no significant difference between the two groups on the period when the total hip replacement was done (p=0,925). Quality of life assessed by the ASQOL and the SF-36 was comparable between the two groups (p=0,666 and 0,326; respectively).
Conclusion: Our study shows the high prevalence of hip involvement in the juvenile group of SpA. This complication occurs within the five years of disease outcomes and constitutes a turning point in their lives.
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POS1314 VALIDATION OF A PEDIATRIC-SPECIFIC ULTRASOUND SCORING SYSTEM FOR THE EVALUATION OF WRIST, FINGER, AND ANKLE SYNOVITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is the most common chronic rheumatic disease in children. Clinical evaluation of arthritis is a subjective measurement. Musculoskeletal ultrasound (MSUS) is increasingly being utilized in children. In order to provide objective assessments of arthritis, reliable and validated MSUS scoring systems are needed. Recently, a joint-specific scoring system for the assessment of arthritis of the pediatric ankle, wrist and finger joints were proposed[1, 2].
Objectives: This study aims to further validate the MSUS scoring system for the assessment of finger, wrist, and ankle arthritis
Methods: JIA patients with finger, wrist, and ankle arthritis as per expert clinician evaluation are eligible for this study. A comprehensive wrist, ankle, and finger (2-5th metacarpal and 2-5th proximal interphalangeal joints) MSUS examination by an American College of Rheumatology MSUS certified pediatric rheumatologist is performed an all enroll subjects. MSUS are scored using the semiquantitative (grade 0 to 3) scoring systems previously proposed. A subset of participants receives an MRI with contrast of the targeted joint immediately after MSUS performance. MRI findings are read for presence of synovitis, tendonitis and enthesitis by a pediatric radiologist with expertise on musculoskeletal imaging. For the analysis of the current report, MRIs were classified as having presence or absence of findings of JIA disease based on the pediatric radiologist expert opinion. MSUS were classified as normal (grade 0 and 1) or abnormal (grade 2 and 3). Cohen's Kappa Coefficient was used to assess the level of agreement between MSUS (normal and abnormal) and MRI with contrast (absence or presence of disease) for each targeted joint. Tetrachoric Correlation was used to assess the strength of the association. Fisher's Exact test was used to determine statistical significance at $p < 0.05$ level.
Results: A total of 52 children aged 2 – 18 years old have been enrolled in this study. To date 20 MSUS of the finger(s), 33 MSUS of the wrist, and 43 MSUS of the ankle joints have been collected. Three MRI of the 2-5 fingers (12 fingers total), 6 MRI of the wrist, and 5 MRI of ankle have been obtained through the study. Preliminary results of this effort reveal that for the ankle joint there is moderate agreement (Kappa coefficient 0.53 (confidence interval (CI)=0.14-0.92)) between MRI and US and a strong positive tetrachoric correlation (0.79) ($p = 0.03$). While the Kappa coefficient for comparing MRI and US finding on wrist joint indicated moderate agreement (Kappa 0.62 [0.15-1.00]) with a strong tetrachoric correlation (0.83) the Fisher's exact test indicated a trend rather than statistically significant results ($p = 0.07$). The Kappa coefficient for MCPs and PIPs joints indicated strong agreement between MRI and US (Kappa 0.83 [CI=0.52-1.00] and 0.80 [CI=0.43-1.00] respectively) and were supported by an almost perfect Tetrachoric Correlation of 0.99 ($p < 0.01$). We anticipate to complete enrollment of subjects by the summer of 2022. Analysis of collected data is underway.
Conclusion: The strong to moderate association of MSUS with contrast-enhanced MRI, suggest that MSUS can provide an objective and accurate assessment of ankle, wrist and finger arthritis at the bedside. Further refinement and validation of these pediatric-specific MSUS scoring systems may support the use of MSUS as a clinical tool and outcome measure in JIA.
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POS1315

PREVALENCE OF SARCOPENIA IN YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: In the 2019 sarcopenia consensus update (EWGSOP2 [1]) experts emphasize low muscle strength as a key characteristic of sarcopenia, adding low muscle mass to confirm the diagnosis of sarcopenia. Thus, the presence of the first criterion indicates probable sarcopenia, the presence of the first and second criteria confirms the diagnosis of sarcopenia, and the presence of all three criteria indicates severe sarcopenia. There are no available data about severe sarcopenia in young adults with juvenile idiopathic arthritis (JIA).
Objectives: This study aims to assess the prevalence of severe sarcopenia in young patients with JIA.
Methods: To confirm the diagnosis of severe sarcopenia we used dual X-ray absorptiometry (DXA) to assess low muscle mass (cut off points for ASM/height2 <7 kg/m2 for men and <5,67 kg/m2 for women); dynamometry - to determine the low muscle strength (grip strength <27 kg for men, <16 kg for women); gait speed and short physical performance battery (SPPB) to assess physical function (cut off points <8 m/sec and score ≤8, respectively). Patients were divided into two groups according to the presence or absence of all three criteria for severe sarcopenia.
Results: We studied 40 young adults with JIA, including 23 female patients and 17 male patients. The mean age of the patients was 24,4±5 years; the mean age at the onset of the disease was 10,1±4,4 years. Patients were divided into 2 groups according to all three criteria for severe sarcopenia. The first group (I group) included 25 patients with reduced muscle mass, strength, and physical function, and the second group (II group) included 15 patients without criteria of severe sarcopenia. In the I and the II groups mean ASM/height2 was 5,1±0,8 kg/m2 vs 7,7±1,01 kg/m2; p=0,01; handgrip strength 14,8 ±4,8 kg vs 27,1±8,3 kg; p=0,01; gait speed 0,6±0,1 m/sec vs 1,4±0,6 m/sec; p=0,01; SPPB score 6,5±1,5 vs 10,9±1,3; p=0,01. The research found out: the height and weight of patients in the group with severe sarcopenia were lower than in the group without severe sarcopenia (height 1,67±0,07 m vs 1,75±0,08 m; p=0,01; weight 56,1±9,2 kg, 72,0±12,8 kg; p=0,01, respectively). The age of patients was not significantly different between the two groups, but the duration of the disease was longer in the I group 16,4±8,2 vs 9,2±5,3; p=0,01. The data of DXA differed between groups: the patients of I group had statistically reduced total BMD 1,07±0,1 g/cm2 vs 1,15±0,14 g/cm2; ultra-distal radius BMD 0,35±0,1 g/cm2 vs 0,51±0,12 g/cm2; femoral neck BMD 0,85±0,1 g/cm2 vs 1,04±0,2 g/cm2; p=0,01, respectively. Comparing the two groups, we found important differences: the level of ESR was higher in the I group 25,05±18,3 vs 11,5±10,02; p=0,01; the index of disease activity either (DAS28 4,0±1,5 vs 2,7±1,2; JADAS27 15,8±9,2 vs 8,3±4,8; p=0,01, respectively). Articular and extraarticular damage index were higher in I group: JADI-A 5,08±7,3 vs 0,5±0,7; p =0,01; JADI-E 1,7±1,8 vs 0,3±0,6, p=0,02.
Conclusion: The study confirms the presence of severe sarcopenia despite the young age of patients with JIA. Severe sarcopenia occurs in patients with a higher level of inflammatory activity, articular and extraarticular damage, reduced bone mineral density, and longer duration of the disease. Further study of the factors influencing the development of sarcopenia in this category of young patients is required.
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POS1316

PERFORMANCE OF THE KOBAYASHI SCORE AND MODIFIED KOBAYASHI SCORE IN PREDICTING RESISTANCE TO INTRAVENOUS IMMUNOGLOBULIN IN PATIENTS WITH PEDIATRIC INFLAMMATORY MULTISYSTEM SYNDROME ASSOCIATED WITH SARS-COV-2.

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Background: Pediatric Inflammatory Multisystem Syndrome Associated With SARS-CoV-2 (PIMS) is a new insidious disease which in several points may mimic Kawasaki disease. Patients diagnosed with one of the aforementioned conditions are initially treated with intravenous immunoglobulin (IVIG). However, up to 20% of children diagnosed with Kawasaki disease appear to be resistant to such therapy. Similarly, substantial portion of PIMS patients requires second line treatment including systemic glucocorticoids. There are several calculative models, including the Kobayashi Score, which are utilized to predict patients' response to such treatment. To our best knowledge, the scoring systems derived from Kawasaki disease have not yet been assessed whether they can fulfil similar role in PIMS patients.
Objectives: There were two essential questions to be addressed in the study: (1) Can the Kobayashi Score be utilized in making clinical decisions regarding concomitant treatment in PIMS patients? (2) Is there any modification that may increase the accuracy of the original score?
Methods: First step of the study involved 19 patients diagnosed with PIMS between July 2020 and June 2021. The statistical analysis including each parameter of the Kobayashi Score has been performed in order to determine potential alterations of the score. Then, the numerous variants of modified score have been compared in terms of their positive and negative predictive values in order to determine new PIMS IVIG Resistance Score (PIRS). In the next phase of the study, both scores have been validated in the second cohort involving 16 patients diagnosed with PIMS between July and December 2021. The final assessment has been performed in the unified study group (35 PIMS patients).
Results: The Kobayashi Score (see Table 1) significantly differentiated PIMS patients in terms of good response or resistance to IVIG (p=0.03967). However, the score returned a few false positive (3 out of 9) and false negative (2 out of 10) results. After step-by-step verification of clinical and laboratory parameters, authors developed a tentative PIRS (see Table 1) including the following criteria: hyponatremia, days of fever and platelet count (derived from the Kobayashi Score but with different cut-off levels) supplemented with procalcitonin level and percentage of lymphocytes. In the validatory phase of the study, both scores had equal accuracy to predict treatment response. The analysis of receiver operating characteristic curve in the unified study group has shown better performance of PIRS (Youden index 0,72) than the Kobayashi Score (Youden index 0,49).

Table 1. List of criteria included in both scores assessed in the study.

Criteria	The Kobayashi Score		PIMS IVIG Resistance Score (PIRS)	
Sodium	≤133 mmol/L	2 points	≤137 mmol/L	1 point
Days of illness at initial treatment	≤4	2 points	≤4	2 points
Aspartate aminotransferase	≥100 IU/L	2 points	-	-
Percentage of neutrophils	≥80%	2 points	-	-
Percentage of lymphocytes	-	-	≤16%	1 point
C-reactive protein	≥100 mg/L	1 point	-	-
Procalcitonin	-	-	≥3.5 ng/mL	1 point
Age	≤12 months	1 point	-	-
Platelet count	≤300 G/L	1 point	≤200 G/L	2 points
Increased risk of resistance to IVIG	**≥4 points**		**≥4 points**	

Conclusion: The Kobayashi Score is worth being considered to estimate the risk of resistance to IVIG in PIMS patients. Nonetheless, it is not free from false positive and false negative results. The postulated modified score called PIRS can become a promising alternative but it requires further validation in larger cohorts of patients.
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POS1317

HOW CAN WE ASSESS CARDIOVASCULAR RISK IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS? PRELIMINARY RESULTS REGARDING MEASUREMENTS OF CAROTID INTIMA-MEDIA THICKNESS DURING THE COVID-19 PANDEMIC.

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Background: There is growing body of evidence that adults who were diagnosed as children with juvenile idiopathic arthritis (JIA) have significantly increased risk of developing cardiovascular disease. Risk factors including prolonged sedentary screen time, insufficient physical activity and unhealthy diet are even more essential in the era of the COVID-19 pandemic. However, there is lack of simple and reliable prognostic marker identifying children at higher risk of early development of cardiovascular disease. Non-invasive tests utilized in adults to screen for early phase of atherosclerosis involve examination of the carotid intima-media thickness (cIMT). Only a few research projects have evaluated performance of cIMT measurement in JIA patients and the results remain inconclusive.
Objectives: The aim of this study was to evaluate the usefulness of cIMT testing as a screening method to determine cardiovascular risk in JIA patients. The secondary objective was to assess the frequency of risk factors related to the patients' lifestyle during the COVID-19 pandemic.
Methods: The study involved forty-five patients at mean age 13.4±3.2 years who were already diagnosed with JIA and thirty-seven age- and sex-matched healthy controls. Children were enrolled in the study between March 2020 and

September 2021. Study database included demographic data, conventional risk factors for developing cardiovascular disease (e.g. abnormal body mass index and exposure to secondhand smoking), inflammatory markers and disease activity score. Measurements of cIMT were performed by a qualified physician according to the standardized protocol using high resolution ultrasonography.

Results: Measurement of cIMT revealed values above 94th percentile in four children (three males and one female) who were all diagnosed with JIA. The quantity of abnormal results was not enough to verify the hypothesis of increased cardiovascular risk in JIA patients, though (p=0.06296). However, children diagnosed with JIA are more likely to have abnormal body mass index than their healthy peers (51.1% vs. 21.6%, p=0.00614). Children who doubled their sedentary screen time during the COVID-19 pandemic skipped the sufficient physical activity (p=0.03352). Correlation between elevated ESR and higher cIMT values in right carotid artery was marginally significant (r=0.292, p=0.051443). Regardless of JIA, exposure to secondhand smoking was proved as a significant risk factor of atherosclerosis (18.2% vs. 2.8%, p=0.02771).

Conclusion: Screening measurements of cIMT should be considered in the follow-up of JIA patients with higher disease activity with concurrent elevated ESR. Defining other indications for performing such examination requires further investigation involving larger study group. Healthy lifestyle, including reducing secondhand smoke exposure, needs to be promoted with utmost importance during the COVID-19 pandemic, especially in children with chronic diseases like JIA.

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POS1318 JUVENILE IDIOPATHIC ARTHRITIS DISEASE ACTIVITY IN TRANSITIONAL CARE

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Background: Juvenile Idiopathic Arthritis (JIA) is a group of heterogeneous arthritis with onset earlier than 16 years old. According to previous studies, these patients experience an improvement of their disease activity, functionality and even remission probability as they become young adults.[1] Transitional care units aim to coordinate an uninterrupted follow-up in patients with chronic diseases in order to accomplished the objective of improving the ability of manage their own disease.[2] Our transitional care unit attend patients from 18 to 25 years old who have been previously diagnosed with any pediatric rheumatic disease

Objectives: Our primary objective was to describe the disease activity of JIA patients at the transference to our unit and the remission maintenance during follow-up.

Methods: We conducted an observational retrospective longitudinal study from a cohort of patients with JIA who have been transferred to our transitional care unit. We selected patients with at least one clinical visit and active follow-up. We collected demographic data, JIA classification, previous treatments and the treatment at time of transfer, articular and ocular flares, remission defined by Wallace criteria[3] and changes in treatment during follow-up.

We calculated the percentage of patients who had active disease activity at the transference to the Unit and the proportion of patients who had an inflammatory flare (ocular or articular) during the follow-up.

Results: From December 2016 to December 2021 we received 184 patients in our Transitional Care Unit, from them 127 had a JIA and 1 had asymptomatic chronic uveitis. Demographics of JIA patients is shown in Table 1. From 127 JIA patients, 34 (26,8%) were active at the transference and 53 (41,8%) had at least one flare during the follow-up.

Table 1. Demographic data from JIA included in the study, divided according to disease activity at the transference to our transitional care unit.

	Total (n: 127)	Actives (n:34)	Not actives (n:93)
Sex (female) n (%)	84 (66.1)	24 (70.6)	60 (64.5)
Age median (IR)	8.64 (3-13)	9.1 (3-13)	8.4 (3-12.9)
Previous joint injections n(%)	43 (33.9)	16 (47.1)	27 (29)
sDMARD prior transference n (%)	98 (76.6)	26 (76.5)	72 (77.4)
bDMARD prior transference n (%)	79 (61.7)	20 (58.8)	59 (63.4)
Uveitis n (%)	23 (18.1)	8 (23.5)	15 (16.1)
JIA subcategory n (%)			
oligo persist	43 (33.9)	12 (35.3)	31 (33.3)
oligo extend	16 (12.6)	3 (8.8)	13 (14)
poly RF -	25 (19.7)	6 (17.6)	19 (20.4)
poly RF +	3 (2.4)	1 (2.9)	2 (2.2)
ERA	24 (18.9)	8 (23.5)	16 (17.2)
systemic	9 (7.1)	2 (5.9)	7 (7.5)
psoriatic	7 (5.5)	2 (5.9)	5 (5.4)

We calculated the percentage of patients who had active disease at the transference to the Unit and the percentage of patients who had an inflammatory flare during the follow-up. Figures 1 and 2 showed the proportion of flares depending on the inflammatory status at transference to the Transitional care unit and the use of biological therapy before transition.

Conclusion: JIA patients remain active in one quarter of the cases at the transference to the Transitional care unit and flares are twice frequent when they were active at the transference.

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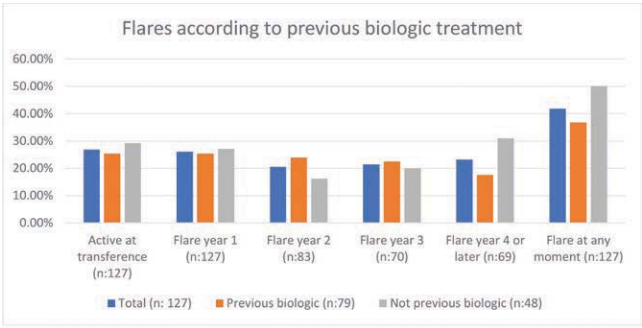

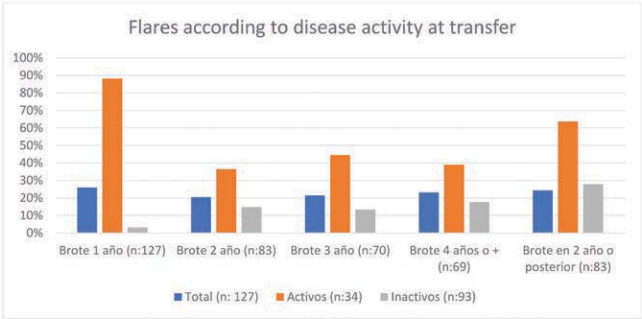

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POS1319

RISK OF CORONARY ARTERY INVOLVEMENT IN KAWASAKI DISEASE.

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Background: Kawasaki disease (KD) is a nonspecific systemic vasculitic disease that frequently occurs among children, and coronary artery lesion (CAL) is the most serious complication

Objectives: We aimed to study the risk factors for CAL in children with KD

Methods: There were examined 188 patients (boys:girls – 2:1, median age Me = 24 months [11;38]) with KD hospitalized in Morozovskaya Children's City Clinical Hospital in 2014-2019. 19 (10,1%) of them were <6 months, 29 (15,4%) - 6-<12 months, 117 (62,3%) - 12 months-<5 years, 23 (12,2%) - ≥5 years. Univariate and multivariate logistic regression analyses were conducted to explore the relationships between CAL and gender, age, clinical diagnosis, laboratory biomarkers, initiation time of IVIG administration.

Results: The enrolled 188 KD children were divided into a CAL group (n = 61) and an NCAL group (n =127) according to cardiac color Doppler ultrasonography. The incidence rate of CAL in the acute period was 26 %. The two groups had significantly different gender (p=0,0184), initiation time of IVIG administration (p=0,0209;)increase in platelets more than 700 000 at 2 weeks (p=0,0089), higher levels of NT-proBNP (p=0.002) and proANP (p=0,0005). Patients with CAL were found to have higher levels of NT-proBNP and proANP, suggesting a prognostic role. The NT-proBNP level was significantly higher in patients with CAL, and a cutoff value of 984 pg/mL yielded a sensitivity and specificity of 79 and 84.8 %, respectively. The area under the curve of the NT-proBNP for predicting CAA was 0.794 (95 % CI 0.620-0.967). The proANP level was significantly higher in patients with CAL, and a cutoff value of 1.015 nmol/L yielded a sensitivity and specificity of 87.5 and 75.8 %, respectively. The area under the curve of the proANP for predicting CAA was 0.805 (95 % CI 0.656-0.954).

Conclusion: Male gender, delayed use of IVIG, high platelets, NT-proBNP, proANP were independent risk factors for KD complicated with CAL. Current evidence suggests that NT-proBNP and proANP may be used as a diagnostic tool for KD complicated with CAL

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POS1320

SAFETY AND EFFICACY OF RITUXIMAB IN PATIENTS WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: THE PRELIMINARY DATA OF RETROSPECTIVE COHORT STUDY

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Background: juvenile systemic lupus erythematosus (jSLE) is the most frequent pediatric connective tissue disease with multiorgan involvement and different outcomes and prognosis. Corticosteroids remain the base treatment option and steroid-sparing treatment is strongly required to avoid steroid toxicity. Rituximab (RTX) is one of biologics, which efficacy was proved in case reports and case series of SLE, but no data from big randomized trials, confirming the efficacy have existed.

Objectives: to evaluate safety and efficiency of RTX in jSLE.

Methods: in the retrospective observation study the information of 48 jSLE patients (12 boys, 36 girls) who received at least one RTX dose before 18 years, included. Diagnosis was made using SLICC criteria. The main indications for RTX were high disease activity with lupus nephritis (LN), CNS and hematology disturbances (hemolytic anemia, thrombocytopenia) and avoiding steroid toxicity. RTX was prescribed in dosage 375 mg/m^2 every week (2-4 infusions) with repeated courses every 6-12 months according disease activity, the degree of B-cell depletion and hypoIgG-emia. The dynamics of clinical, laboratory data, activity of the disease by SLEDAI, GCS doses were assessed in the onset and during RTX trial.

Results: The main patient's characteristics were: onset age 13.0 (11.5; 15.0) years, inclusion age 18.0 (16.0; 20.0) years, LN 25 (52%)/III+IV class 9/11 (82%), CNS involvement 26 (54%). Pre-RTX non-biologic conventional treatment includes: cyclophosphamide 24 (50%), MMF 14 (29%), azathyoprine 7 (15%), methotrexate 6 (13%), cyclosporine A 2 (4%). Observation period ranged from 6 months to 6 years with median time 0.75 (0.2; 2.75) years. Initial pre-RTX treatment (GCS, hydroxychloroquine, non-biologic DMARDS) partially reduced SLE activity (SLEDAI, ANA titer, anti-dsDNA level), and median GCS dose by 25% from the initial dose, without changes in proteinuria, hematuria, C3, C4, WBC, hemoglobin, PLT and ESR levels. Administration of the RTX realized in prominent reducing of SLEDAI, anti-dsDNA level, proteinuria, hematuria, C4, ESR, number of patients with anemia, thrombocytopenia, and median GCS dose by 90% from the initial. The hemoglobin level and WBC have increased. 19 patients received IVIG for treatment of MAS (n=3), infection (n=5) and as replacement treatment in cases where IgG<4.5 g/l (n=11). 3 deaths were observed due to catastrophic SLE with MAS, accompanied severe infection (invasive aspergillosis, n=2). 6 patients realized SAE: pneumonia (n=3), transient agranulocytosis (n=1) after 3rd RTX infusion and meningitis, caused by Lysteria monocytogenis, after 1st RTX infusion (further RTX treatment continued without adverse events), patella osteomyelitis (n=1). 10 patients received antibiotics for respiratory infections. On pre-RTX 13 had antibiotics (p=1.0).

Table 1. Dynamics of SLE features pre-RTX and during RTX trial

Parameter	SLE onset	RTX (baseline)	p	Last visit	p*
SLEDAI	16 (11.0; 23.5)	13.5 (6.5; 21.5)	0.0002	4 (0; 8.0)	0.00002
Patients with elevated anti-dsDNA n, (%)	33 (69)	20 (42)	0.008	11 (23)	0.034
Anti-dsDNA, U/ml (n.v.<25)	112 (1; 200)	24.7 (1; 130)	0.059	0 (0; 27)	0.008
Proteinuria, g/l	2.6 (0.8; 4.4)	3.8 (0.3; 7.5)	0.687	0 (0; 0.2)	0.004
Hematuria, # cells	40 (8; 86)	50 (6; 120)	0.191	0 (0; 1)	0.0016
C4, g/l	0.12 (0.1; 0.24)	0.12 (0.06; 0.19)	0.398	0.15 (0.11; 0.21)	0.016
Patients with leucopenia, n(%)	12 (25)	10 (21)	0.629	5 (10)	0.00001
Patients with anemia n (%)	19 (40)	16 (33)	0.09	7 (15)	0.0015
Hemoglobin, g/l	113 (95;131)	115 (91; 132)	0.830	128 (107; 134)	0.063
Patients with thrombocytopenia n (%)	17 (35)	9 (19)	0.005	2 (4)	0.00001
ESR, mm/h	17 (8; 31)	15 (7; 22)	0.134	7 (2; 20)	0.054
Patients with GCS therapy n, (%)	45 (94)	45 (94)	1.0	40 (83)	0.00001
GCS, mg/kg	1.0 (0.6; 1.0)	0.75 (0.2; 1.0)	0.035	0.1 (0.08; 0.28)	0.000001

*compare to RTX baseline

Conclusion: RTX showed effectiveness in the cases, where previous non-biologic treatment was insufficiently effective. Randomized controlled trials are required to evaluate the efficacy and safety of RTX.

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POS1321

FEATURES OF MACROPHAGE ACTIVATION SYNDROME IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN THE ERA OF BIOLOGIC THERAPY

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Background: Macrophage activation syndrome (MAS) is a severe hyperinflammatory response that develops against the background of juvenile idiopathic arthritis (JIA). It is known that the clinical feature of MAS on biologic therapy has other clinical manifestations, different from biologically naive patients.

Objectives: To study the clinical and laboratory features of macrophage activation syndrome in patients with juvenile idiopathic arthritis with systemic onset (sJIA) on the biologic therapy.

Methods: The study included 100 patients with MAS (114 cases of MAS) who observed in the rheumatological department of the National Medical Research Center for Children's health of Ministry of health. All patients met the criteria for the diagnosis of sJIA and MAS. There were children in our study who did not receive biologic therapy – 84 (74%) cases, and children who had MAS in the biologic therapy – 30 cases (26%). The drugs are distributed as follows: tocilizumab - 7 cases (6%), kanakinumab - 20 cases (17%), etanercept – 2 cases (2%), adalimumab – 1 case (1%). For pairwise intergroup comparisons of quantitative variables, the nonparametric Mann-Whitney test was used.

Results: In comparative analysis of biologic-naive and on biologic patients, the greatest differences were obtained for the following clinical manifestations: rash, lymphadenopathy, myalgia (p<0.05). Fever was the most common symptom in both groups and was present in almost all patients (99%). All patients had

elevated level of ferritin in the blood serum (773 ng/ml to 130149 ng/ml). Laboratory picture of MAS in the group of on biologic patients differed significantly from the group of patients naive for biologic therapy (Table 1). The most significant differences were found among the following laboratory parameters: hemoglobin level, the number of erythrocytes and platelets, erythrocyte sedimentation rate (ESR), levels of C-raective protein (CRP), ferritin, lactatedehydrogenase (LDH), albumin.

Table 1. Laboratory data of patients with MAS.

		n	Reference values	Median	Minimum	Maximum	Mann-Whitney Criterion (p)
Biologic-naive cases of MAS (n= 84)	Hemoglobin, g/l	84	120-145	96,50	61,00	145,00	0,008
	Red blood cells, 10^{12}/l	84	4,5-5,3	3,78	2,13	5,01	0,001
	Platelets, 10^9/l	84	150-440	149,00	41,00	523,00	0,025
	White blood cells, 10^9/l	84	4,5-11,5	4,42	0,69	25,84	0,074
	ESR, mm/h	84	2-20	45,00	2,00	111,00	0,001
	CRP, mg/l	84	0-5	111,56	7,54	368,31	0,006
	Ferritin, ng/ml	84	14-124	4195,21	702,38	130149,20	0,022
	LDH, U/l	84	91-295	413,50	162,00	5245,00	0,059
	Albumin, g/l	84	38-54	29,00	16,10	63,00	0,001
On biologic cases of MAS (n = 30)	Hemoglobin, g/l	30	120-145	104,50	67,00	163,00	0,008
	Red blood cells, 10^{12}/l	30	4,5-5,3	4,17	3,10	6,15	0,001
	Platelets, 10^9/l	30	150-440	101,50	4,00	362,00	0,025
	White blood cells, 10^9/l	30	4,5-11,5	3,22	0,70	15,58	0,074
	ESR, mm/h	30	2-20	17,50	2,00	98,00	0,001
	CRP, mg/l	30	0-5	55,77	1,86	407,12	0,006
	Ferritin, ng/ml	30	14-124	2319,59	773,90	121396,00	0,022
	LDH, U/l	30	91-295	600,00	10,60	2148,57	0,059
	Albumin, g/l	30	38-54	32,80	20,30	51,90	0,001

Conclusion: On biologic patients may also develop MAS, which is often difficult to diagnose due to the poor clinical picture and low laboratory activity. In this case, hyperferritinemia remains as a highly specific marker of MAS.

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POS1322 DISCONTINUATION OF LONG-TERM ADALIMUMAB TREATMENT IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED UVEITIS

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Background: Uveitis is the most common extra-articular manifestation of JIA which may lead to sight-threatening ocular complications. Topical corticosteroids are still used in the initial treatment for JIA-associated uveitis. The goal of treatment in these patients should be topical corticosteroid-free remission and prevention of recurrences. The most commonly used corticosteroid-sparing immunomodulatory are TNF-α inhibitors (TNFi), especially adalimumab.
Currently, limited data are available about when or how to stop adalimumab when remission of JIA-associated uveitis is presumed.

Objectives: To evaluate rates of relapse after discontinuation adalimumab in patients with JIA-associated uveitis.

Methods: Medical records of 33 patients with JIA-associated uveitis who were successfully treated with adalimumab to a state of topical corticosteroid-free remission and discontinued adalimumab due to a long-term remission were analyzed retrospectively.
Remission of uveitis was defined as <1+ cells in the anterior chamber and <1 + vitreous haze grading; relapse was defined as ≥1 cell in the anterior chamber or ≥1 vitreous haze grading [1].

Results: Corticosteroid-sparing control of inflammation was achieved in all patients. Adalimumab was discontinued after 50 (range 12–120) months after initiation of adalimumab. Duration of remission prior to discontinuing adalimumab was 42 (range 6 – 114) months. The mean duration of remission after adalimumab discontinuation was 14 (range 1–59) months. 13 (40%) of patients had flares after less than 12 months after discontinuing adalimumab, 5 (15%) had flares after 12 – 24 months, 15 (45%) had not flared due to 24 months after discontinuation adalimumab and had had a long-term non-biological remission. Disease was successfully controlled in 11(33%) patients with non-biological DMARDs, 22 (66%) patients restarted biological therapy after flares, due to lack of improvement after non-biological DMARDs. All patients in whom biological therapy was reinitiated responded satisfactorily. None of the flared patients didn't require restarting corticosteroids.

Conclusion: Corticosteroid-sparing control of inflammation was achieved in all patients. Data from our experience with adalimumab in patients with JIA-associated uveitis suggest that 45 % of patients can be successfully withdrawn from biologics for at least 24 months without disease recurrence.

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POS1323 ACCELEROMETER-ASSESSED DAILY PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) – FIRST RESULTS FROM THE GERMAN ACTIMON STUDY

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Background: Although regular physical activity (PA) is known to have many health-related benefits for children and adolescents with chronic conditions, JIA has been associated with reduced physical activity (PA) and increased time spent sedentary [1]. Sedentary behaviour is an important consideration alongside PA when examining the contribution of both behaviours to the health of young patients. Because young people show more complex but less structured movement behaviour than adults, capturing their many spontaneous and impulsive movements is a great challenge for PA assessment.
Objectives: Since accurate, objective measures of PA related to potential factors promoting PA have been scarce, this study aimed i) to objectively assess moderate to vigorous PA (MVPA) as well as sedentary behaviour and ii) to identify facilitators for PA in patients with JIA.
Methods: Within the framework of the ActiMON study as part of the TARISMA research network, data were collected at several German paediatric rheumatology centres. Objectively assessed PA of adolescent patients with JIA was recorded exclusively during school months in the period June - December 2021 using the accelerometer ActiGraph wGT3X-BT laterally on the right hip. In accordance with the International Children's Accelerometry Database criteria [2], ActiGraphs were worn on seven consecutive days during all waking hours, including at least 4 valid weekdays and 1 weekend day (wear time >8 hours) in the evaluation. Self-reported PA-related data were measured using a physical activity questionnaire (PAQ), while clinical parameters were used from the National Paediatric Rheumatologic Database (NPRD). Achievement of the WHO recommendation of at least 60 minutes MVPA per day and compliance with the national recommendation of no more than 120 minutes of daily screen time were determined among 12- to 18-year-olds.
Results: Data of 41 patients (mean age 14.6 ± 1.9 years, female 73%, patients' disease duration 7.9 ± 4.6 years, polyarthritis 40%, cJADAS-10 2.3 ± 2.4) were available for evaluation. Almost 71% of participating patients met the WHO-recommended minimum level of MVPA, while the average daily step count achieved was 7804. Almost 80% of the patients rated their motor and coordination skills as being good. The most frequently mentioned reasons for doing sports (multiple answers possible) included feeling good (78%), giving energy (70%), pleasure (65%) and enjoyment (60%). Patients whose parents are active in sports and support their child in finding a suitable offer were more likely to fulfil the WHO recommendation than patients without family support. The average daily time spent sedentary was 10.5 ± 1.9 hours. About half of the patients reported spending more than 4 hours a day with screen-based media, especially video games.
Conclusion: These preliminary results suggest that while a large proportion of patients achieve the WHO recommended minimum level of PA, they exhibit very pronounced sedentary behaviour with increased screen use. In addition to controlled disease activity as a well-known prerequisite for achieving PA recommendations, these results also point to the importance of family support and emotional well-being. With ongoing recruitment, further potential facilitators and barriers to PA should be identified in more in-depth analyses.

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POS1324

THE IMPORTANCE OF MRI IMAGING FOR THE MANAGEMENT AND UNDERSTANDING OF THE DISEASE ORIGIN IN FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

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Background: Fibrodysplasia ossificans progressive (FOP) is ultra-rare autosomal dominant inherited genetic disorder which is caused by mutation in ACVR1 gene and provokes severe heterotopic ossification (HO) as a «second skeleton disease». Our long-term experience of the largest group of FOP patients in single Russian center makes possible to interpretate clinical findings and imaging as the evidences that FOP may belong to special kind of axial spondyloarthritis. Because of new bones formation process X-Ray and CT scans recognize as the main imaging methods for the FOP. But MRI method may present important information for the understanding of the disease origin in FOP.
Objectives: To analyze the MRI findings in FOP patients in relation to clinical manifestations, and therapy options.
Methods: The study was based on retrospective and prospective observation and included 40 pts (21 males; 19 females). Diagnosis of FOP was established on typical clinical features and detecting mutation. X-ray, CT and MRI were performed in most patients excluding the severe disabled status of FOP. Some patients failed to perform MRI due to the presence of severe skeletal deformities or artificial metal constructions (because of previous orthopedic operations). Blood assessment has never shown specific elevated markers.
Results: Among of all 40 FOP patients MRI of sacroiliac joints was performed in 14 patients. Chronic sacroiliitis was detected in 10/14 pts, including active sacroiliitis in STIR regimen in 6/14 pts by. Also 7/14 pts have MRI evidence of severe coxitis (see Figure 1). This imagines findings and other features of axial involvement (X ray imagines of ankylosis of the facet joints and vertebral bodies by the type of syndesmophytes) allowed us to establish alternative diagnosis of juvenile spondyloarthritis (JAS) in 7 pts and juvenile idiopathic arthritis (JIA) in 5 cases. It was needed for the legal possibility to administer tofacitinib (TOFA) in 12 pts (the youngest pt of 2 y.o, the oldest – 19 y.o) with strong uncontrolled progression of FOP. The dosage of TOFA was up to 5 mg twice a day. We noticed that all 12 pts have severe coxitis with synovia proliferation (with MRI and ultrasound evidence). Duration of TOFA therapy is from 2 to 25 months. Drug tolerance was good in all pts, no AE were registered. New nodes formation immediately stopped in most pts, significant improvement of motions was observed in 10 (83%) pts. Also, we noticed fast regression of sacroiliitis and coxitis activity by MRI in 5 (42%) pts under TOFA therapy. All other patients didn`t have repeated MRI examination yet. So MRI seems to be important method to confirm the anti-inflammatory effects for sacroiliitis and coxitis signs in patients with FOP. It seems to expect that inflammation control may prevent the sacroiliac and hip ankyloses. In spite of the absence of new HO in our 16 y.o. pt, we found continuous intraskeletal ossification between C3-C4, C5-C7 vertebral bodies, facet joints that leads to subtotal stenosis of spinal canal without any neurological symptoms. Because of «protection effect» of external heterotopic ossification severe neurological damage was not developed.

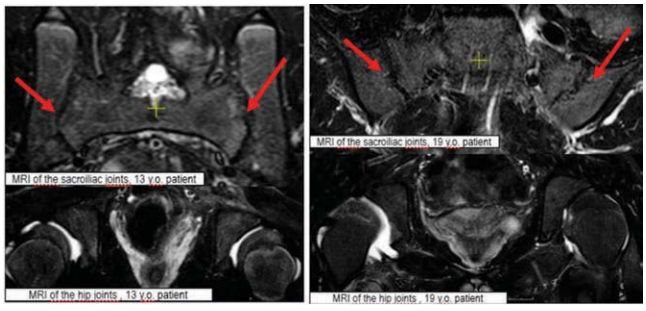

Figure 1. Two different patients with severe FOP and similar evidences of sacroiliitis and bilateral hips synovitis by MRI

Conclusion: According to MRI findings, hip damage was characterized for all ages of FOP patients. Sacroiliitis we found mostly in patients older 10 y.o. Based on our experience of JAK-inhibitor therapy we can suggest about positive effect and advantages of TOFA over other therapy approaches. Dynamics of MRI imaging may be good option for the confirmation of therapeutic anti-inflammatory effects.

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POS1325 CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO): NEW INSIGHTS INTO EXTRA-OSSEOUS MANIFESTATIONS.

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Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a rare inflammatory disease of the skeleton characterized by chronic and recurrent episodes of osteo-articular inflammation. The median age of onset is 10 years old. Clinical manifestations include musculoskeletal symptoms that are well described (pain, tenderness, swelling). Sometimes, skin lesions or digestive manifestations occur. Whole body magnetic resonance imaging (MRI) is the gold standard for assessing the multifocal pattern of the CRMO. Treatment is still empirical and mainly relies on non-steroidal anti-inflammatory drugs (NSAIDs). Bisphosphonates and biologics are used as second-line treatments. To date, the focus has been set on bone involvement and very few data are available on extra-osseous manifestations in CRMO.

Objectives: This study aims to further describe these extra-osseous clinical manifestations in CRMO.

Methods: A historical cohort was designed using 61 CRMO patients at the Pediatric Rheumatology Department in a tertiary university hospital in Paris (Hôpital Bicêtre, France). All patients underwent a MRI that confirmed the diagnosis according to the criteria of Jansson. Skeletal involvement was characterized with 1/axial, 2/ peripheral, 3/ axial and peripheral lesions. Extra-osseous manifestations were divided into 1/ skin lesions, 2/ gastro-intestinal manifestations, 3/ enthesitis and 4/ others. Pain was evaluated thanks to the Visual Analog Scale (VAS, from 0 to 10). Treatments used were recorded. The study complied with ethical requirements.

Results: Forty one patients were included in the study, with 31 females (75.6%). The mean ± SD age at onset was 79.1 ± 59.8 months, with a delay at diagnosis beyond six months (6.71 ± 6.96). Twenty-one patients had a familial history of inflammatory diseases (51.2%), with a majority of psoriasis or ankylosing spondylitis (n=13/21, 61.9%). At diagnosis, the level of pain was 5.71 ± 3.24. Eleven patients (42.3%) had blood inflammation. Bone lesions were reviewed thanks to whole body MRI: four patients had isolated axial involvement (10.0%), nine had peripheral involvement (22.5%) and 27 patients harbored both types of lesions (67.5%). The mean number of lesions was 6.65 ± 4.23. After 12 months of follow-up, all parameters regarding disease's activity decreased (pain, blood inflammation, number of lesions). Regarding extra-osseous symptoms, fever occurred in seven patients (17.1%). Twenty-four patients had skin manifestations (58.5%) with palmoplantar lesions (n=3, 12.5%), acne (n=6, 25.0%), psoriasis (n=5, 20.8%) and aphthous (n=10, 41.7%). Four patients (9.76%) had gastro-intestinal symptoms and seven (17.1%) had enthesitis. One patient had uveitis. Almost all patients received NSAIDs (n=39/41, 95.1%) and half of the cohort were treated with bisphosphonates (n=21/41, 51.2%). Nine patients (22.0%) received biologics with a majority of TNF inhibitors. All patients that received TNF inhibitors had either a cutaneous involvement or digestive symptoms or enthesitis (Figure 1).

Conclusion: Extra-osseous manifestations have to be carefully searched in CRMO, especially in the presence of familial history of inflammatory diseases. While the severity of bone involvement can lead to use bisphosphonates, the introduction of biologics seems to rely on extra-osseous symptoms. These conclusions are drawn on a retrospective study and need to be confirmed in larger cohort.

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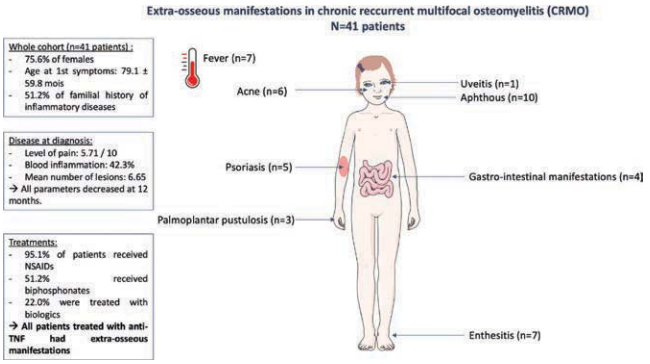

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POS1326 PIMS THROUGH THE WAVES OF COVID 19: DATA FROM THE JIR COHORT

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Background: Paediatric inflammatory multisystem Syndrome (PIMS) is a new systemic inflammatory disease linked to SARS-CoV2 that affects children. It was first reported in may 2020 [1-2].

Objectives: The objectives of this study were to describe patients with PIMS through the international JIR cohort registry and to compare the different profiles and treatments of these patients over the different waves.

Methods: Study patients with international PIMS criteria were included from March 2020 to June 2021. Patients were identified in the JIR cohort, an international registry collecting demographic, clinical and paraclinical data on patients with pediatric inflammatory diseases. Two groups were distinguished: from March 2020 to July 2020 for patients in the first wave, from July 2020 to June 2021 for patients in the 2nd and 3rd waves. These two groups were compared using a Fischer test for categorical data and a Mann-Whitney test for quantitative data

Results: 136 patients meeting the PIMS criteria were included (64 patients in the 1st wave, 72 patients after). Patients had less frequent myocarditis (51 patients in wave 1 vs. 36 patients after, p=0,0003) and respiratory distress (34 patients vs 10 patients, p<0,0001). Corticosteroids were used more frequently in the second wave (32 patients in wave 1 vs. 67 patients after July 2020, p<0,0001). Intravenous immunoglobulins were used as much over the waves (58 patients in wave 1 vs 68 patients after, p=0.5). Antibiotics were less used since the second wave (53 patients received antibiotics before July 2020 vs 11 after, p<0,0001). The duration of hospitalization decreased significantly (p<0,0001) with a median duration of 9 days during the first wave (interquartile range, 7-12) and 7 days (interquartile range, 5-10) after the first wave.

Conclusion: There was a decrease in the number of complications of PIMS, particularly cardiac and respiratory complications, and a decrease in the length of hospitalization over time. The treatment of PIMS has also evolved, with a clear increase in the use of corticosteroids and a decrease in the use of antibiotics.

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Other orphan diseases

POS1327 AMYLOID STORM DEVELOPS IN PATIENTS WITH AA AMYLOIDOSIS AND ASSOCIATED WITH HIGHER AMYLOID BURDEN AND INCREASED MORTALITY

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Background: Amyloid storm is an emerging condition which was described recently also associated with poor prognosis in patients (pts) with AA amyloidosis (AA-a).
Objectives: We herein aimed to evaluate the amyloid storm and its associated factors in pts with AA-a.
Methods: We retrospectively evaluated AA-a pts who followed in our tertiary referral amyloidosis center. Diagnosis of AA-a was made by Congo red straning and immunohistochemistry. Amyloid storm was defined as follows; developing within two weeks, increase in creatinine and proteinuria levels at least two times from baseline or reach the CRP levels more than 10 times [1].
Results: Data of 175 pts with AA-a were evaluated and after exclusion of 11 pts who had missing data, 164 pts were included into the analysis. We identified 9 pts (5.5%; of 4 male) who developed amyloid storm. Five pts were FMF-associated AA-a (FMF-AA) and 4 pts were non-FMF-AA (two pts had ankylosing spondylitis, one patient idiopathic and one patient non-FMF periodic fever syndrome) (p=0.1). Median±interquartile range (IQR) patient age, diagnosis age of FMF and amyloidosis were lower in pts had amyloid storm than had not, but they were not statistically different (p=0.2, p=0.3 and p=0.2 respectively). All pts were M694V homozygous among FMF-AA. Etiology of amyloid storm was infection in 5 pts (56%), treatment non-adherence in 3 pts (33%) and surgery in one patient (11%). Overall, 3 pts with amyloid storm died (33%), but mortality was 10% (n=16) in the remaining pts with AA-a. One patient died during the amyloid storm, and others died within one year after the diagnosis of amyloid storm (median 5 months). In univariable analysis, involvement of ≥3 organs, bone marrow involvement and current proteinuria levels (p=0.4, p=0.05 and p=0.04, respectively) were higher; median number of organ involvement and mortality (p=0.09 and p=0.07) were tended to be higher in pts with amyloid storm than those without it. End stage renal disease (ESRD) development was also higher in pts who had amyloid storm (67%; n=6) than in pts who had not (46 % n=71) but did not reach statistical significance (p=0.3). Median±IQR CRP (48 ±77 vs 9 ±17 p=0.08), creatinine (4.8 ±5 vs1.2 ±0.6 p=0.01) and proteinuria (11 ±12 vs 0.85 ±2.3 p=0.02) levels were higher during the amyloid storm than their previous records. In multivariable analysis, amyloid storm was associated with higher mortality (p=0.045 OR 4.6; 95 % CI 1.03-20). In survival analysis, development of amyloid storm tended to be higher in pts with non-FMF-AA compared to FMF-AA (Log-rank p=0.057). Mortality rate was higher in pts who had amyloid storm than those without it (Log-rank p=0.038).

Table 1. Comparison of clinical and laboratory features of pts with and without amyloid storm

Variables	Amyloid storm (n=9)	Control (n=155)	p value
Age*[ɪ]	37±10	45±20	0.2
Gender, male[#]	4 (44)	86 (56)	0.7
Diagnosis[#]			
FMF	5 (4)	122 (96)	0.1
non-FMF	4 (11)	33 (89)	
Organ distribution[#]			
Renal	9 (100)	152 (98)	1
Gastrointestinal	4 (44)	33 (21)	0.1
Heart	2/6 (33)	32/111 (29)	1
Liver	1 (11)	5 (3)	0.3
Bone marrow	2 (22)	5 (3)	***0.05***
Diagnosis age of FMF*[ɪ]	17.5±30	24±20	0.3
Diagnosis age of AA-a*[ɪ]	26±26	31±22	0.2
Duration of AA-a*[ɪ]	10±14.6	11.2±11	1
Number of organ involvement*	2±2	1±1	0.09
≥3 organ involvement[#]	3/5 (60)	20/122 (16)	***0.04***
Baseline			
CRP*[ᴋ]	10±8	20±20	0.06
proteinuria (g/dL)*	5.3±4.3	4±5.7	0.9
creatinine (mg/dL)*	0.8±0.6	0.8±0.6	0.6
Current			
CRP*[ᴋ]	2.7±5.2	2.7±7.3	0.7
proteinuria*	3.1±23	0±1.9	***0.04***
creatinine*	1.5±3	0±1.9	***0.04***
Two exon 10 MEFV variant (n=108, %)	3 (100)	94 (87)	0.5
M694V homozygous (n=3, %)	3 (100)	73 (68)	0.2
ESRD development[#]	6 (67)	71 (46)	0.3
Mortality[#]	3 (33)	16 (10)	0.07

• .*median±IQR [ɪ]years [#](n, %) [ᴋ]mg/L

Conclusion: This study showed that 5.5% of pts with AA-a may develop amyloid storm, and this condition was associated with higher amyloid burden. Amyloid storm may develop in AA-a pts associated with both FMF and other diseases, and the mortality rate may reach to 33% within one year.
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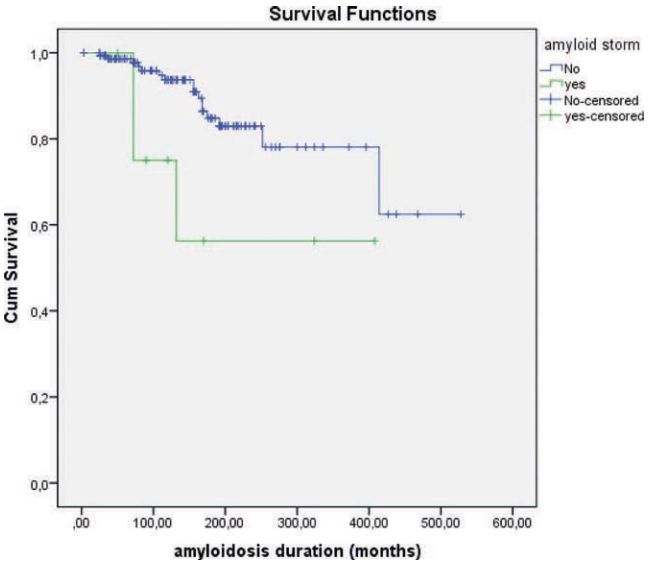

Figure 1. Comparison of survival rate between pts with and without amyloid storm Log-rank: p=0.038

Disclosure of Interests: None declared
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POS1328 DO IL-1 ANTAGONISTS DEFINITELY PROTECT FROM THE DEVELOPMENT OF NEW DAMAGE: A SINGLE-CENTER STUDY

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Background: Ongoing inflammatory episodes of familial Mediterranean fever (FMF) disease can cause damage in nearly all organ systems. Colchicine and interleukin1β blocking agents are successfully used to control the disease activity [1]. Although the effect of IL-1 blockers are known for controlling disease activity and amyloidosis [2], it is unclear whether they prevent organ damage
Objectives: In our study, we assessed the organ damage in patients with FMF treated with colchicine and IL-1 antagonists (IL-1A). It was evaluated whether new damage occurred after IL-1 antagonist treatment.
Methods: A total of 111 patients fulfilling Tel-Hashomer criteria and treated with IL-1A due to colchicine resistance were included in the study. All patients were also treated with colchicine with a maximum-tolerable dose. Patients were grouped according to their recent damage status (no damage, pre-existing damage, and damage developed under IL-1A treatment). The degree of damage was determined using Autoinflammatory Disease Damage Index (ADDI) and modified form of ADDI (mADDI) [3, 4].
Results: 44 patients (42,3%) had damage according to the modified ADDI (mADDI) index; three patients experienced new damage under IL-1 antagonist treatment while four patients showed progression of damage and mADDI score. In patients with a positive mADDI score, the most common damage was amyloidosis (n=28, 63%), the second most frequent was musculoskeletal findings (N=14, 31%), and the third was infertility (N=2, 0,04%). The most common domains of FMF-related damage with IL-1 antagonist treatment were musculoskeletal (n=4), renal (n=2) and reproductive system (n=2)
Conclusion: Our study was the first study to evaluate the progression of damage in patients with FMF and treated- with IL-1 antagonists. Although it is known that IL-1A is effective in colchicine-resistant patients, physicians should be aware that damage can still develop under IL-1A treatment.
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Table 1. Comparison of clinical and laboratory parameters between groups according to damage

	No damage	New damage	Any damage	P value
Age (years)	48,4	56,4	67,5	0,002
Sex (K/E)	34/33	2/5	25/19	NS
Follow-up time (years)	40	43	56	0,33
Dominant attack type	Peritonitis (63,7%)	NA	Arthritis (34,1%)	NS
Persistent inflammation	33,6	42,3	44,3	0,05
AIDAI score	39	40	48	NS
Mutations				
M694V/M694V	26	2	14	NS
M694V/any	44	4	38	
M694V/M680I	3	1	4	
M680I/any	11		9	

• SAIDAI: Auto-Inflammatory Diseases Activity Index

Acknowledgements: All participants were confirmed for both participation and publication. Local Ethical Committee approved the study
Disclosure of Interests: None declared
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POS1329 SECONDARY HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: A SINGLE-CENTRE EXPERIENCE

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Background: Haemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome characterised by fever, organomegaly, cytopaenias, activated macrophages in haematopoietic organs and elevated ferritin. Primary HLH is caused by inherited defects in cytolytic pathway proteins and manifests in infancy[1]. Secondary HLH (sHLH) develops in individuals with a genetic susceptibility to hyperinflammation triggered by strongly immunogenic stimulus such as autoimmune conditions, haematological malignancy, organ transplantation or infection[2].
We present a cohort of patients with sHLH and detail their characteristics.
Objectives: To evaluate the characteristics and aetiology of sHLH patients at our Centre.
Methods: A single-centre retrospective observational study of all cases of sHLH between January 2018 and July 2021. Patients were identified from referrals and included if there was a diagnosis of HLH made by a rheumatologist with an H-score of 169 or greater. P-values were calculated using the Mann-Whitney test, unpaired t-test or Fisher exact as appropriate.
Results: 30 patients (10 female) with sHLH were identified with a median age of 46, a mean H-score of 238 (range 186-317). 15 (50%) had pre-existing immunosuppression, which did not influence mortality (p=0.26). The following primary drivers were identified: lymphoma (n=8), non-HIV viral infections (n=9), first presentation of HIV/AIDS with opportunistic infections (n=4), Adult-onset Still's disease (n=4), miliary tuberculosis (n=1), *M. falciparum* infection (n=1), meningococcal meningitis (n=1), checkpoint inhibitor therapy-related (n=1), and no diagnosis (n=1) - Table 1.
Non-HIV viral infections were the most common cause overall. 6 of 9 were caused by Herpes virus family and all were primary infections. Two followed yellow fever viraemia following live vaccination and both patients died.
Mortality varied with aetiology. All four patients with AOSD survived, while 7 of 8 with lymphoma died, as per previous reports[3]. There was a strong association between lymphoma and mortality vs non-lymphoma sHLH (p=0.0025). Four patients post-solid organ transplantation were identified (three liver, one kidney), three with post-transplant lymphoproliferative disorder and one with CMV viraemia (50% mortality).
There was no significant difference between age, ferritin or H-score between surviving and deceased patients (Figure 1), but H-score trended higher in the deceased (p=0.059). Number of treatments given for HLH was higher in the deceased group vs survival (mean 3.41 deceased, mean 2.44 in survived). Anakinra was used in all 30 patients as treatment, including as monotherapy in one patient with HSV viraemia who survived.

Table 1. **[§] = Mann Whitney U test, [τ] = unpaired t-test, [φ] = Fisher exact**

	Total (n=30)	Survived (n=18)	Died (n=12)	p-value
Demographics				
Male	20	10	10	0.78[§]
Female	10	8	2	
Mean age	43	41	47	0.348[§]
Median H-score	240	230	254	0.059 [τ]
Ferritin (ng/ml)	40277	34690	48404	0.0949
Trilineage cytopenia, n (%)	9 (33%)	5 (31%)	4 (36%)	0.28[§]
Subgroup (not mutually exclusive)				1 yr survival
Lymphoma	8	1	7	12.5% (p=0.0025 [φ])
HIV/AIDS	4	4	0	100%
AOSD	4	4	0	100%
Transplant recipient	4	1	3	25%
Other viral infection	9	5	4	44%
HSV	*3*	*3*	*0*	*100%*
CMV	*1*	*1*	*0*	*100%*
EBV	*1*	*0*	*1*	*0%*
Yellow fever	*2*	*0*	*2*	*0%*
Influenza A	*1*	*1*	*0*	*100%*
Tuberculosis	3	2	1	66%
with HIV	*2*	*2*	*0*	*100%*

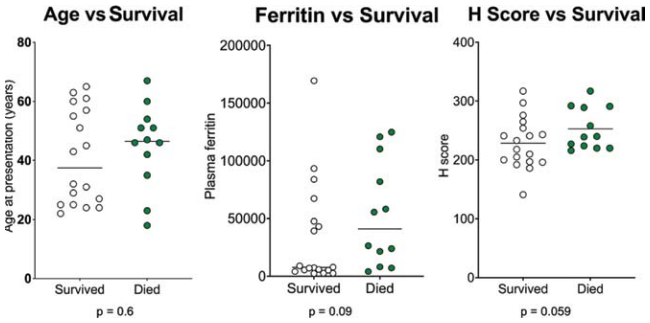

Figure 1.

Conclusion: Ferritin, H-score at diagnosis or age do not appear to correlate with mortality in sHLH. Lymphoma is associated with a significantly worse outcome. Poor response to treatment and increasing numbers of treatment options is associated with increased mortality. Causes are varied and often co-exist.
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POS1330 COMPARISON OF CLINICOPATHOLOGICAL FEATURES BETWEEN PATIENTS WITH AND WITHOUT HYPOCOMPLEMENTEMIA IN IGG4-RELATED KIDNEY DISEASE (IGG4-RKD): A MULTI-CENTER STUDY BY THE JAPANESE SOCIETY OF NEPHROLOGY IGG4-RKD WORKING GROUP

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Background: Although hypocomplementemia has been frequently reported in IgG4-related kidney disease (IgG4-RKD), few studies have investigated differences in the clinicopathological features of IgG4-RKD with and without hypocomplementemia in a relatively small cohort1,2).
Objectives: To compare the clinicopathological features of Japanese patients with and without hypocomplementemia in IgG4-RKD.
Methods: We retrospectively examined the clinicopathological features of 60 patients with definitively diagnosed IgG4-RKD, collected from the institutions associated with the Japan IgG4-RKD working group between December 2010 and May 2019, with reference to the presence of hypocomplementemia.
Results: Among the patients included, 42 (70%) had hypocomplementemia. In the latter group, serum levels of IgG and non-IgG4 IgG, calculated as total IgG minus IgG4, were significantly higher (mean IgG level, 3832 vs 2626 mg/dl, p=0.005, mean non-IgG4 IgG level, 2775 vs 1627 mg/ml, p =0.000). Renal function at diagnosis tended to be lower (mean eGFR level 42.4 vs 53.6 ml/min), although not to a significant degree (p=0.07). There were no significant inter-group differences in the levels of serum IgG4 and IgE, or in the number of extra-renal involved organs. Renal pathology specimens were obtained from 53 patients, 70% of whom had hypocomplementemia. In the hypocomplementemia group, light microscopy demonstrated a significantly broader extent of interstitial inflammatory cell infiltration (p=0.035), and immunofluorescence revealed a higher frequency of IgG or complement deposition on the renal tubular basement membrane (TBM) (p=0.048). C1q deposition on the TBM was evident only in the hypocomplementemia group. There was no significant inter-group difference in the presence of storiform fibrosis, the degree of interstitial fibrosis, the number of infiltrating IgG4-positive cells, or the frequency of membranous glomerulonephritis.
Conclusion: Hypocomplementemia in IgG4-RKD is associated with elevated levels of IgG subclasses other than IgG4, and may be related to progression of renal inflammation.
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POS1331 CERTOLIZUMAB PEGOL IN UVEITIS. RETENTION PROBABILITY AND CAUSES OF DISCONTINUATION.

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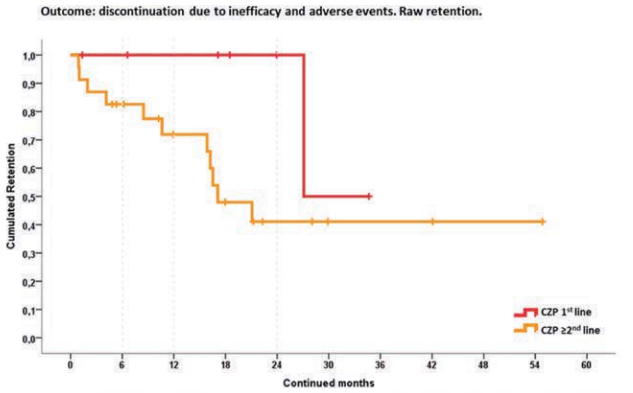
Background: A personalized disease-specific treatment for non-infectious uveitis (NIU) is challenging. Around 50% of adults with NIU who required classic DMARDs or adalimumab in clinical trials, failed at 6 months during open label phase [1,2]. Therefore, to investigate treatment alternatives for NIU are most needed.
Objectives: To study Certolizumab pegol (CZP) retention rate (RR) at 24 months in NIU and susceptibility factors for discontinuation.
Methods: Adults with NIU who received CZP for this indication were included. Data were gathered from the BioÚvea Spanish registry, detailed elsewhere[3]. Demographics, clinical, and therapeutic data was recorded from Nov 2016 to Nov 2017. The primary endpoint assessed was CZP RR at 24 months. Causes and susceptibility factors for definitive discontinuation of CZP were analyzed as well. CZP RR was calculated with the Kaplan-Meier method, Log-rank test was used for the univariate, and the Cox proportional hazard model was implemented for the multivariate analysis.
Results: Thirty patients with a median of 41 (IQR 16) years, 18 (60%) females, were included. NIUs were bilateral in 19 (63%) patients and were active at CZP onset in 20 (71%). Half of the patients suffered from non-anterior NIUs, and etiologically 2 (7%) were unclassifiable, 7 (23%) had ocular syndromes, and 21 (70%) were associated to systemic disorders. Seven (23%) patients were bionaïve, whereas 23 (77%) started CZP as a 2nd (5, 17%) or ≥ 3rd (18, 60%) biologic. With a median follow-up of 21.2 (Range 0.2 to 54.8) months, 12 (40%) patients discontinued CZP, 6 (20%) due to adverse events and 6 (20%) due to lack of efficacy. The overall CZP RR at 24 months was 53.6%, with a median Retention Time (RT) of 27.1 months. In the multivariate analysis, CZP started as a first biologic (HR 0.053, 95%CI 0.003 to 0.809; p = 0.035), and male gender (HR 0.1, 95%CI 0.015 to 0.694; p = 0.02) were protective factors for discontinuation. CZP RR at 24 months as a 1st line biologic was 100% with a median RT of 27.1 months. Conversely, CZP RR at 24 months as a ≥2nd line was 41.1% with a median RT of 17.1 months. When given as a 1st biologic, one (14%) patient discontinued CZP due to loss of efficacy at 27.1 months. Conversely, discontinuation of CZP when administered in ≥2nd line was more frequent, either due to lack or loss of efficacy in 5 (22%) patients or adverse events (AEs) in 6 (26%) (Figure 1).



CZP 1st line *vs.* ≥2nd line					6 m		12 m		24 m		36 m	
Biotherapy line	n	DRT (median, months)	Follow-up median (range), months	LTFU	DRR %	PAR, n	DRR %	PAR, n	DRR %	PAR, n	DRR %	PAR, n
CZP 1st line	7	27.1	18.5 (1.4-34.7)	0	100	6	100	5	100	3	50	1
Cause of discontinuation												
Lack/loss efficacy	1				0		0		0		1	
AE	0				0		0		0		0	
CZP ≥2nd line	23	17.1	22.3 (0.9-54.8)	1	82.6	17	71.9	12	41.1	4	41.1	2
Cause of discontinuation												
Lack/loss efficacy	5				1		2		2		0	
AE	6				3		0		3		0	

Figure 1. Retention rate of Certolizumab pegol in bio-naïve and bio-experienced patients with non-infectious uveitis.Abbreviations: DRT, Drug Retention Time; LTFU, lost to follow-up; DRR, Drug Retention Rate; PAR, Patients at Risk; AE, adverse event.

Conclusion: CZP in NIU showed an excellent retention rate at 24 months in bio-naïve patients. However, it was more than halved when CZP was started as a ≥2nd biologic. Discontinuation of CZP in bio-experienced patients was due to lack or loss of efficacy in 22% and to adverse events in an additional 26% of patients.
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POS1332 TOWARD SAFER GLUCOCORTICOID THERAPY OF POLYMYALGIA RHEUMATICA

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Background: SPI-62 is a potent 11β-hydroxysteroid dehydrogenase type 1 (HSD-1) inhibitor entering Phase 2 development as adjunctive therapy to prednisolone in polymyalgia rheumatica, as well as for treatment of Cushing's syndrome and autonomous cortisol secretion. HSD-1, an intracellular enzyme, activates glucocorticoids in target tissues in which glucocorticoid medicines are associated with morbidity including liver, adipose, muscle, and skin. In Phase 1 clinical trials SPI-62 was generally well tolerated and associated with maximal liver and brain HSD-1 inhibition.

Objectives: To demonstrate mitigation by SPI-62 of corticosterone (CORT) adverse effects in mouse.

Methods: C57BL/6 male mice (age 7 weeks; n=14 per group) were administered CORT (100 g/mL in drinking water) and SPI-62 (by gavage in 0.5% HPMC; 0, 1, or 10 mg/kg/day or 10 mg/kg twice daily) for 35 days. A control group received no CORT or SPI-62. Body weight was assessed daily and food consumption twice weekly. Whole body muscle and fat amounts were measured at Days 0, 14, and 28 using an EchoMRI-130H body composition analyzer. Blood samples for fasting glucose and insulin were obtained at Days 1 (pre-dose), 15, 29, and 35. An open field test was conducted on Day 22. A grip strength test was performed on Day 28. After sacrifice on Day 36, gonadal, subcutaneous, retroperitoneal, and mesenteric fat, quadriceps, and tibialis anterior were dissected and weighed, and skin was formalin fixed and paraffin embedded.

Results: One control mouse died due to accidental gavage injury. Two mice who received CORT + 0.5% HPMC died on Days 11 and 19. CORT resulted in increased food consumption which was normalized by SPI-62 in a dose-dependent manner. CORT-treated mice showed reduced body weight gain for 2 weeks then accelerated body weight gain. SPI-62 prevented body weight gain acceleration in a dose-dependent manner. CORT effects on dermal thickness and structure were less prominent in mice who also received SPI-62. No effect of CORT or SPI-62 was observed in the open field test. SPI-62 prevented CORT adverse effects of insulin resistance, increased adiposity, skeletal myoatrophy, and grip strength reduction (Table 1).

Table 1. Observed percentage difference of treatment group mean, compared to control group mean, in CORT-treated mice

SPI-62 treatment	none	1 mg/kg 1x/day	10 mg/kg 1x/day	10 mg/kg 2x/day
HOMA-IR Day 15	+422	+428	+104	+8
HOMA-IR Day 29	+788	+472	+204	+14
HOMA-IR Day 35	+3620	+1270	+324	+92
Body fat content Day 14*	+110	+72	-13	-7
Body fat content Day 28*	+166	+102	+63	-12
Gonadal fat weight*	+151	+74	+39	-1
Subcutaneous fat weight*	+471	+121	+83	+7
Retroperitoneal fat weight*	+227	+89	+36	+25
Mesenteric fat weight*	+240	+133	+124	+71
Body muscle content Day 14*	-10	-7	0	+1
Body muscle content Day 28*	-15	-8	-6	+3
Quadriceps weight*	-54	-43	-24	-16
Tibialis anterior weight*	-35	-29	-5	+5
Grip strength	-12	+16	+15	+26

*Normalized by body weight.

Conclusion: SPI-62 prevented several CORT adverse effects in mouse, demonstrating that blockade of local intracellular glucocorticoid activation by a HSD-1 inhibitor in target tissues can mitigate glucocorticoid toxicity. These results suggest that SPI-62 has potential to similarly mitigate adverse effects of glucocorticoid medications in human. A placebo-controlled Phase 2 clinical trial has been initiated to compare prednisolone effects with and without SPI-62. Up to 48 patients diagnosed with polymyalgia rheumatica, on stable prednisolone 10 mg daily for at least 2 weeks, and with stable disease inactivity based on acute phase biomarkers will continue prednisolone 10 mg daily for 4 weeks, during which they will receive SPI-62 or placebo for 2 weeks each. Acute phase and other immune function biomarkers, symptom measures, and biomarkers of prednisolone adverse effects will be assessed at baseline and after each 2-week period. After analysis of data from a first cohort of 12 patients the prednisolone dose might be adjusted, in blinded fashion, during the SPI-62 period to maintain equipotency on acute phase biomarker suppression.

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POS1333 STUDY OF THE RELATIONSHIP BETWEEN THE TREATMENT TYPE AND THE THERAPEUTIC RESPONSE ACCORDING TO THE SAPHO SYNDROME CLINICAL FORM IN ADULTS FROM A RETROSPECTIVELY ANALYSED MULTICENTER COHORT

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Background: SAPHO syndrome (Synovitis, Acne, Palmoplantar Pustulosis, Hyperostosis and Osteitis) is a radio-clinical entity associating joint, bone and inflammatory skin disorders. The clinical presentation is very heterogeneous making the diagnosis difficult. The therapeutic strategy in SAPHO syndrome is poorly defined. The first-line treatment remains NSAIDs on demand, which are effective in treating painful flare-ups but rapidly become insufficient in 60% of cases during the course of the disease. TNF-αNF-O syndrome (S necrosis factor-alpha) are reserved for refractory forms and their efficacy is uncertain [1]. Bisphosphonates (BPs) seem to have potential interest [2].

Objectives: The main objective of this study was to investigate the response to treatment with BPs and/or immunosuppressive drugs (DMARDs - *Disease modifying anti-rheumatic drugs*), *c*onventional synthetic *c*s-DMARDs or biologic (*b*-DMARDs), according to the clinical form of rheumatological SAPHO (bony predominantly versus articular or mixed predominantly.

Methods: All patients aged 18 years or older with SAPHO syndrome meeting Benhamou's criteria whose clinical, biological and radiological data were available in the files and who received at least one DMARD or BP treatment for their disease were included in Rouen (thanks to the health data warehouse), Caen, Le Havre/Lillebonne and Dieppe Centres. Each imaging examination was reviewed blinded to the treatments by a radiologist with expertise in osteoarticular disease. Patients were classified into 2 groups (bony versus joint/mixed) according to imaging data and clinical history. The response to treatment was considered positive if symptoms were improved by at least 50% (cut-off used in the literature). An χ^2 patients aged 18 years or older with SAPHO syndrome meeting Benhamou's criteria whose clinical, biological and a Mann-Whitney test for quantitative variables using SPSS software.

Results: Thirty-four patients with SAPHO who had received DMARD or BP treatment were included and classified as follows: 13 in the bone group and 21 in the joint or mixed group. The 2 groups were comparable on demographics, duration of follow-up, previous chest involvement, existence of associated dermatological or inflammatory bowel disease, exposure to smoking, duration of exposure to a previous NSAID or antibiotic. Only the age of onset of symptoms differed between the two groups, with a younger onset of disease in the bone group (p=0.043). The prescribers' therapeutic attitude differed significantly between the 2 groups (p=0.043) with a greater prescription of BPs as first line in the bone group (5/13 patients) and a DMARD in the joint/mixed group (19/21). Regarding treatment efficacy, 10/13 patients had effective treatment without escape during their follow-up in the bone group, which was not significantly different from the joint/mixed group (17/21). BPs achieved escape-free efficacy in significantly more cases in the bone group than DMARDs in the joint or mixed group (p= 0.002). The bone group used significantly fewer specific treatment lines (DMARDs or BP) than the joint/mixed group (1 specific line vs. at least 2) (p =0.046).

Conclusion: BPs appear to be more effective in SAPHO with predominantly bone involvement. This appears to be easier to treat compared to SAPHO with articular or mixed forms.

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POS1334 OCULAR CICATRICIAL PEMPHIGOID: IS THERE AN ASSOCIATION WITH AUTOIMMUNE DISEASES?

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Background: Ocular Cicatricial Pemphigoid (OCP) is an infrequent, systemic cicatricial immune-mediated disease, belonging to the group of membranous-mucosal pemphigoids (MMP). Due to the possibility of coexistence of multiple autoimmune diseases (ADs), OCP could be associated with other diseases. In the literature, association of OCP and ADs is reported in 9-35% of patients, but most reports correspond to MMP.
Objectives: To assess the prevalence of autoimmune diseases associated with OCP and to analyse clinical, laboratorial and treatment associations between these entities.
Methods: A multicentre cross-sectional study of patients with a diagnosis (clinical and/or by biopsy) of OCP derived from ophthalmology was performed.
The population was divided into two groups according to their association or not with other ADs. Clinical, laboratorial and treatment variables were described and compared between both groups. In addition, a multivariate descriptive logistic regression analysis was performed to identify variables that could suggest the association between OCP and ADs.
Results: A total of 88 patients were recruited, 66 (75%) females, with a mean age at diagnosis of 64.3 years (SD 11.9). The median follow-up time was 1 year. The diagnosis was done by biopsy in 86,8%. Ocular bilateral disease was present in 95,3% of patients. There was a median delay from symptoms onset to diagnosis of 2 years. A history of malignancy was reported in 13,6%. Extraocular involvement was evidenced in 11,5% (4% compromised skin and 9,1% other mucous membranes). Regarding the previous clinical findings, no statistically significance was found between the groups with and without ADs. Systemic treatment was depicted as follows: oral corticosteroids (60,2%) (p-value < 0.001), corticosteroids pulses (5,7%), dapsone (3,4%), methotrexate (79,5%), mycophenolate (15,9%), azathioprine (23,9%), rituximab (5,7%), immunoglobulin (1,1%); topical corticosteroids (96,6%) and ocular infiltration (2,3%). The group associated ADs included 24 patients (27.3%). Within them, the most prevalent diagnosis was Sjogren's syndrome (13.6%), followed by Hashimoto´s thyroiditis (9,1%) and rheumatoid arthritis (3,4%). Most of the patients presented Foster stages 1 (45.3%) and 2 (29.3%) at diagnosis. In the ADs group, statistically significant associations were observed with ANA, SS-A and SS-B antibodies, rheumatoid factor, and hypergammaglobulinemia. In the descriptive multivariate logistic regression model, it was detected that hypergammaglobulinemia was associated with ADs and OCP, adjusted for age, sex, smoking, skin and mucosal involvement, and erythrocyte sedimentation rate (OR 8.7; 95% CI 1.6 to 46.8; p= 0.012), Table 1.

Table 1. Multiple logistic regression analysis with OCP associated with ADs as dependent variable.

	OR	CI95	P value
Gender	0.2	0.04 - 1.1	0.07
Age at diagnosis	1.02	0.9 - 1.1	0.25
Smoking	0.5	0.1 - 1.7	0.26
Skin and mucosa compromise	1.2	0.2 - 8.2	0.83
ESR	0.98	0.95 - 1.02	0.58
Hypergammaglobulinemia	8.7	1.6 - 46.8	0.012

ESR: Erythrocyte Sedimentation Rate. OR: Odd Ratio. CI95: confidence interval

Conclusion: Due to the autoimmune nature of OCP, it could coexist with other ADs. In this research, it was observed that more than a quarter of the population presented with such association and hypergammaglobulinemia could suggest it. A systematic search for this coexistence should be carried out to avoid sequelae or incomplete treatment in pathologies that are currently potentially treatable.
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POS1335 ADHERENCE TO COLCHICINE PROPHYLAXIS AMONG PATIENT WITH FAMILIAL MEDITERRANEAN FEVER TREATED WITH INTERLEUKIN-1 INHIBITORS

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Background: Colchicine is the only drug proven to prevent secondary amyloidosis among familial Mediterranean Fever (FMF) patients. Therefore, the common recommendation is to continue colchicine during the treatment with IL-1 inhibitors, despite clinical remission.
Objectives: Our aim was to estimate the adherence to colchicine among FMF patient treated with IL-1 inhibitors.
Methods: The databases of Maccabi Health Services (MHS), a 2.6 million member state-mandated health provider in Israel was searched for patients with FMF diagnosis. Medication possession ratio (MPR) was used as main outcome measure. Patients treated with IL-1 inhibitors ("combination group") were matched in a ratio of 1:4 to patients on colchicine only ("single treatment"). In the second phase, patients with IL-1 inhibitors were matched to themselves, before and after starting the treatment.
Results: The final cohort included 4526 patients. Among them, 108 patients were treated with IL-1 inhibitors. They were matched to 432 "single treatment" patients. The total MPR in each groups was similar (78.9 ±41.4 versus 82.5 ± 80.6, P=0.5). In sub-analyses females treated with IL-1 inhibitors had less MPR than in the matched group (81.4 ± 33.2 versus 85.1 ± 91, P=0.03). In the second phase, The MPR was higher after starting IL-inhibitors among the total population (19.7±13.1 before versus 32.2±14.5 after, p<0.01).
Conclusion: Contrary to initial concerns, the adherence to colchicine is excellent among patients treated with IL-1 inhibitors and is similar to the general FMF population. Moreover, the adherence increases among the same patients after starting IL-1 inhibitors, which may reflect the improvement in disease perception following the need to start the biological treatment.
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Table 1. Comparison of medication possession ratio (MPR) of colchicine between FMF patients treated with IL-1 inhibitors Versus patients without IL-1 inhibitors treatment

Parameter	With IL-1 inhibitors – "study group" (n=108)	Without IL-1 inhibitors – "matched group" (N=432)	P-value
Age category, years			
≤6	74.9±24.9 (N=32)	75.8±33.7 (N=23)	0.9
7-14	90.2±53.6 (N=24)	75.6±70.3 (N=93)	0.09
15-29	76.5±47.9 (N=29)	91.1±123.3 (N=101)	0.3
≥30	75.8±33.7 (N=23)	77±49.9 (N=112)	0.6
Sex			
Male	75.7±49.9 (N=48)	79.2± 65.5 (N=192)	0.9
Female	81.4±33.2 (N=60)	85.1±91.0 (N=240)	0.03
Time of colchicine use			
	102.8±46.2 (N=42)	100.9±99.5 (N=245)	0.2
< 8 years			
8-15 years	66.6±35.8 (N=26)	56.7±36.5 (N=103)	0.2
> 15 years	61.9±24.8 (N=40)	60.4±25.8 (N=84)	0.7

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POS1336 BEHCET'S DISEASE AND PREGNANCY OUTCOMES

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Background: Behcet's disease (BD) is multisystemic disease of unknown cause. The relationship between BD and pregnancy is reported in limited number of studies.
Objectives: To evaluate outcomes of pregnancies in BD patients (pts).
Methods: We retrospectively collected data of 45 women with BD diagnosis (according to ISGBD 1990 and ICBD 2014) and their 118 pregnancies. Pts' mean age was 31,3 [27;35] years., disease duration 6,0 [3;8] years. 11,1% pts had severe BD according to Ch.Zouboulis classification (due to generalized uveitis, retinal vasculitis and parenchymatous CNS lesions), 31,1% pts had a moderate disease, 57,8% pts had a mild disease with mainly dermal-mucous manifestations.
Results: 118 pregnancies in 35 pts resulted in 75 live birth (6 cesarean section in 3 pts). Thirty-nine incomplete pregnancies were observed in 26 patients. Ten patients had 20 medical abortions on request before 12 weeks of gestation, one patient had an abortion due to medical reasons (rubella on the 7 th week of gestation), two patients had premature birth at 28 and 32 weeks with subsequent perinatal death of the baby. Fifteen out of 35 pts had 20 adverse pregnancy outcomes: 8 spontaneous abortion, 12 missed miscarriage. Nine patients had 12 Missed miscarriage at 6-11 weeks of gestation, one patient had 3 missed miscarriage, two had 2, and the others had 1 missed miscarriage. Six patients had 8 spontaneous abortions (early miscarriage). In the control group of 15 women, 7 had 15 pregnancies, 13 live birth of healthy children on time. Table 1 presents a comparison of pregnancy outcomes in patients with BD and healthy control.

Table 1. Pregnancy outcomes

Pregnancy, n	BD, n=118 (%)	Control, n=15 (%)	*p*
Birth	77 (65)	13 (87)	0,01
Abortion	21 (18)	0	0,00
Unfavorable pregnancy outcome	20 (17)	2 (13)	ns
Missed miscarriage	12 (10)	0	ns
Spontaneous abortion	8 (7)	2 (13)	ns

Patients with BD were more likely to terminate pregnancy of their own volition compared to control group. All women with unfavorable pregnancy outcomes are re-pregnant, have healthy children born on time, all had a second or subsequent pregnancy with an unfavorable outcome. Immunosuppressive therapy of BD was not received by any of the pregnant women, which makes it possible to exclude the connection of the outcome of pregnancy with BD therapy.
The manifestation of BD with skin-mucous lesion of the patient in the first and third trimester of pregnancy was noted by 3 patients. In one patient, the appearance of a recurrent ulcer on the vulva was an indication for cesarean section.
Only three women had one favorably completed pregnancy, all the others had from 2 to 7 pregnancies. Out of 45 patients, 10 patients did not have pregnancies, 9 of them are not married, 1 patient is planning a pregnancy.
Table 2 shows the frequency of pregnancy pathology with varying degrees of severity of BD.

Table 2. BD Severity and pathology of pregnancy

BD Severity	N = 45 (%)	Intrauterine deaths/Miscarriage
Mild	25 (57,8)	5/6
Moderate	6 (31,1)	1/1
Severe	14 (11,1)	2/5

Adverse pregnancy outcomes were observed with varying severity of BD. Out of 77 babies children born by BD patients only two had relapsing aphthous stomatitis and one – congenital glaucoma ("Neurobehcet" inherited from the mother).

Conclusion: Patients with BD were more to terminate pregnancy compared to control group. Unfavorable outcomes of pregnancy were documented in pts regardless (with all grades of) BD severity.
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POS1337 ADULT-ONSET STILL'S DISEASE WITH ELDERLY ONSET, RESULTS FROM A MULTICENTRE STUDY AND ASSESSMENT OF AGE INFLUENCE ON CLINICAL FEATURES AND DISEASE OUTCOMES.

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Background: Aging is a physiological, multidimensional, and irreversible process, occurring in humans over time. Interestingly, multiple lines of evidence have recently suggested that some diseases, generally affecting young adults, are nowadays described in the elderly, although possibly associated with different symptoms or complications. In this context, a possible occurrence of adult onset Still's disease (AOSD) in elderly has been suggested. This is a rare inflammatory disorder of unknown origin usually observed in young adults [1-3].
Objectives: In this study, we aimed at describing the clinical characteristics, life-threatening complications occurrence, and mortality of AOSD patients with an elderly onset. The manifestations of these patients were also compared with those with a younger onset. Furthermore, the predictive role of age was evaluated on clinical features and disease outcomes. Finally, in these patients, an assessment of associated comorbidities was also performed.
Methods: A retrospective assessment of prospectively followed patients, from January 2001 to April 2021, was provided to analyse clinical features, life-threatening complications occurrence, and mortality in AOSD patients with onset in elderly. AOSD patients, who were included in multicentre *Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale* (GIRRCS) cohort, were evaluated.
Results: Out of 221 assessed patients, 37 (16.7%) had an onset of the disease aged over than 60 years. When compared with younger patients, these were characterised by a higher prevalence of pericarditis (p=0.008), comorbidities (p<0.0001), and mortality (p=0.023).
Additionally, our analysis showed that pleuritis and pericarditis positively correlated with age (coefficient=0.227, p=0.001; coefficient=0.213, p=0.001, respectively). Furthermore, the occurrence of parenchymal lung disease was significantly related with age (coefficient=0.168, p=0.012). The presence of comorbidities positively correlated with age (coefficient=0.443, p<0.0001). Moreover, age was negatively related to the polycyclic pattern (coefficient=-0.209, p=0.002). A correlation between mortality and age was also retrieved (coefficient=0.158, p=0.019).

Age predicted the presence of serositis in both univariate (HR: 1.02, 95%CI: 1.01-1.03, p=0.007) and multivariate analyses (HR: 1.02, 95%CI: 1.01-1.04, p=0.007). Age was also a significant predictor of parenchymal lung disease in both univariate (HR: 1.03, 95%CI: 1.01-1.05, p=0.017) and multivariate analyses (HR: 1.03, 95%CI: 1.00-1.05, p=0.048). No significant results were observed assessing the predictive role of age on occurrence of macrophage activation syndrome. Furthermore, age resulted to be a negative predictor of polycyclic pattern only in univariate analysis (HR: 0.99, 95%CI: 0.97-1.00, p=0.048). Finally, age significantly predicted the mortality in both univariate (HR: 1.03, 95%CI: 1.00-1.06, p=0.034) and multivariate analyses (HR: 1.05, 95%CI: 1.01-1.08, p=0.012).

Conclusion: Clinical features of AOSD patients with elderly onset were described in our multicentre cohort. Although the main clinical characteristics were similar comparing older and younger patients, patients aged over 60 years at disease onset were characterised by an increased prevalence of serositis, comorbidities, mostly cardiometabolic, and a higher mortality rate. Age predicted the presence of parenchymal lung disease and mortality, and it could be considered a further negative prognostic factor in AOSD.

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POS1338 CENTRAL SENSITIZATION AND RELATED FACTORS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Central sensitization (CS) is an increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input is an important manifestation involved in many different rheumatic diseases [1].

Objectives: This study aims to investigate the CS in patients with Familial Mediterranean Fever (FMF) and its associations with other parameters.

Methods: This ongoing study included 73 patients (57 female, 16 male) who were diagnosed with FMF according to the Tel-Hashomer criteria. Clinical characteristics including age, gender, disease duration, age at onset, genetic mutations, comorbid disease and medications were noted. Disease activity was assessed with a PRAS disease activity score. Evaluations included the Health Assessment Questionnaire (HAQ), FMF quality of life (FMF-QoL), Pittsburg Sleep Quality Index (PSQI), Fibromyalgia Rapid Screening Tool (FiRST), and the Hospital Anxiety and Depression Scale (HADS). The symptoms of CS were assessed with the Central Sensitization Inventory (CSI; range 0-100) which is a self-report outcome measure designed to identify patients who have symptoms that may be related to CS or central sensitivity syndromes (CSS) such as fibromyalgia, neck injury, temporomandibular joint disorder or migraine/tension headaches [2]. Descriptive analysis was performed for all parameters. The Mann-Whitney U-test and chi-squared test were used in statistical analysis. P<0.05 was considered statistically significant.

Results: The mean age of the patients was 37.6 (SD:13.6) years. Sacroiliitis occurred in 8 patients (11%), amyloidosis in 1 (1.4%), and erysipelas-like erythema in 8 (11%). The most prevalent genetic mutation was M694/any compound heterogeneous (16.4%) followed by M69V homogeneous (15.1%). Disease activity was mild in 42.5%, moderate in 32.9% and severe in 12.3% of the patients. The mean CSI was 38.4 (SD:18.7) and thirty-four (46.6 %) of 73 patients had CS according to the CSI. CSI scores were significantly higher in females than in males (p=0.009). Eleven (15%) patients had colchicine resistance, and those with colchicine resistance had significantly higher CS scores. In patients with central sensitization, PRAS, HAQ FMF-QoL, FiRST, PSQI, and HADS scores were significantly higher than in patients without central sensitization (Table 1).

Table 1. Disease characteristics in terms of central sensitization

	Central sensitization *Yes (n=34)*	Central sensitization *No (n=39)*	*p*
Gender, female	31 (91.2%)	26 (66.7%)	**0.02**
BMI, kg/m^2	28.8 (8.8)	26.2 (6.8)	0.282
Disease duration	9.3 (6.9)	12.9 (9.9)	0.156
Number of attacks in the last 3 months	2.05 (2.1)	0.8 (1.6)	**<0.001**
Number of attacks in the last 6 months	3.7 (3.3)	1.5 (3.2)	**<0.001**
PRAS	6.3 (2.1)	4.8 (2.3)	**0.004**
HAQ	0.4 (0.6)	0.08 (0.2)	
FMF-QoL	38.2 (13.7)	17.3 (15.2)	**<0.001**
FiRST	3.9 (1.9)	1.7 (1.7)	**<0.001**
PSQI	9.9 (3.9)	6.4 (2.8)	**<0.001**
HAD-Anxiety	9.6 (4.4)	4.9 (3.8)	**<0.001**
HAD-Depression	7.08 (4)	4.4 (3.2)	**0.003**

BMI: Body Mass Index, HAQ: Health Assessment Questionnaire, FiRST: Fibromyalgia Rapid Screening Tool, FMF-QoL: Familial Mediterranean Fever Quality of Life, PSQI: The Pittsburgh Sleep Quality Index, HADS: the Hospital Anxiety and Depression Scale

Conclusion: CS is present in approximately half of FMF patients. CS in patients with FMF was associated with high disease activity, fibromyalgia, anxiety, depression, impaired function, poor quality of life and sleep.

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POS1339 FACTORS RELATED TO SERUM IGG4 ELEVATION AND DEVELOPMENT OF IGG4-RELATED DISEASE: DATA FROM RESIDENT EXAMINATION

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Background: Elevated serum IgG4 levels are one of the characteristic findings in immunoglobulin G4 (IgG4)-related disease (IgG4-RD). Serum IgG4 levels have an impact to a certain extent on the diagnosis of IgG4-RD although there are some issues in their sensitivity and specificity. In the reports from Japan, China, USA, and Europe, elevated serum IgG4 levels were reported to be observed in 83-97% of patients with IgG4-RD [1-5]. In the past investigations of hospital patients, some studies reported that 10-15% of hospital patients with elevated serum IgG4 levels had IgG4-RD [6,7]. However, in general adults with no symptom, investigations of prevalence of elevated serum IgG4 levels and/or IgG4-RD have rarely been conducted.

Objectives: This study aimed to investigate the frequency of serum IgG4 elevation in the general Japanese population and its associated factors using data from resident examinations.

Methods: We measured the serum IgG4 levels in 1,204 residents who underwent a general medical examination in Ishikawa prefecture, Japan. Logistic regression analysis was used to search for factors related to elevated serum IgG4 levels. Secondary examinations were conducted for participants in whom elevation was identified.

Results: The mean serum IgG4 level was 44 mg/dL, and elevated serum IgG4 levels were observed in 42 patients (3.5%). Univariate logistic regression analyses showed that male sex, older age, lower estimated glomerular filtration rates based on cystatin C (eGFR-CysC), serum high-density lipoprotein cholesterol levels, and higher hemoglobin A1c (HbA1c) levels were associated with elevated serum IgG4 levels. Subgroup analyses in men showed that older age, lower eGFR-CysC levels, and higher serum HbA1c levels were associated with elevated serum IgG4 levels. In contrast, the analyses in women found no significant factors. One of the 10 residents who underwent secondary examinations was diagnosed with possible IgG4-related retroperitoneal fibrosis.

Conclusion: In the general population, elevated serum IgG4 levels are more common in elderly men, which is similar to the epidemiological features of IgG4-RD.

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POS1340 BASELINE CLINICAL DISEASE ACTIVITY IS NOT CRITICAL FOR PREDICTING REMISSION OF ADULTS ONSET STILL´S DISEASE

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Background: The clinical course of adult-onset Still's disease (AoSD) is highly variable, ranging from subtle constitutional symptoms to life-threatening complications such as macrophage activation syndrome. Therefore, it is of interest whether baseline disease activity in AoSD predicts the clinical course, i.e. clinical and serological remission.
Objectives: The aim of this study was to compare whether two instruments to measure AoSD disease activity, Pouchot-Score and Still-Activity-Score (SAS), at baseline predict later remission of disease. We also assessed whether serum levels of calprotectin (S100A8/A9) are associated with clinical disease activity as measured by SAS at follow up.
Methods: AoSD was diagnosed according to the Yamaguchi criteria. In all patients Pouchot-Score and Still-Activity Score (SAS) were assessed at baseline and SAS score also at follow-up. Clinical remission was defined as absence of all AoSD symptoms (i.e. fever and arthralgia), while serological remission was defined as normalization of Ferritin, IL-18 and S100A8/A9 (calprotectin) levels. To investigate the prediction accuracy of the baseline Pouchot-Score and SAS for clinical and serological remission, a calculation of the areas under the receiver operating characteristic (ROC) curves was performed.
Results: 42 AoSD patients (19 males/23 females; mean+/-SD age:41+/-17 years) were assessed. Baseline Pouchot-Score was 5.3 +/- 1.6, baseline SAS was 5.7 +/- 1.0. With treatment of AoSD, clinical disease activity decreased reaching a mean SAS of 2.2 +/- 1.8 after a mean follow up time of 48 +/- 90 months. Glucocorticoids were used by 33%, methotrexate by 21%, IL-1 inhibitors by 33% and IL-6 inhibitors by 29% of the patients. 62% (N=26) of the 42 patients obtained clinical remission and 36% (N=15) serological remission. Neither Pouchot-Score (0.57) nor SAS (0.51) at baseline predicted clinical remission of AoSD. Furthermore, also serological remission was not predicted by baseline SAS (0.62) or Pouchot-Score (0.56) (Figure 1). With respect to activity of AoSD during treatment serum calprotectin levels were closely associated with SAS disease activity ($r = 0.54$, $p < 0.0003$) (Figure 2).
Conclusion: Baseline AoSD disease activity as measured by Pouchot-Score and SAS does not predict clinical or serological remission. Serum calprotectin level is closely related to AoSD disease activity during the treatment phase.
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Disclosure of Interests: Jennifer Groetsch: None declared, Koray Tascilar: None declared, Georg Schett: None declared, Dirk Foell: None declared, Jürgen Rech Speakers bureau: Abbvie, Biogen, BMS, Chugai, GSK, Lilly, MSD; Novartis, Roche, Sanofi, Sobi, UCB, Consultant of: Abbvie, Biogen, BMS, Chugai, GSK, Lilly, MSD, Novartis, Roche, Sanofi, Sobi, UCB, Grant/research support from: Sobi, Novartis
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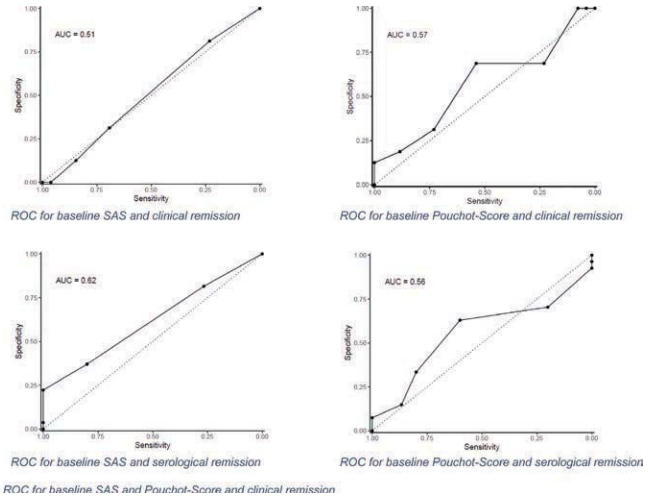

Figure 1. ROC for baseline SAS and Pouchot-Score and clinical remission

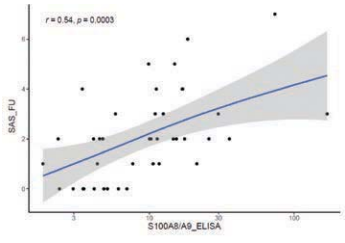

Figure 2. Association between S100A8/A9 protein measured by the ELISA method and disease activity by the SAS at follow-up

POS1341 EVALUATION OF DAMAGE CAUSED BY SEPTAL PANNICULITIS ASSOCIATED WITH ACUTE SARCOIDOSIS

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Background: Joint involvement in combination with septal panniculitis, erythema nodosum (EN), febrile reaction, and intrathoracic lymphadenopathy is the criteria for acute sarcoidosis (Löfgren's syndrome, LS) – a granulomatous multisystem inflammatory disease of unknown etiology.
Objectives: to develop an index of damage caused by septal panniculitis for express-assessment of the X-ray stage of LS.
Methods: We examined 142 patients (31 men and 111 women) in case of EN associated with LS, average age 39.3±11.1 years. All patients underwent a comprehensive clinical, laboratory and instrumental examination, including ultrasound of the joints and computed tomography (CT) of the chest organs.
Results: In 96% of cases, widespread EN was detected, which correlated with the level of CRP ($p=0.006$; $r=0.38$). In 124 patients (87%) there were signs of joint damage with predominantly periarticular changes in the area of ankle joints. The relationship between the duration of the articular syndrome and the duration of inflammatory changes in the subcutaneous tissue and the number of nodes was registered ($p=0.02$; $r=0.45$). The level of CRP had a significant direct correlation with the number of nodes ($p=0.008$; $r=0.29$) and the severity of articular syndrome ($p=0.003$; $r=0.29$). An elevated level of angiotensin-converting enzyme was detected in 97 patients (78%). The assessment of the probable radiological stage (c) of LS was performed according to the formula obtained using step-by-step discriminant analysis:
$c= 1,06*X1+0,98*X2+5,21*A+ 1,68*CRP$
X1 – the number of sides of the lower/upper limbs with the detected diffuse lesions of the skin and subcutaneous fat; X2 – the number of erymatous nodes (or induration); A – the number of arthritis; CRP – concentration of C-reactive protein in absolute values. The value of $c\leq 28.72$ indicated x-ray Stage 0; $28.72<c<109.02$ – x-ray Stage I, $c \geq 109.02$ – x-ray Stage II of the LS of the chest organs. The developed technique made it possible to determine Stage I of LS in 69% of cases and Stage II in 15% of cases, which was confirmed by CT of the lungs. For the selected total value of the discriminant function of 3.984, the sensitivity is 79%, the specificity is 96%.
Conclusion: The developed assessment is a low-cost, affordable and fast way to assess the verification of the X-ray stage of LS at any stage of the disease, which contributes to the immediate prescription of adequate therapy.
Disclosure of Interests: None declared
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POS1342 DEPLETION OF KLRG1+ T CELLS IN A FIRST-IN-HUMAN CLINICAL TRIAL OF ABC008 IN INCLUSION BODY MYOSITIS (IBM)

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Background: Inclusion body myositis (IBM), a relentlessly progressive autoimmune skeletal muscle disease, has no effective available pharmacological therapy. A prominent feature of IBM on microscopy is highly differentiated effector CD8+ cytotoxic T (Tc) cells invading non-necrotic myofibers [1]. These Tc cells, known to be relatively resistant to apoptosis, express markers including killer cell lectin-like receptor G1 (KLRG1) [2]. ABC008, a first-in-class humanized, afucosylated monoclonal antibody (mAb) specific for KLRG1, selectively depletes these highly differentiated Tc cells while sparing other blood cell populations, e.g., naïve, central memory, and regulatory T cells and B cells. ABC008 has been designed to treat diseases mediated by these Tc cells, including IBM and T-cell large granular lymphocytic leukemia (T-LGLL). IBM and rheumatoid arthritis overlap clinically with T-LGLL and share similar expansions of large granular lymphocytes (LGLs), which also express KLRG1. We report here our preliminary data from our ongoing trial of ABC008 in IBM (NCT04659031).
Objectives: Evaluate the safety, pharmacodynamics (PD), and pharmacokinetics (PK) of ABC008 administered subcutaneously (SC) in adults with IBM.
Methods: In this first-in-human, open-label, single ascending dose trial with 3 + 3 design evaluating ABC008 SC, eligible participants must have clinicopathologically defined, clinically defined, or probable IBM according to the European Neuromuscular Centre 2011 research diagnostic criteria [3] and an IBM Functional Rating Scale (IBMFRS) score ≤38. Four dose cohorts are planned: ABC008 0.1, 0.5, 2.0, and 5.0 mg/kg. PD, PK, safety, and disease severity assessments are performed pre-dose (Day 0) and during the 6-month follow-up period.
Results: Five of the 6 (83.3%) participants were male with baseline mean age = 65.7 years, mean IBM disease duration = 6.8 years, and mean IBMFRS score = 27.5 (Table 1). Each received a single dose of ABC008 SC: Cohorts 1 (C1) and 2 (C2) received 0.1 and 0.5 mg/kg and have completed 168 and 56 days of follow-up, respectively.

Table 1. Baseline Demographics

Baseline Characteristics	ABC008 SC Treatment Groups		
	Cohort 1 0.1 mg/kg SC (n=3)	Cohort 2 0.5 mg/kg SC (n=3)	ABC008 Overall (N=6)
Age (years), mean ± SD	64.0 ± 11.36	67.3 ± 6.66	65.7 ± 8.52
Male sex, n (%)	3 (100)	2 (66.7)	5 (83.3)
Caucasian	3 (100)	3 (100)	6 (100)
Body Mass Index (kg/m^2)	28.5 ± 3.58	28.3 ± 4.25	28.4 ± 3.52
Disease Duration (years), mean ± SD	9.7 ± 5.97	3.9 ± 4.48	6.8 ± 5.70
IBMFRS score, mean ± SD	30.0 ± 4.08	25.0 ± 6.16	27.5 ± 5.80

Abbreviations: IBMFRS, Inclusion Body Myositis Functional Rating Scale; n or N, number; SC, subcutaneous; SD, standard deviation.

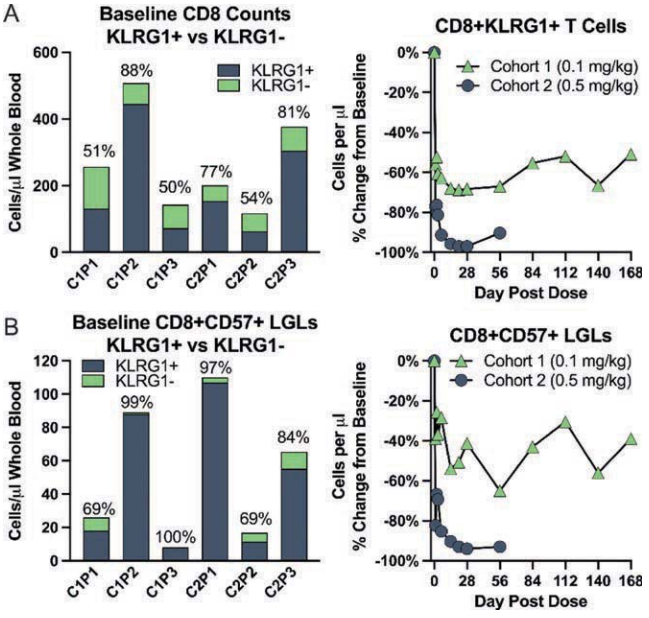

Figure 1. Key pharmacodynamic parameters in Study ABC008-IBM-101. Baseline and change (A) of KLRG1+CD8+ T cells and (B) CD8+CD57+ large granular lymphocytes (LGLs). C1 and C2 are Cohorts 1 and 2; P1, P2, and P3 are Participants 1, 2, and 3.

Maximum depletion of CD8+KLRG1+ cells for C1 and C2 ranged from 46-96% and 98-99%, respectively (Figure 1A), with depletion evident by the next assessment on Day 1. Recovery in C1 began at Day 84 with Day 168 depletion at 29-71%. Other hematologic parameters generally were stable (e.g., T regulatory and B cells). CD8+CD57+ LGLs, mostly KLRG1+, were also depleted (Figure 1B). Preliminary PK showed that ABC008 SC displays a long absorption phase and slow clearance properties typical of mAb therapies. No severe adverse events (AEs) or discontinuations due to AEs have been reported. One unrelated serious AE of fall with muscle tear in a C1 participant with a prior history of falls occurred.
Conclusion: In study participants with IBM, single SC doses of 0.1 and 0.5 mg/kg of ABC008 resulted in the depletion of CD8+KLRG1+ cells and CD8+CD57+ LGLs with clear evidence of a dose response for KLRG1+ T cell depletion and no apparent safety signals. Based on these results, a study evaluating ABC008 for the treatment of T-LGLL is planned.

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POS1343

TREATMENT OF RESISTANT RAYNAUD'S PHENOMENON WITH SINGLE-PORT THORACOSCOPIC SYMPATHICOTOMY: ONE-YEAR FOLLOW-UP

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Background: Raynaud's phenomenon (RP) usually results in discoloration of the extremities when provoked by cold or emotional stress [1]. Some patients do not respond to conventional therapies, such as lifestyle interventions and vasodilatory medication. These patients are confronted with limited options for treatment. In a previous study we have shown that minimally invasive Single-Port Thoracoscopic Sympathicotomy (SPTS) objectively and subjectively improves treatment-resistant RP, after one month [2]. This procedure for treatment-resistant RP is minimally invasive and potentially highly effective, because it specifically targets the sympathetic nerve at the third rib (R3), while leaving the ganglia untouched [3]. The procedure was only performed on the left side in the pilot study, which objectively resulted in improvement of left-hand perfusion in all patients after one month, when compared to the right hand. Furthermore, patient satisfaction after surgery was high and RP attacks of the left hand were less frequent and of shorter duration. Previous studies have shown that long-term effects of conventional sympathectomy is stable in the long run in the majority of patients [4, 5]. We have previously published the one-month results of SPTS for treatment-resistant RP in a concise report [2]. In the current study we sought to report the one-year follow-up results of SPTS for treatment-resistant RP in the same cohort of patients.
Objectives: Follow-up of patients with treatment-resistant Raynaud's phenomenon (RP) one-year after single-port thoracoscopic sympathicotomy (SPTS).
Methods: Eight patients (six males, two females, median age of 45 years) with treatment-resistant RP underwent left-sided SPTS at the third rib (R3), unilaterally. Perfusion was assessed with a cooling and recovery procedure at baseline and one year after SPTS. Furthermore, laser speckle contrast analysis, pulse wave velocity, heart rate variability and nailfold capillaroscopy were performed. In addition, questionnaires were taken, and number and duration of RP attacks were reported over a 2-week period.
Results: One year after SPTS the duration of the attacks of was reduced with 1.9 hours in the left hand versus 0.9 hours in the right hand. Furthermore, three aspects of the questionnaire showed a significant improvement (role limitations due to physical health (p=0.017), pain (p=0.027) and physical functioning (p=0.025)). The total area under the curve of the total cooling and recovery procedure of the left hand was larger one year after surgery (101 (75–140) at baseline versus 118 (95–190) one year post-operatively, p=0.012), implying a better perfusion in the fingers. This was mainly due to the improvement during the recovery phase (21 (1–41) at baseline versus 38 (24–43) one year post-operatively, p=0.028).
Conclusion: One year after unilateral R3 SPTS there is clear benefit with regard to the majority of outcome variables, though some effects seem to attenuate. Long-term effects and five-year follow-up results will be investigated in an on-going study.

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POS1344 USEFULNESS OF TRADITIONAL AND NOVEL BIOMARKERS FOR EVALUATION OF ADULT-ONSET STILL's DISEASE ACTIVITY

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Background: Adult-onset Still's disease (AOSD) is a rare systemic autoinflammatory disorder with unknown etiology. The main problem for rheumatologists is a lack of generally accepted methods for assessing AOSD activity.
Objectives: To compare the usefulness of traditional and novel biomarkers for assessing the AOSD activity
Methods: The cross-sectional study included 27 patients over the age of 18 with a relapse of AOSD who were examined at the Almazov National Medical Research Centre from 2018 to 2021. All patients fulfilled the AOSD classification criteria by Yamaguchi. Clinical manifestations were scored in a Pouchot AOSD activity score. The serum concentrations of IL-1, IL-6, IL-18, ferritin, calgranulin, procalcitonin and the level of glycosylated ferritin (GF) were examined. Standard commercial reagents were used for detection clinical analysis of blood, C-reactive protein (CRP) and aminotransferases. Statistical analysis was performed using the licensed statistical applications Statistica 10.0 for Windows (StatSoft Inc., USA), and Prisma GraphPad 8.0 (GraphPad Software, USA). Results were expressed as median (25th–75th percentile) and analysed for statistical significance using nonparametric tests. For quantitative features comparison, the Mann–Whitney U test was used. The correlation coefficient was obtained by nonparametric Spearman's rank correlation test. P values < 0.05 were considered statistically significant. Data from commercial test systems are taken as the basis for normal biomarker indicators.
Results: Clinical data were available from 27 patients with AOSD (6 male and 21 female). The median age was 41.3 [26;50]. The median Pouchot activity score was 6 [4.5;7]. The course of AOSD was monocyclic in 1 patient, polycyclic in 23, and chronic in 3. Elevated leukocyte count > 10,000/μl was detected in 17 patients (63%), 9 patients (33%) had an elevated leukocyte count > 15,000/μl.
An increase in biomarkers was detected in most patients: calgranulin was increased in 24 out of 26 patients (92.3%), ferritin was increased and GF was decreased in 21 out of 25 patients (84%). Among those 25 patients, the decrease in GF was less than 20% in 13 patients (52%). IL-18 increased in 17 patients (63%), IL-6 increased in 22 patients (81.5%), and procalcitonin increased in 16 out of 26 patients (61.6%). The median of procalcitonin concentration was 0.08 [0.01; 30.1]. No increase in IL-1 beta was detected.
A correlation analysis revealed a direct relationship between the concentration of IL-18, ferritin and the Pouchot system score. An inverse relationship existed between these indicators and the level of GF (rs=0.803, p=0.001) and between calgranulin and IL-6 (rs=0.46, p=0.02). It was noted that the younger the age of the patients, the higher the concentration of IL-18 (rs=-0.449, p=0.019).
Conclusion: The most promising additional laboratory biomarkers for assessing AOSD activity are calprotectin, IL-18, and ferritin. Despite a slight increase in procalcitonin as one of the indicators of the acute phase of inflammation, it remains an effective biomarker of sepsis; however, it is recommended to focus on threshold concentrations above 0.5.

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POS1345 BEYOND PULMONARY ARTERY ANEURYSM; PULMONARY INVOLVEMENT IN BEHCET'S SYNDROME

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Background: Pulmonary involvement (PI) other than pulmonary artery aneurysm (PAA) in Behcet's syndrome (BS) is still an area of investigation.
Objectives: Herein, we aimed to retrospectively evaluate all types of pulmonary involvement associated with Behcet's syndrome (BS).
Methods: Among 800 BS patients according to International Study Group for Behcet's Disease (ISG) criterias, 28 patients were selected based on their radiologic examination consistent with BS-related PI. Demographic features, other clinical manifestations of BS, treatment modalities and types of PI were analyzed.
Results: The overall prevalence of PI was estimated 3,5% among all BS patients. PI was more common in males (82.1% vs 17.9%). Mean age for BS diagnosis and onset of PI were as following; 32 ± 10,9 and 37 ± 11,4 years. Deep vein thrombosis (DVT) was the most common accompanying vascular involvement (53,6%). PAA, pulmonary vasculitis (PV), and pulmonary thromboembolism (PTE) were seen in 7 (25%), 13 (46,3%), and 18 (64,4%) of patients, respectively. In 5 patients, intracardiac thrombosis was present simultaneously in the right ventricle. Cyclophosphamide (CYC) was the most common preferred agent (78%) followed by azathioprine (AZA) as first line. Warfarin used in 18 patients (Table 1) Mortality was seen in 3 patients during follow up (1 due to PAA bleeding, others with unknown causes).

Table 1. Characteristics of pulmonary involvement in BS patients

Male/Female, (n), (%)	23/5 (82,1%/17,9%)
Age of diagnosis, years (Mean± SD)	32 ± 10,9
Age of pulmonary involvement, years (Mean ± SD)	37 ± 11,4
Oral ulcer, (n), (%)	28 (100%)
Genital ulcer, (n), (%)	20 (71,4%)
Osteofollicular lesion,(n), (%)	20 (71,4%)
Erythema nodosum, (n), (%)	13 (46,4%)
Uveitis, (n), (%)	8 (28,6%)
DVT, (n), (%)	15 (53,6%)
Cardiac involvement, (n), (%)	5 (17,8%)
Pulmonary involvement, (n)	28
-PAA, (n), (%)	7 (25%)
-PV, (n), (%)	13 (46,4%)
-PTE, (n), (%)	18 (64,3%)
Immunosuppression (first line agents)	26/28
-Steroid, (n), (%)	26/28
-CYC, (n), (%)	22/26 (84,6%)
-AZA, (n), (%)	4/26 (15%)
Anticoagulation (warfarin), (n), (%)	18

PAA; pulmonary artery aneurysm, PTE; pulmonary thromboembolism, PV; pulmonary vasculitis, CYC; cyclophosphamide, AZA; azathioprine, DVT; deep vein thrombosis

Conclusion: Despite the importance of PAA in BS patients, capillaritis and thromboembolism other than PAA may occur commonly in BS as well. Onset at young age, male gender and previous DVT seem to be significant risk factors for the development of PI.
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Table 1. Main clinical features and treatment of 23 patients with NBD

	n (%)	Mean maximum oral prednisone dose, (SD) mg/day	Conventional immunosuppressants, n (%)	monoclonal anti-TNFα, n (%)	Tocilizumab, n (%)	Anakinra, n (%)
Parenchymal phenotype	**10 (43.5)**	**51.7±19.3**	**6 (46.2)**	**4 (57.1)**	**0**	**0**
-Hemiparesis	*5 (50)*	*52.5±75*	*2 (50)*	*3 (75)*		
-Optic neuropathy	*3 (30)*	*52.3±26.3*	*2 (66.7)*	*0*		
-Encephalopathy	*1 (10)*	*45*	*1 (16.7)*	*0*		
-Ophtalmoparesis	*1 (10)*	*0*	*1 (16.7)*	*1(25)*		
Non-parenchymal phenotype	**10 (43.5)**	**42±12.5**	**5 (38.5)**	**2 (28.6)**	**0**	**0**
-Aseptic meningitis	*10 (43.5)*	*42±12.5*	*5 (38.5)*	*2 (28.6)*		
Mixed	**3 (13)**	**45±15**	**2 (15.4)**	**1(14.3)**	**1 (14.3)**	**1 (14.3)**
-Aseptic meningitis and ophtalmoparesis	*1 (33.4)*	*60*	*0*	*0*	*0*	*0*
-Aseptic meningitis and other cranial nerve involvement	*1 (33.4)*	*0*	*1 (50)*	*0*	*0*	*0*
-Encephalopathy and intracranial hypertension	*1 (33.4)*	*30*	*1(50)*	*1(100)*	*1(100)*	*1(100)*

POS1346

PREVALENCE, PHENOTYPICAL CLINICAL CLUSTERS AND TREATMENT OF NEUROBEHÇET'S DISEASE. STUDY IN NORTHERN SPAIN

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Background: Behçet's disease (BD) may present with different clinical phenotypes. Ocular and Neurobehçet's Disease (NBD) are severe complications [1-4]. Data on NBD epidemiology, clinical phenotype and therapy are scarce and controversial.

Objectives: In a wide unselected single-center series of BD our aims were to assess **a)** NBD prevalence, **b)** associations with other clinical clusters and **c)** treatment.

Methods: Cross-sectional study of all 120 patients diagnosed with BD in Northern Spain, between January 1, 1999 to December 31, 2019. Finally, 96 patients were included in this study according to 2014 International Criteria for Behçet Disease (ICBD) [5]. NBD was diagnosed according to the International Consensus Recommendation (ICR) criteria [4].

Results: NBD was diagnosed in 23 of 96 (24%) patients (15 women/8 men) (mean age: 44±13.9 years). NBD was classified as parenchymatous (n=10, 43.5%), non-parenchymatous (n=10, 43.5%) and mixed (n=3, 13%). HLAB51 was positive in 5 out of 13 (38.4%) patients tested. The main cluster of clinical associations were oral aphthae (n=20, 87%); ocular (n=14, 60.9%), cutaneous (n=10, 43.5%), articular (n=9, 39.1%), vascular (n=4, 17.4%) and intestinal (n=1, 8.7%) involvement (Figure 1).

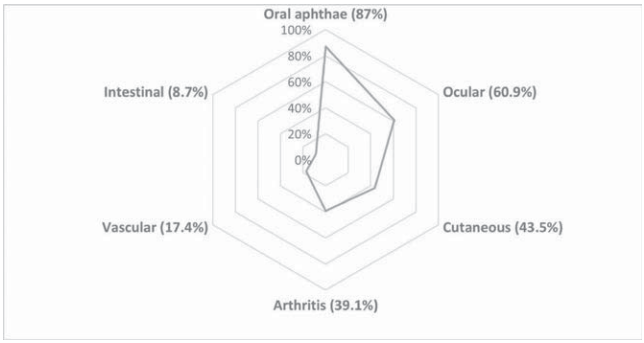

Figure 1. Clusters of clinical associations of NBD

Treatments were oral corticosteroids (n=16; 69.6%; mean maximum dose 42±12.5 mg/ day, conventional immunosuppressants (n=13, 56.5%) and Biological Therapy (BT) (n= 7; 30.4%). BT was used in patients who were refractory to conventional immunosuppressants. Monoclonal anti-TNFα were used as the first option in all patients who received BT. In 3 out of 7 (42.7%) patients BT was switched due to inefficacy. Table 1 shows the main NBD clinical subtypes and treatment.

Complete remission was achieved in 18 of 23 cases (78.2%), partial response in 2 out of 23 cases (8.7%). No severe adverse effects were observed.

Conclusion: NBD was observed in 24% of patients with BD. The most frequent clinical clusters of NBD were oral aphthae and ocular involvement. All patients treated with either conventional immunosuppressant or BT achieved clinical remission.

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POS1347

BIOLOGICAL THERAPY IN NEUROSARCOIDOSIS. STUDY OF 30 PATIENTS FROM A SERIES OF 234 SYSTEMIC SARCOIDOSIS FROM A UNIVERSITY HOSPITAL

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Background: Neurosarcoidosis (NS) is a severe complication of sarcoidosis [1,2]. NS may be classified according to several subtypes [1]. Data on therapy, including biological therapy (BT) is scarce.

Objectives: To assess efficacy and safety of BT in refractory NS subtypes.

Methods: Study of NS from a large cohort (n=234) of all consecutive patients diagnosed with sarcoidosis in a single university hospital from January 1, 1999 to December 31, 2019. Diagnosis of sarcoidosis was established according to ATS/ERS/WASOG criteria [3].

Efficacy was considered as complete or partial response and no-response according to the resolution of the neurological syndrome (signs and/or symptoms) after the BT onset.

Results: NS was observed in 30 (19 women/11 men) of 234 (12.8%) patients; mean age, 55.0±15.8 years. NS subtypes were chronic headache (n=13, 43.4%), peripheral neuropathy (n=6, 20%), cranial neuropathy (n=5, 16.7%), spinal cord abnormalities (n=3, 10%) and aseptic meningitis (n=3, 10%). A total of 26 (86.7%) patients received oral corticosteroids (CT) (mean maximum dose: 50±19.2 mg/dL) and 7 (23.3%) IV CT. In addition, conventional immunosuppressants were administered to 18 (60%) patients and BT to 12 (40%) patients. No treatment was administered to 4 (13.3%) patients. Table 1 shows treatment according to NS subtypes. A total of 12 patients received treatment with 22 BT. Most used BT were monoclonal anti-TNFα (n=18, 81.8%), infliximab (IFX) (n= 10, 45.5%) and adalimumab (ADA) (n=5, 22.7%). After 12 months since the initiation of BT, complete, partial or no response was observed in 14 of 17 (82.4%), 2 (11.8%) and 1 patient (5.9%), respectively (Figure 1). Severe allergic reaction was

Table 1. Treatment of 30 patients with neurosarcoidosis

Neurosarcoidosis subtype	n (%)	Other clinical manifestations n (%)	Conventional immunosuppressant, N=23 n (%)	monoclonal anti-TNFα, N=22 n (%)	Etarnecept, N=1 n (%)	Tocilizumab, N=1 n (%)	Secukinumab, N=1 n (%)	Rituximab, N=1 n (%)
Chronic headache*	13 (43.4)	P (n=9, 69.2%) A (n=9, 69.2%) C (n=6, 46.2%) O (n=4, 30.8%) D (n=4, 30.8%)	MTX (n=6, 26.1%) AZA (n=1, 4.3%)	IFX (n=1, 4.5%) ADA (n=1, 4.5%) GLM (n=1, 4.5%)	0 (0)	0	1 (4.5)	1 (4.5)
Peripheral neuropathy	6 (20.0)	P (n=5, 83.3%) A (n=3, 50%) O (n=3, 50%) C (n=2, 33.3%)	MTX (n=4, 17.4%) AZA (n=2, 8.7%)	IFX (n=3, 13.6%) ADA (n=2, 9.1%) GLM (n=1, 4.5%)	1 (4.5)	0	0	0
Cranial neuropathy	5 (16.7)	P (n=4, 80%) O (n=3, 60%) C (n=1, 20%) A (n=1, 20%) D (n=1, 20%)	AZA (n=4, 17.4%) MTX (n=3, 13.1%)	IFX (n=3, 13.6%) ADA (n=1, 4.5%)	0	0	0	0
Spinal cord abnormalities	3 (10.0)	P (n=3, 100%) O (n=1, 33.3%) C (n=1, 33.3%) A (n=1, 33.3%)	MTX (n=1, 4.3%)	IFX (n=1, 4.5%) GLM (n=1, 4.8%)	0	0	0	0
Aseptic meningitis	3 (10.0)	P (n=2, 66.7%) O (n=1, 33.3%) C (n=1, 33.3%) A (n=1, 33.3%)	MTX (n=2, 8.7%)	IFX (n=2, 9.1%) ADA (n=1, 4.5%)	0	1 (4.5)	0	0
TOTAL (n= 30)	30 (100)	P (n=23, 76.7%) A (n=15, 50%) O (n=12, 40%) C (n=11,36.7%) D (n=5, 16.7%)	MTX (n=16, 69.6%) AZA (n=7, 30.4%)	IFX (n=10, 45.5%) ADA (n=5, 22.7%) GLM (n=3, 13.6%)	1 (4.5)	1 (4.5)	1 (4.5)	1 (4.5)

Abbreviations: A: Articular, ADA: Adalimumab, AZA: Azathioprine, C: Cutaneous, D: Digestive, GLM: Golimumab, IFX: Infliximab, MTX: Methotrexate, O: Ocular, P: Pulmonar*With MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system after rigorous exclusion of other causes and not meeting criteria for other neurosarcoidosis subtypes.

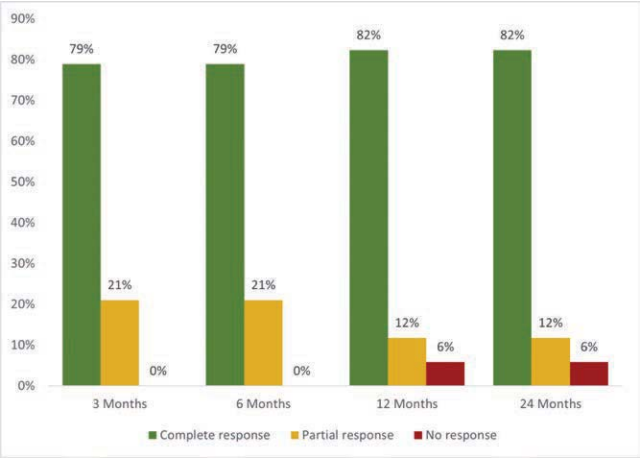

Figure 1. Neurological clinical response to biological therapy

observed in one patient on both IFX and ADA. No more severe adverse events were observed.

Conclusion: BT, especially monoclonal anti-TNFα, seems to be effective and safe in NS, regardless of subtype.

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POS1348

PATIENTS WITH VEXAS DIAGNOSED IN A DANISH TERTIARY RHEUMATOLOGY SETTING HAVE HIGHLY ELEVATED INFLAMMATORY MARKERS, MACROCYTIC ANEMIA, AND NEGATIVE AUTOIMMUNE BIOMARKERS.

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Background: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome was described in 2020 with overlapping features of rheumatology and hematology. VEXAS is an autoinflammatory condition caused by somatic mutations in the *UBA1* gene at methionine-41.

As patients present with highly variable clinical symptoms [1], their path in the clinical system is often complicated, and characterized by many strenuous examinations and biopsies. It is pivotal, that we familiarize with the VEXAS phenotype and advance identification of patients with VEXAS.

Objectives: We aimed to characterize patients diagnosed with VEXAS in a tertiary rheumatology referral center since December 2020 when the syndrome was described [2].

Methods: All patients were identified and diagnosed at the department of Rheumatology, Aarhus University Hospital (AUH), Denmark. Patients underwent testing for the *UBA1* somatic mutations using sanger sequencing at the department of Clinical Immunology, AUH. Sequencing analyzed for somatic variants in/at exon 3 (NM_003334.4: c.118-1G>C, c.121A>C/G, c.122T>C og c.167C>T). Clinical and biochemical data were retrieved from the hospital electronic patient chart. Continuous variables are presented as median with interquartile range (IQR) and categorical variables as percentages.

Results: A total of 11 male patients with clinical suspicion of VEXAS underwent sequencing. Five men were identified in the period December 2020 to December 2021 with *UBA1* somatic mutations. Median age at diagnosis was 84 (75-87). Symptoms debuted on average 22 months (IQR 20-40) before diagnosis. All patients had significantly elevated markers of inflammation: median CRP 297 (196-386), IL-2-receptor, and ferritin and presented with macrocytic anemia. None of the patients were positive for autoimmune biomarkers like ANA, ACPA, MPO-, or PR3-ANCA.

Conclusion: This is, to the best of our knowledge, the first report of Danish patients with the VEXAS syndrome. Patients are males with persistent inflammation, constitutional symptoms, and heterogeneous clinical presentations.

Common features for all patients in this study were highly elevated inflammatory markers, macrocytic anemia, and negative autoimmune biomarkers.

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Table 1. Clinical, biochemical characteristics at diagnosis and treatment of Danish VEXAS patients.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Total n(%) or median (IQR)
Clinical characteristics						
Age at diagnosis	73	89	77	84	85	84 (75-87)
Time from symptom onset till diagnosis (months)	18	21	47	30	22	22 (20-40)
UBA1 variant	c.122 T>C p.Met41Thr	c.122 T>C p.Met41Thr	c.122 T>C p.Met41Thr	c.121 A>C p.Met41Leu	c.118-1 G>C p.(splice)	
Macrocytic anemia	+	+	+	+	+	5 (100%)
CRP	+	+	+	+	+	5 (100%)
(max, mg/ml)	(335)	(436)	(220)	(172)	(297)	(297 (196-386))
Constitutional symptoms*	+	+	+	+	+	5 (100%)
Vasculitis	+	+	+	-	+	4 (80%)
Chondritis	-	-	+	-	+	2 (40%)
Ocular inflammation	-	-	+	-	-	1 (20%)
Arthritis	+	-	+	+	-	3 (60%)
Lung involvement	-	+	+	+	+	4 (80%)
Proteinuria	-	+	+	-	+	3 (60%)
Thrombosis	+	-	-	+	-	2 (40%)
BM vacuoles	-	+	+	NA	-	2/4 (50%)
Biochemical characteristics						
ANA	-	-	-	-	-	0 (0%)
ACPA	NA	-	-	-	NA	0 (0%)
PR3 or MPO-ANCA	-	-	-	-	-	0 (0%)

IQR: inter quartile range, BM: bone marrow, ANA: anti-nuclear antibodies, ACPA: anti-citrullinated protein antibody, PR3-ANCA: proteinase-3 anti-cytoplasmatic antibody, MPO: myeloperoxidase, NR: within normal range, NA: not available.*Constitutional symptoms (fever, night sweats, weight loss).

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POS1349 IMMUNOGLOBULIN G4-RELATED KIDNEY DISEASE'S PREDISPOSITION TO CHRONIC RENAL DYSFUNCTION, COMPLICATIONS OF MALIGNANCY, AND MORTALITY: A LONG-TERM NATIONWIDE MULTICENTER STUDY IN JAPAN

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Background: In immunoglobulin G4-related kidney disease (IgG4-RKD), persistent renal insufficiency may be observed despite the good initial response to glucocorticoids[1, 2]. However, its long-term prognosis in relation to renal function as well as malignancy and mortality has not been well clarified.

Objectives: To clarify the long-term renal prognosis, complications of malignancy, mortality, and factors related to those outcomes in IgG4-RKD.

Methods: We retrospectively reviewed the medical records of patients with IgG4-RKD diagnosed by the expert members of the IgG4-RKD working group in the Japanese Society of Nephrology. We investigated clinical, radiological, and histopathological features at baseline and course of renal function, complications of malignancy, and mortality during the long-term observation periods (median 71 months) in 75 patients. Using collected data, we calculated the crude incidence rates (IR) of chronic kidney disease (CKD) status, malignancy, and death. Cox regression analyses were performed to assess CKD-related factors. Additionally, we calculated the standardized incidence ratio (SIR) of malignancy and standardized mortality ratio (SMR) using national Japan statistics.

Results: Fifty-nine patients were male, and 16 were female (median age 70 years). At diagnosis, their median eGFR was 45.1 mL/min/1.73m^2 (interquartile range [IQR] 28.6-69.9). Seventy-two patients (96%) were treated with prednisolone at a median initial dose of 30 (IQR 30-39) mg/day, leading to a reasonable initial improvement of renal function. The IR of CKD was 30.2/100 person-years, and 66.7% (50/75) of the patients showed CKD at the last visit. Age- and sex-adjusted Cox regression analyses indicated that lower eGFR (per 10 mL/min/1.73m^2, hazard ratio [HR] 0.70, 95% confidence interval [CI] 0.61-0.80), pre-existing hypertension (HR 2.39, 95% CI 1.32-4.34), and wider areas with inflammation (>50% vs. <10%, HR 2.55, 95% CI 1.07-6.08) or fibrosis (>50% vs. <5%, HR 2.84, 95% CI 1.18-6.85) in the biopsied renal specimens at treatment initiation had a significant impact on the time to CKD. Eight patients (10.7%) died during follow-up due to malignancy, severe infection, cerebral hemorrhage, or myocardial infarction. The crude mortality rate was 1.76/100 person-years, and a SMR calculated according to national Japan statistics was 0.97 (95% CI 0.42-1.90). On the other hand, 15 patients were diagnosed as having malignancies during follow-up. The IR of malignancy was 3.71/100 person-years, and the SIR of malignancy was 1.80 (95% CI 1.03-2.93).

Conclusion: This study suggests that pre-treated renal insufficiency and extensive renal inflammatory and fibrotic lesions are related to CKD under glucocorticoid therapy in IgG4-RKD. Similarly with the whole IgG4-related disease, IgG4-RKD may have an increased incidence of malignancy but a mortality rate equivalent to the age- and sex-matched Japanese population.

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POS1350 UVEITIS DUE TO IMMUNE-MEDIATED INFLAMMATORY DISEASES TREATED WITH CERTOLIZUMAB PEGOL. MULTICENTER STUDY OF 80 PATIENTS.

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Table 1. main ocular parameters analyzed in 80 patients with uveitis due to IMID and treated with CZP.

	Baseline	1st week	1st month	3rd month	6th month	1st year
BCVA (mean±SD)	0.68±0.27	0.73±0.26*	0.79±0.26*	0.82±0.25*	0.85±0.24*	0.86±0.23*
Tyndall improvement, n (%) *Patients with Tyndall + at baseline (n=57)*	-	23 (40.3)	45 (78.9)	47 (82.4)	57 (100)	57 (100)
Vitritis improvement, n (%) *Patients with Vitritis at baseline (n=14)*	-	5 (35.7)	8 (57.1)	13 (92.8)	14 (100)	14 (100)
OCT (µm) (mean±SD)	297.5±48.1	297.1±45.5	286.5±39.8*	277.6±43.3*	271.5±38.6*	269.0±38.8*
Choroiditis, affected eyes, n (%)	3 (2.4)	3 (2.4)	2 (1.6)	2 (1.6)	1 (0.8)	1 (0.8)
Retinal vasculitis, affected eyes, n (%)	3 (2.4)	2 (1.6)	1 (0.8)	0 (0)	0 (0)	0 (0)

*p<0.01

Background: Adalimumab remains the only biologic approved by the EMA and FDA for the treatment of non-infectious uveitis [1-6]. The reports on efficacy of other anti-TNF drugs such as Certolizumab Pegol (CZP) are scarce.
Objectives: to determine the efficacy and safety of CZP in refractory uveitis secondary to Immune-mediated Inflammatory Diseases (IMIDs).
Methods: national multicenter study of 80 patients with uveitis due to IMID refractory to glucocorticoids and conventional immunosuppressants treated with CZP. Efficacy was assessed with the following ocular parameters: best corrected visual acuity (BCVA), anterior chamber cells, vitritis, macular thickness and presence of retinal vasculitis. The efficacy of CZP was compared between the baseline visit, 1st week, 1st and 6th month, and 1st year. Statistical analysis was performed with IBM SPSS Statistics v.23.
Results: we studied 80 patients/111 affected eyes (33 men/47 women) with a mean age of 41.6±11.7 years. The IMIDs included were: spondyloarthritis (n=43), Behçet's disease (10), psoriatic arthritis (8), Crohn's disease (4), sarcoidosis (2), JIA (1), reactive arthritis (1), rheumatoid arthritis (1), relapsing polychondritis (1), TINU (1), pars planitis (1), Birdshot (1) and idiopathic uveitis (6). Anterior was the most frequent uveitis pattern (n=61).
In 20 patients, besides the presence of refractory uveitis, desire of pregnancy was the reason for CZP initiation.
Prior to CZP, patients had received: methotrexate (n=38), sulfasalazine (28), azathioprine (14), cyclosporine (10), leflunomide (3), mycophenolate mofetil (4), and cyclophosphamide (1). Previous biologic therapy was administered in 52 patients (63%), with a median [IQR] of 2 [1-3] drugs per patient. The most used biologic was adalimumab (n=48), followed by infliximab (32), golimumab (15), tocilizumab (5), etanercept (7), rituximab (1), anakinra (1) and secukinumab (1). CZP was administered as monotherapy in 39 patients.
After 24 [12-36] months of follow-up, all parameters analyzed showed a rapid and maintained improvement (Table 1). A decrease in the mean number of uveitis flares was observed before and after CZP, (2.6±2.3 vs. 0.6±0.4, p<0.001). CZP was discontinued in 16 patients due to: ocular remission (n=3), insufficient ocular response (4) and incomplete response of extraocular manifestations (9). No serious adverse effects were found.
Conclusion: CZP seems to be effective and safe in the control of uveitis associated to different IMIDs.
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POS1351

CERTOLIZUMAB PEGOL VS ADALIMUMAB IN THE TREATMENT OF REFRACTORY CYSTOID MACULAR EDEMA DUE TO BEHÇET'S DISEASE. MULTICENTER STUDY.

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Background: Cystoid Macular Edema (CME) is the leading cause of blindness in non-infectious uveitis. Behçet's disease (BD) is one of the diseases most frequently associated with CME [1-4].
Objectives: to compare the efficacy and safety of Certolizumab (CZP) and Adalimumab (ADA) in CME due to BD refractory to conventional therapy.
Methods: multicenter study of patients with CME secondary to BD refractory to glucocorticoids (GC) and at least 1 conventional immunosuppressant. All patients had CME (OCT>300µ) at baseline. Efficacy was assessed with the following ocular parameters: macular thickness (µm), visual acuity (BCVA) and GC-sparing effect. The efficacy of CZP vs. ADA was compared between the baseline visit, 1st and 6th month, and 1st and 2nd year. Statistical analysis was performed with IBM SPSS Statistics v.23.
Results: We studied 21 patients/38 affected eyes were studied. 10 patients were treated with CZP (200 mg c/2 weeks) and 11 with ADA (loading dose of 80 mg and subsequently 40 mg c/2 weeks).
No statistically significant baseline differences were observed in both groups (CZP vs. ADA) in sex (♂/♀; 3/7 vs 5/6; p=0.65) and mean age (36.1±8.0 vs 42.2±8.6; p=0.10). However, CZP group was more severe with a longer time between EB diagnosis and biologic initiation (91.6±71.4 vs 34.4±21.3 months, p=0.02), and a greater median [IQR] number of previous biologic drugs (2 [0.75-3] vs 0 [0-0]). In CZP group, 8 patients were previously treated with ADA.
Combined therapy with conventional DMARDs was used with ADA in 81.8% vs. 18.2% of CZP patients.
Regarding the efficacy outcomes analyzed, a rapid and maintained improvement in macular thickness, measured by OCT, was observed after 2 years of follow-up in both groups with no statistically significant differences between them (Table 1). Improvement in visual acuity and a GC-sparing effect was also observed (Table 1). No serious adverse events were observed in either group.
Conclusion: Our study suggests that both CZP and ADA are effective in the treatment of CME due to BD refractory to conventional treatment. CZP was equally effective despite most patients were refractory to ADA.
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Table 1. main ocular parameters compared in the CZP-treated group and in the ADA-treated group.

	CZP (n=10)	ADA (n=11)	P
Baseline			
OCT (µm, mean±SD)	380.7±96.4	416.9±171.1	0.56
BCVA (mean±SD)	0.72±0.30	0.57±0.20	0.21
Prednisone (mg/dl, mean±SD)	13.1±11.4	34.1±18.9	0.07
1st month			
OCT (µm, mean±SD)	333.7±60.4	302±44.2	0.19
BCVA (mean±SD)	0.80±0.27	0.72±0.18	0.45
Prednisone (mg/dl, mean±SD)	8.1±5.5	112.1±6.4	0.31
6th month			
OCT (µm, mean±SD)	284.4±45.5	272.8±38.9	0.53
BCVA (mean±SD)	0.82±0.23	0.86±0.16	0.65
Prednisone (mg/dl, mean±SD)	6.8±6.6	6.1±2.8	0.92
1st year			
OCT (µm, mean±SD)	269.0±46.8	260.9±39.5	0.67
BCVA (mean±SD)	0.82±0.23	0.89±0.17	0.48
Prednisone (mg/dl, mean±SD)	6.2±3.0	5.8±2.1	0.87
2nd year			
OCT (µm, mean±SD)	289.4±49.3	248.0±42.0	0.16
BCVA (mean±SD)	0.87±0.20	0.87±0.17	1.0
Prednisone (mg/dl, mean±SD)	3.7±1.2	3.1±2.3	0.90

Other orphan diseases

POS1352 A PROSPECTIVE, ONE-YEAR FOLLOW-UP STUDY OF PATIENTS NEWLY DIAGNOSED WITH NEUROSARCOIDOSIS

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Background: Sarcoidosis is a granulomatous inflammation of unknown etiology. Neurosarcoidosis (NS) occurs in 5–10% of patients with sarcoidosis and is a severe manifestation of sarcoidosis. The clinical presentation is heterogeneous and depends on the inflammation within the nervous system.
Objectives: This study aimed to describe NS patients and their clinical course of treatment. Our outcomes were changes in 1) enhancing lesions on MRI of the central nervous system (CNS), 2) cerebrospinal fluid (CSF), 3) disability and dependency in daily activities assessed by the modified Rankin Scale (mRS), 4) cognitive function assessed by the Symbol Digit Modality Test (SDMT), 5) quality of life assessed by Short-Form 36 Health Survey (SF-36), 6) fatigue assessed by Fatigue Assessment Scale (FAS), and 7) depression measured by Beck Depression Inventory-II (BDI-II).
Methods: In this observational cohort study with a one-year follow-up, we consecutively recruited NS patients (N=20), not including patients with polyneuropathy, from the Departments of neurology and rheumatology at Odense University Hospital between January 2016 and August 2020. Patients were examined clinically, with questionnaires and MRI at baseline (V) and after three months (V3), six months (V6), and 12 months (V12). Cerebrospinal fluid (CSF) was examined at baseline, V6, and V12.
Results: The median age was 51.6 years, and the median duration of sarcoidosis symptoms was 8 months before inclusion.
At baseline, 60% of NS patients had headache, followed by vertigo (55%) and tinnitus (50%). Objective neurological findings were peripheral sensory signs (50%), peripheral motor signs (40%), and cranial nerve involvement (30%). At V12, there were significant improvements in vertigo (p=0.03), cranial nerve involvement (p=0.03), and joint symptoms (p=0.03).
At baseline, 60% of patients had abnormal findings on MRI of CNS. During the study, the number of contrast-enhancing lesions on MRI decreased significantly (p<0.0001).
The mRS declined significantly from mean (SD) 3.0 (0.8) at baseline to 1.8 (1.1) at V12 (p<0.0001), and 75% of patients experienced clinically important improvement (mRS≥1).
The SDMT score improved significantly from mean (SD) 38 (9) at baseline to 45 (12) at V12 (p<0.0001).
The SF-36 Physical (PCS) and Mental Component Summary scores (MCS) improved significantly from baseline: PCS mean (SD) 35 (11) to 41 (12) at V12 (p=0.003) and MCS mean (SD) 41(9) to 48 (10) at V12 (p=0.03).
The proportions of patients with substantial fatigue (75%) and high depression score (35%) were unchanged.
Conclusion: One year of immunosuppression in NS patients improved several outcomes, and 75% of patients experienced clinically important improvement.
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POS1353 COMPOSITION AND ASSOCIATIONS OF THE GUT MICROBIOTA IN BECHET'S DISEASE WITH PERIPHERAL LYMPHOCYTE SUBSETS AND CYTOKINES

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Background: Bechet's disease (BD) is a chronic multisystemic vasculitis with genetic and abnormal immune response. Growing evidences suggests gut microbiota compositional alteration may have an association with immune dysfunction in patients with BD.
Objectives: This study aims to investigate the gut microbiota between BD and healthy controls (HCs) and analyse relevancy between bacterial and peripheral lymphocyte subsets and cytokines.
Methods: Fecal samples obtained from 22 BD patients and 22 normal-age and gender-matched HCs in this study. The gut microbiota were assessed with 16s rRNA sequencing and the flow cytometry was used to dectect peripheral lymphocyte subsets. C-reaction protein (CRP), Erythrocyte sedimentation rate (ESR), complement C3 and C4 were also assigned for disease activity measure. The edgeR package was used for differential abundance analysis. Difference of alpha diversity indices, bacterial abundances, and the F/B ratio were carried out using the Wilcoxon rank-sum test (R v.4.0.1). The differential abundance of flora and CRP, ESR, C3 and C4 between BD patients and HCs was assessed by pearson's correlation analysis.
Results: As for alpha diversity, the Shannon ($p < 0.05$) and Simpsonance analysis. Difference of alpha diversity indices, bacterial abundances, and the F/B ratio were carried out using the Wilcoxon rank-sum test (R v.4.0.1). The differential abundamicrobial community structures between BD and HCs ($R = 0.053$, $p = 0.051$; Figure 1B). The gut microbiota compositions of BD differed form those of HCs (Figure 1C). Four species of flora distinctly difference were found in BD ($p < 0.05$; Figure 1D). There was significant positive correlations between Tregs and Verrucomicrobiota ($p < 0.05$), and Proteobacteria ($p < 0.05$), Th1 and Proteobacteria ($p < 0.05$), ESR and Verrucomicrobiota ($p < 0.01$), but negatives correlation between TNF-α and Desulfobactbiota ($p < 0.05$; Figure 1E).
Conclusion: Pattients with CTD had disbiosis of gut microbiota charaterized by impared diversity and abnomal composition, which was closely correlated with peripheral lymphocyte subsets and disease activity measures.
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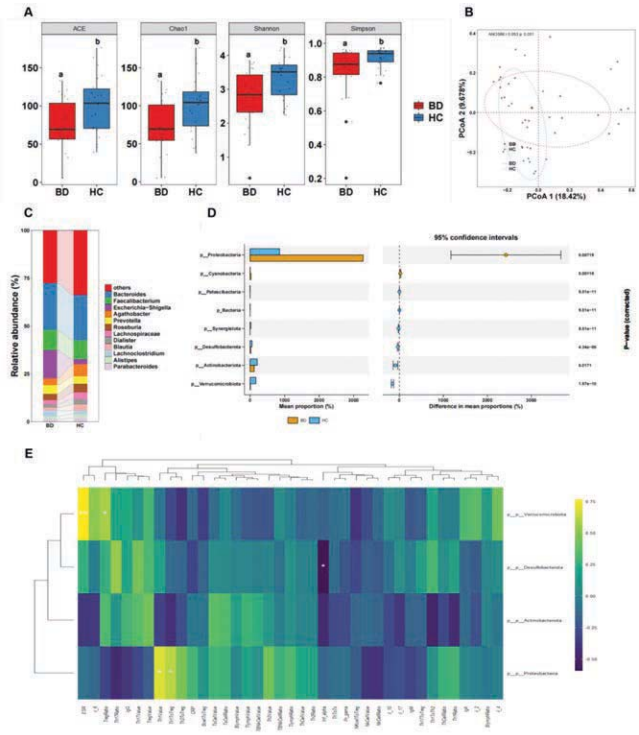

Figure 1: Feature of gut microbiota in BD patients and HCs. (A) Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson), Median estimates compared across cohorts. (B) Principal component analysis (PCoA) plot generated from the Bray-Curtis distances. (C) Microbiota composition based on relative abundance at the genera levels. (D) Panel demonstrated the average relative abundance of different phylum in BD and HCs. (E) Correlation analysis of these differential phyla and lymphocyte subsets and clinical indicators between any two groups using Spearman's correlation analysis.The correlation effect is indicated by a color gradient from green(positive correlation) to purple(negative correlation). *p<0.05. **p<0.01. ***p<0.001.

POS1354

ANALYSIS OF FACTORS ASSOCIATED WITH GOOD THERAPEUTIC RESPONSE TO IMMUNOSUPPRESSIVE DRUGS IN PATIENTS WITH NON-INFECTIOUS UVEITIS: A SURVIVAL ANALYSIS

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Background: Non-infectious uveitides (NIUs) encompass a varied group of inflammatory diseases affecting the uvea and adjacent tissues, with evidence suggesting an immune-mediated cause. A correct management of these conditions is essential to prevent substantial and sometimes permanent visual loss and the development of ocular complications. Although immunosuppressive drugs (ISDs) have shown effectiveness in achieving a sustained control of the inflammatory process, not all patients achieve a satisfactory response.
Objectives: To identify factors affecting the response rate to ISDs in subjects with NIUs.
Methods: Longitudinal retrospective study, with patients collected from the Hospital Clinico San Carlos Uveitis Clinic, included from 1991 until December 2018, and followed-up until December 2019. Patients entered the study at ISD prescription and were followed-up until a) the achievement of a good therapeutic response (GTR), b) ISD treatment change (withdrawal of the prescribed ISD and/or addition of a new ISD), c) 12 months of follow-up, or d) loss of follow-up or end of the study (December 31th, 2019). GTR was defined as the complete resolution of the eye inflammatory manifestations and oral corticosteroid ≤10 mg of prednisone equivalent a day. Furthermore, this situation had to be maintained in at least two consecutive visits spanned at least 28 days. Kaplan-Meier (KM) curves were set to account for GTR. Associated demographic, clinical and treatment-related factors were analyzed using bivariate and multivariate Cox robust regression models. Different models were compared using the Akaike Information Criteria, to select the fittest model to the data. Proportional hazard assumption was tested using Schoenfeld residuals and the scaled Schoenfeld residuals. In case a variable or certain category of a categorical variable were non-proportional, they were included in the Cox models with a time-varying effect, in case the interaction with time was significant ($p<0.05$).
Results: 73 patients (100 episodes of ISD prescription) were analyzed. In 44 episodes, a GTR was achieved (incidence rate 102.0 [95% Confidence Interval (CI): 75.9 to 137.1] per 100 patient-years). Figure 1 shows the KM curve for GTR. In the bivariate analysis, several variables showed a significant association with GTR, including gender, diagnosis of Behçet Disease, prescription of Cyclosporine A (CYA), number of previously prescribed ISDs, previous use of the same ISD, previous discontinuation of a ISD due to inefficacy, higher systemic corticosteroid use in the previous year before ISD prescription, presence of macular edema (ME), and longer intermediate and posterior activity before ISD prescription. Table 1 shows the results of the multivariate analysis. Prescription of CYA was associated with a higher hazard of GTR, compared with the use of other ISDs (methotrexate, azathioprine or biologic drugs). In addition, the higher dosage of oral corticosteroids used in the previous year before ISD prescription, the lower the hazard of achieving a GTR. Finally, presence of ME at prescription was associated with lower hazard of GTR, although this risk diminished with time.

Table 1. Multivariate Cox robust regression to analyze variables independently associated with the achievement of good therapeutic response.

Variable	HR (95% CI)	p value	Schoenfel test p value
CYA prescription	2.04 (1.14-3.67)	0.017	0.56
Number of previous ISDs			
0	Reference	-	-
1	12.61 (2.07-76.73)	$5.9x10^{-3}$	0.001
≥2	3.54 (1.55-8.05)	$2.6x10^{-3}$	0.56
1 previous ISD X Time	0.01 (0.001-1.00)	0.005	
Higher oral corticosteroids dosage (mg) in the previous year	0.98 (0.97-0.99)	0.013	0.83
Macular edema	0.14 (0.04-0.45)	$9.3x10^{-3}$	0.001
Macular edema X Time	14.20 (1.55-103.10)	0.019	

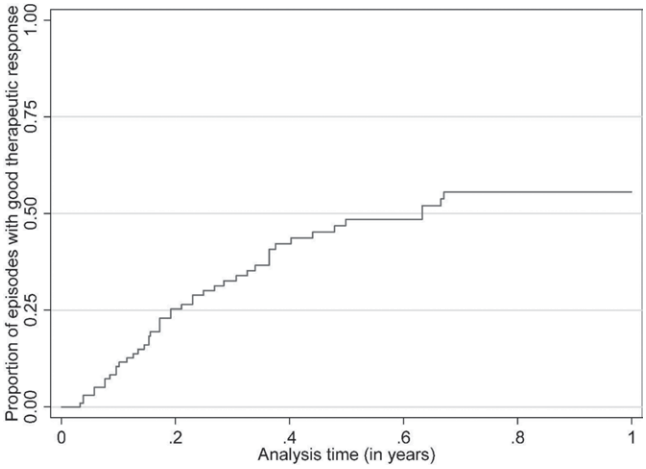

Figure 1. Kaplan-Meier failure curves representing good therapeutic response after immunosuppressive drug prescription for non-infectious uveitis.

Conclusion: We have identified several variables associated with therapeutic response to ISDs in NIUs patients.
Disclosure of Interests: None declared
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POS1355

TO COMBINE OR NOT TO COMBINE: INFLUENCE OF IMMUNOSUPPRESSIVE DRUG COMBINATION IN THE INDUCTION OF THERAPEUTIC RESPONSE IN NON-INFECTIOUS UVEITIS

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Background: Non-infectious uveitides (NIUs) include a heterogeneous group of sight-threatening and incapacitating conditions. Their correct management sometimes requires the use of immunosuppressive drugs (ISDs), prescribed in monotherapy or in combination. Several observational studies showed that the use of ISDs in combination could be more effective than their use in monotherapy. However, a direct comparison between these two treatment strategies has not been carried out yet.
Objectives: To analyze the effect of ISDs combination therapy (CT) on the response rate in patients with NIUs.
Methods: Patients attending a Uveitis Outpatient Clinic from a tertiary care center in Madrid, Spain, and prescribed with ISDs from 1991 to 2018 were included. Patients were assigned as controls or cases based on whether they were prescribed with ISDs in monotherapy (MT) or CT. ISD treatment changes during the observation period were also considered. The primary outcome was good therapeutic response (GTR), defined as the complete resolution of the eye inflammatory manifestations and oral corticosteroid dosage ≤10 mg of prednisone equivalent a day. Furthermore, this situation had to be maintained in at least two consecutive visits spanned at least 28 days. Several propensity score based and non-based weighting techniques for data balancing, followed by Cox regressions, were performed to estimate the effect of CT on the response rate. Random forest (RF) models and clinical appraisal were used to select the variables to be balanced.
Results: 100 episodes of ISD prescription belonging to 73 patients were included in this analysis. In 32 episodes, patients were prescribed with CT (in 3 episodes CT was the initial therapeutic strategy; in 29, combination was the result to adding a second or third ISD). The most frequent drug used in MT was cyclosporine A (CYA; n=39), and the most frequent CT was synthetic + biological ISD (n=21). After RF, the number of previously used ISDs, the prescription of CYA, the dosage of oral corticosteroids at prescription, a previous ISD withdrawal due to inefficacy, and duration of disease were selected for balancing. In addition, after clinical appraisal, uveitis diagnosis, prescription with azathioprine, prescription

with methotrexate, and eye activity features at prescription (presence of cells in anterior chamber, vitreous haze, macular edema, active chorioretinal lesions) were also balanced. The Energy balancing method showed the best balance for GTR. After Cox-regression, CT prescription did not show a statistically significant effect in the hazard of response (p=0.43; Table 1).

Table 1. Cox models showing the effect of combination therapy in the hazard of good therapeutic response after balancing covariates using the Energy method.

Variable	HR (95% CI)	p value	Schoenfel test p value
Combination Therapy	0.66 (0.24-1.83)	0.43	0.82
Cyclosporine A prescription	3.36 (1.22-9.27)	0.019	0.96
Methotrexate Prescription	2.20 (0.72-6.71)	0.16	0.95
Presence of cell in anterior chamber	1.75 (0.83-3.72)	0.14	0.89

Conclusion: The use of CT in our study was not associated with a better therapeutic response in NIU patients compared with the prescription of MT. Considering that most CT episodes were the result of the addition of a new ISD in a patient already treated and still active, the effectiveness of CT as the initial therapeutic strategy remains unanswered.

Disclosure of Interests: None declared

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POS1356 TREATMENT OF IMMUNE CHECKPOINT INHIBITOR-INDUCED INFLAMMATORY ARTHRITIS AND POLYMYALGIA RHEUMATICA

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Background: Therapy with immune check point inhibitors (ICIs) has revolutionized cancer treatment during the last years. Despite their high efficacy, ICIs are associated to a new spectrum of adverse events, the immune-related adverse events (irAEs). Inflammatory arthritis and polymyalgia rheumatica (PMR) are two of the most common rheumatic irAEs. The optimal management of irAEs remains unclear. Treatment guidelines largely support the use of glucocorticoids (GCs) as first line therapy [1]. Preclinical data raise concerns regarding the potential risk of impaired antitumoral effect with use of GCs. The high efficacy and potential synergistic effect (according to recent findings) [2] of targeted immunomodulation, such as interleukin 6 (IL-6) blockade, could support a paradigm shift, where targeted treatments are considered earlier in the treatment sequence.

Objectives: To assess how frequently a disease modifying anti-rheumatic drug (DMARD) treatment in patients with ICI induced arthritis and/or PMR, after inadequate response to GCs, is initiated and to assess its effectiveness.

Methods: We retrospectively identified patients who were diagnosed with inflammatory arthritis and/or PMR at the rheumatology department at Karolinska University Hospital, after referral from the oncology department due to suspicion of a rheumatic irAE, between Jan 2020 and Dec 2021. Treatment response was defined as sustained low disease activity or remission according to the rheumatologist evaluation at 6 months (+/- 1 month) after initiation of DMARD.

Results: A total of 20 patients were identified, who were diagnosed with arthritis (N=11), PMR (N=6) or both (N=3). The median (IQR) age was 70 (46-76) years; 50% of patients were females. The type of cancer was urogenital (N=8), melanoma (N=6), lung cancer (N=2), and other (N=4). 14 patients received a PD-1 inhibitor (9 nivolumab, 4 pembrolizumab, 1 cemiplimab), 3 received a PDL-1 inhibitor (2 atezolizumab, 1 avelumab), 2 received a combination of nivolumab and the CTLA-4 inhibitor ipilimumab and one patient combination of nivolumab and pembrolizumab. The median time from start of ICI treatment to symptom debut was 2 (1.25-3.75) months.

83% of patients with PMR and/or arthritis responded well to GCs without the need for treatment escalation. On the contrary,

11 out of 14 patients (79%) with inflammatory arthritis (with or without PMR) responded inadequately to GC treatment, despite receiving moderate-high doses (median 20mg/day Prednisolone or equivalent), or flared when the dose was reduced below 10mg/day. A conventional synthetic DMARD was initiated in 7 patients (methotrexate N=6, hydroxychloroquine N=1), with a response rate of 71%. 3 patients received a biologic DMARD as first-line DMARD, either because of contraindication for methotrexate and/or high disease activity, and 2 patients after methotrexate failure. All 5 patients tocilizumab, with a response rate of 100%. Subsequently 1 of these patients discontinued tocilizumab due to suspected side effects, and started with a TNF inhibitor. After initiation of tocilizumab all patients were able to reduce the dose of GCs to less than 5mg/day.

Conclusion: The majority of patients developing ICI-induced arthritis are refractory to GCs and need a DMARD treatment, although selection bias cannot be formally excluded, since the most severe forms of arthritis might be referred to the rheumatology department. csDMARDs are effective in a significant proportion of patients. Tocilizumab is highly effective and well tolerated in ICI-induced arthritis. ICI-induced PMR seems to respond adequately to GCs.

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POS1357 THE 10-YEAR OUTCOME OF PATIENTS WITH BEHCET'S SYNDROME: A SINGLE-CENTER EXPERIENCE

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Background: Behcet's syndrome (BS) is a vasculitis characterized by recurrent oral and genital ulcers, as well as ocular, cutaneous, vascular, gastrointestinal, musculoskeletal, and central nervous system manifestations.

Objectives: The study aimed to evaluate the 10-year outcome of patients with BS.

Methods: A cohort of 682 patients diagnosed with BS between January 2007 and December 2009 in the rheumatology outpatient clinic of Gulhane Training and Research Hospital were re-evaluated in November 2021. The data regarding the clinical course of 84 patients (84/682) were obtained from patients' files and detailed telephone interviews.

Results: The study included 84 patients (63 male, 21 female) with a mean age of 47.1±10.6 years. The mean disease duration was 17.6±5.7 years. At the time of the diagnosis, the mean age of the patients was 29.5±9.4 years. Oral ulcer (100%), papulopustular lesions (82.1%), genital ulcer (77.4%), and erythema nodosum (59.5%) were the most frequent manifestations at the time of diagnosis. Ocular (46.4%), musculoskeletal (35.7%), vascular (19%), gastrointestinal (3.6%), and neurological (1.2%) manifestations were seen in decreasing frequency. The most frequent ocular disease was posterior uveitis, whereas superficial thrombophlebitis and deep venous thrombosis were the most prevalent forms of vascular involvement. One patient had transverse myelitis as neurological involvement. Colchicine (88.1%) and corticosteroids (57.1%) were the most preferred drugs for the initial treatment. Fifty-one (60.7%) patients received at least one immunosuppressive agent. After 10-year, there was a statistically significant decrease in all manifestations of BS (Table 1). Nevertheless, 9 (10.7%) patients (8 male, 1 female) had new clinical findings. Five patients had (5.9%) mucocutaneous, 2 (2.4 %) arthritis and 2 (2.4%) vascular lesions as new clinical manifestations. The mean age of the patients with newly onset clinical findings was 48±8.9 years. There was no statistically significant difference between patients with and without new clinical findings with respect to age (p=0.79). The new onset mucocutaneous manifestations were genital ulcer and erythema nodosum. Besides, new onset vascular lesions were superficial and deep venous thrombosis of the lower extremities. The mean age of the patients who developed venous thrombosis at the time of the assessment was 37.0±7.07 years. Vascular involvement was detected more frequently in younger patients

Table 1. Clinical manifestations of Behcet's syndrome

		Initial	After 10 years		p
			No	Yes	
Oral ulceration, n (%)	No	0	0	0	<0.001*
	Yes	84 (100)	42 (50)	42 (50)	
Genital ulceration, n (%)	No	19 (22.7)	16 (84.2)	3 (15.8)	<0.001**
	Yes	65 (77.4)	54 (83.1)	11 (16.9)	
Erythema nodosum and Papulopustular lesions, n (%)	No	6 (7.1)	4 (66.7)	2 (33.3)	<0.001**
	Yes	78 (92.9)	44 (56.4)	34 (43.6)	
Arthritis, n (%)	No	54 (64.3)	52 (96.3)	2 (3.7)	<0.001**
	Yes	30 (35.7)	21 (70)	9 (30)	
Vascular involvement, n (%)	No	68 (81)	66 (97.1)	2 (2.9)	0.013**
	Yes	16 (19)	12 (75)	4 (25)	
Gastrointestinal involvement, n (%)	No	81 (96.4)	81 (100)	0	<0.001*
	Yes	3 (3.6)	3 (100)	0	
Ocular involvement, n (%)	No	45 (53.6)	45 (100)	0	<0.001**
	Yes	39 (46.4)	29 (74.4)	10 (25.6)	
Neurological involvement, n (%)	No	83 (98.8)	83 (100)	0	<0.001*
	Yes	1 (1.2)	1 (100)	0	

*McNemar-Bowker Test, **McNemar Test

(p=0.03). However, ocular involvement is a frequent symptom after mucocutaneous involvement at the beginning, none of the patients had new eye involvement at the end of the follow-up. Colchicine, corticosteroid, and azathioprine were associated with the highest drug survival. Twenty-one (41.1%) patients of who were administered immunosuppressive agents as initial therapy were still using immunosuppressives 10 year later. The most frequently prescribed immunosuppressives were azathioprine and cyclosporine during the follow-up.

Conclusion: The frequency of newly onset clinical manifestations decreases with age in BS, especially after age 40. Besides, especially male Behcet's patients should be followed-up regularly for complications that may develop regardless of age.

Disclosure of Interests: None declared

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POS1358 CLINICAL PRESENTATION AND MANAGEMENT OF IDIOPATHIC GRANULOMATOUS MASTITIS IN A MIDDLE EASTERN POPULATION

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Background: Idiopathic Granulomatous mastitis (IGM) is a rare inflammatory disease of the breast with poorly understood aetiology or risk factors. IGM has a predilection towards women of child-bearing age with a history of breastfeeding, particularly among Hispanic and Asian ethnicities. However, the true prevalence is unknown with IGM being poorly studied in Middle Eastern Arab and Levantine women who have different genetic, epidemiological, and environmental characteristics.

Objectives: To study the clinical features of Middle Eastern women diagnosed with biopsy-confirmed IGM.

Methods: A retrospective observational study of patients with a biopsy-confirmed diagnosis of IGM, referred to two different private outpatient rheumatology clinics in Amman- Jordan between 2016-2021. The Patients' characteristics, clinical presentation, treatment, and outcomes were recorded

Results: A total of 25 patients were identified in this study. The mean age was 34.9 ± 5.2 years. All females presented with a breast nodule and tenderness, while only 16% reported associated skin changes in the breast and 12% reported galactorrhoea. Bilateral breast involvement occurred in only 4 patients (16%) while 21 patients had unilateral breast involvement. Systematic manifestations including myalgia/arthralgia, skin changes, fever, and axillary lymphadenopathy were reported by 44%, 16%, 20%, and 16% of patients, respectively.

Notably, all enrolled females were married at the time of presentation and 3 of them were pregnant or postpartum during the onset of symptoms. The majority of patients (n= 21, 84%) had a prolonged period of breastfeeding (> 6 months). Moreover, 80% of patients had ≥3 pregnancies with 60% having their youngest child aged 3-5 years.

20 patients (80%) had a complete resolution of symptoms, and 20% (n=6) were lost to follow-up. Among patients who completed follow-up, treatment duration lasted for ≥ 1 year in 36% (n=9) of patients, whereas 11 patients had a complete resolution in less than a year. Azathioprine, methotrexate, antibiotics, and steroids were used in the treatment of 20%,36%, 60%, and 68%, respectively. Of note, only 1 patient underwent surgical intervention during treatment.

Conclusion: Many theories had suggested different aetiology for IGM but, in our cohort, it appears that being multiparous and prolonged breastfeeding carry higher risks of developing granulomatous mastitis. Although the aetiology is unclear, early diagnosis and the introduction of treatment using steroid therapy and immunosuppression can improve prognosis and prevent unnecessary surgery. Most of our patients that were treated with corticosteroid, Azathioprine, and Methotrexate had a complete resolution of symptoms after one year of therapy.

Disclosure of Interests: None declared

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POS1359 TRANSIENT ELASTOGRAPHY (FIBROSCAN) AS A NON-INVASIVE METHOD FOR DETECTING AMYLOID DEPOSITION IN TRANSPLANTED KIDNEYS IN PATIENTS WITH AA AMYLOIDOSIS

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Background: Amyloidosis is characterized by accumulation of insoluble fibrils composed of different monomers in extracellular spaces of different organs, and demonstration of deposits by non-invasive methods is important especially for organs difficult to sample. Transient elastography (Fibroscan) is a diagnostic method of measuring liver stiffness (LS) being used in chronic liver diseases.

Objectives: We herein aimed to search potential of fibroscan detecting kidney stiffness (KS) associated with amyloid deposition in patients with AA who received kidney transplants.

Methods: Renal transplant recipients (RTR) because of AA amyloidosis-related kidney failure (amyloidosis group; AG) and RTR due to other underlying diseases (control group; CG) enrolled into this study. KS and LS were measured by the same physician blinded to diagnosis. The stiffness results were expressed in kilopascals (kPa). Local ethics committee approval and patient consents were obtained.

Results: Nineteen AG and 16 CG patients included into the study. Patient age (p=0.4), gender (p=1), body mass index (BMI) (p=0.4), donor type (p=0.2), donor age (p=0.3), frequency of rejection history (p=0.4) and graft loss (p=0.2) did not show significant difference between two groups. Frequency of diabetes mellitus (DM) (p=0.01), median creatinine (p=0.015) and proteinuria (p<0.001) were higher in AG group than CG. Although median KS was higher in CG group (19.8 [IQR:34] vs 15.8 [IQR:16]), the difference was not significant (p=0.5). Baseline clinical and laboratory features were similar in AG patients with recurrent-amyloidosis (n=6) and non-recurrent AG patients (n=13). Median KS score was higher in recurrent compared to non-recurrent AG patients (p< 0.001). However median LS did not differ between two groups (p=0.4). In multivariate analysis only KS was associated with renal recurrence of AA (p=0.031; OR=1.18, 95% CI 1.015-1.362). In ROC analysis, a cut-off value of 24.55 kPa provided 83.3% sensitivity and 92.3% specificity (LR=10.8, AUC=0.936, p=0.003). Median KS was higher in patients with a history of rejection both among the patients with AG and CG, but the difference was not significant. Additionally, LS scores were similar between two groups.

In FMF-associated AA, median KS was higher in patients with one MEFV variant compared to those with two variants and tended to be higher in other MEFV variants compared to M694V homozygotes (p=0.027 and p=0.08, respectively). There was no correlation between the patient age, disease duration, duration of renal transplantation, donor age, BMI, LS, creatinine, CRP, proteinuria, and KS both in patients with AG and CG.

Table 1. Comparison of clinical and laboratory features between patients had amyloidosis recurrence and not

Variables	Total	Recurrence -	Recurrence +	p value
Age (years)*	48 (22)	47 (17)	50 (27)	1
Gender, male ‡	13 (68.4)	9 (69.2)	4 (66.7)	1
Duration of amyloidosis (months)*	206 (89)	220 (99)	163 (203)	0.08
Diagnosis age of amyloidosis (years)*	28 (17)	27.5 (17)	28 (20)	1
Duration of renal transplantation (months)*	145 (137)	144 (110)	123 (50)	0.7
Kidney stiffness (kPa)*	15.8 (15.8)	10.9 (7.7)	29.3 (18.9)	***<0.001***
Liver stiffness (kPa)*	5.45 (2.8)	5.4 (2.7)	5.9 (8.9)	0.4
Rejection ‡ (n, %)	3 (15.8)	2 (15.4)	1 (16.7)	1
Creatinine (mg/dL)*	1.4 (0.6)	1.4 (0.7)	1.7 (0.5)	0.24
CRP (mg/L)*	2.7 (4.4)	1.3 (4.1)	3.5 (13.9)	0.3
Proteinuria ‡	3 (15.8)	1 (7.7)	2 (33.3)	0.2
Proteinuria (g/day)*	0.4 (1.2)			0.4

*median; IQR ‡ n, %

Conclusion: Median KS scores were similar between AG and CG groups; however it was higher in AG patients with recurrent kidney amyloidosis than those without recurrent disease, which may support using the fibroscan method as a useful screening method for establishing AA recurrence. Additionally, higher KS scores in patients with one MEFV variant compared to those with two variants need further studies to be able to identify other yet unidentified amyloidogenic factors.

Disclosure of Interests: None declared

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POS1360

TRANSIENT ELASTOGRAPHY (FIBROSCAN); AS A NEW NON-INVASIVE DIAGNOSTIC METHOD FOR DETECTING HEPATIC INVOLVEMENT OF AMYLOIDOSIS

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Background: Demonstration of deposits by non-invasive methods is important especially for organs difficult to sample in amyloidosis. Transient elastography (fibroscan) is a diagnostic method being used to measure liver stiffness (LS) in different chronic liver diseases.

Objectives: We herein aimed to test the place of fibroscan method for detecting increased LS associated with amyloid deposition in patients (pts) with amyloidosis.

Methods: Six categories of pts enrolled into this cross-sectional study; AA amyloidosis (AA-a), AL amyloidosis (AL-a), Familial Mediterranean Fever (FMF) pts without amyloidosis, cirrhotic chronic liver disease, non-cirrhotic chronic hepatitis B infection (CHB) and healthy controls (HC). LS assessment by fibroscan were categorized as normal for kPa<7, significant stiffness for kPa≥7, advanced stiffness for kPa≥9.5 and kPa≥F4 stiffness. FIB-4 and APRI scores were calculated for each patient when they indicated chronic liver disease. Pts with known chronic liver disease and viral hepatitis excluded from amyloidosis and FMF groups.

Results: A total of 165 pts (AA-a, n=65; AL-a, n=15; FMF, n=20; cirrhotic pts, n=16; CHB, n=22; HC, n=27) constituted the study group. Average age was higher in the AL-a group compared to others. Median LS was highest in cirrhotic pts, and it was also higher in AA-a and AL-a pts compared to FMF and HC. Median LS was numerically higher in AL-a compared to AA-a, but it did not reach statistical significance. Median LS was also higher in FMF pts compared to HC. FIB-4 and APRI scores were lower compared to cirrhotic patients in AA-a and AL-a. ALP levels were higher in AA-a and AL-a groups compared to FMF, CHB and HC. FIB-4 and APRI scores, ALP and GGT levels were correlated with LS both in AA-a (r=0.534***,r=0.485***,r=0.437***, r=0.506***) and, AL-a (r=0.536*, 0.579*, r=0.645*, r=0.752**) and FMF-AA (r=0.584***, r=0.566***,r=0.322*, r=0.306*; *p<0.001, **p<0.01, *p<0.5) groups. Higher patient age, age at diagnosis of amylodosis, FIB-4 and LS scores, ALP levels, non-FMF causes of AA were associated with hepatic AA amyloid involvement in biopsy-proven pts. A cut-off value 12.05 kPa of LS provided 100% sensitivity and 85.5% specificity (LR=6.9, AUC=0.901, 95% CI 0.81-0.99) for pts with AA-a.

Conclusion: In our single center cohort, we showed a higher median LS by fibroscan in both AL-a and AA-a pts compared to CHB, FMF and HC. It was thought to be that fibroscan may be useful in detecting hepatic amyloid involvement.

Disclosure of Interests: None declared

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POS1361

THE CANADIAN RESEARCH GROUP OF RHEUMATOLOGY IN IMMUNO-ONCOLOGY (CANRIO): A NATIONWIDE MULTI-CENTER PROSPECTIVE COHORT

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Background: Immune Checkpoint Inhibitors (ICI) have altered the landscape of cancer therapy. However, toxicities are common and up to 80% of patients will develop immune-related adverse events (irAE), including rheumatic irAEs (Rh-irAE), which can often limit their cancer treatment. Our knowledge of clinical manifestations and optimal management of patients with Rh-irAE continues to evolve as these agents are being used to treat a wider variety of cancers. Currently available data is limited to retrospective case series and case reports. There is also scarce data on the use of ICI in patients with pre-existing autoimmune disease (PAD) as these patients are often excluded from clinical trials.

Objectives: To describe the clinical presentation, management and early outcomes of patients exposed to ICI with Rh-irAE or PAD recruited and followed prospectively from multiple sites across Canada.

Methods: Adult patients with Rh-irAE from cancer immunotherapy (CTLA-4, PD-1 or PDL-1 inhibitors) or those with PAD exposed to cancer immunotherapy are prospectively recruited across 9 academic sites in Canada. Standardized clinical and biologic data are also collected. We describe clinical characteristics and management of patients recruited between January 2020 and October 2021, stratified based on the presence or absence of PAD.

Results: 103 patients were recruited from 9 sites. From those, 85 had Rh-irAE, 47 had pre-existing musculoskeletal and rheumatic diseases, and 20 had other PAD. The most frequent Rh-irAE were joint manifestations (n = 73). Other Rh-irAE included muscle symptoms (n = 7), connective tissue disease (n = 6), vasculitis (n=2) and sarcoid (n = 3). Prednisone was the most common treatment (n = 53). Intraarticular corticosteroids were used in 7 patients. Eleven patients required conventional synthetic disease-modifying anti-rheumatic drugs (DMARD) and only one required biologic DMARD to control the Rh-irAE. Anti-PD-1 therapies were the most used ICI (56.3%), followed by combination therapy (35.9%). Response to index immunotherapy at 6 months was available for 21 patients. Most patients had partial response (57.1%) and only 4 patients had tumor progression (19.1%). The ICI was permanently discontinued due to an irAE in 21 patients (38.1% with PAD and 61.9% without PAD). There were no deaths related to Rh-irAE.

Conclusion: The initial sample of the CanRIO prospective national cohort suggests that demographic characteristics and tumor representation in people with PAD and without PAD is similar. Patients with PAD are less likely to receive

Table 1.

	AA-a (n=65)	FMF (n=20)	AL-a (n=15)	Cirrhosis (n=16)	Chronic Hepatitis B (non-cirrhotic) (n=22)	HC (n=27)	p[1]	p[2]	p[3]	p[4]	p[5]	p[6]
Age (years)*	46 (19)	42.5(13)	58 (16)	49 (15)	45 (21)	45 (23)	0.4	0.3	0.8	0.5	0.8	***0.002***
Gender (n, %)												
Male	38 (59)	10 (50)	6 (40)	10 (62.5)	13 (59)	17 (55)	0.5	0.8	1	0.7	0.7	0.2
Female	27 (41.5)	10 (50)	9 (60)	6 (37.5)	9 (40.9)	14 (45.2)						
Diabetes Mellitus (n, %)	5 (8)	2 (11)	2 (13)	3 (15)	2 (13)	3 (10)	0.7	0.6	0.4	0.8	0.9	0.6
Body Mass Index (kg/m^2) *	25.7 (1.4)	25.6 (5.4)	24.8 (3.6)	26.7 (6.7)	25.5 (7)	26 (5.7)	0.9	0.4	1	0.7	0.7	0.3
Liver stiffness (kPa)*	6.7 (5.6)	6.45 (2.7)	9.8 (12)	26.7 (22)	5.7 (5)	4.9 (1.6)	***<0.001***	***<0.001***	***0.03***	***<0.001***	***<0.001***	0.16
Significant stiffness (kPa≥7)	31 (48)	11 (55)	8 (58)	16 (100)	4 (18)	2 (6.5)	0.4	***<0.001***	***0.012***	***<0.001***	***<0.001***	0.6
Advanced stiffness (kPa≥9.5)	17 (26)	4 (20)	7 (50)	16 (100)	3 (14)	0	0.4	***<0.001***	0.2	***0.001***	***0.02***	0.1
S4 stiffness (kPa≥12.5)	10 (15)	0	5 (36)	16 (100)	2 (9)	0	0.057	***<0.001***	0.4	***0.02***		0.1
FIB-4 score	0.97 (0.9)	0.76 (0.56)	1.3 (0.95)	2.5 (3.4)	0.85 (0.8)	0.7 (0.5)	***<0.001***	***<0.001***	0.4	***0.005***	0.6	0.1
APRI score*	0.25 (0.2)	0.26 (0.2)	0.24 (0.2)	0.77 (1.3)	0.22 (0.2)	0.16 (0.08)	***<0.001***	***<0.001***	0.3	***0.002***	***0.02***	0.4
ALP (U/L)*	97 (65)	79 (55)	103 (54)	79 (126)	76 (39)	67 (22)	***<0.001***	0.5	***0.002***	***<0.001***	***0.002***	0.7
GGT (U/L)*	18 (18)	17 (26)	24 (61)	24 (51)	16 (14)	14 (14)	0.07	0.2	0.2	0.07	0.2	0.08

p[1]: AA-a and FMFp[2]: AA-a and cirrhosisp[3]: AA-a and chronic liver diseasep[4]: AA-a and HCp[5]: FMF and HCp[6]: AA-a and AL-a*Median, interquartile of range

combination therapy (n= 12 vs. n=25) and are less likely to have tumor progression on ICI (n=1) compared to those without PAD (n=3). Selection bias is noted in this initial sample since half of recruited patients have PAD. The CanRIO cohort provides valuable insight into real-world spectrum and management of Rh-irAE secondary to immunotherapy for cancer.

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POS1362 THE EFFICACY AND CYTOKINE PROFILES DURING TREATMENT WITH APREMILAST IN PATIENTS WITH BEHÇET 'S DISEASE

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Background: Apremilast has been shown to be effective in patients with Behçet's disease (BD) in domains other than oral ulcers; however, its long-term efficacy is yet to be determined. Although serum cytokine modulation by increasing intracellular cAMP levels has been suggested as a mechanism for the efficacy of apremilast on skin areas of psoriasis [1], the relationship between efficacy and cytokine on various domains in BD has not been fully investigated.

Objectives: This study aims to evaluate the long-term clinical efficacy of apremilast in BD and its effect on serum cytokines.

Methods: In this study, patients with BD who received apremilast for active oral ulcers were included. For 12 months, the improvement rates of oral and genital ulcers, skin lesions, and arthritis were assessed every three months. Serum levels of cytokines, including interferon-gamma (IFN-γ), interleukin 10 (IL-10), and IL-17A were determined using Simple Plex (Protein Simple, CA, USA) at baseline and three months after apremilast treatment. Other cytokines, including tumor necrosis factor-alpha (TNF-a), IL-6, IL-8, and IL-23, were also measured in serum using a multiplex immunoassay (Luminex Assay, R&D Systems).

Results: Fifteen patients were included in this study. Table 1 shows the characteristics of the patients who participated in this study. Oral ulcers disappeared in 66.7% and 92.3% of the patients after 3 and 6 months of apremilast treatment, respectively. Genital ulcers disappeared in all patients after 6 months of apremilast treatment and were maintained for 12 months. The efficacy of apremilast in oral ulcers could be divided between two groups: 8 patients in the oral ulcer remission group (OU-R group) whose oral ulcers completely disappeared after 3 months of apremilast administration and persisted for 1 year, and 7 patients in the oral ulcer non-remission group (OU-NR group) whose oral ulcers persisted after 3 months of apremilast treatment. Genital ulcers improved more rapidly in the OU-R group than in the OU-NR group, and completely disappeared within 3 months. Skin and joint lesions generally improved after 6 months, but recurred after 9 months.

Table 1. Baseline characteristics of the studied patients with Behçet's disease

Characteristics	N = 15
Age (years), mean ± SD	46.7 ± 13.0
Sex (female), n (%)	11 (73.3)
Disease duration (years), mean ± SD	10.4 ± 8.8
Active Behçet's disease manifestation at the time of enrollment, n (%)	
Oral ulcer	15 (100)
Genital ulcer	5 (33.3)
Skin lesion (erythema nodosum or pustules)	10 (66.7)
Arthralgia	9 (60.0)
Arthritis	5 (33.3)
Ocular involvement	0 (0)
Gastrointestinal involvement	1 (6.7)
Neurological involvement	0 (0)
Vascular involvement	0 (0)

SD, standard deviation; n, number.

Serum cytokines could be analyzed in seven of the 15 cases. There was no significant association between serum baseline cytokine levels and the presence of lesions or severity of disease. Compared to baseline, TNF-α and IL-23 levels were significantly lower after apremilast treatment and IFN-γ levels were trending upwards; however, IL-6, IL-8, and IL-10 levels showed no constant trend (TNF-α and IL-23: p <0.05, IFN-γ: p = 0.078). In addition, the rate of decrease in serum IL-6, IL-10, and IL-23 levels was significantly greater in the OU-R group than in the OU-NR group (Figure 1). However, the rate of change in serum cytokines was not associated with efficacy of apremilast for skin lesions, arthralgia, or arthritis.

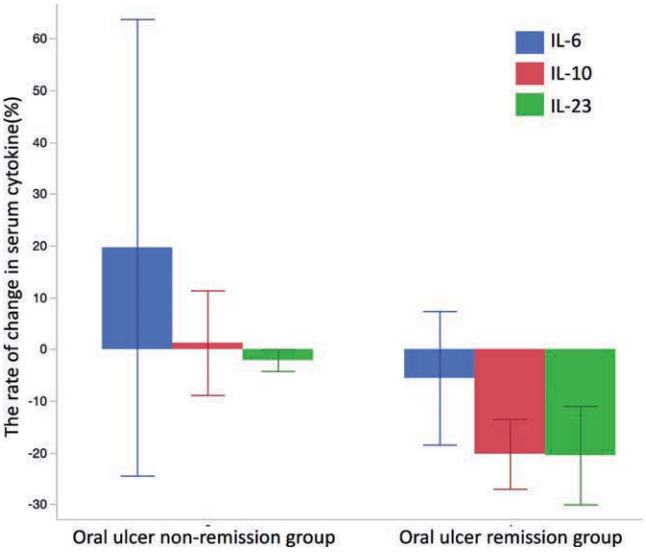

Figure 1. The rate of change in serum interleukin (IL)-6, IL-10, and IL-23 levels up to 3 months after apremilast treatment in the oral ulcer remission group and the oral ulcer non-remission group.

Conclusion: Apremilast has shown long-term efficacy in the treatment of oral and genital ulcers in patients with BD. The efficacy of apremilast against oral ulcers in BD may be attributed to its modulatory effect on serum cytokines as previously reported. Future exploratory studies for biomarkers associated with the presence of efficacy against genital ulcer and arthritis are needed.

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POS1363 THE VALIDITY AND RELIABILITY OF THE TURKISH VERSION OF BEHÇET'S SYNDROME OVERALL DAMAGE INDEX IN A RETROSPECTIVE COHORT

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Background: Behçet's syndrome Overall Damage Index (BODI) is a newly developed damage index specific to Behçet syndrome (BS).

Objectives: We aimed to evaluate validity, reliability and feasibility of the Turkish version of BODI and evaluate its performance for use in retrospective cohort studies for different phenotypes of BS.

Methods: The study included 295 patients with at least 3 visits at 6 months intervals out of 590 consecutive BS patients who were admitted between January 2015 and August 2017. Turkish version of the BODI form was developed by translating into Turkish and backwards by 2 people. BODI scores were calculated for each year during the follow-up period. The test-retest reliability of BODI was assessed by scoring the same 50 patients at 6-month intervals by the same observer (YYO). Two different observers (YYO- YO) assessed the same 50 patients for inter-observer agreement. The intra-class correlation coefficient (ICC) was used to assess the inter and intra-observer agreement. We also evaluated the median time to fill out the form in patients with different types of involvements.

Results: Among the 295 (158 F/137 M) patients, mean age was 39 (9.9) and the mean disease duration was 8.8 (5.9) years. Clinical features of BS patients were summarized in the Table 1. BODI median score was 1 (IQR=0-1). We observed

an increase in BODI score in 111 (38%) patients during follow-up. The main reasons for increasing BODI scores were eye, vascular and neurological involvement (Table 1). The mean ICC for inter-observer agreement was 0.94 (95% CI, 0.89-0.96) and for intra-observer agreement was 1. The median (range) time to complete the form was 2 (1-8) minutes.

Table 1. Clinical features and BODI scores of Behçet syndrome patients.

Oral ulceration	99.7
Genital ulceration	81.3
Erythema nodosum	57.1
Papulopustular lesions	89.5
Joint involvement	25.2
Ocular involvement	47.3
Vascular involvement	21.4
Neurologic involvement	3.1
Gastrointestinal involvement	2.7
N of patients with more than 3 BODI scores*(%)	194 (66)
Causes for increase in BODI score**(n=111) (%)	
Ocular involvement	77 (69)
Vascular involvement	17 (15)
Neurological involvement	8 (7)
Gastrointestinal involvement	3 (3)
Mucocutaneous inv.	6 (5)
Cardiovascular inv.	1 (0.9)
Diabetes mellitus	4 (4)
Avascular necrosis	2 (2)
Osteoporosis related fracture	1 (0.9)

*All patients had at least 3 BODI scores, **Some patients had more than 1 type of involvement

Conclusion: This study showed that the Turkish version of BODI was a reliable and feasible instrument that could capture the change over time in damage, and could be used in retrospective cohort studies. Ocular involvement was the most common cause of progressive damage in this cohort.

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POS1364 ATTACKS OF MYALGIA IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: OTHER THAN CALF PAIN

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by recurrent attacks of fever, serositis, and musculoskeletal symptoms [1, 2]. Arthritis is the most common musculoskeletal symptom of attacks and also included in diagnostic criteria of FMF [3]. If it is specifically queried, myalgia may be detected in up to 20-25% of the patients with FMF. [4, 5].

Objectives: In our study, we aim to assess the localization of attack-related myalgia and associated parameters in patients with FMF.

Methods: A total of 349 consecutive patients followed by FMF in our clinic were enrolled in the study and asked for attack-induced myalgia and if present, localization of muscle groups on the mannequin body parts diagram.

Attack frequency, duration, and disease activity were evaluated with the Auto-Inflammatory Diseases Activity Index (AIDAI) scoring system [6]. Patients were also asked for work/study day loss during attacks and patient acceptable symptom state (PASS) status [7].

Results: 126 patients showed attack myalgia (36%); attack duration, frequency, severity were significantly higher in patients with attack-myalgia (p<0,005). Most common muscle groups were calves, lower back, and latissimus dorsi muscles in order. Myalgia was most commonly accompanied by arthritis (p<0,002). Patients with myalgia have a higher frequency of colchicine resistance and work/study day loss due to attacks.

Conclusion: Our results conclude that myalgia is an important domain of attacks and causes absenteeism and uncontrolled disease activity.

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Table 1. Comparison of clinical and laboratory parameters between patients with /without myalgia attacks

	Patients with myalgia attack	Patients without myalgia attack	p value
Age (years)	36,33 ±10, 68	37,9±11, 48	>0,05
Sex (female/male)	78/43	138/87	>0,05
Follow-up time (years)	16,1	17,6	>0,05
Dominant attack(number)			
Peritonitis	42	55	>0,05
Arthritis	11	39	**0,012**
Pleuritis	13	10	>0,05
Only fever	4	7	>0,05
AIDAI score (mean, 0-175)	127,40	80,68	**<0,05**
VAS score for pain (median score, during attack. 0-10)	8	5	**<0,05**
Colchicine resistance (number of patients)	69	25	**0,003**
Colchicine-resistant	29	84	**0,002**
Colchicine-sensitive			
PASS status (number)	41	6	**0,016**
Need additional treatment	34	74	**0,010**
Satisfied from treatment			
Work/study day loss (number)	48	6	**0,003**

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POS1365 THE FMF&AID SURVEY - A PATIENT ORGANIZATION DRIVEN SURVEY FOR AUTOINFLAMMATORY DISEASES

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Background: Autoinflammatory diseases (also referred to as hereditary periodic fever syndromes) are caused by defects in the innate immune system. Many autoinflammatory syndromes arise from inherited genetic mutations which begin in childhood and persist throughout adult life. These diseases are often present in several members and generations within a family. Newer research also reflects that, cases can often present at any age through-out childhood, teenage years, and even into older adulthood. These cases appear to be acquired, perhaps due to the interplay of genetic, immune, and environmental factors (somaticism). It

is not uncommon that a patient is diagnosed with rheumatoid arthritis, multiple sclerosis or another autoimmune issue, as many physicians are not aware of monogenic inborn errors, nor how to conduct a thorough work up due to a lack of medical knowledge.

Objectives: Unfortunately, the knowledge base that many doctors have with regards to autoinflammatory genetic diseases is minimal to non-existent, when compared to the well-established expertise of autoimmune disease management. Concerns about the increasing patient accounts detailing lack of medical diagnosis, treatment, and pain management, lead to the important decision to collect further data from the autoinflammatory patient community. The aim of the survey responses collected, and post data aggregation will help identity patient trends and use this information to educate and increase awareness amongst the medical community as to the unmet diagnostic and treatment requirements for the autoinflammatory population.

Methods: A questionnaire comprised of thirty questions was developed by members of the patient organization FMF & AID Global Association (Executive Director, Malena Vetterli with Research Director, H. Ellen Cohen) under the guidance of Dr. med. Juergen Rech focused on collecting basic information (e.g. age, country, onset and duration of symptoms, pain and fatigue). The survey was published at the end of 2020 on social media (Facebook) and on the FMF&AID website (www.fmfandaid.org). Participation was voluntary and the patients agreed that the anonymised response information of the survey may be evaluated and published. This international survey was approved by the ETHICS Committee FAU in Erlangen-Nuremberg, Germany.

Results: Worldwide, over a thousand patients or parents/caregivers of patients (younger than 18 years) in fifty-two countries took part in this survey and answered the questionnaire. Eighty percent (80%) of the participants had already been diagnosed with an autoinflammatory disease. However, despite classic periodic symptom presentation, twenty percent (20%) of the participants were still without a concise diagnosis. FMF - forty-three percent (43%) was cited as the most common diagnosis and M. Behçet thirty percent (30%) as the second, with a variety of others (e.g. PFAPA, CAPS, HIDS, TRAPS, DADA, Yao syndrome, and uSAID). The minimum age at diagnosis ranged from 1 to 70+ years old with an average age of 33 years when properly diagnosed. Three-hundred and nine (309) patients reported that their pain had not been taken seriously and adequately treated in the past. Pain and fatigue, as measured by the standard visual analogue scale (VAS 0-10), was high in the past 30 and 7 days, respectively. VAS pain 30 days was 4.8 (SD +/-2.7) or 7 days with 4.2 (SD +/- 3), as well as fatigue VAS 30 days 5.7 (SD +/- 2.8) or fatigue VAS 7 days with 5.5 (SD +/- 3).

Conclusion: One-fifth of patients with classic symptoms of autoinflammatory diseases remain undiagnosed and therefore not specifically treated. Although, the rest of the participants eighty percent (80%) have a diagnosis of an autoinflammatory disease, therapy does not appear to be sufficient to manage their wide-ranging and debilitating symptoms, in particular pain and fatigue. Patients continue to carry the burden of receiving mental diagnosis vs actual medical diagnosis and are still forced to seek additional medical support, often incurring travel or relocation costs to obtain proper care.

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POS1366 RITUXIMAB IN IGG4-RD: AN OPEN-LABEL NON-RANDOMIZED OBSERVATIONAL STUDY

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Background: IgG4-related disease (IgG4-RD) is a rare, heterogenous and potentially severe disease. An open-label trial demonstrated efficacy of rituximab (RTX) in IgG4-RD [1]. Recently, four distinct phenotypes of IgG4-RD were identified [2]. There is a paucity of studies investigating RTX efficacy across these phenotypes.

Objectives: Investigate efficacy and safety of RTX in IgG4-RD and segregated by phenotypes.

Methods: This is an open-label non-randomized single center observational study. All patients with IgG4-RD (diagnosed by expert opinion) at the Oslo University Hospital treated with ≥ 1 dose of RTX with 12 months follow-up were included. Two experts (JV, ØMi) assigned patients to phenotypes. Glucocorticoid (GC) treatment was allowed. We measured disease activity by the IgG4-RD Responder Index (IgG4-RD RI) at baseline, 6 months, and 12 months. We defined a composite primary outcome consisting of two measures; (i) reduced disease activity (i.e., ≥2 points improvement in IgG4-RD RI from baseline and/or IgG4-RD RI score 0 at follow-up), and (ii) no disease flares (i.e., no ≥2 points worsening of IgG4-RD RI and no need to increase GC dose) at 6 months. Secondary outcomes were (a) reduced disease activity at months 6 or 12, (b) remission (IgG4-RD RI score 0 and GC dose ≤ 7.5 mg) at 6 or 12 months and (c) safety. Descriptive statistics were applied.

Results: We included 40 patients, of which 30 (75%) were male and 35 (88%) Caucasian. Mean age and disease duration at time of first RTX infusion was 58 and 3 years, respectively. Seventeen of the 40 patients (43%) received RTX as add-on therapy (following GC for > 3 months), while 13 (33%) received RTX as upfront combination therapy with GC, and 10 (25%) received RTX as upfront monotherapy. All 40 patients received an infusion of 1000 mg RTX at study baseline (dose 1A at week 0) and 39 of these 40 patients (98%) received a second RTX infusion (dose 1B) at week 2. Additional infusions of 500-1000 mg RTX were administered at weeks 26 (dose 2A) and 28 (dose 2B) in 24 (60%) and 7 (18%) patients, respectively. The composite primary endpoint was met by 31/40 patients (78%). Reduced disease activity at 6 and 12 months were seen in 34 (87%) and 35 (90%) patients, respectively. Fifteen patients (38%) were in remission at 6 months, and 22 (56%) were in remission at 12 months. "Retroperitoneum and Aorta" showed lowest response rates, while "Head and Neck-Limited" had the highest rate of flares (Table 1). Mild infusion reaction occurred in 8 (20%) patients. Hypogammaglobulinemia was observed in 4 (10%). Infection requiring hospitalization occurred in 6 (15%), including one fatal infection which was the only death in the study period.

Table 1.

	All 40 (100)	Pancreato-Hepato-Biliary 9 (23)	Retroperitoneum and Aorta 6* (15)	Head and Neck-Limited 14 (35)	Mikulicz and Systemic 11 (28)
Baseline (n=40)					
Male, n (%)	30 (75)	8 (89)	5 (83)	8 (57)	9 (82)
Caucasian (%)	35 (88)	9 (100)	6 (100)	12 (86)	8 (73)
Age, years (SD)	58 (14)	63 (9)	66 (3)	49 (18)	60 (11)
Disease duration, years (SD)	3 (4)	4 (3)	3 (4)	2 (2)	5 (6)
2019 ACR/EULAR classification criteria (%)	28 (70)	8 (89)	3 (50)	6 (43)	11 (100)
IgG4-RD RI at diagnosis (SD)	10 (6)	10 (5)	7 (4)	7 (3)	17 (4)
IgG4-RD RI at RTX 1A, (SD)	8 (6)	9 (4)	5 (4)	6 (4)	12 (7)
6 months (n=39)*					
IgG4-RD RI (SD)	2 (2)	3 (3)	2 (2)	1 (1)	1 (2)
Primary outcome, n (%) (n=40)	31 (78)	9 (100)	3 (50)	9 (64)	10 (91)
Reduced disease activity, n (%)	34 (87)	9 (100)	3 (60)	12 (86)	10 (91)
Remission, n (%)	15 (38)	4 (44)	0	6 (43)	5 (46)
Flare, n (%)	3 (8)	0	0	3 (21)	0
12 months (n=39)*					
IgG4-RD RI (SD)	1 (1)	1 (1)	0 (1)	1 (1)	1 (2)
Reduced disease activity, n (%)	35 (90)	9 (100)	4 (80)	12 (86)	10 (91)
Remission, n (%)	22 (56)	7 (78)	3 (60)	7 (50)	5 (45)
Flare, n (%)	4 (10)	1 (11)	1 (20)	2 (14)	0

*One patient died shortly after 1A, and is not included in secondary efficacy outcomes

Conclusion: In our observational study, RTX appears safe and effective in IgG4-RD, with the highest response in patients with Pancreato-Hepato-Biliary phenotype. Relatively low remission rates across all phenotypes indicate an unmet need for improved treatment.

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Wallenius: None declared, Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Jansen, Lilly, Medscape, Merck Sharp & Dohme, Roche, Consultant of: Actelion, ARXX, Bayer, Boehringer Ingelheim, Jansen, Lilly, Medscape, Merck Sharp & Dohme, Roche, Grant/research support from: Boehringer Ingelheim

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POS1367 THE PREVALENCE AND RISK FACTORS FOR CARDIAC DISEASE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is a genetic disorder manifested by recurrent attacks of peritonitis, pleuritis and arthritis, and characterized by clinical and laboratory evidence for localized and systemic inflammation. Colchicine treatment usually prevents the attacks and the associated inflammation. Inflammation may play an important role in the initiation and progression of atherosclerosis. Recently colchicine was suggested as a therapy that help to prevent coronary heart disease.

Objectives: To study the effect of FMF and colchicine treatment on the cardiovascular morbidity and the overall mortality.

Methods: We studied using the data base from health insurance in Israel (Maccabi Healthcare Services-MHS) the presence of IHD and its risk factors in 492 FMF patients aged 40 years or more, and in a control groups matched by age gender and socioeconomic status.

Results: The incidence of cardiac disease in FMF patients was similar to the control group (6.5% vs 5.7% p- 0.594), smoking kidney disease and gout were higher in FMF compared to the control group (16.1 % vs 12.8% p- 0.022, 9.3% vs 5.1 p- 0.01 and 4.5% vs 0.2% p<0.001 respectively), but hypertension and diabetes were similar. The overall mortality in average follow up of 3174.37 ±1738.84 days was similar in both groups.

Conclusion: The incidence of cardiac disease among FMF patients was not increased compared to the control group, despite the exposure to recurrent inflammation. We suggest that colchicine may have a protective role in these patients. Further studies are required.

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POS1368 DIVERSITY OF HEMODYNAMIC TYPES IN CONNECTIVE TISSUE DISEASE ASSOCIATED PULMONARY HYPERTENSION: MORE THAN A SUBGROUP OF PULMONARY ARTERIAL HYPERTENSION

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Background: Connective tissue disease (CTD) associated pulmonary hypertension (PH) is classified as a subgroup of WHO group 1 PH, also called pulmonary arterial hypertension (PAH). However, not all CTD-PH fit the hemodynamic definition of PAH. This study investigates the diversity of hemodynamical types of CTD-PH, their different clinical characteristics and outcomes.

Objectives: This study investigates the diversity of hemodynamical types of CTD-PH, their different clinical characteristics and outcomes.

Methods: We performed a retrospective cohort study. CTD-PH patients underwent right heart catheterization (RHC) were enrolled and divided into WHO group1 PH, WHO group 2 PH and high output PH (PVR<3WU and PAWP<15mmHg) according to hemodynamic features. Patients with obvious lung diseases, left heart disease and pulmonary embolism were excluded. Baseline characteristics, inflammatory markers, autoantibodies, cardiac function status, echocardiogram parameters, hemodynamics and survival rates were compared.

Results: 207 CTD-PH patients were included, including 139 in WHO group 1 PH, 36 in WHO group 2 PH and 32 in high output PH. Incidence of anti-ribonucleoprotein antibody was lower in WHO Group 2 PH. High output PH is less severe, presenting lower NT-proBNP level, better WHO functional class, lower mPAP and PVR, higher cardiac output, and less cardiac remodeling. Among patients with elevated PAWP, combine pre& post-capillary PH had higher mPAP and larger right ventricle diameter. Association of mild to moderate interstitial lung disease didn't show significant difference in disease characteristics. Short-term survival was significantly worse in WHO group 2 PH, yet 5-year survival rates didn't differ between groups.

Conclusion: Pre-capillary PH is not the only hemodynamic type of CTD-PH. Different types of CTD-PH present different clinical phenotypes and outcome. Carefully phenotyping PH in CTD-PH patients is important.

Disclosure of Interests: None declared

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POS1369 PULMONARY ARTERY WALL THICKNESS IS INCREASED IN BEHÇET'S DISEASE

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Background: Behçet's Disease (BD) is a unique systemic vasculitis that mainly involves veins, in contrast to other vasculitides [1, 2]. Prior studies showed that pulmonary arteries have a similar structure with systemic veins in terms of wideness, thin-walled, increased compliance, and low resistance [3]. We have recently shown increased venous wall thickness in lower extremity veins of BD patients.

Objectives: In this study, we aimed to assess pulmonary artery (PA) wall thickness by transthoracic echocardiography (TTE) in BD compared to healthy controls and patients with non-inflammatory pulmonary embolism (NIPE).

Methods: Patients with BD (n=77), NIPE (n=33) and healthy controls (n=57) were included in the study. PA wall thickness was measured with TTE by a cardiologist blinded to cases. PA wall thickness was measured from the mid-portion of the main PA (approximately 1 to 2 cm distal to the pulmonary valve) as demonstrated in Figure 1.

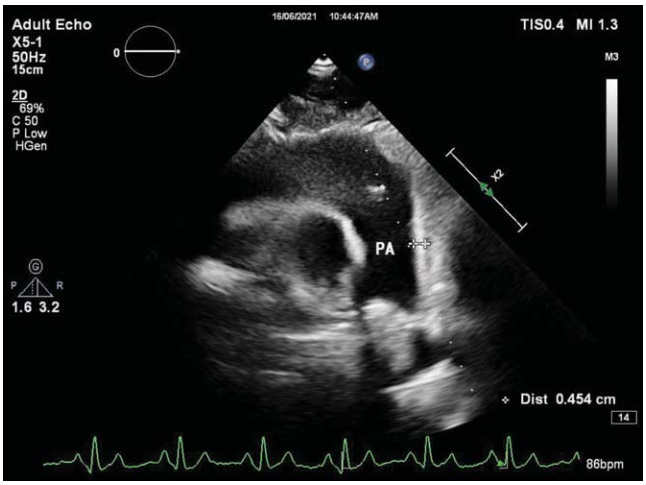

Figure 1. Measurement of pulmonary artery wall thickness by Transthoracic Echocardiography

Results: PA wall thickness was significantly lower in controls (0.36 mm (SD:0.03) compared to NIPE (0.44 mm (SD:0.05) and BD (0.44 mm (SD:0.06) (p<0.001 for both). PA wall thickness was also found to be significantly higher in BD patients with major organ involvement (0.47 mm (SD:0.04) compared to healthy controls and NIPE (p <0.001 and p=0.006, respectively). PA wall thickness was similar between BD and NIPE (p= 0.6). Among patients with BD, PA wall thickness was significantly lower in patients with only mucocutaneous involvement compared to patients with major organ involvement (0.37 mm vs 0.47 mm, p< 001), it was also similar between patients with only mucocutaneous involvement and healthy controls (0.37 mm vs 0.36 mm, p= 0.3). PA wall thickness was comparable between patients with vascular and non-vascular major organ involvement (0.46 mm vs 0.47 mm, p= 0.3). Patients with vascular and non-vascular major organ involvement had significantly higher PA wall measurements compared with NIPE patients (p= 0.04, p= 0.02, respectively).

Conclusion: We found that PA wall thickness was significantly higher in BD with major organ involvement compared to BD patients with only mucocutaneous

involvement regardless of major organ involvement type. These results suggest that increased PA wall thickness in BD may be the predictor of the major organ involvement during follow-up.

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POS1370 INCREASED INFERIOR VENA CAVA WALL THICKNESS AS A SIGN OF VENOUS INFLAMMATION IN BEHÇET'S DISEASE

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Background: Vascular involvement of Behçet's disease (BD) involves both arterial and venous vessels of all sizes [1]. Femoral (superficial, deep, and common) and popliteal veins are the most frequently affected veins. We have previously shown that femoral wall thickness is increased in BD patients and can be used as a diagnostic test [2].

However, many other sites including vena cava inferior/superior and pulmonary arteries may also be involved [3]. Despite the dominance of venous vessel involvement, there is limited data assessing the large veins in BD.

Objectives: In this study, we aimed to assess inferior vena cava wall thickness (IVC) by transthoracic echocardiography (TTE) in BD compared with healthy controls.

Methods: Patients with BD (n=70) and age and sex-matched healthy controls (n=51) were included in this study. Assessment of inferior vena cava (IVC) wall thickness was performed by an experienced cardiologist blinded to cases. Measurement of IVC wall thickness was made at end-expiration and approximately 0.5 to 2.0 cm proximal to the ostium of the right atrium as demonstrated in Figure 1.

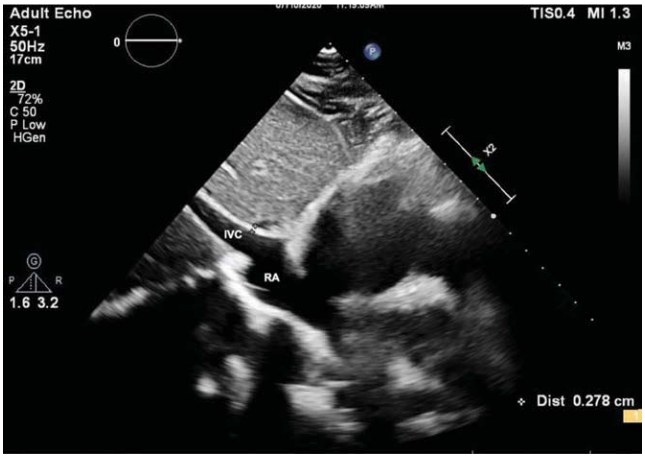

Figure 1. Measurement of inferior vena cava wall thickness by transthoracic echocardiography

Results: IVC wall thickness of patients with BD (0.29 mm (SD: 0.03) was significantly higher than healthy controls (0.26 mm (SD: 0.03) (p<001). Although IVC wall thickness was higher in patients with BD with vascular involvement (0.30 mm (SD:0.04) and history of pulmonary embolism (0.30 mm (SD:0.04)), the difference did not reach statistical significance. There was no difference between IVC wall thicknesses in patients who used immunosuppressive and anti-TNF treatments due to major organ involvement, compared to those who did not. Similarly, no difference is observed between IVC thicknesses among Behçet's patients according to age, gender, and activity status at the last visit. Although no correlation was found between IVC wall thicknesses, disease duration, and BDCAF scores at the last visit in the BD group, there was a low-grade correlation between age and IVC wall thickness (r=0.31, p=0.09)

Conclusion: Increased IVC wall thickness shows vasculitic involvement of large venous structures in BD and can be easily measured by TTE which is an easily accessible, noninvasive modality without radiation. The role of IVC wall thickness assessment for the diagnosis or management of BD requires further studies.

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POS1371 HYPOMETHYLATION OF CIRCULATING IMMUNE CELLS IN PATIENTS WITH GRAVES' ORBITOPATHY – A PRELIMINARY STUDY

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Background: Graves' orbitopathy (GO) is an eye disease occurring in patients with autoimmune thyroid disorders (AITD), most commonly Graves´ disease. It is characterized by inflammation affecting soft tissues of the orbit. A recent study demonstrated an association between fibroblast hypomethylation and disease activity in GO (Virakul *et al*., Front Endocrinol, 2021). Because procurement of fibroblast from GO patients require an invasive sampling, we wondered whether analysis of global DNA methylation in circulating immune cells obtained from peripheral blood could contribute to early detection of GO from patients with AITD.

Objectives: To compare global DNA methylation pattern in circulating immune cells obtained from AITD patients with GO and without GO history and healthy controls.

Methods: Global DNA methylation was quantified in circulating immune cell populations by flow cytometry using 5-methylcytosine antibody in patients with GO (n=10), AITD without GO history (n=9) and healthy controls (n=8). Immune populations ($CD4^+$ and $CD8^+$ T cells, B cells, monocytes and $CD56^{dim/bright}$ NK cells) and their activation status were identified using CD3/4/8/14/16/19/25/45/56/69 antibodies.

Results: In patients with GO, global DNA methylation was reduced by ~50% in the activated ($CD25^+$) $CD8^+$ T cells and by ~35% in the whole $CD8^+$ T cell population compared to patients with AITD (p=0.006). Moreover, percentage of $CD8^+$ T cells, but not activated subpopulation, was higher in GO when compared to AITD (p=0.04). Hypomethylation by ~20% was detected in monocytes as well as in $CD56^{dim}$ NK cells and their activated ($CD69^+$) subpopulation when GO was compared with AITD (p≤0.02). Of these cell populations, percentage of monocytes was also higher in GO when compared to AITD (p=0.04). Global methylation in B cells, $CD4^+$ T cells and $CD56^{bright}$ NK cells did not differ between patients with GO and patients with AITD (p>0.05). Of these populations, higher percentage of B cells was detected in GO when compared to AITD group (p=0.02). Analysis of larger patient cohorts is in progress with particular emphasis on the relationship of methylation patterns to GO disease activity.

Conclusion: This is the first study identifying the different global methylation profile of circulating immune cells in patients with GO characterized by DNA hypomethylation in $CD8^+$ T cells, $CD56^{dim}$ NK cells and monocytes compared to patients with AITD. Our study nominates hypomethylation as a non-invasive biomarker of GO and should be validated in a larger cohort of patients.

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POS1372

THE 2021 EULAR AND ACR POINTS TO CONSIDER FOR DIAGNOSIS, MANAGEMENT AND MONITORING OF THE IL 1 MEDIATED AUTOINFLAMMATORY DISEASES: CAPS, TRAPS, MKD, AND DIRA

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Background: The Interleukin-1 (IL-1) mediated systemic autoinflammatory diseases (SAIDs), including the cryopyrin-associated periodic syndromes (CAPS), tumor necrosis factor receptor-associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), and deficiency of the IL-1 receptor antagonist (DIRA) belong to a group of rare immunodysregulatory diseases that primarily present in early childhood with variable multiorgan involvement. When untreated, patients with severe clinical phenotypes have a poor prognosis, and diagnosis and management of these patients can be challenging. However, recently-approved treatments targeting the pro-inflammatory cytokine IL-1 have been life-changing and have significantly improved patient outcomes.

Objectives: We aimed to establish evidence-based recommendations on diagnosis, treatment, and monitoring to standardize the management of these patients.

Methods: A multinational, multidisciplinary task force consisting of physician experts including rheumatologists, patients or caregivers, and allied health care professionals was established. Evidence synthesis including systematic literature review and expert consensus (Delphi) via surveys were conducted. Consensus methodology was utilized to formulate and vote on statements to guide optimal patient care.

Results: The task force devised five overarching principles, 14 statements related to diagnosis, 10 on therapy, and 9 focused on long-term monitoring that were evidence and/or consensus-based for patients with IL-1 mediated diseases. An outline was developed for disease-specific monitoring of inflammation-induced organ damage progression and reported therapies of CAPS, TRAPS, MKD, and DIRA.

Conclusion: The 2021 EULAR/ACR points to consider provide state-of-the-art knowledge based on published data and expert opinion to guide diagnostic evaluation, treatment, and monitoring of patients with CAPS, TRAPS, MKD and DIRA, and inform the various stakeholders about optimized patient care to improve disease outcomes.

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POS1373

THE DIAGNOSTIC ROLE OF PATHERGY TEST IN PATIENTS WITH BEHÇET'S DISEASE FROM WESTERN EUROPE

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Background: pathergy is the term used to describe the hyper-reactivity of the skin in response to a minimal trauma, as the consequence of an exacerbated response of the innate immune system [1]. Pathergy test has a central role for the diagnosis of Behçet's disease (BD), especially in doubtful and atypical cases. However, while its incidence has been decreasing over the past few decades, there are significant variations in the frequency of pathergy among different geographic contexts [2]. These aspects affect the diagnostic role of pathergy test for patients with suspected BD.

Objectives: to evaluate the frequency and features of positive pathergy test (PPT) in Italy, its role in the diagnosis of BD, and any association with other BD-related manifestations.

Methods: 29 BD patients, 15 patients with spondyloarthritis (SpA) and 19 healthy controls (HCs) underwent two types of pathergy test, which were performed on the hairless part of the volar forearm ipsilaterally: intradermal injection of 0.5 ml normal saline and intradermally needle soaked with fresh self-saliva. Both pricks were done with a monouse 25 gauge hypodermic needle inserted with a vertical approach at a depth of 5 mm into the skin. The needle was withdrawn with a twisting movement. Skin reactions were observed 48 hours after prick. The results of pathergy tests were statistically analysed in the light of demographic, clinical, and therapeutic features of subjects enrolled. The BD activity at the time of the pathergy test was assessed with the Behçet's Disease Current Activity Form (BDCAF) [3].

Results: pathergy test performed with saline solution resulted always negative in all groups. Skin prick test using self-saliva resulted in the occurrence of a papule in 2 (6.9%) BD patients and in 1 (6.7%) patient with SpA. A ≥15 mm erythematous area surrounding the needle prick site was observed in 12 (41.4%) BD patients, in 4 (26.7%) patients with SpA (including the patient with the papule), and in 1 (5.6%) HCs (p=0.022). The frequency of skin erythema was significantly higher among BD patients compared to HCs (p=0.015); no statistically significant differences were observed between BD and SpA patients (p=0.53) as well as between SpA patients and HC (p=0.21). The occurrence of skin erythema was not associated with any of the BD-related clinical manifestations. No statistically significant differences were observed between BD patients with positive and negative pathergy test according to sex (p=0.873); HLA-B51 positivity (p-value=0.461); age at the pathergy test (p=0.929); and disease duration at the pathergy test (p=0.487). The mean BDCAF was 1.33±0.65 among patients with PPT and 0.82±0.72 among patients with negative pathergy test (p=0.092). Erythema at self-saliva prick test showed a sensitivity of 41.4% (C.I. 23.52%-61.06%) and a specificity of 85.3% (C.I. 68.94%-95.05%); the positive likelihood ratio was 2.81 (C.I. 1.12-7.05) and the negative likelihood ratio was 0.69 (C.I. 0.49-0.96).

Conclusion: this study confirms the lower frequency of PPT in Western European BD patients if considering the development of a papule or a pustule in the site of pathergy test. Conversely, the onset of a ≥15 mm erythematous area surrounding the prick site could be sufficient to unveil the hyper-reactivity of the innate immune system in BD patients from Western Europe. Pathergy test is not pathognomonic of BD, as its positivity can be also observed in other innate immune system disorders, as observed for SpA patients.

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POS1374

LONG-TERM SAFETY OF CANAKINUMAB IN PATIENTS WITH AUTOINFLAMMATORY DISEASES - INTERIM ANALYSIS OF THE RELIANCE REGISTRY

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Background: Autoinflammatory diseases (AID) are characterized by severe systemic and organ inflammation as well as high burden of disease for patients and their families. Treatment with the monoclonal antibody canakinumab (CAN), an interleukin-1β inhibitor, has been proven to be safe and effective in clinical trials and real-life.

Objectives: The present study explores the long-term efficacy and safety of CAN in routine clinical practice conditions in pediatric (age ≥2 years) and adult patients with CAPS (cryopyrin-associated periodic syndromes), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

Methods: RELIANCE is a prospective, non-interventional, observational study based in Germany. Patients with clinically confirmed diagnoses of AID routinely receiving CAN are enrolled. Besides efficacy parameters regarding disease activity and remission, safety parameters were recorded at baseline and assessed at 6-monthly intervals.

Results: Here, we present the interim analysis of patients with AID (N=199) enrolled in the RELIANCE Registry between October 2017 and December 2021. Mean age in this cohort was 24.4 years (2–79 years) and the proportion of female patients was 53% (N=104). At baseline, median duration of prior CAN treatment was 2 years (0–12 years).

A total of 123 patients (62%) experienced any AE (N=653) among which nasopharyngitis, increase of inflammatory markers and pyrexia were the most frequent AE with incidence rates per 100 patient years (IR) of 8.3, 6.2, and 6.2, respectively. 29 patients (15%) were affected by severe AE (SAE, total number N=90) including 11 patients (6%) with SAE suspected to be drug-related (SADR; total number N=30) with IR from 0.2 to 0.7 (Table 1). Overall, 16 AE comprised upper respiratory tract infections (URI). One death (COVID-19, not related) and one malignancy (skin papilloma, not related) were reported. No vertigo and no hypersensitivity reactions were observed. N=10 (IR 2.36) vaccination reactions were reported (no SAE).

Table 1. Overview of the CAN safety data of the RELIANCE study across all study indications (N=199 patients).

Type of event	Number of events	IR‡
AE total	653	154.43
AE non-serious	563	133.15
AE, non-serious, not related	317	74.97
AE, URI	16	3.78
AE, non-serious adverse drug reaction	246	58.18
SAE, total	90	21.28
SAE, not related	60	14.19
SADR#, total	30	7.09

#Abdominal pain; Alport's syndrome, appendicitis, arthralgia, blister, cardiovascular disorder, chest pain, circulatory collapse, dehydration, diplopia, dyspnoea, erythema, febrile convulsion, gastroenteritis, glomerulonephritis, Haemophilus test positive, myalgia, oedema, pneumonia, premature delivery, skin discoloration, tachycardia, tonsillitis bacterial, tonsillitis streptococcal, vision blurred (each n=1 event, IR 0.24‡), tonsillectomy (2 events, IR 0.47‡), pyrexia (3 events, IR 0.71‡), not yet coded (hospital admission due to exsiccosis upon gastroenteritis, 1 event, IR 0.35‡)‡IR, incidence rate per 100 patient years; AE, adverse event; URI, upper respiratory tract infection; SAE, severe adverse event, SADR, severe adverse drug reactionIncidence rate = number of events * 36,525 / sum of observation days (=154,442)

Conclusion: The interim data from the RELIANCE study, the longest running real-life canakinumab registry, confirm safety of long-term canakinumab treatment across the entire study population. A trend for dose-related increase of SAE/SADR requires continuous close monitoring and awareness in patient groups (children, severe phenotypes, certain genotypes) requiring greater than standard dose treatment regimens.

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POS1375 THE EVALUATION OF OBESITY IN ADULT-ONSET STILL'S DISEASE, DATA FROM A LARGE MULTICENTRE COHORT.

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Background: Over the last few decades, obesity has become an increasing public health problem worldwide [1]. This is a complex disease characterised by as an abnormal or excessive fat accumulation which is usually assessed by body mass index (BMI). A value of BMI over 30 identifies the threshold to define the obesity. High BMI is common feature among patients with rheumatic disease and it is associated with higher disease activity and disability [2]. Thus, the presence of obesity may be considered as a negative prognostic factor in these patients. Against this background in rheumatic disorders, the prevalence of obesity in adult onset Still's disease (AOSD) has not been entirely clarified so far. Similarly, the impact of being obese on disease features and outcomes has not been fully elucidated in these patients. AOSD is a rare inflammatory disease usually characterised by fever, arthritis, and evanescent skin rash associated with a typical hyperferritinemia [3].

Objectives: In this study, we aimed at evaluating the prevalence of obesity in patients with AOSD. Furthermore, we descriptively assessed the clinical characteristics of these patients. We also described the occurrence of life-threatening complications, the disease courses, and the rate of mortality of obese patients with AOSD than non-obese ones.

Methods: A retrospective assessment of prospectively followed patients, from January 2001 to April 2021, was provided to analyse clinical features of patients with AOSD characterised by a BMI≥30. AOSD patients were evaluated among those included in the multicentre *Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale* (GIRRCS) cohort. This is a large cohort of patients with AOSD comprising almost 200 patients [4]. The presence of obesity was evaluated at the time of diagnosis of the disease. In this evaluation, only patients with available data about BMI were included.

Results: In this assessment, 139 patients, who had BMI registered in our database, were evaluated. Out of those, 26 (18.7%) had a BMI≥30 and were defined as having obesity. These patients had a mean age of 39.3±13.6 years and were 46.2% male. Concerning main clinical features, obese patients with AOSD were characterised by fever (96.2%), skin rash (84.6%), arthralgia (76.9%), myalgia (65.4%), and arthritis (61.5%). An explorative comparison between obese and non-obese patients was performed. A lower rate of obese patients showed sore throat (38.5% vs 63.7%, p=0.026) than others. The prevalence of serositis was observed at lower frequency in obese patients with AOSD. Pericarditis (7.7% vs 29.2%, p= 0.024), and pleuritis (7.7% vs 25.7%, p=0.035) were less frequently recorded in obese patients when compared with non-obese ones. In addition, obese patients with AOSD showed higher values of C-reactive protein (CRP) [99.2 (117.0) mg/L vs 52.0 (84.3) mg/L, p=0.046] than others. Conversely, no significant differences were retrieved assessing systemic score, ferritin, erythrocyte sedimentation rate, life-threatening complications, disease patterns, and mortality in obese than non-obese patients.

Conclusion: Clinical features of obese patients with AOSD were described in our multicentre cohort. Almost 20% of patients with AOSD were obese at the time of diagnosis of the disease. These patients were characterised by a lower prevalence of sore throat, pericarditis and pleuritis, and by higher values of CRP. However, obesity did not appear to influence the main disease features and outcomes in AOSD, although further studies are needed to fully elucidate this issue.

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POS1376 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH HIDS (HYPER-IGD SYNDROME) - INTERIM ANALYSIS OF THE RELIANCE REGISTRY

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Background: Hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) is a rare autoinflammatory condition caused by a defect in the gene coding for mevalonate kinase. This periodic fever syndrome is characterized by severe systemic and organ inflammation. Treatment with interleukin-1β inhibitor canakinumab (CAN), approved and applied for treatment of HIDS/MKD patients since 2017 [1], resulted in rapid remission of symptoms and normalization of laboratory parameters in most patients in clinical trials [2] as well as in real-life.

Objectives: To explore the long-term efficacy and safety of CAN under routine clinical practice conditions in pediatric (age ≥2 years) and adult HIDS/MKD patients.

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up period. Patients with clinically confirmed diagnoses of TRAPS, CAPS, FMF or HIDS/MKD who routinely receive CAN are enrolled in order to evaluate efficacy and safety of CAN under standard clinical practice conditions at baseline and at 6-monthly intervals.

Results: The present interim analysis shows baseline data of 8 HIDS/MKD patients enrolled by December 2021 as well as preliminary 18-month data. Of these patients, 5 (63%) were females and median age at baseline was 8 years (2–39 years). The median duration of prior CAN treatment at baseline was 1.5 years (0–5 years). Standard, low, and high dose CAN treatment was evenly distributed at every interval.

Table 1. Baseline characteristics and interim analysis data of patients with HIDS.

	Baseline (N=8)	6 months (N=7)	12 months (N=6)	18 months (N=4)
Number (%) of patients in disease remission (physician assessment)	4 (50)	6 (86)	4 (67)	3 (75.0)
Physician assessment of disease activity, percentage of absent/mild-moderate/severe rating	37 / 50 / 13	71 / 29 / 0	50 / 33 / 17	50 / 50 / 0
Patient´s assessment of current disease activity; 0–10, median (min; max)	0 (0; 7)	2.0 (0; 7)	0.0 (0; 8)	0.0 (0; 0)
Patient´s assessment of current fatigue; 0–10, median (min; max)	2.5 (0; 7)	3.0 (0; 7)	1.0 (0; 4)	1.0 (0; 2)
Number (%) of patients without impairment of social life by the disease	3 (50)	4 (67)	4 (80)	1 (33)
Number (%) of patients with days absent from work/school during last 6 months	2 (25)	3 (43)	0 (0)	1 (25)
CRP, median (mg/dl)	0.2	0.5	0.3	2.1
SAA, median (mg/dl)	0.6	0.7	0.8	0.5
ESR, median (mm/h)	10.0	6.0	8.0	13.0

CRP, c-reactive protein; SAA, serum amyloid A; ESR, erythrocyte sedimentation rate

Preliminary results indicate stable remission and disease control by physicians´ and patients´ assessment as well as laboratory parameters (Table 1). In total, 4 patients were affected by adverse drug reactions, however, none of these events was classified as serious.

Conclusion: Baseline characteristics and preliminary data of HIDS/MKD patients from the RELIANCE study indicate good clinical and laboratory disease control and no unexpected safety concerns at the 18 months interim analysis.

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POS1377 LUNG INVOLVEMENT IN VEXAS SYNDROME

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Background: Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS) syndrome is a recently identified disorder caused by somatic mutations in the *UBA1* gene of myeloid cells. Various manifestations of pulmonary involvement have been reported, but a detailed description of lung involvement and radiologic findings is lacking.

Objectives: To describe lung involvement in VEXAS syndrome.

Methods: A retrospective cohort study was conducted of all patients identified at the Mayo Clinic with VEXAS syndrome since October 2020. Clinical records and chest high resolution computed tomography (HRCT) scans were reviewed.

Results: Our cohort comprised 22 white men with a median age of 69 years (IQR 62-74, range 57-84). Hematologic disorders including multiple myeloma, myelodysplastic syndrome and pancytopenia were present in 10 patients (45%), rheumatologic diseases including granulomatosis with polyangiitis, IgG4-related disease, polyarteritis nodosa, relapsing polychondritis, and rheumatoid arthritis were found in 10 patients (45%), and 4 patients had dermatologic presentations including Sweet syndrome, Schnitzer-like syndrome or drug rash with eosinophilia skin syndrome (DRESS). VEXAS syndrome-related features included fever (18, 82%), skin lesions (20, 91%), lung infiltrates (12, 55%), chondritis (10, 45%), venous thromboembolism (12, 55%), macrocytic anemia (21, 96%), and bone marrow vacuoles (21, 96%). Other manifestations observed were arthritis, scleritis, hoarseness and hearing loss. Median erythrocyte sedimentation rate (ESR) was 69 mm/1st hour (IQR 34.3-118.8) and median C-reactive protein (CRP) of 55.5 mg/dL (IQR 11.4-98.8). The somatic mutations affecting methionine-41 (p.Met41) in UBA1 gene were: 11 (50%) p.Met41Thr, 7 (32%) p.Met41Val, 2 (9%) p.Met41Leu, and 2 (9%) in the splice site. All patients received glucocorticoids (GC) (median duration of treatment was 2.6 years); 21 (96%) received conventional immunosuppressive agents (methotrexate, azathioprine, mycophenolate, leflunomide, cyclosporin, hydroxychloroquine, tofacitinib, ruxolitinib) and 9 (41%) received biologic agents (rituximab, tocilizumab, infliximab, etanercept, adalimumab, golimumab, abatacept). Respiratory symptoms included dyspnea and cough present in 21 (95%) and 12 (55%), respectively, and were documented prior to VEXAS diagnosis. Most of the patients were non-smokers (14, 64%) and obstructive sleep apnea (OSA) was present in 11 patients (50%). Seven patients (32%) used non-invasive ventilation, 6 used C-PAP, and 1 used Bi-PAP. Bronchoalveolar lavage (BAL) was available in 4 patients, and the findings were compatible with neutrophilic alveolitis in 3. Two patients had lung biopsies (2 transbronchial and 1 surgical) that showed ATTR amyloidosis and organizing pneumonia with lymphoid interstitial pneumonia, respectively. Pulmonary function tests were available in 9 (41%) patients and showed normal results in 5; 3 patients had isolated reduction in DLCO and 1 with mild restriction. On chest HRCT, 16 patients (73%) had parenchymal changes including ground-glass opacities in 9, septal thickening in 4, and nodules in 3; pleural effusions were present in 3 patients, air-trapping in 3 patients and tracheomalacia in 1 patient. Follow-up chest HRCT was available for 8 patients (36%), the ground-glass opacities resolved in 5 patients, 3 patients manifested new or increased ground-glass opacities, and 1 patient had increased interlobular septal thickening. After 1 year of follow-up, 4 patients (17%) had died; 3 due to pneumonia (2 COVID-19,1 bacterial) and 1 due to heart failure. VEXAS flares occurred in 18 patients (82%), the maximum number of relapses was 7, and they were mainly managed with GC and with changes in the immunosuppressive regimen.

Conclusion: Pulmonary involvement was documented by chest HRCT in most patients with VEXAS syndrome. Respiratory symptoms occurred in over one half of patients and about 20% had PFT abnormalities. The pulmonary manifestations of VEXAS are nonspecific and characterized predominantly by inflammatory parenchymal involvement.

Disclosure of Interests: None declared

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POS1378 ARTHRITIS IN PATIENTS WITH FAMILY MEDITERRANEAN FEVER

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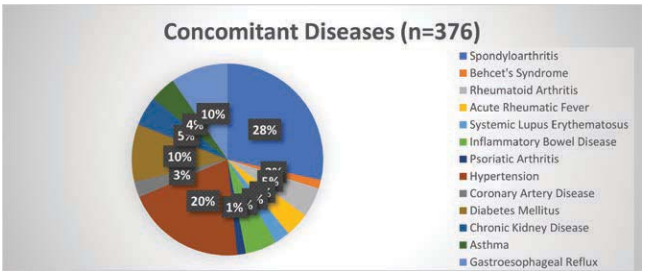
Background: Familial Mediterranean fever (FMF) is an inherited autoinflammatory disease characterized by recurrent episodes of fever and serositis. Arthritis is one of the most common attack manifestations. Arthritis in FMF is usually in the form of acute mono- or oligoarthritis of the large joints of the lower extremities. While acute attacks of arthritis usually heal without causing permanent deformity, the severe, long-lasting form of chronic arthritis can last for months or even years and result in permanent deformity.

Objectives: In this study, we described the characteristics of joint involvement in FMF in a single cohort.

Methods: The medical records of patients with joint involvement from our cohort of 2350 patients who were diagnosed with familial Mediterranean fever were retrospectively scanned through the files and hospital database. The prevalence, demographic information, genetic test results, clinical features, features of joint involvement, treatments and responses, acute phase values in the attack and remission periods, and family history of patients with joint involvement were recorded.

Results: 953 patients (n=953) from a total of 2350 patients had arthralgia or arthritis (40%). In our study, the male/female ratio was found to be

Table 1. Concomitant diseases of our FMF cohort



0.49 (male n=316, female n=637). The number of patients who underwent genetic testing was 787 (82%), and 702 (89%) of these patients had mutations in the MEFV gene. The most common pathogenic mutation is the M694V mutation with a rate of 43%. Concomitant diseases and their frequencies are shown in Table 1, the most common accompanying disease was spondylarthritis at a rate of 27%. Arthritis was present in the first attack in 55% (n=531), while arthritis was found in the ongoing attacks in 45%. The duration of the attack was between 24-96 hours in 77% (n=837) of the patients, and the duration was longer than 96 hours in 23% (n=116). The most common finding accompanying the attacks was exercise-related leg pain. Family history was present in 61% (n=580). 73% of the patients (n=696) were involved in the ankle and 51% were involved in the knee (n=492). The incidence of sacroiliitis was 14% (n=142). As for the number of joints, 91% of the patients had mono- and oligoarthritis. Asymmetric involvement was detected in 77% of the patients. Red arthritis was present in %73 of our study group. HLA-B27 was examined in 185 patients, 24 of them were positive (12%). It was found that 43% of the patients had treatment changes due to arthritis. Colchicine dose increases and changes were performed in 32% of these patients. NSAIDs were started in 21%, corticosteroids in 15%, DMARDs in 12%, anti-TNF in 10%, and anti-IL-1 in 8%. The mean dose of colchicine was as 1.56 ± 0.5 mg. Unresponsiveness to colchicine was found in 21% (n=122).

Conclusion: FMF diagnosis should definitely be considered in people with red mono-oligoarthritis in the large joints of the lower extremities. One of the most important features of joint involvement in FMF patients is the short duration of arthritis. The accompanying effort-related leg pain is an important symptom that should suggest FMF. In patients with a diagnosis of FMF and arthritis, the required colchicine dose in the treatment and the rate of colchicine unresponsiveness are higher than in other attack types. The incidence of sacroiliitis and spondyloarthropathy increases in patients with FMF, and joint involvement features are similar. FMF should be considered in the differential diagnosis of patients with inflammatory low back pain.

Disclosure of Interests: None declared

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POS1379 HYPERMETABOLIC BONE SARCOIDOSIS ON 18F-FDG PET-CT: IMPACT ON TREATMENT AND DISEASE RELAPSE IN A COHORT OF 165 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

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Background: Sarcoidosis is a multisystemic granulomatosis of unknown cause. Prevalence of bone sarcoidosis is estimated between 3 and 30%. Bone sarcoidosis is symptomatic in about half of the cases. 18F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) is a useful imaging modality in sarcoidosis, to search for a biopsiable site, evaluate organ involvement or assess disease activity. It is a sensitive imaging modality to detect bone involvement. However, clinical and prognostic significance of hypermetabolic bone involvement of sarcoidosis is not well known.

Objectives: The aim of this study was to compare the characteristics of patients with and without hypermetabolic bone involvement of sarcoidosis and to evaluate the impact of metabolic bone involvement on treatments and outcomes.

Methods: This was an observational, comparative, retrospective monocentric study of prospectively collected data. Inclusion criteria were a diagnosis of sarcoidosis according to the World Association of Sarcoidosis and Other Granulomatous diseases (WASOG) criteria and at least one 18F-FDG PET-CT during follow-up. Metabolic bone involvement of sarcoidosis was defined as bone hypermetabolism for which alternative causes had been reasonably excluded, following the WASOG criteria of « at least probable » bone sarcoidosis. Characteristics of patients with and without bone involvement were compared using bilateral Fisher or Mann-Whitney tests. Relapse-free survival curves were constructed following the Kaplan-Meier method and compared using a log-rank test. A p-value < 0.05 was considered significant.

Results: Among 503 patients with sarcoidosis, 165 with definite sarcoidosis who had undergone at least one 18F-FDG PET-CT were included. Fourteen patients had positive bone PET-CT findings which were attributed to other cause than sarcoidosis. Metabolic bone involvement of sarcoidosis was found in 29 patients (18%), among which 9 (31%) had structural bone lesions on CT. Metabolic bone involvement of sarcoidosis was associated with more frequent intrathoracic lymph node involvement (28 [96%] and 107 [79%], $p < 0.001$), extrathoracic lymph node involvement (15 [52%] and 40 [30%], $p = 0.03$) and a higher number of organ involvements (median [interquartile range], 6 [4-7] and 4 [2-5], $p < 0.001$). Patients with metabolic bone involvement received more frequently corticosteroids (29 [100%] and 99 [73%], $p < 0.001$), methotrexate (26 [90%] and 66 [48%], $p < 0.001$), tumor necrosis factor (TNF) alpha inhibitors (22 [76%] and 41 [30%], $p < 0.001$), and a higher number of treatments (3 [3-4] and 2 [1-3], $p < 0.001$). Despite more intensive treatments, disease relapse occurred significantly sooner in patients with metabolic bone involvement of sarcoidosis (median time to the first relapse, 63 [44-84] months and 96 [72-156] months respectively, $p = 0.01$).

Conclusion: Metabolic bone involvement on PET-CT was present in 18% of patients with sarcoidosis. It was predominantly axial and without structural lesions. In this comparative study, patients with metabolic bone involvement received significantly more treatments and had a shorter time to relapse. It could therefore reflect a more severe multisystemic involvement and chronic evolution of the disease. This could help adjust individual therapeutic strategy for patients with sarcoidosis.

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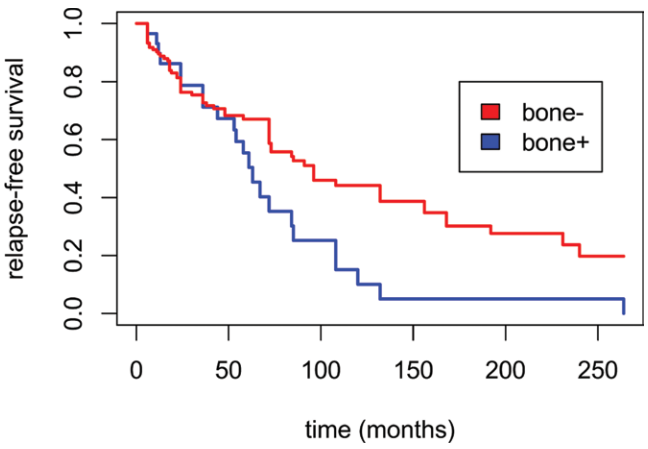

Figure 1.

Disclosure of Interests: None declared

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Diagnostics and imaging procedures

POS1380 AUTOANTIBODIES ARE ASSOCIATED WITH EROSIVE DAMAGE IN THE SECOND AND THIRD METACARPOPHALANGEAL JOINTS ASSESSED BY HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: The presence of anti-citrullinated protein antibodies (ACPAs) and rheumatoid factor (RF) are prognostic for erosive severity by radiography in patients with rheumatoid arthritis (RA) [1]. However, others have shown that RF mainly acts as an enhancer for ACPAs mediated bone loss [2]. High-resolution peripheral quantitative computed tomography (HR-pQCT) has a very high resolution with a voxel size of 82 μm^3, and has been proposed to monitor disease activity in patients with RA. In the current study, erosive damage was assessed by HR-pQCT according to the presence of autoantibodies. The hypothesis is that the presence of RF and especially ACPA is associated with erosive damage in two metacarpophalangeal (MCP) joints assessed by HR-pQCT; this has previously been shown using 44 joints assessment of both hands and feet by conventional radiography.

Objectives: The objective was to investigate if the presence of the autoantibodies, RF and ACPAs, was associated with a higher erosive burden in two MCP joints assessed by HR-pQCT.

Methods: Patients with RA and disease duration ≥ 5 years had their second and third MCP joints imaged by HR-pQCT. Age, sex, disease duration, ACPAs and RF status were acquired. From the Danish Clinical Quality Program – The Danish Rheumatologic Database (DANBIO) [3], the average 28-joint Disease Activity Score (DAS28-CRP) and Health Assessment Questionnaire (HAQ) from five years before inclusion were extracted. Statistical significance was investigated for the following groups, who were ordered according to the expected erosive burden: RF+/ACPA+ patients, RF-/ACPA+ patients, RF+/ACPA- patients, and autoantibodies negative patients. Analysis of variance was used to investigate the difference between the groups for age and sex. Cuzick's Rank-sum test for trend of ordered groups was used to test for trend for disease duration, 5-year average HAQ, 5-year average DAS28, number of erosions, total erosive volume, and average erosion volume.

Results: A total number of 353 patients with RA were included in this study. 203 was RF+/ACPA+ positive, 52 was RF-/ACPA+ positive, 24 were RF+/ACPA- positives, and 74 were autoantibodies negative. The groups were comparable with respect to age, sex distribution, disease duration and mean disease activity during the last five years, according to mean DAS28-CRP and mean HAQ during the previous five years.

There was a statistically significant test for trend for total erosive volume (p = 0.016) and average erosion volume (p = 0.043), but not for the number of erosions (p = 0.053) (Figure 1). A significant difference between the groups was only observed between double-positive patients and patients negative for autoantibodies.

Conclusion: In the current study, HR-pQCT scanning of only two MCP joints supports previous findings by radiography of both hands and feet, showing the accumulated erosive burden is higher in patients double-positive for RF and ACPA.

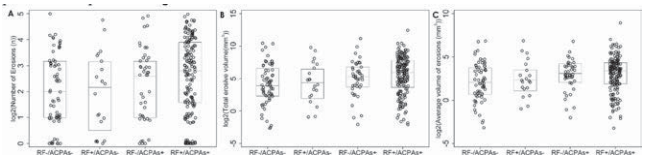

Figure 1. Scatterplot showing the number of erosions (A), total erosive volume (B) and the average volume of erosions (C) in the second and third MCP joint per patient according to the presence of the autoantibodies, ACPAs, as well as RF. Boxes denote the median and 25th and 75th percentile of the groups.

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POS1381 ULTRASONOGRAPHIC EVALUATION OF ENTHESOPATHY IN IDIOPATHIC DIFFUSED SKELETAL HYPEROSTOSIS. APPLICABILITY OF THE MASEI INDEX

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Background: In Diffuse idiopathic Skeletal Hyperostosis (DISH) o Forestier-Rotés disease the enthesis is also the hallmark of extraspinal manifestations. Despite being a characteristic hallmark of the disease, it has been poorly investigated.

Objectives: To assess the usefulness of the Madrid Sonographic Enthesitis Index (MASEI) to classify patients with DISH and to analyse the ultrasound findings in hyperostotic entheses.

Methods: We recruited 35 patients with DISH, according to Resnick classification criteria, who were compared with 33 healthy patients age, sex and body mass index-matched. An ultrasound was performed strictly following the MASEI protocol. The ultrasound examiners, with extensive experience in musculoskeletal ultrasound (ECOCAT group), were blinded to the diagnosis of the patients. The interobserver reliability of MASEI index measured by an ICC was 0.97 (95%, CI 89-99) [1]. Demographic, cardiovascular risk factors, clinical, radiological and MASEI-related variables were collected. We categorized into MASEI- inflammatory (MASEI-I) and MASEI-damage (MASEI-D) as previously published [2] but also into MASEI-DISH, which included the variables of thickness, structure and calcification. In the statistical analysis, patients' data were depicted by using descriptive statistics and the comparison between groups with the Chi-square test for categorical variables and the T-Student test for numerical variables. The validity of the index was examined using the area under the ROC curve and its corresponding 95% confidence interval (CI). The optimal cut-off point was defined as the one that maximizes sensitivity (S) and specificity. (Spe). The statistical program used was R software.

Results: In the analysis of the elemental lesions, the alterations in structure, thickness and calcification of the distal quadriceps (DQT) and Achilles tendons (AQT) stood out (p <0.05). In the total MASEI, the ultrasound score of ≥ 16.50 (S80%, Spe 85%), obtained with an AUC of 0.877 (95% CI, 0.79 to 0.96), was the best cut-off to differentiate patients from healthy subjects. In the categorized indices, MASEI-I: cut-off 5.50 (S 89%, Spe 76%) and AUC 0.835 (95% CI 0.73 to 0.94); MASEI-D: 7.50 (S 86%, Spe 76%) and AUC 0.850 (95% CI, 0.75 to 0.94) and MASEI-DISH: 16.50 (S 74%, Spe 91%) and AUC (95% CI 0.76 to 0.95).

The total MASEI in the DISH group was 27.46 (SD 14.4) compared to 10.30 (SD 6.4) in healthy controls (p<0.001) as well as in those categorized as MASEI-I, MASEI-D or MASEI-DISH (p <0.001).

Conclusion: Entheses lesions of the AQT and the DQT mark the differences between DISH and healthy patients. The optimal cut-off point was 16.50, and we did not observe any advantages in establishing MASEI categorizations that could be useful in clinical practice. Although the MASEI is an index designed to classify patients with spondyloarthritis, our study shows that it also allows differentiating DISH patients from healthy subjects. It would also be interesting to analyse the capacity of the MASEI to distinguish DISH from spondyloarthritis.

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POS1382 AN OVERVIEW OF NAILFOLD CAPILLAROSCOPY IN ITALY: RESULTS FROM A NATIONAL SURVEY

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Background: In May 2020, the executive committee of the Italian Society of Rheumatology (SIR) endorsed the Italian study group (SG) on capillaroscopy and microcirculation in rheumatic diseases (CAPSIR) that first convened at the virtual annual meeting the same year. Nowadays capillaroscopy is a well-established, non-invasive technique with useful clinical applications in the assessment of connective tissue diseases (CTDs) [1] and mandatory for the differential diagnosis of Raynaud's phenomenon (Rp) [2]. Despite growing interest in the use of this imaging technique in clinical and research settings, data on its current usage to assess microcirculation in rheumatic diseases in Italy are not available.

Objectives: To obtain an insight into the current utilization of capillaroscopy in the assessment of rheumatic patients in the Italian clinical setting.

This survey aimed: 1) to obtain an overview on the usage of capillaroscopy in rheumatological clinical practice in Italy, and 2) to gauge expert's attitudes on factors influencing its use and the potential critical issues.

Methods: This online survey was devised to evaluate the opinions of the members of the SIR about nailfold capillaroscopy. It was designed with the contributions of the steering committee of CAPSIR SG, and emails with a link to the survey were sent to physicians affiliated with the SIR between July and August 2021 on behalf of the CAPSIR SG. At the beginning of the survey, the physician most experienced in capillaroscopy was asked to complete the questionnaire on behalf of his/her center. Questions were about the use of this technique in clinical practice and its critical issues. Data were reported with a descriptive analysis.

Results: One hundred and one centers, with at least one representative for each of the twenty Italian Region, completed the survey. 51.5% of respondents were in non-university hospitals, and 70 (69.3%) centers perform more than 100 capillaroscopy per year. The respondents were mainly practicing capillaroscopy for more than 5 years (85%) and gained certification of national or international dedicated training courses (84%). 43% of respondents had at least one scientific publication on this topic. Videocapillaroscope with 200X magnification was the most used instrument (91%). In public health services, the waiting time to schedule capillaroscopy is less than 3 months in 62.4% of centers. The survey has identified attitudes toward the use of capillaroscopy in the assessment and management of CTDs. In the screening phase of Rp, it is performed every 12 (mean value) months in patients with antinuclear antibodies (ANA) negative and every 6 months for those with positive ANA. Capillaroscopy is performed every 12 months (mean value) as part of the staging of CTDs (including systemic sclerosis). In more than 60% of centers, there is no specific diagnostic program for the screening of Rp and there is no connection with the general practitioners. 70% of the centers use capillaroscopy to follow the effect of therapies at least in systemic sclerosis.

Conclusion: At least one center for each Italian Region participated in this national survey, thus ensuring good geographical coverage. Moreover, the personnel who perform the exam had certified training and experience thus supporting the reliability of results. This survey indicates that the Italian public health system allows an acceptable waiting time to schedule the exam (less than 3 months). Italian Rheumatologists prescribe capillaroscopy as part of the clinical routine in the screening of Rp and as part of the annual checkup of CTDs. Critical issues remain the lack of a specific program and network with the general practitioners. To have a wider vision on this topic, our survey could be further extended to other European countries.

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POS1383 DIFFERENTIAL DIAGNOSTICS OF POLYMYALGIA RHEUMATICA IN A UNIVERSITY HOSPITAL IN FINLAND

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Background: Polymyalgia rheumatica (PMR) is an inflammatory disease that causes muscle pain and morning stiffness, especially in the shoulders and hips. Diagnosing PMR can be difficult, as the diagnosis is mainly clinical without a definitive diagnostic test, and many symptoms and findings of PMR may also be present in other conditions. There is little recent data on differential diagnostics of PMR.

Objectives: The aim of our study was to analyse patients diagnosed with polymyalgia rheumatica (PMR) in Turku University Hospital in Finland and determine how often a competing diagnosis better explaining the patients' symptoms was found during further evaluation and clinical follow-up. We also aimed to find out what are the most common conditions initially misdiagnosed as PMR.

Methods: All patients with a new primary diagnosis of PMR (International Classification of Diseases – 10th revision [ICD-10] code M35.3) on at least one (in- or outpatient) visit during years 2016–2019 were identified from the hospital discharge register of Turku University hospital in Finland. We did a chart review of the patient charts including the full clinical follow-up period (median 34 months). We studied how often the primary diagnosis of PMR changed after further diagnostic evaluation or during follow-up.

Table 1. Demographic and clinical characteristics of the study sample.

Number of patients	382
Female (%)	218 (57.1%)
Age at diagnosis in years [IQR]	70.0 [64.0–77.8]
Follow-up in months [IQR]	34.0 [21.0–49.0]
Diagnosed in rheumatology (%)	299 (79%)
Treated in rheumatology (%)	310 (81%)
Nr. of visits [IQR]	6.5 [3.0–12.0]
Diagnosis changed during follow-up (%)	125 (32.7%)
Final diagnosis in 125 patients whose initial diagnosis of PMR changed	
Inflammatory arthritides (%)	45 (36.0%)
Degenerative or stress-related musculoskeletal disorder (%)	16 (12.8%)
Infection (%)	12 (9.6%)
Malignancy (%)	12 (9.6%)
Giant cell vasculitis (%)	8 (6.4%)
Other vasculitis (%)	8 (6.4%)
Other rheumatological disease (%)	7 (5.6%)
Fibromyalgia or other chronic pain syndrome (%)	4 (3.2%)
Gout or other crystal arthropathy (%)	2 (1.6%)
Endocrinological disease (%)	2 (1.6%)
Other or unknown (%)	14 (11.2%)

Continuous variables are expressed as medians with interquartile ranges, and categorical variables are described as counts with percentages.

Results: In 125 (32.7%) of the 382 patients, the initial diagnosis of PMR changed during further diagnostic evaluation or follow-up. Most common diagnoses initially misdiagnosed as PMR were inflammatory arthritides 36.0% (45/125), degenerative or stress-related musculoskeletal disorder 12.8% (16/125), infection 9.6% (12/125), malignancy 9.6% (12/125), giant cell vasculitis 6.4% (8/125) and other vasculitis 6.4% (8/125) (Table 1). Diagnosis changed in 19% (39/207) of patients fulfilling the 2012 ACR/EULAR PMR classification criteria and in 49% (86/175) of patients who did not.
Conclusion: In a university hospital setting, a third of initial diagnoses of PMR were changed during further evaluation and follow-up. Our findings highlight that thorough consideration of differential diagnosis is always essential when diagnosing PMR. Especially in patients with atypical presentation, there is a substantial risk for misdiagnosis.
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POS1384 NON-INVASIVE IN VIVO METABOLIC PROFILING OF INFLAMMATION IN JOINTS AND ENTHESES BY OPTOACOUSTIC IMAGING

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Background: An in-depth metabolic characterization of joints and entheses at the tissue level can help in the early diagnosis and treatment selection for patients with inflammatory arthritis [1]. However, current knowledge about the metabolic profiles of synovitis and enthesitis is limited. Multispectral optoacoustic tomography (MSOT), a novel metabolic imaging technology, could be used to undertake metabolic profiling of joints and entheses non-invasively using near-infrared multispectral laser to stimulate tissues and detect the emitted acoustic energy, enabling quantification of tissue components in vivo based on differential absorbance at multiple wavelengths [2, 3].
Objectives: To explore the metabolic characteristics of arthritis and enthesitis using MSOT.
Methods: We performed a cross sectional study on healthy controls (HC) and patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) (Table 1). Participants underwent clinical, ultrasound (US), and MSOT examination of metacarpophalangeal joints, wrists, entheses of lateral epicondyles, patellar, quadriceps and Achilles tendons. MSOT-derived hemoglobin, oxygen saturation, collagen and lipid levels were measured. We calculated scaled mean differences (SMD) between affected and unaffected joints and entheses as defined by clinical examination or US using linear mixed effects models.
Results: We obtained 1535 MSOT and 982 US scans from 87 participants (36 HC, 34 PsA, 17 RA). Entheseal tenderness was not associated with metabolic changes, whereas US enthesitis was associated with increased total hemoglobin, oxygen saturation and collagen content. In contrast, clinical and US arthritis showed increased hemoglobin levels but reduced oxygen saturation and reduced collagen content. Synovial hypertrophy was associated with increased lipid content in the joints (Figure 1).
Conclusion: MSOT allows a non-invasive characterization of metabolic changes in arthritis and enthesitis. These findings can be interpreted as a reflection of increased synovial cellularity, collagen degradation, and metabolic demand in synovitis, and of an increased tissue apposition and vascularization in enthesitis. Our results suggest that synovitis and enthesitis do not only differ at the clinical and anatomical-functional level, but also exhibit divergent metabolic changes.
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Conflict of Interest: AR., FK, MW are co-inventors, together with iThera Medical GmbH, Germany on an EU patent application (no. EP 19 163 304.9) relating to a device and a method for analysis of optoacoustic data, an optoacoustic system and a computer program. All other authors declare no conflict of interest.

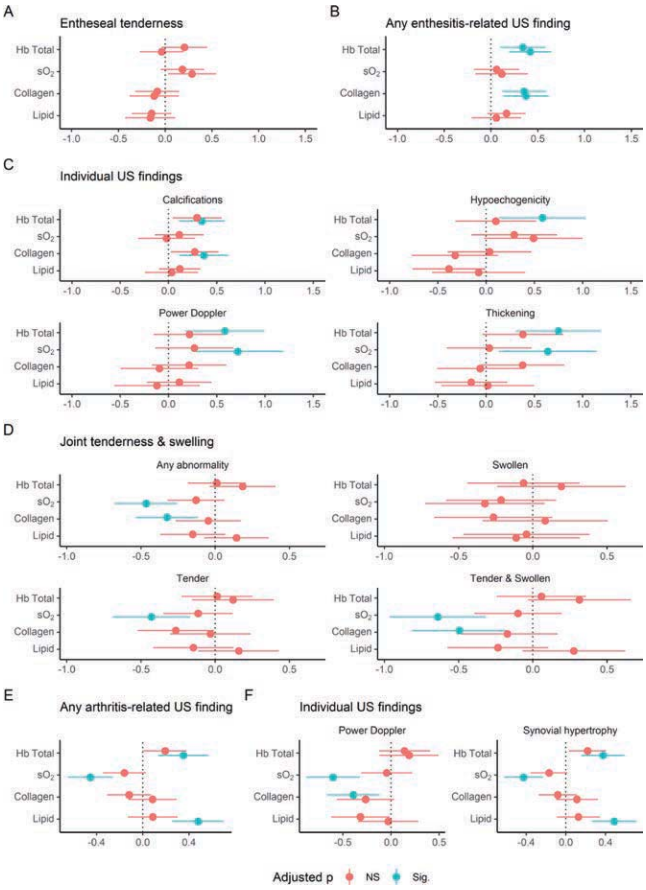

Figure 1. Scaled differences and 95% confidence intervals of MSOT-measured metabolite values by clinical and ultrasonographic findings of enthesitis (A-C) and arthritis (D-F). Two differences are plotted for each metabolite indicating two multispectral processing algorithms used for estimation. P values were adjusted for multiple testing using a false discovery rate of 5%. NS, not significant. sO_2, oxygen saturation.

Table 1. Baseline characteristics.

	Overall	Healthy	PsA	RA
N	87	36	34	17
Age, mean (SD)	47.0 (15.7)	34.7 (12.0)	52.4 (11.5)	62.5 (9.1)
Sex, n (%)				
Female	48 (55.2)	18 (50.0)	17 (50.0)	13 (76.5)
Male	39 (44.8)	18 (50.0)	17 (50.0)	4 (23.5)
Tender joints, median (IQR)	0 (0-2)	0 (0-0)	1 (0-5)	2 (1-6)
Swollen joints, median (IQR)	0 (0-1)	0 (0-0)	0 (0-2)	2 (1-6)
Tender entheses, median (IQR)	0 (0-2)	0 (0-0)	1 (0-3)	0 (0-0)
csDMARD, n (%)	22 (25.3)	-	13 (38.3)	9 (53.0)
b-tsDMARD, n (%)	31 (35.6)	-	20 (58.8)	11 (64.7)

SD, standard deviation; IQR, interquartile range; csDMARD, conventional synthetic disease modifying anti-rheumatic drug; b-tsDMARD, biologic or targeted synthetic disease modifying anti-rheumatic drug.

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POS1385 INTERNATIONAL CONSENSUS FOR ULTRASOUND DEFINITIONS OF TENOSYNOVITIS IN JUVENILE IDIOPATHIC ARTHRITIS: RESULTS OF A DELPHI PROCESS

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Background: Musculoskeletal Ultrasonography (US) is a suitable tool for the clinical assessment in juvenile idiopathic arthritis (JIA). Recently US definitions for normal components of pediatric joints and synovitis have been developed by the OMERACT US working group. Currently this group is working on development and validation of US definition for tenosynovitis as it is also an essential prerequisite for the reliable use of this technology in the pediatric age group.
Objectives: To produce consensus-based definitions for US tenosynovitis in JIA through a Delphi process.
Methods: We undertook a Delphi process on US-defined tenosynovitis in children that consisted of two steps. As a prior systematic literature review showed that US anatomy of the tendons is similar to adults, a Delphi questionnaire was written based on the consensual definitions developed for and used in adults with rheumatoid arthritis [1, 2]. The Delphi questionnaire was sent to rheumatologists and pediatricians who perform pediatric US examination, asking them to rate their level of agreement with each statement of US-defined tenosynovitis. Group agreement was considered if ≥80% of responders scored an item as either 4 or 5.In the second step, the definitions were validated on 88 standardized US images displaying various degrees of tenosynovitis obtained from JIA patients at various ages. Tendons often involved in JIA were selected (foot and ankle tendons, hand and wrist tendons, bicep tendon.). US images of both normal and tenosynovitis elementary lesions were collected by the 18 experts participating in the OMERACT US task force on pediatric tenosynovitis. An agreement ≥70% was considered mandatory for accepting the definition as applicable in the rated image.
Results: The response rate was 75% (28 out of 37) from the first Delphi questionnaire. Strong group agreement (≥86%) was obtained for the US definitions tested. The response rate was 88.9% (16 out of 18) from the Web-exercise after four rounds. The final definitions were validated on still images for all tendons, except for the biceps tenosynovitis in the age group 2-4 years (the definitions of elementary lesions and the global definition of tenosynovitis) as no image was available for this location and age group. Despite not reaching group agreement after the second and the third round for the US-defined normal finger pulley in children aged 8 years and younger (roughly 68% and 69% respectively), it reached a score of 99.8% after the fourth round.
Conclusion: US definitions of tenosynovitis and its elementary components covering a wide pediatric age range were successfully developed through a Delphi questionnaire and validated in a web-based still images exercise. These results provide the basis for the standardized US assessment of tenosynovitis in clinical practice.
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POS1386 THE OCCURRENCE OF INFUSION-RELATED REACTIONS TO RITUXIMAB IS ASSOCIATED WITH LOW PLASMA LEVELS OF MYELOPEROXIDASE-DNA COMPLEXES.

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Background: Rituximab (RTX), a chimeric anti-CD20 antibody, is used in the treatment of rheumatic diseases. Infusion-related reactions (IRRs) are the most common adverse event, and premedication may reduce the incidence [1]. To date, there is still no effective predictor for the occurrence of IRRs.
Objectives: To identify factors predicting the occurrence of IRRs during the first course of RTX therapy in patients with rheumatic diseases.
Methods: We prospectively enrolled 29 patients with rheumatic diseases underwent the first course of RTX infusion, which consisted of two 500-mg intravenous infusions separated by about 2 weeks. Each patient received 100 mg intravenous methylprednisolone 60 minutes prior to each RTX infusion. Complete blood counts and C-reactive protein tests were performed before each infusion. The plasma levels of IL-1β, IL-6, IL-8, TNF-α, B-cell activating factor (BAFF) and plasma levels of myeloperoxidase (MPO)-DNA complexes were measured. All-grade IRRs occurring within 24 hours after infusions were recorded. Mann-Whitney U test was conducted to analyze factors associated with IRRs.
Results: The demographics and characteristics of the patients were shown in Table 1. Two patients reported IRRs in the first infusion, and three patients had IRRs in the second infusion of the first course. Among the five IRRs, four were skin rashes and one was headache. No serious events were found. A significant association between the low levels of MPO-DNA complexes and IRRs in the second infusion was noted (p = 0.011). The low plasma levels of MPO-DNA complexes also tended to be associated with the occurrence of IRR in the first infusion. The IRRs were not significantly correlate with absolute neutrophil counts, absolute lymphocyte counts, and the plasma levels of IL-1β, IL-6, IL-8, TNF-α, and BAFF.

Table 1. The characteristics of the patients received the first course of RTX treatment (n = 29).

Age (years)‡	44.9 (38.4 to 50.9)	
Gender, female (%)	26 (89.7)	
Diagnosis		
Antiphospholipid syndrome, n (%)	11 (37.9)	
Autoimmune thyroid disease, n (%)	6 (20.7)	
Sjögren's syndrome, n (%)	4 (13.8)	
Systemic lupus erythematosus, n (%)	2 (6.9)	
Rheumatoid arthritis, n (%)	1 (3.4)	
Others, n (%)#	5 (17.2)	
Blood test during each infusion	Before first infusion	Before second infusion
MPO-DNA complexes levels‡¶	11% (3% to 53%)	15% (3% to 32%)
IL-6 (pg/mL)‡	8.3 (6.9 to 11.2)	12.1 (8.5 to 13.8)
IL-8 (pg/mL)‡	14.4 (12.6 to 15.9)	13.0 (12.1 to 14.9)
TNF-α (pg/mL)‡	8.9 (6.9 to 12.7)	8.1 (6.1 to 11.2)
BAFF (pg/mL)‡	155.1 (121.3 to 231.9)	276.8 (201.3 to 331.2)
IL-6 (pg/mL)‡	8.3 (6.9 to 11.2)	12.1 (8.5 to 13.8)
Absolute neutrophil count (/μL) ‡	4380 (3441 to 5890)	4360 (3286 to 8195)
Absolute lymphocyte count (/μL) ‡	1511 (1198 to 1799)	1214 (854 to 1465)
C-reactive protein (mg/dL) ‡	0.03 (0.01 to 0.10)	0.04 (0.02 to 0.21)

‡ Data are presented in median and interquartile range.# Other diagnoses include systemic sclerosis, dermatomyositis, vasculitis, pemphigus, myasthenia gravis.¶ Data are presented in ratio to positive control.

Conclusion: Plasma MPO-DNA complexes represent neutrophil extracellular traps released by activated neutrophils. Neutrophils could be involved in the response to RTX therapy [2]. In this study, the risk of IRRs to RTX tended to increase when the plasma level of MPO-DNA complexes is low. Further research is needed to clarify the impact of activated neutrophils on RTX therapy.
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POS1387 ULTRASOUND FINDINGS OF JOINTS AND ENTHESES FOLLOWING ONE HOUR OF AGE AND GENDER ADJUSTED WEIGHT TRAINING

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Background: Joint effusion and enthesitis are common ultrasound findings in rheumatologic diseases like rheumatoid arthritis or spondyloarthritis. Physically active individuals and athletes were also found to exhibit structural and vascular changes in their entheses, as well as joint effusion through different imaging approaches [1, 2].
Objectives: The aim of this study was to evaluate the development of joint and entheseal ultrasound findings in large and medium joints of young healthy individuals after one hour of standardised weight training.
Methods: A total of three musculoskeletal ultrasound examinations were performed in healthy individuals under the age of 30 years. The first examination was carried out before the individuals conducted one hour of standardized weight training, the second examination 24 hours later and the third examination 48 hours later. The examination comprised shoulder, elbow, wrist, hip, knee, and ankle joints, as well as associated entheseal sites. Poisson mixed effects models were applied to analyse the development of the ultrasound findings within 48 hours after the weight training.
Results: Fifty-one healthy individuals with a mean age of 23.7 years (± 2.5, range: 19-30) (52.9% female) were enrolled in this study. Fourteen participants (27.5%) presented with at least one abnormal enthesis at baseline, increasing to 24 (47.1%) after 24 hours and to 29 (56.9%) 48 hours after the weight training. Hyperperfusion was the only entheseal pathology detected by ultrasound after the training.
The number of individuals with at least one joint effusion increased from 37 (72.6%) at baseline to 45 (88.2%) after 24 hours and to 48 (94.1%) 48 hours after the weight training. The Poisson mixed effects models showed a significant increase of the number of joints with effusion and entheses with pathologies with time after the weight training ($p < 0.001$, Exp(b) = 1.63 and $p < 0.001$, Exp(b) = 1.58).
Conclusion: Prevalence of joint effusion in large and medium joints as well as the prevalence of entheseal pathology increase significantly within 48 hours after one hour of weight training. As a result, the individual's physical activity should be considered when performing a musculoskeletal ultrasound examination.
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Disclosure of Interests: None declared
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POS1388 CLINICAL RELEVANCE OF ANTI-SSA ANTIBODIES: A SINGLE-CENTRE EXPERIENCE

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Background: Anti-Ro/SSA antibodies are directed against different proteins of intracellular small ribonucleic acid (RNA)-protein complexes, Ro60 (60 kDa) and Ro52 (52 kDa) and are the most frequently detected autoantibodies in patients´ sera. The clinical associations with antibodies to the Ro60 protein is well documented and includes systemic lupus erythematosus (SLE) and Sjögren syndrome (SS). [1]The presence of anti-Ro52 antibodies has been reported in a large variety of diseases, such as neoplastic diseases or viral infections [1, 2].
Objectives: The aim of this study was to analyze the clinical relevance and the disease phenotype of patients with anti-Ro52 and/or anti-Ro60 autoantibodies in a single portuguese tertehospital.
Methods: Retrospective and descriptive study included all patients screened for anti-nuclear antibodies (ANA) in the database of the immunology laboratory of our Hospital between 2017 and 2021. Only adult patients (≥ 18-years-old) with positive anti-Ro52 and/or Ro60 were included in the study and divided into three groups: group 1 – Ro52+/Ro60-, group 2 – Ro52+/Ro60+ and group 3 – Ro52-/Ro60+. The presence of ANA was tested by indirect immunofluorescence (threshold of positivity established at titer 1/160) and further screened for anti-extractable nuclear antigen (ENA) antibodies. Socio-demographic and clinical data were collected. Descriptive analysis was performed, p-value≤0.05 was statistically significant.
Results: Among 1210 patients, 277 were positive for the antibody anti-Ro52 and/or Ro60. Most of the patients included were women (79.8%) with a mean age of 58.87±16.12. Immune-mediated rheumatologic diseases were diagnosed in 173 (62.5%) patients, while 104 (37.5%) had non-rheumatologic disease. About 38.6% were exclusively anti-Ro52 positive, 30.3% of patients were anti-Ro60 positive alone and 31% tested positive for both. The clinical data of the patients in these three groups is represented in Table 1. In each of the three groups, the most frequent pattern was nuclear fine speckled (AC-4). In group 2, SS was the most frequent diagnosis (46.5%), followed by SLE (19.6%). Regarding ANA titers, a higher amount was observed in this group ($p<0.05$). The most frequently associated autoantibodies were anti-La (15.1%). In group 3, the diagnosis of SS was the most frequent (23.8%) followed by undifferentiated connective tissue disease (16.7%). Lupus anticoagulant (7.1%) and anti-RNP (6.0%) were more represented in this group. Finally, in group 1, non-rheumatologic disease was the most represented group of disease. In the case of SLE and systemic sclerosis, there were no statistically significant differences between the three groups and the different types of organ involvement. In SS, sicca symptoms were more prevalent in group 2, with statistically significant differences between the groups (p=0.027).

Table 1.

	Group 1 Ro52+/ Ro60- (n=107)	Group 2 Ro52+/ Ro60+ (n=86)	Group 3 Ro52-/ Ro60+ (n=84)	*p*
Immune-mediated rheumatologic diseases (n)	**51**	**69**	**53**	**0.004**
Systemic lupus erythematosus	10	16	7	0.396
Sjögren syndrome	21	40	20	**0.050**
Systemic sclerosis	2	1	2	0.618
Inflammatory myositis	4	0	1	**0.024**
Rheumatoid arthritis	9	2	7	**0.020**
Undifferentiated connective tissue disease	4	9	14	**0.025**
Other diseases	1	1	2	0.824
Non-rheumatologic disease (n)	**56**	**17**	**31**	0.369
Infections	3	1	2	0.978
Neoplasms	7	2	1	0.319
Liver cirrhosis	6	2	8	0.178
Interstitial lung disease	2	0	2	0.637
Chronic kidney disease	2	0	1	0.736
Unclassified	36	12	17	0.444

Conclusion: In line with published studies, our work demonstrated that, among the sera tested, autoreactivity to anti-Ro52 alone was the most often observed and in most patients the presence of this antibody alone was not associated with immune-mediated rheumatologic disease, but mainly with malignancies. We also identified the clinical phenotype of patients with positive anti-Ro52 and/or anti-Ro60. Thus, we reinforce the importance of specific detection such as Ro-52 or Ro60 as they present individual diagnostic utility.
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POS1389 SUGGESTION OF OPTICAL SPECTRAL TRANSMISSION IMAGING (HANDSCAN) CUT-OFF VALUES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CORRELATIONS WITH CLINICAL AND LABORATORY DISEASE ACTIVITY MARKERS.

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Background: Optical spectral transmission (OST) is a modern diagnostic modality able to assess the blood-specific absorption of light transmitted through a tissue, promising quantification of inflammation in the finger and wrist joints of

patients with rheumatoid arthritis (RA) (HandScan -Demcon/Hemics, The Netherlands). Early data on OST revealed both correlations with clinical and arthrosonographic activity markers of RA, as well as a high diagnostic value during disease follow-up [1-3]. However, in a previous work we could detect and describe several OST confounding factors that complicate the establishment of universal cut-off values [2].

Objectives: Aim of this study was to examine and suggest OST-cut-off values after adjusting for the effect of statistically identified confounding factors. Moreover, we sought to describe a clinical model that would represent the probability of a positive RA diagnosis on the basis of OST values and presence of confounders in every individual patient.

Methods: Newly diagnosed RA patients (ACR-EULAR Classification Criteria 2010) were examined by OST and compared with healthy controls. Moreover, RA patients underwent clinical (tender & swollen joint counts, DAS28) and laboratory (inflammation markers) examinations. To identify factors that could have a confounding effect on OST, we performed logistic multivariate regression analyses, taking into account patient-associated characteristics such as age, gender, BMI, hand size, nicotine use. After identifying confounders, we determined OST cut-offs for different patient categories. In addition, we calculated the probability of the presence of an RA-diagnosis, based on the measured OST value and the presence of the identified influencing factors. Finally, we examined correlations of OST with clinical and laboratory RA activity parameters.

Results: 74 early RA patients [64%♀; median age 59 years (53-70, IQR); median DAS28 4.58 (3.5-5.3, IQR)] and 101 controls [80%♀; median age 45 years (35-56, IQR)] were recruited. Male gender and advanced age were statistically identified as OST influencing factors. Receiver operating characteristics (patients vs. controls) revealed an OST cut-off value of 11.2 (sensitivity 85%, specificity 72%) for female and an OST cut-off of 16.07 (sensitivity 75.7%, specificity 72.7%) for male patients. Two models were shown to be statistically appropriate for calculating the probability of the presence of RA based on the measured OST values and confounders: one model with included age for females and one model with included age and smoking status for males (Table 1). OST showed statistically significant moderate correlations with DAS28 (r=0.42, p<0.001), swollen joint count (r=0.437, p<0.001), VAS (r=0.355, p=0.002) and a weak significant correlation with CRP (r=0.23, p=0.045).

Table 1. Statistical models for calculating the probability of the presence of rheumatoid arthritis based on measured OST values and OST confounding factors.

Statistical model
Women $P(RA)=\frac{e^{(-7.85+(0.057xX_1)+(0.347xX_2)}}{1+e^{(-7.85+(0.057xX_1)+(0.347xX_2)}}$
Men $P(RA)=\frac{e^{(-7.561+(0.109xX_1)+(0.113xX_2)+(2.53xX_3)}}{1+e^{(-7.561+(0.109xX_1)+(0.113xX_2)+(2.53xX_3)}}$

OST: optical spectral transmission; P(RA): probability of RA diagnosis X1 for age, X2 for OST; X3 for nicotine use

Conclusion: The establishment of OST cut-off values adjusted for confounding factors and the suggested statistical models could contribute to an increase of the diagnostic value of HandScan and assist clinicians during patient screening. To our knowledge, this is the first report in the literature on the specific topic. Further patient recruitment and research regarding additional confounders are currently taking place with the aim of improving the diagnostic capabilities of this new and promising diagnostic technology.

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POS1390 **ULTRASOUND BASED WITHDRAWAL OF BIOLOGICS IN RHEUMATOID ARTHRITIS (RA-BIOSTOP)**

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Background: Discontinuation of biological (b)DMARDs may be considered in rheumatoid arthritis (RA) patients in persistent clinical remission [1]. Some earlier studies reported that baseline ultrasound may predict successful tapering or withdrawal of bDMARDs, while others found that ultrasound had little additional value over clinical parameters alone [2-4]. The majority of these studies, however, were limited by small sample size, inadequate remission criteria and variable tapering regimens.

Objectives: To test the hypothesis whether ultrasound-verified subclinical inflammation might predict a relapse in RA patients in stringent clinical remission who discontinue bDMARDs.

Methods: Prospective, phase IV clinical trial including RA patients in persistent clinical remission according to the ACR/EULAR criteria treated with a combination of conventional synthetic (cs)DMARD plus bDMARDs. Upon stopping the bDMARD, 9 study visits were conducted within 52 weeks. At each visit, patients underwent clinical examination and ultrasound of 14 joints. The primary hypothesis was that a Power Doppler (PD) score >0 predicted a relapse until week 16 after bDMARD cessation. Relapse was defined as change from remission to moderate/high disease activity according to the simplified disease activity index.

Results: Although 110 patients were required by the protocol, inclusion had to be stopped after reaching 38 (34.5%) due to insufficient recruitment. There were 9, 10 and 13 relapses between baseline and weeks 16, 24 and 52, respectively. Relapses till week 16 tended to be more common in patients with PD score >0 at baseline than in those without [9/30 (30.0%) vs. 0/7 (0%), p=0.160)]. Similar observations were made for weeks 24 [9/30 (30.0%) vs. 1/7 (14.3%), p=0.647)] and 52 [12/30 (40.0%) vs. 1/7 (14.3%), p=0.383)]. Kaplan-Meier plot indicates the relapse-free survival in patients with and without PD+ synovitis at baseline (Figure 1).

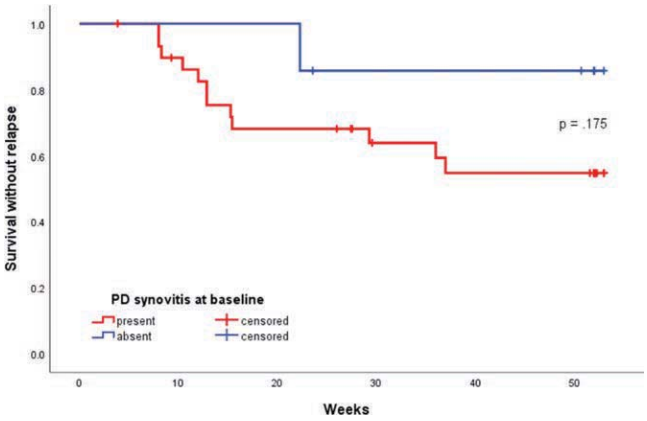

Figure 1. Kaplan-Meier analysis of relapses according to presence or absence of Power Doppler (PD) synovitis at baseline.

PD scores were higher at the time of relapse as compared to the preceding visits [mean difference in the PD score 3.2 (±4.5) points, p=0.034]. PD scores were also higher at visits preceding a relapse [mean 5.6 (±3.9), n=13] as compared to the mean PD score across all visits of patients without a relapse [mean 2.0 (±1.5), n=24, p=0.003, respectively]. There were trends towards a higher mean baseline PD score in patients who had a relapse between baseline and week 16 as compared to those who remained in remission (5.2 ± 5.8 vs. 2.3 ± 3.0, p=0.079). Similar observations were made for relapses until weeks 24 and 52. No difference was observed comparing mean residual swollen or tender joint counts at baseline between patients with and without a relapse. There were 9 adverse events. All of them were mild to moderate.

Conclusion: In RA patients in strict clinical remission, PD assessment at baseline but not clinical joint count could help identify patients who will relapse after the cessation of a bDMARD. Due to insufficient recruitment and limited power of the present trial, however, no definitive conclusion can be made.

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POS1391 DEEP LEARNING-BASED PANNUS LOCALIZATION SOFTWARE IN THE HANDS OF INFLAMMATORY ARTHRITIS USING TIME-INTENSITY CURVE (TIC) SHAPE CLASSIFICATION ON DYNAMIC MRI DATASET

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with significant functional impairment and disability, linked to inflammatory and structural articular and peri-articular damage [1]. Synovitis is a characteristic feature of RA, and is considered an important factor in disease activity and the best predictive marker of joint damage [2]. Therefore, accurate quantification of synovitis can play an important role in clinical evaluation and treatment serving as a biomarker. Pixel-by-pixel time–intensity curve (TIC) shape analysis is a dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) technique to help visualize differently shaped TICs [3]. Pixels having TIC shape type 4, which is characterized as early enhancement followed by washout phase, were regarded as synovitis pixel [4]. A deep residual network called ResNet-50 model, a convolutional neural network (CNN) that is 50 layers deep, might effectively classify TIC shapes.

Objectives: This study aimed to develop software that can automatically demonstrate the distribution of enhancing synovial pannus of patients with inflammatory arthritis on DCE-MRI.

Methods: Modified ResNet-50 was used on MATLAB. Two investigators drew regions of interest (ROIs) of muscle, bone, and synovitis under expert guidance and obtained TICs for each tissue on DCE-MRI of ten rheumatoid patients. Through cross-validation and batch evaluation, we verified the confusion matrices for the performance of the classifier. Then we identified the pixels of enhancing synovial pannus by image classification from the obtained pixel-by-pixel TIC shape and displayed them in color. The software performance was evaluated using a visual assessment on seven hand joints of one patient.

Results: 150 ROIs for muscles, 150 ROIs for bones, and 59 ROIs for synovitis on DCE-MRI of the hand joints were drawn in ten patients and obtained 4049, 3825, and 1041 TIC shape images, respectively. The classifier's accuracy, precision, sensitivity, and specificity were 99.6%, 99.3%, 98.4%, and 99.7%, respectively. Out of seven joints, four were assessed as good, two as fair, and one as fail.

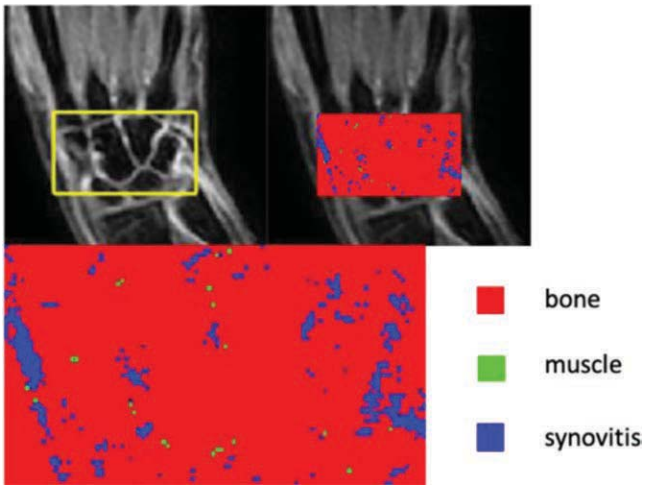

Figure 1. Software performance on contrast enhanced dynamic MRI of the wrist

Conclusion: Our classifier showed high accuracy, precision, sensitivity, and specificity. And through the comparison between manual outlining and the result of software, our software had relatively good performance. This automatic software developed using deep learning with CNN might accurately display the enhancing synovial pannus in RA.

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POS1392 TISSUE DOPPLEROGRAPHY AS A DIAGNOSTIC TOOL FOR MYOCARDIAL DYSFUNCTION IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Pathology of the cardiovascular system has a significant impact on the mortality rate in the population of patients with rheumatic diseases, including rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Involvement of the cardiovascular system determines the course and prognosis of many rheumatic diseases. In the general population, left ventricular diastolic dysfunction is an independent predictor of mortality and symptomatic chronic heart failure. However, routine screening for diastolic dysfunction is rarely performed in patients with RA and AS, especially in those who do not have clinical symptoms.

Objectives: to identify early preclinical signs of myocardial dysfunction in patients with RA and AS.

Methods: 142 people with verified rheumatic diseases were examined. All patients were divided into 2 groups. The first group consisted of patients with RA - 95 pts (average age 46.5±11.1 years). The second group consisted of patients with AS, 47 pts (average age 42.3±10.3 years). The control group included 70 healthy individuals (average age 43.7±12.1 years). All patients underwent standard laboratory and instrumental diagnostic tests, which included joint radiography

(group 1), magnetic resonance imaging of the spine and ileosacral joints (group 2). In addition, we performed echocardiography and tissue dopplerography of the heart on the GE Vivid E9 ultrasound machine.

Results: The parameters e'L, e'S, e'R were the lowest in patients with RA (9.95 [8; 12], 8.2 [6; 10], 12 [10; 14], respectively) compared to both the group with AS (11.1 [9; 13.7], 9.8 [7.2; 12], 13.1 [12; 14], respectively), and with the control group (12.1 [10; 14], 9.8 [8; 11], 13.4 [11; 15], respectively) (p<0.005). This indicates a significant deterioration in the diastolic function of both ventricles in patients with RA. We found a similar picture when comparing the systolic velocities of the fibrous ring of the left and right atrioventricular openings S'L, S'S, S'R. In the group of patients with RA, these parameters were the smallest (9.1 [8; 10], 7.4 [7; 8], 12.9 [12; 14], respectively) compared to the other two groups (p<0.0005). These results indicate a significant deterioration in the diastolic and systolic function of both ventricles in patients with RA. Diastolic dysfunction of both the left ventricle (25.3%) and both ventricles (16.8%) was more common among patients with RA compared to the control group (5.7%, 0%, respectively) (p<0.01). The same pattern was found in the group with AS: 17 and 10.6%, respectively (p<0.01). At the same time, there were no statistically significant differences between the 1st and 2nd groups. In addition, the calculation of the relative risk showed that the presence of RA 4.42 times increases the risk of developing diastolic dysfunction of the left ventricle compared with control group (CI 1.6-12.2). It should be noted that in the control group, diastolic dysfunction of the left ventricle was diagnosed only type 1, whereas among people with RA out of 24 pts, 10 had a pseudonormal type, and among patients with AS out of 8 pts, it was detected in four pts.

Conclusion: Patients with RA and AS are characterized by deterioration of the diastolic function of the left ventricle or both ventricles simultaneously. Quantitative characteristics obtained during tissue dopplerography confirm these changes. In addition, in people with RA, there is also a decrease in the systolic function of both ventricles. Thus, in order to detect early myocardial dysfunction in patients with RA and AS, it is advisable to conduct not only two-dimensional echocardiography, but also tissue dopplerography.

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POS1393 ULTRASOUND AS A POTENTIAL TOOL TO DETECT INTERSTITIAL LUNG DISEASE IN DAILY CLINICAL SETTING OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Interstitial lung disease (ILD) is the most common and relevant pulmonary complication, that contributes significantly to increased morbidity and mortality in rheumatoid arthritis (RA). Thus, increased awareness of this complication is a real challenge in the clinical setting; in particular, an accurate strategy to detect RA-ILD is crucial to assure the survival and quality of life of RA patients. In the last years, the pulmonary ultrasound (US) has been proposed to assess ILD in rheumatic diseases [1, 2]. Preliminary results have demonstrated a positive correlation between their findings and those of HRCT and diffusion capacity of carbon monoxide (DLCO).

Although these results are exciting, the value and potential application of US in detect ILD in daily clinical setting of patients with RA remain to be clearly delineated.

Objectives: To investigate the potential role of US in the detection of ILD in a real-life cohort of patients with RA.

Methods: Patients with diagnosis of RA were consecutively enrolled. All patients underwent pulmonary examination, laboratory data, DLCO measure, chest HRCT and radiographs, and US examination. A healthy group was included as control group.

US was performed according the 14-intercostal space scanning protocol using the following semiquantitative scale [0 = normal (≤5 B-lines); 1 = slight (≥6 and ≤15 B-lines); 2 = moderate, (≤16 and ≥30 B-lines); 3 = severe (≥30 B-lines)].

Results: A total of 74 RA patients and 74 healthy controls were included. Thirty of 74 patients (40.5%) showed US signs of ILD with respect to the healthy controls (3 subjects, 4.1%) (p=0.0001); whereas HRCT showed ILD in 27 (36.4%) of 74 patients.

Among the 30 patients that showed US findings of ILD, 17 (56.6%) were asymptomatic from respiratory view-point. The sensitivity and specificity of US were 92% and 89% respectively.

A positive correlation between US and HRCT findings were found (p= < 0.0001) whereas no correlation was found with chest radiographs and DLCO findings (p = 0.2971 and 0.7856 respectively). Positive association between US findings and DAS28-ESR, RF and anti-CCP (p=0.0076, 0.0044, 0.0074 respectively) was found.

Feasibility, represented by the mean time spent to perform the pulmonary US assessment was 7.8 minutes (± SD 1.2, range 6 to 10 minutes).

Conclusion: Our results support the potential of US in detect accurately ILD in a real-life cohort of patients with RA and provide a rationale to consider it as a friendly screening tool to be implemented in early phases of the disease.

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POS1394 ULTRASOUND MAY DETECT SUBCLINICAL INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS.

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Background: Interstitial lung disease (ILD) is common in systemic sclerosis (SSc) patients and despite recent advances in the treatment represents still the major cause of death. It may be established within the first 4 years of SSc and frequently is subclinical [1].

To evaluate the presence of ILD, there are different available tools in addition to the clinical evaluation including respiratory functional tests (RFT) and imaging methods, especially HRCT which remain the mainstay for the diagnosis of SSc-ILD.

It has been recently proposed that pulmonary ultrasound (US) may have a potential role for the assessment of ILD in patients with SSc [2, 3]. Despite the growing body of evidence, there are no established data regarding its potential role in both detecting ILD in subclinical stages and on the follow-up of SSc patients.

Objectives: To investigate the validity of US in detecting subclinical ILD in SSc and to determine its potential in the follow-up of these patients.

Methods: 133 patients without respiratory symptoms and 133 healthy controls were included. Borg scale dyspnea index, Rodnan skin score (RSS) and pulmonary auscultation were performed. X-ray and respiratory function tests (RFT) were performed the same day. An expert rheumatologist blinded to clinical assessment performed the US. To determine the concurrent validity high-resolution CT (HRCT) scans was performed. HRCT findings were scored according to Warrick score whereas US findings were classified according the previously proposed scale. An inter-observer reliability was performed. A follow-up including US, RFT and Borg scale was done every 3 months for 12 months.

Results: A total of 54 of 133 SSc patients (40.6%) showed US signs of ILD in contrast to healthy controls (4.8%) (p=0.0001). The clinical and laboratory variables associated with ILD were anti-centromere antibodies (p=0.005) and RSS (p=0.004). A positive correlation was demonstrated between the US and HRCT findings (p=0.001). Sensitivity and specificity of US in detecting ILD was 91.2% and 88.6% respectively. A good inter-observer reliability was also observed (k = 0.72).

In the follow-up, a total of 30 patients (22.6%) that demonstrated US signs of ILD at baseline showed US worsening. Nine patients (30%) developed symptoms of ILD.

Conclusion: US is valid to detect subclinical ILD-SSc. Our results showed a high prevalence of this complication. Despite encouraging data, it seems still controversial its role in monitoring the ILD progression in SSc.

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POS1395 NEUROFILAMENT LIGHT CHAIN, AN EARLY BIOMARKER FOR POLYNEUROPATHY IN HEREDITARY ATTR AMYLOIDOSIS.

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Background: Serum neurofilament light chain (sNfL) is a sensitive marker for polyneuropathy (PNP) in hereditary transthyretin-related (ATTRv) amyloidosis patients and correlates with the severity of polyneuropathy [1-4]. We hypothesized that sNfL may diagnose neuronal damage in patients with hATTR amyloidosis before the onset of symptoms and before PNP can be detected by electromyography (EMG) examination.
Objectives: To establish the course of sNfL in three different groups: 1. persistently asymptomatic variant carriers (with and without detected amyloid), 2. ATTRv amyloidosis patients with PNP on treatment, 3. variant carriers who develop PNP.

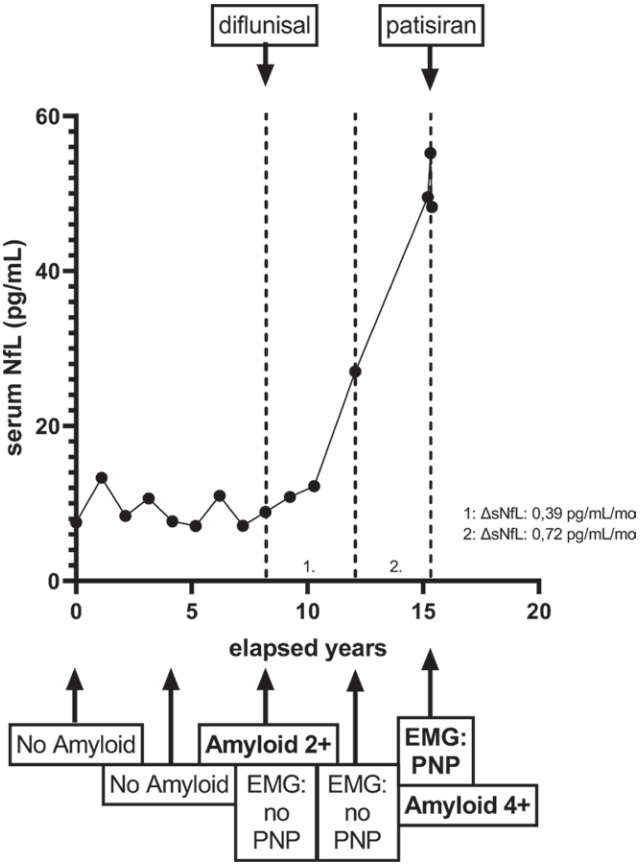

Figure 1.

Methods: sNfL levels were assessed longitudinally in asymptomatic variant carriers (with and without detectable amyloid), ATTRv amyloidosis patients with PNP on treatment (either a transthyretin (TTR) stabilizer or patisiran, an RNA interference therapeutic), and variant carriers who developed PNP. PNP was established by EMG examination. The single-molecule array (Simoa) assay was used to assess sNfL levels.
Results: sNfL levels significantly increased over 1 year in 20 persistently asymptomatic carriers (p<0.001), with the strongest increase in variant carriers (n=8) with detectable amyloid in the subcutaneous abdominal fat tissue. In 21 symptomatic ATTRv amyloidosis patient with PNP on treatment with a TTR stabilizer, sNfL levels remained stable over 1 year. In 24 patients treated with patisiran, sNfL levels significantly decreased after 1 year of treatment (p=0.01). In 8 out of 9 variant carriers who developed PNP a rise in the sNfL level could be observed before the onset of symptoms and establishment of PNP by EMG examination (Figure 1).
Conclusion: sNfL is a marker for early neuronal damage since a rise in sNfL level occurs before abnormalities can be detected by EMG examination. Our data support the use of sNfL in monitoring disease progression, screening asymptomatic variant carriers and monitoring of treatment effect.
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POS1396 PSORIASIS, WITHOUT RHEUMATOLOGICAL MANIFESTATIONS, IS ASSOCIATED WITH STRUCTURAL CHANGES OF THE SACROILIAC JOINT, A CONTROLLED STUDY USING CT SCAN

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Background: Plaque Psoriasis (PsO) is an inflammatory disorder that could be associated with rheumatological manifestations defining Psoriatic arthritis. Moreover, recent studies showed that the presence of plaque psoriasis is associated with more structural damage In axial Spondyloarthritis [1]. To our knowledge, no study has specifically evaluated the extent of structural lesions of the sacroiliac joints (SIJs) on computed tomography (CT) in patients with PsO, without rheumatological manifestations, compared with healthy controls.
Objectives: To describe SIJ CT characteristics in patients with PsO and compare them with those of age- and sex- matched controls.
Methods: An observational, retrospective study was performed using medical records from Besançon University Hospital's rheumatology and dermatology departments, which were screened to identify patients with PsO, diagnosed by a dermatologist. A search was then carried out for patients in the hospitals' imaging archiving system to identify those who had undergone a CT which included the SIJs in their entirety. Non-inclusion criteria were the existence of pelvic bone lesions and a history of pelvic radiotherapy. Each patient was then matched with a control of the same age and sex, recruited through the hospital's imaging archiving system.
For each individual, CT was interpreted by two independent readers using a score previously used by Diekhoff et al. [2], dividing each SIJ into 12 regions, for each of which joint space narrowing (JSN), erosions, and sclerosis are assessed. For this study, we also observed the existence of intra-articular gas and diffuse idiopathic skeletal hyperostosis (DISH) lesions for each region. Quantitative variables were compared using Student's t-test. Qualitative variables were compared using the Chi-2 test.
Results: 60 patients and 457controls were included. Mean (SD) age was 52,2 ± 17,7 in the PsO group and 53,6 ± 16.7 in the control group. 31 (52%) were male in PsO group and 30 (54%) in the control group. In the PsO group, BMI was 27,7± 6 versus 26,9 ± 6,44 in control group (p= 0.55). There is a trend for more frequent active smoking in PsO (69% in PsO group versus 54% in control group; p=0.075). In PsO patients, mean disease duration was 20.2 ± 17,6 years, the skin area affected was 41,8% ± 22,6 and the mean number of bDMARDs used was 2.25 (± 1.16). The global SIJ score was higher in the PsO group (6,63 ± 10,7) in comparison with the control group (2,84 ± 4,87). Erosion and sclerosis scores were similar in both group but joint space narrowing score was significantly higher in the PsO group (0.873

(±4.62) versus 4.15 (±10.8); p =0.035). There were no correlations between the global score and the disease duration (Pearson score 0.166 (-0.131; 0.435)) and the severity of the psoriasis (Pearson 0.00937 (-0.259; 0.276)).The number of gestation, active smoking, alcohol intake and physical work have no impact on the global Score.
Conclusion: The CT characteristics of SIJs from patients with Pso were different to those of age- and sex-matched controls essentially secondary to joint space narrowing.
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Table 1. CT scan findings between PsO patients and matched controls

	Controls	PsO	
Erosion	0.42 (±0.91)	0.2 (±0.48)	0.18
Joint space narrowing	0.873 (±4.62)	4.15 (±10.8)	**0.035**
Sclerosis	1.76 (±2.07)	2.17 (±2.73)	0.37
Global score	2.84 (±4.87)	6.63 (±10.7)	**0.015**
Gas	34 (62%)	34 (57%)	0.57
DISH	11 (20%)	9 (15%)	0.48

Disclosure of Interests: None declared
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POS1397 USEFULNESS OF ^{18}F-FDG PET/CT FOR POLYMYALGIA RHEUMATICA DIAGNOSIS

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Background: Polymyalgia rheumatica (PMR) is an inflammatory disorder affecting elderly people. The diagnosis is based on clinical and imaging findings such as ultrasonography. The interest of ^{18}F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (^{18}F-FDG PET/CT) in PMR is increasing. However, its exact place in the diagnosis or management of PMR patients remains unclear.
Objectives: We aimed to describe the utility ^{18}F-FDG PET/CT for PMR diagnosis.
Methods: We performed an observational retrospective study of patients with new onset of PMR having a ^{18}F-FDG PET/CT. Diagnosis of PMR was done according to ACR/EULAR 2012 classification criteria. A control group, including patients with sarcoidosis, neoplasia or infection, was also analyzed. The following sites were assessed for the presence of hypermetabolism (SUVmax ≥ 2): shoulders, acromioclavicular and sternoclaviculaire joints, hips, symphysis pubis, ischial tuberosities, great trochanters, cervical and lumbar interspinous process and large vessels. The number of hypermetabolic sites (0-18), the median SUVmax and the highest SUVmax were analyzed.
Results: A total of 85 PMR patients (60% of female, mean age 70.7 years) and 75 controls (51% of female, mean age 65 years) were analyzed. Among PMR patients, hypermetabolism was mostly observed in shoulders (93%), hips (91%), great trochanters (87%), ischial tuberosities (89%) and lumber interspinous process (71%). Large vessel vasculitis was only observed in 7% of PMR patients. In comparison to control patients, PMR had higher number of hypermetabolic sites (11.3 ±3.3 vs. 0.85 ±1.1, p<0.001), and mean SUVmax score (3.9 ±0.8 vs. 2.7 ±0.4, p<0.001). After adjustment to age, the number of hypermetabolic sites (OR 2.57 [1.84; 4.51], p<0.001) and the mean SUVmax were associated with the diagnosis of PMR (OR 1.49 [1.30; 1.78], p<0.001). Among PMR patients, the C-reactive protein (CRP) levels were correlated with the mean SUVmax (r=0.38, p<0.001), the number of hypermetabolic sites (r=0.34, p<0.01) and the highest SUVmax (r=0.38, p<0.001).
Conclusion: ^{18}F-FDG PET/CT appears to be a sensitive imaging for PMR. The number of hypermetabolic sites and the man SUVmax are correlated with CRP levels and PMR diagnosis.
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POS1398 ASSOCIATION OF FUNCTIONAL SALIVARY TESTS WITH SALIVARY GLAND ULTRASOUND AND BIOPSY IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME.

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Background: Salivary gland ultrasonography is useful to assess salivary gland involvement in primary Sjögren Syndrome. Different publications have describes the association between decreases salivary flow and the degree of involvement with ultrasound.
Objectives: This study aims to assess the association of functional salivary tests evaluated by stimulated and unstimulated salivary flow (SSF and USF) with salivary major gland ultrasound scores (SGUS) and a positive focus score in a minor salivary gland biopsy.
Methods: A cross-sectional study including 98 subjects fulfilling the ACR-EULAR 2017 classification criteria for pSS. All patients underwent salivary functional tests, an ultrasound of salivary glands and a minor salivary gland biopsy requested as per clinical practice. The ultrasound images were graded using three different scoring systems: De Vita (0-3), Salaffi (0-4) and Omeract (0-3), obtained as the highest score achieved in the four evaluated glands, left and right parotid and submandibular. Positive biopsy was considered if focus score ≥1
Results: This study included 98 patients with pSS. We evaluated the different ultrasound scoring systems and each score individually assessed in parotid and submandibular gland with the salivary functional tests. USF is associated with all SGUS independently of the measurement, with a 2.5 ml/15min higher in negative compared to positive SGUS. Similar results were shown for SSF, with a 3 ml/5 min higher in negative compared to positive SGUS (Table 1). We observed no association between USF or SSF and a positive focus score in the minor salivary gland biopsy.

Table 1. Association between salivary flows and ultrasound scoring systems.

		Unstimulated Salivary Flow			Stimulated Salivary Flow		
Ultrasound score	Group	N(%)	Means[95%CI]	p-val	N(%)	Means[95%CI]	p-val
Vita	N	54 (55.1%)	4.076 [3.056, 5.096]	0.004	54 (55.1%)	6.745 [5.042, 8.447]	0.011
	P	44 (44.9%)	1.839 [0.709, 2.969]		44 (44.9%)	3.436 [1.550, 5.322]	
Vita Parotid	N	60 (61.2%)	3.886 [2.912, 4.861]	0.008	60 (61.2%)	6.575 [4.961, 8.190]	0.011
	P	38 (38.8%)	1.784 [0.560, 3.008]		38 (38.8%)	3.182 [1.153, 5.210]	
Vita Submandibular	N	55 (56.1%)	4.002 [2.986, 5.017]	0.007	55 (56.1%)	6.668 [4.977, 8.358]	0.014
	P	43 (43.9%)	1.881 [0.733, 3.030]		43 (43.9%)	3.458 [1.546, 5.370]	
Salaffi	N	52 (53.1%)	4.050 [3.005, 5.095]	0.007	52 (53.1%)	6.754 [5.015, 8.493]	0.014
	P	46 (46.9%)	1.965 [0.854, 3.076]		46 (46.9%)	3.570 [1.721, 5.419]	
Salaffi Parotid	N	58 (59.2%)	3.857 [2.861, 4.853]	0.016	58 (59.2%)	6.578 [4.931, 8.225]	0.014
	P	40 (40.8%)	1.932 [0.733, 3.132]		40 (40.8%)	3.347 [1.365, 5.330]	
Salaffi Submandibular	N	54 (55.1%)	4.011 [2.985, 5.037]	0.007	54 (55.1%)	6.689 [4.982, 8.396]	0.014
	P	44 (44.9%)	1.918 [0.782, 3.054]		44 (44.9%)	3.505 [1.614, 5.395]	
Omeract	N	56 (58.9%)	3.727 [2.727, 4.726]	0.01	56 (58.9%)	6.313 [4.612, 8.014]	0.043
	P	39 (41.1%)	1.854 [0.656, 3.051]		39 (41.1%)	3.574 [1.536, 5.613]	
Omeract Parotid	N	61(64.2%)	3.562 [2.598, 4.526]	0.040	61 (64.2%)	6.227 [4.599, 7.854]	0.036
	P	34 (35.8%)	1.874 [0.582, 3.165]		34 (35.8%)	3.326 [1.147, 5.506]	
Omeract Submandibular	N	57 (60.0%)	3.661 [2.667, 4.656]	0.028	57 (60.0%)	6.246 [4.557, 7.935]	0.052
	P	38 (40.0%)	1.903 [0.685, 3.120]		38 (40.0%)	3.603 [1.534, 5.671]	

N: Negative, P: Positive

Conclusion: USF and SSF are associated with SGUS system independently of the salivary gland evaluated but not with positivity in the biopsy, pointing to salivary ultrasound as a good technique to evaluate functionality. Neither USF nor SSF are associated with positivity in the biopsy indicating no link between histology and functionality.
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POS1399 THE INTEREST OF DOPPLER ULTRASOUND IN THE EVALUATION OF THE CARPAL TUNNEL SYNDROME SEVERITY

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Background: Several studies have proven the value of Doppler ultrasound (DpUS) in the diagnosis of carpal tunnel syndrome (CTS) with satisfactory sensitivity and specificity. Yet, unlike the Nerve Conduction Studies (NCS), the interest of this technique in the severity diagnosis in CTS remains uncertain to this day. Several studies have focused on this subject. However, the morphological signs of gravity are not yet consensual.

Objectives: Compare US data with clinical and electromyographic data in order to determine the place of DpUS in the severity diagnosis in CTS.

Methods: A bicentric cross-sectional study including patients with uni or bilateral CTS, confirmed by NCS, referred from the plastic surgery department. All the patients underwent a clinical examination, a NCS of both hands as well as a DpUS of the wrists by the same rheumatologist.

Results: After screening and application of all exclusion criteria, a total of 72 wrists of 47 patients were included. The median age was 54,23 ± 11 years [21-77 years] and 89,4% of wrists were from female patients. Hand numbness was the most frequent functional sign (94.4%) and the Phalen sign was the most noted examination sign (73.6%). Clinically, the patients presented respectively 32 mild, 14 moderate and 26 severe lesions. According to the NCS, there were 18 mild, 21 moderate and 33 severe CTS with 73.6% of the wrists with sensorimotor impairment. On US, the hypoechoic image was the dominant qualitative sign (84.7%). Regarding the quantitative measures, the mean Median Nerve (MN) cross sectional area (CSA) was 14.5 mm2 [9-30 mm2] and the mean flattening index was 3 [1.8-8.92]. Intraneural hypervascularisation was present in 57 writs (79,2 %). Statistically significant associations were detected between the MN CSA and both history of diabetes mellitus (p=0.045), diabetes duration (p=0.040) and disease duration (P=0.021). But there was no association between MN CSA and age (p=0,406), gender (p=0,690) and BMI (p=0,414). the mean MN CSA during mild clinical stage was 13.5 mm2. For moderate stage it was 17 mm2 while for severe stage it was 15 mm2.No relationship was found between US quantitative and morphological parameters and clinical severity grades. We detected significant correlation between MN hypervascularization and the CTS severity grades on NCS (p=0,044). For the other qualitative US signs, there was no statistically significant difference between the different grades of electromyographic severity (Notch sign (p=0.364), Hypoechoic image (p=1.000), Disappearance of the fascicular aspect (p=0.248), Decreased mobility of the tunnel contents of the canal during wrist movements (p=0.140)). the mean MN CSA during mild electromyographic stage was 13 mm2. For moderate stage it was 14 mm2 while for severe stage it was 15 mm2 and We did not find a statistically significant difference in MN CSA (P=0.494) between the different grades of severity of CTS on NCS. There is no statistically significant association between qualitative US signs and the type of NCS impairment; pure sensory or sensorimotor. However, we found a significant association between the MN CSA and pure sensory or sensorimotor damage on NCS (P=0,009).

Conclusion: MN DpUS could be a complementary procedure to the clinical examination which allows, in addition to the positive diagnosis, to evaluate the severity of the CTS based on the MN CSA and the intraneural vascularization in power Doppler.

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POS1400 CLINICAL EVIDENCE OF THE DIFFERENCE IN CIRCULATING CALPROTECTIN LEVELS BETWEEN RHEUMATOID ARTHRITIS AND HEALTHY INDIVIDUALS, NON-INFLAMMATORY ARTHRITIS OR OTHER INFLAMMATORY ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease mainly characterized by a chronic inflammation of the joints. Early diagnosis and treatment with disease-modifying antirheumatic drugs (DMARDs) is essential to prevent or slow down the structural damage. Diagnosis might be difficult in patients with mild and unspecific clinical signs and symptoms though. A differential diagnosis in patients presenting arthritis is needed for an appropriate patient management. Acute-phase reactants (ESR or CRP) are non-specific inflammatory biomarkers used to aid in the diagnosis of RA and to assess disease activity. In the recent years, studies published have shown that calprotectin may be an alternative biomarker of active inflammatory disorders as well as a prognostic or monitoring biomarker.

Objectives: To collect all available evidence on the difference between circulating calprotectin (cCalpro) levels in rheumatoid arthritis (RA) patients and other control populations such as healthy individuals (HI), osteoarthritis (OA), psoriatic arthritis (PsA) or spondyloarthritis (SpA).

Methods: Electronic databases searches (Scopus, Pubmed and Cochrane Library), complemented by registry and hand searching, were conducted (February 4th, 2021) to identify fully paired studies comparing cCalpro levels in RA and HI, non-inflammatory arthritis (NIA), or other inflammatory arthritis. As recommended by Cochrane, the Hedge´s standardized mean difference (SMD) and its 95% confidence intervals were used to synthetize the difference in cCalpro levels from studies using different matrices (serum or plasma) or laboratory methods. Sample size, mean and standard deviation of each group were extracted from the individual studies to conduct a random-effects model meta-analysis in STATA MP v17.0. When cCalpro levels were reported in median and range or inter-quartile, a formula was used to estimate the mean and standard deviation. Sensitivity analysis, subgroup analyses and meta-regression analyses on matrix type (serum or plasma) and cCalpro commercial test were performed, when feasible, to investigate heterogeneity.

Results: The systematic review retrieved 27 studies comparing cCalpro levels between RA and controls. One study reported cCalpro levels in three different RA and HI cohorts. Most of RA and controls were age and gender matched. Calprotectin was measured in serum in 72,4% of the comparisons. Thirteen different commercial calprotectin tests and four homemade tests were used. In 21 studies cCalpro levels were measured in 2678 RA and 1096 HI. cCalpro levels were significantly higher in RA than in HI (SMD=2,13;95%CI=1,27-2,98;p<0,0001), and significant heterogeneity was observed. A meta-regression on matrix and assay manufacturer indicated that 22% of the between-study variance might be explained by the type of calprotectin test used. Five studies compared cCalpro levels in 207 RA and 187 NIA (78,57% OA). cCalpro levels were significantly higher in RA than in NIA (SMD=2,914;95% CI=0,957-4,872;p=0,0035), significant heterogeneity was observed. cCalpro levels in 1217 RA and 411 PsA patients were reported in 5 studies. cCalpro levels were slightly higher in RA than in PsA (SMD=0,54; 95%CI=0,424-0,656; p<0,0001), while no significant heterogeneity was observed. A comparison between cCalpro levels in RA and SpA was included in 4 studies. cCalpro levels were slightly higher in RA than in SpA (SMD=0,35; 95%CI=0,129-0,576; p=0,0020), and no significant heterogeneity was observed.

Conclusion: In this systematic review and meta-analysis, rheumatoid arthritis patients showed significantly higher circulating calprotectin levels than healthy individuals, non-inflammatory arthritis, psoriatic arthritis and spondyloarthritis. Pooled standardized mean difference between groups should be interpretated with cautious due to substantial heterogeneity or small number of studies.

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POS1401 **PROGNOSTIC VALUE OF COMMON FEMORAL VEIN WALL THICKNESS IN BEHÇET DISEASE: A PROSPECTIVE FOLLOW-UP STUDY**

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Background: We reported the first controlled doppler ultrasound study showing increased common femoral vein (CFV) thickness in Behçet Disease (BD). Following that, we recently showed that increased CFV thickness is a distinctive feature of BD, rarely present in other inflammatory or vascular diseases such as ankylosing spondylitis, systemic vasculitides, venous insufficiency, and non-inflammatory DVT (deep venous thrombosis) with a specificity higher than 80% for the cut-off value of ≥ 0.5 mm. However, the association between CFV thickness and any organ involvement, disease course or treatment during the prospective follow-up has not been demonstrated so far.
Objectives: This study aimed to assess the longitudinal course and prognostic value of CFV thickness measurement during prospective follow-up BD patients.
Methods: In this prospective study, we included 195 patients with diagnosed BD. The clinical, demographic, treatment data and laboratory were recorded during the routine visit. Bilateral CFV thickness was measured with ultrasonography by an experienced radiologist at the same day. Patients were started to follow up prospectively with 3-6 months intervals and in any urgent visit. In 47 patients, the second CFV thickness measurement was done mean 19.79 (10.10) months after the first visit.
Results: At baseline, 98.6% of patients had increased CFV thickness above the cut-off value of ≥0.5 mm. The baseline and last follow-up clinical characteristics were shown in Table 1.

Table 1. The baseline and follow-up clinical characteristics of patients with Behçet's Disease.

	Baseline (n=139)	Last Follow-up (n=139)	Relapses or New Involvement during follow-up
Age mean (SD)	34.85 (8.27)		
Gender F/M ratio	43/96		
Pathergy (positive/negative)	59/44		
Right CFV Wall Thickness mean (SD) mm	0.791 (0.253)		
Left CFV Wall Thickness mean (SD) mm	0.797 (0.207)		
Oral aftous n (%)	134 (95)	134 (95)	13 (9.4)
Genital Ulcer n (%)	84 (60.4)	89 (64.5)	6 (4.3)
Eritema Nodosum n (%)	62 (44.6)	69 (49.6)	9 (6.5)
Arthritis (%)	48 (34.5)	48 (34.5)	10 (7.2)
Major Organ Involvement n (%)	103 (74.1)	110 (78.6)	39 (28.1)
Vascular Involvement n (%)	84 (60.4)	96 (69.1)	35 (25.2)
Deep Venous Thrombosis (%)	61 (43.9)	65 (46.8)	6 (4.3)
Pulmonary trombosis n (%)	35 (25.2)	52 (37.4)	23 (16.5)
Neuro-Behcet n (%)	14 (9.9)	16 (11.5)	2 (1.4)
Uveitis n (%)	33 (23.7)	40 (28.8)	7 (5)

In 47 patients, the second CFV thickness measurement was done mean 19.79 months after the first visit. There was no statistically significant difference between the first and second CFV venous wall thickness measurements for both right and left of our patients (First vs. second for right CFV: 0.791 mm vs. 0.755, p=0.264; first vs. second for left CFV: 0.787 mm vs. 0.753, p=0.264). We did not find any change in CFV wall thickness with the treatment, new organ involvement and relapses. 139 of 195 patients had prospective clinical follow-up data with the mean of 26.52 (16.94) months. New major organ involvement or relapse leading to treatment change was seen in 39 (28%) patients. While 22 (15.8%) patients had new major organ involvement, 12 (8.6%) of them were diagnosed with new vascular involvement, seven (5%) with new uveitis. Among 36 patients with only mucocutaneous disease at baseline, new major organ involvement developed in 9 patients during follow-up. These nine patients had had higher baseline CFV thicknesses compared to patients not developing major organ involvement despite not achieving clinical significance (0.83 mm vs 0.73 mm for right CFV; 0.80 mm vs 0.73 mm for left CFV: p >0.05 for both)
Conclusion: CFV wall thickness measurement with ultrasonography which is a new non-invasive diagnostic tool for BD, does not show a major change over time with treatment, new organ involvement or disease relapses. However, our preliminary results suggest that mucocutaneous BD patients with higher CFV thickness may have a higher risk of developing major organ involvement during follow-up. The results of our prospective cohort with longer follow-up and increased patients' number would clarify the prognostic value of CFV thickness in BD.
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Public health, health services research, and health economics

POS1402 **COST-EFFECTIVENESS AND COST-UTILITY OF ADD-ON, LOW-DOSE PREDNISOLONE IN RA PATIENTS AGED 65+: THE PRAGMATIC, MULTICENTER, PLACEBO-CONTROLLED GLORIA TRIAL**

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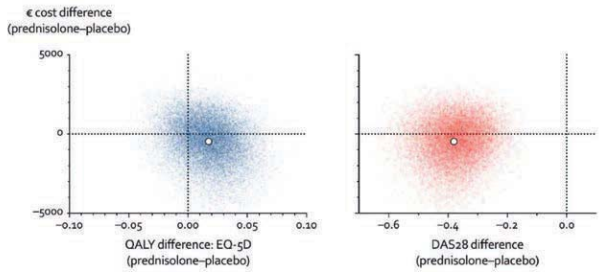
Background: Rheumatoid arthritis (RA) is a disease with substantial impact on quality of life, healthcare and societal costs [1]. Current treatment strategies, especially biologic drugs, result in high costs [2]. Previous studies have already found that a combination treatment strategy of disease-modifying antirheumatic drug(s) with initially medium-to-high doses of prednisolone resulted in better effects and lower costs compared to the treatment strategies without prednisolone [3, 4]. However, to our knowledge the cost-effectiveness of low-dose glucocorticoids (GCs), and that of GC overall in established RA has not been examined separately.

Objectives: To evaluate the cost-effectiveness and cost-utility of low-dose prednisolone in RA patients aged 65+.

Methods: The economic evaluation was performed as part of the placebo-controlled GLORIA trial of RA patients aged 65+ with a disease activity score in 28 joints (DAS28) ≥2.60. Eligible patients were randomized to 2 years 5 mg/day prednisolone or placebo. Patients were recruited from 28 clinical centers in seven European countries. All co-treatment, except for chronic oral GC, was allowed. The economic evaluation had a societal perspective with a time horizon of two years. Cost data were collected with questionnaires and from recorded events, and valued with unit prices of 2017. The primary effectiveness outcome was the DAS28. For cost-utility, quality-adjusted life years (QALYs) were estimated from the EuroQol-5 Dimension (EQ-5D) questionnaire. Standard regression models were used to estimate incremental costs and effects between the treatment groups. Bootstrapping assessed the uncertainty around the average differences in costs and health outcomes.

Results: In total, 444 of 451 randomized patients were included in the modified-intention-to-treat analysis (see main GLORIA study abstract). Patients were on average 72 years and had median 4 active comorbidities at baseline. Mean total costs over 2 years were k€10.8 in the prednisolone group, k€0.4 (95% CI –3.7; 1.9) lower than in the placebo group. Total direct medical costs were k€0.5 (95% CI –4.0; 1.5) lower in the prednisolone group. The mean number of QALYs was similar in both groups (difference 0.02 [–0.03; 0.06] in favor of prednisolone). The DAS28 was 0.38 lower in the prednisolone group than in the placebo group (0.19;0.56). The cost-effectiveness plane shows that the majority of the bootstrapped cost-effect pairs was situated in the southwest quadrant of the plane confirming the larger effects (i.e. decrease in DAS28) and non-significant lower costs in the prednisolone group (Figure 1). The cost-utility plane shows that the number of QALYs was similar for both groups and that the bootstrapped cost-utility pairs were slightly more located in the southeast quadrant confirming a very small increase in QALYs and slightly lower costs in the prednisolone group (Figure 1).

Figure 1. Cost-effectiveness and cost-utility planes representing the differences in cost (€) and health (EQ-5D and DAS28) between prednisolone and placebo treatment.



Conclusion: With greater effectiveness at non-significantly lower costs, low-dose, add-on prednisolone is cost-effective for RA compared to placebo over two years. QALYs were equal in both groups, most likely due to the impact of multiple comorbidities.

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POS1403 CLINICAL CHARACTERISTICS, HEALTH CARE RESOURCE UTILIZATION, AND COSTS ASSOCIATED WITH FLARES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN GERMANY

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Background: Longitudinal data describing real-world systemic lupus erythematosus (SLE) disease characteristics, health care resource utilization (HCRU), and costs associated with flares in Germany are limited.

Objectives: To evaluate the clinical characteristics of patients with SLE and estimate the impact of flares on HCRU and costs in a cohort of adults with SLE in Germany.

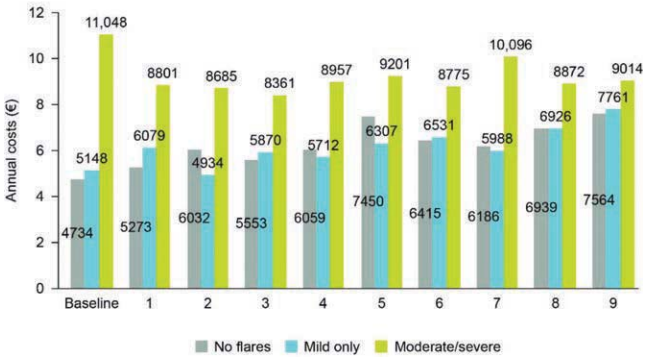
Methods: CHaracteristics and impact of flares on clinicAl and econoMic OutcoMes In patients with systemic Lupus Erythematosus: a German Claims Database Study (CHAMOMILE) was an observational, retrospective cohort study. Adult patients with SLE were identified from the German Betriebskrankenkassen health insurance fund database between 1 July 2010 and 31 December 2013, and followed for up to 9 years. Baseline period was defined as the first year since the first quarter with the earliest SLE diagnosis during the identification period, including this quarter. Resource utilization measures included number of hospitalizations, duration of stay, and associated costs per person-year (PY) by follow-up year for patient subgroups defined by flare exposure (no, mild, or moderate/severe flares) during baseline. Cost measures included total PY costs in flare-exposure subgroups.

Results: Of 2088 patients included in the study, the mean (SD) age was 51.4 (16.1) years and 1767 (84.6%) were female. The most common SLE manifestations were cutaneous (66.8%), osteoarticular (28.7%), and vascular (23.0%). Patients were receiving treatment with glucocorticoids (54.8%), antimalarials (40.2%), nonsteroidal anti-inflammatory drugs (39.1%), and/or immunosuppressants (32.7%). During the baseline period, 750 patients (35.9%) experienced moderate/severe flares, 622 (29.8%) experienced mild flares, and 716 (34.3%) experienced no flares. Patients with no flares or mild flares during the baseline period had similar costs, and a similar number and duration of hospital stays per PY, which remained consistent from baseline up to 9 years of follow-up. Patients with moderate/severe flares during the baseline period had 2- to 3-fold higher hospital costs, 1- to 2-fold more hospital stays, and hospital stays that were 2-fold longer in duration, compared with the no-flares or mild-flares groups during baseline and each year of follow-up (Table 1). During the baseline period, annual total costs were more than 2-fold greater for patients with moderate/severe flares (€11,048/PY) than patients with mild (€5148/PY) or no flares (€4734/PY). In all subsequent years, costs for patients with moderate/severe flares exceeded costs for patients with mild or no flares. Annual total costs gradually increased over time to €7761/PY for patients with mild and to €7564/PY for patients with no flares at Year 9, whereas costs reduced sharply at follow-up Year 1 to €8801/PY and remained similar to Year 9 for patients with moderate/severe flares (Figure 1).

Table 1. Mean Costs, Number, and Duration of Hospital Stays per Person-Year by Baseline Flares

	Flare-Exposure Subgroup	Year									
		Baseline	1	2	3	4	5	6	7	8	9
Patients, n	**No**	716	716	701	676	658	634	603	526	444	315
	Mild	622	622	613	596	575	559	534	455	348	239
	Moderate/severe	750	750	721	690	669	646	624	503	391	263
Costs of hospital stays, mean, €	**No**	1325	1798	2296	1725	2233	3126	1759	1786	1795	2047
	Mild	1779	1944	1545	1820	1652	2261	2390	1974	2290	2451
	Moderate/severe	5517	3550	3403	2798	2725	2999	2663	3695	2714	2977
Number of hospital stays, mean, n	**No**	0.49	0.46	0.47	0.44	0.51	0.53	0.44	0.41	0.44	0.45
	Mild	0.46	0.48	0.40	0.50	0.42	0.47	0.47	0.48	0.51	0.43
	Moderate/severe	1.39	0.85	0.76	0.64	0.62	0.67	0.63	0.76	0.60	0.74
Duration of hospital stays, mean, days	**No**	3.51	4.66	4.98	3.91	5.02	5.41	3.98	4.58	4.46	4.73
	Mild	4.55	4.91	4.11	4.41	3.76	4.33	4.13	4.05	4.68	4.19
	Moderate/severe	13.89	8.18	7.58	7.68	6.88	7.10	6.59	7.89	6.54	6.03

Figure. Annual Total Person-Year Costs by Baseline Flare Exposure Subgroups



Conclusion: Patients with moderate or severe flares following diagnosis place a large burden on the health care system in Germany. Earlier diagnosis and treatment may reduce flare severity and the associated high health care costs.

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POS1404 SHARED DECISION MAKING AND INTERNET USE FOR GATHERING HEALTH INFORMATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTICENTER CROSS-SECTIONAL STUDY

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Background: It is well known that providing appropriate health information to patients with systemic lupus erythematosus (SLE) has an advantage in the treatment decision making process. In modern information society the growing popularity of smartphones and social networking services, patients have more access to online health information. However, there are concerns that Internet use may inversely affect the shared decision making (SDM) process with their attending physicians if they receive inaccurate information.

Objectives: This study aimed to investigate how online information gathering behavior affects SDM with their attending physicians.

Methods: In this cross-sectional study, information of 386 patients with SLE, which were enrolled from five Japanese institutions between June 2020 and August 2021, were analyzed. The main exposure was time spent on the Internet per day (excluding time used for working). It was divided into four categories (none, <1 hour, 1-2 hours, > 2 hours). Patients were asked to select the source of health care information they would like to access first and were categorized into physicians, the Internet, and other media sources (family and friends, healthcare professionals other than physicians, or TV and radio, etc.). Outcome was shared decision making measured via the 9-item Shared Decision Making Questionnaire (SDM-Q-9 [scores 0-100]). To assess the relationship between the time of Internet use and SDM, we fitted general linear models adjusted for age, gender, education level, household income, marital status, history of cancer, disease duration, and disease activity. Chained equations were used to impute missing values of covariates.

Results: This study ultimately employed 334 patients whose mean age and female ratio were 45.3 years (standard deviation 13.8) and 87.7%, respectively. 68.9% of the patients indicated that they would like to access their physicians first, and 19.5% indicated that they would like to access the Internet first. Compared to patients who chose their physician as their first access to health information, there was no difference in SDM-Q-9 among patients who chose the Internet, but patients who chose other media had significantly lower SDM-Q-9 (-7.7 point, 95% confident interval [CI] -14.4 to -0.92, P=0.026). Besides, SDM-Q-9 scores were significantly lower in patients who did not use the Internet compared to those who used it for more than two hours except for their work activities (-9.6, 95%CI -18.9 to -0.26, P=0.044).

Conclusion: The present study suggests that SDM between physicians and patients is positively rather than adversely associated with online information-gathering behavior. Rheumatologists also need to be aware that how patients prefer to access health information to establish a good physician-patient relationship for SDM. In addition, rheumatologists may need to introduce their patients to websites offering appropriate health information.

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POS1405 LESS THAN 50% FEMALES WITH CHRONIC RHEUMATIC INFLAMMATORY DISEASES CONTINUE A DMARD DURING PREGNANCY: A DESCRIPTIVE ANALYSIS OF THE NATIONAL FRENCH SOCIAL SECURITY DATABASE

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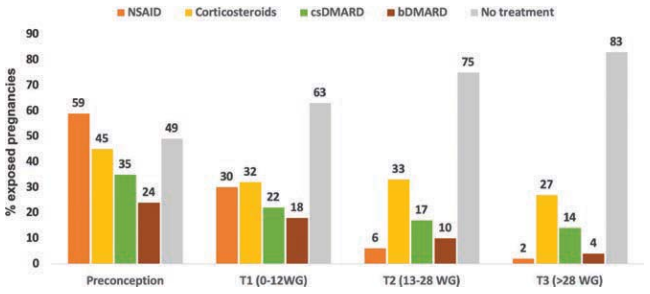
Background: Treatment of patients with chronic rheumatic inflammatory diseases (CRID) during pregnancy has changed in the last decade, namely due to the availability of new DMARDs labelled to be used during pregnancy.
Objectives: To describe the anti-rheumatic drug use during pregnancy in women with CRID (i.e. rheumatoid arthritis (RA) or spondyloarthritis (SpA)) in France over the past decade.
Methods: This is a retrospective cohort study within the French Healthcare database (SNDS), which covers 98% of the French population. Adult women were included if they had RA or SpA according to CIM-10 codes, had started a singleton pregnancy between 2008 and 2017 (index date), and were continuously covered by this health insurance from 1-year before pregnancy onset to 1-year after end of the pregnancy or death (whichever comes first). The treatment exposures of interest were: NSAIDs, oral corticosteroids, csDMARD (methotrexate, leflunomide, sulfasalazine, azathioprine, hydroxychloroquine), biologics (anti-TNF, rituximab, abatacept, tocilizumab, ustekinumab, anakinra). Exposure during pregnancy was defined as at least one drug reimbursement from the 6 months before the last menstrual period (LMP) to the end of pregnancy period.
Results: Among the 35,737 adult women with a CIRD (40.7% with RA and 59.3% with SpA) who had a past history of DMARD reimbursement, 11,274 (41.7%) started a singleton pregnancy during the study period. In total, during preconception and pregnancy, 4,773 (42.3%) women were not delivered any DMARD nor corticosteroids, 769 (6.8%) were delivered corticosteroids alone, 3,639 (32.2%) a csDMARD alone and 2,862 (25.4%) a biologic (among whom 33.1% associated a csDMARD). Biologics delivered during pregnancy were mainly anti-TNFs (92.1%). Exposure to NSAIDs was more frequent during the first trimester (30% patients) of pregnancy but occurred all along the pregnancy (6% and 2% in the second and third trimesters, respectively). Conversely, exposure to oral corticosteroids was stable during the pregnancy (33% to 27%); however, more than half of the prescriptions corresponded to doses higher than 10mg. Exposure to DMARDs including bDMARDs during pregnancy was more frequent during the first trimester, compared to the rest of the pregnancy (see graph).



Conclusion: Overall, less than 50% of women with a CRID who received a DMARD prior to the pregnancy continued to retrieve such treatment during pregnancy, and overall less than 20% were delivered biologics during pregnancy. Whether the withdrawal of DMARDs led to unfavorable maternal and pregnancy outcomes needs to be evaluated.
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POS1406 EVALUATING THE QUALITY OF CARE FOR HEART FAILURE HOSPITALIZATIONS IN INFLAMMATORY ARTHRITIS- A POPULATION-BASED COHORT STUDY

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Background: Individuals with inflammatory arthritis (IA) have an increased risk of heart failure (HF). Little is known if the quality of HF care differs among patients with IA compared to other chronic diseases such as diabetes mellitus (DM).
Objectives: We examined adherence to quality-of-care indicators for HF hospitalizations among patients with IA compared to those with DM but no IA and the general population (without IA or DM).
Methods: We linked multiple population-based health datasets to construct a cohort of adults living in Ontario, Canada on January 1, 2011 and followed to December 2020. The IA cohort was identified using validated case definitions and included patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. Comparison cohorts included adults with DM but no IA and general comparators without DM or IA. We included all subjects with a first HF hospitalization and who were alive at the time of discharge. We summarized the percentage of subjects in each of the 3 exposure groups who achieved recommended quality process measures [1]: (1) % receiving echocardiogram, (2) % receiving electrocardiogram, (3) % receiving a chest x-ray; and (4) % seen by a physician within 7 days of discharge. For those over the age of 65 years in whom medication information was universally available, we examined how many were dispensed evidence-based therapies: (5) % prescribed β-blocker, (6) % prescribed angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, (7) % prescribed mineralocorticoid receptor antagonist. We categorized adherence as perfect, moderate, or poor based on the number of measures achieved and compared proportions using pair-wise chi-squared tests.
Results: A first HF hospitalization occurred in 5,836 IA patients, 33,553 DM patients and 62,256 general comparators. The crude incidence rate for HF in IA was 2.70 per 1000/PY and was significantly higher compared to the general population (0.84 per 1000/PY), but lower compared to the DM cohort (5.01 per 1000/PY, p< 0.001). Mean age at time of HF hospitalization was significantly higher in the IA group (78 years) with more females affected (58%) compared to either the DM or general population group (p<0.001). All groups had high achievement of testing process measures and there were no differences in perfect adherence between the IA vs. DM and IA vs. general population comparators (Table 1). For those >65 years of age, patients with IA were less likely to achieve perfect adherence for medication quality indicators compared to either the DM or general population.

Table 1. Percentage in each of three exposure groups achieving the recommended HF quality measures.

Process Measure	IA Group	DM Group	General Population
1.Echocardiogram	90.6%	91.1%	89.5%
2.Electrocardiogram	97.4%	97.4%	97.3%
3.Chest x-ray	99.7%	99.6%	99.6%
4.Health care provider visit within 7 days of discharge	39.0%	38.9%	38.7%
Perfect Adherence (achieving 1, 2,3 and 4 above)	33.0%	33.0% (p=0.43, IA vs. DM)	32.2% (p=0.15, IA vs general population)
5.Beta-blocker prescribed	64.8%	70.5%	66.6%
6.Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker prescribed	54.8%	61.3%	56.2%
7.Mineralocorticoid receptor antagonist prescribed	20.3%	19.9%	21.2%
Perfect Adherence (achieving 5, 6 and 7 above)	10.6%	12.0% (p=<0.001, IA vs. DM)	12.0% (p=0.02, IA vs general population)

Conclusion: HF quality indicators are adhered to in a high proportion of patients with IA following HF hospitalization. However, reasons for lower HF medication prescribing in IA compared to other high-risk conditions, such as DM, requires further evaluation. It will also be important to determine if adherence to HF quality of care translates to reduced long-term outcomes such as repeat HF hospitalizations and cardiovascular mortality, which we are currently exploring.
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Disclosure of Interests: Bindee Kuriya Speakers bureau: Abbvie, Gilead, Pfizer, Lihi Eder Speakers bureau: Abbvie, UCB, Pfizer, Eli Lily, Novartis and Sandoz, Jessica Widdifield: None declared, Laura Ferreira-Legere: None declared, Irene JH Jeong: None declared, Jiming Fang: None declared, Anna Chu: None declared, Jacob Udell: None declared
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Epidemiology, risk factors for disease or disease progression

POS1407

THE MANAGEMENT OF CONTEMPORARY EARLY UNDIFFERENTIATED ARTHRITIS: DATA ON EULAR'S RECOMMENDATION ON THE RISK OF PERSISTENT DISEASE

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Background: EULAR recommendations for early arthritis recommend assessing the following risk factors for persistent disease in Undifferentiated Arthritis (UA): polyarthritis, acute phase reactants (i.e. c-reactive protein(CRP), erythrocyte sedimentation rate(ESR)), rheumatoid factor (RF), ACPA and imaging findings/erosions. However, these recommendations are based on an outdated definition of UA: not fulfilling 1987 RA criteria and having no alternative diagnosis ('conventional UA'). Since the introduction of the 2010 RA criteria the characterization of UA has changed. The contemporary definition of UA is: not fulfilling 1987- nor 2010 criteria, and having no alternative diagnosis. Therefore, predictors for persistent disease in conventional UA may not be applicable in contemporary UA.
Objectives: Our objective was to assess which risk factors for persistent disease, as mentioned in the EULAR recommendations, are applicable in contemporary UA.
Methods: Patients consecutively included in the Leiden Early Arthritis Clinic cohort with contemporary UA between 2006-2019, when DMARD start in UA was recommended, were studied. The outcome was sustained remission, defined as absence of clinical synovitis without DMARD use (including corticosteroids) for the entire follow-up (at least one year). Cox regression was used to test the association between the risk factors as mentioned in EULAR-guidelines and sustained remission. For comparison, patients with conventional UA (not fulfilling the 1987 criteria and no other diagnosis) were studied using similar analyses.
Results: Contemporary UA patients (n=710) were mostly ACPA negative (95%) and had a median of 2 swollen joints. Radiographic erosions were rare (1.8%). 60% of contemporary UA patients achieved sustained remission after median 1.5 years (IQR 1-3). After achieving remission patients were followed for 5.5 years without clinical arthritis, demonstrating sustainability. Univariably, CRP, ESR, ACPA and RF were associated with time to sustained remission, while polyarthritis was not. In multivariable analysis, only ACPA and CRP were independently associated with sustained remission (HR 0.10 (95%CI:0.03-0.32) and HR 0.67(0.50-0.91), respectively). 67% of contemporary UA patients had none of these risk factors. In contrast, only 2% had both CRP and ACPA. For comparison, multivariable analysis in conventional UA patients showed that ACPA, RF, CRP and polyarthritis were all independently associated with sustained remission.
Conclusion: The contemporary UA population is different from conventional UA and risk factors for disease persistence are partly dissimilar. ACPA and CRP remain to be predictive in contemporary UA. Other factors included in the current EULAR recommendation were uninformative (RF, ESR, polyarthritis) or rare (erosions). Therefore, risk factors recommended in future EULAR recommendations may require alterations.
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POS1408

AN ULTRASOUND NEGATIVE FOR SUBCLINICAL SYNOVITIS IN PATIENTS WITH ARTHRALGIA: IS IT HELPFUL IN IDENTIFYING THOSE WHO WILL NOT DEVELOP INFLAMMATORY ARTHRITIS? A LONGITUDINAL STUDY IN FOUR ARTHRALGIA COHORTS

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Background: Ultrasound (US) has become an established method in the evaluation of joints and is often used in clinical practice to guide management decisions in arthralgia-patients. To date, studies on the prognostic value of MSUS in arthralgia focused on the positive predictive value of subclinical inflammation. However, also the absence of imaging-detected subclinical synovitis is now increasingly used in daily practice to exclude arthralgia-patients from further follow-up. Though, evidence on the value of a negative US in ruling out future IA development in arthralgia-patients (the negative predictive value) is mostly absent. According to the rules of Bayes, predictive values are highly dependent on the prior-risk of developing the disease. The NPV therefore, is strongly related to the prior-risk of not getting IA, which is quite considerable in arthralgia-patients.
Objectives: To investigate the negative predictive value (NPV) of musculoskeletal ultrasound (MSUS) in arthralgia patients at risk for developing inflammatory arthritis (IA).
Methods: An MSUS examination of hands and feet was performed in arthralgia-patients at risk for IA in four independent cohorts. Patients were followed for one-year on the development of IA. Subclinical synovitis was defined as greyscale≥2 and/or power Doppler≥1. NPVs were determined and compared with the prior risks of not developing IA. Outcomes were pooled using meta-analyses and meta-regression analyses. In sensitivity analyses, MSUS-imaging of tender joints only (rather than the full US-protocol) was analyzed and ACPA-stratification applied, the latter being in line with the use of US in daily care.
Results: After one-year 78%, 82%, 77% and 72% of patients in the four cohorts did not develop IA. The NPV of a negative US was 86%, 85%, 82% and 90%, respectively. The meta-analysis showed a pooled non-IA prevalence of 79%(95%CI: 75%-83%) and a pooled NPV of 86%(95%CI:81-89%) (Figure 1). Imaging tender joints only (as generally done in clinical practice) and ACPA-stratification showed similar results.

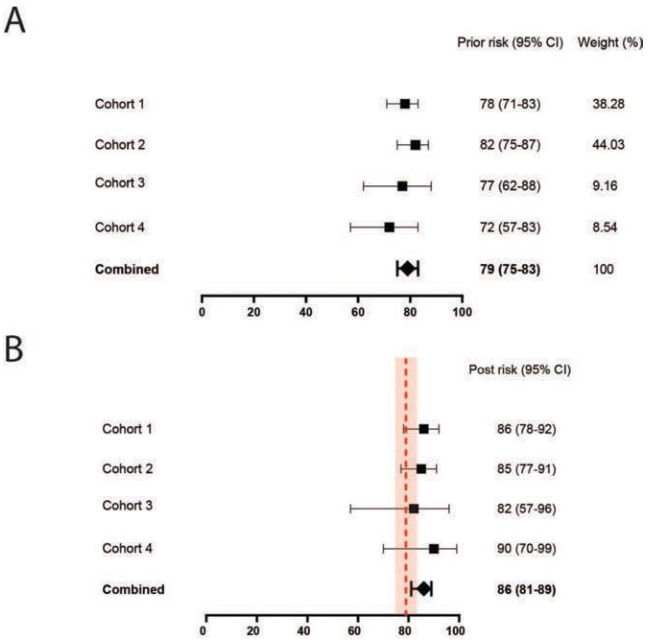

Figure 1. Full US protocol; Prior risks of not developing IA (A) and negative predictive values of MSUS (B) in the four cohorts. For comparison, the pooled prior risk and confidence interval from A are depicted in the red column in B.

Conclusion: A negative US result in arthralgia has a high NPV for not developing IA, which is mainly due to the high a-priori risk of not developing IA. The added value of a negative US (<10% increase) was limited.
References: N.A.
Disclosure of Interests: Cleo Rogier: None declared, Giulia Frazzei: None declared, Marion Kortekaas: None declared, Marloes Verstappen: None declared, Sarah Ohrndorf: None declared, Elise van Mulligen: None declared, Ronald van Vollenhoven Speakers bureau: Speaker, for which institutional and/or personal honoraria were received: AbbVie, Galapagos, GSK, Janssen, Pfizer, UCB, Consultant of: Consultancy, for which institutional and/or personal honoraria were received: AbbVie, AstraZeneca, Biogen, Biotest, BMS, Galapagos, Gilead, Janssen, Pfizer, Sanofi, Servier, UCB, Vielabio, Grant/research support from:
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POS1409

ASSOCIATION BETWEEN SHORT-TERM EXPOSURE TO ENVIRONMENTAL AIR POLLUTION AND PSORIASIS FLARE

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Background: Psoriasis is a chronic inflammatory disease with a relapsing-remitting course. Selected environmental factors such as infections, stressful life events or drugs may trigger disease flares. Whether the air pollution could trigger psoriasis flares is still unknown.

Objectives: To investigate whether the short-term exposure to environmental air pollution is associated to psoriasis flares.

Methods: Observational study with both case-crossover and cross-sectional design was conducted. We retrospectively analyzed longitudinal data from 2013 to 2020 of patients with psoriasis attending the outpatient dermatologic clinic of the University Hospital of Verona. For the case-cross over analysis patients with at least one disease flare, defined as PASI increase ≥5 between 2 consecutive assessments in a time frame of 3-4 months, were considered. In the case-crossover analysis each patient serves as its own control; the exposure of interest is compared in two different periods in the same group of patients followed longitudinally (Figure 1). For the cross-sectional analysis, patients receiving any systemic treatment for ≥6 months, with ≥2 consecutive PASI assessment were included. We compared the mean and cumulative (area under the curve) concentrations of several air pollutants (CO, NO2, NOx, C6H6, PM10 and PM2.5) in the 60 days preceding the psoriasis flare and the control visits.

Results: A total of 957 patients with plaque psoriasis with 4,398 follow-up visits were included in the study. More than 15,000 measurements of air pollutants concentration from the official, open-source, bulletin of the Italian Institute for Environmental Protection and Research (ISPRA) were retrieved. Among the overall cohort, 369 (38.6%) patients with psoriasis flare were included in the case-crossover study. We found that concentrations of all pollutants were significantly higher in the 60 days before psoriasis flare (median PASI at the flare 12, IQR 9-18), compared to the control visit (median PASI 1, IQR 1-3, p <0.0001). In the cross-sectional analysis, exposure to mean PM10 over 20 µg/m3 and mean PM2.5 over 15 µg/m3 in the 60 days before assessment were associated with a higher risk of PASI ≥5 point worsening, aOR 1.55, 95% CI 1.21-1.99 and aOR 1.25, 95% CI 1.0-1.57, respectively (Figure 1). Sensitivity analyses that stratified for trimester of evaluation, with various lag of exposure and adjusting for type of treatment yielded similar results.

Conclusion: Air pollution may be a trigger factor for psoriasis flare.

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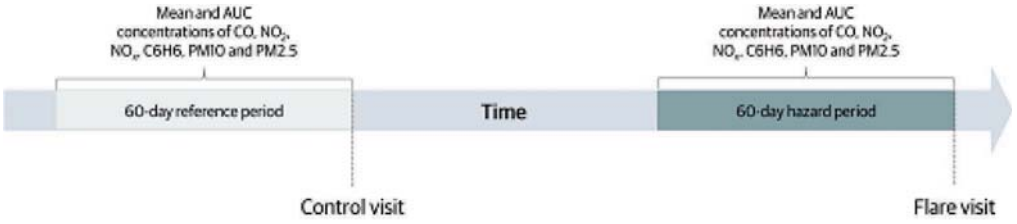

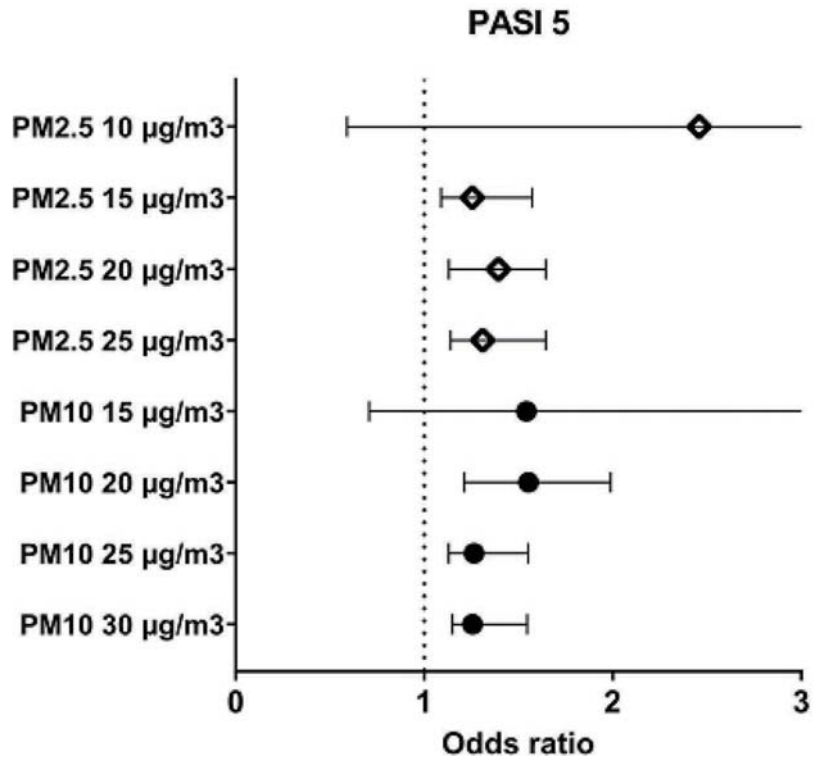

POS1410

DEVELOPMENT OF PREDICTION MODELS FOR SENIOR PATIENTS WITH RHEUMATOID ARTHRITIS AND COMORBIDITIES TREATED WITH CHRONIC LOW-DOSE GLUCOCORTICOIDS IN THE GLORIA TRIAL

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Background: Rheumatoid arthritis (RA) is a systemic, inflammatory disease primarily located in the joints resulting in pain, joint damage, functional disability and reduced quality of life. Treatment of RA is essential to prevent these outcomes, but the treatment itself may also result in adverse events and comorbidity [1]. Although many investigators are working on personalized medicine [2], better models to predict harm and benefit from a certain drug need to be developed before they can be used in daily clinical practice [3].

Objectives: To develop prediction models for individual patient harm and benefit outcomes in senior patients with RA and comorbidities treated with chronic low-dose glucocorticoid therapy or placebo.

Methods: In the GLORIA trial 451 RA patients aged 65+ were randomized to 2 years 5 mg/day prednisolone or placebo. Eight prediction models were developed from the dataset in a stepwise procedure. In preparation, to limit excessive statistical testing and false positive results, possible predictors were grouped into five predictor sets based on prior knowledge (Table 1). The first set of four models disregarded study treatment and examined general predictive factors. The second set of four models was similar but examined the additional role of study treatment, as main factor and as interaction factor with other predictive variables. In each set two models focused on harm (1: occurrence of ≥1 adverse event of special interest (AESI); 2: number of AESIs per year) and two on benefit (3: early clinical response–disease activity; 4: lack of joint damage progression). AESI comprised all serious adverse events, events leading to discontinuation of study treatment, and events related to glucocorticoid exposure (see main GLORIA study abstract). Linear and logistic multivariable regression methods with backward selection were used to develop the models. The final models were assessed and internally validated with bootstrapping techniques, and their performance was evaluated with model fit and discrimination measures.

Table 1. Predictor sets.

Personal factors	Disease factors	Comorbidities
Age	DAS28	Active comorbidity: cont, dich,
Sex	RA duration	GC-related
Education	RF	Prior comorbidity: cont, dich,
Smoking	Anti-CCP	GC-related
Alcohol	Damage (cont, dich)	# comorbidity medications
BMI	Coping RA	Joint surgery
Blood pressure	Impact RA	# patient symptoms
Medication	Health and daily functioning	
# concomitant medications	HAQ	
Previous use DMARD, bDMARD, GC	QoL	
Current use bDMARD	VAS health	
Adherence	SF36 physical, mental	
Switch antirheumatic drugs		

cont=continuous; dich=dichotomous; GC=glucocorticoid.

Results: Study treatment (i.e. prednisolone) was highly predictive as a main factor in models 5-8, increasing the risk of both benefit and harm. In addition, a few additional variables were slightly (but not relevantly) predictive for the outcome in one of the models (Figure 1). Their association was much weaker than that of study treatment. In three instances, prednisolone interacted with another predictive factor (see Figure 1). The quality of the prediction models was sufficient, the performance low to moderate: explained variance: 12-15%, AUC 0.67-0.69.

Figure 1. Baseline predictive factors for benefit and harm (other than prednisolone), and their interaction with prednisolone.
For benefit red means less benefit, for harm red means increase of harm.

To predict: / Baseline predictive factor:	Benefit*		Harm			
	Early response	No damage progression	≥1 AESI	Prednisolone effect	# AESIs	Prednisolone effect
More prior comorbidities						
More medication						
More joint damage				neutralized		
More adherence						decreased
No change of antirheumatic treatment at baseline						
No prior treatment with biologicals						
Prior occurrence of GC-related comorbidity						
More disability (HAQ)						

*For benefit prednisolone showed no interaction with other predictive variables.
AESI=adverse event of special interest; GC=glucocorticoid; HAQ=health assessment questionnaire.

Conclusion: Baseline factors are not helpful to select senior RA patients for treatment with low-dose prednisolone given their low power to predict the chance of benefit or harm.

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POS1411

ARTIFICIAL INTELLIGENCE FOR IDENTIFYING NEW DISEASE CLUSTERS IN PATIENTS WITH PSORIATIC ARTHRITIS/PSORIASIS: A PROOF-OF-CONCEPT STUDY

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Background: Psoriatic arthritis (PsA)/Psoriasis (PsO) patients present with multiple long-term conditions (MLTCs), and more than half of PsA patients have ≥1 LTC, which have an impact on the quality of life. We used the Clinical Practice Research Datalink (CPRD) in the UK to determine multimorbidity in patients with PsA/PsO. CPRD is a database of routinely collected UK patient data that can be used to examine multimorbidity over the life course of the disease. A understanding of clusters and timing may allow the development of tailored programmes for surveillance and early interventions to reduce MLTcs in PSA/PO.

Objectives: The overall objective of our study was to use CPRD to identify and interpret new and frequently-occurring disease clusters in the PsA/PsO population.

Methods: We identified PsA/PsO patients from the CPRD GOLD for the UK from 2009 to 2018 with at least one year of follow up but excluded patients in practices that had migrated to Aurum, a different electronic health record system held by CPRD. All patients were matched to controls at a 1: 4 ratio by age, sex, practice. We analysed 40 common MLTCs outlined by Barnett et al. to identify and interpret multimorbidity clusters. Multimorbidity clusters were identified using the network bi-clustering. Our methodology can be divided into three steps- (a) Separate the "case" and the "control" population, (b) Create a patient-condition matrix for each of "case" and "control" population and (c) From the patient-condition matrix in each case use a the Euclidean distance criterion to compute a similarity matrix of all the possible conditions among those patients.

Results: We identified 67,827 incident or prevalent PsA/PsO patients aged 20 years and above who were matched to 271,308 controls by age, sex and practice (Table 1). The median number of long-term conditions (LTCs) was higher in the cases than in the controls.

Table 1.

Characteristic	CASE, N = 67,827	CONTROL, N = 271,308
Age Group, n (%)		
<20	6,491 (9.6%)	27,897 (10%)
20-54	42,357 (62.4%)	169,008(62.3%)
55 and above	19,148 (28.2%)	74,403 (27.4%)
Ethnicity, n (%)		
White	28,200 (41.6%)	93,485 (34.5%)
Black, S.Asian and other	956 (1.4%)	3,735 (1.4%)
Unknown	38,671 (57%)	174,088(64.2%)
Sex, n (%)		
F	35,431 (52%)	141,724 (52%)
BMI category, n (%)		
20 to <25	11,183 (16.5%)	43,240 (15.9%)
25 to <30	13,565 (20%)	45,783 (16.9%)
30 to <35	7,584 (11.2%)	22,690 (8.4%)
35 to 40	3,048 (4.5%)	8,172 (3.0%)
Alcohol status, n (%)		
Non-drinker/ Ex-drinker	8,649/2,159 (15.9%)	33,983/7,579 (15.3%)
Drinker/Heavy drinker	47,316/3,030 (74.2%)	180,888/8,831 (69.9%)
Smoking status, n (%)		
Ex-smoker/Non-smoker	14,137/29,289 (64%)	48,110/142,295 (70.2%)
Smoker	24,018 (35%)	71,779 (26%)
Long term condition, Median (IQR)	1.00 (0.00, 3.00)	1.00 (0.00, 2.00)

We present the results obtained via spectral clustering on the similarity matrix obtained in each “case” and “control” population via Euclidean distance. There are 40 LTCs which are represented via two clusters in the “case” and the “control” population network (Figure 1). The LTCs in the same cluster are strongly connected within themselves compared to those in the other cluster. The noticeable part was clustering of diabetes, hypertension and chronic heart diseases in one group, especially in the “case” population over the “control” population. Interestingly depression, dementia and chronic heart diseases were in the same group in the clustering results for both the “case” and the “control” population. There are a central group of diseases (HYP, DEM, DIV, CHD etc.) in Figure 1, which seems to be connected with both sets of clusters. As mentioned earlier, diabetes has connections with these central groups of diseases, and it tends to be more pronounced in the “case” population.

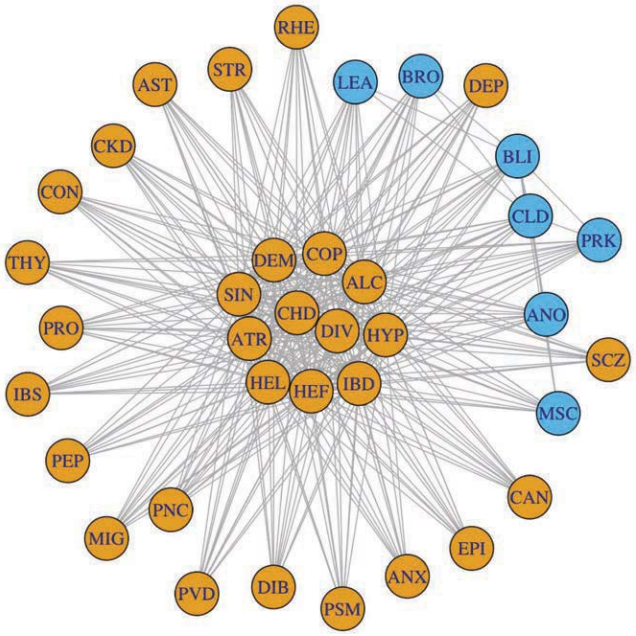

Figure 1.

Conclusion: MLTCs including diabetes, hypertension, chronic kidney disease and heart disease occurred together more commonly in patients with PsA/PsO than those without PsA/PsO.

The future goal is to identify frequently occurring clusters of MLTCs in the immune-mediated inflammatory disease population.

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POS1412

FIRSTS RESULTS OF THE PRAISE STUDY (PATIENT-REPORTED AUTOIMMUNITY SECONDARY TO CANCER IMMUNOTHERAPY): MULTICENTRIC PROSPECTIVE COHORT STUDY ON AUTOIMMUNE DISEASES SECONDARY TO CANCER IMMUNOTHÉRAPY

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Background: In cancer immunotherapy, T-lymphocyte activation can lead to secondary autoimmune diseases named OASI for Opportunistic Autoimmunity Secondary to cancer Immunotherapy [1]. The epidemiology of OASI deserves to be further studied due to the unadapted reporting of clinical trials and the lack of prospective studies. Moreover, literature focuses on the most severe OASI and/or on specific OASI (myocarditis, colitis, arthritis).

Objectives: Our goal was to determine incidence, severity of all grade OASI using a multicentric prospective patient cohort starting treatment with cancer immunotherapy.

Methods: We present a multicentric, prospective, observational, longitudinal, real life, French e-cohort. 900 patients treated with ipilimumumab and/or nivolumab will be included. Data is collected from the patient and the oncologist at inclusion, then patients report directly any symptom that could be suggestive of OASI with the help of monthly digital questionaries. In case an OASI is suspected, further confirmation is made with the practician in charge and by a paired analysis with the Système National De Santé (SNDS), the French health insurance registry.

Results: On the 19/01/2022, 439 patients were included, 310 males (70.6%) and 129 females (29.4%). Mean age is 66 years old with a median follow up of 192 days. 354 patients (80.6%) are treated with Nivolumab alone, 7 (1.6%) with Ipilimumab alone and 76 (17.8 %) with combined Nivolumab + Ipilimumab. 136 patients (31.6%) are treated for a non-small cell lung carcinoma, 107 patients (24.9%) for a clear cell renal carcinoma, 91 patients (21.2%) for a skin melanoma, 49 patients (11.4%) for a head or neck epidermoid carcinoma, 24 patients (5.6%) for another lung cancer sub-type, and 32 patients (5.3%) for another histological cancer type. The mean follow-up is 294 days (+/- 192). 83 patients (18.9%) died since the beginning of the follow up.

47 patients (10.7%) developed 63 OASI. The mean delay between the beginning of cancer immunotherapy and the OASI is 134.7 days (+/- 103.4).

Approximately, one third of the OASI were musculoskeletal diseases. The OASI included polymyalgia rheumatica (3 patients), psoriatic arthritis (1 patient), polyarthritis (1 patient) systemic lupus (1 patient), arthralgias and myalgias (8 patients), colitis (11 patients), dysthyroïditis (6 patients), hepatitis (4 patients), nephritis (3 patients), pneumonitis (2 patients), hypophysitis (2 patients), adrenal insufficiency (4 patients), myocarditis (1 patient), hemophagocytic lympho-histiocytosis (1 patient), and other types of OASI (15 patients).

26 patients (55% of patients with OASI, 5,9% of all patients) had to stop cancer immunotherapy due to an OASI, one because of a rheumatic disease (systemic lupus). 52 patients were treated with corticosteroids, 1 patient with methotrexate (psoriatic arthritis), 3 patients with infliximab (colitis) and 1 patient with abatacept (myocarditis). 1 patient died after an OASI (colitis).

Conclusion: The first results of this prospective study, using an original patient-centered methodology, confirm the expected incidence of autoimmune events secondary to cancer immunotherapy and the role of rheumatologists in their therapeutic management.

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POS1413 INTERSTITIAL LUNG DISEASE(ILD) PREVALENCE AND TRENDS IN SYSTEMIC LUPUS ERYTHEMATOSUS(SLE), RHEUMATOID ARTHRITIS(RA), SCLERODERMA(SCL), MYOSITIS AND MIXED CONNECTIVE TISSUE DISEASES(MCTD) ALONG WITH COMPARISON OF LENGTH OF HOSPITALIZATION STAY(LOS), COST AND RACIAL PREDISPOSITION AMONG THESE PATIENTS

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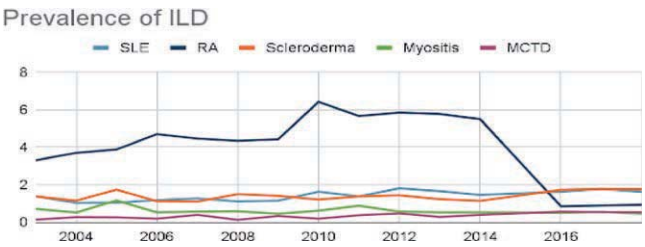
Background: ILD includes a category of lung disorders seen in a variety of autoimmune conditions. Prevalence of ILD in autoimmune diseases is variable and poorly studied. ILD is more commonly seen in systemic sclerosis, with 90% of patients showing some interstitial changes on High resolution CT scan. ILD is less common in SLE compared to SCL, with ILD not only a complication but also a poor prognostic factor in these patients. Prior studies have shown increased prevalence of ILD in RA patients over the years. For myositis, ILD can develop during the course of disease or can precede the diagnosis in a small subset of patients.

Objectives: Our study aims to determine the prevalence of ILD in diseases like SLE, Scleroderma, RA, MCTD, and Myositis over the years as well as identify racial predisposition, LOS, Cost of hospitalization in these patients

Methods: We used the Nationwide Inpatient Sample database (years 2003-2018) and extracted patients with ILD using validated International Classification of Disease (ICD) codes. Data from 2015 was excluded from the study in light of the transition of the coding system from version 9 to 10. We identified cases having the diagnosis of SLE, RA, Scleroderma, MCTD or Myositis. Prevalence as well as demographics, cost of hospitalization, and length of stay (LOS) was analyzed and charted. Data was analyzed using statistical analysis system 9.4 software.

Results:



We identified a total of 149,691 cases of ILD over 15 years. Patients with RA had the highest prevalence of ILD amongst the 5 studied autoimmune diseases. The prevalence rate of RA in ILD patients in 2003 was 3.3% which significantly reduced to 0.93% in 2018, with a peak of 6.42% seen in 2010 (p <0.0001). Prevalence rate of ILD with myositis decreased from 0.72% in 2003 to 0.46% in 2018 (p 0.0001). The prevalence rates of SLE, Scleroderma, and MCTD in cases with ILD significantly increased from 1.38% to 1.63%, 1.38% to 1.76%, and 0.14% to 0.54% from 2003 to 2018 respectively.

The average age of ILD cases with SLE was significantly younger compared to ILD without autoimmune disease (59.28 vs 72.32 years, p <0.0001), RA (69.72 vs 72.17 years, p <0.0001), Scleroderma (62.01 vs 72.28 years, p < 0.0001), Myositis (59.56 vs 72.19 years, p <0.0001) and MCTD (59.6 vs 72.18 years, p <0.0001). On examining the racial distribution, the African American population with ILD when compared to other races were more likely to have underlying SLE, MCTD, Myositis or Scleroderma. In ILD with RA, Native Americans were the most affected racial demographic followed by African Americans.

Average cost of hospitalization was higher in ILD with MCTD ($104,631 vs $71,264.6, p<0.0001), Myositis ($105,623 vs $71,232.9, p<0.0001) and Scleroderma ($88,736.2 vs $71,135.5, p<0.0001). Average LOS was significantly longer in RA (7.17 vs 6.66 days, p value 0.0006), MCTD (7.71 vs 6.67 days, p value 0.0008), Myositis (8.33 vs 6.66 days, p value <0.0001) and Scleroderma (7.07 vs 6.67 days, p value 0.0176). Though not significant, average LOS was longer in SLE (6.79 vs 6.67 days, p value 0.4999).

Conclusion: Our study shows that the prevalence of RA in ILD cases has significantly reduced through the years. This can be attributed to the better understanding of the disease and its risk factors as well as the availability and use of newer biologic agents to obtain better control. However, the prevalence of SLE, Scleroderma, and MCTD in ILD cases has increased over the years. This points to the need for better therapies as well as highlights the fact that the overall recognition and diagnosis of these diseases have increased over the years. Racial predilection also comes to light, suggesting the need for special attention to certain races to diagnose the autoimmune disease earlier. Average LOS and cost of hospitalization were also higher in ILD cases with autoimmune disease, reflecting the higher socioeconomic burden.

Disclosure of Interests: None declared

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POS1414 RISK OF CANCER IN CONNECTIVE TISSUE DISORDERS IN THE NORTH EAST OF ITALY OVER 15 YEARS OF FOLLOW-UP

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Background: Connective tissue diseases (CTD) include systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), polymyositis (PM), and dermatomyositis (DM). CTD are characterized by dysfunction of the immune system that leads to the loss of tolerance to self-antigens [1]. Shared genetics, environmental factors, medical treatment of autoimmune diseases and dysregulated immune function have led to speculation of an elevated cancer incidence in patients with autoimmune diseases [2].

Objectives: The present study aimed to evaluate the cancer risk associated with the most relevant CTD in the northern Italian region of Friuli Venezia Giulia over the years 2002-2017. The primary objective was to determine whether the risk of malignancy was higher among these rheumatic conditions than the age- and sex-corresponding general population.

Methods: A retrospective population-based cohort study was conducted using data from healthcare databases of the Friuli Venezia Giulia region, north-east of Italy (1,206,000 inhabitants). Information on demographic characteristics, hospital discharges, exemption from medical charges, drug prescriptions, were individually matched with data from the population-based cancer registry. The cancer risk was assessed in people diagnosed with the following diseases: SLE, SS, SSc, PM, and DM. To compare the cancer incidence in the cohort with the general population, Standardized Incidence Ratios (SIRs) were calculated as the ratio between the observed and the expected number of cancer cases. The cohort included subjects resident in the Friuli Venezia Giulia region, diagnosed with at least one of the following diseases: SLE, SSc, SS, DM, and PM. To guarantee the highest homogeneity and comparability of the exemptions codes, the analysis was restricted to the years 2002-2017.

Excluding criteria were: (1) follow-up shorter than 90 days; (2) concurrent diagnoses of rheumatoid arthritis (RA), psoriatic arthritis or ankylosing spondylitis; (3) ever use of biologic drug specific to treat RA (with the exception of rituximab), psoriatic arthritis or ankylosing spondylitis.

The patients were observed starting from 90 days after the first date when the diagnosis was mentioned in hospital discharges or exemptions, and they were followed until cancer diagnosis, death, change of regional residence, or December 31, 2017, whichever came first.

For the aim of this study, we excluded from the analysis NMSC (ICD-10: C44) and diagnoses based on autopsy only or Death Certificate Only.
Results: 2504 patients were followed-up for a total of 18,006 person-years (median follow-up: 6.8 years). After 5 and 10 years of follow-up, the cumulative cancer incidence was 2.6% and 8.5%, respectively. The most common cancers were breast (n=34), lung (n=24), colon-rectum-anus (n=20), and non-Hodgkin lymphomas (NHL) (n=20). Overall, no excess cancer risk was noted (SIR=0.87, 95% CI: 0.75-1.00), whereas the number of observed NHL cases was more than two-fold significantly higher than expected (SIR=2.52, 95% CI: 1.54-3.89). The subgroup analysis showed a higher risk of NHL among SS patients (SIR=3.84, 95% CI: 1.92-6.87) and SLE patients (SIR=2.69, 95% CI: 0.99-5.84). Conversely, the study population showed a decreased risk for cancers of breast (SIR=0.61, 95% CI: 0.42-0.85) and corpus uteri (SIR=0.21, 95% CI: 0.03-0.77).
Conclusion: The incidence of NHL was higher among patients with SS and SLE. A careful surveillance for haematological malignancies in these patients is recommended. The lower risk of cancer for breast and corpus uteri in CTD indirectly supports cancer screening programs and highlights the role of the continuous clinical follow-up for these chronic conditions.
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POS1415 A MACHINE LEARNING ANALYSIS OF FACTORS PREDICTING ORGAN DAMAGE PROGRESSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS USING THE SPANISH SOCIETY OF RHEUMATOLOGY LUPUS REGISTRY (RELESSER)

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Background: Evidence shows that around half of the patients with systemic lupus erythematosus (SLE) develop irreversible organ damage due to the disease itself or to other factors (e.g., steroid treatment). It is essential to have a comprehensive understanding of factors that predict organ damage progression to identify at-risk patients and inform clinical decision making.
Objectives: To develop an algorithm, using machine learning (ML) methodology, that predicts organ damage progression in SLE patients.
Methods: The Spanish Society of Rheumatology Lupus Registry (RELESSER) with patient records from 45 Rheumatology Units across Spain was used. RELESSER data were collected from 2011 to 2021 and captured demographic and comprehensive clinical information. In this analysis, a sample of 2,676 patients was used. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was used to measure organ damage progression between 2015 (start of the prospective data collection in RELESSER) and 2020.To predict the risk of an increase in the SDI, 102 variables were identified as potential predictors. A ML model (gradient boosting trees) was developed and validated by a simple logistic regression (LG) model. The area under the receiver operating characteristic curve (AUCROC) was used to quantify the improvement over random chance (an AUCROC of 0.5). Shapley Additive Explanation (SHAP) values were used in the ML model to identify predictors and their contribution to damage progression.
Results: Of all patients, 13% experienced organ damage progression, with 2-year patient follow-up. The ML algorithm was better at identifying these patients (AUCROC 0.68) than the LG model (AUCROC 0.63) (Figure 1). ML model performance can be contextualized using a random sample of 100 SLE patients of whom 13 suffered organ damage progression, the model would successfully identify 12. However, 66 additional patients would be incorrectly identified (True Positive 90%; False Positive 79%). The top 5 predictors of damage progression, across all patients, were patient age >49 years,

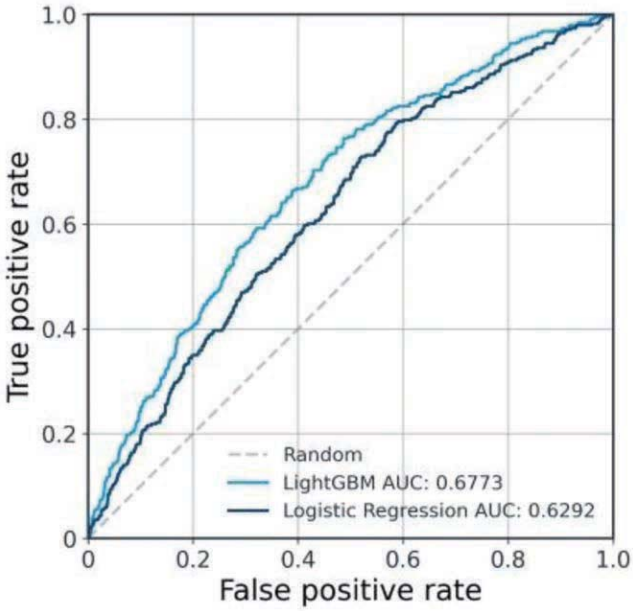

Figure 1. ROC AUC plot

Creatinine > 0.9 mg/dl, cardiovascular-related disease complications (> 3 complications), low hematocrit level recorded recently (<41.9 months ago), and triglycerides > 81.5 mg/dl. At the patient level, the 5 patients with the highest predicted risk had strong predictors of progression, with key predictors being patient age at study entry >49 years, age at diagnosis >40 years, cardiovascular-related disease complications, and increased creatinine >0.9 mg/dl. The 5 patients with the lowest predicted risk had strong predictors of no change with key predictors being not having a low hematocrit level recorded recently, triglycerides <81.5 mg/dl and patient age at study entry <49 years.
Conclusion: We developed a machine learning model, using an exhaustive set of variables in RELESSER which successfully predicted short-term organ damage progression in SLE patients, and outperformed a standard regression model. If the model were to be used as a clinical tool, only light-touch interventions should be carried out due to high false positive rate. Further model optimizations, including exposing the model to longer follow-up data and testing it in non-Spanish patients is needed.
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POS1416 LONG-TERM OUTCOME OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE); DATA FROM THE LARGE POPULATION-BASED SOUTHEAST SLE COHORT (NOR-SLE)

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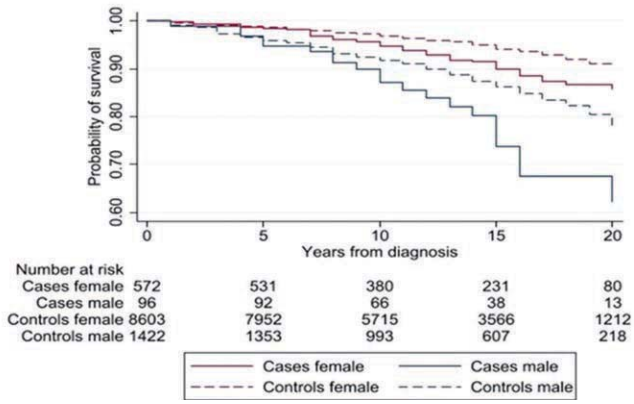
Background: Population-based studies on Systemic Lupus Erythematosus (SLE) patients with a verified diagnosis is considered the gold standard to find true outcomes in SLE, but few population-based SLE cohorts have follow-up over 15 years [1]. Norway is among the few countries worldwide where social and structural factors facilitate the gathering of complete population-based cohorts in rare disease like SLE due to its healthcare organization.
Objectives: To examine long-term outcome of SLE in a population-based setting and determine if immediate cause of death differs between SLE patients and the general population.
Methods: The study included all SLE patients who were resident in the South-east region of Norway during 1999 - 2017 and met the 1997 American College of Rheumatology classification criteria for SLE. All SLE diagnosis was confirmed by chart review. SLE patients and 15 controls for each case (matched by age, gender and ethnicity) were linked to the Norwegian Cause of Death Registry. We examined survival by means of Kaplan-Meyer estimates and used log rank test to test for differences. To estimate risk of death, we performed calculations of standard mortality rate (SMR) by dividing the number of deaths on the number of years observed. The excepted number of deaths referred to the number of deaths for the matched control group. All SLE cases were included in SMR. The 95 % confidence interval (CI) of SMR was calculated with Mid-P exact test. We defined immediate cause of death as the final event directly leading to death. An International Classification of Diseases 10th revision code of I00-99 or R96 classified as death from cardiovascular disease (CVD) (except pulmonary embolism and cerebral bleeding) and of infections A00-B99, J10-18, N39, M86 or U07.
Results: We identified 1298 SLE patients in the region, of whom 673 was incident cases; all captures within one year from diagnosis. Of the incident cases, 76 (11%) died during 8434 years of follow-up (Table 1). The five-, ten-, 15- and 20-year survival for incident SLE patients (controls) was respectively 98 (98), 94 (96), 87 (94) and 82 (88) % and differed significantly first after ten years of disease duration compared to controls. Figure 1 shows 20-year survival for incident SLE patients and matched controls; stratified by gender. SMR for all SLE cases was 2.3 (95 % CI 1.5. - 4.0); female SLE 2.5 (95 % CI 1.6 – 3.9) and male SLE 1.9 (95 % CI 1.3 – 2.2). The most common immediate cause of death in SLE patients was CVD; whereof myocardial infarction (21 %) was most frequent. SLE patients died more often of CVD than controls (29 % vs. 21 %, p = 0.01) and had a tendency to more infections (23 % vs. 18 %, p = 0.07), whereof pneumonia (58 %) was most frequent.

Table 1. Patient demographics, follow-up time and number of deaths in the total Systemic Lupus Erythematosus (SLE) cohort and in incident SLE patients.

	Total SLE cohort	Incident SLE	
		Female	Male
	n = 1298	n = 577	n = 96
Of European descent, n (%)	1140 (88)	472 (82)	86 (90)
Juvenile onset[a], n (%)	93 (7)	31 (5)	6 (6)
LN[b], n (%)	470 (36)	177 (30)	49 (51)
Cumulative ACR criteria[c], μ (SD)	5.4 (1.2)	5.3 (1.2)	5.1(1.1)
Follow-up years, total	19252	6160	1217
Deaths, n (%)	282 (23)	54 (9)	22 (23)
Age at diagnosis, years μ (SD)	35.5 (15.7)	37.4 (15.6)	44 (17.9)
Disease duration at death, years μ (SD)	20.4 (12.5)	9.6 (5.8)	10.6 (10.5)

μ: mean, n: number, SD: standard deviation[a] Diagnosed before age of 16 [b] Lupus Nephritis defined by 1999 American College of Rheumatology classification criteria for Systemic Lupus Erythematosus [c]1997 American Collee of Rheumatology classification criteria for Systemic Lupus Erythematosus

Figure 1. **Estimated 20-year survival in Systemic Lupus Erythematosus patients compared to controls; stratified by gender.**



Conclusion: Mortality in SLE is substantially increased. Differences in survival compared to the general population only appear after ten years of disease duration. CVD was the most common immediate cause of death and more frequent in SLE patients.

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POS1417

INTEROSSEOUS TENDON INFLAMMATION IN THE HANDS: A NOVEL FEATURE OF DEVELOPING RHEUMATOID ARTHRITIS? RESULTS FROM A LARGE MRI STUDY IN CLINICALLY SUSPECT ARTHRALGIA

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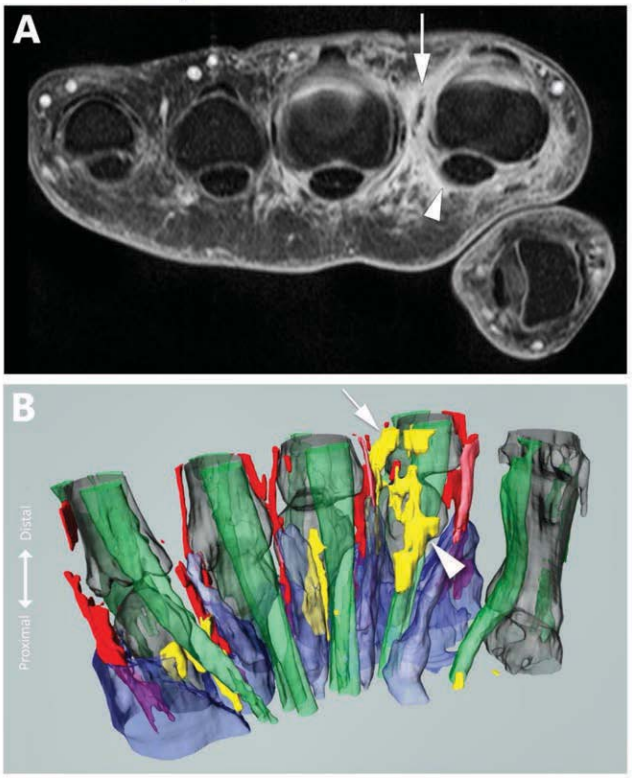
Background: Inflammation around the tendons of the hand interosseous muscles (interosseous tendon inflammation; ITI) on MRI was recently reported in rheumatoid arthritis (RA) patients and in ACPA-positive individuals with musculoskeletal symptoms. We therefore hypothesized that ITI is an early RA-feature that precedes clinical arthritis.
Objectives: To examine this we assessed the frequency of ITI in clinically suspect arthralgia (CSA) patients and compared this to the frequency in the general population. Additionally we investigated the relation between ITI and other locally inflamed tissues (synovitis/tenosynovitis/osteitis) in MCP-joins of CSA patients as well as the association with future arthritis development.
Methods: 667 consecutive patients presenting with CSA and 193 symptom-free controls from the general population underwent contrast-enhanced hand-MRI. MRIs were evaluated for ITI and for synovitis/tenosynovitis/osteitis, using the rheumatoid arthritis MRI scoring system (RAMRIS). CSA patients were followed for clinical arthritis development (median follow-up 25 months). Logistic and Cox-regression were used. ACPA-stratification was performed. To gain a better understanding of the anatomical relationships, 3D MRI-reconstruction of the interosseous and lumbrical muscles and tendons was performed in a patient with ITI.
Results: At presentation, 10% of CSA patients had ITI, compared to 1% of symptom-free controls (p<0.001). ITI was more frequent in ACPA-positive than ACPA-negative CSA (27% versus 7%; p<0.001). 72% of patients with ITI also had synovitis and/or tenosynovitis at the MCPs (37% synovitis; 7% tenosynovitis; 27% both synovitis and tenosynovitis). Also in multivariable analyses, adjusted for simultaneous presence of synovitis/tenosynovitis/osteitis, ITI was more likely if synovitis (OR 2.2 (95%CI 1.2-4.2)) or tenosynovitis (9.7 (5.5-17.0)) was present at MCPs. The 3D MRI-reconstruction indicated that ITI is continuous with MCP flexor tenosynovitis (Figure 1). CSA patients with ITI developed arthritis

more frequent than those without (HR 4.5 (2.8-7.2)); this relation was stronger in ACPA-negative (3.9 (1.9-7.9)) than ACPA-positive CSA (1.8 (0.9-3.4)).

Figure Example MR-image (A) and 3D MRI-reconstruction (B) at the level of the MCP-joints in a CSA-patient with ITI continuous with flexor tenosynovitis at the 2nd MCP-joint



Legend

(A&B)	Arrows:	ITI
	Arrowheads:	flexor tenosynovitis
(B)	Yellow:	inflammation around interosseous and flexor tendons
	Grey:	metacarpal bones and phalanges
	Red:	interosseous tendons
	Green:	flexor/extensor tendons of the fingers
	Blue:	interosseous and lumbrical muscles

Conclusion: ITI is present in CSA and precedes clinical arthritis, suggesting that this peritendinous inflammation is an early RA-feature.

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Disclosure of Interests: None declared

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POS1418 SEPARATING THE EFFECTS OF CHILDHOOD AND ADULT BODY SIZE ON INFLAMMATORY ARTHRITIS: A MENDELIAN RANDOMISATION STUDY

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Background: Obesity is strongly associated with inflammation and inflammatory arthritis, but most studies to date have only examined adulthood body mass index (BMI). Whether childhood obesity has a direct and long-term influence on risk of inflammatory arthritis is unclear. This question is important as childhood obesity becomes a growing and global public health crisis [1], but traditional epidemiologic approaches may be limited by reverse causation (obesity can be cause and consequence of disease) and confounding. Mendelian randomisation (MR) uses genetic variants as instrumental variables to estimate the effect of an exposure on an outcome. Since variants are randomly allocated at conception, MR is less susceptible to reverse causation and confounding.

Objectives: To examine whether childhood body size affects risk of inflammatory arthritides – rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), gout and systemic lupus erythematosus (SLE) – after accounting for the effect of adult body size using two-sample univariable and multivariable MR.

Methods: Genetic instruments for childhood (age 10 years) and adult body size were derived using data from 453,169 individuals from the UK biobank study (313 and 580 variants respectively; r^2<0.001, p<5x10^{-8}), which have been previously validated using BMI data from three independent populations [2]. Participants recalled their body size at age 10 as "thinner", "about average" or "plumper". Adult body size was determined using BMI at a mean age of 57 years and, to facilitate comparison, split into three groups to match the proportions for childhood body size. Genome-wide association data comprised of 22,350 RA, 9,069 AS, 3,609 PsA, 13,179 gout and 5,201 SLE cases. We conducted univariable MR to estimate the total effects of childhood and adult body size on outcomes and multivariable MR to examine the independent effect of childhood body size after accounting for adult body size. F statistics were calculated for each exposure with a value >10 considered suggestive of adequate instrument strength.

Results: The F statistic for childhood and adult body size instruments were 30 and 23 respectively. Genetically predicted childhood body size had a total effect on risk of PsA (OR 2.18 per change in body size category; 95%CI 1.43, 3.31), gout (OR 2.18; 1.43, 3.31) and SLE (OR 2.44; 1.14, 5.22), but not RA (OR 0.95; 0.70, 1.29) or AS (OR 0.96; 0.61, 1.52). After accounting for adult body size, the direct effect of childhood body size was little changed for PsA (OR 1.92; 1.14, 3.25) and SLE (OR 2.69; 1.24, 5.87), but was attenuated for gout (OR 1.40; 0.94, 2.09).

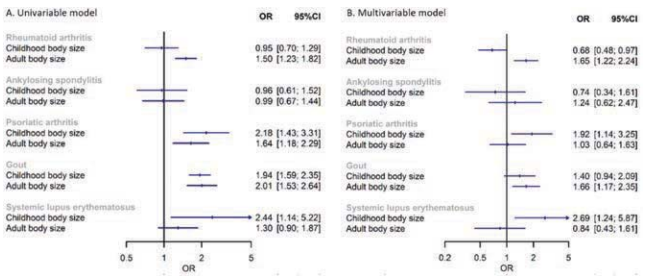

Figure 1. Mendelian randomisation estimates of the effect of childhood and adult body size on inflammatory arthritis.

Conclusion: Results of this study suggest that the risk conferred from having a larger body size during childhood may not be fully reversable even when a healthy size is achieved in adulthood. How the immune system is altered by early life adiposity to increase risk of PsA and SLE is unclear. Differential effect estimates of body size on each inflammatory arthritis (PsA vs AS, RA vs SLE) may help shed light on their unique pathophysiology in future studies.

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POS1419 CANCER INCIDENCE IN PATIENTS WITH AUTOIMMUNE DISEASES TREATED WITH CYCLOPHOSFAMIDE

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Background: Cyclophosphamide (CYC) is one of the first-line drugs for some serious manifestations of autoimmune diseases [1]. It has been associated with the appearance of a secondary cancer [2]. Several studies showing a higher incidence of cancer in small-vessel vasculitis in relation to CYC treatment have been carried out [3], but there is not much evidence about this complication in other autoimmune diseases.

Objectives: -Estimating the incidence of cancer in patients treated with CYC for serious manifestations of autoimmune diseases.
-Comparing the incidence of cancer in autoimmune diseases treated with immunosuppressants (IS) against the incidence of cancer in the general population.

Methods: This is a single-center retrospective cohort study. We included patients over 18 years old assessed in outpatient clinics of the Rheumatology service at the Ramón y Cajal Hospital from 1990 to 2018. They had been diagnosed with: diffuse or limited cutaneous systemic sclerosis (dcSSc/LSSc), systemic lupus erythematosus (SLE), vasculitis or others. We divided the patients into two groups; those exposed to CYC throughout the follow-up and those not exposed to it (being treated with other IS). Patients who had an active cancer at the time of starting the immunosuppressive therapy were excluded.
A descriptive analysis was carried out. The incidence of cancer was compared to the incidence of cancer in the general population according to the 2020 Spanish

Network of Cancer Registries data. A multivariate analysis was subsequently performed.

Results: Regarding the baseline characteristics of the patients included, there were no significant statistical differences in the sex, median age, and personal history of cancer. There was a bigger percentage of smokers in the non-exposed group. The incidence of cancer was similar y both groups (7.5% vs. 4.1%; p0.211). The cumulative incidence of cancer in our sample was 55.55/1.000 patients (95% CI 32.1-94.6). The standardized incidence ratio was 2.19 (95% CI 3.30-11.92) and it was stratified by sex and age. The bivariate analysis is shown in Table 1.

Table 1. Comparison between patients with or without appearance of cancer during the follow-up.

	Cancer (n 12)	No cancer (n 204)	P value
Male sex	7 (58,33%)	31 (15,19%)	0,001
Age at the time of the study	69,92 (±7,54)	53,88 (±16,75)	0,001
Smoking habit	6 (50%)	45 (22,06%)	0,027
Personal history of cancer	5 (41,66%)	5 (2,45%)	<0,001
Treatment with classical IS	1 (8,33%)	49 (24,02%)	0,303
Treatment with cDMARDs	1 (8,33%)	21 (10,29%)	1
Treatment with bDMARDs	1 (8,33%)	8 (3,92%)	0,408
Treatment with corticosteroids	2 (16,66%)	38 (18,63%)	1
Method of administration of CYC			
Intravenous	7 (58,33%)	78 (38,24%)	1
Oral	0 (0%)	6 (2,94%)	1
Both	0 (0%)	2 (0,98%)	1
Total administered dose of CYC (grams)	7,28 (±2,36)	6,59 (±3,68)	0,626

Regarding the multivariate analysis, the variables that demonstrated a statistically significant association with the appearance of cancer were age at the time of the study (OR 1.18 [1.02-1.36], p 0.024) and personal history of neoplasia (OR 7.86 [1.30-47.47], p 0.010).

Conclusion: The incidence of cancer in patients with autoimmune diseases treated with CYC is not higher with respect to patients with similar diseases treated with other IS. The increased incidence of cancer is associated with the personal history of cancer and older age. Studies with a larger sample size and prospective studies are necessary to verify these results and determine more clearly the associated risk factors.

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POS1420

DOUBLY ROBUST ESTIMATOR FOR AVERAGE TREATMENT EFFECT AS SENSITIVITY ANALYSIS FOR COMPARATIVE EFFECTIVENESS RESEARCH. AN EXAMPLE COMPARING DRUG MAINTENANCE BETWEEN BARICITINIB AND ALTERNATIVE BIOLOGIC DMARDS.

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Background: Drug maintenance is a common outcome measure of real world effectiveness studies, because it combines a measure of drug effectiveness and its tolerance / safety. Major hurdles of observational studies are potential selection biases and confounding. Cox proportional hazard ratio models address this issue by adjusting for potential confounders, but misspecification of the model may lead to biased estimates. 'Augmented Inverse Probability Treatment Weighting' (AIPTW) has the attractive property of being doubly robust, meaning that only one of the two underlying models has to be correctly specified to obtain consistent estimates. It can be used as a sensitivity analysis for Cox models, when analyzing time-to-event data.

Objectives: To evaluate AIPTW estimator and test the robustness of the results obtained by a Cox model.

Methods: Previous analyses in the Swiss rheumatoid arthritis (RA) registry (SCQM) had demonstrated that time to all-cause-discontinuation was significantly longer in RA patients on bariticinib (BARI, N = 273) compared to TNF-inhibitors (TNFi, N = 473); but not compared to other mode of actions biologics (OMA, N = 378) [1], in an adjusted Cox regression including age, gender, BMI, concomitant csDMARD, prednisone, CDAI score, disease duration, smoking status, line of therapy and seropositivity. Here we repeat the same analysis using AIPTW, including the same potential confounders. We combine a propensity score using a logistic regression model and an inverse probability weighted Cox regression. Two implementations of the AIPTW estimator are considered. First we use the *RiskRegression* package in R, to obtain risk ratios. Then we implement the AIPTW manually to obtain the average treatment effect as the difference in median survival time.

Results: Time to treatment discontinuation measured with Cox model was significantly longer for RA patients on BARI compared to patients on TNFi according to the adjusted Cox model (HR = 1.79), and a similar non-significant trend existed when compared to OMA (HR = 1.29). When considering 90-day treatment discontinuation measured with the AIPTW, the results were qualitatively very similar: the risk ratio between BARI and TNFi groups is statistically significant (RR = 2.51), while that of BARI against OMA is larger than one (RR = 1.47), but not statistically significant. Confidence intervals are larger with the AIPTW estimation.

Table 1. Cox Regression HR and AIPTW risk ratios

	Cox Regression Hazard Ratio (95% CI)	AIPTW Estimate of 90-day risk ratio of treatment discontinuation (95% CI)
BARI vs. TNFi	1.79* (1.34-2.38)	2.51* (1.19 – 3.83)
BARI vs. OMA	1.29 (0.96-1.73)	1.47 (0.76 – 2.18)

Legend: BARI: baricitinib; TNFi: TNF-inhibitors; OMA: Other Mode of Actions biologics; AIPTW: Augmented Inverse Probability Treatment Weighting. 95% CI: 95% Confidence Interval. *: statistically significant result at the p<0.05 level.

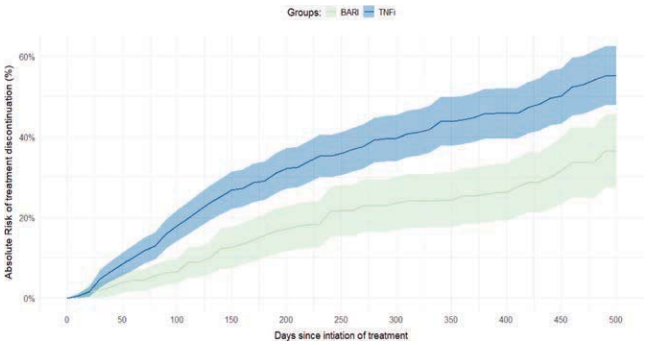

Figure 1. Absolute risk of treatment discontinuation over time between patients on baricitinib and patients on TNF inhibitors, estimated with AIPTW.

Conclusion: Time to treatment discontinuation measured with Cox model was significantly longer for RA patients on BARI compared to patients on TNFi according to the adjusted Cox model (HR = 1.79), and a similar non-significant trend existed when compared to OMA (HR = 1.29). When considering 90-day treatment discontinuation measured with the AIPTW, the results were qualitatively very similar: the risk ratio between BARI and TNFi groups is statistically significant (RR = 2.51), while that of BARI against OMA is larger than one (RR = 1.47), but not statistically significant. Confidence intervals are larger with the AIPTW estimation.

Conflict of Interest: : This analysis has been made possible by financial support of Eli Lilly (Suisse) SA to the Geneva University Hospitals (HUG).

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POS1421

AROMATASE INHIBITORS AND SKELETAL HEALTH – NATURAL HISTORY AND INTERVENTIONAL EPIDEMIOLOGY

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Background: Breast cancer remains the most common cancer diagnosed in women worldwide. Aromatase inhibitors (AI) are employed for hormone sensitive disease in mainly postmenopausal women. AI related bone loss (AIBL) is a known complication; although data regarding the natural history in the real-world, long-term outcomes and the role of bone active therapy in fracture prevention is sparse.
Objectives: Our aim was to determine the real-world impact of AIBL and whether bone sparing therapy utilising standard risk stratification model is sufficient for fracture prevention.
Methods: We undertook a longitudinal study of patients prescribed AI for breast cancer over a seven-year period at our university teaching hospital. All the data was recorded electronically with full access to demographics, disease parameters, investigations and drug management. DEXA scans performed prior to initiation of AI were compared with subsequent imaging over a mean follow up of 3 years. Outcome data for cancer and all fractures was collected. Statistical analysis was done to investigate significant relationships amongst the variables of interest.
Results: 1001 women were identified during the study period. The mean age of the cohort was 64 years (range 29-93). 929 (93%) were Caucasian, 57 (6%) were Asian and 15 (1%) were Afro-Caribbean. 723 women (72%) were diagnosed with invasive ductal carcinoma and 863 women (86%) were postmenopausal. At diagnosis, 428 women (43%) had node positive disease and 35 women (4%) had metastases. 91 women (9%) had sustained fractures prior to their breast cancer diagnosis.
All women had a baseline DEXA: 496 (49.6%) had osteopenia, 151 (15%) had osteoporosis and 354 (35.4%) had a normal result. 478 (48%) of women had a repeat scan available. Overall, there was a decline (from a mean of 0.888 g/cm2 to 0.858 g/cm2, p<0.0001) in left neck of femur (LNOF) bone mineral density (BMD) over time (mean of 3 years, with a range of 1-6).
334 (33%) were prescribed bone active therapy with 276 women (83%) given oral bisphosphonates. This group had an improvement in BMD by 0.4% (LNOF mean BMD of 0.785 g/cm2 at baseline compared to LNOF mean BMD of 0.788 at repeat DEXA, p=0.82).
Women who were not offered any treatment (n=667, 66%), showed a significant decline in bone density with the decline being -5%. (LNOF mean BMD of 0.939 g/cm2 at baseline compared to LNOF mean BMD of 0.888 g/cm2 at repeat DEXA, p< 0.0001).
The rate of fractures remained the same between the treatment (19 fractures, 5.67%) and non-treatment group (38 fractures, 5.70%)
Conclusion: Our study provides long term data for AIBL and confirms a significant decline in BMD over seven years. It confirms that bone sparing therapy is effective in reducing the pace of decline in BMD. However standard risk stratification model such as FRAX based intervention thresholds in mainly those with WHO defined osteoporosis (T ≤-2.5) is ineffective in fracture prevention in keeping with prior literature. Since our study period overlaps with publication of newer guidelines recommending different T score-based risk model, further studies are required to confirm their utility.

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POS1422

USE OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS AND RISK OF MULTIPLE MYELOMA IN PERSONS WITH RHEUMATOID ARTHRITIS

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Background: Biologic therapies used in the management of rheumatoid arthritis (RA) target several cytokines that have been implicated in the pathogenesis of multiple myeloma (MM). Yet little is known about the association between use of biologic or targeted synthetic disease modifying anti-rheumatic drugs (b or tsDMARDs) in RA and the incidence of MM.
Objectives: Our objective was to estimate the association between b/tsDMARD use and the risk of MM among persons with RA using Veterans Health Administration (VHA) data. We hypothesized that b-/tsDMARD use is associated with a lower incidence of MM compared with conventional synthetic DMARDs (csDMARDs).
Methods: In this retrospective cohort study, we identified patients >18 years of age diagnosed with RA in any United States VHA facility from 1/1/2002 and 12/31/2018. All patients met the following inclusion criteria: 1) two or more International Classification of Diseases Version 9 or 10 (ICD9 or ICD10) codes for RA at least 7 days apart but no more than 365 days apart 2) a prescription for a csDMARD within 90 days of the first RA diagnosis 3) one inpatient or outpatient visit 30 days to 2 years preceding first RA diagnosis (indicating a regular user of VHA). Medication data was derived from the outpatient prescription fills, bar coded medication administration (BCMA), and intravenous (IV) data domains. The csDMARDs included in these analyses were: methotrexate, sulfasalazine, leflunomide, and hydroxychloroquine. The bDMARDs included were tumor necrosis factor inhibitors (TNFi) and non-TNFi biologics such as tocilizumab, rituximab, abatacept, and biosimilars; tsDMARD was tofacitinib. Patients with MM before the diagnosis of RA were excluded. Incident MM was determined by 1 or more ICD9/10 code or ICD-oncology codes. Multivariable Cox proportional hazards model were performed to estimate the hazard ratio for developing MM among those during and following the use of a b-/tsDMARD relative to b-/tsDMARD-naïve persons adjusting for age, gender, race, and ethnicity.
Results: 27,540 veterans with RA met study eligibility criteria, of whom 8,322 (30%) had taken a b-/tsDMARD. Over the study period there were 77 incident MM over a total of 192,000 person years. There were 55 events in users of csDMARDs, an incidence rate (IR) of 0.40 (95% CI 0.30-0.52) per 1000 person-years and 22 in persons currently or formerly using b-/tsDMARDs (IR 0.41, 0.25-0.61 per 1000 person years). The unadjusted hazard ratio for MM following bDMARD use relative to csDMARD only use was 1.04 (0.63, 1.73), which increased to 1.28 (0.76, 2.16) after adjusting for demographic characteristics (Table 1).

Table 1. Multivariable Cox proportional hazards model for association between use of disease modifying anti-rheumatic drugs and incident multiple myeloma.

Clinical characteristic	Hazards ratio (95% CI)
csDMARD	Reference
b-/tsDMARD use	1.28 (0.76-2.16)
Age*	**1.04 (1.02-1.07)**
Female	0.58 (0.20-1.62)
Race	Reference
White	**2.11 (1.15-3.86)**
Black	0.70 (0.10-5.08)
Other	
Hispanic Ethnicity	0.71 (0.17-2.92)

Abbreviations: b-/tsDMARD- biologic or targeted synthetic disease modifying anti-rheumatic drug; CI: confidence interval*Hazards ratio reflects risk per every 1-year increase in ageModel adjusted for age, gender, race, and ethnicity

Conclusion: In this nationwide VA study, we did not observe an association between bDMARD use and the incidence of MM. Of note, the median interval from initiation of a bDMARD to the end of follow-up was approximately 5.8 years, which does not allow for an examination of a possible longer term influence.

Disclosure of Interests: None declared
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POS1423

CHARACTERISTICS OF CYTOMEGALOVIRUS-POSITIVE VERSUS NEGATIVE, AND CYTOMEGALOVIRUS-TREATED VERSUS UNTREATED PATIENTS DURING IMMUNOSUPPRESSIVE THERAPY FOR RHEUMATIC DISEASES.

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Background: Immunosuppressive treatment is a common cause of cytomegalovirus (CMV) reactivation.
Objectives: To elucidate the characteristics of CMV-positive and negative patients during the treatment for rheumatic diseases.

Methods: We retrospectively evaluated consecutive patients admitted to our department from January 2006 to October 2021 whose C7-HRP antigen were measured. We collected their age, sex, primary problem and its lesion, and test results within 3 months before C7-HRP measurement. We also investigated the use of immunosuppressants, and maximum and cumulative dose of administered prednisolone within 6 months before C7-HRP measurement. Maximum and cumulative dose of prednisolone contained methylprednisolone pulse, which was converted into prednisolone equivalent. We investigated the characteristics of CMV-positive and negative patients, and those of CMV-positive patients with or without anti-CMV drug use.
Results: Of a total of 472 patients, 85 were positive and 387 were negative for C7-HRP. The average age was 71.2 vs. 64.4 (p=0.0021). Their male-to-female ratio was 20/65 vs. 120/267 (p=0.0290). The following diseases were significantly common among CMV-positive patients: microscopic polyangiitis (21.2% vs. 3.9%, p<0.0001), adult-onset Still's disease (7.1% vs. 1.3%, p=0.0002), and systemic sclerosis (4.7% vs. 2.1%, p=0.0273). Significantly common comorbidities of CMV-positive patients were interstitial lung disease (35.3% vs. 16.0%, p<0.0001), nephritis (23.5% vs. 11.6%, p=0.0005), peripheral nervous system disorders (11.8% vs. 5.7%, p=0.0070), alveolar hemorrhage (5.9% vs. 0.8%, p=0.0001), and peripheral circulatory disorders (4.7% vs. 1.6%, p=0.0111). Average neutrophil counts (7720 /μL vs. 6440 /μL, p=0.0001), serum creatinine (1.0 mg/dL vs. 0.9 mg/dL, p=0.0104), and hemoglobin A1c (6.3% vs. 5.7%, p=0.0030) were significantly higher among CMV-positive patients, whereas hemoglobin (10.1 g/dL vs. 11.1 g/dL, p<0.0001), lymphocyte counts (820 /μL vs. 1190 /μL, p<0.0001), platelet counts (233000 /μL vs. 259000 /μL, p<0.0001), and serum albumin (2.9 g/dL vs. 3.4 g/dL, p<0.0001) were lower. Higher maximum dose of prednisolone (534.9 mg/day vs. 135.5 mg/day, p<0.0001), intravenous cyclophosphamide (27.1% vs. 11.4%, p<0.0001), rituximab (9.4% vs. 2.1%, p<0.0001), azathioprine (23.5% vs. 14.2%, p=0.0053), cyclosporin (8.2% vs. 3.6%, p=0.0101) were significantly more often used among CMV-positive patients. Average cumulative dose of prednisolone was 3022.6 mg vs. 1408.7 mg (p<0.0001). We also performed multivariate analysis, including the patients' age, sex, maximum and cumulative dose of prednisolone, and the use of intravenous cyclophosphamide, rituximab, azathioprine, and cyclosporin. Elderly (p=0.0006), female (p=0.0293), high cumulative dose of prednisolone (p=0.0155), and the use of cyclosporin (p=0.0479) were significantly associated with CMV-positivity. Anti-CMV drug was administered to 63.5% of CMV-positive patients. The average age was significantly higher in anti-CMV-drug-treated patients than untreated patients (73.7 vs. 67.1, p=0.0492). The CMV-treated patients had significantly higher neutrophil counts (8540 /μL vs. 6280 /μL, p<0.0001), erythrocyte sedimentation rate (57.6 mm/h vs. 40.5 mm/h, p<0.0001), and C-reactive protein (5.3 mg/dL vs. 2.6 mg/dL, p<0.0001) than the untreated patients while the other data such as complete blood counts and serum chemistry revealed no significant difference. Average maximum dose of prednisolone was significantly higher in CMV-treated patients (617.1 mg/day vs. 391.1 mg/day, p=0.0261) while average cumulative dose of prednisolone and the use of any other immunosuppressants revealed no significant difference.
Conclusion: Intense immunosuppression, especially with higher dose of glucocorticoids, seemed to be the major risk factor of CMV reactivation. These medications may often require anti-CMV therapy.
Disclosure of Interests: None declared
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POS1424 RISK FACTORS FOR ADVERSE EVENTS OF SULFAMETHOXAZOLE-TRIMETHOPRIM PROPHYLAXIS IN PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES

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Background: The prophylactic use of sulfamethoxazole-trimethoprim (SMX/TMP) can reduce the risk for developing pneumocystis pneumonia in immunosuppressed patients with systemic rheumatic diseases, whereas discontinuation of SMX/TMP prophylaxis is frequent due to adverse events (AEs) with this drug.
Objectives: The purpose of this study was to identify risk factors for AEs of SMX/TMP in patients with systemic rheumatic diseases.
Methods: All consecutive patients who were admitted in our hospital for induction treatment between 2012 and 2019 and newly received prophylactic SMX/TMP were included in the study. We divided them into two groups according to the presence or absence of AEs of SMX/TMP leading to discontinuation of the drug and compared clinical characteristics between the AE and non-AE groups. Multivariable analysis was performed to identify risk factors for AEs of SMX/TMP prophylaxis.
Results: A total of 438 patients were included in the study. Rheumatic diseases of the patients were systemic lupus erythematosus (25.3%), anti-neutrophil cytoplasmic antibody associated vasculitis (15.5%), rheumatoid arthritis (11.6%), polymyositis/dermatomyositis (10.7%), IgG4-related disease (8.5%), large vessel vasculitis (7.1%), adult-onset Still's disease (AOSD; 4.1%), and others (17.2%). Among them, 82 patients (18.7%) stopped SMX/TMP due to AEs. Most frequent AEs were skin rash (36.6%), followed by liver dysfunction (29.3%), thrombocytopenia (19.5%), elevation in serum creatinine levels (15.9%), hyperkalemia (14.6%), hyponatremia (11%), leukopenia (6.1%), and fever (6.1%). Baseline age (61.4±16.4 vs 56.3±16.9 years, p=0.014) and prednisolone dose for remission induction treatment (0.97 vs 0.91 mg/kg/day, p=0.03) were significantly higher in the AE group than in the non-AE group, respectively. In terms of disease type, significantly higher rates of AEs were observed in patients with AOSD than in those with the other diseases (66.7% vs 16.7%, p<0.001; Figure 1). Blood tests at SMX/TMP initiation demonstrated lower lymphocyte counts (10.1 vs 10.8 x10^2/μl, p=0.049), lower platelet counts (20.9 vs 25.8 x10^4/μl, p=0.045), lower albumin levels (3.2 vs 3.4 g/dl, p=0.007), higher AST levels (26 vs 23 U/L, p=0.04), higher creatinine levels (0.71 vs 0.67 mg/dl, p=0.047), and higher ferritin levels (167 vs 154 ng/ml, p=0.047) in the AEs group compared with the non-AEs group, respectively. Multivariable analysis identified an older age (OR 1.03, p=0.002) and AOSD (OR 9.72, p<0.001) as independent risk factors for AEs leading to SMX/TMP withdrawal (Table 1).

Figure

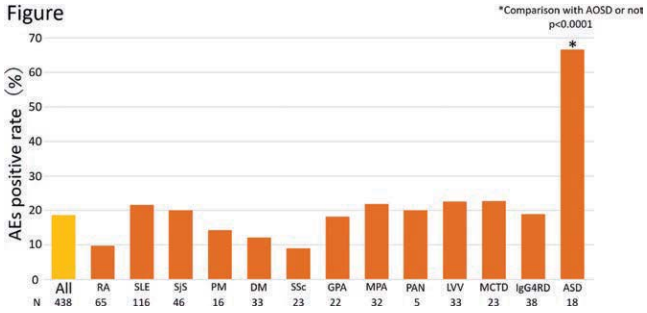

Table Risk factors for AEs due to SMX/TMP in systemic rheumatic disease patients

	Unadjusted odds			Adjusted odds		
	Odds ratio	95 % CI	P values	Odds ratio	95 % CI	P values
Gender (female)	0.913	0.544-1.532	0.73	0.837	0.472-1.483	0.543
Age	1.019	1.004-1.034	0.015	1.027	1.010-1.045	0.002
ASD	9.999	3.631-27.54	<0.001	9.718	3.224-29.29	<0.001
Induction PSL dose	3.588	1.143-11.26	0.029	2.569	0.778-8.484	0.122
Lymphocyte	0.9996	0.9991-0.9999	0.034	0.9996	0.9991-1.0002	0.066
Plt	0.999	0.9965-1.0006	0.165	0.998	0.9959-1.0005	0.120
Cr	1.198	0.739-1.940	0.46	0.906	0.519-1.585	0.731

Conclusion: Old age and AOSD were associated with AEs of SMX/TMP prophylaxis in patients with systemic rheumatic diseases.
Disclosure of Interests: None declared
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POS1425 THE BURDEN OF OSTEOARTHRITIS ACROSS THE STATES OF INDIA, 1990–2019: FINDINGS FROM THE GLOBAL BURDEN OF DISEASE STUDY 2019

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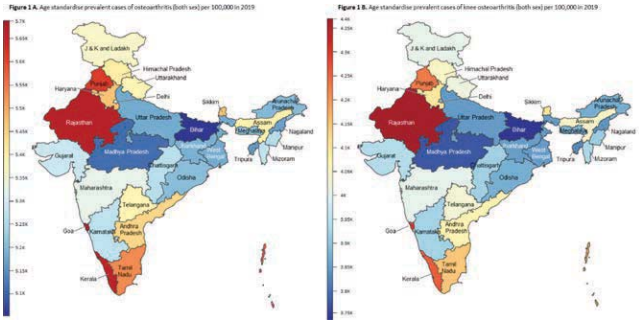
Background: Few studies have reported the burden of osteoarthritis (OA) in different parts of India. However, no study has reported the detailed estimates of incidence, prevalence, and years lived with disability (YLDs) and its trends for OA (and its various sites) across the states of India over a long period of time.

Objectives: We aim to describe the state-wise prevalence, incidence, and YLDs for osteoarthritis (OA) in India from 1990 to 2019 according to age and sex.
Methods: Data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 were used. The burden of OA –including knee OA, hip OA, hand OA, and other OA– was estimated for India and its states from 1990 to 2019 through a systematic analysis of prevalence, incidence, and YLDs modelled data using the methods reported in the GBD 2019 Study. All estimates are presented as counts and age-standardised rates per 100,000 population, with uncertainty intervals (UIs).
Results: Around 23.46 million individuals in India had OA in 1990; this increased to 62.35 million in 2019. The age-standardised prevalence of OA increased from 4,895 (95% uncertainty interval (UI): 4,420–5,447) in 1990 to 5313 (95%UI: 4,799–5,898) in 2019, per 100,000. OA was the 20th most common cause of YLDs in India in 2019, accounting for 1·48% (95%UI: 0·88–2·78) of all YLDs; increasing from 23rd most common cause in 1990 (1·25% (95%UI: 0·74–2·34)). Knee OA was the most common form of OA, followed by hand OA. The prevalence, incidence, and YLDs for OA and knee OA were consistently higher in females than males. Uttar Pradesh (8.53 million (95%UI: 7.63–9.53), Maharashtra (6.37 million (95%UI: 5.75–7.06), and West Bengal (4.90 million (95%UI: 4.39–5.46) had the three highest levels of OA prevalence. Goa (5689 (95%UI: 5,125–6,282)), Rajasthan (5667 (95%UI: 5,097–6,305)), and Kerala (5658 (95%UI: 5,107–6,263)) had the highest age-standardised prevalence of OA in 2019, per 100,000 (Figure 1 A and B).



Conclusion: The burden and impact of OA in India are substantial and is increasing; however, it varied among states. Females were affected more commonly than males. Knee OA was the most prevalent site. With improvement in life expectancy and population ageing, greater increases are expected. Adopting suitable control and preventive community measures to reduce modifiable risk factors (such as obesity, injuries, occupational stress) are needed now to reduce the current and future burden of OA in India.
Disclosure of Interests: None declared
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POS1426 INCIDENCE, CLINICAL FEATURES AND OUTCOMES OF PATIENTS WITH POLYMYALGIA RHEUMATICA IN SLOVENIA

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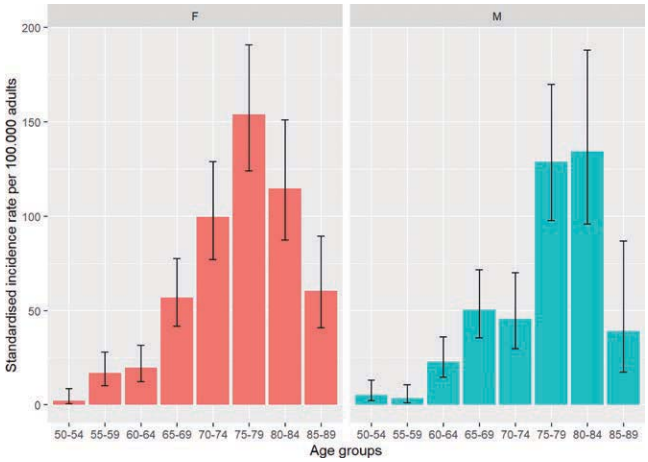
Background: Polymyalgia rheumatica (PMR) is common in patients over the age of 50 years. Clinical symptoms promptly respond to glucocorticoid therapy, but there are wide variations of dosage tapering, treatment duration and rate of relapses. In Slovenia epidemiology of PMR is unknown.
Objectives: We aimed to determine the incidence rate of PMR, the clinical characteristics, the relapse frequency and length of glucocorticoid therapy.
Methods: A detailed single centre retrospective review of medical records of all patients diagnosed with PMR between 1 January 2014 and 31 December 2016 was performed at the Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia–the only secondary level rheumatology institution in serving the Central Slovenian and Gorenjska regions, which represent ~40% (7×105) of the Slovenian adult population. The outcomes were assessed up to1 October 2021.
Results: During the 3-year period 494 patients (460 from Ljubljana and Gorenjska regions) were diagnosed with PMR (64% females, median (IQR) age 75 (69, 80) years), resulting in an annual sex- and age-standardised incidence rate (IR) per 105 adults ≥ 50 years of 46.0 (95% CI 42.0, 50.4), with a female/male ratio of 1.5 (95% CI 1.3, 1.7). The IR peaked between 70–85 years (Figure 1). There was no seasonal variation in IR. The median (IQR) times from symptom onset, and from referral to rheumatology consultation were 6 (4, 11) weeks, and 1 (1, 1) day, respectively. 86% were referred by their GPs, 7% by other internists, and 6% by infectious disease specialists, and the rest by other specialists. At presentation, 96% had morning stiffness (71% lasting >45 minutes), 99% shoulder pain, 94% pelvic girdle pain, 49% weight loss, 13% peripheral arthritis, and 12% body temperature >37°C. Data on US of shoulders and hips was complete, partial, or missing for 38%, 24%, 39%, respectively. Elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) was present in 98% of patients, the median (IQR) ESR was 55 (42, 71) and CRP 49 (26, 79) mg/l, and 58% had anaemia. RF and ACPA were positive in 4% and 3%, respectively. 8/12 had ACPA values less than 2× the reference value. During follow-up ACPA was repeated in 8/12 patients and negativized in 6/8 patients. Among other pre-existing conditions, 51 (10%) had history of malignancy diagnosed a median 7 (3–11) years prior to diagnosis of PMR. EULAR/ACR classification criteria for PMR were fulfilled in 68% and 71% based on clinical and extended ultrasound criteria (missing items were imputed with 0), respectively. 14 (3%) patients had clinically overt concurrent giant cell arteritis (GCA). All patients were treated with methylprednisolone, administered orally in 99.4%, 93% started at 16mg qd. By the end of follow-up, 295 (60%) patients successfully discontinued methylprednisolone after a median of 117 (104, 143) weeks. Steroid sparing leflunomide and methotrexate were used by 66 (13%) and 27 (6%) patients, respectively. During a median follow-up of 150 (98, 244) weeks, 146 (30%) had at least one relapse. Median time to first relapse was 111 (50, 141) weeks. 54% relapsed after glucocorticoid discontinuation after a median time of 4 (2, 18) weeks, 9% presented with GCA, 12% relapsed due to treatment non-adherence. During the follow-up 6% were diagnosed with malignancies.



Conclusion: (1) With the IR of 46 per 105 adults ≥50 years, PMR is more common as rheumatoid arthritis in Slovenia. (2) A considerable proportion of patients required long-term glucocorticoid treatment, leaving a huge unmet need for safer therapeutic options.

Disclosure of Interests: None declared
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POS1427 CLINICAL COURSE IN PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF): REAL-LIFE DATA FROM A MULTICENTER ILD REGISTRY

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Background: Several patients with Interstitial Lung Disease show autoimmune characteristics but do not meet the classification criteria for a connective tissue disease. In order to define this condition, the classification of patients with interstitial pneumonia with autoimmune features (IPAF) has been adopted (Fischer's criteria).
Objectives: To describe the sociodemographic, clinical, functional characteristics and therapeutic management of IPAF in clinical practice and to evaluate the incidence rate of functional respiratory impairment.

Methods: A longitudinal observational study was performed (NEREA registry). Patients diagnosed with IPAF according to Fischer's criteria were included from ILD diagnosis (Feb 2007 to Dec 2019) and followed until loss of follow-up or Jan 2021. The study was carried out by a multidisciplinary team (pneumologists and rheumatologists) in seven Hospitals of Madrid. The relative functional respiratory impairment, defined as a ≥ 5% decline in percent predicted forced vital capacity (FVC%) compared to the previous visit was set as main outcome. Respiratory function was measured at baseline and every 6-12 months. Covariates included: a) sociodemographic, b) clinical, c) radiological pattern (non-specific interstitial pneumonia [NSIP]; usual interstitial pneumonia [UIP], others); d) FVC% DLCO%; e) laboratory tests; f) therapy used. Survival techniques were used to estimate the incidence rate (IR) of relative functional respiratory impairment, expressed per 100 patient-semester with their respective confidence interval [95 % CI].

Results: 79 IPAF were included, with a follow up of 462.8 patients-semester and a maximum follow-up of 12.3 years. 79% were women with a mean age of 66±11 years. Along with obesity (40%), the most frequent comorbidities at baseline were hypertension, hypercholesterolemia, followed by ischemic heart disease. Baseline FVC% and DLCO% were 88.5±22.7 and 64.2±19.3, respectively. Distribution of IPAF classification criteria was: a) clinical domain: arthritis (46.2%), Raynaud`s phenomenon (35.8%) and mechanic hands (9.3%); b) serological domain: 80.8% positive ANA at >1/320 titer; 29% RF (> 40 IU/ml); 25% positive anti-Ro; c) morphological domain: 46.8% of NSIP and 36.7% of UIP. During the study period, 77.2% of patients (n=61) received treatment: glucocorticosteroids (n=52), mycophenolate (n=25), azathioprine (n=21), rituximab (n=15) and antifibrotics (n=11). During the follow-up, 50 patients presented 111 relative functional respiratory impairment events over time. The estimated IR was 23.9 [19.9-28.8] per 100 patient-semester, and 50% of the patients developed functional respiratory impairment at 16 months from diagnosis. IR was similar between patient gender, baseline overall comorbidity, baseline pulmonary functional tests, and age strata, with slight difference in patients >80 years of age. Patients with baseline associated emphysema (IR: 17.6 [10-31]) or without baseline associated fibrosis (IR: 21.1 [15-28]) had lower IR compared to the opposite (IR without emphysema: 24.5[19.3-31]; IR with fibrosis emphysema: 27.5 [19.9-37.9]). As expected, IR was higher in UIP (32.2 [24-42]) compared to NSIP or any other pattern. With respect to serologic markers, patients with ANA titers >=1/320 had a higher IR (26.7 [21-33]) in comparison with those with lower or non-titers of ANA (IR: 15.7 [9.9-25.1]).

Conclusion: In a multicenter registry of Madrid, we have performed a descriptive longitudinal study. IPAF were mostly women in their sixties. The most frequent clinical criteria were arthritis and Raynaud`s phenomenon. An NSIP radiological pattern predominated. At onset, patients have a slightly diminished lung function. The incidence rate of functional deterioration was estimated in 23.9% patient-semester and 50% of the patients developed pulmonary functional deterioration at 16 months from ILD diagnosis. This Incidence rate was higher in patients with an UIP pattern, baseline fibrosis or ANA at medium-high titers.

Disclosure of Interests: None declared

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POS1428 IDENTIFICATION OF A WARM AUTOIMMUNE HEMOLYTIC ANEMIA (WAIHA) POPULATION USING PREDICTIVE ANALYTICS OF A KNOWN CLINICALLY PROFILED COHORT

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Background: The disease burden of warm autoimmune hemolytic anemia (wAIHA), a rare disorder characterized by the destruction of red blood cells (RBCs) by pathogenic IgG autoantibodies, has not been well studied. At the time this claims database analysis was carried out a diagnostic code specific for wAIHA did not exist, which presented challenges in identifying patients with wAIHA.

Objectives: Despite the absence of a diagnostic code specific for wAIHA we aimed to 1) identify a wAIHA cohort using a collection of diagnostic codes, 2) bisect severe versus non-severe wAIHA patients, 3) compare the frequency of comorbidities, anemia symptoms, treatments, diagnostic tests, and healthcare provider visits in these two groups, and 4) use a predictive model to validate clinical variables and prevalence estimates.

Methods: A de-identified, longitudinal, patient-level claims database of >300 million US patients was used for this study. Patients with wAIHA were identified based on a diagnosis code of "autoimmune hemolytic anemia" (AIHA), chronic use of steroids (≥30 days) in the last 36 months, and chronic use of non-steroidal immunosuppressants. Patients were classified as severe if claims related to transfusion, high frequency of blood testing, high frequency interactions with a hematologist, and/or ≥2 ER visits per year were observed in the 36-month period. Codes for anemia symptoms, comorbidities, treatments, and diagnostic tests were grouped and analyzed within the most recent 12 months for each patient. Prevalence was estimated using Artificial Intelligence/Machine Learning (AI/ML) lookalike modeling, using known patients with wAIHA as the positive training class.

Results: A cohort of 1,548 patients with wAIHA was identified (n= 631 were classified as severe while n= 917 as non-severe). Median patient age was >65 years, and patients were evenly distributed by gender. The rate of disease-relevant claims was disproportionately higher in the severe cohort versus the non-severe cohort. Over the 12-month study period, there was a 61% higher rate for anemia symptomatology codes and a 570% higher rate for wAIHA specific testing and monitoring codes in the severe cohort. Primary hypertension, hyperlipidemia, gastro-esophageal reflux, and evidence of chemotherapy use were also present in wAIHA patients. All these conditions were observed more frequently in severe patients with the exception of lupus. Almost 44% of wAIHA claims for the full cohort were associated with Hospital/Emergency care - 48% for the severe group. AI/ML modeling predicted patients using claims variables for hemolytic anemia, other blood count abnormalities, and medical procedure claims commonly used for the diagnosis and management of wAIHA. The predicted population supports reported US prevalence estimates of 30,000-49,000 patients.

Conclusion: We developed and validated a method for defining wAIHA patients using de-identified claims data based on AIHA ICD-10 codes and relevant treatments. We observed that while disease manifestations are generally the same in the severe and non-severe wAIHA cohorts, there is an increased rate of occurrence in the severe cohort during the same 12-month period. This increase was also associated with higher utilization of healthcare resources. The comorbidity of lupus was more commonly associated with non-severe wAIHA patients. This may indicate that patients with a known diagnosis (in this case lupus) who are more closely monitored are less likely to reach the level of severity that would categorize them as patients with severe wAIHA.

Disclosure of Interests: Keith R McCrae Consultant of: Momenta and Novartis, Tricia Gooljarsingh Employee of: Momenta and Janssen (previously), Graham K Jones Consultant of: Momenta, Employee of: IPM AI, May Lee Tjoa Employee of: Janssen

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POS1429 IMPROVING ACCURACY OF SELF-REPORTED DIAGNOSES OF POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS IN THE FRENCH PROSPECTIVE E3N COHORT: A VALIDATION STUDY

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two associated inflammatory diseases that probably share common pathophysiological mechanisms. Data on environmental risk factors are lacking. Population based cohort studies are the most adequate and less biased sources for identifying such factors. But case validation of disease diagnoses is the first necessary step for running such studies, even though it is not easy to perform.

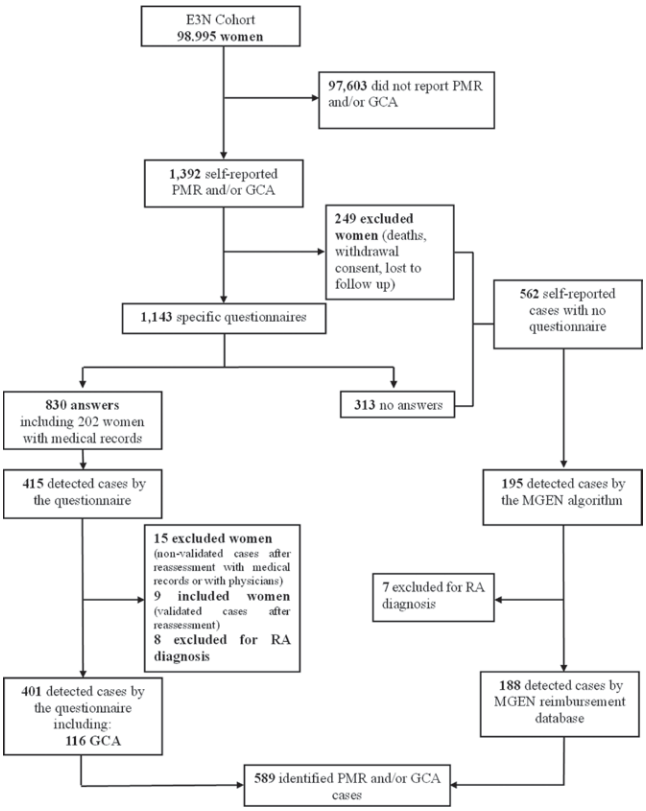
Objectives: To assess the accuracy of self-reported GCA/PMR diagnoses and to develop algorithms to ascertain GCA/PMR in a large French population-based cohort, using combined data of a dedicated questionnaire and medication reimbursement database.

Methods: The E3N cohort study (*Etude Epidémiologique auprès des femmes de la Mutuelle générale de l'Education Nationale*) includes 98,995 healthy French women born between 1925 and 1950, recruited in 1990 and was designed to investigate lifestyle and environmental factors associated with chronic conditions. Participants completed biennially mailed questionnaires to update their health-related information, lifestyle characteristics, and newly diagnosed diseases. Women who self-reported a diagnosis of GCA and/or PMR were sent a specific validation questionnaire designed to ascertain the diagnosis including clinical, biological, and therapeutic data, along with ACR 1990 classification criteria for GCA and ACR/EULAR 2012 classification criteria for PMR. We then devised algorithms based on self-reported answers and a medication reimbursement database, and evaluated their accuracy, comparing them with diagnoses obtained from medical chart review.

Results: Among the 98,995 participants, 1,392 women self-reported GCA/PMR. The specific questionnaire was sent to 1,143 (82.1%) of the eligible women (249 women could not be contacted because of death or withdrawn consent) and response was obtained for 830 women (59.6%). Among them, 202 women provided sufficient medical data to ascertain a diagnosis and study accuracy of developed algorithms. 56 women were classified as ACG and 121 as PMR. Self-reported diagnoses alone had an accuracy of 87.6% with medical chart review. If women additionally self-reported a diagnosis confirmation by a physician and the use of glucocorticoids for ≥ 3 months, the accuracy was improved to 89.9%. For patients who did not respond to validation questionnaire, adding the use of glucocorticoids for ≥ 3 months in the reimbursement database also improved the diagnosis accuracy to 92.8%. These two designed algorithms also had the benefit of reducing the number of false positive cases by 10 and 16 respectively. Finally, 589 GCA and/or PMR cases were confirmed by our two devised algorithms: 401 cases with algorithm using the specific GCA/PMR questionnaire and 188 with medication reimbursement database. The mean age at diagnosis was 70.3 (± 8.0) years [73.4 (± 6.2) years for cases detected using the specific GCA/PMR questionnaire and 68.9 (± 8.3) years for cases detected with medication reimbursement database]. Demographic and clinical data were similar between our population of validated cases by medical chart review and the cases detected by our algorithms in the cohort.

Conclusion: The accuracy of self-reported diagnosis of GCA/PMR was high in the E3N-cohort. Using additional data such as medication reimbursement and/or other self-reported data from a specific questionnaire, particularly the prolonged use of glucocorticoids led to a better accuracy with a very small number of false positive cases and seemed to be sufficient to correctly ascertained GCA and/or PMR diagnoses. With the validation of nearly 600 GCA and/or PMR cases in our cohort, we will be able to conduct epidemiological studies to identify risk factors of these diseases.

Figure 1: Study population in E3N



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Disclosure of Interests: None declared

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POS1430 WATCH OUT FOR THE INFLAMMATORY RESPONSE IN AUTOIMMUNE DISEASES WITH INTERSTITIAL PNEUMONIA. A RETROSPECTIVE STUDY

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Background: Chronic interstitial pneumonia (IP) is often a feature of autoimmune rheumatic diseases (ARD). While potentially a life-threatening complication, it is however highly heterogeneous both as regards its presentation and its progression over time. Some patients may have a predominantly lung involvement, a context which hampers their classification and/or management. The recently coined concept of interstitial pneumonia with autoimmune features (IPAF) may help to identify these cases, albeit some others might remain unclassified (UAIP). Either with or without an overt underlying ARD, real-life data are regarded fundamental to shed light on the natural course of autoimmune IP (AIP) and to identify prognostic markers in order to tailor follow-up and therapeutic approaches

Objectives: To find prognostic markers in our cohort of patients with autoimmune diseases with AIP (comprising ARD-IP, IPAF and UAIP), which may guide our therapeutic strategies.

Methods: We set a retrospective study including all patients diagnosed with AIP from our Clinic with a minimum follow-up of 3 yr -or until death-. The end of the study was set at January 2020. We collected demographic data and classified the disease according to the updated criteria for the ARDs, Fischer's preliminary criteria of IPAF and Solomon's proposed criteria of anti synthetase (ARS) syndrome. We registered morphological, serological and clinical features of the disease. Besides, available laboratory parameters were recorded as dichotomous variables (absent/present; normal/increased). The dependent variable of our study was death. Student's t, Fisher's exact test and survival techniques were employed in the univariate analysis. Logistic regression analysis was done to assess death prediction models. One way ANOVA and Dunnett 2 sided t were employed in multi-group comparisons of means.

Results: A total of 118 patients (69% women), comprising 63 patients (53%) with ARD-IP, 37 (31%) with IPAF and 18 (15%) with UAIP, were included. There were 22 patients fulfilling RA criteria, 16 patients SSc criteria and 20 patients meeting criteria for IM. Twenty one patients could be diagnosed with ARS syndrome. Disease duration was not different between subgroups, with a total follow-up of 984 patient-years. Age at onset was significantly younger in ARD-IP cases (54 ± 2), than in IPAF (61,7 ± 2,7), p 0.035, and also in 2 group comparison with UAIP (72,1 ± 1,9), p < 0.001, p 0.019, respectively. Thirty one deaths occurred during follow-up. In the univariate analysis, older age at presentation (difference: -11,2 ± 3,3 y.o. [CI95: -17.9; -4.6] p 0,001), a shorter course of the disease (difference: 4,5 ± 1,1 y [CI95: 2,3; 6,8] p < 0.001) and the presence of pulmonary hypertension (OR 6,08 ± 1,69 [CI95 2,18; 16,96] p 0.001) were associated to fatal cases. On the other hand, none of clinical subgroups, morphological patterns or autoantibodies conveyed death risk. As regards laboratory parameters, increases of ferritin, triglycerides, ESR, CRP and LDH were strong predictors of death (Table 1). With logistic regression, the combination of older age, pulmonary hypertension, increased ferritin an increased ESR was the best model for death prediction (OR 14,57, p < 0.001), while the elevation of LDH and CRP could be explained by the mentioned 4-factor model.

Table 1.

Laboratory parameter	alive	dead	OR	p
increased ferritin	19p (22,9%)	16p (51,6%)	3,59 ± 1,56 [CI95 1,50; 8,58]	0,004
increased ESR	47p (55,3%)	24p (77,4%)	2,77 ± 1,62 [CI95 1,08; 7,13]	0,034
increased CRP	49p (57,6%)	27p (87,1%)	4,96 ± 1,78 [CI95 1,59: 15,43]	0,006
increased triglycerides	6p (7%)	7p (22,6%)	3,84 ± 1,83 [CI95 1,18: 12,53]	0,026
increased LDH	34p (40%)	23p (74,2%)	4,31 ± 1,59 [CI95 1,73; 10,76]	0,002

Conclusion: According to our data, markers of macrophage activation and the activation of acute phase response could be taken as risk factors of a poor outcome in patients with AIP, regardless of clinical diagnosis and process-related features. Nonetheless, due to our study design and sample, these resutls warrant replication in other cohorts.

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POS1431 FISH CONSUMPTION AND RISK OF RHEUMATOID ARTHRITIS: FINDINGS FROM THE E3N COHORT STUDY

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Background: Rheumatoid arthritis (RA) is an inflammatory rheumatic disease of multifactorial aetiology, which preferentially affects women. To date, active personal smoking has been the most reproducibly reported risk factor for anti-citrullinated protein antibodies (ACPA) positive RA. Fish consumption has been thought to reduce the risk of rheumatoid arthritis (RA), but reported data were conflicting.

Objectives: To assess the association between fish consumption (overall, lean fish, and oily fish) and the risk of RA.

Methods: The E3N study (Etude Epidémiologique auprès des femmes de la Mutuelle générale de l'Education Nationale) is a French prospective cohort investigating environmental factors associated with chronic diseases. It follows 98,995 healthy French women since 1990 covered by a national health insurance primarily involving teachers. RA cases have been previously identified with specific questionnaires and medication reimbursement database. Dietary data were collected via a validated food-frequency questionnaire in 1993. Cox proportional hazards models were used to calculate HRs and 95% CIs for incident RA depending on the tertiles of consumption of overall, lean and oily fish. Models were adjusted for age and for the main potential confounders. Stratified analyses were conducted depending on the active smoking status (never or ever-smoker).

Results: Among 62,629 women, 480 incident cases of RA were identified. In the overall population, we did not find a linear association between overall fish consumption and RA risk (p for trend 0.65), but a moderate consumption of fish (16.7–31.1 g/day, roughly corresponding to 1 to 2 servings a week) was associated with a decreased risk of RA (HR 0.74; 95% CI 0.59—0.94 for tertile 2 compared with tertile 1), especially among ever smoking women (HR 0.61; 95% CI 0.44—0.85). Although not statistically significant, a trend towards an inverse association was only found with oily fish consumption (HR 0.81; 95% CI 0.65—1.02 for tertile 2), but not with lean fish.

Conclusion: In our large population-based cohort study of French women, there was a U-shaped relationship between overall fish consumption and the risk of RA, with a reduced RA risk only in moderate consumers. The inverse association was restricted to ever-smokers. When separately considering oily and lean fish, the second tertile of oily fish consumption was inversely associated with the risk of RA only in never-smokers, while there was no association with lean fish.

Table 1. Hazard ratios (95% confidence intervals) for the risk of rheumatoid arthritis (RA) by tertiles of fish consumption (N = 62,629)

Fish consumption	Non-cases	RA	Model 1	Model 2
	N (%)	N (%)	HR (95% CI)	HR (95% CI)
All population	N=62,149	N=480		
Tertile 1 (0–16.7 g/day)	20,509 (33.00)	172 (35.83)	Reference	Reference
Tertile 2 (16.7–31.1 g/day)	19,628 (31.58)	121 (25.21)	0.74 [0.58; 0.93]	0.74 [0.59; 0.94]
Tertile 3 (31.1–261 g/day)	22,012 (35.42)	187 (38.96)	0.99 [0.80; 1.22]	0.99 [0.80; 1.22]
P_{trend}			0.63	0.65
Never smokers	N=33,314	N=244		
Tertile 1 (0–16.7 g/day)	11,322 (33.99)	79 (32.38)	Reference	Reference
Tertile 2 (16.7–31.1 g/day)	10,556 (31.69)	66 (27.05)	0.89 [0.64; 1.24]	0.90 [0.65; 1.25]
Tertile 3 (31.1–261 g/day)	11,436 (34.33)	99 (40.57)	1.19 [0.88; 1.60]	1.21 [0.90; 1.64]
P_{trend}			0.15	0.12
Ever smokers	N=28,835	N=236		
Tertile 1 (0–16.7 g/day)	9,187 (31.86)	93 (39.41)	Reference	Reference
Tertile 2 (16.7–31.1 g/day)	9,072 (31.46)	55 (23.31)	0.60 [0.43; 0.84]	0.61 [0.44;0.85]
Tertile 3 (31.1–261 g/day)	10,576 (36.68)	88 (37.29)	0.81 [0.60; 1.09]	0.81 [0.60; 1.08]
P_{trend}			0.39	0.36

M1: Adjusted for total daily intake and age M2: M1+ body mass index (kg/m^2), smoking status (current smoker, non-smoker, former smoker, except for stratified analyses), passive smoking in childhood (no, yes), gastrointestinal transit (normal, diarrhoea, constipation, alternating diarrhoea/constipation), educational level (< High School, up to 2-level university, 3-4 level university), and physical activity (in quartiles)

Disclosure of Interests: None declared

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POS1432 ROLE OF FAT AND MUSCLE TISSUE ON QUALITY OF LIFE OUTCOMES IN OSTEOARTHRITIS: RESULTS FROM THE KHOALA COHORT

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Background: The study of associations between body composition and osteoarthritis is still incomplete. While fat-related components are associated with pain in cross-sectional studies, longitudinal studies are rare and the impact on other quality of life (QOL) dimensions is not known.

Objectives: The main objective of the study was to analyze the impact of body composition on the evolution of the perceived health of patients followed for hip and knee osteoarthritis (OA).

Methods: Longitudinal data from the Knee and Hip Osteo Arthritis Long-term Assessment (KHOALA) cohort, a multicenter cohort of 878 patients with symptomatic knee and/or hip OA, were used. Body composition measures were obtained from DXA scans at year 3. Only 3 of the 6 investigating centers with Lunar Prodigy Advance DXA equipment recruited patients for this study. The main outcome criteria were the changes in Patient-Reported Outcomes Measures (PROms) (physical functioning, pain, mental health and vitality of the SF-36 0=worst,100=best) between 3 and 7 years of follow up. Body composition variables were as follows: fat mass index (FMI (kg/m^2)), percentage of fat mass and trunk to leg fat mass ratio (TFM/LFM), skeletal muscle Mass Index (SMI (kg/m^2)) and low lean mass if SMI <7.00 kg/m^2 for men and <5.5 kg/m^2 for women. To account for the correlation of repeated measurements of the same individual, generalized estimating equation (GEE) models were used to assess the associations between body composition measurements and the 4 SF-36 scores. The GEE models were adjusted for potential confusion covariates (age, sex, education level, occupation, smoking, comorbidity, hand OA, number of painful joints, joint of inclusion and Kellgren grade (KL)) showing a significant association at the 0.2 threshold in the bivariate analysis.

Results: 290 patients with knee and 114 patients with hip OA have been included in the analysis: women 254 (66.7%), mean age 60.3 (SD 8.4) years old, IMC 29.5 (5.7), KL grade2 135 (46.6%) for knee OA, 79 (69.3%) for hip OA.

The results of the multivariate analysis of associations between anthropometric measures and quality of life dimensions are presented in Table 1.

Table 1.

	Physical functionning			Bodily pain			Mental health			Vitality		
	β	CI* 95%	p	β	CI* 95%	p	β	CI* 95%	p	β	CI* 95%	p
FMI*	-0.02	(-0.03;-0.01)	<.0001	-0.007	(-0.02;0.002)	0.14	0.0012	(-0.006;0.008)	0.76	-0.01	(-0.02;0.002)	0.02
TLF/LFM*	0.06	(-0.02;0.14)	0.12	0.03	(-0.06;0.12)	0.53	0.09	(0.02;0.15)	0.008	0.08	(0.002;0.17)	0.04
SMI*							0.01	(0.006;0.02)	<.0001	0.02	(0.01;0.02)	<.0001
Low LM	-0.21	(-0.02;0.02)	0.02									

Positive coefficients indicate that the outcome variable increased more for the observed group than for other participants. *The estimator expresses the variation of risk for an increase of 1 units of the variable. Analyses were adjusted on age, sex, education level, occupation, smoking, comorbidity, hand OA, number of painful joints

Conclusion: Increased FMI and the presence of low muscle mass (SMI) were associated with impaired functional ability, but not with pain, the associations of which disappeared after adjustment. Increased TFM/LFM and SMI were associated with improved mental health and vitality over time

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POS1433 OBSTETRIC OUTCOMES OF MEXICAN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES.

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Background: Autoimmune rheumatic diseases(ARDs) are more prevalent in women during childbearing age. These women have an increased risk of adverse pregnancy outcomes and maternal morbidity than general obstetric population(GOP)

Objectives: The objective this study was to evaluate the obstetric outcomes in Mexican women with ARDs

Methods: A retrospective and descriptive study was conducted in a pregnancy and rheumatic disease clinic of a university hospital in Northeast Mexico from Jan 2017 to Dec 2020. All data were collected from the medical records of childbearing age women with ARDs enrolled in our clinic at the time of their pregnancy and childbirth. Patients with non-inflammatory rheumatic diseases were excluded. The obstetric, maternal, and fetal outcomes were compared with the rate of adverse perinatal outcomes of the GOP (n=31,254) database from the same institution. Sociodemographic and clinical characteristics of the population are described. We used the Mann–Whitney U, Chi-square, or Kruskal–Wallis tests to analyze the differences between groups. A p<0.05 was considered statistically significant. The statistical analysis was performed with SPSS v.24 statistical software (IBM, NY).

Results: A total of 62 pregnancies in women with ARDs were included. RA (n=24, 38%) was the most frequent diagnosis followed by SLE (n=14, 22.5%) and APS (n=9, 14.5%). The median maternal age at conception was higher in pregnancies with ARDs than GOP(p<0.001). Table 1 shows the pregnancy and product outcomes between groups. Maternal age ≥ 35 years was also more frequent in the ARDs group(p<0.001). The birth weight was lower in ARDs group than GOP(p=0.007). The odds of preterm delivery were increased in ARDs group(p=0.038)

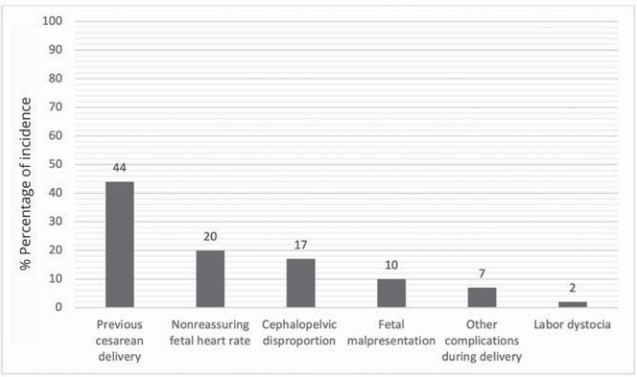
Table 1. Pregnant outcome, maternal, fetal, and neonatal adverse events

	ARD(n=62)	GOP(n=31254)	OR(CI 95%)	p
Pregnancy outcome				
Pregnancy loss[a]	6(9.68)	1560(4.99)	1.94(0.84-4.49)	0.122
Live births[a]	60(90.9)	29694(95)	0.96(0.67-1.35)	0.8
Gestational age,	37.6(37-39)	39(38-40.2)	-	**0.001**
median (IQR)(weeks)[b]				
Birth weight,	2831.6	3022.2	-	**0.007**
mean (CI)(Kg)[c]	(2677.4-2985.8)	(2986.8-3057.6)		
Maternal adverse events				
Preterm deliveries <37 weeks[a]	14(23.7)	3821(12.2)	1.85(1.03-3.3)	**0.038**
<34 weeks[a]	3(5.1)	1065(3.4)	1.42(0.45-4.53)	0.553
Gestational diabetes[a]	4(6.5)	1406(4.5)	1.43(0.52-3.95)	0.485
Preeclampsia[a]	5(8.1)	2471(7.89)	1.02(0.41-2.54)	0.97
Postpartum hemorrhage[a]	0	930(2.97)	0.27(0.017-4.35)	0.355
Emergency cesarean section[a]	8(12.9)	1844(5.9)	2.19(1.05-4.57)	**0.037**
Maternal death[a]	0	31(0.09)	7.94(0.48-131.2)	0.148
Fetal adverse events				
Miscarriages[a]	3(4.8)	663(2.12)	2.28(0.71-7.29)	0.164
Stillbirths[a]	3(4.8)	897(2.87)	1.69(0.53-5.38)	0.377
Congenital anomalies[a]	4(6.5)	1094(3.5)	1.84(0.67-5.08)	0.237
Neonatal adverse events				
Low birthweight (<10th percentile)[a]	7(12.3)	3782(12.1)	0.933(0.43-2.04)	0.862
Very low birthweight (<3rd percentile)[a]	3(5.3)	813(2.6)	1.86(0.58-5.93)	0.294
Low Apgar scores at 5 minutes (<7)[a]	4(7.02)	1781(5.7)	1.13(0.41-3.12)	0.81

Values in bold denote statistical significance (<0.05)[a] n, % [b] IQR, interquartile range (25th–75th percentile) [c] CI, confidence interval (95%)

The most common fetal adverse event was congenital anomalies in both groups with no significant difference(p=0.237). The most frequent neonatal adverse events were low birthweight(<10th percentile) and a low Apgar score at 5 minutes(<7pts) in both groups

The prevalence of cesarean section was higher in the ARDs group(p=0.016). The distribution of indications for cesarean sections is shown in Figure 1.



Conclusion: Pregnant women with ARDs had a higher median maternal age at conception, lower birth weight, increased preterm delivery, and more emergency cesarean sections than pregnant women without ARDs. Close monitoring and multidisciplinary care are necessary to prevent and timely treat complications in this population

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POS1434 USE OF BIOLOGIC OR TARGETED SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS AND THE RISK OF LYMPHOMA IN RHEUMATOID ARTHRITIS

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Background: Epidemiologic studies suggest that disease duration and degree of inflammatory activity of rheumatoid arthritis (RA) contribute to lymphoma

development (1). Whether the decrease in inflammatory burden seen with use of biologic or targeted synthetic disease modifying anti-rheumatic drugs (bDMARDs or tsDMARDs) translates into a lower risk of lymphoma in RA needs to be studied.

Objectives: The objective of our study was to examine the effect of administration of b/tsDMARDS on the incidence of lymphoma relative to conventional synthetic DMARDs (csDMARDs) in an inception cohort of Veterans with RA.

Methods: We identified patients >18 years of age diagnosed with RA in any US Veterans Affairs (VA) facility from 1/1/2002 and 12/31/2018 using the VA Corporate Data Warehouse (CDW). To be included, each patient was required to meet the following criteria: 2+ RA diagnostic codes at least 7 days apart but no more than 365 days apart; 2) a prescription for a csDMARD within 90 days of the first RA diagnosis; and 3) an inpatient or outpatient visit 30 days to 2 years preceding first RA diagnosis (indicating they are a regular user of the VA). The csDMARDs included in these analyses were: methotrexate, sulfasalazine, leflunomide, and hydroxychloroquine. The bDMARDs included were tumor necrosis factor inhibitors (TNFi) and non-TNFi biologics such as tocilizumab, rituximab, abatacept, and biosimilars; tsDMARD was tofacitinib. Patients with prevalent lymphoma were excluded. Lymphoma diagnoses were identified using International Classification of Diseases Version 9, 10 and Oncology (ICD9, ICD10, ICDO) codes.

We used marginal structural models as described by Hernan et al (2) and time-varying Cox models to control for confounding by indication while evaluating this association. We adjusted for baseline demographics (age, sex, race, ethnicity, year of cohort entry, rheumatology visits), and time-varying CRP and time-varying Rheumatoid Disease Comorbidity Index (RDCI) (3) to control for confounding.

Results: 27,421 Veterans with RA met our eligibility criteria. Most of the Veterans (56%) were in the age range 61-80 years old; 89% male, 76% White, 14% African American. 8,225 (30%) patients were treated with a b-/tsDMARD. The crude incidence rates were 1.71 (95% CI 1.5-1.94) per 1000 person-years for those only on csDMARDs and 1.78 (95% CI 1.44-2.18) for patients during or following use of a b/tsDMARDs. After adjustment with both time-fixed and time-varying covariates using marginal structural models, the incidence of lymphoma was not different between patients who did and did not use a b/tsDMARD (hazard ratio=1.06, 95% CI= 0.82-1.37) (Table 1).

Table 1. Estimates of Effect of bDMARD or tsDMARD use on Lymphoma relative to use of csDMARDs

Marginal Structural Models; adjusted for:		
[@]Demographics	1.04	(0.80, 1.34)
[#]Demographics + CRP	1.06	(0.82, 1.37)

* per 1000 person-years [@]Demographics = age, gender, race, ethnicity, rheumatology visits, and year of cohort entry [#]Adjusts for CRP, baseline rheumatology visits (yes/no) and RDCI. CRP = C-Reactive Protein, RDCI = Rhematic Disease Comorbidity Index, CI = Confidence Interval, b/tsDMARD = biologic or targeted synthetic DMARD, csDMARD = conventional synthetic DMARD

Conclusion: In this large study using the nationwide VA data, we did not observe an association between the use of b/ts DMARDs and an increased risk of lymphoma.

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POS1435 FACTORS ASSOCIATED WITH THE RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A NATIONWIDE, POPULATION-BASED CASE-CONTROL STUDY

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Background: Ankylosing spondylitis (AS) is a chronic, systemic inflammatory disease with major pharmacological treatment with long-term nonsteroidal anti-inflammatory drugs (NSAIDs). Patients with AS are notably at risk for comorbidities involving the cardiovascular system [1]. Development of a predictive chart score or algorithm for risk of major adverse cardiovascular events (MACE) in patients with incident AS requiring pharmacologic therapy based on identified risk factors is a clinical necessity for a better holistic management. The related epidemiologic studies are still lacking currently.

Objectives: To investigate factors associated with major adverse cardiovascular events (MACE) in patients with incident ankylosing spondylitis (AS) requiring medical therapy.

Methods: We conducted a population-based case-control study using the Taiwanese National Health Insurance Research Database, and 42,595 newly-diagnosed AS patients requiring medical therapy without previous MACE (the composite outcome of myocardial infarction, ischemic stroke, or patients who underwent coronary artery bypass graft or percutaneous coronary intervention) from 2004 to 2012 was identified. Totally 1,151 patients (2.7%) developed MACE during the follow-up period. We matched MACE cases with non-MACE controls at a 1:4 ratio for age, gender and AS follow-up duration and included 947 AS patients with MACE and 3896 matched controls for final analyses. Using conditional logistic regression analyses, we examined the associations of MACE with low income (≤ 21000 new Taiwan dollars per month), urbanisation, extra-articular manifestations (uveitis, psoriasis and inflammatory bowel disease), comorbidities and use of medications within a year before MACE development. We also examined the influence of NSAIDs of three categories (traditional NSAIDs, selective cyclooxygenase-2 inhibitors [COX-2i] and preferential COX-2i) with their annual cumulative defined daily dose (cDDD) on MACE risk with a Bonferroni correction of the cut-off of probability value for statistical significance. The risk was shown as adjusted odds ratio (aOR) with 95% confidence intervals (CIs).

Results: MACE development was associated with selective COX-2i use especially with annual cDDD > 132 (aOR, 1.61; 95% CI, 1.12-2.32, p = 0.011), corticosteroid use with a dose–response relationship (prednisolone equivalent dose < 5 mg/day: aOR, 1.25; 95% CI, 1.02-1.54, p = 0.028; ≥ 5 mg/day: aOR, 4.75; 95% CI, 3.51-6.43, p < 0.001), residence in rural region (aOR, 1.32; 95% CI, 1.03-1.69, p = 0.028), hypertension (aOR, 3.12; 95% CI, 2.57-3.80, p < 0.001), diabetes mellitus (aOR, 1.69; 95% CI, 1.37-2.07, p < 0.001), hyperlipidaemia (aOR, 5.00; 95% CI, 4.14-6.03, p < 0.001), chronic kidney disease (aOR, 1.98; 95% CI, 1.35-2.90, p = 0.001), heart failure (aOR, 4.04; 95% CI, 2.74-5.94, p < 0.001) and valvular heart disease (aOR, 2.06; 95% CI, 1.33-3.20, p = 0.001), but not with use of traditional NSAIDs, preferential COX-2i, biologics, methotrexate, sulfasalazine, uveitis, psoriasis or inflammatory bowel disease.

Conclusion: The risk factors of MACE in AS patients include use of selective COX-2i, corticosteroids, residence in rural region and other well-known associated comorbidities. The major limitation of this study was a lack of information on individual smoking status. The findings might aid in the development of a predictive chart score or algorithm for MACE risk in patients with AS.

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POS1436 CLINICAL CHARACTERISTICS AND RISK FACTORS OF INVASIVE FUNGAL INFECTION DURING IMMUNOSUPPRESSIVE INDUCTION THERAPY IN PATIENTS WITH CONNECTIVE TISSUE DISEASE

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Background: Invasive fungal infection (IFI) is a life-threatening complication among immunosuppressed patients. Whereas intensive immunosuppressive therapy during remission induction phase in patients with connective tissue disease is a major risk of IFI, little is known about the clinical characteristics and risk factors of IFI.

Objectives: This study aims to reveal prevalence, clinical characteristics, and associated risk factors of IFI during immunosuppressive induction therapy in patients with connective tissue disease.

Methods: We reviewed consecutive patients with connective tissue diseases who underwent immunosuppressive remission induction therapy in Keio University Hospital Rheumatology Department from January 2012 to August 2020. Patients with 0.5mg/kg or more equivalent dose of daily prednisone use were included for IFI, diagnosed according to the definition of invasive fungal diseases from EORTC/MSG 2008. Infections caused by *Pneumocystis jirovecii* were not included.

Results: Among 2701 hospitalized cases, 627 patients had undergone induction or re-induction therapy. Total of 24(3.8%) patients were diagnosed as IFI,

of whom there were 8 proven cases and 16 probable cases; 14 aspergillosis, 5 candidiasis, 2 cryptococcosis, 1 phaeohyphomycosis, and 2 cases with unknown pathogen. Median duration from the start of immunosuppressive therapy to the onset of IFI was 95 days (interquartile range, 36,249 days; range, 13-1397 days) and the mean dose of daily prednisolone was 0.53±0.29 mg/kg at the onset of IFI. Total of 11 patients died; 6 patients (25.0%) due to IFI and 5 patients (20.8%) due to the exacerbation of underlying disease. Univariable analysis comparing the IFI and non-IFI groups, age (65.8±3.7 vs. 56.1±0.7; P=0.01), initial prednisolone dose (0.87±0.01 vs 0.95±0.04 mg/kg; P=0.037), the history of methylprednisolone (mPSL) pulse therapy (54.2% vs. 20.0%; P<0.001), tumor necrosis factor (TNF) inhibitor use (8.3% vs. 1.1%; P=0.039), 2 or more immunosuppressant or biologic use (33.3% vs. 12.9%; P=0.010), HbA1c 6.5% or higher (58.3% vs. 28.9%; P=0.003), lowest serum IgG during the clinical course (599.4±62.1 vs 787.7±12.4 mg/dl; P=0.003), and cytomegalovirus reactivation defined by pp65 antigen 6 or higher (33.3% vs. 11.2%; P=0.004) were significantly different, respectively. Sex, body mass index, presence of interstitial lung disease, and the use of cyclophosphamide, rituximab, or interleukin-6 inhibitors were not significantly different. Multivariable analysis revealed older age (for each 10-year increase: OR 1.40, 95% CI 1.03-1.91; P=0.023), the history of methylprednisolone pulse therapy (OR 2.60, 95% CI 1.06-6.77; P=0.049), TNF inhibitor use (OR 11.2, 95% CI 1.70-74.0; P=0.012), and serum IgG less than 550 mg/dl (OR 2.59, 95% CI 1.03-6.55; P=0.041) as the independent risk factors of IFI.

Conclusion: Patients with connective tissue disease with older age, lower serum IgG, mPSL pulse therapy, or TNF inhibitor use are at higher risk of IFI. Further studies are needed to determine the benefit of prophylactic anti-fungal treatment in such patients.

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POS1437 ASSOCIATION BETWEEN BEVERAGE CONSUMPTION AND RISK OF RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY FROM THE FRENCH E3N COHORT

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Background: The role of nutrition in the pathogenesis of RA has been suggested in many studies but remains controversial.

Objectives: To assess the relationship between consumption of the most frequently drinked specific beverages (coffee, tea, alcohol, and soft drinks) and the risk of RA.

Methods: The E3N Study (*Étude Épidémiologique auprès des femmes de la Mutuelle Générale de l'Éducation Nationale*) is a French prospective cohort including 98,995 women since 1990. RA cases have been previously identified with specific questionnaires and medication reimbursement database (1). Food and beverage consumption was assessed using a validated food-frequency questionnaire. Hazard ratios (HR) and their 95% confidence intervals (CI) for incident RA were estimated by Cox proportional hazards models, adjusted for age and the main potential confounders, including smoking. Tests for linear trends were performed. As smoking is a major risk factor for RA, stratified analyses were conducted according to the smoking status (ever or never-smoker) even in the absence of statistically significant interaction between the smoking status and beverage consumptions. Sensitivity analyses were performed in the subgroup of seropositive cases (positive RF and/or ACPA).

Results: During a total follow-up of 21 years (mean 20.78 (SD 2.26) years), 62,630 women contributed 1,300,874 person-years, and 481 developed RA (incidence 37/100 000 person-years). Incident RA cases were diagnosed a mean 11.7 (SD 5.9) years after baseline. Of the 179 (37.2%) RA cases with known antibody status, 153 (31.8%) were seropositive. Consumptions of total alcohol, tea and sugar-sweetened soft drinks were not associated with RA risk. Coffee consumption was associated with RA risk with a dose-effect relationship (≥4 cups/day *versus* ≤ 1cup/day, HR 1.24, 95% CI [0.94; 1.64], p_{trend} = 0.04), only in never-smokers. According to the type of coffee consumed, only high caffeinated coffee consumption was associated with an increased risk of RA among never-smokers (≥ 3.5 cups/day *versus* ≤ 1 cup/day, HR=1.62 95% CI [1.12;2.34], p_{trend} = 0.006, $p_{interaction}$ = 0.07). Decaffeinated coffee consumption was not associated with RA risk. Risk of RA was higher with artificially-sweetened soft-drinks consumption (consumers *versus* non-consumers, HR 1.66 [1.12; 2.45]), in never-smokers. No association was observed with other soft drinks. Moderate liquor (spirits or aperitifs) intake was associated with a reduced risk of RA among ever-smokers (consumption of 1 - 3 glasses/week *versus* non-consumers HR 0.63, 95% CI [0.43; 0.91]) and moderate wine consumption was associated with a decreased risk of seropositive RA (consumption of 4 -10 glasses/week *versus* ≤ 1glass/week HR 0.57, 95% CI [0.35 to 0.94], whereas no association was observed with other alcohols.

Conclusion: Consumptions of tea, total alcohol, and sugar-sweetened soft drinks were not associated with RA risk, whereas consumptions of coffee (especially caffeinated coffee), and artificially-sweetened soft drinks were associated with higher RA risk, among never-smokers. By contrast, moderate liquor consumption was associated with a decreased risk of RA in ever-smokers, and moderate wine consumption was associated with a decreased risk of seropositive RA. If further confirmed, these results could lead to novel mechanistic hypotheses and to simple prevention measures.

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POS1438 FRYQ QUESTIONNAIRE DISTINGUISHES INFLAMMATORY FROM NON-INFLAMMATORY DISEASE IN NEWLY REFERRED PATIENTS

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Background: Inflammatory Rheumatic Diseases (IRDs) affect 5% of the general population, while 35% of the population experiences Musculoskeletal Complaints (MSCs) [1]. IRDs cause early disability, reduced life-expectancy and considerable health care costs. Early diagnosis is essential to prevent long-term damage, similarly important is the early identification of patients with MSCs without IRDs to prevent unnecessary health care expenses. Of the population referred to the rheumatologist, 60% have non-inflammatory MSCs while only 20% of patients with an IRD see a rheumatologist within three months of symptom onset [2]. The need for digital predictive (triage) tools for Rheumatic and Musculoskeletal Diseases led to the development of the Frysian Questionnaire for differentiation of MSK complaints (FRYQ).

Objectives: To assess if FRYQ questionnaire can distinguish inflammatory rheumatic disease from non-inflammatory MSCs in newly referred patients.

Methods: The Frysian Questionnaire for differentiation of MSK complaints (FRYQ) is an 87 item questionnaire (consisting of 20 open questions and 67 closed questions), which is used in regular care in the rheumatology outpatient clinic of the Medical Center Leeuwarden to triage newly referred patients. Results of FRYQ, referral work diagnosis, resulting diagnoses and demographic data of 854 patients were collected. Elastic Net regularization was used to extract the most informative questions. The data was split: 75% to construct the elastic net and 25% to perform an independent validation. The classification performance was evaluated according to the area under the ROC-curve.

Results: The group consisted of 287 males (33%) and 570 (66%) females. Table 1 shows the characteristics of the 854 studied referrals.

Table 1.

Table 1	Referral or work diagnosis Number (%)	Diagnosis by rheumatologist Number (%)	Correct work diagnosis GP Number (%)
Rheumatoid arthritis	146 (16.9)	87 (10.1)	53 (36.3)
Psoriatic arthritis	41 (4.8)	29 (3.4)	17 (41.5)
Spondylarthropathy	64 (7.4)	52 (6.0)	30 (46.9)
Undifferentiated oligoarthritis	97 (11.2)	10 (1.2)	5 (5.2)
Polymyalgia rheumatica	55 (6.4)	27 (3.1)	22 (40.0)
Gout	55 (6.4)	49 (5.7)	40 (72.7)
Calcium pyrophosphate deposition	4 (0.5)	13 (1.5)	2 (50.0)
Sarcoidosis	10 (1.2)	10 (1.2)	5 (50.0)
Arthralgia	124 (14.4)	0 (0) Varied: mostly non inflammatory	NA
Clinically suspect arthralgia	0	18 (2.1)	NA
Reactive arthritis	2 (0.2)	12 (1.4)	1 (50.0)
Sjögrens' syndrome	14 (1.6)	6 (0.7)	2 (14.3)
Systemic sclerosis	3 (0.3)	5 (0.6)	2 (66.7)
Systemic lupus erythematosus	8 (0.9)	5 (0.6)	3 (37.5)
GPA vasculitis	0	1 (0.1)	0 (0)
Suspicion systemic auto immune disease	57 (6.6)	0 (varied: mostly non inflammatory)	0 (0)
Tendomyalgia	27 (3.1)	117 (13.6)	10 (37.0)
Fibromyalgia	79 (9.2)	110 (12.7%)	57 (72.2)
Osteoarthritis	29 (3.4)	153 (17.7%)	22 (75.9)
Hypermobility syndrome	0	23 (2.7)	0 (0)
Unknown	6	0	NA
Other	33 (3.9)	127* (14.8)	NA
total	854 (100)	854 (100)	NA
Inflammatory	293 (34.3 %)*		
Non-inflammatory	560 (65.7 %)*		

*including missing data

After elastic net regularization the 87 items could be reduced to 33 items that were able to differentiate inflammatory disease from non-inflammatory disease with an AUC of 0.70 in the ROC curve below (Figure 1).

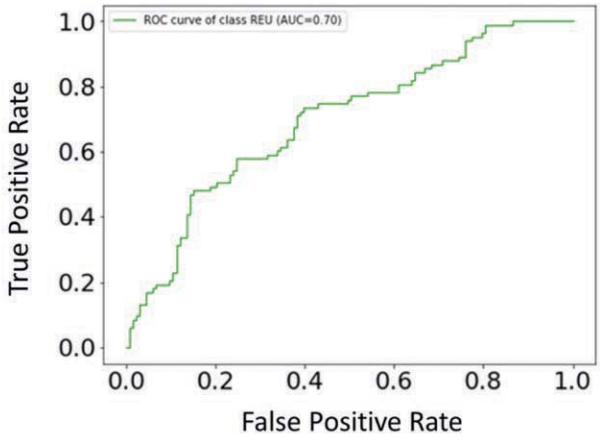

Figure 1. ROC-curve highlighting performance of FRYQ after regularization in the validation set

Conclusion: FRYQ questionnaire can differentiate inflammatory rheumatic disease from non-inflammatory musculoskeletal complaints. To officially validate FRYQ a prospective cohort study is needed.

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POS1439 CANCER IN PATIENTS WITH RHEUMATIC DISEASES EXPOSED TO DIFFERENT BIOLOGIC AND TARGETED SYNTHETIC DMARDS IN REAL-WORLD CLINICAL PRACTICE: DATA FROM A MULTICENTER REGISTER

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Background: Extensive evidence has confirmed no increased risk of cancer associated to either conventional synthetic DMARDs or anti-TNF in patients with rheumatic diseases. The risk of cancer in biologic (bDMARDs) different to anti-TNF and targeted synthetic (tsDMARDs) is considerably less investigated. As new therapies are emerging, more data in real-world registries are needed to confirm safety in other treatment groups.

Objectives: To compare the risk of cancer of tsDMARDs and other bDMARDs versus anti-TNF in patients with rheumatic diseases.

Methods: Data of patients enrolled in BIOBADASER 3.0 up to October 2021 with the start of any bDMARD or tsDMARD were analyzed. For each group, demographic and clinical variables were estimated. Changes to therapy and occurrence of serious adverse events collected annually. Incident cancer was defined as any cancer during the exposure classified according to Meddra dictionary leading to therapy discontinuation. Incidence rate ratios of cancer per 1000 patients-year (PYs) and 95% confidence interval were estimated. Incidence rate ratio was calculated for each group versus anti-TNF.

Results: We identified 271 cancers in BIOBADASER 3.0, corresponding to a cancer incident rate of 7.4 (6.5-8.3) per 1000 PY of exposure. Patients exposed to anti-TNF and anti-IL17 were younger, with lower disease duration and comorbidity versus other groups. Proportionally more malignancies were identified in the anti-CTLA-4 group (3.4%) versus the anti-TNF group (2.9%). The rates of incident cancer ranged between 2.6 events/1000 PY in the anti-IL17 group and 15.3 events/1000 PY in the anti-CTLA-4 group. The rate of cancer did not differ significantly in patients exposed to JAKi [0.8 (95% CI 0.4-1.5)], anti CD20 [1.1 (95% CI 0.6-1.8)], or anti-IL6 [1.3 (95% CI 0.9-1.9)] versus anti-TNF; it was significantly lower in patients exposed to anti-Il17 [0.4 (95% CI 0.2-0.9)], and significantly higher in patients exposed to anti-CTLA-4 [2.2 (95% CI 1.4-3.2)]. The most frequent malignancy was non-melanoma skin cancer, followed by solid cancer (mainly breast cancer with 24 events and lung cancer with 14 events) and melanoma (13 events).

Conclusion: In this register-based study, rates of incident cancer did not differ between patients treated with anti-TNF and other bDMARDs or tsDMARDs, with the possible exception of a potential increased risk in patients treated with anti-CTLA-4.

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Table 1. New Cancer Diagnosis Among Patients with anti-TNF versus other therapies

	Anti-TNF (N=6356)	JAKi (N=1079)	Anti-CD20 (N=667)	Anti-IL6 (N=1178)	Anti-CTLA-4 (N=783)	Anti-IL17 (N=1051)
Female, n (%)	3738 (58.8)	868 (80.4)	523 (78.4)	947 (80.4)	598 (76.4)	492 (46.81)
Mean age, (SD)	54.8 (14.7)	58.5 (12.4)	60.9 (13.6)	59.8 (15.1)	64.0 (12.8)	52.2 (11.6)
Mean start age, (SD)	49.1 (14.0)	56.6 (12.3)	57.9 (13.5)	55.7 (15.2)	59.7 (13.0)	49.8 (22.2)
Disease duration, median (IQR)	6.2	10.4	11.0	8.3	10.3	3.1
	[2.2-13.0]	[4.7 -17.2]	[5.1-18.5]	[3.2-15.1]	[5.2-17.0]	[0.3-10.7]
Charlton Index	1.9 (1.3)	2.4 (1.6)	2.4 (1.7)	2.4 (1.7)	2.8 (1.9)	1.8 (1.3)
First line biologic, n (%)	99 (53.2)	2 (22.2)	1 (7.1)	6 (20.0)	5 (18.5)	2 (66.7)
New cancer diagnosis, n (%)	186 (2.9%)	9 (0.8%)	14 (2.1%)	30 (2.5%)	27 (3.4%)	5 (0.5%)
Median years of follow-up months	4.2 [2.3-7.3]	2.4 [1.4-3.2]	1.0 [1.0-1.0]	2.6 [1.3-6.6]	4.4 [1.5-5.7]	1.8 [1-5-2.2]
Time of exposure, yrs	26233.5	1652.7	1871.5	3196.7	1762.1	1921
Cancer Incidence Rate (per 1000 PY)						
ancer Incide	7.1 (6.1-8.2)	5.4 (2.8-10.5)	7.5 (4.4-12.6)	9.4 (6.6-13.4)	15.3 (10.5-22.3)	2.6 (1.1-6.3)
.6 (1.1-6.3).	5.2 (4.4-6.1)	6.3 (1.6-8.1)	5.9 (3.3-10.6)	7.5 (5-11.2)	10.8 (6.9-16.9)	1.6 (0.5-4.8)
.6 (0.5-4	0.3 (0.2-0.6)	0 (0-0)	1.1 (0.3-4.3)	0.3 (0-2.2)	0.6 (0.1-4)	0 (0-0)
(0-0)1-4)3)9)) Rate (per	1.6 (1.2-2.2)	1.8 (0.6-5.6)	0.5 (0.1-3.8)	1.6 (0.7-3.8)	4 (1.9-8.3)	1 (0.3-4.2)
Rate ratio	NA	0.8	1.1	1.3	2.2	0.4
(vs anti-TNF)		(0.4-1.5)	(0.6-1.8)	(0.9-1.9)	(1.4-3.2)	(0.2-0.9)

POS1440

HEMATOLOGICAL MALIGNANCIES AND ANTI-TNF IN INFLAMMATORY ARTHRITIS: THE REAL LIFE DATA FROM THE HUR-BIO REGISTRY

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Background: TNF inhibitors (TNFi) is highly effective in inflammatory arthritis (IA) treatment. However, concerns are raised about the possible association between TNFi and hematologic malignancies (HMs).
Objectives: To assess the incidence of HMs among IA patients receiving TNFi compared with the general Turkish population.
Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a single center biological disease modifying anti-rheumatic drug (bDMARD) registry since 2005. Patients with IA including rheumatoid arthritis (RA), spondyloarthritis (SpA), and psoriatic arthritis (PsA) patients who had at least 1 visit after the TNFi usage were screened from 2005 to November 2021. HM diagnosis was determined from the each patient files according to the hematologists' decision and/or bone marrow/lymph node biopsy. Demografic data, disease characteristics, and death status were recorded. Standardized incidence rates (SIR) were calculated after adjustment for age and gender and compared with age- and gender-specific SIR values abstracted from the 2017 Turkish National Cancer Registry (TNCR).
Results: Of the 6139 patients registered in the HUR-BIO database, 5355 [3116 female (58.2%)] used any TNFi at least once. Median follow-up duration was 2.6 years for all patients receiving TNFi. 13 patients [8 (61.5%) female] had HM on follow-up. In these patients, median age at the IA onset was 38 (range 26 to 67) and the number of patients with SpA, RA, and PsA was 7, 4, and 2, respectively. The median duration of IA was 17.7 years (range 1 to 33). The median age at the HM onset was 55.5 (range 38 to 76) and the type of HM as follow: 8 lymphoma, 2 multiple myeloma, 1 large granular lymphocytic leukemia, 1 plasma cell dyscrasia, and 1 myelodysplastic syndrome. The median duration of the TNFi usage onset to HM was 36 (range 4-112) months. The TNFi was as follows: etanercept (n=8), adalimumab (n=6), infliximab (n=4), golimumab (n=1), and certolizumab (n=1). 5 patients used more than one TNFi. Patients using TNFi had an increased incidence for HMs (SIR 4.23, 95% CI 2.35-7.05). These results were also valid for both gender. 10 patients with HMs were under the age of 65. In this group, there was a higher incidence of HMs in both men (SIR 5.15, 95% CI 1.88-11.43) and women (SIR 4.76, 95% CI 1.74-10.55). 5 patients deceased on follow-up.
Conclusion: The risk of HMs in inflammatory arthritis patients receiving TNFi being four times higher in comparison with the general Turkish population. There is a plethora of information that discusses the association between HMs and rheumatic disease. To determine whether the increased risk is from rheumatic disease or from TNFi usage, it would be ideal to compare patients receiving TNFi with bDMARD naive IA patients.

Table 1. SIR for diferent age cut-ofs in both sexes for patients with hematologic malignancies

Gender	Age	Observed/expected cases	SIR	%95 confidence interval
Total	All ages*	13/3.07	4.23	2.35-7.05
Male	20-64 years (n=2059)	5/0.97	5.15	1.88-11.43
	≥ 65 years (n=180)	0/0.39	NA	-
	Overall (n=2239)	5/1.36	3.67	1.34-8.14
Female	20-64 years (n=2667)	5/1.05	4.76	1.74-10.55
	≥ 65 years (n=449)	3/0.66	4.54	1.15-12.37
	Overall (n=3116)	8/1.71	4.67	2.17-8.88

*: Includes patients ≥18 years. NA: Not applicable, SIR: standardized incidence rates

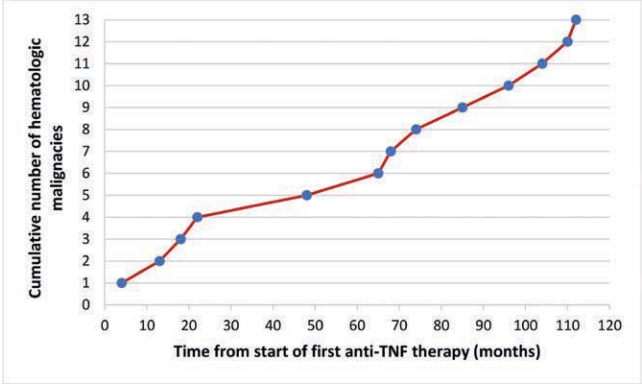

Figure 1. Cumulative number of hematologic malignancies in function of time from start of first anti-TNF therapy

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POS1441

INFLUENCE OF ENVIRONMENTAL AND GENETIC FACTORS ON SERUM IGG4 DURING HEALTH CHECKUPS IN NAGASAKI ISLAND STUDY

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Background: Although serum IgG4 levels are important for the diagnosis of IgG4-related diseases (IgG4-RD), few studies have validated IgG4 levels in healthy individuals in large resident medical examination cohorts and investigated background factors associated with serum IgG4.
A report on genetic factors shows that HLA loci associate with IgG4-RD found in Japanese nation-wide IgG4-RD registry[1)]. However, environmental and genetic factors related to the elevated serum IgG4 levels, which may closely associate with development of IgG4-RD, have previously been unclear in healthy subjects. The nephelometric immunoassay (NIA) is conventionally used to measure IgG4, but it requires a relatively large amount of serum. The magnetic bead panel assay (MBA), which can evaluate IgG4 levels with only a few ml of serum, has an advantage compared with NIA regarding to required sample volume, but the correlation between the two methods is unclear.
Objectives: First, we attempted to verify the accuracy of the MBA compared to the standard NIA in the first cohort. Next, we examined the relationship between IgG4 measured by the MBA and background information of healthy subjects to identify variables that correlate with serum IgG4 in the second cohort.
Methods: First, Kanazawa University collected 947 samples from the resident health examination, and IgG4 levels were measured by both MBA and NIA, and

the correlation between the two was verified using Spearman's rank correlation coefficient (first cohort). Next (second cohort), serum IgG4 of 3240 samples of Nagasaki Island Study (NaIS), which had started in 2014 collaborating among Nagasaki University and Goto City, Nagasaki Prefecture, intended for research of varying conditions and diseases including IgG4-RD, were then measured by MBA. These subjects were stratified into the two groups as IgG4-high and IgG4-within normal limit using the aforementioned cutoff values, and compared with background information such as age, gender, drinking, smoking, uric acid, serum creatinine, comorbidities and HLA typing, including *DRB1*04:06, *04:03, *04:05, *04:10* as disease-susceptibility gene, *DRB1*09:01* and *DQB1*03:03* as protective gene[1)].

Results: IgG4 by MBA correlated well with IgG4 by NIA (r=0.94, p-value<0.001) which was determined from Kanazawa samples (N=947). 1,463.6 mg/mL of IgG4 of MBA corresponded to 135 mg/dl, the normal cut-off value for IgG4 by NIA. In the analysis of NaIS samples (N=3240), the overall high IgG4 positivity rate was 6.3%. Multivariable analysis including age, gender, smoking and drinking, led by univariate analysis, showed that gender and smoking were significantly associated with high serum IgG4 positivity (male: odds ratio = 1.8, 95%CI =1.2-2.7, p = 0.009, smoking: odds ratio = 1.7, 95%CI =1.1-2.5, p = 0.012). There was no association between high serum IgG4 level and HLA genotyping.

Conclusion: We concluded that MBA is a good method to measure serum IgG4 even by the very small sample volume. In our study, the prevalence of serum IgG4 positivity was high tendency than previous report[2)]. Our data showed that male and smoking are independent factors associated with high serum IgG4 positivity. There were no association between serum IgG4 level and HLA genotyping in healthy subjects. Further comprehensive investigation is necessary to clarify high risk subjects who will develop IgG4-RD.

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POS1442

THE PREVALENCE OF RHEUMATOID ARTHRITIS IN WESTERN AUSTRALIA EXTRAPOLATED FROM HOSPITALISATION AND BIOLOGICAL THERAPY USAGE DATA

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Background: Rheumatoid arthritis (RA) is a heterogeneous chronic autoimmune disease that affects the synovial joint lining and may result in permanent joint destruction, premature death, and socio-economic burden.[1] Although RA is one of Australia's national health priority areas and gathering information about the RA burden of disease was one of the national action plans[2], no published epidemiological study adequately describes RA prevalence and risk factors for frequent hospitalisations in Western Australia (WA) to date. An accurate prevalence estimate of this disease offers a framework for predicting present and growing healthcare service requirements in the future.[3]

Objectives: We estimated RA period prevalence and identified risk factors of frequent RA hospitalisations, using linked administrative health and state-specific Australian Pharmaceutical Benefits Scheme (PBS) datasets in WA from 1995–2014.

Methods: RA prevalence was calculated per 1000 hospital separations and biological therapy users. RA patients were identified in the WA linked health dataset using ICD codes 714.0–714.9 and M05.00–M06.99. Dispensing data on biological therapy for RA were obtained from PBS records and converted to defined daily doses/1000 population/day. Multivariate logistic regression was used to analyse risk factors for frequent RA hospitalisations (>2/year), controlling for sex, age, and geographic locations.

Results: A total of 17,125 RA patients were admitted to WA hospitals between 1995–2014. The total number of RA hospital separations was 50,353, averaging three hospitalisations per patient over 20 years. The RA period prevalence was 3.4 per 1,000 separations (0.34%), while the RA period prevalence based on biological therapy use was 0.36%. The corrected RA prevalence based on biological therapy usage was 0.36% and 0.72% for the 2005–2009 and 2010–2014 periods, respectively (Table 1). Female gender, age 60–69 years, and living in rural areas were all risk factors for frequent RA hospitalisations.

Conclusion: Based on hospital and biological therapy data, the minimal prevalence of RA in Western Australia is 0.34–0.36%, which falls within the literature range. Older female RA patients in rural areas were more likely to be hospitalised, suggesting unmet needs in primary care access.

Table 1. Total number of Rheumatoid Arthritis patients in Western Australia taking a standard dose daily (DDD) of RA biological therapy from 1995 to 2014.

Year	Total RA bDMARDs utilisation (DDD/1000 population/day)	WA general population	Prevalence of RA bDMARDs use in WA population (%)	Number of RA patients use standard dose daily of bDMARDs at WA
2003	0.01	1,952,741	0.00	14
2004	0.08	1,979,542	0.01	158
2005	0.16	2,011,207	0.02	329
2006	0.23	2,050,581	0.02	476
2007	0.31	2,106,139	0.03	643
2008	0.50	2,171,700	0.05	1,094
2009	0.60	2,240,250	0.06	1,338
2010	0.59	2,290,845	0.06	1,361
2011	0.63	2,353,409	0.06	1,475
2012	0.77	2,425,507	0.08	1,859
2013	0.66	2,486,944	0.07	1,649
2014	1.00	2,517,608	0.10	2,510

Abbreviations: bDMARDs, biologic disease-modifying anti-rheumatic drugs included Abatacept, Adalimumab, Certolizumab, Etanercept, Golimumab, Infliximab, Rituximab, Tocilizumab; DDD, defined daily doses; RA, Rheumatoid arthritis; WA, Western Australia.

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POS1443

IDENTIFYING THE NEW EMERGENCE OF RACIAL DISPARITIES IN GOUT OVER THE PAST 3 DECADES – US NATIONAL SURVEY AND PROSPECTIVE COHORT DATA

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Background: Several studies published after 2010 reported a higher frequency of gout and hyperuricemia among US Blacks than Whites.[1-4] However, Blacks (in the US and Africa) were previously thought to suffer gout less often than Whites.[5] We hypothesized that the racial disparity in Blacks emerged over the past several decades, with flipped prevalence between the two races.

Objectives: To assess trends in racial differences in gout prevalence in the US using both national survey and cohort study data over the past 3 decades.

Methods: Using data from the NHANES (National Health and Nutrition Examination Survey) III (**1988-1994**) and latest decade (**2007-2016**), and data from 5 examination periods in the ARIC (Atherosclerosis Risk in Communities) Study between **1988 through 2013**, we compared age- and sex-adjusted prevalences and odds ratios (OR) to determine the trend of racial differences in gout prevalence between Blacks and Whites. A time-race interaction term was used to assess differences in the rate of change between the two races.

Results: Among Whites, the sex- and age-standardised prevalence of gout in the NHANES rose from 2.8% (95% CI: 2.4 to 3.2) in 1988-94 to 3.7% (3.2 to 4.1) in 2007/16. Prevalence of gout among Blacks was lower than Whites in 1988-94 (2.6% [2.2 to 3.0]) but rose more sharply over the subsequent decades (p for race-time interaction=0.003), and in 2007/16 came to exceed that of Whites (5.0% [4.4 to 5.6]). Corresponding age-sex-adjusted ORs for gout in Blacks vs. Whites were 0.93 (0.73 to 1.17) in 1988-94, increasing to 1.46 (1.22 to 1.74) in 2007/16 (**Table 1**). This disproportionate rise in gout prevalence among Blacks tended to be more prominent among women (OR 1.81 [1.29 to 2.53]) than men (OR 1.26 [1.02 to 1.55]; p for race-time interactions of 0.002 and 0.01, respectively). Similar trends were observed in the ARIC cohort, where the OR for gout among Blacks vs. Whites rose progressively from 0.82 (0.65 to 1.02) in 1987-89 to 1.81 (1.49 to 2.19) in 2011-13.

Table 1. Temporal Trend of Racial Disparity in Gout Prevalence in NHANES Survey and the ARIC Study Cohort, overall and by sex

		Odds Ratio (95% CI) for Gout Among Blacks vs. Whites				
OVERALL	NHANES	**1988-1994**			**2007-2016**	
	Age- and sex-adjusted	0.93 (0.73 to 1.17)			1.46 (1.22 to 1.74)	
	ARIC	Visit 1: **1987-89**	Visit 2: **1990-92**	Visit 3: **1993-95**	Visit 4: **1996-98**	Visit 5: **2011-13**
	Age- and sex-adjusted	0.82 (0.65 to 1.02)	0.99 (0.81 to 1.22)	1.24 (1.03 to 1.50)	1.60 (1.35 to 1.90)	1.81 (1.49 to 2.19)
WOMEN	NHANES	**1988-1994**			2007-2016	
	Age-adjusted	0.98 (0.65 to 1.47)			1.81 (1.29 to 2.53)	
	ARIC	Visit 1: **1987-89**	Visit 2: **1990-92**	Visit 3: **1993-95**	Visit 4: **1996-98**	Visit 5: **2011-13**
	Age-adjusted	0.92 (0.64 to 1.32)	1.14 (0.82 to 1.59)	1.45 (1.07 to 1.96)	1.89 (1.45 to 2.46)	2.28 (1.73 to 3.01)
MEN	NHANES	**1988-1994**			2007-2016	
	Age-adjusted	0.91 (0.68 to 1.21)			1.26 (1.02 to 1.55)	
	ARIC	Visit 1: **1987-89**	Visit 2: **1990-92**	Visit 3: **1993-95**	Visit 4: **1996-98**	Visit 5: **2011-13**
	Age-adjusted	0.73 (0.54 to 0.97)	0.87 (0.66 to 1.14)	1.03 (0.79 to 1.33)	1.29 (1.02 to 1.64)	1.34 (1.00 to 1.78)

Conclusion: Gout prevalence tended to be lower in Blacks than Whites until late 80's, then rose and surpassed that of Whites over the past several decades. These trends closely parallel the worsening obesity epidemic during this period,[6] particularly in Blacks, partly due to enhanced Western lifestyle. Gout risk genetic profile change would not contribute to this emergence of racial differences, particularly among the same individuals in ARIC, although it remains to be clarified whether Blacks carry genetic profiles that enhance the effect of lifestyle risk factors for gout.

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POS1444

FLT1 AND EPHB2 ARE NOVEL GENETIC MARKERS ASSOCIATED WITH PANCREATITIS IN PATIENTS TAKING AZATHIOPRINE FOR IMMUNE-MEDIATED CONDITIONS: INTEGRATING GENOME- AND TRANSCRIPTOME-WIDE ASSOCIATION STUDIES

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Background: Azathioprine (AZA) is a thiopurine immunosuppressant medication used to treat a variety of immune-mediated diseases. Unfortunately, its use is limited by adverse effects. Pancreatitis, a potentially severe, life-threatening side effect is independent of dose and necessitates AZA discontinuation given the high risk of recurrent pancreatitis with continued use or re-challenge. The mechanisms driving pancreatitis are unclear. While classic thiopurine-induced acute pancreatitis (TIAP) has been associated with HLA haplotypes, most patients taking AZA and presenting with pancreatitis do not fulfill the stringent criteria for TIAP.

Objectives: To identify genetic risk factors for pancreatitis in patients taking azathioprine for immune-mediated conditions.

Methods: Using a biobank linked to electronic health records (EHR) from a tertiary center, we identified new users of AZA. Patients were excluded if the primary indication for AZA was organ transplant or if there was a history of pancreatitis prior to AZA use. The analysis was restricted to patients with EHR-reported race as White due to insufficient case counts for the non-White group. We then identified patients with amylase or lipase values that exceeded twice the upper limit of normal (">2x ULN") or with ICD-9/ICD-10 codes for acute pancreatitis. Each record was manually reviewed to confirm the timing of AZA use in relation to laboratory derangements or ICD coding, as well as to further classify patients into three increasingly strict, but not exclusive categories: 1) pancreatic injury (amylase or lipase >2x ULN); 2) acute pancreatitis[1], or 3) TIAP[2]. We completed genotyping with Illumina Infinium Expanded Multi-Ethnic Genotyping Array plus custom content data, employed Michigan Imputation servers for genetic imputation, and used PrediXcan (GTEx v8) to impute gene expression. We then conducted genome-wide association and transcriptome-wide association studies (GWAS, TWAS). Acknowledging the relatively small overall cohort, and possible imbalance of cases vs controls, we used the Firth logistic regression method, which is a penalized likelihood-based method.

Results: We studied 2127 AZA users (35.4% male; mean 44.5+/-17.2 years). The median AZA dose was 100mg/day (IQR: 50-125mg/day). Rheumatologic conditions (56.9%) and inflammatory bowel disease (40.4%) comprised the most common primary indications for AZA. Pancreatic injury, pancreatitis, and TIAP were diagnosed in 42 (2.0%), 16 (0.8%), and 9 (0.4%) patients, respectively. GWAS identified several significantly associated genes, many with overlapping TWAS findings in the pancreas and liver (Figure 1). From these, the two protein-encoding genes *Fms Related Receptor Tyrosine Kinase-1* (*FLT1*) and *Ephrin type-B receptor-2* (*EPHB2*) overlapped in two or more pancreatitis phenotypes in the TWAS and GWAS, respectively. *EPHB2* was associated with a 8.6-fold (P=1.84 x 10^{-8}) and a 31.4-fold (P=2.87x 10^{-8}) higher likelihood of pancreatic injury and TIAP, respectively.

Conclusion: *FLT1*—a gene that encodes a receptor tyrosine kinase and is a member of the vascular endothelial growth factor receptor (VEGFR) family—and *EPHB2*—a gene that encodes a member of the Eph receptor family, which is the largest subgroup of the receptor tyrosine kinase family—are novel genetic markers associated with pancreatitis in patients taking AZA. VEGF can potentiate inflammation and the pancreas microenvironment is known to promote VEGF expression, which has been linked to pancreatic cancer development; anti-VEGF treatments have been investigated both for mitigating inflammation and also anti-pancreatic cancer treatment. Future studies validating our findings in AZA-induced pancreatitis are warranted.

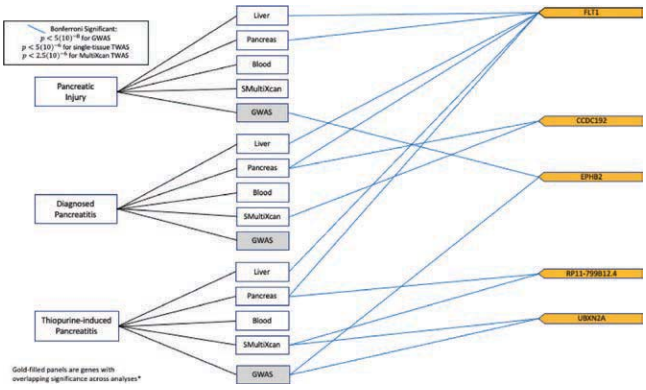

Figure 1.

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POS1445 EARLY DETECTION OF AXIAL PSORIATIC ARTHRITIS IN PATIENTS WITH PSORIASIS: A PROSPECTIVE, MULTICENTER STUDY.

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Background: In the absence of reliable serological and/or imaging biomarkers that can support an early diagnosis of psoriatic arthritis (PsA) in patients with psoriasis (PsO), and considering the known diagnostic delay there is a need for screening tools for detection of early PsA. While different validated screening/referral tools focusing on peripheral manifestations of PsA exist, validated referral algorithms for PsA with axial involvement (also referred to as axial PsA - axPsA) are still missing.
Objectives: In this prospective, multicenter study we applied a dermatologist-centered screening tool and a structured rheumatologic examination including magnetic resonance imaging (MRI) of sacroiliac joints (SIJs) and spine to detect axPsA in patients with psoriasis (PsO).
Methods: Patients with PsO were systematically screened by their dermatologist for eligibility for referral to a rheumatology clinic. Eligible patients were ≥ 18 years with a confirmed diagnosis of PsO who reported having chronic back pain (≥ 3 months) with onset prior to 45 years of age and who had not been treated with any biologic or targeted synthetic DMARD 12 weeks prior to screening. For those patients who qualified for referral a rheumatologic investigation including clinical, laboratory and genetic assessments as well as imaging with conventional radiography and MRI of sacroiliac joints and spine was performed. The primary outcome of the study was the proportion of patients diagnosed with axPsA among all referred PsO patients.
Results: In total 355 patients were screened at 14 dermatology sites, of whom 151 (42.5%) qualified for referral to rheumatology clinic and 100 (28.2%) were seen by a rheumatologist. The diagnosis of axPsA was confirmed in 14 patients (3/14 with both, axial and peripheral involvement) and the diagnosis of peripheral PsA (pPsA) without axial involvement was made in five patients. The ASAS classification criteria for axSpA were fulfilled in nine (64.3%) of the patients diagnosed with axPsA. All but one patient diagnosed with PsA (13/14 with axPsA and 5/5 with pPsA) fulfilled the CASPAR criteria for PsA.
Patient characteristics are presented in Table 1. All patients diagnosed with axPsA had active inflammatory and/or structural (post)inflammatory changes in the sacroiliac joints and/or spine on imaging. In five patients (35.7%), MRI changes indicative of axial involvement were found only in the spine as illustrated in Figure 1.

Table 1. Clinical characteristics of all referred patients with PsO and suspicion of axSpA.

Patient characteristic	pPsA (N=5)	axPsA (N=14)	No PsA (N=81)	p-value[1]
Age (years) – Mean (SD)	42.8 (9.0)	46.2 (13.6)	45.7 (13.3)	0.883
Female – n (%)	2 (40.0)	9 (64.3)	45 (55.6)	0.543
PASI – Mean (SD)	3.3 (2.1)	4.3 (4.9)	4.0 (4.5)	0.971
Inflammatory back pain – n (%)	5 (100.0)	8 (57.1)	36 (44.4)	0.379
HLA-B27 positive – n (%)	0	4 (28.6)	12 (14.8)	0.204
Elevated CRP (>5 mg/L) – n (%)	1 (20.0)	5 (35.7)	11 (13.6)	0.041
Peripheral arthritis, current (last 7 days) – n (%)	5 (100.0)	3 (21.4)	3 (3.7)	0.012
Radiographic sacroiliitis as per mNY criteria – n (%)	0	4 (28.6)	1 (1.2)	<0.001
Active inflammation, sacroiliac joint (MRI) – n (%)	0	8 (57.1)	0	<0.001
Structural (post)inflammatory changes, sacroiliac joint (MRI) – n (%)	0	8 (57.1)	0	<0.001
Active inflammation, spine (MRI) – n (%)	0	13 (92.9)	0	<0.001
Structural (post)inflammatory changes, spine (MRI) – n (%)	0	8 (57.1)	0	<0.001

[1]Statistically significant differences between the axPsA and No PsA groups of patients were determined by using Mann–Whitney U test for continuous data and Chi-square test for categorical data

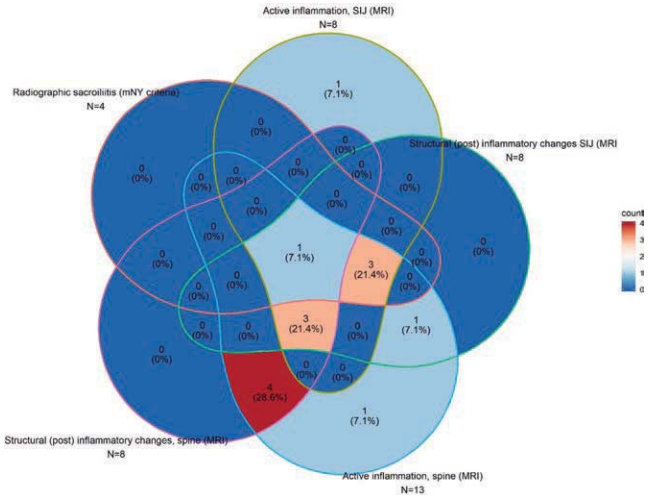

Figure 1. Imaging features of axial involvement in PsO patients diagnosed with axPsA

Conclusion: Our study revealed that applying a dermatologist-centered screening tool may be useful for the early detection of patients with a high probability of PsA (and specifically axPsA) in PsO patients. Given the high prevalence of isolated spinal involvement (without SIJs), imaging of the entire axial skeleton may be required as a part of diagnostic procedure in patients with suspected axPsA.
Acknowledgements: Caroline Höppner, Rebecca Bolce, David Sandoval, Hagen Russ, Burkhard Muche, Judith Rademacher, Hildrun Haibel, Laura Spiller and all cooperating dermatologists.
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POS1446 CREATINE KINASE COULD BE A MARKER OF CHRONIC INFLAMMATION-INDUCED SARCOPENIA IN FRAIL PATIENTS

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Background: Frailty is a hallmark of unhealthy ageing characterized by a decline in the general physiological state, strength and endurance of the patient and consequently, a greater vulnerability to endogenous and/or exogenous stressors. Behind this condition there are multiple pathophysiological processes affecting different systems, such as the musculoskeletal, reflected in sarcopenia, where anabolism is reduced in turn of catabolism. Underlying these processes, chronic inflammation is a well-known but not properly dissected mechanism that contributes to frailty. Although several studies suggest an association of TNF-α, IL-6, IL1-β with systemic inflammation in frail patients, the results are not conclusive. Some authors have explored other molecules related to inflammation, including creatine kinase (CK), a muscle enzyme involved in energy metabolism. Decreased serum CK levels have been observed in chronic inflammatory diseases associated with sarcopenia such as rheumatoid arthritis. In turn, CK is increased not only after myocardial infarction and post-traumatic myolysis, but also associated with muscle mass anabolism.
Objectives: To study the clinical significance of CK levels and their association with other inflammatory and anabolic regulators in frail patients.
Methods: We randomly selected 152 individuals (76 frail and 76 robust) that were 80.86 (±5.49) years and 50% were female, from the second wave of Toledo Study of Healthy Aging cohort (1). CK was measured by routine analysis; serum TNF-α, sgp130, Growth Differentiation Factor (GDF)-15, soluble IL-6R (sIL-6R) and IGF-1 by Multiplex-Luminex. Serum C-Reactive Protein

(CRP) and Myostatin (MSTN) were assessed by ELISA. Differences between robust and frail patients were tested using Mann-Whitney and Kruskal-Wallis test for continuous variables and Chi-square test for discrete variables. For each variable, normality was tested using Shapiro-Wilk normality and Kolmogorv-Smirnov tests. Non-normal variables were natural logarithm transformed to achieve normality. The association between each biomarker and frailty was assessed using multivariate logistic models. Additionally, a sensitivity analysis was performed including a second biomarker in the model in order to detect those biomarkers that influenced the association. All analyses were done using R.

Results: Inflammatory markers CRP and GDF-15 were increased in frail patients, OR (95% CI) 1.59 (1.22-2.05; p<0,001) and OR 1.93 (1.01-3.68; p=0,006), respectively, in comparison to robust. There were no significant changes in the inflammatory parameters TNF-α, sgp130, sIL-6R between groups. The anabolic marker IGF-1 did not change significantly between groups, while the anti-anabolic mediator MSTN was reduced in frail patients, OR 0.40 (0.19-0.86; p=0.02). Finally, CK levels were decreased in frail patients when compared to robust subjects, OR 0.37 (0.18-0.76; p=0.007). In sensitivity analysis, this association remained statistically significant with ORs ranging from 0.33 to 0.40 regardless of a second biomarker.

Conclusion: We identified chronic inflammation in a cohort of frail patients given the significant increase in CRP and GDF-15, although we did not find association with other inflammation parameters such as TNF-α, sgp130 or sIL-6R, highlighting the difficulty of characterize the status of systemic inflammation. The decrease in CK levels in frailty suggest that this marker could be an indicator of cumulative muscle mass loss due to chronic inflammation. Since CRP can be sensitive and altered by a multitude of pathological conditions in frail patients, we propose CK as a more specific marker of inflammation-induced muscle impairment.

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POS1447 SOCIODEMOGRAPHIC, CLINICAL AND TREATMENT DIFFERENCES OF RHEUMATIC DISEASES IN THREE MEXICAN REGIONS.

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Background: Rheumatic diseases prevalence and characteristics in Mexico may vary depending on the country´s region[1]. To acknowledge these differences is needed to develop focused strategies for early diagnosis and treatment[2].

Objectives: Identify the sociodemographic, clinical and treatment characteristics of the rheumatic diseases in the different regions in Mexico using data from the Mexican Adverse Events Registry (BIOBADAMEX).

Methods: In this analysis we included all patients registered from 2016 to 2021. We described the prevalence in the northern region of Mexico (NR), central (CR) and southern region (SR). We compared sociodemographic, clinical and treatment characteristics between these three regions. We used descriptive statistics, Chi square and Kruskal Wallis tests to analyze differences between the groups.

Results: A total of 780 patients were included in this study, 248 patients (32%) were from the NR, 471 (60%) were from the CR and 61 (8%) from the SR. At baseline, patients had a median (IQR) age of 50 (40-58) years and median disease duration of 7 (3-15) years. NR patients had longer disease duration (9.7 years, p <0.001) and SR patients had higher BMI (29, p 0.001). Overall, 351 (45%) had comorbidities. In CR and SR more than the half of the patient had comorbidities, while in NR only 29% (p 0.001).

The most common diagnosis was rheumatoid arthritis with 512 (66%) patients, followed by ankylosing spondylitis in 115 (15%), psoriatic arthritis in 44 (6%), systemic lupus erythematosus in 30 (4%) and idiopathic juvenile arthritis in 27 (3%), this proportions were maintained when analyzed by regions. We found SR had higher DAS 28 and higher BASDAI (Table 1).

Table 1. Baseline characteristics by region.

	Northern region n=248	Central region n=471	Southern region n=61	p
Age, median(IQR)	49.7 (42-58)	49.9 (38-58)	51.6 (43-61)	0.4
Female, n(%)	193 (78)	383 (81)	52 (85)	0.33
Body Mass Index, median (IQR)	28 (25-32)	26 (22-29)	**29 (26-32)**	0.001
Disease duration (years), median (RIC)	**9.7 (5-16)**	5.9 (2-14)	4.5 (1-10)	0.001
Diagnostic, n(%):				
Rheumatoid arthritis	**173 (70)**	300 (64)	39 (64)	0.001
Idiopathic Juvenile Arthritis	3 (1)	**23 (5)**	1 (2)	
Ankylosing Spondylitis	**47 (19)**	59 (13)	9 (15)	
Laboratory studies, n(%)				
Rheumatoid factor	97 (39)	274 (58)	**38 (62)**	0.001
ACPA	15 (6)	68 (14)	**12 (19)**	0.001
Disease activity scores, median (IQR)				
DAS28	4.8 (3-6)	5.1 (4-6)	**5.2 (5-7)**	0.001
BASDAI	2.8 (0-7)	4.9 (2-7)	**8.0 (5-9)**	0.003
Comorbidities, n(%)	72 (29)	**247 (52)**	**32 (52)**	0.001
Previous bDMARD, n(%):	**136 (55)**	149 (32)	1 (2)	0.001
Steroids, n(%):	93 (38)	155 (33)	**42 (69)**	0.001
cDMARD, n(%)	200 (81)	373 (79)	53 (87)	0.4
Cause of bDMARD discontinuation, n(%) [a]				
Lack of efficacy	**85 (62)**	45 (33)	2 (22)	0.001
Adverse Event	4 (3)	25 (18)	**3 (33)**	
Pregnancy	1 (1)	**3 (2)**	0(0)	
Loss of patient follow up	10 (7)	0 (0)	**2 (22)**	
Remission	**23 (17)**	5 (4)	0 (0)	
Others	14 (10)	**59 (43)**	2(22)	

a) 238 patients.

Glucocorticoids were used by 290 (37%) patients, SR had the highest use rate (69%, p <0.001) and 80% of the patients used conventional DMARDs (cDMARDs) with no differences between regions. Overall, the most used bDMARDs were adalimumab, certolizumab, tocilizumab and abatacept.

At the time of the analysis 238 (36%) had discontinued bDMARDs treatment, 132 (47%) due to lack of response, being this the most frequent cause reported overall, with the highest rate in NR (62%, p <0.001). All NR patients have social security compared to 83% in CR and 79% in SR.

Conclusion: There are regional differences between patients with rheumatic diseases registered in Biobadamex. It was remarkable that all patients form NR had social security, which may impact in the access to treatment. There were differences in the treatments between regions. The data from this analysis may be useful to policy makers, pharmaceutical companies and physicians. Differences in size samples between regions could have influenced in the results, further analyses will be performed in the future including more patients.

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Validation of outcome measures and biomarkers

POS1448 DICKKOPF HOMOLOG 3 (DKK3) AS A PROGNOSTIC MARKER IN LUPUS NEPHRITIS: A PROSPECTIVE MONOCENTRIC EXPERIENCE

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Background: Lupus nephritis (LN) is a major cause of mortality/morbidity in patients affected by systemic lupus erythematosus (SLE). Reliable prognostic markers, especially related to the degree of interstitial fibrosis, are still lacking and renal biopsy still represents the gold standard. Recent data suggests a role of Dickkopf homolog 3 (DKK3) as a marker of tissue fibrosis in different diseases, however its role in autoimmune diseases still needs to be elucidated.
Objectives: To investigate DKK3 serum levels in SLE patients with and without LN, assessing its changes in relation to kidney function, flares and interstitial renal fibrosis, as well as its association with the IFN signature.
Methods: 132 SLE patients, 57 of whom diagnosed with LN, were included in this study, as well as 50 healthy donors. DKK3 and Myxovirus resistance protein 1 (MxA) were measured in serum samples, using enzyme-linked immunosorbent assays. Biopsies were evaluated for glomerular involvement, interstitial renal fibrosis and tubular atrophy according to 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification and the revised 2018 version. Patients were followed-up for at least 36 months.
Results: DKK3 serum levels were significantly higher in patients with biopsy-proven LN when compared to those without (median[min-max]: 215ng/ml [81-341] vs 21.1ng/ml [1-69], p<0.01). When focusing on patients with LN, DKK3 levels resulted to be associated with the presence of chronic kidney disease (OR: 4.31[C.I. 2.01-6.61] per DKK3 doubling, p<0.01), higher chronicity index at biopsy (OR: 1.75[C.I. 1.59-2.13] per DKK3 doubling, p<0.01) and flares rate (OR: 1.45[C.I. 1.1-5.71] per DKK3 doubling, p<0.044). DKK3 levels correlated with the IFN signature as expressed by MxA (correlation coefficient: 0.71, p<0.037).
Conclusion: While kidney biopsy remains the gold standard for diagnostic and prognostic assessment in LN, DKK3 could represent an additional useful prognostic tool to monitor SLE patients and eventually to guide therapeutic choices.
Disclosure of Interests: None declared
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POS1449 VALIDATION OF THE GERMAN LUPUSPRO QUESTIONNAIRE TO MEASURE LUPUS-SPECIFIC HEALTH-RELATED QUALITY OF LIFE IN LUPUS ERYTHEMATOSUS PATIENTS

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Background: To date, there is no validated lupus-specific questionnaire for health-related quality of life (HRQoL) in German language. Regular assessment of health-related quality of life is recommended for monitoring and outcome in current management guidelines [1][2]. Given that about 20% of the EU population are native German speakers, it is therefore essential to validate a Lupus-specific questionnaire in German.
Objectives: The aim of this study is to present the validity (content, construct, and criterion) and reliability (internal consistency and test-retest) of the German translation of the LupusPro questionnaire, which captures both generic and lupus-specific HRQoL domains.
Methods: The German LupusPRO was professionally translated and then administered to consecutive patients with systemic lupus erythematosus treated at our tertiary centre. At each visit, clinical and laboratory data were collected, including disease activity and damage (SLEDAI-2K resp. SLICC/SDI). Additional questionnaires were used for validity testing, including questionnaires for HRQoL (SF-36v2), fatigue (FACIT), depression (CES-D), sleep (PSQI) and health impairments (IMET).
We calculated Cronbach's alpha to test reliability. An alpha >0.70 is considered acceptable. Test-retest reliability was tested by evaluating the consistency between the LupusPro at two time points (T0 and T1 after 2-3 days). Criterion and construct validity was assessed by comparing the results of the LupusPRO with the generic HRQoL questionnaire, established clinical endpoints (disease activity, disease damage), and the domains of the additional questionnaires. The confirmatory factor analysis was performed with the Lavaan package (Ver. 0.6-9) in R using the relative fit indices, the Tucker-Lewis index (TLI) and the comparative fit index (CFI).
Results: 148 patients with confirmed SLE took part in the study of which 111 participated in the test-retest analysis. About 84% were female with a mean age of 45.5 (SD 12.0) and mean disease duration of 17.7 (SD 9.7) yrs. The mean SLEDAI-2K was 3.1 (SD 3.2) and SLICC/SDI 1.4 (SD 2.1).
The LupusPro domain's internal consistency by Cronbach's alpha exceeded >0.7 except for the domains lupus symptoms (α=0.64), lupus medication (α=0.59), procreative ability (α=0.58), and coping strategies (α=0.43). The overall test-retest correlation was excellent (ICC=0.94). The correlation of the corresponding LupusPRO and SF-36v2 domains were moderate to strong (ρ=0.54–0.78), whereas correlation with disease activity and damage (SLEDAI-2K and SLICC/SDI) was weak (ρ=-0.23 resp. -0.08). Correlation of the selected LupusPRO domains with the above mentioned other dedicated outcome measure instrument emphasized construct and criterion validity.
The results of the confirmatory factor analysis showed good construct validity of the LupusPRO. The observed model fit for the hypothesized item-scale relationships was very good (CFI = 0.98, TLI = 0.98). Items generally had loadings of >0.6 with their respective factor. Exceptions were especially the domain coping strategies where all items loaded <0.4.
Conclusion: The GermanLupusPRO is a valid instrument for measuring health-related quality of life. It shows comparable psychometric properties as the original versions. Minor difference in individual domains may be explained by sociocultural factors.
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Disclosure of Interests: Veronika Mevissen: None declared, Tim Filla: None declared, Christina Duesing: None declared, Matthias Schneider: None declared, Jolly Meenakshi Consultant of: GSK, Aurinia., Gamal Chehab: None declared
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POS1450 PSYCHOMETRIC PROPERTIES OF THE CENTRAL SENSITIZATION INVENTORY IN PATIENT WITH FIBROMYALGIA

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Background: Patients with fibromyalgia (FM) complain many symptoms besides musculoskeletal pain: e.g. fatigue, sleep difficulties, a swollen feeling in tissues, paresthesia, cognitive dysfunction, dizziness, and symptoms of overlapping conditions such as irritable bowel syndrome, headaches and restless legs syndrome. These conditions can be grouped under the umbrella term of central sensitization (CS) syndromes.
Objectives: The goal of the present study was to explore additional evidence of convergent and discriminant validity of the Central Sensitization Inventory (CSI) in a large sample of subjects with fibromyalgia (FM).
Methods: Patients were consecutively enrolled for a cross-sectional assessment comprehensive of three FM-specific measures (the revised Fibromyalgia Impact Questionnaire [FIQR], the modified Fibromyalgia Assessment Status [modFAS], and the Polysymptomatic Distress Scale [PDS]) and of CSI. To test the convergent validity, the Spearman's rho was used to measure the degree of correlation between the variables CSI and the FM-specific measures. To assess discriminant validity, CSI scores were grouped according to FIQR disease severity states, and differences between these groups studied with the Kruskal-Wallis test. Interpretative cut-offs were established with the interquartile reconciliation approach.
Results: The study included 562 FM patients, 199 (35.4%) were classified as having central sensitization syndrome (CSI ≥40). CSI was largely correlated with modFAS (rho = 0.580; p <0.0001), FIQR (rho = 0.542; p <0.0001), and PDS (rho = 0.518; p <0.0001). The differences between the CSI scores in accordance with the FIQR were significant (p <0.000001). CSI cut-offs proposed for FM: 21 between remission and mild severity, 30 between mild and moderate severity, 37 between moderate and severe disease, and 51 between severe and very severe disease.
Conclusion: The current study successfully showed additional evidence of the convergent and discriminant validity of the CSI in FM patients.
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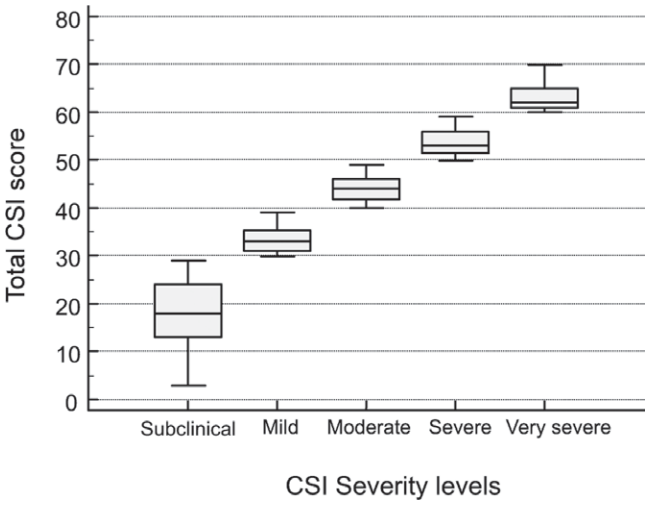

Figure 1. *Distribution of the CSI score according to the different CSI score ranks of the overall cohort. Bars show median and interquartile range. CSI, central sensitization inventory*

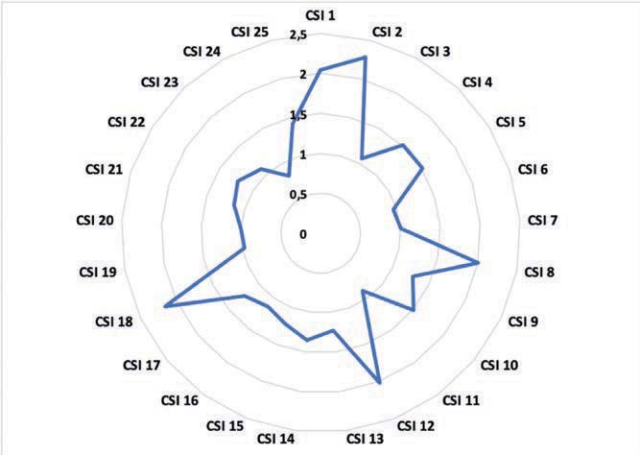

Figure 2. *Spydergrams of the individual CSI scores in FM patients (n° 562)*

Disclosure of Interests: None declared
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POS1451

DISCRIMINATORY CAPACITY OF THE ASAS HEALTH INDEX IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED IN A TIGHT CONTROL SETTING VERSUS STANDARD OF CARE

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Background: Improvement in functioning and health as assessed by the ASAS Health Index (HI) is an important outcome of interventions in patients with axial spondyloarthritis (axSpA). ASAS HI thresholds for measuring improvement have been proposed but not yet tested in an independent intervention trial to study its discriminant capacity.
Objectives: To test the discriminant capacity of the ASAS HI using data from a randomized, active-controlled trial.
Methods: In this post-hoc analysis from the tight-controlled, treat-to-target (T2T) trial TICOSPA [1], data of active axSpA patients randomized to either the T2T arm (visits every 4 weeks, prespecified strategy of treatment intensification until achieving low disease activity) or standard of care (SOC; visits every 12 weeks, treatment at the rheumatologist's discretion) were compared to test whether different thresholds for improvement or achieved state of ASAS HI could discriminate between treatment arms. Week 48 effect sizes (ES) of improvement from baseline were calculated for each treatment arm as Phi Coefficient (higher means better discrimination) and OR (95% CI).
Results: The table shows the ES between treatment arms for all tested improvements and health states achieved in ASAS HI. Overall, absolute improvement outcomes performed better than percentage changes outcome followed by status outcomes. The absolute improvement of ≥2.0, ≥2.5, and ≥3.0 performed best followed by the 20% improvement. As the ASAS HI ≥3.0 is the smallest detectable change for this outcome, this seem to be the most appropriate proposed outcome.

Table 1. Thresholds by treatment groups.

	Non-responder imputation at 48 weeks		Effect size measures	
	TC/T2T	UC	Phi Coefficient*	OR [95% CI]
ASAS HI 20% improvement	56.9%	45.8%	**0.11 [0-1.0]**	0.64 [0.33-1.23]
ASAS HI 25% improvement	51.4%	41.7%	0.10 [0-1.0]	0.68 [0.35-1.30]
ASAS HI 30% improvement	43.1%	34.7%	0.09 [0-1.0]	0.70 [0.36-1.38]
ASAS HI 35% improvement	40.3%	31.9%	0.09 [0-1.0]	0.70 [0.35-1.38]
ASAS HI 40% improvement	37.5%	31.9%	0.06 [0-1.0]	0.78 [0.39-1.56]
ASAS HI 50% improvement	29.2%	22.2%	0.08 [0-1.0]	0.69 [0.33-1.47]
ASAS HI 60% improvement	26.4%	18.1%	0.10 [0-1.0]	0.61 [0.28-1.36]
ASAS HI 70% improvement	16.7%	12.5%	0.06 [0-1.0]	0.71 [0.28-1.82]
ASAS HI 80% improvement	13.9%	11.1%	0.01 [0-1.0]	0.78 [0.29-2.09]
ASAS HI 90% improvement	9.7%	9.7%	0.0[0-1.0]	1.0 [0.33-3.01]
ASAS HI improvement ≥1.0	66.7%	61.1%	0.06[0-1.0]	0.79 [0.40-1.55]
ASAS HI improvement ≥2.0	55.6%	41.7%	**0.14 [0.0-1.0]**	0.57 [0.30-1.11]
ASAS HI improvement of ≥2.5	44.4%	31.9%	**0.13 [0-1.0]**	0.59 [0.30-1.16]
ASAS HI improvement of ≥3.0	41.7%	29.2%	**0.13 [0-1.0]**	0.58 [0.29-1.15]
ASAS HI improvement of ≥ 3.5	29.2%	22.2%	0.08 [0-1.0]	0.69 [0.33-1.47]
ASAS HI improvement ≥4.0	29.2%	22.2%	0.08 [0-1.0]	0.69 [0.33-1.47]
ASAS HI improvement ≥5.0	16.7%	12.5%	0.06 [0-1.0]	0.71 [0.28-1.82]
ASASHI, end of study, ≤12.0	87.5%	80.6%	0.09 [0.0- 1.0]	0.59 [0.24, 1.47]
ASASHI, end of study, ≤5.0	37.5%	33.3%	0.04 [0.0, 1.0]	0.83 [0.42, 1.65]

A value of PHI = 0.1 is considered to be a small effect, 0.3 a medium effect, and 0.5 a large effect.

Conclusion: In this active-controlled trial an absolute improvement in the ASAS HI discriminated best between treatment arms. A similar evaluation is needed in a placebo-controlled trial to be able to propose the best outcome for the ASAS HI in a trial.

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Rehabilitation

POS1452 EFFECT OF PHYSICAL ACTIVITY ON CHRONIC FATIGUE IN RHEUMATOID ARTHRITIS PATIENTS

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Objectives: To evaluate the dynamics of fatigue indices in RA patients depending on the intensity of physical activity (aerobic exercise) in the short term.
Methods: The study included 111 women with RA (mean age 54.4±11.03 years old, mean disease duration 11.9±9.3 years, DAS28-ESR score 2.84 [2.32;3.05]; mean VAS fatigue score 71.6±8.93). All patients underwent a 3-week post-hospital rehabilitation program (PHRP), and aerobic exercise was the main component of this program (dosed walking, daily, up to 1 hour) and outdoor walks up to 3-3.5 hours per day [1].The level of fatigue was estimated using the British Rheumatoid Arthritis Fatigue Scale - Numerical Rating Scale (BRAF-NRS V2). The 50-meter walking test was used to assess the functional state of patients in dynamics, the 6-minute walking distance test (6MWD) - to assess patients' tolerance to physical activity. The intensity and duration of exercise were compared with serum levels of free fatty acids (FFA), triglycerides (TG), and angiopoietin-like protein type 4 (ANGPTL4), an inhibitor of lipoprotein lipase, which plays an important role in the regulation of lipid metabolism and energy balance.
Results: After completion of PHRP, RA patients showed a significant decrease in fatigue aspects of the NRS severity scale (6.83 ± 1.21 vs. 6.51 ± 1.18 points, p=0.003), NRS-effect (6.24 ± 1.07 vs. 5.95 ± 1.08 points, p=0.037); a decrease in time taken to complete the 50 m. walk test was noted (79.3 ± 8.64 vs. 78.91 ± 8.15, p=0.01) [2]. Increased concentration of ANGPTL4 (p<0.02), FFA (p<0.01) and decreased TG level (p<0.05) were also determined in serum of RA patients. There was a significant correlation between ANGPTL4 and FFA (r=0.54, p<0.02), but not with TG (r= -0.18, p>0.05). The increase in serum ANGPTL4 during exercise may be mediated by increased serum FFA content and increased lipid oxidation processes. Previously, it was shown that muscle tissue, along with liver and adipose tissue, significantly affect to the increase in circulating ANGPTL4 during exercise [3, 4].
Based on the results of the first phase of the study, patients (n=102) were retrospectively divided into two groups: Group I (n=53) included patients with < 5-6 thousand steps/day (sedentary lifestyle); Group II (n=49) included patients with ≥ 7-8 thousand steps/day (mobile lifestyle).Group II of RA patients significantly improved their physical parameters - reduction of walking time (p<0.001) and number of steps in the 50-meter test (p=0.013) at the end of PHRP. There was a reduction in fatigue severity on all scales: VAS (p<0.001), NRS severity (p<0.001), NRS effect (p<0.001), and NRS-overcoming (p=0.001). In group I, there was an increase in VAS fatigue (p=0.008) and NRS effect (p=0.01). No intergroup differences were found among lipid metabolism indices before and after PHRP (p>0.05).
Conclusion: Aerobic exercise (walking) is an effective method of increasing physical activity and reducing fatigue in patients with RA during the post-hospital rehabilitation phase. Increased physical activity during walking (≥7-8 thousand steps/day) has a positive effect on physical indices and fatigue components in the short term. Lipid metabolism markers can be used in determining the degree of activity, optimization of the duration and intensity of exercise in RA patients.
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POS1453 INTERVAL HYPOXIC-HYPEROXIC TRAINING IN REHABILITATION OF PATIENTS WITH OSTEOARTHRITIS AND POST-COVID SYNDROME

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Background: Intermittent hypoxia conditioning reduces the levels of inflammatory parameters and cytokines (C-reactive protein, TNF-α, IL-4, IL-6, IL-8), increases the tolerance to acute hypoxia, the functional capacity and improves parameters of respiratory and cardiovascular systems [1–4].
Objectives: To evaluate the efficiency of the interval hypoxic-hyperoxic training (Reoxy therapy) in the rehabilitation of patients with osteoarthritis (OA) and post-COVID syndrome.
Methods: 36 patients with OA (78% females, age of 43 to 68 years, generalized OA, OA of the knee or hip joints) where included in the randomized placebo-controlled study. Coronavirus infection COVID-19 were diagnosed from 12 to 26 weeks before the study. The main symptoms of post-COVID syndrome were dry cough, smell loss, breathlessness, weakness, fatigue, sleep disorders, cognitive symptoms, memory problems, anxiety, depression, headache, dizziness, joint and muscle pain. All patients were randomized into 3 groups. 13 study group patients received 10 Reoxy therapy procedures, 9 placebo group patients – 10 placebo procedures of Reoxy therapy, 14 control group patients – only standard rehabilitation. The patients of all groups underwent 2-week standard rehabilitation program: 10 procedures of electrostatic massage for muscles and periarticular tissues, 10 sessions of general magnetic therapy, 10 group sessions of physical exercises with elements of breathing exercises. All patients received NSAIDs and SYSADOA at standard dosages. Intra-articular corticosteroids was not used. The study group patients were breathing hypoxic (FiO2 13–15%) and hyperoxic (FiO2 up to 40%) gas mixture through the mask in the interval mode with biofeedback using device «ReOxy» (Ai Mediq S.A., Luxembourg). 10-min hypoxic test (FiO2 12–13%) was performed before the first and fourth procedures. The duration of 1–4 procedures was 30 min, 5–10 procedures – 40 min. The placebo procedures were performed using the mask with the atmospheric air hole. Joint pain and general health on 100-mm VAS, Lequesne and WOMAC indexes, Spielberger-Khanin anxiety test, Beck depression inventory and breathlessness on Modified Borg scale were evaluated at baseline and at 2 weeks.
Results: After 2 weeks in the study group pain on VAS decreased by 49,6% (p<0,05), Lequesne index – by 39,3% (p<0,05), WOMAC – by 1,4 times (p<0,01), anxiety level on Spielberger-Khanin test – by 40,9% (p<0,05), depression level on Beck depression inventory – by 64,1% (p<0,01), general health on VAS improved by 69,3% (p<0,01). The level of breathlessness on Modified Borg scale in the study group initially was 2,5±0,9 score (moderate – slight breathlessness). After rehabilitation in the study group the level of breathlessness decreased to 0,3±0,4 score (extremely slight – no breathlessness). In the study group there were statistically significant differences from the placebo group (p<0,05) and the control group (p<0,05) in all parameters.
Conclusion: 2-week complex rehabilitation program, including interval hypoxic-hyperoxic training (Reoxy therapy), reduces pain, breathlessness, depression and anxiety, improves functional status and general health in patients with OA and post-COVID syndrome.
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POS1454 NEUROPLASTICITY STIMULATION-BASED REHABILITATION IMPROVES PAIN AND HAND FUNCTIONALITY IN PATIENTS DIAGNOSED WITH CARPAL TUNNEL SYNDROME: A PILOT STUDY

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Background: Carpal tunnel syndrome (CTS) is the most commonly diagnosed entrapment neuropathy, characterized by sensory and motor disorders. Physiotherapy interventions based on neuroplasticity stimulation, such as mirror therapy (MT) and cross-education (CE) have been demonstrated effective in pain and impaired function. In those therapies, mirror neurons that are activated when observing an action are considered the possible underlying neural mechanism, creating organized new pathways between two cerebral hemispheres and enabling brain plasticity. However, MT and CE effects have not been widely studied on unilateral CTS.
Objectives: To analyze the effectiveness of MT and CE rehabilitation protocols in a sample of patients with CTS on pain intensity and functionality.
Methods: A randomized-controlled trial was conducted. Subjects diagnosed with unilateral CTS were enrolled in this study. MT group (MTG) (N=9)

performed a rehabilitation protocol consisting of six-weeks of MT training, five days/week. The healthy hand was trained in front of a mirror placed in the middle of the body, while the affected hand was hidden and quiet on the opposite side. CE group (CEG) (N=10) intervention was designed to perform the same training protocol, but without a mirror. Thus, the difference between interventions was the use of the mirror. Training consisted of mobility, strength and functional exercises. Minimum, maximum and average perceived pain were assessed through Visual analog scale (VAS), and upper limb function through Quick-DASH, before and after the intervention. Regarding statistical analyses, a two-factor mixed multivariate analysis of variance (MANOVA) was carried out with a between-subjects factor "treatment group" (MTG and CEG) and a within-subject factor "time measuremets" (pre and post-intervention) for all variables. (Clinical trial Id: NCT05115396).

Results: Nineteen participants (4 men and 15 women) between 30 and 60 years were included in the study. There were no statistically significant differences between groups at the beginning of the study. After treatment, there was a significant decrease in maximum pain (p<0.05), minimum pain (p<0.05) and average pain (p<0.05) of the affected hand in both groups, being larger the experienced changes of the MTG compared to that of the CEG (Table 1). Regarding hand functionality, both groups significantly improved compared with baseline (p<0.01). This study suggests that activation of mirror neurons either by MT or CE, is effective on hand pain and functionality in people with unilateral CTS.

Table 1. Pre and post-intervention results on pain and functionality.

Group		N	Pre-treatment	Post-treatment
VAS maximum	MTG	9	4.22 (2.64)	2.11 (2.26)*
	CEG	10	4.70 (2.87)	2.80 (2.15)*
VAS minimum	MTG	9	2.22 (2.22)	0.33 (0.50)*
	CEG	10	2.50 (2.64)	0.90 (1.10)*
VAS mean	MTG	9	3.22 (2.44)	1.56 (1.59)*
	CEG	10	3.80 (2.82)	2.20 (1.75)*
Quick-DASH	MTG	9	34.35 (21.36)	23.74 (21.71)**
	CEG	10	31.14 (26.48)	19.77 (19.87)**

Data are shown as mean (SD). MTG: Mirror Therapy Group; CEG: Cross-education Group; VAS: Visual Analog Scale; *: p-value <0.05 between pre and post-intervention; **p-value <0.01 between pre and post-intervention.

Conclusion: Neuroplasticity stimulation-based rehabilitation, using a MT protocol or a CE protocol, improves pain and functionality in patients with unilateral CTS.

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POS1455 EFFICIENCY OF PASSIVE MECHANOTHERAPY IN COMPLEX REHABILITATION OF PATIENTS WITH OSTEOARTHRITIS

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Background: Different types of physical exercises relieve pain, improve functional status and quality of life in patients with osteoarthritis (OA) in addition to drug treatment [1–4].

Objectives: To evaluate the efficiency of robotic mechanotherapy (continuous passive motion) in the complex rehabilitation of patients with OA.

Methods: 58 patients with OA of the knee, hip, wrist and hand joints (76% females, age of 49 to 65 years, disease duration of 3 to 11 years) were included in the study and randomized into 2 groups. 28 study group patients underwent robotic passive mechanotherapy (continuous passive motion) for the knee and hip joints using «ARTROMOT K1» machine (Ormed gmbh, Germany), for the wrist and hand joints using «Kinetec Maestra hand and wrist CPM» machine (Kinetec, UK) (10 sessions for 20–25 min) in addition to the standard rehabilitation program (2 weeks). 30 control group patients received only the standard rehabilitation program, which included 10 group sessions of physical exercises for the joints for 45 min under the supervision of a trainer, 10 procedures of electrostatic massage for muscles and periarticular tissues, 10 sessions of occupational therapy for 45 min (joint protection strategies, use of assistive devices and adaptive equipment). All patients received NSAIDs and SYSADOA at standard dosages. Intra-articular corticosteroids were not used. Tender joint count, joint pain on 100-mm VAS, Lequesne and WOMAC indexes, the amplitude of flexion in the knee joint measured by goniometer, the march test (passage time of 20 meters per sec), hand grip strength measured by a dynamometer were evaluated at baseline and at 2 weeks.

Results: After 2 weeks in the study group pain on VAS decreased by 40,9% (p<0,05), tender joint count – by 38,7% (p<0,05), Lequesne index – by 1,53 times (p<0,01), WOMAC – by 1,21 times (p<0,01). In the study group the amplitude of flexion in the knee joint increased by 34,2% (p<0,05), the march test decreased by 3,5±1,2 sec (28,8%) (p<0.05), the grip strength of the more affected hand enhanced by 22,3% (p<0,05), of the less affected hand – by 18,5% (p<0,05). In the study group there were statistically significant differences from the control group in all parameters (p<0,05), excluding the grip strength of the less affected hand (p>0,05).

Conclusion: 2-week complex rehabilitation program, including robotic mechanotherapy (continuous passive motion), relieves pain, improves functional ability, motor activity (march test, range of motion in the knee joint, hand grip strength) in patients with OA.

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Education

POS1456 TEACHING NAILFOLD CAPILLAROSCOPY USING THE "FAST TRACK ALGORITHM" VIA AN ONLINE PLATFORM: THE ASIAN EXPERIENCE

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Background: Nailfold capillaroscopy (NFC) is being increasingly used in the early identification of systemic sclerosis (SSc) related disorders. Recent studies have shown that an optimised simple capillaroscopic definition of normal and abnormal capillary morphology is reliable and a multi-centre consensus 'fast track algorithm' was developed by the European League against Rheumatism (EULAR) Study Group on Microcirculation in Rheumatic Diseases (SG MC/RD) to allow trainees to identify scleroderma patterns from non-scleroderma patterns.

Objectives: To validate the "fast track algorithm" taught via an online teaching platform to identify scleroderma patterns from non-scleroderma patterns on NFC.

Methods: Trainees participated in the NFC teaching workshops conducted via an online platform by the same SSc expert (AL) over 3 separate sessions. In the first part of the workshop (training), all trainees attended a talk on NFC by the SSc expert (AL) whereby they were taught the fast track algorithm to identify and classify NFC image patterns using a training set of images. The "fast track algorithm" (Figure 1) consists of three easy rules: 1) Rule number 1: the presence of ≥ 7 capillaries (capillary density) AND the absence of giant capillaries (capillary dimension) allows the rater to call the capillaroscopic image a "non-scleroderma pattern (category 1)"; 2) Rule number 2: the presence of giant capillaries or the presence of an extremely lowered capillary density (≤ 3 capillaries) in combination with abnormal shapes (= "late" scleroderma pattern) allows the rater to call the capillaroscopic image a "scleroderma pattern (category 2)"; 3) Rule number 3: if the image does not meet rule number 1 or rule number 2 then the image is automatically classified as a "non-scleroderma pattern (category 1)". In the second part of the workshop (evaluation), each trainee independently rated 45 NFC images (30 seconds for each NFC image) in the same session, and submitted their answers in real time using an electronic form. The reading of the expert (AL) was considered the gold standard. AL is a SSc expert who had previously attended the EULAR workshop on NFC and has had more than 10 years of experience in NFC. Within 2-4 weeks of the initial rating exercise, trainees re-evaluated the same set of images for the intra-reader exercise under supervised conditions via the online platform. We computed the inter- and intra-rater agreement using

mean [standard deviation (SD)] Cohen's Kappa, with the following values representing the degrees of agreement: <0 –poor; 0-0.20 –slight; 0.21-0.40 –fair; 0.41-0.60 –moderate; 0.61-0.80 –substantial; and 0.81-1.00 –almost perfect agreement.

Results: Ninety-eight trainees from Singapore, Malaysia, Indonesia, Hong Kong, Philippines, Taiwan, Myanmar and Brunei included rheumatologists, rheumatology trainees, pediatric rheumatologists, internists and nurses. Fifty-four participants were novices with no prior NFC experience, 38 participants were "moderately experienced" (< 5 years of NFC experience) and 1 participant was "experienced" with more than 5 years of NFC experience. The mean (SD) inter-rater kappa of the 98 trainees was 0.71 (0.13). For the 61 trainees who participated in the re-evaluation session, mean (SD) inter-rater and intra-rater kappa were 0.74 (0.16) and 0.71 (0.15), respectively.

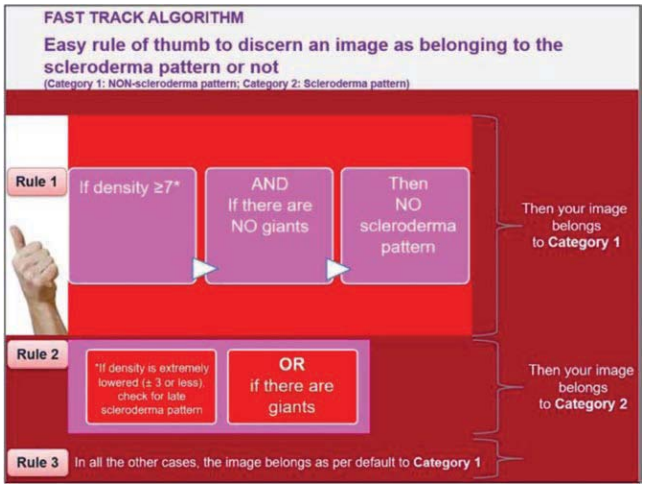

Figure 1. Fast Track algorithm

Conclusion: There was substantial inter- and intra-rater agreement. This is the first study in Asia examining NFC training using the EULAR SG MC/RD fast track algorithm and our results support the importance of standardized teaching for NFC.

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POS1457

ANALYSIS OF WORLDWIDE RHEUMATOLOGY POSTGRADUATE TRAINING CURRICULA: A MAPPING EXERCISE TO INFORM THE DEVELOPMENT OF EULAR STANDARDS FOR THE TRAINING OF EUROPEAN RHEUMATOLOGISTS

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Background: Previous work has highlighted considerable heterogeneity in the organization of postgraduate rheumatology training programs. EULAR strives to harmonise rheumatology training across Europe with defined standards of key aspects of training including knowledge, skills and professional behaviors.

Objectives: To analyse existing documents on postgraduate training in rheumatology and other related specialties available within Europe and the rest of the world.

Methods: As most documents were unpublished, key documents on specialty training in Rheumatology and 28 related specialties were retrieved by hand-search. We started with the collection of documents developed by UEMS (Europe), ACGME (USA), CanMEDS (Canada) and RACP (Australia). Then we searched for specialty training documents developed by other international Boards and we also sent emails to the boards or associations if no document could be found in their websites. Finally, we retrieved national documents from European Countries with a structured rheumatology training process, translated them into English using DeepL/Google translate and, in case of doubt, liaised with native speakers familiar with the documents. The content of all the above documents (including information about the structure of each document) was extracted into a standardized data extraction sheet.

Results: 133 documents were retrieved. UEMS, ACGME, CanMEDS documents were available for all the mapped specialties, while RACP documents were retrieved for only 18 specialties. No American or Canadian specialty board developed additional documents on training, while in Europe non-UEMS boards of 11 specialties did (Table 1). With regard to Rheumatology, 2 separate documents for adult and pediatric rheumatology training were available from UEMS and ACGME while one document

Table 1. Documents retrieved and extracted for each specialty. Rheumatology national training documents are not listed.

Specialty	Europe		USA		Canada		Australia		ALL
	UEMS	*Other board*	*ACGME*	*Other board*	*CanMEDS*	*Other board*	*RACP*	*Other board*	
Rheumatology	x		x		x		x		6*
Allergology	x	x	x		x		x		5
Anaesthesiology	x		x		x		0		3
Cardiology	x	x	x		x		x		5
Child and Adolescent Psychiatry	x		x		x		0		3
Clinical Genetics	x		x		x		x		4
Dermatology and Venereology	x		x		x		x		4
Emergency Medicine	x	x	x		x		0		4
Endocrinology	x	x	x		x		x		5
Gastroenterology	x		x		x		x		4
General practice	x		x		x		x		4
Geriatrics	x		x		x		x		4
Gynaecology and Obstetrics	x		x		x		0		3
Infectious Diseases	x		x		x		x		4
Internal Medicine	x	x	x		x		0		4
Medical Oncology	x	x	x		x		x		5
Nephrology	x	x	x		x		x		5
Neurology	x		x		x		x		4
Occupational Medicine	x		x		x		x		4
Ophthalmology	x		x		x		0		3
Orthopaedics	x	x	x		x		0		4
Otorhinolaryngology	x		x		x		0		3
Paediatrics	x	x	x		x		x		5
Physical Medicine and Rehabilitation	x		x		x		x		4
Psychiatry	x		x		x		0		3
Public Health Medicine	x		x		x		x		4
Radiation Oncology and Radiotherapy	x	x	x		x		0		4
Respiratory medicine	x	x	x		x		x		5
Sport and exercise medicine	x		x		x		0		3
TOTAL	**30**	**11**	**30**	**0**	**30**	**0**	**18**	**0**	**119**

*2 UEMS and 2 ACGME document on adult and pediatric rheumatology

on adult rheumatology training was retrieved for CanMEDS and RACP. Upon assessment of the content of these 133 documents, we observed that their organisation could be competence-based (48%), role-based (47%), or problem-based (5%). When focusing on Rheumatology, content was fairly similar across international curricula, but several differences emerged in national curricula. These were mainly related to national regulations (e.g. rheumatology training as part of internal medicine training) and a different definition of mandatory/optional competences. The number of listed competences in the rheumatology documents ranged from 18 to 196.
Conclusion: We collected and analysed documents on specialty training in Rheumatology and other related specialties across a broad set of international sources. Most documents followed a competence-based or role-based framework; similarities and differences in the content of Rheumatology documents were detected. This mapping exercise informed the EULAR Task Force on the development of standards for the training of European rheumatologists.
Disclosure of Interests: None declared
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POS1458 HOW EASY IS IT FOR PATIENTS TO READ AND UNDERSTAND AVAILABLE PATIENT EDUCATIONAL MATERIALS FOR LUPUS?

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Background: Health Literacy (HL) informs health behaviors such as follow-up with health care providers & management plans. Poor HL is linked to poor health outcomes & healthcare disparity. In addition to personal HL, health care providers/systems & Organizations can also empower patients by developing & providing educational resources that foster HL & support a patient's understanding of their health condition (organizational HL). Patient educational handouts are frequently provided after a physician visit to supplement instructions/education & are often obtained from online resources accessible to both physicians & patients. Lupus, a multisystem disease, preferentially effects people of color, a group at higher risk of health disparities, & poor HL. It is paramount for lupus patients to understand their disease & management to optimize health outcomes & reduce health disparities. The provision of easy to read & comprehend patient educational resources are one way to address this need.
Objectives: The Center for Disease Control (CDC) recommends the readability of patient educational material to be at eight-grade level, while the National Institute of Health (NIH) & the American Medical Association (AMA) recommend a level no higher than sixth-grade. The Readability & Comprehension (RC) of commonly available lupus-related patient educational materials are not known & may offer an opportunity to improve patient care & outcomes.
Methods: We searched for the RC of Lupus-related patient educational materials, available at the American College of Rheumatology (ACR) & Lupus Foundation of America (LFA) websites. These reputable national organizations are at the forefront of Lupus education & research. RC were evaluated using the following measures: Flesch Kincaid Readability Ease (FKRE), Flesch Kincaid Grade Level (FKGL), Gunning Fog Score (GFS), Simple Measure of Gobbledygook (SMOG) Index, Coleman Liau Index (CLI) & Automated Readability Index (ARI).
FKRE score is a widely used measure of readability with scores ranging from 0-100 & higher scores denoting greater reading ease (Goal is >60). FKGL represents the U.S. school grade needed to comprehend the text (Target is 7th grade). GFS estimates the years of formal education required to understand the text on the first reading (Goal is 7-8). SMOG index estimates the years of education needed to comprehend written materials. CLI is used to assess the U.S. grade level necessary to comprehend text material. The ARI assesses how easy a text material is to learn & estimates the U.S. grade level necessary to comprehend a passage.
Descriptives for RC were obtained & compared using t test between the two sources.
Results: There were 12 patient educational pamphlets on Lupus available (4 from ACR & 8 from LFA). Mean (SD) FKRE & FKGL were 52.73 (11.44) & 10.46 (2.14) respectively (Table 1). Mean GFS & CLI exceeded 12, while mean ARI was 18.

Table 1. Reading & Comprehension of Patient Educational Materials on Lupus

RC Test (Values are Mean (SD))	All	ACR	LFA	P
Flesch Kincaid Reading Ease	52.73 (11.44)	47.18 (4.93)	55.50 (13.00)	0.25
Flesch Kincaid Grade Level	10.46 (2.14)	10.73 (0.64)	10.33 (2.64)	0.78
Gunning Fog Score	12.19 (1.78)	12.65 (0.31)	11.96 (2.19)	0.41
SMOG Index	8.94 (1.41)	9.6 (0.67)	8.61 (1.60)	0.27
Coleman Liau Index	13.51 (2.04)	14.65 (1.34)	12.94 (2.15)	0.18
Automated Readability Index	18.02 (23.13)	11.1 (1.45)	21.47 (28.27)	0.49

There were no significant differences in the RC scores among patient educational materials from the ACR or LFA.
Conclusion: Patient educational materials on Lupus, available at the ACR & LFA websites, are not easy to read or comprehend, using standardized RC metrics. Additionally, they are not aligned with recommended reading levels suggested by leading organizations (CDC, NIH or AMA). Patient's understanding is critical in a complex disease like lupus to optimize health outcomes. Revision of patient lupus educational resources at these websites, to target 6-7th grade RC metrics, is recommended & could be overseen by the development of a new taskforce.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3848

POS1459 THE IMPLEMENTATION OF AN EDUCATIONAL PROGRAM TO IMPROVE PHARMACOLOGICAL ADHERENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS. RESULTS FROM A QUASI-EXPERIMENTAL STUDY

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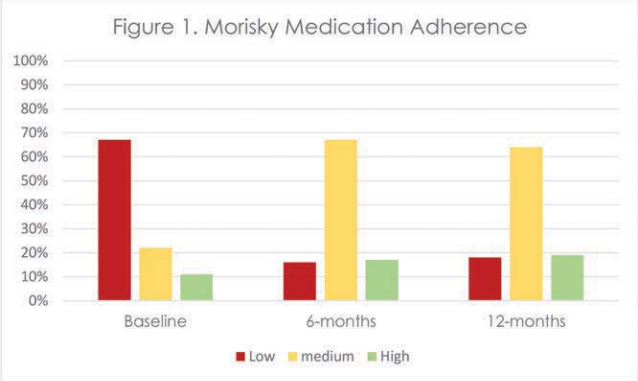
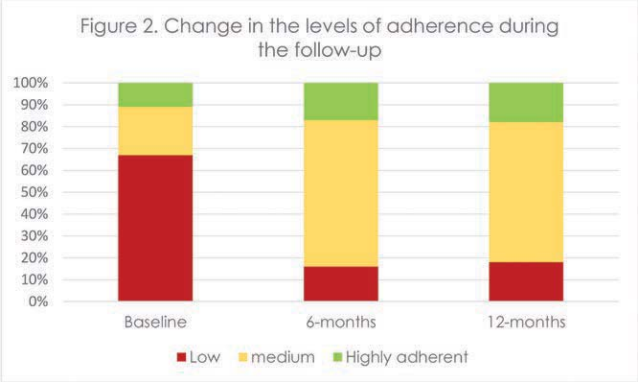
Background: Pharmacological therapy is the principal intervention in rheumatoid arthritis (RA) patients. Currently, adherence to DMARDs therapy is a challenge that needs to be addressed[1]. On the other hand, educational programs have shown an improvement in the health status of RA patients[2].
Objectives: This study aimed to determine if a 12-month educational program developed for patients with RA can improve medication adherence.
Methods: A quasi-experimental design was conducted. Patients who attend a specialized center in RA were invited to participate in an educational program. The program was called UNIVERSITAR: PATIENT UNIVERSITY. An interdisciplinary team provided educational workshops for the patients; we included coaching sessions and leisure activities such as yoga and art lessons to avoid a conventional classroom program and provide a dynamic program. A rheumatologist with experience in centers of excellence for RA led the team. Patients attended during a year. Follow-up was planned at 6 and 12 months after enrollment. Medication adherence was assessed using the self-reported 8-item Morisky Medication Adherence Scale (MMAS-8). Patients were considered adherent when they scored 8 points, moderately adherent with a score of 6 or 7, and non-adherent with less than 6 points. The Wilcoxon signed-rank test was used to evaluate differences in MMAS-8 scores between baseline and 16 and 12-months. We also assessed if there were changes in DAS 28 in the participants who improved the level of adherence.





Results: In total, 252 patients were enrolled in the study, and 206 completed the follow-up at 6 and 12 months (82%). The median age was 60 years IQR (54-67), 94% were female. In our study, 54% of patients received conventional and 46% Biological therapy. The proportion of patients with high adherence at baseline was 11%, at 6-months was 17% and at 12-month was 19%. At the end of the follow-up, 49% of the participants moved from being non-adherent to a moderate or high adherence level. When we compared the MMAS scores at baseline and follow-up, they showed a significant improvement (P<0.05) Figures 1-2. The majority of participants (65%) were in remission at baseline, according to DAS28. Therefore, we found no differences between the level of adherence and DAS28.

Conclusion: Our educational program improved medication adherence among patients with RA. Educational interventions are helpful to sustain remission in patients with RA. Further studies focused only on patients with moderate and high disease activity are necessary to assess the impact on clinical outcomes.

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Disclosure of Interests: Pedro Santos-Moreno Speakers bureau: Pfizer, Janssen, Abbvie, Biopas-UCB, Bristol, Roche, Novartis, Lilly, Consultant of: Pfizer, Janssen, Abbvie, Biopas-UCB, Bristol, Roche, Novartis, Lilly, Grant/research support from: Pfizer, Janssen, Abbvie, Biopas-UCB, Bristol, Roche, Novartis, Lilly, Diana Buitrago-Garcia: None declared, Fernando Rodriguez: None declared, GUILLERMO SÁNCHEZ: None declared

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POS1460 CONTRIBUTING TO THE TRAINING OF IMAGING IN RHEUMATOLOGY BY EXPERTS WORLDWIDE VIA INTERACTIVE MOBILE E-TEACHING: BERLINCASEVIEWER.

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Background: Rheumatology education today can be very diverse, and you can find everything from structured textbooks to YouTube channels to social media accounts. Peer-reviewed content is still recognized as a very high-quality source of information. App-based content has the advantage of bundling information in one place, always available on the go. However, the majority of offerings are only available in English.

Objectives: An app was to be created to learn about imaging in rheumatology in a very easy to understand way in different languages, with experts being able to create translated content very easily.

Methods: Using mySQL, Java, Objective C and JavaScript, a case database with specific structure and numerous interactive elements was created for academic teaching. Special functions for the annotation of images were provided. The development was initially for devices with the iOS operating system, and later for Android. Rheumatologists and radiologists worldwide were invited to participate via the social media channels LinkedIn, Instagram, Facebook, Twitter, and TikTok.

Results: The app, called BerlinCaseViewer, was developed for smartphones, tablets and Mac computers. All information is entered and processed in a web-based database. Using XML files and ZIP archives, the relevant data is then transferred to the mobile apps. Case of the month and learning modules on rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthritis are available, many in English, Spanish, French, Italian, Portuguese, German, and other languages (Figure 1). In addition to the medical image data, the patient's medical history is also presented in an exciting way with the help of multiple-choice questions. Only when all questions are answered, the diagnosis becomes visible. Timeline functions can be used to visualize medical courses as well. Colored overlays are used to annotate images and can be placed with pixel precision. The user can decide whether these should be displayed as aids. Content is peer-reviewed before publication.

Figure 1. Multi-lingual presentation of medical training cases.

Conclusion: BerlinCaseViewer is a new approach not only to train medical professionals, but also to connect colleagues and overcome language barriers. As a platform, BerlinCaseViewer is open to all medical professionals to collaborate, whether to contribute their own cases or translate existing cases for use in the local language.

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Disclosure of Interests: : Kay-Geert Hermann Shareholder of: Co-founder of BerlinFlame GmbH, Mikhail Protopopov: None declared, Aline Serfaty: None declared, Ihsane Hmamouchi: None declared, Fernando Sommerfleck: None declared, Fabio Macori: None declared, Katharina Ziegeler: None declared, Torsten Diekhoff: None declared, Denis Poddubnyy Shareholder of: Co-founder of BerlinFlame GmbH, Joachim Sieper Shareholder of: Co-founder of BerlinFlame GmbH

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Educational cases

POS1461 GIANT CELL ARTERITIS-RELATED STROKE IN A MAN WITH ELDERLY-ONSET RHEUMATOID ARTHRITIS

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Background: Giant cell arteritis-related stroke is rare, with high early mortality and major morbidity in survivors.

Objectives: To increase the awareness of coexistence of giant cell arteritis-related stroke and rheumatoid arthritis.

Methods: A case report and discussion.

Results: A 73 year-old man with seronegative elderly-onset rheumatoid arthritis (EORA) presented to the emergency department (ED) with a one week history of frontal headache, vomiting and dizziness. He had multiple cardiovascular comorbidities and took multiple medications, including methotrexate and sulfasalazine. He also had long-standing history of thrombocytopenia without requiring any treatment. Neurological examination performed in the ED was unremarkable. His C-reactive protein (CRP) was 69mg/L and erythrocyte sedimentation rate (ESR) 82mm/hour. Computed tomography (CT) of the brain was normal. The headache settled with analgesia. A diagnosis of probable tension-type headache, with underlying active EORA, was made. One month later, he presented to an ophthalmologist with recurrence of headache associated with visual disturbance and was diagnosed with giant cell arteritis (GCA). Both CRP (77mg/L) and ESR (85mm/hour) remained raised. Neither temporal artery biopsy nor temporal artery ultrasound were possible due to the coronavirus disease 2019 (COVID-19) pandemic. The headache and visual symptoms resolved completely a week after prednisolone 60mg daily was prescribed. In parallel, the CRP dropped to 2mg/L and ESR 16mm/hour. The patient's glucocorticoid dose was then tapered. While on prednisolone 20mg daily, about 3 weeks later, he developed slurred speech and generalized weakness. Examination showed cerebellar signs and MRI brain showed acute cerebellar infarct. He was treated pragmatically as an atherosclerotic stroke with clopidogrel, and the steroid was rapidly tapered in view of absence of headache and normalization of inflammatory markers. Four weeks later, he was noted to have persistent confusion and unsteadiness of gait. CRP was elevated at 92mg/L. An urgent positron emission tomography-CT (PET-CT) scan showed inflammation in the vertebral arteries [Figure 1] and cerebellar stroke. Prednisolone 40mg daily was restarted which led to a rapid improvement in his symptoms and normalization of inflammatory markers. The glucocorticoids were tapered in a slower manner this time.

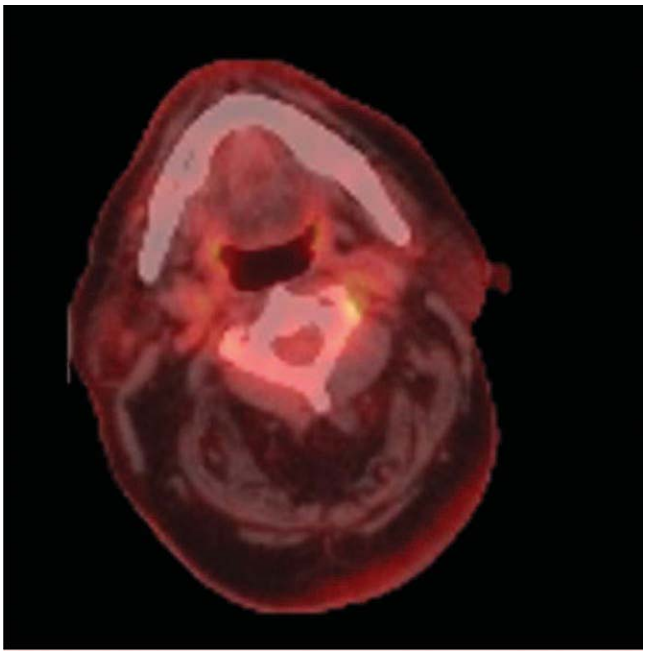

Figure 1. Fused axial image of a PET-CT scan demonstrating increased uptake in the region of the left vertebral artery within the vertebral foramen.

A diagnosis of GCA-related cerebellar stroke with vertebral vasculitis was made and, with glucocorticoids, the patient made a good clinical recovery. His inflammatory joints pain also improved in parallel.

Conclusion: Stroke or transient ischemic stroke are rare complications, reported in 2.8-16% of patients with active GCA. Most studies report strokes as occurring between the onset of GCA symptoms and 4 weeks after commencement of glucocorticoids[1-3]. Vertebrobasilar territory is involved in 60–88% of cases of GCA-related stroke[1-3]. In contrast, the vertebrobasilar territory is affected only in 15-20% of atherosclerotic strokes[1,2]. One study reported fatal outcomes in 11 out of 40 patients (28%) with GCA-related stroke, 7 within 2-13 days of stroke[2]. To conclude, this case demonstrates that high-dose glucocorticoids with slower tapering were able to control GCA-related stroke due to vertebral vasculitis in patient with EORA on background methotrexate and sulfasalazine.

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POS1462 **CAUSES OF DEATH IN PATIENTS WITH RHEUMATIC AND AUTOIMMUNE DISEASES: A 15-YEAR-OLD AUTOPSY-BASED STUDY.**

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Background: Patients with rheumatic and autoimmune diseases have susceptibility to fatal outcomes and may seem less deadly than they actually are.
Objectives: To describe the main causes of death as determined by autopsy findings, in patients with rheumatic and autoimmune diseases in a central hospital of the Colombian north-east. Stress the importance of autopsy as a teaching, research tool and education in medicine.
Methods: A retrospective, descriptive study of the database from the Pathology Department at UIS in Bucaramanga, Colombia. A total of 4,430 autopsies were performed between January 2004 and December 2019 in patients whose death occurred at Hospital Universitario de Santander or other hospitals in the Bucaramanga metropolitan area. Perinatal autopsy cases were excluded (2,181) and 2,249 autopsy protocols were analyzed, of which 47 corresponded to patients with a rheumatic and autoimmune disease (Figure 1).

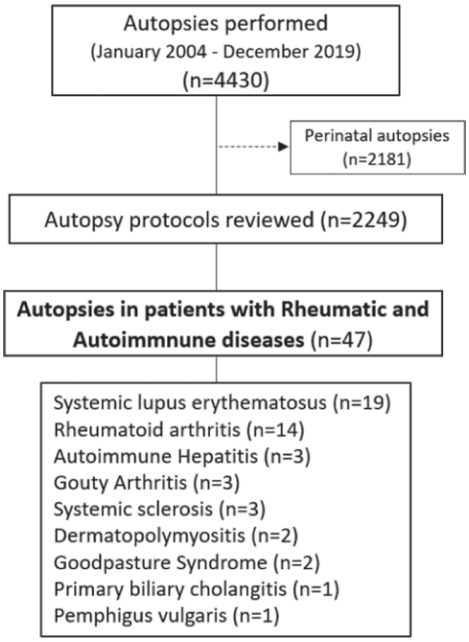

Figure 1. Flowchart of case selection

Results: A total of 47 cases were included, 27 (57.5%) were female and 20 (42.5%) were male. The mean age was 39 years old with a range from 13 to 69 years old. The most common disease was systemic lupus erythematosus (40.5%) and rheumatoid arthritis (29.8%), followed by autoimmune hepatitis and gouty arthritis with 3 cases (6.4%) each one. The most common cause of death determined by the autopsy findings was infections (66%) of which more than half were due to opportunistic pathogens, with tuberculosis being the predominant cause with 12 cases. The second cause was organic compromise due to disease activity (23.4%), and lastly other causes (10.6%) such as pulmonary embolism or myocardial infarction, which conditions more likely to present in patients with a rheumatic and autoimmune disease. A detailed description of the case series is displayed in Table 1. Almost all patients were receiving immunosuppressive therapy. The most used agents were prednisone (85%), methotrexate (19%), and azathioprine (15%). The other immunosuppressive medications were cyclophosphamide and tumor necrosis factor inhibitors in 2 cases each one.

Table 1. Causes of death determined at autopsies findings.

Disease n (%)	SLE	RA	AH	GA	SSc	DMPM	GS	Others*
Cause of death	19 (40,5)	14 (29,8)	3 (6,4)	3 (6,4)	2 (4,2)	2 (4,2)	2 (4,2)	2 (4,2)
Pneumonia (CAP)	5 (26,2)	3 (21,4)	1 (33,3)	-	1 (50)	-	-	-
Septic shock	2 (10,5)	2 (14,3)	-	-	-	-	-	-
Opportunistic Infection	5 (26,2)	6 (42,9)	-	2 (66,6)	1 (50)	2 (100)	-	1 (50)
Renal failure	3 (16)	-	-	-	-	-	2 (100)	-
Respiratory failure	-	-	-	-	-	-	-	-
Hepatic failure	-	-	2 (66,6)	-	-	-	-	1 (50)
MODS	3 (16)	-	-	-	-	-	-	-
Pulmonary embolism	1 (5,1)	1 (7)	-	-	-	-	-	-
Myocardial infarction	-	2 (14,3)	-	1 (33,3)	-	-	-	-

*Others: Primary biliary cholangitis 1 case and Pemphigus vulgaris 1 case. SLE= Systemic lupus erythematosus; RA= Rheumatoid arthritis; AH= Autoimmune Hepatitis; GA= Gouty Arthritis; SSc= Systemic sclerosis; DMPM= Dermatopolymyositis; GS= Goodpasture Syndrome; CAP= Community-acquired Pneumonia; OI= opportunistic infections; MODS= Multiple organ dysfunction syndrome.

Conclusion: The causes of death in our autopsy series match previous studies in these population. The leading cause of death were infections and most cases occurred in young and middle-aged women. These results support previous reports regarding the importance of infections as a cause of death in patients with rheumatic and autoimmune diseases and the fatal outcomes of a severe activity of the uncontrolled disease. It is a challenge for the clinician to treat patients with these conditions and to achieve a balance between obtaining an effective treatment (usually high doses of immunosuppressive drugs) and minimizing the risks of adverse events related to the medications, such as infections.

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Disclosure of Interests: None declared

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POS1463 TUBERCULOSIS AS A FATAL OUTCOME IN PATIENTS WITH RHEUMATIC DISEASES: AN AUTOPSY-BASED STUDY

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Background: Tuberculosis (TB) is still a worldwide health problem and patients with rheumatic disease (RD) have an increased risk of this infection and fatal outcomes.

Objectives: We aim to report an autopsy case series in patients with an RD whose deaths were caused by TB in a high-level hospital of the Colombian north-east and stress the importance of autopsy as a teaching and research tool.

Methods: A retrospective, descriptive study of the database from the Pathology Department at UIS in Bucaramanga, Colombia. A total of 3390 autopsies were performed between January 2009 and December 2019 in patients whose death occurred at Hospital Universitario de Santander. A total of 1713 autopsy reports were analyzed, of which 10 corresponded to patients with RD whose deaths were caused by Mycobacterium tuberculosis.

Results: A total of 12 patients with a premortem diagnosis of RD were included who additionally had autopsy findings consistent with a mortal infection by a Mycobacterium tuberculosis. Nine cases (75%) were male and 3 were female (25%). The mean age was 49 years old with a range from 32 to 69 years old. The most common RD was rheumatoid arthritis (33,3%) followed by systemic lupus erythematosus, dermatopolymyositis and gouty arthritis with 2 cases (16,6%) each one. In 9 cases the autopsy findings were extrapulmonary TB, of which more than half were disseminated and only 3 cases were exclusively pulmonary TB. All patients were receiving immunosuppressive therapy. The most commonly used therapies were prednisone (100%), methotrexate (25%), and anti-TNF agents (16,6%). A detailed description of the reported cases is displayed in Table 1 and Figure 1.

Table 1. Description of the reported cases

Case	Sex	Age	RD	IST	Autopsy findings
1	Male	32	RA	PRED, MTX, Anti-TNF	Disseminated tuberculosis
2	Male	37	DMPM	PRED	Disseminated tuberculosis
3	Female	42	SLE	PRED	Disseminated tuberculosis
4	Male	43	DMPM	PRED, MTX	Pulmonary tuberculosis
5	Male	45	GA	PRED	Meningeal tuberculosis
6	Male	45	RA	PRED	Meningeal tuberculosis
7	Male	49	GA	PRED	Pulmonary tuberculosis
8	Male	53	PV	PRED, AZA	Pulmonary tuberculosis
9	Female	56	RA	PRED, Anti-TNF	Miliary tuberculosis
10	Male	57	SLE	PRED	Disseminated tuberculosis
11	Male	60	RA	PRED, MTX	Pulmonary tuberculosis and tuberculous endocarditis
12	Female	69	SSc	PRED	Pulmonary and meningeal tuberculosis

RD= Rheumatic Disease; RA= Rheumatoid Arthritis; DMPM= Dermatopolymyositis; SLE= Systemic Lupus Erythematosus; GA= Gouty Arthritis; PV= Pemphigus Vulgaris; SSc= Systemic Sclerosis; IST= Immunosuppressive therapy; PRED= Prednisone; MTX= Methotrexate; Anti-TNF= Tumor Necrosis Factor Inhibitor; AZA= Azathioprine.

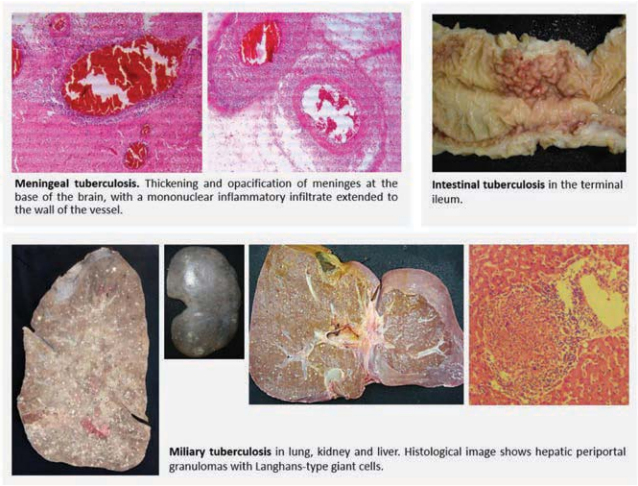

Figure 1. Pictures of some autopsy findings of the reported cases

Conclusion: TB remains one of the leading causes of death worldwide and patients with RD have an increased risk of TB as compared to the general population. In patients with rheumatic conditions, TB most commonly presents in its extrapulmonary form likely from the reactivation of latent infection, hence we stress the importance of screening for the most prevalent infections before the initiation of immunosuppressive therapy. The diagnosis and early treatment of latent TB infection are vital to preventing the progression of the disease and avoid fatal outcomes related to this infection.

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POS1464 TOXOPLASMOTIC CHORIORETINITIS IN A PATIENT WITH RHEUMATOID ARTHRITIS

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Background: Biological disease-modifying antirheumatic drugs (bDMARD) are one of the most effective in the treatment of rheumatoid arthritis. Infectious complications are one of the most common complications of this type of therapy. Before the therapy is started, patients are examined for tuberculosis, human immunodeficiency virus and hepatitis B and C, but the spectrum of chronic infections is much wider, for example toxoplasmosis infection is widespread. Toxoplasma gondii mainly affects the brain, lungs, liver and organ of vision.

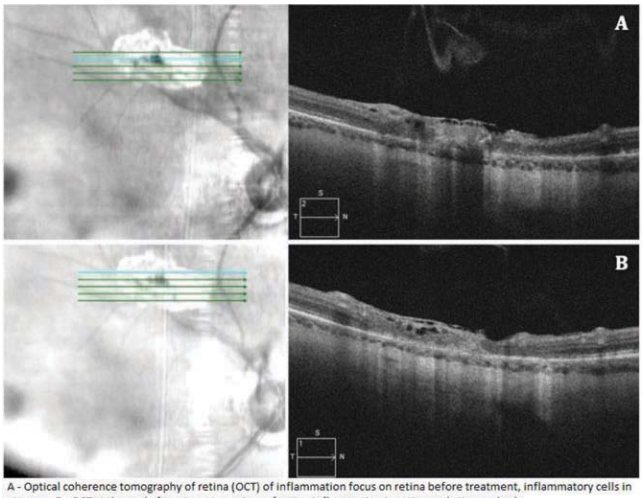
Objectives: To present a clinical case of toxoplasma chorioretinitis in a patient with rheumatoid arthritis.

Methods: Case report. The patient was treated and examined based on real clinical practice.

Results: A 59-year-old woman was admitted to the rheumatology department with symmetric arthritis of the hand joints, long morning stiffness duration (up to 4 hours). The diagnosis of rheumatoid arthritis was previously verified according to the ACR / EULAR 2010 criteria (three years ago). She received treatment in accordance with the clinical guidelines of the Ministry of Health of the Russian Federation: methotrexate 12.5 mg per week with a subsequent increase in dosage to 20 mg per week. Due to the increase in transaminases, the dosage of methotrexate was reduced to 17.5 mg per week, the daily intake of glucocorticosteroids (prednisone 7.5 mg per day). Nevertheless she had high disease activity (Disease Activity Score (DAS28) 5.54, Clinical Disease Activity Index (CDAI) 26.6, Simplied Disease Activity Index (SDAI) 30.12). Considering the continued high activity of the disease against the background of ongoing therapy lasting more than 6 months,

infliximab was added to the treatment at a dose of 3 mg per kg of body weight. A good clinical response was achieved (DAS28 2.67, CDAI 4.0, SDAI 9.4, prednisone canceled). After 4 months, there were complaints of acute decrease in vision in the right eye. Referred to an ophthalmologist. Visual Acuity: best corrected visual acuity (BCVA) on right eye is 0.4 (Snellen Chart), BCVA on left eye is 0.9 (Snellen Chart), intraocular pressure: right eye - 18 mmHg (non-contact), left eye - 19 mmHg (non-contact). Right eye: palpation is painful; cornea and anterior chamber humor are transparent; mild cataract in lens; inflammation cells in vitreous body (3+). Fundus (right eye): disc of optic nerve is normal; edema along upper-temporal vessels in macular region, exudates with pigmentation; periphery is normal. Left eye: findings are not clinical significant. Optical coherence tomography of retina (OCT): macular depression is normal; in paramacular region is epiretinal membrane, no traction; along upper-temporal vessels in macular region is chorioretinal focus with retina layer disorganization and tractions. Laboratory: Diaskintest is negative; Toxoplasma IgG = 170 ME / ml (positive is> 8 ME / ml). Diagnosis: Toxoplasma chorioretinitis, infiltration phase of right eye. Topical therapy: dexamethasone 0.1% - 1 x 6 times / day - 20 days, nepafenac 0.1% - 1 x 3 TID - 20 days. Oral: rovamycine 3 mil. ME - 2 TID - 20 days. Infliximab and methotrexate were canceled for the entire period of toxoplasma chorioretinitis treatment. Ophthalmologist's follow-up after 20 days: no complaints on visual acuity, BCVA on right eye is 1.0 (Snellen Chart). No cells in vitreous body. Fundus: decrease evidence of edema. OCT: decrease evidence of edema. Taking into account the presence of chronic toxoplasmosis infection, the patient was prescribed sulfasalazine 3 g per day as a basic therapy.

Conclusion: In this clinical case we demonstrated the possibility of activating chronic infections such as toxoplasmosis during therapy with bDMARD infliximab. To avoid risk of activating toxoplasmosis patients with rheumatoid arthritis should be screened for this infection before start bDMARD therapy.



A - Optical coherence tomography of retina (OCT) of inflammation focus on retina before treatment, inflammatory cells in vitreous. B - OCT at the end of treatment: no signs of active inflammation in retina and vitreous body

Figure 1.

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POS1465 **COMPLICATED QUESTIONS YET SIMPLE ANSWERS. A CASE OF THIAMIN DEFICIENCY MISTAKEN FOR SJOGREN'S SYNDROME.**

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Background: Sialosis is a non inflammatory nor neoplastic expansion of the salivary glands. it is a common mimicker for obstructive, inflammatory and malignant salivary gland disorders.(1) It had been described in acromegaly, vitamin A, and Thiamin deficiency and in amylophagia and bulimia.(2-5) Imaging should be normal in Sialosis(6) Here we describe a case of Sialosis due to Vitamin deficiency who was treated for a few months with anti-tuberculous and anti inflammatory drugs.

Objectives: To raise awareness about this cause of parotid swelling and encourage practice of exclusion prior to treatment.

Methods: A 30 year old lady with no significant past medical history presented to us with 2 years of slowly progressive, non tender bilateral facial swellings, with no excess or reduced salivation and no pain upon eating, she had negative history of preceding upper respiratory tract infection. the condition was associated with feeling a lump in her right axilla, and cervical region, there was no fever or systemic manifestations. she consulted a surgeon during that period, an exisional biopsy of the lump revealed the presence of fatty lumps, she was then prescribed antituberculosis medications since her symptoms were vague and because TB is quite common in Iraq. She denied any improvement with these medications. She then was prescribed treatment with hydroxyChloroquin and prednisolone by another physician assuming she had sjogren's syndrome. When we saw the patient she was extremely distressed and depressed, had bilateral diffused parotid swellings, along with submandibular swelling, no mass could be felt during the exam, her mandibles and neck appeared large, she had normal tear film production and negative eye test, with no articular or muscular abnormalities.

Results: Her Labs were negative, and ultrasound for the parotids revealed enlarged glands with normal texture, MRI showed enlarged both parotids and submandibular glands with no other abnormality, minor salivary gland biopsy showed normal tissue with no inflammatory cell infiltrates. she had normal thyroid, parathyroid and growth hormone levels, normal metabolic panel and denied history of Alcohol consumption of Bulimia, but rarely consumed meat. a trial of Vitamin A, Thiamin and pilocarpine was started, the patient reported regression in the size of the swellings after 2 weeks of therapy but then developed mucosal dryness, afterwards, Vitamin A was stopped, she developed bone pain with normal bone markers and for that reason, pilocarpine was stopped. despite stopping these medicines, the size continued to regress on thiamin supplement alone, and she was prescribed anxiolytics and antidepressants by a Neurologist.

Figure 1. Showing the appearance A, before and B after one month of treatment.

Conclusion: Sialosis can be a manifestation of variable metabolic and endocrine conditions and it should be kept in mind when facing a patient with parotid swelling being a potentially treatable cause.

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POS1466 A CASE REPORT OF IRAQI CHILD WITH MONA SYNDROME AND GALACTOSEMIA

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Background: MONA) Multicentric Osteolysis, subcutaneous Nodulosis and Athropathy(is a rare autosomal recessive disorder caused by inactivating mutations in the matrix metallopeptidase 2 (MMP2) gene.It is manifested by osteolysis of the carpal and tarsal bones, progressive joint contractures, and fibrocollagenous nodules (1,2). In addition, there are reports of gingival hypertrophy, pigmented skin lesions, coarse face, corneal opacities, and cardiac defects (1,3). Because of joint contractures and dysmorphic features and radiological findings, it can be misdiagnosed as juvenile idiopathic arthritis and mucopolysaccharidoses respectively(4). Most affected children are apparently normal at birth with symptoms' onset usually between six months and six years of age (5); the range is from birth to 11 years (2).To date, 51 individuals have been identified with biallelic pathogenic variants in MMP2 (3,6).Here we report a case of child MONA and galactosemia which is not known before.
Objectives: To share this interesting extremely rare presentation and new association
Methods: An eight year old Iraqi boy with Galactosemia at the 4th month of life presented with 4 years history of fractures of his long and short bones after trivial traumas with progressive painful deformities in hands and feet with limitation motion He has seizures, and Atrial septal defects. Intellect is normal, He had coarse facial features, hypertelorism, gum hypertrophy with high arched palate and hirsutism. Painful subcutaneous nodules involving both palms and soles (Figure 1).

Figure 1.

Results: The immunological, hematological and ultrasound were normal. The X-rays showed osteopenia, decrease in joint space and resorption of phalanges with cortical thinning and expansion of the phalangeal and metacarpal bones was a distinct finding (Figure 1). Genetic study revealed Homozygous *MMP2* mutation.
Conclusion: Diagnosis of MONA Combined with galactosemia was made.
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POS1467 SEPTAL PANNICULITIS AS A MANIFESTATION OF COVID-19 INFECTION

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Objectives: to study the clinical and laboratory features of septal panniculitis in the form of erythema nodosum (EN) in a cohort of patients with COVID-19 referred to a rheumatological center.

Methods: In 2020–2021 we examined 21 patients (18 women and 3 men, average age 43.2±11.4 years) with EN and polyarthralgia/arthritis. Depending on the time of EN and articular syndrome associated with COVID-19 development, patients were divided into three groups: 1) up to 4 weeks – acute COVID (symptoms potentially associated with infection); 2) from 4 to 12 weeks – ongoing symptomatic COVID and 3) more than 12 weeks – post-COVID syndrome (persistent symptoms not associated with an alternative diagnosis). All patients underwent a comprehensive clinical, laboratory and instrumental examination, including ultrasound of the joints and chest computed tomography (CT), as well as pathomorphological examination of skin and subcutaneous adipose tissue from the node area (in 9 cases).

Results: Based on the history data, COVID-19 in the study cohort had mild (in 3 patients), moderate (12) and severe (6) severity. Two patients (21 and 23 years old) with a mild severity of the disease on the 2nd-3rd day of the development of the respiratory symptom for the first time noted red painful (45 mm on a visual analogue scale) nodes on the legs and polyarthralgia. In 9 patients (52.3%), similar skin changes were detected 24.5 ± 7.6 days after stopping active COVID-19, i.e. during the period of ongoing symptomatic COVID. In 8 patients (38%), including 6 with moderate severity of the disease, nodules appeared after 85.6 ± 12.3 days, which corresponded to post-COVID syndrome. At the time of examination, 100 and 71.4% of patients complained of skin rashes and joint pain, respectively. Shortness of breath, weakness, cough, sweating and myalgia disturbed 67% of patients. An increase in body temperature to subfebrile was observed in 43% of cases, mainly with ongoing symptomatic COVID. In the overwhelming majority of cases (86%), UE was located on the anterior and lateral surfaces of the legs, less often on the posterior and medial surfaces. It is noteworthy that the lesion of more than 50% of the surface of the lower and upper extremities was associated with the number of nodes ($p < 0.02$), CRP level ($p < 0.03$) and post-COVID syndrome ($p < 0.2$). Sixteen patients (76.1%) had signs of arthralgia, mainly ankle (81%) and knee (56%) joints. In a laboratory study, the median ESR was 39 [14; 62] mm/h, the level of CRP was 17 [2; 79] mg/l. The results of the polymerase chain reaction for SARS-CoV-2 were negative in 90.4 % of patients. In 90.4 % of cases, IgG antibodies were detected and in 52.3% - IgM to the SARS-CoV-2 virus. At CT of the chest, ≤25% of lung lesions were detected in 51% of patients, from 25 to 50% - in 33% and from 50% to 75% - in 9.5 % of cases. Pathomorphological examination of the nodes showed signs of septal panniculitis.

Conclusion: When EN associated with SARS-CoV-2 appears it is important to timely suspect a post-infectious manifestation, based on the clinical picture of the disease and to determine the scope of further examination and adequate treatment
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POS1468

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN A PATIENT WITH A BACKGROUND OF LUPUS NEPHRITIS AND CEREBRAL LUPUS

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Background: Progressive multifocal leukocencephalopathy (PML) is a potentially fatal degenerative condition caused by reactivation of the human polyomavirus 2 (JC virus) in immunodeficient individuals. It is well recognised in individuals who have received Rituximab, but patients treated with other immunosuppressants are at risk also (1). Moreover, patients with SLE may be at increased risk, even when they are not taking immunosuppressants (1, 2).
Objectives: Describe the case of a patient with a history of lupus nephritis and cerebral lupus, on long-term Mycophenolate mofetil (MMF) and Prednisolone, diagnosed with PML complicated by immune reconstitution inflammatory syndrome (IRIS).
Methods: Case report.
Results: This patient first presented in 2010 at the age of 18 with ankle swelling and proteinuria. She had high ANA and anti-dsDNA titres, and renal biopsy showed class IV lupus nephritis. She went into remission on high dose Prednisolone and MMF and elected to stop her MMF. Four months later, she developed behaviour changes and worsening proteinuria. MRI showed a mild high signal lesion in the right cerebral hemisphere, and she was diagnosed with cerebral lupus. She recovered after treatment with IV methylprednisolone and MMF. Over the subsequent eight years, she had three flares of her lupus nephritis, with repeat biopsies in 2013 and 2018 showing active proliferative (class IVA) glomerulonephritis. Consequently she was treated with varying doses of oral Prednisolone and MMF for most of this period. She never received any B-cell depleting therapies. In October 2020, she presented to A&E with numbness in her left face and down her left arm and leg. MRI demonstrated signal abnormalities in her right hemisphere, involving the cortex, white matter and leptomeninges. She was lymphopenic (0.58x10^9/L) with a low CD4 count of 136 cells/uL (normal range 620-1990 cells/uL). A recent dsDNA had risen to 70 IU/ml. Her cerebrospinal fluid revealed mildly raised white cells and a weakly positive JC virus PCR. The differential diagnoses included cerebral lupus, opportunistic infection and malignancy. During this period of diagnostic uncertainty, she was treated with an increased dose of oral Prednisolone and plasma exchange. She went on to have a brain biopsy that showed peri-vascular lymphocytic infiltration and JC virus was present in high copy numbers in the brain tissue (49221.8 IU/mL), confirming a diagnosis of PML. Her MMF was stopped but she continued a low dose Prednisolone with the addition of Hydroxychloroquine. She was re-admitted two weeks after discharge in December 2020 with a right-sided headache, left facial weakness and loss of dexterity in her left hand. MRI showed evidence of IRIS in the right hemisphere with cerebral oedema causing midline shift. She was treated with IV Dexamethasone then Prednisolone 30 mg daily, with a gradual taper over a year.She has made a good recovery with minimal neurological deficit; she had recurrent seizures which responded well to anticonvulsant therapy. Her SLE has not flared.
Conclusion: This describes a case of PML in the context of longstanding lupus nephritis, treated with prednisolone and MMF. Her longstanding lymphopenia with low CD4 counts were attributed to the combined consequences of active lupus and her cumulative immunosuppressive burden. CD4 lymphopenia is associated with PML in the HIV population, and may provide information about which patients on immunosuppressive treatments are at risk of developing PML (3). However, not enough is known to routinely screen patients and the counts of other lymphocyte subsets are likely to be important too. The case highlights that PML can be associated with different immunosuppressants, other than B-cell depletion. The prompt diagnosis, facilitated by brain biopsy, and appropriate management led to a good medium-term outcome for this patient, showing that PML is eminently survivable.
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POS1469

POLYAUTOIMMUNITY AS THE PRESENTING FEATURE OF LIPOPOLYSACCHARIDE RESPONSIVE BEIGE-LIKE ANCHOR PROTEIN DEFICIENCY IN A YOUNG INDIAN BOY

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Background: LPS-responsive beige-like anchor protein(LRBA) deficiency is an autosomal recessive disorder caused by biallelic mutations in the LRBA gene leading to a syndrome of autoimmunity, lymphoproliferation and humoral immune deficiency.LRBA protein plays a major immuno-regulatory role in the expression, function and trafficking of cytotoxic T lymphocyte-associated protein 4 (CTLA4) in Tregs which is an immune effector molecule that acts as an inhibitory checkpoint for the immune response.[1,2,3]
Objectives: We report a 7 years old boy with LRBA deficiency who was presented with polyautoimmuity primarily affecting gut, pancreas & joints with recurrent infections.
Methods: He was born to a non-consanguineous Indian parents with uneventful birth, development and vaccination history.He had been unwell from the age of one with multiple episodes of lower respiratory tract infections warranting usage of prolonged antibiotics. 2.5 years of age, he had been diagnosed as Type 1 Diabetes Mellitus and he was commenced on insulin therapy. 3.5 years, he developed chronic diarrhoea.Evaluation revealed sterile blood, urine and stool cultures with normal abdominal imaging(USG & CT scan), elevated TTg-IgA & HTTP/DGP screen and negative HLADQ2-DQ8. He failed gluten-free diet. Gastrointestinal endoscopy showed duodenum and terminal ileum nodularity & biopsy was suggestive of non-celiac autoimmune enteropathy. 4 years, he developed two episodes of stridor, tetany and breathing difficulty which were promptly reversed by IV calcium infusion. He had low serum calcium, low parathyroid hormone with normal vitamin D level, serum phosphorous, magnesium, thyroid profile, anti-thyroid antibodies, renal and liver functions. 5.5 years, he first presented to us with chronic unexplained polyarthritis involving small and large joints in an additive pattern. Family history was significant for a death of the previous male sibling at 7 months of age due to chronic unexplained diarrhoea. Examination revealed facial dysmorphism and failure to thrive with no systmic findings.
Results: Investigations showed HB 8.1gm%,TLC6700/cumm with normal differential counts and platelet counts 233000/ul. ESR was 39mm/hr and CRP was negative. Direct coomb's test, RF, ANA were negative. He had a mild elevation in IgG levels with normal B-T cells populations. Genetic evaluation revelaed pathogenic homozygous splice site mutation in intron 11 of *LRBA* gene. Both the parents are heterozygous carriers. A largest systematic review[3] of 212 cases of LRBA deficiency showed autoimmunity(70%), non malignanat lymphoproliferation(54%), enteropathy(41%), endocrinopathy(41%) and lower respiratory tract infections(41%) as the most common clinical manifestations with normal or abnormal immunoglobulin level and B-T cells populations. Arthritis(8%) was amongst the rare manifestations. Hypoparathyroidism was the rarest endocrine manifestations. No data available regarding prevalence of positive celiac disease antibodies. There was no haematological manifestations in our case.
Conclusion: LRBA deficiency should be strongly considered in a child recurrent infection and polyautoimmunity including arthritis. Abatacept could be used as a steroid sparing agent and as a bridging agent awaiting transplant.
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HPR Measuring health (development and measurement properties of PROs, tests, devices)

POS1470-HPR KNOWING WHAT TO DO WITH THE DATA - A QUALITATIVE STUDY ON CHALLENGES OF USING SMARTPHONE-BASED EPROS IN RHEUMATOID ARTHRITIS

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Background: Using patient-reported outcomes (PROs) has a long tradition in rheumatology, and PRO measurement is included in many composite indices evaluating disease progression and treatment response [1]. However, little is known about patients´ and health professionals´ (HPs) perceptions of using digitally collected PROs, the so-called ePROs, with a personal smartphone app.

Objectives: To identify main challenges in utilising ePROs for management and treatment of rheumatoid arthritis from patients' and HPs' perspectives.

Methods: We interviewed 25 people with rheumatoid arthritis (RA) and 17 HPs (nurses, rheumatologists, and physiotherapists) from Austria and Denmark. We used the RheumaBuddy app as a practical example to illustrate the digital data collection and the feedback that patients would get from entering their self-reported outcomes. Interviews were recorded and transcribed. We applied a qualitative thematic analysis to identify major themes using a procedure of rigorous coding. Analysis was done by two researchers, and conflicts were solved by consensus. Ethical approval was obtained in both countries.

Results: Three main themes emerged: 1) Being simple yet comprehensive; 2) Resources to interpret, use and act upon the collected data; and 3) Being reminded of the disease. Within the first theme, many valued the intuitiveness and simplicity of ePROs, especially when used as a monitoring tool in between clinical visits. HPs were concerned about not to overwhelm the patients with too many questions. On the other hand, the short ePROs asked in the app were not comprehensive enough to capture psychosocial and lifestyle aspects of the disease which were considered important both by patients and HPs. Within the second theme, patients and HPs expressed that ePROs could be the basis for shared decision making. Nevertheless, some patients had clearer ideas on making use of the feedback they could get from their self-reported data than the others. Participants from Denmark, who experienced a higher level of digital health maturity in official institutions, expressed more proactive use of the data than participants from Austria who were on average younger than their Danish counterparts. One patient in Austria even asserted having no idea what to do with the collected data but believed that the "doctor will make good use of it". HPs in both countries, however, indicated that they needed more resources, skills, and time to make sense of the ePRO data and act accordingly. Under the third theme, patients considered the collection of ePROs to be very important when pain and disease activity were high. HPs, on the other hand, were more concerned that the regular collection of ePROs might constantly remind patients that they are living with the disease.

Conclusion: The potential adoption of ePROs in practice depends on both patients and HPs' motivations and ideas to use the feedback they would get from the collected data. This might be influenced by the level of digital health maturity of a country, as well as available resources. In addition, ePROs need to be intuitive and simple, but at the same time comprehensive and reliable enough so that they can be used for shared decision making. Challenges remain for the ePROs to be used as supporting and empowering tools, and not as reminders of the disease and pain.

Table 1. Demographic data of the participants (N=42)

Demographic	Austria				Denmark				Total			
Data	Patient		HP		Patient		HP		Patient		HP	
N	14		10		11		7		25		17	
Women (%)	10	(71)	6	(60)	7	(64)	5	(71)	17	(68)	11	(65)
Men (%)	4	(29)	4	(40)	4	(36)	2	(29)	8	(32)	6	(35)
Age												
Mean (Range)	54	(30-76)	41	(29-63)	65	(37-77)	47	(31-59)	60	(30-77)	44	(29-63)

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POS1471-HPR PAIN CATASTROPHIZING AND ITS ASSOCIATION WITH PAIN OF PATIENTS WITH RHEUMATOID ARTHRITIS IN A NON-INFLAMMATORY CONDITION.

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Background: Pain in rheumatoid arthritis (RA) is considered to be linked with non-inflammatory factors, including physical disabilities, psychiatric disorders, and pain catastrophizing (PC) [1].

Objectives: We investigated the role of PC in the possible link between physical disabilities and psychiatric disorders in RA patients in a non-inflammatory condition.

Methods: In this cross-sectional study, a total of 81 RA patients in a non-inflammatory condition were included; all patients had serum C-reactive protein levels <0.5 mg/dL, without any inflammatory joints. We examined the demographic and clinical data and administered the pain visual analog scale (VAS), the pain catastrophizing scale (PCS), the Health Assessment Questionnaire Disability Index (HAQ-DI), and the patient version of the Brief Scale for Psychiatric Problems in Orthopedic Patients (pBS-POP). A series of multivariate-adjusted multiple regression analyses were performed to examine the associations between PC and pain intensity, physical disabilities, and psychiatric disorders.

Results: We found associations between all the above-mentioned variables in separate models associated with HAQ-DI, pBS-POP, and PCS scores. However, in the model associated with pain VAS, the PCS score (β=0.34, p=0.0073) emerged as the only variable showing statistically significant association.

Conclusion: PC is associated with pain in RA patients in a non-inflammatory condition, and this association may be mediated through pathways involving physical disabilities and psychiatric disorders.

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Table 1. Multiple linear regression analysis of factors associated with each outcome

Outcome	Variables	ß	95% CI	P value
Pain VAS	Age	0.044	-0.32 to 0.51	0.66
	Sex (female)	0.0089	-4.65 to 5.09	0.93
	Stage	0.0092	-4.34 to 4.70	0.94
	Disease duration	0.19	-0.13 to 0.88	0.14
	HAQ-DI	0.23	-0.23 to 1.76	0.13
	pBS-POP	0.038	-1.06 to 1.45	0.76
	PCS	0.34	0.13 to 0.81	0.0073
pBS-POP	Age	-0.18	-0.15 to 0.00	0.046
	Sex (female)	-0.0081	-0.95 to 0.86	0.93
	Stage	-0.033	-0.97 to 0.71	0.77
	Disease duration	0.10	-0.053 to 0.14	0.40
	Pain VAS	0.033	-0.037 to 0.050	0.76
	HAQ-DI	0.41	0.10 to 0.45	0.0026
	PCS	0.31	0.02 to 0.16	0.0088
HAQ-DI	Age	0.16	0.01 to 0.20	0.029
	Sex (female)	0.14	-0.10 to 2.10	0.93
	Stage	0.17	-0.06 to 2.00	0.77
	Disease duration	0.22	0.017 to 0.25	0.025
	Pain VAS	0.14	-0.01 to 0.09	0.76
	pBS-POP	0.29	0.15 to 0.70	0.0026
	PCS	0.26	0.03 to 0.19	0.0088
PCS	Age	-0.10	-0.42 to 0.12	0.27
	Sex (female)	-0.21	-6.77 to -0.60	0.02
	Stage	-0.082	-4.10 to 1.83	0.45
	Disease duration	-0.13	-0.53 to 0.14	0.25
	Pain VAS	0.28	0.06 to 0.35	0.0073
	pBS-POP	0.30	0.28 to 1.85	0.0087
	HAQ-DI	0.36	0.23 to 1.50	0.0080

ß: standardized regression coefficient; CI: confidence interval; HAQ-DI: Health Assessment Questionnaire Disability Index; pBS-POP: the patient version of the Brief Scale for Psychiatric Problems in Orthopedic Patients; PCS: Pain Catastrophizing Scale; VAS: visual analog scale

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POS1472-HPR

CONSTRUCT VALIDITY OF THE PROMIS PHYSICAL FUNCTION 10-ITEM SHORT FORM IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES AND SEVERE LIMITATIONS IN PHYSICAL FUNCTIONING

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Background: Physical functioning in patients with inflammatory arthritis (IA) can be severely affected and is often measured using the disease-specific questionnaires Health Assessment Questionnaire-Disability Index (HAQ-DI) or Bath Ankylosing Spondylitis Functional Index (BASFI). Also, the Patient Reported Outcome Measurement Information System (PROMIS) Physical Function Item Bank[1] has been increasingly used. This is a generic instrument to assess physical functioning and compare health status across conditions. Several short forms can be derived, including the PROMIS PF 10-Item Short Form (PROMIS PF-10). To date, experience with this PROMIS PF-10 in research with IA is limited and more insight is needed in its construct validity in specific IA populations.
Objectives: To assess the construct validity of the PROMIS PF-10 in patients with rheumatoid arthritis (RA) or axial spondyloarthritis (axSpA) and severe limitations in physical functioning.
Methods: Baseline data from patients with RA or axSpA and severe limitations in physical functioning participating in two randomized controlled trials on the effectiveness of longstanding physical therapy[2] were used. Patients completed the PROMIS PF-10 (score range 13.5-61.9 worst-best, standardized to the Dutch population) and several measures of physical functioning and quality of life: i.e. the 36-item Short Form Health Survey (SF-36) (Physical and Mental Component summary Scores (PCS and MCS) were calculated), the EuroQol 5-dimensions 5-levels (EQ5D5L; index and VAS) and the 6 Minute Walk Test (6MWT). In addition, RA patients completed the HAQ-DI and axSpA patients the BASFI. Spearman rho correlation coefficients were computed between the PROMIS PF-10 and the other measures. Correlations were considered 0.3<r<0.5 weak, 0.5 <r<0.75 moderate to good, r >0.75 good to excellent. The PROMIS PF-10 was expected to correlate moderately to good with instruments measuring physical functioning and weak with other instruments (e.g. SF-36 MCS). All analyses were stratified for RA and axSpA.
Results: Data from 181 patients with RA and 139 with axSpA (92% and 48% female, mean (SD) age 59 (13.1) and 54 (11.4) years, respectively) were analyzed. The mean score of the measures of physical functioning and quality of life are summarized in the Table 1. The PROMIS PF-10 correlated moderately to good with HAQ-DI, BASFI, SF-36 PCS and EQ5D5L-index (Spearman r >0.5, all p-values <0.001). The PROMIS PF-10 correlated weak with the 6MWT, EQ-VAS and the SF-36 MCS (Spearman r <0.5).

Table 1. Mean score and Spearman r correlation coefficients of PROMIS PF-10 with measures of physical functioning and quality of life

	PROMIS PF-10	HAQ-DI (RA) BASFI (axSpA)	SF-36 PCS	SF-36 MCS	EQ5D5L index	EQ-VAS	6MWT
RA Mean(SD)	34.1 (5.0)	1.6 (0.5)	39.4 (19.7)	46.8 (12.0)	0.5 (0.3)	56.4 (18.7)	300 (100)
Spearman r	-	-0.724*	0.611*	0.101	0.617*	0.450*	0.469*
AxSpA Mean(SD)	35.4 (4.2)	6.2 (1.8)	44.4 (17.6)	45.5 (11.6)	0.5 (0.3)	54.5 (19.0)	390 (108)
Spearman r	-	-0.686*	0.539*	-0.014	0.598*	0.438*	0.434*

*Correlation is significant at <0.001 level

Conclusion: The moderately to good correlations of the PROMIS PF-10 with measures of physical functioning support the construct validity in RA and axSpA patients with severe limitations in physical functioning. However, the correlation of the quality of life questionnaire EQ5D5L was also moderately to good. Future research is needed to better understand this relatively high correlation. Also clinimetric properties (responsiveness to change and ability to discriminate between intervention and control conditions) in this population should be determined in future.
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POS1473-HPR

THE RELATIONSHIP BETWEEN PHYSICAL ACTIVITY LEVEL AND EXERCISE SELF-EFFICACY, BODY AWARENESS, AND FATIGUE SEVERITY IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL AND PILOT STUDY

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease in which, for many reasons of the nature of the disease, patients tend to perform less physical activity (PA) than recommended in the guidelines (1). Many variables associated with a level of PA in patients have been described (2). However, there are limited studies about related factors with PA in RA patients.
Objectives: To investigate the relationship between PA level and exercise self-efficacy, body awareness, and fatigue severity in RA patients.
Methods: A total of 80 RA patients (women/men=61/19, age=56.83±11.56 years) who were diagnosed according to the ACR 2010 criteria and followed in university outpatient clinic were included in our study. All patients were assessed regarding physical characteristics (age, body-mass index), exercise status (yes/no), and occupational status (working/not working/retired). Physical activity level by International Physical Activity Questionnaire, exercise self-efficacy by Exercise Self-Efficacy Scale, body awareness by Body Awareness Questionnaire, and fatigue by Bristol Rheumatoid Arthritis Multidimensional Scale was assessed.
Results: Patients' characteristics are presented in Table 1. It was observed that patients have low PA levels. Significant correlation was found between PA and exercise self-efficacy (r=0.410, p<0.001), body awareness (r=0.374, p=0.001), and fatigue (r=-0.482, p<0.001).

Table 1. The characteristics of patients

	Mean ± SD, median (25/75 quartiles) or n (%)
Age, years	56.83 ±11.56
Body mass index, kg/m^2	27.84 ±5.57
Time of diagnosis, years	11.49 ±10.92
Exercise status	
Yes	53 (66.3)
No	27 (33.8)
Occupational status	
Working	16 (20.0)
Not working	30 (37.5)
Retired	34 (,42.5)
IPAQ	
Walking, MET-min/week	371 (198/693)
Moderate, MET-min/week	270 (0/840)
Vigorous, MET-min/week	0 (0/0)
Total, MET-min/week	693 (268/ 1533)
IPAQ sub-group	
Inactive	55 (68.8)
Minimal Active	19 (23.8)
Very Active	6 (7.4)
Exercise self-efficacy score, 0-1800	646.62 ±339.40
Body awareness score, 18-126	84.77 ±16.41
Bristol rheumatoid arthritis multidimentional fatigue score, 0-70	19.06 ±12.83

IPAQ: International Physical Activity Questionnaire.

Conclusion: Our study showed that RA patients had low PA and PA was related to exercise self-efficacy and fatigue moderately and body awareness weakly. We think that it may be important to assess these variables and to plan interventions to improve these variables while planning PA programs of the patients.

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POS1474-HPR FATIGUE IS AN IMPORTANT COMORBIDITY FOR RA PATIENTS. HOW CAN WE MEASURE IT EASILY IN CLINICAL PRACTICE?

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Background: Fatigue is highly prevalent (40-70%) in Rheumatoid Arthritis (RA)[1]. Patients describe fatigue as an important symptom, in discrepancy with rheumatologist´s perception. Different validated questionnaires are available to measure fatigue, without any standarised preference in their use. In randomized controlled trials, FACIT-F is a unidimensional tool for fatigue widely used. MDHAQ is a multidimensional tool exploring different dimensions of RA, providing a VAS 0-10 for fatigue as a simple scale to measure it[2].

Objectives: We studied fatigue in RA patients with two different questionnaires, FACIT-F and VAS 0-10 included in MDHAQ, and evaluated their utility in clinical practice.

Methods: Patients with RA (ACR/EULAR criteria, 2010) who agreed to participate in this study were included consecutively in the Arthritis Unit for 3 months. They fulfilled 2 questionnaires to evaluate fatigue: 1. FACIT-F(FS)=FACIT-Fatigue, 13 questions (0-4 score) with a global score of 0-52 (lower scores indicate worse fatigue). 2. VAS 0-10 of fatigue (=VAS-Fatigue) included in the question 9 in MDHAQ. Other self-reported queries of the MDHAQ were collected: 1-10 physical function (FN) according to modified HAQ (0-10), VAS 1-10 for pain (PN) and patient global assessment (PATGL) to calculate RAPID3, a review of 60 symptoms (ROS60) and self-assessment 48 joint count (RADAI48). Physical articular examination (TJC 0-28, SJC 0-28), laboratory test (CRP, ESR), composite EULAR disease activity indices (DAS28-ESR, SDAI), demographic (sex, age, BMI) and patient´s disease characteristics, also screened for depression with Patient Health Questionnaire 9= PHQ9≥10) were collected. A descriptive analysis of the variables was done, and Pearson´s correlation between FACIT-Fatigue and VAS-Fatigue scores, and between each questionnaire (FACIT-Fatigue and VAS-Fatigue) and the rest of variables was performed.

Results: A total of 75 patients (84% females) with RA were recruited, with a mean age of 62 (±11.6) years, a mean disease duration of 14.6 (± 5) years, a mean BMI of 22.8 (± 8.0), 64% with bDMARD and 45.3% with glucocorticoids treatment. Depression (PHQ9≥10) was observed in 16%. Correlation between the two studied questionnaires (FACIT-Fatigue and VAS-Fatigue) was almost very good (-0.79, p<0.001). Statistically significant (p<0.05) similar correlation ~0.70 were obtained between VAS-Fatigue (range: 0.60, 0.76) and ~0.80 between FACIT-Fatigue (range:-0.70,-0.87) and self-reported MDHAQ queries (FN, PN, PATGL, RAPID3, ROS60, and RADAI48). Similar but moderate correlation~0.50 (range:0.42,-0.61) was obtained in both questionnaires with TJC and EULAR indices of disease activity (DAS28-ESR, SDAI), and similar but lower ~0.20 (range:0.24, -0.29) with inflammatory variables (CRP, ESR, SJC) except for ESR and FACIT-Fatigue, no correlation was observed. Depression (PHQ9≥10) obtained the highest correlation with -0.92, p<0.001 in FACIT-Fatigue, and less for VAS-Fatigue 0.66, p<0.001 (Table 1).

Table 1. Correlation between VAS-Fatigue and FACIT-Fatigue and the different disease activity variables.

	VAS-Fatigue (0-10)	p-value	FACIT- Fatigue (0-52)	p-value
FACIT-Fatigue (0-52)	-0.79	<0.001	1	
VAS-Fatigue (0-10)	1		-0.79	
TJC (0-28)	0.42	<0.001	-0.58	<0.001
SJC (0-28)	0.24	0.040	-0.29	0.014
CRP	0.27	0.021	-0.28	0.017
ESR	0.25	0.032	-0.20	0.096
DAS28-ESR	0.52	<0.001	-0.61	<0.001
SDAI (0-86)	0.49	<0.001	-0.58	<0.001
FN (0-10)	0.76	<0.001	-0.87	<0.001
PN (0-10)	0.70	<0.001	-0.62	<0.001
PATGL (0-10)	0.75	<0.001	-0.73	<0.001
RAPID3 (0-30)	0.77	<0.001	-0.75	<0.001
ROS60 (0-60)	0.66	<0.001	-0.77	<0.001
RADAI48 (0-48)	0.60	<0.001	-0.70	<0.001
PHQ9 (0-27)	0.66	<0.001	-0.92	<0.001

Conclusion: VAS (1-10) is a good tool compared to FACIT to easily measure of fatigue in daily routine for RA patients. The use of this simple scale integrated in the MDHAQ allows capturing important clinical information for the disease.

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POS1475-HPR THE MINIMALLY IMPORTANT DIFFERENCE AS THE INTERPRETABILITY OF EMOTIONAL HEALTH DOMAIN IN JAPANESE VERSION OF LUPUSPRO FOR SLE PATIENTS; PRELIMINARY RESULTS OF A PROSPECTIVE COHORT STUDY

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Background: The minimally important difference (MID) required to interpret the magnitude of changes in lupus patient-reported outcome (LupusPRO), which is a widely used outcome measure of quality of life in SLE patients, remains unclear.

Objectives: We report preliminary results of an ongoing prospective observational study that assesses the MID as the interpretability of emotional health (EH) domain in Japanese version of LupusPRO.

Methods: We recruited subjects at three university hospitals in Japan participating in an ongoing multidisciplinary cohort study (the Lupus registry of Nationwide institutions (LUNA). Of a total of 210 SLE patients enrolled during the 17-month recruitment period, patients with low disease activity, defined as SLE Disease Activity Index 2000 (SLEDAI-2K) ≤ 4, and who were seen at least twice of three months'

duration and responded to both the LupusPRO and health status change questions were included in this subcohort. The second questionnaire was given an allowance period of 30 days before or after the three months from starting date. Descriptive statistics were presented as means and standard deviations (SD) or counts and percentages (%). The emotional health score ranges from 0 to 100; a higher score indicates less frequent presence of symptoms. The change in health status was assessed using the 7-point Global Rating of Change [1], and the score = 0 and the score ≥ +1 were considered in the 'unchanged' and the minimal 'improved' category, respectively. MID was mainly estimated using the mean change of the groups with the score ≥ +1 as the anchor-based method, and the area under the curve (AUC) was also calculated as a sensitivity analysis to estimate MID thresholds [2] and 95% confidence intervals (CI) were constructed using 1000 bootstrapping.

Results: The mean age of the 24 eligible patients was 48 (SD 14), and 88% were female. The glucocorticoid dose, SLEDAI-2K, and Systemic Lupus International Collaborating Clinics /American College of Rheumatology Damage Index were 3.4 (2.1) mg, 1.0 (1.1) and 1.1 (1.9), respectively. The mean EH score was 67.5 (30.3), five patients (21%) had the maximum EH score at baseline, 73.4 (25.0) after three months, 7.2 (18.0) for the change in EH. The correlation coefficient and the AUC for the change in health status and the EH were 0.23 and 0.60. The mean changes were 4.1 (18.4) of the groups with 'unchanged' health status and 12.3 (17.1) of the groups with 'improved' health status. The MID for improvement was estimated at 12.3 using the anchor-based method, and the cutoff point corresponded to 9.3 [95%CI -6.7 to 25.3]) of the EH change score by the receiver operating curve method.

Conclusion: In this study, the MID (3 months) for the EH domain in the Japanese version of LupusPRO was estimated to be between 9 and 12, which was similar to the results of the previous cross-sectional study [3]. The challenge in estimating the MID in our setting was the low correlation with external anchors, even though the study population was limited to patients with low disease activity, because disease activity at baseline can generally influence 'improved' health status.

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POS1476-HPR FEASIBILITY OF USING OPTOELECTRONIC MEASUREMENT OF HAND MOVEMENT FOR CHARACTERIZING HAND FUNCTION IN RHEUMATOID ARTHRITIS

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Background: Physical function is an important factor determining disease burden in arthritis. Monitoring function in rheumatoid arthritis (RA) patients is essential for effective treatment [1]. The currently used tools to assess physical function (e.g. patient reported outcomes) have limitations with respect to sensitivity and specificity to measure functional impairment in RA [2,3]. A marker-based optoelectronic measurement of hand function enables detailed analysis of hand movements such as spatial-temporal parameters and joint angles [4]. This may provide new possibilities to quantitatively and qualitatively analyze the changes of hand function in patients with RA in so far unprecedented way.

Objectives: To test the feasibility of optoelectronic measurement of hand function in RA patients and healthy controls (HC) when performing standard functional tests such as the Moberg Pick-Up-Test (MPUT) as well as standard movements such as finger flexing and to detect disease specific patterns.

Methods: RA patients (ACR/EULAR 2010 criteria [1]) recruited from the Internal Medicine 3 outpatient clinic, Erlangen, Germany and HC were included (Ethics #125_16B). Participants were asked to perform the MPUT and a simple movement of flexing the interphalangeal (DIP) and proximal interphalangeal joint (PIP). Spatial-temporal data of hand movements and hand segment kinematics were captured using an optoelectronic measurement system (Qualisys AB, Sweden) with 29 retroreflective markers (Figure 1). Transport time for each of the 12 MPUT objects was divided into a grasping phase (GP) (first touch to safe grip) and a manipulation phase (MP) (safe grip to drop) using the video recording or marker trajectories. For the flexing movement, the ratios between the flexion angle of the DIP and PIP joint (DIPPIP) were calculated. We used linear mixed-effects models accounting for within-participant clustering of hands and adjusting for age and sex differences to compare RA with controls.

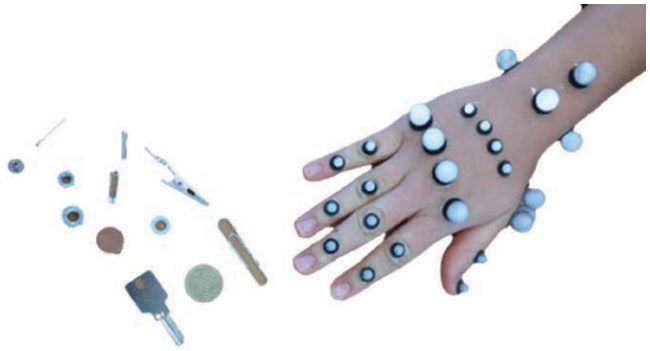

Figure 1. Marker setup and the 12 objects transported during the MPUT.

Results: Twenty-four RA patients and 23 healthy controls were evaluated (Table 1). Mean GP times across all objects showed higher absolute differences between the groups (RA 0.43 [0.35-0.52]; HC 0.33 [0.27-0.40] sec) while MP times were identical (RA 0.36 [0.30-0.44]; HC 0.36 [0.30-0.44] sec) showing a significant group-phase interaction ($p<0.001$). Objects safety pin, key, and paper clip showed the highest absolute between-group mean differences for unadjusted time data (0.41, 0.36, 0.34 sec respectively). Measured angle ratios (RA 0.60±0.15; HC 0.68±0.17 (DIPPIP)) and their linear fit (RA 0.96±0.05; HC 0.97±0.03 R^2) were similar for RA and controls ($p>0.05$).

Table 1. Subject characteristics; mean (SD)

	RA	HC
male: female [N]	7: 17	11: 12
Age [years]	62.3 (9.1)	50.2 (16.1)
Disease duration [years]	11.8 (10.8)	
Disease Activity Score (DAS28)	2.5 (1.3)	

Conclusion: Optoelectronic measurement of hand function is feasible and allows to gain a more detailed picture of impairment in hand function in RA patients. For instance, tasks like reaching for an object are significantly impaired. Further, objects causing the greatest difficulty for RA patients in the GP were identified. The previously described linear relationship of angle ratios for the distal finger joints in healthy individuals [5] seems also valid for RA patients in our cohort and no significant group differences for the ratio could be observed. This may reflect that DIP and PIP joints are less affected in RA compared to e.g. psoriasis arthritis [6]. In conclusion, optoelectronic hand movement analysis allows a more accurate and differentiated analysis of hand function in RA patients.

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POS1477-HPR IS ECO-INTENSITY A PREDICTIVE FACTOR IN DETERMINING THE PHYSICAL PERFORMANCE OF WOMEN WITH KNEE OSTEOARTHRITIS?

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Background: Researchers are increasingly using echo-intensity (EI) as an index of muscle quality or fatty and fibrous tissue infiltration. EI is moderately associated with muscle strength and/or power and a better predictor of muscle performance than measures of muscle mass. In this regard, ultrasound-derived EI may be a promising skeletal muscle assessment tool for monitoring the progression of physical performance. However, there has been no study that investigated the relationship between muscle EI and physical performance in women with knee osteoarthritis (OA).
Objectives: The aim of our study is to investigate the relationship between the physical performance and muscle echo-intensity in women with knee OA.
Methods: Ninety-six women with radiological and clinical knee OA participated in this cross-sectional observational study. Quadriceps femoris (Rectus Femoris-RF, Vastus Intermedius-VIM, Vastus Medialis-VM, Vastus Lateralis-VL) and hamstring (Biceps Femoris-BF, semitendinosus-STT and semimembranosus-SMM) muscles were evaluated using B-Mode ultrasonography. Ultrasound images were analysed offline using an image analysis software (Image J) program and EI of muscles was determined the same researcher. All patients completed Knee Injury and Osteoarthritis Outcome Score (KOOS) that is a knee related disorder-specific questionnaire. Physical performance measures included the Five times Sit to Stand test (FTSS), the Twenty-meter Walk Test (20WT), and the Stair Climbing Test (SCT).
Results: The mean age of patients participating in the study was 58.73±9.42 years. A positive correlation was found between EI of quadriceps femoris and hamstring muscles and the total KOOS scores. EI of RF, VIM, VM, VL and BF presented a significant negative correlation with FTSS, 20WT and SCT (Table 1).

Table 1. Correlation coefficients between Echo-Intensity of Quadriceps Femoris And Hamstring Muscles and KOOS, Physical Performance Parameters (n=96)

Knee Injury and Osteoarthritis Outcome Score Subscales					
EI (au)	Pain	Symptoms	Function in daily living	Function in Sport and Recreation	Quality of Life
RF	0.129	0.237	0.443*	0.365*	0.186
VI	0.220	0.94	0.210	0.162	0.201
VL	0.071	0.116	0.444*	0.482*	0.312
VM	0.105	0,191	0.432*	0,454*	0.112
BF	0.456*	0.227*	0.436*	0.402*	0.502
SMM	0.070	0.239	0.078	0.015	0.357
STT	0.224	0.179	0.456	0.312	0.522

Physical Performance Parameters			
EI (au)	**Five times Sit to Stand test**	**Twenty-meter Walk Test**	**Stair Climbing Test**
RF	0.439*	0.454*	0.643**
VI	0.322*	0.435*	0.432*
VL	0.444*	0.623**	0.556**
VM	0.431*	0.584**	0,571**
BF	0.448*	0.419*	0.433**
SMM	0.126	0.414*	0.125
STT	0.145	0.315*	0.319**

EI, Echo-intensity; au, Arbitrary Unit; RF, Rectus femoris; VIM, Vastus Intermedius; VM, Vastus Medialis; VL, Vastus Lateralis; BF, Biceps Femoris; STT, Semitendinosus; SMM, Semimembranosus; *P < 0.05; **P < 0.001

Conclusion: We concluded that muscle EI may be an important predictor of functional performance in women with knee OA.

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POS1478-HPR INCREMENTAL SHUTTLE WALK TEST IN ANKYLOSING SPONDYLITIS PATIENTS

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Background: Functional exercise capacity might be affected in ankylosing spondylitis (AS) patients due to factors such as pulmonary function impairment, reduced physical activity, peripheral arthritis, fatigue, muscle weakness and systemic inflammation. In addition to laboratory-based exercise tests, field tests are also used to measure functional exercise capacity. The six-minute walk test (6MWT) which is the most frequently used field test, is valid, reliable, and cost-effective. However, the main disadvantage of the 6MWT is that it allows the patient to set the walking speed. The incremental shuttle walk test (ISWT) is a valid field exercise test of functional capacity. The test requires patients to walk at increasing speeds up and down a 10 m course. The walking speed, which increases every minute, is controlled by audio signals. Performance on the test relates strongly to $VO2_{max}$, the traditional indicator of cardiorespiratory capacity [1]. Although there are studies evaluating functional exercise capacity in AS patients, no study using ISWT has been found.
Objectives: The aim of this study was to investigate the ISWT results and factors associated with this test in patients with AS.
Methods: Fifty AS patients aged between 25-58 years (27 males,23 females,) participated in the study. Age, height, weight, body mass index (BMI) were recorded. Disease-specific indices such as Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), Bath AS Metrology Index (BASMI) were used. Sit-up test and push-up test were used to measure muscular endurance. Incremental Shuttle Walk Test (ISWT) was used to assess functional exercise capacity The test was performed in a 10 m course defined by two cones placed 0.5 m from each endpoint. The test was terminated if the patient was unable to maintain the required speed and failed to complete a shuttle in the time allowed for the second time. The total number of shuttles was recorded and distance calculated. Heart rate (HR), blood pressure, perceived dyspnea and leg fatigue (modified Borg Scale) were assessed before and after the test. Age-predicted maximal heart rate (HR_{max}) was calculated as 220 minus age. Spearman's correlation coefficients were used to examine the relationship between the ISWT distance and the variables.
Results: The mean incremental shuttle walk distance (ISWD) of the patients was 458.40± 98.63 m (min 290 m-max 710 m). Subjects reached 50% of the predicted ISWD according to the reference equation for healthy people [2]. The maximal heart rates were lower than predicted values anticipated for the patients' age. At the end of the test, subjects reached 57.97±8.62 % of HR_{max}. ISWD showed significant correlations ($p<0.05$) with gender ($r = 0.488$), height ($r = 0.474$), BASFI ($r = -0.313$), BASMI ($r = -0.397$), sit-up test ($r = 0.620$), push-up test($r = 0.476$). However, no relationship was found between ISWD and age, weight, BMI, BASDAI, dyspnea, fatique. Dyspnea and fatigue were not limiting factors for the test. The most common reason for stopping the test was the inability of the patients to maintain the set pace. ISWD has been reported to be associated with age [2], but in our study, unlike the literature, no relationship was found between ISWD and age in AS patients.
Conclusion: According to the results of our study, we found that the incremetal shuttle walk test distance in AS patients decreased compared to the reference values reported for healthy individuals. ISWT is associated with factors such as gender, height, functionality, spinal mobility and muscular endurance. ISWT may be appropriate for measuring exercise capacity of AS patients, however, more research is needed.

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POS1479-HPR INVESTIGATING THE RELIABILITY OF THE SOLLERMAN HAND FUNCTION TEST AND THE ASSOCIATIONS WITH DISEASE- AND HAND-RELATED PARAMETERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Although the hand involvement is one of the first manifestations in the disease course of Systemic Sclerosis (SSc), hand functions are generally inquired by using patient-reported tools. Sollerman Hand Function Test (SHFT) is developed to evaluate the performance-based hand functions.
Objectives: The aim of this study was to investigate the reliability of the SHFT and the associations with disease- and hand-related parameters in patients with SSc.
Methods: Thirty-six patients (30 females) were included in the study. SHFT includes 20 different hand functions which are scored between 0 (unable to perform) and 4 (performed within 20 seconds with normal quality) (1). In the present study, item 12 'put on Tubigrip stocking on the other hand' was not evaluated, thus, the SHFT was scored over a total score of 76. Inter-rater reliability was investigated by comparing the scores of two different investigators, and test-retest reliability was investigated by assessing the scores obtained at 2-hour intervals. Modified Hand Mobility in Scleroderma Test (mHAMIS), modified Rodnan skin score (mRSS), grip and pinch strengths were measured to evaluate hand-related physical characteristics. Duruoz Hand Index, Disability of Arm, Shoulder and Hand Questionnaire (DASH), Health Assessment Questionnaire (HAQ), and Scleroderma Health Assessment Questionnaire (SHAQ) were used as patient-reported outcomes.

Table 1. Associations between the Sollerman Hand Function Test scores and disease- and hand-related parameters

n= 36	Median (IQR 25/75)	rho	*p*
mHAMIS (score 0-4)	0 (0/0)	-0.366	0.072
mRSS-Fingers (score 0-3)	2.5 (2/3)	-0.070	0.684
mRSS-Hands (score 0-3)	1.5 (1/2)	-0.056	0.747
mRSS-Forearms (score 0-3)	1 (0/2)	-0.032	0.855
mRSS-Upper Arms (score 0-3)	0 (0/1)	0.008	0.962
mRSS-Total (0-51)	10 (6/27.5)	-0.158	0.356
Hand Grip Strength (kg)	19.9 (12.0/24.9)	**0.612**	**<0.001***
Tip to Tip Pinch Strength (kg)	3.1 (2.3/3.9)	**0.517**	**0.001***
Three Jaw Pinch Strength (kg)	2.7 (1.9/3.4)	**0.554**	**<0.001***
Lateral Pinch Strength (kg)	3.9 (3.3/5.3)	**0.461**	**0.005***
Duruoz Hand Index (score 0-90)	5.5 (0/17)	**-0.751**	**<0.001***
DASH (score 30-150)	61.5 (47/84)	**-0.645**	**<0.001***
HAQ (score 0-3)	0.3 (0.1/0.9)	**-0.632**	**<0.001***
SHAQ-Raynaud's Phenomenon (score 0-3)	0.9 (0.1/1.4)	-0.246	0.161
SHAQ-Digital Ulcers (score 0-3)	0.1 (0/1.2)	**-0.372**	**0.030***
SHAQ-Gastrointestinal (score 0-3)	0.2 (0/1.5)	-0.177	0.315
SHAQ-Pulmonary (score 0-3)	0.6 (0.1/1.5)	-0.270	0.123
SHAQ-Patient Global Assessment (score 0-3)	1.4 (0.1/2.1)	**-0.547**	**0.001***

p<0.05, rho: Spearman correlation coefficient, mHAMIS: modified Hand Mobility in Scleroderma Test, mRSS: modified Rodnan skin score, lcSSc: limited cutaneous Systemic Sclerosis, dcSSc: diffuse cutaneous Systemic Sclerosis, DASH: Disability of Arm, Shoulder, and Hand Questionnaire; HAQ: Health Assessment Questionnaire; SHAQ: Scleroderma Health Assessment Questionnaire

Results: SHFT demonstrated excellent inter-rater reliability (75 (72/76) vs. 75 (72/76), ICC: 0.987) and moderate test-retest reliability (75 (72/76) vs. 76 (75/76), ICC: 0.645). SHFT scores correlated significantly with grip and pinch strengths, Duruoz Hand Index scores, HAQ scores, SHAQ-Patient Global Assessment scores, and SHAQ-Digital Ulcer Scores ($p<0.05$). No significant correlations were observed between other parameters and SHFT ($p>0.05$). The hardest task was determined as 'do up buttons' which cannot be completed within 20 seconds by the half of the patients. All the patients completed 'put key into Yale lock, turn 90°', 'lift iron over edge 5 cm in height', and 'lift telephone receiver, put to ear' tasks within 20 seconds with normal quality.
Conclusion: The results of the present study suggest that SHFT is a reliable tool to evaluate hand functions in patients with SSc.
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POS1480-HPR SCREENING WITH THE ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3 QUESTIONNAIRE CAN REDUCE THE NUMBER OF CLINIC VISITS

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Background: The long-term and frequent evaluation of disease activity in patients with rheumatoid arthritis (RA) leads to a large burden of planned consultations at outpatient clinics. It might be possible to reduce that burden by prescreening to identify patients with low disease activity with the electronic Routine Assessment of Patient Index Data 3 (RAPID3), with the aim to let them skip their visits. For this purpose, accurate classification of patients in the low category with the RAPID3 is required.
Objectives: To evaluate the test characteristics and agreement between the Disease Activity Score 28 (DAS28) and the RAPID3 in patients with RA and low disease activity.
Methods: We performed a retrospective database study with clinical data collected as part of usual care from the electronic medical record at Reade Amsterdam, a secondary care center for rheumatology patients. The dataset comprised each completed RAPID3 between June 2014 and March 2021, that was followed by a DAS28 within 2 weeks in patients with RA. We dichotomized the disease activity for both the RAPID3 and DAS28 into 'low' and 'high', with cutoffs at 2.0 for RAPID3 and 3.2 for DAS28. We report test characteristics and agreement (Cohen's kappa).
Results: The dataset comprises 5009 combined RAPID3 and DAS28 measurements recorded in 1681 unique RA patients. Mean age was 60 years, 76% of patients were female with a median disease duration of 4 years. Overall agreement was 0,58, ƙ was fair at 0.26, with 1426 (28%) of the RAPID3 measurements in the 'low' category (Table 1). Sensitivity to detect low disease activity was 0.39, specificity 0.94 and positive predicted value 0.92.

Table 1. Crosstabulation of dichotomised RAPID3 and DAS28* results.

		DAS28		Total
		Low (<3,2)	**High (>3,2)**	
RAPID3	**Low (≤2,0)**	1309 (26%)	117 (2%)	1426 (28%)
	High (>2,1)	2005 (40%)	1578 (32%)	3583 (72%)
Total		3314 (66%)	1695 (34%)	5009 (100%)

*Disease activity score 28 (DAS28), Routine Assessment of Patient Index Data 3 (RAPID3).

Conclusion: With a positive predictive value of 0.92 for low disease activity, a RAPID3 score of 2.0 or lower is a good threshold to propose a postponement of the consultation and substantially reduce the clinic burden. Such a proposal is safe if the patient can overrule it.
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[1] With a positive predictive value of 0.92 for low disease activity, a RAPID3 score of 2.0 or lower is a good threshold to propose a postponement of the consultation and substantially reduce the clinic burden. Such a proposal is safe if the patient can overrule it.
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POS1481-HPR CROSS-CULTURAL ADAPTATION, VALIDITY AND RELIABILITY OF THE QUIPA TOOL: TURKISH VERSION

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Background: The Quality Indicators for Physiotherapy Management of Hip and Knee Osteoarthritis (QUIPA) is the only patient-reported outcome measure assessing the quality indicators of physiotherapy management of hip/knee osteoarthritis (OA). It consists of 3 subscales and a total of 18 questions.
Objectives: The purpose of this research was to translate and cross-culturally adapt the QUIPA into the Turkish language and test its validity and reliability in Turkish-speaking patients with hip/knee OA.
Methods: Ninety-two patients with hip/knee OA were enrolled in the research. The QUIPA was cross-culturally adapted according to guidelines defined by Beaton et al. Participants completed QUIPA tool twice, with an interval of 7 days. Construct validity was tested via Exploratory Factor Analysis. Test-retest reliability and internal consistency were determined interpreting Intraclass Correlation Coefficient (ICC) and Cronbach's alpha coefficient, respectively.
Results: The Exploratory Factor Analysis demonstrated that QUIPA has 3 factors. For the first, second and third subscales and total score of QUIPA, ICC was found to be as 0.895, 0.947, 0.665, and 0.925, respectively. Cronbach's alpha coefficient was determined to be as 0.682, 0.797, 0.593, and 0.812, respectively for the first, second and third subscales and total score of QUIPA. These results indicate that Turkish version of QUIPA has excellent test-retest reliability and good internal consistency.
Conclusion: Turkish version of the QUIPA determined to be a valid and reliable tool to assess the quality indicators of physiotherapy management of hip/knee OA in Turkish-speaking patients. It is suggested to be used in clinical settings and researchs.
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Table 1. Test-retest reliability analysis of the QUIPA

QUIPA	ICC	95% CI (Lower-upper bound)
1st question	0.814	0.731-0.873
2nd question	0.686	0.560-0.780
3rd question	0.782	0.688-0.850
4th question	0.655	0.521-0.758
5th question	0.727	0.614-0.811
6th question	0.616	0.471-0.728
7th question	0.768	0.669-0.841
8th question	0.631	0.490-0.739
9th question	0.723	0.609-0.808
10th question	0.785	0.692-0.853
11th question	0.879	0.812-0.923
12th question	0.772	0.674-0.843
13th (a) question	0.842	0.770-0.892
13th (b) question	0.752	0.615-0.845
14th question	0.543	0.381-0.672
15th question	0.498	0.327-0.637
16th question	0.514	0.347-0.650
17th question	0.866	0.804-0.909
1st Subscale, (Q1-Q6)	0.895	0.845-0.929
2nd Subscale, (Q7-Q13)	0.947	0.921-0.965
3rd Subscale, (Q14-Q17)	0.665	0.534-0.765
Total	**0.925**	**0.888-0.950**

ICC: Intraclass correlation coefficient, CI: Confidence interval

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POS1482-HPR ASYNCHRONOUS TELECONSULTATION BY WHATSAPP CHATBOT IN CONTROLLED AXIAL SPONDYLOARTHRITIS (SPA) PATIENTS UNDER BIOLOGICAL THERAPY: 10 MONTHS EXPERIENCE AT A SINGLE CENTRE

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Background: The use of telehealth in the control of rheumatic diseases had been scarce, but COVID pandemic forced rheumatologists to try alternatives to classic face-to-face consultation. In times of lockdown phone calls and video calls were easy to perform, but later on an asynchronous model of teleconsultation would probably fit better. The purpose of this study is to prove that asynchronous whatsapp teleconsultation is an effective alternative to classic healthcare consultation models out of pandemic. So, we selected axial spondyloarthritis (SPA) patients with stable controlled disease under biological therapy and we offered teleconsultation with a whatsapp platform chatbot, that´s been created for this purpose as a way to send PROMS (BASDAI, VAS for patient global disease assesment, ASDAS, and 3 questions for extraarticular disease), and receive feedback and schedule for the following visits
Objectives: To prove that teleconsultation through whatsapp platform was not inferior to face-to-face consultation in terms of mantaining axial SPA patients disease under control. And to prove that teleconsultation model was less time and resources consuming for the patient and the system, and probably preferred by a group of patients.
Methods: Prospective study with retrospective control of patients diagnosed of Axial SPA, fullfilling ASAS criteria and with stable disease under biological therapy for the previous year, recruited from 01 jan to 30 nov 2021. We offered them two teleconsultation visits using their personal mobile device, once every four months and a face-to-face visit at the end of the study (one year since inclusion). If there is a deviation in the lab test or PROMs or if the patient asks for contact (via whatsapp) he is called up by the person in charge (nurse/doctor) that solves the question and arranges an aditional presential visit when needed. We consider disease controlled if BASDAI <4, ASDAS < 2,1 or if in rheumatologist´s opinion there is no need to change treatment. We collect patient and disease information (age, gender, employment, use of mobile devices, duration and characteristics of the disease, previous and actual treatment), activity (BASDAI, PCR, ASDAS), physical function (BASFI), Quality of life (AsQol) ansd productivity (WAPAI), and we also check number of face-to-face and phone consultations and patient´s preferences.
Results: 62 patients (52 men and 10 women) were recruited, mean aged 47,7 years (range 26-72), 36% were under 45 years at the time of inclusion. They were mostly Ankylosing Spondylitis (AS) (90%; only 6 non radiographic SPA), positive HLA B27 (90%) and with longstading disease (mean 24 years), and only 6 patients less than five years. 16% had peripheral involvement (arthritis/dactylitis), and 40% presented extraarticular manifestations, mainly uveitis (20%). 70% were under their first biological (TNF inhbitor, mostly adalimumab), 24% were refractory to the first, 3 patients to 2 previous biologicals and just 1 patient was refractoy to 5. 50% of patients were treated with tapered dose of TNF inhibitors. We have now a mean followup of 10 months, in which we have had 109 scheduled teleconsultations with aditional need of 36 phone calls and 10 aditional presential visits for the whole group. To date, 3 patients with reduced dose increased to standard dose of biological drug and none change of biological was required.
Conclusion: Asynchronous teleconsultation seems promising, specially for followup in patients with stable rheumatic disease, less interfering with daily activities, less time consuming for the patient and less resource consuming for healthcare systems, with no impairment of disease control and quailty of healthcare. This study will also show patient´s preference, and we´ll try to describe a profile of patient more prone to teleconsultation.
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POS1483-HPR DYSFUNCTIONAL COPING CORRELATES WITH DEPRESSION AND ANXIETY AND PREDICTS WORSE OUTCOME IN PATIENTS WITH A HIGH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Disease flares of rheumatoid arthritis (RA) are important stressors for patients (pts) who may use coping for disease management. Some coping styles are thought to be beneficial and may help to improve disease outcome whereas others are thought to be harmful.
Objectives: We investigate the frequency and intensity of different coping styles in pts with an acute flare of seropositive RA and its impact on disease outcomes after 12 month of therapy.
Methods: Coping was analysed with the Brief-COPE (1) using a 4 point Likert scale in 222 pts participating in the ERFASS study (2). Coping styles were analysed by confirmatory and exploratory factor analysis (CFA, EFA). Disease activity was measured via DAS28 (CRP), depression and/or anxiety using Hospital Anxiety and Depression Scale (HADS) and Patient Health Questionnaire 9 (PHQ-9). Repeated measures ANOVA was used to identify the effect of different coping strategies on disease activity and Spearman-Rho to identify correlations.
Results: Factor analysis revealed five dominant coping styles (problem oriented, emotion oriented, dysfunctional, religion, alcohol/drugs) which were consistent during 6 and 12 months follow up. When analysing the relative intensity of each coping strategy over time there was no significant change during treatment (Table 1). The usage of only a single coping style at baseline ("I am doing this a medium amount" or "a lot") was reported by 70 pts (31,5%). 65 pts (29,3%) reported the use of 2 coping styles simultaneously, 25 pts (11,3%) 3 coping styles and 4 pts (1,8%) four coping styles. Problem oriented coping was used by 125 pts (56,3%), emotional coping by 97 pts (43,7%), dysfunctional coping by 41 pts (18,5%), religion by 24 pts (10,8%) and alcohol/drugs by only 4 pts (1,8%). 58 pts (26,1%) reported not to use any of the coping styles ("I am doing this not at all" or "only a little bit") and these pts had a lower DAS28 during the course of the study (p=0.036) as compared to pts who use one or more coping strategies. When analysing the group with high disease activity (DAS28 >5.1) at baseline (n=60), pts with medium or high dysfunctional coping had a significantly higher disease activity after 12 months as compared to those with no or little dysfunctional coping (U = 187,00, Z = -2.025, p = 0.043) (Figure 1). The other coping styles did not significantly predict the outcome of disease activity. We observed a strong correlation between dysfunctional coping and depression (PHQ9 r = 0.590; HADS depression r = 0.569) as well as anxiety (HADS anxiety r = 0.639) but not for the other coping strategies at baseline.

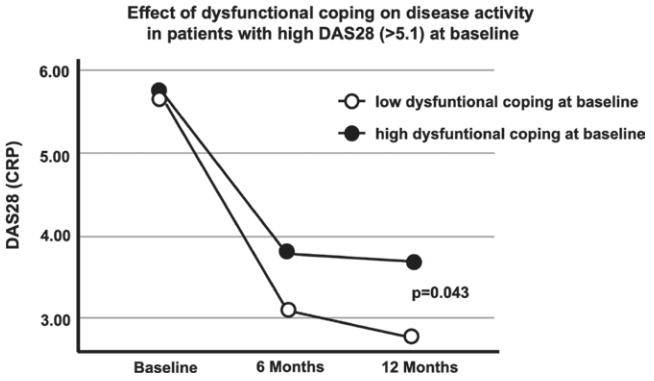

Figure 1.

Table 1. Development of disease activity (DAS28) and coping strategies over time

	Time		
	Baseline mean (SD)	Month 6 mean (SD)	Month 12 mean (SD)
DAS28	4.32 (1.14)	2.79 (1.23)	2.47 (1.05)
Problem oriented	53.10 (14.93)	49.69 (14.10)	47.43 (14.00)
Emotion oriented	49.94 (13.00)	50.73 (12.76)	50.46 (13.45)
Dysfunctional	40.25 (14.59)	36.44 (11.76)	36.00 (12.26)
Religion	36.15 (18.30)	35.53 (17.02)	34.68 (16.64)
Alcohol / Drugs	27.03 (7.81)	27.15 (8.75)	26.53 (6.07)

Conclusion: Different ways of coping may be used simultaneously during an acute flare of seropositive RA. In pts with high disease activity dysfunctional coping is the only coping strategy predicting a worse disease outcome after 12 months and dysfunctional coping correlates with depression and anxiety.

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POS1484-HPR LUMBOPELVIC STABILITY, TRUNK POSITION SENSE, AND SPINE POSTURE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial Spondyloarthritis (ax-SpA) are chronic systemic inflammatory rheumatological diseases characterized by axial skeletal involvement and enthesitis. The trunk is the central key point of the body, playing an essential role for postural control, the coordination of the extremities, and functional activities. The systemic, inflammatory nature of ax-SpA, chronic pain, inflammatory cytokines, changes in the bone and ligaments of the spine may affect lumbopelvic stability, trunk position sense, and spine posture.

Objectives: We aimed to investigate lumbopelvıc stability, trunk position sense, and spine posture in patients with ax-SpA.

Methods: Twenty ax-SpA patients (mean age; 33.65± 5.72, 75% female) and 20 age- and gender-matched healty controls were included in the study. In ax-SpA patients, mean time since symptom onset was 9.75±4.82 years and mean time since diagnosis was 6±3.97 years. Lumbopelvic stabilization was evaluated by a pressure biofeedback unit (Stabilizer Pressure Biofeedback Unit, Chattanooga Group Inc., Hixson, TN, USA). Trunk position sense, as indicated by trunk reposition errors (TRE), was assessed with a digital inclinometer. Thoracic and lumbar curvature tests werw performed with a digital inclinometer.

Results: Comparisons of lumbopelvıc stability, trunk position sense and posture were shown in Table 1. Lumbopelvic stabilization values were significantly lower in the ax-SpA group when compared to the control group (p<0,001). TRE, in which higher scores indicate poorer trunk position sense, was higher in the ax-SpA group compared to the control group (p<0,001). The degree of thoracic curvature was higher (p = 0.001) in the ax-SpA group compared to controls whereas the degree of lumbar lordosis was not significantly different between the groups (p = 0.444).

Table 1. Comparison of lumbopelvıc stability trunk position sense, and posture of the groups

Characteristics	AxSpA group (n=20)	Control group (*n* = 20)	p
Lumbopelvic stabilization (mmHg, median; min–max)	43.65 (41.3;51.3)	48,6 (46;62,6)	p<0.001[*b]
Trunk position sense (TRE) (°,median; min–max)	3.6 (0.66; 8.6)	1.3 (0.66; 2)	p<0.001[*b]
Spine posture			
Thoracic curvature (°,median; min–max)	39,95 (29.3;53.3)	34.3 (29.6;3)	p = 0.001[*b]
Lumbar curvature (°, mean ± SD)	39,78 ± 7,60	37,9 ± 7,82	p = 0.444[a]

TRE trunk reposition error, AxSpA Axial Spondyloarthritis, SD standard deviation*p < 0.05. *a Independent samples t test. b Mann–Whitney U test.*

Conclusion: According to our results, patients with ax-SpA had poor lumbopelvic stability, trunk position sense, and spine posture. The multiplicity and complexity of the symptoms of patients with ax-SpA require multifaceted symptom management interventions. For this purpose, consideration of the training of lumbopelvıc stability, trunk position sense, and spine posture might be beneficial in optimal treatment planning.

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POS1485-HPR DIGITALLY ENHANCED TREAT-TO-TARGET AND SHARED DECISION-MAKING APPROACH WITH A DIGITAL HEALTH APPLICATION: INTERIM RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: Digital health applications (DHA) became indispensable patient companions accelerated by the current COVID pandemic [1]. In 2020, for the first time worldwide, a regulatory framework to reimburse DHA was established in Germany. To get listed as a DHA, preliminary evidence needs to be generated – next to fulfilling highest standards in quality and safety. The DHA ABATON RA consists of two parts; 1) digital shared-decision-making (SDM) including choosing an appropriate electronic patient reported outcome (ePRO) instrument and the respective ePRO target for the next visit, 2) remote patient monitoring and ePRO tracking by the patient. Hereby, ABATON RA supports a digitally guided Treat-to-Target (T2T) approach.

Objectives: The objective of this study is to evaluate a potentially beneficial effect for the patient by using ABATON RA.

Methods: Three-armed, partially blinded multicenter trial (RCT) including RA patients who regularly use a smartphone. Patients attend 3 visits, 3 months apart (T0, T3, T6), with one follow-up visit (T9). Intervention group (IG): Patients use ABATON RA. Via SDM patients and rheumatologists choose a specific ePRO and respective treatment target for the next visit in three months, e.g. RAID ≤4. Control group (CG): Standard of care treatment (no DHA). Placebo group (PG): Usage of a placebo version of ABATON RA providing only Regensburger Insomnie Skala (RIS) and Epworth Sleepiness Scale (ESS) as ePROs. No SDM is conducted and ePRO results are not presented to HCP.

Results: This interim analysis evaluated the first 38 patients that completed T3. IG: 13 patients (Av. age 55.9, 61.5% females); PG: 12 (Av. age 50.7, 66.7% females); CG: 13 (Av. age 56.1, 76.9% females). We observe a significant improvement in the mean over time in a pairwise comparison within the intervention group for the following: Pt-GA mean difference of 2.98 (p = 0.025, partial η^2

= 0.353), pain mean difference of 1.46 (p = 0.049, partial η^2 = 0.286) whereas all pairwise comparisons for the two parameters were non-significant in PG and CG. The patient reactions assessment (PRA) score, measuring patient perceived quality of the patient-provider relationship, increased by a mean of 4.15 points in IG, compared to a slight decrease of 1.92 for PG and 2.77 for CG.

Conclusion: These preliminary findings show beneficial differences among the groups in favor of IG: 1) for quality of life and 2) the physician-patient-relationship. A digitally enhanced therapy is non-inferior to the gold-standard of exclusive in-person treatment. Patients seem willing and able to get involved in an enhanced treat-to-target and shared decision-making approach.

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POS1486-HPR DETECTION OF ASSOCIATED FIBROMYALGIA IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE ACCORDING TO THE MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE/ FIBROMYALGIA ASSESSMENT SCREENING TOOLS (MDHAQ/FAST4).

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Background: Osteoarthritis is the most prevalent joint pathology. knee Osteoarthritis is one of the most frequent locations and has the greatest impact on the health of patients. It can be associated up to 11% with depression and 23% with neuropathic pain. It has also been reported that it can coincide with fibromyalgia (FM) between 6% and 22.83%. This difference may be attributed to some factors, e.g., sample size and/or socioeconomic status. Therefore, the clinical interpretation of symptoms in knee osteoarthritis may be overestimated by the presence of FM. Pincus T. et al. used the FAST4 to identify the coexistence of FM in patients with various rheumatic pathologies. The FAST4 consists of using the MDHAQ (symptom checklist, painful joint count, fatigue and pain). A FAST4 score ≥ 3 allows the association of FM to be considered. The authors demonstrated good concordance with the 2011 FM criteria according to the ACR (with a sensitivity of 70.4% and a specificity of 97.1%)

Objectives: To detect the presence of associated FM in patients with early and established knee osteoarthritis employing the MDHAQ/FAST4

Methods: Patients ≥18 years, of both sexes, from our community with early and established knee osteoarthritis (Luyten, FP 2018 and Altman, R 1986 Classification Criteria respectively). All answered the MDHAQ/FAST3-F questionnaire, in addition to the Patient Health Questionnaire (PHQ9) and the Neuropathic Pain 4 Questions (DN4). Depression was considered respectively with a score ≥3 of the PHQ9 and neuropathic pain with 4 points of the DN4

Results: 100 patients (96 with a diagnosis of early knee osteoarthritis and 4 with established knee osteoarthritis [Luyten - ACR]) with a median age of 58 (RIC 16) and female sex were included 72%.We observed associated FM (FAST4-F) in 31% of patients (27 with early knee osteoarthritis and 4 with established knee osteoarthritis). Median VAS pain, patient and physician global assessment of the disease was higher in patients with FM (p<0.0001). Disease activity by RAPID 3 was low in 4%, moderate in 38% and high in 58% of patients. The cohort had a median pain score of 60 (RIC 60) with absence of neuropathic pain (DN4) in 90% of patients. Depression (PHQ9) was observed in 29% of cases.OA evolution time in months in patients with FM 48 (RIC 12) vs. 36 (RIC 24) without FM (p< 0.0001).Binary logistic regression was performed. In the bivariate analysis, it was observed that the presence of early OA by Luyten's criteria (p=0.002), the presence of depression by PHQ9 (p=0.001), patients of white ethnicity (p=0.03), sobrepeso (p=0.002), low RAPID 3 disease activity (p=0.001), kellgren and lawrence grades II and III (p=0.001), were significant in the bivariate model, although none were statistically significant in the multivariate model

Conclusion: The evaluation of knee osteoarthritis can be complicated in those patients who coexist with FM. In our study 31% met criteria for this entity according to MDHAQ/FAST4. We consider this questionnaire to be single and practical for detecting associated FM. The results obtained give hierarchy to the use of PROMs (Patient Reported Outcomes Measures) that can recognize clues of associated diseases such as FM and/or depression. And thus be able to establish a timely and appropriate treatment when these pathologies are overlapping, in order to change the patient's prognosis and improve their quality of life

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POS1487-HPR THE RELATIONSHIP BETWEEN SEXUAL QUALITY OF LIFE AND CLINICAL FEATURES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is associated to a significant economic and social burden, due to the fact that it affects young individuals during their most productive years of life. Sexuality is one of the health areas affected by axSpA, owed to pain and inflammation, loss of axial and peripheral mobility, joint deformity, joint replacement surgeries, and adverse events secondary to therapy.

Objectives: To assess the relationship between disease related variables, treatment and sexual quality of life in patients with ax-SpA.

Methods: Thirty-nine ax-SpA patients (69.2% female) were included in the study. Median age was 36.0 (IQR 25/75: 25.32/41.7) years, mean body mass index was 26.34±4.64 kg/m^2, median time since symptom onset was 10.0 (IQR 25/75: 9.59/14.72) years, median time since diagnosis was 6.0 (IQR 25/75: 5.70/8.66) years, and treatment with anti-TNF alpha was 64.1%. All the patients completed the Qualisex questionnaire to assess the quality of sexual life. Axial mobility according to the Bath Ankylosing Spondylitis Metrology Index (BASMI) was calculated. All the patients completed the questionnaires Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and, to evaluate disease activity and functional status respectively. Furthermore, patients fulfilled Ankylosing Spondylitis Quality of Life (AsQoL) and Musculoskeletal Health Questionnaire (MSK-HQ) to evaluate quality of life and musculoskeletal health respectively. Spearman's rank-order correlation test was used to analyse the relationships between sexual quality of life and clinical features.

Results: The results of BASMI and the self-reported questionnaires Qualisex, BASDAI, BASFI, AsQoL and MSK-HQ scores of patients with ax-SpA were summarized in Table 1. Moderate relationships were found between Qualisex questionnaire and BASMI, MSK-HQ (Table 1, p<0.05). Qualisex questionnaire has the strongest association with BASFI (rho: .703, p<0.001) and average association with BASDAI (rho: .648, p<0.001) and AsQoL (rho: -.612, p<0.001).

Table 1. The relationships between Qualisex questionnaire and BASMI, self-reported questionnaires BASFI, BASDAI, AsQoL, MSK-HQ in patient with axSpA

Characteristics	Median (IQR 25/75) (n:39)	The correlation results, rho, p values
		Qualisex questionnaire
BASFI	3.1 (2.87/3.9)	.703* p<0.001
BASDAI	4.3 (3.67/4.74)	.648* p<0.001
AsQoL	10 (8.88/11.18)	-.612* p<0.001
BASMI	2.2 (2.26/3.15)	.403* p=0.016
MSK-HQ	30 (30.18/34.5)	-.522* p=0.001
Qualisexquestionnaire	3.7 (2.69/3.73)	

IQR 25/75: Interquartile range between 25th and 75th percentiles; axSpA, Axial spondyloarthritis; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; AsQoL, Ankylosing Spondylitis Quality of Life; MSK-HQ, Musculoskeletal Health Questionnaire
*Spearman's rank-order correlation test, p<0.05.

Conclusion: According to our results; especially high disease activity and lower functional status were highly associated with worse sexual health in axSpA patients. Improving disease activity, funnctional status and axial mobility may help to improve sexual health in those patients.

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POS1488-HPR DETERMINANTS OF PATIENT AND PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN LARGE VESSEL VASCULITIS.

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Background: Factors influencing disease activity assessment by patients and physicians are unknown, but are highly relevant in the context of PROs development.
Objectives: To compare the patients' and physicians' global assessment of disease activity in large vessel vasculitis and investigate factors influencing the assessment of disease activity.
Methods: Between 2010 and 2020, patients with large vessel vasculitis and their routine caring physicians assessed a global disease activity score (numerical rating scale 0 – 10) in our outpatient clinic. We compared these global scores of disease activity. In a multiple linear regression analysis we examined the influence of potential demographical and clinical factors on the disease activity assessment.
Results: 138 Patients with 866 assessments were available for analysis. At timepoint of assessment they had a mean age of 76 (± 9) years and a mean disease duration of 5 years (± 5). The median global score of patient-reported disease activity was 3 points, the median physicians' disease activity assessment was 2 points. In 28,2% (n=244) there was a deviation of more than 2 points between the patients' and physicians' assessment of disease activity. Only 5 times the physicians, but 232 times the patients rated their disease activity higher than 5 points. In this group the patient-reported disease activity was associated with the patients age (β 0.025), the patients BMI (β 0.071) and the extent of pain (β 0.19), p<0.05. The disease duration, CRP level and the psychological well-being of the patient showed no association.
Conclusion: In our cohort, physicians and patients showed greater divergence in disease activity assessment with higher disease activity. Age, BMI and the extent of pain were associated with higher disease activity ratings by the patients. This results are relevant for the development and interpretation of PROs for activity assessment in large vessel vasculitides.
Disclosure of Interests: Anna Kernder: None declared, Marius Rohde: None declared, Hasan Acar: None declared, Oliver Sander Speakers bureau: SOBI Pharma, EUSA Pharma, AbbVie Pharma, Consultant of: SOBI Pharma, EUSA Pharma, Boehringer Pharma, Jutta Richter: None declared, Rebecca Fischer-Betz: None declared, Matthias Schneider Speakers bureau: Astra-Zeneca; Biogen; BMS; Celgene; Chugai; GSK; Janssen-Cilag; Lilly; Pfizer; UCB, Paid instructor for: Lilly, Consultant of: Abbvie; Astra-Zeneca; Boehringer-Ingelheim; GSK; Lilly; Novartis; Pfizer; Protagen; Roche; Sanofi-Aventis; UCB, Grant/research support from: Abbvie; Astra-Zeneca; GSK; UCB, Gamal Chehab: None declared
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POS1489-HPR ASSESSMENT OF TREATMENT ADHERENCE IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH SUBCUTANEOUS ANTI-TNF WHO WERE EXPOSED TO A COMPREHENSIVE CARE MODEL

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Background: Rheumatoid arthritis (RA) is an autoimmune, chronic, and inflammatory disease, which can be treated with effective medications, but requires a high level of adherence to treatment. Offering a comprehensive care model by a multidisciplinary team could increase the adherence levels of these patients and improves disease outcomes.
Objectives: Compare the level of adherence to treatment before and after the implementation of a comprehensive care model in a cohort of patients with RA, treated with subcutaneous anti-TNF, in a reference center in Bogotá-Colombia.
Methods: An analytical study was conducted before and after the implementation of a comprehensive care model on a cohort of patients over 18 years of age, diagnosed with RA, who have been prescribed management with a subcutaneous anti-TNF by their doctor during the last 12 months. Convenience sequential sampling was performed to reach a defined sample size of 130 patients to estimate a baseline versus final adherence difference of 20%, at an alpha value of 5% and a beta value of 20%. The comprehensive care model (CCM) consisted of the approach by a multidisciplinary team, offering a comprehensive care not fragmented, based on evidence (guidelines and protocols) and proposing a treatment by objectives (T2T). Adherence was measured using the CQR-19 scale, with a cut-off point ≥80.7 to consider an adherent patient.
Results: The cohort consisted of 131 patients who were followed semiannually for 24 months, and who were incorporated into the CCM. 83.9% were women (n=110), in an age range between 30 and 84 years (Average: 62; DS: 9.9 years). 37.4% of patients were treated with etanercept (n=49), 29% with golimumab (n=38) and 33.6% with adalimumab (n=44). The median baseline of CQR-19 was 87.7 points (RIQ:84.2-91.2); while at month 24 it reached 91.2 points (RIQ: 87.7-94.7). The difference between the distributions was statistically significant (p<0.00). According to the cut-off point for CQR-19, the baseline percentage of adherent patients was 87.8% (n=115) and increased to a percentage of 96.2% at 24 months of follow-up (n=126). The difference between these two percentages of adherence was 8.39% (95% CI: 1.9-14.9%) (p: 0.012). The results of a generalized linear model binomial family, for the outcome of difference in proportions (PD) of basal and final adherence, are presented in Table 1. The estimator is adjusted for activity level (DAS28), disability level (HAQ) and anti-TNF. Golimumab appears to have an effect that increases adherence by 4.5% compared to adalimumab and etanercept, adjusting for the other predictors.

Table 1. Model of the effect of MAI on adherence to treatment.

Dependent variable: Adhesion according to cut-off point CQR-19(≥80.7). Proportion Difference (DP) Estimator

Variable	DP	CI 95%	P-value
Intervention: MAI	9,4%	3,2-15,5%	0,003
Golimumab vs. Etanercept-Adalimumab	4,5%	0,5-8,5%	0,024
DAS28	(-)0,85%	(-)3.2% to 14.9%	0,47
HAQ	0,00	(-)0.03% to 0.045%	0,85

MLG-Binomial family. Identity function.

Conclusion: The CCM, after a follow-up of 24 months in patients with RA in treatment with subcutaneous anti-TNF increases the percentage of adherence by 9.4%, adjusting for treatment, activity level and degree of disability. Golimumab appears to have an effect that increases adherence by 4.5% compared to adalimumab and etanercept, adjusting for the other predictors.
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POS1490-HPR INVESTIGATION OF THE RELATIONSHIP BETWEEN EXERCISE CAPACITY AND PSYCHOSOCIAL VARIABLES IN WOMEN WITH FIBROMYALGIA: A PRELIMINARY STUDY

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Background: Various studies have showed that patients with fibromyalgia have lower exercise capacity than healthy individuals (1, 2). This reduced exercise capacity affects these patients' independence in performing daily activities (3). Although it was shown that exercise capacity related physical status, it is not quite clear that relationship between exercise capacity and patients' psychosocial variables in patients with fibromyalgia.
Objectives: To identify whether there is any direct link between the exercise capacity of women with fibromyalgia and their psychosocial status.
Methods: Nineteen women with fibromyalgia meeting the criteria of the American College of Rheumatology were included in the preliminary cross-sectional study (age=46.26±6.25 years, BMI=27.64±3.86 kg/m^2). Exercise capacity was assessed by 6-min walking test. For psychosocial variables, alexithymia, fatigue, self-efficacy, and social support were measured by Toronto Alexithymia Scale, Multidimensional Fatigue Index, General Self-Efficiacy Scale, and MOS Social Support Survey, respectively. Spearman' correlation was used to investigate the relationship.
Results: The average distance walked was 468.15± 57.50 m. It was found that a significant correlation between 6-min walking test and alexithymia (r=-.517, p=.023), fatigue (r=-.475, p=.040), and self-efficacy scores (r=.607, p<.001). However, no link was observed between 6-min walking test and social support scores (r=.170, p=.486).
Conclusion: As a result of our study, the exercise capacity of fibromyalgia patients was reduced as in other studies. there was a strong positive correlation between exercise capacity and self-efficacy in patients with fibromyalgia. Furthermore, exercise capacity was negatively associated with multidimensional fatigue scores and alexithymia. In the light of all this, it may be said that exercise capacity is related to patients' psychosocial status in women with fibromyalgia. We think that the structure of exercise programs aimed at improving the exercise capacity of patients should include strategies that also improve psychosocial factors.

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POS1491-HPR THE USEFULNESS OF THE PATIENT ACTIVITY SCORE-PASS-II TO ASSESS DISEASE ACTIVITY DURING THE COVID-19 LOCKDOWN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Many measurement tools are designed to assess disease activity for Rheumatoid Arthritis (RA) patients. One of the most used tools is the Disease Activity Score- DAS28 which assesses the number of painful joints, erythrocyte sedimentation, and a patient's global assessment. The assessment is performed by a clinician and requires laboratory exams. Unfortunately, from March to August 2019, Colombia had one of the strictest responses to the COVID-19 pandemic according to the COVID-19 stringency Index(1). One of the main restrictions was the preventive isolation of older populations, especially those with comorbidities. These restrictions challenged the rheumatology practice because face-to-face consultations were not possible. Due to the above, measurements like the PAS-II score should be used to assess disease activity during the pandemic.
Objectives: To describe disease activity according to the Patient Activity Score-PAS-II score patients with RA and compare its results to the most recent DAS28 assessment before the COVID-19 pandemic.
Methods: We conducted a descriptive study; patients were followed during the COVID-19- lockdown in a video consultation. The PAS-II score was applied to assess disease activity as an alternative to the DAS28 assessment. The patients were part of an educational program, clinical charts were reviewed to collect the study variables. We collected demographic data and DAS28 before the pandemic started. We present a descriptive analysis of DAS28 severity and the results obtained by the PASS-II score.
Results: The educational program enrolled 250 participants; 196 patients had complete data. 93% of participants were women, mean age was 64 years IQR (54-67). 43% of participants were married or had a civil union, 26% were single, 20% divorced, and 11% were widowed. Regarding educational level, 25% had finished elementary school and 39% high school; the remaining 36% had higher education. When we compared the last DAS28 assessed by a rheumatologist between January, and March 2019, 67% of patients were in remission, while in July 2019, the PASS-II score reported that 7% of patients were in remission and 75% had low or minimal activity. Figure 1- Table 1.
Figure 1.

Table 1.

DISEASE ACTIVITIY	DAS28	PASS-II
Remission	67%	6%
Low (Minimal)	14%	75%
Moderate	15%	18.5%
High/Severe	4%	0.5%

Conclusion: The PASS score is a helpful tool to assess disease activity in patients with RA, especially in situations where the patient cannot see a rheumatologist in a face-to-face consultation; however, patients in severe disease activity should not delay the consultation with a clinician. As other studies have demonstrated, patient-reported outcome measures should be adopted in clinical practice as an alternative for treat- to- targe strategies(2). Further studies should be conducted to assess the impact of the pandemic in countries with high levels of restrictions in the course of RA.
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POS1492-HPR PSYCHOMETRIC PROPERTIES OF THE FIBROMYALGIA IMPACT QUESTIONNAIRE – REVISED IN FIBROMYALGIA AND CHRONIC WIDESPREAD PAIN: A RASCH ANALYSIS

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Background: The Fibromyalgia Impact Questionnaire - Revised (FIQR) is one of the most commonly used self-rating instruments developed to quantify the severity of disease burden and impact of disease on functional ability and social participation in patients with fibromyalgia (FM) [1]. The FIQR consists of 21 individual items categorized within three different domains; 'function', 'overall impact' and 'symptoms' [2]. The FIQR that has been translated into several languages, has mainly been validated based on classical test theory (CCT) - except for the Italian version [3]. The psychometric properties of the Italian version of the FIQR was evaluated by Salafi et al. based on item response theory using Rasch analysis [3]. The benefit of using Rasch measurement models, is that it allows for a detailed analyses of an instrument's rating scale properties and aspects of validity, including fit of individual scale items to a unidimensional model [4]. Although the FIQR demonstrated adequate psychometric properties in the original studies based on CCT, the Rasch analysis in the Italian study revealed problems with the rating scale properties [2,3]. The FIQR is a frequently used questionnaire when assessing patients with FM in Denmark, but the Danish version of the FIQR has not yet been validated.
Objectives: The aim of this study was to evaluate the psychometric properties of the Danish version of the Fibromyalgia Impact Questionnaire Revised (FIQR), when used to quantify the severity of disease burden in a Danish population of patients with Chronic widespread pain (CWP) including Fibromyalgia (FM).
Methods: A total of 924 participants diagnosed with CWP and/or FM completed an electronic version of the FIQR via touchscreens in the clinic at referral for specialist care. Data was collected from January 1st, 2018 to September 3rd, 2020. Rasch measurement methods were applied.
Results: Rating scale analysis suggested multiple threshold disordering in the 0 to 10-category rating scale. A principal component analysis suggested assessment of a multidimensional construct. Thus, the Rasch analysis of the full FIQR was discontinued. Instead Rasch analyses were performed on the two subscales: 'function' and 'symptoms'. By collapsing the rating scale to a 0 to 4-category scale, the remaining threshold disordering of both subscale was solved. Only the symptom subscale indicated a multidimensionality. There was underfitting misfit of item 21 and overfitting misfit of item 12. No significant Differential Item Functioning was found defined by sex, ethnicity, or education.
Conclusion: The FIQR should be considered as an instrument consisting of three separate subscales representing 'function', 'overall impact' and 'symptoms'. We recommend calculating and reporting on both a 0 to 10- and a 0 to 4-category scale. Also, if using the total FIQR score as an outcome measure, this should be done with caution, until revision of the rating scale.
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HPR Epidemiology and public health (including prevention)

POS1493-HPR FACTORS ASSOCIATED WITH THE OCCURRENCE OF MENTAL DISORDERS IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES DURING THE COVID-19 PANDEMIC.

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Background: Mental disorders constitute a serious and underestimated problem in Latin America and they could have worse features in comparison with Europe or North America [(1)]; that was the case even before the COVID-19 epidemic ensued in 2020.
Objectives: The objective of this study was to determine the factors associated with the occurrence of mental health disorders (MHD) in patients with autoimmune rheumatic disease (ARD) from Perú, a high COVID-19 incidence country.
Methods: Patients with ARD from a single center (Hospital Guillermo Almenara -EsSalud, Lima-Perú) were included during the first and second waves of the COVID-19 pandemic (March to November 2020). Interviews, medical records reviews, and an electronic survey were performed. MHD explored were depression (assessed with the Patient Health Questionnaire 9: PHQ-9), anxiety (ascertained with the Generalized Anxiety Disorder-7: GAD-7) and post-traumatic stress disorder: PTSD (evaluated with the Event Scale-Revised: IES-R). Variables examined were sociodemographic (age, gender, educational level, marital status, living alone, job status, religiosity), previous diagnosis and treatment for mental disorders, living with a COVID-19 patient, COVID-19 diagnosis (current or past), fear of COVID-19 (assessed with the COVID-19 Scale: FCV-19S) and the ARD type. Multivariable logistic regression models using backward elimination procedure were performed to determine the variables associated with depression, anxiety, and PTSD. (See Table 1).

Table 1. Variables associated with depression, anxiety an PSTD on ARD patients: Multivariable analysis.

	Depression		Anxiety		PTSD	
variables	OR (CI=95%)	p value	OR (CI95%)	p value	OR (CI95%)	p value
Previous treatment for mental disorders	2.35 (1.37-4.0)3	0.002	2.42 (1.37-4.26)	0.002	2.42 1.39-4.21	0.002
Fear for COVID-19	1.07 (1.05-1.10)	<0.001	1.09 (1.06-1.12)	<0.001	1.41 1.11-1.17	<0.001
COVID-19 diagnosis		NS		NS	1.75 1.06-2.89	0.028
Educational level						
University/ postgraduate						
High School		NS	0.43 (0.82-0.21)	0.009		NS
Elementary		NS	0.52 (0.28-0,95) Ref.	0.032		NS
Marital status						
Single		NS		NS	0.57 (0.34-0.96)	0.033
Divorced/ separate		NS		NS	1.02 (0.73-1.41)	0.919

Results: Nine hundred and thirteen ARD patients were evaluated. The most frequent diagnosis was rheumatoid arthritis in 446(48.8%) patients followed by systemic lupus erythematosus in 279 (30.6%). Depression, anxiety, and PTSD were observed in 128 (14.0%), 112 (12.30%) and 485 (53.1%) patients, respectively. In the multivariable analyses, previous treatment for mental disorders and fear of COVID-19 were associated with depression: OR=2.35 (95% CI 1.37-4.03; p=0.002) and OR=1.07 (95% CI 1.05-1.10; p<0.001) respectively; also with anxiety: OR= 2.42 (95% CI 1.37-4.26; p=0.002) and OR=1.09 (95% CI 1.06-1.12; p <0.01) and with PSTD: OR=2.42 (95% CI 1.39-4.21;p=0.002) and OR=1.41 (95% CI=1.11-1.17; p<0.001). A diagnosis of COVID-19 was associated with PTSD: OR=1.75 (95% CI 1.06-2.89, p=0.028), while being single was associated with a decreased probability of PTSD occurrence: OR=0.57 (95% CI=0.35-0.96; p=0.03). Finally, having a high educational level was associated with less anxiety: OR=0.43 (95% CI=0.82-0.21; p=0.009), for university /postgraduate studies and OR=0.52 (CI 95%=0.28-0.95; p=0.032) for secondary studies.
Conclusion: Fear of COVID-19 and previous treatment for mental disorder were associated with all MHD explored on our ARD patients during the COVID-19 pandemic.
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POS1494-HPR INCIDENCE OF PSYCHIATRIC DISORDERS AND FIBROMYALGIA IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS DURING COVID 19 PANDEMIC: THE ROLE OF TELEMEDICINE.

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Background: The management of patients with immuno-rheumatological diseases has profoundly changed during the COVID 19 pandemic and telemedicine has played an important role in the disease follow-up.
In addition to monitoring disease activity and any adverse events, especially infectious events, assessing the psychological situation of the patient can be fundamental in particular considering that COVID-19 has also a serious impact on mental health and it has been demonstrated a significantly higher incidence of anxiety disorders and depressive symptoms especially in younger people
Objectives: The aim of this study is to evaluate the incidence of depressive disorders, anxiety and fibromyalgia in our patients with rheumatoid arthritis and psoriatic arthritis during the lockdown period due to the COVID 19 pandemic and validate the use of telemedicine in the clinical management of these patients.
Methods: Patients affected by rheumatoid and psoriatic arthritis treated with biological disease-modifying drugs were contacted to evaluate the state of health and the presence of any adverse events and a nurse administered the clinimetric questionnaires assessment to evaluate the disease activity, the impact of rheumatic disease on the health status and the presence of anxiety, depression and fibromyalgia. In particular the following scales have been used: The Rheumatoid Arthritis Impact of Disease (RAID), the Psoriatic arthritis impact of disease (PsAID), Beck Depression Inventory BDI-II, State-Trait Anxiety Inventory (STAI) and The Fibromyalgia Rapid Screening Tool questionnaire (FIRST), The VAS scale for the assessment of pain. Patients who reported disease flare-up or adverse events underwent an outpatient visit and during visit Disease Activity Score (DAS 28) and Disease Activity Index for Psoriatic Arthritis (DAPSA) were used.
Results: 171 patients with rheumatoid arthritis (RA) and 129 patients with psoriatic arthritis were enrolled. The incidence of fibromyalgia was increased in the two groups during the lockdown compared to the previous evaluations and in particular in patients with psoriatic arthritis (AR p =0.013, AP p= 0.001).Our analysis did not report significant differences between the two groups for the presence of fibromyalgia and anxiety-related disorders during lockdown, but a prevalence of depressive disorders in patients with rheumatoid arthritis was observed.During lockdown in RA patients, (n=50), no correlation was found between DAS28 and RAID score (r=0.112, p=0.438) and in PsA patients (n=34), no correlation was found between DAPSA and PSAID score (r=0.131, p=0.459) while median value of RAID was higher in STAI I and II positive and median value of PSAID was higher in STAI I and II positive. Patients positive at BDI had higher RAID score (median 6.28 vs 1.14) and PSAID (median 4.95 vs 2.85) score (Mann Whitney p<0.001 and p=0.003)
Conclusion: In conclusion, mental and physical stress during COVID-19 pandemic can greatly worsen FM symptoms and intensify the patients' suffering without a clinical flare of the inflammatory disease for patients affected by rheumatoid arthritis. Telemedicine has allowed us to identify patients who needed a face-to-face approach for therapeutic reevaluation even if not related to a flare of the disease.
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POS1495-HPR COVID-19, INFLUENZA AND PNEUMOCOCCUS VACCINATION UPTAKE IN PATIENTS WITH RHEUMATIC DISEASE: A PROSPECTIVE AUDIT

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Background: Patients with autoimmune inflammatory rheumatic diseases are susceptible to infections. This could be attributed to theimmunosuppressive effect of the underlying condition or the use of immunomodulatory medications. According to the Department of Health guidelines inthe UK and the European League Against Rheumatism (EULAR), patients who are immunosuppressed should be vaccinated against influenza and pneumococcal infection, as well as COVID-19 infection.
Objectives: Our aim was to explore the Pneumococcal, Influenza and COVID-19 vaccination uptake of our patients with different autoimmune inflammatory rheumatological conditions. In addition, to assess the side effects profile and the status of their underlying rheumatological diseases following COVID-19 vaccination.
Methods: We undertook a prospective audit of consecutive patients with regards to their vaccination update for influenza, pneumococcus, and COVID-19, utilizing a standard questionnaire and compared the results to our 2017 data.
Results: Some 81% of patients received the influenza vaccination (compared to 47% in 2017) representing a 172% improvement, p<0.001. Some 53% received the pneumococcus vaccination compared to 28% in 2017, indicating a 185% improvement, p=0.003. With regards to COVID-19 vaccination, 98/101(97%) of eligible patients received at least one dose and 66% received two doses. 47% received Astra Zeneca, 52% Pfizer and 1% unsure. 46% of patients mentioned, no one specifically discussed the COVID vaccine with them - got information via SMS/ from media, However, 37% of patients were informed by GP Doctor/ Nurse, 14% from the person giving the vaccine, and 7% from specialist hospital doctor. Safety concerns were indicated by all 3 patients who deferred vaccination.
Most side-effects were observed following the first dose (74 patients) vs. the second dose (13 patients) and were mainly mild (66%), but also moderate (19%) and severe (15%). The sore arm was the commonest side-effect, whilst the majority of side-effects resolved within two days. Crucially, 28% reported a flare of the rheumatological condition following the vaccination. No patients receiving at least one dose were diagnosed with COVID-19 infection subsequently.
Conclusion: Vaccination rates for influenza and pneumococcus have improved substantially since 2017, although the population with rheumatic diseases still has low uptake in pneumococcal vaccination. The COVID-19 vaccination uptake has been extremely high in this cohort.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3355

HPR Interventions (educational, physical, social and psychological)

POS1496-HPR HARD TIMES: ADAPTING A FATIGUE MANAGEMENT PROGRAMME IN A PANDEMIC

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Background: Fatigue is a symptom of many Rheumatology Conditions (1). Hewlett et al have shown that a Fatigue Management programme (FMP) is effective in reducing fatigue in Rheumatoid Arthritis patients (2). In 2019, a 7-week group-based FMP was developed using a cognitive behavioural approach for Rheumatology patients in NHS Lothian (Scotland). In 2020, due to COVID-19, the in person FMP was adapted for virtual delivery. Referral criteria included Visual Analogue Scale-Fatigue (VAS-F) of ≥6/10 and an inflammatory rheumatic disease diagnosis. The FMP participants recorded Patient Reported Outcome Measures (PROMs) prior to and on completion of the FMP. In August 2021 demand for the FMP far outweighed the capacity of the delivery team and therefore the original 7-week FMP was further adapted to a 4-week programme. This was achieved by focusing on four core elements (i) sleep, (ii) thoughts, emotions and behaviours, (iii) energy conservation, (iv) setbacks.
Objectives: The primary objective was to evaluate whether the 4-week programme produced comparable PROMs results to the 7-week programme. In doing so, the aim was to maintain efficacy of the programme and provide increased capacity by offering more groups in the same timeframe.
Methods: Fatigue Severity Scale (FSS) and VAS-F were selected for comparison between pre and post FMP PROMs results, these being the main indicators of improvement in fatigue management. Fisher's exact test was used to determine any difference between the PROMs results reported at the end of both programmes. Participants who reported that their PROMs result were the same, worse or who did not respond, were all placed into the category "Other". The FMP team recorded the average waiting time for those attending each group. The length of the waiting list at any one time was calculated by removing those who were not interested, had been referred elsewhere, or who did not respond to the invitation, from the total number of referrals received by the FMP team.
Results: There was no significant difference in FSS and VAS-F results reported by the participants in both groups at the end of the FMPs as determined by Fisher's exact test (Table 1). Waiting list times reduced from 24 weeks in August 2021 to 6 weeks in December 2021 as a result of the adaptation of the FMP from a 7-week programme to a 4-week programme (Figure 1).

Table 1. Reported differences between pre-FMP and post-FMP PROMs.

		7 Week FMP (n = 25)	4 Week FMP (n = 13)	Fischer Exact
FSS	Improved	72%	77%	p = 1.000
	Other	28%	23%	
VAS	Improved	80%	69%	p = 0.689
	Other	20%	31%	

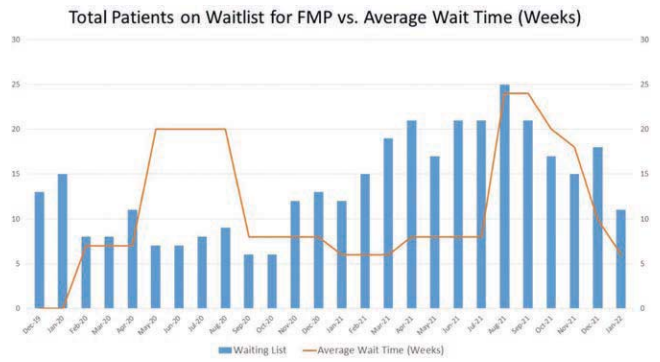

Figure 1. *- Review of average waiting times experienced by each group. In August 2021, the decision was made to trial a 4-week FMP to counter large increases in average waiting times.*

Conclusion: A 4-week FMP is as effective at improving the management of fatigue in Rheumatology patients as a 7-week FMP and reduces patient waiting times. More research is required to bolster the evidence base to support this novel approach.
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POS1497-HPR FEASIBILITY OF A PHYSIOTHERAPIST LED, BEHAVIOUR CHANGE INTERVENTION TO IMPROVE PHYSICAL ACTIVITY IN PEOPLE WITH RHEUMATOID ARTHRITIS

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Background: Physical activity (PA) is an important component in the management of people with rheumatoid arthritis (RA) (1). Interventions incorporating Behaviour Change (BC) theory are needed to target physically inactive people with RA. The study Physiotherapist-led Intervention to Promote Physical Activity in Rheumatoid Arthritis (PIPPRA) was designed using the Behaviour Change Wheel (BCW) and a pilot study of feasibility undertaken (ClinicalTrials.gov Identifier: NCT03644160).
Objectives: To obtain reliable estimates regarding recruitment rates; participant retention; protocol adherence and possible adverse events, and to producing estimates of the potential effect sizes of the BC intervention on changes in outcomes of physical activity; fatigue; disability and quality of life.
Methods: Participants were recruited at University Hospital (UH) rheumatology clinics and randomly assigned to control group (physical activity information leaflet) or intervention group (four BC physiotherapy sessions in eight weeks). Inclusion criteria were diagnosis of RA (ACR/EULAR 2010 classification criteria), aged

Table 1. Mean (sd) for secondary outcome measures in PIPPRA feasibility study

	Intervention			Control		
Outcomes and instruments	Baseline Mean (sd)	Time 1 Mean (sd)	Time 2 Mean (sd)	Baseline Mean (sd)	Time 1 Mean (sd)	Time 2 Mean (sd)
Physical Activity – self report (YPAS[1])	146.27 (193.73)	120.88 (70.80)	132.00 (70.65)	91.75 (85.86)	58.03 (50.61)	124.31 (69.75)
Physical Activity – objective (Step Count)	32,616.91 (11,415.85)	32,190.00 (9,291.57)	27,793.33 (7,426.92)	30,476.15 (12,642.97)	42,117.25 (21,714.67)	34,288.77 (17,677.90)
Pain (VAS[2])	4.18 (2.40)	4.90 (1.91)	4.50 (1.90)	3.71 (2.55)	5.10 (2.77)	4.79 (4.50)
Disability (HAQDI[3])	0.85 (0.57)	0.94 (0.57)	1.03 (0.65)	0.71 (0.56)	0.71 (0.52)	1.52 (0.69)
Fatigue (BRAF MDQ[4])	18.18 (8.98)	14.82 (13.15)	18.55 (11.84)	15.71 (12.29)	13.93 (15.27)	20.21 (10.85)
Psychological Constructs (TPB[5])	22.00 (4.84)	19.91 (7.76)	20.27 (8.63)	21.79 (5.67)	15.50 (11.43)	25.36 (6.86)
Quality of Life (RA QoL[6])	15.18 (6.08)	14.73 (7.23)	17.09 (7.33)	18.43 (5.06)	11.50 (10.02)	14.86 (6.47)
Sleep (PSQI[7])	11.55 (3.56)	8.50 (3.27)	9.91 (3.62)	10.21 (3.47)	9.09 (4.32)	10.14 (4.42)

[1]YPAS – Yale Physical Activity Scale [2]VAS – Visual Analogue Scale [3]HAQDI – Health Assessment Questionnaire Disability Index [4]BRAF MDQ - Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire [5]TPB – Theory of Planned Behaviour Questionnaire [6]RA QoL – Rheumatoid Arthritis Quality of Life Scale [7]PSQI – Pittsburgh Sleep Quality Index

18+ years and classified as insufficiently physically active. Ethical approval was obtained from the UH research ethics committee. Participants were assessed at baseline (T0), 8-weeks (T1), and 24-weeks (T2). Descriptive statistics and t-tests were used to analyse the data with SPSS v22.

Results: 320 participants were identified through chart review with direct contact then with people meeting the inclusion criteria at rheumatology clinics. Of the clinic attendees n=183 (57%) were eligible to participate and n=58 (55%) of those consented to participate. The recruitment rate was 6.4 per month and refusal rate was 59%. Due to impact of COVID-19 on the study n=25 (43%) participants completed the study (n=11 (44%) in intervention and n=14 (56%) in control). Of the 25, n= 23 (92%) were female, mean age was 60 years (sd 11.5). Intervention group participants completed 100% of BC sessions 1 & 2, 88% session 3 and 81% session 4. No serious adverse events were reported. Secondary outcome measures data is Table 1.

Conclusion: The PIPPRA study designed using the BCW to improve promote physical activity was feasible and safe. This pilot study provides a framework for larger intervention studies and based on these findings a fully powered trial is recommended.

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Disclosure of Interests: None declared

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POS1498-HPR NEWLY DIAGNOSED WITH INFLAMMATORY ARTHRITIS – DEVELOPMENT OF A COMPLEX SELF-MANAGEMENT INTERVENTION

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Background: People newly diagnosed with inflammatory arthritis (IA) request regular consultations and support from health professionals (HPRs) in rheumatology to manage physiological, emotional, and social challenges. Evidence suggests that providing a tailored tailormade multi-component self-management program may benefit disease management (1). However, there is a lack of evidence in interventions with multiple components targeting people newly diagnosed with IA.

Objectives: To develop a complex evidence- and theory-based intervention in co-creation with patients and HPRs for better self-management in newly diagnosed people with IA in a rheumatology out-patient clinic.

Methods: This study followed the Medical Research Council (MRC) Framework (2,3) for developing a complex intervention. The development phase comprised 1) identifying the evidence base, 2) identifying theory, 3) modelling process and outcomes, resulting in 4) a final description of all components and outcomes of the intervention.

1) Identifying the evidence base

We conducted two literature reviews, on which, we described a preliminary nurse-led intervention.

2) Identifying theory

Given the fact that the theory of Self-management is built upon Social Cognitive Theory (4) this was chosen as the underlying theory along with Acceptance and Commitment Theory (5) to support our communication strategy.

3) Modelling process and outcomes

The preliminary intervention was discussed and further developed in seven workshops to ensure that the intervention was in accordance with patients' needs and feasible in clinical practice. Three patients and 38 HPRs (nine therapists, 10 rheumatologists, one psychologist, one social worker, and 17 registered nurses) attended. During the workshops we identified the competencies needed in the HPRs delivering the intervention. In addition, relevant outcomes to measure self-management in a subsequent feasibility study were discussed. Discussions were digitally recorded and analysed using Thematic Analysis (6). Subsequently, the project group discussed the analysis and consensus was reached.

Results: *4) Description of all components and outcomes of the intervention*

Our intervention, ready for testing in a feasibility study, was a 9-month nurse-led intervention, and consisted of four individual and two group sessions. A physiotherapist and an occupational therapist should attend the group sessions along with the nurse (Figure 1). All sessions should target inflammatory arthritis-specific self-management.

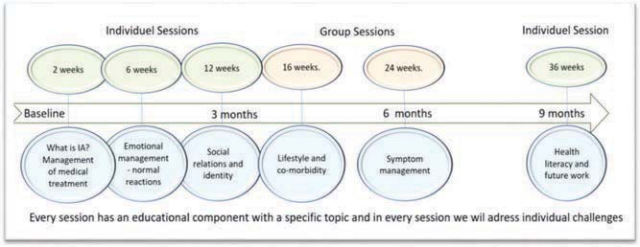

Figure 1. Intervention activities and

A comprehensive intervention manual has been developed. Our patient research partner and experts in rheumatology and self-management commented on the content to secure content validity. Subsequently, we conducted cognitive interviews with the HPRs to determine the face validity of the manual. In addition, we completed a two-day competence program to train HPRs in delivering the intervention. The selected patient reported outcomes were: Physical activity levels, Health assessment, Fatigue, Quality of life, Anxiety and depression, Illness intrusiveness, Illness perception, and Self-efficacy, supplemented with objective measures for diseases activity.

Conclusion: NISMA - a nurse-led complex self-management intervention embedded in a multidisciplinary team has been developed and described based on MRC's framework for the development of complex interventions. The intervention is currently being tested in a feasibility study.

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Disclosure of Interests: None declared
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POS1499-HPR ANKYLOSING SPONDYLITIS AND TELE-YOGA DURING COVID-19 PANDEMIC: PRELİMİNARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: Yoga is an ancient discipline that emerged thousandans of years ago in India to unite the mind, body and spirit. Yoga is widely used by patients with various rheumatic diseases. Although it is recommended for ankylosing spondylitis (AS) patients, there is no randomized controlled study on this subject in the literature. Due to Covid-19, which has changed the world and the people's lifestyle, tele-yoga practice can be considered as an alternative to traditional face-to-face yoga classes. The use of online platforms provides a safe environment for yoga training at home.
Objectives: The aim of this study was to investigate the effects of tele-yoga on disease activity, functional status, spinal mobility, sleep quality, depression, anxiety, stress and quality of life in ankylosing spondylitis patients.
Methods: Thirty-six volunteer AS patients (21 male, 15 female) who applied to Dokuz Eylül University, Department of Internal Medicine, Division of Rheumatology and Immunology were included in the study. Participants were randomly assigned to a tele-yoga (n=18, mean age 43.22 ±8.54 years) or waiting-list control group (n=18, mean age 44.9 ±8.01 years) by block randomization method. Patients in the tele-yoga group participated in 1-hour tele- yoga sessions with a maximum of 5 people in each group using Zoom (online video-conference method) 3 days a week for 8 weeks. Assessments were performed before and after 8 weeks of yoga training. The waiting list control group did not receive any intervention, participants were advised to maintain their usual activities and continue their routine medical treatments. Assessments were performed at baseline and after an 8-week waiting period. After assessments, patients who wished participated the tele-yoga program. The following inventory was used for assessment: Bath AS Disease Activity Index (BASDAI) for disease activity, Bath AS Functional Index (BASFI) for functionality, Bath AS Mobility Index (BASMI) for spinal mobility, ASAS Health Index, Pittsburgh Sleep Quality Index (PSQI), Short Form-36 (SF-36), Hospital Anxiety and Depression Scale (HADS), Perceived Stress Scale (PSS).
Results: The groups were similar at baseline in terms of age, height, weight, body mass index, gender and physical activity level ($p>0.05$). While all parameters improved significantly in the tele-yoga group ($p<0.05$), no change was observed in the control group after 8 weeks ($p>0.05$). When the changes in the tele-yoga group and the control group were compared, the improvements in the BASDAI, BASFI, BASMI, ASAS Health Index, SF-36 Physical Function, SF-36 Role Physical, SF-36-Bodily Pain, PSQI and PSS were found to be statistically significant in the tele-yoga group ($p<0.05$).
Conclusion: According to our preliminary results, tele-yoga is beneficial in reducing disease activity and stress, improving functional level, spinal mobility, sleep quality and quality of life. Due to its therapeutic effects, tele-yoga can be considered as an alternative approach for AS patients.
Disclosure of Interests: None declared
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POS1500-HPR BABS ON A MISSION: AN EXPERIMENTAL STUDY ON THE EFFECTS OF MESSAGE FRAMING AND THE USE OF A PATIENT TESTIMONIAL ON BELIEFS AND INTENTIONS OF OSTEOARTHRITIS PATIENTS

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Background: It is important that patients receive appropriate and reliable information that effectively targets beliefs in order for them to adhere to health behaviors. Framing (focusing on either gains or losses; [1]) is one of the most commonly used techniques in health communication to influence beliefs. In addition, the use of a testimonial in educational material might strengthen effects as intentions to adhere to health behaviors seem to rely strongly on testimonies of other patients. However, little is known about the potential of framing and patient testimonies to impact beliefs and change in health behaviors in osteoarthritis (OA).
Objectives: To study the effects of 1) message framing and 2) patient testimonies on beliefs about and intentions to be physically active and use pain medication.
Methods: We conducted an experiment consisting of a 2 (gain-frame vs loss-frame) x 2 (testimonial versus informative message) factorial design. Members of a research panel (n=639) with a self-reported diagnosis of knee OA were invited to participate. Participants were randomized into one of four video messages applying framing and the use of either a testimonial or facts. The messages (mean (SD) words 1073 (129)) were audiotaped by the same female speaker, subtitled, and complemented with images (duration of ~10 minutes). The four different combinations were: informative-loss ("If you are not physically active, this can lead to more pain[…]."), informative-gain ("If you are physically active, this can lead to less pain[…]."), testimonial-loss ("When I wasn't physically active, I experienced more pain[…]."), testimonial-gain ("When I was physically active, I experienced less pain[…]."). After this video, participants filled out a questionnaire on socio-demographic and disease characteristics, and rated 3 statements concerning beliefs on a 7-point Likert scale (completely disagree – completely agree), and one 7-point Likert scale item on intentions (I do not do this now and am not planning doing this – I am doing this already for more than 6 months) each for both physical activity and pain medication based on the Theory of Planned behavior questionnaire [2]. ANOVA was used to assess the main and interaction effects of framing and the use of a testimonial on mean beliefs and intentions.
Results: A total of 154 respondents completed the questionnaire (Table 1). Framing nor the use of a testimonial impacted beliefs and intentions on physical activity. Loss framing resulted in more positive beliefs about pain medication (mean (SD) 5.5 (1.6)) than gain framing (mean (SD) 4.9 (1.9), p=.04, 95% CI [0.0, 0.1]). Within the loss frame, the patient testimonial scored significantly more positive on pain medication beliefs (mean (SD) 5.0 (1.7)) than the informative message (mean (SD) 6.0 (1.1), p=.02, 95% CI [0.1, 1.6]) (Figure 1).

Table 1. Characteristics of participants (n=154)

Female, n (%)	110 (71)
Age (in years), mean (SD)	62.3 (7.9)
BMI, mean [kg/m^2], (SD)	27.3 (4.4)
Daily functioning (KOOS[a]; 0-100), mean (SD)	64.5 (18.0)
Pain VAS (0-10), mean (SD)	4.6 (2.2)
Symptoms for more than five years, n (%)	96 (62.3)
Presence of OA in other joints, n (%)	85 (55.2)
Knee replacement, n (%)	32 (20.8)
Presence of comorbidities, n (%)	111 (72.0)

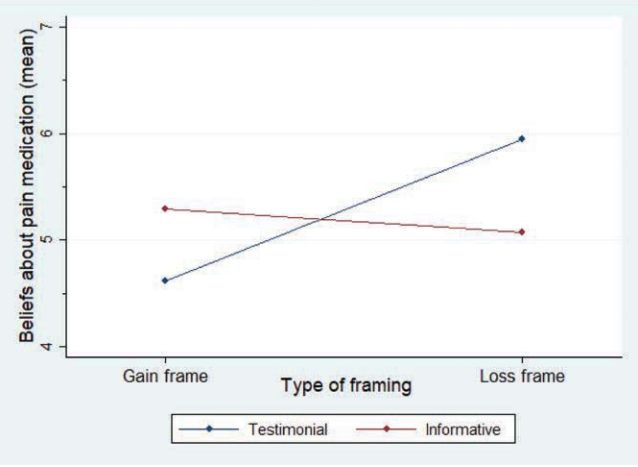

Figure 1. Interaction of framing and the use of a patient testimonial on beliefs about pain medication

Conclusion: This study showed that stating the disadvantages of nonadherence to pain medication resulted in more positive beliefs about pain medication than stating the advantages of adherence. The use of a patient testimonial within this loss frame strengthened the effect. Our findings indicate that health care providers should be aware of the potential effects of emphasising either gains or losses in educational messages to their patients.
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POS1501-HPR ADDRESSING THE VOCATIONAL DEVELOPMENT OF YOUNG PEOPLE WITH LONG-TERM HEALTH CONDITIONS IN HEALTH CARE SETTINGS: A SYSTEMATIC REVIEW AND MIXED METHODS SYNTHESIS

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Background: Long term health conditions (LTHC) such as rheumatic conditions have significant impact on the biopsychosocial development of young people (YP) including vocational development. Educational transitions are prominent during adolescence and young adulthood yet not all transitional care programmes in rheumatology address this area [1].

Objectives: To identify and synthesise the benefits and experiences of addressing the vocational development of YP with LTHC in health care settings.

Methods: A mixed methods synthesis approach [2] was employed. We systematically searched 10 bibliographic databases. Restrictions were applied on publication date (1996-2020) and publication language (English). Articles reporting quantitative and/or qualitative primary research on addressing vocational needs/issues of YP with LTHC in health care settings were included. YP was defined as 10-24 years [3]. Two reviewers independently screened records using predetermined inclusion/exclusion criteria [4]. Quality appraisal was undertaken following study selection. Qualitative data were synthesised thematically. Quantitative data were synthesised narratively, given that a pooled synthesis was not considered appropriate. A cross-study synthesis integrated findings from both the qualitative and quantitative syntheses.

Results: 43 articles were included. The quality of qualitative evidence was generally good; but the quality of quantitative evidence was generally poor. The thematic synthesis of stakeholders' perspectives (n=23 qualitative studies) resulted in seven recommendations for interventions: provide skills training; provide psychological support; offer to liaise with key stakeholders in educational/workplace settings; provide specialist career advice; provide information, signposting and facilitate access to supporting services; provide/facilitate access to social support; provide flexible care and optimal disease management to support education/employment transitions. The narrative synthesis summarised results of 17 interventions (n=20 quantitative studies). The cross-study synthesis mapped interventions against recommendations arising from stakeholders' perspectives: Four interventions met five recommendations; two interventions met four recommendations; five interventions met three recommendations; six interventions met two recommendations. Transitional care interventions were the type of intervention that most comprehensively met the recommendations. The way in which interventions addressed vocational issues was not always clear, with some interventions addressing them explicitly/directly (reporting vocational intervention components) and others implicitly/indirectly (reporting vocational outcomes only). Interventions where vocational issues were the core, defining component of the intervention were lacking.

Conclusion: Stakeholder evidence suggests vocational development is an important area to address in the care of YP with LTHC such as rheumatic diseases. The resulting set of recommendations provides guidance for future research in this area and transitional care developments in rheumatology. Further work in this area should address these aspects to enable better quality evidence and ensure consistency.

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Disclosure of Interests: None declared

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POS1502-HPR A PHYSICAL EXERCISE PROGRAM FOR THE MANAGEMENT OF FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AT THE TIME OF PANDEMIC: A PILOT STUDY

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Background: Fatigue in SLE has a multifactorial origin and disease activity seems to contribute only minimally to its genesis. Therefore, non-pharmacological therapeutic strategies should also be considered in the management of fatigue. There is some evidence on the effectiveness of aerobic exercise programs in improving fatigue, without a negative impact on disease manifestations.

Objectives: the aim of this study was to analyze fatigue and Health Related Quality of Life (HRQoL) in a monocentric cohort of patients with SLE, in a condition of stable remission or low disease activity, before and after a program of physical exercise, through the administration of validated Patient Reported Outcomes (PROs).

Methods: this is a cross-sectional interventional study which included patients with SLE, aged between 18 and 55 years, in a condition of stable (≥12 months) remission (DORIS)[1] or low disease activity (LLDAS)[2]. Patients enrolled had a FACIT score ≤40 in the previous 6 months. Patients with other possible causes of fatigue (e.g.: anemia, hypothyroidism, severe vitamin D deficiency), active arthritis or physical disabilities were excluded. For each patient, demographics, comorbidities, treatment, clinical and laboratory data were collected. Disease activity was evaluated with the SELENA-SLEDAI and organ damage with the SLICC/DI. Each patient completed the following PROs before and after the interventional program: SF-36, FACIT-Fatigue, LIT, HADS. Due to the limitations related to the COVID-19 pandemic, the physical exercise sessions were carried out using the Google Meet digital platform. Patients were asked to participate to at least 70% of the lessons. The physical exercise program included moderate intensity aerobic exercises (muscle strengthening, joint mobility, breathing, static and dynamic stretching, balance and neuro-dynamics); workouts were performed 3 times a week, consisting of 60 minutes each. The program lasted for 12 weeks.

Results: we enrolled 12 female patients, regularly followed at the Rheumatology Unit of Pisa; only 9 of them completed the study (mean age 38.56 ± 9.1 years; median disease duration 7 years (IQR 5,25-9,75)). 8/9 were in stable remission, while 1/9 was in LLDAS for the presence of leukopenia. 2/9 patients presented organ damage, one for cataract and one for renal insufficiency, while none presented damage in the musculoskeletal system. 33.3% of patients had fibromyalgia. 88.8% was on treatment with Hydroxychloroquine, 55.5% was on low dose steroids (2±1.9 mg/daily), 33.3% was on Mycophenolate Mofetil; only 1 patient was on Belimumab. All PROs showed a trend to improvement at the end of the 12-week program of physical activity (Table 1). We demonstrated a statistically significant improvement of: FACIT, LIT, depression score of the HADS and MCS of the SF-36. The items of role physical (RP), vitality (VT) and mental health (MH) of the SF-36 also showed a significant improvement.

Table 1. Scores of PROs before and after the physical exercise program.

PROs	Mean scores at baseline	Mean scores after the 12-week exercise program	p
FACIT	30.2 ± 4.9	39.3 ± 7.2	0.01
PF	73.18 ± 10.9	78.9 ± 10.5	0.18
RP	50 ± 13.2	67.4 ± 18.6	0.03
BP	52 ± 12.1	54.1 ± 11.1	0.73
GH	41.7 ± 11.1	48.4 ± 11.1	0.07
VT	34.7 ± 12.5	59.0 ± 14.2	0.002
SF	58.3 ± 15.6	66.7 ± 16.7	0.3
RE	55.5 ± 21.5	69.4 ± 18.0	0.13
MH	58.3 ± 15.8	67.2 ± 16.2	0.03
PCS	43.8 ± 4.0	46.1 ± 4.8	0.19
MCS	38.6 ± 8.8	45.6 ± 8.7	0.03
LIT	36.9 ± 14.2	27.5 ± 14.1	0.05
HADS (A)	9 ± 4.4	7.7 ± 3.2	0.4
HADS (D)	7.9 ± 4.4	5.1 ± 2.96	0.05

Conclusion: In a small cohort of SLE patients in remission but with severe fatigue, in the difficult context of COVID-19 pandemic, we demonstrated that an online program of physical exercise may determine a significant improvement of fatigue, perception of disease burden and mental health. In the context of a multidisciplinary management, finding effective intervention programs to improve fatigue and HRQoL in SLE patients appears of utmost importance, with the final aim of improving patients' health status.

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[1] PMID 27884822; [2]PMID 26458737

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POS1503-HPR **THE VALUE OF REMOTE CONSULTATIONS WITH A PHYSIOTHERAPIST, SPECIALISED IN AXIAL SPONDYLOARTHRITIS DURING THE COVID 19 PANDEMIC: EVALUATION OF A MEMBER-SUPPORT PROJECT WITH THE NATIONAL AXIAL SPONDYLOARTHRITIS SOCIETY.**

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Background: COVID-19 caused significant disruption to Axial Spondyloarthritis (AxSpA) services during the intial 2020 lockdown[1]. In response, The National Axial Spondyloarthritis Society (NASS) piloted provision of remote consultations with a physiotherapist specialised in the management of AxSpA to their members in urgent need. This project was funded by the UK National Lottery Fund
Objectives: To provide a total of 130 hrs of remote consultation to members of NASS, unable to access specialist care and in need of self-management advice for their condition
Methods: Remote consultations were offered to NASS members from Sept 2020 to Feb 2021. The preferred format being 1hr assessment and 2 x 30 min at 1 and 3 weeks from assessment. Participants consented to video consultations via Zoom and the inclusion of anonymised outcomes and comments in the project evaluation. Patient Reported Outcomes (BASDAI and BASFI) were collected immediately prior to assessment, at final consultation and in April 2021, between 8- 16 weeks from final consultContent was individually tailored, centring on self-management (pacing, sleep management), education (AxSpA pathology, medication) and individualised exercise plans. Exercise plans were formulated through "Rehab My Patient" software, including links to YouTube video references and daily exercise log sheets.
Results: 67 members received online consultations, 63 receiving the full 3 sessions. Missed appointment rate = 2.5%
Participants represented a wide geographical area across England and a spread in time since diagnosis.
Patient Reported Outcomes Measures (PROMs) on assessment:

- Mean BASDAI score (n=55) on assessment = 5.8
- Mean BASFI score on assessment (n=56) = 5.5

24 participants returned PROMS at final consultation, 10 at longer follow-up (8-16 weeks). Results for complete data set (n=10):

Table 1.

PROMS	Assessment	Final consultation	Follow-up
Mean BASDAI	5.0	4.3	4.0
Mean BASFI	5.1	4.0	4.1

Satisfaction:
60 members completed an online feedback survey provided by NASS:
9 Feedback to questions were asked, with a satisfaction scale of 1-5 (ascending positivity)
99.6% of all scores were 3 or above.
Example responses:

- How would you rate the overall experience: 92% = 5, 100% = 3-5
- To what extent do you feel more confident to manage your condition: 40% = 5, 100% = 3-5
- How useful was it to be in direct contact with a Physiotherapist: 93% = 5, 100% = 3-5

46 members chose to leave additional, overwhelmingly positive comments, with 2 obvious themes arising:
1)The **value of the experience and knowledge of the therapist**. "was great to have the guidance and support of a professional who knows what they are talking about when it comes to AxSpA"
2)The **value of education in condition management** "set me back on track", "very helpful for my mental strength in dealing with this enduring disease", "I learned so much about my AS and ways to keep mobile"
Conclusion: A set of 1-3 sessions per person achieved desirable patient reported outcomes with modest and enduring improvements seen in disease activity and function. This pilot project enabled those living with Axial SpA across England access to a Physiotherapist highly experienced in treatment of their condition. The majority of participants reported having no previous experience of seeing a therapist with specialised knowledge of their condition. The knowledge and experience of the clinician was a key theme in the positive nature of feedback linking to another key theme of improved confidence to manage their condition. These results highlight the value to patients of specialised knowledge amongst health professionals. Remote consultations may provide access to specialist knowledge "out of area" and may be an efficient method of delivering self-management advice
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POS1504-HPR **THE EFFECT OF REMOTE AND FACE-TO-FACE STABILIZATION EXERCISES ON FUNCTIONAL CAPACITY OF ASYMPTOMATIC INDIVIDUALS**

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Background: In recent years, it has been emphasized that preventive rehabilitation approaches for problems such as low back and neck pain, which are very high in health expenditures, are more cost-effective than treating them. Due to the Covid-19 pandemic, risk factors for individuals' spinal health have increased and access to health care has become difficult (1). Therefore, interest in tele-rehabilitation, which is an important part of telehealth, has increased recently.
Objectives: This study aims to investigate the effectiveness of remote and face-to-face spinal stabilization exercise training on functional capacity tests in asymptomatic individuals.
Methods: Individuals who did not have chronic low back and neck pain and between the ages of 18-55 were included in the study. While the face-to-face group traditionally exercised under the supervision of a physiotherapist, the tele-rehabilitation group exercised with videoconferencing and asynchronous video recordings. Both groups performed progressive spinal stabilization exercises 3 days a week for 8 weeks (2). Before and after the training functional capacity tests (repetitive reaching, lifting object overhead, and sustained overhead work) were performed (3).
Results: Twenty (11 female, 9 male) individuals with a mean age of 30,252±9.06 and a mean body mass index of 24.36±4.09 were included in the study. There was no difference between the baseline values of functional capacity test scores of both groups ($p>0.05$). There were significant improvements in the repetitive reaching and sustained overhead work tests after the exercise program in both groups ($p< 0.05$), while there was no difference in the lifting object overhead test ($p> 0.05$). There was no difference between the changes in functional capacity test scores between the groups after the training ($p> 0.05$).
Conclusion: According to our preliminary results, face-to-face and remote spinal stabilization exercise programs caused similarly positive changes in functional capacity test scores (repetitive reaching, sustained overhead tests) of asymptomatic individuals. These exercises are known to improve deep muscle activation. This development may have led to improvements in tests, which mostly evaluate speed, coordination and endurance. Weight lifting capacities have not changed. This may be because stabilization exercises focus more on deep muscle activation and not on developing superficial muscle strength like upper extremity strength(2). Success of exercise training with telerehabilitation may have contributed to the younger population and possibly better adaptation to technology. It is planned that these preliminary results will be extended and make greater contributions to the current literature.
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POS1505-HPR **FEASIBILITY OF AN ONLINE "FATIGUE AND ACTIVITY MANAGEMENT EDUCATION IN WORK" (FAME-W) INTERVENTION FOR INDIVIDUALS WITH INFLAMMATORY ARTHRITIS**

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Background: A **FA**tigue **M**anagement **E**ducation in **W**ork (FAME-W) programme was developed for individuals with inflammatory arthritis to manage fatigue in work (McCormack et al, 2018).
Objectives: This study tested the feasibility and acceptability of an online format of FAME-W for a future definitive intervention trial.
Methods: This was a mixed methods study. Participants were randomly allocated to intervention (IG) or control group (CG). The IG received a four-week online FAME-W. The CG received a FAME-W handbook. Participants were required to complete questionnaires on work presenteeism, fatigue, mood, Health Related Quality of Life (HRQOL) and pain at baseline (T0), and two weeks following intervention (T1). They also attended a focus group and individual interviews. Data were analysed using descriptive statistics
Results: Seven of ten individuals recruited participated in the study (intervention = 3, control =4). The majority of participants in both groups had Rheumatoid Arthritis and were working full-time in non-manual jobs. The mean age of intervention participants was 53 ± 10.4 and 56.5 ± 3.7 for the controls. Most of the intervention group were males and the majority of controls were female. Disease activity at baseline was similar for both groups: 3.33 ±2.5 intervention; 3.0 ± 1.8 control. At follow-up, disease activity did not change for intervention group (3.3 ±.57) and reduced slightly for CG (2.7 ±2.4). Slight improvements were noted for both groups in presenteeism and fatigue between T0 and T1 (Table 1). There was no change in anxiety levels of the intervention group, with improvements noted for controls. Greater improvements were noted for the intervention group for depression and HRQOL. Pain measures showed increased pain for controls at T1 in comparison to the intervention group.

Table 1.

Measure	Intervention (n=3) Median (min-max)		Control (n=4) Median (min-max)	
	T0	T1	T0	T 1
Work Role Function	84.1 (81.9-92.1)	85.7 (83.4-97.2)	84.8 (63.7-93.9)	84.9(72.9-94.5)
Fatigue	13.0 (8.0-14.0)	10.0 (10.0-14.0)	14.0 (12.0-17.0)	12.5 (12.0-17.0)
HADS Anxiety	5.0 (3.0-6.0)	5.0 (3.0-6.0)	10.0 (7.0-14.0)	8.0 (6.0-12.0)
HADS Depression	5.0 (3.0-5.0)	3.0 (2.0-4.00)	5.0 (3.0-11.0)	6.0 (3.0-9.0)
HRQOL	68.0 (47.0-90.0)	75.0 (65.0-90.0)	70.00 (50.00-95.00)	66.5 (50.0-95.0)
Pain Level	4.0 (100-5.0)	2.0 (2.0-4.0)	1.5 (1.0-4.0)	4.5 (200-10.0)
Pain Intensity	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.5 (0.0-1.0)	1.5 (0.0-2.0)

Those allocated to FAME-W attended all four sessions. FAME-W participants reported that the programme content was comprehensive and relevant. They stated that the occupational therapist facilitator was able to "*see things from a different perspective for managing symptoms*". Participants also reported a better understanding of fatigue: "*It helped me understand my fatigue. If you understand it you can manage it better*". The online delivery format was favored over attending a centre-based programme. Control participants reported the handbook content as "*informative and reassuring*". All participants fully completed all study questionnaires and attended focus groups and interviews.
Conclusion: This feasibility study showed that an online programme to improve work ability was feasible and acceptable to individuals with Rheumatic Diseases. Study measures were completed in full and adherence rate was 100% for the intervention. The findings support a definitive intervention trial of FAME-W.
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POS1506-HPR **SYSTEMATIC LITERATURE REVIEW TO INFORM THE EULAR TASK FORCE FOR RECOMMENDATIONS/ POINTS TO CONSIDER FOR THE NON-PHARMACOLOGICAL MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS**

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Background: The heterogeneity and complexity of the chronic autoimmune diseases systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) necessitate comprehensive person-centred management, including non-pharmacological approaches. Recommendations for non-pharmacological management are currently lacking.
Objectives: To perform a systematic literature review to inform the EULAR task force for recommendations/points to consider for the non-pharmacological management of adult patients with SLE and SSc. Among research questions formulated by the task force, we aimed at identifying (i) non-pharmacological interventions that have been evaluated and (ii) their target health domains or organ systems.
Methods: We searched the Medline, Embase, Web of Science Core Collection and CINAHL for articles published between January 2000 and June 2021. From the initial search (n=15,803), 2 researchers independently performed the article selection. Conflicts were discussed until consensus with 2 additional researchers. Subsequent data extraction from the selected articles was performed by 4 researchers, with an overarching guidance by 2 additional researchers. Risk of bias assessment was performed according to Joanna Briggs Institute Critical Appraisal Checklists.
Results: A total of 111 articles for SLE and 75 for SSc were selected for analysis. Non-pharmacological interventions identified for SLE included physical exercise (n=34), psychological support (n=21), dietary therapy and nutrition (n=15), patient education and self-management (n=14), photoprotection (n=5), medication adherence interventions (n=5), complementary and alternative medicine (CAM) e.g., Chinese medicine (n=5), multidisciplinary care (n=4), and phototherapy/laser modalities (n=4). Interventions identified for SSc included physical exercise e.g., hand, oral and general exercise (n=21), phototherapy/laser modalities or shockwave therapy (n=15), patient education and self-management (n=10), CAM (n=8), hand-bathing e.g., in paraffin (n=5), manual therapy e.g., osteopathic manipulative treatment (n=5), dietary therapy and nutrition (n=5), oral hygiene (n=2), hyperbaric oxygen or ozone therapy (n=2) and multidisciplinary care (n=2). Target health domains and organ systems identified within SLE included (in descending order) (i) disease activity, (ii) health-related quality of life (HRQoL), (iii) depression/anxiety, (iv) fatigue, (v) organ damage, (vi) inflammatory markers, (vii) psychological stress, (viii) pain, (ix) body composition/ anthropometry, and (x) aerobic capacity. Intervention targets in SSc included (i) functional impairment e.g., hand mobility, (ii) skin sclerosis including microstomia, (iii) HRQoL, (iv) pain, (v) circulation e.g., Raynaud's phenomena and telangiectasias, (vi) skin ulcers, (vii) oral hygiene, (viii) fatigue, (ix) digestion, and (x) depression/anxiety.
Conclusion: Physical exercise was a frequently researched non-pharmacological intervention within both SLE and SSc. While psychological support and dietary therapy/nutrition were frequently investigated in SLE, phototherapy modalities were common in SSc. Patient education and self-management was advocated in both SLE and SSc literature. HRQoL was a frequent target domain in both diseases; while disease activity and psychosocial domains emerged as important targets in SLE, functional impairment and skin-related aspects constituted predominant targets in SSc. Efficacy of interventions varied considerably across studies. Current evidence is limited by the overall small study populations, and the lack of large RCTs.

Table 1. Studies categorised by design.

Study design	SLE	SSc
Meta-analysis of RCTs	5	1
RCT (including long-term follow-up or post-hoc analysis)	41	28
Non-randomised longitudinal controlled/cohort studies	28	7
Retrospective cohort study, cross-sectional or case-control study	16	2
Case series or open pilot studies	21	37

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POS1507-HPR INVESTIGATION OF THE EFFECTS OF PELVIC FLOOR TRAINING ON PAIN, SEXUAL DYSFUNCTION, AND QUALITY OF LIFE IN FEMALE PATIENTS WITH SJOGREN

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Background: Sjogren's syndrome is a chronic systemic inflammatory disorder (classified as an autoimmune disorder) characterized by lymphocyte infiltrates in exocrine organs. This syndrome is classified as primary sjogren's or secondary sjogren's. Dryness of the eyes, oral cavity, larynx, pharynx and vagina is common in primary sjogren's syndrome. Although vaginal dryness is a symptom seen after menopause in the healthy population, it often occurs at a young age in cases with primary sjogren's. The presence of urogynecological complaints in women with pSS adversely affected the health-related quality of life of pelvic floor function. However, it has been shown that the sexual functions of women with pSS are also negatively affected. Sexual dysfunction and increased pain were seen with increasing pelvic floor dysfunctions. Many studies showing that pelvic floor training has been accepted in the literature as the first step in the treatment of pelvic floor dysfunctions to increase pelvic floor strength and effectiveness. In addition, the positive effects of pelvic floor exercises on sexual functions have been supported by studies.

Objectives: The aim of this study was to investigate the effects of pelvic floor training on pain, sexual dysfunction and quality of life in female patients with pSS and determine whether pelvic floor training was superior to education program.

Methods: 46 pSS patients (46 female) with an average age of 47.78±9.18 were included in the study. Patients were divided into two groups by block randomization method. Group 1 received 30 minutes of pelvic floor training program every day as a home exercise for 8 weeks. Group 2 received education about pelvic floor muscles and daily living activities. Health Assessment Questionnare (HAQ) was used to evaluate the quality of life, Visual Analog Scale (VAS) and Pelvic Pain Impact Questionnaire (PPIQ) was used to evaluate degree of pelvic pain, Pelvic Floor Disability Index-20 (PFDI-20) was used to evaluate the degree of certain discomfort caused by pelvic symptoms in women, Female Sexual Function Scale (FSFI) was used to evaluate the sexual dysfunction, Pelvic Floor Impact Questionnaire (PFIQ-7) was used to evaluate the effect of bladder, bowel, and pelvic symptoms on the individual's activities of daily living, social relationships, and emotions. All evaluations were performed at baseline and at the end of the 8th week.

Results: When the groups were compared before training, there was no significant difference (p> 0.05). In post-training comparisons, there was a significant difference in FSFI, VAS, PPIQ, PFIQ-7, PFDI-20 in pelvic floor training group (p:0.02-0.00); in FSFI-lubrication, PFIQ-7 and PFDI-20 (p:0.00-0.03) in education group. In addition, after post-training, pelvic floor training group was found to be superior in terms of FSFI total (Z: -3.40, p: 0.01), FSFI-orgasm (Z: -3.13, p: 0.02), FSFI-satisfaction (Z: -2.27,p: 0.02), FSFI-pain (Z: -2.42, p: 0.01), PFDI-20 (Z: -3.42, p: 0.00), POPDI-6 (Z: -3.00, p: 0.00), CRADI-8 (Z: -2.18, p: 0.02), UDI-6 (Z: -3.64, p: 0.00) compared with education group.

Conclusion: As a result of our study, pelvic floor training has a positive effect on sexual dysfunction and discomfort caused by pelvic symptoms in patients with pSS. Pelvic floor training should be included in rehabilitation programs as a home exercise to improve sexual function and pelvic floor dysfunctions for patients with pSS.

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POS1508-HPR USE OF PHYSICAL THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS OR AXIAL SPONDYLOARTHRITIS: THE PATIENT´S PERSPECTIVE

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Background: In national and international management guidelines physical therapy (PT) is a recommended treatment for people with inflammatory arthritis (IA). Based on multiple systematic reviews, concluding that supervised exercise therapy and exercise promotion is an effective and safe PT treatment option in patients with IA, recommendations in particular endorse active PT treatment. In order to monitor and enhance the quality of PT in clinical practice, knowledge about its delivery, including its active content, is needed.

Objectives: To assess the use, frequency, duration and content of PT in patients with IA.

Methods: In this cross-sectional, national study a link to an electronic questionnaire addressing people with rheumatic and musculoskeletal diseases was published between December 2020-July 2021 by the Dutch Arthritis Foundation via their website, newsletter and various social media. It comprised questions on demographic and health characteristics, the EuroQol 5-Dimensions 5-Levels (EQ5D5L) and 29 questions on the usage of PT currently and/or in the past 12 months and, if applicable, the duration, frequency and content of the PT treatment. The content of PT was categorized into exercises (active aerobic, muscle strengthening, range of motion and/or functional exercises), manual treatment, physical modalities and counseling/education. Only data from patients self-identifying as diagnosed with rheumatoid arthritis (RA) and/or axial spondyloarthritis (axSpA) were used for the current study.

Results: A total of 267 people with RA (mean (SD) age 54 (12) years, 96% female) and 104 people with axSpA (age 47 (13) years, 88% female) (10 patients with both diagnoses) completed the questionnaire. More than 90% were treated by a rheumatologist; the mean (SD) EQ5D5L of people with RA was 0.62 (0.2) and of axSpA 0.59 (0.2). 172 RA respondents (64%) reported the use of PT related to their RA (162 individual PT, 1 group PT, 9 both individual and group PT). In axSpA, the rate was 87 (84%; 77 individual PT, 2 group PT, 8 both individual and group PT). Of those reporting individual PT treatment, the duration was long-term (> 3 months) in 134 (89%) and 70 (89%) of the respondents with RA and axSpA respectively, with a duration of more than 2 years in 67 (44%) and 38 (48%). In all users of individual PT, the mean frequency was once per week or less in 116 (77%) of the RA and 63 (80%) of the axSpA patients. Proportions were based on number of respondents to questions on individual PT. Concerning the content of individual PT, and taking into account both short-term and long-term use, for active exercises, the proportion of patients reporting aerobic, muscle strengthening, range of motion or functional exercises ranged from 40-66% in RA and 24-73% in axSpA patients. Regarding manual treatment, the proportions were 61% and 58%, in RA and 73% and 72% in axSpA for massage and passive mobilizations, respectively. With respect to physical modalities (passive), the modality most frequently mentioned were kinesiotaping and dry needling (40 and 25% and 43 and 32% in RA and axSpA). For counseling/education, exercises to perform at home (70 and 78%) and physical activity (PA) promotion (48 and 49%) were most often reported in both RA and AxSpA.

Conclusion: Long-term use of PT is common in patients with RA and AxSpA. Apart from active treatment modalities (exercises) and promoting recommended PA, passive treatment options appear to be relatively often used. The results must be interpreted with caution, as the respondents may not constitute a representative sample of the IA population, yet warrant further research.

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POS1509-HPR CHANGES IN SELF-EFFICACY AND USE OF ENERGY CONSERVATION STRATEGIES FOLLOWING PARTICIPATION IN THE FATIGUE MANAGEMENT EDUCATION FOR INDIVIDUALS WITH SYSTEMIC SCLEROSIS (FAME-ISS)

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Background: Fatigue is one of the most prevalent and disabling symptom of systemic sclerosis (SSc). No fatigue specific programs exist for people with SSc despite the negative impact on daily life activities. However, recent literature has shown that using pacing and other energy conservation strategies, has been associated with reduction in fatigue.
Objectives: The purpose of this pilot study was to evaluate changes in self-efficacy and use of energy conservation strategies after participation in Fatigue and Activity Management Education for Individuals with Systemic Sclerosis (FAME-iSS).
Methods: Adult participants were recruited from the Scleroderma Foundation chapters and social media to participate in a 6-week, virtual group program focused on SSc-related fatigue. Inclusion criteria: ≥18 years of age, access to device with videoconferencing capabilities, and at least moderate fatigue determined by degree, severity, and distress (scales: 1-10). The program, led by occupational therapists included sessions on factors related to fatigue, management of energy, pain, stress, physical activity and nutrition. At baseline, participants completed a demographic questionnaire, the Self-Efficacy for Performing Energy Conservation Strategies Assessment (SEPESCA) to measure confidence using energy conservation strategies. At post-intervention and 3-month follow-up, participants also completed the Energy Conservation Strategies Survey (ECSS) to identify use and effectiveness of 14 energy conservation strategies (e.g. changing body positions, planning and prioritizing, communicating needs) and a qualitative interview to contextualize their responses. Descriptive statistics (means, standard deviations) were used to analyze quantitative data.
Results: The sample for the pilot study included 18 participants (89% women; age 52 ± 11.6 years) with established SSc (disease duration= 13.7 ± 14.5 years). 83% participants completed 100% of FAME-iSS sessions. Directly following the program all 14 energy conservation strategies were used by at least seven (39%) participants. The most frequently used strategy was "*planned day to balance rest and activity*" which was used by 17 participants post-intervention. (see Table 1). At the three-month follow-up the there was a decline in use for 50% of the strategies and an increase in use for the other 50%. Of those who reported not using energy conservation strategies, the most frequent reason provided by participants was that they were already using the strategy prior to attending FAME-iSS. The mean strategy effectiveness scores varied at both time points with "*adjusting priorities*" the most effective strategy at T2 and "*delegating activities*" the most effective at T3. While not statistically significant, participants trended towards improved self-efficacy scores for energy conservation strategies (baseline: 6.8 (2) post-intervention: 8.1 (1.4); 3-month follow-up: 8.4 (2.8) Participants qualitatively reported that FAME-iSS led to the sharing of new fatigue management strategies and increased attention to their daily activities.
Conclusion: This pilot study showed that FAME-iSS resulted in increased self-efficacy in use of energy conservation strategies in participants with established SSc. New behaviors were adapted that participants felt reduced their fatigue. The virtual format allowed for sharing of strategies and availability to more people.
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POS1510-HPR IDENTIFYING THEORY-DRIVEN THERAPEUTIC CONTENT FOR A SMARTPHONE APP FOR THE SELF-MANAGEMENT OF SJOGREN'S SYNDROME

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Background: Technology-supported self-management of long-term conditions (e.g., through the use of smartphone apps) provides easily accessible support. However, currently there are no systematically developed, evidence-based smartphone apps for Sjogren's Syndrome. We took an agile approach to developing such an app: instead of starting "from scratch" we deemed it more efficient and scientifically sound to digitalise relevant components from existing, evidence-based interventions for the symptoms of SS.
Objectives: The present study was desk research, which aimed to deconstruct interventions and resources down to units of theory-driven therapeutic content, to then select from, for the inclusion in an app for the self-management of SS.
Methods: We used deductive and inductive content analysis, to identify behaviour change techniques (BCTs)[1] and behaviour change methods (BCMs)[2]. The materials consisted of published fatigue, pain and sleep interventions (e.g. [3] and [4]), as well as private-facing clinician notes and public facing resources on self-management from Versus Arthritis and the UK NHS's CRESTA fatigue clinic.
Results: We found 38 active ingredients from the BCT Taxonomy and the BCM intervention mapping approach frameworks, of which at least 14 were overlapping in function. Importantly we noted that BCTs and BCMs were formulated in various ways pertaining to how the interventions should be delivered (form of delivery-FoD) [5]. Further qualitative analysis revealed 6 themes relating to FoD. The theme *Interactivity* involved presenting information in ways that would involve the reader in actively responding to it in various ways. The theme *Reflection* was about engaging the recipient in in-depth consideration of their own experience with symptoms and self-management processes. The theme *Validation* encompassed all the ways in which the illness and management experience was socialised and normalised to remove stigma and sense of isolation. The theme *Treatment Rationale* was about providing an a-priory transparent, sound, and compelling justification for the self-management actions required from recipients. The theme *Discourse* pertained to how information was being communicated, e.g., with language that is warm, simple, assertive, etc. Finally, the theme *Approaches* was about the therapeutic origins of the active ingredients, e.g. Second and Third Wave CBT. These themes indicate that meaningful therapeutic content is missing from commonly used theoretical frameworks for the development of interventions.
Conclusion: Our findings indicate that meaningful therapeutic content is missing from commonly used theoretical frameworks for the development of interventions. Interventions should not just include BCTs and methods, but also active ingredients pertaining to how these techniques and methods are delivered, i.e., active ingredients relating to FoD. Reflection deserves particular attention in self-management, as it is unclear empirically in apps what is the most effective way to produce the most useful psychological and behavioural insight, and for whom. FoD is a component of intervention development that requires systematising and the present findings can contribute to such efforts.
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HPR Patients- perspectives, functioning and health (descriptive: qualitative or quantitative)

POS1511-HPR "I LEARNT SO MUCH ABOUT MY APPROACH TO BEING ACTIVE": EXPERIENCES OF PEOPLE WITH RHEUMATOID ARTHRITIS ON THE IMPACT OF A PHYSIOTHERAPIST LED INTERVENTION TO PROMOTE PHYSICAL ACTIVITY

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Background: Physical activity is an important component in the management of people with rheumatoid arthritis (RA) [1]. A Physiotherapist-led Intervention to Promote Physical Activity in people with RA (PIPPRA) was undertaken using the Behaviour Change Wheel, with the aim of examining the feasibility of promoting physical activity in RA. This qualitative study involved participants and health care professionals who participated and were involved in a behaviour change pilot RCT intervention.
Objectives: To determine, qualitatively, the acceptability of PIPPRA to participants with RA and health care professionals, in order to capture their reality.
Methods: A qualitative study design of face-to-face semi-structured interviews was undertaken. The interview schedule explored the following areas: experience of the intervention; unintended consequences; experience and suitability of outcome measures used; views regarding the intervention; perceptions of behaviour change and physical activity. Interviews were transcribed verbatim by a professional transcriber. Thematic analysis was used as an analytical approach [2]. The research team searched for patterns, analysed and coded the data, and generated themes and sub-themes. Themes were reviewed by the research team to check if they worked in relation to the coded extracts and the entire data set. The COREQ checklist provided guidance throughout [3].
Results: Fourteen participants [13 female/1 male; mean age of 59 (SD 6.3); mean RA diagnosis of 8.6 (SD 6.8) years; moderate to severe disability (HAQ-DI: 1.4 (SD 0.50)] and 8 healthcare staff [4 female/4 male; mean age of 41 (SD 5.6)] participated. Three main themes were generated from participants:- 1) Positive experience of behaviour change intervention - *"I found it very knowledgeable to help you get stronger"*; 2) Improvement in self-management - *"…….motivate me maybe to go back to doing a little bit more exercise"*; 3) Negative impact of COVID-19 on intervention – *"I don't think doing it online again would be really good at all"*. Two main themes from health care professionals:- 1) Positive learning experience of behaviour change delivery – *"Really made me realise the importance of discussing physical activity with patients"*; 2) Positive approach to recruitment – *"Very professional team showing the importance of having a study member on site"*.
Conclusion: The findings demonstrated that participants had a positive experience of being involved in a behaviour change intervention in order to improve their physical activity and found it acceptable as an intervention. However, if given the choice they would prefer the intervention delivery face to face rather than telehealth. Healthcare professionals also had a positive experience and in particular found it beneficial to their own development, in particular the importance of recommending PA to patients.
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POS1512-HPR FATIGUE AND MOOD DISORDERS AS DETERMINANTS OF QUALITY OF LIFE IN PATIENTS WITH RA TREATED WITH BIOLOGICS

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Background: Rheumatoid arthritis (RA) includes many conditions that affect joints, the tissues surrounding the joints, and other connective tissues.[1] In 2012, the prevalence of RA in the USA was estimated to be 22.7% (52.5 million adults over 18 years of age) and projected to increase to 49% (about 78 million Americans) by 2040.[2] The disease causes pain and limits physical function.[3] It is accompanied by fatigue, anxiety and even depression, which may not be considered important by those around the patient, but may be crucial for the patient.[4] Research on the impact of psychosocial factors on the quality of life (QoL) of patients receiving biologic therapy is still limited. There is a need to identify new psychological determinants affecting the course of treatment of patients with RA and their quality of life and perception of health.
Objectives: The aim of the study was to assess the level of QoL and the association of selected psychosocial (depression, anxiety, fatigue) and clinical (pain) factors with the quality of life of patients with RA treated with biologics.
Methods: Standardized questionnaires were used in the study to assess the level of anxiety and depression (Hospital Anxiety and Depression Scale), quality of life (WHOQoL-BREF), pain (Visual Analogue Scale) and fatigue (Modified Fatigue Impact Scale).
Results: A total of 63 RA patients (61.9% women) aged 52.38±16.97 years treated with biologics were enrolled in the study. Mean disease duration in the study group was 13.54±9.51 years. The level of fatigue in MFIS questionnaire was 25.96±16.14, the level of depression and anxiety assessed by HADS, respectively was (17.1±2.2 vs (20.0±2.3)). In QoL assessment, the highest scores were obtained in psychological (16.5±1.86) and environmental (14.47±- 2.22) domains, and the lowest in physical domain (11.4±-2.41). In regression analysis, pain negatively affected the psychological domain (5.11±2.55) and social life of 6.03% of patients. Patients assessed their QoL as average and almost half of the respondents (42.86%) were dissatisfied with their health. In correlation analysis, anxiety ($r=-0.472$, $p<0.001$), depression ($r=-0.322$, $p=0.01$) and mental fatigue ($r=-0.271$, $p=0.047$) significantly decreased patients' QoL in psychological domain. In multivariate analysis, depression ($R=-0.126$,$p=0.002$) was a significant independent determinant of QoL perception, disease duration ($R=-0.104$, $p=0.001$) was a significant determinant of QoL in the psychological domain, and obesity ($R=-2.427$, $p=0.013$) and depression ($R=-0.244$, $p=0.008$) were significant in the physical QoL domain.
Conclusion: The quality of life of RA patients treated with biologics is moderate. The independent determinants of QoL are obesity, depression and disease duration. There is a need to introduce diagnostics recognizing mood disorders in order to implement individual remedial projects aimed at prevention and re-education of depression and improvement of QoL.
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POS1513-HPR ASSESSMENT OF WORK CAPACITY AND PRODUCTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The main task of rheumatologists in the treatment of SLE was to reduce mortality and increase patient survival. At the same time, insufficient attention was paid to improving the quality of life, which includes getting an education, building a career and starting a family.
Objectives: Study the effect of SLE on the ability to work and productivity of patients.
Methods: 110 patients with SLE participated in a one-time anonymous survey conducted using Google Forms. A mean age of the patients included in the study was 32.8 ± 7.97 years. A mean duration of SLE was 4 years. 95.45% of patients received glucocorticoids as monotherapy or in combination with immunosuppressive medications: 63.64% hydroxychloroquine, 2.73% methotrexate, 10% azathioprine, 10% cyclosporine, 1.82% mycophenolate mofetil, and 6.36% biological therapy. Work capacity and labor productivity were assessed using the Work Productivity and Activity Improvement (WPAI) questionnaire.

Results: 110 respondents of working age took part, including 105 women (95.45%) and 5 men (4.55%). A mean age of the study participants was 32.8 ± 7.97 years, women were a mean age 32.6 ± 7.80, and men - 36.4 ± 11.44. The men surveyed have experience of SLE a mean experience of 6.8 ± 4.08 and women 6.4 ± 5.77. High activity disease was observed in 37 people (35.2%), and mild and moderate activity - in 73 (64.8%). 59 women (56%) and 2 men (40%) responded positively to the question about the availability of paid work. Ehe activity of the majority of working patients was associated with mental labor - 58 people (95%). Among the unemployed group of respondents, which made up 44.5% of the total number of survey participants, 76% of respondents associate the lack of paid work with the presence of SLE. Absenteeism was zero in 38 patients (62.3%), which indicates that more than half of the patients did not miss work during all the analyzed days. 6 out of 38 (15.8%) had a high activity disease. 5 people (8.2%) with paid work were absent from the workplace for the entire week under study (absenteeism 100%), of which 4 people had a high activity disease. A mean value of presenteeism in the group of actual workers during the study period was 50.45 ± 28.60% of working time. A mean value of absenteeism was 41.78 ± 36.73%. Work productivty loss in 61 patients with a job was 52.73 ± 30.55%. activity impairment, which was determined in all patients included in the study, was reduced by 51.68 ± 28.44%. In the course of our study, it was revealed that 44.5% of the surveyed patients with SLE of working age do not have a paid job. The absolute majority associate this fact with the influence of the disease on their ability to work. It is also important to say that 23 (37.7%) people out of 61 employees missed work due to their illness. Damage to the musculoskeletal system during the progression of SLE affects the ability to work, labor productivity and daily activity of the adult population is confirmed by the above indicators (presenteeism 50.45 ± 28.60%, absenteeism 41.78 ± 36.73%, work productivty loss 52.73 ± 30.55%, activity impairment 51.68 ± 28.44%).

Conclusion: Activity disease, functional insufficiency and damage developing as a result of the progression of SLE and ongoing therapy have a direct relationship with a decrease in labor productivity, disability and disability, which is confirmed by the values of presenteeism, absenteeism, work productivty loss and activity impairment.

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POS1514-HPR UNDERSTANDING AND CHARACTERISING PATIENT PATHWAYS TO TREATMENT FOR VERTEBRAL FRACTURES: A QUALITATIVE STUDY

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Background: Osteoporosis involves thinning of the bones, making them more prone to break. The most common osteoporotic fracture is a vertebral fracture (OVF). People with OVFs are at high risk of further fractures. To reduce this risk, guidelines recommend prescription of bone protection therapies to people who have experienced a fracture. However, many patients do not receive diagnosis. Understanding patient pathways to treatment for OVFs will provide information to improve practice and aid in effective identification and management.

Objectives: To understand and characterise patient pathways to treatment for OVFs.

Methods: Twenty-three semi-structured qualitative interviews were conducted with patients aged ≥50 years with diagnosis of OVF. Patients were recruited through two hospitals in England and were purposively sampled to capture variation in pathways to diagnosis, sex, age, comorbidities and other relevant characteristics. Interviews were audio-recorded, transcribed and analysed thematically, with themes transposed onto key stages of the patient pathway.

Results: Several factors influenced patient pathways to treatment: *Patient appraisal and self-management*: Characteristics and attitudes towards back pain impacted treatment-seeking behaviour. Patients who appraised their pain as 'different', severe or disruptive, or associated with an injury such as a fall, were more likely to seek help. Limited availability of information about OVFs and risk factors meant most patients did not associate symptoms with a potential OVF. Factors contributing to delayed consultation included the normalisation of back pain and prioritisation of comorbid conditions. Several misappraised their symptoms as a "pulled muscle" or other minor injury. Many adopted strategies to manage pain, including use of painkillers, lying flat or resting. For some, a lack of improvement in symptoms over time, combined with worsening pain, created a '*tipping point'* in seeking care. There was a moral dimension for some patients who did not want to "bother" healthcare professionals.

Healthcare professional appraisal: Differential diagnosis was a barrier to treatment and healthcare professionals interpreted OVF pain as broken ribs, muscular pain, kidney pain or sciatica. GPs tended to instigate watchful waiting, in which patients were asked to re-consult if pain did not improve. Feeling disbelieved caused some patients to become disillusioned and reluctant to re-consult and a small number of patients presented at Accident and Emergency. Those already having treatment for musculoskeletal conditions with access to specialist care, were more likely to receive timely diagnosis.

Communication of diagnosis: Patients discussed multiple methods of communication, including written communication and clinical conversations. Several expressed confusion around the use of unfamiliar medical terminology, the implications of OVFs, how many OVFs they had experienced and how they had been identified.

Treatment initiation: Bone protection therapies were not consistently prescribed after diagnosis. Patients who were familiar with these therapies were unsure whether treatment should be initiated in primary or secondary care. Patients described how they felt a need to be proactive by arranging appointments and asking for treatment.

Conclusion: The study provides novel findings about patient pathways to treatment and will be used to identify targeted solutions to improve management of OVFs. This work addresses stages of the Model of Pathways to Treatment[1] and provides detailed understanding of patients' experiences of these stages. Further work with healthcare professionals in primary care is underway to identify additional system-level factors that may impact patients' journeys to treatment.

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POS1515-HPR CONJUGAL RELATIONSHIPS IN MARRIED PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISMS

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Background: The consequences of chronic inflammatory rheumatisms (CIR) on the sexuality and the relationships between the subject and his/her partner are still underestimated and insufficiently studied.

Objectives: The aim of this study was to investigate the impact of CIR on conjugal relationships.

Methods: We conducted a cross-sectional study involving patients with rheumatoid arthritis (RA) (2010 ACR/EULAR criteria) and spondyloarthritis (SpA) (2009 ASAS criteria). All the patients included in the study were married. We collected demographic data, and participants were asked to complete a questionnaire on their conjugal relationships.

Results: We enrolled 75 patients (40 RA and 35 SpA) with a sex ratio of 0.4 and a mean age of 55.35 ± 9.81 years [22-85]. The mean chronic CIR duration was 11.85 ± 3.4 years. The mean duration of marriage was 9.5 ± 2.6 years. The mean age at marriage was 27 ± 6.41 years [19-33]. The mean number of off-springs was 4. Forty-nine percent of patients and 22.3% of the partners had a profession, respectively. Forty one percent of the partners had a chronic disease: diabetes (n=12), hypertension (n=10), dyslipidemia (n=7), CIR (n=7), coronary disease (n=3), and other conditions (n=5). A psychiatric illness was noted in 22.6% of cases: depression (n=9), anxiety (n=6), and bipolar disorder (n=2). Sixty-four percent of patients consider their spouses sympathetic to their illness. Eighty-nine percent of participants have noticed a change in their life as a couple before and after the CIR onset. According to 64% of participants, the CIR had a negative impact on their married lives. The spouses' emotional reactions to the disease were as follows: indifference (30.6%), denial (29.3%), anger (26.6%), and fear (13.6%). Patients reported being accompanied by their spouses to their medical appointments in 36% of cases, and 40% of them were asked questions by their spouses about their disease and treatment. The CIR has resulted in the termination of the marriage in 2.6% of cases.

Conclusion: Patients suffering from chronic diseases such as CIR are more frequently exposed to difficulties in their conjugal relationships. The disease has thus important consequences on the subject's quality of life, emotional and interpersonal state. A better compliance with the chronic disease and its treatment may improve the couples' relationships.
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POS1516-HPR CHRONIC INFLAMMATORY RHEUMATISMS: DOES PERIODIC FASTING REDUCE THE DISEASE ACTIVITY?

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Background: Many experimental studies have emphasized the role of periodic fasting in the adaptive responses that reduce inflammation.
Objectives: Our purpose was to assess the impact of periodic fasting on the activity of chronic inflammatory rheumatisms (CIR).
Methods: We conducted a cross-sectional study involving patients with rheumatoid arthritis (RA) (2010 ACR/EULAR criteria) and spondyloarthritis (SpA) (2009 ASAS criteria). CIR activity was assessed during the period of Ramadan (periodic fasting) and three months following Ramadan using clinical parameters including the Patient's Global Assessment of disease activity (PGA), 10-cm Visual Analog Scale (VAS) pain score, morning stiffness, nocturnal awakenings, and joint count for RA (tender joint count (TJC) and swollen joint count (SJC)); biological parameters including C-reactive protein (CRP); disease activity scores including the SDAI, CDAI and $DAS_{28\ CRP}$ for RA, BASDAI and $ASDAS_{CRP}$ for SpA. An analysis of variance (ANOVA) was used to assess the statistical relationship between fasting and CIR activity.
Results: We enrolled 75 patients (40 RA and 35 SpA) with a sex ratio of 0.4 and a mean age of 55.35 ± 9.81 years [22-85]. The mean chronic CIR duration was 11.85 ± 3.4 years. RA was erosive in 92% of cases. Rheumatoid factor and anti-citrullinated peptides antibodies were positive respectively in 82% and 84% of cases. Seventy-five percent of RA patients were on corticosteroids with a mean dose of 10.20 mg/day of prednisone equivalent, and 81% of SpA patients were on non-steroidal anti-inflammatory drugs. Eighty-three percent of our patients were treated with conventional synthetic DMARD, and 40% with biological DMARD. The following parameters were lower in the month of Ramadan compared to the period following Ramadan in RA patients: mean PGA 4.3 vs 4.6 (p=0.01); mean morning stiffness 1.1 vs 1.5 (p=0.01); mean SJC 4.7 vs 8.5 (p=0.01); mean $DAS_{28\ CRP}$ 3.56 vs 4.25 (p= 0.05); mean CDAI 17.5 vs 20.35 (p= 0.01), and mean SDAI 13.87 vs 18.44 (p=0.01). As for SpA, the following parameters were lower in the month of Ramadan compared to the period following Ramadan: mean morning stiffness 1.3 vs 2.1 (p= 0.01); mean $ASDAS_{CRP}$ 2.9 vs 3.3 (p= 0.01), and mean BASDAI 3.6 vs 4.9 (p= 0.05). However, we found no statistically significant correlation between periodic fasting and VAS pain score, nocturnal awakenings, TJC, and CRP.
Conclusion: Our study concluded that periodic fasting was associated to a lower CIR activity. The incorporation of periodic fasting may promote optimal health and reduce the activity of some chronic inflammatory diseases.
Disclosure of Interests: None declared
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POS1517-HPR PATIENT AND CLINICIAN PERSPECTIVES ON IMPLEMENTING THE RADAI-F5 TOOL TO HELP INFORM THE ASSESSMENT AND MANAGEMENT OF FOOT DISEASE IN RA: A QUALITATIVE STUDY

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Background: While patient-reported outcome measures (PROMs) are widely recommended in clinical care, their application is limited [1]. The RADAI-F5 is a validated PROM to determine RA foot disease activity [2]. Patients' and clinicians' perceptions of the RADAI-F5's clinical utility have yet to be captured.
Objectives: This study aims to explore patient and clinician opinions and perceptions of the clinical utility of the RADAI- F5's in managing rheumatoid foot disease.
Methods: A 60-minute semi-structured interview using video conference calls with adult RA patients and rheumatologists, physiotherapists, and podiatrists was conducted as part of the interpretive phenomenological analysis research. The interviews included open-ended questions about the effect of foot disease, current clinical utilization of PROMS, and barriers and facilitators to the clinical application of the RADAI-F5. Inductive thematic data analysis with Nvivo12 identified emerging themes.
Results: Eight participants with rheumatoid arthritis: seven females; mean [standard deviation, SD] age 52.4 [9.5] years; mean [SD] disease duration 16.1 [16.4] years; eight clinicians; mean [SD] age 46.75 [5.3] years; mean [SD] years of clinical experience 19.5 [2.21] years. Four main themes were identified (Table 1); 'Feet are a priority' as the impact of RA on the feet was substantial and had a negative impact on quality of life. The second theme was 'Need for a clinically feasible foot PROM' as clinicians and patients recognised the lack of a clinically feasible tool that can determine RA foot disease. The third emerging theme was 'RADAI-F5 facilitators' as the tool can promote communication, guide management, help screen foot symptoms, monitor foot disease status and treatments longitudinally, and promote patient education. The final theme was 'RADAI-F5 barriers' as there were associated practical difficulties, including lack of appointment time, administrative burdens associated with PROM use, lack of trust in the RADAI-F5's validity and IT barriers since there is no universal electronic system for reporting RADAI-F5 results.

Table 1. Themes with respective quotes that emerged as part of the individual interviews to understand the clinical utility of the RADAI-F5

Theme	Quotations
Theme 1: Feet are important	*"Foot disease is common and it's troublesome for patients" (C16)* *"I couldn't see my friends because I was always so tired and in pain. It is very lonely." (P07)*
Theme 2: Existing methods for measuring foot disease activity are inadequate	*"The feet are under-represented in the clinical tools for assessing disease activity, and clinicians don't look at feet enough." (C11)* *"We've tried numerous PROMS. Historically, I think probably it's time-consuming for our clinical consultation". (C12)*
Theme 3: RADAI-F5 facilitators	*"I think [The RADAI-F5] improves the clinician-patient relationship" (C15)* *"Using the RADAI-F5 could measure the success of the treatments that we are implicating." (C12)*
Theme 4: RADAI-F5 barriers	*"I mean, this (RADAI-F5) will obviously go along with other tools. You know, the blood tests and things as well." (P01)*

Conclusion: The RADAI-F5 has significant potential as a therapeutic tool to aid in managing foot disease in RA. However, several implementation barriers need to be overcome before widespread use in rheumatology clinics can occur.
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POS1518-HPR BELIEFS ABOUT MEDICATION IN A POPULATION OF PATIENTS WITH INFLAMMATORY ARTHROPATHY

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Background: The beliefs that patients have regarding their medication, namely about its need and concerns regarding possible adverse effects, are a determining factor for adherence and therapeutic success[1].
Objectives: Determine which sociodemographic and clinical factors are associated with beliefs related to medication, either in terms of necessity or concerns about medication, in patients with Rheumatoid Arthritis (RA) or Psoriatic Arthritis (PsA).
Methods: Observational study, with a sample consisting of 58 patients (female 72,4%, male 27,6%; mean age = 51,0 ± 13,2 years; education < 9 years 39,7%, ≥ 9 years 60,3%). Of these, 33 had a diagnosis of RA and 25 of PsA (mean years of disease duration = 8,2 ± 7,3 years; mean disease activity by DAS28-PCR or DAS28-PCR 3 variables = 2,32 ± 0,95). Between March 2021 and June 2021, a brief questionnaire was applied with sociodemographic and clinical variables, such as the use of classic or biological DMARDs and their administration´s route. The Specific Beliefs About Medication Scale (BMQ) was anonymously applied, adapted from the Beliefs About Medicines Questionnaire, comprising 2 sections: section 1 – Specific Needs, patients beliefs about the need for medication;

section 2 – Specific Concerns, beliefs related to the dangers of addiction and long-term toxicity or side effects. Higher scores (scale from 5 to 25 points), in sections 1 and 2, reflect the belief of greater need and greater concern regarding medication, respectively. The average scores in section 1 and in section 2 of the BMQ were 9 and 15,7 points, respectively. Statistics: descriptive, Student t-Test, Pearson Correlation and ANOVA, p<0,05.

Results: Patients with PsA and younger age had a higher mean score in section 2 of the BMQ (p= 0,049 e p<0,01, respectively). The variables male gender, education ≥ 9 years and shorter duration of the disease also showed a tendency to be associated with the higher score in section 2 of the BMQ, with p-values close to statistical significance (p=0,091, p=0,074 and p=0,094, respectively). In the multivariate analysis with the above variables, only the diagnosis of PsA showed a statistically significant association with the score in section 2 of the BMQ (B=4,269; p<0,001; CI 95%=[2,060-6,477]). There was also a statistically significant correlation (p=0,007) between the scores in section 1 and section 2 of the BMQ. Regarding analysis of the sample by diagnosis, there was an association between the subcutaneous route of drug administration in individuals with RA and greater concern with the adverse effects of the medication (p=0,007), and between low disease activity and greater belief in the specific need for medication for the disease (p=0,006).

Conclusion: In this study, patients with PsA were more concerned about the possible adverse effects of medication than patients with RA. RA patients who take subcutaneous drugs are more afraid of the drug's toxic potential, and those with lower disease activity have a greater need to comply with the prescribed therapy, which can be explained by the previous effectiveness of the drug in disease control. It was also found that the greater the belief in the need for medication, the greater the concern with its possible long-term harmful effects.

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POS1519-HPR IMPACT OF SYSTEMIC LUPUS ERYTHEMATOSUS ON FOOT FUNCTION, PAIN, AND ASSOCIATED DISABILITY.

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Background: Systemic lupus erythematosus (SLE) is an inflammatory pathology of autoimmune origin with high morbidity and a great impact on daily life. Hindfoot pain is often an area of the musculoskeletal system that is severely affected and causes walking difficulties. The alterations in the structure and posture of the foot can contribute to altered gait patterns in people with SLE, reducing health-related quality of life.

Objectives: This work's objective was to know the impact of SLE on pain, disability, activity limitation, foot function in activities of daily living and life quality.

Methods: The study of the population included people with SLE. A cross-sectional observational study was carried out. 47 subjects with a diagnosis of SLE recruited in a Rheumatology Unit between March and May 2021 were included. The inclusion criteria were: patients with a diagnosis of SLE according to the EULAR / ACR 2019 criteria11, and a diagnosis of at least one year of evolution and age equal to or greater than 18 years. Sociodemographic, clinical and therapeutic data were collected. Cumulative damage was measured using the Systemic Lupus International Collaborating Clinics Damage Index (SLICC) and disease activity using the Systemic Lupus Erythematosus Disease Activity Measure (SLEDAI). Pain, disability and activity limitation were assessed using the Foot Function Index (FFI) scale where higher scores indicate greater pain, disability, and activity limitation and therefore poorer foot health. Pain nowadays was also measured using the Visual Analog Pain Scale (EVAD), foot function was assessed using the Foot and Ankle Ability Measures (FAAM) scale for activities of daily living (FAAM-ADL) and for physical activity (FAAM-S) where higher scores indicate higher levels of function, and perceived health-related quality of life was evaluated through the EUROQoL-5D scale where higher scores indicates poorer quality of life.

Results: 47 subjects participated (93.6% women) with a mean age (SD) of 49.2 (10.8) years (range 23-66). The mean (SD) SLICC and SLEDAI scores were 0.74 (1.33) and 1.17 (1.80), respectively. Mean foot pain was 4.38 (SD 2.97) on a VAS of 10 at the current time. The mean overall score (SD) on the FFI was 37.08 (26.41). The FAAM score on the ADL subscale was 0.64 (0.234). Of a total of 31 subjects who reported that they practiced some type of physical activity, the mean score (SD) on the Sport subscale of the FAAM was 0.51 (0.30). Regarding the quality of life measured through the EQ5D, a mean score (SD) of 0.56 (0.25) was obtained. In addition, a mean score (SD) of 63.76 (23.40) was obtained on the EVAEQ5D. A significant association was only obtained between SLICC and the overall value of the FFI (r = 0.305; p = 0.037), where the less accumulated damage, the less impact of foot problems on pain, disability and activity limitation. There was no significant correlation between the SLEDAI and the FFI, FAAM and ED5D.

Conclusion: The foot's function is moderately affected and a third of the patients evaluated are unable to carry out any physical activity, despite having low activity of the disease measured by SLEDAI. Furthermore, we found a direct correlation of the damage measured by SLICC-DI with problems of pain, disability and limitation in activity related with the foot.

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POS1520-HPR RHEUMATOLOGY PATIENTS TREATED WITH A BDMARD PERSPECTIVE TOWARDS THERAPEUTIC DRUG MONITORING

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Background: Therapeutic Drug Monitoring (TDM) is a tool to determine the optimal dose of a drug for individual patients using measurement of blood concentrations and, optionally, anti-drug antibodies (ADA). In the field of rheumatology interest in applying TDM is increasing. A recent study by *Syversen et al.,* the NOR-DRUM B trail, supports TDM as a treatment strategy. This study showed that treatment with proactive TDM was more effective then treatment without TDM. Applying TDM creates a more personalized treatment for individual patients, therefore it is relevant to understand the patients perspective towards TDM.

Objectives: To study the perspective of rheumatology patients treated with a bDMARD in a personalized fashion using TDM.

Methods: Adult rheumatology patients from the Amsterdam Rheumatology and immunology Center who participate in the COVID-19 prospective cohort study (Nederlands Trial Register, trial ID NL8513) received a digital questionnaire which comprised, in addition to demographic items, of three TDM topics: familiarity, attitude and risk assessment.

Results: Participants were selected based on the following criteria: treatment with a bDMARD and a fully completed questionnaire (n=888). Table 1 shows characteristics of study population.

Table 1. Characteristics of study population

	Total N= 888	
Age, yr Mean (SD)	55	(13)
Gender, female - N (%)	575	(65)
Diagnosis* - N (%)		
RA	511	(58)
PSA	172	(19)
AS	203	(23)
Axial and peripheral SpA	21	(3)
Other	17	(2)
bDMARD** - N (%)		
Adalimumab	242	(27)
Etanercept	352	(40)
Other	297	(33)

* Some patients reported more than one diagnosis** Three patients reported more than one bDMARD

Sixty-six percent (n=582) of the participants had never heard of the concept 'personalized dosing, using TDM'. After explaining the concept 60% (n=535) of the participants answered they have a positive attitude towards the concept (Figure 1). Participants with a positive attitude received a follow-up question. They were asked which of the following related aspects: individual dosing, costs, safety and other, they thought was most relevant regarding the concept. Multiple answers were possible. Ninety-four percent (n=502) reported as the main reason for having a positive attitude, that the treatment can be personally adjusted. The second and third reasons, respectively, were safety 43% (n=230) and costs 27% (n=142) of the treatment.

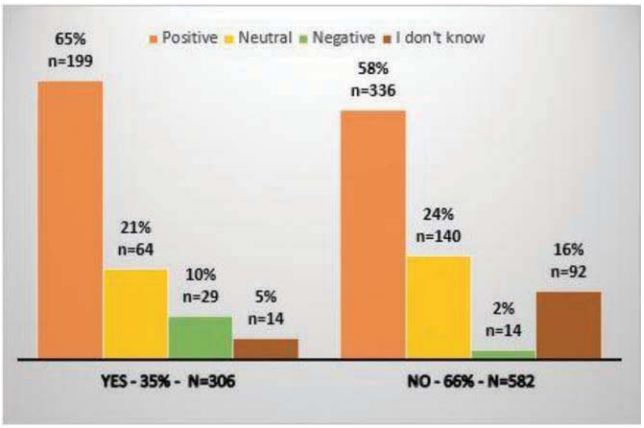

Figure 1. ***Attitude towards concept of TDM against being familiar with concept of TDM***

Five percent (n=43) of the participants had a negative attitude towards the concept. Main reasons were; previous experience with unsuccessful dose reduction and unwillingness to change current treatment due to the fact that several previous treatments were ineffective. Participants were also asked what amount of risk they are willing to take when presented with five different situations; worsening rheumatologically symptoms: e.g. pain and swelling, increased fatigability, necessary treatment with prednisone, switching to another bDMARD or more frequent visits to rheumatologist. Majority of the patients reported for each of the five situations, respectively: 37% (n=330), 40% (n=359), 51% (n=453), 48% (n= 426) and 29% (n=262) that they would only be willing to take a negligible risk, < 0.1%.

Conclusion: Majority of participants was not familiar with the concept of personalized dosing using TDM. However, the majority had a positive attitude towards the concept. The main reason for a positive attitude is that the treatment can be personally adjusted. On the other hand, patients who are currently being treated with a bDMARD were only willing to take a negligible risk when it comes to their own treatment.

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POS1521-HPR

UNDERSTANDING AND IDENTIFYING KEY CONTEXTUAL FACTORS THAT INFLUENCE THE PRACTITIONER-PATIENT ENCOUNTER IN THE MANAGEMENT OF OSTEOARTHRITIS: A QUALITATIVE SYSTEMATIC REVIEW

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Background: Contextual factors (CFs) related to the patient, healthcare practitioners, and their therapeutic relationship are integral to the overall treatment effect of any given intervention (1). In osteoarthritis (OA), around 75% of the treatment effect is directly attributable to CFs (2). Identifying and understanding the role of CFs may encourage healthcare practitioners to develop and enhance the contextual aspects of care.

Objectives: To explore and understand the experience and perspectives of patients and health practitioners regarding CFs in consultations for OA.

Methods: A systematic search was conducted between March 15 and May 18, 2020, on the following databases: MEDLINE via Ovid, EMBASE, AMED, PsycINFO and CINAHL. The search for unpublished studies included ProQuest Dissertations and Google Scholar. The search was not limited to any language or publication year. The Joanna Briggs Institute (JBI) methodology for quality assessment, study selection, data extraction and synthesis were used. Findings were assessed for credibility, categorised based on similarity in meaning and subjected to a meta-aggregation. The ConQual approach was used to assess the confidence of the synthesised findings (3).

Results: Of 1808 records generated from the systematic search of databases and grey literature, eight studies were included in the meta-aggregation (Figure 1). All included papers were moderate to high quality based on the JBI qualitative critical appraisal tool. Meta-aggregation generated three synthesised findings. According to the ConQual criteria, all the synthesised findings' level of evidence was rated as moderate (Table 1). The key, potentially modifiable, factors identified were positive communication; clear and relevant information provided by the health practitioner; patient expectation concerning their outcome and the consultation experience; sufficient consultation time; and easy access to consultations.

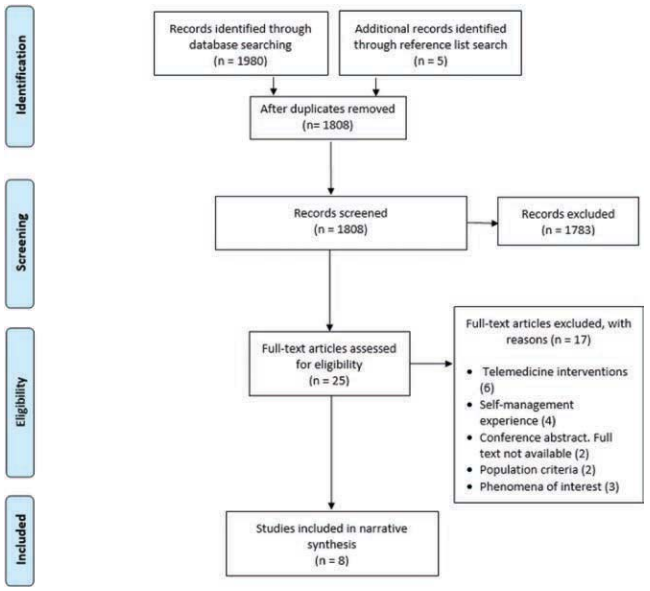

Figure 1. PRISMA flowchart of the study selection and inclusion process

Table 1. ConQual summary of findings

Synthesized finding	Type of research	Dependability	Credibility	ConQual score
I. People with OA will likely experience comprehensive and satisfactory management of their condition if the key contextual enhancers are implemented.	Qualitative	Unchanged*	Downgrade 1 level**	Moderate
II. Health providers acknowledged that information provision and efficient communication skills are likely to enhance management during consultations for OA.	Qualitative	Unchanged*	Downgrade 1 level**	Moderate
III. Effective consultations are affected by an intersection of organizational challenges and patient and provider characteristics. Limited experience with OA of some practitioners, unrealistic patients' expectations, and short consultation duration are barriers that need to be adjusted for better management.	Qualitative	Unchanged*	Downgrade 1 level**	Moderate

* The average score was (4/5) for dependability.** Downgraded one level due to a mix of unequivocal and credible findings.

Conclusion: This qualitative systematic review has defined three synthesized findings. Identification of modifiable CFs that are deemed important by both patients and health practitioners can inform the development of a training package for healthcare professional.

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POS1522-HPR COMPARISON OF EDUCATIONAL NEEDS AMONG PATIENTS WITH ANCA ASSOCIATED VASCULITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS – A PILOT STUDY USING THE EDUCATIONAL NEEDS ASSESSMENT TOOL.

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Background: Patients with chronic disease need to learn and adapt to symptoms, treatment, and the impact of disease. Knowledge about the specific disease is one way to empower the patients to cope. We previously reported that disease duration and sex, rather than disease characteristics associate with an increased need of educational support in ANCA associated vasculitis (AAV) (1). Data on how specific educational needs vary between different inflammatory rheumatic diseases are lacking.
Objectives: The aim of the study was to compare educational needs among two chronic systemic inflammatory diseases, AAV and Systemic lupus erythematosus (SLE) using the Educational Needs Assessment Tool (ENAT).
Methods: This pilot study included cross-sectional data from two separate cohorts, AVV and SLE, from the Rheumatology clinic at Karolinska University Hospital in Sweden during 2009-2022. Inclusion criteria were minimum age of 18 years and literate in Swedish. Exclusion criterion was cognitive impairment interfering with literate capabilities. Educational needs were captured by patients' answers to the questionnaire ENAT. The ENAT consists of 39 questions, presented as total ENAT and seven domains (managing pain, movement, feelings, disease process, treatment, self-management and, support systems) each containing 4-7 items (from 'not at all important' = 0, to 'extremely important' = 3). The participants' responses were presented as "mean % of the domain score", from 0 interpreted as no educational need to 100 as highest educational need. Participants with AAV and SLE respectively were individually matched for disease duration, sex, and education. For comparisons paired samples t-test were used.
Results: Twenty-two matched pairs (86% female), mean (SD) disease duration 5.7 (8) years, were included. The mean age were 43 (14.0) years for AAV 61 and (14.7) years for SLE (p=0.001). Educational length was reported as mean 14 (3.6) years among SLE patients and 13 (2.9) years among AAV patients (p=0.111).
In all patients, the mean total ENAT was 60.4% (range 23-100%) and did not differ between the two cohorts (p=0.2) (Table 1). In the pooled group the highest educational need was found in the domains 'Disease process' (mean 78.3%) and 'Self-management' (mean 75.9%). Lowest educational need was found in the domains 'Movement' (mean 46.7%) and 'Managing pain' (mean 51.6%).

Table 1. Comparison of ENAT scores (mean % of max) (SD) between patient with SLE and AAV

ENAT domain	All *n=44*	SLE *n=22*	AAV *n=22*	p
Managing pain	51.6 (29.8)	50.8 (28.7)	52.4 (32.2)	0.867
Movement	46.7 (35.1)	41.9 (34.2)	49.2 (35.7)	0.500
Feelings	63.1 (31.0)	54.6 (30.6)	70.4 (30.3)	0.087
Disease process	78.3 (22.1)	73.9 (23.0)	83.4 (20.9)	0.130
Treatments	60.7 (35.1)	46.4 (36.0)	74.2 (30.4)	**0.021**
Self-management	75.9 (21.1)	75.8 (18.8)	76.9 (24.3)	0.886
Support systems	54.0 (30.2)	49.2 (31.4)	58.7 (28.8)	0.302
Total ENAT	60.4 (24.0)	55.7 (22.8)	65.0 (24.8)	0.216

Patients with AAV report a higher educational need in total ENAT as well as in all individual domains, compared to SLE (Table 1), but only significantly in the domain 'Treatments' where the educational need among AAV was mean 74.2% (30.4) and for SLE mean 46.4% (SD 36.0) (p = 0.02).
Conclusion: In this pilot study with SLE and AAV, we found educational needs regarding 'Treatments' to be substantially increased among the participants with AAV, compared to SLE, despite that the participants were matched for disease duration and sex, two variables previously found to be indicators of increased educational needs. AAV patients with higher educational needs were older, this result needs to be further explored in a larger sample.
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POS1523-HPR PATIENT SATISFACTION SURVEY OF A SPECIALIST PHARMACIST RUN RHEUMATOLOGY BIOLOGIC AND JAK INHIBITOR CLINIC

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Background: Hereford Rheumatology Department, UK, treats over 850 patients on biologic disease-modifying anti-rheumatic drugs (bDMARDs) and JAK inhibitors (JAKi). The multidisciplinary team (MDT) includes a Specialist Rheumatology Pharmacist running clinics for all adult Rheumatology patients who have been identified for bDMARD or JAKi initiation or switch by their responsible Consultant. Patients can feel anxious during the pre-treatment screening process and require reassurance about medication safety. This innovative role has been a well-received asset to the Rheumatology MDT, but patients' perceptions of the role are unknown. To our knowledge, there is no similar study within British Rheumatology practice.
Objectives: The survey aims to gauge patient satisfaction of the consultation from a pharmacist-run bDMARD and JAKi initiation and switch clinic.
Methods: A generic patient satisfaction survey was piloted with positive results. Following this, a bespoke survey was developed, specifically enquiring about patients' perceptions of the consultation skills, clarity, education and reassurance provided by the pharmacist. A Likert scale was used where appropriate and a space for free text was included. The Trust's Patient Experience Team was consulted to ensure clarity for patients. In consecutive weekly clinics from July 2021 to January 2022, the survey was given to all patients immediately following Specialist Rheumatology Pharmacist clinic. The majority of patients were seen face-to-face however the survey was posted to the patient if telephone consultation was necessary. Clinic staff collected the completed surveys to ensure patient anonymity.
Results: 57 of 58 patients completed the survey, with 100% stating they were pleased to receive counselling from a pharmacist. Patients were asked to score their knowledge of the medication out of 10, before and after the consultation; they reported a mean increase in knowledge of 3.9/10. The remaining survey results show mostly positive feedback (Table 1).

Table 1. Patient rating of experience in pharmacist clinic.

Statement	No answer	Strongly disagree	Disagree	Neither	Agree	Strongly agree
The pharmacist put me at ease	0	0	0	0	**11**	**46**
The information provided was easy for me to understand.	**1**	0	0	**1**	**13**	**42**
The pharmacist listened to what I had to say.	0	0	0	0	**9**	**48**
The pharmacist showed care and sensitivity to my Rheumatological condition.	0	0	0	0	**11**	**46**
The pharmacist appeared knowledgeable about the medication to be started.	0	0	0	0	**8**	**49**
I feel that the medication I am starting has been chosen for me as an individual.	**1**	0	0	**1**	**17**	**38**
I understand why we are starting the new medication.	0	0	0	**2**	**10**	**45**
I have been told about the side effects the medication could cause.	0	0	0	0	**11**	**46**
I feel that it is safe to start the new medication.	**1**	0	**1**	**6**	**15**	**34**
I was able to discuss my concerns and ask questions about the new medication.	0	0	0	0	**11**	**46**
I felt included in the decision to start or change to new medication.	**1**	0	0	**2**	**11**	**43**
Overall, my experience in the pharmacist clinic today was a positive one*	**4**	0	0	0	**10**	**43**

*Statement excludes results from 4 patients who did not complete the second page of the survey.

Conclusion: The results demonstrate the high level of patient satisfaction attained from the Specialist Pharmacist clinic. A small number of patients remain sceptical about medication safety, despite discussion. Inclusion of a pharmacist is especially useful to manage the increasing number of patients starting these medications, maintaining excellent patient experience, reducing the workload for other Rheumatology staff, and ensuring a robust MDT.

REFERENCES: Not applicable.

Disclosure of Interests: Claire Jones Speakers bureau: Presented to rheumatology pharmacists at King's College hospital London, Dec 2017. Purpose: to share my role to aid their development. Paid by UCB: £1000., Consultant of: Focus group for Fresenius Kabi Sept 2021. Received £500 honorarium, Jeanette Trickey: None declared

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POS1524-HPR HPR 2020 GRANT. AWARENESS OF NON-PHARMACOLOGICAL AND NON-SURGICAL TREATMENTS FOR OSTEOARTHRITIS: A SURVEY OF PEOPLE WITH OSTEOARTHRITIS IN SWEDEN.

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Background: International clinical practice guidelines for the management of osteoarthritis (OA)[1 2] recommend exercise, education and diet as first-line interventions since they are safe, low cost and reported to be effective, in reducing OA pain and disability, regardless of the severity of the disease. However, these treatments require high levels of adherence, which may be difficult to achieve. One of the possible reasons that can jeopardise patients' adherence with first-line interventions for OA is the lack of awareness of the role that these treatments play in their care.

Objectives: To investigate the level of awareness of non-pharmacological and non-surgical treatments for hip and knee OA in a cohort of people with this disease in Sweden.

Methods: A cross-sectional, online survey-based study was conducted in Sweden. People with diagnosed knee or hip OA were recruited through social media outlets and patients' associations. The survey was divided into two sections: (i) participants' demographic and clinical characteristics (e.g. gender, age, income, work, height, weight, level of physical activity, previous surgeries, pain, level of disability) and (ii) a set of items with 22 treatments (e.g., weight advice, physical activity, drugs, supplements etc) where participants were asked to report whether each treatment was 'recommended', 'optional', 'not recommended', or 'I don't know' - for the management of knee or hip OA. In the analyses, we grouped the 22 proposed treatments into 'recommended', 'optional', and 'not recommended' according to existing international guidelines.[1 2] Based on the responses, participants were categorised as "aware" if they correctly identified all the treatments, "partially aware" if they correctly identified at least one treatment, and "not aware" if they did not correctly identify any of the treatments.

Results: Participants comprised 123 people with OA of the knee, hip or both (N=65, 22%; N=27, 22% and N= 33, 26% respectively). Their mean (SD) age was 60.3 (8.8) and 108 (88%) were women. Forty-eight (39%) were "aware" of the recommended treatments, 63 (50%) "partially aware" and 14 (11%) were "not aware". Regarding the optional treatments, 2 (2%) were "aware", 103 (82%) "partially aware" and 20 (16%) were "not aware". For the treatments that were not-recommended, none was "aware", while 69 (55%) and 56 (45%) were considered "partially aware" and "not aware", respectively. Figure 1 summarises the responses of the participants to each treatment item.

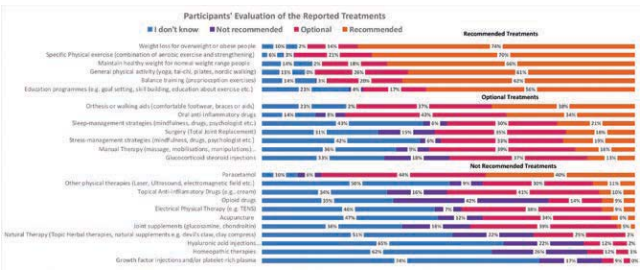

Figure 1. Participants' responses to each treatment

Conclusion: Survey participants seem to be more aware of the recommended treatments than the optional and not-recommended ones. A more holistic approach in the education of people with OA should be pursued, providing them with a complete overview of the possible OA treatments. This would help patients identify the most appropriate treatment option for their OA and facilitate a shared decision-making with their health professionals.

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POS1525-HPR BODY SELF-ESTEEM AND SEXUAL FUNCTION IN IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Background: The Immune-Mediated Inflammatory Diseases (IMID) are a group of pathologies that have in common an altered immune system causing a chronic inflammatory process. IMIDs usually have a significant impairment of quality of life, including affective and sexual components.

Objectives: To describe body self-esteem and sexual function in patients with IMIDs. Secondly, to compare outcomes between rheumatic IMIDs patients and those with other IMIDs.

Methods: A cross-sectional comparative study was performed including 38 patients with rheumatic IMIDs (including rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis), compared to 34 patients with other IMIDs (psoriasis and inflammatory bowel disease). All participants fulfilled the Body Self-Esteem Scale (EAC) to measure body self-esteem, and also the International Index of Erectile Function (IIEF-15) for men, and the Female Sexual Function Index (FSFI) for women.

Results: The prevalence of sexual dysfunction in our study was 66.7%. A trend of greater impairment in sexual function was observed in women. There was a higher percentage of sexual dysfunction in the gastrointestinal IMIDs group (79.2%), compared to rheumatic diseases (60.5%) and dermatological diseases (60%), but no significant differences were found regarding the sexual dysfunction between groups ($\chi^2 = 2.53$, $p = 0.28$). Our results showed a significant inverse relationship between body self-esteem and sexual function ($p = 0.012$), i.e., the lower the body self-esteem, the higher the probability of presenting sexual dysfunction.

Conclusion: Sexual function was impaired in all IMIDs. Body self-esteem problems were an important factor of sexual dysfunction in IMIDs. Healthcare professionals should be aware of these potential problems, promote self-care, and address sexual issues.

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POS1526-HPR WHICH FACTORS INFLUENCE PATIENTS' PREFERENCES FOR TELEHEALTH APPLICATIONS IN RHEUMATIC DISEASES? A QUALITATIVE STUDY

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Background: Telehealth has the potential to improve patients' health outcomes and patient empowerment by increasing access to care and medical information.[1,2] As patients with rheumatic diseases are known to experience drug-related

problems at various moments along their patient journey,[3] this population can benefit from more continuous information about their medication and healthcare provider support to manage drug-related problems. To most effectively employ telehealth for this purpose, it is important that offered technologies match with patients' needs and preferences.

Objectives: Identify factors influencing the preference of patients with rheumatic diseases regarding telehealth applications.

Methods: A qualitative descriptive study was performed in the Netherlands between May and June 2021. Using a semi-structured interview guide, patients with a rheumatic disease were interviewed face-to-face. First, patients were presented four telehealth applications (frequently asked questions page, digital human, and chatting and video calling with healthcare providers). Second, patients were asked to use each application to answer one medication-related question predefined by the research team. During the process of finding an answer to the question, patients were asked to think aloud and were questioned on which factors influenced their experience and preference for each application. Third, patients were given additional hypothetical questions after which they were asked to explain their preferred application for answering the question, to elicit additional factors influencing preference. Interviews were audio recorded, transcribed verbatim and analysed thematically.

Results: Fifteen patients (aged 19 – 73 years, 53% female) participated. Three domains influenced patients' preference for telehealth applications. First, preference for telehealth applications was influenced by *factors related to individual patients* such as medication-related information needs, literacy, and skills with digital applications. Second, preference was influenced by *factors related to the specific applications* such as speed of answer, level of interaction, extent of privacy, the perceived usefulness of an application, and usability of the application. Third, preference was influenced by *factors related to the context* in which telehealth applications are offered, such as the support from healthcare providers in using telehealth applications, reliability of information source, and potential of telehealth to save time for healthcare providers.

Conclusion: Patients' preference for telehealth applications is influenced by patient-related, application-related and context-related factors. To effectively support patients with rheumatic diseases, telehealth applications should match with these patients' preferences. Furthermore, it is important to offer a variety of telehealth applications as preferences differ among patients and circumstances.

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POS1527-HPR HEALTH PROMOTION IN INDIVIDUALS WITH KNEE PAIN – DIFFERENT WAYS TO ENABLE AND MAINTAIN A BALANCE IN EVERYDAY LIFE BASED ON THE ABILITIES

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Background: Most individuals with knee pain develop radiographic knee osteoarthritis over time [1], and up to 30% develop chronic widespread pain (CWP) [2]. Many studies only focus on physical activity or weight loss when it comes to managing knee osteoarthritis (KOA) and chronic pain. There is a challenge to get more individuals to follow the existing recommendations for KOA, including physical activity and weight loss [3]. However, the interaction between the various physical, mental, and social factors regarding health promotion is complex. More research is needed to understand health-promoting activities applied amongst individuals with knee pain.

Objectives: To explore health-promoting activities in individuals with knee pain.

Methods: The study was a part of the Halland Osteoarthritis cohort (ClinicalTrials.gov NCT04928170), including 306 individuals with knee pain without earlier diagnosed KOA, cruciate ligament injury or other rheumatological disorder. A purposeful sample of 22 individuals (13 women, 9 men; median age 52 years) participated in the study. Ten had radiographic KOA, 12 had chronic regional pain, 9 reported CWP, 16 were overweight, and 13 met the WHO recommendations for physical activity with moderate intensity. Semi-structured interviews were conducted and followed a pilot-tested interview guide initiated with open-ended questions such as "What do you do to maintain your health?" and "What enables you to keep health?". The interviewers followed the participants reasoning, and to obtain depth in the data, the participant received follow-up questions such as "Please, can you tell me more about…?". The interviews were audio-recorded and transcribed verbatim. Data analysis was performed by latent qualitative content analysis and revealed an overall theme including two categories and six sub-categories.

Results: Health-promoting activities in individuals with knee pain were interpreted in the overall theme; *enabling and maintaining a balance in everyday life based on abilities*. Two categories explored the content in health-promoting activities as 1) *Using facilitators to take care of the body* with the sub-categories: being physically active, having a healthy diet, and using external resources. For example, the participants took care of the body by being physically active to decrease pain, reducing sugar intake and using external resources such as online workouts or help from health care. 2) *Managing stressors of everyday life* with the sub-categories: promoting vitality, allowing for recovery, and safeguarding healthy relationships. The participants managed stressors of life by, for example, being in nature, planning their work- and private life and spending time with friends and family. See Table 1.

Table 1. Overview of the results exploring health-promotion activities in individuals with knee pain.

Theme	**Enabling and maintaining a balance in everyday life based on abilities**					
Category	**Using facilitators to take care of the body**			**Managing stressors of everyday life**		
Sub-categories	Being physically active	Having a healthy diet	Using external resources	Promoting vitality	Allows for recovery	Safeguarding healthy relationship

Conclusion: Individuals with knee pain described various health-promoting activities, ranging from physical activity to social interactions, included in the theme of enabling and maintaining a balance in everyday life based on abilities. We suggest that a broader approach to everyday life can be helpful in treatment plans and health promotion to manage and prevent KOA and chronic pain while maintaining a healthy lifestyle.

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POS1528-HPR FACTORS ASSOCIATED WITH FRAILTY STATUS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Frailty is characterized by increased fatigue and vulnerability which leads to adverse health outcomes. Recent studies have reported the increased prevalence of frailty in various rheumatological diseases regardless of age. However, information about the prevalence of frailty in patients with axial spondyloarthritis (axSpA) is limited.

Objectives: This study aims to determine prevalence of frailty and its assocaited factors in patients with axial spondyloarthritis (axSpA).

Methods: In this monocentric cross-sectional study 50 patients (26 women) with axSpA aged between 40 to 65 were included. Frailty status was determined using Kihon checklist. Patients were groups as pre-frail, frail and robust according to the Kihon Checklist and <4 was accepted as robust, ≥4 pre-frail, 8≥ frail. Nutritional status, disease activity, functional level and quality of life were assessed using Mini Nutritional Assessment (MNA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankilozan Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) respectively. Analysis of variance and multivariate linear regression analyses were used to assess group differences and factors associated with frailty status.

Results: The mean age of the patients was 51.78±6.77, the mean disease duration was 7.8±8.41 years, the mean body mass index was 29.98 ±4.72 kg/m^2. Twenty-one patients were classified as frail, 16 was pre-frail and 13 was robust. Compared to robust patients, pre-frail and frail individuals had significantly higher BASFI, BASDAI and ASQoL scores. There was a significant high correlation between the Kihon chekclist score and worse BASFI ($r=0.62$, $p<0.001$), BASDAI (0.69, $p<0.001$), ASQoL scores (0.73, $p<0.001$). Poor nutritional status was moderately correlated with frailty index score ($r=-0.53$, $p<0.001$). In multivariable linear regression analysis, nutrition status and level of quality of life were independently associated with frailty index score ($p<0.001$).

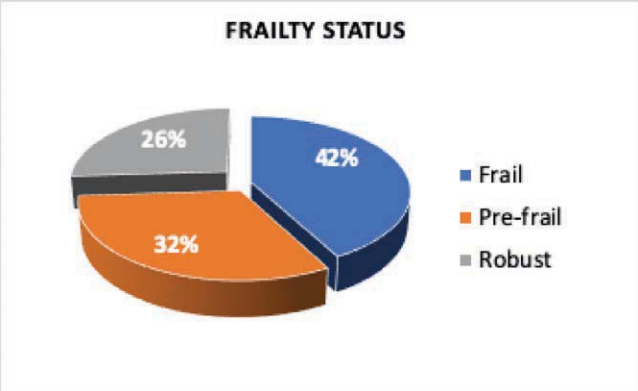

Figure 1. Percentages of patients according to their frailty status.

Table 1. Comparison of patients according to their frailty status

	Robust (n= 13)	Pre-frail (n=16)	Frail (n=21)	P_1	P_2	P_3
Age (years)	53.84±7.27	49.75±6.22	52.04±6.74	.24	.73	.56
Sex, women/men (n)	2/11	10/6	14/7	-	-	-
BMI (kg/m^2)	27.86±5.61	28.31±3.15	30.19±5.07	.96	.35	.46
BASDAI	2.39±1.81	4.83±1.60	5.93±1.83	.00	.00	.15
BASFI	1.96±2.01	2.87±2.10	5.41±2.19	.48	.00	.00
ASQoL	4.23±3.94	7.75±4.76	12.61±4.22	.08	.00	.00
Mini Nutritional Assessment	25.61±1.47	24.59±2.13	23.59±2.16	.36	.01	.29

BMI; body mass index, BASDAI; Bath Ankylosing Spondylitis Disease Activity Index, BASFI; Bath Ankilozan Spondylitis Functional Index, ASQoL; Ankylosing Spondylitis Quality of Life Questionnaire. P_1; P value between robust and pre-frail individuals, P_2; P value between robust and frail individuals, P3; P value between robust and frail individuals.

Conclusion: Frailty or pre-frailty is common in patients with axSpA and the main factors associated with frailty status were poor nutritional status and level of quality of life. Since it is a reversible condition, identifying the frailty status and its associated factors may help to prevent further decline in functional level and to design appropriate treatment interventions. Further studies are needed to determine frailty prevalence and its predictors in patients with axSpA.

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POS1529-HPR SEXUAL DYSFUNCTION AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Sexual health is a major component of human well-being. The World Health Organization (WHO) defines sexual health as "a state of physical, mental, emotional, and social well-being in relation to sexuality". Sexuality is a very important, inherent part of human functioning. As repeatedly shown in research, satisfaction with sex life and sexual fulfillment correlate positively with quality of life (QoL) in most of its aspects. It is thus true that a reduced quality of one's sex life and lack of sexual fulfillment can contribute to poorer QoL overall. As poor sex life quality and sexual dissatisfaction result from sexual dysfunction, effective treatment of such a dysfunction can be assumed to contribute significantly to a better QoL.

Objectives: To describe an assessment of sexual problem among RA patients as a part of patient-reported outcome measures assessment.

Methods: 171 consecutive RA patients (mean age 48.3±14.6) attending the rheumatology outpatients clinic over 6 months in 2021. Standardized questionnaires were used in the study: The Sexological Questionnaire to assess self-assessment of the incidence of sexual disorders, WHOQOL-BREF to assess QoL level, Disease Acceptance Scale and VAS scale to assess pain intensity.

Results: The mean duration of the disease in the study group was 13±9 years. The mean score of subjective assessment of mobility was 6.2 ± 1.6, and the mean score of the DAS-28 disease activity index was 4.0±1.9. The study group presented a mean level of disease acceptance (AIS 29.6 ± 11.6). The comparative analysis showed significant differences in reaching orgasm and declared sexual dysfunctions. These problems occurred more often in women than in men (34.2% vs. 18% and 43% vs. 40% respectively p=0.002). In univariate analysis, factors correlating positively with the frequency of declaring sexual dysfunction were: subjective motor score less than 6 points, AIS<36 points, WHOQOL-BREF<59 points, disease activity ≥3.5 points and VAS>3. In multivariate logistic regression analysis independent factors positively correlating with frequency of sexual dysfunction declaration were: general QoL (β=1.255; p=0.035) and pain limiting social life (β=1.564; p=0.030). The absence of comorbidities correlated negatively and reduced the prevalence of sexual dysfunction (β=-1.030, p=0.043). Patients with reduced QoL had 3.5 times and patients with pain limiting social life had 4.8 times higher risk of sexual dysfunction than other patients. In contrast, those without comorbidities were 2.8 times more likely to be free of sexual dysfunction than those diagnosed with other chronic diseases besides RA.

Conclusion: Sexual dysfunction is a problem found both in women and in men with RA. The most common problems include lack of orgasm, vaginal dryness in women, and erectile dysfunction in men. Psychological factors that contribute to sexual dysfunction include low or no illness acceptance and poor QoL. The absence of comorbidities is an independent determinant of lower sexual dysfunction incidence, whereas low QoL and pain limiting the patient's social life are independent determinants of increased incidence of sexual dysfunction in both sexes.

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POS1530-HPR RHEUMATIC MUSCULOSKELETAL DISEASES (RMDS) DURING THE FIRST WAVE OF THE COVID19 PANDEMIC: PATIENTS' POINT OF VIEW ON THE ROLE OF TELEMEDICINE

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Background: The COVID19 pandemic has caused health problems in people's daily lives with a significant psychological impact. In fact, patients with RMDs have experienced diseases' flare and also psychological problems. The lockdown and the "social quality changes" have impacted the life and the well-being of RMDs patients, influencing directly the implementation of telemedicine during daily practice.

Objectives: A descriptive observational study was designed to analyse the short-term effect of the first wave on RMDs patients on social quality changes and the usefulness of telemedicine.

Methods: The survey was carried out by administering a questionnaire consisting of 30 questions, developed *ad hoc* using Likert scales. Items such as family and work environment, access to healthcare facilities, healthcare provided to the patient, disease activity and the mental health status of individuals (anxiety / depressive symptoms) were investigated. Preliminary data on the first wave were collected between September and November 2021 through patient associations and social networks.

Results: 40 RMDs patients (Rheumatoid Arthritis 57.5%, Psoriatic Arthritis 35%, Fibromyalgia and others 7.5%) prevalently women (97.5%) were included in the survey. During the pandemic, 72% of respondents reported cancellation or delays in scheduled appointments and 50% did not have alternative contacts (telephone consultations, e-mail prescriptions, telematics training) with the hospital. 40.5% of patients reported difficulty in finding DMARDs and material for the treatment of ulcers, 28.2% reported difficulties in accessing the health facilities. In particular, 34.2% reported the total closure of the hospital facilities.

Moreover, our data show a worsening of health status due to an increased anxiety concerning the management of their RMDs, an increased stress within the

family, a reduced access to care facilities due to their closure or travel restrictions. In 57% of patients, a worsening of health status was reported, while in 90% stress and a feeling of abandonment was developed since the beginning of the pandemic. In this context, telemedicine was considered useful by 97.5% of patients, although patients felt that an improvement was necessary with an integration with the regular follow up.

Conclusion: Patients with RMDs reported that the significant delays or cancellation of the outpatient visits provoked an increase of stress, worry and anxiety for their health. The majority was very concerned about the overall management of their RMDs. The worsening of symptoms in more than half of the patients was the most worrisome observation. Almost all patients agreed that Telemedicine might help the clinical evaluation of their RMDs, also providing a significant support to their psychological condition because of the direct contact with the caring physician and health professionals.

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POS1531-HPR PATIENT-REPORTED ADVERSE DRUG REACTIONS ATTRIBUTED TO THE USE OF ETANERCEPT: DISTINCTION BASED ON NATURE, FREQUENCY AND BURDEN

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Background: Research regarding adverse drug reactions (ADRs) associated with the use of etanercept in patients with inflammatory rheumatic diseases (IRDs) usually focuses on the nature and frequency of ADRs without considering the burden of the ADRs. However, not every ADR causes the same burden for patients. Information is lacking about the degree of experienced burden per ADR by patients with IRDs.

Objectives: First, to describe ADRs of etanercept based on nature, frequency and burden, and second, to propose a new model for identification of relevant ADRs for health care professionals.

Methods: Data of the Dutch Biologic Monitor (DBM) was used to categorize patient-reported ADRs into high and low burden. In this prospective cohort event monitoring system patients were asked to fill out bimonthly questionnaires on experienced ADRs that they attributed to the use of a biological DMARD. The questionnaire included a quantification of the burden of the reported ADRs using a five-point Likert scale ranging from 1 (no burden) to 5 (very high burden). The nature of the reported ADRs were grouped into preferred terms (PTs) according to the Medical Dictionary for Regulatory Activities (MedDRA). Inclusion criteria for this study were patients with IRDs using etanercept and who reported an ADR with at least one burden score. For every patient, the mean burden scores per ADR (MedDRA PT) were analyzed. The burden was classified in two categories: 'high' when the mean burden score was equal to or more than 2.5, and 'low' when it was less than 2.5. Text analytics of the reported ADRs (MedDRA PTs) and a comparison word cloud were used to visualize ADRs that were more often reported with high burden or more often reported with low burden. For this, the relative ADR frequencies of the low burden classes were subtracted from the relative frequencies of the high burden class, resulting in a percentual difference between the high and low burden class for every ADR. Therefore, the highest percentual difference corresponds to the ADRs that are experienced as most burdensome.

Results: A total of 187 patients (70% female) met the inclusion criteria and reported 905 ADRs, of which 373 (41%) were reported with high burden (see Table 1). The word cloud (Figure 1) visualizes which ADRs were more often reported with high or low burden. These ADRs correspond to the greatest difference in relative class frequency. Patients experienced the burden of headache, pneumonia and pruritis mainly as high, and the burden of injection site pruritus and injection site erythema as low.

Table 1. Characteristics of patients and reported adverse drug reactions (ADRs)

Characteristics	Total		
Patients (n = 187)			
Gender (female, %)	130 (70)		
Age (years) (mean ± SD)	58.1 ± 14.1		
Indication[a]			
Rheumatoid arthritis (%)	132 (71)		
Ankylosing spondylitis/axial spondyloarthritis (%)	19 (10)		
Psoriatic arthritis (%)	46 (25)		
Adverse drug reactions	Total	High burden	Low burden
Adverse drug reactions (ADRs) (%)	905 (100)	373 (40)	532 (60)
Drug-induced ADR burden (mean ± SD)	2.5 ± 0.9	3.3 ± 0.7	1.9 ± 0.5
High burden ADRs:			
Headache	30	22	8
Pruritus	23	17	6
Pneumonia	20	15	5
Feeling cold	11	11	0
Skin atrophy	11	11	0

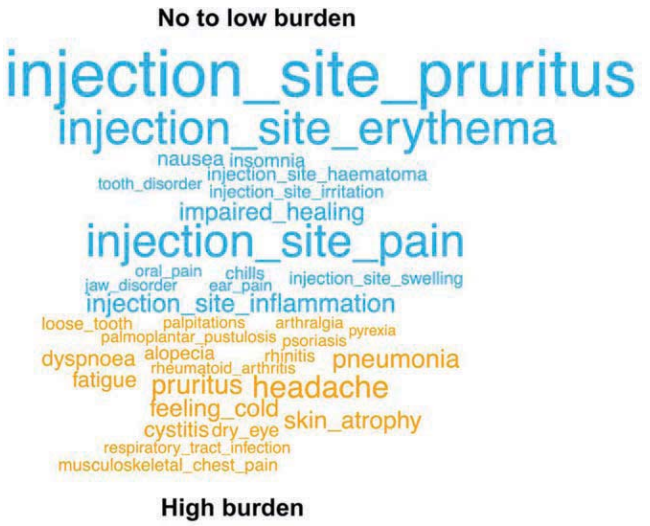

Figure 1. Comparison word cloud visualizing adverse drug reactions (ADRs) that patients reported more often with high burden (orange) and with no to low burden (blue). An ADR increases in size if the relative difference in frequency between classes increases.

Conclusion: The outcomes of the word cloud reveal that headache is more often experienced as burdensome which is an unexpected outcome. Visualizing the nature, the frequency and the burden of ADRs in one picture, provides simple guidance to the degree of relevance for the reported ADRs in clinical practice.

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POS1532-HPR

SEX DIFFERENCES IN THE EXPERIENCED BURDEN OF ADVERSE DRUG REACTIONS ATTRIBUTED TO ADALIMUMAB AND ETANERCEPT BY PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Background: Patients experience burden of adverse drug reactions.[1] So far, it is not known whether men and women experience adverse drug reactions (ADRs) with the same burden.

Objectives: To examine sex differences in regard to the burden of mutually reported ADRs in patients with immune-mediated inflammatory diseases (IMIDs) treated with adalimumab or etanercept.

Methods: Patients with rheumatoid arthritis (RA), psoriatic arthritis or (axial) spondyloarthritis using etanercept or adalimumab were included from the Dutch Biologic Monitor (DBM).[1] In the DBM, questionnaires concerning experienced ADRs and corresponding burden were filled out bimonthly. ADRs were coded according to Medical Dictionary for Regulatory Activities (MedDRA) terminology. The burden of ADRs (Preferred term level, PT) was reported on a five-point Likert scale ranging from no burden (1) to very high burden (5). If ADRs were present over multiple questionnaires, burden was only assessed the first time the ADR was mentioned. Likert scales reported for burden were compared between male and female patients for mutually reported ADRs that were reported at least four times by both male and female patients, using the Cochran-Armitage test for trend, which considers the ordinal nature of Likert scales.

Results: In total 748 consecutive patients participated, of which 55% were female (Table 1). Almost half (48%) reported at least one ADR during the study. More than half of female patients (55%) reported at least one ADR as compared to 38% of male patients. In total 882 ADRs were reported comprising 264 distinct ADRs, of which the majority (74%) was reported by female patients. 71 (27%) distinct ADRs were mutually reported by male and female patients and 12 (5%) distinct ADRs were reported at least four times by females and males. Pneumonia and headache impose the highest burden of the mutually reported adverse drug reactions. 'Arthralgia' (p=0.052) showed the largest differences burden Likert scale scores between male and female patients. Even though male patients experienced higher burden, these differences were not statistically significant (Figure 1).

Table 1. Demographics of females and males that reported at least one of the 12 distinct adverse drug reactions (ADRs) that are included in the analysis of sex-specific burden of ADRs.

Participants	Female	Male
N	138	70
Age, mean ± SD[a]	53.7 ± 13.5	57.6 ± 11.8
Indication for bDMARD therapy[b], N (%)		
Ankylosing spondylitis/axial spondyloarthritis	15 (10.9)	14 (20.0)
Ankylosing spondylitis/axial spondyloarthritis and Psoriatic arthritis	1 (0.7)	-
Ankylosing spondylitis/axial spondyloarthritis and Rheumatoid arthritis	1 (0.7)	3 (4.3)
Psoriatic arthritis	26 (18.8)	25 (35.7)
Rheumatoid arthritis	95 (68.8)	28 (40.0)
bDMARDs, N (%)		
Adalimumab	60 (43.5)	32 (45.7)
Etanercept	77 (55.8)	38 (54.3)
Switched adalimumab/etanercept	1 (0.7)	-
Comedication, N (%)[c]		
Methotrexate	55 (39.1)	21 (30.0)
Corticosteroids	17 (12.3)	11 (15.7)
Thiopurines	3 (2.2)	1 (1.4)
Sulfasalazine	9 (6.5)	3 (4.3)

[a]Age was missing for 1 male and 1 female patient. [b]Patients could report multiple indications. 5 male and 14 female participants also reported other indications. [c]Reported comedication at the moment of inclusion. Eleven patients (male=3, female=8) did not start with etanercept or adalimumab at the moment they were included. In these cases, comedication is counted from the moment they reported the start of adalimumab or etanercept treatment.

Conclusion: Although women reported the majority of the ADRs, there was a trend that that men experienced certain ADRs as more burdensome in comparison to women, albeit this did not reach statistical significance.

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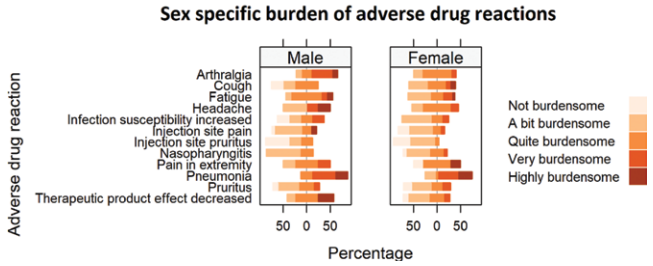

Figure 1. Sex-specific burden of mutually reported adverse drug reactions.

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POS1533-HPR

COMPARISON OF HAND FUNCTIONS AND FUNCTIONAL STATUS IN PATIENTS WITH LIMITED CUTANEOUS SYSTEMIC SCLEROSIS AND DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is an autoimmune connective tissue disorder which is characterised by the fibrotic changes in the skin effecting especially fingers and hands. Regarding skin manifestations, SSc is classified into two different subtypes as limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc).

Objectives: The aim of the present study was to compare hand functions and functional status in patients with lcSSc and dcSSc.

Methods: Twenty-three patients with lcSSc and thirteen patients with dcSSc were included in the study. Modified Hand Mobility in Scleroderma Test (mHAMIS), modified Rodnan skin score (mRSS), grip and pinch strengths were measured to evaluate hand-related physical characteristics. Duruoz Hand Index, Disability of Arm, Shoulder and Hand Questionnaire (DASH), Health Assessment Questionnaire (HAQ), and Scleroderma Health Assessment Questionnaire (SHAQ) were used as the outcomes.

Results: While differences were detected in mRSS scores between disease subtypes ($p<0.05$), hand functions and functional status were comparable between groups ($p>0.05$).

Table 1. Comparison of the groups

	lcSSc Group Median (IQR 25/75) (n= 23)	dcSSc Group Median (IQR 25/75) (n=13)	p*
mHAMIS (score 0-4)	0 (0/1)	0 (0/0)	0.745
mRSS Fingers (score 0-3)	2 (1.5/3)	3 (2/3)	0.100
mRSS Hands (score 0-3)	1 (0.5/2)	2 (2/3)	**0.020***
mRSS Forearms (score 0-3)	0 (0/1)	2 (1/2)	**0.013***
mRSS Upper Arms (score 0-3)	0 (0/0)	1 (0/1)	**0.003***
mRSS Total (0-51)	8 (5/13)	27 (18/29)	**0.006***
Hand Grip Strength (kg)	19.7 (11.2/24.6)	20.9 (14.4/24.8)	0.649
Tip to Tip Pinch Strength (kg)	3 (2.2/3.9)	3.3 (2.4/2.9)	0.721
Three Jaw Pinch Strength (kg)	2.4 (1.7/3.2)	2.8 (2/3.5)	0.226
Lateral Pinch Strength (kg)	3.8 (3.4/5.1)	4 (3.2/5.3)	0.948
Duruoz Hand Index (score 0-90)	5 (0/17)	6 (0/15)	0.770
DASH (score 30-150)	62 (47/84)	61 (53/77)	0.770
HAQ (score 0-3)	0.3 (0.1/0.9)	0.3 (0.8/0.9)	1.000
SHAQ-Raynaud's Phenomenon (score 0-3)	0.8 (0/1.4)	1.3 (0.3/1.5)	0.363
SHAQ-Digital Ulcers (score 0-3)	0 (0/0.6)	0.3 (0/1.7)	0.136
SHAQ-Gastrointestinal (score 0-3)	0 (0/1.5)	0.7 (0.1/1.4)	0.466
SHAQ-Pulmonary (score 0-3)	0.5 (0/1.5)	1 (0.2/1.5)	0.534
SHAQ-Patient Global Assessment (score 0-3)	1.1 (0.1/2)	1.4 (0.8/2.2)	0.345

p<0.05, *: Mann-Whitney U test, IQR 25/75: Interquartile range between the 25th and 75th percentiles, n: number, mHAMIS: modified Hand Mobility in Scleroderma Test, mRSS: modified Rodnan skin score, DASH: Disability of Arm, Shoulder, and Hand Questionnaire, HAQ: Health Assessment Questionnaire, SHAQ: Scleroderma Health Assessment Questionnaire, lcSSc: limited cutaneous Systemic Sclerosis, dcSSc: diffuse cutaneous Systemic Sclerosis

Conclusion: According to our results, even though, patients with dcSSc present higher skin thickening compared to patients with lcSSc, hand functions and functional status seem to be similar between SSc subtypes.

Disclosure of Interests: None declared

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POS1534-HPR **WRIST JOINT POSITION SENSE AND MANUAL DEXTERITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS**

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Background: Joint position sense is a marker of proprioception and is defined as being aware of the body position and individual body parts in the space. Position sense in the wrist joint is especially important for the manual dexterity. A possible damage due to arthritis may lead a decrease in joint position sense. However, the status of joint position sense was not investigated in children with juvenile idiopathic arthritis (JIA).

Objectives: To compare the wrist position sense and a motor performance test related to manual dexterity among children with JIA with wrist arthritis history (JIAWrist+), children with JIA without wrist arthritis history (JIAWrist-), and healthy controls.

Methods: A total of sixty children (20 children for each group) were included in the study. Wrist joint position sense was evaluated by measuring joint re-position error. The wrist was passively placed in a pre-determined position (30° for flexion, 30° for extension, 10° for radial deviation, and 15° for ulnar deviation). Then passively was returned to baseline position. The patient was asked to reposition their wrist into the target degree actively. The absolute error in degrees between each position and reposition was calculated. Manual dexterity was evaluated by using Purdue Pegboard Test. The test was repeated three times and the average number of the correctly placed pines was used in the analysis.

Results: Joint position sense (in all directions except radial deviation) and manual dexterity (except assembly) was found negatively affected in JIAWrist+ patients compared to healthy controls. No differences (except radial deviation) were observed between JIAWrist- patients and healthy controls.

Conclusion: Joint position sense and related manual dexterity is diminished in JIA patients with wrist involvement. The results of this study suggested that children with wrist arthritis should be followed with special attention focusing on manual abilities. Hand therapy programs might help improving joint position sense acuity.

Disclosure of Interests: None declared

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Table 1. Comparison of the groups

	JIAWrist+ (n:20)	JIAWrist- (n:20)	Healthy Controls (n:20)	
Physical Characteristics	Median (IQR 25/75)	Median (IQR 25/75)	Median (IQR 25/75)	p*
Age (years)	14.0 (10.5/16.0)	12.5 (11.0/14.5)	12.0 (10.0/13.0)	0.131
Body-Mass Index (kg/m^2)	20.1 (18.8/22.6)	18.9 (15.7/23.9)	18.6 (16.8/21.9)	0.477
Disease Related Data	Median (IQR 25/75)	Median (IQR 25/75)	Median (IQR 25/75)	p**
Disease Duration (months)	27.5 (10.5/64.0)	31.5 (11.0/63.0)	NA	0.903
Gender	n (%)	n (%)	n (%)	p***
Female	19 (95%)	10 (50%)	13 (65%)	0.007
Male	1 (5%)	10 (50%)	7 (35%)	
Joint Re-position Error	Median (IQR 25/75)	Median (IQR 25/75)	Median (IQR 25/75)	p*
Flexion (°)	5.2 (3.3/6.7)	2.7 (2.0/4.0)	2.0 (1.3/2,7)	p<0.001 p1: 0.061 p2< 0.001 p3: 0.148
Extension (°)	3.8 (2.2/6.0)	3.5 (2.8/4.5)	1.8 (1.3/4.0)	p: 0.038 p1: 1.000 p2: 0.045 p3: 0.171
Radial Deviation (°)	2.8 (2.0/5.2)	3.3 (1.8/4.7)	2.0 (1.3/2.7)	p: 0.022 p1: 1.000 p2: 0.051 p3: 0.048
Ulnar Deviation (°)	3.5 (2.5/4.3)	2.3 (1.5/3.0)	1.7 (1.2/2.7)	p: 0.003 p1: 0.084 p2: 0.003 p3: 0.805
Flexion (°)	5.2 (3.3/6.7)	2.7 (2.0/4.0)	2.0 (1.3/2,7)	p<0.001 p1: 0.061 p2< 0.001 p3: 0.148
Manual Dexterity	Median (IQR 25/75)	Median (IQR 25/75)	Median (IQR 25/75)	p*
Purdue Pegboard Test Single Hand (score)	15.2 (13.5/15.5)	15.2 (14.5/16.2)	16.2 (15.0/18.0)	p: 0.022 p1: 0.981 p2: 0.019 p3: 0.244
Purdue Pegboard Test Both Hands (score)	11.0 (9.8/12.0)	11.0 (10.3/12.3)	12.5 (11.7/13.2)	p: 0.006 p1: 1.000 p2: 0.007 p3: 0.051
Purdue Pegboard Test Assembly (score)	26.5 (23.0/28.5)	26.0 (23.5/29.0)	28.0 (25.5/30.0)	p: 0.243

*Kruskal-Wallis Analysis, **Mann-Whitney-U Test, ***Chi-Square Test, p<0.05. JIAWrist+: children with JIA with wrist arthritis history; JIAWrist-: children with JIA without wrist arthritis history, NA: not applicable, p1: JIAWrist+ vs. JIAWrist-; p2: JIAWrist+ vs. healthy controls; p3: JIAWrist- vs. healthy controls.

POS1535-HPR

THE RELATIONSHIP BETWEEN SCAPULAR STABILIZATION AND HAND FUNCTIONS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Distal stabilization is an essential component for high quality proximal movement. In this regard, scapular stabilization is important for upper extremity and hand functions. Moreover, scapular stabilization might have a role as a support point for hand functions in patients with joint problems. However, the relationships between scapular stabilization and hand functions were not investigated in children with juvenile idiopathic arthritis (JIA).
Objectives: To investigate the relationship between scapular stabilization and hand function in children with JIA with wrist arthritis history (JIAWrist+), and children with JIA without wrist arthritis history (JIAWrist-).
Methods: A total of forty children (20 children for each group) were included in the study. Scapular stabilization was measured by using scapular muscle endurance test. General functional status, subjective hand functions, and objective hand functions were assessed by using Childhood Health Assessment Questionnaire (CHAQ), Duruoz Hand Index, and Purdue Pegboard Test, respectively.
Results: JIAWrist+ patients reported poorer hand functions compared to JIAWrist- patients. No significant differences were detected for other parameters. Scapular muscle endurance was moderately related to CHAQ Disability Index score, Purdue Pegboard Test (single hand score and assembly score) in JIAWrist+ patients, while there was only a significant relationship between scapular muscle endurance and Purdue Pegboard Test both hand score in JIAWrist- patients.

Table 1. Comparison of the Groups and Relationships between Scapular Muscle Endurance and Hand Functions

	JIAWrist+ (n:20)	JIAWrist- (n:20)	
	Median (IQR 25/75)	Median (IQR 25/75)	p*
Age (years)	14.0 (10.5/16.0)	12.5 (11.0/14.5)	0.512
Scapular Muscle Endurance (sec)	21.9 (10.7/35.8)	22.5 (15.8/50.8)	0.383
CHAQ Discomfort Index (score)	20.0 (7.5/48.2)	27.5 (10.0/50.0)	0.489
CHAQ Health Status Index (score)	45.0 (30.0/75.0)	45.0 (30.0/57.5)	0.558
CHAQ Disability Index (score)	0.8 (0.1/1.0)	0.3 (0.0/0.7)	0.104
Duruöz Hand Index (score)	5.5 (2.5/13.5)	0.5 (0.0/4.0)	0.006
Purdue Pegboard Test Single Hand (score)	15.2 (13.5/15.5)	15.2 (14.5/16.2)	0.981
Purdue Pegboard Test Both Hands (score)	11 (9.8/12.0)	11.0 (10.3/12.3)	1.000
Purdue Pegboard Test Assembly (score)	26.5 (23.0/28.5)	26.0 (23.5/29.0)	0.779
Relationships between Scapular Muscle Endurance and Hand Functions			
CHAQ Discomfort Index (score)	rho: -0.086, p: 0.718	rho: -0.174, p: 0.464	
CHAQ Health Status Index (score)	rho: 0.090, p: 0.706	rho: 0.005, p: 0.982	
CHAQ Disability Index (score)	rho: -0.560, p: 0.010	rho: -0.219, p: 0.353	
Duruöz Hand Index (score)	rho: -0.442, p: 0.051	rho: -0.158, p: 0.506	
Purdue Pegboard Test Single Hand (score)	rho: 0.503, p: 0.024	rho: 0.313, p: 0.179	
Purdue Pegboard Test Both Hands (score)	rho: 0.400, p: 0.081	rho: 0.459, p: 0.042	
Purdue Pegboard Test Assembly (score)	rho: 0.594, p: 0.006	rho: 0.218, p: 0.355	

*Mann-Whitney-U Test, p<0.05, CHAQ: Childhood Health Assessment Questionnarie, JIAWrist+: children with JIA with wrist arthritis history; JIAWrist-: children with JIA without wrist arthritis history, rho: Spearman's Rank Correlatio

Conclusion: According to our results, scapular endurance was found more related to hand functions in wrist involved JIA patients. It seems that scapular stabilization contributes to hand functions differently related to joint involvement in JIA patients. It might be a beneficial strategy to work on scapular muscles in JIA patients with wrist involvement and poor hand functions.
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POS1536-HPR

THE RELATIONSHIP BETWEEN POSTURAL CHANGES AND TRUNK MUSCLE ENDURANCE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Body posture is defined as relative biomechanical alignment of body's head, trunk, and extremities as well as position of the body in the space. Body posture might be altered due to different musculoskeletal pathologies. Juvenile Idiopathic Arthritis (JIA) is a chronic inflammatory disease characterized by musculoskeletal problems including bone and muscle geometry alterations which may lead a deteriorated posture. However, it is not known whether trunk muscle endurance is associated with body posture in children with JIA.
Objectives: To investigate the relationship between postural changes and trunk muscle endurance in children with JIA.
Methods: Thirty-four children (eighteen female, sixteen male) were included in the study. Postural changes were assessed by a three-dimensional evaluation system (PosturePrint System, Biotonix, Canada). The system provides Posture Index (PI) score which is a composite score from three postural regions including head, ribcage, and pelvis. Higher PI scores indicate a more deteriorated posture. Biering–Sørensen Test (BST), Flexor Endurance Test (FET), Lateral Endurance Test (LET) were used to assess trunk muscle endurance, and Static Scapular Endurance Test (SSET) were used to assess scapular muscle endurance. Spearman Rank Correlation test was employed to determine the possible relationships.
Results: Enthesitis related arthritis was the most common JIA subtype in the study (38.2%) followed by oligoarthritis (26.5%), polyarthritis (20.6%), and systemic arthritis (14.7%). Significant negative correlations were detected between SSET and PI-head score (rho= -0.467, p=0.005), SSET and PI-ribcage score (rho= -0.381, p=0.026); FET and PI-head score (rho= -0.469, p=0.005); LET and PI-head score (rho= -0.441, p=0.009).

Table 1. Demographics, muscle endurance and Posture Index scores of children

Variable	Median (IQR 25^{th}/75^{th})
Age (years)	12.0 (10.0/14.0)
Height (cm)	145.50 (140.00/158.25)
Weight (kg)	42.75 (33.00/49.50)
Body mass index (kg/m^2)	19.17 (16.09/21.42)
Biering– Sørensen Test (sec)	49.70 (28.42/80-78)
Flexor Endurance Test (sec)	38.91 (30.59/60.19)
Lateral Endurance Test (sec)	32.52 (19.99/59.68)
Static Scapular Endurance Test (sec)	23.19 (15.93/44.74)
Posture Index-Head (score)	7.0 (5.0/8.0)
Posture Index-Ribcage (score)	5.0 (4.0/6.0)
Posture Index-Pelvis (score)	6.0 (3.0/8.0)

IQR: Interquartile range

Conclusion: These results indicated that postural displacements of head and ribcage are linked with decreased trunk and scapular muscle endurance in children with JIA. Exercise and physical activity programs targeting muscle endurance may result improvements in posture in these children.
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POS1537-HPR

PERCEIVED BARRIERS AND FACILITATORS TO PHYSICAL ACTIVITY AND ITS ASSOCIATED FACTORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Physical activity is a core treatment method in the management of axial spondyloarthritis (axSpA). Barriers to physical activity including high disease activity, symptoms such as pain, stiffness and fatigue and lack of time have been reported in qualitative and quantitative studies in patients with axial spondyloarthritis (axSpA). Inflammatory Arthritis FAcilitators and Barriers (IFAB) questionnaire has been developed to assess perceived barriers and facilitators to physical activity in patients with inflammatory arthritis. Identifying barriers and facilitators to physical activity using a rheumatic-specific tool may help to plan better patient management strategies in clinical practice.
Objectives: To determine barriers and facilitators of physical activity in patients with axSpA and explore associations between perceived barriers and facilitators to physical activity and education level, disease duration, functional status, anxiety, depression.
Methods: Between September and December 2021, 93 patients with axSpA were included in this study. Besides demographic and clinical variables, patients completed the IFAB questionnaire to determine the perceived barriers and facilitators to physical activity or exercise. Also, anxiety and depression status was determined with Hospital Anxiety and Depression

Scale (HADS) and functionality was measured with Health Assessment Questionnaire (HAQ). Physical activity level was assessed using the International Physical Activity Questionnaire Short-Form (IPAQ-SF). Multiple linear regression analysis was used to investigate the association of HADS score, HAQ score, disease duration, educational status and the IFAB score.

Results: Of the 102 patients included, 93 were analyzed, 46 % were women. The mean age was 44.81±10.71 and the mean disease duration was 6.91 ± 6.92 months. According to the IPAQ-SF scores, 47.3 % of the patients were inactive, 49.5 % were moderately active and 3.2 % were active. The mean IFAB score was 4.61 ± 22.22, and 26 % of patients' score was below -5. One level increase in educational status resulted in an increase of 3,55±1,77 points in the IFAB score and a one-point increase in HADS-Depression score lead to a 2,00±0,57 decrease in the IFAB score.

Conclusion: In this axSPA population, 26 % scored below -5, indicating significant barriers and a need for a physical activity intervention. IFAB score was independently associated with education status and level of depression. Our results may propose that a comprehensive physical activity program should be designed considering psychological factors and should be prepared according to the educational status of the patients.

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Table 1. Characteristics of the included patients.

Characteristics	Mean ± SD (Median)
Age (years)	44.81±10.71 (47)
Time since diagnosis (years)	6.95±6.95 (5)
BMI (kg/m^2)	27.17±4.75 (27)
BASDAI	4.49±2.22 (4.5)
HAQ	0.35±0.36 (0.25)
HADS-anxiety	7.89±5.44 (7)
HADS-depression	6.76±4.78 (6)
IFAB-total score	4.61 ± 22.22 (5)

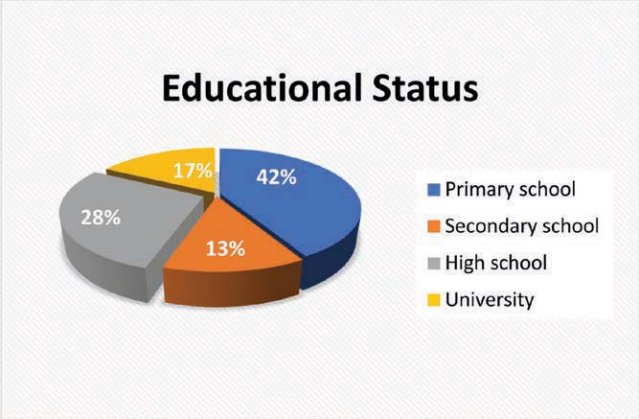

Figure 1. Educational status of the included patients.

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POS1538-HPR INVESTIGATION OF BALANCE FUNCTIONS IN INDIVIDUALS WITH NEURO-BEHCET: A PILOT STUDY

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Background: Behcet's disease is a vasculitis, causing multisystem inflammation and resulting in oral and genital ulcers and eye and skin lesions (1). A proportion of patients also have neurological involvement, termed Neuro-behcet's disease (2). We think about that Neuro-behçet's disease can impact balance functions in patients due to neurological involvement. However, there is no study investigating the balance functions in patients with Neuro-behcet.

Objectives: To investigate the balance functions in individual with Neuro-behçet's disease.

Methods: In this study 8 Neuro-behcet patients with a mean age of 38.37±16.96 who were followed in the PAU Rheumatology outpatient clinic and diagnosed by a rheumatologist according to the criteria of the International Behcet Study Group and 8 healthy control with a mean age of 42.62±13.94 with similar demographic characteristics were included. Exclusion criteria for the study were age <18 years old, having any disease which mimics BD (including systemic lupus erythematosus, vasculitis of central nervous system). Demographic data of the participants were recorded. Then, balance functions were evaluated with a balance board (Sensamove Mini-Board, NL) in Neuro-behcet and control groups. This assesment included static balance, proprioception, and reaction. Results were analyzed with Mann Whitney U Test.

Results: Participants were similar in terms of age and gender ($p>0.05$). Neuro-behcet group showed a significant decrease in static balance in all directions except the right side compared to the control group ($p<0.05$). A significant decrease was observed in the right and left reaction times in Neuro-behcet group compared to control group ($p<0.05$). There was no significant difference between the two groups in proprioception assesment ($p>0.05$).

Conclusion: This results show that patients with Neuro-behcet may experience disturbances in static balance and reaction time. Balance and reaction exercises should be included in rehabilitation. Further research is needed on the effect of balance functions and the effectiveness of balance exercises in Neuro-behcet's disease.

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POS1539-HPR EXPLORING TASK- SHIFTING IN HAND OSTEOARTHRITIS CARE FROM THE PERSPECTIVE OF THE SERVICE USER.

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Background: The demand for and provision of health care is in constant change. People live longer and have more complex health requirements, challenging the functioning of the health care system in responding adequately to present and future needs. For persons with hand osteoarthritis (HOA), access to recommended treatment is poor (1) and what can be offered in primary health care is not optimal. A reorganization of the workforce through task-shifting can be a solution where the aim is to use existing human resources in health in more efficient ways. Through task- shifting, tasks and knowledge can be shifted between health professionals, between levels of the health care system, and from health professionals to service users, changing the current division of labor (2).

Objectives: The aim of this study is to gain a broader understanding of the distribution of tasks among health professionals and service users in HOA care from the perspective of service users to guide future task- shifting initiatives.

Methods: In- depth interviews with 21 service users with HOA were conducted, including 15 women and six men from 47 to 86 years of age. All had received services from primary and specialized health care services. A theme based semi- structured interview guide was used. All interviews were audio- recorded and subsequently transcribed verbatim. Reflexive thematic analysis was used to generate codes and develop three main themes.

Results: *Tasks by different professionals*: service users describe general practitioners (GPs) as entry points to health service provision. Contact is initiated with

the aim to have signs and symptoms recognized for referrals to diagnostic tests and specialized services. As such, tasks beyond referrals are not expected by service users in primary health care in their encounters with GPs. Upon entering specialized health care services, service users describe diagnostics and prescription of medication for pain as key tasks of the rheumatologists, highlighting the role of the rheumatologists in ruling out severe pathology. Service users attribute the tasks of providing information about the condition, exercises, and assistive devices to occupational therapists (OTs). A lack of familiarity with the OT- profession prior to consultations is also expressed. This shows how patients attribute different tasks to GPs, rheumatologists, and OTs based on experiences in consultations.

Profession secondary to competence about HOA and interpersonal skills: service users say they do not have preferences related to who executes what professional tasks in addressing their needs. On the contrary, service users highlight competence about HOA as a key factor independent of whether the health professional is a GP, rheumatologist, or OT, saying professional orientation is secondary to professional knowledge about HOA. At the same time, service users underline interpersonal skills of health professionals as another key element, further downplaying the specific professional background of health professionals and levels of the health care system in meeting service user needs.

Transfer of tasks to service users: service users experience that they are presented with few treatment options beyond self- management in encounters with health professionals, leaving service users to cater for their own needs through the self- administration of exercises, medicines, and assistive devices.

Conclusion: In the division of labor, service users highlight the importance of professional knowledge and skills within the field and interpersonal skills independent of professional background and levels of the health care system. They also underline few treatment opportunities beyond self- management resulting in task- shifting to service users.

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POS1540-HPR CENTRAL SENSITIZATION PLAYS A PROMINENT ROLE IN DISEASE ACTIVITY, FUNCTIONAL IMPAIRMENT AND QUALITY OF LIFE IN PATIENTS WITH SPONDYLOARTHRITIS.

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Background: Pain in rheumatic diseases is substantially due to an excess of nociception in response to chronic inflammation. However, the share of nociplastic pain in these disorders shouldn't be overlooked. Different tests have been evaluated but some of them require expensive equipment.

Objectives: to assess The Central Sensitization in young patients with spondyloarthritis (SpA) using a simple and validated tool: The Central Sensitization Inventory (CSI).

Methods: We conducted a cross-sectional study including patients with SpA, fulfilling the Assessment of SpondyloArthritis International Society (ASAS) 2009 criteria. For all patients, we collected the following data: age, age at onset of SpA, disease duration, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing spondylitis quality of life score (ASQOL) and functional statement by Bath ankylosing spondylitis functional index (BASFI). Nociceptive pain was assessed by VAS pain, neuropathic pain was assessed by DN4 and nociplastic pain was assessed by CSI.

Univariable and multivariable linear regression analyses were used to investigate the association between CSI scores, patient-related parameters and disease characteristics.

Results: Sixteen SpA patients (50 axial SpA, 8 axial and peripheral SpA, 1 psoriatic arthritis and 1 SpA associated with inflammatory bowel disease) were enrolled. There were 22 females and 38 males. Mean age was 39,4 years ± 11,08, mean age at onset was 23,61 years± 8,5 and mean disease duration was 11,37 years ±7,23. Mean night awakenings was 0,92 [0, 3], mean VAS pain was 5,27 [1, 9]. Mean BASDAI was 3,53 ± 3,34, mean BASFI was 4,01 ± 2,53, mean ASQOL was 6,3 ± 5,128 and mean DN4 was 1,72 [0, 7].

Mean CSI score was 20,38 ± 18,657. Six patients (10%) had a CSI score≥ 40, which indicates a central sensitization. CSI score>40 was not associated with the gender (p=0,659), nor axial presentation of SpA (p=0,644), nor the presence of coxitis (p=0,217). CSI score was not correlated with disease duration (p=0,306) nor age at onset (p=0,376). It was however associated with a BASDAI>4 (p=0,039).

A positive correlation was found between higher CSI score and higher ASQOL (p<0,001, r=0,744), VAS pain (p=0,061, r=0,282), more frequent night awakenings (p=0,009, r=0,433), higher BASDAI (p=0,006, r=0,379) and higher BASFI (p=0,055, r=0,270).

Conclusion: Higher CSI score was associated with higher disease activity, more frequent night awakenings, poorer quality of life and greater functional impairment. A global and comprehensive management including these factors as well as nociplastic pain should help the patient achieve better outcomes.

Disclosure of Interests: None declared

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POS1541-HPR PAIN CATASTROPHIZING IS FREQUENT AND IMPACTS THE LIFE AND FUNCTION OF PATIENTS WITH SPONDYLOARTHRITIS

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Background: Psychological care for patients with spondyloarthritis (SpA) should be standard practice if we aim to achieve better outcomes. In fact, pain catastrophizing, anxiety, and depression are to look for when the patient remains unsatisfied despite the clinicobiological control of the disease.

Objectives: To assess the presence of pain catastrophizing among patients with SpA.

Methods: We conducted a cross-sectional study including patients with SpA, fulfilling the Assessment of SpondyloArthritis International Society (ASAS) 2009 criteria. For all patients, we collected the socio-demographic data and disease characteristics, the following scores: the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath ankylosing spondylitis functional index (BASFI), the Ankylosing spondylitis quality of life score (ASQOL) were used to evaluate respectively disease activity, functional status and quality of life. The presence of pain catastrophizing was assessed by the arabic validated version of Pain catastrophizing score (PCS) and nociplastic pain by Central Sensitization Inventory (CSI).

Results: We included 60 SpA patients (sex ratio=1,72). Mean age was 39,4 years ± 11,08. Mean disease duration was 11,37 years ±7,23. Mean BASDAI score was 3,53± 3,34, mean BASFI was 4,01 ±2,53 and mean ASQOL score was 6,3 ±5,12. Mean PCS was 15,73 ± 13,893. thirteen patients (21,7%) had PCS >30 which indicates clinically relevant level of catastrophizing. PCS was significantly higher in men (mean PCS was 19,29 in men versus 9,59 in females), p=0,003. Clinically relevant level of catastrophizing (PCS>30) was significantly associated with age: mean age was 45,61 years in patients with PCS>30 compared to 37,47 in patients with lower PCS (p=0,022). Higher PCS was correlated with greater central sensitization assessed by the CSI (p<0,0001, r=0,621), poorer quality of life assessed by the ASQOL (p<0,0001, r=0,818) and greater functional impairment appraised by BASFI (p=0,009, r=0,347). No correlation was shown between PCS and age (p=0,640, r=0,062), age at disease onset (p=0,580, r=-0,84), disease duration (p=0,805, r=0,037), patient's global assessment (p=0,211, r=0,197), CRP value (p= 0,425, r=-0,130) and BASDAI score (p=0,073, r=0,244).

Conclusion: Pain catastrophizing was not influenced by inflammation parameters. PCS was correlated with greater central sensitization, poorer quality of life and greater functional impairment. Therefore, psycho-education should be investigated among patients with SpA.

Disclosure of Interests: None declared

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POS1542-HPR QUALITY OF LIFE AND PHYSICAL FUNCTIONING OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS FAST TRANSLATE ICON TRANSLATE FAST TRANSLATE ICON TRANSLATE

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Background: Quality of life (QoL) due to World Health Organization (WHO) is an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. QoL can be decreased during chronic illnesses, including juvenile idiopathic arthritis (JIA). This severe chronic disease of childhood afflicts both joints and body`s system inducing various comorbid conditions, among which eye damage (uveitis) is the most common[1]. Considering the fact of involved joints it was set up that physical functioning (PF) shows the lowest values in some studies, which is associated with joint damage, activity, and duration of the disease[2].

Objectives: To establish the overall level of QoL and physical functioning in patients with JIA, considering the subtype of the disease, duration and the therapy complex.

Methods: The study involved 118 patients with JIA, among which 47 had polyarticular subtype, 43 had oligoarticular one, 28 were with uveitis-associated (JIA-u) subtype. The investigation included 77 girls and 41 boys in age from 2 till 18 years old. The therapy by methotrexate was provided in 112 patients, among them 30 had MTX with immunobiological therapy (29 adalimumab, 1 – tocilizumab), 6 – sulfasalazine. The disease duration due to disease subtype in polyarthritis was (49,2±6,7), oligoarthritis – (35,4±4,2), JIA-u – (76,8±10,2) months. Disease activity was assessed using the JADAS27 questionnaire, functional state (FS) according to CHAQ and QoL according to PedsQLTM 4.0 Generic Core Scales.

Results: It was found that high JIA activity was observed in 31 (26.2%) patients, equally often in all subgroups of children. FS did not show a significant decrease either in the whole group or in each of the arthritis subgroups. The overall indicator of QoL in children with JIA was reduced in the whole group (71.2±1.4 and 72.9±1.4 per week and month). There was no significant difference between the QoL indicators of boys and girls. The polyarticular subtype showed the lowest results in QoL and PF, especially in children in the first year of the disease. They also turned out to be worse in children with JIA-u with the disease from one to three years (QoL – 63,3±2,6*; PF – 66,6±3,9) The highest level of the physical component of QoL was observed in children with oligoarthritis older than 14 years (84,9±4,7) and in children under 8 years of age in the JIA-u group (96,8±1,8). There was no significant effect on the physical indicators of QoL of the start treatment timing. ($p \leq 0,05$). Finally, the strong correlation was determined between QoL and PF ($r=-0,842$; $p \leq 0,05$).

Conclusion: A decrease in QOL and its physical component is typical for children with different types of JIA (oligoarticular, polyarticular, and JIA-y). It has been established that children with polyarticular subtype of arthritis have the greatest decrease in QoL and physical functioning.

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POS1543-HPR **JOINING TELEMEDICINE SERVICES IN RHEUMATOLOGY: THE ROLE PLAYED BY PERSONALIZED EXPERIENCE FROM PATIENTS' PERSPECTIVE**

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Background: With the beginning of the Covid-19 pandemic, many hospital departments worldwide, including rheumatology ones, were forced to implement telemedicine strategies. Telemedicine revealed to be an umbrella term, with various practical implementations and different degrees of preparedness1. Some practitioners were already familiar with telemedicine, as in the case of the Rheumatology Unit of ASST Niguarda Hospital in Milan (Italy), where telemedicine projects have been implemented for more than a decade with structured design and organized processes. Moreover, patients in Niguarda have experimented telemedicine with personalized mixes of channels, including e-mails and phone calls, Patient Reported Outcomes questionnaires, and home delivery of drugs. This represents a paradigmatic case study that enables us to deepen essential questions on the success of telemedicine.

Objectives: Given that the last decision on joining telemedicine rests with patients[2], we decided to adopt their perspective. We deepened three main aspects: i) the benefits perceived, ii) the willingness to enrol in future projects, iii) the preference on the service-mix, i.e., on-distance contacts rather than in-person visits. Most importantly, we investigated differences in the three areas among all patients based on the type of personalized experience had.

Methods: We conducted a survey from November 2021 to January 2022, enrolling randomly outpatients who attended the rheumatology unit for any reason. The survey originated from well-known surveys, such as the Tele-Health Usability Questionnaire[3] and the Intention to use telehealth services[4]. However, we decided to overcome the usual separation that makes surveys addressed either to users or no users of telemedicine. Our survey comprised an introductory set of questions related to personal, social, clinical and ICT skills information, followed by the central part on telemedicine, which explored the three areas mentioned: benefits, adherence, preferences on service-mix. For this part, questions were the same for all patients apart from the tense used, being conditional tense for no-users and past tense for users. All the answers were analysed with descriptive statistics and regression models.

Results: A complete response was given by 400 patients: 71% were female, 59% were 40-64 years old, 53% of them declared to work, and the diseases most represented were Rheumatoid Arthritis (36%) and Osteoporosis/arthrosis (21%).

The descriptive statistics revealed interesting differences between users and no users, e.g., the desire to participate in future projects was stated by 95% of users, 81% of no users. These results were confirmed by multivariate logistic regression models that controlled for the influencing patients' characteristics (such as being old or a frequent hospital attender).

It emerged that no-users imagined wide-ranging benefits. As for the willingness to participate to future telehealth projects, even if personal characteristics showed an impact (e.g., being a worker increased the probability to adhere), other things being equal, having had a more intense experience of telemedicine increased the odds of accepting by 3.1 times (95% C.I. 1.04-9.25), compared to no users. Furthermore, the more telemedicine was experienced, the higher the willingness to substitute in-person with online contacts.

Conclusion: Our study contributes to enlighten the crucial role played by the telemedicine experience in determining patients' preferences. On one side, users appeared more aware of the realistic benefits to be expected from telemedicine. On the other side, it seemed that the more telemedicine was experienced, the higher the willingness to adhere to future projects and to increase on-distance contacts.

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HPR Service developments, innovation and economics in healthcare

POS1544-HPR RHEUMATOID ARTHRITIS CONTROL USING SYNCHRONOUS TELEMEDICINE MODALITY IN THE PANDEMIC PERIOD

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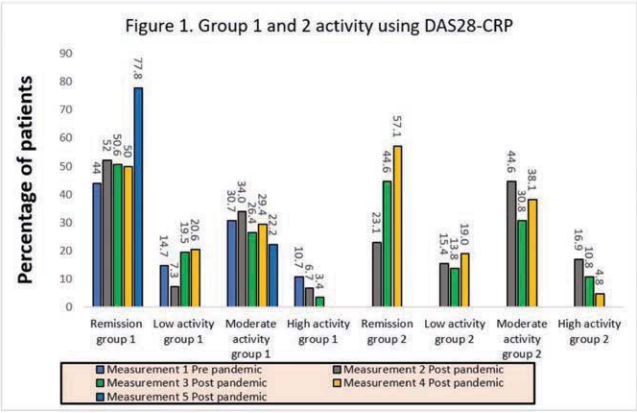
Background: Telemedicine is a useful tool in the control of patients with rheumatological conditions, even more so in the pandemic period. The evolution of patients with rheumatoid arthritis (RA) treated exclusively under this modality has been scarcely described.
Objectives: Evolution of clinical activity in RA patients controlled exclusively by the synchronous telemedicine (ST) modality in the COVID-19 pandemic period.
Methods: An observational study was carried out.Two group of patients were analyzed separately, first group who had been treated using ST before the declaration of a health emergency in Colombia in march 2020 and second who were admitted to ST after this date. ST consists of a real-time video call with a trained general physician help on the referral site to performed physical examination. Assessments of disease activity was measured by DAS28 using C-reactive protein.
Results: Data was obtained from 150 and 65 patients in the first and second group. For the first group, more than a half of the patients had 2 controls with DAS28 assessment after march 2020, only 33% obtained 3 assessments, and very few with 4 or more. We found that the number of patients with high activity decreased significantly from 10% to 3%, remission increased from 44% to 50% and low activity from 14% to 19%, without major changes in the moderate activity group that remained close to a third. Same tendencies happened in group 2, with a difference in reduction of the moderate activity group from 44% to 38% (Figure 1)



Conclusion: When in person attention with rheumatologist is not possible, telemedicine is a useful and efficient way to control patients with RA, mainly finding a reduction in high activity and an increase patients in remission.
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POS1545-HPR PATIENT SELF-SAMPLING IN RHEUMATOID ARTHRITIS: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: Rheumatoid arthritis (RA) requires early diagnosis and tight surveillance of disease activity. Patient self-sampling of blood for the analysis of autoantibodies and inflammation markers could facilitate the identification of patients at-risk for RA and improve tight disease monitoring [1].
Objectives: A randomized, controlled trial to evaluate the feasibility, acceptability and accuracy of an upper arm self-sampling device (UA) and finger prick-test (FP) to measure capillary blood from RA patients for C-reactive protein (CRP) levels and the presence of IgM rheumatoid factor (RF IgM) and anti-cyclic citrullinated protein antibodies (anti-CCP IgG).
Methods: 50 RA patients were randomly assigned in a 1:1 ratio to self-collection of capillary blood via UA or FP. Venous blood sampling (VBS) was performed as gold standard in both groups to assess the concordance of CRP levels as well as RF IgM and CCP IgG. General acceptability and pain during sampling were measured and compared between UA, FP and VBS. The number of attempts for successful sampling, requests for assistance, volume and duration of sample collection were also assessed.
Results: 49/50 (98%) patients were able to successfully collect capillary blood. Overall agreement between capillary and venous analyses for CRP (0.992), CCP IgG (0.984) and RF IgM (0.994) were good. In both groups 4/25 (16%) needed a second attempt and 8/25 (32%) in the UA and 7/25 (28%) in the FP group requested assistance. Mean pain scores for capillary self-sampling (1.7/10 ± 1.1 (UA) and 1.9/10 ± 1.9 (FP)) were lower on a numeric rating scale compared to venous blood collection (UA: 2.8/10 ± 1.7; FP: 2.1 ± 2.0). UA patients were more likely to promote the use of capillary blood sampling (net promoter score: +28% vs. -20% for FP) and were more willing to perform blood collection at home (60%) vs. 32% for FP).
Conclusion: This study shows that self-sampling is accurate, feasible and well accepted among patients. The implementation could allow tight remote monitoring of disease activity as well as identifying patients at-risk for RA and potentially other rheumatic diseases.
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POS1546-HPR DISEASE ACTIVITY BURDEN FOR LONG TERM RHEUMATOLOGY FOLLOW-UP PATIENTS

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Background: There has been a lot of emphasis for early diagnosis and treatment for immune mediated rheumatology conditions such as Treat to target (T2T) for inflammatory arthritis, Fast track pathway for Giant cell arteritis. However, the data regarding burden of disease activity, nature and proportion of long term rheumatology follow up patients in rheumatology clinics have not been explored. There are conditions which are refractory to treatment or affected by recurrent flare-ups requiring long term follow-ups and constant monitoring. With increasing life expectancy and better treatment of the long term conditions, emphasis on long term disease activity monitoring is under strain. It is important to understand the nature of illnesses and treatment of long term follow-up patients to decide management strategies.
Objectives: The aim of this quality improvement project was to understand profile of disease and management of patient being seen as long term follow-up (defined as >2 years follow-up after their first presentation in specialist clinic).
Methods: This was a single point, retrospective cohort analysis of patients seen in rheumatology clinics in a district general hospital, UK in March 2021. We reviewed consecutive 120 follow-up patients and recruited 80 patients who

had >2yrs follow-up. We have a community rheumatology service arm where all patients with stable inflammatory arthritis on non-biologic treatments are reviewed while patients with multisystem complicated illness and biologics are seen in secondary care. The stable patients from community clinics have not been included in this analysis. The data was reviewed using clinic letters, date of first appointment & last appointment. We looked at gender, age, diagnosis, number of follow ups in the first and last year, disease activity scores of the respective diagnosis and treatment given.

Results: Sixty six percent of follow-up patients are long term with complicated illness or treatment. Of these 52 patients (65%) were female with median age 64 years (range 23-94 years). Median duration of follow up for this group of patients was 6 years (range 2-11 years). Inflammatory arthritis was the most common diagnosis in 75% of patients (11 patients were Psoriatic arthritis, 30- Rheumatoid arthritis, 7- undifferentiated inflammatory arthritis and 7- Axial spondyloarthritis), 17.5% connective tissue disease, 11.2% vasculitis and others (Still's disease) 3.7%. Some patients had more than one diagnoses. The number of follow ups in the first year ranged from 1-13 (median 4). In final year of analysis, patients were seen median of 3 times (range1-8). Amongst them, 25% of patients were seen 4 or more times. The commonly prescribed drugs were methotrexate (41.2%), sulfasalazine(17.5%), hydroxychloroquine(15%), leflunomide (7.5%),biologics (8.7%), mycophenolate mofetil and azathioprine (6.5%).The activity scores such as DAS28, BVAS, PsARC and BASDAI were documented in 46 patients (57.5%).

Conclusion: This study shows that 66.6% of follow-up patients in rheumatology clinics are complicated long term conditions on immunomodulatory treatment. Despite T2T approach, use of combination DMARDs and early use of biologics, majority are inflammatory arthritis. It also shows that even after median follow-up of 6 years, these patients require an average review 3 or more times per year. The reasons for this may be poor disease control, disease complications, comorbidities and medication side effects. Further analysis is ongoing to look into these aspects for better disease control and long term outcome.

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POS1547-HPR CREATION OF A MULTI-DISCIPLINARY TEAM (MDT) RHEUMATOLOGY CLINIC AT UNIVERSITY COLLEGE LONDON HOSPITAL (UCLH) TO TACKLE THE BACKLOG OF PATIENTS WAITING FOR TREATMENT AS A RESULT OF THE COVID-19 PANDEMIC.

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Background: Covid-19 has consumed hospital resources since January 2020. In the UK, routine care has been disrupted with an estimated 30 million fewer outpatient attendances (2020/21) and over 6 million patients waiting for consultant led care (1). The British Society for Rheumatology 'Rheumatology Workforce: a crisis in numbers (2021)' highlights the challenges facing National Health Service rheumatology departments in managing rising caseloads (2). In 2021, UCLH wait time for follow up rheumatology appointments was 9 months. We were inundated with patients requiring urgent treatment. Innovative ways of running outpatients were required which led to the formation of an MDT clinic.

Objectives: Create a Rheumatology MDT clinic to:

Reduce follow up time

Increase clinic capacity

Reduce number of hospital attendances

Add value to each clinic encounter

Methods: The consultant lead identified an existing clinical nurse specialist (CNS) interested in supporting the MDT. With a UCLH Outpatient Transformation grant of £15,000 we recruited an advanced physiotherapy practitioner (APP) and administrator for a 6 month trial period. Managerial support was provided by the board. We met weekly to agree aims and allocate responsibilities. We did the following:

- Reviewed clinic lists for 6 months to identify duplicate appointments.
- Identified patients with CNS and consultant follow up scheduled in a short time frame and cancelled unnecessary appointments.
- Reviewed the clinic list weekly to identify patients suitable for APP management. This allowed overbooking of urgent cases.
- Embedded hand ultrasound appointments in the clinic template.
- Created CNS 'Zoom' virtual drop-ins for routine enquiries to reduce the administrative burden of patient emails/phone calls occurring outside the clinic.
- Organised patient participation sessions to help shape the service and collected patient feedback questionnaires.

Results: We reduced our waiting time for follow up appointments from 9 months to 2 months. Pre-MDT the average wait from consultant referral to physiotherapist appointment was 55 days. The MDT allows for same day assessment (reducing 2-3 patient journeys a clinic) and where suitable, facilitates discharge or onwards referral to the appropriate service i.e. pain management, hand therapy, APP-led hypermobility programme. A dedicated MDT CNS has shortened treatment times, reduced email traffic between CNS and consultant and allows for same day, joint decision making resulting in fewer appointments. Patients welcomed the Zoom sessions as an efficient, reliable method of raising concerns/queries. Our administrator helps to facilitate communication between patients and clinicians and streamline MDT processes. Embedding point of care ultrasound reduces hospital visits and enhances treatment decision making thereby reducing follow up attendances.

Conclusion: Our MDT model has reduced waiting lists, decreased treatment delays and cut the number of hospital visits. Performing ultrasound in clinic helped prevent patients being sent for scans at private providers. This cost saving likely covers the APP, ensuring the project is close to cost neutral. Shared decision making added value to outpatient attendances, reflected in patients positive feedback. The MDT enhances the role of APP and CNS, utilising their unique skill set. Administrative support is crucial, enhances team working and places added value on this often underappreciated role. We encourage other Rheumatology departments to adopt an MDT approach to tackle the backlog of patients awaiting treatment, add value to clinic encounters and maximise the skill set of clinicians involved in patient care.

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POS1548-HPR USEFULNESS OF AN ELECTRONIC CONSULTATION SYSTEM BETWEEN PRIMARY CARE HEALTH CENTERS AND RHEUMATOLOGY DEPARTMENT OF A TERTIARY HOSPITAL

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Background: The EPISER study is the first Spanish epidemiological study that has confirmed the great burden of rheumatic diseases in the general population: they consume a large quantity of health resources (doctor visits, medical products) and imply a high social impact in terms of work absenteeism. Rheumatic diseases represent almost 30% of Primary Care medical consultations in Spain[1,2]. Electronic consultation could be an alternative response to the increase of this demand, both to make an early diagnosis and derivation and to improve communication with Primary Care physicians[3,4].

Objectives: To analyze the demand of Primary Care and its resolution through the electronic consultation system of the Rheumatology Department of a tertiary hospital.

Methods: Retrospective descriptive study of the data collected in the request and information system (Sistema de Peticiones Electrónicas, SIPE) that supports electronic consultation between primary care physicians of the health area and the Rheumatology Department of a tertiary hospital, between July 2020 and May 2021.The following variables were collected: age, sex, reason for consultation, response time in days and destination (primary care/outpatient follow-up). Descriptive statistics were used to present the results.

Results: The last 500 consecutive electronic consultations registered in the system, referring to 496 patients, were collected. Mean age was 59.5±17.7 years; 74.2% women. Mean response time was 2 days, median response time 1 day and range 0-45. The reasons for consultation (see Graph 1) were: osteoporosis assessment 55 (11%), treatment adjustment 50 (10%), appointment request 49 (9.8%), loss to follow-up 43 (8.6%), local-regional pathology assessment 39 (7.8%), infiltration request 28 (5, 6%), suspected rheumatoid arthritis 19 (3.8%), flare 18 (3.6%), suspected polymyalgia rheumatica or giant cell arteritis 16 (3.2%), COVID vaccine consultation 14 (2.8%), Raynaud's phenomenon 13 (2.6%), monoarthritis assessment 12 (2.4%), assessment of polyarthritis 11 (2.2%), adverse effects of treatment 11 (2.2%), suspected spondyloarthritis 11 (2.2%), suspected psoriatic arthritis 8 (1, 6%), generalized pain 7 (1.4%), suspected Sjögren's syndrome 5 (1%), suspected systemic lupus erythematosus 1 (0.2%), suspected other systemic autoimmune diseases 9 (1.8%), others 81 (16.2%). Fifty-seven and four % (287) of the patients required an appointment at the Rheumatology outpatient clinic and in 42.6% of the patients (213) the electronic consultation was successful, so it was not necessary to refer the patient to the hospital.

Conclusion: Forty-two and six percent of the queries were resolved thanks to the electronic consultation system in an average of two days, otherwise that patients would have been referred to specialized care. The main reasons for consultation were osteoporosis assessment and clarification of doubts about the treatment of patients who were already being followed up by the Rheumatology Department.

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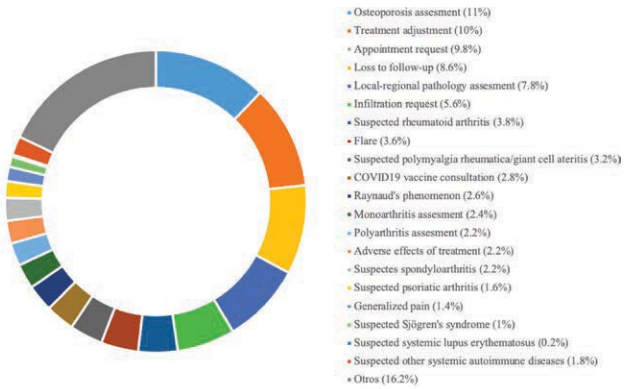

Graphic 1. Reasons for electronic consultation.

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POS1549-HPR IMPROVING EFFICACY AND SAFETY OF BLOOD MONITORING IN RHEUMATOLOGY PATIENTS ON DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS) USING A NEW AUTOMATED ALGORITHM

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Background: Most patients in Rheumatology require early management with DMARDs to control their disease. In our department, around two hundred patients start a DMARD therapy every month and monitoring their blood test results whilst on DMARDs play an essential role to detect toxicity and the need for further action. This process has been done manually, which has been prone to error. Over the past six months, a minimum of three patients have had abnormalities which were missed, consequently identifying the need to improve the quality of the blood monitoring.

Objectives: The aim of the project was to develop, test and implement an automated algorithm to review multiple blood test results and highlight any changes, trends or abnormalities in patients starting DMARD therapy efficiently.

Methods: We designed a system to automatically review blood tests from patients newly started on DMARD therapy, following the recommended British Society for Rheumatology (BSR) schedule for blood monitoring. Results are processed in our local laboratory, subsequently uploaded to our unique database and analysed automatically using an algorithm against BSR guided threshold values for each blood test. According to the value, each blood result is identified as normal, mildly abnormal, missing, trending, or abnormal. A trained clinician or pharmacist will review the data and endorse the results after taking any appropriate action. Based on the results, if any actions are needed, patients are contacted either by phone or via a letter automatically generated by this software, recommending them to have a repeat test or temporarily stop the medication as required.

Results: The system was tested on two cohorts, comprised of 100 and 227 blood tests. It was faster and more efficient than the manual alternative. Following this test, each record was compared manually, based on the data stored on a spreadsheet.

This new system led to the identification of more abnormalities versus the manual inspection (29% vs 10%, Chi square P<0.001). Additionally, it took less than a minute compared to the manual method, which took three hours to complete. Follow up manual inspection confirmed that the new system had correctly identified every abnormality, based on test records.

To date, we have analysed 3568 blood results using this technique. 1564 (44%) results have been normal and endorsed within seconds. 374 (10%) were mildly abnormal, 17 (0.5%) results have been abnormal requiring action and 311 (9%) were abnormal requiring no action. 265 (7%) results showed a trend within the blood results. Trending results were defined as being out of range and worsening on two consecutive occasions but not reaching the limits for stoppig a drug. 1032 (29%) results contained missing results, a consequence of the different timings of results uploaded by various laboratory sections.

Conclusion: We have developed an efficient and safe blood monitoring system for Rheumatology patients starting on a DMARD, proven to be more accurate compared to previous manual alternatives and able to process up to 10,000 results at a time.

Disclosure of Interests: None declared

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POS1550-HPR DRIVE-THROUGH PHLEBOTOMY – DOES IT WORK FOR CDMARDS MONITORING?

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Background: Centralised phlebotomy services have been an integral part of providing blood monitoring facility for people with chronic diseases prescribed vital therapies. However the patient experience is not always optimal due to the issues of congestion, parking, long waiting times and have been accentuated during COVID-19 pandemic with the need for minimising physical contact. Expert panels have advocated for the creation of innovative approaches to provide safe patient care while maintaining precautions against COVID-19 spread. Several groups have published the concept and experience of using a drive-through clinic for anticoagulation monitoring and management. There is limited data on how this model of care can impact other clinical services such as rheumatology where patient groups are more vulnerable.

Objectives: In response to the growing pressure on phlebotomy service at our institution enhanced by COVID-19 pandemic, our rheumatology service implemented a drive-through phlebotomy clinic to provide the option for patients and families to stay in their vehicles whilst having venepuncture. The objectives were to evaluate the feasibility and patient experience of the service.

Methods: At our large university teaching hospital, we set up a drive-through phlebotomy service provided by a senior health care assistant supervised by the lead nurse. It was located near the hospital entrance where vehicles could park for a few minutes without disrupting traffic flow. Patients were identified from the departmental database and were offered the facility via telephone. Eligibility was assessed using a standardised proforma focusing on logistics such as ability to drive and access to a mobile phone. Appointments were scheduled in advance with patients choosing this care option. On the day, patients were screened for COVID-19–related symptoms before their appointment and were encouraged to stay in their vehicles wearing a mask before being approached by the HCA. At the end of clinic, all samples were submitted to the central laboratory.

All the data was prospectively collated with patients' consent and anonymised for analysis. In addition to demographics, diagnosis and drug record, duration of visit and patient feedback was collected.

Results: 112 patients were offered the service during a 12-week pilot. Mean age of the participants was 49.5 yrs (19-91) with 73 (65%) women. 74 (65%) were of Caucasian and 28 (25%) of Asian origin. 94 (84%) had inflammatory arthritides and all were prescribed DMARDs and/or bone active agents.

69 (61%) had blood samples taken using this service. Most common reason to decline was an already arranged appointment with standard phlebotomy (n=14, 12.5%). Six (5%) could not be bled due to difficult venepuncture. Mean duration of appointment was 12.5 mins (5-60). 68 (60%) provided feedback with 61 (90%) rating 5/5 and 60 (89%) rating it better than standard phlebotomy. All would like to have the option for future and 67 (98%) were highly likely or likely to recommend the service to family and relatives.

Conclusion: To our knowledge, this is the first study to demonstrate the utility of drive-through phlebotomy for people with rheumatic diseases prescribed DMARDs. Excellent feedback of the participants confirms the need and desire for such innovation in health care. Prior publications have shown the benefits of such clinics in anticoagulation services. Arguably, it's more prudent to have this facility for those where there is no alternative such as point-of-care or home INR monitoring. In post COVID-19 services reconfiguration with telemedicine and innovative models of care, this allowed flexibility for our department to develop

and establish an alternative process. The availability of drive-through appointments and the close physical proximity to the clinic made it an appealing option for a vulnerable group of patients evidenced by their outstanding experience and feedback. Overall, an HCA-delivered, nurse-supervised drive-through pathway is highly effective, safe and provides an innovative solution to strained phlebotomy services.

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POS1551-HPR MEDICAL EXPERT KNOWLEDGE MEETS AI: HOW EXPERT KNOWLEDGE CAN IMPROVE SYMPTOM ASSESSMENT APPS - A NEW APPROACH IN RARE DISEASES

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Background: By definition, rare diseases occur in fewer than 5 in 10,000 people. However, in Germany alone, there are approximately 4 million people affected (1). Due to their rarity, rare diseases are often overlooked by general practitioners with limited knowledge about them. There are often only a handful of specialized experts for each condition. Yet, those experts are frequently not evenly distributed across the healthcare system, and often, patients lack access. Therefore, the time to diagnosis is often long and poses many challenges. Artificial intelligence (AI) approaches, such as those used in symptom assessment apps can potentially help to detect disease and thus, shorten the time to diagnosis (2).

The general approach underlying the AI of symptom assessment apps is to gather medical knowledge from data (e.g. electronic health record or literature searches). However, for rare diseases, there is only limited research available. In this study we used a new approach: to abstract medical expert knowledge by conducting guided interviews and transforming them into clinical vignettes.

Objectives: There are two objectives. First, we aimed to integrate expert knowledge on the lysosomal storage diseases (LSDs) Fabry, Gaucher and Pompe into the Ada symptom assessment application and use this expert knowledge to optimize Ada's LSD condition models. LSDs are of particular importance as they represent import differential diagnoses to rheumatic diseases.

Second, we will conduct questionnaires with patients and LSD experts, comparing the optimized to the previous condition models' performance. We will investigate whether the novel approach of guided interviews, in combination with literature research, results in a better performance than literature research alone.

Methods: Our novel approach is to curate expert medical knowledge from guided interviews with medical experts. The interviews aim to gather knowledge on the symptom constellations with which patients typically present to their physicians. This knowledge is subsequently used to create prototype clinical cases and transform them into structured case vignettes. The rare disease structured case vignettes can be readily transcribed into Ada's knowledge base.

Results: We conducted guided interviews with clinical experts from the Medizinische Hochschule Hannover (MHH) to create clinical vignettes for the LSDs Fabry, Gaucher and Pompe disease. We conducted interviews with four medical experts and created a total of 11 clinical vignettes: five vignettes for Fabry disease, four for Gaucher disease and two for Pompe disease. Figure 1 demonstrates the vignette creation process. Then, in combination with systematic literature searches, the vignettes were used to update Ada's existing condition models for Fabry and Gaucher disease and to add Pompe disease.

Figure 1. The novel medical model creation approach uses guided expert interviews to create prototypic clinical vignettes, which can be readily transcribed in a medical modeling language to create individual disease models

Conclusion: Participants will complete two assessments: an Ada version with the old knowledge base and an Ada version with the updated models. The study plans to enroll 15 LSD patients - five per condition - and nine LSD experts. For the conditions Fabry and Gaucher disease, we will ask the participants to rate both Ada versions. For Pompe disease, we will ask participants to rate the latest Ada version with the updated knowledge base. This novel approach has various clinical implications, including potentially shortening the 'time to diagnosis' for rare diseases, thus giving patients faster access to the treatments they need.

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POS1552-HPR A SYNTHESIS OF GUIDANCE AVAILABLE FOR ASSESSING METHODOLOGICAL QUALITY AND GRADING OF EVIDENCE FROM QUALITATIVE RESEARCH TO INFORM CLINICAL RECOMMENDATIONS: A SYSTEMATIC REVIEW

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Background: Qualitative research is crucial to understand key stakeholders experiences and perspectives of care and health services. However, there is a lack of explicit frameworks and guidelines about how best to use qualitative evidence to formulate clinical recommendations. Part of the problem includes uncertainties about the contributions of qualitative research to the evidence, and the empirical and theoretical basis for appraising and synthesizing qualitative evidence in a standardized manner. In addition, most existing grading systems of qualitative research originates from quantitative research, and there is no clear guidance about how to incorporate qualitative research into the evidence hierarchy.

Objectives: To conduct a systematic literature review (SLR) to answer two research questions (RQ):

RQ1) *What guidance (e.g., tools, checklists, frameworks) exists to assess the methodological quality of qualitative research employed to inform clinical recommendations?;*

RQ2) *What methods exist specifically to grade levels of evidence for qualitative research?*

Methods: The protocol for this review was registered on www.researchregistry.com (reviewregistry1240). Electronic databases (PubMed/Medline, EMBASE, Web of Science, COCHRANE, Emcare, PsycINFO, ERIC, Academic Search

Premier, Sociological Abstracts, ProQuest Dissertations and Thesis Global) were searched for published and unpublished studies. Searches were completed from inception to 23rd October 2020. No restrictions were applied to clinical population. Eligible studies for both questions included primary articles and guideline documents available in English, describing the: i) development; ii) application of validated tools (e.g., checklists); iii) guidance on how to assess methodological quality of qualitive research and iv) guidance on how to grade levels of qualitative evidence. Opinion pieces and conference abstracts were excluded. Manual searches of the reference lists of full text articles were conducted. Two reviewers independently screened the titles, abstracts, and full text. A narrative synthesis was conducted to identify key aspects between the included studies.

Results: 9071 records were retrieved (Figure 1). After de-duplication and title/abstract screening, 51 full-articles articles were assessed for eligibility yielding 15 included articles. For RQ1, six articles were included that described six tools *(1) The society for Critical Care Medicine Family – Cantered Care Guidelines; 2) Nursing Management of the Second Stage of Labour evidence based clinical practice guidelines; 3) Jonna Briggs Institute Critical Appraisal of Qualitative Studies; 4) Critical Skill's Appraisal Programme (CASP) and 6) the Modified CASP checklist).* All tools ranged from 10 to 30 items, and evaluated research design, recruitment, ethical rigour, data collection and data analysis. Seven articles described one approach *(GRADE CER-Qual)* to assess methodological quality of qualitative research. This approach advised on the importance for assessing methodological limitations. For RQ2, two articles were included, one described a qualitative hierarchy of evidence, and another described a research pyramid that included a section on qualitative research.

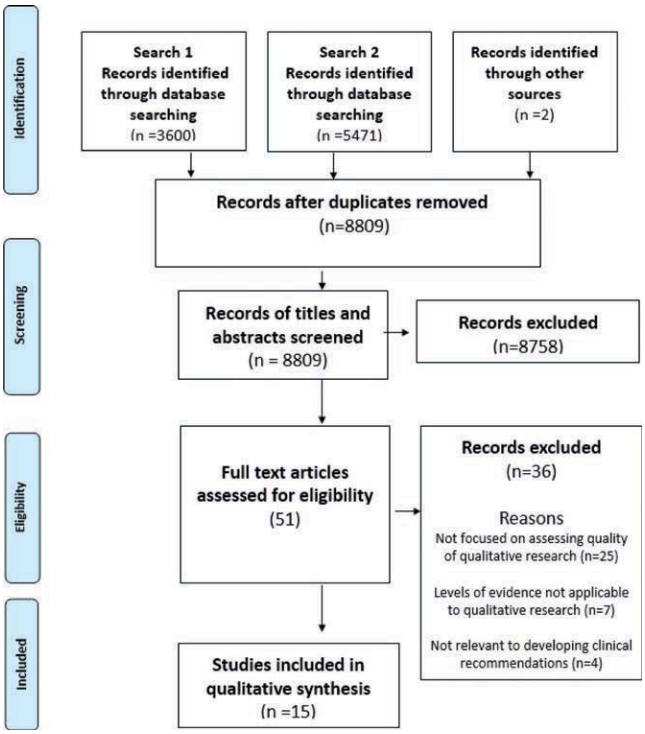

Figure 1. PRISMA diagram of included papers

Conclusion: This review highlights lack of consensus and limited availability of tools, checklists, and approaches to 1) appraise the methodological quality of qualitative research used to inform clinical recommendations and 2) grade levels of evidence for qualitative research. Current research agendas will need to determine the most relevant and appropriate method for the quality appraisal of qualitative research. This way, qualitative research could be more consistently and appropriately applied to the development of clinical recommendations.

REFERENCES: N/A

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POS1553-HPR

A VIRTUOUS IMPLEMENTATION OF TELEMEDICINE SERVICES IN RHEUMATOLOGY: DESCRIPTION OF CHANGE MANAGEMENT PRACTICES ADOPTED BY THE NIGUARDA HOSPITAL

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Background: Over the past few decades there have been an increasing debate around the use of telemedicine. Despite this, there is still a slow rate of adoption of telemedicine services. According to a recent scoping review this may be due to a piecemeal approach to the change process, and a lack of understanding of how to plan, manage and reinforce change when implementing telemedicine service[1]. A virtuous example of implementation of telemedicine services can be found within the rheumatology unit of Niguarda Hospital in Milan (Italy), where the whole staff has been involved in experimenting with new multichannel interactions to communicate with patients for more than a decade. Developed in 2011 with the introduction of the iAr Plus app for the collection of Patient Reported Outcomes (PROs), the project was first targeted to patients with Rheumatoid arthritis, Psoriatic arthritis and Spondylarthritis. In 2019 the project consolidated and added the home delivery of biological drugs for the stable patients. During spring 2020, this experience was further enhanced and extended to all patients treated with biological drugs to facilitate patient interaction during Covid-19 and was characterized by three elements: remote monitoring, triage through phone calls and home delivery of medication. What contextual factors and mechanisms adopted to plan, manage, and reinforce change where more successful?

Objectives: This study aimed to highlight what were the distinctive and successful elements of this implementation experience, what we could learn from it, and which managerial implications we could derive for future implementations.

Methods: We adopted a realist evaluation approach[2] to identify the underlying generative mechanisms that explain 'how' the outcomes were caused and the influence of context. Thus, we deepened how the change management process has been managed by conducting semi-structured interviews with the unit director, and the staff members involved in the phases of the project (i.e., clinicians, nurses, and administrative staff). The interviews were recorded and analyzed through an ad-hoc framework[1] for the analysis of change management practices. This framework identifies 10 change steps divided into 13 strategic practices and 6 operational practices that are important during the preparatory phase of the change process, for managing the change, and to sustain and reinforce long-term change.

Results: Our study identified the most relevant actions put in place by the rheumatology unit during the three major steps of preparing for change (e.g., developed telemedicine App, assigned coordinating role, identified champions), managing change (e.g., developed and articulated a clear vision, provided training, developed ownership), and reinforcing change (e.g., continued to engage partners). The analysis highlighted four main lessons learned: first the characteristics of the context and a strong managerial structure were a prerequisite for success. The generative mechanisms that explain how these successful outcomes were caused are: a leadership role able to define a clear vision and a clear specialization of tasks and roles; the involvement of all team members; regular meetings and interactions. Second, patients should be involved as central actors in the definition of the care pathway. The final decision on the kind of services to be used was made by the patient. Third, the relevant stakeholders should be involved since the co-design of the app. Finally, change should be incremental. The Rheumatic unit introduced one change at a time, and this brought to constant improvements.

Conclusion: The framework adopted can be used either to retrospectively analyze the experiences developed but may also act as a tool to guide future telemedicine service implementation and research. As well as the lessons learned can guide the implementation of future telemedicine experiences

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Disclosure of Interests: Lucia Ferrara: None declared, Elisabetta Listorti: None declared, Antonella Adinolfi Speakers bureau: JANSSEN, BMS, Maria Chiara Gerardi: None declared, Nicola Ughi Speakers bureau: ROCHE, PFIZER, ALFASIGMA, ABBVIE, JANSSEN, GALAPAGOS, BRISTOL MYERS SQUIBB, oscar massimiliano epis: None declared, Valeria Tozzi: None declared
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HPR Professional education, training and competencies

POS1554-HPR

HEALTH PROFESSIONALS' PERSPECTIVES ON THE USE OF JANUS KINASE INHIBITORS TO TREAT PATIENTS WITH INFLAMMATORY ARTHRITIS

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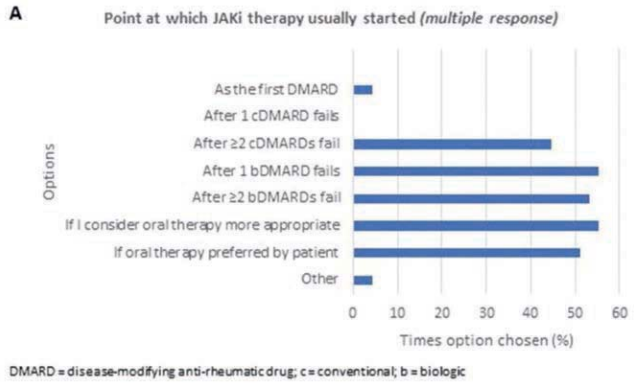
Background: Janus kinase inhibitors (JAKi) are relatively new to the field of rheumatology and provide health professionals in rheumatology (HPRs) with more therapeutic options for treating inflammatory arthritis (IA), specifically rheumatoid arthritis (RA) and psoriatic arthritis (PsA) [1]. Aside from a different target, JAKi differ from often currently prescribed biologics by being administered orally. To date, there is a lack of evidence on what HPRs think about their real-world use and how the COVID-19 pandemic affects JAKi prescription.
Objectives: To explore UK-based HPRs' perspectives towards JAKi use in IA patients, and in the context also of the COVID-19 pandemic.
Methods: A 15-item anonymous online survey, with both closed and open-ended questions, was designed and piloted on 5 HPRs with amendments made based on their feedback. The survey was advertised on Twitter and shared by email in September 2021. Data were exported from the online survey platform and analysed descriptively with the assistance of statistical software.
Results: Fifty-one HPRs responded to the survey: 37 Consultants, 7 Registrars, 5 Clinical Nurse Specialists, 1 Clinical Fellow and 1 'other rheumatology role' (not stated). Responses were received from 11/12 UK regions. Most represented was Greater London (18%) and North-West England (16%). 69% of respondents worked in secondary care, with the remaining 31% in tertiary care. The majority (40%) spent 1-25% of their job role doing research, followed by 27% who were not research active. 60% of HPRs indicated that 1-5% of their RA and/or PsA patients take a JAKi (no HPRs had more than 15% of their RA/PsA patients on a JAKi). 96% of HPRs indicated that they prescribe JAKi in their clinical practice, with 91% of those who prescribe following their local guidelines. 72% of respondents who prescribe JAKi, prescribed them 'frequently' as a monotherapy. Figure 1 shows responses chosen for when JAKi therapy is usually started and for feeling less confident with JAKi prescription. Of those HPRs who prescribe, 17% have continued JAKi in their patients. When discontinuation occurred, the most common reasons chosen (multiple responses allowed) were 'due to inefficacy' (60%), 'due to other adverse events' i.e., non-major adverse cardiovascular events (32%) and 'due to herpes zoster infection' (28%). 55% of HPRs would consider switching patients to another JAKi after initial failure. Across prescribers, 49% indicated no impact of the COVID-19 pandemic on their prescribing of JAKi. Common reasons chosen for a change in prescribing patterns for JAKi as a result of the pandemic (multiple responses allowed) included: prescribing them more as 'an alternative to infusions, in order to reduce hospital visits' (23%) and as 'an alternative to injections, in order to reduce at-home training visits' (21%). This was followed by 'other reason' (15%) with the free text from all 7 respondents highlighting the benefits of the shorter half-life of JAKi e.g., "Prescribed more as quick on and quick off so can be discontinued quickly in event of severe infection" (Registrar, Greater London). Safety concerns around the use of JAKi were raised in 13/14 free text comments left at the end of the survey e.g., "I am concerned about recent reports of increased VTE [venous thromboembolism] and malignancies" (Consultant, Yorkshire and the Humber) and "Concerns about cardiovascular safety" (Clinical Fellow, Scotland).
Conclusion: A large proportion of HPRs indicate confidence in prescribing JAKi to their patients with IA, adhering to local guidelines. JAKi are largely prescribed as monotherapy, with the most frequent reason for discontinuation being inefficacy. The COVID-19 pandemic seems to have positively impacted JAKi prescription, however, safety concerns over JAKi use remain for some HPRs.



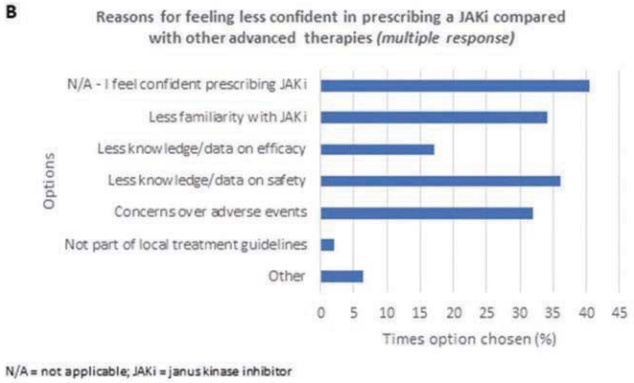


Figure 1. Initiation and confidence in prescribing JAKi

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POS1555-HPR

EVALUATION OF CONVERSATIONS IN MOTION: A PROGRAM DESIGNED TO IMPROVE PATIENT-PROVIDER COMMUNICATION IN THE CARE OF RHEUMATOID ARTHRITIS

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Background: Previous studies have found a need for improvement in communications between healthcare professionals (HCPs) and patients with rheumatoid arthritis (RA), especially in relation to shared-decision making (SDM), management of expectations, and goal-setting.[1-2] *Conversations in Motion* (CIM) is an educational program, consisting of four modules, that teaches HCPs how to use validated communication techniques to improve the quality and efficiency of their consultations with RA patients.
Objectives: This pilot study assessed the impact of CIM deployed in the United Kingdom (UK) on HCPs' knowledge, skills, confidence, beliefs, and performance using validated communication techniques in interactions with RA patients.
Methods: A longitudinal mixed-methods study, consisting of three surveys (pre/before the program, 2-3 weeks post, and 5-6 months follow-up) and semi-structured interviews (4-6 weeks post) was used to evaluate CIM based on the outcome model by Moore et al.[3] Surveys assessed outcomes via multiple choice or 11-point rating scale questions (0-none, 10-extreme). Participants included UK rheumatology physicians, nurses, and allied HCPs, all of whom had a minimum yearly caseload of 10 RA patients and participated in CIM between September and October 2020. Survey data was descriptively analysed in SPSS by comparing pre with post and pre with follow-up (matched samples). Interviews were thematically analysed using NVivo.
Results: Almost half (15/34) of registrants completed all four CIM modules. Of those, 53% (n=8) completed pre and post surveys; 33% (n=5) pre and follow-up surveys; and 27% (n=4) completed interviews. Post surveys showed greater knowledge for strategies to build trust and empathy with RA patients and practice efficiency than at pre (Figure 1). A decrease in helplessness was noted for dealing with a patient who is nonadherent (pre=3.9/10; post=1.6/10). Interviewees described CIM as "thought provoking" and reported improvement in their ability and confidence to use patient's own stories and words as a strategy to build trust and empathy (n=4). Post and follow-up surveys showed changes in skills and confidence were more pronounced for practice efficiency and discussing nonadherence (Table 1). At follow-up, most participants reported practicing at least one

technique to build trust and empathy with patients (80%, 4/5), save time (100%, 5/5), engage in SDM, or discuss nonadherence (60%, 3/5).

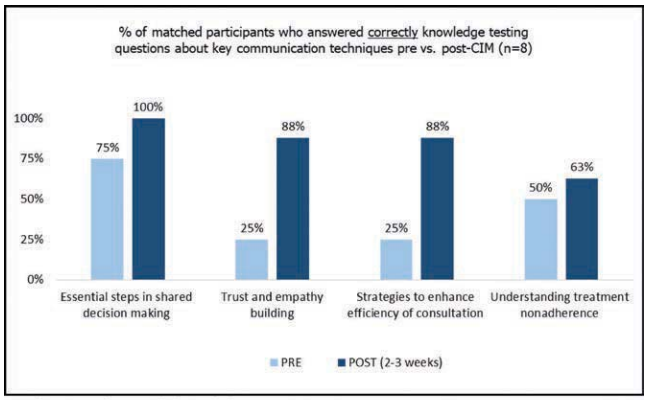

Figure 1 – Changes in knowledge post-CIM

Table 1. Changes in skill and confidence post-CIM

		Matched respondents (n=8)			Matched respondents (n=5)		
	Survey item	Pre	Post	Δ	Pre	Follow-up	Δ
Skill	Assisting patients in the conceptualization of treatment pros and cons	5.6	7.1	+15%	5.4	6.4	+10%
	Listening to and understanding patients' emotions, expectations, and personal needs	6.6	8.1	+15%	7.0	8.2	+18%
	Simplifying complex terminology related to RA	5.4	7.8	+24%	5.4	7.2	+16%
	Discussing reasons for nonadherence	5.4	7.8	+24%	4.2	6.4	+22%
Confidence	Engaging in shared decision making	6.1	7.9	+18%	5.0	6.2	+12%
	Building trust and empathy via telemedicine	5.9	6.9	+10%	5.0	6.0	+10%
	Addressing patient concerns in limited consultation	5.2	6.6	+14%	4.0	5.6	+16%
	Support patients through treatment adherence	6.0	7.5	+15%	4.0	6.2	+22%

Table description: All items were rated on an 11-point scale (0-none, 10-extreme). The matched sample of participants who completed the pre and 2-3 weeks post-CIM survey was not the same as the one who completed the pre and 5-6 months follow-up survey. Change (Δ) was measured as the percent difference between means.

Conclusion: This pilot evaluation suggests that CIM has a measurable impact on HCPs' learning and use of techniques that can enhance communication and collaboration with RA patients. Future studies should validate CIM impact in a larger sample size and/or by evaluating patients' perspective on observed changes in their communication and collaboration with HCPs.

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Disclosure of Interests: Elena Nikiphorou Speakers bureau: Celltrion, Pfizer, Sanofi, Gilead, Galapagos, AbbVie, Eli Lilly, Grant/research support from: Pfizer and Eli Lilly, Sophie Péloquin: None declared, Monica Augustyniak: None declared, Andra Negoescu Speakers bureau: Eli Lilly, Bristol Myers Squibb, Galapagos, Abbvie, David Walker Speakers bureau: Eli Lilly, Galapagos, Consultant of: Galapagos, Gilead Sciences, Grant/research support from: Gilead Sciences, Fasiha Haq Shareholder of: Eli Lilly, Employee of: Eli Lilly, Patrice Lazure: None declared, Suzanne Murray: None declared

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POS1556-HPR RECOMMENDATIONS FOR NURSES ON THE MANAGEMENT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOUS: A DELPHI CONSENSUS

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Background: Nurses play a key role in the management of Systemic Lupus Erythematosus (SLE) due to their close contact with the patient. Well-structured resources and specialized training are necessary to ensure comprehensive and quality care. However, no complete clinical practice guidelines for nurses have been developed for the management of SLE in Spain or Europe [1].

Objectives: In this context, the OpenReuma scientific society decided to promote the RECOMIENDAles project, the aim of which is to create consensus-based recommendations for the management of SLE patients by nurses in Spain.

Methods: Following a bibliographic review, the Delphi method [2] was followed to reach the consensus and a structured survey was sent to nurses with expertise in SLE. Two successive rounds were conducted. Consensus was established when at least 70% of the panelists agreed or disagreed on a topic.

The final questionnaire contained 90 items divided into 3 sections (Figure 1).

Figure 1. Structure of the RECOMIENDAles project questionnaire.

Results: In Spain, few nurses could be considered experts in SLE, hence the number of panelists was small: 25 nurses from different specialties (Rheumatology: 80%, Autoimmune Disease Units: 4%, Internal Medicine: 4%, and Day Hospital Services: 12%) with sufficient experience to ensure validated recommendations that could translate into practice. All the participants worked in public hospitals and had more than 2 years of experience treating SLE patients.

A high consensus was reached on the role and responsibilities that nurses should have in relation to SLE patient management. The main results are summarized in Table 1.

Table 1. Summary of the main recommendations reached in the RECOMIENDAles Project.

RECOMMENDATIONS	% of agreement (7 – 9 score)
General recommendations	
• Multidisciplinary teams with at least one nurse trained in SLE	100%
• Participate throughout the SLE patient care process and have their own agenda of visits and content	92%
• Psychological and social worker support	96%
• Access to continuous training (SLE management, individual and group counselling and communication techniques)	100%
• Access to research projects	96%
Specific recommendations	
Diagnosis:	
• Inform the patient about the diagnosis (manage expectations and resolve doubts and fears)	100%
• Provide contact channels with the service and reliable sources of information	100%
• Collaborate in the physical examination	92%
• Collaborate performing diagnostic tests	76%
Education:	
• Have a structured plan for patient education, engaging family and friends	100%
• Inform about the pathology (disease course, symptoms indicating aggravation, comorbidities)	96%
• Inform about healthy lifestyle habits (diet, hydration, exercise, rest patterns, photoprotection measures), avoiding toxic habits such as alcohol or smoking	100%
Treatment:	
• Play an active role in treatment training, including self-administration and adherence monitoring	100%
• Take part in the decision to introduce injectable therapy at home	76%
• Prepare a youth-adult therapeutic transition plan	100%
Follow-up:	
• Supervise patient condition to prevent comorbidities (diabetes, obesity, osteoporosis, cardiovascular problems)	96%
• Promote family planning measures	100%
• Monitor patient needs during the youth-adult transition	96%

Conclusion: Despite the high consensus achieved, to bring these recommendations to fruition it is necessary to: 1) Reinforce the role and presence of the specialized nurse in multidisciplinary teams treating SLE patients; 2) Establish a specific training plan for nurses: accredited, subsidized and supported by the Scientific Societies; and 3) Create detailed clinical practice guidelines for the SLE nurse specialist.

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POS1557-HPR PATIENT-CENTRIC INTERPROFESSIONAL EDUCATION AS A MEANS TO INCREASE HEALTH PROFESSIONAL STUDENTS' AWARENESS AND UNDERSTANDING OF SCLERODERMA

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Background: Incorporating a complex chronic disease into an interprofessional education (IPE) event is an appropriate method to increase knowledge and awareness of diseases that require multiple disciplines to manage. Scleroderma is one example of a rheumatic condition that requires an interprofessional (IP) team management approach. In practice, the rheumatologist must rely heavily on other healthcare professionals to provide optimal care to a scleroderma patient. Core competencies such as teamwork, leadership, and accomplishing common patient care aims are promoted by IPE[1]. The foundation of the patient-centric approach is seldom learned in a classroom setting while IPE can promote the observation of the patient-lived experience, the value of patients as a knowledge resource, and the emphasis of patient diversity[2].

Objectives: At each event we aim to increase awareness and understanding of scleroderma among health care professional students and enable patients to draw on their health histories to act as lead educators. Based on the success to date, we hope to promote replication of this model at other scleroderma centers.

Methods: Over four years, approximately 800 students from Russell Sage College, Albany College of Pharmacy and Health Sciences, and most recently The State University of New York at Albany, have participated in an IPE event which included individuals living with scleroderma and/or caregivers. For the first three years the event was held in person and the most recent was hosted virtually following the same structure as years prior. The event includes introductions of the moderators and words from a patient advocate followed by guidance on active listening and patient interview techniques. Eight to ten students enrolled in health-related programs including nutrition, psychology, occupational therapy, physical therapy, pharmacy, nursing and public health are assigned into small IP teams. Each team joins a round table or breakout room with one patient and/or caregiver. Students ask discipline specific questions which allows the patient and/or caregiver to share their narrative(s), enabling students to cultivate active listening skills and elicit the perspective of the patient. As the disease presentation and symptoms vary, the student IP teams will then interview another patient and/or caregiver. During the event students also hear best practices through a facilitated patient interview. An expert panel reflective of the disciplines represented on the student IP teams who have experience working with those diagnosed with scleroderma and other chronic conditions answer student questions. All attendees are asked to complete an anonymous pre and post event survey.

Figure 1.

Results: Including patients with scleroderma as educators is effective in increasing student awareness and knowledge of the disease. The implementation of this model into IPE also allows students to practice IP collaboration specific to the needs of an individual living with scleroderma, as it would occur in the health care setting.

Conclusion: This patient-centric IPE enables patients to share their medical journey as lead educators in increasing future health care professionals' awareness and knowledge of scleroderma. Replication of this pilot model at other scleroderma centers worldwide could promote the collaboration needed from healthcare professionals to assure the best quality of care for those living with scleroderma.

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POS1558-HPR INFLUENCING FACTORS ON WORK BURNOUT OF PRE-EXAMINATION AND TRIAGE NURSES UNDER THE NORMAL EPIDEMIC PREVENTION AND CONTROL

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Background: Nurse is a high-risk groups work fatigue feeling, which seriously affects the quality of conventional work efficiency and bureden pressures for contradiction between nurses and patients especially during the COVID-19 pandemic.Normalized epidemic prevention and control during the preview triage nurse need to all patients to the hospital and the accompanying personnel carries on the preliminary screening.COVID-19 fixed point hospital preview triage

Table 1. Univariate analysis of job burnout of pre-examination triage nurses from different dimensions.

		Job Burnout								
		Emotional exhaustion			Depersonalization			Personal accomplishment		
Item	Number	score	*F(t)*	*P*	score	*F(t)*	*P*	score	*F(t)*	*P*
gender			0.020	0.888		0.162	0.689		0.319	0.575
female	100	20.10±13.67			6.98±6.15			28.40±13.41		
male	10	21.00±12.08			8.20±9.52			25.98±8.70		
age(year)			5.511	**0.007**		4.143	**0.021**		0.750	0.477
18~25	30	20.33±12.40			8.40±7.33			28.07±6.97		
26~30	40	13.60±11.62			4.00±3.55			26.65±10.70		
31~40	40	27.00±13.48			9.20±6.99			24.35±8.79		
marriage			-0.939	0.352		-1.155	0.253		0.615	0.541
unmarried	52	18.38±13.30			6.04±6.40			27.00±9.99		
married	58	21.79±13.57			8.03±6.40			25.48±8.29		
job title			5.739	**0.006**		2.320	0.108		0.611	0.547
junior nurse	52	16.12±12.94			5.96±5.98			27.26±8.33		
senior nurse	38	19.68±12.53			6.63±6.14			26.50±10.62		
supervisor nurse	20	31.70±10.38			10.90±7.22			23.40±5.60		
work experience(year)			1.277	0.292		0.938	0.429		0.659	0.581
< 1	20	24.80±15.87			7.60±6.98			27.90±5.67		
1 ~3	24	18.42±12.05			6.33±6.51			24.25±13.00		
4 ~9	34	16.00±10.53			5.47±6.03			24.69±9.16		
10 ~20	32	23.06±15.10			9.06±6.43			28.00±7.46		
department			-3.875	**0.000**		-2.337	**0.023**		0.401	0.690
out-patient	54	13.81±10.50			5.11±4.38			26.70±10.65		
emergency	56	26.32±13.23			9.00±7.50			25.71±7.42		
average working time per day(hour)			0.791	0.459		1.125	0.332		2.173	0.124
6~6.9	18	15.33±7.92			5.11±5.28			30.56±8.35		
7~7.9	44	20.26±13.61			6.43±7.28			27.09±9.33		
≥8	48	22.00±14.88			8.52±5.81			23.61±8.62		
education degree			-0.643	0.523		-1.000	0.322		2.465	**0.017**
junior college	18	16.00±14.76			4.00±5.48			36.50±8.43		
college	92	20.51±13.42			7.33±6.47			25.39±8.70		
SAS(score)			2.080	**0.042**		1.637	0.108		0.498	0.621
≤50	34	17.74±12.71			6.16±5.33			27.12±8.74		
>50	76	25.65±13.75			9.18±8.16			25.79±9.31		
SDS(score)			0.240	0.811		0.825	0.413		0.428	0.671
≤50	72	19.58±12.94			6.11±3.96			26.58±9.66		
>50	38	20.50±13.85			7.61±7.40			25.47±8.05		
PSQI(score)			2.379	**0.021**		2.029	**0.047**		-0.521	0.604
≤7	40	17.06±12.17			5.80±4.98			26.69±9.33		
>7	70	25.65±14.08			9.35±8.02			25.35±8.79		

nurse with an infected person contact, more prone to anxiety,depression, results in the decrease of efficiency, to treat the service object formulation work sense of fatigue performance, etc.

Objectives: To explore the influencing factors of work burnout of pre-test and triage nurses under normal epidemic prevention and control.

Methods: A total of 110 pre-test and triage nurses from 4 Grade-A hospitals in Shanxi Province were enrolled in this study. The general data questionnaire, Nurse Job Burnout Scale, Pittsburgh Sleep Quality Index Scale, Self-Rating Anxiety Scale and Self-Rating Depression Scale were investigated towork burnout of pre-examination and triage nurses. Comparison between groups using two Independent sample t-test and single factor variance analysis. Multiple regression were applied to analysis factors affecting nurse fatigue feeling dimensions by SPSS22.0. P values<0.05 were considered significant.

Results: As shown in Table 1, different professional title, department, and the sleep quality of preview triage nurses emotional exhaustion dimension comparison(P<0.001), different department nurses to personalized level dimension comparison(P<0.05), nurse personal accomplishment dimension comparison of different cultural levels(P<0.05). Professional title, working department, sleep quality and educational level were the influencing factors of job burnout of pre-test and triage nurses.

Conclusion: In the COVID-19 epidemic, managers should pay more attention to the main factors that affect the sense of exhaustion of pre-test and triage nurses, and take targeted intervention measures to alleviate the sense of exhaustion of nurses, so as to ensure the safety of nursing.

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POS1559-HPR

PHYSIOTHERAPISTS MAKE LIMITED USE OF BEHAVIOUR CHANGE TECHNIQUES DURING PHYSICAL ACTIVITY COUNSELLING FOR PEOPLE WITH AXIAL SPONDYLOARTHRITIS

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Background: The 2018 EULAR recommendations for physical activity (PA) in people with inflammatory arthritis and osteoarthritis state that PA in generally recommended dose is effective, safe and feasible (1). Based on the recommendations, the Ankylosing Spondylitis Association of Switzerland (SVMB) developed a concept for their exercise groups, consisting of guidance on exercising, regular fitness assessments and individual PA counselling by the group-leading physical therapist (PT). The use of behaviour change techniques (BCTs) during PA counselling ought to support counselees' adherence to individual, unsupervised exercising.

Objectives: To assess the BCTs used by the PTs during their PA counselling sessions with the members of their axSpA exercise groups.

Methods: An observational cross-sectional study was performed with the first cohort of PTs (n=16) who applied the new concept and provided PA counselling, and their group members who agreed to participate. All first counselling sessions with an individual with axSpA were audiotaped, transcribed and analysed using a coding manual for BCTs (2). The manual includes 38 BCTs across the determinants 'knowledge' (2 BCTs), 'awareness' (8 BCTs), 'social influence' (3 BCTs), 'attitude' (4 BCTs)', 'self-efficacy' (6 BCTs), 'intention (6 BCTs)', 'action control' (2 BCTs), 'facilitation' (2 BCTs), 'maintenance' (5 BCTs). Two raters familiar with BCTs identified the BCTs used by the PTs. They repeatedly discussed and agreed about their classifications of PTs' phrasings to BCTs in an iterative process to achieve consistency over all counselling sessions. A BCT could be used several times within one counselling session.

Results: A total of 12 PTs (75%) who counselled 41 people with axSpA participated. All 41 PA counselling sessions, lasting between 30-55 minutes were analysed. Overall, 15 out of the 38 BCTs were identified. Across each determinant (with its number of BCTs), the most and least frequently used BCTs were as follows: 1) determinant 'knowledge' (1 of 2 BCTs used): 'provide general information' (469 times by 12 PTs); 2) 'awareness' (3 of 8 BCTs used): reflective listening and 'self-monitoring of behaviour' (328x by 12 PTs and 39x by 9 PTs respectively); 3) 'social influence': none of 3 BCTs used; 4) 'attitude' (1 of 4 BCTs used): persuasive communication (184x by 11 PTs); 5) 'self-efficacy' (3 of 6 BCTs used): verbal persuasion and guided practice (77x by 11 PTs and 3x by 3 PTs respectively); 6) 'intention' (4 of 6 BCTs used): general intention formation and develop training schedule (250x by 12 PTs and 18x by 5 PTs respectively); 7) 'action control' (1 of 2 BCTs used): use of cues (199x by 12 PTs), 8) 'facilitation': none (of 2) BCTs used; 9) 'maintenance' (2 of 5 BCTs used): continuous professional support and individualize regimen (137x by 12 PTs and 70x by 10 PTs respectively).

Conclusion: The study identified that PTs used only a limited number of BCTs. BCTs considered less effective such as providing information were widely used, whereas BCTs that are considered effective, such as specific aims or coping with barriers were much less or not at all used. This study provides an insight in real clinical practice and may help to develop counselling training for PTs. There is a need to translate theoretical BCTs into effective measures that are easy to use in clinical practice.

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HPR Interdisciplinary research

POS1560-HPR "MY GUT FEELING IS…": IDENTIFYING HOW HEALTHCARE PROFESSIONALS COMMUNICATE ABOUT PAIN IN PAEDIATRIC RHEUMATOLOGY MULTIDISCIPLINARY TEAM MEETINGS

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Background: Multi-disciplinary teams (MDTs) are common in paediatric rheumatology where UK standards of care state that all children/young people should have access to a paediatric rheumatologist, nurse, physiotherapist, occupational therapist and a psychologist. MDTs in paediatric rheumatology regularly meet for the broader purpose of discussing the assessment of and future management plans for children/young people with a range of complex conditions in which chronic pain may feature. The content of these discussions has not been previously researched. Little is known about healthcare professional to healthcare professional communication and how this may influence the care of children/young people with chronic pain.

Objectives: The objective of the current study was to investigate healthcare professionals communication about children and young people with chronic musculoskeletal pain during MDT meetings in paediatric rheumatology.

Methods: This study was a non-participant ethnographic observation of virtual and face-to-face MDT meetings in three paediatric rheumatology centres in the UK. A structured observation checklist was used to capture and organise field notes which were analysed using an inductive thematic approach amongst research team members. Interpretation of field notes was guided by discussions with healthcare professionals from each of the teams involved.

Results: Forty-two healthcare professionals from across the three teams participated. Ten meetings from each team (n=30) were observed, with meetings ranging from 1-2 hours. Analysis was organised into three themes;

1)*Describing the child/young person with pain*: Healthcare professionals' perceptions about personality characteristics (e.g. "He is mature", "She is sensitive") were frequently used to introduce a child/young person to the team. A child/young person description was always accompanied by a description of parents and perceptions about their behaviour (e.g. "Dad is very disengaged", "Mum can shout").

2)*Interpreting the pain of the child/young person*: A core component of interpretations was professional's familiarity with the child/young person and parents (e.g., "I haven't got a handle on them yet"). Professionals also discussed how their interpretations of pain were influenced by "gut feelings" or "vibes that something else is going on at home".

3)*Managing the child/young person with pain*: Healthcare professionals discussed the need for acceptance of pain and treatment from children/young people (e.g., "She wasn't buying into that"; "He needs to get used to it"). Setting boundaries for children/young people and parents for accessing the team also featured in discussions (e.g., "We need to re-assure them but not always be available").

Conclusion: This study highlights a range of healthcare professional approaches and processes to communicating about and discussing children/young people with pain at paediatric rheumatology MDT meetings. Findings suggest that healthcare professionals in paediatric rheumatology describe, interpret and manage the child/young person presenting with pain alongside the broader psychosocial (and less frequently the biological) context. These findings will inform the content and methods of a behaviour change intervention to improve pain communication in consultations with children/young people, parents and amongst the paediatric rheumatology team of healthcare professionals in the UK.

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POS1561-HPR HEALTH CARE PROVIDERS' PERSPECTIVE ON CONTINUATION VERSUS TEMPORARY INTERRUPTION OF IMMUNOMODULATORY AGENTS IN CASE OF AN INFECTION: AN INTERVIEW STUDY

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Background: Immunomodulatory agents (IA) are often used in the treatment of immune mediated inflammatory diseases (IMIDs). The use of some of these IA is associated with a slightly increased infection risk (1), which raises concerns especially during the current COVID-19 pandemic. It is however unknown whether it is best to continue or temporary interrupt IA in case of an infection, and what the views of health care providers are on this subject.

Objectives: To obtain insight in the health care providers' perspective regarding continuation and temporary interruption in case of an infection and to assess barriers and facilitators for both treatment strategies.

Methods: Health care providers, involved in the pharmacological treatment of different IMID patients, were interviewed by phone or face-to-face using semi-structured interviews. Recruitment was done using purposive sampling based on age, gender, function, specialty and affinity with the topic. Interviews were conducted until data saturation and analyzed by two researchers using inductive thematic analysis.

Results: Thirteen health care providers with three different functions (medical specialist, physician assistant, resident in training) from three different medical specialties (rheumatology, gastroenterology and dermatology) were interviewed. Mean age was 49 years (range 34 to 66) and the majority was female (69%). Ten main themes were constructed, yielding 77 barriers and facilitators across the two treatment strategies (see Table 1 for themes and a selection of barriers/facilitators). Health care providers mentioned that the choice between continuation and temporary interruption is often about balancing infection severity, IMID severity (e.g. risk of flare) and patient characteristics (comorbidities/vulnerability). They struggled with the lack of evidence on these two treatment strategies, which leads to choices being made based on previous experiences or intuition.

Table 1. Identified themes

Theme	Example of barrier/facilitator
1. IMID characteristics	Low disease activity (facilitator for interruption)
2. IA characteristics	Large administration intervals: interruption not possible (barrier for interruption)
3. Effects of IA on infection / immune system	Belief on positive effect (facilitator for continuation)
4. Patient characteristics	Patients with comorbidities / history of previous infections (facilitator for interruption)
5. Infection characteristics	Mild infection (facilitator for continuation)
6. Guidelines / current practice	Current practice = interruption of IA during infection (barrier for continuation)
7. Health care provider characteristics	Peer influence (facilitator for interruption; health care providers state that they would interrupt IA if for example an infectious diseases specialist would recommend so)
8. Financial	Higher costs (barrier for continuation)
9. Stopping IA in general	Chance to stop/taper IA (facilitator for interruption)
10. Interruption characteristics	Short duration: no impact on disease activity (facilitator for interruption)

Conclusion: A wide variety of barriers and facilitators for temporary interruption and continuation of IA during infection were identified. These perceived barriers and facilitators –together with emerging evidence on the risk and benefits of IA use during infections (2)– will aid implementation of the most optimal strategy regarding IMIDs, IA and infections.

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Patient information and education

POS1562-PARE CAN EDUCATION PROGRAMS REDUCE ANXIETY IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: Persistence of pain syndrome is accompanied by emotional changes and contributes to the formation of anxiety disorders in patients with rheumatoid arthritis (RA). Models of training patients with RA are aimed at developing the correct behavioral stereotype and improving the psychological status. To evaluate the effectiveness of these educational programs, it is required to study the impact of these programs on the level of anxiety in patients with RA.

Objectives: To assess the impact of education in an educational program in patients with RA on the level of anxiety.

Methods: The study was conducted in the Chuvash Republic, the city of Alatyr, from December to January 2020. 90 patients with RA of varying severity were examined. The inclusion criterion was a diagnosis of RA in accordance with the criteria of the European Antirheumatic League (EULAR) / ACR 2010. All patients were randomized into two groups: the main group (n=45), which, on the background of drug therapy (methotrexate at a dose of 7.5 to 15 mg/week and nimesulide 200 mg/week) was trained in the educational program: lectures and practical exercises. In the practical part, most of the time was devoted to the skills of self-control of the disease (taught how to self-assess swollen and painful joints). The training was carried out in two stages. The first stage (lecture-practical course) - twice a week for 1.5 hours, for two weeks, full-time education. The second stage (lecture course) - twice a week for 1.5 hours for two weeks, distance learning. In the control group (n=45), patients received the same treatment but were not trained in the educational program. Patients in these groups were representative by sex and age. All patients before and after completing the training program (after 1 month) were determined the level of situational and personal anxiety according to the Spielberger questionnaire modified by Yu.L. Khanina. The results obtained were interpreted: up to 30 points - a low level of anxiety, 31-45 corresponded to an average level, over 45 - a high level of anxiety. Statistical processing was carried out in the MS Office Excel package with the determination of average values (M), standard deviation. In each group, anxiety levels before and after training were compared using Student's t-test for normally distributed data, otherwise Wilcoxon's test. Differences were considered statistically significant at $p<0.05$.

Results: Before training in the main group, the structure of personal anxiety was represented by a high level of 62.14 ± 4.46 points (83.0% of patients), while reactive anxiety was represented by average values of 39.24 ± 3.29 (62% of patients). 2% of respondents had a low level of personal anxiety, 5.2% of patients had low levels of reactive anxiety. Anxiety scores were about the same in the two groups. After training in the main group, the level of personal anxiety decreased in 41% of respondents (53.22±6.87 points), reactive anxiety decreased by more than 2 times in 27% of patients. The number of patients with low levels of both personal and reactive anxiety increased to 40% and 40.2%, respectively. The differences were statistically significant ($p<0.05$). In the control group, the level of anxiety did not change statistically significantly.

Conclusion: Patients with RA who were trained in an educational program had a two-fold decrease in the level of personal anxiety and more than a two-fold decrease in the level of reactive anxiety, compared with patients who did not receive training. It is possible that the decrease in the level of anxiety in patients with RA occurred both due to a higher level of awareness of patients about this disease, and due to changes in the psycho-emotional state.

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POS1563-PARE SELF-MANAGEMENT STRATEGIES FOR ADVERSE DRUG REACTIONS AS REPORTED BY TNF-ALPHA INHIBITOR USERS: AN OBSERVATIONAL STUDY

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Background: Self-management strategies of adverse drug reactions (ADRs) are outside the vision of healthcare professionals (HCPs). Nevertheless, patients consider this information as one of the most important domains regarding ADR information (1). Therefore, identifying these strategies is important for both HCPs and patients.

Objectives: To identify which self-management strategies are applied by patients with immune-mediated inflammatory diseases (IMIDs) who encountered injection site reactions, local/systemic infections, or skin reactions during the use of adalimumab or etanercept.

Methods: Data of the Dutch Biologic Monitor (DBM), a prospective cohort event monitoring system, was used. Patients using biologics for IMIDs were asked to fill out bimonthly questionnaires on biologic use and experienced ADRs including questions on applied self-management strategies in an open-ended text field. For this study we included patients who used adalimumab or etanercept and reported injection site reactions, infections or skin reactions with self-management strategies. Self-management strategies were identified with thematic-analysis of the open-ended text fields.

Results: We included 160 patients and the characteristics are presented in Table 1. Most patients experienced injection site reactions (n=149), followed by infections (n=133), and skin reactions (n=101). Of these patients, the lowest number of applied self-management strategies was reported for injection site reactions (n=42, 28%), followed by skin reactions (n=62, 61%), and infections (n=88, 66%). The self-management strategies included themes such as 'Changing methods of administration' for injection site reactions, 'Change of personal care' for skin reactions, and 'Additional treatment for the ADR' for infections. Figure 1 shows which items are covered by these themes.

Table 1. Patient characteristics.

Patient characteristics, n=160	**n (%)**
Gender	
Female	110 (68.8)
Age (mean (SD))	
53.6 y (±14.8)	
Indication	
Psoriatic arthritis	33 (20.6)
RA	74 (46.3)
Crohn's disease	17 (10.6)
Ulcerative colitis	3 (1.9)
Bechterew's disease / axial SpA	23 (14.4)
Other[a] and RA	2 (1.2)
Other[b]	8 (5.0)
bDMARD	
Adalimumab	84 (52.5)
Etanercept	76 (47.5)
Most frequently reported ADRs	
Injection site reactions (pain, pruritis, erythema)	85 (100)
Infections	231 (100)
Cystitis	25 (10.8)
Infection susceptibility increased	24 (10.4)
Nasopharyngitis	21 (9.1)
Skin reactions	266 (100)
Eczema	42 (15.8)
Psoriasis	29 (10.9)
Dry skin	25 (9.4)

Note: n= number of patients, y= years, RA= rheumatoid arthritis, SpA= spondyloarthritis, bDMARD= biological disease-modifying antirheumatic drug[a]Rheumatoid arthritis-associated lung disease (n=1), systemic scleroderma (n=1) [b]Uveitis posterior and panuveitis (n=1), birdshot chorioretinopathy (n=1), hemochromatosis (n=1), hidradenitis suppurativa (n=1), juvenile idiopathic arthritis (n=1), psoriasis (n=1), Bechterew's disease and RA (n=1), RA and Crohn's disease (n=1).

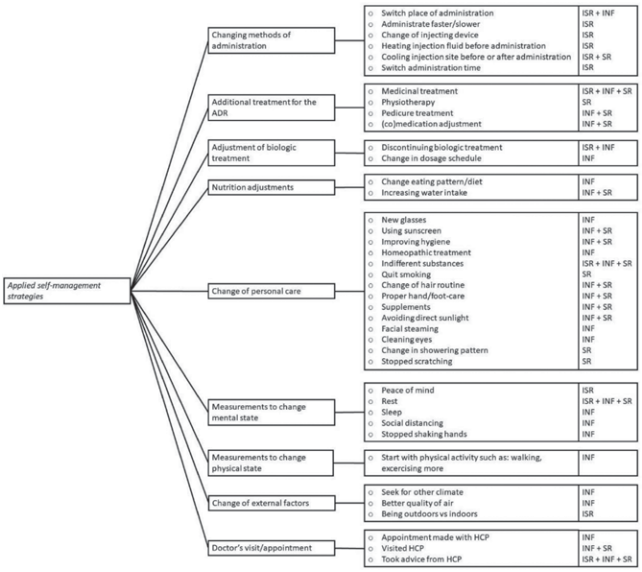

Figure 1. Applied self-management strategies divided in themes. ADR= adverse drug reaction, HCP= Healthcare professional, ISR= injection site reactions, INF= infections, SR= skin reactions.

Conclusion: This study shows that patients apply a wide range of self-management strategies for their ADRs. Further research should focus on the effectiveness of these actions and subsequently dissemination or (de)implementation of these strategies if deemed (in)effective.

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POS1564-PARE EDUCATION TOPICS AND SMARTPHONE APP FUNCTIONS PRIORITIZED BY PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Generating information that people living with a rheumatic and musculoskeletal disease (RMD) find useful while making decisions about their treatment requires identifying and understanding educational needs and interests directly expressed from people living with RMD.

Objectives: To identify what types of information US adults with RMD perceive as important to know about their disease and how they express and prioritize such information.

Methods: Using nominal group technique, focus groups of participants (pts) with RMD generated sets of rank-order educational items which were then aggregated across groups into themes. Based on nominal group results, a survey with the final 28 items was administered online, along with a question about desired functions of a smartphone app for RMD, to members of the ArthritisPower registry in January 2022.

Results: Six nominal groups (n=47) yielded 28 unique items for the online survey of educational priorities. To date, a total of 570 pts completed the survey, of whom 85.4% were female, 89.5% white, mean age of 59.6 (SD 11.2) years. Rheumatoid arthritis (52.5%), osteoarthritis (16.0%), psoriatic arthritis (12.5%), and axial spondyloarthritis (7.5%) were the most common RMDs. Knowing how to tell when a medication is not working, how RMD affects other medical conditions, understanding the results of tests used to monitor their RMD, available treatment options and possible side effects, and how life will change as an RMD progresses were each items that > 75% of pts considered extremely important (Table 1). Top functions pts listed as useful for a smartphone app included being able to participate in research, view lab results, record symptoms or flares, share how they are doing with their provider, and get educational information about their disease (Table 2).

Table 1. Top Education Topics Adults with Rheumatic and Musculoskeletal Disease Consider Extremely Important (N=570).

Item	n (%)
Knowing when the medication is not working	505 (88.6)
Knowing how a rheumatologic condition can affect your other health conditions or medical issues	481 (84.4)
Understanding the results of tests used to monitor your condition	471 (82.6)
Knowing the side effects of available drugs, and how the drugs interact with each other	461 (80.9)
Finding the right rheumatologist	453 (79.5)
Having realistic expectations of the effectiveness of the medications	445 (78.1)
Knowing how the disease will progress, even if the news is bad	439 (77.0)
Knowing the available medications and treatments for your rheumatologic condition	437 (76.7)
Knowing how long it takes drugs to work	436 (76.5)
Understanding how your life will change as your disease progresses	434 (76.1)

Table 2. Desired Smartphone App Functions Rated By Adults with Rheumatic and Musculoskeletal Disease (N=570).

App Function	n (%)
Participate in patient-centered research	299 (52.5)
View my lab results	283 (49.7)
Record my symptoms (e.g. pain, fatigue) or disease flares to track my health over time	278 (48.8)
Record my symptoms and share how I am doing with my rheumatology provider to know if I am meeting my treatment goals	230 (40.4)
Get educational information about my disease	225 (39.5)
Keep track of the medications prescribed by doctor	200 (35.1)
Schedule and keep track of my medical appointments, rheumatology and other	199 (34.9)
Track the vaccines I get (i.e. vaccination record)	188 (33.0)
Help me improve some of my health habits (e.g. sleep, diet, exercise)	187 (32.8)
Keep track of my use of over-the-counter, complementary or alternative therapies (herbs, tinctures, acupuncture, massage, stretching, etc.)	174 (30.5)
Get support for my disease from trained patients with my same health condition (i.e. 'peer coaching')	144 (25.3)

Conclusion: People with RMD prioritized information about medications and prognosis in educational materials, providing guidance for the development of educational tools. A sizeable minority felt educational materials were an important component of a smartphone app, but also identified other important features such as participation in research.

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POS1565-PARE ASSESSMENT OF QUALITY AND RELIABILITY OF YOUTUBE VIDEOS FOR PATIENT AND PHYSICIAN EDUCATION ON INFLAMMATORY MYOSITIS

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Background: Nowadays 80% of internet users access health information online, with YouTube being the second most popular search website worldwide. This study was undertaken to assess the reliability and quality of videos pertaining to myositis on YouTube and identify lacunae in information material on the platform.
Objectives: This study aims to assess the quality and profile of myositis information videos on YouTube, and to compare and delineate attributes of useful and not useful videos using standard metrics.
Methods: A thorough search was carried out on YouTube using 9 search terms related to myositis. The inclusion criteria were primary English content related to myositis, acceptable audio-video quality, and multi-part videos to be considered as one, while duplicates and advertisements were excluded. The videos were classified as useful, not useful or misleading, and patient experiences (Figure 1).

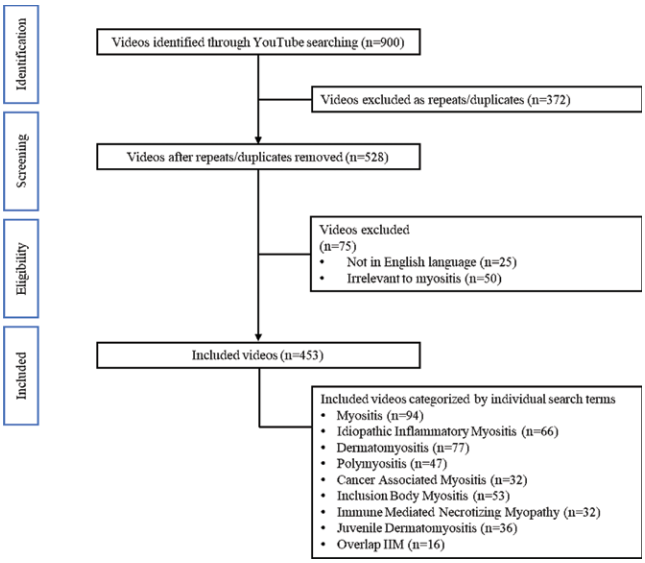

Figure 1. Flowchart of selection of YouTube videos for the study

Reliability of the videos was determined using the 5-point modified DISCERN (mDISCERN) criteria and quality by the 5-point Global Quality Scale (GQS) and 4-point JAMA scoring system. Score-based usefulness was defined as mDISCERN >4 or GQS >4 or JAMA >3. All values are in median and IQR.
Results: Of 453 analyzed videos 74% and 2% provided useful and not useful information respectively. 24% were patient experiences, and 324 (71%) were intended specifically for patients while 313 (69%) were for healthcare providers and students. Nearly one-thirds (n=143) reported information related to treatment of myositis.
Noteworthily, useful and not useful videos had similar views count. However, number of likes and daily viewership were higher for useful videos (p=0.024, p=0.046). Nearly half (47%) of useful videos were by professional medical societies/patient support groups while not useful ones were often by nonmedical media (38%).
Useful videos had higher mDISCERN reliability scores [4(3-4) vs 2(1-3), p<0.001] and better quality on GQS [4.5 (3.5-5) vs 1 (1-2.8), p<0.001] and JAMA [3 (3-4) vs 2.25 (2-3), p=0.004]. Physician predicted usefulness was discordant with score-based usefulness(κ=0.129). However, GQS score emerged significant (p=0.008) for predicting video usefulness in multivariate analysis (Table 1).

Table 1. Factors predicting usefulness of video in binary logistic regression.

Variable	B coefficient	S.E.	Exp (B) and 95% CI	p value
Intended audience	-5.45	2.586	0.004 (0.0-0.68)	0.035
Anyone/General public Average GQS	-2.86	1.076	0.05 (0.007-0.47)	0.008

GQS Global Quality Scale. Exp (B) is odd's ratio, p<0.05 is significant

Conclusion: Majority of English YouTube videos on myositis provide useful information for patients, largely related to treatment of myositis. However, the dynamic nature of YouTube could potentially change this equation in the future and physicians should correct any misinformation identified in face-to-face meetings or teleconsultations. High quality useful videos, often predicted by validated scores and produced by professional medical societies should be promoted as the first line of content consumed.
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POS1566-PARE BEYOND MEDICATION – SELF MANAGEMENT AS A COMPLEMENTARY APPROACH FOR TREATING RMDS

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Background: Upon diagnosis Rheumatoid Patients declare that the feeling that prevails is fear. Fear over the unknown over their health condition, their professional future, and their personal and social life. The person experiences a vicious cycle. Loss of control leads to anxiety which triggers pain which enhances psychological distress, thus the person feels completely helpless.
Objectives: The Self-Management education workshop is offered as a complementary aid, next to the arranged medical plan and the medications prescribed. The primary goal of the Workshop is for patients to accept their new reality which is, living with RMD. Further on, grounds for change are set. Patients within the program are taught in great detail how to engage new healthy, daily activities, such as appropriate exercise, appropriate use of medications, healthier nutrition, communicating effectively their fatigue, anxiety and psychological distress to family and friends. Patients are also taught, how to communicate to health professionals their condition, seek for information so as to evaluate new treatments, and demand the right for shared decision over their treatment. Moreover they receive information about the Cyprus League of people with Rheumatism, the social and psychological help provided, practicalities that concerns them, availability of Doctors, and new medications. Information, provides a strong Know-how, to deal with everyday problems. Such achievement enhances the confidence that a new well-being could be within the persons reach.
Methods: Participants meet for two hours once a week, for five weeks. Two trained leaders conduct the workshop, one being a health professional and one patient. Participants are to the maximum 15. Major rules of a therapeutic group apply, such as empathy, confidentiality, respect in every sharing, time keeping, simple language. All activities are Interactive. Discussions, questions and answers, brain storming, action-planning exercises and feedback, role playing, problem-solving techniques, and decision making. Moreover, symptom management activities are included, such as exercise, relaxation, communication, healthy eating, medication management, and managing sleep and fatigue. During the workshop, participants experience rapport, and trust thus they are motivated to manage the challenges associated with their condition.
Results: Participants demonstrated significant improvements in exercise, ability to do social and household activities, less depression, less fear and frustration about their health, reduction in symptoms like pain, improve mobility, increase energy, and boost confidence in their ability to manage their condition. Results of every workshop are scientifically documented.
Conclusion: Self-Management workshops are often described by new coming participants as "render of last hope". The structure and the facilitators create a safe environment for the patient to release the pain, seek knowledge, express the despair, set all the nightmares free. Acceptance, Respect, Rapport, Trust, knowledge aid the participants to experience the rebirth of hope. Self-Management workshops, are designed to complement clinical treatment and when delivered with empathy, lead RMD patients to physical and psychological well-being.
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POS1567-PARE **ASSESSMENT OF ADHERENCE AMONG GREEK PATIENTS WITH RHEUMATIC DISEASES DURING THE COVID-19 ERA**

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Background: Patient's (pts) adherence is a EULAR important recommendation for an optimal disease course and outcome. COVID-19 pandemic has globally challenged the issue of adherence. As relevant Greek data are lacking, the Pan-Hellenic Federation "Rheumazein" (i.e., co-living with a Rheumatic Disease) conducted a survey among their members to assess adherence and a possible COVID-related negative impact.
Objectives: The main endpoint of the study aimed to capture the degree of pt adherence to treatment, either with conventional synthetic or/and biologic DMARDS (csDMARDS, bDMARDS). The secondary endpoints were: a. To record pts'–physicians' interactive communication to assess the level of shared disease making (SDM). b. The emerged barriers to medication access during the pandemic and consequent restrictive measures. c. To record pt perceptions on the usefulness of mobile reminder applications towards an uninterrupted regimen.
Methods: A 29-item quantitative questionnaire was uploaded in the social media of the Federation and its associations, in order to register pts' responses on the aforementioned sections. The questionnaire was accessible for a 58-day period (21/09/2021-17/11/2021).
Results: Participants' characteristics: The responses of 303 adults with RD (M:F 63:240), aged (in yrs) 18-44: 35%, 45-54: 26%, >55: 38% respectively, were available for analysis. The RD types were RA 33%, AS 18%, PsA 13%, SLE 18%, Juvenile Arthritis 5% and Other RD 13%, respectively. The education level was low/moderate 39%, high 30%, post-graduate 31%, respectively. Receivers of a monotherapy with either cs- or bDMARDS were 93(31%) and 83(27%), of a combined regimen cs+bDMARDs 114(38%) and off treatment 13 (4%). BDMARD receivers were mostly AS pts (93%) while the least, SLE pts (48%). The route of bDMARD administration (sc vs iv did not significantly differ (57% vs. 43%). Since diagnosis, the mean disease trajectory was 7.6 yrs, the mean time on medication 6.9 yrs, while the mean duration on the current regimen 3 yrs, respectively. Adherence: At least one skipped dose during the last trimester was reported, significantly more often by pts under csDMARDs than by those under bDMARDs, (60% vs. 40%, p<0.001) with a mean number of 2.7 vs. 1.8 skipped doses, respectively. Additionally, the main reasons of non-adherence under csDMARDs and bDMARDs significantly differed only in respect to pt responsibility (56% vs.19% p<0.001), but not for COVID-related reasons, namely fear either of getting infected, or due to a performed COVID vaccination (35% vs 42%), or due to physician recommendations (22% vs. 32%). Regarding the pt-physician interactive discussions on emerging new treatments, 90% of the pts reported this policy, but only 40% of them in a rather frequent to more frequent rate. In respect to satisfaction, 67% expressed a moderate to high satisfaction regarding the level of provided information, while the degree of their satisfaction was positively related with the frequency of these discussions. The main topics focused on the route and frequency of the medication, especially with bDMARD receivers. Of note, 80% of the bDMARD group participated in the SDM before commencing this therapy, but just 20% in the selection of the brand name. Only a minority of pts (17%) were aware of the existence of mobile applications, reminding the scheduled drug administration; however, they rated these programs as very useful (4.3 according to a 0-5 scale). Despite the difference source of supply of cs and bDMARDs on pt access to treatment, the impact of COVID-19 and consequent restrictive measures had not impaired it (1.5/5 and 1.7/5 by the above scale, respectively).
Conclusion: A significant percentage of pts skip scheduled DMARD administrations, especially those (60%) under csDMARDs. The relationship with the physician was considered relatively satisfactory. Most of the pts did not have any mobile phone reminder application regarding their dose. Finally, the COVID-19 pandemic appeared to have had little effect on pts' access to both cs- and bDMARDs and consequently, adherence to their treatments.
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POS1568-PARE **THE BRIEF-ILLNESS PERCEPTION QUESTIONNAIRE: A METHOD FOR ASSESSING THE COGNITIVE REPRESENTATION OF RHEUMATIC DISEASE**

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Background: The common-sense model proposes that illness perception (IP), is how patients make sense of their illness and respond emotionally to it, influencing the way they cope with the illness and subsequently illness outcomes. This proposition has gained considerable empirical support, and the relevance of IP in understanding illness-related behaviors or outcomes has also been supported in patients with rheumatic diseases (RD). The Brief Illness Perception Questionnaire (B-IPQ) was designed to provide a simple and rapid assessment of IP. This questionnaire has been widely used in diverse ages, illness types, countries, and languages.
Objectives: This study aimed to examine the construct of IP as measured by the B-IPQ in patients with RD.
Methods: A cross-sectional study was conducted at a Tunisian rheumatology department on 80 patients with RD. Sociodemographic, disease-related variables were reported. Participants completed a questionnaire on illness beliefs (B-IPQ).
Results: Subjects were aged 22-74 years (mean 51 years), 61.6 % were female. Diagnoses included Rheumatoid arthritis (RA) (63%), axial spondylarthritis (AS) (37%). The mean disease duration was 11 years and 7 years for RA and AS respectively. The proportion of physical comorbidities was higher in RA patients (36%) versus AS patients (11%). Disease activity was low in 28.8% of patients. All patients were on medications for their rheumatic disease, and 34,6 % were on biological therapy.
In both diseases, the participants perceived their rheumatic illness as a chronic condition (9.4) that could be controlled by treatment (6.6) but not strongly influenced by personal actions (4.3). Overall, Rheumatic disease was seen as having an important impact on their life (7.9) without significant difference between patients with low or high activity disease (p=0.23). The majority believe that they have a moderate understanding of their illness (6.6). The frequency of symptoms was highly evaluated in RA patients than AS patients (7.3 vs 5.6) (p=0.01). In RA patients, 76% were extremely affected emotionally by their disease, however, the majority of AS patients were moderately affected emotionally with a significant difference (p=0.02). In addition, RA patients considered their disease mainly a result of psychological factors (66.8%). On the other hand, AS patients (73%) attributed their illness to various risk factors (especially physical overexertion).
Conclusion: High scores of B-IPQ shown in our studies, encourage the design of psychotherapeutic trials targeting disease-related cognitions in AS and RA in an attempt to improve patients' reported outcomes and disease outcomes.
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Building patient led organisations

POS1569-PARE **TESTING A NEW APPROACH TO IDENTIFY AND ASSESS PATIENT-VALUED TREATMENT GOALS IN RHEUMATOID ARTHRITIS (RA): A PATIENT-ENGAGED HEALTHCARE VALUATION STRATEGY**

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Background: Common approaches to valuing health technologies often fail to capture outcomes that matter to patients and families. The treatment goals of people living with rheumatoid arthritis (RA) include common trial endpoints but also include other facets of disease impact. Identifying a feasible and rigorous approach to inclusion of the patient perspective is needed as trialists increasingly seek to incorporate patient-important outcomes in trial design and as varied patient-centered value assessment frameworks emerge. No standard approach is available to systemically identify and quantify patient-important outcomes, nor to include those outcomes in deliberative decision-making. We developed the Patient-Engaged Healthcare Valuation strategy, using principles of goal attainment scaling to frame survey-based goal collection directly from adults.

Table 1. Top Goals based on rating as "Very Important" by >70% of subjects, from set of 36. "My goals for living with RA are to…"

Goals	Not Important	Somewhat Important	Important	Very Important
Symptom Management				
improve the quality of my life with RA	0% (0)	0% (0)	23% (11)	77% (36)
manage my RA pain	0% (0)	2% (1)	11% (5)	87% (41)
reduce how my RA pain interferes with my life	0% (0)	9% (4)	17% (8)	74% (35)
Life Impact				
reduce the ways in which RA interferes with my life	0% (0)	2% (1)	21% (10)	77% (36)
be independent in my daily functioning	0% (0)	4% (1)	15% (4)	81% (22)
Managing my RA				
feel like I can manage my RA	0% (0)	2% (1)	26% (12)	72% (34)
Treatment Features				
understand my RA treatment options	0% (0)	4% (2)	21% (10)	74% (35)
have the information I need to make treatment decisions	0% (0)	0% (0)	19% (9)	81% (38)
know what to expect with my RA treatment	0% (0)	2% (1)	23% (11)	74% (35)
find treatments that are effective	0% (0)	0% (0)	6% (3)	94% (44)

Objectives: To develop and test a goal-based method for collecting RA patient input for use in clinical trials and value assessment and evaluating the feasibility of this approach in people with RA.

Methods: Patient goals and domains were identified from (1) a literature review (2010-2020) of patient outcomes, goals, and preferences in RA, and (2) discussions with patients and clinicians during two meetings with a steering committee (SC) consisting of clinicians, outcomes researchers, patients/advocates, and health economists. These goals informed the development of a draft survey. Adults with RA were recruited from online patient networks to rate goal importance and suggest additional goals. SC members reviewed the survey findings and assessed feasibility of scaling up goal collection for HTA.

Results: Of 135 articles identified, 17 were retained. An inductive and iterative approach was used to identify and thematically group the final set of 36 goals into 4 domains. The draft survey was cognitively debriefed with 4 adults with RA. The first survey was administered to 20 participants; results informed item revisions and additions for the second round of data collection (n=27).

The 47 respondents were mostly White (87%), college-educated (72%) women (93%) living with RA for an average of 15 years; 75% rated their RA as moderate to severe. Free-text goals added in round 1 include: 1) finding specialists who listen to patient input on symptoms; 2) addressing loneliness or isolation; and 3) finding support from or helping others with RA. All Symptom and Life Impact goals were rated as *Important* or *Very Important* by ≥85% of participants; endorsement for Management and Treatment goals was somewhat more variable, with ≥85% endorsing these as *Somewhat* to *Very Important*. Results suggested that domains match key goals. Steering committee ratings supported the feasibility of this method.

Conclusion: Goals relevant for RA treatment evaluation can be efficiently identified and rated for importance by patients. Patient-important goals can be incorporated into deliberative healthcare valuation using this method to permit "crowd-sourced" input from people living with RA and to capture heterogeneous patient perspectives in healthcare valuation.

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Arthritis research

POS1570-PARE

A PATIENT-LED SURVEY INTO THE BENEFITS AND LIMITATIONS OF TELEMEDICINE APPOINTMENTS FOR ASSESSING CHILDREN AND YOUNG PEOPLE WITH RHEUMATIC CONDITIONS: COMPARING EUROPEAN AND CANADIAN COHORTS

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Background: During the COVID-19 (coronavirus) pandemic, some provision of healthcare shifted to remote, technology-assisted appointments (telemedicine). Whilst parents/carers of children and young people with rheumatic conditions have reported benefits of telemedicine, concerns remain.

Objectives: This patient and parent-led project sought to understand the views of parents/carers about telemedicine, identifying the benefits and limitations of remote technology-assisted appointments, and comparing views between Canadian and European cohorts.

Methods: An online survey was developed, translated into multiple languages and shared via social media and patient organisations, targeted at parents of children and young people with rheumatic, autoimmune and autoinflammatory conditions. Fieldwork took place in April 2021 in Europe and May 2021 in Canada. Consent was provided during enrollment.

Results: A total of 290 responses were received (133 Europe; 157 Canada). Of these, 73% were female, median age 12.

Over half of respondents (53%) in Europe reported travelling over an hour to in-person appointments with their paediatric rheumatologist, compared to a significantly higher proportion of respondents in Canada (87%). Consequently, in-person appointments represent a greater time burden amongst Canadian caregivers, though both groups report appointments taking over three hours in total (51% Europe, 69% Canada).

Prior to COVID-19, most had never had a telemedicine appointment (92% Europe, 95% Canada). Since March 2020, the majority (71% Europe, 82% Canada) had at least one telemedicine appointment.

Table 1. Shows the scores (1 worst, 5 best) given by parents about their telemedicine experience. Overall, most aspects scored positively (p<.05). However, parents felt telemedicine was not as good as in-person appointments.

	Europe	Canada	P
Easy to schedule	3.50 (3.18, 3.82) *	4.33 (4.14, 4.52) *	†
On time	3.22 (2.89, 3.55)	4.07 (3.85, 4.28) *	†
Enough time with doctor	3.51 (3.19, 3.83) *	4.24 (4.02, 4.45) *	†
As good as in-person visit	2.21 (1.96, 2.46) **	2.66 (2.42, 2.90) **	†
Easier to see doctor	2.84 (2.55, 3.13)	3.51 (3.25, 3.77) *	†
Easy to sign-in	3.52 (3.22, 3.82) *	4.25 (4.06, 4.43) *	†
Quality of video	3.23 (2.93, 3.53)	3.87 (3.66, 4.07) *	†
Quality of sound	3.54 (3.26, 3.81) *	3.94 (3.75, 4.14) *	†
Able to speak freely	3.61 (3.34, 3.88) *	4.05 (3.85, 4.24) *	†
Able to understand doctor	3.61 (3.32, 3.90) *	4.09 (3.90, 4.28) *	†
Quality of care provided	3.43 (3.12, 3.73) *	3.78 (3.56, 4.00) *	†
Overall telemedicine experience	3.23 (2.91, 3.55)	3.78 (3.57, 3.99) *	†

Table 1. Mean scores for a range of aspects of telemedicine (1-worst; 5-best). * Positive score (p<.05) ** Negative score (p<.05) † Difference between Canadian and European cohorts is statistically significant (p<.05), chi-square.

When asked about aspects of telemedicine, a greater proportion of respondents from Canada answered favourably compared to those from Europe with the majority reporting telemedicine appointments had saved them time, enabled them to have an appointment and that it made the appointment safer. However, most felt that their consultant could not properly assess their child (72% Europe, 78% Canada, P<.05).

Overall respondents said they would prefer the next appointment to be in-person (82% Europe, 62% Canada, p<.05), although 31% from Canada were amenable to a combination of in-person and telemedicine-based care.

Conclusion: There are advantages to telemedicine, notably saving time and making appointments accessible. Families from Canada tended to view telemedicine more favourably than those from Europe, although the majority from both cohorts reported concerns about the ability to assess their child. There may be value in providing training to parents to enhance the accuracy of home-based assessments, particularly when the disease is stable. However, parents continue to report the value of in-person appointments.

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Innovations in arthritis health care

POS1571-PARE ONLINE COUNSELLING FOR PATIENTS WITH ARTHRITIS

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Background: The Covid-19 pandemic has changed many aspects of our lives. Perhaps the biggest changes have been in medical services. Institutes specializing in RMD in Serbia were part of the covid system and patients only had access in emergency cases, there was no regular examinations.
Objectives: The paper will show how the "Online Counselling for Arthritis Patients (OCAP)" worked during the pandemic, how many rheumatologists and patients were involved and were patients satisfied with the service provided.
Methods: Through the platform "Lekarinfo" ORS,[1] in cooperation with pharmaceutical companies, organized an OCAP. Patients were informed about the possibility of using online consultations with rheumatologists via social networks, viber groups. email ... and they were given instructions how to use it, they were advised to send medical documentation before, so the doctor has time to look at it, which gives more time for conversation. Consultations were held by phone or online, depending of patient's wishes and abilities. The time set aside with a rheumatologist was 20 minutes and with a psychologist 30 minutes. One psychologist and 23 rheumatologists were available. The ORS distributed cards to rheumatogists with all necessary data about OCAP to inform their patients.
Results: ORS conducted a Survey about OCAP. It was completed by 100 respondents, aged 20 to 75 of whom 75% were women. The 44% of respondents were from Belgrade, but it also included respondents from all over the country. RA have 61% of respondents, but patients with other types of arthritis were also included. 4/5 of patients are non-smokers and half of them are on biological therapy. All but one respondents are ORS's members.
The results of Survey are the following: OCAP was used by 27% of respondents and all of them were satisfied except one. Everyone would use it again and would advise others to do so. Online consultation can replace live examination, when the disease is in remission, thinks 62% of respondents. The majority (90%) found it technically easy to use it, but also the majority of respondents felt that there is a space for improvement (70%). One third prefers to have online consultations with their rheumatologist, Half of them understand the importance of telemedicine, 61% think that C-19 pandemic has increased the need for it and 64% think that digital solutions are our perspectives and it should be further developed.
Conclusion: It is desirable to continue with this kind of telemedicine. Patients and their families should be encouraged and educated about using digital platforms, aim is to explain them the benefits of telemedicine and that consultations do not necessarily have to be with their rheumatologists. Regardless of the pandemic, digitalization is in every aspect of our life, it is inevitable, but also it is a great advantage that should not be missed. Investments in the development of online platforms, that will facilitate patients access to doctors are an investment in self-control of chronic diseases in extraordinary circumstances, but also in normal conditions when because of the overscheduled doctors, lack of time for employed patients or other reasons, it is not possible for frequent examinations. Telemedicine is an investment not only in physical health but also in mental health of patients, having a doctor "just a step from you" has calming and positively affects for patients. And without positive attitude it's hard to keep a chronic disease under control.
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POS1572-PARE HELPER'S WAY OF WORKING IN ORS BRANCH – NIS DURING THE COVID-19 PANDEMIC IN 2021

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Background: Helper is a person with RMD educated to help other patients. Based on the clearly defined authorizations this person helps in advising and information sharing among the ORS members.[1] Association of patients with rheumatic diseases of the Republic of Serbia (ORS) operates across the country through the reference centers/ branches, but in pandemic the functioning of helper in an regular way was significantly impacted.
Objectives: In order to continue with the functioning in Association and with Helper during the Covid-19 pandemic, new communication and info-sharing methods has been applied. In this work will be shown how the strategy of communication was shifted from physical to digital, methods used for information sharing and communication tools of the modern world has been used for this purposes. Also, functioning of the branch in Niš and its Helper will be shown through statistical comparison of data prior and during the Covid19.
Methods: In the definition phase of Association's response on the new circumstances, it has been concluded that most of the members are using some of IM platform or e-mail. Based on this fact, out of 247 members of branch in Niš, 168 members have been joined through the most popular IM platform in Serbia – Viber. Through the group the patients has been sharing the information, notifications and other news important for the patients. Group administrators supported discussions, but also identified patients who did note use IM platforms and those members were notified by phone or e-mail. This method of communication was symbiotic with other projects of the Association because we used the same communication channels to increase the awareness of members about the activities of the Association.
Results: During 2019, Helper's work took place under normal conditions. At the Niska Banja Institute, Helper used the office where patients with rheumatic diseases used to come. Four lectures by eminent experts in the field of rheumatology and physiatry were organized, as well as socializing in the form of meetings and field trips. We marked the World Arthritis Day and the World Osteoporosis Day.[2]
During 2021, most activities took place online or outdoors, depending on the intensity of the Covid-19 wave. Helper's work took place from home in January and February 2021, and from March to the end of 2021, Helper worked in the office. The lectures that were organized were exclusively online. We have marked the World Arthritis Day with a small number of participants. The event was realized with media support. [3]
Analysis and participation of members in 2019 and 2021 are shown below:

- In 2021, 208 vs 260 live contacts in 2019;on average 17 vs 22 contacts per month
  - In 2021, 216 contacts through online meetings; on average 18 per month. IN 2019 no such exercise.
  - In 2021, 2.000 vs 239 contacts in Viber group in 2019; on average 167 vs 20 members
  - In 2019, alternative communication methods were not used. In 2021, 1,023 contacts were made with messages, calls and emails, or 85 per month.

Conclusion: Based on the fact mentioned above, 2019 was richer and more fulfilling with lectures, socializing and direct contacts with members, while in 2021 communication was dominated by digital tools and methods (Viber groups, calls, emails) and consultation with doctors via e-consultations and by phone[4].
The pandemic disabled direct contact with members of the Association and live lectures, but the Association used digitalization as a complement to new ways of working that connected us more than ever before, enabled instant transmission of information and created a basis for support at times when it was necessary the most. With this process in place, we not only fulfilled the goal of the Association, but we went a step further - we became the first contact for patients with RMD.
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[3] Danijela Janković – Izveštaj Podružnice Niš za 2021 godinu.
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POS1573-PARE PATIENT-REPORTED OUTCOME MEASURES OF PAIN ALLEVIATION WITH CANNABINOID USAGE IN RHEUMATOID AND PSORIATIC ARTHRITIS: A CROSS-SECTIONAL STUDY.

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Background: Patient-Reported Outcome Measures (PROMs) give us direct, immediate evidence of patient experience. Pain is a chronic, debilitating, multifactorial, presenting symptom that remains a difficult target to treat in populations with Inflammatory Arthritides.[1] Increasingly, cannabis products are being utilized and investigated for their potential analgesic and immune-modulatory effects.[2] The legislation and form of cannabis products deployed as therapy varies around the world and across populations. More data on usage and patient reported outcomes is needed to guide better clinical practice and inform sound legislative policy.

Objectives: To describe PROMs of pain, stiffness with cannabis use in a population of patients with Rheumatoid Arthritis (RA) or Psoriatic Arthritis (PsA).
Methods: This investigation was a monocentric, cross-sectional study. Inclusion criteria were adults receiving care at a University Rheumatology practice in Central Florida, USA from December 2019 to March 2020 who provided informed, written consent. Those who consented were provided with a brief, voluntary, and anonymous Qualtrics survey which queried patient-reported prevalence and outcome measures of short and long-term pain relief. 236 RA and 43 PsA patients were enrolled in this study. All subjects met the criteria for Rheumatoid, Psoriatic, or Inflammatory Arthritis (seronegative RA). Subjects' scores before and after cannabinoid use were compared with a paired T-test after the parametric nature of the data was established. Ethical approval was obtained from the University of Central Florida Institutional Review Board (Study00001041).
Results: Cannabis product usage was reported in 16.95% of RA subjects (40/236) and 11.63% of PsA subjects (5/43). Of this group, 71% (RA) and 40% (PsA) endorsed current usage. Inhalation was the most prevalent form used in RA (27.50%). In PsA, the most commonly reported forms were liquid (30%) and topical/skin (30%). On the 10-point pain scale, RA patients reported a significant reduction in average pain by 1.83±1.91 points in the long-term and 2.28±2.10 points in the short-term. Those with PsA reported a significant reduction in average pain by 1.60±0.89 points in the long-term and 1.80±0.84 points in the short term. Stiffness was also reduced in the RA group (7.3%). 17.5% of patients with RA using cannabinoids reported side effects not leading to cessation.
Conclusion: In an academic rheumatology practice population, a substantial number of RA and PsA patients are choosing to self-treat with cannabis therapy to manage their pain and other symptoms. Subjects reported significant reductions in both short- and long-term pain; some patients reported total pain resolution with ongoing cannabinoid therapy. Stiffness was also reduced in a subset of RA patients. Subjects that reported adverse effects did not find these severe enough to warrant cessation. These study results may allow for a more open discussion to improve safety and optimize outcomes. Additionally, the significant prevalence of usage and pain reduction reported provide a compelling rationale for further interventional studies in populations with Inflammatory Arthritides.
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Psychosocial support

POS1574-PARE PATIENTS REPORT HIGH LEVELS OF CONCERNS ABOUT MEDICATION FOR PSORIATIC AND RHEUMATOID ARTHRITIS: UNMET NEEDS REVEALED BY A UK PILOT WEB SURVEY.

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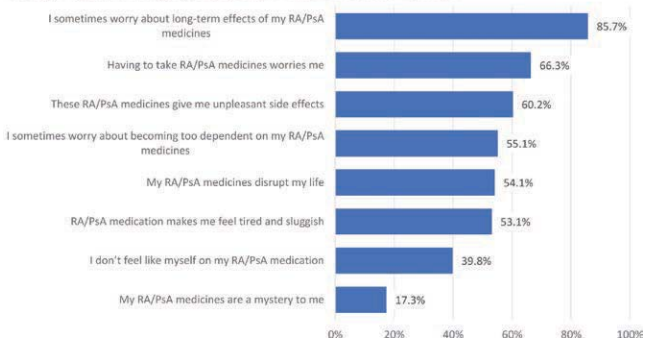
Background: Patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are often nonadherent to prescribed symptom-modifying drugs. [1] Concerns about the potential negative effects of medication have been implicated in medication nonadherence. Few evidence-based interventions to address concerns about medication and support medication-taking are available in the UK context.
Objectives: To inform the development of intervention to support people with RA and PsA to manage medication we conducted a survey of unmet needs relating to perceptions of arthritis and arthritis medication, medication-taking behaviour and experience of side effects.
Methods: We recruited people with arthritis via local and national patient groups for participation in an online survey. The survey included clinical and demographic questions, validated measures of treatment (Beliefs about Medication Questionnaire; BMQ) and illness perceptions (brief Illness Perception Questionnaire; bIPQ), medication adherence (Compliance Questionnaire Rheumatology; CQR), and patient-reported side effects. Participants were asked about consequences of taking and not taking their arthritis medication as free text to contextualize scores.
Results: Questionnaire responses from 98 participants (42 with PsA, 56 with RA, 89.8% female) indicated participants typically viewed arthritis negatively with ratings on the bIPQ indicating high emotional impacts, symptoms and affects on everyday life, and doubts about their ability to control their arthritis. Analysis of the BMQ indicated ambivalence about RA/PsA medications; while few people expressed doubts about their personal need for medication, concerns about RA/PsA medications were common, see Figure 1). Most, 85.7% (n=84), reported a side effect in the last month, with a mean of 10 'moderately severe' or 'very severe' side effects (m=10.02, sd = 5.98). Just over a quarter (26.0%, n=25) were classed as low adherers using the CQR with 54.6% reporting they had missed some of their arthritis medication over the last year. Free text responses indicated that some participants had additional concerns about medication (e.g. worries about impact on life expectancy) not addressed in the questionnaire measures.

Figure 1: Concerns about arthritis medication
Percentage of participants strongly agreeing/agreeing with statements about their medication



Conclusion: In this pilot survey, many participants reported concerns about medication, doubts about whether medication controls arthritis symptoms, severe side effects and medication nonadherence. Although our small sample is unlikely to be generalizable to all arthritis patients, these findings suggest potential targets for intervention and indicate that some patients have needs for support with medication that are not currently being addressed.
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Work and rehabilitation

POS1575-PARE WORKING AND HEALTH STATUS IN NORWEGIAN PATIENTS WITH TAKAYASU ARTERITIS

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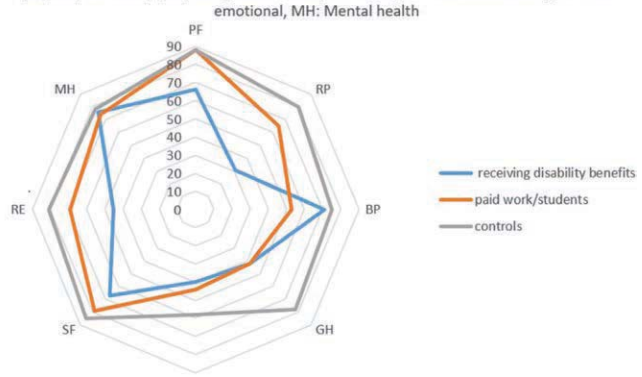
Background: Takayasu arteritis (TAK) is a rare vasculitis of large vessels, mainly in young women, with a point prevalence of 25.6/10^6 in a Norwegian population. TAK is most prevalently limited to the aortic arch and its branches (Type 1) among North Europeans (1). Early symptoms include fever, myalgia and loss of appetite. Later, irreversible vascular damage and ischemic symptoms with claudication of the extremities may occur. We have previously observed a reduced life expectancy, mainly due to cardiovascular complications and a median age among those deceased of only 58 years (2). These findings clearly indicate that TAK may have severe impact on the wellbeing of the patients and their physical capacity. Furthermore, being part of the working life is a major component of life but is affected in chronic autoimmune diseases (3,4)
Objectives: (i) To describe general health status and quality of life in patients with different working status.
(ii) To estimate the rates of patients having paid work or receiving disability benefits, compared to the general Norwegian population.
Methods: Patients with TAK registered in "The Norwegian Systemic Connective Tissue Disease and Vasculitis Registry" (NOSVAR) were included. All patients fulfilled the American College of Rheumatology classification criteria and/or the modified Ishikawa diagnostic criteria for TAK. (3). General health status was measured with 10-cm visual analogue scale (VAS) of pain and fatigue, ranging from 0 (best possible score) to 10 (worst possible score) and with Patients´ global assessment (PtGA) of health measured by a five-point Likert scale with scores ranging from 1 (very good health) to 5 (very bad health). The SF-36 was applied

to measure health related quality of life and included 8 scales with score ranging from 0 (worse) to 100 (best). Disease duration was defined as the time from diagnosis to date of registration. Working full- or part time was defined as paid work. We adjusted for age, gender and residence counties in southeast Norway using reference data from Norway Statistics. Indirect standardization with 95% confidence interval rates was calculated. Descriptive analyses were conducted.

Results: Patients with paid work were more educated compared with those receiving disability benefits (81% vs 19% p=0.031). Patients receiving disability benefits reported higher levels of pain (3,4 vs.1,4, p=0.024) and disease activity (3,8 vs. 0,8, p=0.025), more frequently claudication in legs (83% vs. 17%, p= 0.009) and impaired quality of life measured with SF- 36, physical functioning (66 vs 88, p=0.002) and role physical (32 vs 65, p=0.017) compared to patients with paid work/students (Figure 1).

Compared with the age and gender matched general population, the disability rate of female patients was 16 % higher, adjusted ratio (CI 95%) 2 (1,2-3,3), p=0.038. The paid work rate was 51% lower in women with TAK compared to the general population, adjusted ratio (CI 95%) 0,38 (0,23-0,64), p=0.001 .

Figure 1 Comparison between patients groups and controls. PF: physical functioning, RP: role physical, BP: bodily pain, GH: general health, VT: vitality, SF: social functioning, RE: role emotional, MH: Mental health



Conclusion: TAK-patients receiving disability benefits reported lower health status and lower quality of life by physical functioning and role physical in SF 36. Work disability in female TAK patients was 16 % higher and for paid work 51 % lower compared to the general population.

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Disclosure of Interests: None declared

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Best practice campaigning

POS1576-PARE IMPROVING METHOTREXATE PRESCRIBING AND DISPENSING SAFETY THROUGH A SIMPLE ADJUSTMENT TO ELECTRONIC PRESCRIBING.

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Background: Methotrexate (MTX) is the most commonly prescribed disease-modifying antirheumatic drug (DMARD) in rheumatoid arthritis, as well as being frequently used in other rheumatic conditions. Having been discovered in 1948 [1], its use is established and the toxicity profile is well recognised. In the rheumatology setting, it is prescribed as a once weekly dosing regimen. However, despite experience in the use of MTX, there still remains a concern for patient safety with regards to more frequent ingestion than the weekly dose. This can result in severe complications such as acute kidney injury, myelosuppression, mucositis and even death. According to Medicines and Healthcare products Regulatory Agency (MHRA), there were 11 adverse event reports between 2006 and 2020, and as a result, in 2020 the MHRA outlined guidance to reduce the potentially fatal dosing errors associated with the prescription of MTX [2].

Amongst this guidance, prescribers are instructed to discuss, document and include in the prescription, the specific day of the week MTX is to be taken. Dispensers are also advised to document the day of the week on the MTX drug dispensing label. At King's College Hospital (KCH) there is an existing mandatory field for day of the week when prescribing inpatient non-cancer MTX treatment. However, this does not exist currently for outpatient electronic prescribing.

Objectives: To update practice in the KCH Rheumatology department, in line with MHRA guidance on MTX prescription.

Methods: A retrospective audit of 30 MTX new and renewal prescriptions over 1 month was conducted to assess concordance with MHRA guidance. The safety-nets of documentation of day of the week on most recent clinic letter, drug prescription and drug dispensing label were reviewed. Following this the electronic prescription system was updated to make "day of the week" a mandatory field required to complete MTX prescriptions. A sample of 30 patients post intervention was then re-audited.

Results: The percentage of new prescriptions across the 2 groups were roughly equivalent (30% vs 33%).

Prior to intervention, 44% of new MTX prescriptions had no form of documentation of the day of the week across all 3 safety-nets, and only 33% had at least 2 of the 3 safety-nets completed. Post-intervention this has increased to 100%. Of those newly prescribed MTX, the inclusion of day of the week on clinic letters rose from 22% to 40%. There were similar improvements seen in safety-nets achieved for repeat prescriptions.

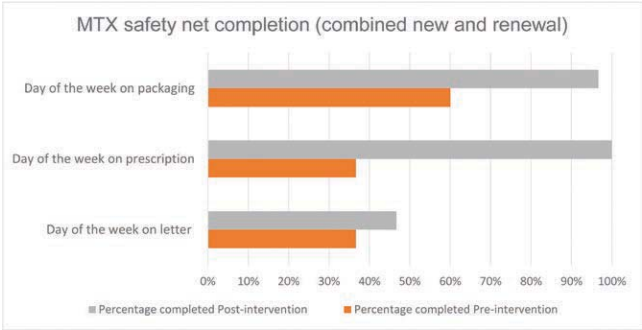

Figure 1.

Table 1.

	Percentage completed			
	Pre-intervention		Post-intervention	
	New	Renewal	New	Renewal
Day of the week on letter	22%	43%	50%	45%
Day of the week on prescription	33%	38%	100%	100%
Day of the week on packaging	33%	71%	90%	100%
None of the above	44%	14%	0%	0%
At least 2 of 3 of the above	33%	52%	100%	100%
All 3 completed	22%	14%	40%	45%

Conclusion: A significant improvement in concordance with MHRA guidance on MTX prescribing and dispensing can be easily achieved by making "the day of the week" a mandatory field to be included on all electronic MTX prescriptions. This change also produces a significant improvement in drug dispensing label safety and clinic letter documentation for patients newly initiated on MTX.

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Disclosure of Interests: None declared

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POS1577-PARE WHAT PATIENTS VALUE AND NEED FROM HEALTHCARE IN THE DIAGNOSIS AND MANAGEMENT OF AXIAL SPONDYLOARTHRITIS

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Background: The clinician's understanding of what constitutes good quality care for axial spondyloarthritis (axial SpA) has been explored (1) and used to define quality standards (2,3). However, research into the patient perspective on what constitutes good quality care was lacking. The UK's National Axial Spondyloarthritis Society (NASS) commissioned Headstrong Thinking, and its research partner, Community Research, to investigate this issue.
Objectives: The objectives of the research included: to explore the lived experience of those with an axial SpA diagnosis, to identify all the stages (domains) and milestones they identify and describe in their journey; to identify tangible person-centred indicators of "quality" in each of those stages, covering clinical care, patient care (non-clinical) and support for their mental health needs; to capture the everyday language used to articulate their values and needs around "quality"; and to understand possible differences between individual/subgroup experiences.
Methods: The project will use both qualitative and quantitative methods sequentially.
This paper reports only on the qualitative stage of the project, which comprised twelve individual depth interviews, conducted online, across a broad spectrum of people living with axial SpA in the UK, allowing for variation in age, sex, socioeconomic status, presence of children, length of time since diagnosis, physical symptoms and comorbidities.
Findings from the qualitative stage will inform the questionnaire for the quantitative stage (target n=1,500), which will seek to validate and refine initial hypotheses and quantify differences between sub-groups.
Results: This paper presents a rich understanding of the impacts on mental, emotional, cognitive and practical aspects of life with axial SpA. A detailed picture of a wide range of clinical, psychological and practical adverse impacts around delayed diagnosis is described.
Further, the qualitative research found that, from the perspective of people with axial SpA, quality care consists of three elements, defined by patients as: to be seen, heard and believed; to experience a purposeful, consistent pathway of care, underpinned by effective administration and communication (rather than a series of care "snapshots"); and to be helped to know what they can do to help themselves, including making a care plan that evolves as needs change.
Individuals with multiple or complex comorbidities were less likely to report having experienced good quality care, as they defined it, in part due to the challenges of accessing a joined-up patient journey and their greater reliance on an effective cross- disciplinary (NHS) healthcare system.
Conclusion: Patients define quality care in the diagnosis and management of axial SpA differently to clinicians. Professionals involved in the diagnosis and care of people living with axial SpA (including rheumatologists, but also those involved in the wider care of people living with axial Spa, such as physiotherapists and even mental health professionals) would benefit from a greater understanding of the patient perspective.
The individual stories uncovered in this qualitative phase underline the importance of collecting and analysing quantitative data by demographics, life stage and by discrete phases in the diagnostic /ongoing patient (self) management journey.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3056

POS1578-PARE TO OBTAIN GREATER AWARENESS OF ARTHRITIS AND THE DANISH ARTHRITIS ASSOCIATION BY MEDIA COVERAGE

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Background: Despite arthritis being among the most common diseases in Denmark, the overall personal consequences followed are generally unknown. You don't die of arthritis. This is reflected in the population's general knowledge of The Danish Arthritis Association of a mere 57 %, despite being Denmark's third largest patient organisation.
Objectives: To obtain greater awareness of arthritis and the Danish Arthritis Association by media coverage
Methods: We use case stories strategically in our offensive political agenda. By presenting a good case story with a personal, yet wide perspective, we quite often succeed in getting our agenda in the media – as personal and emotional case stories are more likely stories to be chosen by journalists than political solutions from organisations like ours.
On social media (especially Facebook and Instagram) we also use case stories to a great extent – 2 – 3 times a week. Our followers like to read stories about people who struggle with the same issues as themselves – and to reflect their own issues. Whether they are newly diagnosed or have lived with arthritis for a long time.
In general, we get good response on these personal case stories. Many likes, and often our followers share their own experience with each other and pass on good advice.
Helping out the media: The media and journalists are always in need of case stories to back up their articles and agendas. We have introduced the principle of always being willing to help the media with case stories. By providing cases with arthritis– even though the issues aren't exclusively about arthritis, we help solving a problem, as well as we manage to turn the agenda into a story about arthritis as well. Examples are corona, vaccination, deferred surgeries, lack of coherence in the health system.
What does it take to use cases?: As an organisation, you have a responsibility to take care of your cases by informing them of what it means to be in the media. They must be prepared and helped out – also along the way. It is also important to choose cases who are well spoken and not afraid to express themselves.
Debate group: Some of the topics such as coherence in health care, are immediately academic topics, and difficult to understand – and therefore more difficult to get covered in the media. We have successfully initiated a debate group consisting of a small group of young arthritis patients, whom we have taught how to write debate posts. By telling their own personal stories – often with an underlying political angle – these articles have been published in the major national newspapers.
Results: We have succeeded in getting media coverage in both women's magazines, tabloid newspapers, national newspapers as well as radio and television.
Conclusion: It is a fairly simple concept that easily can be copied by other patient organisations despite size.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.4734

POS1579-PARE LET'S TAKE AN HEALTHY WALK IN THE PARK

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Background: Patients with RMDs are not yet used to live phisical activity such as an important part of their therapy;
Covid 19 pandemic, with the restrictions imposed on interpersonal approaches and the the fear of being infected and spreading the virus, has further slowed down the way towards these kind of empowerment.
During the pandemic, in Italy the number of pets (mainly dogs) had an exponencial increase.
Animal Assisted Interventions /Animal Assisted Therapies seems to be really successful.
Objectives: Our project aims:
to offer people with RMDs the opportunity to move playing fitwalking under control of WALKin trainers who can teach them the right way to practice this new discipline or simply walking properly with their dogs or playng rehabilitative exercises (specific for each one) with the help of animals specially trained.
a number of meetings (at least 12) in which experts will discuss about RMDs, comorbidities, nature, animals, man-animal relationship adn so on.
Methods: Thanks to an agreement with a natural park (UNESCO MAB Collina Po reserve), we could draw 4 different routes (3-4-5-7 Km) and a safe area in which all the participants can play different activities.
Based on the medical prescription, people will be assigned to different groups (no more than 7 people in each group) and to different activities (walking, rehabilitative exercises, alone or with animals).
Twice a week during an hour the groups will meet and practice their activity, not only working together, but also sharing experiences, sesations, feeling.
Each group will be lead by an expert (walking trainers, health pofessionals, teamsters).
Either each group leader or each participant will wright a diary at the end of the activity session, to let us have a number of encoded informations which drive us to verify all progresses in term of improvement of mobility and mood and reduction of drugs cosumption.
Results: The participation (face to face and virtual) in the first three meetings (October, November 2021 and January 2022 has been continuously increasing and we have a good core of "fans", but also every time a lot of new people who want to join us.
We are collecting the first inscriptions and we preview to start the activity on March 20 when the first goups will be leaded by Maurizio Damilano, twice world and Olympic running champion and inventor of fitwalking.
First preliminary results will be available in December 2022.
Conclusion: With this project we hope to help people with RMDs to live physical activity as an important part of their therapeutic pathway and to rediscover how nice it is to be together, finding new friends (either humans or animals)
Disclosure of Interests: None declared
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Publication Only

Genomics, genetic basis of disease and functional genomics

AB0001

ALLELIC POLYMORPHISM OF INFLAMMATORY CYTOKINES GENES FOR PREDICTION OF CARDIOVASCULAR DISORDERS IN CHILDREN WITH JIA

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Background: It is known that defects in the synthesis and structure of cytokines or their receptors can lead to modification of many pathological processes in the organism: inflammation, coagulation, impaired cell regeneration, which makes it appropriate to further study the genetic preconditions for the violation of immunoregulatory mechanisms. Great attention is paid to the study of allelic polymorphism of genes in chronic inflammatory diseases as a potential marker of functional activity of proteins encoded by them and related features of the course of various disease.
Objectives: To assess the impact of allelic polymorphism of TNFα (G308A) & IL6 (G174C) genes on the development of cardiovascular disorders in children with JIA.
Methods: 102 children with JIA were examined. Allelic polymorphism of TNFα (G308A)& IL6 (G174C) genes was determined by PCR using specific oligonucleotide primers, subsequent analysis of polymorphism of restriction fragments was made. Activity of disease was calculated using JADAS27. Functional state of the myocardium was assessed using software-hardware complex "Cardioplus P", an ECG of 4th generation. Cluster analysis of obtained data was performed. K-means and EM algorithms were used. The number of children who finally entered this stage of the analysis was 25.
Results: According to the disease activity, the number of mutations and the complex indicator of the functional state of the myocardium (CI FS, %), two clusters were identified. In cluster 1 (10 children, group 1) the higher score of CI FS (median 78%) and lower disease activity degree (JADAS 27 median 9.5) was noted, and in cluster 2 (15 children, group 2) high disease activity (JADAS 27 median 14) was observed and a decrease in the CI FS (median 62%). The CI FS according to the ECG of 4th generation differed significantly (p = 0.00001) in clusters. It is noted that in the second group the disease debuted relatively earlier (p>0.01). Among these cluster groups of patients with JIA there were a number of significant differences in general clinical laboratory parameters: the activity of AST in the blood of patients with JIA was 29±3.1 IU/ l in the first group vs 24±2.2 IU/l in the second group (p = 0.07 Wald-Wolfowitz), serum creatinine was higher in the first group 68.8±11.0 μmol/l (against 57.0±9.3 μmol/l in the second group; t = -2.24, p = 0.044), also in the second group according to the results of the study according to the general analysis of blood there was leukocytosis (11.6±4.1 $x10^9$ vs. 6.69±0.8 $x10^9$, p = 0.075 Wald-Wolfowitz).
According to the obtained data of the cluster analysis, the total number of mutations in the genes IL6 and TNF-α was significant for the course of disease. In cases with a larger number of mutations, a more aggressive course of the disease, a more pronounced degree of inflammation, a higher frequency of extra-articular lesions, including changes in the CVS, was noted.
Conclusion: The overall number of mutations in TNFα (G308A) & IL6 (G174C) genes makes impact on the course of the disease; two and more mutations are associated with a more aggressive course of the disease and can lead to cardiovascular lesions more likely. Determination of allelic polymorphism should be recommended to patients who have changes on ECG performed by a 4th generation ECG.
Disclosure of Interests: None declared
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AB0002

ATTEMPTS TO LINK EXONIC GENE POLYMORPHISMS TO ANKYLOSING SPONDYLITIS (AS)- ASSOCIATED PROTEIN MODIFIED FUNCTIONALITY: A STRUCTURAL BIOLOGY APPROACH

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Background: Genome wide association studies (GWAS) have played a primary role in depicting genetic contributions to ankylosing spondylitis (AS) development, while accommodating the exonic polymorphisms on the protein structure level, when available, enhances our understanding of protein function modification. AS is a polygenic disorder and it is the archetype of a group of inflammatory conditions known as spondyloarthropathies because of their tendency to involve the spine [1]. Linking human genetics with therapeutic targets requires understanding of the biological function and structure of the expressed protein by the causal gene variant to be known.
Objectives: We sought to investigate recently identified AS-associated functional gene polymorphisms, such as *ERAP1*, *PON1*, *CARD9* and *JARID1A* [2-5] by correlation to protein structure and function.
Methods: The experimental 3D model structures of the human ERAP1, PON1, CARD9 and JARID1A proteins were used for the localization of the polymorphisms under study. Molecular mechanics/dynamics studies were applied to determine the impact of the polymorphisms on the structural stability of the enzyme and the conformational changes caused were structurally analyzed. The mutants were constructed using molecular modeling with the program MOE (Molecular Operating Environment V.2019.01, Chemical Computing HPC), which was also used to analyze the conformational changes caused by the mutation. All figures depicting 3D models were created using the molecular graphics program PyMOL V.2.2 [6].
Results: ERAP1 plays a role in trimming peptides for optimal binding to MHC1 molecules by utilizing a complex catalytic mechanism. High resolution structures of ERAP1 have shown that K528 and Q730 are located distal from the active site of the enzyme (Figure 1a). Recent enzymatic and computational studies have demonstrated that the presence of Lys or Arg at position 528 and of glutamine or glutamic acid in position 730 affects differently the conformational distribution of the protein ensemble by altering the conformational plasticity of the enzyme and, therefore, indirectly affecting dissimilarly its activity [7]. The *PON1* rs662 (Gln192Arg) variant affects stability and recognition of the ligand recognition site and plays a functional role in inflammatory disorders (Figure 1b). The caspase recruitment domain (CARD) interaction of CARD9 with Bcl10 promotes downstream activation of factors including NF-κB and the mitogen activated protein kinase (MAPK) p38 [8]. The *CARD9* rs4077515 (Ser12Asn) variant affects the conformational flexibility of the interacting N-terminal [9] (Figure 1c). *JARID1A* gene codes for lysine demethylase 5A (KDM5A) a histone demethylase that specifically demethylates 'Lys-4' of histone H3. The *JARID1A* rs11062385 (Met865Thr) SNP that is strongly correlated with expression has been associated with a protective role for the disease but is located in a region of the KMD5A protein with an undefined yet function.
Conclusion: Based on several examples, we have tried to define a rational link from AS-associated gene polymorphisms to structure and to modified function, including metagenomic analysis of SNPs, protein crystallography, protein molecular modeling, molecular mechanics and dynamics. Locating, shaping and understanding the target protein interaction interface plays a decisive role in most cases and provides clues for further pharmacological or medical actions.

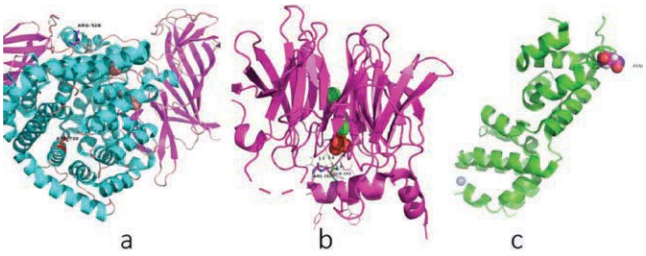

Figure 1. The structures of huERAP1 (a), huPON1 (b) and huCARD9 (c) with the mutations highlighted and labeled

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Disclosure of Interests: None declared
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AB0003

PHENOTYPIC EFFECTS OF GENETIC LOSS OF FUNCTION IN TYROSINE KINASE 2 USING LARGE-SCALE BIOBANKS

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Background: We used a naturally occurring germ-line genetic variant in tyrosine kinase 2 (*TYK2* [P1104A, rs34536443]), which has been shown to cause partial loss of function and protect against autoimmune disease,[1] to survey the phenotypic consequences of reduced TYK2 function.

Objectives: Survey the phenotypic consequences of a naturally occurring partial loss of TYK2 function, and directly test for an effect of naturally occurring TYK2 partial loss of function on risk of cardiovascular disease, thromboembolism, and lymphoma.
Methods: We performed phenome-wide association studies (PheWAS) in 2 large biobanks (FinnGen and UK Biobank) and across public case-control genetic studies using Open Targets Genetics.
Results: This study found additional support for a protective effect (odds ratio [OR] ≤0.8, $P<1x10^{-4}$) of TYK2 partial loss of function in multiple autoimmune diseases, including rheumatoid arthritis, psoriasis, psoriatic arthritis, systemic lupus erythematosus, sarcoidosis, type 1 diabetes, inflammatory bowel disease, and hypothyroidism. We did not observe any novel phenotypic associations that could highlight safety concerns for TYK2 inhibition. Additionally, we used well-powered and focused analyses to demonstrate that TYK2 partial loss of function is not associated with nonselective Janus kinase inhibitor safety concerns in any of the genetic studies. Our meta-analysis across the included studies showed no association with increased risk of cardiovascular disease (OR=0.97; *P*=0.02; 258,279 cases / 549,387 controls), venous thromboembolism (OR=0.97; *P*=0.52; 11,966 cases / 260,704 controls), and lymphoma (OR=1.06; *P*=0.47; 2687 cases / 220,721 controls).
Conclusion: TYK2 P1104A, a partial loss-of-function polymorphism, enables assessment of TYK2 involvement in immune-mediated disease and other pathologies. Loss of function in TYK2 reduces risk of immune-mediated disease but does not significantly increase risk of cardiovascular disease, thromboembolism, or lymphoma.
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Disclosure of Interests: Narayanan Raghupathy Shareholder of: employee and shareholder of Bristol Myers Squibb, Employee of: employee and shareholder of Bristol Myers Squibb, Erika Kvikstad Shareholder of: employee and shareholder of Bristol Myers Squibb, Employee of: employee and shareholder of Bristol Myers Squibb, Emily Holzinger Shareholder of: employee and shareholder of Bristol Myers Squibb, Employee of: employee and shareholder of Bristol Myers Squibb, Ian Catlett Shareholder of: employee and shareholder of Bristol Myers Squibb, Employee of: employee and shareholder of Bristol Myers Squibb, Joseph Maranville Shareholder of: employee and shareholder of Bristol Myers Squibb, Employee of: employee and shareholder of Bristol Myers Squibb
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AB0004 PTPN22 AND TNFAIP3, BUT NOT STAT4, ARE RISK FACTORS FOR IGG4-RELATED DISEASE

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Background: The etiology of IgG4-related disease (IgG4-RD) is not yet clear, but environmental and genetic factors are thought to be involved. Little is known about the genes that confer susceptibility to this disease, which is why various *loci* related to inflammation or autoimmunity have begun to be studied. Such studies are limited to Asian and European cohorts. To date, no study has searched susceptibility genes for the development of IgG4-RD in the Mexican Mestizo population.
Objectives: To determine whether three single nucleotide variants (SNVs) located in classic genes associated with systemic lupus erythematosus and rheumatoid arthritis, namely, *TNFAIP3* (rs2330926T/G), *STAT4* (rs7574865G/T), and *PTPN22* (rs2476601C/T), confer susceptibility for the development of IgG4-RD in the Mexican Mestizo population.
Methods: Patients who met the 2019 ACR/EULAR classification criteria for IgG4-RD were included. For each patient, two healthy controls were matched by sex who had no history of chronic, inflammatory, or autoimmune diseases. Both patients and controls were unrelated and self-reported with Mexican Mestizo ancestry by linage (at least three generations including their own). Genomic DNA was extracted from peripheral blood cells. SNVs were genotyped using TaqMan probes and the 5' exonuclease assay. The Chi-square test was used to determine odds ratios.
Results: We included 124 controls and 60 patients with IgG4-RD (31 (51.6%) female and 29 (48.4%) male). Patients with IgG4-RD had a mean age of 52.1 ±15 years. Ten (16.6%) had single organ involvement, 10 (16.7%) had two involved organs, and 40 (66.6%) had ≥ 3 involved organs. Thirteen (21.7%) belonged to the pancreato-hepato-biliary, 5 (8.3%) to the retroperitoneal/aortic, 19 (31.7%) to the head/neck-limited, 18 (30%) to the Mikulicz/systemic, and 5 (8.3) to the undetermined phenotype, while 43 (71.7%) belonged to the proliferative and 17 (28.3%) to the fibrotic phenotypes.
The allelic and genotypic frequencies of the SNV rs7574865G/T of *STAT4* did not show statistically significant differences between cases and controls ($p>0.05$); while the *PTPN22* variant rs2476601C/T showed association with IgG4-RD: allele C vs T, OR 10.6, CI 95% 1.22 - 91.37, $p=0.02$ and CC vs CT, OR 11.0, CI 95% 1.25 - 96.2, $p=0.008$; and the SNV rs2230296T/G of *TNFAIP3* showed the following association: T vs G, OR 2.8, 1.03 - 7.87, $p=0.04$ and TT vs TG, OR 3.0, 95% CI 1.07 -8.60, $p=0.03$.
Conclusion: This is the first study to suggest that the *STAT4* variant rs7574865G/G is not a risk factor for the development of IgG4-RD, while the variants rs2476601C/T of *PTPN22* and rs2230936T/G of *TNFAIP3* confer susceptibility to the development of this disease in the Mexican Mestizo population. Our study provides new information on the genetic basis of IgG4-RD.
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Disclosure of Interests: None declared
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AB0005 INTEGRATED ANALYSIS OF LNCRNAS AND MRNAS EXPRESSION PROFILING IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by over-activity of lymphocytes, production of autoantibodies and effects on multiple organs 1. Growing evidences suggest long noncoding RNAs (lncRNAs) and mRNAs widely participate in physiological and pathological processes. However, knowledge of related lncRNAs and mRNAs in SLE remains limited.
Objectives: The aim of our study is to investigate the levels of differential expression of lncRNAs and mRNAs in the peripheral blood mononuclear cells (PBMCs) of SLE patients and their correlation with disease activity, clinical features and cell differentiation.
Methods: Peripheral venous blood 4ml were collected from 11 patients with SLE before and after treatment and 11 sex-and age-matched healthy individuals and saved in EDTA tubes. PBMCs were isolated from peripheral blood samples by Ficoll-Histopaque density gradient centrifugation. Total RNA was extracted from PBMCs with TRIzol reagent. RNAs amount and quality were quantified by using a NanoDrop ND-1000. Peripheral blood samples were sent to Novogene Co. Ltd (Beijing, China) for sequencing. The DESeq package in R language was used to analyze the differential expression of lncRNAs and mRNAs in the two groups. GO and KEGG databases analyze the potential biological functions and signal transduction and disease pathways affected by abnormal expression of lncRNAs and mRNAs[2].
Results: According to the RNAs expression profiles, 338 lncRNAs (173 upregulated and 165 downregulated) and 2020 mRNAs (1292 upregulated and 728 downregulated) were differentially expressed between SLE patients and control groups. In addition, 17 lncRNAs were significantly downregulated and 66 mRNAs (47 upregulated and 19 downregulated) were differentially expressed between active and treated SLE patients. There were 1645 RNAs up-expression in active

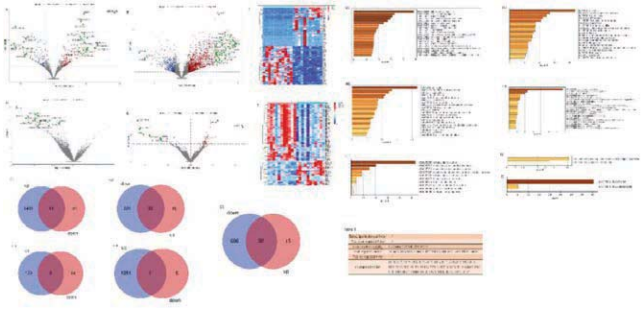
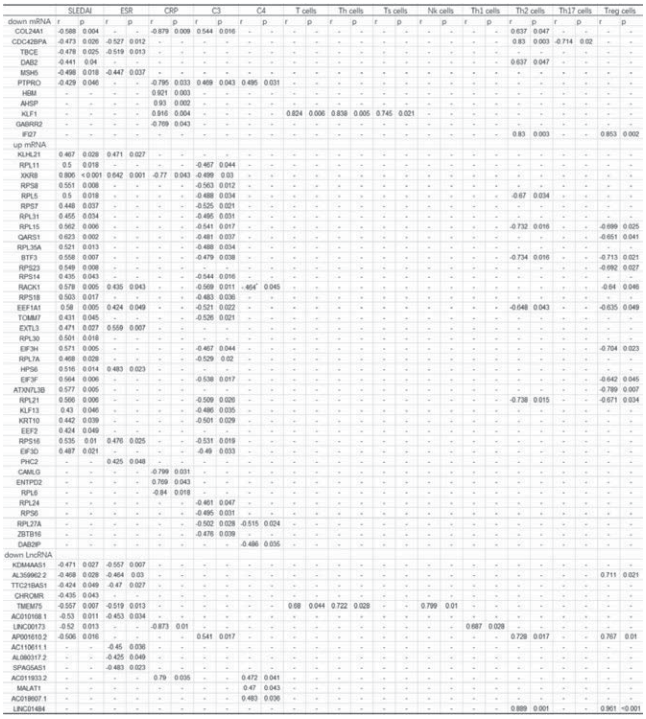


Figure 1. (A-C) Analysis of DElncRNAs and DEmRNAs of pre-treated SLE and cotrols. (A) The volcano plot with the DElncRNAs. (B) The volcano plot with the DEmRNAs. (C) The hierarchical clustering heatmap of DElncRNAs and DEmRNAs. (D-F) Analysis of DElncRNAs and DEmRNAs between pre-treated and treated SLE. (D) Volcano plot with the DElncRNAs. (E) Volcano plot with the DEmRNAs. (F) The hierarchical clustering heatmap of DElncRNAs and DEmRNAs. (G1-G5) Partial RNAs expression changed in active and treated SLE patients. Table 1 showed specific changed RNAs. (H1-H4) The top 20 GO and KEGG terms related to the up-regulated and down-regulated DEmRNAs. (I1-I3) GO and KEGG analyses of DEmRNAs between active and treated SLE patients.



	SLEDAI		ESR		CRP		C3		C4		T cells		Th cells		Ts cells		Nk cells		Th1 cells		Th2 cells		Th17 cells		Treg cells	
down mRNA	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
COL24A1	-0.588	0.004	-	-	-0.879	0.009	0.544	0.016	-	-	-	-	-	-	-	-	-	-	-	-	0.637	0.047	-	-	-	-
CDC42BPA	-0.473	0.026	-0.527	0.012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.83	0.003	-0.714	0.02	-	-
TBCE	-0.478	0.025	-0.519	0.013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
DAB2	-0.441	0.04	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.637	0.047	-	-	-	-
MSH5	-0.498	0.018	-0.447	0.037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PTPRO	-0.429	0.046	-	-	-0.795	0.033	0.469	0.043	0.495	0.031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HBM	-	-	-	-	0.921	0.003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AHSP	-	-	-	-	0.93	0.002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
KLF1	-	-	-	-	0.916	0.004	-	-	-	-	0.824	0.006	0.838	0.005	0.745	0.021	-	-	-	-	-	-	-	-	-	-
GABPB2	-	-	-	-	-0.769	0.043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
IFI27	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.83	0.003	-	-	0.853	0.002
up mRNA																										
KLHL21	0.467	0.028	0.471	0.027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL11	0.5	0.018	-	-	-	-	-0.467	0.044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
XRN1	0.806	< 0.001	0.642	0.001	-0.77	0.043	-0.499	0.03	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPS8	0.551	0.008	-	-	-	-	-0.563	0.012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL5	0.5	0.018	-	-	-	-	-0.488	0.034	-	-	-	-	-	-	-	-	-	-	-	-	-0.67	0.034	-	-	-	-
RPS7	0.448	0.037	-	-	-	-	-0.525	0.021	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL31	0.455	0.034	-	-	-	-	-0.495	0.031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL15	0.562	0.006	-	-	-	-	-0.541	0.017	-	-	-	-	-	-	-	-	-	-	-	-	-0.732	0.016	-	-	-0.699	0.025
QARS1	0.623	0.002	-	-	-	-	-0.481	0.037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.651	0.041
RPL39A	0.521	0.013	-	-	-	-	-0.488	0.034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BTF3	0.558	0.007	-	-	-	-	-0.479	0.038	-	-	-	-	-	-	-	-	-	-	-	-	-0.734	0.016	-	-	-0.713	0.021
RPS23	0.549	0.008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.692	0.027
RPS14	0.435	0.043	-	-	-	-	-0.544	0.016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RACK1	0.578	0.005	0.435	0.043	-	-	-0.569	0.011	-.464	0.045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.64	0.046
RPS18	0.503	0.017	-	-	-	-	-0.483	0.036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EEF1A1	0.58	0.005	0.424	0.049	-	-	-0.521	0.022	-	-	-	-	-	-	-	-	-	-	-	-	-0.648	0.043	-	-	-0.635	0.049
TOMM7	0.431	0.045	-	-	-	-	-0.526	0.021	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EXTL3	0.471	0.027	0.559	0.007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL30	0.501	0.018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EIF3H	0.571	0.005	-	-	-	-	-0.467	0.044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.704	0.023
RPL7A	0.468	0.029	-	-	-	-	-0.488	0.034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HPS6	0.516	0.014	0.483	0.023	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EIF3F	0.564	0.006	-	-	-	-	-0.538	0.017	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.642	0.045
ATXN7L3B	0.577	0.005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.789	0.007
RPL21	0.566	0.006	-	-	-	-	-0.509	0.026	-	-	-	-	-	-	-	-	-	-	-	-	-0.738	0.015	-	-	-0.671	0.034
KLF13	0.43	0.046	-	-	-	-	-0.486	0.035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
KRT10	0.442	0.039	-	-	-	-	-0.501	0.029	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EEF2	0.424	0.049	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPS16	0.535	0.01	0.476	0.025	-	-	-0.531	0.019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EIF3D	0.487	0.021	-	-	-	-	-0.49	0.033	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PHC2	-	-	0.425	0.048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CAMLG	-	-	-	-	-0.799	0.031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ENTPD2	-	-	-	-	0.769	0.043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL6	-	-	-	-	-0.84	0.018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL24	-	-	-	-	-	-	-0.461	0.047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPS6	-	-	-	-	-	-	-0.495	0.031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPL27A	-	-	-	-	-	-	-0.502	0.028	-0.515	0.024	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ZBTB16	-	-	-	-	-	-	-0.476	0.039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
DAB2IP	-	-	-	-	-	-	-	-	-0.486	0.035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
down LncRNA																										
KDM4A-AS1	-0.471	0.027	-0.557	0.007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AL359962.2	-0.468	0.029	-0.464	0.03	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.711	0.021
TTC21B-AS1	-0.424	0.049	-0.47	0.027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CHROMR	-0.435	0.043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
TMEM75	-0.557	0.007	-0.519	0.013	-	-	-	-	-	-	0.68	0.044	0.722	0.028	-	-	0.799	0.01	-	-	-	-	-	-	-	-
AC010168.1	-0.53	0.011	-0.453	0.034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LINC00173	-0.52	0.013	-	-	-0.873	0.01	-	-	-	-	-	-	-	-	-	-	-	-	0.687	0.028	-	-	-	-	-	-
AP001610.2	-0.506	0.016	-	-	-	-	0.541	0.017	-	-	-	-	-	-	-	-	-	-	-	-	0.729	0.017	-	-	0.767	0.01
AC110611.1	-	-	-0.45	0.036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AL080317.2	-	-	-0.425	0.049	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SPAG5AS1	-	-	-0.483	0.023	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AC011933.2	-	-	-	-	0.79	0.035	-	-	0.472	0.041	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
MALAT1	-	-	-	-	-	-	-	-	0.47	0.043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AC018697.1	-	-	-	-	-	-	-	-	0.483	0.036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LINC01484	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.889	0.001	-	-	0.961	<0.001

Table 1: The relativity between aberrantly expressed mRNA and LncRNA and clinical characteristics of active and treated SLE patients.

SLE patients and 36 RNAs under-expression in treated SLE patients, and total 14 RNAs changed direction of expression. GO and KEGG pathway analysis showed most of mRNAs were related to transcription, inflammation and immunity. The relativity between aberrantly expressed RNAs and clinical characteristics of active and treated SLE patients were shown in Table 1.

Conclusion: Dysregulation of lncRNAs and mRNAs involves in molecular regulation of SLE, which may support for diagnosis or determination of the susceptibility of individuals of SLE.

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AB0006

ESTABLISHED RISK LOCI FOR SYSTEMIC LUPUS ERYTHEMATOSUS AT NCF2, STAT4, TNPO3, IRF5 AND ITGAM ASSOCIATE WITH DISTINCT CLINICAL MANIFESTATIONS: A DANISH GENOME-WIDE ASSOCIATION STUDY

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Background: Systemic lupus erythematosus (SLE) has been associated with more than 100 genetic loci. This parallels positively to the clinical diversity that is reflected by the classification of SLE.

Objectives: We aimed to investigate associations between disease manifestations of SLE and risk gene variants relevant to Danish subjects of European ancestry.

Methods: We included 427 SLE patients of European ancestry similar to previous reports.[1] We also included 89,699 controls from the Danish Blood Donor Study Genomic Cohort. SLE risk loci in this population were identified by

Table 1. Associations between five SLE risk loci and specific disease manifestations in 427 Danish patients with SLE*.

		NCF2	STAT4	IRF5	TNPO3	ITGAM
		rs17849502_T	rs7574865_T	rs4728142_A	rs13239597_A	rs11860650_T
	N (%)					
Malar rash	233 (55%)	1.28 (0.84-1.96)	0.83 (0.62-1.11)	1.01 (0.74-1.38)	1.44 (0.97-2.12)	1.14 (0.80-1.61)
Discoid rash	46 (11%)	1.49 (0.81-2.73)	0.90 (0.56-1.45)	1.01 (0.62-1.66)	1.16 (0.63-2.12)	0.76 (0.42-1.41)
Photosensitivity	219 (51%)	0.96 (0.63-1.46)	1.09 (0.81-1.47)	0.98 (0.71-1.34)	0.84 (0.57-1.25)	**0.67 (0.47-0.97)**
Oral ulcers	132 (31%)	0.96 (0.61-1.50)	0.90 (0.65-1.23)	0.83 (0.60-1.16)	1.30 (0.87-1.96)	1.43 (0.99-2.05)
Non-erosive Arthritis	342 (80%)	0.84 (0.52-1.37)	**1.49 (1.02-2.18)**	0.93 (0.63-1.36)	1.04 (0.64-1.68)	1.16 (0.74-1.80)
Serositis						
-Pleuritis	124 (29%)	0.63 (0.38-1.05)	**1.38 (1.01-1.89)**	1.22 (0.87-1.72)	0.85 (0.56-1.29)	0.84 (0.57-1.24)
-Pericarditis	72 (17%)	0.75 (0.41-1.40)	1.35 (0.93-1.96)	1.05 (0.70-1.58)	1.15 (0.70-1.89)	1.09 (0.70-1.72)
Persistent proteinuria	158 (37%)	**1.63 (1.07-2.49)**	1.08 (0.80-1.46)	**0.68 (0.49-0.94)**	**1.74 (1.16-2.61)**	1.09 (0.76-1.57)
Neurologic disorder						
-Seizures	23 (5%)	1.58 (0.75-3.35)	1.49 (0.80-2.76)	**2.10 (1.04-4.25)**	0.61 (0.26-1.44)	0.93 (0.42-2.06)
-Psychosis	8 (2%)	0.76 (0.097-5.87)	2.77 (0.94-8.15)	0.35 (0.10-1.23)	0 (0)	2.96 (0.85-10.3)
Haematologic disorder						
-Haemolytic anaemia	38 (9%)	0.78 (0.34-1.76)	1.37 (0.85-2.22)	0.75 (0.44-1.29)	1.11 (0.57-2.19)	1.24 (0.70-2.20)
-Leukopenia	130 (30%)	1.04 (0.67-1.61)	1.19 (0.87-1.63)	1.00 (0.72-1.39)	0.90 (0.60-1.37)	0.94 (0.64-1.37)
-Lymphopenia	228 (53%)	0.95 (0.63-1.44)	**1.35 (1.01-1.81)**	0.95 (0.70-1.29)	1.16 (0.79-1.70)	1.09 (0.77-1.54)
-Thrombocytopenia	102 (24%)	1.42 (0.91-2.22)	0.84 (0.60-1.18)	0.83 (0.58-1.18)	1.35 (0.86-2.11)	0.91 (0.60-1.37)
Immunologic disorder						
-anti-DNA ab.	330 (77%)	0.69 (0.44-1.09)	1.02 (0.72-1.44)	0.94 (0.65-1.35)	0.97 (0.62-1.53)	1.08 (0.71-1.65)
-anti-Smith ab.	44 (10%)	1.44 (0.79-2.64)	**1.58 (1.00-2.49)**	1.23 (0.73-2.07)	1.47 (0.80-2.69)	1.07 (0.61-1.84)
-anti-phospholipid ab.	183 (43%)	**1.63 (1.07-2.49)**	1.05 (0.79-1.41)	0.84 (0.61-1.14)	1.14 (0.77-1.68)	1.14 (0.80-1.62)

* Logistic regression models for each manifestation included all five lead variants (multivariate) and were adjusted for age and sex

genome-wide association methodology and hereafter correlated to cumulative occurrence of SLE classification items.
Results: Fourteen variants mapped to the following genes: *NCF2, STAT4, TNPO3/TPI1P2, IRF5,* and *ITGAM,* were significantly associated (p<5E-8) with SLE.
The five lead variants were associated (p<0.05) with the following manifestations; *NCF2*: proteinuria and anti-phospholipid antibodies, *STAT4*: arthritis, serositis, neurologic disorder, lymphopenia, and anti-Smith antibodies, *IRF5*: seizures and proteinuria, *TNPO3*: proteinuria, and *ITGAM*: photosensitivity (Table 2).
Conclusion: Our findings support the future use of select, relevant genetic markers in predicting various SLE phenotypes.
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AB0007 ASSOCIATION OF RS172378 VARIANT IN C1Q GENE CLUSTER WITH SOME CLINICAL AND IMMUNOLOGICAL ASPECTS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN BULGARIAN PATIENTS

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Background: Single nucleotide polymorphisms (SNPs) in complement C1q component are found to be linked with systemic lupus erythematosus (SLE), but less is known about their association with the clinical and immunological aspects of the disease.
Objectives: The aim of the study was to examine five SNPs – rs665691, rs682658, rs172378, rs294179, rs292001 in C1q gene cluster for association with some clinical (age at disease onset, organ involvement, BILAG score, SLICC/ACR DI) and immunological (ANA, anti-dsDNA, complement factors C3 and C4) aspects of SLE.
Methods: 53 SLE patients were enrolled in this cross-sectional study and relevant clinical information was collected. SNP genotyping was performed on extracted DNAs from patients using a TaqMan allelic discrimination assay. ANA, anti-dsDNA and complement proteins C3 and C4 were measured by IIF, ELISA and radial immunodiffusion resp.
Results: G-allele and GG-genotype of rs172378 were overrepresented among patients with LN compared to the other SLE patients – 64% vs 31% for G-allele and 48% vs 7.7% and were associated with renal involvement – OR=3.96 (95%CI: 1.53 – 10.23), p=0.005 for G-allele and OR=10.86 (95%CI: 1.29 – 91.58), p=0.028 for GG-genotype.
G-allele and GG-genotype were also associated with increased levels of anti-dsDNA antibodies – OR=2.95 (95%CI: 1.21 – 7.18), p=0.017 and OR=6.33 (95%CI: 1.41 – 28.39), p=0.016, resp.
G-allele showed weak correlation with earlier age at disease onset (point biserial r=-0.22, p=0.03) and patients, carrying it (GG- and AG-genotypes) were younger at disease onset then those with AA-genotype (p=0.05 and p=0.02 resp.).
Conclusion: rs172378 associates with some clinical and immunological parameters of SLE, traditionally linked to disease severity, therefore it may possibly play a role in disease pathogenesis.
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AB0008 ACESO APPLICATION: AN INTEGRATED GENOTYPE ANALYSIS WEB SERVER FOR CLINICAL GENOMICS IN CROHN'S DISEASE AND IBD-RELATED ARTHRITIS

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Background: Genome Wide Association Studies (GWAS) observe the set of different variants throughout the genome of different individuals and study whether a particular trait is due to one variant. Many autoimmune diseases have been identified to have a linkage with specific loci and metabolic pathways, but the exact cause of disorders is still remaining unknown [1]. Aceso Application is an integrated bioinformatics web-tool designed for researchers and medical experts towards to estimating the clinical genomic profile of a candidate patient with Crohn's Disease (CD)[2-4].

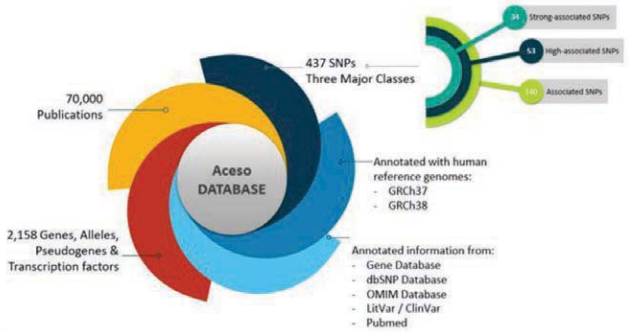

Figure 1. The Aceso app web-server Database. Left are shown the three identified SNPs classes of the genomic "grammar" of CD.

Objectives: To identify the most reliable gene variants, single nucleotide polymorphisms (SNPs) and epigenetic related SNPs that causing CD using the genomic data provided for the patient and aid the medical expert in CD diagnosis.
Methods: In the present study, we have analyzed more than 149.000 CD related publications using data mining and semantic techniques towards extracting the Crohn's Disease-related genes, non-coding regions and generally candidate SNPs. The extracted knowledge has been filtered, evaluated, annotated, classified, and stored in the Aceso Application Database (AAD). This was followed by the design and development of the Aceso application, in which the generated datasets and results were included. The application has been tested and presented here with whole-exome sequencing data from several related patients with CD.
Results: CD-related SNPs and variants identified in genome-wide association studies (GWAS), whole-genome (WGS), whole-exome (WES), or targeted sequencing information are classified, annotated, and analyzed in an integrated patient profile with clinical significance information. Probable genes associated with the patient's genomic profile are visualized with chromosome ideograms, statistic bars, and regulatory networks through data mining studies with relative publications. An evaluation study was performed on 2 patients from a three-generation family with CD [5].
Conclusion: The Aceso application was designed to assist early stage diagnosis by using the patients's genomic data. It provides the patient's genomic profile which is generated based on the list of the most predictable candidate gene variants related to CD and has implications also for IBD-related arthritis. This novel and accessible webserver tool of CD to assist medical experts in the clinical genomics and precision medicine procedure is available at http://geneticslab.aua.gr/aceso.

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AB0009 DIFFERENTIALLY EXPRESSED GENES BETWEEN FLARE OF PALINDROMIC RHEUMATISM AND ACTIVE RHEUMATOID ARTHRITIS

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Background: Although the mechanisms of palindromic rheumatism (PR) is still unclear, an association between PR and rheumatoid arthritis (RA) has been well recognized in previous studies, with one to two-thirds of PR patients developing RA during a period of follow-up. RNA sequencing (RNA-Seq) is a next-generation sequencing (NGS) method that measures genome-wide RNA abundance. Using RNA-Seq to identify the DEGs between flare PR and active RA could help elucidate the pathogenic mechanisms of PR flare and find novel genes to predict RA progression.
Objectives: The aim of this study is to identify gene expression signatures between PR flare and active RA using whole blood RNA-seq.
Methods: We collected clinical data, and blood samples from 12 flare PR patients and 12 active RA (defined as DAS28-ESR≥3.2) patients from Taichung Veterans General hospital. We obtained high-quality RNA by using PAXGene tube for whole blood sampling and PAXGene blood RNA Kit to extract RNA. Cuffdiff (Cufflinks option) output was filtered for differentially expressed genes (DEGs) with p-value < 0.05. Gene set enrichment analysis (GSEA) were performed using the GSEA version 4.0.0 with immunologic gene sets (C7 sets containing 4872 gene sets) from The Molecular Signatures Database (MSigDB). According to GSEA web suggestion, a false discovery rate (FDR) < 0.25 with a p-value < 0.05 was considered statistically significant. We obtained rank ordered gene list from GSEA.
Results: We compared flare PR and active RA using GSEA. Five of the top 12 enrichment in phenotype with flare PR was related to lipopolysaccharide (LPS), which was found in the outer membrane of Gram-negative bacteria. And other pathways were also related to immune response, e.g., B cell, T cell and macrophage. In active RA, the characteristic gene expressions were associated with immune response, such as genes up-regulated in dendritic cells, genes down-regulated in B cell, and genes up-regulated in T cells.
We obtained top 3 differential gene expressions in flare PR patients and top 3 differential gene expressions in active RA patients. FCGBP, GLRX3 and RTN4R genes were significantly associated with immune response in flare PR patients. And we observed that 3 genes had statistically significant *t-test* result (FCGBP, p-value< 0.001; GLRX3, p-value< 0.001; RTN4R, p-value< 0.001) (Figure 1**a, 1b and 1c**). This result showed that FCGBP, GLRX3 and RTN4R may play an important role on immune response related to flare PR. In active RA patients, 3 genes had statistically significant *t-test* result (HK3, p-value< 0.001; HIST1H2AI, p-value= 0.002; BST1, p-value<0.001) (Figure 1**d, 1e and 1f**).

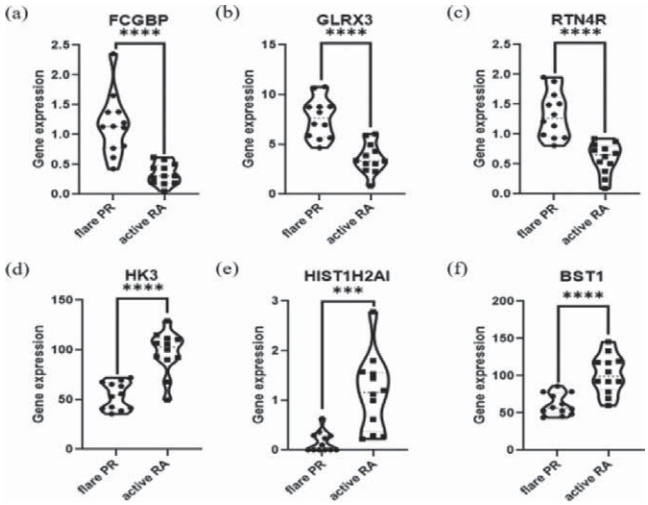

Figure 1. Differential gene expressions between flare PR and active RA. (a) FCGBP, (b) GLRX3, (c) RTN4R, (d) HK3, (e) HIST1H2AI, (f) BST1

Conclusion: GSEA analyses showed that five of the top 12 enrichment in flare PR was related to LPS and other pathways were related to immune responses of B cell, T cell and macrophage. However, in active RA, the characteristic gene expressions included genes up-regulated in dendritic cells, genes down-regulated in B cell, and genes up-regulated in T cells, suggeting different physiological pathways from flare of PR.
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AB0010 ASSOCIATION OF SOME NON-HLA GENE POLYMORPHISMS WITH SUSCEPTIBILITY TO SYSTEMIC LUPUS ERYTHEMATOSUS IN WOMEN IN BELARUSIAN POPULATION

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Background: Despite the recent progress in our understanding of the genetic predisposition to systemic lupus erythematosus (SLE) its clinical and functional significance is not fully clarified yet and needs to be implemented in personalized care [1].
Objectives: To estimate the association between some single nucleotide polymorphisms (SNPs) of 9 non-HLA genes-candidates as STAT4 rs7574865, PTPN2 rs2542151, PTPN22 rs2476601, AGER rs1035798, TRAF1/C5 rs3761847, SLC7A11 rs13128867, RUNX1 rs9979383, IL6 rs1800795, IL6R rs2228145, IL6R rs4845618 and susceptibility to SLE in Belarusian women for the following predictive model development.
Methods: We examined 316 women: among them 59 SLE patients (mean age 39.84, CI95% 36.62-43.06) classified according to the 1997 American College of Rheumatology (ACR) revised classification criteria and 257 age-matched healthy controls (blood donors, mean age 38.12, 95% confidence interval (CI95%) 36.77-39.46). Deoxyribonucleic acid was extracted from peripheral blood samples by phenol-chloroform method. Genotyping was performed by real-time PCR with fluorescent probes. Descriptive analysis, test for Hardy–Weinberg equilibrium, multiple inheritance models (co-dominant, dominant, recessive, over-dominant and log-additive) for single SNPs, Akaike information criteria (AIC) and Bayesian information criteria (BIC) were analyzed using SNPStats web tool [2]. Pearson χ^2 (χ^2), two-way Fisher exact test (F, $p_{2\text{-t}}$), odds ratio (OR), likelihood ratio of positive (LR^+) and negative (LR^-) tests with corresponding $CI_{95\%}$ were also calculated.
Results: Exact test for all genotype frequencies distribution of all studied SNPs didn't reveal significant differences with Hardy-Weinberg equilibrium in all controls and SLE groups. We noted significant increase of minor TT genotype frequency of STAT4 rs7574865 in SLE vs healthy women with recessive inheritance model as the best-fitting one according to its less AIC and BIC values (OR=3.78 ($CI_{95\%}$ 1.35-10.62); p=0.016; LR^+=3.45 ($CI_{95\%}$ 1.37-8.60); LR^-=0.91 ($CI_{95\%}$ 0.84-0.98)). We revealed protection of minor A allele of AGER rs1035798 carriership with log-additive model of inheritance as the best-fitting one according to AIC and BIC values against SLE development in women (OR=0.52 ($CI_{95\%}$ 0.33-0.83); p=0.004; LR + =0.70 ($CI_{95\%}$ 0.50-0.93); LR – =1.47 ($CI_{95\%}$ 1.10-1.86)). We also noted significant increase of minor allele G frequency of TRAF1/C5 rs3761847 in SLE vs healthy women with dominant inheritance model (OR=3.61 ($CI_{95\%}$

1.05-12.38); p=0.019; LR $^{+}$ =1.30 ($CI_{95\%}$ 1.03-1.43); LR $^{-}$ =0.36 ($CI_{95\%}$ 0.12-0.92)) and increase of AA genotype frequency in healthy women (p_{2-t} =0.041). We revealed that minor allele G of PTPN2 rs2542151 is more frequent in SLE women vs healthy controls and has overdominant model of inheritance (OR=1.98 ($CI_{95\%}$ 1.09-3.59); p=0.026; LR $^{+}$ =1.57 ($CI_{95\%}$ 1.07-2.20); LR $^{-}$ =0.79 ($CI_{95\%}$ 0.62-0.97)). There were no significant differences in genotypes and alleles distribution for PTPN22 rs2476601, RUNX1 rs9979383, SLC7A11 rs13128867 and IL6 rs1800795 in studied population and we noted only non-significant tendency in minor SNP genotypes distribution of IL6R rs4845618 and IL6R rs2228145 between healthy controls and women with SLE.

Conclusion: Our data suggest the susceptibility to SLE in women with TT genotype of STAT4 rs7574865 polymorphism and allele G carriers of both TRAF1/C5 rs3761847 and PTPN2 rs2542151 as well as protective role of AGER rs1035798 A allele carriership againt SLE development in women of Belarusian population.

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AB0011 DNA METHYLATION AS A BIOMARKER OF TOCILIZUMAB RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Tocilizumab (TCZ) is a disease-modifying antirheumatic biologic drug, which targets the IL-6 signalling pathway and is effective in ameliorating disease activity in rheumatoid arthritis (RA). However, approximately 50% of patients do not respond adequately to TCZ and some patients report adverse events. Considering there is growing evidence that DNA methylation is implicated in RA susceptibility and response to some biologics (1, 2), we investigated DNA methylation as a candidate biomarker for response to TCZ in RA.

Objectives: To identify differential DNA methylation signatures in whole blood associated with TCZ response in patients with RA.

Methods: Epigenome-wide DNA methylation patterns were measured using the Infinium EPIC 850k BeadChip (Illumina) in whole blood-derived DNA samples from patients with RA. DNA was extracted from blood samples taken pre-treatment and following 3 months on therapy, and response was determined at 6 months using the Clinical Disease Activity Index (CDAI). Patients who had good response (n=10) or poor response (n=10) to TCZ by 6 months were selected. Samples from secondary poor responders (n=10) (patients who had an improvement of CDAI and were in remission at 3 months, followed by a worsening of CDAI at 6 months) were also analysed. Differentially methylated positions (DMPs) were identified using linear regression, adjusting for gender, age, cell composition, smoking status, and glucocorticoid use.

Results: In the pre-treatment samples, 20 DMPs were significantly associated with response status at 6 months (unadjusted p-value $<10^{-6}$), whilst in the 3 month samples, 21 DMPs were associated with response. One DMP, cg03121467, was significantly less methylated in good responders compared to poor responders in the pre-treatment samples. This DMP is close to *EPB41L4A* and may play a role in β–catenin signalling. Interestingly, cg10136146 was significantly less methylated in secondary poor responders compared to both good and poor responders in the 3 month samples. This DMP maps close to *CD81*, which plays a role in mediating the development and activation of B and T lymphocytes.

Conclusion: These preliminary results provide evidence that DNA methylation patterns may predict response to TCZ. Further regional and pathway analyses is in progress and validation of these findings in other larger data sets is required.

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AB0012 IDENTIFICATION OF NEW BIOMARKERS FOR SINOMENINE TREATMENT IN RHEUMATOID ARTHRITIS BASED ON BIOINFORMATICS ANALYSIS

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Background: Sinomenine (SIN) were extracted from Caulis Sinomenii and achieved an remarkable therapeutic effect for Rheumatoid Arthritis (RA). However, the mechanism of SIN acting on RA is not clear yet.

Objectives: To excavate potential targets and mechanisms of SIN for RA through bioinformatics.

Methods: The microarray data were downloaded from the Gene Expression Omnibus (GEO) database. GEO2R was used to identify differentially expressed genes (DEGs) and the unique value was retained. The potential targets of active compounds from various databases were screened. Based on the overlapping genes, Cytoscape 3.7.2 software was used to construct a protein-protein interactions (PPI) network and to visualize the mechanisms of the treatment by Gene Ontology (GO) enrichment analysis Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis by DAVID database. Finally, we used AutoDockTools 1.5.6 for molecular docking.

Results: A total of 5053 DEGs and 1070 intersections were obtained, including 486 up-regulated and 584 down-regulated targets. 298 SIN targets were collected from various databases, 84 potential targets were obtained by intersecting with DEGs. There are 80 nodes and 305 edges were obtained in PPI network. Based on the degree, the top 10 target genes were AKT1, RGFR, MTOR, JAK2, NOS3, IL2, IL6, MMP9, MAPK8, HSP9OAA1. The core targets was most relevant to protein phosphorylation, signal transduction though GO analysis. The results of the KEGG enrichment analysis included PI3K-Akt signaling pathway and Neuroactive ligand-receptor interaction. Following analysis found that AKT1, EGFR, MTOR and JAK2 existed in the PI3K-Akt signaling pathway. Molecular docking was used to confirm that the binding energy of AKT1 was -7.68 kJ mol $^{-1}$, EGFR was -5.33kJ mol^{-1}, and MTOR was -4.77 kJ mol^{-1},JAK2 was -3.25 KJ mol^{-1}. AKT1 and EGFR was further identified as the core targets.

Conclusion: Present study show that AKT1 and EGFR may be the key targets of SIN acting on the PI3K-Akt signaling pathway, thereby inhibiting the progression of disease and improving RA.

Keywords: Sinomenine; Rheumatoid Arthritis; bioinformatics;

Disclosure of Interests: None declared

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Identification of new biomarkers for Sinomenine treatment in Rheumatoid Arthritis based on bioinformatics analysis

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AB0013

THE COHESIN COMPLEX PROTEIN SMC1A IS A PUTATIVE REGULATOR OF SEX-BIASED INFLAMMATORY RESPONSES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: A strong female predisposition is characteristic of Systemic Lupus Erythematosus (SLE), with female-to-male ratio ranging from 7:1 to 15:1. The molecular basis of this gender bias remains incompletely understood. In a previous whole-blood RNA profiling study, we identified genes with differential expression in SLE males versus females but not in their healthy counterparts. Among these genes, the cohesin complex protein SMC1A (Structural Maintenance of Chromosomes 1A) displayed the highest statistical significance [1].
Objectives: To (a) determine the immune cell type that displays the strongest gender-biased SMC1A expression in SLE versus healthy individuals, and (b) elucidate the role of SMC1A in regulating immune/inflammatory responses in the context of SLE.
Methods: Multiple immune cell types ($CD19^+$ B cells, $CD4^+$ T cells, $CD14^+$ monocytes, neutrophils) were purified from peripheral blood specimens of SLE and healthy individuals, followed by Taqman PCR and Western blot to measure SMC1A mRNA and protein levels, respectively. The genome-binding properties of SMC1A were assayed by chromatin immunoprecipitation (ChIP)-sequencing in monocytes cultured under lupus-inducing conditions (lupus-like monocytes) [2]. To recapitulate the female/male difference in SMC1A expression, *ex vivo* cultured lupus-like monocytes were transfected with si-SMC1A (to downregulate SMC1A) versus si-control reagent, followed by genome-wide transcriptome analysis by RNA-sequencing.
Results: Among the various tested immune cell types, $CD14^+$ monocytes best recapitulated the initial whole blood RNA-seq findings, demonstrating significantly decreased SMC1A mRNA and protein expression in male versus female SLE patients but not in their healthy counterparts. In blood monocytes cultured under lupus-inducing conditions and tested by ChIP-sequencing, SMC1A binding was increased on enhancers and promoters of genes associated with inflammation (including type I/II interferon and other inflammatory cytokines) and cell migration. In accordance, lupus-like monocytes with lowered SMC1A expression (i.e., male-like) displayed significantly reduced expression of inflammatory genes like *IL6*, *GBP5*, *ADA* and *IL1A*, as compared to monocytes with unaffected SMC1A (i.e., female-like). Furthermore, *IL6* mRNA synthesis was significantly enhanced in female versus male monocytes cultured under lupus-inducing conditions.
Conclusion: SMC1A may transcriptionally regulate genes associated with the inflammatory response of monocytes. Our findings of gender-biased SMC1A levels in SLE monocytes raise the hypothesis that differential SMC1A expression and function might contribute to the disease gender bias and/or sexual dimorphism.
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AB0014

THE ROLE OF NLRP3 INFLAMMASOME POLYMORPHISMS IN THE GOUT SUSCEPTIBILITY

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Background: Recent reports have demonstrated that polymorphisms within NLRP3 inflammasome signaling pathway are key factors in the risk to develop some joint inflammatory diseases (1). To date, there is still uncertain information about the presence of these genetic variants and their association with risk of gout.
Objectives: To determine the association between the single nucleotide polymorphisms (SNPs) within NLRP3 inflammasome genes and the risk of developing gout.
Methods: We included 220 gout patients and 243 healthy subjects as control group. Clinical examination was performed and laboratory including glucose concentration, total cholesterol and triglycerides were obtained. The frequency and the allelic distribution of eight SNPs from seven different genes within the NLRP3 inflammasome signaling pathway were analyzed using the Step One Plus Real-Time PCR Systems. SNPs were selected by the criterion of minor allele frequency (MAF) (above 1 %), using the 1000 Genomes Project. Genetic variation data for all the SNPs were obtained from the HapMap project (http://www.hapmap.ncbi.nlm.nih.gov/) and the public National Center for Biotechnology Information dbSNP database (http://www.ncbi.nlm.nih.gov/snp). The SNPs should not to be in linkage disequilibrium. Ancestry was analyzed using ancestry informative markers differentiating mainly Amerindian, African, and European ancestries.
Results: The missense SNP rs45520937 in PPARGC1B, showed enhanced association with the risk of developing gout when it was analyzed using the dominant model, evidencing that gout patients carried the A/G-A/A genotype have an elevated risk compared to the control group [OR (95% CI) = 2.30 (1.09-4.86), p=0.030]. While, the adaptor molecule CD14 rs2569190 SNP could be associated with lower risk of gout under an additive model [OR (95 % CI)= 0.41 (0.16-1.05), p= 0.064]. No significant association were identified for the remaining SNPs.
Conclusion: Our findings suggest that genetic variant rs45520937 of PPARGC1B is significantly associated with the gout susceptibility.
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AB0015

HOMEOBOX D13 TRANSCRIPTION FACTOR MODULATES THE FORMATION OF THE PRIMARY CILIUM IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: Differences in gene expression and functions of synovial fibroblasts between distinct joints might lead to site-specific activation of arthritis-relevant pathways. We previously showed that the transcription factors HOX-D10, -D11 and -D13 are higher expressed in synovial fibroblasts from hands and feet compared to shoulder and knee, and that this expression pattern is epigenetically imprinted[1].
Objectives: To investigate the functional role of HOXD13 in synovial fibroblasts.
Methods: Synovial fibroblasts from patients with rheumatoid arthritis (n=2) were cultured and transfected with HOXD13 antisense LNA GapmeRs (12.5 nM). Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000). Pathway enrichment analysis of RNA-seq data was performed using web-based tools (ToppGene, EnrichR and Cytoscape) (± fold change > 1.5, FDR < 0.05). The expression of histone deacetylases (HDACs) and sirtuins was measured by quantitative real-time PCR and immunofluorescence staining. Ciliogenesis of synovial fibroblasts was assessed by measuring the expression of *PKD2, ARL13B, KIF3A*, and *IFT88* using qPCR. Acetylation of alpha-tubulin was assessed by immunofluorescence staining. Imaging was performed with the CellInsight™ CX7 platform.

Primary cilia were manually counted. Approximately 500 cells for each replicate were recorded for the presence of a primary cilium. The length of primary cilia was measured using Image J (Version 1.53o). Synovial fibroblasts were treated with Trichostatin A (2μM), an inhibitor of HDACs (HDACi), for 24h.

Results: Pathway enrichment analysis of genes changed after HOXD13 silencing of synovial fibroblasts showed that HOXD13 regulated genes are involved in primary cilia related pathways. We confirmed lower mRNA expression of the ciliary proteins, *PKD2*, *KIF3A* and *IFT88* after HOXD13 silencing (n=4; *PKD2*: 0.65 ± 0.4, p<0.05; KIF3a: 0.6 fold ± 0.3, p<0.05; IFT88: 0.7 fold ± 0.3, p<0.05), and higher expression of *ARL13B (ARL13B*: 1.8 fold ± 0.4, p<0.05). An increase in the number and length of primary cilia, as well as acetylation of alpha- tubulin, a characteristic feature of primary cilia, was seen after HOXD13 silencing (n=4). Accordingly, expression of *HDAC4, -5* and *-7* was decreased after HOXD13 silencing (n=4; *HDAC4*: 0.25 fold ± 0.1, p<0.05*; HDAC5*: 0.4 fold ± 0.1, p<0.05; *HDAC7*: 0.3 fold ± 0.2, p<0.05). *SIRT1* expression was higher (n=4; 1.7 fold ± 0.4, p<0.05), but *SIRT2* expression was lower (n=4; 0.1 fold ± 0.03, p<0.05) in HOXD13 silenced synovial fibroblasts. Trichostatin A treatment increased the acetylation level of alpha tubulin (n=4) as well as the expression of *ARL13B*, *KIF3A*, and *IFT88* in synovial fibroblasts (n=4; *ARL13B*: 2.3 fold ± 0.9, p<0.05; *IFT88*: 1.5 fold ± 0.3, p<0.05; *KIF3A*: 3.7 fold± 1.8, p<0.05). The length and number of primary cilia was not changed by Trichostatin A treatment.

Conclusion: Our data show that HOXD13 plays a role in regulating the assembly of primary cilia in synovial fibroblasts. This effect seems partly mediated by the expression of HDACs and partly by the expression of ciliary proteins. The primary cilium is a sensory organelle mediating reactions to mechanical and chemical signals from the environment. Thus, our results suggest joint specific regulation of synovial fibroblasts in response to stimulation via the primary cilium.

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AB0016 GENETIC VARIANTS OF PREDISPOSITION TO RHEUMATOID ARTHRITIS IN BELARUSIAN POPULATION

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by autoimmune inflammatory response focused in the synovium. RA is a complex disorder with significant genetic component and it is also known to have possible environmental triggers. Microbiota and bacterial infections play a significant role in RA etiology. The onset of RA may be accompanied by the previous or ongoing chlamydia infection in some cases.

Objectives: to determine genetic variants of susceptibility to RA in Belarusian population

Methods: 650 individuals were divided into 2 cohorts: 305 patients with RA (59.69 ± 12.20), and 345 controls (mean age 37.42 ± 10.62). Patients with RA were further stratified into two subsets – those with catamnestic *Chlamydia trachomatis*/*Chlamydophila pneumoniae* infection (43, "RAChl+") and those without (262, "RAChl-"). 11 SNPs of 10 genes (*IL6* (rs1800795), *IL6R* (rs2228145 and rs4845618), *STAT4* (rs7574865), *TRAF1/C5* (rs3761847), *RUNX1* (rs9979383), *RUNX3* (rs11249215), *PTPN2* (rs2542151), *PTPN22* (rs2476601), *AGER* (rs1035798), *SLC7A11* (rs13128867)) were genotyped using Real-time PCR or PCR-RFLP.

Results: It was found that homozygous TT genotype at the rs7574865 locus of the *STAT4* gene and CT+TT genotypes at the rs2476601 locus of the *PTPN22* gene are associated with RA in general (OR 2.71 [1.31 – 5.61]; p = 0.005 and OR 2.47 [1.75-3.48] p<0.000, respectively). CC genotype at the rs9979383 locus of the *RUNX1* gene and AG+GG genotypes at the rs11249215 locus of the *RUNX3* gene revealed protective effect (OR 0.63 [0.40-0.98] p=0.036 and OR 0.58 [0.36-0.92] p=0.02, respectively). The lack of association with RA was shown for polymorphic loci of the *IL6* (rs1800795), *IL6R* (rs2228145 and rs4l45618), *SLC7A11* (rs13128867), *AGER* (rs1035798), *PTPN2* (rs2542151) and *TRAF1/C5* (rs3761847) genes. For RA subsets stratified according to presence/absence of the *C. trachomatis*/*C. pneumoniae* infection it was shown that CC genotype at the rs1800795 locus of the *IL6* gene and AA genotype at the rs11249215 locus of the *RUNX3* gene were associated specifically with the risk of developing Chlamydia infection-associated RA (OR 5.22 [1.85–14.71] p=0.0024 and 2.63 [1.09-6.35] p=0.037). In addition, TG+GG genotypes at the rs2542151 locus of the *PTPN2* gene is also associated with RAChl+ clinical phenotype (2.10 [1.10-3.99] p=0.025). No association with either of disease subtypes was revealed for polymorphic loci *RUNX1* (rs9979383), *IL6R* (rs2228145, rs4845618), *AGER* (rs1035798), *SLC7A11* (rs13128867), *TRAF1/C5* (rs3761847).

Conclusion: Thus, the polymorphic variants of *STAT4*, a key gene of autoimmunity, and *PTPN22* gene, that is involved in the JAK/STAT pathway of immune response, increase the RA susceptibility in general cohort for the Belarusian population. At the same time, CC genotype at the rs1800795 of the *IL6* gene, its product being central proinflammatory cytokine, and AA at the rs11249215 locus of the *RUNX3* gene, that is involved in T-cell initiated immune response, as well as the genotypes TG+GG at the rs2542151 locus of the *PTPN2* gene, involved in signaling pathways of immune response through T-cell activation, are associated only with RAChl+ clinical phenotype. Our data may indicate that genetic variants of *STAT4* and *PTPN22* contribute to genetic basis of the pathogenesis of RA through renewal of T-cell initiated immune response.

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Disclosure of Interests: None declared

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

AB0017 T HELPER /REGULATORY T CELLS RATIOS IMBALANCE IN DIFFERENT STAGING RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that results in the destruction of the bone and cartilage of the joints[1]. The imbalance between Th17 and Treg cells has been demonstrated to play a role in RA pathogenesis[2].With the advances in the RA field, curing and even preventing RA has become a new direction of efforts. To explore the immune characteristics in multi-staging RA is helpful for the development of accurate strategies.

Objectives: To observe the immune characteristics in different staging rheumatoid arthritis patients

Methods: A total of 127 patients with RA were recruited for this study, in cluding 30 early RA(newly diagnosed and treatment-naive,duration of disease ≤3months), 30 midddle RA (newly diagnosed and treatment-naive, duration of disease >3months and≤1 year), 30 advanced RA(newly diagnosed and treatment-naive,duration of disease >1 year) and 37 active treated RA (remissioned after target treatment and this time due to disease recurrence in hospital). All patients were hospitalized in the second hospital of Shanxi medical university and diagnosed with RA fulfilled the ACR 1987 or 2010 criteria.The percentage and absolute numbers of lymphocyte phenotypes and CD4+ T subsets in peripheral blood were examined by flow cytometry.

Results: There were no significant difference in the percentage and value of T,B,NK,CD4+T,CD8+T andCD4+T subsets. But the Th1/Th2 cell ratios in active treated RA group were increased than that in early RA, middle RA and advanced RA group.The Th17/Treg cell ratios in middle RA and advanced RA group were higher when compared with those of active treated RA group.In addition, the Th1/Treg cell ratios were decreased in middle and advanced RA group as compared with those in active treated RA.

Conclusion: Th1/Th2,Th17/Treg and Th1/Treg imbalance varied with disease staging.The different disease staging in RA, the immune function is different. Providing targeted immunotherapy according to disease staging is helpful to improve remission rates and even prevent disease.

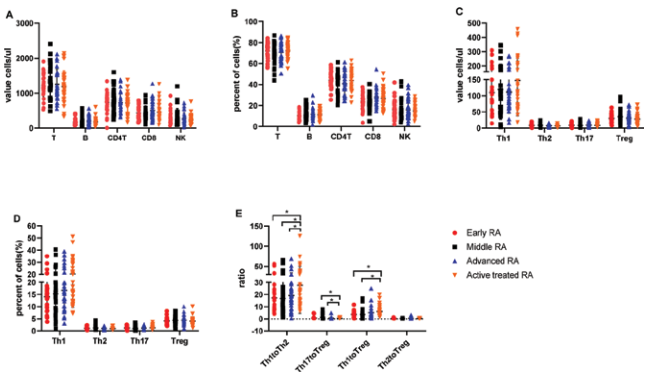

Figure 1. The comparsion about the lymphocyte subsets and cell ratios in peripheral blood of different stage RA patients.(*p<0.05)

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.377

AB0018 SERUM ANTIBODIES AGAINST ORAL AND INTESTINAL BACTERIA IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS, CHRONIC RA PATIENTS, AND NEW ONSET PATIENTS WITH DIFFERENT RHEUMATIC DISEASES

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Background: Evidence about the influence of microbes in autoimmune diseases such as rheumatoid arthritis (RA) has grown in recent years. However, the precise role of specific bacteria remains largely unknown. Previous investigations identified several oral pathobionts to be specifically targeted by serum antibodies in RA patients.[1] In addition, Pianta et al.[2] identified recognition of *Prevotella copri* by the immune system of RA patients. It has to be noted, however, that such findings have neither been reproduced, nor studied in different disease stages. Also, the assumptions made for *P. copri* relied on a single strain, the type strain DSM18205, isolated from a healthy individual.[3] However, there is recent evidence suggesting *P. copri* to be a non-monotypic species, meaning it clusters into several subspecies displaying geno- and phenotypic differences[4].
Objectives: This study aimed to quantify serum antibodies targeting different *P. copri* strains, as well as known oral pathobionts in patients with different rheumatic diseases or in various stages of RA development.
Methods: We used custom-made ELISA assays measuring pathogen-specific IgG levels in patient's serum. Samples were tested against *P. copri* strains isolated from stool samples of healthy donors and RA patients, as well as the following oral pathobionts: *Porphyromonas gingivalis*, *Prevotella intermedia* and *Prevotella melaninogenica*. We analyzed 120 samples from a Swiss cohort of first-degree relatives, individuals in various pre-clinical RA stages (SCREEN-RA), and 45 samples of patients with established RA (SCQM cohort). These participants were categorized as asymptomatic seronegative individuals (FDR), individuals with 'systemic autoimmunity associated with RA' (ACPA and/or RF autoantibodies) (preRA 1), individuals with 'clinically suspect arthralgia' or 'undifferentiated arthritis' with/without autoantibodies (preRA 2) and chronic RA patients (cRA). Additionally, we included 92 serum samples from new-onset patients diagnosed with RA, psoriatic arthritis (PsA) axial spondyloarthritis (SpA), or other non-rheumatic diseases (NRD) recruited via the german RheumaVOR cohort (Table 1).

Table 1. Overview human cohort studies

cohort	SCREEN-RA			SCQM	RheumaVOR			
patient group	FDR	preRA 1	preRA 2	cRA	NRD	RA	PsA	axSpA
total numbers	42	40	38	45	32	14	30	16
age median	54	54	59	56	43.5	51.5	50.5	33
sex (F/M)	32/10	35/5	34/4	35/10	19/13	9/5	15/15	10/6
ACPA positivity	0	25	9	31	0	7	0	0
RF positivity	0	19	8	34	0	7	0	0

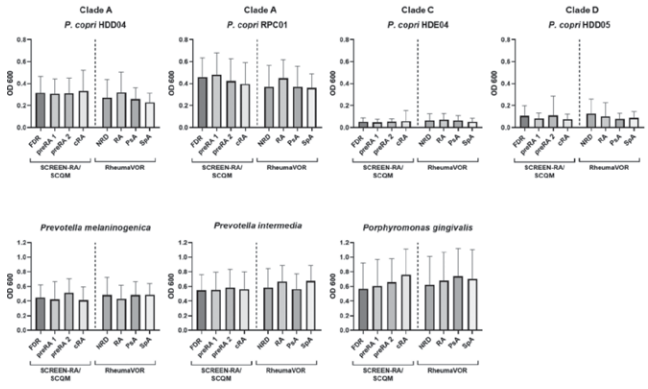

Figure 1. Serum IgG responses against different microbes from individuals recruited via SCREEN-RA, SCQM or RheumaVOR cohort

Results: Overall, there were no significant differences in the IgG reactivity profiles between the patient groups against the distinct *P. copri* strains or oral pathobionts (Figure 1). However, performing this assay with *P. copri* strains from distinct subspecies identified clear differences and revealed important variability in the IgG reactivity.
Conclusion: Our study failed to reproduce previous results and could confirm neither *P. copri* nor the three oral pathobionts to be particularly targeted by systemic IgG immune reactions in RA patients. However, we identified strain-specific differences in the IgG reactivity against *P. copri*, regardless of disease type or state. The latter suggests that the overall immunostimulatory potential of *P. copri* might be dependent on its strain/subspecies level. Our findings underline the necessity of *P. copri* strain-level characterization when studying host-microbiota immune interactions.

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Disclosure of Interests: None declared
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AB0019 RITUXIMAB TREATMENT DOES NOT ALTER EXPRESSION OF CO-STIMULATION MARKER CD19 ON B CELLS IN SYSTEMIC SCLEROSIS PATIENTS

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Background: CD19 is a membrane glycoprotein interacting with different surface molecules like the B cell receptor (BCR) and is crucial for antigen-independent development as well as immunoglobulin-induced activation of B cells.[1] Alterations in this signalling pathway can incline autoantibody production and systemic autoimmunity in humans. Rituximab (RTX), a CD20 antagonist appears to be an effective candidate in the treatment of different autoimmune diseases that are partly driven by autoreactive B cells, such as systemic sclerosis (SSc).[2] It has been speculated that RTX might work not only by depleting B cells but also to down regulate activation markers, such as CD19.
Objectives: In-depth analysis of CD19 abundancy and activation on B cells in SSc patients with and without RTX treatment
Methods: Peripheral blood samples from 41 patients suffering from SSc (median ± standard deviation SD, age: 54.3 ± 10.6 years, female ratio: 0.8) and 45 age- and sex-matched healthy controls (HC) (age: 51.0 ± 13.9 years, female ratio: 0.8) were drawn and PBMCs were isolated on-site. We performed flow cytometry analysis on a standardized BD LSRFortessa platform to identify B cell (CD19+CD20+) subpopulations. The geometric mean fluorescence intensity (gMFI) for CD19 in all B cell subtypes was extracted from the data set and used for further statistical analysis. Additionally, a quantitative flow cytometric bead-based assay (QuantiBRITE PE kit from Becton Dickinson) was used for the estimation of CD19 antibodies bound per cell.
Results: 3 out of 41 SSc patients were in high disease activity at the time of blood drawal. 23 SSc patients were under RTX therapy of whom 5 patients still displayed measurable B cells frequencies. Naïve B cells made up the most abundant B cell population in SSc patients. Thus, the frequency of IgM+/IgD+/CD27- B cells was 67.9% ±13.2 (mean ±SD), followed by class-switched memory B cells (IgM-/IgD-/CD27+, 10.5 ± 4.9), non-switched memory B cells (IgM+/IgD+/CD27+, 4.0 ± 3.6) and plasmablasts (0.3 ± 4.4). Pairwise Wilcoxon Tests (Bonferroni-corrected for multiple testing) showed significant differences ($p < 0.001$) between frequencies of naïve B cells and all other cell types. In contrast, naïve B cells displayed the second lowest CD19 gMFI levels (7601.0 ± 1912.0) in the dataset. Non-switched memory B cells in SSc patients showed the highest CD19 gMFI (10620.0 ± 15689.8), followed by class-switched (9388 ± 3048.6). As expected, Plasmablasts displayed the lowest CD19 gMFI levels (4799.0 ± 4185.7). The decrease in CD19 gMFI was again highly significant. This trajectory in decreasing CD19 gMFI was found in both HCs and SSc patients. We saw a significant reduction in percentages of non-switch B cells and class-switched B cells in SSc patients compared to HCs (4.0 ± 3.6 vs 6.5 ± 4.2, $p = 0.029$, 10.5 ± 4.9 vs 13.2 ± 7.2 $p = 0.04$) but an increase in CD19 gMFI in non-switched B cells (HC: 9204.5 ± 2116.8, $p = 0.05$). Interestingly, SSc patients under RTX treatment had significantly lower class-switched memory B cell frequencies compared to HCs (6.4 ± 4.2 vs. 13.2 ± 7.2, $p = 0.015$). However, RTX did not affect CD19 gMFI or bound CD19 in SSc.
Conclusion: RTX treatment in SSc is not associated with downregulation of the co-stimulation marker CD19. Thus, the main effect of this drug is the reduction of B cells, especially class-swtched memory B cells that might have a high capacity to activate other cells involved in the pathogenesis of SSc.

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AB0020 COMPARATIVE DESCRIPTION OF CYTOKINES AND MATRIX METALLOPROTEINASES IN A GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHROSIS UNDER A STRICT FOLLOW-UP COMPARED WITH COVID-19 PATIENTS

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Background: COVID-19, rheumatoid arthritis (RA) and osteoarthrosis (OA) are diseases characterized by the secretion of cytokines related to the stimulation of the inflammatory response.
Objectives: To identify the differences in the cytokine and matrix metalloproteinases (MMP) profile within one acute infectious disease and two chronic inflammatory rheumatic diseases.
Methods: Analytical cross-sectional study. RA patients under a strict follow-up program (T2T evaluated every two months), OA patients without strict clinical follow-up, evaluated once or twice a year, and Severe (mortality) COVID-19 patients were included. Eleven proteins (cytokines, MMPs and its tissue inhibitors) were quantified through Luminex multiplex assay in serum samples. Univariate and bivariate analyzes were performed. Approval of Ethics Committee and informed consent were obtained.
Results: A total of 108 patients with RA and OA were compared with 20 severe COVID-19 patients. There were no significant differences through the method of Kruskall–Wallis, between RA and OA patients. IL1-B and MMP-2 were significantly lower in COVID-19 patients. Levels of IL-10, IL-1RA, IL-6, MMP-1, MMP-9, and TIMP-1 were significantly higher in COVID-19 patients. There were no differences in TNF-A, TIMP-2 and INF-G. (Table 1)

Table 1. Significant correlations between cytokines related to Covid-19, RA and OR.

Cytokine (pg/ml) Median values	RA (%)	OA	COVID-19	P-value
IL-10	54.92	54.49	116.38	<0.0001[a]
Il1-RA	62.19	51.82	110.08	<0.0001[a]
IL1-B	67.09	55.30	46.17	0.045
IL-6	56.09	51.34	84.98	<0.0001[b] 0.003[c]
TNF-A	17.5	14.6	16.3	NS
MMP-1[d]	57.84	54.84	90.81	<0.0001[b] 0.045[c]
MMP-2 [d]	70.38	70.59	48.56	0.040
MMP-9 [d]	66.25	58.16	86.4	0.007 [b]
TIMP-1 [d]	51.59	60.99	111.67	<0.0001[a]
TIMP-2 [d]	45.2	47.7	49.6	NS
INF-G	5.75	5.32	3.07	NS

[a] Between RA and Covid-19 and OA and Covid-19, without differences between RA and OA. [b] Between OA and Covid-19.[C] Between RA and Covid-19. [d] ng/ml.

Conclusion: Compared with RA and OA patients, severe COVID-19 patients have a great impact on the cytokines and MMPs addressed in this study, proving that COVID-19 patients suffer from a cytokine storm [1] when severely infected.

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AB0021 FEATURES OF IMMUNOLOGICAL MANIFESTATIONS OF COMMON VARIABLE IMMUNODEFICIENCY COMBINED WITH RHEUMATOID ARTHRITIS

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Background: The prevalence rate of common variable immunodeficiency (CVID), the most common symptomatic form of primary immunodeficiency disease (PID), is growing every year. In the Republican Register of PID in the Chuvash Republic (Russia) there are 32 patients with CVID, 5 (15.6%) of whom have CVID combined with an autoimmune disease - rheumatoid arthritis (RA). The immunological studies occupy a large place in the diagnosis of PID and autoimmune diseases.
Objectives: The aim of the study was to search for immunological criteria for the differentiation of RA from CVID combined with RA.
Methods: The object of the study were 2 groups of patients. Group 1 consisted of 20 RA patients; group 2 consisted of 5 patients with CVID in combination with RA. Patients with CVID, who had the results of an immunological study conducted before the appointment of immunoglobulin replacement therapy, were selected for this study. The control group consisted of 20 practically healthy people.
Results: The significant changes were revealed in the concentration of serum immunoglobulins in the studied groups of patients, in particular, a sharp decrease in IgG levels in group 2 (1.9±0.3 g/l vs. 15.2±2.3 in group 1, p<0.001), IgA (0.1±0.02 g/l vs. 3.1±0.7 g/l in group 1, p<0.001), IgM (0.2±0.03 g/l vs. 1.7±0.2 g/l in group 1, p<0.001). Immunoglobulin levels in both groups of patients were lower (p<0.001) compared to the control group. In both groups, the number of regulatory cells – Treg (CD4+CD25+FoxP3) was reduced: in group 1 - to 2.5±0.03%; in group 2 - to 2.3± 0.02%, while in the control group it was 4.2± 0.5%, p<0.001. The result of our study confirms that the development of RA and CVID is associated with the decrease in the number of Treg cells responsible for ensuring peripheral tolerance and preventing the development of autoimmune diseases.
Conclusion: CVID and RA have a common immunopathological sign - a decrease in the content of Treg cells in the blood. In the differential diagnosis between RA and CVID, combined with RA, it is necessary to rely on the results of the determination of immunoglobulins in the blood serum.
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AB0022 SELECTIVE ESTROGEN RECEPTOR MODULATORS AND TISSUE-SELECTIVE ESTROGEN COMPLEX DO NOT SHARE ESTROGENIC EFFECTS ON IGG SIALYLATION IN AUTOIMMUNE CONDITIONS

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Background: Women entering menopause, with a decrease in estrogen levels, display an increased incidence of rheumatoid arthritis (RA). Estrogen (E2) treatment has beneficial effects on IgG pathogenicity by altering the sialylation grade which affect the binding ability to FcR[1]. E2 replacement may therefore be beneficial in pre-RA patients having autoantibodies. Exposure to estrogen is associated with negative side effects, therefore selective estrogen receptor modulators (SERMs) have been developed with estrogenic protective effect on bone but minimal impact on the reproductive system[2]. The SERM, Bazeodoxifene (BZA), as well as tissue-selective estrogen complex (TSEC), a combination of conjugated estrogen and BZA, have been approved for treatment of postmenopausal bone loss[3-5]

Objectives: The purpose of this study was to investigate the impact of BZA and TSEC on IgG sialylation grade which affects the pathogenicity as well as to determine the effects on total serum protein sialylation.
Methods: C57Bl6 mice were subjected to ovariectomy to stop the endogenous E2 production and mimicked the postmenopausal status. Mice were then treated with E2, BZA, TSEC, or vehicle, followed by ovalbumin (OVA) immunization to induce the IgG levels. Blood was collected before treatment started and at termination. In serum total IgG, OVA specific IgG and the degree of IgG-sialylation were quantified with ELISA. Sialyation of total serum proteins was determined with sialic acid assay quantification kit. Expression of sialyltransferase protein was analyzed in the bone marrow (BM) and spleen cell compartment using flow cytometry. The mRNA expression of glycosyltransferase was analyzed by qPCR analysis.
Results: Neither BZA nor TSEC significantly altered the total IgG levels or sialylation grade of IgG. Indeed, E2 significantly altered IgG sialylation. We showed that BZA increased sialyltransferase protein in plasma cells in a similar manner as E2. Further, neither E2, BZA or TSEC had any significant impact on sialic acids in whole serum protein and not in the mRNA expression of glycosyltransferase in the liver, BM, or gonadal fat.
Conclusion: In this study, we were not able to detect any alteration by TSEC or BZA treatment on IgG-sialylation grade and thereby pathogenicity of the IgG. Neither E2 nor BAZ or TSEC show any significant alteration on general sialylation, but our results suggest that further studies are required to understand E2, SERM, and TSEC full effect on protein sialylation in autoimmune conditions.
Keywords: IgG sialylation, protein glycosylation, SERMs
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AB0023 JAK-INHIBITORS DISRUPT CD14+/CD4+ CELL INTERACTION SUPPRESSING RHO-GTPASE DEPENDENT LEUKOCYTE RECRUITMENT TO JOINTS OF RA PATIENTS

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Background: While examining arthritis development due hyperactivated Rho-GTPases in a mouse model, we found that macrophages with hyperactive Rho-GTPases regulate the migration of thymic T regulatory cells to peripheral lymphoid organs, which contributed to arthritis development Interestingly, T cells reciprocally upregulate Rho-GTPases leading to suppression of homing and formation of a mechanosensory complex of centered around β_1-intergrin facilitating migration.
Objectives: In response to the finding in mice we sought to explore this relationship in patients diagnosed with RA, aiming to expand understanding how different treatments affect the molecular mechanisms we observed in mice.
Methods: To confirm if similar interaction mechanisms between macrophages and T cells are present in RA patients, we used paired transcriptome (RNAseq) of $CD14^+$ and $CD4^+$ cells from 80 RA patients active on conventional DMARDs prior to treatment with TNF-inhibitors (exploratory cohort) and from 56 RA patients with inactive disease on various DMARD treatment (confirmatory cohort). In both cohorts, patients were stratified by mean expression of *CDC42* in $CD14^+$ cells to mimic hyper activation of Rho-GTPases. Transcriptomics of $CD14^+$ and $CD4^+$ cells were analyzed and translated into clinical correlates.
Results: Examining the exploratory cohort, we found a reciprocal upregulation of Rho-GTPases across the cell types. The $CDC42^{hi}$ group had upregulation of *RHOA* and *RAC1* in $CD14^+$ cells and *CDC42, RAC1* and *RHOA* in $CD4^+$ cells. Upregulation of *IL6*, *TLR4* and inflammasome units *IL18R1* and *IL1R2*, *NLRP3* signified pro-inflammatory phenotype of those cells. Furthermore, $CDC42^{hi}CD14^+$ and $CD4^+$ cells shared the upregulation of AP-1 TFs, and the circadian rhythm controlling molecules *PER1*, *AHR* and *KLF6* assisting cell migration. Next, $CDC42^{hi}$ cells were enriched with a synovial macrophage marker CD163, and *ITGB1* to facilitate focal adhesion and migration into joints. Moreover, high expression of CXCL-chemokines and *CCL5* on $CDC42^{hi}CD14^+$ cells indicated the ability to recruit T cells, and high *CXCR4* on $CDC42^{hi}CD4^+$ cells suggested their synovial destination. Unexpectedly, $CDC42^{hi}CD14^+$ and $CD4^+$ cells were not recognized by strong production of the key pro-arthritis cytokines TNF-α and IFN-γ. Consequently, the $CDC42^{hi}$ profile of $CD14^+$ and $CD4^+$ cells was not predictive for clinical response to TNF-inhibition in the exploratory cohort.
Examination of the confirmatory cohort revealed the majority of $CDC42^{hi}CD14^+$ cells belong to the patients treated with conventional DMARDS, while $CDC42^{lo}$ group were treated with JAK-inhibitors (20 vs 4, *OR*= 11.87, 95 % CI [3.387, 49.72], $p<0.0001$). We also found a correlation between *CDC42* expression in $CD14^+$ cells and DAS28 in patients treated with JAK-inhibitors ($r=0.5$, $p=0.0072$) pointing at tight relation between the treatment effect and Rho-GTPase dependent processes. This significantly affected the Rho-GTPase dependent interaction between $CD14^+$ and $CD4^+$ cells.
Transcriptional profile of $CDC42^{hi}CD14^+$ cells of the confirmatory cohort showed many similarities with the exploratory cohort including upregulation of the canonical Rho-GTPases, *ITGB1* and the inflammasome activation that were enhanced by upregulation *of* the vast number of ITGA and chemokines. Transcriptional regulation through *AHR* and *KLF6* persisted, while AP-1 and *PER1* was downregulated. In contrast to CD4+ cells of the exploratory cohort, $CD4^+$ cells of the patients with $CDC42^{hi}CD14^+$ cells were low in *CDC42*, *RAC1* and *RHOA* expression. Also, $CD4^+$ cells were deficient in AP-1, *AHR*/*KLF6* and *PER1*.
Conclusion: Taken together, these data show that Rho-GTPases regulate interaction between $CD14^+$ and $CD4^+$ cells and their migration to RA joints. Treatment with JAK-inhibitors suppress the Rho-GTPase dependent recruitment to joints by changing communication between $CD14^+$ and $CD4^+$ cells. This finding opens new perspective to use Rho-GTPase signature to identify patients suitable for treatment with JAK-inhibitors and in predicting the treatment response.
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AB0024 PLURIPOTENCY MARKER PBX1 PREDICTS TREATMENT EFFECT IN RHEUMATOID ARTHRITIS

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Background: Accelerated immunosenescence with contraction of T cell repertoire, demise of thymic function and expansion of $CD28^{null}$ T cells with poor T cell reconstitution is the hallmark of rheumatoid arthritis (RA)[1].
Objectives: In this study we assessed if PBX1 transcription factor that maintains the pluripotency of hematopoietic stem cells could be used to predict treatment response in RA patients.
Methods: $CD4^+$ T cells of 87 RA female patients (age, median 61y (23-76); disease duration, median 9y (0-45)) were isolated from the perpheral blood, activated with aCD3 and subjected to transcriptional analysis by RNAseq (Illumina). External RNAseq of $CD4^+$ T cells of 80 RA patients (f 56, m 24) was used for validation. The genes differentially expressed (DEG, nominal $p<0.05$) between $PBX1^{hi}$ and $PBX1^{lo}$ groups were identified by R-studio using Benjamini-Hochberg correction (Bioconductor, DESeq2 package). DEGs were clustered by covariance to identify PBX1 associated genes and biological processes. Clinical variates and treatment regimens in $PBX1^{hi}$ and $PBX1^{lo}$ groups were compared.
Results: The patients of $PBX1^{hi}$ and $PBX1^{lo}$ groups were of similar age and disease duration but differed in anti-rheumatic treatment. $PBX1^{hi}$ group was often treated with conventional DMARDs and monotherapy, while $PBX1^{lo}$ group was mostly treated with biologics and/or JAK-inhibitors in combination with cDMARDs (χ^2, $p=0.0099$). This treatment led to sufficient disease control in both PBX1 groups (median DAS28; 2.6 and 2.7, respectively). In the external RA cohort of the patients resistant to conventional DMARDs, $PBX1^{hi}$ patients had significantly fewer frequency of non-responders to anti-TNF treatment compared to $PBX1^{lo}$ (χ^2, $p=0.026$).
Pathway analysis of the DEGs identified strong enrichment for regulation of transcription ($cor.p=10^{-23}$), RNA metabolic processes ($cor.p=10^{-18}$) and differentiation ($cor.p=10^{-7}$) in $PBX1^{hi}$ $CD4^+$ cells, which corresponds to the known biological properties of $PBX1^2$. $PBX1^{hi}CD4^+$ cells in both datasets had imprinted features of pluripotency[3] and expressed higher levels of KIT and CAT, low proliferation

markers Ki67 and BIRC5, and had virtually no cytokine production. In the main cohort, PBX1^{hi}CD4^{+} cells were recognized by naïve T cell marks CD62L (SELL) and CD45 (PTPRC), and also PECAM1, CR2, and CD28, indicating recent thymic egress. In the validation cohort, PBX1^{hi}CD4^{+} cells were enriched with stem cell markers CD34, MEG3, and DNMT3B. Lineage specific TFs (TBET, GATA3, FOXP3, RORC) and cytokines (IFNG, TNF, IL10, IL17F, etc.) were accumulated in PBX1^{lo}CD4^{+} cells indicating terminally differentiated effector CD4^{+} T cells.

Conclusion: This study shows that enrichment with PBX1^{hi} CD4+ cells is associated with naïve pluripotent phenotype of CD4 lymphocytes. Patients with high PBX1 expression are less heavily treated and respond better to treatment. This suggests boosting of PBX1-expression to be a way of treating RA.

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AB0025 PERIPHERAL BLOOD CD4+ AND CD8+ RECENT THYMIC EMIGRANTS IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS DISPLAY AN ACTIVATED PHENOTYPE

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Background: T cells play a major pathogenic role in Rheumatoid Arthritis (RA). Their pro-inflammatory potential, interaction with B-cells (CD4) and cytotoxic capacities (CD8) have a high impact on disease progression, at the site of inflammation as well as in the periphery. T cells in RA have an altered glucose metabolism, which further amplifies their pro-inflammatory and auto-immune profile.[1,2] This phenotype is even displayed by RA naïve CD8 T cells, and several studies propose that defects in RA T cell development occur already during thymic development. Thus, acquisition of an activated (auto)inflammatory phenotype may occur at very early stages of RA T cell development.

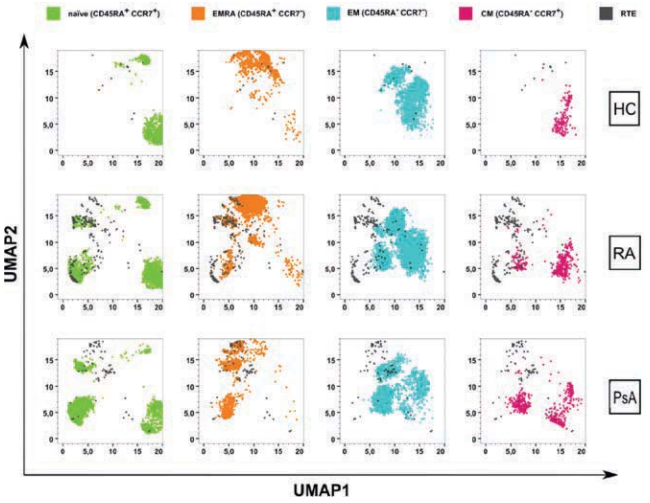

Figure 1. UMAP analysis of total RTEs. Previously downsampled CD4^{+} and CD8^{+} T cells were clustered by UMAP (FlowJo™) and total RTEs were mapped on the naïve, effector (EMRA), effector memory (EM) and central memory (CM) compartments of the respective groups.

Objectives: We studied Recent Thymic Emigrants (RTEs) in peripheral blood to establish, whether the activated pro-inflammatory signature present in naïve RA T cells can already be found at such an early stage of T cell development.

Methods: We analysed previously described RTE surface markers [3] on CD8 and CD4 T-cells of human adult thymus samples, as well as on cord-blood samples and additionally confirmed the identified cells as RTEs based on their TREC (T cell Receptor Excision Circle) content. Next, we phenotypically characterised RTEs in the peripheral blood of 10 RA patients, 6 PsA (Psoriatic Arthritis) patients and 5 healthy donors (HC) by 24-parameter Flow Cytometry. Cell clustering was analysed using the UMAP algorithms.

Ethic approval NR: S-969/2020

Results: As expected, RTEs only made up a small proportion of the total CD4 and CD8 T cells, on average 1.3 % and 2.5 % respectively. Contrary to previous reports [4], we could see no significant differences between patients and controls. A first global analysis of CD45RA and CCR7 on CD4 and CD8 via UMAP revealed that RA and PsA RTEs cluster together with naïve and effector cells (Figure 1).

We further analysed several functional surface markers for homing (CD11a, CD49a), effector functions (CD69, CD27, CD107a), regulatory functions (CD25) and exhaustion (CD95, PD-1, CTLA-4.

In CD4 RTEs we observed more cells expressing homing, effector and exhaustion markers in RA and PsA when compared to HC. CD11a and CD69 were expressed on 3 times more CD4 RTEs in RA and PsA and CD95 and PD1 expressing CD4 RTEs were 2 times more frequent in the arthritic groups compared to HC, while PD1 expressing CD4 RTEs in patients were 10 times more frequent. The CD25^{+} CD4 RTE population was 3 times larger in RA and PsA than in HC.

In CD8 RTEs the frequency of CD11a expression was similar, whereas the CD49a^{+} population was 3 times larger in RA compared to PsA and HC. CD69 expressing CD8 RTEs were increased in RA and PsA compared to HC, while the degranulation marker CD107a was expressed on similar amounts of HC and PsA RTEs and 2 fold increased compared to RA. CTLA-4 and PD1 expressing CD8 RTEs were 5 - and 2 times more frequent in the RA group than in HC.

Conclusion: Overall, the RTE populations of RA and PsA patients displayed a more active and exhausted phenotype than the control group. However, this seemed to be more prominent for CD4 RTEs than CD8 RTEs. According their CD45RA/CCR7 profiles, both CD4 and CD8 RTEs fall into the less active naïve compartment, corresponding to the early developmental stage, but also into the effector compartment. The RTEs from RA and PsA patients also express markers that are usually associated with pro-inflammatory activity and even exhaustion. This implies that indeed even RTEs are already biased towards a more active phenotype in RA and PsA, compared to RTEs from healthy individuals, suggesting alterations in T cell development in the RA and PsA thymus.

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AB0026 CELL TYPE-SPECIFIC DYSREGULATION FOUND TO DIFFERENTIATE PATIENT SUBSETS OF SJÖGREN'S DISEASE

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Background: Sjögren's disease (SjD) is a chronic, heterogenous autoimmune disorder characterized by inflammatory destruction of the exocrine glands and Ro autoantibodies. Previous studies, most in whole blood, reported transcriptional and cell type differences between SjD subphenotypes.
Objectives: Evaluate the role of cell type-specific dysregulation in subpopulations of SjD patients having focal lymphocytic sialadenitis and/or anti-Ro/SSA and/or ANA positivity using single-cell RNA-seq (scRNA-seq).
Methods: Peripherical blood mononuclear cells (PBMCs) stored at -120°C from 30 SjD patients and 10 healthy controls (HCs) were selected from our OMRF Sjögren's Research Cohort based on ACR/EULAR 2016 criteria. PBMCs were captured, libraries processed using 10X Genomics Chromium v3.1 and sequenced to a depth of ~45,000 reads/cell. 10X Genomics Cell Ranger (v 6.1.2) cell multiplexing pipeline was used to align reads to the GRCh38 human genome and separate combined data to per-sample output files. Seurat R package was used for quality control (QC), integration, clustering, and cell type assignment. Differential expression (DE) analysis was done using Seurat for genes with 10% or more of the cells showing expression. DE transcripts (defined as p_{adj}<0.05) were evaluated using Ingenuity Pathway Analysis (IPA).
Results: After removing cells with low feature counts, high mitochondrial gene counts, and/or other QC criteria, a total of 331,981 cells were captured. Cells were mapped to 28 clusters using Seurat, then cell types were predicted using marker genes developed from an in-house reference panel of publicly available scRNA-seq datasets. Mapping condensed the 28 observed cell clusters to 19 clusters of specific cell types; 4 clusters remained unidentified. Percentages of each cell type were compared across various subsets of SjD (Ro+; Ro-; Ro-/ANA+; Ro-/ANA-) and HCs. CD14 monocytes were decreased in Ro-/ANA- vs. Ro+ or Ro-/ANA+ cases (p<0.05) and trended downward when compared to HCs (p=0.057). CD8 central memory T cells (TCM) were decreased in Ro+ vs. Ro- or Ro-/ANA- cases (p<0.02) and trended downward when vs. HCs (p=0.076). Conventional dendric cells (DCs) were increased in Ro+ vs. Ro-/ANA- SjD cases (p=0.036) and trended upward in Ro+ vs. Ro- cases (p=0.08) but were not significantly different from HCs. Natural killer (NK) cells were increased in both Ro-/ANA- and Ro- vs. Ro+ (p<0.05).
DE analysis between immune cell subsets revealed potential subphenotype-specific differences in pathophysiology. Interferon signaling was upregulated in CD14 monocytes, naïve B, and CD4 central memory (TCM) cells from the Ro+ subset. Ro+ subset also showed upregulation of genes involved in T cell receptor signaling in CD4 cytotoxic T (CTL), CD4 TCM, and CD4 effector memory T (TEM) cells, but downregulation of this pathway in CD8 TCM cells. Ro+ subset also exhibited increased B cell receptor signaling pathway in naïve and memory B cells. Ro+ subset showed downregulation of autophagy in naïve B, CD4 CTL, CD4 TCM, and CD4 TEM cells. Several cell types in Ro+ and Ro-(ANA+/-) subsets showed decreased DE of genes involved in nitric oxide production and NRF2 oxidative stress pathways. Ro- (ANA+/-) vs. HCs showed increased IL6 and TREM1 signaling pathways in CD14 and CD16 monocytes. While Ro+ subsets showed upregulation of B and T cell pathways (shown previously in lupus), Ro- (ANA+/-) showed dysregulation of osteoarthritis and neuroinflammatory pathways. Interestingly, among the DE long intergenic non-coding (linc)RNAs found herein, we observed that *LINC01871*, which we previously reported as DE in all subsets of SjD, was overexpressed in CD4 CTL and NK cells in both Ro+ and Ro- (ANA-) vs. HCs.
Conclusion: This interim analysis shows similarities and differences in the dysregulation of genes and pathways for specific cell subsets from our Ro+ and Ro- (ANA+/-) subsets of SjD, potentially allowing for more tailored diagnostics and interventions for the disease in the future.
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AB0027 XANTHINE OXIDOREDUCTASE: ENZYME PROFILE OF PLASMA AND LYMPHOCYTES IN RHEUMATOID ARTHRITIS

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Background: Disorders of acquired and adaptive immunity play an important role in the rheumatoid arthritis (RA) pathogenesis. Important changes can nevertheless be detected at the metabolic level in the immune cells along with immune disorders. The imbalance between generation and neutralization of the free radicals during oxidative stress may cause damage of both cellular structures and components of extracellular matrix. One of principal free radical generators is xanthine oxidoreductase (XOR), the prooxidant enzyme complex which could be active either in its oxidase or dehydrogenase form. The study of plasma and lymphocytic xanthine oxidase (XO) and xanthine dehydrogenase (XDG) activities is of emerging interest because of their putative role in initiation and chronization of RA.
Objectives: Evaluation the relationship between RA activity and XO and XDG activities using both plasma and lysed lymphocyte samples.
Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles after the local ethical board approval. RA diagnosis was verified using ACR/EULAR criteria (2010). RA activity was measured using the Disease Activity Score of 28 joints (DAS28). Blood lymphocytes were isolated by means of density gradient centrifugation in lymphosep (JCN Biomedicals), 1.077-1.079 g/ml. XO (EC 1.17.3.2) and XDG (EC 1.17.1.4) activities in plasma and lysed lymphocytes were measured using spectrophotometric techniques and expressed as nmol/ml/min [1]. Data are presented as median and quartiles (Me (Q_{25}; Q_{75}). Differences were considered significant when p<0.05.
Results: 77 RA patients (57 women and 20 men) were enrolled in the study. Mean age of patients was 45 (37; 49) years, mean RA duration was 8 (6; 10) years. 16 (21%) RA patients had low disease activity, 49 (63%) patients moderate, and 12 (16%) patients had high one. 30 (19 women and 16 men) healthy persons comprised the control group. Reference ranges for plasma XO and XDG activities were 2.60–3.96 nmol/min/ml and 4.49–5.93 nmol/min/ml, respectively. Reference ranges for XO and XDG activities in lysed lymphocytes were 14.11-31.33 nmol/min/ml and 18.62-39.64 nmol/min/ml, respectively. Plasma enzymatic pattern in RA patients was characterized by increase in XO activity (p<0.001) and a somewhat decrease in XDG activity (p=0.059). Lymphocytic enzymatic pattern in RA patients was characterized by decreased activity of both enzymes (p<0.001 for both cases). Plasma XO activity was increased and lymphocytic XO activity was decreased in all the grades of RA activity. XO activity reached its highest changes at maximum disease activity. Plasma XDG activity was increased in low disease activity (p<0.001), while patients with moderate or high disease activities were characterized by decreased activity of this enzyme (p=0.008). Lymphocytic XDG activity was decreased in all the grades of disease activity (p<0.001). XDG activity reached its highest changes at maximum disease activity. Activities of XO and XDG in lymphocytes negatively correlated with RA activity. Activities of XO in plasma positively correlated with RA activity, while XDG activity negatively correlated with RA activity.
Conclusion: Plasmatic and lymphocytic enzymatic patterns in RA patients were characterized by multidirectional changes of XO and XDG activities. Multiple correlations were found between RA activity and enzyme activities in both studied compartments. These changes in oxidant enzyme activities may point at involvement of free radical oxidation in the RA pathogenesis. Free radical generation triggers metabolic cascades that lead to cell damage, premature death, promote endothelial dysfunction, extracellular neutrophil trap formation, support chronic inflammation and joint destruction, and other organs and systems under oxidative stress.
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AB0028 IL-2 DEPRIVED PHENOTYPE OF FOXP3+ REGULATORY T CELLS AND PHENOTYPIC ALTERATIONS CONVENTIONAL CD4+ T CELLS IN PATIENTS WITH INFLAMMATORY MYOPATHIES AND PRIMARY SJOGREN´S SYNDROME

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Background: A defect in regulatory T cell (Treg) homeostasis due to an acquired deficiency of interleukin-2 (IL-2) plays an important role in the pathogenesis of systemic lupus erythematosus (SLE).[1,2] However, it is still unclear whether a defect in the Treg-IL-2 axis is also involved in other connective tissue disease such as inflammatory myopathies or primary Sjogren´s syndrome (pSS).
Objectives: The aim of our study was to investigate whether Treg from patients with poly- and dermatomyositis (PM/DM) and pSS display typical features of IL-2

deficiency in parallel to phenotypic alterations of conventional CD4+ T cell (Tcon) subsets compared to healthy controls (HC).
Methods: PBMC were isolated from patients with PM/DM (n=22) and pSS (n=17) and from age- and sex-matched HC (n=19) using gradient density centrifugation. Treg and Tcon subsets were analyzed by using multicolor flow cytometry. Mann-Whitney test was used for statistical analyses.
Results: Frequencies of FoxP3+CD127lo Treg among CD3+CD4+T cells were higher in pSS compared to PM/DM patients ($p<0.001$) and to HC ($p<0.05$). However, in both, PM/DM and pSS patients, frequencies of CD25+ cells among FoxP3+CD127lo Treg were significantly lower compared to HC (PM/DM: $p<0.05$, pSS: $p<0.0001$), while the frequencies of Helios+ cells among the CD25- Treg subset were substantially higher in pSS patients compared to DM/PM and HC (both $p<0.001$). Conversely, we found lower frequencies of CXCR5+ follicular Treg only in PM/DM patients ($p<0.05$). In parallel, there were higher frequencies of CD45RO+CCR7- effector/memory cells ($p<0.01$) and of Ki67+ proliferating cells ($p<0.05$) among CD3+CD4+FoxP3- Tcon in pSS patients compared to HC, which was not observed in PM/DM patients.
Conclusion: The loss of the CD25+ Treg subset in PM/DM and pSS patients is similar to previous findings in SLE patients[1] and represents a hallmark of IL-2 deficiency. This suggests that shortage of IL-2 is pathophysiologically relevant also in PM/DM and pSS providing a rationale for low-dose IL-2 therapy in these diseases. In addition, activation and expansion of effector/memory Tcon appears to be more pronounced in pSS compared to PM/DM. The different distribution of Treg and of Tcon subsets between pSS and PM/DM patients might reflect differences in the availability of IL-2 and in the regulation of Tcon responses in these diseases.
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AB0029 CIRCULATING CD39+ TREG CELLS IN EARLY RHEUMATOID ARTHRITIS FACILITATE THE ANTIINFLAMMATORY ACTION OF METHOTREXATE AND SERVE AS EARLY BIOMARKERS OF CLINICAL RESPONSE

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Background: FoxP3+ regulatory CD4+ T cells (Tregs) are key to the homeostasis of the immune system [1-3]. Stressed cells at inflammatory foci release adenine nucleotides to the extracellular space[4] that can act as enhancers of inflammation[4] but are rapidly hydrolysed by the sequential action of ectonucleotidases CD39 and CD73 rendering the antiinflammatory agent adenosine[4]. CD39, the rate-limiting enzyme in this cascade, is highly expressed by a subset of human FoxP3+Tregs (Treg39+)[1-3]. Methotrexate (MTX), the first line of treatment in Rheumatoid Arthritis (RA)[4], inhibits AICAR transformylase which results in an enhanced release of extracellular adenine nucleotides[4] to be metabolized by Treg39+ cells; hence MTX may cooperate with Treg39+ cells in the control of inflammation.
Objectives: To examine the relation of CD39 expression on Treg cells of early RA (ERA) patients with the ex vivo and in vivo effect of MTX.
Methods: Peripheral blood was obtained from 63 DMARD- and steroid- naïve ERA patients with a disease duration < 24 weeks and 63 age and gender-matched healthy controls (HC). 33 ERA patients donated blood again 12 months after initiating MTX (ERA-R). The frequency of Treg and Treg cell subsets was assessed by flow cytometry. CD4+CD25+CD127- (total T reg), CD4+CD27+CD127-CD39+ Treg (Treg39+) and CD4+CD25-CD39- responder T (Tresp39-) cells were isolated by sorting. The suppressor potency of Tregs was determined in cocultures of isolated Tregs with Tresp. Proliferation was determined by CFSE dilution; cytokine secretion was measured by ELISA of culture supernatants. Disease activity was assessed using the DAS28-ESR score. Low disease activity (LDA) was defined as a DAS28 ≤ 3.2.
Results: The proportion of Tregs that expressed CD39 (Treg39+) was significantly increased in ERA. Total ERA Tregs were more potent suppressors than HC Tregs, and the difference was reduced by adenosine A2AR antagonists. In vitro, MTX further heightened the total Treg cell potency, with greater amplification in ERA vs HC and this was also reversed by A2AR antagonists. The potency of isolated Treg39+ and its enhancement by MTX were comparable for ERA and HC; the potency of isolated Treg39- was inferior to that of Treg39+ cells in both groups of subjects and was not modified by A2AR antagonists; this further suggests that the differences observed in assays using total Tregs are due to the increased ERA Treg39+ frequency. Patients who achieved LDA had significantly higher basal frequencies of Treg39+ cells and multiple logistic regression (OR 1.93, 95% CI 1.33-4.51) showed that this was independent of basal disease activity, RF or ACPA titres. The Receiver Operating Characteristic (ROC) analysis area under the curve (AUC) was 0.97 (0.94-0.99) for Treg39+ cells. The relative risk (RR) of achieving LDA for patients with a cTreg39+ frequency above the p75 value observed in HC was 13.4 (2.9-75.6) (Fisher's exact test). The proportion of Treg39+ significantly decreased in all patients whether they had or not achieved LDA, and the frequency and function of ERA-R Treg cells were not different from HC. In fact, 12 months after initiating treatment with MTX, the circulating Treg39+ cell frequency was no longer elevated in ERA; however, its association with the clinical response remained: the cTreg39+ cell frequency observed at 12 months was still significantly higher in those patients who had achieved LDA. This suggests that Treg cell expression of CD39 is upregulated during the initial stages of ERA as a negative feedback mechanism of inflammation.
Conclusion: MTX cooperates with Treg39+ cells to control inflammation and the pretreatment Treg39+ frequency in ERA is associated with the clinical response to MTX at 12 months.
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AB0030 THE BIOLOGICAL FUNCTION AND MECHANISM EXPLORATION OF TACI IN SJOGREN'S SYNDROME

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Background: primary Sjogren's syndrome (pSS) is a chronic autoimmune disease that affects the lacrimal, salivary and other exocrine glands. More and more studies have shown that B cells play a central role in the pathogenesis of SS.
Objectives: We intended to explore the expression of the transmembrane activator, calcium modulator and cyclophilin ligand interactor (TACI) on the B cells, its role in pSS, and possible signal transduction pathways.
Methods: We included 34 naive pSS patients who visited the rheumatology department of Peking University First Hospital, and 37 gender- and age-distribution matched healthy controls (HCs). (1) To compare the B cell subsets, expression of TACI and relevant receptors in pSS patients, peripheral blood mononuclear cells were separated to analyze the ratio of B subsets, TACI, and BAFF-R by flow cytometry; ELISA was applied to detect the serum BAFF and soluble TACI (sTACI) concentration. (2) As for functional research of TACI, CD19+ B cells separated by magnetic sorting were treated under in vitro culture circumstances with raw TACI, TACI knocked down by siRNA, and sTACI analog (telitacicept) intervention with varing doses. The apoptosis, proliferation, differentiation and regulatory capacity on T cells were analyzed by flow cytometry, inflammatory cytokines and immunoglobulin levels in the culture supernatants were detected by CBA. (3) As for TACI-associated signaling pathway exploration, based on our previous miRNA data and relevant report of high quality, miRNA associated with

TACI with significantly biased expression was confirmed by RT-qPCR. Screening the target gene of the candidate miRNA, and miRNA overexpression and inhibition experiments were conducted to validate the targeted relationship in B cells. And TACI-associated signaling pathway was explored via overexpressing and inhibiting the target gene.

Results: (1) Compared to HC, peripheral blood B subsets of pSS patients exhibited a significant bias, manifesting as increased proportion of CD19+CD24hiCD38hi Breg and decreased ratio of CD19+CD24+CD38- memory B cells. The expression of TACI in all B subsets was down-regulated, while that of BAFF-R was up-regulated. Both the serum concentration of BAFF and sTACI in pSS patients increased significantly. (2) As for functional research of TACI, in the setting of raw TACI, B cells in the pSS group showed higher apoptosis rate than HC under culture in vitro, where the ligand of TACI (APRIL or BAFF) addition turned the rate comparable; more active proliferation, and impaired capacity of inducing Treg cells to secrete IL-10. When TACI was knocked down by 50%, B cells performed less late apoptosis, significantly increased proliferation, impaired differentiation, significant dysfunction of Breg itself and impaired induction of Treg cells to secrete IL-10. While telitacicept intervention increased early apoptosis rate of B cells, significantly inhibited proliferation in 500ng/mL group and impaired ability of Breg and Treg cells to secrete IL-10. Besides, increased TACI on B cells treated with telitacicept, decreased IgG and increased IgA in the culture supernatants were observed. (3) As for TACI-associated signaling pathway exploration, hsa-miR-30b-5p showed satisfactory correlation between both transmembrane and sTACI. Besides, the expression of hsa-miR-30b-5p was significantly down-regulated, and inhibition its expression in vitro could lead to differentiation retard, impaired secretion of IL-10 by Breg cells. SMAD1 was screened based on database and validated as its target gene by overexpressing and inhibiting hsa-miR-30b-5p in B cell. After targeted up- or down-regulating the transcription of SMAD1 further, the transcription of ID2 downstream the TGF-β/Hippo signaling pathway changed accordingly.

Conclusion: The expression of TACI on peripheral blood B cells was deficient in pSS patients. TACI deficiency was closely associated with the downregulation of hsa-miR-30b-5p, activating TGF-β/Hippo pathway mediated by its target gene SMAD1 and taking part in the pathogenesis of pSS.

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AB0031 DEEP IMMUNE PHENOTYPING OF SLE AND RA BY MACHINE LEARNING

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Background: Breakdown of self-tolerance is an important common mechanism in autoimmunity. Despite considerable clinical heterogeneity, many autoimmune diseases exhibit common immunological mechanisms leading to a breakdown of self-tolerance. Identification of unique and similar patterns across different autoimmune disease may help to understand their pathophysiology behind.

Objectives: Establishing workflows for the multi-parameter deep immune phenotyping of T- and B-cells by unsupervised machine learning (ML) methods for feature extraction, cluster analysis and anomaly detection.

Methods: We use machine learning to identify common patterns and dissimilarities between type 1 diabetes (T1D, n=69), rheumatoid arthritis (RA, n=63), systemic lupus erythematosus (SLE, n=38) and healthy controls (n=69) samples based on multi-plex immune phenotyping. PBMCs were isolated from patients with T1D, RA, SLE, and controls. A flow cytometry-based approach was applied, and a traditional analysis was compared to a ML method implemented in R [1] and based on self-organizing maps (Figure 1). Our pipeline includes unsupervised pre-gating, normalization, FlowSOM clustering [2], and a statistical model

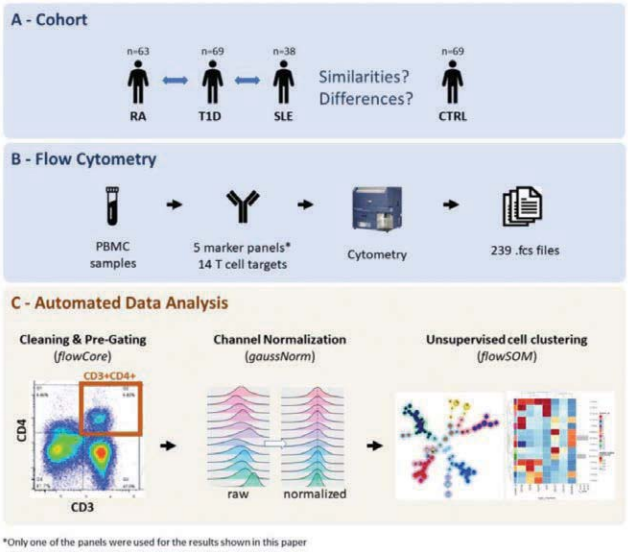

Figure 1.

(GLMM), to check for significant differential abundances of cell populations among the autoimmune conditions.

Results: After applying our automated workflow to one T cell panel we could identify 14 cell clusters present in all the samples. The GLMM test revealed a cluster with a significant difference (p=0.035) and a trending one (p=0.059) on the abundance across the different diseases. In particular, $CD4^{pos}$ T cells expressing high IL-7 receptor (CD127) levels and median amounts of CD15s but low CD25, CD161 and FoxP3 are increased in T1D whereas $CD4^{+}CD25^{++}CD15s^{+}FoxP3^{low-}CD161^{low}CD45RA^{-}$ cells are increased in SLE.

Conclusion: This unbiased, unsupervised ML workflow was able to identify canonical and novel clusters of T cells that are similar in RA, SLE and T1D. Additionally, a novel memory T cell population expressing CD15s was shown. This unsupervised analysis approach for large datasets enables the discovery of new immune cell populations complementing traditional workflows.

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AB0032 CHARACTERIZATION OF PERIPHERAL BLOOD B-CELL SUBSET IN UNTREATED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS

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Background: B-cells play a critical role in the regulation of systemic autoimmune diseases pathogenesis, that extends beyond antibodies production.
Objectives: To examine B-cell subsets in peripheral blood of patients (pts) with untreated systemic lupus erythematosus (SLE) and systemic sclerosis (SSc), to analyze of their associations with disease-specific autoantibodies.
Methods: Thirty six untreated SLE pts (31F/5M) and 32 untreated SSc pts (25F/7M) were enrolled. SLE pts had median age of 37(range)(32-41)years, disease duration of 3.5(1-11)years, SLEDAI 2K of 7(4-8), BILAG of 14,5(10,2-23). SSc pts had median age of 42(38-50)years, disease duration of 3.5(1-10) years, Disease Activity EScSG of 2.5 (1-3.2). The control group consisted of 29 volunteers (23F/6M, median age 38(35-48)years. CD19+B cells, memory B cells (CD19+CD27+), switched memory B cells (CD19+CD27+IgD-), non-switched memory B cells (CD19+CD27+IgD+), naive (CD19+CD27-IgD+), double-negative (CD19+CD27-IgD-), transitional (CD19+CD38++CD10+IgD+CD27-) B cells, and plasmablasts (CD19+CD38+++CD27+IgD-CD20-) were analyzed using multicolor flow cytometry.
Results: Differences in the median percentage and of absolute B-cells subset levels in untreated pts with RA and SLE were not found. The absolute counts of memory B cells (CD19+CD27+), switched memory B cells (CD19+CD27+IgD-), transitional B cells (CD19+CD38++CD10+IgD+CD27-), and plasmablasts (CD19+CD38+++CD27+IgD-CD20-) were higher in SLE and SSc pts compared to healthy donors, p<0,01 for all cases. The absolute counts of double-negative B cells (CD19+CD27-IgD-) were lower in SLE pts than in donors, p=0,03 (Table 1). At significant correlation was found in SLE pts between anti-dsDNA levels and absolute counts of the following B-cell subtypes: CD19+B cells (r=0,72), memory B cells (CD19+CD27+) (r=0,76), switched memory B cells (CD19+CD27+IgD-) (r=0,75) and naive B cells (CD19+CD27-IgD+) (r=0,73); the a-Sm levels and absolute counts of the switched memory B cells (CD19+CD27+IgD-) (r=0,51); the antibodies to cardiolipin (aCL) IgG levels and absolute counts of CD19+B cells (r=0,64), and with naive B cells (CD19+CD27-IgD+) (r=0,59), p<0,01 for all cases. There was a correlation between the anti-topoisomerase-1 antibodies (a-Topo-1) and the absolute counts of double-negative B cells (CD19+CD27-IgD-) (R=0,62, p=0,01) in SSc pts.

Table 1. Levels of the blood B-cell subsets in SLE pts, SSc pts and in control.

Parameters, n (x10^9/l)	SLE	SSc	Control group
CD19+B cells	0,15 (0,12-0,25)	0,14 (0,12-0,20)	0,1 (0,08-0,2)
memory B cells (CD19+CD27+)	0,036 (0,031-0,006) *	0,042 (0,027-0,053) *	0,003 (0,001-0,007) *
switched memory B cells (CD19+ CD27+IgD-)	0,02 (0,016-0,046) *	0,026 (0,017-0,034) *	0,01 (0,005-0,02) *
non-switched memory B cells (CD19+CD27+IgD+)	0,012 (0,007-0,027)	0,016 (0,01-0,027)	0,02 (0,01-0,04)
naive B cells (CD19+CD27-IgD+)	0,09 (0,06-0,2)	0,09 (0,06-0,16)	0,1 (0,06-0,1)
double-negative B cells (CD19+CD27-IgD-)	0,011 (0,006-0,014) *	0,02 (0,01-0,03)	0,02 (0,01-0,02) *
transitional B cells (CD19+CD38++CD10+IgD+CD27-)	0,011 (0,004-0,026) *	0,011 (0,005-0,012) *	0,0001 (0-0,0003) *
plasmablasts (CD19+CD38+++CD27+IgD-CD20-)	0,001 (0,001-0,002) *	0,001 (0-0,002) *	0,0001 (0,00006-0,0003) *

Note: * - Differences in B-cell subset of the control group with SLE and SSc groups.

Conclusion: Immunophenotyping showed similar levels of B-cell subset in untreated SLE and SSc pts, an increase in the absolute counts of memory B cells (CD19+CD27+), switched memory B cells (CD19+CD27+IgD-), transitional B cells (CD19+CD38++CD10+IgD+CD27-), and plasmablasts (CD19+CD38+++CD27+IgD-CD20-) in untreated SLE and SSc pts compared with healthy subjects. Positive correlation between the counts of B-cell subsets and values of disease-specific autoantibodies (anti-dsDNA, a-Sm, aCLIgG, a-Topo-1) suggests that B-lymphocytes may be involved in SLE and SSc pathogenesis.
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AB0033

T- AND B-CELL SUBSETS AS ADDITIONAL DIAGNOSTIC TOOL FOR PRIMARY SJOGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) and primary Sjogren's syndrome (pSS) are chronic autoimmune diseases with complex pathogenesis. T-lymphosytes are known to be prime effectors of autoimmune diseases, while B-lymphosytes play a key role as sources of antibodies and antigen presenting cells. Considering the implications of T- and B-cells in the pathophysiology of SLE ans pSS, the assessment of their distribution in the blood could be helpful in the complex process of determining a precise diagnosis.
Objectives: The study aimed to compare composition of peripheral blood T- and B-cell subsets and investigate their diagnostic utility in patients with SLE and pSS.
Methods: The study was performed with 37 patients suffering from SLE, 57 patients with pSS, and 49 apparently healthy volunteers (HVs). The diagnosis of SLE was performed according to the 2019 EULAR – ACR classification criteria, the diagnosis of pSS- according to the 2016 EULAR – ACR criteria. 11 patients in pSS group met the criteria for both pSS and SLE. The relative distribution and percentage of T- and B-cell subsets were evaluated by flow cytometry. T helper (Th) and cytotoxic T-cell subsets (Tcyt) were identified by using CD3, CD4, and CD8 antibodies. Regulatory T cells (Tregs) were characterized by the expression of CD3, CD4, and high IL-2R alpha chain (CD25high) levels. All peripheral blood B-cells were identified by using CD19 antibody, detection of subpopulations of B cells based on expression of IgD, CD38, CD27. The absolute and relative values of B-lymphocyte subpopulations were evaluated using three main classifications: based on IgD / CD38 expression (classification Bm1-Bm5), co-expression of IgD / CD27 and CD38 / CD27. The statistical analysis of data was performed with STATISTICA Version 12.0 Inc. Method of discriminant analysis was performed to evaluate diagnostic utility of relative values of T- and B-cell subsets.
Results: In the discriminant model the top significance was documented while assessing the percentage of naive B-cells (Bm1, IgDdimCD38low), germinal center B-cells (Bm 3+Bm4, IgDlowCD38hi), naive B-cells (IgDdimCD27low), unswitched memory B-cells (IgDdimCD27dim), naive mature B-cells (CD27dimCD38low), transient B-cells (CD27lowCD38hi), all T-cells (CD3hi), Tregs (CD3hiCD4hiCD25hi), Tcyt (CD3hiCD8hi) and Th (CD3hiCD4hi), model percent correct was 78%, p <0,05. The discriminant function was either f1 for distinguishing HVs versus ill patients SLE and pSS (all participants are accounted) or f2 for SLE versus pSS (only participants with disease are accounted). During ROC analysis, performed for the differential diagnosis of healthy and sick patients, this discriminant model had a sensitivity of 86,5% and a specificity of 72,8%, the area under the curve (AUC) 0.94, p <0.001. Among the group of ill patients, the differential diagnosis between SLE and pSS had a sensitivity of 69,6% and specificity of 64,8%, AUC 0.87, p <0.001. Graphic representation of the discriminant analysis is performed on Figure 1. The group of patients, meeting the criteria for both pSS and SLE, is between the main groups.

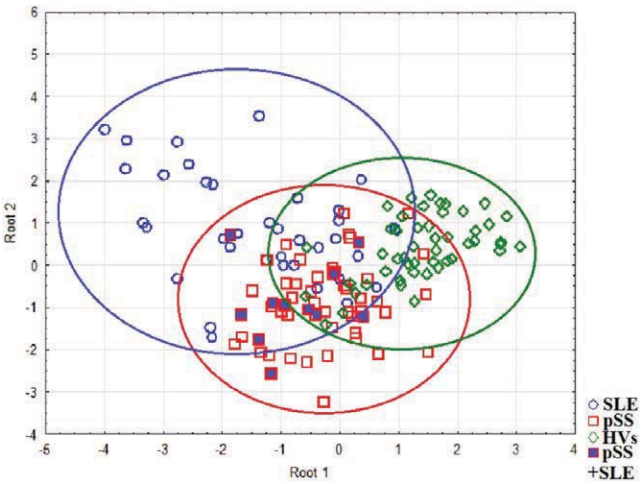

Figure 1. Graphic distribution of SLE, pSS and pSS+SLE patients, as well as HVs analyzed by discriminant analysis.

Conclusion: T- and B-cell peripheral blood subsets might provide an additional diagnostic tool for distinction SLE, pSS and HVs. Differential diagnosis between pSS and SLE is difficult, because this diseases may coexist.

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AB0034 INVESTIGATING THE ROLE OF ACCELERATED IMMUNESENESCENCE IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

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Background: Advancing age is recognised as a major risk factor for autoimmune inflammatory conditions, such as Rheumatoid Arthritis (RA). Despite strong associations with older age we understand little of the role ageing processes play in disease pathogenesis in RA. The immune system undergoes a dramatic remodelling with age, termed immunesenescence, which contributes towards increased risk of autoimmunity[1]. Previous research in patients with established RA has shown certain features of immunesenescence, such as thymic atrophy and telomere shortening in T cells, at a younger age[2,3].

Objectives: In this study we aimed to determine if immunesenescence is seen in the very earliest stages of RA and therefore might be a contributor to RA pathogenesis rather than a result of the disease.

Methods: We have assessed aspects of the aged immune phenotype by immunostaining and flow cytometry[4] in adults with arthralgia (n=25), undifferentiated arthritis (UA; n=41), confirmed RA of less than 3 months (n=25) and more than 3 months duration (n=78) and compared these to age and sex matched healthy controls (n=38). Nanostring methodology was used to determine gene expression changes associated with the development of RA.

Results: We observed increased features of T and B cell immunesenescence in DMARD-naïve recently diagnosed RA patients driven by reduced naïve T cells ($p<0.01$) and B cells ($p<0.01$), increased senescent (CD28-ve, CD57+ve, KLRG1+ve) T cells ($p<0.01$), an increased Th17/Treg ratio ($p<0.01$) and increased frequency of age-associated B cells ($p<0.01$). With the exception of naïve T cell frequency, which was reduced in UA patients ($p<0.05$), these changes were not seen in the very early stages of RA, namely patients with arthralgia and UA. These data suggest that immunesenescence only occurs once disease is established. Furthermore, using nanostring we have identified several biological ageing processes (DNA damage, autophagy) associated with this state of immunesenescence in RA.

Conclusion: Accelerated immune ageing is an early feature of RA and biological ageing processes represent novel targets to modulate disease progression.

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AB0035 FREQUENCY OF LYMPH NODE STROMAL CELLS HLA-DR+ IS REDUCED IN INGUINAL LYMPH NODES FROM HUMAN DONORS WITH RHEUMATOID ARTHRITIS COMPARED TO CONTROLS

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder where the immune system gradually damages a wide variety of body systems, including the skin, eyes, lungs, heart, and blood vessels[1]. Animal studies have shown that lymph node stromal cells (LNSCs) are key players in peripheral tolerance through their capacity to present self-antigen to T cells thereby controlling auto reactivity and regulating autoimmunity and humoral response[4,5]. Although self-antigen presentation by human LNSCs needs to be formally proven in human, this study speculates that malfunctioning LNSCs might be associated with loss of tolerance in autoimmune diseases like RA.

Objectives: The objective of this study is to assesses and compare the frequency of main LNSC subsets in human lymph node needle biopsies of healthy controls, autoantibody positive individuals at risk of developing RA (RA-risk) and RA patients. We especially focussed on markers for antigen presentation expressed by LNSCs.

Methods: RA at risk, RA and healthy (n=1) participants underwent an ultrasound-guided inguinal LN needle core biopsy as previously described[6]. We included RA-risk participants (n = 6) with elevated IgM-RF and/or ACPA levels, but without any evidence of arthritis upon examination; RA patients (n =13) with established disease based on fulfilment of the American College of Rheumatology and European League Against Rheumatism (ACR/EULAR) 2010 criteria as assessed by the rheumatologist. For comparison we included healthy participant (n = 17) The healthy control was without any joint complaints and without elevated IgM-RF and/or ACPA level and without active viral infection or any history of autoimmunity or malignancy. To increase the number of healthy participants in the control group, we included lymph node biopsies from individuals receiving a kidney transplant (n= 16). After collection, tissue samples were enzymatically digested to obtain a single cell suspension, followed by flowcytometry analysis with the following cell surface markers CD40, CD80, CD86, PD-L1, HLA-DR, CD45, PDPN, CD31, CD235a, Viability dye.

Results: Antigen presentation related co-stimulatory molecules (CD40, CD80, CD86, PD-L1) and HLA-DR were detected at low levels. Blood endothelial cells having the highest expression of HLA-DR followed by LECs, FRCs, DNs. WE observed a reduced frequency of HLA-DR+ lymph node stromal cell (CD45-, CD235a-) in RA and at RA at risk compared to control. After we found that FRCs, DNs, and BECs were reduced in RA and RA at risk compared to healthy control population.

Conclusion: Our findings show that the frequency of HLA-DR positive LNSCs is lower in RA-risk individuals and RA patients compared to controls. As HLA-DR is crucial to present self-antigens and promote self-tolerance, it will be of interest to investigate whether the antigen presenting capacity of LNSCs is diminished already before onset of disease and how we could restore this.

Disclosure of Interests: None declared

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Innate immunity in rheumatic diseases

AB0036 BUTYRIC ACID SUPPRESSES MIGRATION OF MONOCYTE-DERIVED DENDRITIC CELLS BY INHIBITING MDIA1-MEDICATED ACTIN POLYMERIZATION

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Background: Butyric acid is known to improve chronic inflammation such as inflammatory bowel disease and arthritis [1, 2]. Dendritic cells activate in inflammatory condition, migrate to regional lymph nodes, and activate naive T cells.
Objectives: In this study, we investigated the effect of butyric acid on the migration ability of monocyte-derived dendritic cells (moDC).
Methods: Human CD14+ Monocytes were purified by positive selection from PBMC using CD14 magnetic beads. Cells were cultured in the presence of GM-CSF (50 ng/ml) and IL-4 (20 ng/ml) for 5 days. After culturing for 5 days, cells were matured with LPS (1ug/ml) for 24 hours. Butyric acid was administered at different dose or period. Surface antigen on moDC was analyzed by flow cytometry (BD FACS VERSE). Migration assay was performed on Boyden chamber CytoSelect 24-Well Cell Migration Assay (5um). Actin was stained with Alexa Fluor 488 Phalloidin before and after migration assay. After administration with butyric acid assigned to each period and concentration, moDC were lysed for western blot analysis for evaluating signaling. Chemiluminescent signals were detected and calculated by Amersham Imager.
Results: We demonstrated that butyric acid decreased the CCR7 expression of moDC, which has a key role in DC homing to the lymph nodes and intestinal Peyer's patches. We also showed that butyric acid decreased the migration ability of moDC. Furthermore, moDCs cultured with butyric acid showed a round shape and poor formation of dendrites and pseudopodia. Then we studied the effect of butyric acid on cytoskeleton, which plays an important role in migration and pseudopodia formation of DCs. Polymerized Actin (F-Actin) staining revealed that butyrate suppressed actin polymerization of moDC in a dose dependent manner. CDC42 works important role of lamellipodia and membrane protrusions. RhoA is upstream of mDia1, and mDia1 was reported to accelerate actin nucleation and elongation. We revealed that butyrate decreased the protein expression of mDia1, RhoA, and CDC42, while beta actin was not downregulated, by Western blot analysis. Our results suggested that butyric acid suppresses migration of moDCs by inhibiting mDia1-medicated actin polymerization.
Conclusion: Butyric acid suppresses migration of moDCs by inhibiting mDia1-medicated actin polymerization.
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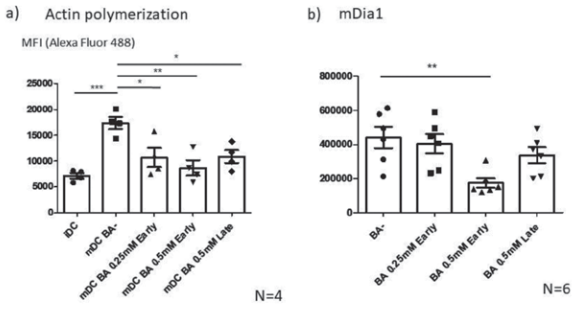

Fig. 1.
a) Butyric acid inhibited actin polymerization of moDC after migraton for FBS. Actin was stained with Alexa Fluor® 488 Phalloidin. MFI was analyzed by FACS.

b) Butyric acid downregurated expression of mDia1. Chemiluminescent signals were detected and calculated by AmershamTM Imager.

All data are presented as mean ± sem
$P < 0.05$; $^{**}P < 0.01$, $^{***}P < 0.001$ Based on Turky

Disclosure of Interests: None declared
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AB0037 APE1 REGULATES THE MIGRATION OF FIBROBLAST-LIKE SYNOVIOCYTES FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The level of apurinic/apyrimidinic endonuclease 1 (APE1) is elevated in synovial fluids from patients with rheumatoid arthritis (RA). However, the role of APE1 in RA pathogenesis remains unclear.
Objectives: To explore whether APE1 affects cell migration through reactive oxygen species (ROS) level, fibroblast-like synoviocytes (FLS) from patients with RA were stimulated with human recombinant APE1.
Methods: Synovial tissues were obtained from RA patients who were undergoing synovectomy or joint replacement. The isolated cells were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum and maintained in a 5% CO_2 incubator at 37 °C. FLS were used for experiments after three to six passages. Cells were stimulated with or without recombinant interleukin 17 (IL-17; 10 ng/ml), tumor necrosis factor alpha (TNF-α; 10 ng/ml), and long-lasting recombinant human APE1 (MR201; 1, 10, 100 ng/ml) for 24 h. ROS levels were analyzed using MitoSOX dye. Cell migratory ability was examined using wound migration assay.
Results: RA FLS treated with APE1 showed slightly decreased level of mitochondrial specific ROS. To induce pro-inflammatory conditions, RA FLS were incubated with IL-17 and TNF-α. These cytokines are highly detected in RA synovium and directly stimulate FLS activation. Stimulation with IL-17 and TNF-α upregulated ROS by 30% compared to control. Cytokines-induced increase of ROS was inhibited by 22% in APE1 treatment. When FLS cultures were approximately 90% confluent, FLS monolayers were wounded with pipette tips and treated with IL-17/TNF-α and APE1 for 24 h. Cell migration was increased after treatment with IL-17/TNF-α. Cytokines-induced cell migration was remarkably attenuated by APE1 treatment.
Conclusion: Recombinant APE1 markedly inhibited mitochondrial specific ROS production and IL-17/TNF-α-induced cell migration in RA FLS.
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Disclosure of Interests: None declared
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AB0038 DUAL TARGETING PEPTIDE RLS-0071 REDUCES AND INHIBITS MYELOPEROXIDASE (MPO) IN HEALTHY HUMAN VOLUNTEER

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Background: RLS-0071-101 was a first in human clinical trial to evaluate safety of the peptide RLS-0071 in healthy volunteers in a single ascending dose and multiple ascending dose format. RLS-0071, previously referred to as Peptide Inhibitor of Complement C1 (PIC1) is a dual-targeting peptide being developed for clinical use to moderate humoral and cellular inflammation via inhibition of complement activation and neutrophil effectors including myeloperoxidase (MPO) and Neutrophil extracellular trap formation (NETosis).[1,2] Humans that are otherwise asymptomatic are considered at risk for cardiovascular complications if they have a plasma MPO level of > 420 pmol.[3] A post hoc analysis of plasma samples from subjects participating in RLS-0071-101 identified an individual with mildly elevated baseline MPO level (142 pmol/L).
Objectives: Evaluate if RLS-0071 dosing would change MPO level or activity in a subject with elevated baseline MPO.
Methods: Frozen plasma samples prepared from blood collected by venipunture into K2EDTA tubes (BD) was utilized to determine MPO quantity and activity levels. MPO quantity in the plasma was analyzed using a human MPO ELISA kit (BMS2038INST, Invitrogen) and MPO activity within the plasma was analyzed using a fluorescence-based myeloperoxidase assay kit (K745-100, BioVision).
Results: Upon screening 54 subjects from RLS-0071-101 we identified one individual with a mildly elevated MPO level at baseline, a 21-year-old white female with BMI of 21.7. The subject received 9 intravenous infusions of RLS-0071 each at a dose of 10 mg/kg. Her vital signs and body temperature remained normal

throughout the study and the only blood laboratory abnormality were a mildly low plasma protein concentration of Day 2 and Day 4 which was noted both among recipients of the peptide and placebo subjects. Analysis of MPO blood concentrations demonstrated a mildly elevated baseline plasma MPO concentration that decreased after multiple doses of RLS-0071 with partial recovery to baseline 24 hours after cessation of dosing. MPO activity analyzed using a fluorescence-based myeloperoxidase assay kit demonstrated an elevated baseline plasma MPO activity level that decreased after multiple doses of RLS-0071 with partial recovery after 24 hours.

Conclusion: These results suggest promise for RLS-0071 to reversibly moderate plasma MPO activity and potentially affect MPO-mediated diseases including acute coronary syndrome (ACS), atheromatous plaque vulnerability and auto immune conditions.4,5,6,7.

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AB0039 MONOCYTE EXTRACELLULAR TRAPS: A NEW POTENTIAL DIAGNOSTIC BIOMARKER IN RHEUMATOID ARTHRITIS?

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Background: Studies demonstrating the important role of neutrophil extracellular traps (NETs) in the pathogenesis of autoimmune diseases, including rheumatoid arthritis (RA), have been published extensively in recent years. The researchers are also discussing the possibility of considering NET as a source of potential diagnostic biomarker in RA. As compared with NETs, the monocyte extracellular traps (METs) formation by mononuclear phagocytes, although they have also been implicated in the development of autoimmune reactions, has been studied insufficiently. No studies have been reported on the MET formation in active RA patients.

Objectives: Assesssment of METs generation by peripheral blood monocytes from RA patients in association with the disease exacerbation.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles after the local ethical board approval. Circulating monocytes were isolated with one-step density gradient centrifugation using double layers of the in-lab-made ficoll-amidotrizoate gradient. Composition of isolated cellular fractions, their viability, and non-specific activation were evaluated by light microscopy using common Romanowsky-Giemsa staining, trypan blue exclusion test as well as NBT test. METs were induced by LPS. Monocyte fractions contained low extents of activated and dead cells. Spontaneous and induced formation of extracellular traps was assessed using fluorescence microscopy [1]. Results were presented as values (95%CI).

Results: 30 healthy volunteers (9 males and 21 females, mean age 37.2 years) were enrolled as a reference group. 37 patients (6 males and 31 females, mean age 42.7 years) with verified RA according to the ACR/EULAR 2010 criteria were included in the study. RA disease activity was assessed using DAS28 score did not exceeded 2.6 in every patient at the inclusion timepoint. In 16 (15.4%) patients, the activity of DAS 28 exceeded 3.2 at subsequent visits (after 3, 8 and 12 months). Spontaneous and induced MET formation by isolated monocytes in RA patients (DAS 28<2.6) was 8.7 (8.3-9.1)% and 26.2 (24.5-27.9)%, respectively. Spontaneous and induced MET formation by isolated monocytes in RA patients (DAS 28>3.2) was 18.1 (17.8-18.4)% and 38.2 (38.0-38.4)%, respectively. Spontaneous and induced MET formation by isolated neutrophils in active RA patients (DAS 28>3.2) was significantly higher than in inactive RA patients and in comparison to the reference group. Induced MET formation was also significantly higher than spontaneous one ($p<0.05$). Monocytes did not demonstrate any difference between ACPA-positive and ACPA-negative RA patients in their MET production. The growth rate of spontaneous MET formation was 114.7%, for induced MET formation – 44.2%. The growth rate of spontaneous MET formation is 2.6 times higher than the induced MET formation.

Conclusion: METs formation by isolated monocytes can be considered as a new potential diagnostic biomarker associated with RA flare. Further study of the mechanisms of MET formation and their composition may improve our understanding of the role of monocytes and METs in the pathogenesis of RA.

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Disclosure of Interests: None declared

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AB0040 STUDYING THE MACROPHAGE ACTIVATION AND THE INTIMA-MEDIA THICKNESS OF THE CAROTID ARTERIES IN UNTREATED PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS (PRELIMINARY DATA)

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Background: Autoimmune Rheumatic Diseases (ARDs) occur with a high risk of atherosclerosis development. The macrophages are at the same time a part of the inflammatory response, and also tightly linked to the foam cell formation, thus taking part in both crucial for atherogenesis processes.

Objectives: To evaluate the macrophage activation, and the intima-media thickness (IMT), subclinical atherosclerosis of the carotid arteries in untreated pts with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Methods: Thirty six untreated RA pts (30F/6M) and 36 untreated SLE pts (31F/5M) were enrolled.

RA pts had median age of 39 years (range) (33-45), disease duration of 2.5 years (1-5), moderate clinical disease activity DAS of 28 5.3 (3.5;5.8), SDAI of 17 (15;19), HAQ of 1 (0.75;1).

SLE pts had median age of 37 years (range) (32-41), disease duration of 3.5 years (1-11), SLEDAI 2K of 7 (4-8), BILAG of 14,5 (10,2-23).

Isolation of monocytes was carried out according to the standard procedure for obtaining a leukocyte fraction in a Ficoll gradient and subsequent selection of CD14 + cells using magnetic separation. After isolation, the cells were cultured in X-Vivo medium. To assess the degree of monocyte activation, cells were stimulated by the addition of LPS. The value of monocyte activation was expressed as a ratio of the level of secretion of proinflammatory cytokines by monocytes cultured with and without LPS addition. Secretion levels were determined by ELISA. The belonging of the isolated cells to CD14 + monocytes was additionally confirmed by flow cytometry. All pts undertook carotid duplex ultrasonography.

Results: Macrophage activation was 8.9 (range) (2.7;40.8) in RA pts and 4.8 (2.3;5.6) in SLE pts ($p=0.09$). In RA and SLE pts macrophage activation was independent of age, sex, body mass index, cardiovascular risk (CVR) factors (arterial hypertension, overweight, smoking, family history of cardiovascular diseases), activity scores (DAS28, SDAI, SLADAI 2K), and disease-specific autoantibodies levels.

In RA pts and SLE pts, the carotid mean IMT (m-IMT) was 0.66 ± 0.12mm and 0.61 ± 0.10mm, the maximum IMT (M-IMT) was 0.76 ± 0.16mm and 0.69 ± 0.14mm, respectively, $p>0.05$ in both cases. The prevalence of raised lesions (IMT>0.9 mm) were observed in 5 RA pts (14%) and 2 SLE pts (5%); the atherosclerotic plaques (ASP) (IMT ≥ 1.2 mm) – in 7 RA pts (20%) and 6 SLE pts

(17%). In RA pts, there was a significant correlation between carotid m-IMT and age (R=0.76), level of total cholesterol (R=0.51), LDL cholesterol (R=0.27), systolic blood pressure (R=0.71), diastolic blood pressure (R=0.78), aMCV levels (R=0.79), p<0,05 in all cases. No correlation between carotid m-IMT/M-IMT and the disease's duration, stage or activity was found in RA pts. In SLE pts, carotid m-IMT was associated with the mean SLICC/ACR Damage Index score (R=0.50, p=0.01), with antibodies to cardiolipin (aCL) IgG levels (R=0,42, p=0,02), and with antibodies to beta2-glycoprotein 1 (anti-beta2GP1) IgG levels (R=0.49, p=0.01). No correlation between carotid m-IMT/M-IMT and the traditional CVR factors and disease's activity was found in SLE pts. No association was found between the carotid m-IMT/M-IMT and macrophage activation.

Conclusion: No differences in macrophage activation were found in RA and SLE pts. Macrophage activation was independent of CVR and ARD-related factors. Subclinical atherosclerotic lesions of the carotid arteries were observed in a every fifth untreated RA and SLE pts. Carotid m-IMT correlated with traditional CVR factors in RA pts, and SLICC/ACR Damage Index score in SLE pts. Our results suggest that there is an association between carotid IMT and immunoinflammatory markers: aMCV in RA pts and antiphospholipid antibodies in SLE pts. A study on a larger number of pts will clarify the link between macrophage activation, autoimmune disorders and carotid atherosclerotic lesions.

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Disclosure of Interests: None declared

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AB0041

THE PHENOTYPE OF PERIPHERAL BLOOD DENDRITIC CELLS OF PATIENTS WITH ADULT-ONSET STILL´S DISEASE COMPARED TO HEALTHY DONORS AND PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Adult-onset still´s disease (AOSD) is a rare autoinflammatory disease. A triad of high fever, arthritis and skin rash is described, but multiple forms of manifestation, as the lack of detectable biomarkers, aggravate making the diagnosis (1).

Psoriatic arthritis (PsA), another autoimmune disease with jointal manifestation, affects approximately 30% of all patients with psoriasis (2).

Dendritic cells (DCs) are potent antigen presenting cells linking adaptive and innate immunity. In various autoimmune diseases alterations of DCs were detected (4).

Objectives: The etiology and effect of peripheral blood DCs on the arthritis in both diseases is not cleared yet (1,3). This project tried to examine alterations of DCs in AOSD patients compared to those with PsA and a healthy control group (HC).

Methods: 13 patients with AOSD were analysed and compared.

Leukocytes were separated with density gradient centrifugation and sorted with flow cytometry. The contingent of DC subsets in the peripheral blood (pDCs, CD1c+DCs, CD141+DCs) was compared between AOSD patients and the other two groups (n=12).

Monocytes of the peripheral blood were incubated with IL-4 and GM-CSF to differentiate to DCs. The addition of lipopolysaccharides helped gaining immature (n=11) and mature (n=9) DCs. Their phenotype was characterized by CD1a, CD206, Osteoactivin (OA), CCR7, CD14, DC sign, CCR7, CD14, CD40, HLA-DR, CD80, CD83, CD86. The expression levels of the surface proteins were again compared.

Results: The DC subset rates did not differ significantly between AOSD patients and both other groups.

The surface markers showed a significant difference in expression of CD80 on mature DCs of AOSD patients and those with PsA. Immature DCs presented a significantly different level of OA on patients with AOSD and HCs. All other measured surface markers did not vary between the groups.

Conclusion: The DC subsets analysis did not show significant differences. An arthritic manifestation in AOSD might not depend on the fraction of DCs in the peripheral blood.

OA inhibits T cell responses strongly as coinhibitory molecule on antigen presenting cells. The lower expression of OA on DCs of patients with AOSD might represent a lower inhibition of T cells in comparison to HCs (5).

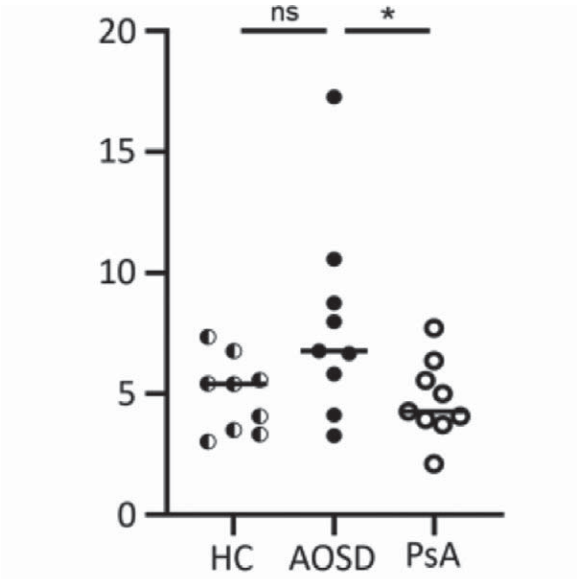

Figure 1: CD80 expression on mature DCs of patients with AOSD compared to patients with PsA is significantly different (p=0,04). HC does not express CD80 differently.

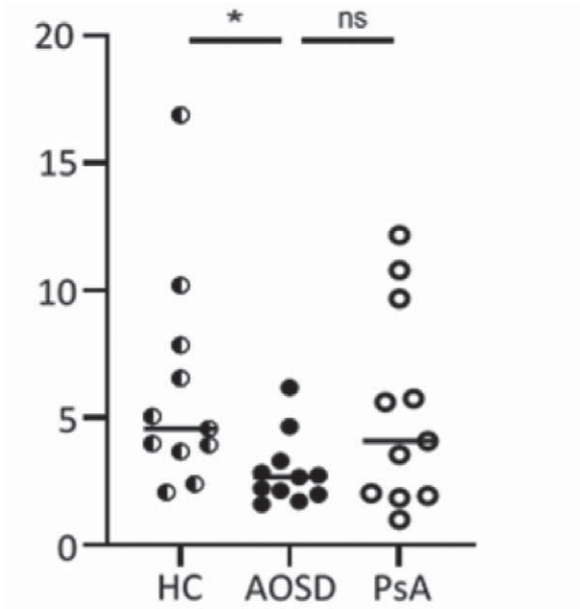

figure 2: OA expression on immature DCs is statistically different between HC compared to patients with AOSD (p= 0,0128). The expression levels of AOSD patients and those with PsA do not differ significantly.

The interaction of CD80 and CD86 with CD28 is necessary to produce IL-6. The pro-inflammatory effect is limited by CD80/ CD86 itself (6). CD80, in contrast to CD86, is expressed differently in patients with AOSD and PsA. As CD80 and CD86 function as cofactors, an alteration of both might have been expected.

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AB0042 OPTIMAL CONDITIONS FOR THE DETECTION OF INFLAMMASOME ACTIVATION IN CD14+ CD16- MONOCYTES FROM HUMAN BLOOD BY FLOW CYTOMETRY

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Background: The inflammasome activation is linked to the aggregation of the adaptor protein ASC into a multimeric structure, known as the ASC speck. The aggregation of cytosolic ASC into ASC specks is therefore used as a readout parameter for inflammasome activity. The direct detection of ASC speck formation on a single cell basis through flow cytometry, can analyze inflammasome activated cells. This allows the investigation of inflammasome activity in a clinical setting.
Objectives: Investigating the optimal conditions for a reliable identification of inflammasome activated ASC speck positive cells *ex vivo* using flow cytometry.
Methods: Freshly donated blood from five different healthy donors was used for all experiments. The choice of anticoagulant, storage time and storage temperature were examined. PBMCs were isolated from blood collecting tubes with ethylenediaminetetraacetic acid (EDTA) or lithium heparin (LH). PBMCs were also isolated from LH blood stored at 4 °C, room temperature (RT), 37 °C and after different storage times. After isolation, PBMCs were fixed immediately and stained for flow cytometric analysis. ASC speck positive $CD14^+$ $CD16^-$ monocytes and THP-1 cells can be generated through incubation with nigericin in PBS.
Results: We adapted a method for flow cytometric analysis of ASC specks, with was previously described by Sester *et al*. [1]. As expected, we observed ASC speck formation after inflammasome activation, in $CD14^+$ $CD16^-$monocytes through a decrease in ASC fluorescent pulse width and an increase in ASC fluorescent pulse area. Monocytes in PBMCs collected from tubes with EDTA compared with LH showed significantly higher numbers of unspecific ASC speck positive cells. Blood storage at RT for 24 h can lead to an unspecific ASC speck formation. Storage at 37 °C resulted in contamination of the PBMC interface with erythrocytes, while blood stored at 4 °C resulted in severe cell clumping. Since storing LH blood for 24 h at RT lead to unspecific ASC speck formation in $CD14^+$ $CD16^-$ cells, but not monocytes from freshly isolated PBMCs, the determination of the time until unspecific ASC speck signals occur was investigated. A significant increase in ASC speck positive $CD14^+CD16^-$ monocytes was detected after 4 h storage at RT compared to directly processed samples and the number of ASC speck positive monocytes further accumulated over time. The incubation with nigericin in PBS leads to a significant increase in ASC speck positive $CD14^+$ $CD16^-$ monocytes and THP-1 cells compared to incubation in RPMI media.
Conclusion: The flow cytometric detection of ASC specks is adapted for practical clinical usability. To reduce background signals, LH- instead of EDTA blood collecting tubes are recommended. The LH blood should be processed within 2 h after blood collection and be stored at RT. To avoid nonspecific activation and formation of ASC specks, the PBMCs should be isolated directly after venipuncture and fixed immediately. It is also possible to freeze the PBMCs until further usage. However, this will cause some loss of ASC speck positive cells. With these settings, clinical samples can now be examined.

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Disclosure of Interests: None declared
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AB0043 THE IMPACT OF ANTI-RO52 ANTIBODIES ON THE EXPRESSION OF ANTIVIRAL RESPONSE-RELATED GENES – PRELIMINARY STUDY

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Background: Ro52, also known as TRIM21, is an essential agent of the innate host defence, especially of the antiviral responses[1]. It was found to be induced by type I and II interferons. Due to its activity of E3 ligase, TRIM21 is involved in the ubiquitination of several IFN regulating factors (IRFs)[2]. Ro52 enables antibody-dependent intracellular neutralization as a high-affinity Fc immunoglobulin receptor[1]. The auto-ubiquitination of the TRIM21-related complex induces signalling pathways with the production of pro-inflammatory cytokines[1]. Anti-Ro52 autoantibodies are found in versatile autoimmune conditions. The hypothesis of our project assumes that viral infections in genetically susceptible individuals trigger overexpression of Ro52, followed by the production of autoantibodies, which suppress its function as the negative regulator of type I interferon responses, leading to enhanced production of proinflammatory agents that uphold autoimmune process.
Objectives: To compare the expression of antiviral response-related genes in patients with anti-Ro52 autoantibodies and healthy volunteers in order to assess the significance of anti-Ro52 in the antiviral defence.
Methods: Anti-Ro52+ patients, hospitalized at the Department of Rheumatology, Medical University of Lodz or treated in the united outpatient clinic were recruited. 19 patients with anti-Ro52 antibodies were included in the study group (mean age: 54,2 years, F:M ratio 14:5). Among them, 5 patients were diagnosed with primary Sjogren syndrome, 5 with idiopathic inflammatory myopathies, 4 with systemic lupus erythematosus, 1 with rheumatoid arthritis, 3 with overlapping syndromes and 1 was undergoing diagnosis of connective tissue disease at the time of the recruitment. Data on the diagnosis, clinical symptoms and laboratory results were collected from the patients and the available medical records. 10 healthy individuals without autoimmune disorders were recruited to the control group. Whole blood samples were collected from both anti-Ro52+ patients and healthy controls, PBMC were isolated using Biocoll reagent. RNA was isolated from each sample with RNeasy and cDNA synthesis was performed by RevertAid™ H Minus First Strand cDNA Synthesis Kit. The mRNA expression levels of TRIM, IRF3, IRF5, IRF7, NFκB, RIG-1, MDA5 genes were examined by quantitative real-time PCR with TaqMan™ Universal PCR Master Mix according to the manufacturer's instructions. The expression levels of genes relative to that of GAPDH were calculated by delta Ct (ΔCt). The ΔCt value is the Ct value of the target gene subtracted its Ct value of GAPDH, $\Delta Ct = Ct (Gene) - Ct (GAPDH)$. Therefore, the smaller the ΔCt values, the higher the expression levels of the target mRNA. The Mann–Whitney rank sum test was used to compare the control group and anti-Ro52+ patients.
Results: The ΔCt values for TRIM, IRF3, IRF5, IRF7, NFkB, RIG-1, MDA5 were found to be lower in the anti-Ro52+ group as compared to the control group, indicating higher mRNA expression of these genes in anti-Ro52+ patients. Statistical significance was reached for all of the examined genes but IRF3. Detailed results are presented in Table 1.

Table 1. The ΔCt values for antiviral response-related genes in anti-Ro52+ patients and healthy controls. P – statistical significance

	Anti-Ro52+ group ΔCt	Control group ΔCt	*p*
TRIM	4,91	6,64	<0,0001
IRF3	5,70	5,92	0,8482
IRF5	4,45	5,68	<0,0001
IRF7	5,14	6,54	<0,0001
NFκB	4,78	5,66	<0,0001
RIG-1	3,77	4,33	0,0188
MDA5	5,08	6,82	<0,0001

Conclusion: Presented results confirm the enhancement of the antiviral defence in anti-Ro52+ patients. As overexpression is observed independently in various connective tissue diseases, impaired response to viral infections via Ro52 pathways could indicate a common trigger factor of autoimmunity.

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Disclosure of Interests: None declared
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AB0044 **REDUCED PERIPHERAL BLOOD MYELOID CELLS IN PATIENTS WITH VEXAS SYNDROME**

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Background: Systemic inflammatory or dysimmune diseases (SIDDs) are encountered in up to a quarter of patients with myelodysplastic syndromes (MDS). Recently identified VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, associated with somatic mutations in UBA1, encompasses a range of severe inflammatory conditions along with hematologic abnormalities, including myelodysplasia. Only limited data are available on the pathophysiology of MDS-associated SIDDs, and especially about the role of different myeloid cell subsets.

Objectives: The aim of this study was to describe the phenotype of myeloid immune cells (dendritic cells and monocytes) in MDS patients with associated SIDDs, and to compare their distribution with MDS patients without SIDDs and controls.

Methods: Phenotype analysis by flow cytometry from PBMCs of 14 MDS patients with SIDDs, 23 MDS patients without SIDDs and 7 controls without MDS and SIDDs. Eight of the 14 MDS/SIDDs patients (57%) had a somatic *UBA1* mutation.

Results: In this study analyzing peripheral blood myeloid immune cells in MDS patients with and without SIDDs, we observed a quantitative reduction of different DC and monocyte subsets in MDS/SIDDs patients, especially in patients with active SIDDs and above all in patients with newly described VEXAS syndrome.

Conclusion: Further functional studies are warranted to better understand the mechanisms and the consequences of the phenotypic modulations of immune myeloid cells in the pathophysiology of MDS-associated SIDDs, especially in VEXAS syndrome.

Disclosure of Interests: None declared
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Osteo arthritis, aetiology, pathology and animal models

AB0045 **EFFECTS OF AEROBIC EXERCISE AND PREBIOTIC FIBRE SUPPLEMENTATION ON THE VASTUS LATERALIS AND SOLEUS MUSCLES IN A RAT MODEL OF DIET-INDUCED OBESITY**

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Background: A high-fat/high-sucrose (HFS) diet leads to osteoarthritis-like damage in the knee and shoulder (Collins et al., 2018), and to a low-level systemic inflammation that is accompanied by a decrease in insulin sensitivity. Recently, we demonstrated in a rat model, that when prebiotic fibre supplementation, aerobic exercise, or their combination is started at the onset of the HFS diet exposure, the development of the osteoarthritis-like lesions in the knee joints and the metabolic dysfunction is prevented (Rios et al., 2019).

A central role in the altered metabolic state of rats fed a HFS diet is thought to be played by skeletal muscle (Collins et al., 2018). Besides the detrimental effect on metabolic and inflammatory regulation, muscular dysfunction might be a contributor to the decline in running endurance and coordination observed with prolonged exposure to a low quality diet (Clayton et al., 2022).

Objectives: To evaluate the changes in insulin sensitivity and vastus lateralis and soleus muscle composition in a HFS diet rat model and determine whether the expected muscle alterations can be prevented with a prebiotic fibre supplementation, aerobic exercise, or their combination.

Methods: Twelve-week-old male Sprague Dawley rats fed a high-fat/high-sucrose diet (HFS, Diet #102412, Dyets) were randomized into a sedentary (HFS, n=12), moderate aerobic exercise (HFS+E, n=12), prebiotic fibre supplementation (HFS+F, n=12), or moderate aerobic exercise combined with prebiotic fibre supplementation (HFS+F+E, n=12) group for 12 weeks. Eight chow-fed (Diet #5001) age- and sex-matched animals were used as controls.

Whole body insulin sensitivity (composite insulin sensitivity index – CISI) was determined at the end of the intervention period and, after sacrifice, the VL and soleus muscle composition was evaluated through a triglyceride colorimetric assay and histological analysis of collagen with picrosirius red staining. Non-parametric Kruskal-Wallis testing with pairwise comparisons was used to compare groups.

Results: HFS group rats had less than half (40%, p = 0.001) of the whole-body insulin sensitivity of control rats while rats in the HFS+E, HFS+F and HFS+F+E groups were similar to control.

Rats that were fed the HFS diet showed increased VL (p = 0.033) but not soleus (p = 0.644) triglycerides content compared to control (Figure 1 A). Both VL and soleus showed increased collagen content in the groups fed the HFS diet compared to the control group (p<0.001 for VL and soleus) (Figure 1 B). Moderate aerobic exercise, prebiotic fibre supplementation, or their combination did not prevent the observed alterations in muscle composition in the groups fed the HFS diet.

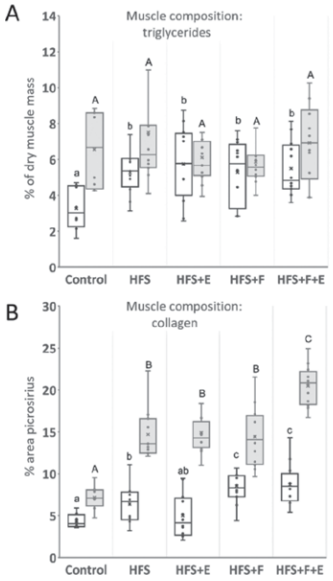

Figure 1. Vastus lateralis (white) and soleus (shaded) composition. In A) intramuscular triglyceride content and B) intramuscular collagen content. Equal letters represent similar values across groups with capital letters used for comparisons regarding the soleus muscle.

HFS: high fat/high sucrose diet; F: prebiotic fibre; E: aerobic exercise.

Conclusion: While a positive effect of prebiotic fibre and exercise in managing metabolic disturbance was present with a clear recovery of insulin sensitivity to control levels in the groups that were fed the HFS diet, the protective effect of exercise and prebiotic fibre that has been previously described for knee joints in this model was not observed for the VL and soleus muscles. The HFS diet led to alterations in muscle composition that seem to be muscle-specific

and cannot be prevented by combining prebiotic fibre or exercise with the HFS diet.

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Disclosure of Interests: None declared

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AB0046 RESISTANCE TO OXIDATIVE DEGRADATION OF A FORMULATION COMBINING HYALURONIC ACID AND NIACINAMIDE

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Background: Hyaluronic acid plays a major role in the homeostasis of cartilage. In cases of osteoarthritis, hyaluronic acid is subjected to significant oxidative stress linked to the inflammation cascade leading to drastic diminution of its quantity at the level of the joint. This decrease in hyaluronic acid reduces dramatically the lubricating properties of the synovial fluid.

Several preparation methods have been developed to further stabilize the hyaluronic acid used as viscosupplement such as crosslinking or adding adjuvants.

Objectives: A new formulation intended for intra-articular administration has been developed consisting of a combination of hyaluronic acid and vitamin B3 commonly called Niacinamide.

The addition of niacinamide has a protective effect against hyaluronic acid under heat stress and under oxidative stress.

Methods: In order to assess the resistance to free radicals, 4 products were compared (HA 2.2%+vitamin B3 vs HA at 2.2% vs 2 cross-linked HA). 1 gram of sample were placed on Peltier Plate of a Rheometer – TA instrument and submitted to a temperature of 37°C. 50µL of H2O2 was introduced on the sample.

The rheological properties of the mixture were followed-up at a shear stress of 1Hz until full degradation of the sample (i.e. until reaching a viscosity close 0).

The degradation was calculated at each time point and plotted on a graph to compare the enzymatic degradation kinetics.

To assess the thermal resistance, 2 products were compared (HA 2.2%+ vitamin B3 vs HA 2.2%). The samples consisting of 2 grams of gel packaged in glass syringe were placed in a dry oven at 50°C. The viscosity was measured at 3 different timepoints.

Results: This study demonstrates a significant better resistance to free-radical degradation for the HA+Niacinamide vs comparative products.

The viscosity follow-up under heat stress demonstrated that the adjunction of Niacinamide does have a positive effect in preserving the HA viscosity consistently throughout time.

Conclusion: Vitamin B3 commonly called Niacinamide exhibits a dual positive effect when associated with Hyaluronic Acid.

The study demonstrates a better resistance to oxidative degradation for the HA+Niacinamide most probably due to the antioxidant effect of Niacinamide.

This study confirmed the adjunction of the Niacinamide into the HA-based gel formulation does increase the stability of HA against thermal degradation.

References: Data on file

Disclosure of Interests: Farid HADJAB Consultant of: Albomed GmbH, Grant/research support from: Albomed GmbH

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AB0047 CARTILAGE DEGRADATION STATUS OF KNEE OSTEOARTHIRTIC PATIENTS CAN BE PREDICTED BY CHONDROCYTE GENE EXPRESSION ANALYSIS

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Background: Osteoarthritis (OA) is the most common degenerative joint disease, but its pathogenesis is still poorly understood. OA is characterized by articular cartilage loss due to an imbalance in anabolic and catabolic gene expression of the chondrocyte, together with aberrant expression of transcription factors and inflammatory mediators.

Objectives: We aim to evaluate de genes implicated in the chondrocyte failure regarding the four issues assessed to evaluate cartilage integrity using Mankin score (MkS): surface integrity, cellularity, cell cloning and staining.

Methods: Knee OA (KOA) patients aged 60-75 undergoing a total knee replacement, were recruited. At surgery, tibial plateau and femur condyles were deposited in DMEM medium and sent to the laboratory within 4 hours of the extraction. Punches from areas located at low, medium and high load (1) were excised from each sample (approximately 11 areas per patient). For RNA analysis, punches were kept in RNAlater at -20ºC until analyzed. RNA extraction, cDNA synthesis and cDNA amplification of the selected genes were performed previous to gene expression quantifycation by OpenArray Assay with custom plates. ΔCt was analyzed by ExpressionSuite V1.3 using 6 housekeeping genes. For histology study, punchs were fixated in formalin and embedded in parafin. Sections of 4 µm were stained with hematoxilin eosin and Safranin O-Fast Green. Slices were scored using the modified MkS (2) by 3 independent observers. R (v3.3.2) analysis was used to explored the results with principal components analysis (PCA) and linear regression (LR).

Results: Surgical samples were obtained from a total of 27 patients and 219 different areas were analyzed. ΔCt of the 51 genes analyzed by PCA showed that 9 components were enough to represent >80% of variance of the model. The genes associated with each component are summarized in Table 1. LR shows that second and first component were significantly associated to all or most of the fields included in the MkS, respectively. In contrast, component 4, 5 and 9 were not associated with any field. Lower expression of genes represented in component 1 (mainly related with extracellular matrix content) are associated with higher MkS values. On the other hand, component 2 summarizes data of genes mainly related with factors regulating cell metabolism. In this case, higher expression of TNFαIP6, NGF, IGFBP1, CRLF1, TNFα, and lower expression of ACAN, COL11A2, COL2A1, COL10A1, SOX9 and TGFβ1, among others, are associated with increased MkS values.

Table 1. Genes that most contribute (by order) to component 1 & 2 (due to space limitation). Data of LR analysis for each component and MkS item. Significant association marked in bold.

		Mankin score item (β coefficient; p-value)			
Component	Genes	Surface integrity	Cellularity	Cell cloning	Staining
1	SERPINE2, COL8A2, OGN, COL5A, TIMP3, BMP6, CRLF1, TIMP2, WISP1, ST3GAL1, SERPINE1, TNFSF10, ASPN, NGF, CD44, TNFRSF11B, TGFA, ADAMTS5, COL15A1, LUM, TNFAIP6, PTGS2, BMP2	**-0.092; 0.006**	**-0.025; 0.047**	-0.028; 0.078	**-0.043; 0.015**
2	ACAN, GPC5, CFH, FGFR3, COL11A2, TGFB1, GREM1, TNFAIP6, NGF, SOX9, IGFBP1, MMP3, FGF2, CRLF1, TNFa, COL2A1, COL10A1	**0.261; 2.54 10^{-7}**	**0.050; 0.010**	**0.066; 0.005**	**0.072; 0.007**
3		**-0.174; 0.003**	-0.029; 0.191	**-0.076; 0.006**	0.004; 0.898
4		0.068; 0.410	-0.019; 0.543	-0.055; 0.161	-0.021; 0.627
5		-0.082; 0.364	0.051; 0.146	0.020; 0.644	-0.052; 0.283
6		0.050; 0.605	0.023; 0.548	**0.111; 0.017**	0.062; 0.228
7		-0.120; 0.266	**-0.090; 0.032**	0.010; 0.839	-0.113; 0.052
8		-0.134; 0.274	0.006; 0.892	**-0.198; 0.001**	**-0.131; 0.047**
9		-0.220; 0.096	-0.041; 0.425	-0.101; 0.110	0.020; 0.780

Conclusion: There is a correlation between the expression level of the studied genes and the MkS values, although the role played by each gene might be

different according to the MkS issue evaluated. These results could be useful to describe biomarkers that identify burden of disease in KOA.

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AB0048 THE SUPPRESSION OF INFLAMMATORY PROCESSES AND MODULATION OF MAPK SIGNALING BY SHIKONIN DERIVATIVES IN PRIMARY OA CHONDROCYTES

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Background: Osteoarthritis (OA) is one of the most common joint disorders and is characterized by the degeneration and loss of articular cartilage with chronic arthritis of the joint edge and subchondral bone. OA is causally influenced by several factors, including age, gender, familial susceptibility, as well as local biomechanics, cartilage cell apoptosis, and the action of degenerative enzymes. Despite intensive research, there are still few effective therapeutic approaches.
Objectives: In the rat OA model, shikonin was shown to inhibit inflammatory processes and chondrocyte apoptosis by regulating the PI3K/AKT pathway. Therefore, we investigated the effect of shikonin and its derivatives acetylshikonin and cyclopropylshikonin on inflammation, MMP expression, and regulation of MAPK signaling in human OA chondrocytes.
Methods: Viability was analyzed using the CellTiter 96 AQ_{ueous} Luminescence Assay on human healthy chondrocytes (HC) and primary OA chondrocytes (pCH-OA). For the study of inflammatory processes, we performed a proteome profile screening assay. As MAPK signaling pathways play a key role in cartilage destruction in OA, we analyzed the effects of shikonin and its derivatives using protein expression analysis of the phosphorylation pattern and the corresponding downstream gene regulation using RT-qPCR.
Results: Both HC and pCH-OA showed a dose-dependent inhibition of cell viability after treatment with shikonin derivatives, whereby the strongest effects were found for shikonin with IC_{50} values of 1.2 µM and 1.3 µM, respectively. Shikonin counteracts inflammatory response caused by IL-1β by massively reducing the expression of pro-inflammatory mediators.
Phosphorylation level of ERK changed slightly, pJNK and pp38 showed a significant increase after treatment with the shikonin derivatives both in HC and pCH-OA cells. The downstream targets c/EBPs and MEF2c may play a role in the homeostasis of joint cartilage under physiological and pathological conditions. The phosphorylation level of STAT3 significantly decreased in a dose-dependent manner after treatment. STAT3 blockade has a chondroprotective function through a regulation of cyclin D1 or Sox9.
Conclusion: Our results demonstrate for the first time that shikonin and its derivatives acetylshikonin and cyclopropylshikonin have extensive effects on inflammatory processes, MAPKs, and IL6/STAT3 downstream regulation in human healthy chondrocytes and primary OA chondrocytes.
References: none
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.1544

AB0049 ASSOCIATION WITH LEPTINEMIA AND Q223R (RS1137101) POLYMORPHISM OF LEPR GENE IN FEMALE PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Knee Osteoarthritis is the most common form of arthritis, affecting millions of people worldwide. Poor early diagnostics, growing share of seniors in the population structure, the need for genetic or other molecular biomarkers to improve safety, efficacy, and outcome of treatment of OA patients make up the key issues of scientific interest.
Objectives: To assess the association between serum leptin concentrations, the *LEPR* gene *Q223R(rs1137101)* polymorphism in patients with knee OA.
Methods: The participants in this study (knee OA patients = 99, control group (healthy women) = 62) underwent blood measurement to *LEPR Q223R(rs1137101)* genotyping assay and leptin serum levels. We analyzed the relationship with multivariate regression models using generalized linear models with binomial link function.
Results: In this way, allele frequency and genotypic variant specificity for polymorphic variant Q223R(rs1137101) of LEPR gene in women with OA of knee joints were determined. The frequency of the variant allele G(Arg) in the group of patients with OA of the knee joints was 0.54 and in the control group 0.43. The results were unreliable, although the nature of the trend was small (p = 0.06). In patients with OA, the genotype Q223R(rs1137101) of the LEPR gene was significantly subdivided according to the Hardy-Weinberg law (p = 0.002), which was due to the higher frequency of homozygotes of both types, while theoretically scoring with the same status. The association of the Q223R(rs1137101) polymorphism of the LEPR gene with the risk of developing OA of the knee joints in the recessive model of decay (GG/AA + AG) was revealed: odds ratio (OR) = 2.15 (95% CI: 1.03-4.50), p = 0.04. There was no correlation between the Q223R(rs1137101) polymorphism of the LEPR gene and such clinical and laboratory indicators as clinical form, body mass index, and blood serum leptin concentration. Carriers of AG (Gln/Arg) + GG(Arg/Arg) genotypes have a significantly higher risk of developing rapid X-ray progression of OA (II and III X-ray stages, due to I) after 5 years of diseases: OR = 5.17 (95% CI: 1.04 - 25.57), p = 0.03.
Conclusion: Our results suggest that the patients with knee OA the *AG (Gln/Arg)* and *GG (Arg/Arg)* genotype carriers have statistically significant higher risk of OA.
Further study of this issue is needed.
Disclosure of Interests: None declared
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AB0050 ALTERED NAMPT, ADIPOKINE AND CYTOKINE LEVELS CHARACTERIZE MONOCYTE ACTIVITY AND CORRELATE WITH DISEASE SEVERITY IN OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a chronic, debilitating, aging-associated disease (1), characterized by chronic low-grade inflammation, the underlying mechanisms of which are poorly understood (2). Intracellular nicotinamide phosphoribosyltransferase (iNAMPT) is the rate-limiting enzyme in the NAD^+ salvage pathway, in charge of maintaining cellular homeostasis through redox reactions. NAD^+ promotes the expression of sirtuin-1 (SIRT1), which regulates the mobilization of myeloid-derived suppressor cells from the bone marrow. Extracellular eNAMPT, the secreted form of NAMPT also known as visfatin, is an adipokine involved in OA pathogenesis (3,4).
Objectives: We aim to analyse the cytokine and adipokine profile and the role of i- and eNAMPT in OA-related inflammation.
Methods: Peripheral blood and, whenever possible, synovial fluid from knee joint were collected from patients with OA older than 50 years. Samples from subjects without OA older than 50 (non-OA>50y) and younger than 30 (non-OA<30y) were used as controls. Serum, plasmatic, and synovial fluid adipokines and cytokines were measured by ELISA. Peripheral blood mononuclear cells were purified with Ficoll gradient and monocytes were selected with anti-human CD14 microbeads; RNA was extracted for polymerase chain reaction for NAMPT, SIRT1 and pro/anti-inflammatory cytokines. Monocyte intracellular NAD^+ was measured at baseline and 1 hour after nicotinamide (a NAMPT substrate and precursor of NAD^+) supplementation. Results were correlated with clinical data.
Results: Peripheral blood was obtained from 51 patients with OA (19 with synovial fluid also), 44 from non-OA>50y, and 35 from non-OA<30y controls. Plasmatic chemerin and leptin were higher in OA patients, visfatin was higher in OA and in non-OA>50y group ($p<0.01$ for all analyses). Plasmatic and synovial levels of leptin and resistin were correlated ($p<0.001$, $r=0.6$ for both comparisons); synovial leptin and resistin correlated with synovial IL-6, VEGF, and TNFα and these were higher in polyarticular OA (vs monoarticular, p=0.01 and p=0.03, respectively) and in OA with more severe Kellgren-Lawrence score (p=0.003 and p=0.03, respectively). Monocyte expression of NAMPT and anti-inflammatory cytokines IL-10 and Arginase-1 was increased in non-OA<30y controls compared to OA patients and non-OA>50y subjects ($p<0.05$ for all analyses). At baseline, monocyte intracellular NAD^+ content was higher in the non-OA>50y cohort; after niacin supplementation, non-OA>50y subjects had the highest content, whereas

OA patients had higher NAD levels than at baseline, but significantly lower than non-OA>50y controls (Figure 1).

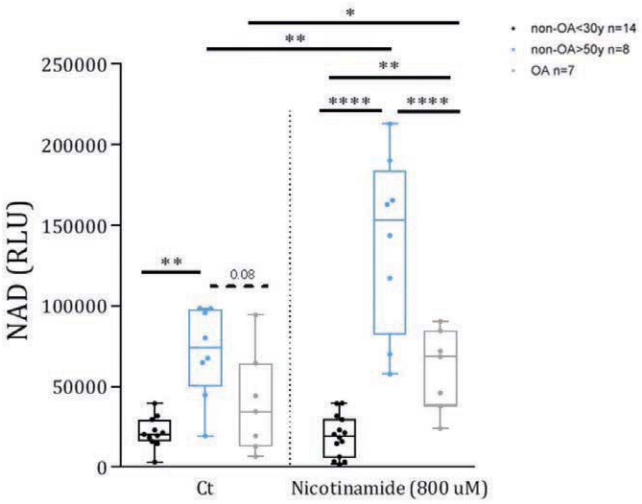

Figure 1. Monocyte NAD^+ content at baseline and 1 hour after nicotinamide supplementation. *p<0.05 **p<0.01 ****p<0.0001.

Conclusion: A specific plasmatic and synovial adipokine signature characterizes OA and patients with more severe disease. In monocytes there is a age-related reduction of iNAMPT and anti-inflammatory cytokine expression, whereas eNAMPT is higher in elderly compared with younger subjects. In non-OA>50y subjects there might be an increase of iNAMPT activity which leads to NAD^+ production, while in OA patients this mechanism seems to be impaired and can be only partially enhanced by nicotinamide supplementation, leading to reduced intracellular redox efficiency. These results suggest that NAMPT activity might be a key component of the mechanisms underlying inflammation in OA patients.

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AB0051 EVIDENCE OF VERY EARLY CARTILAGE DAMAGE IN EXPERIMENTAL OSTEOARTHRITIS USING SCANNING ELECTRON MICROSCOPY

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Background: Early, reproducible, sensitive imaging biomarkers are an unmet need in experimental osteoarthritis (OA) evaluation. Electron microscopy may reveal joint changes prior to soluble biomarkers.

Objectives: This study describes very early, quantitative, articular cartilage surface damage in posttraumatic experimental OA models allowing determination of disease severity.

Methods: Mice (5/group) were subjected to anterior cruciate ligament transection (ACLT), ACLT plus meniscectomy (MNCT), as OA models, or sham surgery and sacrificed 3, 7 or 14 days later. Articular cartilage was collected and processed for optical (H&E; Safranin O staining) or scanning electron microscopy (SEM) analysis. Histology was graded using Osteoarthritis Research Society International (OARSI) parameters whereas cartilage thickness, roughness and damage index were evaluated under SEM.

Results: Optical microscopy did not reveal significantly relevant cartilage changes in OA models *vs* controls. Femoral and tibial cartilage thickness were significantly reduced in mice subjected to ACLT or MNCT at 7 and 14 days postsurgery (P<0.05). Cartilage roughness was significantly increased in MNCT agroup as early as 3 days postsurgery, as compared to sham and ACLT groups, being sustained up to 14 days in both femoral and tibial extremities. Articular damage index using SEM was more severe at 14 days postsurgery in ACLT and MNCT *vs* control groups (P<0.05).

Conclusion: Posttraumatic experimental OA display quantitative cartilage changes at SEM with increased roughness and thickness as early as 3 days post induction. In addition to unravel very early ultrastructural cartilage damage, these changes may be used as early surrogates for joint damage in experimental OA.

Disclosure of Interests: None declared

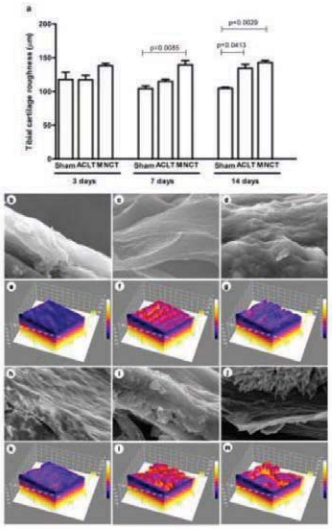

Figure 3. Assessment of roughness of tibial cartilage.
Mice were subjected to a sham procedure or transection of the medial collateral and anterior cruciate ligaments (ACLT) or ACLT followed by transection of the medial meniscus (MNCT). Groups were sacrificed 7 or 14 days post surgery. (A) Data represent mean±sem of cartilage roughness (µm) using scanning electron microscope (SEM) images (9/group), compared using Student's "t" test. Representative SEM imaging and roughness plots of the tibial cartilage of animals of the sham [(B,H) and (E,Q)], ACLT [(C,I) and (F,L)], and MNCT [(D,J) and (G,M)] groups sacrificed at 7 or 14 days post surgery, respectively.

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AB0052 CHANGES IN THE MOLECULAR ARCHITECTONICS OF PLASMA MEMBRANES (PM) OF NEUTROPHILIC LEUKOCYTES (NL) FROM SYNOVIAL FLUID (SF) IN GONARTHROSIS (GA)

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Objectives: Changes in the spectrum of phospholipids (PL) in NL membranes correlate with the activity of their metabolic and phagocytic processes. The aim of the work was to study PL homeostasis of NL from SF in GA.

Methods: SF of knee joints of 12 patients with GA with active synovitis and 7 conditional donors postmortem (D) were researched. PL analysis: phosphatidylcholine (PC), sphingomyeline (SM), phosphatidylethanolamin (PEA), phosphatidylinositol (PI), phosphatidylserine (PS), lysophosphatidylcholine (LPC) were performed by conventional lipid-gas and fluid chromatography methods. Active forms of oxygen (AFO2) have been registered by applying EPR. Electrokinetic motility (EM) of NL determined by the automatic microscope.

Results: With GA, against the background of the sharp increase (2.7 times) of free radical processes, there are quantitative changes in the FL plasma membranes NL, expressed in the decreases in the percentages of PC, SM, PEA, PI and the increases in PS and LPS.

Table 1. Phospholipids concentration (%), AFO2 (units/mg of protein) and EM (m/v sec) NL from SF in GA

NL	PC	SM	PEA	PI	PS	LPC	AFO2	EM
D	25,8±0,9	18,7±0,3	27,3±0,7	19,7±0,4	9,5±0,9	5,1±0,2	21,7±4,9	1,20 ♦ 10-8
GA	20,4±0,7*	12,3±0,4*	11,7±0,6**	10,9±0,8**	13,2±0,4*	8,9±0,7*	59,4±7,5**	0,27♦ 10-8***

* - p <0.05; ** - p <0.01; *** - p <0.001

A decrease in the level of PC and SM in GA indicates an increase in the sensitivity of NL membranes to reactive oxygen species and a decrease in their structural stability, an increase in microviscosity and fluidity. A decrease in the PEA level in GA is also associated with the sharp increase in the active forms of oxygen radicals, which leads to "loosening" of the membranes and the formation of hydrophilic pores. PI is an effector of many membrane enzyme-substrate complexes, and with GA, the percentage of PI is halved. An increase in the level of PS and LPC in GA indicate the presence of structural rearrangements and loosening of the hydrophobic region of the lipid layer of the NL membranes. The PEA / PS ratio in the control group was 2.87, and with GA - 0.89. This indicates a change in the saturation of the lipid bilayer of the NL membrane, an increases in microviscosity and fluidity. Quantitative shifts in the FL composition in NL membranes during GA lead to their pronounced depolarization and the 4.4 -fold decrease in EM.

Conclusion: FL form the NL apoptotic response, determine their plastic and energy potential. In GA, FL homeostasis of NL is disturbed and membrane-destructive processes development. Modification of the lipid bilayer of plasma membranes NL causes their depolarization, a decrease in plasticity, viscosity, electrical conductivity and EM. The noted changes in the molecular architectonics of NL membranes in GA inhibit their membrane-protective properties, antioxidant potential, and stimulate the apoptotic response.
Disclosure of Interests: None declared

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AB0053 **LNCRNA NUTM2A-AS1 ALLEVIATED OSTEOARTHRITIS BY REGULATING MIR-183-5P/TGFA PATHWAY**

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Background: Osteoarthritis(OA) is a common comorbidity in the elderly, characterized by articular cartilage degeneration, hyperosteogeny and synovitis. Long non-coding RNAs (LncRNAs) have been shown to be involved in several human diseases, including OA. However, the effect of NUTM2A-AS1 on chondrocytes remains unknown.
Objectives: The purpose of this study was to evaluate the role of LncRNA NUTM2A-AS1 in OA pathological changes in vitro.
Methods: Chondrocyte cells were treated for 24 hours to mimic OA pathological conditions. The experimental center used chondrocytes with interleukin-1 beta (IL-1β) Intervention to simulate the pathological state of OA.The expression levels of LncRNA NUTM2A-AS1, miR-183-5p and TGFA mRNA were detected by quantitative real-time PCR (qRT-PCR), along with CCK-8 to determine cell viability. Inflammatory response was assessed by determining the release of pro-inflammatory factors such as TNF-α and IL-6 using ELISA kits. Cell apoptosis was examined by flow cytometry assay. The binding relationship between miR-183-5p and LncRNA NUTM2A-AS1 or TGFA was confirmed by dual-luciferase reporter assay.
Results: IL-1β induced chondrocytes to express LncRNA NUTM2A-AS1 and TGFA, and the miR-183-5p expression was decreased in IL-1β-treated cells. Low expression of LncRNA NUTM2A-AS1 or TGFA mitigated IL-1β-caused chondrocyte viability reduction and apoptosis promotion. miR-183-5p overexpression alleviated IL-1β-mediated chondrocyte apoptosis and inflammatory injury via decreasing TGFA expression. In addition, our work revealed that miR-183-5p is a target of LncRNA NUTM2A-AS1. Rescue experiments showed that TGFA overexpression could reverse the effects of low expression of LncRNA NUTM2A-AS1 on the pathological changes in IL-1β-induced chondrocytes.
Conclusion: Low expression of LncRNA NUTM2A-AS1 significantly mitigated the chondrocytes damage induced by IL-1β through regulating miR-183-5p/TGFA axis, which might be an important target to regulate the promotion of OA.
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Bone diseases, aetiology, pathology and animal models

AB0054 **NEW THERAPEUTICAL TOOLS FOR HETEROTOPIC OSSIFICATION TREATMENT AND PREVENTION**

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Background: Heterotopic ossification (HO) consists in abnormal bone growth in soft tissues, in a non-porrostoeblastogenic environment. This pathology origin can be congenital (progressive osseus heteroplasia, progressive osseous fibrodysplasia, …) or acquired (burnt, big traumas, electrocutions, articular replacement surgeries, …). Currently, the available therapies (radiotherapy and removal surgery) are aggressive, associated to multiple adverse effects, and not suitable for every populations. Therefore, new therapeutic tools are needed to HO.
Osteoblast is the cell type in charge of bone growth. These cells share a mesenchymal origin with adipocytes. Interestingly, osteoblastogenesis and adipogenesis are opposed and mutually controlled processes.
Objectives: The aim of this work is to study osteoblastogenesis inhibition through adipogenesis promotion using a new therapy (Tri-therapy) composed by a PPARG agonist, a NSAID, and a corticoid.
Methods: Mice mesenchymal stem cells (C3H10T1/2) were differentiated towards adipogenesis and osteoblastogenesis for 7 days, in the presence of the Tri-therapy compounds alone and combined. Simultaneously, human preosteoblast cells (SaOS2) were differentiated to osteoblast for 14 days, being treated with the Tri-therapy. Human HO cells (acquired HO and congenital HO independently), obtained from HO explants, were exposed to an adipogenic environment in the presence of the Tri-therapy for 7 days.
Osteoblastogenic (ALPL, SPP1, GPNMB, RUNX2) and adipogenic (FABP4, PLIN2, ADIPOQ, PPARG) marker genes mRNA expression measured by RT-PCR was used to evaluate differentiation processes. All the results were expressed as the media± SEM of, at least, 3 independent replicates.
Results: In C3H10T1/2 differentiations Tri-therapy synergically induced FABP4, PLIN2, ADIPOQ expression in both cell fates, demonstrating therefore its ability to promote adipogenesis. In SaOS2, the proposed therapy diminished osteoblastogenic marker genes expression (SPP1, GPNMB, RUNX2), being this effect greater than PPARG agonists' themselves. In HO cells, Tri-therapy augmented adipogenesis markers expression, showing a partial effect in osteoblastogenic marker genes expression.
Conclusion: Pro-adipogenic switch in differentiation marker genes expression induced by the Tri-therapy suggested the clinical use of this drugs combination to treat and prevent HO and abnormal bone growth.
Disclosure of Interests: None declared
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AB0055 **BONE AND MINERAL DISORDERS IN RENAL HEMODIALYSIS PATIENTS**

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Background: Chronic kidney disease causes many mineral and bone disorders, secondary hyperpathyroidism, adynamic bone disease and osteomalacia which can reduce the bone mineral density (BMD).
Objectives: To analyze the prevalence of osteoporosis in group of patients with chronic renal failure and to evaluate the relation between bone mineral density (BMD) and specific markers of bone turnover in hemodialysis (HD) population.
Methods: This is a cross sectional study conducted in rheumatology department of Taher Sfar university hospital in mahdia, Tunisia. The study involved 61 patients with chronic hemodialysis. they were invited to participate and were included after signing informed consent until the calculated sample size was reached. Patients were asked to undergo a hip and lumbar (L2-L4) densitometry by DXA to measure bone mineral density (BMD). Serum levels of iPTH and alkaline phosphatase (ALP) were measured before the dialysis session.
Results: The studied group of 61 patients was 26 females (42,6%) and 35 males (57.4%), there mean age was 53.9 [17-83] years, with mean dialysis duration 6,1 years. The mean onset age of hemodialysis therapy was 44.7 +/- 15.4 years. It was diabetic nephropathy in 25 cases (41%) vascular nephropathy in 15 cases and tubulointerstitial nephropathy in 21 cases (34,4). 23 patients (37,7%) had osteoporosis using the WHO criteria (T-score < -2,5), 26 patients (42,6%) had osteopenia and 12 patients had normal BMD. The mean serum level of iPTH with normal BMD and lower BMD 167,84 vs 535,71 respectively. the mean serum level of ALP with normal BMD and lower BMD 144,59 vs 271,99 respectively (p<0,001). The mean duration of dialysis therapy with normal BMD and lower BMD 4,57 years vs 6,55 years (p<0,001).
Conclusion: Our study showed that osteoporosis is common in dialysis patients. The main determinants of BMD is PTH activity and the duration of dialysis therapy. the importance of prevention and treatment of metabolic bone disease has become better appreciated.
Disclosure of Interests: None declared
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Rheumatoid arthritis - aetiology, pathogenesis and animal models

AB0056 COMPARATIVE ANALYSIS OF THE DISTRIBUTION OF LYMPHOCYTES, MACROPHAGES AND MAST CELLS IN THE MARGINAL SYNOVIUM AND JOINT CAPSULE IN GENERAL AFTER ANTENATAL ANTIGENIC STIMULATION

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Background: The joint capsule is one of the main pathogenetic points of arthritis development [1]. In addition, the initial signs of the inflammatory joint diseases are identified primarily in the marginal transitional zone [2]. The joint capsule morphology was studied using hip joints of Wistar rats during the postnatal period in norm and after antigenic stimulation. The last one was modeled through the transuterine intrafetal interscapular subcutaneous injection of antigen (0.05 ml of human normal immunoglobulin) for the rat foetus on the 18th day of its antenatal life under general anesthesia and sterile conditions via laparotomy for the pregnant female (Voloshyn's method (1981). The control group of rats was injected with 0.05 ml of physiological saline in the same manner. The earlier recovery of certain parameters (total cells quantity, vessels, collagen fibers and ground substance) to normality in the marginal synovium compared to the rest (larger) part of the joint capsule in antigen-suppressed rats was previously revealed.
Objectives: A comparative analysis of the distribution of lymphocytes, macrophages and mast cells in the marginal synovium in relation to the rest (larger) part of the joint capsule after antenatal antigenic stimulation was conducted.
Methods: Collection of the biomaterial was carried out on the first, seventh, 14th, 30th, 45th, 60th and 90th day of postnatal life under general anesthesia (intact, antigen-suppressed and control rats; six rats in each group, 126 rats in total). The joints were fixed, decalcified and dehydrated. Paraffin-embedded tissue sections were stained with hematoxylin and eosin. Cells of the synovial subintima of the marginal synovium and rest (larger) part of the joint capsule were counted using the light microscopy (x100) and morphometric lattice. The obtained data were processed using the statistical methods. The parameters of intact and control rats did not differ significantly from each other.
Results: In the joint capsule of antigen-suppressed rats compared to intact and control rats, an increased number of lymphocytes till the 90th day (in the marginal synovium – till the 45th day), macrophages till the seventh day (in the marginal synovium – also till the seventh day) and mast cells till the 90th day (in the marginal synovium – till the 14th day) was found. The integrity of the synovium-cartilage barrier is of fundamental importance, failing which it would lead to excessive synovial tissue penetration into the articular cartilage, recognition of it by immunocompetent cells and initiation of immune-mediated cartilage destruction. The previously premature appearance (on the seventh day) of strong expression of receptors for peanut agglutinin (PNA) in the marginal cartilage of antigen-suppressed rats I detected could lead to the assumption about the premature appearance of "chondroprotective substances" such as fibronectin, laminin etc. and their intensive glycosylation. This fact might be considered a compensatory mechanism to create the „defensive wall" for adhesion and deactivation of the immunocompetent cells, therefore reducing their influence on cells and contributing to accelerated return the parameters to normality.
Conclusion: The compensatory defence mechanisms, occurring in the marginal cartilage after the antigenic stimulation, contribute to earlier recovery of parameters in the marginal synovium compared to the joint capsule in general. In so doing, the marginal transitional zone forms the important innate, nonspecific, immunobiological, anatomical and physiological barrier between the joint capsule and articular cartilage.
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Disclosure of Interests: None declared
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AB0057 REGULATION OF TYPE I INTERFERON SIGNATURE BY VGLL3 IN THE FIBROBLAST-LIKE SYNOVIOCYTES OF RHEUMATOID ARTHRITIS

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Background: The upregulation of interferon (IFN)-stimulated genes (ISGs) induced by type I IFNs (namely type I IFN signature) in RA patients had implications in early diagnosis and prediction of therapy responses. However, factors that modulate the type I IFN signature in RA are largely unknown.
Objectives: To explore the involvement of VGLL3, a homologue of the vestigial-like gene in Drosophila and a putative regulator of the Hippo pathway, in the modulation of the type I IFN signature in RA.
Methods: FLS were isolated from RA and osteoarthritis patients. Expression of VGLL3 in the synovial tissues and FLS was analyzed by immunohistochemistry and PCR. RNA sequencing was performed in RA-FLS upon VGLL3 overexpression. The expression of ISGs was examined by PCR and Western blotting.
Results: VGLL3 was upregulated in the RA synovium and RA-FLS compared to OA. Overexpression of VGLL3 promoted the expression of ISGs in RA-FLS. The expression of STAT1 and MX1 was also upregulated in RA synovium compared to OA. The expression of STAT1 and MX1 was associated with the expression of VGLL3 in RA and OA patients. VGLL3 promoted the IRF3 activation, IFN-β1 expression, and IFN-β1 autocrine signaling in RA-FLS. VGLL3 also modulated the expression of the Hippo pathway molecules WWTR1 and AMOTL2, which mediated the regulation of IRF3 activation and IFN-β1 production by VGLL3 in RA-FLS.
Conclusion: VGLL3 drives the IRF3-induced IFN-β1 secretion in RA-FLS by inhibiting WWTR1 expression and subsequently promotes the type I IFN signature expression through autocrine IFN-β1 signaling.
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AB0058 SERUM ANTIGENOME PROFILING REVEALS DIAGNOSTIC MODELS FOR RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that leads to joint damage, systemic inflammation and early mortality. Though the precise molecular mechanism in the triggering immune response are not fully understood, the emergence of antibodies against self-antigens can serve as diagnostic biomarker. Multiple antigens have been confirmed. However, the profiling of serum antigen, antigenome, remains poorly known.
Objectives: The study aimed to investigate the serum antigenomic profiling and determine potential diagnostic biomarkers using label-free proteomic technology implemented with machine-learning algorithm.
Methods: We captured serum antigens from a cohort consisting of 60 RA patients (45 ACPA-positive RA patients and 15 ACPA-negative RA patients), sex- and age-matched 30 osteoarthritis patients and 30 healthy controls. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed. We then trained a machine learning model to classify RA, ACPA-positive RA and ACPA-negative RA based on proteomic data and validated in the cohort.
Results: We identified 62, 71 and 49 differentially expressed proteins (DEPs) in RA, ACPA-positive RA and ACPA-negative RA respectively, compared to OA and healthy controls. Among these DEPs, the pathway enrichment analysis and protein-protein interactions networks were conducted. Three panels were constructed to classify RA, ACPA-positive RA and ACPA-negative RA using random forest models algorithm based on the molecular signature of DEPs, whose area under curve (AUC) were calculated as 0.9949 (95% CI = 0.9792-1), 0.9913 (95%CI = 0.9653-1) and 1.0 (95% CI = 1-1).
Conclusion: This study presented serum antigen profiling of RA. Among them, three panels of antigens were identified to classify RA, ACPA-positive and ACPA-negative RA patients as diagnostic biomarkers.
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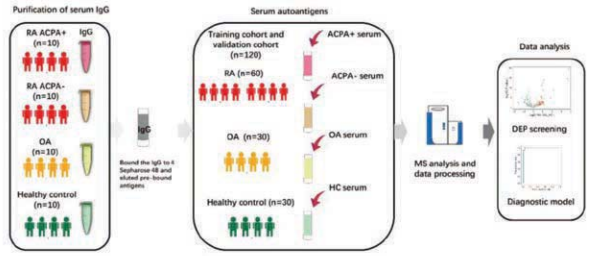

Figure 1. Study overview and antigenome characterization

Disclosure of Interests: None declared
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AB0059

SRC-LIKE ADAPTOR PROTEIN DEFICIENCY DOSE-DEPENDENTLY PROTECTS MICE AGAINST COLLAGEN-INDUCED ARTHRITIS

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Background: Src-like adaptor protein (SLAP), an adaptor between E3 ubiquitin ligase c-Cbl and the TCR complex, is a negative regulator of T-cell activation. SLAP regulates the expression of the CD3 ζ-chain. In accordance with our previous data, SLAP expression is increased in the CD4+ T-cells of patients with rheumatoid arthritis (RA). Recent data demonstrate that SLAP deficiency can prevent zymosan-induced arthritis in mice.
Objectives: We investigated the role of SLAP in collagen-induced arthritis (CIA).
Methods: Homozygous and heterozygous SLAP knock out and wild type (WT) C57BL/6J mice were used. After the isolation of genomial DNA, the genotype of the mice was determined. Then the animals were injected once (primary immunization) or twice (secondary immunization) with type II. collagen, or left untreated (the first injection was applied together with complete Freund's adjuvant). Mice were monitored twice a week for 70 days, and the severity scores were evaluated. The scores were calculated for each limb (1 limb score: 0=no swelling; 4=the severe swelling).
Results: SLAP deficiency provided almost complete protection from the primary immunization of CIA. By contrast secondary immunization led to similar arthritis of the SLAP-KO, heterozygous or WT mice.
Conclusion: The authors' present data suggest that SLAP deficiency protects dose-dependently from CIA.
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Disclosure of Interests: None declared
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AB0060

SYSTEMIC INFLAMMATORY EFFECT ON HIPPOCAMPAL VOLUME IN RHEUMATOID ARTHRITIS AND ULCERATIVE COLITIS

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Background: Autoimmune diseases represent a large and heterogeneous group of disorders that afflict specific target organs. However, multiple factors point to common links between the differing presentations of autoimmune disorders. With increased interest in further understanding the neuro-immune axis, autoimmune diseases represent an important opportunity to explore whether systemic inflammation from these autoimmune pathways has a central effect and, if so, whether there is a common or discrete central effect caused by different autoimmune diseases.
Objectives: The present study aimed to analyse hippocampal volume in patients with rheumatoid arthritis (RA) and ulcerative colitis (UC) as compared to healthy control groups. The hippocampus was chosen as a region of interest given the regulatory role it exhibits in the hypothalamic–pituitary–adrenal (HPA) axis[2]. Additionally, the hippocampus has been identified as a region that is affected in other autoimmune diseases such as systemic lupus erythematosus (SLE).
Methods: Data from 1,040 individuals in the UKBiobank Imaging sub-study were included in the present study. This was divided into two separate patient populations with separate control groups. Data from 267 individuals (mean age ± SD =65.52 ± 7.02, 70.8% females) were included in the RA patient group with 267 age and sex matched controls (mean age ± SD = 65.51 ± 7, 70.8% females). Data from 253 individuals (mean age ± SD = 64.09 ± 7.03, 51.6% females) were included in the UC patient group with 253 age and sex matched controls (mean age ± SD = 63.4 ± 7.02, 51.6% females).
The UKBiobank is a prospective observational study with a proposed cohort of 500,000 participants. The imaging substudy is planned to scan 100,000 of those participants with a standardised scanning protocol including MRI of the brain. Multi-modal images were acquired on a 3T scanner[3]. From the T1w data, volumetric imaging derived phenotypes (IDPs) are provided using the FMRIB Integrated Registration and Segmentation Tool (FIRST); http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIRST. This study utilised the right and left hippocampal volume outputs from that tool.
Results: We observed a smaller hippocampal volume in UC patients when compared to healthy controls (difference right: 99.78 mm^3, SD ± 38.97, p = 0.01; left: 74.30 mm^3, SD ± 39.41, p = 0.06). The Cohen's effect size was *d* = -0.24 [95% CI -0.43, -0.05] for right hippocampal volume and *d* = -0.18 [95% CI -0.36, 0.00] for left hippocampal volume.

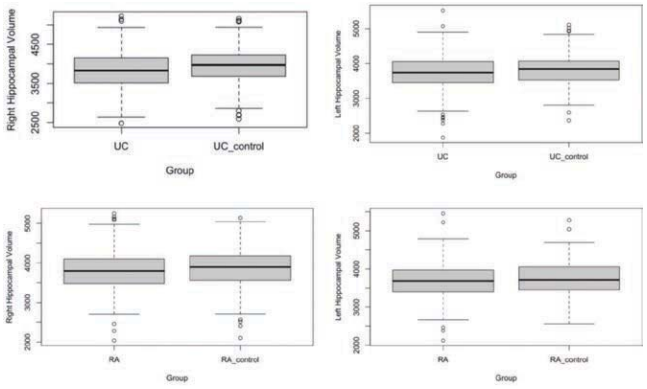

Figure 1. Right and left hippocampal volume in UC patients versus controls and right and left hippocampal volume in RA patients versus controls.

There was no significant difference seen in hippocampal volume in RA patients compared to controls (difference right: 61.32 mm^3, SD ± 40.33, p = 0.13; left: 39.00 mm^3, SD ± 38.19, p = 0.31). The Cohen's effect size was *d* = -0.12 [95% CI -0.30, 0.06] for right hippocampal volume and *d* = -0.08 [95% CI -0.27, 0.10] for left hippocampal volume.
Conclusion: This study provides evidence of moderate reduction in hippocampal volumes in patients with ulcerative colitis as compared to age and sex matched healthy controls. This same effect was not seen in a similarly matched rheumatoid arthritis patient population. Further analysis of additional subcortical regions could provide further context for whether there are alternative regions affected in both RA and UC.
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de Groot Shareholder of: Employee of GlaxoSmithKline, Employee of: Employee of GlaxoSmithKline, James Cole: None declared, Steven Williams: None declared
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AB0061 PHARMACOKINETICS OF METHOTREXATE POLYGLUTAMATES IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF RA PATIENTS IS SIMILAR AFTER SUBCUTANEOUS OR ORAL ADMINISTRATION IN THE METHOTREXATE MONITORING (MEMO) TRIAL

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Background: Pharmacokinetics of methotrexate (MTX) after oral and subcutaneous administration to RA patients differs: MTX levels in plasma and MTX-polyglutamate (MTX-PG) accumulation in erythrocytes are higher during equidosed subcutaneous compared to oral MTX treatment. (1,2) No data are available whether administration route of MTX differentially impacts the intracellular concentrations of MTX-PGs in peripheral blood mononuclear cells (PBMCs) during MTX therapy.
Objectives: To investigate the pharmacokinetics of MTX-PGs in PBMCs of newly diagnosed RA patients receiving oral or subcutaneous MTX in the early phase (1, 2, 3 and 6 months) of MTX treatment.
Methods: In a clinical prospective cohort study (MeMo study (NTR7149)), RA patients were
administered oral (n=24) or subcutaneous (n=22) MTX up to 25 mg MTX/week, as described before. (1) At 1, 2, 3 and 6 months after the start of therapy, PBMCs were isolated via Ficoll density gradient centrifugation. Individual MTX-PG forms ($MTX\text{-}PG_{1\text{-}6}$) in PBMCs were analyzed by a UPLC-MS/MS method including custom-made stable isotopes of $MTX\text{-}PG_{1\text{-}6}$ as internal standards (3). UPLC-MS/MS measurements of the PBMCs were performed with a Waters Acquity BEH C18 column coupled to an AB Sciex 6500+ with the ESI operating on the positive mode. Dosing, concomitant treatments and DAS28-ESR assessments were in conformity with clinical practice. (4)
Results: 46 consecutive patients were included in this study; 76% female, mean age: 57.8 years, BMI: 25.8, smokers: 20%, mean baseline DAS28-ESR: 3.5, as described before. (1) MTX dose at baseline was 10.5 mg (SD: 1.5) for both groups, 15.4 mg (4.4) and 16.8 mg (1.8) at 1 month, 22.8 mg (3.9) and 22.4 mg (5.2) at 2 months, 20.1 mg (6.3) and 20.8 mg (5.6) at 3 months, and 19.7 mg (6.1) and 18.5 mg (6.7) at 6 months for oral and subcutaneous use, respectively. MTX-PG analyses in PBMCs for individual and total MTX-PGs revealed no significant differences between oral and subcutaneous administration groups at 1, 2, 3, and 6 months (Figure 1). Linear regression of LN transformed MTX-PG levels in PBMCs and administration route, corrected for age, baseline DAS28, smoking, BMI, eGFR and MTX dose, showed a trend towards higher MTX-PG levels in PBMCs after subcutaneous MTX administration compared to oral administration (data not shown). MTX-PG distribution in PBMCs was mainly composed of $MTX\text{-}PG_1$ (58%), and to a lesser extent $MTX\text{-}PG_2$ (27%) and $MTX\text{-}PG_3$ (15%). Longer chain MTX-PGs beyond $MTX\text{-}PG_4$ were detectable in PBMCs, but at levels lower than $MTX\text{-}PG_{1\text{-}3}$ (mean: 4.0 – 6.7 fmol/10^6 cells). Total MTX-PG accumulation in PBMCs was approximately 10-20 fold higher than in erythrocytes. PBMC accumulation was rather stable, whereas RBC MTX-PG accumulation increased between 1 to 3 months to reach a plateau (Figure 1).

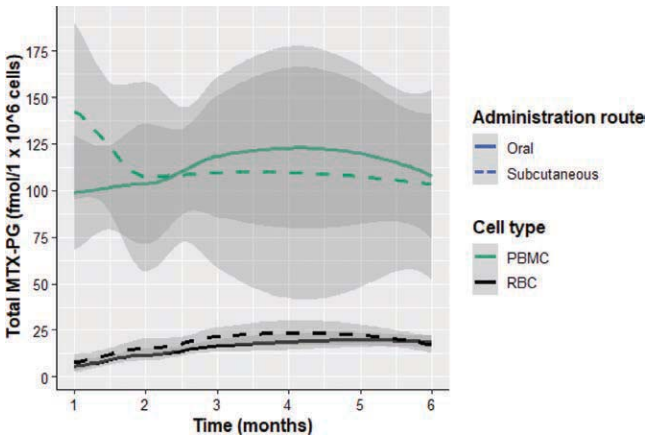

Figure 1. Loess regression of MTX-PG concentrations in PBMCs (MTX-PG1-3) and RBCs (MTX-PG1-6) of RA patients during the first 6 months of oral or subcutaneous MTX administration. At 6 months, 18 patients using oral and 18 patients using subcutaneous MTX were still continuing MTX treatment. Means (lines) and SE (grey areas) are depicted.

Conclusion: This study demonstrated that MTX-PG accumulation in PBMCs early on in the MTX treatment of RA patients was not significantly different between oral or subcutaneous MTX administration routes.
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AB0062 ANGIOTENSIN CONVERTING ENZYME ACTIVITY IN ANTI-TNF-TREATED RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS PATIENTS

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Background: Angiotensin-converting enzyme (ACE) and ACE2 have been implicated in the regulation of vascular physiology. Elevated synovial and decreased or normal ACE or ACE2 levels have been found in rheumatoid arthritis (RA). Very little is known about the effects of tumour necrosis factor α (TNF-α) inhibition on ACE or ACE2 homeostasis.
Objectives: In this study, we assessed the effects of one-year anti-TNF therapy on ACE and ACE2 production in RA and ankylosing spondylitis (AS) in association with other biomarkers.
Methods: Forty patients including 24 RA patients treated with either etanercept (ETN) or certolizumab pegol (CZP) and 16 AS patients treated with ETN were included in a 12-month follow-up study. Serum ACE levels were determined by commercial ELISA, while serum ACE2 activity was assessed using a specific quenched fluorescent substrate. Ultrasonography was performed to determine flow-mediated vasodilation (FMD), common carotid intima-media thickness (ccIMT) and arterial pulse-wave velocity (PWV) in all patients. In addition, CRP, rheumatoid factor (RF) and ACPA were also measured. All assessments were performed at baseline and 6 and 12 months after treatment initiation.
Results: Anti-TNF therapy increased ACE levels in the full cohort, as well as in the RA and AS subsets. ACE2 activity increased in the full cohort, while the ACE/ACE2 ratio increased in the full cohort and in the RA subset ($p<0.05$). Uni- and multivariable regression analyses determined associations between ACE or ACE/ACE2 ratios at different time points and disease duration, CRP, RF, FMD and IMT ($p<0.05$). ACE2 activity correlated with CRP. The changes of ACE or ACE2 over 12 months were determined by treatment together with either RF or FMD ($p<0.05$).
Conclusion: Anti-TNF treatment may increase ACE and ACE2 in the sera of RA and AS patients. ACE and ACE2 may be associated with disease duration, markers of inflammation and vascular pathophysiology. The effects of TNF inhibition on ACE and ACE2 may reflect, in part, the effects of these biologics on the cardiovascular system.
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AB0063

AMPA CANNOT BE DETECTED IN FAECES OF SEROPOSITIVE RA PATIENTS: NO EVIDENCE FOR LOCAL AMPA PRODUCTION IN THE LOWER GASTRO-INTESTINAL TRACT

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Background: Rheumatoid arthritis (RA) patients harbor antibodies against several post-translational modifications (AMPA), for example anti-citrullinated protein antibodies (ACPA) and anti-acetylated protein antibodies (AAPA). The exact mechanism underlying the development of these autoantibodies is currently unclear, but the mucosal immune system has been hypothesized to play a role. ACPA IgA have been detected in sputum and saliva of seropositive RA patients (1-2), suggesting local production of autoantibodies in the lung and oral mucosa. This raises the question whether ACPA can also be produced at other mucosal sites. The intestines are an interesting candidate, as microbiome dysbiosis has been described in RA patients and intestinal content may represent a source of post-translationally modified antigens. However, it is currently unknown whether AMPA are also produced locally in the intestine.
Objectives: To determine whether AMPA are produced locally in the intestine, we set out to detect ACPA and AAPA in faeces samples of seropositive RA patients. These findings were compared to the ACPA/AAPA levels found in paired serum and saliva samples of the same patients.
Methods: Paired faeces, saliva and serum samples of 16 established seropositive RA patients and 16 healthy volunteers were collected. All patients fulfilled the ACR/EULAR 2010 criteria. Saliva was collected using the passive drooling method. Faeces was self-collected by participants at home and immediately frozen. Faeces samples were homogenized in PBS containing protease inhibitors and supernatants were used in ELISA. Saliva was diluted 1:4. Total IgA and anti-E. Coli IgA were measured using commercial and in-house ELISA, respectively. ACPA/AAPA IgA (serum, saliva) and ACPA/AAPA Ig (faeces) were detected using in-house ELISAs, coated with citrullinated and acetylated CCP2 or the unmodified arginine and lysine variants as control. Saliva samples were considered AMPA positive when the value was above the cut-off (mean + 2 times standard deviation of healthy donors) and the delta OD between the modified and unmodified peptide was larger than 0.1.
Results: 9/16 ACPA IgG-positive RA patients were also ACPA IgA positive in serum. In the faecal supernatants total IgA was clearly detectable by ELISA: the supernatants contained on average 85 µg/ml total IgA, only slightly less compared to the mean 117 µg/ml total IgA found in the pre-diluted saliva. However, in none of the faecal supernatants ACPA Ig could be detected. Differences in optical density (OD) between the CCP2 and unmodified arginine peptide were close to 0 (Figure 1A). On the contrary, 8 RA patients were positive for ACPA IgA in saliva (Figure 1B). Similar results were found for AAPA (Figure 1C-D). To control whether the lack of an AMPA signal is explained by technical difficulties associated with measuring IgA in an antigen-specific manner in faeces, we determined anti-E. Coli IgA in the same samples. Anti-E. Coli IgA was clearly detectable in 11/32 faeces samples, indicating intact antigen-specific IgA was present in the faecal samples (Figure 1E).

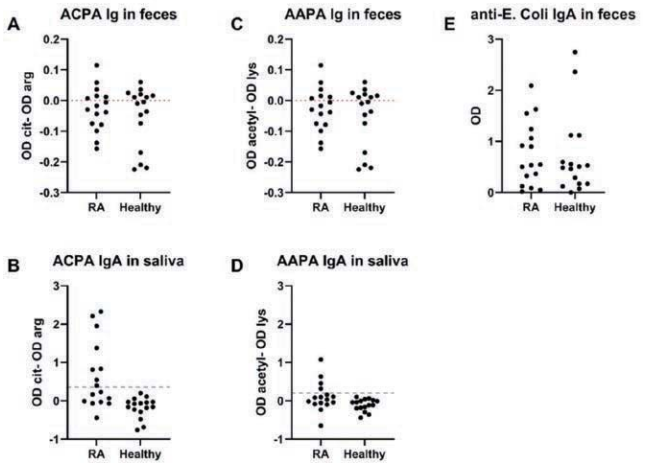

Figure 1.

Conclusion: No ACPA or AAPA Ig antibodies could be detected in faeces of RA patients, even though these patients were positive for ACPA/AAPA IgA in both serum and saliva. The fact that it was possible to detect other antibodies in faeces, indicates that the absence of an AMPA signal is not due to inherent methodological issues. These findings indicate that the lower gastro-intestinal tract does not contain measurable levels of AMPA IgA and suggest that it is not a main site of ACPA production in RA patients.

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AB0064

PHARMACOLOGICAL INHIBITION OF IL-6/JAK/STAT AXIS INCREASES MUSCLE MASS IN AN EXPERIMENTAL MODEL OF SARCOPENIA ASSOCIATED TO RHEUMATOID ARTHRITIS

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Background: Sarcopenia is a frequent comorbidity of rheumatoid arthritis (RA) due to an imbalance in muscle remodelling with dominance of catabolism over anabolism. IL-6/JAK/STAT axis is of particular importance in this regulation because of its dual activity. According to local and acute factors, it promotes muscle healing and hypertrophy, whereas in chronic inflammation, this signalling substantially increases muscle catabolism activating pro-atrophic pathways involving atrogene expression and ubiquitin proteasome system (UPS). JAK/STAT blockade suppresses muscle wasting induced by IL-6, through STAT3 activation. Interestingly, different clinical trials have shown that JAK inhibitors produce an asymptomatic increase in serum creatine kinase (CK) and creatinine levels in RA patients, suggesting an impact on muscle.
Objectives: To evaluate the effect of JAK inhibition and its effect in muscle remodelling in an experimental model that accurately mimics human rheumatoid sarcopenia.
Methods: An experimental model of antigen-induced arthritis (AIA) was carried out in 14 rabbits by immunization against ovalbumin followed by 4 intra-articular (i.a) injections of this protein. One week after the first i.a injection, 7 of these rabbits received tofacitinib (TOFA, orally 10mg/kg/day) for 2wk. Animals were euthanized one day after the last i.a injection, when tibialis anterior (TA), extensor digitorum longus (EDL) and gastrocnemius (GN) were isolated from both hind limbs. Histological changes and ATPase staining were analysed in TA, while the number of myonuclei was evaluated in EDL fibres by immunofluorescence studies. C-reactive protein (CRP) and myostatin (MSTN) serum concentration were determined by ELISA. The gene expression of proinflammatory cytokines (IL-1β, IL-6, TNF-α, MCP-1), atrogenes (Atrogin-1, MuRF-1) and MSTN was measured by quantitative PCR, while proliferative muscle marker (PAX-7), differentiation muscle markers (MyoD, Myogenin), pSTAT3, pSTAT1, MSTN and CK protein expression was analysed by western blot in GN. Creatine presence in GN was analysed by a colorimetric assay.
Results: A significant increase in body weight was observed in the AIA+TOFA group vs. AIA at the end of the study. A significant increase in TA cross-sectional area and diameter in the AIA+TOFA, in comparison to AIA, was found, while the decrease in the area of type II fibres observed in the AIA animals was not noticed in AIA+TOFA. Moreover, the number of myonuclei in the EDL that was increased in the AIA group when compared to healthy animals, was significantly decreased in AIA+TOFA. However, systemic inflammation measured by CRP was not modified by TOFA treatment at the end of the study, in comparison to AIA, and so did serum MSTN concentration. TOFA evoked a significant reduction in the gene expression of IL-6, MCP-1, atrogin-1 and MuRF-1 in GN in comparison to untreated AIA rabbits. Notably, AIA+TOFA showed higher protein levels of CK and lower creatine compared to AIA in muscle. Simultaneously, no differences in the proliferative marker PAX-7 were found between groups, while AIA rabbits showed an increase in the differentiation markers MyoD and Myogenin in the muscle that was prevented in AIA+TOFA.
Conclusion: These data provide novel insights into the effects of JAK inhibitors in muscle remodelling during rheumatoid cachexia. Despite an elevated systemic inflammatory status, JAK inhibition was able to rapidly increase muscle mass through attenuating IL-6/JAK/STAT activation, decreasing atrogene expression, and restoring to baseline the muscle cell differentiation markers in the tissue. The increase in muscle mass was accompanied by an increase in CK presence, supporting the role of CK as a valuable marker of muscle gain following treatment with JAK inhibitors. However, the low levels of MCP-1 and the disorganization of muscle fibre myonuclei raise the question of whether these treatments could trigger a complete regeneration of muscle fibre cell or just hypertrophy of cells already present.
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AB0065

ASSOCIATION OF SERUM LEVELS OF NESFATIN-1 WITH RHEUMATOID ARTHRITIS ACTIVITY AND ANXIETY-DEPRESSIVE DISORDERS

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Background: Rheumatoid arthritis (RA) is primarily associated with pain levels and limited function. Depressive disturbances and anxiety levels are not usually assessed, the focus is on the physical aspects of the disease. At the same time, patients with high disease activity often experience a decrease in body weight and lack of appetite, which is referred to as rheumatoid cachexia. Nesfatin-1 (NF-1), discovered as an anorexigenic protein. The participation of NF-1 in the regulation of eating behavior and reactions to emotional stress together with oxytocin, melatonin, serotonin, and histamine receptors has been proven. Elevated levels of NF-1 are detected in more severe forms of depression, correlating with the level of inflammation markers - C-reactive protein and interleukin-6. Recent work confirms an increase in NF-1 levels in RA, although its role in inflammation has not yet been clearly defined.
Objectives: To determine the correlation of the level of NF-1 in the blood serum of patients with RA with the level of anxiety and depression.
Methods: 110 patients with RA were examined. NF-1 level concentration was determined by indirect enzyme-linked immunosorbent assay (RaiBiotech, cat no. EIA-NESF). The PHQ-9 scale was used to assess the severity of depressive symptoms, and the GAD-7 scale was used to assess the severity of anxiety symptoms.
Results: Mood disorders of varying severity were detected in 48% of patients with RA. The highest levels of NF-1 were found in patients with high RA activity according to DAS-28 and disease duration of more than 10 years. The level of anxiety was more correlated with the severity of the disease activity ($r = 0.351$; $p<0.01$), and the level of depression was more correlated with the duration of the disease ($r = 0.273$; $p<0.01$).
Conclusion: In our study depression and high levels of anxiety were found in 48% of patients with RA, which is consistent with well-known data (the prevalence of mood disorders in RA ranges from 30 to 75%). The severity of depression and anxiety correlates with the level of NF-1, the frequency of occurrence depends on the activity and duration of the disease.
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AB0066

EFFECT AND MECHANISM OF QINXITONG ON BIOLOGICAL BEHAVIOR OF SYNOVIAL FIBROBLASTS IN RHEUMATOID ARTHRITIS

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Background: Chinese medicine has been used widely for the treatment of RA for a long history in China. The Fifth Hospital of Xi'an has treated patients of RA with QinXiTong(QXT) for 40 years which is mainly based on the water extract from Caulis Sinomenii(CS). However, the molecular mechanism of its anti-rheumatism effect remains unclear.
Objectives: To investigate the effects of Qinxitong on proliferation, apoptosis, migration and invasion of synovial fibroblasts in rheumatoid arthritis and its mechanism.
Methods: Taking rheumatoid arthritis synovial fibroblast cell line MH7A as the research object. The cells were divided into four groups according to the different dosage of Qinxitong intervention, namely control group, low dose group (QXT-20), medium dose group (QXT-50) and high dose group (QXT-100). CCK-8 assay was used to detect cell proliferation, flow cytometry was used to detect cell apoptosis, Transwell assay was used to detect cell migration and invasion, and Western blotting was used to detect total Erk protein (t-Erk) and phosphorylated Erk protein (p-Erk) expression levels.
Results: CCK-8 assay showed that Qinxitong could inhibit the proliferation of MH7A cells, compared with the control group, cell proliferation in QXT-50 and QXT-100 groups was significantly reduced ($p<0.05$) after 24h, 48, and 72h intervention, the effect of QXT-100 was even more significant ($p<0.001$); flow cytometry showed that QXT could promote apoptosis of MH7A cells, compared with the control group, the apoptosis rate of QXT-50 and QXT-100 groups was significantly increased ($p<0.05$); Transwell assay showed that QXT could inhibit the migration and invasion of MH7A cells, compared with the control group, the QXT-50 and QXT-100 groups showed significantly higher inhibition of migration and invasion of MH7A cells ($p<0.05$); Western blotting showed that QXT could reduced p-Erk expression level, compared with the control group, the decrease of p-Erk expression level in QXT-50 and QXT-100 groups was statistically significant ($p<0.001$).
Conclusion: Qinxitong can inhibit the proliferation, promote apoptosis, inhibit migration and invasion of rheumatoid arthritis synovial fibroblasts by regulating Erk signaling pathway, providing scientific basis for clinical application of Qixintong.
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AB0067

INTERLEUKIN-1 RECEPTOR ANTAGONIST: RELATION TO CARDIOVASCULAR DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The interleukin-1 receptor antagonist (IL1-Ra) belongs to the IL-1 family. IL1-Ra has an inhibitory function on the inflammatory reaction consisting of preventing the binding of IL-1α and β to their respective receptors. IL-1, in its different subtypes, has been implicated in the pathogenesis of both rheumatoid arthritis (RA) and cardiovascular disease (CV) in the general population.
Objectives: In the present work we aim to study the relation of IL1-Ra serum levels to RA's features, and its CV comorbidity and subclinical carotid atheromatosis in a large RA cohort.
Methods: This was a cross-sectional study that included 430 RA patients. A complete panel of clinical and analytical information related to CV disease was collected: CV risk factors, full lipid profile, insulin and C-peptide serum levels, insulin resistance and β-cell function (%B) indexes by Homeostatic Model Assessment (HOMA2). A carotid ultrasound examination was performed to assess carotid intima-media thickness in the common carotid artery and to detect focal plaque in the extracranial carotid tree. Similarly, IL1Ra and IL-6 serum levels were assessed and disease activity indices, extra-articular manifestations and RA therapies were collected. A multivariable regression analysis was performed to determine how IL1Ra serum levels is associated with disease-related characteristics, CV comorbidity and subclinical atheromatosis in RA patients.
Results: Regarding CV risk factors, IL1-Ra serum levels were related with waist circumference (coefficient beta -β- 8 [95% confidence interval -CI- 5-11] pg/ml, $p<0.001$) and obesity (body mass index >= 30 kg/m2) (β 169 [95% CI 78-260] pg/ml, $p<0.001$). After adjusting for confounders, IL1-Ra was related with higher levels of several lipid profile molecules, such as total cholesterol (β 12 [95%CI 2-22] mg/dl, $p=0.023$), apolipoprotein A1 (β 13 [95% CI 0.5-25] mg/dl, $p=0.042$) and apolipoprotein C3 (β 3 [95% CI 2-5] mg/dl, $p<0.001$). Furthermore, higher IL1-Ra serum levels were associated with pancreatic beta cell dysfunction as measured by HOMA2-%B (β 22 [95%CI 2-42], $p=0.031$). Disease activity using different scores showed a positive relationship with IL1-Ra after multivariable adjustment: DAS28-ESR (β 60 [95% CI 28-92] pg/ml, $p<0.001$), DAS28-PCR (β 65 [95%CI 26-104] pg/ml, $p=0.001$) and CDAI (β 99 [95%CI 3-14] pg/ml, $p=0.002$). Likewise, ESR (β 2 [95% CI 0.07-5] pg/ml, $p=0.044$) and IL-6 plasma levels (β 3 [95% CI 1-6] pg/ml, $p=0.003$) were positively associated with IL1-Ra levels after adjusting for covariates. Hydroxychloroquine use, but not other therapies, was associated with lower IL1-Ra serum levels (β -131 [95% CI -260- -2] pg/ml, $p=0.046$), independently of confounding variables. No association was found between IL1-Ra and intima-media thickness or carotid plaque.
Conclusion: In RA patients, IL1-Ra serum levels are related to the clinical and biological disease activity, as well as with different CV comorbidities such as dyslipidemia, beta cell dysfunction and obesity. Our findings highlight the beneficial effect that blocking IL-1 activity can have both in the control of RA disease activity and in the management of the CV disease that accompanies the disease.
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AB0068

INTERLEUKIN 40 SERUM LEVELS ARE ELEVATED IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AND ASSOCIATE WITH NEUTROPHIL ACTIVATION

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Background: IL-40 is a newly described cytokine associated with immune system function and malignant transformation. We have recently shown that IL-40

is up-regulated in rheumatoid arthritis (RA) and associates with disease activity, autoantibodies and NETosis[1].

Objectives: As autoantibodies and neutrophil activation are factors thought to drive the pathological processes at early phase of RA development, we aimed to investigate IL-40 in relation to neutrophils and early stages of RA (ERA).

Methods: The levels of serum IL-40 were determined in a cohort of treatment naïve patients with ERA at baseline (n=60) and three months after initiation of conventional treatment (n=60). Serum IL-40 was also determined in sex- and age- matched healthy controls (n=60). Levels of IL-40, cytokines and NETosis markers (proteinase 3, PR3 and neutrophil elastase, NE) were measured by commercially available ELISA kits. The levels of autoantibodies were analysed by routine laboratory techniques. *In vitro* experiments were performed on peripheral blood neutrophils from patients with ERA (n=15).

Results: Levels of IL-40 were elevated in ERA patients at baseline compared to healthy controls ($p<0.0001$) and normalised after three months of the treatment ($p<0.0001$). Baseline serum IL-40 was associated with the levels of autoantibodies RF (IgM) ($p<0.01$) and anti-CCP ($p<0.01$) and markers of NETosis PR3 and NE) (both $p<0.0001$). Moreover, significant decreases in the serum IL-40 following the therapy correlated with the decrease of NETosis markers PR3 ($p<0.01$) and NE ($p<0.05$). *In vitro*, neutrophils from patients with ERA significantly enhanced the release of IL-40 following NETosis induction ($p<0.05$) or after exposure to pro-inflammatory cytokines such as IL-1β, IL-8 ($p<0.05$), TNF ($p<0.01$) or to LPS ($p<0.05$). Lastly, recombinant IL-40 induced the secretion of IL-1β ($p<0.05$) and TNF ($p<0.05$) by ERA neutrophils.

Conclusion: We demonstrated for the first time that IL-40 is upregulated in ERA and decreases after three months of conventional therapy. Moreover, we showed that neutrophils are an important source of IL-40 in RA and its release is potentiated by pro-inflammatory cytokines and NETosis. Our results suggest that IL-40 may play an important role in early stages of RA.

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AB0069 ASSOCIATION OF NUCLEAR FACTOR OF ACTIVATED T CELLS CYTOPLASMIC 1 (NFATC1) EXPRESSION WITH CARDIOVASCULAR RISK IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Nuclear factor of activated T cells (NFAT) is a transcription factor family that plays a crucial role in physiological and immune processes, modulating intracellular and extracellular signaling pathways related with several diseases[1,2]. In this regard, it has been involved in the pathogenesis of rheumatoid arthritis (RA) and in the development of cardiovascular (CV) disease[3-5]. Given that CV disease is one of the main causes of morbidity and mortality in patients with RA[6], functional studies focused on the implication of *NFAT* in CV disease in RA are of potential interest.

Objectives: To study the role of the gene expression of two members of the NFAT family, *NFATc1* and *NFATc2*, in the risk of developing CV disease in patients with RA.

Methods: A total of 79 disease-modifying antirheumatic drug-naïve patients with early RA[7] from Hospital Universitario Marqués de Valdecilla (Santander, Spain) were included in this study. The relative mRNA expression of *NFATc1* and *NFATc2* in peripheral blood was determined by qPCR. Carotid ultrasound data were used as surrogate markers of subclinical atherosclerosis. The association between *NFATc1* and *NFATc2* expression in RA patients and their clinical characteristics was evaluated. Results were adjusted by sex, age at the time of the study and traditional CV risk factors.

Results: A statistically significant increase of *NFATc1* mRNA expression was found in women compared to men (fold change=+1.18, $p=0.035$). In addition, a higher *NFATc1* mRNA expression was observed in patients with dyslipidemia compared to those with normal lipid profile (fold change=+1.18, $p=0.006$). With respect to this, we also disclosed a positive correlation between *NFATc1* mRNA expression and low-density lipoprotein cholesterol levels ($r=0.27$, $p=0.039$). No significant associations were detected between *NFATc2* mRNA expression and clinical characteristics of our RA patients. Carotid ultrasound findings were not related to *NFATc1* and *NFATc2* expression.

Conclusion: Our study suggests that a higher expression of *NFATc1* in peripheral blood is associated with abnormalities in the lipid profile and, consequently, with an increased risk of CV disease in patients with early RA.

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AB0070 INHIBITION OF STAT3 IN PBMCS FROM RHEUMATOID ARTHRITIS PATIENTS: CLUES TO UNDERSTAND SELECTIVITY OF JANUS KINASE INHIBITORS

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Background: The Janus kinase (Jak) - signal transducer and activator of transcription (STAT) pathway has 4 Jak proteins and 7 STAT factors that mediate intracellular downstream of cytokine receptors. Targeted small-molecule therapies with different bond affinity to Jak proteins have been demonstrated effective in rheumatoid arthritis (RA) treatment, but the clinical significance of selective inhibition remains unclear.

Objectives: To explore the effect of selective inhibition of Jak-STAT pathway in peripheral blood mononuclear cells (PBMC) from RA patients compared to healthy donors (HD).

Methods: In vitro Jak inhibition of the subunit 3 of phosphorylated (p) than activated STAT was measured by flow cytometry in peripheral blood mononuclear cells (PBMC) from RA patients with active disease (DAS28>5.1) naïve to any DMARDs (n.5) and HD (n.5), following recombinant human 0.1 ng/ml IL-6 (Peprotech – NJ, USA) stimulation. After blood separation, PBMC were overnight incubated with IC50 concentrations of selective Jak1-, Jak2-, Jak3- and Tyk2-inhibitors (Biovision Inc. – CA, USA) with or without IL-6 stimulation. Mean fold-increase of pSTAT3 was then compared in presence of different compounds stimulation.

Results: Mean pSTAT3 activity after overnight incubation was significantly higher in RA patients compared to HD (37%; 95CI 8.2-56.7 vs 17.9%; 95CI 4.6-21 – $p=0.01$). After IL-6 stimulation, a 2-fold and a 1.4-fold increase in pSTAT3 levels was observed in PBMC from RA patients and HD, respectively. In unstimulated PBMC from HD Jak-inhibitors didn't significantly reduced pSTAT3 activity. In CD14+ cells from RA patients, pSTAT3 activity was reduced with no differences between all four selective Jak-inhibitors, while in CD4+ cells only Jak1-inhibition was able to reduce by 40% pSTAT3 activity. After IL-6 stimulation, the co-culture with Jak1- or JaK3- selective inhibitors was able to significantly reduce pSTAT3 levels in CD4+ lymphocytes, by an average of 20%. While in CD14+ monocytes Jak1-, Jak2- and Jak3- selective inhibitors were able to reduce pSTAT3 activity by a mean of 30%. Tyk-2 selective inhibitor did not interfere with STAT3 activation by IL-6 stimulation of PBMC from RA patients and HD.

Conclusion: Jak/STAT3 activity of PBMC from RA patients with active disease may be differently modulated by specific inhibitors. Selectivity of Jak-inhibitors seems more relevant in lymphocytes after IL-6 stimulation. These preliminary findings may explain discrepancies in effectiveness of selective Jak-inhibitors and pave the way for different choices in clinical practice.

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Disclosure of Interests: None declared

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AB0071 ANTI-ACETYLATED PROTEIN IGM-ANTIBODIES AS THE STARTING POINT OF AUTOANTIBODY FORMATION IN RHEUMATOID ARTHRITIS?

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Background: Anti-modified protein antibodies (AMPA) are an important hallmark of rheumatoid arthritis (RA) and the fact that they have consistently been found to develop years before disease onset, has provided important insights into the immunopathology underlying RA. In (auto)antibody development, IgM is the first isotype to be produced. However, it is unclear whether IgM-autoimmunity differs between AMPA targeting different post-translational modifications (citrulline, homocitrulline and acetylated residues), which could provide clues about the starting point of the AMPA response.

Objectives: We therefore investigated IgM-levels of anti-citrullinated protein antibodies (ACPA), anti-carbamylated protein antibodies (anti-CarP) and anti-acetylated protein antibodies (AAPA) in healthy individuals, non-RA and RA patients.

Methods: Autoantibodies were investigated in 2 cohorts:

1) a Japanese cohort of healthy individuals (community based Nagasaki Island study) known to be ACPA-positive (n=65) or ACPA-negative (n=197) were compared to Dutch healthy donors (n=30) and ACPA-positive RA patients (n=29). ACPA, anti-CarP and AAPA IgG were measured by ELISAs using CCP4, CHcitP4 and CAcetylP4 peptides with sequences similar to the commercial CCP2 antigen and native control peptides.

2) early arthritis patients from the Leiden Early Arthritis Clinic who had RA (n=648) or another form of arthritis (non-RA, n=555) and healthy controls (n=80). ACPA and AAPA were determined by ELISAs using CCP2 and cACP2 peptides and their native control peptides, while anti-CarP was measured on homocitrullinated versus native fetal calf serum. Mann-Whitney U-tests were performed for statistical comparisons.

Results: ACPA IgM reactivity was mainly present in established ACPA-positive RA patients (Figure 1A) and to a lesser extent in ACPA-positive healthy Japanese individuals, and non-RA arthritis patients (Figure 1D). A similar picture was observed for anti-CarP IgM reactivity, for which again highest levels were found in established RA patients (1B and 1E) and ACPA-positive compared to ACPA-negative healthy Japanese individuals (1B). Intriguingly, AAPA IgM reactivity-levels displayed a different pattern as these were comparable between healthy individuals and ACPA-positive RA patients (1C and 1F). Likewise, AAPA IgM reactivity-levels were also not increased in ACPA-positive healthy Japanese individuals, who instead had lower levels compared to their ACPA-negative counterparts. Furthermore, the AAPA IgM-reactivity levels did not differ between non-RA arthritis patients, healthy controls and RA patients (1F). AAPA IgG-levels on the other hand were clearly elevated in RA patients compared to healthy controls and non-RA arthritis patients (1G).

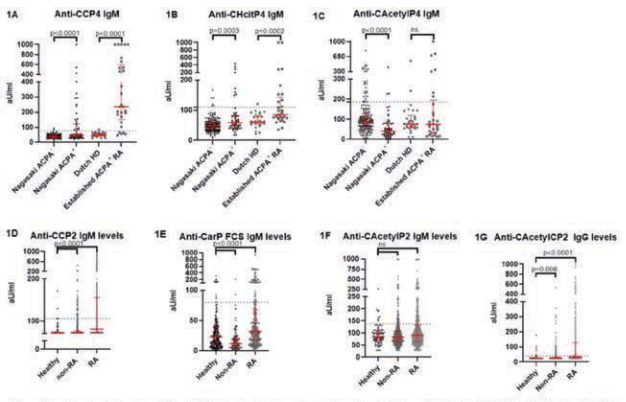

Figure 1. Levels of anti-modified protein antibodies (AMPA) in healthy individuals and rheumatoid arthritis patients. Figure 1A-C: levels of ACPA IgM (anti-CCP4), anti-CarP IgM (anti-CHcitP4) and AAPA (anti-CAcetylP4) IgM in healthy Japanese ACPA-negative and ACPA-positive individuals, as well as Dutch health donors (HD) and established ACPA-positive RA patients. Figure 1D-G: levels of ACPA IgM (anti-CCP2), anti-CarP IgM (anti-CarP FCS),AAPA (anti-CAcetylP2) IgM, AAPA (anti-CAcetylP2) IgG in Dutch healthy controls, non-RA arthritis patients and RA patients.

Conclusion: AAPA are exceptional compared to other AMPA because IgM AAPA-levels are similar among healthy individuals, non-RA arthritis and RA patients. This suggests that AAPA IgM is part of the "normal" immune repertoire and could constitute the starting point for RA-associated AMPA responses, with isotype switching and epitope spreading to other post-translational modifications leading to the typical RA-associated mature AMPA response.

Disclosure of Interests: None declared

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AB0072 GLUCOCORTICOIDS MODIFY NOT ONLY THE PROPERTIES OF DENDRITIC CELLS, BUT ALSO PROGENITOR CELLS

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Background: Dendritic cells (DCs) are universal antigen-presenting cells that can have both tolerant and immunosuppressive properties. Tolerogenic properties of DCs are mediated by activation T-regulatory cells, production of anti-inflammatory cytokines and activation T cell apoptosis. Currently, DC is an attractive object of study as a new treatment for rheumatoid arthritis. It is known that glucocorticoids make it possible to control properties of DCs to the tolerogenic side.

Objectives: The aim of the study is to investigate the effect of pulse therapy by glucocorticodes on the properties of DCs and peripheral blood monocytes from which DCs were generated.

Methods: Twenty five patients with rheumatoid arthritis were recruited in this study. All patients follow ACR/EULAR criteria (2010). All studies were performed after receiving informed consent. All patients received conventional synthetic DMARDs. DCs were generated from blood monocytes culturing for 5 days with GM-CSF and IFN-α, LPS as maturation stimuli was added on fourth day. The functions of DCs were evaluated by allostimulatory activity in mixed lymphocyte culture. The properties of DC were studied before pulse therapy (methylprednisolone 500mg №3) and 4 days after pulse therapy.The relative number of monocytes (classical $CD14^{++}CD16^{+}$, intermediate $CD14^{+}CD16^{+}$ and nonclassical $CD14^{+}CD16^{++}$) before and after pulse therapy was also studied in comparison with healthy donors.

Results: Prior to pulse therapy, the DCs from RA patients were characterized by a high ability to stimulate the proliferation of allogenic T-lymphocytes about 20000 cpm. After pulse therapy, the stimulating ability of DCs significantly decreased (9800 vs. 2000 cpm, p=0.04). Evaluation of the relative content of classical ($CD14^{++}CD16^{-}$), intermediate ($CD14^{++}CD16^{+}$) and nonclassical ($CD14^{+}CD16^{++}$) monocytes of healthy donors (n=18) and RA patients (n=25) revealed a decrease in the relative content of $CD14^{++}CD16^{-}$ cells in patients (Me 78 vs. 90%; p=0.02) and an increase in the proportion of $CD14^{++}CD16^{+}$ (Me 4.0 vs. 2.0%; p=0.034) and $CD14^{+}$ $CD16^{++}$ monocytes (Me 5.0 vs. 1.5%; p=0.02). After the end of pulse therapy in RA patients, the relative content of $CD14^{++}CD16^{-}$cells increased (89 vs. 78%), and the proportion of $CD14^{+}CD16^{++}$ monocytes decreased (1 vs. 5%), and RA patients no longer significantly differed in these indicators from healthy donors. Thus, a decrease in the content of $CD14^{+}CD16^{++}$ cells in the monocytes population after pulse therapy was associated with a decrease in the effectiveness of DCs generated to stimulate the proliferation of allogenic T cells.

Conclusion: The effect of pulse therapy of glucocorticoids is associated not only with the ability of glucocorticoids to inhibit the maturation of IFN-DC and induce their tolerant phenotype at the stage of differentiation of monocytes into DCs, but also with the effect on the subpopulation of circulating monocytes that are precursors of DC.

Disclosure of Interests: None declared

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AB0073 NEUTROPHIL EXTRACELLULAR TRAPS: COUPLING WITH RHEUMATOID ARTHRITIS FLARES AND ANTI-CITRULLINE AUTOANTIBODIES PERSISTENCE

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Background: Rheumatoid arthritis (RA) is characterized by dysregulation of the adaptive immune system. Detection of subcellular structures with localization of most typical citrulline-containing rheumatoid autoantigens in a single compartment is of special interest considering importance of anticitrulline autoantibodies for autoimmune response in RA. Neutrophil extracellular traps (NETs) can be suggested as a most likely candidate for the role of such structures.
Objectives: To study of peripheral blood neutrophils from RA to generate NETs, associated with diseases exacerbation.
Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles after the local ethical board approval. Circulating neutrophils were isolated with one-step density gradient centrifugation using double layers of ficoll-amidotrizoate gradient. Composition of isolated cellular fractions, their viability, and non-specific activation were evaluated by light microscopy using common Romanowsky-Giemsa staining, trypan blue exclusion test as well as NBT test. Neutrophil fractions contained minute percentages of impurities and low extents of activated and dead cells. NETs were induced by PMA. Spontaneous and induced formation of extracellular traps was assessed using fluorescence microscopy [1]. Results were presented as values (95%CI).
Results: 37 patients (6 males and 31 females, mean age 42.7 years) with verified RA according to the ACR/EULAR 2010 criteria were included in the study. RA disease activity at the inclusion timepoint shouldn't exceed 2.6 DAS28 points. 16 (15.4%) patients had subsequent increase of the DAS28 score above 3.2 at following visits (3, 8 and 12 months after the inclusion). 30 healthy volunteers (9 males and 21 females, mean age 37.2 years) were enrolled as a reference group. Mean proportions of spontaneous and induced NET formation by isolated neutrophils of inactive RA patients (DAS 28<2.6) were 6.0 (5.7-6.3)% and 26.9 (24.0-29.8)%, respectively. Active RA patients (DAS 28>3.2) had dramatic increase of the respective values: 16,6 (16,4-16,8)% and 38,0 (37,7-38,3)%.
Both active and inactive RA patients had significant increase of NET-generating neutrophils proportion comparing to the reference group as well as significant difference of both these parameters between active and inactive phase (p<0.05). The growth rate of spontaneous NET formation in the active RA was 183.8%, the respective value for induced NET formation was 46.7%. The growth rate of spontaneous NET formation is 3.9 times higher than the induced NET formation. Neutrophils from ACPA-positive RA patients were found to have increased spontaneous and induced NETs formation compared to ACPA-negative RA patients (p>0.05).
Conclusion: Thus, our study demonstrated a strong relationship between onset of RA flare and increase of spontaneous and induced NET formation by circulating neutrophils. There was also a clear distinction between ACPA negative and positive RA patients as to higher spontaneous and induced NET formation in the latter subgroup. The comparison using larger group of patients will magnify the differences above significance limit. Continued research in this direction can promote the development of new therapies of RA.
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DOI: 10.1136/annrheumdis-2022-eular.2620

AB0074 RAPAMYCIN INHIBITS IL-1B INDUCED RA SYNOVIAL FIBROBLAST ACTIVATION, AN EFFECT ASSOCIATED WITH ALTERATION IN THEIR METABOLIC PROFILE

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Background: Rheumatoid Arthritis (RA) is a common autoimmune disease characterized by systemic polyarthritis affecting the joints, most notably of the hands and feet. A fundamental feature of RA is inflammation within the synovial joint due to neo-angiogenesis which facilitates an influx of immune cells and release of pro-inflammatory mediators.
Objectives: In this study we investigate the effect of metabolic reprogramming on IL-1β regulation of stromal cell activation and invasiveness in RA.
Methods: Primary RA synovial fibroblasts (RAFLS) and human umbilical vein endothelial cells (HUVEC) were cultured with IL-1 β (2 ng/mL) alone or in combination with the metabolic inhibitor rapamycin (100nM). Pro-inflammatory cytokines IL-6, MCP-1 and Rantes were quantified by real-time PCR and ELISA. Cellular adhesion and network formation were quantified by adhesion binding assays and Matrigel invasion assays. pS6 (a surrogate marker of the mTOR pathway) was quantified by flow cytometry. Cellular bioenergetics was assessed using the Seahorse-XFe-technology and key glycolytic genes (HK2, PKM2, G6DP) were quantified by real-time PCR. YAP was measured by Western-Blot.
Results: IL-1β significantly induced secretion of IL-6 (p<0.05), MCP-1 (p<0.01) and Rantes (p<0.01) from RAFLS. IL-1β induced leukocyte adhesion to RAFLS (p=0.062) and HUVEC (p=0.051), in addition to an increase RAFLS and HUVEC network formation. This was accompanied by a change in the cellular bioenergetic profile of cells, where IL-1β increased the ECAR/OCR ratio in favour of glycolysis for RAFLS (p<0.05) and HUVEC, and induced the % frequency in the cell surface expression of pS6 on RAFLS. Rapamycin inhibited IL-1β -induced leukocyte adhesion and network formation in RAFLS (p<0.05; p<0.05 respectively) and HUVEC (p<0.05). Rapamycin inhibited IL-1β -induced Rantes secretion (p<0.05), no effect observed for IL-6 and MCP-1. Rapamycin also inhibited IL-1b-induce YAP protein expression which is involved in FLS invasive capacity through cytoskeletal rearrangement. This was accompanied by a shift in the metabolic profile from a glycolytic/energetic state back towards a more quiescent state.
Conclusion: Rapamycin inhibits IL-1β -induced pro-inflammatory mechanisms in key stromal cells involved in the pathogenesis of RA. Targeting metabolism may lead to new potential therapeutic or adjuvant strategies, particularly for those patients who have sub-optimal responses to current treatments.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.2642

AB0075 IDENTIFICATION OF NOVEL ACETYLATED ANTIGENS IN IMMUNE COMPLEXES OF SYNOVIAL FLUID FROM RA PATIENTS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by genetic predisposition and associated immunological features including the production of autoantibodies against various epitopes. Several pathways have been implicated in the induction of autoantibodies against novel epitopes through post-translational modifications such as citrullination, carbamylation and acetylation (1). However, the contributions of these anti-modified protein antibodies (AMPAs) in the pathogenesis and formation of immune complexes (IC) in the synovial fluid has not been fully uncovered.
Objectives: To analyze reactivity of monomeric and IC antibodies of RA patients to citrullinated, carbamylated and acetylated modified antigens in comparison to disease control group and healthy donors.
Methods: Synovial fluid (SF) was collected from 17 RA patients and 40 individuals from a disease control group (CG) including reactive arthritis and psoriasis arthritis. Paired serum and SF samples were used from 16 RA and 19 CG compared to serum from 70 healthy donors (HD). Immune complexes (IC) were purified from sera and SF by applying a technique using purified human C1q, which was immobilised on magnetic tosylactivated microparticles (Dynabeads M-280) according to the manufacturer's recommendations for activation of amine groups. Additionally, sucrose gradient centrifugation was used to fractionate SF and sera into 21 fractions and according to protein markers, protein G was used to isolate monomeric IgG from fractions 3-9 and IC IgG from fractions 11-22. ELISA kits for anti CCP-IgG, anti-mutated citrullinated vimentin (MCV)-IgG, anti-acetylated Lysine Antibody (anti-HC55)-IgG and anti-carbamylated vimentin (carbVim)-IgG were used to test reactivity against modified proteins. Extracted antigens from the IC were investigated with Western blot for specific modifications or individual antigens with the corresponding antibodies. Citrullinated and acetylated vimentin was identified as part of IC via mass spectroscopy. Purified AMPAs from serum or SF (isolated from IC or as soluble antibodies) were investigated on a custom-made LineBlot array containing 24 different antigens either citrullinated, carbamylated, acetylated or unmodified/native counterparts.
Results: Titers of anti-CCP, anti-MCV and anti-acetylated (anti-HC55) reactivity were higher in SF of RA patients compared to CG. AMPAs were detected in SF in IC as well as free antibodies. Some isolated IgG (monomeric and IC) showed reactivities against citrullinated and acetylated peptides that could not be detected in native samples. Surprisingly, in addition to citrullinated vimentin, the acetelylated form was also detected in the IC eluted fractions. Haptoglobin and fibrinogen fragments were identified as carbamylated modified proteins in small concentrations. The spectrum of identified acetylated proteins included human proteins such as histones as well as fragments of bacterial filament proteins. SF of RA patients showed reactivity against MCV and citrullinated desmin in LineBlot array.

Conclusion: AMPAs recognize different modified antigens and form immune complexes in the SF of RA patients. The elevated titer of anti-acetylated protein antibodies and the inclusion of its epitope in immune complexes in the synovium points to its contribution in the pathogenesis of RA.

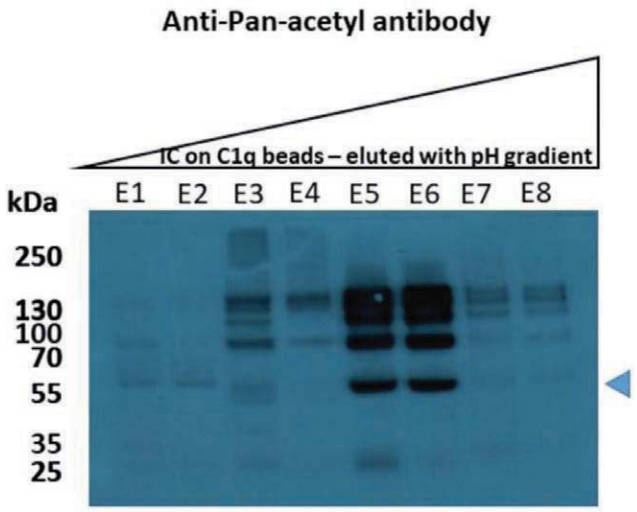

Figure 1. The identification of acetylated antigens in the synovium of RA patients is especially intriguing, as infections (bacteria) are known to not only acetylate their own proteins, but also modify host proteins.

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AB0076 DOES HELICOBACTER PYLORI HAVE AN IMPACT ON RHEUMATOID ARTHRITIS?

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Background: Rheumatoid arthritis (RA) is an autoimmune disease of not completely defined pathogenesis. A growing body of studies shows that microbiota may be a critical environmental trigger in the development of RA. Helicobacter pylori (Hp) is a common human pathogenic bacterium and is associated with multiple autoimmune diseases. However, the role of H.pylori in RA is far less well understood.

Objectives: The study aims to investigate the impact of Hp on RA.

Methods: We recruited 81 RA patients (disease duration >1 year) in this study, and all patients met the 2010 ACR/EULAR diagnostic criteria. They were divided into two groups depending on their infection status: the Hp-uninfected group (9 male, 33 female) and the Hp-infected group (10 male, 29 female). C-reactive protein (CRP), Rheumatoid factor (RF), and Anti-citrullinated protein antibodies (ACPA) were measured in serum of patients for assessing disease severity.

Results: The results, as shown in Figure 1, indicated that the serological levels of CRP (P=0.004), RF (P=0.0004), and ACPA (P=0.009) were significantly elevated in the Hp-positive group compared to the Hp-negative group.

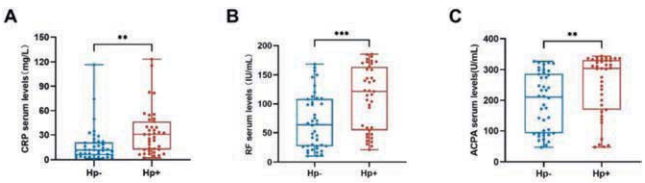

Figure 1. The serological levels of CRP (A), RF (B), and ACPA (C) in two groups. *P<0.05, **P<0.01, ***P<0.001.

Conclusion: Hp-positive RA patients present with higher levels serological of CRP, RF, and ACPA, which suggested that Hp infection could influence the disease progression or severity of RA. Thus, further research is required to investigate the pathogenic mechanism of Helicobacter pylori in rheumatic diseases.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2022-eular.2705

AB0077 IN RHEUMATOID ARTHRITIS PATIENTS, TOTAL IGA1 AND IGA2 LEVELS ARE ELEVATED: IMPLICATIONS FOR THE MUCOSAL ORIGIN HYPOTHESIS

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Background: Mucosal surfaces may be involved in the pathophysiology of rheumatoid arthritis (RA) (1). IgA is the most abundant class of immunoglobulin at mucosal sites. Therefore, it is worthwhile to study this isotype in RA patients in more detail. Humans have two IgA subclasses, IgA1 and IgA2, which are not evenly distributed. IgA1 is dominant in serum, whereas IgA1 and IgA2 are more balanced at mucosal surfaces (2). Besides these differences in location, IgA2 has also been ascribed pro-inflammatory properties (3).

Objectives: As IgA subclasses might provide new insights into mucosal involvement and potential pro-inflammatory mechanisms, we investigated total and autoantibody-specific IgA subclasses responses in sera of rheumatoid arthritis patients.

Methods: Sera from two cohorts of RA patients, the IMPROVED (baseline visit) and the EAC (1-year visit), were selected based on previous autoantibody measurements. All patients fulfilled the 1987 (EAC) or 2010 (IMPROVED) ACR criteria for RA. Total IgA subclasses and IgA subclasses of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) were measured using (in-house) ELISA's, and compared to healthy donors. Associations between these IgA subclass levels and markers of inflammation (CRP and disease activity score (DAS)) were investigated using Spearman's rank correlation. Mann–Whitney U tests were performed to investigate the association between IgA1 and IgA2 levels and smoking, a proxy for chronic mucosal inflammation. To correct for confounders, a multivariate linear model including age, gender, CRP and smoking was used.

Results: Total IgA1 and IgA2 levels were increased in RA patients compared to healthy donors in both cohorts (Figure 1A-C, data IMPROVED). This increase was more pronounced in seropositive RA versus seronegative RA. Both total IgA subclasses were raised to the same extent, since the percentage of IgA2 of total IgA in serum did not differ between patients and healthy donors. In seropositive patients, RF and anti-CCP2 IgA1 and IgA2 could be detected, but measurements of anti-CCP2 IgA2 levels proved challenging due to interference of RF IgA. Although IgA2 has been postulated to be more proinflammatory, no correlations were found between total, RF and ACPA IgA subclass levels and DAS. An association between CRP and RF IgA2 was observed, but the effect size was small and did not remain significant after correction for multiple testing in the EAC. In smoking seropositive RA patients, a trend towards a selective increase in total IgA2 and RF IgA1 and IgA2 was observed (Figure 1D, data IMPROVED seropositive RA).

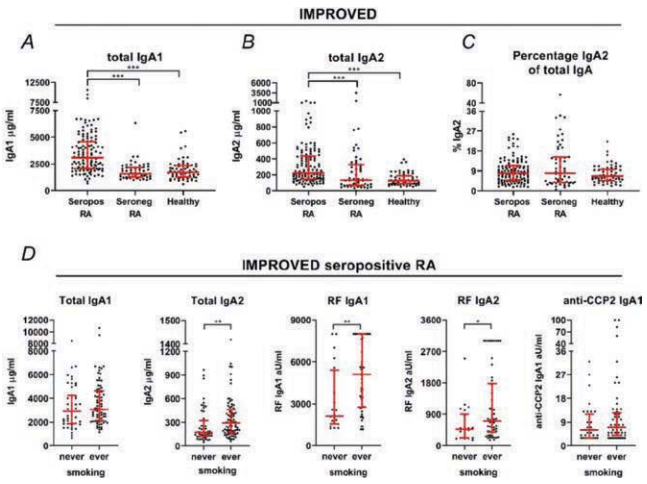

Figure 1.

Conclusion: Seropositive RA patients have raised IgA1 and IgA2 levels and can also harbor RF and ACPA IgA subclasses. No shift towards IgA2 was observed,

indicating that the increase in total IgA is not due to translocation of mucosal IgA into the bloodstream. However, chronic mucosal inflammation might be one of the mechanisms involved in the raise in IgA(2) levels in RA, given the association between smoking and total IgA2 levels. Despite its' pro-inflammatory properties, no strong associations between IgA2 and markers of inflammation were found, which suggests that IgA2 does not play a essential role in the ongoing pro-inflammatory processes in RA patients.

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AB0078 NESFATIN-1 EXPRESSION ASSOCIATED WITH A MARKER FOR BONE MATRIX FORMATION P1NP IN RHEUMATOID ARTHRITIS

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Background: Currently, the role of tissue cytokines in the pathogenesis of various diseases is being actively studied [1,2]. Nesfatin-1 (NF-1) is an endogenous peptide with pleiotropic activity. Recently, there have been works on the involvement of NF-1 in osteogenesis. In the experiment, intravenous administration of NF-1 to ovariectomized rats (OVX) leads to an increase in bone mineral density (BMD). There are works showing inhibition of osteoclastogenesis in mice [3,4]. We assume that the level of NF-1 affects the processes of bone matrix formation. The aim of the study was to determine the relationship between the level of NF-1, bone mineral density, composite body composition and markers of bone metabolism in patients with rheumatoid arthritis (RA).

Objectives: The study randomized 110 patients with RA according to the ACR/EULAR criteria, 2010 and 30 people in the control group.

Methods: All of them underwent osteodensitometry LUNAR DPX-Pro with the determination of composite body composition (BCT) and bone mineral density (BMD). NF-1 levels and bone turnover markers were determined using a commercial ELISA test.

Results: The average concentration of NF-1 in patients with RA was 50.49±34.05 ng/ml, which is significantly higher than in healthy individuals. The average level of NF-1 in the blood serum of healthy individuals was 31.61±3.17 ng/ml (M±σ). The level of reference indicators of NF-1 in healthy individuals, defined as M±2σ, ranged from 25.27 to 37.95 ng/ml.

According to the level of NF-1, all patients with RA were divided into 2 subgroups. The 1st group included patients (n=44) with normal serum NF-1 concentration (less than 37.95 ng/ml), the 2nd group (n=66) included patients with elevated NF-1 levels (more than ng/ml).

During the analysis of the results of the study, we revealed a statistically significant correlation between NF-1 and the N-terminal propeptide of type I procollagen (P1NP)) ($r = 0.218$, $p = 0.022$). The level of CRP and the erythrocyte sedimentation rate positively correlated with the indicators of NF-1.

However, we found no relationship between NF-1 levels and BMD; composite body composition; as well as the level of C-terminal type I collagen telopeptide (β-CTx).

Conclusion: Thus, the relationship between nesfatin-1 and a marker of bone matrix formation (P1NP) was revealed. This may indicate a possible effect of nesfatin-1 on the differentiation and function of osteoblasts.

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AB0079 THERAPEUTIC EFFECT OF ANTIGEN B, A PROTEIN FROM ECHINOCOCCUS GRANULOSUS, IN EXPERIMENTAL ARTHRITIS

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Background: Antigen B (AgB) is a lipoprotein secreted in the hydatic cyst by *Echinococcus granulosus* larval stage and seems to be responsible for regulating the immune balance of host via Th2 response to promote survival of the parasite. A Th2 response can suppress the pro-inflammatory Th1 response generated in several immunopathologies, such as rheumatoid arthritis.

Objectives: To evaluate the anti-inflammatory and immunomodulatory effects of AgB in mice models of Zymozan-induced arthritis (ZIA), Antigen-induced arthritis (AIA) and Collagen-induced arthritis (CIA).

Methods: In all models, mice were divided into three groups: vehicle (saline), AgB 2 µg and AgB 10 µg (intraperitoneal once a day). In ZIA, arthritis was induced in Balb/c mice with an intra-articular (ia) injection of zymosan in the left knee joint thirty minutes after treatment. Nociception was analyzed over a 6h period and mice were euthanized 6h after arthritis induction to assess leukocyte migration into the joint. In AIA, Balb/C mice were sensitized by subcutaneous (sc) injection of methylated bovine serum albumin (mBSA) on day 0. Booster was administered on days 7 and 14. On day 21, arthritis was induced by ia injection of mBSA in the left knee joint. The treatment was performed 24h and 30min before the ia injection of mBSA. Nociception was analyzed over a 24h period and mice were euthanized 24h after arthritis induction to assess leukocyte migration into the joint. Male DBA/1J mice had CIA by subcutaneous injection of an emulsion containing Freund's adjuvant and bovine collagen type II on days 0 and 18. The treatment took place between the 18th and 45th day after induction, as well as the evaluation of clinical arthritis score and nociception. Serum concentrations of IL-2, IL-4, IL-6, IL-10, IL-17, IFN-γ and TNF were evaluated in AIA and CIA.

Results: In ZIA, both doses of AgB diminished leukocytes migration to the knee joint compared with vehicle (AgB 2µg: 5.8±2.7; AgB 10µg: 5.6±2.7; vehicle: 4.8±3.1, $p<0.05$), but did not affect nociception. In AIA, both doses of AgB reduced nociception (AgB 2µg: 7.3±1.6; AgB 10µg: 7.2±1.6; vehicle: 6.0±2.1, $p<0.01$). Moreover, treatment with 2 µg of AgB inhibited in 70% the neutrophils migration (12.0±9.0, $p<0.001$) as well as it was reduced in mice treated with 10 µg of AgB as much as 58% (8.9±7.5, $p<0.001$), compared with control/vehicle (55.9±30.9). In addition, both doses reduced serum levels of IL-6 (AgB 2µg: 2.85±2.63; AgB 10µg: 3.10±3.18; vehicle: 27.07±30.28, $p<0.01$) and the dosage of 2 µg reduced the levels of IFN-γ (AgB 2µg: 0.53±0.27; vehicle: 1.47±0.46, $p<0.05$). In CIA, AgB treatment did not affected clinical score of arthritis (AgB 2µg: 4.6±3.8; AgB 10µg: 2.6±2.9; vehicle: 4.8±3.8, $p>0.05$), but the 2 µg dose improved nociception at day 32 after disease induction (7.1±1.2, $p<0.05$) and diminished serum levels of IL-6 (AgB 2µg: 68.9±71.8; vehicle: 475.7±362.3, $p<0.05$;) and TNF (AgB 2µg: 49.3±31.1; vehicle: 115.9±19.58; $p<0.01$), while the dose of 10 µg improved nociception at days 25, 32 and 34 after CIA induction (7.2±1.2, $p<0.05$).

Conclusion: These results suggest an effect of AgB on the initial pathophysiology of arthritis, reducing the influx of inflammatory cells to the knee joints of mice with acute arthritis. It also showed analgesic and anti-inflammatory potential on murine models of rheumatoid arthritis, highlighting the immunomodulatory role of parasitic helminth proteins on immune-mediated diseases.

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AB0080 GDF-11 AND GDF-8 INVOLVEMENT IN MUSCLE IMPAIRMENT OF COLLAGEN-INDUCED ARTHRITIS MODEL

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Background: Rheumatoid arthritis is an autoimmune, inflammatory disease which affects primarily synovial joints and can induce skeletal muscle wasting (1). It is known that growth differentiation factors 8, 11 plays an important role in muscle homeostasis (2-3).

Objectives: Evaluate muscle mRNA and protein expression of GDF-8, GDF-11 in early and established stages of collagen-induced arthritis.

Methods: DBA1/J mice, were randomized into 5 groups: baseline animals (BL=6); control animals evaluated at days 25 and 50 (CO25=8, CO50=8) and collagen-induced arthritis mice evaluated at day 25 and 50 (CIA 25=8; CIA 50=8). Clinical score, paw edema, and body weight were evaluated. Clinical score, hind paw edema, and body weight were assessed. Grip strength, nociception, fatigue time, and walking speed were assessed on days 0, 18, 25, 50 of experimentation. Animals were euthanized on days zero (BL group), 25 (CIA 25 and CO 25) and 50 (CIA 50 and CO 50) after disease induction. TA muscle was used to myofiber cross-sectional and GA muscle was used to evaluate gene expression of GDF-8, GDF-11 levels via qRT-PCR. Protein expression of GDF-8, GDF-11 levels in GA muscle was performed by ELISA.

Results: RA in the early CIA 25 and established CIA 50 groups was confirmed by high values of clinical score, nociception, paw edema and histological score when compared to the respective controls ($p<0.0001$; $p=0.001$; $p=0.001$). There was a decrease in grip strength in the CIA 25 group and a worsening in this decrease at CIA 50 ($p=0.0021$, $p=0.007$). Fatigue time was shorter in CIA 25 compared to CO 25 ($p= 0.002$) and maintained in CIA 50 ($p= 0.006$). Walking speed showed a decrease in both time points ($p=0.001$; $p=0.000$). After normalization by body weight, only the GA muscle had weight loss in CIA 50 when compared to CO 50 (-34.5%). Similarly, the CSA TA muscle myofiber showed a reduction of 14.04% only at CIA 50 group compared to the CO 50 ($p=0.026$). The GA muscle GDF-11 mRNA levels were higher in the CIA 25 group compared to the CO 25 and BL groups ($p=0.004$; $p=0.0087$, respectively); in CIA 50, there was a trend towards increased muscle GDF-11 mRNA levels ($p=0.07$). The protein expression of GDF-11 in serum samples did not show differences between the analyzed groups; however, in GA muscle, GDF-11 protein expression showed differences at the CIA 25 ($p=0.0023$) and the CIA 50 group ($p=0.017$) compared with the respective controls and a significant difference in muscle protein expression between the CIA 25 groups and CIA 50 ($p=0.0138$). There was a decreased of mRNA content GDF-8 on muscle, in CIA 50 and a decreased between the CIA 25 and CIA 50 in GA muscle ($p= 0.0377$; $p= 0.0019$); GA muscle had an increase of GDF-8 protein levels comparing the CIA 25 and CIA 50 group ($p=0.001$), while protein levels in serum of GDF-8 were decreased in CIA 50 compared with CO 50 ($p= 0.037$). Low muscle strength was associated with higher protein levels of GDF-11 in GA muscle ($r= -0.64$, $p=0.01$) and decreased walking speed ($r=-0.534$, $p=0.04$). Higher serum levels of GDF-8 were associated with higher muscle strength ($r= 0.74$, $p=0.02$) and increased walking speed ($r= 0.64$, $p=0.01$).

Conclusion: At early arthritis, GDF-11 mRNA and protein expressions were increased and are related to the physical impairment, while GDF-8 expression is reduced at established disease and increased in serum over time in CIA model, possibly as GDF-8 had a more systemic role in inflammatory arthritis. Thus, the GDFs may have a role in muscle outcomes in the CIA model and can be involved in muscle atrophy and loss of physical function in RA.

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AB0081 BIODISTRIBUTION OF NIPOCALIMAB (ANTI-HUMAN FCRN ANTIBODY) IN HUFCRN TRANSGENIC MICE

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Background: Nipocalimab (JNJ-80202135, M281) is a fully human IgG1 monoclonal antibody (mAb) designed to bind to the human FcRn receptor with high affinity at both neutral and acidic pH, and is currently in investigational clinical trials. The primary role of FcRn is to extend the half-life of IgG due to its ability to bind, salvage, and recycle IgG in the circulation. Nipocalimab specifically targets the FcRn IgG binding site, thereby interfering with the binding of native IgG, reducing IgG recycling and accelerating IgG clearance (1).

Objectives: To determine the biodistribution of nipocalimab compared to an isotype control IgG in huFcRn transgenic (Tg32) mice. This type of study is well suited to non-invasively determine the blood PK of labeled antibodies, as well as the kinetic biodistribution into various organ systems.

Methods: Four formulations were prepared for dosing: nipocalimab-VT680XL (N027a), nipocalimab-VT680XL plus 2x unlabeled nipocalimab (N027b), isotype control IgG-VT680XL and control vehicle. The biodistribution assessment experiments were performed in Tg32 mice (n=3/group, strain: B6.Cg-Fcgrttm-1Dcr Tg(FCGRT)32Dcr/DcrJ). A time series of *in vivo* fluorescence-mediated tomography (FMT) imaging sessions of body and brain was collected to follow the biodistribution of antibodies (Abs) after single IV administration. *In vivo*, whole body fluorescence was assessed immediately after administration of each formulation, and at 1, 5, 24, 48, 72, 96 and 144 hrs post administration. Mice were sacrificed after the final *in vivo* imaging timepoint, followed by resection of tissues and *ex vivo* imaging. The *in vivo* tissues were also assessed *ex vivo* at the terminal time point by epifluorescence. *Ex vivo* epifluorescence measurements were obtained for gall bladder, muscle, spleen, pancreas, white blood cells, lymph nodes, and intestines, which were flushed prior to imaging to remove fecal material.

Results: Biodistribution of nipocalimab and control IgG1 mAb were similarly observed to exhibit 2-compartment blood pharmacokinetics, dominant liver accumulation with minimal kidney and bladder signal and a prolonged terminal half-life in circulation (70-90 h). Nipocalimab showed only subtle differences compared to IgG1 control antibody, attributed to specific binding to target antigen. Early tissue accumulation/binding was seen between 1 and 5 hrs post-injection, which yielded an apparent, modest increase in blood clearance and a slightly lower AUC as compared to control IgG. The bulk of increased tissue binding could be attributed to liver retention, with trends for lower accumulation/binding in other tissues, such as pancreas, lung, and muscle. Addition of 2-fold excess of unlabeled nipocalimab to the labeled nipocalimab yielded some small trends of changes in biodistribution of the labeled material.

Conclusion: Whole body biodistribution and blood pharmacokinetics of nipocalimab were similar to that observed for the isotype control IgG1 antibody. Nipocalimab exhibited a subtle trend towards higher liver distribution within the first 5 hours after dosing and a more rapid distribution phase compared to the control antibody. This is possibly related to its FcRn targeting and its shorter anticipated half-life compared to isotype control IgG or other human IgG mAbs. Overall results for both nipocalimab and control IgG were typical for IgG mAbs.

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AB0082

ANTI-INFLAMMATORY EFFECTS OF TOTAL SAPONINS OF PANAX JAPONICUS ON RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a common autoimmune disease with inflammation[1]. Total saponins of *Panax japonicus* (TSPJs) are effective components extracted from *Panax japonicus*[2]. They are known to exhibit anti-inflammatory and immunosuppressoive properties, but their effect of anti-inflammation in collagen-induced arthritis (CIA) remains unclear.
Objectives: To investigate the anti-inflammatory targets of TSPJ predicted by bioinformatics and the verification in CIA mice.
Methods: The targets of RA are obtained in the GeneCards database. we used Cytoscape 3.7.2 software to construct a protein-protein interactions (PPI) network and obtain the hub genes. There are four effective components of TSPJ: Araloside A, chikusetsusaponin IVa, ginsenoside Rg2, and ginsenoside Ro. Through molecular docking between the screened hub genes and the four effective components of TSPJ, the possibility of TSPJ treating CIA mice can be predicted. The collagen II (CII) and complete Freund's adjuvant (CFA) were used to induce the CIA model. After establishing the model, 32 DBA1/J mice were divided into C group (n=8), M group (n=8), L group(n=8), and H group(n=8). The L and H groups were gavaged with TSPJ at 30 mg/kg or 150 mg/kg, and the C and M groups were gavaged with normal saline. The thickness of the hind paw, number of swollen joints, and arthritis index were evaluated. After 11 days of treatment, all the mice were sacrificed after anesthesia. Sera were collected to centrifuge tubes and the levels of inflammatory factor were determined by the ELISA kit following the instruction.
Results: A gene list that enriches 263 genes was obtained by searching RA from the GeneCards database. The hub genes of the top 3 obtained from Cytoscape 3.7.2 software were tumor necrosis factor (TNF), interleukin-1β (IL-1β), and interleukin-6 (IL-6). In addition, interleukin-17A (IL-17A), a classical inflammatory index in the top 10, was selected and included in the predicted target. The results of molecular docking between the predicted target and the components of TSPJ showed that the combined pose has good stability. The numerical value of hind paw thickness, swollen joint counts, and arthritis index in the intervention groups were lower than those in the M group, suggesting TSPJ played a critical role in improving pathological changes. Compared to those of the C group, the serum levels of TNF-α, IL-1β, IL-6, and IL-17A were increased in the M group. Compared to those of the M group, the levels of TNF-α, IL-1β, IL-6, and IL-17A in the L and H groups were decreased. Compared to those of the L group, the levels of TNF-α, IL-1β, IL-6, and IL-17A in the H group were decreased. The results suggested that TSPJ may decrease the levels of TNF-α, IL-1β, IL-6, and IL-17A in CIA mice. These results suggest that TSPJ may inhibit the inflammatory effects of CIA mice.
Conclusion: Current study demonstrated a novel inhibitory effect of TSPJ on inflammation in CIA mice, and TSPJ can act on the targets predicted by bioinformatics of CIA mice, suggesting the potential of TSPJ as a therapeutic agent for RA and providing new ideas for the clinical treatment of RA.
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AB0083

RELATIONSHIP BETWEEN APOLIPOPROTEIN C-III AND ACTIVATED FACTOR VII-ANTITHROMBIN COMPLEXES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Both rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are associated with increased cardiovascular risk and thrombosis. Alterations in plasma lipids levels, including apolipoproteins are recognized as the important risk factors of cardiovascular disorders. Activated Factor VII -anti- Thrombin complex (FVIIa-AT) is a marker of the extrinsic coagulation cascade activation, the pathway accelerated by interaction with plasma apolipoprotein C-III (Apo-CIII) (1).
Objectives: To investigate the associations between plasma FVIIa-AT concentration, lipid profile including apolipoprotein CIII, and markers of disease activity in patients with RA and PsA.
Methods: 41 patients with RA, 38 with PsA, and 22 healthy controls, all not taking anticoagulant drugs were selected for the study. The lipid profile comprised triglycerides (TG), total cholesterol (TCh), low (LDL), and high-density lipoprotein (HDL). Serum levels of Apo C-III were measured using a Human ApoCIII ELISA kit CellBiolabs Inc.Austria. FVIIa–AT plasma concentrations were determined using ELISA test. C-reactive protein (CRP) level was measured using the immunoturbidimetric assay. All measurements were performed by a technician blinded to sample origin. The Mann-Whitney test and Kruskal Wallis tests were applied for intergroup comparisons, and correlations were assessed using Spearman's rank tests, due to data non-normal distribution.
Results: The highest serum levels of Apo C-III were found in RA patients (median: 99.9μg/ml, min.-max. 8.7–199) compared to PsA (30.86μg/ml, 12.4–125.8) and controls (9.5 μg/ml, 3.7–29.2), p<0.001. RA and PsA patients revealed higher FVIIa-AT plasma levels than controls (RA median 153.8 pM, min.—max. 57.0–397.8, PsA 157.6 pM, 64.9– 323.8 vs controls 104.5 pM, 68.9–150.9, p<0.001). In RA and PsA patients ApoCIII correlated positively with TG levels (r=0.35, p=0.027 and r=0.38, p=0.018 respectively). In all patients and controls, Apo C-III levels correlated positively with FVIIa-AT concentrations (r=0.45 p<0.001). No significant differences were found in the serum concentrations of TCh, LDL, HDL, TG, and CRP, between the groups of RA and PsA patients.
Conclusion: Elevated concentrations of both, apolipoprotein CIII and activated FVII-AT complexes in rheumatic patients suggest associations between plasma lipoproteins and activation of coagulation cascade leading to a pro-thrombotic state in patients with RA and PsA. Further studies on these relationships are necessary taking into account various clinical conditions of patients and treatment.
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AB0084

INCREASED LIVER DISEASE RISK IN RHEUMATOID ARTHRITIS IS ASSOCIATED WITH DISEASE ACTIVITY, INFLAMMATORY MARKERS, INSULIN RESISTANCE AND ACPAS. INFLUENCE OF METHOTREXATE

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Background: Liver alterations, especially nonalcoholic fatty liver disease (NAFLD) are associated with Rheumatoid Arthritis (RA). This abnormality appears as asymptomatic and can progress to a severe liver damage rapidly. Chronic inflammation, treatment with methotrexate (MTX) or even autoimmunity are factors that might be involved, however the mechanisms related to this comorbidity in RA are not completely stablished yet.
Objectives: 1) To evaluate the liver disease risk in RA patients through feasible indexes to be used in the daily clinical practice and its relationship with clinical features of the disease; 2) To analyze the impact of antibodies to citrullinated proteins antigens (ACPAs) on hepatic function; 3) To examine the influence of MTX treatment on classical parameters and new indexes of hepatic dysfunction in a cross-sectional and longitudinal cohort.

Methods: 1) Cross-sectional study in 307 body mass index matched subjects: 55 healthy donors (HDs), 190 RA patients and 62 non-RA patients diagnosed with NAFLD through echography. Obese patients were excluded from the study. 2) Longitudinal study with 50 RA patients treated with MTX for 6 months. Clinical and laboratory parameters, subclinical liver disease biomarkers and 4 indexes to evaluate the presence of fibrosis and steatosis (APRI, "AST to platelet ratio index"; FIB-4, "fibrosis 4 score"; HSI, "hepatic steatosis index" and TyG, "triglycerides and glucosa index") were measured. Association studies of hepatic dysfunction with clinical parameters were performed; A panel of 15 proteins directly involved in hepatic disease was analyzed in serum (C1QTNF1, IL7R, TIE1, CCL5, REG3A, CA3, LCN2, CCL14, NRP1, ICAM3, CD59, TIMP1, CNDP1, GNLY, IGFB6). 3) *In vitro* experiments were carried out in hepatocyte cell line (HEPG2) treated with ACPAs.

Results: Using NALFD patients as positive controls for the four liver disease indexes, RA patients showed significantly higher levels of HSI and TyG biomarkers. In fact, a high proportion of these patients (42.7%) were estimated to suffer NALFD. The association studies in RA patients showed that liver disease biomarkers (HSI and TyG) were related to the insulin resistance state, inflammation, complement component 3(C3), disease activity, and the levels of ACPAs. Serum levels of CNDP1, CCL5, GNLY, TIMP-1, CD59 and CCL14 were significantly increased in RA patients and correlated with hepatic damage indexes. Treatment with ACPAs on hepatocytes promoted the secretion of C3 in parallel with a significant alteration of genes related to glucose and lipid metabolisms, inflammation, fibrosis and apoptosis. MTX treatment, from the point of cross-sectional approach, was not associated with an increase of hepatic enzymes, serum proteins nor liver disease indexes. Treatment with MTX for 6 months did not affect those levels either.

Conclusion: 1) A high proportion of RA patients present an alteration in markers of NAFLD, associated with insulin resistance state, disease activity, inflammation, component C3 and ACPAs levels; 2) the autoantibodies could directly impact hepatocyte biology altering the expression of genes related to glucose and lipid metabolisms, inflammation, fibrosis and apoptosis, 3) Treatment with MTX did not promote any alteration in subclinical liver disease biomarkers after 6 months of treatment. Funded by Institute of Health Carlos III (PI20/00079).

Disclosure of Interests: None declared

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AB0085 TIGLYLCARNITINE AS KEY FACTORS IN LIVER–JOINT AXIS

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Background: Gut microbiota could promote RA progression metabolites mediated gut–joint axis [1]. We previously reported that liver metabolism has a close linkage with Rheumatoid arthritis (RA) [2]. However, the inter-relational mechanisms between liver and joint are still unclear.

Objectives: This article aimed to explore the shared metabolites signatures of liver, plasma and joint in RA.

Methods: We integrated multiomics datasets metabolites of liver and plasma from in the healthy group (n=10) and CIA group (n=10), and metabolites of knee-joint fluid (synovial fluid) from 40 participants in osteoarthritis (OA) group (n=20) and RA group (n=20). The Weighted Gene Co-Expression Network Analysis (WGCNA) was used to identify the co-expression modules related to liver, plasma and joint.

Results: The blue modules were negativelycorrelated with CIA (r =-0.74, p <0.001), included 200 liver metabolites. The black modules were positively correlated with CIA (r = 0.63, p <0.001), included 78 plasma metabolites. The yellow modules were positively correlated with RA (r = 0.53, p =0.008), included 55 synovial fluid metabolites. There were only 1 metabolite (Tiglylcarnitine) overlapped in RA-related module of liver, plasma and joint.

Conclusion: Tiglylcarnitine may be the key factors to liver–joint axis.

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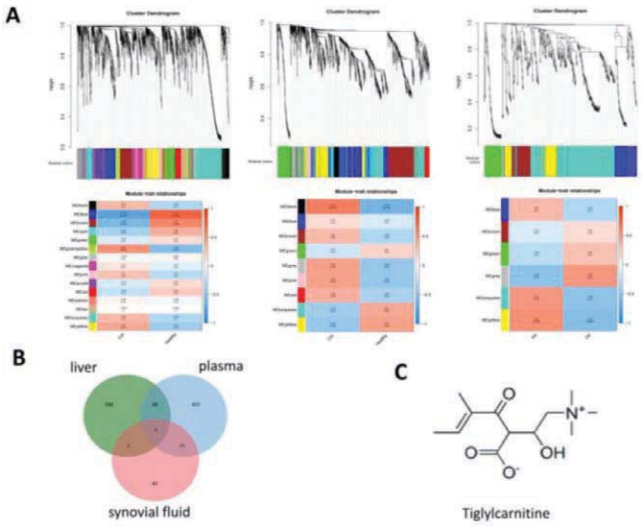

Figure 1. Tiglylcarnitine as Key Factors in liver-joint axis. A The cluster dendrogram of co-expression genes and modulexis.es Collagen-Induced Arthri B The shared metabolites between the blue module of liver, the black module of plasma, and yellow modules of synovial fluid. C The chemical structures of Tiglylcarnitine.

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AB0086 PORPHYROMONAS GULAE INFECTION IS NOT RELATED TO EXOGENOUS CITRULINATION OR DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: *Porphyromonas gulae (P. gulae)* is a Gram negative microorganism of the Porphyromonadaceae family. It presents in its structure virulence factors similar to *P. gingivalis*, including the PAD enzyme. An enzyme responsible for catalyzing citrullination, related to the formation of autoantibodies against citrullinated peptides associated with Rheumatoid Arthritis (RA).

Objectives: To evaluate the presence of *P. gulae* and anti-citrullinated peptide antibodies of *P. gulae* PAD in patients with RA and their possible association with clinical markers of activity.

Methods: Ninety RA patients and 90 controls matched for age and sex were included. Serum levels of rheumatological markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti-citrullinated protein antibodies (Anti-CCp/ACPA) and rheumatoid factor (RF) were measured. Disease activity was assessed using Disease Activity Indices-28 (DAS28) and SCDAI. The periodontal diagnosis was according to CDC and American Academy of Periodontology. The presence of *P. gulae* was established by qPCR, verifying the specificity and confirmed due to the high homology between *P. gingivalis* and *P. gulae*. The presence of antibodies against 2 peptides called VDK and LPQ were evaluated in their native structure and citrullinated at one end and inside the PPAD molecule of *P.gulae*. It was determined by ELISA in-house. Prediction of B and T epitopes of PPAD from *P. gulae* was made taking into account the location of arginines within the molecule, restricting it to HLA alleles associated with RA. Associations were established by Kruskal Wallis, Mann Whitney U tests and multiple correspondence discriminant analysis (MCDA) in SPSS V24 and STATA for Windows software, with a significance of 95%,$p \leq 0.05$.

Results: A frequency of *P. gulae* was observed in the RA group of 15.8% versus controls of 9.5%, p=0.1925, A Despite finding a diagnosis of periodontitis in 70.5% of the patients, it was not associated with clinical severity or diagnosis of periodontitis. Comparisons were made classifying the patients according to periodontal diagnosis, the presence of *P. gulae* was observed more frequently in the RA group with a diagnosis of periodontitis, compared to the control group (6.7% vs 2.5%, respectively) without statistical significance (p=0.2576). Of the 180 individuals evaluated, 17 had the presence of anti-citrullinated peptide antibodies of *P. gulae* PAD. Despite a higher frequency in the RA group of antibodies against two citrullinated peptides, the results were not significant (p=0.378 and p=0.346), there was no evidence of a relationship with activity or disease markers in RA. The MCDA test generated two dimensions, one with the clinical activity variables of RA with CC: 0.218, and a second dimension in which the presence of anti-citrullinated peptide antibodies of PAD CC were related to each other CC: 0.749; No positive correlation was found between the clinical variables of RA and the anti-citrullinated peptide antibodies of *P. gulae* PAD.

Conclusion: Despite the presence of *P. gulae* and PPAD citrullinated peptide antibodies from *P. gulae* in patients with RA, it was not possible to establish the relationship with clinical variables, which could indicate a lower contribution of this microorganismto the biological mechanism and molecular of citrullination common between RA and periodontitis. However, an additive effect of *P. gulae* with *P. gingivalis* in the citrullination process cannot be ruled out.

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AB0087 THE EFFECT OF BARICITINIB ON STAT1 PHOSPHORYLATION IN MONOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS

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Background: Baricitinib is a Janus kinase (JAK)1/JAK2 inhibitor approved for the treatment of rheumatoid arthritis (RA)[1-2]. STAT proteins bind JAK kinase dimers coupled with cytokine receptors and regulate gene transcription. The JAK/STAT system is responsible for the intracellular signaling of different cytokines contributing to the activation process of the monocyte lineage, therefore the use of JAK inhibitors can affect cell functionality[3-6].

Objectives: The aim of the present study was to verify the effects of baricitinib on STAT phosphorylation in peripheral mononuclear cells (PBMCs) of RA patients and to evaluate any correlation between STAT phosphorylation and response to therapy.

Methods: At baseline (BL) and after 4 weeks (w4) of treatment, we evaluated patients' disease activity ($DAS28_{PCR}$, CDAI and SDAI), dividing them into responders and non-responders according to the Minimal Clinically Important Difference for $DAS28_{PCR}$ (1.2 points) at w4. The phosphorylation of STAT1, STAT4 and STAT5 was analyzed at BL and w4 in gated monocytes, Treg, CD8 + and CD4 + lymphocytes from 4 responder and 4 non-responder patients through flow cytometry, at basal conditions and after IL2, IFNα and IL6 stimulation.

Table 1. Clinical and demographic characteristics of Rheumatoid Arthritis patients.

Clinical and demographic characteristics	N=8
Age (years), median (IQR)	59 (8)
Female:Male	7:1
Etnicity	
-Caucasian n (%)	6 (75)
-Hispanic n (%)	2 (25)
Disease duration (months), median (IQR)	156 (201)
Rheumatoid Factor, n (%)	3 (37.5)
ACPA, n (%)	4 (50)
Number of previous csDMARDs, n (%)	
-1	2 (25)
-2	1 (12.5)
-3	1 (12.5)
-≥ 4	4 (50)
Number of previous bDMARDs, n (%)	
-1	2 (25)
-2	2 (25)
-3	1 (12.5)
-≥ 4	3 (37.5)
Baricitinib in monoterapy, n (%)	5 (62.5)
Daily PDN dose, median (IQR)	5 (6)

ACPA: anti-citrullinated protein antibodies; csDMARDs: conventional syntetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs; PDN: prednisone.

Results: Baseline clinical and demographic characteristics of patients are reported in Table 1. We showed that monocyte count decreased from BL to w4 mostly in responders. Basal pSTAT1 phosphorylation tent to be higher in monocytes of non-responder patients; after 4 weeks of treatment, the reduction of the cytokine-induced pSTAT1 was significantly greater in monocytes from responders compared to non-responders (Figure 1). The phosphorylation of STAT4 and STAT5 was not affected by treatment in any cell type and at any time point. We further studied the STAT1 phosphorylation pathway isolating the effect of stimulation with IFNα and stratifying monocytes according to their surface marker expression of CD14 and CD16 in classical, intermediate and non-classical. We observed the same pattern with a significant greater reduction of pSTAT1 in monocytes from responder patients, compared to non-responders, after the treatment with baricitinib.

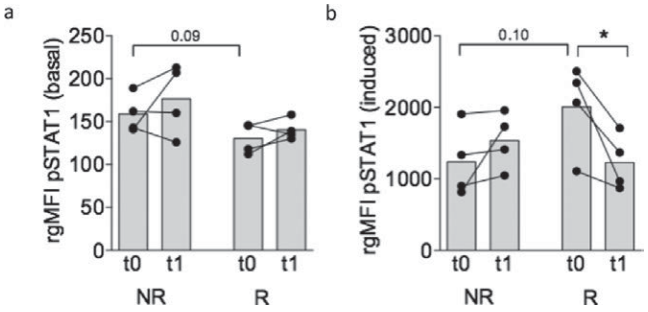

Figure 1. STAT1 phosphorylation in responder (R) and non-responder (NR) patients at basal conditions (before stimulation) (a), and after cytokine (IL2, IFNα and IL6) stimulation (b) at baseline and at T1 (week 4).

Conclusion: These results may suggest that monocyte count and STAT1 phosphorylation in circulating monocytes could represent early markers of response to baricitinib therapy.

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AB0088 DOUBLE-STRANDED DNA BREAKS ARE A MARKER OF THE INFLAMMATORY ACTIVITY OF RHEUMATOID ARTHRITIS

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Background: Double-strand DNA breaks (DNA-DSB) are one of the most biologically significant DNA damage lesions that leads to chromosome breakage and/or rearrangement, mutagenesis and loss or gain of genetic information. The phosphorylation of H2AX histone proteins which are located in the vicinity of the DSBs is known as one of the earliest responses to DNA DSBs in cells. Induction

of DNA DSBs in live mammalian cells triggers the phosphorylation near the C-terminal of H2AX protein, which results in the phosphorylated form of H2AX, termed yH2AX. [1,2].

Objectives: To examine DNA-DSB among patients with systemic autoimmune rheumatic diseases (SARDs) by evaluating phosphorylation yH2AX and 53BP1 at the site of injury.

Methods: The analysis included 25 patients with SARDs (19 with RA (16 women, Me;IQR the disease duration 60 (20-103) months, DAS28-ESR 5.05(4.06-5.9)); 4 - with systemic lupus erythematosus (4 women, the disease duration 324 (204-372) months, SLEDAI-2K 9.5 (4.5-16.5) and 2 women with Sjogren's disease. The control group consisted of 14 healthy donors, comparable in gender and age with the examined patients. DNA-DSB breaks were determined as a discrete focus during immunofluorescence staining with anti-yH2AX and anti-53BP1 antibodies of the lymphocyte culture, followed by analysis on the automated platform AKLIDES (Medipan, Berlin/Dahlewitz, Germany).

Results: There were no significant differences in the number of DNA breaks among patients with SARDs and healthy donors (p>0.05). There was a positive correlation between % pos. cells by yH2AX and CDAI (r=0.45 p=0.035), Nuclei with foci by 53BP1 and ESR (r=0.53 p=0.02) and IgM RF (r=0.63 p=0.005). Among patients with high CDAI activity (n=10), there was a greater number of Nuclei with foci by yH2AX - (22.5 (6.0-43.0); a higher average number of foci mean (0.39 (0.19-0.62) and a higher % pos. cells (32.6 (18.7-39.1) comparing with patients with low/moderate inflammatory activity (9,0 (2-12); 0,12 (0,02-0,28); 11,5 (1,8-23,5) accordingly, p<0.05, n=9).

Conclusion: The evaluation of double-stranded DNA breaks can be beneficial as an additional marker for assessing the disease activity among patients with RA.

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Disclosure of Interests: None declared

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AB0089 INTEGRIN A11B1 DEFICIENCY AFFECTS THE COURSE OF DISEASE IN THE ARTHRITIC HTNFTG MOUSE

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder conducted by fibroblast-like synoviocytes (FLS), which acquire a tumor-like phenotype causing irreversible cartilage and bone damage. FLS attache to the extracellular matrix (ECM) invading the joints, a process mediated by integrins. Integrins are transmembrane proteins regulating several cell functions like cell migration, cell proliferation, tissue invasion and cytokine expression – key mechanisms during the pathogenesis of RA. The collagen-binding Integrin $\alpha 11\beta 1$ ($\alpha 11$) is expressed on FLS mediating their adhesion to the ECM and in this study, we analysed its implication in RA.

Objectives: We examined the pathogenesis of RA in a murine arthritis model (hTNFtg) lacking $\alpha 11$ to analyze its contribution to joint destructions and the disease course.

Methods: Expression levels of $\alpha 11$ were analysed by Western Blot and immunofluorescence staining using FLS and synovial tissue of patients with RA and hTNFtg mice in comparison to their respective controls. Crossbreeding hTNFtg with $\alpha 11$ deficient (*itga11*$^{-/-}$) mice enabled us to evaluate arthritis progression using clinical parameters like paw swelling and grip strength. Inflammation area and cartilage damage were quantified by histomorphological techniques such as toluidine blue staining of in paraffin-embedded sections from hind paws. Bone erosion was visualized by µCT imaging and quantification of the bone volume in the tarsal bone area.

Results: High expression levels of $\alpha 11$ could be detected in hTNFtg and human RA samples in comparison to their controls. The progression of arthritis in *itga11*$^{-/-}$hTNFtg was slower and less severe in comparison to hTNFtg mice, visible in a stronger grip strength and reduced paw swelling at the same timepoint. The histomorphology analysis confirmed these results showing higher cartilage area (3.21% vs 5.22%, $p < 0.05$), less cartilage destruction (51.73% vs 35.65%, $p < 0.05$) and reduced inflammation (28.28% vs 12.00%) in *itga11*$^{-/-}$hTNFtg compared to the hTNFtg mice. Also, the quantification of the tarsal bone area revealed a higher bone volume (77.94% vs 84.92%, $p < 0.01$) in *itga11*$^{-/-}$hTNFtg.

Conclusion: This study showed the important role of $\alpha 11$ in the progression of joint destruction as it is highly expressed in hTNFtg mice and in human synovial tissue of patients with RA. Its absence results in less severe arthritis progression and joint destruction, therefore a possible and interesting target for RA treatment.

Disclosure of Interests: None declared

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AB0090 BASELINE IGG-FC N-GLYCOSYLATION PROFILE IS ASSOCIATED WITH LONG-TERM OUTCOME IN A COHORT OF EARLY INFLAMMATORY ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease which causes chronic joint inflammation and functional limitation[1,2]. The diagnosis of rheumatoid arthritis (RA) is mainly based on clinical data and RA specific autoantibodies, while the prediction of long-term prognosis from disease outset is not clinically reliable[3,4]. The importance of immunoglobulin G (IgG) and its Fc *N*-glycosylation in inflammation of RA has been described, with changes in the glycosylation profiles observed years before the diagnosis of RA[5].

Objectives: We herein sought to assess the value of total serum IgG Fc *N*-glycosylation as a diagnostic and prognostic biomarker in patients with early inflammatory arthritis (EIA). Specifically, we aim to assess whether IgG *N*-glycoform levels may predict the diagnosis of RA or undifferentiated arthritis (UA) and the long-term disease's outcome in patients with EIA arthritis patients naïve to treatment.

Methods: The "Early Arthritis Clinic" of the University Hospital of Heraklion is a prospective cohort of patients with inflammatory arthritis. For the present study, we selected a group of patients naïve to any immunosuppressive treatments with available serum at baseline evaluation (n=118). At baseline, demographics, RA clinical characteristics (DAS28, HAQ-DI) and laboratory tests [autoantibodies (RF and/or ACPA)], were also recorded. The patients were prospectively followed for two years, with clinical, laboratory and disease-related treatments documented. A diagnosis of RA or UA was based on established classification criteria[6]. In order to assess long-term prognosis we formulated a combined "index" of favourable outcome if the patients fulfilled all the following at 24 months of follow-up: remission or low disease activity (based on DAS28 < 3.2) and normal functionality (based on HAQ ≤ 0.25) while on treatment with csDMARDs and never use bDMARDs. We applied a state-of-the-art liquid chromatography - mass spectrometry (LC-MS) based workflow for analysis of subclass-specific IgG Fc *N*-glycosylation at the baseline[7].

Results: We studied 118 EIA patients [age (mean, SD) (53, 15.6) years, females (80.5%), symptoms duration (53.8, 8.7) years, ACPA positive (16%), DAS28 (4.8, 0.14)]. During the 2 years of follow-up, 60% of the patients were diagnosed with RA and 40% with UA. Although patients with UA had higher relative abundances of galactosylated and sialylated *N*-glycoforms (H4N4F1, H5N4F1 and H5N4F1S1) in all IgG subclasses at baseline compared to RA patients, differences were not statistically important. Interestingly, we observed a significant association between high levels of IgG2/3 galactosylation for H5N4F1 [effect 0.63, adjusted p=0.036)] and H3N4F1 [effect -0.55122, adjusted p=0.0496) and favorable outcome after two years of treatment.

Conclusion: In our cohort of EIA we found IgG2/3 Fc *N*-glycoforms to be associated with a favorable prognosis after 2 years of follow-up. Should the present data be confirmed in a larger cohort could be of clinical value. Since currently available prognostic tools have significant limitations, further research should aim to the development of a predictive tool of high specificity and sensitivity based on the combination of clinical, serological data and novel biomarkers.

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AB0091 INCREASED BIOLOGICAL AGE IN MALE PARTICIPANTS OF SWEDISH AND UK RHEUMATOID ARTHRITIS COHORTS IS NOT LINKED TO DISEASE

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Background: Immunesenescence in the adaptive immune system, subsequent to thymic involution, results in compromised immunity and increased susceptibility to autoimmune disease and chronic inflammation. There are reports in the literature that immunesenescence, including thymic atrophy and telomere shortening, is accelerated in patients with rheumatoid arthritis (RA)1. What is unclear is whether RA includes accelerated biological ageing overall in addition to immune ageing which may help to explain the increased risk of age-related diseases in RA2. Recent studies have identified a set of DNA methylated sites across the genome that are highly correlated with chronological age and mortality, termed epigenetic clocks3,4 or DNAm age (DNAma), and can be used to determine an individual's biological age.

Objectives: The aim of our study is to determine if the biological epigenetic clocks of RA patients are accelerated.

Methods: We evaluated the Horvath[3] and Hannum[4] epigenetic clocks of control and RA patients using published DNAm data sets, accessions GSE42861 (EIRA, Swedish cohort of 342 RA patients and 328 non-RA controls) and E-MTAB-6988 (77 RA discordant monozygotic twins).

Results: We did not detect significant differences between DNAma of RA and non-RA twins. Similarly, there were no significant differences between the DNAma of RA patients and controls from the Swedish EIRA cohort. However, we detected a significant acceleration in DNAma of male discordant twins, both RA and non-RA, by 5.4 years (p=3.29e-5) and 2.8 years (p=0.04) using the Hannum and Horvath clocks, respectively. Male participants, both control and RA patients, from the EIRA cohort also exhibited an accelerated DNAma, by 1.5 years (p=7.55e-5) using the Hannum clock but using the Horvath clock a significant DNAma acceleration, by 1.4 years (p=0.002) was detected in male RA patients from the EIRA cohort.

Conclusion: Overall, we detected a significant biological age acceleration in male participants from both RA and control groups and only found a significant difference between DNAma of Non-RA controls and RA patients for one of the epigenetic clocks. Further analysis using additional cohort data and biological clock algorithms is needed to confirm our findings.

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AB0092 CTLA4-IG PROMOTES THE M1-M2 SHIFT IN CULTURED MACROPHAGES OF RHEUMATOID ARTHRITIS PATIENTS WITH ACTIVE DISEASE: IN VITRO STUDY

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Background: In rheumatoid arthritis (RA), macrophages play an important role in modulating the immunoinflammatory response through their polarization into "classically" (M1) or "alternatively activated" (M2) phenotypes and the release of pro-inflammatory cytokines (1). In the active inflammatory phase of RA, circulating intermediate monocytes and synovial tissue macrophages show a M1 phenotype, whereas MerTK$^+$M2 macrophages seem to characterize the synovial tissue of RA patients under remission (2-4). In RA, CTLA4-Ig fusion protein (abatacept) reduces the pro-inflammatory activity of macrophages by interacting with the costimulatory molecule CD86 on surface cell membrane of activated cells, including macrophages (2).

Objectives: The *in vitro* study investigated the efficacy of CTLA4-Ig treatment to induce the shift from the M1 phenotype into an M2 phenotype in cultured monocyte-derived macrophages (MDMs) obtained from active RA patients.

Methods: Cultured MDMs obtained from peripheral blood mononuclear cells of 5 active RA patients (mean age 54±13 years) and 5 age-matched healthy subjects (HSs) after overnight stimulation with phorbol myristate acetate (5ng/ml), were treated with CTLA4-Ig at the concentrations of 100mg/mL or 500mg/mL for 3, 12, 24 and 48 hours. A part of cultured RA-MDMs as wells as cultured HS-MDMs were maintained in growth medium (RPMI at 10% of fetal bovine serum) without any treatment and used as unstimulated cells. Gene expression of CD80, CD86 and toll-like receptor-4 (TLR4), as M1 markers, as well as macrophage scavenger receptors (CD163, CD204), mannose receptor-1 (CD206), as surface M2 markers, and MerTK (functional M2 marker) were evaluated by quantitative real-time polymerase chain reaction (qRT-PCR). Protein synthesis of surface M2 markers was investigated by Western blotting. The statistical analysis was performed by Wilcoxon t-test.

Results: Cultured RA-MDMs showed a high basal gene expression of TLR4, CD80 and CD86 compared to HS-MDMs, confirming to be activated M1 macrophages. In these macrophages, CTLA4-Ig treatment downregulated the gene expression of M1 markers at both concentrations and all timings, but significantly limited to TLR4 and CD80 markers (500mg/mL,12 hours: $p<0.05$). Conversely, both concentrations of CTLA4-Ig significantly upregulated the gene expression of CD163, MerTK and CD206 ($p<0.05$), whereas only the high concentration of CTLA4-Ig significantly upregulated CD204 gene expression ($p<0.05$). The protein synthesis of all M2 surface markers was increased after 24 hours of treatment primarily by the high concentration of CTLA4-Ig, and significantly for CD204 and CD206 ($p<0.05$).

Conclusion: CTLA4-Ig treatment seems to exert an important anti-inflammatory effect by promoting the shift from a M1 to an M2 phenotype in cultured RA macrophages The results suggest a further mechanism for CTLA4-Ig in the modulation of the RA synovitis (5).

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AB0093 MODELING OF ANTIGEN-COLLAGEN-INDUCED ARTHRITIS IN BALB/C MICE

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Background: Rheumatoid arthritis (RA) is one of the most common autoimmune diseases. Currently, disease-modifying drugs and biological agents are used to treat RA [1]. The available drugs are not perfect: they have serious side effects and do not always cause a stable improvement or remission [2]. The above sets the task of finding new approaches to treatment that will be effective, more specific and safe. In this connection, it is necessary to develop and apply experimental models as close as possible in pathogenesis to rheumatoid arthritis. One such model, rarely used at present, is the combined antigen-collagen-induced arthritis [3].
Objectives: To show immunological and histological changes similar to RA in the AIA/CIA model and the validity of its application in research activities.
Methods: Experimental AIA/CIA was induced according to 2 different protocols in 50 BALB/c mice. Clinical assessment of arthritis was made by measuring the swelling of the paws with a caliper at different times. The assessment of immunological changes included the analysis of the content of antibodies to type II collagen by ELISA, the content of T-regulatory cells by flow cytometry. Also, a histological analysis of the obtained data was carried out.
Results: On the 10th day, a significant increase in paw thickness was recorded in animals induced both according to the first and second protocols. The intensity of swelling subsided by the 23rd day. A significant increase in the content of antibodies to type II collagen was observed in all experimental groups, but in animals from Protocol No. 1, the amount of antibodies to type II collagen was significantly higher. A high level of T-regulatory cells was registered only in mice induced according to the first protocol on the 10th day. Histological changes in the form of synovial hyperplasia, pannus, usurations were observed to varying degrees in all experimental groups, but the most pronounced changes were in animals from the first protocol.
Conclusion: In experimental animals, in all the presented protocols, changes were observed that were closest to RA, when compared with classical models of experimental arthritis induction. Based on the fact that protocol 1 animals showed an increase in the content of T-regulatory cells, the levels of antibodies to type 2 collagen were consistently high, and the histological changes were the most pronounced, it can be assumed that protocol 1 of the combined AIA/CIA model on the line of Balb/c mice, is the most suitable for testing and developing new methods of RA therapy.
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AB0094 DENDRITIC CELLS AS TARGETS OF PATHOGENETIC THERAPY FOR AUTOIMMUNE DISEASES

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of autoimmune diseases through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. DCs are a heterogeneous population and can be divided into groups: myeloid (mDCs) and plasmacytoid (pDCs). DCs can induce both immune response and tolerance.
Objectives: The study is aimed at investigating the subpopulations of peripheral blood DCs (myeloid and plasmacytoid) in patients with rheumatoid arthritis (RA) and axial spondyloarthritis (axSpa) under disease-modifying antirheumatic drugs (DMARDs) treatment as a target of pathogenic therapy.
Methods: There are thirty patients were included in the study. Twenty patients with early RA (ACR/EULAR criteria, 2010, duration of the disease up to 12 months,) and ten patients with axSpa (ASAS criteria) were recruited. RA patients received methotrexate, leflunomide, sulfasalazine or their combination. All patients received NSAID in combination with conventional synthetic DMARDs. Analysis of the content of the B-lymphocytes, myeloid and plasmacytoid DCs was carried out by flow cytometry. B-lymphocytes, subtypes of peripheral blood DCs were characterized by the following phenotypes: myeloid DCs (CD3-CD14-CD19-HLA-DR + CD11c + CD123-), plasmacytoid DCs (CD3-CD14-CD19-HLA-DR + CD11c-CD123 +), B-lymphocytes (CD19 +). Analyses were performed before treatment and 6 months later.
Results: RA patients were characterized by high activity of the disease (DAS28=5.46). At the beginning we revealed significant increasing of the population of myeloid DCs (1.6%) and B-lymphocytes (5.4%). No significant differences were observed in the number of plasmacytoid DCs. After 6 months of treatment, most of the patients had a decrease in the activity of the disease (DAS28=3.5vs5.46, p=0.05, n=12) coupled with a significant decrease mDCs (0.85 vs1.6%, p=0.03) and B-cells (4.2 vs 5.4%, p=0.05). In the remaining patients (n=8), there was no clinically significant improvement (DAS28=4.96) or differences in mDCs (1.45 vs1.6%) and B-cells (5.0vs5.4%). Six months later, there was a decrease in ASDAS activity among axSpa patients (2.56 vs 2.09). We were revealed no differences in amount in mDCs between RA and axSpa patients (1.4 vs 1.6%). After 6 month of investigation we detected decreasing mDCs (1.4 vs 0.9%, p=0.05). We have also found a decrease in B lymphocytes among axSpa patients (5.1 vs 4.1%) that is consistent with some authors' data on B lymphocytes in spondyloarthritis pathogenesis.
Conclusion: Reduction in the number of DCs in the context of treatment combined with reduced activity of diseases confirm the role of DCs in the pathogenesis of autoimmune diseases. In addition, probably being a target of pathogenetic therapy, they can serve as a marker of a good clinical response to the therapy.
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AB0095 CHARACTERISTICS OF TUMOR NECROSIS FACTOR-ALPHA AND INTERLEUKIN-6-INDUCED OSTEOCLASTS IN PERIPHERAL BLOOD AND BONE TISSUE FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: We have previously reported that stimulation of mouse bone marrow–derived macrophages with tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) induces differentiation of osteoclast-like cells having bone resorption ability[1]. Recently, we have shown that the combination of TNF-α and IL-6 can induce osteoclasts from human peripheral blood mononuclear cells (PBMCs) via RANKL-independent pathways, and that there are functional differences between TNF-α and IL-6-induced osteoclasts (T6-OCs) and RANKL-induced, conventional osteoclasts (cOCs). In particular, the number of T6-OCs differentiated from PBMCs in patients with rheumatoid arthritis (RA) positively correlated with the modified total Sharp score (mTSS)[2]. On the other hands, no such correlation was observed between the number of cOCs from RA and mTSS.
Objectives: Objectives of this study were to compare the differentiational potential into T6-OCs of PBMCs from RA patients with those from healthy donors, to clarify mRNA and protein expressions of T6-OCs derived from PBMCs from patients with RA, and to identify tartrate resistant acid phosphatase (TRACP) positive multinuclear cells with the same characters as T6-OCs histologically in the sub-chondral bone tissues from patients with RA and osteoarthritis (OA).
Methods: PBMCs and CD14+ monocytes derived from RA patients and healthy volunteers were stimulated with TNF-α and IL-6 or RANKL. Real-time quantitative PCR and immunofluorescence staining were used to measure expression levels of osteoclast-associated mRNA and protein. Consecutive sections of the proximal tibial bone tissue from patients with RA and OA (n=6 each) were stained by TRACP, and analyzed expression levels of osteoclast-associated molecules by immunohistochemistry.
Results: The number of T6-OCs differentiated from PBMCs in RA patients was significantly increased compared to that in healthy volunteers. Expression levels of *RANK* mRNA and protein were clearly up-regulated in cOCs differentiated from CD14+ monocytes and were down-regulated in T6-OCs. In contrast, expression levels of *MMP-3* mRNA and protein were obviously up-regulated in T6-OCs and down-regulated in cOCs. Therefore, we believe T6-OCs and cOCs were differently identified on bone tissue as TRACP+RANK-/MMP-3+ cells and TRACP+RANK+/MMP-3- cells, respectively. The numbers of TRACP+ osteoclasts in subchondral cancellous bone were significantly increased in RA patients compared to those in OA patients. Interestingly, numerous TRACP+/

RANK-/MMP-3+ osteoclasts were present in the subchondral bone from patients with RA, on the other hands, no such cells observed in OA patients.

Conclusion: The PBMCs of RA patients have definitely increased differentiation capacity into T6-OCs, which have potential of degrading chondral tissue. Additionally, cells having same characteristics with T6-OCs are observed in subchondral bone of patients with RA. These results suggest that novel T6-OCs may be involved in the pathogenic mechanisms of inflammatory bone destruction in patients with RA.

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AB0096 MECHANISM OF SHIP IN NEUTROPHIL EXTRACELLULAR TRAP IN RHEUMATOID ARTHRITIS

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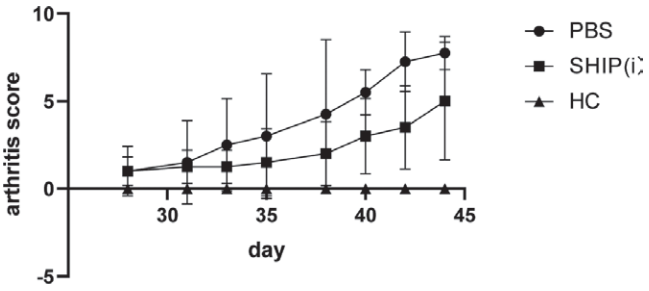
Background: Rheumatoid arthritis (RA) is a common autoimmune disease with unknown etiology. RA is characterized by the destruction of cartilage and bone. Neutrophils are abundant in synovial fluid of RA and are closely related to the development of RA [1]。In recent years, it has been reported that neutrophils can release neutrophil extracellular traps (NET) , which can not only kill different bacteria and viruses, but also closely related to autoimmune diseases [1,2] Studies have shown that NET is involved in the development of RA[3]. The Src homologous 2 domain containing inositol 5-phosphatase 1 (SHIP-1) controls the level of intracellular inositol 3-phosphate kinase product phosphatidylinositol-3,4,5-triphosphate. SHIP can be used as a positive or negative regulatory signal in different stimuli.And So has studied that the inflammation of CIA mouse model is reduced after SHIP is inhibited.

Objectives: Therefore, we want to study whether SHIP is involved in the formation of rheumatoid arthritis NET and its relationship with NET.

Methods: We isolated neutrophils from RA peripheral blood, stimulated NETosis with PMA, and detected the changes of NETosis in the group with SHIP inhibitor by flow cytometry and immunofluorescence. In addition, DBA mice were divided into three groups: HC, CIA and SHIP inhibitor intraperitoneal injection group. The degree of paw swelling and HE staining were used to detect the inflammation of mice, and the release of NET in CIA model was detected by flow cytometry.

Results: In the DBA model, the generation of neutrophil extracellular traps decreased significantly in the intraperitoneal injection group of SHIP inhibitor. SHIP inhibitor can significantly inhibit the formation of NET in RA patients. In addition, we also found TNF- α Monoclonal antibodies reduced NETosis in RA patients, while SHIP inhibitors inhibited the generation of NET in RA patients. The results suggest that SHIP may inhibit the inflammatory factor TNF- α. In turn, it is involved in the release of NET in rheumatoid arthritis

Conclusion: SHIP participates in the formation of NET in rheumatoid arthritis and affects the production of NET through pro-inflammatory cytokines. Therefore, SHIP is expected to become a new target for the treatment of RA.



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AB0097 EFFECT OF CYTOCHROME P450 METABOLITES OF ARACHIDONIC ACID IN RHEUMATOID ARTHRITIS

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Background: Arachidonic acid (AA) is a polyunsaturated fatty acid, released in inflammatory disease, such as rheumatoid arthritis (RA). Cyclooxygenase (COX) and lypooxygenase (LOX) pathways have received greater attention than cytochrome P450 (CYP) pathway of AA, which also plays a significant role in RA. AA is a substrate of CYP enzymes through two different pathways: the ω-hydroxylase, and epoxygenase pathways, respectively. The epoxygenase gives rise to epoxyeicosatrienoic acids (EETs) (5,6-EET, 8,9-EET, 11,12-EET, 14,15-EET), whereas ω- hydroxylase produces hydroxyeicosatetraenoic acids (HETEs) [1].

Objectives: The aim of this study is to evaluate the role of Cytochrome P450 metabolites of arachidonic acid and their therapeutic targeting in rheumatoid arthritis.

Methods: Pubmed and Scopus databases were the main databases used to identify all the studies conformed to the eligibility criteria.

Results: CYP enzymes (CYP3A, CYP2C19, CYP2C9, CYP1A2) suppression was observed in the synovial fluid of RA patients with higher IL-6 levels. EETs inhibit bone resorption and osteoclastogenesis, have an important role in blocking inflammation by reducing TNFα, and are negatively linked with pro-inflammatory cytokines (IL-1, IL-6, IL-8)[2]. The anti-inflammatory effects of EETs are potentially attributed to peroxisome proliferator–activated receptor gamma (PPARγ) activation. EETs are also metabolized through soluble epoxide hydrolase (sEH) to dihydroxyeicsatrienoic acids (DHETs), which have a pro-inflammatory activity. On the other hand, 20-HETE deriving from CYP ω-hydroxylase pathway has pro-inflammatory effect [3]. Data have shown that the genetic variations of CYP could affect the individual susceptibility to RA [4].

Conclusion: sEH inhibitors (sEHi) can not only block the inflammation caused by EETs metabolite, but can also act on LOX and COX pathway, and can be used in chronic-phase arthritis to reduce both inflammation, and the pain. In a mouse model of RA, sEHi showed decent RA assessment score improvement [5]. Moreover, data suggest that sEHi inhibit also PGE2 production, and exert an additional anti-inflammatory effect in arthritis. Since NSAIDs can lead to gastric and cardiovascular problems, sEHi are considered a better pharmacological approach in inflammatory rheumatic disease. Despite the failure of some of sEHi to reach clinical trials, we believe that CYP-derived eicosanoids should be further studied as potential target in rheumatic disease. Dual inhibitors sEHI/5-LOX activating protein (FLAP) are also very promising compounds as they can inhibit leukotriene formation, without effecting the levels of anti-inflammatory pro-resolving mediators. In perspective we suggest that multiple ligands targeting different AA pathways or mediators should be further explored as potential targets for designing new compounds to treat RA patients.

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AB0098

TOFACITINIB IS SUPERIOR TO DEXAMETHASONE IN MODULATING MAIT CELLS, INNATE LYMPHOID CELLS, AND TH9 CELLS IN PSORIATIC ARTHRITIS

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Background: Tofacitinib is a potent and selective oral inhibitor prevalently of JAK1 and JAK3and is currently included in the international recommendations for the management of psoriatic arthritis (PsA). Nonetheless, the mechanisms of the immune response to the treatment remain unclear, particularly regarding the effects on overlooked immune cell subpopulations specifically involved in the pathogenesis of PsA, i.e. mucosal-associated invariant T cells (MAIT), innate lymphoid cells (ILCs), both relevant sources of IL-17, and T lymphocytes producing interleukin 9 (Th9). We thus investigated the effect of tofacitinib on these cell population function and compared with glucocorticoids.
Objectives: To investigate the effect of tofacitinib and dexamethasone on MAIT cells, ILCs, and Th9 cells in PsA.
Methods: We investigated synovial fluid and peripheral blood mononuclear cells from patients with PsA that were cultured with phorbol myristate acetate (PMA)/ionomycin in the presence or absence of 100 or 300nM Tofacitinib or 1000uM Dexamethasone for 24 hours and the addition of brefeldin in the last 2 hours. FACS analysis allowed to identify MAIT cells by CD3+CD161+Valpha7.2TCR; ILCs by CD3+CD45+CD127+, from this population ILC1 were arrayed as cKit-CRTH2-; ILC2 as cKit +/- and CRTH2+, and ILC3 as cKit+ and CRTH2-; Th9: CD3+CD4+IL-9+.
Results: A significant decrease in IL-17 production was observed in CD8+ MAIT cells treated with tofacitinib 300 nM compared to untreated conditions, with a magnitude similar to what observed with dexamethasone [mean fluorescence intensity-MFI median 1920 (interquartile range-IQR 1597-2761), 18.6% (3.9-31.4) in untreated cultures; 1481 (1325-3163), 13.4% (4.5-9.3) in tofacitinib-treated cultures; 1511 (1147-2882); 11.5% (2.5-49) in Dexamethasone-treated cultures; Figure 1]. A reduction of IL-17 production was observed also in ILC3 [52.1% (4.2-59.4) in untreated cultures; 25.8% (5.3-40.3) in Tofacitinib-treated cultures; 35.4% (6.3-47.9) in dexamethasone-treated cultures]. A reduction of IL-9 production was observed in peripheral blood T cells [2.19% (1.3-2.3) in untreated cultures; 0.6% (0.0-1.8) in Tofacitinib-treated cultures; 0.97% (0.07-1.13) in Dexamethasone-treated cultures].

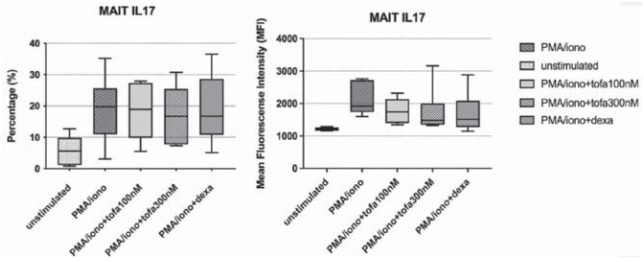

Figure 1.

Conclusion: In PsA, tofacitinib is superior to dexamethasone in reducing the production of IL-17 by synovial fluid MAIT cells and ILC3 cells and of IL-9 by peripheral blood T cells.
Disclosure of Interests: Maria De Santis Grant/research support from: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme, Actelion, Boehringer, Italfarmaco, Grunenthal, Roche, Natasa Isailovic: None declared, Angela Ceribelli Speakers bureau: Amgen, Paid instructor for: SPA Farmaceutici, Grant/research support from: Eli-Lilly, Grunenthal, GSK, Novartis, Pfizer, Francesca Motta Consultant of: Thermo-Fisher, Matteo Vecellio: None declared, Marta Caprioli: None declared, Giacomo Maria Guidelli Speakers bureau: Amgen, UCB, Galapagos, Eli-Lilly, Consultant of: Amgen, UCB, Galapagos, Eli-Lilly, Nicoletta Luciano Speakers bureau: Eli-Lilly, Galapagos, Consultant of: Eli-Lilly, Galapagos, Carlo Selmi Speakers bureau: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme), Paid instructor for: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme), Consultant of: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme), Grant/research support from: AbbVie, Amgen, Janssen, Pfizer
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AB0099

KNEE SYNOVIAL FLUID AND SERUM TNF-A IN RHEUMATOID ARTHRITIS: CORRELATION WITH SONOGRAPHIC PARAMETERS

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Background: Rheumatoid arthritis (RA) is a chronic, inflammatory joint condition that affects about 5 out of 1000 persons of the general population [1]. Environment, genetics, and autoimmunity may all have a role in the pathogenesis of the disease [2]. Overproduction of pro-inflammatory cytokines like tumor necrosis factor-α (TNF-α) is the end result of these mechanisms [3].However, little is known about its soluble concentrations in synovial fluid and serum and its association with clinical and ultrasonographic joint parameters.
Objectives: The aim of this study was to assess the presence of TNF-α in serum and synovial fluid of the knee in RA patients with knee effusion and to evaluate its correlation with musculoskeletal ultrasound (MSUS) parameters of the affected knee joint.
Methods: This study included 40 patients (20 RA,10 systemic lupus erythematosus (SLE) and 10 osteoarthritis (OA)) who had knee effusion (unilateral or bilateral) upon clinical examination. The sample size was selected as convenient sample; all patients who fulfilled the inclusion criteria were offered to participate in the study, unless they qualify for any of the exclusion criteria or refuse to participate. The inclusion criteria included the following: a) age ≥ 18 years old, b) patients with knee effusion detected by clinical examination and confirmed by MSUS, c) patients with RA diagnosed according to 2010 ACR /EULAR classification criteria [4],SLE according to SLICC criteria [5] or knee OA diagnosed according to EULAR criteria [6].
Demographic, clinical, and therapeutic data were recruited from all participants. Visual analogue scale (VAS) was used to determine the pain intensity in the affected knee. MSUS examination of the affected knee was performed, and a sample of synovial fluid was aspirated. TNF-α was measured in the aspirated synovial fluid and serum of each patient.
Results: There was a total of 40 patients (20 RA, and 20 age and sex matched non_RA (10 SLE, and 10 OA)). The mean age of RA patients was 48.4 years, most of them were females (80%) with median duration of knee pain of 2 months. Serum TNF-α was barely significantly higher in RA vs. non-RA cases (3.66 ± 0.76 vs 3.24 ± 0.58 U/ml, p= 0.052), while in synovial fluid, difference was not statistically significant (3.73 ± 0.72 vs 3.48 ± 0.58 U/ml, p= 0.252). Also, there was a statistically significantly higher serum TNF-α in RA vs. OA (3.66 ± 0.76 vs 3.06 ± 0.32, p= 0.022). Figure 1 shows that serum TNF-α at cut point of >3.24 U/ml can significantly discriminate RA from OA with 65% sensitivity, and 90% specificity (AUC = 0.725, P = 0.018). There was no statistically significant correlation between synovial TNF-α and MSUS parameters of thee knee either in RA or non_RA patients.

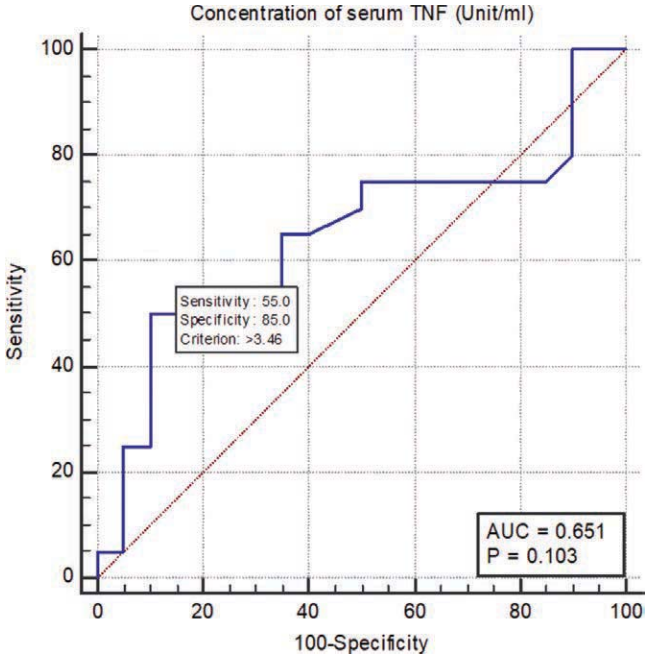

Figure 1. ROC curve for serum TNF as a discriminator of RA from non-RA

Conclusion: Serum TNF-α is higher in RA than non_RA patients. However, synovial fluid TNF-α level do not differ in RA from non_RA patients. No role of synovial TNF-α in knee pathologies in RA patients.
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Disclosure of Interests: None declared
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AB0100

LONGER DISEASE DURATION OF RHEUMATOID ARTHRITIS IS ASSOCIATED WITH TNF RECEPTORS REDISTRIBUTION ON IMMUNOCOMPETENT CELLS AND CHANGES IN CELL SENSITIVITY TO CYTOKINE

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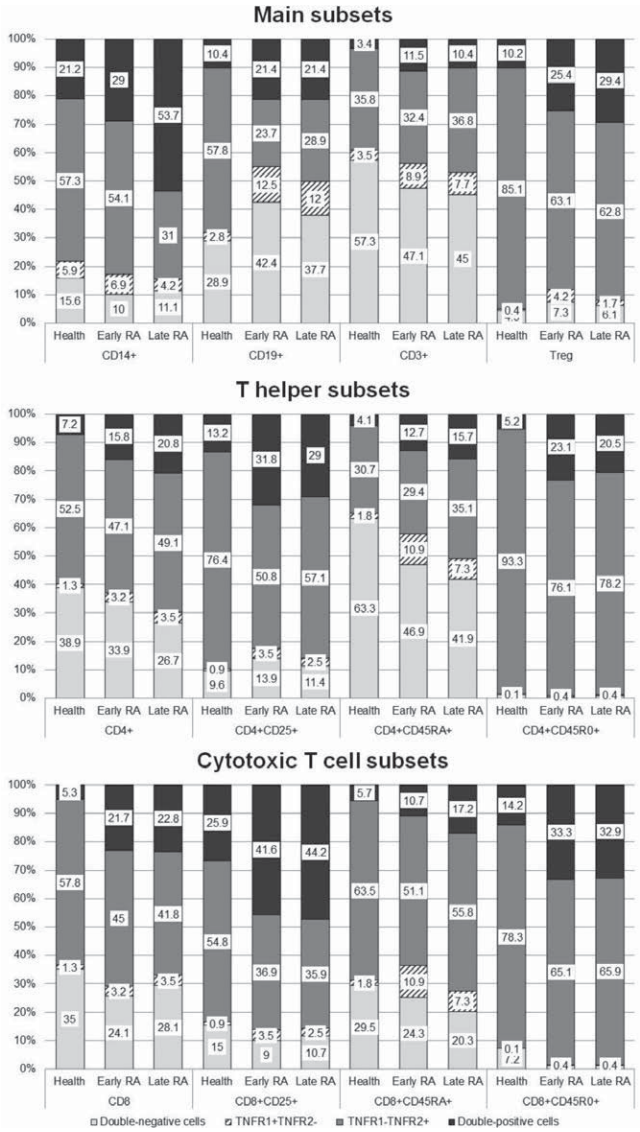
Background: Longer duration of rheumatoid arthritis (RA) is associated not only with higher disease severity, but also with lower treatment efficacy including anticytokine therapy. One of key mechanisms implementing this is changing in expression of cytokines and their receptors actively involved in the pathological process, such as tumor necrosis factor (TNF).



Objectives: The aim of the study was to study the redistribution of TNF receptors in patients with different duration of RA and depending on the severity of the disease.
Methods: Subanalysis of RA patients with disease duration less than 10 years (Early RA group, n=34) and more than 10 years (Late RA group, n=30) was performed. Late RA patients had DAS-28 activity comparable with Early RA group (4.98 vs 4.69, p=0.68), but had higher radiological stage, higher levels of inflammatory markers, and more often received biologics and had systemic features. As a control group, data from 43 comparable healthy donors were used. Co-expression profile of TNF receptors type 1 and 2 (TNFR1/2) were assessed in main mononuclear subsets: T cells, B cells, monocytes, Tregs, T helpers, cytotoxic T cells. Dynamics of percentage of cells with different co-expression combination was estimated as well as receptors expression density per cell.
Results: The redistribution of receptors on 12 subpopulations of immune cells was studied. Two types of cell responses were associated with disease duration increase. The first trend was presented by monocytes, regulatory T cells and general pool of cytotoxic T cells and consisted in significant decrease in TNFR2 expression density with simultaneously increase of double-positive TNFR1+TNFR2+ cells percentage and decrease of TNFR1-TNFR2+ cells percentage with no changes in proportion of cells without receptors, as compared with health and with disease progression. The second type of response was presented by B cells, T cells, T helper naïve cells and activated T cells and represented a significant increase in TNFR1 expression density and increase of double-positive cells proportion compared to health without influence of disease duration and tendency to decrease in proportion of cells without receptors over time.
Conclusion: Two trends in the response of immunocompetent cells to changes in the level of TNF that occur during chronic inflammation in RA were established. These two trends demonstrate the reactive and adaptive mechanisms of immune cells actively involved in pathological process and are of significant interest for the possibilities of modulating cell sensitivity to the proapoptotic and proinflammatory effects of cytokine and for futher development of targeted RA therapy.
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Disclosure of Interests: None declared
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AB0101

INCREASED DNA DAMAGE AND LACK OF DNA REPAIR IN FIBROBLAST-LIKE SYNOVIOCYTES OF INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory immune-mediated disease leading to synovial tissue inflammation and bone destruction. Inflammation-induced DNA damage in fibroblast-like synoviocytes (FLS) is thought to play an important role in RA pathogenesis. However, since a recent functional genomics study revealed a causal role for FLS in the genetic susceptibility of RA and synovial inflammation is absent in autoantibody positive individuals at risk for RA, we aimed to investigate whether DNA damage in FLS is present before onset of disease.
Objectives: Determine the extent of DNA damage in FLS and their capacity to repair this damage during the earliest phases of systemic autoimmunity.
Methods: We included individuals with arthralgia who were IgM rheumatoid factor (RF) and/or anti-citrullinated protein antibody (ACPA) positive but without any evidence of arthritis (RA-risk individuals, n=6), RA patients (n=6), osteoarthritis (OA) patients (n=6) and controls without inflammatory disease (n=6). Synovial tissue biopsies were collected either during joint surgery or individuals underwent a mini-arthroscopy of a knee joint. Subsequently, FLS were *in vitro* expanded upon enzymatic synovial tissue digestion. DNA damage in FLS (passage 6) was assessed by immunofluorescence staining for γH2AX. DNA damage repair was assessed by first irradiating the cells with 1 gray to induce DNA damage and assess γH2AX staining directly and after 3 and 24 hours of culture to allow for DNA repair.
Results: Preliminary immunofluorescence staining for γH2AX shows that DNA damage is present in RA-risk and RA FLS to more extent compared with FLS from non-inflammatory controls. OA FLS exhibit even more DNA damage and their nuclei show signs of impaired chromosomal segregation, forming micronuclei with high γH2AX staining intensity. Overall, DNA damage repair is slower in FLS from RA-risk individuals, RA and OA patients compared with controls as shown by persistent γH2AX staining after inducing DNA damage.
Conclusion: These findings reveal increased DNA damage and concomitant impaired DNA repair in FLS of not only patients with synovial inflammation but also in FLS from RA-risk individuals, suggesting that DNA damage is already present in absence of overt synovial tissue inflammation and before clinical

disease onset. More research is needed to investigate DNA damage or lack of DNA repair as potential driver in development of RA.
Disclosure of Interests: None declared
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AB0102 GPX4 - ASSOCIATED FERROPTOSIS OF MACROPHAGE EXACERBATES IMMUNE IMBALANCE IN RHEUMATOID ARTHRITIS

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Background: Reactive oxygen species accumulation and iron overload are involved in the pathogenesis of rheumatoid arthritis (RA). Ferroptosis, as a non-apoptotic form of programmed cell death, characteristically depends on iron and lipid peroxidation. However, the role of ferroptosis in RA has not been explored.
Objectives: To explore the role of ferroptosis in immune imbalance of rheumatoid arthritis.
Methods: Iron content in synovial fluid was determined by colorimetry. Lipid peroxidation was assessed by flow cytometry and immunofluorescence. MDA and GSH were used as markers to assess iferroptosis. K/BxN spontaneous arthritis mice and serum-induced arthritis mice were used as in vivo animal models of ferroptosis.
Results: Iron overload and hyperlipid peroxidation of mononuclear-macrophages were found in the synovial fluid of RA patients. Liproxstatin-1, the specific inhibitor of ferroptosis, alleviated the progression of arthritis mice model by increasing M2-like macrophage numbers. Mechanistically, iron overload in arthritis lesion induced anti-inflammatory macrophage ferroptosis by promoting glutathione peroxidase 4 (GPX4, a classical anti-ferroptosis molecule) to undergo P62 - dependent autophagy degradation.
Conclusion: Our results provide compelling evidence that macrophages ferroptosis plays a major role in RA. M2-like macrophages are more sensitive to ferroptosis than M1-like macrophages under iron overload circulation. This finding heavily contributes to the immune imbalance of rheumatoid arthritis.
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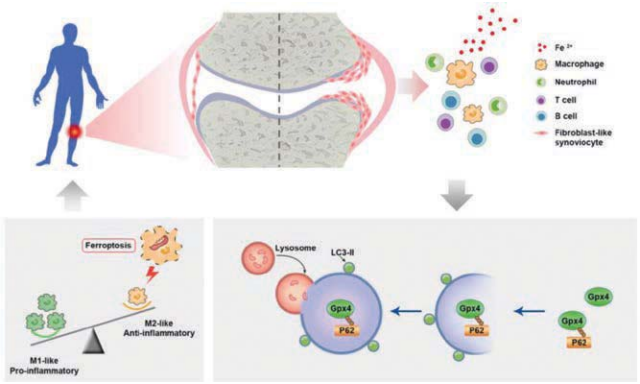

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AB0103 SITE SPECIFICITY OF RHEUMATOID ARTHRITIS INFLAMMATION: A SECONDARY ANALYSIS OF BIOPSIES FROM RADIAL AND ULNAR ASPECTS OF MCP JOINTS

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Background: Ulnar drift is a common complication of Rheumatoid Arthritis (RA) (1,2). There is no clear consensus regarding the etiology of the hand deformity. Observations from corrective hand surgery and other studies have noted more pronounced inflammation in the radial site of the MCP-joints (3,4). This could partly explain the pathophysiology behind the ulnar deviation.
Objectives: To determine if there is more pronounced inflammation, measured by increased CD-68 expression (5) and Krenn-synovitis score (6), at the radial side of the MCP joints when compared to the ulnar side, in patients with verified RA.
Methods: We included RA patients from a previous study who had biopsies taken from the most affected joints based on clinical examination and ultrasound (7). Twenty-nine PIP-, MCP- and wrist-joints were biopsied. Biopsies from the MCP-joints were taken from the dorso-ulnar and dorso-radial concavity. Inflammation was graded by the Krenn-synovitis score (0-9) and the density of CD-68-positive cells (%). The difference between radial and ulnar joint inflammation was calculated by paired t-test. P-value <0.05 was considered statistically significant.
Results: In 8 patients biopsies were taken from both the ulnar and the radial site of the same MCP-joint. The mean difference in inflammation on the radial and ulnar site of MCP-joints was based on differences in CD-68 density: 0,67% (95%-CI -4,77 to 6,10; P = 0,77) (Figure 1) and Krenn-score: 0,83 (95%-CI -1,31 to 2,98; P = 0,36), respectively.

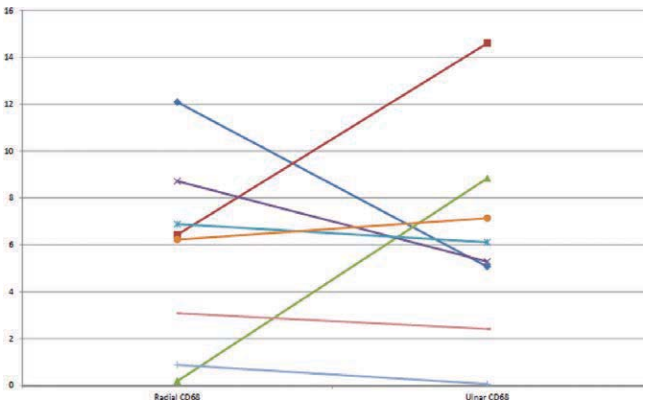

Figure 1. Paired data on CD-68 percentage in radial and ulnar sites

Conclusion: There was no difference in concentration of inflammatory cells or overall synovial pathology between the radial and ulnar site of MCP-joints in RA patients. The impression of a more pronounced inflamed synovium on the radial site of MCP joints, as observed during surgery, does not seem to arise from an immunological preference, but rather to be linked to a larger synovial volume.
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Spondyloarthritis - aetiology, pathogenesis and animal models

AB0104 CHANGES IIN SECRETION OF TH17 EFFECTOR CYTOKINES IN SYNOVIAL FLUID CELL CULTURES BY THE ATOPIC DERMATITIS BIOLOGIC DUPILUMAB (ANTI-IL-4 RECEPTOR ALPHA)

M. P. Hundahl[1], S. Lomholt[1], T. W. Kragstrup[1]. [1]*Aarhus University, Institute of Biomedicine, Aarhus, Denmark*

Background: Inflammatory arthritis and enthesitis has been documented as adverse events in patients with atopic dermatitis treated with dupilumab targeting the interleukin 4 (IL-4) receptor alpha subunit (1,2). The disease mechanisms underlying atopic dermatitis are primarily driven by a substantiated Th2 response. Therefore, blockade of IL-4 and IL-13 signaling rationally inhibits Th2-mediated atopy. However, IL-4 and IL-13 are also well-known suppressors Th17 cells. Therefore, we hypothesize that dupilumab-induced arthritis could be caused by increased production of Th17 effector cytokines.
Objectives: Here, we tested the effect of dupilumab on in vivo activated peripheral blood and synovial fluid mononuclear cells from patients with active inflammatory arthritis.
Methods: We used peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) from patients with immune mediated inflammatory arthritis (juvenile idiopathic arthritis, spondylarthritis, polyarthritis, psoriatic arthritis, and arthritis with intestinal bowel disease (IBD), n=8). PBMCs and SFMCs were either unstimulated or stimulated with CD3/Cd28 beads, and then cultured with three different concentrations of dupilumab (0.2 µg/mL, 1.0 µg/mL or 5.0 µg/mL). Supernatants were analyzed by the two MSD Multi-Spot Assay System in the Proinflammatory Panel 1 (INF-γ, IL-1β, IL-2, Il-4, IL-6, IL-8, IL-10, IL-12p70, IL-13 and TNF-α) and the Th17 Panel 1 (IL-17A, IL-21, IL-22, IL-23, IL-27, IL-31 and CCL20). All data were transformed to ratios by dividing the value of the samples treated with dupilumab with the value of untreated samples. Data were then analyzed with repeated measures one-way ANOVA or the paired t-test depending on the number of groups. P-values <0.05 were considered statistically significant.
Results: In SFMCs not cultured with CD3/CD28 beads, dupilumab decreased the production of IL-17A, IL-22, CCL20 and IL-1β (P-values: 0.0007, 0.0002, 0. 0025 and 0.0432 respectively). IL-6 was decreased by dupilumab in both PBMCs and SFMCs not cultured with CD3/CD28 beads (P-value = 0.013 and P-value = 0.001). The concentration of cytokines measured in supernatants from the PBMCs cultured without CD3/CD28 were low in both the Proinflammatory Panel and the Th17 panel. Interestingly, the response to increasing concentrations of dupilumab in PBMCs and SFMCs pre-conditioned with CD3/CD28 showed a biphasic curve. Thus, the low concentration of dupilumab (0.2 µg/mL) resulted in increased concentration while the higher concentrations of dupilumab (5.0 µg/mL) decreased the concentration. This was particularly seen in CD3/CD28-stimulated SFMC cultures for IL-17A, IL-22, IL-4, IL-13, IL-31, IL-10 and IL-1β (P-value for UT vs. 0.2 µg/mL: 0.0117, 0.0379, 0.0052, 0.0002, 0.0456, 0.0003 and 0.0484) In CD3/CD28-stimulated PBMC cultures, the biphasic response curve was seen for TNF-α, IFN-γ, IL-2 and IL-10 (P-value for UT vs. 1.0 µg/mL: 0.4978, 0.3922, 0.0373 and 0.0008).
Conclusion: This data contradicts the hypothesis and indicates that dupilumab does not increase the production of Th17 related cytokines. However, the increase in proinflammatory cytokines seen with the low concentrations of dupilumab suggest that partial blockade of the IL-4 receptor alpha under some conditions could lead to augmented inflammation.

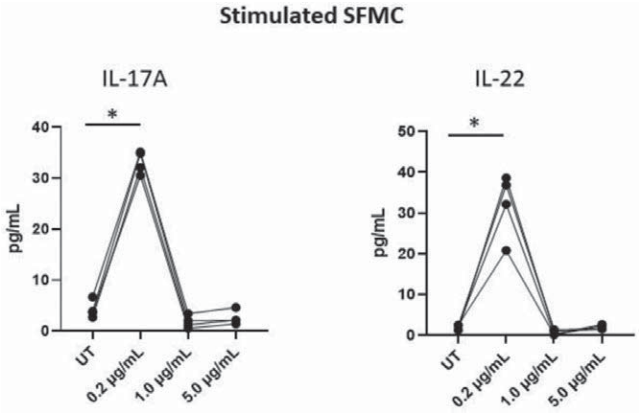

Figure 1. The biphasic response to dupilumab treatment shown for the analytes IL-17A and IL-22. An increase is seen in UT vs. 0.2 µg/mL with a P-value of 0.0117 and 0.0379.

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AB0105 A HIGHLY SENSITIVE NEO-EPITOPE BIOMARKER OF TYPE II COLLAGEN C- TERMINAL IS ASSOCIATED WITH CARTILAGE FORMATION

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Background: Altered extracellular matrix (ECM) remodeling is a common event in rheumatic diseases. Type II collagen is the most abundant ECM protein in the cartilage and provides tensile elasticity and strength to enable support to the joints. Chondrocalcin, also known as the C-terminal propeptide of type II collagen, is among the most highly synthesized polypeptides in cartilage. It is cleaved off by BMP-1/C-endopeptidase during maturation and plays a role in assembly of type II collagen and in calcification of cartilage matrix. When cleaved off, the chondrocalcin fragments are released into circulation, where they can be quantified in a blood sample.
Objectives: This study aimed at developing an immunoassay targeting a neo-epitope of chondrocalcin, named CALC2. Moreover, we explored its biomarker potential to evaluate type II collagen formation in an *ex vivo* human osteoarthritis (OA) cartilage explant model (HEX) with anabolic treatment, and in serum from healthy controls, patients with rheumatoid arthritis (RA) and patients with ankylosing spondylitis (AS).
Methods: A novel direct immunoassay targeting the neo-epitope of type II collagen C-terminal (PIICP) was developed and technically validated. The technical validation included inter- and intra-variation, linearity, spiking recovery, stability, and specificity. Specificity of the monoclonal antibody was tested using an elongated peptide, a truncated peptide, and a non-sense peptide to exclude possible cross-reactivity. CALC2 levels were measured in supernatant from HEX cultured for 35 days in serum free DMEM/F12 medium with IGF-1 (Insulin-like Growth Factor-1) (100 ng/mL), including a control group without (w/o) treatment. The supernatant was harvested 3 times weekly and replaced with new culture medium with IGF-1. Biomarker results were confirmed by western blot. Serum samples from 18 healthy donors (mean age 35.8 ± SD 3.8, 100% Caucasian), 19 patients with AS (mean age 35.8 ± SD 3.2, 100 % Caucasian) and 18 patients with RA (mean age 35.8 ± SD 3.4), 100% Caucasian) were also measured by CALC2. Linear regression models with pairwise comparisons were performed.
Results: A technically robust and specific assay was developed. The inter- and intra-assay variation of CALC2 was determined as 12% and 7% respectively. CALC2 showed a good dilution recovery, spiking recovery, and storage /freeze-thaw stability (All, 100%±20%). CALC2 showed specificity towards the targeted sequence and did not show any reactivity towards the truncated peptide, elongated peptide, or non-sense peptide. CAL2 neoepitope levels were significantly elevated after 14, 21 and 28 days of IGF-1 treatment compared to untreated ($p<0.01$, $p<0.0001$ $p<0.001$, respectively). The western blot confirmed the CALC2 results by the presence of a band of ~35 kDa in all explants, corresponding to the weight of chondrocalcin previously stablished (1). Furthermore, the bands were more pronounced at day 21 in the IGF-1 treated explant compared to the untreated explant. CALC2 also showed significantly lower levels in patients with RA compared to controls (p=0.003; mean 0.32 ng/mL ± SD 0.16 vs 0.64 ng/mL ± SD 0.31).
Conclusion: Higher levels of CALC2 were detected in supernatants from explants after 14, 21 and 28 days of IGF-1 treatment compared to untreated. Lower levels of CALC2 were present in patients with RA compared to healthy controls. Overall, this suggests that CALC2 may have potential as biomarker for type II collagen formation. However, further preclinical and clinical studies are required to validate these findings.

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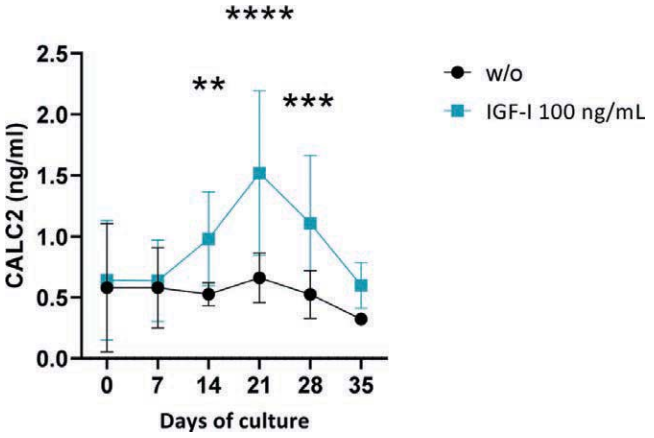

Figure 1. CALC2 measurements in HEX model.

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AB0106 THE PATTERN OF JOINT INFLAMMATION IN THE CAIA MOUSE MODEL OF ARTHRITIS

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Background: Animal models of inflammatory arthritis such as the collagen-antibody induced arthritis (CAIA) have a variable disease incidence in hind paw arthritis, complicating experimental design.
Objectives: To investigate the use of 18FDG µPET/CT as a guide for inflammation in joints otherwise inaccessible for clinical scoring, enabling the use of additional joints for histological analysis.
Methods: CAIA was induced in 8 male DBA/1 mice using the ArthritoMab Antibody cocktail (4 mg/mouse on day 0), followed by 100 µg LPS at day 3. Body weight, clinical signs of arthritis such as paw swelling and grip strength loss were recorded 3 times per week in both front and hind paws. Whole body 18FDG µPET/CT was performed at day 11, the estimated time of peak inflammation, and inflammation was scored visually on images scaled to the same standardised uptake value. At day 28, animals were euthanized and peripheral joints were collected for histological analysis.
Results: Cumulative disease incidence based on paw swelling dropped from 100% to 87.5% when looking only at hind paws, and to 75% when taking into account only the region suitable for histological analysis, namely the ankle and midfoot of the hind paws. Symmetrical, bilateral hind paw arthritis was not observed. While hind paw arthritis showed a tendency to be less severe in comparison to front paw arthritis, grip strength was equally affected, indicating possible involvement of other hind limb joints. µPET/CT images detected inflammation in the hind paws (at least unilateral involvement in 62.5% of the mice, bilateral involvement in 0%), knee joints (at least unilateral in 75%, bilateral in 50%), hip joints (at least unilateral in 50%, bilateral in 0%), elbow joints (at least unilateral in 50%, bilateral in 37.5%) and shoulder joints (at least unilateral in 25%, bilateral in 25%). Histology could confirm this inflammation with the presence of inflammatory infiltrates and bone erosions. Grip strength loss in hind limbs without paw swelling correlated only weakly with knee inflammation detected by µPET/CT.
Conclusion: In the CAIA model, inflammatory arthritis can develop in all peripheral joints, in particular with a high incidence in knee joints, which are highly suitable for subsequent histological analysis. Since clinical scoring seems insufficient for detecting these affected joints, implementation of in vivo imaging modalities such as µPET/CT, offers a substantial benefit in disease monitoring and assessment.
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AB0107 IMPACT OF SARS-COV-2 INFECTION ON THE DISEASE ACTIVITY OF PATIENTS WITH PSORIATIC ARTHRITIS UNDER BDMARDS: REAL LIFE DATA

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Background: SARS-CoV-2 infection can lead to severe inflammation and has been suggested to induce Psoriatic Arthritis (PsA) flares.[1] However, the impact on disease activity and response to biological disease modifying anti-rheumatic drugs DMARDs (bDMARDs) remains unknown.
Objectives: To evaluate the effect of SARS-CoV-2 infection on disease activity and bDMARDs responses in patients with PsA.
Methods: We performed a retrospective analysis including all the patients with PsA, meeting the CASPAR criteria and under biologic therapy, followed in the Rheumatology department of a tertiary university hospital. Demographic and clinical data, including occurrence of SARS-CoV-2 infection, were collected from our national database (reuma.pt). Disease activity (CDAI, SDAI, DAS28 4v, BASDAI, ASDAS) and bDMARDs responses (EULAR, ASDAS, ASAS, ACR and PsARC responses) were evaluated before and after SARS-Cov-2 infection. Statistical analysis was performed with SPSS. Continuous variables were compared through paired samples t-test.
Results: A total of 102 patients with PsA were included. Fifty-two were females (51%).The mean age was 53 ± 11.09 years and the median disease duration was 15 years [min 2, max 47]. Overall, 54 (53%) patients had predominant axial involvement, 26 (26%) peripheric and 36 (37%) enthesopathic. The most used bDMARD was etanercept (n=28, 27.5%) followed by adalimumab (n=22, 21.6%) and secukinumab (n=18, 17.6%).
The prevalence of SARS-CoV-2 infection was 15.7% (n=16). Sixty-three per cent received the BNT162b2 (Pfizer/BioNtech) vaccine, 31% received mRNA-1273 (Moderna), 13% received AZD1222 (AstraZeneca) and 13% received AD26.COV2.S (Janssen/Johnson & Johnson). Sixty-three percent were infected before any vaccination, 13% after the first dose and 25% after the second. The most common symptoms were anosmia (65%), dysgeusia (56%) and cough (56%). All patients fully recovered from the infection, with no need for hospitalization.
Regardless of the score used, the difference between the mean disease activity after SARS-CoV-2 infection and that at baseline did not reach statistical significance. At baseline and after infection, mean (SD) disease activity parameters were, respectively: CDAI 8.6±5.7 vs 8.6±5.7, p=0.997; SDAI 9.3±6.6 vs 9.2±6.1, p=0,928; DAS 28 4v 2.9±1.2 vs 2.9 ±1.2, p= 0.818; BASDAI 3.6 ±2.6 vs 3.2±2.7, p=0.506; ASDAS 2.2±1.2 vs 2.2±1, p=0.721.
The number of patients unresponsive to bDMARDs (according EULAR, ASDAS, ASAS, ACR and PsARC) before the infection wasn't different from post-infection.
Conclusion: Our study suggests that SARS-CoV2 infection has no negative impact on PsA disease activity and bDMARD responses. However, more studies are still needed to better understand the long-term effects of SARS-CoV2 infection.
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AB0108 INFLAMMATION IN AXSPA AS A DISRUPTOR OF BONE METABOLISM – THE EFFECT OF PATIENTS' SERA ON AN IN VITRO BONE MODEL

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Background: In axial spondyloarthritis (axSpA), two opposing processes of bone resorption and neogenesis are closely related, with a common denominator – chronic inflammation. This pathological condition affects osteoblasts, among other cells, residing in sites of inflamed tissue, but it can also activate mononuclear precursors in the blood to form osteoclasts [1,2]. To this day, it is not

yet clear how the interplay between osteoblasts and osteoclasts affects pathogenesis of axSpA.

Objectives: The aim was to evaluate the effect of sera from patients with different forms of the disease, non-radiographic (nr-axSpA) and radiographic (r-axSpA) including ankylosing spondylitis, in comparison to the effect of sera from healthy individuals (axC) on osteoblasts and osteoclasts co-culture.

Methods: The inflammation characteristic for each diagnose was simulated by age- and sex-matched pools of 12 nr-axSpA and 12 r-axSpA patients' sera, healthy condition by a pool of 12 axC sera. We used THP-1 monocytic cell line and SaOS-2 osteosarcoma cell line co-culture to model bone physiology. After THP-1 adhesion, SaOS-2 cells were added with 10 % of nr-axSpA, r-axSpA or axC sera, respectively, in the media for 14 days. Activity of osteoblastic alkaline phosphatase (ALP) and osteoclastic enzymes tartrate-resistant acid phosphatase (TRAP), cathepsin K (CTSK) and carbonic anhydrase II (CAII) on days (D) 1, 7 and 14 were measured. Simultaneously, we examined metabolic activity (MTS assay), cell proliferation (PicoGreen assay) and mRNA expression of selected genes in co-culture.

Results: In all three studied co-cultures the ALP activity increased with length of the cultivation; nevertheless, the onset of the activity in D1 was more rapid in axC sera compared to nr-axSpA ($P<0.05$) and r-axSpA ($P<0.001$). The ALP activity increase from D1 to D14 was 4.9 fold in axC, 5.7 fold in nr-axSpA and 6 fold in r-axSpA. Moreover, rise of ALP gene expression corresponds well with rise of ALP activity. TRAP activity peaked in all sera on D7 and decreased again towards D14, mirroring the same mRNA expression profile. The TRAP activity on D7 was highest in axC sera and lowest in r-axSpA ($P<0.01$). Gradual drop of CA II activity from D1 to D14 was detected in co-cultures with axC and nr-axSpA sera; in r-axSpA, however, the activity increased 1.42 times from D7 to D14 and was thus significantly higher on D 14 compared to cultures in other two sera ($P<0.0001$). In all cultures, CTSK activity increased from D7 to D14. Activity was highest in culture with axC sera (nr-axSpA D7 and D14 $P<0.0001$; r-axSpA D7 $P<0.0001$, D14 $P<0.05$). A gradual increase in cell proliferation was observed in axC sera and was thus significantly higher compared to both patients' sera on D14 ($P<0.0001$). In contrast, the proliferation in patients' sera peaked on D7 with the significantly highest D7 proliferation observed in r-axSpA ($P<0.05$). While the metabolic activity per cell followed U shape trend in all co-cultures, the changes were more distinct in patients' sera: 2 fold drop in r-axSpA, 1.6 fold in nr-AxSpA and 1.3 fold in axC sera on D7 followed by increase of 3.4 fold in r-AxSpA, 2.9 fold in nr-AxSpA and 1.8 fold in axC on D14.

Conclusion: Data acquired from the *in vitro* bone model point to an imbalance in the enzymatic activity of osteoclasts and to changes in the metabolic activity and proliferation of both, osteoblasts and osteoclasts. These changes seem to be caused by inflammatory agents in patients' sera. However, the changes are not the same in both forms of disease, which may explain differences between nr- and r-axSpA symptoms.

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AB0109 INCREASED NEUTROPHIL FREQUENCY IN LYMPH NODES OF PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Increased presence of neutrophils in the skin[1], synovium[2,3], and entheses[4] of patients with Psoriatic Arthritis (PsA) and their downregulation upon successful treatment[2,5,6], suggests a role for neutrophils in PsA pathogenesis. As neutrophils have been implicated in Th17 differentiation, gaining insight in the presence and function of neutrophils within lymph nodes, which are the epicentre of T cell activation and differentiation, could be important in unravelling disease pathogenesis.

Objectives: We hypothesize that activated neutrophils migrate from inflamed peripheral tissues to lymph nodes, where they steer inflammation by interaction with tissue resident cells and immune cells, ultimately resulting in activation of IL-17 producing T cells. To investigate this, we studied the presence of neutrophils in lymph node biopsies of patients with inflammatory arthritis, including PsA, and compared their frequencies to controls.

Methods: Ten PsA patients, 34 seropositive individuals at risk of developing rheumatoid arthritis (RA-risk), 26 ACPA- RA patients and 10 healthy controls (HC) underwent ultrasound-guided inguinal lymph node biopsy. These biobanked biopsies were analysed using qPCR and immunohistochemistry. Flow cytometry on fresh biopsies was used to determine cell frequencies in six active PsA patients (defined as arthritis in ≥1 joint) and two RA-risk individuals.

Results: qPCR analyses showed significantly increased mRNA levels of Cathepsin G (CTSG), which is highly expressed by neutrophils, in PsA patients compared to HC ($p = 0.020$). Immunohistochemistry showed that the neutrophil marker CD15 is significantly increased in PsA patients compared to HC ($p = 0.008$). Preliminary flow cytometry analyses indicates a clear population of CD45+CD16+CD66b+ neutrophils in lymph node biopsies of PsA patients while this was not observed in RA-risk individuals.

Conclusion: Overall, we show for the first time an increased presence of neutrophils in lymph nodes of PsA patients when compared to controls. Future studies are needed to investigate their functional role in immunoregulation within lymph node organs.

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AB0110 TRANSCRIPTOMICS-BASED INVESTIGATION OF THE MECHANISM OF ANKYLOSING SPONDYLITIS WITH UVEITIS

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Background: Spondyloarthritis is a large group of autoimmune diseases that are associated with HLA-B27. Among them, Ankylosing spondylitis is a typical representative of these diseases. In addition to spine and joint involvement, AS has many extra-articular manifestations, among which uveitis is one of the most common extra-articular manifestations of AS.[1]Untreated or inappropriate treatment can lead to serious consequences such as blindness. However, there are few studies on the mechanisms of AS-related uveitis, and the pathogenesis of AS-related uveitis is not fully understood, so there is no way to prevent it.

Objectives: We performed a whole-blood gene expression profiling and then analyzed gene expression differences between AS-associated uveitis patients and normal controls by bioinformatics methods. Protein–protein interaction network was constructed to predict the relationship among the products of the differentially expression genes (DEGs). Furthermore, module mining and function

annotation were applied to assess the interaction network of DEGs.The aim is to find predictive biomarkers for AS-associated uveitis, to further discuss the pathogenesis of AS-associated uveitis in depth, and to provide a reference for clinical precision treatment.

Methods: This microarray-based discovery study used samples from three patients with AS,classified according to the New York criteria,four patients with AS-associated uveitis, and three gender- and age-matched controls. Total RNA was extracted from whole blood samples and enriched for mRNA after DNA digestion using DNase, and then constructed cDNA libraries were quality-checked with an Agilent 2100 Bioanalyzer and sequenced using an Illumina HiSeq TM 2500 sequencer.The data were normalized and initially screened for differential genes using the DESeq R package in R 4.1.0 Prediction of relationships between products of differentially expressed genes (DEGs) using String database prediction and construction of protein-protein interaction networks in Cytoscape. GO with KEGG analysis of differential genes using ClueGO and CluePedia. Screening for hub genes associated with AS-associated uveitis using cytoHubba.

Results: We initially screened 14607 differential genes, from which 112 significantly differential genes with p-values<0.05 and |log2FC|>2 were selected. Among them, 82 were up-regulated genes and 30 were down-regulated genes. Sixty-six relationships between 49 nodes were shown in the PPI network interactions graph constructed from the String database results.The results of GO analysis showed that most genes were involved in biological processes related to immune response, such as positive regulation of inflammatory response, integrated stress response signaling and toll-like receptor 4 signaling pathway. The molecular functions were mainly focused on chemokine receptor binding. the results of KEGG analysis showed that the gene products were mainly involved in cytokine-cytokine receptor interaction, IL-17 signaling pathway. The target genes screened included CXCL8 CXCL2 NFKBIZ NFKBIA IL11 IL1A,all of which have adequate immune response effects(Figure 1)

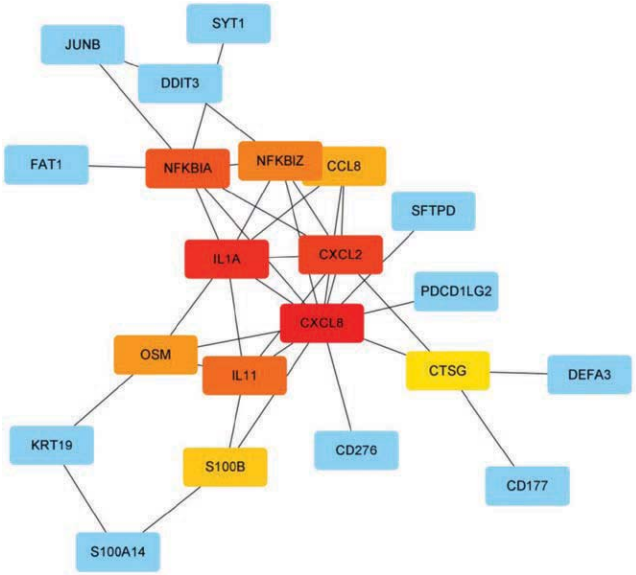

Figure 1. Using the EPC algorithm in cytoHubba to screen hub genes, the graph shows the top 10 scoring genes, with different colors representing higher scores.

Conclusion: We have identified a series of genes associated with immunity in this study.These DEGs may provide a basis for insight into the pathogenesis of AS-associated uveitis. Further experimental studies are needed to confirm our hypothesis.

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AB0111 EFFECT OF TOFACITINIB AND GLUCOCORTICOIDS ON INTESTINAL PERMEABILITY, EPITHELIAL DAMAGE AND BACTERIAL TRANSLOCATION IN RAT ADJUVANT-INDUCED ARTHRITIS

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Background: Growing evidence indicated that the intestine is not only a target but also an actor of the pathogenesis in chronic inflammatory rheumatic diseases (CIRD). Consistently, increased intestinal permeability (IP) and damage (ID) as well as bacterial translocation (BT) have been described in patients with CIRD. However, the effects of treatments used in patients with CIRD on gut health are unknown.

Objectives: To determine the effect of glucocorticoids (GCs) and tofacitinib on IP, ID and BT in rats with adjuvant-induced arthritis (AIA).

Methods: AIA was induced in 6-week-old male Lewis rats by a tail injection of *Mycobacterium butyricum* in incomplete Freund's adjuvant. At onset of arthritis, rats were treated daily with prednisolone at low (0.1 mg/kg/day, i.p.) or high dose (10 mg/kg/day, i.p.), or with Tofacitinib (10 mg/kg twice a day, s.c.) or with vehicle. After 21 days, IP, ID and BT were assessed by measurement of plasma levels of zonulin, intestinal Fatty Acid Binding Protein (iFABP) and serum levels of soluble CD14 (sCD14) by ELISA), respectively. Arthritis severity was daily evaluated through the determination of an arthritis score.

Results: Compared to vehicle, Tofacitinib and high-dose of GC both reduced arthritis score ($p<0.001$) and levels of sCD14 (-44%, $p<0.001$ and -41% $p<0.001$ respectively) in AIA. High dose of GC decreased iFABP (-17%, $p<0.05$) levels but had no effect on zonulin levels. Tofacitinib did change nor iFABP neither zonulin levels. As compared to vehicle, the low-dose of GC had no effect on arthritis severity, sCD14, iFABP and zonulin plasma levels.

Conclusion: Prednisolone at a dose efficient on arthritis did not worsen but on the contrary reduced intestinal bacterial translocation and epithelial damage. These results are consistent with the positive effects of GCs on intestinal dysfunction observed in case of sepsis or colitis. The lack of efficacy of the sub-therapeutic dosage of prednisolone suggested that effects of GC are, at least partly, related to their anti-inflammatory effects. Consistent with the positive effect of jakinibs in patients with inflammatory bowel disease, Tofacitinib blunted intestinal bacterial translocation in AIA. Given the suspected pathophysiological link between bacterial translocation and arthritis, our results identified a new mechanism involved in the positive effects of GC and tofacitinib in arthritis diseases.

Disclosure of Interests: None declared

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AB0112 DECOY RECEPTOR 3 AND ITS SIGNAL PATHWAY CONTRIBUTE TO PATHOGENESIS IN ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic progressive disease with invasion of spine and sacroiliac joint as the main clinical manifestation, which can be combined with systemic inflammation or abnormalities in multiple parts at the same time. There are complex changes of immune function in patients with AS, and its immune and genetic pathogenesis is still unclear. Decoy receptor 3 (DcR3), as a new immune molecule discovered in recent years, plays an important role in regulating T cell activation, proliferation, differentiation and apoptosis. Studies have confirmed that DcR3 is involved in the immune disorder process of rheumatoid arthritis, SLE, AS and other autoimmune diseases, so that the role of DcR3 in AS has attracted attention. However, the expression of DcR3 related pathway genes[1-3].However, studies evaluating the DcR3 related pathway genes in AS are scarce.

Objectives: To assess the contribution of DcR3 and its signal pathway to AS and the clinical importance of these genes in AS.

Methods: The mRNA expression levels of DCR3 and its signal pathway(DR3、TL1A、Fas、FasL、Ligth、LigthR、LTgthRNA expresured in peripheral blood mononuclear cells (PBMCs) from 50 AS patients and 50 healthy subjects. The relationship between DCR3 related molecular pathway expression levels and laboratory features was analyzed in AS patients.

Results: The expression levels of DCR3、DR3、Fas、Light were much lower in the AS group than in the HC groups ($p<0.05$)(a,b,c,d), and the expression levels of LT The relationship between DCR3 related molecular pathway expression l

Conclusion: Compared with HC group, DCR3 and its signal pathway in PBMCs of AS patients are differentially expressed. It is speculated that DcR3 related molecular pathway gene may be involved in the pathogenesis of AS.

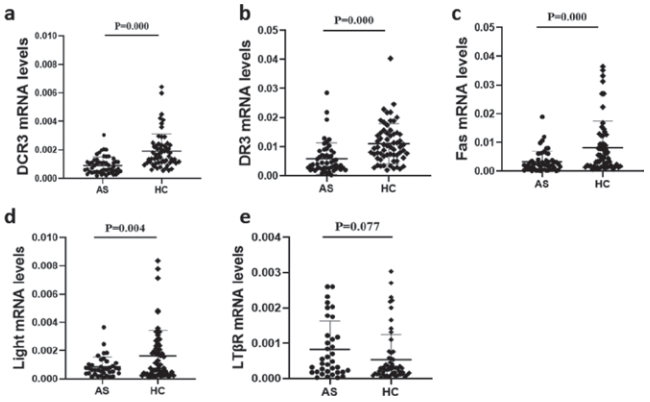

Figure 1. Relative Expression of DcR3 related molecular pathway gene in the PBMCs of Patients. The mRNA levels in PBMCs from AS patients(n=50) and HCs(n=50) were measured by RT-qPCR. The expression levels of DCR3、DR3、Fas、Light were much lower in the AS group than in the HC groups ($p<0.05$)(a,b,c,d), and the expression levels of LTβR was much higher in the AS group than in the HC groups ($p<0.05$)(e).

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AB0113 A MINIMAL-INVASIVE METHOD TO RETRIEVE AND IDENTIFY ENTHESEAL TISSUE FROM PSORIATIC ARTHRITIS PATIENTS

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Background: Enthesitis represents a hallmark feature of spondyloarthritis, including psoriatic arthritis (PsA).[1] So far, most of the data on enthesitis in PsA are based on clinical assessment of tenderness as well as MRI or ultrasound examinations.[2] These approaches, however, do not allow molecular analysis of entheses, which will require acquisition of entheseal tissue. Up today, it is unknown, which entheseal structure in humans would qualify for a feasible biopsy and how correct sampling of entheseal structures could be ascertained within such biopsy material. These technical challenges have led to substantial lack of knowledge on human entheseal tissues.

Objectives: To establish a minimally invasive biopsy technique of human entheses for the analysis of entheseal tissue in patients with PsA.

Methods: Human cadavers were used for establishing the technique to retrieve tissue from the lateral humeral epicondyle enthesis (cadaveric biopsies). After biopsy, the entire entheses was surgically resected (cadaveric resections). Biopsies and resections were assessed by label-free second-harmonic-generation (SHG) microscopy. The same biopsy technique was then applied in PsA patients with subsequent definition of entheseal tissue by SHG.

Results: Entheseal biopsies were performed in five cadavers and allowed the retrieval of entheseal tissue, validated by analysis of the resection material. Thus, microscopy of biopsy and resection sections allowed differentiation of entheseal, tendon and muscle tissue by SHG and definition of specific intensity thresholds for entheseal tissue. The same method was then successfully applied to 10 PsA patients. Hence, the fraction of entheseal tissue within the PsA biopsy specimens was high (65%) and comparable to the fraction retrieved in cadaveric biospies (68%) as assessed by SHG microscopy.

Conclusion: Entheseal biopsy of the tendon plate of the lateral epicondyle is feasible in PsA patients allowing reliable retrieval of entheseal tissue and its identification by SHG microscopy.

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Disclosure of Interests: None declared

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AB0114 IMPROVEMENT OF GUT MICROBIOTA DYSBIOSIS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AFTER ONE YEAR OF BIOLOGICAL TREATMENT

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Background: Emerging evidence suggests that dysbiosis of the gut microbiota is involved in the initiation and perpetuation of spondyloarthritis (SpA). Biological disease-modifying antirheumatic drugs (bDMARDs) are a successful treatment to improve symptoms and reduce structural damage occurring in SpA; however, non-responders are frequent and few predictive factors for clinical response have been identified. Whether or not a patient responds to treatment could be related to gut microbiota composition.

Objectives: To investigate the gut microbiota changes in patients with radiographic axial SpA (r-axSpA) after receiving one year of treatment with bDMARDs and identify potential microbial biomarkers predictive of treatment response.

Methods: Patients with r-axSpA were recruited between 2015 and 2019 in an extension of the prospective GErman SPondyloarthritis Inception Cohort (GESPIC) before beginning bDMARD therapy. All patients had high disease activity (BASDAI >=4 and/or ASDAS >=2.1) despite previous treatment with nonsteroidal anti-inflammatory drugs, and had not received treatment with bDMARDs for at least three months before enrollment in the study. The choice of bDMARD was left to the discretion of the clinical rheumatologists in accordance with standard practice. Disease activity measures (BASDAI, CRP and ASDAS) and fecal samples were assessed at baseline prior to treatment and after one year of treatment. Patients with back pain negative for inflammatory disease served as a control group. Microbiota composition was determined by 16S rRNA gene sequencing, followed by taxonomic profiling with the SILVA138 database. Response to bDMARD therapy was defined as a clinically important improvement of ASDAS (>=1.1).

Results: A total of 99 patients with r-axSpA and 63 control individuals were included based on the availability of clinical and microbiome samples. Average age (mean±SD) was 36.4±10.4 years and 64 patients were males. The prevalence of HLA-B27 was 89.9% among r-axSpA patients compared to 7.9% among control individuals. Simpson indices showed an increase in alpha diversity between baseline and year 1 in r-axSpA patients which was statistically insignificant (paired Wilcoxon p=0.154) but brought the r-axSpA cohort nearer to controls. Likewise, Bray-Curtis dissimilarities to measure beta diversity showed a qualitative normalization to healthy individuals after treatment when visualized in principal coordinate space.

At the genus level, patients were mainly depleted in Lachnospiraceae taxa such as *Blautia*, *Roseburia*, and *Fusicatenibacter*, and enriched in *Collinsella* compared to the control group at baseline. After one year of treatment, most SpA patients exhibited increased abundances of these taxa, most notably *Blautia*. Patients also exhibited depletions in *Bacteroides* and

Faecalibacterium, which was strongly enriched in HLA-B27+ individuals at baseline (adjusted Wilcoxon p<0.001). *Collinsella* showed a very slight median increase after one year of treatment, with no significant difference between responders and non-responders (adjusted Wilcoxon p=0.33). Shifts in highly abundant *Prevotella* and *Bacteroides* were strongly correlated with the change in ASDAS after one year when controlling for intra-individual variance and overall changes in alpha diversity.

Conclusion: The gut microbiota composition of r-axSpA patients who underwent treatment with bDMARDs for one year more closely resembled the controls. The unique enrichment of *Collinsella* in r-axSpA patients remained stable across time and treatment, suggesting it may be a disease biomarker.

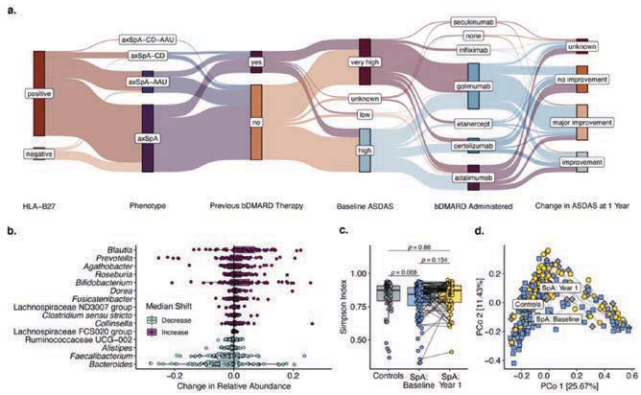

Figure 1. a) Flowchart of axSpA patients summarizing the main clinical and disease activity parameters of the cohort. b) Taxa with the most pronounced shifts in median relative abundance in patients with axSpA after receiving biological treatment for one year. c-d) Alpha and beta diversity analyses, respectively, of axSpA patients before and after treatment compared to control individuals. Labeled points in d represent group means.

Disclosure of Interests: None declared
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AB0115

MONOCYTE CHEMOATTRACTANT PROTEIN-1 IN PATIENTS WITH PSORIATIC SPONDYLOARTHRITIS CORRELATES WITH COMPONENTS OF PATIENT FUNCTIONAL STATUS

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Background: Activated monocytes represent the main source of pro-inflammatory chemokine, Monocyte Chemoattractant Protein-1 (MCP-1) in psoriatic skin lesions and synovial tissue during active psoriatic arthritis (PsA) (1). Osteoclast precursors binds MCP-1, implying the involvement of MCP-1 in the pathogenesis of bone erosion (2). MCP-1 is present in the plasma of patients with psoriasis at higher levels than in healthy subjects (3).

Objectives: The aim of this study was to determine the relationship between serum MCP-1 concentration and disease activity in PsA patients.

Methods: We enrolled 52 patients with PsA in the study and assessed Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Disease Activity in Psoriatic Arthritis (DAPSA), Bath Ankylosing Spondylitis Disease Functional index (BASFI), and the spread of psoriasis using Body Surface Area (BSA) method. In the serum, C-reactive protein (CRP) was measured using immunoturbidimetric assay and MCP-1 concentration using ELISA. Relationship between two parameters was analyzed applying Spearman correlation and p<0.05 was considered significant.

Results: Serum MCP-1 concentration did not correlate with the BSA, the DAPSA, CRP, the number of tender joints from 68 evaluated, the number of swollen joints from 66 evaluated, the patient's assessment of the intensity of pain and overall disease activity during the last week. The concentration of MCP-1 did not correlate with the fatigue, the intensity of pain in axial and peripheral joint structures, the sensitivity to touch, the duration of morning stiffness, BASDAI and BASFI.

MCP-1 statistically significantly correlated with the score for getting up from a sitting position without the help of hands, for getting up from a floor without the help, for standing up without supporting for 10 minutes and for performing physically demanding activities (Figure 1).

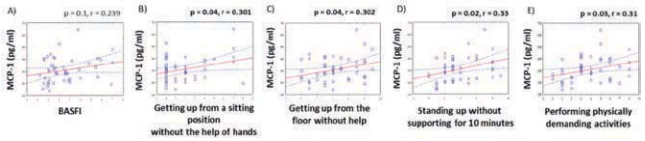

Figure 1. Correlation of serum MCP-1 concentration and BASFI components in patients with PsA.

Conclusion: Serum MCP-1 concentrations in PsA patients seem to reflect some components of patient functional status.

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SLE, Sjögren's and APS - aetiology, pathogenesis and animal models

AB0116

NEW INFLAMMATORY MARKERS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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Background: Thromboinflammation is a pathological process that is associated with uncontrolled inflammation, leading to hypercoagulability and thrombotic complications. Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are prototypical chronic thromboinflammatory diseases. Neutrophils are important cells in the development of systemic inflammation and thrombosis. Neutrophil reactivity (NEUT-RI), neutrophil granularity (NEUT-GI), immature granulocytes (IG), and neutrophil-to-lymphocyte ratio (NLR) are considered as inflammatory markers.

Objectives: To determine the role of parameters of neutrophil activation (NEUT-RI, NEUT-GI), immature granulocytes (absolute (IG#), relative (IG%) counts), NLR, ESR in assessing inflammation in SLE, primary APS (PAPS), and SLE with APS.

Methods: The study included 80 patients and 40 healthy donors (HD). Patients were classified into three groups: Group 1 included 37 patients with SLE. The median age of patients with SLE was 34 years [28-43]. Group 2 included 20 patients with SLE+ APS (45 years [37-49]). Group 3 included 23 patients with PAPS (38 years [34,5-47,5]). Current disease activity was evaluated with SLE-DAI-2K and adjusted GAPSS (aGAPSS).

A complete blood count (WBC-white blood cell, NEUT#-absolute neutrophil count, NEUT-RI, NEUT-GI, IG%, IG count, NLR, thrombocytes, ESR-erythrocyte sedimentation rate) was performed with XN-1000 automated hematology analyzer (Sysmex, Japan).

Results: Patient characteristics are shown in Table 1. IG# and IG% levels were significantly increased in patients with SLE and SLE+APS compared to controls and PAPS. ESR levels was significantly higher in patients with SLE, SLE+APS, and PAPS compared to HD. There was no significant difference between NEUT-RI, NEUT-GI, NLR, fibrinogen and CRP levels in patients with SLE, SLE+APS, PAPS, and HD. The aGAPPS was positively correlated with the IG# (r_s=0.46; p=0.028) and IG% levels (r_s=0.49; p=0.017) in patients with PAPS. No correlation was found between the IG and SLEDAI 2K. The ESR was positively correlated with SLEDAI 2K in SLE patients (r_s =0.54; p≤0.001).

Conclusion: Patients with SLE and SLE+APS had significantly higher levels of immature granulocytes than controls and PAPS patients. In PAPS, immature granulocytes were positively correlated with aGAPSS values.

The study was performed at V.A. Nasonova Research Institute of Rheumatology within the framework of the fundamental research FURS-2022-003.

Disclosure of Interests: None declared
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Table 1. Characteristics of patients with SLE, PAPS, SLE+APS, and healthy controls.

Parameters M±SD, Me [25%; 75%], n (%)	SLE (n=37)	PAPS (n=23)	SLE+APS (n=20)	Healthy donors (n=40)	p
SLEDAI 2K	7 [3.5-13]	-	4 [2-8]	-	p=0.03*
Anti-dsDNA, IU/ml	41.6 [13.6-101]	-	22.2 [10.7-69.9]	-	NS
aCL IgG,n,%	2 (5.4)	16 (69.5)	11 (55.0)	-	p<0.001*
aCL IgM,n,%	0	4 (19)	1 (5)	-	P=0.034*
aB2GP1 IgG,n,%	2 (5.4)	15 (65.2)	11 (55.0)	-	p<0.001*
aB2GP1 IgM,n,%	1 (2.7)	5 (21.7)	1 (5)	-	P=0.053*
LA positivity, n,%	1 (2.7)	15 (65.2)	9 (45)	-	p<0.001*
Triple positive,n, %	-	14 (60.8)	7 (35)	-	NS
WBC, 10^9/l	5.1 [3.8-7]	5.6 [4.7-6.7]	6.4 [4.9-7.7]	6.2 [5.3-6.9]	NS
Thrombocytes, 10^9/l	231 [201-300]	223.5 [189.5-270]	226 [168-278]	251 [210-290]	NS
NEUT#,10^9/l	2.89 [1.84-3.71]	3.6 [2.71-4.4]	3.3 [3.1-5]	3.55 [2.9-4.4]	NS
NEUT-RI, FI	45.5 [43.8-47.3]	44.2 [43.1-45.9]	45.1 [43.5-47.3]	44.0 [42.7-46.2]	NS
NEUT-GI, SI	155.6 [151.6-158.0]	154.85 [153.7-156.1]	154 [151.2-157.8]	153.7 [150.2-155.7]	NS
NLR	1.8 [1.3-2.5]	2.1 [1.4-3.1]	2.3 [1.6-2,8]	1.9 [1.5-2.4]	NS
ESR, mm/h	13 [7-20]	14 [6.5-18]	16 [13-19]	7 [4-11]	p<0.001*
IG#,10^9/l	0.02 [0.01-0.07]	0.01 [0.01-0.02]	0.03 [0.02-0.05]	0.01 [0.01-0.02],	p=0.002*
IG%	0.4 [0.3-1.1]	0.2 [0.2-0.4]	0.4[0.3-0.7]	0.2 [0.2-0.3]	p<0.001*
CRP, mg/l	2.2 [0.6-3.8]	1.15 [1-1.4]	2.5 [1.7-6.3]	-	NS
Fibrinogen, g/l.	3.15 [2.8-3.6]	3.35 [2.84-3.76]	3.21 [2.9-3.8]	-	NS

*a statistically significant test result (p < 0.05); NS-not significant;FI- fluorescence intensity; SI- scatter intensity; fl- femtoliter.

AB0117

IMMUNE CELL IMBALANCES IN PLACENTAS OF SYSTEMIC LUPUS ERYTHEMATOSUS AND SJÖGREN'S SYNDROME PATIENTS

J. J. Fierro[1], G. M. Verstappen[1], J. R. Prins[2], J. Westra[1], H. Bootsma[1], K. de Leeuw[1]on behalf of Rheumatology and Clinical Immunology. [1]*University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands;* [2]*University Medical Center Groningen, Obstetrics and Gynecology, Groningen, Netherlands*

Background: Systemic lupus erythematosus (SLE) and primary Sjögren's syndrome (pSS) are associated with adverse pregnancy outcomes (APOs) [1,2]. During pregnancy, maternal immune activation is related to a higher risk of hypertension, preeclampsia, preterm labor, and fetal growth restriction in SLE patients [1]. Furthermore, these patients have an increased risk of neonatal lupus due to the transplacental passage of maternal anti-RO/SSA antibodies to the fetus [3]. Nevertheless, there is no compelling evidence about the type of immune cell imbalances in the placenta in patients with SLE and pSS.

Objectives: Identify immunologic imbalances, focusing on interferon (IFN) and immune cell subtypes in placenta tissue of patients with SLE or pSS.

Methods: Retrospective analysis of immune cell composition of paraffin-embedded placental tissue from 6 SLE, 4 pSS, and 12 healthy women was conducted. For each case, one full-thickness sample of normal-appearing parenchyma from the central two-thirds of the placental disc was taken. APOs history and pregnancy outcomes were recorded. Placenta immunohistochemistry stainings were done for myxovirus resistance protein A (MxA, an interferon induced protein), CD3, CD20, CD45 and CD68. Statistical analysis was performed with a non-parametric T-test.

Results: A significantly higher MxA expression in the placenta of SLE and pSS patients compared to healthy controls was observed (Figure 1A). SLE patients had an increased MxA expression in decidua and villi compared with controls, while in pSS patients this increase was found in amnion and villi.

The count of T cells, B cells, total leukocytes, and macrophages in the decidua tissue were comparable between groups (Figure 1B). However, a significantly higher macrophage per total number of cells index was observed in SLE and pSS patients compared to healthy controls (Figure 1C). Only two patients had no APOs. Therefore, no analysis was performed comparing patients with or without APO.

Conclusion: A higher macrophage count and an increased IFN expression were identified in the placentas of SLE and pSS patients. These findings suggest a proinflammatory placental environment that could be related to APOs presentation in patients with SLE and pSS. However, to establish the relation with APOs further studies are needed including more patients especially without APOs.

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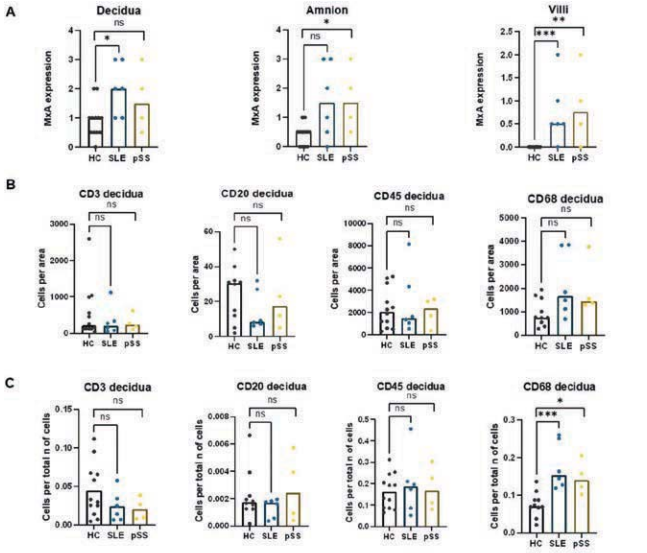

Figure 1. Immune cell imbalances in placentas of systemic lupus erythematosus and Sjögren's syndrome patients. (A) Placental MxA expression by disease. (B) Immune cell count per area of the decidua tissue. (C) Immune cells per total number of cells in the decidua tissue. Statistically significant results *p value <0,05; **p value <0,01, ***p value <0,001. Abbreviations. HC, healthy controls; SLE, systemic lupus erythematosus; pSS, primary Sjögren's syndrome.

Disclosure of Interests: None declared

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AB0118

PORPHYROMONAS GINGIVALIS AMOUNT IN THE TONGUE BIOFILM IS ASSOCIATED WITH EROSIVE ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

F. Ceccarelli[1], M. Saccucci[2], F. Natalucci[1], G. Olivieri[1], E. Bruni[3], R. Iacono[2], T. Colasanti[1], G. Di Carlo[2], C. Alessandri[1], D. Uccelletti[3], P. Russo[2], A. Pilloni[2], F. Conti[1], A. Polimeni[2]. [1]*Sapienza Università di Roma, Reumatologia, Dipartimento di Scienze Cliniche, Anestesiologiche e Cardiovascolari, Roma, Italy;* [2]*Sapienza Università di Roma, Department of Oral and Maxillofacial Science, Roma, Italy;* [3]*Sapienza Università di Roma, Department of Biology and Biotecnology Charles Darwin, Roma, Italy*

Background: Several data have demonstrated the occurrence of erosive arthritis in Systemic Lupus Erythematosus (SLE) patients. However, few studies have focused on the pathogenic mechanisms involved in this feature. The implication of oral pathogens has been proved in Rheumatoid Arthritis: in particular, Porphyromonas gingivalis (Pg), by inducing citrullination, could trigger autoimmune response.

Objectives: We evaluated amount of Pg of the tongue in a cohort of SLE patients with arthritis, focusing on the association with the erosive phenotype.

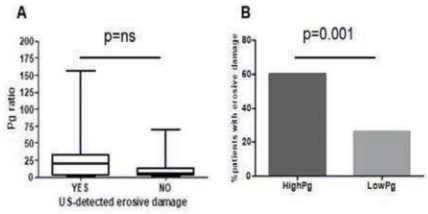
Methods: SLE patients with arthritis were enrolled. We evaluated the presence of ACPA and RF by using commercially enzyme-linked immunosorbent assay kits. SLEDAI-2k was applied to assess disease activity and DAS28 to assess

joint inflammatory status. Erosive damage was evaluated by ultrasound at level of metacarpophalangeal and proximal interphalangeals joints. All subjects underwent a tongue cytologic swab in order to quantify the amount of Pg (real-time PCR). The bacterium expression was obtained from the ratio between the patient's DNA amount and that obtained from healthy subjects.

Results: The present analysis included 33 SLE patients (M/F 3/30; median age 47 years, IQR 17; median disease duration 216 months, IQR 180). Concerning activity at the time of the enrollment, we found a median DAS28 value of 3.8 (IQR 2.8) and a median SLEDAI-2k of 4 (IQR 5). Twelve patients (36.4%) showed US-detected erosive damage in at least one joint, significantly associated with ACPA positivity (p<0.0001). Furthermore, patients with erosive damage showed significantly higher median DAS28 values in comparison with those without [4 (IQR 3.1) versus 3.2 (IQR 2.1), p=0.03]. Moving on the oral pathogen analysis, we found a mean Pg ratio of 19.7±31.1 (median 6.6, IQR 22.3). When dividing patients according to the presence of erosive damage, we found higher Pg amount in SLE patients with this phenotype in comparison with those without (31.4±44.3 versus 12.9±19.2, p=ns; Figure 1A). Thus, we used Pg mean values as threshold, identifying two groups of patients, namely highPg and lowPg. In a receiver operating characteristic curve analysis (ROC), this threshold resulted in the most sensitive and specific one (sensitivity of 85%; specificity of 50%). As reported in Figure 1B, erosive damage was significantly more frequent in highPg patients in comparison with lowPg (60.0% versus 26.0%, p=0.001). Furthermore, highPg patients showed higher prevalence of skin manifestations, serositis and neurological involvement compared to lowPg patients (p=0.005, p=0.03, p=0.0001, respectively).

Conclusion: The possible contribution of oral microbiota in SLE erosive arthritis was here evaluated for the first time, finding a significant association between erosive damage and higher expression of Pg at tongue level.

Figure 1. (A) Box and whisker plot representing Pg ratio in SLE Patients with and without erosive arthritis.
(B) Prevalence of erosive arthritis in SLE patients with HighPg and LowPg ratio.



Disclosure of Interests: None declared
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AB0119

ROLE OF COSTIMULATORY MOLECULES IN SYSTEMIC LUPUS ERYTHEMATOSUS: FOCUS ON CD137

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Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by a wide autoantibodies production. The traditionally concept of a B-cell driven disease has been changed in the last years due to the evidence demonstrating the crucial role of T cells in SLE pathogenesis. In particular, regulatory (Treg) and memory T cells seem act through co-stimulatory and co-inhibitory molecules, such as CD137, PD1-1 and CTLA4. The over-expression of this molecules on lymphocytes may contribute to immune system dysregulation.

Objectives: The primary objective of the present case-control study was to evaluate the expression of CD137, PD1-1 and CTLA4 on T cell surface of SLE patients by using flow-cytometry. Secondly, we evaluated the percentage of Treg and memory T cells.

Methods: We enrolled patients SLE patients (2019 ACR/EULAR criteria) and sex/age-matched healthy subjects (HS). Demographic, clinical, and laboratory data were collected in a standardized computerized electronically filled form. Disease activity was assessed by SLEDAI-2k. Each subject underwent peripheral blood sample collection. By using flow-cytometry we evaluated the expression of FOXP3, CD137, PD1-1 and CTLA4, CD45, CD25, CCR7 to determine the percentage of Treg and memory T cells.

Results: The present analysis included 21 SLE patients [M/F 1/20 median age 48 years (IQR 17), median disease duration 144 months (IQR 204)]. The Treg percentage was significantly lower in SLE compared to HS [median 4.2 (IQR 0.32) *versus* 2.5 (IQR 2.44); p=0.001, Figure 1A]. Moving on effector Treg (eTreg), SLE patients with high disease activity (SLEDAI > 4) showed a significantly higher prevalence for these cells compared to patients with SLEDAI ≤ 4 [1.16 (IQR 0.51) *versus* 0.53 (IQR 0.8), p=0.014, Figure 1B]. Moreover, inverse correlation was found between eTreg percentage and SLEDAI-2k [p=0.029, r=-0.47 (CI 0.75 – 0.04) Figure 1C]. The evaluation of CD137 expression was significantly higher in SLE patients compared to HS on CD3+ cells [median 5.32 (IQR 6.11) *versus* 3.3 (IQR 1.7), p=0.001, Figure 1F]. On CD4+ cells, CD137 expression positively correlated with disease activity [p=0.0082, r=0.58 (CI 0.15-0.82)]. Finally, when analysing memory T cells subpopulations, inverse correlation has been found between effector memory T cells (TEM, CD45RA-CCR7-) and SLEDAI-2k when considering CD3+ [p=0.029, r=-0.56 (CI 0.81 – 0.12)] and CD4+ cells [p=0.016, R=-0.54 (CI -0.80 - -0.1)]. Of note, CD137 expression on T central memory cells (TCM, CD45RA-CCR7+) positively correlated with SLEDAI-2k [(p=0.019, r=0.52 (CI 0.09 – 0.79)].

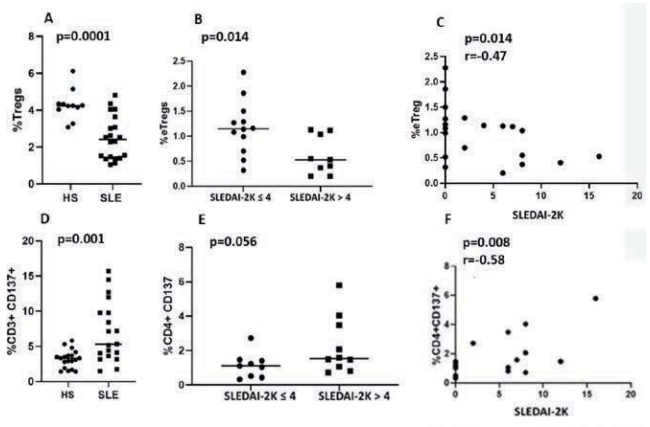

Figure 1. A) Comparison of the percentage of Treg in HS and SLE patients. B) Comparison of the percentage of eTreg in SLE patients with high disease activity and low disease activity C) Correlation between % eTreg and SLEDAI-2k. D) Comparison of the percentage of CD3+CD137+ cells in HS and SLE patients. E) Comparison of % of CD4+CD137+ cells in SLE patients with high disease activity and low disease activity F) Correlation between % of CD4+CD137+ cells and SLEDAI-2k.

Conclusion: Our results suggest a possible role of CD137-CD137L axis in SLE pathogenesis. The stimulatory role of this molecule is indicated by the positive correlation between SLEDAI-2k values and surface expression of CD137. Moreover, inverse correlation between SLEDAI-2k and eTreg percentage suggests a possible Treg dysregulation in SLE.

Table 1. SLE cohort features

Clinical and Laboratory Features	
Mucocutaneous	80.9%
Articular	76.1%
Serositis	19.0%
Kidney	23.8%
Haematological	48.2%
CNS/PNS	9.5%
Thrombotic events	4.7%
anti-dsDNA	68.4%
anti-SSA/anti-SSB	47.6%
anti-RNP	19.0%
anti-Sm	33.0%
Antiphospholipid antibodies	14.2%
Low C3/C4	57.1%
Previous Therapy	
Glucocorticoid	90.5%
Hydroxychloroquine	95.2%
Methotrexate	23.8%
Mofetil Mycophenolate	33.3%
Ciclosporin	28.5%
Cyclophosphamide	9.5%
Azathioprine	33.3%
Rituximab	14.3%
Antiplatelet	23.8%
Anticoagulant therapy	4.7%

Disclosure of Interests: None declared
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AB0120 ENZYMATIC PATTERN OF CIRCULATING XANTHINE OXIDOREDUCTASE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Generalized autoimmune inflammation underlies the pathogenesis of systemic lupus erythematosus (SLE). At the same time metabolic disorders at the cellular and subcellular levels are involved in the development of the disease. The literature contains data confirming the role of reactive oxygen species and oxidative stress in SLE multi-organ involvement [1,2].
Objectives: to evaluate the changes in XOR activities in plasma, lysed white blood cells (WBC), and lysed red blood cells (RBC) of SLE patients.
Methods: Diagnosis of SLE was verified using the SLICC criteria (2012). Activities of XOR interconvertible forms, xanthine oxidase (XO) and xanthine dehydrogenase (XDG), were measured in plasma, lysed WBC and lysed RBC by the spectrophotometric method [3]. The enzymatic activities were expressed as nmol/min/ml and normalized to 1×10^7 cells/ml in lysed WBC, and to 1×10^9 cells/ml in lysed RBC. The results were expressed as Me (Q_{25}; Q_{75}). Statistical comparison tests were selected in according to the common guidelines. Differences were considered significant when $p<0.05$. Reference ranges were calculated as 95th percentile interval.
Results: 56 adult SLE patients (mean age 35 (31; 42) years; mean disease duration was 8 (5; 11) years)) and 35 healthy individuals were enrolled in the study. Reference intervals of plasma XO and XDG activities were 2.29 – 4.31 and 4.52 – 5.97 nmol/min/ml, respectively. Reference intervals of XO and XDG activities in lysed WBC were 14.11 – 31.33 and 18.62 – 39.65 nmol/min/ml, respectively. Reference intervals of XO and XDG activities in lysed RBC were 20.62 – 25.46 and 41.89 – 55.04 nmol/min/ml, respectively. Enzymatic activities of SLE patients were significantly different from healthy controls. Increased XO activity and decreased XDG activity were observed in plasma of SLE patients ($p<0.001$ for both enzymes). The activities of both XOR forms were decreased in lysed WBC ($p<0.001$ for both enzymes). Lysed RBC were characterized by a decrease in XDH activity ($p<0.001$).
Conclusion: Significant changes in the balance of XO and XDG activities were revealed in plasma, lysed WBC and RBC of SLE patients., These enzymes can also exhibit NADH oxidase and nitrate reductase activities under conditions of low pH and hypoxia. Such conditions are formed in SLE due to the development of pronounced inflammation and microthrombosis in various tissues. Reactive forms of oxygen and nitrogen, which production is increased as a result of XOR activity, have a damaging effect on cellular structures, initiate the processes of lipid peroxidation, participate in the stimulation of NF-kB, and contribute to the formation of neutrophil extracellular traps. It can be assumed that the imbalance of XOR enzymatic activities in WBC indicates the previous stages of purine metabolism disturbances, which leads to a change in functional state and death of these blood cells. Free radicals generated by the XOR may have a damaging effect on RBC.
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AB0121 STUDY OF SLAMF7 EXPRESSION IN PRIMARY GOUGEROT-SJÖGREN SYNDROME

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Background: SLAMF7 (CD319, CS1) is a lymphocyte signaling activation molecule (SLAM) belonging to the CD2 receptor family. It regulates many immune functions following its activation by homotypic interaction (SLAMF7 as ligand and receptor). Its expression is observed on different hematopoietic cells such as plasma cells and NK cells and its activation leads to increased cytotoxic degranulation and IFNg secretion. SLAMF7 is a therapeutic target in multiple myeloma where plasma cells over-express SLAMF7. Elotuzumab, which binds to SLAMF7, induces an antibody-mediated cytotoxicity mechanism and an increase in the anti-tumor activity of NK cells.
Objectives: We investigated SLAMF7 expression in primary Sjögren's syndrome (pSS).
Methods: SLAMF7 expression was studied using flow cytometry on different subpopulations (CD4 T cells, CD8 T cells, NK cells, plasma cells (CD19+ CD38+ CD27high) and naive (CD27-) or mature (CD27+) B cells before (IgD+) or after (IgD-) class switching in pSS patients and healthy donors (HD). SLAMF7 protein expression was measured by the difference in expression (condition with antibody recognizing SLAMF7 - condition without antibody) of the mean fluorescence intensity (delta MFI).
Results: The pSS cohort consisted of 18 patients (17 women). 71% of patients were anti-SSA+, 41% anti-SSB+, 44% had rheumatoid factors (RF). The median IgG level was 13.3 g/l (9.88-21.45). 8/18 patients had evidence of systemic activity (ESSDAI score >0). Twenty-one healthy donors (19 women) were used as controls. No overall difference in SLAMF7 expression was observed between pSS and healthy donors, or among pSS patients between patients with or without systemic complications. SLAMF7 expression was higher in patients with than in patients without autoantibodies or markers of B-cell activation.
1/RF-positive patients had a higher expression of SLAMF7 than RF-negative patients by IgD- CD27+ B cells (median delta MFI: 397 for RF+ pSS vs 185 for RF- negative pSS [p=0.001] vs 187 [p<0.0001] for HD) and by C27+ IgD+ B cells (median delta MFI: 450 for RF+ pSS vs 307 for RF- negative pSS [p=0.005] vs 329 [p=0.001] for HD).
2/ Anti-SSA-positive patients had a higher expression of SLAMF7 than anti-SSA-negative patients by CD27+ IgD- B cells (median delta MFI: 346 for anti-SSA+ pSS vs 149 for anti-SSA-negative pSS [p=0.019] vs 187 [p=0.007] for HD) and by C27+ IgD+ B cells (median delta MFI: 403 for anti-SSA+ pSS vs 264 for anti- SSA negative pSS [p=0.021] vs 329 [p=0.012] for HD). The same association with a higher expression of SLAMF7 was observed for anti-SSB.
3/SLAMF7 expression was correlated with IgG levels in pSS patients on IgD-CD27+ B cells (r=0.51, p=0.044).
Conclusion: This study shows for the first time an overexpression of SLAMF7 on the surface of mature B cells in patients with pSS. This overexpression of SLAMF7 is associated with the presence of markers of B-cell activation. The therapeutic targeting of SLAMF7 therefore deserves further investigation in pSS. A study of its expression in the target tissue of the disease, minor accessory salivary glands, will allow a more precise analysis of the potential pathogenic role of SLAMF7 in pSS.
Acknowledgements: Necessity project
Disclosure of Interests: None declared
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AB0122 DETECTION OF ANTINUCLEAR ANTIBODY AND ANTIBODIES TO EXTRACTABLE NUCLEAR ANTIGENS IN SERUM-DERIVED EXOSOMES

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Background: Antinuclear antibody (ANA) and antibodies to extractable nuclear antigens (anti-ENAs) are important diagnostic biomarkers for autoimmune disease. In-direct immunofluorescence (IIF) and EUROLINE-Western Blot technology are used to detect ANA and anti-ENAs in serum respectively. However, the sensitivity of some anti-ENAs are not high, which often lead to the misdiagnosed or missed diagnosis of autoimmune disease. Much more methods are needed to increase the sensitivity of anti-ENAs. The protein of serum-derived exosomes have been used to explore the biomarker of many disease. As the level and significance of ANA and anti-ENAs in serum-derived exosomes, it has not been reported yet.
Objectives: Our study aims to detect the level of ANA and anti-ENA in serum-derived exosomes and compare the difference between serum and serum-derived exosomes.
Methods: Twenty-four patients with ANA positive in serum were enrolled into the study. Exosomes were separated from the serum by the ExoQuick^{TM} kit combined with ExoQuick^{TC} kit. ANA and anti-ENAs were further detected by IIF and EUROLINE-Western Blot technology in serum and serum-derived exosomes.
Results: The ANA levels in serum-derived exosomes were the same as serum. The anti-ENAs levels of serum-derived exosomes in 70% (16/24) patients were different from serum. Besides, anti-nRNP, anti-Sm, anti-SSA, anti-Ro52, anti-SSB, anti-Jo1, anti-CENPB, anti-dsDNA, anti-AHA, anti-ARPA levels of serum-derived exosomes in 11.11% (1/9), 33.30% (1/3), 46.15% (6/13), 54.55% (6/11), 50% (1/2), 100% (1/1), 66.67% (2/3), 75.0% (3/4), 66.67% (2/3), 40% (2/5) patients were different from that of serum.
Conclusion: The levels of most anti-ENAs in serum-derived exosomes are higher than that of serum, which may help to improve the sensitivity of diagnose in autoimmune disease.

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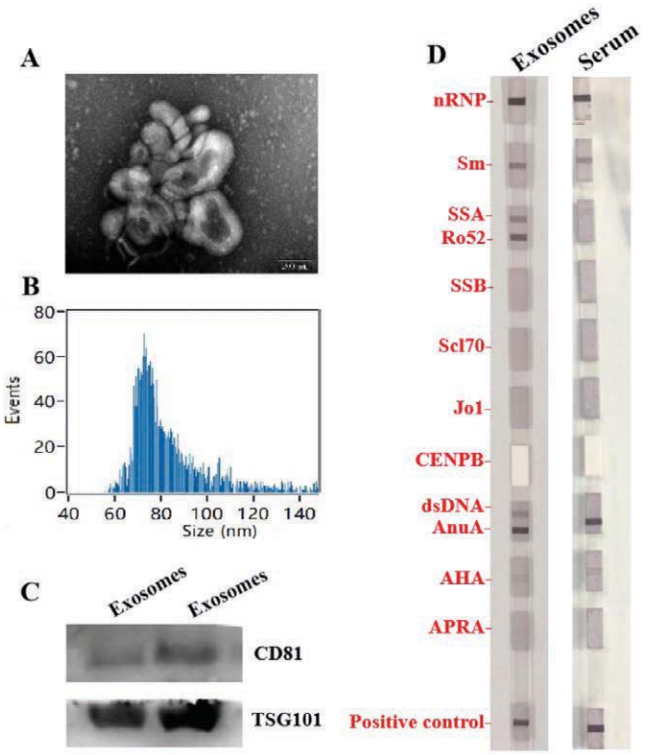

Figure 1. The identification and anti-ENAs detection of serum derived exosomes. A: The morphology of EVs were detected by TEM; B: The size of EVs were detected by high sensitivity flow cytometry for nanoparticle analysis; C: The expression of CD81 and TSG101 were detected by western blot; D: The anti-ENAs detection of serum and serum derived exosomes in patient 1#.

Disclosure of Interests: None declared
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AB0123

IMPACT OF TOBACCO ON PRIMARY SJÖGREN SYNDROME: ANALYSIS OF THE FRENCH COHORT ASSESS

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Background: It has been shown that smoking could be negatively associated with the risk of developing primary Sjögren's Syndrome (pSS), and that amongst smoking pSS patients, seropositivity for anti SSA antibodies and frequency of focal sialadenitis were lower. However, data are scarce concerning the impact of smoking on disease activity, glandular features, patient reported outcomes (PROs) and disease progression.
Objectives: To describe the impact on smoking on pSS disease characteristics and outcome.
Methods: ASSESS (Assessment of Systemic Signs and Evolution in Sjögren's Syndrome) is a French prospective multicenter, longitudinal cohort involving 395 patients with pSS enrolled in 15 French centers between 2006 and 2009 and followed since then. In these patients, we compared baseline characteristics and outcome (change in activity and PROs) during the first 5 years of follow-up, according to their smoking status (ever/never). For change during follow-up, any change of ≥ 3 points of ESSDAI or ≥ 1 point of ESSPRI or individual VAS, ≥ 25% of unstimulated salivary flow (UWSF) were considered.
Results: Data on smoking at inclusion were available for 394 patients, 106 (26.9%) of them were ever-smokers. Compared to never smokers, ever-smokers were significantly younger (54.0 ± 11.3 vs 59.2 ± 12.2, p < 0.001), and more frequently men (14 (13.2%) vs 12 (4.2%), p = 0.0013). The mean ESSDAI did not differ according to smoking status, (5.0 ± 4.9 vs 5.5 ± 5.8, p = 0.436).
There were no significant differences regarding the use of corticosteroids (49 (46.2%) vs 159 (55.2%), p = 0.113), immunosuppressive drugs (21 (19.8%) vs 77 (26.7%), p = 0.158), or hydroxychloroquine (49 (46.2%) vs 165 (57.3%), p = 0.05), even though numerically less smokers were taking these treatments. Smokers tended to have a lower dryness VAS and were less likely to use treatment for dry mouth (64 (60.4%) vs 210 (73%), p = 0.016).
No difference was observed in PROs (ESSPRI 5.2 ± 2.2 vs 5.5 ± 2.1, p = 0.259), and in UWSF (0.5 ± 0.75 vs 0.4 ± 1.0, p = 0.672) between smokers and non-smokers.
After five years, no difference in change of disease activity (ESSDAI change ≥ 3 points: 12/77 (15.6%) vs 30/207 (14.5%), p = 0.818), or in PROs (ESSPRI change ≥ 1: 30/70 (42.9%) vs 91/198 (46%) p = 0.654) was observed according smoking status, as well as no change in dryness (p = 0.968), pain (p = 0.280), fatigue (p = 0.605) or in UWSF (p = 0.132).

Table 1. ***Baseline characteristics and change in patient-reported outcomes at 5 years***

Baseline	Smokers n = 106	Non smokers n = 288	*p*-value
Age (years)	54.0 ± 11.3	59.2 ± 12.2	0.00008
Sex, females	92 (86.0)	276 (95,8)	0.0013
Disease duration (years) median [IQR]	3.9 [1.1; 8.7]	5.5 [2.6; 9.7]	0.257
ESSPRI	5.2 ± 2.2 (n = 97)	5.5 ± 2.1 (n = 267)	0.259
Dryness	4.9 ± 2.5 (n = 98)	5.5 ± 2.2 (n = 270)	0.053
Fatigue	5.9 ± 2.8 (n =101)	6.0 ± 2.6 (n = 275)	0.924
Pain	4.6 ± 2.8 (n = 101)	4.9 ± 2.9 (n = 274)	0.359
Unstimuled salivary flow (mL/min)	0.5 ± 0.75 (n = 89)	0.4 ± 1.0 (n = 241)	0.672
Treatment for dry mouth	64 (60.4)	210 (73.0)	0.016
ESSDAI	5.0 ± 4.9 (n = 104)	5.5 ± 5.8 (n = 281)	0.436
Corticosteroids	49 (46.2)	159 (55.2)	0.113
Hydroxychloroguine	49 (46.2)	165 (57.3)	0.050
Immunosuppresive drugs	21 (19.8)	77 (26.7)	0.158
Lymphocytes count (/mm^3)	1661.1 ± 919.3	1492.1 ± 1072.0 (n = 280)	0.128
After five years			
Change in ESSDAI ≥ 3	12 (15.6) (n = 77)	30 (14.5) (n = 207)	0.818
Change in ESSPRI ≥ 1	30 (42.9) (n = 70)	91 (46.0) (n = 198)	0.654
Change in salivary flow ≥ 25%	29 (44.6) (n = 65)	55 (34.0) (n = 162)	0.132

Data are given as mean ± SD or n (%) unless otherwise specified. SD, standard deviation; IQR, interquartile range; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index.
Continuous variables were compared using student t test and qualitative variable using chi-square

Conclusion: Smokers pSS patients are more likely to be men and younger than non-smokers. Ever smokers tended to have less dryness, and take less frequently treatment for dryness, corticosteroids, hydroxychloroquine or immunosuppressants. After five years, no difference was observed, according to smoking status, in terms of change in disease activity or PROs.
Disclosure of Interests: None declared
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AB0124

EFFECTS OF INHIBITOR K-CARRAGEENAN ON HAECS INFLAMMATORY RESPONSE TO LDLS ISOLATED FROM SLE PATIENTS

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with a high risk of atherosclerosis and cardiovascular events. It was previously reported by our group that low-density lipoprotein (LDL) particles isolated from SLE patients, during an active state of the disease ('flare'), promoted an exaggerated inflammatory response in human aortic endothelial cells (HAECs). However, the molecular mechanisms underlying this response still remain elusive.
Objectives: The hypothesis of this study is that these SLE-LDLs would be using receptor LOX-1, associated with inflammatory conditions and altered lipoproteins, to generate the proatherogenic response in HAECs.
Methods: LOX-1 pharmacological inhibitor k-carrageenan was used before the stimulation of HAECs with LDLs isolated from healthy controls (10), non-active (13), or active-SLE patients (13). Gene expression, protein, and cell migration assays were performed to evaluate HAECs inflammatory response.
Results: LOX-1 inhibition with k-carrageenan significantly reduced the expression of vascular cell adhesion molecule 1 (VCAM-1) and restored the gene expression of endothelial nitric oxide synthase (eNOS) in HAECs incubated with non-active SLE LDLs.
Conclusion: While VCAM-1 down-regulation was expected, the immediate next step derived from the observed results will be a deeper understanding of how LOX-1 inhibition may restore the endothelial ability to synthetize NO in the presence

of altered LDL. This will allow gaining insight not only on the development of atherosclerosis but also on the clue mechanisms involved in the pathogenesis of SLE.
Disclosure of Interests: None declared

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Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models

AB0125 IL-25 PARTICIPATES IN KERATINOCYTE-DRIVEN DERMAL MATRIX TURNOVER AND IS REDUCED IN SYSTEMIC SCLEROSIS (SSC) EPIDERMIS

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Background: Evidence shows that dysfunctional SSc keratinocytes contribute to fibrosis by altering dermal homeostasis (1, 2). Whether interleukin-25 (IL-25), an IL-17 family member regulating many epidermal functions (3), takes part in skin fibrosis is unknown.
Objectives: To investigate the role of IL-25 in skin fibrosis.
Methods: The expression of IL-25 was evaluated by immunofluorescence and *in situ* hybridization in 10 SSc and 7 healthy donors (HD) skin biopsies. Epidermal equivalents (EE) reconstituted by primary HD keratinocytes were used as a model to study transcriptomic changes induced by IL-25 in the epidermis. RNA expression profile in EE was characterized by RNAseq. The conditioned medium (CM) from primary SSc and HD keratinocytes primed with IL-25 was used to stimulate fibroblasts. IL-6, IL-8, MMP-1, type-I collagen (col-I), and fibronectin production by fibroblasts was assessed by ELISA.
Results: SSc epidermis expressed lower levels of IL-25 compared to HD. In EE, IL-25 regulated several molecular pathways related to wound healing and extracellular matrix (ECM) remodeling. Compared to control CM, the CM from IL-25-primed keratinocytes enhanced the fibroblast production of MMP-1, IL-6, IL-8, but not of Col-I nor fibronectin. However, IL-25 significantly reduced the production of Col-I when applied directly to fibroblasts and partially inhibit α-smooth muscle actin (α-SMA) expression promoted by TGFβ. The activation of keratinocytes by IL-25 was receptor-dependent and evident after a very short incubation time (10 min), largely mediated by IL-1, suggesting enhanced and specific release of preformed mediators.
Conclusion: These results show that IL-25 participates to skin homeostasis and its decreased expression in SSc may contribute to skin fibrosis by favoring ECM deposition over degradation.
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Acknowledgements: We thank Natacha Civic and Mylène Docquier (Genomics Platform) for performing the RNA sequencing; Nicolas Laudet (Bioimaging Core Facility) for quantification of immune-histology, François Prodon and Olivier Brun for microscope imaging (Bioimaging Core Facility), Marie Ebrahim Malek and Laura de Luca (Histology Core Facility) for contribution to tissue preparation (all at University Medical Center, Geneva, Switzerland).
Disclosure of Interests: Barbara Russo: None declared, Julia Borowczyk: None declared, Pietro Cacialli: None declared, Philippe Moguelet: None declared, Marie-Elise Truchetet Speakers bureau: Abbvie, Lilly, SOBI and Boehringer Ingelheim, Ali Modaressi: None declared, Nicolò Brembilla: None declared, Julian Bertrand: None declared, Wolf-Henning Boehncke Speakers bureau: Abbvie, Almirall, BMS, Celgene, Leo, Lilly, Novartis, and UCB, Carlo Chizzolini Speakers bureau: GSK, Roche, Boehringer Ingelheim
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AB0126 MULTIPARAMETER LINEBLOT IMMUNOASSAY FOR AUTOIMMUNE INFLAMMATORY MYOPATHIES: ADDITION OF CN-1A FOR THE DETECTION OF AUTOANTIBODIES ASSOCIATED WITH INCLUSION BODY MYOSITIS

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Background: Autoantibodies against cN-1A (Mup44) are primarily used as a biomarker for inclusion body myositis (IBM), they also occur with lower prevalence in systemic lupus erythematosus (SLE) and Sjögren's Syndrome (SjS). cN-1A has been included as a parameter on the multiparameter lineblot Autoimmune Inflammatory Myopathies 16 Ag et cN-1A (EUROIMMUN), allowing the detection of 17 myositis-specific and myositis-associated autoantibodies.
Objectives: The prevalences of anti-cN-1A autoantibodies were determined in different patient collectives and healthy blood donors.
Methods: A lineblot immunoassay containing a highly purified, recombinant cN-1A expressed in *E.coli* was incubated according to the instructions. Sera of 197 patients with IBM, 48 with collagenosis (systemic sclerosis, undifferentiated collagenosis and mixed tissue collagenosis), 52 with polymyositis/dermatomyositis and 75 with SLE/SjS were screened for cN-1A autoantibodies. Additionally, 151 apparently healthy blood donors as well as a disease control collective comprising sera of 20 patients with thyroiditis, 26 with neuromuscular disorders, 24 with primary biliary cholangitis (PBC), 19 with Wegener's Disease, 17 with Coeliac disease, and 2 with autoimmune liver disease (ALD) were analyzed. Signal intensities were automatically evaluated using the EUROLineScan software (EUROIMMUN).
Results: Prevalences of cN-1A autoantibodies were 34.5% in IBM, 10.4% in collagenosis, 7.7% in polymyositis/dermatomyositis, 13.3% in SLE/SjS, 2% in the blood donor cohort and 4.6% in the disease control collective.
Conclusion: The addition of cN-1A to a multiparametric lineblot immunoassay now reduces the risk of underdiagnosing IBM in patients with autoimmune inflammatory myopathies and increases the overall diagnostic sensitivity.
Disclosure of Interests: Julia Janz Employee of: EUROIMMUN Medizinische Labordiagnostika AG, Anthonina Ott Employee of: EUROIMMUN Medizinische Labordiagnostika AG, Marius Richter Employee of: EUROIMMUN Medizinische Labordiagnostika AG, Thomas Scheper, Employee of: EUROIMMUN Medizinische Labordiagnostika AG, Wolfgang Schlumberger Employee of: EUROIMMUN Medizinische Labordiagnostika AG, Wolfgang Meyer Employee of: EUROIMMUN Medizinische Labordiagnostika AG
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AB0127 BRONCHOALVEOLAR LAVAGE (BAL) FLUID AND SERUM FROM PATIENTS WITH SYSTEMIC SCLEROSIS WITH INTERSTITIAL LUNG DISEASE (SSC-ILD) PROMOTE A PRO-INFLAMMATORY GENE SIGNATURE IN HUMAN PRIMARY LUNG FIBROBLASTS

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Background: While circulating cytokines are frequently investigated in SSc patients, they may also play a role in local tissue, such as the lungs. Although most SSc patients show limited systemic inflammation, some studies have demonstrated that BAL fluid obtained from patients with SSc contains elevated levels of pro-inflammatory and pro-fibrotic cytokines. However, the relevance of the local milieu of the bronchial tree on the development of ILD has not been studied. We hypothesized that the bronchial milieu as represented by BAL fluid will have pro-inflammatory and pro-fibrotic effects on lung fibroblasts as the major effector cells in lung fibrosis. We also anticipated a greater pro-inflammatory and pro-fibrotic effect of BAL fluid obtained from patients with ILD (SSc-ILD) compared to patients without ILD (SSc). Finally, we hypothesized that serum obtained from both SSc-ILD and SSc will have a similar and concordant effect on lung fibroblasts, due to the systemic nature of the disease.
Objectives: To show the differential effect of BAL fluid and serum obtained from SSc patients with and without ILD on mRNA expression of pro-inflammatory and pro-fibrotic markers in human primary lung fibroblasts.
Methods: Serum and BAL fluid were collected from 3 SSc-ILD and 3 without ILD who were all treatment-naïve. ILD diagnosis was based on HRCT and lung function tests. Normal human primary lung fibroblasts were cultured and treated with either BAL fluid (5%) or serum (0.5%) from all individual patients. No treatment (CTRL) or treatment with pooled serum from healthy controls were used as control. After 4h, fibroblasts were harvested in TRIzol. The mRNA expression levels of inflammatory markers (Interleukin-6: IL-6, Interferon gamma-induced protein 10: IP-10), fibrotic markers (Connective Tissue Growth Factor: CTGF, Transforming Growth Factor: TGF-β and Alpha- Smooth Muscle Actin: α-SMA) were assessed using RT-qPCR. Nonparametric Mann-Whitney U test was used for comparison between groups. Correlation between BAL and serum treated fibroblast were calculated for the expression of the markers using Pearson correlation coefficient method.
Results: Fibroblasts treated with either SSc or SSc-ILD BAL fluids showed a significantly higher mRNA expression of IL-6 compared to control (Figure 1 a). The same was observed for IP-10, except for SSc serum which was not significant (Figure 1 b). When comparing the effects of BAL fluids between SSc or SSc-ILD patients, the effect of SSc-ILD BAL fluid was strikingly more profound

than observed with SSc on both IL-6 and IP-10 (Figure 1 a,b). Similar effects were seen when fibroblasts were treated with SSc serum, where serum from SSc-ILD resulted in significantly higher expression of IL-6 and IP-10 compared to SSc (Figure 1 a,b). The effect of serum and BAL on IL-6 gene expression were strongly and significantly correlated (r=0.9; P=0.015) while were weakly correlated regarding IP-10 expression (r=0.4; P=0.3) (not shown). The fibrotic markers TGF-β and α-SMA showed no difference in expression in BAL or serum-treated fibroblasts compared to controls (Figure 1 c,d). Only the fibroblasts treated with SSc-ILD serum showed a significant increase in mRNA expression of the early fibrosis marker CTGF when compared to control or SSc serum (Figure 1 e).

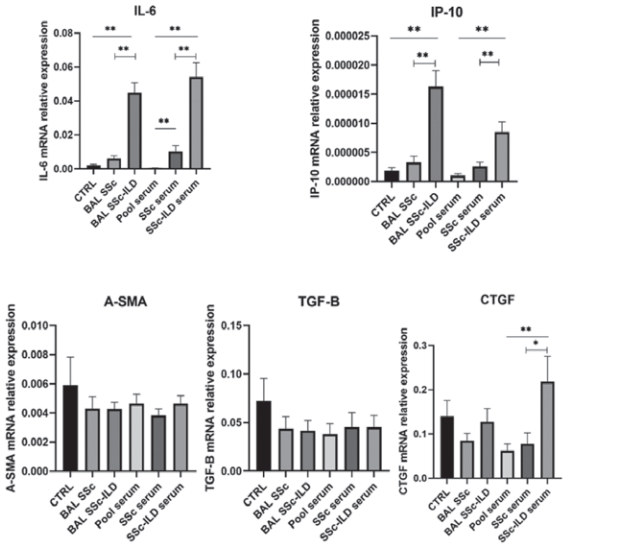

Fig.1: Effects of systemic and local fluids from SSc patients with ILD (SSc-ILD) and those without ILD (SSc) on lung fibroblasts. (a-e) mRNA relative expression of inflammatory (IL-6 and IP-10) and fibrotic (A-SMA, TGF-B and CTGF) genes, respectively, of lung fibroblasts treated with BAL or serum obtained from SSc or SSc-ILD patients, or healthy controls. CTRL, control (untreated); *, p<0.05; **, p<0.01. Three technical replicates were performed (n=3) using materials from 6 patients (N=6) and pooled healthy serum.

Conclusion: We showed a clear pro-inflammatory effect of BAL fluid obtained from patients with SSc on human fibroblasts as demonstrated by mRNA expression of IL-6 and IP-10. This pro-inflammatory effect was 5-10 times more profoundly observed in SSc patients with ILD compared to those without ILD. Similar effects were observed when fibroblasts were treated with serum obtained from the same SSc patients where the BAL fluid and serum of each patient seemed to provoke a concordant pro-inflammatory effect. Although further studies are warranted, our results underline the systemic nature of SSc and provide new insights into the role of and interaction between the local bronchial and systemic milieu in ILD development.

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AB0128

IMMUNE RESPONSE GENE 1 (IRG1) IS DYSREGULATED IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune idiopathic connective tissue disease in which there is inflammation and fibrosis of the skin. The innate immune system is intricately linked in the disease. IRG1 is a gene that codes for an enzyme that is essentially to make itaconate a metabolite of the TCA cycle. Itaconate has recently been ascribed function in immunity by negatively regulating inflammation through mechanism that involve upregulation of nrf2 and possibly downregulation of nf-kb to act as a molecular rheostat to balance the positive and negative aspects of inflammation. IRG1 is known to be robustly upregulated in macrophages after LPS stimulation.

Objectives: To determine the expression of IRG1 in systemic sclerosis macrophages.

Methods: Early diffuse SSc patients (< less than 2 years from first non-Raynaud's symptom) had blood drawn and monocytes were isolated on CD14 using MACS. Healthy controls blood was also taken and CD14+ monocytes were isolated. All female (3 donors each). After isolation cells were differentiated to macrophages using M-CSF for a set period. After which they were treated with ultrapure LPS for 18 hours. Cells were lysed and mRNA expression for IRG1 and Nqo1 was quantified by qPCR. Data is normalized to housekeeping gene 18S for normalization. In some experiments macrophages were stimulated with the itaconate derivative 4 Octyl Itaconate (4OI) at 100 μM for 2 hours, then stimulated or not with LPS for a further 24 hours. IL-1β and IL-6 cytokines were measured by ELISA. Bleomycin mouse model of skin fibrosis was employed by repeated intra dermal injections of bleomycin or sodium chloride vehicle. Skin biopsies were taken in the lesioned skin and H&E performed and fibrosis markers by qPCR was analysed.

Results: Healthy monocytes in response to LPS stimulation robustly upregulated IRG1 expression but in comparison to SSc monocytes this upregulated was significantly attenuated (n=3). Pretreatment of SSc monocytes with the itaconate derivative 4OI prior to LPS stimulation led to significantly reduced IL-1β and IL-6 secretion. The also led to upregulation of the nrf2 target gene Nqo1 6 fold compared to LPS treated alone. No difference in nf-kb was observed. mRNA expression of bleomycin skin found significantly downregulated nrf2 expression in association with elevated fibrosis markers compared to vehicle control treated mice (n=3 per group).

Conclusion: Failed upregulation of IRG1 in SSc macrophages may lead to a failure of inflammatory resolution and subsequent fibrosis. The itaconate derivative 4OI could be a possible anti-fibrotic through restoration of homeostasis via upregulation of nrf2 target genes.

Disclosure of Interests: Steven O'Reilly Employee of: I am employed by STipe therapeutics

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AB0129

MYOSITIS-SPECIFIC AUTOANTIBODIES IN CLINICAL PRACTICE: IMPROVING THE PERFORMANCES OF THE IMMUNODOT

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Background: Idiopathic inflammatory myopathies (IIM) or myositis are a group of rare autoimmune diseases that combine muscle weakness and multi-visceral damage. The discovery of IIM-specific autoantibodies (aAbs) and their associations with clinical phenotypes has improved diagnostic and classification criteria. Faced with the large number of these aAbs, multiplexed techniques have emerged. Among them, the immunodot is simple, rapid, and inexpensive, but has been several times criticized for its lack of specificity.

Objectives: Our objective was to evaluate the current interpretation criteria of the D-Tek immunodot and to propose new interpretation rules based on clinical criteria in order to improve its reliability.

Methods: Were included in this retrospective study patients tested positive result on the semi-quantitative myositis/synthetase immunodots at manufacturer threshold (≥ 5 UA), for at least one of the 15 aAbs: anti-SRP, anti-NXP2, anti-TIF1, anti-SAE (1 and 2), anti-Mi2, anti-MDA5, anti-Jo1, anti-PL7, anti-PL12, anti-EJ, anti-OJ, anti-KS, anti-ZO, anti-HA. Specificity of the immunodots was further evaluated using 60 healthy and anonymous subjects (French blood bank, Toulouse, France). The clinical diagnosis and sub-classification retained by the clinician in charge of the patient was used as a reference for attribution to the myositis/non-myositis group and subgroups. For the myositis group, 7 subgroups were considered: immune-mediated necrotizing myopathy (n=4); dermatomyositis (n=66); anti-synthetase syndrome (n=36); inclusion body myositis (n=1); overlap myositis with another connective tissue disease (n=7); polymyositis (n=8); and unclassified myositis (n=6). For the non-myositis group, patients were subdivided in 4 subgroups: autoimmune or inflammatory diseases (n=72); isolated and diffuse interstitial lung disease (n=26) not associated with other myositis criteria; other non-inflammatory myopathies (n=8) including genetic, metabolic, and toxic myopathies; and other diseases (n=36). The immunodot interpretation thresholds were evaluated both in relation to the manufacturer's threshold, and by considering the phenotypes and clinical diagnoses using a ROC method (Youden's index).

Results: Among 270 patients included between 01/07/2016 and 30/06/2020, 128 (47%) were classified as myositis (median age 58 years, 60% women, 52% DM and 28% AS) and 142 (53%) in non-myositis. Among the 15 aAbs analyzed, none were detected in the healthy control group but they were represented in both myositis and non-myositis group. Among them only 2 (anti-Jo1, anti-Mi2) predominate in the myositis group, and 1 (anti-TIF1) in the non-myositis group (Fisher's test). As quantitative values were found different for 5 aAbs (Mann Whitney test), a clinical threshold was calculated to discriminate myositis from non-myositis groups (ROC curve) allowing to determine an odds ratio (OR). Accordingly, 4/15 (%) aAbs were found associated with myositis: anti-SRP (at 28UA: OR=3.24 95% CI [1.01-10.46], p=0.048), anti-MDA5 (at 15UA: OR=4.36; 95% CI [1.19-15.99], p=0.048), anti-Mi2 (at 5UA: OR =3.24; 95% CI [1.01-10.46], p=0.026), anti-Jo1 (at 5UA: OR= 12.20; 95% CI [2.78-53.52], p<0.0001). All positive predictive values were improved by using a clinical threshold although some of did not reach significance due to their infrequency.

Conclusion: In this retrospective work, despite missing data, the clinical phenotypes of myositis patients and their distribution according to aAbs were

comparable to those in the literature. Our study confirms the lack of specificity of D-tek immunodots for IIM-specific aAbs and allows establishing new thresholds improving their performance. Our results should encourage medical biologists to establish local rules of interpretation and reinforce the interest of the discussion between Clinicians and Biologists around the interpretation of these immunodots.

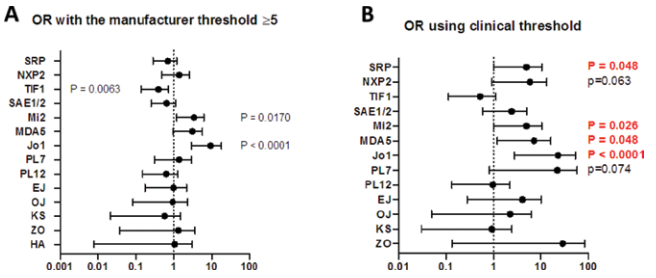

Figure 1. A: Odd Ratio (OR) evaluated with the manufacturer threshold ≥ 5 and B: OR using Youden's index (clinical threshold).

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AB0130 DEREGULATION OF TFAM EXPRESSION PROMOTES MITOCHONDRIAL DAMAGE AND FIBROBLAST ACTIVATION IN SYSTEMIC SCLEROSIS

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Background: Transcription factor A, mitochondrial (TFAM) is a transcription factor with essential function in the mitochondrial homeostasis, such as mitochondria biogenesis and mtDNA replication. Deregulation of TFAM expression has been linked to mitochondrial dysfunction. However, its role in the pathogenesis of rheumatic diseases has not been studied so far.
Objectives: We aimed to study the role of TFAM in the pathological fibroblast activation in SSc.
Methods: The expression of TFAM in SSc skin fibroblast and skin biopsies was analyzed by immunofluorescence and Western blot. The role of TFAM in fibroblast activation was investigated by TFAM knockdown in cultured fibroblasts. The role of TFAM in skin and lung fibrosis was further studied in mice with fibroblast specific knockout of TFAM in three independent mouse models: Bleomycin-induced skin and lung fibrosis as well as TβRI^{act}-induced skin fibrosis.
Results: Dermal fibroblasts from SSc patients express lower level of TFAM in the skin and also after prolonged culture in vitro. The downregulation of TFAM impairs mitochondria homeostasis with decreased mitochondrial number, accumulation of damaged mitochondria with release of mtDNA, accumulation of deletions in mtDNA, metabolic reshaping with impaired OXPHOS and release of the mitokine GDF15. Long time, but not acute exposure of normal fibroblasts to TGFβ mimicked the finding in SSc fibroblasts with downregulation of TFAM and mitochondrial homeostasis disruption and damage. Knockdown TFAM of normal fibroblasts promotes fibroblast activation with increased myofibroblast differentiation and collagen release in a SMAD3 dependent manner. RNA sequencing demonstrated upregulation of pro-fibrotic genes and pathways. Mice with fibroblast-specific knockout of TFAM demonstrate are more sensitive to fibrotic stimuli such as bleomycin injection and TβRIact-overexpression and even demonstrate responses to NaCl instillation.
Conclusion: Alterations in the key mitochondrial transcription factor TFAM in response to prolonged activation of TGFβ and associated mitochondrial damage induce transcriptional programs that promote fibroblast activation and tissue fibrosis.
Disclosure of Interests: Xiang Zhou: None declared, Thuong Trinh-Minh: None declared, Cuong Tran Manh: None declared, Andreas Giessl: None declared, Christina Bergmann: None declared, Andrea-Hermina Györfi: None declared, Georg Schett: None declared, Jörg H.W. Distler Consultant of: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB.,, Grant/research support from: Anamar, Active Biotech, Array Biopharma, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB.
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AB0131 INDUCTION OF COLLAGEN CHAIN FORMATION IN RESPONSE TO FIBROTIC FACTORS IN DERMAL AND PULMONARY FIBROBLASTS

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Background: Systemic sclerosis (SSc) patients who develop pulmonary fibrosis, have an increased mortality rate[1]. Excessively activated fibroblasts deposit extracellular matrix (ECM), which leads to fibrosis resulting in stiffening of the tissue in both skin and lung. Currently there is no cure for fibrosis in SSc, only drugs which can slow the fibrotic process, and there is therefore, a medical need for further understanding of the pathogenesis. Fibrosis is associated with growth factors, including tumor growth factor beta 1 (TGF-β1) and platelet derived growth factor-ab (PDGF-ab).
Objectives: We investigated how TGF-β1 and PDGF-ab stimulation affected the gene and protein expression of specific collagen chains of type I, III and VI collagens in primary healthy human dermal (DF) and pulmonary fibroblasts (PF).
Methods: The fibroblasts were grown in 0.4% fetal calf serum DMEM, ficoll (to produce a crowded environment) and ascorbic acid for up to 12 days. They were stimulated with TGF-β [0.01 nM], PDGF-ab [3 nM] or a combination of TGF-β [0.01 nM] and PDGF-ab [3 nM], while non-stimulated fibroblasts served as control. ECM protein formation was assessed in supernatant from day 0, 4, 8 and 12, by ELISAs which detects the N-terminal of the pro-collagen of type I and III collagen, and the C5 domain of the α3 chain of type VI collagen. Gene expression was analyzed after 4 days and the relative gene expression was calculated based on multiple reference genes[2]. Statistical analysis includes one-way and two-way ANOVA.
Results: TGF-β increased the gene expression of Col1α1 in DF (p<0.0001) and Col1α2, Col3α1 and Col6α3 in both DF (p<0.01, p<0.001, p<0.05, respectively) and PF (p<0.0001) compared to control. PDGF-ab showed no difference in gene expression of the DF but decreased multiple genes in PF (p<0.01). The combination of TGF-β and PDGF-ab increased the gene expression of Col1α1 in DF (p<0.01), Col3α1 in PF (p<0.0001) Col1α2 and Col6α3 in both DF (p<0.05 and p<0.01) and PF (p<0.0001) compared to control. None of the stimulations lead to an increase in the Col6α1 and Col6α2. The TGF-β induced gene expression corresponded with increased ECM formation of type I and VI collagen from day 4 (p<0.01), and type III collagen from day 8 (p<0.05) in both DF and PF. PDGF-ab stimulation led to an increased ECM formation of type I and VI collagen in both DF and PF (p<0.01), and type III collagen in DF (p<0.01). The combination stimulation with TGF-β and PDGF-ab induced a corresponding increase in both gene expression and ECM formation of type I and VI collagen in both DF and PF (p<0.01). While the combination increased the ECM formation of type III collagen in both fibroblast types, the gene expression of Col3α1 were only increased in PF (p<0.0001).
Conclusion: This study demonstrates that TGF-β stimulation alone and in combination with PDGF-ab results in increased gene and protein expression of type I and VI collagen in both DF and PF, and additionally type III collagen in PF. However, there was a disconnect between the gene and protein expression profiles after PDGF-ab stimulation, which have to be investigated further. This study may provide new insights to the differences between fibroblast of different origin and their response to fibrotic factors.

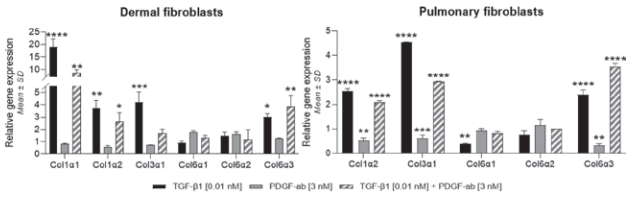

Figure 1: Relative gene expression type I, III and VI collagens of dermal (DF) and pulmonary fibroblasts (PF) after stimulation with TGF-β and/or PDGF for 4 days. The gene expression was calculated based on multiple reference genes.

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AB0132 STIMULATION OF SOLUBLE GUANYLATE CYCLASE (SGC) FOSTERS ANGIOGENESIS AND BLUNTS ENDOTHELIAL-TO-MESENCHYMAL TRANSITION (ENDOMT) OF SYSTEMIC SCLEROSIS (SSC) DERMAL MICROVASCULAR ENDOTHELIAL CELLS

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Background: In SSc, early abnormalities in microvessel morphology and angiogenic impairment in parallel advance with the development of tissue fibrosis orchestrated by myofibroblasts. Increasing evidence suggests that the EndoMT process, in which endothelial cells transdifferentiate into profibrotic myofibroblasts, may take centre stage in SSc pathogenesis [1,2]. sGC is an enzyme regulating cell growth/proliferation and vascular tone/remodelling by catalysing the production of cyclic guanosine monophosphate. Previous studies reported that sGC stimulation inhibits TGFβ-induced fibroblast-to-myofibroblast differentiation and collagen synthesis by blocking non-canonical ERK-dependent TGFβ signalling, and that sCG stimulators (sGCS) may exert antifibrotic effects in experimental models of fibrotic disorders.
Objectives: To investigate the possible modulatory effects of sGC stimulation on impaired angiogenesis and EndoMT of SSc dermal microvascular endothelial cells (SSc-MVECs).
Methods: To evaluate the effects of treatment with sGCS on endothelial cell viability/proliferation, 5 lines of SSc-MVECs and 5 lines of healthy dermal MVECs (H-MVECs) were challenged with sGCS (here MK-2947) and assayed with both annexin V/PI flow cytometry and WST-1. To analyse the modulation of angiogenesis by sGCS, SSc-MVECs were challenged with MK-2947 and subsequently tested for wound healing and capillary-like tube formation capabilities. To study the effects of MK-2947 on EndoMT, the same cells were assayed for the expression of endothelial and mesenchymal/myofibroblast markers by quantitative real-time PCR, western blotting and immunofluorescence, as well as for their contractile ability by collagen gel contraction assay. Phosphorylation of ERK1/2 was assessed by western blotting.
Results: Treatment with MK-2947 did not affect viability/proliferation of H-MVECs, while it significantly increased the proliferation of SSc-MVECs ($p<0.001$ vs. basal). Compared to basal condition, the MK-2947 challenge ameliorated both wound healing capability ($p<0.001$) and angiogenic performance (number of nodes: $p<0.01$; segments: $p<0.001$; meshes: $p<0.01$; and junctions: $p<0.001$) of SSc-MVECs. Upon stimulation of sGC, SSc-MVECs exhibited increased gene expression of proangiogenic matrix metalloproteinase (MMP)-9 ($p<0.05$) and decreased expression of both antiangiogenic MMP-12 ($p<0.05$) and pentraxin-3 ($p<0.001$) respect to basal SSc-MVECs. A significant increase in both gene and protein expression of the endothelial markers CD31 and VE-cadherin, and a parallel decrease in the expression of the mesenchymal/myofibroblast markers α-SMA, S100A4, and type I collagen were found in MK-2947-treated SSc-MVECs. MK-2947 also downregulated the EndoMT-driving transcription factor SNAIL1 in SSc-MVECs. Stimulation with MK-2947 was able to significantly counteract the intrinsic ability of myofibroblast-like SSc-MVECs to contract collagen gels ($p<0.001$) and effectively reduce phosphorylated-ERK1/2 protein levels ($p<0.01$) respect to basal cells.
Conclusion: Stimulation of sGC effectively ameliorates the angiogenic performance and blunts the pathogenic myofibroblast-like profibrotic phenotype of SSc-MVECs.
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Disclosure of Interests: Eloisa Romano: None declared, Irene Rosa: None declared, Bianca Saveria Fioretto: None declared, Dilia Giuggioli: None declared, Mirko Manetti Speakers bureau: has received consulting fees or honorarium from MSD, Marco Matucci-Cerinic Speakers bureau: has received consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Grant/research support from: has received consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche

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AB0133 TARGETING INFLAMMATION RESOLUTION IN SYSTEMIC SCLEROSIS: PRECLINICAL DATA OF A NEW DISEASE MODIFYING BIOLOGIC DRUG CANDIDATE RESOLVIX

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Background: Systemic sclerosis (SSc) is a complex immune-mediated connective tissue disorder characterized by microvascular damage, inflammatory cell infiltration, and excessive deposition of extracellular matrix proteins (ECMs) resulting in fibrosis in the skin and various internal organs.
Limited treatment options are currently available in the clinic and are mostly focusing on symptom control with limited impact on disease progression. New treatment approaches are needed to address the complex dysregulated pathways and disease drivers to develop effective therapies.
While the pathophysiology of SSc remains incompletely understood it is well-recognized that progressive chronic inflammation is a part of the disease and its progression. Accumulation of apoptotic cells in tissues and defective clearance of these cells contributing to unresolved tissue repair is emerging as a root cause leading to sustained uncontrolled chronic inflammation and fibrosis. Naturally ending and resolving chronic inflammation to initiate healing and repair processes could present a novel therapeutic approach for SSc.
Resolvix, a next generation biological drug candidate under development, harnesses a complex mix of naturally occurring pro-resolutive factors emitted by human cells, has demonstrated promising disease modifying effects in models of experimental arthritis and inflammatory bowel disease.
Objectives: The objective of our preclinical study presented here, was to evaluate the potential therapeutic effects of Resolvix in experimental models of SSc.
Methods: Two established inducible preclinical models of SSc (bleomycin (BLM) and HOCl) were used to monitor the impact of Resolvix mouse equivalent versus a control treatment on skin (thickness and collagen deposition), lung (leucocyte infiltration and alveolar macrophage efferocytosis) and lymphoid organs/blood (Tregs) as well as selected plasma proteins. A single treatment or respective controls were administrated intra-venously at 3 weeks post disease induction and mice were monitored daily and sacrificed for analysis after 3 weeks post treatment.
Results: In our hands both preclinical models clearly show phenotypes associated with sclerosing processes of SSc. In both models we could show a significant reduction of skin thickening and collagen deposition in skin samples after a single treatment with Resolvix when compared to controls. Leucocyte infiltrates particularly evident in the HOCl model were significantly reduced by the Resolvix treatment in skin and lung tissues. Interestingly, alveolar macrophages collected from broncho-alveolar lavage (BAL) fluids of the diseased mice in both model systems demonstrated a significant reduction of efferocytosis capacity (eliminating apoptotic cells) a sign of uncontrolled ongoing chronic inflammation and recently reported in SSc patients[1]. Resolvix treatment successfully restored the efferocytosis activity to comparable levels detected in healthy mice.
In addition, $Foxp3^+$ regulatory T cells were increased in the blood of BLM-mice treated with Resolvix.
Plasma concentrations of IL-6 and TNF-α were not modified between controls, treated and non-treated mice.
Conclusion: Collectively our preliminary data demonstrate that harnessed pro-resolutive factors making up Resolvix are able to revert skin fibrosing processes, control inflammatory cell infiltration and restore defective macrophage efferocytosis as a novel a therapeutic approach in SSc.
Resolvix should be considered as a next generation disease modifying biological drug candidate for further development for the treatment of SSc.
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AB0134 IN-VITRO STUDY ON THE EFFECT OF SELECTIVE JAK-INHIBITORS ON PBMCS STAT3 PHOSPHORYLATION FROM SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is a rare autoimmune connective tissue disease characterized by autoimmunity-driven damage and vasculopathy leading

to fibrosis of the skin and internal organs (1). The Janus kinase (Jak) - signal transducer and activator of transcription (STAT) pathway has been evidenced markedly activated in SSc patients (2, 3), and its inhibition has been proved in preclinical and clinical trials (4), but no data on Jak selective inhibition are available.
Objectives: To explore the effect of selective inhibition of Jak/STAT pathway in peripheral blood mononuclear cells (PBMC) from SSc patients.
Methods: In vitro Jak inhibition of the subunit 3 of phosphorylated (p) than activated STAT was measured by flow cytometry in peripheral blood mononuclear cells (PBMC) from SSc patients naïve to any immunosuppressive and/or corticosteroids (n.5). pSTAT3 activity was also assessed after stimulation with recombinant human 0.1 ng/ml IL-6 (Peprotech – NJ, USA). The PBMC were overnight incubated with IC50 concentrations of selective Jak1-, Jak2-, Jak3- and Tyk2-inhibitors (Biovision Inc. – CA, USA). Percentages of pSTAT3 positive cells were compared in presence of different compounds stimulation.
Results: After overnight incubation, percentage of pSTAT3 positive cells was significantly higher in $CD14^{pos}$ compared to $CD4^{pos}$ (16.3%; 95CI 10-22 vs 10.7%; 95CI 4--18, – p=0.02). $pSTAT3^{pos}CD14^{pos}$ cells were halved only by selective Jak3-inhibitor, while $pSTAT3^{pos}CD4^{pos}$ cells were reduced by 36% by selective Jak1-inhibitor. Selective Jak2- or Tyk2-inhibitors did not interfere with STAT3 phosphorylation in PBMC from SSc patients. After IL-6 stimulation, we observed a 2- and a 1.5-fold increase in percentage of $pSTAT3^{pos}CD4^{pos}$ and $pSTAT3^{pos}CD14^{pos}$ cells, respectively. $pSTAT3^{pos}CD14^{pos}$ cells were reduced in the PBMC co-culture with IL-6 and Jak-selective inhibitors, in contrast no effects were found in $CD4^{pos}$ cells. Specifically, selective Jak1- and Jak3-inhibitors reduced $pSTAT3^{pos}CD14^{pos}$ cells by an average of 37% and 25%, respectively. No effects were observed after co-culture with IL-6 and selective Jak2- or Tyk2-inhibitors.
Conclusion: Jak/STAT3 pathway of PBMC from SSc patients with active disease may be differently modulated by specific inhibitors. Selectivity of Jak1- and Jak3-inhibitors seems more relevant, especially in $CD14^{pos}$ monocytes after IL-6 stimulation. These preliminary findings highlight some evidence for effectiveness of selective Jak-inhibitors in SSc treatment.
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AB0135 PROTEIN CONFORMATIONAL CHANGES AND FUNCTIONAL ALTERATIONS IN DERMAL FIBROBLASTS FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Despite intensive studies and clinical trials, there is still no available precise diagnostic tool and treatment of the patients affected by systemic sclerosis (SSc). Proteopathies are diseases characterized by the production of aberrant conformers of certain proteins that lead to a disturbance of their cellular functions and disease. It is believed that the structure of a protein is principally responsible for its function. By identifying altered protein structures on a proteome-wide scale, there is a possibility to detect protein functional changes.
Objectives: To screen for changes in the protein conformation and to correlate with cell function in SSc dermal fibroblasts compared to fibroblasts from healthy donors (HC) using a novel approach of limited proteolysis followed by functional assays.
Methods: Diffuse cutaneous SSc and HC dermal fibroblasts were used for recently established Limited Proteolysis-coupled Mass-Spectrometry (Lip-MS)[1] to examine protein structural alterations in a proteome-wide scale. A change in conformation was defined as having a foldchange greater than 1 or smaller than -1 and a significant p-value of -log10 > 1.3 (≤0.05). Further, the responsive signalling targets in these cells, including the NF-κB-dependent pathway and energy metabolism, were evaluated. Fibroblasts were stimulated with inflammatory cytokines, highly relevant in SSc, including TNFα, IL-1β, TGF-β, IL-17A, and a combination of IL-17A and TGF-β. To examine the NF-κB activity, cells were transduced with a pseudo-typed HIV-1-based lentiviral vector. The measurements of luciferase signal were analysed. RT-qPCR was used to assess the expression of NF-κB-dependent genes for non-transduced cells. ATP measurements were analysed and presented as the amount of luminescent signal.
Results: LiP-MS analysis detected 53263 common peptides in SSc (n=6) and HC fibroblasts (n=6), of which 41 peptides showed conformational changes in SSc fibroblasts in comparison with HC fibroblasts. The 41 conformationally altered peptides showed significant enrichment in GO pathways for: biological processes (9), molecular function (7) and cellular components (21). SAE1, CTNND1, CDC37, and PPP1R13L were related to the NF-κB-dependent pathways, while ATP5A1, GSTM1, PCK2, ANPEP, GM2A, GNS, CAD, ACOT2 were connected with metabolic processes. There was a tendency of lower levels of mRNA *RELA, NFKBIA, MMP1* and *TNC* expression levels in untreated and stimulated SSc fibroblasts (n=6) compared to HC fibroblasts (n=6). The assessment of the NF-κB activity in untreated SSc fibroblasts (n=9) showed a trend to lower fold change compared to HC fibroblasts (n=9) (0.63 vs 1, SE 0.19, p=0.07). A statistically significant difference between SSc (n=8) and HC (n=8) fibroblasts was found in TGF-β stimulated fibroblasts (0.64 vs 1, SE 0.16, p=0.046). SSc fibroblasts (n=9) showed a lower ATP level compared to HC fibroblasts (n=9) in untreated condition (0.82 vs 1, SE 0.09, p=0.07), after stimulation with IL-1β (0.85 vs 1, SE 0.08, p=0.07) and TGF-β (0.81 vs 1, SE 0.09, p=0.05). Of note, a statistically significant difference between SSc and HC fibroblasts was found in IL-17A stimulated cells (0.82 vs 1, SE 0.07, p=0.02).
Conclusion: LiP-MS approach allowed for the identification of conformational changes in SSc fibroblast mainly related to signal transduction and metabolic pathways. Confirmatory functional studies showed deregulated NF-κB activity and ATP levels in SSc fibroblasts. Therefore, LiP-MS approach may create a distinctive opportunity to discover new disease biomarkers and functionally transformed pathways. This method may advance therapeutical approaches, where only structurally altered proteins could be specifically targeted, without interfering with non-changed proteins.
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AB0136 ELUCIDATING THE PATHOGENIC EFFECTS OF ANTI-TOPOISOMERASE-1 ANTIBODIES IN SYSTEMIC SCLEROSIS

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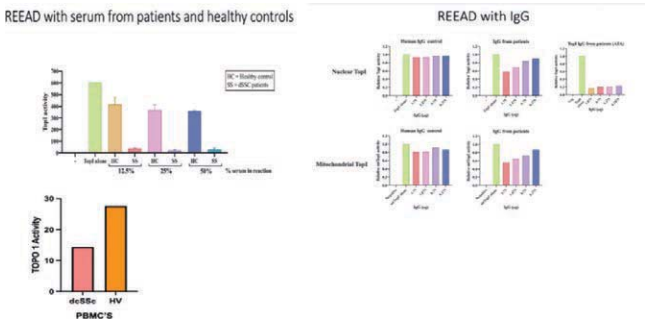
Background: Prediction of the pattern of organ involvement in patients with diffuse cutaneous systemic sclerosis (dcSSc) is supported by the specificity of autoantibodies. These autoantibodies are generally mutually exclusive and highly specific for dcSSc[1]. The autoantibody reactivity allows patients to be stratified early in the disease course, leading to a tailored approach and management. Anti-topoisomerase I antibodies (ATA) are predictors of the development of interstitial lung disease (ILD) and digital ulcers but appear to be protective against pulmonary artery hypertension (PAH).
Objectives: The aim of this project was to elucidate the functioning of ATA and their role in the pathogenicity of the disease.
Methods: Sera from healthy volunteers (HV) and dcSSc patients with and without ATA were collected from Aarhus University Hospital. Total IgG was purified from the sera using a Protein G column. ATA was further purified from the total IgG fraction by passing it through a column packed with the functional domains of human topoisomerase-1 (TOP1) expressed from *E.coli.*
Sera, total IgG and purified ATA fractions were utilized in preliminary experiments. The ability of ATA to inhibit TOP1 was tested by a in house developed REEAD assay in which the generation of closed DNA circles, by the cleavage-ligation activity of TOP1, is monitored after rolling circle amplification[2].
Results: Serum from patients with dcSSc, but not from HV, could inhibit TOP1 activity at various dilutions. Similarly, purified total IgG fractions from dcSSc patients could also inhibit TOP1 activity. ATA was successfully separated from IgG from dcSSc patients who were positive for ATA. This could inhibit TOP1 activity even at lower concentrations than total IgG. This was the case for both mitochondrial and nuclear TOP1 activity.
Fully in line with presence of ATA, PBMC's from dcSSc patients contained a lower TOP1 activity compared to HVs PBMCs.
Conclusion: To our knowledge we are the first group to be able to successfully separate ATA from total IgG from dcSSc patients. our unique in house developed REEAD assay clearly demonstrates the function of ATA and provides the opportunity to better understand



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AB0137 SERA DERIVED EXTRACELLULAR VESICLES FROM SYTEMIC SCLEROSIS PATIENT AND AUTOANTIBODIES MEDIATE PERIPHAL BLOOD MONOCYTES ACTIVATION

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Background: In SSc, autoantibodies (abs) directed against G protein-coupled receptors (GPCR) are prominent and for example induce release of inflammatory and profibrotic proteins by monocytes (1-3). Increased levels of autoantibodies against angiotensin II type 1 receptor (AT1R abs) have been found in patients with renal involvement in systemic sclerosis (SSc) (4-5). The elevated amount of anti-GPCR abs is accompanied by increased secretion of extracellular vesicles (EVs) in SSc (6). The importance of EVs in the pathogenesis is also based on packing and horizontal transfer of AT1R to different tissues and immune cells, exemplary shown by activated cardiomyocytes leading to higher responsiveness to Angiotensin II of recipient cells and vessels (7). Taken together, the relevance of studying anti-GPCR abs together with GPCR-EVs in SSc pathogenesis becomes evident (8). Interestingly, CCL18 is found to be upregulated in SSc patients and suggested to be upregulated by AT1R abs (9), indicating CCL18 and CCR8 cross-talk via EVs plays an essential role in the pathogenesis of SSc.
Objectives: Unravel the immune response of peripheral blood monocytes mediated by anti-AT1R abs and EVs to gain new insights into the pathomechanism in SSc.
Methods: Human peripheral blood monocytes of healthy donors were stimulated by the endogenous AT1R ligand angiotensin II as well as by a monoclonal anti-human AT1R ab and, in comparison, by purified IgG from HD (HD IgG) versus those from SSc (SSc IgG). Further, human peripheral blood monocytes of HD were treated with EVs derived from sera of SSc patients versus sera of HD, in the presence or absence of a monoclonal recombinant anti-AT1R ab. Monoclonal AT1R ab has been generated by hybridoma technique, sequenced and recombinantly expressed in HEK cells. The specificity of AT1R abs was tested by using an AT1R blocker (telmisartan, TEL). EVs were isolated from sera by differential centrifugation to exclude large particles and microvesicles and further by one-step polymer precipitation procedure utilising ExoQuick Exosome Precipitation Solution (System Biosciences, Palo Alto, CA) and subsequent purification by size exclusion. Further, primary human peripheral blood monocytes of HD (n=6) were treated with EVs derived from sera of SSc patients (n=6) versus sera of HD (n=6), in the presence or absence of a monoclonal recombinant anti-AT1R ab. The response of the monocytes was measured via CCL18 secretion by ELISA.
Results: The recombinant monoclonal anti-human AT1R antibody induced secretion of CCL18, a profibrotic cytokine, by primary monocytes derived from HD. Similarly, the purified IgG fractions derived from SSc patients also induced an increased CCL18 release by monocytes compared to IgG fractions derived from HD. Further, complete amelioration of the AT1R ab effect on CCL18 secretion was found, when monocytic AT1R expression was blocked with TEL. In addition, antagonistic effects of Angiotensin II to the monoclonal AT1R ab were observed. In line, enhanced CCL18 secretion of human monocytes stimulated with SSc-EVs alone and together with the monoclonal AT1R ab was induced.
Conclusion: The secretion of pro-fibrotic CCL18 by human monocytes in response to a monoclonal AT1R antibody as well as to SSc IgG indicates that anti-AT1R abs are involved in the SSc pathogenesis. Further, this effect could also be due to SSc-EVs potentially presenting anti-GPCR abs to their receptors on immune cells.
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AB0138 XANTHINE OXIDOREDUCTASE: BLOOD PROFILE IN SYSTEMIC CONNECTIVE TISSUE DISEASES

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Background: Systemic lupus erythematosus (SLE) and systemic scleroderma (SSc) are systemic connective tissue diseases. Their development is based on a generalized immune inflammatory process. Deep immunological and metabolic disorders in these diseases have along with general characteristic distinctive features. XOR is a multifunctional enzyme. The reactions catalyzed by XOR are a source of reactive forms of oxygen and nitrogen, nitric oxide, which are of great physiological importance, and are also responsible for the development of many pathophysiological reactions. Analysis of changes in the activity of interconverting forms of XOR (xanthine oxidase (XO), EC 1.17.3.2 and xanthine dehydrogenase (XDG), EC 1.17.1.4) in plasma and blood cells is of interest.
Objectives: to characterize differences of XO and XDG activities profiles in blood of SLE and SSc patients.
Methods: The researcher was carried out in agreement with the WMA Declaration of Helsinki principles. 56 SLE patients and 51 SSc patients were enrolled in this study. Diagnosis of SLE was verified using the SLICC criteria (2012). SSc was verified according to ACR/EULAR criteria (2013). The reference group consisted of 35 healthy controls. XO and XDG activities were measured in plasma, lysed WBC, lysed RBC using spectrophotometric method [1]. Results were expressed as Me (Q_{25}; Q_{75}). The Mann-Whitney U test was used for statistical analysis, differences were considered significant when $p<0.05$.
Results: Mean age of SLE patients was 35 (31; 42) years, mean duration of disease was 8 (5; 11) years. Mean age of SSc patients was 43 (38; 48) years, mean SSc duration was 8 (6; 9) years. The enzyme indices included in the study did not depend on the sex and age of healthy individuals. XO activity was increased in plasma of SLE and SSc patients ($p<0.001$ for both disease). The activity of XO was higher in SLE ($p<0.001$). XO activity of lysed WBC was decreased in both diseases ($p<0.001$). XDG activity was decreased in lysed WBC and lysed RBC of patients with SLE and SSc (all $p<0.001$). Activity of this enzyme was lower in lysed WBC and higher in lysed RBC in SLE compared with SSc (all $p<0.001$). In contrast to SLE, accompanied by low levels of plasma XDH activity ($p<0.001$), SSc was characterized by increased activity of this enzyme ($p<0.001$). Also, increased XO activity was revealed in lysed RBC of SSc patients ($p<0.001$). The values of this enzymatic activity did not differ between the group of SLE patients and healthy controls ($p=0.977$).
Conclusion: Changes in the activity of oxidase and dehydrogenase forms of XOR were revealed in plasma, lysed WBC, lysed RBC of SLE and SSc patients, which determine characteristic blood profiles in these diseases. Changes in the balance of XOR enzymatic activities can affect the exchange of purine nucleotides, the pool of reactive oxygen and nitrogen species in body tissues, participating in the processes inherent in these diseases.
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AB0139 **DEEP IMMUNE PHENOTYPING OF T LYMPHOCYTE SUBSETS IN SYSTEMIC SCLEROSIS PATHOPHYSIOLOGY AND FOLLOWING RESPONSE TO TARGETED CYTOTOXIC TREATMENT**

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Background: Abnormalities in T lymphocyte populations are associated with the pathogenesis of many autoimmune diseases, such as systemic sclerosis (SSc). Various studies report on the aberrations of different T cell cytotoxic (CTL) and helper (Th) subsets that appear to be linked with inflammatory and/or fibrotic manifestations of patients with SSc. Since T cells seem to play a pivotal role in the pathophysiology of SSc, targeting the pathogenic T cell subsets might be a promising therapeutic option.
Objectives: Here we set out to comprehensively compare T lymphocyte phenotypes between SSc patients and healthy donors. We further test the in-vitro efficacy of a combination of anti-CD3/CD7 immunotoxins (CD3/CD7-IT), that have been developed to eliminate activated CD4+ and CD8+ T cells, to study specific sensitivity of T-cell subpopulations to CD3/CD7-IT.
Methods: 30 SSc patients and 15 age and sex matched healthy donors were included. Of these patients, lymphocyte populations were quantified by 17-parameter flow cytometry of peripheral blood mononuclear cells (PBMCs) to identify CD4+ T helper cells (Th1, Th2, Th17, T peripheral helper), CD8+ naïve, memory, effector CTLs and senescent/exhausted subsets. We next developed a cell killing assay to evaluate the effect of T cell depletion. To address this, patients' (N=6) PBMCs were first activated for 24 hours in the presence of phytohemagglutinin, followed by CD3/CD7-IT addition for 48 hours. Subset-specific T cell depletion was assessed by using a combination of CellTiter-Glow luminescent cell viability assay and multi-parameter flow cytometric (FCM) quantification of CD3/CD7-IT-induced cell death.
Results: Frequencies of effector CD8+ CTLs,Th2 and T peripheral helper cells were elevated in SSc patients compared to healthy controls. Furthermore, SSc patients exhibited lower percentages of the anti-fibrotic Th1 subset. A striking expansion of the senescent CD4+CD28- and CD8+CD28- populations was noted in patients, while these subsets were barely detectable in healthy controls. In-vitro adittion of anti-T cell immunotoxins effectively depleted 50 % of patients' CD8+ T cells (including the CD8 effector subset) and 62% of CD4+ T cells (including Th2 and T peripheral helper cells). No difference in cytolytic sensitivity between different T cell subsets was observed.
Conclusion: Our findings demonstrate that deep FCM immunephenotyping reveals pathophysiological differences in peripheral T cell subsets of SSc patients. Strikingly, the developed cytolytic assays show that CD3/CD7-IT is able to target the potential disease-associated T cell subsets in an in-vitro setting.
References: Not applicable
Disclosure of Interests: None declared
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AB0140 **ROLE OF ENDOGLIN IN THE PATHOGENESIS OF SYSTEMIC SCLEROSIS: A PRISMA-DRIVEN SYSTEMATIC REVIEW**

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Background: Systemic sclerosis (SSc) is a rare autoimmune disease characterized from peculiar vascular alteration and fibrosis of the skin and internal tissues. SSc pathogenetic mechanisms are still partially unclear but an involvement of the TGFβ pathway, known for being responsible of both angiogenesis and fibrosis, has been proven. Endoglin (ENG) is a TGFβ receptor type III involved in signal regulation, and mutations in *ENG* gene cause Hereditary Hemorrhagic Telangiectasia type I, a rare disease that shares with SSc the presence of mucocutaneous telangiectasias and disturbed angiogenesis.
Objectives: The aim of this systematic review is to highlight the role of ENG in the pathogenesis of SSc focusing on a subset of clinical manifestations.
Methods: We performed a systematic review following the PRISMA guidelines, searching the MEDLINE (PubMed), Web of Science and EMBASE databases using as keywords: "Endoglin", "sENG", "CD105", "Systemic sclerosis", "SSc", "Scleroderma", "CREST". The last search was made on November 2nd 2021. This review includes both conference abstracts (without subsequent publication) and articles that evaluated the relationships between SSc and ENG; we excluded the papers that used CD105 only as a cell marker. We then consulted the references from the papers found in order to search possible articles that escaped our first search.
Results: Of the 656 records identified from the database research, 42 were included in our systematic review (16 abstracts and 26 original papers) (Figure). The majority of these studies (25) measured serum ENG (sENG) looking for correlations with cutaneous, pulmonary and cardiac disease in patients with SSc.

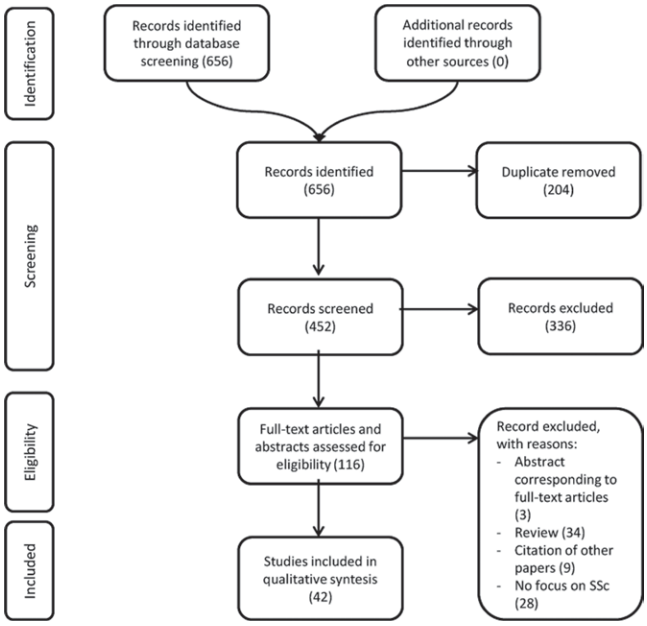

Figure. PRISMA flow diagram.

High levels of sENG demonstrated an independent association with telangiectasia in 2 studies, with the presence of digital ulcers (DU) in 6 studies but was not related to the occurrence of new DU (2 studies) and it was related to scleroderma pattern late in 2 studies. Between limited and diffuse cutaneous SSc, sENG showed no differences in one study and significantly higher values in lcSSc in another, this latter study also found sENG to be higher in lcSSC compared to systemic lupus erythematous and healthy controls (HC). sENG, moreover, demonstrated a positive correlation with anti-centromere antibodies (two studies). Regarding pulmonary involvement, no correlation between sENG and mean pulmonary arterial pressure was recorded, and two studies found sENG elevated in patients with pulmonary arterial hypertension while no correlation was found from two other papers. High sENG concentrations demonstrated a positive correlation with subclinical atherosclerosis and with high sensitivity troponin, but its concentration did not relate to right heart dysfunction (1 study each). Two different groups evaluated sENG concentration in Localized Scleroderma and found no differences with other connective tissue diseases. One study searched for genetic alterations in the expression of *ENG* gene and found no difference between SSc patients and HC. Four studies evaluated Eng expression on fibroblast surface: SSc fibroblasts from both systemic circulation and lung showed higher production of Eng than HC. Tissue Eng, moreover, is up regulated in SSc patients where it acts as a regulator of TGFβ signaling and of extracellular matrix production.
Conclusion: As suggested by the role of Endoglin in the TGFβ pathway, several authors demonstrated an altered expression of Endoglin in SSc patients. A particular focus of interest is the role of ENG in PAH and DU that occur in SSc. A direct involvement of *ENG* in PAH is known as mutation in this gene are one of the genetic causes of PAH. However, particularly in pulmonary vascular disease, there are still controversial and insufficient data to draw definitive conclusions. As PAH is a leading cause of mortality in SSc patients this is an area of clinical interest and the study of the TGFβ pathway could lead to useful clinical findings.

Disclosure of Interests: None declared
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AB0141 DIFFERENTIAL CYTOKINE PRODUCTION PROFILES IN STIMULATED MONONUCLEAR CELLS OF PATIENTS WITH SYSTEMIC SCLEROSIS AND CONTROLS

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Background: Altered innate and adaptive immune responses represent the link between microvascular injury and fibrosis in systemic sclerosis (SSc) pathophysiology. Peripheral monocytes and lymphocytes are responsible for the secretion of cytokines with proven pro-inflammatory and pro-fibrotic activities. Chronic immune activation in SSc is supported by distinct serum and peripheral blood mononuclear cell (PBMC) cytokine profiles in relation to disease duration, autoantibody subtype, as well as severity of clinical manifestations.
Objectives: This pilot study aimed to: (1) evaluate the PBMC cytokine production in SSc patients versus healthy controls (HC) after in vitro stimulation with lipopolysaccharide (LPS) and heat-killed *Candida albicans* and (2) distinguish different SSc clinical phenotypes based on their cytokine signature.
Methods: Eighteen SSc patients (8 limited cutaneous, 9 diffuse cutaneous, 1 sine scleroderma) and 17 age and gender matched HC were enrolled between February 2020 and October 2021. PBMCs were isolated and further subjected to stimulation with LPS and *Candida albicans*. Cytokine production was measured after 24 hours using ELISA kits for interleukin (IL)-1β, IL-1 receptor antagonist and IL-6. IL-17 and interferon gamma (IFN-γ) concentrations were determined at 7 days from samples stimulated with *Candida albicans*-in the presence of 10% human pooled serum. Non-parametric data was analyzed using Mann-Whitney test while T.test was used for parametric data.
Results: Significantly elevated IL-1 β and IL-6 concentrations were detected in SSc patients compared to HC after stimulation with either LPS or *Candida albicans*. IL-17 cytokine production was also enhanced in SSc patients compared to HC after stimulation with *Candida albicans* for 7 days, but no difference was identified with respect to IFN-γ. No significant statistical difference was demonstrated between cytokine levels and extent of cutaneous involvement. Furthermore, no association was observed between autoantibody subtypes and cytokine production. Patients with diffuse cutaneous SSc and those positive for anti-Scl-70 antibodies revealed elevated C-reactive protein (CRP) levels.
Conclusion: SSc patients exhibit a pro-inflammatory phenotype irrespective of the extent of cutaneous involvement or autoantibody profile. This appears to be mediated through increased production of innate immune cytokines, which correlated to elevated Th-17 responses on later time-points. Elevated CRP levels might define a subgroup of SSc patients with specific disease characteristics. Validation of these findings and mechanistic assessment is warranted in larger cohorts of patients.

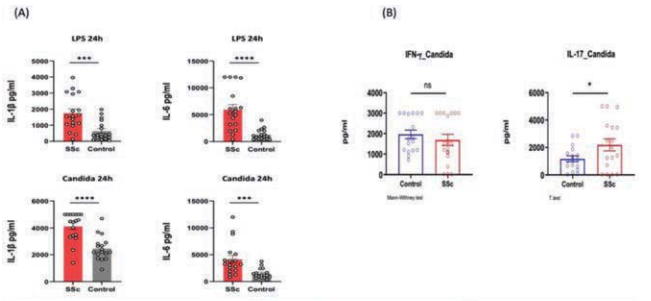

Figure 1. Cytokine production at 24 hours and 7 days respectively after stimulation with LPS and Candida albicans. (A) Higher IL- 1β and IL-6 levels were detected in SSc patients versus HC at 24 hours. (B) IL-17 concentrations are elevated after stimulation with Candida albicans for 7 days in SSc patients compared to HC. No difference was observed with respect to IFN-γ production.

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AB0142 EVIDENCE OF TYPE I INTERFERON ACTIVATION DURING VASCULAR MANIFESTATIONS OF SYSTEMIC SCLEROSIS

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Background: Vascular involvement in Systemic Sclerosis (SSc) is known to start even before clinical diagnosis, to drive Digital Ulcer disease and later in the disease natural history to cause Pulmonary Artery Hypertension, among other manifestations. Despite the proven immune origin of Scleroderma, vascular involvement is not currently targeted by immune driven interventions. Similarly, little data is available on immune or inflammatory biomarkers and outcome measures of vascular disease in SSc. Digital Artery Volume Index (DAVIX) has been recently proposed as imaging surrogate outcome measure of vascular disease activity in SSc [1].
Objectives: Here we aimed to determine the value of DAVIX as overall biomarker of vascular involvement and its correlation with Type I IFN activation in patients with SSc.
Methods: Eighty-six patients attending our Scleroderma Program were consecutively enrolled for the evaluation of serum IFN score as previously described [2]. Clinical features including presence or history of Digital Ulcers, Presence of Pulmonary Artery Hypertension (PAH) and DLCO, were recorded. Digital Artery Vascular Index (DAVIX) of the dominant hand's fingers was calculated using time of flight magnetic resonance images analysed through IAG proprietary algorithm, as previously described [1]. Medians were compared by Mann-Whitney-Wilcoxon test, correlation with clinical parameters was performed using Spearman's or Pearson test, as appropriate (R).
Results: Sixty-two patients fulfilled the 2013 ACR/EULAR classification criteria for SSc (diffuse cutaneous 24.6%, limited cutaneous 75.4%) whereas 23 were classified as Very Early Diagnosis of Scleroderma (Criteria score between 6 and 8). Twenty-three patients had DU disease (History of DUs in the previous 24 weeks, presence of DUs at baseline assessment, or onset of new DUs during the following 24 weeks). Eighteen patients had reduced DLCO (<70) with FVC/DLCO>1.8 (suspected PAH). DAVIX showed a negative correlation with disease duration (r=-0.33 and p=.003) and with FVC/DLCO ratio (r=-0.34 and p=.009). Patients with DU disease presented lower DAVIX than patients without (p=.018).
DAVIX showed a significant correlation with Serum IFN score (r=-0.24, p<0.032). Accordingly, patients classified as IFN-HI had lower DAVIX than those within the IFN-LO group (p=0.016).
Conclusion: DAVIX correlated both with presence of Digital Ulcer disease, DLCO and disease duration. The correlation of DAVIX and Serum IFN score does support the notion of innate immune involvement in vascular disease manifestations of SSc. Prospective testing in the context of Randomised controlled trial will determine the value of DAVIX as surrogate outcome measure of vascular disease severity in SSc.

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Vasculitis - aetiology, pathogenesis and animal models

AB0143 CHARACTERIZATION OF CELLULAR INFILTRATE IN TEMPORAL ARTERITIS USING IMAGING MASS CYTOMETRY IN GIANT CELL ARTERITIS

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Background: Imaging mass cytometry (IMC) is a high-plex imaging technique that incorporates flow cytometry principles while preserving the histological and architectural components of the tissue sample. Characterizing the entire cellular component of temporal artery (TA) in patients with giant cell arteritis (GCA) may provide clues towards novel diagnostic and therapeutic approaches.
Objectives: We aimed at a comprehensive summary of the immune cells and pathways involved GCA by using IMC approach.
Methods: TA samples from biopsy-proven GCA patients (n=2) and controls (CTLs, n=2) were analyzed using IMC with a panel of 15 staining antibodies.
Results: Eleven cell populations were identified in arterial wall from GCA patients including both immune (CD20+ B cells, CD8+ T cells, CD4+ T cells, FOXP3+ Tregs, CD66b+ granulocytes, CD11b+ myeloid cells, CD14+ monocytes, CD68+ macrophages) and non-immune (aSMA+ smooth muscle cells, CD31+ endothelial cells, Vimentin+ fibroblasts) cells (Figure 1). The 3 layers (intima, media and adventitia) of the arterial wall was enriched by all the immune cell subsets in GCA except for granulocytes and myeloid cells. CD8+, CD4+ and FOXP3+ regulatory T cells were significantly increased in any layer of the TA. The proportion of B cells was also enhanced in both intima and adventitia and displayed a high level of Ki67 expression.

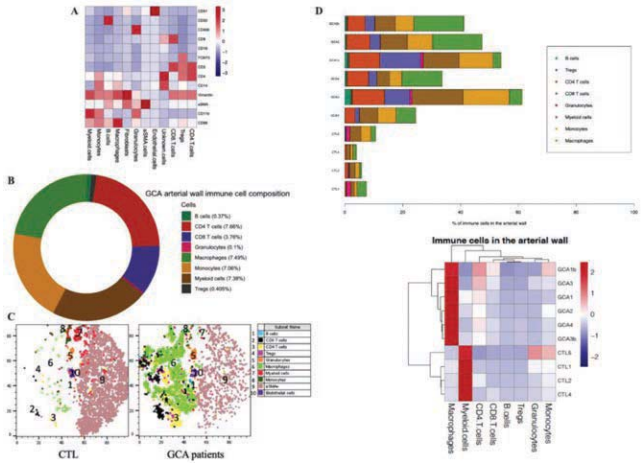

Figure 1. Unbiased clustering of cellular infiltrate in temporal arteritis using Imaging Mass Cytometry.

Heatmap of different cell type markers expressed by the 11 cell populations identified in the arterial wall of GCA patients: CD20+ B cells, CD8+ T cells, CD4+ T cells, FOXP3+ Tregs, CD66b+ granulocytes, CD11b+ myeloid cells, CD14+ monocytes, CD68+ macrophages, Vimentin+ fibroblasts, aSMA+ smooth muscle cells and CD31+ endothelial cells. A population of unidentified cells is also represented (A). Donut chart representing the relative composition of immune cells in the arterial wall of GCA patients (B). tSNE dimensional plots of the different cell clusters identified in the arterial wall of CTL and GCA patients (C). Percent and Heatmap of immune cells identified in the arterial wall of each patient (D).

GCA: giant cell arteritis, CTL: controls, Tregs: regulatory T cells.

Conclusion: Our study provides an exhaustive overview of the distinct cell lineages involved in GCA and supports IMC approach to further characterize the immune networks active in GCA.
Disclosure of Interests: None declared
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AB0144 PD-1 DEFICIENCY IN THE REGULATORY T CELL MAY BE INVOLVED IN THE PATHOGENESIS IN TAKAYASU'S ARTERITIS

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Background: Regulatory T cell (Treg cell) has been demonstrated decreased in peripheral blood of TAK patients in recent researches. PD-1 may regulate Treg cell differentiation and apoptosis as an important checkpoint molecule.
Objectives: This study aims to investigate whether PD-1 is involved in the abnormal of Treg cell in TAK.
Methods: This study enrolled 49 patients with TAK and 23 healthy controls. Treg cell related serum cytokines IL-10, IL-7, IL-2 and IL-15, as well as serum chemokines CCL2, CCL3 and CXCL10 were detected using cytokine cytometric bead array. The expression of PD-1 in $CD4^+Foxp3^-$ T cells and Treg cells were analyzed by flow cytometry analysis in 15 patients with TAK and 18 healthy controls.
Results: Mean fluorescence intensity of PD-1 in $CD4^+PD\text{-}1^+$ cells decreased in TAK patients [72.2 (45.8, 84.7) vs. 363.00(335, 431), P = 0.000]. The frequency of $CD4^+Foxp3^-PD\text{-}1^+$ cells in $CD4^+$T cells decreased in peripheral blood (9.05 ± 1.06% vs. 12.61 ± 1.17% , P = 0.034) of TAK patients. The percentage of $CD4^+CD25^+Foxp3^+PD\text{-}1^+$ cells in $CD4^+CD25^+$T cells (0.40 ± 0.05% vs. 0.63 ± 0.09% , P = 0.047) is lower in TAK patients than healthy controls. Higher serum levels of IL-10[4.84 (0.07,409.57) vs.3.16 (0,69. 15) , P = 0.004] and IL-7[10.05 (2.68,227.2) vs. 7.4 (2.68,16.77) , P = 0.014] level were observed in TAK patients. Compared to healthy controls, serum CCL2[30.64 (0 , 686.84) vs. 10.31 (0 , 32.92) , P = 0.000] and CCL3[3.01(0.69,19.24)vs.1.84 (0.87 , 4.6) , P = 0.000] increased obviously.
Conclusion: The frequency of $CD4^+Foxp3^-PD\text{-}1^+/CD4^+$T cells and $CD4^+CD25^{+-}Foxp3^+PD\text{-}1^+/CD4^+CD25^+$T cells decreased. This study suggested that PD-1 may contribute to the imbalance of regulatory T cell in TAK.
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AB0145 IGA VASCULITIS AND IGA NEPHROPATHY SHARE A SIMILAR IL33-IL1RL1 ASSOCIATION PATTERN

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Background: IgA vasculitis (IgAV) and IgA nephropathy (IgAN) are inflammatory conditions that share pathogenic and molecular mechanisms [1] and may represent different outcomes of a continuous spectrum of the disease [2]. Interleukin (IL)-33 is a cytokine that exerts its biological functions by binding to its receptor, IL-1 receptor like 1 (IL-1RL1) [3]. Several lines of evidence demonstrate that genetic variants located both in *IL33* and *IL1RL1* genes are implicated in the increased risk of numerous immune-mediated diseases [4].

Objectives: To determine whether IgAV and IgAN exhibit a different *IL33-IL1RL1* association pattern.

Methods: Three tag genetic variants within *IL33* (rs3939286, rs7025417 and rs7044343) and three tag polymorphisms within *IL1RL1* (rs2310173, rs13015714 and rs2058660), which cover the major variability of these loci and that were previously associated with several inflammatory diseases were genotyped in 380 Caucasian patients with IgAV, 96 patients with IgAN and 845 sex and ethnically matched healthy controls.

Results: Similar genotype and allele frequencies were observed in the whole cohort of patients with IgAV when compared to those with IgAN when *IL33-IL1RL1* genetic variants were analyzed independently (Table 1). In accordance with that, no *IL33-IL1RL1* genotype or allele differences were detected between IgAV patients who developed nephritis and patients with IgAN (Table 1). Additionally, no statistically significant differences between the whole cohort of patients with IgAV and healthy controls as well as between patients with IgAN and healthy controls were observed when each *IL33-IL1RL1* genetic variant was also analyzed independently (Table 1). Similar results were disclosed when haplotype frequencies were compared between the different comparative groups above mentioned (data not shown).

Conclusion: Our results reveal that IgAV and IgAN share a similar *IL33-IL1RL1* association pattern.

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Table 1. Genotype and allele frequencies of *IL33* and *IL1RL1* in the whole cohort of patients with IgAV, patients with IgAV who developed nephritis, patients with IgAN and healthy controls.

Polymorphism	Change	Data set	Genotypes, % (n)			Alleles, % (n)	
	1/2		1/1	1/2	2/2	1	2
IL33 rs3939286	C/T	IgAV	49.1 (186)	40.9 (155)	10.0 (38)	69.5 (527)	30.5 (231)
		IgAV with nephritis	48.5 (66)	39.7 (54)	11.8 (16)	68.4 (186)	31.6 (86)
		IgAN	43.8 (42)	49.0 (47)	7.3 (7)	68.2 (131)	31.8 (61)
		Controls	49.0 (414)	41.4 (350)	9.6 (81)	69.7 (1178)	30.3 (512)
IL33 rs7025417	T/C	IgAV	68.1 (254)	29.5 (110)	2.4 (9)	82.8 (618)	17.2 (128)
		IgAV with nephritis	69.9 (93)	27.1 (36)	3.0 (4)	83.5 (222)	16.5 (44)
		IgAN	61.5 (59)	37.5 (36)	1.0 (1)	80.2 (154)	19.8 (38)
		Controls	70.8 (598)	25.9 (219)	3.3 (28)	83.7 (1415)	16.3 (275)
IL33 rs7044343	T/C	IgAV	42.3 (160)	42.1 (159)	15.6 (59)	63.4 (479)	36.6 (277)
		IgAV with nephritis	44.5 (61)	39.4 (54)	16.1 (22)	64.2 (176)	35.8 (98)
		IgAN	40.6 (39)	49.0 (47)	10.4 (10)	65.1 (125)	34.9 (67)
		Controls	44.5 (376)	43.9 (371)	11.6 (98)	66.4 (1123)	33.6 (567)
IL1RL1 rs2310173	G/T	IgAV	29.2 (111)	46.1 (175)	24.7 (94)	52.2 (397)	47.8 (363)
		IgAV with nephritis	32.1 (44)	43.1 (59)	24.8 (34)	53.6 (147)	46.4 (127)
		IgAN	20.8 (20)	46.9 (45)	32.3 (31)	44.3 (85)	55.7 (107)
		Controls	30.2 (255)	46.7 (395)	23.1 (195)	53.6 (905)	46.4 (785)
IL1RL1 rs13015714	T/G	IgAV	56.3 (211)	39.5 (148)	4.3 (16)	76.0 (570)	24.0 (180)
		IgAV with nephritis	61.8 (84)	33.8 (46)	4.4 (6)	78.7 (214)	21.3 (58)
		IgAN	54.2 (52)	40.6 (39)	5.2 (5)	74.5 (143)	25.5 (49)
		Controls	57.2 (483)	37.2 (314)	5.7 (48)	75.7 (1280)	24.3 (410)
IL1RL1 rs2058660	A/G	IgAV	56.9 (215)	38.6 (146)	4.5 (17)	76.2 (576)	23.8 (180)
		IgAV with nephritis	62.2 (84)	31.9 (43)	5.9 (8)	78.1 (211)	21.9 (59)
		IgAN	53.1 (51)	42.7 (41)	4.2 (4)	74.5 (143)	25.5 (49)
		Controls	56.7 (479)	37.5 (317)	5.8 (49)	75.4 (1275)	24.6 (415)

IgAV: IgA vasculitis; IgAN: IgA nephropathy.

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AB0146 **BAFF, APRIL Y BAFFR: DIFFERENTIAL BIOMARKERS BETWEEN IGA VASCULITIS AND IGA NEPHROPATHY?**

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Background: IgA vasculitis (IgAV) and IgA nephropathy (IgAN) are inflammatory conditions [1, 2], that share pathogenic mechanisms [1], in which B-lymphocytes are described as key cells implicated in these processes. BAFF, APRIL and BAFF-R are cytokines implicated in the development of B-lymphocytes [3, 4] and in autoimmune processes [5, 6]. In this regard, an influence of *BAFF, APRIL* and *BAFFR* polymorphisms was observed on several immune-mediated conditions, being *BAFF* GCTGT>A a shared insertion-deletion variant for inflammatory conditions [7, 8].

Objectives: To determine whether *BAFF, APRIL* and *BAFFR* could be used as differential biomarkers between IgAV and IgAN.

Methods: *BAFF* rs374039502 (which colocalizes with *BAFF* GCTGT>A), two tag variants within *APRIL* (rs11552708 and rs6608) and two tag variants within *BAFFR* (rs7290134 and rs77874543) were genotyped in 394 Caucasian IgAV patients, 95 patients with IgAN and 832 matched healthy controls.

Results: Similar genotype and allele frequencies were observed in the whole cohort of patients with IgAV when compared to those with IgAN when *BAFF, APRIL* and *BAFFR* variants were analyzed independently (Table 1). In accordance with that, no *BAFF, APRIL* and *BAFFR* genotype or allele differences were detected between IgAV patients who developed nephritis and patients with IgAN (Table 1). Additionally, no statistically significant differences were observed between the whole cohort of patients with IgAV and healthy controls as well as between patients with IgAN and healthy controls when each when *BAFF, APRIL* and *BAFFR* genetic variant was also analyzed independently (Table 1). Similar results were disclosed when haplotype frequencies of *APRIL* and *BAFFR* were compared between the different comparative groups above mentioned (data not shown).

Conclusion: Our results reveal a similar *BAFF, APRIL* and *BAFFR* genetic distribution in IgAV and IgAN, suggesting that these genes could not be used as differential biomarkers between these pathologies.

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Table 1. Genotype and allele frequencies of BAFF, APRIL and BAFFR in the whole cohort of patients with IgAV, patients with IgAV who developed nephritis, patients with IgAN and healthy controls.

Polymorphism	Change	Data set	Genotypes, % (n)			Alleles, % (n)	
	1/2		1/1	1/2	2/2	1	2
BAFF rs374039502	T/A	IgAV	92.1 (363)	7.9 (31)	0.0	96.1 (757)	3.9 (31)
		IgAV with nephritis	90.1 (128)	9.9 (14)	0.0	95.1 (270)	4.9 (14)
		IgAN	91.6 (87)	8.4 (8)	0.0	95.8 (182)	4.2 (8)
		Controls	91.8 (764)	7.8 (65)	0.4 (3)	95.7 (1593)	4.3 (71)
APRIL rs11552708	G/A	IgAV	78.7 (310)	20.1 (79)	1.3 (5)	88.7 (699)	11.3 (89)
		IgAV with nephritis	81.1 (116)	18.9 (27)	0.0	90.6 (259)	9.4 (27)
		IgAN	75.8 (72)	23.2 (22)	1.1 (1)	87.4 (166)	12.6 (24)
		Controls	78.7 (655)	19.7 (164)	1.6 (13)	88.6 (1474)	11.4 (190)
APRIL rs6608	C/T	IgAV	72.6 (286)	25.4 (100)	2.0 (8)	85.3 (672)	14.7 (116)
		IgAV with nephritis	75.5 (108)	23.1 (33)	1.4 (2)	87.1 (249)	12.9 (37)
		IgAN	65.3 (62)	30.5 (29)	4.2 (4)	80.5 (153)	19.5 (37)
		Controls	71.0 (591)	26.6 (221)	2.4 (20)	84.3 (1403)	15.7 (261)
BAFFR rs7290134	A/G	IgAV	58.9 (232)	35.5 (140)	5.6 (22)	76.6 (604)	23.4 (184)
		IgAV with nephritis	60.1 (86)	32.2 (46)	7.7 (11)	76.2 (218)	23.8 (68)
		IgAN	57.9 (55)	38.9 (37)	3.2 (3)	77.4 (147)	22.6 (43)
		Controls	58.7 (488)	35.1 (292)	6.3 (52)	76.2 (1268)	23.8 (396)
BAFFR rs77874543	G/C	IgAV	83.2 (328)	15.5 (61)	1.3 (5)	91.0 (717)	9.0 (71)
		IgAV with nephritis	83.1 (118)	16.9 (24)	0.0	91.5 (260)	8.5 (24)
		IgAN	86.3 (82)	13.7 (13)	0.0	93.2 (167)	6.8 (13)
		Controls	83.7 (696)	16.0 (133)	0.4 (3)	91.6 (1525)	8.4 (139)

IgAV: IgA vasculitis; IgAN: IgA nephropathy.

declared, PAZ COLLADO: None declared, Antonio Fernandez-Nebro: None declared, Gisela Díaz-Cordoves: None declared, Secundino Cigarrán: None declared, Jesús Calviño: None declared, Carmen Cobelo: None declared, Diego de Argila: None declared, Esther F. Vicente-Rabaneda: None declared, Esteban Rubio-Romero: None declared, MANUEL LEON LUQUE: None declared, Juan María Blanco-Madrigal: None declared, E. Galíndez-Agirregoikoa: None declared, Oreste Gualillo: None declared, Javier Martin Ibanez: None declared, Santos Castañeda: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Miguel A González-Gay Speakers bureau: Abbvie, MSD, Jansen, and Roche, Grant/research support from: Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene, MSD and GSK, Raquel López-Mejías: None declared

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AB0147 INFLAMMATORY AND NEUTROPHIL ACTIVATION MARKERS IN PATIENTS WITH BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is a systemic variable vessel vasculitis with different clinical manifestations. BD does not have specific laboratory findings. Neutrophil hyperactivation is a major pathogenic factor in BD-related inflammation and tissue damage. Neutrophil reactivity (NEUT-RI), neutrophil granularity (NEUT-GI), immature granulocytes (IG), neutrophil-to-lymphocyte ratio (NLR), mean platelet volume (MPV), and platelet-lymphocyte ratio (PLR) are considered as inflammatory markers. Their role in BD remains unclear.
Objectives: to determine the importance of parameters of neutrophil activation (NEUT-RI, NEUT-GI), immature granulocytes (absolute (IG#), relative (IG%) counts), NLR, MPV, PLR in assessing inflammation in BD.
Methods: 29 patients with a reliable BD according to ICBD 2014 and 40 age-matched healthy donors (HD) without acute infectious diseases or cancer were included in the study (Table 1). Patients with BD were separated into two groups: 22 with active and 7 with inactive BD. Active BD was defined as involvement of at least two of the following features: oral ulcers, genital ulcers, uveitis, intestinal involvement, skin lesions, neurological involvement, arthritis, and vascular involvement. Current disease activity was evaluated with transformed Behçet's Disease Current Activity Form (BDCAF). A complete blood count (WBC-white blood cell, NEUT#-an absolute neutrophil count, NEUT-RI, NEUT-GI, IG%, IG#, NLR, thrombocytes, MPV, PLR, ESR-erythrocyte sedimentation rate) was performed with XN-1000 automated hematology analyzer (Sysmex, Japan).

Table 1. Comparative characteristics of patients with active/inactive BD and healthy controls.

Parameters M±SD, Me [25%; 75%], n (%)	Active BD (n=22)	Inactive BD (n=7)	Healthy donors (n=40)	p
Gender: male/female, n	16/6	4/3	16 /24	NS
Vascular involvement,n	7	3	-	NS
BDCAF	5 [5; 8]	1 [0; 3]	-	p<0.001*
WBC, 10^9/l	7.4 [5.9; 8.6]	6.9 [6.5; 8.4]	6.05 [5.2; 6.9]	p=0.04*
Thrombocytes, 10^9/l	264.33±56.95	305.11±104.82	257.46±53.18	NS
NEUT#, 10^9/l	3.91 [3.34; 5.03]	3.89 [3.78; 5.5]	3.41 [2.86; 4.13]	NS
NEUT-RI, FI	45.95 [44.1; 47.1]	46.25 [44.95; 47.75]	43.7 [42.7; 46.2]	p=0.049*
NEUT-GI, SI	154.84±4.05	157.04±5.55	153.37±4.7	NS
NLR	1.64 [1.39; 1.91]	1,9 [1.73; 2.6]	1.83 [1.4; 2.28]	NS
ESR, mm/	6.5 [4.5; 17.0]	12.0 [4.0; 15.0]	7.0 [4.0; 11.0]	NS
IG#,10^9/l	0.02 [0.01; 0.04]	0.04 [0.01; 0.07]	0.01 [0.01; 0.02]	p=0.036*
IG%	0.3 [0.2; 0.4]	0.45 [0.25; 0.65]	0.2 [0.2; 0.3]	p=0.018*
CRP, mg/l	2.5 [1.2; 7.4]	2.45 [1.28; 4.65]	-	NS
MPV, fl	10.4 [9.7; 11.0]	9.85 [9.6; 11.0]	10.5 [10.1; 11.2]	NS
PLR	116.45 [83.5; 138.6]	151.55 [119.5; 171.1]	137.1 [104.4; 160.1]	NS
Fibrinogen, g/l	3.48±0.8	2.88±0.4	-	NS

*a statistically significant test result ($p \leq 0.05$); NS-not significant;FI- fluorescence intensity; SI- scatter intensity; fl- femtoliter.

Results: A WBC count was significantly higher in BD patients compared to controls (Table 1). Patients with active BD had a higher WBC count than inactive. Patients with BD were found to have significantly higher levels of IG#, IG%, and NEUT-RI compared to HD. There was no significant difference between NEUT-GI, NLR, MPV, PLR, and ESR levels in patients with BD and HD. No significant difference in NEUT-RI, NEUT-GI, NLR, IG #, IG%, PLR, or MPV between active and inactive BD was found. These hematological parameters did not correlate with the transformed BDCAF score. IG# levels positively correlated with total leukocyte count (r_s=0.656, p<0.001) and the absolute neutrophil count (r_s=0.548, p=0.002). There was a tendency to a positive correlation between IG# and NEUT-GI (r_s=0.354, p=0.050) and a negative correlation between IG# and PLR (r_s=-0.356, p=0.052).
Conclusion: Patients with BD had significantly higher total WBC counts, immature granulocyte levels, and neutrophil reactivity than controls. Except for the leukocytes, there was no statistically significant difference in the studied parameters between patients with active and inactive BD.
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Disclosure of Interests: None declared

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AB0148 COULD THE RENIN-ANGIOTENSIN SYSTEM AFFECT THE PROGNOSIS OF GIANT CELL ARTERITIS? SINGLE-CENTRE RETROSPECTIVE OBSERVATIONAL STUDY

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Background: About half of patients with giant cell arteritis (GCA) relapse while tapering glucocorticoid therapy[1]. A previous observational study reported that blockade of the renin-angiotensin system, with angiotensin II receptor blockers (ARBs), was associated with lower relapse risk[2].
Objectives: To determine whether angiotensin blockade, with angiotensin converting enzyme inhibitor (ACEi) or ARB, is associated with differential relapse risk in GCA.
Methods: GCA patients from a tertiary centre diagnosed 2012–2020 with two years follow-up were identified from UK GCA Consortium. All provided written informed consent. Retrospective review of medical records included demographics, comorbidities, drug history, inflammatory markers and relapses. Relapse was defined as return of symptoms, raised inflammatory markers, or active vasculitis on imaging confirmed by the treating clinician. Relapse-free survival was analysed using Kaplan Meier (KM) curves and Cox proportional hazards.
Results: 111 patients were included (Table 1: demographic data), all were initially treated with 40–60mg Prednisolone. 42% received further immunosuppressants due to relapse or disease severity. 50% patients relapsed in two years, presenting with cranial symptoms (72%), PMR-like symptoms (30%) and/or raised inflammatory markers (48%). There was no association between relapse and age, gender, comorbid HTN/IHD or pre-steroid inflammatory markers and relapse. Rate of steroid taper can affect relapse. EULAR recommend 15–20mg of steroid by three months[3]. 9 patients relapsed within that time and were excluded, there was no difference in steriod dose at three months between the two groups. KM analysis showed ACEi did not significantly affect time to relapse compared to no angiotensin blockade (HR 0.57, 95% CI 0.28 – 1.18, unadjusted p-value=0.128), and neither did an ARB (HR 0.78, 95% CI 0.31 – 1.98, unadjusted p-value=0.605).

Table 1. *demographic data at baseline.*

	Relapse (n = 56)	No Relapse (n = 55)
Patient Factors		
Age *median (IQR)*	70 (65-74)	73 (67-78)
Male Sex *n (%)*	16 (29)	20 (36.36)
Medications *n (%)*		
ACEi	9 (15)	16 (29)
ARB	7 (12)	7 (13)
Comorbidities *n (%)*		
CKD	4 (7)	9 (16)
IHD	6 (11)	5 (9)
Prediabetes	11 (20)	10 (18)
DM	1 (2)	5 (9)
HTN	22 (40)	23 (42)
Current Smoker	6 (10)	2 (4)
GCA Factors *median (IQR)*		
CRP pre-treatment	69 (32 – 131)	64 (23 -115)
ESR pre-treatment	50 (37 -95)	4 (22 -72)
Steroid dose at 3 months	19 (15 -20)	15 (10-20)

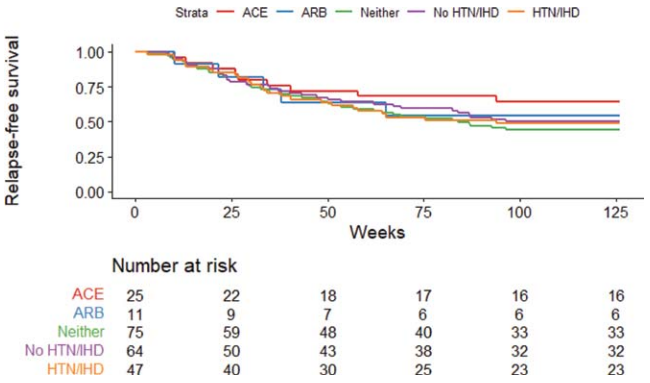

Figure 1. Unadjusted KM survival curve showing probability of relapse in patients 1) taking ACEi, 2) taking ARB, 3) taking neither ACEi or ARB, 4) with no comorbid HTN or IHD at diagnosis, and 5) experienced comorbid HTN/IHD. There was no significant difference in relapse free survival in patients on an ACEi compared to those taking neither ACEi or ARB.

Conclusion: In the two years following GCA diagnosis 50% relapsed. There was no significant difference in the rate of relapse in patients taking an ACEi or ARB. The main limitation, in this retrospective, observational study was the inability to exclude a reluctance of clinicians to diagnose GCA relapse in the presence of cardiovascular comorbidity. A randomised controlled trial would be needed to determine whether starting an ACEi could reduce relapse risk in patients with new-onset GCA.

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AB0149 RNA SEQUENCING OF SKIN BIOPSY SAMPLES REVEALS UNIQUE BIOLOGICAL PROCESSES AMONG SPECIFIC GROUPS OF ADULT PATIENTS WITH IGA VASCULITIS

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Background: Immunoglobulin A vasculitis (IgAV) is a small vessel leukocytoclastic vasculitis, characterized by vascular IgA deposits, and clinically by skin, join, kidney and bowel involvement. Renal involvement, present in up to 84% of adult patients, is associated with an increased risk of progression to chronic kidney failure. A skin or renal biopsy is still the golden standard for diagnosis. Omics data from NCBI-GEO and Array Express databanks are lacking from IgAV samples of adult patients.

Objectives: Our aim was to perform RNA sequencing and to identify differentially expressed genes and dysregulated molecular pathways in the affected skin of adult IgAV patients with renal involvement, patients with skin-limited IgAV and healthy controls (HC).

Methods: Skin biopsy samples were collected from treatment-naive adult IgAV patients at time of diagnostic procedure: 1) skin-limited disease (n=3), 2), IgAV with renal involvement (n=3), and age-/sex-matched HC (n=3). RNA was isolated and 100 bp paired-end sequenced using the Illumina HiSeq 4000 platform (25.9 to 30.8 million reads were obtained per sample). Reads were mapped with Salmon tool against the human transcriptome (Ensemble Release 104). Differentially expressed genes (log2 fold change $\geq |1|$, padj < 0.05) were computed using the R package DESeq2. Data were clustered using principal component analysis (PCA), and KEGG pathway over-representation analysis (ORA) was performed with R package clusterProfiler.

Results: We identified 72 differentially expressed genes (34 up- and 38 down-regulated) between skin-limited IgAV and HC, while 686 genes were differentially expressed (421 up- and 265 down-regulated) in the affected skin between adult IgAV patients with renal involvement and healthy controls (HC). PCA distinguished between IgAV (renal and skin-limited) and healthy controls, suggesting specific transcriptome signatures in IgAV. 21 overlapping genes were differentially expressed in both groups of patients in comparison to HC. 196 genes were differentially expressed between IgAV patients with renal involvement compared to skin-limited IgAV.

Genes, differentially expressed in patients with skin-limited disease were enriched in the oxidative phosphorylation (padj = 3.08×10^{-5}) and cell adhesion molecules (padj = 6.32×10^{-4}) KEGG Pathways. Differentially expressed genes in patients with renal involvement exhibited enriched KEGG Pathways involved in the ribosome (padj = 0×10^{-7}), the regulation of lipolysis in adipocytes (padj 9,066 x 10^{-4}), cell adhesion molecules (padj = 8.0008 x 10^{-3}), renin secretion (padj = 4.2882 x 10^{-3}), complement and coagulation cascades (padj = 3.58547 x 10^{-2}), vascular smooth muscle contraction (padj = 3.76132 x 10^{-2}) and aldosterone synthesis and secretion (padj = 3.76132 x 10^{-2}).

Conclusion: Deregulated genes in skin of adult IgAV patients with renal manifestation could serve as biomarkers for organ-specific involvement. Further studies are needed that would support deciphering the involvement of perturbed molecular pathways and the contribution of individual cell types to skin manifestations of adult IgAV patients.

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AB0150 CIRCULARRNA AS A POTENTIAL BIOMARKER OF GRANULOMATOSIS WITH POLYANGIITIS

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Background: Granulomatosis with polyangiitis (GPA) belong to ANCA-associated vasculitides, a heterogeneous group of disorders whose clinical presentation ranges from isolated lesions affecting a single organ to life-threatening conditions. The etiology of the disease is not fully understood, and there is a lack of reliable and unambiguous diagnostic and prognostic markers.

Research in recent years points to the potential use of circulating free nucleic acids as a potential biomarkers in human pathology. Circular RNAs (circRNAs) belong to the group of non-coding RNAs, a group of potentially regulatory RNAs generated by linkage between a downstream 3′ splice site and an upstream 5′ splice site in a process known as backsplicing. CircRNAs were found in in nearly all tissues and recently have been reported to regulate gene expression by sponging miRNA. However their role in specific human conditions is largely unknown.

Objectives: The aim of our study was to assess the potential role of circRNA in diagnosis and monitoring of GPA.

Methods: CircRNAs were selected using bioinformatic analysis of RNA-seq data. Serum samples were obtained from 30 patients with GPA and 30 healthy controls. Levels of circRNA weres assessed using qPCR with specific primers

and probes. Statistical analysis was performed using dedicated packages for R and R Studio software.

Results: Levels of at least 10 serum circRNAs distinguished GPA patients from controls and 6 of them reached statistical significance. There was also an apparent difference in the levels of selected molecules between GPA exacerbation and remission (hsa_circ_0015167 – RQ 5.97, p<0.05; hsa_circ_0045266 – RQ 4.53, p<0.05). CircRNAs that differentiate patients from healthy individuals were associated with genes for P-selectin, VCAM and interleukins, among others. In contrast, molecules derived from catherins do not differentiate between the study and control groups.

Conclusion: Our results suggest that circRNA could be potentially used as a biomarker facilitating GPA diagnosis. Moreover, the observed differences depending on the stage of the disease could allow for monitoring the disease and predicting its progression. The association of molecules which levels differ between the test and control groups with genes previously associated with the development of the disease strongly suggests their potential involvement in its pathogenesis, which in turn strengthens the diagnostic specificity of the proposed markers.

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AB0151 THE ROLE OF PLASMA MICROVESICLES IN LVVS: NOT ONLY BIOLOGICAL MARKERS

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Background: Microvesicles (MVs) are membrane enclosed extracellular vesicles released upon cellular activation and stress, which maintains features and maintain features and constituents of their parental cells. Large vessel vasculitides (LVVs) are inflammatory conditions of the wall of large-sized arteries, mainly represented by giant cell arteritis (GCA) and Takayasu arteritis (TA). Arterial stenosis and dilatation directly affect prognosis and, according to latest EULAR guidelines can be investigated by positron emission tomography and magnetic resonance angiography. Endothelial cells are believed to play a role in the pathogenesis of LVVs and circulating microvesicles could be a biomarker of vessel wall injury.

Objectives: To verify whether arterial wall derived-MVs detectable in the blood of TA patients and expressing bioactive molecules potentially involved in arterial injury, inflammation and remodeling could correlate with clinical and radiological features of those patients.

Methods: Platelet was obtained from 112 LVV pts (73 TA, 39 GCA). Plasma flow cytometry was performed with anti-CD14, CD16, anti-CD144 (VE-cadherin, an endothelial marker), anti-CD140a/b (PDGF receptor A/B a vascular stromal marker), anti-HMGB1, anti-PTX3, Mitotracker green and MitoSox, which are expression of mitochondrial moieties and ROS. Vascular imaging was carried out by angio-RM and PET. Circulating microvesicles from LVVs patients were correlated with disease characteristics, namely CRP, NIH activity, PGA, ITAS2010, ITAS2011 activity, immunosuppressant intake (IS), intake of glucocorticoids (yes/no) and biologics, and daily dose of glucocorticoids as well as radiological parameters. Pearson's and Spearman's correlation tests were used for parametric and non-parametric analysis. The SPSS IBM Software was used for statistics.

Results: The number of total MVs negatively correlate to CRP levels positively correlate to IS (p 0.052 and 0.013). CD 14 and 16 + MVs do not correlate with disease activity, extent or vascular inflammation at either MR or PET. PTX3+ MVs positively correlate to disease activity (NIH criteria and VAS), steroid intake, and disease extent (number of vessels at imaging). CD144+ MVs negatively correlate to IS and positively to SUV max at FDG PET. CD140a+ MVs significantly correlate to disease activity (PGA, VAS, and ITAS2010). Mitotracker+ Mvs negatively correlate to SNR max and positively to FDG-PET positivity.

Conclusion: Monocyte-derived MVs, despite being increased in LVV, do not correlate with disease activity, extent and vascular inflammation. Despite this, endothelial and stromal-derived MVs reflect some disease-related domains including clinical activity and imaging activity at PET. Furthermore, bioactive signals on MVs such as the long pentraxin PTX3 and mitochondria are more promising biomarkers. Accordingly, other studies have shown that systemic pentraxin-3 levels reflect vascular enhancement and progression in Takayasu arteritis, being PCR and ESR more a mirror of the burden of systemic inflammation. However, further studies are required to verify the pathogenic role of MVs in LVVs and to assess the impact of potential confounders such as therapy.

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AB0152 MITOCHONDRIAL DNA IS ELEVATED IN PLASMA OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) represents the most prevalent form of systemic vasculitis in elderly, and characterized by a remarkable heterogeneity regarding clinical and histological phenotype, pathogenetic mechanisms and treatment choice (1). The pathophysiology of GCA is driven by an interplay between cells of both innate and adaptive immune systems (2). Neutrophils seem to hold a cardinal role in GCA pathology, given their abundance in vicinity to the foci of tissue injury (3). Most importantly, neutrophils eject neutrophil extracellular traps (NETs) which are decorated with a series of immunocompetent epitopes, essential for the dissemination of the inflammatory response (3, 4).

Objectives: The diagnostic and prognostic value of cell-free DNA in GCA is still unknown. The aim of the present study was therefore to examine the clinical utility of cell-free DNA quantification as a biomarker in GCA.

Methods: Total DNA was isolated from platelet-free plasma samples of matched healthy controls (HC) and consecutive GCA patients. Plasma and clinical data were collected at baseline and follow-up. Copy numbers were quantified by quantitative PCR for mtDNA (ATP-6 gene) and nuclear (n) DNA (GAPDH gene) (5).

Results: Twenty-one GCA patients (median age 64.0 ± 9.0, 49% female) and 22 sex matched HC were enrolled for analysis.

mtDNA levels were significantly elevated in GCA plasma ($2.0x10^8$ copies/ml plasma, 95% CI: $7.0x10^7$ to $3.8x10^8$), compared to HC plasma ($7.0x10^6$ copies/ml plasma, 95% CI: $2.8x10^6$ to $1.1x10^7$, p<0.0001). nDNA levels in contrast did not differ between GCA ($5.1x10^6$ copies/ml plasma, 95%CI: $2.5x10^6$ to $9.5x10^7$) and HC ($4.1x10^6$ copies/ml plasma, 95%CI: $2.3x10^6$ to $9.3x10^7$, p=0.74). Receiver *operating characteristic* curve analysis showed that a cut-off value of $2.8x10^7$ mtDNA copy numbers differentiated between GCA and HC with 90.5% sensitivity, 95.2% specificity and an AUC of 0.95.

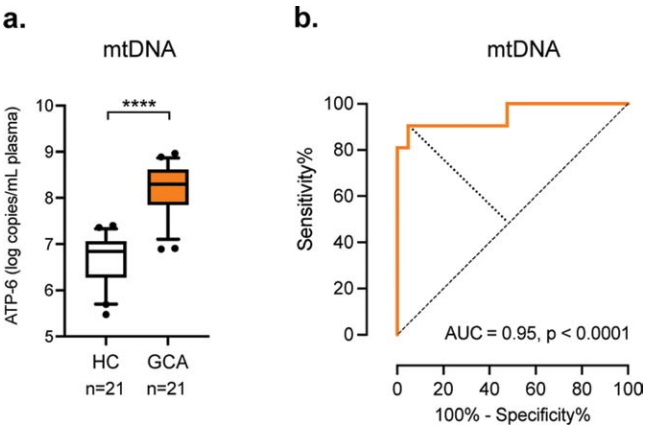

Figure 1. (a.) Plasma mtDNA levels in GCA patients are elevated (2 orders of magnitude) compared to healthy controls. Whiskers represent 95% CI. (b.) Receiver operating characteristic curve for mtDNA plasma concentrations discriminate between HC and GCA patients. AUC: area under the curve.

There was no association of mtDNA elevation with any particular type of intra-, extra-cranial or ocular vessel involvement).
Conclusion: The quantification of cell free mtDNA - but not nDNA - copy numbers allows a sensitive and specific distinction between healthy individuals and patients with GCA and raises the possibility that circulating nucleic acids contribute to the pathogenesis of GCA. Plasma mtDNA quantification may aid in the diagnosis of GCA and in monitoring GCA activity.
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Basic and translational science in paediatric rheumatology

AB0153 **EFFECT OF STANDING FRAMES USED IN REAL LIFE ON BONE REMODELING IN NON-WALKING CHILDREN WITH CEREBRAL PALSY**

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Background: Children with severe cerebral palsy are prone to low bone mineral density. Standing frames are recommended as postural management for these children. The beneficial effects in promoting bone health remain unclear.
Objectives: To determine whether static standing frames enhance bone remodeling in real life in severe cerebral palsy.
Methods: 24 children with severe cerebral palsy GMFCS IV & V were included in the study and were divided into two groups: 13 were using a passive standing frame and 11 were not. We performed a single center retrospective cross-sectional study comparing the two groups using dual X-ray absorptiometry data and tests on biological samples, including bone remodeling factors.
Results: Total body (less head) bone mineral content was significantly higher in children who used a standing frame for an average of 30 min/day. This was confirmed in the lumbar spine. Although the total body bone mineral density (less head and proximal femur) densitometric data were not significantly higher, a positive trend favored the use of a standing frame in the children. Bone resorptive factors (CTX) were higher in the non standing-frame group, whereas there was no difference among osteoformation factors. No difference in fracture history was found.
Conclusion: Used in real life, we showed that static standing practice improved mineralization by reducing osteoresorption in non-ambulant children with cerebral palsy. Further studies are needed to determine how standing practice could impact bone mineralization over time in real life and to explore more bone remodeling factors.
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AB0154 **PHYSICAL FUNCTION ASSESSMENT TOOLS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: JAFAS VERSUS CHAQ**

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Background: Children with juvenile idiopathic arthritis (JIA) frequently experience impairments in one or more body systems. These may include pain, fatigue, muscle weakness, and poor exercise capacity. Functional disability can be evaluated by means of questionnaires and observed performance tests. Only the Juvenile Arthritis Functional Assessment Scale (JAFAS) and the Childhood Health Assessment questionnaire (CHAQ) were developed specifically for children with juvenile arthritis.
Objectives: The aim of this study was to investigate the relationship between JAFAS and CHAQ in the evaluation of physical function.
Methods: This is a cross sectional study including patients with JIA. Assessment of disease activity (DAS28), number of tender joints (NTJ) and swollen joints (NSJ) were determined. The JAFAS (range 0-20) includes 10 items of activities of daily living (dressing, cutting food, getting in and out of bed, picking up an object from the floor while standing, moving from standing to the floor and returning to standing, walking 50 feet unaided, and walking up a flight of 5 steps). The score range for each item is 0–2, based on the time in seconds the child takes to complete each task. Higher scores indicate greater activity limitation (1). The original CHAQ including 30 activities in eight different domains, with a total score ranging from 0 (no limitation) to 3 (maximal limitation) was completed by interviewing the patient (2). Spearman correlation test and Cohen's kappa coefficient (k) were used. Significance level was set at $p \leqslant 0.05$.
Results: Twenty-nine patients with a median age of 25 years [8-40] and median disease duration of 16 years, were included. Age of onset of the disease was 8 years [2-16] years. The median JAFAS score was 3 [0-12] and the median CHAQ score was 0.05 [0-3]. There was a slight agreement between JAFAS and CHAQ k=0.1 (p = 0.05). A positive correlation was found between NTJ and CHAQ (r=0.54, p=0.03) and JAFAS (r=0.5, p=0.05). A correlation was noticed also between NSJ and CHAQ(r=0.51, p=0.05). Both the JAFAS and CHAQ scores correlated with DAS28 (r=0.55, p=0.01and r=0.44, p=0.02, respectively). At the level of the individual joints, coxitis was the most frequent complication (13 patients out of 28), six of them had surgery of total hip prosthesis. There was a linear relationship between JIA complicated with coxitis and the level of functional disability measured with JAFAS (p=0.027).
Conclusion: Our study shows that, even though JAFAS had a slight agreement with CHAQ, both were correlated with the level of disease activity and the number of swollen and tender joints.
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AB0155 VASCULAR ENDOTHELIAL GROWTH FACTOR IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Vascular changes are preceding the development of fibrosis in juvenile idiopathic arthritis (JIA). Signs of angiogenesis, the process of new vessel formation, cannot be fully detected, especially in childhood. Vascular endothelial growth factor (VEGF) is considered to play a crucial role for angiogenesis regulation [1,2].
Objectives: To evaluate serum levels of vascular endothelial growth factor in the treatment of juvenile idiopathic arthritis.
Methods: 104 consecutive JIA patients aged 10 to 18 years (13.3 ± 0.3) were included in this 4-years prospective study. VEGF levels were determined by VEGF ELISA kits. Serum levels of VEGF were analyzed depending on patients' gender, age, and age of JIA onset, its variant, duration, activity, and presence of methotrexate (MTX) in treatment and its dose.
Results: We evaluated VEGF level for children with JIA (min: 23.68 pg/ml; Me:244.75 pg/ml; max: 2158.91 pg/ml). VEGF in JIA was related to onset of JIA in patients older than 15 years and high disease activity according JADAS-27 pattern ($p<0.05$). Levels of circulating immune complex (CIC) and antistreptolysin-o (ASL-O) was associated with VEGF level. Mostly VEGF was correlated with CIC (among: girls r=0.53, patients with oligoarthritis r=0.55, inactive disease activity according to JADAS-27 r=0.47, dose of MTX, 10–12,5mg/m2/week r=0.67 $p < 0.05$) and with ASL-O (among: girls r=0.47, inactive disease activity according to JADAS-27 r=0.51, MTX treatment r= 0.36, dose of MTX, 10–12,5mg/m2/week r=0.90 $p < 0.05$).
Conclusion: Children with JIA had a higher VEGF level in patients older than 15 years and high disease activity. Also, CIC and ASL-O showed high impact on VEGF level which is the critical factor of angiogenesis.
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Basic and translational pain science

AB0156 INTRA-ARTICULAR AGRIN PROVIDES DIRECT PAIN RELIEF IN OSTEOARTHRITIS AND CARTILAGE DEFECTS

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Background: Osteoarthritis is the leading cause of disability worldwide with a financial burden estimated between 1.5 and 2% of the GDP in all westernised countries. The main driver of progression in osteoarthritis is cartilage loss, which may be associated with bone changes, low degree synovitis and lesions to menisci and ligaments. These pathological features result in pain, which contributes to chronic disability.
Improving cartilage integrity without pain relief does not help patients and results in failure in clinical trials. Therefore, there is a need for therapeutics that induce rapid pain relief and long-term cartilage regeneration.
We previously showed that Agrin results in cartilage regeneration and in this study, following on the serendipitous finding of rapid pain relief after Agrin administration we explore its analgesic effect in animal models of osteochondral defects and osteoarthritis.
Objectives: Test the analgesic potential of Agrin in post-surgical pain associated with osteochondral defects in mice and sheep.
Determine whether Agrin can relieve chronic pain induced by osteoarthritis in mice.
Investigate the therapeutic potential of Agrin in models of primary and injury-induced secondary osteoarthritis.
Methods: Acute post-surgical pain: Surgery was performed on skeletally mature male mice and female sheep to create critical-sized osteochondral defects; defects were filled with collagen gel containing PBS or Agrin. Animals were sacrificed 8 weeks (mice) and 6 months (sheep) after surgery. Pain was measured in mice using von Frey filaments and incapacitance readings. Sheep were fitted with accelerometers for the duration of the study.
Osteoarthritic pain: Osteoarthritis was surgically induced in skeletally mature male mice by menisco-ligament injury (MLI). Control mice received sham surgery. Nine weeks post-surgery, once chronic pain was established, mice were injected intra-articularly with recombinant Agrin. Pain was measured by von Frey filaments and incapacitance.
Treatment in therapeutic regime: Tamoxifen-inducible transgenic mice overexpressing Agrin under the AggrecanCre promotor were generated. Skeletally mature male mice were subjected to menisco-ligament injury surgery. Four weeks later, tamoxifen was administered to overexpress Agrin in the cartilage. Pain was measured by von Frey filaments and incapacitance.
Ex-vivo: MicroCT, X-ray, Kellgren-Laurence scoring, histology, OARSI scoring and immunohistochemistry.
Results: In sheep, Agrin administration induced regeneration in osteochondral defects and, more importantly, reduced the levels of secondary osteoarthritis. This was associated with a rapid and sustained symptomatic relief.
In mice, Agrin expression was lost in the dorsal root ganglia corresponding to the limb subjected to MLI but not in the dorsal root ganglia corresponding to the sham operated limbs.
Intra-articular recombinant Agrin in mice with established OA (9 weeks after MLI surgery) resulted in pain relief as early as three hours after administration. Acute administration of recombinant Agrin does not have any analgesic effects in sham operated mice.
Inducible, cartilage-specific Agrin-overexpression mice were protected from developing pain associated with instability-induced osteoarthritis.
In mice with acute osteochondral defects, intra-articular Agrin administration resulted in pain relief for at least five days.
In humans, the loss of Agrin in the articular cartilage correlated significantly with the Mankin score of patients undergoing knee replacement surgery.
Conclusion: Agrin has analgesic properties in both the acute phases of cartilage damage and in established osteoarthritis. Our findings support the therapeutic use of Agrin for joint surface regeneration and pain relief.
Disclosure of Interests: Suzanne Eldridge: None declared, Aida Barawi: None declared, Anne-Sophie Thorup: None declared, Beatriz F Fernandez: None declared, Sabah Bharde: None declared, Shafaq Sikandar: None declared, Zeyu Guan: None declared, Magdalena Kaneva: None declared, Helen Lydon: None declared, Fran Henson: None declared, Cosimo De Bari: None declared, Andrew McCaskie: None declared, Francesco Dell'Accio Consultant of: Prof Dell'Accio has consulted for Samumed, Grant/research support from: A PhD studentship unrelated to this abstract is funded by UCB

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Rheumatoid arthritis - prognosis, predictors and outcome

AB0157 EFFICACY AND SAFETY OF FILGOTINIB IN ACTIVE RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO METHOTREXATE: COMPARATIVE STUDY WITH FILGOTINIB AND TOCILIZUMAB EXAMINED BY CLINICAL INDEX AS WELL AS MUSCULOSKELETAL ULTRASOUND ASSESSMENT (TRANSFORM STUDY): STUDY PROTOCOL

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Background: The administration of Janus kinase (JAK) inhibitors as well as biological disease-modifying anti-rheumatic drugs has dramatically improved even the clinical outcomes in rheumatoid arthritis (RA) patients with inadequate response to methotrexate (MTX). The dysregulation of JAK- signal transducer and activator of transcription (STAT) pathways via overproduction of cytokines, such as interleukin-6 (IL-6) is involved in the pathogenesis of RA (1). Filgotinib, a preferential JAK1 inhibitor, is effective in suppressing disease activity and preventing the progression of joint destruction due to inhibition of the JAK-STAT pathway. IL-6 inhibitors such as tocilizumab also inhibit the JAK-STAT pathways due to inhibition of IL-6 signaling. Thus, it should be desirable to investigate whether the effectiveness of filgotinib monotherapy is non-inferior to those of tocilizumab monotherapy in RA patients with inadequate response to MTX. In addition, it is important to accurately evaluate disease activity at the joint level by using musculoskeletal ultrasound (MSUS) and clinical disease activity indices, including subjective parameters (2).
Objectives: This study's principal objective is to evaluate the effects of filgotinib monotherapy is non-inferior to those of tocilizumab monotherapy in RA patients with inadequate response to MTX. In addition, we will evaluate changes in patients' parameters, including clinical disease activity indices, MSUS scores, serum biomarkers, patient-reported outcome (PRO), and modified total Sharp score (mTSS) after the administration of filgotinib or tocilizumab. Herein, we describe the study protocol for this study.
Methods: This study is an interventional, multicenter, randomized, open-label, parallel-group and non-inferiority clinical trial with a 52-week follow-up. In total, 400 RA patients with at least moderate disease activity during treatment with MTX will be included. Patients will be randomized in a 1:1 ratio to administration of filgotinib 200mg/day monotherapy or subcutaneous tocilizumab 162mg/biweekly monotherapy switched from MTX (Figure 1). We will evaluate disease activity by measuring clinical disease activity indices and by using MSUS. The primary endpoint is the proportion of patients who achieve an American College of Rheumatology 50 response at week 12. Important secondary endpoints are the changes from the baseline of the MSUS scores, PRO, and mTSS. We will also comprehensively analyze the serum levels of multiple biomarkers such as cytokines and chemokines.

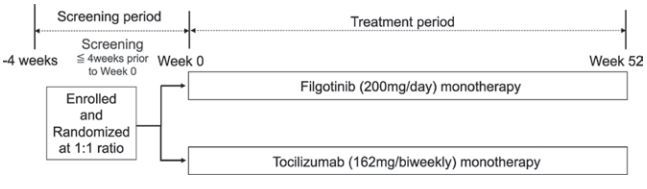

Figure 1.

Results: Although the study results cannot be shown because the research entry is in progress, they are expected to show the non-inferiority of filgotinib monotherapy to tocilizumab monotherapy in RA patients with inadequate response to MTX.
Conclusion: The strength of this study is its prospective evaluation of therapeutic efficacy using not only clinical disease activity indices but also MSUS, which accurately and objectively evaluate disease activity at the joint level among patients drawn from multiple centers with a standardized evaluation by MSUS. In addition, we will evaluate the effectiveness of both drugs by integrating multilateral assessments, i.e., clinical disease activity indices, MSUS findings, and serum biomarkers.
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AB0158 PREDICT OF PROGNOSIS AT ONE YEAR AFTER THE ADMINISTRATION WITH B/TSDMARD FOR PATIENT WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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Background: Patients with difficult-to-treat rheumatoid arthritis (D2T RA) are the most serious problem in recent systemic RA treatment protocols [1].
Objectives: Prognosis after biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) is beneficial when predicted in patients with D2T RA. Predictors of post b/tsDMARDs in D2T RA patients were investigated using retrospective cohort data.
Methods: RA patients more than 1 year after the start of newly administered b/tsDMARDs were recruited. The patients were divided into two groups according to the EULAR definition of D2T RA [2]. Patients who met the criteria were classified into the D2T RA group and others into the non-D2T RA group. The incidence of the clinical features described in the criteria of D2T RA and the rheumatoid disease comorbidity index (RDCI) [3] were compared between the two groups at the time of drug initiation (baseline). The primary endpoint was "Success or Failure" 1 year after baseline. Success was defined as b/tsDMARD persisted in remission as the 28 joint disease activity score with erythrocyte sedimentation rate (DAS28) ≤ 2.6, or as b/tsDMARD was discontinued upon achieving clinical remission. The Failure was defined as other decisions such as discontinuation due to failure, adverse events, or characteristic patient problems. In the discontinued cases, the monitoring value at the last observation was carried forward to 1 year.
Cox regression analysis was used to assess each variant as a potential risk factor for Failure. Receiver operating characteristic analysis (ROC) was tested on variants with significantly higher risk ratios, and Kaplan-Meier survival analysis was also tested for cut-off indices.
Results: 71 cases of the D2T RA and 259 cases of the non-D2T RA group were analyzed. As shown in Table 1, the clinical characteristics of the D2T RA group were significantly worse than those of the non-D2T RA group.
Higher DAS28 had a significantly higher risk ratio for the Failure from month 3 in the D2T RA group, whereas from baseline in the non-D2T RA group (Figure 1-A). Other factors in the D2T RA group at and after baseline listed in the Table 1 had no significant risk ratios. PS-VAS and EQ5D score had significant higher risk ratios in the non-D2T RA group using univariate models, however, only DAS28 had significant higher risk ratio using multivariate model. The cut-off index (COI) and the area under the curve (AUC) using ROC for each observational period in the two groups were shown in Figure 1-B. Results of Kaplan-Meier survival analyses were shown in Figure 1-C. Hazard ratios of DAS28 > COI exceeded 2.5 even from months 3 with high sensitivity ($p < 0.001$) in the D2T RA group.

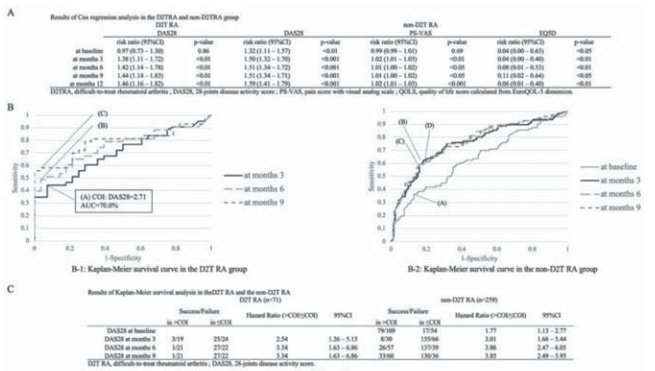

Figure 1

Conclusion: These results indicated that higher DAS 28 suggested a failure prognosis at 12 months after initiation in D2T RA and non-D2T RA patients. Even in patients with D2T RA, strict disease activity control is most important for prognostic management, with 1-year prognosis predictable in the first 3 months. However, this study is a short-term prognostic predictor, and accumulation of short-term predictions is a long-term predictor.
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AB0159 HEALTH RELATED QUALITY OF LIFE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AT TIKUR ANBESSA SPECIALIZED HOSPITAL. A HOSPITAL-BASED CROSS SECTIONAL STUDY

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Background: Rheumatoid Arthritis (RA) is a chronic disorder associated with substantial morbidity and mortality. Patients with active RA suffer from significant decline in functional capacity and many become work disabled within five years, from onset of symptoms despite treatment. Measurable outcome of these can be done with the help of HRQoL questionnaires. There is a need to study the HRQoL in RA patients, as there is no available data in Ethiopia.
Objectives: This study was conducted to evaluate HRQoL in patients with Rheumatoid Arthritis and factors associated with it.
Methods: A Cross sectional study was conducted at Rheumatology Clinic in Tikur Anbessa specialized Hospital, Addis Ababa, Ethiopia from June1 to October 31. Data was collected using a structured interviewer administered questionnaire and data extraction form. Data was entered and it was analyzed using SPSS Version 26. To identify associated factors in Health related quality of life of patients with rheumatoid arthritis, bivariable and multivariable analysis were done. Statistical significance was considered at 5%, and beta weight with 95% confidence interval was used to present the estimates of the strength of the association.
Results: A total of 213 participants were included in this study. The mean age of participants was 44.7(±14). Majority 191(89.7%) of participants were female. In this study all the 8 domains of RAND 36 are reduced. The mean value of two scales from physical component and one scale from the mental component are below 50. These are Role limitation due to physical problems, General Health Perception and Role limitation due to emotional problems. Both summary score are affected with the PCS more affected than MCS. The multivariable analysis identified rural residence and modified health assessment questionnaire score as factors associated with PCS. For each shift of a patient from urban to rural residence, the PCS decreases by 9.1. For each one score increase in modified health assessment questionnaire score, the PCS score decreases by 26.25. Whereas factors associated with MCS are rural residence, adherence score, MHAQ score, peptic ulcer disease, and rheumatoid nodule. For each shift of residence from urban to rural, the MCS decreases by 15.2 . For each one score increase in adherence score, the mental component score increases by For each one score increase in MHAQ score, the MCS decreases by 14.3. For each shift of peptic ulcer disease from absent to present, the mental component score decreases by 16.Finally, for each shift of rheumatoid nodule from absent to present, the MCS by 20.8.
Conclusion: This study showed that Rheumatoid Arthritis has a significant effect on the Health Related quality of life of patients. Rural residence and functional disability was the most influencing factor on both the physical and mental function. Routine assessment of the Health Related quality of life in those patients is recommended to detect and monitor the impact of the disease and its medications on different aspects the patient's life.
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Disclosure of Interests: None declared
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AB0160 THE RELATIONSHIP BETWEEN THE LEVEL OF FETUIN-A AND LABORATORY MARKERS OF CONNECTIVE TISSUE DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: It is known that there are biochemical markers of cartilage and bone tissue destruction, which reflect the metabolic processes occurring in tissues. For example, in rheumatoid arthritis (RA), routine markers such as CTX-I, a bone degradation marker (C-terminal telopeptide of type I collagen) and CTX-II, a cartilage degradation marker (C-terminal telopeptide of type II collagen), can be used. Also, to assess the state of cartilage tissue, the determination of type II collagen fragments by Urine CartiLaps is widely used, which allows not only primary diagnosis, but also dynamic monitoring of metabolic processes.
Objectives: The aim of our research was to study the relationship between the level of fetuin-A (FeA) and laboratory markers of bone and cartilage tissue degradation in the blood serum of patients with RA.
Methods: We observed 110 patients with a verified diagnosis of RA, the control group consisted of 30 practically healthy individuals without joint diseases. The group of patients with RA and the control group were comparable in terms of age (p=0.083), gender (p=0.116), BMI (p=0.302). The diagnosis of RA was based on the clinical classification adopted at the EULAR/ACR in 2010. The level of FeA in the blood serum was determined once by enzyme immunoassay using commercial test systems (Human Fetuin-A ELISA Biovender Cat No. 191-0371).
Results: We have assessed the FeA level in the group of RA patients and healthy donors. The normal level of FA in healthy individuals, calculated as M±2σ, ranged from 653.55 μg/ml to 972.19 μg/ml. FeA level was normally distributed (K-S d=0.062, p>0.2). We also studied the relationship between indicators of bone metabolism and the concentration of FeA. In patients with normal FeA levels (n=87), the mean CTX-1 level was 35 ng/mL; in patients with reduced FeA levels (n=23), the mean CTX-1 level was 51 ng/ml (t=-2.42 p =0.016). Thus, with a decrease in the FeA level, CTX-I (an indicator of osteodestruction) tended to increase.
Next, we analyzed the relationship between low and normal levels of FeA and the Cartilaps/urine creatinine ratio using intragroup analysis methods. In the group with low FeA level Cartilaps/urinary creatinine was 598.9±223.72 μg/mmol versus 481.17±226.93 μg/mmol in the group with normal FeA level (Z=-2.311; p=0.021). Our data probably allow us to associate the FeA level with the rate of cartilage tissue destruction.
Conclusion: Considering that the levels of laboratory markers of cartilage and bone collagen degradation Cartilaps and CTX-I were statistically lower in the presence of an elevated serum level of FeA, we can conclude that FeA has chondro- and osteoprotective properties. It can also be assumed that the level of this marker can be used to predict the rate of cartilage destruction in patients with RA, but this issue requires further study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.810

AB0161 THE RELATIONSHIP OF TRYPTOPHAN CATABOLISM WITH RHEUMATOİD ARTHRITIS DİSEASE ACTİVİTY ABSTRACT

A. Kor[1], S. Erten[1], E. F. Yurt[2], I. Dogan[1], H. Apaydın[3], M. A. Serdar[4], C. Bİçer[5]on behalf of ankara city hospital working group. [1]*Ankara Yıldırım Beyazıt University Faculty of Medicine, Rheumatology, ANKARA, Turkey;* [2]*Beypazari Public Hospital,, Medical Biochemistry,, ANKARA, Turkey;* [3]*Ankara Şehir Hastanesi, Rheumatology, ANKARA, Turkey;* [4]*Acibadem Hospital Ankara, Medical Biochemistry, ANKARA, Turkey;* [5]*Ankara Yıldırım Beyazıt University Faculty of Medicine, Medical Biochemistry,, ANKARA, Turkey*

Background: Tryptophan (Trp) is an essential amino acid. The immunosuppressive effect caused by Kynurenine (Kyn) and its metabolites formed by the catabolism of Trp is thought to be an important physiological mechanism.
Objectives: This study aims to evaluate the relationship of Kyn and its metabolites formed in Trp catabolism with rheumatoid arthritis (RA) disease activation and to investigate the usability of these markers in the diagnosis and treatment of RA.
Methods: 50 RA patients followed in our rheumatology clinic and 41 healthy controls without chronic disease were included in this study. Disease Activity Score 28 (DAS28) was used to evaluate the association of Kyn metabolites and Indolamine 2,3 dioxygenase (IDO) enzyme activity with RA disease activity. The task of this enzyme is to provide Kyn formation with Trp catabolism.
Results: In this study, lower Trp levels were found in the RA group compared to the control group (11285.47±2318.93-13320.31±3771.27, respectively) compared to the Trp mean (p<0.01). In terms of the Kyn/Trp ratio, a significantly higher Kyn/Trp ratio (4.42±1.77-3.27±0.71, respectively) was found in the RA compared to the control group (p<0.001). There was no significant difference between the study groups in terms of Kyn averages (p>0.05). A significant correlation was found between Trp levels and morning stiffness (r: -0.321, p<0.05) and the DAS28 score (r:-0.566, p<0.01). A significant positive correlation was found between the Kyn/Trp ratio and C-reactive protein (r:0.317, p<0.05), sedimentation (r:0.319, p<0.05), morning stiffness (r:0.287, p<0.05) and DAS28 score (r:0.322, p<0.01).

Table 1. Comparison of study parameters between RA and control group.

Parameter	Rheumatoid arthritis	Control group	P-Value
Tryptophan (ng/ml)	**11285,47±2318,93**	13320,31±3771,27	**<0.01**
Kynurenine (ng/ml)	477,68±158,38	437,51±162,10	>0.05
Kyn/Trp ratio	**4,42±1,77**	3,27±0,71	**<0.001**

All values were expressed as mean ± SD. All values were calculated using independent sample t-test for normal distribution.

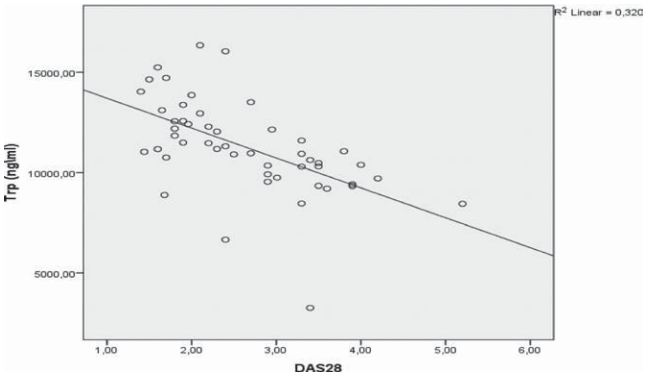

Figure 1. Correlation relationship between DAS 28 and Trp levels (r: -0,321, p < 0.01)

Conclusion: In this study, we observed that RA has a significant relationship with Trp levels and Kyn/Trp ratio. In addition to the literature, we found that RA activation indicator DAS28 score and Kyn/Trp ratio and Trp level showed a statistically significant correlation. Our study has shown that the Trp catabolic pathway can be an important field of study for more effective and safe treatment of RA.

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Trp: Tryptophan, DAS28: Disease Activity Score

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AB0162 PREDICTION OF TREATMENT DISCONTINUATION DUE TO ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS USED BIOLOGICAL DMARDS AND TARGETED SYNTHETIC DMARDS

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Background: The main goal of rheumatoid arthritis (RA) patients therapy is to achieve low activity or remission of the disease (T2T strategy). However, it is sometimes necessary to interrupt effective treatment due to the development of adverse events.

Objectives: To reveal predictors of target drug withdrawal due to adverse RA.

Methods: The study includes patients with RA used bDMARDs, total 1217 treatment events. Search for predictors was carried out in two steps. At the first step were selected variables which demonstrated significant correlation with time to treatment discontinuation in Kaplan-Meier analysis. At the second step selected factors were included in the Cox regression model. The final set of independent significant predictors was obtained by backward stepwise variable selection.

Results: Of 661 patients 85,8% were women, the mean age of onset disease 58,7 ± 12,9 years, the mean disease duration 14,6 years. The longest mean time till withdrawal due to adverse events had Abatacept, Toficitinib, Tocilizumab, the shortest time had Infliximab. There were 146 cases of therapy discontinuation due to adverse events. The side effects that caused the cancellation of treatment were: infections of respiratory system, skin, urinary system, allergic and infusion reactions, drug-induced hepatitis, changes in the hematopoietic system, death and other. Presence of rheumatoid nodules ($p < 0.001$), higher doses of glucocorticoids ($p<0.001$), lower doses of methotrexate ($p = 0.009$) were independent significant predictors of increased risk of bDMARDs withdrawal due to adverse events. Used target drug also showed independent significant correlation with this risk. Relative risk (compared to Etanercept) was for Infliximab - 6.57 (CI: 3.69-11.73), Certolizumab pegol - 2.61 (CI: 1.23-5.56), Abatacept - 1.23 (CI: 0.65-2.30), Adalimumab - 1.37 (CI: 0.75-2.50), Rituximab - 0.56 (CI: 0.26-1.20), Tofacitinib - 0.46 (CI: 0.15-1.40), Tocilizumab - 0.77 (CI: 0.37-1.60).

Conclusion: Growth glucocorticoid doses for every 1 mg increases the risk of discontinuation of therapy by 8.7%. Reducing the methotrexate doses for every 1 mg increases the risk of discontinuation of bDMARDs and tsDMARDS by 3%. There are significant differences between target drugs for the risk of cancellation due to adverse events. High risk of infliximab discontinuation was associated more with infusion reactions and infection, discontinuation of certolizumab pegol was associated with infection.

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[1] The identified predictors for the treatment withdrawal due to side effects may be discussed to identify measures necessary to prevent adverse events in patients with RA who are using bDMARDs and tsDMARDs. These measures are: the use of full doses of methotrexate, avoid long-term use of glucocorticoids, or prescription of the targeted drug with lower risk of adverse events.

Disclosure of Interests: None declared

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AB0163 SERUM LEVELS OF CHEMERIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Chemerin (Ch) is one of the relatively new representatives of adipokines. Numerous studies have shown that adipokines are actively involved in inflammation and immune responses in rheumatoid arthritis (RA) [1]. Data have been obtained, on the basis of which it can be assumed that an increase in the level of Ch in the blood serum in patients with certain systemic diseases is associated with systemic inflammation [2, 3].

Objectives: The aim of the work was to study the level of chemerin in blood serum in a group of healthy donors and patients with RA.

Methods: The group of patients included 92 patients diagnosed with RA, corresponding to the diagnostic criteria developed by ACR and EULAR (2010). The age of the surveyed ranged from 18 to 75 years. The average duration of the disease was 11 years [(Me) [3(25%);16(75%)]. The control group consisted of 30 practically healthy persons aged 26 to 62 years. The group of patients with RA and the control group were comparable in age (p=0.089) and gender (p=0.121). Serum chemerin levels were determined using the commercial HUMAN CHEMERIN ELISA kit (BioVendor, Cat. No.: RD191136200R) according to the instructions provided.

Results: The level of the normal Ch value in healthy individuals ranged from 134.7 μg/ml to 241.6 ng/ml. The average Ch level in RA patients (calculated as M±2σ) was 462.6±159.82 ng/ml, which is significantly higher than in healthy donors — 169.9±43.47 ng/ml (t=-10.49; p<0.0001). The Ch level was normally distributed (K-S d=0.10653, p>0.2). We also found a moderate correlation between the Ch level and the age of patients with RA (r=0.232008, p<0.05).

Conclusion: Thus, the level of Ch in the blood serum of patients with RA is significantly higher than in healthy individuals. It can be assumed that Ch in RA patients can be used as one of the potential markers of inflammation activity.

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Disclosure of Interests: None declared

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AB0164 ARE PATIENTS WITH RA IN REMISSION IN FINLAND DURING THE COVID TIMES? RESULTS FROM THE FINNISH QUALITY REGISTER

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Background: Worries have been expressed, concerning the care of chronic diseases during the Covid times (1).

Objectives: To study the current status of patients with RA in the Finnish quality register database.

Methods: Patients who receive care for RA were identified in the database. Clinical and demographic data from the last visits during 2020-21 were collected, including swollen (SJC46) and tender joint counts (TJC46), doctor assessment of disease activity (Dr global), laboratory tests for inflammatory and serology markers, patient reported outcomes (PROs), and DAS28. Regression models were applied to compare measures of clinical status between the health care regions, adjusted for gender, age, ACPA status, and disease duration.

Results: A total of 14163 patients (72% female, mean (SD) age 62 (14) years, median (IQR) disease duration 8.5 (2.6, 20) years, 84% ACPA positive) were identified. For the entire population, the median (IQR) SJC46 was 0 (0, 1), TJC46 0 (0, 2), ESR 8 (5, 18), CRP 3 (1, 6), and dr global 8 (0, 19). Among PROs, median (IQR) HAQ was 0.5 (0, 1), pain 26 (10, 51), fatigue 28 (8, 54) and patient global 29 (11, 51). Between health care regions, statistically significant differences were found for all variables due to a large sample size. The mean (SD) DAS28 was 2.3 (0.9) for the entire group and 69 % of all patients had DAS28<2.6. The median DAS28 ranged from 2 to 2.7 among health care regions (Figure 1) (p<0.001). Majority of patients were taking csDMARDs only.

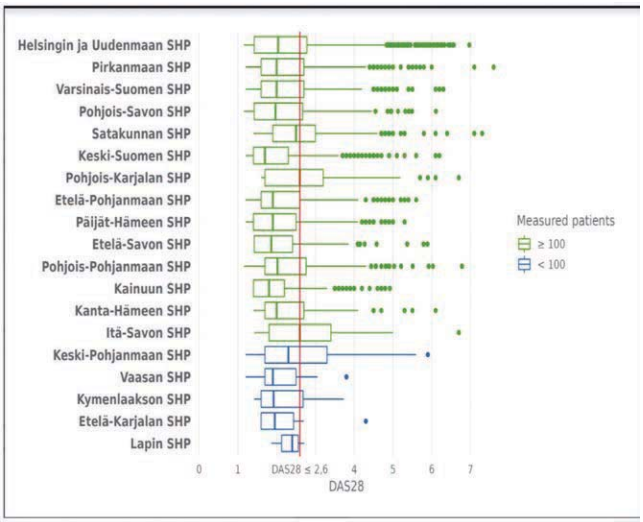

Figure 1. Rheumatoid arthritis in 2020-21: The median DAS28-values in 19 regions in Finland.

Conclusion: The quality register provides comprehensive real-world data on the current status of patients with RA. A majority of patients can be considered being in remission even during the Covid times.

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AB0165 MALIGNANCY AS PREDOMINANT CAUSE OF DEATH IN RHEUMATOID ARTHRITIS: REVIEW OF DATA FROM 'BASILDON EARLY ARTHRITIS COHORT'

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Background: Rheumatoid arthritis is a chronic inflammatory autoimmune condition historically linked to increased mortality with predominant contribution from cardiovascular, respiratory, infectious and neoplastic causes. There is evidence of decreasing cardiovascular mortality through improvements in preventative and treatment strategies. Recent literature has also suggested overall improvement in RA-associated mortality attributed to contemporary advances in disease control. There is a need to assess if such outcomes are reflected in the real world setting and to identify elements that continue to promote poorer outcomes.

Objectives: To assess long-term outcome in patients diagnosed with rheumatoid arthritis from the 'Early Arthritis Cohort' at a district general hospital in UK.

Methods: A retrospective cohort study was conducted on 185 patients newly diagnosed with rheumatoid arthritis between 2009 & 2013. Patients fulfilling the ACR/EULAR 2010 criteria were included. Anonymised data from the Basildon Early Arthritis registry was analysed. Measured parameters included patient demographics, disease activity score (DAS28), treatment regime, development of co-morbidity & mortality.

Results: Complete data was available for analysis in 171 patients. This comprised 60 men & 111 women with median age of 57 years (IQR 47 - 67 years) and median follow-up time of 90 months (IQR 63 - 108 months). Thirty nine percent were current or ex-smokers. At baseline, 40% of patients had DAS28 score > 5.1, this reduced to 2.5% at time of their last follow up. 74% of patients were in clinical remission at last follow up with 11.7% achieving drug-free remission, 40.4% remaining on single csDMARD, 29.8% on combination csDMARD & 18.1% on biologic therapy.

Analysis of new comorbidities revealed cancer burden of 12.9% (22/171) with lung cancer having highest incidence (n= 9). Other comorbidities recorded were cardiovascular 11.1% (19/171), pulmonary 5.8% (10/171) and cerebrovascular disease 5.3% (9/171).

A crude mortality rate of 19.3% (33/171) was observed in our cohort over a median period of 7.5 years follow-up. The incidence mortality rate was 174/10,000 person-years of follow-up and standardised mortality ratio was 2.09 (95% CI 1.44 – 2.86). Majority of patients died five or more years after initial diagnosis (67%) with most deaths occurring in the 6th year after disease onset. Patients in the mortality group had higher disease activity scores at their last follow-up compared to the remaining cohort (p=0.017).

More deaths were recorded from underlying malignancy 7.6% (n= 13) than with cardiovascular disease 4.7% (n= 8). Eight out of 13 cases were identified as lung cancer deaths. Breast, bladder, pancreatic and ovarian cancer constituted remaining cases. Other causes of death were from chronic obstructive pulmonary disease (n= 3), dementia/frailty (n = 3), interstitial lung disease (n= 2), infection (n= 2), stroke (n = 1) and chronic liver disease (n= 1).

Conclusion: Despite achieving remission in majority of patients, long-term analysis reveals that mortality in this cohort is significantly elevated compared to the general population. To best of our knowledge this is the first real-world study showing malignancy as the predominant cause of morbidity and mortality in rheumatoid arthritis.

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AB0166

PROTOCOL VIOLATIONS IN AN OPEN, RANDOMIZED, TRIAL IN EARLY RA PATIENTS: POTENTIAL IMPACT OF SHARED DECISION MAKING

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Background: Modern trials in RA often have a strict protocolized treat-to-target design, whereas in daily practice shared decision making is the preferred way to manage treatment.
Objectives: To document the protocol violations in an early RA trial that illustrate potential conflicts between these strategies.
Methods: In the COBRA treat-to-target trial, treatment-naive early RA patients were classified into a low- and high-risk group, and treated according to two different protocols. Treatment target was minimal disease activity (DAS44 <1.6) or EULAR good response. Non-responders at 13 weeks were randomized to treatment intensification or continuation, with as primary endpoint the proportion of patients achieving the treatment target at 26 weeks.
Results: In total 190 patients were included. High-risk patients (n=150) were initially treated with COBRA-light (30 mg/day oral prednisolone, tapered in 8 weeks to 7.5 mg/day, and MTX increasing to 25 mg/week): 110 (73%) patients reached the treatment target at 13 weeks. The 31 non-responders were randomized to treatment intensification (n=15) or treatment continuation (n=16) for weeks 14 to 26. Intensification comprised 60 mg/day prednisolone, tapered in 6 weeks to 7.5 mg/day, and addition of sulfasalazine 2000 mg/day and hydroxychloroquine 400 mg/day (COBRA-plus).
The low-risk group (n=40) was treated with MTX monotherapy increasing to 25 mg/week: only 20 (50%) reached the target at week 13. The 15 non-responders were randomized to treatment intensification with a COBRA-light oral pulse of prednisolone (n=8) or continuation (n=7).
Over the whole study period 79 of 190 patients (42%) had a protocol violation. In the first 13 weeks, 27 (18%) high-risk and 8 (20%) low-risk patients had a protocol violation. In the responders at week 13, 15 (14%) high-risk and 3 (18%) low-risk patients had a protocol violation in week 14-26. In the high-risk non-responders, 18 of 31 had a protocol violation (58%) after randomization at 13 weeks, 11 in the intensification group and 7 in the continuation group (Table). Remarkably, increased intensification of therapy was only found in the continuation group (3 patients); decreased intensification was mainly found in the intensification group (11 patients, vs 3 patients in the continuation group). In the low-risk non-responders, violations occurred in 8 out of 15 (53%) patients after randomization, 4 in both groups.

Table Protocol treatment violations after randomization of non-responders at week 13 by risk group.

	High-risk		Low-risk	
	Continuation (16)	Intensification (15)	Continuation (7)	Intensification (8)
Week 14-26				
Number of violations	7	11	4	4
Increased intensity				
Rheumatologist	3			
Other physician			1	
Decreased intensity				
AEs MTX	1		1	
No MTX due to AEs			1	
Rheumatologist	1	3		1
Rheumatologist, patient	1	7		
Patient		1		2
Mixed (increase + decrease)				
AEs MTX, rheumatologist			1	
Rheumatologist, patient	1			1

Violations are categorized by direction of intensification and by reason/initiator.
AE=adverse event; MTX=methotrexate.

Conclusion: In this study almost half of the patients had a protocol violation. The high frequency is most likely related to the open design of the trial, the risk of adverse effects through intensification with high dose prednisolone and other DMARDs, the randomization phase, and, last but not least, by the shared decision making. Shared decision making by physician and patient may jeopardizes protocol adherence in trials with an open treat-to-target design.
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AB0167

FUNCTIONAL DISABILITIES IN HANDS PRECEDE THOSE IN FEET IN PATIENTS PROGRESSING FROM CLINICALLY SUSPECT ARTHRALGIA TO RHEUMATOID ARTHRITIS; A LONGITUDINAL OBSERVATIONAL STUDY

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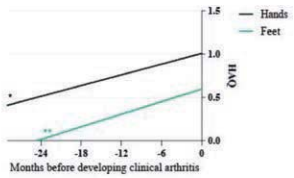
Background: In the pre-arthritis phase of Rheumatoid Arthritis (RA), symptoms resulting in physical disabilities already occur. It is unknown whether functional disabilities start in hands or feet, and whether such information on functional disabilities is related to arthritis development.
Objectives: To study the course of functional disabilities in hands and feet during progression from arthralgia to RA, and whether questions assessing specifically these disabilities contribute to predicting progression to RA.
Methods: 600 patients with clinically suspect arthralgia were studied for development of clinical inflammatory arthritis (IA) (median follow-up 25 months). Functioning was measured with the Health Assessment Questionnaire Disability-Index (HAQ) at baseline and after 4,12,24 months. HAQ-items assessing hands-functioning (dressing/eating/grip) and feet-functioning (walking) were studied. In patients who developed IA, the longitudinal course of functional disabilities towards IA-development was studied, using linear mixed models with date of IA-development as timepoint zero. ACPA-stratification was applied. Associations between HAQ-questions at presentation and future IA-development were studied with cox-regression analysis, including age, sex, CRP, ACPA and RF.
Results: 99 patients developed IA. In these patients, feet-functioning at presentation with arthralgia was less impaired than hands-functioning. Disabilities involving hands and feet both rose significantly towards IA-development (hands 0.25units/year, 95%CI=0.04-0.45, p<0.019; feet 0.29units/year, 95%CI=0.08-0.50, p=0.008, on HAQ-scale of 0-3; see Figure). However, hands-disabilities were reported earlier and were more severe than feet-disabilities during the total course (overall difference=0.41units; 95%CI=0.28-0.55, p<0.001). This was similar in both ACPA-subtypes. In the total arthralgia-population, a single question on difficulties with dressing (a HAQ-question involving hands-functioning) was as predictive as total HAQ≥1 for IA-development. This was independent of regularly used predictors; HR 2.3 (95%CI=1.5-3.6, p<0.001).

Figure. Functional disabilities involving hands and feet during progression from CSA to RA



Legend: lines depict the course of functional disabilities involving hands (average of dressing, eating, grip) and feet (walking) in CSA-patients prior to arthritis-development, derived from linear mixed model analyses. In these analyses, date of clinical arthritis is defined as t=0 and functional disabilities prior to clinical arthritis is studied. *Functional disabilities of the hands increased with 0.25 units per year on the HAQ-scale of 0-3, compared to **0.29 units per year for disabilities of the feet. Overall, functional disabilities of the hands was 0.41 units higher than those of the feet.

Conclusion: Functional disabilities in hands precede those in feet during RA-development. A single question on dressing difficulties adds value to risk stratification in patients with clinically suspect arthralgia and is easy to use in practice.
Disclosure of Interests: None declared
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AB0168

DISEASE BURDEN MEASURED BY PROS: DOES PSORIATIC ARTHRITIS (PSA) FEEL WORSE THAN RHEUMATOID ARTHRITIS (RA)? A CROSS-SECTIONAL STUDY

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Background: Little comparative research has been done comparing disease burden between PsA and RA. Previous studies from Nordic countries and the US have shown small differences (0-10/100 VAS units) in patients with PsA vs. RA. The mean and median VAS levels for PsA and RA ranged between 30-40 for pain and 40-50 for fatigue and patient global health in cross-sectional settings (1, 2, 3).
Objectives: To study the current differences in PROs between PsA and RA in Finland.
Methods: 3731 patients receiving care for PsA and 14163 for RA were identified in the national quality register for inflammatory arthritides in 2020-21. Patients were divided into groups by sex and age; <50 years, 50-60 years, 60-70 years and ≥70 years. The VAS values of pain, fatigue and patient global health at the most recent visit were compared in PsA vs. RA between the groups. Descriptive statistics and regression models were used for comparison.
Results: Patients with PsA vs RA were younger (mean (sd) age 54(14) vs 62(14)) and less often women (51% vs. 72%). Median (IQR) disease duration after the first symptoms was 8.6 (3.7, 17) years for PsA and 9.5 (3.3, 21) years for RA. The median (IQR) pain was 29 (10, 56) for all patients with PsA and 26 (10,51) for patients with RA. The corresponding values were: fatigue 28 (9, 60) in PsA vs 28 (8, 54) in RA, and patient global health 28 (10, 51) in PsA and 29 (11, 51) in RA.
Median pain was slightly higher in female PsA patients compared to RA patients in all age groups (29 and 18, 35 and 28, 32 and 27 and 48 and 38) (p<0.001). In males, higher levels of pain in PsA vs. RA were seen in age groups older than 50 years old. Figure 1 illustrates the mean (95% CI) pain for PsA and RA in the age and sex groups.
Median fatigue levels were quite similar between the groups. The median patient global health was higher in female PsA compared to RA patients in age groups <50 years and 50-60 years (20 vs. 29 and 30 vs 37) (p<0.001).

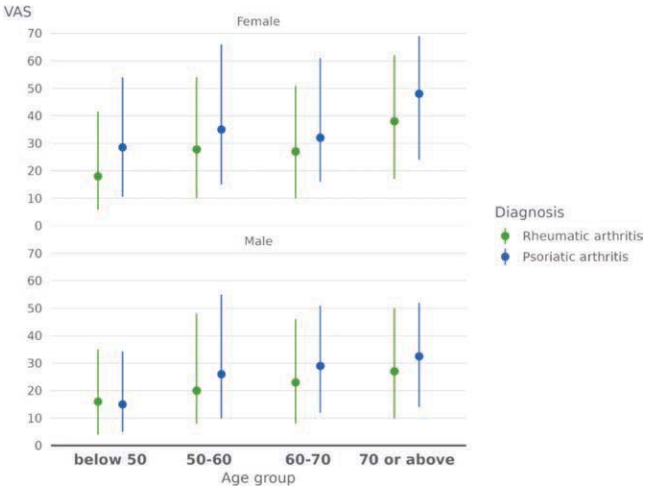

Figure 1. Mean (95 % CI) pain in VAS-units for women and men by age groups in 2020-2021

Conclusion: Female patients with PsA report higher levels of pain in all age groups compared to patients with RA. The same was seen in men >50 years old. Concerning fatigue and patient global health, the differences between PsA and RA were smaller. Compared to earlier research in other countries, disease burden observed by PROs appears lower both in PsA and RA in Finland.

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AB0169 EARLY REMISSION AT 6 MONTHS AS A PREDICTOR OF LONGTERM REMISSION IN NEW ONSET RHEUMATOID ARTHRITIS

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Background: Early therapeutic intervention is crucial for patients with early rheumatoid arthritis (ERA). The goal of remission is achievable in a large proportion of ERA patients.
Objectives: To evaluate the rate of patients in remission at 6 months and to correlate the 36 and 60 months remission rate in the Belgian CAP48 cohort and the UCLouvain Brussels cohort. To identify baseline characteristics differences between patients achieving remission or not.
Methods: We included patients with ERA from the CAP48 cohort and from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 RA classification criteria. All patients were naïve to csDMARDs therapy. We collected patient characteristics at baseline and clinical response was analysed at 6, 36 and 60 months.
Results: 287 RA patients from our UCLouvain Brussels Cohort and the CAP48 cohort were analysed (211 Females, 76 Males, mean age 46.2 years, 43.4% with baseline erosion, 70.1% with ACPA, 70.3% with Rheumatoid Factor, mean HAQ 1.16, mean DAS28-CRP 4.67, mean SDAI 24.9 and mean CDAI 24.1).

Table 1. The clinical results are summarized in the Table.

	DAS28-CRP Mean(±SD)	SDAI Mean(±SD)	CDAI Mean(±SD)	Remission (DAS28-CRP), %	HAQ Mean(±SD)
Baseline n=287	4.67 (±1.38)	26.5 (±15.5)	24.1 (±14.4)	/	1.16 (±0.70)
Months 6 n=287	2.97 (±1.34)	11.3(±12.3)	10.5 (±11.8)	44,9%	0.60 (±0.62)
Months 36 n=287	2.24 (±1.04)	7.5(±8.6)	6.2 (±7.8)	71,1%	0.52 (±0.59)
Months 60 n=196	2.41 (±1.00)	6.4(±6.5)	5.7 (±6.2)	66,3%	0.56 (±0.63)

We divided the patients according to whether they achieved remission DAS28-CRP < 2.6 (group 1), or not (group 2) at 6 months.
Patient baseline characteristics were similar in the two groups respectively: age (46.7 vs 45.4 yrs); female (68.5 vs 77.3%); smoker (25.6 vs 27.0%); ACPA positive (70.1 vs 75.4%); baseline X-ray erosion (45.0 vs 54.7%).
DAS28-CRP, SDAI and CDAI at 6 months could predict long-term remission at 36 and 60 months, Figure:

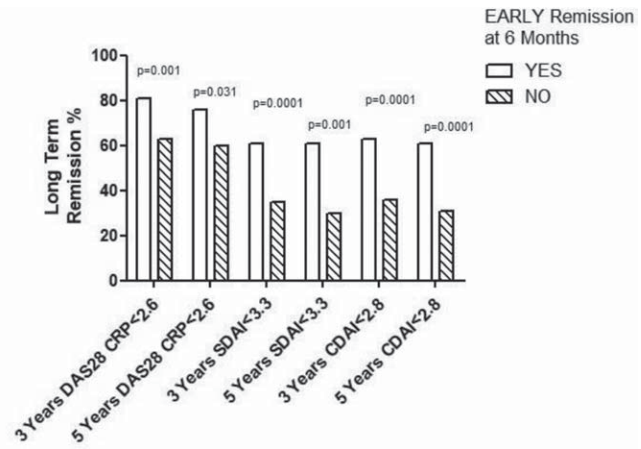

Figure 1.

In group 1 global remission (DAS28-CRP<2.6, HAQ<0.5 and no X-ray progression) was observed in 75.6% at 60 months. The majority of these patients (69.4%) are still treated with Methotrexate, the others were treated with combination therapy.
Conclusion: Early and long term remission is an achievable goal in our two cohorts. Early diagnosis is critical in standard of care. At 6 months, all remission index criteria are good predictor for long term remission and could be used in daily care.

Disclosure of Interests: None declared
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AB0170

AMCV POSITIVITY AND HIGHER SERUM IP-10 (CXCL-10) LEVEL ARE ASSOCIATED WITH A MORE PRONOUNCED EFFECT OF ABATACEPT THERAPY

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Background: With the advent of medications with different mechanisms of action in the treatment of rheumatoid arthritis (RA), clinicians face the challenge of personalizing the approach to the treatment of RA patients. One of the steps in this direction is to identify predictors of the effectiveness of the therapy. This work is devoted to the identification of predictors of the therapy effectiveness with the blocker of T cells co-stimulation - abatacept (ABA).
Objectives: Search for clinical and immunological predictors of the effectiveness of ABA therapy.
Methods: 91 patients were included in the study, most of them women, with high disease activity of RA (DAS28=5.1±1.0, SDAI=28±13.4, CDAI=25±12) and failure of previous biologics (51, 6%) and DMARDs (100%). Moreover, in 20% (n=18) of patients the inefficiency more than 2 biologics were recorded. The average duration of the disease was 3.0 (1.4–12) years, most patients were positive for RF 72.5%, ACCP 77%, AMCV 86%. In 44 patients the levels of RF, ACCP, AMCV and MMP-3 were assessed after 24 weeks of ABA therapy. In 36 patients enzyme-linked immunoassay was used to measure serum concentrations of biomarkers IL-1β, IL-6, IL-17AF, TNF-α, VEGF-A, IP-10, YKL-40 at baseline and after 24 weeks of ABA therapy. The effectiveness of therapy was assessed according to the EULAR criteria. ABA IV infusions were performed according to the standard schedule. Methods of parametric and non-parametric statistics were used in statistical analysis.
Results: ABA treatment led to a significant decrease of disease activity assessed by DAS28, SDAI, CDAI starting from 3 months of therapy ($p<0.05$). More than half of the patients were in remission and had low disease activity according to the DAS28 (65.7%, n=35) after 48 weeks of treatment. After 48 weeks, the highest percentage of patients with RA remission was registered by the DAS28 (37.4%, n=20), the lowest — SDAI (21.6%, n=11). After 24 weeks of therapy, ABA led to a significant decrease in the serum levels of IL-6 from 2.4 [1.1 - 6,4] to 1.29 [0.9-2.2] pg/ml, ($p=0.0006$), IP-10 from 21 [12,9-49,8] to 14 [7.5-28] pg/ml, ($p=0.007$) and matrix metalloproteinase 3 (MMP3) from 30.1 [13-82] pg/ml to 10 [7.4-55] pg/ml, ($p = 0.0003$). A decrease in the serum level of IL-6 significantly correlated with a decrease in the DAS28 and SDAI ($r=0.5$ and $r=0.479$, $p<0.05$), IP-10 with DAS28 ($r=0.326$, $p<0.05$). Initially, the serum level of TNF-α was significantly lower in patients who achieved low disease activity by the SDAI (72.6%, n=37) after 48 weeks of therapy, compared with the rest. On the contrary, a significantly higher level of IP-10 before treatment was recorded in patients with a good response according to the EULAR criteria (39%, n=29) after 48 weeks of ABA treatment (Figure 1). The ROC-analysis revealed that an initially high concentration of TNF-α may indicate with 71% sensitivity and 77% specificity about the possible ineffectiveness of ABA therapy after 48 weeks of treatment, the area under the curve was 0.7, 95% CI (0.5– 0.9). In patients initially positive for AMCV, low RA activity by SDAI was significantly more often registered after 24 ($p=0.04$) and 48 weeks. ($p=0.01$). 89% (n=34) of AMCV-positive patients achieved low disease activity after 48 weeks therapy by the SDAI and CDAI. It is noteworthy that a cohort of patients with insufficient effect after 48 weeks consisted entirely of AMCV-negative patients.

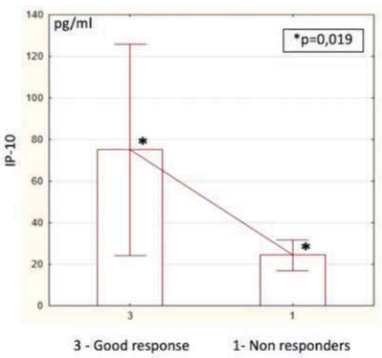

Figure 1 The ratio of the baseline level of IP-10 depending on the response to ABA therapy. The efficacy of therapy was assessed by the EULAR criteria. Error bars represent 95% CI. CI, confidence interval.

Conclusion: ABA therapy led to a significant decrease in disease activity according to the main indices (DAS28, SDAI, CDAI). During ABA treatment, there was a decrease of important immunoinflammatory markers - IL-6, IP-10, MMP-3. AMCV positivity is significantly associated with higher efficacy of ABA therapy. Also, a high basal concentration of TNF-α could use as a predictor of possible failure of ABA therapy, and a high initial level of IP-10, on the contrary, indicates the possible efficacy of ABA therapy.
References: None
Disclosure of Interests: None declared
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AB0171

TOWARDS A BETTER IMPLEMENTATION OF TREAT-TO-TARGET STRATEGY IN RHEUMATOID ARTHRITIS: A COMPARISON OF TWO REAL-WORLD COHORTS

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Background: Treat-to-target (T2T) strategy has been the core of rheumatoid arthritis (RA) management for over a decade, however implemented distinctly varied in real practices.
Objectives: We tried to investigate the differences in disease activity and target achievement of two cohorts with different T2T implementations.
Methods: We used data of the CENTRA (Collaboratively intENsive Treat-to-target in RA) and TARRA (Treat-to-TARget in RA) cohorts. The CENTRA is a RA cohort prospectively follow-up by a fixed team with tight control, while the TARRA is a longitudinal observational cohort follow-up by a rheumatologist with casual control. Patients from two cohorts were matched 1:3 by propensity score matching (PSM). The primary outcome was simplified disease activity index (SDAI) at 1-year follow-up.
Results: 102 patients from the CENTRA cohort and 271 patients from the TARRA cohort were included. Both groups were comparable in terms of age, gender, disease course, and seropositivity. At the end of 1 year follow-up, the SDAI of patients in the CENTRA cohort was significantly lower than that of patients in the TARRA cohort (2.1 vs 3.4, $p < 0.001$). The follow-up interval of patients in the CENTRA cohort was significantly shorter than that in the TARRA cohort when patients have not achieved remission (3.1 vs. 3.3 months, $p=0.019$).
Conclusion: RA patients may benefit more from a tight control T2T strategy with closer follow-up and appropriate education compared with a casual T2T strategy.
Disclosure of Interests: None declared
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AB0172

METABOLIC AND LIPOPROTEIN PROFILING IN RHEUMATOID ARTHRITIS WITH THE USE OF NMR-BASED METABOLOMICS

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Background: Rheumatoid arthritis (RA) remains a disease with high morbidity, due to the greater prevalence of cardiovascular disease. In contrast to the general population, systemic inflammation in RA lowers the circulating levels of lipids, a phenomenon called "the lipid paradox". In addition to that, therapy is withdrawn in 50% of patients within 5 years, due to loss of efficacy or side effects. Momentarily predictive biomarkers for drug efficacy or side effects are missing, while a personalized approach in RA therapy is imperative. Several reports support the notion that specific metabolomic profiles are good predictors for response to MTX and anti-TNF therapy.
Objectives: The aim of this work is to depict in detail the metabolic profile of RA patients at different time-points of therapy DMARDs/bDMARDs in order to retrieve biomarkers related to their response to a given therapy, to monitor the disease progression and to predict the optimal disease management approaches.
Methods: Plasma was collected from fasted RA patients according to their therapy timepoint and organized in the following groups: a) newly diagnosed, without therapy (Naïve, n=15); b) patients having received therapies previously, with unstable disease, who were evaluated before receiving a new therapy (RAb, n=23); c) patients after having received a new therapy (RAa, n=14); and d) patients receiving any standard therapy (RAs, n=54), either DMARD or bDMARD, being in a stable condition. Finally, healthy subjects were enrolled as controls (n=33). Metabolomic profiling was carried out firstly with untargeted ^{1}H NMR spectroscopy, and secondly with in vitro diagnostic (IVDr) NMR spectroscopy with the lipoprotein subclass analysis (B.I.LISA), to quantify absolute concentrations of metabolites and lipoproteins. The acquired data were subjected to univariate and multivariate statistical analysis to investigate clustering of the

groups and define the responsible molecules. Clinical parameters, including inflammation markers, DAS28, and comorbidities, were also included in the analysis, and Spearman correlation coefficient was calculated.

Results: Untargeted NMR data were analyzed with multivariate supervised approach (PLS-DA) revealing distinct metabolic signatures for the 6 groups under investigation. The most defined groups being RAb and RAs, compared to controls, which indicated changes in alanine, tyrosine, lactate and acetone. Besides small molecule, significant changes were also observed in various plasma lipoproteins. For the thorough investigation of these findings, a targeted lipoprotein subclass analysis was conducted and highlighted significantly higher lipoprotein subclass concentrations, including free cholesterol (FC), cholesterol (CH), phospholipids (PL) and apolipoprotein A1 subfractions in RAs compared to controls and Naïve. Concerning metabolite differentiations, RAs patients exhibited reduced ketone bodies and organic acids compared to RAb and control individuals, respectively. All RA groups had lower concentrations of sarcosine. Correlation analysis highlighted the association of DAS28, ESR and CRP with ketone body acetoacetate ($p<10^{-4}$) and sarcosine ($p<10^{-2}$). VAS correlated with HDL triglyceride subfractions (H1TG and H2TG, $p<10^{-5}$) and sarcosine ($p=1.8x10^{-4}$). All therapies were found to correlate with lipoproteins; MTX with LDL-2 subfractions ($p=5x10^{-4}$), intermediate-density lipoprotein ($p=2.7x10^{-5}$) and acetate ($p=5.9x10^{-6}$), Anti-IL-6R with VLDL cholesterol subfraction V1CH, ($p=1.9x10^{-3}$) and V2CH ($p=1.5x10^{-3}$), and Anti-CD20 with triglyceride fractions, IDTG and TPTG ($p<10^{-3}$).

Conclusion: Overall, these data reveal that RA patients have a distinct metabolic signature depending on the time-point of therapy. Clinical parameters correlated with changes in ketone bodies, amino and organic acids, while therapies correlated with lipoproteins. The above analysis indicates that biomarkers revealed by metabolomic profiling can be useful in RA therapy monitoring.

Disclosure of Interests: None declared

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AB0173 MORPHOLOGICAL PARAMETERS ASSESSED BY ULTRASOUND IN QUADRICEPS MUSCLE WERE ASSOCIATED WITH CLINICAL FEATURES, MUSCLE STRENGTH, FUNCTIONAL CAPACITY AND PHYSICAL FUNCTION OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients usually present extra-articular manifestations (1,2), which affect muscle mass and, consequently, physical function (3). Among the various methods to assess muscle mass we tested muscle morphology by ultrasound (MU) to verify the associations of the quadriceps muscle with clinical features, muscle strength, functional capacity and physical function.

Objectives: To assess the MU of the quadriceps muscle and verify the muscle quality assessed by the pennation angle and its associations with clinical features, muscle strength, functional capacity and physical function in RA patients.

Methods: RA women, age ≥18years and who met 2010 American College of Rheumatology (ACR) criteria were included. Morphological parameters in quadriceps muscle consisted of the pennation angle of rectus femoris (RF), vastus intermedius (VI) and vastus lateralis (VL). RA activity was measured by 28-joint disease activity score (DAS28), muscle strength by handgrip and chair stand tests, functional capacity by health assessment questionnaire (HAQ), and physical function by timed-up-and-go (TUG) test and short physical performance battery (SPPB). Pearson's or Spearman's correlation coefficients were explored. The significance level was set at $p \leq 0.05$ for all analyzes.

Results: Eighty-one patients were included (age: 58.64±9.52 years old; DAS28: 3.24±1.34). Smaller pennation angle in rectus femoris (RF) were associated with lower handgrip strength (r= 0.224, p=0.044), chair stand test (r= -0.372, p=0.004), HAQ (r= -0.404, p=0.001), SPPB (r= 0.262, p=0.047), as well as higher disease activity by DAS-28 (r= -0.415, p<0.0001) and age (r= -0.290, p=0.009). Smaller pennation angle in vastus intermedius (VI) were associated with worse chair stand (r= -0.281, p=0.033), HAQ (r= -0.302, p=0.015) and higher disease activity by DAS-28 (r= -0.304, p=0.006). Lastly, smaller pennation angle in vastus lateralis (VL) were associated with worse chair stand (r= -0.290, p=0.027), as well as higher DAS-28 (r= -0.237, p=0.033) and age (r= -0.272, p=0.014).

Conclusion: The pennation angles of the quadriceps muscle evaluated by ultrasound (RF, VI and VL muscles) were associated with chair stand test and DAS-28. In addition, the level of disease activity assessed by DAS-28 also appears to be affecting the quadriceps muscle. Finally, MU may be a useful method to evaluate the impact of the disease on skeletal muscle.

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Table 1. Associations between the quadriceps muscle morphology by ultrasound (pennation angle) with clinical features, muscle strength, functional capacity and physical function in rheumatoid arthritis patients.

Variables	n	Components of the quadriceps muscle	R	p-value
Age (y)	81	RF	-0.290	0.009
		VI	NS	NS
		VL	-0.272	0.014
Disease duration (y)	81	RF	NS	NS
		VI	NS	NS
		VL	NS	NS
Das-28 (CRP)	81	RF	-0.415	<0.0001
		VI	-0.304	0.006
		VL	-0.237	0.033
Handgrip strength test (kg)	81	RF	0.224	0.044
		VI	NS	NS
		VL	NS	NS
Chair stand test (s)	58	RF	-0.372	0.004
		VI	-0.281	0.033
		VL	-0.290	0.027
HAQ (score)	65	RF	-0.404	0.001
		VI	-0.302	0.015
		VL	NS	NS
TUG test (s)	68	RF	NS	NS
		VI	NS	NS
		VL	NS	NS
SPPB (score)	58	RF	0.262	0.047
		VI	NS	NS
		VL	NS	NS

RF: rectus femoris; VI: vastus intermedius; VL: vastus lateralis; n: number; y: years; s: seconds; kg: kilogram; DAS28: Disease Activity Score 28; CRP: C-reactive protein; TUG: Timed-up-and-go; SPPB: Short Physical Performance Battery; NS: Not significant.

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Disclosure of Interests: None declared

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AB0174 MOST RHEUMATOID ARTHRITIS PATIENTS IN POST–2010 REPORTS FROM ROUTINE CARE REMAIN IN DAS28, CDAI OR RAPID3 MODERATE ACTIVITY/ SEVERITY, NOT LOW/REMISSION: EXPLAINED IN PART BY LIMITS OF INDICES AND/OR STRATEGIES FOR DIAGNOSIS AND TREATMENT?

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Background: Availability of powerful biological agents to treat rheumatoid arthritis (RA) has led to a strategy of treat-to-target toward remission or low disease activity according to a quantitative index, although higher levels of disease activity according to shared decisions are recognized as appropriate for certain patients.[1] Substantial improvement in patient status was documented quantitatively in 2000 compared to 1985,[2] maintained in 2008[3] and 2010[4], but few reports in recent years compare patient status in routine care to earlier data.

Objectives: To analyze post-2010 reports concerning mean or median or categories of DAS28, CDAI, and RAPID3 to depict patient status, and compared to pre-2011 reports.

Methods: PubMed searches were conducted for 2011-2021 reports for "DAS28 (disease activity score) categories not trial," and repeated twice, replacing "DAS28" with "CDAI" (clinical disease activity index) and "RAPID3" (routine assessment of patient index data). Activity/severity levels for high, moderate, low, and remission, respectively, are: DAS28 (0-10) >5.1, 3.2–5.1, 2.6–3.2, ≤2.6; CDAI (0-76) >22, 10.1–22, 2.9-10, ≤2.8; RAPID3 (0-30) >12, 6.1–12, 3.1-6, ≤3.0. Mean and/or median DAS28, CDAI, or RAPID3, and/or proportions of patients who were in remission, low, moderate, and high activity/severity were compiled. Results were compared to 3 pre-2011 reports, 2 of which included all 3 indices.[2-4]

Results: Results from 1985 vs 2000 indicate >50% improvement in swollen joints and physical function,[2] maintained in 2008[3] and 2010[4] (data not shown). The

search identified 32 reports with 98 comparisons of 1, 2, or 3 indices for mean or median levels or activity/severity categories (Table). Analyses of 57 means or medians indicated 10 high, 39 moderate, 8 low; for DAS28-ESR 2, 18, 2; for DAS28-CRP 1, 6, 3; for CDAI 4, 9, 3; and for RAPID3 3, 6, 0 (Table). Analyses of 41 reports of comparisons of disease activity/severity categories indicated more high/moderate in 35 vs low/remission in 6, 1 of 5 for DAS28–CRP and 5 of 15 for CDAI (Table). Remission according to DAS28, CDAI, or RAPID3 was reported in 17.1%, 10.2%, and 13.7% of patients, respectively, and low activity/severity or remission in 33.3%, 39.6%, and 29.7%, respectively (data not shown).

Table 1. Means and/or Medians and categories of DAS28-ESR, DAS28-CRP, CDAI and RAPID3.

Index:	# of compa-risons	DAS28-ESR	DAS28-CRP	CDAI	RAPID3
		Mean/Median of Index			
Total means and medians	57	22	10	16	9
High activity/severity	10	2	1	4	3
Moderate activity/severity	39	18	6	9	6
Low activity/severity	8	2	3	3	0
Remission	0	0	0	0	0
		Categories of High or Moderate Activity/ Severity vs Low or Remission			
Total classified by categories	41	12	5	15	9
High or Moderate> Low or Remission	35	12	4	10	9
Low or Remission> High or Moderate	6	0	1	5	0

Conclusion: Most RA patients in post 2011 reports from routine care were in moderate activity according to means or medians or categories, unchanged from 2008 and 2010. Only a minority were classified as in remission or low activity/severity. Optimal RA treatment may require modification of treatment goals, further recognition of differences between patients in clinical trials and routine care, and possible new strategies for earlier identification of RA patients for treatment, in addition to new therapeutic agents.

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Disclosure of Interests: None declared

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AB0175 THE ROLE OF MONITORING THE CYTOKINE PROFILE TO PREDICT THE EFFECTIVENESS OF THERAPY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background:

Objectives: To evaluate the changes in cytokine profile in methotrexate (MTX)-naive patients (pts) with early rheumatoid arthritis (RA) during MTX therapy and identify predictors of the effectiveness of therapy.

Methods: The study included 45 early RA DMARD-naive pts (35 females, 10 males with median age 53.5; interquartile range 46-59.5 years, disease duration 7.0;4.0-11.5 months, DAS 28 5.8;4.9-6.4, RF positive 91%, anti-CCP positive 96%). MTX was administered to all patients as the first-line DMARD at 10 mg/week with a rapid escalation of the dose up to 20-25mg/week. The levels of IL-1b, IL-1Pa, IL-2,-4,-5,-6,-7,-8,-9,-10,-12,-13,-15,-17, Eotaxin, FGF-basic, IFN-γ, IP-10, MCP-1, MIP-1α, MIP-1β, RANTES, TNF-α, VEGF (pg/ml) were tested by multiplex technology xMAP at baseline and weeks 12 and 24.

Results: After 3 months the efficacy of SC MTX have met the goal in 23(51%) of pts. MTX induced reduction in proinflammatory (IL-6,-17,TNF-α), anti-inflammatory (IL-4,-5,-9,-13) cytokines, chemokines (IP-10) and growth factors (FGF) at week 12; IL-6,-9, IP-10, PDGF-bb at week 24 (p<0.05). The serum levels of IL-10, IFN-γ increased at week 24 (p<0.05), Figure 1. Among the "respondents" to MT therapy, by week 12, a significant decrease in levels of IL-1Ra, IL-2,-4,-6,-7,-9,-13, IP-10, TNF-α, VEGF was detected. In the "non-responders" group, the level of cytokine profile indices did not change (p>0.05), Figure 2.

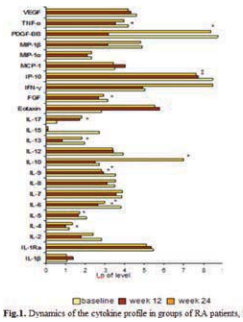

Fig.1. Dynamics of the cytokine profile in groups of RA patients, *p<0,05 from baseline

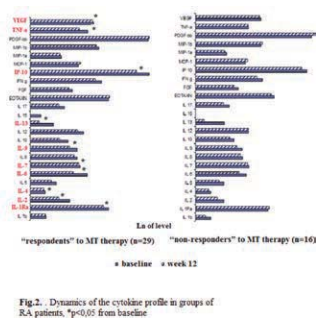

Fig.2. . Dynamics of the cytokine profile in groups of RA patients, *p<0,05 from baseline

Conclusion: Clinical efficacy of SC MTX therapy is associated with reduced of proinflammatory cytokines, chemokines and growth factors at weeks 12-24 of therapy. The dynamics of cytokine profile after 12 weeks of MT therapy can be considered as a predictor of the effectiveness of MT therapy.

Disclosure of Interests: None declared

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AB0176 THE ROLE OF IL-6 IN PREDICTING INFLAMMATORY ACTIVITY BASED ON ULTRASONOGRAPHIC (US) EVIDENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS DURING RITUXIMAB BIOSIMILAR (ACELLBIA «BIOCAD») THERAPY

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Background:

Objectives: To assess the role of laboratory markers in predicting the persistence of inflammatory activity according to US evidence in patients with RA during therapy with a rituximab biosimilar (RTX) – Acellbia.

Methods: 20 RA pts (18 woman, Me;IQR age 61.5[54-66.5] years, disease duration 39.5[20-84] months, mean DAS 28 5.6[4.9-6.8]) received two intravenous RTX infusions (600 mg №2) in combination with DMARDs and glucocorticoids. Ultrasound with gray scale (GS) and power Doppler (PD) were performed at baseline, 12, 24 weeks after initiation of therapy. The wrist, MCP2, MCP3, PIP2, PIP3, MTP2 and MTP5 joints of the clinically dominant side were examined by US according to the European League Against Rheumatism (EULAR) guidelines. ESAOTE MyLabTwice and GE Logiq 9 US machines with 13–18 MHz-transducer were used. The levels of IL-1b, IL-1Pa, IL-2,-4,-5,-6,-7,-8,-9,-10,-12,-13,-15,-17, Eotaxin, FGF-basic, IFN-γ, IP-10, MCP-1, MIP-1α, MIP-1β, RANTES, TNF-α, VEGF (pg/ml) were tested by multiplex technology xMAP at baseline and weeks 12 and 24 after the first infusion of RTX.

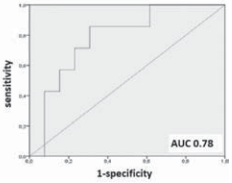
Results: After 24 weeks of RTX therapy values DAS 28 was 4.1 [3.1-4.7]; DAS 28 remission/low disease activity was achieved in 8 (40%) pts, while RTX failure based on EULAR response was documented in 3 (15%) pts. The baseline value of PD was 2.0 [1.0–3.5]; the proportions of PD(+) and PD(–) patients were 65% and 35%, respectively. After 24 weeks of therapy, the PD value was 0.5 [0.0–2.0] points; active inflammation persisted in 7 (35%) patients, p<0.05. Depending on the presence of active inflammation according to PD after 24 weeks of therapy, all patients were divided into two groups (Table 1).

According to the ROC analysis, it was found that the basal level of IL-6 more than 100.0 pg/ml is associated with the preservation of inflammatory activity according to PD by the 24th week of therapy with a sensitivity of 85% and a specificity of 62% (AUC = 0.78, 95% CI 0.57–0.99).

Table 1. Basal clinical and laboratory parameters in groups of patients depending on US changes after 24 weeks of therapy

Parameters	PD (+), *n*=7	PD (-), *n*=13
DAS 28	6.6 [5.4–7.2]	5.4 [4.7–5.7]
ESR, mm/h	62.0 [22.0–130.0]	40.0 [17.0–73.0]
CRP, mg/l	37.1 [9.2–46.0]	10.0 [8.6–44.4]
IgM RF, IU/ml	318.0 [170.0–519.0]	201.0 [79.3–502.0]
Anti-CCP, U/ml	159.6 [17.2–265.1]	119.3 [51.9–264.5]
IL-1β pg/ml	18.5 [4.5–63.3]	10.5 [4.8–30.5]
IL-1Ra pg/ml	3355.7 [448.5–14548.3]	953.2 [475.1–2206.7]
IL-2 pg/ml	253.1 [0.01–850.9]	18.9 [0.01–75.8]
IL-4 pg/ml	7.0 [5.9–9.3]	7.8 [6.5–9.6]
IL-5 pg/ml	15.2 [2.7–30.8]	5.3 [2.7–27.0]
IL-6 pg/ml	**286.4 [106.8–590.7]**	**95.1 [31.5–108.5]** *
IL-7 pg/ml	10.6 [3.8–361.5]	8.5 [5.3–28.8]
IL-8 pg/ml	47.0 [36.4–54.9]	39.2 [33.9–46.2]
IL-9 pg/ml	127.0 [50.8–385.9]	192.3 [62.2–323.2]
IL-10 pg/ml	148.2 [21.2–1877]	66.1 [19.2–332.1]
IL-12 pg/ml	154.4 [35.7–1064.4]	72.1 [46.1–237.7]
IL-13 pg/ml	22.7 [6.2–275.5]	11.6 [2.7–21.1]
IL-15 pg/ml	317.6 [23.5–845.3]	94.9 [58.5–176.5]
IL-17 pg/ml	67.9 [64.0–74.6]	77.8 [74.9–101.6]
Eotaxin pg/ml	857.7 [423.2–3681.3]	340.9 [216.1–584.3]
FGF basic pg/ml	40.9 [35.7–54.1]	43.9 [35.7–48.2]
G-CSF pg/ml	102.3 [94.1–258.5]	130.6 [91.4–382.5]
GM-CSF pg/ml	0.01 [0.01–418.7]	0.01 [0.01–72.7]
IFN γ pg/ml	535.7 [175.2–2939.2]	317.5 [181.3–892.2]
IP-10 pg/ml	2555.2 [1934.8–3289.9]	2471.0 [1764.3–2850.8]
MCP-1 pg/ml	308.7 [42–1119.3]	90.7 [48.7–246.7]
MIP-1α pg/ml	5.0 [4.4–7.7]	5.1 [4.4–8.0]
MIP-1β pg/ml	83.7 [63.6–99.1]	110.9 [84.9–151]
PDGF bb pg/ml	2925.9 [2656.1–3308.7]	3975.8 [3418.5–4275.6]
TNF-α pg/ml	1566.9 [169.9–3472]	324.6 [171.2–705.4]
VEGF pg/ml	116.2 [73.6–599.6]	106.6 [61.2–200.6]

*p<0.05 between groups



Conclusion: IL-6 is the most promising marker for predicting persistent inflammatory activity according to PD in patients with RA on the RTX biosimilar therapy, other analyzed parameters have worse sensitivity and specificity.

Disclosure of Interests: None declared

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AB0177 ASSOCIATION OF SEROLOGICAL STATUS WITH THE FREQUENCY OF CLINICAL AND RADIOLOGICAL REMISSION IN RHEUMATOID ARTHRITIS

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Background: Achieving remission is one of the main goal in the management of patients (pts) with rheumatoid arthritis (RA). According to the literature, one of the determining predictor of the disease course is the serological variant of RA [1]. However, there are conflicting data in scientific publications concerning relationship between the presence/titre of antibodies to cyclic citrullinated peptide (ACCP) or rheumatoid factor (RF) and the frequency/rate of remission [1].
Objectives: To examine associations of ACCP- and RF-status with possibility and timing of clinical and radiological remission in Ukrainian pts with RA while taking the main non-biological disease modifying anti-rheumatic drugs (DMARD).
Methods: In enrolled pts RF titer was determined by the latex agglutination method (Humatex, Germany), reference values <20 IU/ml; ACCP level - by ELISA (IBL-Hamburg, Germany), the diagnostic limit of ACCP was ≥15U/ml, the maximum value ≥ 345U/ml. All pts received non-biological DMARD: methotrexate, leflunomide, sulfasalazine or its combination with hydroxychloroquine. At baseline and after 6, 12 and 24 months (mth) of treatment the disease activity and achievement of remission (by DAS28; Sharpe-van der Heide scale) in different subgroups of RA pts were analysed.
Results: 128 pts with RA were included in the study; the mean (SD) age was 54 (12.7) years and follow-up was for 2.0 (1.3) years. Most were women (72.4%), mean disease duration 18.4± 3.18 mth. ACCP-positive were 64.8% and RF - 57.1% pts. According to serological status at baseline, pts were stratified into four classes: ACCP+RF- (n=19), RF+ACCP- (n=9), dual positive (n=64) and dual negative (n=36). There were no significant differences between the analysed groups in age, sex, RA duration, disease activity, radiological changes and prescribed therapy (p>0.05).
During the 2-year follow-up, clinical remission was achieved in a total of 27 (21.1%) pts, including early remission (during first 6 mth) in 25 (19.5%). The percentage of pts in remission were 36.1, 33.3, 15.8, and 12.5 respectively for RF–/ACCP–, ACCP–/RF+, ACCP+/RF–, and ACCP+/RF+ ($\chi 2$ = 7.74, p<0.05 RF–/ACCP– vs ACCP+/RF+; $\chi 2$ = 4.55, p <0.05 ACCP–/RF+ vs ACCP+/RF+). The rate of remission (frequency of early remission in the structure of general remission) in four analysed groups did not differ significantly and was 75%, 66.6%, 66.6% and 84.6%, respectively. The ACCP titer in pts who achieved and didn't achieve remission were respectively 240.8 ± 38.5U / ml and 187.8 ± 13.7U / ml, p>0.05. There also wasn't difference between RF titer and the frequency of remission in these groups (257.9±233.8 IU / ml vs 293.2±257.3 IU / ml, p> 0.05). According to our data, there was no correlation between the level of RF / ACCP and the frequency of remission.
Radiological remission was achieved in 46.7% of ACCP-negative patients and only in 10.6% of ACCP-positive patients (p <0.01). The absence of RF in the blood was also associated with a more frequent achievement of radiological remission (in 34.2% of pts) compared with the RF-positive cohort of pts (in 15.4%, p <0.05). Double seronegative pts achieved remission three times more often (48.1% pts) than double seropositive (13.9%, p<0.01).
Conclusion: Our data suggest that the frequency of clinical remission, including early, is three times higher in patients with RA, negative for ACCP. The rate of clinical remission (ratio of early in the structure of the general) doesn't depend on the serological variant of RA: about two thirds of pts in all analysed groups achieve remission in the first 6 mth of DMARD therapy. ACCP- and RF-titers in the onset of the disease don't influence on the possibility of achieving clinical and radiological remission. Radiological remission is observed three times more often in seronegative (for ACCP or RF) pts. Double seropositivity has an additive effect on subsequent joint destruction.
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AB0178 INDICATORS OF DISEASE ACTIVITY DURING HOSPITALIZATION IN A RHEUMATOLOGICAL HOSPITAL IN PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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Background: Patients (pts) with Difficult-to-Treat Rheumatoid Arthritis (D2T) (EULAR 2021 criteria) are distinguished by a history of failure of two or more biological disease modifying antirheumatic drugs (bDMARDs)/targeted synthetic DMARDs (tsDMARD) with different mechanisms of action and a more aggressive course of RA generally. In this study, we wanted to identify differences in the manifestation of RA activity during an exacerbation of the disease in such pts, compared with similar pts, but not meeting the D2T EULAR criteria.
Objectives: Describe the features of manifestations of rheumatoid arthritis (RA) activity in pts with D2T.
Methods: In pts with RA, with ineffectiveness of bDMARD/tsDMARD taken before hospitalization, admitted to the V.A.Nasonova Research Institute of Rheumatology from January to December 2021 due to an RA exacerbation (n=113), the duration of morning stiffness in the joints, tender joint count (TJC), swollen joint count (SJC), VAS general health pt, ESR, blood CRP levels, and DAS28 calculated indices. Pts Patients Eligible for D2T RA EULAR 2021 were allocated to the D2T group (n=26/23%), the remaining pts were assigned to the C control group (n=87/77%). Pts at D2T and C were matched for sex, age (D2T: 44.6±14.1 years vs. C: 48.8±15.6 years; p>0.05) and duration of RA (D2T: 15.8 ±11.4 years vs. C: 13.7±8.6 years, p>0.05).
Results: Inflammatory activity in terms of CRP in D2T was significantly higher than in C (p=0.04). At the same time, the frequency of taking classical DMARDs in D2T was slightly lower (p>0.05), and systemic glucocorticoids (GC) was significantly higher (OR=3.7 [1.3-10.8]; p=0.01).
TJC, SJC, VAS general health pt, ESR, CRP, duration of morning joint stiffness, as well as the estimated DAS28 indices at the time of admission to the hospital in pts with D2T RA were comparable to those in C. (Table 1)

Table 1. Indicators of disease activity and concomitant therapy in the study groups

	D2T (n=26)	C (n=87)	p
TJC, M±SD	9.1±4.8	10.6±5.7	>0.05
SJC, M±SD	6±3.7	6.6±4.5	>0.05
VAS general health pt, M±SD, мм	66.2±11	66.9±12	>0.05
ESR, Me [25; 75%], mm/hr	53.5 [8;98]	27 [14;56]	>0.05
CRP, Me [25; 75%], mg/l	28.3[3.5;67.7]	7.9[5.7;44.2]	0,04
DAS28^{CO3}, M±SD	5.5±1.3	5.7±1.1	>0.05
DAS28^{CPБ}, M±SD	5.2±0.9	5.3±1	>0.05
Duration of morning joint stiffness, min	120±79	135.5±94	>0.05
Taken classic DMARDs, n/%	18 / 69,2	74 / 85,1	>0.05
Taken GC per os n/%	21 / 80,8	46 / 52,9	OR=3,7 [1,3-10,8]; p=0,01
GC dose in terms of prednisolone, mg/day	7,6±4,1; 5 [5;10]	6,6±3; 5[5;10]	>0.05

Conclusion: Pts with D2T RA during an exacerbation of the disease differed from other RA patients with the ineffectiveness of previous bDMARD/tsDMARD by a higher inflammatory activity in CRP (p=0.04) with a higher frequency of systemic GCs (OR=3,7 [1,3-10,8]; p=0,01).
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Disclosure of Interests: None declared
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AB0179 PATIENT'S SATISFACTION WITH TREATMENT IN RHEUMATOID ARTHRITIS: AN UNMET NEED

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Background: Shared decision between rheumatologists and their patients has become an overarching principle in current treatment recommendations in rheumatoid arthritis (RA). Therefore, assessing satisfaction with pharmacological therapy, among patients, is becoming increasingly important in clinical settings.
Objectives: In this study, we aimed to assess the satisfaction of patients with RA about their treatment and to investigate the predictive factors.
Methods: A cross-sectional study was conducted including adults diagnosed with RA for more than a year and receiving their current Disease-modifying anti-rheumatic Drug(s) (DMARD(s)) for at least 12 months.
We used the treatment satisfaction questionnaire for medication (TSQM v1.4) to assess the treatment satisfaction among patients. Multivariable regression analysis was applied to determine the factors associated with treatment satisfaction.
Results: We included 70 patients (63F/7M) with a mean age of 57.8 ±10.6 [29-81] years at the time of the study. The mean disease duration was 13.71±7.2 [2-30] years. Twenty-four (34,2%) patients were on a biologic DMARD (bDMARD).
Regarding the Disease Activity Score 28 (DAS28-ESR), 14.3% of patients had a low disease activity, 47.1% a moderate disease activity, 7.1% a high disease

activity, and 31.4% were in clinical remission. The mean (SD) Rheumatoid Arthritis Impact Disease (RAID) overall score was 4.72 ±2.11. Mean (SD) TSQM scores were 65.42±14.77 for convenience, 68.71±18 for effectiveness, 70.60±24.5 for side effects, and 67.95±17.10 for global satisfaction.

Twenty percent of patients were satisfied with convenience, 38.6% were satisfied with effectiveness, 45.7% were satisfied with side effects and 30% were globally satisfied.

The multivariable regression analysis showed that the RAID overall score was inversely associated to global satisfaction (p=0.001) and to satisfaction with effectiveness (p=0.032).

Difficulty of coping (one of the RAID domains) was inversely associated to satisfaction with effectiveness and convenience.

It was, also, showed that satisfaction with side effects was inversely associated to the degree of interference of the RA on domestic work (p=0.020) and positively correlated to the degree of participation in treatment decision-making (p=0.014). In addition, satisfaction with current physician was positively associated to global satisfaction (p=0.029).

Satisfaction with convenience was inversely associated to bDAMARs (p=0.027).

Conclusion: We conclude from our data that despite the diversity of therapeutic strategies, almost two-thirds of patients remain not satisfied with their treatment. A better understanding of patients' unmet needs and an individualized patient-centric approach would improve outcomes in RA.

Disclosure of Interests: None declared
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AB0180 CLINICAL AND ULTRASOUND-BASED COMPOSITE DISEASE ACTIVITY INDICES AND RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Musculoskeletal ultrasound (US) has been reported to predict radiographic progression in rheumatoid arthritis (RA).

Objectives: To test the predictive value of composite disease activity indices (DAI) based on solely clinical as well as clinical and US (USDAI) information to predict radiographic progression in RA.

Methods: Data from the Swiss Clinical Quality Management (SCQM) database were extracted from patients with RA; USDAIs were created based on previous publications (1) (Table 1). In summary, the disease activity score in 28 joints (DAS28) and the simplified disease activity index (SDAI) were modified by supplementing or replacing the clinical swollen JC with joints showing signs of power Doppler (PD) and/or grey scale (GS) synovitis. Series with two standard x-rays of the hands (difference ≥ 183 days) and ≥1 visit with clinical and US data in between were analyzed. Progression was defined as an increase of ≥6.27 points of the Ratingen-Rau x-ray score. Receiver operating curve (ROC) analyses were used to assess predictive ability of every DAI for radiographic progression. As a subanalysis, ROCs using the median DAIs of series with ≥2 DAIs between two x-rays were run. Clinical DAS28/SDAIs were compared to their respective USDAI counterpart with the highest area under the curves (AUC).

Results: We included 649 series in 475 patients. Progression was observed in 84/649 (12.9%) series. Mean difference between the x-rays was 27.6±18.0 months. Mean age was 56.3±12.7 years, 474/649 (73%) series were from female patients. There was no significant difference between the AUC of the ROC of SDAI vs. SDAI_PD (p=0.19) nor between DAS28 vs. DAS28_PD: (p=0.17) (Figure 1A, Table 1). Similarly, when analyzing only series with ≥2 DAIs (143 series) we observed no difference between the AUC of the ROC of SDAI vs. SDAI-PD (p=0.28) nor between that of DAS28 vs. DAS28_PD (p=0.23) (Figure 1B, Table 1).

Table 1. Area under the curves (AUC) of receiver operating characteristic curves for the predictive value of the composite disease activity indices for radiographic progression. ***DAI disease activity index*; *DAS28, disease activity score for 28 joints; GS, grey scale; PD, power Doppler; SDAI, simplified disease activity index; SJC: swollen joint count; + positive***

Disease activity indexes		All series AUC	All series 95% CI Lower	All series 95% CI Upper	Series with ≥ 2 DAIs AUC	Series with ≥ 2 DAIs 95% CI Lower	Series with ≥ 2 DAIs 95% CI Upper
DAS28		.58	.52	.58	.62	.45	.78
DAS28_GS	SJC replaced by GS+ joints	.56	.49	.56	.62	.44	.80
DAS28_PD	SJC replaced by PD+ joints	.60	.53	.60	.63	.46	.81
DAS28_GSPD	SJC replaced by GS AND PD+ joints	.57	.50	.57	.62	.44	.80
DAS28_plus_GS	SJC supplemented by GS+ joints	.57	.50	.57	.62	.44	.80
DAS28_plus_PD	SJC supplemented by PD+ joints	.59	.52	.59	.61	.43	.79
DAS28_plus_GSPD	SJC supplemented by GS AND PD+ joints	.57	.50	.57	.62	.44	.79
SDAI		.57	.50	.57	.48	.26	.70
SDAI_GS	SJC replaced by GS+ joints	.53	.46	.53	.47	.23	.71
SDAI_PD	SJC replaced by PD+ joints	.58	.52	.58	.51	.27	.75
SDAI_GSPD	SJC replaced by GS AND PD+ joints	.53	.46	.53	.47	.23	.71
SDAI_plus_GS	SJC supplemented by GS+ joints	.54	.47	.54	.47	.23	.70
SDAI_plus_PD	SJC supplemented by PD+ joints	.58	.51	.58	.48	.25	.72
SDAI_plus_GSPD	SJC supplemented by GS AND PD+ joints	.54	.47	.54	.46	.23	.70

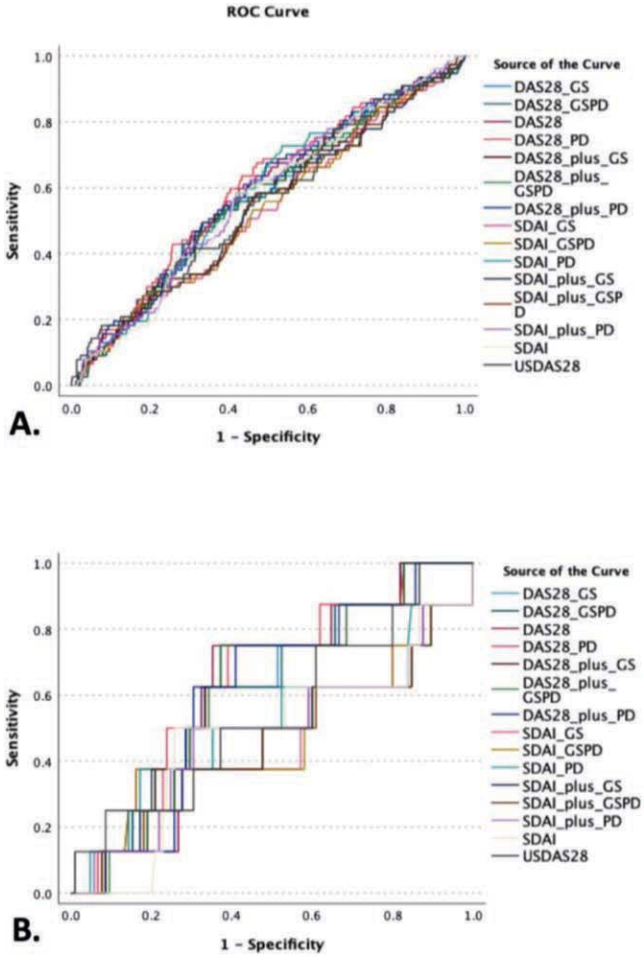

Figure 1. Receiver operating characteristic (ROC) curve of clinical and ultrasound-based composite disease activity indices (A) overall and (B) for the subgroup with series with ≥ disease activity indices. DAS, disease activity score; GS, grey scale; PD, power Doppler; SDAI, simplified disease activity index;

Conclusion: The predictability of radiographic progression by disease activity measures was generally limited. The composite USDAIs containing sonographic JC were not superior for predicting radiographic progression compared to their clinical counterparts although there was a trend for higher predictive value for indices containing PD.

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AB0181

RADIOGRAPHIC DESTRUCTION OF CARPAL BONE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: The pharmacotherapy for rheumatoid arthritis (RA) has changed dramatically and caused a paradigm shift with the advent of methotrexate (MTX) and biological disease-modifying antirheumatic drugs (bDMARDs).
Before the paradigm shift of RA therapy, the frequency of carpal collapse was high in patients with RA.
It has been reported that certain numbers of patients with RA rapidly advance the destruction of the carpal bones during the early onset in the natural course of it [1].
Another report showed that hand function was positively correlated with disease activity[2]
In Japan, bDMARDs were approved in 2003, and the maximum allowable dose of MTX was raised from 8 mg/week to 12 mg/week in 2012.
We hypothesize early aggressive therapy for the patients with early RA may have improved outcomes of carpal bone destruction in this last decade.
In this study, we investigated the change of drug therapy and carpal height ratio (CHR) in patients with early RA in the last decade.
Objectives: The aim of this study was to investigate CHR and drugs for the patients with early RA who developed it and started the therapy in 2009, 2014, and 2019.
Methods: Patients with early RA diagnosed in our department in 2009, 2014, and 2019 were included in the study.
The CHR was measured at the first visit and two years later on radiographs of both hands.
The drug history for RA was obtained in the medical records retrospectively.
All statistical analyses were performed with EZR version 1.55.
Results: This study included 43 cases (36 females, 7 males). The number of cases in 2009, 2014, and 2019 was 16, 13, and 14, respectively.
The mean age at the time of initial examination was 55 years (30-72).
There was no significant difference in the mean value of DAS28-CRP at the time of the first visit in each year.
The left hand CHR of initial diagnosis was 0.554 (0.484-0.632), 0.551 (0.490-0.618), and 0.567 (0.517-0.632) in 2009, 2014, and 2019, respectively, with no significant difference.
Two years later, the left-hand CHR was 0.541 (0.475-0.651), 0.549 (0.502-0.617), and 0.562 (0.528-0.591), respectively, with no significant difference.
There was also no significant difference in the amount of change.
The right hand CHR of initial diagnosis was 0.525 (0.475-0.607), 0.539 (0.459-0.589), and 0.557 (0.506-0.635) in 2009, 2014, and 2019, respectively, with no significant difference.
Two years later, the right-hand CHR was 0.532 (0.444-0.627), 0.529 (0.478-0.588), and 0.548 (0.491-0.593), respectively, with no significant difference.
There was also no significant difference in the amount of change.
The DAS28-CRP of initial diagnosis for cases in 2009, 2014, and 2019 was 4.68 (3.11-6.83), 4.19 (1.21-6.15), and 4.23 (2.41-6.38), respectively.
The DAS28-CRP at 2 years after treatment for cases in 2009, 2014, and 2019 was 2.12 (0.96-3.60), 2.25 (1.13-4.81), and 2.04 (0.99-3.45), respectively.
Although DAS28-CRP was improved, there was no significance among the three groups.
The usage rate of MTX was 56.3% in 2009, 76.9% in 2014, and 50% in 2019, with mean doses of 6.2 mg (2-8 mg), 8.6 mg (4-12 mg), and 9.1 mg (4-16 mg), respectively. There was no significant difference in the rate and dosage of MTX use in each year.
bDMARDs were used in one case in 2009, two cases in 2014, and one case in 2019.
Conclusion: In this study, DAS28-CRP showed a trend of improvement in this decade, but there was no obvious improvement in the progression of carpal collapse.
Further early aggressive therapy may be necessary to prevent the destruction of the carpal bones.

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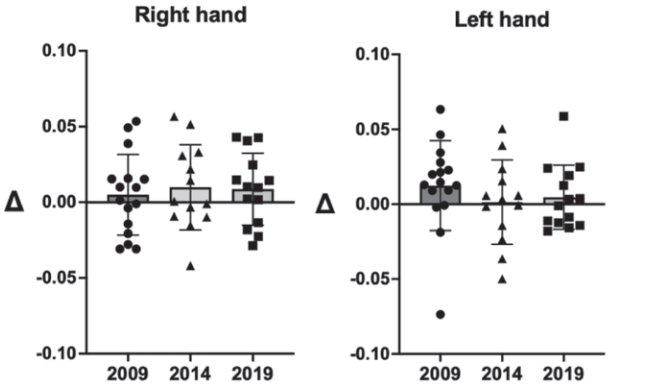

Figure
Amount of change in carpal height ratio between initial visit and 2 years later in each year. Δ; Amount of change in carpal height ratio

Disclosure of Interests: None declared
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AB0182

THE PROFILE OF POOR PROGNOSTIC FACTORS BASED ON EULAR RECOMMENDATIONS IN CHINESE RA PATIENTS: A SINGLE-CENTER OBSERVATIONAL STUDY

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Background: Despite the constant updating of rheumatoid arthritis (RA) treatment strategies, whether poor prognostic factors (PPFs) can guide RA treatment is still controversial. There are limited data about the presence of PPFs in Chinese RA patients.
Objectives: To describe the profile of PPFs based on European League Against Rheumatism (EULAR) recommendations in Chinese RA patients, and explore the significance of these factors in adjusting treatment therapy.
Methods: In this real-world study, RA patients were enrolled from 2012 to 2020. The baseline characteristics and prognostic factors based on EULAR recommendations include acute-phase reactant levels, rheumatoid factor (RF), anti-cyclic citrullinate peptide (anti-CCP antibody), swollen joint counts (SJC), early bone erosions, and responses to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) at month 3 or month 6 were collected. Disease activity was assessed by disease activity score of 28 joints-erythrocyte sedimentation rate (DAS28-ESR), DAS28-C-reactive protein (DAS28-CRP), simple disease activity index (SDAI), and clinical disease activity index (CDAI). The association of different factors was represented by a Venn diagram. The number of patients presenting with different combinations of prognostic factors was graphically displayed by UpSetR. Correlation between binary variables was analyzed by the Chi-square test.
Results: 1252 registered RA patients were enrolled. 901/1252 (72.0%) patients had elevated ESR or CRP and 1027/1164 (88.2%) patients had positive RF or anti-CCP antibody. 397/1252 (31.7%) patients had ors was graphicas. 166/444 (37.0%) patients had early bone erosions, which usually coexisted with other PPFs. 394 (34.4%) of the 1105 patients who received csDMARD therapy as prescribed had persistent moderate or high disease activity (MDA/HDA). Failure of two or more csDMARDs was found in 245 (22.2%) patients. 99% of RA patients had at least one PPF. Patients with MDA/HDA usually coexisted with other PPF. MDA/HDA was significantly correlated with elevated ESR/CRP or high SJC and is not correlated with positive RF/anti-CCP antibody or early bone erosion.
Conclusion: PPFs are prevalent in RA patients in real-world data. It is inappropriate to guide treatment strategies just based on the presence or absence of PPFs. The categories of PPFs should be simplified and the role of different combinations of PPFs in guiding treatment therapies remains to be explored.

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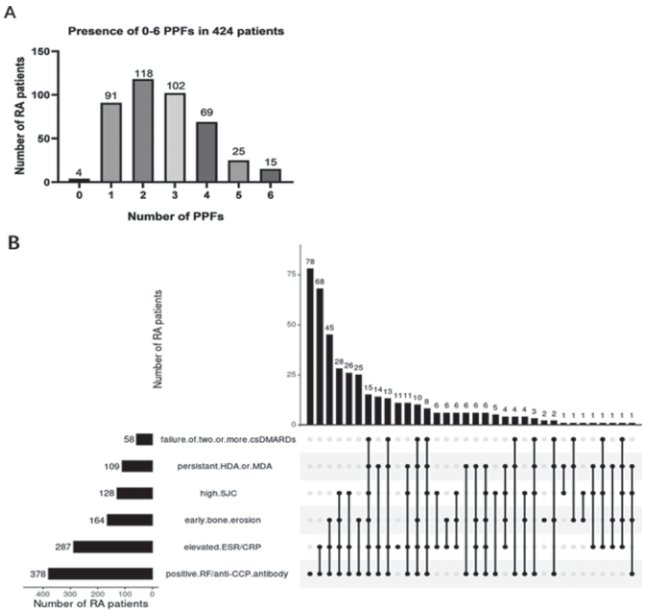

Figure 1. Coexistence of 6 PPFs including positive RF/anti-CCP antibody, elevated ESR/CRP, high SJC, persistent MDA/HDA, failure of two or more csDMARDs, and early bone erosion.

Acknowledgements: This study was based on the contributions of all colleagues in our department during the outpatient visits over the past decade.
Disclosure of Interests: None declared
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AB0183 DOWNREGULATION OF TUMOUR NECROSIS FACTOR A GENE EXPRESSION IN CULTURED PERIPHERAL BLOOD MONONUCLEAR CELLS IN THE PRESENCE OF TOFACITINIB PRIOR TO THERAPY AS A PROGNOSTIC BIOMARKER OF CLINICAL REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial hyperplasia, mononuclear cell infiltration, bone erosion and joint destruction. Recently we have shown that changes in energy generation-related gene expressions in the peripheral blood of tofacitinib (TOFA)-naïve patients with RA are associated with clinical response to treatment [1]. Therefore, considering metabolic status of patients with RA, may be useful for identification of prognostic biomarkers for personal responsiveness to TOFA therapy in TOFA-naïve RA patients by baseline gene expression analysis in peripheral blood mononuclear cells (PBMCs) cultured with TOFA prior to therapy.
Objectives: To examine the association of changes in expression of the genes responsible for cell growth and proliferation [mammalian target of rapamycin, mTOR], bone and articular cartilage resorption [matrix metalloproteinase (MMP)-9, cathepsin K], and inflammation [tumour necrosis factor (TNF)α] in the PBMCs obtained at baseline from patients with RA and cultured with TOFA with therapy outcome.
Methods: 12 patients with RA (median age 55 years), median disease duration 28.5 months (without previous history of therapy with TOFA) were examined. 6 of these patients with RA gained remission after 3 months of TOFA therapy while 6 patients, maintained high and moderate disease activity. Control group consisted of 26 healthy subjects. PBMCs were isolated prior to therapy using Ficoll density gradient and cultured with 10 nM tofacitinib citrate (TOFA) during 48h. Cell viability was monitored with 0.2% Trypan blue staining. Total RNA isolated from these cells was used for mTOR, MMP-9, cathepsin K, and TNFα gene expression studies performed with quantitative real-time RT-PCR.
Results: TOFA was capable of modifying gene expression in cultured PBMCs from the examined patients with RA compared with untreated cells. Baseline expression of all the examined genes was significantly upregulated in cultured with TOFA PBMCs from patients who maintained high and moderate disease activity after TOFA therapy compared with untreated counterparts. In contrast, TNFα gene expression was significantly downregulated in cultured with TOFA PBMCs of patients who gained remission compared with untreated cells. No significant changes in the expression of other examined genes was observed in cultured with TOFA PBMCs from the examined patients with RA who gained remission after TOFA therapy compared with untreated counterparts.
Conclusion: Downregulation of TNFα gene expression in cultured with TOFA PBMCs compared with untreated counterparts in TOFA-naïve patients with RA prior to therapy might serve a prognostic biomarker of personal positive response to TOFA therapy while upregulation in the expression of the same gene suggests non-response to TOFA therapy.
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AB0184 IDENTIFYING TRAJECTORIES OF REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN A TERTIARY CARE CENTRE

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Background: The main goal of treatment for patients (pts) with rheumatoid arthritis (RA) is remission to preserve physical function and prevent radiographic damage. However, less than 50% of pts with early RA have achieved remission in clinical studies and inception cohorts [1]. Little is known about the course of disease and the clinical patterns when remission is tried to be achieved in pts with RA.
Objectives: To identify subgroups with distinct trajectories of DAS28-CRP in pts with RA.
Methods: Longitudinal data from adult RA pts presenting to a tertiary centre were used. Socio-demographic data, disease characteristics and standard assessments including established outcome parameters for disease activity (DAS28-CRP) and physical function (FFbH) were retrospectively analysed. Group-based

Table 1. Patients demographics and disease characteristics at baseline in trajectory groups

	Class 1 (N=10)	Class 2 (N=36)	Class 3 (N=56)	Class 4 (N=23)	Class 5 (N=9)
Age, years	65.8 (12.7)	60.6 (10.6)	56.7 (16.0)	50.5 (15.4)	56.8 (12.0)
Gender, female	80.0% (N=8)	77.8% (N=28)	82.1% (N=46)	52.2% (N=12)	66.7% (N=6)
Education level university	0.0% (N=0)	11.1% (N=4)	16.1% (N=9)	21.7% (N=5)	0.0% (N=0)
Employment	10.0% (N=1)	33.3% (N=12)	53.6% (N=30)	69.6% (N=16)	33.3% (N=3)
Body mass index	30.6 (5.4)	27.8 (4.3)	27.1 (4.7)	25.2 (4.2)	29.0 (6.4)
Symptom duration, years	12.8 (7.3)	10.4 (8.3)	9.5 (9.6)	6.7 (3.6)	12.4 (13.2)
Anti-CCP	49.2 (63.9)	101.3 (89.7)	98.6 (95.6)	94.9 (78.2)	114.5 (84.6)
CRP	1.0 (1.1)	0.7 (0.9)	0.4 (0.4)	0.4 (0.5)	1.2 (1.1)
Erosions	20.0% (N=2)	36.1% (N=13)	28.6% (N=14)	45.5% (N=10)	44.4% (N=4)
At least one Comorbidity	100.0% (N=10)	94.4% (N=34)	78.6% (N=44)	65.2% (N=15)	88.9% (N=8)
Charlson Comorbidity Index (0-29)	1.1 (1.4)	1.1 (1.3)	0.6 (0.9)	0.4 (0.7)	1.2 (1.3)
No. of patients on steroids	0.0% (N=0)	0.0% (N=0)	2.9% (N=1)	15.4% (N=2)	0.0% (N=0)
No. of patients on bDMARD	77.8% (N=7)	45.8% (N=11)	41.2% (N=14)	30.8% (N=4)	71.4% (N=5)
No. of patients on tsDMARD	0.0% (N=0)	0.0% (N=0)	5.9% (N=2)	7.7% (N=1)	0.0% (N=0)
Pain (NRS 0-10)	6.1 (1.8)	5.8 (1.8)	4.2 (2.0)	2.3 (2.6)	4.2 (2.0)
Patient Global (NRS 0-10)	5.8 (2.8)	5.3 (1.7)	3.7 (2.1)	2.8 (3.0)	6.3 (2.2)
DAS28-CRP	5.3 (1.2)	3.9 (0.7)	2.5 (0.7)	2.1 (1.0)	4.6 (0.9)
FFbH	38.5 (29.0)	48.8 (21.8)	74.2 (18.9)	90.4 (8.8)	61.1 (19.4)
RAID (0-10)	6.5 (2.0)	5.3 (2.1)	3.8 (1.9)	1.8 (1.8)	4.6 (1.8)

trajectory modelling (GBTM) was used to identify homogeneous classes of DAS28-CRP trajectories, where the number of classes was selected using Nagin's Bayesian information criterion (BIC). Differences between the identified classes and clinical variables were studied.

Results: Data of 134 pts with 849 DAS28-CRP values were analysed. Retrospective chart data were available for a follow-up of 33.7 (SD 18.0) months. One third of pts already had erosions and severe limitations in physical functioning. About half of the pts were on bDMARDS and <20% on steroids. Five distinct classes of DAS28-CRP trajectories were identified (Figure 1). These groups were subsequently categorized as 1) high-increasing, 2) high-stable, 3) low-increasing, 4) low-decreasing disease activity, and 5) remission. Pts.' characteristics at baseline in each trajectory group are shown in Table 1. Group 4 had a shorter disease duration but more erosions, a better function and a higher educational level than seen in other groups. The increase of disease activity in group 3 was modest.

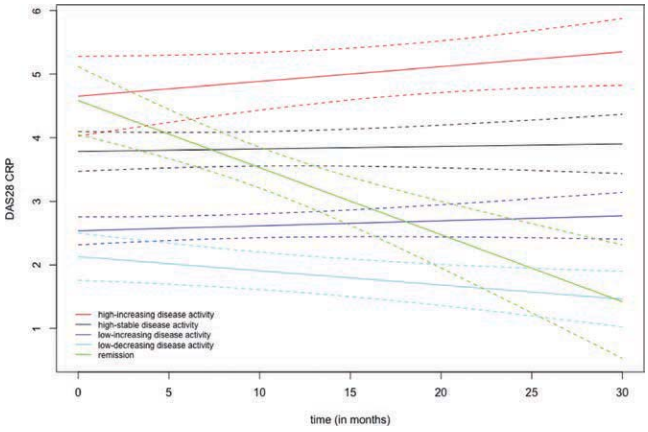

Figure 1. Longitudinal DAS-28-CRP in trajectory groups

Conclusion: Using GBTM five distinct trajectories in pts with RA were identified. Only a small proportion of pts showed a reduction in disease activity over time, whereas the largest proportion of pts showed rather constant high or constant low disease activity. The cohort size may have impacted the modelling and further analyses in larger cohorts are needed. Importantly, even though well established in our hospital it is unclear how consequent the T2T strategy was followed and which intervention was successful to reach remission. The impact of pts global assessment on DAS28 values also needs further study.

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AB0185

PHENOTYPES OF DRUG-FREE RHEUMATOID ARTHRITIS FLARE AND IMPACT OF RESIDUAL SUBCLINICAL ECOGRAPHIC JOINT INJURY IN ACPA POSITIVE AND ACPA NEGATIVE DISEASE

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Background: The mechanisms of flare across the pathogenic spectrum of RA remain unclear. To what extent RA flare reproduces the dynamics of disease onset or is primarily driven by new dynamics is not known. Furthermore, the hypothesis of a role for circulating auto-antibodies in determining different mechanism behind flare has never been challenged.

Objectives: To evaluate whether RA flare after remission achievement reproduces the phenotype of onset or it is characterized by a different phenotype primarily driven by the pattern of residual joint injury after treatment, in ACPA positive and negative patients.

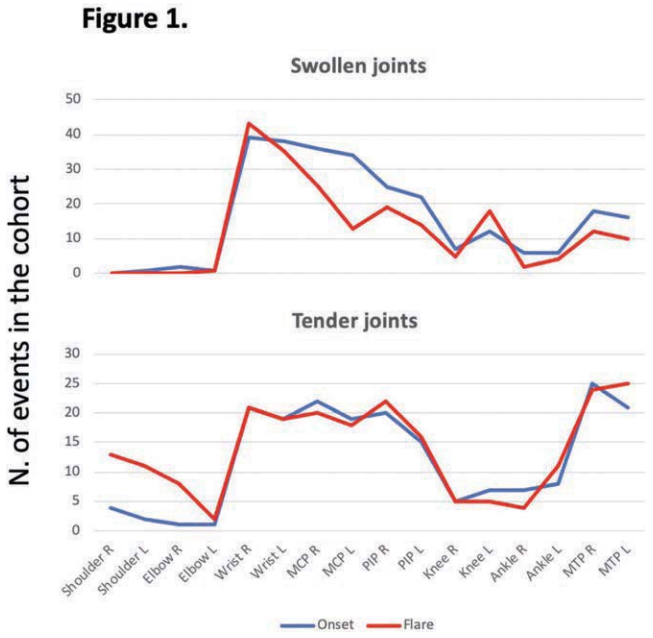
Methods: 53 RA patients, in stable drug-free remission (DFR) after early csDMARDS introduction and displaying clinical flare across 60 months of follow-up were analysed for clinical, laboratory and ultrasound (US) characteristics at diagnosis, treatment discontinuation, and flare (DAS28- and/or physician-based flare). We compared the synovitis clinical phenotype (ACR 1987 criteria defined districts), PROs and the inflammatory status at disease flare versus onset. We then measured the impact of residual subclinical US joint injury (absence of objective synovitis and GS>1 and/or PD>0) at the time of drug discontinuation, on the synovitis clinical phenotype of flare. Finally, we explored differences in the outcomes in ACPA positive and negative RA.

Results: Cohort characteristics are shown in Table 1. As inferred by paired analyses, no significant differences were observed between onset and flare concerning composite indices of disease activity, and subjective/semi-objective domains. However, flare appeared to be significantly less inflammatory in terms of CRP, ESR, SJC, morning stiffness and HAQ ($p<0.05$). These differences remained after adjustment for diagnostic delay including only very early RA patients (<3 months from symptoms' onset). The evaluation of the frequency of articular districts' involvement revealed no difference between onset and flare both for SJC and TJC (Figure 1). However, the percentage of SJs at flare being present at onset showed a high variability among patients. Stratification for ACPA status demonstrated a significantly higher recurrence of synovitis in joints involved at onset in ACPA negative vs ACPA positive patients ($p<0.05$). The percentage of SJs at flare presenting residual subclincal US injury at the time of drug discontinuation was significantly higher in ACPA negative vs ACPA positive patients ($p<0.05$) and negatively correlates with the ACPA titer (R 0.354, $p>0.05$).

Table 1. Comparison between Onset and Flare

	Onset, median (IQR)	Flare, median (IQR)
Sex, female (%)	34 (64)	\
Age at Symptoms onset (yrs)	57 (43-65)	\
Diagnostic delay(months)	3 (2-7)	1.5 (1-2) *
ESR (mm/h)	20.0 (12.0-38.5)	17 (9.00-27.0)§
CRP (mg/dL)	0.640 (0.307-2.11)	0.370 (0.220-1.05) *§
HAQ	0.625 (0.375-1.13)	0.438 (0.125-0.875)
GH	40.0 (26.5-50.0)	40 (30.0-50.0)
PGA	50.0 (27.0-66.5)	49 (20.0-70.0)
EGA	38.0 (27.0-60.0)	40 (30.0-60.0)
SJC/66	7 (4.00-10.0)	4 (3.00-6.00) *§
TJC/68	5 (2.00-10.0)	5 (2.00-11.0)
DAS28-ESR	4.55 (3.29-5.36)	3.98 (3.56-4.61)
DAS28-CRP	3.98 (3.08-4.88)	3.83 (3.00-4.27)
Morning Stiffness (minutes)	60.0 (11.3-90.0)	10 (1.00-30.0) *§

Index: *significant compared to onset, § significant compared to onset considering only VERA



Conclusion: RA flare in patients achieving DFR seems to be less severe in terms of inflammatory markers and synovitis recurrence, despite a similar degree of joint tenderness and patients' perception compared to disease onset. The arthritis phenotype undergoes detectable changes more in ACPA positive than negative patients. The residual subclinical US joint damage seems to drive the localization of synovitis recurrence in ACPA negative more than positive patients, supporting the existence of pathologic differences in the process of disease reactivation in the two groups.

Disclosure of Interests: None declared

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AB0186

IMPROVEMENT OF RADIOGRAPHIC JOINT DESTRUCTION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS IN THE LAST DECADE

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Background: The paradigm shift has caused in the treatment for rheumatoid arthritis (RA) before the last decade [1]. The advent of high-dose MTX and biologics has maked it possible to treat RA with early and aggressive therapy, and prevent the joint destruction [2].
Objectives: To aim of this study, we investigated the joint destruction and clinical outcomes in patients with early RA every 5 years in the last decade.
Methods: 81 patients with early RA (within 1 year from their onset of RA) enrolled retrospectively in this study. The number of patients with early RA were 21 in 2009, 23 in 2014, and 37 in 2019, respectively. They had 17 males and 64 females. Mean age was 59 years (19-92) at the first visit to our department. The following items were investigated: age, disease duration from onset to consultation, anti-cyclic citrullinated peptide antibody (ACPA) positivity (positivity was defined as >4.5 U/ml), CRP, DAS28CRP4, medications, and modified total sharp score (mTSS) at the time of initial consultation and 1 year later. Kruskal-Wallis test was used for statistics (PASW 25 software, SPSS Institute Inc., Chicago, IL, USA, p<0.05).
Results: The ACPA positivity rates were 71.4% (15/21) in 2009, 78.3% (18/21) in 2014, and 78.4% (29/37) in 2019, respectively. The mean value of DAS28CRP4 was 4.7 (2.4-6.8) in 2009, 4.2 (1.2-6.2) in 2014, and 4.2 (2.1-6.7) in 2019 at the time of the first visit to our department respectively. DAS28CRP4 under 2.6 was 29% (6/21) in 2009, 61% (14/23) in 2014, and 54% (20/37) in 2019 1 year after the first visit. The mean improvement of DAS28CRP4 (ΔDAS28CRP4) was -1.2 (-3.9 - 2.1) in 2009, -1.5 (-4.0 - 1.7) in 2014, and -1.7 (-4.1 - 0.4) in 2019, respectively. It had tended to improve gradually, however, it was not significantly different (p= 0.20, Figure 1).

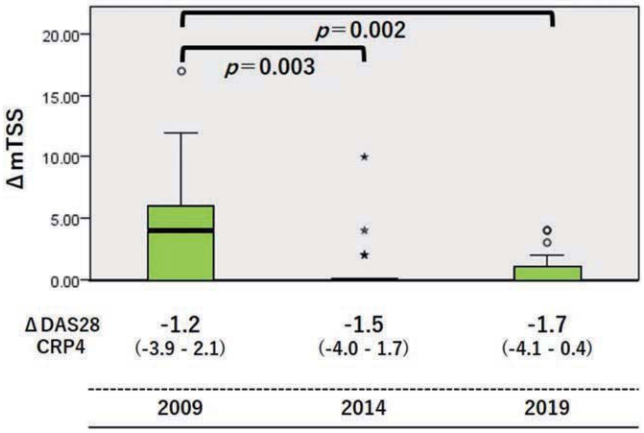

Figure 1. Mean value of improvement of mTSS and DAS28CRP4 (ΔmTSS and ΔDAS-28CRP4) from initial visit to 1 year later at 2009, 2014 and 2019.

The changing of mTSS for a year (ΔmTSS) was 4.2 (0-17) in 2009, 0.9 (0-10) in 2014, and 0.6 (0-4) in 2019, respectivly. ΔmTSS in 2014 and 2019 was significantly lower compared to that in 2009 (p<0.05, Figure 1).
One year after the first visit to our department, the mean dose of MTX increased to 9.2 mg/week (2-14) in 2014 and 8.7 mg/week (4-16) in 2019 compared to 6.6 mg/week (2-8) in 2009 (p=0.19). The mean dose of PSL decreased 4.2 mg/day (1-8) in 2014, and 3.8 mg/day (1-10) in 2019 compared to 4.9 mg/day (2-10) in 2009, respectively (p=0.11). On the other hand, biological DMARDs were introduced in 24% (5/21) in 2009, 13% (3/23) in 2014, and 13% (1/37) in 2019, respectively.
Conclusion: Jonit destruction has been already reported to begin in patients with early-stage of RA [1, 2]. Based on the results of this study, joint desctruction in early RA was decreased in the last decade, because of more early and aggressive therapy for early RA with increasing mean dose of MTX gradually, not biologic DMARDs in real world. In addition, the mean dose of PSL in 2014 and 2019 decreased compared to that in 2009. The intensive therapy for early RA at our hospital has shown the improvement of joint destruction in the last decade.
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AB0187

UNTREATED EARLY RHEUMATOID ARTHRITIS WITH ONSET IN THE YOUNGER (18-49 YEARS) AND OLDER (50 YEARS AND OLDER) AGE ACCORDING TO PRACTICAL HEALTH CARE. COMPARATIVE STUDY

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Background: Comparative characteristics of various clinical manifestations in untreated early rheumatoid arthritis (RA) in younger and older age patients is not sufficiently covered in the literature.
Objectives: To compare the frequency of different clinical manifestations in younger (18-49 years) and older (50 years and older) age patients with early RA who had not received background therapy yet.
Methods: 292 patients (men-65, women - 227, mean age 53.57±16.08 years) with early-stage RA were selected from 5327 patients included in the All-Russian register of patients with arthritis OREL from 01/01/2012 to 31/12-2018. They were studied during the first visit before prescription of background therapy (DMARDs: synthetic, biologics or other targeted drugs and systemic glucocorticoid therapy). 141/227 patients had RA onset at 18-49 years age (group 1): men-25, women-116, mean age (m±SD) 39.27±7.97 years. 151/227 patients had RA onset at 50 years or older age (group 2): men -41, women -110, mean age 66.05±7.34 years. RA was diagnosed according to ACR 1987 and ACR/EULAR 2010 criteria. Disease activity was assessed according to DAS-28 index, radiological stage – Steinbrocker classification, functional disorders - according to functional class (FC).
Results: The male/female ratio in group 1 was 1:4.6, in group 2 - 1:2.8 (p=0.055). Following disorders developed more often in group 2 than in group 1: morning stiffness (82% vs. 59%) (p< 0.05), lesions of small joints of the hands (76% vs. 65%) (p >0.05), wrist joints (65% vs. 52%) (p< 0.05), elbow (33% vs. 17%) (p< 0.05), knee (53% vs. 36%) (p< 0.05), shoulder (44% vs 19%) (p< 0.05), the total number of affected symmetrical pairs of joints (452 vs 285) (p< 0.001). Patients of group 2 showed more pronounced inflammatory process than in group 1: high activity - 66% vs. 35%, respectively (p< 0.05), as well as destructive changes in joints (erosive arthritis - 52% vs. 29%; p< 0.05) and functional disorders (FC 3 - 68% vs. 15%, respectively). RF was detected with equal frequency in both groups (72% vs 72%, respectively; p>0.05), and ACPA was more frequently positive in group 1 (89 vs 78%, respectively; p<0.037).
Conclusion: Comparative study of the clinical characteristics of the natural course of early RA with onset in younger age (18-49 years) and with onset in older age (50 years and older) according to the data of the All-Russian register of patients with arthritis OREL showed that RA with onset in older age is characterized by stronger inflammatory process, destructive and functional disorders in the joints than RA with onset at a younger age.
Disclosure of Interests: None declared
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AB0188

ULTRASONOGRAPHIC RESIDUAL INTRA-ARTICULAR SYNOVITIS IS MORE SEVERE IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH PREDNISOLONE

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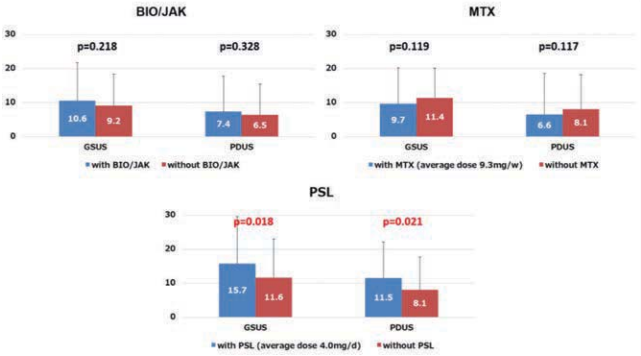
Background: The treatment option including biological DMARDs (BIO) and JAK inhibitor (JAK) was expanded, and the number of patients reached to the

treatment target are increasing in rheumatoid arthritis (RA). On the other hand, it is also true that some patients are still using prednisolone (PSL). Recently, ultrasound has played a role of sensitive imaging modality in the diagnosis and follow-up of patients with RA. It is known that residual synovitis was found in ultrasound even in patients with clinical remission.

Objectives: We investigated the differences of ultrasonographic intra-articular synovitis findings between treatment drugs in patients with RA.

Methods: From January 2017 to August 2020, 750 RA patients who underwent ultrasound examination were included. A US examination was performed at the bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) joints, wrist joints (three part of radial, medial and ulnar) and first to fifth metatarsophalangeal (MTP) joints, by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18-6 MHz). The gray scale and power Doppler findings were assessed by the semi-quantitative method (0-3). All patients were divided into with or without BIO / JAK, methotrexate (MTX) and PSL. Then, patients were matched using the propensity score adjusted for gender, age, RA disease duration, disease activity, CRP value, and MMP-3 value. The total gray scale and power Doppler score (GSUS / PDUS) were compared between treatment drugs of RA by using propensity score matching methods.

Results: The average age of 750 RA patients were 64.5 years and an average disease duration of RA was 13.9 years and females were 581 (77.5%). There were 517 patients (68.9%) treated with BIO/JAK and 233 patients treated without BIO/JAK. The 205 patients in each group were matched. GSUS were 10.6±11.1 vs 9.2±10.4 (p=0.218) and PDUS 7.4±9.2 vs 6.5±9.0 (p=0.328). Ultrasound residual synovitis was not different between with or without BIO/JAK in matched patients. There were 525 patients (70.0%) treated MTX, the average MTX dose was 9.3mg, and 225 patients treated without MTX. The 203 patients with or without MTX in each group were matched. GSUS were 9.7±10.6 vs 11.4±12.0 (p=0.119) and PDUS 6.6±8.8 vs 8.1±10.1 (p=0.117). Ultrasound residual synovitis was not different between with or without MTX in matched patients. There were 111 patients (14.8%) treated PSL, the average dose was 4.0mg, and 639 patients treated without PSL. The 105 patients with or without PSL in each group were matched. GSUS were 15.7±13.9 vs 11.6±10.6 (p=0.018) and PDUS 11.5±11.4 vs 8.1±9.6 (p=0.021). Ultrasound residual synovitis was more severe treated with PSL than without PSL in matched patients.



Conclusion: In a comparison between RA patients matched backgrounds such as disease activity, there was no difference in ultrasound residual synovitis between patients with or without BIO/JAK and MTX. However, there was significant difference in patients with or without PSL. This suggests that PSL use suppresses clinical symptoms but does not improve synovitis. Thus, it should be noted that joint destruction may progress in patients treating with PSL.

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AB0189 WHAT BIOMARKERS ARE ASSOCIATED WITH LOCAL BONE LOSS AND RISK OF FRACTURES IN RHEUMATOID ARTHRITIS AT LONG-TERM FOLLOW-UP?

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Background: Local and generalized bone loss in patients with rheumatoid arthritis (RA) is a manifestation of disease progression or a negative consequence. Various endogenous and exogenous factors have an effect on bone loss.

Objectives: To study the association between the underlying osteoimmunological and immunological RA markers and local bone loss (erosion score) according to the fracture risk.

Methods: There are presented the preliminary results of a prospective long-term research to study the outcomes of local and generalized bone loss in 44 women with rheumatoid arthritis, whose age at baseline was 56.8 ± 6.9 years, the duration of follow-up 8.3 ± 1.5 years. In all patients at baseline and in dynamics serum RF, ACCP, CRP levels were measured by standard methods; serum IL-6, RANKL, CTX-I, osteocalcin and BAP (bone alkaline phosphatase) were measured by ELISA. The immunological control group was composed of healthy donors (n = 12). X-rays of hands and feet were evaluated using the Sharp-Van der Hejde method, in both groups it was observed a significant increase in the erosions score ($p < 0.05$). Bone mineral density (BMD) was measured at lumbar spine (L1-L4) and total hip using dual-energy X-ray absorptiometry (DXA) at baseline and in dynamics (at baseline in all patient by Hologic). The 10-year probability of fractures was measured using the fracture risk assessment tool (FRAX) in 41 (93%) patients. A high risk of fractures was estimated in 25 (61%) patients, a low risk in 16 (39%). Statistical analysis was carried out using standard parametric and non-parametric methods in Statistica. Pearson tests were used for assessing the correlation between serum levels of these molecules and erosion scores in RA.

Results: Over the follow-up period, 12 (48%) patients from high-risk group and 2 (12%) patients of low-risk group has had peripheral fractures ($p = 0.01$). At baseline and in dynamics in the high-risk group it was noted the higher erosion score than in the low-risk group ($p = 0.001$ and $p = 0.002$, respectively), while the delta of erosion between the groups did not significantly differ. The correlation analysis showed that in the high-risk group the erosion score and in dynamics was positively correlated ($p < 0.05$) with the baseline CRP level. In the low-risk group the erosion score was positively correlated ($p < 0.05$) with osteocalcin level (at baseline and in dynamics for both indicators), and the erosion delta was positively correlated with ACCP positivity at the second visit. In the same group, there was a significant positive correlation between the baseline erosion score and CTX-I level in dynamics. No reliable correlation between erosion score and other immunological markers levels was reported.

Conclusion: Preliminary analysis of long-term follow-up results showed an increase in erosion score in the high and low fracture risk groups, and fractures in the high-risk group. Higher baseline CRP values in the high- risk group were associated with a larger count of erosions both initially and in dynamics. The increase in erosion score (delta) in the low-risk group was influenced by ACCP positivity (visit in dynamics) and it was noted that the level of osteocalcin, marker reflecting osteoblast activity, was positively correlated with the erosion score, possibly reflecting remodeling/bone turnover activity.

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AB0190 THE LONG-TERM PREDICTORS OF FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: Fatigue is one of the major complaints of patients with rheumatoid arthritis (RA). However, the literature relating fatigue to other disease-related parameters has presented discrepant results and longitudinal studies with multivariate analyses are scarce.
Objectives: To explore potential associations between fatigue and demographic variables and other patient-reported outcomes (PROMs) in patients with RA treated with biological disease-modifying antirheumatic drugs (bDMARDs) over the time.
Methods: A 24-month (24M) monocentric observational retrospective cohort study was conducted. Patients diagnosed with RA, according to the 2010 American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) criteria, and registered on the Rheumatic Diseases Portuguese Register (Reuma.pt) who started their first bDMARD between 2015 and 2021 were included. Age, gender, disease duration, body mass index (BMI) and PROMs were obtained by consulting Reuma.pt. Fatigue was monitored at baseline, 12 and 24M using Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), a 13-item questionnaire with a total score ranging from 0 to 52. A score ≤ 39 indicates the presence of clinically significant fatigue. Health Assessment Questionnaire (HAQ), EuroQol-5D (EQ-5D), 36-Item Short Form Survey (SF-36), patient global assessment visual analogue scale (VAS) and pain VAS were assessed at baseline, 12 and 24M. Multivariate linear regression models were conducted with FACIT-F as the dependent variable.
Results: A total of 40 patients (47.4±11.4 years; 90.2% female) with a BMI of 29.87±8.54 kg/m^2 and a mean disease duration of 10.4±5.6 years were included. A total of 47.5% of patients were treated with an anti-TNF. About 85% of patients had clinically significant fatigue at baseline (FACIT-F 26.9±11.8). At baseline, patient global assessment VAS (β=-0.4, 95%CI [- 0.68; -0.095]) and pain VAS (β=- 0.34, 95%CI [-0.6; -0.068]) predicted fatigue. SF-36 predicted fatigue at baseline (β=0.35, 95%CI [0.14;0.56]), 12M (β=0.23, 95%CI [0.084;0.37]) and 24M (β=0.26, 95%CI [0.13;0.39]). HAQ predicted fatigue at baseline (β=- 12.2, 95%CI [- 19.8; - 4.5]) and 24M (β=- 11.4, 95%CI [- 17.47; - 5.38]). EQ-5D (β=39.5, 95%CI [15.84; 63.22]) predicted fatigue at 24M.
Conclusion: Our results showed that pain levels and patient global assessment of disease activity predicted a higher level of fatigue at baseline. The decrease in physical function and a worse overall health status perceived by patient predicted higher fatigue over the time. Previous research has suggested that disease-related factors, such as inflammation, pain or decreased physical function are associated with greater fatigue in RA (1). These findings encourage the pre-treatment screening of fatigue in patients with RA in order to design individualized non-pharmacological approaches in addition to bDMARDs therapy.
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AB0191 OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS: IMPACT ON BIOLOGIC DRUGS TOLERANCE AND SURVIVAL

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Background: Osteoporosis is one of the main comorbidity of RA and leads to an increased risk for fragility fractures, which further impair functional ability, quality of life, and life expectancy. The influence of this condition on the maintenance and survival of biotherapies has rarely been studied.
Objectives: To assess the influence of osteoporosis on efficacy, tolerance, and biologic drugs survival.
Methods: We conducted a cross-sectional and observational study. Files of patients with RA on biologics drugs (archived from the files of patients on the National Health Insurance Fund of Tunis) were studied. Epidemiological characteristics such as age, sex, and comorbidities, were collected. All patients had a bone mineral density measurement. The patients were divided into two groups (a group with G1 osteoporosis and a group without osteoporosis G2). The therapeutic maintenance rate at 12, 24, 36, and 48 months as well as the biologic survival were analyzed using Kaplan-Meier survival curves and compared using the Log-Rank test.
Results: Three hundred and seventy-four files were selected. The average age of our cohort was 55±12.54 years [20-90]. A female predominance was noted with a sex ratio M/F=0.147. The average duration of RA was 11.7±6.76 years [2-41]. Osteoporosis was observed in 78 patients (20.9%). First biogics prescription was: tocilizumab 6% and rituximab 7%, etanercept 54%, adalimumab 14%, certolizumab pegol 13%, infliximab 6%.The maintenance of the first biotherapy was 40.53 [35.64-45.43] in G1 and 41.44 [39.01-43.86] in G2. The biologic survival curve study did not find any significant difference between the two group p= 0.598.
The presence of osteoporosis would increase the risk of stopping biotherapy without being a statistically significant factor (HR = 1.109, p = 0.602)
The therapeutic maintenance of the 1st biotherapy, in the presence of osteoporosis, was on average 40.53 months [35.64-45.43].
Conclusion: Osteoporosis has not hitherto been retained as a determining factor in therapeutic maintenance (1), as was indeed the case in our study. Nevertheless, screening and early management of osteoporosis are necessary since it alone constitutes a risk factor for mortality.
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Disclosure of Interests: None declared
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AB0192 ANTIBODIES AGAINST MODIFIED PROTEIN/PEPTIDE SPECIFICITIES IN RECENT-ONSET PALINDROMIC RHEUMATISM MAY DETERMINE THE EVOLUTION TO RHEUMATOID ARTHRITIS

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Background: Palindromic rheumatism (PR) may evolve to rheumatoid arthritis (RA), particularly in patients with autoantibodies such as rheumatoid factor (RF) or antibodies against modified proteins (AMPA), anti-citrullinated peptide antibodies (ACPA) or anti-carbamylated antibodies (anti-CarP) (1,2). We hypothesized that the specificities and isotype usage of ACPA and anti-CarP may differ between recent-onset PR and established RA, and this could help ascertain the evolution to RA in PR patients.
Objectives: To determine differences in the recognition of epitopes between patients with recent-onset PR and established RA by analysis of AMPA specificities and isotypes.
Methods: Subanalysis using preliminary data of the PALABA study. Two populations included: patients with recent-onset PR include in the PALABA multicenter randomized clinical trial (abatacept vs hydroxychloroquine) at study entry (NCT03669367) and patients with established RA (ACR/EULAR 2010) as controls previously selected from an observational study(3). Only RF and/or ACPA (CCP2) positive patients were selected. PR patients were DMARD naïve and RA patients receiving rituximab or abatacept were excluded. AMPA specificities and isotypes in sera were determined by in-house ELISA tests using as antigens two carbamylated proteins and a panel of chimeric peptides derived from fibrin and filaggrin proteins bearing one to three post-translational modifications (citrullination, carbamylation and acetylation) (4). The cut-off for ELISA tests was established by ROC curves, with a specificity of 95% compared with a healthy population. The frequency and titers of the AMPA isotypes (IgA,IgG,IgM) was analyzed.
Results: 45 PR patients (77.6% female), with a mean age of 49.3 (±11) years and a mean disease duration of 9.6 (±6.1) months and 125 RA patients (75.6%

Table 1. Anti-CarP autoantibody status in RA vs PR patients.

		RA (n 125)	PR (n 45)	p value
Fetal calf serum carbamylated (FCS-CarP)	anti-FCS-CarP-IgG positive,n (%)	78 (62.4)	14 (31.1)	<0.005
	median titer, AU/mL (IQR)	238 (571)	75 (249)	<0.005
	anti-FCS-CarP-IgA positive,n (%)	41 (32.8)	2 (4.4)	<0.005
	median titer, AU/mL (IQR)	161 (308)	14 (97)	<0.005
	anti-FCS-CarP-IgM positive,n (%)	30 (24.0)	5 (11.1)	NS
	median titer, AU/mL (IQR)	90 (165)	32 (101)	<0.005
Fibrinogen carbamylated (Fib-CarP)	anti-Fib-CarP-IgG positive,n (%)	87 (69.6)	9 (20)	<0.005
	median titer, AU/mL (IQR)	249 (304)	70 (104)	<0.005
	anti-Fib-CarP-IgA positive,n (%)	25 (20.0)	10 (22.2)	NS
	median titer, AU/mL (IQR)	0 (76)	36 (72)	<0.005
	anti-Fib-CarP-IgM positive,n (%)	33 (26.4)	8 (17.8)	NS
	median titer, AU/mL (IQR)	82 (117)	57 (84)	NS
Chimeric fibrin/ filaggrin homocitrullinated peptide (CFFHP)	anti-CFFHP-IgG positive,n (%)	54 (43.2)	10 (22.2)	<0.05
	median titer, AU/mL (IQR)	9 (227)	0 (12)	<0.005
	anti-CFFHP-IgA positive,n (%)	20 (16.0)	1 (2.2)	<0.05
	median titer, AU/mL (IQR)	0 (5)	0 (0)	NS
	anti-CFFHP-IgM positive,n (%)	14 (11.2)	2 (4.4)	NS
	median titer, AU/mL (IQR)	0 (7)	0 (0)	<0.05

females) with a mean age of 59.6 (±13) years and a mean disease duration of 77.2 (±59.7) months. RF and ACPA (CCP2) were positive in 80% and 91.1% of PR patients and 77.6% and 88% of RA patients (p>0.05). Although both populations presented a similar frequency of RF and ACPA(CCP2), PR patients had fewer AMPA specificities than RA patients. The differences were statistically significant for two IgA ACPA antigens (doubly citrullinated/homocitrullinated peptides) and most anti-CarP specificities and isotypes (Table).

Conclusion: The immune response against post-translational modified peptides/proteins has a lower frequency and less isotype usage in PR for some AMPA specificities in comparison with RA. The absence of IgA ACPA isotypes and, especially, anti-CarP in the early stages of PR may be associated with a lower rate of progression to RA.

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AB0193 BIOLOGIC DRUGS RETENTION IN ELDERLY RHEUMATOID ARTHRITIS: WHAT FEATURES?

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Background: The elderly RA population is expanding. The management of RA in elderly patients can be challenging because of comorbidities, the frequency of adverse events. The efficacy and safety of RA therapies; particularly biologics drugs (bDMARDs); are poorly studied in this age group.

Objectives: To investigate the therapeutic response to bDMARDs in elderly rheumatoid arthritis.

Methods: We conducted a cross-sectional and observational study. Files of patients with RA on biologics drugs (archived from the files of patients on the National Health Insurance Fund of Tunis) were studied. The characteristics of RA, and the current treatments were studied. We have divided our population into two age groups. G1 aging under 65 years and G2 aged 65 or over. The therapeutic maintenance rate as well as the biologics survival was analyzed using Kaplan-Meier survival curves and compared using the Log-Rank test.

Results: Three hundred and seventy-four files were selected. Their average age was 55±12.54 years [20-90]. A female predominance was noted with a sex ratio M/F=0.147. The average duration of RA was 11.7±6.76 years [2-41]. Subjects over the age of 65 represented 22.2% of the workforce, i.e. 83 patients. The first biotherapy prescribed was etanercept in 54% of cases, adalimumab in 14% of cases, certolizumab pegol 13%, infliximab 6%, tocilizumab 6% and rituximab in 7% of cases. The 4-year survival was 54.41% and 60.94% for subjects under 65 and 65 or older, respectively. Treatment maintenance for RA in the elderly (≥ 65 years old) was 42.21 months, [53.51–46.92]. In our study, age did not influence the survival of biologics with a Hazard Ratio (HR) = 0.997 (p=0.667).

Conclusion: RA therapy is generally effective and safe in elderly patients. We did not find any influence of age on survival and therapeutic maintenance of biological treatments. Further studies with a broader spectrum are needed to better understand this notion

Disclosure of Interests: None declared

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AB0194 VALIDATION OF ANDROID OPERATED SMARTPHONE PEDOMETER IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Impact of disease and disease activity in RA is measured with questionnaires such as the health assessment questionnaire (HAQ) or composite scores such as the disease activity score (DAS-28). These methods may miss signs of disease activity because they are typically performed only at hospital visits. Measuring physical activity continually may assist in the early discovery of relapses in the future. In addition, measuring physical activity may be relevant for predicting the risk of developing comorbidities such as cardiovascular disease [1]. Activity tracker devices have been tested in RA patients for this purpose, but the disadvantage is that they can only be carried for a limited period of time and are expensive, which makes them unsuitable for long-term cohort studies [2]. As an alternative, obtaining physical activity data from the patient's own smartphone using a dedicated and secure activity tracker app incurs no added costs, but the reliability of this method has never been tested in patients with RA.

Objectives: The aim of this study was to validate the use of the standard Android-operated smartphone step-counter pedometer in patients with RA.

Methods: Clinical characteristics were obtained. Two typical Android smartphones running the Android virtual step counter sensor were tested in a treadmill test-bed setup at 6 different speeds, ranging from 2.5 km/h to 5 km/h. Patients walked 100 steps at each test speed wearing the Android devices placed in a stomach pouch. Software running on a Windows PC communicated in real time with both phones, and the PC software also allowed the investigator to easily record the manually observed steps using clicker functionality, which were then automatically linked to the steps recorded from the smarthphones.

Results: Median (interquartile range) disease duration was 13 (4-21) years, DAS-28 2.2 (1.6-2.9), and MHAQ 0.2 (0-0.9). Seventy-six % of the patients were rheumatoid factor positive, 75% were Anti-citrullinated peptide antibody positive, and 70% had erosive disease.

The overall difference in device step counts versus the observed was 5.9% mean average percentage error for both devices. Most of the error was introduced at the 2.5 km/h speed tests where the mean error of the two devices was 18.5%. From 3 km/h, the mean average percentage error of the two devices was below 5% and from 3.5 km/h and up the mean average percentage error of the two devices was below 3%. A box plot of the data is demonstrated in Figure 1.

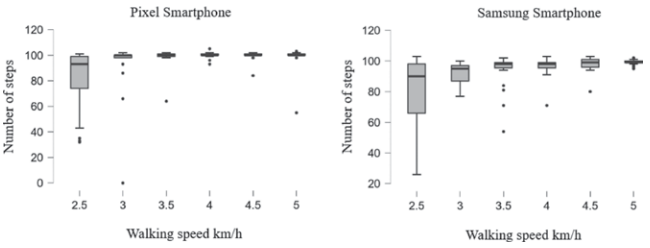

Figure 1. Box plot of number of steps with both devices at the six different speeds.

Both walking speed and walking cadence had a significant impact on the pedometer validity, as both speed and cadence were negatively correlated to the absolute percent error measured by both devices (p<0.001), which indicates, that the greater the speed and/or cadence, the lower the step counting error rate.

Conclusion: The two tested Android pedometer applications were valid in patients with rheumatoid arthritis, but walking with very low speed may represent a challenge. Next step will be field tests evaluating the setup including active measured time in patients with rheumatoid patients.

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AB0195 PLATELET TO LYMPHOCYTE RATIO: A BIOMARKER OF STRUCTURAL DAMAGE IN RHEUMATOID ARTHRITIS

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Background: A regular monitoring of structural damage in patients with rheumatoid arthritis (RA) is necessary to adjust the treatment. However, the rhythmicity of new radiographs to assess the structural damage is not codified. There is no biomarker able to reflect structural damage.
Objectives: Our study aimed to assess the relationship between the modified Sharp score and the platelet to lymphocyte ratio.
Methods: We performed a cross-sectional study including 53 patients with RA. A cell blood count was performed for each patient, and PLR was calculated. Modified Sharp score and its components (erosion score and joint space narrowing score) were evaluated using the radiograph of hands and feet.
Statistical analysis was performed using SPSS (Statistical Package for Social Sciences).
Results: Of the 53 patients, 39 were female (Sex Ratio: 2.8). The mean age was 53.9 ± 12.7 years. The mean age of the onset of the disease was 43.8±13.5 years. The mean disease duration was 10.1 ± 8.2 years. The mean DAS 28-ESR score was 4.64 ± 1.23.
The mean value of PLR was 161.62 ± 86.59. The mean modified Sharp score was 46.33 ± 37.74. Thirty-two percent of patients had a modified Sharp score greater than 50. The mean scores of joint erosion and joint space narrowing were 12.76 ± 15.05 and 33.57 ± 25.80.
Modified Sharp score was correlated to the PLR (r: 0.501; p <10-3).
Moreover, joint space narrowing score and joint erosion score were correlated to the PLR (r: 0.558; p <10-3 and r: 0.299; p: 0.033, respectively).
Patients with a modified Sharp score ≥ 50 had a higher PLR (203.12 ± 101.71 versus 142.33 ± 74.07).
As shown in Figure 1, the ability of PLR to distinguish patients with a modified Sharp score ≥ 50 was good with an AUC of 0.704 (p= 0.021) with a cut-off of 130.5 (sensitivity=75%, specificity=65.7%).

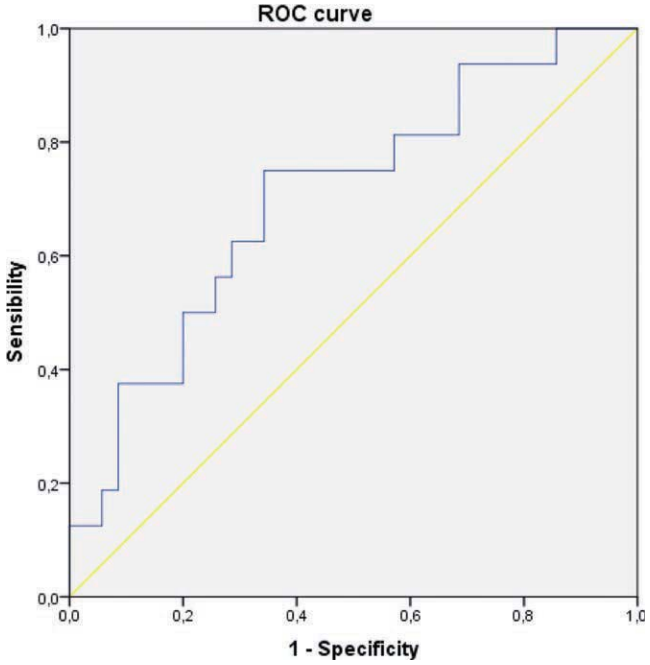

Figure 1. ROC curve assessing the ability of PLR to distinguish patients with a modified Sharp score ≥ 50

Conclusion: Our study showed that the modified Sharp score correlated with PLR, which can be useful to distinguish patients with severe structural damage with a cut-off of 130.5. This finding suggests that this ratio is a reliable marker to reflect radiographic joint damage.
Disclosure of Interests: None declared
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AB0196

ABATACEPT VERSUS HYDROXYCHLOROQUINE IN PALINDROMIC RHEUMATISM: A MULTICENTER RANDOMIZED CLINICAL TRIAL (PALABA STUDY): TRIAL DESIGN AND PATIENTS CHARACTERISTICS

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Background: Many patients with palindromic rheumatism (PR), mainly those with positive autoantibodies, evolve to rheumatoid arthritis (RA). Management of PR is empirical, and hydroxychloroquine (HCQ) is the most used antirheumatic drug. Abatacept (ABA) has been investigated in preclinical RA with good results. There are no randomized clinical trials in PR.
Objectives: To present the design of a randomized clinical trial in PR (PALABA study). To describe the characteristics of the patients at study entry. The main objective is to test the hypothesis that ABA can reduce the progression of RA in seropositive (ACPA+ and/or RF+) PR patients in comparison with HCQ.
Methods: Phase IV multicenter open label randomized controlled clinical trial with 42 months duration. The enrollment period was 18 months and the open randomized period 24 months. Fourteen spanish centers were included. The sample size was 70 patients (35 per arm). ABA sc 125mg/week first year, 125mg eow second year and HCQ oral 5mg/Kg daily were administered, both therapies in monotherapy. The main inclusion criteria were age >18 years with PR according to Guerne and Weissman modified criteria and disease evolution >3 and <36 months. Positive ACPA (ELISA or chemiluminescence (CCP2) and/or RF tests are required. Patients with arthritis in ≥1 joint >1 week at baseline, with criteria of other rheumatic diseases, radiographic erosions or previous antirheumatic therapy with synthetic DMARDS were excluded. The main outcome measure is achievement of RA classification criteria (EULAR/ACR 2010) at any time during the 24-month follow-up. Secondary outcomes were the number and intensity of joint attacks, adverse events, and effects on serum ACPA and anti-carbamylated antibodies at 0,3,12,24 months of follow-up. STATISTICS: Modified Full Analysis Set and Per Protocol Population analysis.
Results: Patient one was included in June 2018. The inclusion period has been extended until April 2022 due to low recruitment rates, partly due to the COVID-19 pandemic. As of 15 Jan 2022, 51 patients have been randomized and 49 (37F/12M) have received at least one drug dose. The mean onset of symptoms was 9.9±6.3 months. In 22 patients the follow-up time was greater than 12 months. RF and ACPA (CCP2) were positive in 81.6% and 89.8% of patients respectively; 24 patients were included in the ABA arm and 25 in the HCQ arm. Seven patients withdrew from the study during follow-up due to: progression to RA (n=3), adverse events (n=2) and other reasons (n=2). The demographic, clinical and laboratory characteristics of PR patients at study entry are shown in Table 1. No significant differences in patients' characteristics between arms were observed at enrollment except a higher prevalence of CCP2 in the HCQ arm.

TABLE 1 Baseline demographic, clinical and laboratory characteristics at study entry

Age, mean (sd)	*49.6 (11.2)*	*49.8 (12.0)*	*49.4 (10.7)*	*NS*
Female, n (%)	*37 (75.5)*	*19 (79.2)*	*18 (72)*	*NS*
Body mass index, mean (sd)	*27(5.7)*	*26.6 (5.5)*	*27.4 (5.9)*	*NS*
Month of symptom duration, mean (sd)	*9.9 (6.3)*	*9.8 (6.8)*	*9.9 (5.9)*	*NS*
Current Smokers, mean (sd)	*15 (30.6)*	*6 (25)*	*9 (36)*	*NS*
Number attacks 6 months before inclusion, mean (sd)	*4.65 (4.07)*	*4.24 (2.78)*	*5.0 (5.0)*	*NS*
PIP/MCP involvement n (%)	*35 (71.4)*	*16 (66.7)*	*19 (76)*	*NS*
Wrist involvement, n (%)	*32 (65.3)*	*17 (70.8)*	*15 (60.0)*	*NS*
Involvement of other joints, n (%)	*30 (61.2)*	*14 (58.3)*	*16 (64.0)*	*NS*
ESR (mm), mean (sd)	*20.71 (16.8)*	*23.13 (18.8)*	*18.30 (14.8)*	*NS*
RF positive, n (%)	*40 (81.6)*	*19 (79.2)*	*21 (84)*	*NS*
ACPA (CCP2) positive, n (%)	*44 (89.8)*	*19 (79.2)*	*25 (100)*	*0.022*

PIP: proximal interphalangeal MCP: metacarpophalangeal

Conclusion: We present the design of the first randomized clinical trial in PR of the efficacy of antirheumatic drugs (ABA vs HCQ) to avoid progression towards RA in patients with a high risk (recent onset PR and positive autoantibody status) of persistent arthritis. The characteristics of patients included until now are similar to those reported in recent onset PR.
Acknowledgements: PALABA study investigators: Beatriz Frade-Sosa, Rosa Maria Morlà, Lola Tobalina, Maria López-Lasanta, Helena Borrell, Georgina Salvador, Andrea M Cuervo, Noemí Busquets, Eduard Graell, Carolina Pérez-García, Luciano Pocino, Delia Reina, Oscar Camacho, Hector Corominas Ana M Millan. Miquel Sala, Sonia Castell, Eduardo Kanterewicz, Josep R. Rodriguez Cros, Alejandro Escudero, Usansolo Irati, José Francisco Garcia, Francisco Javier Toro, Natividad Oreiro, Alejandro Olivé, Maria J Gómara, Cristina García-Moreno, Isabel Haro and Raimon Sanmarti.
Disclosure of Interests: Beatriz Frade-Sosa: None declared, Rosa Morlà: None declared, Lola Tobalina: None declared, Carolina Perez-Garcia: None declared, Isabel Haro: None declared, Raimón Sanmartí Speakers bureau: received speaker honorariafrom Abbvie, BMS, Gebro-Pharma, Lilly, MSD, Pfizer, Sanofi and Roche, Grant/research support from: investigation grants from Abbvie, BMS, Gebro-Pharma, Lilly, MSD, Pfizer, Sanofi and Roche
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AB0197 **RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND CERVICAL SPINE INVOLVEMENT**

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Background: The prevalence of cervical spine involvement in rheumatoid arthritis (RA) varies between 17 and 86%. Cervical spine involvement is in third place after hand-wrist and foot involvement. The activity of RA is manifested by inflammation of all joints.
Objectives: To study the characteristics of patients with rheumatoid arthritis and research a relationship between cervical spine involvement and disease activity in rheumatoid arthritis.
Methods: We conducted a multicenter, prospective, descriptive, cross-sectional study in 300
patients with RA between 2013-2018. We collected demographic data, Body mass index (BMI), disease duration, Disease Activity Score of 28 joints (DAS28), (Health Assessment Questionnaire (HAQ), CRP, ESR, the rheumatoid factor (RF), ACPA. A radiological assessment of the cervical spine was requested for all patients, including a radiograph of the cervical spine from the front with the mouth open, a neutral profile, and dynamic flexion and hyperextension views. The activity of RA was assessed by DAS28. We study the relationship between cervical spine involvement (CSI) and disease activity in RA.
Results: 80, 3% were female), sex ratio H/F) was 0,24, the mean age was 51, 17±12,68 years, the BMI was 26,11±5,25, 67, 66 % had comorbidities, the most frequent were osteoporosis (30%), obesity (24%), hypertension (21,7%). RA mean duration was 13±9 years, mean DAS 28 was 4,68±1,5 mean HAQ was 1,01±0,69, mean CRP was 15,50 ±12 mg/L, mean ESR was 41,89 ±26,8mm, rheumatoid factor was positive in 70,6% and ACPA were positives in 77,3%. The standard radiographs of cervical spine found 53 (17, 66%) patients with CSI The various lesions of the cervical spine were atlantoaxial subluxations 13%, 3,66% of lateral atloïdo-axoïd subluxations, vertical subluxations in 0,66%, C1C2 arthropathies in 2,33% spondylolisthesis in 2%, and 0,33% of spondylodiscitis. The results of the univariate and multivariate analysis did not find a relationship between CSI and DAS28A (p=0, 66).
Conclusion: Cervical spine involvement in rheumatoid arthritis was common in our study. We did not find a relationship between cervical spine involvement and disease activity in rheumatoid arthritis.
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AB0198 **BASELINE FUNCTIONAL CAPACITY IN RHEUMATOID ARTHRITIS PREDICTS SUBCLINICAL ATHEROSCLEROSIS ON FOLLOW-UP**

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Background: The main cause of death in patients with rheumatoid arthritis (RA) is due to cardiovascular disease1. Cardiovascular mortality is strongly associated with the cumulative severity of the disease. Functional disability, as measured by the Health Assessment Questionnaire (HAQ), has been used to predict premature mortality in RA2. There are no studies relating its baseline score to the development of subclinical atherosclerosis by carotid ultrasound.
Objectives: To determine whether baseline HAQ score is an independent factor for the development of subclinical atherosclerosis assessed by carotid ultrasound.
Methods: Prospective, observational study. Patients with a diagnosis of RA who met ACR/EULAR 2010 criteria and who were recruited at the Cardio-Rheumatic Clinic in 2014-2015 were included. Patients underwent a clinical history and physical examination and completed the HAQ. The presence of subclinical atherosclerosis was identified by carotid Doppler ultrasound at the end of follow-up. Subclinical atherosclerosis was defined by the presence of carotid plaque or carotid intima-media thickness (c-IMT) ≥0.8mm. Distribution was assessed with the Kolmogorov-Smirnov test. Correlation between cIMT value and baseline HAQ score was determined using Spearman's correlation coefficient. Binary logistic regression was used to determine the independent factor for the development of subclinical atherosclerosis.
Results: A total of 48 patients were followed up. The median follow-up was 4.5 years (4.3-4.9). The baseline characteristics of the patients are shown in Table 1. A correlation was found between the GIMc value and the baseline HAQ score statistically significant (r=0.625, p=<0.001). In multivariate analysis that included scales to assess disease activity (DAS28-CPR, DAS28-ESR, CDAI, HAQ) and disease duration, and HAQ score was found to be an independent factor with MR 5.94 95% CI (1.65-21.41) (p=<0.001). DAS28-CRP with MR 1.52 95% CI (0.39-5.87), DAS28-ESR MR 0.27 95% CI (0.05-1.41), CDAI with MR 0.66 95% CI (0.82-1.12), disease duration 0.32 95% CI (0.07-1.49), but these were not statistically significant.

Table 1. Baseline characteristics.

	Basal (n=48)
Age, years ± SD	55.8 ± 9.7
Female, n (%)	44 (91.7)
Disease duration, years (IQR)	9.5 (4.3-16.5)
DAS28-ESR ± SD	4.4 ± 1.2
DAS28-CPR ± SD	3.3 ± 1.1
CDAI ± SD	13.0 ± 10.2
HAQ, (IQR)	0.87 (0.25-1.25)
HT, n (%)	19 (39.6)
DM, n (%)	2 (4.2)
Active tabaquism, n (%)	4 (8.3)
Obesity, n (%)	19 (39.6)
BMI, kg/m^2 ± SD	29.1 ± 4.6
Methotrexate, n (%)	40 (83.3)
Glucocorticoids, n (%)	30 (62.5)

DAS28, disease activity score using 28 joints; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; CDAI, clinical disease activity index; HAQ, Health Assessment Questionnaire; HT, hypertension; DM, diabetes mellitus; BMI, body mass index.

Conclusion: Our data show that at 4.5 years of follow-up, baseline HAQ score is a significant independent predictor of the presence of subclinical atherosclerosis by carotid ultrasound in patients with rheumatoid arthritis.
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AB0199 **RELATIONSHIP BETWEEN EXERCISE AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is a chronic, autoimmune, inflammatory disease in which cardiovascular disease is the leading cause of death (1). Exercise has been shown to have certain benefits in chronic diseases such as RA, decreasing symptoms and disease activity (2).
Objectives: To correlate exercise and minutes of physical activity performed per week with the disease activity level in a Mexican RA population.
Methods: This was a cross-sectional study in which a total of 240 Mexican patients with a diagnosis of RA were included. They were divided into two groups (120 in each): those who self-reported performing at least 30 minutes of exercise 3 or more times per week and were matched with patients who did not perform it by age, gender, and comorbidities. The disease activity level was determined with Disease Activity Score 28-joint erythrocyte sedimentation rate (DAS28-ESR) and Disease Activity Score 28-joint C-reactive protein (DAS28-CRP).
Distribution was evaluated with Kolmogorov-Smirnov. Comparisons with Chi-square test, Student's t-test, and Mann-Whitney U test. Correlation between disease activity level and minutes of exercise per day with Spearman-rho coefficient.
Results: DAS28-ESR was significantly higher in patients who did not exercise [4.024 (3.08-5.31) vs 4.73 (3.6-54.82), *p=0.*006]. DAS28-CRP had similar trend [2.76 (1.89-4.14) vs 3.51 (2.28-4.63), *p=0.*004] (Table 1).
The Spearman-rho coefficient showed a significant correlation between the minutes of exercise performed per week and DAS28-ESR (rho=-0.193, *p=0.*003) and DAS28-CRP (rho=-0.207, *p=0.*001) (Figure 1). A multivariate analysis was performed in which minutes of exercise performed per week, treatment, and comorbidities were included, showing an independent association between

minutes of exercise performed per week and the disease activity level assessed by DAS28-ESR (B=-0.001, 95% CI= -0.002- -0.0003, *p=0.*011) and DAS28-CRP (B=-0.001, 95% CI= -0.002- -0.0003, *p=0.*011).

Table 1. Demographic characteristics of the patients.

Characteristics	RA patients who exercise (n=120)	RA patients who do not exercise (n=120)	Value of *p*
Age, mean ± SD	54.4±8.1	54.5±8.2	NS
Female gender, n (%)	106 (88.3)	106 (88.3)	NS
Obesity, n (%)	23 (19. 1)	31 (25.8)	NS
T2DM, n (%)	15 (12.5)	12 (10.0)	NS
Hypertension, n (%)	30 (25.0)	24 (20.0)	NS
Dyslipidemia, n (%)	39 (32.5)	34 (28.3)	NS
Methotrexate, n (%)	93 (77.5)	107 (89.1)	**0.015**
bDMARD, n (%)	6 (5)	5 (4.1)	NS
Glucocorticoid, n (%)	61 (50.8)	74 (61.6)	NS
Minutes of exercise per week, median (p25- p75)	180 (150-300)	0	-
DAS28ESR, median (p25-p75)	4.024 (3.08-5.31)	4.73 (3.6-54.82)	**0.006**
DAS28CRP, median (p25-p75)	2.76 (1.89-4.14)	3.51 (2.28-4.63)	**0.004**

RA, rheumatoid arthritis; NS, not significant; T2DM, type 2 diabetes mellitus; bDMARD, biological disease-modifying anti-rheumatic drugs; DAS28, Disease Activity Score 28-joints; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

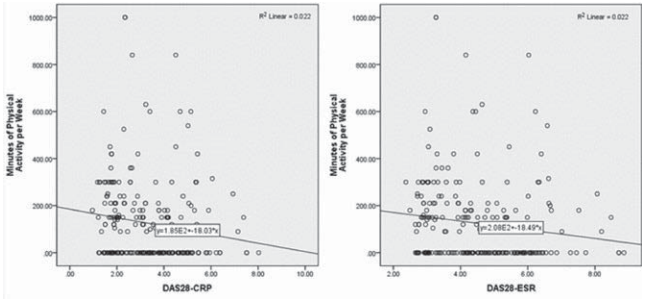

Figure 1. Correlation between exercise time and disease activity level in RA.

RA, rheumatoid arthritis; DAS28, Disease Activity Score 28-joints; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Conclusion: Mexican RA patients who exercise presented lower levels of disease activity. Emphasis should be placed on their practice to improve the patients' symptomatology.

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AB0200 COMPARISON OF TREATMENT AND DISEASE ACTIVITY OF BETWEEN EORA AND YORA PATIENTS IN A NATIONWIDE DATABASE OF RHEUMATOID ARTHRITIS IN JAPAN "NINJA"

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Background: Elderly-onset rheumatoid arthritis (EORA) has different characteristics from younger-onset RA (YORA), however, few reports have conducted large-scale and long-term comparisons of treatment and disease activity between EORA and YORA.

Objectives: To compare the changes in treatment and disease activity of between EORA and YORA patients and to examine the characteristics of patients who achieved remission between them using data of a real-world database in Japan.

Methods: Analysis was performed using data from 2010, 2013, 2016, and 2019 of the National Database of Rheumatic Diseases in Japan (NinJa). Patients were grouped according to age of disease onset into G1: <65 years (divided into G1a <65 years and G1b ≧65 years by the age at analysis), G2: 65-74 years, and G3:≧75 years.

Results: MTX usage rate decreased over time in G2 (58.3% in 2013→55.1% in 2016→54.4% in 2019) and G3 group (41.1→39.5→37.9%). Biologics/JAKi usage rate increased (G1b:24.4→28.2→ 33.3%, G2:19.1→20.3→23.7%, G3:12.3→14.5→19.1%) and steroid usage rate decreased (G1b:49.1→41.8→35.1%, G2:42.2→36.8→29.5%, G3:50.9→45.9→39.2%) in all groups. TNFi usage rate decreased (G1b:19.5→18.0→17.3%, G2:15.4→ 14.1→12.7%, G3:6.2→4.3→5.1%) but IL-6i usage rate increased (G1b:5.2→7.4→9.5%, G2:4.1→4.3→5.9%, G3:2.7→3.4→3.3%) except for the G3 group. CTLA-4Ig usage rate also increased (G1b:3.7→5.3→6.7%, G2:2.7→5.5→5.9%, G3:3.6→6.5→8.1%) in all groups.

The SDAI remission rate was increased over time in all groups (G1a:34.4→41.2→44.6%, G1b:25.1→31.4→35.2%, G2:33.1→37.1→42.2%, G3:30.0→35.9→39.3%) and EORA showed similar rate of remission with YORA. In the analysis stratified by SDAI using NinJa 2019, the positive rate of RF and ACPA decreased (ex RF. G3: 71.0→64.5→53.2%, ACPA. G3: 66.4→56.2→46.5%) and the proportion of male increased (ex G3: 23.0→30.3→35.1%) as the disease activity decreased (moderate / high → low → remission) in all groups. Also, the proportion of patients using two or more DMARDs decreased (ex G3: 43.8→35.2→22.4%) and the usage rate of steroid decreased (ex G3:52.5→37.9→30.2%). Furthermore, in a comparison of remission patients in each group, MTX usage rate (G1b:62.9→G2:61.7→G3:40.9%) and biologics/JAKi usage rate decreased (32.5→23.6→15.3%) as the age of onset increased, but the steroid usage rate increased (20.3→20.6→30.2%).

Conclusion: Disease activity improved over time, regardless of age of onset. EORA showed the same remission achievement rate as YORA, but the treatment content of those who achieved remission differed greatly depending on the age of onset.

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AB0201 INTAKE OF FISH RICH IN N-3 POLYUNSATURATED FATTY ACIDS IS ASSOCIATED WITH GOOD RESPONSE TO TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING TARGETED THERAPIES.

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Background: The management of rheumatoid arthritis (RA) has been transformed by the use of molecular targeted therapies. Early treatment and treat-to-target approach leads to good clinical response and remission (responders), but not in all patients.

Environmental factors including diet contribute to the development, activity and severity of RA. Evidence from clinical trials suggested that dietary interventions, such as Mediterranean diet or supplementation with fish oil rich in n-3 polyunsaturated fatty acids (n-3 PUFA), have positive effects on RA. Japanese and Mediterranean diets are associated with longevity and characterized by high fish intake. Clinical studies have identified predictors of treatment response in individual RA patients, however, the influence of fish consumption on treatment response in RA patients treated with targeted therapies has not been elucidated.

Objectives: To assess whether fish consumption is associated with a good response to targeted therapies in RA patients with Japanese and Mediterranean dietary patterns.

Methods: The study is a collaborative international cross-sectional retrospective study enrolling patients with RA on treatment with biologics or JAK inhibitors attending to Hokkaido University Hospital, Japan or Hospital Virgen de las Nieves, Spain.

Enrolled patients were asked to complete a brief-type self-administered diet history questionnaire (BDHQ) and a detailed fish frequency questionnaire (DFFQ) referring to consumption frequency in the previous month. At study entry, alcohol consumption, tobacco habits, educational level and employment status were recorded and RA disease activity evaluated by qualified rheumatologists. Demographic, clinical/laboratory data were retrospectively extracted from the medical records.

By December 2021, 279 patients (Japan 217, Spain 62) returned the questionnaires. A preliminary analysis was carried out with the first 58 Japanese patients in which all clinical and laboratory data could be collected. A descriptive analysis was performed and the relative risks approximated by odds ratios.

Results: Fifty-eight Japanese RA patients, 45 females, median age at entry 66 yrs [IQR 54-73], median disease duration 11yrs [IQR 7-20] were included in this

analysis. Fifty-three (93%) of patients were on biologic therapies and four (7%) on JAK inhibitors with a median treatment duration of 4.5 yrs [IQR 1-7]. Concomitant treatment with conventional DMARDS and glucocorticoids were reported in 69% and 48% of patients, respectively. Forty-two (72%) patients were responders to treatment defined as DASESR ≦3.2. Another systemic autoimmune disease, hypertension, diabetes mellitus, dyslipidemia or gout history were present in 29%, 29%, 9%, 33% and 10% of patients, respectively.

All patients had consumption of fish in the last month and an intake of n3-PUFA rich fish (fatty fish) was indicated by 82% (<1 time/week 34%, ≧ 1 time/week 48%).

The patients' fatty and non-fatty fish intake scores were calculated with a mathematical formula based on the intake of each of the fish included in the DFFQ and number of responses. In the group of high fatty fish score patients (≧ 1 time/week) 94% were responders to treatment vs. 6% non-responders, [OR 8.75, CI [1.0-73.54, p= 0.022] while only 63% of patients in the high non-fatty fish score group respond to the treatment.

Conclusion: Fatty fish intake associated with a good response to treatment in patients receiving targeted therapies, suggesting that fish consumption may have some beneficial effects on RA treatment.

References: There is no reference.

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Disclosure of Interests: None declared

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AB0202 GUT MICROBIOTA DYSBIOSIS WERE CLOSELY CORRELATED WITH LYMPHOCYTE SUBSETS AND CYTOKINES IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: Inflammatory arthritis includes a group of chronic conditions, particularly rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA)[1].Growing evidences link gut microbiota dysbiosis with the development of inflammatory arthritis[2].

Objectives: The aim of this study was to discover the characters of microbiota in inflammatory arthritis patients and compare the relationship between the microbiota and peripheral lymphocyte subsets and cytokines.

Methods: Fecal samples were collected from 73 arthritis patients (13 PsA, 30 AS, 30 RA patients) and 140 sex- and age-matched healthy controls (HCs). The gut microbiota was studied by sequencing the V3-V4 variable regions of bacterial 16S rRNA genes by the Illumina Miseq PE300 system. Peripheral lymphocyte subsets in these participants were assessed by flow cytometry. Measures of disease activity such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) were recorded. Alpha and Beta diversity was assessed using results from QIIME2 and gut microbiome profiles were compared using linear discriminant analysis (LDA) effect size (LEfSe). R (version 4.0.1) was used for comparative statistics, using pearson correlation analysis to assess the correlation between the relative abundance of genus in the sample and clinical parameters.

Results: Compared with HCs, the richness of gut microbiota (ACE and Chao 1) was significantly lower ($p < 0.05$) in arthritis patients, and bacterial diversity including Shannon and Simpson indices ($p < 0.001$) was also significant in arthritis decreased (Figure 1A). β-diversity analysis based on Bray-curtis distance revealed significant differences in microbial communities between arthritis and HCs (Figure 1B, r=0.098, p=0.001, ANOSIM). In addition, compared with HCs at the genus level, 9 bacterial groups were significantly different in PsA ($p < 0.05$), 19 bacterial groups in AS ($p < 0.05$), and 17 bacterial groups in RA($p < 0.05$) (Figure 1C). There was a significant positive correlation between CD4+T and Prevotella(p<0.01), T and Prevotella(p<0.05), Blautia(p<0.05) as well as Megamonas(p<0.05), Th17 and Prevotella(p<0.01), CD8+T and Megamonas(p<0.01), Th1 and Megamonas(p<0.05), Prevotella(p<0.01),Coprococcus(p<0.05), B and Erysipelotricbaceae_UCG-003(p<0.01), and Erysipelotricbaceae_UCG-003(p<0.01), Anaerostipes(p<0.01), CRP and Fusobacterium(p<0.05) as well as Roseburia(p<0.05). There were negative correlations between T and Erysipelotricbaceae_UCG-003 (p<0.05),CD8+T and Fusobacterium(p<0.01), CD4+T and Fusobacterium(p<0.05), NK and Fusicatenibacter(p<0.05).

Conclusion: The gut microbiota of patients with inflammatory arthritis differs from HC and also varies among individual arthritis, which was closely related to lymphocyte subsets.

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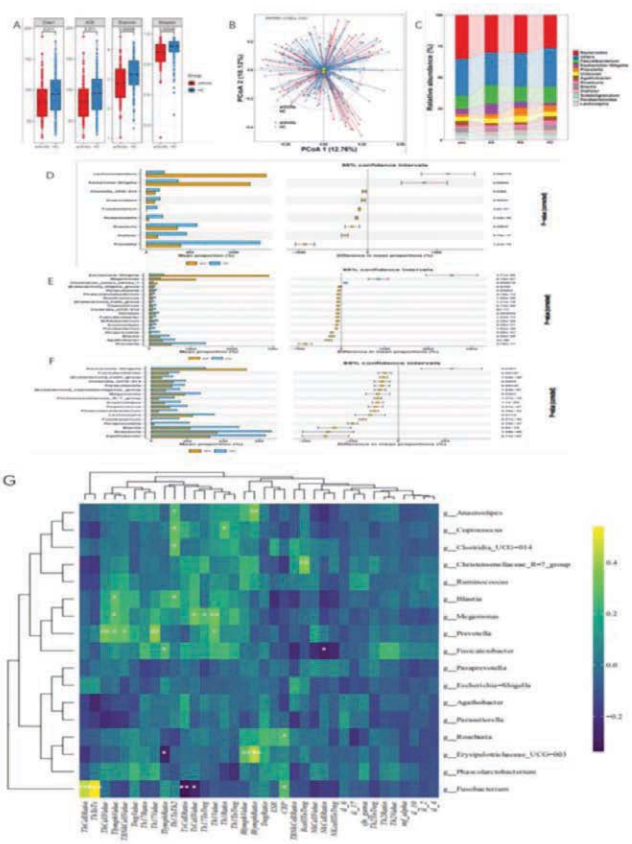

Fig1. Feature of gut microbiota in arthritis patients and HCs. (A) Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson), Median estimates compared across cohorts. (B) PCoA plot based on the Bray curtis distance of gut microbiota samples from arthritis vs. HC (p = 0.001, ANOSIM). (C) Distribution of gut microbiota at genus level.(D-F) Panel demonstrated the average relative abundance of different genus in PsA and HCs., AS and HCs. as well as RA and HCs.(G)Correlations between the relative abundance of significantly different bacteria and clinical variables. *p<0.05, **p < 0.01, ***p <0 .001,****p < 0.0001.

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Disclosure of Interests: None declared

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AB0203 25-HYDROXYVITAMIN D [25 (OH) D] LEVEL IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS, ITS RELATIONSHIP WITH THE COURSE OF THE DISEASE, VDR (FOKI) GENE POLYMORPHISM AND BONE MINERAL DENSITY.

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Background: Osteoporosis is known to be a common concomitant state in postmenopausal women with rheumatoid arthritis, but its development cannot be explained only by increasing of age, hormonal disorders, disease duration and glucocorticosteroid intake. Vitamin D deficiency may be one of the major risk factors, but its prevalence in the Ukrainian cohort of postmenopausal RA patients is unknown, and the factors on which it depends have not been established.

Objectives: To analyze the level of 25-hydroxyvitamin D [25 (OH) D] in postmenopausal women with rheumatoid arthritis (RA) and to investigate its relationship with the course of the disease, VDR (FokI) gene polymorphism and bone mineral density (BMD).

Methods: The study included 81 postmenopausal RA patients and 21 postmenopausal age-matched women without RA as a control group. All patients

were screened for demographic, disease course and treatment data. Serum 25-hydroxyvitamin D [25 (OH) D] level and VDR (FokI) gene polymorphism were measured by enzyme-linked immunosorbent assay (ELISA). Levels of 25-hydroxyvitamin D [25 (OH) D] 20-30 ng / ml were defined as insuficiency and less than 20 ng/ml as deficiency. BMD was measured in the lumbar spine and proximal femur using double X-ray absorptiometry. Osteoporosis was diagnosed in case of BMD> -2.5 T.

Results: The analysis has showed that serum vitamin D level in RA group was significantly lower than in control group (11.54 ng/ml vs. 15.25 ng/ml; p <0.01). In addition, the incidence of vitamin D insuficiency and deficiency was higher in RA patients than in control group. In particular, abnormal vitamin D level was diagnosed in 74.1% of RA patients, among whom 25 (30,9%) patients had vitamin D insuficiency and 35 (43.2%) patients had vitamin D deficiency. In control group 8 (38.1%) persons had vitamin D insuficiency, and 6 (28.6%) persons had vitamin D deficiency. There was an inverse correlation between vitamin D levels and RA activity assessed by DAS28 (p <0.001), CDAI (p = 0.001), ESR and CRP (p <0.001) but not with age, daily glucocorticosteroid dose and disease duration. In addition, significant correlation was revieled between VDR (FokI) gene polymorphism and vitamin D deficiency, as well as low BMD in postmenopausal women with rheumatoid arthritis (p <0.001)

Conclusion: Low 25-hydroxyvitamin D [25 (OH) D] level and VDR (FokI) gene polymorphism are independent risk factors of osteoporosis in postmenopausal women with RA. Vitamin D deficiency is associated with RA activity and not depends on age, glucocorticosteroid daily dose and disease duration.

Disclosure of Interests: None declared

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AB0204 DOES THE PRESENCE OF COXITIS IN RHEUMATOID ARTHRITIS CHANGE THE DISEASE SEVERITY PROFILE?

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by intra-articular manifestations affecting small and large joints. Hip involvement is not common but it can predict a severe disease course [1].

Objectives: Our study aimed to investigate the prevalence of coxitis in RA patients and to compare patients with RA coxitis (+) and RA coxitis (-) according to their clinical, biological outcomes and their therapeutic findings.

Methods: This was a retrospective and comparative study, which include patients diagnosed with RA according to the ACR/EULAR 2010. Sociodemographic, clinical, biological, and therapeutic data were collected. The diagnosis of coxitis was made on plain x-rays or MRI.

Results: Among 255 RA, there were 30 RA coxitis (+) (11.8%). Coxitis was unilateral in 28 patients and bilateral in 2 patients. The mean delay onset of coxitis was about 11.6 ± 8.4 years (1-27). The mean age was 57.5 ± 12.2 years for RA coxitis (+) and 59.1 ± 10.5 years for RA coxitis (-) (p=0.5). The gender distribution was (70% female and 30% male) for RA coxitis (+) and (85% female and 15% male) for RA coxitis (–) (p= 0.04). The mean Body Mass Index was 24.8 ± 4.8kg/m^2 in RA coxitis (+) and 28 ± 5.8 kg/m^2 in RA coxitis (-) (p= 0.03). Comorbidities were present in 46% of RA coxitis (+) and 48% of RA coxitis (–) (p=0.8). Extra articular manifestations were noted in 76% RA coxitis (+) and 66% RA coxitis (–) (p=0.8). RA was seropositive in 76% RA coxitis (+) and in 82% RA coxitis (–) (p=0.4). RA was immunopositive in 51% RA coxitis (+) and 69% RA coxitis (–) (p=0.04). The mean DAS28 (CRP) was respectively 4.6± 1.1 in RA coxitis (+) vs 4.8 ± 1.1 RA coxitis (-) (p=0.7). Atlanto-axial dislocation was noted in 60% RA coxitis (+) and 22% RA coxitis (–) (p<10^{-3}). The use of corticosteroid was noted in 92% RA coxitis (+) and in 90% RA coxitis (–) (p=0.7). Biologic drugs were prescribed in 43% RA coxitis (+) and in 25% RA coxitis (–) (p=0.04).

Conclusion: Our study showed that coxitis in RA patients is associated with a higher risk of Atlanto-axial dislocation and a more frequent use of biologic drugs reflecting a more severe and mutilating disease. We highlight the importance of an early diagnosis and treatment to prevent complications.

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Disclosure of Interests: None declared

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AB0205 TENDERNESS AND RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: In inflammatory arthritis swelling is regarded as a sign of synovitis and is associated with radiographic progression. However, the association of tenderness with radiographic progression is not clear.

Objectives: To assess the predictive value of tenderness alone and with consideration of sonographic signs for synovitis, disease duration and baseline radiographic damage for subsequent radiographic progression in rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

Methods: Clinical and sonographic (grey scale (GS) and power Doppler (PD)) examination of 22 joints of the hand were performed cross-sectionally in consecutive patients with RA and PsA with at least one tender joint. Radiographs were scored for erosions and joint space narrowing (JSN) at inclusion and radiographic progression of each joint was assessed after 2 years. The impact of tenderness on progression was analyzed in non-swollen joints for RA and PsA separately with logistic regression analyses. As a second step, the association of PD, GS, disease duration, C-reactive protein, baseline erosions and JSN and global joint counts with subsequent structural damage was assessed using univariate logistic regression in tender non-swollen joints again on the joint level.

Results: We included 1207 joints in 54 RA patients and 396 joints in 18 PsA patients. Tenderness was associated with subsequent radiographic progression in non-swollen joints in PsA (OR 3.44, 95%CI 1.78-6.62, p<0.01) but not in RA (OR 1.60, 95% CI 0.99-2.48, p=0.55) (Figure 1). In tender non-swollen joints in RA patients, PD (OR 3.74, 95% CI 1.10-13.30, p=0.04) and baseline erosions (OR 4.42, 95% CI 1.22-15.95, p=0.02) had a significant impact on radiographic progression. In PsA patients, PD (OR 8.46, 95% CI 1.72-41.72, p<0.01), baseline erosions (OR 6.71, 95% CI 1.43-31.39, p=0.02), baseline JSN (OR 7.27, 95% CI 1.47-35.89, p=0.02) and SJC (OR 1.26, 95%CI 1.07-1.48, p<0.01) were associated with radiographic progression.

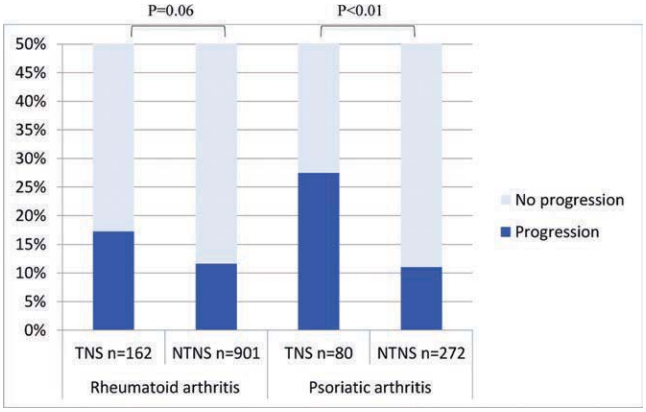

Figure 1. The proportion of joints with progression in tender non-swollen and non-tender non-swollen joints in patients with rheumatoid and psoriatic arthritis; NTNS: non-tender non-swollen; TNS: tender non-swollen

Conclusion: Our findings indicate that tenderness in non-swollen joints is associated with subsequent radiographic progression in PsA, while in RA it is a risk factor for radiographic progression only in the presence of additional factors, such as sonographic signs for synovitis.

Disclosure of Interests: Irina Gessl: None declared, Mihaela Popescu: None declared, Gabriela Supp: None declared, Thomas Deimel: None declared, Paul Studenic: None declared, Martina Durechova: None declared, Michael Zauner: None declared, Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO, Janssen, Lilly, Merck Sharp & Dohme, Novartis- Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB, Grant/research support from: Abbvie, AstraZeneca, Lilly and Roche, Daniel Aletaha Speakers bureau: Abbvie, Amgen, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Grant/research support from: Abbvie, Amgen, Lilly, Novartis, Roche, SoBi, Sanofi
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AB0206 STUDY ON THE SIGNIFICANCE OF SERUM COMPLEMENT C5 IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Recent studies have pointed out that complement system activation is a major alteration in early atherosclerotic plaques, and complement C5 has promising value as a novel circulating biomarker of atherosclerosis, but the relationship between C5 and carotid atherosclerotic (CAS) plaque in rheumatoid arthritis (RA) is still unclear.
Objectives: To investigate the clinical significance of serum complement C5 and the association with CAS plaque in patients with RA .
Methods: 143 patients with RA were included in the study, and 46 cases with age- and sex- matched healthy physical examination without RA or CAS plaque served as a normal control. All RA patients were divided into RA with CAS plaque group and RA without CAS plaque group according to the presence or absence of plaque formation in the carotid artery. The subject's demographic data, laboratory investigations and serum samples were collected. Body mass index (BMI) and Disease Activity Score 28-joint counts (DAS28) were calculated. Glucocorticoid and DMARDS use were recorded in the past 3 months. ELISA method was used to determine the concentration of complement C5 in the serum of each participation. CAS plaque was determined by color Doppler ultrasound.
Results: Serum complement C5 in RA group was significantly lower than that in control group (P<0.05), whereas C5 level in RA with CAS plaque group was significantly higher than that in RA without CAS plaque group (P<0.05). In RA group, serum C5 level was positively correlated with CAS plaque, high-sensitivity C-reactive protein (hs-CRP) and fibrinogen (FIB) (r=0.204, P=0.017; r=0.225, P=0.009; r=0.186, P=0.029;). In addition, there was no significant correlation between serum C5 and sex, age, BMI, course of disease, DAS28, lipid profile (TG, serum triglyceride; TC, total cholesterol; LDLC, low density lipoprotein cholesterol; HDLC, high density lipoprotein cholesterol; TC/HDLC; LDLC/HDLC), immune markers (RF, rheumatoid factor; anti-CCP, anti-cyclic citrullinated peptide antibodies), cytokine (IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-α), erythrocyte sedimentation rate (ESR) (all P>0.05), or drug therapy (all P>0.05).
Conclusion: C5 may be a novel circulating marker of atherosclerosis in RA patients, it might promise to assist in risk stratification for cardiovascular disease in the future.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3636

AB0207 SOME TARGET JOINTS PERSIST SWOLLEN ACROSS THE FOLLOW-UP IN RHEUMATOID ARTHRITIS: RESULTS FROM A REAL LIFE REGISTRY

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Background: Rheumatoid arthritis (RA) is an inflammatory chronic disease, affecting peripheral joints. For the assessment of these joints, rheumatologists use mostly 28 joint swollen and tender count. Although there has been a development of new drugs and therapeutic strategies, there is new information (1) regarding the persistence of some joints that seem to be refractory to treatment.
Objectives: The aim of this study is to describe the pattern of swollen joint affection and its change during followup in real-life RA patients from a rheumatology clinic registry.
Methods: RA patients from an outpatient registry were included if they fulfilled ACR-EULAR 2010 criteria, had ≥ 18 years old, and attended between October 2010 to September 2021. Only those who a 28-joint swollen count available performed by an experienced rheumatologist (EB) in ≥ 5 visits were included. Each joint from the 28-joint count was analyzed individually, the percentage of swollen affection at baseline, last registered visit and during the follow-up was registered. Descriptive statistical analysis and comparisons was performed, depending on the type of data and its distribution.
Results: 403 patients with RA diagnosis were in the registry, 247 (61%) had descriptive 28-joint count, from which 154/247 (62.3%) had ≥ 5 visits and were finally included. When comparing those with < 5 with ≥ 5 visits, the latter had more bDMARD/tsDMARD treatment at baseline (16.9% v 6.5%, p = 0.01). In 154 patients, the mean period between visits was 6.7 months (SD +/- 5.8), the mean follow-up was 5.8 years (SD +/- 3.1), and the mean of visits per patient was 13 (DS +/- 8.8). At baseline the most affected swollen joints were 35.7% right wrist, 35.1% Left Wrist, 35% 2nd right MCP, 32.5% 3rd right PIP. At the last registered visit, the same joints were the most affected, and the percentage of affection persisted across the follow-up. [Figure 1]. When the change from baseline to the last registered visit was analyzed for other variables, a significative improvement was found (baseline v last visit, ESR-DAS28: 3.8 v 3, p = 0.0001, CRP-DAS28: 3.5 v 2.7, p = 0.001).

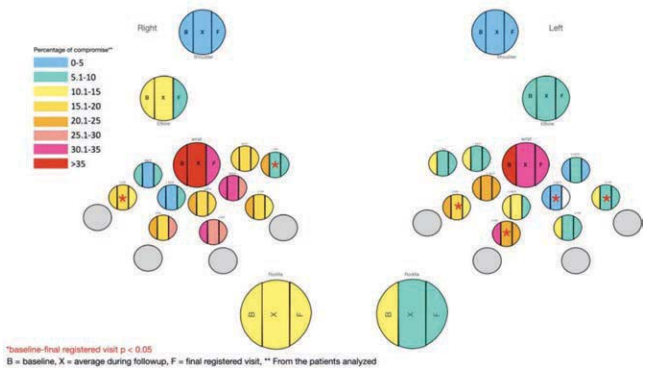

Figure 1. Percentage of swollen joint affection at baseline, final registered visit and average followup

Conclusion: In this registry, some swollen joints were persistently affected across the follow-up, and did not improve from baseline to the last registered visit. However, the burden of the disease improved, measured by DAS28 or its individual components. The improvement of other swollen joints and other components of DAS28 can be the reason. The detection and local treatment (vg: intra-articular injections) of this persistent swollen joints could be the better approach to this issue. Weaknesses of this study: a possible bias in the included patients (they were from single clinic), joint assessment not blind and performed by a single rheumatologist, patients included could be more severe since they were more frequently bDMARD/tsDMARD users.
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Table 1. Change from baseline to the last registered visit (n = 154)

VARIABLE		Basal	Final	p =
Methotrexate – n (%)		89 (57.8)	119 (77.3)	0.0001
Leflunomide – n (%)		31 (20.1)	37 (24)	0.3
Prednisone – n (%)		57 (37)	75 (48.7)	0.01
bDMARD / tsDMARD – n (%)		26 (16.9)	49 (31.8)	0.0001
Swollen Joints – X (SD)		4.64 (4.8)	3.03 (3.8)	0.0001
Tender Joints – X (SD)		3.9 (4.5)	2.49 (3.6)	0.002
VAS global (mm) – X (SD)		38.5 (24)	31.04 (22.7)	0.004
VAS physician (mm) – X (SD)		35.6 (26.4)	24.2 (22.4)	0.0001
ESR (mm/1h) – X (DS)		33.7 (23.2)	27.3 (23.2)	0.01
CRP (mg/dl) – X (DS)		3.7 (5.7)	1.7 (2.6)	0.02
ESR-DAS28 – X (DS)		3.8 (1)	3 (1.1)	0.0001
CRP-DAS28 – X (DS)		3.5 (1)	2.7 (1.1)	0.001
ESR-DAS28	≤ 2.6 – n (%)	22 (14.3)	50 (32.5)	0.0001
	2.7-3.2 – n (%)	16 (10.4)	16 (10.4)	1
	3.3-5.1 – n (%)	78 (50.6)	43 (27.9)	0.0001
	≥ 5.2 – n (%)	9 (5.8)	8 (5.2)	0.8

Disclosure of Interests: None declared
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AB0208 LONG-RUN RELATIONSHIP ASSESSMENT OF AIR POLLUTANTS ON RHEUMATOID ARTHRITIS DISEASE ACTIVITY SCORE: EVIDENCE FROM THE VECM APPROACH

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Background: Current findings on the impact of air quality conditions on rheumatoid arthritis (RA) are sparse and not conclusive.
Objectives: To investigate the relationship between air pollutants and RA disease activity scores on a short and a long time period using a multivariate time series model.
Methods: Data on RA patients were extracted from the Kuwait Registry for Rheumatic Diseases (KRRD) from four major hospitals in Kuwait from January 2013 to December 2017. Data on air ambient pollutants (ozone O3, sulfur dioxide SO2, nitrogen dioxide NO2) were extracted from four Kuwait Environmental Public Authority (K-EPA) Air Monitoring Stations through Environmental Monitoring Information System of Kuwait (eMISK), corresponding to the patients residential

areas from January 2013 till December 2020. A multivariate time series approach using Evidence from vector error correction model (VECM) was employed to investigate the effect of air ambient pollutants emissions on DAS28 over that period.

Results: A total of 1,809 RA patients and 10,215 hospital visits were included, 63% females, mean age 54 years, mean disease duration 9.2 years and 77% had rheumatoid factor positive. A significant correlation was found between DAS-28 and SO2, NO2 and O3 (p=0.012, 0.029, 0.039 respectively). According to the Granger causality test and VECM, emissions of NO2, and O3 had a positive short-term effect on DAS28 among RA patients. Impulse response test results showed that for some locations in Kuwait there is a short-term positive causal relationship between emissions of NO2 and DAS28, due to sources of pollution surrounding the locations. The results showed that the short run effect for NO2 with lags 1 to 4 days had a positive relationship with DAS-28 which means, there is 1% increase in DAS-28 for every 0.0182 increase in NO2 emission. Our results revealed that 36% of discrepancy between the overall relationship between DAS-28 and air pollution is corrected each year.

Conclusion: Increased concentrations of air pollutants may increase the risk of RA activity. VECM time series model can be used as a tool to predict changes in disease activity based on air pollutants up to 8 days. We recommend that a regular broadcast is issued by health authorities to RA patients to help predict changes in disease activity. Warning about air pollution may be tailored according to the patient's residential area. Government should take serious decisions to help minimize air pollution in the residential areas.

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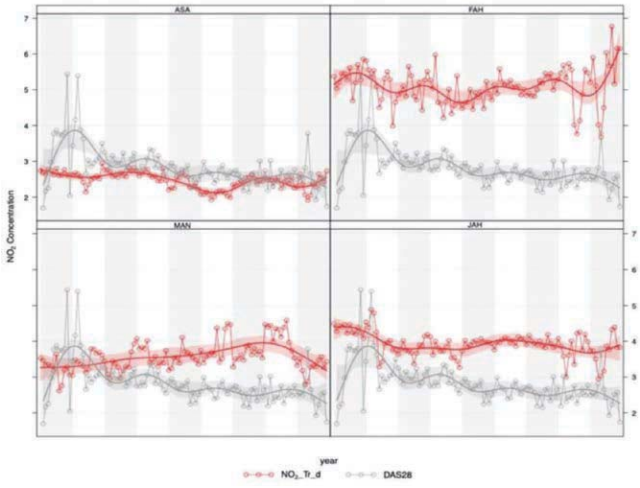

Figure 1. Long-term (2012-2020) trends of NO2 concentrations and DAS-28 calculated using the smooth trend method based on the mean measurements for four locations in Kuwait

Disclosure of Interests: None declared

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AB0209 PHYSICIAN TRUST RATHER THAN RHEUMATOID ARTHRITIS KNOWLEDGE RELEVANT IN DISEASE OUTCOMES IN ETHNIC MINORITY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Ethnic minority (EM) patients with Rheumatoid Arthritis (RA) have more severe disease, more disability, and less use of biologic disease modifying anti-rheumatic drugs (bDMARDs). A Treat to target (T2T) strategy has been recommended to improve clinical outcomes but barriers include patient preference, access to specialty care and increased administrative effort. Additionally, EM patients in the US often have low health literacy, express greater reluctance to accept physician recommendations, in part due to sociocultural preference and mistrust of a historically biased healthcare system. It is unknown whether improving knowledge of RA would improve T2T outcomes in EM active RA patients.

Objectives: To assess the proportion of EM RA patients who achieve low disease activity or remission following implementation of a coordinator-based education program highlighting T2T RA strategy.

Methods: Adult participants with active RA (RAPID3>6 or CDAI > 10) were invited to participate in a series of five one-on-one 20-minute educational sessions, co-occurring with scheduled routine clinic visits (6 -12-week intervals). Sessions were facilitated by a rheumatology care coordinator, a non-healthcare professional with intensive training over 4 weeks to conduct RA patient education. Sociodemographic data was collected, and disease activity measures (TJC, SJC, RAPID3, CDAI) and validated patient questionnaires on RA Knowledge (ACREU), compliance (CQR5), and physician trust (Trust in Physician Scale) were recorded at baseline and after the final educational session. Descriptive statistics were applied and medians and ranges for instrument scores are reported. Paired T-test was used to test for significant differences in scores after the education sessions. Correlations between the ACREU scores and clinical-demographic variables were measured using Pearson's correlation coefficient.

Results: 20 EM patients (75% Female, mean age, 58.8 years (12.2) seen by EM physicians were enrolled, with mean RA disease duration of 7 years and poor prognosticators (75% double seropositivity). ACREU scores were low at baseline (mean 0.45 (0.16)), with no significant improvement on completion of educational sessions, and no correlation with years of education or duration of RA. There was a positive correlation between ACREU and compliance scores at baseline (r=0.3). Average duration of the education period was 9.72 months, with a 33% decrease in average RAPID3 over time, and 42% of patients achieving a target of remission or LDA. Trust in Physician scores were high at baseline and persisted with >50% of patients completing at least one medication change during study period.

Conclusion: RA knowledge did not impact RA patient outcomes in this cohort of EM patients. However, patients had high trust in their providers and achieved clinical remission or LDA despite risk for poor outcomes highlighting the importance of the provider- patient relationship in achieving targeted goals of therapy. Limitations include the small sample size from a single institution, and the lengthy time between initial and final assessment of RA knowledge.

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AB0210 REAL-LIFE DAS28-DEFINED REMISSION IN RHEUMATOID ARTHRITIS – INFLAMMATION CONTROL IS NOT ENOUGH

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Background: Remission of rheumatoid arthritis (RA) is currently a reachable target in real-life settings under treat-to-target strategies, meta-analytical data

showing an overall success of 16.3% for its 6-month DAS28 definition [1]. Baseline high levels of inflammation and activity markers have been consistently shown to negatively influence this endpoint.
Objectives: The study aimed to evaluate the prevalence of DAS28-defined remission in naïve RA patients after their first 6 months of b/tsDMARD treatment and whether the degree of baseline activity independently predicts treatment outcomes (remission, switch) in a real-life setting.
Methods: Medical records of naïve RA patients who initiated b/tsDMARDs (according to Romanian criteria [2]) from 20.12.2016 to 20.12.2021 were retrieved retrospectively from the database of the Clinical Center for Rheumatic Diseases in Bucharest, Romania. Children, cases with missing data (baseline and 6 months), patients who were previously exposed to b/tsDMARDs, patients exposed to b/tsDMARDs less than 6 months and patients who were not actually exposed to b/tsDMARDs were excluded. Prediction of dichotomous outcomes (remission and switch at 6 months) was evaluated using binary logistic regression.
Results: The study included 157 patients with established RA, mostly women (80.3%), 56.2±11.8 years-old on average. The group included predominantly positive rheumatoid factors (77.7%) and positive anti-citrullinated protein antibodies (81.5%), with only 12.1% both negative. At baseline, 58.0% were receiving one csDMARD (especially leflunomide - 49.7%, and methotrexate - 43.3%), 38.9% were receiving 2 csDMARDs, and 57.3% were on chronic oral glucocorticoids (7.6±4.4 mg/day on average). All patients had high baseline disease activity (average DAS28 of 6.3±0.8). Accordingly, all patients were initiated on either original/biosimilar TNF inhibitors (adalimumab - 22.3%; certolizumab - 7.0%; etanercept - 31.2%; golimumab - 1.3%; infliximab - 17.8%), other bDMARDs (abatacept - 3.8%; rituximab - 1.9%; tocilizumab - 6.4%) or tsDMARDs (baricitinib - 5.7%; tofacitinib - 2.5%). After 6 months, 29.3% of patients were in DAS28-defined remission, 22.9% in LDA, 35.7% in MDA and 12.1% in HDA. Therefore, 12.7% switched their initial bDMARD and 10.8% stopped b/tsDMARDs, because 10.8% exhibited primary non-responsiveness (PNR) and 11.5% had adverse events (7 dermatological conditions, 6 cases of non-tuberculosis pneumonia, 1 case of clinical pulmonary tuberculosis, 1 case of latent tuberculosis, 1 transaminitis, 1 gastric cancer, 1 neutropenia). High baseline levels of DAS28 were associated with a lower probability to attain DAS28-remission after 6 months (OR = 0.64) and with a higher probability to switch the initial b/tsDMARD due to PNR (OR = 2.44), suggesting that pharmaceutically influencing the inflammation cascade is not enough. Addition of b/tsDMARDs reduced at 6 months the prevalence of oral glucocorticoids to 28.0% (5.9±2.6 mg/day on average).
Conclusion: Although reachable, disease remission seems difficult to attain, despite using advanced therapies. High baseline levels of DAS28 are negative predictors for not attaining remission and switching of therapy due to PNR in real-life.
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AB0211 FOOT IMPAIRMENT IS NOT A BARRIER TO PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Physical activity is increasingly promoted for patients with Rheumatoid arthritis (RA) and strongly recommended. However, adherence to regular physical activity remains low. Identifying the barriers to physical activity is a key element to understanding physical activity behavior in RA.
Objectives: Our objective was to assess the impact of foot involvement on physical activity among patients with RA.
Methods: We conducted a cross-sectional study including patients with RA, fulfilling the ACR-EULAR 2010 criteria. We collected the socio-demographic data and disease characteristics. Regarding the foot involvement, we assessed the presence of foot static disturbances and foot deformities through clinical examination, and radiographic damage. Physical activity was assessed by the Arabic version of validated International Physical Activity Questionnaire (IPAQ). According to this questionnaire, patients were subdivided into three groups: low, moderate and high physical activity.
Results: We included 94 RA (60 rheumatoid factor (RF) positive RA and 57 Anti Citrullinated Peptides Antibodies (ACPA) positive RA) patients. Eighty-six were females, mean age 52,12 ±9,743 years. The mean disease duration was 14,78 years ± 9,425. RA was erosive in 81 cases. Sixty-four patients had extra articular manifestations: pulmonary (n=15), dry syndrome (n=46), rheumatoid nodules (n=7) and osteoporosis (n=25). Mean DAS28CRP score was 3,67 ±1,58 and mean HAQ score was 0,88 ± 0,65. Eighty patients were treated by cs-DMARDS and 31 by biologics: infliximab (n=3), etanercept (n=3), adalimumab (n=2), golimumab (n=3), certolizumab (n=1), tocilizumab (n=11), rituximab (n=4).
Forty-six patients complained of fore foot pain, 34 of mid foot pain and 19 of hind foot pain. Mean visual analogue scale for foot pain was 3,6 ±3,05, and no significant correlation was shown with IPAQ score (p=0,19, r=0,138). Foot static disturbances were present in 66 patients: bilateral flat foot (n=31), hallux valgus (n=59), claw toes (n=33) calcaneal valgus (n=25), peroneal tenosynovitis (n=24), tibialis posterior tenosynovitis (n=18), ankle arthritis (n=15) and mid-foot arthritis (n=18). We didn't find a significant association between lower IPAQ score and foot deformities (p=0,235), the presence of peroneal tenosynovitis (p=0,438) and tibialis posterior tenosynovitis (p=0,113).
As regards X-rays findings, bone erosions were found in 58 patients, joint narrowing in 65 patients, and dislocation of the MTP joints in 17 patients. No positive association with lower IPAQ score was found with structural damage: erosions (p=0,938); joint narrowing (p=0,258) and dislocation of the MTP joints (p=0,884). DAS28 was higher among patients with low physical activity (mean DAS28crp among this population was 4,16 compared to 3,63 among patients with high physical activity), but without reaching a significant threshold (p=0,432, r=-0,85).
Conclusion: Increasing physical activity in RA patients is an ongoing challenge. In this study, no association was found between foot involvement in RA and a lower IPAQ score.
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AB0212 COMPARISON OF THE EFFECTS OF POLYPHARMACY IN THE TREATMENT OF RHEUMATOID ARTHRITIS PATIENTS AND PSORIATIC ARTHRITIS PATIENTS WITH PERIPHERAL JOINT INVOLVEMENT

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Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are chronic, progressive inflammatory diseases that can be accompanied by other diseases. These patients use several medications, especially due to their comorbidities and widespread pain. In recent years, with the increase in the lifespan of individuals, the concept of polypharmacy has become more prominent. Accordingly, in our study, we aimed to present the prevalence of polypharmacy and its effects on these diseases.
Objectives: Demonstrating the prevalence of polypharmacy in RA and PsA, which are among the most frequently encountered inflammatory arthritides, and the effects of polypharmacy on disease activity.
Methods: This study included PsA patients with only peripheral joint involvement and no distal interphalangeal joint involvement and RA patients. The numbers of medications used by the patients at the onset of their treatment and in the sixth month of their treatment were recorded. Non-prescribed (over the counter), topical and herbal/homeopathic medications were excluded. Polypharmacy was accepted as the simultaneous use of at least five medications by the person. Disease activity score in 28 joints C-reactive protein (DAS-28 CRP) was used for disease activity for both diseases. In addition to these, the scores of the patients who attended their follow-ups in the 12th month were calculated and analyzed. The Charlson Comorbidity Index (CCI) scores of the patient were calculated based on their chronic diseases.
Results: The sample of the study included 232 RA and 73 PsA patients. Demographic and some clinical characteristics are shown in Table 1. The mean numbers of medication used by the patients at the onset of their treatment were respectively 5.09±2.89 and 4.03±2.7 for the RA and PsA patients, whereas these mean numbers were found consecutively as 8.67±3.58 and 7.71±3.3 in the sixth month of their treatment. Polypharmacy was present in the sixth month of the treatment in 217 (93.5%) RA and 61 (83.6%) PsA patients.

Table 1. Demographic and some clinical features

	RA (n=232)	PSA (n=73)
Age (mean±SD)	55.2±13.66	48.4±13.43
Age Group		
<65 years	171(73.7)	65(89)
≥65 years	61(26.3)	8(11)
Sex		
Female, n (%)	172(74.1)	50(68.5)
Male, n (%)	60(25.9)	23(31.5)
Current smoker, n (%)	82(35.3)	33(45.2)
The numbers of medication used	8.67±3.58	7.71±3.3
Polypharmacy at the Beginning of Treatment	115(49.6)	28(38.4)
Polypharmacy in the sixth month of treatment	217(93.5)	61(83.6)
CCI (n=232/72) (mean±SD)	1.25±0.88	1.31±0.71
0th month DAS-28 CRP (mean±SD)	4.91±1.28	4.68±1.03
6th month DAS-28 CRP (mean±SD)	3.14±1.06	2.86±0.99
12th month DAS-28 CRP (n=83/29) (mean±SD)	2.73±1.18	2.8±1.12

While the mean ages of the RA and PsA patients who had polypharmacy treatment at the beginning were respectively 59.21±12.65 and 53.5±13.81, their ages were significantly higher than the ages of those who did not receive polypharmacy treatment (respectively, 51.26±13.53 and 45.22±12.3).
In RA ve PsA patients, the status of polypharmacy is higher in the groups in the groups aged 65 and over than those under 65 years of age, and it is statistically significant (p=0.001 and p=0.048, respectively). The risk of polypharmacy in people over 65 years of age in RA patients was 8.2 times, and the risk of polypharmacy in people over 65 years old in PSA patients was increased 6.3 times (p=0.015).
In both the RA and PSA groups, patients with baseline polypharmacy had statistically significantly higher DAS-28 CRP scores at 6 months of treatment than those without baseline polypharmacy. (p<0.001). While the higher DAS-28 CRP score was maintained at 12 months in the RA group with polypharmacy at baseline (p=0.006), this was not significant in the PSA group (p=0.07).
Conclusion: Polypharmacy was present both at the time of diagnosis and in the treatment process in the RA and PsA patients, and the presence of polypharmacy at the beginning of the treatment was among the factors that affected the treatment of these patients by significantly affecting their 6th-month DAS-28 CRP values.
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AB0213 CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING TOTAL JOINT REPLACEMENT: A 20-YEAR TREND ANALYSIS

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Objectives: To examine time trends in the characteristics of patients with rheumatoid arthritis (RA) undergoing total joint replacement (TJR).
Methods: A total of 271 patients (399 joints) with RA underwent TJR of large joints (hip, knee) at Republican Clinical Hospital, Kazan between 2002 and 2021. Of these, 98 patients were retrospectively examined between 2002 and 2011; 183 patients were observed prospectively in the perioperative period by a rheumatologist and orthopedist from 2012 to 2021. Of the 183 patients, 65,5% underwent one joint replacement, 19,1% underwent two joint replacements, 13,7% underwent three joint replacements, and 1,7% underwent four joint replacements during the study period. All patients met the 1987 ACR classification criteria or the ACR/ EULAR diagnostic criteria. Median [interquartile range (IQR)] age at surgery was 56 (49, 63), the time from the onset of RA to TJR was 11 (7, 18) years. During the study period, total knee replacement was performed most often (67.9%). Joint pain (VAS), disease activity - DAS28, functionality of the HAQ index were assessed before the operation, after 6 and 12 months in the active observation group.
Results: In patients in 2002-2011, TJR were performed earlier from the time of the onset of RA compared to the 2012-2021 group [median (IQR), 10 (7-17) vs. 12 (8-19) years, p = 0.01], and there were more complications of surgery (16.3% vs. 5.4%, p < 0.001). In the later period (2012-2021), there was a decrease in blood loss and operation time, p < 0.05. With respect to RA treatment, a significant increasing trend was observed in the proportion of subjects receiving methotrexate (p 0,006) and biological drugs and biologics (p < 0.001).
In the prospective observation group (n=183), patients were significantly older at the time of TJR with low and moderate activity RA (n=106) compared with high activity (n=77) [median (IQR), 57 (51, 64) vs. 55 (46, 63), p = 0.034]. A significantly less time from RA onset to TJR was observed in patients with high activity, using glucocorticoids. Patients who had the use of glucocorticoids TJR was performed earlier than non-users [median (IQR) 11 (6, 16) and 13 (8, 19) years, respectively, p=0.041] There was no significant difference in time from the onset of RA to TJR, stratified by gender and the use of MTX, biological drugs. At the same time, there was no significant difference in dependence on the activity RA to reduce pain syndrome (VAS), improve function (HAQ) after surgery and presence of postoperative complications.
Conclusion: Over a 20-year period changes were observed in the characteristics of patients with RA undergoing TJR with an increase in the time before surgery. Perioperative management of patients by a rheumatologist and orthopedist can reduce blood loss, the number of complications after surgery. Patients with high RA activity and using glucocorticoids need TJR at an earlier time. Arthroplasty in patients with highly active RA is also effective in improving functional ability.
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AB0214 SERUM IMMUNOGLOBULINS LEVEL IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS ON DIFFERENT TREATMENT OPTIONS

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Background: Serum immunoglobulins (Ig) A, G, and M (IgA, IgG, and IgM) are not routinely evaluated in rheumatoid arthritis (RA). There are some reports that rituximab (RTX) may induce hypogammaglobulinemia (1). Under normal conditions, IgM provides a rapid immune response and is involved in tissue homeostasis, whereas IgG and IgA are long-lasting high-affinity antibodies, the latter mainly providing mucosal immunity (2).
Objectives: The evaluate serum Ig levels (IgG, IgM, IgA) in a cohort of RA patients and potential therapeutic influences.
Methods: We performed a retrospective study in a cohort of 104 patients with RA exposed to different therapeutic agents, without switch for at least 1 year (conventional synthetic disease modifying drugs - csDMARDs, biologics and JAK inhibitors - JAKi); the collected data included demography, disease characteristics, treatment exposure (molecules, treatment line), serum level of IgA, IgG, IgM.
Results: 104 patients, mean age 60.3 years (±11.9), with a disease duration of 15years (±9.8), 83.7% women; the mean exposure to the current treatment option (without switch) was 3.7 years (±3.8); 20.2% (21 pts) were on csDMARDs, 70.2% (73pts) on biologics and 9.6% (10pts) on JAKi. 90.4% (83pts) used combination therapy along with biologics and JAKi. The biologics used were: 58.9% RTX, 31.5% TNFinhibitors, 8.2% IL-6 blockers and 1.3% abatacept. At cohort level, we found hypogammaglobulinemia in 12.5% for IgG, 9.6% for IgM and 7.7% for IgA, independent of the treatment duration. Low IgG levels were related mostly to RTX exposure (53.8%) followed by TNFi (23.1%) and with equal values anti-IL-6, JAKi and csDMARDs (7.7%). Low IgA levels were noted almost in RTX exposure (75%), followed by TNFi and anti-IL-6 (12.5%, each). Low IgM levels appeared in RTX group (90%) and csDMARDs (10%). No relations between Ig levels and the treatment option (the line of intervention). The Ig mean values were significantly different across treatment groups; for IgG: 9.55g/L in RTX vs 11.68 g/L in TNF inhibitors (p<0.05) and 12.64 g/L in csDMARDs (p<0.05); for IgA: 2.17 g/L in RTX vs 3.35 in JAKi (p<0.05); for IgM: 0.84 g/L in RTX vs 1.82g/L in TNF inhibitors (p<0.001) and 1.58 g/L in JAKi (p<0.05); also IgM were significantly lower in csDMARD group (1.22g/L compared to TNF inhibitors values (1.82g/L), (p<0.05). The serum levels of IgG and IgM (not IgA) were negatively associated with disease duration r = -0.22, p<0.05 and r = -0.2, p<0.05) and age (r =-0.3, r=-0.26, p<0.01). No impact of disease activity, nor patient gender or seropositivity of rheumatoid factor or ACPA.
Conclusion: Low serum levels of IgG, IgM and IgA are seen mostly with RTX exposure, but appear with other treatment exposures as well, which may influence the rate of future infections. Even if our study lacks assessment of baseline Ig levels, it is clear that treatment option has an influence on Ig levels. Future studies are needed to clarify all contributors to these results.
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AB0215 DOES THE PARITY IMPROVE THE RHEUMATOID ARTHRITIS ACTIVITY?

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Background: The parity seems to decrease the risk of auto-immune diseases like Rheumatoid arthritis (RA). The risk reduction appeared when the parity number reached two [1]. The activity of RA improved during pregnancy and flares postpartum, but the relationship of parity to RA prognosis is unclear. The impact of childbirth on disease activity is less studied.
Objectives: We aimed to investigate the impact of parity on rheumatoid arthritis activity.
Methods: We conducted a retrospective study including patients fulfilling the American Congress Of Rheumatology / European League Against Rheumatism (ACR EULAR) 2010 criteria.
We collected epidemiological, clinical, biological (C-reactive protein: CRP, erythrocyte sedimentation rate (ESR), immunological status (rheumatoid factor RF and anti-citrullinated protein/peptide antibody ACPA), and disease activity index (The Disease Activity Score 28 DAS 28). We divided our patients into two groups: group (G1): the nulliparous women; group 2 (G2): women who gave birth.
Results: Ninety-two patients were enrolled. There were 14 men and 78 women. The mean age was 59.56 ± 11.7 years. The mean disease duration was 9.32 ± 8.22 years. Among 78 women, we found 50 patients with parity. The main swollen joint was 3.34 ± 3.6 in G2 versus 4.44 ± 4.04 in G1 (p=0.94). The mean painful joints were 6.74 ± 5.12 and 9 ± 9.19 (p=0.28), respectively. However, the inflammatory syndrome is higher among women in G2. The mean CRP level was 15.1 mg/l, and the mean ESR was 37.7 mm. In G1, the RF and ACPA were 131 UI/l and 281 UI/l, respectively compared with 568 UI/L and 315UI/l, respectively in G2.
A significant difference was noted in the DAS28-CRP between the two groups (G2: 4.18 ±1.23 versus G1: 4.49 ± 2.5, p=0.04).
However, no association was found between parity and disease activity using the DAS28-ESR.
Conclusion: Our study showed that parity could have a protective effect on disease activity. It seems to be associated with a lower joint count and a lower rate of RF and ACPA. However, more studies are necessary to conclude these issues.
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AB0216 FATIGUE ASSESSMENT IN RHEUMATOID ARTHRITIS, SANTO DOMINGO, DOMINICAN REPUBLIC

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Background: Rheumatoid arthritis (RA) is an inflammatory, systemic autoimmune disease affecting the synovial membrane of small joints.[1] Wagan A. et al demonstrated that the frequency of fatigue in rheumatoid arthritis is 62%,[2] Hammam et al described a higher rate of fatigue associated with higher disease activity. Fatigue is as a feeling of exhaustion, also as a reduction in physical and mental capacity,[3,4] it can be measured with the scale FACIT-F (Functional Assessment of Chronic Illness Therapy-Fatigue), which evaluates the last 7 days, with a score of 0-52. For the severity analysis, 4 grades are used: no or mild fatigue (40-52), moderate (27-39), severe (14-26) and extreme fatigue (0-13).[2,5]
Objectives: To evaluate the frequency and degree of fatigue in rheumatoid arthritis.
Methods: Prospective, observational, cross-sectional study of a cohort of patients of the Rheumatology Service of the Hospital Docente Padre Billini. Patients were interviewed in July 2021. Inclusion criteria: ≥ 18 years, diagnosis of RA according to the ACR/EULAR 2010 classification criteria. Exclusion criteria: previous diagnosis of fibromyalgia, depression or anxiety, treatment with antidepressants, antihistamines, beta-blockers. Scales measured: FACIT-F, DAS28, CDAI, and HAQ-DI. Statistical analysis was performed with the Pearson correlation (r_p). Data were analyzed in IBM-SPSS v23.
Results: 597 patients met inclusion criteria. 93% female, mean age 58.5±12.4 years, mean disease duration 7.5 years. HT 73.9% (441), DM 14.2% (85), dyslipidemia 21.3% (127), obesity 17.9% (107), smoking 9.9% (59), high ESR 60.0% (358), high CRP 49.7% (297), scDMARD8 2.7% (494), bDMARDS 36.8% (218), tsDMARDS 18.1 (108). Frequency of fatigue 19.9% (119): moderate 12.9% (77), severe 7.0% (42). Correlation of FACIT-F with DAS28, CDAI and HAQ-DI: No fatigue FACIT-F 80.1% (478): DAS28 remission or low activity 84.9% (406), CDAI remission or low activity 93.5% (447), moderate 4.0% (19), high activity 2.5% (12), HAQ-DI mild 75.9% (363), moderate 16.5% (79), severe 7.5% (36). Moderate FACIT-F 12.9% (77): DAS28 remission or low activity 19.5% (15), moderate 80.5% (62), CDAI moderate 48.1% (37), high activity 51.9% (40), HAQ-DI mild 24.7% (19), moderate 63.6% (49), severe 11.7% (9). Severe FACIT-F 7.0% (42): DAS28 remission or low activity 4.8% (2), high activity 95.2% (40), CDAI low activity or remission 35.7% (15), high activity 64.3% (27), HAQ-DI mild 7.1% (3), moderate 23.8% (10), severe 69.0% (29). Correlation between FACIT-F/DAS28 (r_p= .673, p< .001) and FACIT-F/CDAI (r_p= .701, p < .001) were strong.
Conclusion: The study showed a low frequency of fatigue; the degree of fatigue most found was moderate. The group of patients with fatigue had a statistically significant linear association with disease activity and degree of functional limitation. There were no patients with extreme fatigue.
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AB0217 FREQUENCY OF SEXUAL DYSFUNCTION IN RHEUMATOID ARTHRITIS, SANTO DOMINGO, DOMINICAN REPUBLIC

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Background: Rheumatoid arthritis (RA) is an inflammatory, autoimmune systemic disease that affects the synovial membrane of small joints.[1] Kamissoko et al found the frequency of sexual dysfunction in RA to be 69.2%.[2] Pain is considered to have a fundamental role associated with the decrease in the frequency of sexual intercourse.[3] The CSFQ-14 (Changes in Sexual Functioning Questionnaire), evaluates the changes in sexual functioning due to a disease and/or treatment in 5 domains with a score range of 14-70; cut-off point indicating sexual dysfunction <41 men and <47 women.[4]
Objectives: To evaluate the frequency and degree of sexual dysfunction in patients with rheumatoid arthritis.
Methods: Prospective, observational, cross-sectional study of a cohort of patients of the Rheumatology Service at Hospital Docente Padre Billini. Patients were interviewed in July 2021. Inclusion criteria: > 18 years, diagnosis of RA according to the ACR/EULAR 2010 classification criteria, at least 1 sexual intercourse. Exclusion criteria: previous diagnosis of another autoimmune disease, depression, diabetes, treatment with antidepressants, antiepileptics, narcotics. Scales measured: CSFQ-14, DAS28. Statistical analysis was performed with the Pearson correlation (r_p) with p>0.05. Data were analyzed in IBM-SPSS v23.
Results: Of the RA cohort, 483 met inclusion criteria. 93.4% (451) female, mean age 58±12.6 years, mean duration of diagnosis 8 years, married 53.8% (260), single 27.7% (134), widowed 16.6% (80), hypertension 73.9% (357), dyslipidemia 21.5% (104), obesity 18.0% (87), smoking 9.9% (48). Frequency of sexual dysfunction 61.3% (296). Sexual dysfunction in women 93.9% (278) and men 6.1% (18). Global domains: desire/interest 55.7% (165), desire/frequency 56.4% (167), pleasure 58.1% (172), arousal/excitement 67.2% (199), orgasm/completion 50.0% (148). Female: desire/interest 94.5% (156), desire/frequency 93.4% (156), pleasure 93.6% (161), arousal/excitement 93.0% (185), orgasm/completion 93.9% (139). Male: desire/interest 5.5% (9), desire/frequency 11.6% (11), pleasure 6.4% (11), arousal/excitement 7.0% (14), orgasm/completion 6.1% (9). Desire/interest dysfunction: DAS28 remission or low activity 28.5% (47), moderate 53.3% (88), high activity 4.8% (8). Desire/frequency: DAS28 remission or low activity 35.3% (59), moderate 47.3% (79), high activity 3.6% (6). Pleasure: DAS28 remission or low activity 30.2% (52), moderate 50.0% (86), high activity 2.9% (5). Arousal/excitement: DAS28 remission or low activity 25.1% (50), moderate 55.8% (111), high activity 6.0% (12). Orgasm/completion:

DAS28 remission or low activity 43.2% (64), moderate 38.5% (57), high activity 6.1% (9).

Conclusion: The study showed a high frequency of sexual dysfunction, observing greater dysfunction in females. In the population, the most affected global domain was arousal/excitement, and it was the most frequent in female and male.

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AB0218 ASSOCIATION OF PULSE PRESSURE AND CAROTID INTIMA MEDIA THICKNESS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients have increased cardiovascular risk than the general population. Systemic inflammation causes a proatherogenic state in this group of patients (1). The carotid ultrasound is a useful diagnostic tool for the detection of subclinical atherosclerosis; however, it is not available for all patients. Pulse pressure, defined as the difference between systolic and diastolic blood pressure, has been associated with atherosclerosis in the general population (2). Information in RA patients is lacking.

Objectives: We aimed to correlate pulse pressure and carotid intima media thickness (cIMT) in RA patients.

Methods: This was a cross-sectional study. We recruited a total of 92 patients with RA diagnosis, according to the 2010 EULAR/ACR classification criteria, aged 40-75 years. Patients with a previous cardiovascular event, another connective tissue disease or pregnancy were excluded. A B-mode carotid ultrasound was performed in all patients by a certified radiologist blinded to clinical information. cIMT was measured in the left and right carotid arteries. An average of both cIMT was obtained for each patient for this analysis. Correlation between pulse pressure and cIMT was determined with the Spearman's correlation coefficient (rs). A p-value <0.05 was considered statistically significant.

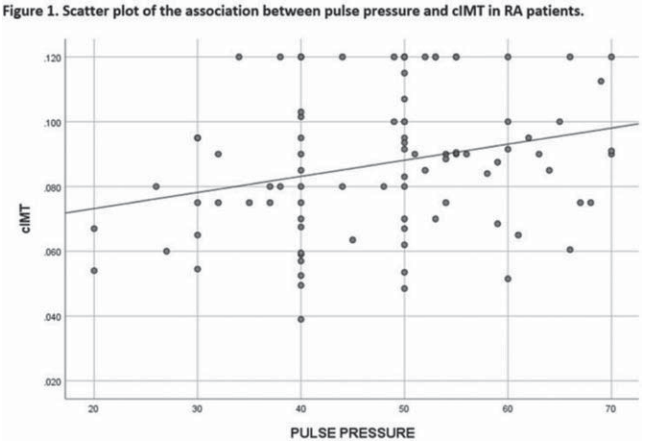
Results: Mean age of RA patients was 58.9 ± 6.6 years. Most of them were women (92.4%), with a median disease duration of 10.5 (4.2-17.5) years. Median cIMT was 0.08 (0.07-0.10) mm, and median pulse pressure was 50 (40-55) mmHg (Table 1). We found a significant positive correlation between pulse pressure and cIMT in RA patients (rs = 0.254, p = 0.015) (Figure 1).

Table 1. Demographic and disease characteristics.

Characteristics	RA patients (n=92)
Age, years, mean ± SD	58.9 ± 6.6
Women, n (%)	85 (92.4)
T2DM, n (%)	17 (18.5)
Hypertension, n (%)	33 (35.9)
Dyslipidemia, n (%)	30 (32.6)
Obesity, n (%)	30 (32.6)
Active smoking, n (%)	11 (12.0)
Disease duration, years, median (IQR)	10.5 (4.2-17.5)
CRP, mg/dL, median (IQR)	0.70 (0.51-1.22)
ESR, mm/h, median (IQR)	21.0 (13.0-33.2)
Pulse pressure, mmHg, median (IQR)	50 (40-55)
cIMT, mm, median (IQR)	0.08 (0.07-0.10)

RA, rheumatoid arthritis; T2DM, type 2 diabetes mellitus; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; cIMT, carotid intima media thickness.

Figure 1. Scatter plot of the association between pulse pressure and cIMT in RA patients.



Conclusion: Higher pulse pressure was associated with higher cIMT in RA patients. Pulse pressure may be useful for the detection of high-risk patients who would benefit from a carotid ultrasound evaluation, to identify patients with high cIMT.

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Disclosure of Interests: None declared

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AB0219 ASSOCIATION OF DISEASE ACTIVITY AND THE PRESENCE OF BILATERAL CAROTID PLAQUE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Cardiovascular (CV) disease is the major cause of death of RA patients. There is a direct association of systemic inflammation and an accelerated process of atherosclerosis, which is related to higher CV morbimortality (1). Additionally, RA patients with bilateral carotid plaque (CP) had a two-fold risk of developing a CV event compared to patients with unilateral CP (2).

Objectives: To compare disease activity and other disease characteristics of RA patients with bilateral and unilateral CP.

Methods: This was a cross-sectional study nested of a RA patients' cohort. We recruited RA patients who fulfilled the 2010 ACR/EULAR classification criteria. Patients with a previous CV event, another connective tissue disease, or pregnancy were excluded. Disease activity was assessed with DAS28-CRP. A carotid ultrasound was performed to all RA patients, and the presence of CP was considered as a carotid intima media thickness ≥ 1.2 mm or a focal narrowing ≥ 0.5 mm. All RA patients with bilateral CP were included in this study and matched by age (± 5 years), gender, and traditional CV risk factors to RA patients with unilateral CP by a rheumatologist blinded to clinical information. Comparisons were done with Chi-square test for qualitative variables and Student's T test or Mann-Whitney's U test for quantitative variables. A p-value < 0.05 was considered statistically significant.

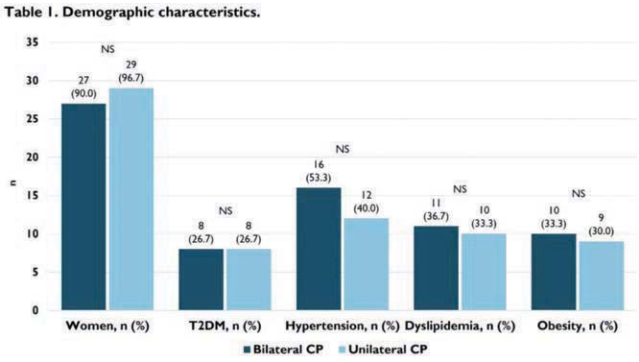
Results: Mean age of RA patients with bilateral CP was 61.98 ± 6.82 years as compared to 59.70 ± 6.74 years in patients with unilateral CP (p = NS). Demographic characteristics are shown in Figure 1. When comparing disease characteristics, we found a difference in C-reactive protein (CRP) levels, higher in patients with bilateral CP (1.06 mg/dl vs 0.64 mg/dl, p = 0.012), in disease activity assessed with DAS28-CRP as a continuous variable, higher in patients with bilateral CP (3.83 vs 3.05, p = 0.023), and as moderate-high disease activity classification, more prevalent in patients with bilateral CP (70.0% vs 43.3%, p = 0.037) (Table 1). A binary logistic regression, including traditional CV risk factors and disease activity, showed that classification of disease activity in the

moderate-high activity category is an independent risk factor for the presence of bilateral CP, OR 3.18, 95% CI 1.033-9.812, p = 0.044.

Table 1. Comparison of disease characteristics.

Variables	RA patients with bilateral CP (n=30)	RA patients with unilateral CP (n=30)	*p-value*
Disease duration, years, median (IQR)	7.86 (2.97-19.18)	9.02 (6.45-13.66)	NS
CRP, mg/dl, median (IQR)	1.06 (0.67-1.93)	0.64 (0.43-1.06)	0.012
DAS28-CRP, mean ± SD	3.83 ± 1.27	3.05 ± 1.32	0.023
Moderate-high activity, n (%)	21 (70.0)	13 (43.3)	0.037
Anti-CCP, median (IQR)	15.30 (3.16-196.15)	115.73 (1.60-196.05)	NS
FR IgG, median (IQR)	5.84 (2.00-17.13)	5.25 (2.00-20.41)	NS
FR IgM, median (IQR)	156.86 (27.91-200.00)	197.22 (65.71-200.00)	NS
FR IgA, median (IQR)	85.87 (13.60-200.00)	46.83 (5.33-129.93)	NS
MTX, n (%)	22 (75.9)	21 (70.0)	NS
GC, n (%)	16 (55.2)	11 (36.7)	NS
bDMARD, n (%)	3 (10.3)	6 (20.0)	NS

NS, no significant; RA, rheumatoid arthritis; CRP, C-reactive protein; anti-CCP, anti-cyclic citrullinated peptide antibodies; RF, rheumatoid factor; MTX, methotrexate; GC, glucocorticoids; bDMARD, biologic disease modifying antirheumatic drugs.



Conclusion: We found that RA patients with bilateral CP had higher levels of CRP levels, higher DAS28-CRP, and a higher prevalence of being classified in the moderate-high disease activity category, which was independently associated to the presence of bilateral CP. Emphasis should be placed on tight disease control to prevent the development of a major CV events in RA patients.

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AB0220

FACTORS ASSOCIATED WITH CAROTID INTIMA MEDIA THICKNESS REDUCTION IN RHEUMATOID ARTHRITIS PATIENTS: A FOLLOW-UP STUDY

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Background: Rheumatoid arthritis (RA) patients have higher risk of developing cardiovascular (CV) events than the general population. Traditional CV risk algorithms have been shown to underestimate the real CV risk of RA patients (1). For this reason, current CV risk guidelines state that a carotid ultrasound could be considered as part of the CV evaluation of these patients.

Objectives: To describe the carotid ultrasound changes in the follow-up of RA patients, and to compare demographic and disease characteristics in patients who had a reduction of carotid intima media thickness (cIMT) and those who did not.

Methods: Longitudinal, observational, and prospective study. A total of 39 RA patients were included in this study. A first evaluation, including a carotid ultrasound, laboratory analyses, and clinical history, was performed at the time of inclusion. Posteriorly a follow-up carotid ultrasound was performed. Patients were divided into two groups, those with reduction of cIMT in both carotid arteries, and those who remained with the same measurements or had an increase of cIMT. Comparisons were done with Chi-square test or Fisher's exact test for qualitative variables and Student's T test or Mann-Whitney's U test for quantitative variables. A *p*-value < 0.05 was considered statistically significant.

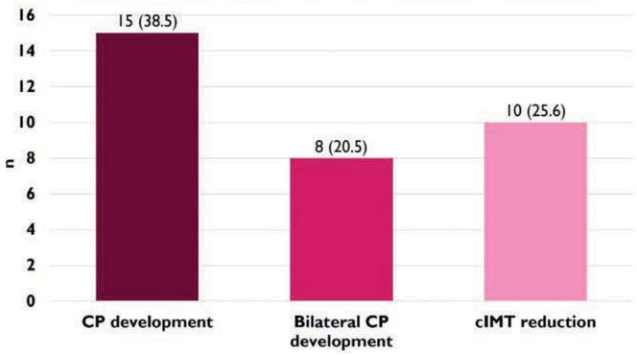
Results: Median follow-up was 4.66 (4.33-5.00) years. When evaluating changes in the carotid ultrasound findings, 15 (38.5%) patients developed CP, 8 (20.5%) patients developed bilateral CP, and 10 (25.6%) patients had a reduction of cIMT at the follow-up (Figure 1). When comparing baseline characteristics, we found that patients with reduction of cIMT were younger (48.88 years vs 59.30 years, $p = 0.004$), with a lower prevalence of dyslipidemia (0% vs 34.5%, $p = 0.040$), had lower levels of erythrocyte sedimentation rate (ESR) (14.50 mm/h vs 28.0 mm/h, $p = 0.024$), and had higher prevalence of normal levels of ESR (<20 mm/h) (80.0% vs 27.6%, $p = 0.007$) than patients who remained with the same measurements or had an increase of cIMT (Table 1). A multivariate analysis was performed, including variables with a *p*-value < 0.05, and we found that normal ESR was an independent factor associated with reduction of cIMT, with an OR 8.63 (1.27-58.33), $p = 0.027$.

Table 1. Baseline characteristics of patients with and without reduction of cIMT.

Baseline characteristics	Patients with cIMT reduction (n=10)	Patients without cIMT reduction (n=29)	*p-value*
Demographic characteristics			
Age, years, mean ± SD	48.88 ± 8.59	59.30 ± 9.46	0.004
T2DM, n (%)	0 (0)	3 (10.3)	NS
Hypertension, n (%)	1 (10)	11 (37.9)	NS
Dyslipidemia, n (%)	0 (0)	10 (34.5)	0.040
Active smoking, n (%)	0 (0)	2 (6.9)	NS
Obesity, n (%)	6 (60)	8 (27.6)	NS
Treatment			
Statins, n (%)	2 (20)	7 (24.1)	NS
MTX, n (%)	9 (90)	23 (79.3)	NS
GC, n (%)	6 (60)	16 (55.2)	NS
Disease characteristics			
ESR, mm/h, median (IQR)	14.50 (9.00-21.25)	28.0 (17.0-42.0)	0.024
ESR <20 mm/h, n (%)	7 (70)	8 (27.6)	0.027
CRP, mg/dl, median (IQR)	0.75 (0.45-1.26)	0.91 (0.66-1.26)	NS
DAS28-ESR, mean ± SD	4.30 ± 1.04	4.66 ± 1.09	NS
DAS28-CRP, mean ± SD	3.23 ± 0.90	3.49 ± 1.06	NS

cIMT, carotid intima media thickness; T2DM, type 2 diabetes mellitus; MTX, methotrexate; GC, glucocorticoids; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28, disease activity score 28 joints.

Figure 1. Carotid ultrasound changes in follow-up of rheumatoid arthritis patients.



Conclusion: Our results show that patients without dyslipidemia and with lower ESR levels, a proinflammatory biomarker, had a reduction in cIMT, which decreases the risk of developing a major CV event. Emphasis should be placed on tight control of disease activity and traditional CV risk factors. A follow-up carotid ultrasound evaluation in RA patients may be necessary, to identify those who would benefit from an opportune treatment.

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Disclosure of Interests: None declared

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AB0221 DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS IN THE CLINICAL PRACTICE OF A RHEUMATOLOGY CENTER

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Objectives: To compare the features of the disease course and the therapy in rheumatoid arthritis (RA) patients who meet and do not meet the difficult to treat (D2T) criteria.

Methods: RA patients admitted to the V.A. Nasonova Research Institute of Rheumatology for therapy correction from March to October 2021were included. All patients fulfilled the RA criteria of ACR/EULAR 2010. According to the opinion of the attending physician, they needed correction of therapy, so they were sent to the expert commission to confirm the expediency of using biologic or targeted synthetic (ts) disease-modifying antirheumatic drugs (DMARDs).

Results: 295 RA patients with high or moderate disease activity according to DAS28 were included. The expert commission in all cases confirmed the validity of administration of biologic or ts DMARDs. 111 (37.6%) patients (group A) were prescribed these drugs for the first time due to the unsatisfactory result of the use of conventional synthetic (cs) DMARDs, 105 (35.5%) patients were planned to continue treatment with previously used biologic or ts DMARDs after a break associated with various reasons (group B). In 54 (18.3%) cases, first biologic or ts DMARD failed so second biologic or ts DMARD was prescribed (group C). The D2T group included 25 (8.4%) patients with a history of inefficiency or intolerance of 2 or more biologic or ts DMARDs of different mechanisms of action. The duration of RA in the D2T group was significantly longer than in the rest of the patients (respectively 15.9±11.8 and 11.9±9 years, p=0.04). Radiological changes of joints in D2T RA were more significant than those in the rest of the patients. The III or IV Steinbrocker stage og RA in the D2T group was detected in 18 (72%) while in the remaining patients - in 130 (48.1%) cases (p=0.02). At the same time, there was a correlation between the duration of RA and the X-ray stage (p<0.0001). At the time of hospitalization, patients with D2T had higher inflammatory activity than group B patients who continued therapy with biologic or ts DMARDs. In groups A and C, all the analyzed signs of inflammation were also significantly higher than in group B (p <0.05). Methotrexate had been most often prescribed as the first cs DMARD in all groups but at the time of hospitalization, patients with D2T RA were more likely than other patients to remain without DMARDs (in 8 (32%) and 39 (14.4%) cases respectively, p=0.03). 73.3 - 84% of patients in all groups earlier received glucocorticoids (GC). At the time of hospitalization, the dose of GC in D2T group was higher than in other patients and averaged 8.3±5.1 mg /day and 6.4±2.9 mg / day, respectively, p=0.02. The proportion of patients taking GC in the D2T group was also higher than that among other patients, but these differences did not reach statistical significance. In D2T RA, adverse events associated with biologic DMARDs occurred more often than in groups B and C (respectively in 9 (36%) and 15 (9.4%) patients; p=0.001).

Conclusion: The formation of D2T RA in our patients could be associated with the prescribing of higher doses of GC and insufficient use of DMARDs. The development of D2T RA was accompanied by a more pronounced progression of radiological changes of the joints than in other patients.

Disclosure of Interests: None declared

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AB0222 THE ALBUMIN TO GLOBULIN RATIO AS A NOVEL INFLAMMATORY MARKER OF RHEUMATOID ARTHRITIS

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Background: The albumin to globulin ratio (AGR) has recently been identified as a new prognostic factor in patients with several types of cancer. However, the correlation of AGR and the disease activity in patients with rheumatoid arthritis (RA) have not been reported.

Objectives: This study aimed to explore the clinical value of AGR in RA and its association with disease activity.

Methods: This retrospective study collected 137 RA patients and 82 age- and sex-matched healthy controls. Neutrophil, lymphocyte, monocyte, platelet, albumin, globulin, AGR, neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), platelet to lymphocyte ratio (PLR), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Disease Activity Score of 28 joints-ESR (DAS28-ESR) and other laboratory parameters were recorded. Receiver operating characteristic (ROC) curves were used to determine the area under curve (AUC) value. The relations between inflammatory indexes and DAS28-ESR were checked.

Results: The AGR was lower in RA patients than in healthy subjects ($P < 0.05$) and decreased significantly along with the disease activity of RA patients ($P < 0.05$). According to the ROC curve which was conducted to discriminate RA patients from healthy individuals, the AGR (0.881, 95% CI: 0.837 - 0.924) showed the highest AUC than albumin (0.868, 95% CI: 0.823 - 0.914), globulin (0.789, 95% CI: 0.729 - 0.849), NLR (0.801, 95% CI: 0.742 - 0.859), MLR (0.762, 95% CI: 0.699 - 0.826) and PLR (0.803, 95% CI: 0.745 - 0.860). Spearman analyses showed that AGR was reversely associated with DAS28-ESR (r = -0.545, $P < 0.001$). Besides, the relevance between AGR and DAS28-ESR was higher than albumin (r = -0.381, $P < 0.001$), globulin (r = 0.492, $P < 0.001$), NLR (r = 0.444, $P < 0.001$), MLR (r = 0.189, $P = 0.027$) and PLR (r = 0.423, $P < 0.001$).

Conclusion: The results demonstrated that the AGR was decreased in RA patients and may be a potential marker for monitoring the disease activity of RA patients.

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Disclosure of Interests: None declared

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AB0223 COXITIS AND ATLANTOAXIAL SUBLUXATION IN RHEUMATOID ARTHRITIS: IS THERE A LINK?

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Background: Rheumatoid arthritis (RA) is an autoimmune chronic inflammatory disease that can over time be debilitating and life threatening vital prognosis through Atlantoaxial subluxation(ASS) and functional prognosis through coxitis.

Objectives: The aim of this work was to determine the correlation between coxitis and AAS in RA.

Methods: We performed a cross-sectional comparative study including 182 patients with RA meeting the ACR-EULAR 2010 criteria in a rheumatology department during the period from 2000 to 2021. The socio-demographic, clinical and radiological features were collected.

Results: Among the 182 patient enrolled, 16.4% (n=30) of patients had coxitis: unilateral in (90.24%; n = 27) and bilateral in (9.76%; n = 3). The coxitis was significantly found in males with a percentage of 40% vs 13.5% in females (p=0.01). As it for the AAS, it was noted in 13.3% of our patients more frequently in males 41.2% vs 17.8% in females (p=0.044).

The discovery of AAS on standard radiographs was fortuitous in 70.4% of cases (systematic radiographic assessment for structural assessment of RA) and in 29.6% of cases presenting an inflammatory neck pain.

Cervical MRI was pathological in 63.4%. The abnormalities observed on MRI were: C1 – C2 synovitis (47.6%), confirmed LAA (42.9%) and basilar impression (9.5%).

C1-C2 instability was presumed anterior (90.9%), lateral (6.1%) and rotatory (3%). Two patients had basilar impression.

The occurrence of an atlantoaxial subluxation was significantly correlated to the anterior presence of a coxitis (p=0.000).

Conclusion: Our study suggest that in RA, the presence of a coxitis;mostly in males; can be a predictive factor for the occurrence of AAS but further studies are needed to confirm these results.

Disclosure of Interests: None declared

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AB0224 JAK-INHIBITORS ATTAIN A RAPID AND PERSISTENT EFFECTIVENESS ON SEVERAL PATIENT-REPORTED OUTCOMES IN LONG-STANDING RHEUMATOID ARTHRITIS

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Milan, Italy; [3]AO Mauriziano, Università degli Studi di Torino, Academic Rheumatology Centre, Torino, Italy; [4]Spedali Civili di Brescia, Department of Rheumatology, Brescia, Italy

Background: Janus kinase inhibitors (JAKi) are efficacious drugs for the control of disease activity in rheumatoid arthritis (RA). The effect on patient-reported outcomes (PROs) has been shown in randomized clinical trials, but is still largely unknown in real-life scenarios.
Objectives: To assess the time to onset and magnitude of improvement across a number of different PROs in patients with RA treated with JAKi.
Methods: Patients were selected from centres involved in the LORHEN Registry. Patients with a diagnosis of RA initiating a JAKi (Baricitinib or Tofacitinib) between May 2019 and February 2020 were clinically assessed at baseline, 8 weeks and 16 weeks with DAS28 and SDAI. PROs were collected at baseline, 2 weeks, 4 weeks, 8 weeks and 16 weeks from JAKi initiation. The PROs assessed at each timepoint were: Patient Global Assessment (PGA), General Health (GH), 0-100 mm visual analogue scale (VAS)-pain, VAS-fatigue, Health Assessment Questionnaire (HAQ), The Clinical Arthritis Activity (PRO-CLARA) questionnaire.
Results: Thirty-eight patients (female 76%, mean age 57±15) were enrolled for a total of 152 visits for PROs assessments. Patients had received a median of 2 (IQR 1;3) previous conventional synthetic DMARDs (csDMARD) and a median of 2 (0;3) biological DMARDs. Mean disease duration at time of JAKi initiation was 10±9.5 years. JAKi was prescribed as combination therapy with a csDMARD in 20 (53%), concomitant glucocorticoids (GC) in 28 (73%) patients, at a mean dose of 6±2 mg/day. Twenty-one (55) patients were on regular analgesics. DAS28-ESR reduced from 4.5±0.9 at baseline to 2.6±0.9 at 8 weeks (p<0.001). DAS28-ESR remained stable between 8 and 16 weeks (mean values 2.3±0.1; p=0.17). Similarly, DAS28-CRP reduced from 4.1±0.8 to 2.1±0.6 at 8 weeks (p<0.0001). Between 8 and 16 weeks there was a further significant reduction of DAS28-CRP under the effect of JAKi treatment to a mean value of 1.4±0.5 (p<0.0001). SDAI reduced over the period of observation from 19±8 to 6±5 at 8 weeks (p<0.0001), and to 4±3 at 16 weeks (0.03). By week 8 the intake of concomitant GC reduced to 28% of patients (p=0.0001), and of analgesics to 2% of patients (p<0.0001).
By two weeks, all PROs had a significant reduction compared to baseline (Figure 1). For PGA, VAS-pain, VAS-fatigue a further significant reduction was observed by week 4 to then stabilize between week 8 and 16. GH and HAQ had a significant reduction by week 2 and remained stable thereafter. All PROs were significantly lower during all time-points compared to baseline. The PRO-CLARA Road score to assess physical function significantly improved starting from week 2 from a score of 4±2 to 2±2 at the end of follow-up. The PRO-CLARA self-administered tender joint count was stable at week 2 (mean score 4±2) but recorded an improvement from week 4 onwards (p<0.03).

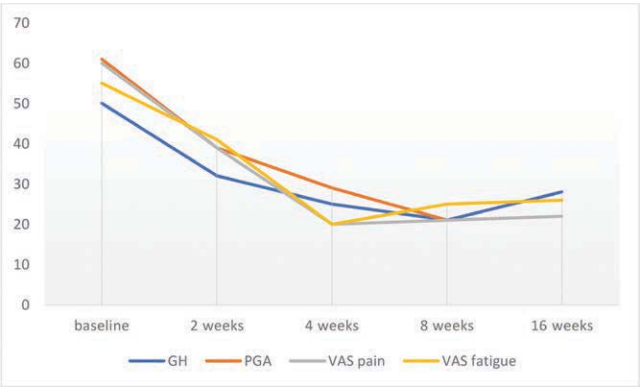

Figure 1. Improvement of patient-reported outcomes over the period of observation

Conclusion: Treatment with JAKi ensures a very rapid and persistent improvement of several PROs, including pain, fatigue and physical function, as early as 2 weeks treatment even in patients with long-standing RA treated with several lines of previous DMARDs.
Disclosure of Interests: None declared
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AB0225 FRAX ASSESSMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS PREDICTED THE REAL INCIDENCE OF CLINICAL FRACTURES FOR 10 YEARS FROM THE RESULTS OF THE 10-YEAR TOMORROW STUDY

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Background: To investigate if FRAX in patients with RA can predict the incidence of new clinical fractures for 10 years by using the 10-year data of the TOMORROW study (UMIN000003876) which is a prospective cohort study.
Objectives: To investigate if FRAX in patients with RA can predict the incidence of new clinical fractures for 10 years by using the 10-year data of the TOMORROW study (UMIN000003876) which is a prospective cohort study.
Methods: We calculated ten-year probability of major osteoporotic fracture (FRAX) in 208 RA patients and 205 sex- and age-matched volunteers (Vo), and compared FRAX with the incidence of clinical fractures for 10 years.
Results: The mean FRAX were 14.5 and 8.8% in 175 RA patients and 168 Vo, respectively, in whom we could calculate FRAX at baseline and complete to investigate the incidence of clinical fractures for 10 years from baseline. The mean FRAX in RA patients was significantly higher than that in Vo (P<0.001). The actual incidence of clinical fractures for 10 years in RA patients was significantly higher than that in Vo (33.9 vs 22.9%, P=0.031). In both groups, the actual incidence of clinical fractures was higher than FRAX prediction. Logistic regression analysis revealed that FRAX and FRAX≧15% were the significant risk factors for clinical fractures for 10 years in both groups (Odds ratio (OR), 1.055, P<0.001, 2.943, P=0.043, respectively). The mean FRAX in RA patients with and without clinical fractures for 10 years were 18.5 and 12.5%, respectively (P=0.002). In RA patients, FRAX was also the significant risk factor for clinical fractures (OR, 1.046, P=0.004).
Conclusion: FRAX and the incidence of clinical fractures for 10 years were significantly higher in RA patients than them of Vo. We confirmed that FRAX was the risk factor for clinical fractures in actual clinical practice.
Disclosure of Interests: None declared
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AB0226 CLINICAL SIGNIFICANCE OF SOLUBLE ST2 IN PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE THE APPOINTMENT AND AFTER 12 MONTHS OF TREATMENT WITH BIOLOGICAL DRUGS (PRELIMINARY DATA).

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Background: The role of soluble ST2, the IL-33 receptor, in the pathogenesis of rheumatoid arthritis (RA) is discussed in the literature.
Objectives: to assess the levels of soluble ST2 marker initially (against the background of ineffective basic anti-inflammatory therapy (DMARD) and after 12 months of combination therapy (DMARD + biological therapy).
Methods: The study included 47pts (39 women /8 men) with RA, 51 [39,0; 63,0] years old. Pts were seropositive for IgM RF (79%) and anti-CCP (62%), with highly active RA (DAS28 5,7 [5,2; 6,4]; SDAI 35,0 [29,1; 43,6], CDAI 34,0 [25,0; 43,0]) scores, and median disease duration of 4.0 [3,0;14.0] years. All patients with RA had a history of insufficient effect or intolerance to two or more basic anti-inflammatory drugs (DMARDs). At the time of inclusion in the study, patients received DMARDs: 44% of patients received methotrexate (median dose - 15 (15; 20) mg /week), 35% - leflunomide (20 mg / day), 9.3 % - sulfasalazine (2000 mg / day), 7% - hydroxychloroquine (200 mg / day), 67.4% - glucocorticoids (5 (4; 8) mg / day). Patients did not receive biological

therapy at the time of inclusion in the study. Due to lack of efficacy or intolerance, patients with RA (n=21) were prescribed biological therapy: 52.4% - anti-B-cell therapy, 38% - TNF-alpha inhibitors, 9.6% - IL-6 inhibitors. The control group consisted of 20 age-matched donors without rheumatic diseases. The concentration of soluble ST-2 was determined by enzyme immunoassay (Cristal Diagnostics, San Diego). The upper limit of normal when testing 20 sera from healthy donors was 17,65 ng/ml, corresponding to the 95th percentile.

Results: The serum level of soluble ST2 in patients with late RA (n=47) was higher than in the control group (n=20) (14.2 [11.5;20.1] ng/ml versus 10.65 [9.3; 13.1 ng/ml) (p<0.001). Patients with RA and elevated serum ST2 levels (≥17.65 ng/mL) were older than patients with ST2 levels ≤17.65 ng/mL (58.5 [50;68] vs 47, 0 [38;59] years) (p=0.007). In the group of patients (n=21) who received combination therapy for 12 months, there was a statistically significant decrease in clinical and laboratory activity, levels of RF IgM and soluble ST2 in blood serum, compared with baseline (13.8 [11.5; 18.4] ng/ml vs 12.5 [9.6;13.8] ng/ml (p<0.05 in all cases).(Table 1). In the group of patients (n=21), after 12 months of combination therapy, direct correlations were noted between the delta (Δ) of the level of soluble ST2 and Δ DAS28 (R=0.59; p=0.006), Δ CRP (R=0.55; p =0.01), Δ anti-CCP (R=0.49; p=0.04).

Table 1.

	Patients with RA (n=21) with insufficient effect of basic anti-inflammatory therapy	Patients with RA (n=21) after 12 months of receiving combination therapy	Δ,%	p
BMI, kg/m^2	24,16 (21,23; 26)	25,15 (23,43;26,7)	+4,1	0,8
DAS28	5,6 (5,3; 6,7)	3,97(3,36;4,63)*	-30,4	**0,0001**
SDAI	38,17 (29,5; 45,8)	17,2(9,57;25,6)*	-54,8	**0,0001**
CDAI	35,0 (26,0; 43,5)	17,0(9,0;23,5)*	-51,4	**0,0001**
CRP,mg/l	20,6 (11,7;34,1)	3,15(1,2;7,2)*	-84,7	**0,003**
ESR,mm/h	27,0 (16,0;45,0)	16,0 (10,0;23,5)*	-40,7	**0,003**
IgM RF, ME/ml	84,4 (20,8;163,0)	32,2(10,6;107)*	-61,8	**0,01**
ST-2, ng/ml	13,8 (11,5;18,4)	12,5(9,6;13,8)*	-9,4	**0,008**

* -p <0.05 reliability of differences in indicators before and after 12 months of combination therapy (Wilcoxon); Δ,% - the difference in indicators between the groups by the 12th month of combination therapy.

Conclusion: In patients with high RA activity and the ineffectiveness of basic anti-inflammatory therapy, the level of soluble ST2 in serum was increased compared to the control group. After 12 months of effective anti-rheumatic therapy, the level of this marker decreased. The association of this marker with the clinical and laboratory activity of RA suggests its role in the development of rheumatoid inflammation.

Disclosure of Interests: None declared

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AB0227 TREATMENT SEQUENCING PATTERNS AND COMPARATIVE EFFICACY IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM A REAL-WORLD SETTING

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Background: The European League Against Rheumatism (EULAR)[1] recently provided updated guidelines regarding the initiation and modification of disease-modifying antirheumatic drug (DMARD) therapy in patients with Rheumatoid Arthritis (RA). Therefore, real-world evidence studies are warranted to provide insights into first-line DMARD utilization and durability of response in the second-line setting.

Objectives: To analyze RA treatment patterns in real-world data and compare durability of response between second-line DMARDs + anti-TNF (TNFi) therapies vs. TNFi monotherapy.

Methods: Electronic health records (EHRs) from a large health system in the Northeast US were used to identify RA patients. Lines of therapy were defined based on confirmed prescriptions for DMARDs and TNFi therapies. Time to next treatment (TTNT) was the primary outcome to estimate durability of response. Time-to-event analyses were performed using Kaplan-Meier and log-rank test methods. In addition, a Cox Proportional-Hazards (CoxPH) model was used to evaluate covariates as independent predictors of disease progression.

Results: Our study cohort consisted of 8,040 patients who had at least one line of therapy for RA. Conventional synthetic DMARDs (csDMARDs) were the predominant first line of therapy in this dataset (71.3%), followed by TNFi alone (11.1%) or TNFi combined with csDMARD (9.1%) (Figure 1).

For patients who had csDMARD as their first line of therapy, 22.93% progressed to second line treatment. Among them 36.2% patients were TNFi with or without in combination with csDMARDs. In the second-line, TNFi + csDMARDs were associated with a longer TTNT (median time: 13.1 months vs 6.1 months, P < 0.005) compared to TNFi monotherapy. The multiple variable CoxPH model (adjusted for age, gender, and race) demonstrated that second-line TNFi + csDMARDs had a lower hazard rate when compared to TNFi monotherapy (HR = 0.74, 95% CI: 0.36 - 1.12, p < 0.005).

Conclusion: We demonstrated the first comprehensive treatment sequencing patterns in RA from a real-world setting. As a second-line therapy for patients with inadequate response to csDMARDS, the TNFi + csDMARDs combination may improve duration of response when compared to TNFi monotherapy. Results from this study will inform future sequencing strategies to improve patient outcomes.

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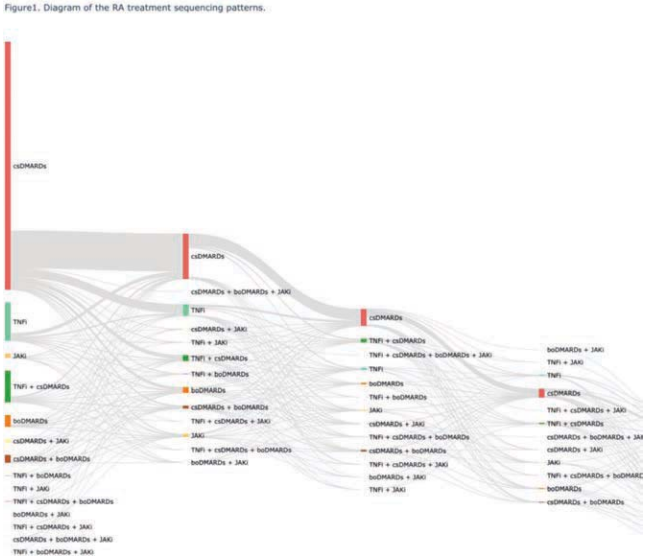
Figure1. Diagram of the RA treatment sequencing patterns.



Disclosure of Interests: Lei Ai: None declared, Mitchell Higashi: None declared, Kyeryoung Lee: None declared, Zongzhi Liu: None declared, Lan Jin: None declared, Kalpana Raja: None declared, Yun Mai: None declared, Tomi Jun: None declared, William Oh Consultant of: Janssen
Pfizer, Aviva Beckmann: None declared, Emilio Schadt: None declared, Zachary Schadt: None declared, Rick Wallsten: None declared, Ediz Calay: None declared, Andrew Kasarskis: None declared, Qi Pan: None declared, Eric Schadt Speakers bureau: Eli Lilly, Consultant of: SAB of Eli Lilly
Celgene, Xiaoyan Wang: None declared

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AB0228 THE CONNECTION BETWEEN NUTRITIONAL STATUS AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Nutritional status is closely associated with a person's physical condition. As for patients with autoimmune disease, nutritional status may affect the balance of immune system, which successively affects disease activity.

Objectives: The prognostic nutritional index (PNI), nutritional risk index (NRI), controlling nutritional status (CONUT) score and body mass index (BMI) are four widely used nutritional indices [1]. This study aimed to investigate the relationship between nutritional status and disease activity of rheumatoid arthritis (RA).
Methods: 168 RA patients and 50 healthy volunteers were retrospectively enrolled. According to the disease activity score using 28 joint counts-erythrocyte sedimentation rate (DAS28-ESR), the cohort of RA patients was divided into the lower disease activity groups (DAS28-ESR≤3.2) and the higher disease activity groups (DAS28-ESR>3.2). We recorded clinical assessment and laboratory data for further analysis. Spearman's correlation, receiver operation characteristic (ROC) curves, binary logistic regression analysis were carried out.
Results: Compared to the higher disease activity group, the lower disease activity group had low-level total protein (TP), ESR and CRP (all P<0.05), while high-level albumin and PNI (all P<0.05). PNI and NRI were negatively correlated with DAS28-ESR (r=-0.395, and r=-0.200, all P<0.05), while CONUT score was positively correlated with DAS28-ESR (r=0.324, P<0.05). ROC curve illustrated that area under the curve (AUC) of PNI for RA patients with higher disease activity was superior to NRI, CONUT score and BMI. The AUC of PNI was 0.693.

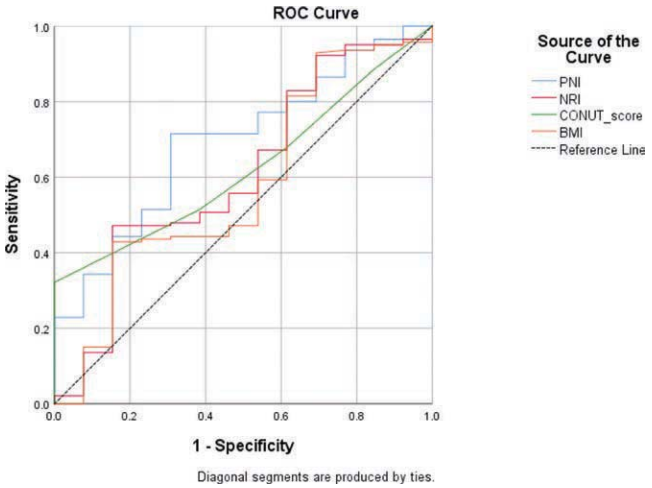

Figure 1. The diagnostic value of variables for disease activity in rheumatoid arthritis using ROC curve

Table 1. The correlation between nutritional indices and disease activity score using 28 joint counts-erythrocyte sedimentation rate (DAS28-ESR)

	PNI		NRI		CONUT score		BMI	
	r	*P* value	r	*P* value	r	*P* value	r	*P* value
Neutrophil(×10^9/L)	-0.061	0.434	0.045	0.568	0.025	0.757	0.079	0.313
Monocyte(×10^9/L)	0.183	0.163	0.145	0.064	-0.104	0.193	0.152	0.052
Lymphocyte(×10^9/L)	0.472	0.000	0.201	0.010	-0.436	0.000	0.208	0.007
ESR (mm/h)	-0.561	0.000	-0.258	0.001	0.393	0.000	-0.182	0.020
CRP (mg/L)	-0.520	0.000	-0.077	0.326	0.391	0.000	0.003	0.967
RF(IU/ml)	-0.224	0.004	-0.116	0.151	0.260	0.001	-0.082	0.306
CCP(IU/ml)	-0.139	0.088	-0.201	0.014	0.195	0.018	-0.188	0.022
DAS28-ESR	-0.395	0.000	-0.200	0.011	0.324	0.000	-0.142	0.072

Conclusion: PNI may become a manageable marker for detector disease activity of RA patients.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.4657

AB0229 ACHIEVING GLUCOCORTICOID FREE MIGHT DECREASE RISK FOR CLINICAL FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS - TEN-YEAR FINDINGS FROM THE TOMORROW STUDY

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Background: Patients with rheumatoid arthritis (RA) who have muscle weakness and stiff or painful joints might be at increased risk of falls and fractures.
Objectives: The present study prospectively investigates correlations between decreasing doses of glucocorticoid (GC) and the incidence of clinical fractures in patients with RA based on the ten-year findings of the TOMORROW study (UMIN000003876) that started in 2010.
Methods: We evaluated anthropometric parameters, bone mineral density, disease activity, RA medication, and the incidence of clinical fractures over a period of ten years in 202 patients with RA (mean age, 58.6 years; mean disease duration, 14.0 years). We also investigated the effects of GC doses on the incidence of clinical fractures over the same period in patients with RA using multivariate regression analysis.
Results: The incidence of clinical fractures for ten years in patients with RA was 0.036/person-year. There were 89 patients (44.1%) treated with GC at least once during ten years. The incidences of clinical fractures in patients with RA treated with and without GC during ten years were 0.052 and 0.026/person-year, respectively. After adjusting for fracture risk factors including age, sex, smoking, and body mass index, cox proportional hazard model revealed that GC dose of ≥ 2 mg/day at baseline was a significant risk factor for clinical fractures (Hazard ratio [HR]:2.430; 95%CI, 1.040-5.675, p=0.040). Although the risk for clinical fractures did not decrease by just reducing the dose of GC (HR:4.505; 95%CI, 0.589-34.457, p=0.147), it was significantly lower if the dose of GC could be reduced to zero during ten years (HR:0.407; 95%CI, 0.194-0.857, p=0.018).
Conclusion: Medication with even low dose of GC are apparently significantly associated with an increased frequency of clinical fractures among patients with RA. However, if the dose of GC was reduced to free during ten years, the clinical fracture risk could become lower. We concluded that we should decrease the dose of GC to free after controlling disease activity of RA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.4682

AB0230 THE INFLUENCE OF THE PATIENT'S PSYCHOLOGICAL STATUS ON THE INFLAMMATORY ACTIVITY OF RHEUMATOID ARTHRITIS

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Objectives: To examine the relationship between rheumatoid arthritis (RA) activity indicators and psychological factors of patients receiving the therapy according to the "Treat to target" (T2T) strategy.
Methods: The research included 93 patients with early RA (16 men and 77 women), average age Me;IQR (58 [49; 66] years), the duration of the disease 7 [4-11,5] months. All patients were prescribed a subcutaneous form of methotrexate (MT) at an initial dose of 10 mg / week with a rapid escalation of the dose to 20-30 mg / week. If the effectiveness of the therapy was insufficient, biologics were prescribed. During the first year, patients received the therapy according to the concept of T2T, then they were observed in the «real-life» clinical practice. After 6 years, the patients were re-examined. Clinical examination was performed including patient global assessment (PGA), functional status was determined by HAQ, the nature of pain by painDETECT, the presence of anxiety and depression – by HADS.
Results: Before the start of the therapy, the DAS 28-ESR was 5.31 [4.79; 6.14], SDAI – 28.27 [18.79; 40.73], CDAI-25 [17; 36], HAQ – 1,32 [0,75; 1,25]. After 6 years DAS28-ESR 4 [3,4; 4,59], SDAI-15,06 [9,32; 21], CDAI-15 [9; 21], HAQ - 0.5 [0.25; 1], PGE - 35 [20; 50].; activity of disease according to DAS28-ESR: remission in 7.8%, the low activity in 21.3%, the moderate activity in 60.6%, the high activity in 11.2% of patients.
29 patients had subclinically or clinically expressed anxiety (≥8 according to HADS), of whom10.3% had remission/low disease activity, 89.7% had moderate/high disease activity.
18 patients had subclinically or clinically expressed depression (≥8 according to HADS), of whom remission/low disease activity in 16.6%, the moderate/high activity was in 83.4%. In 35 patients, the painDETECT questionnaire revealed possible or probable neuropathic pain, remission/low disease activity of the was revealed in 20%, moderate/high activity in 80%. Depending on the presence of anxiety and depression, all patients were divided into two groups

(Table 1). Among patients with depression, there was a greater severity of PGE pain, and more expressed functional disorders. In the group of patients with anxiety, there was a higher disease activity (according to DAS28-ESR), the severity of pain according to PGE and functional disorders; there were no significant differences between the groups in terms of ESR and CRP indicators (Table 1).

Table No1. Influence depression and anxiety symptoms of inflammatory activity

Parametres	Depression positive, n=18	Depression negative, n=75
DAS28-ESR	4,4 [3,8; 5]	3,9 [3,1; 4,5]
ESR, mm/hr	16 [13; 25]	16 [9; 27]
CRP, mg/l	1,5[0,6; 2,9]	2,4 [1; 5,9]
HAQ	1[0,75; 1,37]*	0,5[0; 1]*
PGA	52,5 [35; 70]*	30 [15; 50]*
	Anxiety positive, n=29	Anxiety negative, n=64
DAS28-ESR	4,4 [3,8; 4,9]*	3,18[2,9; 4,4]*
ESR, mm/hr	20[11; 33]	15[9; 25]
CRP, mg/l	1,9 [1; 3,3]	2,5[1; 5]
HAQ	1[0,5; 1,37]*	0,5[0; 0,8]*
PGA	50 [35; 70]*	25[10; 40]*

Conclusion: The presence of depression and anxiety negatively influences the activity of RA, leading to an increase in pain and worsening of the functional disorders. To prescribe an adequate anti-rheumatic therapy, it is necessary to take into account not only the activity of RA, but also the psychological status of the patient

Disclosure of Interests: None declared

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AB0231 PROGNOSTIC UTILITY OF METACARPAL BONE MINERAL DENSITY MEASUREMENT IN PATIENTS WITH RECENT-ONSET ARTHRITIS BY ASSESSMENT OF RADIOGRAPHIC PROGRESSION AT 2-YEAR FOLLOW-UP

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Background: Rheumatoid arthritis (RA) and osteoporosis (OP) have a complex interplay in terms of pathogenic mechanisms. In this regard, radiogrammetry (DXR) of the hand, a technique that measures the bone mineral density (BMD) at the central metacarpals (MC), is associated with a worse prognosis in patients with RA (1). However, DXR is an expensive technique, and not very accessible in our environment. Our group demonstrated an excellent reproducibility of the MC measurement by DXA (2) and good correlation between BMD measurements obtained by DXR and DXA (3).

Objectives: To evaluate if baseline BMD of the non dominant MC measured by DXA can be used as a prognostic marker, resembling DXR, in patients with early arthritis (EA).

Methods: A total of 378 subjects from the PEARL (Princesa Early Arthritis Register Longitudinal) study underwent DXA measurement of the 2nd to 4th MC's diaphyseal area of the non dominant hand (Hologic 4500). In PEARL sociodemographic, clinical and laboratory parameters, therapeutic data and radiographic findings are collected by protocol. Radiographic progression was evaluated in hands by a blind expert rheumatologist assessing the erosion scale of modified SvdH index in both the baseline and two year follow-up visit. To study the predictive value of MC baseline BMD by DXA, two multivariate models were fitted using generalized linear models with Stata 14.0 for Windows (Stata Corp LP, College Station, TX, USA). The dependent variables were remission (SDAI<3.3) and radiographic progression after two 2 years of follow-up. Both models were adjusted by the classic variables that affect BMD such as age, sex and body mass index (BMI), cumulative DMARD treatment and baseline disease activity for the remission model.

Results: After adjustment by age, sex and BMI: a) those patients at remission tended to show higher baseline MC's BMD by DXA (p=0.328); and b) those patients with higher radiographic progression had significantly lower baseline MC's BMD as shown in Figure 1(p=0.001).

Conclusion: In our registry of patients with EA, we have detected that a lower basal BMD in the diaphysis of the central MC bones, assessed by DXA, is associated with greater radiographic progression at 2 years of follow-up after adjusting for the main factors influencing BMD. Therefore, we could conclude that a low initial bone mass could constitute a poor prognostic factor in patients with EA.

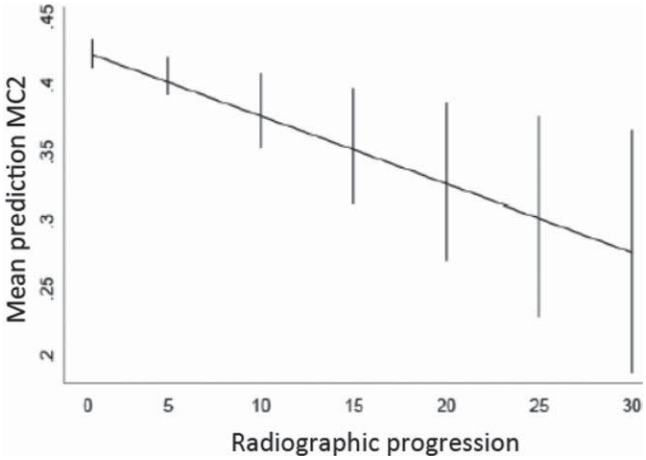

Figure 1. Correlation of mean BMD of 2-4th MC bones with radiographyc progression assesed by the modified SvdH radiological index at 2 years, after adjusting for age, sex and BMI, calculated using Stata margins command base don the data obtained from multivariate analysis.

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AB0232 THE USEFULNESS OF THE PROGNOSTIC NUTRITIONAL INDEX (PNI) FOR THE DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Many prognostic factors and laboratory biomarkers have been put forward to correlate disease activity in Rheumatoid arthritis (RA). The prognostic nutritional index (PNI) was first established to assess perioperative immunonutritional status and surgical risk in patients undergoing gastrointestinal surgery. The PNI, which reflects albumin concentration and lymphocyte count, is a newly established inflammation-based nutritional score.

Objectives: In this study, we aimed to determine the relationship between this simple risk index, which was first adapted and analyzed in malnourished patients, and disease activity in RA patients.

Methods: This prospective study included 77 RA patients who fulfilled the 2010 revised criteria of the American College of Rheumatology for RA. The demographic characteristics of the patients, duration of the disease and clinic characteristics of the patients such as the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate (DAS28-ESR), Visual Analogue Scale, Health Assessment Questionnaire-Disability Index were collected. Labotaruvary findings including erythrocyte sedimentation rate, C-reactive protein levels, lymphocyte count, albumin were noted. The PNI was calculated using the following formula: 10 x serum albumin value (g/dL) + 0.005 x total lymphocyte count in the peripheral blood (per mm^3). Based on the DAS28-ESR level, the included patients were categorized into two groups, namely, inactive to mild active RA (n=31; DAS28-ESR level <3.2) and moderate to highly active RA (n=46; DAS28-ESR level ≥3.2). These groups were compared with the parameters described above.

Results: Seventy-seven patients (90.9% female) with a mean age of 53.6 (SD:10.2) years were recruited into the study. The age, gender and disease therapy duration of the patients were similar in both groups. Patients who DAS28-ESR ≥3.2 had a significantly lower PNI compared to those who did not [41,57 (SD:3,64) *vs*. 43,78 (SD:2,30), *p*=0.017] (Table 1). Multivariate logistic regression analyses revealed that PNI was an independent predictor of moderate to highly active RA (OR: 0.770, 95%CI: 0.635–0.935; *p*=0.008). A receiver operating characteristic curves analysis yielded that the optimal cut-off value of PNI for moderate to highly active RA was 42.01 with sensitivity 67.7% and specificity 47.9% (AUC: 0.662, 95%CI: 0.541-0.782, p=0.017) (Figure 1).

Table 1. Demographic, clinical features and laboratory findings of the patients with rheumatoid arthritis based on disease activity measured by DAS28-ESR

	DAS28-ESR <3.2 n=(31)	DAS28-ESR ≥3.2 n=(46)	P value
Age (years; mean SD)	55,80 SD 9,39	52,13 SD 10,67	0.124
Female, gender, n (%)	26(%83,9)	44(%95,7)	0.111
Prognostic Nutritional Index (mean SD)	43,78 SD 2,30	41,57 SD 3,64	***0,017***
Disease symptoms duration (month; mean SD)	112,2 SD 97,3	120,9 SD 79,7	0.316
Disease therapy duration (month; mean SD)	93,2 SD 94,2	110,0 SD 76,0	0.126
DAS28-ESR (mean SD)	2,55 SD 0,47	4,47 SD 0,85	<0.001
Visual Analogue Scale (mm, mean SD)	7,38 SD 16,58	20,17 SD 25,76	<0,001
Health Assessment Questionnaire-Disability Index (mean SD)	0,69 SD 0,62	0.84 SD 0,60	0,259
ESR (mm/h, mean SD)	26,35 SD 18,98	31,73 SD 16,95	0.083
CRP (mg/L, mean SD)	6,30 SD 4,49	12,75 SD 19,54	0.106
Albumin (g/dl, mean SD)	4,37 SD 0,23	4,15 SD 0,36	0.010
Lymphocyte (cells/µL, mean SD)	2,01 SD 0,62	2,07 SD 0,65	0.570

Abbreviations: DAS28-ESR, the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

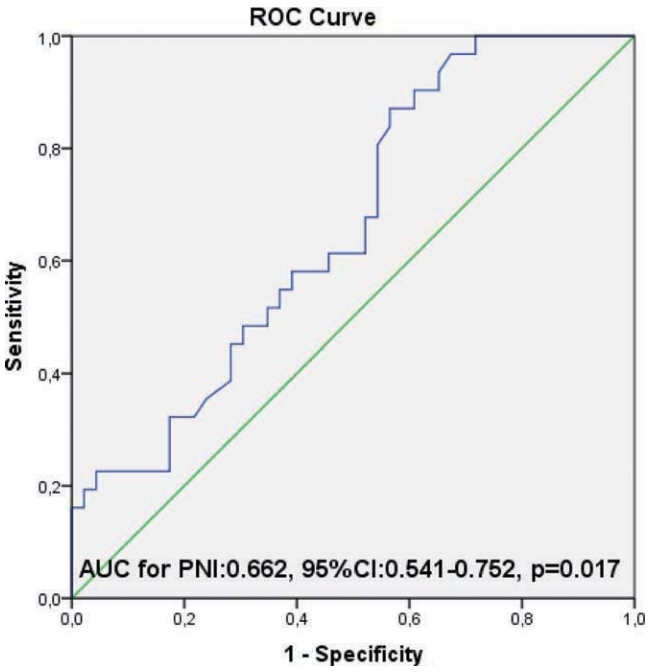

Figure 1.

Conclusion: Based on the study findings, we were able to show that simple and easily obtained PNI could be an independent predictor of disease activity in rheumatoid arthritis patients.

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AB0233

CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A TWO YEARS OBSERVATIONAL STUDY.

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Background: The risk of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) is higher than individuals from the general population due to chronic inflammation. Current CV risk screening and management strategies underestimate the actual CV risk in RA. Thus, an adequate CV risk stratification has special relevance in RA to identify patients at risk of CV disease.

Objectives: To assess the incidence of cardiovascular events in a RA cohort after a 2 years follow-up.

Methods: A cohort study was performed in which inclusion criteria were adult RA patients and matched adults in terms of age, sex and CV risk factors (controls). Population over 75 years old, patients with established CV disease and/or stage III chronic kidney disease were excluded. Controls with other inflammatory diseases, pregnant women or any malignancy were also excluded. This study was performed from July-2019 to January-2022. CV risk assessment included risk factors collection and US evaluation consisted in detection of plaques and measurement of the intima-media thickness in both right and left carotid.

Results: Overall, a total of 200 cases and 111 healthy controls were enrolled in the study. Demographical and clinical variables were comparable between cases and controls and are shown in Table 1. US study revealed a higher IMT in both right and left carotid arteries with greater presence of plaques in patients than in controls (CI 95% [1.542; 3.436], p<0.001). Plaques were found in both carotid arteries in the 32% of cases and 9.91% of controls. The longer duration of RA was related to a higher presence of carotid plaques (95% [1.015; 1.056], p<0.001).

Table 1. Demographic, clinical characteristics and Ultrasound results of patients and controls.

Characteristic	RA cases n=200	Healthy controls n=111
Age - years	62.05 (10.75)	58.3 (12.14)
Female sex – number (%)	163 (81.5)	73 (65.77)
BMI – value (ds)	26.38 (5.03)	26.2 (5.19)
Smoking habit		
Never Smoked	107 (53.5%)	71 (63.96%)
Ex-smoker	51 (25.5%)	20 (18.02%)
Active smoker	42 (21%)	20 (18.2%)
Race – number (%)		
Caucasian	186 (93)	62 (93.94)
Comorbidities – number (%)		
High blood pressure	83 (41.5%)	34 (30.63%)
Dyslipemia	93 (46.5%)	39 (35.14%)
Blood pressure -- mmHg	127.2(18.36)/78.67(10.21)	127.77(19.42)/78.28 (10.59)
Ultrasound findings		
Right carotid cIMT	0.78 (0.15)	0.62 (0.11)
Left carotid cIMT	0.77 (0.14)	0.64 (0.12)
Plaques	101 (50.5%)	32 (28.83%)
Bilateral	64 (32%)	11 (9.91%)
Right carotid	17 (8.5%)	7 (6.31%)
Left carotid	20 (10%)	14 (12.61%)

Eight patients (4%) presented a cardiovascular event, and one of them died (0.5%). The events consisted in 2 angina pectoris, 3 transient ischemic attack, 1 acute myocardial infarction, 1 lacunar stroke and 1 cardiac arrest. Six out those 8 patients demonstrated bilateral plaque presence at baseline. Two patient caused loss of follow up due to death related to Covid-19. Not a single cardiovascular event was reported in the control group.

Conclusion: Our results shows that cardiovascular events are increased in RA patients and US study may be useful in predicting an event.

Disclosure of Interests: None declared

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AB0234 POTENTIAL CREDIBILITY IN RHEUMATOID ARTHRITIS PATIENT REPORTED DAS28 SCORES

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Background: Due to COVID-19 and the reduction of face to face clinic, the rheumatology telephone advice line service has been an integral part in identifying patients that need assessment the most (1). This however means relying on a patient's ability to conduct their own disease activity score (DAS28), which clinicians conduct to help drive patients with rheumatoid arthritis (RA) into remission. Current literature suggests that patient self-assessed joint counts are reliable and when compared to the joint count of the physician, have an acceptable level of accuracy (2-5). We present data from an NHS audit where we incidentally found that patients could conduct their own joint counts.
Objectives: Our objective was to compare self-reported DAS28 scores with the clinical opinion of physicians during a face-to-face appointment.
Methods: We identified 10 patients with RA who attended a face-to-face appointment following a call to the helpline where a telephone DAS28 score was undertaken (with guidance from rheumatology specialist nurses). These scores were contrasted against the clinician's assessment of whether synovitis was present or not in a face-to-face consultation. Co-morbidities: fibromyalgia (FM), osteoarthritis (OA) or both, were also recorded to examine whether these conditions influenced a patient's ability to perform an accurate DAS28 score.
Results: There were 10 patient self-reported DAS 28 scores in total. 70% (7/10) of patients DAS 28 scores were over 4.01. In all these cases, clinicians confirmed evidence of synovitis during their face-to-face consultation. 30% (3/10) of patients self-reported DAS 28 score was <4.01. Of these patients 2/3 have no evidence of synovitis according to their clinician. When considering co-morbidities, one individual also suffered from OA. This individual's self-assessed DAS28 score was over 4.01 and was also evidenced to have synovitis during their consultation with the clinician.

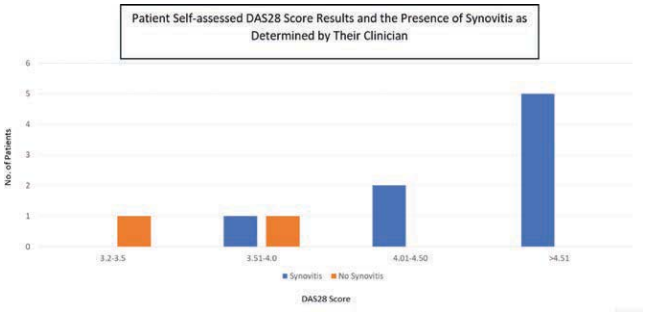

Figure 1. Shows patient's self-assessment DAS28 scores and whether synovitis was identified following a face to face consultation with a clinician.

Conclusion: This regional NHS audit found that patients who self-reported DAS28 scores over 4.01 accurately identified a flare up, as confirmed by a diagnosis of synovitis at a face-to-face appointment. This is significant as it demonstrates that patients who score above 4.01, can reliably assess their own joint count. This may enable the Rheumatology service to become more patient-driven, empowering patients to accurately assess their condition.
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AB0235 TREAT TO TARGET PATHWAY (T2T) IN INFLAMMATORY ARTHRITIS-DESIRABLE RESULTS? AND IF CERTAIN GROUPS RESPOND TO TREATMENT BETTER?

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Background: There is established evidence that treat to target strategy in inflammatory arthritis helps achieve early remission rates or low disease activity. This approach is more effective for improved outcomes at no additional costs and more likely to achieve rapid and sustained disease control. It is important to aim for early diagnosis to limit the structural damage that occurs with prolonged inflammation. Commencing disease modifying anti-rheumatic drugs (DMARD) therapy and glucocorticoids as early as possible and titrating therapy as appropriate improves clinical outcomes.
Objectives: Aim of this study was to analyse ACR20 response within different subgroups of inflammatory Arthritis patients enrolled in Treat to Target program.
Methods: Data collection was performed by assessing electronic medical records of 374 inflammatory arthritis patients who participated in Treat to Target pathway for inflammatory arthritis between 2014 to 2020.
In total 374 patients were enrolled in treat to target inflammatory pathway led by Rheumatology ANP with consultant supervision. Majority of the patients had diagnosis of Rheumatoid arthritis as per ACR/Eular criteria. 213(51%) were seropositive RF+, 83(19.9%) were seronegative RF-, 44(10.5%) were diagnosed as psoriatic arthritis, and 34(8.1%) were labelled as undifferentiated inflammatory arthritis. In terms of age and gender, 158(42%) were under 50, and 216(58%) were aged 50 and over, majority females 207(55%). Smoking status 118(32%) current, 211(56%) never, 45(12%) ex-smokers. DMARD started at baseline was Methotrexate only and Starting dose was 15mg for all patients. 326(88%) were on oral methotrexate and only 48(12%) were on SC form between weeks 1-20. ACR 20,50,70 responses were analysed for these subgroups with majority (61%) seen at week 6 for their visit 1 after starting T2T pathway while all patients seen by week 20.
Results: ACR 20,50 and 70 responses were calculated for all subgroups enrolled in T2T program. The results showed that ACR 20 response rate was same among patients aged under and over 50(67% responders), ACR 50 (38.3%) responders and ACR 70 (20.1%) responders. There was no significant difference in ACR 20 response among females and males (66.9% response) both groups. In terms of seropositivity, 75% responded to treatment in RF+ group vs 60% in RF-group. Higher response rates were seen among not current smokers vs active smokers(70%vs65%). ACR 20 response was greater in patients on Sc form of methotrexate. Overall, 65 % achieved remission within 15 months of starting T2T pathway while remaining achieved low disease activity. Further analysis and discussion will follow.
Conclusion: Treat to target strategy in inflammatory arthritis are consistent with real world data in achieving early response rates with methotrexate (ACR responses) and specific subgroups within T2T cohort respond better to treatment.

Disclosure of Interests: None declared
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Rheumatoid arthritis - comorbidity and clinical aspects

AB0236 PRESENCE OF ANTI-CITRULLINATED POLYPEPTIDE ANTIBODIES DECREASES BONE MINERAL DENSITY IN BODY OF PATIENT WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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Background: Presence of anti-citrullinated polypeptide antibodies (ACPA) is one risk factor of bone erosion of the joint in patients with rheumatoid arthritis (RA). However, bone absorption in the whole body is still not clarified in a longitudinal study.
Objectives: The aim of this study is to clarify effects of ACPA on bone mineral density (BMD) decrease using dual-energy X-ray absorptiometry (DXA) in patient with RA using retrospective longitudinal cohort study.
Methods: Patient with RA who were measured BMD in lumbar spine (LS) and total hip (TH) using dual-energy X-ray absorptiometry (DXA) at first consultation (baseline) and were treated for more than five years, were recruited. Follow-up started at BMD measurement and continued until the development of the first fracture or censoring at death, loss to follow-up or end of the study. Every patients have been followed up with monitoring of SDAI and Health Assessment Questionnaire Disability Index (HAQ) at every another to three months. Sharp/van der Heijde Score (SHS) was measured at baseline and every another year thereafter. BMD were measured every six months. Relationship between BMD and candidate risk factors including ACPA positivity and serum titer level, and other variants for BMD loss were evaluated statistically using linear regression analysis. Evaluations were performed for the absolute value of BMD and Z-score at baseline, mean value of these during follow-up, and change from baseline. Change of Z-score during follow-up was also compared between groups what classified according to ACPA positivity (ACPA positive/negative group).
Results: A total of 222 patients were recruited including 17 male (7.7%) and 205 female (92.3%). The mean age of the patients was 69.2 years old. Mean disease duration at baseline and follow-up length after baseline were 6.4 and 63.3 months, respectively. Mean SDAI score, HAQ score and SHS at baseline were 22.2, 0.516, and 6.6, respectively. The mean ACPA level and positive rate were 202.1 and 77.5%, respectively.
Higher ACPA titer level correlated significantly low BMD and Z-score in TH (p<0.05), whereas ACPA positivity significantly correlated with low Z-score in LS and TH during follow-up using univariate models (p<0.05). The ACPA positivity also correlated with decrease of Z-score in both LS and TH using univariate models (p<0.05), whereas no significant correlation demonstrated using multivariate model.
Change of Z-score in the ACPA positive group was significantly lower than in the ACPA negative group despite no significant difference of disease activity between the two groups demonstrated (p<0.05) (Table 1).

Table 1. Comparison of the two groups

	parameters	ACPA-positive (n=172)	ACPA-negative (n=50)	p-value
	female (%)	91.3	96.5	0.10
at baseline	age (year-old)	65.4	71.3	**<0.001**
	disease duration (months)	7.7	4.6	**<0.001**
	RF (IU/L)	138.3 (197.1)	21.5 (49.3)	**<0.001**
	SDAI	26.3 (24.0)	21.0 (17.8)	**<0.05**
	HAQ	0.496 (0.618)	0.553 (0.639)	0.48
	SHS	8.4 (8.2)	3.5 (5.0)	**<0.001**
	BMD in LS (g/cm2)	0.825 (0.167)	0.849 (0.156)	0.23
	BMD in H (g/cm2)	0.700 (0.140)	0.710 (0.132)	0.75
	Z-score in LS	-0.246 (1.300)	0.123 (1.392)	**<0.05**
	Z-score in TH	-0.062 (1.034)	0.261 (1.020)	**<0.05**
at follow-up	follow-up length (months)	64.8	65.4	0.65
	SDAI	4.5 (3.1)	5.1 (4.4)	0.22
	HAQ	0.495 (0.616)	0.516 (0.544)	0.32
	SHS	8.1 (8.2)	3.4 (4.8)	**<0.001**
	BMD in LS (g/cm2)	0.839 (0.171)	0.870 (0.165)	0.16
	BMD in TH (g/cm2)	0.710 (0.118)	0.713 (0.115)	0.99
	Z-score in LS	-0.008 (1.361)	0.368 (1.426)	**<0.05**
	Z-score in TH	0.129 (0.902)	0.396 (0.891)	0.11
	anti-osteoporotic drug administered, ever (%)	73.4	69.8	0.72
	GCS administered, ever (%)	35.8	32.9	0.68

The values are presented as mean (SD) unless indicated otherwise.Statistically significant within 0.05 are shown as bold styles.

Conclusion: Presence of ACPA potentially have an independent risk of BMD decrease. Its action affects regardless gender and age.

Disclosure of Interests: None declared
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AB0237 CHANGES AND CLINICAL SIGNIFICANCES OF PERIPHERAL REGULATORY T CELLS IN RHEUMATOID ARTHRITIS PATIENTS WITH CARDIOVASCULAR DISEASE

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Background: Rheumatoid arthritis (RA) is an independent risk factor for cardiovascular diseases (CVD), driven by the underlying chronic systemic inflammation [1]. The imbalance of $CD4^+$ T lymphocyte subsets, especially between T helper (Th) 17 cells and regulatory T (Treg) cells, can mediate autoimmune inflammatory process, promoting the overproduction of cytokines and abnormal antibodies [2,3]. However, the levels of peripheral Th17 and Treg cells in RA patients with CVD are still unknown.
Objectives: To explore the expression of circulating Th17 and Treg cells in RA patients with CVD and analyze its clinical significance.
Methods: A total of 192 patients with RA and 86 healthy controls (HCs) were enrolled from January 2019 to January 2021. The peripheral blood $CD4^+$T lymphocyte subsets of all participants were assessed by flow cytometry. Patients were divided into RA-CVD group (n=72) and RA only group (n=120), and the clinical data were recorded. The statistical differences between two groups were analyzed by independent-samples t test, χ^2 test or Mann-Whitney U test, and risk factors of CVD were analyzed using Logistic regression.
Results: ① The median age and the percentage of male patients in the RA-CVD group were significantly higher than those in the RA only group. ② The absolute numbers of peripheral Treg cells in the patients with RA only and RA-CVD were all significantly lower than those in HCs [24.94 (19.32, 34.12) cells/μl *vs.* 33.13 (24.96, 45.83) cells/μl , Z=-4.135 , P < 0.01; 19.13 (13.76, 27.34) cells/μl *vs.* 33.13 (24.96, 45.83) cells/μl , Z=-5.354 , P < 0.01]. While the numbers of peripheral Th17 cells in two groups of patients were not significantly different with those in HCs. The ratios of Th17/Treg cells in two group patients were higher than those of HCs, but only the difference between RA-CVD patients and HCs were significant [0.40 (0.23 , 0.63) *vs.* 0.18 (0.13 , 0.29) , Z=-4.696 , P < 0.01]. ③ Compared to the RA only patients, the absolute counts of Treg cells in RA-CVD patients were significantly lower [Z=-3.047 , P < 0.01], the numbers of Th17 cells were significantly higher [7.48 (3.72, 13.63) cells/μl *vs.* 5.59 (3.49 , 8.91) cells/μl , Z=-1.989 , P < 0.05], and the ratio of Th17/Treg cells was significantly higher [0.40 (0.23 , 0.63) *vs*. 0.23 (0.14 , 0.35) , Z=-4.289 , P < 0.01]. ④ Logistic regression analysis showed that the level of circulating Treg cells (*OR*=0.936, 95%*CI*: 0.906-0.968) was a protective factor, while Th17 cells (*OR*=1.068, 95%*CI*: 1.020-1.119), elder age (*OR*=1.039, 95%*CI*: 1.004-1.076) and hypertension (*OR*=2.712, 95%*CI*: 1.254-5.865) were independent risk factors of RA patients complicated with CVD.
Conclusion: It is suggested that the immune imbalance caused by the deficiency of Treg cells may be involved in the occurrence and development of RA complicated with CVD, and to restore Treg numbers and function may be a promising preventive strategies.
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AB0238 HEALTH-RELATED QUALITY OF LIFE AND CORRELATION WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with active rheumatoid arthritis (RA) are at risk for poor functional outcomes, affecting quality of life (QoL). SF-36 is a validated instrument to measure health-related quality of life (HRQoL) in various domains of physical and mental health[1], and has been validated in RA. Nevertheless,

data on the impact of RA disease activity on SF-36 scores in Greek patients are lacking.
Objectives: To compare SF-36 scores in Greek RA patients versus the general population and to assess the impact of disease activity on HRQoL.
Methods: Cross-sectional study in RA patients followed in the Department of Rheumatology, Asklepieio Voulas General Hospital (05-10/2021). Demographic characteristics, state of disease activity and current treatment for RA were recorded at most recent visit. All patients completed SF-36 questionnaires and were classified in three subgroups of DAS28-disease activity: i) Remission or Low disease activity (LDA), ii) Moderate disease activity (MDA), and iii) High disease activity (HDA). Data from the SF-36 validation study in the Greek general population with 1007 participants, were used as historical controls[2]. Descriptive statistics, one-way ANOVA and linear regression were used for statistical analyses.
Results: 107 patients participated in the study (80,4% females, mean (SD) age 63.3 (12.1) years, 64.5% seropositive, 72% overweight or obese). One third (n=36) were active smokers and 63% (n=67) were receiving a biologic disease modifying antirheumatic drug (bDMARD).
Patients with RA exhibited low scores in all SF-36 domains and reported significantly worse results compared to the general population (Figure 1).

Figure 1.

Physical component score (PCS) and Mental component score (MCS) of the SF-36 showed a negative correlation with DAS28 (β= -8.28, p= <0.001 and β= -6.2, p= <0.001, respectively). Patients with remission or LDA exhibited better SF-36 scores compared to the other subgroups; moreover, patients with MDA had better SF-36 scores than those with HDA (Table 1). When patients with MDA were further divided into low- and high-moderate disease activity (DAS28: 3,21-4,19 and 4,2-5,1, respectively), no significant difference in any SF-36 domain was found between the two groups.

Table 1.

SF-36 domain mean±SD	RDA or LDA 51%	MDA 37,2%	HAD 11,7%	p-value
PF	48,43 ±34,23	32,14 ±19,83	20 ± 19,75	**0.003**
RP	34,9 ±43,68	20,71 ± 32,92	0 ± 0	**0.015**
BP	51,2 ±30,47	28,24 ± 24,49	18,86 ± 23,54	**<0.001**
GH	48,83 ±45	41,57 ± 24,25	32,27 ± 19,54	**0.043**
VT	49,48 ±22,22	34,14 ± 18,57	30,91 ± 15,94	**0.001**
SF	52,16 ±35,33	40,36 ± 27,13	28,41 ± 14,89	**0.041**
RE	39,01 ±44,68	27,62 ± 40,81	18,18 ± 34,52	0.246
MH	54,08 ±23,24	47,57 ± 21,75	40 ± 18,59	0.124

Conclusion: HRQoL assessed by SF-36 is dampened in RA patients, in both physical and mental component. Disease activity had a negative impact on both physical and mental components of HRQoL. Patients with remission or LDA showed better HRQoL outcomes, suggesting that the treat-to-target approach may also positively affect QoL.
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AB0239 **HOW SOLID MALIGNANCIES ARE DETECTED IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: According to a meta-analysis reported in 2015[1)], among solid malignancies (cancers), only lung cancer was at an increased risk in patients with rheumatoid arthritis (RA) compared with the general population. A Japanese cohort study reported that the incidence of cancers in patients with RA treated with biological DMARDs was not significantly elevated compared to the Japanese general population[2)]. However, in recent years, malignancy has been one of the major causes of death in Japanese patients with RA[3)]. It has been reported that there was an increased incidence of malignancies in patients treated with tofacitinib compared to TNF-alpha inhibitors. Clinicians need to pay more attention to emerging malignancies.
Objectives: We explored how to detect cancer early in patients attending rheumatology outpatient clinics.
Methods: In this retrospective study, we studied 545 patients with RA who visited our rheumatology clinic between April 2011 and December 2021. Forty-five cases of cancer in 38 patients (31 women, 7 men) with RA were reviewed.
Results: Cancer types: 9 breast, 8 lung, 6 colon, 5 uterus, 4 stomach, 2 prostate, 2 pancreas and 9 others. Five female patients had metachronous or simultaneous double cancers and one male patient had metachronous triple cancers. The median age at diagnosis of 45 cancers was 72 years old (IQR 63–76.5) and the median duration of RA prior to cancer diagnosis was 10 years (IQR 5–20.5).
Lung: Seven cases were found by chest CT at the outpatient clinics; two at the start of bDMARDs and five during RA treatment.
Stomach and Colon: Two cases of four stomach cancers were discovered due to the progression of anemia. Both patients were at an advanced stage with distant metastasis and died 2 months after diagnosis. On the other hand, four of six colon cancers were detected by the fecal occult blood test, and three were in remission.
Of the 45 cases, only 8 cases were detected by cancer screening. In 15 cases, blood samples or imaging tests were the triggers cancer detection. Eight of the 15 cases were detected by routine examinations in the rheumatology outpatient clinic, but five cases were already in the advanced stage.

Table 1. Forty-five cancers in 38 patients with rheumatoid arthritis

		Clue to cancer diagnosis and prognosis at the final visit (death - under treatment - remission)					
Site of cancer	n	noticing symptoms		Various tests in outpatient clinic symptoms(-)		Cancer Screening	
Breast	9	8	(1-4-3)			1	(0-0-1)
Lung	8	1	(1-0-0)	7	(2-3-2)		
Colon	6			1	(1-0-0)	5	(0-1-4)
Stomach	4	1	(0-0-1)	3	(3-0-0)		
Cervix uteri	3	1	(0-0-1)			2	(0-0-2)
Corpus uteri	2	2	(0-2-0)				
Pancreas	2			2	(0-2-0)		
Prostate	2	2	(0-1-1)				
Skin*	2	2	(0-0-2)				
Oral/throat	2	2	(0-2-0)				
Duodenum	1	1	(0-0-1)				
Biliary tract	1	1	(0-1-0)				
Anus	1					1	(0-0-1)
Bladder	1			1	(0-0-1)		
Brain	1			1	(0-1-0)		
Total	45	21	(2-10-9)	15	(6-6-3)	9	(0-1-8)

Conclusion: We have been performing cancer screening before RA treatment and performing routine blood, urine, and imaging tests to identify adverse effects. However, they cannot always find cancers at the early stage. Screening procedures for malignancy are strongly recommended[4)], but the consultation rates for breast and cervical cancer screening are lower in Japan than in European nations. We should encourage our patients to undergo usual age- and sex-appropriate cancer screening.
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Disclosure of Interests: None declared
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AB0240 CORRELATION BETWEEN KLOTHO LEVELS AND ANKLE-BRACHIAL INDEX IN FEMALE RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) that is a chronic systemic and disabling disease affecting 0.5–1% of the general population, have been strongly linked to accelerated aterosclerosis and increased incidence of cardiovascular events and mortality. Klotho is a membrane-bound or soluble antiaging protein, whose protective activity is essential for a proper function of many organs. The association between serum Klotho and the classic risk factors, as well as the clinical history of cardiovascular disease, was also shown. There are a lot of evidences that Klotho deficiency correlates with the occurrence and development of coronary artery disease, atherosclerosis, myocardial infarction, and left ventricular hypertrophy.

Objectives: The aim of this study was to examine the possible association between serum Klotho levels and ankle-brachial index in women with RA.

Methods: This cross-sectional study was performed in Vega-Baja Hospital (Orihuela-Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive female patients affected by RA and followed at the Vega-Baja Hospital (Orihuela-Spain). All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/ European League Against Rheumatism (ACR/EULAR) criteria for RA. Ankle-brachial index were evaluated using a BIDOP model ES-100V3 vascular screening system (Hadeco, Inc, Kawasaki, Japan). Serum Klotho (Elabscience, USA) was analysed using ELISA.

Results: Our study included 63 female patients, with a mean (SD) age of 53 ± 8 years. The majority were Caucasian (90.5%). The mean duration of RA was 8.5 ± 5.8 years. Mean 28-joint disease activity scores (DAS28) based on erythrocyte sedimentation rate (ESR) indicated low disease activity 3.0 ± 1.3. The mean of the health assessment questionnaire (HAQ) was 0.75 ± 0.67. Mean serum Klotho levels were 4.68 ± 1.14 ng/mL. The mean value of the ankle-brachial index was 1.14 ± 0.1.

Lower serum Klotho levels were significantly associated with a lower ankle-brachial index (r 0.27, p<0.05).

Conclusion: Decreased serum Klotho levels are associated with peripheral arterial disease in women with RA.

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AB0241 COGNITIVE FRAILTY AND RISK OF FALLS AMONG EGYPTIAN OLDER ADULTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is chronic autoimmune disease, affecting bone cartilage and predominantly joints, and causing inflammation and pain [2]. RA patients have disease-specific risk factors, including greater impaired balance, tender and swollen joints, lower muscle strength in their lower limbs, fatigability and medication side effects which contributes to a predisposition for falls [1]. Frailty, which was originally considered a geriatric syndrome, is an age-related decline in physiological reserve (3). It is associated with reduced muscle strength, exhaustion and with high inflammatory markers contributing to perpetuation of the frailty cycle (4). The concept of frailty is a recent issue in the rheumatologic field; by now, the prevalence of frailty among elderly individuals with RA has not been extensively examined and few studies on frailty in RA adults have been conducted.

Objectives: To assess the prevalence of cognitive frailty in people with rheumatoid arthritis and the relationship between cognitive frailty and falls.

Methods: In this cross-sectional study we evaluated 105 patients 60 years old or more with rheumatoid arthritis who fulfilled the ACR 2010 criteria and attended to rheumatology outpatient clinic in Ain-Shams University hospitals. Data was collected regarding demography and comorbidities. For cognitive and frailty screening, the Montreal Cognitive Assessment (MOCA) and frail scale were used respectively. Cognitive frailty (CF) is a clinical condition characterized by the simultaneous presence of physical frailty and mild cognitive impairment without functional impairment.

Results: 105 older adult patients with RA were studied of whom (72.4%) were females. The mean age of the study population was 66.03. We found that (12.4%) of the study group were cognitively frail and the prevalence of falls among cognitively frail patients was 92.3%.

Table 1.

		No.= 105
Age	Mean±SD	66.03 ± 4.29
	Range	60 – 77
Gender	Female	76 (72.4%)
	Male	29 (27.6%)
Age/onset	Mean±SD	36.41 ± 4.65
	Range	27 – 48
Education	Not educated	40 (38.1%)
	Educated	65 (61.9%)
Cognitive frailty	No	92 (87.6%)
	Cognitively frail	13 (12.4%)
Frailty sore	Frail	47 (44.8%)
	Pre frail	41 (39.0%)
	Robust	17 (16.2%)

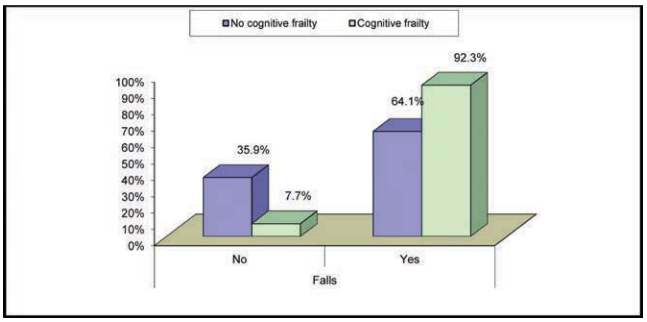

Figure 1.

Conclusion: The prevalence of cognitive frailty in geriatric people with rheumatoid arthritis was high and highly related to falls so screening for cognitive frailty in geriatric practice and the implementation of specific care is recommended.

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AB0242 RELATIONSHIP BETWEEN FALLS AND FALL RISK MEDICATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Falls are a serious event that can lead to disability and death. The use of hypnotics, anxiolytics, and antidepressants has been reported drugs associated with higher risk of falls. Rheumatoid arthritis (RA) is associated with a high risk of falls, which is an important issue because it can lead to fractures. Patients with RA have a higher incidence of sleep disorders, depression, and anxiety disorders. They are likely to be prescribed fall risk medications.

Objectives: We conducted a retrospective study of the incidence of falls in patients with RA, who are more prone to fractures and falls, using fall risk medications, especially hypnotics and anxiolytics, which aimed to determine the relationship between falls and fall risk medications in patients with RA.
Methods: This study is a retrospective cohort study conducted in Showa University Hospital between December 1, 2019 and March 31, 2020. We included of RA patients who visited the outpatient and fulfilled the American College of Rheumatology (ACR) /European League against Rheumatism (EULAR) classification 2010 criteria. The main exposure was the fall risk medication. The fall risk medication group was defined as RA patients who were prescribed fall risk medication (sedative/hypnotic, antidepressants, antipsychotics, and anxiolytic (benzodiazepines) drugs) for all the observational period. The comparison group was defined as RA patients who had never been prescribed any fall risk medications. Outcome measure was the prevalence of fall incidents in the past one year, obtained by using questionnaires to patients. Logistic regression analysis was performed to investigated the relationship between the prevalence of fall incidents and the use of fall-risk medications. The co-variables we selected were as follows: age, sex, stroke, dementia, diabetes and osteoarthritis as covariates.
Results: We obtained data from 331 patients, of which 303 were included in the analysis. Among the 303 patients, the median age was 67 years (56-75), and 78.5% were women. Of the 303 patients, 45 patients used fall risk medication and 69 patients experienced at least one fall in a year. Of the 45 patients who used fall risk medication, 18 patients experienced at least one fall in a year. Of the 69 patients who experienced falls, 30 patients experienced twice or more falls in a year. Of the 18 patients who used fall risk medication and experienced falls, 9 patients experienced twice or more falls. 4 patients were admitted to the hospital as result of falls, 2 patients used fall risk medication. These results are shown as percentages in Figure 1. The group of fall risk medication was significantly higher than using non fall risk medication. (adjusted odds ratio (AOR) 2.31, 95% Confidence Interval (CI) 1.14-4.68, p=0.02).

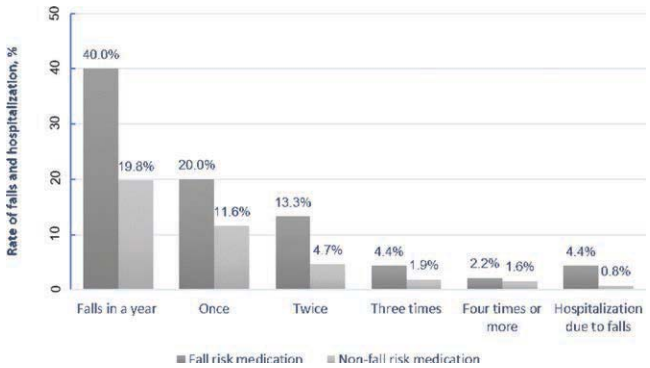

Figure 1.

Conclusion: Use of fall risk medications may have increased falls for patients with RA.
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AB0243 **ASSOCIATIONS BETWEEN JOINT DEFORMITY, DISEASE DURATION, DISEASE ACTIVITY, ACTIVITIES OF DAILY LIVING, QUALITY OF LIFE, PAIN, AND FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Patient with rheumatoid arthritis (RA) have disease-related problems such as joint deformity, disease duration, disease activity, activities in daily life (ADL), quality of life, pain, and fatigue. All these problems correlate interactively.
Objectives: Aim of this study is to clarify association among these problems statistically using retrospective cohort data.
Methods: Patients with RA who were followed up more than three years were recruited. Their EuroQol-5th dimension (EQ5D) as an indicator of quality of life (QOL), simplified disease activity index (SDAI) as an indicator of disease activity, Health Assessment Questionnaire Disability Index (HAQ) as an indicator of ADL, pain score using visual analog scale (PS-VAS), and fatigue score using visual analog scale (FS-VAS), were monitored every three months. Sharp/van der Heijde score (SHS) as an indicator of joint deformity was calculated annually. Association among average values of these factors and patient's sex, age, disease duration (DD), and anti-citrullinated polypeptide antibodies (ACPA) titer were evaluated using multivariate linear regression analysis. Statistical significance was set within 5%.
Results: A total of 447 patients, in whom 120 male and 327 female included, were analyzed. Mean age, disease duration, EQ5D score, SDAI score, HAQ score, SHS, PS-VAS, and FS-VAS during follow-up were 71.6-year-old, 12.9 years, 0.831, 4.26, 0.413, 46.9, 22.5, and 23.2, respectively.
EQ5D score correlated significantly with age, HAQ score, SDAI score, SHS, PS-VAS, FS-VAS, and DD using univariate models. In these, age, HAQ score, and FS-VAS correlated significantly using multivariate model (correlation coefficients (CC): 0.927). HAQ score correlated significantly with age, EQ5D score, SDAI score, SHS, PS-VAS, FS-VAS, and DD using univariate models. In these, EQ5D score, SHS, and FS-VAS correlated significantly using multivariate model (CC: 0.910). SDAI score correlated significantly with female gender, EQ5D score, HAQ score, SHS, PS-VAS, and FS-VAS using univariate models. In these, SHS and PS-VAS correlated significantly using multivariate model (CC: 0.620). SHS correlated significantly with age, female gender, EQ5D score, HAQ score, SDAI score, PS-VAS, and DD using univariate models. In these, HAQ score, SDAI score, and DD correlated significantly using multivariate model (CC: 0.685). PS-VAS correlated significantly with EQ5D, HAQ score, SDAI score, SHS, and FS-VAS using univariate models. In these, SDAI score and FS-VAS correlated significantly using multivariate model (CC: 0.732). FS-VAS correlated significantly with EQ5D score, HAQ score, SDAI score, and PS-VAS using univariate models. In these, EQ5D score, HAQ score, and PS-VAS correlated significantly using multivariate model (CC: 0.715). ACPA did not correlated with any factors significantly.
Conclusion: These results suggested that EQ5D score, namely QOL is influenced by various disease-related factors and aging, especially correlated with ADL and fatigue closely. The HAQ score, namely ADL level is influenced by fatigue level and joint deformity directly. The SDAI score, namely disease activity level correlated with pain level and joint deformity level, and correlates with the other factors indirectly. A schematic figure that represents relationships among factors were shown in Figure 1. These information would beneficial for conducting treatment protocol of RA.

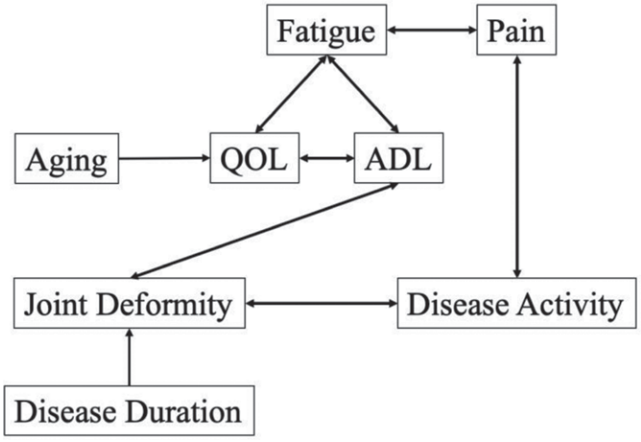

Figure 1

Disclosure of Interests: None declared
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AB0244 **MEDICATION ADHERENCE AND BELIEFS ABOUT MEDICATION IN PATIENTS WITH RHEUMATOID ARTHRITIS.**

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Background: Consistent immunosuppressive treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drugs (DMARDs) is crucial for reduced progression and improved long-term outcome of the disease. Therefore, drug adherence is a prerequisite, which is often insufficient according to literature.
Objectives: Our aim was to investigate the relationship between adherence and beliefs about medication in patients with RA.

Methods: The study included 137 RA patients (102 female, 35 male; age range 28-86 years, Ø 64.8 ± 12.6 yrs; SDAI Ø 9.9 ± 6.8; 61 % DMARD monotherapy, 31 % DMARD combination therapy, 9 % currently treated without DMARD). Medication adherence was measured with the Compliance-Questionnaire-Rheumatology (CQR). This is a self-report questionnaire with 19 items (4 response options each). The sum score is mapped to a scale from 0 to 100 % (CQR%), where 100 % corresponds to optimal adherence. A CQR% ≥ 80 % was defined as satisfactory adherence. In addition, the specific part of the Beliefs about Medicines Questionnaire (BMQ) was used to assess patients' opinions about the necessity of their medication therapy and their concerns. Besides correlation analyses (Spearman-Rho) multiple linear regression was applied to determine factors influencing adherence (coefficient of determination: adjusted R^2).
Results: Adherence was satisfactory in 93 RA patients (67.9 %) and insufficient in almost one-third (n = 44, 32.1 %). Analyses showed that adherence was significantly related to belief in necessity ($r = 0.46$; $p < 0.001$) and concerns about drug therapy ($r = -0.27$; $p = 0.001$). Furthermore, it became apparent that adherence is closely linked to the age of the patient ($r = 0.30$; $p < 0.001$). Younger RA patients (< 60 yrs) had significantly lower CQR%-scores than older RA patients (≥ 60 yrs; $p < 0.01$). Belief in the necessity of therapy, medication concerns and patient age accounted for almost half of the patient-specific variability in adherence (each $p < 0.001$; $R^2 = 42.9$ %), suggesting a strong dependence of adherence on these three factors.
Conclusion: Adherence is insufficient in about one-third of RA patients. Additionally, adherence appears to be strongly dependent on the patient's belief in the necessity of therapy, medication concerns and age. Physicians should strive for all RA patients to have sufficient knowledge about their medication, strengthen the belief in the necessity of the therapy and be mindful of adherence when talking to patients.
Disclosure of Interests: None declared
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AB0245 PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS AND SECONDARY SJÖGREN SYNDROME

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Background: Rheumatoid arthritis (RA) is a severe inflammatory disease that affects the joints and other organs such as the lung. Gougerot-Sjögren's syndrome (GSS) is an autoimmune disease. Secondary GSS can be primary or secondary and is defined by (1) the presence of another connective tissue disease, (2) the existence of dry eyes or dry mouth, and (3) objective evidence of ocular or salivary involvement. The presence of anti-SSA or anti-SSB antibodies is not necessary for the diagnosis of secondary SMS (4). The association of the two pathologies (RA-SGS) is frequent, and apart from osteoarticular involvement, various organs can be affected, in this case the lungs, by one or the other pathology with similar pulmonary lesions.
Objectives: To determine the incidence of pulmonary involvement in a population of RA-SGS patients.
Methods: Retrospective study, conducted from January 2019 to October 2021, at the rheumatology department of the CHU Ibn Rochd of Casablanca. Inclusion criteria: patients followed for RA according to the diagnostic criteria (EULAR/ACR 2010) associated or not with secondary GSS. Exclusion criteria: patients followed for primary GSS alone or other inflammatory rheumatic diseases with pneumopathy.
Results: 139 patients were included in our study, with a female predominance of 96.40%. The mean age was 56.31 years, the mean duration of RA was 9.89 years (4 months - 34 years). GSS was associated in about 1/3 of the patients, 33.81%. In the study population 24.46% of patients had pulmonary involvement which was present in the majority of RA-SGS patients (63.83%). Clinically, exertional dyspnea was found in all these patients and chronic dry cough in 66.67%. On standard radiography, an interstitial syndrome was found in all of these patients and on the pulmonary CT scan, 2 patients were at the stage of pulmonary fibrosis, i.e. 6.67% (PR-SGS).
Discussion: Secondary GSS is found in 30% of patients with rheumatoid arthritis (3). Pulmonary infiltrative disease is similar in both conditions. In RA these diseases are in the foreground after pleural involvement. They have the same clinical, radiological and functional characteristics, associated to varying degrees with exertional dyspnea, dry cough, crepitus rales, and digital hippocrasis (5,6). Pulmonary involvement is frequent in SSc, mainly represented by diffuse interstitial lung disease and bronchial and bronchiolar involvement (7). In SSc, the prognosis is rarely life threatening (8). In RA, the overall prognosis of rheumatoid lung disease remains poor with significant morbidity and mortality. A particular evolutionary mode characterized by acute exacerbation of interstitial lung disease associated with connective tissue diseases has been reported, particularly in RA (9,10).
Conclusion: In our series, the frequency of association of secondary SSG with RA is similar to the data in the literature and lung involvement is particularly frequent in these patients. No study in the literature has looked specifically at the clinical and prognostic features of lung involvement in RA-SGS patients.

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AB0246 EXAMINATION OF THE FACTORS CONSTITUTING DEPRESSIVE STATE IN RHEUMATOID ARTHRITIS PATIENTS AND THEIR ASSOCIATIONS.

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Background: About 15% of patients with rheumatoid arthritis (RA) have depression, with an odds ratio of 1.42 (95% CI: 1.3-1.5) compared with healthy control. In previous reports, depressed mood and sleep disorders were reported separately, and no report has examined the factors that constitute depression. In addition, there is no report that examines the relationship between them.
Objectives: In the present study, we investigated the factors that constitute depression in RA patients.
Methods: One hundred and twenty-four patients with RA attending Showa University Hospital who gave written consent to the study were included in the study. Age, gender, body mass index, smoking history, presence of hypertension, presence of diabetes, steroid use, methotrexate use, erythrocyte sedimentation rate, CRP, and serum MMP-3 levels were investigated. The simplified disease activity index (SDAI) was used to assess disease activity in RA, the health assessment questionnaire disability index (HAQ-DI) was used to assess activity of daily living, and the Hamilton depression rating scale (HAM-D) was used to assess depression. All patients were interviewed for the HAM-D by the same interviewer, and the relationship between each item of the HAM-D and each index was examined.
Results: Forty-two patients (33.9%) reported experiencing "Depressed mood". On the other hand, a higher percentage of patients reported "Anxiety Somatic (79, 63.7%)," " Somatic Symptoms General (69, 55.6%)," "Work and Activities (57, 46.0%)," "Hypochondriasis (53, 42.7%)," and "Genital Symptoms (49, 36.5%)" than depressed mood. Depressed mood" was correlated with SDAI (r=0.31) and HAQ-DI (r=0.26), while " Somatic Symptoms General " was correlated with SDAI (r=0.30) and HAQ-DI (r=0.29). "Somatic Symptoms General" correlated with SDAI (r=0.30) and HAQ-DI (r=0.29). "Anxiety Somatic" correlated only with age (r=0.24), and other factors showed no correlation.
Conclusion: Higher percentage of RA patients reported "Somatic Symptoms" than " Depressed mood " as a factor of depression. These factors were mildly correlated with RA disease activity and HAQ-DI.
Disclosure of Interests: None declared
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AB0247 THE ROLE OF AUTOIMMUNITY ON THE RELATION BETWEEN EROSIONS AND BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS: A CLINICAL RESEARCH

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Background: Rheumatoid arthritis (RA) is the most frequent chronic inflammatory rheumatism. It is characterized by peripheral articular destruction and it is

well known that erosions are correlated with the presence and titer of anti-citrullinated peptide antibodies (ACPA)[(1)]. RA is also known to be an independent factor of osteoporosis[(2)] and it has already been demonstrated that ACPA is associated with bone mineral density (BMD) at the hip and spine[(3)]. The physiopathology of erosion and bone loss in RA is related to osteoclast activation via RANK-L pathway stimulation, that can possibly be lead by ACPA[(4)].

Objectives: Our aim was to determine if there is an association between local and systemic bone damage in RA, represented respectively by erosion and BMD, and whether it may be driven by ACPA and/or other autoimmunity-related antibodies.

Methods: Patients followed in the Department of Rheumatology between January 2008 and May 2019 satisfied the 1987 ACR or 2010 ACR-EULAR criteria. To be included, they had to undergo radiographs and biology at intervals of less than 2 years from DXA. Bone mineral density (BMD) was evaluated in g/cm^2 and by T-score at the hip on DXA. Erosions were evaluated by the modified Sharp/van der Heidje erosion score (SHSe) on radiographs and the presence and titers of ACPA, rheumatoid factor (RF) and anti-nuclear antibodies (ANAs) were recorded.

Results: A total of 149 patients met the inclusion criteria, represented by 75.8% of women. They had a mean age of 62 (SD 9.61) and a long median disease duration of 132 [60; 240] months. A total of 61.1% patients were ACPA positive, 79.9% were erosive and 10.7% had a hip or spine T-score ≤-2.5. A higher erosion score was associated with a lower BMD (R^2: 0.049 and value: -0.222; p=0.009) and T-score (R^2: 0.158 and value -0.397; p<0.0001) at the hip. ACPA status, but not titer, was associated with a higher erosion score (63.0 (53.2) *vs.* 45.5 (44.1) for ACPA – (p= 0.04)). ACPA titers were associated with lower BMD at the hip (value -0.216; p=0.01) but not with T-score. In linear regression, erosion and bone mineral density were still associated but this association does not seem to be driven by ACPA status or titer. RF and ANA did not demonstrate any role in this association.

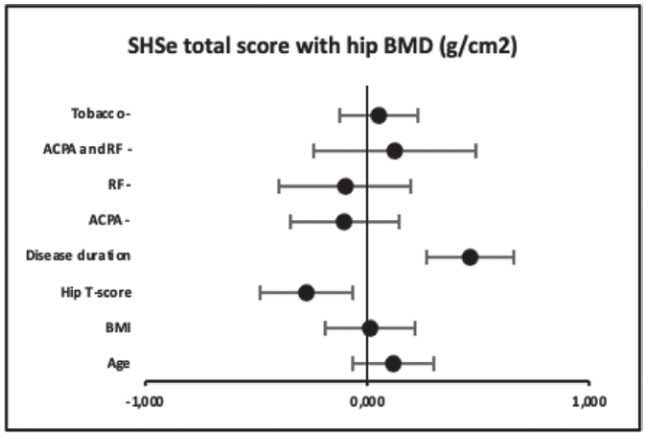

Figure 1. SHSe total score and associated variables in linear regression

Conclusion: We have shown that erosions were associated with lower BMD and T-score at hip but also at spine. Nevertheless that relation does not seem to be driven by ACPA or other autoimmunity-related antibodies. However, the presence of ACPA or erosion should lead to osteoporosis assessment.

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AB0248 LIPID PROFILE CHANGES FROM PRE-CLINICAL TO ESTABLISHED RHEUMATOID ARTHRITIS: A 12 YEARS FOLLOWUP PILOT STUDY

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Background: Patients with rheumatoid arthritis (RA) have an increased risk for developing cardiovascular diseases (CVD). This is partly due to the systemic inflammation characteristic to the disease, but also due to an increased prevalence of 'traditional' risk factors such as dyslipidemia. The inflammation in RA often leads to an increased catabolism of lipids, resulting in a subsequent decrease in HDL and LDL, while treatment with anti-inflammatory medication reverses these effects. This decreased cholesterol level in active disease is, unexpectedly, associated with an increased incidence of CVD (the lipid paradox). Additionally, we previously demonstrated pro-atherogenic lipid profile changes in preclinical RA patients.

Objectives: To explore the lipid profile changes in RA patients through different phases of the disease, i.e. from the preclinical stage and RA onset through treatment with biological disease modifying anti-rheumatic drugs (bDMARDs).

Methods: Thirty-nine consecutive patients who were previously included in both Reade's RA prevention cohort and biological cohort were included in the current study. The prevention cohort consisted of individuals with arthralgia and rheumatoid factor and/or anti-citrullinated protein antibodies without arthritis, and the biological cohort comprised RA patients using bDMARDs. Lipid spectrum was measured longitudinally, at the following points in the disease course identified in each patient (time from baseline was different in each patient due to the natural course of disease progression):

1.Baseline, months prior to RA diagnosis (Start Prevention cohort)
2.Moment of RA diagnosis (End Prevention cohort)
3.Period between diagnosis and start bDMARD treatment
4.Start treatment with bDMARDs
5-7.Continued treatment with bDMARDs

Results: From baseline, high density lipoprotein cholesterol (HDLc) and apolipoprotein A1 (ApoA1) increased up to the start of biological treatment, thereafter they slightly decreased. Low density lipoprotein cholesterol (LDLc) and apolipoprotein B (ApoB) both decreased with higher disease activity, increasing again after starting bDMARD therapy. Total cholesterol/HDL ratio decreased substantially from baseline and onwards and stabilized in the bDMARDs treatment phase. Lipoprotein(a) (Lp(a)) increased slightly up to treatment with bDMARDs, after which it stabilized. Figure 1 shows the progression of HDLc, LDLc and total cholesterol (TC) plotted against C-reactive protein (CRP) over time.

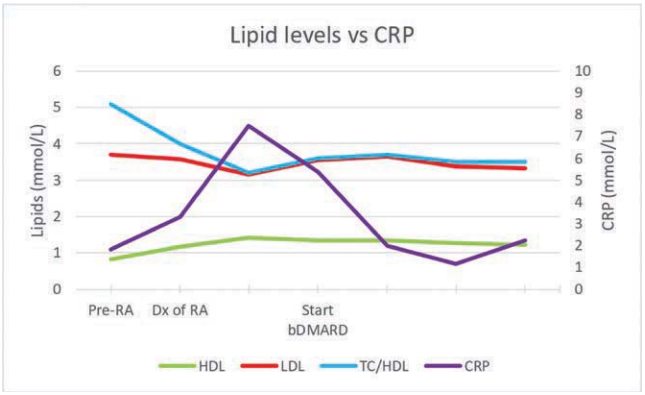

Figure 1. Time course of cholesterol parameters vs disease activity. CRP = C-reactive protein, RA = rheumatoid arthritis, Dx = diagnosis, TC = total cholesterol, HDL = high-density lipoprotein, LDL = low-density lipoprotein

Conclusion: Our study uniquely shows the change of lipid parameters during the course of RA disease. While LDLc, ApoB and cholesterol/HDL ratio decreased with higher disease activity, HDLc and ApoA1 increased, affirming the expectations. Larger cohort studies are necessary to accurately elucidate the development of lipids through different disease stages in RA patients, to better understand one of the key risk factors for CVD in RA.

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AB0249 EVALUATION OF BELIEFS AND FEARS DURING RHEUMATOID ARTHRITIS TOWARDS CONVENTIONAL BACKGROUND TREATMENTS: STUDY BY BMQ (BELIEF ABOUT MEDICATION QUESTIONNAIRE)

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Background: Poor adherence is one of the main causes of therapeutic failure in chronic inflammatory rheumatism, particularly in rheumatoid arthritis (RA). Thus to improve regular intake especially of conventional background treatments (cs-DMARDs), it is important to assess patients' beliefs and fears about their treatments.
Objectives: Evaluate the beliefs and fears of patients with Rheumatoid arthritis towards their conventional background treatments.
Methods: This is a cross-sectional study with RA follow-up patients meeting the ACR/EULAR criteria. Epidemiological, clinical and paraclinical data were collected. The evaluation of beliefs and fears towards csDMARDs was carried out by the BMQ score which has two five-item scales rated according to a 5-point Likert scale, ranging from 1 (not at all agree) to 5 (strongly agree). The scores of necessity, fear, overuse and nuisance were calculated. Patients were divided into 4 groups according to their beliefs of csDMARDs: accepting, ambivalent, indifferent and septic.
Results: The mean Disease Activity Score (DAS28crp) was 3.5 ±1.54, the mean value of Visual analogue scale of pain (VAS) was 40.5± 20.5, and the mean value of Health Assessment Questionnaire (HAQ) was 1.05± 0.85. All patients were treated with methotrexate and 12.5% with Salazopyrine in combination. The average need score was 20± 2.4, fear score was 16.45± 3, overuse score was 13.67± 2.25 and nuisance score was 10.8± 2.6. Patients' beliefs about the need for their background treatments were more important than their concerns and fears about the potential consequences of these treatments (p=0.03). A higher necessity score was correlated with the number of painful joints (NAD) (p=0.02) and a higher DAS28 (p=0.05). Patients who were more afraid of their treatments had more joint deformities (p=0.03), higher HAQ functional index (0.007) and a higher VAS value (p=0.01). The belief profile study concluded that 60% of patients were ambivalent, 27.5% accepting, 10% indifferent and 2.5% were septic towards their background treatments.
Conclusion: Our study showed that during RA, knowledge of the profiles of our patients, their beliefs and fears about their treatments especially cs-DMARDs is essential, and could help us to adapt strategies for improving compliance.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.1026

AB0250 DESCRIPTION OF ARTERIAL STIFFNESS, INFLAMMAGING AND VASCULAR AGE IN A GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS UNDER A STRICT FOLLOW-UP COMPARED WITH UNCONTROLLED OSTEOARTHRITIS PATIENTS

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Background: The risk of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) is higher than in individuals in the general population. The fundamental risk factor for CVD is age, related to alterations at the arterial level, called vascular aging reflected by arterial stiffness and endothelial dysfunction
Objectives: The aim of the study was to compare vascular age and arterial stiffness (PWV-Pulse Wave Velocity) in two groups of patients with RA and with osteoarthritis (OA) and to assess the influence of inflammaging (persistent low-grade inflammation that develops with age) and metabolic markers in these outcomes.
Methods: Analytical cross-sectional study. RA patients under a strict follow-up program (T2T evaluated every two months) and OA patients without strict clinical follow-up, evaluated once or twice a year, were included. Patients with history of uncontrolled hypertension, CVD and/or current smoking were excluded. Waist-hip ratio, body mass index (BMI), DAS28 (RA), C-Reactive protein (CRP), Erythrocyte sedimentation rate (ESR), glycemia and lipid profile were measured. PWV and vascular age (in years) were evaluated through oscillometric method, arteriograph-TensioMed. Eleven proteins components of the inflammaging (cytokines, Matrix metalloproteinases - MMPs and its tissue inhibitors), were quantified through Luminex multiplex assay in serum samples. Univariate and bivariate analyzes (Chi-square and non-parametric correlations) were performed. Approval of Ethics Committee and informed consent were obtained.
Results: A total of 106 patients (74% women) were included (52/RA and 54/OA). Mean age was 57±5.6 years without differences between groups. There were significant differences in CRP and ESR (higher in RA) and in BMI, waist circumference and weight (higher in OA). RA patients had low disease activity level (DAS28: Median 2.6, IQR 1.3). There were no differences in PWV, vascular age or inflammaging (except for MMP-1, higher in RA), between the groups. PWV had a positive correlation with LDL (Rho Coef. 0.218 p=0.025). Patients who performed physical activity had a lower vascular age than those who did not [43 Interquartile range (IQR)23 vs 60 IQR 17, p=0.032). Vascular age was higher in RA patients who did not receive methotrexate 60 (IQR 19.3) compared with patients under methotrexate treatment 44.5 (IQR 23) (p = 0.017). Also, vascular age was lower in OA patients under prescribed physical activity (43 IQR 24.8 vs 56.5 IQR 20, p=0.03). MMP-9 in RA patients (Rho 0.283, p=0.042) and IL-10 in OA patients (Rho 0.290, p= 0.036) correlated with diastolic pressure. The components of inflammaging did not correlate with vascular age. The Framingham Risk Score was strongly associated with vascular age.

Table 1. Significant correlations with vascular age

Variable	Spearman's Rho	p-value
LDL levels	0.200	0.040
Systolic blood pressure	0.300	0.002
Mean arterial blood pressure	0.210	0.031
Daily coffee cups intake	-0.212	0. 045
Framingham Risk Score	0.340	<0.0001
MDHAQ score in RA patients	0.417	0.002

LDL: low density lipoprotein; MDHAQ: multidimensional health assessment questionnaire.

Conclusion: In RA strictly controlled patients, there are no differences in endothelial dysfunction, vascular age or inflammaging, when comparing with uncontrolled overweight OA patients. Physical activity, LDL levels and coffee consumption corelate with vascular age in OA and RA patients. OA patients under physiatrists follow-up and RA patients under methotrexate treatment or with low MDHAQ levels have lower vascular age levels.
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AB0251 * FATIGUE IN RHEUMATOID ARTHRITIS: DOES PATIENT AGE INFLUENCE?

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Background: Fatigue in RA has a multi-causal pathway. It is recommended that it should be measured in all RA studies using a validated instrument. Fatigue in elderly patients could have a different perception than in younger patients, identifying the associated factors could be a key to the management of this complex symptom.
Objectives: To compare fatigue and its associated factors in young and elderly patients with RA from two university hospitals.
Methods: A cross-sectional analysis was performed in 167 RA patients diagnosed according to the 2010 ACR-EULAR criteria. Patients were divided into two groups based on age (≥60 and <60) for comparative purposes. Fatigue was assessed using 4 instruments: the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ), the fatigue subscale of the Short-form 36 survey (fatigue-SF36), the Visual Analogic scale of fatigue (VASf) and the Functional Assessment of chronic illness Therapy Fatigue Scale (FACIT-F). To compare the mean of fatigue between groups we used a T-Test.
To determine in each group of patients (young and elderly patients) the relationship between the 4 subscales of fatigue (assessed by BRAF-MDQ) and the other variables (DAS28, CPR, ESR, hemoglobin, vitamin D, HAQ, RAID [Rheumatoid Arthritis Impact of Disease], SF36, Hospital Anxiety and depression Scale [HAD] and Brief Pain Inventory) a Spearman correlation was performed. A value of $p < 0.05$ was accepted as statistically significant.
Results: A total of 167 patients were included, 81 (48.5%) young and 86 (51.5%) elderly patients. We found fatigue (using 4 instruments) has not significant differences in young and elderly patients (Table 1). In young and

elderly patients, physical, living, cognitive and emotional fatigue were correlated to RAID, SF36, HAD and pain but they were not associated to CRP, ESR, hemoglobin and vitamin D. In young patients, all dimensions of fatigue were associated with DAS28. Furthermore, in elderly patients we found a relationship between physical (p-value 0.044) and living fatigue (p-value 0.012) with DAS28, nevertheless cognitive and emotional fatigue (p-value 0.078 and 0.079 respectively) were not related.

Table 1. Scores of the Fatigue Questionnaires used to assess fatigue in young and elderly patients with RA.

	Young Mean (SD)	Elderly Mean (SD)	p-value
FACIT-F	36.5 (12.5)	35.9 (11.7)	0.2963
VAS-F	4.3 (2.8)	3.8 (2.8)	0.119
SF36-Fatigue	50.9 (23.9)	51.0 (21.9)	0.628
BRAF-MDQ			
Physical	9.2 (6.2)	8.5 (6.3)	0.4670
Living	5.3 (5.6)	4.2 (4.6)	0.1446
Cognitive	3.3 (3.8)	4.2 (4.6)	0.2932
Emotional	3.5 (3.5)	2.6 (2.7)	0.0932

Conclusion: In young and elderly patients, all dimensions of fatigue appear to be related with subjective but not with objective variables. In young patients, all dimensions of fatigue were associated with DAS28 but in elderly patients only physical and living fatigue were correlate to disease activity. These results could indicate that it is important to evaluate fatigue in a multidimensional perspective in elderly patients.

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AB0252 INTOLERANCE TO METHOTREXATE IN RHEUMATOID ARTHRITIS: AN ASSESSMENT WITH THE MISS (METHOTREXATE INTOLERANCE SEVERITY SCORE)

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Background: Methotrexate (MTX) is a cornerstone in the treatment of rheumatoid arthritis (RA), in monotherapy or in combination with biological agents. Its prolonged use requires regular clinical and biological monitoring. The purpose of our study is to assess intolerance to MTX and its consequences.

Objectives: The purpose of our study is to assess intolerance to MTX and its consequences.

Methods: This is a cross-sectional study with RA follow-up patients meeting the ACR/EULAR 2010 criteria. An assessment of MTX intolerance was conducted using the Arabic version of the MISS (Methotrexate Intolerance Severity Score). It is a questionnaire containing 12 items covering four areas: abdominal pain, nausea, vomiting and behavioral disorders. A score of six indicates an intolerance.

Results: Forty patients were included: 35 women (87.5%) and 5 men (12.5%) of average age 51.7 years ±12.7 years. The average duration of disease progression was 12.2 years 9.2 [1-40 years]. All patients were treated with methotrexate and supplemented with folic acid. 50% of patients were under 10mg/week of MTX, 27.5% under 15mg/week and 22.5% under 20 mg/week. Patients had been on this treatment for an average of 8.7 years [1-25 years]. The majority of them (97.5%) received corticosteroids in combination, 12.5% received Salazopyrine and 27.5% received biotherapy. Methotrexate intolerance was observed in 16 patients (42.1%). Nausea was observed in 13 patients (81.2%), vomiting in 5 patients (31.2%), abdominal pain in 11 patients (68.8%) and behavioral disorders in all patients. As a result of this intolerance, 18.8% of patients had to stop their treatment, 12.5% decreased the dose on their own, 6.2% took the MTX irregularly, 12.5% switched from the oral route to the intramuscular route and 50% continued to take their treatment in the usual way. The study of correlations did not reveal statistically significant associations between MTX intolerance and age, sex, dose and duration of MTX, the associated intake of salazopyrin, biotherapy and other symptomatic treatments.

Conclusion: The occurrence of an intolerance to MTX is common in patients followed for RA, which may lead to poor adherence to therapy or even a discontinuation of treatment thus decreasing the effectiveness of management. Hence the need to systematically detect this intolerance and react in time.

Disclosure of Interests: None declared

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AB0253 CARDIOVASCULAR OUTCOMES IN PREVENTION RANDOMIZED CONTROLLED TRIALS IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A SYSTEMATIC REVIEW.

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Background: Cardiovascular disease (CVD) risk in patients with chronic inflammatory arthritis (IA), including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS), is substantially increased compared to the general population. New evidence strengthens the notion that the excess risk of CVD morbidity and mortality in patients with IA is related to both traditional (e.g. hypertension, diabetes, smoking) and novel CVD risk factors, including chronic inflammation, leading to an accelerated atherosclerosis. How to minimize such increased CVD prevalence is still poorly understood, and whether more intensive traditional risk factor control or disease specific risk factor should be targeted is still matter of debate.

Objectives: The aim of this systematic review was to identify intervention targeting CVD or inflammatory arthritis associated with improvement of CV risk outcomes (estimated CV risk, CV events, endothelial function, arterial stiffness, subclinical atherosclerosis) in adult patients with diagnosis of inflammatory arthritis (RA, PsA and AS).

Methods: Two independent reviewers retrieved randomized controlled trials of interest from systematic searches of Medline, Embase and Cochrane database (20th April 2020). Data extraction was performed using standard template; the quality of each included trials was assessed with the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) [1]. Systematic review was conducted following the Preferred Reporting Items for systematic reviews and Meta-analysis (PRISMA) statement.

Results: Out of total of 4823 articles, 27 met the inclusion criteria. Among these, most (n=22) involved RA patients, one trial was based on mixed IAs patients and the remaining (n=4) were performed on spondylarthritis population. Total number of patients was 8045. Overall risk of bias was high in most of per protocol analysis trials (90%) and in 26.7% of intention-to-treat analysis trials. Four trials evaluated major adverse cardiovascular events (MACE) incidence and one of these demonstrated a significant reduction in incidence of MACE in RA patients underwent a treat-to-target strategy of CV risk factor. The same study also demonstrated a significant reduction in progression of subclinical atherosclerosis (carotid Intima-media thickness, cIMT), while other trials (n= 8) exploring effect of rosuvastatin, enalapril, tocilizumab and TNF-inhibitors failed to reach a similar result. Endothelial dysfunction, predominantly measured as reduce flow mediated dilatation (FMD), was widely used as surrogate outcome of CVD and it appeared to be significantly improved by treatment with statins, ACE-inhibitors, anakinra and tocilizumab. Treatment with pioglitazone, anakinra or tocilizumab in three trials significantly ameliorated arterial stiffness, estimated with pulse wave velocity (PWV), Cardio-ankle vascular index (CAVI) or augmentation index (AI). Two studies explored how a reduction of estimated CV risk could be achieved after treatment with enalapril and tight-control strategy aiming to SDAI ≤ 3.3. Results of both trials didn't demonstrate any variation in QRISK3-2018 and Framingham risk score, respectively.

Conclusion: Optimal CVD management in IA patients remains undefined and it should be implemented as stated in international guidelines. Randomized controlled trials exploring efficacy of prevention strategy are few and predominantly focused on surrogate outcome measures of cardiovascular risk.

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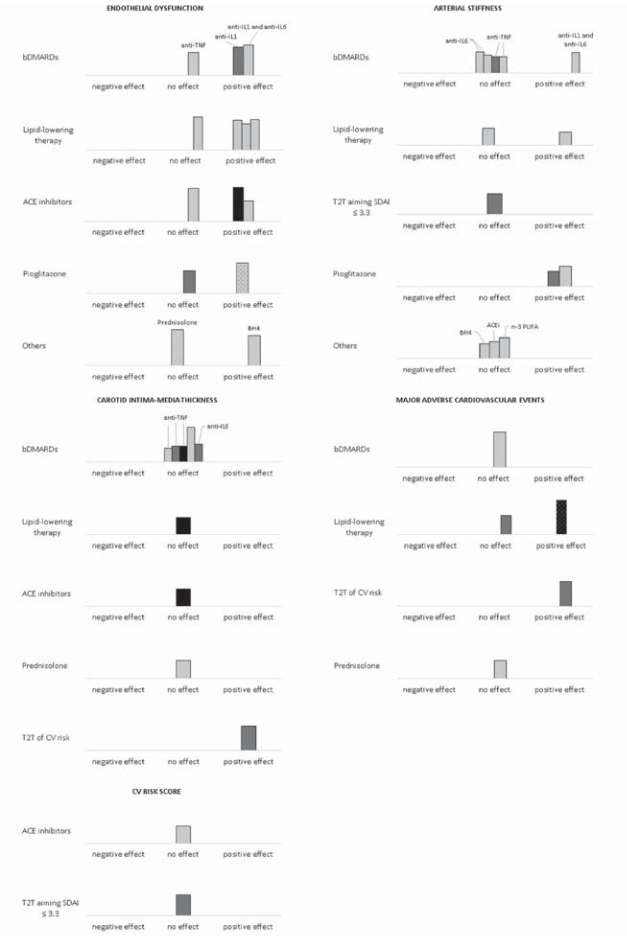

Fig.1 - Harvest plot of included trials and effect on specific cardiovascular outcomes. Each bar counts as a study, height of bar correlates with sample size. Color of bar correlates with risk of bias. Light grey: high risk of bias, grey: some concerns, black: low risk of bias. Dot pattern indicates positive result without statistical significance.
bDMARDs: biologic disease modyfing antirheumatic drugs, T2T: treat-to-target, CV: cardiovascular, BH4: tetrahydrobiopterin, n3-PUFA: n-3 polyunsaturated fatty acids.

Disclosure of Interests: Carlo Garaffoni: None declared, Antonio Marangoni: None declared, Marcello Govoni Speakers bureau: Abbvie, Pfizer, Galapagos, BMS, Eli-Lilly, Paid instructor for: Pfizer, Consultant of: Abbvie, BMS, Novartis, Astrazeneca, Pfizer, Carlo Alberto Scirè Grant/research support from: AbbVie, Lilly

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AB0254

ASSOCIATED FACTORS WITH TREATMENT ADHERENCE IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL ANALYTIC STUDY OF COLOMBIAN PATIENTS.

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Background: Rheumatoid arthritis (RA) represents an essential public health problem regarding vast influence on the individual's global health. Adherence to pharmacological therapy has been shown to be a relevant outcome to ensure the desired therapeutic objectives and thus avoid the recurring concern of flares, the perpetuation of inflammation, and its consequences, not only physiological but also structural and socioeconomic.
Objectives: Our aim was to identify clinical-epidemiological variables associated with treatment adherence in an outpatient clinic-based cohort of Colombian RA patients.
Methods: We conducted a cross-sectional analytic study with data obtained from August 2020 to October 2021. Treatment adherence was assessed on each visit through the Compliance Questionnaire on Rheumatology (CQR); moreover, patients were stratified into those who were adherent to the treatment and those who didn't, according to their CQR score. Additional information regarding the quality of life (QOL-RA), disease activity (DAS28 ESR), and functionality (HAQ) was recovered from electronic clinical charts. Data was gathered on a database stored in REDCap. T-test and Chi-squared test were used for comparisons and a multiple logistic regression with backward selection was performed to build the final fitted model.
Results: Data from a total of 564 patients were included in the analysis. Our population was constituted of 79.1% women with a mean age of 53 (± 13.1); the CQR mean score was 77.7 (± 9.26) and treatment adherence, defined as a CQR score of ≥ 80.7, was seen in 49.3% of the cases. Mean DAS28 ESR, QOL-RA, and HAQ scores were 3.3 (± 1.62), 7.24 (± 1.43), and 0.671 (± 0.716), respectively; with a reported preserved quality of life (QOL-RA >7) in 60,5% of patients. Monotherapy (42.7%) and combined therapy (49-6%) were the two most common treatment schemes, being MTX the more frequent DMARD (58.9% oral, 20.9% subcutaneous). Noncompliant patients showed higher mean disease activity (3.52 (±1.66) vs 3.08 (±1.54); p 0.001) and lower quality of life (6.94 (±1.43) vs 7.56 (±1.35); p <0.001) scores. Having a higher DAS28 score (OR 1,19), drug dispensing delay (OR: 1,71), and infection as an adverse effect (OR 2.53) were recognized as risk factors for an impaired treatment adherence after adjustment for the effects of possible confounders. Complete results of the multiple logistic regression model are shown in Table 1.

Table 1. Associated factors with treatment adherence in RA patients.

	Odds Ratio (95% Confidence Interval)	p-value
Age	0,99 (0,97 – 1)	0,12
Male	**1,54 (0,98 – 2,43)**	**0,065**
Having a stable partner	0,75 (0,52 – 1,09)	0,13
Comorbidities		
Hypothyroidism	0,69 (0,41 – 1,15)	0,16
Dyslipidemia	0,52 (0,22 – 1,16)	0,12
Dyspepsia (AE)	**1,48 (0,97 – 2,28)**	**0,07**
Infection (AE)	**2,53 (1,31 – 5,08)**	**0,007**
Perception of the information received by health professionals		0,45
Unsatisfied	Ref.	
Satisfied	2,23 (0,06 – 28,1)	0,55
Very satisfied	1,37 (0,09 – 17,2)	0,81
Healthcare barriers	**1,98 (0,92 – 4,45)**	**0,088**
Drug dispensing delay	**1,71 (0,99 – 2,99)**	**0,058**
Disease duration (months) until rheumatology consultation	**1,00 (0,99 – 1,00)**	**0,004**
DAS28 ESR score	**1,19 (1,06 – 1,33)**	**0,003**

AE: adverse effect. Bold values indicate a p value < 0,1

Conclusion: In our study population, there were evident trends regarding the effects of dispensing delays, adverse effects, and barriers to access to the health system on reducing treatment adherence. Moreover, there was a subtle association of treatment adherence with the DAS28 score, as well as with a better quality of life. Taken together, these results suggest the need for the implementation of educational programs that will support a comprehensive approach that considers not only patient-related factors but also the proper functioning of the healthcare system itself. Further research with a follow-up period could assess the long-term effects on several clinical outcomes and explore if proposed trends change with time.

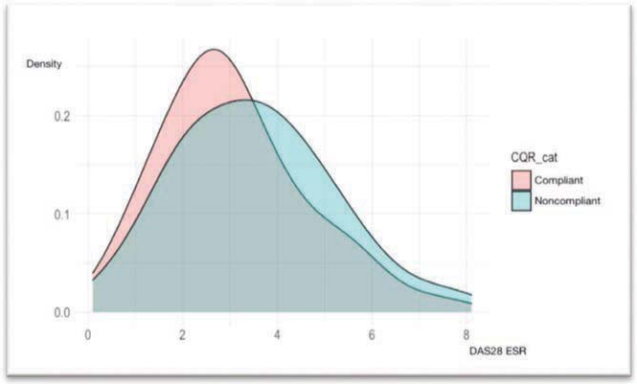

Figure 1. Density plot comparing disease activity in patients that are compliant and noncompliant to treatment.

Disclosure of Interests: None declared

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AB0255 SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS OVER 65 YEARS OF AGE: PREVALENCE AND PREDISPOSING FACTORS.

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Background: Sarcopenia is a muscle disease which is characterized by loss of muscle mass and function. This condition is associated with chronic disease and ageing which predicts inability, hospitalization and death.
Objectives: Describe sarcopenia prevalence and risk factors in patients with reumathoid arthritis (RA) over 65 years of age.
Methods: Design:
A case-control study.
Subjects
Cases: Recruitment was performed by random sampling between patients over 65 years of age with RA (ACR/EULAR 2010 criteria) attended at 4 Spanish University Hospitals.
Controls: Recruitment of subjects without rheumatoid disease was performed asking for case patients who attended to medical center with a similar-age (age of range +/- 5 years) and same-gender person from same social or family environment.
Variables: The main variable was sarcopenia which was defined according to European Working Group on Sarcopenia in Older People (EWGSOP) 2019. Sarcopenia risk factors assessed were: economic status, malnutrition, measured with Mini Nutritional Assessment (MNA), dual-energy x-ray absorptiometry (DEXA) in spine and hip to osteoporose screening, toxic habits, comorbidities and Charlson index, physical activity measured with Global physical activity questionnaire (GPAQ) and Short Physical Performance Battery (SPPB).
Other variables were: haemoglobin, calcium, D and B12 vitamins, total proteins, albumin, C reactive protein, body mass index (BMI), polimedication, quality of life measured with EQ-5D and RA related factors, activity disease measured with DAS28, SDAI and CDAI; physical function measured with HAQ (Health assessment questionnaire) and global functional status according ACR criteria.
Statistical analysis:
Descriptive and multivariative analysis was performed to identify factors associated to sarcopenia in RA.
Results: 76 patients and 76 controls were included in the study, 120 were women (78,9%), with media ± SD of age 74,7 ±6,98 of media and 32 (21,1%) were men, with age 70,1 ±3,78 of media. In comparation with controls, RA patients presented more frequency of sarcopenia (30 [19,53%] vs 6 [3,94%]; p=0,005). RA patients who presented sarcopenia, were upper average age (p=0,001), worse results in Short Physical Performance Battery (SPPB) (p=0,037), higher DAS28 (3,55 ± 1,09 vs 2,78 ± 1,05; p=0,017), higher score HAQ (1,18 ± 0,79 vs 1,69 ± 0,68; p=0,024), worse score in EQ5D (0,27 ± 0,28 vs. 0,54 ± 0,25; p=0,001) and Visual analogic scale VAS EQ5D (45,7 ± 17,4 vs. 56,9 ± 17,6; p=0,035).
By the way, RA patients presented lower levels of total proteins (p=0,018), worse results in MNA (p=0,001) and they performed less physical activity by GPAQ (p=0,011). Multivariative models (Table 1) identified as independent predictors of sarcopenia in RA: age (p=0,014), proteins levels (p=0,044) and disease activity measured by DAS28 (p=0,030). This model could explain 37% of sarcopenia in RA (R2=0,37).

Table 1. ***Multivariativeanalysis (VD: Sarcopenia)***

	OR(IC)	p
Age, years	1,213 (1,041-1,414)	0,014
Proteins (g/dL)	0,185 (0,036-0,958)	0,044
DAS28	2,146(1,076-4,881)	0,030

R2=0,37

Conclusion: Sarcopenia is more prevalence in over 65 years-old RA people. Older age and higher activity disease measured by DAS28 more risk of sarcopenia. Proteins levels have a protected association with sarcopenia.
Disclosure of Interests: None declared
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AB0256 EFFECTS OF BIOLOGICAL-DMARDS ON THE SERUM URIC ACID LEVEL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Hyperuricemia associated with rheumatoid arthritis (RA) has been reported to be a risk factor for cardiovascular disease. It has been reported that uric acid (UA) levels decrease with the use of leflunomide and increase with tumor necrosis factor (TNF) inhibitor therapy. However, the effects of long-term biological disease-modifying antirheumatic drugs (bDMARDs) therapy and the effects of non-TNF inhibitor biologic therapy on UA levels have not been reported.
Objectives: We aimed to investigate the changes in UA levels during the use of TNF inhibitors and non-TNF inhibitors therapy.
Methods: Patients with RA treated with bDMARDs from 2008 to 2018 were studied based on the All Showa University of RA (ASHURA) database. The association between uric acid level reduction and treatment was evaluated. Of 629 patients treated with the bDMARDs, 256 patients with available uric acid levels medical records were included. The following background factors were investigated: age; sex; type of bDMARDs; dosage of methotrexate and prednisolone; usage of conventional synthetic DMARDs, dyslipidemia drugs and nonsteroidal anti-inflammatory drugs; body mass index; smoking history; HbA1c; presence or absence of hypertension and dyslipidemia; and serum creatinine, C-reactive protein, and matrix metalloproteinase-3 levels. We also used the simplified disease activity index (SDAI) to evaluate RA disease activity. The analysis was performed in two groups, TNF inhibitor-treated group (148 patients) and non-TNF inhibitor-treated group (108 patients, tocilizumab and abatacept). The primary endpoint was UA levels before, and after 6 months and 1 year, which was determined using the repeated-measures analysis of variance (ANOVA) and secondary endpoint was proportion of patients with hyperuricemia (uric acid level of 7.0 or higher was defined), determined using spearman's correlation coefficient by rank test.
Results: In TNF inhibitor-treated group, the UA levels were not increased from 4.9 ± 1.4 (mg/dl) to 4.9 ± 1.4 and 5.1 ± 1.7 before treatment and after 6 months and 1 year, respectively (p=0.50). The number of patients with hyperuricemia increased from 7 to 12 and 16 (p=0.026). In non- TNF inhibitor-treated group, the UA levels were not increased from 5.2 ± 1.4 (mg/dl) to 5.2 ± 1.4 and 5.3 ± 1.4 (p=0.78). The number of patients with hyperuricemia increased from 8 to 16 and 12 (p=0.193). There was a difference in the type of drug, but no difference in the duration of administration by repeated-measures ANOVA.
Conclusion: Our study suggests that TNF inhibitor therapy may affect increased percentage of patients with hyperuricemia. On the other hand, non-TNF inhibitor therapy may not affect increased percentage of patients with hyperuricemia and bDMARD treatment has a mild effect on UA levels in patients with RA.
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AB0257 ADHERENCE TO TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adherence is defined as the degree of agreement between a patient's behavior (taking medication, changing lifestyle, or adhering to treatment recommendations) and the prescriptions of a physician or medical staff. The patient's adherence to treatment is an important factor influencing the effectiveness of therapy, the course of the disease. In Russia, a universal questionnaire was developed to assess the level of adherence to drug therapy, medical care, lifestyle changes, and general adherence to treatment.
Objectives: To analyze the adherence to treatment, medical care and recommendations for lifestyle changes in patients with RA.
Methods: The cross-sectional study included 88 women with RA (ACR/EULAR 2010), the mean age - 63.0±8.1 years, the duration of the disease - 22.4±9.3 years. Adherence was assessed using the Russian questionnaire, which determines the low, average, and high levels of adherence to drug therapy, medical care, recommendations for lifestyle changes, and general adherence to treatment. All patients completed The Hospital Anxiety and Depression Scale (HADS) for the evaluation of anxious and depressive symptoms and HAQ (Health Assessment Questionnaire) to explore functional disability. All patients took a clinical examination, assessment of the anamnestic data, X-ray of hands, feet.

Results: Most of RA patients had an average level of adherence to drug therapy - 51 (58%); medical care - 45 (51%); low level of adherence to lifestyle recommendations – 63 (72%). Assessment of general adherence to treatment showed: 30 (34%) people had a low level of adherence, 51 (58%) - medium, and 7 (8%) - high. Elderly age (p=0.00), anxiety (p=0.02) and depression (p=0.04) were associated with low adherence to medical care. The use of glucocorticoids (GCs) was associated with high adherence to drug therapy (p=0.01). The number of patients taking disease-modifying anti-inflammatory drugs and biologic disease-modifying antirheumatic drugs, functional disability (HAQ) and the radiographic stage of RA (classified according to Steinbrocker) did not differ significantly in patients with different levels of adherence.
Conclusion: Most of RA patients had an average level of adherence to drug therapy, medical care, and a low level of adherence to recommendations for lifestyle changes. Patients taking GCs have a high level of adherence to drug therapy. Mental disorders (anxiety and depression) and elderly age are associated with low adherence to medical care.
Disclosure of Interests: None declared
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AB0258 STATE OF ADIPOCYTOKINES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adipose tissue is actively involved in the development of systemic inflammation in rheumatoid arthritis (RA), producing proinflammatory cytokines and adipocytokines that can independently modulate inflammatory and destructive processes in the joints [1-2].
Objectives: To establish the relationship between serum adiponectin and leptin in patients with RA with clinical and laboratory indicators of disease activity and the results of ultrasound examination (US) of the hand joints.
Methods: The study included 72 women with RA according to the ACR / EULAR criteria of 2010 who visited the adaptation therapy clinic of Orenburg State Medical University. The mean±SD age was 46.4±7.5 years and the mean±SD disease duration was 7.9±4.4 years.
Clinical study of patients with RA included an assessment of the tender joint count (TJC) (11.3±6.8), the swollen joint count (SJC) (4.6±2.7), duration of morning stiffness (107.5±49.3 min) and the patient's global assessment according to a 100-millimeter visual analogue scale (46.2±23.5 mm). Disease activity was assessed by the DAS28 index (4.4±1.7).
The mean body mass index (BMI) in patients with RA was 26.3 ± 6.2 kg/m^2.
We evaluated for the following laboratory tests: rheumatoid factor (RF), antibodies to cyclic citrullinated peptide (A-CCP), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), interleukin-17 (IL-17), adiponectin and leptin in blood serum.
We carried out US to determine the inflammatory and destructive changes in 30 joints in each RA patient (wrist joints, metacarpophalangeal, proximal and distal interphalangeal joints and the first interphalangeal joint on the palmar and dorsal sides of both hands) by the device "Philips Epiq 7" with linear transducer with a frequency of 5-18 MHz and the use of Power Doppler (PD) which included the identification of synovitis, tenosynovitis, erosive changes in the hand joints.
At the time of examination, 30 (41.7%) patients with RA received therapy that included methotrexate (MTX); 9 patients (12.5%) intook glucocorticosteroids (GCS) perorally, MTX+GCS – 15 patients (20.8%).
The program STATISTICA, 12.0 was used for statistical analysis.
Results: The level of serum adiponectin negatively correlated with the level of CRP (r=-0.3, p <0.05). At the same time, significant correlations were found between the number of erosions of the joint space and the level of adiponectin (r=0.5, p <0.0001). Also, additional correlations were noted between adiponectin levels and the intake duration of MTX (r=0.3, p <0.05) and GCS (r=0.4, p <0.001). We found a positive correlation between the level of leptin and BMI (r=0.5, p <0.0001). In addition, there were significant correlations between the level of serum leptin and the morning joint stiffness duration (r=0.4, p <0.0001), TJC (r=0.5, p <0.0001), as well as the level of CRP (r=0.4, p <0.001) and the DAS 28 index (r=0.4, p <0.001) in patients with RA. An increase in IL-17 concentration was associated with an increase in leptin levels (r=0.3, p <0.05) in RA patients. However, we did not find a significant correlations between serum adipokine concentrations and RF and A-CCP levels.
Conclusion: Level of adiponectin is associated with pronounced destructive changes in the joints and the intake duration of MTX and GCS. There is a positive relationship between the level of leptin and indicators of disease activity (TJC, level of CRP, DAS28-CRP index) and an increased blood flow during Doppler imaging, which indicates its role as a proinflammatory cytokine.
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AB0259 THE IMPACT OF LOCKDOWN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The COVID-19 pandemic has impacted on face to face assessments of patients with rheumatic diseases, including rheumatoid arthritis (RA) and telemedicine has offered a valid opportunity to follow these patients. DEDICARE is a Patient Support Program (PSP) which has been active at our center since 2016, which allows the telemonitoring of PROs (Patient Reported Outcomes) for patients being treated with abatacept. Since 2016, 98 RA patients followed at out Unit entered the DEDICARE program. During COVID19 pandemic these patients continued their monitoring using this PSP.
Objectives: To evaluate the impact of the first COVID wave on PROs and CROs (Clinical Reported Outcomes) in patients with RA included in the DEDICARE programme
Methods: Data collected in the dedicated platform three months before (from December 2019 to February 2020, pre-lockdown), during (from March 2020 to May 2020, lockdown) and after (from June 2020 to August 2020, post-lockdown) the first lockdown period in Italy were compared. In detail DAS28 (CRP, ESR), CDAI and SDAI were evaluated before and after the lockdown period; while VAS-pain, Global Health (GH); Patient Global Assessment of Disease Activity (PGA); Health Assessment Questionnaire (HAQ); Functional Assessment Chronic Illness Therapy (FACIT) were evaluated pre, during e post lockdown with the DEDICARE platform.
Results: 36 RA patients, all females, were included in the study; mean age was 62.4 (32-85) years; mean disease duration 15.5 (5-38) years; 18 were ACPA and RF+. All patients were treated with abatacept, 13 as monotherapy and 23 in association with csDMARDs. No patients had COVID19 disease during the evaluated period.
A significant worsening of global health and patient global assessment of disease activity was observed; while no differences were observed regarding the CROs and other PROs (Figure 1)

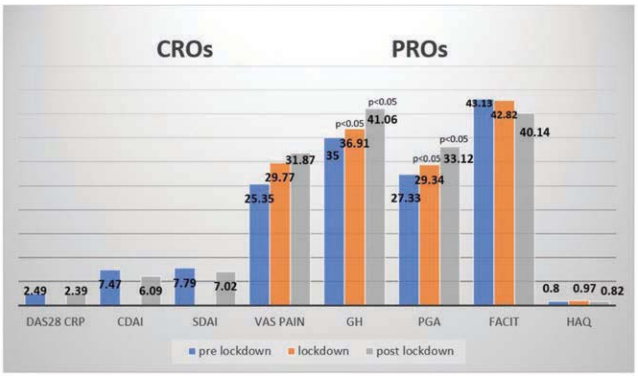

Figure 1.

Conclusion: In the present study we were able to compare PROs in patients with RA before and after the first COVID wave in Italy. While no significant changes in disease activity were observed, patients experienced an increased perception of disease activity and a decline in their overall health status which began during the lockdown and continued over the following 3 months.
This may highlight a discordance between the patient and the physician perception of the disease, which may partly due to the psychological impact of pandemic on the general perception of health particular in patients with chronic diseases.
Since this discrepancy may have consequences on disease management, and particularly on treatment adherence, there is a need to promote studies to better understand the reasons for these discrepancies and to improve the patient perception of their disease particularly in difficult situations such as COVID 19 pandemic.
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AB0260 ASSOCIATION BETWEEN INFLAMMATION AND DEPRESSIVE SYMPTOMS IN RHEUMATOID ARTHRITIS PATIENTS.

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Background: Rheumatoid arthritis (RA) is an autoimmune, progressive disease characterized by an inflammatory process mediated by CD4+T lymphocytes leading to damage of the synovial membrane[1]. Its prevalence is estimated between 0.2 and 1.2% worldwide, affecting women in the fourth and fifth decades[2]. In 2013, the Mexican College of Rheumatology estimated a 1.6% prevalence[3] in Mexico.
RA may affect patients´ social, psychological, economic and physical areas. Among its psychological implications, depression is one of the most important (with a prevalence of 40%) beyond the general population[4]. Several studies assess either prevalence or prognosis, despite its higher prevalence and a lesser likelihood of remission in these patients. Some investigations looked for a relationship between inflammation and depressive symptoms considering only clinical or biochemical parameters, despite the evidence supporting better results with imaging methods, such as musculoskeletal ultrasound (MSU).
Objectives: To identify the association between MSU demonstrated inflammation and the presence of depressive symptoms in RA patients.
Methods: In 2021 a cross-sectional study on RA patients (according to ACR/EULAR 2010 criteria) was conducted. The subjects were from the *Instituto Nacional de Rehabilitación "Luis Guillermo Ibarra Ibarra"* and *Hospital Juárez de México* Rheumatology out-patient clinic. Each patient underwent a clinical (SDAI, CDAI, and EVA), psychological (PHQ9 and InCaViSa questionnaires), and MSU assessment (7 joints score). Data described with central tendency and dispersion measures for quantitative variables and frequencies and proportions for qualitative variables. Kruskal Wallis, U Mann-Whitney and Spearman correlation tests for analysis done.
Results: Fifty-two patients (94% women) were evaluated, with a mean age of 56.06 (±12.31) years and duration of disease 13.66 (±9.44) years. Depression prevalence was 54%. Patients with disease activity had the highest depression scores (p=0.009), those with triggering events in the last six months (p=0.177), the leading event was the death of a close relative in 30% of the patients. A moderate correlation between the depression score (PHQ9) and clinical disease activity scores (SDAI, CDAI, VAS, and painful joints) (rho=0.553 [p<0.001], 0.559 [p<0.001], 0.492 [p<0.001], and 0.57 [p<0.001], respectively) were found. Furthermore, we found a moderate correlation between depression scores and psychological, social and physical quality of life. A mild correlation between MSU synovitis and depression scores (rho=0.315 [p=0.03]) found.
Conclusion: Patients with disease activity reported higher depression scores in comparison to remission patients. We demonstrated a relationship between depressive symptoms, social factors, disease perception and ultrasound synovitis. It is crucial to conduct longitudinal studies with a large number of patients, including a control group, and perform an adequate stratification of the demographic characteristics of the patients and their confounding variables.
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AB0261 CARDIOMETABOLIC COMORBIDITIES MAY IDENTIFY A MORE SEVERE SUBSET OF RHEUMATOID ARTHRITIS, RESULTS FROM A "REAL-LIFE" STUDY

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Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease associated with a significant increased rate of cardiometabolic comorbidities contributing to an increased risk of morbidity and mortality of these patients [1,2]. RA patients with cardiometabolic comorbidities might differ from those without in their clinical presentation and prognosis.
Objectives: This "real-life" cross-sectional study was designed to describe disease features of RA consecutive participants affected by cardiometabolic comorbidities than those without, among those attending recruiting centres from January 1, 2021 to December 31, 2021. Our purpose was also the identification of possible associations between these diseases and clinical characteristics of patients (i.e. fulfilment of ACR1987 criteria, ACPA positivity, presence of extra-articular manifestations, remission, and bDMARD failure).
Methods: Consecutive RA patients were assessed, all fulfilling 2010 ACR/EULAR criteria for RA. We have defined the participant as having such comorbidities if affected by 2 or 3 among high blood pressure (HBP), type 2 diabetes (T2D), and/or dyslipidaemia. The presence of cardiometabolic comorbidities for each participant was verified by reviewing the clinical charts, interview, and extensive medical examinations. Patients with and without cardiometabolic comorbidities were grouped and compared. After that, regression models were built to assess the influence of the presence of cardiometabolic comorbidities on RA features of disease severity.
Results: 757 consecutive RA participants were evaluated [(female 56.6%, age 64.7 ± 12.3years, median disease duration 6 years (IQR 12)]. Among assessed participants, 13.5% showed cardiometabolic comorbidities. These were older (63.9 ± 13.1 vs 70.4 ± 9.0 years, p<0.001) and characterised by a longer disease duration with 64.7% between 5 and 10 years (p=0.003). They were more often affected by extra-articular manifestations (8.2% vs 17.7%, p=0.029) and frequently displayed smoking habit (36.6% vs 50.0%, p=0.003). A lower percentage of participants with these comorbidities was in remission (15.7% vs 8.5%, p=0.048) and they showed a higher prevalence of history of bDMARD failure (40.4% vs 78.4%, p<0.001).
Finally, regression models showed that cardiometabolic comorbidities were significantly correlated with RA features of disease severity. Participants with cardiometabolic comorbidities more frequently fulfilled ACR1987 criteria in both univariate (OR: 1.47, 95%CI: 1.15-1.89, p=0.002) and multivariate analyses (OR: 1.48, 95%CI: 1.15-1.91, p=0.002). These participants had a higher probability of ACPA positivity in both univariate (OR: 1.52, 95%CI: 1.10-2.09, p=0.009) and multivariate analyses (OR: 1.47, 95%CI: 1.06-2.04, p=0.020). Cardiometabolic comorbidities also predicted the presence of extra-articular manifestations in both univariate (OR: 3.26, 95%CI: 1.77-5.89, p<0.001) and multivariate analyses (OR: 2.41, 95%CI: 1.30-4.87, p=0.005). Participants with cardiometabolic comorbidities had a higher probability of previous bDMARD failure in both univariate (OR: 1.73, 95%CI: 1.24-2.43, p<0.001) and multivariate analyses (OR: 7.17, 95%CI: 3.61-14.2, p<0.001). Cardiometabolic comorbidities resulted to be a negative predictor of being in remission in both univariate (OR: 0.53, 95%CI: 0.39-0.97, p=0.041) and multivariate analyses (OR: 0.61, 95%CI: 0.41-0.96, p=0.035).
Conclusion: We described disease features of RA participants with cardiometabolic comorbidities, identifying a disease subset characterised by clinical features of disease severity and to be considered as "difficult-to-treat". Thus, cardiometabolic comorbidities may represent a considerable burden for RA patients requiring an appropriate management which should focus, in addition to cardiovascular risk prediction, on targeting these metabolic components.
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AB0262 PATIENTS WITH RHEUMATOID ARTHRITIS WHO DEVELOP SARCOPENIA FALL FREQUENTLY: 5-YEAR DATA FROM THE CHIKARA STUDY

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Background: Patients with rheumatoid arthritis (RA) are likely to have sarcopenia due to decreased muscle mass and physical function. Some patients develop sarcopenia even if disease activity is well-controlled. We previously reported that 13.2% of RA patients without sarcopenia at baseline developed sarcopenia over a year[1].
Objectives: The aim was to longitudinally investigate sarcopenia status and the characteristics of RA patients using data from the prospective, observational CHIKARA study.

Methods: Body composition, laboratory data, disease activity, physical function (HAQ), treatment, and history of falls and fractures were investigated in 100 RA patients who participated in the CHIKARA study at baseline and at 5 years. They were divided into 4 groups depending on their sarcopenia status: no sarcopenia developed (N group; sarcopenia absent at baseline and 5 years); sarcopenia developed (S group; sarcopenia absent at baseline, but present at 5 years); cured (C group; sarcopenia present at baseline, but absent at 5 years); and persistent (P group; sarcopenia present at baseline and at 5 years).
Results: Seventy RA patients completed the survey. There were no differences among the 4 groups in disease activity, physical function, and treatment. The N group, accounting for 67.1% of all patients, was young and had high body mass index, muscle mass, fat mass, estimated bone mass, and body metabolic rate at baseline. On the other hand, the S group, accounting for 4.3% of all patients, fell significantly more frequently (p=0.035), 3.3 times during 5 years. The P group, accounting for 18.6% of all patients, had significantly higher MMP-3 at baseline (p=0.006). The C group accounted for 10.0% of all patients (Table 1).

Table 1. Characteristics of 77 RA patients by sarcopenia status at baseline and at 5-year follow-up

	no development (n=47)	development (n=3)	cured (n=7)	persisted (n=13)	p value
age, years	63 (57.5, 70)	76 (74.5, 81)	66 (54, 70)	73 (65, 82)	0.006
disease duration, years	6.5 (1.1, 10.7)	15.2 (14.9, 20.7)	11.4 (7.2, 14.8)	3.5 (1.1, 6.5)	0.021
MTX dose, mg/day	8.1 ± 3.7	6.0 ± 2.0	7.4 ± 3.8	6.2 ± 4.8	0.406
biologics use, %	36.2	66.7	28.6	23.1	0.513
GC use, %	23.4	0	28.6	15.4	0.701
average GC dose, mg/day	3.5 ± 1.1	0	3.7 ± 1.8	6.3 ± 1.8	0.833
CRP, mg/dl	0.1 (0.04, 0.18)	0.04 (0.04, 0.23)	0.2 (0.12, 0.47)	0.19 (0.08,0.82)	0.22
MMP-3, ng/ml	62.2 (50.3, 98.6)	58.9 (47.8, 71.3)	74.9 (58.3,147.2)	160 (90.8,262)	0.006
DAS28ESR	3.34 ± 0.91	4.11 ± 0.72	3.36 ± 1.38	3.79 ± 1.20	0.355
mHAQ	0.25 (0, 0.5)	0.63 (0.56, 1.25)	0.87 (0.25, 1.0)	0.25 (0.13, 0.75)	0.132
BMI, kg/m^2	23.22 ± 3.51	21.4 ± 2.25	18.69 ± 2.08	19.56 ± 2.39	<0.001
SMI, kg/m^2	6.73 ± 0.7	6.1 ± 0.2	5.51 ± 0.14	5.79 ± 0.6	<0.001
fat percentage, %	30.39 ± 8.77	30.03 ± 9.12	25.04 ± 6.23	23.75 ± 6.56	0.051
estimated bone mass, kg	2.2 (2, 2.4)	1.9 (1.75, 1.95)	1.6 (1.55, 1.9)	1.9 (1.7, 2.2)	0.001
BMR, kcal	1101 (1051, 1198)	986 (934, 1010)	896 (872, 994)	978 (902,1107)	<0.001
ΔDAS28ESR	-0.15 ± 0.84	-0.43 ± 1.73	0.04 ± 0.89	-0.59 ± 1.33	0.445
ΔSMI, kg/m2	-0.06 ± 0.34	-0.38 ± 0.57	0.25 ± 0.22	0.08 ± 0.42	0.038
fall, times	1.6	3.33	1.29	0.38	0.045

Data are shown as mean ± standard deviation (SD) or median (25th, 75th percentile). GC: glucocorticoids, MMP-3: matrix metalloproteinase 3, DAS: disease activity score, HAQ: health assessment questionnaire, BMI: body mass index, SMI: skeletal muscle mass index, BMR: body metabolization rate, Δ:change during 5 years.

Conclusion: Overall, 4.3% of RA patients developed sarcopenia and fell frequently during 5-year follow-up. Patients who develop sarcopenia require special care because they are at high risk of falls.
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AB0263 CLINICAL AND LABORATORY FACTORS ASSOCIATED WITH THE RHEUMATOID CACHEXIA.

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Background: Rheumatoid arthritis (RA) is associated with reduced physical performance capacity, leisure activities and self-service [1]. These changes are the results of the destruction of the joints, as well as the decrease in muscle strength, which is known as sarcopenia. However, patients with RA beset with a rheumatoid cachexia (RC), a specific form of sarcopenia, characterized with a decrease in fat-free mass index and an increase in fat mass index [2]. RC leads to a dramatic decrease in the life quality and increase in mortality rate [3].
Objectives: To study the clinical and laboratory factors associated with the RC.
Methods: 110 patients (102 females and 8 males) were enrolled in our study. All patients fulfilled the 2010 ACR/EULAR classification criteria for RA. Standard clinical, laboratory and instrumental examinations were performed. Additionally, hsCRP, ACPA, CTX-1, P1NP and 25(OH)D were defined. Dual-energy X-ray absorptiometry with Total Body program was performed. The diagnosis of RC was based on the next criteria: fat-free mass index less than 10th percentiles with fat mass index above 25th percentiles [2]. Statistical analysis was performed using a software package "Statistica 12.0". Parametric parameters are presented as M±std.dev. (95% CI), non-parametrics as Me (Q1-Q3). Intragroup analysis of quantitative indicators was carried out using Student's or Mann-Whitney test. The multiple logistic regression analysis was performed with a stepwise direct search procedure. Results are presented as odds ratio (OR) and 95% confidence interval (95% CI). ROC curve was plotted to assess the diagnostic significance of quantitative signs in predicting rheumatoid cachexia.
Results: Mean patients age was 53,7±12,07 (10,8-13,7) years. More than 85% had severe of terminal progression of the RA. Most patients were RF (77,3%) and ACPA (67,3%) positive, had moderate disease activity (3,79 [2,89-4,40]), cartilage erosions (79%) and II (56,4%) functional class. RC was diagnosed in 25 patients. Prevalence of RC was lower in RF-negative patients (OR 0,11 (95% CI 0,01-0,83). Also, prevalence of RA was associated with the duration of RA (1,06 (1,01-1,11)). Mean cumulative dose of glucocorticoids (GCs) was higher in patients with RC (8,5 g [6,2-17,5 g]), than without (5,8 g [3,6-13,7 g]) (Z=-1,98; p=0,047). Mean daily dose of GCs was lower in patients with RC (5 mg [4-8 mg] and 8 mg [5-10 mg] (Z=2,58; p=0,01)). The median duration of RA was higher among patients with RC (14,0 years [9,0-22,0] vs 8,0 years [3,0-16,0] (Z=-2,18; p=0,029)).
ROC-curve was employed to assess the significance of the RF-negativity and RA duration in the diagnosis of RC. Results are presented in Figure 1.

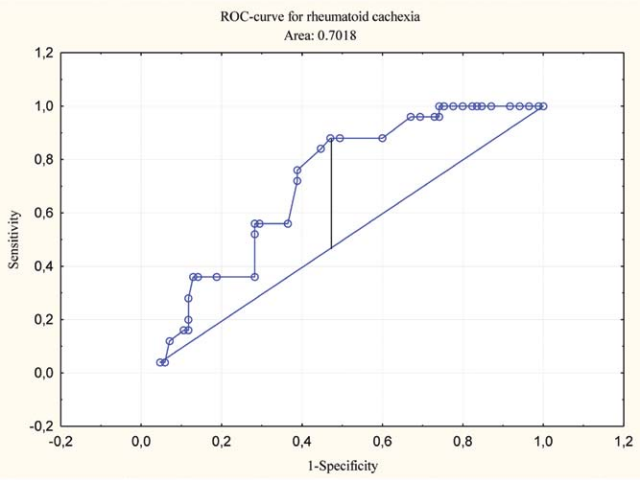

Figure 1. ROC-curve for the RC based on the duration of RA and the presence of RF.

The optimum cut-off point of 9,5 years of RA was defined using Youden's J, with a sensitivity of 88% and specificity of 53%.
Conclusion: RC is associated with the duration of RA, positivity for RF, higher cumulative dose of GCs and lower daily dose of GCs. Due to clinical practice, higher doses of GCs are usually prescribed as a "bridge-therapy" at the start of the treatment or while switching the therapy. On the other side, patients with low daily dose of GCs are more often hormone dependent, with high total cumulative dose. With the sensitivity of 88% patients with the duration of RA 9,5 years and more have RC.
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AB0264 ASSOCIATION BETWEEN DIFFERENT HLADRB1 ALLELES AND SEVERITY IN RHEUMATOID ARTHRITIS

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Table 1. Characteristics of the patients with the different alleles

Variables	SE- (n= 43)	*01:01 (n= 18)	*01:02 (n= 10)	*04:01 (n= 12)	*04:04 (n=10)	*04:05 (n= 4)	*10:01 (n= 5)	*03:01 (n= 15)	*07:01 (n= 17)	*p*
Age at diagnosis (years), mean (SD)	54.1 (16.2)	48.5 (14.8)	55.5 (10.7)	45.7 (12.9)	50 (11.4)	56.8 (20.9)	55.1 (21.2)	50.5 (11.3)	59.7 (17.9)	0.336
Female sex, n (%)	30 (69.7)	12 (66.6)	7 (70)	10 (83.3)	9 (90)	0	3 (60)	12 (80)	12 (70.6)	0.096
Time since diagnosis (years), mean (SD)	12.8 (7.8)	15.3 (3.6)	11.8 (7.6)	14.1 (6)	11.03 (7.9)	9.3 (6.8)	11.8 (7.4)	16.4 (6.9)	12.3 (7.3)	0.420
RF +, n (%)	32 (74.4)	17 (94.4)	9 (90)	12 (100)	10 (100)	4 (100)	4 (80)	12 (80)	13 (76.5)	0.216
ACPA +, n (%)	27 (62.7)	16 (88.8)	9 (90)	11 (91.6)	10 (100)	4 (100)	5 (100)	9 (60)	8 (47)	**0.004**
Erosions, n (%)	12 (27.9)	9 (50)	3 (30)	8 (66.7)	5 (50)	2 (50)	2 (40)	7 (46.7)	7 (41.2)	0.422
Noduls, n (%)	0	1 (5.5)	0	1 (8.3)	1 (10)	2 (50)	1 (20)	0	1 (5.9)	**0.003**
Osteoporosis, n (%)	14 (32.5)	3 (16.7)	4 (40)	1 (8.3)	3 (30)	0	0	1 (6.6)	4 (23.5)	0.194
Sjogren S., n (%)	4 (9.3)	0	0	1 (8.3)	0	0	0	2 (13.3)	0	0.515
ILD, n (%)	5 (11.6)	1 (5.5)	1 (10)	2 (16.7)	2 (20)	0	0	2 (13.3)	2 (11.8)	0.937
CVD, n (%)	11 (25.6)	4 (22.2)	1 (10)	1 (8.3)	1 (10)	1 (25)	1 (20)	2 (13.3)	4 (23.5)	0.872
Serious infections, n (%)	11 (25.6)	1 (5.5)	1 (10)	0	2 (20)	2 (50)	0	2 (13.3)	2 (11.8)	0.646
Cancer, n (%)	4 (9.3)	3 (16.7)	1 (10)	1 (8.3)	2 (20)	1 (25)	1 (20)	2 (13.3)	2 (11.8)	0.972
Multiresistants, n (%)	2 (4.6)	2 (11.1)	0	1	0	1	0	2	0	0.465
Deaths, n (%)	12 (27.9)	2 (11.1)	0	0	0	2 (50)	0	1 (6.6)	7 (41.2)	**0.005**

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Objectives: To evaluate the association between different HLADRB1 alleles and the development of serious complications in patients with rheumatoid arthritis (RA).
Methods: We performed an observational, longitudinal and retrospective study of a cohort of 134 patients with established RA (ACR/EULAR 2010) from the registry of our department, older than 18 years and without other associated autoimmune pathologies except secondary Sjogren's syndrome and who had the requested HLADRB1 genotype. Patients with ≥ 1 of the following HLA-DRB1 alleles were considered positive shared epitope carriers (SE+): *01:01, *01:02, *04:01, *04:04, *04:05, * 10:01, *03:01 or *07:01. The remaining patients without any of these alleles were considered shared epitope negative (SE-). Serious complications of RA were included: interstitial lung disease, cardiovascular events, cancer, admissions for serious infections, vasculitis, Felty's syndrome, or death. Other severity data: erosions, rheumatoid nodules, multiple resistance to biologicals (3 or more biologicals), secondary Sjogren's syndrome or osteoporosis. Descriptive and bivariate analysis was performed between the different alleles (χ^2/ANOVA). Cox regression analysis was performed to estimate the influence of the different alleles on mortality.
Results: A total of 134 patients (91 SE+ and 43 SE-) were included. The main differences between the different alleles are shown in Table 1. The most frequent alleles were *0101 (n=18), *0301 (n=15) and *0701 (n=17). When the different alleles were compared, it was seen that the carriers of the alleles *04:05 presented positive ACPA more frequently (100%), rheumatoid nodules (50%) and showed higher mortality (50%) together with the carriers of *07:01 (41.2%), in a statistically significant way. There was no difference in the rest of the complications or severity data. The causes of death were varied in patients with both alleles (cardiovascular events, cancer, interstitial lung disease, and infections). There were no differences in age at death [mean 82.8 years (SD 3.8) vs 84.5 (6.6); p= 0.836, respectively]. Cox regression analysis adjusted for sex, age and ACPA showed that patients with alleles *04:05 (HR 9.1 (95% CI 1.1-72.3; p=0.036) and *07:01 (HR 10.9 (95% CI 1.5-81.2; p= 0.019) had a higher risk of mortality from any cause.
Conclusion: Our results suggest that RA patients carrying the *0405 and *0701 alleles have an increased risk of mortality. Studies with larger numbers of patients are needed to confirm these results.
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AB0265

RHEUMATOID ARTHRITIS PATIENTS HOSPITALIZED FOR A SERIOUS INFECTION HAVE HIGH INCIDENCE OF SEPSIS WHILE THOSE ON BDMARDS HAVE LOWER MORTALITY COMPARED TO THOSE ON CSDMARDS

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Background: The treatment of rheumatoid arthritis (RA) includes conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biologic DMARDs (bDMARDs). RA is associated with an increased risk of serious infections (SI) and the use of bDMARDs almost doubles this risk. SI can lead to sepsis, a life-threatening condition manifested by organ failure caused by a dysregulated host response to a pathogen. bDMARDs target pro-inflammatory cytokines which mediate the inflammation cascade activated both in RA and sepsis. However, very few data exist regarding the incidence of sepsis in patients with a SI while on treatment with bDMARDs.
Objectives: To assess the outcomes of sepsis and death in RA patients with a SI and compare them between patients on bDMARD and csDMARDs. Secondary aims were the comparison of subgroups of patients treated with different bDMARD classes [Tumor necrosis factor inhibitor (TNFi) vs. non-TNFi] and subgroups based on age (geriatric vs. younger patients).
Methods: Single-center retrospective analysis of adult RA patients registered in the University of Crete Rheumatology Clinic Registry (UCRCR), who were hospitalized for ≥1 SI between 2004-2020. Patients were assigned to "bDMARD group" if they were receiving bDMARDs at the time of the SI or "Control group" if there was no bDMARD exposure at least 3 months before the SI. Demographics, RA characteristics, and comorbidities were retrieved from UCRCR database, while details regarding hospitalization were sought in the patients' electronic and paper files. Together with the "Sequential Organ Failure Assessment" (SOFA) criteria at admission and during 76-92 hours of hospitalization used to define the diagnosis of sepsis, we also analyzed the criteria of septic shock and in-hospital mortality.
Results: A total of 117 hospitalizations for SI in RA patients were included: 66 in patients receiving bDMARDs and 51 in the control group (65% bDMARD-naive and 35% bDMARD-experienced). The majority of the patients (76%) were women in both groups, however, patients on bDMARDs were younger than control patients [70 (IQR 62-77) and 78 (IQR 68-82) years old respectively, p=0.002]. Other demographics, disease characteristics, disease activity at baseline, and comorbidities did not differ between the two groups, except for a higher prevalence of one or more previous hospitalizations for infection in patients on bDMARDs.
During hospitalization, 14 patients (12%) died. Mortality was significantly higher in the control group (19.6% of patients) compared to the bDMARD group (6%) (p=0.025). Sepsis criteria were fulfilled in 56 patients (47.9%) at admission and/or at 76-92 hours of hospitalization. Sepsis was marginally more frequent in the control group versus the bDMARD group (56.9% vs. 40.9% respectively, p=0.087). In the subgroup analysis based on the type of bDMARD, no statistical difference was found for the outcomes of sepsis or death between patients on TNFi versus those on non-TNFi. However, in the subgroup of patients ≥65 years old, there was a tendency for a lower incidence of sepsis or death in patients on TNFi compared to those on non-TNFi or the control group [14% vs 53%, vs 85% respectively (p=0.120) for the outcome of sepsis and 7% vs. 21%, vs. 71% (p=0.138) for the outcome of death].
Receiver operating characteristic (ROC) analysis indicated older age (p<0.001), higher SOFA score at admission (p<0.001), septic shock at 76-92 hours (p<0.001), and non-exposure to TNFi (p=0.040) as predictors of in-hospital death. However, in multivariable logistic regression analysis, older age was the only significant predictor of sepsis and death during hospitalization.
Conclusion: In the present study, we found a high incidence of sepsis (47.9%) and mortality (12%) in RA patients hospitalized for a serious infection. Older age is the most significant predictor of adverse outcomes, however, patients on bDMARDs showed lower mortality and a tendency for a lower incidence of sepsis compared to the control group.
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AB0266

PREGNANCY PLANNING AND FOLLOW-UP IN MULTIDISCIPLINARY UNITS IMPROVES THE OUTCOMES IN WOMEN WITH INFLAMMATORY ARTHROPATHIES

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Background: Women with inflammatory arthropaties (IA) have fertility problems and complications during pregnancy and frequently biological therapy (BT) is required for the disease control.
Objectives: To evaluate pregnancy in women with IA in a multidisciplinary unit composed of Rheumatologists and Obstetricians: describe disease evolution, complications and treatment.
Methods: Retrospective and descriptive study of the evolution of pregnancy in patients with IA [Rheumatoid Arthritis (RA), Spondyloarthritis (SpA), Psoriatic arthritis (PsA) and Juvenile Idiopathic Arthritis (JIA)] and follow-up in a multidisciplinary unit for more than 15 years (until December 2021). Demographics, maternal disease, time until conception, previous abortions and presence of antibodies were collected. In addition, during follow-up, treatment, abortions, cesarean sections (C-section), preterm births, disease activity and maternal/fetal complications were collected.
Results: We registered 49 pregnancies (39 women): 27 RA (55.1%), 9 SpA (18.4%), 9 PsA (18.4%) and 4 JIA (8.1%). Maternal average age at diagnosis was 26.8±6.7 years and average age at childbirth/abortion was 34.5±5.3 years. It took an average time of 9±7.7 months to conceive. 8.2% received fertility treatment with in vitro fertilization techniques.
AntiRo antibodies were registered in 6.3% of patients and 28.6% had at least 1 antiphospholipid antibody.
At the time of gestational desire/gestation 24 women (13 RA, 5 SpA, 3 PsA, 3 JIA) were receiving BT: 14 certolizumab (CZP), 5 adalimumab (ADA), 4 etanercept (ETN). 1 patient was being treated with baricitinib (BARI). Due to pregnancy, ADA was changed to CZP in 3 women and BT was stopped in 6 cases (3 ETN, 2 ADA, 1 CZP) as well as BARI. In 2 cases, ADA was stopped at week 17 of pregnancy (medical indication). Pregnancy was completed with BT (CZP) in 15 cases. 9 abortions were registered prior to follow-up in the unit (0.23 abortions/mother) and 3 (2 RA, 1 PsA) during follow-up (0.07 abortions/mother): 2 (1 RA, 1 PsA) of them in women with CZP. RA patient had positive antiphospholipid antibodies and was a smoker and the other one had moderate disease activity by the time of the abortion. C-section was performed in 26.1% of cases. Preterm birth (<37 weeks) happened in 8.2% (n: 4) of the pregnancies: 2 in women with CZP.
A total of 19 different fetal/maternal complications were registered during follow-up: 8 in the BT group (42.1%) compared to 11 (57.9%) in the group without BT, being Intrauterine Growth Restriction (IUGR) more frequent among women with BT. Infections were not more common in patients with BT. Table 1.

Table 1.

COMPLICATIONS	WITH BT (n, %) n: 17	WITHOUT BT (n, %) n: 32
IUGR	3 (17.6)	1 (3.1)
LBW	2 (11.8)	2 (6.2)
INFECTION	1 (5.9)	4 (12.5)
CHOLESTASIS	0 (0)	2 (6.2)
PREECLAMPSIA	0 (0)	1 (3.1)
DM	2 (11.8)	1 (3.1)
HIGH BLOOD PRESSURE	0 (0)	0 (0)
NEPHROPATY	0 (0)	0 (0)
NEONATAL LUPUS	0 (0)	0 (0)
HEART BLOCK	0 (0)	0 (0)
MALFORMATION	0 (0)	0 (0)
HELLP SYNDROME	0 (0)	0 (0)
TOTAL	**8**	**11**

Regarding concomitant treatment, low dose prednisone was used in 32.7% of pregnancies, hydroxychloroquine in 44.9%, sulfasalazine in 8.2% and acetylsalicylic acid in 51%. We didn´t find differences in the use of these treatments between the two groups.
Median DAS28 among RA patients with available data was under 2.6 throughout pregnancy as well as previously and posteriorly. No differences in median DAS28 were found between women with BT and without BT. SpA patients had BASDAI lower than 4 in both groups during pregnancy and previously.
Conclusion: In our series, as described in the literature, women with IA are older and more likely to have preterm births compared to general population. Appropriate disease control was maintained during pregnancy, also previously and afterwards. We registered more IUGR, low birth weight (LBW) and diabetes mellitus (DM) among women with BT but lower rate of infections. Given the low number of patients with BT no statistically significant conclusions about complications can be drawn. Therefore, more studies among pregnant women with BT are necessary.
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AB0267

FEATURES OF CARDIAC PATHOLOGY IN PATIENTS WITH SECONDARY OSTEOARTHRITIS ON THE BACKGROUND OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis, being one of the most common rheumatic diseases, is often accompanied by systemic (extra-articular) manifestations and various complications. In particular, the inflammatory process often leads to damage to the tissues of the joint and the subsequent development of secondary arthrosis. RA is accompanied by a high cardiovascular risk. Patients with OA also have an increased risk of developing cardiovascular diseases.
Objectives: To identify the features of cardiac pathology in patients with rheumatoid arthritis (RA) in combination with osteoarthritis (OA).
Methods: The study involved 282 patients with secondary OA on the background of RA. The first group consisted of 48 patients who underwent endoprosthetics of at least one large joint due to severe OA, the second group consisted of 234 patients with RA and secondary OA of functional class 1-3 who did not require endoprosthetics. The patients underwent determination of the level of rheumatoid factor, circulating immune complexes, C-reactive protein, ESR, ECG with calculation of the QT interval variance, vectorcardiography and echocardiography.
Results: Patients with RA who underwent endoprosthetics due to secondary osteoarthritis were characterized by later clinical and radiological stages ($p<0.0001$), as well as a higher functional class compared to patients of group 2 ($p<0.0005$). Both groups differed in the level of ESR: 1st - 29 [16;40] mm/h, 2nd - 20[12.5;31] mm/h ($p<0.05$). In other words, the severity of osteoarthritis is more associated with the inflammatory component of the underlying disease than with the autoimmune one. During the correlation analysis in group 1, the following correlations were found: inverse, average and reliable relationship between age and the E/a transmittal flow index ($r=-0.63$, $p<0.0001$); direct, average relationship between the DAS level and the relative wall thickness of the left ventricle (LV) ($r=0.39$, $p<0.05$); inverse, average relationship between the level of rheumatoid factor and the vectorcardiographic parameter MV-rise ($r=-0.32$, $p<0.05$); direct, strong the relationship between the relative thickness of the LV wall and the area of the loop P on vectorcardiography ($r=0.76$, $p=0.01$); the inverse, average relationship between the final LV diastolic size and the loop area T ($r=-0.65$, $p=0.03$). Thus, in this group of patients, the older a person is, the more the diastolic function of the left ventricle is impaired. In this study, we found out that with an increase in the activity of the disease, the structural geometry of the heart becomes more concentric, which affects the results of vectorcardiography. In the 2nd group, a direct, average correlation was revealed between the DAS index and the value of the maximum vector according to vectorcardiography ($r=0.6$, $p<0.05$); the inverse, strong relationship between the E/a of the transmittal flow and the dispersion of the QT interval ($r=-0.73$, $p=0.02$). It follows from this that in group 2, an increase in the activity of the disease is accompanied by an increase in the electrical activity of the ventricles of the heart, determined by the maximum vector. And with an increase in diastolic dysfunction of the left ventricle, there is an increase in readiness for the initiation of life-threatening arrhythmias and electrical instability of the myocardium.
Conclusion: In patients with RA and severe secondary OA, high activity of the disease contributes to structural and geometric remodeling of the heart, and in the milder form of secondary OA is accompanied by electrophysiological remodeling in the form of increased electrical activity of the ventricles and, accordingly, the risk of malignant arrhythmias.
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AB0268

SURVEY OF ELDERLY RHEUMATOID ARTHRITIS (RA) PATIENTS: REAL-WORLD DATA OF PRE-OLD (65 TO 74 YEARS) AND OLD (≥ 75 YEARS) RA PATIENTS

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Background: The number of patients (pts) with rheumatoid arthritis (RA) is highest in persons in their late 60s, and the age at onset has increased in recent years. In many countries, including Japan, 'elderly' is defined as 65 years or older, but recently, the Japan Geriatrics Society and Japan Gerontological Society have advocated a newer classification of elderly: pre-old as 65 to 74 years, old as 75-89 years and super old as ≥90 years[1)]. Disease activities, renal functions, treatments and other parameters in thus classified elderly RA pts have not been investigated yet.
Objectives: Elderly pts with RA were classified, and then disease activities, treatments, renal functions and other parameters compared between the groups to clarify the real-world picture of pre-old and old RA pts.
Methods: We enrolled 359 RA patients (85 males, mean age 65.0 ± 13.6 years) treated at our hospital and affiliated hospitals. They were divided into three groups: under 65 years as a control group, 65-74 years as a pre-old (group I), and 75 years or older as an old (group II). Urine examination, serum Cr, eGFR, BUN, other biochemical tests, serological tests, disease activity, treatment, smoking, and comorbidities were evaluated. Difficult-to-treat RA pts (D2T RA) were evaluated according to EULAR criteria[2)].
Results: Group C contained 148 pts (28 males, mean age 51.7 ± 9.6 years), Group I 123 pts (28 males, mean age 70.1 ± 2.9 years) and Group II 88 pts (29 males, average age 80.2 ± 4.5 years). Among the three groups, the frequency of males was 33.0% in group II, which was significantly higher than in the other groups. There was no significant difference in disease activity among the three groups. There was a significant difference in eGFR among the three groups (77.3 ± 17.3 ml/min. in group C, 69.4 ± 15.8 ml/min. in group I, 62.7 ± 18.7 ml/min. in group II). There was a significant difference in frequencies of treatment with NSAIDs (40/133 (30.0%) in group C, 23/102 (22.5%) in group I, 9/67 (13.4%) in group II), methotrexate (MTX) (87/148 (58.8%) in Group C, 62/123 (50.4%) in Group I, 28/88 (31.4%) in Group II). There was no significant difference in frequencies of treatment with prednisolone (55 / 148 (30.2%) in group C, 55/123 (43.1%) in Group I, 45/88 (51.1%) in Group II), with biologics (44/148 (29.7%) in Group C, 29/123 (23.6%) in Group I, 26/88 (29.5%) in Group II) and with JAK inhibitor (15/148 (10.1%) in Group C, 7/123 (5.7%) in Group I, 5/88 (5.7%) in Group II). There was no significant difference in D2TRA pts among the three groups (21/148 (14.2%) in Group C, 12/123 (9.8%) in Group I, 13/88 (14.8%) in Group II). There were significant differences in the frequency of stage IV and comorbidities among the three groups.
Conclusion: In the pre-old and old RA pts, renal function was lower than in the control group. MTX was administered even in them, but less frequently. We were able to clarify the current situation that JAK inhibitors and biologics are actively used even in pre-old and old RA pts with impaired renal function, and the frequency of D2T RA pts could be suppressed to almost that in the control group. Patients with impaired renal function are more likely to develop side effects of MTX, and it is necessary to pay particular attention to pre-old and old RA patients.
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AB0269

UTILITY OF DAS28-ΓGT IN THE ASSESSMENT OF DISEASE ACTIVITY AND CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS

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Background: γGT has been identified as a maker of systemic inflammation and cardiovascular (CV) risk. The composite index DAS28-γGT has been developed to allow an evaluation of both joint disease activity and CV risk.
Objectives: To assess the value of the DAS28-γGT in a population of patients with rheumatoid arthritis (RA) requesting cardiologic assessment.
Methods: Retrospective analysis of RA patients referred to cardio-metabolic day hospitalization in the Rheumatology department of Cochin hospital between February 2021 and January 2022. Criteria for referral were age > 50 years and presence of at least one CV risk factor. DAS28-GGT index was calculated as follows: 0,56 * √TJ-28 + 0,28 * √SJ-28 + 2 * ln (γGT) + 0,14 * GH. This index was analysed according to disease activity measured with the DAS28-CRP, CV risk assessed by the Framingham score and the decision taken by the cardiologist (requirement of complementary explorations and/or therapeutic intervention).
Results: We included 22 RA patients (17 women), with a mean age of 66±10 years, a disease duration of 21±12 years. Rheumatoid factor was positive in 15 patients, anti-CCP antibodies in 17, and bone erosions in 16. 15 patients received methotrexate, 13 corticosteroids (dose < 10 mg per day), 15 targeted biologic therapies and 3 JAK inhibitors. The mean DAS28-CRP was 2.5±0.9 and the mean DAS28-γGT was 7.90±1.90.
2 patients had a DAS28-γGT < 5.5, defined in our previous study as high probability of RA remission and low probability of CV risk. These two patients were in remission and their Framingham score was < 10% (low CV risk). No complementary exploration was requested by the cardiologist.
8 patients (6 women, 2 men) had a DAS28-γGT index between 5,5 and 7,5, defined in our previous study as high probability of RA remission or low disease activity (LDA) and increased probability of CV risk. As expected, all patients were in remission or in LDA. This population were at higher CV risk: 2 patients had a Framingham score > 20% (high risk), 3 patients a score ranging from 10 to 20% (intermediate risk), and 3 patients a score < 10%. One patient presented carotid atheroma. 4 patients required additional CV explorations and 3 patients necessitated escalation of blood hypertension therapy.
Twelve patients (9 women, 3 men) had a DAS28-γGT index > 7,5, defined in our previous study as high probability of active RA and/or increased probability of CV risk. 4 patients were in remission, 3 were in LDA and 5 presented moderate disease activity. One patient had a Framingham score > 20%, 4 had a score ranging between 10 and 20% and 6 had a score < 10%. The score was not applicable in an 80-year-old patient. Three other patients had coronary artery disease, including a patient who presented both coronary artery disease and carotid atheroma. 5 patients requested additional CV explorations and 4 required CV therapy escalation (introduction of statin and aspirin in 2 patients and increased blood hypertension therapy in 2 patients). Among these 12 patients, 3 with the highest DAS28-γGT values presented CV complications: a 64-year-old woman with a DAS28-γGT of 12.8 (DAS28-CRP: 2.89) had carotid atheroma and intermediate lesion of the right artery on coroscanner justifying a coronarography; a 81-year-old woman with a DAS28-γGT of 10.67 (DAS29-CRP: 4.62) had atrial fibrillation and aortic stenosis requiring Transcatheter Aortic Valve Implantation; and a 77-year-old woman with a DAS28-γGT of 10.35 (DAS28-CRP: 3.89) had ischemic chest pain necessitating rapid explorations in cardiology.
Conclusion: The DAS28-γGT allowed a reliable classification of patients according to the RA activity disease and CV risk. This index may be relevant for CV risk stratification decision making to refer RA patients to a cardiologist. Its validation is in progress in a prospective cohort.
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AB0270

EFFECT OF METHOTREXATE USE ON JOINT AND LUNG DISEASE OUTCOMES IN PATIENTS HAVING RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a frequent complication of rheumatoid arthritis (RA). Although methotrexate (MTX) is an anchor drug for RA management, its use may worsen lung disease severity in patients with RA related ILD (RA-ILD). The safety and efficacy of MTX use in RA-ILD treatment have not been elucidated.
Objectives: We aimed to clarify the clinical characteristics of patients with RA-ILD and the effect of MTX use on joint and lung disease outcomes.
Methods: In this retrospective study, we included patients with RA-ILD who visited our department from 2011 to 2019 and underwent chest computed tomography (CT). RA was diagnosed using the 1987 ACR criteria or the 2010 ACR/EULAR classification criteria. During the abovementioned period, we defined the baseline as the time of the first chest CT scan; moreover, the final observation was defined as the time of the final chest CT scan in patients who underwent CT more than once, or as the final visit in those without a second chest CT scan. We excluded patients whose RA-ILD status could not be fully evaluated using chest

CT scans due to other causes, including respiratory infections. Severe infections were defined as infectious events requiring hospitalization.
To identify the clinical characteristics of patients with RA-ILD, we compared the features of RA with versus without ILD at baseline. To clarify the effect of MTX use on RA-ILD outcomes, we compared the outcomes of patients with RA-ILD with versus without MTX use. Furthermore, we investigated factors associated with RA disease activity or ILD deterioration using multivariate analyses.
Results: In this study, we included 452 patients (mean age, 60.2 years; females, 78.5%; mean observational period, 77.5 months), 325 (71.9%) of whom underwent chest CT more than two times.
Patients with ILD (ILD; n=90, 19.9%) were older and had a higher RF positivity rate than those without ILD. Moreover, patients with ILD were treated with lower MTX use (20.2% vs. 52.9%, p<0.001; 1.46 vs. 3.53 mg/week, p<0.001) and TNF inhibitors exposure (21.1% vs. 13.1%, p<0.044) than those without ILD, albeit with similar uses of prednisolone and other bDMARDs, including tocilizumab and abatacept. DAS28-CRP was higher in patients with than in those without ILD at baseline (4.60 vs. 3.42, p=0.063) and at the final observation (2.42 vs. 2.09, p=0.025). Linear regression analysis showed that baseline age and ILD were significantly associated with DAS28-CRP at the final observation (β=0.206 and 0.173, respectively). Kaplan Meier analysis revealed that patients with ILD experienced severe infections and respiratory infections more frequently than those without ILD (log-rank test, p<0.001 and p<0.001).
Seventeen patients (20.2%) with ILD were treated with MTX. At baseline, these patients had similar ages and RF/ACPA positivity rates, as well as prednisolone and tDMARDs exposures, with higher bDMARD exposure (41.2 vs. 13.4%, p=0.016) compared to that in ILD patients without MTX use. DAS28-CRP was comparable in patients with and without MTX use at baseline, but was lower at the final observation in MTX-treated patients with ILD (1.41 vs. 2.73, p<0.001). Kaplan Meier analyses revealed no differences in the frequencies of severe infections, respiratory infections, or ILD deterioration between patients with and without MTX use. Cox regression analysis demonstrated that the risk factors for ILD deterioration included baseline age (hazard ratio [HR] 1.088; 95% confidence interval [CI] 1.037-1.147), but not MTX use (HR 1.666; 95% CI 0.472-5.876).
Conclusion: RA-ILD were treated with lower MTX use, which resulted in higher RA disease activity. In contrast, patients with RA-ILD treated with MTX had lower RA disease activity without ILD deterioration. As RA-ILD is undertreated, appropriate MTX use may be required for effective RA-ILD treatment
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Disclosure of Interests: None declared
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AB0271 ALEXITHYMIA IN A PATIENT WITH RHEUMATOID ARTHRITIS: CONNECTION WITH DISEASES AND FUNCTIONAL ABILITY.

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Background: Rheumatoid arthritis (RA) is the chronic, destructive, immune-mediated inflammatory disease that has a progressive course and causes the early disability of approximately 50% over the next five years. Acute pain syndrome in RA often leads to a violation of the psycho-emotional sphere with manifestations in the form of depression, anxiety and alexithymia.[1] Alexithymia is defined as a personal emotional disorder characterized by difficulty in identifying and describing subjective feelings and related to cognitive impairment.
There is insufficient data regarding the prevalence of alexithymia in patients with RA.
Objectives: To investigate the prevalence of alexithymia and the relationship with disease activity and functional ability in patients with RA.
Methods: RA patients diagnosed according to the ACR/EULAR 2010 classification criteria. The presence of alexithymia was determined by the «Toronto Alexithymia Scale» questionnaire (TAS-20). RA activity was assessed by the Disease Activity Score (DAS28-ESR), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI). Functional ability - by the Health Assessment Questionnaire (HAQ). In the study were included 98 patients with RA (83.7% of women). The mean age was (M±SD) 49.5 ± 11.7 years, the duration of the disease ranged from 1 to 21 years, and averaged 7.8 ± 4.9 years. Statistical analysis was performed by IBM Statistics SPSS 20.
Results: Among 98 examined, alexithymia (≥ 61) was detected in 24 persons (24.5%), including 23 women, mean age (M±SD) 54 ± 7.16 years with disease duration 9.96 ± 5.23 years. The activity of RA in persons with alexithymia was: DAS-28 (6.4 ± 0.71); SDAI (41.15 ± 8.64); CDAI (39.46 ± 9.03) and ESR (27.6 ± 15.1), which was significantly higher than in patients without alexithymia: DAS-28 (5.52 ± 1.05); SDAI (32.72 ± 11.28); CDAI (31.98 ± 11.07) and ESR (22.7 ± 15.27). Functional disability in individuals with RA and alexithymia according to HAQ was (1.7 ± 0.59) in contrast to the group of patients with RA without alexithymia - (1.04 ± 0.62). The value of TAS-20 had a direct correlation with the activity by DAS-28 (0,379; p < 0,01), SDAI (0,39; p < 0,01) and CDAI (0,359; p < 0,01)), radiological stage (0.260; p < 0.01) and HAQ (0.393; p < 0.01).
Conclusion: Alexithymia is quite common comorbid condition in patients with RA associated with disease activity and functional disability. Further studies are needed to assess the clinical significance of alexithymia in this category of patients.
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AB0272 DEEP BREATHING INCREASES HEART RATE VARIABILITY IN HEALTHY PARTICIPANTS AND IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS: AN INTERVENTIONAL DOSE-RESPONSE STUDY

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Background: Patients with Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) are known to have an autonomic dysfunction, especially reduced parasympathetic activity. The dysfunction can be measured through heart rate variability (HRV), an indicator of vagus nerve tone. Studies have found a potential anti-inflammatory effect of the vagus nerve and proposed vagus nerve stimulation (VNS) as an anti-inflammatory treatment. A way of stimulating the vagus nerve non-invasively could be through deep breathing (DB).
Objectives: The aims of this study were to examine the dose-response of DB on HRV in healthy participants and to examine the reliability of the effect of DB on HRV in patients with RA and SLE across two days.
Methods: The study was designed as an interventional study, more specifically the healthy subjects participated in a dose-response study and the patients with RA and SLE participated in a study of reliability. Forty-one healthy participants performed DB for 5, 15, and 30 minutes (4 seconds of inspiration and 6 seconds of expiration) in a randomized order on three different days. Fifty-two patients with RA and SLE performed the optimal dose of DB found in healthy participants, and the intervention was repeated on two different days to examine the reliability of the effect. The outcome measure was HRV, which was derived from a 5-minute electrocardiogram recording measured twice before and three times after DB. The extracted HRV measures included in the further analysis were the time domain parameters: a) The standard deviation of the R-R intervals (SDNN), b)

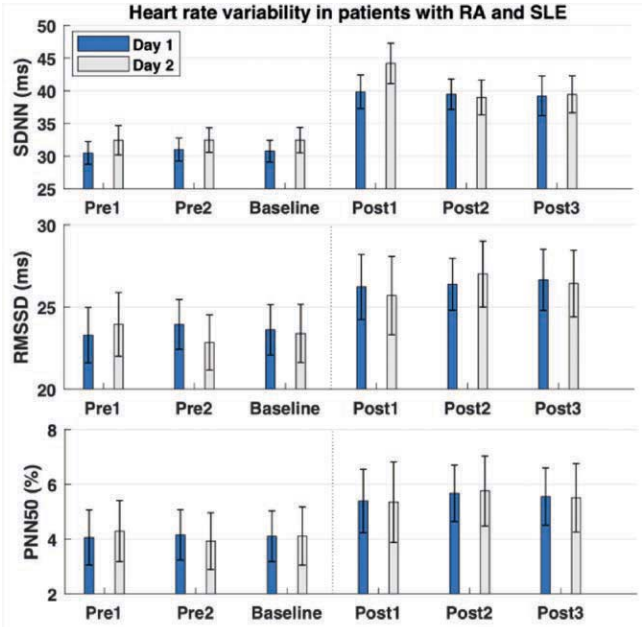

Figure 1. Bar chart showing the heart rate variability-parameters plotted as mean ± standard error in patients with RA and SLE. RA: Rheumatoid Arthritis. SLE: Systemic Lupus Erythematosus. SDNN: The standard deviation of the R-R intervals. RMSSD: The root mean square of successive R-R intervals. PNN50: The proportion of NN50 (pairs of successive R-R intervals that differ more than 50 milliseconds) divided by the total number of R-R intervals.

the root mean square of successive R-R intervals (RMSSD), and c) the proportion of NN50 (pairs of successive R-R intervals that differ more than 50 milliseconds) divided by the total number of R-R intervals (PNN50).
Results: Thirty minutes of DB increased HRV and was the optimal dose of DB in healthy participants. In patients with RA and SLE 30 minutes of DB increased all HRV-parameters similarly across two days indicating reliability, see Figure 1. The effect of DB remained for at least 30 minutes after the intervention.
Conclusion: DB increases HRV in healthy participants and in patients with RA and SLE, indicating a stimulation of the vagus nerve. Future studies are needed to investigate the potential anti-inflammatory effect as well.
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AB0273 IDENTIFICATION OF RED FLAGS FOR INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Interstitial lung disease (ILD) in Rheumatoid Arthritis (RA) can be subclinical or underestimated. Data from the literature report male sex, seropositivity and old age as known risk factors for ILD in RA. However, the correct timing for referral to pneumologists and eligibility for CT chest scan is undefined.
Objectives: To identify potential red flags of ILD diagnosis for referral to a multidisciplinary team analyzing clinical and radiological findings associated with the establishment of ILD.
Methods: Retrospective study on CT chest scan from RA patients evaluated and categorized into usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP) and unclassifiable RA-ILD (Un-ILD), by two radiologists. RA-ILD was diagnosed by two pneumologists considering radiological and clinical factors.
Results: 80 CT chest scans from RA patients (F 59, age 66,6 ± 11,4, disease duration 7,8 ± 4,4) were evaluated. 36,5% of patients had performed CT-chest scan for suspect of ILD, 11,2% for probable pulmonary infection, 8,7% for oncological screening or follow up, 13,7% for COPD disease, 8,7% for screening or active TBC, 3,7% for screening or previous pleuritis and 17,5% for other reasons. A RA-ILD pattern was identified in 35% of patients, with a defined UIP pattern in 17,8%, a defined NSIP pattern in 42,8% and a 39,3% of Un-ILD, while 65% of patients had a non-ILD lung involvement by CT-scan. The mean age at ILD diagnosis was 67,2 years and the mean time between RA diagnosis and onset of ILD symptoms was 7,4 years.
In the multivariate analysis female sex (HR=0,33; p=0,006) and disease duration (HR=0,8; p=0,06) were protective factors for ILD diagnosis. Age (HR=1,1; p=0,03), use of leflunomide (HR=10,1; p=0,03) were negative prognostic factors for ILD. Pulmonary clinical symptoms as dry cough (HR=17,6; p=0,02), bibasilar inspiratory crackles (HR=11,5; p=0,01) and pleural rubs (HR=18,1; p=0,03) predicted ILD while negative predictors were the presence of linear opacities (HR=99,9; p=0,006), interstitial abnormalities (HR=12,1; p=0,07) and cystic areas (HR=33,3; p=0,06) at chest CT scan.
Conclusion: In our cohort the first ILD symptom appeared 7.4 years after RA diagnosis. Clinical variables and radiological abnormalities were identified as highly predictive of ILD diagnosis and may represent red flags for an early diagnosis and referral to pneumologists and radiologists in a multidisciplinary approach.
Disclosure of Interests: None declared
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AB0274 PRESCRIPTION, SWITCH RATE AND THERAPEUTIC RESPONSE DURING BIOLOGIC THERAPY IN INFLAMMATORY RHEUMATIC DISEASES: AN OBSERVATIONAL STUDY IN SOUTHERN MOROCCO

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Background: The use of biological treatment has improved the prognosis of patients with rheumatic diseases. It is important to know the different effects leading to switch in order to adapt the prescription to the patients' profile.
Objectives: To study the prescription profile of biological agents (bDMARD) during chronic inflammatory rheumatic diseases, their impact on disease activity, frequency and causes of switch.
Methods: This is a retrospective study including 106 patients followed for chronic inflammatory rheumatism treated by biological agents.
Results: We included 106 patients, sex ratio (0.44), mean age was 41.5 (±12 .97). 64.4% were followed for spondyloarthritis (41 cases of ankylosing spondylitis, 10 cases of psoriatic arthritis, 11 cases of spondyloarthritis and chronic inflammatory bowel disease). 35.6% of the cases had rheumatoid arthritis, Seropositive in 32%, associated with (Sjorgen's syndrome in 7.5% of cases, lupus in 1.9% of cases, vasculitis in 2% of cases). The mean time between diagnosis and initiation of biotherapy was 54 months (±57.34). The first biologic prescribed for rheumatoid arthritis was Rituximab (94%), Infliximab was the first choice for spondyloarthritis (71%). Conventional treatment was combined with biotherapy in 79% versus 21% just treated by a biological treatment, the switch rate was high in the in the group receiving monotherapy with a significant difference (P=0.024). The initial mean DAS-28 and BASDAI were 4.01 (±2.12) and 4.76 (±2.2) respectively, versus 2.45 (±1.98) and 3.78 (±2.01) after initiation of biologic therapy (P=0.0082). The first cause of switch was therapeutic escape in (82.36%), followed by ineffectiveness in (11.76%) and a paradoxical reaction such as skin psoriasis in (5.85%). Switching was made to an Anti TNF alpha in 14 patients and to another therapeutic class in 3 patients.
Conclusion: Regular monitoring of the efficacy and tolerance of biological treatment is an integral part of the management of chronic inflammatory rheumatism.
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DOI: 10.1136/annrheumdis-2022-eular.2907

AB0275 THE FREQUENCY, PREVALENCE OF CORONARY ARTERY DISEASE AND PRE-MATURE CAD IN PSA AND RA PATIENTS

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Background: An increased incidence of coronary artery disease (CAD) is known in inflammatory arthritis patients compared to the normal population. In the Veterans With Premature Atherosclerosis (VITAL) registry, the frequency of premature CAD (CAD < 55 in men, < 65 years in women) in autoimmune rheumatic diseases was 1.72 (95% CI 1.63-1.81) in Rheumatoid arthritis (RA) compared to the healthy population in approximately 135,000 patients, while a similar situation was not observed in Psoriatic arthritis (PsA) patients 1.09 (95%CI 0.98-1.21) (1).
Objectives: In this study, we aimed to compare the frequency of CAD and premature CAD in RA and PsA patients using bDMARDs.
Methods: The Hacettepe University biological database (HUR-BIO), database was established in 2005 and prospective follow-up of patients using bDMARDs is being carried out. The frequency of CAD was recorded in 486 PsA and 524 RA patients using bDMARDs. CAD was determined according to the angiography reports or Coronary Computed-Tomography results. Premature CAD is defined as a history of CAD before the age of 55 in men and before the age of 65 in women. Demographic characteristics and other comorbid conditions of the patients were also noted. Disease activity (DAS-28) and functional status (HAQ-DI) of the patients before the first DMARD initiation were recorded.
Results: 581 (75.4% female) RA and 520 (69.4% female) PsA patients were evaluated. The ages of the patients and the duration of the disease are as follows; RA, mean (SD) years of age 52.1 (13.9), disease duration 5.3 (2.1) years, PsA mean (SD) years of age 48.7 (12.5), disease duration 9.2 (6.4). At the time of first bDMARD initiation, 43/581 (7.4%) patients with RA and 12/486 (2.4%) patients with PsA had CAD (p<<0.001). After a median (IQR) follow-up of 32 (23) months in RA patients and 49 (88.5) months in PsA patients, CAD was detected in 59 (11.2%) patients, 32 (6.6%) in PsA patients, p=0.01. While 39/59 (66.1%)

Table 1. Characteristics of RA and PsA patients with/without premature CAD

	RA			PsA		
	Premature CAD n=38	Non-premature CAD n=21	p	Premature CAD n=18	Non-premature CAD (n=14)	p
Gender, n (%)	29 (76.3)	9 (42.8)	0.01	10 (55.5)	10 (71.4)	0.36
Age, mean (SD), years	56.6 (8.9)	72.7 (7.1)	<0.001	59.9 (8.2)	69.1 (6.3)	0.002
PsA duration, mean (SD), years	5.5 (2.1)	6.0 (1.7)	0.34	13.3 (8.9)	12.6 (9.5)	0.83
Smoking (ever), n(%)	22 (57.9)	11 (52.4)	0.80	16 (88.9)	5 (35.7)	0.002
BMI > 30, n(%)	19 (52.3)	7 (35.0)	0.20	8 (44.4)	11 (78.5)	0.051
HT (ever), n(%)	23 (63.9)	14 (66.7)	0.89	11 (61.1)	13 (92.8)	0.040
DM (ever), n(%)	20 (57.1)	9 (52.9)	0.77	4 (22.2)	6 (42.8)	0.45
LDL > 130 (ever), n(%)	29	12	0.13	11 (61.1)	5 (35.7)	0.14
DAS-28	4.7 (1.1)	4.2 (1.2)	0.11	4.7 (1.4)	4.5 (1.5)	0.72
HAQ (0-3)	1.41 (0.7)	1.05 (0.8)	0.079	0.7 (0.6)	1. 3 (0.7)	0.13

RA: Rheumatoid arthritis, PsA: Psoriatic arthritis, CAD; Coronary artery disease, BMI; Body-mass index, HT: Hypertension, DM: Diabetes mellitus

of RA patients had premature CAD, 18/32 (56.3%) PsA patients had premature CAD (Table 1).

Conclusion: While the frequency of premature CAD is 10% in the normal population, CAD has a premature character in two-thirds of RA patients and 55% of PsA patients (2). In a large community-based study, the frequency of premature CAD was found to be increased in RA patients compared to the normal population, but no similar difference was observed in PsA patients (1). In real-life data in which we examined a large group of patients using bDMARDs, it is seen that the subtype of CAD is of pre-mature character in both RA patients and PsA patients.

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Disclosure of Interests: None declared

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AB0276

COMPARISON OF METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE WITH NON-ALCOHOLIC FATTY LIVER DISEASE IN IDENTIFYING CARDIOVASCULAR RISK IN CHINESE INDIVIDUALS WITH RHEUMATOID ARTHRITIS

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Background: The nomenclature from non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD) is considered to identify more cardiovascular disease (CVD) risk in general population, and patients with rheumatoid arthritis (RA) carry an excess risk for CVD.

Objectives: To compare MAFLD with NAFLD in identifying CVD risk in RA patients.

Methods: Clinical data from a Chinese RA cohort were retrospectively analyzed. Hepatic steatosis was defined by abdominal ultrasound examination. CVD risk in RA patients was estimated by the Prediction for Atherosclerotic Cardiovascular Disease Risk in China.

Results: Among 513 included RA patients, 78.4% were female and the mean ± SD age was 51.8 ± 12.6 years. The prevalence of MAFLD and NAFLD was 21.4% and 20.5%, respectively. 10.9% RA patients concomitated with CVD events and 32.4% had a high 10-year CVD risk. Multivariate logistic regression analysis showed that both MAFLD and NAFLD were associated with an increase in CVD events (MAFLD: AOR = 2.303 [95% CI 1.197, 4.429]; NAFLD: AOR = 2.478 [95% CI 1.185, 4.779] and high 10-year CVD risk (MAFLD: AOR = 3.184 [95% CI 1.777, 5.705]; NAFLD: AOR = 2.870 [95% CI 1.597, 5.156]; all p < 0.05). The NRI and IDI was -0.011 (95% CI -0.025, 0.003) and -0.002 (95% CI -0.007, 0.002) for CVD events, and 0.012 (95% CI -0.014, 0.038) and 0.005 (95% CI -0.003, 0.013; all p > 0.05) for high 10-year CVD risk, which indicated no additional CVD events and high 10-years CVD risk were identified when replacing NAFLD with MAFLD in RA patients.

Conclusion: Both MAFLD and NAFLD are associated with an increased CVD risk which implies the importance of early detection and management of MAFLD or NAFLD in RA patients. However, new nomenclature of MAFLD identify no additional CVD risk in RA patients.

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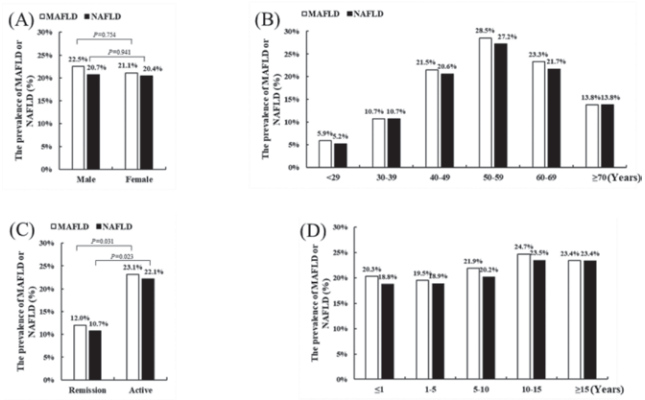

Figure 1. The prevalence of MAFLD and NAFLD in RA patients with different stratification.The prevalence in different genders (A) and ages groups (B); The prevalence in different disease activity groups (C) and disease duration (D); remission (CDAI ≤ 2.8); active (CDAI > 2.8).

Disclosure of Interests: None declared

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AB0277

DYSLIPIDEMIA TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS USING BDMARDS IS BETTER THAN PSA, BUT THERE IS STILL A WAY TO GO

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Background: Patients with inflammatory arthritis have an increased risk of cardiovascular disease. Dyslipidemia is one of the primary modifiable risk factors.

Objectives: Comparasion of the frequency of dyslipidemia and the use of anti-hyperlipidemic agents in patients with Rheumatoid Arthritis (RA) and Psoriatic arthritis (PsA) receiving bDMARDs.

Methods: The Hacettepe University biological database (HUR-BIO), was established in 2005 and 581 (75.4% female) patients with RA and 520 (69.4% female) patients with PsA enrolled up to 2021 were analyzed. Dyslipidemia was defined according to the Turkish Endocrine and Metabolism society criteria (TC > 240, Triglycerides (Tg) > 150, LDL-C > 160, HDL-C (< 40 in men, < 50 in women) (1). The anti-hyperlipidemic (anti-HL) agents used by the patients during follow-up and at their last visit were recorded.

Results: The mean (SD) age of the patients and diseases duration were as follows; RA vs. PsA [age: 52.1 (13.9) vs. 48.7 (12.5) years; disease duration: 5.3 (2.1) vs. 9.2 (6.4) years]. Lipid profiles were known in 289 (49.7%) patients with RA and in 175 (33.6%) patients with PsA at the initiaiton of bDMARD. Lipid profiles were evaluated in 356 (61.2%) patients with RA and 226 (43.4%) patients with PsA during follow-up and at the last visit. Lipid profiles were similar in patients with RA and PsA at the initiation of bDMARDs (Table 1). At the initiation of bDMARD, 29 (5.0%) of RA patients and 10 (3.2%) of PsA patients were receiving anti-HL agents. During the entire follow-up, 65 (12.6%) patients with RA and 22 (4.8%) patients with PsA have used anti-HL agents (p<0.001).

Table 1. Lipid values in patients with RA and PsA at the initiation of bDMARD and at the last visit

	Rheumatoid arthritis, n (%)		Psoriatic arthritis, n (%)		p1*	p2**
Lipid values	bDMARD initiation	Last visit	bDMARD initiation	Last visit		
Total Cholesterol > 240	47/270 (17.4)	98/339 (28.9)	32/161 (19.8)	57/203 (28.1)	0.30	0.13
Triglyseride > 150	62/242 (25.6)	108/320 (33.7)	45/159 (28.3)	80/193 (41.4)	0.79	0.20
HDL-C < 40 (males), < 50 (females)	88/267 (32.9)	70/343 (20.4)	57/157 (36.3)	20/207 (9.6)	0.48	0.001
LDL-C > 160	53/289 (18.3)	91/356 (25.6)	43/175 (24.5)	65/226 (28.7)	0.38	0.55

*p1, bDMARD initiation visit comparison **p2, last visit comparison

Conclusion: In real-life cohort, lipid profile was not assesed in half of the patients during entire follow-up. Although, LDL-C levels are high in about a quarter of the patients in both groups, use of anti-hyperlipidemic drug was inadequate. This is even more evident in PsA patients. Despite the significant emphasis on comorbidities in treatment guidelines, there is still a long way to go in real life.

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AB0278 IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING BDMARDS, THE CHARLSON COMORBIDITY INDEX IS MORE PRONOUNCED THAN PSORIATIC ARTHRITIS

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Background: According to international recommendations, co-morbidities must be taken into account in the management of patients with inflammatory arthritis.

Objectives: To evaluate the distribution of pre-treatment comorbidities in the bDMARD cohort including patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

Methods: The Hacettepe University biological database (HUR-BIO) was established in 2005, 581(75.4% female) patients with RA and 520 (69.4%female) patients with PsA enrolled up to 2021 were analyzed. Diagnosis of RA and PsA were based on the clinical evaluation of the rheumatologist who followed the patients. Comorbidities of the patients were reviewed retrospectively from the biological database, hospital electronic records, ICD-10 diagnostic codes and prescriptions of patients. Diabetes mellitus (DM), Hypertension (HT), Dyslipidemia (DL), Coronary artery disease (CAD), Body mass index (BMI) and smoking were recorded. DL was grouped in terms of lipid values according to the classification of the Turkish Society of Endocrinology and Metabolism Dyslipidemia Guide(1). Detection of coronary artery disease before the age of 55 in men and of 65 in women was classified as premature - CAD. Data on Chronic Kidney Disease, obstructive pulmonary disease, Cerebro-vascular disease, Thyroid Diseases were also recorded. The Charlson comorbidity index (CCI) was calculated by summing the comorbidities in the patients' medical history before the bDMARDs.

Results: The distribution of comorbidities in patients with RA and PsA prior to initiation of bDMARDs was given in Table 1. Patients with RA were older and smoking was more common. HT(28.5% for RA, 21.9% for PsA) and thyroid diseases (22.7% for RA, 14.7% for PsA) were the most comorbidities in both groups. Compared to PsA, patients with RA had higher rate of comorbidities (64.8% vs. 40.4%, p<0.001). Multimorbidity was detected in 231/581 (39.7%) of patients with RA, and it is significantly more common than the patients with PsA (21.8%) (p<0.001). There was no difference between the groups in terms of cardiovascular comorbidities such as BMI, DM, and dyslipidemia. When adjusted for age, the comorbidity burden according to CCI was 3.96 (2.57-6.13, p<0.001) times higher in patients with RA than in patients with PsA.

Table 1. Comorbidities in RA and PsA patients

Features	RA n=581	PsA n=520	p
Gender, female n (%)	438 (75.4)	361 (69.4)	0.027
Age at PsA diagnosis, mean (SD) years	46.7 (13.7)	39.3 (12.0)	<0.001
Age at bDMARD start, mean (SD) years	49.5 (13.8)	42.2 (12.3)	<0.001
CCI			
-No comorbidity	205/581 (35.2)	290/486 (59.6)	<0.001
-1 comorbidity	145/581 (24.9)	90/486 (18.5)	
-≥ 2 comorbidity	231/581 (39.7)	106/486 (21.8)	
CCI mean, (SD)	1.56 (1.77)	0.78 (1.18)	<0.001
Smoking (ever), n	292/581	282/506	<0.001
BMI, mean (SD)	29.3 (6.7)	29.6 (5.9)	0.50
BMI ≥ 30 n	261/577	221/498	0.77
Diabetes Mellitus, n	68/581	49/402	0.30
Hypertension, n	166/581	110/502	0.012
Dyslipidemia* n			
-High TC	47/270	32/161	0.30
-High TG	62/242	45/159	0.79
-High LDL -C	53/289(	43/175	0.38
-Low HDL-C	88/267	57/157	0.48
Uric acid (>6 mg/dl), n	150/554	136/437	0.16
CAD n	59/524	32/486	0.010
Premature CAD, n	39/581	18/486	0.030
CKD, n			
G1 (GFR > 90)	437/523	0	<0.001
G2 (GFR 60-90)	68/523	0	
G3a (GFR 45-60)	11/523	0	
G3b (GFR 30-45)	5/523	28/370	
G4 (GFR 15-30)	2/523	342/370	
Lung disease, n			
-COPD	15/519	3/485	0.007
-Asthma	66/520	19/485	<0.001
Thyroid disease, n	132/581	65/440	<0.001

*TC > 240, TG 150-499, LDL-C> 160, HDL-C erkek < 40, kadın < 50CCI: Charlson comorbidity index, CAD: Coronary artery disease, CKD: Chronic Kidney Disease, COPD: Chronic Obstructive pulmonary disease

Conclusion: The burden of comorbidities in patients with RA before bDMARDs is more pronounced than in patients with PsA. Although, cardiovascular risk factors were similar, with the exception of hypertension and smoking, the age-adjusted CCI was 3.96 times higher in patients with RA than in patients with PsA.

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AB0279 HERPES ZOSTER IN RHEUMATOID ARTHRITIS. PROSPECTIVE SINGLE UNIVERSITY CENTER STUDY

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Table 1. Main features of different groups

Variables	RA patients N= 393	RA with HZ N=31	RA without HZ N=362	P HZ vs noHZ	Variables (continued)	RA patients N= 393	RA with HZ N=31	RA without HZ N=362	P HZ vs noHZ
Age (years) (men±SD)	59.4±12.9	64.7±11.8	59.1±12.9	**0.02**	MTX	365 (92.87)	29 (93.54)	336 (92.81)	0.87
Sex (women)(%)	309 (78.62)	25 (80.6)	284 (78.5)	0.95	LFN	127 (32.31)	12 (38.70)	115 (31.76)	0.42
RA Evolution(months) (mean±SD)	136.9±109.8	155.3±117.0	135.30±109.2	0.33	SSZ	94 (23.91)	7 (22.58)	87 (24.03)	0.78
Hypertension, n(%)	165 (42.0)	19 (61.3)	146 (40.3)	**0.04**		**Anti-TNFa, n (%)**			
Diabetes Mellitus, n(%)	55 (14.0)	7 (22.6)	48 (13.3)	0.24	ADA	144 (36.6)	15 (48.4)	129 (35.6)	0.22
Dislypidemia, n(%)	149 (37.9)	15 (48.4)	134 (37.0)	0.29	ETN	139(35.4)	16 (51.6)	123 (33.9)	**0.05**
RAfeatures, n(%)					IFX	40 (10.1)	5 (16.1)	35 (9.7)	0.25
PositiveRF	224 (57.0)	17 (54.8)	207 (57.2)	0.95	GLM	33 (8.4)	3 (9.7)	30 (8.3)	0.74
PositiveACPA	207 (52.7)	13 (41.9)	194 (53.6)	0.29	CZP	13 (3.3)	1 (3.2)	12 (3.3)	0.97
Erosions	145 (36.9)	10 (32.3)	135 (37.3)	0.71		Non anti-TNFa n (%)			
Subcutaneousnodules	22 (5.6)	1 (4.6)	21 (5.8)	0.85	TCZ	134 (34.1)	16 (51.6)	118 (32.6)	**0.05**
Pulmonary fibrosis	20 (5.1)	3 (9.7)	17 (4.7)	0.20	RTX	69 (17.5)	9 (29.0)	60 (16.7)	0.13
Associated Sjögren Syndrome	20 (5.1)	1 (3.2)	19 (5.3)	0.95	ABA	55 (13.9)	6 (19.3)	49 (13.5)	0.41
Vasculitis	23 (5.9)	2 (6.5)	21 (5.8)	0.7	SARI	2 (5.1)	1 (3.2)	1 (0.3)	**0.03**
RATreatment, n (%)						JAK inhibitors n (%)			
Prednisone	139 (35.4)	19 (61.3)	120 (33.1)	**0.04**	BARI	32 (8.14)	3 (9.67)	29 (8.01)	0.73
Prednisona>5mg/d	13 (3.30)	5 (16.1)	8 (2.20)	**0.001**	TOFA	17 (4.32)	3 (9.67)	14 (3.87)	0.14
ConventionalDMARDs					UPA	4 (1.01)	1 (3.22)	3 (0.83)	0.20

Background: Patients with Rheumatoid arthritis (RA) have an increased risk of infections due to the disease itself, and/or immunosuppressive therapy. The risk of herpes zoster (HZ) including disseminated HZ is also increased**(1)**

Objectives: In an unselected series of RA patientswe assess**a)**prevalence, **b)**general features and **c)** predictive factors of HZ.

Methods: Study of 393 RA patients included in the prospective vaccination program of the Preventive Medicine and Rheumatology department of a University hospital, from October 2011 to October 2016. The minimum follow-up was of 12 months; therefore, it was made until December 2020. HZ vaccination is not included in our vaccination program.

RA was diagnosed according to the ACR/EULAR 2010 criteria. HZ was diagnosed if presented: characteristic skin rash and blisters, paresthesia and local pain, in one (localized) or more dermatomes (generalized).

Information on patients and HZ characteristics was retrieved from the hospital and general physician records.

Results: We studied 393 patients (310 women), mean age 61.5±11.9 years. They were followed-up during a mean period of 82.6±15.2 months(range; 50 months-9 years).

HZ infection was observed in 31 of 393 patients (7.9%) (26 women); mean age 67.5±11.6ys. Prevalence of HZ in this period (122months) was 7.88% with an annual incidence rate of 0.73/100 patients/year. A comparison between patients with and without HZ was performed (Table 1**).**

HZ locations were intercostal (n=6), dorsal (5), abdominal (3), lumbar (3), facial (3), cervical (1), gluteus (1), submmamary fold (1), intermmamary fold (1) and upper extremity (1). Main HZ complications were post-herpetic neuralgia (n=7), visual alteration in facial HZ (n=1) and disseminated HZ(n=1).

HZ treatment was anitiviral agents (n=23) (brivudine=7; acyclovir 6; famciclovir6; valaciclovir4), topic (n=2) and none (n=6).

Predictive factors for HZ(Figure 1) were older age (>65 years), hypertension and treatment with high prednisone dose and antiTNF.

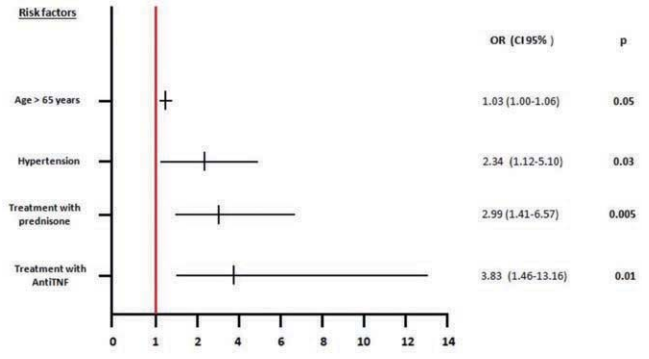

Figure 1. Predictive factors for Herpes zoster

Conclusion: HZ is a relative frequent complication of RA. In our series, although are usually localized, post-herpetic neuralgia is relatively frequent. Probably to include HZ vaccine in our vaccination program of RA may be useful.

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AB0280

SERIOUS INFECTIONS-RELATED HOSPITALIZATION IN RHEUMATOID ARTHRITIS. OBSERVATIONAL STUDY OF 392 PATIENTS FROM A SINGLE UNIVERSITY CENTER

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Background: Patients with Rheumatoid Arthritis (RA) have an increased risk of infections. This may belinked to disease-related, the immunosuppressive therapy and the co-morbidities.

Objectives: in an unselected group of RA patients, our aim was to assess the **a)**incidence **b)**features of disease and **c)**predictive factors of serious infections-related hospitalization.

Methods: Observational study of all patients diagnosed with RA that were included in the vaccination program of our university hospital between October2011 and October 2016.The minimum follow-up was of 12 months; therefore, it was made until December 2020.

Patients with serious infections-related hospitalization were **a)** compared with those not requiring hospital admission and, **b)**identified predictive factors (multivariate analysis adjusted by age and sex).

Vaccination program in our hospital includes vaccination for Influenza, Streptococcus pneumoniae and Haemophilus influenzae.

Information on patients, infections and hospitalizations was retrieved from the hospital and general physician records.

Table 1. Comparative study of different groups

	Patientswithserious infections-related hospitalization N=88	Patients without serious infections-related hospitalization N=304	p
Demographic features and comorbidities			
Age (years),mean±SD	69.7±11.2	59.2±12.6	0.005
Women, n (%)	60 (68.2)	249 (81.9)	0.33
Active smokers, n (%)	41 (46.6)	114 (7.5)	0.32
Hypertension, n (%)	56 (63.6)	109 (35.8)	0.004
Hypercholesterolemia, n(%)	47 (53.4)	101 (33.2)	0.02
Diebetes Mellitus, n(%)	25 (28.4)	30 (9.9)	0.0002
RA features			
Duration of RA (months) mean±SD	165.8±130.1	128.6±102.6	0.005
Positive RF, n (%)	52(59.1)	171(56.2)	0.80
Positive ACPA, n (%)	48 (54.5)	158 (52.6)	0.81
Erosive disease, n (%)	32 (36.4)	113 (51.9)	0.89
Associated Sjögren Syndrome, n (%)	4 (4.5)	16 (5.3)	0.79
Interstitial lung disease n (%)	11 (12.5)	9 (2.9)	0.0008
Subcutaneousnodules n (%)	6 (6.8)	16 (5.3)	0.57
Prednisone (or equivalent) dose mg/day, mean±SD	5.3±4.5	3.3±3.8	0.001
Number of convencional DMARDs, mean±SD	1.9±1.4	1.5±1.3	0.05
Number of biologic DMARDs, mean±SD	0.1±0.2	0.1±0.4	0.03
Number of JAK inhibitors, mean±SD	69.7±11.2	59.2±12.6	0.1

Results: We studied 392RApatients (309women/83men); mean age 63.1±13.7 years. After a mean follow-up of 71.8±20.6 months, in 88 of 392patients (22.4%) (60 women) 187serious infections-related hospitalizations were required. The median [IQR] number of hospitalizations were 1.5 [1-2]. The main serious infections were respiratory (44 patients; 78 hospitalizations), urinary (33 patients; 48 hospitalization), cutaneous (19 patients; 28 hospitalizations), abdominal (17 patients, 20 hospitalizations), septic arthritis (7 patients; 8 hospitalizations), maxillofacial(2 patients, 2 hospitalizations), bacterial endocarditis (2 patients, 2 hospitalizations) and genital (1 patient, 1 hospitalization).
Patients with serious infections-related hospitalization were older, with a longer RA, with more co-morbidities (hypertension, hypercholesterolemia diabetes mellitus, and Interstitial lung disease) and with more conventional and biological DMARDS (Table 1).
The predictive factors for hospitalization were hypertension and Diabetes Mellitus, RA related interstitial lung disease and treatment with biologic DMARDs. (Figure 1)

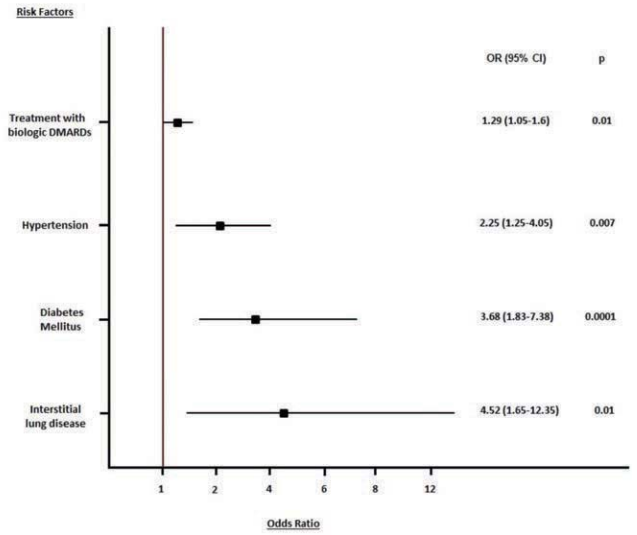

Figure 1. Predictive factors for serious infections-related hospitalization

Conclusion: Despite to be included in a vaccination program up to 22% of patients required hospitalization due to serious infection. The main predictive factors were co-morbidities, interstitial lung disease and treatment with biologic DMARDs. Serious infections in RA remain to be an unmet need.
Disclosure of Interests: None declared
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AB0281 THE 2016 REVISED ACR FIBROMYALGIA CRITERIA IDENTIFY A HIGHER PREVALENCE OF FIBROMYALGIA IN RHEUMATOID ARTHRITIS PATIENTS: A CROSS-SECTIONAL STUDY FROM INDIA.

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Background: Fibromyalgia (FM) prevalence in rheumatoid arthritis (RA) is reported around 5-50% as per older American College of Rheumatology (ACR) FM Criteria, while in India reported around 15% (1). The Revised 2016 ACR FM criteria has greater sensitivity and specificity of 94% and 91% respectively compared to older criteria (2). To best of our knowledge, no study has evaluated presence of FM in RA as per revised 2016 ACR FM criteria.
Objectives: 1) To study prevalence of FM as per revised 2016 ACR FM criteria in RA patients.
2) To compare Disease activity, Disability status, Quality of life, Anxiety and Depression in RA with and without FM.
Methods: This cross-sectional study included 200 RA patients and equal number of controls. FM was diagnosed using revised 2016 ACR FM Criteria. Disease activity, quality of life and functional disability in RA patients was assessed using disease activity scores (CDAI, SDAI, DAS-28 CRP, WHO-Qol BREF and Health Assessment Questionnaire CRD HAQ-DI). Presence of depression and anxiety was determined using validated Hospital Anxiety and Depression Scale (HADS).
Results: FM was present in 31% and 4% of RA patients and healthy controls respectively in our study using 2016 ACR FM criteria. This is significantly higher compared to the 15% and 2.5% in RA and healthy control populations respectively of the study by Dhir V. et studying a similar population of Indian patients, using 1990 ACR FM criteria. RA patients with FM were older, predominantly females, had longer disease duration, were more on steroids, had higher disease activity and more functional disability. In a multivariable linear regression analysis, FM was important predictor of DAS28 score & CDAI, even after adjusting for other independent variable like disease duration, CRP, SJC, functional disability. RA patients with FM had a poorer quality of life and had higher prevalence of anxiety and depression. No difference was noted in use of disease modifying agents, biological or ts-DMARDs in RA patients with or without FM.

Table 1. Characteristics of RA with FM and RA without FM patients.

	RA without FM (n=138)	RA WITH FM (n=62)	P VALUE
	Mean ± sd	Mean ± sd	
Age, yrs.,	47.17±12.44	51.37±12.33	0.028
Duration of RA	4.1±3.59	6.46±6.09	0.006
TJC, 0-28	4.57±2.86	6.87±3.08	<0.001
SJC,0-28	2.3±2.37	3.37±2.87	0.011
Pain VAS,0-100	36.38±16.16	55.24±11.18	<0.001
ESR	39.01±20.67	46±20.39	0.028
CRP	11.61±11.15	16.43±15.72	0.032
CDAI	14.6±6.69	19.68±6.71	<0.001
SDAI	15.74±7.33	21.34±7.48	<0.001
DAS-28 CRP	4.1±1.1	4.85±0.84	<0.001
PDS,0-31	8.68±3.22	16.27±2.33	<0.001
Physical score*, 0–100	54.83±12.16	34.37±9.41	<0.001
Psychological score, 0–100	59.78±14.34	39.84±12.74	<0.001
Social score, 0–100	60.68±12.75	51.5±12.76	<0.001
Environmental score, 0-100	59.21±11.04	49.35±9.73	<0.001
CRD HAQ-DI	1.04±0.64	1.8±1.03	<0.001
Anxiety, n (%)	23(17%)	53(85%)	<0.001
Depression, n (%)	44(32%)	59(95%)	<0.001

TJC: tender joint count (28 joints); SJC: swollen joint count (28 joints); CDAI: Clinical disease activity index; SDAI: Simplified disease activity index; DAS 28: disease activity score (28 joints); PDS: Polysymptomatic distress score of fibromyalgia; *Domain scores of quality of life (WHO-Qol BREF).

Conclusion: The prevalence of FM in RA patients is significantly higher with 2016 ACR FM Criteria as compared to older criteria in similar population of RA patients. A significant number of patients had anxiety and depression that needs to be clinically attended. The presence of FM in RA adversely affects the Disease activity, quality of life, functional disability.
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Disclosure of Interests: None declared
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AB0282 COMORBIDITIES ARE MORE IMPORTANT THAN JAK INHIBITORS: VENOUS THROMBOEMBOLISM IN RHEUMATOID ARTHRITIS

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Background: The risk of Venous thromboembolisim (VTE) is increased and is an important cause of mortality and morbidity in rheumatoid arthritis. In addition to the underlying Rheumatoid arthritis(RA), there are a number of predisposing risk factors for VTE(1).
Objectives: In this study, we aimed to evaluate the demographic and clinical features of rheumatoid arthritis patients with VTE.
Methods: Patients who were refered to Hacettepe University Medical Rheumatology department from January 2021 to December 2021 retrospectively analyzed. A total 981 RA patients were detected according to the ICD code(M05, M06, MO07). RA diagnosis was confirmed in 400 patients according to 2010 ACR/EULAR criteria. Venous thrombosis was confirmed by ICD code(I26,I74,I82), computed torax tomography, lower extremity venous doppler and medical treatment report in these 400 patients with RA. Thromboembolism was detected in 58 patients during follow-up. The patients' clinical characteristics, serological features, co-morbidities, and treatment were systematically analysed.

Results: VTE was diagnosed in 58 patients with RA. Of these patients, 84,5% was female and mean (SD) age was 67.5 ± 11,1 years. The majority of patients had deep venous thrombosis (53.4%). Rate of rheumatoid factor and/or anti-cyclic citrullinated peptid positivity was 72.5% and ANA positivity was 68% respectively. Distribution of cDMARDs and bDMARDs before VTE was as follows: methotrexate 18 (45%), leflunomide (35%), sulfasalazine (22.5%), hydroxychloroquine (47.5%), steroid (47.5%), biological agents (22.5%). Comorbidities were common and The Charlson Comorbidity Index score was ≥3 in 89.6% of patients with VTE. VTE frequency of patients in the last 1 year was %1.27.

Conclusion: All RA patients with VTE had at least one comorbidity and 89% of patients had multi-morbidities. RA patients with multimorbidity may have an increasded risk of VTE. In the management of RA, comorbidities should be taken into account.

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Table 1. Demographic, Clinic and treatment Features of venous thromboembolisim with RA

Demographic, Clinic and treatment Features	VTE in RA patients N=58(%)
Age, years, mean(SD)	67,5 (±11.1)
Female, n(%)	49(84.5)
Charlson Comorbidity Index score(CCI)	
○ CCI1	2(3.4)
○ CCI2	4(6.8)
○ CCI3 and higher	52(89.6)
Smoking, ever, n(%)	20 (41.6)
Presentation of Venous thromboembolism	
○ deep vein thrombosis, n(%)	27(46.6)
○ pulmonary thromboembolism, n(%)	26(44.8)
○ DVT+PTE, n(%)	5(8.6)
Treatment before venous thrombosis, n(%)	
○ Methotrexat	18(45)
○ Leflunomid	14(35)
◦ ○ Sulfasalazin	9(22.5)
• Hydroxychloroquine	19(47.5)
• Biologic agents	9(22.5)
• Steroid	19(47.5)
Treatment, ever, n(%)	
• Methotrexat (n=44)	39(88.6)
• Leflunomid(n=42)	24(52.1)
• Sulfasalazin(n=47)	29(62)
• Hydroxiclorokine(n=49)	44(89)
• Steroid(n=54)	50(92.5)
• Tofacitinip	19(34.5)
• Biologic agents	2(0.03)
○ Abatacept	3(0.05)
○ Adalimumab	5(0.09)
○ Etanercept	3(0.05)
○ Rituximab	9(16)
○ Certolizumab	1(0.01)
○ İnfliximab	1(0.01)
Comorbidity, n(%)	35(60.3)
	10(17.2)
	40(70.2)
	11(19)
	8(13.8)
	8(13.8)
	15(30.6)
	5(8.6)
	7(12.5)
	10(25.6)
	8(13.8)
	54(93.1)
CRP/mg/dl at venous thrombosis, mean, (SD)	0.98(±5.2)
Erytrochyte Sedimentation rate/mmhour at venous thrombosis, mean,(SD)	25 (±22.3)
Seropositive, n(%)	41 (73.2%)
ANA positive, n(%)	34 (68%)

Disclosure of Interests: None declared

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AB0283 FATIGUE AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS. A RESIDUAL FATIGUE OF HIGH LEVEL CAN BE OBSERVED EVEN IN LOW DISEASE ACTIVITY.

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Background: Fatigue is a major symptom suffered by patients with rheumatoid arthritis (RA), with a high prevalence (40%-70%)[1]. Different questionnaires and scales (BRAF, FACIT, SF36v, MDHAQ, VAS...) have been validated, but none have been standardized to measure it. In observational studies, the VAS (0-10) scale was reported as a good measure for fatigue; cut-off>5/10 indicates high level[2]. A residual fatigue in low activity/remission of the disease has been described in a significant proportion of patients[3].

Objectives: We studied the association with high level of fatigue and the clinical disease activity in non-selected RA patients.

Methods: RA patients (ACR/EULAR criteria, 2010) were included consecutively in our Arthritis Unit during a period of 3 months. Patients completed 2-pages MDHAQ that includes a VAS 0-10 for fatigue at question 9, in addition to other queries: physical function (FN) + pain (PN) + patient global assessment (PATGL), checklist of 60 symptoms (ROS60) and self-assessment 48 joint count (RADAI48). VAS for Fatigue was calculated with a cut-off point ≥5/10 to obtain the group with high fatigue. Demographic variables (age, sex, BMI) and clinical variables: disease duration, treatment with bDMARDs and glucocorticoids, joint physical examination (TJC 0-28, SJC 0-28), acute phase reactants (ESR, CRP), physician global assessment (PhyGL), and the rates of clinical activity with their respective clinically significant differences (DAS28-ESR>0.6; SDAI>10; RAPID3>3.8) were also calculated.

A descriptive analysis (mean and SD) of all the variables, a bivariate analysis to compare groups (Student t for quantitative and Chi^2 tests for categorical variables) and calculation of numerical differences between indices was performed.

Results: A total of 75 RA patients (84% females) were recruited, of mean age of 62 (SD:11.6) years, with media BMI of 22.8 (SD:8.0), mean disease duration of 14.6 (± 5) years, 16% depressed (PHQ9≥10), treated with bDMARD (64%) and glucocorticoids (45,3%). Means of disease clinical indexes were as follows: DAS28-ESR (2.55, SD:1.21), SDAI (8.7, SD:8.00) and RAPID3 (5.97, SD:5.85).

In 31 (41.2%) of patients we observed high fatigue (VAS-fatigue≥5/10). When comparing with those with low or no fatigue levels, these patients have higher disease activity measured by the composite activity indices and acute phase reactants except for the SJC. All self-reported variables evaluated by MDHAQ (FN, PN, RADAI48, ROS60) were also higher in patients with high fatigue levels (Table 1).

Table 1. Descriptive and comparison variables between groups, expressed as mean and SD.

	All patients, n=75	Non-high fatigue group, n=44 (58.6%)	High fatigue group, n=31 (41.3%)	p value
TJC (0-28)	1,45 (2,81)	0,59 (1,21)	2,68 (3,84)	0.001
SJC (0-28)	1,23 (2,18)	0,96 (1,94)	1,63 (2,47)	0.200
PCR	0,7 (0,97)	0,47 (0,29)	1,02 (1,42)	0.014
ESR	13,9 (15,0)	10,52 (9,44)	18,68 (19,56)	0.019
FN (0-10)	1,26 (1,82)	0,72 (1,23)	3,20(2,39)	0.004
PN (0-10)	3,56 (3,12)	1,90 (2,28)	5,30 (2,98)	<0.001
PATGL (0-10)	3,27 (2,86)	2,07 (2,24)	5,18 (2,77)	0.001
RADAI48 (0-48)	7,85 (8,81)	4,14 (5,50)	12,87 (9,99)	<0.001
ROS60 (0-60)	10,06 (8,84)	5,78(5,03)	15,71 (9,64)	<0.001
PhyGL (0-10)	2,43 (1,94)	1,90 (1,47)	3, 18 (3,27)	0.004
DAS28-ESR	2,55 (1,21)	2,13 (0,97)	3,15 (1,27)	0.001
SDAI	8,7 (8,0)	6,18 (4,80)	12,33 (10,01)	0.001
RAPID3 (0-30)	5,97 (5,85)	3,08 (3,48)	10,29(0,06)	<0.001

The mean differences in the three activity indices between both groups were statistically significant, in the DAS28-ESR and RAPID3 were also considered clinically relevant: 1.02 (>0.6) and 7.2 (>3.8) respectively, but not for SDAI: 6.15 (>10).

Conclusion: Even non-selected RA patients but with low disease activity, high fatigue level was common. For a better approach to fatigue in RA patients, it would be interesting not to forget this residual fatigue.

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AB0284 COGNITIVE AND DEPRESSIVE DISORDERS IN PATIENTS WITH RA, THEIR CONNECTION WITH THE LEVEL OF BRAIN - DERIVED NEUROTROPHIC FACTOR

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Background: Rheumatoid arthritis (RA) is a common pathology among other rheumatic diseases. Chronic inflammation, prolonged pain, early disability of

patients - all these factors contribute to the development of depressive and cognitive disorders in this category of patients. Still, the mechanisms of these disorders remain poorly understood. Recently, the role of brain-derived neurotrophic factor (BDNF) as one of the factors of cognitive and depressive disorders in various pathological conditions has been widely discussed in the literature.

Objectives: To study cognitive and depressive disorders in RA patients and their association with serum BDNF levels.

Methods: 79 women with RA, aged 21 to 74 years, on average (M ± SD) 48.7 ± 10.2 were examined. Diagnosis RA was established according to EULAR / ACR criteria (2010). Patients' cognitive function was assessed by the MMSE (Mini Mental State Examination). The presence and severity of depression were determined by the QIDS-SR16 (Quick Inventory of Depressive Symptomatology Self-Report). Serum BDNF was detected by enzyme-linked immunosorbent assay (ELISA) using standard BDNF Quantikine ELISA kits (R&B Systems, USA). The control group consisted of 30 age matched healthy women.

Results: It was found that the level of BDNF in the serum of women with RA was 1.5 times higher than in healthy individuals and was 16.8 ± 10.8 ng/ml and 11.32 ± 4.89 ng/ml, respectively. Cognitive disorders (MMSE <28 points) were registered in the majority (78.5%) of patients with RA, while in the control group, there were only 10%. The mean MMSE values in RA patients and the control group were 27.2 ± 1.45 and 29.1 ± 0.99, respectively. Depressive disorders (QIDS-SR16 ≥ 6 points) were reported in 53% of patients, while in the control group, it was 3.3%. It was found that depressive disorders in RA patients were associated with BDNF levels ($r = 0.208$; $p<0.05$) and age ($r = 0.159$; $p<0.05$). There was no significant association between BDNF levels and MMSE in RA patients. In the control group it was found negative correlation (-0.257; $p <0.05$). We found also close negative correlation between MMSE and age in patients with RA ($r = -0.689$; $p<0.001$). A significant relation with age was also registered in the healthy group ($r = -0.257$; $p<0.05$).

Conclusion: Patients with RA had an increased level of BDNF compared with the control group. Most of them had cognitive and depressive disorders. Depressive disorders in RA patients are associated with higher levels of BDNF in the blood and with age. No association of cognitive impairment with BDNF has been established in patients. Cognitive disorders in RA patients are most closely associated with age. Moderate association between MMSE and BDNF levels was established in control group.

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AB0285 MTX REDUCED THE CARDIOVASCULAR RISK IN RHEUMATIC DISEASES

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Background: The relationship between cardiovascular risk (CVR) and inflammatory rheumatic diseases (IRD) remains certain [1].

The aggressive suppression of systemic inflammation by the CsDMARDs or biologics may lower this risk.

Objectives: The purpose of this study was to assess the protective role of the different treatments in rheumatoid arthritis (RA) and spondyloarthritis (SpA).

Methods: We carried out 107 patients followed up for IRD between March and December 2020. We collected the socio-demographic data of patients, the clinical and biological characteristics of the disease. Prescribed treatments were specified.

CVR was assessed by measuring, in centimeters, the Intima-media Thickness (IMT) at the level of the left (LCC) and right (RCC) common carotid arteries and by calculating the Framingham risk score (FRS) for each patient. Individuals with IMT≥0.9 mm or an FRS≥20% were considered as those with high CVR (HCVR).

Results: Of the 107 surveyed patients, 56% had RA (n=47) and 44% had SpA (n=60). Among them, 55% were male. The mean age was 43.9±14.2 years. The mean disease duration was 117.3±89 months. The mean BASDAI was 4.98 ±2.7. The mean DAS28 was 4.13±1.5. Seventy percent of patients had active disease. Conventional DMARDs were prescribed in 54.7% of cases: Methotrexate (95% in RA versus 5% in SpA) and Sulfasalazine (13% in RA versus 30% in SpA), NSAIDs in 57.3% of patients (4.5% in RA versus 96.6% in SpA), corticosteroids (CT) in 25% (47.5% in RA versus 8.5% in SpA), and biotherapy in 9% of cases (12.8% in RA versus 6.7% in SpA).

The mean FRS was 5.98 ± 6.6. The mean IMT was 0.58±0.15. About 60% of patients were considered with HCVR.

NSAIDs were associated with an increase in IMT in the LCC ($p<0.001$) and in the RCC ($p<0.001$). MTX had a significant protective effect on IMT in LCC ($p=0.001$). However, there was no association between CT use and IMT. Regarding FCS, no significant association was found based on MTX ($p=0.09$), NSAIDs ($p=0.11$), CT ($p=0.45$) nor biologic use ($p= 0.74$).

Conclusion: In our study, patients taking MTX had a lower IMT than those not taking this molecule. NSAIDs were associated with an increase in IMT. However, we didn't observe any effect of CT and biologic treatment on CVR in our population.

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AB0286 BENEFICIAL EFFECT OF OLIVES AND OLIVE OIL CONSUMPTION ON RHEUMATOID ARTHRITIS DISEASE ACTIVITY

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Background: The main goal for the management of rheumatoid arthritis (RA) is to control symptoms to reach clinical remission or low disease activity as the best possible alternative [1]. Although the number of available therapeutic options, a substantial proportion of patients remain symptomatic. Recent EULAR recommendations [2] shift focus to lifestyle interventions whose concurrent approach could help in controlling potential inflammatory triggers. In this context, olives and olive oil have beneficial properties on health mainly attributed to their high monounsaturated fatty acid content, and to the presence of phenolic compounds. To our knowledge, very few studies addressed the anti-inflammatory effects related to olives and olive oil consumption on RA disease activity.

Objectives: To study the attitude of consumption of olives and olive oil in RA patients from northern Italy, and to assess the effect on disease activity.

Methods: In this observational cross-sectional study, all consecutive adult RA with disease duration ≥ 3 months were enrolled. Disease Activity Score on 28 joints (DAS28-CRP), Simple Disease Activity Index (SDAI) were recorded. Dietary habits in the previous six months were collected with a with a 110-item food frequency questionnaire. In this analysis, we focus on olive oil consumption with original response categories ranging from "never" to "more than 2 times per day" (in spoon units). We created a food group composed by olive oil, black and green olives (frequencies/day). Olive oil consumption was entered as the independent variable into multiple regression models. When disease activity was entered in continuous in the regression models, we estimated the effect on a 1-point increment/decrease in RA disease activity. When disease activity was modeled as a dichotomous variable, we estimated the odds ratios (ORs) of disease activity and the corresponding 95% confidence intervals (CIs) within unconditional multiple logistic regression models. We included in each model the potential confounding variables: age, sex, education, body mass index (BMI), cigarette smoking status, alcohol drinking intensity, disease duration, rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA), and therapies.

Results: 365 RA patients (median age: 58.46 years, 78.63% females) were included. Most of the patients (60.55%) finished the high school and/or the university. The median BMI was 23.63 (IQR: 21.00-26.78) Kg/m^2; never smokers or drinkers were 51.64% and 29.04%, respectively. The median disease duration was 12.81 (IQR: 8.08-20.72) years, with RF positivity being 53.70% and ACPA positivity 50.96%. Disease activity measures DAS28-CRP and SDAI showed medians of 2.21 (IQR: 1.613.02) and 6.30 (IQR: 3.01-11.81), with high disease activity present in 3.84% and 5.75% of the sample, respectively. Major comorbidities included arterial hypertension (33.42%), gastro-esophageal reflux (19.18%), and gastritis (8.77%). After adjustment for the mentioned confounding factors, the ORs (and the corresponding 95% confidence interval) of RA disease activity was equal to 0.78 (95% CI: 0.76-1.31) for DAS28-CRP and to 0.76 (95% CI: 0.75-1.34) for SDAI, suggesting significant protection of about ~20% for both outcomes. Similarly, robust

regression models for estimating the increment in the mean outcome disease activity scores, DAS28-CRP and SDAI in continuous, provided beta coefficients equal to -0.17 (Standard Error, SE: 0.06) with a p-value equal to 0.06 for DAS28-CRP and a beta coefficient of -1.13 (SE: 0.37) with a p-value equal to 0.04.

Conclusion: Increasing frequency of consumption of a food group composed by olive oil, black and green olives is significantly associated to a lower risk of disease activity, as measured by both DAS28-CRP and SDAI, after adjustment for socio-demographic factors, therapy, disease duration and severity. Robust regression models allowed to quantify the mean reduction of DAS28-CRP in 0.17 points and that of SDAI in 1.13 points.

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AB0287 INFLUENCE OF COPING ON RHEUMATOID ARTHRITIS RELATED PAIN

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Background: Most patients with rheumatoid arthritis (RA) have chronic pain. Nowadays dealing with pain is no more focused on traditional treatment only.

Objectives: Our study aimed to assess the impact of coping strategies on the chronic pain in RA subjects.

Methods: We performed a 6-month study including patients followed for RA according to ACR / EULAR 2010 criteria. The visual analogue scale (VAS) was used to assess the perception of pain. Coping was assessed by the Brief COPE questionnaire according to which five grouped strategies were identified: Problem solving that includes active coping and planning. Cognitive restructuring that combines humour, acceptance and positive reinterpretation. Support seeking that combines the search for instrumental support, the search for emotional support and religion. Avoidance that includes denial, blame, substance use and behavioural disengagement. Distraction that includes distraction and expression of feelings.

Results: We included 65 RA patients with 58 women and 7 men, the sex ratio was 0, 12 H/F. Mean age of the patients was 58, 6 [24 – 73 years]. Disease duration was superior to 10 years in 66, 2% of patients. RA was immunopositive in 87, 7% of cases and erosive in 83, 1 % of cases. The DAS28 (ESR) was on average 3, 4(IQR 25-75: 2, 8- 4, 6). The average of VAS was 5 ± 2,2. The perception of pain was positively associated with coping strategies based on problem solving, negatively associated to cognitive restructuring and distraction (Table 1).

Table 1. Impact of coping strategies on chronic pain RA subjects

	B	p
Problem solving	0,411	**0,001**
Cognitive restructuring	-0,371	**0,002**
Support seeking	-0,095	0,452
Avoidance	0,243	0,252
Distraction	-0,292	**0,018**

Conclusion: Our study revealed that having coping strategies based on problem solving increased the perception of pain whereas strategies based on distraction and cognitive restructuring decreased it.

Disclosure of Interests: None declared

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AB0288 ECHOCARDIOGRAPHIC FINDINGS BY SPECKLE TRACKING IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory joint disease characterized by infiltration of the synovial membrane by B cells, T cells, and monocytes. Among the most important extra-articular manifestations are those of the cardiovascular system. Cardiovascular involvement in this group of patients is highly relevant as it is an important cause of morbidity and mortality (1,2). Subclinical involvement is underestimated and currently, conventional cardiovascular risk stratification methods are insufficient to detect early stages of cardiovascular disease. Speckle tracking has emerged as a tool to measure early myocardial dysfunction and has been shown to be useful as a predictor of cardiovascular events. Normal reference values have recently been published (3).

Objectives: To describe the echocardiographic findings by speckle tracking (ST) of the left atrium (LA) and left ventricle (LV) in patients with RA without prior known cardiovascular disease and to compare it with healthy controls. To establish if there is an association of echocardiographic findings with characteristics of the disease.

Methods: Thirty-four patients with RA without a history of previous cardiovascular disease and 50 healthy controls were included. Echocardiographic measurements were made by Speckle Tracking of the LA in its 3 phases and of the LV expressed as Global Longitudinal Strain (GLS), in addition to conventional measurements. Quantitative variables were expressed as proportions, continuous data were reported as means and standard deviations. Both groups were compared with t-student test and a linear regression model was used to evaluate age and RA presence in relation to the abnormality or normality of Speckle tracking findings. SPSS was used for statistical analysis.

Results: A significant difference was found in LA global longitudinal strain compared to controls (45.14% vs 57.34%, p=0.020), LA conduit strain (25.69% vs 36.74%, p=0.002) and LV global longitudinal strain (- 17.6% vs. -22.62%, p=0.000). There was no significant difference in LA contractile strain and LA strain rate. In the echocardiographic measurements by conventional technique, no differences were found in the measurement of the LV ejection fraction or LA volume index, but LA ejection fraction was lower in the RA group (53.8% vs 78.2%, p=0.000). Rheumatoid arthritis was associated with LA speckle tracking abnormality in the reservoir, conduit, and LV global longitudinal phases.

Conclusion: The patients with rheumatoid arthritis presented subclinical echocardiographic alterations of myocardial deformation measured by speckle tracking both in the left ventricle (assessed as GLS) and in the left atrium, these were associated with RA regardless of age.

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AB0289 DEPRESSION AND METABOLIC DISORDERS PREVENT REMISSION IN RHEUMATOID ARTHRITIS

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Background: Epidemiological data and clinical observations suggest an increased risk of depressive disorders in rheumatoid arthritis (RA) patients with metabolic syndrome (MS) [1, 2].

Objectives: To study the prevalence of depressive symptoms depending on the presence of MS components in RA patients and to evaluate their combined effect on achieving remission of RA.

Methods: 100 RA patients aged 18 to 69 years old (91% women; mean duration of disease 9 [3.5;15] years; body mass index (BMI) 28.8 [IQR 25.1-32.8]) were examined. MS was confirmed in RA patients with three or more harmonized National Cholesterol Education Program/ Adult Treatment Panel III (NCEP/ ATPIII; 2004) criteria. RA patients were assigned a binary MS score ("yes/no") and a categorical MS score (from 0 to 5 criteria) was calculated. The severity of depression in patients with RA was determined using the Beck Depression Inventory (BDI).

Results: 46% of RA patients met the criteria for MS. The presence of three categorical signs of MS was noted in 26%, four - in 16% and of all five signs - in 4% of cases. The combination of elevated fasting glucose, elevated triglycerides (TG), and decreased high-density lipoproteins (HDL) was the most frequent (19.6%; 9/46). The combination of the four MS criteria (increased waist circumference (WC), elevated TG, decreased HDL, and arterial hypertension) occurred in 17.4% (8/46) of cases. RA patients with MS had more severe systemic inflammation (C-reactive protein 9.3[3.9; 23.1] versus 3.35[2.3; 12.0] mg/L, p=0.028), higher levels of TG (p=0.001) and total cholesterol (p=0.003), and higher BMI (p=0.018) and WC (p=0.007).

Depression scores of BDI ≥10 were noted in 64 RA patients: 26% were mild, 28% were moderate and 10% were severe. Symptoms of depression were more frequent in RA patients with longer duration (β=0.25, p=0.012) and high activity (β=0.37; p=0.001) of the disease. There were statistically significant differences in the incidence of depression (BDI ≥10 points) depending on the absence or presence of MS in RA patients (Phi-square=0.42; association coefficient φ=0.65). When comparing groups of RA patients stratified by the presence of MS, significant differences in the severity of depressive disorders according to BDI were found (RA without MS: 8,35 ± 5,1 points; RA with MS: 23,6 ± 12,8 points, p < 0,001). In RA patients without MS, only mild (26%) and moderate (9.3%) depression were detected. In RA patients with MS, depressive symptoms from mild to severe were present in almost equal poportions. Two-factor analysis of variance showed no significant effect of BDI and MS on DAS28-ESR activity in RA patients (p>0.05). The presence of MS had a significant effect on BDI depression (p<0.001), and there was no relationship between MS and the degree of disease activity (p=0.33).

Re-examination (6-7 months later) of patients with initially moderate RA activity (n=58) revealed that remission of the disease was not achieved in 25% of patients from the group with no signs of depression and MS. In the group of RA patients with MS and BDI ≥10 there were almost 2.5 times more cases of deterioration (63.3%) (χ2 with Yates correction = 4.7, p=0.03).

Conclusion: Progression of depression against the background of marked metabolic disorders can lead to a decrease of RA patients' quality of life and complicate disease prognosis [3, 4, 5]. This requires an early multidisciplinary treatment and increased knowledge of the risks associated with depression and MS among health care professionals and patients. Identification and correction of symptoms of depression and MS in RA patients should be a part of the optimal patient care.

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AB0290 COMPARATIVE FEATURES AND LONGITUDINAL BEHAVIOUR OF RHEUMATOID ARTHRITIS-ASSOCIATED UIP VERSUS IDIOPATHIC PULMONARY FIBROSIS: A SINGLE CENTRE COHORT STUDY

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Background: Interstitial lung diseases (ILDs) are a group of heterogeneous lung disorders with variable prognosis. Idiopathic pulmonary fibrosis (IPF) is the main idiopathic interstitial pneumonia and rheumatoid arthritis (RA) is the commonest cause of connective tissue disease related-ILD. In fact, ILD is the most frequent form of respiratory involvement in RA, with 10% patients having clinically significant disease, frequently imposing significant morbi-mortality. RA-ILD can potentially comprise different disease patterns with distinct prognosis, with usual interstitial pneumonia (UIP) being the most frequent radio-histological pattern. Several studies have suggested that the RA-UIP disease course and survival may be clinically similar to IPF.

Objectives: This study aimed to investigate comparative clinical features, longitudinal behaviour and healthcare resource utilization between local cohorts of RA-UIP and IPF patients.

Methods: Retrospective and descriptive study including all IPF and RA-ILD cases diagnosed and followed in the ILD outpatient clinic of secondary hospital between 2015 and 2020. All patients with RA diagnosis met classification criteria of 2010 ACR/EULAR and IPF patients were diagnosed according to 2018 ATS/ERS/JRS/ALAT clinical guidelines. Socio-demographic, clinical data and longitudinal lung function (functional vital capacity (FVC) and lung diffusion capacity for carbon monoxide (DL_{CO})) were collected. A statistical analysis was performed; p-value <0.05 was statistically significant.

RESULTS:

Table 1. Baseline clinical characteristics of all patients are listed in table.

	IFP n=22	RA-UIP n=14	*p*
Age, years (mean±SD)	74.5±1.8	75.5±9.4	0.75
Sex (M/F), n	17/5	4/10	**0.006**
Smoking Status			0.31
Smoker (%)	0	0	
Ex-smoker (%)	64.6	42.9	
Smoking load	53.1±7.9	35.8±22.2	0.48
Baseline dyspnea (mMRC)			0.07
0 (%)	0	7.1	
1 (%)	13.6	28.6	
2 (%)	54.5	50.0	
3 (%)	18.2	14.3	
4 (%)	13.6	0	
Cough (%)	86.4	42.9	**0.01**
Time from respiratory symptoms until diagnosis (months)	20.5±3.4	11.6±9.7	0.09
Elevated titers of Rheumatoid Factor, n	-	10	
Elevated titers of anti-CCP, n	-	11	
Baseline lung function			
FVC, % predicted	73.0±14.9	91.3±19.8	**0.007**
DLCO, % predicted	42.1±18.6	60.3±21.2	**0.04**
6-minute walking distance at baseline (meters)	341.8±147,7	346.2±132.3	0.95

In RA-UIP group, 86% of patients reported preceding articular symptoms, with lung disease being diagnosed after a median of 11 years (IQ range 2-13). All patients had a UIP/probable UIP pattern in HRCT. Regarding baseline FVC and DLCO, the RA-UIP group revealed better lung function compared to the IPF group. All patients with RA-UIP received some form of immunomodulation treatment. Around 78.4% of patients were on low dose prednisolone. Additionally, 64.2% received treatment with mycophenolate mofetil, 21.4% with rituximab, 7.1% with azathioprine and 7.1% with hydroxychloroquine. Regarding IPF patients, about 86.4% were treated with antifibrotics (nintedanib or pirfenidone). From the global population study only 27.3% and 14.3% of IPF and RA-UIP patients, respectively, were referred for respiratory rehabilitation. There were significant differences regarding FVC (p=0.002) and DLCO (p=0.003) decline over time between groups. Comparing to RA-UIP, IPF patients experienced a greater number of acute exacerbations (4 vs 27;p=0.06) and had more respiratory-related emergency visits. IPF patients also had a higher rate of hospitalizations, most of them respiratory-related. There was a clear trend towards higher mortality during follow-up in the IPF group compared to the RA-UIP group (40% vs 21,4%;p=0.23), although not reaching statistical significance.

Conclusion: RA-UIP patients appear to be less symptomatic and have a shorter symptomatic period at diagnosis. IPF patients had worse lung function at diagnosis. IPF patients showed a higher tendency to acute exacerbations and had a greater unplanned health care resources utilization. There was also a non-significant trend towards higher mortality during follow-up in the IPF group.

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AB0291 COMORBIDITIES PROFILES IN SEROPOSITIVE RHEUMATOID ARTHRITIS VERSUS SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: Patients with seropositive rheumatoid arthritis (RA) (positive Rheumatoid Factor (RF)) are more susceptible to extra-articular manifestations [1]. The role of RF in the occurrence of comorbidity is not clear.
Objectives: We aimed to compare comorbidities among patients with seropositive RA versus patients with seronegative RA.
Methods: We conducted a retrospective study in our rheumatology department including 255 patients with established RA according to the ACR/EULAR 2010 criteria. Patients were divided in two groups according to their Rheumatoid Factor (RF) profile: seropositive RA (positive RF), seronegative RA (negative RF). Comorbidities were investigated and compared between the two patients groups.
Results: There were 206 seropositive RA and 49 seronegative RA. Gender distribution was similar in the two groups: 82% female and 18% male in seropositive RA; 85% female and 15% male in seronegative RA (p=0.5). Smoking was noted in 15% patients with seropositive RA and in 11% patients with seronegative RA without any difference (p=0.5).
Comorbidities were noted in 49% of seropositive RA and in 45% of seronegative RA without any significant difference (p=0.6). Obesity (BMI ≥ 30kg/m^2) was noted in 31% of seropositive RA and in 36% of seronegative RA (p=0.7). Diabetes was noted in 18 % seropositive RA and in 26% seronegative RA patients (p=0.1). Hypertension was noted in 31% seropositive RA patients and in 30% seronegative RA (p=0.8). Heart disease was present in 6% seropositive RA and in 7% seronegative RA (p=0.9). Dyslipidemia was noted in 40% seropositive RA and in 20% seronegative RA (p=0.1). Gastrointestinal comorbidities were observed in only seropositive RA patients (11%). Respiratory comorbidities were noted in 27% seropositive RA and in 28% seronegative RA without any significant difference (p=0.6). Regarding mental health problems, depression was noted in 7% seropositive RA and in 14% seronegative RA without any significant difference (p=0.4).
Conclusion: Our study showed that comorbidities were comparable in seropositive and seronegative RA. It seems that RF does not influence the prevalence of comorbidities in RA patients.
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AB0292 ASSOCIATION OF RHEUMATOID CACHEXIA WITH BONE, VERTEBRAL FRACTURES, AND STRUCTURAL JOINT DAMAGE IN MOROCCAN RHEUMATOID ARTHRITIS PATIENTS

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Background: The concurrent decrease in the fat-free mass index (FFMI) and increase in the fat mass index (FM) in rheumatoid arthritis (RA) is called rheumatoid cachexia (RC). There is limited data on RC association with osteoporosis, vertebral fracture (VF), and structural joint damage in RA.
Objectives: To explore rheumatoid cachexia association with bone, vertebral fractures, and radiographic damage in RA patients.
Methods: This was a cross-sectional study on RA patients fulfilling the ACR/EULAR 2010 criteria and recruited from December 2021 at our rheumatology department. Patients with prior cancer, chronic kidney disease, severe heart failure, severe chronic obstructive pulmonary disease, cirrhosis, hyperparathyroidism, thyroid dysfunction, diabetes, dysphagia, illicit drug use, alcohol abuse, and a body mass index (BMI) above 36kg/m^2 were excluded. RC was defined according to Engvall et al. (1) (as a fat-free mass index (FFMI) below the 10th percentile and a fat mass index (FMI) above the 25th percentile) and Elkan et al. (FFMI<25 and FMI>50) (2). Body composition, bone mineral density (BMD), and trabecular bone score (TBS) were obtained by dual-energy X-ray absorptiometry (DXA). Osteoporosis was defined as a T-score under 2.5. The radiographic joint damage was measured by the modified total Sharp /van der Heijde score (mTSS) using standard X-ray images of hands and feet. VFs were defined using the Genant semiquantitative approach as grade 2 or higher.
Results: We included 82 RA patients with a mean age of 51.90 ± 13.12 years. Their mean disease duration under treatment was 7.54 ± 5.69 years, and the mean mTSS was 93.84 ± 56.77. RC was observed in 11 (13.4 %) and 9 (11%) patients using both definitions, respectively. Osteoporosis was observed in 44 (53.7 %) patients. BMD was numerically lower in rheumatoid cachexia patients without significance while mean TBS was similar. The mTSS and particularly the mTSS erosion scores were significantly lower in RC patients (p < 0.01). RA patients with RC (according to Elkan's definition) had significantly more VF (p = 0.039).
Conclusion: RC was positively associated with VF, and RC patients were less erosive.
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AB0293 INDICATIONS AND THERAPEUTIC IMPLICATIONS OF HAND AND WRIST JOINT ULTRASOUND IN RHEUMATOID ARTHRITIS

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Background: Ultrasound (US) has been increasingly used in the recent years for the diagnosis and follow-up of rheumatoid arthritis (RA) [1]. It is considered as a complement to physical examination with high sensitivity, specificity, and accuracy in detecting synovial thickening, synovial hypervascularization as well as cortical bone erosions [2].
Objectives: We aimed to study the indications of hand and wrist joint ultrasound and the implications of its findings on the management of RA.
Methods: A cross-sectional study was conducted on a sample of RA patients, fulfilling the ACR/EULAR 2010 RA classification criteria. We collected data about characteristics of the disease, its activity assessed by the Disease Activity Score 28 using C-Reactive Protein and erythrocyte sedimentation rate (DAS28-CRP, DAS28-ESR), treatment of RA (conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), biologics (bDMARDs), and corticosteroids (CS)), indication of hand and wrist joint US and the implications of its findings.
Results: Fifty-eight patients were enrolled in the study with 83% females, with a mean age of 58.5±11.8 years and a mean age at diagnosis of 46.8±12. years. RA was seropositive in 89.7% of patients and erosive in 84.5%. Most patients underwent csDMARDs treatment (67.3%), 29.3% underwent bDMARDs treatment, and 67.3% used oral CS with a mean dose of 4.9±4.4 mg/day of prednisone equivalent. Mean DAS28-CRP was 4.1±1.4, and mean DAS28-ESR was 4.9±1.5. Hand and wrist joint US was performed for RA activity assessment in 93.1% of patients (n=54), for erosion assessment in recently diagnosed RA in 5.2% of patients (n=3), for erosion assessment in established RA in 1.7% of patients (n=1).
In patients who had US signs of active RA, treatment was modified in 73% of patients with initiation of a 3-day parenteral CS pulses (18.9%), initiation of oral CS (2.7%), escalation of oral CS dose (2.7%), escalation of csDMARD's treatment (24.3%), adjunction of another csDMARD (5.4%), reintroduction of a csDMARD (2.7%), initiation of bDMARDs (24.3%), and switch of bDMARDs (5.4%). US findings had no implication in 27% of these patients. When inactive RA was assessed (31,5%), there was no implication on treatment strategy in 82.4% of patients, a decrease of oral CS dose in 11.8% and a single intra-articular CS injection in 5.9%.
Detecting ultrasonographic activity signs of RA in hand and wrist joint was more likely to have implications on treatment strategy than finding no activity signs (75% vs 22%, $\chi 2=14.25$, $p<10^{-3}$).
The group of patients who had an implication of US findings on treatment strategy had significantly higher DAS28-ESR (5.53 vs 4.18, p=0.002).
Conclusion: Hand and wrist US had significant implications on treatment strategy of RA especially in patients with higher disease activity. However, it had no implications in some patients suggesting the complementary role of US compared to clinical determinants in RA treatment decision.
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AB0294 VITAMIN D LEVEL AND LOCOMOTIVE FUNCTIONS IN WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Muscle health is an important aspect of rheumatoid arthritis (RA). A decrease in muscle mass and physical performance is a frequent complication of RA that contributes to inability to work and reduced quality of life. Vitamin D deficiency is also common in these patients.
Objectives: To assess the relationship between vitamin D level, muscle strength and physical performance in RA patients.
Methods: 135 women (mean age 58.5±8.9) with confirmed RA according to ACR/EULAR criteria (2010) were enrolled in the study. Muscle strength of upper extremities was measured using a mechanical dynamometer, of lower extremities – using "Chair stand test" (CST) – assessment of the ability to rise from a chair and sit back down 5 times. Handgrip strength 16 kg and less or CST for more than 15 seconds were the criteria for low muscle strength. All patients underwent "Gate speed test" (GST) and "Timed Up and Go test" (TUG) to assess the physical performance. Serum level 25 (OH)D was performed using the Cobas E411 immunochemiluminescence analyzer and Elecsys Vitamin D total kit, Roche.
Results: Median 25(OH)D level was 23.7 [18.2; 30.7] ng/ml in RA women with minimum 7.9 ng/ml and maximum 70.0 ng/ml.
Insufficiency and deficiency of vitamin D were detected in 56 (41,5%) and 42 (31,1%) women, respectively, with median level 24.1 [21.8; 26.6] ng/ml in the patients with insufficiency and 15.6 [13.6; 17.9] ng/ml – in deficiency group.
Vitamin D level was compared between patients with low muscle strength and/or physical performance and women with normal locomotive functions (Table 1). 25(OH)D level was significantly higher in RA women with normal CST and GST >0,8 m/s than in patients with the worst results of these tests. At the same time, we didn't find differences in handgrip strength and TUG depending on vitamin D level.

Table 1. 25(OH)D in women with RA according to locomotive functions

Test	25(OH)D	*p*
CST		
≤15 seconds	26,7 [20,4; 32,2]	0,036
>15 seconds	21,0 [17,9; 25,1]	
GST		
>0,8 m/s	26,1 [19,6; 32,0]	0,043
≤0,8 m/s	21,1 [17,0; 26,8]	
Handgrip strength		
≥16 kg	23,8 [17,8; 30,2]	>0,05
<16 kg	27,7 [19,5; 32,2]	
TUG		
<20 seconds	23,7 [17,9; 30,1]	>0,05
≥20 seconds	18,8 [18,1; 21,0]	

Conclusion: The frequency of low vitamin D level was 72,6% in women with RA including deficiency in 31,1% patients. Patients with reduced lower limb strength and low walking speed had significantly lower vitamin D levels, but there were no differences in 25(OH)D and other tests (handgrip strength and TUG).
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AB0295 HIGHER PREVALENCE OF DEPRESSION WITH LINK TO CHILDHOOD TRAUMA IN AN EARLY ARTHRITIS COHORT – A SELECTIVE DATA ANALYSIS (PSYRA-STUDY)

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Background: In patients with arthritis, psychological co-morbidities are very common. Previous studies have found a relatively high prevalence of depression, anxiety, and post-traumatic stress disorder (PTSD), especially in long-term disease. Recent research has begun to study psychiatric co-morbidities not just as an outcome, but also as a probable risk factor, evaluating patients in the early disease stages. [1] Furthermore, some sources suggest that childhood adversities could impact the autoimmune process in adulthood. [2]
Objectives: To compare the prevalence of depression, anxiety, PTSD, and childhood trauma in a prospective early arthritis cohort to a healthy age- and gender-matched control group. Moreover, to explore whether these factors may contribute to the early arthritis development.
Methods: This selective data analysis of prospective single-centre, observational study included 60 patients with an early arthritis and 60 healthy controls. The control group was defined as no inflammatory joint pain and further subdivided into 2 subgroups, differentiating 24 patients with arthralgia and 36 with no arthralgia and not from the outpatient consultation. Early arthritis was defined as the presence of at least one inflammatory joint from 4 weeks to 12 months, independent of rheumatic diagnosis. For the assessment of current and prior psychological co-morbidities, included patients underwent semi-structured interview and received the standardized questionnaires for depression/anxiety (Hospital Anxiety and Depression Scale (HADS)), childhood trauma (Childhood Trauma Questionnaire (CTQ)) and PTSD (Posttraumatic Diagnostic Scale (PDS)) respectively. Differences among the groups were analyzed with Chi Square and Mann-Whitney U tests. A backwards binominal logistic regression model in reference to the healthy patients was performed to identify the significant factors for the early arthritis group.
Results: The mean age of the total group was 47.4 ± 16.0 (♀ 58.3%, mean symptom duration 4.5±3.3 months). Depression rate of 41.7% according to interview was significantly higher in early arthritis group compared to 16.7% in healthy patients (p=0.03). Regarding arthralgia subgroup, depression was also high with 34%. HADS-D score was also significantly higher in early arthritis (5.4±4.8) to healthy cohort (3.6±3.3) (p=0.047). Compared to 3.3% in healthy patients, PTSD rate of 13.3% was also significantly higher in the arthritis group (p=0.048). We could not detect a significant difference between these two groups using the U test while evaluating CTQ dimensions. We performed a subsequent subgroup analysis and found that childhood trauma dimensions were relevant in arthralgia group, as 25% presented with high emotional abuse score. The logistic regression model showed that emotional neglect, sexual abuses in childhood as well as HADS-D were significant covariates for early arthritis. (p=0,048 OR=1.2; p=0.040 OR=1.4, p=0.025 OR=1.2 respectively).
Conclusion: As the rates of depression and PTSD, as well as HADS-D score were significantly higher in the early arthritis cohort compared to healthy individuals, our findings suggest a potential link between psychiatric outcomes and inflammation. According to our regression model certain childhood adversities and depression are significant factors for an early arthritis group. Arthralgia group had similar aberrant scores regarding childhood trauma, implying that early-life stress might be an important factor in understanding this condition.
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AB0296 RELATIONSHIP BETWEEN OBESITY AND ACUTE PHASE REACTANTS IN RHEUMATOID ARTHRITIS

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Background: Obesity plays an important role in autoimmune and inflammatory diseases such as rheumatoid arthritis (RA). It has been demonstrated a paradoxical relationship between increased body mass index (BMI) and disease activity (1). Acute phase reactants (APR) play an essential role in determining the disease activity level (2).
Objectives: To compare APR levels in obese and non-obese patients with RA, and to establish their relationship with the disease activity level.
Methods: A total of 272 patients with a diagnosis of RA were included in a cross-sectional study. They were divided in two groups, 136 obese patients and 136 non-obese patients, matched by age, gender and comorbidities. The C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) level were measured, and the activity level was determined with Disease Activity Score 28-joint erythrocyte sedimentation rate (DAS28-ESR) and Disease Activity Score 28-joint C-reactive protein (DAS28-CRP).
The distribution was evaluated with Kolmogorov-Smirnov. Comparisons with Chi-square test for qualitative variables, Student's t-test, and Mann-Whitney U test for quantitative variables. Correlation between BMI and APR with Spearman-rho coefficient.
Results: The Spearman-rho coefficient showed a significant correlation between CRP level and BMI (rho=0.187, *p=0.*002) (Figure 1). No difference was found between activity level when comparing both groups (Table 1).

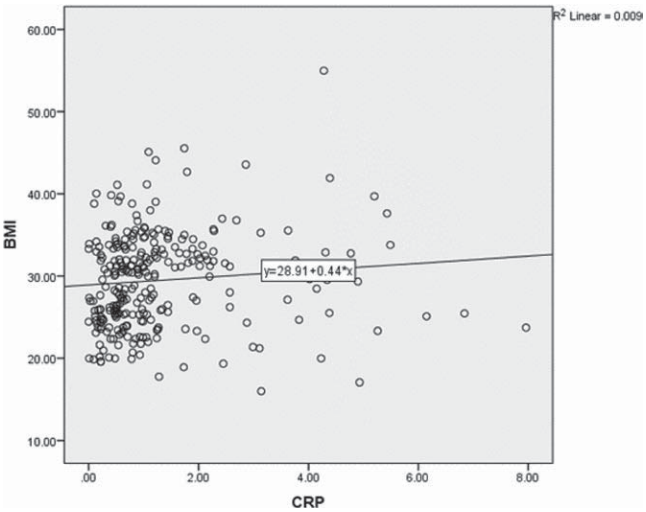

Figure 1. Correlation between BMI and CRP
BMI, body mass index; CRP, C-reactive protein

Table 1. Demographic Characteristics of the Patients

Characteristics	Obese RA Patients (n=136)	Non-Obese RA Patients (n=136)	*P* Value
Age, mean ± SD	55.32±8.67	55.38±8.64	NS
Female, n (%)	130 (95.5)	130 (95.5)	NS
BMI, mean ± SD	34.22±3.74	24.70±2.89	-
T2DM, n (%)	30 (22.0)	23 (16.9)	NS
Hypertension, n (%)	62 (45.5)	48 (35.2)	NS
Dyslipidemia, n (%)	39 (28.6)	48 (35.2)	NS
Methotrexate, n (%)	119 (87.5)	114 (83.8)	NS
bDMARD, n (%)	7 (5.1)	11 (8.0)	NS
Glucocorticoid, n (%)	89 (65.4)	77 (56.6)	NS
CRP, median (p25-p75)	1.00 (0.58-1.73)	0.68 (0.38-1.25)	NS
ESR, median (p25-p75)	25.00 (16.00-36.00)	24.50 (14.25-37.75)	NS
DAS28ESR, mean ± SD	4.74±1.45	4.57±1.38	NS
DAS28CRP, mean ± SD	3.62±1.46	3.37±1.39	NS

RA, rheumatoid arthritis; NS, not significant; BMI, body mass index; T2DM, type 2 diabetes mellitus; bDMARD, biological disease-modifying anti-rheumatic drugs; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; DAS28, Disease Activity Score 28-joint.

Conclusion: Obese RA patients presented higher CRP levels compared to non-obese patients, suggesting that a higher BMI level may be related to a higher degree of inflammation and consequently worse systemic manifestations in patients.
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AB0297 EVALUATION OF FACTORS RELATED TO POSITIVE THORACIC COMPUTERIZED TOMOGRAPHY FINDING IN RHEUMATOID ARTHRITIS

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Background: Lung involvement is one of the common extra-articular involvements in rheumatoid arthritis (RA). There are some studies in the literature evaluating the risk factors related to lung involvement in RA. Male gender, smoking, seropositivity, uncontrolled disease activity, and long disease duration are the characteristics known for increased lung involvement in RA. There is ongoing debate about when and how we should screen RA patients for lung involvement. In addition, little is known about the importance of patients' comorbidities as a risk factor for RA lung involvement.
Objectives: In this study, we evaluated the role of demographic and disease-related features and comorbidities as risk factors for positive lung computed tomography (CT) findings associated with RA lung involvement. Our aim here was not to evaluate the risk factor for RA lung involvement. Instead, we try to guide clinicians to risk stratification of RA patients for possible lung involvement. In previous studies, the authors compared risk factors between RA patients with and without known lung involvement. In addition, not all patients in these RA cohorts had thoracic CT. Therefore, they may miss preclinical or asymptomatic patients. In our study, we compared the characteristics of two groups of patients with and without positive thoracic CT findings.
Methods: We included 76 RA patients from our cohort who applied to our outpatient clinic for routine follow-up and had thoracic CT for any purpose in the past year. All RA patients met the 2010 ACR-EULAR RA criteria. Thoracic CT findings were classified as associated with RA according to the article by Esposito AJ et al. Patients with any known pulmonary involvement, malignancy, nursing, and known COVID-19 infection in the past year were excluded from the study. We divided the patients into two groups (positive or negative) according to thoracic CT findings. We compared the two groups in terms of patient and disease-related characteristics. We used qi-square test for comparing categorial variables and Mann-Whitney U test for comparing continuous variables. We then performed multivariate analysis with a model that includes significantly different features in univariate analyses and age to find the amount of risk attributed to the factors for positive thoracic CT. P<0.05 was accepted as significant.
Results: Of the 76 (56.5 %) RA patients, 43 (56.5 %) had positive findings related to RA in thoracic CT (Table 1). Male gender (p=0.008), ACPA positivity (p=0.04), thyroid diseases (p=0.03) were found significantly more common in the patients with positive thoracic CT findings. The frequencies of all other demographic and disease related features and comorbidities are similar between the groups. Additionally, multivariate analyses found thyroid diseases (OR 6.1, %95 CI 1.5-24.3, p=0.009) and male gender (OR 7.8, %95 CI 1.6-35.7, p=0.008) were related to positive CT findings.

Table 1. Positive thoracic CT features of RA patients

	n=43 (%)
Pulmonary nodules	15 (34.8)
Ground glass opacities	13 (30.2)
Bronchial diseases	12 (27.9)
Pleural diseases	9 (20.9)
Mosaic attenuation	7 (16.2)
Mediastinal lymphadenopathy	6 (13.9)
Honey combing	5 (11.6)
Emphysema	5 (11.6)
Interstitial fibrosis	3 (6.9)
Pulmonary vascular diseases	2 (4.6)

Conclusion: In our study conducted in our cohort, we found that male gender and thyroid disease were risk factors for positive thoracic CT findings associated

with RA. Clinicians may consider these factors when classifying RA patients for lung involvement and planning thoracic CT for screening.

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AB0298 THE RISK OF SULPHA ALLERGY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Sulpha drugs have been used such as sulfasalazine for the treatment of rheumatoid arthritis (RA), and trimethoprim-sulfamethoxazole (TMP-SMX) for the treatment or prevention of pneumocystis pneumonia. However, some patients with RA delay treatment because of allergy to sulpha drugs[1]. We reported that 16.7% of RA patients presented drug allergies[2]. It was not clear what is a risk factor for drug allergies in patients with RA.

Objectives: The aim of this study was to evaluate the clinical features with sulpha allergy in patients with RA.

Methods: We prospectively examined consecutive patients diagnosed with RA in our hospital from March 2021 to January 2022. The patients with RA met the EULAR/ACR 2010 criteria. We included patients with RA with other rheumatic diseases. A careful allergic history was obtained from patients with RA and physical examination performed.

The first analysis was performed on patient baseline laboratory data at diagnosis of patients with RA with or without sulpha allergy. Sulpha allergy (rash, angioedema and anaphylaxis after drug exposure) was allergy to sulfasalazine or TMP-SMX. The second analysis was performed on seven types of allergic reactions: (1) drug allergies other than sulpha drugs (rash, angioedema and anaphylaxis after drug exposure), (2) food allergy (rash, angioedema and anaphylaxis after foods exposure), (3) allergic contact dermatitis such as metals, and other cosmetics, (4) seasonal allergic rhinitis and/or conjunctivitis (AR and/or AC), and AR and/or AC associated with house dust, (5) asthma, and (6) atopic dermatitis.

Results: There were 513 patients with RA in our study. In the first analysis, 17 patients with sulpha allergy and 496 patients without sulpha drugs were enrolled (Table 1). The median ages (with supha allergy and without sulpha allergy) were 66.0 and 72.0 years old (p=0.40). Females were 82.3% and 77.0%(p=0.4). The median observation period was 97.0 and 69.0 months (p=0.20). Patients with other rheumatic diseases were 11.6 and 6.8% (p=0.34).

Table 1. Characteristics of RA patients at diagnosis of RA

	With sulpha allergy (n = 17)	Without sulpha allergy (n = 496)	P
Female	83.4%	76.9%	0.77
Age, year, y	66.0 (56.0-78.5)	72.0 (60.0-80.0)	0.40
Observation period, m	97.0 (45.5-182.0)	69.0 (31.0-123.8)	0.20
Patients with other rheumatic diseases	11.8%	6.8%	0.34
ANA-positive patients(>1:80)	52.9%	28.2%	0.052
Anti-SSA antibody-positive patients	46.2%	18.2%	0.02
RF-positive patients	40.0%	66.8%	0.049

The RA patients with sulpha allergy had higher positivity rate of anti-nuclear antibody (ANA) (>1:80) (52.9%, 28.2%: p=0.052), higher positivity rate of anti–Sjögren's-syndrome-related antigen A autoantibody (anti-SSA antibody) than those without sulpha allergies (46.2%, 18.2%: p = 0.02) and lower positivity rate of rheumatoid factor(RF) than those without sulpha allergies (40.0%, 66.8%: p = 0.049).

In the second analysis drug allergies other than sulpha allergy were more frequent in patients with sulpha allergy. Drug allergies other than sulpha allergy were such as antibiotics and nonsteroidal anti-inflammatory drugs. There were no significant differences in other allergies.

Conclusion: Among patients with RA, patients with sulpha allergy had higher positivity rate of ANA and anti-SSA antibody, and lower positivity rate of RF than those without sulpha allergy. RA patients with sulpha allergy had a higher prevalence of the other drug allergies than those other than sulpha allergy.

Table 2. Allergic disorders in RA patients with and without sulpha allergy

	With sulpha allergy (n = 17)	Without sulpha allergy (n = 496)	P
drug allergies other than sulpha allergy	61.6%	12.7%	<0.01
food allergy	11.8%	13.5%	1.00
allergic contact dermatitis	23.5%	24.2%	1.00
AR and/or AC	58.8%	46.6%	0.34
asthma	17.7%	13.1%	0.48
atopic dermatitis	5.9%	6.3%	1.00

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AB0299 ASSOCIATION OF RHEUMATOID CACHEXIA WITH DISEASE PARAMETERS IN MOROCCAN RHEUMATOID ARTHRITIS PATIENTS

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Background: Low muscle mass occurs in patients with rheumatoid arthritis without weight loss. This condition has been studied lately (1) and was referred to as rheumatoid cachexia (RC).

Objectives: To study the prevalence of rheumatoid cachexia and its associated factors in rheumatoid arthritis (RA) patients.

Methods: We designed a cross-sectional study on RA patients recruited from December 2021 at our rheumatology department. Exclusion criteria were patients with prior chronic kidney disease, severe heart failure, severe chronic obstructive pulmonary disease, acute liver failure, uncontrolled diabetes, thyroid dysfunction, dysphagia, illicit drug use, and alcohol abuse. Body composition was measured with dual-energy X-ray absorptiometry (DXA), and patients' data were collected. RC was defined by Engvall et al. (2) as a fat-free mass index (FFMI) below the 10th percentile (under lean) and a fat mass index (FMI) above the 25th percentile (fat excess). Inflammatory activity was measured by C-reactive protein (CRP) and used to assess disease activity score for 28 joints (DAS28CRP). The physical disability was assessed by the Health Assessment Questionnaire (HAQ) and the physical activity by the International Physical Activity Questionnaire (IPAQ). Nutrition was evaluated by the Mini Nutritional Assessment (MNA).

Results: We included 91 RA patients with a mean age of 52.61 ± 12.99 years. The prevalence of rheumatoid cachexia was 12.1 %. Twenty-six patients (28.6 %) were under lean, and six patients (6.6 %) had excess fat. DAS28CRP (p = 0.004) and fasting glucose (p = 0.03) were significantly lower in RC patients. RC did not show any significant association with HAQ, MNA, physical activity, gender, menopause, seropositivity, lipid levels or BMI. RC was significantly associated with DAS28CRP (p = 0.01, OR = 0.305, 95%IC [0.114, 0.818]) and fasting glucose level (p = 0.02, OR = 0.0002, 95%IC [0.00000001, 0.311]) when adjusting on IPAQ categories and ACPA seropositivity.

Conclusion: Rheumatoid cachexia was frequent in our RA patients. This condition was significantly associated with low fasting blood sugar levels and disease activity.

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AB0300 REDUCTION OF LACHNOSPIRA IS CLOSELY RELATED TO AUTOIMMUNE DISEASE COMPLICATED WITH PULMONARY FIBROSIS

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Background: Autoimmune diseases (AD) are a group of heterogeneous disorders caused by both genetic and environmental factors. Rheumatoid arthritis (RA) and Sjögrens syndrome (SS) are typical autoimmune diseases[1], Pulmonary fibrosis (PF) is the most common complication of AD. Despite the extensive study of the human gut microbiome in AD complicated with PF(AD-PF),the question of whether there are common microbial features characterizing AD-PF still remains[2].
Objectives: This study focused on exploring differences between the microbiota diversity and peripheral lymphocyte subpopulations as well as cytokine in AD with PF is different from that of AD without PF.
Methods: A total of 64 AD patients (44 AD without PF and 20 AD with PF) as well as 100 age- and sex- matched healthy controls (HCs) were enrolled in this study. The peripheral lymphocyte subsets were analyzed by flow cytometry and the gut microbiota were investigated via 16s rRNA sequencing. Alpha and Beta diversity (bray curtis distance-based) analysis was used to define the difference of gut microbiota profiles between patients and HCs. To explore the specific bacterial taxa associated with AD-PF, the STAMP software was used to compare the fecal microbiota composition. Spearman correlation analysis was used to determine the similarities in the microbiota community with clinical meatures among fecal samples.
Results: There is a decrease that the richness and diversity index between HCs, AD and AD-PF patients. Principal co-ordinates analyses suggested that these three microbiota states explained a reasonable proportion of observed variance in gut microbiota composition (ANOSIM R2 = 0.113, p < 0.001; Figure 1b). Compared with HCs, there are obvious differences among 19 species of flora in AD without PF at the genus level, of which 2 species of flora (Lachnospira,Muribaculaceae) belong to AD-PF patients were showed much fewer. The relative abundance of Lachnospira was positive correlated with the absolute numbers of Th17, IL-6 and THF-α (P<0.05,Figure 1D-E) , which indicated Lachnospira may be the most critical among the AD-RF patients' own species of flora. Therefore, the reduction of Lachnospira may influence the immune status of the intestinal tract of patients by producing less short-chain fatty acids.
Conclusion: Our results suggest that the decrease of Lachnospira may lead to the occurrence of AD with pulmonary interstitial fibrosis, which was closely correlated with lymphocyte subsets and Cytokines, maintaining the flora balance might be a potential therapeutic target for AD-PF.

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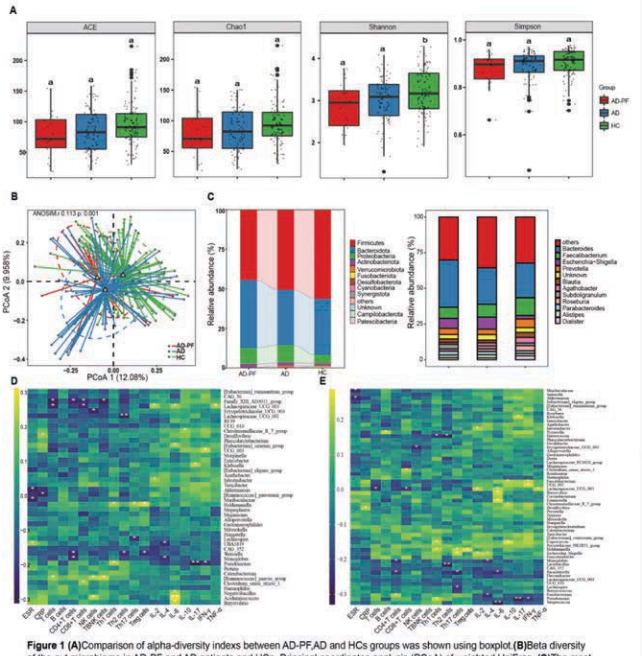

Figure 1 (A) Comparison of alpha-diversity indexs between AD-PF,AD and HCs groups was shown using boxplot.**(B)**Beta diversity of the gut microbiome in AD-PF and AD patients and HCs. Principal coordinates analysis (PCoA) of weighted UniFrac. **(C)**The most abundant gut microbiota for AD-PF at genus level.**(D-E)**Correlations between gut microbiota, and Lymphocyte subsets as well as clinical variables.*p<0.05,**P<0.01,***P<0.001.

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AB0301 ANALYSIS OF INTESTINAL MICROBIOTA IN PATIENTS WITH OSTEOPOROSIS SECONDARY TO RHEUMATOID ARTHRITIS

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Objectives: To analyse of intestinal microbiota in patients with osteoporosis (OP) secondary rheumatoid arthritis (RA).
Methods: Design: A cross-sectional observational study nested in a prospective cohort of incident RA patients.
Patients: Patients with RA (ACR/EULAR 2010) from a prospective baseline cohort (incident cases between 2007-2011), >16 years, from whom information on bone mineral densitometry (BMD) was collected.
Protocol: all subjects were evaluated in a specialized outpatient unit. Clinical-analytical variables of the cut-off date and clinical history were registered. Blood, urine and faeces samples were obtained from all subjects. A BMD was done by dual energy X-ray absorptiometry (DXA) for osteoporosis diagnosis.
Variables: Dependent variable: osteoporosis according World Health Organization (WHO) definitions. The fecal microbiota (continuous var., 0-100%) was analysed using the Ion Torrent S5 next-generation sequencing platform, and the sequences obtained were processed using the QIIME2 (Quantitative Insights Into Microbial Ecology 2) software. Others variables included demographics characteristics, comorbidities, inflammatory activity measured by mean accumulated Disease Activity Score-28 (DAS-28) throughout the disease, severity variables: smoking, erosions, anticitrullinated peptide antibody (ACPA) titres, rheumatoid factor (RF) and physical function measured by HAQ. Treatment with bDMARD (biological disease-modifying antirheumatic drug) and/or sDMARD (synthetic disease-modifying antirheumatic drug).
Statistical Analysis: descriptive, bivariate using $\chi 2$ and T-Student followed by logistic multivariant regression model in patients with RA. (Vd: Osteoporosis).
Results: 110 patients with RA were included. The majority of the subjects were women (80%) with an average age of 56 years. The majority of patients were seropositive (81.8% with positivity for RF and 80% with positive for ACPA) and the accumulated DAS-28 average was 3. A total of 49/110 (44.5%) had normal BMD, 46/110 patients (41.8%) had densitometric osteopenia and 15/110 OP (13.6%). Patients with OP were older (p=0.025), higher RA length (p=0.003), higher CRP (p=0.046), higher inflammatory by DAS-28 (p=0.051) and higher ACPA titres (p=0.043). Furthermore, they showed higher levels of Lentisphaerae (p=0.035), Synergistetes (p<0.001), Actinobacteria (p=<0.001) y Verrucomicrobia (p=0.034).

Table 1. Epidemiological, clinical and analytical characteristics of patients

Variable	Patients n=110
Epidemiological characteristics	
Age in years, mean (IQR)	55.9 (49.3-64.4)
Sex, female; n (%)	88 (80.0)
Tobacco	
Never smoker, n (%)	47 (42.7)
Ex-smoker, n (%)	30 (27.3)
Active smoker, n (%)	33 (30.0)
Comorbidities	
High blood pressure, n (%)	28 (25.5)
Diabetes Mellitus, n (%)	6 (5.5)
Dyslipidemia, n (%)	25 (22.7)
Cardiovascular Disease, n (%)	18 (16.4)
BMI (Kg/m^2), mean (SD)	28.4 (5.1)
Clinical and analytical characteristics	
RA evolution time, months, median (IQR)	93.2 (77.6-123.4)
Diagnosis delay, months, median (IQR)	8.1 (4.5-17.0)
Erosions, n (%)	68 (61.8)
RF >10, n (%)	90 (81.8)
ACPA >20, n (%)	88 (80.0)
DAS-28 average, mean (±SD)	3.0 (0.7)
HAQ average, median (IQR)	0.71 (0.3-0.9)
sDMARD, n (%)	93 (84.5)
bDMARD, n (%)	42 (38.1)
Osteopenia, n (%)	46 (41.9)
Osteoporosis, n (%)	15 (13.6)

The variables independently associated with OP in RA were: age (OR [IC 95%],1.099 [1.012-1.193]; p=0.025), ACPA (OR [IC 95%],1.005 [1.001-1.010]; p=0.036), RA length (OR [IC 95%],1.039 [1.016-1.062]; p=0.001) y Actinobacteria (OR [95% CI] 1.124 [1.004-1.257]; p=0.042), R2=0.367.

Conclusion: Osteoporosis in Rheumatoid Arthritis is associated with severity factors as the age, the disease length or the presence of ACPA, as well as the *Actinobacteria* predominance in the intestinal microbiota.

Disclosure of Interests: Alba María Cabezas-Lucena: None declared, Maria Morales-Águila: None declared, Patricia Ruiz-Limon: None declared, Isabel Moreno-Indias: None declared, Natalia Mena-Vázquez: None declared, Sara Manrique Arija Speakers bureau: Abbvie, Gedeon, Jansen, Lilly, Menarini, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Consultant of: Abbvie, Jansen, Lilly, Novartis, Sanofi, Antonio Fernandez-Nebro: None declared

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AB0302 DIASTOLIC DYSFUNCTION IN RHEUMATOID ARTHRITIS PATIENTS: A COMPARATIVE CROSS-SECTIONAL STUDY

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Background: Cardiac failure is an independent risk factor for mortality in Rheumatoid arthritis (RA) and diastolic dysfunction (DD) may act as a precursor for cardiac failure.

Objectives: The aim of our study is to determine the frequency of diastolic dysfunction in rheumatoid arthritis (RA) patients compared to a control group and to focus on associated factors.

Methods: This was a comparative cross-sectional study, including patients diagnosed with RA according to the ACR/EULAR 2010 criteria and control subjects. Each patient underwent transthoracic echocardiography and the DD was assessed by E/A and E/a ratio.

Results: Seventy-two patients with RA and 72 control subjects were included. In our study, there was a clear female predominance in both groups (93.1% vs 94.4%). The mean age of RA patients was 52.9 ± 11.72 years [21-75 years] and that of the control group was 49.26 ± 10.74 years [19-76 years]. In RA group, the mean duration of disease was 12.4 ± 9.9 years [6 months-40 years]. The means of DAS 28 (CRP), DAS 28 (ESR) and HAQ score were respectively 3.4 ± 1.4 [1.2-6.7]; 3.9 ± 1.4 [1.4-7.4] and 0.9 ± 0.7 [0-2.5]. 51.4% of patients had an increased ESR and 37.5% of cases had an increased CRP (CRP>6). In RA group, DD was present in 26 patients (36.1% of cases). The mean value of the impaired E/A ratio was 0.7 ± 0.1 [0.4-0.9] and the mean value of the impaired E/a ratio was 9.8 ± 1.5 [8.5-14.4]. These patients (23 women and 3 men) had a mean age of 56 ± 10.4 years [33-74 years]. Among them, 7 patients had hypertension, 9 patients had cardiac symptoms, 21 patients had a long-standing RA, 17 patients had positive ACPAs and 11 patients had positive RF. In control group, DD was present in 10 patients (13.9% of cases). The mean value of the impaired E/A ratio was 0.6 ± 0.1 [0.4-0.9] and the mean value of the impaired E/a ratio was 9 ± 0.6 [8.4 to 10.1]. Left ventricular diastolic dysfunction was more frequent in RA patients compared with the control group with a significant difference (p<0.01). No significant association was found between diastolic impairment and RA parameters.

Conclusion: Subjects with RA have a higher frequency of diastolic dysfunction than those without RA. Therefore, correct assessment of diastolic function should be considered of pivotal importance in the routine follow-up of RA patients. The identification of predictor factors requires further study.

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AB0303 RELATION BETWEEN CLINICAL ANTHROPOMETRIC MEASUREMENTS AND MALNUTRITION IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is associated with an increased risk of malnutrition, especially among the elderly. However, nutritional assessments in this population are scarce in the clinical situation. Various anthropometric measurements can help to assess malnutrition.

Objectives: To evaluate the nutritional status using anthropometric measurements in elderly patients with RA.

Methods: A prospective study was conducted, including RA patients aged 65 years or older and followed in rheumatology department. Clinical findings, disease activity and nutritional profile were studied. The mini-nutritional assessment (MNA) was used to identify altered nutritional status. The anthropometric measurements studied were: Weight loss, Body mass index (BMI), Triceps skin fold thickness (TSF) which reflects fat mass, Mid-arm circumference (MAC), Arm muscle circumference (AMC) which indicates lean mass and the calf circumference (CC).

Results: Sixty-three patients were included, 82% were female. Their mean age was 68.17±4.35 years. The mean duration of RA was 11 years. The average DAS28 was 3.72±1.48. The mean MNA total score was 20.19 ± 4.71 with a range of 8 to 27.5. The prevalence of malnutrition in our population was 20.6%. 55.6% of the patients were at risk of malnutrition. Only 23.8% had a normal nutritional status. The average BMI was 27.97 ± 5.44 kg/m2 [14.85 - 43.2]. The diagnosis of malnutrition according to the BMI (< 21 kg/m2) was made for 7.9% of patients, of which 4.8% were severely malnourished. The average weight loss was 2.26 ± 2.51 kg during the last month [0 – 10]. The average percentage of weight loss in the last month was 3.39 ± 4% [0-11%]. Among our patients, 26 patients (41.3%) did not report a weight loss, 19 patients (30.2%) had a weight loss of less than 5%. Eighteen patients (28.6%) had malnutrition defined as weight loss greater than or equal to 5% in one month, of whom 7 patients (11.1%) had severe malnutrition with a loss of at least 10% of their habitual weight. The mean TSF was 18.38 ±6.77 mm [5 - 30] (19.15±6.72 mm in women and 14.72±6 mm in men). 28.6% of patients had decreased values of TSF. The mean MAC was 29.48 ± 4.52 cm [18 - 40]. The mean AMC was 23.7 ± 3.64 cm [15.86-34.43] (24±3.57 cm in women and 22.19±3.75 cm in men). The AMC was decreased in 20.6% of cases. The mean CC was 33.25 ± 4.62 cm [20-43]. 31.7% of patients had a decreased CC. There were significant association between the nutritional status using the MNA and BMI, loss of weight and TSF (p=0.013, p<0.001 and p=0.05, respectively). MNA was not associated with MAC, ACM or CC (p=0.6, p=0.8 and p=0.4, respectively).

Conclusion: This study showed that the prevalence of malnutrition varies depending on the used anthropometric tool. BMI, weight loss and TSF are, according to our study, reliable tools to detect the malnutrition in elderly patients with RA.

Disclosure of Interests: None declared

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AB0304 CHRONIC KIDNEY DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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Background: Prevalence and incidence estimates for chronic kidney disease (CKD) in rheumatoid arthritis (RA) vary and it may result from comorbidities, chronic inflammation, aging, or effects of drugs used for the disease.

Objectives: To calculate the prevalence and incidence of CKD in a cohort of patients with RA.

Methods: This was a retrospective cohort study in which well-characterized patients with RA (fulfillment of 1987 ACR criteria) were included from 2014 to 2021. Patients were evaluated at a single rheumatology outpatient center in Bogotá, Colombia. Baseline and follow-up estimated glomerular filtration rate (eGFR) were calculated according to CKD-EPI equation. CKD was defined as an eGFR <60 mL/min/1.73 m2.

Results: A total of 783 outpatients were included. Baseline characteristics were as follows: female gender 81.6%, mean age 51.8±11 years, mean disease duration 8 (IQR 3-15) years, RF positive 80.1%, ACPA positive 58.2%, and erosions 24.9%. Most patients have received glucocorticoids (89.8%), and conventional synthetic DMARDs (97.8%), being prednisone and methotrexate the most frequently prescribed. Hypertension was the most frequent comorbidity (27.7%). CKD was found in 43 (5.5%) patients at the time of inclusion, being hypertension the most common cause (24, 55.8%). Only 12 (1.5%) patients had a documented history of CKD at the beginning of the

follow-up. The median of follow-up was 73 months. Fifteen incident cases of CKD were found (15/358, 4.1%) in patients with follow-up data of at least 1 year and without prior CKD. Main characteristics of the patients are shown in Table 1.

Table 1. Cardiovascular disease and main comorbidities in RA patients.

	Baseline (n/783)	Prevalent CKD (n/43)	Incident CKD (n/15)
Cardiovascular Disease	n (%)	n (%)	n (%)
Hypertension	217 (27,7)	24 (56)	6 (40)
Coronary artery disease	27 (3,4)	3 (7)	2 (13)
Thrombosis	14 (1,8)	2 (5)	2 (13)
Stroke	11 (1,4)	1 (2)	-
Chronic occlusive arterial disease	4 (0.5)	1 (2)	1 (7)
Comorbidity	n (%)	n (%)	n (%)
Dyslipidemia	209 (26,7)	16 (37)	9 (60)
Diabetes mellitus type 2	55 (7)	3 (7)	-

Conclusion: There is an underestimation of the prevalence of CKD in patients with RA in routine clinical practice due to the absence of a systematic estimation of eGFR. The incidence of CKD is low in the Colombian population.

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Disclosure of Interests: None declared

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AB0305 RELATIONSHIP BETWEEN IMMUNOLOGICAL ASSESSMENT AND PERIODONTAL STATUS IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) and Periodontitis are two chronic inflammatory diseases, which can share similarities such as the patho-physiological progression and immune regulation.

Objectives: The present study aimed to determine the link between immunological assessment and periodontal status in RA.

Methods: A cross sectional study including RA patients, which consulted or were hospitalized in Rheumatology department in Taher Sfar University Hospital of Mahdia Tunisia, between March 2020 and February 2021. The diagnosis of RA was based on ACR/EULAR 2010 criteria. Oral and periodontal examination was practiced by a trained dentist in the same hospital. Oral hygiene, teeth status (missing teeth) and paradental parameters (bleeding index of Loe and Silness (GI), plaque indexed O'Leary (PI)) were determined for each patient, to assess oral and periodontal diseases in RA.

Results: Our study included 73 patients with an average age of 51.7 years ±11.8 [21-74years]. Sixty-two patients (93.9 % of cases) were women, in which 35 (54.7%) were menopausal. Only one patient was a smoker. Nine patients (13.6% of cases) were diabetic. The mean duration of RA was 11.2 years ± 8.4 [10 months-37 years]. Rheumatoid factor (RF) was positive in 31 Patients (57 % of cases). Anti-citrullinated peptide antibodies (ACPA) were positive in 39 patients (72 %). Antinuclear antibodies (ANA) were positive in 5 patients (9.3%). Fifty patients (80.6%) had radiological impairments and 36 (54.5%) had specific deformations of RA. The disease activity score (DAS28-VS) and (DAS28-CRP) were very high (>5.1) in respectively 14 patients (21.2%) and 8 patients (12%).

Oral examination revealed xerostomia in 37 patients (62.7% of cases). Three patients (4.7% of cases) were toothless. Gingivitis was diagnosed in 45 Patients (65.2% of cases): localized in 13 patients (31.7%) and generalized in 28 patients (68.3%). Periodontitis was seen in 36 (50.7% of cases). Basing on bleeding index of Loe and Silness (GI), 36 patients (51.4%) had degree 2 and 11 patients (15.7%) had degree 3. Supragingival plaque and subgingival plaque were detected respectively in 62 patients (88.6 %) and 60 patients (88.2 %).

We performed statistical analysis which showed that the positivity of ACPA was significantly associated with the presence of gingivitis. The RF or the ANA were not associated with periodontal abnormalities.

Conclusion: In addition to the functional handicap, rheumatoid arthritis has an impact on the oral status, which may be related to the immunological status of patients.

Disclosure of Interests: None declared

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AB0306 PNEUMOCOCCAL VACCINATION REDUCES THE RISK OF RESPIRATORY INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TARGETED THERAPY. DATA FROM MOSCOW UNIFIED ARTHRITIS REGISTRY (MUAR)

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Background: The incidence of infections, mainly pneumonias, is significantly increased in patients with rheumatoid arthritis (RA). The risk increases more in persons treated with targeted anti-inflammatory drugs (tDMARDs), biological or targeted synthetic.

Pneumococcal vaccination is recommended for most patients with rheumatic diseases. However, only the immunological effectiveness of such vaccination has been sufficiently confirmed. There is sparse evidence of its clinical efficacy in patients with rheumatic diseases.

Objectives: to evaluate the effect of 23-valent pneumococcal polysaccharide vaccine (PPV23) and 13-valent pneumococcal conjugate vaccine (PCV13) on the risk of infections in RA patients receiving tDMARDs.

Methods: The data from the Moscow Unified Arthritis Registry (MUAR) for the period 2018-2020 were analyzed. We included patients with RA, over 18 years old, received tDMARDs (all available biologics or tofacitinib).

The analysis included episodes of observation from the moment of vaccination with pneumococcal vaccine until the development of the analyzed event (any infection, respiratory infection or serious infection) or until the end of follow up. For unvaccinated patients, episodes began since October 20, 2018 (the average date of vaccination of persons who received immunization).

The risks were compared using Cox regression. An adjustment was made for confounders identified in an earlier study: age and smoking.

Results: The analysis included 832 patients: 40 were vaccinated with PCV13, 35 – with PPV23. There were 144 men (17.3%). The mean age was 55.4 ± 12.1 years. The duration of observation was 319 ± 198 days.

A total of 237 infectious events were registered, of which 201 were respiratory and 21 serious (Table 1). There was a significantly lower risk of any infection (relative risk (RR) – 0.39 CI: 0.18 - 0.84, p = 0.015) and the risk of respiratory infection (RR - 0.32; CI: 0.13 -0.79; p = 0.014) in the group of patients vaccinated with PCV13 compared with unvaccinated. The differences remained statistically significant after adjusting for the age and smoking, Figure 1.

Table 1. Registered infectious events

Event groups	Localisation	Number	Of them serious
Respiratory infections	Ear, paranasal sinuses, tonsils	16	2
	Upper respiratory tract	166	0
	Pneumonia	18	14
	Lung abscess	1	1
Other infections	Eye and appendages	3	0
	Skin and subcutaneous tissue	7	1
	Bones and joint	2	2
	Urogenital tract	6	0
	Digestive system, including the oral cavity	2	1
	Herpes infections*	16	0

* - events are included in the group, regardless of localization, these events were not included in other sections

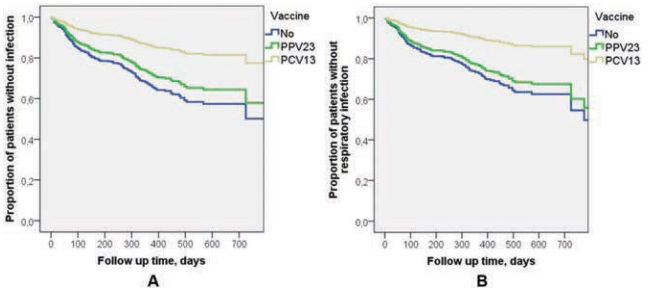

Figure 1. Survival without infectious events (A) and without respiratory infections (B) adjusted for age and smoking

The interaction of the effects of vaccination with the factor of the used tDMARD, as well as with the factor of the use of methotrexate in their effect on the risk of any and respiratory infections was evaluated. There was no significant interaction between these variables.

There were no significant differences in the risk of serious infections due to a small number of events of this kind. No serious infections were registered among patients vaccinated with PCV13.

Conclusion: Vaccination with 13-valent conjugated pneumococcal vaccine in patients with rheumatoid arthritis receiving tDMARDs can significantly reduce the risk of infectious complications, mainly due to acute respiratory infections. We found no significant effect of targeted drug and treatment with methotrexate on the effectiveness of vaccination.

Disclosure of Interests: Evgeniy Zhilyaev Speakers bureau: UCB Pharma, Biocad, Galina Lukina Speakers bureau: Pfizer, MSD, Biocad, Ekaterina Koltsova: None declared, Dzhamilya Murtazalieva: None declared, Evgeniya Shmidt: None declared, Karine Lytkina Speakers bureau: UCB Pharma, Anna Shmitko: None declared, Dmitry Blagovidov: None declared, Mikhail Kostinov: None declared

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AB0307 MERKEL CELL CARCINOMA RECURRENCE RISK IS LOWER IN PATIENTS WITH AUTOIMMUNE DISEASE THAN IN THOSE WITH OTHER TYPES OF IMMUNE SUPPRESSION

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Background: Merkel cell carcinoma (MCC) is twice as likely to recur in immunosuppressed (IS) patients as in immunocompetent (IC) patients. Iatrogenic IS due to autoimmune disease (AD) may influence prognosis differently than intrinsic IS such as due to hematologic malignancy. Moreover, modification of IS medication may improve prognosis.

Objectives: Our objective was to evaluate the risk of MCC recurrence among patients with AD diseases relative to other immunosuppressive conditions among 762 MCC patients from an Institutional review board-approved registry.

Methods: We categorized patients into 3 groups: IS due to AD (IS^{AD}); IS from other causes ($IS^{non\text{-}AD}$) such as hematologic malignancy, solid organ transplant, human immunodeficiency virus; or immune competent (n=31, 70, and 661 respectively). IS^{AD} patients were subcategorized into rheumatoid arthritis (RA) (AD^{RA}, n=13) vs. AD except for RA ($AD^{non\text{-}RA}$, n=18). Descriptive statistics were used to compare the features of different characteristics in each group. Kaplan-Meier survival curves were constructed to assess the cumulative incidence of recurrence in different patient groups. In order to estimate the associations between baseline patient characteristics and the risk of MCC recurrence, Fine and Gray regression models were used with death as a competing risk for recurrence. The multivariable models adjusted for age, sex, and extent of MCC at initial presentation.

Results: Patients with IS^{AD} had lower stage disease (local disease: 58% vs. 36%, p = 0.003) and smaller primary tumors than $IS^{non\text{-}AD}$ (<= 2 cm: 83% vs. 57%, p=0.023). After adjusting for age, sex, and stage, IS^{AD} patients (AD^{RA} and $AD^{non\text{-}RA}$) overall had a 54% higher recurrence rate (hazard ratio (HR): 1.54, p=0.21) than IC patients. In comparison, $IS^{non\text{-}AD}$ group had a 165% higher recurrence rate (HR: 2.65, p<0.001) than IC patients (Figure 1). When considered separately, AD^{RA} pts appeared to have a similar recurrence rate as IC pts (HR: 1.19, p=0.76) while $AD^{non\text{-}RA}$ pts had a higher recurrence rate (HR: 1.83, p=0.16) relative to IC pts. At the time of MCC diagnosis, 80% (n=24) of AD pts were on IS medication including conventional disease modifying drugs, biologics, or oral steroids. After MCC diagnosis, 22% (5 patients) stopped all immunosuppressive medications. Among patients on biologics, 89% (8/9 pts) elected to stop the drug. Eleven pts with AD experienced recurrences. Our study was underpowered to demonstrate associations regarding use of a particular immunosuppressive medication and MCC recurrence.

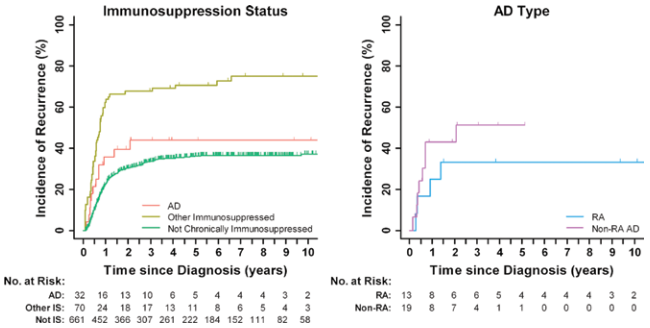

Figure 1. Cumulative incidence of Merkel cell carcinoma recurrence in different patient groups.

AD = autoimmune disease; IS = immunosuppressed; RA = rheumatoid arthritis.There were 4/13, 8/18, 49/70, and 217/661 recurrences in the RA, $AD^{non\text{-}RA}$, other immunosuppressed, and not chronically immunosuppressed groups, respectively. Follow-up time ranged from 26 days to 16 years, with median follow-up times of 4.7 years, 1.6 years, 1.6 years, and 3.9 years for the RA, $AD^{non\text{-}RA}$, other immunosuppressed and not chronically immunosuppressed groups, respectively.

Conclusion: In this cohort, pts with AD appeared to have a better prognosis than intrinsic IS, with RA conferring very little risk above that for immune competent pts.

Acknowledgements: I have no acknowledgements to declare.

Disclosure of Interests: None declared

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AB0308 FALL RISK EVALUATION WITH COMPUTERIZED DYNAMIC POSTUROGRAPHY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Patients with rheumatoid arthritis (RA) have a higher risk of falling due to pain and physiological/biomechanical deformities (decreased muscle density, decreased functional stability, changes in gait, etc.) [1]. Although high incidences of falls have been reported in RA patients [1], there are not sufficient data regarding patient-specific fall risk.

Objectives: The aim of this study was to evaluate patient-specific fall risk, via computerized dynamic posturography, in RA patients, and to compare the results with those of age-matched healthy participants.

Methods: A total of 29 patients with RA (9 males, 20 females; mean age: 54.4±6.5 years) and 18 healthy participants (7 males, 11 females; mean age: 53.6±7.1) were included in the study. Detailed demographic, physical, and medical characteristics of the participants were recorded. Dynamic balance was tested with a computerized dynamic posturography, which assesses balance responses to induced postural disruption [2]. A translational ramp test (speed: 0.1 m/s), sinusoid tests (frequencies: 0.25 Hz - 0.50 Hz), and limits of stability evaluations were applied. Ramp and sinusoid tests were evaluated with the eyes open and closed, in the antero-posterior direction, and the participants were instructed to keep their balance during the tests. Limits of stability was evaluated on a static platform, with the eyes open. During the test, the participants were told to carry their pressure center as far as possible by performing the movement only from the ankle (in all directions), without lifting their feet, and trying not to fall.

Results: The groups were similar in terms of demographic and physical characteristics (p>0.05). Patients with RA showed statistically significant dynamic balance alterations compared to healthy participants (p<0.05) (Table 1). The fall test was positive in 31% of the RA patients and 5.6% of the control group (Figure 1).

Table 1. Comparison of the groups in terms of the fall risk assessment criteria

Test Parameters		RA Group (n=29)	Control Group (n=18)	p
1.Ramp	Energy in AP (J)	2051 (1071-2258)	1409 (1224-1644)	0.005*
Eyes Open				
1.	Energy in ML (J)	213 (122-414)	208 (138-259)	0.369
1.	Time in ML (s)	3.9 (3.0-4.4)	3.5 (2.6-3.9)	0.083
2.Ramp	Energy in AP (J)	1939 (1856-2147)	1718 (1334-1929)	0.024*
Eyes Closed				
1.	Energy in ML (J)	224 (174-364)	189 (155-381)	0.539
1.	Time in ML (s)	3.9 (3.5-4.9)	3.4 (3.2-4.5)	0.007*
3.Sinusoid	Gain in AP	1.1 (1.0-1.3)	1.1 (1.0-1.3)	0.809
Eyes closed	Gain in ML	0.3 (0.3-0.4)	0.2 (0.2-0.3)	<0.001*
Eyes open	Gain in AP	1.0 (0.8-1.3)	0.7 (0.6-0.8)	0.003*
4.Limits of Stability	Surface (cm^2)	13.0 (10.0-15.0)	21 (17.7-21.5)	<0.001*

Data are presented as median and interquartile range. p value; Mann Whitney U Significance Test results between groups. (*): statistically significant difference (p<0.05). AP: Antero-posterior, ML: Medio-lateral

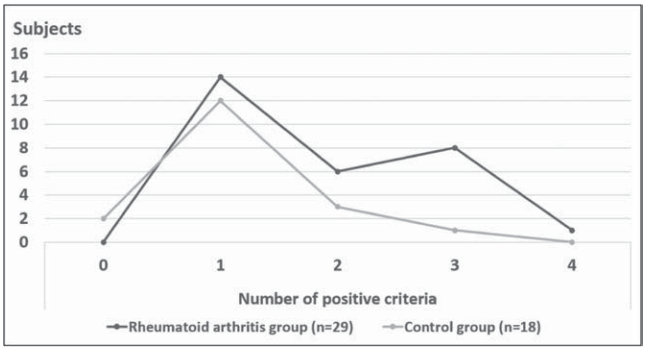

Figure 1. Distribution of participants according to the number of positive criteria. The fallers met at least three criteria.

Conclusion: The results of this study showed that dynamic postural responses to destabilizing conditions are significantly altered in patients with RA compared to healthy controls. Determining the patient-specific fall risk is important in designing personalized rehabilitation programs and reducing the risk of injury.

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AB0309 ASSOCIATION BETWEEN RHEUMATIC DISEASE COMORBIDITY INDEX AND PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS

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Background: Pulmonary involvement is one of the primary contributors of morbi-mortality among patients followed for Rheumatoid Arthritis (RA) [1]. Comorbidities are also independent factors of poor outcomes on those debilitated population.

Objectives: We aimed to assess association between comorbidity and pulmonary involvement in rheumatoid arthritis

Methods: We conducted a retrospective study in our rheumatology department including patients with established RA according to the ACR/EULAR 2010 criteria. Rheumatic Disease Comorbidity Index (RDCI) was calculated for each patient. Clinical characteristics, radiological findings, and respiratory function tests (PFTs) for pulmonary involvement were collected.

Results: There were 255 patients: 212 female (83.1%) and 43 male (16.9%). The mean age was 58.92 ± 10.72 years [25-85]. The mean RDCI was 1.14 ± 1.25 [0-6]. Pulmonary involvement was noted in 115 patients (45.3%). It was asymptomatic in 50.6% of cases. Reported clinical symptoms were dyspnea (36.1%), chronic cough (8.4%), and dyspnea with chronic cough (4.8%).

PFT showed a restrictive syndrome in 34.9% of cases, an obstructive syndrome in 4.8%, a mixed syndrome 3.6% and was normal in 56.6% of patients. Non-specific interstitial pneumonia was noted in 26.6% of patients, followed by nodular lung disease in 11.4 %, usual interstitial pneumonia in 11.4%, BOOP in 6.3%, and then pleural nodules in 6.3%.

An association was noted between RDCI and pulmonary involvement (presence: 1.7 ± 1.3 vs absence: 0.6 ± 0.8, $p<10^{-3}$).

Conclusion: In conclusion, there was an elevated comorbidity index in patients with pulmonary involvement. Comorbidities may be a predictive factor of extra-articular manifestations. The early management may improve outcomes in RA patients.

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Disclosure of Interests: None declared

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AB0310 STUDY "AR-CAT INICI": MANAGEMENT OF EARLY RHEUMATOID ARTHRITIS IN CATALONIA

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Background: Given the progressive change in the management of inflammatory diseases,an observational study was conducted on the management of Early Rheumatoid Arthritis (ERA) in Catalonia.

Objectives: To know the management of ERA in Catalonia, to assess whether the recommendations of the EULAR/ACR guidelines are followed and to study the causes of management variability,to set improvement objectives.

Methods: An observational,descriptive,and cross-sectional study was conducted,with data collection from June 15 to 30, 2021.The rheumatologists' partners of the Catalan Society of Rheumatology were the object of study. An online survey was conducted with 304 members on the management of the ERA. Variables related to the characteristics of the respondents,the derivation and variables of the disease including clinical variables,type of treatment and outcomes used for follow-up including the impact of the SARS-CoV2 pandemic were included. The univariate study was performed using a study of proportions with Pearson's correlation.

Results: A total of 105 members (34.5%) responded to the survey.11.6%>60 y, only 7.8% <30y. 99% were in public assistance.The number of rheumatologists per service is 7.2[1-17],but 34.2% had< 5 rheumatologists,with a reference population of 200,000-300,000p in 42% of respondents.The number of weekly visits made is 67.5[20-130].42.2% do not have a monographic RA or ERA dispensary and 30.4%not have specialized nursing.**Characteristics of ERA**:77.5% are derived from primary care(PC),52% have been between 6 weeks,42.1%>3 months.54.9% make a first visit within 2-4 weeks of PC referral and 14.7%> 8 weeks.100%provide previous analysis,only 47% had had RX performed.98% were previously treated(50.4%NSAIDs + CG,36.1%NSAIDs,12.3% CG).4.3% had GC doses>10 mg/day,11.3%> to 20mg/day.**The treatment**:DMARDs of choice in 100% is MTX,44.1% start doses of 10mg/week and 3.9%7.5 mg/week.The route of choice is oral(55.9% vs 44.1%).92.2% associate GC and 31.7% have not withdrawn them after 6 m.57.8% consider the maximum of MTX 25mg/W.87.1% use doses<10 mg/day,with the most used dose being 5 mg/day(35.6%).Follow-up after the

start of DMARDs is performed 72.5% between 4-6 weeks and 12.7% is performed by nursing.100% use DAS 28 and 53.5% also CDAI.31.4% perform **PROs**(HAQ 83.3%,RAPID 3 14.3%).The use of **systematic ultrasound** is collected in 33%, being himself who performs it in 59.9% and an expert rheumatologist in 46.1%.Finally, when asked about **incidence of pandemic** in the follow-up,53.3% consider that it is doing the same as before. 46.1% consider that telephone visits are not suitable for the follow-up of the ERAvs14.7% who consider that Yes.When questioning the situations in which they consider them to be appropriate,75.9% that it was adequate in the control after the beginning of the DMARDs.Regarding the treatment of ERA, 66% delayed the onset of biological DMARDs, 72.1% due to difficulty of follow-up and only 8.8% due to an increased risk of infection. When performing the **univariate analysis**, it is evident that having a monographic dispensary is associated with earlier onset of MTX($p< 0.001$)and at doses≥15 mg/W($p = 0.05$),greater nursing intervention($p< 0.001$),greater use of PROs($p = 0.008$)and there is a tendency to a shorter waiting time for first visits($p = 0.07$).It is also associated with not considering telephone visits($p< 0.001$), making them in less than 25%($p< 0.0001$).Similarly,hospital level is directly proportional to initiation at higher doses of MTX($p< 0.0001$),lower use of GC<10mg.Among the rest of the variables, no association has been found.

Conclusion: The recommendations of EULAR/ACR in the treatment and follow-up of ERA are consistently followed,although the wide use of MTX orally is striking.It is evident that the variable that most influences the early onset of FAME and at higher doses,is a monographic dispensary,as well as greater presence of nursing and performance of PROs.

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AB0311 RHEUMATOID ARTHRITIS AND OSTEOPOROSIS: FREQUENCY AND ASSOCIATED FACTORS

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Background: In rheumatoid arthritis (RA), persistent systemic inflammation may cause bone and cartilage destruction and systemic osteoporosis (OP).

Objectives: We conducted this study to determine the frequency of OP in RA patients and to focus on associated factors.

Methods: This is a retrospective descriptive and analytic study including consecutive RA patients. The epidemiological, clinical, biological data and the measurement of bone mineral density were collected from patients' records. A statistical analysis was performed to study the clinico-biological profile of osteoporotic patients and determine factors associated with the development of OP in RA patients.

Results: Seventy-one of RA patients were recruited: 67 females (94.4%) and 4 males (5.6%) with a mean age of 54.28 years ± 11.09 [30-75]. OP was noted in 45.1% of cases (32 patients). The mean T-scores at the lumbar and femoral sites were -2.7 ± 0.6 SD and -1.3 ± 1 SD, respectively. Patients with OP were older (58.8 ± 7.6 years vs 50.5 ± 12.1 years; p <0.01) and with a greater number of postmenopausal women than patients with normal bone density (68.7% vs 41%; p=0.02). Osteoporotic patients had RA duration longer than the other group (15.2 ± 12.5 years vs 11.9 ± 8.2 years; p=0.02) and more extra-articular manifestations associated with RA (100% vs 76.9%; p < 0.01). Both groups were treated with corticosteroid drugs with similar frequency, although patients with normal bone density received biotherapy more frequently than patients with OP (23% vs 18.7%; p= 0.03). The two groups had almost similar disease activity DAS28 ESR (44,3 ± 34 vs 42.7 ± 30.7; p=0.2). The following parameters were not associated with the occurrence of OP in our series: gender, smoking, BMI, ESR, CRP, ACPA, RF, erosive and deforming character of RA.

Conclusion: OP is an extra-articular disease that must be systematically screened throughout the follow-up. In our study, there was no significant difference in disease activity at both groups of patients. However, patients with OP had longer duration of RA, more extra-articular manifestations and were less frequently treated with biotherapy.

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AB0312 BODY COMPOSITION AND BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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Objectives: To assess body composition and bone mineral density (BMD) in rheumatoid arthritis (RA) women compared to patients with osteoarthritis (OA).

Methods: 133 women with RA and 45 women with OA aged 50 and over were enrolled in the study. Body composition (fat mass (FM), lean mass and bone mineral component (BMC)) and BMD of the lumbar spine, femoral neck and total hip were measured using dual-energy X-ray absorptiometry (DXA). Appendicular muscle mass (AMM) and appendicular mass index (AMI) were calculated. Muscle strength was assessed in all patients. The criteria of the European Working group on Sarcopenia in Older people 2 (EWGSOP2) were used for low muscle mass and sarcopenia. Osteoporosis was determined in accordance with WHO criteria.

Results: Mean age of RA patients and women with OA was 61.3±7.1 and 61.9±6.2 years, respectively ($p>0.05$). BMC and AMM were lower in RA patients than in women with OA: BMC - 1948.6±425.7g and 2167.1±398.1g, respectively ($p=0.004$); AMM - 17.5±2.9 kg and 20.1±2.7 kg, respectively ($p<0.001$). 27 (20.3%) RA women and only 1 (2.2%) person with OA had low AMM ($p=0.004$). The mean value of AMI was 6.8±1.0 kg/m^2 and 7.5±0.9 kg/m^2 in RA and OA patients, respectively ($p<0.001$). Total FM was 28.3±8.5 kg and 33.2±9.8 kg in RA and OA women, respectively ($p=0.003$). At the same time, we found no differences in the percentage of fat mass: 39.2±5.7% in RA patients and 39.9±5.8% in persons with OA ($p>0.05$). Overfat was discovered in 99 (77.4%) and 38 (84.4%) in women with RA and OA, respectively ($p>0.05$). All women with low AMM/AMI had low muscle strength and were diagnosed with confirmed sarcopenia.

In RA patients BMD at any region was less than in women with OA: in the lumbar spine – 1.026±0.174 g/cm^2 and 1.114±0.177 g/cm^2, respectively ($p=0.009$); in the femoral neck – 0.844±0.151 g/cm^2 and 0.914±0.137 g/cm^2, respectively ($p=0.005$) and in the total hip 0.878±0.148 g/cm^2 and 0.986±0.117 g/cm^2, respectively ($p<0.001$). Normal BMD was found in 33 (24.8%) and 24 (53.3%) women with RA and OA, respectively ($p=0.0004$). 42 (31.6%) patients with RA and 6 (15.4%) women with OA had osteoporosis ($p=0.017$).

Conclusion: RA patients had lower BMC, AMM/AMI, total FM and BMD compared to women with OA, and they were significantly more likely to have sarcopenia and osteoporosis.

Disclosure of Interests: None declared

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AB0313 CLINICAL FEATURE OF 100 CASES OF METHOTREXATE ASSOCIATED LYMPHOPROLIFERATIVE DISORDERS WITH RA PATIENT

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Background: Lymphoproliferative disorders (LPDs), including malignant lymphoma, are known to occur in RA patients treated with disease modified antirheumatic drugs (DMARDs). In particular, LPD associated with methotrexate (MTX)-treated RA is often referred to as MTX-associated LPD (MTX-LPD). MTX-LPD have various clinical feature and histological findings[1)]. We have accumulated MTX-LPD cases in patients with rheumatoid arthritis (MTX-RA-LPD).

Objectives: We clarified the clinical characteristics of MTX-RA-LPD. In addition, we examine the prognosis of MTX-LPD in RA patients.

Methods: We enrolled 100 RA patients who diagnosed MTX-LPD from 2005 to 2021. We collected as follow data based on clinical reports retrospectively; 1) age, 2) gender, 3) duration from RA onset to LPD onset, 4) total dose of MTX, 5) duration of MTX administration, 6) presence of extranodal lesion 7) histological findings, 8) treatment for LPD, 9) 5-year survival rate.

Results: The mean age of 100 MTX-RA-LPD patients (M:F=30:70) were 66.7 ± 10.7 years old, and the duration from RA onset to LPD onset were 25.2 ± 11.0 years. The total dose of MTX and duration of MTX administration were over 2,600mg and over 5 years, respectively. The extranodal lesions were found in 51%, and diffuse large B cell lymphoma was the most common histological findings. Spontaneous regression was observed in 68%. The 5-year survival rate of MTX-RA-LPD was as high as over 85%.

Conclusion: The clinical features of MTX-RA-LPD were similar to those previous reports. Furthermore, we suggested a good prognosis for MTX-RA-LPD.

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AB0314 MULTIMORBIDITY BURDEN IN RHEUMATOID ARTHRITIS

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Background: Multimorbidity in patients with rheumatoid arthritis (RA) has been described as the coexistence of two or more chronic diseases and is the most common cause of death in this population.

Objectives: To describe the prevalence of multimorbidity and mortality trends in a well-characterized cohort of patients with RA.

Methods: A retrospective cohort study of patients with RA (1987 ACR criteria) was conducted. Each patient was evaluated and followed by a rheumatologist in a single outpatient private center in Bogotá, Colombia, from 2014 to 2021. Categorical variables were expressed in frequency and percentage and quantitative variables in mean and standard deviation or median with interquartile range, depending on the distribution of the data. Statistical package: SPSS 25.

Results: A total of 783 patients were included. 11% of patients with RA present multimorbidity. Baseline characteristics were as follows: female gender 81.6%, mean age 51.8±11 years, mean disease duration 8 (IQR 3-15) years, RF positive 80.1%, ACPA positive 58.2%, and erosions 24.9%. Most patients have received glucocorticoids (89.8%), and conventional synthetic DMARDs (97.8%), being prednisone and methotrexate the most frequently prescribed. Hypertension was prevalent in 27.7%, osteoporosis 19.3%, malignancies in 5.5% and principal infection was urinary infection 14.3%. Polyautoimmunity was present in 5.7% most frequently Autoimmune thyroid diseases 10.6% and Sjögren syndrome 9%. After a median of 73 months of follow-up, the mortality rate was 1% of the entire cohort, being cardiovascular disease and COVID-19 infection the main causes.

Conclusion: Patients with RA have an important multimorbidity burden and this increased risk of adverse outcomes and mortality.

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Table 1. Prevalence of the diseases.

Disease	Prevalence
Chronic disease	
Hypertension	27.7%
Dyslipidemia	26.7%
Osteoporosis	19.3%
Obesity	7.7%
Diabetes Mellitus	7%
Cardiovascular disease	
Myocardial infarction	3.4%
Cerebrovascular disease	1.4%
Thrombosis	1.8%
Infections	
Urinary infection	14.3%
Tuberculosis	11.2%
COVID-19	8.2%
Autoimmune disease	
Autoimmune thyroid diseases	10.6%
Sjögren syndrome	9%
Systemic Lupus Erythematosus	2%

Disclosure of Interests: None declared

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AB0315 HYPERURICEMIA AS A FACTOR INTERRELATED WITH COMORBIDITY AND TREATMENT RESULTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Uric acid (UA) is a risk factor of cardiovascular comorbidity in total population [1,2]. However, data about role of hyperuricemia (HU) in rheumatoid arthritis (RA) are limited.

Objectives: to evaluate the interrelations between HU and disease activity, comorbidity, treatment results in patients (pts) with RA.

Methods: Three age and sex matched groups of the pts were formed on the base of Saint-Petersburg rheumatological register (01JAN 2011 - 31DEC2021): group of RA pts with HU (n=292, criteria EULAR2010), group of RA pts without HU (n=292), and group of pts with gouty arthritis (GA, n=300). HU registered if patient had serum level of UA ≥360 μmol/l in ≥3 tests in absence of GA. Pts with secondary HU excluded. RA activity was measured with DAS28. Statistics was performed with SPSS 2020.

Results: Demographic, clinical characteristics, RA treatment in both RA groups were comparable, however decrease of DAS28 during 6-month RA treatment in RA pts with HU was lower than in RA with absence of HU, Table 1.

Table 1. Clinical, laboratory characteristics, and treatment efficacy in RA and GA

Parameter	RA with HU (n=292)	RA without HU (n=292)	GA (n=300)
Age (Mean±SD), years	60.53±12.47	58.07±13.24	57.7±11.85
Female, n (%)	253 (86,64)	282 (96.57)	275 (91.67)
Duration of clinical manifestation, years (mean±SD)	3.56±1.58	4.13±1.75	3.42±2.12
ESR, mm/h (mean±SD)	29.25±14.67	28.22±14.39	30.14±14.43
C-reactive protein, mg/l (mean±SD),	21.10±20.88	23.69±29.93	22.48±21.49
6 months decrease of DAS28 (mean±SD)	1.09±0.28	1.48±0.35*	NA
Medicamental ULT, n (%)	25	NA	100
Efficacy of ULT, n (%)	68 (23.29)	NA	160 (53.33)

ESR – Erythrocyte Sedimentation Rate; ULT – urate-lowering treatment; DAS28 – Disease activity score; NA – not applicable; intergroup difference with p<0.001.

Presence of the HU in RA pts was associated with increased comorbidity as compared with age, sex and activity matched RA pts without HU, and with GA, Figure 1.

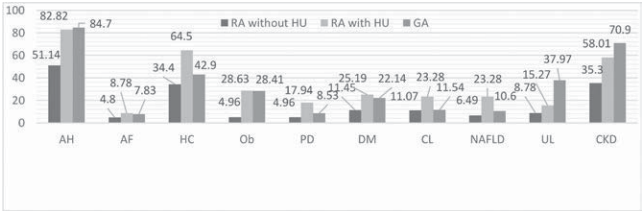

Figure 1. Comorbidity in pts with RA without and with HU, and in GA pts.

Intergroup difference of comorbidities between pts with RA without and with HU or with GA is significant with p <0.000. Intergroup difference between RA with HU and GA is significant with p<0.01.

AH - arterial hypertension, AF - atrial fibrillation, HC – hypercholesterolemia, Ob – obesity, DM - diabetes mellitus type 2, CL – cholelithiasis, NAFLD - non-alcoholic fatty liver disease, UL – urolithiasis, CKD – chronic kidney disease (st.1-4).

ULT was administered to pts with RA and HU 4 times less frequently than to pts with GA. The effectiveness of ULT in RA and HU is two times lower than in GA.

Conclusion: 1) HU negatively affects the decrease of RA activity. 2) HU in RA is associated with increased comorbidity 3) ULT is assigned to pts with RA and HU 4 times less frequently than to pts with GA and is ineffective in 76.71% of cases.

Additional research is needed to evaluate the influence of UAs' serum levels' normalization as factor that could improve results of RA treatment and comorbidity.

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AB0316 SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: PREVALENCE AND ASSOCIATED FACTORS

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Objectives: To evaluate the prevalence of sarcopenia (SP) and associated factors in patients with rheumatoid arthritis (RA).

Methods: 159 women (mean age 58.7±8.8) with confirmed RA according to ACR/EULAR criteria (2010) were enrolled. Hand grip strength was measured using mechanical dynamometry. Dual-energy X-ray absorptiometry (DXA) was performed to assess the body composition and bone mineral density (BMD) of the lumbar spine, femoral neck and total hip. SP was defined as muscle strength < 16 kg and appendicular lean mass index (ALMI) <5.5 kg/m^2 or appendicular lean mass (ALM) <15 kg. RA activity was assessed by C-reactive protein (CRP) and disease activity score using 28 joint counts and erythrocyte sedimentation rate (DAS28-ESR). The relation between low ALM with disease parameters was analyzed using Spearman's r. Factors associated with SP were evaluated using regression analysis.

Results: SP was diagnosed in 33 (20.8%) women with RA. Patients with SP did not differ in age from those without it (59,0±8,9 and 58,7±8,8 years, respectively, p>0,05). 75.8% patients with SP and only 27.8% women without SP had normal BMI (p<0.001). Osteoporosis was diagnosed significantly more often in patients with SP than in women without SP (54.5% and 23.0%, respectively, p<0.001). In women with RA, ALM and ALMI correlated with body mass index (BMI), bone mineral component, BMD and total fat mass. ALM and ALMI did not correlate with age, disease duration, the use of glucocorticoids, DAS28, CRP, total protein, and creatinine levels. In univariate regression analysis, SP was associated with BMI, bone mineral component, BMD of lumbar spine and proximal femur, total fat mass. In multivariate regression analysis, SP was positively associated with the presence of osteoporosis [OR 2.98, 95%CI (1.22-7.30), p = 0.017] and BMI < 25 kg/m^2[OR 6.75, 95%CI (2.45-18.56), p <0.001]. No other significant associations were found.

Conclusion: Among patients with RA, 1/5 of them had SP, which was positively associated with BMI and the presence of osteoporosis, but not with the age, activity and duration of the disease.

Disclosure of Interests: None declared

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AB0317 QUALITY OF LIFE AND LOCOMOTIVE FUNCTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objectives: To evaluate quality of life and its relationship with muscle strength and physical performance in patients with rheumatoid arthritis (RA).

Methods: 157 women with RA (median age was 58.6±8.8 years, median duration of RA was 8.0 [4,0; 14] years) were included in the study. Assessment of functional disability and quality of life was carried out using Health Assessment Questionnaire Disability Index (HAQ), EQ-5D (index and visual analog scale, VAS), Hospital Anxiety and Depression Scale (HADS, with two subscales for anxiety and depression, HADS-A and HADS-D), Rheumatoid Arthritis Impact of Disease (RAID). Also, all patients underwent tests to determine muscle strength by hand dynamometry and test "Chair stand" and physical performance by the Short Physical Performance Battery (SPPB). Dual-energy X-ray absorptiometry of the whole body, lumbar spine and proximal hip was done. Spearman's correlation test was performed.

Results: 88.5% of RA patients had low muscle strength, 61.1% of people had low physical performance. No correlation was found between physical performance and age, RA activity, body composition and BMD. In persons with reduced physical performance, HAQ, EQ-5D index, VAS and RAID were worse than in women with normal physical function (p<0.0001; p<0.0001; p=0.004; p=0.010, respectively). Also, these patients had more pronounced signs of anxiety and depression, assessed using HADS-A (p=0.004) and HADS-D (p=0.001). HAQ positively correlated with the number of comorbidities (r=0.35, p<0.001) and negatively correlated with the SPPB and gait speed (r=0.35, r=-0.39 and r=-0.37, respectively, p<0.001). EQ-5D index positively correlated with SPPB and gate speed (r=0.44 and r=0.39, respectively, p<0.001). HADS-A and HADS-D positively correlated with the number of comorbidities (r=0.35 and r=0.34, respectively, p<0.001). HADS-A negatively correlated with the biological therapy duration (r=-0.36, p=0.032) and with BMI (r=-0.34, p<0.001). HADS-D negatively correlated with the SPPB (r=-0.36, p<0.001). RAID negatively correlated with the biological therapy duration (r=-0.35, p=0.032) and with SPPB (r=-0.35, p<0.001).

Conclusion: 88.5% of RA patients had low muscle strength and 61.1% - low physical performance. Quality of life negatively correlated with physical performance.

Disclosure of Interests: None declared

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AB0318 PREVALENCE OF SECONDARY SJOGREN'S SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS- A SINGLE CENTER STUDY FROM NORTHERN INDIA

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Background: Sjogren's syndrome (SS) is a systemic autoimmune disease characterized by lymphocytic infiltration of salivary and lacrimal glands leading to dry eyes and dry mouth. Sjogren's syndrome either present alone (primary Sjogren's syndrome) or sometimes can occur with other autoimmune diseases like rheumatoid arthritis, systemic lupus erythematosus, and scleroderma. In such instances, the condition is termed secondary Sjogren's syndrome. SS may be a marker of more aggressive joint disease in patients with RA, and hence it is essential to characterize the symptoms in the RA cohort, which may help in the management and treatment of the disease.

Objectives: Primary Objective

The primary objective of the current study is to estimate the prevalence of secondary Sjogren's syndrome in a cohort of patients with rheumatoid arthritis.

Secondary Objective

To compare the clinical characteristics in rheumatoid arthritis patients with Sjogren's syndrome and in rheumatoid arthritis patients without Sjogren's syndrome.

Methods: The study was conducted from 2016-2018 in a tertiary care hospital in the Department of Rheumatology, New Delhi, India. Patients with a rheumatologist-diagnosed RA were enrolled. There were 726 patients with rheumatoid arthritis. Patients were enquired about their symptoms. Out of 726, 193 had secondary Sjogren's syndrome (26.58%). In patients without Sjogren's syndrome, complete clinical data were available only for 377 patients hence the analysis on the comparison of clinical characteristics was limited to 377 patients. The other patients were excluded due to lack of the data required for the study.

Results: It was identified that out of 726 patients, 193 had symptoms of secondary Sjogren's like dry eyes dry mouth, or both. It was found that in patients with secondary Sjogren's syndrome (n=193), the mean age was significantly higher than those patients without secondary Sjogren's syndrome (n=377) [52.58 ± 12.36 Vs. 48.42 ± 13.98, p=0.0005]. Similarly, the mean disease duration was significantly higher among RA patients with secondary SS than those without SS [10.76 ± 8.34 Vs. 6.81 ± 7.29, p<0.0001]. Similarly, co-morbidities like hypertension, diabetes mellitus, and hypothyroidism were more seen in patients with rheumatoid arthritis with Sjogren's syndrome.

In a meta-analysis involving 18 studies[1], it was identified that the prevalence of SS in RA was 19.5%. The differences in the prevalence of secondary SS in RA patients could be attributable to inter-ethnic variation, disease duration, and clinical scores employed in the studies. Similar to our study, Santhosh et al.[2] reported that patients with secondary SS had a longer disease duration than those without secondary SS.

Conclusion: The prevalence of Sjogren's syndrome among patients with rheumatoid arthritis in the North Indian cohort of patients with RA was 26.58%.

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Disclosure of Interests: None declared

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AB0319 PREALBUMIN SERUM LEVEL AS A USEFUL TOOL IN THE ASSESSMENT OF MALNUTRITION IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Protein-energy malnutrition is a common condition among elderly patients with RA associated with a poor prognosis. Although many screening tools are developed, there's no consensus on which test is more reliable in clinical practice. Serum prealbumin (PAB) may be a useful malnutrition biomarker.
Objectives: Our objective is to evaluate the usefulness of serum PAB in the assessment of malnutrition in elderly patients with RA.
Methods: We conducted a prospective study including RA patients who were followed in rheumatology department and aged 65 years or older. We studied malnutrition prevalence, risk of complications related to malnutrition and PAB serum concentrations. The mini-nutritional assessment (MNA) score was used as the reference method to determine malnutrition. We also dosed inflammatory proteins: Orosomucoide (Oroso), C-reactive protein (CRP) and Haptoglobine (Hapto). For the prognosis assessment, we calculated the Geriatric nutritional risk index (GNRI) and the Prognostic Inflammatory and Nutritional Index (PINI).
Results: Sixty-three patients (52 female and 11 male) were included. Their mean age was 68.17±4.35 years. The average DAS28 was 3.72±1.48. The mean MNA total score was 20.19 ± 4.71. According to MNA, the prevalence of malnutrition was 20.6%. 55.6% of the patients were at risk of malnutrition and only 23.8% of patients had a normal nutritional status. The median PAB was 0.16 g/L with an IIQ of [0.04-0.24] and extremes ranging from 0.01 to 0.37 g/L. According to PAB, 35.8% of patients had a normal level above 0.20 g/L, 17% had PAB levels between 0.15 and 0.19 g/L, indicating moderate malnutrition and 47.2% of patients had PAB levels below 0.15 g/L, indicating severe malnutrition. Concerning inflammation proteins: the mean CRP was 18.96 ± 27.8 mg/L. 28.6% of patients had a CRP > 15 mg/L, of which 9.5% had a CRP > 50 mg/L. The mean Oroso was 1.29 ± 0.46 g/L [0.6-2.2]. 52.5% of our patients had an elevated oroso value. The mean Hapto was 2.07 ± 0.97 g/L [0.31-5.29]. 42.9% of patients had an increased value above 2.5 g/L. Concerning prognosis indexes, the median GNRI was 116.47 with an IIQ of [106.6-125.12] and extremes ranging from 70.06 to 145.02. The median PINI was 1.77 with an IIQ of [0.47-10.21] and extremes ranging from 0.05 to 222.16. Statistical analysis showed a significant association between PAB and MNA with p=0.05. Negative correlation was found between PAB and inflammatory proteins; with Oroso (p=0.001), CRP (p=0.006) and Hapto (p=0.03). By analysing prognosis indexes, significant negative correlation of the serum PAB was found with the GNRI (p=0.003) and the PINI (p=0.001).
Conclusion: We conclude that PAB could represent a feasible and reliable tool in the diagnosis of malnutrition. It is a good biomarker for the prognosis and the assessment of the risk of complications related to malnutrition among the elderly patients with RA.
Disclosure of Interests: None declared

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AB0320 ASSOCIATION OF THE BIOMARKERS SOLUBLE ST2, GALECTIN-3, N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE, PENTRAXIN WITH MYOCARDIAL DYSFUNCTION DETECTED BY SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS PRIOR TO BIOLOGICAL THERAPY

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Background: Risk of developing cardiovascular complications and death in rheumatoid arthritis (RA) is 50% higher than in the total population. The biomarkers soluble ST2 (sST2), galectin-3, pentraxin and N-terminal pro-brain natriuretic peptide (NT-proBNP) provide prognostic information in pts with heart failure.
Objectives: To determine the frequency of myocardial dysfunction (lower global longitudinal epicardial strain of left ventrical (GLES LV) using echocardiographic method of speckle tracking, the level of NT-proBNP, pentraxin, galectin-3 and sST2 in patients (pts) with RA prior to therapy with bDMARDs.
Methods: A total of 41 pts with RA (ACR/EULAR criteria, 2010) were included in the study: 63% of women, age 56 [37;66] years, disease duration 24 [8;96] months; DAS28 6,01 [5.3;6.3], positive for ACCP (92%), RF (78%), without cardiovascular diseases and prior administration of bDMARDs. All pts underwent echocardiography, tissue Doppler imaging and the speckle tracking assessment of GLES LV. 44% of RA pts received methotrexate (median dose - 15 (15;20) mg / week.), 35% - leflunomide, 9.3% - sulfasalazine, 7% - hydroxychloroquine, 67.4% - glucocorticoids (median dose - 5 (4;8) mg / day.), 74% - nonsteroidal anti-inflammatory drugs. In each RA pts, we measured plasma concentrations of sST2 (Cristal Diagnostics, San Diego), galectin-3 (Bender MedSystems GmbH Biocenter, Vienna Austria) NT-proBNP (Roche Diagnostics, Switzerland) and pentraxin (Hycult Biotech, Netherland). The control group consisted of 10 healthy subjects, which were matched by sex and age.
Results: : In pts with RA speckle-tracking method detected lower global longitudinal epicardial strain (GLES)(–16.5 [-14.6; -18.5]%), compared to the healthy control group (–21.58 [-22.1;-20.4] %, p=0.0001). 27(67%) RA pts showed a decrease GLES. RA pts also had higher levels of NT-proBNP (114.8 [45.1; 277.5] pg/ml vs 52 [40.5; 69.1] pg/ml, p<0.05), lower levels of sST2 (10.6 [9.2; 13.1] ng/ml vs 13.5 [11.0; 19.7] ng/ml, p<0.04) compared to control group.
All RA pts were divided into 2 groups: group 1- with low GLES, group 2 - with preserved GLES. In group 1, the levels of ST2 were significantly lower than in group 2 (Table 1). There were no differences in left ventricular ejection fraction, LV sizes, LV myocardial mass index, NT-proBNP, pentraxin, galectin-3 levels between groups.

Table 1. Levels of biomarkers in groups

	low GLES, (n=27)	Normal GLES, (n=14)	p
sST2, ng/ml	13.2 [10.6;17.0]	18.3 [13.7;60.9]	<0.05
Pentraxin, ng/ml	0.29 [0.05;0.42]	0.3 [0.02;0.79]	>0.05
galectin-3, ng/ml	4.0 [2.6;6.9]	4.3 [3.2;5.3]	>0.05
NT-proBNP, pg/ml	105 [42;260]	94 [35.5;378.8]	>0.05

There were negative correlations between the global longitudinal epicardial strain and age (r=-0,9, p<0,02), E velocity LV (r=-0,5, p<0,04), sST2 (r=-0,5, p<0,02). Galectin-3 correlates with left atrial volume (r=0,4, p<0,04), septal e' velocity (r=0,6, p<0,008). ST2 levels correlate with ESR (r=0,6, p<0,04), CRP (r=0,5, p<0,002).
Conclusion: In pts with RA frequently (67%) were detected lower global longitudinal epicardial strain, higher levels of NT-proBNP and lower levels of sST2. In RA pts the sST2 biomarker is better associated with inflammatory activity and myocardial dysfunction.
Disclosure of Interests: None declared

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AB0321 ADHERENCE TO MEDITERRANEAN DIET AND PREVALENCE OF CARDIOVASCULAR RISK FACTORS IN RHEUMATIC DISEASES

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Background: Rheumatic diseases (RD) are autoimmune inflammatory arthritis. However involvement to other organs can occur and leads to atherosclerosis and cardiovascular (CV) risk factors. Mediterranean diet (MD) has attracted considerable interest because it seems to offer significant benefits to that end.
Objectives: To evaluate the role of MD in the development of the cardiovascular risk factors in RD.
Methods: We conducted a cross-sectional study including patients with RA (ACR-EULAR 2010 criteria) or with SA (ASAS 2009 criteria), in remission or in low activity disease and with no history of cardio vascular risk factors before the diagnosis of their RD. Sociodemographic and disease related data were collected: Disease Activity Score (DAS28-CRP), Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) and medication. We asked the patients to complete the 14-items MD adherence questionnary. We evaluated the association of adhrence to MD with cardiovascular risk factors: obesity, type-2 diabetes, hyperlipidemia and hypertension. We estimated odds ratios for each cardiovascular risk factors and their 95% confidence intervals. In all analyses, the

high adherence category of MD adherence score [10–14) was considered the reference category.

Results: We included 61 patients (40 women and 21 men) with a mean age of 42.2 ± 1.1 years old [20-66]. Among them, 32.7% belong to urban environment and 26.2% were professionally active. The mean disease duration was 83.2 months [9-180]. The mean DAS28-CRP was 1.2 [0.8-1.9] and the mean ASDAS-CRP was 1.8 [1.1-2.01]. Methotrexate was used by 52.4%, either as monotherapy or combination and biological in 47.6 %. Thirty patients had high adherence to MD (H-MD) and thirty-one had medium or low adherence to MD (L-MD). We found that higher adherence to the MD is inversely associated with the prevalence of each of the four cardiovascular risk factors, results are shown in Table 1.

Table 1. Prevalence of cardiovascular risk factors and odds ratio in high adhrence to Mediterranean diet in rheumatic diseases.

	Prevalence %	Odds ratio	95% confidence intervals
Obesity	57.4	0.017	[0.03-0.93]
Type-2 diabetes	50.8	0.01	[0-0.019]
Hyperlipidemia	50.8	0.126	[0.04-0.3]
Hypertension	42.6	0.13	[0.43-0.4]

Conclusion: Our results suggest that the healthy effects of the MD observed in epidemiologic studies are exerted partly through plausible mechanisms: low prevalence of obesity, of type2 diabetes, of hyperlipidemia and of hypertension. Interventional studies may eventually provide stronger evidence. In the meantime, an increasing of knowledge supports the Mediterranean diet as a useful tool in managing individuals with RD, who are at high risk ofcardiovascular diseases.

Disclosure of Interests: None declared

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AB0322 INTESTINAL DISBIOSIS IS ASSOCIATED WITH INADEQUATE RESPONSE TO MULTIPLE ANTIRHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS.

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Objectives: To evaluate the relationship between inadequate response to multiple antirheumatic biologic or targeted synthetic drugs (IRM-b/tsDMARDs) and intestinal microbiota and other inflammatory and severity factors in patients with rheumatoid arthritis (RA).

Methods: Design: A case-control study nested in a prospective cohort of RA patients.

Patients: Patients with RA (ACR/EULAR 2010) from a prospective baseline cohort (incident cases between 2007-2011), >16 years. Controls: subjects without inflammatory disease matched by sex and age.

Protocol: All subjects were evaluated in a specialized outpatient unit. Clinical, analytical and therapeutic variables were registered using a data collection protocol. Blood, urine and faeces samples were obtained from all subjects.

Variables: Dependent variable: "RA patients with IRMD", defined as failure >2 different bDMARDs (biological disease-modifying antirheumatic drug) or dsDMARDs (targeted synthetic disease-modifying antirheumatic drug). Faecal microbiota (continuous var., 0-100%) was analysed using the Ion Torrent S5 next-generation sequencing platform, and the sequences obtained were processed using the QIIME2 (Quantitative Insights Into Microbial Ecology 2) software. Inflammatory activity was measured by mean DAS-28 (disease activity score-28) throughout the disease and RA severity variables included erosions, anticitrullinated peptide antibody (ACPA) titres and HAQ (health assessment questionnaire). Other variables included socio-demographic, clinical-analytical characteristics, type of treatment with bDMARDs and reason for suspension.

Statistical Analysis: descriptive, bivariate using χ^2 and T-Student followed by two logistic regression model in order to identify the factors associated with both bDMARDs and IRM-b/tsDMARDs in patients with RA.

Results: 220 subjects, 110 RA patients and 110 controls, were included. A total of 90/110 RA patients were seropositive (81.8%) and 68/110 were erosive (61.8%). A total of 61/110 (55.5%) were treated with any bDMARD, being more frequent the anti TNF (35.5%). Ninety-three (84.5%) of RA patients took associated sDMARD. Thirteen patients (21.3%) presented IRMD. The variables independently associated with biological therapy in RA were: physical activity (OR [95% CI], 0.990 [0.989-0.999]; p=0.043), erosions (OR [95% CI], 2.450 [1.056 -4.683]; p=0.037) and Actinobacteria family (OR [95% CI], 1.182 [1.016-1.375]; p=0.030), R2= 0.283. The variables that were independently associated with IRMD in patients with RA were: ACPA (OR [95% CI], 1.005 [1.001-1.010]; p=0.039), diagnostic delay (OR[95% CI] 1.025 [1.001-1.050]; p=0.044), age (OR [95% CI], 0.933 [0.872-0.998];p=0.032), *Bacterioidetes* (OR [95% CI],1.080 [1.014-1.150]; p=0.016), *Synergistetes* (OR [95% CI], 2.277 [1.094-4.741]; p=0.028), R2=0.329.

Table 1. Epidemiological, Clinical and analytical characteristics of patients and controls.

Variable	Patients n=110	Controls n=110	p-value
Epidemiological characteristics			
Age, mean (IQR)	55.9 (49.3-64.4)	56.2 (48.3-65.3)	0.917
Sex, female; n (%)	88 (80.0)	88 (80.0)	1.000
Clinical and analytical characteristics			
Erosions, n (%)	68 (61.8)	-	-
RF >10, n (%)	90 (81.8)	0 (0.0)	<0.001
ACPA >20, n (%)	88 (80.0)	0 (0,0)	<0.001
CRP (mg/dl), median (IQR)	2,9 (2.9-6.2)	2.9 (2.9-3.3)	<0.001
ESR (mm/h), median (IQR)	13.0 (8.0-21.0)	11.0 (6.0-16.0)	0.008
DAS28 average, mean (±SD)	3.0 (0.7)	-	-
HAQ average, median (IQR)	0.71 (0.3-0.9)	-	-
sDMARD, n (%)	93 (84.5)	-	-
bDMARD, n (%)	61 (55.5)	-	-
Anti TNF-α, n (%)	39 (35.5)	-	-
Anti IL-6, n (%)	9 (8.2)	-	-
Rituximab, n (%)	7 (6.4)	-	-
Abatacept, n (%)	2 (1.8)	-	-
JAK inhibitor, n (%)	4 (3.6)	-	-
Multiresistance, n (%)	13 (21.3%)	-	-

Conclusion: Biological treatment in RA was associated with less physical activity, erosions and a greater presence of *Actinobacteria.* Bad prognosis factors such as delayed diagnosis and elevated ACPA titres were associated with multiresistance in RA patients, in addition to higher levels of *Bacteriodetes* and *Synergistetes.*

Disclosure of Interests: None declared

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AB0323 FACTORS ASSOCIATED TO CLINICAL INERTIA IN RHEUMATOID ARTHRITIS

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Background: Clinical inertia in rheumatic diseases is defined as inability or undue delay to initiate or intensify therapy when the disease is active or de-escalate therapy when the disease is in remission. Understanding the various contributory factors to clinical inertia is helpful in ensuring appropriate planning to tackle the issue and achieving Treat-To-Target (T2T) goals.

Objectives: We aimed to identify medical therapeutic inertia in Rheumatoid Arthritis (RA) patients and to assess its contributing elements.

Methods: We conducted a monocentric study including 42 patients, fulfilling the 2010 ACR/EULAR classification criteria for RA, who consulted our outpatient department from november 2021 to January 2022. Study data collection included demographics, clinical and disease characteristics, and treatment history. The survey also contained the Satisfaction Questionnaire for Medication (TSQM) which provides validated score for four subscales: effectiveness, side effects, convenience, and global satisfaction. Treatment satisfaction was measured using a cutpoint global satisfaction score ≥ 80.

Results: Most patients were female (86%) with a mean age of 57±13 years and a mean disease duration of 10.8±4.7 years. The education level for most patients (62%) was secondary school education or less. Fifteen percent of patients were in full-time work, 27% were unemployed, and 54% were retired. RA impact on patients' work-life was considerable, as 14.3% had retired early due to RA. Patients had moderate-to-high disease activity, with a mean DAS28 with C-reactive protein (CRP) of 4.2±1.4. Radiographic structural damage was apparent in 79% of patients. RA was immunopositive in 92% of patients. Most

common comorbidities were cardiac disorders (32%), pulmonary disorders (13%), and metabolic/nutrition disorders (11%). Psychiatric disorders was present in 9.5% of patients. CsDMARDs were the most frequently prescribed medications, used in 69% cases, followed by bDMARDs used in 34% cases. A total of 54% received the anchor drug methotrexate as part of their treatment regime. Only 12% of patients used systemic glucocorticoids for RA. Only half (52%) of all patients had a planned switch of medication, despite long-standing disease and suboptimal symptom control with current DMARD therapy. Statistical analysis revealed that factors for switch decision to a different DMARD by the treating physician was: younger patient age (p=0.002), having a high disease activity by DAS28-ESR (p<0.001), worse HAQ score (p<0.001), lower global satisfaction score (p<0.001), and patient preference for oral administration (p=0.006). Predictors for not switching to a different DMARD included a higher number of comorbidities (p<0.001), lower current DAS28-ESR score (p<0.001) and lower number of concomitant medications (p=0.002). Mean TSQM scores were 62 for effectiveness, 45 for side effects, 65 for convenience, and 60 for global satisfaction. Only 16 % of patients were satisfied with their RA treatment.
Conclusion: Our study showed that patients with active RA may not be managed in consistency with recommendations. This phenomenon defined as clinical inertia, is multi-factorial including healthcare set-ups and providers, patients and their caregivers. That's why before labelling management of rheumatic disease in an individual as a 'failure', careful consideration of relevant factors linked to clinical inertia may be helpful.
Disclosure of Interests: None declared

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AB0324 SAFETY PROFILE OF JAK INHIBITORS IN REAL WORLD FROM A SINGLE CENTER COHORT

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Background: Recent published data have emerged some concerns about safety of Janus kinase (JAK) inhibitors and FDA have established prescribing restrictions.
Objectives: The aim of this study was to analyze the safety profile of current approved JAK inhibitors in Europe with data from a Real World cohort.
Methods: A single center observational study was performed including patients who had initiated treatment with Tofacitinib, Baricitinib or Upadacitinib from September, 2017 to January, 2022. Demographic, clinical, laboratory and safety variables were collected from baseline and at months 1, 3, 6 and every six months. Safety data was collected including any adverse event (AE) due to any cause. An AE was considered serious if it was life-threatening or result in hospitalization, disability or in death. All AE and SAE were expressed adjusted by exposure (E/100 PY).
Results: A total of 194 patients were included whom baseline demographic and disease characteristics are exposed in Table 1. Drug exposure was 265.5 patient-years. Overall, 214 AE were detected being mild upper tract respiratory infection the most frequently registered (15.82 E/100PY) followed by Urinary tract Infection accounting 7.16 E/100PY. 10 Serious Infections were detected in 10 patients of which 5 were pneumonia (1.88 E/100PY), 1 cellulitis (0.38 E/100PY) and 2 COVID-19 (0.76 E/100PY). 12 herpetic infection were detected in 9 patients (4.52 E/100PY) of which 7 were caused by herpes zoster (2.64 E/100PY) and 5 by herpes simplex (1.88 E/100PY) 3 cases were mono-metameric and 4 multi-metameric. Moreover, 2 patient developed postherpetic neuralgia. A patient with RA developed Miliary Tuberculosis (0.38 E/100PY) with a negative IGRA test prior to the JAKi. A patient with RA suffered a Myocardial Infarction (0.38 E/100PY). 7 RA patients developed malignancy (2.64 E/100PY), one with oral squamous cell carcinoma, two Bowen carcinoma, one breast cancer, 2 basal cell carcinoma and a colorectal metastatic cancer. Not a single case of thromboembolic event nor Hepatitis B Virus reactivation were registered. 2 patients died, one with cancer and the other suffered a severe COVID-19 (unvaccinated).

Table 1. DEMOGRAPHIC, DISEASE AND TREATMENT BASELINE CHARACTERISTICS.

Characteristic	Rheumatoid arthritis n=163 (84.02%)	Psoriatic arthritis n=18 (9.28%)	Juvenile idipathic arthritis n=7 (3.61%)	Other n=6 (3.09%)
Age - years	55.23 (16.84)	54.71 (11.89)	27.14 (5.18)	48 (12.95)
Female sex – number (%)	142 (87.12)	12 (66.66)	6 (85.71)	4 (66.67)
Race – number (%)				
Caucasian	135 (82.82)	16 (88.89)	7 (100)	6 (100)
Asian	2 (1.23)	0 (0)	0 (0)	0 (0)
Latin	26 (15.95)	2 (11.11)	0 (0)	0 (0)
Comorbidities – number (%)				
High blood pressure	118 (72.39)	11 (61.11)	0 (0)	0 (0)
Dyslipemia	54 (33.13)	6 (33.33)	0 (0)	1 (16.67)
Diabetes Mellitus	10 (6.13)	3 (16.66)	0 (0)	1 (16.67)
Positive HBV serology	12 (7.36)	1 (5.55)	0 (0)	0 (0)
Latent Tuberculosis	15 (9.20)	1 (5.55)	0 (0)	0 (0)
JAKi				
Baricitinib	61 (37.42)	0 (0)	2 (28.57)	1 (16.67)
Tofacitinib	83 (50.92)	15 (83.33)	4 (57.14)	3 (50)
Upadacitinib	19 (11.66)	3 (16.67)	1 (14.29)	2 (33.33)
Patients taking glucocorticoids – number (%)	112 (68.71)	9 (50)	3 (42.86)	1 (16.67)

Conclusion: In this updated analysis of 194 patients treated with JAKi, the three approved JAKi showed a safety profile consistent with data from RCT. The patients under JAK therapy should be carefully evaluated on their follow-up.
Disclosure of Interests: None declared

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AB0325 SERUM HEPCIDIN LEVEL IN REFRACTORY RHEUMATOID ARTHRITIS: ITS RELATIONSHIP TO DISEASE ACTIVITY AND CHRONIC HYPOXIA

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Background: Difficult-to-treat rheumatoid arthritis (D2T RA) was recently defined by a EULAR study group and, as a disease category it is largely complicated and under-researched. Patient multimorbidities, in particular chronic hypoxia, may play a significant role in the response to therapy with biologic disease-modifying antirheumatic drugs (bDMARDs) and in the disease classification as D2T RA. Iron metabolism disorders are the leading pathogenic factors in progression of anemia of chronic disease and chronic hypoxia. Hepcidin is a key negative acute-phase regulator of duodenal iron absorption, mobilization and considered as a mediator of anemia in inflammation. However, present studies on serum hepcidin levels in patients with RA and multimorbidity are inconsistent
Objectives: To investigate the relationship between hepcidin levels, markers of inflammatory activity and hemoglobin (Hb) levels in patients with RA and multimorbidity.
Methods: The investigation enrolled 71 patients (mean age, 54.8±14.8 years) with RA according to the 2010 ACR/EULAR criteria, who had been examined and treated at the V.A. Nasonova Research Institute of Rheumatology. The median disease duration was 5.0 [1.5; 9.5] years; the mean DAS28 score was 5.0±1.3. Documentation and anamnesis data were analyzed with emphasis on associated diseases. The Cumulative Illness Rating Scale (CIRS) was used to assess the profile of multimorbidity.
Anemia of inflammation (AI) was diagnosed in 42 patients. Anemia was defined as hemoglobin <12g/dL and <13.5g/dL, in men and women, respectively. AI was diagnosed on the basis of a combination of the following: a) normal or elevated ferritin b) lowered serum iron and total iron binding capacity and c) normal percent iron saturation. Serum hepcidin, as well as IL-6 levels were also measured. Patients with iron-deficiency anemia were excluded.
Results: Chronic kidney disease that occurred in almost half (42.5%) of cases was most commonly undiagnosed in the cohort under study; on average, every three patients were not found to have signs of metabolic syndrome (hyperglycemia in 29%, hypercholesterolemia in 20%, obesity in 13.5%), chronic hypoxia (new-onset anemia verified in 24% of cases).

RA patients with AI and with normal Hb levels (n=29) were comparable (p>0.05) in age (44.4±14.8 and 49.8±9.3 years), disease duration (73.5±65.4 and 59.8±48.3 months) and DAS28 (6.3±1.6 and 5.9±1.9).

In RA patients with AI we found a strong positive correlation between serum hepcidin and ferritin levels (r=0.623, p=0.009). There was a positive correlation between serum hepcidin and IL-6 levels (r=0.546, p=0.023). We found a strong negative correlation between serum hepcidin concentrations and Hb levels (r=0.528, p=0.029), but reliable correlation between DAS28, CRP and ESR was not revealed.

In RA patients without anemia, the level of hepcidin positively correlated with the inflammatory activity parameters including CRP, ESR and DAS28, no correlation between the Hb and ferritin levels was revealed.

Conclusion: Our data support the hypothesis that IL-6-driven hepcidin production mediates AI in RA patients and might play a role in the pathogenesis of anemia associated with RA. In RA patients with chronic hypoxia, serum hepcidin level was significantly higher and perform better than traditional yardsticks in identifying anemia inflammation.

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[1] The study was carried out within the framework of topic No. AAAA-A19-119021190149-0

Disclosure of Interests: None declared

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AB0326 EVALUATION OF BONE DENSITY PARAMETERS IN A COHORT OF PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS: HOW THERAPY WITH GLUCOCORTICOIDS, METHOTREXATE AND BDMARDS CHANGES BONE MINERAL DENSITY, T-SCORE AND TRABECULAR BONE SCORE

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Background: Osteoporosis (OP) can affect patients with Rheumatoid Arthritis (RA). This can be due to long-time use of glucocorticoids (GCS) or to the activation of proinflammatory pattern, via TNFα signalling, that leads to osteoclast (OC) activation with bone resorption.

Objectives: Aim of this study is to assess how therapy with GCS, methotrexate (MTX) and bDMARDs may change bone density parameters.

Methods: 66 RA patients were enrolled in this study. Bone Mineral Density (BMD), T-score of spine and femur, Trabecular Bone Score (TBS) and TBS T-score were evaluated at baseline and after 18 months of treatment with GCS, MTX, bDMARDs. Comparison among different patient groups were evaluated by ANOVA. P-value < 0.05 was considered significative.

Results: At baseline, 66% of patients were female and 44% male, mean age was 62.2 (± 8.4) years, mean disease duration was 17.8 (± 11.2) years, 76% of patients were Rheumatoid Factor (RF) positive and 24% were RF negative, 71% were ACPA positive and 29% were ACPA negative, mean DAS-28 was 3.67 (± 1.34), mean L1-L4 BMD was 0.930 (± 0.175) g/cm^3, mean neck's femur BMD was 0.705 (± 0.102) g/cm^3, mean L1-L4 T-score was -1.11 (± 1.54), mean neck's femur T-Score was -1.17 (± 1.02), mean TBS was 1.239 (± 0.132) and mean TBS T-score was -2.36 (± 1.42). Among the entire population in study, 24.4% were affected by OP, 74.6% were in therapy with GCS, 57.8% with MTX and 16.6% were under OP treatment with bisphosphonate or teriparatide or denosumab. At baseline, 51.6% of patients started an TNFi treatment, 3.1% started an anti IL-6 treatment, 9.3% started an anti-CTLA4 treatment and 23.4% started a JAKi treatment. By ANOVA analysis, patients at baseline in therapy with MTX had mean L1-L4 BMD and L1-L4 T-score higher than those not in therapy with MTX, respectively 0.985 (± 0.184) g/cm^3 vs 0.866 (± 0.144) g/cm^3 (p < 0.05) and -0.73 (± 1.70) vs – 1.62 (± 1.13) (p < 0.05). At 18 months patients treated with MTX had higher L1-L4 T-score than those not in therapy with MTX, respectively -0.48 (± 1.68) vs – 1.68 (± 1.18) (p < 0.05). Percentage variations in BMD, T-score, TBS and TBS T-score between baseline and 18-month endpoint were not significative; nevertheless, we observed a positive trend in lumbar and femur BMD percentage variations in patients treated with JAKi (2.89%), and in TBS percentage variations in patients in TNFi treatment (2.98%).

Conclusion: In this study we confirmed the high prevalence of OP in RA-patients. Therapy with MTX seems to prevent bone resorption, but it does not improve bone density parameters. Moreover, we observed a positive trend in JAKi-patients BMD and TNFi-patients TBS percentage variations, even though these data are not statistically significative due to the small sample.

Disclosure of Interests: None declared

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AB0327 CARDIOVASCULAR RISK ASSESSMENT IN RHEUMATOID ARTHRITIS WITH CAROTID ULTRASONOGRAPHY AND CARDIOVASCULAR RISK SCORES: A CASE CONTROL STUDY

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Background: The risk of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) is higher than individuals from the general population. This excess risk might be explained by the chronic inflammation.

Objectives: To assess the Cardiovascular Risk (CV) in Rheumatoid Arthritis (RA) patients using the Framingham Score, SCORE (systematic coronary risk evaluation) and carotid ultrasound additionally to the traditional cardiovascular risk factors.

Methods: A single center case control study was performed. Inclusion criteria were adult RA patients (cases) and matched healthy adults in terms of age, sex, and CV risk factors (controls). Population over 75 years old, patients with established CV disease and/or stage III chronic kidney disease were excluded. Controls with other inflammatory diseases, pregnant women or any malignancy were also excluded. This study was performed from July-2019 to January-2020. The US study included presence of plaques, plaque number and measurement the intima-media thickness in both right and left carotid. Scores were multiplicated x1.5 according to EULAR recommendations.

Results: Overall, a total of 200 cases and 111 healthy controls were included in the study. Demographical and clinical variables were comparable between cases and controls and are shown in Table 1. In both groups a relationship between age, BMI and high blood pressure was detected (p<0.001). RA patients had a Disease duration of 18.93 years (11.36); 163 (81.5%) Erosions (X-Ray of hands/feet), Extra-articular symptoms 44 (22%), Prednisone use 103 (51.5%) with Median dose of Prednisone last year 2.34 (2.84). In treatment with Methotrexate 104 (52%), bDMARDs 89 (44.5%) and JAK inhibitor 26 (13%). US study revealed a higher IMT in both right and left carotid arteries with greater presence of plaques in

Table 1. Demographic, clinical characteristics, Ultrasound Results, SCORE and Framingham of patients and controls.

Characteristic	RA cases n=200	Healthy controls n=111
Age - years	62.05 (10.75)	58.3 (12.14)
Female sex – number (%)	163 (81.5)	73 (65.77)
BMI – value (ds)	26.38 (5.03)	26.2 (5.19)
Smoking habit		
Never Smoked	107 (53.5%)	71 (63.96%)
Ex-smoker	51 (25.5%)	20 (18.02%)
Active smoker	42 (21%)	20 (18.2%)
Race – number (%)	186 (93)	62 (93.94)
Caucasian		
Comorbidities – number (%)		
High blood pressure	83 (41.5%)	34 (30.63%)
Dyslipemia	93 (46.5%)	39 (35.14%)
Blood pressure -- mmHg	127.2(18.36)/78.67(10.21)	127.77(19.42)/78.28 (10.59)
Ultrasound findings		
Right carotid cIMT	0.78 (0.15)	0.62 (0.11)
Left carotid cIMT	0.77 (0.14)	0.64 (0.12)
Plaques	101 (50.5%)	32 (28.83%)
Bilateral	64 (32%)	11 (9.91%)
Right carotid	17 (8.5%)	7 (6.31%)
Left carotid	20 (10%)	14 (12.61%)
SCORE		
Very Hihg	13 (6.5%)	5 (4.5%)
High	31 (15.5%)	15 (13.51%)
Low	156 (78%)	91 (81.98%)
Framingham		
High	76 (38%)	33 (29.7%)
Low	124 (62%)	78 (70.3%)

patients than in controls (CI 95% [1.542; 3.436], p<0.001). Plaques were found in both carotid arteries in the 32% of cases and 9.91% of controls. The longer duration of RA was related to a higher presence of carotid plaques (95% [1.015; 1.056], p<0.001). US and blood test results are shown in Table 3. SCORE and Framingham correlated with the CV estimation with US (p<0.001), however, seemed to underestimate the global findings in cases (p<0.001).

Conclusion: Cardiovascular risk calculators such as Framingham and SCORE are useful in RA risk estimation. However, those tools may underestimate the real risk, so carotid US might be valuable.

Disclosure of Interests: None declared

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AB0328 ASSESSING THE MULTIMORBID PROFILE (CIRS) IN REFRACTORY RHEUMATOID ARTHRITIS

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Background: The World Health Organization assigns cardiovascular diseases, cancers, chronic respiratory diseases, as well as diabetes mellitus and some other nosological entities, including mental and musculoskeletal disorders, to main non-communicable diseases. These are considered to be a major public health challenge of the 21st century. In this case, one patient frequently has a set of several age-related chronic diseases that develop simultaneously or sequentially. The management of these patients requires an integrated approach based on the multimorbid nature of pathology. Unlike the definition of comorbidities, which assumes to identify the underlying and related diseases, the concept of multimorbidity of such gradations fails to provide and interprets a patient's chronic diseases as equivalent.

Objectives: To assess the presence and nature of multimorbidity in patients with refractory rheumatoid arthritis (RA) and the impact of multimorbidity on disease activity

Methods: The investigation enrolled 153 patients (mean age, 54.8±14.8 years) with RA according to the 2010 ACR/EULAR criteria, who had been examined and treated at the V.A. Nasonova Research Institute of Rheumatology in 2019–2020. The median disease duration was 5.7 [1.5; 10.5] years; the mean DAS28 score was 5.0±1.3. Documentation and anamnesis data were analyzed with emphasis on associated diseases. The Cumulative Illness Rating Scale (CIRS) was used to assess the profile of multimorbidity.

Results: The patients with RA had a high index of the spectrum of multimorbidity; concomitant diseases were detected in 125 (82%) patients with RA. Their number ranged from 0 to 8 and increased in direct proportion to the age of the patients. The average total score of CIRS was 6.7 ± 3.3 points, the maximum score was 18, the minimum score was 2; The multimorbidity index is 2.5 [1; 6], the maximum number of categories with a score of ≥2 points is 6, the minimum is 1.

The number of concomitant diseases diagnosed in patients with RA before using CIRS was significantly lower (by 52%; p <0.01) than the results of our study showed. Most often, the following disorders were observed in patients at the time of inclusion in the study: comorbid cardiovascular diseases in 44%, anemia in 14.5%, hypercholesterolemia in 18%, obesity in 9.5%, thyroid disease in 11.5% (hypothyroidism criterion – in 3.5%) and diabetes – in 4%. CIRS allowed the first time to identify chronic pathology. The results reflect the cautiousness of doctors regarding comorbid cardiovascular diseases in RA: only 4% of patients were diagnosed with hypertension for the first time. At the same time, before inclusion in the study, no patient with RA revealed chronic kidney disease(CKD), which occurred in almost half of the cases (44.5%). On average, every third person had no previous signs of metabolic syndrome (hyperclycemia in 29%, obesity in 13.5%) and chronic hypoxia (anemia first diagnosed was verified in 24% of cases)

There was a correlation of the quantitative equivalent of multimorbidity with the clinical and laboratory measures of RA activity, including the number of painful joints (r = 0.39; p<0.001), overall patient assessment (r=0.37; p=0.03), physician's global assessment of disease activity (r = 0.37; p < 0.01), DAS28 (r = 0.42; p<0.001), CDAI (r=0.37; p<0.001), SDAI (r=0.34; p< 0.001), HAQ (r=0.34; p<0.001).

Conclusion: Systematic screening for multimorbidity should be performed in each patient with RA. It is advisable to use CIRS in subsequent studies to assess the prevalence of multimorbidity and its consequences. CIRS allows you to more accurately determine the contribution of each chronic disease or syndrome to the development of «multimorbid disease»

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AB0329 IS THERE A LINK BETWEEN INFLAMMATION AND AN ABNORMAL LIPOPROTEIN PROFILE IN RHEUMATOID ARTHRITIS?

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Background: The management of cardio vascular risk in rheumatoid arthritis (RA) is essential and involves the assessment of the blood lipid profile. Studies have shown that patients with active untreated RA, by the presence of a pro-inflammatory state, have a decrease of total cholesterol (TC), HDL cholesterol (HDLc) and LDL cholesterol (LDLc) [1]. The relationship between blood lipids and inflammation is the so-called `lipid paradox' in RA [2].

Objectives: To study the lipoprotein profile of patients with RA and its association with markers of inflammation and disease activity.

Methods: We conducted a cross sectional study among patients with established RA. We analyzed their lipoprotein profile. We further evaluated possible associations between dyslipidemia, disease activity score using the DAS28 and markers of inflammation C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)]. A disturbed lipid profile was defined by a Total Cholesterol level (TC) ≥ 5.17 mmol/L or High density lipoproteins (HDLc) ≤ 1.03 mmol/L or Low Density Lipoproteins (LDLc) ≥ 4.13 mmol/L or Triglycerides (TG) ≥ 1.69 mmol/L.

Results: The mean age of the 136 patients included was 55.19±11.84 years, with a female predominance (n=120). Disease duration was 16.27±11.84 years. Mean lipid concentrations were 4.73±0.95 mmol/L for TC, 1.29±0.36 mmol/L for HDLc, 2.87±0.72 mmol/L for LDLc and 1.19±0.54 mmol/L for TG. The inflammatory syndrome was present in 70% of patients. Mean ESR and CRP values were 32.81±22.19 mm at H1 and 26.17± 6.17 mg/L.

A significant association was objectified between the inflammatory syndrome and low concentrations of TC (4.57 ±0.93 vs 5.09 ±1.06; p=0.010) and LDLc (2.74 ±0.69 vs 3.15 ±0.85; p=0.007). However, no relationship was found between lipid profile and disease activity.

Conclusion: Although there was no relation between lipids plasma levels and disease activity in our population, inflammation was linked to a decrease in CT and LDLc. Contrary to the general population, this decrease is at high cardiovascular risk joining the lipid paradox theory in RA.

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Rheumatoid arthritis - biological DMARDs

AB0330 EXPERIENCE IN THE CURRENT PRACTICE WITH BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INTERSTICIAL LUNG DISEASE OF THE DONOSTIA UNIVERSITY HOSPITAL

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Background: Baricitinib (BARI) is a selective and reversible oral Janus kinase (JAK) inhibitor for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients with inadequate response or intolerance to one or more antirheumatic drugs disease modifiers (DMARDs). Interstitial lung disease (ILD) is a common extra-joint manifestation of RA. Symptomatic ILD occurs in 5-17% of patients with RA and influences the natural course of the disease and substantially affects morbidity and mortality, which is why we wanted to review our patients with RA and ILD who are under treatment with BARI.
Objectives: To assess the safety and persistence of BARI, as well as the evolution of lung function in patients with RA and ILD who are undergoing treatment with BARI, in the Rheumatology Service of the Donostia University Hospital.
Methods: A retrospective search was carried out of all patients undergoing BARI treatment until June 2020. The electronic medical records were reviewed. The variables collected were: sex, age, date of diagnosis of RA, history of smoking, presence of erosions, positivity for rheumatoid factor (RF), citrullinated cyclic antipeptide (anti-CCP) and previous treatments. Regarding BARI, the dose, the time since the start of treatment, related adverse effects, reason for suspension and other relevant data were collected. The quantitative variables are shown with the median and interquartile range, the qualitative variables are shown with the absolute value and its percentage.
Results: 17 patients with RA and ILD treated with BARI were found. Table 1 shows the clinical characteristics, Table 2 shows the treatments and Table 3 shows the respiratory function tests (RFT). All patients were positive for RF and anti-CCP, the presence of erosions was observed in 10 (59%), a history of smoking in 8 (47%), the most frequent type of ILD was Usual Interstitial Pneumopathy (UIP) 7 (41%), at the diagnosis of ILD Abatacept was the most used drug 14 (82). Before the start of BARI, the median FVC 90% (80.5-111), DLCO 69% (57-83.5) and the last control after the use of BARI the median FVC 94% (87-107), DLCO 63% (51-87), the median time of exposure to BARI was 34 months. To date, 10 (59%) patients continue with BARI and the most frequent cause of suspension was failure 2º.
Conclusion: A good persistence of BARI was observed (59%), it also proved to be a safe drug and kept lung function stable in these patients, so BARI can be a therapeutic option in these cases, although more studies are needed to better elucidate these findings.

Table 1

Sex	Mean age (years)	RA diagnosis (years)	ILD diagnosis (years)	Erosive RA	Tabacco	ILD type on CT	Mean time with BARI (months)	BARI dosis	Control CT (n=10)
M 13 (76) W 4 (24)	71 (63-68)	10 (7-15)	4 (3-7)	Yes 10 (59) No 5 (29) NR 2 (12)	Yes 3 (18) Ex 5 (29) No 6 (35) NR 3 (18)	NIU 7 (41) pNIU 2 (12) NINE 3 (18) NO 1 (6) PND 4 (24)	34 (29-36)	4 mg 12 (70) 2 mg 5 (30)	Stable 9 (53) Improvement 1 (6)

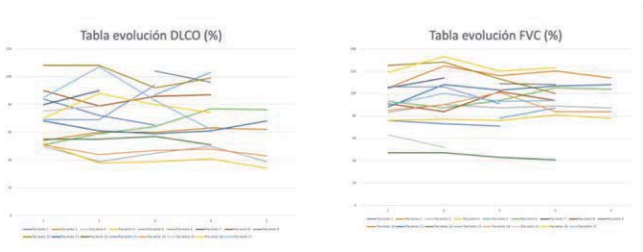

Figure 1.

Disclosure of Interests: None declared
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AB0331 REDUCED C-REACTIVE PROTEIN LEVEL AT HOSPITAL ADMISSION IN PATIENTS TREATED WITH TOCILIZUMAB IN COMPARISON WITH OTHER ADVANCED ANTIINFLAMMATORY TREATMENTS- AN ATTENTION MAY BE REQUIRED

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Background: C-reactive protein (CRP) is a marker of inflammation and infection. The main proinflammatory cytokine that leads to CRP gene expression is IL-6[1]. Different DMARDS may influence CRP levels due to their specific mechanisms of action and alter its usage as an important indicator of acute infection/inflammation
Objectives: The study aimed to compare CRP level between patients who were treated with Tocilizumab (TCZ), an il-6 receptor blocker, and other advanced anti-inflammatory treatments (AAIT), as well as with other admitted and non-admitted populations.
Methods: A cross-sectional study of all patients (≥18 years) hospitalized at tertiary medical center between 12/2009 and 02/2020 and treated before hospitalization with (AAIT). Data on background DMARDS treatment was collected and then categorized to one of the two following groups: tocilizumab treatment and other treatments. In further investigation, the other treatments groups were divided into 3 subgroups: anti-TNF subgroup which included Infliximab (IFX), Adalimumab (ADA), etanercept (ETN), Golimumab, and Certolizumab, JAK-inhibitor subgroup which included Tofacitinib and Baricitinib, and another subgroup which included Rituximab, Abatacept and Anakinra Only the first hospitalization of each patient was included. Women admitted to obstetrics department were excluded. Demographic data, first blood tests results, and comorbidities were collected.
Results: The study included 563 patients treated with AAIT (2.5% received TCZ). Patients treated with TCZ were older (median 75 vs. 50 years, p<0.001), had higher Charlson score (median 5 vs. 1, p<0.001) and more infectious diseases at admission (50% vs. 23.4%, p=0.05). Patients treated with TCZ had lower CRP levels (median 0.5 vs. 25mg/l, p<0.001) and more common normal values (64.3% vs. 20.8%, p<0.001) compared to patients treated with other AAIT. CRP level in patients treated TCZ (median 0.5mg/l) was lower than that of 58,548 patients admitted to the hospital between 2010-2020 (median 12.55mg/l, p<0.001) and not statistically different from 140 non-admitted randomly selected individuals without acute disease (1.33 mg/l, p=0.294).
Conclusion: When compared to other anti-inflammatory drugs, tocilizumab is associated with lower CRP levels in individuals admitted to an acute care hospital. This finding must be considered by treating physician to avoid misinterpretation of CRP results.
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AB0332 EVALUATION OF THE RABBIT RISK SCORE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS NEWLY TREATED WITH BIOLOGIC DMARDS: DATA FROM THE IORRA COHORT

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Background: Serious infection is one of the most critical adverse events in patients with rheumatoid arthritis (RA) using biologic disease-modifying antirheumatic drugs (bDMARDs). During the first year, infections occur more frequently. Therefore, estimating the risk of developing a serious infection is important for the safe use of bDMARDs. The Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) risk score predicted the incidence rate of serious infection during 1 year in patients with RA taking DMARDs. Moreover, it has been validated using data from various observational cohort studies and nationwide registries with favorable results, with a reported area under the receiver operating characteristic curve (AUROC) of 0.68–0.87[1–5]. However, the RABBIT risk score has not been validated in RA patients starting a first bDMARD.

Objectives: To investigate the discriminatory ability of the RABBIT risk score for predicting the development of serious infection during 1 year after starting first bDMARDs in Japanese patients with RA using data from the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort.
Methods: The IORRA cohort is a large observational cohort at the Institute of Rheumatology, Tokyo Women's Medical University. Japanese patients with RA visiting our institute were registered and clinical parameters were assessed biannually. This study enrolled patients with RA who were registered in the IORRA cohort and treated with a first bDMARD. Patients who were missing data needed to calculate the RABBIT risk score were excluded. The RABBIT risk score was calculated using the patient's age, comorbidities, Japanese-Health Assessment Questionnaire score, history of previous infections, and types of DMARDs used. Serious infections were defined as those requiring hospitalization or treatment with intravenous antibiotics. The occurrence of serious infection during 1 year after starting the first bDMARDs was identified using data from the biannual IORRA cohort and confirmed using medical records. The discriminatory ability of the RABBIT risk score was analyzed by the AUROC.
Results: A total of 1,081 patients with RA and a median age of 55.3 years, in which females were the majority (88.2%), were included. Serious infection occurred in eight patients during 1 year before starting their first bDMARDs. The number of patients starting a TNF inhibitor, IL-6 inhibitor, and abatacept were 830 (76.8%), 170 (15.7%), and 81 (7.5%), respectively. A total of 23 patients (1.7%) had serious infections during 1 year after starting the first bDMARD; the most frequent infection was pneumonia (n=16, 69.6%). The median RABBIT score was 2.3 (IQR 1.6–5.4) in patients with serious infections during the follow-up period, and 1.6 (IQR 1.2–2.5) in patients without serious infections. The discriminatory ability of the RABBIT risk score was slightly poor, with an AUROC of 0.67 (95% CI, 0.52– 0.79).
Conclusion: The RABBIT risk score is highly practical; however, our present study suggested that some adjustments may be required to predict the risk of serious infection in Japanese patients with RA starting a first bDMARD.

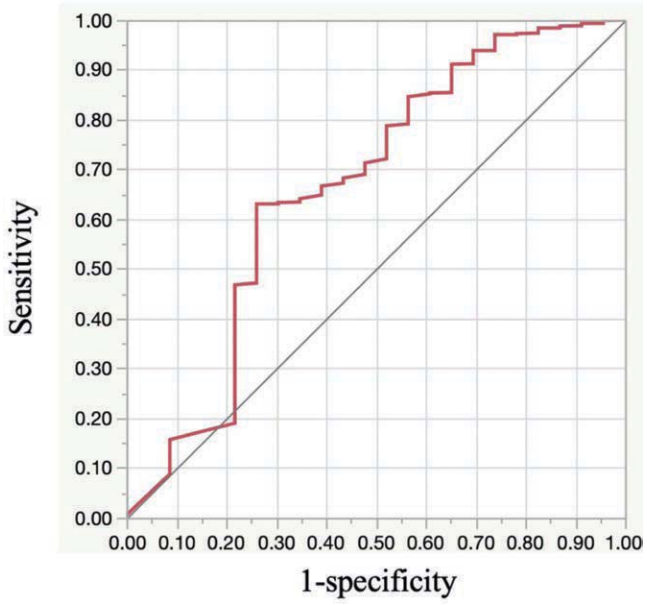

Figure 1. ROC curve of serious infection and RABBIT score with an AUROC of 0.67 (95% CI, 0.52– 0.79).

Disclosure of Interests: Tomoaki Higuchi: None declared, Eiichi Tanaka Speakers bureau: Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Paid instructor for: Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Eisuke Inoue Speakers bureau: Bristol-Meyers and Pfizer, Consultant of: Nippontect systems, Mai Abe: None declared, Kumiko Saka: None declared, Eri Sugano: None declared, Naohiro Sugitani: None declared, Yoko Shimizu: None declared, Moeko Ochiai: None declared, Rei Yamaguchi: None declared, Katsunori Ikari Speakers bureau: Asahi Kasei Pharma Corp., Astellas Pharma Inc., AbbVie Japan GK, Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Janssen Pharmaceutical K.K., Kaken Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corp. Pfizer Japan Inc., Takeda Pharmaceutical Co. Ltd., Teijin Pharma Ltd and UCB Japan Co. Ltd., Yamanaka Hisashi: None declared, Masayoshi Harigai Speakers bureau: AbbVie Japan, Ayumi, Boehringer Ingelheim Japan, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly Japan, GlaxoSmithKline, Kissei, Pfizer Japan Inc, Takeda, Teijin, Consultant of: AbbVie Japan, Boehringer Ingelheim Japan, Bristol-Myers Squibb, Kissei, Teijin, Grant/research support from: AbbVie Japan, Asahi Kasei, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Kissei, Mitsubishi Tanabe, Nippon Kayaku, Sekiui Medical, Shionogi, Taisho, Takeda, Teijin.
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AB0333

SUSTAINABILITY OF RESPONSE TO UPADACITINIB AMONG PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS REFRACTORY TO BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Sustained clinical remission (REM) is the primary treatment goal for patients with rheumatoid arthritis (RA), with low disease activity (LDA) being an appropriate target for treatment-refractory patients.[1,2]
Objectives: To evaluate the sustainability of response to the JAK inhibitor, upadacitinib (UPA) 15 mg once daily (QD), among patients with prior inadequate response or intolerance to biologic DMARDs.
Methods: Data come from the 12-week, phase 3 randomized, placebo (PBO)-controlled SELECT-BEYOND trial of UPA 15 mg or 30 mg QD in patients with moderate to severe RA on stable background conventional synthetic (cs) DMARDs. Initiation, change, or discontinuation of background RA medications, including ≤2 csDMARDs, was allowed starting at Week 24. Patients completing the 12-week trial were able to enter a long-term extension of up to 5 yrs with all PBO patients switching to UPA.[3] This post hoc analysis evaluated REM (CDAI ≤2.8; SDAI ≤3.3), LDA (CDAI≤10; SDAI≤11), and DAS28(CRP) <2.6/≤3.2 at first occurrence of response before Week 60, as well as at 3, 6, and 12 months following initial response in patients randomized to UPA 15 mg. For those patients who achieved REM/LDA, Kaplan-Meier was used to define the time from when the response was first achieved to the earliest date at which the response was lost at two consecutive visits or discontinuation of study drug. The predictive ability of time to REM/LDA was evaluated using Harrell's concordance (c)-index (range: 0 to 1, where 0.5 indicates a model that is no better at predicting an outcome than random chance). The date of the last follow up was 16 April 2018, when all patients had reached the Week 60 visit. Non-responder imputation was used for missing data. Only data from the approved 15 mg dosage are reported here.
Results: In patients with active RA despite prior treatment with at least one bDMARD, 34% and 79% of those receiving UPA 15 mg + background csDMARD(s) achieved CDAI REM or LDA through Week 60, respectively. Sustained CDAI REM was attained by 30%, 26%, and 16% of patients randomized to UPA at 3, 6, and 12 months post initial response, while CDAI LDA was achieved by 68%, 61%, and 50% of patients during the same time points (Figure 1). Time to initial clinical response weakly predicted sustained REM but did not predict sustained LDA, with a c-index (95% CI) of 0.62 (0.49, 0.74) and 0.52 (0.44, 0.61), respectively. Through the last follow-up visit at Week 60, 39/61% of patients on UPA remained in CDAI REM/LDA (Figure 2). Of those who lost CDAI REM, 58% remained in CDAI LDA, and 22% recaptured REM by the cut-off date; 18% of patients who lost CDAI LDA recaptured response. Similar results were observed for REM and LDA based on SDAI and for DAS28(CRP) <2.6/≤3.2.
Conclusion: Among patients with inadequate response or intolerance to bDMARDs, over three-quarters on UPA 15 mg achieved CDAI LDA, a relevant therapeutic target for these treatment-refractory patients, and nearly two-thirds of those maintained this response through 60 weeks. Additionally, about one-third of UPA-treated patients attained CDAI REM and maintained that response over 60 weeks.
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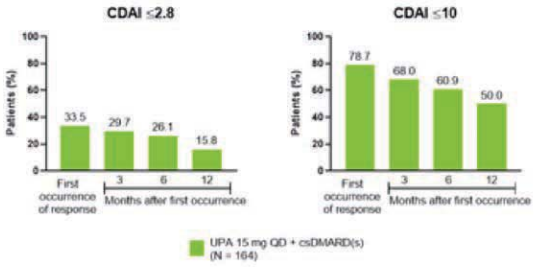
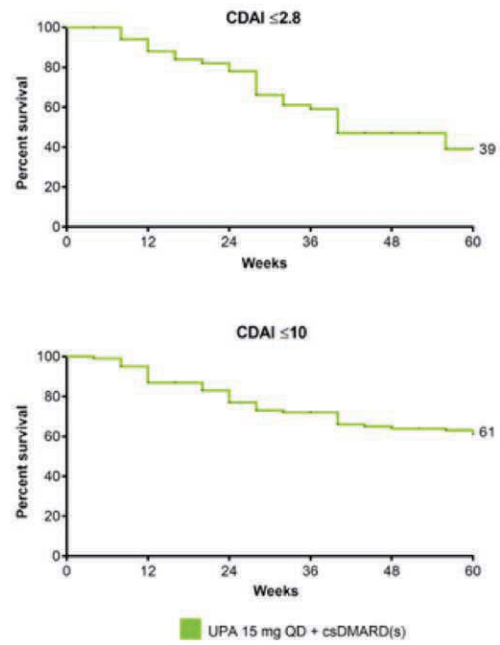
Figure 1. Proportion of Patients Sustaining CDAI Remission or Low Disease Activity at 3, 6, and 12 Months After Initial Occurrence of Response Among the Total Randomized Population



Treatment group is by initial randomization, non-responder imputation was used for missing data.

CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drugs; QD, once daily; UPA, upadacitinib.

Figure 2. Kaplan-Meier Analysis of Time to Loss of CDAI Remission or Low Disease Activity After the First Occurrence of Response



Treatment groups are by initial randomization. Results are for patients who had achieved CDAI remission or low disease activity. UPA 15 mg QD + csDMARD(s): CDAI ≤10: n = 129; CDAI ≤2.8: n = 55.Data were censored at the cut-off (16 April 2018, when all patients had reached the Week 60 visit; censored = stopped collecting data). Non-responder imputation was used for missing data. Week 0 indicates the first occurrence of response. CDAI, Clinical Disease Activity Index; QD, once daily; UPA, upadacitinib.

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AB0334

EFFICACY AND SAFETY OF ABATACEPT IN CHINESE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: REAL-WORLD DATA

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Background: Abatacept (ABA) has demonstrated efficacy and safety in active rheumatoid arthritis (RA) patients in Europe and the United States as one of bDMARDs [1]. However, the clinical activity of Abatacept (ABA) has not been sufficiently investigated in patients with RA from a real-world clinical setting in China.
Objectives: This study was designed to investigate the efficacy and safety of Abatacept in the RA patients in Chinese population who were refractory to csDMARDs, aiming to provide further reference for clinical rational drug use.
Methods: Clinical data of 55 patients with active RA who were admitted in the Affiliated Hospital of North Sichuan Medical College from June 2020 to June 2021 and did not respond to csDMARDs was retrospectively analyzed. Patients in this study were treated with Abatacept (125 mg by subcutaneous injection once weekly combined with csDMARDs. Changes in clinical manifestations, including DAS28-ESR, CDAI, ACR 20/50/70 at week 12 and 24 from baseline and AEs during 24 weeks were observed and recorded.
Results: 55 patients (46 women and 9 men) were included in this study with a mean age 50.80 ± 12.46 and a mean disease duration of 6.29 ± 6.22 years. The ACR 20 response at week 12 and 24 was 50.91% (28/55) and 87.27% (48/55), respectively. Besides, DAS 28-ESR score were significantly lower at week 12 and 24 compared to baseline (P <0.05) with 19 patients (34.55%) achieving clinical remission or low disease activity. Changes in CDAI scores revealed that 80% patients achieved clinical remission or low disease activity at week 24. DAS28-ESR score was significantly lower in previously untreated patients (Biologic-naive) (n=36) (3.40 ± 0.81) than in the previously treated patients (Biologic non-naive) (n=19) (3.83 ± 0.68) (P = 0.02) (Figure 1). RF, CCP antibody and GLOB levels were significantlyreduced in RA patients after 24-week ABA treatment compared to baseline (*P*<0.05) (Table 1). Two hepatitis B virus (HBV) carriers, two patients with active tuberculosis and one patient with latent tuberculosis status showed no reactivation of HBV and no new active tuberculosis lesions 24 weeks after treatment with ABA. AEs were reported in 9.1% (5/55), but no serious infections occurred.

Table 1. Analysis of clinical and serological parameters at baseline and after treatment with Abatacept.

Indexes	Baseline	12 weeks	24 weeks
TJC	6 (4 , 10)	3 (2 , 4)*	2 (1 , 3)**
SJC	2 (1 , 4)	1 (0 , 2)*	0 (0 , 1)**
PtGA-VAS (0-10cm)	8 (7 , 10)	5 (3 , 6)*	2 (2 , 3) **
HAQ	2 (0 , 4)	1 (0 , 2)*	0 (0 , 1)**
ESR (mm/h)	51 (41 , 89)	37 (28 , 51)*	23 (17 , 37)**
HsCRP (mg/L)	14.08 (3.7 , 35.0)	5 , 77 (2.27 , 20.78) *	4.12 (1.34 , 9.37) **
GLOB	34.47±5.69	-	30.33±3.81*
RF-IgM (IU/mL)	408.55 (68.8,566.5)	-	167.41 (34.9, 171.25) *
RF-IgG (U/mL)	8.63 (4.55, 11.1)	-	7.94 (3.13, 6.23) *
RF-IgA (U/mL)	90.18 (25.63, 99.12)	-	58.20 (16.81, 59.09) *
CCP (RU/mL)	1095.45 (66.79, 1033.28)	-	782.0 (58.49, 857.5) *

*p<0.05,TJC=Tender joint count, SJC=Swollen joint count, GLOB= immunoglobulin.

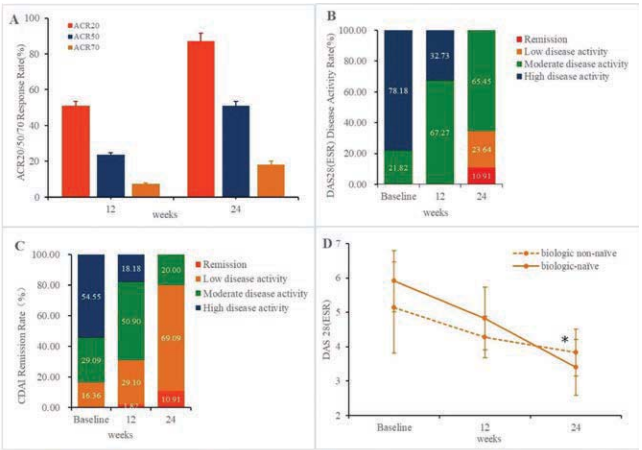

Figure 1 Efficacy of Abatacept at week 12 and week 24. (A) ACR20/50/70 response rate of all patients at week 12 and week 24. (B) DAS28 (ESR) disease activity of patients at baseline, week 12, and week 24; (C) CDAI remission rate of patients at baseline, week 12, week 24; (D) Efficacy of abatacept with biologic-naïve and biologic non-naïve. *P < 0.05 compared with week 24.

Conclusion: In the Chinese patients with active RA refractory to csDMARDs, the combination of ABA and csDMARDs showed great clinical efficacy and a favorable safety profile. Moreover, ABA resulted in better efficacy in patients previously untreated with biologics than previously treated with biologics.

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Disclosure of Interests: None declared
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AB0335 THE FREQUENCY OF SWITCH FROM ANTI-TNF ORIGINATORS TO BIOSIMILARS AND THE CLINICAL OUTCOMES – REAL-WORLD RETROSPECTIVE STUDY IN FOUR ITALIAN CENTRES

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Background: Biologics, such as tumor necrosis factor inhibitors (TNFi), are highly effective in the treatment of inflammatory arthritis, i.e., rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA). The importance of collecting real-world evidence data on switching patients from an originator to a corresponding biosimilar is well recognized in the field (1).

Objectives: The aim of the study was to evaluate the frequency and clinical outcomes of the switch in patients with RA, PsA and axSpA to determine whether a switch could cause a reactivation of the disease.

Methods: We searched electronic patient's records in four Italian centers for consecutive adult patients treated with TNFi for RA, PsS and axSpA. For these patients, we extracted data on age, gender, age and diagnosis and disease duration, the history of a switch from a TNFi originator to a biosimilar, and swollen joints, tender joints, global health, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP). We calculated composite indices of disease activity, DAS28-ESR, DAS28-CRP, CDAI and SDAI, at baseline, and at 3 and 6 months of follow-up. Response was calculated as the difference between DAS28 at baseline and at 3 or 6 months and stratified into good, moderate, no response according to EURAL response criteria. Chi-square test was used to assess if lower response rates were encountered in the switch versus no-switch groups. The Generalized Linear Regression Model was used to study the relationship between DAS28-ESR/CRP responses at 3 and 6 months and DAS28-ESR/CRP, age, sex, smoke or switch at baseline as predictors.

Results: We identified 195 patients; cohort's descriptive statistics are given in Table 1. A total of 140 (74%) patients were switched from adalimumab to a biosimilar. At 3 months after the switch, 25 (19%) and 17 (13%) of patients were defined as good responders, 48 (36%) and 41 (31%) as moderate responders and 61 (46%) and 76 (57%) patients as non-responders, on DAS28-ESR and DAS28-CRP, respectively. At 6 months, 28 (24%) and 22 (19%) of patients had a good response, 29 (25%) and 32 (28%) – a moderate response and 59 (51%) and 62 (53%) patients did not respond, on DAS28-ESR and DAS28-CRP (Figure 1), respectively. The results of the Chi-squared test indicated no difference in the frequency of good/moderate/no response at 3 and 6 months on DAS28-ESR/CRP between patients switched and not. There was a significant association between age and DAS28-ESR/CRP response at 6 months ($p<0.001$ and $p=0.025$) respectively.

Table 1. Patients characteristics

Variables	N = 195[1]
Age	
Mean (SD)	55.05 (13.95)
Median (IQR)	57.00 (48.00, 64.00)
Minimum	18.00
Maximum	86.00
(Missing)	6
Sex	
F	120 (62%)
M	74 (38%)
(Missing)	1
Smoke	
no + ex-smokers	150 (79%)
yes	39 (21%)
(Missing)	6
ANTI-CCP	
neg	130 (75%)
pos	40 (23%)
(Missing)	25

[1]Mean (SD), Median (IQR), Min, Max or Frequency (%)

Conclusion: About three quarters of the patients included in this study underwent a switch from an originator to a biosimilar TNFi. The response rates were similar in those who did and who did not undergo a switch. The switch did not determine a reactivation of the disease.

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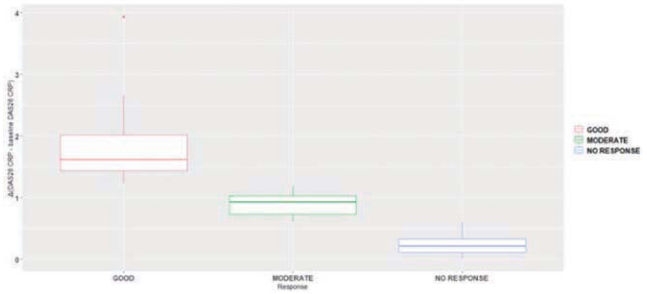
Figure 1. Boxplot of DAS28-CRP responses at 6 months.



Disclosure of Interests: None declared
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AB0336 MANAGEMENT OF INFLAMMATORY ARTHROPATHIES IN SUSTAINED REMISSION: UNIFICATION OF TAPERING CONCEPT IS ON TIME (THE RESULTS OF E-SURVEY OF UKRAINIAN RHEUMATOLOGISTS)

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Background: Changes in the management paradigm (early diagnosis, new therapeutic options, implementation treat-to-target (T2T) concept) in patients with inflammatory arthropathies (IA) have led to the fact that disease activity in most cases is suppressing effectively. On the one hand, this improves of long-term outcomes of IA; on the other - it increases risks of overtreatment, adverse events, and financial costs.

Objectives: The study aimed to estimate trends and approaches among Ukrainian rheumatologists to the tapering disease-modifying antirheumatic drugs (DMARDs) in patients with IA in sustained T2T remission.

Methods: The anonymous and validated e-survey, based on the initial research hypothesis, was conducted by the Ukrainian Association of Rheumatologists. Its structure consists of 10 questions agreed by the members of the Task Force and approved by the ethics committee. E-survey was designed with digital toll SurveyMonkey and disseminated via email among rheumatologists of Ukraine from the national database. All data received is stored and processed per privacy protection laws. Descriptive statistics were used for the analysis.

Results: During one month period, 107 responses had received. 82.2% of Ukrainian rheumatologists used validated diseases activity measures in their daily clinical practice regularly. To assess the trends for DMARDs tapering for further analysis, 71 (66.4%) responses are taken from specialists who often/very often prescribe bDMARDs to patients with IA. Only 12 (17.1%) rheumatologists rarely taper DMARDs; 39 (55.7%) - periodically and 20 (28.2%) - very often deescalate DMARDs therapy in their practice. For 35 (49.3%) of responders, the decision doesn't depend on the type of IA. In the case of combined therapy, 43 (60.6%) start tapering of synthetic DMARD, 19 (26.8%) – of bDMARDs, and 9 (12.7%) with simultaneously tapering of bDMARDs and cDMARDS, respectively. The main criteria for Ukrainian rheumatologists to start dose reduction of DMARDs were state of sustained remission - 30 (42.3%), significant disease activity suppression - 17 (23.9%), financial inability to purchase the drug - 17 (23.9%), adverse events development - 7 (9.9%). The optimal remission duration before tapering for 23 (32.4%) responders was 6-12 months, for 17 (23.9%) – up to 6 months, and for 12 (16.9%) more than 12 months, respectively. Only 19 (26.8%) believe that disease activity suppression and improvement of patient status are enough to start tapering DMARDs. During tapering DMARDs, it was found that for clinical status monitoring, 30 (42.3%) of rheumatologists examine patients monthly, 31 (43.7%) – every 3-months, 7 (9.9%) - on-demand, and only 3 (4.2%) – every 6-months. 43 (60.6%) of specialists had noted that due to the loss of T2T response - full-dosing regimens have to be restored. Financial inability to purchase the drug for 49 (69%) responders is the strong argument to start a dose reduction due to the lack of bDMARDs reimbursement in Ukraine.

Conclusion: DMARDs dose reduction has become a part of clinical rheumatology practice. The lack of unified recommendations leads to decisions tapering

DMARD based mainly on rheumatologists' knowledge and experience. The standardized approach introduction to DMARD de-escalation would help clinicians support treatment decisions.

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AB0337 BASELINE C-REACTIVE PROTEIN PREDICTS ADHERENCE TO ADALIMUMAB THERAPY AT 3 MONTHS IN AN OBSERVATIONAL COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adherence to biologic treatment in rheumatoid arthritis (RA) is often self-reported and little is known about the predictors of adherence to biologic medications. Many studies have reported the predictors of adherence to be linked to psychological factors. A systematic review [1] identified several predictors of adherence to methotrexate in RA patients with the strongest predictors related to psychological factors including beliefs in medication necessity and absence of low mood. Mild disease activity was also found to be a significant predictor of adherence from this study. It is unknown whether similar factors will predict adherence in an established cohort of patients with RA starting biologic therapy.

Objectives: To investigate levels of self-reported adherence to adalimumab treatment and identify the contribution of demographic, physical and psychological factors to medication adherence in an RA cohort.

Methods: Patients with RA who were commencing on adalimumab were recruited through the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS), a large UK multicentre prospective observational cohort study. Demographics, baseline clinical and psychological measures including illness and medication beliefs were collected. Self-reported adherence, defined as the patient has never stopped, altered, missed, forgot to take, or took a lower dose than prescribed of adalimumab, were recorded at 3 months. Potential baseline predictors of adherence to adalimumab therapy were determined using logistic regression analyses.

Results: 202 patients were included; 76% female, median (IQR): age 59 (52-67) years, pre-treatment DAS28-CRP score 5.6 (5.1-6.1) and disease duration 5 (2-15) years. During the first 3 months following commencement of adalimumab, 176 (87%) patients reported full adherence. Univariable analyses found that high baseline C-reactive protein (CRP) [odds ratio (OR) 1.04 per mg/L, 95% CI 1.01, 1.09] was associated with adherence to adalimumab at 3 months. However, there were no associations identified from the psychological variables and this includes perceived necessity towards medication [OR 0.92, 95% CI 0.79, 1.05], hospital depression score [OR 0.94, 95% CI 0.84, 1.06] and hospital anxiety score [OR 0.97, 95% CI 0.88, 1.08].

Conclusion: These findings suggest that the psychological measures were less able to predict adherence to adalimumab therapy. The high percentage of adherence during the first three months of therapy may limit power to detect small effects in this cohort. Further research to investigate whether psychological variables correlate with drug levels as an alternative surrogate for adherence and to consider including other biological agents with a longer follow-up timeline are needed.

High baseline CRP levels were associated with adherence. This finding suggests active disease with higher levels of inflammation in RA may be a factor for adherence in patients who are commencing biologic therapy.

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AB0338 BELIEFS ABOUT BIOLOGIC DRUGS AMONG RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease requiring a long-term follow-up and the use of chronic therapies. The management of this disease is based on a multidisciplinary care, requiring total patient involvement. Previous personal experiences, the experiences of others and the daily impact of the disease on patients fuel their perceptions of the treatment especially biologic one. There are few studies evaluating patient's beliefs about these drugs [1,2].

Objectives: The aim of our study was to investigate beliefs about biologic Disease-Modifying Anti-Rheumatic Drugs (bDMARDs) among patients with RA and to identify factors related to specific beliefs.

Methods: We conducted a bi-centric cross-sectional study, including patients with RA fulfilling the ACR/EULAR 2010 criteria. All patients were on bDMARDs associated or no to conventional synthetic (sc) DMARDs. Sociodemographic, clinical, biologic, and therapeutic data were collected. Patients were interviewed about their medication beliefs using the Beliefs about Medicines Questionnaire (BMQ).

Results: There were 75 RA patients: 60 female (80%) and 15 males (20%). The sex ratio was about 0.25. The mean age was 56.92 ± 9.06 years [34-80]. Thirty-three percent of patients were illiterate. Twenty patients were employed. Sixty-four patients (85.3%) were married. The mean disease duration was 14.85 ± 8.5 years [2-39]. Thirty-three patients had joint deformities. Twenty-seven patients had extra-articular manifestations and thirty-six patients had comorbidities. The mean disease activity scale (DAS28 CRP) was 3.94 ± 1.32 [1.21-7.15]. Fifteen patients (20%) had high disease activity, 11% had low disease activity, and 19% were in remission. The mean functional impairment scale (HAQ) was 0.64 ± 0.48 [0-2.2]. Twelve patients had moderate to severe disability and only one patient had severe to very severe disability. The mean duration of the current bDMARD was 37.17 ± 39.44 months and the mean rank of the current biotherapy was 1.41 ± 0.9 [1-5].

Regarding the BMQ, the mean score for General Overuse was 14 ± 2.37 [6-20]. The mean score for General Harm was 10.82 ± 4.42 [4-20].

The mean score of patients' specific beliefs regarding the necessity of taking the current bDMARD (Specific Necessity) was 20.62 ± 5.71 [5-25]. The mean Specific Concerns score regarding the current bDMARD was 10.33 ± 3.29 [5-25]. Necessity about taking bDMARD was reported by 77.3% patients in the present and 61.3 % patients consider maintaining the bDMARD in the future.

There were 4% of patients who reported concerns about taking bDMARD. Twenty four percent of patients reported concerns about long term effects, and 16% about becoming too dependent on bDMARD.

Beliefs about the necessity to stop occasionally chronic therapies were reported by 13.3% of patients.

Specific necessity was correlated to the current bDMARD duration (p=0.01), Patient Global Evaluation (p=0.03), VAS pain scale ($p<10^{-3}$), the number of nocturnal awakenings (p=0.01), tender joint count ($p<10^{-3}$), swollen joint count (($p<10^{-3}$), HAQ (p=0.005), DAS28 (CRP) ($p<10^{-3}$). Specific concerns were correlated to the actual bDMARD rank (p=0.01).

Conclusion: Our study showed stronger beliefs in the necessity of taking biologic drugs if indicated. Disease activity parameters and functional impairment influence those beliefs. Further studies are required to evaluate the impact of beliefs on biologic drug adherence.

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AB0339

EFFICACY, PHARMACOKINETICS AND SAFETY BETWEEN CT-P13 AND CHINA-APPROVED INFLIXIMAB: 54 WEEK RESULT FROM A PHASE III RANDOMIZED CONTROLLED TRIAL IN CHINESE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: CT-P13 is an approved biosimilar to EU-approved and US-licensed Infliximab (INX) for the indications of rheumatoid arthritis (RA), adult and paediatric Crohn's disease, adult and paediatric ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis.

Objectives: The purpose of this study was to demonstrate equivalence of efficacy and compare PK and safety profiles of CT-P13 and China-approved INX.

Methods: In this randomized, double blinded, multicenter, parallel-group, phase III study, patients with active RA who had been responding inadequately to methotrexate for at least 3 months, were randomized to receive either CT-P13 or China-approved INX. Patients were treated with doses of 3 mg/kg at Weeks 0, 2, 6, then every 8 weeks up to Week 54. Prior to dosing at Week 30, patients randomized to China-approved INX underwent a second randomization either to continue China-approved INX or to switch to CT-P13 at Week 30. Results of patients who underwent transition to CT-P13 were included in the China-approved INX group. The primary efficacy endpoint was change in DAS28 (CRP) from baseline to Week 14, which was analyzed using an analysis of covariance. Equivalence was determined if the 90% CI for the estimate of treatment difference was entirely contained within the predefined equivalence margin of -0.6 to 0.6.

Results: 270 patients were randomly assigned to 2 treatment groups in a 1:1 ratio (136 and 134 patients in the CT-P13 and China-approved INX groups, respectively) and 184 patients completed the study. The least square mean change (standard error) of DAS28 (CRP) from baseline to Week 14, -1.566 [0.1419] and -1.547 [0.1491], was similar between the CT-P13 and China-approved INX groups, respectively. The 90% CI for the estimate of treatment difference (-0.29, 0.25) was contained within the predefined equivalence margin, which demonstrated therapeutic equivalence between the groups. The mean actual values for DAS28 (CRP) decreased from baseline to Week 54 and were similar between the groups (Figure 1). Additional efficacy endpoints, including ACR responses (ACR20 at Week 14; 60.6%, 54.8% and at Week 54; 65.1%, 60.6% in the CT-P13 and China-approved INX groups, respectively), EULAR responses, CDAI, and SDAI, were similar between the groups, even after switching at Week 30. During the study, mean serum INX concentrations were similar between the groups. Between Weeks 14 and 22, mean (percent coefficient of variation) AUC_{τ} were 11156333.615 (44.796) ng·h/mL and 11462884.280 (51.057) ng·h/mL, and $C_{max,ss}$ were 66577.2 (31.4) ng/mL and 66356.1 (21.0) ng/mL in the CT-P13 and China-approved INX groups, respectively, which were similar between the groups. Most treatment-emergent AEs were grade 1 or 2 in intensity. One malignancy was reported in the CT-P13 group and no deaths were reported. The proportions of patients with anti-drug antibodies were similar between the groups, even after switching at Week 30. The overall safety profile of CT-P13 was comparable to that of China-approved INX and no new safety issues were observed (Table 1).

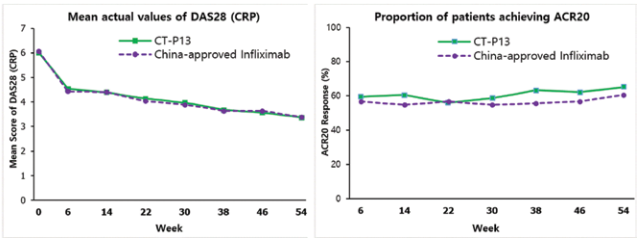
Table 1. Summary of Safety Results

Number of patients (%)		CT-P13 (N=136)	China-approved Infliximab (N=133)
Treatment-emergent AEs	Total	115 (84.6%)	107 (80.5%)
	Related	97 (71.3%)	86 (64.7%)
Treatment-emergent serious AEs	Total	17 (12.5%)	12 (9.0%)
	Related	10 (7.4%)	6 (4.5%)
Infusion related reaction/ hypersensitivity/ anaphylactic reactions	Total (=Related)	20 (14.7%)	19 (14.3%)
Infections	Total	45 (33.1%)	43 (32.3%)
	Related	36 (26.5%)	40 (30.1%)

Note: Summary is presented for the safety population who received at least 1 dose (full or partial) of study drug.

Conclusion: The study demonstrated that efficacy of CT-P13 is equivalent to that of China-approved INX. Also, the PK and safety profiles of CT-P13 were comparable to those of China-approved INX. No loss of efficacy or difference in safety or immunogenicity was observed after switching from China-approved INX to CT-P13 at Week 30.

Figure 1. Key Efficacy Results up to Week 54



Disclosure of Interests: Jonathan Kay Consultant of: Boehringer Ingelheim GmbH; Pfizer Inc.; Samsung Bioepis; Sandoz Inc., Grant/research support from: Pfizer Inc. (paid to UMass Chan Medical School), Xiaofeng Zeng Grant/research support from: Celltrion, Inc, Lin Chen Grant/research support from: Celltrion, Inc, Kaijiang Tang Grant/research support from: Celltrion, Inc, guixiu shi Grant/research support from: Celltrion, Inc, Lin Liu Grant/research support from: Celltrion, Inc, Lijun Wu Grant/research support from: Celltrion, Inc, Yi Liu Grant/research support from: Celltrion, Inc, Jiankang Hu Grant/research support from: Celltrion, Inc, Shengyun Liu Grant/research support from: Celltrion, Inc, Zheng Yi Grant/research support from: Celltrion, Inc, Sung Hyun Kim Employee of: Celltrion, Inc, YunJu Bae Employee of: Celltrion, Inc, JeeHye Suh Employee of: Celltrion, Inc, Seungjin Rhee Employee of: Celltrion, Inc, SeulGi Lee Employee of: Celltrion, Inc, Chankyoung Hwang Employee of: Celltrion, Inc

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AB0340

SHORTENING THE DOSING INTERVAL OR DOSE ESCALATION OF BIOLOGICAL DMARDS SUPPRESSED RESIDUAL ULTRASOUND SYNOVITIS AND JOINT DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS -STARBOARD STUDY-

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Background: In patients with rheumatoid arthritis (RA) who have residual synovitis even after using biological disease modified anti-rheumatic drug (bDMARDs), joint destruction may progress[1]. The enhanced treatment such as shortening the dosing interval or dose escalation of bDMARDs are recommended for these patients, if allowed in package inserts[2, 3].

Objectives: We investigated the effects of enhanced treatment in RA patients with residual synovitis under treatment with standard dose of bDMARDs.

Methods: Forty RA patients treated with standard dose of infliximab, tocilizumab or golimumab were included in this study. Ultrasound (US) examination was performed at the bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) joints, wrist joints (three parts of radial, medial and ulnar) and first to fifth metatarsophalangeal (MTP) joints, by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18-6 MHz). Residual synovitis was defined as Power Doppler score (PD) ≥2. In patients with residual synovitis, we recommended enhanced treatment. The patients were divided into 3 groups, PD≥2/ET+ group (patients agreed enhanced treatment), PD≥2/ET- group (patients rejected enhanced treatment), and PD<2 group. We assessed ultrasound (PD score), laboratory data

(CRP, MMP-3), disease activity (Simplified Disease Activity Index; SDAI), physical function (Health Assessment Questionnaire; HAQ), and joint destruction (modified Total Sharp Score; mTSS) at baseline and 1-year follow-up.

Results: There were 9 patients in PD≥2/ET+ group and 31 patients in PD<2 group. PD≥2/ET+ group had significantly higher SDAI (p=0.027), MMP-3 (p=0.005), and PD (p<0.001) at baseline compared with PD<2 group, but their MMP-3 (p=0.019) and PD (p=0.042) were significantly decreased over 1 year. PD≥2/ET+ group had joint destruction before ET (p=0.022), but it was suppressed after ET and there was no significance in change in mTSS compared with PD<2 group (p>0.99) (Figure 1).

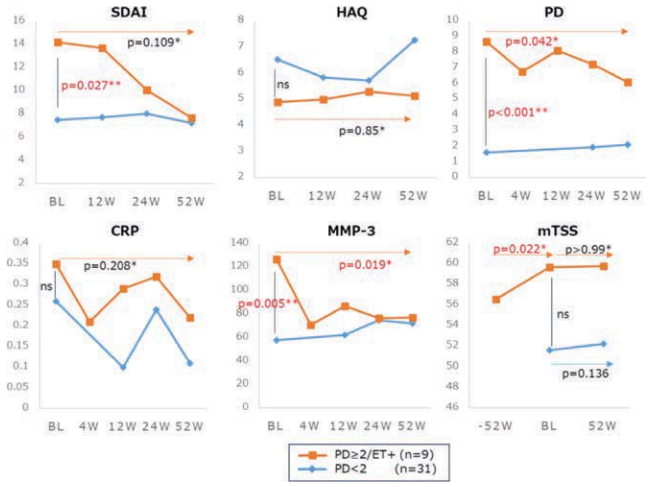

Figure 1. Disease activity, ultrasound assessment and radiographic change from baseline (BL) to 1-year follow-up in RA patients with residual synovitis who had enhanced treatment (PD≥2/ET+) and those without active synovitis (PD<2). *Each parameter at BL and 1-year was statistically analyzed by Wilcoxin signed rank test only in PD≥2/ET+ group.**Difference in two groups at BL was statistically analyzed by Student t test or Mann-Whitney U test. SDAI: simplified disease activity index, HAQ: health assessment questionnaire, PD: Power Doppler, MMP-3: matrix metalloproteinase 3, mTSS: modified Total Sharp Score.

Conclusion: In RA patients with the residual synovitis under treatment with standard dose of bDMARDs, enhanced treatment decreased the synovitis and suppressed the joint destruction.

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AB0341

EFFICACY AND DRUG SURVIVAL AFTER MULTIPLE-SWITCHING FROM ADALIMUMAB ORIGINATOR TO THE BIOSIMILARS ABP501 AND SB5: A REAL-LIFE STUDY

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Background: AntiTNF-α biosimilars are broadly available for the treatment of inflammatory arthritis. There are a lot of data concerning the maintenance of clinical efficacy after switching from originators to biosimilars. However, there is lack of data on the switch between biosimilars. The current evidence on the safety, efficacy, and immunogenicity of switching multiple times from a biosimilar to another biosimilar comes from a limited number of randomized-controlled trials and real world evidence studies.

Objectives: The aim of our work was to evaluate the disease activity trend after multiple switching from ADA originator-Humira (oADA) to its biosimilars (bsADA; ABP 501 and SB5 subsequently) in a cohort of inflammatory arthritis patients.

Methods: In this real-life study, we selected patients with clinical diagnosis of rheumatoid Arthritis (RA), psoriatic Arthritis (PsA) and ankylosing spondylitis (AS). Patients had been previously treated with oADA and switched to the bsADA (first ABP 501 and then SB5). At each outpatient visit, we recorded demographic features (age, sex, and time since diagnosis) and the following disease activity measures: DAS28, DAPSA, BASDAI and the HAQ. Rheumatoid factor (RF), anti-citrullinated protein antibody (ACPA), C-reactive protein (CRP) and HLAB27 were also measured over the observational period (visits 0, 12, 24 and 36 months). The disease activity was evaluated during the year before the introduction of the bsADA, and then evaluated in the following 36 months during the first and the second bsADA treatment. We also examined whether some baseline characteristics, such as the duration of ADA treatment, concomitant therapy, comorbid disease and baseline disease activity, could influence the bsADA discontinuation.

Results: We evaluated the 3-year drug survival and efficacy of the multiple switch of bsADA in RA, PsA and AS patients, previously treated with oADA in 127 patients (Table 1). All the patients enrolled underwent a first switch lasting one year and then a second switch with a follow up of one year too. The 1-year retention rate for ABP501 was 84.4%, 78% and 76% in AS, RA and PsA patients, respectively. The 1-year retention rate for SB5 was 82.1%, 78,7% and 77,5% in AS, RA and PsA patients, respectively. Disease activity, as measured by DAS28, DAPSA and BASDAI remained stable over the 3 years (Figure 1). Comorbid disease (HR: 3.04, $p < 0.001$) and HAQ at baseline (HR: 2.12, $p = 0.001$) significantly increased the risk of ADA discontinuation, while previous ADA duration was positively associated with bsADA retention rate (HR: 0.83, $p = 0.0024$). 27.4% patients left the study due to the interruption of the bsADA, 76.5% discontinued due to inefficacy and 23.5% due to adverse events.

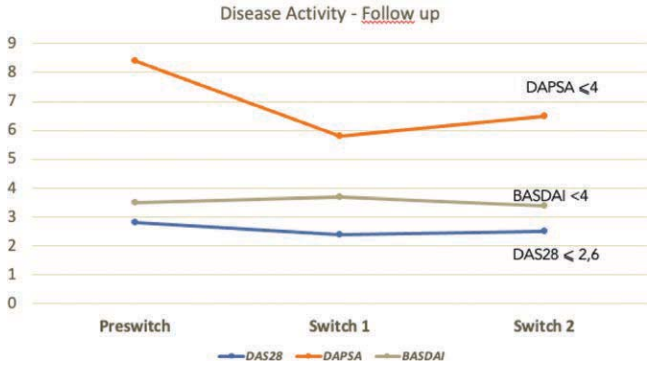
Table 1. Baseline characteristics of RA, PsA and AS patients

Characteristics	Total cohort N=127	RA N=41	PsA N=52	AS N=34
Female gender (%)	75 (60)	35 (85)	31 (59)	9 (26)
Age (years)	61.7±12.78	60.5±12.64	61.55±11.6	56.3±10.71
Disease duration (years)	15.86±9.49	17.23±10.64	13.75±6.57	14.92±9.50
Comorbidities, (%)	17,8 (14)	5,7 (14)	9,8 (19)	2 (6)
ACPA+, n (%)	-	25 (63.3)	-	-
RF+, n (%)		24 (62.5)		
HLAB27+, n (%)	-	-	8 (15)	17 (50)
CRP (mg/L)	1.65±2.27	2.31±1.90	0.42±0.27	1.36±1.91
DAS 28	-	2.65±0.75		
DAPSA	-		8.25±3.69	
BASDAI	-			3.23±1.58
HAQ	0.73±0.57	0.72±0.55	0.73±0.52	0.76±0.69
Prednisone, n (%)	46 (36)	23 (55)	20 (44)	3 (13)
Combo Therapy	65 (51)	29 (68)	25 (48)	11 (32)
oADA duration (months)	49.74±40.75	56.43±41.27	25.00±13.67	40.08±37.78
ABP501 duration (months)	12.42±2.41	12.77±2.34	12.82±1.49	12.49±2.95
SB501 duration (months)	11.92±1.41	12.47±1.74	12.72±1.49	12.41±1.95

ABP501 (Adalimumab biosimilar, Amgevita), SB501 (Adalimumab biosimilar, Imraldi)

Conclusion: No difference was found between oADA and bsADA in terms of efficacy. This real-life study confirms the similar efficacy profile of multiple switch bsADA with long-term retention and a good safety profile in inflammatory arthritis patients.

FIG.1



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AB0342 EVALUATION OF SELF-CARE SAFETY SKILLS AND THERAPEUTIC KNOWLEDGE OF RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGIC DRUGS

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Background: The management of rheumatoid arthritis (RA) was revolutionized by the use of biologic therapies (bDMARD). Nevertheless, bDMARDs may carry some specific risks such as infection. However, data about self-care safety skills are poor [1]. An assessment of the level of information and education is therefore essential for patients followed for RA.
Objectives: The purpose of our study was to assess knowledge and safety skills of RA patients under bDMARDs.
Methods: We conducted a descriptive, bi-centric, and cross-sectional study, including RA patients receiving intravenous (IV) or subcutaneous (SC) bDMARD for at least 3 months. Sociodemographic, clinical, and paraclinical data were collected. Knowledges and self-care safety skills were assessed by a pre-specified questionnaire.
The questionnaire was divided into three domains:
- Five questions about general theoretical knowledge domain: assessing patient's knowledge of the name of the current bDMARD, duration and rate of intake, and a question on annual cost estimation.
- Three questions about the current bDMARD management: assessing cold chain compliance and management of the biologic in SC emphasizing adherence to the steps to be taken prior to giving the injection.
- Tow questions about knowledge regarding safety skills in special situations: infection, cough, contraception, surgery, vaccination, and regarding the need to inform others about the use of bDMARD.
Based on the data analysis, patients were divided into 3 groups according to their knowledge level:
- Group A (low knowledge level: percentage of correct answers <40%)
- Group B (moderate knowledge level: percentage of correct answers >40% and <60%)
- Group C (high level of knowledge: percentage of correct answers > 60%).
Results: Seventy-five patients with RA were collected. Their mean age was 56.92 ± 9.06 years [34-80]. The mean duration of bDMARD was 37.17 ± 39.44 months [4-248] with a mean rank of 1.41 ± 0.9 [1-5]. The SC route was used in 41 patients (54.7%) followed by the IV route in 34 patients (45.3%)
The most prescribed molecules were Infliximab, Certolizumab and Tocilizumab (22.7% respectively). The average order of the current biologics was 1.41 ± 0.9 [1-5] in combination with a csDMARD in 48 patients (64%).
Safety skills were low in 24 patients (32%), moderate in 36 patients (48%), and high in 15 patients (20%).
The mean percentage of correct answers for each domain was respectively: 56.53 ± 18.4% [20-100] for general theoretical knowledge domain, 68.44 ± 26.21% [0-100] for the management of current biologic treatment domain, and 40.8 ± 16.87% [6.67-80] for knowledge regarding safety skills in special situations.
Safety skills levels were significantly related to occupational status (p=0.001), DAS28 CRP (p=0.04), joint deformities (p=0.01) and radiographic erosions (p=0.006), number of previous bDMARDs (p=0.009), and the rank of the current bDMARD (p=0.009).
Conclusion: The major finding of our study was the insufficient level of knowledge and safety skills of RA patients under bDMARDs. We highlight the importance of involving patients in the decision-making process and emphasize the role of the therapeutic patient education programs.
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Disclosure of Interests: None declared
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AB0343 LONG-TERM TOCILIZUMAB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS IN DAILY CLINICAL PRACTICE

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Background: Tocilizumab (TCZ) is a humanized anti-IL-6 receptor monoclonal antibody that improves the signs and symptoms of rheumatoid arthritis (RA). In previous clinical trials, long-term outcomes have been increasingly evaluated in daily clinical practice. We report the five-year outcomes of TCZ treatment at our institute.
Objectives: This retrospective study determined the long-term trends in TCZ use in clinical practice.
Methods: Data from the Toyohashi RA database (TRAD) were used. The TRAD is single-center retrospective data. Last observation carried forward was used as a complementary method for missing data. Participants were 59 RA patients in whom TCZ therapy was started at our institute from September 2009 to May 2016. Subsequent items, baseline patient characteristics, disease activity, treatment continuation rates of TCZ using the Kaplan-Meier method, reasons for stopping TCZ, concomitant use of methotrexate (MTX) and prednisolone (PSL) were investigated.
Results: Baseline characteristics at the start of TCZ treatment were 17 men and 42 women with a mean age of 58.6 years (30–81). The mean RA duration was 8.7 years (0–31). The mean SDAI score was 27.9 ± 11.6; the mean DAS28-CRP was 5.0 ± 1.0. CRP was 4.1 ± 3.0 mg/dl and MMP-3 388.3 ± 311.5 ng/ml. Methotrexate (MTX) was administered in 37 patients (62.7%, mean 6.0 mg, mean MTX dose administered in cases, 9.6 mg/week). Prednisolone (PSL) was administered in 37 patients (62.7%, mean 3.6 mg; the mean PSL dose administered in cases 5.7 mg/day).
Regarding disease activity, the mean SDAI was 27.9 at baseline; 12.3 at three months; 8.1 at one year; 7.3 at two years; 6.5 at three years; 46.7 at four years; 5.6 at five years, and 5.2 at final observation. The SDAI significantly improved after two years compared to baseline. Remission and low disease activity also significantly improved at one year and gradually improved after one year (Figure 1). The remission rate at the final observation was 55.2%, with an SDAI ≦3.3. TCZ continuation rates were 86.9% at one year, 78.7% at three years, and 68.9% at five years (Figure 2). TCZ was discontinued due to adverse events in 11 cases (18%), and inadequate efficacy occurred in 9 (14.8%). The adverse events were respiratory infection (5), purulent arthritis (1), infectious endocarditis (1), subarachnoid hemorrhage (1), breast cancer (1), pruritis (1), and skin ulcer (1). Other reasons for discontinuation were dialysis (2), suspension of hospital visits (2), kidney transplant (1), and financial difficulties (1). Concomitant use from baseline to final observation declined from 62.7% to 15.3% for MTX and from 62.7% to 23.7% for PSL.
Conclusion: Long-term treatment with TCZ was acceptable. We found that with TCZ therapy, the remission and low disease activity rates significantly improved at one year and continued to improve after one year. Treatment persistence was high, but careful monitoring for infection is necessary.

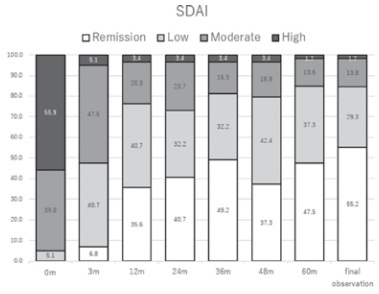

Figure 1 Time-course of Disease Activity Category in RA patients who passed 5 years afterTCZ initiation (Last Observation Carried Forward, including cases who stopped TCZ therapy before 5 years after initiation)

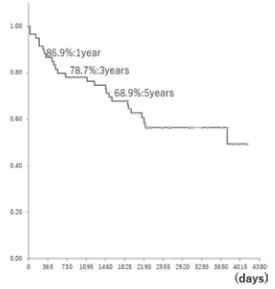

Figure 2 Continuation rate of TCZ therapy

Disclosure of Interests: None declared
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AB0344 EFFICACY OF SUBCUTANEOUS INFLIXIMAB (CT-P13 SC) COMPARED WITH INTRAVENOUS INFLIXIMAB IN RHEUMATOID ARTHRITIS: A POST-HOC ANALYSIS OF A PHASE 3 RANDOMIZED CONTROLLED TRIAL

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Background: Subcutaneous (SC) CT-P13 is the first and only subcutaneous formulation of infliximab (IFX) approved by the EMA.[1] In the pivotal study (NCT03147248), non-inferiority of SC IFX to intravenous (IV) was demonstrated in rheumatoid arthritis (RA) patients using 28-joint Disease Activity Score (DAS28) C-reactive protein (CRP) improvement at Week 22, with a statistically significant treatment difference of 0.27 (95% CI 0.02, 0.52) favoring the SC versus the IV arm.[2,3] At Week 30, numerical differences in efficacy outcomes were shown between SC and IV IFX favoring SC IFX. IV group patients switched to SC IFX by Week 30, and the difference between the groups was reduced at Week 54.[2]
Objectives: To investigate whether there was a statistically significant difference between SC and IV IFX at Weeks 30 and 54 in the phase 3 pivotal study of CT-P13 SC using conservative missing imputation methods.
Methods: Patients with active RA who had an inadequate response to MTX received IV IFX 3mg/kg at Weeks 0 and 2 for induction and were randomized at a 1:1 ratio to receive SC IFX 120mg every 2 weeks or IV 3mg/kg every 8 weeks thereafter for maintenance. Patients who were randomized to receive IV IFX switched to SC at Week 30. In this post-hoc analysis, non-responder imputation (NRI) and last observation carried forward (LOCF) methods were used to investigate whether the difference in efficacy outcomes between SC and IV IFX at Weeks 30 and 54 was statistically significant. Assessments included EULAR (CRP/ESR)/ACR response; remission rate and low disease activity (LDA) rate based on DAS28 (CRP/ESR), Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI); Boolean remission rate; and the proportion of patients achieving a minimal clinically important difference (MCID) in Health Assessment Questionnaire (HAQ).
Results: Of the 343 randomized patients, 165 patients who received SC IFX and 174 patients who received IV IFX from the efficacy population were included in the analysis. There was a statistically significant difference in SC IFX compared to IV treated patients at Week 30 using both NRI and LOCF methods in almost all the clinical variables. However, the difference in efficacy outcomes between SC IFX and IV was reduced at Week 54 after the IV group switched to SC. This supports the improved efficacy of SC IFX at Week 30. Some of the key results (EULAR [CRP] responses, LDA rates based on DAS28 [CRP], CDAI, and SDAI) were presented in Figure 1. Analysis using LOCF and NRI methods yielded consistent results across most of the efficacy outcomes.

Figure 1. Comparison of clinical outcomes between SC IFX and IV IFX in patients with active rheumatoid arthritis. *P<0.05. P-value for difference in proportion between SC and IV treatment group was obtained by asymptotic Wald test. Low disease activity based on DAS28 (CRP) (< 3.2), CDAI (eatment group AI (≤ 11.0).

Conclusion: Statistical analyses using conservative missing imputation methods showed significantly greater improvements in clinical outcomes with SC IFX compared to IV at Week 30 in patients with RA. Between-group differences was reduced at Week 54, suggesting improved responses after switching from IV to SC.
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AB0345

THERAPEUTIC DRUG LEVELS TO ACHIEVE GOOD EULAR RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ADALIMUMAB: RESULTS FROM THE BIOLOGICS IN RHEUMATOID ARTHRITIS GENETICS AND GENOMICS STUDY SYNDICATE (BRAGGSS) COHORT

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease often treated with biologic disease-modifying anti-rheumatic drugs (bDMARDs) such as Adalimumab (ADL), a tumour-necrosis factor inhibitor (TNFi). However, it is known that about a third of patients do not respond to ADL treatment. Previous studies have reported associations between poor response, decreased serum drug levels (SDLs) and poor adherence, but a therapeutic SDL has not been defined nor applied in clinical practice.
Objectives: To assess median ADL SDLs in RA European Alliance of Associations for Rheumatology (EULAR) good vs non/moderate responders, and to determine cut-off SDLs associated with a "Good" response in fully adherent RA patients.
Methods: In a prospective observational cohort study, patients with RA were treated with ADL. At baseline, 3-, 6-, and 12-months patients had 4-component DAS28 scores, self-reported treatment adherence data and SDLs measured. Median drug levels and receiver-operator characteristics (ROC) curves were used to compare SDLs between responders and non-responders, and to establish cut-off SDLs in

self-reported fully adherent patients. Serum drug levels were measured using a sandwich ELISA produced by Progenika Biopharma. Patients were considered fully adherent if they self-reported never having altered, forgotten or omitted any dose of their biologic drug at follow-up. Between group comparisons were assessed using Fisher's exact test, with a threshold for significance set at p<0.05. Statistical analyses were performed in R Version 4.1.0 and RStudio Version 1.4.1106.

Results: A total of 283 RA patients taking ADL were included in the analysis. Baseline characteristics are shown in Table 1. Of these patients 93 (32.9%) self-reported being fully adherent to treatment at 3 months follow-up and had SDLs measured.

Table 1. Baseline characteristics of patient cohort with RA taking ADL (n=283)

Characteristic	n	Missing (%)
Age at baseline, median years (IQR)	58 (51, 64)	0
Disease duration, median years (IQR)	7 (3, 16)	0
Female Sex, n (%)	206 (73)	0
BMI, median (IQR)	27.4 (23.7, 31.9)	0
Smoking Status		132 (46)
Current, n (%)	57 (38)	-
Ex, n (%)	32 (21)	-
Non, n (%)	62 (41)	-
On concurrent DMARD(s)		1 (0.4)
No, n (%)	34 (12)	-
Yes, n (%)	248 (88)	-
Baseline DAS Score, median (IQR)	5.61 (5.18, 6.14)	
On MTX at baseline		38 (13)
No, n (%)	44 (18)	
Yes, n (%)	201 (82)	

In 93 fully adherent RA patients taking ADL at 3 months, good EULAR responders had significantly higher SDLs compared to non/moderate EULAR responders (p=0.0234). In 47/93 (50.5%) fully adherent good responders median SDL at 3 months was 10.94mg/L (IQR 7.75 to 12.0), whereas in 46/93 (49.5%) non/moderate responders, median SDL at 3 months was 9.014 (IQR 6.96 to 11.1).

ROC analysis (see Figure 1) reported a 3-month non-trough ADL SDL cut-off of 7.5mg/L in fully adherent RA patients which discriminated Good EULAR responders compared to non/moderate responders with an AUC of 0.63 (95% CI 0.52 – 0.75), 39.1% specificity, and 80.9% sensitivity.

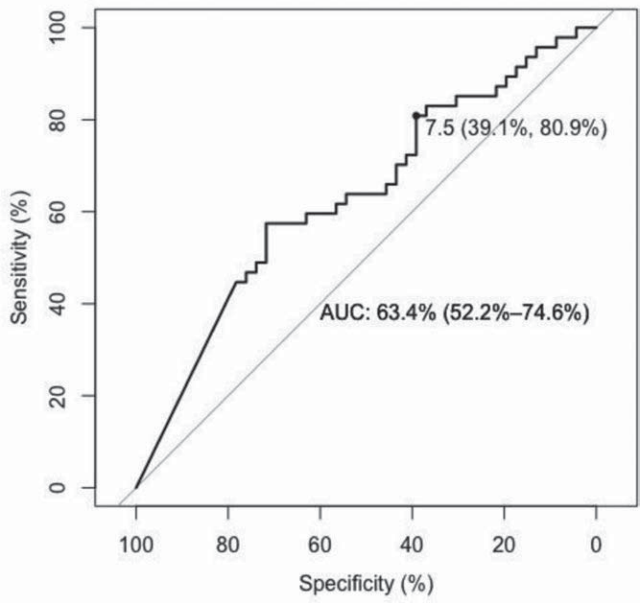

Figure 1. ROC curve analysis: EULAR non/moderate vs good responders with 3 month ADL SDLs.

Conclusion: In keeping with previous work, SDLs were higher in adherent compared with non-adherent patients, but this is the first study to demonstrate that SDLs are higher in fully adherent good EULAR responders compared with non/moderate responders. Based on our methods, cut-offs of 7.5mg/L for ADL may be useful targets in clinical practice to achieve good EULAR response.

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AB0346 REASONS FOR DISCONTINUATION OF TNF INHIBITORS IN PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS ACCORDING TO DRUG HISTORY

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Background: TNF-alpha inhibitors (TNFi) are considered the drugs of choice for initiating biological therapy in rheumatoid arthritis (RA). Rreview of the reasons for their cancellation is included in a comprehensive study of the group of patients (pts) with Difficult to Treat RA (D2T).

Objectives: To make a comparative assessment of the reasons for discontinuation of TNFi in pts meeting the international EULAR (2021) criteria for D2T, comparing them with other pts who had experience in taking a biological disease modifying antirheumatic drugs (bDMARDs)/targeted synthetic DMARDs (tsDMARDs).

Methods: We analyzed the drug history of 505 pts with RA who were hospitalized at the V.A.Nasonova Research Institute of Rheumatology hospital from January to December 2021(inclusive) due to an RA exacerbation, and who were approved for the introduction of bDMARD/tsDMARD. Pts with no prior experience with bDMARD/tsDMARD were excluded from the analysis (n=179/35.4%). Pts meeting the EULAR criteria for D2T RA (the main of which: failure of two or more bDMARDs/tsDMARDs of different mechanisms of action) were allocated to the D2T group (n=35/6.9%), the rest of the pts made up the control group C (n=291/57.6%). The middle age (±SD) of patients in D2T was less than in C (D2T - 46.3±15.1 years vs. C - 51.6±14.8 years, p=0.047), the duration of RA in the groups was comparable (D2T - 15 .7±10.7 years vs. C – 13.1±8.9 years, p>0.05).

Results: The frequency of prescribing a history of TNFi in D2T (85.7%) was higher than in C (38.5%; OR=2.9 [1.3-6.6]; p<0.0001). The total duration of their intake (in cases of prescription) and the average number of TNFi drugs in the groups were comparable (p> 0.05), but in D2T pts more often had the experience of taking 3 or more TNFi (OR = 6.4 [2 -20.4]; p=0.002) (Table 1).

Table 1. Reasons for discontinuation of TNFi in study groups (n/%)

		D2T (n=35)	C (n=291)	p
Pts taking TNFi in anamnesis, n/%		**30** / 85,7	**112** / 38,5	<0,0001; OR=9,6 [3,6-25,4]
Total duration of taking TNFi M±SD, Me [25; 75 percentile], months		22,8±22,5* 15[6;35]	23,2±27,5* 11[4;34]	>0,05
Pts taking 3 or more TNFi, n/%		8 /26,7*	6 /5,4*	0,002; OR=6,4 [2-20,4]
Cancellation for administrative reasons, n/%		2 /6,7*	37 /33*	0,004 $^{CHI\text{-}Square}$;OR=6,9 [1,6-36,6]
Adverse reactions, n/%		9 /30*	23 /20,5*	>0,05
insufficient efficiency	Total	28 /93,3*	49 /43,8*	<0,0001 $^{CHI\text{-}Square}$; OR=18 [4,1-79,3]
	Secondary non-responsiveness to TNFi	**17** /56,7*	**35** /31,3*	0,01; OR=2,9 [1,3-6,6]
	Gradual fading effect	7 /41,2**	22 /62,9**	>0,05
	After the break	9 /52,9**	7 /20**	0,02; OR=4,5 [1,3-15,9]
	After changing to generic	1 /5,9**	7 /20**	>0,05

*the percentage is calculated from the number of pts who took TNFi

**percentage calculated from the number of pts with a history of secondary efficacy of any TNFi

Withdrawal of TNFi due to their ineffectiveness was more often performed in D2T (93.3%/n=28) than in C (43.8%/n=49; OR=18 [4.1-79.3];p<0.0001). At the same time, secondary non-responsiveness (NR) prevailed in D2T - in 56.7% (17 of 28 cases of NR), which is more often than in C (31.3% / 35 of 49 cases of NR; OR = 18 [4.1-79.3]; p<0.0001).

Secondary NR in D2T in 59.9% of pts (9 of 17 cases of secondary NR) developed after the break for administrative reasons in taking a previously effective drug, which is significantly more common than in C (20%/7 of 35 cases of secondary NR; OR = 4.5 [1.3-15.9], p=0.02).

Withdrawal of TNFi for administrative reasons was more common in C (33%/n=37 vs. in D2T -6.7%/n=2; OR=6.9 [1.6–36.6]; p =0.004). The incidence of adverse reactions in both groups was comparable (in D2T 30%/n=9 vs. in C - 20.5%/n=23; p>0.05).

Conclusion: In patients with D2T RA, TNFi were discontinued more often due to their ineffectiveness (93.3%; compared with C: p<0.0001). This inefficiency was more often secondary (56.7%; compared with C: p=0.01). In the structure of secondary inefficiency, the variant of its development after a break in reception for administrative reasons prevailed (52.9%; compared with C: p=0.02). The incidence of adverse reactions in both groups was comparable.

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AB0347 TREATMENT RESPONSE WITH ABATACEPT PLUS METHOTREXATE TREATMENT FOR RHEUMATOID ARTHRITIS: REAL-WORLD EVIDENCE FROM THE UK

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Background: A previous real-world study has reported the characteristics, treatment patterns and clinical outcomes of patients with rheumatoid arthritis (RA) who received abatacept in UK clinical practice.[1,2] However, many of the eligible population received abatacept monotherapy rather than as indicated. A subgroup analysis of patients treated with abatacept in combination with methotrexate (ABA + MTX) was therefore undertaken to explore the treatment effect in this specific patient population.

Objectives: Present a subgroup analysis describing the clinical outcomes of patients with RA treated with ABA + MTX in UK real-world clinical practice.

Methods: A multi-centre, retrospective observational study was undertaken in patients with RA treated with abatacept at any line of therapy between 1 January 2013 and 31 December 2017, across four UK centres. Data were collected from patient medical records from index date, defined as the date of first bDMARD initiation, to most recent RA clinic visit, death or end of study (31 December 2017). Clinical outcomes (disease activity and response to treatment) were measured using the 28-joint Disease Activity Score based on erythrocyte sedimentation rate (DAS28-ESR) and European League Against Rheumatism (EULAR) response criteria. Patients that received abatacept outside indication (i.e., without concomitant methotrexate) were retrospectively excluded from the analysis dataset. Statistical analyses for the ABA + MTX subgroup were repeated in line with the methodology previously reported.[1,2]

Results: This subgroup analysis included 133 patients, of 213 patients included in the original study, with RA that received ABA + MTX (mean age 54.6 years, 77.4% female, 7.5 years mean duration of RA at index date). At index date, 64.8% of patients were positive for both anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF), where data were available. In total, 77.8% of patients were categorised with high disease activity at index, with mean DAS28-ESR of 6.2 (SD 1.1).

Irrespective of line of treatment (LOT), patients tended to have a more favourable distribution of good/moderate/no EULAR response when receiving ABA + MTX (31.8%/34.1%/34.1%; n=44) compared with receipt of other bDMARDs (12.7%/36.4%/50.9%; n=55) at 6 months. Similarly, a favourable distribution of good/moderate/no EULAR response in favour of those receiving ABA + MTX compared with other bDMARDs was observed at 12 months (30.6%/41.7%/27.8% versus 20.0%/35.0%/45.0%, respectively).

Patients receiving ABA + MTX remained on treatment for significantly longer than patients in receipt of other bDMARDs as first LOT (median time on treatment 53.4 vs 18.1 months; p<0.01). A similar trend was observed at second LOT, although differences were not statistically significant (median time on treatment 40.1 vs 19.7 months; p =0.08).

Conclusion: Patients with RA who received treatment with any bDMARDs, including ABA + MTX, experienced reduced disease activity. However, those receiving ABA + MTX persisted with treatment significantly longer than when receiving other bDMARDs.

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AB0348 THE PROPER STUDY: A 48-WEEK ANALYSIS OF A PAN-EU REAL-WORLD STUDY OF SB5 BIOSIMILAR FOLLOWING TRANSITION FROM REFERENCE ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS OR PSORIATIC ARTHRITIS

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Table 1. Patient clinical characteristics, SB5 dose, flare

	RA (N=207)		axSpA (N=127)		PsA (N=162)	
Age at SB5 initiation (years), mean (SD); IQR	60.1 (11.8)	53.0, 68.0	50.3 (13.4)	38.0, 61.0	53.3 (12.0)	45.0, 62.0
Duration of disease (years), mean (SD); IQR	13.3 (11.4)	5.0, 19.5	18.8 (13.5)	9.0, 25.0	12.2 (9.9)	4.0, 19.0
	n	%	n	%	n	%
Women	150	72.5	40	31.5	73	45.1
Patients receiving SB5 40mg Q2W						
Baseline	152	73.4	115	90.6	149	92.0
Week 48	132	72.5	93	87.7	124	91.9
Episodes of Flare						
0	187	90.3	107	84.3	139	85.8
1	20	9.7	18	14.2	20	12.3
2	0	0.0	2	1.6	3	1.9
How was Flare diagnosed						
Disease score	11	55.0	7	31.8	10	38.5
Patient-reported symptoms	19	95.0	22	100.0	26	100.0
Secondary Loss of Response	3	15.0	0	0.0	7	26.9
Action taken for Flare						
Biologic therapy dose adjusted	4	20.0	2	9.1	5	19.2
Non-biologic therapy dose adjusted	8	40.0	3	13.6	9	34.6
Clinical investigation	0	0.0	1	4.5	3	11.5
Other*	9	45.0	13	59.1	16	61.5

*Includes cessation of therapy, prescription of corticosteroids, physical exercise, no action.IQR, interquartile range; SD, standard deviation; Q2W once two-weekly.

Switzerland; [8]Biogen Idec Ltd, Clinical Research, Maidenhead, United Kingdom

Background: SB5, a biosimilar to reference adalimumab (ADL), received EU marketing authorisation in 2017, based on pre-clinical and clinical phase I and III studies that demonstrated bioequivalence and comparable efficacy, safety and immunogenicity to ADL.
Objectives: The real-world study 'PROPER' is designed to provide insights into outcomes of the transition from ADL to SB5 outside the randomised, controlled, clinical trial setting.
Methods: Under an umbrella design, 1000 patients with immune-mediated inflammatory disease were enrolled at centres in Belgium, Germany, Ireland, Italy, Spain and the UK, and followed for 48 weeks post-transition. Eligible patients with a diagnosis of rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA), ulcerative colitis or Crohn's disease had been transitioned to SB5 as part of routine treatment following a minimum of 16 weeks' treatment with ADL. Data were captured from patient charts retrospectively for 24 weeks prior to and prospectively and/or retrospectively up to 48 weeks after SB5 initiation. This analysis of the rheumatology cohort reports clinical characteristics, disease scores, persistence on SB5, clinical management and safety up to the closing date of November 30th, 2021.
Results: Of the 496 patients included in this analysis, the majority were enrolled in UK (n=174), Germany (n=145) and Spain (n=73); Italy, Ireland and Belgium enrolled 45, 44 and 15 patients respectively. At study close, 487 patients had completed 48 weeks of follow-up; 397 of those remained on SB5 throughout.
Methotrexate was received as concomitant therapy by 37% of patients and 20% had received a biologic therapy prior to reference ADL. Most patients (89.3% of RA, 92.1% of axSpA, 97.3% of PsA) transitioned to SB5 at the same dose regimen received for ADL.
Clinical characteristics, SB5 dose and flare are detailed in Table 1, disease scores in Figure 1.

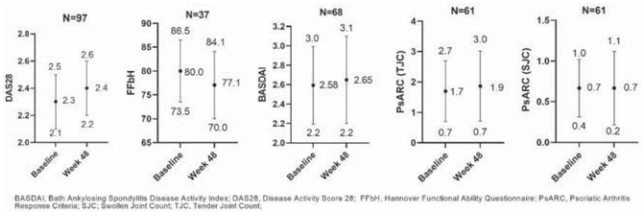

Figure 1. Disease scores (paired patients), mean (95% CI)

Fifteen patients each experienced one unrelated Serious Adverse Event (SAE): 2 in the axSpA cohort [tachycardia, intracranial haemorrhage]; 6 in the PsA cohort [myocardial infarct (2), breast carcinoma, COVID-19, gallbladder calculus, dyspnoea]; 7 in the RA cohort [facial numbness, depression, COVID-19, pneumonia, diverticulitis, parvovirus, coronary occlusion]. Two patients reported SAEs considered causally related to SB5: Herpes zoster and pneumonia (RA cohort), and ALS with worsening (PsA cohort).
Conclusion: This analysis of a large, contemporary cohort of EU patients with established RA, axSpA or PsA shows treatment effectiveness maintained at 48 weeks after switching from ADL to SB5, with most patients continuing on SB5 Q2W throughout. Episodes of flare were uncommon, and the importance of patient-reported symptoms in recognition of flare is evident. No new safety signals were observed.
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AB0349 ANALYSIS EFFICACY OF ABATACEPT TREATMENT IN BIOLOGIC-NAÏVE AND BIOLOGIC-EXPERIENCED PATIENTS.

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Background: Despite the high efficacy of rheumatoid arthritis (RA) therapy, in routine clinical practice, clinicians face questions about the choice of a second biologics, as well as the possibility of biologics monotherapy. Therefore, the specialties of biologics use in these categories of patients are of great clinical interest. This work is devoted to the study of the effectiveness of abatacept (ABA) therapy in biologic-naïve and biologic-experienced patients and in the subgroup of ABA monotherapy.
Objectives: To evaluate the effectiveness of ABA therapy between biologic-naïve and patients who had experienced an inadequate response to biological agents and in the subgroup of ABA monotherapy.
Methods: We prospectively enrolled and followed 91 patients with high RA activity (SDAI=28±13.4, CDAI=25±12) and an inadequate response of conventional synthetic DMARDs (mainly methotrexate, 70.3%) and biologics (mainly TNF-α blockers, 93%) were included in the study. Most of the patients were middle-aged (49±13.5), positive for RF (72.5%) and ACCP (77%) with moderate functional impairment - 1.4 (0.9-2). Patients were divided into two groups: biologic-naïve (48.4%, n=44) and biologic-experienced patients (51.6%, n=47). 18% (n=17) of patients had a history of an inadequate response of 2 or more biologics. The ABA monotherapy group (13%, n=12) was assessed separately. ABA were administered IV, 10 mg/kg according to the standard scheme. The evaluation of the effectiveness of the therapy was carried out according to the EULAR/ACR 2011 criteria using the intention-to-treat approach and SDAI, CDAI and the functional state using the HAQ.
Results: ABA led to a significant ($p<0.05$) decrease in RA activity after 3 months of ABA therapy in all groups. After 6 months of treatment, there was a tendency towards an increase in the number of patients who achieved remission and low RA activity in the group of biologic-naïve patients, which continued to 12 months of therapy. So, after 6 months and 12 months in the group of biologic-naïve patients, the frequency of remission and low disease activity was 71% (n=25) and 76% (n=19) by SDAI, 75.6% (n=28) and 81.5% (n=24) by CDAI, respectively. Whereas, in the group of biologic-experienced patients - SDAI - 61.8% (n=21) and 69.2% (n=18), CDAI - 64.8% (n=22) and 77.8% (n=21), respectively. However, these differences didn't reach significance. Similar results were obtained according to the EULAR criteria: after 12 months of treatment, the percentage of patients with a good response in both groups did not differ, 38% (n=14) in biologic-naïve and 38.4% (n=15) in biologic-experienced patients. ABA significantly improved functional status of patients, after 12 months the median HAQ of biologic-naïve and biologic-experienced patients were 0.7 (0.2–0.8) and 1.18 (0.7–1.6), respectively. More biologic-naïve patients achieved functional remission by HAQ after 6 and 12 months compared with biologic-experienced patients: 67% (n=23) vs. 33% (n=17), 62.5% (n=11) vs. 37.5% (n=9), respectively, but these differences didn't reach significance. In the ABA monotherapy group after 6 months treatment, a good response by EULAR criteria was achieved in 10% (n=1) patients, while in the group of ABA+csDMARDs therapy in 43.5%, p=0.04. After 12 months the trend towards a more pronounced response in the combination therapy group persisted (11%, n=1 and 42%, n=28, respectively), but no significant differences were obtained.
Conclusion: Abatacept has shown significant improvement clinical and functional status in all studied groups. There were no significant differences in response to ABA therapy between biologic-naïve and biologic-experienced patients. ABA monotherapy were significantly worse compared with the combination therapy of ABA and csDMARDs after 6 months. After 12th month observation, this tendency continued, but no significant differences were achieved. This is probably due to the small number of patients on ABA monotherapy and, as a result, to the insufficient statistical representativeness of the sample.
Disclosure of Interests: None declared
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AB0350

ASSESSMENT OF REAL-LIFE PATIENT HANDLING EXPERIENCE OF AVT02 ADMINISTERED SUBCUTANEOUSLY VIA AUTOINJECTOR IN PATIENTS WITH MODERATE-TO-SEVERE ACTIVE RHEUMATOID ARTHRITIS: AN OPEN-LABEL, SINGLE-ARM CLINICAL TRIAL, THEN AN EXTENSION PHASE OF AVT02 ADMINISTERED WITH A PRE-FILLED SYRINGE (ALVOPAD-PEN)

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Background: AVT02 is an investigational biosimilar to adalimumab. It is approved in Europe, Canada, and the UK. It is not approved by the US Food and Drug Administration (FDA).
Objectives: To assess the real-life patient handling of an autoinjector (AI) in adult patients with moderate-to-severe active rheumatoid arthritis (RA) who self-inject AVT02 subcutaneously (s.c.).
Methods: This open-label study enrolled 107 adalimumab-naïve subjects with moderate-to-severe active RA to self-inject AVT02 with the proposed AI 40 mg s.c. in Week 1, and every other week thereafter through Week 8. In an optional extension phase through Week 56, subjects were switched from AVT02 AI to pre-filled syringe and followed for safety and efficacy. The primary endpoint was the percentage of successful self-injections as reported by both the trial site and by subjects using standardized questionnaires at Week 8. Additional endpoints included ease of use and robustness of the AI at Week 8, and efficacy in RA, assessment of serum trough levels of AVT02, and detection of antidrug antibodies (ADA) throughout the study.
Results: The AI success rate was 100% as reported by both the trial site and by subjects. No handling events were noted through Week 8. Approximately 80% (78.1–84.9%) of subjects found the AI 'very easy' to use and, in general, less difficulty was reported as the study progressed. The first 110 AIs used were inspected for robustness and none showed any sign of damage or malfunction.
All subjects who completed Week 8 (n = 106) took part in and completed the optional extension phase through Week 56.
At Week 8, 49.1%, 5.7% and 0.9% subjects achieved ACR20, -50 and -70 responses, respectively. Improvement was also reported for the SDAI, DAS28 CRP and HAQ, with scores consistently decreasing through Week 8. In the extension phase, 70.8%, 47.2% and 13.2% subjects achieved ACR20, -50 and -70 responses at Week 56. Improvement was also reported for the SDAI, DAS28 CRP and HAQ, with scores consistently decreasing through Week 56.
From Baseline through Week 8 the mean serum concentrations of investigational AVT02 increased consistently at each visit, reaching a peak at Week 24. There was no significant difference in serum concentrations of AVT02 based on injection subsite (abdomen or thigh).
ADAs were detected in 65.1% of subjects through Week 8, reducing to 49.1% by Week 56. Of ADA-positive subjects, most were also positive for neutralizing antibodies through Week 8 (62.3%) increasing through Week 56 (90.4%). Subjects who were ADA-positive had lower serum concentrations of study drug compared with the overall population at Week 8 and Week 56 as expected.
There were no clinically relevant safety or tolerability issues. Overall, treatment-emergent adverse events reported in at least 5% of subjects at the PT level were anaemia and influenza (6 subjects [5.6%)] reported 6 events each), and no local ISRs were reported.
Conclusion: The fully successful self-injection with the AI in this study supported the use of the device while administering AVT02. Furthermore, subjects typically found the AI easy to use, with ease of use increasing as time progressed.
The ACR20, -50, and -70, SDAI, DAS28 CRP and HAQ results supported the use of AVT02 to treat adult patients with moderate-to-severe RA, with the treatment effect persisting beyond Week 8 and through Week 56.
The safety and immunogenicity profiles were as expected for adalimumab.
ClinicalTrials.gov Identifier: NCT04224194
Disclosure of Interests: Nemanja Damjanov: None declared, Heimo Stroissnig Employee of: Alvotech, Matjaz Steiger Employee of: Alvotech, Joanna Sobierska Employee of: Alvotech, Eric Guenzi Employee of: Alvotech, Hendrik Otto Employee of: Alvotech, Abid Sattar Employee of: Alvotech, Halimu N. Haliduola Employee of: Alvotech, Elin Edwald Employee of: Alvotech, Fausto Berti Employee of: Alvotech
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AB0351

IMPACT OF FCGR2A, FCGR3A AND FCGR3B POLYMORPHISM ON RITUXIMAB EFFICACY IN RHEUMATOID ARTHRITIS

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Background: Identifying reliable biomarkers of response to biologics in rheumatoid arthritis (RA) is necessary to improve responsiveness, preserve functions and structure of joints, as well as to reduce treatment's cost. Single nucleotide polymorphisms (SNP's) of Fc-gamma receptors genes (FCGRs), by inducing a variation of receptors' affinity to Fc fragment of Gamma immunoglobulin, might influence the efficacy of therapeutic monoclonal antibodies by modifying their clearance.
Objectives: The aim of this study was to investigate whether FCGR2A, FCGR3A and FCGR3B SNP's were predictive factors of response to rituximab (RTX) in Tunisian RA patients.
Methods: A cross-sectional, observational and analytic multicentric cohort study was conducted in a group of patients suffering from RA treated with RTX. Treatment outcome was evaluated after 6 months, using DAS_{28} variation from baseline and EULAR response criteria. R131H-FCGR2A, F158V-FCGR3A and NA1/NA2-FCGR3B SNPs were studied using PCR-SSP and direct sequencing process.
Results: Thirty-four patients were enrolled with a sexe ratio M/F=5/29. The mean age at inclusion was 54,24±11,78 years [29-77]. All patients received at least one cs-DMARDS priorly to the prescription of RTX. Concomitant treatment with methotrexate was pursued in 77,3% of patients. As shown in Table 1, an

Table 1. Correlation of FCGR SNPs with response to rituximab at 6 months of treatment

Genetic study	$\Delta DAS_{28}CRP$	p	ΔDAS_{28ESR}	p	EULAR (R-) (n=7)	EULAR (R+) (n=27)	P
FCGR2A R131H*		0,138		0,761			0,301
Genotypes							
RR	**2,53±1,56**	**0,053**	1,83±0,75	0,480	0(0)	7 (100)	0,131
HH	2,05±2,51	0,868	2,29±1,64	0,683	1 (33,3)	2 (66,7)	0,576
RH	1,09±1,36	0,06	2,00±1,73	0,855	6 (25)	18(75)	0,324
Alleles							
R	1,45±1,52	0,868	1,96±1,49	0,683	6 (0,194)	25(0,806)	0,576
H	**1,17±1,43**	**0,053**	2,1±1,60	0,480	7 (0,259)	20(0,741)	0,131
FCGR3A F158V*		0,428		0,873			0,370
Genotypes							
FF	1,35±1,57	0,860	1,91±1,86	0,705	2 (16,7)	10(83,3)	0,676
VV	0,95±0,98	0,288	2,85±0,32	0,637	1 (10)	9(90)	0,324
FV	2,06±1,83	0,237	1,84±1,51	1	4 (33,3)	8(66,7)	0,175
Alleles							
F	1,72±1,70	0,288	1,87±1,56	0,637	6 (0,25)	18(0,75)	0,324
V	1,56±1,57	0,860	2,13±1,33	0,705	5(0,227)	17(0,773)	0,676
FCGR3B NA1/NA2*		0,217		0,485			0,645
Genotypes							
NA1NA1	2,29±1,81	0,09	2,13±1,08	0,715	2(22,2)	7 (78,8)	0,888
NA2NA2	0,79±1,30	0,329	0,6	0,343	2 (33,3)	4 (66,7)	0,395
NA1NA2	1,23±1,36	0,391	2,28±2,07	0,345	3 (15,8)	16(84,2)	0,436
Alleles							
NA2	1,15±1,33	0,09	1,95±1,95	0,715	5 (0,20)	20(0,80)	0,888
NA1	1,60±1,58	0,329	2,19±1,45	0,343	5 (0,179)	23(0,821)	0,395

DAS**: disease activity score, **ΔDAS**: mean variation of DAS at 6 months, **:Comparison of the global distribution of the 3 genotypes, ******: p while comparing the prevalence of R/R genotype to R/H and H/H genotypes, **R+**: good or moderate EULAR response, **R-**: bad EULAR response*

association, that tend to signification, was found between R/R FCGR2A receptors and a greater variation in DAS28 score (p=0,053). This association was also found using EULAR criteria, since all patients with R/R genotypes had a good or moderate response to RTX but was not significative (p=0,131).

Conclusion: The low affinity receptor R/R FcgRIIa might be predictive of good response in RA patients treated with RTX. More studies need to be conducted in larger cohorts to confirm this association, with the aim of identifying reliable biomarkers of response to biologics to improve responsiveness, preserve joints functions and structure, as well as reduce treatment's cost.

Disclosure of Interests: None declared

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AB0352

IMPACT OF SEROLOGIC STATUS ON CLINICAL RESPONSES TO UPADACITINIB OR ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO BIOLOGIC DMARDS: SUB-GROUP ANALYSIS FROM THE PHASE 3 SELECT-CHOICE STUDY

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Background: In patients with RA who had a prior inadequate response or intolerance to biologic DMARDs, the oral Janus kinase inhibitor, upadacitinib (UPA), demonstrated superiority in change from baseline in DAS28(CRP) and DAS28(CRP)<2.6 at week 12 and improved responses across additional endpoints compared to abatacept (ABA) in the phase 3 SELECT-CHOICE study. Seropositive patients have been reported to respond better to treatment than seronegative patients.

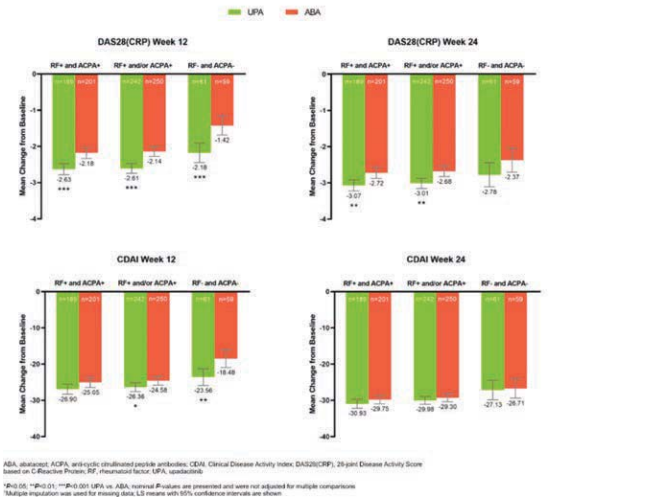
Objectives: To evaluate clinical responses with UPA versus ABA among RA patients based on serologic status.

Methods: In SELECT-CHOICE (24-week, phase 3, double-blind, controlled trial), RA patients were randomized to oral UPA (15 mg once daily) or intravenous (IV) ABA (at day 1 and weeks 2, 4, 8, 12, 16, and 20; <60 kg, 500 mg; 60-100 kg, 750 mg; >100 kg, 1000 mg).[1] UPA patients also received IV placebo and ABA patients also received oral placebo. All patients continued stable background conventional synthetic DMARDs. Starting at week 12, background RA medications were adjusted or added if patients did not experience ≥20% improvement compared to baseline in tender and swollen joint counts at two consecutive visits. For this sub-group analysis, patients were categorized as follows: RF+ and ACPA+, RF+ and/or ACPA+, and RF- and ACPA-. Mean change from baseline in DAS28(CRP), Clinical Disease Activity Index (CDAI), ACR responses, HAQ-DI, patient's assessment of pain, and Functional Assessment of Chronic Illness Therapy - Fatigue scale (FACIT-F) were evaluated at weeks 12 and 24. Statistical inference was conducted using Chi-square tests or analysis of covariance (ANCOVA) with non-responder imputation or multiple imputation used for missing data and nominal *P*-values shown.

Results: Of the total population (N=612), the majority of patients were seropositive for RF and/or ACPA at baseline (80.4%) (Table 1). Most patients were female (~80%), ~55 years old, and one-third had previously experienced ≥2 biologic DMARDs. Mean change from baseline in DAS28(CRP) and CDAI were numerically higher with UPA vs ABA at weeks 12 and 24 across all sub-groups (Figure 1). Regardless of serologic status, UPA demonstrated numerically higher responses vs ABA for ACR 20/50/70 and proportions of patients in low disease activity and remission at both timepoints (Table 1). Mean change from baseline in the HAQ-DI and the patient's assessment of pain was numerically higher with UPA compared to ABA across all sub-groups and timepoints (data not shown). Clinical responses were generally numerically higher at week 24 compared to week 12, and for the seropositive groups compared to the seronegative group, with both UPA and ABA.

Conclusion: Across serologic statuses, clinical responses with UPA 15 mg vs ABA were numerically higher at weeks 12 and 24 among RA patients with prior inadequate response or intolerance to biologic DMARDs. In addition, clinical responses were numerically higher for seropositive patients compared to seronegative patients across all endpoints assessed, although the seronegative group had a smaller sample size in this post-hoc analysis.

Figure: Mean Change from Baseline in DAS28(CRP) and CDAI with UPA 15 mg or ABA Across Serologic Status Sub-Groups at Weeks 12 (A, C) and 24 (B, D)†



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Disclosure of Interests: Andrea Rubbert-Roth Speakers bureau: AbbVie, BMS, Chugai, Roche, Gilead, Janssen, Lilly, Sanofi, Amgen, Novartis, Consultant of: AbbVie, BMS, Chugai, Roche, Gilead, Janssen, Lilly, Sanofi, Amgen, Novartis, Jeffrey Sparks Consultant of: Bristol-Myers Squibb, Gilead, Inova Diagnostics, Optum, and Pfizer., Arnaud Constantin Speakers bureau: AbbVie, BMS, Galapagos, Janssen, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant of: AbbVie, BMS, Galapagos, Janssen, Lilly, Novartis, Pfizer, Sanofi, and UCB, Ricardo Xavier Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Yanna Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Jessica Suboticki Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Roy M. Fleischmann Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer Inc, Sanofi-Aventis, and UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers

Table 1. Clinical Responses with UPA 15 mg or ABA in RA Patients Across Serologic Status Sub-Groups at Weeks 12 and 24

		RF+ and ACPA+ (n=390)		RF+ and/or ACPA+ (n=492)		RF- and ACPA- (n=120)	
		UPA n=189	ABA n=201	UPA n=242	ABA n=250	UPA n=61	ABA n=59
Proportion of Patients (%) (NRI)[†] Week							
ACR20	12	81*	71	79*	71	62	47
	24	84	78	82	77	67	59
ACR50	12	51*	40	51**	40	26*	12
	24	63*	53	63*	54	44	32
ACR70	12	23	16	24*	15	11	7
	24	39*	28	40**	28	25	20
DAS28(CRP) ≤3.2	12	54***	34	54***	33	33**	10
	24	65**	49	65**	50	54	37
DAS28(CRP) <2.6	12	32***	17	33***	15	18*	5
	24	46**	33	48***	33	39	25
CDAI ≤10	12	42	39	43	39	33*	17
	24	59	55	60	56	51	34
CDAI ≤2.8	12	10*	3	10**	3	2	0
	24	23*	14	23**	14	11	12

*P<0.05; **P<0.01; ***P<0.001 UPA vs. ABA; nominal P-values are presented and not adjusted for multiple comparisons [†]NRI was used for missing data

Squibb, Celgene, Eli Lilly, Genentech, Janssen, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis and UCB
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AB0353 BDMARD CHOICES FOR INFLAMMATORY ARTHRITIS WITH CHRONIC KIDNEY DISEASE; HUR-BIO REAL-LIFE REGISTRY

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Background: Rheumatic disesases may involve multiple systems and chronic kidney disease (CKD) can be seen during the course of diseases. Accompanying CKD affects the the choice of treatments in patients with rheumatic disease. There is limited data on the use of biological DMARDs in rheumatic patients with chronic kidney disease.
Objectives: To determine the preferred first and second bDMARDs in patients in the CKD in the bDMARD cohort.
Methods: The Hacettepe University biological database (HUR-BIO), was established in 2005. A total of 2160 RA patients, 3744 SPA patients, were registered in HUR-BIO until November 2021. The CKD was confirmed and classified according to 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. . Patients were evaluated for the presence of CKB before the initiation of bDmard and during follow-up under bDMARDs. Age and sex matched RA patients without CKD were selected for the control group.
Results: 142/5904 (2.4%) patients have CKD. 102(%71.8) patients had CKD prior to initiation of bDMARD and 40 (28.1%) patients had developed during follow-up. The median time to CKD development after starting bDMARD was 4.13 years(±4.05). Of the patients with CKD, 98 (69.0%) had RA and 44 (31.0%) had SpA. RA patients followed for CKD were older than SpA (66.0 (±11.1) vs 59.1 (±13.0) years, p=0.001), female gender was more common (73.5% vs 36.4%, p<0.001), disease duration was similar (19.3 (±13.8) vs 17.1 (±10.5) years, p=0.40). The first bDMARD choices of patients with and without CKD in RA and SpA patients were shown in Table 1. There was no difference between the SPA patients with or without CKD regarding TNF-i preferences. In patients with rheumatoid arthritis there was no difference in terms of TNFi and non-TNF-i preferences, but tocilizumab was more prefered in CKD group.

Table 1. Relationship between remission according to bDMARD and CKD

	Rheumatoid arthritis		p	Spondyloarthritis		p
	w CKD n=98	wo CKD n=91		w CKD n=44(%)	wo CKD n=80(%)	p<0,05
Etanercept, n(%)	34 (34.6)	30 (33.0)	0.46	17 (38.6)	22 (27.5)	P=0.14
Adalimumab, n(%)	17(17.3)	17 (18.7)	0,48	10 (22.7)	22 (27.5)	P=0.36
Infliximab,n(%)	3 (3)	8 (8.8)	0.85	14(31.8)	32 (40.0)	p=0.24
Golimumab, n(%)	4 (4)	3 (3.3)	0,54	1 (2.2)	3 (3.8)	p=0.55
Certolizumab, n(%)	0 (0)	3 (3.3)	0,11	1 (2.2)	1 (1.3)	p=0.58
Anti-TNF therapy, n(%)	58 (59.2)	61 (67.0)	0,61	43	80	0.352
Non-TNF biologics, n(%)	40 (40,8)	30 (33.0)	0,13	1	0	0.355
Rituximab, n(%)	14 (14.3)	12 (13.2)	0,57			
Abatacept, n(%)	14(14.3)	12 (13.2)	0,49			
Tocilizumab, n(%)	**6 (6.1)**	**1**	**0.041**	1(2.2)		p=0.35
Jak-kinase inhibitors, n(%)	6(6.1)	5 (5.5)	0.55			

Conclusion: In our biologic cohort, 2% of patients with RA and SpA had accompanying CKD. In one-third of the patients with CKD, it was developed during the follow-up after bDMARDs. In patients with RA, there was no difference in terms of TNFi and non-TNF-i preferences. It should be kept in mind that CKD may develop during the follow-up of patients using bDMARDs.
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Disclosure of Interests: None declared
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AB0354 THERAPEUTIC DRUG MONITORING: PERFORMANCE OF THE FIRST LATERAL FLOW-BASED POINT OF CARE TEST FOR THE QUANTIFICATION OF INFLIXIMAB IN A FINGER PRICK

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Background: Promonitor Quick IFX is a lateral flow test (LFT) for the quantification of infliximab (IFX) in human whole blood (finger prick or venous) or serum in 20 minutes. This LFT is based on a sandwich immunoassay to quantify either the reference IFX or biosimilars.
Objectives: The objective of this study was to perform the required analytical studies to establish the specifications of the product.
Methods: Clinical and Laboratory Standards Institute (CLSI) guidelines were followed for the evaluation of the analytical specifications of the LFT in whole blood and serum matrices: Linearity (EP-06-A), Detection capability (EP17-A2), Interfering substances (EP07, 3rd Edition) and Intermediate precision (EP05-A3). Results were obtained in combination with the automated portable reader PQreader. A Datamatrix provided with each Promonitor Quick IFX kit contains the calibration information required for the PQreader to measure the Control and Test lines and report the IFX concentration.
Results: The linear assay range was determined to be 1-58 µg/mL in whole-blood and 0.6-67 µg/mL in serum according to the processes indicated in the Package Insert. The Limit of Blank is 0.8 µg/mL, the Limit of Detection and Lower Limit of Quantification (LLoQ) are 1.1 µg/mL, and the Upper Limit of Quantification (ULoQ) is 15.4 µg/mL. There was no effect on assay performance when each of the following substances were added to samples with 0, 3, and 7 µg/mL of IFX: Haemoglobin (>1000 mg/dL), Bilirubin (>40 mg/dL), Triglycerides (>1500 mg/dL), HAMA (160 AU/mL), Rheumatoid factor (200 IU/mL), EDTA (5.4 mg/mL), Heparin (51 U/mL), Citrate (11.4%), Vedolizumab (60 µg/mL) and Adalimumab (20.25 µg/mL). Repeatability and within-device precision results obtained for the positive samples are shown in Table 1.
Conclusion: Promonitor Quick IFX is the first LFT available for true Point of Care testing of patients treated with IFX with just a finger prick sample. It provides quick turnaround time to facilitate therapeutic drug monitoring and aid immediate decision making in the doctor office or hospitals with an excellent analytical performance.
Disclosure of Interests: Amagoia Ametzazurra Employee of: Employee of Progenika Biopharma - Grifols, Javier Pascual Employee of: Employee of Progenika Biopharma - Grifols, Lorena Del Rio Employee of: Employee of Progenika Biopharma - Grifols, Ainara Maguregui Employee of: Employee of Progenika Biopharma - Grifols, Daniel Nagore Employee of: Employee of Progenika Biopharma - Grifols, M. Begoña Ruiz-Argüello Employee of: Employee of Progenika Biopharma - Grifols
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Table 1.

	Whole blood samples					Serum samples				
IFX theoretical concentration (µg/mL)	Mean observed IFX concentration (µg/mL)	Repeatability		Within-device precision		Mean observed IFX concentration (µg/mL)	Repeatability		Within-device precision	
		SD	CV%	SD	CV%		SD	CV%	SD	CV%
3	3.2	0.6	18	0.8	25	3.6	0.5	15	0.6	17
7	7	1.3	18	1.7	24	8.3	1.4	16	1.8	21
10	9.8	1.8	18	2.7	28	10.9	1.8	16	2.3	21

The negative samples showed a negative result in all the measurements.

AB0355

THE DIFFERENCES BETWEEN THE FIRST PREFERRED BIOLOGICAL DMARD AND THE DRUG SURVIVAL IN GERIATRIC AND YOUNGER ADULT POPULATION WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS: TREASURE REAL-LIFE DATA

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Background: Inflammatory musculoskeletal diseases are frequent in the elderly population, and this number is expected to increase significantly near future. The exclusion of older adults from the studies due to their age and comorbidities causes insufficient data about this population. Insufficient data cause clinicians to have difficulties using and selecting biological therapy in the elderly patient group. In real life, physicians' approaches to the selection and use of biological disease modifying anti-rheumatic drugs (DMARDs) in the geriatric population with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) have not been well studied.

Objectives: To compare the clinicians' first choice of biological DMARDs in elderly and younger RA and PsA patients and investigate the drug survival of first biological DMARDs in both populations.

Methods: The traditional chronological age for the human to be classified in the geriatric population is ≥ 65 years (1). The TReasure web-based registry, created in 2017, is a multicenter observational cohort established to collect data on RA and spondyloarthritis (SpA) patients from the participating 17 rheumatology centers in different regions of Turkey. Physicians' first choice biological and targeted synthetic DMARDs in younger and elderly patients with RA and PsA was evaluated using the descriptive statistical method. The survival of the first b/tsDMARDs was assessed using the Kaplan-Meier method.

Results: 3136 RA and 738 PsA patients were evaluated. 12% of 3136 patients with RA were in the geriatric population. In patients with RA, the first choice of biologic DMARDs was adalimumab (20.6%), followed by etanercept (19.9%), and tofacitinib (13.6%) in patients < 65 years of age, while rituximab (24%) was the first choice in patients ≥ 65 years, tofacitinib (20.9%) in the second place and etanercept (13%) in the third. Of 738 PsA patients, 3% were over 65 years. Adalimumab (41.1%) was the first choice of <65 years of age, etanercept (17.6%) was the second choice, and infliximab (15.5%) was the third choice, while adalimumab (28.6%) was the first choice in patients ≥ 65 years followed by etanercept (17.9%) and certolizumab (17.9%). In RA group, drug survival was significantly higher in patients ≥ 65 years (estimated median drug survival; <65 age: 37.5 (34.1-41.1) months vs ≥65 age: 53.5 (24.9-82.2) months; log-rank p=0,016) (Figure 1). In PsA group, drug survival was significantly higher in patients < 65 years (estimated median drug survival; <65 age: 31.2 (26.4-36.1) months vs ≥65 age: 9.1 (0.4-17.7) months; log-rank p<0,001) (Figure 1).

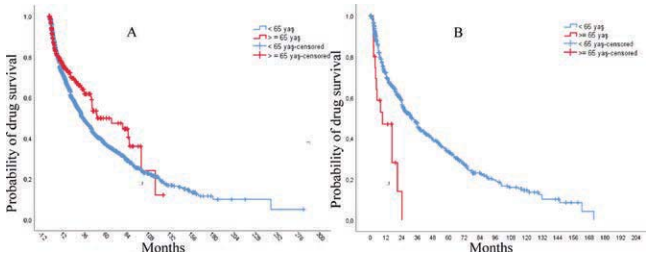

Figure 1. Comparison of first bDMARD retention rates between <65 years and ≥ 65 years. A: In rheumatoid arthritis patients, B: In psoriatic arthritis patients

Conclusion: With these findings, it is thought that in Turkey, the limited socioeconomic support in the geriatric patients has led physicians to prescribe treatments such as rituximab, which are administered in the hospital under the supervision of a physician, are relatively preferred in malignancies, and are considered to be relatively less risky in terms of tuberculosis. Adalimumab and etanercept were chosen in the first two lines in both geriatric and young populations in the patient group with PsA. While the drug survival was significantly higher in patients with RA geriatric age group than the younger group, in PsA in which tumor necrosis factor-alpha (TNF-α) inhibitors were chosen as initial therapy in both age groups was lower in the geriatric population.

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Disclosure of Interests: None declared

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AB0356

THERAPEUTIC DRUG MONITORING: STANDARDIZATION OF PROMONITOR QUICK IFX AND PROMONITOR QUICK ADL POINT OF CARE TESTS WITH WHO INTERNATIONAL STANDARDS FOR THE QUANTIFICATION OF INFLIXIMAB AND ADALIMUMAB IN WHOLE BLOOD AND SERUM

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Background: Promonitor Quick IFX and Promonitor Quick ADL are rapid point of care lateral flow tests (LFT) based on a sandwich immunoassay for the quantification of infliximab (IFX) and adalimumab (ADL), respectively, in human whole blood (finger prick or venous) or serum. These tests are to be used as an aid in Therapeutic Drug Monitoring (TDM) of rheumatic and inflammatory bowel disease patients under anti-TNFα therapy. The international standards (IS) developed by World Health Organization (WHO) for IFX and ADL allow harmonization and comparability among different assays.

Objectives: The aim of this study, was to show that Promonitor Quick IFX and Promonitor Quick ADL can measure either reference or biosimilar drugs, as well as to evaluate the agreement of Promonitor Quick IFX and Promonitor Quick ADL tests and the WHO IS.

Methods: Clinical and Laboratory Standards Institute EP10-A3 guidelines were followed to estimate the bias of Promonitor Quick assays when used to quantify IFX or ADL in samples containing the reference drugs, biosimilars or the WHO IS. Briefly, whole blood was spiked with four known concentrations of IFX or ADL, including current clinical decision levels. Ten replicates were measured of each level along two days. Promonitor Quick IFX was evaluated using the reference drug, SB2 and CT-P13 biosimilars, and the WHO IS (NIBSC 16/170). Promonitor Quick ADL was evaluated using the reference drug, ABP501 and SB5 biosimilars, and the WHO IS (NIBSC 17/236). Results were obtained in combination with the automated portable reader PQreader.

Results: Bias was estimated by comparing the observed concentration of drug spiked whole blood samples. Each biosimilar was compared to the reference at the different drug levels tested. Results showed that Promonitor Quick IFX and Promonitor Quick ADL are able to measure equivalently any molecule (see Table 1).

Table 1.

Promonitor Quick IFX bias results in whole blood samples. Each molecule was compared to the reference drug.

IFX concentration (µg/mL)	Bias (%)			
	CT-P13	SB2	GP1111	WHO IS
3	14%	3%	4%	8%
7	9%	0%	5%	15%
10	1%	5%	6%	8%

Promonitor Quick ADL bias results in whole blood samples.
Each molecule was compared to the reference drug.

ADL concentration (µg/mL)	Bias (%)		
	ABP501	SB5	WHO IS
3	17%	2%	3%
5	13%	3%	12%
8	2%	2%	7%
10	5	17%	2%

Similar results were obtained when serum matrix was used.

The accuracy or closeness of the agreement between the result provided by Promonitor Quick IFX and Promonitor Quick ADL and the true value of the measur- and was assessed by measuring the IS developed by the WHO (see Table 1).

Conclusion: Promonitor Quick IFX and Promonitor Quick ADL allow monitoring of patients treated with IFX and ADL, respectively, with just a finger prick sample. Both tests can quantify reference and biosimilar drugs with equivalent results. Moreover, comparable results were obtained with the WHO IS, and thus, demonstrate that Promonitor Quick tests are suited to accurately determine drug levels at the clinical decision points in both whole blood and serum, proving to be an effective and valuable tool in TDM and immediate decision making in the doctor office or hospitals.

Disclosure of Interests: Amagoia Ametzazurra Employee of: Employee of Progenika Biopharma - Grifols, Javier Pascual Employee of: Employee of Progenika Biopharma - Grifols, Lorena Del Rio Employee of: Employee of Progenika Biopharma - Grifols, Ane Urigoitia Employee of: Employee of Progenika Biopharma - Grifols, Daniel Nagore Employee of: Employee of Progenika Biopharma - Grifols, M. Begoña Ruiz-Argüello Employee of: Employee of Progenika Biopharma - Grifols

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AB0357 INCIDENCE AND DETERMINANTS OF INFECTION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH GOLIMUMAB IN REAL-WORLD PRACTICE

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Background: Although biologic use in rheumatoid arthritis (RA) has a well-characterized infections risk factor, most studies evaluating this association were conducted on first-generation anti-tumor necrosis factor (TNFi) agents or in early years post-drug development (early 2000).

Objectives: To (i) characterize the long-term incidence of infection in a real-world cohort of RA patients treated with subcutaneous golimumab (GLM) in Canadian routine care; (ii) assess the impact of infections on GLM retention, and (iii) explore factors associated with the risk of infection.

Methods: BioTRAC registry was a prospective, multicenter study that collected real-world clinical, laboratory, safety and patient-reported data from TNFi naïve patients or treated with biologics for a period of <6 months before enrolment. This post-hoc analysis included patients with RA who initiated GLM treatment. The incidence density rates (IDR) of total serious (SI) and non-serious (NSI) infections were calculated for the overall follow-up (90 months) period as well as by 6-month interval. Time to first infection and time to treatment discontinuation were assessed with the Kaplan-Meier estimator of the survival function. Determinants of infection over time or within the first 6 months were explored using generalized estimating equation models and logistic regression, respectively.

Results: 530 patients were included with a mean (SD) age of 57.7 (13.0) years and disease duration of 8.0 (8.3) years. Of these, 404 (76.2%) were females, 74 (14.0%) were treated with ≤15mg/week MTX, 280 (52.8%) with >15mg/week MTX, while 173 (32.6%) were not on MTX. In terms of corticosteroids (CS), 72 (13.6%) were treated with ≤5mg/day, 63 (11.9%) with >5mg/day, and 391 (73.8%) were not on CS. Diabetes (4.5%), pulmonary disease (8.9%), and renal disease (18.5%) were present.

Over a mean follow-up duration of 27.0 months, the IDR for total infections, NSI, and SI was 35.10 events/100 PYs, 32.90 events/100 PYs, and 2.23 events/100 PYs. Median estimated time to first infection was 52.9 months (SI: 84.9 months; NSI: 55.1 months) (Table 1). The incidence of total infections was 44.0, 37.3, 35.1, 29.4, 31.1, 35.7, 19.3 and 7.4 events/100 PYs at 0-6 months, 6-12 months, 12-24 months, 24-36 months, 36-48 months, 48-60 months, 60-72 months, 72-84 months, respectively and no infections between 84-90 months. In terms of determinants, no significant associations were identified for the incidence of infections within the first 6 months. However, presence of pulmonary disease was identified as a significant determinant of total infections (OR [95%CI]: 2.19 [1.36-3.52]) and NSI (2.22 [1.35-3.66]) over time, while higher age (1.08 [1.00-1.26]) and high (≥5 mg/day) CS dose (7.25 [1.12-46.80]) were associated with significantly higher odds of SI. Incidence of SI (6.48 [1.16-36.13]), but not NSI, was associated with significantly higher odds of GLM discontinuation; additional predictors of discontinuation were increased baseline CDAI (1.06 [1.04-1.08]) and use of concomitant MTX at low dose (0.52 [0.30-0.91]) or high dose (0.71 [0.49-1.04]).

Table 1. Incidence Density Rate (IDR) by Infection Type.

Infection Type	IDR (Events/100 PYs)	Median Time to 1st Infection (months)
Total Infections	35.1	52.9
Non-serious Infections	32.9	84.9
Serious Infections	2.2	55.1

Conclusion: The infection rates reported with GLM in this cohort are low compared to the rates reported in earlier registry studies with TNFi. Changes in the characteristics of patients starting TNFi (lower disease activity, shorter disease duration, less exposure to CS) in recent years may explain the decreased risk of infection. Compared to the available literature, treatment with GLM was associated with relatively low infection rate. Most infections occurred during the first 6 months of treatment and decreased thereafter. Presence of pulmonary disease, higher age, and higher CS dose were identified as significant predictors of infections. SIs, but not NSIs, were associated with significantly higher odds of treatment discontinuation-TNFi.

Disclosure of Interests: Louis Bessette Speakers bureau: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilead, Sandoz, Fresenius Kabi, Teva, Consultant of: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilead, Sandoz, Fresenius Kabi, Teva, Grant/research support from: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilead, Sandoz, Fresenius Kabi, Teva, Proton Rahman Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, and UCB, Grant/research support from: Janssen and Novartis, John Kelsall: None declared, Jane Purvis: None declared, Emmanouil Rampakakis Consultant of: Janssen, Allen Lehman Shareholder of: Johnson & Johnson, Employee of: Janssen Pharmaceutical Companies of Johnson & Johnson, Meagan Rachich Shareholder of: Johnson & Johnson, Employee of: Janssen Pharmaceutical Companies of Johnson & Johnson, Francois Nantel Shareholder of: Johnson & Johnson, Employee of: Retiree from Janssen Pharmaceutical Companies of Johnson & Johnson, Marilise Marrache Shareholder of: Johnson & Johnson, Employee of: Janssen Pharmaceutical Companies of Johnson & Johnson, Odalis Asin Milan Shareholder of: Johnson & Johnson, Employee of: Employees of Janssen Pharmaceutical Companies of Johnson & Johnson

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AB0358 SAFETY, TOLERABILITY, PHARMACOKINETICS, RECEPTOR OCCUPANCY, AND SUPPRESSION OF T-CELL-DEPENDENT ANTIBODY RESPONSE IN A PHASE 1 STUDY WITH KPL-404, AN ANTI-CD40 MONOCLONAL ANTIBODY

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Background: T-cell priming and T-cell-dependent B-cell responses require an intact cluster of differentiation (CD)40/CD40L pathway. CD40 is expressed on the surface of B-cells, dendritic cells, antigen-presenting cells, and non-immune cell types; its ligand, CD40L (CD154), is expressed on the surface of activated

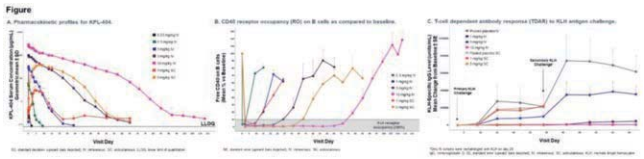
T-cells, platelets, and other cell types. Blockade of CD40/CD40L interaction has been shown to ablate primary and secondary T-cell dependent antibody response (TDAR).

Objectives: We hypothesized that KPL-404, an anti-CD40 monoclonal antibody which inhibits interaction between CD40 and CD40L, would block T-cell dependent, B-cell-mediated autoimmunity in this Phase 1 study in healthy participants.

Methods: This randomized, double-blind, placebo-controlled, first-in-human study of KPL-404 in healthy participants was designed with two single-ascending-dose arms: single intravenous (IV) doses of 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, or 10 mg/kg and single subcutaneous (SC) doses of 1 mg/kg or 5 mg/kg. The primary objective was safety and tolerability of KPL-404; secondary and exploratory objectives included pharmacokinetic (PK) parameters, TDAR inhibition, and receptor occupancy (RO). To evaluate TDAR inhibition, participants post-KPL-404 administration were immunized with 1 mg intramuscular injection of the test antigen *Keyhole* Limpet Hemocyanin (KLH) on day 4 and day 29 to elicit a primary and secondary Immunoglobulin (Ig) response, respectively. To evaluate RO, free and total CD40 receptor levels (percent change from baseline) on B-cells (whole blood) were measured using flow cytometry.

Results: There were no dose-limiting or dose-related safety findings in healthy participants after KPL-404 administration. One unrelated serious adverse event (patella fracture following a fall) occurred in the 10 mg/kg IV arm. The PK profile of KPL-404 in serum after IV or SC administration had low to moderate variability between individuals; elimination was dose-dependent and consistent with target-mediated drug disposition (TMDD) (Figure 1a). For participants receiving 10 mg/kg IV, full receptor occupancy was observed through day 71 (Figure 1b), complete TDAR suppression was observed through Day 57 (Figure 1c), and anti-drug antibodies to KPL-404 were suppressed for at least 57 days; the suppression of antibody responses to the drug itself is an independent indicator of target engagement and pharmacodynamic effect. For participants receiving 5 mg/kg SC, full receptor occupancy was observed through day 43 (Figure 1b), and complete TDAR suppression was observed through Day 29 (Figure 1c). The TDAR response to KLH antigen correlated with the observed full RO.

Figure



Conclusion: The safety and tolerability data and the PK/PD profile of KPL-404 support further investigation of KPL-404 in a broad range of autoimmune diseases, including rheumatoid arthritis. These data support the optionality for studying chronic KPL-404 dosing in patients with subcutaneous and/or intravenous administration.

Disclosure of Interests: Manoj Samant Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Alistair Wheeler Consultant of: Kiniksa Pharmaceuticals Corp., Guang-Liang Jiang Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Moses Njenga Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Madeline Spiers Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Arian Pano Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., John F. Paolini Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp.

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AB0359

TOCILIZUMAB IN AFRO-CARIBBEAN RHEUMATOID ARTHRITIS: THE MARTINICAN EXPERIENCE

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Background: Mortality and morbidity related to rheumatoid arthritis (RA) has remarkably improved over the last twenty years since using biologics DMARDs[1]. However, their effectiveness remains questionable in Afro-descendants (AD) due to their large under-representation in RA clinical trials[2,3]. Martinique is a French Caribbean region with a majority of AD population[4], with free access to healthcare, including biotherapies, and a unique university hospital and rheumatology unit.

Objectives: To evaluate effectiveness of Tocilizumab (TCZ), an interleukin-6 inhibitor, in an afro descendant RA population.

Methods: Retrospective cohort of 171 patients who received at least 1 infusion of Tocilizumab (IV TCZ) at Martinique University Hospital Center between 2008 and 2019. Inclusion Criteria: Patients over 18 y/o meeting RA 2010 ACR/EULAR criteria, having received at least 4 courses of IV TCZ starting at 8mg/kg every 4 weeks, with available baseline clinical/biological data. Exclusion criteria: Patients having received subcutaneous TCZ (SC TCZ) prior to IV TCZ, not living in Martinique. Primary endpoint was proportion of patients in remission (R) and low disease activity (LDA) according to DAS28 CRP at 12, 24, 36 weeks. Secondary endpoint was proportion of patients achieving good (GR) and moderate (MR) EULAR response criteria [5] at 12, 24 and 36 weeks, and TCZ retention at 1 year defined as the proportion of patient receiving TCZ at 1 year follow up.

Results: Out of 171 patients receiving IV TCZ, we identified 138 RA and 80 patients met inclusion criteria: 90% were women, mean age was 56.8 (± 11.8) y/o, mean duration of RA was 11.6 (± 8.9) years, ACPA and Rheumatoid Factor were positive in 72.1% and 73% of cases, 69.6% of patients had erosions and 77.8% had received at least 1 biologic prior to IV TCZ. At baseline, 8 patients were in R, 8 had LDA but presented steroid dependency over 10 mg per day of prednisone and mean dose of prednisone was 6.9 (+/- 6.7) mg per day.

At 12, 24, 36 weeks, R was achieved in 44.8%, 55.2% and 51.2% of patients and LDA in 37.3%, 17.2% and 20.9%, respectively (Figure 1). At 12, 24, 36 weeks, GR was achieved in 44.8 %, 60.3% and 48.8% of patients respectively, MR was achieved in 20.9%, 20.7% and 27.9% of patients respectively (Figure 1) and mean dose of prednisone per day was 5.1 (± 4.9) mg, 4.9 (± 5.6) mg and 3.3 (± 5.1) mg respectively. At 1 year, 78.8% of patients were still on TCZ. During follow up: 15 patients experienced 19 infectious events; 6 patients liver cytolysis; 12 patients neutropenia. No patient died.

Conclusion: This is the first study evaluating efficacy and safety of TCZ in an AD RA cohort. TCZ is safe and effective in our AD population with comparable data observed in other ethnicities[6,7].

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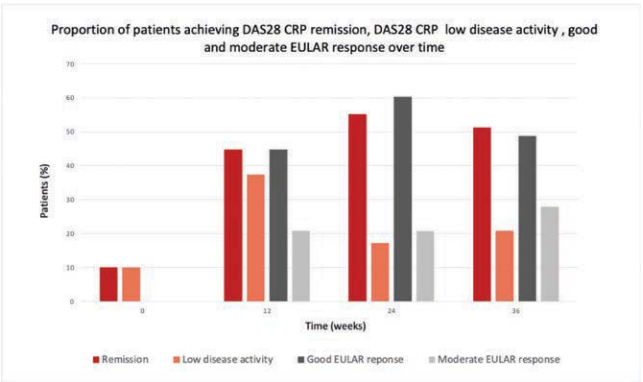

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AB0360

THE LONG-TERM IMPACT OF FATIGUE ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: Fatigue is common among patients with rheumatoid arthritis (RA) with a substantial impact on quality of life (1). Biological disease-modifying antirheumatic drugs (bDMARDs) have been shown to significantly improve fatigue in these patients. However, fatigue is under-assessed by the physicians and evidence is still scarce regarding a possible impact of fatigue on disease activity over time.
Objectives: To explore the long-term impact of fatigue on the disease activity in patients with RA treated with bDMARDs.
Methods: A monocentric observational retrospective cohort study was conducted with 24 months (M) of follow-up. Patients diagnosed with RA, according to the 2010 American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) criteria, and registered on the Rheumatic Diseases Portuguese Register (Reuma.pt) who started their first bDMARD between 2015 and 2021 were included. Demographic, clinical and laboratory data were obtained by consulting Reuma.pt. Fatigue was monitored at baseline, 12 and 24M using Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). This scale is a 13-item self-reported questionnaire with a total score ranging from 0 to 52. A score ≤ 39 indicates the presence of clinically significant fatigue. Disease Activity Score for 28 joints with erythrocyte sedimentation rate (DAS28), DAS28 with C-reactive Protein (CRP) [DAS28-CRP], DAS28 delta, Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI) were calculated to measure disease activity. Clinical response was evaluated by EULAR criteria in three response categories-good, mild and no response- and by ACR criteria (0 to 100%) at 12 and 24M. To correlate fatigue score with EULAR clinical response Chi-square test was used. Multivariate linear regression models adjusted for age, gender and disease duration were used to assess the effect of fatigue on disease activity and ACR clinical response over time.
Results: A total of 40 patients with RA were included, with a mean age of 47.4±11.4 years old and disease duration of 10.4±5.6 years. Most patients were female (90.2%). Rheumatoid Factor was positive in 70% of patients. The majority of patients (85%) had clinically significant fatigue at baseline moment (FACIT-F 26.9±11.8). Treatment characteristics and baseline disease activity scores are described in Table 1. Fatigue at baseline moment predicted DAS28(CRP) (β=-0.061, 95%CI [-0.12; -0.003]) and CDAI (β=- 0.30, 95%CI [-0.57; -0.029]) at 12M. Additionally, fatigue predicted SDAI (β=-0.38, 95%CI [-0.72; -0.047]) and CDAI (β=- 0.39, 95%CI [-0.73; -0.051]) at 24M. In general, for these models, fatigue as a symptom was shown to have negative effects on the different outcomes analysed. Fatigue did not associate with EULAR and ACR responses over time.

Table 1. Baseline characteristics of sample. LEGEND: SD: Standard deviation; DAS28: Disease Activity Score for 28 joints; CRP: C-reactive Protein; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index.

Variable	Descriptive statistic
Treatment options	**n(%)**
Glucocorticoids	37(92.5)
Conventional DMARDs	37(92.5)
Anti-TNF	19(47.5)
Etanercept	13(32.5)
Rituximab	4(10)
Tocilizumab	4(10)
Disease activity score	**Mean±SD**
DAS28	5.4±0.87
DAS28-CRP	4.9±0.69
CDAI	27.6±8.5
SDAI	28.9±8.7

Conclusion: These findings showed that, in our sample, the most RA patients had severe fatigue and its presence may be a predictor of increased disease activity. Indeed, previous research observed a positive association between fatigue and disease activity over the time in patients with RA (2). Therefore, fatigue should be regularly monitored in patients with RA and its impact on treatment must be considered. Moreover, further research with larger samples is needed to explore the impact of fatigue on clinical response and the potential of fatigue relief as an outcome measure of RA treatment.
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AB0361

TOCILIZUMAB VERSUS TOFACITINIB IN THE 12-MONTH TREATMENT OF BIOLOGICAL-NAIVE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: The choice of the most effective disease-modifying antirheumatic drug (DMARD) for the treatment of rheumatoid arthritis (RA) remains relevant. There are several comparative studies between tocilizumab (TCZ), an antibody against interleukin 6 receptor, and tofacitinib (TOFA), a potent selective Janus kinase inhibitor, regarding their efficacy [1,2].
Objectives: To compare the effectiveness of TCZ and TOFA for treatment of biological-naive patients (pts) with active RA according to various indicators of disease activity, physical function, and quality of life during a 12-month (m) follow-up period.
Methods: A total of 80 biological-naive pts with high and moderate RA activity were enrolled (40 pts with TCZ and 40 pts with TOFA). The groups were comparable in terms of sex, age, BMI, and DAS28. All pts were measured: for disease activity using DAS28, SDAI, and CDAI; for quality of life and physical function using EQ-5D, HAQ, and RAPID 3 questionnaires at the beginning of the study and after 12 m of TCZ/TOFA therapy. The EULAR response criteria for treatment of RA were used.
Results: Significant positive changes in major disease activity, clinical and laboratory parameters were found in RA pts after 12 m of TCZ infusion and TOFA intake: DAS28, SDAI, and CDAI decreased significantly in both groups ($p<0.01$ in all cases). There were more good responders among TCZ pts compared to TOFA pts: by DAS28 35 pts (87.5%) vs. 20 pts (50%), $p<0.01$; by CDAI 38 pts (95%) vs. 26 pts (65.7%), $p=0.02$, respectively. There was a more pronounced decrease in DAS28 and CRP levels in TCZ pts (ΔDAS28=-3.8[-4.5;-2.7], ΔCRP=-26.5[-45;-10.7] mg/L) compared to TOFA pts (ΔDAS28=-2,3[-3.2;-1.5]; ΔCRP=-10.1[-32;-8] mg/L, $p<0.01$ in all cases). Both drugs equally improved quality of life and physical function indicators EQ-5D, HAQ, and RAPID during a 12-m follow-up period. Correlations of ΔEQ-5D with ΔESR (R=0.43: $p<0.01$) and with ΔCRB (R=0.46; $p=0.03$) were found after 12 m of TCZ therapy.
Conclusion: TCZ and TOFA both significantly reduce disease activity and improve quality of life and physical function in bDMARD-naive RA patients. Compared with TOFA, TCZ can induce greater improvements during the first 12-m treatment. No unequivocal conclusions on the drugs' effect on pts' quality of life could be made.
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AB0362

NEUTROPHIL COUNT REDUCTION 1 MONTH AFTER INITIATING SARILUMAB AND BASELINE SERUM SOLUBLE GP130 LEVELS CAN INDEPENDENTLY PREDICT CLINICAL REMISSION WITHIN 3 MONTH IN RHEUMATOID ARTHRITIS PATIENTS

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Background: IL-6 contributes significantly to the chronic inflammatory process of rheumatoid arthritis (RA) and is elevated in serum and synovial fluid of RA patients. Sarilumab (SRL), a human anti-human IL-6 receptor alpha monoclonal antibody that blocks the signaling originated by the IL-6/IL-6R complex like tocilizumab (TCZ),is an effective treatment. Recently, an association between the therapeutic effect of TCZ and neutropenia after TCZ initiation was reported[1]. Neutropenia is a common adverse event of SRL in patients with RA, but the relationship between reduced neutrophil count and clinical response to SRL is still inconclusive. In EULAR 2020, we reported the association between serum soluble gp130 levels before SRL treatment and the efficacy of SRL[2]. It is also unclear whether there is a relationship between IL-6 axis cytokines and SRL-induced neutropenia.
Objectives: The purpose of this study was to determine whether neutropenia at 1 month by SRL predicts clinical remission within 3 months and whether there is an association between IL-6 axis cytokines levels and SRL-induced neutropenia.
Methods: This research is a retrospective study. We reviewed medical records of RA patients initiating SRL between February 2018 and August 2021 in our hospital. The Clinical Disease Activity Index (CDAI) was evaluated at baseline (before initiating SRL) and 3 months after administration. Clinical remission was defined when CDAI decreased ≤ 2.8. Of the 66 patients treated with SRL, 42 patients with 3 months follow-up, valid CDAI and serum available were enrolled. The ratio of neutrophil counts 1 month after initiating SRL to those at baseline (neutrophil ratio) was also calculated. Serum samples were tested for IL-6 (Human IL-6 Quantikine ELISA Kit, R&D systems), sIL-6R (Human soluble IL-6R alpha Quantikine ELISA Kit, R&D systems) and sgp130 (Human soluble gp130 Quantikine ELISA Kit, R&D systems) using specific ELISAs according to the manufacturer's instructions. The statistical analyses were performed with EZR 1.55, and p values less than 0.05 were considered significant.
Results: The median age of patients was 69.0 (IQR: 59.3 - 73.8) years and the median of disease duration was 9.0 (3.0 - 16.0) years. Eighteen (42.9%) patients were biologics and Jakinibs naive. The baseline CDAI was median 16.7 (11.5 - 25.8). When comparing CDAI-remission group (clinical remission: CR) and non-CR group, Patients in the CR group had significantly shorter disease duration, were more Biologic and JAKinib naive, and had greater neutropenia 1 month after starting SRL (0.71 vs 0.94, P=0.0252). There was no significant difference in the baseline serum levels of IL-6, sIL-6R between the CR and non-CR groups, but baseline serum sgp130 levels in the CR group tended to be higher than in the non-CR group (264.9 vs 234.2 ng/mL, P=0.0592). Univariate logistic regression analysis suggested Biologics and JAKinibs naive (odds ratio (OR) 6.68, p = 0.0317), baseline serum sgp130 levels (OR 8.608, P=0.0312) as predictors of CDAI remission treated with SRL at 3 months. Although not significant, neutrophil ratio ≤ 0.8 was associated with achieving remission (OR 6.67, P=0.0537). Univariate logistic regression for neutrophil ratio ≤ 0.8 did not show any relevant factors, including higher baseline serum sgp130 levels (OR 1.25, P=0.782).
Conclusion: A 20% or greater decrease in neutrophil count after 1 month of SRL treatment and a high baseline serum sgp130 level independently predict clinical remission within 3 months.

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AB0363

COMPARING THE ULTRASONOGRAPHIC EVALUATION IN PATIENTS WITH JAPANESE RHEUMATOID ARTHRITIS BETWEEN JAK AND TNF INHIBITOR THERAPY

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Background: JAK inhibitor (JAK) and TNF inhibitor (TNF) are the important therapeutic agent for the treatment of rheumatoid arthritis.However there is still few studies of improvement of ultrasonographic findings in RA treated comparison with JAK and TNF.
Objectives: To evaluate the clinical efficacy of JAK and TNF therapy patients with rheumatoid arthritis (RA) using ultrasonography (US).
Methods: Participants comprised 32 and 39 Japanese RA patients who had recently received JAK (BAR23, PEF9) and TNF. All patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria. Patients underwent clinical and laboratory assessments every 4 weeks from baseline to 24 weeks, and US assessments at baseline, 4, 12 and 24 weeks. Gray scale (GS) and power doppler (PD) signals were scored using a semi-quantitative scale from 0 to 3 at 26 (0-78) synovial sites (22 joints) in the following joints: bilateral first to fifth metacarpopharangeal (MCP) joints (dorsal recess); first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) (dorsal recess) joints; and the wrists (dorsal radial, median and ulnar). We evaluated the improvement of GS and PD score from baseline to week 24.
Results: In the patients receiving JAK (n=32) and TNF (n=39), the mean age was 54.7 vs 55.1 years old (p=0.871), disease duration was 7.4 vs 6.1 years (p=0.290), the rate of MTX use was 75% vs 87% (p=0.187), the mean MTX dose was 9.9 vs 10.2 mg/w (p=0.813), the rate of ACPA positive was 94% vs 79% (p=0.086), DAS28-ESR was 4.79 vs 4.65 (p=0.435), CDAI was 22.4 vs 19.1 (p=0.239), GS score was 20.8 vs 18.3 (p=0.995) and PD score was 14.0 vs 11.0 (p=0.940). The degree of improvement respective changes in GS and PD score after 4, 12 and 24 weeks were as follows: GS: -5.1 vs -4.3 (p=0.817) and PD: -5.3 vs -2.7 (p=0.855) after 4 weeks, GS: -9.1 vs -6.6 (p=0.880) and PD: -7.9 vs -4.5 (p=0.476) after 12 weeks, GS: -10.4 vs -9.5 (p=0.463) and PD: -8.1 vs -6.7 (p=0.968) after 24 weeks between JAK and TNF (Figures 1 and 2). Next, The improvement rate of respective changes in GS and PD score after 4, 12 and 24 weeks were as follows: GS: -13.7% vs -18.3% (p=0.489) and PD: -20.4% vs -16.5% (p=0.777) after 4 weeks, GS: -29.7% vs -26.0% (p=0.922) and PD: -30.9% vs -30.8% (p=0.890) after 12 weeks, GS: -38.1% vs -36.4% (p=0.567) and PD: -33.4% vs -50.1% (p=0.977) after 24 weeks between JAK and TNF.
Conclusion: The present study provides evidence supporting the JAK and TNF therapy improved similarly the inflammatory synovitis of US findings.

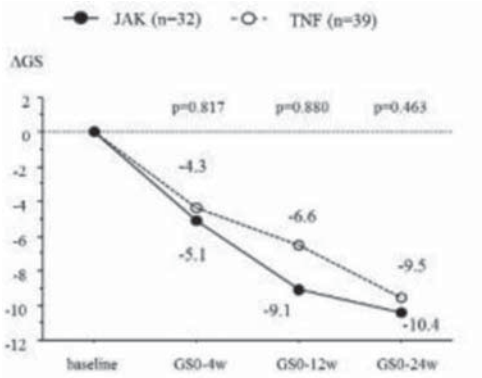

Figure 1 : The degree of improvement respective changesin GS score from baseline to Week 24 between JAK and TNF patients

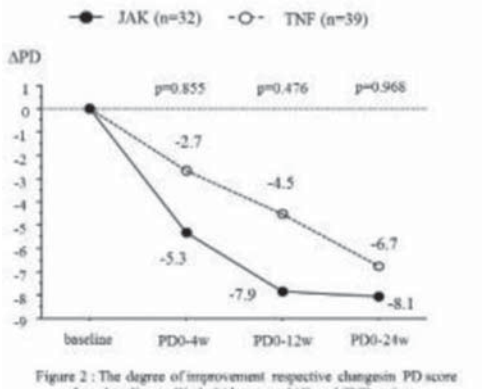

Figure 2 : The degree of improvement respective changesin PD score from baseline to Week 24 between JAK and TNF patients

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AB0364

THE EFFECT OF BIOLOGIC AND TARGETED SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS ON WORK PARTICIPATION IN LONGSTANDING RHEUMATOID ARTHRITIS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

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Background: Work participation (WP) is a top priority for people with RA and a determinant of patients' quality of life. Therefore, assessing the effect of interventions on WP outcomes is important.
Objectives: To review the effect of b/tsDMARDs on employment status (ES), sick leave (SL) and presenteeism in patients with longstanding RA.
Methods: A systematic literature review up to October 2021 was conducted using the PICOT framework (Figure 1). Two researchers independently screened abstracts, then full texts were reviewed to determine eligibility. Data from eligible articles were extracted. Heterogeneity and insufficient reporting of data precluded meta-analysis.
Results: We included 42 studies:16 randomized controlled trials (RCT) and 26 longitudinal observational studies (OBS). All studies were conducted with background therapy with csDMARDs; 33 (78%) in csDMARD-IR patients. RCTs provided short-term data only (≤24 weeks (w)) which have limited relevance for WP outcome domains such as ES[1]. OBS reported long-term data (≤ 5 years), albeit imposing challenges due to lack of random allocation to interventions and often lack of a comparator. Regarding ES, 6 RCTs and 4 OBS did not report significant differences in bDMARD-treated patients vs background csDMARDs. For SL (19 studies), 1 RCT showed that etanercept significantly reduced RA-related SL up to 12-16w; however, one OBS showed no such effect on the long-term. Conflicting results were obtained by 2 RCTs on baricitinib. Most compounds assessed in the 12 OBS without comparator reported improvement in SL up to 104w. For presenteeism (11 studies; Table 1), 4 RCTs showed that etanercept, golimumab, certolizumab pegol, baricitinib and peficitinib were superior to PBO+csDMARDs up to 12w. Two H2H studies assessing sarilumab and baricitinib vs adalimumab observed comparable presenteeism in all treatment arms at 12-16w.
Conclusion: Short-term data from RCTs with background therapy with csDMARDs showed adding b/tsDMARDs was more effective than PBO in improving presenteeism. However, data on SL are conflicting and the positive results come from OBS without comparator. Future studies should consider existing guidance on the assessment of WP outcome domains to allow pooling and meta-analysis[1].

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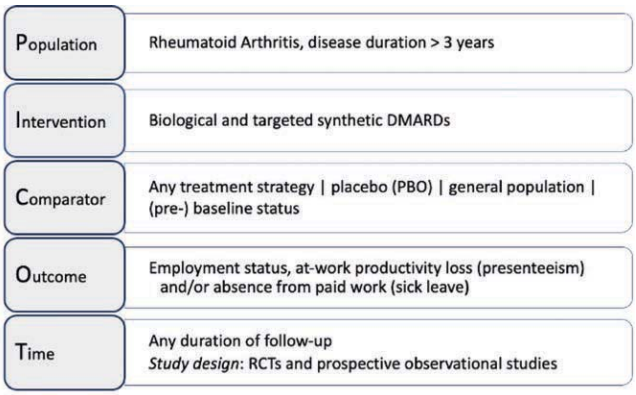

Figure 1. Search strategy according to PICOT framework.

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Table 1. Overview of presenteeism from RCTs and OBS with a comparator in csDMARD-IR patients

Author Year	Instrument Recall period	Intervention (I)¶ Comparator (C)¶	N employed/N total	Effect size	
				From the article	Computed SMD (95% CI)
Bae 2013	WPAI-GH 7 d	I: ETN C: csDMARD	NR/197 NR/103	% improvement 49.6 23.6	-0.24 (-0.5; -0)
Bingham 2014	Self-composed single item 4 w	I: GOL C: PBO	NR/395 NR/197	Mean Δ (SD) –2.4 (2.8) –0.7 (4.5)	-
Emery 2017	WPAI-RA 7 d	I: BARI 2mg I: BARI 4mg C: PBO	88/229 76/227 90/228	LSM Δ from BL (95% CI) –14 (–20 to –8) –16 (–22 to –11) –8 (–13 to –2)	-
Keystone 2017	WPAI-RA 7 d	I: BARI C: PBO	199/487 206/488	LSM Δ from BL (95% CI) -18 (-22, -15) -10 (-13, -6)	-
Kavanaugh 2009	WPS-RA 1 m	I: CZP 200 mg I: CZP 400 mg C: PBO	132/393 139/390 69/199	NR	-0.09 (-0.3; 0.1) -0.17 (-0.3; -0)
Kavanaugh 2009	WPS-RA 1 m	I: CZP 200 mg I: CZP 400 mg C: PBO	101/246 95/246 49/127	NR	-0.11 (-0.3; 0.1) -0.11 (-0.3; 0.1)
Strand 2018	WPS-RA 1 m	I: SARI C: ADA	78/184 185	LSM Δ from BL (SE) -3.74 (0.5) -3.50 (0.5)	-
Kaeley 2018	WPAI-RA 7 d	I: ADA + MTX 7.5mg C: ADA + MTX 20mg	NR/154 NR/155	NR	0.20 (-0.03-0.4)
Tanaka 2021†	WPAI 7 d	I: PEF100mg ± csDMARDs I: PEF150mg ± csDMARDs C: PBO	60/104 53/102 50/102	Mean Δ –12.2 –18.7 3.6	-
Tanaka 2021	WPAI 7 d	I: PEF100mg ± MTX I. PEF150mg ± MTX C: PBO ± MTX	83/174 101/174 99/170	Mean Δ –11.6 –16.9 –2.7	-
Tanaka 2018 & 2020*	WPAI 7 days	I: TCZ C: csDMARDs	167/377 160/347	Mean Δ -17.7 -17.2	-

*OBS**WPAI,** work productivity and activity index; **WPS,** work productivity survey; **GH,** global health; **NR,** not reported; **LSM,** least mean square; **BL,** baseline; **CI,** confidence interval; **SE,** standard error; **SMD,** standardized mean difference; **d**, days; **w**, weeks; **m,** month. ¶Added to background therapy with csDMARDs unless otherwise stated.

AB0365 BELIEFS AND ADHERENCE IN RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGIC DRUGS

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Background: Patients with chronic rheumatic diseases play an important role in their disease management. Adherence to their long-term therapies may depend on their therapeutic beliefs [1].
Objectives: The purpose of our study was to investigate the relationship between beliefs and adherence among patients with rheumatoid arthritis (RA) on biologic therapies (bDMARDs).
Methods: We conducted a multi-centric cross-sectional study, including patients with RA fulfilling the ACR/EULAR 2010 criteria. All patients were on bDMARD. Sociodemographic, clinical, biologic, and therapeutic data were collected. Patients were interviewed about their medication beliefs using the Beliefs about Medicines Questionnaire (BMQ) and about their therapeutic adherence.
Results: There were 75 RA patients: 60 female (80%) and 15 males (20%). The sex ratio was about 0.25. Their mean age was 56.92±9.06 years [34-80]. Thirty-three percent of patients were illiterate. Twenty patients were employed (15%). The mean disease activity scale (DAS28 CRP) was 3.94±1.32 [1.21-7.15]. Fifteen patients (20%) had high disease activity, 11% had low activity, and 19% were in remission. The mean duration of the current bDMARD was 37.17±39.44 months [4-248]. The mean Specific Necessity score was 21.02±5.38 [5-25] for adherent patients and 13.5±7.54 [5-19] for non-adherent patients.
The mean Specific Concerns score was 10.07±3.13 [5-15] for adherent patients and 15±2.82 [5-20] for non-adherent patients.
A statistically significant association was found between Specific Concerns beliefs and adherence behavior (p=0.009) and between Specific Concerns beliefs and adherence behavior (p=0.003). No statistically significant association was noted between general beliefs (General Harm and General Overuse) and adherence behavior (p=0.4 and p=0.6 respectively).
Conclusion: Beliefs about therapeutic were identified as a key factor of adherence among rheumatic disease patients. Practitioners should detect negative patient beliefs and perceptions earlier to prevent nonadherence.
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AB0366 A PROSPECTIVE OBSERVATIONAL STUDY TO ASSESS THE REAL-WORLD EFFECTIVENESS OF GOLIMUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND PREVIOUSLY TREATED WITH INITIAL TNFA INHIBITORY THERAPY

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Background: TNF inhibitor (TNFi) treatment is standard for RA patients even though many reasons may lead to TNFi therapy failures such as lack of effectiveness, patient dissatisfaction or limited therapy adherence, or even safety. As a consequence, patients may switch to a different TNFi. The efficacy of golimumab (GLM) in RA patients with inadequate response to TNFi was demonstrated in the Go-AFTER phase III clinical trial.
Objectives: The objectives of the present Go-BEYOND study were to provide real-world data to evaluate disease activity and treatment persistence with GLM as a second line TNFi therapy in RA patients over a one-year follow-up.
Methods: Go-BEYOND is an observational French multicenter prospective cohort study. All consecutive patients over 18 years of age with a diagnosis of active RA were eligible at the time of initial GLM prescription. To be included, patients had to be previously treated with only 1 TNFi (discontinued for any reason) other than GLM. Patients were ineligible if they had been previously treated with other "non-TNFi" biologics or more than one TNFi.
The study's primary outcome was the percentage of RA patients with a Disease Activity Score (DAS28-CRP score) ≤ 3.2 at the 6-month visit (M6 visit). Patients who permanently discontinued their treatment over the 1-year follow-up were considered as non-responders. The secondary outcomes were analyzed descriptively and included (but not limited to) DAS28-CRP score at 12-month visit (M12 visit), EULAR criteria assessment, treatment persistence analysis, HAQ score, RAPID3 score, and patient acceptable symptom state and satisfaction with the injection. The study was approved by a French Ethics Committee in July 2017.
Results: A total of 128 patients (72.7% female, median age 58.2 years, and duration of RA 13.2 ± 11.4 years) met the inclusion criteria. Anti-CPP antibodies and rheumatoid factors were present in 80 (62.5%) and 81 (63.3%) patients, respectively. In the majority, the initial TNFi was etanercept (n=88, 68.8%), then adalimumab (n=25, 19.5%). The reasons for switching to GLM were secondary non-response (*i.e.,* lack of effectiveness after an initial response to the treatment) for 75 (58.6%) patients, then safety (n=22, 17.2%), primary non-response (n=21, 16.4%), and other personal or medical reasons (n=10, 7.8%).
At the M6 and M12 visits, a small number of patients, 27 (21.1%) and 48 (37.5%) had respectively permanently discontinued their GLM treatment and were considered as non-responders. At the M6 visit, 48 patients over the 128 included (37.5%) had a DAS28-CRP ≤ 3.2 and 32 (25%) < 2.6. At M12 visit, 41 (32%) patients had a DAS28-CRP ≤ 3.2 and 31 (24.2%) < 2.6. According to EULAR response criteria thresholds, 49 (38.3%) and 45 (35.2%) patients had a good or moderate response to GLM at the M6 and M12 visits.
Conclusion: The Go-BEYOND study confirms that in RA, a non-response to a first TNFi does not exclude a response to GLM as a second-line biologic in a substantial proportion of patients in real-life settings.
References: None
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AB0367 THE PARADIGM OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: SUBTYPES AND EARLY IDENTIFICATION.

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Background: Difficult-to-treat rheumatoid arthritis (D2TRA)[1] is an emerging concern for rheumatologists. Multiple failures to biologic or targeted specific disease modifying antirheumatic drugs (b/tsDMARDs) may be due to multi-drug inefficacy or difficulties in the optimum management of treatments due to adverse events, comorbidities, poor adherence, among others. In a previous study[2] we identified that younger patients with erosive disease and especially the early absence of clinical response to the first b/tsDMARDs were associated to multiple drug inefficacy but it is worth knowing whether these factors are the same for those patients who receive multiple b/tsDMARDs due to causes other than inefficacy.
Objectives: i) To describe the characteristics of a cohort of D2TRA patients in clinical practice. ii) To analyze the differences between D2TRA due to inefficacy vs D2TRA to other causes. iii) To compare the different subtypes of D2TRA with non-D2TRA.
Methods: This study involved patients with D2TRA from La Paz Hospital and Clìnic Hospital between 2000 and 2021. D2TRA group included patients who had received ≥2b/tsDMARDs due to inefficacy (D2TRA-inefficacy) or due to: adverse events, poor adherence, contraindications, comorbidities, drug-intolerance etc. (D2TRA-other causes). Patients who achieved low disease activity or remission (by DAS28) with the 1st bDMARD and remained with the same drug for at least 5 years were non-D2TRA patients. For all patients, demographic, clinical characteristics and laboratory parameters were assessed at baseline visit (prior to start the 1st b/tsDMARD) and after 6 months. Descriptive analysis was performed and bivariate logistic regression models were assembled. P<0.05 was considered statistically significant. Odds Ratio (OR) and Confidence Intervals (CI) were calculated. IBM SPSS 21.0
Results: In total, 253 patients were included, 131 were non-D2TRA and 122 D2TRA [86 (70.5%) D2TRA-inefficacy and 36 (29.5%) D2TRA-other causes]. Comparison between both groups of D2TRA patients: no differences in gender, age at b/tsDMARD starting or age at RA diagnosis were found and neither between socioeconomic status, frequency of anxiety-depression or other comorbidities. Patients D2TRA-other causes had less extra-articular manifestations

than D2TRA-inefficacy (8.3% vs 26.7%; p=0.02); lower values of DAS28 at starting 1st b/tsDMARD (4.9±1.4 vs 5.7±1.2; p=0.01), and also at 6 months of treatment (3.5±1.5 vs 4.5±1.5; p=0.02) than those with D2TRA-inefficacy. 2) Comparison between Non-D2TRA patients and D2TRA-other causes: no differences in sociodemographic characteristics were found and neither differences in baseline disease activity, only differences in DAS28 at 6 months were observed, being higher D2TRA-other causes than in non-D2TRA (3.54±1.54 vs 2.93±0.99; p=0.03). Bivariate analysis only showed that high DAS28-6m was slightly associated with D2TRA-other causes (OR=1.45 CI95% 1.11-2.16).

Conclusion: In this cohort, around 3 out of 10 D2TRA patients dropped out multiple b/tsDMARDs for reasons other than inefficacy In contrast to D2TRA-inefficacy, patients with D2TRA-other causes are indistinguishable from non-D2TRA patients at baseline, indicating that patients with D2TRA-other causes does not seem predictable in the early stages of treatment with b/tsDMARDs, unlike what occurs with multidrug ineficacy.

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AB0368 EFFECTS OF SWITCHING FROM ETANERCEPT ORIGINATOR TO ETANERCEPT BIOSIMILAR ON DISEASE ACTIVITY, PHYSICAL FUNCTION, AND PATIENT-REPORTED OUTCOME REGARDING A SELF-INJECTION DEVICE IN PATIENTS WITH WELL-CONTROLLED RHEUMATOID ARTHRITIS

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Background: Although biological drugs have dramatically changed and improved the outcome of patients with rheumatoid arthritis (RA), a lot of unresolved problems still exist. Although comorbidity by which enough treatment drugs cannot be prescribed or RA patients refractory to biological agents are representatives, financial difficulty is another representative. There are RA patients who hesitate biological treatment or treatment with Janus-kinase inhibitor due to financial difficulty. Although biosimilar disease-modifying anti-rheumatic drugs (DMARDs) are promising treatment options for such patients, real-world clinical experiences are still lacking in respect to exchanging from biological originator DMARDs to biosimilar DMARDs.

Objectives: This retrospective study investigated the effects of switching from etanercept originator (ETN-OR) to ETN biosimilar (ETN-BS: LBEC0101 developed by LG Chem) on disease activity, physical function, and patient reported outcome (PRO) regarding a self-injection device in patients with well-controlled RA.

Methods: Data from the Toyohashi RA Database (TRAD) was used, which is a collection of single-center retrospective data. We retrospectively investigated disease activity, modified health assessment questionnaire (mHAQ), and patient characteristics in 42 RA patients that switched from ETN-OR to ETN-BS at least 6 months prior. Patients were also requested to answer the Toyohashi Self-Injection Assessment Questionnaire (T-SAQ), originally designed to assess PRO. T-SAQ consisted of 18 questions about self-injection device such as burden, learning, pain, convenience, handling and so on. Best was 0 and worst was 4 in each question and mean score of 18 questions was called total T-SAQ score.

Results: All the patients were female. The mean age, RA duration, and ETN-OR treatment duration were 63.1 years, 18.3 years, and 3107 days, respectively. Mean disease activity and mean mHAQ after switching were as follows (baseline-3 months-6): DAS28-CRP (1.86-2.00-2.03), SDAI (4.3-5.0-5.3), and mHAQ (0.43-0.44-0.46). SDAI after 6 months was significantly elevated compare to baseline. Among each parameter, tender joints count at 3 months and patients' global assessment at 6 months after switching are significantly increased compared to baseline (Table 1). Other parameters such as swollen joint counts, physician global assessment and CRP were not significantly changed. Total T-SAQ scores before and after switching were 1.3 and 1.1 ($p < 0.01$), respectively. Ease of use, mental tension, and pain were especially improved after switching to ETN-BS.

Conclusion: Switching from ETN-OR to ETN-BS worsened disease activity in well-controlled RA patients in our real-world clinical practice due to not objective findings, but subjective complaints by RA patient. We thought that nocebo effect was one of the reasons to explain the results. On the other hand, the PRO regarding the injection device was improved. This improvement may be due to Finer needle of ETN-BS (ETN-OR: 27G, ETN-OR: 29G).

Table. Time-course of parameters on disease activity

	At starting of ETN-OR (n=34)	At switching to ETN-BS (n=42)	At 3 months	At 6 months
Tender Joints Counts	7.5 (5.0)	1.1 (2.2)	**1.8 (3.3)***	1.4 (2.5)
Swollen Joints Counts	4.7 (4.5)	0.2 (0.6)	0.3 (0.7)	0.2 (0.5)
Patient's Global Assessment (mm)	38.6 (22.3)	14.6 (12.6)	13.5 (12.1)	**21.8 (18.2)***
Physician's Global Assessment (mm)	39.4 (16.6)	10.7 (8.2)	11.4 (8.2)	12.2 (7.9)
CRP (mg/dl)	2.6 (2.7)	0.4 (1.0)	0.3 (0.6)	0.3 (0.6)

Data lacking at starting of ETN-OR exist due to ETN-OR initiation at another institute.
Data is expressed mean value (standard diviation).

* $p<0.05$ compared with data at switching to ETN-BS by Wilcoxon signed-rank test)

Disclosure of Interests: None declared

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AB0369 CORRELATION OF THE FIRST LATERAL FLOW-BASED POINT OF CARE TEST TO QUANTIFY INFLIXIMAB AND ANTI-INFLIXIMAB ANTIBODIES IN A FINGER PRICK SAMPLE WITH THE REFERENCE ELISA TECHNIQUE

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Background: Current techniques to monitor clinical response may require several days and centralised facilities, which may cause delays in effective therapeutic decisions. Therefore, the use of a rapid decentralized test will facilitate patient management and improve patient care.

Objectives: The goal of this study was to validate the use of capillary blood in a real point-of-care (POC) setting for rheumatic patients under infliximab treatment by using Promonitor Quick lateral flow (LF) tests. Results were compared to the Promonitor ELISA reference technique in serum samples used by centralised laboratories.

Methods: A prospective, observational study was designed to evaluate the performance of a rapid LF test (Promonitor Quick IFX, Progenika, Spain). 160 infliximab treated rheumatology consecutive patients (400 samples) were recruited in two hospitals in Galicia, Spain. Prior to the infusion, a finger prick sample was obtained and analysed. Anti-infliximab antibodies were also determined with Promonitor Quick ANTI-IFX[1-4]. Results were read with the automated portable PQreader instrument. Additionally, a serum sample was collected for subsequent comparative analysis with either LF or ELISA tests.

Qualitative (positive (PPA) and negative (NPA) agreements) and quantitative (Pearson correlation and bias) performance of the LF test was compared to ELISA, as well as between different specimens following CLSI EP09-A3.

Results: Overall agreement between Promonitor Quick IFX finger prick and ELISA test was 91% (88% PPA; 100% NPA). The quantitative comparison showed a good correlation (Pearson correlation coefficient: 0.85 and observed bias: 25%) (Table 1).

Table 1.

Performance results: infliximab drug				
Qualitative Comparison				
	N*	**PPA**	**NPA**	**overall**
POC finger prick vs ELISA	274	88%	100%	91%
POC serum vs ELISA	281	98%	100%	98%
Quantitative Comparison				
	N*	**Pearson correlation**	**Bias**	
POC finger prick vs ELISA	165	0.85	25%	
POC serum vs ELISA	181	0.91	6%	
**Only samples in the common measurement range for both methods considered.*				
Performance results: anti-infliximab anti-drug antibodies				
Qualitative Comparison				
	N*	**PPA**	**NPA**	**overall**
POC finger prick visual vs. PQreader	396	100%	99%	99%
POC serum visual vs PQreader	398	100%	100%	100%
POC finger prick PQreader vs ELISA	393	90%	99%	98%
POC serum PQreader vs ELISA	395	89%	100%	99%

Similar results were also observed when serum was used with either the LF or the ELISA tests (98% overall agreement, 0.91 correlation coefficient; 6% bias) (Table 1). Overall agreements for visual and automated (PQreader) interpretations with Promonitor Quick ANTI-IFX were 99% and 100% for finger prick and serum specimens, respectively (Table 1).

Conclusion: Promonitor Quick can be used to reliably quantify infliximab in capillary blood samples and results are comparable to those obtained with the reference ELISA technique. The use of the rapid POC test with finger prick will allow clinicians to monitor their patients in a fully decentralized mode to aid in the decision making process. PQreader is a sensitive portable equipment to report drug as well as antibody levels in the patient samples.

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AB0370 COMPARISON OF A NEW RANDOM-ACCESS SOLUTION FOR THERAPEUTIC DRUG MONITORING OF ADALIMUMAB TO THE REFERENCE ELISA TEST

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Background: Despite numerous studies, Therapeutic Drug Monitoring (TDM) of biological therapies is still debated partly motivated by the accessibility to a ready-to-use monotest device capable of delivering accurate results in a timely manner without the burden of sample batching, therefore allowing immediate decision making.

Objectives: We aimed at comparing the new Chorus Promonitor Adalimumab monotest running in the fully automated random-access Chorus TRIO system to the reference ELISA test Promonitor ADL run in a Triturus system.

Methods: Chorus Promonitor Adalimumab (Diesse Diagnostica Danese, Italy) is an immunoassay kit for the automated quantitative detection of adalimumab (ADL) in human serum using a ready-to-use disposable monotest device applied on the Chorus TRIO (Diesse Diagnostica Danese, Italy) instrument, a random-access single test multiparametric system for immuno-colorimetric assays. The new device implements the same specific reagents as in the reference ELISA test Promonitor ADL (Progenika, Spain) run in a Triturus (Grifols, Spain) system, therefore ensuring the same analytical specificity and applicability for patient monitoring previously demonstrated with the predicate ELISA. The new monotest device contains all the reagents necessary to perform the assay, and a lot-specific master curve method is used for calibrating. The comparison was performed in a set of 53 serum samples from patients under ADL therapy that covered the entire drug trough concentrations found in clinical practice (up to 30 ug/mL). Pearson's correlation, Bland-Altman and Passing-Bablok regression analysis were used to study the association and quantitative comparison between the methods.

Results: Time to first result for the Chorus Promonitor Adalimumab test was 2 hours and 45 min minutes and after this a new result was delivered every 30 seconds. Positive and negative percent agreements between both tests were 100%. A high correlation between both tests was found (coefficient of correlation of 0.959, p<0.01). The Passing-Bablok regression analysis determined an excellent comparability of both data sets with a slope of 1.032 (0.952-1.129) with an intercept of -0.428 (-1.292-0.053).

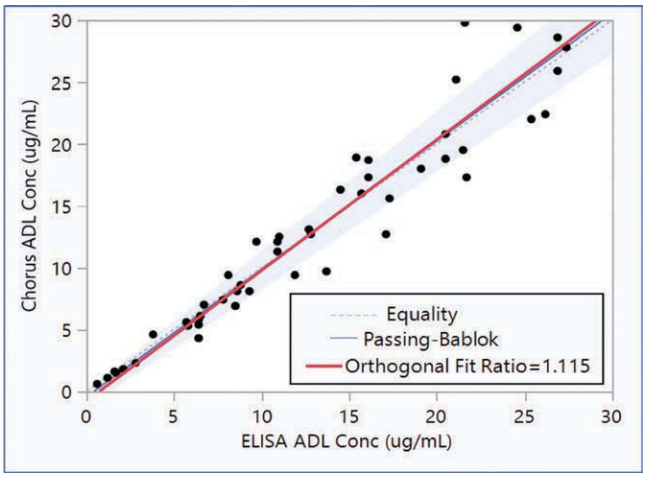

Figure 1.

Conclusion: The Chorus Promonitor Adalimumab represents the first evolution of the gold-standard Promonitor ELISA technology into a monotest random-access technology that enables quick turnaround time to facilitate TDM for ADL and aid immediate decision making.

Disclosure of Interests: None declared

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AB0371 CLINICAL SIGNIFICANCE OF GALECTIN-3 IN PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE THE APPOINTMENT AND AFTER 12 MONTHS OF TREATMENT WITH BIOLOGICAL DRUGS (PRELIMINARY DATA).

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Background: The role of galectin-3, a pro-inflammatory mediator involved in autoimmune disorders in patients with rheumatoid arthritis (RA), is discussed in the literature.

Objectives: To clarify the relationship of clinical and laboratory manifestations of RA with galectin-3 with the ineffectiveness of basic anti-inflammatory therapy and after 12 months of treatment with biological drugs.

Methods: The study included 47pts (39 women /8 men) with RA, 51 [39,0; 63,0] years old. Pts were seropositive for IgM RF (79%) and anti-CCP (62%), with highly active RA (DAS28 5,7 [5,2; 6,4]; SDAI 35,0 [29,1; 43,6], CDAI 34,0 [25,0; 43,0]) scores, and median disease duration of 4.0 [3,0;14.0] years. All patients with RA had a history of insufficient effect or intolerance to two or more basic anti-inflammatory drugs (DMARDs). At the time of inclusion in the study, patients received DMARDs: 44% of patients received methotrexate (median dose - 15 (15; 20) mg /week), 35% - leflunomide (20 mg/day), 9.3 % - sulfasalazine (2000 mg/day), 7% - hydroxychloroquine (200 mg/day), 67.4% - glucocorticoids (5 (4;8) mg /day). Patients did not receive biological therapy at the time of inclusion in the study. Due to lack of efficacy or intolerance, patients with RA (n=21) were prescribed biological therapy: 52.4% - anti-B-cell therapy, 38% - TNF-alpha inhibitors, 9.6% - IL-6 inhibitors. The control group consisted of 20 age-matched donors without rheumatic diseases. Galectin 3 concentration was determined by ELISA (Bender MedSystems GmbH, Biocenter, Vienna Austria). The upper limit of normal when testing 20 sera from healthy donors was 5.32 ng/ml, corresponding to the 95th percentile.

Results: The serum level of galectin-3 in RA patients (n=47) and in the control group (n=20) did not differ statistically significantly (4.27 [2.3;5.26] ng/ml vs 3.83 [2.57;4.11] ng/ml (p=0.1). In the whole group of RA patients (n=47) with inefficiency (insufficient effect) of basic anti-inflammatory therapy, correlations were noted between the level of galectin-3 and age (R=0.34; p=0.02), BMI (R=0.36; p=0.02), SDAI (R=0.33; p=0.02), CDAI (R=0.31; p=0.03). RA patients were divided into 2 groups: group I (n=27) - patients with galectin-3 ≥ 5.32 ng/ml; II (n=20) - less than <5.32 ng/ml. Group I patients were older in age (59.0 (46;67) years vs 42.5(38;53) years), had higher activity according to SDAI (38.2 (30; 48.4) vs 29.7 (26.6; 40.6)), CDAI (35.0 (29; 43) vs 27.0 (23;38)) (p<0.05 in all cases). In the group of patients (n=21) who received combination therapy (DMARDs + biological therapy) for 12 months, there was a significant decrease in clinical and laboratory activity, IgM RF levels (p<0.05 in all cases). (Table 1). The serum level of galectin-3 in RA patients (n=21) decreased by 19% statistically insignificantly after 12 months of combination therapy (4.24 [2.8;5.1] ng/ml vs 3.42 (2.56; 4.36) ng/ml (p=0.2).

Table 1.

	Patients with RA (n=21) with insufficient effect of basic anti-inflammatory therapy	Patients with RA (n=21) after 12 months of receiving combination therapy	Δ,%	p
DAS28	5,6 (5,3; 6,7)	3,97(3,36;4,63)*	-30,4	**0,0001**
SDAI	38,17 (29,5; 45,8)	17,2(9,57;25,6) *	-54,8	**0,0001**
CDAI	35,0 (26,0; 43,5)	17,0(9,0;23,5) *	-51,4	**0,0001**
CRP,mg/l	20,6 (11,7;34,1)	3,15(1,2;7,2) *	-84,7	**0,003**
ESR,mm/h	27,0 (16,0;45,0)	16,0 (10,0;23,5) *	-40,7	**0,003**
IgM RF, ME/ml	84,4 (20,8;163,0)	32,2(10,6;107) *	-61,8	**0,01**
Galectin-3, ng/ml	4,2 [2,8;5,1]	3,42 (2,56; 4,36)	-19	0,2

* -p <0.05 reliability of differences in indicators before and after 12 months of combination therapy (Wilcoxon); Δ,% - the difference in indicators between the groups by the 12th month of combination therapy.

Conclusion: There were no differences in the level of serum galectin-3 in patients with RA and with the ineffectiveness of basic anti-inflammatory therapy and in the control group. At the same time, the association of this marker with RA activity (according to the SDAI, CDAI indices) does not exclude its role in the development of clinical manifestations of rheumatoid arthritis.

Disclosure of Interests: None declared

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AB0372 BIOLOGIC THERAPY IN CHILDREN WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS ACCORDING TO THE FEDERAL REGISTER OF THE RUSSIAN FEDERATION.

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Background: Systemic juvenile idiopathic arthritis (sJIA) is the rarest variant of juvenile idiopathic arthritis, characterized by severe course, frequent exacerbations, the development of life-threatening extra-articular manifestations and complications, which requires the use of expensive medications and frequent hospitalizations of patients. In the Russian Federation, the provision of medicines to patients with sJIA is carried out at the expense of the federal budget, in this regard, the Federal Register of sJIA was created in 2018.

Objectives: To analyze biologic therapy in patients with sJIA according to the data of the Federal Register of the Russian Federation.

Methods: Retrospective analysis of epicrisis of patients receiving biologic therapy with a diagnosis of sJIA included in the Federal Register of the Russian Federation. The analysis included patients receiving the following drugs of biologic therapy: tocilizumab, canakinumab, etanercept, adalimumab.

Results: In 2018, 582 patients receiving biologic therapy were included in the Federal Register. Since 2019, the number of patients has steadily increased: in 2019 there were 796, in 2020 - 949, in 2021 - 1041 patients. The Federal Register of the Russian Federation includes patients under the age of 18 (in 2018 – 471, in 2019 – 666, in 2020 – 806, in 2021 – 790 patients) and patients over the age of 18 (in 2018 – 111, in 2019 – 130, in 2020 – 143, in 2021 – 250 patients). During the four-year follow-up, patients receiving tocilizumab predominate - on average 72.25% (in 2018 – 74%, in 2019 – 73.1%, in 2020 – 70.3%, in 2021 – 71.6% of patients). Therapy with using of TNF-α inhibitors remains without statistically significant dynamics: in 2018 – 38 (6.5%) received etanercept, in 2019 – 42 (5.3%), in 2020 – 44 (4.6%), in 2021 – 46 (4.4%); in 2018 – 22 (3.8%) received adalimumab, in 2019 – 25 (3.1%), in 2020 – 27 (2.9%), in 2021 – 29 (2.8%) patients. The number of patients receiving canakinumab has more than doubled since 2018 (in 2018 – 91 (15%), in 2019 – 147 (18.5%), in 2020 – 210 (22.3%), in 2021 - 220 (21.1%) patients.

Conclusion: The number of patients receiving biologic therapy with sJIA in the Russian Federation has increased, which is due to the natural growth of the disease and more affordable provision of patients with sJIA by the state.

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AB0373 ABATACEPT IN MONOTHERAPY OR IN COMBINATION WITH CONVENTIONAL DISEASE-MODIFYING DRUGS: TREATMENT PERSISTENCE IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: Abatacept is a selective T-cell co-stimulation modulator indicated for the treatment of moderate to severe active rheumatoid arthritis in patients with inadequate response to previous treatment. It is used in routine clinical practice in combination with other conventional synthetic disease-modifying drugs, with some records showing worse results when used in monotherapy[1].

Objectives: To analyse the persistence and efficacy of ABA in monotherapy vs. combined with conventional DMARDs. To determine the prescription patterns and clinical characteristics of patients who have received at least one dose of the drug.

Methods: Retrospective observational study of a cohort of RA patients under treatment with ABA reviewed in Rheumatology consultations at Virgen Macarena University Hospital, from 2010 to 2020. STATA statistical software was used. The study was conducted in accordance with the standards of the CEIC.

Results: 69 patients were included, 80% female. The average age was 63 (53-63) years. RA evolution time was 10 (4-16) years. 92% RF +, 86% ACCP + and 84% double +. 81% with erosions and 47% had extra-articular manifestations: 16 ILD, 10 Dry Syndrome and 9 Rheumatoid Nodules. 96% had relevant comorbidities such as Osteoporosis 33, Hypertensión 31, dyslipidaemia 26, Fibromyalgia 16, Depression 14 or Diabetes 9. Prior to ABA start, all were treated with NSAIDs, GC and conventional DMARDs, 32% with one conventional DMARDs, 31% with two and 37% with three or more; The conventional DMARDs used were MTX 90%, LFN 45%, HCQ 38%, CyA 13%, Gold salts 9% and SSZ 7%. 71% were previously treated with biologic DMARDs; 44% with one biologic DMARDs and 39% with two or more biologic DMARDs. The most commonly used biologic DMARDs were ETA 63.3%, ADA 30.6%, IL-6 inhibitors 20.4% and RTX 24.3%. Of the 29% who started ABA as a first-line. S.C. administration was used in 78%, with the standard dose. ABA was introduced together with conventional DMARDs in 67% patients: MTX 70%, LFN 17%, HCQ 13%, SSZ 4%. Of the 16 patients with ILD, 9 continued with conventional DMARDs in combination. The average ABA persistence was 65.5 (43-100) months; monotherapy 56 (17-76) and associated with conventional DMARDs 73 (59-101), p=0.904 (Figure 1). The differences between ABA in monotherapy or in combination are shown in Table 1. On the last visit, 67% patients with ABA had CG. At the end of the study 38% remained on ABA; 62% discontinued treatment, 68% due to secondary failure, 16% primary failure and 12% adverse events (skin toxicity, haematological toxicity and infections). Six patients died, four due to disease complications, five of whom were on monotherapy.

Table 1.

Variables	Global n=69	ABA monotherapy n=23	ABA + conventional DMARDs n=46	
		Median (p25-p75)		
Age	63 (54 – 70)	70 (63 – 74)	57 (52 – 67)	0,001
Duration of illness	10 (7 – 16)	12 (5 – 20)	10 (4 – 19)	0,04
Exposure time	66 (43 – 100)	56 (20 – 76)	73 (59 – 106)	0,04
DAS28 Basal	4.9 (3.9 - 5.7)	5.3 (3.8 – 6.3)	4.8 (3.8 – 5.5)	0,1
DAS28 Final	4.2 (2.8 – 5.6)	4 (2.7 – 5.4)	4.7 (2.8 – 5.7)	0.4
Basal GC (mg/d)	6 (5 – 10)	6 (5 – 11)	6 (5 – 10)	0,5
Final GC	6 (5 – 10)	7 (5 – 10)	6 (5 – 10)	0,4
	n (%)			
ABA as a first-line	20 (29)	6 (26)	14 (30)	0,7
ABA + GC at the start	54 (78)	18 (78)	319 (63)	1
At the end	31 (67)	12 (75)	6 (78)	0,4
ABA Discontinuation	43 (62)	13 (57)	30 (65)	0,4
ABA Persistence	26 (38)	10 (43)	16 (35)	0,4
EULAR response				
None	32 (64)	11 (64)	21 (63)	0,9
Moderate	11 (22)	4 (23)	7 (21)	
Good	7 (14)	2 (12)	5 (15)	

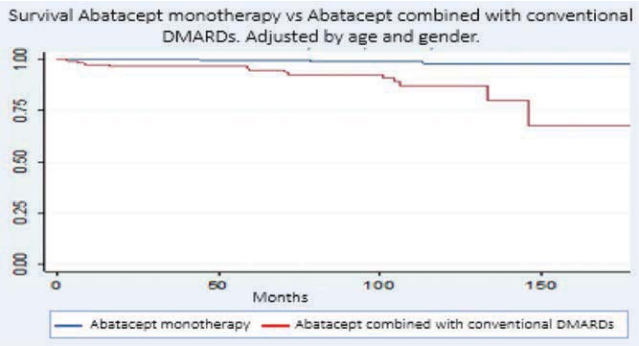

Figure 1.

Conclusion: The results show that Abatacept is mainly used after failure of conventional DMARDs and biologic DMARDs, in patients with long-standing RA and poor prognostic criteria. Combination therapy is used in patients with a higher risk profile (males, antibody positivity, erosions, extra-articular manifestations, comorbidity) and leads to a reduction in the number of patients treated with GC. Survival of ABA in combination is higher than in monotherapy, but this difference is less statistically significant when adjusted by age and gender.

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AB0374 EFFICACY AND SAFETY OF BIOTHERAPY IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE MOROCCAN RBSMR REGISTRY

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Background: Limited data have been published on tolerance and efficacy of biotherapy in elderly patients with rheumatoid arthritis (RA) [1]

Objectives: To assess in real life the efficacy and safety of biological treatments in elderly patients with rheumatoid arthritis (RA) and to identify predictive factors for a good therapeutic response.

Methods: A cross-sectional observational study was conducted, the main data source was the Moroccan registry of biological therapies in rheumatic diseases (RBSMR registry). The duration of this study was 12 months. Patients included were all elderly patients (age > 65 years old), presenting RA,according to ACR /EULAR classification criteria for RA 2010.Demographic and clinical characteristics, disease activity, radiographic damage and functional ability have been compared between two groups of patients: those with response to biotherapy and those without response to biotherapy. Clinical and biological tolerance of biotherapy was assessed at 12 months of follow-up in all patients

Results: Among 224 patients included in the RBSMR registry, 23 patients were over 65 years. The average age of patients was 69,57 years ±4.33 with a sex ratio women/man: 4.75. The mean duration of the disease was 964,79 weeks +/-588,8. RA was seropositive in 87% of patients, with positive anti-cyclic citrullinated antibodies (ACPAs) in 60.9%. It was erosive in 83.3%, with carpitis in 50% of our cases. Concerning biological features, the mean erythrocyte sedimentation rate (ESR) was 55,05 mm H1± 26 and the mean C - reactive protein (CRP) was 26.79 mg/l ± 18. The average initial disease activity score 28-ESR (DAS 28 ESR) was 4,08+/-1,60. The average 12-month DAS was 2,67+ /-1,49. The Health Assessment Questionnaire (HAQ) average was 1.22. Concerning the treatment taken, 8.7% of patients were under Etanercept,4,3% were under Golimumab,69,6% were under Rituximab and 17,4% of patients received Tocilizumab. The analysis did not reveal any statistically significant difference between the two groups regarding demographic, clinical characteristics, disease activity, radiographic damage, biological feature and therapeutic data. 78.3% of our patients had a good tolerance to biotherapies, on the other hand 21.7% had presented undesirable effects.

Conclusion: RA is a common and even more common disease in the elderly, our study as well as The literature data confirms the efficacy of biotherapy and its good tolerance in our Moroccan patients with RA. It represents a therapeutic alternative of choice. Our results further encourage its use in our Moroccan context.

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Disclosure of Interests: None declared

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AB0375 IN PATIENTS STARTING ETANERCEPT, MALE SEX, ABSENCE OF COMORBIDITIES AND NO CSDMARDS CO-ADMINISTRATION ARE INDEPENDENT PREDICTORS OF LONG-TERM (MORE THAN 3 YEARS) PERSISTENCE TO THERAPY, IRRESPECTIVELY OF THE CLINICAL DIAGNOSIS.

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Background: Comparative data among rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA) patients regarding long-term survival of etanercept (ETN) in clinical practice are limited.

Objectives: The first aim of this study was to analyze the long-term (>3 years) ETN survival comparatively between its three main indications. We also aimed to analyze for predictors of long term ETN survival.

Methods: We analyzed data from the University of Crete Rheumatology Clinic Registry (UCRCR), a single center prospective cohort study. All patients with a diagnosis of RA, SpA or PsA starting treatment with a biologic DMARD are recorded prospectively based on a common follow-up protocol. For the first aim, ETN survival >3 years was compared among the 3 diseases. For the 2nd aim patients on ETN >3 years were compared to those stopping ETN during the first 2 years. We analyzed baseline and early on treatment (first 6 months) characteristics, comedications, comorbidities as predictors for long term survival applying univariate and multivariate models.

Results: A total of 711 patients who were started on ETN were analyzed (RA: 450, SpA: 177, PsA: 84). As expected, patients' and disease characteristics at baseline differed significantly between the 3 diagnoses (Table 1). Patients' function was compromised irrespective of the diagnosis, while inflammatory activity was significant across diseases.

Table 1. Baseline parameters [Medians (IQR) unless otherwise specified]

	RA (n=450)	SpA (n=177)	PsA (n=84)	p
Women N (%)	370 (82)	66 (37)	46 (55)	**<0.001**
Age	61.5 (53-70)	44.5 (35-54)	51 (41-62)	**<0.001**
Disease duration	2.6 (0.9-6.5)	0.8 (0.1-5.1)	1.7 (0.6-4.9)	**<0.001**
Follow-up years	1.0 (0.5-2.1)	1.0 (0.4-3.1)	1.1 (0.4-3.6)	0.649
Total comorbidities nr.	3 (1-4)	1 (0-3)	2 (1-4)	**<0.001**
RDCI	1 (1-2)	0 (0-1)	1 (0-1)	**<0.001**
Ever smokers N(%)	124 (39)	82 (67)	30 (61)	**<0.001**
BMI	31 (26-35)	27 (25-32)	29 (23-32)	**0.015**
Treatment line N (%): 1st	264 (59)	87 (49)	43 (51)	**0.012**
2nd	119 (26)	70 (39.5)	24 (29)	
≥ 3rd	67 (15)	20 (11)	17 (20)	
Nr of previous csDMARDs	2 (1-3)	1 (0-2)	1 (1-2)	**<0.001**
Co-administered MTX N(%)	284 (63)	65 (37)	50 (60)	**<0.001**
Monotherapy, N (%)	60 (13)	100 (56.5)	25 (30)	**<0.001**
Ongoing corticosteroids N(%)	153 (34)	25 (14)	17 (20)	**<0.001**
DAS28 - ESR	5.8 (5.0-6.5)	3.7 (2.9-4.7)	5.3 (4.5-6.4)	**<0.001**
ASDAS-ESR	-	3.4 (2.8-4.1)	3.6 (3.2-4.7)	0.067
CRP (mg/dl)	0.4 (0.3-1.1)	1.1 (0.3-2.4)	0.8 (0.4-2.0)	**<0.001**

During a follow-up of 1371 patient-years, 466 (65.5%) patients stopped therapy. The estimated percentage of patients persisting on ETN therapy for > 3 years was 28.4%, 42.8% and 44% of RA, SpA and PsA respectively. The main reason for therapy discontinuation was inefficacy (75% of stop reasons in RA vs. 58% in SpA vs. 69% in PsA). In multivariable Cox regression analyses the most important predictor for ETN survival was the achievement of LDA/remission at 6 months based on DAS28 for RA or ASDAS for SpA [Odds Ratio (OR) 1.98, p=0.008 and 3.02, p=0.001 respectively]. Prognostic factors for ETN discontinuation specifically due to inefficacy were comorbidities number and csDMARDs coadministration (p<0.05 for both), while older age and no co-therapy with MTX predicted ETN stop due to adverse events (p<0.05 for both). Logistic regression analysis indicated that male sex [OR: 2.08, p=0.004], calendar year of treatment start [OR per 3 years: 0.74, p=0.001], comorbidities' number [OR: 0.82, p=0.045] and monotherapy [OR: 1.81, p=0.027] predict persistence on ETN therapy beyond 3 years, while the clinical diagnosis or other baseline parameters are not significant predictors.

Conclusion: In this prospective cohort study, we found that ETN survival was higher for patients with SpA/PsA as compared to RA. Male sex, absence of comorbidities and no csDMARDs co-administration are independent predictors of long-term persistence to therapy, irrespectively of the clinical diagnosis. Notably, both in RA and SpA, 6-month response predicted ETN survival in the long term.

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AB0376 DIFFERENCES IN IMMUNOGLOBULIN LEVELS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND RHEUMATOID ARTHRITIS TREATED WITH RITUXIMAB

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Background: Hypogammaglobulinemia (HGGS) is one of the adverse effects of Rituximab (RTX), a chimeric monoclonal antibody directed against the CD20 receptor, frequently observed in ANCA-associated vasculitis (AAV) patients.

Objectives: To study the characteristics of patients with AAV on RTX treatment and to analyze the factors associated with HGGS, as well as to compare them with patients with rheumatoid arthritis (RA) on the same treatment.

Methods: Retrospective descriptive study of patients with a diagnosis of AAV or RA treated with RTX who had immunoglobulin levels prior to treatment and after each cycle were included. Demographic, clinical and analytical variables were analyzed. Patients who developed HGGS versus those who did not were compared using Student's t and Mann-Whitney U for continuous variables and chi-square for categorical variables.

Results: Ninety-five patients were included, 19 (20%) with AAV and 76 (80%) with RA. Of the 34 (35.8%) who developed HGGS, 19 had RA (25%) and 15 AAV (79%) (p<0.001). The 6 patients who presented with severe HGGS (IgG<500) belonged to the AAV group.

The overall sample was divided into patients with HGGS and patients without (Table 1). Significant differences were obtained in relation to diagnosis (p<0.001), age at diagnosis and at the start of treatment, being higher in patients with HGGS (p 0.005 and p 0.001) and years of disease evolution (p 0.036). Patients with HGGS had a lower mean baseline IgG (p<0.001). The HGGS group had more severe infections (infections requiring admission) (p 0.005) and the time from RTX administration to the development of infection was shorter in this group (p 0.017). The frequency of abdominal infection was higher in the HGGS group (p 0.050), and there were no significant differences with the other types of infection.

Table 1.

	Total sample (n= 95)	HGGS IgG (n= 34)	No HGGS IgG (n= 61)	P
Women n/N(%)	70/95(73.7)	23/34(67.6)	47/61(77)	0.318
Age (m±SD)	64±12	68±10	62±12	0.005
Age at start of treatment (m±SD)	57±12	62±10	54±12	0.001
Years of evolution (m±SD)	11±9	8±9	12±10	0.036
RA n/N(%)	76/95(80)	19/34(55.9)	57/61(93.4)	<0.001
AAV n/N(%)	19/95(20)	15/34(44.1)	4/61(6.6)	<0.001
Glomerular filtration rate <60 n/N(%)	7/91(7.7)	4/34(11.8)	3/61(4.9)	0.164
GCS AD in the previous year (m±SD)	2918±3102	3265±3050	2690±3155	0.238
GC AD during treatment (m±SD)	4656±17713	2889±2778	5576±21775	0.271
Total GC AD (m±SD)	56411±326716	117050±484186	5879±6089	0.159
CFM AD (m±SD)	0.51±2.25	1.1±3.1	0.2±1.5	0.032
Baseline IgG (m±SD)	1107±340	933±346	1203±297	<0.001
Infection n/N(%)	58/95(61.1)	23/34(67.6)	35/61(57.3)	0.325
Severe infection n/N(%)	19/95(20)	12/34(35.3)	7/61(11.5)	0.005
Time to infection (months)(m±SD)	43±43	30±36	57±45	0.017
Exitus n/N(%)	8/95(8.4)	2/34(5.9)	6/61(9.9)	0.270

Conclusion: A significantly higher percentage of HGGS is observed in patients with AAV treated with RTX compared to patients with RA. The development of HGGS seems to be influenced by age at diagnosis and at the start of treatment, years of disease evolution and low levels of IgGs prior to the start of treatment. In addition, there is a higher frequency of severe infections in the HGGS group. Studies with larger sample sizes are needed to confirm these results.

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AB0377 DIFFERENCES OF EFFICACY OF TNF-A INHIBITORS AND THEIR IMMUNOGENICITY IN RHEUMATOID ARTHRITIS AND INFLAMMATORY BOWEL DISEASES

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Background: The immunogenicity of TNF-α inhibitors (TNFi) and its effect on their efficacy can depend on the underlying disease. To date, no studies were performed to directly compare this relation between different groups of immune-mediated diseases.

Objectives: To compare the effect of immunogenicity of TNFi on their efficacy in rheumatoid arthritis (RA) and inflammatory bowel diseases (IBD) (Crohn's disease (CD) and ulcerative colitis (UC)).

Methods: 20 patients with RA and 53 patients with IBD (38 (30.9%) with CD and 15 (12.2%) with UC) were observed for 17 [10; 27] months. 26 (35.6%) of them received infliximab (INX) infusions, 23 (31.5%) – adalimumab (ADM) and 24 (32.9%) – certolizumab pegol (CZP). The following criteria were used for the evaluation of the response to TNFi: EULAR criteria for RA, decrease of CDAI for CD and Mayo Score for UC. Trough level of TNFi and the level of anti-drug antibodies (ADAb) were measured in the serum samples drawn directly before the planned drug administration. The threshold for low trough level was determined as follows: 1 μg/mL for INX[1] in RA group and 5 μg/mL for INX[2] in IBD group, 5 μg/ml for ADM[3], and 20 μg/l for CZP[4].

Results: 17 (85%) patients with RA and 35 (66%) patients with IBD responded well to the treatment. Loss of response to the treatment developed in 3 (15%) cases of RA and 18 (34%) cases of IBD (p>0.05). The median trough level of INX was 0.22 [0.17; 6.19] μg/ml in RA and 1.56 [0.79; 3.87] μg/ml in IBD. The median trough level of ADM was 5.45 [1.05; 12.07] μg/mL in RA and 11.17 [3.19; 13.01] μg/mL in IBD. The tendency toward lower median trough level of CZP in IBD was observed (28.17 [20.69; 42.95] μg/mL in IBD vs 16.92 [8.31; 30.96] μg/mL in RA (p=0.09)). Low trough level of TNFi was found in 11 (55%) patients with RA and 27 (50.9%) patients with IBD. It did not differ significantly either between the diseases or between the TNFi (p>0.05). Loss of response was associated with low trough level of TNFi in all 3 cases of RA and in IBD – in 9 (50%) cases (p>0.05). Positive ADAb were detected in 6 (30%) patients with RA and 8 (15.1%) patients with IBD. The rate of positive ADAb was comparable between different TNFi and immune-mediated diseases (p>0.05). A tendency toward lower prevalence of ADAb to ADM in CD than in RA was observed

(0% vs 40%, OR 0.6, 95%CI 0.362 to 0.995, p=0.08). Association of loss of response to the treatment with ADAb was observed in 2 (66.7%) patients with RA and 2 (11.1%) patients with IBD. Inefficacy of TNFi due to immunogenicity was 6 times more frequent in RA than in IBD (OR 6.0, 95%CI 1.296 to 27.769, p=0.08).

Conclusion: All RA patients not responding to TNFi treatment had either low trough level of the drug or ADAb as opposed to IBD patients with inefficacy, half of which did not have ADAb or low trough level.

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AB0378 EFFECT OF RITUXIMAB ON BONE MINERAL DENSITY IN WOMEN WITH RHEUMATOID ARTHRITIS

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Objectives: To compare the effect of rituximab (RIT) treatment on bone mineral density (BMD) in women with rheumatoid arthritis (RA) and those with RA without biological therapy.

Methods: 78 women over 40 years with confirmed RA according to ACR/EULAR criteria (2010) were enrolled in the study: 48 patients treated with RIT and methotrexate (RIT+) and 30 women received only methotrexate (RIT-). The patients did not differ in the glucocorticoid therapy duration and cumulative dose. BMD was determined in the lumbar spine, femur neck and total hip using dual energy x-ray absorptiometry (DXA, Hologic 4500A) at baseline and after 1 year. RA activity was evaluated by disease activity score using 28 joint counts and erythrocyte sedimentation rate (DAS28 ESR). Nonparametric statistic tests were performed.

Results: There were no differences between patients RIT+ and RIT- in age (median - 58 [53; 63] years and 52 [50; 69] years, p>0.05), RA duration (median – 15 [4; 21] year and 9 [3; 11] year, p>0.05) and DAS28 ESR (median – 5.18 [4.35; 6.25] and 5.71 [4.66; 5.94]). The percentage BMD changes from baseline in lumbar spine, femoral neck and total hip were 0.2% [-3.9%; 4.0%], -1.8% [-6.2%; 2.4%] and -0.3% [-3.5%; 4.5%], respectively, in patients RIT+ and -1.0% [-4.9%; 3.3%], -2.5% [-5.8%; -0.4%], -1.7% [-4.3%; 4.2%], respectively, in persons RIT-. There were no differences in BMD changes in the pair matching test both patients RIT+ and RIT-. No correlations between BMD changes with age, RA duration and DAS28 ESR were found.

Conclusion: RIT had no effect on BMD in women with RA after 1 year therapy. BMD changes were not associated with age, RA duration and disease activity.

Disclosure of Interests: None declared

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AB0379 DOSE-DEPENDENT SUPPRESSION OF T CELL-DEPENDENT ANTIBODY RESPONSE IN HEALTHY VOLUNTEERS BY KPL-404, AN ANTI-CD40 MONOCLONAL ANTIBODY, SUPPORTS CHRONIC DOSING STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: An unmet need remains in patients with failure and/or inadequate response (IR) to biological disease-modifying antirheumatic drugs (bDMARD-IR) and/or Janus kinase inhibitors (JAKi-IR). The CD40/CD40L (CD154) costimulatory pathway is linked to inflammation and joint destruction in RA via production of autoantibodies and inflammatory mediators. KPL-404 is a humanized IgG4 antibody engineered to bind CD40 without triggering Fc effector functions (Muralidharan, 2019), which are known to have been associated with thromboembolic events seen in the first generation of CD40L-targeting therapies. In a first-in-human Phase 1 single ascending dose study, 52 healthy volunteers received single doses of KPL-404 administered either subcutaneously (SC) or intravenously (IV) with no dose-limiting safety findings, infectious episodes, or toxicities (Samant, 2021). The study demonstrated that with 10 mg/kg IV, full receptor occupancy (RO) was observed through day 71, and there was complete suppression of T-cell dependent antibody response (TDAR) to keyhole limpet hemocyanin challenge on day 1 and re-challenge on day 29 through day 57. With 5 mg/kg SC, full RO was observed through day 43, and there was complete suppression of TDAR through at least day 29. Complete suppression of ADA to KPL-404, an independent indicator of target engagement, was also observed while KPL-404 serum concentrations were above approximately 0.1 to 0.2 µg/mL and continued for at least 50 days and 57 days after 5 mg/kg SC and 10 mg/kg IV administration, respectively.

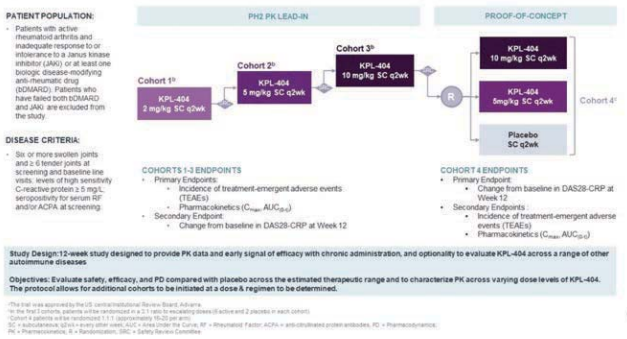
Objectives: Using Phase 1 and nonclinical data, identify chronic dosing regimens anticipated to yield PK in the sub-therapeutic, therapeutic, and supra-therapeutic ranges to be utilized in a Multiple Ascending Dose Phase 2 Study.

Methods: A PK model was used to simulate multiple dosing scenarios, including: 2.5, 5, and 10 mg/kg SC qwk, q2wk, and q4wk, as well as 10 mg/kg IV q4wk. The model was used to identify optimal Phase 2 dosing schedules by generating 1000 virtual subjects using the typical parameter estimates with between-subject variability included.

Results: Following SC administration, all subjects were predicted to achieve complete ADA suppression for the full dosing interval at/above 2.5 mg/kg SC q2wk. At 2 mg/kg SC q2wk (starting dose level), simulated steady-state 8-week data predicted PK in a sub-therapeutic range for most subjects and an approximately 31- and 18-fold safety margin relative to preclinical NOAEL dose. At 5 mg/kg SC q2wk, 100% of patients were predicted to be in a therapeutic range, indicating a potential practical efficacious dose level. At 10 mg/kg SC q2wk, 100% of patients were predicted to be in the supratherapeutic range.

These results support a Multiple Ascending Dose (MAD) Phase 2 study design, with PK lead-in comprised of 3 Cohorts at 2, 5, or 10 mg/kg SC q2wk (each randomized 6:2) and Proof-of-Concept phase (Cohort 4) comprised of 48-60 subjects randomized 1:1:1 to 10 mg/kg, 5 mg/kg, and placebo SC q2wk. The ongoing study will evaluate efficacy (Disease Activity of 28 joints using C-reactive protein [DAS28-CRP]), safety, PK, and pharmacodynamics (PD) of escalating doses levels of KPL-404 compared with placebo in patients with moderate to severe RA (bDMARD-IR or JAKi-IR). The study also allows the flexibility of optional cohorts including additional dosing regimens and/or subpopulations identified based on clinical response and biomarkers.

Figure 1. Study Design of the Phase 2 Trial[a] of KPL-404 in Rheumatoid Arthritis



Conclusion: Inhibition of the CD40-CD154 co-stimulatory interaction holds promise for the management of a spectrum of autoimmune diseases. KPL-404 demonstrated prolonged absorption/excretion capable of suppressing TDAR for extended periods allowing for use of extended dosing intervals irrespective of IV or SC dosing. These analyses supported the design of the ongoing Phase 2 study assessing the efficacy and safety KPL-404 in RA.

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Pfizer, Roche, Sanofi, Consultant of: Abbvie, Amgen, BMS, Kiniksa, Lilly, MSD, Pfizer, Roche, Sanofi, Fang Fang Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Alan Kivitz Shareholder of: Amgen, Gilead Sciences, Inc., GlaxoSmithKline, Novartis, Pfizer, Sanofi,, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, GlaxoSmithKline, Lilly, Merck, Novartis, Pfizer, Sanofi, UCB, Horizon, Consultant of: AbbVie, Boehringer Ingelheim, Flexion, Gilead Sciences, Inc., Janssen, Pfizer, Sanofi, SUN Pharma Advanced Research, Moses Njenga Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Arian Pano Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Costantino Pitzalis Speakers bureau: Abbott/AbbVie, Astra-Zeneca/MedImmune, BMS, Janssen/J&J, MSD, Pfizer, Roche/Genentech/Chugai, UCB.,, Consultant of: Abbott/AbbVie, Astellas, Astra-Zeneca/MedImmune, BMS, CelGene, Grunenthal, GSK, Janssen/J&J, Kiniksa, MSD, Pfizer, Sanofi, Roche / Genentech / Chugai, UCB., Grant/research support from: Abbott/AbbVie, Astellas, Astra-Zeneca/MedImmune, BMS, Janssen/J&J, MSD, Pfizer, Roche/Genentech/Chugai, UCB., Manoj Samant Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Steve Schmitz Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Madeline Spiers Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., Eben Tessari Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp., John Ziemniak Consultant of: Kiniksa Pharmaceuticals, Ltd., John F. Paolini Shareholder of: Kiniksa Pharmaceuticals Corp., Employee of: Kiniksa Pharmaceuticals Corp.

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AB0380 ANTI-TNFA: ORIGINATORS VS BIOSIMILARS, COMPARISON IN CLINICAL RESPONSE ASSESSMENT IN A MULTICENTER COHORT OF PATIENTS WITH INFLAMMATORY ARTHROPATHIES

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Background: Tumor necrosis factor (TNF)-α is one of principal proinflammatory cytokines involved in pathogenesis of different inflammatory arthropathies as Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS). Biotechnological drugs, represented among others by monoclonal antibodies directed against TNF-α, lead to a revolution in RA and spondylarthritis treatment. They were the first biological drugs used to treat these diseases, with good results in terms of safety and efficacy. Also because of high cost of these drugs, for some years biosimilars have been introduced in clinical practice. Biosimilars are less expensive (in Italy, less of 30% than bioriginators); they underwent to a severe process of "*comparability*" to assess safety and efficacy like their originators. In Italy, AIFA authorized SB4 (etanercept biosimilar), SB5 and ABP501 (adalimumab biosimilars) after passing III-phase randomized clinical trials; but *real-life* data and registers are lacking.

Objectives: Aim of this study is to compare biosimilars and bioriginators in terms of safety and efficacy in a real-life contest.

Methods: We consequently enrolled patients, affected by inflammatory arthropathies (RA, PsA, AS) and treated with biosimilars (SB4, ABP501), belonging to any of the main biological prescribing centers in the Lazio region, from 2017 to 2020. Moreover, we enrolled patients, affected by same inflammatory diseases, but treated with corresponding originator. Clinical and laboratory data as well as disease activity indices, were collected at recruitment (T0) and after 4 (T1), 8 (T2), 12 (T3) and 24 (T4) months of therapy. Adverse events were registered.

Results: The multicenter cohort was composed by 455 patients treated with biosimilars (SB4/ABP501 276/179; F/M 307/146; naïve 56%, median age/IQR 55/46-65) and 436 treated with originators (etanercept/adalimumab 186/259, F/M 279/157, naïve 67,2%, median age/IQR 53/43-62). No differences were found about safety, but biosimilar group presented a higher number of discontinuations due to inefficacy (p<0.001), observed at all time-points. Female gender, to be smoker and b-DMARDs naïve, the initial non-response to the drug were predictive factors of reduced drug survival (p=0,05, p=0,046, p=0,001 respectively). Retention rate at 24 months was 81.1% for bioriginators and 76.5% for biosimilars (with a median retention time of 20.7 and 18.9 months, respectively) (p=0.002). Patients with remission/low disease activity achievement at T1 showed a cumulative survival of 90% to biosimilar therapy until at T4 (p=0.001); early adverse reactions instead represented an important cause of subsequent drug discontinuation (p=0.001).

Conclusion: Real-life data demonstrated the same safety between biosimilars and originators but a reduced biosimilar retention rate at 24 months, about 76%. Despite their loss efficacy, biosimilars could be considered valid and safe, and a good and less expensive alternative to the originators, allowing access to these innovative treatments to a wider patient population.

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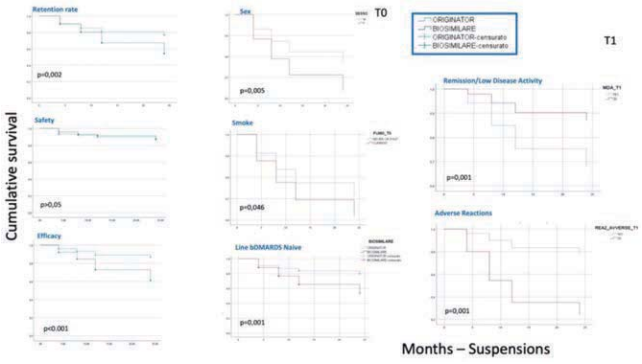

Figure 1.

Disclosure of Interests: None declared
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AB0381 ULTRASONOGRAPHY TO PREDICT FLARE AFTER DISCONTINUATION OF BIOLOGICS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REMISSION

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Background: Ultrasonography (US) has been suggested to be useful in predicting flare in patients with rheumatoid arthritis (RA) after discontinuation of biological disease-modifying antirheumatic drugs (bDMARDs).

Objectives: This study aimed to investigate whether US can predict flare after discontinuation of bDMARDs in RA patients who have achieved stringent remission criteria.

Methods: We prospectively enrolled RA patients who maintained a simplified disease activity index ≤ 3.3 and discontinued bDMARDs and measured clinical assessment and US every 2-3 months for 2 years. The US examination was performed on 40 joints using the semi-quantitative method of 0-3 on the Grey-scale (GS) and Power Doppler (PD), and the total values for each patient were used as the GS score and PD score. Joints graded as GS score ≥ 2 or PD score ≥ 1 were counted as US arthritis. In addition, tendons at 36 sites were counted with or without tendinitis/tenosynovitis to obtain a tendon score.

Results: Thirty-six patients were enrolled and two patients who dropped out early without flare were excluded from the comparative analyses. At baseline, the median GS score was 7, PD score was 0, US arthritis was 0, and tendon score was 0. The total PD score was 0 in 26 patients (72%) and it was 1 in 5 patients (14%). There were no significant differences in US findings between the relapse group (20 patients) and the non-relapse group (14 patients). Positive and negative predictive value for PD-positive findings (total PD score ≥1) were 60% and 42%, and for total PD score ≥2 were 60% and 41%, respectively.

Conclusion: The PD score in the US findings at the time of bDMARDs discontinuation was not predictive for future disease flare.

Disclosure of Interests: Takehisa Ogura Speakers bureau: AbbVie G.K, Ayako Hirata: None declared, Takaharu Kagtagiri: None declared, Yuto Takakura: None declared, Hideto Kameda Speakers bureau: AbbVie G.K., Asahi Kasei Pharma, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Eli Lilly Japan K.K., Gilead Sciences, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma, Novartis Pharma K.K., and Sanofi Pharma, Grant/research support from: AbbVie G.K., Asahi Kasei Pharma, Astellas Pharma Inc., Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Mitsubishi Tanabe Pharma, Novartis Pharma K.K., and Sanofi Pharma
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Rheumatoid arthritis - non biologic treatment and small molecules

AB0382 COMPARISON OF ADVERSE EVENTS (AES) RELATED TO MAJOR ANTI-RHEUMATIC DRUGS, REPORTED TO THE OFFICIAL JAPANESE ADVERSE DRUG EVENT REPORT DATABASE (JADER)

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Background: Currently, many disease-modifying anti-rheumatic drugs (DMARDs) are available for the treatment of rheumatoid arthritis (RA). Among them, methotrexate (MTX), biologic DMARDs (bDMARDs) and Janus kinase inhibitors (JAKi) are the major options. AEs related to these are major concerns. In Japan, the AEs data spontaneously reported to and summarized by Pharmaceuticals and Medical Devices Agency (PMDA) are freely accessible.

Objectives: The major AEs relating to MTX, bDMARDs, and JAKi observed in the real world were compared.

Methods: The number of AEs listed by JADER from 2014 to 2020 was collected. The AEs were classified by System Organ Class (SOC) of Medical Dictionary for Regulatory Activities (MedDRA) and compared using the chi-square test. The bDMARDs included were etanercept (ETN), adalimumab (ADA), golimumab (GOL), tocilizumab (TCZ), and abatacept (ABT), and JAKi was tofacitinib (TOF) and baricitinib (BAR).

Results: The total number of AEs was 27,604. The number was significantly increasing in total and MTX, GOL, TOF during these years, although the number of cases that have each DMARD is not known in this study. The proportion of SOCs among each DMARD was similar throughout the period.

The most frequent was infections/infestations in all DMARDs except for MTX, in which neoplasms were the most. The primary cause of infection was bacterial, including pneumonia. Varicella-zoster virus infection in JAKi, and tuberculosis in ADA and GOL were conspicuous.

Neoplasms were the second major in many DMARDs. Lymphoproliferative disorders were most common in MTX-related neoplasms, whereas solid tumors were more in other DMARDs like ABT or BAR.

Other SOCs include all other categories such as the musculoskeletal, nervous system, cardiac, and vascular disorders. Among them, major adverse cardiovascular events (MACE, including cardiovascular death, myocardial infarction and stroke) and venous thromboembolism (VTE) were both reported in small numbers. However, more MACE was noted in BAR and GOL, and more VTE was in BAR and TOF compared to other DMARDs.

Conclusion: The number of AEs cases related to DMARDs was increasing. Significant difference among AEs related to DMARDs was noted in the JADER database, especially regarding MTX and JAKi.

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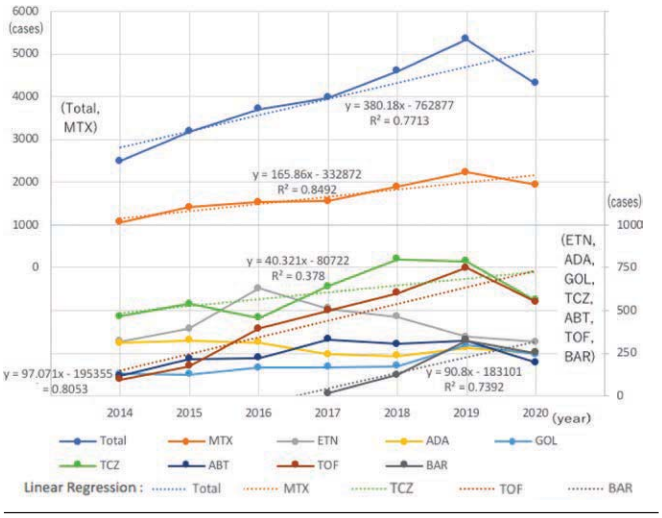

Figure 1. Total number of adverse events reported from 2014 to 2020. Linear regression is shown only for DMARDs with increasing numbers of AEs.

Disclosure of Interests: None declared
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AB0383 COMPARISON OF EFFICACY AND SAFETY IN JAK INHIBITOR DUE TO A DIFFERENCE OF SELECTIVITY – TOFACITINIB VS. BARICITINIB –

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Background: Each Janus Kinase Inhibitor (JAK-i) has different selectivity of JAKs, such as JAK1, JAK2, JAK3, and TIK2. However, little has been known regarding mode of action due to the selectivity difference in clinical practice for treating rheumatoid arthritis (RA).

Objectives: The aim of this study is to compare difference of efficacy and safety in two JAK-i; between tofacitinib (TOF) and baricitinib (BAR) in clinical practice using one-center retrospective cohort.

Methods: Within the case which administered TOF or BAR to the RA patient who the effect was insufficient in the existing treatment and the disease activity was over the middle disease activity using simplified disease activity index (SDAI). At the start of administration (baseline), 5 mg tablets of TOF were taken twice a day or 4 mg tablets of BAR were taken one a day. Patients were divided by drug and included their sex, age at onset, anti-cyclic citrullinated polypeptide antibodies (ACPA) titer, length of RA history at onset, Sharp/van der Heijde score (SHS) at onset, Naïve/Not Naive for biologic DMARDs or JAK-i, 28-joints disease activity score (DAS28), SDAI, Health Assessment Questionnaire Disability Index (HAQ-DI), and pain score with visual analog scale (PS-VAS). It was classified into large joint and small joint, and the point was independently scored by swelling and pressure pain by size and position in each joint. Total score of the

Table 1. Total case numbers and proportion of adverse events related to each DMARD.

DMARDs (year of launch)	Total	MTX (1999)	ETN (2005)	ADA (2008)	GOL (2011)	TCZ (2008)	ABT (2010)	TOF (2013)	BAR (2017)
Number of AEs	27604	11636	2974	1959	1302	4245	1709	3065	714
Blood/lymphatic system disorders	5.8	9.9	2.0	3.2	2.6	4.0	0.9	2.8	3.5
Gastrointestinal disorders	5.0	4.1	3.4	7.5	5.9	7.7	3.9	5.2	4.2
General disorders/administration site reactions	4.6	3.2	11.3	4.1	2.2	3.0	4.0	7.6	2.5
Infections/infestations	28.0	20.3	21.3	32.2	34.2	36.5	37.1	37.0	49.2
Pneumonia (bacterial)	6.6	4.0	6.1	5.2	10.9	7.7	12.5	9.4	15.1
Other bacterial infection	9.1	5.9	5.6	12.3	9.5	17.6	9.1	9.8	10.6
Herpes zoster	2.1	1.1	0.4	1.4	1.2	1.0	1.2	8.2	11.2
Tuberculosis	1.4	0.9	1.9	6.0	3.5	0.6	0.6	0.3	1.0
Investigations	5.0	4.9	5.5	2.3	2.6	5.7	2.2	8.3	2.8
Neoplasms benign, malignant, unspecified	21.1	34.8	11.0	13.5	12.7	7.4	15.6	10.8	15.4
Lymphoproliferative diseases	14.3	29.8	2.8	4.1	4.0	2.2	4.5	2.1	2.2
Solid tumors	5.6	3.8	7.3	7.8	7.5	4.0	9.9	7.3	10.5
Respiratory, thoracic, mediastinal disorders	7.1	6.8	8.3	8.4	9.5	6.5	7.4	6.2	6.7
Other System Organ Class	23.3	15.9	37.3	28.8	30.2	29.2	28.9	22.2	15.7
Major adverse cardiovascular events	1.1	0.4	1.1	1.6	2.5	1.5	1.6	1.3	2.9
Venous thromboembolism	0.4	0.1	0.4	0.5	0.6	0.3	0.2	1.1	1.4

Background colors indicate: comparing to the total cases, higher with *p<0.05*, light pink; higher with *p<0.00001*, dark pink; higher with *p<1E-10*, red. Lower with *p<0.05*, light blue; lower with *p<0.00001*, blue; lower with *p<1E-10*, dark blue, using chi-square test. Yellow indicates System Organ Classes.

involved joints for each part; upper-extremities, lower extremities, big joints, and small joints (UES/LES/BJS/SJS), rheumatoid factor (RF) titer, serum matrix metalloprotease-3 (MMP-3) level, serum creatinine (Cr) level, and estimated glomerular filtration rate (eGFR) of each part were measured. The mean values of each group were obtained at baseline, 1, 2, 3, 6, 9, and 12 months, and the two groups were statistically compared using the Mann-Whitney U-test. As a sub-analysis, each drug group was divided into bio or JAK-i naive, age ≥ 70 years, disease duration ≥ 10 years, SHS ≥ 100. The change of DAS28 under each 2 divided condition was compared using Mann-Whitney U-test. Similar comparison was carried out with RA patient who administered golimumab (GOL) as a control group. The significance level was less than 5%.

Continuation rate (the withdrawal after the remission introduction is put in the continuation) in 12 months after baseline was also compared.

Results: A total of 82 patients were picked up, in whom 22 TOF group, 31 BAR group, and 29 GOL group included. Both DAS28 and SDAI were consistently lower in the BAR than in the other 2 groups from 1 month after baseline. SDAI in the BAR was significantly lower than in the GOL at 3 months after the baseline. The HAQ-DI score at 6 months after baseline was significantly lower in the BAR than in the GOL. PS-VAS in the GOL was significantly higher than the other two groups at 2, 3 and 6 months after baseline. In the joint point, BJS in the BAR was significantly lower than that in the GOL at 2, 3, and 6 month after baseline. SJS in the GOL was significantly lower than that in the TOF at 6 and 12 months after baseline. There was no significant difference in MMP -3, RF, Cr and eGFR between the 3 groups in any observation month, but Cr increased after the start in the BAR group and eGFR tended to decrease.

In the sub-analysis, the decrease of DAS28 at 1 year after baseline with a history of ≥ 10 years was significantly greater than in those with a history of < 10 years in the TOF, as well as DAS28 at 1 year in those with SHS ≥ 100 decreased significantly more than that in those < 100. These phenomena was not observed in the BAR group.

The continuation rate at 12 months after the start of administration was 86.4% in the TOF, 89.3% in the BAR and 69.0% in the GOL.

Conclusion: Even JAK-i characteristics in action differs for each drug. It is needed to choose appropriate drug based on these drug characteristics.

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AB0384

THE EFFECT OF A LIFESTYLE PROGRAM ON PATIENTS AT RISK FOR RHEUMATOID ARTHRITIS:THE "PLANTS FOR JOINTS" PILOT RANDOMIZED CLINICAL TRIAL

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Background: An unhealthy lifestyle increases the risk of developing rheumatoid arthritis (RA). Interventions including plant-based diets, physical activity, and stress management have shown benefits for RA patients but have not yet been evaluated in a program for patients at risk for RA.

Objectives: To investigate preliminary effectiveness of a multidisciplinary lifestyle program on RA risk in patients at risk for RA, in comparison to usual care.

Methods: In the "Plants for Joints" (PFJ) pilot RCT, patients with anti-citrullinated protein antibody (ACPA) positive arthralgia were randomized to the PFJ or control group. Both groups received usual care while the PFJ group additionally followed a 16-week lifestyle program based on a whole food plant-based diet, physical activity, and stress management.[1] The primary outcome was risk of developing RA as quantified by the RA risk score (including family history, symmetry, stiffness, pain level, RF/ACPA level).[2] The maximum score (13 points) was given to participants who developed RA. Secondary outcomes included self-reported pain intensity, inflammatory, anthropometric, and metabolic markers, and serum levels of ACPA and rheumatoid factor (RF). A linear mixed model for between group analysis was used, adjusted for baseline values.

Results: 14 out of 17 included patients completed the study (all female, mean age 47 years). Three patients (n = 2 PFJ group, n = 1 control group) were diagnosed with RA after mean 9.6 weeks and remained in the study. After 16 weeks there was no significant difference in RA risk score between PFJ and control groups (Figure 1). Compared to the control group, the PFJ group had significantly lower fat mass and LDL-cholesterol after 16 weeks (Table 1). After the intervention the PFJ group had an average weight loss of 4.9 kg, of which 2.7 kg was fat mass.

Conclusion: The results of this pilot study do not suggest the PFJ lifestyle program influenced RA risk score, pain, or autoantibody levels, although possible effects cannot be excluded due to the small sample size. However, metabolic health clearly improved in the PFJ group.

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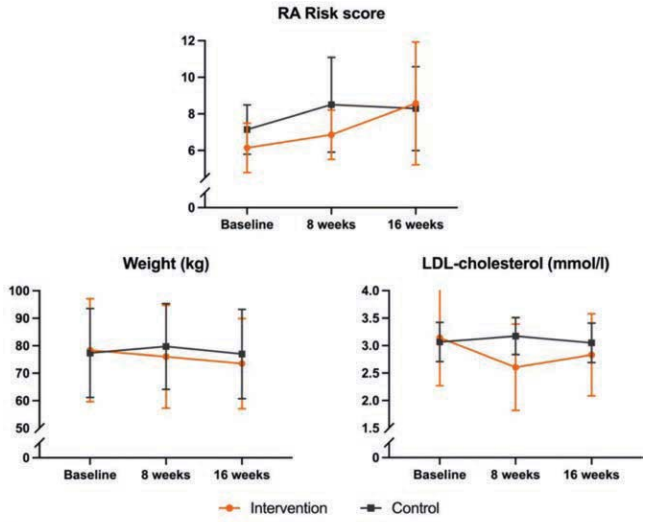

Figure 1. Effect of a 16-week lifestyle intervention on rheumatoid arthritis (RA) risk and secondary outcomes in ACPA positive arthralgia patients. Data shown as mean ± SD.

Table 1. Results reported as mean (SD) when normally distributed and median [Q1 – Q3] when skewed. *P*-value <0.05 = significant. RA = rheumatoid arthritis, ACPA = anti-citrullinated protein antibody, RF = Rheumatoid factor, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein.

	Plants for Joints group (n = 7)		Control group (n = 7)		
	Baseline	**Week 16**	**Baseline**	**Week 16**	***p*-value**
RA risk and related outcomes					
RA risk score	6.1 (1.4)	8.6 (3.4)	7.1 (1.4)	8.3 (2.3)	0.56
Pain intensity	4.9 (2.6)	3.8 (1.9)	5.7 (2.6)	4.0 (2.1)	0.74
ACPA, kU/l	330 [94 - 530]	225 [116 - 550]	256 [79 - 462]	202 [94 - 403]	0.86
RF, kU/l	13 [3 - 68]	11 [3 - 56]	12 [3 - 21]	5 [4 - 12]	0.96
RA diagnosis, *N*	0	2	0	1	-
Inflammation					
ESR, mmol/hour	9 [6 - 15]	7 [6 - 9]	7 [6 - 12]	12 [8 -17]	0.79
CRP, mg/l	0.7 [0.6 - 2.5]	0.6 [0.6 - 1.2]	3.0 [1.1 - 3.6]	3.3 [1.3 - 6.7]	0.58
Anthropometric					
Weight, kg	78.4 (18.6)	73.5 (16.4)	77.4 (16.2)	77.0 (16.3)	0.28
BMI, kgm^{-2}	26.8 (5.3)	25.1 (4.5)	28.2 (6.2)	28.0 (6.0)	0.23
Fat mass, kg	30.6 (14.3)	27.9 (12.3)	31.2 (12.8)	29.8 (13.0)	<0.01
Waist circumference, cm	87.9 (13.3)	86.6 (11.6)	91.6 (15.5)	90.6 (16.1)	0.33
Metabolic					
LDL-cholesterol, mmol/l	3.1 (0.87)	2.83 (0.75)	3.07 (0.36)	3.05 (0.36)	<0.01
HbA1C, mmol/mol	34.9 (3.2)	34.4 (3.1)	35.1 (3.0)	36.9 (3.6)	0.97

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AB0385

BARICITINIB LEADS TO RAPID AND PERSISTENT RESOLUTION OF SYNOVITIS AS MEASURED BY HAND MRI IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS (RA) FAILING CS/BDMARD THERAPY

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Background: RA is characterized by synovial inflammation resulting in local bone loss [1]. Inhibitors of JAK/Stat pathways, such as baricitinib, demonstrated efficacy in reducing signs and symptoms of RA in clinical trials, however, little is known about their effects on synovitis and bone structure [2]. Preclinical and clinical observations suggest a positive effect JAK inhibitors on bone mass and microstructure, however no prospective, interventional clinical trial has been performed so far [3].
Objectives: The aim of this study is to evaluate the effect of baricitinib on local inflammation (synovitis and osteitis) and bone structure (erosions) in RA patients failing on cs/bDMARD therapy using hand MRI.
Methods: BAREBONE is a prospective, interventional, open label, monocentric single center study (EUDRACT 2018-001164-32 / NCT03701789) to assess the effect of baricitinib (4mg/day) on local MRI inflammation and structure in patients with active RA. Besides demographic and clinical characteristics, hand joint inflammation was assessed by magnetic resonance imaging (MRI) using a 1.5 Tesla scanner (Siemens Magnetom Aera T1w TSE cor, T2w TIRM cor, T2w TSE fat-sat trans, T1w TSE fat-sat trans + cor after KM;). at baseline, week 24 and week 48. Scans were assessed for synovitis, osteitis and bone erosions using the RAMRIS scoring system using two independent blinded readers (SK and SB). Intraclass correlation coefficients were calculated for total RAMRIS and synovitis, erosion and osteitis subscores and in a second step differences between cs and bDMARD failure were elaborated. Variables are summarized descriptively using means and 95% bootstrap confidence intervals for continuous outcomes and as number and percentages for categorical outcomes.
Results: Thirty- two RA patients were screened and 30 patients were included (age: 53.4 [SD 12.6] years; sex: f/m N 24/6; disease duration: 3 [IQR 2.0 – 8.0] years; biologic naïve/bDMARD failure 16/14). 27 patients completed the trial while MRI data was available for 24 patients at week 48. Demographics and clinical characteristics can be seen in Table 1. Total RAMRIS scores slightly decreased from 20.6 (95% CI 14.4 -27.8) at baseline (BL) to 18.3 (11.5 -26.5) at week 48. The synovitis subscore mainly contributed to total RAMRIS reduction by significantly improving from 5.3 (4.0 - 6.8) at BL to 2.7 (1.5 - 4.0) at week 48 with a score change of -2.9 (-4.0 to -1.8). At week 48, 12 patients (44.4%) had no signs of synovitis compared to only 3 patients at BL. In contrast, RAMRIS osteitis subscores only marginally decreased from 4.9 (2.2 - 8.4) at BL to 4.0 (1.9 - 6.7) at week 48. RAMRIS erosion score remained stable over the 48-week observation time. A significant difference in RAMRIS synovitis change for biologic naïve -3.8 (-5.2 to -2.6) vs biologic failure -1.0 (-2.2 to 0.4 could be observed at week 48). With respect to clinical disease activity, DAS 28 score decreased from 4.8 (4.5 – 5.1) at BL to 2.9 (2.5 – 3.3) at week 48. Detailed results can be found in Table 1 and Figure 1. Intraclass coefficient (95%CI) for RAMRIS scoring was high for both readers 0.997 (0.994 to 0.998).
Conclusion: Our study shows that baricitinib primarily reduces MRI synovitis in RA patients that have previously failed csDMARD and bDMARD therapy and particularly in patients who are biologic naïve.
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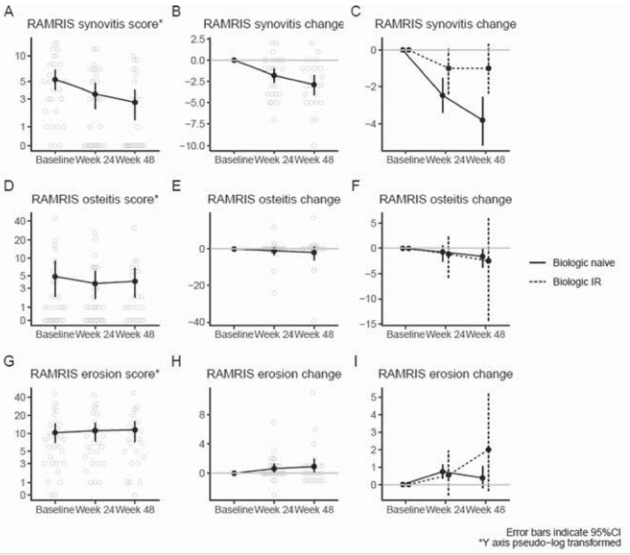

Figure 1: RAMRIS scores for synovitis, osteitis and erosion at baseline, week 24 and week 48 (A, D, G) and their corresponding changes in total (B, E, H) and subgroups naïve to bDMARD/ failing on bDMARD therapy (C, F, I).

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Table 1. Demographics, DAS 28 ESR, RAMRIS total score and RAMRIS subset scores at baseline, week 24 and week 48 are shown as well as number of patients with improvement and resolution of synovitis.

			Baseline	Week 24	Week 48
N			30	30	27
Age		Mean [SD]	53.5 (12.6)		
Gender	female	n [%]	24 (80.0)		
	male	n [%]	6 (20.0)		
Disease duration, years		Median (IQR)	3.0 (2.0-8.0)		
DAS-28 ESR		Mean [95%CI]	4.8 (4.5 to 5.1)	3.0 (2.7 to 3.3)	2.7 (2.4 to 3.0)
MRI available		n [%]	30 (100.0)	28 (93.3)	24 (88.9)
RAMRIS total		Mean [95%CI]	20.6 (14.4 to 27.6)	18.4 (12.6 to 25.4)	18.3 (11.5 to 26.5)
RAMRIS total change		Mean [95%CI]	0.0 (0.0 to 0.0)	-2.1 (-4.0 to -0.4)	-3.9 (-7.2 to -0.5)
RAMRIS synovitis		Mean [95%CI]	5.3 (3.9 to 6.9)	3.5 (2.2 to 4.9)	2.7 (1.5 to 4.0)
RAMRIS synovitis change		Mean [95%CI]	0.0 (0.0 to 0.0)	-1.8 (-2.5 to -1.0)	-2.9 (-4.0 to -1.8)
RAMRIS synovitis improved		patients n [%]		10 (33.3)	13 (48.1)
RAMRIS synovitis resolved		patients n [%]		10 (33.3)	12 (44.4)
RAMRIS osteitis		Mean [95%CI]	4.9 (2.2 to 8.4)	3.7 (1.5 to 6.2)	4.0 (1.9 to 6.7)
RAMRIS osteitis change		Mean [95%CI]	0.0 (0.0 to 0.0)	-0.9 (-3.1 to 1.0)	-1.9 (-5.7 to 1.1)
RAMRIS osteitis improved		patients n [%]		2 (6.7)	4 (14.8)
RAMRIS erosion		Mean [95%CI]	10.4 (7.3 to 14.6)	11.2 (7.7 to 15.0)	11.6 (7.5 to 16.6)
RAMRIS erosion change		Mean [95%CI]	0.0 (0.0 to 0.0)	0.6 (0.1 to 1.2)	0.9 (0.0 to 2.1)
RAMRIS erosion worsened		patients n [%]		2 (6.7)	3 (11.1)

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AB0386 ANALYSIS OF THE RELATIONSHIP BETWEEN THE METHOTREXATE PHARMACOKINETIC PARAMETERS AND RESPONSE TO METHOTREXATE THERAPY IN RHEUMATOID ARTHRITIS

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Background: The key link in the therapeutic drug monitoring of methotrexate (MTX) is the measurement of the concentrations of its most stable metabolites, as well as products of the early and late stages of MTX conversion (short-chain polyglutamates). Metabolic rate of MTX can depend on the clinical characteristics of patients and concomitant drug therapy.
Objectives: To reveal the regularity of the distribution of various metabolites in patients who responded and did not respond to MTX therapy. To compare groups of patients with different responses to MTX according to clinical characteristics.
Methods: The study included 79 RA diagnosis according to ACR/EULAR 2010 criteria, 65 (82%) women and 14 (18%) men, aged 53 ± 11 years, naiive to MTX. All patients had normal renal excretory function (GFR more than 60 ml / min). All patients were prescribed MTX of 10-15 mg/m2 of body surface. Achievement of therapy targets was established according to the EULAR therapy response criteria. The determination of MTX monoglutamate in erythrocytes (ER) and mononuclear cells (MO), as well as the main metabolites of MTX-polyglutamates with 2,3 and 4 glutamate residues (MTXPG 2-4), as well as 7-hydroxymethotrexate (7-OH-MTX) was measured by the tandem chromatomass spectrometry after 4, 12 and 24 weeks of therapy, the result was expressed in nmol/L. The calculation was performed using the statistical data analysis package Statistica 10 for Windows (StatSoft Inc., USA) using the methods of parametric and nonparametric statistics.
Results: By the 24th week of therapy, 34 (43%) (group 1) patients achieved the targets of therapy, 36 (46%) did not achieve (group 2). MTX withdrawn in 5 (6%) patients - due to adverse reactions. 4 (5%) were unable to continue to participate due to SARS-CoV2 pandemic. After 4 weeks of treatment, the concentration of various MTX metabolites did not differ in the groups. After 12 weeks of therapy, significant differences were found in the content of 7-OH MTX in the ER: 28.19 [7.28;58.07] and 5.89 [0.79;20.03], respectively (p=0.002); the concentration of the remaining fractions did not differ. Group 1 showed a higher concentration of 7-OH-MTX in MO after 24 weeks of therapy - 5.23 [1.39;12.52] and 1.05 [0.07;3.55], respectively (p = 0.006). No differences between the concentrations of other MTX metabolites were found. The groups were matched for age, body mass index, duration of RA, and disease activity at the baseline. In group 2, patients used statins more often (2 (6%) versus 6 (37%), p = 0.01), however, there were no statistically significant differences in the concentration of MTX metabolites in the groups of patients taking and not taking statins.
Conclusion: The concentration of 7-OH-MTX after 12 and 24 weeks of therapy is statistically higher in the group of patients who responded to therapy. 7-OH-MTX appears to be a more persistent metabolite of MTX, therefore, it is more applicable for therapeutic drug monitoring of MTX. Patients taking statins may be potential nonresponders to MTX therapy.
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AB0387 THE RELATIONSHIP BETWEEN JAK INHIBITORS AND CREATINE KINASE ELEVATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A REAL-WORLD CLINICAL STUDY

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Background: Some cases of creatine kinase (CK) elevation caused by Janus kinase (JAK) inhibitor treatment for rheumatoid arthritis (RA) have been reported in clinical trials[1]. However, the frequency and patients' background characteristics in clinical practice are unknown.
Objectives: The correlation between JAK inhibitor treatment for RA and changes in CK levels in clinical practice were investigated using a multicenter database.
Methods: The multicenter database of JAK inhibitors was used, and 103 (tofacitinib 46, baricitinib 44, upadacitinib 11, peficitinib 1, filgotinib 1) of 265 RA patients were followed up at 24 weeks, and their CK levels were evaluated. The time-dependent change of CK was evaluated by sex and analyzed by the Wilcoxon signed-rank test. The percentage abnormal from the standard titer was calculated. The factors related to an elevated CK at 24 weeks were investigated using patients' background characteristics at the time of starting JAK inhibitors by univariate analysis.
Results: Women accounted for 85.4% of the patients, the median age was 68 years, disease duration was 15 years, and the mean DAS28ESR was 5.00. The CK levels of both men and women were significantly elevated at 4 weeks and maintained until 24 weeks (men, women: 63, 62 (0 weeks), 101, 95 (4 weeks), 119, 96 (12 weeks), 155, 99 (24 weeks), U/L, P<0.001) (Figure 1). The percentage abnormal was also significantly increased at 4 weeks and maintained until 24 weeks (5.8% (0 weeks), 20.7% (4 weeks), 26.3% (12 weeks), 24.3% (24 weeks), P=0.002). The factors significantly positively related to elevated CK levels at 24 weeks were male, CK, creatinine, and lactate dehydrogenase (LDH), and stage, class, modified health assessment questionnaire, estimated glomerular filtration rate (eGFR), and glucocorticoid use were significantly negatively correlated (Table 1). There were no significant differences in CK elevation among the agents.

Table 1. Characteristics at the time of starting JAK inhibitors related to elevated creatine kinase levels at 24 weeks

	Univariate	
Data at stating JAK inhibitors	R value	P value
Creatine kinase	0.653	<0.001
Gender, men	0.247	0.012
Steinbrocker stage	-0.215	0.039
Steinbrocker class	-0.277	0.008
modified health assessment questionnaire	-0.268	0.008
Creatinine	0.289	0.003
eGFR	-0.231	0.019
LDH	0.201	0.041
Glucocorticoid use	-0.409	0.008

Analyzed by Spearman rank correlation coefficient

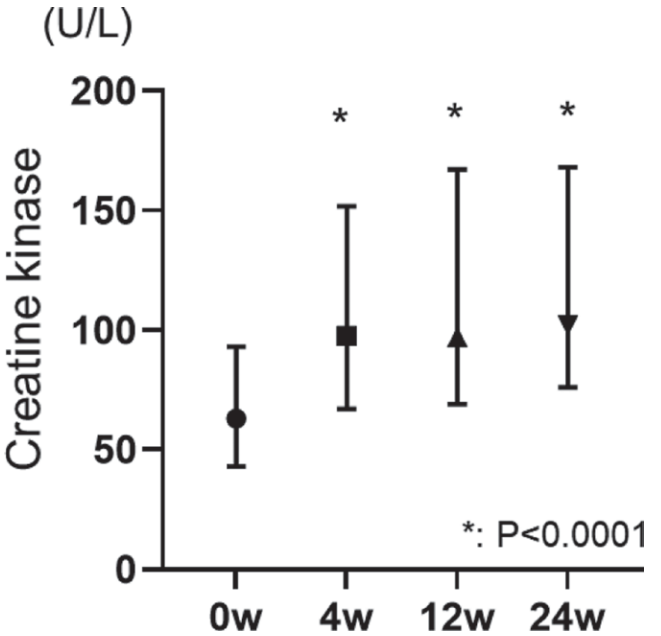

Figure 1. Time-dependent changes of CK in all RA patients

Conclusion: CK was significantly elevated at 4 weeks and maintained until 24 weeks. However, no patients complained of muscle pain and stopped JAK inhibitors. Patients with high CK, low eGFR, high LDH, or maintained activities of daily

living at the time of starting JAK inhibitors tended to have high CK levels at 24 weeks.

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Disclosure of Interests: None declared

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AB0388 FRENCH REAL LIFE SAFETY DATA ON THE USE OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: OBSERVATIONAL STUDY, DEFACTO

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Background: Tofacitinib, an oral Janus Kinase inhibitor, is indicated in the treatment of adult patients (pts) with active, moderate to severe rheumatoid arthritis (RA).

Objectives: The objective of this work is to describe the tofacitinib's safety profile in the DeFacTo study (French prospective observational study).

Methods: The safety profile of tofacitinib was assessed on the basis of interim data from a descriptive analysis of pts having taken at least one dose of tofacitinib in the context of the DeFacTo study.

Results: Of the 313 pts enrolled in the study, 301 had received tofacitinib and were included in the safety analysis. Of these, 276 fulfilled the eligibility criteria and included 219 who had ≥ 1 year follow-up and a mean exposure period of 368 ± 197.1 days. As of 15 March 2021, 122 patients are continuing to take tofacitinib therapy (76 missing prescription data). On inclusion, 77.9% of the 276 pts were females of mean (± SD) age 59.7 ± 11.7 years and a median disease duration of 9.1 years [Q1;Q3: 4.1; 19.2]. A history of cardiovascular disease was found in 12.5% of cases, (4.4% myocardial infraction, 5.5% stroke/transient ischemic attack, 1.5% heart failure and 1.5% peripheral arterial occlusive disease); 5.5% had a history of cancer, 17.5% a prior infection and 46% were smokers/former smokers. Tofacitinib was prescribed in combination with a csDMARD in 58.3% of pts and with corticosteroids in 54.3% of cases. At the cut-off date of 15 March 2021, of the 301 patients, adverse effects (AE) had been reported in 44.9% of cases of which 10.6% were considered serious (SAE). Infections were detected in 18.6% of pts (Table 1).

Table 1. Real life safety data for tofacitinib according to age

N, (%)	< 65 years (n=190)	≥ 65 years (n=110)	Total (n=301*)
Adverse effect	80 (42.1)	55 (50.0)	135 (44.9)
Serious adverse effect	16 (8.4)	16 (14.5)	32 (10.6)
Infection	33 (17.4)	23 (20.9)	56 (18.6)
Severe infection	3 (1.6)	4 (3.6)	7 (2.3)
AE of interest (number of events)			
Infection			
Herpes zoster	5	5	10
Severe infection			
Herpes zoster	1	0	1
Tuberculosis	0	2	2
Cancer			
Small-cell carcinoma	0	1	1
MACE			
Stroke	1	0	1
Thromboembolic events			
Venous thrombosis	0	1	1
Death	0	0	0

*1 patient for whom age is unknown but is counted in the total.

Conclusion: These purely descriptive interim results reveal a safety profile for tofacitinib in patients with RA, similar to that previously reported in clinical and observational studies. [1-2]

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Disclosure of Interests: Cécile Gaujoux-Viala Speakers bureau: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Amgen; Boeringhe; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Andre BASCH Speakers bureau: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB, Consultant of: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB,, Slim Lassoued: None declared, Fabienne COURY-LUCAS Consultant of: AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Novartis and Pfizer, Grant/research support from: AbbVie, Biogen, Roche Chugai, Pfizer, and UCB,, Meriem Kessouri Shareholder of: Pfizer, Employee of: Pfizer, Nadir Mammar Shareholder of: Pfizer, Employee of: Pfizer, Yves Brault Shareholder of: Pfizer, Employee of: Pfizer, Thierry Lequerre Consultant of: Abbvie, BMS, Boeringher, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Roche – Chugai, Sanofi, UCB,, Carine Salliot Consultant of: Biogen, Lilly, Novartis, Roche Chugai, Pfizer

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AB0389 EVOLUTION OF MONOTHERAPY IN RHEUMATOID ARTHRITIS: IMPACT OF THE RISE OF JAK INHIBITOR

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Background: According to different international registries, the frequency of use of biological agents in monotherapy in RA ranges from 12 to 39%. Targeted synthetic DMARDs (tsDMARDs-Jaki) have shown great efficacy when used as monotherapy. The rationale for this study is based on the fact that the frequency has increased with the appearance of the Jaki.

Objectives: To estimate the frequency and reason of the use of biological drugs (bDMARDs) or tsDMARDs in monotherapy since 2013 (Year the Jaki were available in Argentina). To describe the frequency of monotherapy by treatment class and analyze the differential characteristics.

Methods: Retrospective and cross-sectional multicenter study (10 reference centers from Argentina). Consecutive patients, ≥18 years, diagnosis of RA (ACR / EULAR 2010), who were under treatment with bDMARDs or tsDMARDs, started after 2013. Socio-demographic, disease and therapeutic data were collected.

Statistical analysis: descriptive statistics, Chi2 test, Fisher's exact test, Student's T test and Mann Whitney were performed, according to the nature of the variables. A p <0.05 was considered significant.

Results: Total 505 patients were included, 87.7% women, with a mean age 58 years (SD ± 13.5) and disease duration of 13 years (SD ± 7.8). Treatment: TNF blocker 42.1%, JAKi 30.3%, IL-6 blocker 10.9% and other treatments 16.8%.

Since 2013, the frequency of monotherapy was 49% (95% CI: 45-53), in the last visit the current frequency was 41% (95% CI 37-45),of this 40% received JAKi. JAKi and IL-6 blocker were the treatments that were used more frequently in monotherapy vs combination modality (Figure 1).

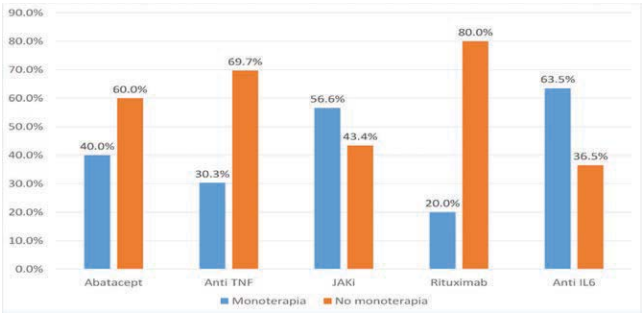

Figure 1.

The main causes of monotherapy were intolerance (39.9%), adverse event (22%), physician's decision (20.2%) and lack of adherence (17.7%) to DMARDs. Patients who were active workers (64% vs 55%, p <0.05), with higher socioeconomic

status (31.4% vs 17.2% p <0.01), better mean HAQ at diagnosis (1.1 vs 1.3, p <0.05) an association was observed with monotherapy. In addition, an association was observed with the use of monotherapy in patients in the 2nd biological line or higher vs 1st line (53% vs 33%, p <0.01), lower polypharmacy (45.6% vs 60%, p <0.02) and a shorter mean time of biological treatment (47 months vs 39 months, p <0.01). These variables were entered in a logistic regression model, the results of the independently associated variables are shown in Table 1.

Table 1.

Variable	p	OR	CI 95%	
Employment status (active).	0,191	1,327	0,868	2,029
Socioeconomic level (medium-high stratum)	**0,002**	**2,15**	**1,323**	**3,494**
HAQ at diagnosis, M (SD)	**0,019**	**0,704**	**0,524**	**0,944**
First Line of biological treatment or Jaki (yes)	**0,02**	**0,459**	**0,3**	**0,7**
Polypharmacy (>4 drugs) (yes)	**0,018**	**0,603**	**0,395**	**0,918**
bDMARDs or tsDMARDs exposure time (months)	0,054	0,994	0,987	1

Conclusion: The frequency of monotherapy, since the Jaki's emergence, was 49% (all follow-up) and 41% (current-last visit). Intolerance to cDMARDs doctor and the patient decision were the main cause. The monotherapy use pattern was greater in those who received JAKi and anti IL6. The use of monotherapy was associated with work activity, socioeconomic status, and functional capacity at diagnosis. An association was also observed with less polypharmacy.

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AB0390 COST-EFFECTIVENESS OF IGURATIMOD IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) BY USING A CLAIMS-BASED ALGORITHM: RETROSPECTIVE ANALYSIS OF REAL-WORLD DATA

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Background: Iguratimod (IGU), as one of the conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), has been approved by National Medical Products Administration (NMPA) to treat Rheumatoid arthritis (RA).

Objectives: This study aimed to compare the cost-effectiveness of well-established RA therapies using a claims-based algorithm in RA patients.

Methods: An electronic medical record (EMR) database from Zhujiang Hospital was utilized to estimate the cost-effectiveness of medication for RA patients, including IGU with MTX, biological DMARDs (bDMARDs) with MTX, and MTX alone for more than 6 months from 2014 to 2020. Patients who were deemed effective must meet all the following criteria according to the algorithm, high adherence; no bDMARDs or IGU switch or addition; no prescription of new csDMARDs; no increase in dose or frequency of index drug; no new use of chronic glucocorticoids or increase in glucocorticoid dose; and no more than one glucocorticoid injection. Average cost was calculated by summing total cost of effective treatment and dividing by number of patients achieving efficacy in each group.

Results: A total of 263 patients were included in the analysis. Based on a claims-based algorithm, the effective rate was 27.1 % (26/96) for IGU with MTX group, 11.2% (7/62) for bDMARDs with MTX group, and 13.3% (14/105) for MTX alone group, respectively. Average cost of effective treatment was $833.46 for IGU with MTX therapy, $2554.57 for bDMARDs with MTX therapy, and $171.48 for MTX alone (Table 1).

Table 1. Effectiveness and Cost per Effectively Treated Patient with RA

Criteria	All patients (n=263)	IGU with MTX group (n=96)	bDMARDs with MTX group (n=62)	MTX (n=105)
Effectiveness:no. of patients (%)[a]	47(17.87%)	26 (27.1%)	7 (11.2/%)	14 (13.3%)
Cost of all RA-related medication per effectively treated patient(SD)	$892.75(911.57)	$833.46 (252.67)	$2554.5 (1273.13)	$171.4 (110.33)
Average cost of all RA medications postindex (excluding biologic DMARDs) per patient (SD)[b]	$146.38(114.60)	$148.81 (123.12)	$86.90 (74.53)	$171.4 (110.33)
Average cost of only biologicDMARDs postindex per patient (SD)[b]	$746.38(926.35)	$684.27(188.67)	$2468.67(1285.91)	/

[a] χ^2showed significant difference in percentage effectiveness for the original algorithm ($p<0.05$). [b]Medication cost was 2020 U.S. dollars.

Conclusion: IGU with MTX therapy was revealed to be both effective and modestly priced, which seemed to be a cost-effective strategy for RA therapy and warranted further cost-effectiveness investigation.

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AB0391 ANALYSIS OF CLINICAL IMPROVEMENT BY 5 JAK INHIBITORS AGAINST JAK INHIBITOR IR RA PATIENTS IN JAPANESE CLINICAL PRACTICE

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Background: Recently, Eular recommended different mode of therapeutic tool to get clinical remission. JAK inhibitors are considered to be one of candidates. Several JAK inhibitors have been used, however there are almost little informations about selection of JAK Inhibitors, especially, informations about secondary JAK for JAK inhibitor iR RA patients.

Objectives: To analyze clinical response by second JAK inhibitors against JAK inhibitor iR RA patientsin in clinical practice.

Methods: In Japan, five JAK inhibitors have been mainly used in MTX iR or biologics iR patients from 2013 (tofacitinib, JAK1,3), 2017 (baricitinib, JAK 1,2), 2019 (Peficitinib, Pan JAK, in Asia, Japan), 2020,April (upadacitinib, JAK1,2, mainly JAK1) and 2020.Nov (filgotinib, JAK1). In our clinic, these JAK inhibitors were sequentially used to get clinical remission. Numbers of patients who used JAK inhibitors are 28 patients in tofacitinib, 38 patients in baricitinib, 27 patients in peficitinib, 34 patients in upadacitinib, and 13 patients in filgotinib. Among them, 22 JAK inhibitor iR RA patients were investigated for clinical effectiveness.

Results: Summery of study were shown in Tables 1 and 2. Biologics were used in 14 patients and satisfied D2T RA (1st row, green color). For pre JAK inhibitors, 12 tofacitinib, 6 baricitinib, 4 peficitinib have been used. JAK inhibitor for JAK inhibitor iR patients, 13 upadacitinib, 3 baricitinib, 3 peficitinib and 3 filgotinib were used. Six months later, 9/13 patients in upadacitinib, 2/3 in filgotinib, 2/3 in peficitinib, 0/3 in baricitinib, totally 13/22 improved clincal disease activity (Eular good+ moderate response). Clinical improvement about ACPA negative (6th row, yellow color) patients, especially RF negative (5th row, blue color) patients, are incomplete. Double negative (ACPA, RF)or RF negative may be a predicter for clinical response about 1st and successive response for upadacitinib treated patients. Since, first JAK in 4 patients (8 th row, dark green)- 3 tofacitinb, 1 baricitinib respond well firstly (secondary unresponsiveness), tofacitinib may be useful for double negative or RF negative RA patients.

Table 1.

No	sex	age(yrs)	Dur (Mo)	RF (IU/ml)	ACPA (U/ml)	pre BIO	pre JAK	csDMARDs	JAK	dose(mg)	Eular response
1	m	67	180	358	1381	TCZ	BARI	n	FIL	200	G
2	f	62	156	287	163.9	ADA,TCZ	BARI	MTX,LEF	UPA	15	M
3	f	62	110	209	163.9	ADA,TCZ	TOF	MTX,LEF	BARI	4	N
4	f	64	144	175	159	ADA.	TOF	MTX	PEF	150	M
5	f	82	348	150	12.5	ADA	PEF	TAC	UPA	7.5	N
6	f	67	192	141	1.7	IFX,TCZ	BARI	n	UPA	15	G
7	f	39	72	59	1.3	n	PEF	n	UPA	15	M
8	f	74	396	56	240	n	TOF	MTX	PEF	100	N
9	f	77	108	51	51.6	GOL,TCZ	TOF	MTX	UPA	15	M
10	f	77	108	51	51.6	GOL,TCZ	TOF	MTX	UPA	15	M
11	f	78	360	44	2.2	TCZ	PEF	n	UPA	15	G

Conclusion: Jak inhibitors are useful for another JAK inhibitor iR RA patients in clinical practice. However, to get good response, baseline immunogenicity, RF/ACPA positivity, JAK specificity need to be considered. To solve, prospective clinical study may be required.

REFERENCES: None

Table 2.

No	sex	age(yrs)	Dur (Mo)	RF (IU/ml)	ACPA (U/ml)	pre BIO	pre JAK	csDMARDs	JAK	dose(mg)	Eular response
13	f	58	240	35	743.6	n	TOF	n	BARI	4	N
14	f	63	192	18	4.7	n	TOF	n	FIL	200	M
15	m	66	264	17	598	n	TOF	LEF	PEF	100	M
16	f	73	468	15	166.3	ADA,TCZ	TOF	n	UPA	15	G
17	m	72	94	15	0.3	ETA,TCZ,ABT,GOL	TOF	MTX	BARI	4	N
18	f	74	144	3	0.6	ADA,CZP,TCZ	BARI	n	UPA	7.5	G
19	m	78	54	3	0.5	n	BARI,PEF	MTX	UPA	15	N
20	f	65	288	3	0.6	n	BARI	n	UPA	7.5	N
21	f	40	120	3	6.4	GOL,CZP	TOF	MTX	UPA	15	N
22	f	78	627	3	1.4	GOL	TOF	n	FIL	100	N

Disclosure of Interests: None declared
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AB0392 EFFICACY AND SAFETY OF UPADACITINIB IN A CHINESE SUBGROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Upadacitinib (UPA) was effective in global Phase 3 trials in rheumatoid arthritis (RA) patients (pts) with inadequate response (IR) to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

Objectives: To assess the efficacy and safety of UPA in csDMARD-IR pts with RA in Chinese subgroup from a Phase 3, randomized, double-blind, placebo (PBO)-controlled study (NCT02955212) [1].

Methods: Pts were randomized to 12 weeks of blinded treatment with UPA 15 mg once daily (QD) or PBO, in combination with csDMARDs. Primary and secondary endpoints were analyzed in a Chinese subgroup, including American College of Rheumatology criteria (ACR) responses, remission and low disease activity measures. Safety was analyzed for pts who received ≥1 dose of study drug.

Results: 228 Chinese pts (67.5% of overall trial population) were randomized and took at least one dose of study drug. Baseline characteristics were generally balanced between UPA and PBO. 46% and 35.1% used methotrexate (MTX) alone as concomitant csDMARD in UPA and PBO group, respectively. 38.9% in UPA and 43.0% in PBO group used concomitant csDMARDs other than MTX and 15.0% and 21.9% respectively used a combination. At week 12, more Chinese pts receiving UPA achieved the primary endpoint of ACR20 compared with PBO (71.9% vs 31.6%, nominal p<0.001). UPA also showed greater improvements in all secondary endpoints vs PBO at Week 12 (Table 1), including ACR50 and ACR70, mean change in Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP), Health Assessment Questionnaire-Disability Index (HAQ-DI), Short-Form 36-item Health Survey-Physical Component Summary (SF-36 PCS), as well as proportion of pts achieving low disease activity based on DAS28-CRP ≤3.2 and Clinical Disease Activity Index (CDAI) ≤10, and clinical remission based on DAS28-CRP <2.6. Onset of response was rapid with more pts receiving UPA achieving ACR20 by Week 1 versus PBO (25.4% vs 5.3%, nominal p<0.001). Through Week 12 treatment-emergent adverse events (TEAEs) occurred in 57.9% of pts on UPA and 49.1% on PBO. The rate of pts with serious AEs (SAEs) was numerically higher with UPA than with PBO (6.1% vs 4.4%). TEAEs reported in ≥ 3% of subjects and with a higher rate on UPA vs. PBO were: upper respiratory tract infection, alanine aminotransferase increased, aspartate aminotransferase increased, hypertension, diarrhea, and leukopenia. Overall safety was consistent with the trial population[1] and similar with the reported safety profile of the global clinical program[2].

Table 1. Summary of Efficacy Endpoint Results at Week 12 in Chinese Subgroup

Endpoint [a]	UPA 15mg (N=114)	PBO (N=114)
Primary endpoint		
ACR20, %	71.9***	31.6
Secondary endpoints		
Δ DAS28-CRP	-2.42***	-0.75
Δ HAQ-DI	-0.55***	-0.11
Δ SF-36 PCS	7.63 [b]***	2.94 [c]
DAS28-CRP ≤3.2, %	46.5***	9.6
DAS28-CRP <2.6, %	28.1***	1.8
CDAI ≤10, %	33.3***	7.0
ACR50, %	39.5***	7.0
ACR70, %	16.7***	2.6
ACR20 at Week 1, %	25.4***	5.3

***Nominal p<0.001 vs PBO [a]Non-responder imputation for binary endpoints; ANCOVA with multiple imputation for DAS28(CRP) and HAQ-DI; mixed model repeated measures for other continuous endpoints. Δ: mean change from baseline [b]N=106 [c]N=104

Conclusion: UPA demonstrated clinical and functional improvement in Chinese csDMARD-IR RA pts. The safety of UPA was comparable with the overall study population and with the safety seen in the global Phase 3 program.

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AB0393 SURVIVAL ON JANUS KINASE INHIBITORS VERSUS OTHER ADVANCED THERAPIES IN RHEUMATOID ARTHRITIS

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Background: Four Janus Kinase inhibitors (JAKi) are licensed in the UK for treating rheumatoid arthritis (Upadacitinib, Tofacitinib, Filgotinib and Baricitinib). Several analyses have examined the survival in these groups of drugs and found them more likely to be tolerated more or equivalently than other modes of action. Recent data suggested an age influence on survival on these drugs.
Objectives: To study the overall survival rates of JAKi compared to the other biologic treatments in a single centre cohort.
Methods: We analysed patients commencing advanced treatments (anti-Tumour necrosis factor, Interleukin 6 blocker, Rituximab and Abatacept) between February 2011 and October 2021. Variables examined included gender and age. The time on drug was compared between JAKi and other treatments using student's T test. Chi squared test was used to compare categorical variables. A Cox regression model was fitted to compare length of stay on each agent JAKi length of stay was compared to length of stay on other agents combined.
Results: 592 patients were included in the analysis. 168 (28%) were started on JAKi. 435 (73.48%) were females. Mean age at drug start was 60.6 years (SD 13.5). The numbers on drug were Filgotinib n=10, Tofacitinib n=35, Upadacitinib n=37, Baricitinib n=86, Adalimumab n=211, Abatacept n=36, Certolizumab n=18, Etanercept n=112, Golimumab n=21 and Tocilizumab n=26. 93 (15.7%) discontinued their drug, mostly due to lack of efficacy. Mean number of days on any biologic treatment was 918.9 (SD 711.5). Patients on JAKi had a significantly shorter survival on drug 652.7 days vs 1024.4 days (P<0.001).
There were no significant differences in age and gender between the groups. Univariate regression showed a hazard ratio of 1.19 (95%CI 0.75,1.98). This remained non-significant after adjusting for age and gender (1.18 95%CI 0.71,1.95). The only predictor of stoppage was age (HR 1.03 95%CI 1.01,1.04).
Conclusion: In this relatively large observational study, there was no difference in predictors of stoppage between JAKi and other advanced therapies. Increasing age was found to be a predictor for stoppage. This is in line with other reports in the literature. Further work looking at the impact of serology and disease activity will be performed.
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AB0394

CLINICAL OUTCOMES UP TO WEEK 48 OF ONGOING FILGOTINIB (FIL) RHEUMATOID ARTHRITIS (RA) LONG-TERM EXTENSION (LTE) TRIAL OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG (BDMARD) INADEQUATE RESPONDERS (IR) INITIALLY ON FIL OR PLACEBO IN A PHASE 3 PARENT STUDY (PS)

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Background: The preferential Janus kinase-1 inhibitor FIL is approved for treatment of moderate to severe active RA in Europe and Japan.
Objectives: Efficacy and safety of FIL were assessed in patients (pts) with IR to bDMARDs in a LTE trial (NCT03025308) enrolled from a Phase 3 PS (NCT02873936).[1]
Methods: bDMARD-IR pts received FIL 200 mg (FIL200), FIL 100 mg (FIL100), or placebo (PBO), all with stable conventional synthetic (cs)DMARDs up to 24 weeks (W). At W14 of the PS, pts with IR to FIL or PBO (<20% improvement in swollen [66] and tender [68] joint counts) switched to standard of care (SOC; investigator's choice of treatment). Pts completing the PS on FIL, PBO, or SOC could enter the LTE. PS FIL pts were maintained, blinded, on their FIL dose; PS PBO and PS SOC pts were rerandomized, blinded, to FIL200 or FIL100. Efficacy data to LTE W48 and safety data to data cutoff (June 1, 2020) are reported.
Results: The PS included 147, 153, and 148 pts on FIL200, FIL100, and PBO. Pts continuing on LTE FIL200 and FIL100 at data cutoff: 80/121 (66%) and 76/110 (69%) from PS FIL200 and FIL100; 35/47 (75%) and 32/46 (70%) from PS PBO, and 13/23 (57%) and 13/22 (59%) from PS SOC. LTE baseline (BL) characteristics were similar in FIL200 and FIL100 pts. During LTE, PS FIL ACR20/50/70 response rates decreased modestly by W48 (Figure 1). Among PS PBO pts, response rates were lower at LTE BL, reaching similar levels to PS FIL pts by W48; rates increased to W48 in PS SOC pts on either FIL dose but not to levels of other groups. Percentages of pts attaining DAS28(CRP) ≤3.2, DAS28(CRP) <2.6, CDAI ≤10, and CDAI ≤2.8 were maintained up to W48 for FIL/FIL pts. PBO/FIL and SOC/FIL pts showed similar patterns to ACR responses (Figure 1). Exposure-adjusted incidence rates (EAIRs)/100 pt-years of exposure for treatment-emergent adverse events (TEAE), serious AEs, and serious infection were higher in SOC/FIL pts vs FIL/FIL or PBO/FIL pts, but samples were small and confidence intervals overlapped. There were 5 deaths (Table 1).
Conclusion: Efficacy was mostly maintained in PS FIL pts up to W48. Response among PS PBO and SOC pts increased from BL to W48, but response in PS SOC pts continued to be lower than in other groups; these pts may represent a refractory population. FIL safety was largely consistent between PS and LTE.
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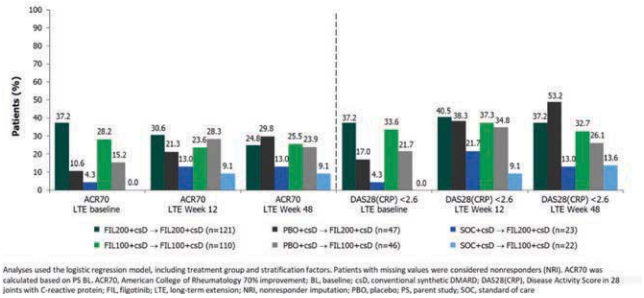
Proportions of patients achieving ACR70 and DAS(CRP) <2.6 at LTE baseline, Week 12 and Week 48 (nonresponder imputation, full analysis set)



Analyses used the logistic regression model, including treatment group and stratification factors. Patients with missing values were considered nonresponders (NRI). ACR70 was calculated based on PS BL. ACR70, American College of Rheumatology 70% improvement; BL, baseline; csD, conventional synthetic DMARD; DAS28(CRP), Disease Activity Score in 28 joints with C-reactive protein; FIL, filgotinib; LTE, long-term extension; NRI, nonresponder imputation; PBO, placebo; PS, parent study; SOC, standard of care

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Table 1. EAIRs of TEAEs in LTE, as of June 1, 2020

EAIR (95% CI)	FIL200+csD → FIL200+csD n=121PYE 228.4	PBO+csD → FIL200+csD n=47PYE 98.1	SOC+csD → FIL200+csD n=23PYE 42.1	FIL100+csD → FIL100+csD n=110PYE 223.3	PBO+csD → FIL100+csD n=46PYE 91.1	SOC+csD → FIL100+csD n=22PYE 38.2
TEAE	46.9 (38.8, 56.6)	38.7 (28.2, 53.2)	52.2 (34.4, 79.3)	40.3 (32.8, 49.5)	40.6 (29.4, 56.1)	49.8 (31.8, 78.0)
TEAE Grade ≥3	10.5 (7.0, 15.7)	10.2 (5.5, 18.9)	19.0 (9.5, 38.0)	10.3 (6.8, 15.5)	13.2 (7.5, 23.2)	18.3 (8.7, 38.5)
TE serious AE	12.3 (8.5, 17.8)	12.2 (6.9, 21.5)	21.4 (11.1, 41.1)	8.1 (5.1, 12.8)	13.2 (7.5, 23.2)	21.0 (10.5, 41.9)
Death	1.3 (0.4, 4.1)	1.0 (0, 5.7)	0 (0, 8.8)	0.4 (0.1, 3.2)	0 (0, 4.0)	0 (0, 9.7)
TE infections	34.2 (27.4, 42.6)	22.4 (14.8, 34.1)	35.6 (21.5, 59.1)	22.4 (17.0, 29.5)	26.3 (17.7, 39.3)	39.3 (23.7, 65.2)
TE serious infections	3.5 (1.8, 7.0)	2.0 (0.5, 8.2)	7.1 (2.3, 22.1)	0.9 (0.2, 3.6)	2.2 (0.5, 8.8)	7.9 (2.5, 24.4)
Opportunistic infections	0 (0, 1.6)	0 (0, 3.8)	0 (0, 8.8)	0 (0, 1.7)	0 (0, 4.0)	0 (0, 9.7)
TE herpes zoster	2.2 (0.7, 5.1)	1.0 (0.1, 7.2)	0 (0, 8.8)	0 (0, 1.7)	2.2 (0.5, 8.8)	2.6 (0.1, 14.6)
TE MACE (adjudicated)	1.3 (0.4, 4.1)	1.0 (0.1, 7.2)	0 (0, 8.8)	0.9 (0.2, 3.6)	1.1 (0.2, 7.8)	0 (0, 9.7)
TE DVT/PE (adjudicated)	0.9 (0.2, 3.5)	0 (0, 3.8)	2.4 (0.1, 13.2)	0.4 (0.1, 3.2)	0 (0, 4.0)	0 (0, 9.7)
Malignancies (excluding NMSC)	1.3 (0.4, 4.1)	3.1 (1.0, 9.5)	4.7 (0.6, 17.2)	1.8 (0.7, 4.8)	3.3 (1.1, 10.2)	0 (0, 9.7)
NMSC	0 (0, 1.6)	0 (0, 3.8)	4.7 (0.6, 17.2)	0 (0, 1.7)	0 (0, 4.0)	0 (0, 9.7)

DVT, deep vein thrombosis; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PE, pulmonary embolism; TE, treatment-emergent

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AB0395 DE-ESCALATION OF DMARDS IN ELDERLY PATIENTS WITH RA

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Background: Rheumatoid Arthritis is the most common form of inflammatory arthritis in older adults, with the mainstay of treatment being the conventional DMARDs (Tutuncu & Kavanaugh, 2007). These drugs are not without side effects, and as elderly people have higher rates of adverse drug reactions and less long-term benefits, the risk/benefit ratio is different compared to other age groups. This research sought to evaluate if the rheumatology department at Southend hospital was sufficiently acknowledging the changing circumstances of their elderly patients and de-escalating conventional DMARDs accordingly. As the average age of rheumatology patients is only likely to increase in the future, contextualising a patients treatment plan for their rheumatological disorder with their overall health status will become an increasingly important skill for clinicians and the observations from this study will be applicable to all who treat elderly patients with inflammatory disorders.

Objectives: 1. Evaluate if major new diagnoses were acknowledged in the rheumatology clinic and if conventional DMARD treatment was reduced in response. 2. Record and compare the outcomes of when conventional DMARD was stopped abruptly vs when it was tapered down slowly.

Methods: Evaluated 10 year's worth of clinic letters from rheumatology and other specialities in 50 patients with a diagnosis of RA over the age of 89. Noted new diagnoses of dementia, cancer and frailty (multiple falls, care home admission or becoming newly house bound) as well as acute hospital admissions and declining renal function and evaluated if this was acknowledged in clinic letters and whether treatment was changed in response. Recorded all instances where conventional DMARDs were stopped or had a dose reduction and evaluated if these dose drops were successful (patient stayed at reduced dose with no flares in disease activity), semi-successful (patient had mild RA flare treated with short course corticosteroids, or stayed at reduced dose for at least a year before returning to original dose) or unsuccessful (patient suffered flare and went back to original dose within 1 year.)

Results: Of the 50 patients, 31 received methotrexate monotherapy, 12 methotrexate and other conventional DMARDs, and 5 DMARDs other than methotrexate. 36 out of 45 patients receiving methotrexate had some decrease in dose by the end of the 10 year period, with the median decrease being 5mg. Patients on multiple DMARDs saw a greater average decrease in methotrexate compared to those on monotherapy. 15 abrupt cessations in methotrexate were recorded, with acute hospital admission being the most common trigger. Of these 3 were successful, 5 were semi-successful and 7 were unsuccessful. 55 planned methotrexate dose reductions in the rheumatology clinic were recorded, with 38 being successful, 9 being semi-successful and 8 being unsuccessful (Figure 1.). Clinic letters did generally acknowledge both new physical diagnoses and changes in social circumstances, but some diagnoses were more likely to trigger a change in treatment, for example in 8 new cancer diagnoses, there were 5 changes to treatment, whereas in 12 dementia diagnoses there were 3 changes to treatment. 6 patients received more methotrexate than guidelines suggest for their level of CKD, with 3 of these having it acknowledged in clinic letters.

Conclusion: Most patients had a reduction in dose of methotrexate over a 10 year period. Planned de-escalations were mostly successful, whereas abrupt stops to treatment were generally less successful. Rheumatologists are good at acknowledging changes to health status but were more likely to change DMARD therapy in response to a cancer diagnosis than a dementia diagnosis or frailty. There is still some work to be done in acknowledging declining renal function and changing methotrexate in response. Overall, these results suggest de-escalation is mostly successful and clinicians can be confident in further expanding this into their day to day practice.

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AB0396 EFFECT OF A MULTIDISCIPLINARY LIFESTYLE PROGRAM IN PATIENTS WITH RHEUMATOID ARTHRITIS: THE PLANTS FOR JOINTS RANDOMIZED CONTROLLED TRIAL

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Background: Lifestyle factors have been associated with the development and progression of rheumatoid arthritis (RA). Interventions involving whole food plant-based diets (WFPDs), physical activity or stress management have shown promising results for people with RA but were not yet evaluated in an integrated program.

Objectives: To determine the effect of a 16-week multidisciplinary lifestyle program on disease activity in patients with RA.

Methods: In the "Plants for Joints" (PFJ) parallel-arm, assessor-blind randomized clinical trial, patients with RA and a 28-joint Disease Activity Score [DAS28] score ≥ 2.6 and ≤ 5.1, were assigned to the PFJ group or the control group. The PFJ group followed a lifestyle program based on a WFPD, physical activity, and stress management in addition to usual care. The control group received usual care. Medication was kept stable three months before and during the trial. Secondary outcomes included anthropometric, and metabolic markers. An intention-to-treat analysis with a linear mixed model, adjusted for baseline values was used to analyze between-group differences of continuous outcomes.

Results: Of 115 people screened, 85 were randomized and 79 completed the study. Participants were 91% female with a mean (SD) age of 55 (12) and body mass index of 26 (4) kg/m^2. After 16 weeks the PFJ group had a mean 0.85-point greater improvement of the DAS28 versus the control group (95% CI 0.40 to 1.30; p < 0.001) (Figure 1). Subgroup analyses showed significant improvements in the seropositive as well as the seronegative subgroup, although the effect was more profound in the seronegative group. Weight, fat mass, HbA1c, LDL and triglycerides also showed significant improvements in the PFJ versus control group, while blood glucose and HDL remained unchanged (Table 1). No serious adverse events occurred.

Table 1. Outcome Measures Plants for Joints Trial

Characteristic	PFJ group (*n* = 40) Mean (SD) baseline	PFJ group (*n* = 40) Mean (SD) 16 weeks	Control group (*n* = 39) Mean (SD) baseline	Control group (*n* = 39) Mean (SD) 16 weeks	Difference in change between groups (95% CI)	*p*-value[1]
DAS28 & components, mean (SD)						
DAS28	3.90 (0.69)	2.88 (1.12)	3.75 (0.72)	3.72 (1.04)	-0.85 (-0.40 to -1.30)	<0.001
DAS28 seropositive group (*n* = 57)	4.00 (0.69)	3.13 (1.18)	3.75 (0.74)	3.78 (1.08)	-0.69 (-1.26 to -0.12)	0.02
DAS28 seronegative group (*n* = 22)	3.72 (0.68)	2.41 (0.86)	3.73 (0.65)	3.52 (0.92)	-1.20 (-1.93 to -0.47)	0.005
ESR, mm/hr	17 (18)	17 (14)	19 (15)	23 (17)	-1.0 (-6.0 to 4.0)	0.7
Patient's global assessment, mm	53 (20)	25 (21)	51 (18)	47 (19)	-15 (-25 to -6)	0.002
Swollen joint count of 28 joints	1.8 (1.9)	1.4 (2.9)	1.8 (2.6)	2.3 (3.2)	-1.6 (-2.9 to -0.4)	0.01
Tender joint count of 28 joints	4.6 (3.6)	1.8 (2.8)	3.9 (3.6)	2.9 (2.8)	-2.2 (-3.6 to -0.8)	0.003
Other outcomes, mean (SD)						
Body mass index, kg/m^2	27.1 (4.6)	25.9 (5.0)	25.2 (3.7)	25.4 (3.9)	-1.5 (-2.0 to -1.0)	<0.0001
Weight, kg	76.8 (13.2)	73.3 (14.0)	72.3 (12.4)	72.7 (12.9)	-4.2 (-5.6 to -2.7)	<0.0001
Fat mass, kg	30.6 (10.0)	27.5 (9.9)	28.0 (8.0)	28.4 (7.9)	-2.7 (-3.7 to -1.7)	<0.0001
Fasting blood glucose, mmol/l	5.1 (0.4)	4.9 (0.5)	5.4 (1.6)	5.1 (0.5)	-0.1 (-0.4 to 0.1)	0.24
HbA1c, mmol/mol	35.5 (5.6)	34.7 (5.2)	37.6 (7.3)	38.4 (6.8)	-1.2 (-2.0 to -0.4)	0.004
LDL, mmol/l	2.92 (1.01)	2.65 (0.78)	3.44 (1.05)	3.21 (0.80)	-0.37 (-0.61 to -0.13)	0.003
HDL, mmol/l	1.63 (0.40)	1.56 (0.40)	1.69 (0.37)	1.65 (0.40)	-0.10 (-0.20 to 0.00)	0.06
Triglycerides, mmol/l	1.14 (0.55)	1.05 (0.43)	1.04 (0.56)	1.03 (0.50)	0.18 (0.04 to 0.32)	0.02

Seropositive subjects: positive for rheumatoid factor [RF] or anti-citrullinated protein antibodies [ACPA], seronegative subjects: negative for RF and ACPA. DAS28 = 28-joint disease activity score, SD = standard deviation, ESR = erythrocyte sedimentation rate, patient's global assessment based on a visual analogue scale (0-100 mm), CI = confidence interval, OR = odds ratio.
[1] P-values based on linear mixed model with random effect for between group analyses, adjusted for baseline values.

Conclusion: The 16-week PFJ lifestyle program substantially decreased disease activity in people with RA with low-moderate disease activity.

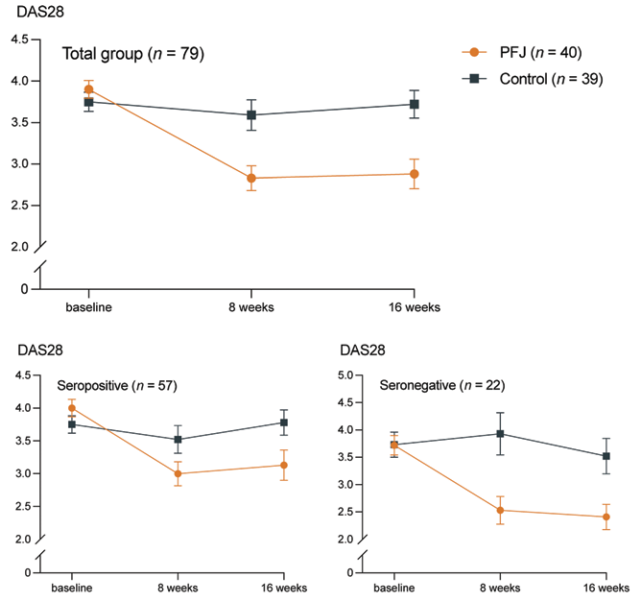

Figure 1. Change in disease activity score based on 28 joints (DAS28, primary outcome) for the total group ($p = 0.0005$) is presented in the top panel with mean ± standard error. The panels below present the same for seropositive subjects (positive for rheumatoid factor [RF] and/or anti-citrullinated protein antibodies [ACPA], $p = 0.02$) and seronegative subjects (negative for RF and ACPA, $p = 0.005$).

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AB0397

DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS WERE SIGNIFICANTLY DECREASED BY SWITCHING JAK INHIBITOR TO ANOTHER JAK INHIBITOR

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Background: With the availability of multiple Jak inhibitors (JAKi) for treatment, patients with RA who have had inadequate response to conventional therapies, including biologics, can now achieve favorable outcomes such as remission and low disease activity. However, it is also true that no single JAKi therapy is effective for all RA. Some RA treatment guidelines recommend a switch strategy from current JAKi to other JAKi or biologics in patients with inadequate response to JAKi therapy [1]. There is insufficient evidence to support the efficacy of switching to another JAKi in patients with inadequate JAKi response (JAKi-IR).
Objectives: The aim of this study is to clarify the effectiveness of the strategy of controlling disease activity by switching to other JAKi in RA cases with JAKi-IR and to analyze the effect on serum cytokines related to the pathogenesis of RA.
Methods: RA patients who switched to other JAKi during treatment with JAKi between September 2017 and January 2022 were included in this retrospective study. The clinical characteristics of the included RA patients were collected from their medical records. The efficacy of the JAKi switch strategy was assessed by changes in composite measure scores of disease activity, including DAS28-CRP, SDAI, and CDAI, at 4 and 12 weeks after the switch. In addition, changes of serum cytokines associated with RA pathogenesis (IL-6, TNF-α) were measured and analyzed by ELISA (Simple Plex, Protein Simple).
Results: Twenty-nine RA patients who received the JAKi switch treatment strategy were included in the analysis. The clinical characteristics of the included patients are shown in Table 1. All patients were receiving JAKi due to inadequate response to biologics. JAKi were switched to control disease activity including 3 cases (10%) who achieved temporary remission. Figure 1 shows the effect of the JAKi switch strategy on the disease activity category. Evaluation using SDAI showed that 65% of patients achieved the immediate treatment goal of low disease activity at 4 weeks after switch, and 69% of patients maintained this goal at 12 weeks. SDAI remission was also observed in 17% of patients at 4 weeks and 31% at 12 weeks, demonstrating the efficacy of the JAKi switch strategy. The efficacy of the JAKi switch strategy was also observed in other measures of disease activity. Changes in serum cytokines (IL-6, TNF-α) associated with disease activity in RA before and after JAKi switch were analyzed in 10 patients. Regardless of the type of JAKi, serum IL-6 was decreased by JAKi switch in most cases at 12weeks (average change of serum IL-6: -27.25pg/ml). However, no trend was observed for changes in serum TNF- disease acti (average change of serum TNF-ed for change) . There was no clear association between changes in these two cytokines and the efficacy of the JAKi switch strategy.
Conclusion: The composite disease activity index showed that about 60% of JAKi-IR patients achieved low disease activity, one of the treatment goals, at 4 weeks after switching to JAKi, and the effect was maintained up to 12 weeks. This effect did not appear to be related to the type of JAKi. The effects of biologic therapy on serum cytokines associated with RA activity differed from the effects of the JAKi switch strategy.

Table 1. Baseline characteristics of the 29 patients enrolled this study

Clinical characteristics	n=29
Age	57 [48.0-66.0]
Sex (F/M)	22/7 (75.9)
Disease duration, years	13 [8.6-18.8]
RF positive	26 (89.7)
ACPA positive, (n=22)	20(90.0)
Concomitant medications	
Methotrexate, dose(mg/week)	10 (34.5), 8.0 [6.0-10.5]
Corticosteroid, dose(mg/day)	17 (59.0), 4.0 [2.0-5.0]
Disease activity	
DAS28-CRP	3.77 [3.2-4.6]
SDAI	15.5 [9.8-21.1]
CDAI	14.5 [9.5-20.0]
Patient global assessment of disease activity (mm)	40 [25-58]
Provider global assessment of disease activity (mm)	32 [15-40]
CRP (mg/dl)	0.9 [0.1-1.7]
TJC/SJC	4 [2-5], 2[2-5]

Date are n (%) or median [IQR].

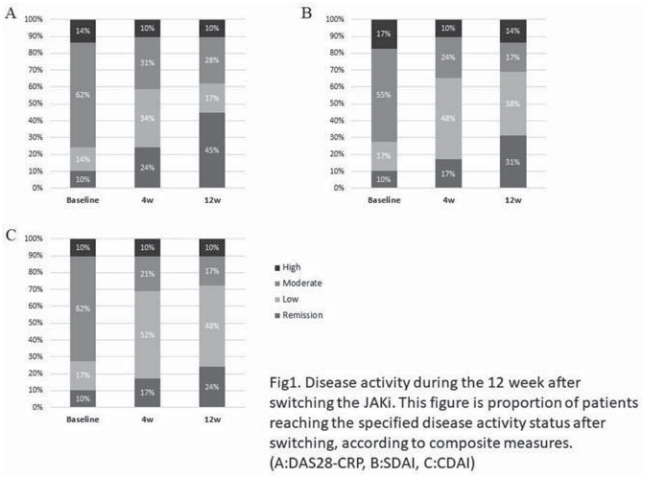

Fig1. Disease activity during the 12 week after switching the JAKi. This figure is proportion of patients reaching the specified disease activity status after switching, according to composite measures. (A:DAS28-CRP, B:SDAI, C:CDAI)

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AB0398

AURICULAR TRANSCUTANEOUS HI-FREQUENCY E-MMUNOTHERAPY SEQUENCES (ATHENS) FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: 1-YEAR CHANGES IN SYNOVITIS, OSTEITIS, AND BONE EROSION

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Background: Current pharmacological treatments remain inadequate for a significant proportion of patients with rheumatoid arthritis (RA), and thus alternative treatment approaches are needed. Prior results from the first 12 weeks of a proof-of-concept (POC) study showed that ATHENS, a non-invasive high-frequency vagus nerve therapy, was well-tolerated with meaningful reductions in RA disease severity as measured by the American College of Rheumatology response criteria (ACR) and the Disease Activity Score using 28 joints (DAS28)[1].
Objectives: The current analysis assessed long-term changes (52 weeks total follow-up) in disease activity as measured by ACR, DAS28, and the following MRI-assessed changes: synovitis, osteitis, bone erosion, and cartilage loss.
Methods: Following the completion of the 12-week POC study, patients achieving a reduction in DAS28-CRP of ≥1.2 were given the option to enroll in the 9-month open-label extension (OLE) study. During the extension phase, patients were to use the wearable device for 15 minutes per day. Adjustment of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or biologic disease-modifying antirheumatic drugs (bDMARDs) were allowed during the OLE. Changes from baseline were assessed at 12 weeks (end of initial POC) and 52 weeks (end of the OLE). Structural damage and disease progression were evaluated by standardized MRI of the wrist and hand, with and without intravenous gadolinium-based contrast. MRIs were evaluated by two independent, central readers, blinded to clinical information and visit-order of the images, and were scored for synovitis, osteitis and bone erosion using the OMERACT-RAMRIS method. Cartilage loss was also determined using the 9-point cartilage loss scale (CARLOS).
Results: Twenty-seven of 30 patients completed the initial 12-week study, of whom 19 consented and entered the OLE. Of those 19 patients, 4 (21%) discontinued due to lack of efficacy, while the remaining 15 completed the 9-month extension. Due to the COVID-19 pandemic, 7 patients were unable to complete a 52-week MRI scan; MRI evaluations at baseline, 12 weeks, and 52 weeks were available for 8 patients. DAS28-CRP mean (standard deviation [SD]) change from baseline was -1.78 (1.01) at 12 weeks (n=19; p<0.0001) and -2.30 (1.22) at 52 weeks (n=15; p<0.0001). ACR20, ACR50, and ACR70 response rates were 68%, 42%, and 21% at 52 weeks (n=19; discontinued participants were deemed non-responders). MRI analysis of synovitis, osteitis, bone erosion, and cartilage loss showed no evidence of disease progression through 52 weeks compared with baseline (Table 1).

Table 1. Change in MRI OMERACT-RAMRIS from baseline to week 52

Score	Baseline (n=8)	Week 12 (n=8)	Week 52 (n=8)	Change Week 12 vs BL (n=8)	Change Week 52 vs BL (n=8)
CARLOS, mean (SD)	3.9 (5.6)	3.9 (5.6)	3.9 (5.6)	0.0 (0.0)	0.0 (0.0)
Erosion, mean (SD)	10.8 (10.3)	10.5 (10.3)	10.6 (10.3)	-0.3 (0.4)	-0.1 (0.8)
Osteitis, mean (SD)	2.8 (4.1)	2.3 (3.7)	1.0 (1.1)	-0.5 (1.1)	-1.8 (3.1)
Synovitis, mean (SD)	4.0 (4.2)	4.1 (4.7)	3.3 (4.0)	0.1 (0.6)	-0.7 (1.0)

CARLOS = Cartilage loss score; OMERACT = Outcome Measures in Rheumatology; RAMRIS = Rheumatoid Arthritis Magnetic Resonance Imaging Scoring System

During the 9-month extension study, two new adverse events were reported (cornea transplant and right hand dysesthesia) in 2 (11%) patients; neither was treatment-related and both resolved without intervention. No serious adverse events were reported.
Conclusion: In patients with an initial treatment response to the Nēsos ATHENS therapy in the 12-week POC study, reductions in DAS28-CRP were sustained through 52 weeks. Although results should be interpreted cautiously given the small sample size and lack of control arm, MRI evaluation of synovitis, osteitis, bone erosion, and cartilage loss suggested no disease progression.
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Disclosure of Interests: Charles Peterfy Consultant of: Nesos Corp, Employee of: Spire Sciences, Héctor Corominas: None declared, Juan Jose de Agustin: None declared, Carolina Perez-Garcia: None declared, Maria Lopez Lasanta: None declared, Helena Borrell Paños: None declared, D Reina-Sanz: None declared, Raimón Sanmartí: None declared, J. Narváez: None declared, Jose Antonio Narvaez: None declared, Vivek Sharma Shareholder of: Nesos Corp., Employee of: Nesos Corp., Konstantinos Alataris Shareholder of: Nesos Corp., Employee of: Nesos Corp., Mark C. Genovese Shareholder of: Nesos Corp. and Gilead, Employee of: Gilead, Matthew Baker Shareholder of: Nesos Corp., Consultant of: Nesos Corp., Sara Marsal Consultant of: Nesos, Pfizer, Sandoz, Novartis, Gilead, Grant/research support from: Nesos, BMS, Celgene, Merck Sharp and Dohme, Pfizer, Sandoz, Novartis, Sanofi, Janssen, Union Chimique Belge Pharma
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AB0399

COMPARISON OF RITUXIMAB VERSUS LEFLUNOMIDE IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE METHOTREXATE TREATMENT- AN OPEN LABEL, RANDOMISED CONTROLLED TRIAL

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Background: Active rheumatoid arthritis (RA) despite methotrexate monotherapy is seen in about 43% of patients[1]. The current American College of Rheumatology (ACR) guidelines recommend adding a biologic or targeted synthetic Disease Modifying Anti-rheumatic Drug (DMARD) to methotrexate (MTX) therapy in such cases. The European Alliance of Associations for Rheumatology (EULAR) guidelines recommend combination DMARDs but the most commonly used combination is that of MTX with sulphasalazine and hydroxychloroquine. In a resource limited country like ours, it is not always possible to give a biological or a targeted synthetic DMARD, and a more cost effective method needs to be implemented. Often, leflunomide (LEF) is added in such cases and is effective.
Objectives: We aimed to study if LEF with MTX combination is non inferior to rituximab (RTX) and MTX combination in patients with active RA despite MTX.
Methods: This open label, randomised controlled trial, carried out on patients with moderate to high disease activity despite MTX therapy for atleast 3 months (Clinical Trials Registry- India - REF/2021/04/042755) was conducted in a tertiary care centre in India. Patients were randomised to receive either LEF (10-20mg/day) or RTX (2 doses of 1gm, 2 weeks apart) along with background MTX (10-25mg/week) and followed up at 12, 18 and 24 weeks. The primary outcome ACR20 response at 24 weeks and secondary outcomes were ACR50 and 70 responses at 24 weeks.
Results: There were 21 patients in each arm. At baseline, all patients in both groups had seropositive RA and had high disease activity according to Disease Activity Score (DAS)28 scores. The ACR20 response at 24 weeks was achieved by 14 (66.6%) and 16 (76.19%) patients respectively in the LEF and RTX arms. The ACR50 response was achieved by 11 (52.38%) patients in both groups and ACR70 response by 4 (19%) and 7 (33.3%) in the LEF and RTX arms respectively (Figure 1). The mean dose of LEF at week 24 was 17.6 mg/day. Improvement of various parameters at week 24 as compared to the baseline values were similar in both groups (Table 1). No major adverse events were noted. Two patients receiving RTX had a mild infusion reaction. Elevation in liver enzymes (<3 times the upper limit of normal) were noted in 4 patients in the LEF arm which normalised subsequently. No patient required drug withdrawal.

Table 1. Responses in both groups at week 24 (p= Not significant for all)

	Leflunomide, n=21	Rituximab, n=21
Mean ±SD reduction in SJC	-4.57 ± 3.4	-5.43 ± 4.6
Mean ±SD reduction in TJC	-6.2 ± 3.9	-7.1 ± 6.1
Mean ±SD reduction in PhGA	-3.42 ± 1.8	-4.04 ± 2.5
Mean ±SD reduction in PGA	-3.05 ± 1.8	-3.42 ± 2.4
Mean ±SD reduction in pain VAS	-33.57 ± 23.2	-38.57 ± 24.4
Mean ±SD reduction in DAS28-ESR	-1.95 ± 1.2	-2.08 ± 1.4
Mean ±SD reduction in DAS28-CRP	-1.81 ± 1.2	-2.07 ± 1.4
Mean ±SD reduction in HAQ-DI	-0.65 ± 0.5	-0.82 ± 0.6
EULAR good response (%)	1 (4.76%)	1 (4.76%)
EULAR moderate response (%)	15 (71.43%)	14 (66.6%)
EULAR non-responders (%)	5 (23.81%)	6 (28.57%)

CRP, C- Reactive Protein; DAS, Disease Activity Score; ESR, Erythrocyte Sedimentation Rate; HAQ-DI, Healthy Assessment Questionnaire-Disability Index; PGA, Patient's global assessment of disease activity; PhGA, Physician's global assessment of disease activity; SJC, Swollen Joint Count; TJC, Tender Joint Count; VAS, Visual analogue scale.

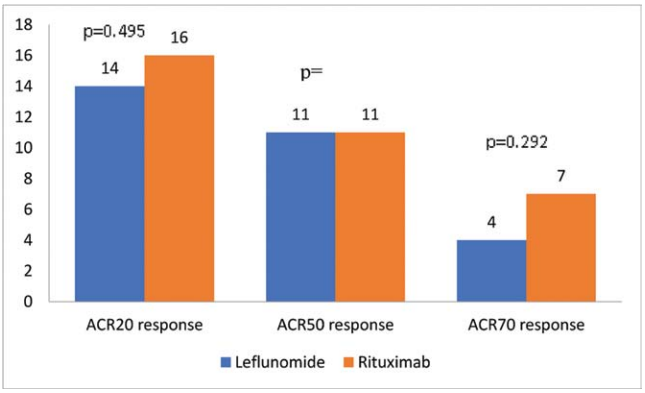

Figure 1. Number of patients achieving ACR20, 50 and 70 responses at week 24

Conclusion: In our study, LEF was comparable to RTX for achievement of ACR20/50/70 responses at 24 weeks. LEF can be considered as an add-on option to MTX instead of more expensive biologic agents in MTX refractory RA. Larger studies are needed to confirm this hypothesis.

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AB0400 A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS INTO THE SUCCESS RATE OF GLUCOCORTICOID DISCONTINUATION AFTER THEIR USE AS INITIAL BRIDGING THERAPY IN RHEUMATOID ARTHRITIS PATIENTS IN OBSERVATIONAL COHORTS AND CLINICAL TRIALS

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Background: Glucocorticoids (GC) are widely used for the initial treatment of rheumatoid arthritis (RA), to induce rapid suppression of inflammation and clinical symptoms and thereby limit radiographic damage progression. There are concerns that GC use in the long term is associated with a dose and duration dependent risk of serious side effects. Therefore, international guidelines have recommended to start GC when initiating a csDMARD, but to discontinue GC as rapidly as clinically feasible, preferably within 3 months (bridging therapy). In contrast, due to the concerns of GC side effects, the ACR guidelines published in 2021 conditionally recommend to start csDMARD monotherapy without GC bridging therapy.

Objectives: We aim to evaluate the success rate of GC discontinuation after using temporary GC as part of initial therapy ('bridging') both in observational cohorts and clinical trials in newly diagnosed RA patients.

Methods: Systematic literature searches were conducted to identify observational cohorts (scoping search) and clinical trials (in-depth search) that included RA patients who were treated with initial GC bridging therapy. GC bridging was defined as oral or intramuscular GC treatment that was discontinued within one year, alongside conventional DMARD therapy. Patient percentages still or again using GC were considered to represent the reverse of successful discontinuation. Random-effects meta-analyses were performed stratified by time point.

Results: The literature search on observational cohort studies could not identify any study answering the research question, since it remained unclear which patients had received GC as part of the initial treatment. The literature search for clinical trials identified 7160 abstracts, resulting in 10 included studies, with varying type and dose of GC and varying tapering schedules (Table 1). Of these included studies, 4 reported sufficient data on GC discontinuation or GC use after the bridging phase. The pooled proportion of patients who were still using GC was 22% (95% Confidence Interval (CI) 8; 37, based on 4 trials) at 12 months and 10% at 24 months (95% CI -1; 22, based on 2 trials) (Figure 1). Thus, the vast majority had stopped GC. Heterogeneity was substantial ($I^2 \geq 65\%$).

Table 1. Overview of included clinical trials.

Study (publication year)	Tapering schedule (mg/day)
COBRA (1997)	In 7 weeks to 7.5. Stop after 28 weeks.*
BeSt (2005)	In 7 weeks to 7.5. Stop in 8 weeks after week 28 if DAS persistently ≤2.4
IDEA (2014)	N.A.
COBRA-light (2015)	arm 1: in 7 weeks to 7.5 arm 2: in 9 weeks to 7.5 Stop after 32 weeks if DAS<1.6.
IMPROVED (2014)	In 7 weeks to 7.5. Stop after 20 weeks if DAS <1.6 at 4 months.
ARCTIC (2016)	In 7 weeks to 0 if DAS <1.6 and no swollen joints present.
tREACH (2013)	In 10 weeks to 0.*
CareRA (2017)	- in 7 weeks to 7.5, further tapered from week 28, stop after 34 weeks.
- *Classic*	- in 6 weeks to 5, further tapered from week 28, stop after 34 weeks.
- *Slim*	- in 6 weeks to 5, further tapered from week 28, stop after 34 weeks.
- *Avant garde*	All if DAS28(CRP) ≤3.2.
Hua et al. (2020)	Tapering after 4 months to 5, stop after 6 months.*
NORD-STAR (2020) - *arm 1A (oral prednisolone)*	In 9 weeks to 5. Stop after 9 months.*

DAS=disease activity score; mg=milligram; N.A.=not applicable. *GC tapered and stopped according to protocol, not depending on disease activity score.

Conclusion: The success rate of GC discontinuation after bridging as part of initial treatment of RA has been described in a limited number of studies. Reports on observational cohorts did not answer the research question and in clinical trials reports, GC (dis)continuation data were also scarce. However, the available data show that GC can be discontinued successfully in a large majority of patients. The paucity of data also reveals that more efforts are needed to provide data towards identifying the optimal GC bridging and discontinuation strategy, combining Treatment to Target with Starting to Stop.

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AB0401 THE BASELINE SERUM SOLUBLE TNF RECEPTOR LEVELS ARE ASSOCIATED WITH THE RESPONSE OF RHEUMATOID ARTHRITIS PATIENTS TO JAKINIBS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that primarily affects the multiple joints.

The elucidation of the pathogenesis of RA has progressed dramatically in recent decades, and among the many cytokines involved in the pathogenesis of RA, interleukin (IL)-6 and TNF-α are known to be the major pro-inflammatory cytokines that are abundant in the bloodstream and synovial tissue. JAK inhibitors (JAKinibs) such as tofacitinib and baricitinib are used in the treatment of RA by inhibiting JAK, which in turn inhibits the signaling of various cytokines including IL-6. However, predictors of the response to JAKinibs are still required.

Objectives: We aimed to combine soluble TNF receptor (sTNFR) I, sTNFR II, IL-6, soluble IL-6R (sIL-6R) and soluble gp130 (sgp130) levels to identify groups of JAKinibs responses in RA patients.

Methods: This research is a retrospective study. We reviewed medical records of RA patients initiating JAKinibs between July 2013 and July 2021 in our hospital. The Simplified Disease Activity Index (SDAI) was evaluated at baseline and 3, 6 months after JAKinibs administration. Clinical remission was defined when SDAI decreased ≤ 3.3. Of the 125 patients treated with JAKinibs, 89 patients with 6 months follow-up, valid SDAI and serum available were enrolled. Serum samples were tested for IL-6 (Human IL-6 Quantikine ELISA Kit, R&D systems), sIL-6R (Human soluble IL-6R alpha Quantikine ELISA Kit, R&D systems) and sgp130 (Human soluble gp130 Quantikine ELISA Kit, R&D systems), sTNFR I (Human TNF RI/TNFRSF1A Quantikine ELISA Kit DRT100) and sTNFR II (Human sTNF RII/TNFRSF1B Quantikine ELISA Kit DRT200) using specific ELISAs according to the manufacturer's instructions. The statistical analyses were performed with EZR 1.55, and p values less than 0.05 were considered significant.

Results: The median age of patients was 62 (IQR: 51 - 72) years and the median of disease duration was 6.0 (2.0 - 16.0) years. Twenty-seven (30.3%) patients were biologics and Jakinibs naive. The baseline SDAI was median 18.9 (12.7 - 27.9). When comparing SDAI-remission group (clinical remission: CR) and non-remission group, there were no significant differences in any of the baseline clinical parameters. There was no significant difference in the serum levels of IL-6, sIL-6R and sgp130 between the CR and non-CR groups, but the serum levels of sTNFR I and sTNFR II in the CR group were significantly lower than non-CR group. Univariate logistic regression analysis suggested Biologics and JAKinibs naive (odds ratio (OR) 3.58, p = 0.015), baseline Log sTNFR II levels (OR 0.013, P=0.034)

as predictors of SDAI remission treated with JAKinibs at 6 months. Although not significant, Stage IV (OR 0.211, P=0.082) and baseline Log sTNFR I serum levels (OR 0.013, P=0.065) were associated with clinical remission.
Conclusion: RA patients could be easily stratified prior to JAKinibs intervention with serum sTNFR II and sTNFR I levels, not but IL-6 axis cytokines (IL-6, sIL-6R and sgp130).

Univariate logistic regression analysis for clinical remission in patients treated with JAKinibs.

	Odds Ratio	[95% C.I.]	P Value
Age, year	0.973	[0.942 - 1.010]	0.104
Female (%)	0.820	[0.231 - 2.910]	0.759
BMI	0.968	[0.847 - 1.110]	0.627
Duration, year	0.952	[0.897 - 1.010]	0.110
Stage	I	referrence	
II	0.857	[0.218 - 3.370]	0.825
III	0.444	[0.072 - 2.740]	0.382
IV	0.211	[0.036 - 1.220]	0.082
Biologic/JAKi naïve	3.580	[1.280 - 9.950]	0.015
JAKi Drug	-Baricitinib	referrence	
-Tofacitinib	1.780	[0.659 - 4.800]	0.256
MTX use	1.640	[0.532 - 5.30]	0.390
PSL use	0.476	[0.176 - 1.290]	0.143
SASP use	0.783	[0.268 - 2.290]	0.654
IGU use	0.328	[0.039 - 2.750]	0.304
BUC use	0.436	[0.051 - 3.760]	0.450
TAC use	0.233	[0.029 - 1.910]	0.175
0W IL-6, pg/mL	0.991	[0.977 - 1.000]	0.198
0W sIL-6R, ng/mL	0.983	[0.947 - 1.02]	0.369
0W sgp130, ng/mL	0.998	[0.994 - 1.000]	0.444
0W sTNFR II/I ratio	0.808	[0.222 - 2.940]	0.746
0W Log sTNFR II, pg/mL	0.002	[0.0000653 - 0.634]	0.034
0W Log sTNFR I, pg/mL	0.013	[0.000126 - 1.300]	0.065

Disclosure of Interests: None declared
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AB0402 THERAPEUTIC ADHERENCE AND PERSISTENCE OF TOFACITINIB AND BARICITINIB IN RHEUMATOID ARTHRITIS PATIENTS IN DAILY CLINICAL PRACTICE.

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Background: The use of Janus kinase inhibitors (JAKi) is approved for adults with rheumatoid arthritis (RA) with moderate to severe activity. Although there is increasing data about baricitinib and tofacitinib in daily clinical practice, data about adherence and persistence in real-life is scarce.
Objectives: (i) To evaluate the adherence and persistence of tofacitinib and baricitinib in RA patients in a real-life setting. (ii) To assess the influence of treatment adherence to therapeutic persistence.
Methods: Retrospective longitudinal observational study that included all patients with RA who were treated with tofacitinib and/or baricitinib between 2017/10 and 2021/05 in a tertiary hospital. Demographic, clinical and pharmacological data were collected from electronic medical and pharmacy claim records. Kaplan-Meier survival analysis and log-rank test were performed to calculate and compare treatment persistence, respectively. Drug adherence was assessed with the Medication Possession Ratio (MPR). The effect of therapeutic adherence on treatment persistence was evaluated with a linear regression model.
Results: We included 136 cases: 30 treated with tofacitinib [28.6%], 44 with baricitinib [41.9%] and 31 with both [29.5%] corresponding to 105 RA patients. In our sample 86.7% of the patients were women with a mean age (± SD) of 63 (± 13) years. At the start of treatment, patients had a mean disease activity score DAS28-ESR (± SD) of 5.1 (± 1.2) and they had previously received a median (range) of 3 (0-8) biologic agents for RA.
During the study period, 40 (29.4%) and 38 (27.9%) patients treated with tofacitinib and baricitinib, respectively, discontinued the treatment.
Mean treatment persistence was 363 days (95%CI=2-1.282) in tofacitinib group and 406 days (CI95%=8-1.300) in baricitinib group. There were no statistical differences in treatment survival (HR=1.01 [95CI%=0.59-1.71]; p=0.97).
Mean MPR was 91% in both groups. There was no statistically significant correlation between therapeutic adherence and treatment persistence (p=0.21).
Conclusion: The results showed no significant differences between treatment persistence and adherence of tofacitinib and baricitinib in our patients with rheumatoid arthritis. In our cohort, therapeutic adherence was high and it did not influence treatment persistence.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.2116

AB0403 EVALUATION OF THE SAFETY AND EFFICACY OF 13-VALENT PNEUMOCOCCAL VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is accompanied by a significant increase in the risk of infection and serious infections, among which pneumonia occupies a leading place. (1) The use of targeted anti-inflammatory drugs is accompanied by an additional increase in the risk of infectious complications. In this regard, vaccination is crucial in the management of such patients.
Objectives: To evaluate the safety and efficacy of the 13-valent pneumococcal vaccine in patients with RA undergoing various types of antirheumatic therapy.
Methods: The study included 60 patients with a reliable diagnosis of RA, according to the criteria of ACR/EULAR, among them 8 men and 52 women, average age 63 years (from 29 to 69 years) with disease activity at the time of inclusion of Das-28 – 4.9 (2.2-7.7), bionaive patients with insufficient response to DMARDs who will be prescribed tofacitinib (TOFA) for the first time or receiving TOFA for at least 3 months (30 patients in each group). Both groups of patients were further subdivided into two groups, 15 vaccinated and unvaccinated patients in each. The exclusion criteria were: age over 70 years; patients with infectious diseases in the acute stage; having a history of intolerance to diphtheria toxoid, patients who had previously been vaccinated with pneumococcal vaccines. For the prevention of pneumococcal infection, a pneumococcal 13-valent polysaccharide conjugated adsorbed vaccine was used. Visits to assess the condition were made in the period of 0-3-12 months. The activity of the disease was assessed by the DAS 28, CDAI, SDAI indices.
Results: Among vaccinated patients with PCV 13 the most common adverse events were: pain at the injection site (16%), fever up to 37.6C (13%), redness at the injection site (6%), infiltration at the injection site (2%), myalgia (2%). These adverse events resolved spontaneously within 3 days. In a comparative assessment of infectious events during 12 months before vaccination and the next 12 months after it, there were no significant differences between vaccinated and unvaccinated patients. In patients who had a history of pneumococcal etiology infections after vaccination, the incidence decreased by 33%.
Conclusion: Vaccination against pneumococcal infection is a safe and effective method of preventing pneumococcal infection in patients with rheumatoid arthritis.
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Disclosure of Interests: Galina Lukina Speakers bureau: Ebbvie, Biocad, Pfizer, Roche, Dzhamilya Murtazalieva: None declared, Ekaterina Koltsova: None declared, Mikhail Kostinov: None declared, Anna Shmitko: None declared, Dmitry Blagovidov: None declared, Evgeniy Zhilyaev Speakers bureau: Ebbvie, Biocad, Pfizer, Roche
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AB0404 DEPENDENCE OF COMPLICATIONS IN TOTAL HIP AND KNEE ARTHROPLASTY ON THE TREATMENT OF RHEUMATOID ARTHRITIS.

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Background: Surgical treatment of patients with rheumatoid arthritis (RA) is associated with an increased risk of complications. This is due to the presence of an inflammatory process, a variety of variants of the course of the disease, reduced physical activity, the severity of functional disorders, prolonged therapy with glucocorticoids, disease-modifying and genetically engineered biological drugs, osteoporosis, as well as the activity of the underlying disease.
Objectives: to conduct a comparative analysis of the effect of RA treatment on local complications, such as periprosthetic infection, periprosthetic fractures, wound complications, ligamentous disorders in hip and knee total arthroplasty in patients with RA.
Methods: 1113 arthroplasties of large joints in patients with RA, which were performed in the period from 2002 to 2020, were analyzed. Of these, 649 total knee replacements (TKA) and 464 total hip replacements (THA) were performed.
Results: In patients with therapy of methotrexate at an average dose of 12.5 mg per week, the incidence of local complications was 7.87%. In patients receiving Leflunomide (Arava), complications were detected in 9.29% of cases. In group

of patients with Sulfasalazine (SSZ) intake, local complications were detected in 7.73% of cases. The complication rate of 7.01% was determined in group of patients who received Glucocorticoids (GC) at an average dose of 7.5 mg (recalculation in Prednisone). 1.87% of complications were observed in patients with intake of genetically engineered biological drugs (bDMARD). The highest incidence of local complications was found in patients with RA who had no therapy (27.27%).
Statistical data analysis revealed a significantly higher number of complications in the group of RA patients ($p<0.005$). Analyzing each type of complications, significant differences were also obtained ($p<0.005$).
Conclusion: The risk of local complications was 3 or more times higher in group of patients with RA without any treatment. So, arthroplasties of large joints in patients with RA without treatment are often accompanied by a high risk of intra- and postoperative complications.
Disclosure of Interests: None declared
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AB0405 JAK INHIBITORS IMPROVE PATIENT-REPORTED OUTCOMES SUCH AS PAIN AND HAQ EARLIER THAN ANTI-IL-6 INHIBITORS

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Background: Clinical feature of Janus kinase (JAK) inhibitor is recognized as not only suppress inflammation but also improve patient-reported outcomes (PRO) such as pain and health assessment questioner (HAQ) in patients with rheumatoid arthritis (RA). This representative clinical feature was known as a results of phase 3 trial compared to TNF inhibitor. One of the mechanisms of JAK in RA is to suppresses interleikin-6 (IL-6). However, the effect for PRO in JAK inhibitor compared to IL-6 inhibitor have not been known.
Objectives: We investigated the effect for patient-reported outcomes such as pain and HAQ in patients with RA treated with JAK inhibitor compared to IL-6 inhibitor.
Methods: This study was analysed a multicenter database included RA patients treated with biological disease-modifying anti rheumatic dugs (bDMARDs) and JAK inhibitors. In 307 patients treated with IL-6 inhibitor (tocilizumab 240 and sarilumab 67) and 220 patients with JAK inhibitor (tofacitinib 101, baricitinib 83, upadacitinib 20, peficitinib 14 and filgotinib 2), 155 patients were treated as first-line bDMARDs/JAK inhibitor (IL-6R inhibitor 104 and JAK inhibitor 51). In this first-line patients, patients treated with IL-6R inhibitor and JAK inhibitor were matched using the propensity score adjusted for gender, age, RA disease duration, baseline charactristics of disease activity, CRP level, and MMP-3 level. The beaseline data and the change of clinical and laboratory data at 4, 12 and 24 weeks were compared between IL-6 inhibitor and JAK inhibitor.
Results: Thirty-six patients in each group were matched and analyzed. The average age was 62.4 and 62.6 years and the average disease duration of RA was 13.2 and 10.1 years in IL-6 inhibitor and JAK inhibitor. The baseline characteristics were not significantly different in both groups. At week 4, tender joint count (TJC) was significantly improved in JAK inhibitor than IL-6 (IL-6: -1.86 vs JAK: -4.12, p= 0.036) and HAQ was significantly improved in JAK inhibitor than IL-6 (IL-6: -0.04 vs JAK: -0.27, p= 0.041). Moreover, Clinical Disease Activity Index (CDAI) was also improved in JAK inhibitor than IL-6 (IL-6: -6.6 vs JAK: -10.9, p= 0.026) at week 4. However, pain VAS and patient global VAS were not significantly different in each group in week4. TJC, HAQ and CDAI was not different in both groups at week 12 and week 24. On the other hand, ESR was significantly decreased in IL-6 inhibitor than JAK inhibitor at week 4, 12 and 24 (IL-6: -26.6 vs JAK: -14.1, p=0.018 at week 4, IL-6: -32.7 vs JAK: -16.5 p=0.004 at week 12, IL-6: -31.3vs JAK: -17.7 p=0.014 at week 24).

	baseline data			Change from baseline at week 4			Change from baseline at week 12			Change from baseline at week 24		
	IL-6	JAK	p value	IL-6	JAK	p value	IL-6	JAK	p value	IL-6	JAK	p value
TJC	7.9	8.0	0.958	-1.9	-4.1	0.036	-3.2	-4.5	0.319	-3.2	-4.6	0.380
SJC	4.9	5.0	0.930	-1.5	-2.4	0.253	-2.3	-2.9	0.585	-2.6	-3.8	0.268
Pt PainVAS	54.3	51.5	0.658	-23.3	-24.6	0.803	-28.3	-31.0	0.672	-27.9	-32.3	0.540
Pt Global VAS	54.6	51.3	0.598	-18.5	-23.7	0.339	-28.4	-31.1	0.653	-23.3	-32.0	0.226
Dr VAS	29.9	29.8	0.971	-13.2	-17.5	0.277	-18.8	-20.9	0.611	-18.3	-22.0	0.446
HAQ	1.0	1.0	0.798	-0.04	-0.27	0.041	-0.14	-0.29	0.212	-0.15	-0.32	0.223
RF	278.9	144.8	0.149	-16.1	-35.6	0.395	-73.1	-54.7	0.770	-42.6	-60.9	0.777
ESR	45.9	49.4	0.644	-26.6	-14.1	0.018	-32.7	-16.5	0.004	-31.3	-17.7	0.014
CRP	1.5	1.2	0.491	-1.3	-0.9	0.477	-1.5	-0.9	0.226	-1.5	-1.0	0.301
MMP-3	256.1	191.8	0.310	-98.6	-79.4	0.772	-154.0	-90.7	0.305	-160.8	-115.5	0.487
DAS28-ESR	5.1	5.3	0.623	-1.4	-1.4	0.985	-2.2	-1.8	0.249	-2.1	-1.9	0.606
DAS28-CRP	4.4	4.3	0.697	-1.2	-1.4	0.391	-1.7	-1.8	0.829	-1.7	-1.9	0.510
SDAI	22.8	22.4	0.872	-7.5	-11.5	0.075	-11.7	-13.5	0.494	-11.6	-14.8	0.266
CDAI	21.3	21.1	0.955	-6.6	-10.9	0.026	-10.2	-12.6	0.358	-10.1	-13.7	0.181

Conclusion: In a comparison between IL-6 inhibitor and JAK inhibitor as a first-line molecular-targeted drug matched baseline charactristics of disease activity, TJC and HAQ was improved in JAK inhibitor earlier than IL-6 inhibitors. JAK inhibitor suppress multi cytokine that might be the reason why JAK inhibitor improve pain. Improvement of patient reported outcome in JAK inhibitor was found also in comparison with IL-6 inhibitor.
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AB0406 LIPID-LOWERING THERAPY IN THE TREATMENT PROFILE OF THE RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder characterized by inflammatory changes in the synovial membranes of the joints, leading to their progressive damage and deformity. Inflammation occupies a prominent place in the pathogenesis of RA making it an essential target to improve the patient's condition.
Objectives: The purpose of this study was to evaluate the influence of lipid-lowering therapy on RA patients given its anti-inflammatory effect.
Methods: We involved 80 patients with established RA diagnosis based on 2010 ACR/EULAR Classification Criteria. The inclusion criteria for our study were the age of patients ≥18 years and the DAS28 index > 2,6. We have excluded from investigation individuals with any prior medical history of myopathies, liver diseases or increased transaminase levels, pregnant or breastfeeding women and patients taking lipid-lowering drugs. The accepted patients were randomized into 2 groups numbering 40 individuals each. The first group of subjects received just basic DMARDs and the second had atorvastatin 40 mg/day in addition. The atorvastatin admission lasted 3 months. To evaluate the possible anti-inflammatory effect of atorvastatin the ESR, CRP, Visual Analogue Scale (VAS), swollen joint count (SJC), tender joint count (TJC) and Disease Activity Score (DAS-28) were used. Moreover, the lipid panel indexes in both groups of patients were assessed. We used the Kolmogorov-Smirnov test for data distribution evaluation. Mann-Whitney U test and unpaired t test were employed for groups comparison, p-value <0.05 was considered as statistically significant.
Results: We found that the administration of atovastatin had a positive effect on pro-inflammatory parameters of patients. In the atorvastatin group the levels of ESR (mm/h) and CRP (mg/L) were significantly lower in comparison with the controls (25.38±9.43 vs 31.85±10.54, p=0.02 and 12.26 [8.21-17.54] vs 15.89 [11.32-21.54], p=0.04 respectively). SJC (p<0.01) and TJC (p<0.05) and DAS-28 (p<0.05) indexes have been improved more significantly in the investigation group as well. The results of lipid panel assessment were better in the atorvastatin group as well. The LDL (mg/dl) level differed between the two groups the most significantly (143.7±23.2 in the control group and 109.8±21.4 in the atorvastatin group, p=0.02).
Conclusion: With this study, we managed to demonstrate the beneficial effect of atorvastatin not only on the lipid profile but also on an inflammatory level and disease course in patients with RA.
Disclosure of Interests: None declared
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AB0407

EFFICACY AND SAFETY OF 144-WEEK TREATMENT WITH TACROLIMUS AS THE FIRST-LINE CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG (CSDMARD) FOR PATIENTS WITH ACTIVE REFRACTORY RHEUMATOID ARTHRITIS： A PROSPECTIVE, COHORT STUDY

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Background: The T2T guideline in RA recommended the normal csDMARDs irresponsive patients (pts) switching to other treatment target. Tacrolimus (TAC), the inhibitor of T cell activation, is candidate for these pts, especially with extrarticular complications (EC).
Objectives: To observe the efficacy and safety of TAC-based csDMARDS regimen refractory RA (RRA) pts and the characteristics of TAC combined treatment.
Methods: This prospective cohort study (ClinicalTrials.gov Identifier NCT02837978) was conducted in China. According to baseline DAS28-ESR, RRA pts (ACR 1987 criteria [1]) were classified to severe (>5.1, S) or moderate (> 3.2,≦5.1, M) groups. The efficacy indicators and AE were recorded untill 144w. The combined medicine with TAC was based on the past history of csDMARD prescription and EC, including TAC with/wo MTX (T+M or T group), Pred, HCQ.
Results: 150 pts (52±14y) were involved, 15 finished 144w observation, 50 still following up and 85 lost.
As shown with GEE analysis, DAS28-ESR, CRP, HAQ were decreased significantly in all pts within 24ws, and maintained stable in later period (Figure 1). The REM or LDA, achieved ACR20, good or moderate EULAR response (G+M) proportion of 103 pts completed the 24w were 41.75%, 56.31%, 76.70%.

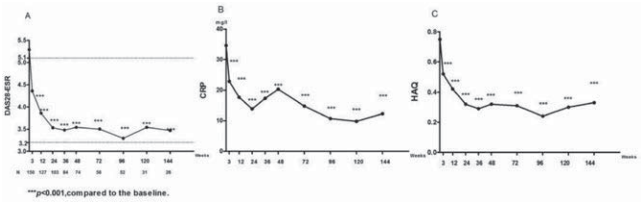

Figure 1. Disease activity index of 150 RRA pts decreased in 144weeks

Similar to the Japanese study [2], DAS28-ESR, CRP and HAQ typically declined rapidly in S group, but still higher than M (Figure 2A-C). According to GBTM analysis, S group, longer disease course or higher HAQ had a higher ACR20 remission rate (Figure 2D).

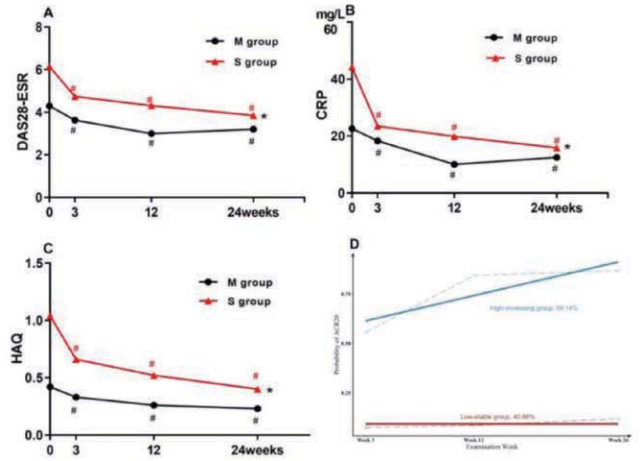

Figure 2. Disease activity index of 103 pts declined rapidly in 24weeks. **(A)**. DAS28-ESR; **(B)** CRP; **(C)**. HAQ declined significantly in S (n=53) than M (n=50) during 24ws. **(D)**.higher increased ACR20 remission group (90.6%), compared with low-stable (0%) in 24ws. *p< 0.05, compared to M; #p< 0.05, compared to baseline.

A total of 69 RA pts (46.0%) had 177 times (23.07%) AE, including 2 SAEs. Infection was the dominating AE (30%) due to asymptomatic positive urinary leucocyte and cold were classified, higher than (3.4%) Japanese study [3]. AEs were mainly happened in pts with higher TAC blood concentration 4.55(3-14.5) ng/ml, compared to No AE group 3.8(2.4-7.8) ng/ml, p=0.048, extremely in those abnormal glucose tolerance and hypertensive pts, p=0.002, 0.022.
The most common reasons of lost were drug ineffective (32.94%), economic reasons (29.1%). There was no difference in efficacy of TAC combined treatment. Combination MTX reduce AE, decrease the usage rate and dosage of Pred. Combination Pred increased AE.
Pts that achieved REM+LDA, G+M, had better TAC survival rate (Figure 3A-B). The combination of MTX, HCQ reduce lost rate (Figure 3C-D).

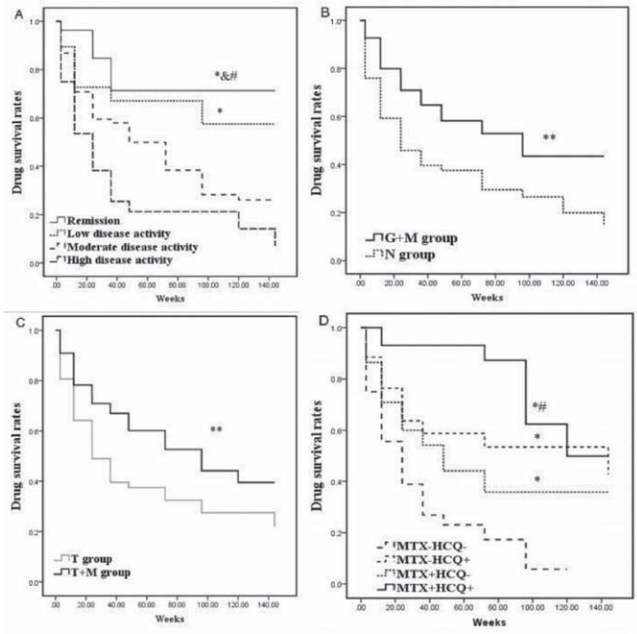

Figure 3. TAC survival ratio were compared in different response and csDMARDs combination groups. **(A)**.The pts acquired remission (n= 31) or LDA (n= 18) had higher TAC survival rate than high (n=28) & moderate (n=73) group, * p < 0.05, compared to group High; # p < 0.05, compared to Moderate; & p < 0.05, compared to Low; **(B)**. The pts G+M (n=95) had better TAC survival rate, compared with no response (N, n=55), ** p < 0.01; **(C)**. Combine MTX reduced lost rate, ** p < 0.01, compared to T; **(D)**. Combine MTX and HCQ reduced lost rate, * p < 0.05 compared to MTX-HCQ-; # p < 0.05 compared to MTX+HCQ-.

The Logistic regression showed baseline DAS28-ESR was an independent protective factor for poor response. Baseline DAS28-ESR and previous Perd use were independent protective factors for ACR20 remission.
Conclusion: TAC-based combined therapies are effective and tolerable for RRA, especially to the higher disease activity pts. TAC blood concentration related to AE. The lower disease activity index and better respond, the higher TAC survival ratio. MTX is recommended as TAC combined treatment.

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AB0408

EXOSOMAL MICRORNAS AS BIOMARKERS FOR VIRAL REPLICATION IN TOFACITINIB-TREATED RHEUMATOID ARTHRITIS PATIENTS WITH HEPATITIS C

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Background: Despite recent advances of direct-antiviral agents (DAA) for Hepatitis C virus (HCV), it is still a prevalent worldwide issue and therapeutic challenge in patients with rheumatoid arthritis (RA). HCV viral replication may respond differently to biological disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) of different mechanism of action. Exosomal microRNA 155 (exo-miR-155) and exo-miR-122 have been implicated in modulating the host immune response and transmit anti-HCV factors to HCV-infected hepatocytes in patients with RA. However, it remains unknown how

exosomal miRNAs may respond following bDMARDs and tsDMARDs treatment in HCV-infected patients with RA.

Objectives: We aimed to study the changes of exo-miR-155 and exo-miR-122 following bDMARDs and tsDMARDs treatment in HCV-infected RA patients.

Methods: We prospectively enrolled RA patients taking anti-tumor necrosis factor-α (TNF-α) inhibitors, rituximab and tofacitinib. The effect of bDMARDs and tsDMARDs on HCV viral replication were assessed using an HCV-tricistronic replicon cell system. Exo-miR-155 and 122 were detected by quantitative PCR.

Results: HCV RNA replication in hepatocytes were not affected by tofacitinib treatment. Exo-miR-155 and exo-miR-122 were significantly increased in RA patients with HCV infection compared with those without HCV infection. We observed a dramatically increase of exo-miR-122 and decreased of exo-miR-155 in patients taking rituximab compared with the TNF-α inhibitors, tofacitinib and conventional synthetic DMARD groups. Finally, a reduction of exo-miR-122 and increase of exo-miR-155 levels were detected following DAA therapy for HCV.

Conclusion: Exo-miR-155 and exo-miR-122 were potential biomarkers for RA patients with HCV infection. Further studies are needed to confirm our findings.

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Table 1. Demographics of HCV-infected RA patients with bDMARDs and tsDMARDs

	anti-TNF-α therapy n=3	Rituximab n=3	Tofacitinib n=3
Age	62.8 (54.0-71.4)	59.9 (49.9-67.6)	63.8 (55.5-70.9)
Gender (female, %)	2 (66.7)	3 (100)	2 (66.7)
Disease duration (years)	11.0 (8.8-14.0)	11.3 (7.6-17.0)	12.0 (8.2-13.8)
RF (IU/ml)	155.0 (102.2-324.4)	363.5 (265.0-538.7)	95.0 (75.4-152.6)
Anti-CCP antibody (units)	132.7 (83.0-210.8)	160.7 (106.9-400.3)	112.0 (88.0-211.8)
DAS28	5.3 (4.9-6.5)	5.3 (4.8-6.4)	5.2 (4.7-6.5)

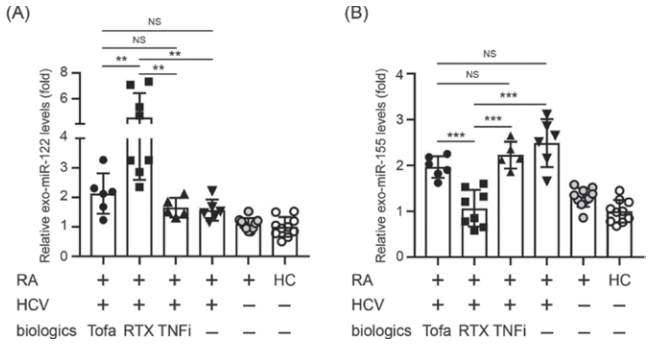

Figure 1. Comparison of exo-miR-122 (left panel) and exo-miR-155 levels (right panel) in RA patients receiving different biologics. All experiments were performed in triplicate and data are presented as the mean ± SD. RTX, rituximab; TNFi: tumor necrosis factor inhibitor; Tofa, tofacitinib. **p<0.01. *** p <0.005. NS, no significantly.

Disclosure of Interests: None declared

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AB0409 FRENCH REAL LIFE EFFECTIVENESS DATA FOR TOFACITINIB AT 1 YEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS: INTERIM RESULTS OF THE OBSERVATIONAL STUDY, DEFACTO

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Background: Tofacitinib, an oral Janus Kinase inhibitor, is indicated in the treatment of adult patients (pts) with active, moderate to severe rheumatoid arthritis (RA). At the present time we have no data concerning its efficacy in a French RA population in a real-life setting.

Objectives: DeFacTo, is an on-going observational study the principal goal of which is to identify factors predictive of Tofacitinib drug survival in RA patients in real life.

Methods: These are the results of interim descriptive analyses of effectiveness data after 1 year of follow up.

Results: Of the 313 pts enrolled in the study, 276 pts were included in the effectiveness analysis (POP1), 219 of whom were patients with a ≥1-year follow-up (POP2) including 122 patients who, as of 15 March 2021, were continuing to take Tofacitinib therapy. At inclusion, POP1 (n=276) was composed of 77.9% females of mean (± SD) age 59.7 ± 11.7 years, having a median disease duration of 9.1 years [Q1;Q3: 4.1; 19.2], TJC 7.5 ± 5.9 and SJC 5.3 ± 5.1; 115 patients presented with erosions, 206 had RF+ and 202 had ACPA+. The median CRP value was 7.4 [: 3.0; 20.0] mg/l, DAS28-4-CRP was 4.6 ±1.1, and the FACIT-Fatigue score was 28.3 ± 11.3. In all, 96.7% of the pts had received prior treatment with ≥1 csDMARDs, 65.2% with b/tsDMARDs (median = 2 [1; 4]). Tofacitinib was prescribed in combination with a csDMARD in 58.3% of cases. The baseline characteristics of the 122 patients still taking tofacitinib at 12 months were comparable to those of POP1. Results showed continued treatment with tofacitinib in 85.3% of pts with mean duration of treatment of 368 ± 197.1 days and reductions from baseline in the parameters of inflammatory markers, pain and the DAS28 activity scores; 20% of 122 pts were in DAS28-CRP remission (Table 1). Safety findings were similar to those reported previously in clinical studies[1 2].

Table 1. Baseline characteristics and effectiveness at 12 months Patient characteristics

Variables: mean ± SD or % pts	Inclusion, n=219	At 12 months, n=122*
PtGA (VAS, mm)	60.6 ± 20.8	29.8 ± 22.8
Pain (VAS, mm)	57.3 ± 24.8	30.1 ± 25.7
CRP (mg/l)	15.5 ± 21.9	7.9 ± 13.3
DAS28-4-CRP	4.6 ± 1.0	2.8 ± 1.1
DAS28-4-ESR	4.9 ± 1.1	3.3 ± 1.2
Effectiveness		
	Inclusion. n=219	At 12 months. n=219‡
LDA, % pts		
- DAS28-CRP ≤3.2	6.8	28.8
- DAS28-ESR ≤3.2	4.6	21.5
Remission, % pts		
- DAS28-CRP <2.6	3.7	20.1
- DAS28-ESR <2.6	2.7	9.6

Conclusion: These real-life interim results for Tofacitinib in RA patients provide information on its use in France: with prescriptions for single drug therapy in 41.7% of cases, the effectiveness of Tofacitinib is confirmed as comparable to that found in clinical studies[1-3].

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Disclosure of Interests: Cécile Gaujoux-Viala Speakers bureau: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Amgen; Boeringhe; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Andre BASCH Speakers bureau: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB, Consultant of: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB,, Slim Lassoued: None declared, Fabienne COURY-LUCAS Consultant of: AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Novartis and Pfizer, Grant/research support from: AbbVie, Biogen, Roche Chugai, Pfizer, and UCB,, Meriem Kessouri Shareholder of: Pfizer, Employee of: Pfizer, Nadir Mammar Shareholder of: Pfizer, Employee of: Pfizer, Yves Brault Employee of: Pfizer, Thierry Lequerre Consultant of: Abbvie, BMS, Boeringher, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Roche – Chugai, Sanofi, UCB,, Carine Salliot Consultant of: Biogen, Lilly, Novartis, Roche Chugai, Pfizer

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AB0410 EVOLUTION OF MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE IN PATIENTS TREATED WITH JAK INHIBITORS FOR RHEUMATIC DISEASES (JAKPIC STUDY)

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Background: Monoclonal Gammopathy of Undetermined Significance (MGUS) is common in patients with inflammatory rheumatic diseases but there are scarce data regarding the effect of disease-modifying antirheumatic drugs (DMARDs) on this pre-malignant condition. Recently, preclinical data and phase I trial have shown efficacy of JAK inhibitors (JAKi) in multiple myeloma.
Objectives: We aimed to evaluate the impact of JAKi on MGUS when initiated for an active rheumatic disease.
Methods: Patients with monoclonal abnormality prior to JAKi initiation for an active rheumatic disease were identified through the MAJIK-SFR Registry, a french multicentre prospective study, and a call for observation via the "Club Rhumatismes et Inflammations" Clinical and biological data were collected using a standardised case report form.
Results: Nineteen patients were identified, 10 women and 9 men, with a mean age of 65 years and a diagnosis of rheumatoid arthritis (n=14), psoriatic arthritis (n=3) or spondyloarthritis (n=2). The JAKi prescribed was baricitinib (n=8), tofacitinib (n=6) or upadacitinib (n=5), with a mean duration of 13 months.
Sixteen patients had individualized serum monoclonal protein (IgG Kappa n=9; IgG Lambda n=6; IgM Kappa n=3; IgA Lambda n=1) ranging from 0,16g/dL to 2,3g/dL. With a follow-up of 2 to 47 months, 8 of 16 patients experienced a decrease in serum monoclonal protein level and 8 had a stable serum monoclonal protein level. The maximal decrease observed was an initial IgG Kappa of 2.3g/dL decreasing to 0.2g/dL at month 14. During follow-up, two patients did not have any detectable serum monoclonal protein on serum electrophoresis (initial value of 5.2g/l and 1.6g/l), but still a positive immunofixation. One patient had bone marrow aspirate with 8% of plasma cells before JAKi introduction and 3% after 4 months of treatment. Three patients did not have initial measurable spike but a positive immunofixation that became negative at month 8 and 11 (IgG Lambda, n=2) or stable (IgG Kappa, n=1).
Conclusion: This study brings reassuring and promising data on the MGUS evolution in patients treated with JAKi for rheumatic diseases, which may guide the choice of treatment in patients with both conditions.
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AB0411 IMPACT OF GENDER IN JAK INHIBITORS PRESCRIPTION: ANALYSIS FROM A SINGLE CENTER COHORT

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Background: Gender differences in demographic and clinical features may have a direct impact in patient prognosis.
Objectives: We aimed to investigate gender differences in disease manifestations, comorbidities and treatment among patients who had started treatment with Janus Kinase Inhibitors.
Methods: A single center observational study was performed including patients who had initiated treatment with Tofacitinib, Baricitinib or Upadacitinib from September, 2017 to January, 2022. Demographic and clinical data was collected and subgroup analysis was performed.
Results: A total of 190 patients were included (84%) and their characteristics are exposed in Table 1. Discontinuation rate was 33% in men and 39% in women. In female patients, age of diagnosis was younger (p=0.04) and the disease evolution, longer (p<0.01). Rheumatoid Arthritis was more frequent in women and Psoriatic Arthritis in men. Smoking habit was more seen in females (p<0.01). High Blood Pressure and Diabetes Mellitus were more frequent in men but dyslipidemia was more seen in women with no statistical signification. Men were more likely to receive a JAKi in first indication (p<0.02). At the time of first dose of JAKi, DAS28 and SDAI were similar between both sexes but HAQ was higher in women. All the laboratory markers (CRP, ESR, RF and ACPA) were higher in women than in men.

Table 1. POPULATION CHARACTERISTICS.

	Men group n=30 (16%)	Women n=160 (84%)
Age – years (ds)	55.73 (14.66)	53.57 (17.29)
Age at diagnosis	46.93 (15.64)	39.9 (15.71)
Disease evolution (years)	10.73 (7.04)	16.79 (11.88)
Rheumatoid Arthritis	21 (70%)	139 (86.88%)
Psoriatic Arthritits	6 (20%)	11 (6.88%)
Juvenile Idiopathic Arthritis	1 (3.33%)	6 (3.75%)
Other	2 (6.67%)	4 (2.5%)
Baricitinib	3 (10%)	59 (36.88%)
Tofacitinib	22 (73.33%)	81 (50.62%)
Upadacitinib	5 (16.67%)	20 (12.5%)
Race – number (%)		
Caucasian	24 (88.89%)	137 (86.16%)
Latin	3 (11.11%)	21 (13.21%)
Other	0 (0%)	1 (0.63%)
Smokers – number (%)	3 (17.65%)	30 (27.03%)
Mean glucocorticoid dosage – mg of prednisone or equivalent	2.85 (3.37)	4.53 (4.24)
Comorbidities – number (%)	10 (33.33%)	39 (24.38%)
High blood pressure	3 (10%)	11 (6.88%)
Diabetes Mellitus	7 (23.33%)	53 (33.12%)
Dyslipidemia	0 (0%)	6 (5.45%)
Fibromyalgia		
Prior bDMARD– number (%)		
Naïve patients	17 (60.71%)	55 (34.59%)
1 bDMARD failure	2 (7.14%)	33 (20.62%)
2 bDMARD failure	3 (10.71%)	21 (13.12%)
3 or more bDMARD failure	6 (21.43%)	45 (28.12%)
DAS 28 – mean total score	5.01 (1.13)	5.02 (0.98)
SDAI – mean total score	22.31 (8.43)	25.21 (9.24)
HAQ – median total score	1.38 (0.91, 1.5)	1.62 (1.25, 1.88)
CRP – mg/L	5 (3.02, 11)	7 (2, 18.9)
ESR – mm/h	16 (8, 32)	29.5 (17, 49.5)
Rheumatoid Factor	16 (10, 166)	37 (10, 169.5)
ACPA	138 (0.7, 340)	204.5 (1.08, 340)

Conclusion: In this analysis of 190 patients treated with JAKi we detect that the men uses JAKi more frequently in first indication than women. Women seems to have a longer disease evolution, more smoking habit and less cardiovascular risk than men.
Disclosure of Interests: None declared
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AB0412 CYCLING OF JAK-INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SINGLE-CENTRE EXPERIENCE

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Background: Despite the availability of multiple effective disease-modifying antirheumatic drugs (DMARDs), discontinuation/switching of treatment is common for many patients with rheumatoid arthritis (RA). Janus kinase (JAK) inhibitors or JAKi, are the latest class of DMARDs approved for RA. Data on the outcomes of cycling JAKi in RA patients is still limited to this day.
Objectives: To assess the outcomes of switching between JAKi baricitinib, tofacitinib and upadacitinib in a real-world cohort of RA patients.
Methods: This was a hospital-based, retrospective observational study of all RA patients treated in a single-centre. Data was collected between 2016 and 2021 for all patients who failed JAKi and were treated with another JAKi. Demographic data, antibody status, history of DMARD use and clinical outcomes were assessed according to change in disease activity scores, time to JAKi discontinuation and reason for switching based on DAS 28-CRP scores.
Results: We identified 26 RA patients, 23 (88%) of which were RhF and/or anti-CCP positive, that failed JAKi and were cycled to another JAKi. 23 (88%) patients had failed treatment with one or more biological therapies prior to initiating JAKi. 13 (50%) patients were prescribed baricitinib and the other 13 patients Tofacitinib as their initial JAKi. During their RA treatment pathway, 9 (35%) of the patients on tofacitinib switched to baricitinib, and 4 (15%) switched to upadacitinib. 7 (27%) patients who started on baricitinib were switched to upadacitinib, and 6 (23%) were switched to tofacitinib. 3 (12%) patients cycled between all 3 JAKi. Reasons for switching first JAKi included primary treatment failure at initial 3-month rescore due to lack of efficacy (7/26; 27%), secondary failure (9/26; 35%), adverse drug reactions (ADR) (2/26; 8%) and others (1/26; 4%). Additionally, 7 (27%) patients on tofacitinib were switched following a drug safety update published by the Medicines and Healthcare products Regulatory Agency (MHRA), in an effort to minimize risk of major adverse cardiovascular events and malignancies. The median time to switching first JAKi was 11.5 months (range 3-23 months). After switching JAKi, 17 (65%) patients were found to have improved DAS 28-CRPs

at their 3-month rescore and continued treatment with their second JAKi. Following their switch, a total of 8 (31%) patients stopped their second JAKi due to inefficacy, 3 (12%) due to ADRs and 2 (8%) for other reasons. Of the 3 patients that went on to receive treatment with a 3rd JAKi (2/3 for primary failure; 1/3 for secondary failure), 2 patients were found to improve at their 3-month rescore.

Conclusion: Cycling through JAKi is an appropriate and safe treatment strategy in RA patients that discontinue first JAKi therapy due to lack of efficacy or ADR.

References: NA

Disclosure of Interests: None declared

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AB0413 STEROID SPARING EFFECT OF JAK-INHIBITORS ACROSS MULTIPLE PATIENTS POPULATION

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Background: JAK-inhibitors (JAK-i) represent an effective choice in achievement of therapeutic target in bio-naïve (bnaïve) and bDMARD-insufficient responders (bDMARD-IR) patients. However, oral glucocorticoids (OGC) are commonly used in clinical practice in combination with b/tsDMARDs in Rheumatoid and Psoriatic Arthritis (RA and PsA) patients in order to reach clinical remission.

Objectives: To assess, in a real-life clinical setting, the reduction of OGC dose during JAK-i treatment in RA and PsA patients that were b-naïve or ≥1-bDMARD-IR or ≥2-bDMARDs-IR with different mechanisms of action.

Methods: Patients with active RA or PsA treated with first JAKi were prospectively enrolled in a single center. Disease activity (DAS28-CRP or DAPSA), pain visual analogic scale (VAS-pain), general health (GH) and mean prednisone dosage (PDN dose) were collected at baseline and after 4, 8 and 12 months (T4, T8, T12) of treatment.

Results: 89 patients with active arthritis (77 RA, 12 PsA) were treated with JAK-i (43 patients received Baricitinib, 41 Tofacitinib and 5 Upadacitinib), with all patients reaching T4, 65 patients T8 and 50 patients T12 (Table 1). 27% patients were b-naïve, 73% ≥1-bDMARD-IR and 34% ≥2-bDMARDs-IR. A mean OGC dose of 4.0 ± 4.6 (mg per day) was used and 39% of patients received JAK-i without csDMARDs. We observed a significant improvement of disease activity by DAS28-CRP or DAPSA, VAS-pain and GH at all time points in whole population (respectively p<0.01, p<0.05, p<0.0001, p<0.001), in b-naïve (p<0.03, p<0.001, p<0.001, p<0.0001), in ≥1-bDMARD-IR (p<0.0001 for all the measures at all time points) and in ≥2-bDMARDs-IR (p<0.006 for DAS28-CRP, p<0.0001 for the others) patients. In all the cohort we reported a statistically significant reduction of PDN dose at T4 (p <0.0001), T8 (p=0.02) and T12 (p=0,002). Likewise, b-naïve patients were able to reduce PDN dose at all time points (p=0.01 for all comparisons); ≥1-bDMARD-IR patients were able to significantly reduce PDN dose at T4 (p<0.0001) and T12 (p=0.03); ≥2-bDMARDs-IR ones also spared steroids at all time points (T4 p=0.0004, p=0.02 at T8 and T12). In patients who completed the follow-up withdraw of OGC was observed at T4 in 42% of patients (44% b-naïve, 41% ≥1-bDMARD-IR and 43% ≥2-bDMARDs-IR patients), at T8 in 31% of patients (25% b-naïve, 33% ≥1-bDMARD-IR and 35% ≥2-bDMARDs-IR patients) and at T12 in 40% of patients (67% b-naïve, 32% ≥1-bDMARD-IR and 38% ≥2-bDMARDs-IR patients).

Table 1.

Women	75% (67)
Age (years)	60 ± 12
Seropositive	66% (51)
Disease duration (months)	132 ± 88
DAS28 CRP	4.0 ± 1.0
DAPSA	40.6 ± 19.7
VAS-pain	67.7 ± 15.8
GH	68.1 ± 15.2

Conclusion: JAK-i administration allows to reduce concomitant OGC regardless of line of b-DMARDs treatment. Chronic OGC may have detrimental bone, metabolic, cardiovascular and infective side effects; therefore JAK-i steroid-sparing effect may be beneficial for patients in long-term treatment.

Disclosure of Interests: None declared

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AB0414 DRUG PERSISTENCE ON JANUS KINASE (JAK) INHIBITORS COMPARED TO BIOLOGIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RETROSPECTIVE STUDY IN THE AUSTRALIAN POPULATION

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Background: In rheumatoid arthritis (RA) persistence on disease modifying anti-rheumatic drugs (DMARDs) can be interpreted as a composite measure of effectiveness, safety, and tolerability. There is limited data available on real-life use of the newest class of drugs, the Janus Kinase (JAK) inhibitors. JAK inhibitors are small-molecule treatments which are administered orally on a daily basis and offer a long-term option in RA treatment.

Objectives: To compare drug persistence on JAK inhibitors tofacitinib, baricitinib and upadacitinib to tumor necrosis factor-α (TNF) inhibitors and other DMARDs in RA patients in Australia.

Methods: A retrospective observational study was conducted among RA patients in the Australian Medicare Database (from January 2006 till October 2021), aged ≥18 and for whom a JAK inhibitor or biologic DMARDs were dispensed. Data were provided by the Australian Department of Health and Aging through PROSPECTION, an Australian healthcare consulting company. A deidentified 10% sample of the database was taken as a random representation of RA patients in Australia.

Kaplan-Meier analysis was used to calculate drug persistence rates, defined as the time from treatment initiation until the date of the last dose when there had not been a script dispensed for 6 months; except for rituximab, where a 12-month gap was applied.

Results: Data from 5,455 patients were analysed. For all patients the 12-month persistence rates were 61% for JAK inhibitors (baricitinib, tofacitinib, upadacitinib), 62% for tocilizumab, 52% for TNF inhibitors (adalimumab, certolizumab, etanercept, golimumab, infliximab), and 51% for abatacept. The JAK inhibitors baricitinib (64%) and upadacitinib (78%) were superior to tofacitinib (54%). Median treatment persistence for upadacitinib was not reached (n = 430); was 27.1 months for baricitinib and 15.2 months for tofacitinib. For TNF inhibitors, treatment persistence was 15.1 months for adalimumab, 14.1 months for certolizumab, 14.0 months for etanercept, 11.1 months for golimumab and 4.5 months for infliximab.

Persistence rates on first-line JAK inhibitors were 70% for baricitinib and 57% for tofacitinib; persistence rates dropped to 63% for baricitinib and 47% for tofacitinib in the second-line setting. First-line persistence rates were 54% for TNF inhibitors and 65% for tocilizumab, rates were sustained for tocilizumab, but dropped to 48% for TNF inhibitors in the second-line setting.

Conclusion: This real-world data highlights that in an Australian clinical practice setting treatment persistence rates on 12 months on JAK inhibitors, in particular baricitinib and upadacitinib, were superior to TNF inhibitors, but not to tocilizumab. Suggesting that persistence rates might differ according to biologics mode of action and line of treatment.

Table 1. Persistence rates at 12 months post treatment initiation

	All patients	First line	Second line
JAK inhibitors			
Overall	61% (2155)	60% (616)	60% (554)
Baricitinib	64% (537)	70% (158)	63% (124)
Tofacitinib	54% (1188)	57% (441)	47% (294)
Upadacitinib	78% (430)	28% (17)	84% (136)
TNF inhibitors			
Overall	52% (6339)	54% (4227)	48% (1561)
Adalimumab	55% (2710)	56% (2030)	48% (590)
Certolizumab	51% (593)	54% (251)	47% (147)
Etanercept	52% (2079)	55% (1354)	47% (623)
Golimumab	49% (814)	49% (506)	47% (174)
Infliximab	35% (143)	23% (86)	53% (27)
Other DMARDs			
Abatacept	51% (952)	56% (263)	46% (310)
Rituximab	49% (284)	41% (70)	65% (79)
Tocilizumab	62% (1156)	65% (279)	65% (351)

In brackets are number of patients.

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AB0415 UPADACITINIB. EFFECTIVENESS AND SAFETY IN PATIENTS WITH REFRACTORY RHEUMATOID ARTHRITIS

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Background: Upadacitinib is the third janus kinase (JAKi) inhibitor approved for rheumatoid arthritis after baricitinib and tofacitinib. Upadacitinib is a selective JAK1 inhibitor, and is indicated for the treatment of moderate to severe active RA in adult patients with inadequate response or intolerance to one or more DMARDs.
Objectives: To describe the effectiveness and safety data of upadacitinib in patients with moderate-severe RA refractory to multiple synthetic and/or biologic DMARDs.
Methods: Descriptive and retrospective observational study conducted in patients who met RA classification criteria, refractory to synthetic and/or biologic DMARDs in the Rheumatology department of the Valme Hospital. Epidemiological, clinical, analytical, and safety and treatment-related variables were collected. A descriptive quantitative analysis of the data was performed.
Results: Forty five patients were included (37 women and 8 men), with a mean age of 53 years and mean time of RA evolution of 11 years. Of the patients, 44.4% had some cardiovascular risk factor. With respect to previous treatment, 100% were on DMARDsc, with a median of 2 DMARDsc per patient. Regarding biologic or targeted therapy, 77.8% had a history of biologic therapy failure with a median of 1 biologic; in addition, 8 patients had received at least 3 previous biologic drugs prior to upadacitinib. A total of 28.9% (13 patients) had previously received JAKi, discontinued due to secondary failure or from clinical trials at other centers. In terms of disease activity at the start of upadacitinib, patients had a mean of number of swollen joints (SJC) 3, number of tender joints (TJC) 4, CRP 11 mg/dl, DAS28 of 4.23 and CDAI of 21.5. When starting upadacitinib, 80% of the patients were on steroid therapy, 51% with doses > 5 mgr/day of prednisone. Combination therapy with DMARDs was maintained in 76.3% of patients (56.7% MTX, 36.7% LFN and the rest with SSZ). The results were analyzed after a median of 7 months from the start of upadacitinib: DMARDsc were discontinued in 4 patients and the steroid dose was reduced in 58.3% of the total, being discontinued in 21.2%. With respect to disease activity analyzed post-treatment in patients who maintained the drug, a mean of SJC 0, TJC 2, CRP 0.8 mg/dl, DAS28 2.7 and CDAI 12.5 were observed (Table 1). The drug was discontinued in 11 patients: 5 for adverse events (headache, hypersensitivity, gastrointestinal discomfort, instability accompanied by photopsia, lymphopenia and irritative cough) that resolved after drug discontinuation, 5 for primary failure and 1 for secondary failure. No cases of herpes, thrombosis or cardiovascular events were recorded.

Table 1. Medians pre-treatment and post-treatment outcomes in patients who maintained upadacitinib: SJC, TJC, C-Reactive Protein (CRP) and disease activity indices DAS28 and CDAI.

	Pre upadacitinib	Post-treatment (medians 7 months)	Statistical significance
SJC	3	0	< 0,05
TJC	4	2	0,03
CRP	11	0,8	< 0,05
DAS28	4,23	2,7	< 0,05
CDAI	21,5	12,5	< 0,05

Conclusion: Upadacitinib managed to control disease activity in a high percentage of our series of patients resistant to multiple synthetic and/or biologic DMARDs, making it possible to reduce or even suspend steroid treatment in a significant number of patients, so it may be an option to consider in patients with refractory RA. Longer-term studies are needed to continue evaluating the effectiveness, safety and survival of the drug in real clinical practice.
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AB0416 CARDIOVASCULAR EVENT, VENOUS THROMBOEMBOLIZM, AND INFECTION RISK WITH TOFACITINIB IN RHEUMATOID ARTHRITIS PATIENTS AGED ≥ 60 YEARS

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Background: Tofacitinib is a targeted synthetic DMARD that selectively inhibits Janus kinase (JAK) and is approved for the treatment of RA by the FDA in 2012. In recent years, an important safety concern related to incidence of adverse events after treatment with tofacitinib has emerged.
Objectives: To evaluate the risk of major adverse cardiovascular events (MACE), venous thromboembolism (pulmonary embolism or deep vein thrombosis), serious infections requiring hospitalization, and herpes zoster with tofacitinib in RA patients aged ≥ 60 years.
Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a single center biological and targeted synthetic DMARD registry since 2005. We analyzed RA patients aged ≥ 60 years receiving tofacitinib who had at least 1 control visit registered in the HURBIO database. Phone calls were made with these patients for the current health status information until the end of January 2022. The data of the patients who lost the follow-up in our clinic were obtained from the personal health record system of the Republic of Turkey Ministry of Health by patients' permission. The coprimary end points were adjudicated MACE, VTE, serious infections, and herpes zoster. These events were identified using patients' medical records. Crude incidence rates were expressed in patients with first events per 100 patient-years, with two-sided 95% confidence intervals.
Results: A total of 132 RA patients (109, 82.6% female) aged ≥ 60 years received tofacitinib at a dose of 5 mg twice daily. The median (25–75% percentiles) age was 67 (63-73) years and median duration under tofacitinib was 18 (5-33) months. Approximately 70% of patients were biologically naive. During a median follow-up of 1.5 years, the incidences of serious infection requiring hospitalization and herpes zoster were higher (5.5% [95%CI 3.12-9.86] and 3.4% [1.67-7.17], respectively) while there was no increase in the incidences of MACE and VTE. The causes for hospitalization were as follows: COVID-19 (n=4), pneumonia (n=3), soft-tissue infection (n=3), and GIS infection (n=1). Two of these patients deceased.
Conclusion: Older patients with RA are at increased infection risk because of age and comorbid conditions. Although adverse events are reported with 10 mg tofacitinib twice daily, clinicians should be careful against the risk of infection at a dose of 5 mg twice daily, especially in elderly patients.
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Table 1. Clinical characteristics of the patients and incidence rates for adverse events

Characteristic*	Tofacitinib, 5 mg Twice Daily (N=132)
Age, years	67 (63-73)
Female/male	109 (82.6)/23 (17.4)
Smoking status	
-Never smoked	78 (59.1)
-Ever smoked	54 (40.9)
History of hypertension	82 (62.1)
History of diabetes mellitus	40 (30.2)
History of coronary heart disease	14 (10.8)
History of congestive heart failure	3 (2.3)
History of chronic kidney disease	11 (8.3)
Family history of coronary heart disease	8 (6.2)
RA disease duration, years	10 (7-18)
Biologic naïve/experienced	92 (69.7)/40 (30.3)
Duration under tofacitinib, months	18 (5-33)
No. of Patients with First Event	***Incidence Rate per 100 Patient-Yr (95% CI)***
MACE, n=1	0.49 (0.07-3.44)
VTE, n=4	1.96 (0.74-5.17)
Infection	
-Requiring hospitalization, n=11	5.55 (3.12-9.86)
-Herpes zoster, n=7	3.46 (1.67-7.17)

* n (%), if otherwise specified; median (IQR) for numeric values. CI: Confidence Interval, MACE: Major adverse cardiovascular events, VTE: Venous thromboembolism (pulmonary embolism or deep vein thrombosis)

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AB0417 SHORT-TERM EFFECT OF METHOTREXATE ON APOLIPOPROTEINS AND LIPID PROFILE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) forms the first line therapy for rheumatoid arthritis (RA). The cardioprotective effect of MTX is well established, but whether this is just due to control of inflammation, or is also via an effect on serum lipoproteins, is unclear. Although a few studies have studied the effect of the MTX on the

traditional lipid profile in RA[1], there is no data on the effect of MTX on apolipoproteins (Apo A1, Apo B, ApoB/ApoA1), which are considered better cardiovascular risk predictors than the traditional lipid profile.
Objectives: To determine the short-term effect of MTX on apolipoproteins and traditional lipid profile in patients with active RA.
Methods: DMARD-naïve patients with active RA (SJC≥2 and TJC≥4) who had been enrolled in the multicentre, RCT comparing two different MTX escalation strategies in RA (MEIRA)[2] and for whom paired serum samples were available before and after MTX treatment were included. All these patients received MTX monotherapy started at 15 mg/week and escalated to 25 mg/week by 4-8 weeks. Serum levels of apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG) were measured before starting MTX and after 16 weeks of MTX monotherapy. Proatherosclerotic indices (TC/HDL and ApoB/ApoA1) were also calculated.
Results: A total of 103 patients [mean age 40 (8) years, 93 (90%) females, mean BMI 25.1 (4.8) kg/m^2, all non-smokers and non-alcoholics] were included. No study participant had comorbid diabetes mellitus or coronary artery disease; none of them were taking glucocorticoids or hypolipidemic drugs. An increase in Apo A1 levels [by a mean of 5.6 mg/dL (p=0.02)], and HDL levels [by a mean of 1.6 mg/dL (p=0.04)] was seen after 16 weeks of MTX monotherapy. Although a numerical increase in levels of TC (mean 4.6 mg/dL, p=0.07), LDL (mean 2 mg/dL, p=0.34) and TG (mean 6.6 mg/dL, p=0.35) was also noted, none of these were statistically significant. No obvious change in Apo B levels and TC/HDL ratio occurred due to MTX therapy. However, the ApoB/ApoA1 ratio decreased significantly from 0.8 to 0.7 (p=0.002) with 16 weeks of MTX therapy (Table 1).

Table 1. Baseline and end of treatment values of apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), and proatherosclerotic indices (TC/HDL and ApoB/ApoA1).

Parameter (mg/dL)	Baseline	After 16 weeks of MTX therapy	p-value
Apo A1	126.0 (25.1)	131.6 (23.4)	**0.02**
Apo B	92.3 (18.9)	92.0 (20.9)	0.84
ApoB/ApoA1	0.8 (0.2)	0.7 (0.2)	**0.002**
TC	164.5 (32.4)	169.1 (36.8)	0.07
HDL	40.9 (9.8)	42.5 (9.7)	**0.04**
TC/HDL	4.2 (1.1)	4.1 (1.1)	0.34
LDL	88.8 (25.2)	90.8 (29.8)	0.34
TG	139.8 (69.6)	146.4 (91.3)	0.35

All values represented as mean (SD). Apo A1=apolipoprotein A1, ApoB=apolipoprotein B, TC=total cholesterol, LDL=low-density lipoprotein, HDL=high-density lipoprotein, TG=triglycerides

Conclusion: MTX therapy led to a mild but significant increase in HDL, ApoA1 and a reduction in ApoB/ApoA1 over short-term. This could potentially represent one of the mechanisms by which MTX exerts its cardioprotective effect; however, these changes need to be carefully interpreted over longer term and in context of the lipid paradox operating in RA.
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AB0418 INCREASED THROMBOEMBOLIC RISK OF JAK INHIBITORS AFTER SWITCHING FROM BIOLOGIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Safety concerns regarding JAK inhibitors have grown since the ORAL surveillance trial reported that their use was associated with an increase in major adverse cardiovascular events compared to TNF inhibitors. However, real-world data on the association between JAKi and thromboembolic events are sparse.
Objectives: We compared the incidence of thromboembolic events (TEs) before and after switching to Janus kinase inhibitors (JAKi) from biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA).
Methods: Among patients with a diagnostic code for RA taking bDMARDs, patients who switched to JAKi or another bDMARD between March 2015 and December 2020 were included in this self-controlled case series study. The outcome was the occurrence of TEs. The incidence rate ratios (IRRs) for TEs in the period after switching to JAKi or another bDMARD compared with the period before switching were calculated based on an assumed Poisson distribution.
Results: There were 1,150 and 2,254 patients who switched to JAKi and another bDMARD, respectively. The mean follow-up duration was 4.5 ± 1.8 years. In the JAKi group, the IRR for TE after drug switching was 1.56 (95% confidence interval [CI] 1.22–1.98, $P < 0.001$) compared with the period before the drug switch; in the bDMARD group, the IRR was 1.16 (95% CI 0.98–1.38, $P = 0.079$).
Conclusion: Switching from bDMARDs to JAKi was associated with an increase in TE incidence in RA patients in a real-world setting.
Disclosure of Interests: None declared
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AB0419 RHEUMATOID ARTHRITIS SWITCHING PATTERNS AND THE GROWTH OF SMALL MOLECULE TREATMENT IN THE EU5

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Background: TNF-α inhibitor therapy has long been the standard of care for adult patients diagnosed with moderate to severe rheumatoid arthritis (RA) across the EU5, though several new biologics, biosimilars, and small molecules have become available for the treatment of RA.
Objectives: This research sought to understand the factors influencing treatment changes when patients are switched from one biologic or small molecule to another, including the reason(s) for their treatment selection.
Methods: An independent market analytics firm collaborated with EU5 rheumatologists (n=250 across France, Germany, Italy, Spain, and the UK) to conduct a retrospective chart review of patients diagnosed with RA (n=1,268) who had switched from one biologic therapy or small molecule agent to another in the prior twelve weeks. Data were collected in August and September 2021 and included clinical and non-clinical patient demographics as well as physician demographics and attitudinal survey responses. This study was a non-longitudinal trending analysis to 2020 (n=1,288), 2019 (n=1,294), 2018 (n=1,312) and 2017 (n=1,235) audits following the same methodology.
Results: 70% of surveyed rheumatologists reported recent changes to the management of their RA patients, with the most recalled treatment shift being an increased use of small molecule agents (JAK inhibitors, 30%), attributable to the introduction of upadacitinib and filgotinib in December 2019 and September 2020, respectively. Despite a plethora of RA treatment options in the EU5, annual physician-reported rates of RA patient switching have remained stable since 2017, with 25% of biologic/small molecule-treated patients switching brands within a given year.
There has been a steady increase in switches from TNF inhibitors to JAK inhibitors over the last few years (2% in 2017 to 19% in 2021). At the same time, the rates of TNF cycling have been on a downward trend (43% in 2017, 40% in 2018, 39% in 2019, 34% in 2020, and 32% in 2021). Rheumatologists indicate 44% of their RA switch patients were switched from a TNF to a JAK inhibitor due to secondary efficacy failure, and their primary reason for selecting a JAK was due to the specific MOA (40%) and dosing delivery (19%).
TNF cycling (both branded and biosimilar) represent one-third of all switches in the EU, making it the most common switch pattern. TNF cycling remains most common in Germany and Spain, while France observes the lowest switch rates between TNFs. The incidence of switches from TNFs to JAK inhibitors is more consistent across countries but remains highest in Germany.

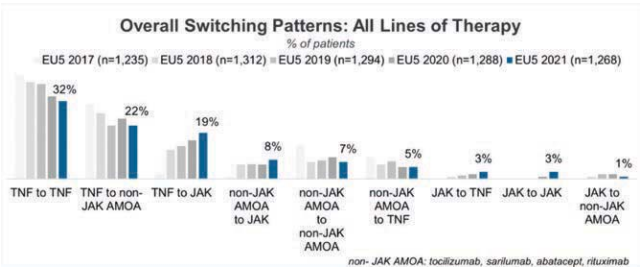

Figure 1.

Conclusion: The introduction of small molecule agents in the EU over recent years (upadacitinib and filgotinib) has provided new options for the treatment of RA, creating a shift in the switching arena from TNF cycling to more utilization of alternate mechanisms of action post first line therapy in favor of JAK inhibitors.
REFERENCES: None
Disclosure of Interests: Maxine Yarnall: None declared, Peter C. Taylor Consultant of: Received consulting fees from AbbVie, Biogen, Eli Lilly, Fresenius, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Nordic Pharma, Pfizer Inc, Roche, and Sanofi., Grant/research support from: Received research grants from Celgene and Galapagos., Phil Pouliot: None declared, Emily Hettel: None declared, Kara Murray: None declared
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AB0420 UNINTENTIONAL MONOTHERAPY IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING TOFACITINIB AND DRUG SURVIVAL RATE OF TOFACITINIB

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Background: Combination of MTX with a bDMARDs or tsDMARDs is considered the most effective treatment regimen currently available for patients with RA who have failed to respond to conventional DMARDs. However, approximately 30% of patients receive bDMARDs as monotherapy in daily clinical practice. Studies in the literature do not assess unintentional monotherapy in general. However, it is thought that some patients may switch to monotherapy unintentionally. In other words, some patients who are prescribed combination therapy switch to monotherapy without informing their physicians.
Objectives: To determine the rate of unintentional monotherapy in rheumatoid arthritis (RA) patients receiving tofacitinib and to evaluate tofacitinib survival rate.
Methods: This national, multicentre, retrospective study included patients' data from the TURKBIO Registry. Data on demographics, clinical characteristics, disease duration and activity, comorbidities, and treatment were analysed.
Results: Data of 231 RA patients (84.8% female, median age, 56 years) were included; 153 were initially prescribed combination therapy and continued to their therapies; 31 were initially prescribed combination therapy but switched to monotherapy of their own will (unintentional monotherapy); 21 were initially prescribed monotherapy and switched to combination therapy; 26 were initially prescribed monotherapy and continued to their therapies. The combination and unintentional monotherapy groups did not differ regarding remission rate assessed by DAS28-CRP (60.5% and 70%, respectively, p=0.328). The rate of comorbidities at the time of data retrieval was significantly higher in the unintentional monotherapy group compared with the combination group (83.3% vs. 60.3%, p=0.031). Presence of comorbidities was a significant factor affecting switching to monotherapy (p=0.039, Odds ratio: 3.29, 95% CI: 1.06-10.18). Drug survival rates of the unintentional monotherapy and combination groups did not differ. The median drug survival duration of tofacitinib was 27+ months with a 1-year and 4-year drug survival rates of 89.6% and 60.2%, respectively, in the unintentional monotherapy group.
Conclusion: Although 13.4% of the study population started monotherapy unintentionally, drug survival rates of the unintentional monotherapy and combination groups were not different. Comorbidity was an important factor affecting transition from combination therapy to monotherapy. This study was sponsored by Pfizer.
Disclosure of Interests: Nevsun Inanc: None declared, Kerem Abacar: None declared, mehmet akif ozturk: None declared, Abdurrahman Tufan: None declared, Hazan Karadeniz: None declared, İsmail Sari: None declared, gercek can: None declared, Yesim Erez: None declared, yavuz Pehlivan: None declared, Ediz Dalkılıç: None declared, Tuğba Ocak: None declared, Ayse Cefle: None declared, Ayten Yazici Grant/research support from: Ayten Yazici has received project grant from Roche Pharmaceuticals, Turkey., Abdurrahman Senel: None declared, Servet Akar: None declared, Elif Durak Ediboglu: None declared, Süleyman Serdar Koca: None declared, Rabia Piskin Sagir: None declared, Sema Yılmaz: None declared, Semral Gulcemal: None declared, Özgül Soysal Gündüz: None declared, Canberk Sami Başıbüyük Employee of: employee of Pfizer Pharmaceuticals, Istanbul, Turkey., Serdar Alkan Employee of: employee and shareholder of Pfizer Inc., Istanbul, Turkey., Teoman Yusuf Cesur Employee of: employee of Pfizer Pharmaceuticals, Istanbul, Turkey., Fatos Onen: None declared
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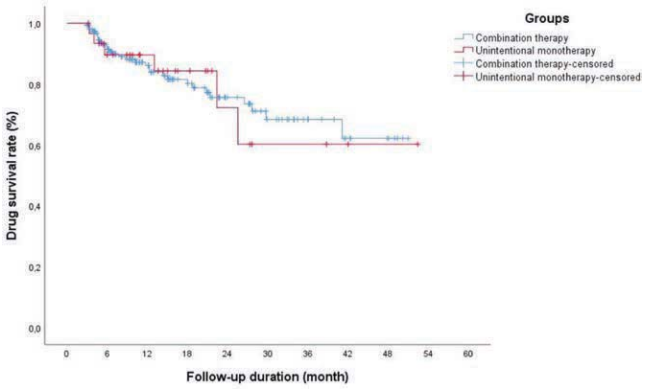

Figure 1.

AB0421 ASSESSEMENT OF LIVER STIFFNESS IN RHEUMATOID ARTHRITIS PATIENTS UNDER METHOTREXATE

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Background: Methotrexate (MTX) is recommended as a first-line disease-modifying antirheumatic drug for treating rheumatoid arthritis (RA) in monotherapy or combinational therapy. A concern about MTX-related liver fibrosis in patients with rheumatoid arthritis (RA) is still unsolved.
Objectives: The aim of the study cutoff of cumulative dose discriminating patients with normal from those with abnormal liver stiffness.
Methods: We conducted a cross-sectional study including consecutive RA patients diagnosed according 2009 ACR-EULAR criteria. Liver stiffness (LS) was assessed by Fibroscan in the gastroenterology department by an experienced operator. The LS is measured in kilopascals (kPa). It is normal when < 6.2 kPa. Above this rate it is considered pathological. Substantial liver fibrosis was defined as liver stiffness of greater than 8 kPa. We collected the following parameters: age, disease duration, disease activity assessed by DAS28, cumulated dose of MTX and duration of this treatment, and the body mass index (BMI). Patients underwent blood testing exploring hepatic function: alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl tansferase (GGT), total bilirubin (TB), albumin (ALB) and prothrombin time (PT). Statistical analysis was performed using SPSS software.
Results: There were 18 men and 36 women. The mean age was 51.9 + 11.49 [22-83]. The mean BMI was 27.27 + 3.40. The mean disease duration 8.08 + 6.28 years. The mean DAS28CRP was 3.96 + 1.49. The mean cumulative dose of MTX was 3670 + 3432.61mg and mean MTX duration was 55.75 + 50.89 months. The mean of LS was 4.6 + 1.64 kPa. The means of the liver blood tests are as follows: AST 20.83 + 8.58 UI/L, ALT 19.60 + 9.39 UI/L, ALP 84.65 + 38.68UI/L, TB 9.50 + 4.79 UI/L, GGT 25.88 + 14.26UI/L, ALB 35.19 + 5.47 g/L, PT 94.60 + 9.02. Eight patients had abnormal LS values and two patients had advanced liver fibrosis. However, hepatic blood tests (AST, ALT, GGT, TB, ALB, PT) were normal in these patients. A correlation was found between LS and following parameters: cumulative dose of MTX (r: 0.347, p: 0.013), the methotrexate duration (r: 0.363, p: 0.010) and total bilirubin rate (r:0.390, p: 0.005). Receiver Operator Curve (ROC) analysis showed the cut-off point of cumulative dose of MTX with the best accuracy in distinguishing patients with normal LS from those with LS higher than 6.2 kPA was 7330 mg, with a sensitivity of 50% and specificity of 91.3% (air under the curve (AUC) value: 0.732 (p=0.03).
Conclusion: Our study showed that LS correlated to both MTX duration and cumulative dose. Patients with a cumulative dose of MTX higher than 7330 mg required a close follow up of liver elastometry and monitoring of hepatic function.
Disclosure of Interests: None declared
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SLE, Sjögren's and APS – treatment

AB0422 SODIUM BICARBONATE MOUTH RINSE IS A USEFUL SELF-CARE METHOD FOR DRY MOUTH IN PATIENTS WITH SJÖGREN'S SYNDROME

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Background: Patients with Sjögren's syndrome (SS) present various symptoms related to dry mouth. While hyposalivation is believed to be the main cause, saliva has various beneficial physiological effects on the intraoral environment, and qualitative changes in its composition should also be considered as a cause of the refractory intraoral manifestations in SS. One of the physiological effects of saliva is buffering, and salivary bicarbonate (HCO3-) is the main determinant of salivary buffering capacity. Since salivary concentration of bicarbonate heavily depends on the rate of salivary secretion, salivary buffering capacity and oral pH decrease in patients with dry mouth; this is associated with the development of dental caries and oral candidiasis. It is considered that sodium bicarbonate mouth rinse is effective for suppressing these intraoral disorders. It is also a practical self-care method because it is inexpensive and can be made at home.
Objectives: To investigate the usability and changes in symptoms associated with dry mouth after use of sodium bicarbonate mouth rinse in SS patients.
Methods: The subjects were 27 SS patients (female: male =24:3, mean age 62.9 years, primary SS: secondary SS =24:3, mean disease duration 12.3 years) who had used sodium bicarbonate mouth rinse (dissolve about 5 g of commercially available baking soda in 500 cc of water in a plastic bottle. Put this sodium bicarbonate water in the mouth and rinse the mouth for 30 seconds to 1 minute so as to reach throughout the oral cavity). We investigated usage status, usability, and changes in subjective symptoms using a questionnaire. During their using the mouth rinse, medication and countermeasures against dry mouth in the daily life continued as usual.
Results: More than half of the patients had no knowledge of sodium bicarbonate mouth rinse (n=15; 55.6%). Highest frequency of use was twice a day (n=9; 33.3%), and common use situations were before bedtime (n=18; 66.7%), after meals (n=17; 63.0%), and at waking up (n=11; 40.7%). Twenty patients (74.1%) had "very good" or "good" sense of use. Eighteen patients (66.7%) had relief of symptoms related to dry mouth. Pros were "feeling refreshed in the mouth" (n=14; 51.9%), followed by "becomes less sticky" (n=8; 29.6%), "easy to make" (n=7; 25.9%), and "inexpensive" (n=6; 22.2%). Some respondents said they had less glossitis, stomatitis, and angular cheilitis (n=4; 14.8%). For cons "troublesome" was the highest (n=10; 37.0%), followed by responses regarding "taste" (n=6; 22.2%). There were also many responses to "none in particular" (n=7; 25.9%). No obvious accidents occurred, and 20 (74.1%) of them replied that they would like to continue to use the sodium bicarbonate mouth rinse.
Conclusion: In addition to the inhibition of dental caries and oral candidiasis, removal of tongue plaque and refreshing feeling in the mouth after rinsing due to its mucolytic effect, reduction of halitosis-causing volatile sulfur compounds, and improvement of gingivitis have been reported as effects of sodium bicarbonate. However, reports on the effects of sodium bicarbonate on dry mouth in SS patients are scarce. These results suggest that sodium bicarbonate mouth rinse is considered to be a useful self-care method that can compensate for the salivary buffering capacity that is impaired in SS patients and may reduce dry mouth symptoms. Since it is easy to continue and safe, it is worth actively incorporating it into the standard treatment for SS. Evaluation in more patients with objective indices is desired in the future.
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AB0423 STRATEGIES FOR GLUCOCORTICOID TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS FLARES: A REAL-LIFE EXPERIENCE

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Background: Glucocorticoids (GC) are a cornerstone for the treatment of Systemic Lupus Erythematosus (SLE) manifestations but there is still open debate concerning their optimal therapeutic employment.
Objectives: To describe and compare the GC therapeutic strategies used in a real-life setting for the initial treatment of SLE flares.
Methods: This study is a retrospective analysis of data from a monocentric cohort of SLE patients who registered a disease flare between 2015 and 2020. Flares were first categorized in "pulse-treated" (PT) and "non pulse-treated" (NPT). PT flares were then divided into "low-dose regimen" (250 mg iv 6MP for 3 consecutive days or less) and "high-dose regimen" (more than 250 mg iv 6MP for 3 days). GC daily and cumulative 6MP doses, rate of remission and relapse were evaluated at 3, 6 and 12 months.
Results: 101 flares were analyzed (30 PT and 71 NPT). PT flares were more severe in terms of median SLEDAI (PT 16(12-22) vs NPT 8(5-10) p=0,00) and BILAG score index (BILAG A PT 71% vs NPT 30% p=0,001). PT patients received significantly higher GC doses at 1 month (PT median cumulative dose 1372 IQR 1028 – 3076 mg of 6MP vs NPT median 160 IQR 120-288 mg of 6MP, p=0,000), 6 months (PT median cumulative dose 2964 IQR 2294 – 4305 mg of 6MP vs NPT 880 IQR 720 – 1284 mg of 6MP, p=0,000) and 12 months (PT median cumulative dose 3510 IQR 3014-5025 vs NPT median cumulative dose 1571 IQR 1098 – 2122 mg of 6MP, p=0,000). Characteristics of flares that were treated with low-dose (N=19) or high-dose (N=11) pulse regimen are summarized in Table 1. As expected, the "low-dose regimen" subgroup received lower cumulative GC dosage over time. However, no statistically significant differences were found neither in term of disease severity at baseline nor in term of disease activity, remission rates or new flares over time.

Table 1. Comparison between low-dose pulse regimen and high-dose pulse regimen in terms of cumulative GC dose and outcome in the first year after a SLE flare

Median GC doses (6MP)	Low-dose regimen N=19 (63,33%)	High-dose regimen N=11 (36,67%)	P value
Median SLEDAI	16 (12 -20)	18 (8-24)	0,6186
BILAG score (A, B, C)	A=14, B=4, C=1	A=10, B=1, C=0	0,488
Cum. dose 1 mo	1350 (1028 – 1534)	1752 (960 – 2356)	0,126
Cum. dose 3 mos	1858 (1604 – 2463)	2784 (2184 – 3240)	0,040
Cum. dose 6 mos	2450 (2218 – 3586)	3456 (2906 – 4380)	0,029
Cumulative doses 12 mos	3150 (2851 - 4448)	4246 (3591 – 5772)	0,011
Remission 3 mos no – (%)	2 (10%)	0 (0%)	0,265
Remission 6 mos no – (%)	8 (42%)	1 (9%)	0,057
Remission 12 mos no – (%)	12 (63%)	5 (45%)	0,346
Median SLEDAI 3 mos	4 (2 – 9)	9 (4 – 12)	0,138
Median SLEDAI 6 mos	3 (0 - 4)	4 (0 – 9)	0,154
Median SLEDAI 12 mos	2 (0 – 5)	2 (0 – 12)	0,363
New flares 6 mos no – (%)	2 (10%)	1 (9%)	0,900
New flares 12 mos no – (%)	2 (10%)	2 (18%)	0,552

GC=glucocorticoids, 6MP=6-methylprednisolone, no=number, Cum.=cumulative, mos=months

Conclusion: These data suggest that in a real-life setting, pulse GC therapy is preferred over oral administration for severe SLE flares and entails administration of high cumulative doses of GC. However, the experience outlined suggests that the low-dose pulse regimen is as effective in remission induction of severe flares as the high-dose regimen, allowing significant GC sparing. Since the cumulative GC dose is a known strong predictor of organ damage, strategies aimed to minimize the GC dosage should be encouraged.
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AB0425

WHAT DOES IT MEAN TO BE A DUAL BICLA AND SRI(4) RESPONDER? A POOLED ANALYSIS OF TWO PHASE 3 TRIALS IN PATIENTS WITH SLE

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Background: The BILAG–based Composite Lupus Assessment (BICLA) and SLE Responder Index ≥4 (SRI[4], based on SLEDAI-2K) are validated composite global measures of clinically meaningful improvement in SLE disease activity. BICLA and SRI(4) responses were endpoints in the phase 2b MUSE and phase 3 TULIP-1/-2 trials.[1–3] In a post hoc analysis, more patients met both the BICLA and SRI(4) response criteria at Week 52 (dual responders) with anifrolumab 300 mg vs placebo across trials (MUSE: 48.5% vs 19.9%; TULIP-1: 42.2% vs 27.9%; TULIP-2: 43.4% vs 26.4%; all nominal $P<0.01$).[4] Whereas the clinical benefit of BICLA responses alone have been characterized,[5] the added benefit of dual BICLA/SRI(4) responses remains unknown.

Objectives: To understand the clinical benefits (SLE clinical assessments, patient-reported outcomes [PROs], and healthcare utilization) of having a dual BICLA/SRI(4) response vs a response for just one endpoint or nonresponse for both, irrespective of treatment assignment.

Methods: This was a post hoc analysis of pooled data from the randomized, 52-week, double-blind TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) trials in which patients with moderate to severe SLE despite standard therapy received intravenous anifrolumab (150/300 mg) or placebo every 4 weeks for 48 weeks.[1,2] Patients were categorized as dual responders (met both BICLA and SRI[4] response criteria at Week 52), single responders (met one of either BICLA or SRI[4] response criteria), or dual nonresponders (did not meet either response criteria). SLE clinical assessments, PROs, and healthcare utilization through Week 52 were evaluated for each group. Statistical comparisons were conducted for dual responders vs single responders and dual nonresponders.

Results: Patient demographics and baseline characteristics were generally balanced across dual responders (n=288), single responders (n=122), and dual nonresponders (n=409). At Week 52, dual responders had greater improvements in SLE-related measures compared with dual nonresponders across all evaluated clinical, PRO, and healthcare utilization outcomes (Figure**, A–E).**

Compared with single responders, dual responders had a significantly greater mean change from baseline in SLEDAI-2K score (–8.2 vs –5.1; nominal $P<0.0001$), PGA score (–1.3 vs –0.9; nominal $P<0.0001$), and swollen joint counts (–6.2 vs –4.5; nominal $P<0.0001$) (**Panel A**); there was also a numerically greater proportion with ≥50% reduction in CLASI-A score (91% vs 76%; nominal $P=0.078$) (**Panel B**). Dual responders had a greater mean reduction in baseline oral glucocorticoid (GC) daily dose (–5.6 vs –3.4; nominal $P=0.006$) vs single responders (**Panel A**).

For PROs, compared with single responders, dual responders had a greater mean change in baseline PtGA score (–17.7 vs –8.6; nominal $P=0.001$), and a higher proportion had clinically meaningful improvements from baseline to Week 52 in fatigue (FACIT-F; 56% vs 43%; nominal $P=0.014$) and SF-36 physical component scores (60% vs 34%; nominal $P<0.0001$) (**Panel C–D**). Healthcare utilization (ED visits and hospitalizations) was lower in dual responders vs single responders; however, this comparison did not reach nominal significance (nominal $P=0.462$ and 0.311, respectively) (**Panel E**).

Conclusion: Patients with SLE with dual responses in two validated outcome measures have significantly better outcomes across a range of clinical, PRO, and healthcare utilization measures compared with dual nonresponders. The higher degree of improvement in disease activity, especially in arthritis, and the greater reduction in oral GC dose compared with single responders is reflected in improved patient well-being, physical functioning, and fatigue. Being a dual responder offers a profound and clinically meaningful outcome for both the clinician and patient.

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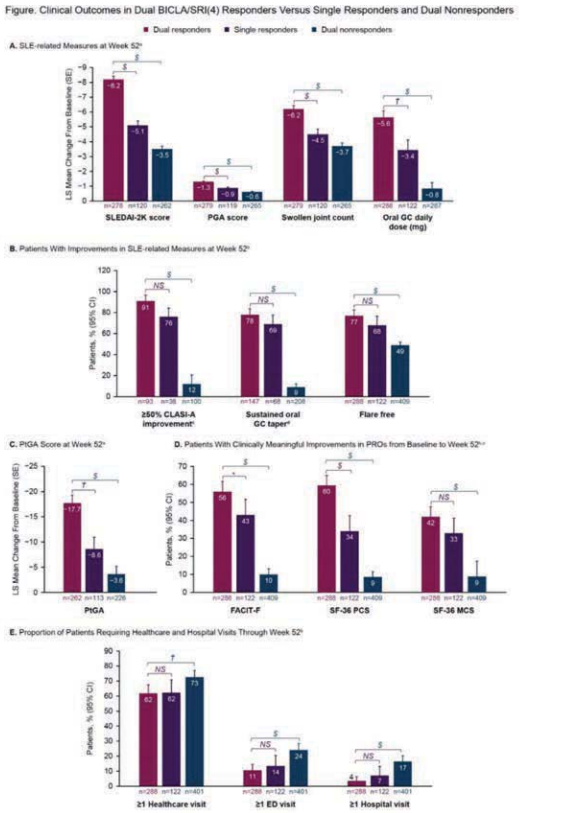

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AB0426 THERAPY WITHOUT GLUCOCORTICOIDS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The effectiveness of glucocorticoid (GC) therapy in SLE is beyond doubt and has been confirmed by the experience gained over many decades of their use. However, with prolonged use of GC, even in low and medium doses, there are many problems. In particular, the development of organ damage associated with GC significantly worsens the prognosis, leads to a decrease in the quality of life, social adaptation. Currently, attempts are being made to use therapeutic programs without the use of GC or with their appointment in minimal doses.
Objectives: Achieving stable remission in patients with SLE. Cancellation of oral GC or the use of therapy without GC in patients with SLE.
Methods: 3 clinical cases. Two patients (N1, N2) had a combination of SLE with Sjogren's syndrome with predominantly musculoskeletal syndrome. In these patients, severe organ lesions (lupus nephritis, vasculitis, central nervous system damage) were excluded. SLEDAI-2K in these patients was 9 and 8 points. Both patients had a decrease in C3, C4 complement component, ANA positivity, arthritis, hematological disorders. In N2, an increase in at to ds-DNA was determined. Therapy with oral GC, immunosuppressive drugs was not carried out in them. Patient N3 with lupus nephritis (hematuria, leukocyturia), exudative pleurisy, polyarthritis, high immunological activity (SLEDAI-2K - 16 points) was prescribed GC at a dose of 2 tab per day. Creatinine and urea were within normal limits. The patient had high immunological activity: low C3, C4 complement, at to dsDNA 200 IU/ml, ANA positivity (1:1280). Due to the presence of lupus nephritis, the patient received mycophenolate mofetil 1500 mg per day. All patients received double anti-B-cell therapy with the sequential use of Rituximab (RTX) 1000 mg intravenously in patients N1 and N2, and N3 at a dose of 2000 mg per day with premedication of 6-methylprednisolone at a dose of 250-500 mg intravenously. After 1-3 months, belimumab infusions were started at a dose of 10 mg/ kg / month. The observation period is 1 year
Results: Anti-B-cell therapy allowed patients to be treated without oral GC. A patient with LN (N3) was prescribed low doses of GC at the time of initiation of therapy with RTX, however, they were subsequently completely canceled by the 6th month of therapy. Clinical remission of the disease was achieved in all three patients. Clinical manifestations of the disease were stopped. SLEDAI-2k was 0-2 points due to minor hypocomplementemia (Figure 1). No new irreversible organ damage and relapse of the disease were registered. Patients continued to receive monthly infusions of BLM, there were no repeated courses of RTM. The patient with kidney damage continued to take MM.
Conclusion: Consistent therapy of **RTX** and BLM allowed to achieve not only a high clinical and immunological effect, but also the possibility of reducing and even abandoning the oral dose of GC, which is consistent with the concept of "Treat to target" in SLE. In addition, all patients were closely monitored by a rheumatologist once a month, which was partly achieved thanks to monthly infusions of BLM, which were carried out in the clinic.
Disclosure of Interests: None declared
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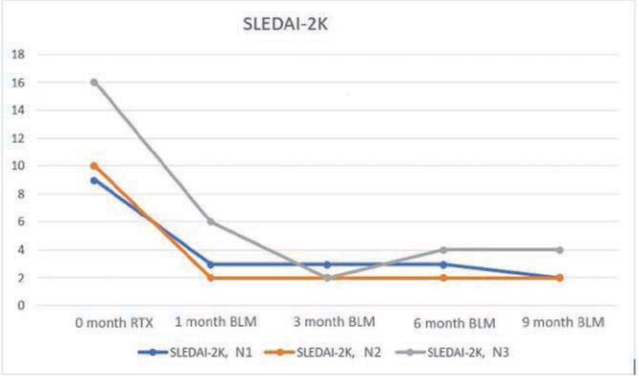

Figure 1.

AB0427 RENAL INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS: A DIFFICULT-TO-TREAT CLINICAL CASE

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Background: Lupus nephritis (LN) is one of the major organ involvement of Systemic Lupus Erythematosus (SLE), causing significant increase of morbidity, mortality and healthcare impact.[1] According to international guidelines, immunosuppressive therapy is indicated for LN class III and IV, while class V usually do not require this treatment, less than there is a proteinuria in the nephrotic range, and so for class II, also with a risk of evolution in a more aggressive form.[2] Immunosuppressive drugs commonly used are mycophenolate mofetil/mycophenolate acid (MMF/MPA) and cyclophosphamide for the initial treatment and MMF/MPA or azathioprine for the maintenance of remission. LN treatment is often difficult because of the drug adverse events and the comorbidities that make therapeutic choices very challenging.
Objectives: We describe the case of a young woman with SLE and other major systemic comorbidities who developed severe LN. This case emphasizes the importance of considering patients in their complexity and the delicate role of the physician in tailoring the treatment strategy on the individual patient.
Methods: A 36-year-old woman presented to our Department for lymphadenopathy, headache, epistaxis, fever and weight loss. In her past medical history, she had a cerebral abscess caused by Streptococcus Constellatus with residual left hemiplegia and cervical HPV-related high-grade dysplasia, treated by ring biopsy. Upon admission, blood tests revealed severe neutropenia and lymphocytopenia, thrombocytopenia and low complement; blood cultures were negative. A total body CT scan showed multiple lymphadenopathies. Lymph node and bone marrow biopsies were performed and histological examination was negative for hematological disease. The autoimmune panel was positive for antinuclear, anti-DNAn, anti-Sm, anti-U1RNP, anti-cardiolipin and anti-beta2glycoprotein antibodies. According to clinical and laboratory results, a diagnosis of SLE was made.
Results: High-dose corticosteroid therapy was started with good clinical response and improvement of blood tests. Because of the gynecological history, immunosuppressive therapy was not started, and a wait-and-see strategy with steroid tapering and careful follow-up was started. A few months later, the patient developed an increase of serum creatinine with proteinuria at nephrotic range. Thus, a kidney biopsy was performed with evidence of class III LN. Following this result, we started high-dose corticosteroid therapy, with only partial response. After executing colposcopy with biopsy, that was negative for HPV-related lesions, we decided to start MMF, continuing with a careful follow-up. After six months, proteinuria reduced but maintained on levels around 1 gr per day. Bearing in mind the growing number of studies reporting the efficacy of belimumab in LN 3,4, we added this drug to achieve a better disease control, continuing to closely monitor the patients and potential adverse events.
Conclusion: In patients with LN the choice of the immunosuppressive therapy can be very challenging. A tailored approach to the individual patient may be the best option to improve the management of this complex disease.
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AB0428

TREATMENT PATTERNS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN TAIWAN – A POPULATION-BASED ANALYSIS

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Background: Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease of an unknown etiology with a broad spectrum of organ manifestations, and patients with SLE have limited treatment options to NSAIDS, glucocorticoids, hydroxychloroquine and immunosuppressants. There is a lack of real-world evidence related to treatment patterns of SLE patients in Taiwan.
Objectives: To describe the real-world patient demographics, clinical characteristics, and treatment patterns of patients with SLE in Taiwan.
Methods: A retrospective observational study using Taiwan's National Health Insurance Research Database (NHIRD) from 1/1/2014 to 12/31/2019 was undertaken. Patients holding catastrophic illness certificates for SLE in 2015-2017 were identified. Enrolled patients aged ≥ 18 years were then divided into three groups (mild, moderate, and severe) based on the highest severity patients experienced in the one year following the enrollment date using a published claims-based algorithm (Garris et al 2013) that incorporates the Systemic Lupus Erythematosus Disease Activity Index, Systemic Lupus Activity Measure, British Isles Lupus Assessment Group Index and expert clinical opinion, and indexed upon the first date of entering the severity group. Baseline patient characteristics and treatment patterns during the follow-up period were measured. The types of treatment considered were NSAIDs, glucocorticoids, hydroxychloroquine and immunosuppressants.
Results: A total of 20,181 patients with catastrophic illness certificates for SLE were included in this study. The mean age of all SLE patients was 46.5 years and patients were mostly female (89.1%). The mean Charlson Comorbidity Index (CCI) score of all SLE patients was 1.5 (SD 1.3). Of these patients, 29.3% (n=5,918) had mild SLE activity, 60.7% (n=12,253) moderate and 10.0% (n=2,010) severe. During the one-year follow-up period, moderate to severe patients had numerically higher utilization rate of all types of treatment compared with mild patients (Table 1). Of all oral glucocorticoid users,27.8% of severe patients used high-dose glucocorticoids (> 15 mg/day) compared to <0.1% for mild and 9.7% for moderate patients. More than 70.0% of moderate to severe patients were prescribed 2 or more types of treatment at the same point of time. Of these patients having concomitant treatment of glucocorticoids with immunosuppressants, glucocorticoid dosage increased with the number of immunosuppressant used, especially in severe patients. 80.4% of moderate to severe patients received glucocorticoid-based therapy as the first-line treatment and the median treatment duration was 3.1 months. The median treatment duration of each first-line immunosuppressant ranged from 0.9 to 4.8 months in moderate to severe patients.

Table 1. SLE treatment utilization during the 1-year follow-up period

	Total (n=20,181)`		Mild (n=5,918)		Moderate (n=12,253)		Severe (n=2,010)	
	n	%	n	%	n	%	n	%
NSAID	7,212	35.7	1,405	23.7	4,983	40.7	824	41.0
Glucocorticoid	14,019	69.5	2,015	34.1	10,297	84.0	1,707	84.9
Hydroxychloroquine	13,278	65.8	2,867	48.5	8,970	73.2	1,441	71.7
Immunosuppressant	7,630	37.8	0	0.0	6,319	51.6	1,311	65.2
Methotrexate	898	4.5	0	0.0	786	6.4	112	5.6
Azathioprine	5,642	28.0	0	0.0	4,843	39.5	799	39.8
Leflunomide	132	0.7	0	0.0	117	1.0	15	0.8
Cyclosporin	854	4.2	0	0.0	715	5.8	139	6.9
Mycophenolate	959	4.8	0	0.0	774	6.3	185	9.2
Cyclophosphamide	790	3.9	0	0.0	17	0.1	773	38.5

Conclusion: The complexity and intensity of therapeutic approaches in SLE were associated with increased disease severity and patients were often resistant to treatment. These findings reflect the disease burden in SLE patients and suggest there is a substantial unmet need in the SLE treatment paradigm for moderate to severe SLE patients.

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AB0429

SAFETY AND OBSTETRIC OUTCOMES OF BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED IMMUNE THROMBOCYTOPENIC PURPURA PATIENTS WITH PREGNANCY

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Background: Immune thrombocytopenia purpura (ITP) is not uncommon in systemic lupus erythematosus (SLE) patients and may lead to severe complications during pregnancy, such as pregnancy loss, and peripartum hemorrhage. [1] However, the treatment options during pregnancy was limited due to fetal safety concerns. Belimumab was approved for SLE and appeared to be safe in pregnant patients [2]. A phase II trial also reported efficacy of rituximab-belimumab combination in treating ITP [3]. However, the safety, influence on pregnancy outcomes, and effects on ITP in SLE patients with pregnancy was unclear.
Objectives: To evaluate the safety and obstetrics outcomes of SLE patients with pregnancy receiving belimumab for ITP.
Methods: This was a retrospective study in National Taiwan University Hospital. Eligible patients were more than 20 years old, had history of ITP, and fulfilled either the 1997 American College of Rheumatology or 2012 Systemic Lupus International Collaborating Clinics classification criteria. The belimumab was administered at 400 mg every 3-4 weeks. The serial full blood counts and immunological markers, unintended hospitalizations, infection episodes, pregnancy complications, and pregnancy outcomes were recorded.
Results: From April 2018 to November 2021, 7 SLE patients were identified. The median (IQR) age at conception was 35.6 (33.0 - 39.5) years. Three (43%) patients had secondary antiphospholipid syndrome, and none had lupus nephritis. The median (IQR) platelet count at conception was 187,000 (146,000 - 195,000) per microliter. The median (IQR) cycle of belimumab was 5 (4.5 - 8.5). Successful delivery was achieved in all patients. The median (IQR) gestational age was 36 (34 - 37) weeks, and four (57%) patients had preterm labor. The median birth weight was 2362 (2269-2477) grams, and three (43%) were small for gestational age. Pre-eclampsia developed in one patient, and none had premature preterm rupture of membrane or peripartum infections, or postpartum hemorrhage.
The median platelet count at labor was 75,000 (59,000 - 116,000) per microliter. During the pregnancy, severe thrombocytopenia with a platelet counts less than 10000 per microliter occurred in two (29%) patients, and one received prophylactic preoperative platelet transfusion. None of the patients had major or minor bleeding episodes throughout the pregnancy. Remarkably, one patient developed severe thrombocytopenia to 15,000 per microliter in the first trimester of pregnancy, and the platelet count recovered to normal range after 4 doses of belimumab administration. (Figure 1)

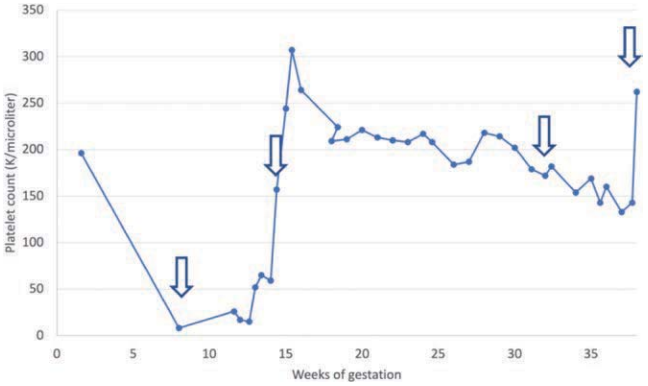

Figure 1. Serial blood platelet count during pregnancy in one patient. Arrow: belimumab 400 mg infusion.

During the pregnancy courses, no patient developed bacterial infections, two (29%) patients developed viral infections (one with upper respiratory tract infection and the other with acute gastroenteritis), and two (29%) had herpes zoster reactivation, which resolved smoothly after five-day course of oral valacyclovir.
Conclusion: The belimumab appeared to be safe in ITP patients with pregnancy, with no obvious increase in the infections and obstetric complications. Based on these observations, belimumab may be considered as one of the pharmacological options for SLE with ITP patients during pregnancy.
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AB0430 EFFECTIVENESS OF RITUXIMAB TREATMENT IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME.

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Background: The therapeutic management of Sjögren's Syndrome remains challenging in clinical practice. Randomized clinical trials with rituximab (RTX) fail to submit primary outcomes; nevertheless, some case series show improvement with this treatment.
Objectives: To evaluate the effectiveness of therapy with RTX in patients with primary Sjögren's Syndrome (pSS).
Methods: A retrospective chart review was conducted among patients with pSS who fulfilled 2002 AECG and 2016 ACR/EULAR criteria and had received RTX in the last 6 years. Patients with Sjögren's Syndrome associated with other autoimmune diseases were not included. Clinical, serological and radiological variables were analyzed (prior and 6 months after RTX therapy). A descriptive statistical analysis was performed.
Results: 18 patients were analyzed, 72.2% women, with a mean age of 60.9 years (36-83) and a mean duration of disease of 9.7 years (2-28). Reasons for treatment initiation were pulmonary involvement (n=5), renal involvement (n=4), arthritis (n=3), severe ocular/oral dryness (n=3), recurrent mumps (n=2) and autoimmune hepatitis with lymphadenopathy (n=1). Initial regimen was 2 doses of 1 g each administered 15 days apart. In 8 patients the dose was reduced in subsequent cycles to a single dose of 1 g or 500 mg. The mean number of cycles received was 3.2 (1 - 12). In 7 patients its administration persists as maintenance treatment every 6 months. In 5 patients, treatment was suspended because of clinical improvement/stability; in 2 it was stopped due to adverse effects (one for psychosis and the other for infusion reaction).; in 1 patient it was discontinued due to lack of efficacy in dryness; in 1 patient with pulmonary involvement, it was replaced by mycophenolate due to COVID-19 pandemic and clinical stability; in 1 patient it was suspended due to initiation of radiotherapy for epidermoid carcinoma of the scalp and 1 died of large cell neuroendocrine carcinoma. RTX was effective in 5 (100%) patients with pulmonary involvement (clinical, radiological and functional stability and/or improvement); in 4 (100%) patients with renal involvement (clinical and analytical improvement); in 3 (100%) patients with arthritis complete improvement was obtained; in 2 (100%) patients with recurrent mumps relapse was avoided; in 1 (100%) patient with autoimmune hepatitis and lymphadenopathy clinical and radiological improvement was obtained. Of the three patients with dryness: 1 experienced subjective clinical improvement, 1 reported improvement coinciding with the use of therapeutic contact lenses and 1 improved only at the beginning. Subjective improvement in asthenia was observed in 4 patients. Complement levels normalized in 4 of 5 patients with hypocomplementemia as well as in 4 of 4 with increased B2-microglobulin; 3 of 6 patients with hypergammaglobulinemia normalized IgG value. No changes were observed in the four patients who were rheumatoid factor positive. 6 of 6 patients receiving corticosteroid treatment, reduced the dose by half and 1 achieved corticoid withdrawal.
Conclusion: The observed data suggest that RTX may be useful in selected patients with pSS. Further research is needed to determine its efficacy.
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AB0431 THE EFFICACY OF BELIMUMAB (BEL) AS A SPARING CORTICOSTEROID AGENCY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Patients with SLE are recommended to continue the maintenance therapy with as less glucocorticoid as possible.1) However, tapering glucocorticoid often results in the recurrence of SLE. Current reports suggested that adding BEL to the standard therapy could lead to the reduction of glucocorticoid and the recurrence of SLE.2)
Objectives: The aim of this study is to evaluate the efficacy and the safety of BEL as co-treatment in the standard therapy of SLE.
Methods: Fourteen patients receiving the maintenance therapy of SLE were enrolled in this study. Dose of prednisolone (PSL), titer of anti-DNA antibody, WBC count, serum complement and SLE disease activity index (SLEDAI) were examined retrospectively at baseline and 24 months after administration of BEL.
Results: At the baseline, the mean age of patients was 48 years old, 11 patients were female, and the mean disease duration was 8.6 years. The mean dose of PSL was significantly reduced (meansease apre-administration of BEL:6.1±1.1 mg/day, 24 months after administration of BEL: 1.2 the baseline,*p=0.001*). Furthermore, six patients (43 %) could withdraw PSL without the flare of the disease. There were also statistical significance about SLEDAI between baseline and after treatment by BEL(2.1patients (43 %) c*p=0.03*) and the titer of anti-DNA antibody (6.8 withdraw PSL without t*p=0.03*). There were no statistical significant in WBC count (6177out the fla7e of the d*p=0.24*) and serum complement (C3 87significant in WBC count (61*p=0.78*, C4 20erum complement (C3 87signif*p=0.54*). As for adverse event, bacterial pneumonia (n=1) and pulmonary cryptococcosis (n=1) was revealed.
Conclusion: Our study is suggested that co-treatment with BEL on standard SLE therapy was enable to prevent the flare of SLE and reduce the dose of PSL with statistical significance among the patients under the maintenance treatment of SLE. In almost half of the cases, patients could withdraw PSL without the flare.
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AB0432 EFAVALEUKIN ALFA, A NOVEL IL-2 MUTEIN, SELECTIVELY EXPANDS REGULATORY T CELLS IN PATIENTS WITH SLE: FINAL RESULTS OF A PHASE 1B MULTIPLE ASCENDING DOSE STUDY

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Background: Defects in regulatory T cell (Treg) number and function are associated with autoimmune diseases including SLE. Interleukin (IL)-2 is essential for the development and suppressive function of Treg, and therapies that exploit the ability of IL-2 to expand Treg have shown disease-modifying potential in SLE[1]. However, low-dose IL-2 has a short half-life and narrow selectivity for Treg over conventional CD4+ T cells (Tcon) and natural killer (NK) cells. Efavaleukin alfa is an IL-2 mutein Fc fusion protein; an introduced mutation decreases binding to IL-2Rβ and increases dependence on IL-2Rα (CD25). This preferential binding to the high-affinity IL-2R, constitutively expressed at high levels on Treg, leads to increased cell surface retention and sustained Treg signaling compared with recombinant IL-2. In healthy subjects, a single dose of efavaleukin alfa was well tolerated and led to robust and selective Treg expansion[2].
Objectives: This final analysis of a phase 1b, double-blind, placebo-controlled, multiple ascending dose study (NCT03451422) reports the safety, tolerability, pharmacokinetics (PK), and pharmacodynamic effects of efavaleukin alfa in patients with SLE.
Methods: The study included five ascending dose cohorts (cohort 1=lowest dose; cohort 5=highest dose). A total of 35 patients with SLE (age 24–71 years; 85.7% female; SLE diagnosed using SLICC or ACR criteria with ANA ≥1:80 and/or elevated anti-dsDNA antibodies) were randomized to receive efavaleukin alfa or placebo (5:2 ratio for cohorts 1–3; 3:1 ratio for cohorts 4–5) subcutaneously every 2 weeks (Q2W; cohorts 1, 2, 4, and 5) or every week (QW; cohort 3) in addition to standard of care therapy for a total of 12 weeks, with 6 weeks of follow-up. The primary endpoint was the incidence of treatment-emergent adverse events (TEAEs). Additional endpoints included serum PK of efavaleukin alfa and changes in numbers of Treg, CD4+ Tcon, CD8+ T cells, and NK cells in peripheral blood.
Results: The most commonly reported TEAEs (occurring in ≥25% of efavaleukin alfa-treated subjects) included non-serious, mild or moderate (grade 1–2) injection site reactions. No grade 4 TEAEs or deaths occurred. Two serious AEs were reported in efavaleukin alfa-treated subjects: one event of syncope (grade 3) was observed in cohort 2 and was not considered related to treatment, and one case of eosinophilia (grade 2) was observed in cohort 5 and was considered related to treatment. Efavaleukin alfa PK was generally linear and dose-proportional, with a terminal half-life ranging from 18–30 hours. Peak Foxp3+ Treg expansion was observed at 8 days post-dose, and the magnitude of the peak was generally sustained after multiple QW or Q2W doses. The mean peak increases in Foxp3+ Treg were 14.8-, 17.4-, 5.7-, 2.4-, and 1.1-fold above baseline for efavaleukin alfa Q2W dosing cohorts 5, 4, 2, and 1 and placebo, respectively. At the final study assessment (42 days after the last dose), the mean Treg count was 1.3-fold above baseline (95% CI, 0.9–1.9). Treatment with efavaleukin alfa also expanded CD25^{bright} Treg (peak 53.8-fold change) and CD31+ recent thymic emigrant (RTE), naïve, and memory Treg subsets. At the highest dose (cohort 5), low-level increases in numbers of CD4+ Tcon (peak 2.3-fold), CD8+ T cells (peak 2.1-fold), and NK cells (peak 2.9-fold) were observed.
Conclusion: Multiple ascending doses of efavaleukin alfa were safe and well tolerated and led to selective and prolonged Treg expansion in SLE patients. Results at the highest dose suggest a plateau in Treg expansion with low-level increases in other IL-2–responsive cells, although interpretation is limited due to small subject numbers. The highest tested dose may be outside the therapeutic window and thus will not be assessed in phase 2 clinical studies. These findings confirm and extend previous results in healthy subjects and support the ongoing phase 2b adaptive randomized controlled trial in patients with SLE.

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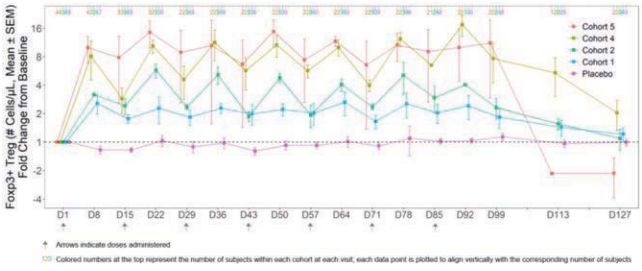
Figure: Fold change from baseline in the number of Foxp3+ regulatory T cells following biweekly administration of efavaleukin alfa.



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Disclosure of Interests: Nadia Tchao Shareholder of: Amgen Inc., Employee of: Amgen Inc., Nandita Sarkar Shareholder of: Amgen Inc., Employee of: Amgen Inc., Xuguang Hu Shareholder of: Amgen Inc., Employee of: Amgen Inc., Rong Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., Cassandra Milmont Shareholder of: Amgen Inc., Employee of: Amgen Inc., Yan Shi Jin Shareholder of: Amgen Inc., Employee of: Amgen Inc., Vincent Chow Shareholder of: Amgen Inc., Employee of: Amgen Inc., Mark Kroenke Shareholder of: Amgen Inc., Employee of: Amgen Inc., Kevin Gorski Shareholder of: Amgen Inc., Employee of: Amgen Inc., Richard Furie Consultant of: Amgen Inc, Grant/research support from: Amgen Inc, Alan Kivitz Shareholder of: Amgen Inc., Gilead, GlaxoSmithKline, Novartis, Pfizer, and Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, GSK, Horizon, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Flexion, Gilead, Janssen, Pfizer, Sanofi, and Sun Pharma, Stanley Cohen Consultant of: Amgen Inc., AbbVie, Eli Lilly, Pfizer, Genentech, and Gilead, Grant/research support from: Amgen Inc., AbbVie, Eli Lilly, Pfizer, Genentech, and Gilead
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AB0433 ANTI-RITUXIMAB ANTIBODIES DEMONSTRATE NEUTRALISING CAPACITY, ASSOCIATE WITH LOWER CIRCULATING DRUG LEVELS AND EARLY RELAPSE IN PATIENTS UNDERGOING TREATMENT FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: A major limitation of biologic therapy is formation of anti-drug antibodies (ADA). We previously found ADA to rituximab (RTX) are more prevalent in patients undergoing treatment for systemic lupus erythematosus (SLE) than rheumatoid arthritis and vasculitis (1). In addition, we demonstrated that ADA to RTX predict subsequent infusion related reactions (2). However, little is known regarding the long-term dynamics of ADA to RTX in patients undergoing treatment for SLE.
Objectives: In this study we evaluated the longitudinal impact of ADA positivity with particular focus on; 1) Risk factors for development of ADA. 2) Impact of ADA on treatment response. 3) Influence of ADA on RTX drug kinetics over time. 4) The capacity of ADA to neutralise RTX.
Methods: Patients with SLE undergoing treatment with RTX were recruited to this study (n=35). Serum samples were collected at the following intervals post-treatment; 1-3 months (defined as 'early' post-treatment), 6 months, 12 months, 36 months (n=114).
Clinical and laboratory data was collected pre-treatment and at each follow-up time point. Response to treatment was assessed by improvement in SLEDAI-2K score from baseline and also according to BILAG as previously described (3).
ADA were detected using an electrochemiluminescent immunoassay. Serum RTX levels were measured by ELISA. ADA status was defined according to the following patterns over time; persistently negative, persistently positive (0-15 AU/ml) and persistently high positive (≥16 AU/ml, upper quartile). A complement dependent cytotoxic assay was used to determine neutralising capability of ADA in a subgroup of positive samples (n=38).

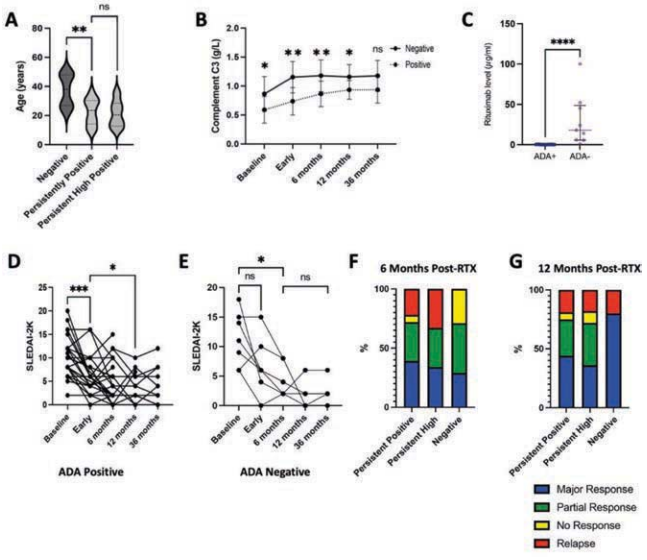

Figure 1.

Results: ADA to RTX were found to be persistently positive in 64.3% of patients over the 36-month follow-up period and there was no significant difference in baseline disease activity (BILAG / SLEDAI-2K) between those who were subsequently ADA positive vs negative. ADA positive patients had a younger age at diagnosis of SLE when compared with ADA negative (mean 22.50 ± 9.10 vs 37.29 ± 11.31 years, p=0.002, Figure 1 A). Multivariate logistic regression found a 22% decrease in risk of ADA positivity for each addition year after diagnosis (p=0.03).

ADA positive patients had a significantly lower C3 level at baseline (mean 0.61 ± 0.23 g/L vs 0.87 ± 0.30 g/L, p=0.026), which remained lower at each subsequent time point post-treatment up to 12 months post-treatment (Figure 1B).

At 1-3 months post-RTX, patients who were ADA positive had a significantly lower circulating drug level than ADA negative (p<0.001, Figure 1 C).

In terms of clinical response, ADA positive patients had an initial significant improvement in disease activity (SLEDAI-2K) by 3 months (p<0.001). However, response was not maintained at 12 months (Figure 1 D). In comparison, ADA negative patients showed a significant improvement in SLEDAI-2K at 6 months and this was maintained across the 36-month follow-up period (Figure 1 E).

BILAG defined relapse was more common at six months post-treatment in ADA positive patients (22%) and ADA highly positive patients (33%) than those who were ADA negative (in which there were no cases of relapse within the first six months, Figure 1 F). At 12-months post-RTX, a higher rate of BILAG defined Major Response was seen in those who were ADA negative (80%) when compared with ADA positive (44%) and high positive (36%) as shown in Figure 1 G.

Finally, antibodies derived from all ADA positive samples (38/38) were found to neutralise RTX *in vitro*.

Conclusion: ADA to RTX were common and persisted over the 36-month period of this study. ADA associated with earlier serum drug elimination, increased relapse rates and demonstrated neutralising capacity suggesting that ADA could be a significant limitation to sustained response to treatment in clinical practice.

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AB0434 EFFICACY AND SAFETY OF OBINUTUZUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH SECONDARY NON-RESPONSE TO RITUXIMAB.

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Background: Secondary inefficacy characterized by infusion reactions and anti-drug antibodies occur in 14% of SLE patients treated with repeat rituximab courses(1). Obinutuzumab is a next-generation humanized type-2 anti-CD20 therapy licensed for hematological malignancies which may overcome this issue(2).

Objectives: We set out to evaluate the clinical efficacy and safety of obinutuzumab in a cohort of rituximab resistant SLE patients.

Methods: We collated data from SLE patients receiving obinutuzumab for secondary non-response to rituximab in BILAG centres. Disease activity was assessed using BILAG-2004, SLEDAI-2K and serology before, and 6 months after, obinutuzumab 2x1000mg infusions alongside methylprednisolone 100mg. Flow cytometry where possible was carried out using a multiple gating highly sensitive strategy.

Results: All 9 patients included in the study received obinutuzumab alongside concomitant oral immunosuppression. At 6 months post-obinutuzumab, there were significant reductions in median SLEDAI-2K from 12 to 6 (p=0.014) and total BILAG-2004 score from 21 to 2 (p=0.009). Complement C3 and dsDNA titres improved significantly (both p=0.04). Non statistically significant numerical improvements were seen in C4 levels.

Of 8/9 patients receiving concomitant oral prednisolone at baseline (all >10mg/day), 5/9 had their dose reduced at 6 months; 4/8 were on 5mg/day and were in Lupus Low Disease Activity State. After obinutuzumab, 6/9 patients with peripheral B-cell data achieved complete depletion including 4/4 assessed with highly sensitive assays. 1/9 obinutuzumab non-responder required cyclophosphamide therapy. 1 unvaccinated patient died from COVID-19.

Conclusion: Obinutuzumab appears to be effective and steroid-sparing in renal and non-renal SLE patients with secondary non-response to rituximab. Obinutuzumab was shown to be effective in patients with severe renal and non-renal disease. Therefore, in those with previous responsiveness to B-cell depletion, switching to humanised type-2 anti-CD20 therapy is a logical approach following loss off efficacy.

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AB0435 LUPUS NEPHRITIS RESPONSE IN TERMS OF KIDNEY FUNCTION, URINE SEDIMENT AND SEROLOGICAL ACTIVITY AFTER SUBCUTANEOUS BELIMUMAB TREATMENT

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease. Kidney affection appears in 40-50% of SLE patients and may condition the prognosis. Belimumab is a monoclonal antibody approved for SLE

Table 1. Baseline characteristics, disease activity and steroid doses before and after last obinutuzumab/rituximab.

Patient	Ethnicity	Disease duration (Years)	Age (Years)	Total BILAG-2004 before Obi	Total BILAG-2004 after Obi	SLEDAI-2K before Obi	SLEDAI-2K after Obi	Prednisolone before Obi (mg)	Prednisolone after Obi (mg)
1	South Asian	10.8	36.4	18	2	14	8	10	5
2	South Asian	6.3	24.4	24	2	12	4	30	10
3	South Asian	11.9	34.8	29	1	10	4	10	10
4	South Asian	8.2	41.9	21	1	6	0	15	15
5	South Asian	6.8	29.4	32	21	18	14	50	60
6	White European	17.5	37.0	12	8	8	8	15	5
7	White European	16.9	30.0	12	1	12	8	10	5
8	Caribbean	6.2	44.2	25	2	13	0	10	15
9	Caribbean	2.6	21.0	9	2	16	6	10	5
Median (Q1, Q3)	**NA**	**8.2 (6, 12)**	**34.8 (29,37)**	**21 (12, 25)**	**2 (1, 2)**	**12 (10, 14)**	**6 (4, 8)**	**10 (10, 15)**	**10 (5, 15)**

Table 1.

		Onset					Currently				
Patient	NL type	Proteinuria (g/24h)	Creatinine (mg/dL)	Glomerular filtration (ml/min)	Anti-DNA	C3, C4	Proteinuria (g/24h)	Creatinine (mg/dL)	Glomerular filtration (ml/min)	Anti-DNA	C3, C4
1	III	1	0.81	90	50	80, 8	0.4	0.73	89	24	80, 20
2	V	0.75	0.40	130	24	normal	0	0.49	130	43	normal
3	III	0.75	0.73	101	164	normal	0	0.80	82.9	78	normal
4	IV	0.96	1.26	55	21	normal	0.70	1.29	71	2.2	normal
5	IV	0.95	1.29	71	15	101, 10	0.17	0.88	84	85	89, 23

since 2011, but it had no lupus nephritis (NL) indication. Recently, promising results from a controlled Belimumab trial in LN were published.

Objectives: To analyze effectiveness of Belimumab in LN patients under follow-up by the rheumatology department of a tertiary hospital.

Methods: Observational, retrospective and cross-sectional study including SLE patients (SLICC/ACR 2012 criteria) treated with subcutaneous and/or intravenous Belimumab. Demographic and serological data, concomitant treatment, kidney function and urine sediment were collected.

Results: Sixteen patients with a median age of 47.56 (11.66) years and with 5.40 (0.55) years since Belimumab onset were included. Five patients had LN demonstrated by kidney biopsy and they were included on analysis data. In this group, median age was 39 (6.96) years, patients had 17.80 (10.38) years since SLE diagnosis and 6.6 (0,89) years since Belimumab onset. The most prevalent nephritis type was III and IV, only one patient presented V type.

Regarding the treatment, every patient received antimalarial drugs (cloroquine 40%, hydroxicloroquine 60%) and mycophenolic acid. Concerning the corticosteroid therapy, all patients receive prednisone, with an average dose of 4 mg per day.

The results obtained were included in the Table 1.

Conclusion: Belimumab can improve LN, in terms of serological activity, kidney function and urine sediment. It could be a promising option associated to standard therapy for SLE patients with kidney affection.

Disclosure of Interests: None declared

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AB0436 EFFECTIVENESS OF BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A REAL-LIFE ANALYSIS

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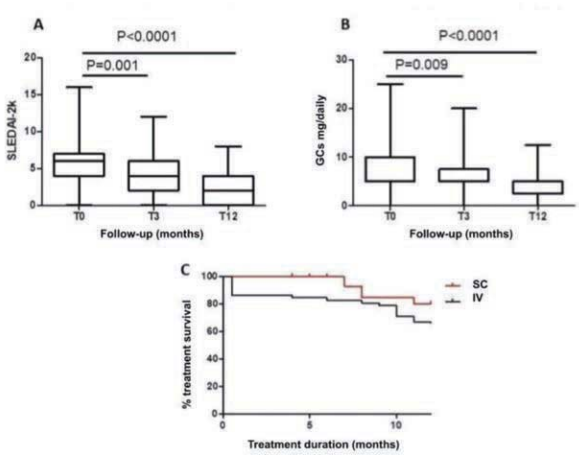
Background: Efficacy and safety of belimumab (BLM) in Systemic Lupus Erythematosus (SLE) patients with active disease have been demonstrated by RCTs [1,2] and confirmed by several observational studies [3-8]. Most of these data have been obtained by the use of BLM intravenous formulation (IV); on the contrary, very few findings are available on the use of the drug subcutaneous formulation (SC).

Objectives: Efficacy and drug survival of BLM have been assessed in a monocentric cohort of SLE patients, exploring any difference between the two routes of administration, IV or SC.

Methods: A longitudinal study on SLE patients (according to ACR 1997 classification criteria [9]) candidates for treatment with BLM has been performed. Demographic, clinical-laboratory and therapeutic data - including glucocorticoid dosage in prednisone-equivalent - have been collected. Disease activity has been assessed by SLEDAI-2k [10]; in patients with inflammatory articular involvement, DAS28-PCR [11] has been used. In compliance with the study protocol, patients were assessed at baseline and at 3 and 12 months after starting treatment.

Results: A total of 85 patients treated with BLM were enrolled, most of whom were female (male/female 2/83), with a median age of 48 years (IQR 13) and a median disease duration of 127 months (IQR 151). Fifty-one patients (60%) were treated with IV formulation and the remaining 34 (40%) with SC route. BLM was prescribed due to the following clinical manifestations: joint involvement (61.2%), cutaneous manifestations (20.0%), renal involvement (for residual proteinuria, 5.9%), haematological modifications (5.9%), constitutional involvement (3.5%), pericarditis (1.2%), headache (1.2%). In both the formulations, joint involvement was the most frequent indication of BLM (IV: 64.7%, SC: 58.8%). Median treatment duration was 15 months (IQR 24). Moving on drug efficacy, after 3 and 12 months of follow-up BLM has determined a significant reduction of SLEDAI-2k median values ($p=0.001$, $p<0.001$ respectively, Figure 1A) as well as of daily prednisone dose ($p=0.009$, $p<0.0001$ respectively, Figure 1B). In patients treated because of musculoskeletal manifestations, DAS28-PCR reduced significantly at 3 and 12 months after treatment ($p<0.0001$). Drug survival at 12 months was 70% in the total cohort (Figure 1C) and was higher in patients treated with SC formulation than with IV route (75.8% *versus* 66.5%, p=ns). During the period of follow-up, 39 patients (45.9%) discontinued BLM: 38.4% of patients due to adverse events, 41% for primary or secondary inefficacy, 15% lost to follow-up, 5.1% for pregnancy. BLM withdrawal for adverse events was more frequent in the group of patients treated with IV formulation than SC one (25.9% *versus* 5.9%, p=0,0001). 11 patients switched from IV formulation to SC one after a median period of 40 months (IQR 20) without loss of efficacy or adverse events.

Figure 1: Change of SLEDAI-2k values (A) and glucocorticoids dosage (GCs - B), graphically represented by Box and Whisker plot; treatment survival calculated by Kaplan-Meier curve (C).



Conclusion: Our results confirm BLM efficacy also in a real-life setting. Notably, our data highlight a better drug survival in patients treated with SC formulation, mainly secondary to a less frequency of adverse events.

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AB0437 MONTELUKAST AS A TREATMENT FOR REFRACTORY CUTANEOUS LUPUS ERYTHEMATOSUS: A CASE SERIES AND PROOF-OF-CONCEPT STUDY

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Background: Treatment of cutaneous lupus relies mostly in avoidance of exposure to sunlight, steroids and hydroxychloroquine. A diverse array of cytokines and chemokines released by resident and migrating inflammatory cells have been implicated in the pathogenesis of skin damage in patients with systemic lupus erythematosus (SLE). Leukotrienes are potent lipid mediators involved in hypersensitivity reactions but very few data exist on their involvement in SLE.

Objectives: Our aim is to report a case series of SLE patients with refractory skin lesions that were successfully treated with sodium montelukast (MLK), a cysteinyl-leukotriene antagonist.

Methods: We present 4 consecutive female SLE patients with refractory skin lesions that were treated with MLK (10mg/d). Skin lesions were scored using

CLASI criteria. Peripheral blood mononuclear cells (PBMC) from those 4 SLE patients and 4 healthy age-matched female controls were collected and the relative expression of the 5-lipoxigenase (ALOX5) and 15-lipoxigenase (15LOX1R) genes against a reference gene (GAPDH) was assessed using a quantitative polymerase change reaction (qPCR) protocol.

Results: All four patients experienced improvement of skin lesions 2-4 weeks following initiation of MLK with over 50% reduction in severity using CLASI score. The response was sustained for at least 3 months follow-up and no adverse events were recorded. All but one of the patients relapsed following MLK withdrawal but response was recovered after restart of MLK. Expression of the ALOX5, but not of 15LOX1R, was significantly ($p<0.001$) increased in PBMC from SLE patients as compared to controls.

Conclusion: This is the first report of a fast and sustained successful response of cutaneous SLE to MLK. There were no safety issues. PBMC from SLE patients showed increased expression of the ALOX5gene. This case series suggests the involvement of MLK in cutaneous lupus and encourage designing a randomized trial.

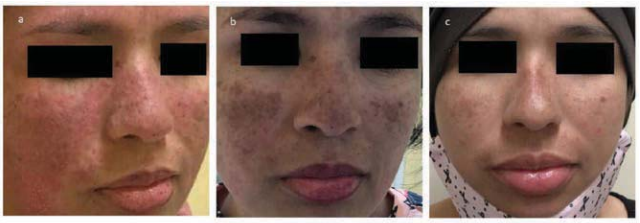

Figure 1 – Severe refractory butterfly rash prior (a) and after (b, c) MLK administration to a lupus patient

Disclosure of Interests: None declared

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AB0438 EFFICACY OF BELIMUMAB TREATMENT FOR SYSTEMIC LUPUS ERYTHEMATOSUS AT OUR HOSPITAL

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Background: Belimumab (BEL), a monoclonal antibody against the soluble counterpart of B-cell activating factor (BAFF) has been recommended to be added in patients with SLE who do not respond adequately to standard therapy [1]. In addition to antibody production, belimumab may also affect other functions of B cells, such as antigen presentation and excretion of inflammatory cytokines. Belimumab may also have an effect on immune cells other than B cells, as they express BAFF receptors. These facts suggest that BEL administration in SLE may have an effect on various pathological conditions including cytokine production, not just antibody production. However, there are few reports on whether cytokine production is actually related to the efficacy of BEL administration in SLE.

Objectives: The purpose of this study was to determine the efficacy of BEL administration in patients with SLE and its effect on cytokines.

Methods: Patients with SLE who were started on BEL between December 2018 and December 2021 at our institution were included in this study. We retrospectively analyzed the reasons for additional BEL administration, adverse events, disease activity indicators (SLE Disease Activity Index (SLEDAI)-2K, lupus low disease activity state (LLDAS) achievement rate, anti-dsDNA antibody titer, serum complement titer, and treatment agents including glucocorticoid dose. Serum cytokine (interferon-alpha, interleukin (IL)-6, IL-10, and IL-17A) levels were measured using ELISA at the start of BEL administration, 3 months, and 6 months later.

Results: Five cases of SLE were included in the study. Four of the five patients were female, with a mean age of 51.4±9.6 years and a mean duration of disease of 17.4±10.0 years. The reasons for additional BEL administration were glucocorticoid reduction in five patients, refractory pericarditis in one patient, skin rash and arthritis in two patients, and immunological activity in two patients. Four of the five patients had decreased renal function below eGFR50 at the baseline. Concomitant medications at the time of BEL induction included steroids in five patients (mean prednisolone dose 12.2±12.2 mg/day), hydroxychloroquine in three patients, mycophenolate mofetil in three patients, tacrolimus in one patient, and methotrexate in one patient. The mean disease activity before the introduction of BEL was SLEDAI 4±4, and LLDAS was achieved in three patients.

Twelve weeks after the start of BEL treatment, two patients had improved SLEDAI, including one patient who achieved LLDAS. Immunological activity parameters improved in one of the two patients. However, two patients flared after BEL administration and were treated with increased glucocorticoid doses. One patient with SLE on hemodialysis had thrombocytopenia, an adverse event that may have been related to belimumab treatment.

Conclusion: At our institution, BEL was additionally administered to SLE patients with refractory disease and was effective; with the exception of one case. Serum cytokine analysis before and after BEL treatment will be included in the discussion.

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AB0439 COMPARATIVE EFFECTIVENESS OF RAPID AND CONVENTIONAL GLUCOCORTICOID TAPERING REGIMENS IN TREATING PATIENTS WITH PROLIFERATIVE LUPUS NEPHRITIS IN THE REAL WORLD SETTING

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Background: Rapid glucocorticoid (GC) tapering is recommended for lupus nephritis (LN) by 2019 EULAR/ERA-EDTA recommendations [1]. However, slower conventional GC tapering regimen is still common in the real world setting, and it is controversial whether a rapid GC tapering regimen is as effective as the conventional regimen.

Objectives: We aimed to compare the renal outcomes between rapid and slower GC tapering regimens in patients with LN.

Methods: We retrospectively surveyed the medical records of 27 patients with proliferative LN (class III or IV) at Kobe City Medical Center General Hospital. These patients were divided into two groups (rapid GC tapering group and conventional GC tapering group) according to GC dosage at month 6. Logistic regression analyses were performed to examine the association of GC tapering regimens with achievement of primary efficacy renal response (PERR) and complete renal response (CRR) which were defined by Furie et al. [2] at month 24.

Results: Twenty-seven patients (19 women and 8 men) with class III or IV LN were included. The mean age was 43 years. The mean eGFR and urine protein-to-creatinine ratio at baseline were 66.7 mL/min/1.73m^2 and 3.125 g/gCr, respectively. Concomitant class V LN was present in 26.0%. The rapid GC tapering group (PSL≦10 mg/day at month 6) and the conventional GC tapering group (PSL>10 mg/day at month 6) were 11 and 16 patients, respectively. Baseline characteristics were balanced between the two groups except for use of cyclophosphamide or mycophenolate mofetil. Mean urine protein-to-creatinine ratio at month 24 were 0.46 g/gCr in the rapid GC tapering regimen group and 1.08 g/gCr in the conventional GC tapering regimen group ($p=0.790$). Achievements of PERR and CRR at month 24 were 54.0% and 43.8% in the rapid GC tapering group and 54.5% and 25.0% in the conventional GC tapering group, respectively. After adjustment of cyclophosphamide or mycophenolate mofetil usage and urine protein-to-creatinine ratio at baseline, adjusted odds ratio was 1.52 (95% confidence interval [0.126 to 18.29], $p=0.743$) and 2.99 (95% confidence interval [0.34 to 28.52], $p=0.341$), respectively.

Conclusion: Our results suggest rapid GC tapering regimen is as effective as conventional slower tapering regimen for patients with proliferative LN.

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Table 1. Baseline patients characteristics.

	Rapid GC tapering group (n=11)	Conventional GC tapering group (n=16)	P value
Age – years	41.7 ± 14.7	43.9 ± 16.2	0.863
Female – no. (%)	9 (81.8)	10 (62.5)	0.405
Class III LN – no. (%)	6 (54.5)	7 (43.8)	0.704
Class IV LN – no. (%)	6 (45.5)	9 (56.3)	0.704
Concomitant Class V LN – no. (%)	4 (36.4)	3 (18.8)	0.391
Induction therapy (use of CY or MMF) – no. (%)	10 (90.9)	8 (50.0)	0.042
Serum creatinine – mg/dL	1.15 ± 0.72	1.14 ± 0.80	0.882
eGFR – mL/min/1.73m^2	65.2 ± 39.0	67.8 ± 34.5	0.835
UPCR – g/gCr	3.29 ± 2.96	3.01 ± 3.25	0.604
C3 – mg/dL	41.1 ± 20.1	45.0 ± 21.5	0.639
C4 – mg/dL	6.8 ± 4.7	10.1 ± 8.0	0.346

GC, glucocorticoid; LN, lupus nephritis; UPCR, urine protein-to-creatinine ratio; CY, cyclophosphamide; MMF, mycophenolate mofetil

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AB0440 USE OF BELIMUMAB IN CLINICAL PRACTICE. CLINICAL AND SEROLOGICAL EFFECTIVENESS AND CORTICOSTEROID-SPARING ACTIVITY

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Background: Since 2011, the use of Belimumab for the treatment of Systemic Lupus Erythematosus (SLE) has demonstrated efficacy and safety in several randomised clinical trials. However, strict inclusion criteria may restrict those results limiting the interpretation of these results to routine clinical practice populations.
Objectives: The aim of this study was to analyse the profile of patients using Belimumab as well as the clinical, serological and corticosteroid-sparing outcomes that may result from it use.
Methods: Retrospective cohort study including patients diagnosed with SLE and treated with Belimumab. Epidemiological, clinical and analytical data were collected at 6, 12 and 24 months before and after starting treatment with Belimumab. To assess effectiveness, the SELENA-SLEDAI, SLICC, clinical changes, concomitant treatments, corticosteroid dose and ds-DNA and C3-C4 levels were used.
Safety was evaluated by assessing the need and cause for discontinuation of Belimumab.
Results: Thirty-one patients were included, mostly 28 (90.32%) women, with a mean age of 48.55 ± 1.95 years and a mean time of disease progression since diagnosis of 16.13 ± 1.77 years. The most prevalent affection before initiation of Belimumab were joint (83.87%), systemic (58.06%), skin (29.03%) and nephropathy (22.58%). The mean SELENA-SLEDAI score before Belimumab was 5.32 ± 0.46; 64.5% had elevated anti-dsDNA, 48.39% and 54.84% had low C3 and C4 levels, respectively. Before starting Belimumab, the most used treatments were both antimalarials (72.4%) and corticosteroids (80.6%). The main reason for starting Belimumab was the ineffectiveness of previous treatments (67.7%). The vast majority of patients were treated subcutaneously (90.3%) and there were no major adverse events leading to drug withdrawal, with a median duration of use of 19.3 months (IQR: 9.75-35.55).
Conclusion: After starting Belimumab, a decrease in the SELENA-SLEDAI activity scale, an increase in C3 and C4 levels, and a significant decrease in anti-dsDNA levels at 6 months were observed. At 12 and 24 months, continuity of this trend was observed, although statistical significance was not reached. As concerns corticosteroids, we observed a decrease in steroid use below 7.5mg/day and even 5mg/day after the introduction of Belimumab avoiding the undesirable effects of prolonged steroid use.

Table 1.

	BEFORE BELIMUMAB (n=31)	6 MONTHS (n=28)	12 MONTHS (n=22)	24 MONTHS (n=9)
ESLEDAI x̄ (SD)	5,32 (0,46)	2,28 (0,44) P<0,001	2,90 (0,72) P<0,005	3,44 (1,39) p>0,05
High dsDNA - n (%)	18 (58,06)	14 (61,29) P<0,001	14 (45,16) P=0,036	4 (12,9) P=0,7
Low C3 (<90mg/dl) - n (%)	15 (48,39)	11 (35,48) P=0,006	9 (29,03) P=0,193	3 (9,68) P=0,06
Low C4 (<16mg/dl) - n (%)	17 (54,84)	14 (45,16) P<0,001	11 (35,48) P=0,003	5 (16,13) P=0,217)

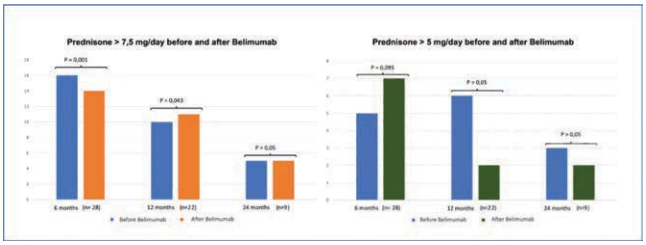

Figure 1.

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AB0441 PREDICTORS OF CLASI RESPONSE OVER TIME IN A MULTICENTRIC REAL LIFE COHORT OF SLE PATIENTS TREATED WITH BELIMUMAB

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Background: Over 80% of patients affected with SLE experience skin involvement. The anti-BLyS drug belimumab was shown effective in ameliorating mucocutaneous SLE manifestations in clinical trials and real-life studies. Cutaneous response is quantified through the CLASI (cutaneous lupus erythematosus area and severity index). Clinically relevant improvements are defined as decreases of ≥50% (CLASI50) or 70% (CLASI70) from baseline values.
Objectives: To assess rates and predictors of CLASI50 and CLASI70 in the Berliss multicentric SLE cohort[1] of patients treated with belimumab.
Methods: Baseline and ongoing features of patients with baseline active skin involvement (CLASI>0) were assessed in relationship to the chosen outcomes CLASI50 and CLASI70 at 24 and 52 weeks. A subanalysis on patients with CLASI≥5 was as well conducted. Logistic regression was employed to identify predictors of response.
Results: 172 patients displayed skin involvement at baseline (CLASI>0). Of those, 124 displayed at least a 12-month-follow-up and were included in the analysis. Seventy-seven (62.1%) patients reached CLASI50 at 24 weeks and 91 (77.8%) at 52 weeks; 87 (70.2%) reached CLASI70 at 24 and 99 (79.8%) at 52 weeks. Baseline predictors of CLASI50 at 24 weeks were CLASI-damage (CLASI-d) (OR [95%CI], p; 0.79 [0.65-0.98] 0.03) and disease duration (0.93[0.86-0.99], 0.011). No baseline predictors of CLASI70 at 24 weeks emerged, however having achieved a CLASI50 response at 24 weeks portended CLASI50 and 70 response through week 52 (p<0.01, Table 1). In the subgroup of patients with CLASI≥5, longer disease and increased CLASI-d at baseline confirmed as negative predictors of CLASI50 at 24 weeks. In this subset, use of antimalarials and active smoking at baseline predicted CLASI70 at 24 weeks (Table 1).

Table 1. Predictors of CLASI-A Response at Week 24 and 52 by Baseline CLASI-A at 50% and 70% Response Thresholds

Timepoint	Outcome	Variable	OR[95%CI] p
CLASI>0			
24 weeks	CLASI50	CLASI-d	0.79 [0.65-0.98] 0.030
		Disease duration	0.93[0.86-0.99], 0.011
	CLASI70	CLASI-d	0.93 [0.74-1.16], 0.51
		Disease duration	0.97 [0.97-1.02], 0.18
52 weeks	CLASI50	CLASI50 at 24 weeks	14.3[4.88-44.42], <0.001
	CLASI70	CLASI50 at 24 weeks	6.22 [2.00-19.34], 0.002
CLASI≥5			
24 weeks	CLASI50	CLASI-d	0.72 [0.53-0.98], 0.037
		Disease duration	0.93 [0.66-1.00], 0.071
	CLASI70	Antimalarials	6.61 [1.20-36.29] 0.032
		Smoking	0.15 [0.03-0.83], 0.034
52 weeks	CLASI50	CLASI50 at 24 weeks	22.0 [2.47-196.05], 0.006
	CLASI70	CLASI50 at 24 weeks	1.24 [0.06-25.08], 0.88

CLASI, cutaneous lupus erythematosus area and severity index; CLASI-d, CLASI damage; CLASI50 and CLASI70: decrease ≥50% or ≥70% in CLASI from baseline. OR and 95%CIs are estimated using a logistic regression model with stratification factors as covariates (SLEDAI-2K at baseline, baseline prednisone dosage).

Conclusion: Earlier use of belimumab favors achievement of skin response among SLE patients and attainment of a prompt response predicts further response. Use of antimalarials reinforces while smoking hampers a more profound CLASI improvement over time.

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Disclosure of Interests: Mariele Gatto Speakers bureau: GSK, Grant/research support from: GSK, Roberto Depascale: None declared, Angela Tincani: None declared, Giacomo Emmi: None declared, Salvatore Scarpato: None declared, Fabrizio Conti: None declared, Marcello Govoni: None declared, Marta Mosca: None declared, Maria Gerosa: None declared, Enrica Bozzolo: None declared, Valentina Canti: None declared, Armando Gabrielli: None declared, Elisa Gremese: None declared, Salvatore De Vita: None declared, francesco ciccia: None declared, Carlo Salvarani: None declared, Maurizio Rossini: None declared, Paola Faggioli: None declared, Antonella Laria: None declared, Amato De Paulis: None declared, Roberto Gerli: None declared, Enrico Brunetta: None declared, Alessandro Mathieu: None declared, Carlo Selmi: None declared, Rossella De Angelis: None declared, Simone Negrini: None declared, Margherita Zen: None declared, Andrea Doria Speakers bureau: GSK, Eli Lilly, Roche, Grant/research support from: GSK, Luca Iaccarino Speakers bureau: GSK, Grant/research support from: GSK

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AB0442

EVEN IN SYSTEMIC LUPUS ERYTHEMATOSUS THAT HAS ACHIEVED SUSTAINED LLDAS, ADDITIONAL ADMINISTRATION OF HYDROXYCHLOROQUINE SHOULD BE CONSIDERED.

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Background: Hydroxychloroquine (HCQ) therapy is recommended as a baseline treatment for all patients with systemic lupus erythematosus (SLE) due to its various benefits (1). However, it is not clear to what extent HCQ contributes to improvement in SLE patients with stable disease activity. It has also been reported that HCQ is effective in improving the prognosis of life caused by atherosclerotic lesions in SLE, but the mechanism of this effect has not been fully elucidated.

Objectives: The purpose of this study was to determine the benefit of additional HCQ administration in SLE with controlled disease activity, who achieved the sustained LLDAS.

Methods: The study included patients with SLE who started additional HCQ treatment between January 2016 and December 2019 at our institution, those who sustained LLDAS achievement for at least 3 months prior to starting HCQ treatment. These patients did not change their immunosuppressant and glucocorticoid regimens for more than three months after starting HCQ. The effect of HCQ was assessed at the beginning and 3 months after administration. The disease activity was measured by SELENA-SLEDAI, SLE-DAS, and immunoserological parameters including serum complement levels and anti-DNA antibodies. The factors that are known to associated with pathogenesis of atherosclerosis, such as serum TNF-α, IL-6, IL-8, MCP-1, adiponectin, leptin, resistin, S100A8, and S100A9, were measured by ELISA.

Results: Of the 110 SLE patients who received additional HCQ at our institution, 27 patients who had achieved LLDAS from at least 3 months prior to HCQ administration were included in this study. Patient characteristics are represented in Table 1. SLEDAI scores, SLE-DAS scores and serum anti-dsDNA antibodies were observed to be significantly reduced after HCQ treatment compared to baseline. After 3 months of HCQ treatment, serum lipid markers such as triglyceride (TG), low-density lipoprotein (LDL) cholesterol and atherosclerotic index, which are associated with the development of atherosclerosis, were significantly reduced compared to baseline (TG, LDL and atherosclerotic index: p<0.05). Cytokines such as TNF-α, IL-6, MCP-1, S100A8, S100A9, leptin, and resistin were found to be significantly decreased, and serum adiponectin was significantly increased. (TNF-α, IL-6, MCP-1, leptin: p < 0.05. S100A8, S100A9, adiponectin, resistin: p < 0.0001, Figure 1).

Table 1. Characteristics of patients with SLE enrolled in this study.

Characteristics	N = 27
Female, no. (%)	24 (88.9)
Age, years, mean ± SD	44.4 ± 11.6
Disease duration, years, mean ± SD	18.3 ± 12.2
BMI, mean ± SD	21.9 ± 3.0
Concomitant immunosuppressive treatments	
Prednisone, no. (%)	n = 23
Median dosage, mg/day[#]	5 (3.0–5.0)
Triglyceride, mg/dL[#]	102 (73–149)
High-density lipoprotein cholesterol, mg/dL[#]	59 (43–66.5)
Low-density lipoprotein cholesterol, mg/dL[#]	108 (96–122)
Arteriosclerotic index[#]	2 (1.7–2.5)
Disease activity	
SLEDAI score[#]	4 (2–4)
SLE-DAS score[#]	2.076 (1.12–3.50)
Anti-dsDNA antibody, IU/ml[#]	5.2 (5–15.6)
dsDNA positive, no. (%)	10 (37.0)
C3, mg/dL[#]	76 (61–100)
C4, mg/dL[#]	14 (10–22)
CH50, U/mL[#]	34.1 (29.7–39.6)

[#]Nonparametric distributions were represented as median (interquartile range). Anti-dsDNA positive means that anti-dsDNA titer increases to >12 IU/mL.

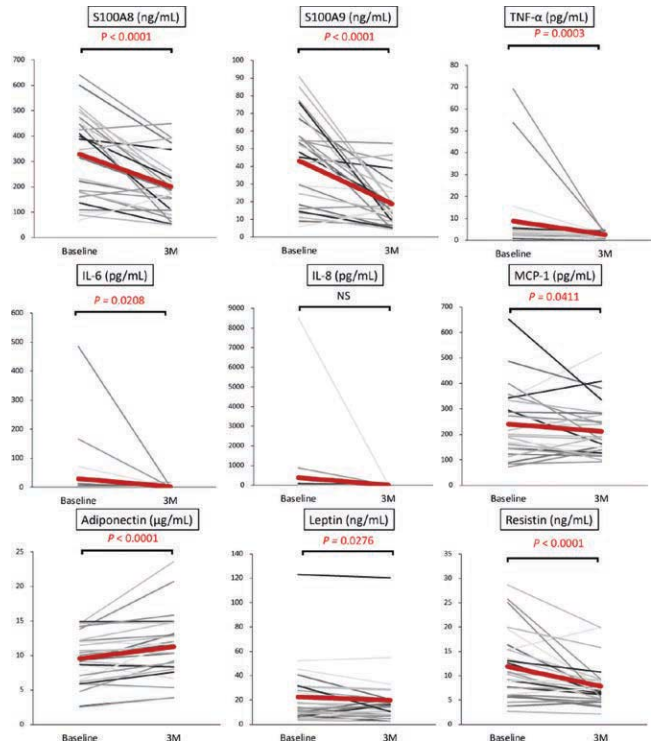

Figure 1. Serum cytokine levels before and after hydroxychloroquine treatment

Serum levels of the indicated cytokines and factors were measured at baseline and after 3 months (3M) of treatment with HCQ. The gray lines show the values for individual patients, and the thick red line shows the average value. P-values were determined using the Wilcoxon signed-rank test. A p-value of less than 0.05 was considered statistically significant.

Conclusion: The addition of HCQ medication to SLE patients who achieve the clinical therapeutic goal of LLDAS without HCQ may prevent progression of atherosclerosis in addition to further reducing disease activity.

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AB0443 LONG-TERM OUTCOMES OF MULTITARGET THERAPY OF MYCOPHENOLATE MOFETIL AND TACROLIMUS IN LUPUS NEPHRITIS: A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Background: Recent studies showed the efficacy of multitarget therapy with mycophenolate mofetil (MMF) and calcineurin inhibitor for induction therapy for lupus nephritis (LN)[1]. However, long-term outcomes have not been well elucidated.
Objectives: We retrospectively analyzed the long-term outcomes of multitarget therapy of MMF and tacrolimus.
Methods: We examined 27 LN patients (4 male, 23 female) treated with multitarget therapy for induction therapy between Oct. 2009 and Nov. 2018 in our department. Complete remission (CR) was defined as 1) UPCR<0.5 g/gCr, and 2) serum creatinine (S-Cr) normal or if abnormal, within 15% of baseline; 1) and 2) were observed in 2 consecutive visits. Relapse was defined as UPCR>1.0 g/gCr or intensification of immunosuppressive treatment after achievement of CR.
Results: The mean age was 38.6±11 . 6 years old. 17 patients were new-onset LN, and 10 patients were relapse LN. UPCR and eGFR before treatment were 4.42±2.98 g/gCr and 71.5±32.9 mL/min/1.73m^2, respectively. Renal histology was Class III in 1, III+V in 4 , IV in 12. IV+V in 9 and V in 1 by ISN/RPS 2003 classification. CR at 6 and 12 months were 59% and 74%, respectively. Patients were treated by multitarget therapy for median of 25 months (IQR, 5.5-37). Finally, 26 (96%) patients achieved CR. During multitarget therapy, there were 15 serious adverse events: deep vein thrombosis in 2, myocardial infarctions in 2, cervical intraepithelial neoplasia in 2, heart failure in 1, herpes zoster in 1, viral myocarditis in 1, cytomegalovirus gastroenteritis in 1, cholecystitis in 1, pyelonephritis in 1, bacterial enteritis in 1, sepsis in 1, and breast cancer in 1. During the median observation period of 94 months (IQR, 63-111.5) after the initiation of multitarget therapy, 1 patient died due to sudden death. No patient reached end-stage kidney disease or doubling S-Cr. 16 patients relapsed at median of 32 months (IQR,13.8-64.5) after CR; 8 patients relapsed on multitarget therapy, and 8 patients relapsed after cessation of multitarget therapy. Relapse was associated with chronic lesions in renal biopsy and normal or higher C4 levels at treatment initiation by Kaplan Meier analysis (Log-rank, P=0.006, P<0.001, respectively).
Conclusion: Multitarget therapy effectively induced CR and maintained renal function in long-term period. However, relapse was often observed during or after withdrawal of multitarget therapy.
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Disclosure of Interests: Yoichi Imai: None declared, Hidekazu Ikeuchi: None declared, Junya Suwa: None declared, Yuko Ohishi: None declared, Mitsuharu Watanabe: None declared, Masao Nakasatomi: None declared, Hiroko Hamatani: None declared, Toru Sakairi: None declared, Yoriaki Kaneko: None declared, Keiju Hiromura Speakers bureau: Chugai, Astellas., Grant/research support from: Chugai, Astellas.
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AB0444 ENPATORAN: PRECLINICAL EVIDENCE SUPPORTING GLUCOCORTICOID DOSE REDUCTION AND PHASE II STUDY DESIGN IN PATIENTS WITH SLE AND/OR CLE (WILLOW)

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Background: Enpatoran is a potent selective dual inhibitor of toll-like receptor (TLR) 7 and TLR8, aberrant activation of which may be involved in systemic lupus erythematosus (SLE) pathogenesis and glucocorticoid resistance.[1,2,3] Enpatoran suppressed disease development in lupus mouse models, improving survival and reducing proteinuria, autoantibodies, and the interferon (IFN) gene signature.[1] In healthy participants and patients hospitalized with COVID-19 pneumonia, enpatoran was well tolerated and demonstrated effective TLR7/8 engagement.[4] Enpatoran is potentially glucocorticoid sparing and may help avoid the detrimental effects of long-term corticosteroid use in SLE management.[5,6]
Objectives: To evaluate the glucocorticoid-sparing effect of enpatoran and design a basket trial to assess its efficacy and safety in patients with SLE and/or cutaneous lupus erythematosus (CLE).
Methods: Cytokine concentrations and gene expression changes were measured in stimulated human peripheral blood mononuclear cells (PBMCs) from healthy donors after treatment with dexamethasone, TLR7/8 inhibitor, or both. A Phase II, basket design proof-of-concept, dose-finding study in patients with SLE and/or CLE (WILLOW) was designed.
Results: In healthy donor PBMCs, synergy was observed between TLR7/8 inhibitor and dexamethasone. Combination treatment inhibited cytokine release (IL-6) with greater potency than either treatment alone and reduced the expression of nuclear factor-kappa B and IFN-regulated genes. WILLOW is a Phase II, basket proof-of-concept, dose-finding, randomized, double-blind, placebo (PBO)-controlled 24-week study with two cohorts (NCT05162586, Figure 1). The primary objectives of WILLOW are to evaluate the dose–response relationship of enpatoran in reducing disease activity based on Cutaneous Lupus Erythematosus Disease Area and Severity Index-A (CLASI-A) or BILAG-Based Composite Lupus Assessment (BICLA) response rate. The secondary objectives are to investigate effects on both BICLA response and clinically meaningful corticosteroid reduction and evaluate disease control (including clinically meaningful corticosteroid reduction) in patients with predominantly active CLE or SLE. Cohort A will enroll patients with CLE (active subacute CLE and/or discoid LE) or SLE with predominantly active lupus rash. Cohort B, in two parts, will enroll SLE patients with moderate to severe systemic disease activity. Part 1 will assess clinical signal and Part 2 may be adapted to improve dose finding. Glucocorticoid-sparing will be evaluated by mandatory tapering to a prednisone-equivalent dose of ≤5 mg/day.

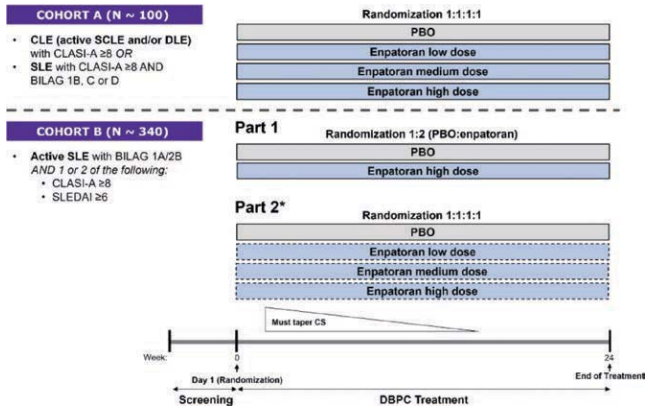

Figure 1. WILLOW study design. Cohort A and Cohort B Part 1 will start in parallel. *Part 2 will be initiated after a pre-specified number of patients are enrolled in Part 1; enpatoran doses in Part 2 may be adapted to improve dose finding (dashed boxes). BILAG, British Isles Lupus Assessment Group; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-A; CLE, cutaneous lupus erythematosus; CS, corticosteroid; DBPC, double-blind placebo-controlled; DLE, discoid lupus erythematosus; PBO, placebo; SCLE, Subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.

Conclusion: Enpatoran is a novel TLR7/8 inhibitor and may enable glucocorticoid dose reduction in patients with SLE and CLE. The WILLOW study incorporates multiple novel elements including a basket design and evaluation of glucocorticoid-sparing.
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Disclosure of Interests: Eric F. Morand: None declared, Andrew Bender Shareholder of: Shares in Merck KGaA, Employee of: EMD Serono Research & Development institute (an affiliate of Merck KGaA), Aditee Deshpande Employee of: EMD Serono Research & Development institute (an affiliate of Merck KGaA), Bharat Vaidyanathan Employee of: EMD Serono Research & Development institute (an affiliate of Merck KGaA), cristina vazquez mateo Employee of: EMD Serono Research & Development institute (an affiliate of Merck KGaA), Melinda Przetak Employee of: EMD Serono Research & Development institute (an affiliate of Merck KGaA), Flavie Moreau Employee of: EMD Serono Research & Development institute (an affiliate of Merck KGaA), Mukhy Khursheed Employee of: Merck Serono Ltd (an affiliate of Merck KGaA), Sanjeev Roy Employee of: Ares Trading SA (an affiliate of Merck KGaA), David Pearson Consultant of: Biogen Inc.
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AB0445 THE BENEFICIAL EFFECTS OF THERAPY ON OBSTETRICAL OUTCOME AND PLACENTAL HISTOLOGY IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: THE EXPERIENCE OF A SINGLE ITALIAN REFERENCE CENTER

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Background: Abnormal placentation plays a crucial role in the pathogenesis of obstetric morbidity in antiphospholipid antibodies syndrome (APS). Placenta is the main target of aPL in obstetric APS, inducing placental thrombosis, inflammatory response and placental dysfunction.
Standard treatment for APS patients during pregnancy includes low-dose aspirin (LDA) plus low molecular weight heparin (LMWH) and, in refractory cases, additional therapies such as hydroxychloroquine (HCQ).
A systematic review of the literature has found five main pathological lesions in the placenta of APS patients: placental infarction, decidual vasculopathy, decidual inflammation, increase of syncytial knots due to syncytiotrophoblast death, and decrease in vasculosyncytial membranes.
Objectives: To analyze placental histology in a group of 23 spontaneously conceived pregnancies in patients with definite APS prospectively followed in a single Italian reference center.
Methods: We analyzed 25 placenta in 23 spontaneously conceived pregnancies in patients with definite APS prospectively followed in the 'Pregnancy at risk' multidisciplinary outpatient clinics at San Raffaele Hospital, Milan, Italy from January 2017 to May 2021. During each trimester of gestation, ultrasonography with Uterine artery Doppler velocimetry was performed. Histological analysis of the placenta was carried out after delivery and placental tissues were examined for the main aforementioned histopathological findings. Statistical relations among clinical and ultrasound evaluations during each trimester, therapeutic approach and placental histology were performed.
Results: 19/25 (76%) patients had primary APS, while 6 patients had APS secondary to SLE. All patients were treated with LDA and LMWH. HCQ was added in a group of patients with concomitant systemic lupus erythematosus (SLE) or in refractory APS. Mean placental weight was 441 ± 129 grams. Histological analysis of placental tissues revealed increased syncytial knots in 17/25 (68%) placenta, decreased vasculosyncytial membranes in 11/25 (44%), infarction in 8/25 (32%), presence of macrophages and decidual inflammation in 2/25 (8%), and atherosis or reduction of spiral arteries remodelling in 3/25 (12%) placenta. Moreover, we observed at least 2 concomitant placental lesions in 12/25 (48%) placentas.
No statistical association between mean UtA-PI values and the number and type of placental lesions described at the histologic analysis were observed. We found a positive correlation between mean titer of aCL IgG, aβ2GPI IgG, aPS/PT IgM and/or aPS/PT IgG and number of placental lesions, and a significant association between aPS/PT IgM and/or IgG mean titer and presence of infarcted areas at placental histology. Moreover, in the placenta of patients treated with HCQ we did not observe any decidual inflammation at histology.
Conclusion: In our study we found some important clinical-pathological correlations between placental histology, clinical evaluations, ultrasound assessments and treatment received during pregnancy. Specifically, it is tempting to speculate that HCQ may have beneficial effects on pregnancy by decreasing the risk of deciduitis in patients with APS.
Further studies on larger numbers of placenta in APS patients will be needed to confirm our findings.
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AB0446 IMPROVEMENT OF BELIMUMAB ON QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Accumulating evidence supports an impaired quality of life in patients with systemic lupus erythematosus (SLE). A study reported the patients concerns centred on fatigue[1].
Objectives: We investigated the effect of belimumab on quality of life in patients with SLE.
Methods: SLE patients from Guangdong Second Provincial General Hospital treated with belimumab (n=19) or control group (n=22) were included. Patients in control group were in traditional treatment without belimumab. Data were collected prospectively at treatment initiation and now, including Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), Pittsburgh Sleep Quality Index (PSQI) and the SF-36 (Table 1).

Table 1.

	SLEDAI		P	PSQI		P	SF-36		P
Group	Pre-treatment	Post-treatment	-	Pre-treatment	Post-treatment	-	Pre-treatment	Post-treatment	-
Belimumab group	11± 4.67	6.11± 3.55	0.001	6± 3.83	3.58± 2.01	0.02	519.47± 187.79	685.62± 141.78	0.004
Control group	8.82± 5.69	3.55±2.11	0.000	6.5± 3.52	5.86± 3.24	0.536	541.73±185.22	700.42± 123.90	0.002
P	0.199	0.007	-	0.665	0.011	-	0.705	0.723	-

Results: Belimumab group showed improvement in SLEDAI, PSQI and the SF-36 ($P < 0.05$). Control group was improvement in SLEDAI and the SF-36 ($P < 0.05$), no changes in PSQI (P=0.536). However, the improvement of belimumab group in SLEDAI and PSQI observably outperformed the improvement of control group.
Conclusion: Belimumab effectively improve quality of life in patients with SLE. Further study of pediatric patients with SLE is still warranted.
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AB0447 LUPUS NEPHRITIS OUTCOMES AFTER DISCONTINUATION OF IMMUNOSUPPRESSION

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Background: Lupus nephritis (LN) is one of the most serious complications of systemic lupuserythematosus (SLE).Immunosuppression (IS) is the standard of care therapy for lupusnephritis(LN).Data on the outcomes of LN patients after discontinuation ofimmunosuppression remain uncertain.

Objectives: To assess the outcomes of patients with LN after discontinuation of immunosuppression.
Methods: Clinical and laboratory data were retrospectively collected on LN patients attending our Lupus Unit.We included 45 patients(41had biopsy confirmedLN)who were treated with immunosuppression including cyclophosphamide, mycophenolate, azathioprine,methotrexate, and/or rituximab.Numeric response variables(median and range)including age, disease duration and length of treatment were collected.Frequencies and percentages categorical variables including gender, ethnicity, lupus nephritis class, autoantibodies, laboratory features, IS therapy used and patients' outcomes (stable versus flared) were analysed.LN flares were defined as: doubling of serum creatinine concentrations and increases in proteinuria after discontinuation of IS.Chi-square tests were applied to comparethese categorical variables between patient's outcomes.Reasons for IS discontinuation: remission, pregnancy planning and patients preference.
Results: We identified the outcomes of 45LN patients who stopped IS therapy. The median age of patients was 55(29 -78)years. The median durationof diseasewas 26.5(15-58)years whereas the median treatment duration was 4(1/2-14) years.Thirty (66.7%)patients were Caucasian ethnicity.Seventeen of 45patients received treatment for more than 5 years.There was only 1(2.2%)male patient in our study. At IS discontinuation, creatinine levels were elevated in9/45 (2%) patient and median creatinine values were 73(41-117umol/L).Median proteinuria values were 20mg/mmol (5-934)(p=0.00).LN histology: classV(24.4%),IV 17.8%and III(17.8%)and eleven patients had a combination of class III IV. Thirteen of 45 (28.9%)patients had relapses after discontinuation of IS. Median time to LN flare was 3(1-17) years and median age of the flared patients was58 years(41-70)years.Median creatinine values and median proteinuria of the flared patients were78(41-111umol/L),361.5 mg/mmol(12-908)respectively.Of these 13relapsed LN patients,4had class III,4had class V and the other patients had combinations of classes.Anti-Sm antibodies were more likely to be associated with relapses(6 patients) compared to stable patients(4 patients)(6% vs.40%) (p=0.030).Anti-*dsDNA* antibodies were positive in 22/32 stable patients(68.8%)compared to 10/13(31.3%)relapsed patients (p=NS).Among 13flared patients, 5 (38.5%)had high creatinine levels and 8(61.5%)had normal serum creatinines(p=0.048)on discontinuation of IS. Of 45 patients,12 had low complement C3, of whom 7(58.3 %) flared and 5(41.7%) were stable(p=0.009).Similarly, of 12patients with lowC4, 8(66.7%)flared compared to 4with stable outcomes(33.3%)p=0.001 .A higher proportion of patients previously taking azathioprine relapsed compared to those with previous use of cyclophosphamide or MMF 30.8%vs15.4%(p=0.011) respectively.
Conclusion: Our data suggests that two thirds of our patients experienced clinical remission with stable LN following cessation of IS therapy for LN.Patients who had elevated serum creatinine values, persistent proteinuria, low complement, positive anti Sm antibodies and previous azathioprine use were more likely to flare after stopping IS.Anti-*dsDNA* antibodies levels did not predict flares after stopping IS.Further prospective studies with larger sample sizes and longer follow-up are needed to estimate LN outcomes after discontinuation of immunosuppression.

Table 1. Patient's characteristics and lupus nephritis outcome

Parameters n (%)	Flared patients (N=13)	Stable patients (N=32)	P value
Abnormal creatinine	5(55.6%)	4(44.4%)	0.048
Significant UPCR	8(88.9%)	1(11.1)	0.000
Anti-sm	6(60%)	4(40%)	0.030
Low C3	7(58.3%)	5(41.7%)	0.009
Low C4	8(66.7%)	4(33.3%)	0.001

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AB0448 **ADVERSE PREGNANCY OUTCOMES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE ROLE OF THERAPY.**

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Background: Our study supports that treatment with glucocorticoids at medium-high doses during pregnancy adversely affects pregnancy outcome with an increased risk of both APO and birth of SGA infants. These data can be related to a direct role of the drug in determining maternal-fetal outcome and to the presence of an incomplete control over disease activity. The comparison between pregnancies followed before 2010 and since 2010 conducted in our study shows that the introduction of drugs such as hydroxychloroquine and azathioprine from the beginning of the pregnancy can reduces the frequency of APO in general. These medications could represent a safety therapeutic strategy both for the mother and for the fetus in order to control autoimmune disease during pregnancy and minimize the occurrence of complications. Further studies on larger numbers of placenta in APS patients will be needed to confirm our findings.
Objectives: To investigate whether treatment in SLE patients during pregnancy may influence the occurrence of APO events and, in particular, the birth of SGA infants.
Methods: We performed a monocentric observational study in SLE pregnant patients prospectively followed at the 'Pregnancy at risk' multidisciplinary outpatient clinics at San Raffaele Hospital, Milan, Italy from January 2003 to June 2021. We collected data from 79 pregnancies in 58 patients with a diagnosis of SLE.
Results: 13/79 (16%) pregnancies ended in a spontaneous abortion. In the other 66/79 (84%) APOs occurred in 29/66 (44%) pregnancies. 17 of the 66 (26%) pregnancies that did not end in spontaneous abortion ended with the birth of SGA infants. Glucocorticoid treatment at medium-high doses (e.i. prednisone ≥ 5 mg) was associated to an increased risk for APO (OR 4.431, p-value 0.018) and for the birth of SGA infants (OR 4.401, p-value 0.019). Preterm delivery (7/43, 16% versus 7/23, 30%), hypertension and/or preeclampsia (4/43, 9% versus 5/23, 22%) were observed with low incidence in pregnancy followed since 2010 than before 2010, even if without reaching statistical significance.
Conclusion: Our study supports that treatment with glucocorticoids at medium-high doses during pregnancy adversely affects pregnancy outcome with an increased risk of both APO and birth of SGA infants. These data can be related to a direct role of the drug in determining maternal-fetal outcome and to the presence of an incomplete control over disease activity. The comparison between pregnancies followed before 2010 and since 2010 conducted in our study shows that the introduction of drugs such as hydroxychloroquine and azathioprine from the beginning of the pregnancy can reduces the frequency of APO in general. These medications could represent a safety therapeutic strategy both for the mother and for the fetus in order to control autoimmune disease during pregnancy and minimize the occurrence of complications. Further studies on larger numbers of placenta in APS patients will be needed to confirm our findings.

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SLE, Sjön-s and APS - clinical aspects (other than treatment)

AB0449 THE PREVALENCE OF AUTOANTIBODIES AGAINST IFNA IS HIGH IN SLE AND ASSOCIATED WITH A HIGH FREQUENCY OF TUBERCULOSIS

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Background: IFNα and anti-IFNα autoantibodies have been implicated in susceptibility both for systemic lupus erythematosus (SLE) and viral infection.
Objectives: We aimed to analyze the SLE disease phenotype and risk for infection associated with anti-IFN-α IgG autoantibodies in SLE patients
Methods: In this multidisciplinary retrospective single referral center study, all consecutive patients with SLE admitted between January 1st and November 30th 2020 were considered. All subjects fulfilled the ACR/EULAR 2019 criteria for SLE. Anti-IFNα IgG autoantibodies were quantified at admission by ELISA. Demographic, medical history, laboratory, treatment, and outcome data were extracted from electronic medical records using a standardized data collection form.
Results: 180 patients [female 87.2%, median age of 44.4 (34-54.2) years] were included. The median disease duration was 10 years [4-20] with a median SLEDAI score of 2 [0-4] at study time. Fifty-four (30%) patients had a past-history of lupus nephritis. One hundred and forty-four (80%) had received long-term glucocorticoids and 99 (55%) immunosuppressive drugs. Overall, 127 infections - mostly bacterial and viral - were reported in 95 (52.8%) patients. Twenty SLE patients (11.1%) had positive anti-IFNα IgG autoantibodies with a titer ranging from 10 to 103 UA/mL. Age, sex, SLE phenotype and treatment did not significantly differ between SLE patients with or without anti-IFNα. Infection rate was similar in both groups except for tuberculosis which was more frequent in patients with anti-IFNα (20% vs 3.1%, p = 0.01).
Conclusion: The prevalence of autoantibodies against IFNα is high in SLE and associated with a higher frequency of tuberculosis
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AB0450 SOLUBLE CD163 IS A BIOMARKER FOR CARDIOVASCULAR EVENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Prediction models based on traditional cardiovascular risk factors underestimate the risk of cardiovascular events (CVE) in systemic lupus erythematosus (SLE).
Objectives: We aimed to determine whether sCD163, a biomarker for SLE-associated atherosclerosis, may predict CVE in SLE.
Methods: All SLE patients included between 2007 and 2010 in the randomized, double-blind, placebo-controlled, multicenter PLUS trial were screened. Patients with no past history of CVE at inclusion and a follow-up period of >20 months were analyzed. sCD163 level was measured using enzyme-linked immunosorbent assay on serum collected at PLUS inclusion. The primary outcome was the incident CVE. Factors associated with incident CVE and sCD163 level were analyzed.
Results: Overall, 442 SLE patients (of the 573 included in the PLUS study) were analyzed for the primary outcome with a median follow up of 110 (interquartile range: 99–120) months. Among them, 29 (6.6%) experienced at least one CVE that occurred at a median of 67 (interquartile range: 31–91) months after inclusion. In the multivariate analysis, dyslipidaemia, age and increased sCD163 were associated with CVE onset. Multivariate Cox models analysis showed that a concentration of sCD163> 263 ng/mL at inclusion increased by 2.7 [hazard ratio 2.7 (95% CI: 1.0, 7.0)] the risk of CVE in SLE. Increased sCD163 was also associated with immunosuppressive treatment, higher body mass index (BMI) and SLEDAI score.
Conclusion: Macrophage-specific sCD163 serum level reflects lupus disease activity and predicts CVE in SLE.
Disclosure of Interests: None declared
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AB0451 FACTORS ASSOCIATED WITH ADVERSE PREGNANCY OUTCOMES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Pregnancies in systemic lupus erythematosus (SLE) are considered high risk and associated with maternal and obstetric complications.
Objectives: Our goal with this study was to determine the most important predictors for each of the main adverse pregnancy outcomes in SLE patients.
Methods: We conducted a retrospective case-controls study by including multiparous women diagnosed with SLE from 1980 to 2020 followed in our unit and compared the clinical profile of patients with adverse pregnancy outcomes to control SLE patients. We excluded elective terminations of pregnancy and cases lost to follow-up. Qualitative data were analyzed by Chi-square test and Fisher's exact test and continuous variables were analyzed by using Student's t test. Multiple logistic regression models were performed to determine the predictive factors for adverse pregnancy outcomes with adjustment of confounding factors. In all tests, P values less than 0.05 were considered to be statistically significant.
Results: 135 multiparous women were included (43% with adverse pregnancy outcomes). The mean age of patients at inclusion was 55.8 (46-64) years. Abortion occurred in 33 patients (57%), pre-eclampsia in 10 patients (17%), ectopic pregnancy in 5 patients (8%), preterm labor in 5 patients (8%), placental abnormalities in 4 patients (6%), stillbirth in 4 patients (6%), premature rupture of membranes (PROM) and neonatal lupus in 3 patients (5%), respectively. 121 patients (89%) have pre-existing lupus and 14 (11%) referred with SLE onset in pregnancy. Renal involvement (p=0.03), anti-DNAds positivity (p=0.002), antiphospholipid antibody (APA) positivity (p=0.001), anti-Ro/SSA (p=0.003) and a younger age at disease onset (p=0.01) were significantly associated with unfavorable pregnancy outcomes. Abortion was correlated with anti-DNAds (β=0.71. p=0.04), renal involvement (β=0,28, p 0.03) and APA (β=0.2, p 0.03). Stillbirth was also correlated with renal involvement (β= 0.26, p =0.04) and APA (β=0.22, p=0.03). Preeclampsia was correlated with direct Coombs positivity (β=0.42, p=0.01) and serositis (β=0.31, p=0.02). Neonatal Lupus was correlated with anti-RNP (β=0.16, p=0.03) and anti-Ro/SSA (β=0.16, p 0.02). Renal involvement and APA had a 2.6-fold increased risk of unfavorable pregnancy outcomes (OR 2.6 95% (1.1-6.1), p 0.03) and APA had a 4.3-fold increased risk of unfavorable pregnancy outcomes (OR 4.3 95% IC 2.1-8.8), p 0.002).
Conclusion: The most unfavorable pregnancy outcomes in women with SLE was spontaneous abortion. Renal involvement, anti-DNAds and anti-Ro/SSA, antiphospholipid antibody positivity, and a younger age at disease onset increased the risk of pregnancy complications.

Table 1. Multiple logistic regression analysis

	Abortion	Stillbirth	Pre-eclampsia	PROM	Ectopic pregnancy	Neonatal Lupus
Anti-DNAds	β =0,71, p=0.04	β =0.26, p=0.04	β =0.12, p=0.38	β =0.15, p =0.24	β = 0.10, p =0.64	β = 0.16, p=0.24
APA	β = 0.2, p = 0.03	β = 0.22, p=0.03	β = 0.11, p = 0.85	β = 0.26, p = 0.04	β = 0.16, p = 0.21	β = 0.83, p = 0.08
Renal involvement	β=0,28, p 0.03	β = 0.26, p = 0.38	β = 0.33, p = 0.83	β = 0.07, p = 0.53	β = 0.17, p = 0.20	β = 0.58, p = 0.07
Serositis	β = 0.85, p = 0.95	β = 0.11, p = 0.41	β=0.31, p=0.02	β = 0.06, p = 0.46	β = 0.13, p = 0.35	β = 0.08, p = 0.46
Direct Coombs positivity	β =0.11, p = 0.41	β = 0.03, p = 0.81	β = 0.42, p=0.01	β=0.03, p =0.83	β= 0.14, p = 0.81	β=0.03, p=0.83
Anti-Ro/SSA	β=0.19, p = 0.13	β=0.03, p = 0.83	β=0.07, p =0.62	β=0.11, p=0.39	β=0.09, p=0.52	β= 0.16, p 0.02
Anti-RNP	β =0.5, p=0.69	β = 0.09, p=0.49	β = 0.16, p= 0.23	β = 0.09, p= 0.81	β=0.03, p=0.81	β=0.16, p=0.03

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AB0452 AGE RELATED DIFFERENCES IN NEUROPSYCHIATRIC MANIFESTATIONS AMONG SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS – A SINGLE RHEUMATOLOGY CENTRE EXPERIENCE IN MALAYSIA

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Background: The prevalence of SLE in Malaysia was reported as 43/100,000 individuals and Chinese (57/100,000) have the highest prevalence followed by Malays (33/100,000) and Indians (14/100,000) [1,2].
The American College of Rheumatology established case definitions and categorised neuropsychiatric syndromes into two groups: central and peripheral system involvement. There were studies showed that cognitive impairment is the commonest neuropsychiatric manifestations with a prevalence of 66% [3].
Objectives: To determine the association between neuropsychiatric manifestation with different age group among SLE patients.
Methods: This was a retrospective study. The electronic medical records of all SLE patients seen in rheumatology clinic of Hospital Sultan Ismail, Malaysia from 1/1/2007 to 31/12/2021 were reviewed. SLE patients with neuropsychiatric manifestations were selected and categorised by age into children (< 12 years old), adolescents (aged 12-18 years), young adults (aged >18 to 35 years), middle-aged adults (>35 -55 years) and elderly (>55 years). The association between neuropsychiatric manifestation with different age group was analysed by using SPSS-Fisher's exact test.
Results: There was a total of 86 patients and female were 77. The majority were Malay (49/86) followed by the Chinese (33/86), Indians (2/86) and others (2/86). Patients were categorized into children (n:6), adolescents (n:18), young adults (n:43), middle-aged adults (n:16) and elderly (n:3) with the mean age of 28.
Our study showed the onset of neuropsychiatric manifestations occurred most during young adulthood (43/86) followed by adolescents (18/86). Seizure disorders is the commonest manifestations (36/86) followed by psychosis (17/86), poly/mononeuropathy (7/86), cognitive dysfunction (7/86), myelopathy (5/86), cranial neuropathy (4/86), mood disorders (3/86), cerebrovascular disease (3/86), movement disorders (2/86), and lastly headache and myasthenia gravis, 1 patient each. 60% of the patients had onset of neuropsychiatric manifestation during first diagnosis and another 7% developed symptoms within 1 year of diagnosis. There was no association between type of neuropsychiatric manifestation with different age group (p = 0.195). Comparison of neuropsychiatric manifestations according to age group was showed in Table 1.

Table 1. Neuropsychiatric manifestations according to age group

Age group (years)	Central nervous system	Peripheral nervous system
Children < 12	Seizure (4), CVD (1), Cognitive dysfunction (1)	
Adolescents 12-18	Seizure (9), Psychosis (5), Mood disorders (1), Cognitive dysfunction (1)	PN/MN (2)
Young adults >18-35	Seizure (18), Psychosis (10), Cognitive dysfunction (4), movement disorders (2), myelopathy (4), CVD (2)	PN/MN (2) CN (1)
Middle-aged adults >35-55	Seizure (4), Psychosis (2), Mood disorders (2), Cognitive dysfunction (1), Myelopathy (1), Headache (1)	PN/MN (3) CN (2)
Elderly >55	Seizure (1)	MG (1), CN (1)

CVD: Cerebrovascular disease, PN/MN: Polyneuropathy/Mononeuropathy, CN: cranial neuropathy

Conclusion: Seizure disorders is the commonest manifestations amongst SLE patients in our study group and there was no association between neuropsychiatric manifestation with the age group.

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AB0453 ROLE OF COMBINATION AUTOANTIBODIES (ANTI-SMITH, RO AND RNP ANTIBODIES) AND ETHNICITY IN ACCELERATED DEVELOPMENT OF LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is an important concern among SLE patients in Asia and its mortality rate was reported to be 6 times higher compared to the general population [1]. A study by McCarty et al suggested that African women with serology showed combination of anti-Smith, Ro and RNP antibodies were at increased risk of developing LN [2]. This is further supported by study done by Majed et al showed this unusual combination accelerated development of LN within the first 5 years after SLE onset [3].
Objectives: To determine the correlation between the combination of autoantibody profile: Smith, Ro and RNP in development of LN amongst Asian ancestry and any association with the duration of LN development from onset of SLE.
Methods: This was a retrospective study. The electronic medical records of all SLE patients seen in the rheumatology clinic Hospital Sultan Ismail, Malaysia from 1/1/2007 to 30/4/2021 were reviewed. Patients who had LN were identified and selected. Data on demography, serology, duration of development of LN from SLE onset were obtained and analysed using SPSS Pearson Chi square and binary logistic regression.
Results: There were a total of 197 patients and 183 were females. The majority were Malays (96/197) followed by the non-Malay (101/197) which included Chinese (86/197) and others (15/197). The mean age group for the studied subjects was 34 (14-80). Of the 197 (100%) patients, 23 (11.7%) patients had the triple combination of Sm, Ro and RNP antibodies while 174 (88.3%) patients did not have the triple combination. For patient with the triple combination, regardless ethnicity, 20/23 (87%) developed LN within 5 years from the SLE onset while the remaining 3/23 (13%) developed LN after 5 years. For patients without this combination, regardless ethnicity, 142/174 (81.6%) of them developed LN within 5 years and 32/174 (18.4%) of them more than 5 years. This showed combination autoantibody does not significantly accelerated development of LN amongst Asian ancestry patients, P = 0.092. There was also no association between the positivity of triple antibody with the duration of development LN from SLE onset, P =0.772. Further stratification was based on ethnicity showed compare to Non-Malay ethnicity, the Malay patients is 3.966 higher odds of developing LN within the 5 years from SLE onset, P = 0.002.
Conclusion: Patient with triple serology combination did not showed significant in accelerating development of LN. Our data showed Malay patients are 4 higher odds of developing LN within the first 5 years after SLE onset compare to Non-Malay patients.

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AB0455 DRUGS, AUTOANTIBODIES AND GENES CONTRIBUTE TO THE DEVELOPMENT OF CHRONIC DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Genetic contribution to development of chronic damage have been scarcely investigated in systemic lupus erythematosus (SLE). In fact, whereas most studies have looked for an association between genetic variants and SLE susceptibility or disease phenotypes, only few have focused on the relationship between these biomarkers and damage development.

Objectives: Moving from these premises, we firstly analyzed the distribution of organ damage in a cohort of SLE patients and secondly we evaluate the role of clinical and genetic factors in determining the development of chronic damage.
Methods: Caucasian SLE patients, diagnosed according with 1997 ACR criteria, were enrolled, and clinical and laboratory data were collected. Based on literature data, we selected a panel of 17 SNPs of following genes STAT4, IL10, IRAK1, HCP5, MIR146a, ATG16L1, IRGM, ATG5, MIR124, MIR1279, TNFSF4, CD40. Genotyping was performed by allelic discrimination assays. A phenotype-genotype correlation analysis was performed by evaluating specific domains of SLICC Damage Index (SDI).
Results: Among 175 Caucasian SLE patients, 105 (60%) exhibited damage (SDI ≥1) with a median value of 1.0 (IQR 3.0). The musculoskeletal (26.2%), neuropsychiatric (24.6%) and ocular domains (20.6%) were involved most frequently. The presence of damage was associated with higher age, longer disease duration, neuropsychiatric (NP) manifestations, anti-phospholipid syndrome and the positivity of anti-dsDNA antibodies. Concerning therapies cyclophosphamide, mycophenolate mofetil and glucocorticoids resulted associated with the development of damage. The genotype/phenotype correlation analysis showed an association between renal damage, identified in 6.9% of patients, and rs2205960 of TNFSF4 (p=0.001; OR 17.0). This SNP resulted significantly associated with end-stage renal disease (p= 0.018, OR 9.68) and estimated GFR<50% (p=0.025, OR 1.06, Figure 1). The rs1463335 of MIR1279 gene was associated with the development of NP damage (p=0.029; OR 2.783). The multivariate logistic regression analysis confirmed the associations between TNFSF4 rs2205960 SNP and renal damage (p=0.020, r=2.53) and between NP damage and rs1463335 of MIR1279 gene (p=0.013, r=1.26)].

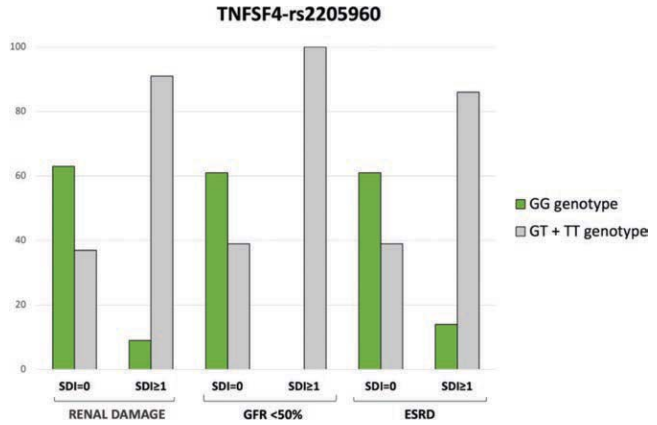

Figure 1. Association between renal damage and rs2205960 of TNFSF4 (p=0.001). In addition, this SNP resulted significantly associated with the development of two specific items of SDI renal domain: estimated glomerular filtration rate (GFR) <50% and end-stage renal disease (ESRD) (p=0.025, p=0.018 respectively).

Conclusion: We showed the role of age, drugs, and autoantibody profile in determining chronic damage.
Our data suggest a possible role of genetic background in determining the development of renal and neuropsychiatric damage, as demonstrated by the association with polymorphisms of TFNSF4 and MIR1279, respectively. These results agree with previous studies suggesting the involvement of TNFSF4 in Lupus nephritis and microRNA in neuroinflammation.
Disclosure of Interests: None declared
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AB0456 DISEASE FLARE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN PATIENTS WITH END-STAGE RENAL DISEASE ON DIALYSIS

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Background: The systemic lupus erythematosus (SLE) disease activity in patients with lupus nephritis (LN) generally declines after the initiation of renal replacement therapy (RRT); this is known as the "burn out" phenomenon that possibly occurs due to the suppression of cellular and humoral immunity in the end-stage renal disease (ESRD) state and elimination of disease pathogenic factor by dialysis [1-4]. However, several studies showed that SLE flares could occur even during RRT [5-8]. Nevertheless, the details of disease flares of SLE in patients under dialysis have not been studied yet.

Objectives: This study aimed to investigate the clinical features, risk factors, and treatment details of SLE patients experiencing disease flare under RRT.
Methods: The medical records of SLE patients who received dialysis at two tertiary referral hospitals in Seoul and Ulsan, South Korea were reviewed. All patients in this study were either clinically or histologically diagnosed with LN
Results: Of a total of 121 patients with SLE on dialysis, 96 (79.3%) were on hemodialysis (HD) and 25 (20.6%) were on peritoneal dialysis (PD). During a median follow-up of 45 months (IQR, 23–120) after the initiation of dialysis, 32 (26.4%) patients experienced SLE flare (HD, n = 25; PD, n = 7). The most common features of SLE flare were hematologic (40.6%) and constitutional manifestations (40.6%). Treatments for disease flares were based on corticosteroids, and 11 (34.3%) patients required additional immunosuppressants including cyclophosphamide and mycophenolate mofetil. There was no case of severe adverse events related to medication. non-renal SLE Disease Activity Index (SLEDAI) score before dialysis initiation (HR 1.235; 95% CI, 1.122–1.359; P = 0.001) was a significant risk factor for disease flare during dialysis.

Table 1. Multivariable analysis of factors associated with SLE flare under dialysis

	Hazard ratio	95% CI	*P*-value
Non-renal SLEDAI at the initiation of dialysis	1.235	1.122–1.359	0.001
Hematologic manifestation prior to dialysis	1.256	0.690–2.826	0.150
Cumulative amount of steroid during 1 year prior to the initiation of dialysis	1.040	0.995–1.087	0.086
Dialysis modality: hemodialysis	0.766	0.262–2.243	0.630

Conclusion: More than one-quarter of SLE patients experienced disease flare during dialysis, which most commonly had hematologic manifestations. Continued follow-up and appropriate treatments including immunosuppressants should be considered for patients with SLE under dialysis.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.696

AB0457 IMPROVED PREGNANCY OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE STUDY OF PREGNANCIES FROM A SINGLE CENTER IN DENMARK FROM 2010-2020 COMPARED WITH THE PERIOD 1990-2010

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Background: Over the past decades, the approach to follow and treat pregnant SLE patients has changed. Today it is recommended that pregnant patients are monitored closely in a multi-professional team throughout pregnancy (1). The importance of low disease activity before pregnancy and continued treatment

during pregnancy has been established (2). Even though many improvements in the management of SLE pregnancies has been made, there is still a high risk of adverse pregnancy outcome (APO).

Objectives: We aimed to evaluate APO in a Danish SLE cohort followed from 2010-2020 and compare the results with a previous study cohort from the same referral area followed from 1990-2010 (3).

Methods: This retrospective cohort study used the local patient registry to identify pregnancies in SLE patients followed at the Department of Rheumatology, Aarhus University Hospital, Denmark from January 2010 to October 2020. All patients were followed regularly and fulfilled at least four of the 1997 American College of Rheumatology (ACR) criteria for SLE classification. Data included demographic, clinical, and laboratory data. Demographics included ethnicity, smoking habits, body mass index (BMI), and concomitant APS (recognized before pregnancy). Data were compared with data from a previous study (1990-2010) from the same department.

Results: In total, 66 pregnancies were registered in 41 women. APO occurred in 65 % of pregnancies. Forty-seven pregnancies resulted in a live birth, while 15 ended in miscarriage. Compared to the 1990-2010 cohort, a reduction in preterm deliveries (7.58 % vs. 17.9 %), acute caesarean (6.1 % vs. 15.5 %), and higher average birth weight (3045 g vs. 2870 g) were found (Table 1). Further, we observed more pregnancies and live births per year (Figure 1). A change in the approach to treatment was found, i.e., significantly more patients were treated with hydroxychloroquine (73 %) compared to the 1990-2010 cohort (6 %).

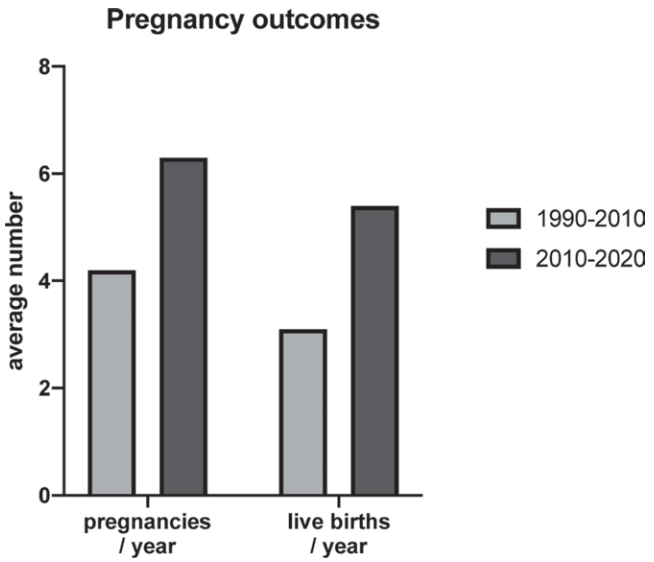

Figure 1. Pregnancy outcome. Average number of pregnancies and live birth per year in the Aarhus SLE cohort in the period 1990-2010 compared with 2010-2020

Table 1. Maternal and fetal/neonatal adverse pregnancy outcomes in our study population (2010-2020) compared with previous study at Aarhus University Hospital (1990-2010).

	1990-2010 n=84	2010-2020 n=66	p-value
Pre-eclampsia/eclampsia, n (%)	7 (8.3)	8 (12.1)	0.59
HELLP syndrome, n (%)	4 (4.8)	0	-
Gestational hypertension, n (%)	20 (23.8)	9 (13.6)	0.05
Preterm deliveries (<37th gestational week), n (%)	15 (17.9)	5 (7.58)	0.07
Acute caesarean delivery, n (%)	13 (15.5)	4 (6.1)	0.07
Elective caesarean delivery, n (%)	11 (13.1)	8 (12.1)	-
Total caesarean delivery, n (%)	24 (28.6)	12 (18.2)	-
Total fetal loss, n (%)	22 (26.2)	19 (28.8)	0.72
Spontaneous abortion <22 weeks, n (%)	18 (21.4)	15 (22.7)	0.85
Therapeutic abortion	3 (3.6)	4 (6.1)	0.47
Still birth	1 (1.2)	0	-
Fetal death after birth	2 (2.4)	0	-
Birth weight, mean ± SD g	2870 (SD,NA)	3045 ± 611	-
IUGR	10 (11.9)	NA	-
SGA	NA	12 (18.18)	-
Congenital heart block, n (%)	1 (1.2)	0	-
Neonatal Lupus Syndrome, n (%)	2 (2.4)	0	-

Conclusion: Improvements in the frequency of APO were found in 2010-2020 compared with 1990-2010. However, even though a specialized multi-professional team closely follows pregnant women with SLE, pregnancy in SLE still carries a high risk of APO.

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Disclosure of Interests: None declared

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AB0458

DISEASE ACTIVITY AT CONCEPTION PREDICTS LUPUS FLARE UP TO 2 YEARS AFTER BIRTH: A MULTICENTRE LONG TERM FOLLOW-UP STUDY

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Background: Systemic lupus erythematosus (SLE) often affects women in their childbearing years, and pregnancy may affect SLE disease activity during pregnancy and post-partum (1,2). Limited data assessing the likelihood and characteristics of SLE activity in an extended time period post-partum which may be relevant as patients may wish further pregnancies exist.

Objectives: To assess predicting factors that might influence SLE disease activity in women in an extended follow-up period of 2 years after giving birth and clinical assessment every three months.

Methods: The study was design as an international retrospective, data-driven case collection study, enrolling 119 women with a first birth and with a strictly monitored follow-up period of 2 years.

Results: Table 1 shows pregnancy outcomes of all pregnancies. When considering disease manifestations, joint involvement was present in 80% of patients, acute cutaneous in 64%, haematological in 54%and renal in 41%; 75% of patients were positive for anti-dsDNA, 49% for anti-ENA and 37% for anti-Ro/SSA positive. The mean SLE disease activity index 2000(SLEDAI-2k) at diagnosis was 13.5±6.8 and at first birth was 2.8±4.4.

Table 1. Pregnancy outcomes of all pregnancies and relative breastfeeding data

Pregnancy Characteristics	All (214)	%
Outcomes		
Live births	169	79
Miscarriages	37	17.3
Stillbirths	8	3.7
Maternal and Foetal Complications		
Prematurity	39	18.2
Pre-eclampsia	23	10.7
HELLP syndrome	4	1.9
Placental Infarction	12	5.6
Breastfeeding (all pregnancies)		
Any breastfeeding (n, %)	109	64.5*
Exclusive breastfeeding (n, %)	87	51.5*
Breastfeeding (after first birth)		
Any breastfeeding (n, %)	87	73.1**
Any breastfeeding duration (months) (m±sd)	10.29±10.04	
Exclusive breastfeeding*** (n, %)	62	52.1**
Exclusive breastfeeding*** duration (months) (m±sd)	6.07±6	

Percentages are calculated considering viable babies (total= 169) Percentages are calculated considering first birth (total= 119)***Exclusive breastfeeding was defined as feeding infants only breast milk*

At follow-up, 51.3% of patients had at least one flare after a mean time after birth of 9±6.3 months(mean flare per patient 0.94±1.1). The most frequent flare manifestations were joint involvement(48%), followed by renal(33%), cutaneous(28%)

and haematologic(20%). Patients with remission of disease(SLEDAI-2K=0; no clinical or laboratory manifestations of SLE) at conception had significantly lower rates of flares than those not in remission (18/49–37% vs. 43/70–61%;p=0.008) (Figure 1).

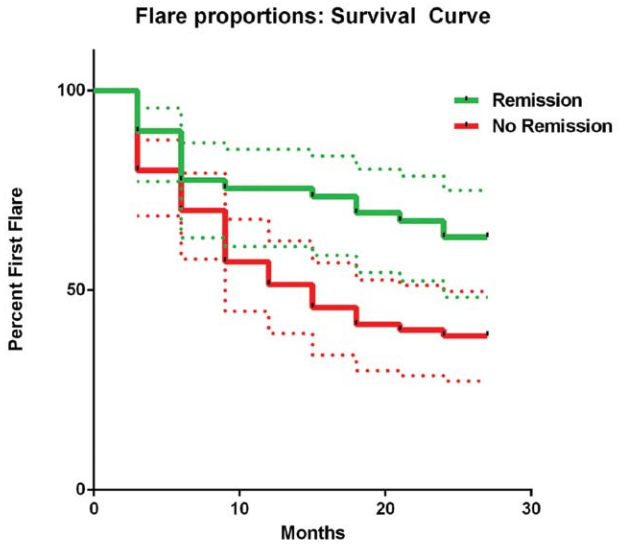

Figure 1. Flare proportion: Survival Curve based on remission status at conception of the patients included in the study.

Patients who experienced a flare during pregnancy (17 patients), when compared to those who did not, had higher rates of flares during follow-up (76% vs. 47%, respectively, p=0.019), lower time for first flare (4.4±2.3 months vs. 10.3±6.5, respectively, p<0.001), lower rate of remission of disease at conception (12% vs. 46%, respectively, p<0.001), lower rates of SLEDAI 2K at conception (5.9±5.6 vs. 2.3±4, respectively, p<0.001) and lower rates of exclusive breastfeeding (24% vs. 57%, respectively, p=0.009). Remission of disease and flares during pregnancy remained significantly associated with the development of flares during follow-up after multivariate analysis.

Conclusion: Remission at conception can influence SLE disease positively, even at long-term. Planned pregnancy counseling is fundamental when managing SLE patients.

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AB0459 NATIONAL TEMPORAL TRENDS IN ALL-CAUSE MORTALITY IN PATIENTS WITH SYSTEMIC SCLEROSIS IN MEXICO BETWEEN 1998-2017

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Background: Systemic sclerosis (SSc) is a rare chronic connective tissue disease characterized by vascular injury, immune dysregulation, and extensive fibrosis of several organs. Due to its rarity, epidemiological data for SSc are sparse.

Objectives: To investigate national temporal trends over time in all-cause mortality rates in patients with systemic sclerosis (SSc) in Mexico between 1998 and 2017.

Methods: All-cause deaths between 1998 to 2017 were extracted from the General Board of Health Information (DGIS) Open Access datasets. We identified all persons aged ≥18 years with a diagnosis of SSc (ICD-10 code M34). We calculated the age-standardized mortality rate (ASMR) for SSc and non-SSc (information provided by the National Institute of Statistics, Geography and Informatics). A Joinpoint regression model was used to determine mortality trends by sex and geographic regions. Annual percentage change (APC) and average APC (AAPC) were calculated using Joinpoint analysis.

Results: From 1998 to 2017, the overall ASMR of SSc increased (AAPC= 2.5%), whereas the ASMR for non-SSc remained stable. By subpopulations, females and males with SSc had a significant uptrend in the ASMR (APC= 4.6% and 4.4%, respectively), between 1998 and 2008 for the former and between 1998 and 2010 for the later. Females had a non-significant ASMR uptrend and males a non-significant ASMR decline. Some variations among geographic regions were found. Women had a higher SSc AMSR to non-SSc ASMR ratio than males. The relative cumulative change between 1998 and 2017 differed between females (78.1%) and males (50.8%), and residents of the Southern region had the largest cumulative change (147.8%).

Conclusion: SSc mortality rate increased in Mexico between 1998 to 2017, with SSc mortality higher than non-SSc mortality with variations by sex and geographic regions.

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Disclosure of Interests: None declared

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AB0460 METABOLOMIC PROFILE OF INSULIN RESISTANCE IN NON-DIABETIC WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is associated with an increased risk of insulin resistance (IR). Metabolomics offers an opportunity to examine markers of IR and their relationship with SLE.

Objectives: 1) to compare the metabolomic profile of IR in SLE patients and controls; 2) to correlate the metabolomic profile with other IR surrogates and 3) to evaluate the relationship between the metabolomic profile of IR and SLE disease variables, vitamin levels and subclinical atherosclerosis in patients with SLE.

Methods: In this cross-sectional analysis, serum samples were collected from patients with SLE (n= 64) and gender- and age-matched controls (n= 71). Serum metabolomic profiling was performed using ultra-high performance liquid chromatography and tandem mass spectrometry (UPLC-MS-MS). Homeostasis model assessment (HOMA) and the quantitative insulin sensitivity check index (QUICKI) were also carried out. Serum 25(OH)D concentrations were assessed by chemiluminescent immunoassay. Carotid IMT was quantified by ultrasound.

Results: In non-diabetic patients with SLE, the metabolomic Quantose score significantly moderately correlated with HOMA-IR, HOMA2-IR and QUICKI. Although levels of IR metabolites did not differ between SLE patients and controls, fasting plasma insulin levels were higher and insulin sensitivity lower in SLE patients. The Quantose IR score was significantly correlated with complement C3 levels (r= 0.7; p= 0.001). Neither 25 (OH)D nor IMT was correlated with any metabolite or Quantose IR index.

Conclusion: This exploratory study found that Quantose IR may be a useful tool for IR assessment. There was a possible correlation between the metabolomic profile and complement C3 levels. The implementation of this metabolic strategy may help develop biochemical insight into metabolic disorders in SLE.

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Disclosure of Interests: None declared

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AB0461

TRIPLE POSITIVE PROFILE IN ANTIPHOSPHOLIPID SYNDROME: PROGNOSIS, RELAPSE AND MANAGEMENT FROM A RETROSPECTIVE MULTICENTER STUDY.

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Background: The antiphospholipid syndrome (APS) is defined by the development of vascular thrombosis, or pregnancy morbidity in the presence of persistent antiphospholipid antibodies (APL). Antinuclear antibodies (ANA) can be detected in primary APS patients without any clinical systemic autoimmune disease. The presence of ANA antibodies could confer a specific phenotype in primary APS.
Objectives: Antiphospholipid syndrome (APS) is defined by the association of thromboembolic and/or obstetrical clinical manifestations and the presence of antiphospholipid antibodies (APL). Patients with all three APL are referred to as triple positive (TP). The objective of our study was to evaluate the impact of the TP profile in a cohort of 204 patients.
Methods: Clinical and biologic data from 195 APS were retrospectively collected. ANA test was considered to be positive when titers were superior or egal to the 1/80 dilution. ANA-positive APS patients did not fulfilled SLE ACR/EULAR classification criteria
Results: 204 patients were included in our study, 68 were TP and 136 were single or double positive (NTP). 122 patients (59.8%) had primary APS. 67 patients (32.8%) had obstetrical APS, with a higher rate among TP patients (45.6% versus 26.5%, P=0.010), and 170 patients (83.3%) had thrombotic APS, without difference between TP and NTP patients. TP patients had more placental complications than NTP patients (17.6% versus 2.9%, P=0.001) and more non-criteria events (48.5% versus 25.7%, P=0.002). 97 patients (47.5%) presented at least one relapse, and the relapse rate was significantly higher in TP patients than in NTP patients (63.2% versus 39.7%, P=0.002). Of the relapses, 30 were obstetric and 74 thrombotic, and the rate of obstetric relapses was significantly higher in TP patients. During follow-up, 21 patients (10.3%) died and this rate did not differ between the two groups. In univariate analysis, TP patients (HR 1.77; 95% CI 1.17-2.68; P=0.007), venous APS (HR 1.74; 95% CI 1.13-2.69; P=0.013), a history of premature birth (HR 2.47; 95% CI 1.24-4.93; P=0.010), and curative anticoagulation (HR 4.91; 95% CI 1.55-15.5; P=0.007) are associated with the risk of relapse. The serological profile was also a factor in relapse: the presence of the anti-β2GP1 antibody (HR 1.70; 95% CI 1.09-2.64; P=0.018) and LA (HR 1.59; 95% CI 1.01-2.50; P=0.046). The non-criteria manifestations of APS are associated with a higher risk of relapse, although not statistically significant (HR 1.49; 95% CI 1.00-2.23; P=0.052). In multivariate analysis, the TP profile remained associated with a risk of relapse (HR 1.63; 95% CI 1.04-2.55; P=0.031), as well as venous APS (HR 2.05; 95% CI 1.30-3.23; P=0.002), and the antecedent of premature delivery (HR 2.33; 95% CI 1.10-4.92; P=0.027). The risk factors associated with relapse in multivariate analysis are summarized in Figure 1.

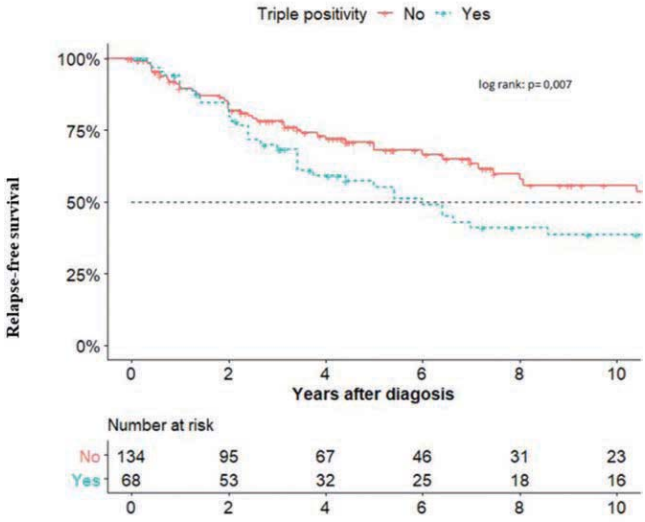

Figure 1.

Conclusion: The TP profile is associated with a higher risk of relapse and obstetrical complications.
Disclosure of Interests: None declared
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AB0462

CORRELATION BETWEEN SAXON TEST AND UNSTIMULATED SALIVARY FLOW RATE IN PATIENTS WITH SUSPECTED SJÖGREN´S SYNDROME

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Background: Sjögren syndrome (SS) is a chronic systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands, which alters their function producing dryness of the mouth, eyes and other mucous membranes. The method used to quantify glandular hypofunction is by whole saliva flow stimulated and unstimulated (UWSF) [1], which takes between 5 and 15 minutes (min). The Saxon test [2], is another tool with the same objective but requires less time: 2 minutes. In the literature, we only have found one study that compares the Saxon test with other diagnostic methods although it is developed in patients without SS [3].
Objectives: To compare the Saxon test and UWSF in a cohort of patients with suspected SS.
Methods: In a consecutive cohort of patients who attended the rheumatology department for suspected SS, UWSF was measured (mL/5 min) and the Saxon test (gr/2 min) was performed. The Index Reported by Patients with Sjögren's Syndrome of the EULAR (ESSPRI) was collected too. This is a patient-reported index designed to assess the severity of patients' symptoms (dryness, pain, somatic and mental fatigue) in SS through an average of single 0–10 numerical scale for each domain. To measure the UWSF, patients were asked to swallow their saliva before the start of the test and then to spit into a container for 5 min. The Saxon test was performed by calculating the difference in the weight of two pieces of sterile gauze that the patient chews for two minutes. An UWSF >0.25 mL/min, a Saxon test >2.75 g/2min and an ESSPRI<5 were considered normal. Spearman's rank correlation coefficient (r_s) was used to determine the correlation between both quantitative variables. The Chi-square test and the Gamma test were used in the comparisons between the groups (altered and normal) and the Mann-Whitney U in the comparisons of the quantitative variables based on the groups (altered and normal) previously defined. *P* values <0.05 were considered statistically significant.
Results: We enrolled 70 patients (63 women/7 men), with a mean age ± standard deviation of 54±13 years. The medians (Me) and interquartile ranges (IQR) obtained were 1.500 (0.6750 – 2.5000) mL/5min for the UWSF, 2.405 (1.6775-3.4925) g/2min for the Saxon test, 6.67 (3.67-7.67) for ESSPRI and 7.00 (4.00-8.00) for ESSPRI-dryness score. A direct and significant correlation between the Saxon test and the UWSF (r_s=0.325; *P*=0.006) was observed. Twenty-four patients (34.3%) presented an altered UWSF and forty-two patients (60%) had an altered Saxon test. When we analysed the intensity of the association between the different groups (altered/normal) of both variables, we observed a direct and significant association (Gamma value=0.583, *P*=0.010) between both tools. We also detected differences in the Saxon test between patients with altered UWSF (Me: 1.89 gr/2min.; IQR: 1.47-2.68) and those with normal UWSF (Me: 2.78 gr/2 min.; IQR: 1.77-3, 75) (*P*=0.029). Similarly, we observed significant differences in UWSF values between patients with altered Saxon test (Me: 1.30 mL/5min IQR: 0.50-2.13) and those with a normal Saxon test (Me: 2.00 mL/5min IQR: 1.5-2.88) (*P*=0.008). Regarding the ESSPRI, 42 (62,7%) patients presented an altered ESSPRI and 49 (73,1%) had an altered ESSPRI-dryness score. The group patients with ESSPRI-dryness score≥5 obtained significantly worse scores on the Saxon test (Me: 2.10 g/2min IQR: 1.58-3.07) and on the ESSPRI (Me:7.33 IQR:5.83-8.00) than the normal ESSPRI-dryness score group: Me:3.02 g/2min, IQR:2.20-3.84, on Saxon test (*P*=0.026); Me: 2.66 IQR:1, 00-4.08, on the ESSPRI (*P*=0.000).
Conclusion: In patients with suspected SS, there is a direct and significant correlation between the Saxon test and the UWSF. Therefore, the Saxon test could be useful in the initial assessment of oral gland dysfunction, to save time and/or to select patients who require performing the UWSF.
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AB0463

PREVALENCE AND PREDICTORS OF COGNITIVE DYSFUNCTION IN PATIENTS WITH LUPUS NEPHRITIS: A CROSS-SECTIONAL COMPARISON WITH PATIENTS WITH OTHER CHRONIC KIDNEY DISEASES

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Background: Cognitive dysfunction (CD) is among the most frequent neuropsychiatric manifestation of systemic lupus erythematosus (SLE) that has a considerable impact on quality of life, but still lacks adequate screening in clinical routine.
Objectives: Our aim was to investigate the distribution and determinants of CD in patients with lupus nephritis, and to compare cognitive function with that in patients with other forms of glomerular chronic kidney disease (CKD) by the Montréal Cognitive Assessment (MoCA).
Methods: We carried out a cross-sectional case-control study with consecutive patients with SLE who fulfilled the 2012 SLICC (Systemic Lupus International Collaborating Clinics) classification criteria(1) and have history of lupus nephritis, using a similarly derived CKD control population matched by age and sex, to assess cognitive function using MoCA scale(2). CD was defined as score < 26/30, adjusted for duration of formal education. Demographic data and disease characteristics were collected. SLE disease activity was evaluated by using Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI2K) (3). The effect of disease-related parameters on the MoCA was examined by regression analysis.
Results: A total of 35 patients with SLE and 35 CKD controls were included in our study (Table 1). Among SLE patients, 7 (20%) patients had biopsy proven active nephritis, 7 (20%) had kidney failure and one a kidney transplant. CD according to MoCA score was found in 64.2% (n=45) patients (Figure 1). The proportion of patients with CD according to MoCA between patients with lupus nephritis and CKD controls was not statistically significant (62.8% vs 65.7%, p>0.05). SLE patients performed bad in all cognitive domains. Memory, abstraction and language skills were the most affected domains. Our study showed that active nephritis and disease duration were associated with poor cognitive performance (OR=1.4, p = 0.03; OR=1.2, p = 0.03). GFR values and other parameters evaluated (end stage renal disease, damage, age at diagnosis, use of glucocorticoids, hydroxychloroquine and immunosuppressive drugs) had no significant effect on development of CD in SLE patients.

Table 1. Demographics and clinical characteristics of SLE patients

	mean	%
Age	44	
Women		94.2
Education		
>16 yrs		51.4
16 -13 yrs		37.1
<13 yrs		11.4
Disease duration (yrs)	16	
Kidney failure		20
Prednisone (% use)		
<20 mg		11.4
≥20mg		88.5
Hydroxychloroquine (% use)		65.7
Immunosuppressants (% use)		57.1
SLEDAI	2.4	
SDI	0.8	

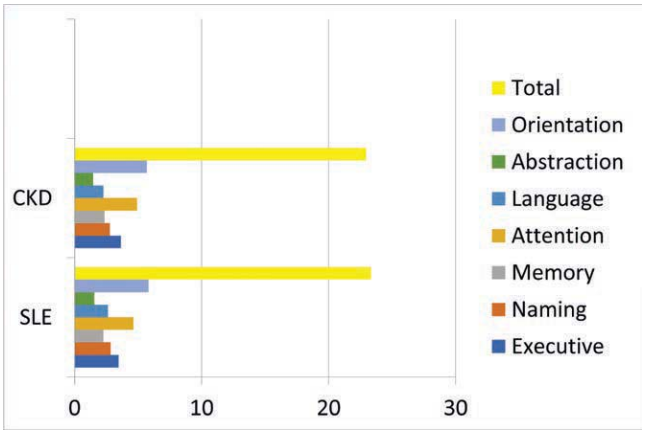

Figure 1. Montréal Cognitive Assessment (MoCA) results in patients with systemic lupus erythematosus (SLE) compared to hemodialysis and chronic kidney disease (CKD) patients.

Conclusion: In this study, two thirds of SLE patients had CD. Patients with lupus nephritis have comparable cognitive function than patients with other CKD. Decline in renal function was not associated with CD in SLE, suggesting that the CD in this population may represent a consequence of lupus itself rather than kidney-related central nervous system damage.

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AB0464 ULTRASONOGRAPHIC FEATURES OF THE PAROTID AND SUBMANDIBULAR SALIVARY GLANDS IN SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by the presence of "sicca syndrome", secondary to the involvement of the exocrine glands. Different studies have been published and have shown that salivary gland ultrasound (SGUS) could be used as a tool for the diagnosis of pSS, especially the score of parenchymal inhomogeneity of salivary glands (SG) [1].
Objectives: To identify relevant ultrasonographic features associated with glandular involvement in patients with pSS, such as size measurements, vascularization, and the characteristics of adjacent lymph nodes of parotid and submandibular SG, and their association with the score of parenchymal inhomogeneity.
Methods: We enrolled patients with pSS (n=53), based on the 2002 American–European Consensus Group (AECG) pSS classification criteria, and non-Sjögren's sicca subjects (n=25), who exhibited sicca symptoms but did not fulfill the AECG pSS classification criteria. We considered SGUS score based on parenchymal homogeneity, presence of hypoechogenic areas, and clearness of posterior glandular border of SG. The score of the highest graded gland was considered and a score ≥2 was defined as a positive SGUS, according to OMERACT US-SG scoring [1]. The size measurements of the SG were the diameters in anterior-posterior, medio-lateral, and vertical directions during dental occlusion, and length and width of anterior prolongation of parotid glands. The vascularization was ranked according to the color doppler ultrasonography pattern without salivary stimulation. For the lymph nodes examination we considered the shape, number, and size of submandibular, superficial parotid (preauricular), and intraparotid lymph nodes, and the jugulodigastric lymph node, considering also that lymph nodes may not be detected. Categorical variables were compared using the Chi-square test and continuous variables were compared using Student's t-test with Welch's correction. p-values <0.05 were considered significant.
Results: SGUS was positive in a higher proportion of patients with pSS, in comparison to non-Sjögren's sicca subjects (60% vs. 24%, p=0.003). The size measurements showed a smaller antero-posterior diameter of both the right (mean 31.3 mm vs. 35.4 mm, p=0.037) and left (mean 30.1 mm vs. 34.2 mm, p=0.004) submandibular glands in pSS patients. A smaller antero-posterior diameter of the left parotid gland was also observed (mean 30.2 mm vs. 34.2 mm, p=0.046) in pSS patients. The lymph nodes evaluation showed that superficial parotid lymph nodes were detected in a lower proportion in pSS patients (45% vs. 72%, p=0.027). No significant differences were found between pSS patients and non-Sjögren's sicca subjects regarding the rest of the size measurements, the vascularization pattern, nor the shape, number, nor size of lymph nodes when they were detected. In addition, positive SGUS in pSS patients was also associated with smaller antero-posterior diameter of both the right (mean 29.9 mm vs. 35.4 mm, p=0.009) and left (mean 32.8 mm vs. 34.2 mm, p=0.008) submandibular glands, and a smaller antero-posterior diameter of the left parotid gland (mean 27.5 mm vs. 34.2 mm, p=0.044).
Conclusion: Ultrasonographic features are a valuable resource for the evaluation of pSS. The score of parenchymal inhomogeneity is associated with clinical diagnosis, and other indices such as the antero-posterior diameter of the submandibular glands and a lower detection of the superficial parotid lymph nodes may be used to assist the evaluation. However, no other macrostructural features of the parotid and submandibular SG, and the adjacent lymph nodes, seem to be different between pSS patients and non-Sjögren's sicca subjects.
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AB0465 COMPARISON OF ULTRASOUND STRUCTURE CHANGES OF SALIVARY GLANDS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME WITH POSITIVE AND NEGATIVE ANTICENTROMERE ANTIBODIES

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Background: Apart from anti-Ro and/or anti-La positive primary Sjögren's syndrome (pSS), there is a unique subtype of pSS with anticentromere antibodies (ACA). At the present time salivary gland ultrasonography (SGUS) is widely used to assess the structure of the salivary glands in pSS, but there are few publications about SGUS changes in ACA-positive patients [1].
Objectives: To investigate SGUS changes in ACA (ACA+) positive pSS patients and compare with ACA-negative (ACA–).
Methods: We examined 141 patients with pSS, including 103 ACA– patients (pSS-ACA–) with the mean age 49,8 ± 14,1 years and 38 ACA+ positive (pSS-ACA+) with the mean age 59,1 ± 10,2 years. All patients underwent standard examination for the diagnosis of pSS (stomatological, ophthalmological, immunological), and SGUS performed using GE LOGIQ 9 of two parotid and two submandibular glands. Ultrasound images were evaluated with the OMERACT SGUS scoring system (SGUS SS) from grades 0 to 3 [2]. Statistical analyses (chi-squared test, p <0.05) were performed using STATISTICA version 12.
Results: Characteristics of patients with pSS-ACA+ and pSS-ACA– are presented in Table 1.

Table 1.

Parameters	ACA–		ACA+	
	N	%	N	%
Oral dryness	86	83,5	36	94,7
Ocular dryness	76	73,8	30	78,9
Enlargement of parotid salivary glands	36	34,9	7	18,4
Recurrent parotitis	23	22,3	7	60,5
ANA ≥1:320	103	100	38	100
Stimulated saliva flow test < 2.5 ml/5 min	65	63,1	30	78,9
Sialectasia on parotid sialography	103	100	38	100
Stimulated Schirmer's test <10 mm/5 min	67	65,0	26	68,4
Tear breakup time <10 seconds	59	57,3	20	52,6
Focus score ≥ 1foci/4 mm2	94	91,3	12/13	92,3
MALT-lymphomas	8	7,7	5	13,1

Characteristics of SGUS SS in pSS-ACA+ and pSS-ACA– are shown in Figure 1.

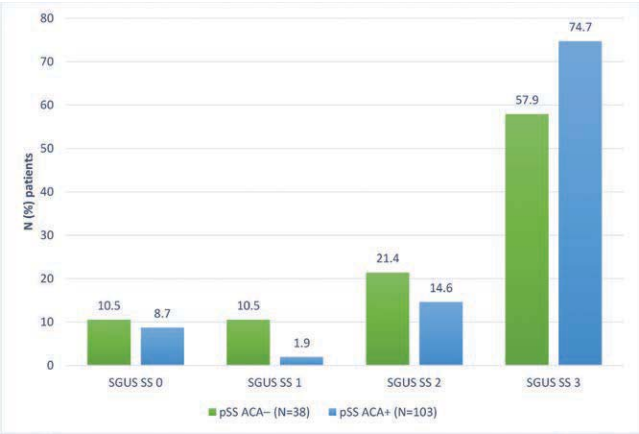

Figure 1.

We did not find significant differences when comparing SGUS SS in patients with pSS-ACA+ and pSS-ACA–.
Conclusion: We did not find significant differences in SGUS and SGUS SS in patients with pSS-ACA+ and pSS-ACA–.
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AB0466

DYSFUNCTION OF THE AUTONOMIC NERVOUS SYSTEM IS ASSOCIATED WITH LOW-GRADE INFLAMMATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background: Systemic lupus erythematosus (SLE) is characterized by chronic, systemic inflammation, organ damage and -dysfunction. Autonomic nervous system dysfunction is highly prevalent in SLE patients (up to 54%); compared to controls the prevalence may be up to 12 times increased.[1] These numbers parallel findings in other chronic conditions such as diabetes.[2]
Heart rate variability (HRV) reflects autonomic activity, and low variability indicates impaired activity, denoted as autonomic dysfunction (AD). AD is associated with low-grade inflammation in healthy subjects and patients with diabetes or cardiovascular disease.[3] The causality hereof is not fully understood: AD may impair the vagally mediated anti-inflammatory reflex, thus leading to increased systemic inflammation, but inflammatory mediated microvascular and neuronal damage may also impair autonomic function.
Objectives: To determine if markers of low-grade inflammation are associated with AD in SLE patients.
Methods: SLE patients (n=111) from the Copenhagen based PLUSheart (Prospective Lupus Study on Cardiovascular Risk Factors) cohort were included for this cross-sectional analysis. The cohort has previously been described[1] with the following characteristics in 2018-2019: 89.2% women, mean age: 51.5 (SD ±12.7) years, mean BMI: 25.1 (±5.0), mean disease duration: 19.9 (±9.5) years, median SLEDAI 2K score: 3 (IQR 1-4), and median SLE Damage Index score: 2 (1-4).
Low-grade inflammation was evaluated by plasma levels of C-reactive protein (CRP) and soluble urokinase-type plasminogen activator receptor (suPAR). Autonomic function was assessed with 5-min resting lead-I electrocardiograms using the Vagus™ device. Subsequent HRV analyses comprised RMSSD (the root mean square of successive interval differences between normal heartbeats), reflecting parasympathetic function, and SDNN (standard deviation of normal-to-normal heartbeat intervals), reflecting mixed parasympathetic-sympathetic function.
Results: All HRV- and inflammatory markers were non-normally distributed. The median SDNN was 30.4 (IQR 24.1-40.4), the median RMSSD was 19.7 (12.6-31.7). The median CRP level was 1 (1-3) and suPAR level was 3.2 (2.5-4.6).
For parametric analyses, all markers were logarithmically transformed. Both SDNN and RMSSD associated with CRP and suPAR levels in univariate analyses. When adjusting for age and SLE disease activity as per the SLEDAI-score, SDNN remained associated with suPAR and CRP and RMSSD with suPAR only (Table 1).

Table 1. Association between low-grade inflammation and autonomic nervous system function

	SDNN *				RMSSD *			
	Univariate		Adjusted		Univariate		Adjusted	
	β	P	β	P	β	P	β	P
CRP *	-0.241	**0.011**	-0.197	**0.035**	-0.215	**0.024**	-0.168	0.072
suPAR *	-0.239	**0.014**	-0.197	**0.038**	-0.268	**0.006**	-0.227	**0.016**

Univariate and multivariate linear regression analyses adjusted for age and disease activity of correlations between log-transformed (*) low-grade inflammation markers (CRP and suPAR) and heart rate variability markers (RMSSD and SDNN). β=standardized coefficients. Statistically significance (P<0.05) is marked with bold.

Conclusion: In SLE, HRV impairments reflecting both decreased parasympathetic and mixed parasympathetic-sympathetic autonomic function were associated with markers of low-grade inflammation independently of SLE disease activity and age. Longitudinal prospective studies are needed to determine causality.
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AB0467

COMPARISON OF 2002 AECG AND 2016 ACR/EULAR CLASSIFICATION CRITERIA AND ROLE OF SALIVARY GLAND ULTRASONOGRAPHY IN A SICCA COHORT

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Background: For the last 20 years, different classification criteria have been used in clinical practice to improve the diagnosis of primary Sjögren's syndrome (pSS) and for research purposes. Several recent studies have assessed major salivary gland ultrasonography (SGUS) as a tool for diagnosing pSS and its inclusion in the classification criteria sets. In addition, some research suggests that it may be important to distinguish between monospecific antibody assays to Ro60 or Ro52.

Objectives: To compare the new 2016 American College of Rheumatology/ European League Against Rheumatism (ACR/EULAR) criteria to the revised 2002 American–European Consensus Group (AECG) criteria in a cohort of subjects with sicca symptoms and to assess the diagnostic accuracy of SGUS. We include monospecific antibody determination to Ro60 or Ro52.

Methods: Patients ≥ 18 years old with diagnosis of sicca syndrome without other associated collagen diseases were included. The initial cohort compromised 72 patients. We assessed features of salivary and lacrimal gland dysfunction and autoimmunity as defined by tests of both AECG and ACR/EULAR criteria. We included separate antiRo52 and antiRo60 antibodies determination, and considered only antiRo60 for the ACR/EULAR criteria as recommended [1]. All the patients underwent SGUS. Agreement between the criteria sets was assessed using Cohen's κ coefficient, and categorical variables were compared using the Chi-square test.

Results: Application of the AECG criteria resulted in the classification of 50 (69%) subjects with pSS, among whom 48 (67%) subjects also met ACR/EULAR criteria. All these patients received a physician diagnosis of pSS. No patients met ACR/EULAR only, and 22 (31%) subjects met neither criteria set. The concordance between AECG and ACR/EULAR criteria was almost perfect (κ = 0.94). The concordance group presented 8% antiRo60+, 4% antiRo52+, and 75% antiRo60+/ antiRo52+, among whom 56% had antiRo60+/antiRo52+/antiLa+. No patients presented antiLa in the absence of both antiRo60 and antiRo52 antibodies. SGUS was abnormal in 63% of these patients. The 2 patients fulfilling only AECG criteria had antiRo52+, and SGUS was abnormal in one of them. SGUS was abnormal in 27% of the 22 patients fulfilling no criteria sets. Thus, SGUS was abnormal in a significantly higher proportion of patients with pSS, in comparison to non-Sjögren's sicca subjects (62% vs. 27%, p=0.007). Including SGUS among the ACR/EULAR criteria would increase the concordance from κ = 0.94 to κ = 0.97 between the criteria set.

Conclusion: The two sets of classification criteria yielded concordant results with an almost perfect agreement in our sicca cohort. The presence of both antiRo60 and antiRo52 antibodies was the most characteristic autoimmune pattern, with no detection of antiLa in the absence of them. SGUS was positive in a higher proportion of patients with pSS and may improve the classification criteria.

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AB0468

COMPARISON OF THE DIAGNOSTIC PERFORMANCE OF SALIVARY GLAND SCINTIGRAPHY AND ULTRASOUND IN SJÖGREN'S SYNDROME

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Background: The 2002 American-European Consensus Group (AECG) criteria included salivary gland scintigraphy (SGS) as one of the possible objective methods for assessing salivary gland involvement in primary Sjögren's syndrome (pSS). However, this test as well as the sialography were not included in the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria and considered obsolete. On the other hand, salivary gland ultrasound (SGUS) is a simple and non-invasive procedure that is readily available and provides important information on the major salivary glands. Several recent studies have assessed SGUS as a tool for diagnosing pSS.

Objectives: To compare the diagnostic performance of SGS and SGUS for pSS patients.

Methods: We included 63 patients with sicca symptoms and suspected pSS. Diagnosis of pSS was established following the 2002 AECG criteria. The patients' scintigraphic grade was determined according to Schall classification (I-IV scale) [1], establishing Schall grade ≥III (moderate functional impairment) as the cut-off. We considered SGUS score based on parenchymal homogeneity, presence of hypoechogenic areas, and clearness of posterior glandular border of salivary glands. The score of the highest graded gland was considered, and a score ≥2 was defined as a positive SGUS, according to OMERACT US-SG scoring [2]. The area under the receiver operating characteristic (ROC) curve was employed to evaluate the screening method's performance.

Results: pSS was diagnosed in 40 (63%) patients, and the remaining 23 sicca subjects (37%) constituted the control group. Abnormal SGS was established in 26/40 (65%) pSS patients and 10/23 (43%) controls. Positive SGUS was established in 24/40 (60%) pSS patients and 6/23 (26%) controls. Thus, the sensitivity and specificity of SGS were 65% and 57%, respectively, and 60% and 74% for SGUS, respectively. The area under the ROC curve (Figure 1) of scintigraphy was 0.73, while for the SGUS was 0.83.

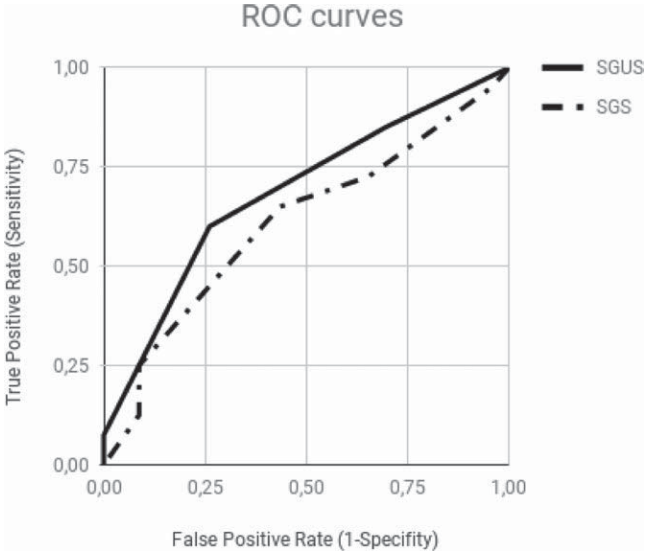

Figure 1. ROC curve comparison of SGS and SGUS for the diagnosis of pSS.

Conclusion: The diagnostic accuracy of SGUS is not only comparable with scintigraphy in pSS patients but also results in a better performance. This result indicates that SGUS is a useful method for evaluating salivary gland involvement in pSS and could be an alternative tool to other diagnostic techniques, such as SGS.

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AB0469

EVALUATION OF SALIVARY GLAND ALTERATIONS IN SJÖGREN'S SYNDROME WITH MULTISPECTRAL OPTOACOUSTIC TOMOGRAPHY

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Background: More than half of all patients with Sjögren's syndrome (SjS) show characteristic sonomorphological changes in the salivary glands. The relevance of this alterations for diagnosis and follow-up has been investigated in multiple studies. However, it is still not known which parenchymal changes cause this sonomorphological picture. Multispectral optoacoustic tomography (MSOT) is based on the photoacoustic effect – by exciting different chromophores with lasers of different wavelengths, information on tissue composition can be generated. With the help of MSOT, knowledge about tissue changes in salivary glands in patients with SjS should be gained for the first time.

Objectives: Can MSOT be applied in the area of the salivary glands and provide new information on the parenchymal changes in SjS?

Methods: In patients with SjS, classified according to the ACR/EULAR classification criteria, the ESSPRI and ESSDAI were recorded and tear flow and unstimulated salivary flow were determined. The sonomorphological changes in the salivary glands were evaluated using the OMERACT scoring system. Using MSOT, collagen, lipids and (de)oxygenated hemoglobin of the parotid and submandibular glands on both sides were measured (MSOT Acuity Echo).

Results: Twenty-three patients were included in the study (21 women, age: 62 years). At the time of the study, the ESSPRI averaged 47 points and the ESSDAI 8.5 points. The Schirmer test gave an average value of 6.4 mm/5 min, the unstimulated salivary flow (UWSF) 0.2 ml/5 min. The evaluation of the B-mode sonography showed predominantly hypoechoic lesions and less hyperechoic bands. In the evaluation of the tissue information obtained by means of MSOT, a correlation between increased lipid content and salivary flow measurement was shown as well as a significant difference between collagen proportion between parotid and submandibular glands.
Conclusion: With the help of MSOT, statements about the actual tissue changes within the salivary glands in SjS can be made for the first time. This project demonstrated for the first time a correlation between tissue composition and clinical parameter. The evaluation of other wavelengths in order to obtain further information on the tissue composition is planned.
Disclosure of Interests: None declared
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AB0470 THE ASSOCIATIONS OF ANTI-DNA ANTIBODIES WITH DISEASE ACTIVITY INDICES AND PATIENT REPORT OUTCOME PARAMETERS OF SLE IN KYOTO LUPUS COHORT.

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Background: Since the goals of remission or low disease activity are becoming more realistic with advances in treatment for SLE, there is a need to examine the measurements for SLE especially in patients with low disease activity. It has been known that disease activities in SLE are correlated with anti-DNA antibodies (Abs). However, it was not clear which measurements of disease activities or patient reported outcomes correlate better with anti-DNA Abs.
Objectives: To examine the association between parameters for SLE and anti-DNA Abs measured with RIA in Kyoto Lupus Cohort, a SLE registry in Kyoto University Hospital from 2019 to 2021.
Methods: 1)Correlations between anti-DNA Abs with SLEDAI, M-SLEDAI (SLEDAI without anti-DNA Abs), VAS, LupusPRO, SF-36, and Systemic lupus erythematosus Symptom Checklist (SSC) were evaluated cross-sectionally (n = 310).
2)The alterations in SLE parameters and anti-DNA Abs between two visits were examined (n = 106). Further, the correlations within 3 months were examined in cases with flare-ups of SLE (the alteration in SLEDAI > 0 and anti-DNA Abs≧0, n = 39). The associations of the alterations of anti-DNA Abs with each item of SLEDAI classified by organs were also examined.
Results: 1)31 percent of the cases in the entire registry was classified as remission or low disease activity (Table 1). SLEDAI (mean±SD) was higher in patients positive for anti-DNA Abs (7.94±5.20) than that in patients negative for anti-DNA Abs (4.56±4.65) ($p < 0.0001$). Anti-DNA Abs were weakly correlated with SLEDAI (R = 0.24 [$p < 0.0001$]), M-SLEDAI (R = 0.15 [$p = 0.014$]), and Physician-VAS (R = 0.19 [$p = 0.0016$]). On the other hand, there were no significant correlations between anti-DNA Abs and LupusPRO and SSC. Some dimensions in SF-36 had weak correlations with anti-DNA Abs, while no component summary scores had significant correlations with anti-DNA Abs.

Table 1. Patients' demographics and disease characteristics in the cohort (n = 310).

Variable	Results
Age (years)	47.7 (39.4, 57.5)
Female sex	n = 284 (91.6%)
Disease duration (years)	15.9 (9.4, 24.5)
Anti-DNA Ab positivity†	n = 106 (34.2%)
Anti- DNA Ab titer (U/mL)	4 (0, 8)
SLEDAI	4 (2, 8)
SLEDAI<=4	n = 162 (52.1%)
SSC	31 (16.2, 52.5)
Remission or LDA	n = 95 (30.7%)
Patient-VAS	38 (15, 52)
Physician-VAS	13.3 (3.3, 23.3)
SF-36 PCS	45.4 (36.6, 52.4)
SF-36 MCS	48.2 (41.5, 53.6)
SF-36 RCS	51.3 (42.6, 58.6)
LupusPRO HQOL	70.2 (54.8, 86.5)
LupusPRO NHQOL	41.7 (31.3, 51.0)
Glucocorticoid (mg/day)	5 (4, 8)

* Data are n (%) or median (Q1, Q3). † Anti-DNA Ab positivity at the time of the cross-sectional observation.

2)No significant correlations were observed between the alterations of SLEDAI and anti-DNA Abs (R = 0.00 [95% CI: -0.23 – 0.22, p = 0.95]) in the total of patients with various range of observation periods (Figure 1A). In contrast, a significant correlation was observed (R = 0.32, p = 0.04) within 3 months after the flare-ups of SLE (Figure 1B). No significant correlations were found between the alterations in VAS and anti-DNA Abs, or the alterations of SSC and anti-DNA Abs. They showed the following organ symptoms: renal involvement, 62.8%; musculoskeletal, 17.1%; neuropsychiatric, 11.4%; hematological, 5.7%; mucocutaneous, 11.4%; serositis, 2.9%, and fever, 2.9%.

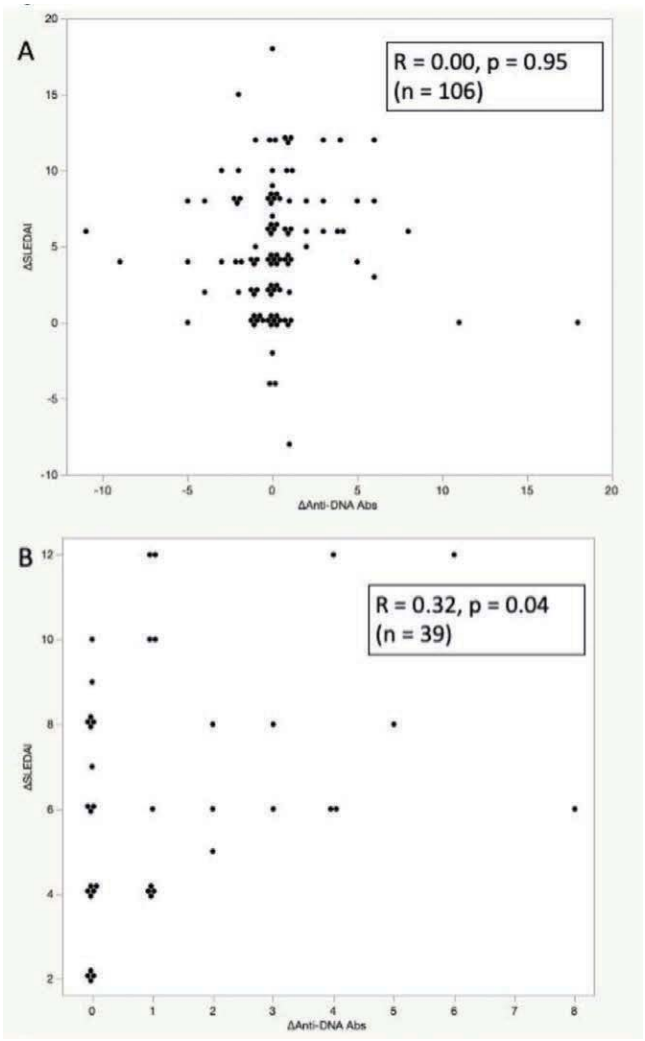

Figure 1. The associations between the alteration in anti-DNA Ab and SLEDAI

Conclusion: The associations between anti-DNA Abs with several parameters of SLE were examined. Anti-DNA Abs correlated with disease activities (SLEDAI) in SLE patients, especially when observed in the condition of flare-up.
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AB0471 FIRST SYMPTOMS AT THE ONSET OF PRIMARY SJÖGREN'S SYNDROME – THE PATIENTS' PERSPECTIVE OF A SNEAKY DISEASE

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Background: Primary Sjögren Syndrome (PSS) is an autoimmune disorder with a diverse spectrum of clinical manifestations ranging from sicca symptoms to severe systemic organ involvement. Little is known about the symptoms at the onset of PSS, as these are often ignored by both, patients and physicians leading to a substantial delay of diagnosis.
Objectives: The aim of this study was to investigate patients' recollection of the first symptoms before diagnosis of PSS in qualitative interviews. The second aim was to verify and quantify these aspects in a representative cohort.

Methods: All PSS patients fulfilled the EULAR/ACR 2016 classification criteria. In the first part of the study, consecutive PSS patients were recruited for individual, semi-structured interviews. A discussion guide with five open-ended questions was developed to explore patients' experiences on the onset of PSS. All interviews were audio-recorded and transcribed verbatim, and an inductive thematic data analysis was performed using MAXQDA software (VERBI, Berlin, Germany).

In the second part, the identified aspects of the qualitative analysis were grouped to a checklist with ten items. Patients were asked to complete the checklist before their routine clinical assessment.

Results: One-hundred and thirty-four patients participated in the study. The qualitative part was completed by 31 PSS patients; 90.3% (n=28) were female and patients had a mean disease duration of 6.9 years (±5.7(SD)) and a mean age of 58.1 years (±12.6).

Four different major aspects emerged of how patients experienced the beginning and first symptoms of PSS: (1) sicca symptoms started after initial swelling of parotis and/or lymph nodes (2) "Classic" PSS symptoms (fatigue, pain, dryness): patients reported wandering joint pain before diagnosis with a long time apart from first symptoms until diagnosis. Patients described joint pain, chronic malaise, and fatigue over months. (3) Hormonal changes (e.g. after birth, hysterectomy) or infections before the onset of PSS symptoms. (4) Slowly progressing discomfort due to sicca: patients reported a slow progression of symptoms with no initial recognition of sicca discomfort. In these patients recurrent dental problems and loss of teeth in the years prior to diagnosis was common.

In the second part of the study, the four themes were verified in an independent cohort of 103 PSS patients. Patients were 59.9 (±13.7) years old and six patients were male. The main symptom before diagnosis was dryness (n=77, 74.8%) with wandering joint pain (n=51, 49.5%) and fatigue (n=47, 45.6%). In 38.8% (n=40), patients reported a swelling/inflammation of the parotid gland at the onset of disease.

Conclusion: We identified four themes describing the initial symptoms of PSS. Raising awareness of these symptoms among physicians and among the general public may allow earlier diagnosis of PSS.

Disclosure of Interests: None declared

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AB0472 DEFINING AN ACCEPTABLE STATE OF QUALITY OF LIFE IN PRIMARY SJÖGREN'S SYNDROME

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Background: The PSS-QoL (the Primary Sjögren's Syndrome Quality of Life Questionnaire) is a disease-specific health-related quality of life (HRQL) questionnaire in primary Sjögren Syndrome (PSS). The psychometric testing showed a valid and reliable assessment, which allows a comprehensive evaluation of the patients' perspective and the extent of the disease in PSS.

Objectives: To define the threshold of an acceptable QoL state (AQLS) and the minimal detectable change (MDC) of the PSS-QoL.

Methods: Data of patients from the PSS registry of the Medical University of Graz fulfilling the 2016 ACR/EULAR classification criteria for PSS were analysed. Patients completed the PSS-Qol and ESSPRI (EULAR Sjögren's syndrome patient-reported index), disease activity was assessed by the ESSDAI (EULAR Sjögren's syndrome disease activity index) and an evaluator's global assessment (EGA, scale from 0 to 10). Receiver operating characteristic curve analyses were used to estimate the AQLS based on patients' assessment on the extent of HRQL. We selected the optimal cut-off of PSS-QoL by the maximal Youden index. At the follow – up visits after 12 months, patients assessed, whether their HRQL had changed. An anchoring method based on this evaluation was used to estimate the MDC of PSS-QoL. Furthermore, clinical data were compared in AQLS and non-AQLS groups.

Results: Data from 152 PSS patients were analysed which of 91.4% (n=139) were female. The mean age was 59.65±12.3 years (± standard deviation) and the mean disease duration was 5.6±5.3 years. The AQLS estimate was defined as PSS-QoL≤29.5. 40.1% (n=61) were categorized to be in AQLS. Although AQLS patients were significantly younger (56.9±13.1years vs 61.5±11.4 years, $p<0.01$) they had a longer disease duration (6.9±5.8 years vs. 4.7±4.7 years, $p<0.05$) compared to non-AQLS patients. AQLS patients had a lower EGA (2 [0-5] vs 3 [0-7], $p<0.01$ (median [range]), higher IgG (15.7[7.7-33.8, range] vs 13.1 [6.5-38.1], $p<0.05$) and higher rheumatoid-factor IgA (84 [0-500] vs 20 [0-500], $p<0.01$). AQLS patients showed significantly lower burden of sicca (measured by ESSPRI and sicca VAS scores). The MDC for PSS-QoL was defined as 12.2 points. After one year, patients' HRQL did not change in 83.3% and got worse 7.1%.

Conclusion: This study determined the AQLS and the minimal detectable change for HRQL. These results will help evaluating the HRQL of patients in clinical practice, as well as possible assistance designing future clinical trials. Patients in AQLS show lower dryness scores but higher immunological activity compared to non-AQLS patients. Longitudinal studies are needed to determine factors affecting patients' HRQL in PSS.

Disclosure of Interests: None declared

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AB0473 EFFECT OF THYROID LESIONS ON THE COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Thyroid disease is a common complication of systemic lupus erythematosus manifesting in 30% of cases due to a disturbance of autoimmune mechanisms.

Objectives: evaluating the effect of thyroid lesion on the course of systemic lupus erythematosus based on clinical and laboratory parameters, and the level of antibodies to thyroid hormones.

Methods: Among 65 examined patients with SLE (63 women and 2 men aged 19-65) we revealed a thyroid disorder in a third of patients. Patients were diagnosed with autoimmune thyroiditis in 16 cases, nodular goiter (degree I and II), and single diffuse toxic goiter in 5 cases. The duration of the disease was 5 years, that concomitant thyroid diseases — 3 years. The concentration of antibodies to thyroid hormones was determined by enzyme immunoassay using immobilized thyroxine and triiodothyronine.

Results: When the thyroid gland (TG) gets involved, there is a pronounced discordance in the parameters of immune and hormonal status in patients with SLE compared with patients without thyroid complications. It was found that 68% of patients had antibodies to nDNA, compared with 46% without concomitant thyroid lesion, CIC - 77% and 32%, respectively, IgG - 54% and 25%. The SLICC/ACR damage index in the SLE group with thyroid involvement was higher than in the second group: 4.55 and 3.6 points. This indicates an increase in the severity of SLE in patients with involvement of the thyroid gland. Joint involvement was seen in 79% with thyroid involvement, and 49% without thyroid involvement. A lesion of serous membranes in the form of pleurisy was in 39% and in 3% without involvement, that of the heart in 66/24%. Lupus erythematosus cell phenomenon in 44 / 31%. Immunological activity prevailed in the group of SLE patients with combined autothyroid disease. Among these patients, 100% had an elevated level of antibodies to thyroid-stimulating hormones, versus 15% in the group without autothyroid disease.

Conclusion: The involvement of the thyroid gland increases the severity of the course of SLE, antibodies to thyroid hormones are produced actively, which is indicative of thyrocyte destruction and of blocking the normal process of hormone synthesis by their antibodies.

Disclosure of Interests: None declared

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AB0474 IMPACT OF HEALTH LITERACY ON TRUST IN PHYSICIANS AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE TRUMP2-SLE PROJECT

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Background: Information technology has expanded the gap in patient health literacy (HL), and HL has various implications on the trust in patient-doctor relationship. Previously, only functional HL, the ability to interpret health information through reading and writing skills, has been studied in patients with SLE (1).
Objectives: We examined how trust in physicians is affected by the broader concept of HL, including communicative HL, the ability to extract health information from communication to use, and critical HL, the ability to discern and use such information (2).
Methods: This cross-sectional study enrolled 362 SLE patients at 5 sites between June 2020 and August 2021. Three domains of HL (i.e., functional HL, communicative HL, and critical HL) were assessed using the 14-item FCCHL scale (range: 1-4 points for each domain). The outcomes were patients' trust in their physicians and physicians in general and were measured using the Japanese version of the 5-item Wake Forest Physician Trust scales (range: 0-100 points for each scale). General linear models adjusted for age, gender, education, income, SLEDAI, disease duration, depression, and hours of Internet use were conducted. Subsequently, a series of general linear models were then fit to each of the three domains of HL to examine whether or not it was associated with the aforementioned covariates.
Results: The median age of the patients was 45 (interquartile range [IQR],34-55), 88% were female. The median value of SLEDAI was 4 ([IQR], 2-8), Trust in one's physician was 80 ([IQR], 70-95) and trust in physicians generally was 65 ([IQR], 50-80). Trust in one's physician increased with higher functional and communicative HL (per 1-pt increase, 3.2 [95%CI 0.7 to 5.9]; 5.4 [95%CI 1.6 to 9.3]). Trust in doctors generally increased with higher communicative HL and decreased with higher critical HL (per 1-pt increase, 6.8 [95% CI 2.0 to 12]; -6.7 [95% CI -12 to -1.9]). Lower functional HL was associated with older age and depression, while higher HL was associated with higher educational level. Higher communicative HL and critical HL were each associated with longer Internet use.
Conclusion: In patients with SLE, higher trust in one's physician was associated with both functional and communicative HL, while higher trust in physicians generally was associated with higher communicative HL and lower critical HL. Our findings suggest that trusting relationships may be fostered by the encouragement of rheumatologists to cultivate patients' ability to share their health problems with their physicians and family members and to obtain useful health information (i.e., communicative HL), rather than to improve their ability to discern health information (i.e., critical HL).

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AB0475

AVASCULAR NECROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF LONG-TERM FOLLOW-UP FROM A SINGLE CENTRE

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Background: Avascular necrosis (AVN) is a major cause of morbidity and loss of quality of life in systemic lupus erythematosus (SLE) patients. AVN is often diagnosed at advanced stages and treatment options are limited.
Objectives: To identify the differences of demographic, clinical, and serological factors in SLE patients with and without AVN, and to investigate associated risk factors of AVN in patients with SLE.
Methods: In this single-centre retrospective cohort study, we included 533 SLE patients [88.6% female, mean (standard deviation, (SD)) age at diagnosis 34.6 (14.3) years] who fulfilled SLICC 2012 classification criteria. AVN diagnosis was confirmed by radiological imaging techniques in symptomatic patients. To investigate the correlation between maximum daily steroid dose and AVN development, we divided our patients into four groups according to the highest dose of prednisolone used for a month or longer during their follow-up (Group 1: 0-19mg/day, Group 2: 20-39mg/day, Group 3: 40-59mg/day, Group 4:≥60mg/day). Pulse steroid administration was also recorded. Multivariable logistic regression analyses were performed to demonstrate the associated factors with AVN. Clinical parameters found to be related to AVN development in univariable analyses were analyzed both in the sex- and age-adjusted model, and the model including sex, age, time to AVN or last follow-up, immunosuppressive therapy, and steroid dosages (multivariable model). To determine the relation of different steroid groups and pulse steroids with AVN, odds ratios (OR) were calculated in the sex- and age-adjusted model and multivariable model.
Results: After a median disease duration of 9.1 years, AVN was detected in 46 (8.6%) patients. There were 85 AVN sites involved, the hips being the most commonly affected (71.7%) (Figure 1). The mean age at SLE diagnosis was significantly younger in the AVN group (mean (SD) 26.8 (11.7) vs. 35.3 (11.4), p<0.001). Fever (21.6% vs. 10.9%), malar rash (52.2% vs. 36.3%), serositis (26.1% vs. 14.6%), renal involvement (65.2% vs. 35.1%) and hemolytic anemia (32.6% vs. 19.3%) were found more frequently in the AVN group compared to non-AVN group, respectively (p<0.05). In the multivariable logistic regression analyses, malar rash was found to be the only clinical feature associated with AVN (OR 2.01, 95% confidence interval (CI) 1.02-3.97). The steroids had an association with AVN development in a dose-dependent manner (Table 1). Pulse steroids did not increase the risk of AVN (Table 1).

Table 1. Factors associated with avascular necrosis.

Association between maximum daily steroid dose and AVN			
	OR Crude (95% CI)	OR Age-sex adjusted (95% CI)	OR fully adjusted* (95% CI)
0-19 mg/day (reference group)	1.00 (reference group)		
20-39 mg/day	7.22 (1.29-40.31)	6.63 (1.18-32.28)	5.86 (1.00-34.37)
40-59 mg/day	14.08 (3.02-65.63)	10.69 (2.25-50.75)	8.79 (1.77-43.61)
≥60 mg/day	31.50 (7.39-134.19)	26.03 (6.02-112.59)	13.93 (3.07-63.16)
Association between pulse steroid treatment and AVN			
	OR Crude (95% CI)	OR Age-sex adjusted (95% CI)	OR fully adjusted* (95% CI)
No pulse steroids	1.00 (reference group)		
Pulse steroids	6.29 (3.35-11.81)	4.86 (2.53-9.37)	1.51 (0.69-3.32)

*In addition to the age at SLE diagnosis and sex, immunosuppressant use, and follow-up duration were also added to the final model.

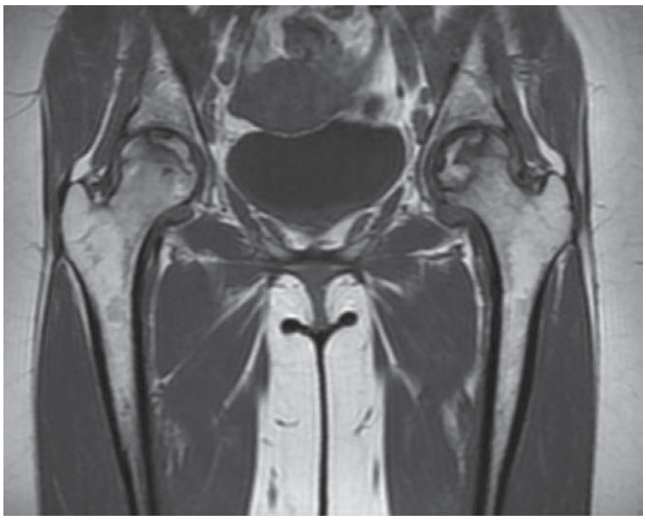

Figure 1. Magnetic resonance imaging of avascular necrosis of bilateral femoral heads in a patient with SLE.

Conclusion: High-dose daily steroid use was associated with an increased risk of AVN in SLE patients. Therefore, to prevent AVN in patients with SLE, the aim should be minimizing the dosage and duration of steroid use as much as possible. Furthermore, we showed that malar rash independently increased the risk of AVN development. Further research is required to explain this finding.

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AB0476 PREDICTIVE FACTORS FOR THE DEVELOPMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS IN PATIENTS WITH IMMUNE THROMBOCYTOPENIA

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Background: Patients with immune thrombocytopenia (ITP) have a risk of developing systemic lupus erythematosus (SLE). We sought to examine the clinical characteristics of patients with primary ITP who later developed SLE, and identified the risk factors for the development of SLE.
Objectives: We retrospectively examined patients who were diagnosed with primary ITP at a tertiary hospital between August 2001 and November 2019. We compared the clinical characteristics according to the development of SLE. Logistic regression analysis was performed to identify the factors associated with the development of SLE.
Methods: Of 130 patients with primary ITP, 10 (7.7%) were later diagnosed with SLE during follow-up (median, 30 months [IQR, 15.5–105]). The presence of skin bleeding, organ bleeding, lymphopenia, anemia, and positive antinuclear antibody (ANA) titer (> 1:160) were more common among patients who later developed SLE than did those who did not develop SLE. Multivariate analysis showed that young age (< 40 years; odds ratio [OR], 8.359 [95% confidence interval (CI), 1.230–56.793]; p = 0.033), organ bleeding (OR, 18.349 [95% CI, 2.771–121.517]; p = 0.003), and ANA positivity (>1:160; OR, 7.692 [95% CI, 1.482–39.910]; p = 0.015) were significantly associated with the development of SLE.
Results: Young age (< 40 years), organ bleeding, and ANA positivity (> 1:160) were risk factors for the development of SLE in patients with primary ITP.
Conclusion: These results suggest that continued follow-up for the detection of SLE development is needed for patients with ITP, particularly those with young age, ANA positivity, or organ bleeding.
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Table 1. Factors associated with the development of SLE in patients with primary ITP

	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	P value
Young age[a]	5.444	1.332–22.250	0.018	8.359	1.230–56.793	0.033
Female	4.333	0.530–35.422	0.17			
BMI	0.873	0.717–1.070	0.20			
Skin bleeding	8.419	1.034–68.533	0.046			
Mucosa bleeding	1.250	0.247–6.330	0.79			
Organ bleeding	14.864	3.633–60.815	< 0.001	18.349	2.771–121.517	0.003
Platelet counts	0.911	0.828–1.002	0.06			
ANA positivity[b]	16.500	3.984–68.341	< 0.001	7.692	1.482–39.910	0.015
Neutropenia[c]	2.111	0.229–19.499	0.51			
Lymphopenia[d]	4.846	1.189–19.759	0.028			
Anemia[e]	10.118	2.044–50.091	0.005			

SLE: systemic lupus erythematosus, ITP: immune thrombocytopenia, BMI: body mass index, ANA: antinuclear antibody, OR: odds ratio, CI: confidence interval. [a]Young age = age < 40 years [b]ANA positivity ≥ 1:160 [c]Neutropenia = Absolute neutrophil count < 1500 µL [d]Lymphopenia = Absolute lymphocyte count < 1500 µL [e]Anemia = Hemoglobin < 12 g/dL

Disclosure of Interests: None declared
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AB0477 REMISSION AND CLINICAL PATTERNS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN SOUTHERN PAKISTAN: RETROSPECTIVE COHORT STUDY

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Background: SLE is a difficult to treat autoimmune disease due to clinical heterogeneity, unpredictability of disease flares and limited therapeutics. These challenges are worsened in a low-middle income country (LMIC) setting, yet clinical epidemiology from LMIC may have global benefits.
Objectives: To determine (i) the clinical pattern of SLE and (ii) the effect of SLE severity and treatment regimen on time to remission.
Methods: A retrospective cohort study of 200 SLE patients' medical records (Mar 2014 to Mar 2020) from ImmunoCure clinic was conducted. Patients fulfilled American College of Rheumatology criteria 1997 for SLE classification. Inclusion criteria were active SLE disease, as measured by SLEDAI-2K [1]. SLEDAI categories were used as outcome measure: mild (score ≤6), moderate (7-10), severe (>10) to evaluate clinical pattern of SLE. ANA subsets and disease phenotypes were used to describe the clinical pattern in each SLEDAI category. ANA was performed using Immunofluorescence on Human Hep2 cells. ANA subsets were performed using immunoblot from Euroimmun [2]. Statistical analyses were performed using STATA v16.0. Kruskal-Wallis test was used for continuous measures, and Pearson's chi square test was used to compare categorical variables across SLEDAI severity. Remission status and time to remission was the secondary outcome. Remission was based on DORIS 4 criteria [3]: immunosuppressives (IS) with Prednisolone (Pred) 5mg or 2.5mg and finally off all drugs (Pred 0 and no IS), along with follow up duration > 1-year. Total doses of all drugs were calculated [4]. Survival regression was used, along with Kaplan Maier curve to estimate median remission time (months).
Results: ANA Speckled pattern is associated with mild to moderate disease (P=0.02). Most frequent antibodies are anti-dsDNA (63%), SSA (24%) and Ku (17.5%). Anti-cardiolipin (aCL) antibodies are significantly associated with severe disease (OR = 3.6, CI: 1.5-8.5, P<0.01). Most common presentations of SLE in this cohort are arthritis (85%), alopecia (53%), anemia (38%), rash (35%) and CNS disease (28%). Nephritis, CNS disease, cytopenias and oral ulcers are significantly associated with severe disease activity (P<0.01). ILD is in 10% of our cohort. Frequency of severe SLE was 47.5%, whereas mild disease was 16.5%. Mean duration of follow up was 41±19 months. For every 1- month increase in duration of follow up, the odds of remission increase by 6% (CI: 1.04-1.09, P<0.05). Clinical remission on treatment (at Pred≤5mg) was successfully achieved in 62% patients. Complete remission (off all IS & Pred) was achieved in 24 patients (14 in severe SLEDAI category) out of 200, with a mean post remission follow-up of 18 ± 15 months. Importantly, no statistical difference was found in SLEDAI category and remission status (p=0.3). However, the hazard of time to remission is 61% (CI: 0.21-0.77, P=0.01) less in severe SLE as compared to mild SLE disease activity (Figure 1).

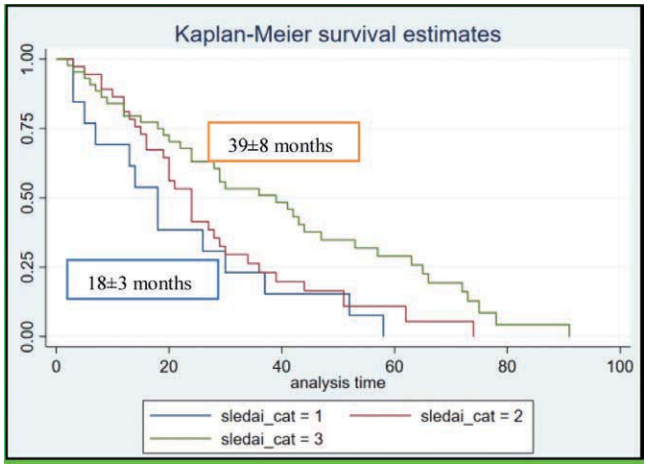

Figure 1. Kaplan Meier curve for remission time in 94 SLE patients followed for >1-year.

Conclusion: Presence of aCL is associated with severe SLE. Sustained remission is possible even in severe SLE in a LMIC setting if adequate immunosuppression is provided with persistent clinical follow-up.
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AB0478

LUPUS ANTICOAGULANT IS ASSOCIATED WITH PROSPECTIVE ECHOCARDIOGRAPHIC CHANGES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A FIVE-YEAR FOLLOW-UP STUDY

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with increased risk of cardiovascular complications such as coronary artery disease, myocarditis, pericarditis, and valvular dysfunction (1–3). The pathophysiological mechanisms are poorly understood and markers to identify high risk patients are warranted.
Objectives: We aimed to identify SLE-characteristics that are associated with progressive cardiac dysfunction.
Methods: A total of 108 patients with SLE (90 % female, mean age 46±13 years, median disease duration of 14 (7-21) years) were included from 2013 to 2014. Blood samples were collected with inclusion of biomarkers, and a standard echocardiography was performed at baseline and at a five-year follow-up. Multivariate regression analyses with five independent lupus-specific baseline variables of interest (disease activity, lupus nephritis, anti-cardiolipin and/or anti-beta-2 glycoprotein I antibodies, and lupus anticoagulant (LAC)) were performed for the association with baseline echocardiographic parameters as well as for changes during follow-up.
Results: During the five-year follow-up period, left ventricular (LV) end-diastolic volume index increased from 43.5±13.9 to 52.5±15.7 ml/m^2 (p <0.001) (Figure 1 A1), and LV diastolic parameters declined (E/A ratio 1.4±0.5 vs. 1.3±0.5, p=0.002; e' velocity 12.8±3.8 vs. 12.0±3.7 cm/s, p=0.02; mitral valve deceleration time 227.9 vs. 200.8 ms, p=<0.001), except for E/e' (7.5±3.8 vs. 6.8±3.4, p=0.02) (Figure 1B1) in the entire SLE population. LV ejection fraction remained stationary (59.5±6.8 vs. 59.6±6.4 %, p=0.81). Presence of LAC was associated with progressive LV dilatation during the follow-up period (p=0.005) (Figure 1 A2) but not baseline LV volumes (p=0.35). LAC was associated with lower E/A ratio at baseline (p=0.006) but did not predict a decrease of E/A ratio during follow-up (p=0.09) (Figure 1 B2). Follow-up changes of other echocardiographic parameters were not associated with any of the lupus-specific variables.

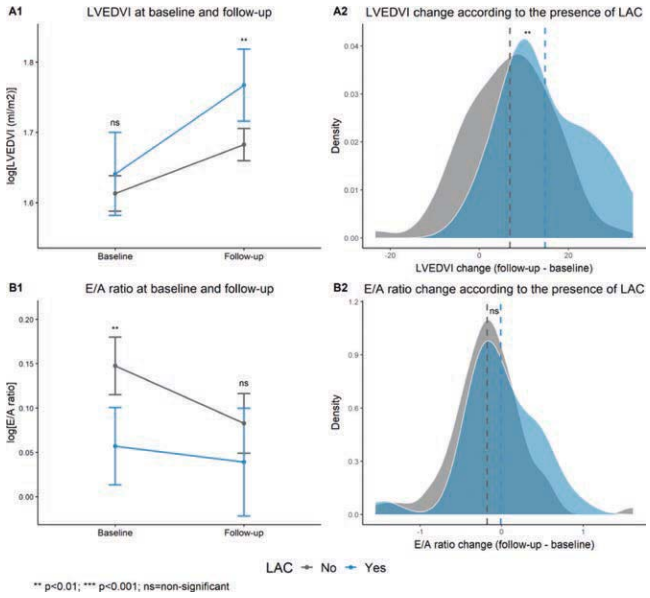

Figure 1. Left ventricular end-diastolic volume index (LVEDVI) (A) and E/A ratio (B) at baseline and follow-up (A1, B1) as well as paired longitudinal changes as density plots (A2, B2) with mean values (dashed lines) according to the presence of LAC (blue). LVEDVI and E/A ratio at baseline were log-transformed due to non-normality.

Conclusion: Presence of LAC was associated with lower E/A ratio at baseline as well as progressive left ventricular dilatation during a five-year follow-up period. Hence, LAC might be a predictor of progressive cardiac dysfunction in SLE patients. LAC is known to have implications for the microvascular circulation, but the clinical significance of the present findings is yet to be elucidated.

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SLE, Sjön-s and APS - clinical aspects (other than treatment)

AB0479 RELATIONSHIP BETWEEN DISEASE ACTIVITY, ORGAN DAMAGE AND HEALTH-RELATED QUALITY OF LIFE AS ASSESSED BY LUPUSQOL AND SF-36 IN 400 RUSSIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives: We conducted this study to compare the efficiency of LupusQoL with the 36-item Short-Form Health Survey (SF-36), a generic quality of life (QoL) scale, in Russian patients with lupus.
Methods: Both questionnaires were conducted for one visit to the clinic. Disease activity was evaluated by the SLEDAI-2K, while the chronic damage was assessed by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI). Associations between the LupusQoL and SF-36 domains were examined according to SLEDAI 2K and SDI.
Results: A total of 400 patients with lupus (F/M 363:37, mean age 34,2±11.5 years, mean disease duration 106,3±91,9.0 months) were included. All patients were divided into 4 groups: SLEDAI 2K ≤4 – 136 pts, SLEDAI-2K ≥4 – 264 pts, SDI =0 – 177 pts, SDI ≥1 – 223 pts.
QOL as assessed by SF-36 and LupusQoL was low in all groups of patients with SLE. The mean scores for each of the domains of the LupusQoL and SF-36 are shown in Table 1.
It was shown that the domain of pain of the LupusQoL questionnaire ($p<0.007$) statistically significantly responds to disease activity in contrast to the comparable SF-36 scale. The domains MH ($p<0.001$) and VT ($p<0.007$) of the SF-36 are more sensitive to change of disease activity.
It was found that in patients with SLE with a high activity of the disease, the noncomparable domains such as Planning ($p<0.0004$), Intimate relationship ($p<0.003$), Burden to others ($p<0.03$), Body image ($p<0.007$) significantly change. The QOL in patients with SLE with SDI ≥1 was poor in the domain of Physical health of the LupusQoL and in the comparable domain of the SF-36 PF. Higher QOL in these domains was in patients without damages. The domains Fatigue and VT are also significantly affected by the damage. So, in patients with SDII ≥1, there was a significant decrease of QOL in these domains up to 60.35±24.0 and 49.55±20.32, respectively, as compared with patients without damages 65.7±25.3 ($p\leq0.03$) and 55.69±20.32 ($p\leq0.02$) respectively.
Conclusion: LupusQoL is more sensitive to changes in SLE activity. Both SF-36 and LupusQoL are equally sensitive to changes in organ damage.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.1515

AB0480 LUPUS ORGAN DAMAGE: WHAT IS DAMAGED IN PATIENTS OF THE RUSSIAN FEDERATION, KIRGIZSTAN AND KAZAKHSTAN?

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Background: Assessment of organ damage has become the standard outcome measure for morbidity and mortality in patients with lupus over the world including the Russian Federation (RF), Kirgizstan and Kazakhstan.
Objectives: The aim of this study was to compare organ damage of patients with systemic lupus erythematosus in the Russian Federation, Kirgizstan and Kazakhstan in real clinical practice.
Methods: 1102 SLE pts who fulfilled SLICC 2012 criteria were enrolled into the study. Disease activity was evaluated by SLEDAI-2K, while chronic damage was assessed by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI).
Results: 400/600/102 Lupus pts from RF, Kirgizstan and Kazakhstan respectively were studied. Pts were predominantly female (91%/93%/98%) with a mean±SD age of 34,2±11,5/35,07±12,2/33,8±10,5 years ($p=0,36$; $p=0,96$) respectively. The mean disease duration (Me) in RF/ Kazakhstan was 6 [3;12]/ 5[2;9] years ($p=0,15$), in Kirgizstan- 2[0,6; 7] years($p\leq0,05$). Kazakh pts ($p=0,00$) had higher disease activity (SLEDAI 2K) 17,6±8,8 than Kirghiz pts 15,1±8,3 and Russian pts 9,4±8,1.
Patients from RF and Kazakhstan appeared to have a higher prevalence of damage compared with patients in Kirgizstan (Table 1). The Russian pts had a higher prevalence of Cataract 27%, damages in Cardiovascular system 77(19%), Diabetes mellitus 4% and premature gonadal failure 4%.
The pts from Kazakhstan had a higher prevalence of Neuropsychiatric 27% and renal 18% failures, skin 71% and Musculoskeletal 39% damages. The fewest damage was found out in Kirgiz pts. The risk factors for damage in our SLE pts such as age, disease duration, number of exacerbations, dosage of corticosteroids, duration of corticosteroids were determined by comparing pts with DAI SLICC =0 (676) with pts with DAI SLICC >1 (426) (*Mann — Whitney test)*
Conclusion: Identification of variations in target organ predilection and accrual of damage across patients of differing ethnicity has implications for treatment, monitoring and prognostication.
Disclosure of Interests: None declared
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Table 1. Relationship between disease activity, organ damage and health-related quality of life as assessed by LupusQoL and SF-36 in 400 Russian patients with systemic lupus erythematosus

LupusQoL domains	SLEDAI 2K≤4 Mean (SD)	SLEDAI 2K ≥4 Mean (SD)	P	SF-36 domains	SLEDAI2K ≤4 Mean (SD)	SLEDAI-2K ≥4 Mean (SD)	P
Comparable							
Physical health	70,1±22,1	64,9±23,6	0,07	PF	65,6±28,2	60,6±28,5	0,1
Emotional health	67,3±24,8	63,2±24,6	0,13	MH	52,2±9,0	49,6±7,8	0,001
Pain	74,7±23,6	67,5±24,8	0,007	BP	46,3±9,5	47,3±8,4	0,09
Fatigue	65,7±24,5	65,5±24,8	0,22	VT	55,5±23,3	48,3±9,5	0,007
Noncomparable							
Planning	71,1±27,9	60,1±28,0	0,0004	SF	71,0±24,0	71,1±24,1	0,003
Intimate relationships	78,3±28,7	69,9±31,1	0,003	GH	55,9±18,7	55,9±18,7	0,34
Burden to others	61,2±26,8	54,2±28,1	0.003	RE	59,3±42,4	59,3±42,4	0,012
Body image	71,1±24,7	62,2±28,5	0,007	RP	65,6±28,2	65,6±28,2	0,028
LupusQoL domains	**SDI =0 Mean (SD)**	**SDI ≥1 Mean (SD)**	**P**	**SF-36 domains**	**SDI =0 Mean (SD)**	**SDI ≥1 Mean (SD)**	**P**
Comparable							
Physical health	71,2±22.5	63,3±23,1	0,002	PF	69,2±27,4	57,1±28,2	0,0007
Emotional health	66,2±25,2	63,3±24,3	0,24	MH	50,31±7,9	50,6±8,7	0,6
Pain	72,3±24,2	68,2±24,8	0,03	BP	47,02±8,4	46,9±9,1	0,84
Fatigue	65,7±25,3	60,35±24,1	0,03	VT	55,6±20,3	49,5±24,9	0.02
Noncomparable							
Planning	67,7±27,3	60,9±29.1	0.03	SF	64,05±28,1	60,5±26,4	0,21
Intimate relationships	76,1±28,4	70,6±32,5	0,22	GH	52,11±20,2	47,41±20,1	0.06
Burden to others	55,7±28,4	57,4±27,3	0,68	RE	56,29±42,1	46,9±41,8	0,06
Body image	66,6±27,9	64,1±27,3	0,33	RP	50,54±42,4	39,15± 13,1	0,0001

Table 1. Organ damage in 1102 Lupus pts from RF, Kirgizstan and Kazakhstan

Features	Russian Federation N=400	Kirgizstan N=600	Kazakhstan N=102
Patients with damage, n (%)	223 (56%)	111(19%)	92 (90%)
Organ damage			
Ocular	144 (36%)	7(1,1%)	14 (14%)
Cataract	109(27%)	6(1%)	7(7%)
Neuropsychiatric	46(11%)	24(4%)	27(27%)
Skin	4(1%)	7(1,1%)	72 (71%)
Renal	12(3%)	36(6%)	18(18%)
Pulmonary	28(7%)	26(4%)	7(7%)
Cardiovascular system	77(19%)	71(16%)	14(14%)
Peripheral vascular diseases	48(12%)	26(4%)	3(3%)
Musculoskeletal	96(24%)	6(1%)	39(39%)
Diabetes mellitus	16(4%)	5(0,8%)	3(3%)
Malignancy	7(2%)	0	2(2%)
Premature gonadal failure	16(4%)	0	0
Predictors for organ damage, (M±SD)	**DAI SLICC =0 N=676**	**DAI SLICC >1 N=426**	**P**
Age, years	31,29±10,13	36,57±12,01	<0,0001
Disease duration, month	25,77±9,13	34,15±12,10	<0,0001
Number of exacerbations	2,10±1,36	3,64±2,55	<0,0001
Dosage of corticosteroids	34,90±21,61	42,12±16,68	0,03
Duration of corticosteroids, month.	69,97±42,30	83,29±66,01	0,04

**p <0,05 Mann — Whitney test*

AB0481

HEALTH-RELATED QUALITY OF LIFE ASSESSED BY LUPUSQOL AND SF-36 IN 400 RUSSIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background: The LupusQoL is a disease-specific health-related quality of life (HRQoL) measure for patients with lupus.
Objectives: We conducted this study to compare the efficiency of LupusQoL with the 36-item Short-Form Health Survey (SF-36), a generic quality of life (QoL) scale, in Russian patients with lupus. Both questionnaires were conducted for one visit to the clinic.
Methods: Disease activity was evaluated by the SLEDAI-2K, and chronic damage by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI). Associations between the LupusQoL and SF-36 domains were examined, while also examining age, disease duration, and disease activity for each questionnaire. Descriptive statistics, Spearman's correlation coefficients, and Students t test were performed to analyze the data.
Results: A total of 400 patients with lupus (F/M 363:37, mean age 34,2±11.5 years, mean disease duration 106,3±91,9.0 months) were included, and 63 % of these were active and 56 % of these had SDI≥1. The mean SLEDAI 2K score was 9,6±8,0.
QOL as assessed by SF-36 and LupusQoL was low in this group of patients with SLE. The mean scores for each of the domains of the LupusQoL and SF-36 are shown in Table 1. The mean scores are < 60 in 8 domains of the SF-36 but not in social functioning (62,03±27,19) and physical function (62,35±28,53).

Table 1. Descriptive statistics and correlation coefficient for SF-36 and LupusQoL

LupusQoL domains	Mean (SD)	SF-36 domains	Mean (SD)	r	P
Comparable					
Physical health	66,20±23,18	PF	62,35±28,53	0,77	0,96
Emotional health	64,65±24,75	MH	50,51±8,40	0,38	0,94
Pain	70,03±24,68	BP	47,0±8,86	-0,33	0,02
Fatigue	62,7±24,73	VT	53,04±22,59	-0,70	0,83
Noncomparable					
Planning	63,90±28,46	SF	62,03±27,19		
Intimate relationships	72,92±30,93	GH	49,14±20,51		
Burden to others	50,68±27,79	RE	49,84±43,86		
Body image	65,18±27,60	RP	40,46±41,35		
		PCS	45,15±7,65		
		MCS	48,46±5,41		

The MCS and PCS scores were both < 50. Despite the fact that the mean score in LupusQoL was always higher than in SF-36 for each of the comparable domains, 3 standardized p values were not statistically significant (mean score in 400 patient visits: physical health/physical function, 66,20±23,18/62,35±28,53, p = 0.96; emotional health/mental health, 64,65±24,75/50,51±8,40, p = 0.94; and fatigue/vitality 62.70 ± 24.73/53.04 ± 22.59, p = 0.83), 1 standardized p value was statistically significant - pain/bodily pain 70.03 ± 24.68/47.00 ± 8.86, p = 0.02. The correlation of the comparable domains of LupusQoL and SF-36 was studied. There was a strong correlation between comparable domains in LupusQoL and SF-36 in 400 patient visits (physical health and physical functioning, r = 0.77; emotional health and role emotional, r = 0.38; pain and bodily pain, r = -0,33; and fatigue and vitality, r =- 0.70; all p values < 0.0001).
For the 4 non-comparable domains of the LupusQoL, there was a correlation between 3 domains of LupusQoL and 1 of the component scores of SF-36: body image and SF-36 MCS, r = 0.20; planning and SF-36 MCS, r = 0.13, r = 0.73; and burden to others and SF-36 MCS, r = 0.19; body image and SF-36 PCS,r=0,38; planning and SF-36 PCS,r=0,66; and burden to others and SF-36 PCS,r=0,38.
Conclusion: The LupusQoL-Russian is sensitive to change in SLE patients with active SLE. LupusQoL and SF-36 were equivalent in assessing the HRQOL in the Russian SLE patients. Both LupusQoL and SF-36 are easily completed by patients and correlate very well with each other.
Disclosure of Interests: None declared
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AB0482

FACTORS AFFECTING QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN 1102 LUPUS PATIENTS FROM THE RUSSIAN FEDERATION (RF), KIRGHIZSTAN AND KAZAKHSTAN

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Background: Patients with systemic lupus erythematosus (SLE) have a better survival as compared to decades ago; nevertheless, they still experience a low health-related quality of life (HRQoL). The study of factors affecting the quality of life will improve medical care for patients in future.
Objectives: The aim of this study was to determine factors affecting quality of life of 1102 Lupus patients (pts) from the Russian Federation (RF), Kirghizstan and Kazakhstan.
Methods: 1102 SLE pts who fulfilled SLICC 2012 criteria were enrolled into the study. The SLEDAI 2K index activity, SLICC damage index, HRQo*L* using the LupusQo*L* (validated for the Russian-speaking population in 2018) and HADS questionnaires were evaluated.
Results: 400/600/102 Lupus pts from RF, Kirghizstan and Kazakhstan were studied, respectively. *The* pts were predominantly female (91%/93%/98%) and of indigenous nationality (Russian 83%/ Kirghiz 88%/ Kazakh 76%) with a mean±SD age of 34,2±11,5/35,07±12,2/33,8±10,5 years (p=0,36; p=0,96), respectively. The mean disease duration (Me) in RF/ Kazakhstan was 6 [3;12]/ 5[2;9] years (p=0,15), in Kirgizstan - 2[0,6; 7] years(p≤0,05). Kazakh pts (p=0,00) have a higher disease activity (SLEDAI 2K) 17,6±8,8 as compared to Kirghiz 15,1±8,3 and Russian 9,4±8,1 pts. SLICC damage index 2,39±1,61 in Kazakh pts (p=0,00) was higher than in Russian 1,57±1,54 and Kirghiz 0,79±0,32 pts.
The mean scores for each of the domains of LupusQoL are shown in Figure 1.

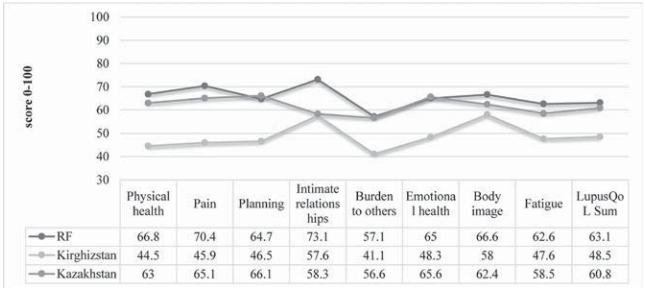

Figure 1. HRQoL in 1102 Lupus Patients from the Russian Federation (RF), Kirghizstan and Kazakhstan

As regards the Sum LupusQoL, 1102 pts were divided into two groups. The first group included 93 pts with SLE with the Sum LupusQoL<20. The second one included 484 pts with SLE with the Sum LupusQoL≥60. Such factors as age, duration of illness before verification of SLE diagnosis, pregnancy, pts without disability, high education, working\ unemployed, SLEDAI 2 K, SLICC damage index, HADS (T), HADS(D) were included into the analysis.

The worst HRQol (Sum LupusQol<20) was associated with older age, duration of illness before verification of SLE diagnosis, unemployed status, high disease activity, organ damage, anxiety and depression (Table 1).

Table 1. Factors affecting quality of life in patients with systemic lupus erythematosus in Lupus Patients from Russian Federation, Kirghizstan and Kazakhstan.

Factors	Sum LupusQol<20 (n=93)	Sum LupusQol>60 (n=484)	P
Age, years, (M±SD)	37,06±12,38	30,09±9,96	0,04
Duration of illness before verification of SLE diagnosis, month., Me [Lower,Upper Quartiles]	36 [12; 84]	10 [4; 24]	<0,0001
Pregnancy, n (%)	0	71(14%)	0,002
Pts without disability, n (%)	30(32%)	242(50%)	0,02
High education, n (%)	38(41%)	281(58%)	0,01
Working, n (%)	33(35%)	266(55%)	0,03
Unemployed, n (%)	46(49%)	131(27%)	0,01
SLEDAI 2 K, score, (M±SD)	11,32±8,16	8,50±7,47	0,04
SLICC damage index, score, (M±SD)	1,83±1,72	1,09±0,96	0,004
HADS (T)≥11, n (%)	30(32%)	19(4%)	<0,0001
HADS(D)≥11, n (%)	26 (28%)	1(0,4%)	<0,0001

**p <0,05 Mann — Whitney test*

Much better HRQoL (LupusQol≥60) was associated with younger age, pregnancy, absence of disability, high education, availability of work.

Conclusion: The most consistent predictors of low HRQoL in SLE Patients from the Russian Federation (RF), Kirghizstan and Kazakhstan are socio-demographic factors such as older age, poverty and lower educational level, working\unemployed. There are some more important factors such as SLE activity, damage and prevalent comorbidities (anxiety and depression).

Disclosure of Interests: None declared

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AB0483 THE ROLE OF PENTRAXIN-3 AS PREDICTOR OF PREGNANCY COMPLICATIONS IN PATIENTS WITH SLE AND/OR ANTI-PHOSPHOLIPID SYNDROME

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Background: Pentraxin-3 (PTX3) seems to be implicated in placentation and foetus tolerance, being mostly secreted in response to inflammatory stimuli by dendritic cells, macrophages, and endothelial cells (1). Although several studies have recently focused on this molecule (2-4), no data on women with SLE/APS are available to date.

Objectives: To assess the role of serum PTX3 and anti-PTX3 Abs as predictors of pregnancy complications in SLE and/or APS.

Methods: This case control study included pregnancies in women with SLE (SLICC, 2012) and/or APS (Miyakis, 2006), recruited at University of Padova in the Out-patient Clinic shared by Obstetrics and Gynaecologists and Rheumatologists. The control group included pregnancies of patients with other rheumatic diseases rather than APS and/or SLE. All pregnancies were recruited from 2015 to 2021 (conception date< 1st Apr 2021). At first-trimester consultation, demographics, clinical, and serological variables were recorded. First-trimester serum PTX3 levels (ng/ml) were detected by a commercially available sandwich ELISA (Alexis, UK); IgG anti-PTX3 Abs were detected by home-made validated ELISA and expressed as Optical Density values, measured at 405 nm by microplate spectrometer. Cut-off of positivity corresponded to 0.234 OD. Maternal complications included SLE flares (increase of ≥1 point in SLEPDAI); preeclampsia/eclampsia, HELLP, pregnancy induced hypertension, maternal death, gestational diabetes mellitus (GDM). Foetal complications included: miscarriage<10 week of gestation (WG); intra-uterine foetal death (IUFD) (≥10 WG); preterm delivery (<37 WG); intra-uterine growth restriction (IUGR); neonatal death within 28 days from birth.

Results: 79 pregnancies occurred in 79 patients (Table 1). Serum IgG anti-PTX3 Abs were found in 11 women (13.9%, 95% CI 7.2-23.5), and they did not differ between cases and controls (p=0.08, 4 SLE/APS women vs. 7 controls). Anti-PTX3 were associated with GDM (p=0.04, stratified for maternal age) but not with IUGR (p=0.09). No other statistical associations were found between anti-PTX3 Abs and other maternal/foetal complications. PTX3 serum levels did not statistically differ between cases and controls (p=0.63, 0.37 ± 0.26 ng/mL in cases vs. 0.33 ± 0.24 ng/mL in controls). Serum PTX3 levels were lower in patients with GDM (0.3 ± 0.2 ng/mL) compared to non-GDM patients (0.4 ± 0.2) but it did not differ between IUGR and non-IUGR, although the mean PTX3 ± SD was lower in the IUGR group (0.25 ± 0.2 in IUGR vs 0.35 ± 0.2 in non-IUGR).

Table 1. Clinical and serological characteristics of our cohort (N=79)

	Patients (N, %)
Age at pregnancy, years (mean ± SD)	35.1 ± 3.9
Cases	13 (16.5)
SLE	9 (11.4)
APS	7 (8.9)
SLE with secondary APS	3 (23.1)
Control Group	66 (83.5)
Serological features	
LAC	11 (13.9)
IgG/IgM anti-cardiolipin	20 (25.3)
IgG/IgM antibeta2-Glycoprotein I	25 (31.6)
Triple positive aPL tests	6 (7.6)
Primiparous	23 (29.5)
IgG anti-PTX3 Abs	11 (13.9)
IgG anti-PTX3 level (cut-off 0.234 OD), (median, IQR)	0.2 (0.1-0.2)
PTX3 ng/mL (mean ± SD)	0.3 ± 0.2
Concomitant treatment	
Heparin	15 (19.0)
Aspirin	44 (55.7)
Immunosuppressants	3 (3.8)
Hydroxychloroquine	21 (26.6)
Prednisone	9 (11.4)
Prednisone dosage (mg/day) (median, IQR)	5 (2.5-7.5)

Legend to Table 1: SD: standard deviation; SLE: Systemic Lupus Erythematosus; APS: antiphospholipid syndrome; LAC: Lupus anticoagulant; aPL: antiphospholipid antibodies; PTX: Pentraxin-3; Abs: antibodies; OD: optical density; IQR: interquartile range.

Conclusion: To our knowledge, this is the first study which assessed the frequency of anti-PTX3 Abs in a cohort of SLE and/or APS pregnant women. These Abs occurred in the minority of patients (13.9%) and did not differ between SLE/APS women and controls. Due to our sample size, these findings need to be confirmed in larger cohorts.

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AB0484 CLINICAL EFFICACY OF 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus have an increased risk of detecting respiratory diseases.

Objectives: To study the efficacy of 23-valent polysaccharide pneumococcal vaccine (PPV-23) in patients with systemic lupus erythematosus (SLE).

Methods: The study enrolled 72 patients diagnosed with SLE, including 64 women and 8 men aged 19 to 68 years with the disease duration ranging from 9 months to 42 years. Nine patients had high activity of disease, 17 - moderate, 40 - low, 6 - remission. Therapy: 68 patients received glucocorticoids (GC) 5-40 mg/day, 55-hydroxychloroquine (HC), 38 -cytostatics (CS), 26 - bDMARD: 14-rituximab (RTM), 10-belimumab (BLM), 2-RTM + BLM. Only 4 of 72 patients received monotherapy (GC-1, HC-1, CS-1, bDMARD-1); the remaining 68 received combined immunosuppressive therapy. PPV-23 in an amount of 0.5 ml (1 dose) was administered subcutaneously. Patients were observed and examined for 1 year after vaccination. Standard clinical and laboratory examinations were performed during the visits, and the serum antibody (AB) level to S. pneumoniae was determined. The presence of respiratory infections, including lower respiratory tract infections, during the year before and after vaccination was detected by questioning, as well as by studying medical records (hospital discharge papers, specialist reports, radiological and CT examinations). 25 patients were followed up for 5-6 years after vaccination.

Results: A year after vaccination, a more than twofold increase in the concentration of antibodies to pneumococcus persisted in 56% of patients. The clinical efficacy of the vaccine was superior to the resulting immunogenicity of PPV-23.

Table 1. Respiratory infections in SLE patients at one year before and after vaccination (n=72)

Respiratory infections	1 year before vaccination	1 year after vaccination	p
Lower respiratory infections	31(43%)	9(12,5%)	0,0001
Pneumonia, (including recurrent,	12(16,7%)	4(5,6%)	0,06
2-5 episodes)	5(7%)	-	
Acute bronchitis	13(18%)	4(5,6%)	0,04
Exacerbation of chronic bronchitis	6(8,3%)	1(1,4%)	0,1
Upper respiratory infections	14(19,4%)	6(8,3%)	0,04
Acute sinusitis,	11(15,3%)	5(7%)	0,1
(Including recurrent)	1(1,4%)	-	
Exacerbation of chronic tonsillitis	2(2,8%)	-	
Acute otitis media	1(1,4%)	1(1,4%)	

During the year after vaccination, a decrease in episodes of infections of the lower respiratory tract by more than 3 times was recorded compared with the year preceding immunization (43% and 12.5%, respectively), p=0.0001. Not a single case of recurrent pneumonia was noted (before vaccination - in 5 patients). The number of infections of the upper respiratory tract has more than halved (19.4% and 8.3%, respectively). In 4 (5.6%) patients, non-severe pneumonia developed within a year after vaccination, all of these patients had risk factors for the development of respiratory infections: anti-B-cell therapy with the absence of an adequate vaccine response (3), interstitial lung damage (1), work activities and home environments associated with an increased risk of viral or bacterial infection (3). After a year of observation, 25 patients were followed up for another 4-5 years, the development of pneumonia was not registered in any case (2 out of 25 had pneumonia in the year prior to vaccination). At the same time, 5 years after vaccination, only 18% of patients had more than a 2-fold excess of the initial anti-pneumococcal antibodies.

Conclusion: Sufficient immunogenicity and clear clinical efficacy of PPV-23 have been demonstrated in SLE patients receiving combined immunosuppressive therapy.

Disclosure of Interests: None declared

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AB0485 TRIGGERS OF DISEASE FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic relapsing-remitting disease characterized by a clinical heterogeneity, an unpredictable pattern and a capricious course. Despite great advances in diagnosis and treatment strategies, lupus flares of varying severity still occur, leading to an increased risk of organs damages and a poorer prognosis. Preventing flares, achieving and maintaining remission represent the main objective in SLE management and remain a major challenge for practitioners.

Objectives: Our study aimed to describe lupus flare-ups and identify its triggering factors, in a cohort of patients with active SLE, in order to optimize disease control.

Methods: We conducted a retrospective study including patients with SLE followed for a period of 20 years. SLE diagnosis was retained according to the American college of Rheumatology classification criteria (ACR) of 1997 and/or to the SLICC 2012 criteria. A lupus flare was defined by the occurrence of new or worsening lupus manifestation, justifying treatment intensification. We evaluated potential flare triggers, disease activity at each outbreak according to the SLEDAI-2K score and flare types. Patients considered at full clinical remission or at low disease activity state (SLEDAI ≤ 3 in patients treated with antimalarials drugs / SLEDAI ≤ 4 in patients treated with a low glucocorticoids dose <7.5 mg of Prednisone per day ± immunosuppressant) during the study period were excluded (31/102; 30.4% of patients).

Results: A total of 72 patients, with a mean age at SLE diagnosis of 31 years [11-66] and a gender ratio (F/M) of 8:1, were enrolled. During follow-up, 186 flares occurred. The average number of flares per patient was 3 [1-13]. The mean SLEDAI score during flare-ups was 8 [6-21]. At least one triggering factor was found in 62.9% of flares. The identified triggers for lupus flares were medication nonadherence in 54.7% of cases (discontinuation of antimalarial drugs and corticosteroid therapy in 38.46% and 16.2% of cases, respectively), an intercurrent infection in 30.7% of cases, a hormonal factor in 11.96% and inadequate photoprotection and/or excessive sun exposure in 8.5% of flares. Elsewhere, lupus flare-ups could be explained by therapeutic inertia or corticosteroid dependence (mean dose of 12.5mg per day) in 3.4% and 13.7 % of cases, respectively. Frequencies of general symptoms, cutaneous and haematological flare-ups were higher in relapses with objectified triggering factors (26.5% vs 8.7%, p=0.02; 40.2% vs 26.1%, p=0.036; 32.5% vs 14.5%, p=0.005). In contrast, renal flare-ups were more frequent in the group of flares in which no triggering factors were identified (21.4% vs 33.3%, p=0,005). Disease activity was comparable in both groups. The average follow-up time was 8 years [1-26].

Conclusion: In our cohort, an avoidable trigger, dominated by poor medication compliance and infections, preceded more than one out of two lupus flares. Formalized and organized therapeutic education should be one of the pillars of SLE management.

Disclosure of Interests: None declared

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AB0486 INFLAMMATORY MUSCULOSKELETAL ABNORMALITIES BY CONTRAST ENHANCED MRI IN SLE PATIENTS

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Background: Joint involvement in SLE is the most frequent manifestation and shows a wide heterogeneity[1]. It has not a valid classification and it is often underestimated. Subclinical inflammatory musculoskeletal involvement is not well known[2].

Objectives: We aim to describe the prevalence of joint and tendon involvement in hand and wrist of SLE patients, either with clinical arthritis, arthralgia or asymptomatic and compare it with healthy subjects using contrasted MRI.

Methods: SLE patients fulfilling SLICC criteria were recruited and classified as follows: group (G) 1: hand/wrist arthritis, G2: hand/wrist arthralgia, G3: no hand/wrist symptoms. Jaccoud arthropathy, CCPa and RF positivity, hand OA or surgery were excluded. Healthy subjects (HS) were recruited as controls: G4. Contrasted MRI of non-dominant hand/wrist was performed. Images were evaluated following RAMRIS criteria extended to PIP, Tenosynovitis score for RA and peritendonitis from PsAMRIS. Groups were statistically compared.

Results: 107 subjects were recruited (G1: 31, G2:31, G3:21, G4:24). Any lesion: SLE patients 74.7%, HS 41.67%; p 0.002. Synovitis: G1: 64.52%, G2: 51.61%, G3: 45%, G4: 20.83%; p 0.013. Erosions: G1: 29.03%; G2: 54.84%, G3: 47.62%; G4: 25%; p 0.066. Bone marrow edema: G1: 29.03%, G2: 22.58%, G3: 19.05%, G4: 0.0%; p 0.046. Tenosynovitis: G1: 38.71%; G2: 25.81%, G3: 14.29%, G4: 0.0%; p 0.005. Peritendonitis: G1: 12.90%; G2: 3.23%, G3: 0.0%, G: 0.0%; p 0.07.

Conclusion: SLE patients have a high prevalence of inflammatory musculoskeletal alterations by contrasted MRI, even if asymptomatic. Not only tenosynovitis but peritendonitis is also present.

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AB0487 SJÖGREN SYNDROME: DESCRIPTIVE AND COMPARATIVE STUDY OF PRIMITIVE AND ASSOCIATED FORMS

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Background: Sjögren syndrome (SS) is an autoimmune disease (AID) characterized by a dysfunction of the exocrine glands (mainly salivary and tear glands). It is responsible for xerostomia and xerophtalmia as well as systemic manifestations that may affect multiple organs. This syndrome comes in two forms: primary when it is isolated (pSS) and associated (aSS) when it is in association with another AID whether it is specific of organs or not. These two entities have different particularities, requiring explorations and adapted treatments. Few studies have taken interest in determining them.

Objectives: The objective of this study was to compare the various clinical and evolutionary manifestations of these two forms.

Methods: We conducted a retrospective analytical study over a period of 33 years. All patients with SS based on ACR 2012 and/or ACR/EULAR classification

criteria were included. Epidemiological, clinical, para-clinical, therapeutic and disease course characteristics in both groups (pSS and aSS) were described and compared.

Results: One hundred and forty-five patients were included. Sixty-three (43.4%) had pSS and 82 (56.5%) had aSS. The pSS group consisted of 58 women (92%) and five men (8%) with a mean age at diagnosis of 51.9 ±15.3 years. Seventy-eight women (95%) and four men (5%) with a mean age at diagnosis of 45.4±16.2 years had a SS. The most common AADs associated with the latter were SLE (39%) and RA (18.3%). The comparison of the two groups concluded that the mean age at the time of diagnosis was significantly higher in patients with pSS (p= 0.01). Glandular involvement was almost constant in both groups. Joint involvement, skin involvement and Raynaud's syndrome were significantly more common in the aSS group (p< 0.01; < 0.001 and 0.02 respectively). Central neurological involvement was significantly more common in the pSS group (p=0.04). The other clinical manifestations were comparable in both groups. Comparison of biological abnormalities between pSS and aSS showed a statistically higher frequency of leukopenia (p=0.04), lymphopenia (p <0.001), Antinuclear antibodies (p=0.001), anti SSA antibodies (p=0.003), rheumatoid factor (p < 0.001) and anti CCP antibodies (p<0.001) in aSS. Synthetic antimalarial drugs, corticosteroids and immunosuppressive treatment were significantly more prescribed for aSS (p= 0.003, p < 0.001 and p=0.02 respectively). After a mean of follow up of 3 ±4.5 years for the pSS and 4 ±4.5 years for the aSS. No cases of lymphoma were observed in both groups.

Conclusion: Differentiating between pSS and aSS is crucial in order to establish an early diagnosis and ensure adequate management and a better prognosis. Larger-scale studies appear to be needed to optimize management.

Disclosure of Interests: None declared

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AB0488 THE UTILITY OF ERYTHROCYTE SEDIMENTATION RATE, C-REACTIVE PROTEIN, AND PROCALCITONIN IN DETECTING INFECTIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A DIAGNOSTIC TEST ACCURACY REVIEW

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Background: Patients with systemic lupus erythematosus (SLE) are at an increased risk of hospitalization for flares or infections. In practice, diagnosing SLE flares versus infection can be challenging as both present with similar signs and symptoms. Strategies are needed to help differentiate between infections and SLE flares in hospitalized patients. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin (PCT) are commonly used to aid in the diagnosis of infection in hospitalized patients, however, their utility in SLE is unclear.

Objectives: To summarize the evidence about accuracy of ESR, CRP, and PCT in diagnosing infection in hospitalized patients with SLE.

Methods: We searched five databases until April 2021. We included studies published in English investigating levels of ESR, CRP, or PCT on adults hospitalized with a diagnosis of SLE comparing infection versus non-infection. We excluded studies with no clinical data, inadequate data to perform analysis, different conditions, and not relevant study types (such as case reports, other reviews). We also excluded studies with overlapping data (e.g., abstracts that are later published as full-text articles). We used the Quality Assessment of Diagnostic Studies to assess for bias and applicability. We obtained pooled sensitivities and specificities from studies that used similar cut-offs. We also generated mean differences for ESR, CRP, and PCT in infection versus non-infection hospitalized SLE patients.

Results: We included 26 studies in our analysis. Most studies had an unclear or high risk of bias. Most patients from both infection and non-infection groups were women aged from 27-40 years. The definitions for infection were heterogenous but mainly included positive culture or biochemical testing, suggestive imaging, response to antibiotics, or obvious signs/symptoms (such as purulence). The CRP had a pooled sensitivity of 0.75 (95%CI 0.57-0.94) and specificity of 0.72 (0.59-0.85), PCT had a pooled sensitivity of 0.68 (95% CI 0.0.59-0.77) and specificity of 0.75 (0.59-0.90), and for ESR pooled estimates were not calculated due to insufficient data but sensitivity ranged from 50 to 69.8 and specificity from 38.5 to 55.6. Modifying cut-offs improved sensitivities and specificities (see Table 1). The ESR, CRP, and PCT mean differences were all greater in infection groups versus non-infection (10.1, 95% CI 3.2-17.0; 46.8, 95% CI 36.5-57.0; 0.53, 95% CI 0.26-0.80; respectively).

Conclusion: Our study showed that although ESR, CRP, and PCT mean values are increased in hospitalized infected SLE patients compared to patients with no infection, the included studies used varying cut-offs for sensitivities and specificities and definitions for infection decreasing the uncertainty on the results and making the clinical usefulness of these biomarkers unclear. Our findings at this time do not support the widespread use of these biochemical markers in SLE patients and highlight the need that more research is needed to investigate the use of these markers in this patient population.

Table 1. Pooled sensitivity and specificities of CRP and PCT

	Studies (n)	Sensitivity (95% CI)	Specificity (95% CI)
CRP			
CRP < 10	3	0.68 (0.48-0.89)	0.70 (0.62-0.77)
CRP > 10	2	0.91 (0.86-0.97)	0.87 (0.81-0.93)
Overall	5	0.75 (0.57-0.94)	0.72 (0.59-0.85)
Procalcitonin			
PCT > 0.2	3	0.66 (0.50-0.81)	0.84 (0.76-0.92)
PCT < 0.2	3	0.70 (0.61-0.80)	0.61 (0.53-0.69)
Overall	6	0.68 (0.59-0.77)	0.75 (0.59-0.90)

Disclosure of Interests: None declared

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AB0489 ORGANIC DAMAGE MEASURED BY SDI IN A LONG-FOLLOW-UP SLE COHORT

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Background: SLICC Damage Index (SDI) index was designed to reflect accrual damage in patients with systemic lupus erythematosus (SLE). It reflects an irreversible change, unrelated to inflammatory activity, that has occurred since the diagnosis of SLE, verified by clinical assessment, and has been present for at least 6 months.

Objectives: Our objective is to determine the factors associated with higher mean SDI and SDI≥1 in patients with SLE in a long-follow-up cohort.

Methods: Single-centre retrospective observational study of SDI in SLE in a Spanish Lupus Cohort (HAPLES cohort: single-center cohort designed for the prospective evaluation of cardiac involvement in SLE). We included 219 SLE patients but 9 were excluded from the study because they did not fulfill the EULAR/ACR 2019 classification criteria.

Results: Two hundred and ten patients with a mean age at diagnosis of 35.3 years (89.1% women) were analyzed. The mean follow-up time was 15.4 years. Mean SDI was 2.21 (range 0-26). The majority (70,9%) of patients presented an SDI≥1. However, an SDI≥1 was more frequent with longer follow-up (p=0.034): 23.8% in ≤5 years vs 74% in ≥10 years. The mean SDI increases over time (follow-up) (p<0.001): in patients with <5 years since diagnosis is 1.16, between 5-10 years 2.14 and in >10 years of follow-up 2.47. A positive correlation was also found between mean SDI and age (p<0.001), hypertension (p<0.001), diabetes (p=0.004), dyslipidemia (p<0.001), obesity (p=0.045), thrombosis (p<0.001), serositis (p=0.005), renal involvement (p=0.012), neurolupus (p<0.001), cardiac involvement (p<0.001) and antiphospholipid antibodies (aPLs) (p=0.002). A negative (protective) correlation was only found with antimalarials (p=0.002). Patients with SDI=0 (no damage) vs. SDI≥1 (any damage) were compared (Table 1) to evaluate the risk factors of presenting some irreversible accrual damage in the follow-up.

Table 1. Damage accrual measured by SDI (SDI=0 vs SDI≥1)

	SDI=0	SDI≥1	p value	OR (IC95%)
Female sex (%)	88.71 %	88.51 %	p=0.967	
Late onset SLE (≥50 years) (%)	6.45 %	23.65 %	p=0.003	3.43 (1.41-8.32)
Obesity (%)	6.45 %	16.89 %	p=0.045	2.83 (1.07-7.48)
Hypertension (%)	24,19 %	53.38 %	p<0.001	2.21 (1.27-3.86)
Diabetes (%)	1.61 %	7.43 %	p=0.097	
Dyslipidemia (%)	22.58 %	45.27 %	p=0.002	1.96 (1.10-3.47)
Thrombosis (%)	3.23 %	18.24 %	p=0.004	6.00 (1.71-21.01)
Serositis (%)	12.90 %	27.03 %	p=0.026	2.08 (1.01-4.26)
Neurolupus (%)	8.06 %	25.00 %	p=0.005	3.12 (1.35-7.26)
Glomerulonephritis (%)	14.52 %	24.32 %	p=0.114	
Cardiac involvement (%)	15.52 %	54.86 %	p<0.001	3.67 (1.95-6.92)
DNAds+ (%)	56.45 %	63.51 %	p=0.338	
Anti-Sm (%)	12.90 %	14.86 %	p=0.711	
Anti-Ro (%)	29.03 %	25.68 %	p=0.616	
Anti-RNP (%)	11.29%	8.11%	p=0.463	
Antiphospholipid antibodies (%)	25.81 %	54.05 %	p<0.001	2.16 (1.25-3.75)
LLDAS (%)	56.14 %	63.51 %	p=0.331	
DORIS (%)	41.38%	48.65%	p=0.347	
Prednisone (or equivalent) >7.5	2.94 %	12.93 %	p=0.019	4.33 (1.20-15.67)
Antimalarials	90.16 %	79.73 %	p=0.022	0.43 (0.17-1.09)
Conventional DMARDs (%)	37.70%	47.97%	p=0.175	
Belimumab (%)	1.64%	5.41%	p=0.223	
Death (%)	0.00 %	2.03 %	p=0.259	

Conclusion: SDI in our SLE-cohort was correlated with age, vascular risk factors, severe organ involvement, aPLs and steroid use. Only antimalarials were associated with a lower mean SDI. SDI increases significantly with longer follow-up time, especially after the fifth year of follow-up. Prevention and early treatment of the aforementioned risk factors could avoid irreversible organ accrual damage in lupus.

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AB0490 INFLAMMATORY MUSCULOSKELETAL ABNORMALITIES BY CONTRAST ENHANCED MRI SHOW A SPECIFIC PROFILE IN SLE PATIENTS

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Background: Joint involvement in SLE is the most frequent manifestation and often it is the first clinical symptom. Despite this, it is not well characterised and demographic, serological and clinicotherapeutic correlations have not been well stablished[1].

Objectives: We aim to determinate if there is a demographic, clinic or serological profile related to inflammatory joint involvement of hand and/or wrist (sinovitis, bone marrow edema, erosions, tenosynovitis or peritendonitis) confirmed by contrasted MRI in SLE patients.

Methods: Consecutive SLE patients fulfilling SLICC criteria both symptomatic and asymptomatic for joint involvement were recruited. Contrasted MRI of non-dominant hand/wrist was performed for joint and tendon evaluation. Sociodemographic, clinicotherapeutic and serological data were collected and statistically analysed along with each MRI abnormality.

Results: 83 subjects were recruited. Erosions and synovitis were more frequent at advanced age (55±12.61 vs 45.06±12.18 years, p 0.001 and 52.78±12.99 vs 44.95±12.49 years, p 0.011). Synovitis is less frequent in patients with renal involvement (6.7% vs 24.3%, p 0.031). No other SLE organ-specific involvement showed statistical correlation. Neither SLE related autoantibodies (ANA, DNAds, Sm, RNP, Ro, La, antiphospholipid), complement fractions, ESR nor CRP correlated with MRI lesions, except for erosions which showed lower DNAds titers (15.94±49.56 vs. 27.23±62.41, p 0.008). Patients with bone marrow edema received more methotrexate (25% vs 6.3%, p 0.033), and those with erosions and peritendonitis received less mycophenolate (5.6% vs 22.9%, p 0.034; y 0% vs 12.8%, p 0.026). Peritendonitis was the only alteration related to higher SLEDAI (7±2.45 vs 3.64±3.34, p 0.018). None of the musculoskeletal abnormalities correlated with accrual damage.

Conclusion: SLE patients with joint and/or tendon abnormalities confirmed by MRI are usually older and have less renal involvement, receiving more methotrexate and less mycophenolate than those who do not show musculoskeletal involvement.

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AB0491 MUSCULOSKELETAL INVOLVEMENT, CONFIRMED BY CONTRAST ENHANCED MRI, CONTRIBUTES TO A WORSE HEALTH-RELATED QUALITY OF LIFE IN SLE PATIENTS

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Background: Joint involvement in SLE is the most frequent manifestation, despite this, its impact on health-related quality of life (HRQoL) has not been well stablished in these patients[1]. Pain, fatigue and functional disability contribute to HRQoL related to SLE[2].

Objectives: We aim to study the relation between joint and tendon involvement confirmed by contrasted MRI and these patient related outcomes (PRO).

Methods: Consecutive SLE patients fulfilling SLICC criteria both symptomatic and asymptomatic for joint involvement were recruited. Gadolinium-enhanced MRI of non-dominant hand/wrist was performed in all subjects for joint and tendon evaluation. Different PRO: numeric scale (NE) of pain (0-10) and fatigue (0-3), Health Assessment Questionnaire (HAQ) and Fatigue Severity Scale (FSS-9) were collected and statistically analysed along with each MRI abnormality.

Results: 83 subjects were recruited. Patients with synovitis, tenosynovitis, peritendonitis and bone marrow edema reported higher values in pain NE (6.03±2.57 vs 4.26±2.49, p 0.005; 6.56±1.95 vs 4.76±2.75, p 0.017; 8.80±1.30 vs 4.95±2.55, p 0.001; 6.47±2.62 vs 4.83±2.58, p 0.026); patients with synovitis reported higher values in fatigue EN (2.32±0.82 vs 1.91±0.84, p 0.035) and patients with tenosynovitis showed worse FSS-9 (61.50±1.73 vs 45.70±16.80, p 0.015) versus patients who did not show these abnormalities by MRI. Patients with synovitis and peritendonitis had a worse HAQ (1.14±0.69 vs 0.75±0.65, p 0.031; 1.69±0.07 vs 0.90±0.69, p 0.018).

Conclusion: SLE patients with joint and/or tendon involvement confirmed by contrast enhanced MRI have a worse HRQoL measured by pain, fatigue and functional disability.

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AB0492 INTESTINAL MICROBIOLOGICAL DISORDER CLOSELY ASSOCIATED WITH PERIPHERAL LYMPHOCYTE SUBSETS AND CYTOKINES IN SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by widespread inflammation and tissue damage in multiple organs[1]. Microbiome is one of environmental factors that has been suggested to contribute to the occurrence and development of SLE[2].

Objectives: This study aims to the understanding of the pathogenesis of SLE from the perspective of intestinal microorganisms and investigate the associations between flora and peripheral lymphocyte subpopulations and cytokines in SLE patients.

Methods: Fecal samples were collected from 96 patients with SLE, and 96 sex- and age-matched healthy controls (HCs). The gut microbiota were investigated via 16s rRNA sequencing and the peripheral T lymphocyte subsets of these participants were assessed by flow cytometry. Indicators of disease activity such as erythrocyte sedimentation rate (ESR), C-reaction protein (CRP), complement C3 and C4 were recorded. Differential abundance analysis was carried out using the edgeR algorithm. The Wilcoxon rank-sum test was used to compare alpha diversity indices, bacterial abundances, and the F/B ratio between groups. R (version 4.0.1) was used for comparative statistics, and pearson's correlation analysis was used to assess the correlations between the relative abundances of bacterial genera and serum levels of ESR, CRP, C3 and C4 in the samples; correlations with $p < 0.05$ were considered significant.

Results: The alpha estimators of richness (ACE and Chao 1) were significantly reduced in SLE feces samples compared with those of HCs ($p < 0.0001$). Bacterial diversity estimators, including the Shannon ($p < 0.001$) and Simpson's ($p < 0.01$) indices, were also significantly lower in SLE (Figure 1A-D). The microbial community structures of the SLE and HCs could be separated by unweighted UnFrac-based principal coordinates analysis (PCoA) ($R = 0.186$, and $p = 0.001$; Figure 1E). Significant differences in gut microbiota composition between SLE and HCs were found using the edgeR algorithm. Compared with HCs, 24 species of flora were discovered to be distinctly different($p < 0.05$). Moreover, there was a significant positive correlation between Tregs and Corynebacterium

(p < 0.05), CD8+T and Corynebacterium (p < 0.05), CD4+T and Corynebacterium (p < 0.05), T and Corynebacterium (p < 0.05), Th1 and Escherichia–Shigella (p < 0.01), Th2 and Dielma (P<0.001) as well as Eubacterium eligens group (p < 0.05), NK and Faecalibacterium (p < 0.01). as well as Corynebacterium (p < 0.001), IL-6 and Coprococcus (p < 0.05), IL-10 and Eubacterium eligens group (p < 0.001) as well as Veillonella (p < 0.05). and Lachnospira (p < 0.01). As for clinical disease measures, there were positive correlations between CRP and Eubacterium ventriosum (p < 0.05). and Coprococcus (p < 0.05), C4 and the abundance of Corynebacterium (p < 0.05) (Figure 1**F**).

Conclusion: Patients with gut dysbiosis that mainly characterized by reduced the diversity and impaired abundance of the intestinal flora. Abnormality of T cell subsets and cytokines, especially the level of CD4+T, CD8+T, NK, Treg, Th, IL-6 and IL-10 cells contributes to the occurrence and progression of SLE, which may be related to the disturbance of gut microbiota. The discovery of the associated intestinal microbiota of SLE may provide a new idea for treatment.

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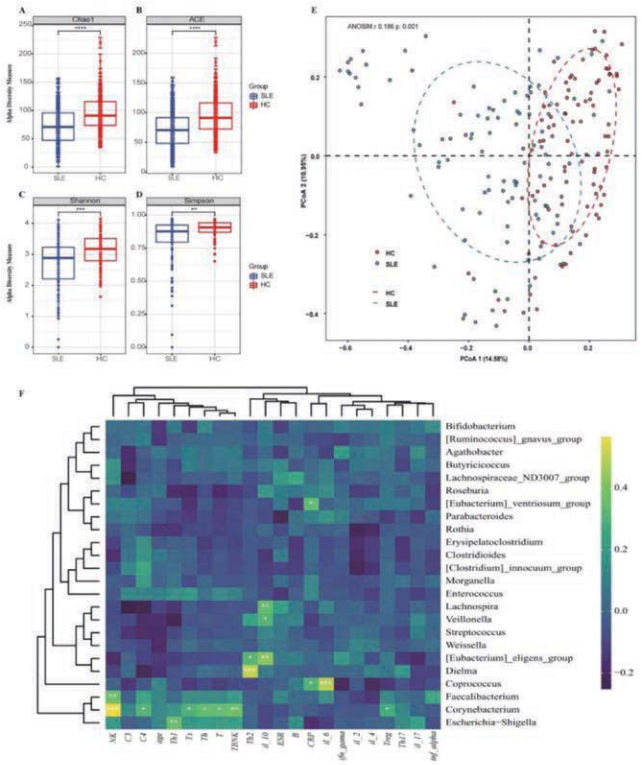

Figure1 Gut microbiome compositions of patients with SLE and HC. **(A-B)** Significantly lower Chao1 and ACE in SLE compared with HC. **(C-D)** Significantly lower Shannon and Simpson's index in SLE compared with HC by the Wilcoxon rank-sum test and Benjamini–Hochberg false discovery rate (FDR) correction. **(E)** Principal coordinate analysis (PCoA) revealed the clustering of bacterial taxa based on the Bray–Curtis distance, with each point corresponding to a subject and colored according to the type of sample. Permutational multivariate analysis of variance showed the separation of bacterial communities in feces samples was significant (q = 0.001), and the disease phenotype explained 18.6% of the variation in the overall bacterial composition of the feces between the SLE and HC, respectively. **(F)** Correlation analysis of these differential genera and cytokinesand lymphocyte subsets and clinical indicators between any two groups using Spearman's correlation analysis. The correlation effect is indicated by a color gradient from green(positive correlation) to purple (negative correlation). *p < 0.05, **p < 0.01, ***p <0 .001,****p < 0.001

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AB0493 FACTORS ASSOCIATED WITH SUICIDAL IDEATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME PATIENTS

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Background: Suicidal ideations in systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) patients are associated with stress related depressive and anxiety disorders and can lead to higher mortality rates.

Objectives: To describe the rates and potential causes of suicidal ideations in SLE and APS patients.

Methods: 159 patients (62 with SLE, 49 with SLE and secondary APS, 48 with primary APS (PAPS)), mostly women (120 (75,5%)), were consecutively enrolled in the study. The mean (M±SD) age was 37,5±12,2 years. SLE activity was measured by SLEDAI. Suicidal ideations and mental disorders were detected by psychiatrist in semi-structured interview. The severity of mental disorders was measured with MADRS, HADS, PHQ9, PSS10, and quality of life with EQ-5D, LupusQoL.

Results: The majority of patients had mental disorders (149 (93.7%)) with a predominance of anxiety and depressive spectrum (143 (89.9%)). Anxiety and depressive disorders in remission were diagnosed in 7 (4.40%) patients. Suicidal ideations in the past were revealed in 20 (12,6%) patients: in SLE - 9 (14,5%), SLE + APS - 8 (16,3%), PAPS - 3 (6,25%); suicidal attempt – in 1 (0,63%) patient with SLE + APS; autoaggressive behavior – in 11 (6,92%) patients (mainly presented as discontinuation of treatment in 10 (6,29%) patients): 6 (9,68%) - SLE, 4 (8,16%) - SLE + APS, 1 (2,08%) - PAPS. Current suicidal ideations were found in 16 (10,1%) patients: SLE - 5 (8,06%), SLE + APS - 5 (10,2%), PAPS - 6 (12,5%). The patients with suicidal ideations had higher depression (according to MADRS, HADS, PHQ-9) and anxiety (according to HADS) severity, they also presented with higher rates of stress perception (PSS-10) and poorer life quality (EQ-5D, LupusQol). The APS duration was significantly longer in patients with suicidal ideations; no differences in activity, severity and duration of SLE or steroid therapy were found, but SLE patients with current suicidal ideations compared to patients without them were 2 times more likely to receive rituximab (Table 1).

Table 1. Description of patients with/without suicidal ideations.

Characteristic, Me [25%; 75%] M±SD	With current suicidal ideations (n=16)		Without current suicidal ideations (n=143)		
	n	%	n	%	p
SLE	5	31,3	57	40,2	n/s
SLE+APS	5	31,3	44	30,9	n/s
APS	6	37,4	41	28,9	n/s
SLE duration, months	156,0 [132,0; 216,0]		84,0 [24,0; 68,0]		n/s
APS duration, months	228,0 [204,0; 348,0]		120,0 [48,0; 180,0]		0,001
MADRS	27,0 [14,5; 31,5]		13,0 [8,0; 18,0]		0,0001
HAM-A	18,5 [10,5; 25,5]		15,0 [10,0; 21,0]		n/s
HADS:					
-depression	7,0 [3,0; 9,0]		3,0 [1,0; 6,0]		0,009
-anxiety	9,0 [5,0; 14,0]		6,0 [3,0; 9,0]		0,04
PHQ-9	12,0 [8,0; 15,0]		6,0 [3,0; 12,0]		0,02
PSS-10	32,7±8,73		27,6±6,50		0,006
EQ-5D	0,56±0,29		0,72±0,22		0,009
Lupus Qol	113,7±24,9		132,0±25,8		0,02
Methylprednisolone intake:					
-Current dose, mg/day	10,0 [0; 22,5]		10,0 [5,0; 15,0]		n/s
-Cumulative dose, g	16,9 [0,9; 61,2]		7,2 [0; 28,9]		n/s
Rituximab treatment	5	31,2	26	18,2	n/s

Conclusion: Suicidal ideations in SLE/ APS patients are mainly caused by anxiety-depressive spectrum disorders provoked by stress factors, no associations with the duration, activity and manifestations of the rheumatic diseases were found. Timely identification and therapy of depressive and anxiety spectrum disorders can prevent suicidal ideations and possible poor outcomes.

Disclosure of Interests: None declared

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AB0494 COMPARISON OF CUTANEOUS SILENT PERIOD PARAMETERS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME WITH THE HEALTHY POPULATION

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Background: Neurological involvement has a great importance in the clinical spectrum of primary Sjögren's syndrome (pSS) (1). The presence of small fiber neuropathy (SFN), which cannot be detected in routine electrophysiological examinations, causes the peripheral nervous system involvement to be underestimated in the course of the disease and causes pain-related symptoms in patients that cannot be explained by routine examinations (2). Various methods can be used in the detection of SFN, and cutaneous silent period (CSP) measurement is gaining popularity recently due to its non-invasiveness and practical application (3).

Objectives: Evaluating SFN involvement in patients with pSS using CSP and evaluating its relationship with clinical parameters.

Methods: Patients with a diagnosis of pSS followed in the rheumatology outpatient clinic and healthy volunteers demographically homogeneous with the patient group were included in the study. The CSP responses were recorded over the abductor pollicis brevis muscle in the upper extremity of all participants. The latency and duration values of the responses were obtained. In patient group, EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), Hospital Anxiety and Depression Scale (HADS), Short Form-36 (SF-36) questionnaire, Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) and Central Sensitization Inventory (CSI) were applied for the evaluation of symptom severity, mood, quality of life, presence of neuropathic pain and central sensitization, respectively. Comparison of CSP parameters between patients with pSS and healthy volunteers was determined as the primary outcome measure. The secondary outcome measure was the relationship between CSP parameters and ESSPRI, HADS, SF-36, LANSS and CSI scores.
Results: A total of 36 patients and 36 healthy controls were included in the final analyses. There was no significant difference between the two groups in terms of demographic data. The mean CSP latency was significantly longer in patients with a mean of 78.18 (±7.51) when compared to controls with a mean of 67.91 (±6.41) (95% CI: 6.98- 13.55, p<0.001). Mean CSP duration was also significantly shorter in patients with a mean of 33.40 (±6.93) (95% CI: 9.57 -15.31, p<0.001). There were no significant differences in CSP parameters (latency and duration, respectively) according to patients' neuropathic pain or central sensitization profile (p>0.05 for all analyses). There were significant correlations of CSP parameters with ESSPRI dryness (r=0.469, p=0.004; r=-0.553, p<0.001), fatigue (r=0.42, p=0.011; r=-0.505, p=0.002), pain (r=0.428, p=0.009; r=-0.57, p<0.001) subscores and mean ESSPRI score (r=0.631, p<0.001; r=-0.749, p<0.001). Significant correlations were not found between CSP parameters and SF-36 scores, other than CSP duration and "pain" subscore (r=-0.395, p=0.017). When the other correlations were investigated there were no significant correlations other than CSP duration and the HADS anxiety score (r=-0.201, p=0.02).
Conclusion: As an indicator of CSP measurement, SFN is more common in patients with pSS than in the healthy population. The association with important clinical symptoms of the disease course such as dryness, fatigue, pain and anxiety highlights the importance of detecting small fiber neuropathy.
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AB0495 SERUM AND URINE GALECTIN-9, IP-10 AND SIGLEC-1 AS BIOMARKERS OF DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Galectin-9, interferon-inducible protein-10 (IP-10) and sialoadhesin (SIGLEC-1) are proteins associated with interferon signature, and considered as potential biomarkers reflecting disease activity in patients with systemic lupus erythematosus (SLE).
Objectives: In this study, we aimed to investigate the association of serum and urine levels of galectin-9, IP-10 and SIGLEC-1 with disease activity in patients with SLE.
Methods: Sixty-three patients with active SLE (31 renal and 32 extrarenal) were included in the study. Thirty inactive patients with SLE (15 renal and 15 extrarenal) and 32 healthy volunteers were selected as control groups. Serum (s) and urine (u) levels of galectin-9, IP-10 and SIGLEC-1 were tested using ELISA. Urine levels of biomarkers were normalized by urine creatinine.
Results: Groups were comparable with regard to sex and age distribution. Of 125 participants, 102 (81.6%) were female and median age was 33 (28-44.5) years. Proliferative lupus nephritis (LN) (class III/III+V and IV/IV+V) were found in 22 patients with active renal SLE (70.9%), while 6 patients (19.3%) had pure class V and 3 (9.7%) had class II LN. Levels of sIP-10, uIP-10, sGalectin-9 and uSIGLEC-1 were significantly higher in the active SLE group compared to the inactive SLE group (sIP-10 p=0.046, uIP-10 p<0.001, sGalectin-9 p=0.031 and uSIGLEC-1 p=0.006); however, no differences were detected in the comparison of uGalectin-9 and sSIGLEC-1 between the groups (uGalectin-9 p=0.180 and sSIGLEC-1 p=0.699) (Table 1). Serum and urine levels of galectin-9, IP-10 and SIGLEC-1 did not differ between patients with active renal and extrarenal SLE. Levels of sIP-10, uIP-10 and uSIGLEC-1 were correlated with SLE Disease Activity Index (SLEDAI). Serum and urine levels of all biomarkers were re-tested in 41 of 63 patients (65%) with active SLE after a median treatment of 8 (5-22.5) months. At the time of the second tests, there was a significant decrease in disease activity as measured by SLEDAI [2 (0-4)] compared to the time of the first tests [10 (6-15.5)]. Comparison of sGalectin-9 levels between the serum at the time of active disease and remission showed a very significant decline (p<0.001) as shown in Figure 1. uGalectin-9, sIP-10 and uSIGLEC-1 also decreased after treatment; however, the difference was not statistically significant.

Table 1. Serum and urine levels of biomarkers across study groups.

Biomarker	Active SLE (n=63)	Inactive SLE (n=30)	Healthy Control (n=32)
sGalectin-9 (ng/ml)	11.73 (7.52-14.15)	8.66 (7.51-10.02)	5.61 (4.56-6.6)
sIP-10 (pg/ml)	279.4 (147.5-430.3)	173.4 (142.2-247.9)	74.3 (58.8-103)
sSIGLEC-1 (pg/ml)	181.2 (157.8-213.9)	182.5 (169.9-203.1)	258.3 (179-602)
uGalectin-9 (ng/ml)	8.83 (4.07-18.11)	11.54 (7.03-15.07)	10.63 (5.55-17.4)
uIP-10 (pg/ml)	34.4 (15.9-73,9)	20.8 (9.9-53.3)	12.2 (1.8-25.7)
uSIGLEC-1 (pg/ml)	321 (236.3-370.9)	297.6 (247.7-371)	290 (205.1-323.5)
uGalectin-9 (ng/mgCre)	15.50 (9.60-32.05)	11.41 (8.78-19.54)	13.57 (11.27-22.08)
uIP-10 (pg/mgCre)	73.4 (40.9-136.9)	26.1 (18.1-55.1)	16.4 (5-32.5)
uSIGLEC-1 (pg/mgCre)	619.6 (389.4-1056.5)	393.2 (248.6-715.8)	425.6 (264.7-925.9)

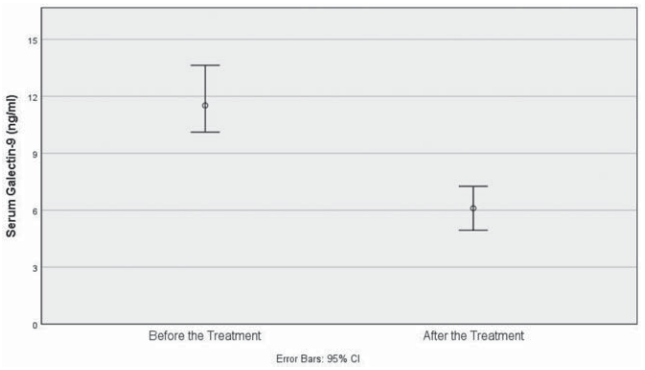

Figure 1. Serum levels of galectin-9 before and after the treatment in 41 patients with active SLE.

Conclusion: sIP-10, uIP-10, sGalectin-9 and uSIGLEC-1 are associated with disease activity in SLE. None is able to discriminate active renal from active extrarenal disease. sGalectin-9 may be a valuable biomarker to monitor response after treatment for active disease (Funded by Scientific Research Projects Coordination Unit of Istanbul University. Project number: TSA-2019-34218).
Disclosure of Interests: None declared
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AB0496 SHOULD ANTIBODIES TO DOMAIN I B2-GLYCOPROTEIN 1 BE INVESTIGATED IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME (APS) AND SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)?

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Background: The role of antiphospholipid antibodies (aPL) not included in the International Classification Criteria for the verification of APS continues to be discussed.
Objectives: To determine the clinical significance of IgG antibody for domain 1 β_2-glycoprotein 1 (IgG-aβ_2-GP1-D1) in patients with APS and SLE.
Methods: The study included 187 patients: 52 - with primary APS (PAPS), 12 - with probable APS (proAPS), 59 - with SLE+APS, and 64 - with SLE without APS. The comparison group included 49 patients with various rheumatic diseases (thrombosis without aPL (n=7), rheumatoid arthritis (RA) (n=10), Behcet's disease (BD) (n=15), systemic sclerosis (SSD) (n=12), pregnant women (n=2),

polymyositis (n=2) and Buerger's endarteritis (n=1)) and a control group of 100 relatively healthy people. IgG/IgM-antibodies to cardiolipin (aCL) and IgG/IgM-aβ_2-GP1 were determined by ELISA, and IgG-aβ_2-GP1-D1 - by chemiluminescence assay (CMA) in all patients and controls.

Results: IgG-aβ_2-GP1-D1 was detected in 37 (71%) of 52 patients with primary APS (PAPS), in 6 (50%) of 12 patients with probable APS (proAPS), in 42 (71%) of 59 patients with SLE+APS, in 17 (26%) of 64 patients with SLE, in 1 (2%) of comparison group and in none of control group. IgG-aβ_2-GP1-D1 was significantly associated with PAPS and SLE+APS compared with patients with SLE (P=0,0002 and P=0,0001, respectively). IgG-aβ_2-GP1-D1 levels were significantly higher in patients with PAPS, proAPS, SLE+APS, and SLE compared to control group (P < 0,000001, 0,03, < 0,000001, and 0,02, respectively). IgG-aβ_2-GP1-D1 levels were significantly higher in patients with PAPS and SLE+APS compared to patients with SLE (P = 0,001 and P = 0,000005, respectively) and patients from the comparison group (P < 0,05). The frequence of IgG-aβ_2-GP1-D1 positivity was associated with both thrombosis and obstetric pathology - the risk of developing clinical manifestations of APS was 9,69 and 4,19 times higher, respectively. A reliable correlation between antibodies to IgG-aβ_2-GP1-D1 and arterial thrombosis can be traced. Obstetric pathology was detected in 32 of 37 women with a history of pregnancy and all were with IgG-aβ_2-GP1-D1, versus 21 of 32 with negative IgG-aβ_2-GP1-D1 (χ2=4,19; P=0,04). Eclampsia/preeclampsia and fetoplacental insufficiency in history was in 19 of 37 women with IgG-aβ_2-GP1-D1, versus 7 of 32 with obstetric pathology but no IgG-aβ_2-GP1-D1 (χ 2=6,35; P=0,01). The incidence of obstetric pathology was significantly associated with the presence of IgG-aβ_2-GP1-D1 compared to women without these antibodies. Isolated IgG-aβ_2-GP1-D1 positivity was reported in 13 (19%) of 70 aPL-negative patients. Obstetric pathology was present in all 6 (100%) women who had pregnancy in their disease course, and thrombosis in 7 (53%) of 13 patients. Sensitivity and specificity of IgG-aβ_2-GP1-D1 depending on APS and its clinical manifestations are presented in the Table 1.

Table 1. ***Sensitivity and specificity of IgG-aβ2-GP1-D1***

	Thrombosis	*Obstetric pathology*	*Diagnosis of APS*
Sensitivity (%)	63	58	71
Specificity (%)	83	92	87

Conclusion: The frequency of IgG-aβ_2-GP1-D1 positivity was higher in patients with APS compared to patients with SLE without aPL, comparison group and controls (P < 0,05). In 19% of cases, isolated IgG-aβ_2-GP1-D1 positivity was observed. Positive IgG-aβ_2-GP1-D1 levels were significantly associated with thrombotic complications and with obstetric pathology (χ2=8,84; P=0,002 and χ2=6,35; P=0,01). Specificity of IgG-aβ_2-GP1-D1 for APS and its clinical manifestations (thrombosis and obstetric pathology) was higher than sensitivity.

The study was performed at the V.A. Nasonova Research Institute of Rheumatology within the framework of the fundamental topic FURS-2022-003.

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AB0497

IMMUNOLOGICAL DISEASE ACTIVITY PARAMETERS AT CONCEPTION ARE RISK FACTORS FOR PRETERM BIRTH AND LOW BIRTH WEIGHT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Women with systemic lupus erythematosus (SLE) are known to have more difficulty in achieving a successful pregnancy than healthy women. They have a higher risk for adverse pregnancy outcomes (APOs) including preterm birth (PB), low birth weight (LBW). (1,2). Many reports revealed that these APOs are related to uncontrolled high disease activity (3,4). Therefore, it is important for SLE women who hope to conceive to control disease activity strictly. However, it is not clear to what extent disease activity should be strictly controlled, including serum parameters such as complement levels and anti-dsDNA antibodies.

Objectives: The purpose of this study was to determine whether disease activity parameters at conception could be a risk factor for PB or LBW among APOs in patients with SLE.

Methods: Disease activity parameters including SLEDAI score, LLDAS achievement rate, serum complement levels (C3, C4, CH50), and anti-dsDNA antibody titer were retrospectively collected from medical records. We then collected information related to each APOs (PB and LBW), and analyzed the association with disease activity parameters.

Results: The subjects were 60 pregnancies of 45 patients. As for a comprehensive disease activity index at conception, SLEDAI score or the rate of LLDAS achievement became risk factors for PB (both of p<0.01, Table 1), and SLEDAI score was also a risk factor for LBW (P=0.04, Table 1). Analysis of immunological disease activity parameters showed that low C3 or high titer of anti-dsDNA antibody were risk factors for PB (P=0.03 and 0.01, respectively, Table 1). In the logistic regression analysis of PB, the cut-off levels of C3 and anti-dsDNA antibody were 62 mg/dl and 5.4 IU/ml, respectively (Figure 1 **[1]-A, [1]-D**). The risk of PB was significantly higher in the cases with low serum C3 and high anti-dsDNA antibody titer at conception (P=0.02). Similarly, low C3 or CH50 were risk factors for LBW (P=0.02 and 0.03, respectively, Table 1). Logistic regression analysis for LBW showed the cut-off level of C3 as 87 mg/dl, and CH50 as 41.8 IU/ml (Figure 1 **[2]-A, [2]-C**). Cases with low C3 and low CH50 were at higher risk for LBW (P=0.03).

Table 1. Association between disease activity parameters and PB or LBW

	Preterm birth (PB)			Low birth weight (LBW)		
	PB (+) (n = 14)	PB (-) (n = 46)	P value	LBW (+) (n = 23)	LBW (-) (n = 37)	P value
Achievement of LLDAS, n (%)##	5 (41.7)	30 (71.4)	0.09	12 (63.2)	23 (65.7)	1.00
Achievement of LLDAS without a glucocorticoid dose, n (%)##	5 (41.7)	37 (88.1)	< 0.01*	13 (68.4)	29 (82.9)	0.31
SLEDAI score#	3.5±2.9	1.1±1.3	<0.01*	2.3±2.1	1.3±2.0	0.04*
C3, mg/dl#	77.3±19.0	94.7±21.2	0.03*	80.5±16.3	96.7±22.7	0.02*
C4, mg/dl#	16.1±9.0	19.2±6.3	0.16	17.6±6.3	19.1±7.4	0.56
CH50, IU/ml#	37.3±10.6	41.1±8.5	0.17	36.5±6.6	42.2±9.7	0.03*
Anti-dsDNA antibody, IU/ml#	32.5±68.5	5.5±11.1	0.01*	20.7±55.8	7.0±12.2	0.34

(Values are presented as mean ± standard deviation or number (%). #Wilcoxon rank sum test; ##Fisher's exact test; *P < 0.05.)

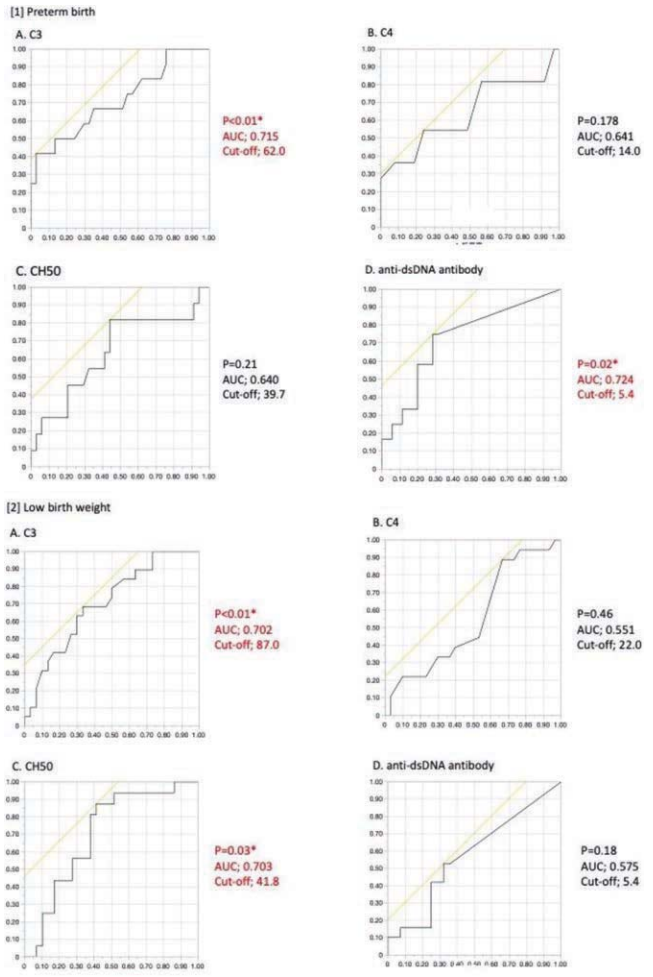

Figure 1. Logistic regression analysis of cut-off value of PB and LBW for C3, C4, CH50 and anti-dsDNA antibody. (ROC curves based on logistic regression analysis of cut-off levels for disease activity parameters, including C3, C4, CH50, and anti-dsDNA antibody titer. [1] showed ROC curves for PB, and [2] showed those for LBW.)

Conclusion: We revealed that disease activity parameters of SLE at conception are strongly associated with negative pregnancy outcomes; PB and LBW. These include low serum C3 and CH50 levels and high anti-dsDNA antibody

titers. In particular, low serum complement is a risk factor for both PB and LBW. Therefore, it is important to strictly control these disease activity parameters at conception in women with SLE.

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AB0498 CONCENTRATIONS OF ADVANCED GLYCATION END PRODUCTS (AGES) CORRELATE WITH INDEXES OF ACTIVITY AND DAMAGE ACCRUAL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).

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Background: It has been postulated that AGES could have a relevant role as inducers in the chronic inflammatory pathway present in various diseases[1]; among them, in immune-mediated diseases such as SLE, as well as that its concentration could be related to some parameters of the disease such as activity [2] or accumulated damage [3], showing studies discrepant results to date.
Objectives: To describe correlations between the concentrations of AGEs measured by cutaneous autofluorescence and various parameters related to the disease in a population of SLE patients.
Methods: AGE concentrations were measured by skin autofluorescence (Age Reader Mu Connect from Diagnoptics Technologies BV) in 66 SLE Caucasian patients and correlations with demographic and clinical data were analyzed, after adjusting for age, smoking and corticosteroids as possible confounding factors, according to previous data. Previous validation studies have shown that skin autofluorescence is strongly related to AGE levels in skin biopsies[4]. The indices were analyzed both as quantitative and categorized variables according to previously established categories or to medians/tertiles/quartiles depending on the distribution of the variable in our population.

Table 1. Descriptive characteristics of the cohort. *c: categorized.*

		Average	SD	%
Age		54	15	
BMI		25.36	4.68	
Smoker	No			68.2
	Yes			31.8
AGEs		2.6	0.7	
Disease duration (years)		16	11	
DAS28		2.22	1.16	
cDAS28	remission			71.2
	low			9.1
	moderate			15.2
	high			4.5
SLEDAI		5	4	
cSLEDAI	remission			21.2
	low			16.7
	moderate			51.5
	high			10.6
SLICC		1	1	
cSLICC	0			0.0
	1			48.5
	>1			30.3
	3			21.2
FACIT Fatigue Scale		18	10	
Patient global assessment (PGA)		3.0	2.4	
cPGA	0-1			31.8
	2-3			28.8
	>3			39.4
Physician global assessment		1.7	1.3	
cPhysician global assessment	0-1			47.0
	>1			53.0
Visual Analogue Scale (VAS)		3.1	3.1	
cVAS	0			34.8
	1-4			30.3
	>4			34.8
Health Assessment Questionnaire (HAQ)		0.527	0.551	
cHAQ	0			33.3
	0-0.75			36.4
	>0.75			30.3
Corticoids	Yes			27.3
	No			72.7

Results: Table 1 shows some descriptive characteristics of our cohort. There were clinically and statistically significant differences in the values of AGEs according to the patient's SLEDAI and SLICC. Specifically, it was observed that AGEs' values in the population with severe activity according to SLEDAI was 0.61 (95% CI 0.85-2.046; p=0.045) points > than in those in remission (p=0.045); as well as AGEs' values in patients with SLICC ≥1 was 1.23 (95% CI 0.49-1.98; p=0.030) points > than in the group without cumulative damage. In all the models, the values of AGEs increased significantly with age, smoking and current treatment with corticosteroids, except for the model including the SLICC variable. Interactions in said model were explored, and it was observed that the concentration of AGES depended on the interaction between the value of SLICC and the intake of corticosteroids, so that differences were only observed between SLICC groups in those who took corticosteroids.
Conclusion: A correlation with elevated values of AGEs was observed in those SLE patients with higher scores in the indexes of activity (SLEDAI) and damage accrual (SLICC). The fact that the differences in SLICC are only observed in those patients treated with corticosteroids suggests that, maybe, only the accumulated damage related to taking corticosteroids could be mediated by AGEs.

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AB0499 LYMPHOID ORGANIZATION IN LUPUS NEPHRITIS: EVALUATING POSSIBLEAUTO ANTIGENS

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Background: Lupus nephritis (LN) represent one of the most frequent organ manifestations and one the major cause of morbidity in Systemic Lupus Erythematosus (SLE) patients. Tubule-interstitial infiltrate (TII) represents an independent prognostic factors of renal outcome[1].
Objectives: The aim of the study was to evaluate the inflammatory infiltrates organization in kidney biopsies obtained from LN patients and to investigate possible autoantigens for in situ immune response.
Methods: Paraffin embedded kidney specimens collected since 2017 from SLE patients who underwent a renal biopsy for diagnostic purpose were re-evaluated[2]. Clinical, laboratory and histological data were collected in a standardized, computerized and electronically filled form, including demographics and past medical history. Disease activity was assessed by using SLEDAI-2K and remission in response to therapy was defined as a score 0 of renal item of the SLEDAI[3]. The cellular infiltrate were assessed by hematoxylin-eosin and by immunohistochemistry with a staining of sequential sections for monoclonal antibodies to CD3, CD20, CD21. Staining for detections of LL-37, vimentin and citrulline was made[4]. Serological levels of CXCL13 and anti-vimentin antibodies (AVAs) were evaluated in a subgroup of patients.
Results: Eighteen paraffin embedded renal specimens with TII, from LN patients were re-evaluated (F:M = 17:1, median age at biopsy-SD years 37-23; median disease duration at date of biopsy-IQR 3-4 years). A histo-morphologic grading score was performed based on the total count of TI lymphocytes and the presence of ectopic lymphoid structures-ELSs (grade 3-G3) (Figure 1). A correlation was found between G3 structures and the absence of renal remission with conventional immunosuppressive therapy (P=0.0026). Samples with G3 foci showed significantly higher intensity of LL37 (P=0.013) and LL37 co-localization (P=0.006) compared to the other lymphocytic infiltrates. No correlation was found among the intensity of vimentin and citrulline and the grade of lymphoid aggregates. A statistically significant inverse correlation between AVAs serum levels and response to therapy was found (P=0.0048). Moreover, higher level of AVAs and CXCL13 were found in patients with G3 structures. To note, two patients underwent anti-CD20 therapy but renal remission was achieved only in the patients displaying G3 structure.

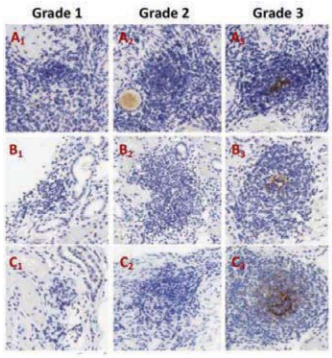

Figure 1. Characterization of the lymphocytic infiltrate and histo- morphologic grading of renal specimens from three patients with lupus nephritis (LN). Renal specimens (3 µm thick) from LN patients were stained for detection of CD21+ follicular dendritic cells (**A3, B3, C3**). Displayed are representative examples of grade 1 (**A1, B1, C1;** cellular aggregates with 10–50 lymphocytes,), found in 12 of the 18 LN patients (66.7%); grade 2 (**A2, B2, C2;** 50 lymphocytes) identified in 10 of the 18 patients (55.6%); and grade 3 (**A3, B3, C3**; > 50 lymphocytes, with ELS) foci, observed in 6 of the 18 patients (33.4%). (Original magnification x50)

Figure 1.

Conclusion: The study demonstrated that tubule-interstitium involvement is associated with the presence of lymphoid aggregation and poor renal outcome. For the first time we demonstrated that patients with G3 structures had a significant decreased response to immunosuppressant conventional therapies compared to those without ELSs. These results suggest a possible phatogenetic, prognostic and therapeutical role of lymphocytic aggregates. In addiction, LL37, thus NETosis, could have a possible role in inducing the formation of lymphocytic structures. Moreover, patients with a G3 foci showed high serological levels of AVAs and CXCL13, thus, promoting their possible role as circulating biomarkers of the presence of ELSs.

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AB0500 THE LEVEL OF PERIPHERAL BLOOD LYMPHOCYTE SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH RESPIRATORY TRACT INFECTION AND ITS CLINICAL SIGNIFICANCE

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disorder. Infections are a most common cause of morbidity and mortality in this patient population[1] and at least 50% of patients with SLE are suffered with infections during the course of their disease [2]. Lymphocytes and Natural killer (NK) cells play an important role in the occurrence and development of SLE[3]. In this study, peripheral blood lymphocyte subsets were detected in these patients, providing reference for early diagnosis and treatment of SLE patients with respiratory tract infection.

Objectives: To analyze the detection level and clinical significance of peripheral blood lymphocyte subsets in patients with SLE with respiratory tract infection.

Methods: A total of 333 SLE patients with no recent infection, 95 SLE patients with respiratory tract infection, and 132 healthy individuals matched in age and sex were enrolled in the second Hospital of Shanxi Medical University from July 2014 to December 2016. The characteristics of lymphocyte subsets in the three groups were compared and receiver operating characteristic (ROC) curves were drawn to analyze the predictive value of lymphocyte subsets in SLE patients with respiratory tract infection.

Results: The counts of T, B, CD4 + T, CD8 + T, NK, Th1, Th2, Th17 and Tregs in SLE non-infection group and SLE infection group were [(1094.235 ± 574.495) / (702.781 ± 432.152), t= -7.169, P < 0.001], [(208.338 ± 210.448) / (177.55 ± 170.256), t = -1.306, P = 0.192], [(503.382 ± 303.498) / (304.075 ± 215.497), t = -7.168, P < 0.001], [(536.705 ± 344.218) / (358.034 ± 235.234), t = -5.802, P < 0.001], [(113.898 ± 101.48) / (61.768 ± 50.127), t = -6.831, P < 0.001], [(86.268 ± 89.081) / (47.92 ± 54.174), t = -3.367, P = 0.001], [(11.363 ± 9.834) / (6.628 ± 6.434), t = -3.622, P < 0.001], [(9.537 ± 10.12) / (5.346 ± 4.731), t = -3.646, P < 0.001], [(25.736 ± 27.013) / (20.78 ± 28.083), t =-1.037,P=0.301] (Figure 1).The above indexes in SLE infection group were lower than those in SLE non-infection groups. When lymphocyte subsets predict pulmonary infection in SLE, the AUC value of CD4 + count is the highest, and the cut-off is 387/ µ l(Table 1). The sensitivity and specificity of predicting SLE pulmonary infection were 75.8% and 38.6%(Figure 2).

Table 1. Predictive value of peripheral blood lymphocyte subsets in SLE complicated with respiratory tract infection

					Susceptibility	Specificity
Indicator	AUC	P value	Jordan index	cut-off	(%)	(%)
B	0.569	0.040	83.9950	0.183	0.421	0.238
CD4	0.714	<0.001	0.372	387	0.758	0.386
CD8	0.682	<0.001	0.325	405	0.726	0.401
CD4+ T /CD8+ T	0.569	0.041	0.000	0.785	0.537	0.370
NK	0.687	<0.001	0.309	82.5	0.768	0.460

Conclusion: The absolute number of these subsets in infected SLE patients is significantly lower than that in uninfected patients, which indicates that the low absolute number of these cells can be used as an indicator of high infection risk in SLE patients. CD4 + T lymphocytes and NK cells in patients with respiratory tract infection are significantly lower, and can play a certain predictive value for SLE respiratory tract infection to a certain extent.

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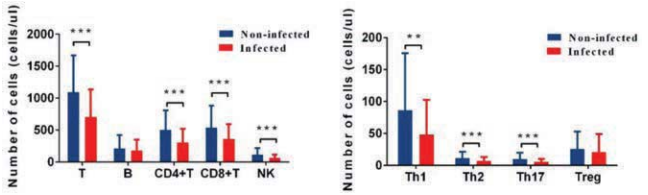

Figure 1 lymphocyte subsets in SLE patients with respiratory tract infection and non-infection

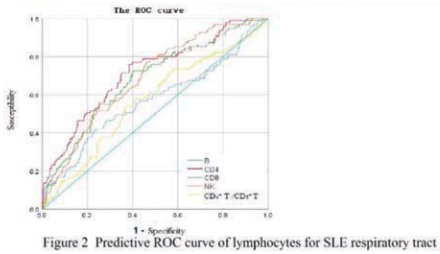

Figure 2 Predictive ROC curve of lymphocytes for SLE respiratory tract

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AB0501 COMPREHENSIVE ASSESSMENT OF PATIENTS WITH SUSPECTED SJÖGREN'S SYNDROME: 5-YEAR RESULTS OF A MULTIDISCIPLINARY SJÖGREN'S SYNDROME CLINIC

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Background: Primary Sjögren's syndrome (pSS) is a systemic rheumatic disease that affects several organ systems, most frequently the ocular, oral and musculoskeletal domains. Multidisciplinary care is thus crucial in the optimal management of SS patients.
Objectives: To report the clinical impact of a Multidisciplinary SS Clinic (MSSC) over a 5-year period.
Methods: We prospectively included patients assessed in the MSSC from September 2015 to October 2020. All patients had a full clinical evaluation, including disease-related questionnaires, specialized oral/ocular assessment, salivary gland biopsy (SGB) and ultrasound (SGUS), tear and salivary flow and ocular staining scores. We compared the results of patient-reported outcomes, comprehensive clinical assessments and specialized complementary exams in patients with pSS and other diagnoses.
Results: 445 patients (96% women, mean age 57±14 years) with sicca symptoms underwent complete multidisciplinary evaluation. Patients were most frequently referred from Rheumatology (91%), but also from Stomatology (5%), Ophthalmology (2%), Internal Medicine (1%) and other medical specialties (1%). Most patients were diagnosed with pSS (n=221; 50%), followed by non-Sjögren sicca syndrome (nSSS, n=134; 30%), secondary SS (sSS, n=60; 13%) and undifferentiated connective tissue disease (n=30; 7%). Positive sicca tests were present in 217/385 patients (56%): unstimulated whole salivary flow (UWSF) ≤0.1ml/min in 84/317 (27%); Schirmer's test ≤5mm/5min in 163/354 (46%); van Bijsterveld score ≥4 in 42/349 (12%); Ocular Staining Score (OSS) ≥5 in 36/343 (11%). Subjective complaints assessed by the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), the EULAR Sicca Score (ESS), the Profile of Fatigue and Discomfort - Sicca Symptoms Inventory (PROFAD-SSI), the Xerostomia Inventory (XI), and the Ocular Surface Disease Index (OSDI) did not differ between patients with pSS and other diagnoses. However, objective dryness measures such as UWSF (31vs20%, p=0.028), Schirmer's test (51vs40%, p=0.040) and OSS (14vs7%, p=0.048) were significantly associated with pSS. A positive SGB (focus score≥1) was seen in 48% of patients with a clinical diagnosis of pSS (p<0.001 vs. other diagnoses), with a mean focus score of 1.1±1.6. Instead, 94% of patients with nSSS had grade 0-1 biopsies. Mean SGUS scores (p=0.006) and the frequency of moderate/severe changes (p<0.001) were higher in pSS patients.
Conclusion: Multidisciplinary evaluation was crucial in the assessment of patients with similar sicca complaints and in the management of ocular/oral/systemic involvement. Objective measurements and specialized complementary exams greatly contribute to establishing or confirming the diagnosis of pSS.
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AB0502 STRESS AS POTENTIAL PATHOGENIC FACTOR IN PRIMARY SJOGREN'S SYNDROME.

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Background: Sjogren's Syndrome (SS) is a common autoimmunological disorder characterized by infiltration of exocrine glands by autoreactive immune cells that lead to the disease's two most common symptoms — dry eyes and a dry mouth, also known as sicca syndrome. The etiopathogenesis considers the coexistence of genetic predisposition and environmental factors, such as viral infections or sex hormones imbalance.
Objectives: The aim of the study was to determine whether major stressful life events are also risk factors for developing SS.
Methods: We performed a matched case-control study. Cases were patients with an established diagnosis of primary SS (pSS) within the previous five years. Controls were patients with osteoarthritis in whom systemic connective tissue disease has been ruled out. Data on major stressful life events were collected using the modified Holmes-Rahe stress scale. Data were collected for the period of the year before the disease onset.
Results: 100 patients were enrolled in the study (pSS group = 50, control group = 50), mean age was 55.8±10.4 years for pSS and 61.3±9.59 years for control group, in both groups 96 % of patients were female. pSS patients had significantly higher total score on Holmes-Rahe stress scale within the preceding 1 year before the onset of disease symptoms than control group (pSS group = 152±66.3 vs control group = 50±54.6; p<0.001). In pSS group 50 % of patients reported the subjective impression that the symptoms were caused by stress, while in control group it was 12 % (p<0.001). The most frequently mentioned life events in the pSS group were divorce or marital separation, death or change in health of family member and stress related to work.
Conclusion: Patients with pSS are significantly more likely to have had a major stressful life event within the preceding 1 year before the disease onset. The relationship between stress and the occurrence of many diseases and their exacerbations is well documented, especially within autoimmune diseases. Stress is a ubiquitous problem these days, therefore it is of fundamental importance to understand the biological mechanisms underlying its influence on the development of diseases. It is crucial to properly recognize the stressful situation in the patient's life and undertake appropriate interventions in order to prevent health consequences.
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AB0503 CLINICAL AND SEROLOGICAL DIFFERENCES BETWEEN CAUCASIAN AND LATIN AMERICAN SLE PATIENTS IN A MULTIETHNIC SPANISH SINGLE-CENTRE COHORT

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Background: Systemic lupus erythematosus (SLE) is a highly heterogeneous systemic autoimmune disease with multiorgan manifestations. There are

Table 1. Caucasian vs. Latin American SLE patients

	Caucasian	Latin American	p-value	Odds ratio (IC95%)
Serositis (%)	22.58 %	26.32 %	p=0.712	
Skin involvement (%)	65.59 %	52.63 %	p=0.261	
Arthritis (%)	24.32 %	52.63 %	p=0.008	2.39 (1.06-5.38)
AIHA (%)	0.00 %	5.26 %	p=0.002	28.69 (1.13-728.60)
Lymphopenia (%)	34.95 %	52.63 %	p=0.084	
Immune thrombocytopenia (%)	4.30 %	10.53 %	p=0.230	
Neurolupus (%)	20.97 %	10.53 %	p=0.278	
Glomerulonephritis (%)	18.82 %	42.11 %	p=0.018	2.51 (1.05-6.02)
ESRD (%)	3.76 %	15.79 %	p=0.020	4.20 (1.01-17.58)
Low C3 (%)	54.30 %	89.47 %	p=0.003	1.65 (0.82-3.31)
Low C4 (%)	49.46 %	84.21 %	p=0.004	1.70 (0.84-3.46)
Low vitamin D (%)	11.29 %	26.32 %	p=0.061	2.33 (0.79-6.89)
High DNAds (%)	61.29 %	63.16 %	p=0.404	
Anti-Sm (%)	12.37 %	36.84 %	p=0.004	2.98 (1.13-7.85)
Anti-Ro (%)	26.34 %	31.58 %	p=0.624	
Anti-RNP (%)	8.06 %	21.05 %	p=0.063	2.61 (0.79-8.66)
Anti-histones (%)	4.30 %	21.05 %	p=0.003	4.89 (1.35-17.77)
Antiphospholipid antibodies (%)	45.16 %	42.11 %	p=0.799	
Steroids (%)	88.71 %	94.74 %	p=0.419	
Antimalarials (%)	94.05 %	89.47 %	p=0.436	
SLEDAI≥6 (%)	34.41%	26.32%	p=0.477	
SDI ≥1 (%)	70.43 %	68.42 %	p=0.855	
LLDAS (%)	60.99 %	66.67 %	p=0.637	
DORIS (%)	48.09 %	38.89 %	p=0.456	
Death (%)	1.61 %	0.00 %	p=0.577	

disparities in its manifestations conditioned by sex, age of onset, and serological characteristics. The ethnic origin of the patients may be a conditioning factor for different organic manifestations, immunological markers, and outcomes.

Objectives: Our objective was to evaluate the clinical and serological differences in Caucasian vs. Latin American patients in a multiethnic Spanish single-center SLE cohort.

Methods: Single-centre retrospective observational study from a Spanish Lupus Cohort of adult SLE patients fulfilling the 2019 EULAR/ACR Classification Criteria. Only patients of Caucasian or Latin American origin were included.

Results: The study included 205 patients: 186 (90.7%) Caucasian and 19 (9.3%) Latin American. The mean age at diagnosis was 35.5 years. The female/male ratio was 9:1 in the Caucasian group and 19:1 in the Latin American group (ns). Serous and cutaneous involvement was similar between groups. The presence of arthralgia was also similar (ns) but there were statistically significant differences with the presence of arthritis (p=0.008). Severe hematologic manifestations were also more frequent in Latin American patients but only statistically significant for autoimmune hemolytic anemia (AIHA). Lupus nephritis and end-stage renal disease (ESRD) were two-fold and four-fold more common in Latin American patients. Among the immunological findings: hypocomplementemia, Anti-Sm, and anti-histones were differential markers between the two groups. Anti-RNP was also more frequent in the Latin American group (ns). Regarding treatments, there were no relevant differences between steroids and antimalarials. There were also no disparities in outcomes measured by activity (SLEDAI), cumulative damage (SDI), low activity (LLDAS), remission (DORIS), or death in our cohort.

Conclusion: In our multiethnic Spanish single-center cohort, SLE patients of Latin American origin had a higher frequency of arthritis, glomerulonephritis, and AIHA. They also presented a higher frequency of hypocomplementemia, anti-Sm, and anti-histones at the immunological level. However, these clinical and serological differences did not correlate with outcomes of activity, damage, remission, or mortality. Future studies are needed to assess the definitive effect of ethnicity on SLE.

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AB0504 DOES THE PRESENCE OF ANTIPHOSPHOLIPID ANTIBODIES AFFECT THE PROGRESSION OF RENAL FAILURE IN PATIENTS WITH LUPUS NEPHROPATHY? LONG-TERM OBSERVATION

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder with various clinical manifestations and diverse courses. Lupus nephropathy (LN) is observed in 30-50% of patients with SLE. 10% of patients with LN will develop renal failure (RF). Antiphospholipid antibodies (aPLs) are known for their pro-thrombotic action. According to the literature data, the presence of aPLs can lead to the development of thrombotic microangiopathy and may influence the progression of RF among patients with LN.

Objectives: The study aims to assess the influence of the presence of aPLs on the course and the progression of LN in long-term observation.

Methods: We conducted a retrospective analysis of the medical history of 34 patients (pts) with SLE and confirmed lupus nephropathy who are under the constant, long-term care of a rheumatology center. The kidney function (creatinine, estimated glomerular filtration rate; eGFR) was assessed at the beginning of the observation and after approximately 7-10 years.

The presence of antiphospholipid antibodies (anticardiolipin antibodies IgG or IgM, anti-beta-2-glycoprotein-I antibodies IgG or IgM, lupus anticoagulants) was taken into consideration. The progression of RF was compared between the pts groups with positive and negative aPLs test results.

Results: A total of 34 patients (median age at the end of follow-up was 50 years; range 24-82) were included. The majority of patients were female (88.2%). Of these patients, 8 (23.5%) had a positive tests for aPLs many times in their medical history. Considering the progression of RF among patients with positive aPLs, significant statistical differences were observed (p <0,01). Moreover, a statistically significant effect of aCL (p <0.03) and antibodies directed against anti-beta2 glycoprotein I (p <0.04) on the reduction of eGFR in the course of the disease was observed.

Conclusion: The presence of aPLs is associated with the risk of the deterioration of kidney function in patients with LN. It affects the decrease of eGFR and an increase of the concentration of creatinine in the blood.

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AB0505 RISK OF SYSTEMIC LUPUS ERYTHEMATOSUS FLARES ACCORDING TO THE POSITIVITY OF AUTOANTIBODIES

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by excessive production of pathogenic autoantibodies. A variety of autoantibodies can be detected in patients with SLE. Presence of particular autoantibody is known to be associated with specific manifestations of SLE: anti-double-stranded DNA antibody (anti-dsDNA Ab) with renal involvement and overall disease activity, anti-Sm Ab with renal involvement, anti-Ro Ab with cutaneous lupus and neonatal lupus, anti-La Ab with cutaneous lupus and neonatal lupus, and anti-U1RNP Ab with Raynaud's phenomenon and pulmonary hypertension. However, little is known about the association between positivity of each autoantibody and risk of SLE flare.

Objectives: We aimed to assess the risk of SLE flare according to the positivity of various autoantibodies.

Methods: A total of 228 patients with SLE who fulfilled the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE were included. SLE flare was defined as an increase of SLE disease activity index-2000 (SLEDAI-2K) of more than 4 points and/or hospitalization for SLE and/or augmentation of SLE therapy. The occurrence of flare was retrospectively reviewed from the date of SLE diagnosis to the date of last follow-up. Multivariable Cox regression analysis was conducted to estimate the hazard ratio (HR) and 95% confidence interval (CI) of SLE flare, according to the positivity of autoantibodies. Multivariable model was adjusted for sex, age at SLE diagnosis, positivity of other autoantibodies, SLEDAI-2K at diagnosis, use of immunosuppressants.

Results: Among the 228 patients, flare occurred in 179 (78.5 %) patients during 635.0 person-years of follow-up (incidence rate: 28.2/100 person-years). Of the 179 flares, 92 were severe flares (necessitating use of glucocorticoid dose > 20mg of prednisolone or equivalent, and/or addition of immunusuppressants), whereas 87 were mild-to-moderate flares (necessitating use of glucocorticoid dose < 20mg of prednisolone or equivalent, and no addition of immunosuppressants). In the multivariable Cox regression analysis, anti-dsDNA Ab positivity (adjusted HR 1.46, 95% CI 1.04–2.05, p = 0.031) and anti-Sm antibody positivity (adjusted HR 1.73, 95% CI 1.16–2.59, p = 0.007) were significantly associated with a higher risk of SLE flares.

Conclusion: Patients with SLE who are positive for anti-dsDNA Ab or anti-Sm Ab at diagnosis have a higher risk of SLE flare during the course of their disease. Careful monitoring of disease activity and prompt adjustment of therapy accordingly could be helpful in these patients.

REFERENCES: Not applicable.

Table 1. Risk of flares according to the positivity of each autoantibodies

	Univariable analysis		Multivariable analysis[a]	
	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Anti-dsDNA antibody positivity	1.47 (1.09–1.99)	0.011	1.46 (1.04–2.05)	0.031
Anti-Sm antibody positivity	1.52 (1.12–2.07)	0.008	1.73 (1.16–2.59)	0.007
Anti-Ro antibody positivity	1.19 (0.88–1.61)	0.252	1.04 (0.71–1.52)	0.836
Anti-La antibody positivity	1.24 (0.89–1.74)	0.211	1.26 (0.83–1.92)	0.278
Anti-U1RNP antibody positivity	1.19 (0.89–1.60)	0.250	0.83 (0.57–1.21)	0.332

[a]Adjusted for sex, age at diagnosis, positivity of other autoantibodies, SLEDAI-2K at diagnosis, use of immunosuppressants

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AB0506

PRELIMINARY STUDY ON IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) is a typical autoimmune disease, which can be classified into primary antiphospholipid syndrome (PAPS) and secondary antiphospholipid syndrome (SAPS) based on the presence or not of other autoimmune diseases. Disorders of peripheral blood lymphocyte and CD4+T cell subsets, especially Th17 and Treg cell subsets, may be involved in the pathogenesis of APS.

Objectives: To investigate the differences of peripheral blood lymphocyte and CD4+T cell subsets between patients with primary and secondary antiphospholipid syndrome and healthy controls, and to evaluate the correlation of antiphospholipid antibody titers and Th17/Treg values in PAPS and SAPS groups, as well as the correlation of cytokines and clinical characteristics in APS patients.

Methods: A total of 67 APS patients (12 PAPS patients, 55 SAPS patients) and 40 healthy controls were enrolled in this study. Retrospectively collected clinical and laboratory data of these patients. The absolute numbers of peripheral blood lymphocyte subsets and CD4+ T cell subsets were detected by flow cytometry, and serum cytokine levels were detected by flow cytometry bead array.

Results: Compared with healthy control group, the absolute values of T [689.26 vs. 1239.00, $p < 0.001$], B (104.69 vs. 177.50, $p < 0.001$), NK (98.97 vs. 300.00, $p < 0.001$) and CD4+T (330.16 vs. 628.50, $p < 0.001$) cells in SAPS group were decreased. While only the NK cells (151.30 vs. 300.00, $p = 0.002$) in the PAPS group were lower than that in healthy control group. However, the absolute values of T (1295.41 vs. 689.26, $p = 0.001$), B (184.44 vs. 104.69, $p = 0.012$), NK (151.30 vs. 98.97, $p = 0.023$) and CD4+T cells (698.34 vs. 330.16, $p = 0.002$) in PAPS group were significantly higher than those in SAPS group. For CD4+T cell subsets, PAPS patients and SAPS patients showed the same trend compared with healthy controls, showing increased Th1(111.50 vs. 23.47, p=0.002 and 71.43 vs. 23.47, p=0.001, respectively), decreased Th2(6.97vs.12.43, p=0.037 and 2.49 vs. 12.43, $p < 0.001$, respectively) and, more importantly, decreased Treg (18.77 vs. 29.53, p=0.031 and 12.01 vs. 29.53, $p < 0.001$, respectively), with increased Th17/Treg ratio (0.39 vs. 0.17, p=0.001 and 0.42 vs. 0.17, $p < 0.001$, respectively). Meanwhile, Th2(6.97 vs. 2.46, $p = 0.006$), Th17 (8.42 vs. 4.00, $p = 0.042$) and Treg (18.77 vs. 12.01, $p = 0.020$) cells in PAPS group were higher than those in SAPS group. As for the correlation study, we concluded that both aCL (r=0.6061, p=0.0405) and aβ2GPI (r=0.6900, p=0.0158) were positively correlated to Th17/Treg ratio in PAPS group. In addition, for APS patients, IL-2 (r=-0.420, p=0.010), IL-4 (r=-0.392, p=0.016), IL-10 (r=-0.331, p=-0.046), IL-17 (r=-0.479, p=0.006), and IFN-γ (r=-0.339, p=0.040) were negatively correlated with titers of aCL. And IL-6 is also associated with ESR (r=0.469, p=0.004) and CRP (r=0.670, $p < 0.001$).

Conclusion: Whether PAPS or SAPS patients, detection and balancing of lymphocyte and CD4+T subsets, especially Th17 and Treg subsets, may help correct immune disorders. Of course, the immune function of primary and secondary APS patients is not completely consistent, at least in terms of immune cells. Also, the role of cytokines in the pathogenesis of APS should not be ignored.

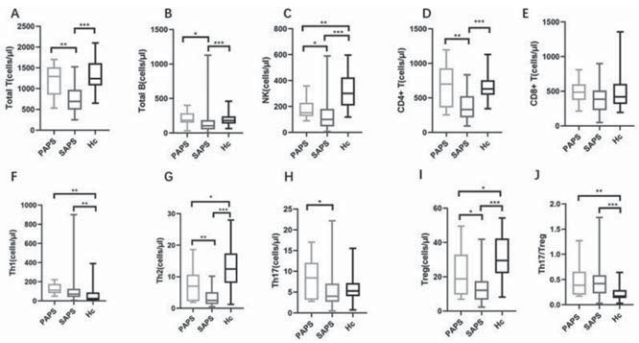

Figure 1. Comparison of lymphocyte absolute values and CD4+ T cell subsets in PAPS group, SAPS group and healthy control group.

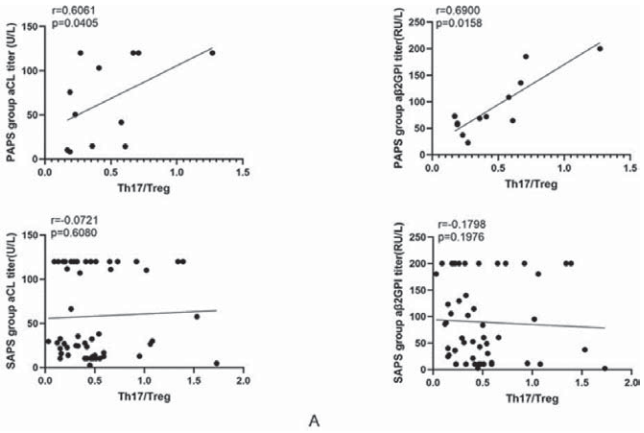

Figure 2. The correlation analysis between the value of Th17/Treg and the titer of aCL and aβ2GPI in PAPS group and SAPS group, respectively.

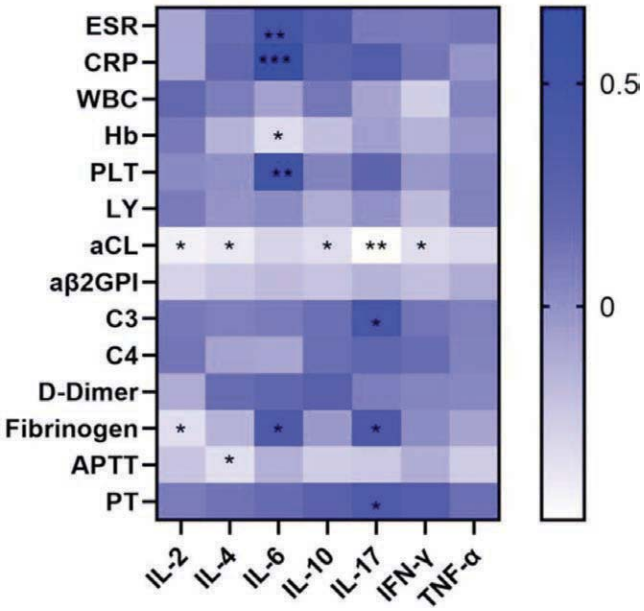

Figure 3. Heatmap of correlation of the serum cytokine levels of a variety of cytokines with clinical and laboratory characteristics of APS patients.

Disclosure of Interests: None declared
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AB0507

IMPACT OF CAFFEINE CONSUMPTION ON ENDOTHELIAL PROGENITOR CELLS SURVIVAL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Circulating endothelial progenitor cells (EPCs) are widely demonstrated biomarkers of endothelial function. Their frequency and function varied in systemic lupus erythematosus (SLE) patients, with a significant association with subclinical atherosclerosis[1]. Caffeine, one of the most widely consumed products in the world, seems to interact with multiple components of the immune system by acting as a non-specific phosphodiesterase inhibitor, and it seems to be able to activate autophagy[2-3]. In terms of cardiovascular disease (CVD), data from the literature showed a U-shaped association between habitual coffee intake and CVD[4]. In this view, Spyridopoulos et al. demonstrated a significant improvement in endothelial cells and EPCs migration after coffee consumption in coronary artery disease both in mouse models and in patients[5]. Finally, we demonstrated the impact of caffeine on SLE disease activity, in terms of SLEDAI2k values and

serum cytokine levels. Moreover, patients with a low caffeine intake seemed to have a more severe disease phenotype[6].

Objectives: The aim of this study was to evaluate the role of caffeine intake on endothelial function in SLE patients, by assessing its effect on number and function of EPCs both *ex vivo* in SLE patients and *in vitro* in healthy donors (HD) treated with SLE sera.

Methods: We performed a cross-sectional study enrolling consecutive SLE patients (revised 1997 ACR criteria), referring to the Sapienza Lupus Clinic. Patients with history of traditional CV risks factors were excluded. Caffeine intake was evaluated using a 7-day food frequency questionnaire. At the end of questionnaire filling circulating EPCs were detected by using a flow cytometry analysis defined as CD34+KDR+ cells. Subsequently, EPCs pooled from 6 HD were co-cultured with caffeine at 0.5 mM and 1 mM with and without SLE sera. After 7 days, we evaluated the cells morphology and the ability to form colonies. Moreover, we analyzed for the percentage of annexin V-positive (AV) apoptotic cells by flow cytometry analysis and for levels of autophagy and apoptotic markers LC3-II, p62 and Bcl2 by western blot.

Results: We enrolled 31 SLE patients (F:M 30:1, median age 43 years, IQR 18; median disease duration 144 months, IQR 180). The median intake of caffeine was 166 mg/day (IQR 194). We found a EPCs median percentage of 0.03% (IQR 0.04) observing a positive correlation between caffeine intake and EPCs percentage (p=0.03, r=0.4). Moving on *in vitro* experiments, after 7 days of cell cultures, HD EPCs treated with SLE sera and caffeine showed an improvement in morphology and in number of EPCs-CFU in comparison with those incubated with SLE sera without caffeine (p=0.0003). Moreover, the colonies treated with SLE sera were poorly organized in comparison with HD; the addition of caffeine restored the colony structure. After treated HD-EPCs with SLE sera we observed an increase in AV positive cells and p62 and LC3-II values and a reduction of Bcl2 values; the addition of caffeine was able to significantly reduce AV positive cells and p62 and LC3-II values and to significantly increased Bcl2 values, without any significant differences between caffeine 0.5 mM and 1 mM treatment (Figure 1A-D).

Conclusion: Our data demonstrated the ability of caffeine in increasing the number of circulating EPCs in SLE patients. Moreover, *in vitro* experiments seem to suggest a protective role of caffeine on EPCs survival and vitality through the promotion of autophagy and the inhibition of apoptosis.

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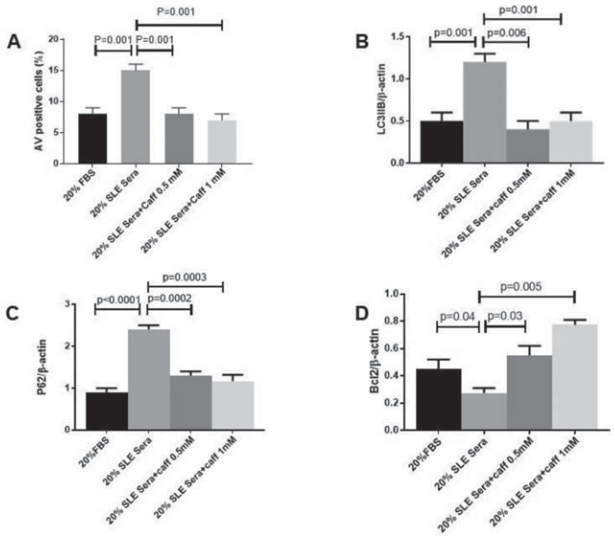
Figure 1. Percentage of AV (A), LC3II (B), p62 (C), Bcl2 (D) positive cells in HD-EPCs co-cultured with caffeine at 0.5 mM and 1 mM with and without SLE sera



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AB0508 RISK FACTORS FOR DEVELOPMENT OF ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) has been strongly linked to accelerated atherosclerosis and increased cardiovascular morbidity and mortality.

Objectives: The goal is to evaluate the traditional cardiovascular risk factors (TRF), intima-media wall thickness (IMT) and cardiovascular events (CVE) in SLE patients as compared to the same-nationality populations.

Methods: This cross-sectional study included 227pts (69% females, aged 35,6±0,7years) with SLE according to SLICC/ACR 2012 criteria, attending a routine visit at our Clinic between February 2018 and February 2020. Carotid plaques were assessed by ultrasound (US). Disease duration was 132,9±7,7months, SLEDAI 2K–9,4±0,5, SLICC/DI–1,89±0,13 score. Briefly, 90% had a history of joint involvement, 72%-hematological involvement, 70%-nephritis, 67%-serositis, 64%-skin lesions, 48%-neuropsychiatric involvement. Out of them 82%pts were on prednisone therapy at 17,3±1,0mg/day, 41%–on HCQ, 22%-immunosuppressants. Forty-one (18%) patients were diagnosed with SLE for the first time and were not receiving therapy at the time of enrollment. Concomitant antiphospholipid syndrome (APS) had 24% of SLEpts: 80% of SLE+APSpts had venous thrombosis, 43%-arterial, 56%-obstetric pathology. The control group (healthy donors) was matched by age and gender (n=99, 79% females, aged 36,2±0,8years).

Results: Patients with SLE compared to controls had a higher incidence of hypertension (52% and 21%,p<0,001), triglyceride concentrations (1,60±0,07 and 0,89±0,09mmol/l,p<0,001), lower levels of high-density lipoprotein (HDL) cholesterol (1,20±0,03 and 1,40±0,04mmol/l,p<0,01) and a higher number of TRF (2,40±0,08 and 2,01±0,13,p<0,05). Following carotid US assessment, atherosclerotic plaques (IMT≥1,5 mm) occurred in 24% of SLEpts versus 5% of controls,p<0,001. SLEpts had hazard ratio (HR) of carotid plaques of 5,22 (95%CI 1,95-13,99). Clinical manifestations of atherosclerosis (CVE) were reported in 19% of SLEpts vs 2% of controls, p<0,001. Out of them coronary artery disease (CAD) was in 13% vs 2%, p=0,002, myocardial infarction (MI)-in 5% vs 1%, p>0,05, stroke – 7% vs 1%, p>0,05. SLEpts had HR of CVE of 9,16 (95%CI 2,26-37,09), of CAD - 6,54 (95%CI 1,59-26,84). In SLEpts carotid plaques were more common than in controls at the age of 30-49 years, p<0,05; clinical manifestations of atherosclerosis occurred after 40 years: CAD - at 40-49 years, stroke - >50 years, p<0,05. No differences were found in other age groups. Patients were found to correlate CVE with age (r=0,384,p<0,001), male gender (r=0,361,p<0,001), hypertension (r=0,227,p<0,001), body mass index (BMI) (r=0,180,p=0,007), number of TRF (r=0,247,p<0,001), SLE duration (r=0,317,p=0,001), SLICC/DI (r=0,273,p<0,001), steroid use duration (r=0,255,p<0,001) and cumulative prednisolone dose (r=0,163,p<0,05).

Conclusion: The frequency of CVE (CAD, MI) and carotid plaques is higher in patients with SLE than in controls. In patients, CAD and carotid plaques were detected more frequently at the age of 30-49 years than in controls. Hypertension, hypertriglyceridemia and low HDL are the most common TRF in young SLE patients. In SLE, not only TRF and their number are associated with CVE, but also SLE duration, SLICC/DI, steroid use duration and cumulative dose.

Disclosure of Interests: None declared

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AB0509

AGREEMENT BETWEEN LABIAL BIOPSIES AND THE OMERACT GREY-SCALE ULTRASOUND SCORING SYSTEM FOR SALIVARY GLANDS IN A SINGLE-CENTER COHORT OF PATIENTS WITH SUSPECTED SJÖGREN'S SYNDROME

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Background: Ultrasound is a promising non-invasive tool in the evaluation of the salivary glands for parenchymal changes related to Sjögrens Syndrome (SS). The OMERACT Ultrasound Grey-scale (GS) Scoring System for SS has been shown to have good sensitivity and excellent specificity for fulfilling the SS classification criteria, when a GS ≥2 in at least 1 gland was considered indicative of SS (1), however others have suggested pathology in at least 2 glands is required (2). Systematic use of ultrasound might reduce the need for labial biopsies if US findings are in agreement with biopsies.
Objectives: To assess the agreement between labial biopsy results and salivary gland ultrasound findings in patients suspected of SS.
Methods: Patients referred to our department with a suspicion of SS from 2017-2021, scheduled for a diagnostic labial biopsy were recruited. All underwent GS ultrasound of the parotid and submandibular glands bilaterally prior to clinical exam, Schirmer's test, unstimulated salivary flow, blood samples including autoantibody analysis. Still images of the four glands were scored 0-3 using a previously developed ultrasound atlas (1) of the OMERACT ultrasound scoring system for SS (2,3). All biopsies were evaluated by a pathologist and focus score ≥1 was considered indicative of SS. Two different ultrasound scores for SS were tested: US-score ≥2 in at least 1 gland and US-score ≥2 in at least 2 glands. Descriptive statistics were used. In these analyses, we used labial biopsy as reference standard.
Results: 103 patients were included and 44 were clinically diagnosed with SS of which 42 (95%) fulfilled the 2016 ACR/EULAR classification criteria and 33 (75%) had positive labial biopsy. Demographics are shown in Table 1.

Table 1. Demographics

	All patients, n=103
Gender, n=females (%)	89 (86)
Age, mean ± SD	55 ± 15.9
Symptoms > 2 years, n=patients (%)	51 (50)
Symptoms < 2 years, ≥ 1 year, n= patients (%)	28 (27)
Symptoms < 1 year, n= patients (%)	24 (23)
Biopsy with focus score ≥ 1, n= patients (%)	32 (31)
US with ≥ 1 gland score ≥ 2, n=patients (%)	36 (35)
US with ≥2 glands score ≥ 2, n= patients (%)	31 (30)
SSA positive (%)	39 (38)
SSB positive (%)	9 (9)
ANA positive (%)	42 (41)
Sialometry positive (%)	67 (65)
Schirmer's test positive (%)	32 (31)

The sensitivity of ultrasound score ≥2 in at least 1 gland was 0.69 and the specificity 0.80. The positive predictive (PPV) and negative predictive values (NPV) were 0.61 and 0.85, respectively. Applying ultrasound score ≥2 in at least 2 glands did not improve specificity (0.83), PPV (0.61) or NPV (0.82) whereas sensitivity dropped to 0.59. The agreement between biopsies and ultrasound for SS is shown Figure 1.

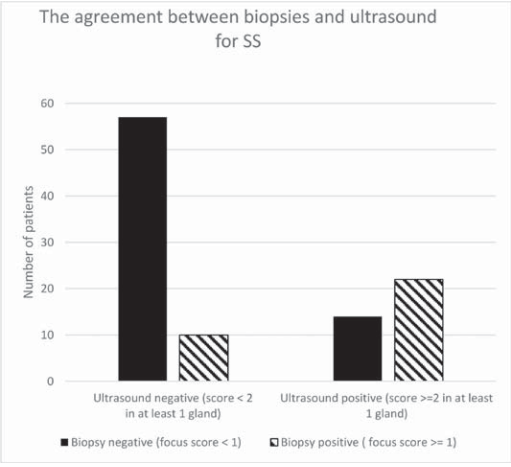

Figure 1

Conclusion: In patients with suspected SS, we found good agreement between US of salivary glands and subsequent labial biopsy. US of salivary glands seems useful in the diagnosis and classification of SS, but labial biopsies may still be needed in select cases.

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Disclosure of Interests: Viktoria Fana: None declared, Nanna Surlemont Schmidt: None declared, Uffe Møller Døhn: None declared, Simon Krabbe: None declared, Lene Terslev Speakers bureau: Novartis, Pfizer, UCB, Janssen and GE

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AB0510

IMMUNOPHENOTYPIC RECLASSIFICATION OF ANA ASSOCIATED AUTOIMMUNE DISEASE: PRELIMINARY ANALYSIS OF FLOW CYTOMETRIC DATA IN A MULTI-DISEASE COHORT.

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Background: The heterogeneity within the connective tissue disease patient cohort is not adequately reflected by current diagnostic labels(1,2). An immunophenotypic classification may be more appropriate for targeting therapy and basket therapeutic trials. DEFINITION is a multi-disease cohort (n=300) containing multiple clinical and immune datasets.
Objectives: To perform preliminary clustering analysis using the flow cytometric dataset from DEFINITION.
Methods: 142 patients with comprehensive flow cytometry data available were selected from the DEFINITION cohort. Highly sensitive flow cytometry was used to identify 7 B cell, T cell, NK cell and monocyte subsets and tetherin/SIGLEC1 expression on each subset.
ANA and ENA titres were assessed via the Bioplex assay. Demographic and clinical data was obtained from the DEFINITION cohort. Multiple classification algorithms were applied to flow cytometry data using R. Including K-means, hierachical, model-based and partitioning around medioids (PAM). Output clusters were retrospectively compared to their legacy diagnoses and serology.
Results: In the first 142 patients, PAM identified 3 clusters with memberships of 45, 49 and 48 patients respectively (Table 1).

Table 1. Key legacy diagnoses and ENA positivity for the identified clusters.

Diagnosis	Total	Cluster 1	Cluster 2	Cluster 3	P value
SLE	57	22	10	25	>0.01
UCTD	25	12	8	5	0.06
Sjogren's	15	2	4	9	0.06
Systemic sclerosis	7	0	5	2	0.07
MCTD	9	2	4	3	0.76
Myositis	8	3	3	2	0.86
Antibody positivity					
dsDNA	43	16	11	16	0.33
Ro60	45	12	7	26	>0.01
Ro52	36	10	7	19	0.01
La	18	2	2	14	>0.01
Sm	14	1	4	9	0.02
Sm_RNP	23	7	5	11	0.23
RNP	14	3	5	6	0.64
SCL-70	1	0	0	1	0.37
Jo-1	4	1	2	1	0.80
Centromere	5	1	4	0	0.08
Chromatin	29	10	8	11	0.68
Ribosomal P	4	1	1	2	0.78

Cluster 1 (**UCTD/CD3+ dominant**) was characterised by a higher proportion of UCTD patients (27%) and larger populations of CD3+ T cells and NK bright cells. Cluster 2 (**SSc dominant/Tetherin low**) was characterised by a higher population of systemic sclerosis (SSc) patients (10%) and a lower proportion of SLE patients (20%). High levels of classical and non-classical monocytes were demonstrated alongside low plasmablast populations and low SIGLEC1/Tetherin expression. Cluster 3 (**SLE/pSS high, Ro/Tetherin high**) included a higher proportion of SLE and primary Sjogren's syndrome (pSS) patients (52% and 19%). This cluster showed larger plasmablast numbers and higher SIGLEC1/Tetherin expression. Serologically this cluster had higher levels of Ro60, Ro52, Sm-RNP and La positivity. There were statistically significant differences in Ro60, Ro52, La, and Sm antibody positivity between the 3 clusters. Significant differences in CD19+CD27+ memory B cell tetherin expression and CD14+CD16- classical monocyte SIGLEC1 expression were observed (both

p < 0.05). A significant difference in SLE distribution was noted between the clusters (p < 0.01).

Conclusion: This preliminary study identified of a flow cytometric dataset identified 3 immunophenotypically distinct subgroups, each comprised of multiple legacy diagnoses within spectrum of ANA+ disease. Future work will evaluate other datasets within the full cohort with a view to conduct basket trials in the baskets defined.

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AB0511 SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY SCORE (SLE- DAS) VALIDATION IN ARGENTINIAN PATIENTS

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Background: Many activity indices have been developed for Systemic Lupus Erythematosus. However, they present important limitations due to the multi-organ compromise. The SLEDAI score and its different versions are widely used in daily practice and in clinical research. Diogo Jesus et al (2018) developed the SLE-DAS (Systemic Lupus Erythematosus Disease Activity Score), that include 17 items, 4 of them continuous. SLE-DAS assesses disease activity in the 28 previous days using an online calculator, with clinical characteristics non-evaluated by SLEDAI. It showed greater precision to measure disease activity, greater sensitivity to detect clinically significant changes and better performance to predict accumulated damage than SLEDAI. It has not yet been validated in Argentina.

Objectives: To determine the validity of the SLE-DAS score in a population of patients with SLE from Argentina.

Methods: A multicenter observational study was conducted. Outpatients and hospitalized patients with SLE from 9 Argentinian centers were included between July to August 2021. Socio-demographic and disease variables were studied and SLE activity was measured by physician's global assessment (PGA), SLEDAI 2K and SLE-DAS. The disease activity categories used for SLE-DAS were: remission ≤2.08; mild activity >2.08 to 7.10, moderate and severe activity >7.10. For SLEDAI 2K, remission was considered 0, mild activity 1 to 5, moderate 6 to 10, high 11 to 19, very high >20 points. To determine construct validity and criterion validity, SLEDAI 2K and PGA were used as the gold standard and correlation between scores was analyzed with the Pearson and Spearman correlation coefficient. Sensitivity and specificity of the points that define each of the activity levels were established by ROC curves to determine the discriminative capacity of SLE-DAS.

Results: A multicenter observational study was conducted. Outpatients and hospitalized patients with SLE from 9 Argentinian centers were included between July to August 2021. Socio-demographic and disease variables were studied and SLE activity was measured by physician's global assessment (PGA), SLEDAI 2K and SLE-DAS. The disease activity categories used for SLE-DAS were: remission ≤2.08; mild activity >2.08 to 7.10, moderate and severe activity >7.10. For SLEDAI 2K, remission was considered 0, mild activity 1 to 5, moderate 6 to 10, high 11 to 19, very high >20 points. To determine construct validity and criterion validity, SLEDAI 2K and PGA were used as the gold standard and correlation between scores was analyzed with the Pearson and Spearman correlation coefficient. Sensitivity and specificity of the points that define each of the activity levels were established by ROC curves to determine the discriminative capacity of SLE-DAS.

Conclusion: In this population of lupus patients from Argentina, the SLE-DAS allowed to discriminate between remission and disease activity, being a useful and practical tool.

Disclosure of Interests: None declared

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AB0512 COMPARATIONS OF SALIVARY GLAND ULTRASONOGRAPHY FINDINGS IN PRIMARY SJOGREN'S SYNDROME VS TYPE 2 DIABETES MELLITUS

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Background: Primary Sjogren syndrome (pSS) is a chronic autoimmune disease that mainly affects the exocrine glands [1]. Type 2 diabetes mellitus (DM) is also autoimmune disease involving not only the pancreas but also salivary glands. In both diseases, sicca symptoms due to different mechanisms were common [1, 2]. The use of salivary gland ultrasonography (SGUS) has become widespread in the diagnosis and follow-up of pSS [3, 4]. In DM, fewer US-based studies have shown abnormalities in the major salivary glands [2].

Objectives: This study aimed to compare the SGUS findings in patients with pSS and DM patients with sicca symptoms and to examine the relationship between these findings with clinical and laboratory parameters.

Methods: In this study, 32 patients with pSS and 28 DM patients with sicca symptoms (not meet ACR/EULAR pSS criteria) were included. Demographic data and patient characteristics were obtained from medical records. Physical examination was assessed by a rheumatologist. In all patients, bilateral parotid and submandibular gland US was performed by a blind another rheumatologist, using the Hocevar and the Outcome Measures in Rheumatology (OMERACT) scoring system. Clinic and ultrasonographic variables were compared between groups. The association between SGUS score and disease duration was analyzed by correlation analysis.

Results: Patients with pSS presented higher SGUS scores than patients with DM significantly (the Hocevar total score; 20.93(±9.65) vs 3.82(±3.71); p<0.05, the OMERACT total score; 5.96(±2.30) vs 2.07(±1.65); p<0.05, respectively). In patients with pSS, the submandibular gland scores higher than the parotid gland scores while in patients with DM showed higher parotid gland scores. Other demographic data is shown in Table 1. In pSS patients, the Hocevar and the OMERACT total SGUS scores were significantly correlated with disease duration (r=0.584, p<0.01 vs r=0.518, p<0.01, respectively). This correlation was not found in patients with DM (Figure 1).

Table 1. Demograpfic data and salivary gland ultrasonography scores in pSS and diabetic patients

	pSS patients(n=32)	DM patients with sicca(n=28)
Age, mean(±SD)	53.90(±9,70)	52.25(±7.65)
Disease duration, mean(±SD)	7.68(±4.01)	8.46(±6.31)
First symptom, n(%)		
Sicca	5(15.62%)	4(14.28%)
Non-sicca	23(71.87%)	20(71.42%)
Parotitis, n(%)	7(21.87%)	2(7.14%)[a]
Anti-Ro positivity, n(%)	22(68.75%)	0(0.0%)[a]
Unstimulated saliva flow rate ≤0.1 ml/m, n(%)	28(87.5%)	13(46.42%)[a]
Schirmer's test≤5 mm/5 m in at least one eye, n(%)	30(93.75%)	8(28.57%)[a]
The Hocevar total SGUS score, mean(±SD)	20.93(±9.65)	3.82(±3.71)[a]
right parotid	4.62(±2.73)	1.25(±1.17)[a]
left parotid	4.34(±2.57)	1.25(±1.08)[a]
right submandibular	6.06(±3.07)	0.67(±0.41)[a]
left submandibular	6.31(±2.95)	0.64(±0.43)[a]
The OMERACT total SGUS score,(mean(±SD)	5.96(±2.30)	2.07(±1.65)[a]
right parotid	1,28(±0.77)	0,71(±0.59)[a]
left parotid	1,21(±0.65)	0,78(±0.62)[a]
right submandibular	1,68(±0.82)	0,44(±0.25)[a]
left submandibular	1,78(±0.83)	0,47(±0.32)[a]

[a] *p<0.05*

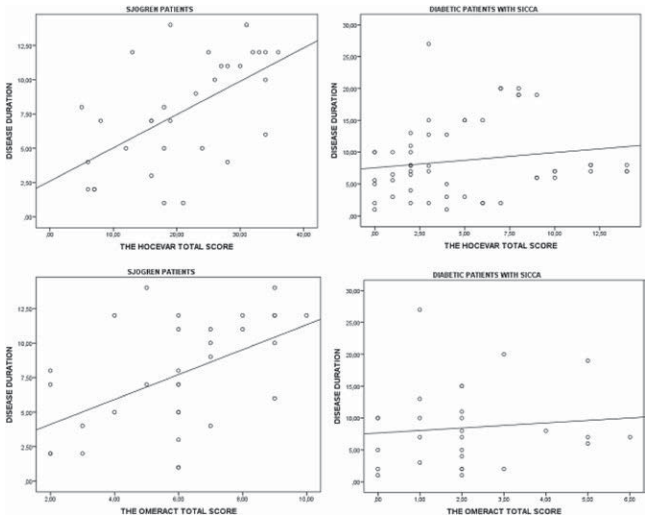

Figure 1. Correlation between SGUS scores and disease duratin in two groups

Conclusion: This study demonstrated that the major salivary gland involvement was more severe, submandibular gland dominant and correlated with disease duration in pSS. Contrarily, in patients with DM, it was mild compared to pSS, parotid dominant and uncorrelated with disease duration.

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AB0513 COVID-19 PREVENTION IN PATIENTS WITH MODERATE-TO-SEVERE LUPUS DURING THE PANDEMIC: RESULTS FROM THE BILAG-BIOLOGICS REGISTER (BILAG-BR)

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Background: There have been concerns over the susceptibility of SLE patients to severe COVID-19 illness since the beginning of the pandemic, and many patients were assigned 'clinically extremely vulnerable' according to the UK's shielding guidance issued in March 2020. Here we report on vaccination and shielding behaviours of a moderate-to-severe SLE cohort with high immunosuppressant burden.

Objectives: To review the shielding behaviours, and the safety and tolerability of COVID-19 vaccines in a real-world cohort of patients with moderate to severe SLE.

Methods: The British Isles Lupus Assessment Group Biologics Registry (BILAG-BR) is a national prospective registry of lupus patients from the UK (2010-21). Patients from the BILAG-BR were invited to complete a paper or online questionnaire which consisted of 17 questions to assess their self-reported shielding behaviour, vaccination status, and any adverse responses following COVID-19 vaccination. Questionnaires were completed between 9th Oct 2021 and 7th Jan 2022. Responses were linked with data collected in the BILAG-BR.

Results: Data were collected from the first 202/1268 patients (186 [92.1%] women) to respond, with a median age of 51 (IQR 38-61) years from 37 UK centres. The majority of patients were Caucasian (78.1%, 150/192). Previous therapy included rituximab (165, 81.7%), belimumab (33, 16.3%) and cyclophosphamide (54, 26.7%). In the past 12 months, over two thirds of patients (138, 68.3%) had received oral prednisolone (current dose median 5mg [IQR 5-8mg, range 2-40mg] daily), and almost a third had received parental steroids (60, 29.7%).

Shielding was reported in the first national lockdown (March-June 2020) by 93.6% (189/202) of patients, and of those in employment at the time, over half (58/100) were unable to work from home. The vast majority of patients complied with the UK government guidance (97.0%, 196/202) and did not socialise with other households indoors during this time period. Fifty-four percent of patients (109/202) reported attending a hospital or GP appointment during the first lockdown, and 24/202 (11.9%) reported regular appointments. During the first lockdown, 13/109 (11.9%) patients reported receiving rituximab infusions and 9/109 (8.3%) belimumab infusions.

Ninety-seven percent (196/202) had received at least 1 COVID-19 vaccination (Oxford AstraZeneca 95/146, 65.1%; Pfizer/ BioNTech 50/146, 34.3%). Approximately half of patients (54.2%, 104/192) reported an adverse reaction to the vaccine (both vaccine doses in 45 (23.9%) patients). The majority of these included lethargy/ flu-like symptoms (82, 78.8%) or local site reactions (32, 30.8%). Six (3.0%) patients reported a lupus flare and 3 (1.5%) patients reported a hospital attendance due to vaccine side effects.

Conclusion: In this cohort of moderate-to-severe SLE patients there was strong engagement with UK shielding guidance, however only half of patients attended a GP or hospital appointment during the earliest peak of the pandemic, highlighting disruptions to routine clinical care. There was high uptake of COVID-19 vaccination, which whilst generally well tolerated in this cohort, may be temporally associated with a flare, albeit in only a small number of patients. We recognise it may be difficult to distinguish between vaccine adverse events and lupus flares in patients with SLE, therefore this may be an overestimation. Of note, three patients reported a hospital attendance post-vaccination which warrants further investigation.

Acknowledgements: Submitted on behalf of the BILAG-biologics register

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AB0514 EXPRESSION OF IMMUNITY-RELATED GTPASE FAMILY M PROTEIN (IRGM) SNPS AMONG EGYPTIAN LUPUS PATIENTS

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Background: Of determinants that drives systemic lupus erythematosus (SLE) triggering and development is autophagy, Immunity-related GTPase family M protein (IRGM) was shown to be linked with immune -mediated diseases.

Objectives: Aim of the current study is to assess whether IRGM-autophagy gene polymorphism has a role in SLE susceptibility among Egyptian population and its relation to diverse clinical manifestations particularly lupus nephritis.

Methods: A cohort where total of 200 subjects (100SLE patients who fulfilling according to 2012 SLICC criteria and 100 controls) were enrolled. All patients underwent a thorough medical history and clinical examination. Lupus activity was evaluated by SLEDAI-2K score. Two single-nucleotide polymorphisms (SNPs) (rs10065172 & rs4958846) were genotyped. Genotypes and Alleles analysis were conducted to compare between cases and controls as well as on the stratification analysis of presence or absence of lupus nephritis

Results: Among selected SNPs of IRGM, no association was considered between both SNPs and SLE susceptibility. For rs10065172, the major expressed genotype was CC (61% and 71%) (Adj OR= 2.9, 95%= 0.545-15.5) followed by TC (34 % and 27%) (Adj OR= 1.985, 95%= 0.357-11.041) in cases and controls respectively. For rs 4958847 AA and AG were comparably expressed in case (43% &39%) and control (41%&43%) with (Adj OR= 1.073, 95%= 0.483-2.382) and (Adj OR= 1.24, 95%= 0.557- 2.763) respectively. Additionally, no relation between both SNPs with gender, lupus nephritis, disease activity, or disease duration.

Table 1. SNPs of rs 10065172, rs 4958847 genotypes and allele frequencies for cases and controls.

IRGM[a] 10065172	Case N (%)	Control N (%)	p value unadjusted OR		p value Adjusted OR		95th CI
TT	5(5)	2(2)	0.445	0.388	0.252		
TC	34(34)	27(27)	0.261	0.707	0.433	1.985	0.357-11.041
CC	61(61)	71(71)	0.161	1.525	0.211	2.9	0.545-15.5
IRGM4958847							
GG	18(18)	16(16)	0.849	0.93	0.835		
AG	39(39)	43(43)	0.565	1.1	0.598	1.24	0.557-2.763
AA	43(43)	41(41)	0.744	0.921	0.863	1.073	0.483-2.382

a IRGM: Immunity-related GTPase family M protein

Conclusion: IRGM SNPs (rs10065172 and rs4958846) is not associated with SLE susceptibility in this Egyptian cohort that necessitates further research to evaluate more the impact of IRGM autophagy-related gene on lupus.

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AB0515 CARDIOVASCULAR RISK FACTORS ASSESSMENT AND CONTROL IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an independent risk factor for cardiovascular disease (1). Studies reporting how cardiovascular risk factors (CVRF) are assessed in clinical practice are scarce.

Objectives: To describe the prevalence of CVRF and characterize the assessment and control of dyslipidaemia and high blood pressure (HBP) in SLE patients.

Methods: Cross-sectional study of all adult SLE patients (SLICC 2012 criteria) followed in a dedicated clinic in 2019. Patients with less than one year of follow-up or less than three in-person visits were excluded. LDL-cholesterol control was defined as desirable (<115mg/dL), ideal (<100mg/dL), and according to the SCORE risk (2) (low, <115mg/dL; moderate, <115mg/dL; high, <100mg/dL; very high, <70mg/dL). Blood pressure (BP) control was defined as desirable (systolic BP [SBP]/ diastolic BP [DBP]<140/90mmHg) and ideal (SBP/DBP<130/80mmHg). Data are shown as number (%) and median (interquartile range [IQR]) for categorical and continuous variables respectively. We used statistical tests as needed.

Results: Among 82 SLE patients followed in 2019, 65 met the inclusion criteria (89% female; median age, 52 years; median disease duration, 15 years; median follow-up, 8 years). The median SLEDAI-2K was 2 (0 - 4). Most patients were on hydroxychloroquine (88%), 43% were on steroids and 31% on other immunosuppressants. Dyslipidaemia was present in 62% of patients, followed by HBP (51%), obesity (n = 9,14%) and diabetes mellitus (n = 4, 6%). Once-a-year CVRF assessment in the five years prior to the study was low: lipid profile (LP) - 25% among all patients (33% of patients with dyslipidaemia); BP - 9% of all patients (15% of patients with HBP) (Table 1). In the study year, LP was assessed in 69% of all patients and in 85% (34/40) of patients with known dyslipidaemia, with a median LDL-cholesterol of 96 (128 – 74) mg/dL. Thirty-five (35/40, 88%) patients were under statins and the LP control was desirable, ideal and in line with the SCORE risk in 56%, 53% and 56% of patients, respectively. In the study year, BP was assessed in 32% of all patients and in 39% (13/33) of patients with known HBP, of whom 94% were under antihypertensive drugs. Among these patients (n=13), 69% had desirable and 23% ideal BP control. Steroid treatment regimen prevalence as well as disease activity as measured by the SLEDAI-2K was similar between patients who had LP and BP assessed and controlled compared to those who did not (all $p>0.05$).

Table 1. Prevalence of diagnosis, clinical recognition, drug prescription and control of HBP and dyslipidaemia.

		Total (n = 65)	Subgroup by disease
HBP, n (%)			**33 (51)**
Clinical assessment	2019	21 (32)	13 (39)
	Annual	6 (9)	5 (15)
Under treatment		31 (48)	31 (94)
Control *	Desirable	17 (81)	9 (69)
	Ideal	10 (48)	3 (23)
SBP / DBP, mmHg		130 (134–120) / 77 (80–70)	134 (141–130) / 80 (87–75)
Dyslipidaemia, n (%)			**40 (62)**
Clinical assessment	2019	45 (69)	34 (85)
	Annual	16 (25)	13 (33)
Under treatment		35 (54)	35 (88)
Control *	Desirable	29 (64)	19 (56)
	Ideal	24 (53)	18 (53)
	According to SCORE	28 (62)	19 (56)
LDL, mg/dL		97 (124–74)	96 (128–74)

*Calculated from the clinical assessment number for each group.

Conclusion: LP was the most frequently evaluated CVRF but only about one third of patients had their BP measured. Despite treatment, dyslipidaemia and BP control are suboptimal.

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AB0516 IN-HOSPITAL MORTALITY IN YOUNG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND ASSOCIATED CLINICAL FEATURES

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Background: Patients with systemic lupus erythematosus (SLE) are three times more likely to die from any cause as compared to patients without SLE.[1] This is largely driven by cardiovascular disease, malignancy, and an increased risk of infection. Alarmingly, recent studies have shown that younger patients with SLE are particularly vulnerable to all-cause mortality.[1] However, there is a paucity in knowledge about patient characteristics and specific etiologies of mortality in this population that needs to be described in order to implement strategies to improve outcomes in younger patients with SLE.

Objectives: To identify disease characteristics and etiologies of mortality in young patients with SLE that died while hospitalized.

Methods: A retrospective chart review of a multi-institutional publicly funded health system in Texas, USA was performed. Deceased patients aged 18-49 with a 2019 EULAR/ACR diagnosis of SLE were identified from 2012 to 2021. Patients with mixed connective tissue disease, missing records, or cardiac arrest in the emergency room that did not have a clear etiology of death were excluded. Data was extracted from the electronic medical records by two independent reviewers to determine the most likely cause of death. If there was any discrepancy between the reviewers, this would be resolved by a third-party reviewer. Baseline demographics, disease activity by the SLE disease activity index (SLEDAI), medications, and reasons for prednisone administration were collected.

Results: Twenty- six patients with SLE (age range 22 to 48) that died in the hospital were identified. The most common cause of death was infection (58%) followed by lupus activity (15%). Of those that died of infection, all but one was on a two-month average dose of prednisone ≥10mg. Furthermore, the majority of patients (71%) that were on prednisone doses of ≥10mg had not undergone a prednisone taper within two months (i.e. were on a consistent dose). This was because of either persistent disease activity or poor follow-up.

Conclusion: To our knowledge, this is the first study to describe characteristics of young patients with SLE that died during hospitalization. Our findings show that young patients with SLE primarily die from infection while on increased doses of corticosteroids that have not been tapered. Further research is warranted to determine association and causality of these findings with mortality. Practitioners should remain vigilant and continue to taper steroids as able as this may be a potential source of mortality in young patients with SLE.

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Table 1. Baseline characteristics of SLE patients that experienced in-hospital mortality.

	SLE Cases (n = 26)
Female, n (%)	20 (77)
Age, range in years	22 to 48
Race and Ethnicity, n (%)	
Black	6 (23)
Hispanic	19 (73)
Asian	1 (4)
Disease manifestations	
Lupus nephritis	18 (69)

End-stage renal disease	3 (12)
SLEDAI before admission (median, IQR)	7 (4 to 11)
SLEDAI on admission (median, IQR)	6 (2 to 11)
Medications	
Prednisone	25 (96)
Hydroxychloroquine	19 (73)
Mycophenolate	9 (35)
Cyclophosphamide	7 (27)
Belimumab	1 (4)
Cause of death	
Infection	15 (58)
Lupus activity	4 (15)
Cardiogenic shock	2 (8)
Cancer	2 (8)
Other	3 (12)

IQR = Interquartile range

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Disclosure of Interests: None declared
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AB0517 IMPAIRED INTESTINAL BARRIER FUNCTION IN SLE MEASURED BY SERUM ZONULIN

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Background: Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease characterized with the secretion of normal autoantibodies, which leads to the involvement of multiple organs. Several observations have showed that the breakdown of immune tolerance was involved in the pathogenesis of SLE, especially the imbalance of Th17/Treg [1], but the mechanism of the impaired immune tolerance is unknown yet. Numerous researches support that intestinal mucosal barrier is an upstream mechanism leading to impaired immune balance [2]. However, the relationship between intestinal mucosal barrier and SLE is little known.
Objectives: To measure the expression of serum zonulin to assess and compare the function of intestinal mucosal barrier in patients with SLE and healthy adults, and to explore the role of intestinal mucosal barrier in the pathogenesis and development of SLE.
Methods: 20 patients with SLE who hospitalized at the Second Hospital of Shanxi Medical University and 10 age and gender-matched healthy adults were enrolled in this study. We collected the blood sample of the patients and healthy controls to examine the function of intestinal mucosal barrier and the absolute number of Th17 and Treg cells. The level of serum zonulin was measured by ELISA to assess the function of intestinal mucosal barrier. The absolute number of Th17 cells and Treg cells was detected by flow cytometry. Disease activity indicators of patients with SLE were collected from laboratory including erythrocyte sedimentation rate (ESR, mm/h), complement 3(C3, g/l) and anti-dsDNA (IU/ml). Then we compared the expression of serum zonulin between the patients and healthy controls and analyzed the correlation of serum zonulin with Th17 cells, Treg cells and disease activity.
Results: The level of serum zonulin of SLE group were significantly higher than that of healthy control group ($p<0.05$). And the expression of serum zonulin was positively correlated with the level of ESR ($r=0.491$, $p=0.033$) and anti-dsDNA, but was negatively correlated with C3 ($r=-0.519$, $p=0.018$). And the expression of serum zonulin was not correlated with the absolute number of Th17 cells and Treg cells ($P>0.05$), but Th17 cells showed a trend of increasing with the increase of zonulin, while Treg cells showed a trend of decreasing with the increase of zonulin.
Conclusion: The results here showed that the level of serum zonulin,a marker of the intestinal mucosal barrier function,was up-regulated in patients with SLE, and the higher level of serum zonulin was positively correlated with the disease activity of SLE, which indicated that impaired intestinal mucosal barrier function in SLE played an important role in the development of the disease.

Table 1. A summary of baseline demographics of all enrolled patients and healthy controls

	HC(n=10)	SLE(n=20)	P value
Age(years)	44.1±18.8	42±12.384	P=0.76
Sex(male/female)	2/8	2/18	P=0.47

Results are expressed as the mean ± standard error. Normally distributed continuous variables were analyzed by the independent-samples Student's t-test.

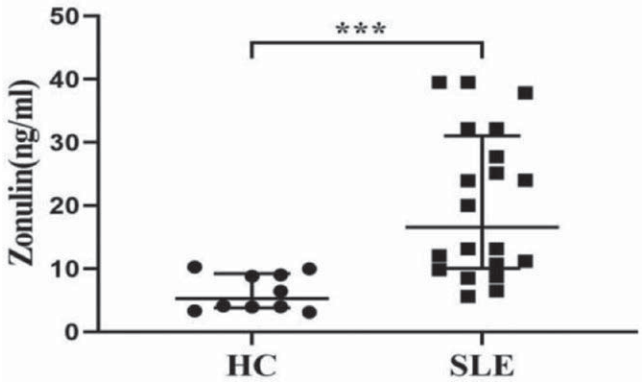

Figure 1. The difference of the expression of serum Zonulin in patients with SLE and healthy controls. Statistical analyses were performed by the Mann-Whitney U test.(***P<0.001)

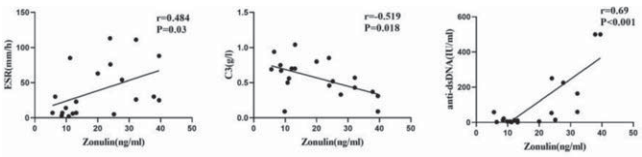

Figure 2. The correlation of disease activity with the level of serum Zonulin.Statistical analyses were performed by the Spearman correlation analysis.

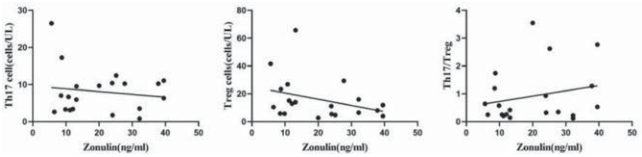

Figure 3. The correlation of disease activity with the level of serum Zonulin. Statistical analyses were performed by the Spearman correlation analysis.

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AB0518 OBESITY PARADOX IN SLE PATIENTS LOWER BMI TRADUCES TO HIGHER DISEASE ACTIVITY.

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Background: Cachexia plays an important role in rheumatoid arthritis (RA), due to its chronic inflammatory process characterized by decreased muscular mass with preservation or increase of fat that occurs in 1-13% of the RA population. A decreased BMI has a paradoxical relationship with disease activity, with an increase in disease activity and mortality (1). Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of nuclear autoantibodies that can form immune complexes and cause inflammation of multiple organs. Cardiovascular events and mortality are nearly twice as high in patients with SLE as in the general population. (2)
Objectives: To determine the relationship between BMI and disease activity in patients with SLE.
Methods: A cross-sectional, observational study was conducted in which a group of 58 patients with SLE were included and their level of disease activity was determined using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and BMI. Distribution was assessed with the Kolmogorov-Smirnov test. Descriptive analysis using measures of central tendency. Correlation between BMI and SLEDAI with Pearson's test. A p value <0.05 was considered statistically significant.

Results: The mean age of SLE patients was 35.4 ± 12.11 years, rest of demographic characteristics in Table 1. Pearson's test showed a correlation between BMI and disease activity (r= -0.304, p= 0.020) Image 1. Multivariate analysis found that a decrease in BMI is independently associated with an increase in disease activity assessed by SLEDAI (B= -0.411, 95% CI= -0.819- -0.003, p=0.049).

Table 1. Demographic characteristics

	SLE n=58
Female n (%)	54 (93.0)
Age, years, mean ± SD	35.4 ± 12.1
DM n (%)	2 (3.4)
AH n (%)	12 (20.6)
DLP n (%)	4 (6.8)
Obesity n (%)	4 (6.8)
SLEDAI mean ± SD	8.06 ± 6.4
ANA positivity n (%)	47 (81.0)
BMI mean ± SD	25.0 ± 4.9

DM; Diabetes Mellitus, AH; Arterial Hypertension, DLP; Dyslipidemia, SLEDAI; Systemic Lupus Erythematosus Disease Activity Index, ANA; Anti-Nuclear Antibodies, BMI; Body Mass Index.

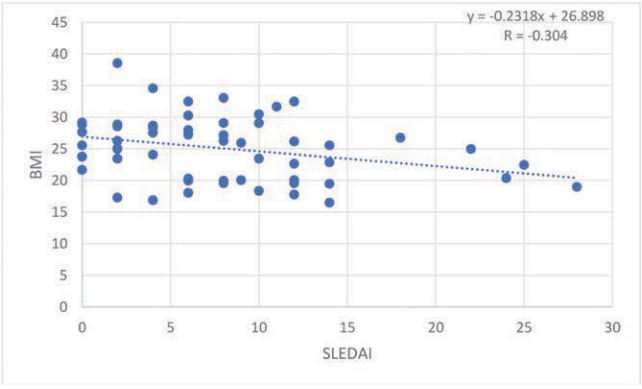

Figure 1. Correlation between BMI and SLEDAI.

Conclusion: The results show an inverse relationship between BMI and disease activity in patients with SLE. Further studies with a larger number of patients should be performed.

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AB0519 ELECTROCARDIOGRAPHIC ALTERATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND CONTROLS.

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with a high prevalence worldwide. Patients with SLE have a higher frequency of developing cardiovascular disease than the general population. There is little evidence on conduction abnormalities and arrhythmias in patients with SLE(1).
Objectives: The aim of this study is to compare electrocardiogram alterations in patients with SLE and a control group.
Methods: A cross-sectional, observational, comparative study was performed. A total of 70 patients with SLE, and 70 controls matched for age (± 5 years) and gender were recruited. An electrocardiogram was performed in all study subjects. Kolmogorov-Smirnov test was used for distribution analysis. Comparisons were performed by Chi-square test for qualitative variables and Student's t-test or Mann Whitney U test for quantitative variables. A p value <0.05 was considered statistically significant.
Results: In electrocardiogram findings, a significant difference was found in QRS segment duration (84.00 vs 89.50 ms, p=0.012), QT segment duration (397.01 vs 384.44 ms, p=0.016) and heart rate (68.60 vs 74.77, p=0.03) (Table 1).

Table 1. ECG comparison between SLE and controls.

Characteristics	Pacientes with SLE (n=70)	Controls (n=70)	*P*
Age (years), median (p25-p75)	35.0 (25.0-50.2)	35.0 (22.7-50.2)	NS
Female, n (%)	63 (90)	64 (91.4)	NS
QRS (ms), median (p25-p75)	89.50 (84.75-95.50)	84.00 (80.00-90.00)	0.012
QT (ms), mean ± SD	384.44 ± 30.84	397.01 ± 30.21	0.016
HR (Bpm), mean ± SD	74.77 ± 12.93	68.60 ± 11.25	0.003

ECG; electrocardiogram, SLE; systemic lupus erythematosus, NS; not significant, HR; heart rate, MS; milliseconds, BPM; beats per minute.

Conclusion: The results suggest that patients with SLE have increased QRS segment, increased heart rate and decreased QT segment duration, which may be related to disturbances of the conduction system.

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Disclosure of Interests: None declared
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AB0520 ASSOCIATION BETWEEN LEFT VENTRICULAR MASS INDEX AND BODY WEIGHT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Rheumatoid cachexia is a clinical spectrum of rheumatoid arthritis in which individuals present increased inflammatory activity, more aggressive joint destruction, and worse cardiovascular prognosis (1). Systemic lupus erythematosus (SLE) is a chronic, inflammatory, autoimmune disease in which there is a high cardiovascular mortality rate (2). Currently, the cachexia phenomenon in SLE patients has not been studied.
Objectives: To correlate body weight with left ventricular (LV) indexed mass in SLE patients.
Methods: This was a cross-sectional study that included a total of 34 patients aged ≥18 years with a diagnosis of SLE according to EULAR/ACR 2019 criteria. Patients with a personal pathological history of cardiovascular disease (myocardial infarction, stroke, or peripheral arterial disease) and pregnancy were excluded. Three certified cardiologists performed a transthoracic echocardiogram in each patient, assessing relative wall thickness, and indexed LV mass. The distribution was assessed with Kolmogorov-Smirnov. Correlations between weight and echocardiographic parameters with Spearman-rho coefficient. A value of p<0.05 was considered statistically significant.
Results: Most patients were female (94.1%), with a mean age of 33.29±9.91. Of the total patients 2 (5.88%) had Type 2 Diabetes Mellitus, 2 (5.88%) hypertension, 1 (2.94%) dyslipidemia, 3 (8.82%) obesity, and 6 (17.64%) smoking. Spearman-rho coefficient showed a significant negative correlation between LV indexed mass and body weight of SLE patients (rho=-0.411, *p*=0.016) (Figure 1).

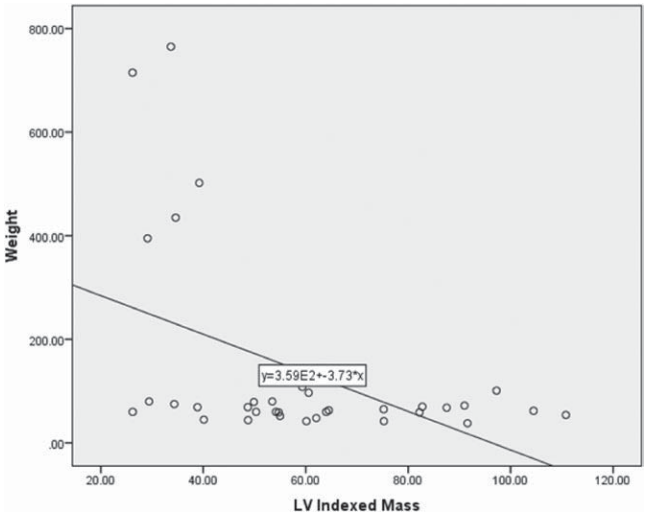

Figure 1. Spearman rho correlation between weight and LV indexed mass.

Conclusion: There is a negative correlation between body weight and LV indexed mass in SLE patients, this suggests that a lower body weight may be related to higher LV mass, which may result in LV hypertrophy and increased cardiovascular morbidity and mortality.

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AB0521 PERICARDITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: CHARACTERISTICS, MANAGEMENT, EVOLUTION AND PREDICTIVE FACTORS FOR RELAPSE. A MONOCENTRIC RETROSPECTIVE STUDY.

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Background: Pericarditis is frequent in Systemic Lupus Erythematosus (SLE) and usually benign. Dedicated studies are scarce. However, recurrences can lead to repeated steroid prescriptions and further immunosuppression. The best management, including the potential benefit of colchicine, remains to be determined.

Objectives: The aim of this study was to describe management, evolution over time and risk factor for relapse in SLE pericarditis in our University Hospital Center.

Methods: Cases were retrospectively collected among hospital discharge data (coding code "SLE" and "pericarditis"), from January 1997 to December 2019. All SLE cases met the ACR/EULAR 2019 classification criteria. Pericarditis cases met ESC 2015 diagnosis criteria. Patients with conditions other than lupus known to cause pericarditis were excluded as well as patients with myocarditis. A minimal follow-up of one year after pericarditis diagnosis was mandatory. Relapse-free survival was described using an actuarial survival model.

Results: Among 103 patients identified in the database, 29 patients (women: n=25, mean age 30 +/- 13 years) were included. Median follow-up was 7 years [range: 1-22].

Description of first episodes: 31% (n= 9) were inaugural of SLE; otherwise, median time elapsed since SLE diagnosis was 65 months [1.7-400]. Fifty-five percent (n=16) of first episodes occurred during a multi-systemic lupus flare. Median SLEDAI-2K was 9 [range: 4-30l. Clinical symptoms and signs were typical chest pain (93%, n=27), dyspnea (55%, n=16); pericardial rub (31%, n=9), fever (38%, n=11). EKG was abnormal in 59% of the cases (n= 17). When present, 79% of effusions (n=17/22) were circumferential, 82% (n= 18/22) were mild to moderate (<20mm), and 25% (n=7) were dry pericarditis. Two Cardiovascular Magnetic Resonance imaging were performed and were pathological.

Biological data showed always high CRP levels (65mg [range: 7-460]), high-titer anti-DNA (79%, n=19) but few patients had low complement levels (C3 21% (n=4/19), C4 26%(n=5/19)).

Prescribed drugs were non-steroidal anti-inflammatory drugs/acetylsalicylic acid (NSAIDs/ASA) (41%, n=12), corticosteroids (66%, n=19; mean daily prednisone dose: 57.2mg +/- 13.9), colchicine 0.5 to 1mg/day (41%; n=12). There was a significant difference in SLEDAI-2K values at pericarditis onset between those treated with NSAIDs/ASA (7.5, [range: 0-16]) and those not (12, [range: 4-30]), (p<0.05). Only 41% (n=5) of colchicine prescriptions lasted at least 3 months; they were associated with a lower SLEDAI-2K at pericarditis onset compared to pericarditis not or insufficiently treated with colchicine (respectively, 7[range: 4-9] and 11[range: 4-30], p=0.04). Immunosuppressive drugs were prescribed in 17% (n=5) of the patients, always due to extra-pericardial involvements.

Recurrences were frequent (55%, 16 patients out of 29) and multiple (1 to 6, average 3 ± 1.26). Short and long-term relapse-free survival tended to be better in patients exposed to at least 3 months of colchicine (100% vs 75% at 1 year, p=0.09) (Figure 1). There was no statistical difference (p=0.25) in terms of short-term relapse-free survival in patients treated with NDAIDs/ASA compared to those who were not. Corticosteroid prescription and previous antimalarial treatment were not associated with a poorer or better outcome during the year following remission (p=0.78). No patient has progressed to constriction.

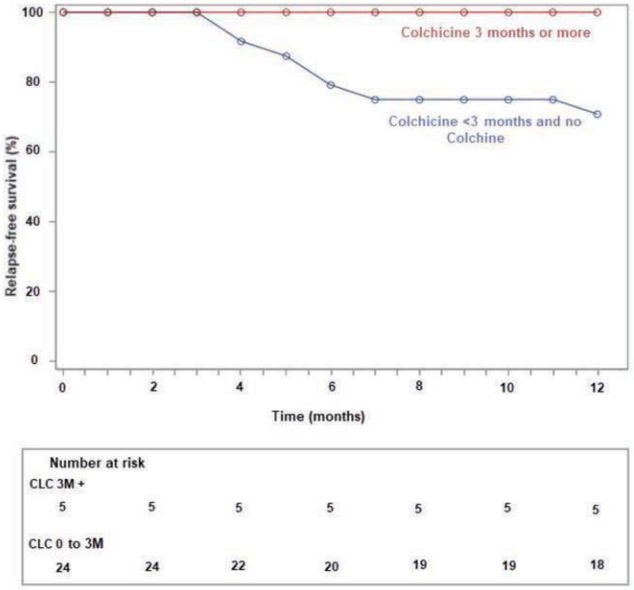

Figure 1. Relapse-free survival at 12 months according to colchicine prescription

Conclusion: Our conclusions are limited due to the small number of patients and lack of multivariate analysis.

Further studies are necessary to confirm the potential benefit of colchicine to prevent incessant pericarditis or relapses in this population.

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AB0522 EARLY DAMAGE AS MEASURED BY THE DAMAGE INDEX FOR ANTIPHOSPHOLIPID SYNDROME (DIAPS) IS NOT A PREDICTOR OF MORTALITY IN THROMBOTIC ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) patients experience damage accrual (1) but correlation with mortality is rarely reported. In systemic lupus erythematosus (SLE), early damage accrued in the first year of disease is a predictor of mortality (2).

Objectives: To determine whether damage accrued within the first year after APS onset as measured by the Damage Index for APS (DIAPS) predicts mortality.

Methods: Single-centre retrospective analysis of thrombotic APS patients (2006 Sydney criteria). The disease onset was determined as the time the first thrombotic event related to APS was diagnosed. Annual DIAPS assessments were determined for each patient. Early damage was considered to be a score ≥1 at the initial assessment (six months). DIAPS is shown as median (interquartile range [IQR]). Survival was analysed by the Kaplan-Meier method. Cox regression analysis was performed to investigate predictors of mortality.

Results: A total of 197 patients (71.1% female; 65.9% primary APS; 72.4% Caucasian) with a median age at APS onset of 40 years (IQR 51 - 28) were followed for up to 43 years (median 10 years). Cumulative damage developed

in 143 (73.6%) patients with a median DIAPS of 1 (IQR 2 - 0) at the last visit. Early damage was present in 69 (35.0%) patients. Patients with early damage had similar sex distribution (p=0.733), age at disease onset (p=0.526) and median time of follow-up (p=0.181) comparing to those without early damage. Secondary APS (SAPS) (odds ratio [OR] 1.89, 95% CI 1.03 - 3.48, p=0.041) and having a first arterial event (OR 7.24, 95% CI 3.74 - 14.03, p<0.001) were associated with early damage. Twenty-three patients (11.7%) died. SAPS (p=0.009), male sex (p=0.008) and age at onset ≥40years (p=0.001) were risk factors for death (Table 1). Early damage was not associated with death (hazard ratio [HR] 1.65, 95% CI 0.73 - 3.78, p=0.231; Figure 1: survival curve) even after adjusting individually for APS category (secondary, p=0.446), sex (male, p=0.374), age at onset ≥40years (p=0.115) and type of event (arterial, p=0.555).

Table 1. Predictors of mortality.

	Crude analysis		Adjusted analysis†	
	HR (95% CI)	*p-value*	HR (95% CI)	*p-value*
Male sex	3.14 (1.35 – 7.33)	**0.008**	1.46 (0.63 – 3.36)	0.374
Age at APS onset ≥ 40 years	5.34 (1.9 – 14.53)	**0.001**	1.95 (0.85 – 4.50)	0.115
Caucasian	0.95 (0.35 – 2.57)	0.918	1.61 (0.70 – 3.70)	0.257
Secondary APS	3.07 (1.32 – 7.12)	**0.009**	1.38 (0.59 – 3.20)	0.446
First event (arterial)	1.85 (0.79 – 4.27)	0.151	1.32 (0.53 – 3.32)	0.555
Early damage	1.65 (0.73 – 3.78,	0.231	-	-

† In this column, we present the *Early Damage* hazard ratio and 95% confidence intervals for death adjusted for the variable in each row. Statistically significant values are presented in bold. APS, antiphospholipid syndrome; CI, confidence interval; DIAPS, Damage Index for Antiphospholipid Syndrome; HR, hazard ratio.

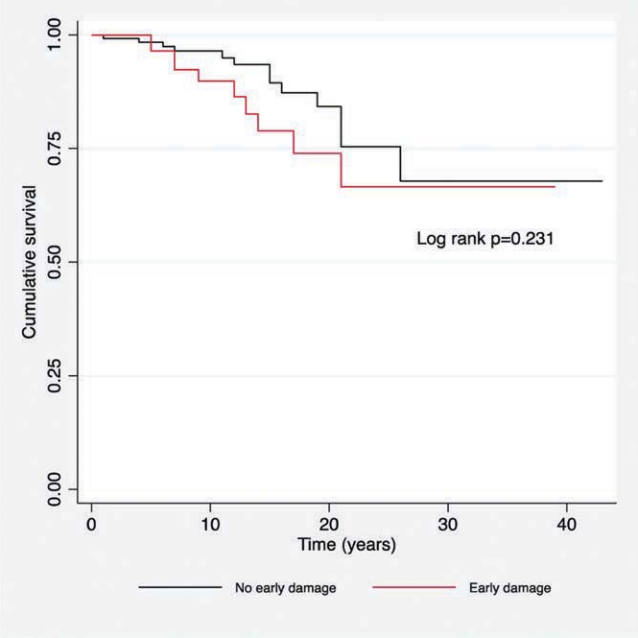

Figure 1. Survival probability in patients with and without early damage.

Conclusion: Unlike SLE, early damage accrual accessed by DIAPS is not a predictor of mortality regardless of the nature of the thrombotic event, gender, APS category and age at APS onset.

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AB0523 THE ENTEROTYPES OF THE GUT MICROBIOTA IN CHINESE POPULATION WITH AUTOIMMUNE DISEASE

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Background: An increasing number of autoimmune disorders (AD) have been associated with microbial dysbiosis[1, 2]. However, this dysbiosis is difficult to characterize for individual patients owing to the high heterogeneity of the gut microbiota. Thus, researchers must find an accurate method of characterizing the AD gut microbiota that is meaningful to clinical diagnosis.

Objectives: The aim of this study was to investigate the enterotype characters of intestinal flora in AD and their associations with peripheral lymphocyte subpopulations and cytokines.

Methods: A total of 339 AD patients and 339 age- and sex- matched healthy controls (HCs) were enrolled in this study. Mathematical modeling using Dirichlet multinomial mixtures (DMM) was applied to describe the variability in the microbiome data and cluster samples into enterotypes. The peripheral lymphocyte subsets were detected by flow cytometry and the cytokines were assessed by ELISA. Differential abundance analysis was carried out the STAMP software. R (version 4.1.0) was used for comparative statistics, and spearman's correlation analysis was used to assess the correlations between the relative abundances of bacterial genera and clinical variables.

Results: Laplace approximation of DMM suggested gut microbiota of AD patients and HCs both can be divided into two distinct enterotypes (Figure 1 A-B), and AD E1 and HC E1 were primarily dominated by Prevotella while AD E2 and HC E2 by Bacteroides. Interestingly, the Prevotella-enriched enterotype (AD E1 and HC E1) had a higher alpha diversity than The Bacteroides-enriched enterotype (AD E2 and HC E2). Patients with AD always had a lower richness and diversity compared with those of HCs in each enterotype (p< 0.001), suggesting gut microbiome was markedly less diverse in composition in AD. Bray curtis distance-based beta-diversity were also different (P<0.001, ANOSIM.R =0.23, Figure 1 C-H). Significant differences in gut microbiota composition at the genus level between AD patients and HCs were found using the STAMP software in each enterotype. Compared with HCs, 37 species in AD E1 patients and 40 species in AD E2 patients of flora were discovered to be distinctly different. In the co-upregulated flora of both enterotypes, Lactobacillus was inversely associated with a variety of lymphocytes such as T, CD4+T, NK, Th2, Th17, Treg cells(P<0.05), and positive correlation with IL-10 and IFN-γ(P<0.05,Figure 1 I). However, in the co-downregulated floras Coprococcus had a positive correlation with B, NK and Treg cells, and anaerostipes had a negativate corrleation with IL-2 and IL-4(P<0.05,Figure 1 J).

Conclusion: There were both two enterotypes in patients and HCs with autoimmune disease, E2 exhibited a loss of Prevotella but a growth of Bacteroides, while E1 presented the opposite results, which were closely correlated with peripheral lymphocyte subsets and cytokines.

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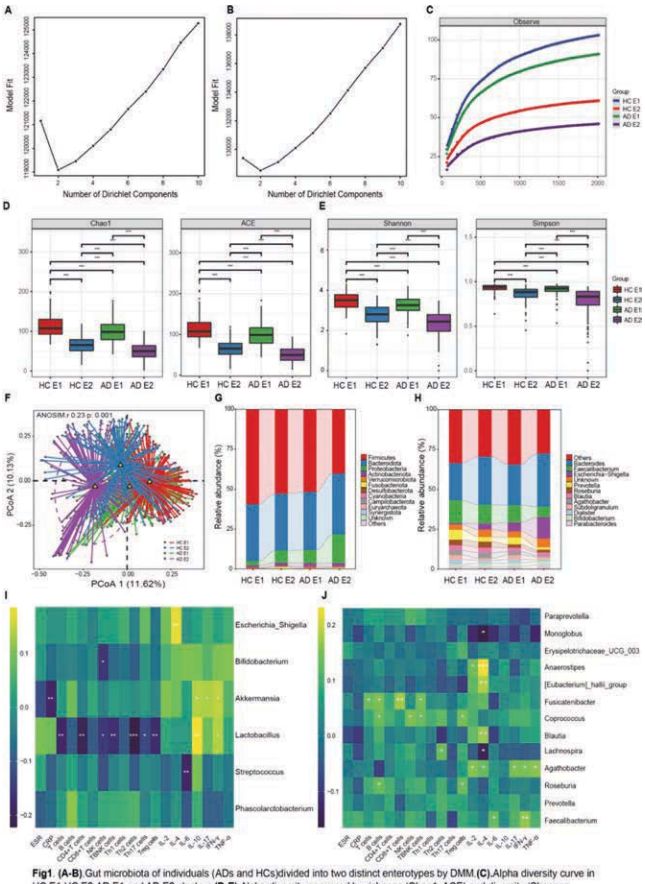

Fig1. (A-B) Gut microbiota of individuals (ADs and HCs)divided into two distinct enterotypes by DMM.**(C)**.Alpha diversity curve in HC E1,HC E2,AD E1 and AD E2 clusters.**(D-E)** Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson), Median estimates compared across cohorts. **(F)** Principal component analysis (PCoA) plot generated from the Bray-Curtis distances. **(G-H)** Microbiota composition based on relative abundance at the phylum and genus levels.**(I-J)** Correlation analysis of these differential genus and lymphocyte subsets and cytokines between two groups using Spearman's correlation analysis.The correlation effect is indicated by a color gradient from green (positive correlation) to purple (negative correlation). *p<0.05. **p<0.01. ***p<0.001.

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AB0524 RELATIONSHIP BETWEEN SERUM URIC ACID, CARDIOVASCULAR RISK AND INFLAMMATORY STATUS IN PRIMARY SJÖGREN'S SYNDROME

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Background: An unhealthy diet, with or without impaired renal urate excretion, is the most frequent cause of hyperuricemia. Despite its pivotal role in the pathogenesis of gout, the clinical relevance of serum uric acid (SUA) levels goes well beyond the simple association with gout and/or nephrolithiasis. Several studies pointed to hyperuricemia as cardiovascular (CV) risk factor in the general population therefore, the 2018 guidelines of the European Society of Cardiology and the European Society of Hypertension included the assessment of uricemia among the screening tests to be performed in hypertensive patients. Furthermore, in view of the association between hyperuricemia and mortality (both CV and all-cause) and CV events, it is conceivable that cardiovascular damage begins with much lower levels of uricemia. In this context, the first results of the URRAH (Uric Acid Right for Heart Health) study identified a uricemia threshold value of 4.7 mg/dL for all-cause mortality and 5.6 mg/dL for CV mortality[1].
Objectives: Since patients with primary Sjögren's syndrome (pSS) have a higher risk of CV events compared to the general population, we aimed to explore how uricemia correlates with other CV risk factors and previous CV events in patients with pSS and without gout.
Methods: A cross sectional study was conducted recruiting consecutive patients with pSS without history of gout. SUA was measured upon recruitment alongside the assessment of disease activity (EULAR Sjögren's syndrome disease activity index, ESSDAI and ClinESSDAI), patient reported symptoms (EULAR Sjögren's syndrome patient reported symptoms, ESSPRI), CV risk factors including hypertension and diabetes among others, and previous CV events. Dietary habits were also explored with various food frequency questionnaires.
Results: One hundred and three patients with pSS were enrolled. SUA levels ranged between 2.9 and 6.8 mg/dl and, according to the cut-off values of the URRAH study, 16 (16%) patients had SUA levels >4.7 mg/dL while 5 (5%) had SUA levels >5.6 mg/dL. Patients with SUA levels >4.7 mg/dL were more likely males (20% vs 3%) with a higher number of CV risk factors compared to patients with SUA levels <4.7mg/dL. No differences were observed regarding dietary habits across groups. Disease activity assessed with both ESSDAI and ClinESSDAI was significantly higher in patients with SUA levels >4.7 mg/dL compared to patients with SUA levels <4.7 (9.3 vs 6.3 p= 0.04 and 9.0 vs 6.0 p=0.03). Conversely, patient reported symptoms (total ESSPRI and individual VAS scales for total dryness, xerostomia, xerophtalmia, pain and fatigue) did not differ across groups. Logistic regression analysis confirmed the association of SUA values >4.7 mg/dL and a higher number of CV risk factors (OR 2.8; 95% CI=1.2-6.5; p=0.016).
Conclusion: Accumulating evidence highlights the emerging role of hyperuricemia as an independent CV risk factor, but no data are available in pSS patients. This is the first study demonstrating that SUA levels >4.7 mg/dL correlate with both a higher number of CV risk factors and a higher disease activity in pSS patients. Large interventional studies are needed to clarify the possible benefits of urate-lowering treatments in pSS patients.
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Disclosure of Interests: None declared
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AB0525 MODELS OF SYSTEMIC LUPUS ERYTHEMATOSUS ACTIVITY (A RESTROSPECTIVE-PROSPECTIVE STUDY)

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous chronic autoimmune rheumatic disease with a wide range of clinical manifestations, characterized by impaired activation of cellular and humoral links of immunity, uncontrolled hyperproduction of autoantibodies of a wide spectrum to nuclear antigens and the formation of immune complexes that cause immuno-inflammatory damage to tissues and organs. This disease is characterized by periods of exacerbation and remission, over time, the activity of SLE may change, mainly in response to therapy. Despite this, patients can be classified according to the current or currently prevailing activity model.
Objectives: To study the activity patterns of patients with SLE.
Methods: The retrospective-prospective study was conducted from 2019 to 2021 based on the study of the history of the disease and annual visits of patients with an assessment of the activity of SLE by SLE Disease Activity Index-2000 (SLEDAI-2K). Depending on the level of SLEDAI-2k flare index, the models of SLE activity, the number of exacerbations during the observation period and the period of the disease, as well as the predominance of organs and systems involved in the process were analyzed. The study included 183 patients with SLE (163 women and 20 men). The average age was 37.5±12.8 y.o. The duration of the disease was Me=9.9 [2.0; 16.0] years.
Results: The clinical and immunological manifestations of SLE were evaluated in the study. The average number of exacerbations of SLE during the period of the disease was 2.9±1.9. The average number of exacerbations during the observation period was 1.1±0.78. The most frequent exacerbation was manifested by a lesion of the musculoskeletal system – 29,5% (54 patients), the skin-mucous system – 21,8% (40 patients) and lupus-nephritis – 21,8% (40 patients). The predominant activity model was relapsing-remitting disease (RRD) – 43,16% (79

patients), then chronic active disease (CAD) - 38,15% (70 patients), and minimal disease activity (MDA) – 7,1% (12 patients). Clinical quiescent disease (CQD) had 21 patients (11,47%). Models of SLE activity and involvement of systems and organs are presented in Table 1.

Table 1. ***Models of SLE activity and involvement of systems and organs in patients with SLE.***

Models of SLE activity / Damage to systems and organs	RRD	CAD	MDA	CQD
Skin-mucosal system	47,5% (19 patients)	37,5% (15 patients)	-	6% (15 patients)
Musculoskeletal system	31,5% (17 patients)	42,6% (23 patients)	11,1% (6 patients)	14,8% (8 patients)
Lupus- nephritis	52,5% (21 patients)	37,5% (15 patients)	-	10% (4 patients)
Polyserosities	42,8% (3 patients)	57,2% (4 patients)	-	-
Nervous system	37,5% (3 patients)	50% (4 patients)	-	12,5% (1 patient)
Hematological disorders	50% (10 patients)	40% (8 patients)	5% (1 patient)	5% (1 patient)
Immunological disorders	42,8% (6 patients)	7,1% (1 patient)	42,8% (6 patients)	7,1% (1 patient)

23 patients with involvement of the skin-mucosal system had 1 exacerbation of SLE in 3 years of the study. 23 patients with involvement of the musculoskeletal system had 1 exacerbation and 19 patients had 2 exacerbation of the disease in observation period. Exacerbation of lupus nephritis 1 time during the follow-up period was noted in 26 patients, 2 times - in 8 patients.

Conclusion: The most frequent model of SLE activity is RRD, which characterizes periods of exacerbation and remission. The most frequent clinical manifestations of exacerbation of SLE are lesions of the skin-mucous and musculoskeletal systems, as well as lupus nephritis.

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AB0526 ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS USING SF-36 SCALE

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Background: Systemic Lupus Erythematosus (SLE) has diverse effects on patients' health-related quality-of-life (HRQoL), affecting both physical and mental domains of well-being. The Medical Outcomes Survey 36-item Short Form (SF-36) is one of the most common generic instruments used to measure HRQoL in SLE.

Objectives: Our objective in this study is to assess the aspects of HRQoL in patients with SLE and to explore the associations between HRQoL and disease-related parameters.

Methods: A cross-sectional study was conducted in patients followed in the departments of Internal Medicine and Rheumatology in Mahdia, Tunisia, who met either the 1997 ACR or the 2012 SLICC criteria for SLE. We evaluated for each patient, the global score and the eight domains of SF-36 (physical functioning (PF), role physical (RP), bodily pain (BP) and general health (GH) gathered into the Physical Component Summary (PCS); vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH)) gathered into Mental component Summary (MCS), scored from 0 (worst) to 100 (best). The disease activity was evaluated by the SLE Disease Activity Index (SLEDAI).

Results: Forty SLE patients were enrolled. 90% of patients were female. The mean age was 47.75±17.59 years. The mean disease duration was 2.3±2.9 years. The mean SLEDAI was 5.78±4.94. The most commonly found manifestations of SLE were; cutaneous, musculoskeletal and neuro-psychiatric in 85%, 82.5% and 40% of cases, respectively. The anti-nuclear antibodies were positive in 100% of cases. Serum levels of complement C3 and C4 were low in 20% and 32.5% of cases, respectively. A biological inflammatory syndrome was found in 37.5% of cases and anemia in 42.5% of cases. Anti-malarial were prescribed for 85% of patients, Glucocortoids were prescribed for 62.5% of patients. The SF-36 global score was 60.5 ± 20.5 ranging from 18.5 to 93.1. Eighteen patients (45 %) had impaired HRQoL (SF-36 < 66.7). The physical domains were more affected than the mental ones with mean scores of PCS and MCS of 59.59 and 61.6, respectively. The means of different domains (PF, RP, BP, GH, VT, SF, RE and MH) were respectively 67.87±28.3; 52.5±50; 62.5±29; 55.49±25.6; 56±21.5; 64±25.7; 67.5 ±47.4 and 58.6±18.6. The most severely impacted domains were RP and GH. Increased age was correlated with reduced PF, BP and PCS (p=0.02, p=0.02, p=0.05 respectively). Longer disease duration was associated with reduced GH (p=0.004). The analysis of organ-specific damage revealed that musculoskeletal involvement was significantly associated with lower scores of PF, RP, BP and PCS (p=0.05, p=0.009, p=0.01 and p<0.001, respectively), While neurological involvement was associated with lower scores of SF, VT and MCS (p=0.01, p=0.05 and p=0.04, respectively). The SF-36 global score and its domains had no significant correlations with the SLEDAI, the biological abnormalities or the received treatments.

Conclusion: Impairment in the quality of life can be significant when suffering from SLE, affecting physical health more than mental health according to our study. HRQoL should be included in routine clinical care in SLE patients.

Disclosure of Interests: None declared

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AB0527 DIFFUSE ALVEOLAR HEMORRHAGE IN LATIN AMERICAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

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Background: Diffuse alveolar hemorrhage (DAH) is an uncommon and life-threatening complication of systemic lupus erythematosus (SLE) with a high mortality rate (estimated average 50%). The presence of respiratory symptoms (dyspnea, cough, hemoptysis), a new drop in hemoglobin levels, and diffuse infiltrates on chest imaging should raise suspicion of this complication.

Objectives: We aimed to describe DAH-SLE patients and compare them with non-DAH SLE patients.

Methods: We conducted a single-center, case-control study that enrolled hospitalized patients between 2012 and 2020 in Colombia. Twenty-three DAH-SLE patients (cases) were matched by age and sex with 23 non-DAH-SLE patients (controls). Descriptive, comparative, and logistic regression analyses were performed.

Results: In seven (30.4%) patients, DAH was the initial manifestation of SLE; 69.5% of DAH-SLE patients were females with a mean age of 35 years. Lupus nephritis was present in 65% of cases, mean hemoglobin decrease was 2.22 g/l [standard deviation (SD) 0.92 g/L], and 78% had hemosiderophages in bronchoalveolar lavage. All patients received intravenous (IV) pulses of methylprednisolone followed by high-dose steroids, 87.0% IV cyclophosphamide pulses, 60.8% plasmapheresis, 21.7% IV immunoglobulin, and 8.7% rituximab. Comparisons between DAH and non-DAH groups are shown in Table 1. Bivariate logistic regression analysis showed that male sex (OR 9.625 CI95% 1.07 - 86.17; p=0.043), higher SLEDAI-2K score (OR 1. 28 CI95% 1.10 - 1.48; p=0.001), and higher C-reactive protein (CRP) levels (OR 1.09 CI95% 1.01 - 1.18; p=0.016) were independently associated with the occurrence of DAH, whereas prior use of corticosteroids (OR 0.029 CI95% 0.003 - 0.25; p=0.001) and antimalarials (OR 0.121 CI95% 0.03 - 0.45; p=0.002), higher hemoglobin levels (OR 0.457 CI95% 0.29 - 0.71; p=0.001), higher C3 (OR 0.94 CI95% 0.91 - 0.97; p<0.0001) and higher C4 levels (OR 0.87 CI95% 0.80 - 0.95; p=0.002) were negatively associated with DAH occurrence (Graph).

Table 1. Demographic, clinical, serological, and therapeutic characteristics in DAH-SLE patients and non-DAH-SLE patients

Variable	Non-DHA SLE (n = 23)	DHA SLE (n = 23)
Female	95.6%	69.5%
Age (years)	27.9 (SD 12.8)	34.82 (SD 17.3)
Hospital stay (days)*	20.7 (SD 29.1)	34.39 (24.4)
SLEDAI-2K*	6.17 (SD 5.9)	21.77 (12.5)
Creatinine (mg/dL)*	2.5 (SD 3.7)	4.23 (SD 5.2)
Leucocyte (cell/mm3)	8907 (5668)	9408 (5477)
Neutrophil (cell/mm3)	7112 (5595)	8063 (5456)
Lymphocyte (cell/mm3)	1236 (759)	952 (425)
Hemoglobin (g/L)	10.5 (2.6)	6.9 (1.5)
Ureic nitrogen (mg/dL)*	33.79 (SD 28.87)	45.73 (SD 25.64)
ESR (mm/Hour)	51.5 (35.72)	64.65 (47.50)
CPR (mg/dL)*	5.21 (SD 8.16)	12.42 (9.63)
Ferritina (ng/mL)	509 (526)	891 (856)
Lactate dehydrogenase (U/L)*	314 (SD 114)	503 (SD 357)
C3 (mg/dL)*	84.8 (SD 23.07)	44.84 (SD 27.91)
C4 (mg/dL)*	20.5 (10.3)	9.5 (8.2)
Anti-dsDNA	42.8%	71.4%
Anti-Ro	38.8%	38.8%
Anti-La	11.1%	10.5%
Anti-RNP	44.4%	47.3%
Anti- Sm	38.8%	35%
IgG ACL	0	9%
IgM ACL	10.5%	13.6%
Lupus anticoagulant	33.3%	33.33%
Mucocutaneous involvement	78.2%	69.5%
Articular involvement	73.9%	60.8%
Hematological involvement	86.9%	69.5%
Renal involvement	91.3%	86.9%
Serosal involvement	34.7%	26.1%
Prior glucocorticoid*	95.6%	39.1%
Prior antimalarial*	69.5%	21.7%
Dead	4.3%	21.7%

***P value** < **0.05**

Conclusion: In about one-third of patients diagnosed with DAH, this life-threatening complication was the initial presentation of SLE. Male sex, higher SLEDAI-2K scores, and higher CRP levels were associated with DAH occurrence, whereas higher hemoglobin levels, elevated complement levels, prior use of glucocorticoids, and antimalarial treatment were negatively associated with the occurrence of DAH.

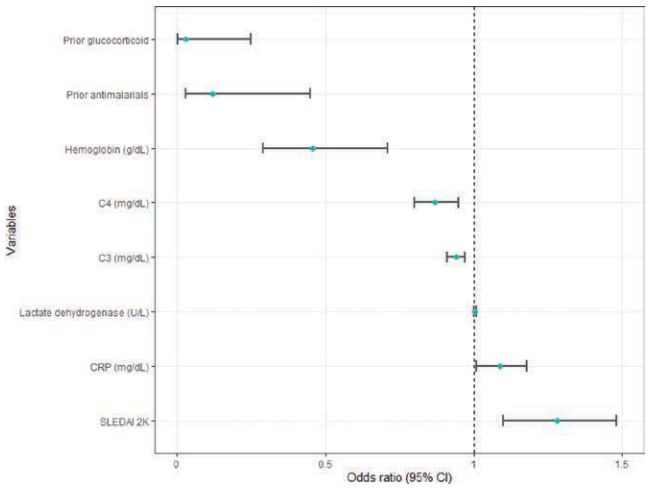

Figure 1. Forest plot of factors associated with DHA-SLE patients. **The Forest plot graph does not include the male sex variable due to its wide confidence intervals.

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AB0528 CORRELATION BETWEEN ALBUMIN TO GLOBULIN RATIO AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been reported as useful inflammatory biomarkers associated with the disease activity of systemic lupus erythematosus (SLE). Recently, the albumin to globulin ratio (AGR) has emerged as a potential indicator to predict the prognosis of some cancers. However, whether AGR can predict the disease activity of SLE has been rarely investigated.
Objectives: This study was to explore the relation between AGR and SLE Disease Activity Index 2000 (SLEDAI-2K) in patients with SLE.
Methods: This retrospective study enrolled 101 SLE patients and 75 age- and gender-matched healthy individuals. According to the SLEDAI-2K score, SLE patients were classified into Group 1 with a score of 9 or lower (patients with mild disease activity, N = 60) and Group 2 with a score > 9 (patients with moderate to severe disease activity, N = 41). Albumin, globulin, NLR, PLR, monocyte to lymphocyte ratio (MLR), AGR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complement 3 (C3), complement 4 (C4), SLEDAI-2K and other clinical data were collected. Receiver operation characteristic (ROC) curves were conducted to discriminate SLE patients from healthy controls and SLE patients with different disease activity. Correlations between the inflammatory markers and SLEDAI-2K were checked. The prognostic value of AGR in the SLE disease activity was tested by logistical regression analyses.
Results: Albumin and AGR in SLE patients were lower compared to those of the healthy controls (P < 0.05), while NLR, PLR, MLR, globulin and CRP were higher (P < 0.05). Patients in Group 2 had lower levels of albumin, AGR, C3 and C4 than those in Group 1 (P < 0.05), NLR and PLR were higher (P < 0.05), while MLR (P = 0.198), globulin (P = 0.704), CRP (P = 0.224) and ESR (P = 0.135) displayed no significant differences. The ROC curves for differentiating SLE patients from healthy individuals showed that the area under curve (AUC) of AGR (0.812, 95%CI: 0.750 - 0.874) and albumin (0.840, 95%CI: 0.782 - 0.898) were higher than NLR (0.786, 95%CI: 0.719 - 0.853), PLR (0.708, 95%CI: 0.629 - 0.786), MLR (0.776, 95%CI: 0.708 - 0.845) and globulin (0.630, 95%CI: 0.548 - 0.713). Similarly, the ROC curves for predicting the disease activity of SLE patients displayed that the AUC of AGR (0.779, 95%CI: 0.689 - 0.870) and albumin (0.827, 95%CI: 0.746 - 0.909) were also higher than NLR (0.644, 95%CI: 0.534 - 0.753), PLR (0.672, 95%CI: 0.565 - 0.780), MLR (0.583, 95%CI: 0.466 - 0.701), globulin (0.521, 95%CI: 0.403 - 0.639), CRP (0.567, 95%CI: 0.452 - 0.683), ESR (0.589, 95%CI: 0.475 - 0.703), C3 (0.709, 95%CI: 0.603 - 0.815) and C4 (0.655, 95%CI: 0.542 - 0.768). AGR was negatively correlated with SLEDAI-2K (r = -0.543, P < 0.001) in SLE patients. Logistical regression analyses showed that AGR (OR = 13.047, 95%CI: 3.407 - 49.966, P < 0.001) was an inverse predictor for SLE disease activity, yielding a highest hazard than other inflammatory parameters.
Conclusion: AGR was significantly decreased in SLE patients compared with healthy subjects and negatively associated with the disease activity of SLE. AGR might be a potential indicator for evaluating inflammation in patients with SLE.

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AB0529 PULMONARY HYPERTENSION (PAH) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IS NOT DEFINED BY AUTO-ANTIBODY AND CLINICAL VARIABLES.

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Background: PAH is a well-recognized but infrequent manifestation of SLE. Often insidious in onset, PAH may have progressed for a while, before symptoms manifest. Prediction of clinical risk of PAH may have clinical benefit during the follow-up of a patient with SLE.
Objectives: The aim of the study was to develop a prediction algorithm for PAH in patients with SLE using clinical and auto-antibody variables.
Methods: The study included patients from the INSPIRE cohort which is, a national multi-center study enrolling patients with disease duration of less than three years. Lupus patients with symptomatic PAH confirmed by a transthoracic

2D ECHO right ventricular systolic pressure of more than 40 mm Hg were enrolled as cases. Controls were age, sex and date of enrolment matched patients from the same cohort without any clinical evidence of PAH. We excluded patients with underlying known heart disease and critical illness. The clinical variables and antibody data was retrieved from records. Outcome of death if any was noted. Using supervised learning, a logistic regression model was built for the prediction of SLE-PAH. The final Prediction model included one clinical variable (RP), sixteen autoantibodies (Sm-RNP, Smith, SS-A, Ro-52, SS-B, SCL-70, PM-SCL, Centromere, Jo1, PCNA, Nucleosome, dsDNA, histone, Ribosomal P and AMA, anticardiolipin antibody) and complement level. To ensure accuracy of the model, a confusion matrix using python was performed. The proportion of right predictions (ρ) is a measure of accuracy of the model. If the model is good, ρ must be close to 1.

Results: A total of 69 patients with symptomatic PAH, confirmed by 2D echo-cardiography were enrolled as cases. Raynaud phenomenon (RP), Interstitial lung disease (ILD) and ischemic stroke were significantly higher in cases than control (p= 0.026,0.001, 0.05 respectively). There was no difference in the prevalence of individual auto-antibodies between the groups except high prevalence of anti-cardiolipin antibody in cases (39% vs 23% p= 0.048). Mortality rate was higher in cases (17% vs 0.06%, p=0.003) during a follow up of 3 years with all the deaths occurring within one year of PAH diagnosis. Ten repetitions of the confusion matrix analysis using Python for this prediction model (both derivation and validation) yielded the following ρ scores 0.60, 0.47, 0.57, 0.63, 0.50, 0.60, 0.57, 0.43, 0.50, 0.57. which exhibited wide variability.

Conclusion: A prediction model using RP and commonly assayed autoantibodies failed to be informative for PAH in Indian lupus patients.

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AB0530 CARDIOVASCULAR RISK STATUS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: WHICH ALGORITHMS IS THE BEST?

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Background: Systemic lupus erythematosus (SLE) has been strongly linked to accelerated atherosclerosis and increased cardiovascular morbidity and mortality. Rheumatological guidelines recommend evaluating the cardiovascular (CV) risk status in SLE patients, for an early identification of patients at high risk to preventive strategies.

Objectives: The aim of our study to compare three algorithms for CV risk estimation, namely Framingham, ACC/AHA (American College of Cardiology/American Heart Association) and QRISK3, in a cohort of patients with SLE.

Methods: This cross-sectional study included 279pts (84% females, median aged 37[28-45]years (median [interquartile range 25%-75%])) with SLE according to SLICC/ACR 2012 criteria, attending a routine visit at our Clinic between February 2018 and February 2020. Traditional risk factors (TRF), ongoing therapies, comorbidities and SLE-specific evaluation were assessed. In those without previous myocardial infarction or stroke (n=254, 83% females, aged 36[27-44]years), Framingham, ACC/AHA and QRISK3 algorithms were then used to estimate the individual risk of developing a CV disease over the next 10 years. In accordance with the NICE (National Institute for Health and Care Excellence) guidelines high-risk was considered for Framingham scores ≥10%, for ACC/AHA - ≥7,5% and for QRISK3 scores - ≥10%.

Results: Patients eligible for CV risk estimation were 254 of 279 enrolled. The median disease duration was 10[4-17]years, SLEDAI 2K-4[2-10], SLICC/DI–1[0-2]score. Framingham index reported (at the age 20-79years, n=238) a median risk score of 1[1-5]%, according to this algorithm 54/238 patients (23%) were classified as high-risk. ACC/AHA index (at the age 40-79years, n=99) showed a median risk score of 2[1-8]%, with 30/99 (30%) at high-risk. QRISK3 revealed (at the age 25-84years, n=211) a median risk score of 7,5[3,5-14,4]%, making it possible to classify 85/211 (40%) at high CV risk. To the same algorithm, the median relative risk (the ratio of the absolute risk of SLE patients to the estimated risk score in an age-, sex- and ethnicity-matched healthy ideal population) was 9,2[4,1-20,3]. «QRISK3 healthy heart age» showed a median of 64[56-71]years. The use of the QRISK3 scale revealed a greater number of SLE patients with CV high-risk compared to the Framingham: 40% vs 23% of patients, p<0,001.

Conclusion: QRISK3 classifies a greater number of SLE patients at high-risk of developing CV diseases over the next 10 years in comparison with classic algorithms as Framingham and ACC/AHA. According to QRISK3 score the absolute CV risk of SLE patients is 9 times higher than the CV risk of healthy individuals. The use of QRISK3 as a tool in the evaluation of SLE patients could lead to the early detection in a considerable part of high-risk CV diseases development individuals who would have otherwise been underestimated by the application of Framingham and ACC/AHA algorithms.

Disclosure of Interests: None declared

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AB0531 GLUCOCORTICOID-ASSOCIATED MORBIDITY IN SLE USING THE GLUCOCORTICOID TOXICITY INDEX

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Background: Systemic glucocorticoid (GC) therapy remains a necessity for a significant subset of patients with SLE. Chronic corticosteroid use is associated with the accrual of irreversible organ damage over time, with the highest risk being among those exposed to a mean prednisone dose of ≥20 mg/day. That is why, CG toxicity assessment should be an important part of routine clinical care as well.

Objectives: The aim of this study is to describe for the first time individual patient GC toxicity in SLE patients using the Glucocorticoid Toxicity Index (GTI)

Methods: A total of 37 patients SLE (30 (81%) women and 7 (19%) men) were enrolled in this study. The mean age was 36± 11,9 years and the median disease duration was 36 [12; 128] months. At the first visit, all patients were assessed for SLE activity by the SLEDAI 2K index, irreversible organ damage by SLICC Damage Index (DAI), GTI *, and current treatment.

Results: The mean disease activity index SLEDAI 2K was 11,3±6,2, DAI SLICC ≥1 was in 20 (54%), 17 (46 %) patients had not any irreversible organ damage DAI SLICC = 0. During the period of illness the maximum GC dose was 33,7 mg ± 19,9 mg, the median of cumulative dose of GC administered intravenously was 1563 mg [293; 6478] mg, median duration of GC treatment was 22 months [8; 112]. 30 (81%) of patients had GTI with median 33 [19; 48] points. 2 (5%) patients had zero GTI, but there were severe organs' injuries from the GTI Specific List (1 patient had cataract and 1 patient had cataract and avascular necrosis). 5 (14%) patients had zero GTI with no severe organs' injuries from the TGI Specific List. In 3 out of 5 patients, the duration of GC treatment did not exceed 6 months, in 2 out of 5 patients, the maximum dose of GC during the period of the disease did not exceed 5 mg/day. In 1 out of 5 patients, the duration of GC treatment was 13 months, and the maximum dose of GC was 15 mg during the period of treatment. The most frequent changes occurred in 5 of 9 main domains: an increase in body mass index was detected in 10 (27%) patients, an increase in blood pressure was detected in 15 (41%) patients, hyperlipidemia was detected in 9 (24%) patients, a decrease bone mineral density was detected in 6 (16%) patients and the development of infectious complications in 5 (14%) patients; The less frequent changes occurred in 5 of 9 main domains: 3 (8%) patients had impaired glucose tolerance, 2 (5%) patients had steroid myopathy; neuropsychiatric intoxication was detected in 2 (5%) patients. Severe organs' injuries were identified, included in a Special list and not scored in points: cataracts were detected in 7 (19%) patients, avascular necrosis was detected in 3 (8%) patients, osteoporotic fractures - in 2 (5%) patients. GTI correlated with disease duration (r = 0.33); the maximum dose of GC per os (r = 0.43); duration of GC therapy (r = 0.37); DAI SLICC (r-0.39), p<0.05 in all cases.

Conclusion: GTI was detected in a significant number of patients with SLE (81%). ITG correlates with the duration of the disease, the maximum dose of GC during the period of illness, the duration of GC therapy, and the SLICC DAI. GTI should be used to evaluate the safety of GC therapy in patients with SLE who receive GC therapy for more than 6 months, together with the SLICC DAI.

**The GTI includes Composite Index and Specific List. Composite Index, consists of 9 domains and 31 elements, each of which is assigned a certain number of points. It contains information on the most common complications of GC therapy: BMI, glucose tolerance, BP, lipids, myopathy, bone mineral density, skin lesions, neuropsychiatric lesions, infections.*

Severe organ damages, which is less common but contributes significantly to GC toxicity, are included in a special list. The specific list includes 11 domains

(9 of which are also used in the Composite index) and 23 elements (avascular necrosis, osteoporotic fractures, cataracts, etc.).
Disclosure of Interests: None declared
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AB0532 LACTATE DEHYDROGENASE AS A PREDICTOR OF FATIGUE IN PRIMARY SJOGREN'S SYNDROME:A POOLED ANALYSIS

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Background: Fatigue is one of the most disabling symptoms in primary Sjogren's syndrome (pSS) and it significantly impacts patient's quality of life[1]. However, the cause of this symptom remains unclear.
Lactate dehydrogenase (LDH), is an enzyme of the anaerobic respiratory pathway. High lactate levels are a marker of inflammation and create a pro-inflammatory microenvironment[2]. LDH levels can be raised in myositis, haemolysis and lymphoma. For this reason, serum LDH is routinely monitored in patients with pSS. However given its role in metabolic pathways, we hypothesize that serum levels of LDH may also be a biomarker of fatigue in pSS.
Objectives: 1. To investigate the bivariate relationship between LDH and fatigue severity, hypothesizing a positive correlation between them.
2. To incorporate factors such as depression, anxiety, serum creatinine and haemoglobin levels as covariates, as these factors may also contribute to fatigue
Methods: We used routinely collected clinical and laboratory data from 512 pSS patients from the Newcastle Sjogren's syndrome cohort. The participants consented for their linked anonymised data to be used in pSS-related research. Severity of fatigue was measured using fatigue subscale of EULAR Sjogren's Syndrome Reported Patient Index (ESSPRI)– a Likert scale of 0-10. Fatigue severity was also categorised into 4 categories: 0-2 being minimal, 3-5 mild, 6-7 moderate and 8-10 severe. Hospital Anxiety and Depression Score was used to measure patients' anxiety and depression levels. Blood parameters including haemoglobin, full blood count, ESR, CRP, serum creatinine, alanine aminotransferase (ALT), alkaline phosphatase (ALP) and LDH were checked during each visit. Dryness was measured using ESSPRI dryness subscale.Statistical analysis of the relationship between the continuous blood parameters and categorical fatigue groups was performed using Kruskal-Wallis for categorical fatigue groups and linear regression for continuous fatigue measures.
Results: The majority of the patients were female (87%) and Caucasian. Baseline measurements of pain, anxiety, depression, abnormal fatigue, mental fatigue and overall ESSPRI score increased with increasing fatigue severity. This is seen most prominently in serum LDH levels. LDH levels increased with increasing fatigue scores. We identified significant differences in baseline LDH levels across the four fatigue groups ($p = 0.002$). Within groups comparisons showed significant differences between mild and minimal, severe and minimal and moderate and minimal fatigue groups only (p-values: 0.026, 0.019 and 0.032 respectively). A baseline linear regression model for fatigue using LDH, CPK, age and gender was performed and showed LDH has a significant relationship with fatigue p=0.007.Findings were also determined using ANOVA where significant difference ($p= 0.0023$) of LDH between fatigue groups were identified using Kruskal-Walis test. A supplementary Tukey-Kramer test was carried out to determine if LDH was significant between two-groups of fatigue severity score, where significant difference was seen between three different sets of fatigue categories: mild-minimal, severe-minimal and moderate-minimal. The test ensured that a relationship between the enzyme and fatigue was present especially between the groups of fatigue severity stated above.The actual-by-predicted and leverage plot further supporting our findings by showing the unique effect of LDH in the models.
Conclusion: The study concludes that a relationship between enzyme lactate dehydrogenase and fatigue exist; however, further study will be required to examine its role as a predictor of fatigue severity in pSS. The complex interconnection between inflammation, disease activity, psychological factors and LDH will have to be further investigated to advance the current understanding of chronic fatigue in Sjogrens syndrome.
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Disclosure of Interests: None declared
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AB0533 THE ASSESSMENT OF CLINICAL CHARACTERISTICS OF MALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is a multisystemic chronic autoimmune disease that is nine times more frequent among females. Due to a female dominancy, the data regarding male patients is limited.
Objectives: This study aimed to evaluate the clinical characteristics of male patients with SLE.
Methods: This retrospective study included male SLE patients who followed up in a tertiary rheumatology outpatient clinic between October 2016 and December 2021. Those who met the Systemic Lupus International Collaborating Clinics (SLICC) criteria were included. The data of the patients and SLE Disease Activity Index-2000 (SLEDAI-2K) values were obtained from files.
Results: There were 40 male SLE patients with a mean age of 42.7 ± 17.3 years. The median age of diagnosis was 30 years, and the median disease duration was 63.5 months (ranges between 5-444). The mean value of the SLICC score was 4.7 ± 0.8. The most frequent initial clinical manifestations were thrombocytopenia and photosensitivity, which were seen in 8 (9.6%) patients each (Table 1). Six (15%) patients had secondary antiphospholipid antibody syndrome. Thirty-five (87.5%) patients achieved remission, but 14 (35%) patients had at least one relapse in the follow-up period. The most frequent manifestation after relapse was nephritis in 9 (22.5%) patients that had no renal involvement at the time of diagnosis. The median SLEDAI score was 2 (ranges between 0-12). The most commonly preferred drug for the treatment was hydroxychloroquine and corticosteroids (92.5% for each). Nineteen (47.5%) patients received pulse steroids. Besides, the most frequently prescribed immunosuppressive drug was mycophenolate mofetil (37.5%). The rates of azathioprine, cyclophosphamide, methotrexate, cyclosporine A, rituximab, intravenous immunoglobulin, and leflunomide usage were 30%, 27.5%, 17.5%, 10%, 7.5%, 7.5%, 5%, respectively. Antinuclear antibody (ANA) was positive in 35 (87.5%) patients, and anti-dsDNA was positive in 9 (22.5%). The median level of anti-dsDNA titers was 40 IU/ml (ranges between 23-200). Other autoantibody positivity rates were; 12 (30%) for anti-Sm, 6 (15%) for anti-histon, 4 (10%) for anti-RNP and 4 (10%) for anti-nucleosome. Thirteen (32.5%) patients had low C3 levels, and 11 (27.5%) patients had low C4 levels. The hospitalisation rate was 55%, and no death was seen during follow-up.

Table 1. Clinical characteristics of the patients (n=40)

Characteristics	Patients	
Clinical manifestations, n(%)	Initial	Relapse
Thrombocytopenia	8 (20)	None
Photosensitivity	8 (20)	None
Anemia	7 (17.5)	None
Malar rash	6 (15)	2 (15)
Nephritis	6 (15)	9 (22.5)
Arthiritis/synovitis	5 (12.5)	6 (15)
Subacute lesions	4 (10)	2 (5)
Leukopenia/lymphopenia	4 (10)	None
Thrombosis	3 (7.5)	4 (10)
Neurological involvement	3 (7.5)	None
Serositis	2 (5)	2 (5)
Pulmonery involvement	2 (5)	None
Discoid lupus erythematosus	1 (2.5)	1 (2.5)
Myositis	1 (2.5)	None

Conclusion: Since SLE is more prevalent among females, it may occur in male patients with mild or life-threatening manifestations. In the current study, the seropositivity was less than in the literature, which may indicate male patients should be cautiously evaluated. Although renal involvement is not an initial manifestation, it may develop during the follow-up.
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AB0534 PROSPECTIVE STUDY OF 24 MONTHS OF EVOLUTION OF A COHORT OF PATIENTS WITH RHUPUS

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Background: Rhupus syndrome (RhS) is a rare combination of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Different studies describe cases of RhS with more frequent initial clinical manifestations in the form of erosive arthritis and the presence of rheumatoid factor (RF) and/or anti-CCP, with later manifestations of SLE appearing.
RhS has a low prevalence and it is useful to know the clinical characteristics of the patients and their evolution over time, since their treatment and clinical management differ from those who present RA or SLE in isolation.
Objectives: Our objective was to study the clinical, analytical and therapeutic evolution of our cohort of patients with Rhupus.

Methods: Prospective study of a cohort of patients with Rhupus during 2020-2021 with systematic review of electronic records for the analysis of clinical, analytical and therapeutic parameters throughout follow-up.
Results: Nine patients with RhS (88.9% women) who met SLICC 2012 criteria for SLE and ACR 2010 for RA were included. The mean age was 62.7 (45-86) years.
During follow-up, the death of one case due to metastatic pulmonary neoplasia was verified, as well as the incorporation of a new patient in the study population.
In 4 cases, RA was the first diagnosis, with a mean evolution of 6.25 years until the diagnosis of SLE. On the contrary, in 5 cases SLE was the first diagnosis with a mean evolution of 7.2 years until the diagnosis of RA. Photosensitivity and arthritis were the predominant clinical manifestations. One patient presented rheumatoid nodules in both elbows and 2 patients presented symptoms of serositis in the form of pleuro/pericarditis. No cases of renal or neurological involvement were recorded.
Clinically, the patients have remained stable, presenting joint manifestations as the predominant clinic.
Regarding the serological evolution, 8 patients presented positive RF at the beginning of the study, 3 of them becoming negative during follow-up. Likewise, the presence of ACPA was positive in 6 patients, maintaining this percentage at the present time.
On the other hand, the ANA were positive at the beginning in all the patients, with ANA becoming negative in 5 of them.
Antiphospholipidic antibodies were positive in 2 patients, however none of them developed antiphospholipidic syndrome..
4 patients were treated with biological drugs/JAK inhibitors (1 abatacept, 1 rituximab, 1 baricitinib and 1 tofacitinib) with a favorable response.
Conclusion: The analysis of our cohort continues to show that, unlike other series, 44.4%% of RhS cases begin with seropositive polyarticular arthritis. 55.6% of these start with manifestations compatible with SLE, in the form of hematological, cutaneous and serological alterations, and these show a more prolonged progression to develop polyarticular involvement. Therefore, a diagnosis of RhS continues to be reached earlier in patients who present with symptoms of RA.
37.5% of patients had a negative RF, maintaining ACPA + in all of them. ANA were negative in 55%. Neither of the 2 patients with anti PL Ab developed APS.
Clinically, joint manifestations in the form of arthralgia of small joints were the predominant clinic.
In general, the evolution has been favourable. Four patients were refractory to treatment with cDMARDs, requiring the use of biological drugs/JAK inhibitors with good response.
Disclosure of Interests: None declared
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AB0535 LEPTIN LEVELS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, CONNECTION WITH COURSE OF THE DISEASE AND ATHEROSCLEROTIC VASCULAR LESIONS

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Background: Atherosclerosis and its complications remain the leading causes of death in patients with systemic lupus erythematosus (SLE). Along with the known pathological factors that significantly accelerate the development of cardiovascular events in patients with SLE (hyperinsulinemia, hypertension, atherogenic dyslipidemia, disease activity, etc.), in recent years the role of dysadipokinemia has been intensively studied. In patients with SLE serum leptin increases, but how its concentration changes under the conditions of the inflammatory process and how it is associated with other factors that aggravate the course, have not been studied enough. Its role in the formation of atherosclerotic vascular lesions in patients with SLE is also unknown.
Objectives: The aim of the study was to assess leptin levels in patients with SLE and to analyze its relationship with the course of the disease, lipid spectrum and atherosclerotic vascular lesions.
Methods: We examined 45 patients with SLE (31 women and 4 men), mean age - 46.23 ± 1.36 years). The average duration of the disease was 9.97 ± 0.82 years. SLE was verified on the basis of ACR / EULAR criteria (2019) and formulated according to the classification recommended by the Association of Rheumatologists of Ukraine (2020). The control group included 20 healthy individuals of the appropriate age and sex.
The content of leptin in the serum was determined by enzyme-linked immunoassay according to the instructions of the manufacturer. The SLEDAI index was used to assess activity. Assessment of endothelial function was determined by the Celermajer method.
Results: The level of leptin in the serum in apparently healthy individuals and patients with SLE differed significantly. In particular, the average hormone content in patients with SLE was 39.4 ± 3.4 ng / ml, while in the control group - 24.4 ± 3.8 ng / ml, ie it was higher by 38.1% (P <0.01). The patient's age and disease duration were weakly related to leptin levels (r = 0.25, r = 0.34, respectively).
It was found out that in patients with SLE serum leptin levels were directly proportional to the disease activity. In particular, a close associative relationship was established between the activity of the disease determined by the SLEDAI index and ESR (r = 0.81, r = 0.42, respectively). The study found a close association between serum leptin concentrations and blood lipid spectrum in patients with SLE. In particular, it was the highest with LDL(low density lipoprotein) (r = 0.54), and probable with total cholesterol and triglycerides (r = 0.32, r = 0.28, respectively). In patients with SLE with a high (≥42.2 ng / ml) leptin level, the endothelium-dependent vasodilation brachial artery (EDV BA) was 52.3% higher and the CCA IMT (common carotid artery intima-media thickness) was 32% higher than in patients with relatively normal leptin levels. In addition, the proportion of patients with a decrease in EDV BA and a thickening of CCA IMT among patients with high leptin levels was 12–25% higher than among patients with relatively normal levels of the enzyme under study. The presence of atherosclerotic plaques, their area and the severity of atherosclerotic lesions of the carotid arteries also determined the tendency to increase in proportion to the increase in serum leptin levels. Thus, hyperleptinemia in patients with SLE is associated with deterioration of vascular function of the carotid artery and the severity of atherosclerotic vascular lesions.
Conclusion: Significantly higher levels of serum leptin were found in patients with SLE, which were associated with inflammatory activity and dyslipidemia, as well as with structural and functional reorganization of blood vessels, which should be considered as an important risk factor for vascular lesions.
Disclosure of Interests: None declared
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AB0536 RELATIONSHIP OF EXERTIONAL ACTIVITY AND MENTAL WELLBEING IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a variety of clinical manifestations [1] and has a profound effect on physical health [2]. Anxiety and depression are common symptoms of SLE which can have a significant impact on the quality of life [3].
Objectives: To study whether or not the physical state of health relates to the extent of anxiety and depression in SLE patients.
Methods: The Physical Component Summary Score (PCS) was determined using the 36-Item Short Form Survey (SF-36) in a cohort of 146 SLE patients consecutively visiting our outpatient clinic. Two groups were compared: one group with low PCS<50 % (LPCS) and the comparison group with high PCS ≥50 % (HPCS). Patients with SLE who visited our Rheumatology clinic between March 2019 and December 2020 as part of a monocentric cross-sectional study completed additional standardized questionnaires: Hospital Anxiety and Depression Scale (HADS), Beck's Depression Inventory (BDI II), Multidimensional Assessment of Fatigue (MAF), Functional questionnaire Hanover (FFbH) and the international questionnaire on physical activity in short form (IPAQ-SF). The data was analyzed with SPSS 27 (IBM, Armonk, NY, USA). The tests include bivariate and partial correlations. Significance tests were performed using non-parametric tests.
Results: In total, 146 patients participated in the study. 14.4 % (n = 21) were male and the mean age was 48.6 ± 12.2 years. The mean state of physical health according to SF36 was 54.9 % ± 25.6 % in the examined cohort.
There were 62 (42.5 %) patients with LPCS, of average age 50.4 ± 10.3 years and 84 (57.5 %) with HPCS, of average age 47.2 ± 13.3 years. The majority of patients in both groups were female (55/7, 88.7 % and 70/14, 83.3 %).
A SLEDAI score > 2 was confirmed in 33.9 % (n = 21) of the patients with LPCS and in 25 % (n = 21) of patients with HPCS, the mean SLEDAI score did not significantly differ between LPCS and HPCS patients (2.4 versus 1.9, p = 0.261). Among patients with LPCS, 54.8 % (n = 34) presented low physical activity and 64.5 % reported functional impairment (FFbH < 80). More than half of LPCS-patients (53.2 %, n = 33) showed a low Mental Health summary score (MCS < 50 %) and over a third of them had moderate to severe depression (BDI II > 19, 38.7 %, n = 24) and indicated pathological anxiety (HADS > 10, 37.1 %, n = 23).
Compared to the LPCS group, a smaller number of patients with HPCS had low physical activity (36.9 %, n = 31, p = 0.031) and the difference in mean weekly MET between the two groups was 2730 counts (p = 0.003). There was no impairment of functional capacity in patients with HPCS (FFbH mean Score 90.9 %, p < 0.001). In contrast to the LPCS group, only 17.9 % (n = 15) of the patients with HPCS showed MCS < 50 % (p < 0.001). Completely free of depressive symptoms were 65.5 % (n = 55) of the patients with HPCS and only 4 patients (4.8 %) reported moderate to severe depression (p < 0.001).
Patients with LPCS reported fatigue (GFI > 20) more often than patients with HPCS (98.4 % versus 54.8, p < 0.001).
Conclusion: SLE patients with low physical health conditions have highly significant mental health impairment, particularly anxiety and depression. Physical functioning and limitations due to physical health should be considered and physical activity needs to be improved. Measurement of the PCS should be a routine tool in the overall assessment of the health conditions of SLE patients.

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AB0537 DRY EYE SYMPTOMS STRONGLY CORRELATE WITH OCULAR AND EXTRAOCULAR PAIN IN PRIMARY SJÖGREN'S SYNDROME. INTERIM REPORT OF A PILOT CROSS-SECTIONAL MONOCENTRIC STUDY.

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Background: Ocular involvement in primary Sjögren's Syndrome (pSS) has been traditionally assessed by Schirmer's test, Tear Break Up Time (TBUT) and Ocular Staining Score (OSS)[1]. The role of Ocular Surface Disease Index (OSDI), Visual Function Questionnaire-25 (VFQ-25) and Numerical Rating Scale (NRS) in measuring ocular pain and discomfort in pSS have not been yet investigated in detail.
Objectives: To explore the prevalence of ocular pain in patients with pSS, and to investigate the potential correlations between dry eye, ocular pain, extraocular patient-reported outcomes and disease activity.
Methods: In this ongoing cross-sectional study, OSDI, VFQ-25 and NRS for ocular pain were administered to 19 consecutive patients with a definite diagnosis of pSS at our outpatient clinic. All patients signed an informed consent for the study. Pearson coefficients were obtained to assess correlation among EULAR Sjögren's Syndrome (SS) disease activity index (ESSDAI), EULAR SS Patient Reported Index (ESSPRI), erythrocyte sedimentation rate (ESR), TBUT, OSDI, VFQ-25 and NRS.
Results: In the study, 19 consecutive patients have been enrolled so far. The sample demographics and disease-related features are representative of a typical pSS population (10% male sex, median age at diagnosis of 49 [IQR 24], median ESSDAI = 1 [IQR 6] being biological, haematological and glandular involvement the most represented). Prevalence of ocular pain of any grade (NRS>0) was 11/19 (58%); 6 patients (33%) reported severe ocular pain (NRS≥5). The correlation analysis was significantly strong for patient-reported dryness (ESSPRId), ocular surface-associated symptoms (OSDI), and stability of the tear film (TBUT) with NRS for ocular pain. Moreover, ocular pain also correlated with generalised pain (ESSPRIp) and fatigue (ESSPRIf), while a significant correlation was outlined for OSDI (but not TBUT) with ESSDAI and ESR. Detailed results are summarised in Table 1.

Table 1. Pearson r coefficients calculated for self-reported ocular pain (NRS), patient-reported outcomes (ESSPRI, OSDI, VFQ-25), physician-assessed dryness (TBUT), disease activity (ESSDAI) and erythrocyte sedimentation rate. *p<0.05 **p<0.01

	NRS	TBUT	ESSDAI	ESSPRId	ESSPRIp	ESSPRIf	OSDI	VFQ-25	ESR
NRS		-0.95**	+0.25	+0.73*	+0.69*	+0.59*	+0.68*	-0.54	+0.19
TBUT	-0.95**		+0.40	-0.56	-0.58	-0.64	-0.57	+0.24	-0.67
ESSDAI	+0.25	+0.40		+0.14	+0.43	+0.12	+0.77**	-0.33	+0.55*
ESSPRId	+0.73*	-0.56	+0.14		+0.73**	+0.36	+0.61*	-0.60*	+0.11
ESSPRIp	+0.69*	-0.58	+0.43	+0.73**		+0.53*	+0.51	-0.63*	+0.32
ESSPRIf	+0.59*	-0.64	+0.12	+0.36	+0.53*		+0.09	-0.31	+0.73
OSDI	+0.68*	-0.57	+0.77**	+0.61*	+0.51	+0.09		-0.60*	+0.56*
VFQ-25	-0.54	+0.24	-0.33	-0.60*	-0.63*	-0.31	-0.60*		+0.05
ESR	+0.19	-0.67	+0.55*	+0.11	+0.32	+0.73	+0.56*	+0.05	

Acronyms: NRS - Numerical Rating Scale (for ocular pain); TBUT - Tear Break Up Time; ESSDAI - EULAR Sjögren's Syndrome (SS) disease activity index; ESSPRI - EULAR Sjögren's Syndrome Patient Reported Index (d= dryness; p=pain; f=fatigue); OSDI - Ocular Surface Disease Index; VFQ-25 - Visual Function Questionnaire-25; ESR: erythrocyte sedimentation rate.

Conclusion: Ocular pain may represent an additional criterion for pSS patient stratification. The unexpected association between ocular pain and extra-ocular symptoms is a novel datum which may suggest that nociceptive mediators could be involved in the genesis of symptoms in pSS[2]. Indeed, OSDI seemed to perform better than TBUT in assessing the sufferance of the ocular surface thus mirroring a systemic inflammatory activity.

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AB0538 INCREASED BURDEN OF MENTAL DISORDERS DESPITE IMPROVEMENT IN DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A PROSPECTIVE STUDY

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Background: Mental disorders such as anxiety and depression are highly prevalent in SLE patients,[1] yet their association with the underlying disease activity remains elusive and has been mostly evaluated at cross-sectional level.[2] This is further complicated by the often-increased rates of treatment non-adherence,[3] an important determinant of heightened lupus activity, among patients with depression.[4]
Objectives: To examine the relationship between longitudinal changes in anxiety (ICD-10-CM F41.9), depression (ICD-10-CM F32.x) and disease activity levels in adult SLE patients. Second, to test the association between the aforementioned mental disorders with treatment adherence and sociodemographic factors.
Methods: A prospective 6-month observational study of outpatients aged 18-65 years who fulfilled the EULAR/ACR 2019 classification criteria and had active disease ascertained by a SLEDAI-2K ≥3 and PGA (physician global assessment; scale 0–3) >1. Patients were enrolled by consecutive sampling technique during May-September 2021. Excluding criteria were overlap rheumatic diseases, active neuropsychiatric lupus, ongoing pregnancy or post-partum period, history of dementia or malignancy. Sociodemographic factors (age, disease duration, education level, working status) and comorbidities were collected. Anxiety and depression levels (assessed with the Hospital Anxiety and Depression Scale [HADS-A/D subscales]), disease activity (SLEDAI-2K, PGA), use of medications, and treatment adherence (Morisky Medication Adherence Scale-4 items scale) were monitored during the observation period.
Results: Forty SLE patients (39 females) with an average [standard deviation] age 50.5 (10.3) years and disease duration 10.3 (7.0) years, were enrolled. Baseline SLEDAI-2K was 6.0 (2.0) driven predominantly from the musculoskeletal and mucocutaneous domains. The prevalence of anxiety (HADS-A >11) and depression (HADS-D >8) were 42.5% and 45.0%, respectively. During follow-up, disease activity was significantly reduced (average [SD] reduction in SLEDAI-2K: 1.90 [2.80], p<0.001), however, anxiety and depression levels remained unchanged (average [SD] change in HADS-A -0.05 [3.76] and HADS-D 0.53 [3.25], respectively, p>0.300 for both). Accordingly, Spearman's non-parametric test showed that longitudinal changes in SLEDAI-2K were not significantly correlated with the corresponding changes in the HADS-A (*rho* = 0.13, p=0.417) or HADS-D (*rho* = -0.05, p=0.781) scores. Treatment non-adherence was found in 19 patients (47.5%) but did not correlate with anxiety and depression (p>0.500 for both). Notably, mental disorders were not significantly associated with comorbidities (including fibromyalgia) but unemployment status predicted the presence of anxiety (odds ratio 7.73, p-value 0.018).
Conclusion: Anxiety and depression are frequent comorbidities in active SLE and do not correlate with short-term disease improvement, thus underscoring the need for adjunct treatment. Physician awareness in the detection of treatment adherence is necessary. Larger studies in early disease and with longer follow-up will be required to further explore the possible interaction between of mental disorder and lupus disease course.

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AB0539 **DEPRESSION, SELF-ESTEEM AND QUALITY OF LIFE IN SJÖGREN'S SYNDROME**

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Background: Sjögren's syndrome (SS) is a connective tissue disease characterized by a triad of fatigue, pain and dryness. SS is a chronic condition with important repercussions on functioning and a source of significant suffering. Therefore, the assessment of depressive symptoms, self-esteem and quality of life (QOL) is important in the clinical and research context.
Objectives: We aimed to describe the clinical picture, depression, QOL and self-esteem of patients followed for SS and to study their association with disease activity.
Methods: This is a descriptive and analytical cross-sectional study including 42 patients with SS diagnosed based on the criteria of the American European Consensus Group of 2002 (AECG). Depression was evaluated by the Beck 13 scale, QOL by the SF-36 and self- esteem by the Rosenberg scale. Disease activity was assessed by EULAR Sjörgen Syndrome Disease Activity Index (ESSDAI).
Results: The average age was 54.5 ±15.67 years and the sex ratio was 0.2. Assessment of disease activity of these patients showed an average activity score of 8.23 ±6.39 with low activity in 16 patients (38.1%), moderate activity in 18 patients (42.9%) and severe activity in 8 patients (19%). The QOL measured by SF-36 was impaired in all areas with averages ranging from 39.76 for physical limit to 66.28 for emotional limit. Depression score evaluated by the Beck scale was 8.42 ±7.05on average with 59.5% of the patients having depression. The self-esteem score evaluated by Rosenberg scale was 32.8 ± 5.7on average. Self-esteem was rated as low to very low in 30.95% of patients.
Disease activity score was correlated to Beck's depression score (r= 0.545; p= 0.001); and Rosenberg's self-esteem score (r= -0.51; p= 0.001). Likewise, we found a correlation between the SF-36 score and Beck's depression score; the SF-36 score and Rosenberg's self-esteem score (p< 0.05).
Conclusion: As QOL, self esteem and depression were correlated to disease activity, taking into account these aspects in SS can improve the overall management of the disease.
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AB0540 **INTERRELATION OF HYPERURICEMIA AND BURDEN OF COMORBIDITIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Comorbidities play an important role in the course and prognosis of systemic lupus erythematosus (SLE) [1]. Hyperuricemia (HP) could cause an increased burden of comorbidities in SLE patients (pts).
Objectives: To evaluate the interrelation between HP and comorbidities in pts with SLE.
Methods: We performed retrospective analysis of the data from 191 SLE pts that were collected in electronic Saint-Petersburg rheumatological register in a period from 01 Jan 2009 until 31 Dec 2020. In analysis were involved data of 85 SLE patients with hyperuricemia (serum uric acid level >360 μmol/l in 3 reports) (group 1) and of 106 SLE pts with normal uric acid level in 3 laboratory reports (≤360μmol/l) – group 2. Pts with rheumatological diseases other then SLE, with gout, active infections, oncological diseases, with glomerular filtration rate <30 ml/min*1.73 m2 and other secondary reasons of HP were excluded. The clinical and laboratory data, presence of comorbidities, Charlson Comorbidity Index, SELENA-SLEDAI were analyzed. SPSS2020 was used to Statistics. Local ethics committee approved the study.
Results: SLE pts with and without HP were matched in age, sex and disease activity characteristics, Table 1(p≥0.05). Uric acids' level did not correlate with activity of SLE (SELENA-SLEDAI), Spearmen' r=0.06, p≥0.05. Hypertension, obesity, hypercholesterolemia, diabetes mellitus, lower renal function were more common in SLE patients with HP than in SLE patients without HP, Table 1. Charlson comorbidity index was higher in SLE pts of than in SLE pts without HP (p<0.05).

Table 1. Clinical characteristics and occurrence of comorbidities in SLE pts.

Patients and Disease' characteristics	Group 1 (n=85)	Group 2 (n=106)	P-value
Age, years, mean ± SD	47.05±13.51	44.84±12.11	≥0.05
Female, n (%)	69 (81.18)	95(89.62)	≥0.05
SELENA-SLEDAI, mean ± SD	7.33±5.03	6.15±3.92	≥0.05
SLE duration, years, mean ± SD	4.73±5.01	0.97±2.15	<0.05
Serum uric acid, μmol/l, mean ± SD	434.6±63.16	238.38±59.36	<0.05
Hypertension, n (%)	52(61.18)	30(28.3)	<0.05
Obesity, n (%)	15(17.65)	5(4.72)	<0.05
Hypercholesterolemia, n (%)	54(63.53)	34(32.08)	<0.05
Diabetes mellitus, n (%)	14(16.47)	3(2.83)	<0.05
Glomerular filtration rate, ml/min*1.73 m^2, mean ± SD	80.29±28.35	95.81±23.38	<0.05

SD - standard deviation

Conclusion: Elevated serum uric acid levels in SLE patients are associated with a higher incidence of hypertension, hypercholesterolemia, obesity, diabetes mellitus, decreased glomerular filtration rate, with a higher Charlson comorbidity index, but not with disease activity.
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Disclosure of Interests: Elizaveta Kornilova: None declared, V Mazurov: None declared, Aleksandra Fonturenko: None declared, Roman Bashkinov: None declared, Oksana Inamova: None declared, Inna Gaydukova Speakers bureau: Novartis, Sandoz, Pfizer, Biocad, MSD, Dr Reddy's, Lilly, Sanofy, not >10000 Euros per year, Consultant of: Novartis, Pfizer, Biocad, MSD, Dr Reddy's, Lilly, Sanofy, not >10000 Euros per year, Grant/ research support from: Novartis, Sandoz, Pfizer, Biocad, MSD, Dr Reddy's, not >10000 Euros per year
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AB0541 **NEUROPSYCHIATRIC MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS: PREVALENCE, MANAGEMENT AND ASSOCIATED FACTORS**

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Background: Neuropsychiatric involvement is one of the major causes of morbidity and mortality in systemic lupus erythematosus (SLE). Its prevalence varies in the literature because of its clinical polymorphism.
Objectives: The aim of our study is to evaluate the clinical, biological, immunological and therapeutic characteristics of neuropsychiatric complications and to analyze the associated factors.
Methods: This is a retrospective descriptive study including patients followed for SLE (ACR 1997/ SLICC 2012) during the period between 2010 and 2021 at the Rheumatology and Internal Medicine departments in Mahdia, Tunisia.
Results: Our study included 82 SLE patients among whom 29 had neuropsychiatric manifestations (NPM) with a frequency of 35.4%. They were 28 women and 1 man. Their mean age was 52.41 ± 18.11 years [21 - 85]. The mean disease duration was 2.4 ± 3 years [15 days-15 years]. The mean

SLEDAI was 9.3 ± 7.85 [0-32]. NPM were inaugural of SLE in 14 cases (17%). Central neurological manifestations consisted of cerebral vasculitis (n=11), epiletic seizures (n=1), ischemic stroke (n=1), aseptic meningitis (n=1) and transverse myelitis (n=1). Peripheral neurological manifestations of mono/polyneuropathy were found in 6 cases. Cranial nerves involvement was described in 2 cases (Optic neuropathy and vestibular nerve damage). Psychiatric manifestations were present in 7 cases (25%): Depression in 4 cases and psychosis in 3 cases. The most frequent associated clinical manifestations were: musculoskeletal (100%), dermatological (89.7%), hematological (72.5%) and cardiovascular (24.1%). Biological findings included: leucopenia (31%), lymphopenia (44.8%), anemia (44.8%) and biological inflammatory syndrome (41.4%). The mean sedimentation rate (ESR) was 53.75 ±34 mm [2-130]. The mean C-reactive Protein was 13.6 ±27.8 mg/dL [0-130]. Anti-nuclear antibodies and anti-DNA were positive in 100% and 41.4% of cases, respectively. Anti-Sm antibodies were positive in 13.5%, anti-SSA in 24.1% and anti-SSB in 13.8% of cases. Antiphospholipid was positive in 8 patients. C3 and C4 consumption was found in 20.7% and 27.6% of cases, respectively. Brain magnetic resonance imaging showed T2 white matter hyperintensities, particularly in the periventricular area, in 8 cases and ischemic brain lesions in 2 cases. The treatment of NPM required: Glucocorticoids (75.9%), Azathioprine (AZT) (24.1%), Cyclophosphamide (13.7%), Mycophenolate Mofetil (3.4%), anticoagulants and antiplatelet agents (40%). The evolution was favorable for our patients except for one patient who developed AZT-induced hepatotoxicity. Statistical analysis showed that NPM were significantly correlated with older age (p=0.003), hematological involvement (p=0.02), lymphopenia (p=0.004), ESR (p=0.01), anti-Sm antibodies (p=0.03) and SLEDAI score (p=0.008).

Conclusion: NPM during SLE are a serious complication of the disease. Our study shows the frequency and variety of neuropsychiatric presentations during SLE. They must be systematically sought, especially if the disease is active, with older patients and anti-Sm antibodies positivity.

Disclosure of Interests: None declared

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AB0542 ANTIPHOSPHOLIPID ANTIBODY CARRIERS WITH THROMBOCYTOPENIA COULD BE AN INDEPENDENT PHENOTYPE OF PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: Among patients with immune thrombocytopenic (ITP), 10-20% of them were found with positive antiphospholipid antibodies (aPLs) but without typical clinical manifestations of antiphospholipid syndrome (APS), especially thrombotic events[1].

Objectives: To compare the clinical characteristics and prognosis between aPLs carriers and patients with APS.

Methods: This is a single center prospective cohort study consecutively enrolling thrombocytopenic patients with continuous positive aPLs. Patients developing thrombotic events are classified as the APS group. The exclusion criteria are other underlying connective tissue diseases such as lupus and other causes that might manifest as thrombocytopenia, such as virus infection, hypersplenism, etc.

Results: This cohort included 47 thrombocytopenic patients with continuous positive aPLs and 55 with diagnosed primary APS. The proportion of thrombotic high risk demographic characteristics including smoking, hypertension, and higher level of homocysteine are higher in the APS group (p = 0.03, 0.04, 0.03, respectively). The prevalence of nephropathy was significantly higher in patients with diagnosed APS [0 vs 7 (12.7%), p =0.01]. Laboratory results and antibody profiles are presented in Table 1. The platelet count of aPLs carriers at admission was lower than APS patients [26×10^9/L (9×10^9/L, 46×10^9/L) vs 64×10^9/L (24×10^9/L, 89×10^9/L), p = 0.0002]. The proportion of positive anti-β2-glycoprotein I, anticardiolipin and lupus anticoagulant separately was similar, but triple aPLs positivity is more common in primary APS patients with thrombocytopenia [24 (51.1%) vs 40 (72.7%), p = 0.04]. There is no significant differences over the complement levels between the two groups [p = 0.2 for low complement 3 (C3), p = 0.8 for low C4]. Regarding the treatment response, the complete response (CR) rate is similar between aPLs carriers and primary APS patients with thrombocytopenia (p = 0.2). Nonetheless, the proportion of response, no response and relapse differed significantly between the two groups [13 (27.7%) vs 4 (7.3%), p < 0.0001; 5 (10.6%) vs 8 (14.5%), p < 0.0001; 5 (10.6%) vs 8 (14.5%), p < 0.0001, respectively]. In Kaplan-Meier analysis (Figure 1), primary APS patients had significantly more thrombotic events than aPLs carriers (p = 0.0006). aPLs carriers with thrombocytopenia share similar clinical manifestations with primary APS patients but hardly develop thrombotic events.

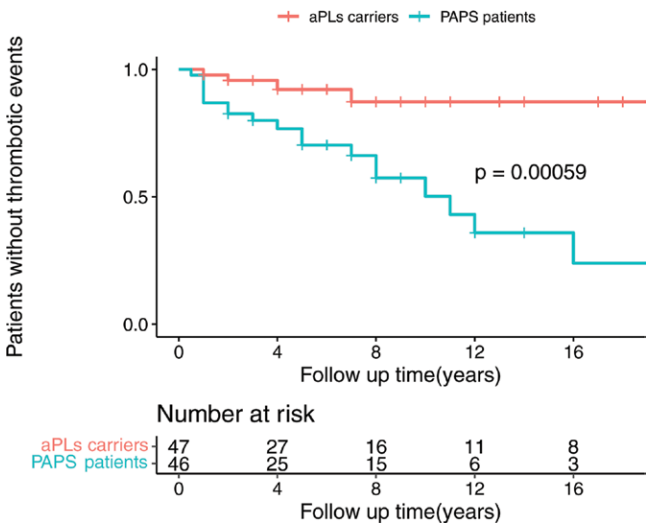

Figure 1. Kaplan-Meier analysis of thrombotic events. aPLs: antiphospholipid antibodies; PAPS: primary antiphospholipid syndrome.

Table 1. Baseline characteristics of laboratory results and antibody profiles.

Characteristics	aPLs carriers (n=47)	Primary APS with thrombocytopenia (n=55)	p-value
Laboratory results, median (Q1, Q3)			
Platelet count ($\times10^9$/L)	26 (9,46)	64 (24, 89)	0.0002*
hsCRP (mg/L)	1.39 (0.475, 2.845)	1.08(0.41, 2.565)	0.8
ESR (mm/h)	5.5 (2.75, 10.75)	7.5 (5, 14.25)	0.06
LDH (U/L)	221 (176, 252)	228 (184.8, 282)	0.3
Low C3, n (%)	3 (6.4)	9 (16.4)	0.2
Low C4, n (%)	5 (10.6)	8 (14.5)	0.8
Antibody profiles, n (%)			
Positive aCL	45 (95.7)	33 (69.1)	0.3
Positive Anti-β2GP I	38 (80.9)	48 (87.3)	0.5
Positive LA	35 (74.5)	50 (90.9)	0.05
Triple positivity	24 (51.1)	40 (72.7)	0.04*
Positive Coombs,	6 (12.8)	10 (18.2)	0.4

*p < 0.05, statistically significant. aPLs: antiphospholipid antibodies; APS: antisphopholipid syndrome; Q1/3: quantile 1/3; hsCRP: hypersensitive C-reactive protein; ESR: erythrocyte sedimentation rate; LDH: lactate dehydrogenase; C3/4: complement 3/4; aCL: anticardiolipin; GP: glycoprotein; LA: lupus anticoagulant.

Conclusion: In the absence of other high risk factor for thrombosis, Thrombocytopenia could be an independent and long-lasting clinical phenotype for aPLs carriers.

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AB0543 HIGHER LEFT VENTRICULAR MASS INDEX IN PATIENTS WITH LUPUS NEPHRITIS

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Background: Systemic lupus erythematosus (SLE) patients have a worse cardiovascular prognosis than the general population. It is estimated that approximately 40% of SLE patients develop lupus nephritis (LN) throughout the evolution of the disease (1). Patients with LN had 8 times more risk of myocardial infarction and 4 times more risk of cardiovascular mortality than SLE patients without LN (2).

Objectives: To compare the echocardiographic parameters between SLE patients with and without LN.

Methods: This was a cross-sectional study nested of a SLE cohort. We recruited patients with SLE diagnosis, according to the 2019 EULAR/ACR

classification criteria, aged ≥ 18 years. Patients with a previous cardiovascular event, another connective tissue disease or pregnancy were excluded. A transthoracic echocardiogram was performed by two certified echocardiographers blinded to clinical information. Patients with LN were included and matched to patients without LN by age and gender. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done with Chi-square test or Fisher's exact test for qualitative variables, and Student's T test or Mann-Whitney's U test for quantitative variables. A p-value < 0.05 was considered statistically significant.

Results: A total of 48 SLE patients, 24 with LN and 24 without LN were included. Mean age of patients with LN was 36.9 ± 10.4 years, compared to 36.5 ± 9.3 years in patients without LN, p = 0.873. There were no significant differences in demographic characteristics between groups (Figure 1). When evaluating echocardiographic parameters we found a significant difference in the left ventricular mass index, higher in LN patients (66.9 g/m^2 vs 54.8 g/m^2, p = 0.035) (Table 1).

Figure 1. Comparison of demographic characteristics between SLE patients with and without LN.

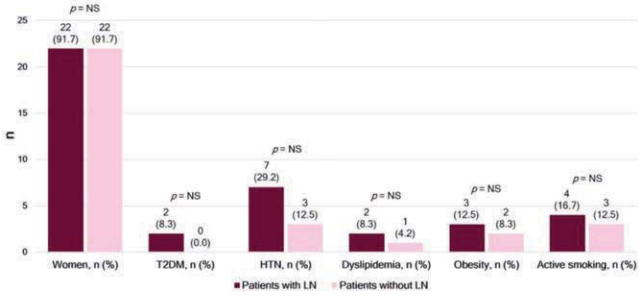

Table 1. Comparison of echocardiographic findings of SLE patients with and without LN.

Variables	Patients with LN (n=24)	Patients without LN (n=24)	p-value
LV mass index, g/m^2, mean ± SD	66.9 ± 21.8	54.8 ± 16.1	**0.035**
RWT, mean ± SD	0.37 ± 0.08	0.34 ± 0.10	NS
LV geometry abnormality, n (%)	7 (29.2)	4 (16.7)	NS
LAESVI, ml/m^2, mean ± SD	29.72 ± 10.80	26.04 ± 8.76	NS
LVEF, %, mean ± SD	58.16 ± 7.42	58.04 ± 7.04	NS
LVESV, ml, median (IQR)	39.0 (26.0-54.5)	32.5 (23.7-39.7)	NS
LVEDV, ml, mean ± SD	92.10 ± 25.09	81.57 ± 27.80	NS

SLE, systemic lupus erythematosus; LN, lupus nephritis; NS, not significant; LV, left ventricular; RWT, relative wall thickness; LAESVI, left atrial end-systolic volume index; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVEDV, left ventricular end-diastolic volume.

Conclusion: SLE patients with LN had higher left ventricular mass index than SLE patients without LN. An increased left ventricular mass could lead to the development of ventricular hypertrophy, which is associated to a higher risk of cardiovascular mortality. A transthoracic echocardiogram should be considered as part of the cardiovascular evaluation of SLE patients, especially those with LN.

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AB0544

LEFT VENTRICULAR GEOMETRY ABNORMALITIES ASSOCIATED WITH DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease. Patients with SLE have higher risk of developing a cardiovascular event than the general population (1), with multiple factors contributing to this increased risk, including systemic inflammation (2).

Objectives: To compare the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and other disease characteristics of SLE patients with and without left ventricular (LV) geometry abnormalities.

Methods: This was a cross-sectional study nested of a SLE cohort. We recruited patients with SLE diagnosis, according to the 2019 EULAR/ACR classification criteria, aged ≥ 18 years. Patients with a previous cardiovascular event, another connective tissue disease or pregnancy were excluded. A transthoracic echocardiogram was performed by two certified echocardiographers blinded to clinical information. Disease activity was assessed with SLEDAI. SLE patients with LV geometry abnormalities were included in this study and matched by age and gender to SLE patients with normal LV geometry by a certified rheumatologist blinded to clinical information. Comparisons were done with Chi-square test or Fisher's exact test for qualitative variables, and Student's T test or Mann-Whitney's U test for quantitative variables. A p-value < 0.05 was considered statistically significant.

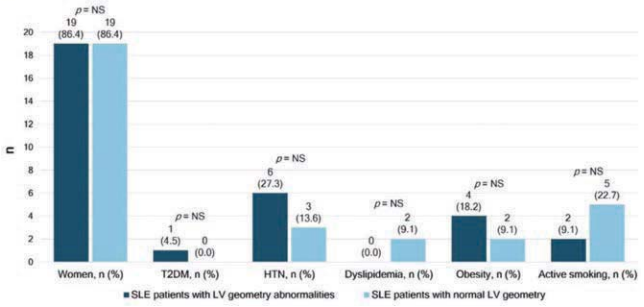
Results: A total of 44 SLE patients were included, 22 patients with LV geometry abnormalities and 22 patients with normal LV geometry. Mean age of SLE patients with LV geometry abnormalities was 35.1 ± 12.2 years, compared to 35.4 ± 9.4 years of SLE patients with normal LV geometry, p = 0.923. The rest of demographic characteristics are shown in Figure 1. When evaluating disease characteristics, the SLEDAI score was significantly higher in SLE patients with LV geometry abnormalities (26.45 vs 17.33, p = 0.016) (Table 1).

Table 1. Comparison of disease characteristics of SLE patients with and without LV geometry abnormalities.

Variables	Patients with LV geometry abnormalities (n=22)	Patients with normal LV geometry (n=22)	p-value
Disease duration, months, median (IQR)	60.0 (12.7-150)	72.0 (43.0-117.7)	NS
SLEDAI, median (IQR)	10.5 (4.0-15.0)	6.0 (2.0-9.0)	**0.016**
CRP, mg/dl, median (IQR)	0.52 (0.33-1.29)	0.60 (0.41-0.85)	NS
ESR, mm/h, median (IQR)	26.0 (13.2-34.2)	29.0 (8.7-58.5)	NS
ANA titers, median (IQR)	640 (160-3200)	480 (160-5120)	NS
Anti-dsDNA, median (IQR)	0 (0-160)	0 (0-200)	NS
C3, mean ± SD	94.6 ± 31.4	100.5 ± 46.1	NS
C4, median (IQR)	13.6 (9.8-14.9)	12.8 (6.4-19.8)	NS
Anti-Ro, median (IQR)	4.5 (2.0-190.5)	3.5 (2.0-82.2)	NS
Anti-La, median (IQR)	2.0 (2.0-4.0)	2.0 (2.0-3.0)	NS
Hydroxychloroquine, n (%)	20 (90.9)	18 (81.8)	NS
Glucocorticoids, n (%)	19 (86.4)	17 (77.3)	NS

SLE, systemic lupus erythematosus; LV, left ventricular; NS, not significant; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ANA, antinuclear antibodies; anti-dsDNA, anti-double stranded DNA.

Figure 1. Comparison of demographic characteristics of SLE patients with and without LV geometry abnormalities.



Conclusion: SLE patients with LV geometry abnormalities had higher SLEDAI score than patients with normal LV geometry. A transthoracic echocardiogram may be useful detect early cardiovascular abnormalities in SLE patients with high disease activity, and therefore should be considered as part of the cardiovascular evaluation of these patients.

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AB0545

THYMUS VARIANTS ON IMAGING IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND POLYMYOSITIS/DERMATOMYOSITIS PATIENTS

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Background: The thymus, a primary lymphoid organ, plays a crucial role in immune system homeostasis [1,2]. Although several studies of an association between radiographic thymus variants and serological features in systemic autoimmune diseases such as systemic scleroderma, have been reported [3-6], information in patients with other systemic autoimmune disease, especially in primary Sjögren's syndrome (pSS) or polymyositis/dermatomyositis (PM/DM) patients, is quite limited.
Objectives: We investigated the association between radiographic thymus variants and clinical and immunological features in patients with pSS and PM/DM, and clarified its significance.
Methods: Patients with pSS and PM/DM were randomly selected from all patients who had visited our department and underwent chest CT scan between April 2009 and March 2019. Patients with thymoma or thymic cyst and those aged less than 30 years were excluded. Thymic enlargement and thymus attenuation score in axial images of CT scans were quantitatively interpreted. We defined thymic enlargement as a thickness of more than 13mm and graded the score by a four-point scale (score 0-3) according to previous studies [7, 8]. Association with radiographic thymus variants and clinical and immunological features was statistically analyzed.
Results: 72 pSS and 47 PM/DM patients were enrolled. 90% and 63.8% were women and mean age was 62.7 ± 12.2 and 56.2 ± 13.7 years in pSS and PM/DM patients, respectively. Thymic enlargement was found in 16 (22.2%) and 14 (29.8%) patients with pSS and PM/DM, respectively. Thymus attenuation (score ≥ 2) was found in 11 (15.3%) and 9 (19.1%) patients with pSS and PM/DM, respectively. These findings were more frequent than in non-connective tissue diseases patients (9.1% and 9.1%, respectively). In pSS patients, radiographic thymus variants, both thymic enlargement and the thymus attenuation score, were significantly positively associated with body weight ($P < 0.0073$ and 0.037, respectively). Although there was no significant difference between immunological features such as titres of serum RF, the ratio of RF-positivity, SS-A antibody-positivity or SS-B antibody-positivity, and radiographic thymus variants, titres of serum RF tended to be positively associated with thymic enlargement ($P = 0.057$). In PM/DM patients, thymic enlargement was significantly positively associated with titres of serum RF ($P = 0.046$), and the thymus attenuation score was significantly positively associated with titres of serum IgG ($P = 0.042$) and significantly negatively associated with age ($P = 0.033$). There was no significant difference between the ratio of myositis specific antibody-positivity and radiographic thymus variants.
Conclusion: Radiographic thymus variants were frequently observed in pSS and PM/DM patients, and particularly, in case of PM/DM, may reflect an abnormal immune response involved in the pathogenesis.
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AB0546

DETERMINANTS OF VASCULITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Among the manifestations of SLE, vasculitic presentation is common. This study was aimed to identify the predictors of vasculitis in SLE patients.
Objectives: To identify the determinants of vasculitis in SLE patients.
Methods: The study was conducted in the Department of Rheumatology, BSMMU, Dhaka from December 2019 to January 2021. A total 168 consecutive confirmed cases of SLE patients were enrolled. The patients were evaluated for the features of vasculitic rashes, digital gangrene, mesenteric vasculitis, mononeuritis multiplex. The cutaneous vasculitis was confirmed by a dermatologist. Study subjects were grouped into vasculitic and no vasculitic groups. The disease activity and damage were assessed using SLEDAI and SLICC/ACR DI. The rate of vasculitis was expressed in percentage. The multivariate logistic regression analysis was done to determine the independent predictors of vasculitis in SLE. P value <0.05 was considered significant.
Results: Rate of lupus vasculitis was 14.3%. The features shown significant difference between vasculitic and no vasculitic groups were: ACLE (79.2% vs. 18.8%, p<0.001), oral ulcer (70.8% vs. 13.2%, p<0.001), alopecia (83.3% vs. 27.1%, p<0.001), Raynaud's phenomenon (20.8% vs. 5.6%, p=0.011), fever (54.2% vs. 25.0%, p=0.002), arthritis (70.8% vs. 29.9%, p<0.001), pregnancy loss (68.8% vs. 32.7%, p=0.003), lupus nephritis (25.0% vs. 45.1%, p=0.032), seizure (8.3% vs. 0.7%, p=0.027), pleurisy (8.3% vs. 0.7%, p=0.027), leucopenia (8.3% vs. 1.4%, p=0.049), anti ds-DNA positivity (87.5% vs. 62.5%, p=0.008), hypocomplementemia (87.5% vs. 59%, p=0.003), higher mean SLEDAI (p<0.001) and SLICC/ACR damage index score (p<0.001). Though not significant the rate of antiphospholipid antibody positivity was high (69.2% vs. 42.9%, p=0.052) in vasculitis group. In multivariate logistic regression analysis, higher SLEDAI score (OR = 1.296, 95% CI =1.114-1.508) was positively and lupus nephritis (OR= 0.055, 95% CI =0.007-0.413) was negatively associated with lupus vasculitis.
Conclusion: In SLE, vasculitic presentation is common. Higher the SLEDAI score greater the chance of lupus vasculitis.
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Table 1. Comparison of clinical features of Lupus vasculitis and without vasculitis (n=168)

Clinical features	Lupus vasculitis (n=24) n (%)	Without vasculitis (n=144) n (%)	p-value
Fever	13 (54.2)	36 (25.0)	**0.002**$^{\gamma}$
SLE specific skin lesions			
ACLE	19 (79.2)	27(18.8)	**<0.001**$^{\gamma}$
SCLE	1 (4.2)	6(4.2)	0.500*
SLE non-specific skin lesions			
Oral ulcer	17 (70.8)	19 (13.2)	**<0.001**$^{\gamma}$
Alopecia	20 (83.3)	39 (27.1)	**<0.001**$^{\gamma}$
Raynaud's	5 (20.8)	8 (5.6)	**0.011***
Arthritis	17 (70.8)	43 29.9)	**<0.001**$^{\gamma}$
Lupus nephritis[a]	6 (25.0)	65 (45.1)	**0.032**$^{\gamma}$
Neuro psychiatric			
Seizure	2 (8.3)	1 (0.7)	**0.027***
Psychosis	1 (4.2)	2 (1.4)	0.186*
Serositis			
Pleurisy	2 (8.3)	1 (0.7)	**0.027***
Pericarditis	1 (4.2)	3 (2.1)	0.231*
Pregnancy loss	11/16 (68.8)	32/98 (32.7)	**0.003**$^{\gamma}$
DVT	1 (4.2)	6 (4.2)	0.500*
APS	3 (12.5)	11 (7.6)	0.213*
AVN	1 (4.2)	2 (1.4)	0.186*
Pulmonary HTN	2 (8.3)	3 (2.1)	0.074*

* Fisher's exact test; γ chi-Square test, $p < 0.05$ is considered statistically significant, n: Number, %: Percent. ACLE: Acute Cutaneous Lupus Erythematosus, SCLE: Sub-acute Cutaneous Lupus Erythematosus, DVT: Deep Vein Thrombosis, APS: Anti Phospholipid Antibody Syndrome, AVN: Avascular necrosis, HTN: Hypertension, a: all diagnosed cases of lupus nephritis, presented with or without flare

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AB0547

PLACENTAL ANGIOGENESIS MARKERS IN THE SCREENING FOR ADVERSE PREGNANCY OUTCOMES IN SLE AND APS

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Background: Pregnancies in patients with systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are at risk for adverse pregnancy outcomes such as preeclampsia or placental insufficiency and prematurity. In these high-risk pregnancies, maternal serum concentration of

the anti-angiogenic factor soluble Fms-like tyrosine kinase-1 (sFlt-1) and the pro-angiogenic factor placental growth factor (PlGF) can predict fetal growth restriction and preeclampsia (1-3).

Objectives: To evaluate the sFlt-1/PlGF ratio in routine assessment of singleton high-risk pregnancies in patients with SLE and APS.

Methods: Patients with SLE and APS that followed in our outpatient clinic were retrospectively analysed for their pregnancy course and outcomes. In these high-risk pregnancies, the sFlt-1/PlGF ratio was measured in the context of screening for preeclampsia and a ratio below 38 was applied to exclude preeclampsia. We compared the sFIT-1/PlGF ratio between patients with and without adverse pregnancy outcome. Adverse pregnancy outcome (APO) was defined as preeclampsia, preterm delivery and small for gestational age newborns.

Results: We analysed sFlt-1/PlGF ratios of 13 singleton pregnancies in 12 patients with SLE and/or APS (4 SLE, 6 SLE with APS or aPL, 2 obstetric APS). Low-dose aspirin was used in all but one pregnancy with de-novo obstetric APS. Low-molecular weight heparin was given in seven pregnancies. Adverse pregnancy outcome occurred in five pregnancies thereof two with preeclampsia. The median sFlt-1/PlGF ratio measured between gestational week 22 and 37 was higher in patients with APO (median 173, range 4 -1904) than in patients without APO (median 7.5, range 1-50) (P=0.03). The sFlt-1/PlGF ratio > 38 was found in 6 pregnancies including two with preeclampsia. Highest sFlt-1/PlGF ratios were found in a case with severe intrauterine growth restriction without signs of preeclampsia (sFlt-1/PlGF=1940) and in a case with early preeclampsia < week 34 (sFlt-1/PlGF=1187). In pregnancies with a sFlt-1/PlGF ratio < 38 there were no signs of preeclampsia or intrauterine growth restriction.

Conclusion: The detection of a dysbalanced sFlt-1/PlGF ratio is clinically useful as it differentiates between pregnancies with adverse outcome and those without. More data are needed to further evaluate the predictive potential of these placental biomarkers in the first trimester and their usefulness for treatment adjustments in order to improve pregnancy outcome.

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AB0548

A COMPARATIVE STUDY BETWEEN THE NEUROPSYCHIATRIC INVOLVEMENTS IN ADULT-ONSET AND CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Neuropsychiatric(NP) manifestations in systemic lupus erythematosus(SLE) encompass a wide spectrum of neurologic and psychiatric features.The nervous system is frequently affected by adult-onset and childhood-onset SLE patients,but disease course and clinical features may differ between both groups.

Objectives: The aim of this study is to evaluate and compare NP manifestations in adult-onset and childhood-onset SLE patients.

Methods: The study included a retrospective analysis of medical records of adult-onset SLE patients and childhood-onset SLE patients following at Hacettepe University from Jan 2015 to Jan 2021.NP events were identified using the ACR established case definitions seen in SLE.Additionally, posterior reversible encephalopathy syndrome, cerebral venous thrombosis, small fiber neuropathy and pseudotumor cerebri were evaluated as having NPSLE in this study.NP were also divided into three categories:neurologic syndromes of the central nervous system, neurologic syndromes of the peripheral nervous system,and diffuse neuropsychological syndromes.

Results: 1062 adult-onset and 161 childhood-onset SLE patients were followed-up median 150 (84-227) months.At least one neuropsychiatric event occurred in 101 (9.51%) adult-onset and 29 (18.01%) childhood-onset SLE patients (p=0.002). NP events were present before or around the time of SLE diagnosis 64.6% of the adult-onset patients and 72.4% of the childhood-onset patients.One-third of the patients in both groups were diagnosed with NPSLE during the follow-up.At the time of NPSLE diagnosis, 60.4% of adult-onset and 86.2% of childhood-onset patients had additional involvement other than neurologic manifestations and overall disease activity(SLEDAI-2k)was higher in childhood-onset patients (17vs.14p=0.036). Almost all patients in the pediatric group and half of the adult patients were given pulse corticosteroids.Cyclophosphamide was the most preferred regimen and was given to 36.6% of the adult patients and 75.9% of the pediatric patients.Rituximab (11.9% and 27.6%) and mycophenolate mofetil (13.9% and 3.4%) were other induction treatments. The adult-onset and childhood-onset NPSLE patients were followed-up median 105(54-165) and 80(40-132) months, respectively.On the last follow-up visit, disease damage scores (SLICC) were similar in both groups,with a median score of 2.

Conclusion: The nervous system was more commonly involved in childhood-onset patients, and disease presentations vary significantly between adult-onset and childhood-onset NPSLE patients.Disease activity appeared to be more severe in children at diagnosis, but permanent organ damage was similar in both groups on follow-up.

Table 1. Demographics, clinical features of adult-onset and childhood-onset NPSLE patients

	Adult-onset NPSLE (n=101)	Childhood-onset NPSLE (n=29)	P value
Cerebrovascular disease	63 (62.4)	8 (27.6)	0.001
Arterial cerebrovascular events	44 (43.6)	5 (17.2)	0.007
Central nervous system vasculitis	25 (24.8)	10 (34.5)	0.209
Parenchymal involvement	18 (17.8)	3 (10.3)	0.256
Demyelinating syndrome	14 (13.9)	2 (6.9)	0.221
Transient ischemic attack	5 (5.0)	-	0.277
Cerebral venous sinus thrombosis	4 (4.0)	6 (20.7)	0.008
Meningeal involvement	5 (5.0)	-	0.277
Posterior reversible encephalopathy syndrome	3 (3.0)	2 (6.9)	0.310
Pseudotumor cerebri	7 (6.9)	3 (10.3)	0.393
Idiopathic intracranial hypertension	2 (2.0)	3 (10.3)	0.073
Lupus headache	38 (37.6)	18 (62.1)	0.017
Acute confusional state	13 (12.9)	4 (13.8)	0.555
Cognitive dysfunction	9 (8.9)	1 (3.4)	0.299
Seizure disorders	31 (30.7)	11 (37.9)	0.302
Movement disorder (chorea)	4 (4.0)	2 (6.9)	0.402
Myasthenia gravis	3 (3.0)	-	0.466
Cranial neuropathy	7 (6.9)	3 (10.3)	0.393
Optic neuritis	4 (4.0)	1 (3.4)	0.690
Peripheral polyneuropathy	9 (8.9)	5 (17.2)	0.173
Mononeuritis multiplex	1 (1.0)	-	0.777
Myelopathy	5 (5.0)	2 (6.9)	0.489
Autonomic dysfunction	-	-	-
Small fiber neuropathy	1 (1.0)	-	0.777

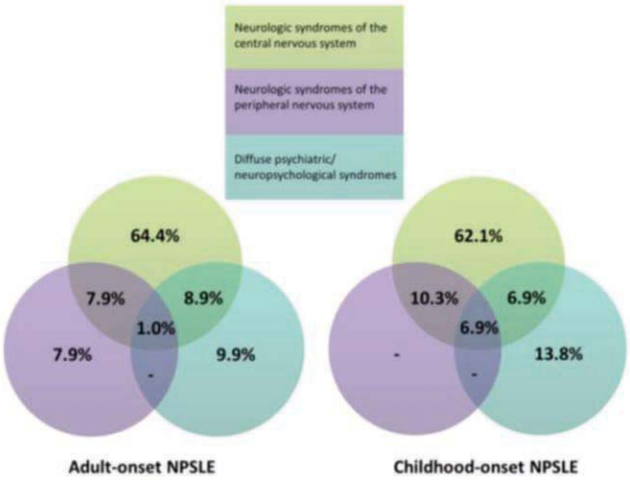

Figure 1. Distribution of adult-onset and childhood-onset NPSLE patients

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AB0549

OBESITY AND TOBACCO SMOKING ARE INDEPENDENTLY ASSOCIATED WITH POOR PATIENT-REPORTED OUTCOMES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS FROM A SWEDISH TERTIARY REFERRAL CENTRE

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Background: Patients with systemic lupus erythematosus (SLE) experience impaired health-related quality of life (HRQoL), pain, fatigue and functional disability. The effect of pharmacotherapy on these aspects has been inconclusive in literature. In light of this, investigation of the impact of lifestyle facets is needed to support complementary non-pharmacological interventions such as weight control strategies and tobacco smoking cessation.
Objectives: To evaluate associations of obesity and tobacco smoking with SLE patients' HRQoL, pain, fatigue and functional disability.
Methods: Patients from the Linköping University Hospital with an SLE diagnosis according to the 1982 American College of Rheumatology (ACR) and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria (n=325) were included in the present cross-sectional analysis of data captured at visits between January 2008 and September 2021. Among consecutive visits, the first visit with complete demographic, clinical and patient-reported data was selected for the present analysis.
Body mass index (BMI) categories were based on the World Health Organization classification: underweight (BMI <18.5 kg/m^2), normal weight (18.5≤ BMI <25 kg/m^2), pre-obesity (25≤ BMI <30 kg/m^2) and obesity (BMI ≥30 kg/m^2). Smoking status was self-reported and categorised into never, prior and current smoking.
HRQoL was self-reported using the 3-level EuroQoL 5-Dimension (EQ-5D-3L) index scores. Visual analogue scales (VAS; 0–100) were used to self-report fatigue, pain and well-being within the preceding 7 days. Functional disability was evaluated using the Swedish version of the Health Assessment Questionnaires Disability Index (HAQ-DI). Disease activity was evaluated using the clinical (c) SLEDAI-2K (serology excluded).
Comparisons of continuous data between different BMI and smoking categories were performed using the Mann-Whitney U test and Kruskal-Wallis test. Multivariable linear regression analysis was employed to assess independence and priority of contributors to HRQoL and functional impairment.
Results: Compared with normal weight, obese individuals reported lower EQ-5D-3L index score [0.73 (0.36–0.80) versus 0.78 (0.68–0.85); P=0.014], as well as higher VAS fatigue [50.0 (27.0–72.5) versus 32.0 (6.5–59.5); P=0.008], VAS pain [40.0 (11.0–67.0) versus 20.5 (5.3–46.5); P=0.011] and HAQ scores [0.63 (0.13–1.13) versus 0.13 (0.0–0.63); P<0.001]. Similarly, ongoing smokers reported higher VAS fatigue [56.0 (28.0–78.0) versus 32.0 (8.0–58.0); P=0.001], VAS pain [45.0 (18.0–62.0) versus 18.0 (5.0–39.8); P=0.001] and HAQ scores [0.63 (0.13–1.13) versus 0.13 (0.0–0.63); P=0.001] compared with individuals who were never exposed to regular tobacco smoking. There were no differences across groups regarding cSLEDAI-2K scores.
In multivariable linear regression models, obesity and current tobacco smoking were independently associated with lower EQ-5D-3L index scores (β=-0.12; P=0.021 and β=-0.11; P=0.029, respectively), and higher VAS fatigue (β=12.8; P=0.007 and β=17.5; P<0.001), VAS pain (β=12.1; P=0.004 and β=15.5; P<0.001), VAS well-being (β=9.6; P=0.028 and β=9.8; P=0.035) and HAQ scores (β=0.30; P=0.001 and β=0.27; P=0.007), but not with cSLEDAI-2K (β=-0.73; P=0.189 and β=0.34; P=0.572).
Conclusion: In a Swedish SLE population, obesity and ongoing tobacco smoking were independently associated with worse outcomes - compared with normal weight and individuals who never smoked, respectively - regarding HRQoL, fatigue, pain and functional disability but were not associated with clinical disease activity.
Disclosure of Interests: None declared
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AB0550

CLINICAL AND PROGNOSTIC SIGNIFICANCE OF ANTINUCLEAR ANTIBODIES IN PRIMARY ANTIPHOSPHOLIPID SYNDROME: FRENCH MULTICENTER RETROSPECTIVE STUDY

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Background: The antiphospholipid syndrome (APS) is defined by the development of vascular thrombosis, or pregnancy morbidity in the presence of persistent antiphospholipid antibodies (APL). Antinuclear antibodies (ANA) can be detected in primary APS patients without any clinical systemic autoimmune disease. The presence of ANA antibodies could confer a specific phenotype in primary APS.
Objectives: To evaluate the characteristics of APS patients with antinuclear antibodies without other autoimmune disease (ANA-positive APS patients) in comparison with primary APS without ANA (ANA-negative APS) or secondary APS patients with associated systemic lupus erythematosus (SLE-APS).
Methods: Clinical and biologic data from 195 APS were retrospectively collected. ANA test was considered to be positive when titers were superior or egal to the 1/80 dilution. ANA-positive APS patients did not fulfilled SLE ACR/EULAR classification criteria.
Results: 40 patients (21%) with ANA-positive APS were included, 77 patients (39%) with primary APS without ANA autoantibodies (ANA-negative APS) and 78 patients (40%) with SLE-associated APS (SLE-APS). Patients with ANA-positive APS presented arterial thrombosis in 20 cases (51%) and venous thrombosis in f 14 cases (41%), adverse obstetrical in 19 cases (51%), non-criteria APS features were noted in 19 cases (51%). ANA-positive APS patients had more non criteria manifestations than ANA-negative APS (48% versus 25%; p=0.01). ANA-positive APS patients had more triple APL positivity and more thrombosis recurrences in comparison with ANA-negative APS patients, respectively (59% versus 18%; p<0.001) and (63% versus 36%; p<0.01). ANA-positive APS and SLE-APS patients had similar clinical manifestations and recurrences. Despite a limited follow-up (28 months (11-50)) none of the ANA-positive APS patients develop SLE. Antiplatelet and anticoagulant therapies were similar for the three groups. SLE-APS patients received more immunomodulatory therapies.
Conclusion: ANA positivity in patients with APS enables to individualize a subset of patients with a more severe phenotype. Whereas the ANA positivity does not seem to be associated with the risk to develop SLE, prospective studies with a longer follow-up are necessary, in particular to evaluate the effect of additional therapies in this subset of APS.

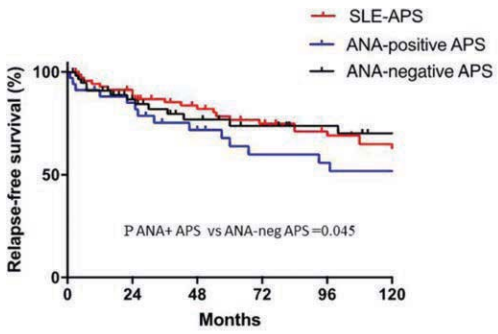

Figure 1 Comparison of relapse free survival

Disclosure of Interests: None declared
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AB0551

CUTANEOUS LUPUS AREA AND SEVERITY INDEX(CLASI) CORRELATES WITH SELF-IMAGE SCORE BUT NOT QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) has multi-system involvement including skin. We explored how skin involvement influenced with the quality of life of patients with SLE.
Objectives: To correlate the domains of SLE QoL with skin involvement and total lupus disease activity.
Methods: A cross-sectional survey of patients with SLE was carried out to assess Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) and SLE-QoL. Lupus disease activity and damage were quantified using Mex-SLEDAI (Mexican SLE Disease Activity Index) and SLICC (Systemic Lupus International Collaborating Clinics) Damage Index respectively. Data is expressed as median (IQR).

Table 1. Correlations between different domains of the SLE(Systemic Lupus Erythematosus) -QoL(Quality of Life) with CLASI (Cutaneous Lupus Area and Severity Index) and Mexican SLE-DAI(SLE Disease Activity Index).

SLE-QoL Domains	Physical functioning	Physical activity	Symptoms	Treatment	Mood	Selfimage	Total
CLASI Activity	.028 (p=0.87)	-.062 (p=0.73)	.242 (p=0.16)	.103 (p=0.56)	.113 (p=0.52)	.252 (p=0.15)	.102 (p=0.56)
CLASI Damage	.125 (p=0.47)	.010 (p=0.95)	.257 (p=0.13)	.239 (p=0.17)	.233 (p=0.18)	.446** (p=0.007)	.243 (p=0.16)
CLASI total	.047 (p=0.80)	-.062 (p=0.75)	.448* (p=0.013)	.331 (p=0.07)	.332 (p=0.07)	.315 (p=0.09	.281 (p=0.13)
Mexican SLEDAI SCORE	.001 (p=0.99)	.130 (p=0.47)	.390* (p=0.025)	.251 (p=0.16)	.115 (p=0.52)	.197 (p=0.27)	.200 (p=0.27)

Results: In the cohort of 35 patients with SLE, with an age of 26(IQR:17-32) years and including eight (22.8%) males, the CLASI score was 5.5(IQR:3-11.5) with an activity score of 3(1-5) and a chronicity score of 1(0-4). The disease duration was 4years (IQR: 2-3) while SLE-QoL was 73(62-86). Overall, most of the patients had active disease at inclusion with a mex-SLEDAI of 8(6.5-11.5). SLICC was 1(0-4).

The correlation matrix of different domains of the SLE-QoL with CLASI, and Mex-SLEDAI is presented in Table 1. Correlation with SLICC was not analysed since it was zero in the majority of participants. Multivariate analyses were not done since there was lack of association on univariate analysis.

Conclusion: In this cohort of patients with active SLE, the SLE-QoL did not correlate with either the overall disease activity score nor the skin specific score. Only the Self-image domain correlated with the skin score. This implies that in active disease, the skin involvement may have only a minor effect on the quality of life.

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AB0552 ELEVATED KYNURENINE LEVELS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Sjögren's syndrome (SS) is a chronic autoimmune systemic inflammatory disease of unknown origin that predominantly affects the exocrine glands (mainly salivary and lacrimal glands). Primary Sjögren's syndrome (pSS) is a disease whose etiology is not yet fully understood, as in most autoimmune diseases, where genetic, epigenetic and environmental factors are hypothesized to play to the pathogenesis of the disease. Metabolism of tryptophan (Trp) via the kynurenine (Kyn) pathway has been proposed to act a substantial role in inflammatory processes.

Objectives: In the present study, we investigated levels of Trp and its metabolites in the Kyn pathway in patients with pSS and in healthy controls. Also, the relationship between Trp metabolites and laboratory parameters, disease activity was evaluated in patients with pSS.

Methods: The study included 34 pSS patients and 42 healthy individuals, and serum Trp and Kyn concentrations were measured by liquid chromatography with tandem mass spectrometry (LC-MS/MS). Trp degradation was predicted using the ratio of Kyn and Trp concentrations (Kyn/Trp). The EULAR Sjögren's syndrome disease activity index (ESSDAI) and the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) were used to evaluate pSS activity.

Results: In our study, the mean serum Trp concentration was found to be considerably lower in the pSS group compared to the control group (p= 0.001). The levels of Kyn (p= 0.019) and Kyn/Trp ratio (p <0.001) were significantly higher in the pSS group compared to the control group (Table 1). Trp concentration was negatively correlated with physician global assessment (r=-0.568, p<0.001), positively correlated with albumin (r=0.384, p=0.025) and hemoglobin (p=0.396, r=0.020). The Kyn/Trp ratio was negatively correlated with CRP (r=-0.369, p=0.032). There was no correlation between the Trp pathway and disease activity parameters ESSDAI and ESRPI.

Table 1. Comparison of the kynurenine pathway results of patients with Sjögren's syndrome and the controls

	Sjögren's syndrome (n=34) median (IQR)	Control(n=42) median (IQR)	p
Kynurenine (ng/ml)	485 (378-601)	386 (356-496)	**0.019**
Tryptophan (ng/ml)	10660 (9160- 12282)	12258 (11442-14711)	**0.001**
Kynurenine/tryptophan ratio (%)	4 (3-6)	3 (3-4)	**<0.001**

*Mann-Whitney U test

Conclusion: In conclusion, we found that kynurenine pathway metabolism was altered in patients with pSS. This suggests that tryptophan metabolism may be closely linked to the disease pathogenesis of pSS.

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AB0553 KIDNEY BIOPSY IN FIRST RENAL FLARE OF SLE – WHAT DOES IT TELL US?

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Background: Lupus Nephritis (LN) is an immune-complex mediated glomerulonephritis affecting up tp 60% of all SLE patients during the disease course. A kidney biopsy is indicated in SLE patients presenting with signs of renal involvement, such as persistent proteinuria, and is generally recommended to evaluate the inflammatory findings but also to rule out other etiologies of renal involvement and to guide the need of immunosuppressive therapy.

Objectives: To investigate the histopathologic findings in first-time renal biopsies from a large cohort of SLE patients. We especially evaluated the type and occurrence of histopathological findings other than LN as these may lead to a risk of inadequate therapeutic interventions.

Methods: Patients from the Karolinska SLE cohort who had a first-time onset of renal involvement from 1995 to 2021 and subsequent renal biopsy were included in the study. All patients fulfilled the American College of Rheumatology (ACR) and/or Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) disease classification criteria (1, 2) for SLE and were biopsied on clinical indication, i.e., proteinuria > 0.5 g/day or active SLE in combination with a rise in plasma creatinine, decrease in glomerular function or new onset proteinuria with concurrent active urine sediment.

Results: In total, 141 patients with first time presentation of renal involvement who had been subject to renal biopsy were included. Of these 107 patients (75.9 %) were female. The median age at the time of biopsy was 34.5 years (range 15.5 - 86.4). For more patient baseline characteristics, see Table 1. One-hundred twenty-five patients (88.7 %) had findings consistent with LN according to ISN/RPS classification system. Twenty-five patients (18.4 %) had class I - II, 43 (30.5 %) class III ± V, 31 (22.0 %) class IV ± V and 26 (18.4 %) class V. Sixteen patients (11.3 %) did not have histological changes in accordance with LN. Of these, 3 had hypertensive nephrosclerosis, 2 had antiphospholipid associated nephropathy, 1 had IgA nephropathy, 1 had tubulointerstitial nephritis and 7 had evidence of systemic vasculitis. Of these, 5 were later found to be ANCA-positive and were re-diagnosed with concomitant ANCA-associated vasculitis. Two patients did not

show any classifiable histological changes. Of the 16 non-LN patients, 6 had proteinuria > 0.5 g/day, 2 had new-onset low-grade proteinuria and concurrent active urine sediment, 2 had new-onset low-grade proteinuria with concurrent increasing SLE disease activity, and 5 patients had isolated persistent low-grade proteinuria. In one case data was missing.

Table 1. Baseline characteristics, 141 patients

Age at SLE diagnosis (years); M (IQR)	**32.2 (22.0 – 44.9)**
SLE duration at biopsy (years); M (IQR)	0.6 (0.2 – 5.3)
Systolic blood pressure (mm Hg); Mean (SD)	127.5 (20.8)
Ethnicity	
Caucasian; n (%)	119 (84.4)
Asian; n (%)	9 (6.4)
African; n (%)	7 (5.0)
Hispanic; n (%)	6 (4.3)
Prednisone equivalent dose (mg/day); M (IQR)	10.0 (0–20.0)
Diagnosis according to ISN/RPS	
Class I-II	25 (17.7)
Class III ± V	43 (30.5)
Class IV ± V	31 (22.0)
Class V ± II	26 (18.4)
TMA/antiphospholipid syndrome	2 (1.4)
Vasculitis	7 (5.0)
Hypertensive nephrosclerosis	3 (2.1)
IgA nephropathy	1 (0.7)
Tubulointerstitial nephritis	1 (0.7)
Nonspecific changes	2 (1.4)

Conclusion: We demonstrate that renal histopathology confirmed other causes than LN in a significant proportion (11.3 %) of SLE patients with signs of renal involvement. Since these patients may need other therapeutic interventions than patients with classic LN, we can conclude that the renal biopsy is important in order to guide the choice of therapeutics.

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AB0554 CLINICAL CHARACTERISTICS AND BURDEN AMONG PATIENTS WITH SLE STRATIFIED BY SLEDAI DERIVED SEVERITY: RESULTS FROM A REAL-WORLD STUDY IN THE US

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Background: Data are limited concerning the distribution of Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores among patients with SLE in clinical practice and the characteristics of patients with specific SLEDAI scores.

Objectives: To investigate SLE patient demographics, clinical status, treatment patterns, and patient reported outcomes (PROs), overall and stratified by SLEDAI score.

Methods: Data were drawn from the Adelphi Real World Lupus IV (2021) Disease Specific Programme™, a point-in-time survey of 79 US rheumatologists and patients with SLE. Rheumatologists completed questionnaires regarding patient demographics, clinical status, and treatment. The same patients were invited to complete questionnaires containing the EuroQoL 5-Dimensions (EQ-5D), Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-Fatigue) and Work Productivity & Activity Impairment questionnaire (WPAI) Patient-Reported Outcomes (PRO) tools.

Physicians completed 24 questions based on the SLEDAI-2K questionnaire regarding their patients' current clinical manifestations, from which a SLEDAI score was derived[1]. Patients were grouped based on their score: SLEDAI=0 (none), SLEDAI=1-6 (mild), SLEDAI=7-12 (moderate), and SLEDAI>12 (severe)[2]. Data from patients without rheumatologist-perceived renal organ involvement and ≥ 1 year of SLE duration were included for analysis using bivariate tests.

Results: A total of 273 patients were included in this analysis. Mean [SD] patient age was 47.0[14.2] years, 83.9% were female, 57.1% were White/Caucasian, and 24.9% were African American.

Conclusion: A disconnect between point-in-time SLEDAI and physician-perceived severity exists. Patients with SLE, irrespective of SLEDAI, had high prevalence of joint symptoms, but higher SLEDAI impacted quality of life.

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AB0555 SYMPTOMATIC NON-SEROSITIC LUNG INVOLVEMENT IN A MONOCENTRIC COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A REAL-LIFE EXPERIENCE

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Background: A growing interest has been addressed to the study of lung involvement in systemic autoimmune diseases. Non-serositic pulmonary manifestations have also been described in SLE. However, little is known about their exact prevalence, clinical features and outcomes.

Objectives: To describe the prevalence, clinical and immunological characteristics of symptomatic non-serositic lung involvement in a monocentric cohort of SLE patients.

Methods: This observational, retrospective study included patients with SLE, regularly followed at the Rheumatology Unit of Pisa, that presented a clinically relevant non-serositic pulmonary involvement during their disease history. Patients with lung manifestations related to other causes (e.g. infections,

Table 1. Point-in-time clinical status, treatment patterns and PROs among patients with SLE stratified by SLEDAI score

Table 1.		**Total Sample (n=273)**	**SLEDAI=0 (n=60, 22%)**	**SLEDAI=1-6 (n=79, 28.9%)**	**SLEDAI=7-12 (n=70, 25.6%)**	**SLEDAI>12 (n=64, 23.4%)**	**p value**
Physician-Reported Clinical Status and Treatment History							
Current SLE severity, n(%)	Mild	221 (81.0)	51 (85.0)	70 (88.6)	53 (75.7)	47 (73.4)	0.057
	Moderate	49 (18.0)	9 (15.0)	9 (11.4)	16 (22.9)	15 (23.4)	
	Severe	3 (1.1)	0 (0.0)	0 (0.0)	1 (1.4)	2 (3.1)	
Current joint symptoms, n(%)	Joint tenderness	109 (39.9)	24 (40.0)	27 (34.2)	28 (40.0)	30 (46.9)	0.498
	Joint stiffness	121 (44.3)	22 (36.7)	33 (41.8)	37 (52.9)	29 (45.3)	0.293
	Joint swelling	60 (22.0)	17 (28.3)	13 (16.5)	19 (27.1)	11 (17.2)	0.190
Mean [SD] Flares in the last 12 months		1.6 [1.5]	1.3 [1.2]	1.7 [1.7]	1.5 [1.3]	1.8 [1.5]	0.550
Currently prescribed, n(%)	Belimumab	58 (21.3)	14 (23.3)	18 (12.9)	8 (10.1)	15 (21.4)	0.011
	Immunosuppressants	48 (17.6)	7 (11.7)	26 (18.6)	10 (12.7)	13 (18.6)	0.052
	Corticosteroids	138 (50.6)	35 (58.3)	62 (44.3)	29 (36.7)	32 (45.7)	0.003
	Antimalarials	206 (75.5)	28 (46.7)	108 (77.1)	64 (81.0)	59 (84.3)	<0.001
Patient-Reported Outcomes							
Mean [SD] EQ5D-5L Utility score (0=death to 1= full health)		0.79 [0.19]	0.83 [0.12]	0.82 [0.21]	0.79 [0.14]	0.69 [0.25]	0.024
Mean [SD] FACIT-Fatigue score (0=worst fatigue to 52= no fatigue)		32.7 [12.2]	36.8 [8.7]	36.1 [12.5]	29.1 [9.8]	26.4 [14.3]	<0.001
Mean [SD] WPAI overall (0= no impact to 100= completely impacted)		26.8 [21.2]	25.2 [15.8]	19.5 [23.6]	35.7 [20.2]	31.9 [26.7]	0.131

49% of SLE patients were categorized as SLEDAI 7-12 or >12 (moderate or severe). Among the SLEDAI 7-12 (moderate) patients, 75.7% were subjectively categorized by their physician as having mild SLE. Of the SLEDAI >12 patients (severe), 73.4% were categorized as having mild SLE. Joints symptoms and flaring in the last 12 months were not significantly different across SLEDAI groups. Patients with greater SLEDAI reported lower EQ5D and greater FACIT-Fatigue scores. There was no statistical difference in WPAI between the SLEDAI groups.

emphysema, Chronic Obstructive Lung Disease, bronchial asthma etc.) were excluded. The following data were collected from clinical charts: demographics, smoke exposure, comorbidities, respiratory symptoms, disease duration and disease activity (SELENA-SLEDAI) at the onset of lung involvement, immunological profile, treatment, CT and spirometry parameters.

Results: Over 450 SLE patients in regular follow-up, we found 11 female patients with a history of clinically relevant non-serositic lung involvement: 7 interstitial lung disease (ILD), 2 acute lupic pneumonitis (ALP), 1 diffuse alveolar hemorrhage (DAH) and 1 shrinking lung syndrome. 45.4% of patients had a history of smoke exposure and had stopped smoking on average 9 years before the onset of lung manifestations. For the 2 patients with ALP, this was the first manifestation of SLE. Among the other 9 patients, lung involvement was diagnosed after a mean disease duration of 14 ± 15 years. At the diagnosis of pulmonary involvement, 10/11 patients presented respiratory symptoms and an overall active disease, with a median SLEDAI of 9 (IQR 6-13). Clinical characteristics are summarized in Table 1. All patients were hospitalized and 2 of them (1 ALP and 1 DAH) were admitted in intensive care unit.

Table 1. Clinical characteristics at the diagnosis of lung involvement

Systemic	Active skin manifestations	36%
	Arthritis	36%
	Fever	36%
	Leukopenia	36%
	Hypocomplementemia	91%
	Anti-dsDNA positivity	36%
Respiratory	Dyspnea	54%
	Exertional dyspnea	18%
	Cough	45%
	Acute respiratory failure	27%

As for the immunologic profile, SSA/Ro60 were positive in 72% of patients and SSA/Ro52, SSB, U1-RNP in 36%; 36% had Sjogren Syndrome (SS) in overlap.

Spirometry was available for 6/11 patients: a restrictive pattern and a moderate/severe reduction of diffusing capacity of the lung for carbon monoxide was found in 5 patients.

In the ILD subgroup, the most prevalent CT pattern was the Non-specific interstitial pneumonia (NSIP) (5/7). 2 patients presented a Bronchiolitis obliterans/organizing pneumonia (BOOP) pattern.

Lung involvement was the driving manifestation in the treatment choice for 6/11 patients: 1 DAH, 2 ALP, 1 Shrinking lung and 2 ILD. All received pulse steroids and in 3 cases (2 ILD and 1 DAH) cyclophosphamide was added for the induction treatment; the patient with Shrinking lung had an overlap SS and was treated with Rituximab.

At last visit (mean follow-up of 8 ± 8.7 years since lung disease onset), 7/11 patients presented no respiratory symptoms and a complete resolution of CT alterations. 3/11 presented a residual exertional dyspnea and mild spirometry alterations. No patients developed respiratory insufficiency; only 1 patient died for cardiovascular complications.

Conclusion: In our large cohort of SLE patients, non-serositic lung involvement seems to be overall rare; the most frequent type of lung manifestation is ILD which appears to be associated with anti-SSA/SSB and anti-U1RNP positivity. The low prevalence of lung involvement (2.4%) in our cohort could be due to the presence of patients with a subclinical involvement. Further studies are needed to assess the real prevalence of subclinical lung manifestations in SLE and to identify the clinical phenotype of patients more prone to develop pulmonary disease.

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AB0556 CHARACTERISTICS OF PATIENTS DIAGNOSED WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE

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Background: Patients with undifferentiated connective tissue disease (UCTD) struggle with physical symptoms as well as diagnostic uncertainty.[1] UCTD diagnosis requires exclusion of other connective tissue diseases (CTD). Prior studies use variable definitions of UCTD that do not account for updated classification criteria thus limiting generalizability.

Objectives: We identified characteristics associated with rheumatologist-diagnosed UCTD, applied strict exclusion criteria, and compared UCTD patients to those with criteria-defined CTD.

Methods: We recruited patients ≥18 years old seen between 2018-2022 who had rheumatologist-diagnosed UCTD with positive ANA and ≥1 sign/symptom of a CTD. We reviewed medical records to identify those who fulfilled ACR/EULAR-endorsed classification criteria for SLE, RA, SSc, Primary Sjögren's, Idiopathic Inflammatory Myopathy, and 2006 Revised Sapporo Criteria for APS. We compared sociodemographic, clinical, serologic, and treatment variables between UCTD and CTD using chi-square, Fisher's exact, and t-tests.

Results: Of 89 patients with rheumatologist-diagnosed UCTD (mean age 49.0 ± 13.7 years, 97.8% female, 66.3% White), 59 (66.3%) had UCTD and 30 (33.7%) had criteria-defined CTD (27 SLE, 3 SLE and RA, 1 RA, and 1 APS).

Patients in both groups had similar non-criteria manifestations, most commonly arthralgia (89.8% UCTD vs. 83.3% CTD, p=0.50) and fatigue (55.9% UCTD vs. 73.3% CTD, p=0.17). Compared to patients with CTD, those with UCTD were less likely to have nonerosive arthritis (27.1% vs. 56.7%, p=0.01) (Table 1).

Table 1. Characteristics of Patients with UCTD or Criteria-Defined CTD

	UCTD[1] (n=57), N (%)	CTD[2] (n=32), N (%)	p-values
Clinical[3,4]			
• ,4nicalN (%))cs of Pa	16 (27.1)	17 (56.7)	0.01
• .0156.7) (%))cs of Patients with UCTD or Criteria	31 (52.5)	18 (60.0)	0.65
• .6560.0) (%))cs of Patient	7 (11.9)	4 (13.3)	1.0
• .013.3)) (%))cs of Patients with UCTD or Criteria-Defined C	27 (45.8)	14 (46.7)	1.0
• .0(46.7) (%))cs of Patien	24 (40.7)	11 (36.7)	0.82
Serology[3]			
• erology) (%))cs of Patients with UCTD or Criteria-Defined CTDth	19 (32.2)	19 (63.3)	<0.01
• 0.013.3) (%))cs of Patien	9 (15.3)	13 (4.3)	<0.01
• 0.01.3)) (%))	22 (37.3)	25 (83.3)	<0.01
• 0.013.3) (%))cs of Patients w	10 (16.9)	6 (20.0))	0.77
• .770.0)) (%))cs of Patients with UCTD or Criteria-D	6 (10.2)	2 (6.7)	0.71
• .71.7))) (%))cs of Patients with UCTD or Criteria-Defined CTDther CTDs. Our fi	18 (30.5)	10 (33.3)	0.81
• .8133.3) (%))cs	11 (18.6)	6 (20.0)	1.0

1. Do not fulfill ACR/EULAR classification criteria for SLE, RA, SSc, PSS, IIM, APS
2. Diagnosed with UCTD and fulfill ≥1 set of listed CTD classification criteria.
3. Defined per listed classification criteria.
4. Criteria with n≤5: fever, proteinuria/cellular casts, pulmonary hypertension, interstitial lung disease, dysphagia/esophageal dysmotility

Patients with UCTD were less likely than those with CTD to have any hematologic manifestation (lymphopenia, leukopenia, thrombocytopenia, or hemolytic anemia) (p=0.02), anti-dsDNA or anti-Smith antibodies (p<0.01), or hypocomplementemia (p<0.01). The frequency of RA, Sjogren's, and APS-related serologies did not differ between groups (Table 1**).** Compared to those with CTD, UCTD patients were less likely to have ever received systemic corticosteroids (71.2% vs. 96.7%, p<0.01); ever use of any disease-modifying antirheumatic drug (DMARD) was similar (35.6% vs. 46.7%, p=0.36).

Conclusion: Among patients diagnosed with UCTD, 66.3% met a stringent definition. Compared to those with criteria-defined CTD, UCTD patients had lower frequency of arthritis, hematologic abnormalities, SLE-specific antibodies, and hypocomplementemia. While use of DMARDs did not differ, UCTD patients were less likely to use systemic corticosteroids. Rheumatologists diagnose UCTD even when criteria are met for other CTDs. Our findings suggest UCTD is nonetheless a distinct clinical entity; more rigorous characterization will enable generalizable prognostic and therapy trials.

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AB0557 THE SPECTRUM OF PEDIATRIC LUPUS: DATA FROM THE KENYA PEDIATRIC RHEUMATOLOGY (KAPRI) REGISTRY

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Background: Childhood-onset systemic lupus erythematosus (cSLE) is a prototype autoimmune condition characterized by systemic organ involvement, high morbidity and mortality (1-5). A pediatric rheumatology registry is critical in defining the spectrum of pediatric lupus within the region The **Kenya Pediatric Rheumatology**

Table 1. Clinico-epidemiological features of paediatric Lupus patients

Patient	Gender	Age	End Organ Involvement	Autoantibody profile	Treatment	Current Clinical Status
1	Female	14 years	Arthritis	ANA +ve Antiphospholipid antibody +ve (B2 glycoprotein IgA)	Declined treatment of Hydroxychloroquine and Methotrexate to seek 2nd opinion	Lost to follow up
2.	Female	14 years 9 months	Skin	ANA +ve Anti ds DNA +ve	Hydroxychloroquine	Lost to follow up
3.	Female	11years	Arthritis Interstitial Lung Disease	ANA+ve >1:640 (fine granular) Anti Rib +ve Anti P protein +ve Anti SSA +ve	Mycophenolate Mofetil Hydroxychloroquine Prednisone 1 dose of Rituximab	Stable with minimally active disease
4.	Female	15 years 2 months	Lupus Gangrene	ANA +1:640 (Homogenpous) Anti Sm +ve Anti RNP +ve Anti ds DNA +ve Anti nucleosome+ve Anti ribosome +ve	Cyclophosphamide Mycophenolate Mofetil Aspirin	Lost to follow up
5.	Female	8 years 7 months	Neurolupus Lupus Gangrene	ANA +VE 1:640(speckled) Anti Sm +ve Anti RNP +ve Anti Ribosome +ve	Cyclophosphamide (6 courses) Rituximab (2 courses) Mycophenolate Mofetil Prednisone Hydroxychloroquine	Minimally Active Disease
6.	Female	6 years 11 months	Arthritis Skin rash Class IV Lupus Nephritis	ANA+VE (1:320 homogenous) Anti ds DNA +ve Anti nucleosome +ve	Mycophenolate Mofetil Hydroxychloroquine Prednisone	Minimally Active Disease
7.	Female	14 years 6 months	Class II Lupus Nephritis	ANA VE 1:320 (Homogenous)	Mycophenolate Mofetil Hydroxychloroquine	Remission

Registry (KAPRI) registry offers a unique opportunity to pioneer and spearhead a systematic and organized format in collecting pertinent clinical information that will offer information on current clinical scenarios and offer a platform to conduct other research projects to improve pediatric lupus healthcare in sub-Sahara Africa.

Objectives: Our objective was to determine the clinic-epidemiological profile of paediatric lupus patients by describing their baseline patient characteristics and clinical features at the Aga Khan University Medical College East Africa who were enrolled into the KAPRI registry from inception in March 2019 to December 2021.

Methods: All patient records were selected from the KAPRI registry database using the ICD 10 code M32 that denotes Systemic Lupus Erythematosus (SLE) Age, gender, laboratory, clinical features at diagnosis, treatment options offered at time of diagnosis were extracted from the database.

Results: Among the 207 patients enrolled thus far in the registry, 7 had a diagnosis of cSLE (3.4%). The commonest symptom among the patients were joint pain, fever and rash. Other clinical features and outcomes are highlighted in the Table 1.

Conclusion: Over a 2 year period, 57% of our cSLE patients (4 of 7) achieved remission while 43% (3of 7) were lost to follow up. Further studies are required to elucidate predictors of good clinical response and reasons for loss to follow up among our cSLE patients.

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AB0558 PREVALENCE OF LATENT TUBERCULOSIS INFECTION AND ITS ASSOCIATIONS WITH CLINICAL AND SEROLOGICAL PARAMETERS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) and Tuberculosis are complicatedly related and studies have shown increased risk of TB in SLE. Studies of Latent TB and SLE are inadequate. This study intended to assess the prevalence of latent TB and its association with disease parameters in SLE.

Objectives: To assess the prevalence of latent TB in patients with SLE. To investigate the demographics and clinical characteristics in patients with SLE and concomitant latent TB compared to those without.

Methods: This is a single center cross sectional study. 124 adult patients with SLE without past h/o TB were recruited. SLE demography, disease activity indices, autoantibody profile and steroid use were noted. Presence of Latent TB infection was assessed in all patients based on the IFN-g release assay (TB-IGRA). Based on the results of IGRA, SLE cases were divided into 2 groups-IGRA positive and IGRA negative. The collected parameters were compared between the 2 groups.

Results: Among 124 patients, 19 had latent TB resulting in a point prevalence of 15.4 %. The average disease duration was 4.3 years in IGRA positive and 4.6 in IGRA negative group(p>0.05). Among antibody profile, though no statistical significance among the groups, proportion of antibodies like anti Ku, Ro 60, Ro 52 and La were numerically higher in the IGRA positive group (21.1%, 42.1%, 42.1% and 21.1% respectively) when compared to the IGRA negative group (11.5%, 28.8%, 28.1% and 7.7% respectively). Likewise, anti nucleosome, histone, U1RNP, PCNA, aCLA IgG and IgM, beta 2 GPI IgG and LAC were numerically higher in IGRA negative group (42.3%, 40.4%, 43.3%, 8.7%, 23%, 18.3%, 28.8%, 14.4%) when compared to IGRA positive group (31.6%, 21.1%, 31.6%, 0, 15.8%, 5.3%, 15.8%, 5.3%). Mean clinical SLEDAI was 2.37 ±5.1 in IGRA positive and 3.5 ±5.77 in IGRA negative group. Among clinical features, 1 person in IGRA positive and none in the IGRA negative group had current gastrointestinal involvement. Comparison of other organ manifestations yielded no statistically significant difference in the 2 groups at this point. Serology revealed greater proportion of C4 in IGRA negative as compared to the positive group(p<0.042).

Conclusion: Prevalence of latent TB in SLE cases was 15.4%. Although comparison of demographic, clinical and autoantibody profile did not yield any statistically significant differences, the early turnover from this pilot study mandates further evaluation with larger sample size.

Table 1. Comparison of clinical and laboratory parameters between IGRA positive and IGRA negative SLE cases

	IGRA POSITIVE(n=19)	IGRA NEGATIVE(n=105)	p VALUE
Age(Mean± SD)	31.79±9.7	29.26 ±10.8	0.199
Female Sex n(%)	19(100)	101(97.1)	0.312
Anti P0 antibody n(%)	3(15.8)	14(13.5)	0.827
Anti Ribo P antibody n(%)	2(10.5)	13(12.5)	0.761
Age of disease onset(Mean± SD)	25.58± 10.6	24.62± 10.57	0.285
Disease duration(Mean± SD)	4.33 ±4.02	4.6± 3.53	0.438
Treatment duration(Mean± SD)	3.84± 4.12	4.03± 3.42	0.439
Clinical SLEDAI(Mean± SD)	2.37 ±5.1	3.5 ±5.77	0.306
SLICC ACR DI(Mean± SD)	0.105±0.32	0.231± 0.66	0.666
Current CNS involvement	1(5.3)	4(3.8)	0.781
Current renal involvement	3(15.8)	26(25)	0.367
Current hematological involvement	1(5.3)	14(13.5)	0.272
Current GI involvement	1(5.3)	0	0.052
Current steroid dose(Mean± SD)	11.32± 11.65	13.03 ± 11.6	0.400
Serum C3(Mean± SD)	0.79 ±0.32	0.89± 0.47	0.477
Serum C4(Mean± SD)	0.19± 0.072	0.1635± 0.13	0.413
Anti dsDNA (Mean± SD)	458± 400.8	379.5± 400.5	0.454
Low C3 n(%)	9(52.9)	37(38.9)	0.108
Low C4 n(%)	2(11.8)	35(36.8)	**0.042**
Elevated Antidsdna n(%)	6(35.3)	37(38.9)	3.343

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AB0559 PATIENTS WITH EARLY-ONSET SJÖGREN'S SYNDROME

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Background: The primary Sjögrens Syndrome (pSS) is an autoimmune systemic disease characterized by chronic inflammation of exocrine glands,

especially lacrimal and salivary glands. The onset of pSS is usually between 50 and 60 years of age, but it may also occur in younger patients, in which case may be associated with a worse progression of the disease and a worse prognosis.
Objectives: To describe the clinical and immunological profile of patients with primary SS, aiming to investigate the clinical and laboratory characteristics of early-onset pSS patients (diagnosis before 35 years old)
Methods: The data of 58 medical records were analysed retrospectively. Based on the disease onset age, the patients were divided into two groups those with the onset age of 35 years old or younger and those with the onset age of older than 35 years old. Data normality was verified with the Shapiro-Wilk test. The comparison between patients' profiles with the late and early diagnosis was done with Pearson's Chi-squared test, Student's t-test, and Mann-Whitney test. P <0.05 was considered statistically significant.
Results: 55 patients were female (94,8%) and 3 were male (5,2%) and the average age on the last medical visit was 45,91±12,46 years old and the time between the diagnosis and the last appointment (follow up time) was 56,90±61,57 months. 14 patients had early-onset pSS and 44 had late-onset pSS. The mean diagnosis age in the early-onset group and the late-onset group. was 30,21±4,21 vs 50,91±9,73 years old (p<0.001) respectively and a mean follow-up time was of 41,40±50,27 vs 61,75±64,64 months respectively. There was no significant difference in demographic profile between the two studied groups, except for the age. There was no significant difference in cutaneous, joint, renal, and nervous system involvement. However there was a significantly higher frequency of xerophthalmia in the late-onset group (88.6% vs 64.3% p=0.036) and a significantly higher frequency of parotid enlargement in the early diagnosis group (42.9% vs 20.5% p=0.036) There was no significant difference in laboratory profiles between the two groups (anti-Ro, anti-La, ANA, rheumatoid factor, hypergammaglobulinemia and low complement).
Conclusion: The profile clinical of early-onset pSS patients may be different to those with later onset, with a higher prevalence of parotid enlargement. This group of patients needs to be monitored to determine the risk of a worse prognosis.
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AB0560 CLINICAL, SEROLOGICAL AND IMAGING CHARACTERISTICS OF LATIN AMERICAN PATIENTS WITH LUPUS MYOCARDITIS: A CASE-CONTROL STUDY

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Background: Lupus myocarditis (LM) is an uncommon manifestation of systemic lupus erythematosus (SLE), with a prevalence of 9% that tends to be lower in recent studies; it can range from subclinical to life-threatening manifestations (1). The clinical and immunological characteristics of LM have not been established in Latin American patients.
Objectives: To determine the clinical, serological, and imaging characteristics of patients with LM.
Methods: We conducted a single-center, case-control study that enrolled hospitalized patients between 2012 and 2020 in Colombia. Fifteen LM patients (cases) were matched by age and sex with thirty non-LM patients (controls). Descriptive, comparative, and logistic regression analyses were performed.
Results: Patients with LM were mostly females (93.3%) with a mean age of 28.2 years. The major affected clinical domains associated was renal (80%). Myocardial involvement occurred after SLE diagnosis with a mean of 5.1 years. Dyspnea (73.3%) was the main clinical manifestation. Troponin was high in 92.3% and echocardiographic findings included decreased left ventricular ejection fraction (LVEF) in the 60% of cases (mean 40%), diastolic dysfunction (61.5%), left ventricular dilatation (53.3%) and global hypokinesia 35.7%. The most common valvulopathy was mild mitral regurgitation. Nine LM patients underwent cardiac magnetic resonance. In this modality, mean LVEF was 38%, increased regional intensity on T2-weighted images, increased myocardial potentiation ratio on T1, and non-ischemic enhancement (mainly epicardial) was presented on 85.7%, 60%, and 57.1%, respectively. All patients received glucocorticoids and cyclophosphamide. Comparisons of the demographic, clinical, serological between LM and non-LM groups are shown in Table 1.

Table 1. Demographic, clinical and serological characteristics.

Variable	LM (n=15)	Non-LM	P-value
Female	93.3%	100%	0.333
Age SLE	24.9 (SD 12)	28.3 (SD 13.9)	0.515
Clinical domains			
Cutaneous	46.7%	90%	0.003
Articular	60%	76.7%	0.245
Hematological	60%	83.3%	0.086
Serosal	53.3%	36.7%	0.227
Renal	80%	76.7%	0.560
Neuropsyquiatric	6.7%	26.7%	0.115
Vascular	13.3%	50%	0.017
PCR mg/dL	10.1 (SD 9.3)	2.8 (SD 4.6)	0.0004
Erythrocyte sedimentation rate mm/H	52.9 (SD 25.7)	43.9 (SD 32.9)	0.267
Creatinine mg/dL	1.4 (SD 0.9)	1.9 (SD 2.5)	0.294
C3 mg/dL	57.4 (SD 22.4)	86.2 (SD 29.9)	0.002
C4 mg/dL	9.6 (SD 8.3)	16.4 (SD 9.3)	0.009
Anti-dsDNA	86.7%	52.4%	0.034
SLEDAI score	14.7 (SD 5.7)	6.8 (SD 7.6)	0.0003

SD: Standard deviation

Bivariate logistic regression showed that LM was independently associated with anti-dsDNA (OR 1.17, IC 1.04 – 1.31, p= 0.004), higher SLEDAI score (OR 1.17, IC 1.04 – 1.31, p=0,006), higher RCP (OR 1.21, IC 1.04 – 1.4, p=0.013), lower C3 (OR 0.96, IC 0.93 – 0.98, p:0,06) and lower C4 (OR 0.90 IC 0.82 – 0.99 P=0,036), highlighting its relationship with disease activity.
Conclusion: LM is a potentially severe manifestation and occurs in patients with higher disease activity, as was evidenced in the present study by low complement, anti-dsDNA and SLEDAI score. In the proper clinical context, noninvasive diagnostic tests should detect myocardial involvement in SLE.
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AB0561 LONG-TERM PERSISTENCE OF ANTIPHOSPHOLIPID ANTIBODIES ANDASSESMENT RISK PROFILE IN WOMEN

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Background: The evidence supporting the prognostic role of risk assessment in antiphospholipid antibodies (APA) positive patients has been obtained from several studies.
Objectives: to assess the association of the persistence of APA ≥ 12 weeks in women with an initial score on the aGAPSS scale, the presence of double and triple antibodies and a history of thrombosis or obstetric events.
Methods: A total of 117 women were included in the case-control study: 44 patients with persistence ≥ 1 antiphospholipid antibodies (APA) for 12 or more weeks (cases); 73 patients with transient circulation of APA less than 12 weeks (controls). An initial examination of women with a subsequent persistence of antiphospholipid antibodies ≥ 12 weeks compared with their transient circulation revealed.
Results: A higher incidence of arterial and venous thrombosis events, and a history of placenta-associated obstetric complications were observed in women with persistence of APA ≥ 12 weeks compared to transient circulation of APA, as well as a higher laboratory risk profile (double and triple positivity of APA. Overall, significantly higher aGAPSS were seen in women with persistence of APA ≥ 12 weeks compared to those with transient circulation of APA (7.37 ± 3.5 vs. 4.8 ± 0.6, p<0.05).
Conclusion: The aGAPSS scale is an additional tool available in clinical practice to clarify the risk profile in patients with APA-positivity in order to choose an adequate antithrombotic strategy. Future studies should evaluate the informativeness of the scale and determine cut-off points for predicting thrombosis and obstetric events.
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AB0562 LIVER ENZYME ABNORMALITIES IN HOSPITALIZED LUPUS PATIENTS – A RETROSPECTIVE STUDY

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Background: Around 25% to 50% of lupus patients may present with alterations in the liver enzymes of variable severity including fulminant hepatic failure.[1]

Table 1. Aetiology and associations of liver enzyme abnormalities

Aetiologies for elevated transaminases						
				Macrophage activation syndrome	33/77(42.9%)	
				Lupus activity	16/77(20.8%)	
				Overlap Myositis	12/77(15.6%)	
				Autoimmune Hepatitis	6/77(7.8%)	
				Sepsis	5/77(6.5%)	
				Primary Biliary Cirrhosis	3/77(3.9%)	
				Drugs	2/77(2.6%)	
Comparison between patients with and without MAS				Comparison between patients with and without mortality among MAS patients		
	MAS (N=33)	No MAS (N=44)	P-value	Mortality (N= 9/33)	No Mortality (N=24/33)	P-value
AST	228(169,377.5)	(128,281)	**0.098 ***	265(232.5,545)	209(139.5,360)	**0.036***
ALT	73(51.5,121.5)	96(54,140)	0.520	58(46,132.5)	94.5(53.5,121.75)	0.505
ALP	202(69.5,382.5)	175(90,318)	0.794	233.5(84,382.2)	202(69.5,407.5)	0.788
GGT	232(77.5, 443)	179(75,333)	0.312	402(139.5,995.7)	202(70.5,373.0)	0.205
AST/ALT RATIO	3.18(1.96,4.45)	2.3(1.4,3.6)	**0.016***	**4.33**(3.07,6.66)	2.58(1.94,3.64)	**0.032***

ABBREVATIONS- AST- Aspartate aminotransferase; ALT- Alanine aminotransferase; ALP- Alkaline phosphatase, GGT- Gamma glutamyl transferase. Statistically significant *P-value = < 0.05.

Objectives: To study the prevalence, aetiology and the outcome in lupus patients hospitalized with liver enzyme abnormalities.

Methods: We analysed liver enzymes of all hospitalized lupus patients from June 2018–June 2021. Patients with abnormal liver enzymes(>2 times Upper Limit Normal)[2] were identified and categorized as per the standard definitions/criteria.[3,4] The outcomes and association of liver enzymes to mortality was analysed.

Results: Liver enzymes were available in 461/535 hospitalisations amongst 383 lupus patients of whom abnormalities were detected in 95/461 (20.6%). Among 77 patients with elevated transaminases, 33/77(42.9%) fulfilled criteria for macrophage activation syndrome (MAS) as per HLH criteria and parodie et.al[4]. Other aetiologies are represented in Table 1. Overall the mortality rate was 12/77(15.58%), highest being MAS 9/12(75%). Higher aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio was associated with adverse outcomes in patients with MAS.

Conclusion: MAS was the most frequent cause of elevated transaminases and was associated with mortality in subset with higher AST/ALT ratio.

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AB0563 ALEXITHYMIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The growth of psychosomatic disorders is the most important medical and social problem of modern healthcare. Particular attention of researchers is attracted by the alexithymic radical in the structure of the patient's premorbid personality, as one of the possible psychological risk factors for the development of psychosomatic disorders. Alexithymia is a psychological phenomenon that described as difficulty in definition one's own feelings, difficulty in distinguishing between feelings and bodily sensations, a decrease in the ability to symbolize, and a focus on external events rather than internal experiences.

Objectives: The aim of this work was to study the level of alexithymia in patients with systemic lupus erythematosus (SLE).

Methods: There were 87 patients under observation, the majority were women (82.8%), of 35.33 ± 1.77 years old in average. The average duration of the disease was 7.09 ± 0.89 years.

The Toronto Alexithymia Scale (TAS) [1] was used to measure alexithymia.

Results: It should be noted that in healthy people [1] the level of alexithymia is 59.3 ± 1.3 points. The mean value of alexithymia in SLE patients was 74.05 ± 2.62 points. The high and medium rates of alexithymia were established in 54 cases from 78 patients, and there were low levels in 24 cases indicating the absence of alexithymia. It was not possible to identify the dependence of alexithymia on gender and age. There was also no significant dependence of the level of alexithymia on the duration of the disease, the course and the activity of the pathological process. However, a significant direct correlation between the severity of alexithymia and depression and anxiety was revealed (see Table 1).

Table 1. Dependence of the level of alexithymia on some characteristics of SLE patients

	Disease course	Disease activity	Age of patients	Disease duration	Asthenia	Depression	Anxiety	Hypochondria
TAS	0.24	0.21	-0.09	0.44	0.33	0.51*	0.46*	0.35

* - p < 0.05

Our data indicate that patients with SLE have a high level of alexithymia. Indeed, patients suffering from this disease experience difficulties in understanding and verbalizing feelings, persistently strive to draw the doctor's attention to their physical sensations, without attaching importance to or denying trouble in the emotional sphere.

Conclusion: The results of the study indicate a certain role of the phenomenon of alexithymia in the pathogenesis of psychosomatic disorders in SLE, and the level of alexithymia does not depend on gender, age, and the main clinical characteristics of the disease, but correlates with general neuroticism. It is possible that the high level of alexithymia in SLE patients leads to an increase in depression and anxiety, and generates psychological distress.

Thus, the study of alexithymia, among other risk factors of a biological and psychosocial nature, is important for a better understanding of the role of psychological mechanisms in the pathogenesis of psychosomatic diseases, the organization of preventive measures aimed at correcting alexithymic features, carried out in individual and group forms of psychotherapy.

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AB0564 PROGNOSTIC ROLE OF PRE-CONCEPTIONAL COMPLEMENT CONSUMPTION ON PREGNANCY OUTCOMES IN ANTI-PHOSPHOLIPID ANTIBODY SYNDROME, POLIABORTIVITY AND RECURRENT IMPLANTATION FAILURE

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Background: In anti-phospholipid antibody syndrome (APS), complement (C3/C4) activation favours the development of adverse pregnancy events. The prognostic role of complement in recurrent pregnancy loss (RPL) and recurrent implantation failure (RIF) has never been clinically studied. Additionally, the influence of hydroxychloroquine and heparin on complement modulation at the molecular level has already been accepted, while few clinical studies on these drugs have been published up to date.

Objectives: The aim of the study was to investigate whether C3/C4 levels represent a risk factor for pregnancy outcomes in a population of patients with APS, patients with RPL and patients with RIF. Moreover, the study investigated the

effects of therapies during pregnancy (low dose aspirin, low molecular weight heparin and hydroxychloroquine and their combinations).
Methods: We collected data of 136 patients (33 APS, 69 RPL, 34 RIF) prospectively followed from September 2018 to June 2021 in the "Recurrent pregnancy loss and Recurrent implantation failure clinic" of the "Centro Scienze della Natalità" department of San Raffaele Hospital, Milan, Italy. For all the patients, serum C3/C4 levels were determined at San Raffaele local laboratory.
Results: 30/136 (22%) patients had pre-conceptional complement consumption. Of these, 5/30 (17%) had anamnestic history of adverse pregnancy outcomes and 29/30 (97%) had at least one abortion in the past. 106/136 (78%) patients had normal pre-conceptional complement levels: 8/106 (7%) had anamnestic history of adverse pregnancy outcomes and 91/106 (86%) had at least one abortion in the past. In 64/136 pregnancies prospectively followed in our centre, 17/64 (26%) had pre-conceptional complement consumption. In patients with complement consumption, abortion (4/17, 24%) and adverse pregnancy outcomes (3/17, 18%) rates were homogeneous to the ones of patients with normal complement levels (16/47, 34% e 5/47, 11% respectively). Hypocomplementemia was associated with a significantly higher (p<0.05) probability of active treatment during pregnancy (both with low dose aspirin, low molecular weight heparin and hydroxychloroquine), which might explain the uniformity of gestational outcomes between the two groups. Thus, additional therapy with hydroxychloroquine provided in our clinic might have improved gestational outcomes in patients with hypocomplementemia.
Conclusion: Measurement of pre-conceptional complement level is an easy and cheap procedure that might be useful to identify those patients at a higher risk of adverse gestational outcomes. The presence of consumed pre-conceptional C3/C4 levels might represent an indication to strengthen therapy in those pregnant patients with history of pregnancy loss. Our study stresses the importance of a personalized diagnostic-therapeutic pathway in patients with RPL and RIF, independently of the presence of APS.
Further studies in larger cohorts with RPL and RIF will be needed to confirm our findings.
Disclosure of Interests: None declared
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AB0565 PREVALENCE OF LIVER FIBROSIS ASSESSED BY TRANSIENT ELASTOGRAPHY IN PATIENTS WITH SJÖGREN'S SYNDROME

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Background: Liver is considered one of the most commonly involved extra-glandular organs in patients with Sjögren's syndrome (SS). Primary biliary cholangitis, hepatitis C virus infection, non-alcoholic fatty liver disease (NAFLD) and drug hepatotoxicity are the major contributors of liver disease among SS patients. Especially, NAFLD comprises a major health problem worldwide with a rapidly rising incidence and a prevalence of approximately 25% in the general population. In both NAFLD and SS, inflammatory and apoptotic pathways are implicated in pathogenesis, pathways that are also linked to fibrogenesis. No studies so far have investigated the net effect of SS in liver fibrosis.
Objectives: To assess whether SS is associated with advanced liver fibrosis (LF) in the absence of viral, alcohol-related, autoimmune hepatitis or primary cholangitis.
Methods: In this prospective study, consecutive SS patients from the rheumatology outpatient clinic of the Department of Pathophysiology, "Laiko" General Hospital, Athens, Greece between June 1st and December 31st, 2021, underwent transient elastography (TE) with measurement of liver stiffness and controlled attenuation parameter, assessing LF and liver steatosis (LS), respectively. For LF the following cut-offs were used: F0-1: 2-7 kPa, F2: 7-10 kPa, F3: 10-14 kPa, and F4: >14 kPa. F0-F1 stages were considered as clinically insignificant and F2-F4 as advanced. For LS the following cut-offs were used: S0-S1: 100-260 dB/m, S2: 260-290 dB/m, and S3: >290 dB/m. LS stage S0-S1 was classified as low and S2-S3 as high. Individuals who were evaluated in the hepatology outpatient clinic for possible NAFLD/LS based on ultrasonographic criteria (higher echogenicity than renal cortex and/or splenic parenchyma) served as a comparator group. In all participants, those with viral or alcoholic hepatitis, autoimmune liver diseases, transaminasemia or liver disease attributed to drug hepatotoxicity were excluded. Clinical, demographic and laboratory data were collected from all participants at the time of TE.
Results: Fifty-two patients with SS (49 females, 94.2%) with a median disease duration (range) of 8 (1-46) years and 198 comparators (104 females, 52.5%) were included in this study. The median age (range) of SS and comparators was 62.5 (30-81) and 55 (19-86) years, respectively. Comparators and SS patients had comparable prevalence regarding type 2 diabetes mellitus (T2DM), hyperlipidemia and body-mass index (BMI). Patients with SS had less frequently high LS (27% vs 62%, p<0.001) and advanced LF [2 (3.8%) vs 34 (17.2%), p=0.014], compared to comparator group. The 2 SS patients with advanced LF had also high LS. Univariable analysis in terms of T2DM, hyperlipidemia, BMI, age, gender, steatosis, and disease status (SS or comparators) between individuals with insignificant and advanced LF revealed age, liver steatosis, BMI, and disease status as the only statistically significant parameters; of these, only age was finally identified as independent risk factor in the multivariable logistic regression analysis (Table 1).

Table 1. Multivariable logistic regression analysis for risk factors associated with advanced liver fibrosis among patients with Sjögren's Syndrome and comparators.

Variables	Coefficient	Odds ratio	p-value	CI low	CI upper
Age	0.057	1.059	0.023	1.019	1.1
Body Mass Index	0.099	1.105	0.121	1.012	1.207
Presence of Sjögren's syndrome	-0.941	0.419	0.346	0.067	2.826
High Liver Steatosis	0.344	1.473	0.62	0.355	6.167

Conclusion: Sjögren's syndrome per se is not associated with advanced liver fibrosis.
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AB0566 CLINICAL AND SEROLOGICAL ASSOCIATION BETWEEN SJÖGREN SYNDROME AND VASCULITIS

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Background: Sjögren Syndrome (SS) is a systemic autoimmune systemic disease which mainly affects the exocrine glands, presenting mainly as persistent eye and mouth dryness as a result of a functional impairment of the lacrimal and saliva glands. Cutaneous vasculitis is one of the most characteristic extraglandular manifestations, especially in patients with anti-Ro antibodies. Although vasculitis may affect a wide range of organs and systems, the clinical characteristics and the diversity of vasculitis associated with SS have not been thoroughly studied.
Objectives: To describe the clinical and analytical characteristics of patients with SS and cutaneous, or systemic vasculitis, as well as their outcome.
Methods: Retrospective, descriptive study, of patients with primary SS and vasculitis attended at a Tertiary Hospital. Collected data were analysed using the SPSS statistical package. Quantitative data were expressed as a mean +/- 2SD and qualitative data as a proportion. A p-value 0.05 was considered significant.
Results: From a total of 395 patients with primary SS, 53 patients presented with both SS and vasculitis (51, 96.2%, women). The mean age at diagnosis was 56.12 (±2.17) years. Globally, 84.9% of patients met the 2002 classification criteria; 90.6% the 2012 criteria, and 83.0% the 2016 criteria. Thirty-two (60.4%) patients presented with cutaneous vasculitis (mainly purpura), and 7 (13.2%) with systemic vasculitis with renal, neurological and/or lung involvement. Extraglandular manifestations were frequent. Out of the 53 patients, twenty-five (47.2%) presented pulmonary involvement; 43(81.1%) articular involvement (19 [35.8%] arthritis); 21(39.6%) Raynaud phenomenon, and 15.1% peripheral neuropathy. Six (11.3%) patients developed a lymphoma. All patients presented positive ANA; 69.8% anti-Ro60, 52.8% anti-La, 75.5% RF; 62.3% polyclonal hypergammaglobulinemia; 33.9% cryoglobulins, 58.5% elevated beta2-microglobulin levels, and 12 (22.65%) hypocomplementemia (4 decreased C3, and 8 decreased C4). Biopsy specimens showed in 8 (15.9%) cases urticaria vasculitis; in 1 (1.9%) PAN; in 2 (3.8%) Cryoglobulinaemic vasculitis, in 5 (9.4%) ANCA associated vasculitis (4 PAM-MPO, and 1 GPA-PR3); and in 1 SNC vasculitis. 64.2% of patients received glucocorticoids and 37.7% hydroxychloroquine. 5 (9.4%) patients received Rituximab. Vasculitis were significantly more frequent in patients with anti-Ro60 (p=0.005, OR2.5 IC95% 1.33-4.74); anti-La (p=0.009, OR 2.39, IC95% 1.29-4.43); RF (p<0.000, OR 3.78, OR 3.72 IC95%1.90-7.26); C4 hypocomplementemia (p<0.00, OR 6.42, IC 95% 2.65-15.56); cryoglobulins (p=0.016, OR 2.29, IC95% 1.21-4.33); hypergammaglobulinemia (p=0.004, OR 2.53, IC95% 1.36-4.71), arthritis (p= 0.001, OR 3.26, IC95% 1.72-6.19), lung fibrosis (p=0.010, OR 2.92, IC95% 1.38-6.17) and lymphoma (p=0.011, OR 4.05, IC95% 1.5-10.94).
Conclusion: In our series, most patients with SS presented repetitive flares of cutaneous vasculitis as previously reported. Nonetheless, our patients showed a greater proportion of lung and articular manifestations as well as anti-La positivity.

Five patients presented with ANCA associated vasculitis, which represents and exceedingly rare and severe manifestation in this context.
Patients with SS may present a wide range of vasculitis, ranging from the most common leucocytoclastic vasculitis to the more severe systemic vasculitis, such as: AAV and cryoglobulinaemic vasculitis.
The association of SS with vasculitis is more common in patients with anti-Ro, anti-La and/or RF, hypocomplementemia, cryoglobulins and hypergammaglobulinemia.

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AB0567 SHORT AND LONG-TERM RENAL OUTCOMES OF PATIENTS WITH PROLIFERATIVE LUPUS NEPHRITIS: DATA FROM A SINGLE INSTITUTE INCEPTION COHORT.

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Background: Renal involvement in SLE is associated with high risk of morbidity with proliferative lupus nephritis (PLN) having the worst prognosis. Although advances in immunosuppressive treatment led to better renal survival rates, response to treatment and short- and long-term outcomes differ among cohorts.
Objectives: To evaluate short and long term renal outcomes in an inception cohort of patients with PLN. We also aimed to define clinical, laboratory, histological and treatment determinants of partial (PR) or complete response (CR), flare, and long-term renal and patient survival.
Methods: An inception cohort of 83 patients with biopsy-proven PLN (class III, IV, or III/IV+V)(diagnosed between 1992 and 2019) was retrospectively studied. Data collected included histologic characteristics at baseline, demographic, clinical, laboratory, and therapeutic parameters at baseline, 6-9-12-18-24-36-72 months after PLN diagnosis, time of renal flare and last follow-up visit.
Univariate logistic and Cox regression analyses were performed to estimate response to treatment, flare and long-term renal survival. Variables found to be significant in the univariate analyses were included in the multivariate models.
Results: Mean age of the patients was 43±12 years, 78% were women, 96% were Caucasians and median duration of SLE before PLN diagnosis was 12 months (IQR 60).Mean SLEDAI score at PLN diagnosis was 12.8±4 and mean proteinuria was 3.69±3.3g/d. At baseline, 73.5% (61/83) had eGFR>60ml/min/1.73m^2, 15.5% (13/83) eGFR 30-60 and 11% (9/83) eGFR<30. 32% (27/83) of patients had class III LN, 46% (38/83) IV, and 22% (18/83) III/IV+V. Median follow-up time was 107 months(IQR 94).
Induction immunosuppressive treatment consisted of cyclophosphamide (CYC) in 71% (59/83) of patients (12/59 in combination with rituximab (RTX)), mycophenolic acid (MPA) in 25% (21/83)(2/21 in combination with RTX) and RTX alone in 2 patients. 1 patient did not receive any immunosuppressive treatment due to ESRD. Patients treated with CYC had a higher baseline SLEDAI score, lower C3 and C4 levels, higher biopsy activity index and higher proteinuria levels than those treated with MPA. 76% (63/83) received MPA as maintenance treatment, 8% (7/83) azathioprine, 7% (6/83) CYC and 8% (7/83) did not receive any maintenance regimen (3/7 due to ESRD, 2/7 received RTX as induction and continued with steroids only, 1/7 due to non-compliance, 1/7 lost to follow-up after 6months). Median duration of treatment was 43.6 months (IQR 44.6).
66% of patients had response (CR or PR) at 6 months (43% CR, 23% PR), 73% at 9 months (46%CR, 27% PR), 77% at 12 months (61%CR, 16%PR) and 91% at the end of follow-up (80%CR, 11%PR)(Figure 1). Median time to complete remission was 9 months (IQR 14) and median time to partial remission was 4 months (IQR 7). In multivariate analysis, baseline eGFR>60ml/min correlated with shorter time to remission (HR 1.7, p=0.05). No clinical, laboratory or histological (PLN class, activity/chronicity index, number of crescents) parameters or any of induction immunosuppressives could predict time to remission.

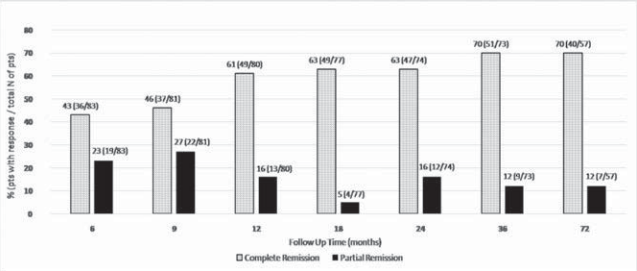

Figure 1.

38.5% of patients (32/83) had ≥1 renal flare in a median time of 40.5 months (IQR 44). In multivariate analysis, proteinuria >1g/d at 12 months correlated significantly with risk of flare (OR 3.65, p=0.039), while induction treatment with MPA was associated with lower risk of flare compared to CYC (OR 0.21, p=0.031) (in combination or not with RTX).
At a median follow-up time of 107 months, 2 patients died, 15.6% (13/83) developed chronic kidney disease (CKD) (<60ml/min/1.73m^2), and 9.6% (8/83) ESRD. In multivariate analysis, baseline eGFR<60ml/min (OR 14.0, p=0.02) and 12-month proteinuria >1g/d (OR 12.0, p=0.02) were the only predictors of CKD.
Conclusion: In our inception cohort of patients with PLN, 66% of patients achieved response at 6 months, 77% at 12 months and 91% at the end of follow-up. Proteinuria >1g/d at 12 months emerged as an important risk factor of renal flare and CKD, while MPA treatment was associated with lower risk of renal flare.

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AB0568 CHRITHIDIA LUCILAE IMMUNOFLUORESCENCE PRESENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS ASSOCIATION WITH POSITIVE CHAGAS TESTS

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Background: Systemic lupus erythematosus (SLE) is characterized by the presence of auto-antibodies, including anti-double strained DNA (dsDNA), which are highly specific for the disease diagnosis and its follow up. Indirect immunofluorescence (IIF) using *chritidia luciliae* (CL) as the antigenic substratum, is the most widely used method to detect it, and its positivity is defined with the staining of the kinetoplast and/or the nucleus. CL is a flagellated parasite, included in *trypanosomatidae* family, which also includes *trypanosoma cruzi*, the cause of Chagas Disease (CD). Some studies suggest that membrane and flagellum fluorescence (considered 'atypical' staining) could be related with positive CD serology.
Objectives: Describe the prevalence of positive IIF-CL images and its association with positive CD test in SLE patients.
Methods: A cross sectional study was designed including consecutive outpatients with SLE diagnosis (SLICC criteria), in which anti-dsDNA antibodies was requested to monitor disease activity. At the same time, two serologic CD tests were performed, since they improve sensibility to detect the disease.
Anti-dsDNA by IIF were performed by an experienced laboratory biochemistry blinded to patients clinical data. Pregnant patients and those ≤ 18 years old were excluded from this analysis.
Standard descriptive analysis was performed, data was compared by exact fisher test or chi2, student's T test or Mann Whitney. A p value < 0.05 was considered as significative.
Results: Thirty five patients were included, 33 (94.3) female, median age 38 (IQR 31-48), with 20 (57.1) patients being from middle-low socioeconomic status (measured by Graffar score). Twenty-six (74.3) patients were receiving glucocorticoids, 28 (80) hydroxychloroquine, 5 (14.3) azathioprine, 12 (34.3) mofetil mycophenolate, 5 (14.3) cyclophosphamide and 4 (11.4) rituximab.
Twelve (34.4) had positive anti-dsDNA test, with atypical staining in membrane and flagellum 31 (88.9), only membrane 4 (11.4) and 9 (25.7) only basal body. One patient had previous chronic CD diganosis without specific treatment.
Five (14.3) CD serologies were positive, and 1 had undefined result. This group of patients had positive staining in membrane and flagellum of CL. No other atypical CL staining images were found. (Table 1)

Table 1. CL staining in CD positive v negative serology

Chritidia luciliae Structure	CD negative (n = 29)	CD positive (n = 5)	p value
Membrane and flagellum – n (%)	25 (86.2)	5 (100)	0.51
Only Membrane – n (%)	4 (13.8)	0	0.51
Basal body – n (%)	7 (24.1)	1 (20)*	0.66

* undefined result

Conclusion: Although we could not find a statistical association between atypical CL staining and positive CD serology, this could be due to the low number of patients included in the study since all the patients with positive CD serology had a positive staining in CL-IIF. A trained biochemistry operator is necessary to avoid false positive tests in regions with high prevalence of CD.
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AB0569 FRECUENCY, TYPE AND DETERMINANTS OF COGNITIVE DEFICIT IN A COLOMBIAN COHORT OF PATIENTS WITH SLE

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Background: Cognitive deficit is part of the neuropsychiatric syndromes associated with systemic lupus erythematosus (SLE) (1). SLE patiens have 2.8 times more risk to develop cognitive deficit (2) and the prevalence is unknown among this population, with variable data from 5% to 80% (3). ACR (American Collegue of Rheumathology) recomends a specific neuropsychological battery (4), but many of the published studies uses variables diagnostic tests. Cardiovascular comorbidities and the use of certain immunosuppressive are involved in the development of cognitive deficit and may be confusors at the time of diagnosis (5). Cognitive deficit affects the quality of life and predisposes to the development of dementia (6). In our setting, the frequency of cognitive deficit as a manifestation of neuropsychiatric SLE is unknown. Determining conditions of it are unknown as well.
Objectives: 1.To define the frequency and degree of cognitive deficit in a cohort of patients with SLE
2.To describe associated factors (including quality of life and depression).
Methods: This was a cross-sectional observational study with 94 patients with SLE. The presence of cognitive deficit was established through a screening test (MoCA test). The diagnosis was confirmed through a battery of specific neuropsychological tests that were performed to patients with abnormal MoCA test. Quality of life was assessed using the LupusCol questionnaire wich is a validated scale for for measuring quality of life in SLE Colombian population. To measure the presence of depression we use the Beck inventory, this scale is also validated in SLE population. An exploratory analysis of the variables was performed and differences were established. A multivariate analysis was performed to find the variables associated with the cognitive deficit.
Results: Of the 94 patients, 90 (95.7%) were women. Of the 94 patients, 43 (51.2%) presented some degree of depression. The median for the loss of quality of life was VIII 21.03% (IQ 10.2 - 40.3). 35 (37.2%) patients had abnormal screening test. Specific neuropsychological tests were applied to 31 (90%) and of those, 11 patients (12.2%) presented a cognitive deficit. An association between cognitive deficit with a greater deterioration in quality of life was found (OR 1.05, 95% CI 1.01,1.09).
Conclusion: The frequency of cognitive deficit is important. There is an association of cognitive deficit with worse scores in quality of life. In addition, it was found that half of the patients presented some degree of depression. The comprehensive assessment of patients with SLE should include the evaluation of cognitive deficit and depression, because of their impact in quality of life, among other clinical aspects.
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AB0570 CLINICAL AND IMMUNOLOGICAL MANIFESTATIONS IN SLE PATIENTS IN A THIRD LEVEL HOSPITAL IN ROSARIO, ARGENTINA

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Background: Systemic lupus erythematosus (SLE) is a chronic and complex inflammatory disease which predominantly affects young females during reproductive ages. Its prognosis is worse in males, young people, Afro-American and Latin patients. Clinical and immunological features had been described around the world but few reports had been done in Argentinian patients.
Objectives: The purpose of this study was to describe the clinical and immunological pattern in SLE patients, characteristics of lupus nephritis (LN), disease male's course of SLE, treatments and causes of hospitalization.
Methods: Retrospective study including patients (>18 years) followed in Rheumatology Department, which had unless two visits in the last year before data collection, its clinical reports were complete, and fulfilled SLICC or EULAR/ACR SLE criteria. We recorded data from the medical reports.
Results: Of the 70 patients, 63 were female (90%). The mean age at diagnosis was 27,86 ± 9,4 years. The most frequent manifestations were arthritis (75,7%), malar rash (65,7%), photosensitivity (31,4%), leukopenia (31,4%), alopecia (31,4%), Raynaud's phenomenon (24,3%) and nasal and oral ulcerations (21,4%). 94,3% of patients were positive for antinuclear antibodies, 45,7% had anti-Ro/SSa, 28,6% anti-RNP and 21% anti-Smith. 75% had low complement and 45,7% anti-DNA antibodies. LN occurred in the 50% of patients, and class IV was the most prevalent in this group. 66% of patients developed LN in the first year of SLE diagnosis. Autoantibodies in this manifestation were: anti-DNA 60%, anti-Ro/SSa 37%, 31% anti-RNP and 26% anti-Smith. The most common comorbidity was high blood pressure followed by hypothyroidism (34,3% and 25,7% respectively). All patients received hydroxychloroquine and 62,9% prednisone; half of the patients who were into prednisone treatment received 5mg or less. Other treatments were cyclophosphamide (42,9%), mycophenolate (28,6%) and methotrexate (15,7%). 60% of patients had been hospitalized because of SLE flares and 15,7% due to infections. 75% of flares were due to LN and 8% because of serositis. Is known that SLE in male patients is more aggressive and with poor prognosis. Although this study had only 7 men, 86% had LN, 29% had pericardial and pleural effusion and 29% thrombocytopenia, were we found several differences in female's SLE presentation.
Conclusion: This study shown similar results reported in other populations. We found that 50% of SLE patients developed LN, which is the most important cause of hospitalization. Although cutaneous and musculoskeletal manifestations were the most frequent, it's important to take into account the clinical and prognostic differences between male and female.
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AB0571

DERIVATION AND INDEPENDENT VALIDATION OF THE LUPUS ARTHRITIS AND MUSCULOSKELETAL DISEASE ACTIVITY SCORE (LAMDA): A MORE SENSITIVE, SPECIFIC AND RESPONSIVE TOOL FOR LUPUS ARTHRITIS

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Background: The MSK components of the BILAG and SLEDAI have limited sensitivity, specificity and responsiveness.
Objectives: To develop a better disease activity tool for MSK lupus.
Methods: "LAMDA" was derived using data from the multicentre USEFUL study (PMID:33792659); 133 patients with inflammatory MSK pain received intramuscular depomedrone then were assessed for 66/68 SJC/TJC, BILAG-2004, SLEDAI-2K, physician MSK-VAS, inflammatory markers, patient pain and disease-activity-VAS and MSK-ultrasound. Baseline variables were modelled against US using penalized (Lasso) regression. For validation we evaluated: (i) responsiveness at week 6 in USEFUL and (ii) association with quality of life and treatment decision in an independent study (n=100).
Results: LAMDA was a composite of SJC, patient-MSK-pain-VAS, physician-MSK-disease-activity-VAS and ESR ranging from 0 to 26.5. Response effect size was greater for the LAMDA (0.37) than the BILAG-MSK (0.31), SLEDAI-MSK (0.27) and total US score (0.33). With active US at baseline, LAMDA's effect size was 0.42.
In the validation study LAMDA score correlated with better physical function (R = -0.49, p<0.001), pain (R = -0.44, p=0.002) and Burden to Others (R = -0.38, p=0.009). LAMDA was higher when therapy was increased (mean (95% CI) difference 12.9 (5.8, 19.9), p<0.001).
Conclusion: LAMDA is a continuous disease activity instrument for MSK lupus that is sensitive to imaging-synovitis without swelling, more responsive than other instruments and correlates with quality of life and treatment decision. LAMDA may improve the ability of clinicians to monitor and treat MSK lupus, and determine the efficacy of therapies in clinical trials.
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AB0572

USEFULNESS OF MINOR SALIVARY GLAND BIOPSY IN THE DIAGNOSIS OF PATIENTS WITH SUSPECTED PRIMARY SJÖGREN'S SYNDROME

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Background: The classification system for Sjögren's syndrome (SS) proposed by the American-European Consensus Group (AECG) and the revised diagrams proposed by the American College of Rheumatology (ACR) include an altered minor salivary gland biopsy (MSGB) or positive antiRo, among other findings. Thus, an altered MSGB is a particularly important finding in patients with autoantibody-negative. A retrospective cohort study showed that a positive biopsy result led to a definitive diagnosis in 80% of patients[1].
Objectives: To assess the usefulness of MSGB in the diagnosis of SS in anti-SSA/SSB (Ro/La) negative patients.
Methods: Retrospective descriptive study in patients with suspected SS in which MSGB were collected according to standard clinical practice over a consecutive period (from September 2020 to May 2021) in the Rheumatology Department of a tertiary hospital.
Patients were grouped according to the reason for requesting the biopsy: 1) Dry eye/oral syndrome (DEOS), 2) DEOS + altered Saxon/Schirmer, 3) DEOS + positive antinuclear antibodies (ANA+), 4) DEOS + (ANA+) + other serological alterations (hypergammaglobulinaemia, rheumatoid factor (RF), hypocomplementemia), 5) DEOS + extraglandular manifestations (EG) + (ANA+) +/- other serological alterations. The following variables were collected: age, sex, dry eye/oral syndrome, Raynaud's phenomenon, EG manifestations (arthritis, autoimmune hepatitis, primary biliary cirrhosis, interstitial lung disease, pleuropericarditis, autoimmune chronic nephropathy suspected or tubulointerstitial nephritis and/or neurological manifestations), ANA, hypergammaglobulinaemia, RF, hypocomplementemia, Saxon and Schirmer tests and histological result of MSGB according to its Focus Score (FS); MSGB was considered altered when FS was ≥1. Descriptive analysis was performed (means and frequencies); Chi-square test was used to compare the reasons for requesting MSGB between patients with altered and unaltered results and to compare whether any of the groups (Groups 2-5) were more frequently associated with an altered MSGB compared to patients presenting only with dry syndrome (Group 1).
Results: Seventy-eight MSGB were collected. Mean age of patients was 55 years; 90% were women. ANA were present in 17% of patients with altered MSGB. DEOS was the suspected manifestation in 83% of patients, 13% had Raynaud's phenomenon and 47% had some EG manifestation. MSGB was compatible with a diagnosis of SS (according to 2002/2016 classification criteria) in 28% of anti-SSA/SSB negative patients. Patients with dry syndrome and positive ANA (Group 3) were significantly associated with MSGB altered (Table 1).

Table 1. Comparative table of patterns inidicated in the reasons for requesting a MSGB. *Not significant (NS).

Reason for request (%)	MSGB altered	MSGB unaltered	p	p vs dryness
DEOS (50)	19	46	0.65	
DEOS + Saxon/Schirmer (38)	15	34	0.47	NS
DEOS + ANA (30)	11	27	0.67	NS
DEOS + ANA + others (8)	6	4	0.41	0.05
DEOS + EG + ANA (14)	9	15	0.69	NS

Conclusion: MSGB was compatible with a diagnosis of SS in 28% of anti-SSA/SSB negative patients. The data suggest that patients presenting with objectified dryness with Saxon and/or Schirmer test, as well as those with extraglandular manifestations and ANA+ and/or other serological alterations, are more likely to have a compatible with SS result on MSGB. Studies with larger numbers of patients are needed.
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AB0573

PERIPHERAL BLOOD B-CELLS SUBSETS IN PATIENTS WITH SJOGREN'S SYNDROME DEPENDING ON SOME IMMUNOLOGICAL PARAMETERS.

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Objectives: To examine B-cell subsets in peripheral blood of Sjogren`s syndrome (SjS) patients (pts) and to analyze the association between B-cell subsets and different clinical and immunological parameters.
Methods: 67 active SjS pts (65F/2M); mean age 51±14,4 years; disease duration 60 (24-120) months were included. SjS was diagnosed based on the ACR-EULAR2016 criteria. Twenty healthy donors composed the control group. CD19+B cells, memory B-cells (CD19+CD27+), non-switched memory B-cells (CD19+IgD+CD27+), switched memory B-cells (CD19+IgD-CD27+), naïve (CD19+IgD+CD27-), double negative (CD19+IgD-CD27-), transitional (CD19+IgD+CD10+CD38+) B-cells, plasmablasts (CD19+CD38+++IgD-CD27+) were analyzed by multicolor flow cytometry using cytometer Navios (Beckman Coulter, USA).

The nonparametric Mann-Whitney test, the Pearson`s x2 criterion, Spearman rank correlation coefficient were used for statistical analysis. Data were shown as median (Me) with an interquartile range of 25 - 75 percentile. The differences were considered statistically significant when p<0.05. Statistica 10 for Windows (StatSoft Inc., USA) package was used for statistical data processing.

Results: The percentages/absolute numbers of plasmablasts, transitional B-cells, memory B-cells in SjS were significantly higher than in healthy donors, p<0.01 for all cases. At the same time percentages/absolute numbers of naïve cells in SjS were reduced compared to healthy donors (p=0.005, p=0.04). Shorter duration of SjS (less than 2 years) correlated with higher rates of naïve cells (p=0.02).

ESSDAI score was ≥5 in 33 pts and <5 in 34 pts. We didn`t find any correlation between B cells subsets and disease activity. The presence of lymphoma in pts (n=5) had no impact on B-cells subsets as well. Significant changes were in B-cells subsets were found depending on immunological parameters. Pts with an isolated increase of antinuclear antibodies (ANA) (ANA positive, RF/aRo/aLa negative) had no plasmablasts in peripheral blood, level of plasmablasts in other pts was 1.5 (1-4.5)x10^3/μL, p=0,004. ARo-positive pts had higher amount of plasmablasts and transitional B-cells than aRo-negative pts (2 (1-5) and 1 (0-1) x10^3/μL, p= 0.004). Higher level of plasmablasts and transitional B-cells also correlated with decrease in C3 and/or C4 (p≤0.03) and increase in IgG (p<0.025).

Conclusion: According to our data elevated level of plasmablasts and transitional B-cells had positive correlation with some immunological diagnostic markers and immunological activity parameters of SjS but didn`t associate with ESSDAI.

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AB0574 PREDICTOR FACTORS IN EMPOWERMENT OF PATIENTS WITH PRIMARY SJOGREN SYNDROME IN THE FRAME OF VALUE BASED HEALTH CARE

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Background: Patient empowerment is a key component in developing awareness of the disease in patient-centred care in the setting of chronic disease management.

Objectives: This study aimed to evaluate predictive factors in the empowerment of patients with Sjögren's Syndrome (pSS), while examining patients reported outcome measures (PROMs) in the setting of value-based health care.

Methods: In this cross-sectional study, 169 patients with pSS (F/M: 162/7; mean age: 52.94±12.20 years) were included. Data was collected from the clinical examination, major salivary gland ultrasonography (SGUS) and a structured questionnaire regarding utilisation of health services and PROMs regarding Oral Health Impact Profile-14 (OHIP-14), Hospital Anxiety and Depression Scale (HADS; HADS-Anxiety and HADS-Depression) and Self-reported General Health Status (100-m VAS; 0: very poor vs 10: very good). Both stimulated (S-SFRs) and unstimulated salivary flow rates (U-SFRs) of patients were measured as ml/min. Patients with hyposalivation were grouped as according to U-SFR (≤0.1 ml/min). Furthermore, Outcome Measures from Rheumatology ultrasonography (OMERACT US) scores (from 0: normal to 3 points: severe inhomogeneity) were collected to evaluate glandular involvement of patients. After initial statistical analyses was carried out, mediation analysis was performed to evaluate the associations.

Results: The rate of patients with hyposalivation was found as 45% and most (85.7%) had elevated SGUS scores (≥2 points). In addition, self-reported oral health problems were common in the study group (from 23.8% to 53.4%). Among this cohort, the patients suffered from Burning oral sensation (27 %) had poor scores in OHIP-14 (29.81±14.48 vs 20.22±12.43), HADS-Depression (10.07±4.49 vs 6.65±4.20) and Self-reported general health status (45.43±17.95 vs 55.56±22.43) compared to those without Burning oral sensation (p=0.006, p=0.019, p=0.018, respectively). Furthermore, significant correlations were observed between OHIP-14 score and HADS-A score (r: 0.4 p: 0.004) and HADS-D scores (r: 0.58 p=0.000). Utilising mediation analysis, the HADS-Depression score was directly mediated by the presence of Burning oral sensation (p=0.0005) and indirectly mediated by OHIP-14 score (p=0.0360). In this group, the interval from the last dental visit was mean: 19 months. Interestingly, 60% preferred to relate their oral discomfort during visits (3 times a year), to rheumatologists.

Conclusion: Better health outcomes could be achieved by reducing oral discomfort, increasing dental visits, improvement of oral health related quality of life and managing depression by a multidisciplinary team with dentists and psychiatrists in patient-centred care. Since these factors have a significant effect on patients' daily life, treatment plans are needed to provide patient empowerment by using suitable strategies in the frame of value-based health care.

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AB0575 MESANGIAL C1Q DEPOSITION, BUT NOT C3 AND C1Q DEPOSITION IN OTHER RENAL COMPARTMENTS, IS A PREDICTOR OF RENAL OUTCOME IN LUPUS NEPHRITIS

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Background: Complement activation is an important pathophysiological process in the pathogenesis and development of systemic lupus erythematosus and lupus nephritis (LN). However, the prognostic value of complement factors deposition in different kidney compartments has received little attention and, to the best of our knowledge, no study examined its association with renal outcomes in LN.

Objectives: To evaluate prognostic significance of C1q and C3 complement factors in renal tissue compartments.

Methods: We have conducted a retrospective cohort study and collected data on demographics, clinical and laboratory parameters and histopathology (light, immunofluorescent and electron microsopy) at the time of biopsy and after long-term follow-up. C1q and C3 expression graded in different kidney compartments (mesangium, glomerular basement membrane (GBM), tubular basement membrane (TBM) and blood vessel wall) and dichotomized into no or low (grades 0 and 1) and high expression (grades 2 and 3). Remission (defined as complete or partial remission) was defined as per EULAR 2019 guidelines.

Results: A total of 51 patients with biopsy-proven LN were followed up for 4.5±2.9 years (80% women, mean age at biopsy 38±14). A total of 29 (71%) achieved complete or partial remission. Complement expression in different kidney compartments was as follows: mesangium (C1q 54%, C3 59%), GBM (C1q 34%, C3 41%), TBM (C1q 5%, C3 5%) and blood vessel wall (C1q 0%, C3 5%). Patients with proliferative lupus had more frequently C1q and C3 deposition in the mesangium (69% vs. 14%, p<0.001 and 72% vs. 29%, p=0.005, respectively), while there were no differences between proliferative and non-proliferative LN in other renal compartments (all p>0.05). Subjects who achieved remission more frequently had C1q deposition in the mesangium (64% vs. 31%, p=0.045), but there was no association between remission and deposition of C1q or C3 in other renal compartments (all p>0.05). Interestingly, the association between C1q mesangial deposition and renal outcome was significant even after adjustment for age at biopsy, gender and lupus type (proliferative vs. non-proliferative) (OR 0.13 [0.02, 0.98], p=0.047).

Conclusion: C1q deposition in the mesangium might be an important prognostic factor in LN and more aggressive treatment of these patients may explain the better outcomes of these patients.

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Vasculitis - large vessel vasculitis

AB0576 SERUM 25-HYDROXYVITAMIN D WAS CORRELATED WITH THE DISEASE ACTIVITY IN TAKAYASU'S ARTERITIS

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Background: 25-Hydroxyvitamin D [25(OH)D] deficiency has been linked to autoimmune disease. However, the relationship between 25(OH)D and Takayasu's arteritis (TAK) disease activity remains largely unknown[1]
Objectives: This study aimed to investigate the association between serum 25(OH)D and disease activity in TAK patients.
Methods: A total of 117 patients with TAK (TAK group) and 75 healthy people (control group) were enrolled in our study. Fifty-nine of the patients were re-evaluated after six months of therapy. The serum 25(OH)D levels were compared between the groups. The correlations between the 25(OH)D levels and TAK disease activity were analyzed.
Results: The serum 25(OH)D levels were markedly lower in the TAK patients than those in the healthy subjects [(12.16±4.9) μg/L vs (21.97±8.33) μg/L] (P<0.001). Serum 25(OH)D in all TAK patients was negatively correlated with IL-6 (r=-0.214, P=0.035). The serum 25(OH)D levels in the TAK patients were significantly higher after six months of therapy with glucocorticoid and immunosuppressive agents than those at baseline [(12.16±4.9) μg/L vs (18.01±7.32) μg/L] (P<0.001). Finally, we showed that elevated changes in the 25(OH)D levels before and after treatment were positively correlated with reduced changes in the NIH, ITAS2010 and ITAS-A scores (r=0.490, P<0.001; r=0.496, P<0.001; and r=0.306, P=0.018, respectively).
Conclusion: The serum 25(OH)D levels were significantly downregulated. The changes in 25(OH)D were positively correlated with changes in disease activity.
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AB0577 CLINICAL MANIFESTATIONS AND VARIANTS OF THE COURSE OF TAKAYASU ARTERITIS IN A KYRGYZ COHORT

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Background: The lack of a unified clinical classification and standardized methods of diagnosis creates additional difficulties for timely verification of the diagnosis in real clinical practice. According to a number of studies, there are some differences in phenotypic manifestations among patients with Takayasu arteritis (TAK) of different ethnicity, which determined the objectives of this study.
Objectives: To study the features of the course of the TAK in the Kyrgyz cohort (KC) of patients.
Methods: The angiographic classification of R. Moriwaki et al. was used to determine the anatomical type of vascular bed lesion [1]. The TAK activity was evaluated according to BVAS index, developed by R. Luqmani et al. R. [2], Jefferson's classification was used to characterize the clinical stage of TAK [3]. K. Ishikawa's classification was used to detect the severity of complications and assess the forecast of the disease [6]. All patients underwent a standard laboratory tests, with the mandatory determination of highly sensitive CRP (hs-CRP) and interleukin 6 (IL6). Degree of peripheral vessels lesion was assessed according to data from Duplex Doppler ultrasound scanning of arteries in the color Doppler imaging mode.
Results: The study included 130 patients who were diagnosed with TAK, verified according to criteria of the American College of Rheumatology (ACR, 1990) [4,5] and who received treatment at the NCCIM from January 2014 to November 2021. The majority of patients were women (93.08%), of Kyrgyz nationality (90.77%), of young age - 32 years old [23; 41], with a disease duration of 6.5 years [3.0; 11.0], with the onset of the disease at the age of 23 [18; 31]. By anatomical type of vascular lesion, the patients were distributed as follows: type I was detected in 18 (13.85%), II (a and b) - in 24 (18.46%) patients, III - in 2 (1.54 %), IV - in 5 (3.85%) and V - in 81 (63.3%) patients, which indicated the prevalence of generalized and diffuse lesions of all parts of aorta. According to the BVAS index, most patients had a severe exacerbation - 74 cases (57%), mild exacerbation observed slightly less (42 cases or 32.3%), partial remission occurred in 13 cases (10%) and complete remission in only 1 case (0,77%). By clinical classification, the majority of patients (119 or 91.54%) had vascular stage; none of the patients had the criteria for the prevasculitis stage. In the overwhelming majority of patients (43.84%) nature of vascular lesion was represented by isolated stenosis while a combination of stenosis with occlusive changes was observed in almost 40% of patients.
Conclusion: In the KC of patients with TAK, the overwhelming majority of cases was among women (90.77%) of young age with the onset of the disease at 23 years. Generalized lesions of the arterial bed (63.3%) and severe exacerbation (57%) were mainly observed. The vascular stage predominated (in 91.54% of cases), with the prevalence of stenotic and occlusive changes (40%).
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AB0578 C-REACTIVE PROTEIN TO ALBUMIN RATIO IN BEHÇET'S DISEASE

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Background: Behcet's Disease (BD) is a systemic variable vessel vasculitis that involves the skin, mucosa, joints, eyes, vascular, nervous and the gastrointestinal system.
Objectives: There is no specific laboratory test for the diagnosis and following of Behçet's disease (BD).This study aims to evaluate the relationship between C-reactive protein (CRP)/albumin ratio (CAR) and other hematological parameters in BD.
Methods: A total of 200 participants (100 BD patients and 100 healthy control) were recruited from the rheumatology outpatient clinic in this cross-sectional study. The laboratory data were obtained from the hospital database. Laboratory tests were conducted to measure complete blood count, erythrocyte sedimentation rate (ESR), CRP, albümin, CAR, neutrophil to lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR). Laboratory findings of BD patients and healthy controls were compared and evaluated. BD Activity scores (BDCAF/Behcet's Disease Current Activity Form) were calculated. The inclusion criteria were fulfilling the international diagnostic criteria of BD, being over 18 years and accepting to participate in the study.
Results: In the BD group, there were 42 male and 58 female participants with a mean age of 42.49 ± 13.15 and in the healthy control group, 44 male and 56 female participants with a mean age of 44.90 ± 10.98. The age and gender distributions of the groups were as similar (P: 0.16 and P: 0.78, respectively). NLR, CRP, ESR and CAR values were significantly higher in patient group than in the healthy controls (respectively p:0.022, p: 0,013, p:0.001, p:0,011). BDCAF score varied between 0 and 4 with a mean of 1.55± 0.64. A statistically significant correlation was observed between BDCAF and CRP, ESR and CAR (p<0.0001).
Conclusion: In this study, a significant correlation was found between CAR and BDCAF, NLR, CRP, albumin and ESR. CAR can be useful in the diagnosis and following of BD patients. However, further studies are needed.
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AB0579 EVALUATION OF PATIENTS WITH PEDIATRIC BEHÇET'S DISEASE: A TERTIARY CENTER EXPERIENCE

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Background: Behçet's disease (BD) is an systemic inflammatory vasculitis characterized by recurrent oral aphthae and genital ulcers. In the course of the disease, skin, eye, musculoskeletal, nervous system and gastrointestinal system involvements can be detected.
Objectives: To evaluate the clinical, laboratory and radiological findings of pediatric cases diagnosed with BD.
Methods: Fifty patients (0-20 years old) who were followed up with the diagnosis of BD at the Pediatric Rheumatology outpatient clinic of Uludag University Faculty of Medicine between January 2011 and July 2021 were included in our study. The patients were diagnosed according to the diagnostic criteria of the International BD Study Group.
Results: Twenty-four (48%) of the patients were male and 26 (52%) were female. The mean age at the diagnosis of patients was 9 ±4.55 years (10.75±4.55 years in boys, 12.35±3.65 years in girls). Twenty patients (36.3%) had a family history of Behçet's Disease. Oral aphthae were present in 96% (n=48) patients, while genital ulcers were in 32% (n=16) (Table 1). Of the nine patients with uveitis, 6 had panuveitis, 2 had anterior uveitis and 1 had posterior uveitis. . There was no difference in the distribution of symptoms according to the gender of the patients. HLA-B51 allel was found in 39 (78%) and ANA was positive in 14 patients (28%). Immunological tests showed that serum immunoglobulins were low in 11 (32.3%) of 34 patients. Low IgG levels were detected in 6 patients, low IgM levels were in 3, and low IgA levels were in 2. Thrombus was presented in three cases (thrombus in the right ventricle in one case, in the intracranial transverse sigmoid sinus and left jugular vein in two cases). The most commonly used drug for aphthae was colchicine (n=45, 82%). The use of biological agents according to patient manifestations is shown in Table 2. In the follow-up, clinical findings improved in 35 patients (70%) Complete improvement was detected only with biological agents in 8 patients with uveitis. One patient was operated due to the development of complicated cataracts secondary to uveitis. Three patients were diagnosed with Covid-19, one of them was followed without treatment, while two of them were treated with favipiravir at home. Three patients with Covid-19 infection were using only colchicine treatment.

Table 1.

Findings at the time of diagnosis	n	%
Uveitis	9	18
Skin findings	18	36
Gastrointestinal tract involvement	19	38
Central nervous system involvement	6	12
Vascular involvement	3	6
Arthritis	17	34

Table 2.

Findings Biological Agents	Uveitis (n)	Arthritis (n)	Venous thrombus (n)	Central nervous system involvement (n)
Azathioprine	2	2	3	1
Methotrexate	2	2	-	-
Adalimumab	3	1	-	-
Infliximab	3	1	-	-

Conclusion: Behçet's disease is rare in childhood. Although it is not common, life-threatening complications can be observed. To reduce morbidity and complications, physicians should be aware of manifestations and rare clinical pictures of the BD.
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AB0580 BEHÇET'S DISEASE IN OSLO NORWAY IN PERIOD 1999 – 2021

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Background: Bechet's disease (BD) is a multisystemic, inflammatory disease, characterized by variety of clinical manifestations, including mucocutaneous, ocular, vascular, neurological (CNS) and gastrointestinal (GI) involvements. The disease can be seen at any age and occurs across gender, ethnic groups, and geographical areas. However, there are only a few studies from northern Europe.
Objectives: To study the demographics and clinical feature of patients with Bechet's disease (BD) in Oslo Norway.
Methods: In this retrospective study we reviewed hospital records from Oslo University Hospital (OUS), a referral hospital for systemic inflammatory vasculitis in Norway. All patients living in Oslo with ICD-10 code M35.2 were identified, and their BD-related data recorded. Those fulfilling either the International Study Group criteria (ISG) or International Criteria for Bechet's disease (ICBD) were included. Patients were defined as non-Norwegian when none of the parents was of Norwegian ancestry. The differences between groups were compared by Chi-square test using the Statistical Package for the Social Sciences (SPSS).
Results: We identified a total of 58 patients fulfilling the inclusion criteria (Table 1). Among them, 30 (52%) were females and 25 (43%) of Norwegian ancestry. Mean age at onset was 26 years, and at diagnosis 32 years.

Table 1. Demographics of Behcet`s patients in Oslo Norway

Counts (%)	Norwegian ancestry	Non-Norwegian ancestry	All (%)
All (%)	25 (43)	33 (57)	58 (100)
Male (%)	8 (29)	20 (71)	28 (48)
Female (%)	17 (57)	13 (43)	30 (52)
ISG Criteria (%)	20 (47)	23 (53)	43 (100)
ICBD Criteria (%)	25 (43)	33 (57)	58 (100)
Age at diagnosis mean (SD) years	33 (11.85)	32 (9.36)	32 (10.41)
Age at onset mean (SD) years	24 (9.34)	27 (9.52)	26 (9.42)

The most prevalent clinical manifestations were oral ulcers (n=58, 100%), genital ulcers (n=49, 84%) and skin lesions (n=40, 69%). Ophthalmic complications (n=21, 36%), arthritis (n=20, 34%), vascular involvement (n=7, 12%), CNS (n=3, 5%) and gastrointestinal (GI) complications (n= 4, 7%) were also present. There was no significant difference of clinical features between patients with Norwegian ancestry and those with non-Norwegian ancestry (data not shown).

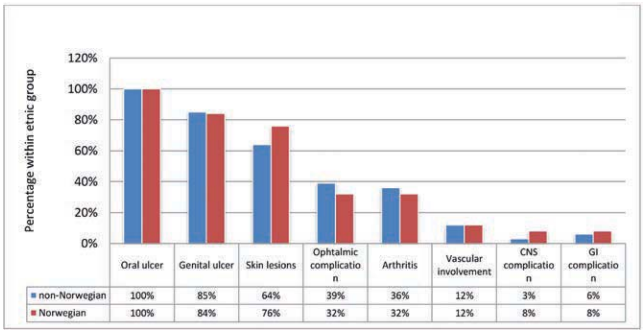

Figure 1.

Conclusion: BD was most prevalent among patients of non-Norwegian ancestry. We found a wide spectrum of clinical manifestations occurring during the disease course. Mucocutaneous lesions were most frequent, but potential serious manifestations were also present. These manifestations were similarly distributed between patients with Norwegian and non-Norwegian ancestry (Figure 1).
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AB0581 TRACHEAL STENOSIS; AN IMPORTANT INVOLVEMENT IN GRANULOMATOSIS WITH POLYANGIITIS

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Background: Granulomatosis with polyangiitis (GPA) is a granulomatous systemic vasculitis of unknown etiology that can affect many organs. Approximately 90% of patients with GPA have upper respiratory tract involvement, including the nasal cavity, sinuses, ear and trachea. Subglottic stenosis (SGS) may develop in some patients due to tracheal involvement.
Objectives: It is aimed to evaluate the general characteristics, treatments and disease prognosis of our GPA cases with tracheal stenosis as it is a significant cause of morbidity and mortality.

Methods: The data of 48 patients diagnosed with GPA between 2000-2021 were analyzed retrospectively and the data of 6 patients with tracheal stenosis (TS) were evaluated.
Results: TS was present in 13% of the patients. All patients with TS were female. The mean age of the patients with TS was 46.5±6.5 years, the mean age of disease onset was 35.5 ±13.4 years, and the mean disease duration was 10.8±10.2 years. Constitutional symptoms were in 17% of patients, and 17% had mastoiditis, sinusitis, otitis, bloody nasal discharge and renal involvement. None of the patients had hearing loss, skin, eye and neurological involvement. 83% of patients had limited disease. While all patients had SGS, one patient also had glottic and bronchial stenosis. The most common symptoms in patients were hoarseness and shortness of breath. All patients received systemic treatment according to their organ involvement, local treatment (dilatation, steroid injection) was also applied to two patients. All patients had anti-neutrophil cytoplasmic antibody (ANCA) positivity. When patients with and without tracheal stenosis were compared, there was a difference in terms of gender, lung and kidney involvement, presence of anemia, increased erythrocyte sedimentation rate, pANCA, cANCA and PR3-ANCA positivity, and myalgia. In addition, our patients with tracheal stenosis had a younger age of onset and a longer delay in diagnosis.
Conclusion: The incidence of SGS in large series has been reported as 8-23% of GPA patients.[1,2] Although the number of cases in our study was small, this rate was 13%. Symptoms range from cough and shortness of breath to progressively life-threatening severe stridor. Early diagnosis and treatment are important. For this reason, TS is strongly emphasized.
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Table 1. Comparison of data from GPA patients with and without tracheal stenosis

N(%)	Tracheal Stenosis +GPA(n=6)	Tracheal Stenosis - GPA (n=42)	P
Gender Female	6 (100)	21(51)	***0.031***
Male	0	20(49)	
Mean Age	46.5±6.5	55.6±13.2	0.095
Symptom Onset Age	35.5±13.4	49.3±14.5	***0.041***
Delay in Diagnosis (months)	44.2±6.5	9.98±14.8	***0.023***
Myalgia	2(33)	33(81)	***0.030***
Fever	1(17)	21(51)	0.194
High ESR	1(17)	31(78)	0.007
High CRP	5(50)	32(80)	0.138
Anemia	1(17)	28(70)	***0.020***
Upper Respiratory Involvement	6(100)	24(59)	0.074
Lung Involvement	3(50)	36(90)	***0.037***
GIS involvement	1(17)	6(15)	1
Eye Involvement	-	11(27)	NA
Skin Involvement	-	12(29)	NA
Urogenital Involvement	-	1(2)	NA
Neurological Involvement	-	13(32)	NA
Renal Involvement	1(17)	29(71)	***0.018***
ANCA positivity	6(100)	38(93)	1
MPO-ANCA	2(33)	4(10)	0.162
PR3-ANCA	1(17)	33(81)	***0.004***
p-ANCA	5(83)	6(15)	***0.000***
c-ANCA	1(17)	31(78)	***0.001***

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AB0582 TAKAYASU ARTERITIS PRESENTS AT AN OLDER AGE IN EUROPEAN POPULATION

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Background: The definition of Takayasu arteritis includes the age of onset of disease as being <50 years. It has been reported most frequently in young females from Asian populations.
Objectives: We investigated whether the epidemiological features are the same in Norfolk, UK, where the population is predominantly of Northern European ancestry.
Methods: In our centre, cases are classified using validated international criteria. The electronic records of our vasculitis clinic were reviewed to identify all individuals with a new diagnosis of large vessel vasculitis between 2011-2020 who met a modified ACR 1990 criteria for Takayasu arteritis. The original criteria include decreased brachial artery pulse, bruit over subclavian arteries or aorta, and arteriogram abnormality. The respective modifications of these three criteria were to accept decreased radial pulse as well as the brachial pulse, bruit over the axillary artery as well as the subclavian artery, and abnormality of positron emission tomography and/or ultrasonography instead of arteriograms.
Results: 15 individuals met the modified ACR 1990 criteria for Takayasu arteritis. 2 of them also met the criteria for GCA and were excluded. 13 individuals were classified as having Takayasu arteritis. 11 were female. The mean (standard deviation) age at diagnosis was 66.9 (8.9) years. None of individuals were <40 years old. On presentation - 9 had upper limb claudication, 7 had pulse discrepancy, 3 had a blood pressure difference >10 mm Hg systolic, 7 had an audible bruit over either subclavian or axillary artery. The diagnosis was confirmed on positron emission tomography in 8. Ultrasonography of extracranial arteries was abnormal in 7. The mean (standard deviation) ESR was 53.2 (33.6) and CRP was 37.5 (32.8).
Conclusion: Takayasu arteritis can present at an older age in Norfolk, UK, where the population predominantly has Northern European ancestry. This has implications for treatment, identification of immunogenetic factors and disease classification.
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AB0583 REFERRAL PATTERN AND TREATMENT OF POLYMYALGIA RHEUMATICA IN GENERAL PRACTICE: AN INTERNATIONAL QUESTIONNAIRE BASED STUDY

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Background: In most countries polymyalgia rheumatica (PMR) is diagnosed and managed by both general practitioners (GP) and rheumatologists. However, the referral pattern from GP's to specialist around the world has not been described. The initial prednisolone dose recommended by EULAR/ACR is between 12.5 and 25 mg[1], but little is known about whether these guidelines are followed everywhere by GP's in clinical practice[2].
Objectives: This study aims to describe the refererral pattern and treatment strategy for PMR in general practice in several countries worldwide.
Methods: An English language questionnaire was drafted by a working group of rheumatologists and GP's from 6 different countries. The questionnaire contained questions on: 1: Respondent, 2: Referral pattern and 3: Prednisolone. Questionnaires were distributed to GP's via members of the International PMR/GCA study group. Answers were collected via an online survey tool (Redcap), from 3rd of November 2021 to 27th of January 2022. Countries with more than 15 responders to the questionnaire were included in the analysis.
Results: Data from 11 countries were analysed. Referral patterns differed widely among countries (Table 1). Almost all patients initially seen by rheumatologists were returned to GP's for treatment. In all countries a proportion of the GP's prescribed higher initial prednisolone doses than recommended, with a large variation between countries (Table 1).

Table 1. Characteristics of responders, referral pattern, and treatment strategy

	Austria	Canada	Colombia	Denmark	Italy	Nether-lands	New Zealand	Romania	Russia	Switzer-land	United Kingdom
Responders											
Responders (n), Completed questionnaire (total)	26 (29)	15 (15)	17 (23)	53 (53)	36 (41)	22 (22)	17 (17)	37 (43)	42 (49)	26 (26)	34 (35)
Experience (years)	20 (12-34)	8 (4-10)	6 (4-9)	12 (10-17)	15 (5-27)	23 (17-30)	14 (9-27)	21 (16-30)	6 (5-9)	26 (15-32)	16 (11-24)
Available PMR/GCA guideline, n (%)	26 (100)	15(100)	17 (100)	53 (100)	36 (100)	22 (100)	17 (100)	37 (100)	42 (100)	26 (100)	34 (100)
Adherence to guideline, n (%)	21 (82)	15 (100)	17 (100)	51 (97)	34 (94)	21 (95)	17 (100)	37 (100)	42 (100)	26 (100)	34 (100)
Referrals											
New PMR patients referred for diagnose (%)	58 (10-100)	50 (2-100)	100 (13-100)	50-(20-100)	60 (28-100)	20 (10-50)	10 (10-20)	60 (10-88)	1 (1-2)	28 (10-50)	10 (1-25)
Patients returned to GP for treatment (%)	100 (50-100)	50 (2-100)	8 (0-50)	85 (40-100)	50 (0-100)	50 (10-90)	100 (90-100)	80 (50-98)	1 (1-1)	80 (10-100)	100 (100-100)
Patients referred during treatment (%)	50 (25-90)	50 (10-100)	100 (50-100)	20 (10-33)	50 (15-80)	15 (10-30)	20 (10-25)	30 (10-80)	1(1-1)	20 (10-30)	10 (10-20)
Prednisolone											
Initial dose (mg)	38 (25-50)	20 (20-50)	20 (10-30)	25 (15-40)	25 (25-25)	15 (15-15)	20 (15-40)	15 (12-20)	15 (15-15)	50 (25-50)	15 (15-20)
Initial dose > 25 mg, n (%)	12 (47)	4 (25)	7 (40)	14 (26)	9 (25)	1 (5)	6 (38)	7 (20)	3 (8)	22 (83)	3 (9)
Duration of treatment (months)	9 (6-12)	6 (2-9)	6 (4-24)	12 (8-18)	5 (3-12)	11 (6-12)	12 (10-18)	2 (2-5)	6 (6-6)	12 (12-14)	15 (12-24)

Data are presented as weighted median (interquartile range) unless otherwise stated. GP: general practitioner, PMR: polymyalgia rheumatica, GCA: great cell arteritis.

Conclusion: Although many patients were referred to the hospital for initial PMR diagnosis or during the disease course, a large proportion of patients received treatment in general practice worldwide. GPs frequently use a higher starting dose of prednisolone and shorter treatment duration than recommended by EULAR/ACR.

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AB0584

MANAGEMENT OF REFERRALS, TREATMENT STRATEGY, AND RESEARCH CHALLENGES IN POLYMYALGIA RHEUMATICA AMONGST RHEUMATOLOGISTS WORLDWIDE: A QUESTIONNAIRE BASED STUDY

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Background: Polymyalgia rheumatica (PMR) is diagnosed and treated by both general practitioners (GP) and rheumatologists. How rheumatologists around the world manage the referral process of patients with PMR from GP's has not been described. EULAR/ACR guidelines recommend initial prednisolone doses between 12.5 and 25 mg, but it is unknown if guidelines are followed in daily clinical practice[1]. In addition, the understanding of challenges for recruitment to clinical trials in PMR is currently limited.

Objectives: This study aims to describe the management of referrals, treatment strategy, and recruitment to clinical trials in PMR among rheumatologists worldwide.

Methods: An English language questionnaire was drafted by a working group of rheumatologists and GP's from 6 different countries. Questions concerned: 1: respondent, 2: referrals, 3: prednisolone, and 4: barriers to research. Questionnaires were distributed to rheumatologists via members of the International PMR/GCA study group. Answers were collected via an online survey tool (Redcap), from 2nd of November 2021 to 27th of January 2022. Countries were grouped by income and geographical region based on the World bank classifications. Data were weighted by number of inhabitants in a country, based on the United Nations age specific population count, divided by number of respondents in a country. Countries with more than 20 respondents were included.

Table 1. Characteristics of reponders, referrals, and treatment.

		Geographical region							Income	
		The world	Europe and Central Asia	North America	Latin America	East Asia and Pacific	South Asia	Middle East and Africa	High- income countries	Low- and middle-income countries
Responders	Responders (n), Completed questionnaire (total)	875 (1000)	294 (304)	78 (81)	136 (152)	53 (53)	53 (72)	261 (338)	446 (458)	429 (542)
	Experience as rheumatologist (years)	11 (6-20)	12 (6-20)	7 (4-20)	11 (6-23)	21 (10-30)	7 (4-10)	9 (5-18)	11 (5-22)	8 (5-12)
Referrals	GP's can discuss patients prior to referral, %	64	79	79	57	58	60	67	74	61
	Referred patients seen (%)	100 (90-100)	100 (90-100)	100 (100-100)	100 (100-100)	100 (95-100)	100 (100-100)	100 (60-100)	100 (100-100)	100 (90-100)
	Evaluation > 2 weeks after referral, %	26	49	80	60	21	6	18	58	15
Prednisolone	Started prior to rheumatological evaluation (%)	50 (20-50)	60 (30-80)	70 (50-80)	50 (10-50)	30 (20-50)	50 (20-80)	20 (0-50)	50 (30-80)	50 (10-70)
	Initial dose (mg)	20 (15-40)	20 (15-20)	20 (15-20)	20 (20-40)	15 (15-15)	20 (15-40)	20 (15-40)	15 (15-20)	20 (15-40)
	Initial dose > 25 mg, %	32	9	6	41	0	41	43	6	42
	Duration of treatment (months)	12 (6-12)	12 (12-18)	12 (10-18)	6 (3-12)	18 (12-18)	12 (6-12)	6 (3-12)	12 (12-18)	9 (6-12)

Data presented as weighted median (interquartile range) unless otherwise stated. GP: general practitioner

Results: Results from 27 countries were analysed including 1000 responders in total (Figure 1). There was large variation in time from referral to first assessment, initial dose of prednisolone was high, duration of treatment was relatively short, and a large proportion of patients with newly diagnosed PMR received prednisolone prior to rheumatological evaluation (Table 1). Concerning the 15% of respondents who performed research in PMR, 52% had participated in clinical trials and 56% of the responders experienced difficulties with recruitment.

Conclusion: This is the first description of current practice in managing referrals and treatment of PMR by rheumatologists worldwide. In general, median treatment duration was according to EULAR/ACR guidelines, but initial dose of prednisolone was often higher than recommended in many parts of the world. PMR patients were often seen more than two weeks after referral, and treatment had started prior to first rheumatological evaluation.

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AB0585 NEURO-BEHÇET'S DISEASE: A TUNISIAN EXPERIENCE

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Background: Behçet's disease (BD) is a systemic inflammatory vasculitis with a wide range of manifestations including neurological involvement. Though neuro-Behçet's disease (NBD) is relatively uncommon, it encompasses some of the most serious manifestations of BD. Its diagnosis can be challenging, as there is no specific diagnostic test.

Objectives: Our study aimed to describe epidemiological, clinical and paraclinical characteristics of BD, and compare them between patients with and without NBD.

Methods: We conducted a retrospective study, including all patients meeting the revised international study group criteria for BD, over an 18-year period. We divided patients into 2 groups, based on the presence or absence of neurological involvement, retained according to the international consensus recommendation criteria for NBD. Epidemiological, clinical and paraclinical features were then analysed and compared between the two groups.

Results: We obtained a cohort of 77 patients with a gender ratio (M/F) of 1.85 and a mean age at diagnosis of 34.4 years [20-60]. Mucocutaneous involvement inaugurated BD in 81.8% of cases, followed by joint involvement (19.5%), vascular involvement (17.9%), neurological involvement (10.7%) and ocular involvement (2.6%). Mucocutaneous involvement was dominated by oral aphtosis (100%) and genital aphtosis (79.2%) with a mean frequency of episodes per year of 8.3 ± 6.2 and 6.9 ± 5.1 respectively, followed by pseudo-folliculitis (66.2%), erythema nodosum (19.5%), and positive pathergic test (13%). Joint involvement (62.3%) was mainly peripheral (arthralgia in 98% and arthritis in 25%), affecting large joints (85.1%) and bilateral in 78.8% of cases (asymmetric in 48.6%). Axial involvement and sacroiliitis were observed in 14.6% and 10.4% of cases, respectively. Only one patient had a popliteal cyst. Vascular manifestations (36.4%) were venous thrombosis (92.9%), arterial thrombosis (12.9%) and arterial aneurysms (6.5%). Ocular manifestations (35%) were uveitis and vasculitis in 77.8% of patients respectively, with predominance of bilateral lesions (70.4%). Other manifestations were cardiac involvement (5.2%), intestinal involvement (3.4%) and fever (23.4%). One patient developed membranous glomerulonephritis without any other underlying aetiology. Biological inflammatory syndrome was found in 42.9% of patients. Twenty-eight patients developed NBD with 34 outbreaks during follow up. The mean delay from onset of BD was 6.3 years [0-26]. Parenchymal NBD was more frequent (73.5%). Non-parenchymal syndromes (38.2%) were acute meningitis (17.6%), cerebral venous thrombosis (11.8%), pseudotumour cerebri (5.9%) and isolated intracranial hypertension (2.9%). One patient developed peripheral neurological involvement. Headache

(59%) and motor deficits (32.4%) were the most common signs. Neurological examination most frequently revealed a pyramidal syndrome (32.3%). Severe forms (modified Rankin scale ≥2) dominated clinical presentations (64.7%). CSF study revealed abnormalities in 10 (35.7%) cases: Increased protein with pleocytosis in 6 cases with lymphocytic predominance (n=3), mixed formula (n=2) and PNN predominance (n=1), decreased glucose levels and increased pressure in 3 cases respectively, and one case of albuminocytological dissociation. The predilection sites of NBD lesions on MRI were brainstem and basal ganglia (35.5%, respectively), periventricular white matter (26.5%), subcortical WM (23.5%), internal capsule (20.6%), centrum semiovale and cerebral cortex (11.8%, respectively) and cerebellum (3%). Comparison between the two groups revealed, in patients with NBD, an older mean age at diagnosis (37.7±11.97 vs 32.3 ±7.14, p=0.023) and a lower frequency of ocular involvement (21.4% in G1 vs 42.9% in G2, p=0.05). We found no statistically significant differences when comparing gender ratio and other clinical and biological features.

Conclusion: Ocular lesions were more frequent in patients without NBD. Large-scale studies are needed in order to determine markers associated to neurological involvement.

Disclosure of Interests: None declared

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AB0586 OCULAR ISCHEMIC SYNDROME CAUSING ACUTE BINOCULAR VISION LOSS IN THREE PATIENTS WITH TAKAYASU ARTERITIS TYPE V: A THERAPEUTIC QUANDARY

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Background: Ocular Ischemic syndrome (OIS) is a rare manifestation in Takayasu Arteritis (TA) which can cause irreversible retinal ischemia and neovascular changes. Ocular Ischemic syndrome denotes hypoperfusion of both anterior and posterior segments of eye and orbital structures as a result of common/internal carotid artery occlusion[1,2]. Although described as a chronic phenomenon, we report three young female patients, diagnosed Takayasu Arteritis Type V (Angiographic Classification) who presented to us with acute binocular loss of vision which were managed with individually tailored approaches to restore vision.

Objectives: 1.To elaborate on three patients diagnosed Takayasu Arteritis type V presenting with acute onset binocular vision loss and discuss critical aspects of management in OIS.

Methods: Case series of three patients of TA satisfying 1990 ACR classification criteria.

Results: 18-year-old female presented with acute onset painless loss of vision in both eyes and severe vertigo. She appreciated hand motion on visual acuity testing. She was started on Methotrexate (MTX)and Prednisolone (PSL). In view of acute vertebrobasilar and carotid insufficiency, she underwent bilateral carotid and vertebral angioplasty. She tested 20/80 on visual acuity in both eyes and ambulated without support by two weeks after procedure.

15-year-old female presented with episodic vertigo, amaurosis fugax and claudication of both upper and lower limbs. She was kept on MTX and tapering doses of PSL and when dose of PSL reached less than 0.25mg/kg, she developed acute binocular vision loss with absent pupillary reflexes. Visual acuity testing revealed perception of hand motion in both eyes which improved to 20/40 within 2 weeks after increasing steroid dose to 0.5mg/kg and tocilizumab.

14-year-old female presented with acute binocular painless vision loss with previous history of limb claudication. Examination revealed no light perception on visual acuity testing in both eyes with absent pupillary reflexes. She was started on tapering doses of PSL and MTX. Also, she underwent a bilateral carotid and vertebral artery angioplasty. By first week, she could identify hand motion in both eyes and is continued on inpatient care.

Conclusion: We suggest that combining vascular surgical and pharmacological intervention in acute vision loss in TA may restore vision, even in active disease. Prompt follow-up and wider sample size is needed to draw insights into ocular involvement in TA.

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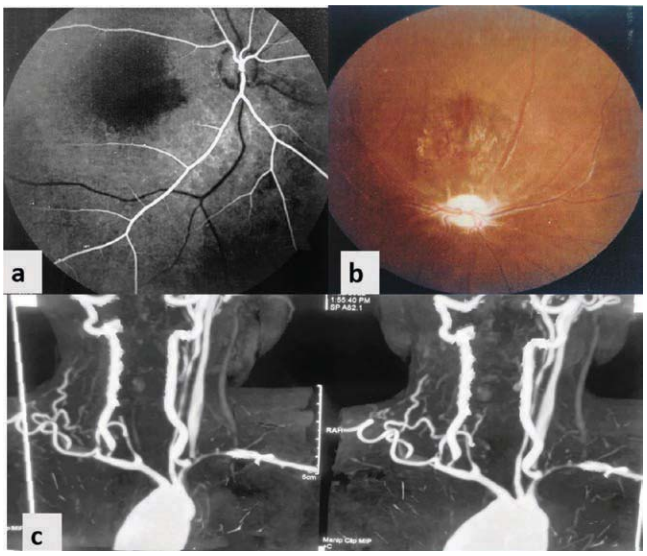
Figure 1. Picture attached showing a)Fundus angiogram – increased foveal avascular zone b)Fundus image -ischemic changes c)CT Aortogram -Bilateral Carotid and subclavian stenosis



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AB0587 THE RISK OF PATIENTS WITH POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS TO DEVELOP DIABETES AND OSTEOPOROSIS ON FOLLOW UP

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Background: Patients with polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are commonly treated with glucocorticoids (GC) in different dosages. Therefore, the most common comorbidities that may develop are osteoporosis (OPO) and diabetes mellitus (DM).

Objectives: To study the development of these comorbidities in the management of PMR and GCA in a real-life setting.

Methods: In a retrospective study design, longitudinal data of patients with a clinical diagnosis of PMR and GCA treated in a tertiary center were studied. Patients and disease characteristics were documented according to clinical routine in patients in whom ≥ 2 documented visits ≥ 3 months apart had been documented.

Results: A total of 550 patients (382 PMR, 168 GCA) was analysed (Table 1). The time period of follow up (FU) ranged between 3 months and 13.6 years (mean 1.4 (0.3) years). The majority of patients received a diagnosis of PMR or

Table 1. Characteristics of patients of TA with acute binocular vision loss

Age	Duration(years)	Absent peripheral pulse	Hypertension	CRP levels	CT aortogram involvement	TA type	Fundus angiogram findings	Fundus examination
18	1	Both brachial and radial	No	High	Both proximal subclavian arteries, common carotid, Infrarenal aorta, coeliac and superior mesenteric arteries	V	capillary non perfusion areas	Normal
15	2	Both brachial, radial, right popliteal and Dorsalis pedis.	Yes	High	Both subclavian arteries, common carotid, renal and iliac arteries with >50% narrowing of abdominal aorta	V	capillary non perfusion areas	Grade II Hypertensive retinopathy
14	4	Left Brachial and radial	Yes	Normal	Both subclavian, renal, iliac arteries and > 70% diffuse stenosis of bilateral carotids	V	increased foveal avascular zone, capillary non perfusion areas	Cotton wool spots, venous engorgements

GCA in our center while 29.5% of patients came for a second opinion. Their mean age was around 70 years, and most patients were female (Table 1). Eight GCA patients were already blind (4.8%) at first presentation, and 77 and 80 patients had a diagnosis of DM (15.5%) and OPO (16.0), respectively, already at baseline. During FU 56 PMR (16.0%) and 7 GCA patients (4.2%) were diagnosed with another autoimmune disease, mainly with rheumatoid arthritis (n=50 (69.4%)). The mean dose of GC differed substantially between groups (Table 1). On FU, 9 (2.4%) and 5 (3.0%) of PMR and GCA patients developed DM and 17 (4.5%) and 14 (8.4%) OPO, respectively. Thus, about 20% and 25% of patients with PMR or GCA finally had DM and OPO, respectively. Almost all patients received vitamin D and antiresorptive agents.

Table 1. Patients and disease characteristics

	PMR patients (n=382)	GCA patients (n=168)	Significance
Age (years)	68,2 (9.3)	71.1 (8,6)	0.9
BMI (kg/m^2)	27.0 (4.9)	26.0 (5,3)	0.44
Female sex, n (%)	216 (56.6)	121 (72,0)	<0.001
Time to rheumatologist (months)	2.1 (9,7)	1.4 (5,4)	0,33
CRP at baseline (mg/dl)	3,8 (4,6)	4,5 (5,5)	0,07
Prednisolone at baseline (mg/d)	25.1 (20,2)	52.0 (69,7)	<0.001
Comorbidities at baseline			
-Number of comorbidities (mean)	1.45 (1.12)	1.51 (1.12)	0.26
-Diabetes, n (%)	61 (16.0)	24 (14.3)	0.36
-Osteoporosis, n (%)	64 (16.8)	30 (17.9)	0.7
-Ischemic heart disease, n (%)	38 (9.9)	19 (11.4)	0.46
Organ manifestation and comorbidities at FU			
-Blindness n (%)	6 (1.6)	8 (4.8)	0.048
-Aneurysm n (%)	1 (0.3)	9 (5.4)	<0.001
-Diabetes, n (%)	70 (18.4)	29 (17.3)	0.89
-Osteoporosis, n (%)	81 (21.4)	44 (26.3)	0.003
-Vascular stenosis	4,6	10,1	0,048

values given as mean (SD)

Conclusion: In this large real-life cohort, patients with PMR and GCA aged around 70 years were seen by rheumatologists about 1-2 months after their first symptom but 8 GCA patients were already blind at first visit. DM and OPO were frequent comorbidities in both, PMR and GCA patients, already at baseline and during follow-up more patients developed these comorbidities despite prophylactic and therapeutic medication. OPO and DM should be a routine concern in the care of PMR and GCA patients - already when glucocorticoids are started.
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AB0588 GIANT CELL ARTERITIS: DO DIFFERENT PHENOTYPES OF PRESENTATION MEAN DIFFERENT CLINICAL ENTITIES?

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Background: Giant cell arteritis (GCA) represents the most common primary vasculitis of the elderly, affecting large and medium-sized arterial vessels. GCA often also involves the aorta and its major branches and may lead to aortic aneurysm/dissection as well as large artery stenoses; it seems that unrecognized extra-cranial involvement may be even more common.
Objectives: The primary aim of this study was to explore the different clinical entities in a large cohort of patients with GCA; a secondary aim was to evaluate long-term outcome of GCA patients with at least 5 years of follow-up.
Methods: A cohort of 278 GCA patients (54 males and 224 females, mean ± SD age 75 ± 6 years) were retrospectively studied. Clinical symptoms at disease onset and during the follow-up, time delay until diagnosis, as well as laboratory findings at the time of diagnosis and therapeutic approach were retrospective evaluated. In order to characterize the different clinical phenotypes, overall clinical symptoms were grouped for macro-area (cranial versus systemic). Moreover, long-term outcomes in patients with a minimum follow-up of 3 years were evaluated. A disease flare was defined as the presence of any further clinical manifestation compatible with the clinical spectrum of GCA and an increase of ESR ≥ 30 mm/hour, not otherwise justifiable, that required higher doses or new introduction of glucocorticoids (GC) therapy and/or the introduction of steroid sparing treatments (e.g. tocilizumab, methotrexate).
Results: The most frequent clinical manifestations presented at the onset included: constitutional symptoms 69%, new onset headache and/or scalp pain 64%, jaw claudicatio 32%, vision loss 30%, abnormal temporal artery on examination 19%, neuropsychiatric symptoms 17%, cough not otherwise justifiable 7%, cerebrovascular accidents 6% and hearing loss 3%. Irreversible (mono- or bilateral) blindness was reported in 7% of patients, mainly due to a latency period between onset and treatment of ≥ 3 months. Temporal artery biopsy was performed in 171 patients, resulting positive in 72%. Globally, about 38% of subjects (was characterized by a clinical profile compatible with extra-cranial GCA. In all cases, extra-cranial involvement was confirmed by (18)F-fluorodeoxyglucose (FDG) positron emission tomography (PET). Moreover, patients who presented symptoms compatible with large-vessel involvement were characterized by a more relapsing course compared with patients with cranial involvement GCA profile (both in terms of dose of corticosteroids and use of steroid-sparing agents).
Conclusion: According to the literature data, different phenotypes of GCA exist and they may probably represent different clinical entities, also in terms of prognosis and therapeutic approach. This is particularly crucial in order to plan a tailored therapy and prevent disease damage in the short and long-term follow-up.
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AB0589 TOCILIZUMAB FOR GIANT CELL ARTERITIS: BASELINE AND TWELVE MONTH AUDIT DATA FROM THE UK BRISTOL AND BATH MULTIDISCIPLINARY MEETING.

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Background: Giant Cell Arteritis (GCA) is a systemic vasculitis involving large and medium-sized blood vessels. Treatment is with high dose glucocorticoids. Steroid-sparing agents and Tocilizumab (TCZ) are used for refractory or relapsing cases. NHS England requires all GCA patients to be discussed in a regional multidisciplinary team meeting (MDT) prior to commencing TCZ. TCZ has only been permitted for a maximum of one year; this time limitation was extended during the Covid-19 pandemic (1). The monthly virtual Bristol and Bath regional MDT started in November 2018.
Objectives: We aimed to review: 1) Baseline data on all patients referred to the Bristol and Bath TCZ for GCA MDT, including demographics, clinical presentation and previous steroid-sparing agents used and 2) 12 month follow up data including number of completions, adverse effects, and flares on treatment.
Methods: The TCZ MDT referral proforma, adapted from the NHS England Blueteq approval form, was reviewed for all patients referred. 12 month follow up data was obtained from clinic letters.
Results: *Baseline data*
Thirty-eight cases were referred between November 2018 and September 2021. Of these, 31 were approved for TCZ usage; 100% fulfilled the criteria for either refractory (n=11) or relapsing (n=20) disease. Mean age was 74 years and 74.2% were female. Average disease duration was 161.5 days for the refractory and 827.3 days for the relapsing group.
77.4% had cranial GCA, 48.4% had large vessel involvement, 45.2% had visual symptoms and 25.8% had ischaemic visual loss. The positive investigations were PET-CT (48.4%), temporal artery ultrasound (41.9%) and temporal artery biopsy (32.3%).
64.5% had trialled a steroid-sparing agent at time of referral (61.3 % methotrexate, 9.7% azathioprine, 6.5% leflunomide), 35.5% had received intravenous methylprednisolone and 58% were receiving greater than 40mg prednisolone at the time of referral.
Glucocorticoid adverse effects of osteoporosis, weight gain, cataracts and hypertension were each seen in 19.4%; whilst diabetes, neuropsychiatric symptoms and sleep disturbance were each reported in 16.1%.
Those with ocular involvement tended to be referred earlier than those without (478.2 days vs 648.1 days), were referred on higher doses of glucocorticoids (71.4% vs 47.1% on ≥ 40mg) and had less steroid-sparing agents prior to referral.
Follow up data
In December 2021, a follow-up audit revealed 14/31 patients had completed at least 12 months of tocilizumab; 5 of these had had an extension under Covid-19 exceptional guidance (mean duration of 5.2 months). Of the remaining 17: 3 patients had stopped early (1 death, 1 moved away, 1 due to adverse effects of headache and gastro-intestinal side effects), 4 had not started tocilizumab and 10 had not completed 12 months of treatment at that point.
Adverse events in the 14 patients at 12 months included: liver abnormalities (2/14; 14.3%), neutropenia (2/14; 14.3%), thrombocytopaenia (1/14; 7.1%), soft tissue

infections (3/14; 21.4%), urinary tract infection (1/14; 7.1%) and lipid derangement (4/14 28.6%). One case of GCA relapse occurred on TCZ (mild headache and raised inflammatory markers settled on small increase in prednisolone). After 12 months, mean prednisolone dose was 3mg (range 0-15mg).

Conclusion: All patients approved for Tocilizumab in the GCA MDT fulfilled NHS England criteria for either relapsing or refractory disease. The majority of cases had cranial disease, but almost half had either ocular or large vessel involvement, reflecting a severe spectrum of disease. Cases showed a high burden of glucocorticoid toxicity. Follow up data suggests that TCZ was effective in allowing glucocorticoid weaning and disease control, but with some adverse effects. Future work to follow up patients after stopping Tocilizumab would be informative, as the twelve month limitation on treatment is likely to be re-instated.

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AB0590 GREATER STEROID-SPARING EFFECT OF TOCILIZUMAB THAN METHOTREXATE: A REAL-LIFE MONOCENTRIC EXPERIENCE

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Background: Glucocorticoids (GCs) are still the mainstay of treatment of Giant Cell Arteritis (GCA), while Tocilizumab (TCZ) has been licensed as the first biologic treatment for GCA. Although GCs are highly effective in GCA, it is well documented the high burden of toxicity of GCs as well as the disease relapse during GC tapering. Therefore, patients with GCA may benefit from GC-sparing treatments[1].

Objectives: The aim is to compare the efficacy as steroid-sparing agents of Tocilizumab (TCZ) or Methotrexate (MTX) in GCA.

Methods: A single-center retrospective study included 39 patients with newly diagnosed GCA confirmed by temporal artery biopsy, temporal artery ultrasound, or TC-PET. Patients were collected from December 2010 to December 2020. The inclusion criterion was the initiation of treatment with MTX or TCZ as GC-sparing agent within the first year of disease, whereas the exclusion criterion was previous treatment with other immunosuppressive agents.

Results: 11 patients received TCZ (162mg/week), while 28 patients MTX (up to 20mg/week) as a GC-sparing agent. Baseline characteristics were reported in Table 1.

Table 1. Baseline characteristics of 39 newly diagnosed GCA patients.

Median (IQR) or n (%)	TCZ (n=11)	MTX (n=28)	All (n=39)	P value
Age, years	66 (57-77)	72 (66-76)	71 (65-76)	0.125
Female	9 (81.8)	20 (71.4)	29 (74.4)	0.504
ESR, mm/h	**89.5 (71-116)**	51.5 (39.5-88.5)	72 (46-92)	**0.026**
CRP, mg/L	**102 (79-169)**	43.9 (20.8-68)	54 (27-102)	**0.006**
Fibrinogen, mg/dL	605 (381-897)	680 (539-800)	680 (492-808)	0.760
≥3 ACR criteria	5 (45.5)	10 (35.7)	15 (38.5)	0.718
AION	**3 (27.3)**	0 (0)	3 (0.8)	**0.018**
Fever	8 (72.7)	13 (46.4)	21 (53.8)	0.138
Extra-cranial symptoms	7 (63.6)	17 (60.7)	24 (61.5)	1.000
TAB positive	6 (54.5)	13 (46.4)	19 (48.7)	1.000
Halo sign positive	5 (45.5)	6 (21.4)	11 (28.2)	0.234
TC-PET positive	6 (54.5)	12 (42.9)	18 (46.2)	0.676
Comorbidities*	5 (45.5)	15 (53.6)	20 (51.3)	0.648

*Presence of at least one among diabetes mellitus, hypertension, ischaemic heart disease, obesity, or osteoporosis.

The follow-up time between groups was 20 (IQR 18.5-24.5) months *vs* 36 (IQR 24-60.5) months, respectively. At the last medical examination, all patients were in sustained remission, 6/11 (54.5%) and 17/28 (60.7%) had discontinued GCs. The prednisone equivalent dosage of 5 mg/day was achieved at 5 (IQR 2.75-5.5) and 7 (IQR 5-10) months (p-value 0.078), respectively, while discontinuation of GCs was achieved at 7.5 (IQR 6.25-11) and 19 (IQR 14-24) months (**p-value 0.015**), respectively. No differences were observed as concerns GC-related adverse events at 1 year after the onset of GCA (1 event in 11 patients [9.1%] vs 3 events in 28 patients [10.7%]). In details, GC-related adverse events were development of diabetes (2/4), hypertension (1/4), or osteoporosis (1/4). Two patients in the first group (18.2%) and 9 in the second one (32.1%) experienced at least one relapse (median time to relapse was 6.5 [IQR 5.75-7.25] and 18 [IQR 12-24] months). Relapses required the association of MTX with TCZ (1/11 [9.1%]) or start of TCZ (1/11 [9.1%] in the former group, while they required an increase in steroid dosage (7/11 [63.6%]), switch from MTX to TCZ (1/11 [9.1%]), or reinstatement of MTX therapy after its discontinuation (1/11 [9.1%]) in the latter.

Overall, both drugs were well tolerated. 1/11 (9.1%) and 5/28 (17.9%) had discontinued TCZ and MTX, respectively, due to mild and reversible drug-related adverse events (4/6 general malaise or discomfort, 1/6 gastrointestinal symptoms, or 1/6 abnormal liver function tests). No serious infections were observed.

Conclusion: TCZ showed a faster steroid-sparing effect than MTX. Both immunosuppressants are safe, effective and allow the discontinuation of GCs.

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AB0591 ANALYSIS OF THE CLINICAL DIFFERENCES BETWEEN THE SUBTYPES OF GIANT CELL ARTERITIS.

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Background: Giant cell arteritis GCA is the most frequent vasculitis over the age of 50. Nowadays, it is known that there are several subtypes of GCA depending on the vessels that are involved: cranial, extracranial and mixed. However, the clinical manifestations that differentiate these three subtypes have not been extensively examined until now. In the future, it is likely that the differential characteristics in the expression of the disease will be relevant in the prognosis and the follow up of these patients.

Objectives: The objective of the study is to investigate the clinical differences associated with these different patterns of GCA involvement.

Methods: This is a retrospective study of new consecutive patients diagnosed with GCA in our hospital for three years. All patients underwent color Doppler ultrasound of both cranial (superficial temporal arteries in the common superficial temporal artery and their frontal and parietal branches) and extracranial arteries (axillary, subclavian and carotid arteries) were explored. The ultrasound diagnosis was made according to the OMERACT definitions of the halo sign and a cut-off the intima media thickness of ≥0.34 mm for the branches of the temporal arteries ≥0.42 in the common superficial temporal artery and ≥ 1 mm for the axillary, subclavian, and carotid arteries was established. The clinical records of the patients were reviewed and their demographic, clinical and laboratory data were compared between the different patterns of ultrasound involvement of GCA. A $p < 0.05$ was established as the limit of statistical significance. The EULAR recommendations of 2019[1] were used to establish the definitions of remission and relapse. The statistical analysis was performed using SPSS version 25.

Results: A total of 74 patients were included, 44(58.7%) women with a mean age of 78.6±8.6 years. Regarding the GCA subtypes, 18 (24.3%) patients had exclusive involvement of cranial giant cell arteritis CGCA, 12 (16.2%) patients had isolated involvement of extracranial giant cell arteritis LVGCA and 44 (59.5%) patients had mixed forms with cranial and extracranial MGCA. The characteristics of the population and of the GCA subtypes are shown in Table 1.

The analysis of the results showed that patients with LVGCA are younger, have less ischemic symptoms and have lower ESR than patients with CGCA $p<0.05$. Cranial involvement was associated with more ischemic symtoms than GCA with large vessel involvement, even in the mixed forms in which the cranial vessels are involved $p<0.05$. Additionally, we observed a trend towards a higher percentage of present greater constitutional syndrome in the LVGCA group. The main limitation of the study is its low sample size when analyzing the subgroups, which does not allow confirming some of the trends observed in Table 1.

Conclusion: There are significant clinical phenotypic differences in the presentation of the different subtypes of vascular involvement in GCA.

Table 1. Clinical characteristics and GCA subtypes.

Clinical characteristics	Total GCA = 74	CGCA = 18	LVGCA = 12	MGCA = 44	CGCA vs. MGCA p	CGCA vs LVGCA p	LVGCA vs MGCA P
Female sex, n (%)	44 (59.4)	10(55.5)	6 (50)	27 (61.3)	0.672	0.765	0.478
Age, mean ± S.D.years	78.6 ± 8.6	79.0 ± 8.1	73.2 ± 9.4	80.7 ± 7.9	0.505	**0.031**	0.077
ESR, (mm/h) mean S.D.	57.1 ± 35.5	66.1 ± 39.2	39.6 ± 24.5	56.6 ± 34.1	0.391	**0.021**	0.115
CRP (mg/dL) mean± S.D.	56.4 ± 57.1	50.1 ± 45.6	52.3 ± 52.5	60.7 ± 63.7	0.179	0.758	0.417
Constitutional symptoms, n (%)	59 (78.7)	12 (66.6)	12 (100)	35 (79.5)	0.282	**0.025**	0.087
Ischemic symptoms, n (%)	66 (82.66)	15 (83.3)	5 (41.6)	35 (79.5)	0.732	**0.018**	**0.010**
Remission for 6 months, n (%)	25 (33.3)	7 (38.8)	5 (41.6)	13 (29.5)	0.847	0.879	0.425
Glucocorticoid free remission, n (%)	8 (10.7)	1 (5.5)	2 (16.6)	5 (11.3)	0.475	0.320	0.622
Major relapse, n (%)	4 (5.3)	0 (0)	1 (8.3)	3 (6.8)	0.479	0.213	0.857
Minor relapse, n (%)	12 (16)	2(11.1)	3 (25)	8 (18.1)	0.492	0.317	0.598

GCA: giant cell arteritis; CGCA: Cranial giant cell arteritis; LVGCA: Large vessel giant cell arteritis; MGCA: Mixed giant cell arteritis; SD: standard deviation; p: value.

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AB0592 IS IT TIME TO DISSECTING GIANT CELL ARTERITIS INTO SUBPHENOTYPES? A CLOSE LOOK TO DATA OF EASTERN MEDITERRANEAN VASCULITIS CENTRE

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Background: Patients with giant cell arteritis (GCA) have heterogeneity in terms of not only symptoms and findings but also extent of arterial involvement. In era of personalized medicine, therapy of patients is based on these diverse parameters.
Objectives: This study is aimed to identify subphenotypes of GCA, treatments have been used and outcomes in a prospective database of Eastern Mediterranean Vasculitis Centre.
Methods: Among 2454 patients recorded into Hacettepe University Vasculitis Research Centre database since October 2014; 181 of them were Takayasu's arteritis and 89 of them GCA. 17 GCA patients were excluded due to missing data. Patients were grouped as Cranial GCA, Cranial GCA+ PMR, Cranial and LV GCA + PMR, Cranial and LV GCA, and LV GCA.
Demographic and clinical findings, histopathological and imaging data as well as outcome was collated for each subphenotype.
Results: Of 72 patients enrolled into further analysis, a female predominance (72.2%) was observed with mean age at diagnosis of 68.3(±8.2) years. Seventy-four percent of patients had cranial GCA (Figure 1) and leading subphenotype of all patients was only cranial GCA. Usage of temporal artery biopsy (TAB), temporal artery and axillary artery ultrasonography, and imaging modalities were different according to phenotypes of GCA.

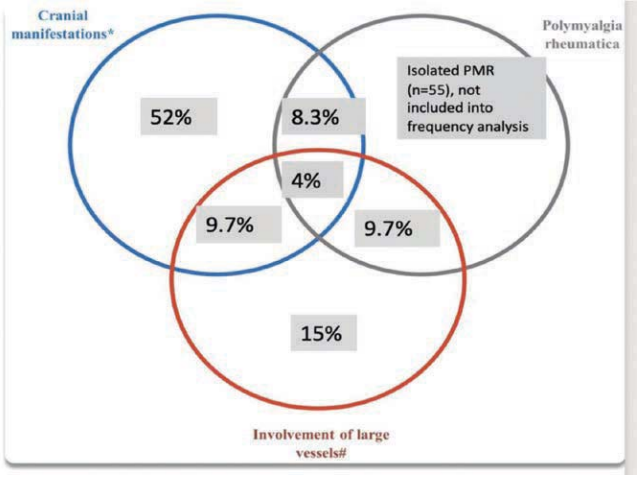

Figure 1. Distribution of GCA subphenotypes

Of the 38 patients having TAB, 20(42.9%) were consisted with GCA. The main histopathological finding were inflammation rich in lymphohistiocytic cells in the temporal artery (44.7%) and fragmentation and loss of integrity of the internal elastic lamina (36.8%).
All of the patients have been used corticosteroids with a median starting dose of 16 mg/day(8-64) had used pulse therapy. Any of conventional DMARDS (AZA, MTX, LEF, CYC) have been used in 60 of patients. In all cases, Tocilizumab was recommended after resistant/intolerant to conventional DMARDs (n=6).
Follow-up data was based on 64 patients. During a median 5,8 (±4.0) years follow-up, 6 (9.3%) patients deceased. Thirteen (20.3%) had one and more relapses, 8(61.5%) from isolated GCA group and 4(30.7%) from Only LV GCA group.
Conclusion: GCA is less frequent than TAK in our centre. Female predominance and a seventh decade of disease onset was observed in our cohort. Heterogeneity of disease was observed in or cohort along with different frequently used diagnostic confirmatory modality among subphenotypes. Relapse rate was 20 percent during a 6-year follow up with a 83% additional DMARD usage.

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Table 1. Confirmatory modality of GCA diagnosis and treatments of subphenotypes

	Only cranial GCA(n=38)	Cranial GCA+ PMR(n=6)	Cranial GCA+ LV GCA+ PMR(n=2)	Cranial+ LV GCA(n=5)	LV GCA+ PMR (n=7)	Only LV GCA (n=14)
Diagnosed confirmed by TAB (Total n=26)	**20**	**4**				**2**
Temporal ultrasonography (Total n=24)	**18**	**2**	**1**	**2**	**1**	
PET CT/Vasculitis MR/ Vasculitis BT (Total n=22)			**1**	**3**	**6**	**12**
Only steroid n=12	**6**	**2**		**1**		**3**
Pulse steroid n=14	**8**	**1**		**1**		**4**
Methotrexate n=35	**17**	**2**	**2**	**1**	**6**	**7**
Leflunomide n=3	**2**					**1**
Azatioprine n=19	**12**	**2**		**1**	**1**	**3**
Cyclophosphamide n=1	**1**					
Tosilizumab n=8	**6**		**2**			

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AB0593 CORRELATIONS BETWEEN PATHOLOGIC SUBSETS AND PET METABOLIC ACTIVITY IN A MONOCENTRIC COHORT OF 46 PATIENTS WITH BIOPSY PROVEN TEMPORAL ARTERITIS. AN OBSERVATIONAL RETROSPECTIVE ANALYSIS.

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Background: Temporal arteritis is the most common systemic vasculitis in patients aged >50 years, the most serious complications of which is visual loss. The arterial biopsy is the diagnostic gold standard; alongside the classic finding of transmural infiltrate and giant cells, other abnormalities have been described, of which it is not yet known whether they identify specific clinical subsets. PET is not yet used for diagnosis, but it can be suggestive in patients with high clinical suspect; it may be useful for assessing the extention of the disease in already diagnosed patients and for ruling out alternative diagnoses as infections and neoplasms. More recently, PET has been used to assess disease metabolic activity

Objectives: The aim of our study is to evaluate, in patients with histologically confirmed temporal arteritis, correlations between pathological subsets, metabolic activity and different clinical behavior.

Methods: We have recovered the medical records of patients with the diagnosis of temporal arteritis made in our Rheumatology service from January 2007 until now. We selected those satisfying the ACR 1990 criteria and, finally, those with a positive biopsy. We analyzed age at onset of symptoms, diagnostic delay, presence of PMR, fever, constitutional symptoms, headache, temporal artery induration, visual loss; we analyzed CRP, ESR, plasmatic Hb, PLT count, hypocomplementemia, ANA, aCL, ANCA. The referring pathologist, who didn't know the history of patients, re-examined all the biopsies performed, focusing on: transmural, periadventitial, limited to small vessels or vasa vasorum infiltrate, presence of giant cells, macrophages, eosinophils, neutrophils, lymphocytes, plasmacells, stenosis, thrombosis, fibrinoid necrosis. The nuclear doctor retrieved the PET images by re-assigning each patient the relative PET VAS score. Descriptive analysis was performed: absolute and percentage frequencies were calculated for categorical variables and mean, standard deviation, range and percentiles for quantitative variables. The relationship between variables was tested by the chi-square test and the Mann-Whitney rank test. All analyzes were performed with the STATA software 14.2.

Results: We analyzed 46 patients (F 32, M 14), average age at onset of symptoms of 75.5 yrs and average diagnostic delay of 3.2 months. Headache was reported by 37 patients, fever and asthenia by 26 and 24 respectively, jaw claudication and PMR by 18 and 7. 11 patients had visual loss while 4 and 2 respectively reported amaurosis and diplopia. Temporal artery induration was described in 24 patients. Tests of systemic inflammation were abnormal (mean CRP 85 mg/L, ESR 72.7 mm /1h); the finding of hypocomplementemia (1/26 patients), ANA, aCL and ANCA positivity (2/31, 1/27 and 1/25) was negligible. Histological analysis showed the prevalence of transmural infiltrate (100% of patients), giant cells (87%) and lymphocytes/macrophages (85% both); small vessel vasculitis (59%) and the presence of plasma cells (53%), neutrophils (48%) and eosinophils (22%) were less represented. Periadventitial infiltrate was described in 29% of patients, with negligibility of vasculitis limited to the adventitia and of the vasa vasorum (2 and 0/46). Intimal hyperplasia and necrosis (22 and 14/46) prevailed over calcifications, stenosis and thrombosis (7-5-1/46). PET was available in 14 patients including 6 positive (43%), with a median PET VAS score of 7 (range 6-21); 8/13 patients had not taken steroids prior to PET.

Conclusion: In our retrospective study we observed, in addition to transmural infiltrate and giant cells, the presence of lymphocytes, macrophages and small vessel vasculitis. No correlation was observed between clinical findings, biological and metabolic activity, apart from the increased presence of giant cells in PET positive patients. Visual loss is slightly more common in PET negative patients. This may be due to severity of the cases which needed early steroid treatment.

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AB0594 ULTRASOUND INTIMA MEDIA THICKNESS CUT-OFF VALUES FOR CRANIAL AND EXTRACRANIAL ARTERIES IN PATIENTS WITH GIANT CELL ARTERITIS

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Background: Ultrasound (US) is a valid imaging tool to detect signs of giant cell arteritis (GCA). Although the halo sign has always been considered the most useful finding for GCA diagnosis, modern high frequency transducers are able to precisely measure the intima-media thickness (IMT) of cranial and extracranial arteries. However, data on optimal cut-off values for IMT to differentiate patients and controls in clinical practice are limited.

Objectives: To determine the optimal cut-off value for IMT of cranial and extracranial arteries in patients with suspected GCA.

Methods: This is a retrospective observational study of patients referred to our US fast-track clinic with suspected GCA. All patients underwent bilateral US examination of the cranial and extracranial (carotid, subclavian and axillary) arteries within 24 hours per protocol. The exam was performed using an Esaote-MyLab8 with a 12-18 MHz frequency transducer for cranial arteries and an 8-14 frequency transducer for extracranial arteries. The IMT was measured in gray scale mode and the presence of a non-compressible halo sign was checked in all arteries. The gold standard for GCA diagnosis was clinical confirmation by the referring rheumatologist after 6 months follow-up. Mean IMT values of each artery were compared between patients with and without GCA by independent samples T-test. Receiver operating characteristics analysis was performed and the Youden index was used to determine the optimal cut-off value for IMT of each artery.

Results: Of the 157 patients with suspected GCA (67.5% female, mean age 73.7 years) referred to the fast-track clinic, 47 (29.9%) had GCA clinical confirmation after 6 months. 41 (87.2%) patients with GCA had positive US findings (61.7% had cranial involvement, 44.7% extracranial involvement and 19.1% a mixed pattern of cranial and extracranial arteries). The following IMT cut-off values showed the highest diagnostic accuracy: 0.44mm for the common superficial temporal artery; 0.34 mm for the frontal branch; 0.36 mm for the parietal branch; 1.1 mm for the carotid artery: 1 mm for the subclavian and axillary arteries. The area under the ROC curve of the IMT for a clinical diagnosis of GCA was 0.984 (95% CI 0.959 - 1) for common superficial temporal artery, 0.989 (95% CI 0.976 -1) for frontal branch, 0.991 (95% CI 0.980 - 1) for parietal branch, 0.977 (95% CI 0.961 – 0.993) for carotid, 0.99 (95% CI 0.979 - 1) for subclavian and 0.996 (95% CI 0.991 -1) for axillary arteries (Table 1).

Table 1. Optimal IMT cut-off values for cranial and extracranial arteries

Artery	Side	Patients without GCA	Patients with GCA	Cut-off (mm)	AUC (CI 95%)	Sensitivity (%)	Specificity (%)
Common superficial	Right	0.33 (0.06)	0.68 (0.28)	0.43	0.997 (0.988 -1)	100	97.1
temporal artery mm, mean (SD)	Left	0.35 (0.11)	0.57 (0.21)	0.45	0.966 (0.905 -1)	100	92.3
	Both	0.34 (0.08)	0.63 (0.25)	0.44	0.984 (0.959 -1)	94.7	95.1
Frontal branch mm, mean (SD)	Right	0.26 (0.05)	0.4 (0.18)	0.34	0.994 (0.983 -1)	100	97.1
	Left	0.27 (0.05)	0.4 (0.18)	0.34	0.985 (0.962 -1)	100	96.1
	Both	0.26 (0.05)	0.4 (0.18)	0.34	0.989 (0.976 -1)	100	96.6
Parietal branch mm, mean (SD)	Right	0.27 (0.05)	0.43 (0.18)	0.36	0.994 (0.981 -1)	100	98.9
	Left	0.27 (0.05)	0.41 (0.16)	0.36	0.987 (0.967 -1)	100	97.6
	Both	0.27 (0.05)	0.42 (0.17)	0.36	0.991 (0.980 -1)	100	98.3
Carotid mm, mean (SD)	Right	0.8 (0.17)	0.88 (0.29)	1	0.974 (0.949 – 0.999)	100	92.6
	Left	0.82 (0.15)	1 (0.42)	1.2	0.982 (0.961 - 1)	90.9	96.2
	Both	0.81 (0.16)	0.96 (0.36)	1.1	0.977 (0.961 – 0.993)	90	94
Subclavian mm, mean (SD)	Right	0.74 (0.18)	0.99 (0.44)	1	0.987 (0.97 - 1)	100	93.4
	Left	0.67 (0.17)	0.9 (0.35)	1.1	0.991 (0.975 - 1)	100	98.3
	Both	0.7 (0.18)	0.94 (0.4)	1	0.99 (0.979 - 1)	100	96
Axillary mm, mean (SD)	Right	0.69 (0.16)	0.99 (0.5)	1	0.992 (0.982 - 1)	100	96
	Left	0.67 (0.17)	0.99(0.49)	1	0.998 (0.995 -1)	100	98.3
	Both	0.68 (0.17)	0.99 (0.49)	1	0.996 (0.991 -1)	100	97.1

Conclusion: Different IMT cut-off values for each artery are necessary to establish a correct US diagnosis of GCA. These proposed IMT cut-off values may help to improve the diagnostic accuracy of US in clinical practice.
Disclosure of Interests: None declared
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AB0595 INFANTILE TAKAYASU: CLINICAL FEATURES AND LONG TERM OUTCOME

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Background: Takayasu arteritis (TA) is a large vessel vasculitis rarely reported in children, and its incidence is extremely low in infants. Most articles on pediatric TA have not focused on infants. We present the largest case series of infantile TA aiming to characterize demographic and clinical data and compare it with existing data on older children.
Objectives: Characterize demographic and clinical data reagrding TA and compare it with existing data on older children
Methods: We conducted an international multi-center retrospective cohort study. Epidemiological and clinical data were collected from patient charts by doctors from six centers.
Results: Twelve patients (50% female) meeting the ACR criteria of TA were included. Median age of symptom onset was 11 months, with a diagnostic delay of 4 months and median time of follow up of 7.5 years. The most common symptoms at presentation were hypertension, BP difference between upper and lower limbs, and fever. The arteries most commonly involved at diagnosis were the abdominal aorta, renal artery, and superior mesenteric artery. Different medications used included steroids, conventional and biological DMARDS, and other immunosuppressive therapies. Half of the patients received biologic agents of which infliximab had the highest complete remission rate (40%). Other medications resulting in complete remission were cyclophosphamide (40%) and methothrexate (38%). Invasive procedures were needed in 58% of patients. The most common complications were cardiac (50%), strokes (42%) and serious infections (33%). None of the patients died.
Conclusion: This study presents the largest series of infantile TA. Compared to reported series on older children, infants with TA were more likely to receive biologic agents, develop complications and require invasive interventions.
Disclosure of Interests: None declared
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AB0596 AORTIC MANIFESTATIONS IN GIANT CELL ARTERITIS: SINGLE CENTRE 10-YEAR EXPERIENCE

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Background: Disease stratification in GCA is an urgent need, with patients categorised into cranial and large-vessel GCA (LV-GCA) subgroups. LV-GCA may have worse outcomes with regards relapsing disease, poor response to glucocorticoids (GC) and aortic involvement.
Objectives: We report a single centre experience using clinical, imaging and treatment outcomes from a specialist clinic.
Methods: 134 patients with LV-GCA were identified over a 10-year period at Southend University Hospital (2012-2022). Medical records were reviewed retrospectively for baseline demographics, clinical presentation, inflammatory markers, imaging (vascular ultrasound, PET-CT, echocardiography), vascular damage and treatment.
Results: There was a female predominance (female n=91). Age at presentation ranged from 46 to 86 years (median 70 years). Co-morbidities implicated in aortic disease included hypertension (n=60), hypercholestrolaemia (n=29), diabetes (n=14), aortic valvular disease (n=5) and atherosclerotic disease including coronary and carotid artery disease (n=19). Constitutional disturbance was most frequently observed presentation (70%, n=94), and the only feature for 11 patients. This was followed by cranial symptoms (62%, n=83), polymyalgia (53%, n=71), ischaemic symptoms i.e., visual disturbance or tongue/jaw claudication (24%, n=32) and cardiovascular presentations (7%, n=9). The latter included limb claudication, stroke, and aortic aneurysm. Although LV-GCA refers to extra-cranial disease, 12 patients (9%) had isolated cranial and/or ischaemic symptoms at initial presentation.
Inflammatory markers were typically elevated at presentation, C-reactive protein ranged from 1-425mg/L and ESR 1-130mm. Vascular ultrasound was used at diagnosis in 93 patients, with positive temporal artery findings in 50% (n=38) and positive axillary findings in 75% (n=57). PET-CT data was available for 125 patients, of which 113 were positive for LV-GCA. Thoracic aorta FDG-uptake was seen in 77%, with 7 ascending and 1 abdominal aortic aneurysm observed. Transthoracic echocardiogram was available for 46% (n=62). Four (6.5%) patients had a dilated aortic root when indexed to height as per British Society of Echocardiography (BSE) guidelines[1] (SOV (mm/m) > 21.8mm in males and > 20.7mm in females). Values for our patients were 22.6 and 21.2 mm/m for the female patients and 29.2 and 25.2 mm/m for the male patients. Furthermore, 32 patients showed some extent of diastolic dysfunction as per BSE criteria (52%).
All patients received GC as part of their treatment, 60% (n=82) needing one or more DMARDs and 17% (n=23) Tocilizumab for relapsing disease. DMARDs used included Leflunomide (n=63), Methotrexate (n=18), Mycophenolate mofetil (n=3) and Azathioprine (n=1). One patient received cyclophosphamide.
Conclusion: By combined imaging modalities, 11 patients (8%) had evidence of ascending aortic damage. Grade 1 diastolic dysfunction can be age related, so this may be association rather than causation[2,3]. Over half of patients had not undergone echocardiogram evaluation, so there may be a hidden burden of disease. Many patients required GC-sparing therapy, showing GC alone are often not enough to halt disease progression, and vascular damage was relatively reduced compared to historical reports. The authors feel GCA services should include standardised protocols for early DMARDs, continuing thorough assessment for LV-GCA and vascular damage, including echocardiography, progressing to cross-sectional imaging if indicated.
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AB0597 FDG-PET/CT IN THE DIAGNOSE AND FOLLOW UP OF TAKAYASU VASCULITIS

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Background: Takayasu vasculitis (TAK) is a chronic disease, where clinic and serological markers as CRP/ESR may fail to predict development of new vascular lesions in the disease course (1). Similarly, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) studies show conflicting results on the association between vessel uptake of FDG and clinical and laboratory finding. A study on new FDG-PET activity scoring system, PETVAS was newly published but has not been validated in other cohorts (2). To date there are limited data on FDG-PET/CT finding at time of diagnoses before treatment induction and 18-FDG uptake and development of new stenosis during follow up.
Objectives: The goal of this study was to see; 1) FDG-PET/CT uptake in newly diagnosed patients before any treatment start 2) FDG-PET/CT uptake and development of new vascular lesions during follow up magnetic resonance angiography (MRA) 3) assess PETVAS score before and after treatment induction.
Methods: All patients in a population-based TAK cohort with FDG-PET/CT at the time of diagnoses before treatment induction were identified. Disease activity was assessed with the NIH activity score (1). Patients had to have clinical, laboratory and MR-angiography prior to/or right after FDG-PET/CT and a minimum of one follow up MRA. The clinical report from the FDG-PET/CT and MRA were reviewed and arteries/aorta regions with reported pathological uptake and stenosis/aneurysm were registrated. Images were reviewed and uptakes in 16 arteries/aorta regions of interest (supraaortic arteries, aorta, iliaca and femoral arteries) scored from 0-3, where 0 represent no uptake, 1 less then liver, 2 same as liver and 3 higher than liver and finally summarized these to PETVAS score.

Results: Twenty-three patients fulfilled the study's inclusion criteria. Twenty-one of the patients were females (91%) and twenty-two were European Caucasian. The mean age was 39.3 (SD 14) at the time of diagnose (Table 1). Five patients were in clinical and laboratory remission at diagnose (NIH=0). Correspondently, none of them had sign of active FDG vessel uptake at PET-CT. They had a median 7 in PETVAS (range 0-13). The remaining 17 patients had clinical active disease (NIH>1) at diagnoses. All 17 patients had uptake on PET/CT in at least one artery/aorta region. The mean PETVAS score at diagnosis was 21.5 (SD 8). At last imaging the patients had developed median 2 new lesions. All the arteries that developed new lesion had active uptake on the original PET/CT. Fourteen patients had FDG PET/CT after treatment start. The PETVAS score decreased from 22.4 (SD 8.7) to 10.7 (SD 6.8) after treatment start (p<0.001).

Table 1.

Patient	Age at pet 1	NIH 0-4	Crp	PETVAS1	PETVAS 2	Treatment at PET2
1	15	1	20	16		
2	64	2	33	16	9	predn 10 mg, mtx 15 mg
3	26	3	207	18	0	predn 15 mg, INF
4	34	3	13	18	7	predn 2.5 mg, mtx 20 mg, INF
5	40	3	317	32	13	predn 10 mg, mtx 15
6	48	3	12	22	16	predn 5 mg, mtx 20
7	55	3	59	37	20	predn 10 mg, mtx 15
8	54	3	182	35	25	predn 5 mg, mtx 15
9	21	4	19	13	3	predn 5 mg, mtx 20
10	36	4	145	18	4	predn 7.5 mg, mtx 17.5 mg
11	27	4	33	14	7	predn 5 mg, mtx 22.5
12	39	4	7	15	7	predn 10 mg, mtx 22.5 mg
13	31	4	75	21	11	predn 10 mg, mtx 25, INF
14	39	4	80	24	16	predn 7.5 mg, mtx 20 mg
15	63	4	106	35	16	predn 10 mg, mtx 20
16	22	4	120	20		
17	27	4	263	21		

Conclusion: All patients with clinical active disease at diagnoses had pathological FDG uptake. Only arteries with increased FDG uptake in the vascular wall subsequently developed new lesion. The study also showed that the PETVAS score fell significantly after treatment induction.

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AB0598

ASSOCIATION OF PROLONGED DISEASE DURATION AND TG/HDL-C RATIO IN ACCELERATING ATHEROSCLEROSIS IN PATIENTS WITH TAKAYASU'S ARTERITIS

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Background: Takayasu's arteritis (TA) is an autoimmune vasculitis that frequently occur in young women.Multiple previous studies have demonstrated that accelerated atherosclerotic changes were commonly found in TA patients[1-4]. More specifically, data indicated that as much as 27% of all TA patients developed carotid artery plaque, while which was only 2% in the age- and sex-matched healthy individuals[1]. In addition, up to 20% of TA patients developed stroke and/or transient ischemic attack(TIA), which both have been known to be associated with atherosclerotic lesions[1-3]. Inflammation of the vascular wall may promotes atherosclerosis (As) in TA,which accelerates the development of As.Higher triglyceride (TG)/HDL-C ratio was found to be associated with presence of endothelial dysfunction and As[5].

Objectives: This study aimed to identify the risk factors associated with the development of atherosclerosis in TA.

Methods: This retrospective study enrolled a total of 101 TA patients. All patients were divided into two groups according to the absence or presence of atherosclerosis(43 vs 58). Baseline demographic features and clinical characteristics were compared between two groups. A logistic model was applied to determine the risk factors associated with the development of atherosclerosis.

Results: Our data suggested that the disease duration of patients in the atherosclerosis group was significantly longer than that of patients in the non-atherosclerosis group [96(18.00,180.00) vs 48.00(12.00,111.00) months] (p=0.015). In addition, the average age of patients with atherosclerosis was significantly older compared to patients without atherosclerosis [44.00 (38.00 , 48.00) vs 28.50 (24.00 , 37.00) years] (p<0.001). Logistic regression analysis showed that the risk of developing atherosclerosis increased by 9.2% per 1 year increase in thedisease duration(p=0.005, OR 1.092,95%CI:1.027-1.162).Patients with TG/HDL-C ratio more than 0.8875 were associated with a 5.861fold increase of risk developing atherosclerosis(p<0.001, 95%CI:2.299-14.939).

Conclusion: Our study indicated that prolonged disease duration and elevated TG/HDL-C ratio are associated with the development of atherosclerosis in TA patients.

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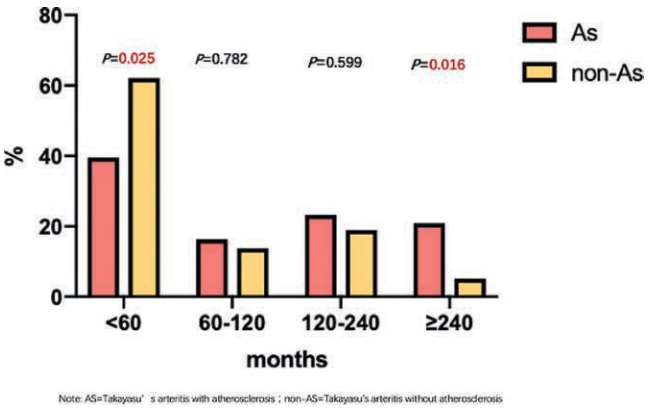

Figure 1.

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AB0599

THE VALUE OF ULTRASOUND IN GCA FOLLOW-UP: RESULTS FROM A SCOTTISH SINGLE CENTRE.

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Background: Ultrasound (USS) is important diagnostically in GCA, but its value during follow-up is unclear[1]. In our centre, ad hoc follow-up USS has been performed routinely.

Objectives: To describe how USS appearances i) changed over time (at defined timepoints), ii) correlated with clinical relapse (at any time), iii) were affected by tocilizumab.

Methods: Patients diagnosed with GCA in NHS Lanarkshire, November 2018 - October 2021, were included. Treatment was in accordance with international guidelines[2]. Follow-up visit data included clinical status (remission, stable, relapse), treatment, and (when USS performed) temporal artery (TA) and axillary artery (LV) intima media thickening (IMT) (TA+ = IMT ≥0.5MM; LV+ = IMT >1mm). Follow-up USS were compared to baseline, pre-relapse or pre-tocilizumab.

Results: 55 patients were diagnosed with GCA; mean (SD) age 73.1 (8.0) years; 31 female (56.4%). Mean (SD) follow-up was 63.8 (40.6) weeks. All patients had baseline USS [48 positive (TA+ or LV+)], 7 negative; 36 (65.5%) had ≥1 follow-up USS. 7 patients had USS at 6-12 weeks; all were clinically stable; all had positive baseline USS; at 6-12 weeks, 3/7 remained TA+, 1/7 remained LV+ (TA-LV+). 25 patients had USS at 16-36 weeks; 9/25 were in remission, 11/25 stable, 5/25 relapsing. Of remission patients, 7/9 had positive baseline USS; at 16-36 weeks, 2/7 remained TA+. Of stable patients, all had positive baseline USS; at 16-36 weeks, 4/11 remained TA+, 3/11 remained LV+. Of relapsing patients, 5/5 had positive baseline USS; at 16-36 weeks, 2/5 remained TA+, 1/5 LV remained LV+.

Table 1. Follow-up and corresponding baseline ultrasound results, at defined timepoints, grouped by clinical status.

			Baseline ultrasound				Follow-up ultrasound			
Time	Clinical status	N[a]	TA+ LV-	LV+ TA-	TA+ LV+	TA- LV-	TA+ LV-	LV+ TA-	TA+ LV+	TA- LV-
6-12 week	All stable	7	6	0	1	0	3	1	0	3
16-36 week	All	25	17	0	6	2	6	4	0	15
	Remission	9	6	0	1	2	2	0	0	7
	Stable	11	7	0	4	0	4	3	0	4
	Relapse	5	4	0	1	0	2	1	0	2
42-62 week	All	15	11	1	2	1	3	5	1	6
	Remission	8	6	0	1	1	3	0	0	5
	Stable	3	2	0	1	0	0	1	1	1
	Relapse	4	3	1	0	0	0	4	0	0

a.Number of patients scanned.

15 patients had USS at 42-62 weeks; 8/15 were in remission, 3/15 stable, 4/15 relapsing. Of remission patients, 7/8 had positive baseline USS; at 42-62 weeks, 3/7 remained TA+. Of stable patients, 3/3 had positive baseline USS; at 42-62 weeks, 1/3 was TA-LV+, 1/3 remained TA+LV+. Of relapsing patients, 4/4 had positive baseline USS (3/4 TA+, 1/4 LV+); at 42-62 weeks, all were TA-LV+. The Table 1 below provides additional detail for each timepoint. 11 patients in total had clinical relapse (any time) and contemporaneous USS; mean (SD) time to relapse was 36.6 (18.3) weeks; median (IQR) prednisolone dose 7mg (4,9). At relapse, 2/11 were TA+LV+, 6/11 LV+, 3/11 TA-LV-. Comparing relapse USS to most recent USS pre-relapse, 4/11 were newly LV+, while other positive findings were seen previously. 11 patients treated with tocilizumab had ≥1 USS post-initiation [at mean (SD) 27.1 (16.7) weeks]. 5/11 were LV+ pre-tocilizumab, 6/11 TA+. At follow-up, all were in remission or stable; 4/5 remained LV+, 4/6 remained TA+.

Conclusion: While many patients had rapid normalisation of USS changes with treatment, others remained abnormal despite stable disease or remission, including at approx. 12 months follow-up. Ad hoc follow-up scans therefore appear unreliable in isolation, but the value of systematic longitudinal scanning warrants further study. Emergence of LV positivity was seen in several cases of relapse and may characterise an evolution in disease phenotype. Positive USS findings largely persisted at approx. 6 months despite disease control on tocilizumab.

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AB0600

ANALYSIS OF RISK FACTORS AND PROGNOSIS IN PATIENTS OF TAKAYASU'S ARTERITIS WITH CORONARY ARTERY LESIONS

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Background: Takayasu's arteritis (TA) can involve coronary artery lesions. The pathogenesis is complex and lacks the best treatment strategy.The coronary artery lesions were typical seen in the ostia of the left and right coronary arteries which were major risk factors for sudden death and ischemia heart failure[1-2].Coronary artery lesions is an important predictor of poor prognosis in TA patients.The incidences of coronary artery lesions were more common in type V TA patients [3-4].The prevalence of metabolic syndrome and its related characteristics (including dyslipidemia, diabetes and hyperinsulinemia) in TA patients are higher compared with healthy people[5].Thus , under the action of vascular inflammation and traditional risk factors, coronary artery stenosis or even occlusion occurs earlier, which can lead to MACE events.

Objectives: The aim of our study is to investigate the risk factors and prognosis of coronary artery lesions in TA patients.

Methods: This retrospective study enrolled a total of 120 TA patients.All patients were divided into two groups according to the absence or presence of coronary artery lesions in TA patients (61 vs 59). A logistic model was applied to determine the risk factors associated with the incidence of coronary artery lesions in TA patients.According to the before and after imaging comparison of TA with coronary artery lesions, the influencing factors of improving TA with coronary artery lesions were analyzed.

Results: The incidence of coronary artery lesions in TA patients increased by 1.618 times for each additional year (p=0.034, OR1.618,95%CI: 1.036-2.529). History of hyperlipidemia indicated 10.124 fold higher risk of coronary artery lesions in TA patients(p=0.003, OR10.124,95%CI: 2.159-47.483).In the follow-up of TA with coronary artery lesions, 27 patients had coronary CTA results before and after comparison. It was found that 11 patients had remission of coronary artery lesions and 16 patients had no remission of coronary artery lesions. The age in the group with improved coronary imaging was significantly younger than that in the group without improved coronary imaging[(39.00±9.81 vs (47.44±10.06) years,p=0.041)].TNF-α and interleukin-6 were significantly higher in the group with improved coronary imaging than in the group without improved coronary imaging[(26.40(10.08 , 165.90) vs 7.80(6.73 , 21.70)pg/dl,p=0.047;12.50(5.83 , 19.30) vs3.71(2.80 , 4.40)pg/dl,p<0.001].Numano type V (75.00% vs 27.27%, p = 0.022) and vascular calcification (56.25% vs 9.09%, p= 0.018) were significantly higher than those in the group without improved coronary imaging, while numano type IIb in the group with improved coronary imaging was significantly higher than that in the group without improved coronary imaging(45.45% vs 6.25% , p=0.027).

Conclusion: Hyperlipidemia and age are the risk factors of coronary artery lesions in Takayasu arteritis.Numano type V and vascular calcification are not conducive to the improvement of TA with coronary artery lesions.All patients with TA of numano type IIb should be screened for coronary artery. Early control of inflammation is more conducive to the imaging improvement of arteritis coronary lesions.

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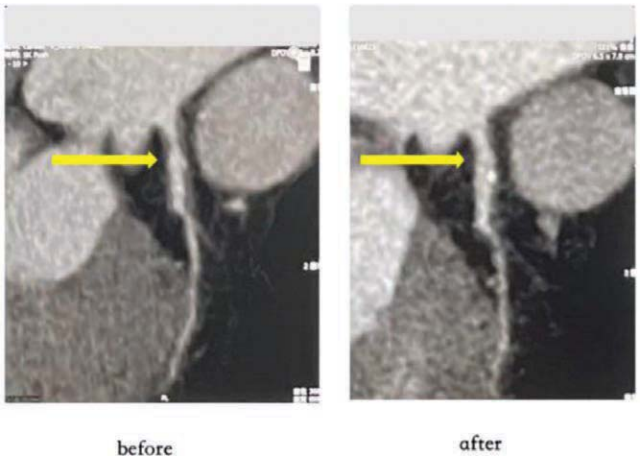

Figure 1.

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AB0601

FACTORS ASSOCIATED WITH THROMBOSIS IN BEHÇET SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Behçet syndrome (BS) is a unique vasculitis that can affect arteries and veins of all sizes. Thrombosis is an important component of vascular involvement in BS. Although several studies were conducted to highlight the mechanism of thromboinflammation in BS, it is still not fully understood.
Objectives: We performed a systematic review and meta-analysis of studies investigating thrombotic, fibrinolytic, and endothelial factors in BS.
Methods: We searched PubMed and EMBASE with the keyword "Behcet*" in four languages (English, German, French and Turkish) from their inception up to April 2020. Titles and/or abstracts of all studies were screened independently by two reviewers (GGO and BY) and conflicts were solved by a third reviewer (GH). Studies comparing BS patients with and without thrombosis and studies comparing BS patients with thrombosis and patients with thrombosis due to other causes were analyzed separately. The pooled odds ratios (OR) with 95%CI were calculated for binary outcomes and standardized mean differences (MD) were calculated for continuous outcomes using RevMan 5.3. We categorized the factors into 4 groups based on acting mechanism 1- those that decrease anticoagulant activity 2- those that increase procoagulant activity 3- those that decrease the activity of fibrinolytic system 4- pathogenetic/endothelial factors.
Results: Of 15548 articles, 15157 were excluded due to duplication and inappropriate study design after reviewing titles and abstracts. Full text review of the remaining 391 articles yielded 103 papers meeting our predetermined inclusion criteria. Factors significantly associated with BS thrombosis compared to BS without thrombosis were high frequency of factor V Leiden mutation (15 studies, OR 2.55, 95%CI 1.66-3.93), high homocysteine level (14 studies, MD: 4.27, 95%CI 2.31-6.22), high protein C level (5 studies, SMD: 0.80, 95%CI 0.15-1.45) and high alpha1-antitrypsin level (1 study, MD: 3.00, 95%CI 0.15-5.85) in Group 1; high factor 8 level (4 studies, MD: 17.17, 95%CI 7.79-6.55), high thrombin level (1 study, MD: 35.90, 95%CI 12.40-59.40), high neutrophil/lymphocyte ratio (2 studies, MD: 1.37, 95%CI 0.24-2.50) and high platelet/neutrophil complex level (1 study, MD: 10.50, 95%CI 0.76-20.24) in Group 2; high TAFI activity (1 study, MD: 28, 95%CI 4.12-51.88) in Group 3; high VEGF level (2 studies, SMD: 1.63, 95%CI 0.21-3.05), high CEC concentration (2 studies, SMD: 1.00, 95%CI 0.22-1.77), high MCP-1 level (1 study, MD: 74.16, 95%CI 61.29-87.03), high anti-C1q level (1 study, MD: 9.11, 95%CI 0.51-17.71), high platelet microaggregate formation (1 study, MD: 75.00, 95%CI 7.62-142.38), high frequency of P-selectin glycoprotein ligand 1 gen polymorphism (heterozygous (AB+AC+BC)) (1 study, OR: 1.88, 95%CI 1.07-3.31), high ADMA level (1 study, MD: 0.16, 95%CI 0.08-0.24), high sICAM-1 level (1 study, MD: 59.30, 95%CI 3.35-115.25) and low brachial artery flow-mediated (endotelium-dependant) dilatation (1 study, MD: -3.22, 95%CI -5.18--1.26) in Group 4.
Factors that were associated with BS thrombosis compared to thrombosis due to other causes including JAK-2 mutation, circulating endothelial cells, activated protein C resistance, tPA, and PAI were assessed in 1 study each. Among these, tPA levels (MD: -6.00, 95%CI -10.99--1.01), APCR (OR: 0.09, 95%CI 0.01-0.73) and JAK-2 mutations (OR: 0.01, 95%CI 0.00-0.06) were significantly less in patients with BS thrombosis compared to patients with thrombosis due to other causes.
Conclusion: Several factors were identified that may potentially be associated with thrombosis in BS. However, the cut-offs used for defining the normal level for these factors, time of blood collection (during acute or chronic stage of thrombosis, use of anticoagulants) and the type of thrombosis (arterial, venous, or cerebral sinus) were not uniform across the studies. Studies investigating these factors together, in a large number of patients, and together with appropriate controls are needed to confirm these results.
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AB0602

TEMPORAL ARTERY BIOPSY POSITIVITY RATES VARY MORE BETWEEN SIMILAR HOSPITALS THAN BY LENGTH, WITH PARTICULAR VARIATION BETWEEN GEOGRAPHIC REGIONS

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Background: Clinical practice surrounding giant cell arteritis (GCA) diagnosis, including the use of temporal artery biopsy (TAB) where appropriate, needs to be consistently accurate to minimise both GCA-related end-organ damage and unnecessary glucocorticosteroid toxicity in all patients. Despite this imperative, the delivery of such clinical care, which can be measured by diagnostic investigation performance characteristics such as TAB positivity rates, varies substantially between different hospitals as it is traditionally reliant on unstructured clinical intuition. While clinical care practices plausibly might be more consistent between neighbouring hospitals given they frequently exchange medical staff and use common teaching sources, these factors are less likely to be applicable when comparing hospitals in different geographical regions within a country, even though educational standards, online information resources, and access to clinical care should be consistent. It therefore stands to reason that variation of diagnostic practice might be greater between geographically distant hospitals.
Objectives: To compare clinical practice surrounding GCA diagnosis, using TAB positivity rates, between similar hospitals in the same city and a geographically distant city in a different region, to understand the contribution of geographic separation to variance in practice.
Methods: TAB histopathological reports were reviewed at three tertiary referral hospital centres: two with neighbouring catchments in the same city, and one in a different city in a neighbouring geographical region in the same country. All three had similar resourcing and catchment demographics during the study period, and none used formal clinical risk stratification scores for GCA pre-test probability. Characteristics including age, sex, biopsy laterality, biopsy length, and hospital were captured, in addition to key histopathological features. Multivariable logistic regression with site-varying intercept was performed, using cubic splines for biopsy length to account for the non-linearity observed.
Results: TAB reports from 708 patients were captured between the three hospitals in two geographical regions. All three sites had a median age of 74 years, had 67-69% of patients being female, and reported median biopsy length between 1.7-2.0cm (Table 1). Despite these similarities, they reported positivity rates varying widely (16% and 24% in Region 1, 29% in Region 2). Apart from age, hospital site was the strongest contributing factor to TAB positivity, with length having little effect outside the very extreme high end and 90% of patients had a biopsy length <4.8cm (Figure 1). For these patients, hospital site differentiated TAB positivity across all biopsy lengths, with Region 2 reporting the highest TAB positivity odds ratio of 2.39 (95%CI: 1.37-4.19).

Table 1.

Characteristic	Site1Region1 N = 218	Site2Region1 N = 361	Site1Region2 N = 129
Bilateral laterality (%)	66 (30%)	105 (29%)	1 (0.8%)
Biopsy length (cm, median (IQR))	2.0 (1.4, 3.0)	1.7 (1.2, 3.5)	1.7 (1.4, 2.2)
Female sex (%)	149 (68%)	249 (69%)	86 (67%)
Age (y, median (IQR))	74 (65, 81)	74 (65, 80)	74 (68, 81)
TAB positivity (%)	34 (16%)	88 (24%)	38 (29%)

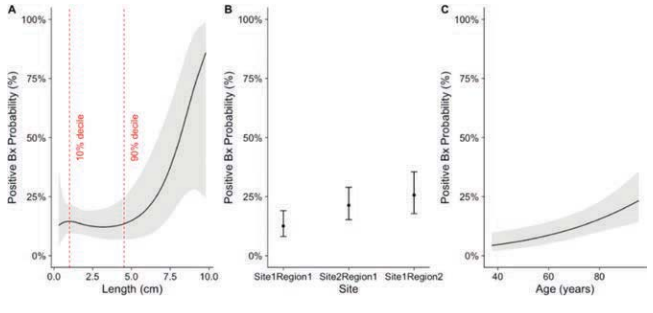

Figure 1. Marginal probabilities of positive TAB obtained from the multivariable logistic regression model (A) across biopsy lengths, with 80% of observed lengths falling between the two vertical red lines (10% and 90% deciles); (B) across hospital sites; (C) across patient age.

Conclusion: Hospital site contributes more greatly to variation in GCA diagnosis clinical practice than demographics or other clinical features do, with particular variation between geographic regions. As part of clinical care standards, using

a replicable pre-test GCA probability score[1] to select patients is likely to be as important to diagnosis as the diagnostic tool characteristics themselves.

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AB0603 INCREASED INCIDENCE OF RAYNAUD'S PHENOMENON IN GIANT CELL ARTERITIS, POSSIBLY ASSOCIATED WITH LARGE VESSEL GIANT CELL ARTERITIS.

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Background: Large Vessel Giant Cell Arteritis (LV GCA) can cause significant narrowing of the subclavian and axillary arteries, either by inflammation or remodelling, which reduces blood pressure in the arms. Also, Raynaud's phenomenon (RP) has been observed in GCA patients.

Objectives: This study aims to investigate the presence of Raynaud's phenomenon in patients with GCA.

Methods: Patients diagnosed with GCA were given a validated questionnaire (CSQ)[1] on symptoms fitting RP, divided into the different phases of RP (white, blue/purple, and red discoloration provoked by cold exposure) as not every patient exhibits all phases. In total, 30 GCA patients were enrolled in this study. Furthermore, imaging data (PET-CT, MRI, ultrasound (US), or temporal artery biopsy (TAB) of all GCA patients were evaluated.

Results: 30 GCA patients were included, with a mean age of 68,6 (±6,5) years, when diagnosed. 76,7% were female. Of the 30 GCA patients, 12 (40%) reported monophasic discoloration. Of these 12 GCA patients, 2 (6,7%) patients reported bi- or triphasic discoloration. Of the 12 GCA patients with at least monophasic discoloration, 6 patients reported a new onset RP (< 1 year of diagnosis). Imaging data of these 6 patients showed severe Large Vessel GCA (with subclavian and axillary involvement) in all of these patients, without displaying cranial GCA. Of these 6 patients, 1 was examined with US alone, 3 with PET-CT, and 2 had both US and a PET-CT. 3 patients reported that the RP complaints, disappeared during treatment of the GCA, 3 still had complaints. Interestingly all these 3 patients had stenosis of either the subclavian, the axillary artery, or both.

Conclusion: We found an increased prevalence of monophasic Raynaud's phenomenon in GCA patients that is 3,7 times higher, when compared to a local background population[2]. When looking at new onset RP in GCA, all patients were found positive for Large Vessel GCA, without cranial symptoms. The data of this study warrants a closer look at LV involvement in patients presenting with Raynaud's phenomenon and GCA or PMR like symptoms.

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Table 1. Presence of Raynaud's phenomenon in GCA.

	GCA new onset RP (n=6)	GCA pre-existing RP (n=6)	GCA Without RP (n=18)	All GCA (n=30)
Age in years at diagnosis, mean (SD)	73 (±3,4)	63,5 (±4,9)	69,3 (±6,5)	68,6 (±6,5)
Gender, women, n (%)	5 (83,3%)	5 (83,3%)	13(72,2%)	23 (76,7%)
Fingers Unusually sensitive to cold, n (%)	6 (100%)	6 (100%)	4 (22,2%)	16 (53,3%)
Have your fingers ever shown any unusual colour changes in the cold, n (%)	6 (100%)	6 (100%)	0 (0%)	12 (40%)
Monophasic RP, n (%)				
Was the colour white? n (%)	6 (100%)	6 (100%)	0 (0%)	12 (40%)
Multiphasic RP, n (%)	2 (33,3%)	0 (0%)	0 (0%)	2 (6,7%)
Was the colour blue/purple? n (%)	1 (16,7%)			1 (3,3%)
Was the colour red? n (%)	1 (16,7%)			1 (3,3%)
LV GCA, n (%)	6 (100%)	2 (33,3)	10 (55,6%)	18 (60%)

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AB0604 INFLUENCE OF THE LOCATION AND SEVERITY OF VASCULAR INVOLVEMENT ON THE BASAL PHENOTYPIC EXPRESSION AND ON THE EVOLUTION OF GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in adults. There is increasing evidence about clinical subtypes of the disease depending on the cranial or extracranial vessels involvement. However, how this type of affectation influences the phenotypic expression of the disease and whether there are differences between them in terms of the thickness of the vessels wall, are still aspects that remain to be clarified.

Objectives: To evaluate the association between the subtypes of GCA and the basal phenotypic expression and severity of the artery walls affectation in the disease.

Methods: This is a retrospective study of new consecutive patients diagnosed with GCA in our hospital from July 2018 to December 2020. The patients underwent Color Doppler ultrasound at the time of diagnosis of cranial arteries (superficial temporal arteries in the common superficial temporal artery and their frontal and parietal branches) and extra-cranial arteries (axillary, subclavian, and carotid arteries). The ultrasound diagnosis was made according to the OMERACT definitions of the halo sign and cut-off the intima media thickness was established as ≥0.34 mm for the branches of the temporal arteries, ≥0.42 in the common superficial temporal artery and ≥1 mm for the axillary, subclavian, and carotid arteries. The "halo score" (HScore) was calculated according to the criteria published by Van der Geest KSM et al. [1] In addition, the clinical records of the patients were reviewed and their demographic, clinical and laboratory data were compared between the different sonographic subtypes of GCA. A $p < 0.05$ limit of statistical significance was established. The Statistical analysis was performed using SPSS version 25.

Results: A total of 74 patients were included, of which 44 (58.7%) were women with a mean age of 78.6 ± 8.6 years. Analyzing the GCA subtypes: 18 (24.3%) had exclusively cranial involvement (CGCA), 12 (16.2%) patients had GCA of extra-cranial large vessels (LVGCA) and 44 (59.5%) patients had mixed forms cranial and extra-cranial (MGCA). The characteristics of the population and of each of the GCA subtypes, as well as thickening of the wall of the arteries are described in Table 1.

Table 1. Clinical characteristics of the study population.

Clinical characteristics	Total GCA = 74	CGCA = 18	LVGCA = 12	MGCA = 44	CGCA vs MGCA p	CGCA vs LVGCA p	LVGCA vs MGCA p
Female sex, n (%)	44 (59.4)	10(55.5)	6 (50)	27 (61.3)	0.672	0.765	0.478
Age, mean ± S.D. years	78.6 ± 8.6	79.0 ± 8.1	73.2 ± 9.4	80.7 ± 7.9	0.505	0.031	0.077
ESR, (mm/h) mean ± S.D.	57.1 ± 35.5	66.1 ± 39.2	39.6 ± 24.5	56.6 ± 34.1	0.391	0.021	0.115
CRP (mg/dL) mean± S.D.	56.4 ± 57.1	50.1 ± 45.6	52.3 ± 52.5	60.7 ± 63.7	0.179	0.758	0.417
Constitutional symptoms, n (%)	59 (78.7)	12 (66.6)	12 (100)	35 (79.5)	0.282	0.025	0.087
Ischemic symptoms, n (%)	66 (82.66)	15 (83.3)	5 (41.6)	35 (79.5)	0.732	0.018	0.010
HScoreCraneal, mean± S.D.	6.29±5.37	9.00±5.10	2.25±3.25	6.27±5.48	0.066	0.000	0.003
HScoreVG, mean± S.D.	5.05±4.35	0.94±1.10	6.25±4.67	6.52±4.02	0.000	0.002	0.856
HScoreTotal, mean± S.D.	11.35±6.17	9.94±4.90	8.50±5.65	12.8±6.48	0.067	0.478	0.035
Right frontal (mm), mean± S.D.	0.40±0.14	0.44±0.19	0.29±0.09	0.40±0.11	0.412	0.022	0.029
Left frontal (mm), mean± S.D.	0.40±0.12	0.41±0.70	0.31±0.17	0.40±0.12	0.711	0.253	0.299
Right parietal (mm), mean± S.D.	0.47±0.27	0.0.48±0.13	0.29±0.07	0.49±0.34	0.879	0.002	0.014
Left parietal (mm), mean± S.D.	0.38±0.13	0.39±0.14	0.34±0.08	0.38±0.12	0.987	0.398	0.354
Right axillary (mm),, mean± S.D.	0.96±0.33	0.72±0.18	1.04±0.42	1.09±0.30	0.000	0.024	0.821
Right subclavian (mm), mean± S.D.	1.00±0.35	0.73±0.13	1.06±.0.41	1.05±0.34	0.000	0.023	0.998
Left axillary (mm), mean± S.D.	0.94±0.29	0.71±0.14	1.04±0.37	0.97±0.27	0.000	0.033	0.598
Left subclavian (mm), mean ± DE	0.91±0.27	0.71±0.17	1.06±0.30	0.93±0.24	0.006	0.007	0.241
Right distal carotid(mm), mean± S.D.	0.95±0.22	0.82±0.14	0.84±0.25	1.02±0.19	0.002	0.821	0.048
Right proximal carotid(mm), mean± S.D.	0.90±0.24	0.68±0.15	0.89±0.21	0.90±0.22	0.001	0.033	0298
Left distal carotid, mean± S.D.	1.01±0.24	0.80±0.13	0.87±0.23	1.10±0.22	0.000	0.520	0.026
Left proximal carotid(mm), mean± S.D.	0.98±0.31	0.73±0.90	0.8±0.15	1.07±0.33	0.001	0.110	0.029

GCA: giant cell arteritis; CGCA: Cranial giant cell arteritis; LVGCA: Large vessel giant cell arteritis; MGCA: Mixed giant cell arteritis; SD: standard deviation; p: value p

Conclusion: The constitutional syndrome was always present in LVGCA but it is also very common in subtypes with cranial involvement. The ischemic syndrome occurs preferentially in groups with cranial vessel involvement, but not exclusively. The thickening of the arterial wall of the cranial arteries shows no difference between CGCA and MGCA; and the same occurs in the large vessels between the LVGCA and the MGCA. Serious adverse effects due to ischemia showed a similar risk regardless of whether it was CGCA or MGCA.

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AB0605 **GIANT CELL ARTERITIS. PREVALENCE OF EXTRACRANIAL LARGE VESSEL VASCULITIS DIAGNOSED WITH 18-FDG POSITRON EMISSION TOMOGRAPHY.**

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Background: The prevalence of extracranial involvement in giant cell arteritis (GCA) is unknown although there are series that has published prevalences of 20-65% depending on the technique used (1).
Objectives: To asses the prevalence of extracranial large vessel vasculitis (LVV) in GCA diagnosed by positron emisión tomography (PET) and to describe clinical and radiological features.
Methods: Prospective and descriptive study of newly diagnosed GCA patients who underwent PET between july 2020 and october 2021. 1990 ACR criteria (2) and/or physician criteria was used to classified patients as having GCA. Clinical and radiological features were described. All patients should not be taken any other inmunosupresant drug but glucocorticoids (GCs).
Results: Fourteen consecutive patients were diagnosed as GCA. Eight patients were female with a median age of 64.4 years. All patients but one underwent temporal artery biopsy (TAB) with a positive result in 54%. PET was positive in 85.7% patients. The median dose of GCs when PET was done was 31.4 (0-45) mg/day and the median delay in PET performance was 8 days (0-22). The 2 patients with negative PET had positive TAB. Proximal thoratic aorta involvement was observed in all patients with positive PET. Late PET images were taken in 6 patients with a median dose of GCs of 43,3 mg/day and median delay of 11,3 days with positive result in all of them (Table 1).

Table 1. PET late images

PET LATE IMAGES	N=6
-SEX (female) %	66
-AGE (years)	60.1
-BAT (positive) %	40
-PET RESULT (positive) %	100
-GCs DOSE (mg)	43.3 (40-45)
-DAYS OF DELAY	11.3 (3-22)

Conclusion: Despite the high dose of GCs and the delay in PET performance, in our serie PET has diagnosed LVV in 85,7% of GCA patients. PET within 3 days after start GCs, has been usefull to diagnosed extracranial involvement in GCA (3). In our series the prevalence of extracranial involvement diagnosed by PET in GCA has been higher than others published until now (2). Further patients are needed to confirm these data.
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AB0606 **HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RITUXIMAB-INDUCED REMISSION OF ANCA-ASSOCIATED VASCULITIS: REGISTRY-BASED COHORT STUDIES**

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Background: Survival rate in ANCA-associated vasculitis (AAV) has significantly improved due to anti-B cell therapy with rituximab (RTX). The main issue now appears to be the management of comorbidities and the improvement of quality of life.
Objectives: Based on a prospective analysis of the single centre registry of AAV patients (pts) treated with RTX, to study the impact of sustained remission on health-related quality of life using Short-Form 36 (SF-36).
Methods: Health-related quality of life was assessed in 70 AAV pts: 35 (50%) with granulomatosis with polyangiitis (GPA), 24 (34.3%) - microscopic polyangiitis (MPA) and 11 (15,7%) - eosinophilic granulomatosis with polyangiitis (EGPA). The mean age was 49,7 ± 15,7 years, 53% women. The median total dose of RTX was 4.3± 2,5 g. As a rule, a reduced dose of RTX 500 mg was used for repeated courses. Mean duration of RTX therapy 46.8 ± 29.4 months. Remission of AAV was defined as a Birmingham Vasculitis Activity Score = 0 regardless of prednisone treatment or dosage. All pts were in remission.
Results: In 70 patients the average indicators of physical functioning: MPA 62.5 (47.5, 78.8), GPA 75 (55, 92.5), EGPA 60 (45, 77.5); social functioning: MPA 25 (0, 56.3), GPA 50 (25, 100), EGPA 50 (12.5, 62.5), physical health component: MPA 41.6 (31.5, 44.8), GPA 43.7 (36.7, 52.5), EGPA 38.7 (33.8, 45). There were no significant differences between men and women within the GPA, MPA, and EGPA groups. There were also no differences between different age groups. When comparing the EGPA group with GPA or MPA, no significant differences were found. At the same time, in patients with MPA, the indicators of physical functioning (p=0.015, w= 3.92) and the physical component of health (p=0.012, w 4.026) were significantly lower than in patients with GPA.
Conclusion: RTX maintenance allows to achieve a good quality of life in AAV pts. SF-36 summary measures were significantly higher in GPA pts compared with MPA. Further research is required to analyze the effect of AAV phenotype and complications on health-related quality of life.
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AB0607 **VASCULAR INVOLVEMENT IN BEHÇET'S DISEASE**

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Background: Behçet's disease (BD) is a multisystemic inflammatory vasculitis, which can affect all types and sizes of blood vessels. It diagnosis is based on a multitude of classification criteria, which include vascular complications associated to this vasculitis.
Objectives: In this study, we reported the main characteristics of vascular involvement in patients with BD.
Methods: In total, 243 patients with BD were, retrospectively, collected in the Internal Medicine Department over 18 years.
Results: Vascular involvement was present in 72 patients (29.6%), whose 57 men and 15 women. The mean age was 32.9 years (range: 5-56 years). It revealed the disease in 26.3% of cases. Venous involvement was predominant, found in 68% of patients. Venous thrombosis interested: the upper limbs (51%), the lower limbs (38.7%), the pulmonary veins (18.3%), the inferior vena cava (12.2%) and the cerebral veins in 1 patient. Superficial venous thrombosis was present in 20.8% of cases. Arterial involvement was present in 11.1% of patients. It included pulmonary artery aneurysms in 8 cases and occlusion of the central retinal artery in one patient. The other associated systemic manifestations were: skin and mucous membrane disorders (100%), joint involvement (34.7%), ocular (29.2%), neurological (27.8%) and cardiac involvement in 7 patients. Treatment was based on long term curative anticoagulation (70%), corticosteroid therapy (50%) and immunosuppressive treatment in 21% of cases. Embolization was performed in two patients with good results.
Conclusion: Our study illustrates the frequency and the polymorphism of vascular involvement in BD.
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AB0608 **TIME OF DIAGNOSIS AND INITIATION OF TREATMENT OF GIANT CELL ARTERITIS (GCA) ACCORDING TO CLINICAL PHENOTYPE AND REFERRAL ORIGIN**

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Background: Giant cell arteritis (GCA) presents two phenotypic patterns: cranial and extracranial. Cranial manifestations are relatively easier to recognize and to diagnose, however since the extracranial are more insidious and less known, it may lead to a delay in diagnosis and in treatment. The main treatment are glucocorticoids (GC) at high doses followed by a descending pattern. The time between the begin of the symptoms and the start of the treatment with GC it's of vital importance in the prognosis of the disease.
Objectives: The present AUDIT describes our cohort's clinical features, the time from symptom onset to rheumatology visit and diagnosis of GCA, as well as the differences in time according to the service originating the referral.
Methods: Audit retrospective, descriptive study of patients diagnosed with GCA by the CGA 1990 criteria. All patients diagnosed with GCA from 2011 to 2021, in a single hospital center and referred to the Rheumatology Service were included. Patients were classified as: cranial phenotype, extracranial or mixed. Demographic and clinical variables and complementary examinations were collected. As well as the time from the first symptom until the patients are referred and diagnosed.
Results: Seventy patients were included in the study. Fifty-one patients (72.9%) were female, their clinical features are shown in Table 1. Twelve of them (17,39%) had a cranial phenotype, sixteen (23,18%) an extracranial phenotype and forty-one (60,42%) a mixed one. Extracranial phenotype patients showed to be younger at the time of the diagnoses than the other groups. Cranial phenotype patients had a lower increase of the acute phase reactants than the other phenotypes (without finding statistically significant differences). In Table 2 are shown the other demographic, clinical and analytic data.

Table 1. Disease Characteristics of the Patients at Baseline according to their phenotype

PHENOTYPE	CRANIAL	EXTRACRANIAL	MIXED	TOTAL
	N=12	N=17	N=41	N=70
Age	75.543 ± 7.48	73.543 ± 8.1	76.356 ±7.46	75.56 ±7.46
Smoker	8.3% (n=1)	11.8% (n=3)	14.6% (n=6)	12.9% (n=9)
Headache	91.7% (n=11)	0%	90.2% (n=37)	68.6% (n= 48)
Ocular involvement	58.3% (n=7)	0%	34.1% (n=14)	30% (n=21)
Fever of unknow origin	0%	29.4% (n=5)	34.1% (n=14)	27.1% (n=19)
Polymyalgia rheumatica	0%	41.2% (n=7)	53.7% (n=22)	41.4% (n=29)
Constitutional syndrome	0%	23.5% (n=4)	36.6% (n=15)	27.1% (n=19)
Cutaneous hyperalgesia	25% (n=3)	0%	31.7% (n=13)	22.9% (n=16)
Anaemia	0%	41.2% (n=7)	46.3% (n=19)	37% (n=26)
C reactive protein	51.33 ± 40.16	77.83 ± 75.30	85.55 ± 81.67	77.58 ± 74.57
Erythrocyte sedimentation rate	60.64 ± 33.13	76.20 ± 36.35	77.93 ± 35	74.65 ± 35.07

Patient referral were made from: Emergency room/ Internal Medicine hospitalization (30%, 21 patients), Primary Care (21.4%, 15 patients), Internal Medicine outpatient clinic (15.7%, 11 patients), Neurology (18.6%, 13 patients) and other specialties outpatient clinic (cardiology, vascular surgery, ophthalmology, hematology and gastroenterology). The median of the time from the first symptom until the patients are diagnosed are 12,9, 13,97 and 7,91 weeks in the cranial, extracranial and mixed respectively. The median of time from the first symptom until the patient referral to rheumatology are 9.34, 12.74 and 5.87 weeks in the cranial, extracranial and mixed respectively. The median of time from patient referral to rheumatology to be assessed are 3.73, 5.59 and 3.43 weeks in the cranial, extracranial and mixed respectively. 75.7% of the patients received treatment with glucocorticoids before being referral to rheumatology.
Conclusion: In our cohort, most of the patients with CGA had a mixed phenotype. The patient referral to rheumatology is made mainly from the emergency room, internal medicine hospitalization and primary care. Patients with mixed phenotype are diagnosed faster than the ones with an exclusively extracranial phenotype. The time between the first symptom and the referral to rheumatology is still long.
Disclosure of Interests: None declared
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AB0609 GAPS IN THE DIAGNOSIS OF TAKAYASU ARTERITIS: A ROMANIAN COHORT

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Background: The diagnosis of Takayasu arteritis still represents a big challenge, even though the disease was first described more than 100 years ago. Proof of that is the continuing effort to develop criteria with high specificity and sensitivity.[1]
Objectives: The aim of the study was to describe the clinical and paraclinical aspects of the disease at the time of diagnosis. Additionally, we wanted to evaluate the damage score in view of the diagnosis delay.
Methods: We retrospectively studied the clinical chart of 17 consecutive patients admitted to the Rheumatology Clinic of Emergency County Hospital from Cluj-Napoca, Romania between 2003 and 2021.
Results: There was just one man in the cohort (0.05%). The average age at the time of diagnosis was 37.5 years old. The average delay in the diagnosis was 33 months, while the biggest delay was of 240 months. The diagnosis was made by rheumatologists in 58% of the cases, while 29% by cardiologists and 11.7% by internal medicine specialists. The most frequent symptoms were limb claudication (64.7%), fatigue (52.9%) and headache (52.9%). Vascular bruits were found in most of the patients at the time of diagnosis (70.5%), as well as blood pressure and pulse difference between arms (52.9%). Unobtainable blood pressure was seen in 5 patients (29.4%). There was a discrepancy in 3 patients (17.6%) between inflammatory markers and inflammation in the vessels' walls, as confirmed by imaging techniques (angioMRI or angioCT). Most of the patients were classified as type V arteritis (35%), followed by type IV (18%), type I (17%), type IIA, respectively type IIB (12% each) and type III (6%). Stenosis of the involved arteries occurred 4.3 times more than aneurysm formation. Eight patients required vascular interventions at the time of diagnosis – four were treated by balloon angioplasty and six by stent placing. The average TADS (Takayasu Arteritis Damage Score) was 1.5 and it was not associated with delay in diagnosis (p>0.05).
Conclusion: Takayasu arteritis is a disease with heterogenous and nonspecific symptoms. For those reasons the delay in diagnosis is usually long, the treatment is started late and damage appears early in the course of the disease. This is reflected by the high amounts of vascular procedures needed at the time of diagnosis. We need better diagnostic criteria and specific monitoring scores.
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Vasculitis - small vessel vasculitis

AB0610 DEVELOPMENT OF MALIGNANCY IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Patients (pts) with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) reported to have an increased risk of malignancy compared to general population [1]. However, studies on risk factors for the development of malignancy in AAV pts are limited.
Objectives: We aimed to evaluate the frequency, clinical features and associated factors of malignancy in pts with AAV.
Methods: In this study, we retrospectively evaluated 287 pts with AAV. Thirty-three pts with EGPA and 14 pts with missing data were excluded. ANCA test was analysed based on immunofluorescence and/or Elisa results and divided into two serological groups; c-ANCA/PR3$^+$ (positive) and p-ANCA/MPO$^+$.
Results: Data of 240 pts (54.6 % female) were analysed. Mean age of diagnosis was 55.6±14 (range; 17-88) years and median disease duration was 67.5 (range; 3-255) months. Of those pts, 175 (73 %) had GPA and 65 (27 %) had MPA. ANCA results were available in 230 pts; 123 were c-ANCA/PR3$^+$ (53.5 %), 85 were p-ANCA/MPO$^+$ (37 %) and 22 were ANCA negative (ANCA$^-$) (9.5 %). Kidney (75.8 %) and lower respiratory tract (74.4 %) were the most common organs involved but they did not differ according to presence of malignancy (9.4 % vs 5.1 %; p=0.4 and 9.4 % vs 5 % p=0.4 respectively.) Twenty-two malignancies were observed in 20 pts (8.3 %; eleven c-ANCA/PR3$^+$, three p-ANCA/MPO$^+$ and two ANCA negative pts). Lung and thyroid papillary cancer in three; bladder, prostate, breast and kidney in two; adrenal gland, oral squamous cavity and sarcoma of retroperitoneum in one patient, hematological (three myelodysplastic syndrome, one chronic lymphocytic leukemia and one lymphoma) in five pts. Six pts (30 %) had prior and/or concomitant AAV diagnosis. Development of malignancy did not differ according to age, gender, diagnosis, seropositivity (ANCA$^+$ vs ANCA$^-$) and ANCA subgroups (Table 1). There was no association between malignancy and cumulative dose of cyclophosphamide (CYC) or history of smoking (p=0.96 and p=0.2, respectively). In univariate analysis, malignancy was associated with presence of cardiovascular disease (CVD) (p=0.003 OR 11.7) and mortality (p=0.04 OR 4.6), higher BVAS score at baseline (p=0.049) and higher VDI score (p=0.02). Significant association was observed between malignancy with CVD (95 % CI 2.2-83 OR 13.4 p=0.005) and mortality (p=0.044 95 % CI 1.03-8.5 OR:2.95) in multivariate analysis.

Table 1. Factors associated with malignancy in pts with AAV

	Univariate analysis		
Variables	**Malignancy + (n=20)**	**Malignancy – (n=220)**	**p value (OR)**
Age (years) ǂ	60±13.4	55.3±14	0.15
Gender (female)	10 (50)	121 (55)	0.7
Diagnosis *			
GPA	15 (8.6)	160 (91.4)	0.8
MPA	5 (7.7)	60 (92)	
ANCA status*			
c-ANCA/PR3	11 (9)	112 (91)	0.16
p-ANCA/MPO	3 (3.5)	82 (97)	
Cardiovascular disease*	8/38 (21)	10/199 (5)	***0.003 (11.7)***
Cerebrovascular accident*	2/15 (13)	16/222 (7)	0.3
Coronary heart disease*	4/18 (22)	19/218 (9)	0.08
Avascular necrosis*	4/35 (11)	14/199 (7)	0.3
Venous thrombosis*	3/21 (14)	15/217 (7)	0.2
BVAS score at admission ǂ	21.3±6	16.6±6.7	***0.049***
Smoking history (ever)*	6/53 (11)	8/156 (5)	0.2
Cumulative CYC dose (g) ᴷ	5 (7.4)	4.5 (7.8)	0.96
VDI scoreᴷ	3.5 (4)	2 (2)	***0.02***
Relapse (n=230, %)	5/80 (6.3)	11/150 (7.3)	0.8
Remission at six months (n=160, %)	8/104 (7.7)	5/56 (9)	0.8
Mortality*	7 (35)	35 (16)	***0.04 (4.6)***

OR: Odds ratio *(n, %) ǂ mean± Std dev. ᴷmedian; IQR

In survival analysis, mortality rate was higher in pts had malignancy compared to those without (Figure 1, p=0.035).

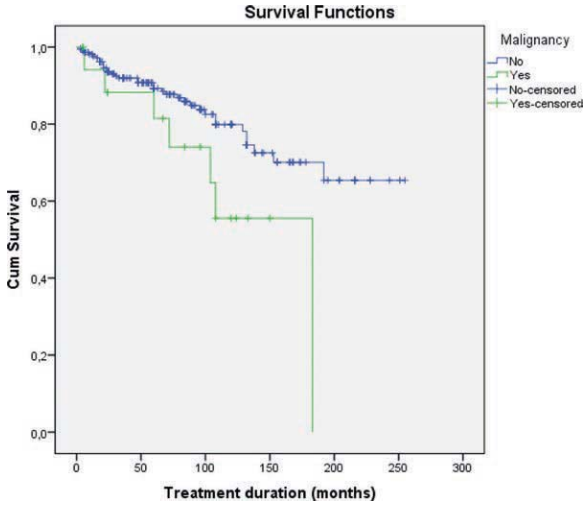

Figure 1. Survival analysis of mortality according to presence of malignancy in pts with AAV. Log-Rank: p=0.035

Conclusion: Significant proportion of pts with AAV developed malignancy in our cohort. Development of malignancy was associated with CVD, higher baseline BVAS and VDI scores. Our study also revealed lower survival rate in patients who developed malignancy. Further studies are needed to clarify risk factors for malignancy in patients with AAV.

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AB0611

NEUTROPHIL EXTRACELLULAR TRAPS AND INTERSTITIAL LUNG DISEASE IN ANCA-ASSOCIATED VASCULITIS: A SCOPING REVIEW

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Background: Deregulated neutrophil extracellular traps (NET) formation is implicated in various diseases, including ANCA-associated vasculitis and pulmonary fibrosis (PF). Lung involvement is frequent in AAV, and interstitial lung diseases (ILD) are strongly related to MPO-ANCA positivity and mainly reported in microscopic polyangiitis. The association between AAV and ILD is a strong indicator of poor prognosis and limited survival. Neutrophils, ANCA and NET interplay in PF development in AAV.

Objectives: This study aimed to review the literature concerning the implications of NET in lung fibrogenesis focused specifically on AAV associated with ILD, and the potential of NET as a theranostic marker.

Methods: Through scoping review methodology, we used a descriptive thematic analysis to understand the pathogenic role of NETs in patients with AAV and pulmonary fibrosis and their further role as a theranostic marker of this disease.

Results: Quality assessment of articles was evaluated through SANRA methodology (Table 1). The implications of NET in the pathogenesis of AAV and ILD (Figure 1), as well as an association between these two diseases, have been identified, but the underlying pathophysiological mechanisms are still unknown. Pharmacological or genetic inhibition of NET release reduces disease severity in multiple inflammatory disease models, indicating that NETs are potential therapeutic targets. In this regard, despite the lack of clinical data, we may hypothesize that an optimal management of AAV-ILD patients would require not only B-cells targeted therapy, but also NETs inhibition.

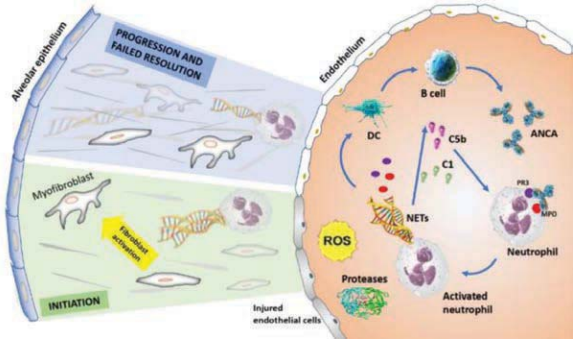

Figure 1. The role of NET in interstitial lung disease associated with ANCA-associated vasculitis

Conclusion: Preliminary findings seem to display a lack of efficacy of traditional immunosuppressants, such as Rituximab, in this subset of patients, while to date no patients suffering from a definite ILD was enrolled in clinical trials. Further insights would be provided by their employment, as a combination treatment, in the common clinical practice. Although we can imagine that inhibition of NETs in patients with AAV-ILD could reduce severity and mortality, we still lack a scientific basis that could improve our understanding of the disease from a molecular point of view.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2022-eular.479

Table 1. SANRA Score for quality assessment

N°.	Authors	Justification of the article's importance for the readership	Statement of concrete aims or formulation of questions	Description of the literature search	Referencing	Scientific Reasoning	Appropriate presentation of data	Total score
1	Pandolfi L et al. 2021	2	2	0	1	2	2	9
2	Radermecker C et al. 2020	1	2	0	2	2	1	8
3	Zhang S et al. 2019	2	1	0	2	2	1	8
4	Skopelja-Gardner S et al. 2019	1	1	0	1	2	2	7
5	Khawaja AA et al. 2020	2	2	0	1	2	1	8
6	Chrysanthopoulou A et al. 2014	2	1	0	2	2	1	8
7	Kraaij T et al. 2018	2	1	0	2	1	2	8
8	Tang S et al. 2015	2	1	0	1	2	1	7
9	Yoshida M et al. 2016	1	2	0	1	2	1	7
10	Nakazawa D et al. 2014	2	1	0	2	2	2	9
11	Hattanda F et al. 2019	2	2	0	1	2	1	8
12	Schreiber A et al. 2017	2	2	0	1	1	2	8
13	van Dam LS et al. 2019	2	2	0	1	1	1	7
14	Roitsch S et al. 2018	1	2	0	1	2	2	8
15	Takeuchi H et al. 2017	2	2	0	2	2	2	10
16	Su B et al. 2021	2	1	0	1	2	2	8
17	Söderberg D et al. 2015	2	1	0	1	2	1	7
18	Surmiak M et al. 2016	1	2	0	1	2	2	8

AB0612

CHRONIC PANCREATITIS DUE TO SYSTEMIC AUTOIMMUNE AND BACTERIAL SEPTIC VASCULITIS IN RHEUMATOID ARTHRITIS – A HYPOTHETIC PATHWAY OF CHRONIC PANCREATITIS IN POST-COVID 19 CONDITION

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Background: The etiology of pancreatitis is heterogeneous; it may be due to chronic excessive alcohol use, gallstones, medications, infections, autoimmune diseases, metabolic disorders, trauma, congenital malformations etc.
Objectives: The **aim** of this study has been to describe a hypothetic pathway of chronic pancreatitis in post-Covid 19 condition, based on the role of autoimmune and bacterial septic vasculitis in the pathogenesis of chronic pancreatitis (**ChrP**) in rheumatoid arthritis (**RA**).
Methods: At the National Institute of Rheumatology **9475** patients died between 1969 and 1992; among them **161** with **RA** and all of them were autopsied.
RA was confirmed clinically according to the criteria of the **ACR**.
Tissue samples of pancreas were available for histologic evaluation in **111** patients. Pancreatitis and vasculitis were determined and characterized histologically [1,2]. The possible role of autoimmune vasculitis and bacterial septic vasculitis in the pathogenesis of **ChrP** was analyzed by Pearson's chi-squared (χ^2) test.
Results: ChrP – characterized by diffuse and/or focal fibrosis and atrophy – was present in **10** (**9.01**%) of 111 patients. Systemic vasculitis complicated **RA** in **28** (25.23%) of 111 patients. **Twenty-five** (89.3 %) of 28 systemic vasculitis proved to be of autoimmune origin. Autoimmune vasculitis involved the pancreatic blood vessels (**pAV**) in **8** (32.0 %) of these 25 patients. Non-specific (n=37), fibrinoid necrotic (n=14), and granulomatous type (n=5) of **pAV** were detected side by side in the same histologic section, involving pancreatic arteries of different sizes. The veins and venules were not involved. **pAV** was not associated with chronic pancreatitis. The relationship between **pAV** and **ChrP** was inverse with a negative colliquation coefficient (c=-1.0, χ^2=0. 0801, p <0.7772 – NS). **Three** (10.7 %) of 28 systemic vasculitis cases proved to be of septic (bacterial) origin. Pancreatic blood vessels (**pSV**) were involved in **2** (66.7 %) of these 3 patients. Granulomatous vasculitis was not seen with **pSV**, and the veins and venules were also spared. Non-specific (n=9), fibrinoid necrotic (n=2) vasculitis involving different size of pancreatic arteries were associated with chronic pancreatitis. The relationship between **pAV** and **ChrP** was significant (c=0.92308, χ^2=6.3201, p <0.012).
Conclusion: Chronic pancreatitis is characterized clinically by abdominal pain and diarrhea, which are common in post-Covid 19 condition [2]. The strong and significant correlation between **pSV** and **ChrP** indicates that subclinical or manifest bacterial septic processes may play a role in the pathogenesis of **ChrP**. Hypothetically a similar pathway is plausible in post-Covid 19 chronic pancreatitis due to viral infection and vasculitis, analogous to bacterial septic vasculitis. Systemic vasculitis of autoimmune origin involving blood vessels of the pancreas may cause a special multifocal relapsing lipo-necrotic pancreatitis [1,2], and according to our results, do not influence the prevalence of **ChrP**. The autoimmune origin of pancreatic vasculitis may be excluded histologically by the presence of granulomatous vasculitis of the most frequently involved arterioles and small arteries.
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AB0613

VASCULAR EVENTS AND ASSOCIATED FACTORS IN ANCA-ASSOCIATED VASCULITIS: ANALYSIS OF 237 PATIENTS WITH LONG-TERM FOLLOW-UP

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Background: Patients with ANCA-associated vasculitis (AAV) reported to have an increased risk of vascular events (VE) compared to general population [1]. However, studies on risk factors for the development of VE in AAV patients (pts) are limited.
Objectives: In our study we aimed to evaluate the frequency, risk factors and mortality risk of VE pts with AAV.
Methods: In this study we retrospectively evaluated 287 pts with AAV. Patients with EGPA (n=33) were not included and 17 pts were excluded due to missing data. Arterial vascular events (a-VE) were recorded as myocardial infarction, unstable angina pectoris, peripheral artery disease, need for revascularization and cerebrovascular accident. Deep venous thrombosis and pulmonary embolism were recorded as venous thrombotic events (VTE). History of a-VE and/or VTE were grouped as all VE. ANCA test results were analyzed based on IFA and/or Elisa results and divided into two serological groups; c-ANCA/PR3$^+$ (positive) and p-ANCA/MPO$^+$.
Results: Data of 237 pts (46 % male) was analyzed. Mean age at diagnosis was 55.6±14 (range; 17-88) years and median disease duration was 77 (range; 3-255) months. Of those pts, 173 (73 %) had GPA and 64 (27 %) had MPA. ANCA results were available in 230 pts; 122 were c-ANCA/PR3$^+$ (53.5 %), 85 were p-ANCA/MPO$^+$ (37 %) and 22 were ANCA negative (ANCA$^-$) (9.5 %). The most common organ involvements were kidneys (75.8 %) and lower respiratory tract (74.4 %). Overall, 22 % (n=52) of the pts developed VE, 17 % (n=40) a-VE, 9 % (n=21) VTE and 3.8 % (n=9) both a-VE and VTE. In univariate analysis; development of VE was significantly higher in males, pts with c-ANCA/PR3 and pts with higher baseline CRP levels, GFR<50 mL/min, history of smoking, severe infection, higher VDI score. Development of a-VE was higher in pts with males, advanced age, pts with c-ANCA/PR3, history of smoking, higher VDI score, GFR<50 mL/min. Additionally, mortality was increased in pts with VE and a-VE. In multivariate analysis; while VE were associated with smoking [95 % CI:1.7-21; OR:6], c-ANCA/PR3 positivity [95 % CI: 1.15-92; OR:10.3] and higher VDI score [95 % CI:1.007-2.4; OR:1.5]; a-VE were associated with advanced age [95 % CI:1.002-1.08; OR:1.04], higher VDI score [95 % CI:1.3-2; OR:1.6] and c-ANCA/PR3$^+$ [95 % CI:1.06-8.6; OR:3]. Development of VTE was associated with higher VDI score (p<0.001) in univariate and multivariate analysis [95 % CI: 1.2-1.8; OR:1.5]. In survival analysis, mortality rate was significantly higher in pts who had a history of VE (Log-Rank: p=0.04).
Conclusion: Our observational data of more than 5 years of follow-up revealed that, one in five pts with AAV developed VE after diagnosis. The risk of VE was significantly higher in c-ANCA/PR3$^+$ pts, smokers and pts with high VDI scores. Older age increased the risk of a-VE. Mortality was increased in AAV pts with VE after diagnosis. Additional studies needed to delineate the mechanism of VE in AAV and precautions should be undertaken to avoid morbidity and mortality.

Table 1.

Prevalence of pAV / pSV Size of involved vessels	Prevalence Ns pAV	Prevalence Fn pAV	Prevalence Gr pAV	Total n/% of pAV	Prevalence Ns pSV	Prevalence Fn pSV	Prevalence Gr pSV	Total n/% of pSV
Arteriole	18	10	3	31 – 55.36	3	0	0	3 – 27.27
small artery	16	4	2	22 – 39.28	3	2	0	5 – 45.46
medium size artery	3	0	0	3 – 5.36	3	0	0	3 – 27.27
Venule	0	0	0	0 – 0.0	0	0	0	0 – 0.0
small vein	0	0	0	0 – 0.0	0	0	0	0 – 0.0
medium size vein	0	0	0	0 – 0.0	0	0	0	0 – 0.0
Total	37 – 66.07%	14 – 25.0%	5 – 8.93%	56 – 100%	9 – 81.82%	2 – 18.18%	0 – 0.0	11 – 100%

Table 1. Factors associated with vascular events in pts with AAV

	Univariate analysis		
Variables	**VE+ (n=52)**	**VE- (n=185)**	**p value (OR) (95 % CI)**
Age*	58.8±14.5	54.9±14	0.08 (0.99-1.04)
Gender, male ‡	31 (60)	78 (42)	***0.03 (5) (1.08-3.8)***
Diagnosis ‡			
GPA (n=173)	40 (23)	133 (77)	0.5
MPA (n=64)	12 (19)	52 (81)	
ANCA status ‡			
c-ANCA/PR3	33 (27)	89 (73)	***0.045 (4) (1.007-4.2)***
p-ANCA/MPO	13 (15)	72 (85)	
Baseline CRP (mg/L)ᵏ	73 (85)	48 (89)	***0.05 (1-1.009)***
GFR<50 ml/min ‡	24 (47)	57 (31)	***0.03 (4.7)***
BVAS score*	19±7	16.3±7	0.06 (1-1.1)
Smoking history (ever) ‡	19/45 (42)	34/162 (21)	***0.004 (8.3) (1.4-5.6)***
Cumulative steroid (MP) dosage (g/12 month) ᵏ	7.9 (17)	7.5 (8)	0.8
Relapse ‡	22/49 (45)	58/180 (32)	0.1
Severe infection ‡	23/46 (50)	57/168 (34)	***0.046 (4) (1.006-3.8)***
VDI score*	4.8±2.7	2.4±1.7	***<0.001 (1.4-1.96)***
Remission at 6. month ‡	19 (56)	85 (68)	0.2
Mortality ‡	15 (29)	27 (14.6)	**0.02 (5.7) (1.1-4.9)**

*mean±std dev ‡ n, % ᵏmedian, interquartile range. OR: Odds ratio

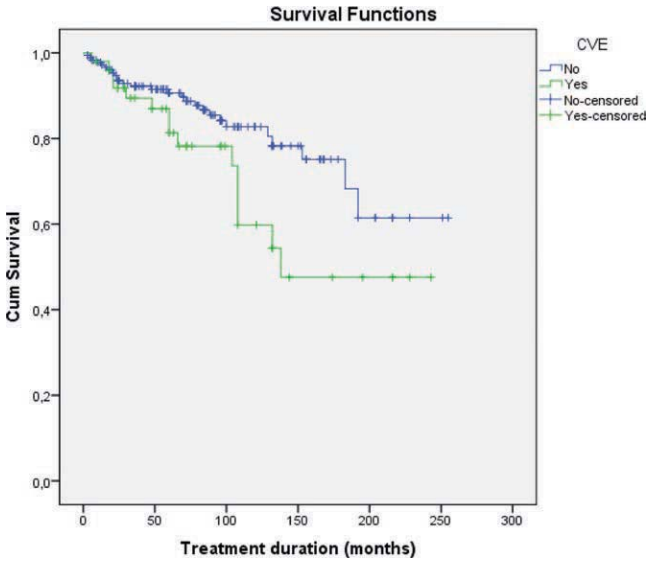

Figure 1. Comparison of mortality rate between pts had VE and had not. Log-rank: p=0.039

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.798

AB0614

LATE-ONSET NEUTROPENIA AFTER RITUXIMAB TREATMENT IN PATIENTS WITH ANCA-ASSOCIATED SYSTEMIC VASCULITIS: A RETROSPECTIVE ANALYSIS OF A REGISTER-BASED PATIENT COHORT

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Background: Anti-B-cell therapy with rituximab (RTX) plays an important role in the induction and maintenance therapy of ANCA- associated vasculitis (AAV). Late-onset neutropenia (LON) has been reported following RTX therapy.
Objectives: Based on a retrospective analysis of the register of AAV patients (pts) treated with RTX, to study the incidence and outcomes of LON.
Methods: 140 AAV pts (median age 52 (20-83) years, 57% women) were treated with RTX between 2009 to 2021: 63 with granulomatosis with polyangiitis (GPA), 45 microscopic polyangiitis (MPA), 24 eosinophilic granulomatosis with polyangiitis (EGPA), and 8 unclassified AAV. The median total dose of RTX was 3.5 (0.5-45) g. As a rule, single 500-mg infusions were used with an interval of 4-6 months for retreatment courses. The duration of follow-up exceeded 6 months after the first dose of RTX. Regular pts monitoring every 3 months included estimation absolute neutrophil count (ANC). LON was defined as unexplained neutropenia occurring 3 weeks after the last RTX infusion.
Results: LON I-IV grade was noted in 16 (11.4%) AAV pts: 6 GPA, 4 MPA, 4 EGPA, and 2 unclassified AAV. In 7 out of 16 cases (43.7%) LON developed after the first course of RTX. Neutropenia grade I was observed in 3 pts (ANC 1.68-2.0x10^9/l, 2-15.5 months after the last RTX infusion), grade II - in 4 patients (1.1-1.5x10^9/l, 3-9 months after RTX). Neutropenia grade I-II resolved independently, without adverse reactions. LON grade IV was noted in 9 pts (0.06-0.3x10^9/l, 1.1-11 months after RTX), 3 of them received leukopoiesis-stimulating drugs with normalization of ANC. In one EGPA pt febrile LON grade IV developed twice (in 2017, 11 months after RTX; in 2019, 4 months after RTX and complicated by uterine bleeding). Fatal outcome occurred in 5 out of 16 cases (31.2%): 1 MPA, 3 GPA, and 1 EGPA. In 3 fatal cases LON was complicated by pneumonia (in 2 with septic shock), in one with acute myocardial infarction and another one with progression of chronic renal failure. According to our registry, the total mortality among 140 AAV pts receiving RTX was 11.4%, while 5 of 16 fatal cases (31.2%) had LON grade IV. Three of the 5 death were noted in 2013-2014, which attributed to the use of cyclophosphamide >2 gm before RTX, as well as insufficient awareness of the risk of LON, which contributed to the delay in control of a full blood count, untimely diagnosis of LON and late treatment. At the beginning, the original drug Mabthera was used, while after 2014 biosimilar Acellbia was mainly used. The disadvantages of this study: the lack of information about the ANC in 4 cases with COVID-19 and fatal outcome.
Conclusion: LON after RTX therapy can develop in 11.4% of AAV pts, which exceeds the data for rheumatoid arthritis (1,3-3%) [1,2]. Our register data are lower than the rate of LON in AAV, presented by D. Tesfa et al. (23%) [1], which could be affected by the use of low-dose RTX for retreatment courses. LON accounts for a significant part in the structure of deaths of AAV pts (31.2%). It needs to careful monitoring of ANC in pts receiving RTX and awareness of both pts and physicians about the risk of LON.
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AB0615

CLINICAL IMPACT OF CERULOPLASMIN LEVELS AT ANCA-ASSOCIATED VASCULITIS DIAGNOSIS

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Background: Myeloperoxidase (MPO) plays a major role in loss of immunological tolerance leading to tissue destruction in ANCA-associated vasculitis (AAV). Ceruloplasmin is a protein with antiproteinase and antioxidant properties that inhibits MPO activity. Whether serum level of ceruloplasmin at AAV diagnosis has an impact is unknown.
Objectives: The objective of this study was to evaluate the prognostic impact of serum level of ceruloplasmin at diagnosis in patients with granulomatosis with polyangiitis or microscopic polyangiitis.
Methods: We conducted a retrospective unicentric study at Caen University Hospital, involving consecutive adult patients with granulomatosis with polyangiitis or microscopic polyangiitis between 2010 and 2021 who had available serum at diagnosis. Data was collected using the health records.
Ceruloplasmin was measured by standardized nephelometry (normal values: 0.15 – 0.50 g/L). Patients in each subgroup (whole cohort, microscopic polyangiitis and anti-MPO patients) were divided into two groups based on the median serum level of ceruloplasmin.
We estimated survival using the Kaplan-Meier survival curve, and between-group differences were evaluated by the log-rank test. The study was approved by the local ethics committee of Caen University Hospital (n° 1947).
Results: Ninety-two patients were included, 46 (50%) granulomatosis with polyangiitis (41 anti-proteinase 3 and 5 anti-MPO) and 46 (50%) microscopic polyangiitis (45 anti-MPO and 1 anti-proteinase 3). The median level of ceruloplasmin was 0.44 g/L. No significant differences in the clinical presentation were observed between patients in the two groups (p>0.05). We observed 9 (19.6%) deaths in the low ceruloplasmin group and 5 (10.9%) in the high ceruloplasmin group (p=0.39). Vasculitis relapse occurred in 10/46 patients (22%) and 11/46 patients (24%) (p=1), renal failure leading to dialysis and/or renal transplant in 6/46 patients (13%) and 8/46 patients (17%) (p=0.77), respectively. No significant difference in survival was found (p=0.07). The same analyses were performed

between the low and the high ceruloplasmin group with the microscopic polyangiitis subgroup (n=46), and no significant differences were found (p>0.05). However, within the anti-MPO subgroup (n=50), the survival was worse in the low ceruloplasmin group (p=0.03).

Conclusion: In anti-MPO AAV patients, serum level of ceruloplasmin at diagnosis seems to be associated with a significant impact on survival.

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AB0616

MYELOPEROXIDASE (MPO) POSITIVE EXTRACELLULAR VESICLES (EVS) EXPRESSING COMPLEMENT SPLIT PRODUCTS IN ANTI - NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) -ASSOCIATED VASCULITIS (AAV)

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Background: Complement activation has a critical role for the development of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). We have previously shown increased expression of complement split products C3a and C5a on myeloperoxidase (MPO) positive EVs (MPO^+EVs) in plasma from AAV patients with kidney involvement compared to the patients with non-renal disease and the EV-levels correlated with disease activity (1).

Objectives: To investigate the expression of a larger set of complement components on circulating MPO^+EVs in relation to disease activity and kidney involvement in patients with AAV.

Methods: Eighty-nine patients with AAV and 23 healthy controls were included. The concentration of MPO^+EVs expressing complement split products C3a, C4d, C5a, terminal complement complex-TCC (C5b-9) or complement factor B (CFB) were analyzed from citrate plasma by flow cytometry. The assessment of vasculitis disease activity was performed using the Birmingham Vasculitis Activity Score (BVAS).

Results: In the AAV group, there were 47 males (52.8%), the median age was 56 years and 33 (37.1%) patients were anti-MPO-positive and 54 (60.7%) were anti-PR3-positive. Two patients were positive for both antibodies. Median disease duration for patients with active AAV (BVAS>0; n=81) was 4 days and for patients in remission (BVAS 0; n=8) 1259 days. 64% had kidney involvement (n=52). Highly active AAV (BVAS ≥12) was noted in 62 patients, of whom 49 patients had kidney involvement. Active disease (0<BVAS<12) was seen in 19 patients. AAV patients had significantly higher levels of MPO^+, MPO^+C3a^+, MPO^+C4d^+ and MPO^+TCC^+ EVs compared to healthy controls (all p<0.001). Patients in remission had higher levels of MPO^+, MPO^+C4d^+ and MPO^+TCC^+ EVs compared to healthy controls (all p≤0.001). There was a significant difference in levels of MPO^+(p=0.02), MPO^+C3a^+(p<0.001), MPO^+C4d^+(p<0.001) and MPO^+TCC^+ EVs (p<0.001) in patients with kidney involvement compared with patients without (n=29) (Figure 1). For patients with BVAS>0 there was a weak correlation between MPO^+, MPO^+C3a^+, MPO^+C4d^+, MPO^+TCC^+ EVs and BVAS. Kidney biopsies from 34 patients were classified according to histopathological class (2): crescentic (n=6), focal (n=18), mixed (n=6), sclerotic (n=4). The level of MPO^+C4d^+EVs was higher in the sclerotic type compared to focal (p=0.04, 95% CI [2.4–103.7]) and mixed (p=0.04, 95% CI [1.4–119.1]).

Conclusion: Levels of EVs expressing complement split products were generally increased in AAV patients and patients with kidney involvement had higher levels of total MPO^+EVs exposing C3a, C4d or TCC compared with patients without suggesting a role in kidney AAV pathogenesis. Patients with sclerotic kidney histotype had higher levels of MPO^+C4d EVs compared with focal and mixed subgroups pointing to that activation of the classical complement pathway may be of importance in severe forms of kidney AAV.

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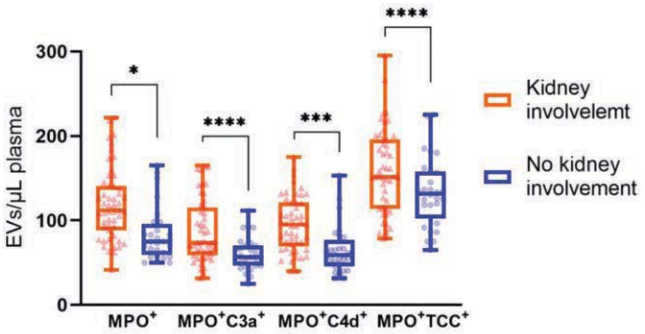

Figure 1. Concentrations of myeloperoxidase positive extracellular vesicles (MPO^+EVs) expressing complement components C3a, C4d or TCC in patients (BVAS>0) with kidney involvement or none. Extreme outliers excluded.

Disclosure of Interests: None declared

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AB0617

HIGH PREVALENCE OF OSTEOPOROSIS AND FRAGILITY FRACTURES IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: A CROSS-SECTIONAL STUDY

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Background: The advent of effective immunosuppressive treatments significantly improved the prognosis of ANCA-associated vasculitides (AAV), which have become chronic relapsing diseases. Patients with inflammatory rheumatic disorders are particularly prone to reduced bone mineral density (BMD) and fragility fractures (FF), due to chronic glucocorticoid therapy, immunosuppressant-induced hypogonadism, systemic inflammation, functional disability and comorbidities. At present, there is paucity of data concerning the risk of osteoporosis and FF in AAV.

Objectives: To describe the occurrence of osteoporosis and major FF in a cross-sectional cohort of patients with AAV.

Methods: Patients diagnosed with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA), according to ACR criteria and/or Chapel Hill definitions and regularly followed-up in our vasculitis center were included. BMD was measured by dual-energy X-ray absorptiometry (DEXA) of the proximal femur and lumbar spine, between March 2016 and September 2021. Osteoporosis was defined by a T-score below –2.5 SD, whereas osteopenia was defined by a T-score between -1 and -2.5 SD, according to the World Health Organization criteria. Vertebral fractures were assessed by X-ray of the dorso-lumbar spine. Data on previous osteoporotic hip fractures were collected.

Results: Sixty-two consecutive patients were included (59.7% female, mean age at time of DEXA 61.8±10.5 years, disease duration 97.0±76.1 months). Sixteen (25.8%), 8 (12.9%) and 38 patients (61.3%) were affected by GPA, MPA and EGPA, respectively. BMD findings indicating osteoporosis and osteopenia, at either the lumbar spine and/or the proximal femur, were observed in 15 (24.2%) and 39 patients (62.9%), respectively, whilst only 8 patients (12.9%) had normal BMD values at both sites. Fifteen patients (24.2%) reported 51 major FF (50 vertebral fractures, 1 hip fracture) during follow-up, with multiple major FF being recorded in 10 patients (16.1%). Osteoporosis, at least at one site, was frequent not only in post-menopausal women (19.4%), but also in 6 males (24%), 3 pre-menopausal women (50%) and 3 patients under 50 years of age (37.5%), respectively (Figure 1). Similarly, major FF occurred in 4 males (16.7%), 1 pre-menopausal female (16.7%) and 1 patient under 50 years of age (12.5%), respectively (Figure 1). Patients with osteoporosis presented a lower body mass index (BMI) (23.1±4.1 vs 25.9±4.4, P=0.03) and a higher prevalence of major FF (53.3% vs 14.9%, P=0.003) compared to patients without osteoporosis. Compared to patients without major FF, those affected by major FF were older (68.8±1.8 vs 59.4±9.3 years, P=0.003), had a higher disease duration (146.9±78.8 vs 81.8±68.9 months, P=0.003) and presented with lower proximal femur BMD values (0.657±0.122 vs 0.761±0.127 g/cm^2, P=0.007) and proximal femur T-score (-2.0±0.9 vs -1.4±0.8 SD). Notably, 7 out 15 patients with FF (46.7%) did not exhibit BMD findings of osteoporosis. Other variables, including sex, disease subtype, ANCA status, chronic kidney disease or treatment with cyclophosphamide were not related to bone loss or FF.

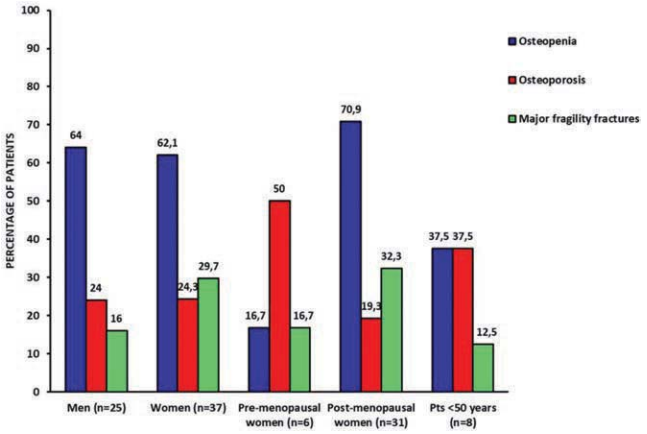

Figure 1. Proportion of patients with osteopenia, osteoporosis and major fragility fractures stratified according to sex, menopausal status and age.

Conclusion: Patients with AAV are particularly susceptible to BMD loss and fractures, with osteoporosis and major FF being reported in about a quarter of patients. Short-term and long-term monitoring for reduced BMD and FF is warranted in all patients with AAV, including male patients, premenopausal females and those under 50 years of age.

Disclosure of Interests: None declared

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AB0618 TOLERABILITY AND SAFETY OF 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE IN PATIENTS WITH SYSTEMIC VASCULITIS, PRELIMINARY RESULTS

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Background: Systemic vasculitis (VS) is a severe autoimmune disease requiring active immunosuppressive therapy. The probability of infectious complications in these patients is very high. Immunization with the 23-valent polysaccharide pneumococcal vaccine (PPV-23) is required to reduce the risk of severe respiratory infections in this group of patients.

Objectives: The aim of the study was to study the tolerability and safety of PPV-23 in patients with SV.

Methods: At this stage, the study included 13 patients with WS: 10 with vasculitis associated with antineutrophil cytoplasmic antibodies (ANCA) (AAV), (5 with granulomatosis with polyangitis (GPA), 4 with eosinophilic granulomatosis with polyangiitis (EGPA), 2 - with microscopic polyangiitis (MPA)), 1 - with polyarteritis nodosa, 1 - with Takayasu's arteritis (AT); of which 10 women, 3 men, aged 22 to 76 years. 9 (69%) patients were older than 50 years. Remission of the disease was observed in 1 patient (EGPA), in 3 - low disease activity, in 9 - active vasculitis (all 9 with AAV, BVAS from 4 to 13). All patients received glucocorticoids (GC): 2 - 55-60 mg/day, 9 - 10-20 mg/day, 2-2.5-5 mg/day; 5 -bDMARD: 4 - rituximab (RTM), 1 - TNF inhibitors; 11 - cytostatics (CS): 4 - mycophenolate mofetil (MM), 3 - azathioprine (AZ), 2 - cyclophosphamide (CPh), 2 - methotrexate (MTX). Two patients were on induction therapy (GC 55-60 mg + CPh) with a plan to switch to RTM. Only 1 patient with EGPA received HA as monotherapy. The 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously in 0.5 ml (1 dose). The follow-up period was 1-6 months. During the visits, standard clinical and laboratory tests and the determination of antibodies to S.pneumoniae were carried out.

Results: Vaccination tolerance was good in all patients. One (7,7%) patient with EGPA (in remission) had a mild local reaction (pain at the injection site) within 1 day. Another 1 (7,7%) patient with severe concomitant pathology (EGPA + multiple sclerosis) had a general reaction in the form of a transient increase in weakness in the lower extremities for up to 5 days (this symptom was a manifestation of polyneuropathy, persisted earlier, and to a greater extent was associated with multiple sclerosis than with EGPA). Vaccinal reactions were completely reversible and did not require additional prescriptions. During the follow-up period, no deterioration in the course of SV was recorded in any case, and no new autoimmune phenomena, both laboratory and clinical, were noted in any of them. 7 (53,8%) patients (all 5 with GPA, 2 with EGPA) had ENT lesions (destructive rhinosinusitis (5), sinusitis (2)) with frequent exacerbations. 1 patient with GPA reported a significant improvement in the condition of the ENT organs (no exacerbations of rhinosinusitis, disappearance of nasal discharge for 5 months). In the remaining 6 patients, the condition also remained stable, no progression of sinusitis was noted during the observation period (1-4 months). No infections of the lower respiratory tract were registered during the observation period.

Conclusion: 1. All patients had a high risk of infectious complications: combined immunosuppressive therapy (92% of patients), age over 50 years (69% of patients), severe lesion of ENT organs (53,8% of patients). 2. The tolerance of PPV-23 vaccination was good. 3. There was no deterioration in the course of SV.

Disclosure of Interests: None declared

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AB0619 RATIONALE AND DESIGN OF THE 52-WEEK, RANDOMIZED, PHASE 3, HEAD-TO-HEAD MANDARA STUDY TO EVALUATE THE EFFICACY AND SAFETY OF BENRALIZUMAB, A HUMANIZED, ANTI-INTERLEUKIN–5 RECEPTOR A MONOCLONAL ANTIBODY IN REFRACTORY OR RELAPSING EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss syndrome) is a rare, potentially organ- and life-threatening disease characterized by systemic eosinophilia, airway disease, and multi-system small-vessel vasculitis. Management of EGPA generally focuses on reducing active inflammation using corticosteroids and immunosuppressants, both of which are associated with serious adverse effects and incomplete disease control. High blood eosinophil (bEOS) levels are a central component of the pathophysiology of EGPA, and studies have shown that bEOS-reducing therapies, such as mepolizumab, are effective in some patients with EGPA. Benralizumab is a humanized, afucosylated, anti-interleukin-5 receptor α monoclonal antibody that induces direct, rapid, and near complete depletion of eosinophils through antibody-dependent cell-mediated cytotoxicity. Eosinophil depletion by benralizumab is effective in eosinophilic asthma, corticosteroid-dependent asthma, and has shown promise in a small phase 2 trial in hypereosinophilic syndrome, which has overlapping organ systems involvement and similar clinical features to EGPA. Collectively, the evidence from these indications supports examination of the efficacy of benralizumab as an eosinophil-depleting therapy in patients with EGPA.

Objectives: The phase 3, head-to-head MANDARA (NCT04157348) study will evaluate the efficacy and safety of benralizumab versus mepolizumab in adults with relapsing or refractory EGPA.

Methods: This randomized (1:1), multicentre, double-blind (DB), active-controlled study is enrolling adults with a diagnosis of EGPA, defined as a history of asthma and eosinophilia together with ≥2 additional clinical features, a history of relapsing or refractory disease, and maintained on a stable prednisolone/prednisone dose ≥7.5 mg/day for ≥4 weeks prior to baseline. Patients will receive either benralizumab 30 mg or mepolizumab 300 mg every 4 weeks over the 52-week DB study period. Patients who complete the DB treatment period will be eligible to continue into an optional open-label extension, during which all patients will receive benralizumab (Figure 1). The primary endpoint is the proportion of patients who achieve EGPA remission, defined as a Birmingham Vasculitis Activity Score (BVAS)=0 and prednisolone dose of ≤4 mg/day, at both Week 36 and 48 of the DB period, and it will assess non-inferiority (NI) between benralizumab and mepolizumab. Secondary endpoints include duration of remission, time to first EGPA relapse, annualized relapse rate, average daily prednisolone dose between Weeks 48 to 52, and the proportion of patients who achieve and maintain remission from Week 24 through the end of the DB period. Other endpoints include safety, symptoms, health-related quality of life, healthcare utilization due to EGPA, and tolerability. The trial also includes a non-interventional patient interview sub-study, which will collect data related to patients' EGPA personal experience and perceived impact on study treatment, and a mechanistic sub-study, which will explore the pharmacodynamic response and mechanism of action of benralizumab compared to mepolizumab.

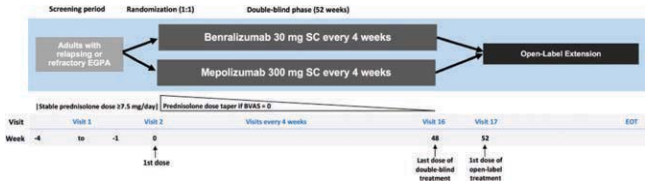

Figure 1. MANDARA Study Design

Results: The study aims to enrol 140 patients which will provide ~90% power to demonstrate NI with a NI margin of -25% at the 2.5% one-sided significance level, assuming each treatment group has a remission rate of 32%. Screening started in Oct 2019 and the trial is ongoing.

Conclusion: MANDARA is one of few multicentre randomized trials conducted to date in EGPA. Results from this phase 3, head-to-head study will characterize the efficacy and safety of benralizumab compared with mepolizumab in adults with relapsing or refractory EGPA. The trial's active comparator design will also provide critical evidence of efficacy and safety in a disease with considerable unmet needs.

Disclosure of Interests: Michael Wechsler Speakers bureau: GlaxoSmithKline, AstraZeneca, Amgen, Sanofi, Regeneron, Novartis, Genentech, and Teva Pharmaceuticals, Grant/research support from: GlaxoSmithKline, AstraZeneca, Amgen, Sanofi, Regeneron, Novartis, Genentech, and Teva Pharmaceuticals, Peter A. Merkel Consultant of: AbbVie, AstraZeneca, Boeringher-Ingelheim, Bristol-Myers Squibb, ChemoCentryx, CSL Behring, Dynacure, EMDSerono, Forbius, Genentech/Roche, Genzyme/Sanofi, GlaxoSmithKline, InflaRx, Janssen, Kiniksa, Kyverna, Magenta, MiroBio, Neutrolis, Novartis, Pfizer, Sparrow, Takeda, Talaris, Grant/research support from: AbbVie, AstraZeneca, Boeringher-Ingelheim, Bristol-Myers Squibb, ChemoCentryx, Eicos, Forbius, Genentech/Roche, Genzyme/Sanofi, GlaxoSmithKline, InflaRx, Sanofi, Sofia Necander Shareholder of: AstraZeneca, Employee of: AstraZeneca, Lena Börjesson Sjö Shareholder of: AstraZeneca, Employee of: AstraZeneca, Elizabeth A. Duncan Shareholder of: AstraZeneca, Employee of: AstraZeneca, Natalya Makulova Shareholder of: AstraZeneca, Employee of: AstraZeneca, Gina D'Angelo Shareholder of: AstraZeneca, Employee of: AstraZeneca, Ron A. Chen Shareholder of: AstraZeneca, Employee of: AstraZeneca, Vivian H. Shih Shareholder of: AstraZeneca, Employee of: AstraZeneca, Rohit Katial Shareholder of: AstraZeneca, Employee of: AstraZeneca, Ubaldo J. Martin Shareholder of: AstraZeneca, Employee of: AstraZeneca

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AB0620 DO PATIENTS WITH ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS (AAV) NEED ANTICOAGULANTS?

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Background: Patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) have a two- to threefold greater risk of developing `thrombotic events. The expediency of thrombosis prevention in AAV continues to be discussed. The issue of prescribing anticoagulants (AC) is being discussed

Objectives: Retrospectively to analyze the parameters of routine blood clotting indicators in patients with AAV depending on receiving AC.

Methods: The study included 45 patients with AAV (15 -with granulomatosis with polyangiitis (GPA), 15 - microscopic polyangiitis (MPA), and 15 - eosinophilic granulomatosis with polyangiitis (EGPA), aged 23 to 73 years. Duration of the disease was in 6 patients had <12 months, in 20 - 1-5 years, in 13 - 5-10 years, in 6 - >10 years. High AAV activity were registered in 22 patients (BVAS > 5)), 21 - low activity (BVAS < 5) points), 2 - remission (BVAS 0-1 points). The VDI damage index in 5 patients was 0, in 30 – from 1 to 3, in 10 – > 3 points. Glucocorticoids (GC) received 44: 78% of patients at a dose of 5-20 mg /day, 16% - >20-40 mg / day, 4% - >40-60 mg /day. AC 23 (51%) of 45 patients took AC. Blood clotting parameters were measured in 40 patients, including activated partial thromboplastin time (APTT), thrombin time (TT), soluble fibrin monomer complexes (SFMC), the number of platelets, 22 of them received AC.

Results: Thrombosis in the past history was registered in 8 (18%) patients, 7 of them continued taking AC. 16 patients received AC without thrombosis for prevention ones. Patients with GPA received AK more often than patients with MPA and EGPA (73%, 40%, 40%, respectively).

AC were prescribed in 51% of patients. AC were prescribed to 51% of patients receiving GC at a dose of up to 20 mg/day and 44% of patients with a dose of GC above 20 mg/day. The appointment of anticoagulants was associated with the duration of the disease. With a disease duration of up to 1 year, AK was prescribed in 33% of cases, with a duration of > 10 years - in 67% of cases. 59% of patients received AC with BVAS>5, 38% of patients - with BVAS<5. The following AC were prescribed to patients: direct oral AC (DOAC) in 16 (69.6%), unfractionated heparin (UH) - 1, low molecular weight heparins (LMWH) -6. LMWH (46%) and DOAC (54%) were prescribed with the same frequency to patients with BVAS>5, while DOAC (87.5%) prevailed in patients with BVAS<5. Hemorrhagic complications during the follow-up period were not registered in any case. Prolongation of APTT, TT was not significantly noted against the background of AC. I. There was a shortening of APTT in 14 (35%) of 40 patients, TT - in 1 (2.5%). An increase in the level of fibrinogen was recorded in 11 (27.5%) patients and in all 40 patients there was an increase in SFMC, which was an indicator of thrombotic readiness. Increased fibrinogen levels were associated with AAV activity (3 out of 11 had a history of thrombosis).

Conclusion: 1. Our retrospective analysis revealed that 51% of 45 patients with AAV received AC, they were more often prescribed with active AAV and more often with GPA. Our retrospective analysis showed that 51% of 45 patients with AAV received AC, more often with active AAV and more often with GPA.

2. DOAC was prescribed more often (in 70% of cases) compared to others.

3. The appointment of AC was associated with the duration of the disease.

4. The dose of GC did not affect the decision to prescribe AC.

5. Hemorrhagic complications during AC therapy were not observed in any case.

Disclosure of Interests: None declared

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AB0621 CHARACTERISTICS OF ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS WITH SEVERE PERIPHERAL NEUROPATHY.

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Background: Peripheral neuropathy is one of major manifestations of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and has a significant impingement on patients' quality of life.[1,2]

Objectives: The aim of this study was to clarify clinical features of AAV patients with peripheral neuropathy and identify risk factors for severe motor neuropathy.

Methods: All consecutive patients with active, treatment-naïve AAV who were admitted to our hospital between April, 2012 and October, 2021 were reviewed. Patients were divided into two groups according to the presence or absence of peripheral neuropathy, and their baseline clinical characteristics were compared.

Results: A total of 76 patients (microscopic polyangiitis, MPA, n=37, granulomatosis with poly angiitis, GPA, n=24, eosinophilic GPA, EGPA, n=15) were included in the study. Among them, 28 patients (36.8%) had peripheral neuropathy including 12 with MPA, 4 with GPA, and 12 with EGPA. The clinical characteristics of all patients with peripheral neuropathy were younger age (66.0 years versus 74.5 years, $p<0.05$) and showed higher white blood cell counts (11500/μL versus 8800/μL, $p<0.05$), higher blood eosinophil counts (788.5/μL versus 139.0/μL, $p<0.05$), higher creatinine clearance (77.3 mL/min versus 56.3 mL/min, $p<0.05$), higher levels of serum immunoglobulin (Ig)E (660 IU/mL versus 125 IU/mL, $p<0.05$), and IgG4 (361.5 mg/dL versus 84.0 mg/dL, p <0.05). In patients with EGPA, the most susceptible type to peripheral neuropathy, 80% of the patients had peripheral neuropathy. Comparison between patients with EGPA with peripheral neuropathy and those without demonstrated significantly younger age (56.0 years versus 80.0 years, $p<0.05$) and higher blood eosinophil counts (7832/μL versus 2340/μL, $p<0.05$) were characteristic for the presence of peripheral neuropathy. Patients with EGPA with motor neuropathy (n=8) showed higher white blood cell counts (26850//μL versus 8650//μL, p <0.05) and higher blood eosinophil counts (13134//μL versus 3436//μL, $p<0.05$) compared with those with only sensory neuropathy (n=4).

Conclusion: Our current study has shown that patients with EGPA are more prone to peripheral neuropathy than patients with MPA or GPA. Severe motor neuropathy was observed only in patients with EGPA and associated with more intense eosinophilic inflammation. Our results suggest that molecular targeted therapy that improves eosinophilic inflammation such as anti-IL-5 therapy is beneficial for peripheral neuropathy.

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AB0622 THE JOINT VASCULITIS REGISTRY IN GERMAN-SPEAKING COUNTRIES (GEVAS) – SUBGROUP ANALYSIS OF 113 GPA-PATIENTS

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Background: Granulomatosis with polyangiitis (GPA) is the second most frequent vasculitis in Germany with an annual incidence of 34 per million and a prevalence of 210 per million [1]. GPA is characterized by its chronic course, frequent relapses, significant overall morbidity and mortality, and substantial socio-economic impact. Multiorgan involvement affecting the respiratory tract, kidney, and other organs is common. Limited variants also occur [2]. So far, prospective long-term observational data on the disease course of GPA are missing in Germany. Therefore, the Joint Vasculitis Registry in German-speaking countries (GeVas) has been established to follow the course of patients recently diagnosed with vasculitis or a change of their treatment due to a relapse (inception cohort). The GeVas registry allows long-term follow-up of a substantial cohort of vasculitis patients in a multicenter setting.

Objectives: To present the first data on the follow-up of newly diagnosed and relapsing GPA enrolled in the GeVas registry.

Methods: GeVas is a prospective, web-based, multicenter, clinician-driven registry for the documentation of organ manifestations, damage, long-term outcomes, and therapy regimens in various types of vasculitis. Recruitment started in June 2019. By January 2022, 17 centers in Germany were initiated and started enrolling patients. Meanwhile, more than 350 patients have been documented in the registry. Sites in Austria and the German-speaking cantons of Switzerland will be integrated soon [3].

Results: By mid-October 2021, the participating centers included 113 patients with GPA. The majority of patients were PR3-ANCA positive and affected by general symptoms, ENT, lung, renal, and neurological involvement. Patients commonly received cyclophosphamide or rituximab in combination with glucocorticoids for the induction of remission. Fewer patients received methotrexate or other immunosuppressants. Patient characteristics and therapy are summarized in Table 1.

Table 1. Patient characteristics (n = 113). *Unless otherwise specified.

Category	Feature	n (%)*
Age	Age (years); median [range]	60 [51 - 70]
Gender	Male	61 (54.0)
	Female	52 (46.0)
Reason for inclusion in the registry	Newly diagnosed vasculitis	57 (51.4)
	Relapse	56 (49.6)
ANCA status	PR3-ANCA	99 (87.6)
	MPO-ANCA	4 (3.6)
	ANCA negative	9 (7.9)
Organ manifestation	General symptoms	86 (76.1)
	ENT	69 (61.1)
	Lung/chest	66 (58.4)
	Renal	35 (31.0)
	Cardiovascular	7 (6.2)
	GI	3 (2.7)
	Neurological	27 (23.9)
Therapy	Glucocorticoid	102 (90.3)
	Rituximab	56 (49.6)
	Cyclophosphamide	37 (32.7)
	Methotrexate and other immunosuppressants, respectively	26 (23.0) and 19 (16.8), respectively

Conclusion: Here, we present the first interim analysis of the GeVas registry. Clinical manifestations of GPA reported herein show less frequent renal involvement in comparison with a recent report from another European registry (POLVAS) and an UK study [4, 5]. This is potentially related to the predominance of recruiting rheumatology centers thus far. By contrast, respiratory tract involvement is more frequent and PR3-ANCA less common in Japan [5]. Further data are prospectively documented and a follow up analysis is in progress.

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AB0623 A REVIEW OF THE EVIDENCE BEHIND THE RECOMMENDATION OF RITUXIMAB FOR ANCA ASSOCIATED VASCULITIS

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Background: Cyclophosphamide (CYC) is currently used to induce remission in patients with ANCA-associated vasculitis (AAV). Once remission induction is successful Azathioprine (AZA) is given as maintenance (1). Concerns surround

the use of cyclophosphamide which has an undesirable safety profile, limiting its use in patients. AZA has shown to be effective at maintenance, however rates of relapse on AZA are high.

Rituximab (RTX) is a biologic with a high specificity to B cells. Its mechanism of action (B cell apoptosis) may mean that it can be used for both the induction and maintenance of remission, with a superior long-term safety profile.

Objectives: To conduct a systematic review of literature to determine the efficacy of rituximab as a remission inducing and maintaining agent.

Methods: A systematic review of literature was conducted by searching PubMed and Cochrane library with the search phrase "rituximab AND ANCA-associated vasculitis". The following criteria was then applied: randomised controlled trial (RCT) in the English language. Only original papers were accepted if it pertained to RTX for either induction or maintenance of remission.

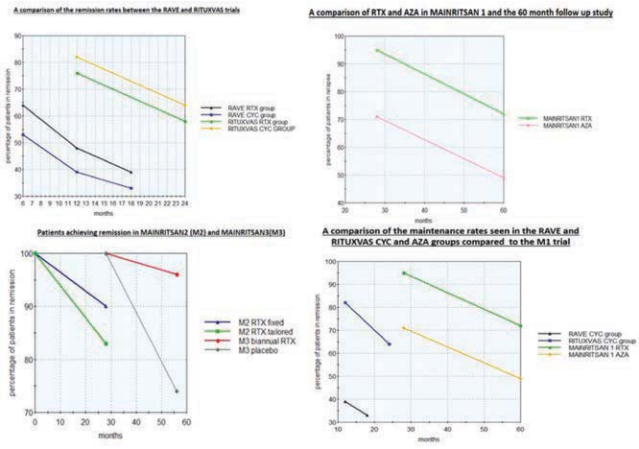
Results: 1008 papers were initially identified and after the search strategy was applied 9 RCTs were analysed.

The RAVE trial compared RTX to CYC in 197 patients with AAV in a double-blind double-dummy trial. The result of the RAVE trial indicated that RTX was as effective as CYC at maintaining remission. The RITUXVAS trial, which was partially blinded and had a sample of 44 patients also came to the same conclusion. Both the RAVE and RITUXVAS trials also showed that an initial dose of RTX was as effective as continuous immunosuppression over the trial length.

Further RCTs were published from the RAVE and RITUXVAS studies including a follow up of patients from the RITUXVAS trial at 24 months which showed no increased rates of relapse or adverse events between the groups. The RAVE study also showed that RTX was effective to be used on multiple occasions to induce remission irrespective of the initial remission inducing agent.

The MAINRITSAN1 study was a non-blinded randomised trial which compared RTX with azathioprine for maintenance in 115 patients with AAV. The results of this trial showed that RTX was superior than AZA at maintenance with only 5% on RTX compared with 29% on AZA relapsing. The long-term follow up of patients in the trial, showed that at 60 months, patients who received RTX were less likely to have relapsed.

The MAINRITSAN2 trial indicated that there was no difference between a fixed vs tailored RTX dose, meaning that a lower tailored dose was as effective as a higher fixed dose. The MAINRITSAN 3 paper was a double-blind trial that indicated that biannual RTX for maintenance was superior than placebo at maintaining remission.



Conclusion: RTX is as effective as CYC at inducing remission, with both the RAVE and RITUXVAS trials sharing similar conclusions.

Currently the research indicates that an initial dose of RTX can maintain remission at similar rates as continuous AZA, however its superiority is yet to be determined. The MAINRITSAN 1 trial was unblinded in its protocol with the data indicating it drastically overestimated the efficacy of both RTX and AZA. Therefore, more research is needed to validate the claim that RTX is superior than AZA at maintenance.

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AB0624 PATIENTS WITH VASCULITIS HAVE A HIGH PREVALENCE OF CORONARY MICROVASCULAR DYSFUNCTION

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Background: Vasculitides are a heterogenous group of diseases characterized by intense vessel wall inflammation, endothelial injury, and systemic inflammation. Several vasculitides are associated with high risk of cardiovascular (CV) disease, an important source of morbidity and mortality in this population. This excess CV risk is attributed both to a high burden of traditional risk factors and to inflammation, but this remains poorly studied. Indeed, inflammation is a known risk factor for CV disease and implicated in coronary microvascular dysfunction (CMD) which may precede obstructive coronary artery disease (CAD).

Objectives: We sought to assess whether vasculitis is associated with CMD in the absence of obstructive CAD.

Methods: We retrospectively identified subjects with systemic vasculitis who underwent symptom prompted rest/stress myocardial perfusion PET. Patients with an abnormal myocardial perfusion study (summed stress score ≥3) or LVEF<40% were excluded. Controls were identified from the same population and matched on age, gender and cardiovascular risk factors (CAD, hypertension, dyslipidemia, diabetes mellitus, and obesity). Coronary flow reserve (CFR), was calculated as the ratio of myocardial blood flow (ml/min/g) at peak stress compared to rest. CMD was defined as CFR <2.

Results: We studied 26 vasculitis cases and 66 matched controls. The most common vasculitides were giant cell arteritis (38%), ANCA-associated vasculitis (31%), and Takayasu's arteritis (12%). Median (IQR) time between diagnosis and PET was 6.5 (2.9, 14.2) years. Seven (27%) cases had active vascultis at the time of PET. Cases and controls were well-matched on age, sex, and CV risk factors (Table 1). Despite a similar prevalence of CV risk factors, coronary flow reserve (reflected by CMD) was abnormal in 38% of vasculitis cases compared to 15% of controls (p=0.004). The mean [SD] CFR was 19% lower in vasculitis cases vs controls (2.11 [0.5] versus 2.6 [0.7], p=0.003).

Table 1. The presence of coronary microvasculature dysfunction in patients with systemic vasculitis without obstructive coronary artery disease

Cohort characteristics	Vasculitis (n=26)		Control (n=66)	P-value
Age at PET, years	62 (18)		61 (17)	0.24
Time from Vasculitis Diagnosis to PET, years (median, IQR)	6.5 (2.9, 14.2)		n/a	
Female, n (%)	18 (72%)		43 (65%)	0.99
Vasculitis Characteristics				
Large Vessel (e.g., giant cell arteritis, Takayasu's), n(%)	13 (50%)		n/a	n/a
Medium Vessel (e.g., polyarteritis nodosa, Kawasaki's arteritis), n(%)	2 (8%)		n/a	n/a
Small Vessel (e.g., ANCA-associated vasculitis, Henoch-Schonlein Purpura), n(%)	11 (42%)		n/a	n/a
Cardiovascular Risk Factors	At Diagnosis	At PET	At PET	
Hypertension, n (%)	12 (46%)	20 (71%)	47 (80%)	0.47
Obesity, n (%)	3 (12%)	2 (32%)	2 (32%)	0.84
Diabetes, n (%)	3 (12%)	5 (20%)	13 (20%)	0.99
Dyslipidemia, n (%)	4 (15%)	15 (58%)	40 (61%)	0.99
Known CAD, n (%)	0 (0%)	1 (4%)	1 (2%)	0.48
Imaging Findings				
Rest myocardial blood flow, ml/min/g	1.0 (0.3)		1.0 (0.3)	0.8
Stress myocardial blood flow, ml/min/g	2.1 (0.6)		2.6 (1.0)	0.008
Coronary Flow Reserve, ml/min/g*	2.1 (0.5)		2.6 (0.7)	0.003
Coronary Microvasculature Dysfunction** (CMD), n (%)	10 (38%)		11 (15%)	0.004

Conclusion: Patients with systemic vasculitis, even in the absence of obstructive CAD, have a high prevalence of CMD compared with non-vasculitis patients. These differences were observed despite matching cases and controls on traditional CV risk factors, highlighting the importance of other factors, such as inflammation and vasculitis treatments on CMD and CV disease in this population. CMD is a known independent risk factor for CV mortality. Future prospective studies are needed to understand the relationship between vasculitis, systemic inflammation, and CMD.

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AB0625 ASSOCIATION BETWEEN CYTOMEGALOVIRUS REACTIVATION AND RENAL PROGNOSIS DURING REMISSION INDUCTION THERAPY FOR ANCA-ASSOCIATED VASCULITIS

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Background: Cytomegalovirus (CMV) has been associated with atherosclerosis in patients with chronic renal failure, and may cause secondary nephrotic syndrome. Therefore, we hypothesized that the reactivation of CMV by immunosuppressive therapy in patients with vasculitis may affect renal function.

Objectives: The purpose of this study was to investigate relationships between CMV infection and renal function during ANCA-associated vasculitis remission induction therapy.

Methods: This retrospective cohort study enrolled microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis patients at 25 sites in Japan who had a first or severe relapse between January 2017 and June 2020. Of these, patients with MPA or GPA who had a positive renal lesion score on BVAS (version 3) at baseline, or vasculitis findings on renal biopsy, CMV assayed by 48 weeks of treatment, were included. Patients were divided into two groups based on the presence or absence of a positive CMV antigen test during the remission induction phase (0–48 weeks of treatment). Outcomes were the rate of change in estimated glomerular filtration rate (eGFR) at 48 weeks after initiation of treatment in both groups, as determined by (eGFR at 48 weeks - eGFR at the initiation of treatment)/eGFR at the initiation of treatment; where lower values were associated with worse renal function. General linear models adjusted for age, gender, presence of diabetes or chronic kidney disease, and the use of rituximab or cyclophosphamide were generated.

Results: A total of 387 patients had CMV antigen measured during ANCA-associated vasculitis treatment, of which 164 had renal involvement and eGFR measured at 48 weeks. Seventy-seven (47.0%) were male and the median age was 75 years (range 69–80 years). CMV reactivation was observed in 44 patients (26.8%). The beta coefficient of multiple regression analysis with CMV positive as 1 and negative as 0 was 0.08 (95% confidence interval -0.13 to 0.29) (p = 0.47). The rate of change in eGFR was higher in the CMV positive group, but not statistically significantly.

Conclusion: Contrary to our hypothesis, renal prognoses tended to be better when CMV reactivation was observed. The patients in the CMV reactivation group may have been treated more aggressively, and some patients with a poor prognosis who were not followed up for 48 weeks dropped out. Further research investigating the adjustment of treatment methods is required.

Disclosure of Interests: None declared

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AB0626 PREVALENCE OF FRAILTY IN AN INTERNET-BASED COHORT WITH A SELF-REPORTED DIAGNOSIS OF VASCULITIS – THE VASCSTRONG STUDY

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Background: Frailty is a syndrome characterized by an increased vulnerability to stressors and is associated with disability and early mortality. Frailty may be accelerated in patients with vasculitis. The prevalence of frailty in patients with vasculitis remains unexplored.

Objectives: To describe the prevalence of self-reported frailty in patients with vasculitis.

Methods: VascStrong is a longitudinal study utilizing the Vasculitis Patient-Powered Research Network (VPPRN), an internet-based prospective longitudinal cohort. Data elements collected included type of vasculitis, demographic, and use of medications. Frailty was measured by the FRAIL scale, a self-report measure which queries on 5 domains: 1. Fatigue, 2. Resistance (inability to climb 10 stairs), 3. Ambulation (inability to walk several blocks), 4. Illnesses (≥5/11 comorbidities), and 5. Loss of Weight (≥5% weight loss in the last year). Patients were classified as robust, pre-frail, and frail based on 0, 1-2, or ≥ 3 criteria, respectively.

Results: The survey collected information from October 8, 2021-January 15, 2022. For this preliminary analysis, 228 responses were included. Clinical characteristics and study data are outlined in Table 1. Prevalence of robustness, pre-frailty, and frailty was 28.5%, 47.8%, and 23.7%, respectively. The majority of patients with each form of vasculitis were rated as frail or pre-frail. Among the individual FRAIL domains, fatigue and loss of weight were the most frequent (48.7% and 42.5%, respectively) while illnesses, was the least common (3.5%). When compared to robust patients, frail and pre-frail patients were younger, more frequently female, more likely to be obese and reported more frequent use of glucocorticoids. Patients with urticarial vasculitis and Takayasu's arteritis were more commonly pre-frail or frail, compared to patients with other types of vasculitis.

Table 1. Characteristics for overall cohort and by frailty classification

	Overall N = 228	Robust N = 65	Pre-frail N = 109	Frail N = 54
Age, years, mean (SD)	57.6 (15.3)	62.4 (14.8)	55.1 (15.6)	57.1 (14.3)
Sex, female	163 (71.5%)	40 (61.5%)	84 (77.1%)	39 (72.2%)
Race, white	204 (89.5%)	60 (92.3%)	98 (89.9%)	46 (85.2%)
Ethnicity, non-Hispanic	195 (85.5%)	57 (87.7%)	97 (89.0%)	41 (75.9%)
Disease duration, years, mean (SD)	8.5 (7.9)	8.6 (6.8)	8.4 (8.4)	8.8 (8.0)
Employment status				
Employed	98 (43.0%)	24 (36.9%)	60 (55.0%)	14 (26.0%)
Retired	66 (28.9%)	29 (44.6%)	24 (22.0%)	13 (24.1%)
Disabled (unable to work)	34 (14.9%)	4 (6.2%)	12 (11.0%)	18 (33.3%)
Other/missing	30 (13.2%)	8 (12.3%)	13 (12.0%)	9 (16.7%)
Diagnosis				
Granulomatosis with polyangiitis	89 (100.0%)	29 (32.6%)	42 (47.2%)	18 (20.2%)
Eosinophilic granulomatosis with polyangiitis	26 (100.0%)	9 (34.6%)	11 (42.3%)	6 (23.1%)
Microscopic polyangiitis	23 (100.0%)	7 (30.4%)	12 (52.2%)	4 (17.4%)
Giant cell arteritis	17 (100.0%)	5 (29.4%)	8 (47.1%)	4 (23.5%)
Urticarial vasculitis	14 (100.0%)	2 (14.3%)	5 (35.7%)	7 (50.0%)
Takayasu's arteritis	10 (100.0%)	0 (0%)	7 (70.0%)	3 (30.0%)
Other*	49 (100.0%)	8 (26.5%)	16 (49.0%)	8 (24.5%)
Body Mass Index[a]				
Underweight	6 (2.6%)	2 (3.1%)	4 (3.7%)	0 (0%)
Normal	86 (37.7%)	35 (53.8%)	40 (36.7%)	11 (20.4%)
Overweight	63 (27.6%)	19 (29.2%)	29 (26.6%)	15 (27.8%)
Obese	73 (32.0%)	9 (13.8%)	36 (33.0%)	28 (51.9%)
Currently on glucocorticoids	104 (45.6%)	19 (29.2%)	52 (47.7%)	33 (61.1%)
Current glucocorticoid dose, prednisone equivalent (mg/d), mean (SD)	13.1 (18.0)	12.6 (17.1)	11.3 (18.6)	16.4 (17.4)

Data presented as n (%), unless specified otherwise *Other diagnosis: Behçet's disease, primary angiitis central nervous system, cryoglobulinemic vasculitis, IgA vasculitis, polyarteritis nodosa, and other/suspected diagnosis [a]Based on World Health Organization Body Mass Index categories

Conclusion: Self-reported frailty or pre-frailty is prevalent in the majority of patients with multiple forms of vasculitis. Future analysis will focus on identifying factors associated with frailty in patients with vasculitis, to allow earlier identification and prevention in this population at high-risk for frailty.

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AB0627

EVALUATION OF INTERNAL CONSISTENCY, FEASIBILITY, AND RELIABILITY OF THE ITALIAN VERSION OF ANCA-ASSOCIATED VASCULITIS PATIENT-REPORTED OUTCOME (AAV-PRO_ITA) QUESTIONNAIRE: PRELIMINARY RESULTS FROM A MULTICENTER STUDY ON A LARGE COHORT OF ITALIAN PATIENTS

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Background: The ANCA-associated vasculitis patient-reported outcome (AAV-PRO) questionnaire is a 29-item disease-specific PRO measure for AAV[1]. The Italian version of the AAV-PRO questionnaire (AAV-PRO_ita) was translated in collaboration with Oxford and Bristol University (UK) and was preliminarily tested on a single-center Italian cohort[2].

Objectives: The main objective of this multicentric study was to assess the internal consistency, feasibility, and reliability of the AAV-PRO_ita in a large cohort of Italian AAV patients. The secondary objective was to investigate the clinical characteristics of AAV patients associated with AAV-PRO_ita domains.

Methods: The AAV-PRO_ita is describes the following disease domains: (1) organ-specific and systemic symptoms and signs (SSS); (2) physical function (PF); (3) social and emotional impact (SEI). In this study, Italian-speaking AAV patients were recruited from Italian Centres (N=13) with a large experience in the diagnosis and treatment of systemic vasculitis, belonging to the Vasculitis Study Group of the Italian Society of Rheumatology. Inclusion criteria were: a confirmed diagnosis of GPA, MPA, or EGPA; ANCA positivity in at least once occasion or biopsy-proven AAV; and age ≥18 years old. Participants completed the AAV-PRO_ita at three different time-points: baseline, after 5-7 days, and at month 3.

Results: 229 AAV-patients (56.3% women) with a median age of 61 (IQR 51-72) were recruited and completed the questionnaires. The subtype of AAV was mainly GPA (131, 57.2%), followed by EGPA (58, 25.3%), and MPA (40, 17.5%). Median BVASv3 at baseline was 0 (IQR 0-3), whereas the median BVASv3 at the onset of disease was 14 (IQR 9-20). Participants had a median duration of disease of 67 (IQR 24-126) months. Patients who experienced at least one relapse, one hospitalization, and one severe infection were 40.2%, 53.3%, and 24%, respectively. 83% of the patients were on immunosuppressant therapy and 71.6% were still receiving glucocorticoids (GC).

AAV-PRO_ita questionnaire had good internal consistency (Cronbach's Alpha range 0.81-0.93) and good test-retest reliability (ICCs range 0.93-0.96). Item response rates were high overall (maximum 0.87% missing data), supporting the feasibility of the questionnaire.

Concerning the domains of the questionnaire, female AAV patients scored higher (i.e. worse) in all three domains, especially in the SEI domain (p-value<0.001). Older participants (≥65 years) scored higher in the PF domain (p-value<0.05) in all three times of self-completions of the questionnaire. The ongoing treatment also influenced the results. In fact, patients on GC showed higher scores in the PF domain (p-value=0.003) and SEI domain (p-value=0.021). The VDI value seemed to be related to AAV-PRO_ita scores more than disease duration or disease activity, especially in the SSS domain (ρ>0.3, p-value<0.001). Conversely, subtype of AAV did not influence the item scores.

Conclusion: The AAV-PRO_ita questionnaire is a new 29-item, disease-specific PRO measure for use in AAV in the Italian language. It is a self-administered Italian questionnaire with good internal consistency, feasibility, and reliability. AAV-PRO_ita proved to be a useful tool to explore the AAV patient's perception of quality of life, and it could become an important way of measuring the unmet needs of AAV patients.

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AB0628

SYSTEMATIC LITERATURE REVIEW INFORMING THE 2022 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF ANCA-ASSOCIATED VASCULITIS: FOCUS ON DIAGNOSTIC AND FOLLOW-UP PROCEDURES

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Background: The 2008 and 2016 European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of ANCA-associated vasculitis (AAV)[1,2] have supported clinicians with recommendations for the accurate diagnosis, monitoring and for the management of the long-term complications of patients with ANCA-associated vasculitis (AAV). Since the publication of the last EULAR guidelines, several high-impact research articles have provided further evidence to improve diagnosis and monitoring of AAV-patients.
Objectives: The aim of this systematic review was collecting evidence supporting the 2022 update of the AAV management recommendations.
Methods: The recommendations were developed based on the 2014 EULAR standardized operating procedures (SOP)[3]. Areas of interest were adopted from the 2016 recommendations and updated by identifying additional items through a Delphi exercise. Key questions were framed in the PICO (Population, Intervention, Comparator, Outcome) format. Keywords identifying topics of interest for the diagnosis and follow up were gathered based on the PICO questions and then incorporated into a search string. A systematic literature research (SLR) was performed according to the EULAR SOP. PubMed (Medline), Embase and the Cochrane Library databases were searched for articles providing data on the search questions. Abstracts of the annual meetings of EULAR, ACR, ERA-EDTA, ASN and the Vasculitis and ANCA Workshops were also screened, but restricted to randomized controlled clinical trials (RCTs).
After deduplication, publications were first sorted by title and abstract and then full text review was done for eligible articles. The data were extracted from included articles and grouped according to the PICO questions. Data extraction results were collected in evidence tables.
The Cochrane revised tool for assessing risk of bias for RCTs (RoB2), ROBINS-1 for observational studies, QUADAS II for diagnostic accuracy studies and AMSTAR II for meta-analyses were used for bias assessment. Evidence was categorized based on the GRADE system as per EULAR SOP[3].
Results: Based on the results of the Delphi, 3 topics related to diagnosis and follow-up were identified that were transformed into PICO questions: the impact of tissue biopsies and positive ANCA testing to support the clinical diagnosis of AAV and the impact of clinical parameters and biomarkers on disease-related outcomes and treatment-related adverse events (Table 1). Other items that received lower scores in the Delphi exercise were added in the format of subquestions (e.g. diagnostic imaging). Based on these research questions, search strings for the SLR were created.
The SLR was still ongoing at the time this abstract has been written and results of the SLR will be presented at the meeting.

Table 1. Topics of interest for diagnostic and follow-up testing identified in the Delphi exercise

Patients	Diagnostic / follow-up procedure	Outcome
Granulomatosis with Polyangiitis	Tissue biopsy	Confirmation of diagnosis of ANCA-associated vasculitis
Microscopic Polyangiitis Eosinophilic Granulomatosis with Polyangiitis	ANCA testing Clinical parameters Imaging Biomarkers	Disease-related outcomes Treatment-related adverse events

Conclusion: This SLR identified recent developments affecting key areas of AAV diagnosis and follow-up. The results of this SLR provide systematic evidence to inform the 2022 update of the EULAR recommendations for the management of AAV, which will also be presented at this meeting.
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AB0629

GLOMERULONEPHRITIS ASSOCIATED WITH ANCA AFTER COVID-19 VACCINE: A SYSTEMATIC REVIEW

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Background: The COVID-19 pandemic has led to widespread vaccination with effective results and a great safety profile. However, as the vaccination rate has increased, more cases of autoimmune diseases after the COVID-19 vaccine have been described. We present a systematic review of ANCA-associated glomerulonephritis after the COVID-19 vaccine.
Objectives: To summarize the existing evidence on ANCA-associated glomerulonephritis after the COVID-19 vaccine.
Methods: We searched all studies from inception till January 27, 2022, that described ANCA-associated biopsy-proven glomerulonephritis after COVID-19 vaccine through Embase and Medline. Methodological quality was evaluated with the 4 domains tool. We included 13 patients from 2 case series and 9 case reports. We extracted demographics, history, lab results, outcomes. We then applied descriptive statistics.
Results: 46% of the patients were males and 54% were females. The median age was 74 years. 54% developed symptoms after the second dose of the 2-dose vaccine. The median interval between the vaccine and the symptom onset was 10.5 days. 85% had anti-MPO antibodies, and the rest – anti-PR3 antibodies. 31% of patients had persistent creatinine (Cr) elevation on follow-up, and 3 patients were requiring hemodialysis. Of those 3 patients, 1 patient had normal renal function prior to presentation, and the rest had chronic kidney disease. The summary of the cases is presented in Table 1.

Table 1.

Gender, age	De novo (1) or relapse (2)	AZD1222 (1), or mRNA-1273 (2), or BNT162b2 (3)	Outcome
M, 75[1]	2	1	Hemodialysis
M, 74[1]	2	1	Improved Cr
F, 82[2]	1	2	Improved Cr
F, 70[3]	1	2	Improved Cr
F, 78[4]	1	3	Improved Cr
F, 79[5]	1	3	Remission
F, 54[6]	1	3	Improved Cr
F, 78[6]	2	3	Hemodialysis
M, 58[7]	1	2	Remission
M, 63[8]	1	1	Improved Cr
F, 29[9]	1	3	Remission
M, 52[10]	1	2	Hemodialysis
M, 84[11]	1	3	Worsened Cr

Conclusion: Although the causality cannot be established on current evidence, the COVID-19 vaccine can probably trigger glomerulonephritis associated with ANCA, primarily anti-MPO type. We need a bigger cohort to identify patients predisposed for disease development or relapse after the COVID-19 vaccine.
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AB0630 ASSESSMENT OF ORGAN DAMAGE ACCRUAL IN BEHÇET'S SYNDROME OVER 2-YEAR FOLLOW-UP: RESULTS FROM THE BODI PROJECT LONGITUDINAL EXTENSION.

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Background: Preventing accrual of organ damage is a major goal in the treatment of Behçet's Syndrome (BS). The BS Overall Damage Index (BODI) is the first damage assessment tool developed and preliminarily validated for BS.
Objectives: To assess the prevalence, extent, and determinants of organ damage accrual in the BODI validation cohort over 24 months of follow-up.
Methods: Overall, 189 patients from the multicenter BODI cohort underwent a 24 ±3 months follow-up (FU) visit. Demographics, ongoing medication, Behçet's Disease Current Activity Form (BDCAF) score, Physician (PGA) and Patient Global Assessment (PtGA) of disease activity, disease relapsing (defined by any treatment change due to increased disease activity), and the BODI score were recorded. Damage accrual was defined as any increase ≥1 in the BODI score between baseline and follow-up visit (Δ-BODI). Logistic regression models were built to identify factors associated with BODI damage accrual.
Results: The mean age (standard deviation) at enrolment and the disease duration was 46.2 (12.1) and 10.8 (8.3) years, respectively, and 92/189 (48.7%) patients were males. During 24 months, 36 (19.0%) patients had an increase in the BODI score of at least 1 point (mean increase of 1.7 points). The BODI score increased from 1.6 (2.1) to 1.9 (2.1), with a mean Δ-BODI of 0.3 (0.8). Overall, 61 new BODI items of damage were recorded (Figure 1); 22 (34%) were steroid-related (diabetes, osteoporotic fractures, cataract). Factors independently associated with increased BODI score were longer glucocorticoids exposure (OR 1.01 per month, 95%CI 1.01-1.02, p<0.001), and occurrence of flares (OR 3.1, 95%CI 1.1-8.9, p = 0.035), whereas stable treatment with conventional and/or biologic immunosuppressants was negatively associated with an increase in the BODI score (OR 0.19, 95% 0.07-0.97, p <0.001) (Table 1).

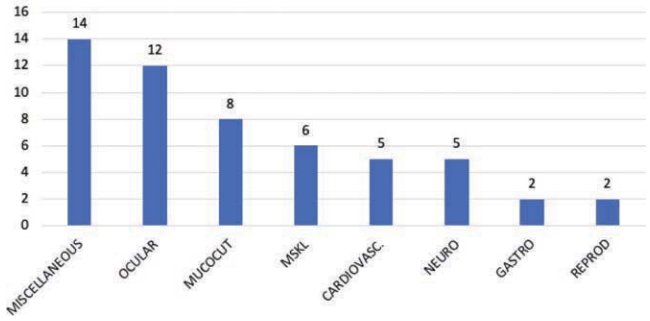
Table 1. Determinants of organ damage accrual over 2 years of follow-up.

	Univariate analysis			Multivariate analysis	
Candidate determinants	**Δ-BODI ≥1 (n 36)**	**Δ-BODI = 0 (n 153)**	**p**	**OR (95%CI)**	**p**
Males	16 (44.4%)	76 (49.7%)	0.572		
Age at enrolment	56.2 (42.9-62.0)	46.6 (35.4-53.1)	**0.001**	--	--
Disease duration	12.9 (7.1-22.0)	11.1 (5.4-21.2)	0.483		
Major organ involv.	22 (61.1%)	72 (47.1%)	0,129		
BDCAF at BL	3 (0-5)	2. (0-5)	0.365		
BDCAF at FU visit	3.0 (3-5)	3 (0-7)	0.188		
GC duration	112 (26.0-147.0)	24.0 (8.0-72.0)	**<0.001**	**1.012 (1.006-1.018**	**<0.001**
cIS or TNFì ever	24 (66.7%)	133 (86.9%)	**0.004**	**0.194 (0.073-0.972)**	**<0.001**
Relapse	9 (25.0%)	20 (13.1%)	**0.070**	**3.093 (1.066-8.972)**	**0.038**
BODI score at BL	1.0 (0-2.0)	1 (0-2)	0.579		

Continuous variables are presented as median (IQR). Dichotomic variable are presented as n (%). BODI, Behçet's Syndrome Overall Damage Index. FU, follow-up. cIS, conventional immunosuppressant. Δ-BODI increase of BODI score from baseline to the FU visit.

Conclusion: Despite the relatively high disease duration in the studied cohort, organ damage accrual was recorded in a relevant proportion of patients. BODI proved to capture the damage associated with major determinants such as inadequate control of disease activity and prolonged exposure to glucocorticoids.

Figure. Distribution of new damage items in different BODI domains



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AB0631 IMPACT OF BEHÇET'S SYNDROME ON WORK ACTIVITY AND PRODUCTIVITY: RESULTS FROM A SUB-ANALYSIS OF THE BODI PROJECT COHORT.

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Background: Behçet's Syndrome (BS) is a multisystem recurring inflammatory disorder characterised by a wide spectrum of clinical manifestations, which can vary from limited mucocutaneous lesions up to severe and even life-threatening events.
Objectives: To evaluate the impact of BS on the patients' work activity and productivity.
Methods: A sub-cohort of 148 patients from the original Behçet's syndrome Overall Damage Index (BODI) Project study was enrolled. The Work Productivity and Activity Impairment: General Health (WPAI:GH) questionnaire was administered. Demographics, disease duration, comorbidity, major organ involvement, ongoing therapy, Behçet's Disease Current Activity Form (BDCAF), Physician Global Assessment (PGA), Patient Global Assessment (PtGA), and the BODI were recorded. Multiple regression models were built to investigate the independent effect of BS features on WPAI.
Results: Overall, 97 (65.6%) out of 148 patients who completed the WPAI:GH questionnaire resulted working for pay; 22 out of 97 (27.8%) patients reported missing work in the past week due to their health, accounting for a mean (SD) of 34.4% (17.8) of their working time (absenteeism). The only factor significantly associated with absenteeism in multivariate analysis was the presence of ocular damage, as assessed by the BODI (β 0.255, p = 0.027).
Although 93 patients reported that they worked in the previous week, mean 27.3% (30.7) of their actual work productivity was impaired due to their health problem (presenteeism), with only 37 (38.5%) patients reporting no such loss. Factors associated with work impairment were female gender (β 0.319, p = 0.001), higher PtGA (β 0.298, p = 0.002), and an increased BODI score in the last 2 years follow-up (β 0.212 for one-point increased BODI score, p = 0.024).
Finally, 99 (66.9%) of the total 148 patients complained of a daily activity impairment, reporting that a mean of 33.3% (30.6) of their regular daily activities had been prevented due to their health problems. Factors significantly associated with patients' daily activity impairment were younger age at enrolment (β 0.187, p = 0.021), higher BDCAF disease activity (β 0.235, p = 0.002) and fibromyalgia (β 0.324, p = 0.033).

Conclusion: BS can lead to missing work time and significantly affect both the patient's work productivity and daily activities. Active disease seems to be one of the major determinants together with a higher burden of damage and the association of some specific comorbidities, such as fibromyalgia.

Table 1. WPAI:GH questionnaire results

Variables	n°	Mean (SD)
All patients	148	
Patients working for pay	97	
Percent work time missed due to health	97	7.9 (21.7)
Percent work time missed due to health (patients with missed time >0) *	22	34.4 (17.8)
Patients who actually worked in the past seven days**	93	
Percent impairment while working due to health	93	27.3 (30.7)
Percent impairment while working due to health (pts with % impairment while working > 0) ***	56	45.4 (27.2)
Percent activity impairment due to health	148	33.3 (30.6)
Percent activity impairment due to health (those with % activity impairment >0)	99	49.8 (23.9)

** Patients working for pay who missed at least on hour of work, 22/97 = 22.7%. ** Patients working for pay, but who worked for > 0 hours in the last week = 93/97 *** Patients with impairment while working > 0 among patients who actually worked in the previous 7 day = 56/93.*

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AB0632 INTRACARDIAC THROMBOSIS AND VASCULAR INVOLVEMENT IN BEHÇET'S DISEASE : TWO SIDES OF THE SAME COIN ?

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Background: Behçet's disease (BD) is a relapsing vasculitis that can affect vessels of all sizes and kinds. Intracardiac thrombosis (ICT) is a serious complication of the disease, which usually presents associated to vascular lesions. However, its mechanism of constitution in BD remains unclear and the link between these manifestations has yet not been fully clarified.
Objectives: Our first objective is to describe the clinical characteristics, imaging features, therapeutic management and outcome of these patients. And secondly, to shed some light on the relation between this rare condition and the vascular involvement of the disease.
Methods: This monocentric study was conducted in the University Hospital Center Ibn Sina of Rabat (Morocco), and retrospectively included 312 Behçet patients admitted to the Internal Medicine department between 2010 and 2021. Twelve patients with ICT related to BD were enrolled.
Results: Patients were mostly male (90%) with a mean age of 30 years. ICT was the presenting symptom of BD in half of the cases. In the other half, it was detected with a mean of 6.4 years after the disease onset. Six patients had a history of deep vein thrombosis (DVT) related to BD, either as a single episode (n=3), recurrent episodes (n=2), or as DVT associated to pulmonary artery occlusion (n=1). The most frequent symptoms were dyspnea (50%), chest pain (50%), dry cough (40%) and hemoptysis (30%). Four patients had signs of right cardiac failure. Peripheral vascular manifestations were noted in five patients. The other Behçet's flares simultaneously observed were mucocutaneous (80%), digestive (10%), ocular (10%) and articular (10%). Inflammatory parameters were raised in all patients with a median ESR of 49 mm/h and CRP of 51 mg/L. On echocardiography, ICT was always located in the right heart, with an extension to the inferior vena cava in half of the cases. Two patients had also the left cavities involved. Multiple thrombi were visualized in three cases. The associated cardiac lesions observed were pericarditis (50%), tricuspid insufficiency (50%), mitral insufficiency (10%), endomyocardial fibrosis (10%) and myocarditis (10%). The right cavities were dilated among five patients. Pulmonary hypertension was found in 60% of the cases. On CT Chest Angiography, 70% of the patients had pulmonary artery thrombosis and 50% of them had pulmonary artery aneurysms. The other vascular lesions detected were Budd Chiari syndrome with mesenteric ischemia (10%), subtotal internal jugular vein obstruction (10%) and cerebral venous sinus thrombosis (10%). All patients were treated with colchicine, glucocorticoids and immunosuppressants. Eleven patients were put under Cyclophosphamide and one under Methotrexate followed by a TNF- alpha inhibitor. Six patients were also on curative anticoagulation. No death or relapse was recorded to our knowledge. Five patients were declared on complete remission, two on partial remission.
Conclusion: ICT is a serious complication that usually occurs in the first years of the BD's onset, among young men with vascular manifestations. We believe that this strong association is highly suggestive that ICT in BD is a direct consequence of the underlying vasculitis.
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AB0633 HEALTH-RELATED QUALITY OF LIFE IN ANCA VASCULITIDES AND RHEUMATOID ARTHRITIS PATIENTS: A CROSS-SECTIONAL COMPARATIVE STUDY

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Background: ANCA associated vasculitides (AAVs) are rare, serious forms of vasculitides. There are limited data regarding the quality of life in patients with AAVs compared to other chronic inflammatory diseases.
Objectives: The purpose of this study was to compare the quality of life between patients with AAV and those with a chronic inflammatory arthritis such as rheumatoid arthritis (RA).
Methods: Multicenter, cross-sectional study of AAV and RA patients followed in three tertiary referral centers. Data from 1007 healthy controls served as historic controls.[1] HRQoL was assessed with the Short Form 36 Health Survey (SF-36) which includes physical and mental component summary scores (PCS and MCS). Disease activity were assessed with the Birmingham Vasculitis Activity Score version 3 (BVAS 3, for AAVs) and the DAS28-ESR (for RA) respectively and organ damage/function with the Vasculitis Damage Index (VDI for AAVs) score and Health Assessment Questionnaire (HAQ for RA) scores, respectively.
Results: 66 patients with AAVs (GPA 62%, MPA 29% and EGPA 9%, females 56%, mean age 63.4 years, generalized disease 74%, mean disease duration 6.2 years, remission 73%) and 71 with RA (females 56%, mean age 63.3 years, remission 72%) were included. Both AAV and RA patients had significantly lower PCS and MCS scores compared to healthy controls ($p < 0.05$) while RA patients had lower PCS and MCS scores compared to AAV patients ($p < 0.05$). According to disease activity status, there was no difference in the SF-36 scores between those with active (BVAS > 1) and inactive (BVAS < 1) AAV, except for the energy-fatigue component (55.0 ± 21.8 vs. 67.2 ± 20.7, p= 0.038) whereas patients with active RA (DAS28-ESR > 3.2) had lower scores for all SF36 components compared to those with low disease activity (DAS28-ESR < 3.2). Additionally, active RA patients had lower both PCS and MCS scores compared to active AAV patients ($p < 0.05$). AAV patients with increased damage scores (VDI > 3) had lower PCS score compared to those with less organ damage (VDI < 3), (33.9 ± 10.1 vs. 49.1 ± 10.2, $p < 0.001$) while RA patients with increased damage/poor functionality (HAQ ≥ 0.75) had lower both PCS and MCS scores compared to those with less damage (HAQ ≤ 0.63), (35.0 ± 7.2 vs. 48.4 ± 8.6, $p < 0.001$) and (40.5 ± 8.6 vs. 48.2 ± 7.6, $p < 0.001$ respectively). Compared to patients with AAV, RA patients with increased damage had lower score for the pain component compared to AAV patients (37.7 ± 28.6 vs. 61.2 ± 29.5, p= 0.024).
Conclusion: In general, patients with AAV and RA, demonstrate impaired quality of life compared to healthy controls. In the AAV group, quality of life correlated more with organ damage and less with disease activity whereas in RA patients, quality of life correlated both with disease activity and damage. These data emphasize the need for more efficacious therapies for AAV patients that could prevent chronic organ damage and improve quality of life.
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AB0634 VARIABILITY IN PHENOTYPE CLUSTERS IN BEHÇET'S SYNDROME: A SYSTEMATIC REVIEW

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Background: The presence of distinct clinical phenotypes with clustering of certain organ manifestations is well-recognized Behçet's syndrome (BS). Differences in demographic features, treatment response, and possibly inflammatory pathways involved in the pathogenesis of different phenotypes have been proposed. However, studies from different BS cohorts have shown variability in the phenotypes that were defined.
Objectives: We aimed to explore the causes of variability in clinical phenotype clustering across different countries and cohorts.
Methods: An electronic search was carried out in PubMed to find articles published in or before November 2021, using the keywords of Behcet, cluster and factor analysis. Two reviewers independently performed a screening of titles, abstracts, and full-texts .
Results: Amongst 496 articles searched, 30 full-texts were assessed, and 10 studies were relevant for data extraction. Ten articles studied 12 different cohorts, 3 from China, 3 from Turkey, 2 from Japan, 1 from South Korea, 1 from Israel, 1 from Greece, and 1 from Italy. 9 out of 10 studies demonstrated clustering of organ manifestations (11 cohorts). There were important differences between the clusters that were identified in these studies (Table 1). Clusters including skin and mucosa manifestations were present in all cohorts, but the skin and mucosa manifestations that clustered together differed from cohort to cohort. Uveitis stood by itself in some studies, whereas it clustered with vascular and central nervous system (CNS) involvement in some cohorts, and certain skin and mucosa lesions in another. Papulopustular lesions (PPL) and arthritis showed a positive correlation in 4 cohorts whereas these manifestations were negatively correlated in 1 cohort. Moreover, no clusters were identified in 1 study. Potential causes of differences in clusters that we have identified in these studies were: study design (database vs multicenter vs single-centre cohort), statistical analysis method (hierarchical cluster vs factor analysis) patient population (pediatric vs adult vs late onset), setting (dermatology vs rheumatology), diagnostic criteria (ISG vs ICBD), disease duration, definition of organ involvement (such as PPL vs folliculitis, or CNS involvement vs dural sinus thrombosis, ascertainment of manifestations (confirmed gastrointestinal involvement vs any diarrhea, lack of ascertainment in diagnosis of nodular lesions as erythema nodosum vs superficial thrombophlebitis), time interval (manifestations throughout the disease course vs manifestations that were active during the last 3 months), and change in the natural history of BS over decades.
Conclusion: Differences in phenotype clusters may result from differences in study characteristics rather than real geographic or ethnic differences. A large multi-national study with uniform inclusion criteria is needed to better understand phenotype clusters and their implication towards management strategies in BS.
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AB0635 CENTRAL NERVOUS SYSTEM INVOLVEMENT AND MIMICKERS IN ANCA ASSOCIATED VASCULITIS

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Background: Central nervous system (CNS) involvement is rare in ANCA associated vasculitis (AAV). Besides, complications of immunosuppressive (IS) therapy or other conditions that mimic CNS involvement may occur in some AAV patients.
Objectives: We aimed to assess the clinical, laboratory and imaging features of our AAV patients with CNS involvement and conditions other than CNS involvement that caused neurologic signs and symptoms.
Methods: We reviewed the charts of our AAV patients with neurologic sign or symptoms and extracted data on their demographics, types of AAV, neurologic symptoms/signs, final diagnoses after neurologic work-up, and their outcome.
Results: Nineteen AAV patients (13 men, mean age: 46.6±16.6 SD years) with neurologic signs or symptoms were identified. Fifteen patients had GPA, 3 had MPA, and 1 had EGPA. Neurologic symptoms were present at disease onset in 9 patients while they developed within a mean follow up of 36.7 ± 40.1 SD months after AAV diagnosis in the remaining 10. At the time of the occurrence of neurologic symptoms, all patients had active disease (median (IQR) BVAS: 13.8 (9.5-18.5)). Eight patients (42%) also had accompanying peripheral nervous system involvement.
Final diagnosis was CNS involvement of AAV in 5 (26%) patients. These were ischemic cerebrovascular accident (CVA) in 2 patients, hemorrhagic CVA in 1 patient, and cranial neuropathy (peripheral facial nerve palsy) in 2 patients. Cranial MRI revealed T2 FLAIR hyperintensities in 2 patients with ischemic CVA. One also had border zone ischemic changes and the other had areas compatible with terminal branch ischemia. Corticosubcortical hematoma in the left parietal lobe and microhemorrhages in the right frontal lobe were observed in a patient with hemorrhagic CVA. Among the 2 patients with facial nerve palsy, cranial MRI was normal in one while the other had nonspecific increased T2 signals in the cerebral cortex. Cranial neuropathy resolved with high dose glucocorticoid (GC) treatment without sequel in 1 patient and regressed with high dose GC and cyclophosphamide (CYC) in the other. One patient with ischemic CVA was lost to follow-up, and the other recovered with high dose GC and CYC treatment without sequela. The patient with hemorrhagic CVA had died.
Neurologic symptoms were diagnosed to be due to other AAV manifestations in 6 (32%) patients. These were sinonasal involvement in 3 patients with sensorineural hearing loss (n=2), and blurred vision (n=1); orbital involvement in 2 patients with headache (n=2) and ocular involvement (scleritis) in 1 patient with blurred vision. Neurologic symptoms of these 6 patients recovered with immunosuppressive therapy including high dose GC (n=6), mycophenolate mofetil (n=2), methotrexate (n=2), rituximab (RTX) (n=1), and both CYC and plasmapheresis (n=1). Three patients (16%) had secondary complications affecting the CNS. One patient with seizures had posterior reversible encephalopathy syndrome (PRES)

Table 1. Clinical phenotype clustering across cohorts

Author, year	n	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6
Zou,2021	69	MC (G, EN, PPL)	U, V, NBS	GI			
Zou ,2021	860	MC (G, EN, PPL)	U	GI	J	CVS, NBS	
Zou ,2021	152	MC (G, EN, PPL)	U, V, NBS	GI	J		
Soejima, 2021	657	MC(O, G and Skin) w/o J	U	Negative correlation of GI &U	MC (O, G and Skin inv.), J	NBS	
Soejima, 2021	6754	MC (O, G and Skin) w/ o J	U, O, G and Skin inv.	Negative correlation of GI &U	MC (O, G and Skin), J	NBS	U, O, Skin
Krause 1999	68	MC(G, PPL)	Negative correlation of STM and EN	GI, PPL	J	DVT, NBS	
Chung 2021	338	EN dominant	Mixt EN and PPL	PPL dominant			
Karaca 2012	186	MC(G, EN)	U	STM, DVT	J, PPL, O		
Karaca 2012	221	MC(O, G, EN)	U	STM, DVT	J, PPL		
Tunc, 2002	272	MC (O, G, EN)	U	STM DVT	J, PPL		
Sota, 2020	396	MC (O, G, EN, PF)	U		Negative correlation of J and PPL		
Arida, 2009	142	No cluster was found					

CVS: Cardiovascular, DVT: deep vein thrombosis; EN: erythema nodosum; G: genital ulcers; GI: gastrointestinal J: joint; MC: mucocutaneous; NBS: Neuro-Behçet syndrome, O: oral ulcers; PF: pseudofolliculitis; PPL: papulopustular lesions; STM: superficial thrombophlebitis; U: uveitis; V: vascular

and recovered with CYC and anti-epileptic drugs. The second patient with blurred vision and headache had cerebral venous sinus thrombosis (CVST) and recovered with anticoagulant therapy. The third patient with muscle weakness died due to spondylodiscitis complicated with aortic pseudoaneurysm.
In 5 patients (26%), neurologic work-up did not lead to an underlying condition. The presenting symptoms of these patients were transient acute vision loss in 2, numbness of extremities in 1, syncope in 1 and vertigo in 1 patient. Neurologic symptoms resolved after high dose GC and RTX in the patient with vertigo. At the onset of neurologic symptoms, 3 patients were using IS therapy including azathioprine, MMF and CYC in 1 patient each. The fourth patient was off treatment. Neurologic symptoms were transient in these patients, and did not recur during our follow-up of 36, 52, 57, and 120 months.
Conclusion: CNS involvement appears to be rare in AAV and non-CNS entities including ocular, orbital and sinonasal involvement and complications such as PRES, CVST and infections may mimic CNS involvement in patients with AAV.
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AB0636 RELATIONSHIP BETWEEN ORGAN DAMAGE AND IMPAIRMENT OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH BEHÇET'S SYNDROME: RESULTS FROM A LONGITUDINAL EXTENSION OF THE BODI PROJECT.

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Background: Preventing accrual of organ damage represents a primary goal in the treatment of Behçet's Syndrome (BS), as it may result in impairment of other outcomes, including the health-related quality of life (HR-QoL).
Objectives: The objective of this study was to investigate whether the recent accrual of organ damage, rather than its extent at a single time point, correlate with an impairment of the HR-QoL.
Methods: A sub-analysis of data from patients recruited in the longitudinal phase of the BODI Project validation cohort was performed. The HR-QoL and damage were measured by the Short-form 36 questionnaire (SF-36) and the BS Overall Damage Index (BODI), respectively, at the baseline visit and at a follow-up (FU) 24 ±3 months later. Then the possible increase of damage over FU was assessed by calculating the difference between the BODI score (Δ-BODI) in the two visits. Then, the relationship between the Δ-BODI and the individual and summary domains of the SF-36 was analysed by building multivariate regression models, including age, gender, concomitant fibromyalgia and/or depression, current disease activity as assessed by the BDCAF, as confounding variables.
Results: From the BODI validation cohort, 147 patients were recruitable for this sub-analysis;73 (49.8%) were males. The mean (SD) age and disease duration at enrolment were, respectively, 46.2 (12.4) and 13.4 (10.1) years. BODI score did not influence the SF-36 domains assessed at the baseline visit. In contrast, a significant correlation was recorded between the Δ-BODI and the following SF-36 domains: physical function (PF) (β -0.158 for 1 unit increase in BODI score, p 0.025), role physical (RP) (β -0.150, p 0.044), general health (GH) (β -0.199, p 0.004), role emotional (RE) (β -0.180, p 0.001), mental health (MH) (β -0.244, p 0.001), and the mental components summary (MCS) (-0.203, p 0.008) (Figure 1). Gender, age, fibromyalgia and disease activity were also confirmed to significantly influence HR-QoL (Table 1).

Table 1. Multiple regression for the assessment of the relationship between Δ-BODI and SF-36 domains

	Δ-BODI	Male	Age	FBM	DPR	BDCAF
Physical function (PF)	-0.158 **(p 0.025)**	0.180 (p 0.010)	-0.299 (p<0.001)	-0.358 (p<0.001)	-- (p 0.552)	-0.141 (p 0.044)
Role-physical (RP)	-0.150 **(p 0.044)**	0.154 (p 0.039)	-0.212 (p 0.001)	-0.278 (p<0.001)	-- (0.086)	-0.251 (p<0.001)
Body-pain (BP)	-- 0.868	0.266 (p<0.001)	-0.286 (p<0.001)	-0.276 (p<0.001)	-- (p 0.799)	-262 (p<0.001)
General health (GH)	-0.199 **(p 0.004)**	0.187 (p 0.010)	-- (0.136)	-0.296 (p<0.001)	-- (0.861)	-0.352 (p<0.001)
Vitality (VT)	-- (p 0.868)	0.238 (p 0.001)	-0.178 (p 0.008)	-0.213 (0.002)	-- (p 0.855)	-0.371 (p<0.001)
Social function (SF)	-- (p 0.239)	0.299 (p 0.004)	-0.166 (p 0.024)	-0.242 (p 0.001)	-- (0.831)	-0.202 (p 0.010)
Role emotional (RE)	-0.180 **(p 0.003)**	0.158 (p 0.047)	-0.157 (p 0.048)	-0.233 (p 0.003)	-- (0.531)	-0.191 (p 0.016)
Mental health (MH)	-0.244 **(p 0.001)**	-- (p 0.142)	-- (p 0.142)	-0.292 (p<0.001)	-- (p 0.073)	-0.254 (p 0.001)
Physical Component Summary (PCS)	-- 0.105	0.229 (p 0.001)	-0.298 (p<0.001)	-0.296 (p<0.001)		-0.254 (p<0.001)
Mental Component Summary (MCS)	-0.203 **(p 0.008)**	-- (p 0.068)	-- (0.246)	-0.255 (p 0.001)	-- (0.122)	-0.302 (p<0.001)

FBM: fibromyalgia; DPR: depression

Conclusion: The recent accrual of organ damage, rather than its extent assessed in a single visit, is associated with impairment of different aspects of heath related quality of life, especially those mental related. Such phenomenon is similar to that observed in other systemic rheumatic disease, may be due to coping mechanisms.

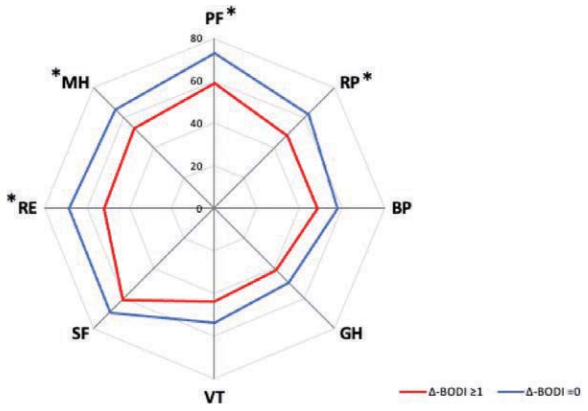

Figure. Impact of increase of damage accrual of 2 years of follow-up on different domains of the SF-36 questionnaire for measurement of the heath related quality of life. PF, physical function. RP, role-physical. BP, body-pain. GH, general health. VT, vitality. SP, social function. RE, role emotional (RE), MH, mental health. * p < 0.005 in univariate analysis using Mann Whitney test.

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AB0637 THE ROLE OF ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) IN ASSESSMENT OF DISEASE ACTIVITY IN SYSTEMIC VASCULITIS

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Background: Despite the proven diagnostic significance, the prognostic role of ANCA, in particular for assessing disease activity, remains questionable. Numerous studies have attempted to estimate the role of ANCA monitoring with different results and a lack of consensus on reported outcomes [1].
Objectives: To analyze the relationship between ANCA level and clinical or laboratory parameters of disease activity.

Methods: This is a retrospective analysis of 38 patients with ANCA-associated vasculitis (granulomatosis with polyangiitis – 25 patients, microscopic polyangiitis – 6 patients and eosinophilic granulomatosis with polyangiitis – 7 patients) from a single center observed from 2015 till the end of 2020. The diagnosis of ANCA-associated vasculitis was performed according to the ACR 1990 criteria or the Chapel Hill Consensus Conference 2012 nomenclature. The study included 20 women (52.6%) and 18 men (47.4%). The average age of patients was 49 (27-62) years, the mean duration of the disease was 26 (6-120) months. The clinical data, initial Birmingham vasculitis activity score (BVAS), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ANCA (ELISA test) against proteinase-3 (PR-3) and myeloperoxidase (MPO) were evaluated. Spearman's correlation analysis was used to investigate the relationship between ANCA levels and ESR, CRP levels, BVAS activity index. The diagnostic value of ANCA in determining the active disease was evaluated by ROC analysis with an estimation of the area under the ROC curve (AUC). The definition of active disease included new, persistent, or worsening clinical signs and/or symptoms attributed to GPA, MPA, or EGPA and not related to prior damage [2].
Results: Positivity for MPO-ANCA was observed in 23.7% of patients, and for PR3-ANCA - in 76.3% of patients. The BVAS activity index averaged 16 (IQR-13) points. The mean CRP level was 47.9 (IQR-90.0) mg/L and the ESR level was 30.1 (IQR-33.5) mm/h. There was a positive correlation between the level of both ANCA and the BVAS index (r = 0.43; 95% CI 0.11-0.66; p <0.01), as well as the level of ESR (r = 0.37; 95% CI 0.05-0.63; p <0.05). No relationship was found between CRP level and ANCA level (r = 0.22; 95% CI -0.15-0.54; p> 0.05), but a positive correlation was observed between CRP level and index BVAS activity (r = 0.41; 95% CI 0.05-0.67; p <0.05). When using ROC-analysis to determine the value of ANCA in the assessment of active disease, it was found that the AUC is 0.93 ± 0.04 (95% CI 0.84-1.01; p <0.01), which indicates excellent ability ANCA diagnose patients with active disease (sensitivity - 87.9%, specificity - 80.0%).
Conclusion: The level of ANCA in patients with ANCA-associated vasculitis correlates with the Birmingham vasculitis activity score, as well as with the level of ESR. Determination of ANCA level can be used not only to diagnose ANCA-associated vasculitis, but also to assess disease activity.

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AB0638 INTRAVENOUS IMMUNOGLOBULIN IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS. STUDY OF 28 CASES FROM A SINGLE UNIVERISTARY HOSPITAL AND LITERATURE REVIEW

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) includes granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) or microscopic polyarteritis (MPA). Standard treatment is often accompained by significant adverse events. Intravenous immunoglobulins (IVIG) may constitute a therapeutic alternative, however, the data are scarce.
Objectives: To assess the utility and safety of IVIG in AAV.
Methods: Observational study of patients with AAV from Spanish referral center treated with IVIG. AAV diagnosis was based on a compatible clinical presentation and/or positive ANCA serology and/or histology. Disease activity was assessed with the Birmingham Vasculitis Activity Score (BVAS).
Results: We included a total of 28 patients; GPA (n=15), MPA (10), and EGPA (3). The main features are summarized in Table 1. The reasons for using IVIG were: **a)** relapse/refractory disease (n=20), or presence/suspicion of infection (8). We observed a rapid and maintained Clinical improvement, since first month of IVIG onset, yielding a BVAS score of zero in 56.5% of patients at 24 months (Figure 1). Serious Adverse event was only observed in 1 patient who developed congestive cardiac failure and had to stop the IVIG therapy.

Table 1. Main general features of 28 patients with antineutrophil cytoplasmic antibody-associated vasculitis treated with intravenous immunoglobulins.

GENERAL FEATURES	RESULTS	GENERAL FEATURES (Continuation)	RESULTS (Continuation)
DEMOGRAPHIC FEATURES		ANALITICAL FINDINGS	
Age of Diagnosis of AAV, mean±SD	57.1±18	CRP (mg/dL), median [IQR]	13.02
Men/ Women; n, (% men)	15/13 (53.6%)	ESR, mm/1st hour, median [IQR]	70.4
AAV Subtype, n (%)		PR3-ANCA, n (%)	11 (39.3)
GPA	15(53.6%)	MPO-ANCA, n (%)	12 (42.8)
EGPA	3(10.7%)	ANCA negative, n(%)	5 (17.8)
MPA	10(35.7%)	FFS at AAV diagnosis, n (%)	
CLINICAL MANIFESTATIONS, n (%)		0	10 (35.7)
Fever	15 (53.6%)	1	11 (39.3)
Constitutional symptoms	26 (92.85%)	2	7 (25)
ORL involvement	7 (25%)	PREVIOUS TREATMENT, n (%)	
Pulmonary involvement	19 (67.9%)	Cyclophospamide	13 (46.4%)
Renal involvement	25 (89.3%)	Methotrexate	6 (21.4%)
Cutaneous involvement)	6 (21.5%)	Azathioprine	3 (10.7%)
Ocular involvement	4 (14.3%)	Cyclophosphamide	13 (46.4%)
Joint involvement	4 (14.3%)	Mycophenolate mofetil	4 (14.3%)
Neurologic involvement	8 (28.57%)	Rituximab	5 (17.9%)

Abbreviations: ANCA:antineutrophil cytoplasmic antibody; EGPA: eosinophilic granulomatosis with polyangiitis; FFS: Five-Factors Score; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis

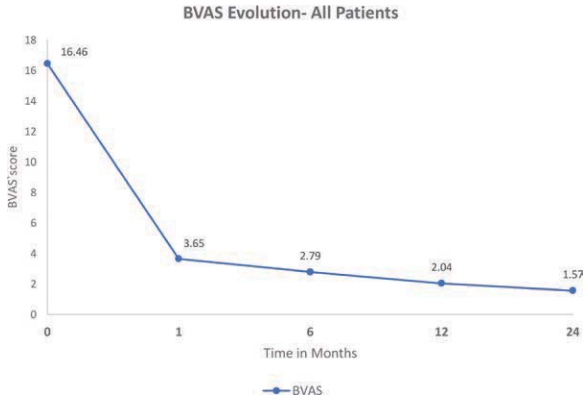

Figure 1. BVAS Evolution with IVIG treatment of all our patients.

Conclusion: IVIG seems to be an effectiveness and relative safe therapeutic option in relapse/refractory AAV or in presence of a concomitant infection.

Disclosure of Interests: None declared
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AB0639 COMMON FEMORAL VEIN THICKNESS MEASUREMENT AS A DIAGNOSTIC TEST IN INCOMPLETE BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is characterized by recurrent oral and/or genital aphthous ulcers accompanied by cutaneous, ocular, articular, gastrointestinal and central nervous system lesions. Diagnosing BD can be a clinical challenge in patients presenting with a limited number of organ manifestations, especially with single major organ involvement. We reported the first controlled doppler ultrasound study showing increased common femoral vein (CFV) thickness in BD (1). We recently also showed that increased CFV thickness is a distinctive feature of BD, rarely present in other inflammatory or vascular diseases such as ankylosing spondylitis, systemic vasculitides, venous insufficiency, and non-inflammatory DVT with a specificity higher than 80% for the cut-off value of ≥ 0.5 mm. We suggest that CFV thickness measurement is an easy, non-invasive diagnostic test for BD (2).
Objectives: In this study, we aimed to assess the diagnostic performance of CFV thickness measurement in patients with 'Incomplete' Behçet's Disease diagnosed by expert opinion.

Methods: We included 28 patients with incomplete BD (15 male, 12 female) diagnosed with expert opinion and followed in the Marmara University Behcet's Clinic. Demographic, clinical characteristics and treatment data were recorded during routine visits. Common femoral vein wall thickness was measured by an experienced radiologist at the same day.
Results: Median age was 34.3 years and median disease duration 2 years (0-16). Four patients were newly diagnosed. At follow-up onset, oral ulcers were present in 22 (78.6%), genital ulcers in 6 (21.6%), papulopustular lesions in 4 (14.3%) and pathergy positivity in 5 (17.9%) patients. Ten (35.7%) patients had familial BD. While 24 (85.7%) patients had major organ involvement, 4 (14.3%) patients had mucocutaneous disease. Distrubution of major organ involvements were given in Figure 1.

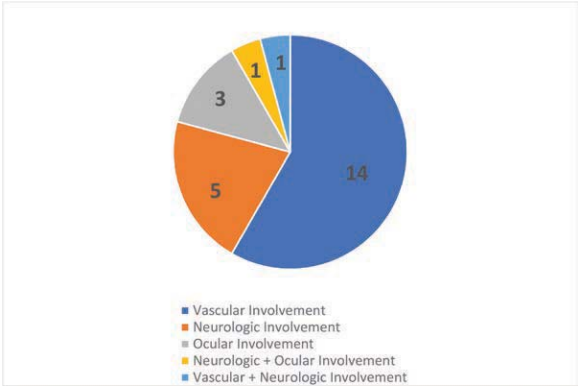

Figure 1. Distribution of major organ involvements (n) in study group

All patients except 1, had CFV thickness value above the cut-off value of ≥0.5 mm. Right CFV thickness was 0.71 (0.3-1.3) mm and left CFV thickness 0.72 (0.4-1.2) mm. Bilateral femoral vein thicknesses were similar in patients with and without an history of familial BD.
Conclusion: Diagnosing BD can be challenging in patients presenting with one major organ involvement such as oral ulcers and posterior uveitis, brain-stem disease or arterial aneurysms, especially in countries with a low prevalence. These patients are generally diagnosed as 'incomplete' BD by 'expert opinion'. Early diagnosis is of utmost importance in some of these cases, especially with venous thrombosis as their management differs from non-inflammatory venous thrombosis, necessitating immunosuppressive use rather than anticoagulant therapy. Our results show that CFV thickness measurement with Doppler US, a non-invasive, fast and cost-effective radiological modality, is a valuable diagnostic test in incomplete BD, especially with major organ involvement.
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AB0640 PREVALENCE AND DETERMINANT FACTORS OF ENDOTHELIAL DYSFUNCTION IN ANCA ASSOCIATED VASCULITIS

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Background: Atherosclerosis and its complications are one the leading cause of death in patients with anti-neutrophil cytoplasmic antibodies (ANCA)- associated vasculitis (AAVs), despite the recent remarkable improvements in prognosis. The mechanism by which atherosclerosis is accelerated in these diseases is not explained by the classical cardiovascular risk factors (CVRFs) and is still under investigation.
Objectives: To evaluate the prevalence of endothelial dysfunction (ED) in AAV patients and to identify the determinant factors of endothelial responses among vasculitis characteristics, such as ANCA status and organ involvement.
Methods: Thirty patients (15 men and 15 women) with AAVs [13 with eosinophilic granulomatosis with polyangiitis (EGPA), 7 with granulomatosis with polyangiitis (GPA), 10 with microscopic polyangiitis (MPA)] were enrolled in the study. For all subjects CVRFs, blood pressure, lipid profile, renal function, acute phase reactants, ANCA status and titers were recorded at diagnosis and at the enrollement in the study. Vasculitis disease activity was measured using the Birmingham Vasculitis Activity Score (BVAS) and organ damage was assessed with the vasculitis damage index (VDI). The prognosis was evaluated through the Five Factor Score (FFS). Patients were excluded from the study if they had previous cardiovascular or cerebrovascular events, liver failure, end stage renal disease under hemodyalisis, or cancer. Microvascular peripheral dysfunction was assessed by pulse amplitude tonometry (PAT) of the small digital artery. In particular, Log-transformed reactive hyperemia index (LnRHI) was evaluated using the EndoPAT2000 device: values of Ln-RHI < 0.51 were considered indicative of peripheral ED.
Results: At diagnosis, 23 subjects (76.7%) were ANCA positive (8 c-ANCA+, 15 pANCA+), and at the enrollment in the study 10 patients (33.3%) were still seropositive. Nineteen patients (63.3%) had inactive disease (BVAS=0), 7 (23.3%) were in low disease activity (1≤BVAS≤2) and 4 (13.3%) had an active disease (BVAS≥3). The presence of ED was documented in 9 AAV patients (30%). AAV patients with ED had higher C-reactive protein (CRP) values at diagnosis compared to subjects without ED (*p=0.05*). Moreover, patients with altered endothelial response were in higher percentage smokers (55.6%) and ANCA positive at enrollment (44.4%), compared to subjects with normal Ln-RHI (28.6%- p=0.12; 19%, p=0.15 respectively). There were no differences regarding age and other traditional CVRFs, disease duration, BMI, BVAS, VDI, FFS. There was an inverse correlation between CRP values at diagnosis and LnRHI (r=-0.42, *p=0.04*). In multiple logistic regression analysis, ANCA positivity at enrollment [OR (95% CI) = 15.68 (0.98-250.28)] (*p=0.05*), and higher CRP concentrations [OR (95% CI) = 1.03 (1.00–1.06)] (*p=0.03*) were independently associated with the presence of peripheral ED.
Conclusion: As observed in other chronic inflammatory autoimmune diseases, ED occurs in AAVs and is mainly related to the chronic systemic inflammation and seems to be also influenced by ANCA positivity, which is probably involved in the accelerated endothelial cell damage.
Further studies are needed to clarify the role of vasculitis related characteristics in the atherosclerotic process.
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AB0641 AN ULTRASONOGRAPHIC STUDY OF THE SALIVARY GLANDS IN A COHORT OF PATIENTS AFFECTED BY CRYOGLOBULINEMIA VASCULITIS: PRELIMINARY RESULTS

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Background: Xerostomia and xerophthalmia can occur in many diseases, rheumatological or not and are often reported by patients affected by cryoglobulinemia vasculitis[1], particularly if related to the Hepatitis C virus infection (HCV)[2]. On the other hand, the Ultrasound (US) was extensively used for detecting pathological findings of the salivary glands[3], possibly associated to many rheumatological diseases.
Objectives: The aim of this study was to detect, in patients affected by cryoglobulinemia vasculitis, the presence and the grade of pathological findings at level of the major salivary glands.
Methods: From January to December 2021, we enrolled consecutive oupatients patients affected by cryoglobulinemia (age ≥ 18 yo and a diagnosis of cryoglobulinemia vasculitis according to 2002 or 2011 classification criteria). Exclusion criteria were a previous diagnosis of other vasculitis/connective tissue diseases/inflammatory arthropathies, concomitant not rheumatological diseases or the intake of drugs possibly related to sicca syndrome symptoms. For each patient, the demographic, anthropometric and clinical history data, particularly about the cryoglobulinemia symptoms (either previous and ongoing) and past or current therapies have been collected. Furthermore, the values of erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], Rheumatoid Factor [RF] and C4 serum complement fraction have been recorded. The presence and the titre of the cryoglobulins have been recorded. For each patient, the Schirmer's Test and the evaluation of the unstimulated whole salivary (UWS) flow were performed. The Schirmer Test was considered positive if < 5 mm/min at least in one eye and the UWS flow was defined pathological if < 1,5 ml/15 min. Each patient was submitted to the US examination (Esaote MyLab Twice) of both parotid and submandibular glands. Each gland was evaluated using a semiquantitative score 0-3, according to the OMERACT definitions[3]. The US score was considered pathological if ≥2. Thus, at patient level, a sum dichotomous score (normal/pathological>) was provided, defining it as "pathological" if any parotid or submandibular glands scored ≥ 2.
Results: We enrolled 20 patients, all females, with a mean age of 68.8 years (SD± 13.32) and a mean disease duration of 11.76 (SD±8.25). For 18 patients was reported a previous HCV infection. 16/18 HCV + subjects reached the remission of the

infection with undetectable HCV viremia. Among the patients enrolled, 10 referred at least one syndrome sicca symptom: 5 patients both xerostomia and xerophthalmia, 4 only xerostomia and 1 only xeropthalmia. Considering blood tests, the cryoglobulins were detected in 14, the ESR title was above the limit in 7 patients and the CRP in 3. The RF was detected in 12 subjects. The Schirmer's test was pathological in 9 patients while the UWS flow was under the limit in 3. As regards the US reports, 2 patients had pathological features scored as≥2, while 7 patients showed minor alterations scored as 1. So, according to the sum score, only 2 patients were classified as pathological. No correlations were identified between the clinical and the US data.

Conclusion: In this cohort of patients with cryoglobulinemia, the US mainly showed mild pathological features at level of the parotid and submandibular structure, suggesting that syndrome sicca symptoms could be related to different pathological mechanisms in these patients, possibly strongly associated to HCV infection. Further and larger studies are necessary to confirm our preliminary data.

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AB0642 DIAGNOSIS OF CEREBRAL VASCULITIS: RETROSPECTIVE STUDY OF 68 CASES

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Background: Cerebral vasculitis, whether primary or secondary, is a group of heterogeneous pathologies characterized by a destructive inflammatory vascular wall lesion of the cerebral tissue. Its physiopathology remains poorly understood. Clinical polymorphism is a major characteristic of this disease.

Objectives: The aim of this work was to describe the epidemiological, clinical, radiological and etiological aspects of Cerebral vasculitis.

Methods: We conducted a retrospective descriptive study based of the records of 68 patients who were hospitalized in the Internal Medicine and Neurology Departments of the Taher Sfar University Hospital in Mahdia over a 12-year period from January 2008 to June 2021.

Results: A total of 68 patients were included: 46 female and 22 male (sex-ratio M/F: 0.47) with an average age of 50.8 ±12.7 [15-75 years]. The revealing symptoms were: Headaches in 52 patients (79.9%) followed by motor deficit in 21 patients (30.8%), sensitivity disorder in 24 patients (35.3%) and neurosensory disorders in 24 patients (35.3 %). These symptoms were insidious in 41 patients (61.2%). The neurological examination was pathological in 75 % of the patients, among them 19 patients (28.7%) had a walking disorder. Strokes were the revealing complication in 5 patients (7%).

Laboratory tests revealed an inflammatory syndrome in 37 patients (55.2%). The lumbar puncture was performed in 76.5% of cases. Cerebral spinal fluid showed aseptic meningitis in 5 cases and High protein level in 6 patients. The immunologic investigations showed that Antinuclear antibodies (ANA) were positive in 41 % and antiphospholipid antibodies were positive in 7.3%.

Cerebral Magnetic Resonance Imagining (MRI) revealed multiple patchy lesions hyperintense on T2 and FLAIR in the white matter in all cases: bilateral and asymmetric in 55 patients (80.9%) with subcortical distribution in 63% and periventricular localization in 45 %. Three patients had Leptomeningeal enhancement.

The etiologies of cerebral vasculitis were: Sjogren Syndrome in 33.8 %, Systemic lupus Erythematosus in 22%, Behcet disease in 19.1 %, Giant cell arteritis in 7.3%, antiphospholipid syndrome in 5.8%, Sarcoidosis in 4.4 %, Susac syndrome in 4.4 % and systemic sclerosis in 2.9 %.

Treatment was based on oral corticosteroids in 89.7 % of cases, associated with intravenous corticosteroids in 52.9% of cases. Immunosuppressive therapy was indicated in 42.4% of patients.

Prompt improvement was obtained in 48,3%, symptoms stability was noticed in 20 %. However, 30% of patients experienced relapse. Worsening of signs was seen in 1.7 %.

Conclusion: Cerebral vasculitis is a rare disorder with a non-specific clinical presentation. Therefore, its diagnosis is a challenge for clinicians who base their investigations on clinical and paraclinical arguments to attribute the neurological and systemic events to vasculitis. An early diagnosis and an appropriate treatment could improve its prognosis.

Disclosure of Interests: None declared

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AB0643 ARE THERE ANY DISTINCTIVE FINDING IN ANCA-ASSOCIATED VASCULITIS RELATED PULMONARY INVOLVEMENT IN COMPARISON WITH CONNECTIVE TISSUE DISEAE OR IDIOPATIC PULMONARY FIBROSIS

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Background: Patients with ANCA associated vasculitis (AAV) have a wide spectrum of pulmonary involvement from parenchymal necrotizing granuloma formation, trecheobronchial inflammation, pulmonary capillaritis to interstitial lung disease. Pulmonary involvement is relatively common in connective tissue diseases (CTDs). Both rheumatologic disorders and idiopatic pulmonary fibrosis (IPF) might cause the usual interstitial pneumonia (UIP) pattern. However, little is known regarding the clinical and radiologic similarities/ dissimilarities of those diseases.

Objectives: We aimed to evaluate the thoracic computed tomography (CT) findings of patients with AAV, CTDs-related interstitial lung disease (ILD) or IPF.

Methods: Patients whose thoracic CT performed at the time of the diagnosis or relapse of AAV (n=64), at the time of the diagnosis of CTD related ILD (n=55) or IPF (n=52) were included in the analysis. Demographic, clinical and serological data were collected retrospectively. Radiological patterns of pulmonary involvement were evaluated by two expert pumonary radiologists and abnormal thoracic CT findings were classified according to Fleischner Society guidelines. Intra- and inter-observer variation were calculated. Multoniminal logistic reggresion was performed to identfy disease specific findings in thoracic CT.

Results: A total of 171 patients were included and of them 64 patients (62.5% with granulomatosis with polyangiitis, 37.5% with microscopic polyangiitis) in AAV group, 55 patients in CTD related ILD (50.9% with scleroderma, 40.0% with rheumatoid arthritis, 9.1% other or undifferensiye connective tisue disease) group and 52 patients in IPF group. Demographic and thoracic CT findings were summarized in Table 1. In univariate analysis according to Fleishner Society definition, patients with AAV had more common pulmonary noduls, cavities, consolidation. However, patients with AAV were less likely to have interlobular septal thickening (ILST), lymph node adenopathy (LAP) and reticulation compared to both CTD related ILD and IPF. In addition, among those groups of rheumatic diseases, cavities and alveolar hemorrhage were detected only AAV. In multinominal logistic reggresion, the presence of nodul and consolidation and the absence of ILST and mediastinal LAP were independent determinant findings in thoracic CT in patients with AAV in comparison with both CTD related ILD or IPF.

Table 1. Demoraphic characteristics and Thoracic CT findings of patients

	AAV patients (n=64)	CTD related ILD (n=55)	IPF (n=52)	p
Characteristics				
Age at diagnosis, yrs, mean (SD)	58.6 (15.0)	61.8 (12.0)	72.4 (9.4)	<0.001
Sex, male, %	70.3	30.9	75	<0.001
Smoking, ever, %	77.8	26.5	62.8	0.29
Chest CT findings according to Fleishner guideline, %				
Ground glass opasity	29.7	38.2	9.6	0.003
Reticulation	19.0	52.7	94.2	<0.001
Interlobular septal thickening	28.6	69.1	98.1	<0.001
Peribronchial thickening	11.1	20.0	3.8	0.03
Honeycombing	14.3	25.5	63.5	<0.001
Bronchiectasis	31.3	47.3	86.5	<0.001
Consolidation	45.3	12.7	5.8	<0.001
Micronodules	6.3	3.6	0	0.07
Nodules	45.3	10.9	3.8	<0.001
Cavities	23.4	0	0	<0.001
Eymphysema	18.8	7.3	19.2	0.96
Mosaic attenuation pattern	7.8	20	38.5	<0.001
Alveolar hemorrage	17.2	0	0	<0.001
Mediastinal lymph node adenopathy	26.7	53.7	57.7	0.002
Pleural effusion	14.1	1.8	0	0.001
Pericardial effusion	6.3	9.1	0	0.16

Conclusion: The results of this study show that in additon to clinical and labaratory characteristics, some thoracic CT imaging findings like the presence of nodules and consolidation and the abscence of LAP and ILST may be useful to differentiate pulmonary involvement of AAV from other relatively common rheumatologic conditions and IPF. In addition, alveolar hemorrhage and cavities may be particular manifestations of AAV.

Disclosure of Interests: None declared

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Scleroderma, myositis and related syndromes

AB0644 INCIDENCE OF CARDIOPULMONARY COMPLICATIONS AND SURVIVAL IN EARLY SYSTEMIC SCLEROSIS (SSC) PATIENTS COMPARING BETWEEN THOSE WITH AND WITHOUT ELEVATED SERUM CREATINE KINASE (CK): INCEPTION COHORT STUDY

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Background: There has been no prior inception cohort data regarding incidence of cardiopulmonary complications and survival in early SSc patients comparing between those with elevated creatine kinase (baseline CK ≥ 500 U/L) and without elevated CK (baseline CK < 500 U/L).
Objectives: The aims of this study were to compare: (1) the prevalence of clinical manifestations; (2) incidence rate (IR) of cardiopulmonary complications and (3) survival, between early SSc patients with and without elevated serum CK levels, using inception cohort study.
Methods: We used an inception cohort of early SSc patients (disease duration from first Non-Raynaud's phenomenon≤ 3 years) seen at the Rheumatology clinic, Maharaj Nakorn Chiang Mai Hospital, Thailand, between January 1st 2010 and 31 December 2019. All patients were assessed for clinical manifestations, creatine kinase (CK) levels and underwent electrocardiography (ECG), echocardiography and high-resolution computed tomography (HRCT) at the study entry and every 12 months thereafter. Interstitial lung disease (ILD) was determined by HRCT. Myocardial disease was defined as presence of dilated cardiomyopathy, non-specific cardiomyopathy or suspected primary right ventricular dysfunction assessed by echocardiography.
Results: One hundred and forty-four patients (84 females, 115 diffuse cutaneous SSc [DcSSc] and 111 anti-topoisomerase I antibody-positive) with mean ± SD age of 53.3 ± 8.9 years, mean disease duration of 11.9 ± 9.2 months and mean follow-up duration of 6.2 ± 2.7 years were recruited. There were 29 early SSc patients with elevated CK (20.1%). Comparing with patients without elevated CK, SSc with elevated CK had significantly higher proportion of clinical manifestations as followings: male gender (58.6% vs. 37.4%, p = 0.038), DcSSc subtype (93.1% vs. 76.5%, p = 0.047) and shorter disease duration (8.2 ± 6.3 vs.12.8 ± 9.5 months, p = 0.009). At enrollment, the elevated CK group had significantly higher prevalence of arthritis (44.8% vs. 25.2%, p = 0.038), weakness (55.2% vs. 10.4%, p < 0.001) and higher modified Rodnan skin score (MRSS) (23.5 ± 10.1 vs. 17.5 ± 10.6, p = 0.005); At last visit, the elevated CK group had significantly higher cumulative prevalence of weakness (58.6% vs. 11.3%, p < 0.001), dysphagia (75.9% vs. 43.5%, p = 0.002), LVEF < 50% (48.3% vs. 12.2%, p < 0.001) and myocardial disease (55.2% vs. 21.7%, p < 0.001). The elevated CK group had significantly higher incidence rate (IR) of: LVEF < 50% (14.24 vs. 2.03 per 100 person-year; incidence rate ratio (IRR) 7.03, p < 0.001), myocardial disease (19.74 vs. 3.87 per 100 person-year; IRR 5.09, p < 0.001) and ILD (60.40 vs. 31.49 per 100 person-year; IRR 1.92, p = 0.006); compared to the non-elevated CK group. The survival rate of early SSc with elevated CK group at 1, 3 and 5 year were 86.2% and 82.5% and 74.3%, respectively. The median survival time of the elevated CK group was lower than those without elevated CK group (6.98 vs. 8.56 years, p = 0.012).
Conclusion: Our study cohort found that early SSc patients with elevated baseline CK levels are predominant in male gender, DcSSc subtype with shorter disease duration. The elevated CK group has more severe clinical presentations including higher MRSS, arthritis and weakness compared to the non-elevated CK group. In addition, significantly higher incidence rate of: LVEF < 50%, myocardial disease, ILD; and poorer survival are also obviously detected in the elevated CK group.
Disclosure of Interests: None declared
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AB0645 NINTEDANIB IN TREATMENT OF PULMONARY FIBROSIS SECONDARY TO CONNECTIVE TISSUE DISEASE:

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Background: Interstitial lung disease (ILD) is a common manifestation of systemic sclerosis and other Rheumatic Diseases, and is one of the major causes of mortality. Nintedanib, a tyrosine kinase inhibitor, has been shown to have antifibrotic and anti-inflammatory effects in preclinical models of systemic sclerosis and ILD.
Objectives: To evaluate efficacy and safety of Nintedanib in pulmonary fibrosis secondary to Connective Tissue Disease.
Methods: Ten patients with pulmonary fibrosis secondary to Connective Tissue Disease treated with Nintedanib were monitored at baseline, 6 and/or 12 months, with clinical assessment, chest CT scan and/or pulmonary function testing (PFT) with assessment of the diffusing capacity for CO (DLCO). 8/10 patients had a diagnosis of Progressive Systemic Sclerosis, while the remaining ones had Polydermatomyositis and Mixed Connectivitis. All patients were dyspnoic at baseline and presented with dry cough. All patients had pulmonary fibrosis according to high-resolution chest CT scan. All patients had been treated with at least one csDMARD or bDMARD (cyclophosphamide, azathioprine, cyclosporine, rituximab, tocilizumab), prior to receiving nintedanib. At baseline 2/10 patients were treated with Nintedanib monotherapy, 7/10 were in combination therapy with Mycophenolate, 1 patient received a combination therapy with cyclosporine.
Results: Compared to baseline values, 4/7 patients showed stationarity of the respiratory function parameters (DLCO), in 2/7 patients it was observed a significant improvement of the DLCO (with a change of 15%) while in only 1 patient there was a worsening over time. FVC remained stable over time except in 1 patient who got a significant improvement. In 5/9 patients cough improved (unchanged in the rest of patients). Dyspnea (NYHA scale) improved in 6/9 patients, remained stationary in 2/6 patients and became worse in 1 patient. 8/9 patients had a stable chest CT at 6 and / or 12 months, while only 1 patient witnessed a further worsening of the fibrosis. 50% of the patients showed good gastrointestinal tolerance to the full dose of nintedaninb. The other half had the dose reduced in order to improve gastrointestinal symptoms.
Conclusion: Our data show that patients with ILD associated with Rheumatic Diseases treated with nintedanib had a clinical benefit over dyspnea and cough symptoms and a stabilization of radiological findings 12 months after starting the treatment. Also, respiratory function parameters remained stable over time. Gastrointestinal adverse events, including diarrhea, were common in these patients, but therapeutic dose adjustment led to fast symptoms resolution and good tolerance.
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AB0646 G- CSF TREATMENT FOR REFRACTORY DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

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Background: Digital ulcers (DU) are a common manifestation of systemic sclerosis (SSc). Despite combination vasodilator therapy, refractory DU are not rare. Granulocyte-colony stimulating factor (G-CSF) had not been evaluated for SSc DU heretofore.
Objectives: To evaluate the efficacy and safety of G-CSF for refractory SSc DU.
Methods: Adult SSc patients with chronic resistant DU despite treatment with maximal tolerated doses of prostacyclin analogue, endothelin receptor antagonist and PDE5 inhibitor, were treated with three consecutive daily doses of G-CSF. Evaluation of DU healing, DUCAS score, antibiotics use, side effects and hospitalizations, was performed.
Results: Ten patients (90% females), mean age 53.5 ± 11.1 years were treated. Fifty percent of the patients had a diffuse SSc disease. All patients suffered from chronic (80%), or recurrent (20%) DU. G-CSF treatment resulted in complete resolution of most DU, after an average of 1.57± 0.76 months. DU recurrence occurred in two patients, after a mean period of two months. The number of DU decreased from 2.23±2.20 at baseline, to 0.84±0.80 at one month (p value= 0.04), and 0.50±0.67 at 3 months (p value= 0.015). DUCAS score dropped from 6.84±1.62 before the treatment, to 1.76±2.00 and 1.16±2.55 at one and three months, respectively (p value <0.0001). No serious adverse events were observed.
Conclusion: G- CSF treatment was found to be beneficial for refractory SSc DU, resulting in DU healing and sustained remission in most cases. No significant side effects were observed. Future trials are needed to evaluate the efficacy and safety of this therapy.
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Table 1. Patients' characteristics:

Parameter	SSc IDU
Mean age at DU onset (years) ±SD	53.5 ± 11.1
Female gender (N, %)	9, 90%
Antibodies	
ATA (N, %)	3, 30%
ACA (N, %)	5, 50%
Negative	2, 20%
Diffuse SSc subtype (N, %)	5, 50%
Treatment (N, %)	
bosentan	10, 100%
sildenafil	6, 60%
CCB	2, 20%
iloprost	10, 100%
Mean Number of DU- baseline	2.23 ± 2.20
Mean Number of DU – 1 month ±SD	0.84 ± 0.80
Mean Number of DU – 3 months ±SD	0.50 ± 0.67
Mean DU duration before G-CSF (months)±SD	4.77 ± 4.53
Mean time to heal- (months)±SD	1.57 ± 0.75
Mean DUCAS before ±SD	6.84 ± 1.62
Mean change in DUCAS- 1M ±SD	5.07 ± 2.75
Mean change in DUCAS- 3M ±SD	5.58 ± 2.53
Adverse reactions (N, %)	0, 0%

Abrreviations: SD- standard deviation, DU- digital ulcers, SSc- systemic sclerosis, ATA- anti topoisomerase antibodies, ACA- anti centromere antibodies, CCB- calcium channel blockers, G- CSF- Granulocyte-colony stimulating factor, DUCAS- digital ulcer clinical assessment score.

Figure 1:

figure 1a: Mean digital ulcers number at baseline, after one month, and after three months:

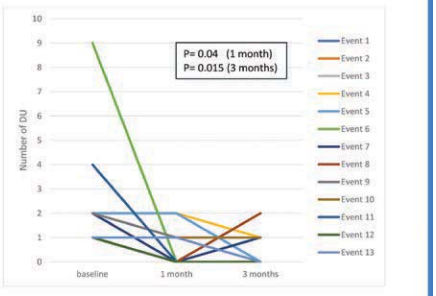
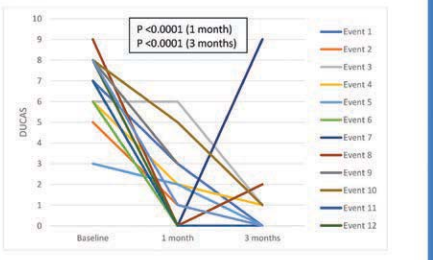


Figure 1b: Mean DUCAS at baseline, after one month, and after three months:



Abrreviations: DU- digital ulcers, DUCAS- digital ulcer clinical assessment

Disclosure of Interests: None declared

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AB0647

CLINICAL PHENOTYPE IN SCLERODERMA PATIENTS WITH LIMITED AND DIFFUSE CUTANEOUS DISEASE BASED ON AUTOIMMUNITY

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Background: Classically, anti-centromere antibodies (ACA) are associated with limited cutaneous involvement (lcSSc) and pulmonary hypertension, whereas anti-topoisomerase I (Sc70) are associated with diffuse skin involvement (dcSSc) and pulmonary fibrosis (ILD). Patients with lcSSc and Sc70 antibodies draw particular attention, which is why characterization of clinical phenotypes can help distinguish patient subgroups and assessing the prognosis of the disease.
Objectives: We aimed to characterize the clinical phenotype of patients with SSc based on autoantibodies.
Methods: We included patients with SSc, fulfilling the 2013 ACR/EULAR criteria, with disease duration ≤10 years. We have compared different subgroups of patients with lcSSc: Scl70-lcSSc (group1), ACA-lcSSc (group 2) and ANA-lcSSc (group 3), (Table 1). Next, we compared patients with Scl70-lcSSc (group 1) to Scl70-dcSSc (group 4) and ANA-lcSSC (group 3) to ANA-dcSSC (group 5). In the ANA subgroup we included patients with negative Scl70 and ACA antibodies. We have assessed the risk of ILD, myositis, scleroderma renal crisis, cardiac and gastrointestinal involvement, myositis, pulmonary hypertension (systolic pulmonary arterial pressure sPAP>45 mmHg at transthoracic echocardiography or sPAP>25 mmHg at right heart catheterization), cancer and all-cause-mortality.

Table 1. Clinical characteristics of patients with lcSSc

	Scl70-lcSSc	P value	ACA-lcSSc	P value	ANA-lcSSc
Female	9 (56.3%)	**0.03**	36 (83.7%)	0.80	12 (52%)
Time from RP to SSc (years)	1.28 (0.25-3.5)	**0.02**	6.23 (3-9)	**0.002**	4.91 (2-5)
Age at SSc onset	56.5 (48-66)	**0.04**	62.5 (54-73)	0.76	59.2 (44-66)
CRP elevation	30 (22-39)	**0.02**	22 (16-29)	0.21	10 (6-19)
mRSS	4 (2-4.2)	**0.03**	3.2 (2.1-4.0)	0.92	3.9 (2.5-4.2)
Joint synovitis	6 (37.5%)	0.47	12 (28%)	0.71	10 (43%)
Tendon friction rubs	2 (12.5%)	0.50	3 (7%)	0.19	0
Myositis	4 (25%)	**0.04**	2 (5%)	0.81	5 (21.7%)
Gastrointestinal involvement	6 (37.5%)	0.19	27 (63%)	**0.04**	16 (69%)
Renal crisis	4 (25%)	**0.04**	2 (5%)	0.18	2 (9%)
ILD	10 (63%)	**0.001**	7 (16%)	**0.04**	7 (30%)
Pulmonary hypertension	4 (25%)	0.47	7 (16%)		3 (13%)
Arrythmia	5 (21.7%)	0.08	6 (14%)	0.35	7 (30%)
Conduction defects	1 (6.3%)	0.59	5 (11.6%)	0.79	1 (4%)
Diastolic disfunction	7 (43.8%)	0.36	17 (39.5%)	0.77	9 (39%)
Immunosuppressants	10 (63%)	**0.01**	13 (30.2%)	0.52	12 (52%)
Steroids	9 (56%)	**0.04**	12 (28%)	0.98	13 (56.6%)
Cancer	8 (50%)	**0.04**	10 (23.2%)	0.22	7 (30%)
Mortality	3 (18.8%)	**0.04**	6 (14%)	0.82	5 (21.7%)

Results: 103 SSc patients were included: 72 (69%) females, 82 (79%) lcSSc and 21 (20%) dcSSc. Among lcSSc patients, 43 (52%) had ACA, 16 (19%) Scl70 and 23 (28%) ANA. Among dcSSC patients, 9 (43%) had Scl70 and 12 (57%) had ANA. Scl70-lcSSc patients had significantly shorter time from Raynaud's phenomenon (RP) to SSc diagnosis (p=0.02), younger age at SSc onset (p=0.04), higher mRSS (p=0.03), higher rate of myositis (p=0.04) and renal scleroderma crisis (p=0.04) than ACA-lcSSc patients. The risk of ILD in Scl70-lcSSC compared to ACA-lcSSC is 3.8 higher (95% IC 1.2-14.5) and 1.5 higher (95% IC 1.05-5.61) than ANA-lcSSC. All-cause mortality was higher in Scl70-lcSSC (p=0.04) compared to ACA-lcSSC. Scl70-dcSSC patients had a shorter time from RP to SSc diagnosis (p=0.02), higher CRP (p=0.04), mRSS (p=0.001), higher rate of myositis (p<0.05) and ILD (p=0.04) and all-cause mortality (p=0.04) than Scl70-lcSSc patients, while renal and cardiac involvement was similar. ANA-dcSSC patients also had a shorter time from RP to SSc diagnosis (p=0.03), higher mRSS (p=0.02) and higher rate of ILD (p=0.02).
Conclusion: Scl70-lcSSc patients show the major organ involvement, followed by ANA-lcSSc and ACA-lcSSc. Scl70-dcSSc and ANA-dcSSC patients exhibit more cutaneous involvement and ILD than Scl70-lcSSc and ANA-lcSSc. These results may provide new ways to help in early diagnosis, management and assessing the prognosis of the disease.

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AB0648

CANCER IN SYSTEMIC SCLEROSIS: ASSOCIATION BETWEEN ANTIBODIES AND MALIGNANCY AND RESULTS FROM A THIRD-LEVEL CENTER

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Background: Systemic sclerosis (SSc) is associated with increased risk of malignancy. Risk factors predisposing a SSc patient for development of malignancy are not well defined, and the pathogenic basis of the association is yet to be explained. Some autoantibodies have been associated with a close temporal relationship with cancer. The absence of malignancy screening guidelines tailored for SSc patients raise the importance of the need for more studies on the association of SSc and cancer.
Objectives: To study the prevalence of cancer in SSc and the association between SSc-specific and SSc-associated autoantibodies and cancer in a third-level center.
Methods: We conducted a retrospective cohort study by including patients diagnosed with SSc followed from 1980 to 2020 fulfilling the 2013 ACR/EULAR SSc criteria. Demographic features, clinical and immunological characteristics were retrieved. The primary outcome was cancer-associated SSc, defined as cancer occurring within 2, 3 and 5 years of first non-Raynaud SSc manifestation. The exposure was defined by the presence of SSc-specific/associated autoantibodies, including anti-centromere (ACA), topoisomerase I (Scl70), RNA polymerase III, fibrillarin, Th/To, PM-Scl, Ku, TIF1g, Ro52. Descriptive analysis was used to compare clinical characteristics of subjects with cancer to those without cancer. Univariate logistic regression was used to compare the odds of cancer-associated SSc between the autoantibody subgroups.
Results: Out of 103 SSc subjects, 27 (26%) had a history of cancer following SSc diagnosis. Mean age was 61.9 (57-69) years, 70% were female and 88% had a smoking history. Median time between cancer and disease onset was 6.33 (3-9) years. Among patients with cancer, 12 (44%), 8 (29%) and 7 (26%) were diagnosed within 2, 5 and 10 years of SSc onset. The most frequent types were breast cancer (n=9), gastrointestinal cancer (n=5), prostatic cancer (n=4), hematological (n=3) cancers, cervical/uterine cancers (n=2), non-melanoma skin (n=2), lung cancer (n=2). Patients with cancer were more likely to be Sc70+(OR 2.55, 95% CI1.03-6.3, p 0.04), anti-TIF1g (OR 19.5, 95% CI 5.6 – 68.3, p 0.001) and RNA pol III (OR 10.9 CI 95% 1.08-109.3, p 0.04), have a history of smoking (OR 7.24, 95% CI 2.6-197, p 0.001), myositis (OR 5.2 IC 95% 2.06-13.2, p 0.005) and older age at SSc onset (61.9 vs 57, p 0.04). Breast cancer was more frequent in anti-TIF1g (OR 3.75 IC 95% 1.8-17.5) and RNA pol-III (OR 7.14 IC 95% 1.56-90.8) subgroups. The risk of cancer-associated SSc was significantly increased among anti-TIF1g-positive subjects at 5 years after SSc onset (OR 2.1 CI 95% (1.45-9.94), p 0.04) and among RNA-pol III-positive subjects at 2 years after SSc onset (OR 3.5 95% CI (1.2-51.4), p 0.02) (Table 1).

Table 1. Logistic regression analysis for the risk of cancer within 2,5 and 10 years of SSc onset according to antibody positivity

	OR 95% CI for cancer diagnosis within 2 years of SSc onset	OR 95% CI for cancer diagnosis within 5 years of SSc onset	OR 95% CI for cancer diagnosis within 10 years of SSc onset
Anti-Scl70	1.56 (0.51-44.5)	1.41 (0.27-12.7)	2.1 (0.55-13.4)
Anti-centromere	1.72 (0.62-52.1)	1.52 (0.32-32.1)	1.69 (0.14-21.3)
Anti-TIF1g	3.9 (0.35-43.4)	**2.1 (1.45-9.94)**	0.42 (0.04-5.32)
ARN Pol III	**3.5 (1.2-51.4)**	1.9 (0.72-62.1)	-
Anti-PM Scl75/100	-	-	0.87 (0.04-1.98)
Anti-Ro52	2.5 (0.66-66.8)	2.0 (0.45-50.2)	0.63 (0.05-7.74)

Conclusion: Anti-Scl70, anti-TIF1g and RNA pol III were predictive of cancer-associated SSc for cancers. Breast cancer was the most frequent. Subjects with cancer were more likely to have a history of smoking, myositis and an older age at SSc onset. Autoantibodies should be taken into account in cancer screening. Larger studies are needed to define the risk of cancer-associated SSc in different autoantibody subgroups.
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Disclosure of Interests: None declared
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AB0649

MYOSITIS SPECIFIC ANTIBODIES - WHO ORDERS THEM AND WHAT ARE THE RESULTS? A RETROSPECTIVE AUDIT OF TWO LARGE REFERRAL CENTERS

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Background: Idiopathic inflammatory myopathies are a group of disorders associated with myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) (1). MSA and MAA are helpful in classifying clinical syndromes with both treatment and prognostic implications (2). Ordering of MSA and MAA has increased in recent years. We report the hospital services that ordered MSA and MAA and follow-up investigations performed in two large referral centers in Melbourne, Australia.
Objectives: To explore and investigate the testing patterns of MSA and subsequent follow up.
Methods: We identified all patients who underwent MSA and MAA testing between January 1 2019 and December 31 2020. Relevant demographic and clinical data were obtained by chart review.
Results: Over the 2-year study period, 294 MSA tests were ordered, alongside 275 ANA and 266 ENA. Of these, 60 (20.4%) were positive and 9 (3.1%) tested positive to more than one MSA. Interstitial lung disease (ILD) was the most common extra-muscular manifestation, 42 (14.2%) had muscle disease manifestations. Respiratory (41%), rheumatology (24%) and neurology (15%) were the top three specialties ordering the most MSA, with the highest proportion of positive MSA originating from rheumatology (38.5%). The rheumatology service was involved in 131 (41.0%) of the MSA ordered as the primary treating unit or as a consultation service. Anti-Scl100 was the most common MSA (n=10, 15.6%). Among the 60 patients with positive MSA, 39 (65%) was given a definitive diagnosis, 13 (21.7%) underwent MRI of muscles, 10 (16.7%) open muscle biopsy, and 5 (8.3%) a skin biopsy. Thirty-two (53.3%) of MSA positive patients underwent high-resolution CT chest; 26 (81.3) % had findings suggestive of a fibrotic process and 12 (20.0%) had a formal diagnosis of ILD. A cancer screen was performed in 23 (38.3%) of the MSA positive patients and no malignancy was identified within the cohort.
Conclusion: Among MSA studies performed in two large centers, 20.4% of results were positive. Respiratory ordered the most numerous tests predominantly to evaluate ILD, a higher proportion of tests recommended by the rheumatology service was positive.
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Disclosure of Interests: None declared
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AB0650

LUNG MANIFESTATIONS OF DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS PATIENTS FROM INDIA

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Background: Lung manifestations in diffuse cutaneous systemic sclerosis (dCSS) are well known. Data on these manifestations in Indian patients are scant or unknown. We aim to present the various lung manifestations in patients with dCSS.
Objectives: To study the clinical and radiological characteristics of pulmonary symptoms such as cough, dyspnea, or hemoptysis, in patients, previously diagnosed with dCSS, in accordance with ACR 2013 classification criteria.
Methods: This was a cross-sectional, point of care study, done at the Government General and Chest Hospital, Hyderabad, Telangana, India. The study was conducted from April 2019 to March 2020 and patients with a confirmed diagnosis of dCSS were included. Patients with known heart disease, diabetes mellitus, cancer, obesity, acute respiratory infections, and HIV infection were excluded.
7 patients were eligible for inclusion. All patients gave their consent to participate in this study. The study was also approved by the institutional ethics committee. All imaging studies were read and confirmed by consultant radiologists at our hospital.
Results: All patients received a confirmed diagnosis of dCSS less than 2 years from the time of presentation to our hospital. The shortest duration from diagnosis of dCSS to first manifestation of pulmonary symptoms was 6 months.
All patients were females. The mean age was 52 ± 14.6 years. All patients had chronic cough, lasting ≥ 1 month. 6 out of 7 patients had exertional dyspnea lasting for ≥ 1 month. None of the 7 patients reported hemoptysis, wheezing, or having a fever. Only 1 patient had anemia, and none had leukocytosis. All patients had their chest x-rays reported as normal.
6/7 (85.7%) patients had subpleural reticular shadowing limited to the lower lobes on HRCT chest, consistent with usual interstitial pneumonia (UIP) pattern. 3/6 (50%) patients with reticular shadowing also had honeycombing suggesting advanced/severe UIP. None of the patients had traction bronchiectasis. 2/6 patients (33.3%) with UIP, also had non subpleural ground glass opacities (GGOs) in the middle and lower zones, suggesting an overlap between UIP and NSIP (non-specific interstitial pneumonia).

Table 1.

S.No.	Age (years)	Sex	Duration from Diagnosis to first pulmonary manifestation	Pulmonary symptoms	CBC	Chest X-ray	HRCT Chest	ECG	2D-Echo	Spirometry	BAL
Patient 1	44	F	16 months	Cough + Dyspnea – 2 months	Normal	Normal	Advanced UIP	Normal	Normal	Restrictive	Normal
Patient 2	56	F	18 months	Cough + Dyspnea – 3 months	Normal	Normal	UIP	Normal	Normal	Normal	Neutrophilic
Patient 3	61	F	12 months	Cough + Dyspnea – 1 month	Normal	Normal	Advanced UIP	Normal	RVSP = 48 mm Hg	Restrictive	Lymphocytic
Patient 4	70	F	21 months	Cough + Dyspnea – 2 months	Normal	Normal	Normal	Normal	Normal	Normal	Lymphocytic
Patient 5	24	F	18 months	Cough + Dyspnea – 2 months	Normal	Normal	Advanced UIP + NSIP (overlap)	Normal	RVSP = 51 mm Hg	Restrictive	Neutrophilic
Patient 6	55	F	12 months	Cough + Dyspnea – 1 month	Normal	Normal	UIP	Normal	Normal	Normal	Not Performed
Patient 7	54	F	6 months	Dyspnea – 1 month	Anemia +	Normal	UIP + NSIP (overlap)	Normal	Normal	Restrictive	Neutrophilic

Notes in the column 'BAL' indicate the predominant cell type noted on cytology. RVSP = Right Ventricular Systolic Pressure

Findings on ECG, 2D-Echo, spirometry and bronchoalveolar lavage (BAL) are summarized in Table 1.

Conclusion: Although limited by a small sample size, UIP appeared to be the most common lung pathology in patients with dCSS. The duration from diagnosis of dCSS to first manifestation of pulmonary symptoms is much shorter in comparison to limited cutaneous systemic sclerosis [1] PAH is commoner with limited cutaneous systemic sclerosis than with dCSS. [2] BAL was neither useful for diagnosis nor required in preparing a therapeutic plan for these patients.

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AB0651 CLINICAL IMPACT AND PROGNOSIS OF CRYOGLOBULINEMIA AND CRYOFIBRINOGENEMIA IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is reported to be a secondary cause of cryoglobulinemia as well as cryofibrinogenemia. However, prevalence, clinical implication and associated pronostic of cryoprecipitates in SSc are unknown.

Objectives: To describe the prevalence, the phenotype and evaluate the prognosis of cryoglobulinemia and/or cryofibrinogenemia associated with systemic sclerosis.

Methods: We included all adult (≥18 years) consecutive SSc patients from the Systemic Scleroderma Toulouse Cohort (SSTC) [1] for whom a cryoglobulin and/or cryofibrinogen measurement was carried out at the immunology laboratory of the Toulouse University Hospital between June 1, 2005 and May 31, 2018 and at least one follow-up visit. We compared SSc-patients characteristics' with and without cryoglobulinemia > 50 mg/l and with and without cryofibrinogenemia. Survival analysis based on presence of cryoglobulin cryofibrinogen was performed using the Kaplan-Meier method. Univariable and multivariable Cox proportional hazards models (ascending step-by-step method) were used to determine baseline variables associated with cryoglobulin or cryofibrinogen presence.

Results: 166 patients were included in the study. 74.6% of patients were women, with a average age at diagnosis of 51.2 years-old. 24% were diffuse cutaneous subtypes and 71.6% limited cutaneous subtypes. Anti-centromere and anti-Scl70 were respectively positive in 44.5% and 21.6% of cases. All these patients were assessed for cryoglobulin detection and 75 cryofibrinogen detection in serum. 43.3% had a cryoglobulinemia >50 mg/l. 46.6% had cryofibrinogenemia. Patients with cryoglobulinemia >50 mg had more cardiac diastolic involvement (22.8% vs. 5.1% p=0.0395). In the multivariate analysis, diastolic involvement (HR=6.23; p=0.0331) was an independent predictor of cryoglobulin >50 mg/l. Survival at 10 years was better for patients with cryoglobulinemia >50 mg/l (log-rank 0.0363) (Figure 1). Survival at 5 and 10 years was 97.6% and 88.8% respectively in patients with cryoglobulinemia >50 mg/l versus 91.9% and 78.4% in patients with cryoglobulinemia <50 mg/l. In cox regression model adjusted for gender, age and type of systemic sclerosis, cryoglobulin >50 mg/l was negatively associated with mortality (HR: 0.09; p=0.03). The presence of cryofibrinogenemia was not associated with any clinical, biological or morphological features. In the multivariate analysis, no variable was predictive of the presence of cryofibrinogenemia in patients with SSc. The presence of cryofibrinogenemia had no influence on the mortality of these patients.

Conclusion: In SSc patients, the presence of cryoglobulin >50 mg/l is an independent predictive factor of cardiac diastolic involvement and is associated with a better survival. However, cryofibrinogenemia does not influence clinical phenotype or impact mortality in SSc patients.

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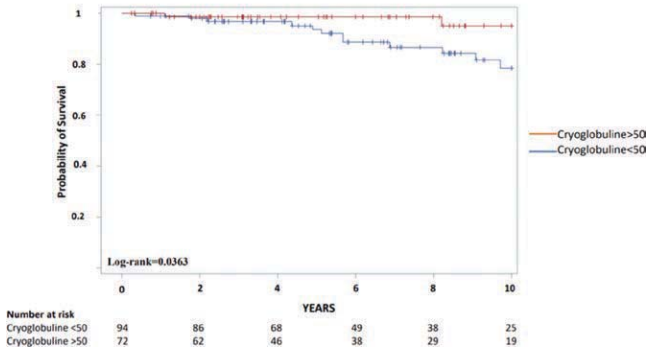
Figure 1: : Kaplan-Meier survival curve for patients with or without cryoglobulin >50 mg/l



Disclosure of Interests: None declared

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AB0652 PREVALENCE OF INTERSTITIAL LUNG DISEASE AND PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS PATIENTS COHORT AT A RHEUMATOLOGY REFERRAL CENTRE IN THE UNITED ARAB EMIRATES

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Background: Scleroderma, also known as Systemic Sclerosis (SSc), is a connective tissue disease that affects multiple organ systems, including the cardiovascular and respiratory systems, namely, pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) as the leading causes of death in this patient population.

Objectives: The purpose of this study is to determine the prevalence of PAH and ILD in a cohort of patients diagnosed with SSc.

Methods: We performed a retrospective chart review of clinical characteristics of all patients diagnosed with SSc Cleveland Clinic Abu Dhabi between April 2015 and April 2020. PAH was estimated by echocardiographic findings and diagnosed based on right heart catheterization (RHC) using 2019 World Symposium on Pulmonary Hypertension. The CT scan of the chest was read by a board-certified radiologist in chest radiology.

Results: Fifty individuals were diagnosed with SSc, with 46% having diffuse cutaneous systemic sclerosis and 54% having limited cutaneous systemic sclerosis. The majority of the patients (88%) were female, with a mean age of 41 ±13 years. The average period from presentation to diagnosis was 5 ±5.4 years. The majority of the cohort (86%) were from the United Arab Emirates. The average BMI was 26.0 kg/m^2. Patients' most prevalent symptoms are fatigue (80%), gastrointestinal symptoms (72%) followed by shortness of breath (58%) and cough (50%). Twenty-six out of fifty patients (52%) underwent a CT chest scan, with 19 (38%) having ILD. Eight patients had more than 30% fibrotic alterations, four patients had 10-30% fibrotic changes, and seven patients had less than 10% fibrotic abnormalities. Patients with more than 10% fibrotic changes were more likely to have usual interstitial pneumonia, whereas those with less than 10% fibrotic changes were more likely to have none specific fibrosis. The majority of patients (92%) had echocardiogram. All except one patient had a normal ejection fraction, and five had grade 1 left ventricular diastolic dysfunction. Five patients were described as having mild, 1 moderate and 2 severe PAH. Only 4 patients underwent RHC. One patient had group II PAH based on elevated wedge pressure. One had group 1 PAH with systemic sclerosis as the only cause for her PAH and two patients had group III PAH due to having more than 30 % pulmonary fibrosis and severe restrictive defect on spirometry. Therefore, the precapillary PAH prevalence was 6% (3/50).

Conclusion: While the prevalence of pulmonary fibrosis in our SSc patients reflects what has been reported in the literature, the prevalence of PAH is significantly lower than the reported 15-20%.[1] This is likely due to underdiagnosis of PAH considering the number of years of systemic sclerosis diagnosis on presentation to our clinic. A systematic approach is needed to assess for the presence and severity of PAH using tools as in Detect algorithm which has been validated and commonly used in Europe and North America to screen for PAH.[2] Validation of such algorithm is likely needed in middle eastern population before it is universally adopted.

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AB0653 **THE ASSOCIATION OF AUTOANTIBODIES WITH MORBIDITY AND MORTALITY OF SCLERODERMA RENAL CRISIS IN JAPAN**

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Background: The morbidity of scleroderma renal crisis (SRC) and autoantibodies in systemic sclerosis (SSc) vary by races and regions. Anti-RNA polymerase III is associated with SRC in America and European countries. However, the association of autoantibodies with SRC had not been elucidated in Japan.

Objectives: We aimed to investigate the association of autoantibodies with morbidity and mortality of SRC in Japan.

Methods: The clinical characteristics and mortality of 330 patients with systemic sclerosis (SSc) at Kyoto University Hospital were retrospectively analyzed, focusing on anti-centromere, anti-RNA polymerase III, anti-topoisomerase I, and anti-U1-RNP. Logistic regression analyses were performed to examine the association of autoantibodies with the development and mortality of SRC. Kaplan-Meier survival analysis was performed comparing the groups classified by autoantibodies.

Results: Anti-centromere (n = 177/318, 56%), anti-topoisomerase I (n = 80/311, 26%), anti-RNA polymerase III (n = 27/204, 13%), and anti-U1-RNP (n = 24/305, 8%) were found in SSc patients (n = 330). SRC was observed in 24 out of 330 SSc patients, including anti-topoisomerase I (n = 12/24, 50%), anti-RNA polymerase III (n = 7/24, 29%), anti-U1-RNP (n = 5/24, 21%), and anti-centromere (n = 3/24, 13%). Anti-U1-RNP (odds ratio [95% confidence interval], 3.63 [1.11–10.2]), anti-RNA polymerase III (3.29 [1.16–8.70]), and anti-topoisomerase I (3.22 [1.37–7.57]) were associated with the development of SRC. All patients with SRC were treated with ACE inhibitors and the 1-year survival rate was 54%. Anti-topoisomerase I was associated with the 1-year mortality of SRC (6.00 [1.11–41.1]). When the survival rate was compared between the patients positive for anti-topoisomerase I (n=12) and negative for anti-topoisomerase I (n=12), the 1-year survival rate was 33% vs 75% (p=0.041), respectively (Figure 1A). Furthermore, the 1-year survival of anti-centromere (100%), anti-RNA polymerase III (83%), and others/not detected (50%) were shown in patients negative for anti-topoisomerase I (Figure 1B).

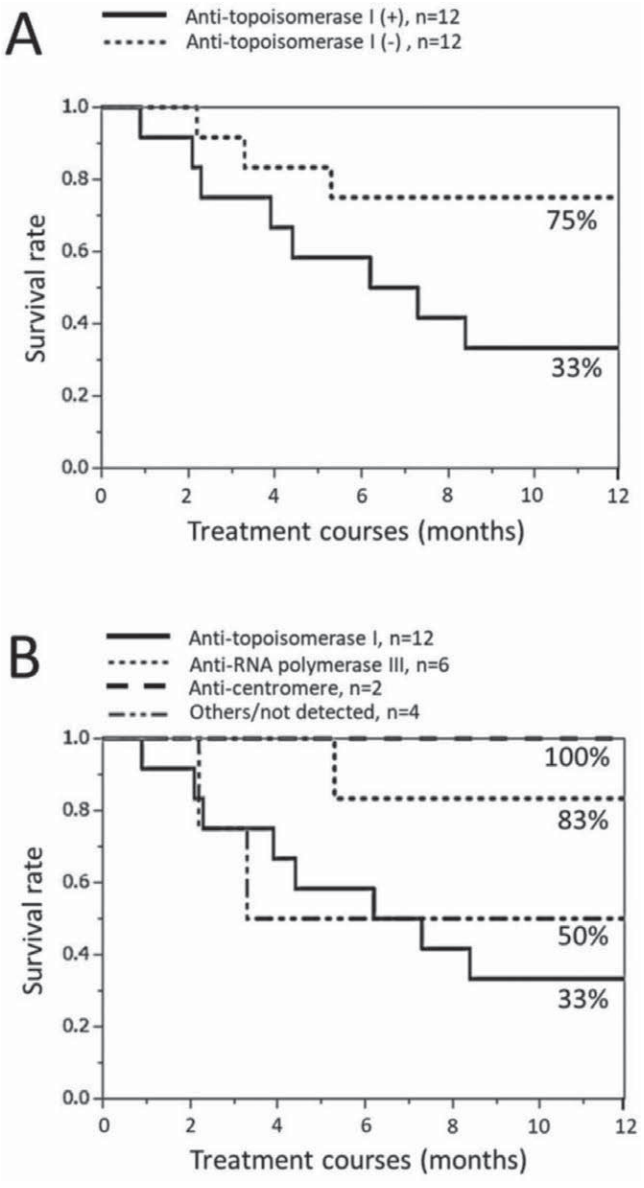

Figure 1. Overall survival of patients with SRC according to the type of autoantibodies. (A) The survival rates in SRC patients who were positive for anti-topoisomerase I (solid line, n = 12) and those who were negative for anti-topoisomerase I (dotted line, n = 12). (B) SRC patients negative for anti-topoisomerase I were classified as patients with anti-RNA polymerase III (dotted line, n = 6), anti-centromere (broken line, n = 2), and others/not detected (chain line, n = 4).

Conclusion: Specific SSc-related autoantibodies were associated with the morbidity and mortality in SRC.

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Table 1. Univariate logistic regression analysis for mortality in SRC (n = 24).

Variables	Odds ratio (95% CI)	P value
Age	1.07 (0.99, 1.16)	0.08
Female sex	3.00 (0.32, 66.6)	0.38
Diffuse/limited (diffuse %)	0.25 (0.04, 1.36)	0.12
BMI	0.67 (0.41, 0.93)	0.049
Modified Rodnan skin score	0.95 (0.88, 1.02)	0.15
Digital ulcer	0.52 (0.10, 2.63)	0.43
Reflux esophagitis	0.60 (0.02, 17.1)	0.73
Pulmonary hypertension	7.50 (1.17, 69.2)	0.046
Pleural effusion	7.20 (1.23, 62.0)	0.04
Glucocorticoid use	3.86 (0.65, 32.4)	0.16
Hemoglobin	0.55 (0.25, 1.01)	0.09
Platelet	1.00 (0.98, 1.01)	0.44
Total protein	0.17 (0.02, 0.69)	0.04
Creatinine	0.95 (0.67, 1.24)	0.69
CRP	0.90 (0.67, 1.17)	0.46
Anti-topoisomerase I	6.00 (1.11, 41.1)	0.048
Anti-centromere	$7.4x10^{-9}$ (--, 0.93)	1.00
Anti-RNA polymerase III	0.36 (0.04, 2.18)	0.29
Anti-U1-RNP	0.74 (0.08, 5.49)	0.77

Disclosure of Interests: None declared

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AB0654 ELEVATED CIRCULATING LEVELS OF IL-33 IN SYSTEMIC SCLEROSIS PATIENTS WITH INTERSTITIAL LUNG DISEASE

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by immune dysregulation, vasculopathy and progressive skin and internal organ fibrosis. Interstitial lung disease (ILD) remains a leading cause of morbidity and mortality in SSc patients. Interleukin 33 (IL-33) is a member of the IL-1 superfamily and has been previously described as a pro-fibrotic cytokine that exerts its function by inducing Th2 cells differentiation and stimulating the expression of TGF-β. Previous reports have revealed the role of IL-33 in numerous fibrotic diseases.

Objectives: The aim of the present study is to examine the serum levels of IL-33 and explore the possible correlation with clinical and laboratory features with a focus on pulmonary involvement in SSc patients.

Methods: A total number of fifty five (n=55) patients fulfilling the 2013 ACR/EULAR criteria for classification of SSc were enrolled in the study. Twenty five (n=25) age and sex matched healthy volunteers were used as controls. Detailed medical history, clinical and laboratory parameters were obtained for all included patients. Serum levels of IL-33 (pg/ml) were determined by enzyme-linked immunosorbent assay. GraphPad Prism 6,SPSS V.28 and RStudio were used for the performance of the statistical analysis.

Results: Of all included patients in the analyses, serum sample was obtained from 55 SSc patients, 51 women (92,7%) and 4 men (7,3%): thirty nine (n=39) with diffuse subset. Mean age was 56±12, mean disease duration was 5.5±6 years. No statistically significant difference was found between IL-33 levels in the patient group and healthy controls. Higher serum IL-33 levels were detected in patients with systemic sclerosis associated interstitial lung disease (SSc-ILD), median 27.9 pg/ml [IQR 4.8-52.9 pg/ml] compared to patients without SSc-ILD 1.12 pg/ml[1.12-45.8 pg/ml]. Decreased percent predicted forced vital capacity (FVC) and vital capacity (VC) correlated inversely with IL-33 levels (p<0,05). The ROC curve analysis with bootstrapping revealed diagnostic accuracy with AUC=0.65, p=0.05 for IL-33 circulating levels as a marker of interstitial lung involvement. A optimal cut-off value of 5 pg/ml was determined with respectively 75 % sensitivity and 60 % specificity.

Conclusion: IL-33 may be involved in the immunopathogenesis of pulmonary fibrosis. The results are consistent with previous studies. The present study is cross-sectional and further analyses and follow-up may be required to determine whether IL-33 may serve as a potential biomarker in the routine practice.

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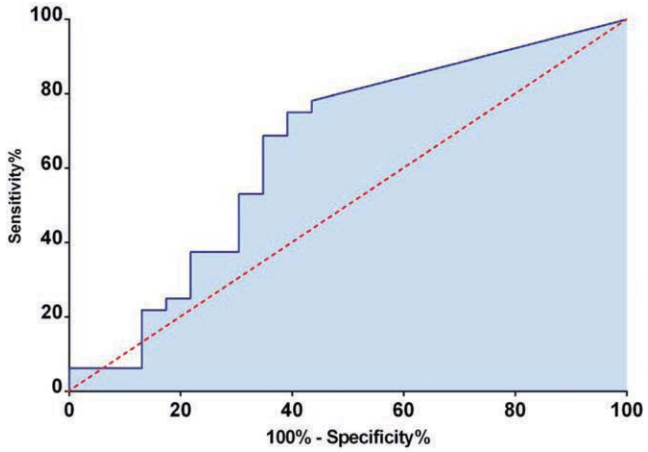

Figure 1.

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AB0655 CLINICAL AND IMMUNOLOGICAL FEATURES OF A PORTUGUESE COHORT OF MIXED CONNECTIVE TISSUE DISEASE

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Background: Various nationwide studies have been already published to better understand Mixed Connective Tissue Disease (MCTD) (1,2). However, Portuguese data is not available.

Objectives: To characterize clinical and immunological features of a Portuguese cohort of patients with MCTD.

Methods: Retrospective, multicenter study including adult-onset patients with clinical diagnosis of MCTD and fulfilling at least one of the following classification criteria: Sharp, Kasukawa, Alarcón-Segovia or the Kahn's criteria. Positivity to other autoantibodies besides anti-U1-RNP were allowed. SPSS was used for statistical analysis and significance level was defined as 2-sided $p<.05$.

Results: A total of 98 patients were included, with a mean age at diagnosis and disease duration of 40.5±13.7 and 7.0±6.5 years, respectively. Most patients were female (87.8%) and Caucasian (70.4%). Raynaud's phenomenon (96.9%), arthralgia/arthritis (94.9/74.5%) and puffy fingers (60.2%) were the most common and early manifestations. Gastroesophageal (GE), respiratory and muscular

involvement were also prevalent, mostly during the follow up, affecting 30.6%, 34.7% and 43.9% of the patients, respectively. Clinical and immunological characteristics are described in Table 1. Males were older at symptom's onset (65.0 VS 46.7, *p*=.035), having more respiratory involvement (OR=4.5, 95% CI 1.3-16.4), and positivity to anti-ACPA (OR=20.0, 95% CI: 3.1-129.4). GE involvement occurred more often in Caucasian patients (OR=3.8; 95% CI: 1.0-14.1), while anemia of chronic diseases (OR=2.7; 95% CI: 1.0-7.2), myositis (OR=3.6; 95% CI: 1.3-9.9) and constitutional symptoms (OR=3.2; 95% CI: 1.2-8.3) were more frequent in Afro-American patients, whose were also younger at disease (34.1 VS 50.6, *p*=.01). After a median follow-up time of 4 (IQR 8) years, 4 deaths occurred (4.1%), mostly (75%) due to infectious complications.

Table 1. Clinical and immunological characteristics

Clinical Manifestations	At presentation	Follow-up
Mucocutaneous system		
Raynaud's phenomenon, n (%)	85 (86.7)	95 (96.9)
Puffy hands, n (%)	48 (49.0)	59 (60.2)
SSc-like, n (%)	43 (44.8)	59 (60.8)
SLE-like, n (%)	28 (28.9)	35 (35.7)
Musculoskeletal system		
Arthralgia/Arthritis, n (%)/n (%)	81 (82.7) / 56 (57.1)	93 (94.9) / 73 (74.5)
Myositis, n (%)	26 (25.6)	43 (43.9)
Hematological system, n (%)	46 (46.9)	70 (71.4)
Respiratory system, n (%)	14 (14.3)	34 (34.7)
Cardiovascular system	3 (3.1)	4 (4.1)
Pulmonary hypertension*	2 (2.0)	15 (15.3)
Gastroesophageal involvement, n (%)	11 (11.2)	30 (30.6)
Renal involvement, n (%)	2 (2.0)	10 (10.2)
Neurological involvement, n (%)	6 (6.3)	14 (14.3)
Constitutional symptoms, n (%)	26 (26.5)	30 (30.6)
Immunological characteristics		
Anti-dsDNA, n (%)	21 (21.4)	
Anti-smith antibody, n (%)	21 (21.4)	
Anti-Ro/SSA, n (%)	31 (31.6)	
Anti-La/SSB, n (%)	7 (7.1)	
Anti-centromere, n (%)	3 (4.1)	
Rheumatoid Factor, n (%)	39 (39.8)	
Anti- anti-citrullinated protein antibodies, n (%)	6 (6.1)	
Antiphospholipid antibodies, n (%)	7 (7.1)	
Myositis antibodies, n (%)	9 (9.2)	
Complement activation, n (%)	27 (27.6)	
Hypergammaglobulinemia, n (%)	51 (52.0)	

Legend: Anti-dsDNA: anti-double stranded deoxyribonucleic acid antibody; SLE: systemic lupus erythematosus, SSc: systemic sclerosis. *No information regarding cardiac catheterism, then compatible alterations in the echocardiogram.

Conclusion: Raynaud's phenomenon, puffy fingers and arthritis were the most common manifestations in Portuguese patients, with similar proportions found in literature (1,2). However, we reported some differences in mucocutaneous, renal and serosa involvement and higher prevalence of probable pulmonary hypertension (1,2), which may be explained by the heterogeneity of the inclusion criteria. Except for respiratory, myositis, GE and constitutional symptoms, there were no differences regarding gender and ethnicity. Here, we characterize the largest cohort of MCTD in Portugal.

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AB0656

CAROTID INTIMA-MEDIA THICKNESS AS POTENTIAL MARKER OF CARDIOVASCULAR RISK IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY.

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Background: In several rheumatic diseases, persistent inflammatory state has been related to an accelerated atherosclerosis. Although the risk of cardiovascular (CV) events and atherosclerosis is increased in patients with Systemic Sclerosis (SSc), the exact underlying process has not been well defined. Indeed, inflammation is not a remarkable feature of systemic sclerosis pathogenesis as in other inflammatory rheumatic diseases.

Objectives: The aim of this study was to evaluate the carotid intima-media thickness (c-IMT) as potential marker of cardiovascular damage in SSc patients.

Methods: Between April and July 2021, 14 consecutive patients with SSc and 14 control subjects were enrolled in the study. Participants were aged > 18 and were able to provide written informed consent. Demographic, anthropometric and cardiovascular risk factors (smoking, arterial hypertension, diabetes and family history of CV events) were collected for each subject. Moreover, an evaluation of the sero-haematological characteristics was also performed. The c-IMT was assessed by the same qualified physician through a B-mode ultrasound examination. C-IMT values ≥ 0.9 mm were considered pathological.

Results: Demographic and clinical characteristics are shown in Table 1. Traditional CV risk factors were similar between groups, although BMI was significantly lower in SSc patients than controls (24±6 vs 26±2; *p*=0.019). Patients' median disease duration was 11 [5.0-16] years. Three patients had limited and 11 patients had diffuse disease according to LeRoy classification. Anti-nuclear antibodies were detected in all SSc subjects. Three patients expressed anti-centromere antibodies (ACA), other 3 are anti-Scl70 antibodies positive, only one patient showed anti-RNA polymerase III antibodies and 7 patients did not presented specific SSc autoantibodies. SSc patients had slightly increased c-IMT compared with controls, however the difference did not reach statistical significance (median c-IMT 0.84 [0.72-0.91] vs median c-IMT 0.68 [0.63-0.82], *p*=0.164).

Table 1.

	Controls (n=14)	SSc patients (n=14)	*p*
Demographic and Anthropometric			
Age (years)	60±4	61±13	0.836
Gender, female (%)	14 (100)	14 (100)	-
Smoking habit, yes (%)	5 (36)	5 (36)	1
AH, yes (%)	7 (50)	8 (57)	0.705
T2DM, yes (%)	5 (36)	4 (29)	0.686
Dyslipidemia, yes (%)	6 (43)	4 (29)	0.430
CVD familiarity, yes (%)	6 (43)	4 (29)	0.430
Total Cholesterol (mg/dl)	189 [167-218]	170 [128-197]	0.094
LDL (mg/dl)	117 [96-139]	100 [80-115]	0.125
HDL (mg/dl)	61 [50-77]	56 [45-63]	0.329
Triglycerides (mg/dl)	107 [62-133]	107 [69-151]	0.667
Treatment			
Iloprost	0 (0)	14 (100)	$1.21x10^{-7}$
ERA, yes (%)	0 (0)	9 (64)	$2.71x10^{-4}$
HMG-CoA reductase inhibitors, yes (%)	6 (43)	4 (29)	0.430

Continuous data are presented as mean ± standard deviation or as median and interquartile range. Binomial data are shown as frequencies and percentages. The overall p-value was calculated by the Mann–Whitney non-parametric test for independent samples and by Chi-squared test as appropriate.

Conclusion: In our study patients with SSc had a non-significative increased c-IMT compared with controls (*p*=0.164), however different results have been reported in previous studies. Although it is not clear whether c-IMT may be considered a marker of cardiovascular damage in SSc, further studies are needed to clarify its role.

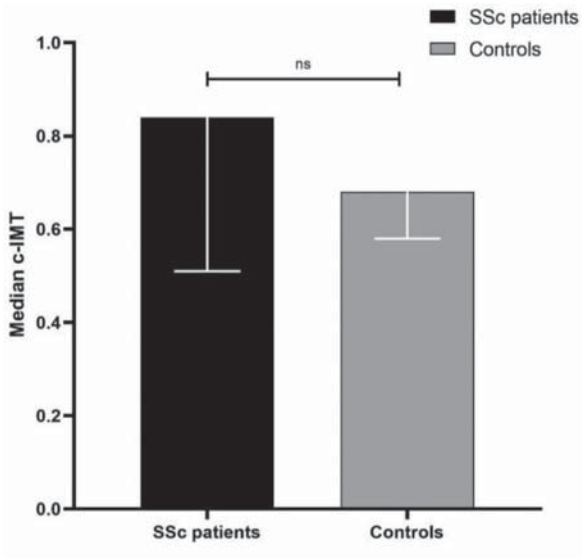

Figure 1. Median c-IMT among groups. Data are shown as median and range. P-values were calculated by the Mann–Whitney non-parametric test for independent samples.

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AB0657

SEVERITY AND IMPACT OF GASTROINTESTINAL SYMPTOMS IN PATIENTS WITH SSC-ILD TREATED WITH NINTEDANIB: DATA FROM SENSCIS-ON

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Background: Gastrointestinal (GI) involvement is a common manifestation of systemic sclerosis (SSc) and a frequent side-effect of drugs used to treat SSc. In the SENSCIS trial, nintedanib reduced the rate of decline in forced vital capacity (FVC) in patients with SSc-associated interstitial lung disease (SSc-ILD), with an adverse event profile characterised predominantly by GI events.

Objectives: To assess the severity and impact of GI symptoms on quality of life in patients treated with nintedanib in the open-label extension trial, SENSCIS-ON.

Methods: Patients with SSc-ILD who completed the SENSCIS trial or a drug–drug interaction (DDI) study of nintedanib and oral contraceptive were eligible to enter SENSCIS-ON. Patients who received nintedanib in SENSCIS (up to 100 weeks) and continued nintedanib in SENSCIS-ON comprised the "continued nintedanib" group. Patients who received placebo in SENSCIS and initiated nintedanib in SENSCIS-ON, or who received nintedanib for a short time in the DDI study, comprised the "initiated nintedanib" group. We assessed changes in scores on the UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract (UCLA SCTC GIT) questionnaire v2.0 from baseline to week 52. This questionnaire comprises 7 scales measuring the severity and impact of GI symptoms: reflux, distension or bloating, faecal soilage, diarrhoea, constipation, emotional well-being, social functioning. Each scale is scored from 0 to 3 except for the diarrhoea scale (0 to 2) and constipation scale (0 to 2.5). The total score, the mean of the scores for the scales except constipation, ranges from 0 to 2.83, with higher scores indicating worse symptoms.

Results: The "continued nintedanib" group comprised 197 patients and the "initiated nintedanib" group comprised 247 patients (231 from SENSCIS). Of these, 178 and 218 patients, respectively, provided a total UCLA SCTC GIT score at baseline. At baseline, mean (SD) total scores were 0.33 (0.33) and 0.33 (0.34) in the continued nintedanib and initiated nintedanib groups, respectively. Mean (SD) scores on the 7 scales ranged from 0.16 (0.52) to 0.70 (0.73) in the continued nintedanib group and from 0.13 (0.43) to 0.64 (0.68) in the initiated nintedanib group. Increases (worsening) in scores were observed in both groups from baseline to week 52, except for on the constipation scale (Figure 1). Based on the total score, between baseline and week 52, the proportion of patients with moderate or severe or very severe GI symptoms increased, but 45.7% and 39.7% of patients in the continued nintedanib and initiated nintedanib groups, respectively, had no or mild GI symptoms at week 52 (Table 1).

Table 1. Changes in severity and impact of gastrointestinal symptoms based on UCLA SCTC GIT total score between baseline and week 52 of SENSCIS-ON

		Baseline				
Week 52		None or mild	Moderate	Severe or very severe	Missing	Total
	Continued nintedanib					
	None or mild	81 (41.1)	5 (2.5)	0	4 (2.0)	90 (45.7)
	Moderate	38 (19.3)	10 (5.1)	0	1 (0.5)	49 (24.9)
	Severe or very severe	13 (6.6)	14 (7.1)	7 (3.6)	1 (0.5)	35 (17.8)
	Missing	6 (3.0)	3 (1.5)	1 (0.5)	13 (6.6)	23 (11.7)
	Total	138 (70.1)	32 (16.2)	8 (4.1)	19 (9.6)	197 (100)
	Initiated nintedanib					
	None or mild	87 (35.2)	6 (2.4)	1 (0.4)	4 (1.6)	98 (39.7)
	Moderate	35 (14.2)	12 (4.9)	2 (0.8)	3 (1.2)	52 (21.1)
	Severe or very severe	8 (3.2)	7 (2.8)	4 (1.6)	1 (0.4)	20 (8.1)
	Missing	37 (15.0)	15 (6.1)	4 (1.6)	21 (8.5)	77 (31.2)
	Total	167 (67.6)	40 (16.2)	11 (4.5)	29 (11.7)	247 (100)

Data are n (%) of patients. None or mild=scores of 0 to 0.49; moderate=scores of 0.5 to 1; severe or very severe=scores of 1.01 to 3.

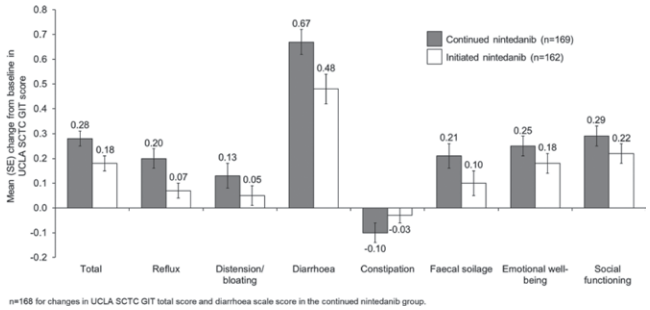

Figure 1. Changes in UCLA SCTC GIT scores from baseline to week 52 of SENSCIS-ON

Conclusion: In the SENSCIS-ON trial, the majority of patients with SSc-ILD treated with nintedanib had no or mild GI symptoms at baseline. A small worsening in GI symptoms was observed over 52 weeks. Diarrhoea had the greatest impact, reflecting the adverse event profile of nintedanib. Recommendations for the management of diarrhoea in patients treated with nintedanib should be implemented in clinical practice.

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AB0658

NOCEBO EFFECT ON DIARRHOEA REPORTED IN THE SENSCIS TRIAL OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD)

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Background: Unfavourable effects observed after administration of placebo that may be attributed to factors such as expectation or conditioning are known as nocebo effects. Prior to initiation of the SENSCIS trial, diarrhoea was a known side-effect of nintedanib.

Objectives: To investigate whether a nocebo effect contributed to reporting of diarrhoea in the SENSCIS trial.

Methods: The SENSCIS trial enrolled patients with systemic sclerosis (SSc) with first non-Raynaud symptom in the prior ≤7 years and ≥10% extent of fibrotic ILD on high-resolution computed tomography. Patients were randomised to receive nintedanib or placebo until the last patient had reached week 52 but for ≤100 weeks. A follow-up visit was conducted 28 days after the end of treatment. Adverse events were reported by investigators irrespective of causality and coded according to the Medical Dictionary for Regulatory Activities. We analysed the incidence of diarrhoea adverse events in the on-treatment period (*i.e.,* events with onset between the first intake of trial drug intake and the last intake plus 7 days) and in the post-discontinuation period (*i.e.,* events with onset between the first day after the on-treatment period and the end of the follow-up period) in the nintedanib and placebo groups. Incidence rates were calculated as the number of patients with diarrhoea adverse events divided by the time at risk.

Results: In the on-treatment period (time at risk: 277.8 patient-years), the rate of diarrhoea adverse events in the placebo group (n=288) was 33.1 per 100 patient-years. In the post-discontinuation period (time at risk: 41.9 patient-years), the rate of diarrhoea adverse events in the placebo group (n=284) was 19.1 per 100 patient-years. In the on-treatment period (time at risk: 105.1 patient-years), the rate of diarrhoea adverse events in the nintedanib group (n=288) was 209.3 per 100 patient-years. In the post-discontinuation period (time at risk: 53.7 patient-years), the rate of diarrhoea adverse events in the nintedanib group (n=283) was 5.6 per 100 patient-years.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, the rate of diarrhoea adverse events in the placebo group fell after trial drug was discontinued. This suggests that a nocebo effect may have contributed to the diarrhoea adverse events reported in the SENSCIS trial.

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Disclosure of Interests: Oliver Distler Speakers bureau: OD has/had relationships with the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three calendar years: Speaker fee: Bayer, Boehringer Ingelheim, Janssen, Medscape, Consultant of: OD has/had relationships with the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three calendar years: Consultancy fee: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, 4P Science, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Prometheus, Roivant, Sanofi and Topadur OD has/had relationships with the following companies in the area of potential treatments for arthritides in the last three calendar years: Consultancy fee: Abbvie, Grant/research support from: OD has/had relationships with the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three calendar years: Research Grants: Boehringer Ingelheim, Kymera, Mitsubishi Tanabe, Kristin Highland Speakers bureau: Actelion Pharmaceuticals (Jansen), Bayer Healthcare, Boehringer Ingelheim, United Therapeutics, Paid instructor for: Acceleron Pharmaceuticals, Actelion Pharmaceuticals, Bayer Healthcare, Boehringer Ingelheim, Gilead Sciences, United Therapeutics, Consultant of: Boehringer Ingelheim, Forsee Pharmaceuicals, Genentech, United Therapeutics, Grant/research support from: Acceleron Pharmaceuticals, Actelion Pharmaceuticals, Bayer Healthcare, Boehringer Ingelheim, Genentech, Gossamer Bio, Eiger Pharmaceuticlas, Lilly Pharmaceuticals, Reata Pharmaceuticals, United Therapeutics, Viela Bio (Horizon Pharmaceuticals), Arata Azuma Speakers bureau: AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Consultant of: Boehringer Ingelheim, Kyorin Pharma, Taiho Co., Toray Medical Co., Grant/research support from: Boehringer Ingelheim, Taiho Co., Corinna Miede Employee of: Corinna Miede is an employee of mainanalytics GmbH that is contracted by Boehringer Ingelheim, Margarida Alves Employee of: Margarida Alves is an employee of Boehringer Ingelheim, Petros Sfikakis: None declared

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AB0659

RECRUITMENT AND PREVALENCE OF MIXED PHENOTYPE MACROPHAGES IS PROMINENT IN BRONCHOALVEOLAR LAVAGE (BAL) OF SYSTEMIC SCLEROSIS (SSC) PATIENTS WITH INTERSTITIAL LUNG DISEASE (ILD).

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Background: ILD is a major problem in SSc for which no disease-modifying therapies are available. Many observations suggest monocyte/macrophage involvement in SSc and might be a key component in the development of ILD. Macrophages polarize into M1 and M2 phenotypes and thereby orchestrate inflammation and subsequent fibrosis by responding to and producing a vast array of cytokines and chemokines. Differences in the levels of the chemokines might explain variations in the recruitment and activation of macrophages in affected organs. In SSc, monocytes with a mixed phenotype (expressing both M1 and M2 markers) are prominent in peripheral blood. No previous study has investigated the mixed phenotype macrophages locally on the lung level.

Objectives: a-to measure macrophage-related chemokines in BAL fluid obtained from SSc-ILD and SSc-no-ILD patients.

b-to investigate levels of M1 and M2 macrophage markers in BAL cells obtained from SSc-ILD and SSc-no-ILD patients.

Methods: A cross-sectional study in which BAL procedure was performed on 15 treatment-naïve SSc patients divided into two groups according to lung involvement determined by HRCT and lung function tests: SSc-no-ILD group and SSc-ILD group (Table 1). Levels of chemokines (CCL18, CXCL-10 and CCR2) were analysed using ELISA. mRNA expression levels of CD86 (M1; inflammatory macrophage marker) and CD206 (M2; fibrogenic macrophage marker) in cells isolated from BAL were assessed using RT-qPCR. In addition, immunofluorescence studies and flow cytometry analyses were performed to evaluate the expression of M1 (CD86) or M2 (CD206) markers in BAL macrophages.

Table 1. Patient characteristics

	no ILD	ILD
Number of patients	8	7
Age	57 (51-68)	60 (53-73)
Female	75%	57%
Raynauds phenomenon	100%	85%
Age start of Raynauds	36 (22-53)	56 (41-66)
Age start of non-Raynauds	50 (33-60)	49 (36-68)
Skin thickening	50%	43%
Digital ulcer at this moment	0%	29%
Digital ulcer in the past	38%	29%
Pitting scars	38%	43%
Telangiectasia	50%	43%
Calcinosis	13%	29%
Cardiac	25%	14%
Gastro-intestinal	88%	43%
Kidney	0%	0%

Results: Macrophages were the predominant immune cell population in BAL of SSc patients (73%). The levels of CCL18, CCR2 and CXCL10 were slightly elevated in the SSc-ILD group compared to the SSc-no-ILD (Figure 1.1). RT-qPCR data showed that CD86 expression was elevated in the SSc-ILD group while no difference was observed in CD206 expression between the two groups (data not shown). The SSc-ILD group had higher proportions of double-positive (CD86+, CD206+) macrophages than SSc-no-ILD which, in contrast, had higher proportions of CD86+, CD206- macrophages (Figure 1.2). These results were supported by fluorescent microscopy images in which the SSc-ILD group had higher CD86 and CD206 expression than the SSc-no-ILD (Figure 1.3). Double staining clearly showed a more prevalent mixed activation of macrophages in the SSc-ILD group.

Conclusion: In this pilot study, recruitment and activation of mixed phenotype macrophages was more prominent in SSc-ILD than in SSc-no-ILD. Although levels of chemokines were not profoundly different between both groups, studying extensively the macrophage activation patterns in BAL provided novel findings regarding differences between the two groups. Since SSc is characterised by inflammatory and fibrotic phases, the mixed polarization of macrophages we showed for the first time in SSc-ILD patients on an organ level is a key aspect in such disease and could potentially serve as a target for therapeutics.

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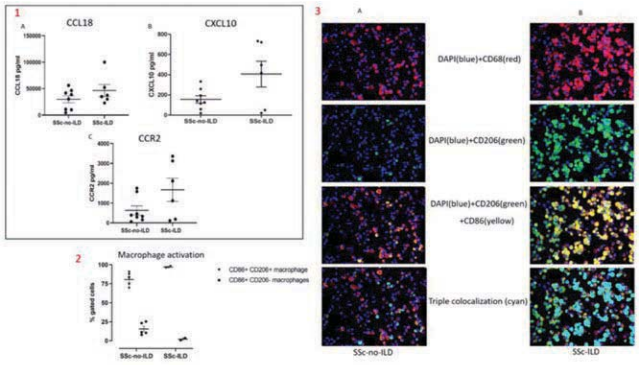

Figure 1: Macrophage-related chemokine levels, and M1/M2 analysis in SSc and SSc-ILD patients. (1) Protein levels in 6x concentrated BAL expressed in pg/mL. (A-C) elevated levels of CCL18, CXCL-10 and CCR2, respectively, in concentrated BAL of SSc-ILD patients compared to SSc-no-ILD, N=14. (2) Percentage of gated cells using CD86 and CD206 surface markers to distinguish M1 from mixed M1 and M2 macrophages in BAL cells, N=7. (3) Fluorescence microscopy images of cytospin preps stained with CD68 (pan-macrophage marker), CD86 and CD206 MoAB-conjugated fluorescence dyes, and DAPI for nuclei visualization (magnification: 20x). A) SSc-ILD cytospin prep showing prevalent staining of both CD86 and CD206 compared to SSc-no-ILD. B) SSc-no-ILD cytospin prep shows less activation of macrophages reflected by low prevalence of CD86 (yellow) and CD206 (green) stainings. No statistical testing was performed due to the small sample size.

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AB0660 LONG-TERM EFFECT OF COMBINATION THERAPY WITH RITUXIMAB AND MYCOPHENOLIC ACID ON CARDIAC MANIFESTATIONS, PULMONARY FUNCTION AND SKIN FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Cardiac manifestations in systemic sclerosis (SSc) can be either due to the fibrotic and vascular process or secondary to pulmonary arterial hypertension (PAH), cardiac inflammation, or renal crisis. Despite being one of the leading causes of death in SSc, cardiac involvement and its therapeutic options have been poorly studied. According to the ACR/EULAR recommendations, therapy with cyclophosphamide (CP) is applied to patients with cardiac manifestations. However, in case of inadequate response to CP, there are no other therapeutics evaluated.

Objectives: The aim of this retrospective analysis was to explore the efficacy of a therapy with rituximab and mycophenolic acid (MPA), especially in cases of CP failure or therapy induced cardiac toxicity

Methods: 14 Patients with SSc and cardiac involvement (defined as troponin T elevation plus right- or left ventricular systolic or diastolic dysfunction, myocarditis, pericarditis, right heart failure secondary to PAH, or arrhythmias) were analysed. Two patients each showed concomitant myositis and rheumatoid arthritis, respectively. Twelve patients were initially treated with CP and two patients with methotrexate (MTX). Due to a disease progress (either cardiac involvement, skin fibrosis or lung function) a therapy with rituximab and MPA was initiated [1] These patients were followed for up to five years.

Results: Before initiation of CP or MTX electrocardiogram showed arrhythmias (atrial fibrillation, conduction blocks, multifocal ventricular extrasystoles (VES)) in 9 patients. Echocardiography revealed abnormalities in 10 patients including reduced left-ventricular ejection fraction (LV-EF), diastolic dysfunction, mitral regurgitation, or aortic aneurysm. 3 patients had PAH, 2 patients were diagnosed with post capillary pulmonary hypertension. Cardiac MRI revealed signs of myocarditis in 4 patients. 4 patients required cardiac resynchronization therapy or pacemaker implantation. Moreover, body plethysmography showed a reduction in forced vital capacity (FVC) in 12 patients, suggestive of restrictive lung disease. Under therapy with CP 11 patients had suffered from disease progress, 1 patient developed relapsing pneumonias and the 2 patients with overlap rheumatoid arthritis developed cardiac disease manifestations on MTX monotherapy. Consequently, rituximab 1000 mg q12weeks and MPA 1000 mg bid were initiated. Under this combination troponin T decreased in all patients (p=0.0002), LV-EF improved in 5, remained normal in 7 and deteriorated in 2 patients. The rate of VES improved in 8 patients. In one patient, myocarditis resolved completely (MRI). Moreover, pulmonary artery systolic pressure, measured by echocardiography, improved in all patients diagnosed with PAH under stable therapy. The modified Rodnan skin score improved in all patients, FVC improved in 7 patients, remained stable in 6 and decreased in the patient with overlap myositis. Rituximab infusions could be extended (1000 mg q24weeks) after 24-36 months of treatment in 11 patients. All patients showed peripheral blood depletion of B cells without noticed severe IgG deficiency. While 11 patients did not develop severe complications 2 patients died during follow-up of pneumonia and cardiogenic shock (overlap myositis), respectively and one patient developed a relapse of lung cancer with cerebral metastasis.

Conclusion: Therapy with rituximab and MPA is a promising alternative. However, its use requires risk stratification of patients with respect to adverse side effects which needs to be explored in future studies.

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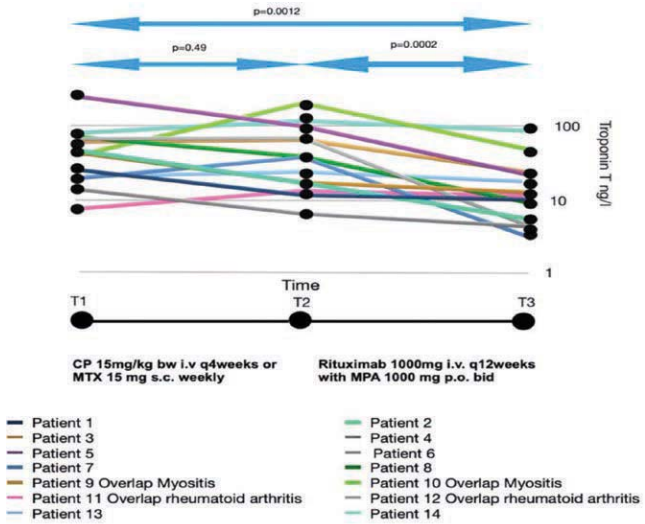

Fig.1: Change in measured level of troponin T before initiation of therapy with CP or MTX (T1), under CP or MTX and before initiation of rituximab and MPA (T2) and after two to five years of therapy with Rituximab and MPA (T3). All patients described showed a decrease in troponin T (T1 to T3 p=0.0012, T2 to T3 p=0.0002 and T1 to T2 p=0.49).

Disclosure of Interests: None declared

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AB0661 NEUROPSYCHOLOGICAL OUTCOME OF CHILDREN BORN TO WOMEN WITH SYSTEMIC SCLEROSIS ASSESSED THROUGH A SELF-ADMINISTERED MULTIDISCIPLINARY QUESTIONNAIRE: RESULTS FROM A MONOCENTRIC COHORT

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Background: In the last years, the rate of successful pregnancies has significantly increased in Systemic Sclerosis (SSc)[1] women. However, the long-term outcome of their children remains an unexplored issue.

Objectives: To evaluate the neuropsychiatric (NP) outcome of children born to SSc mothers.

Methods: An ad-hoc questionnaire, regarding different aspects of child's neurodevelopment (ND) (3 sections: childhood [0-5 years]; scholar age [6-11 years]; adolescence [12-18 years]), was created and administered to female SSc patients (ACR/EULAR 2013 criteria) attending our outpatient clinic during 2021 and who had at least 1 child. Children's NP characteristics were compared between 3 subgroups: A) born >10 years before SSc diagnosis; B) born ≤10 years before SSc diagnosis; C) born after SSc diagnosis. Results below are expressed as number/total number of answers collected for each question.
Results: 100 SSc women reported 189 pregnancies: 152 resulted in 154 live births (2 twin pregnancies).
At least one NP alteration was reported in 42/119 (35%) subjects, more frequently in group B (57%), as compared to group A (31%, *p:0.07*) and group C (30%, *p:0.09*) although not statistically significant (Figure 1). Sleep irregularities were the most frequently reported disorder (15/42, 36%). Comparisons between the 3 subgroups for every NP outcome evaluated are shown in Table 1: overall, a higher rate of NP alterations were reported in children belonging to group B.

Table 1. Analysis of NP outcomes: comparison of the 3 subgroups.

	A n=103	B n=19	C n=32
N° of subjects evaluated for DISORDERS IN CHILDHOOD	103/103	19/19	32/32
Sleep irregularities	6/79 (8)*	4/13 (31)*	5/27 (19)
Motor difficulties	0/77 (3)°	2/13 (15)°	2/26 (8)
Difficulty in relationships	0/78 (0)	1/11 (9)	2/26 (8)
Difficulty in non-verbal communication skills	0/78 (0)	1/11 (9)	2/26 (8)
Difficulty in verbal communication skills	1/77 (1)	1/12 (8)	2/26 (8)
Difficulty in social integration	6/77 (8)	3/12 (25)	1/25 (4)
Cognitive difficulties	0/77 (0)	1/12 (8)	0/26 (0)
N° of subjects evaluated for DISORDERS IN SCHOLAR AGE	103/103	17/19	17/32
Difficulty in school lessons/homework	7/77 (9)	3/12 (25)	0/15 (0)
Behavioral problems during school period	4/76 (5)	1/12 (8)	1/15 (7)
School year repetition	11/76 (15)	2/13 (15)	0/15 (0)
N° of subjects evaluated for DISORDERS IN ADOLESCENCE	101/103	14/19	11/32
Difficulty in managing anger and aggression	4/75 (5)	0/11 (0)	0/10 (0)
Behavioral alterations	0/75 (0)	0/11 (0)	0/10 (0)
Difficulty in conduct	2/73 (3)	0/11 (0)	2/10 (20)
Mood alterations	1/73 (1)	1/11 (9)	0/10 (0)
Alterations of the feeding behavior	1/75 (1)	0/11 (0)	0/10 (0)
Anxiety problems	1/75 (1)	1/10 (10)	0/10 (0)

Results are presented as number/total number (%) of answers collected for each question. Variables were compared with Chi Squared/exact Fisher test. **p=0.03*; *°p=0.02*.

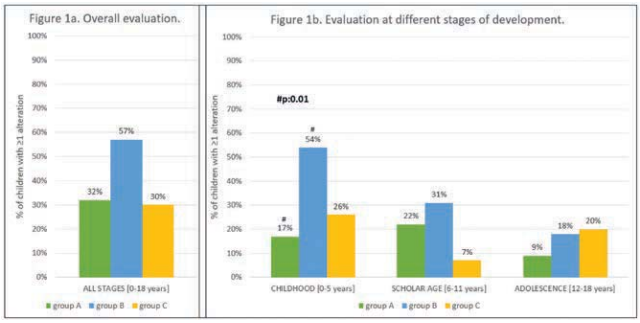

Figure 1. Children with ≥1 NP alteration: comparison of the 3 subgroups.

In addition, SSc mothers declared that 7/123 (6%) children underwent a NP evaluation leading to a diagnosis in 3 cases: 1 cognitive delay, 1 learning disorder (LD) and 1 autism spectrum disorder (ASD). These children were born 1 and 5 years before and 3 years after SSc diagnosis, respectively. The prevalence of these diagnoses (0.8%) does not differ from general pediatric population.
Conclusion: Children born to SSc mothers, had prevalence of major NP alterations (cognitive deficits, LDs, ASDs) similar to general pediatric population. A higher frequency of minor ND disorders, especially sleep irregularities, was observed in children within 10 years before maternal diagnosis, compared to the other groups, possibly suggesting an impact of maternal chronic disease on the relationship with child in the first years of life. To confirm these self-reported preliminary data, the extension of the study will consist in a systematic NP evaluation proposed to all the offspring of SSc mothers aged ≤18 years.

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AB0662 **ELEVATED FECAL CALPROTECTIN IN EARLY SYSTEMIC SCLEROSIS**

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Background: Gastrointestinal (GI) morbidity is prevalent in systemic sclerosis (SSc), causing a reduction in quality of life and increased mortality, but has been difficult to assess objectively [1]. Elevated levels of fecal calprotectin (F-cal), a biomarker of GI inflammation, has previously been observed in patients with SSc [2]. F-cal has not been explored in early SSc and its diagnostic potential in the classification of SSc has not been studied.
Objectives: Our objectives were; 1) study F-cal levels in early SSc; 2) investigate the discriminatory power of F-cal; 3) explore F-cal in relation to GI features of SSc.
Methods: Consecutive referred patients with suspected new-onset SSc without concurrent non-SSc GI disease were invited to this study. Patients were classified as SSc if meeting ACR-EULAR criteria, or SSc mimickers if they did not. GI symptoms and use of NSAID or PPI was noted. F-cal was measured and levels >50ug/g were classified as elevated. F-cal was also measured in age- and sex matched controls without rheumatological disease.
Results: Of 137 patients, 92 were classified as SSc and 45 as SSc mimickers. Elevated F-cal was significantly more common in SSc patients compared to the control group (38% vs 7.3%; p < 0.001) but not compared to the SSc mimicker patients (38% vs 31%; p = 0.427). The median F-cal level was higher in SSc patients compared to controls (35 µg/g vs ≤30 µg/g; p ≤ 0.001) but not compared to the SSc mimicker patients (35 µg/g vs ≤30 µg/g; p = 0.248). Elevated F-cal was not associated with any GI symptoms. Elevated F-cal was more common in patients who used PPI (OR 7.14; 95% CI 2.56-29.93; p < 0.001).
Conclusion: In this study, we demonstrate that elevated levels of F-cal are prevalent already in the early stages of SSc. These results are in line with previous data suggesting that GI involvement may be present in early SSc.

Table 1. Frequency of GI features and association to F-cal elevation (n = 92)

GI features (n, %)	Normal F-cal, n = 57	Elevated F-cal, n = 35	Odds Ratio (95% CI)
Dysphagia	19 (35%)	12 (34%)	0.99 (0.41-2.41)
Reflux symptoms	33 (59%)	23 (68%)	1.46 (0.60-3.56)
Fecal incontinence	9 (16%)	3 (8.6%)	0.50 (0.08-2.22)
Patient-reported involuntary weightloss	11 (20%)	8 (23%)	1.21 (0.43-3.39)
Dilated esophagus on HRCT	8 (16%)	8 (28%)	1.95 (0.64-5.94)
NSAID use	12 (21%)	6 (17%)	0.78 (0.26-2.30)
PPI use	23 (40%)	29 (83%)	7.14 (2.56-19.93)

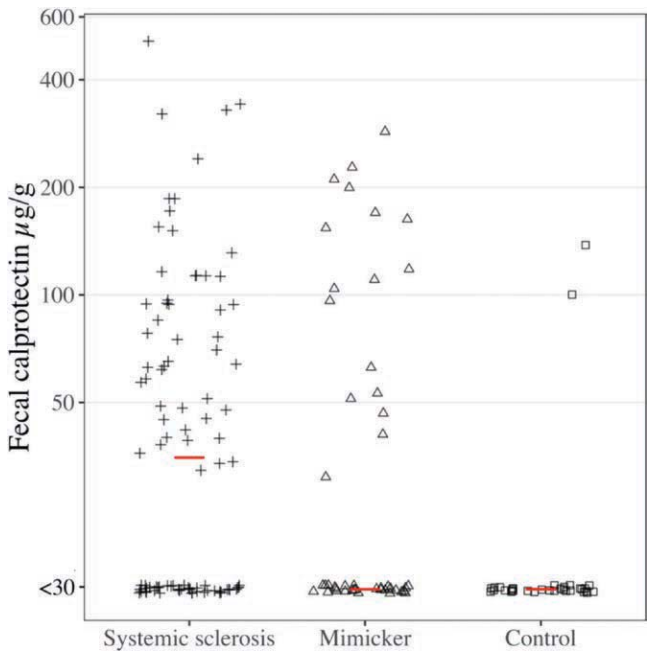

Figure 1. F-cal measurements by group. Median value represented by horizontal bar.

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AB0663 BICENTRIC OBSERVATIONAL STUDY ON THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC SCLEROSIS OVERLAP SYNDROME

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Background: The rheumatoid arthritis (RA)/systemic sclerosis (SSc) overlap syndrome is a rare and understudied association. It affects 5% of patients with SSc. Only open studies evaluating biological drugs (bDMARDs) have reported encouraging results, particularly on joint involvement. The management of these patients is therefore not codified.
Objectives: The objective was to analyze in real conditions the therapeutic strategy and the response to bDMARDs, with a focus on joint involvement.
Methods: We retrospectively analyzed over a 10-year period the clinical, biological, radiographic characteristics and therapeutic management of patients meeting the ACR/EULAR diagnostic criteria for RA and SSc in two academic centers. Response to bDMARDs was assessed according to EULAR and if unavailable according to therapeutic maintenance. The evolution of lung function test was also evaluated.
Results: Twenty-two patients were identified. Interstitial lung involvement was common (n=11). Only 7 patients were treated with csDMARD alone. The most commonly used drug was methotrexate. The use of bDMARDs was frequent (15/22), significantly greater in patients with rheumatoid factors (OR 26.7; p=0.004) and with a trend in patients with higher levels of anti-CCP (160 vs 15 IU; p=0.11) or diffuse interstitial lung disease (OR 10.6; p=0.063). Tocilizumab was the most selected therapy (n = 8) followed by rituximab (n = 5), abatacept, and anti-TNFs (n = 4 respectively). We evaluated 21 treatment sequences, 19 of which were evaluated according to EULAR response criteria. bDMARDS that inhibits the activation of lymphocytes (abatacept, rituximab) generally resulted in a good or moderate response (n = 9/10) with a significant decrease in DAS28 at 6 months (-1.75; p = 0.016). Cytokine inhibitors (tocilizumab, etanercept, infliximab) were less likely to achieve good or moderate control of joint involvement (n = 3/9) with a smaller decrease in DAS28 at 6 months (-0.79; p = 0.36). Two tocilizumab sequences were stopped early due to intolerance and could not be evaluated. One patient received tofacitinib with a good clinical response but was discontinued at 9 months for intolerance. Lung function test data did not change significantly on bDMARD.
Conclusion: In patients with rheumatoid arthritis (RA)/systemic sclerosis (SSc) overlap syndrome, bDMARDS that inhibits the activation of lymphocytes (abatacept, rituximab) resulted in more frequent and greater improvement in joint involvement than cytokine inhibitors (tocilizumab, etanercept, infliximab).
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AB0664 OVARIAN RESERVE IN SYSTEMIC SCLEROSIS

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Background: The low prevalence of pregnancy in women with systemic sclerosis (SSc) is due to multi-factorial causes, including premature ovarian insufficiency (POI). Anti-Mullerian hormone (AMH) is one of the primary parameters for assessing reproductive function and ovarian reserve. The levels of AMH correlates with the residual follicular pool among women of reproductive age.
Objectives: To assess AMH levels in SSc female patients of child-bearing potential, and analyze the relationship between AMH levels and disease severity, as well as the relationship between serum AMH levels and different therapeutic regimens.
Methods: The study group included 48 women with SSc aged 20-40 years, and the control group included 15 age-matched healthy women. Pts' mean age was 32,9 [28;37] yrs, disease duration was 6,3 [3;10] yrs. Diffuse cutaneous subset of the disease had 41,7%, limited in 41,7% and overlap in 16,6% pts. AMH levels was measured using ELISA. AMH reference values ranged within 1.0-10.6 ng /ml. Values <1.0 were interpreted as a decreased ovarian reserve.
Results: Mean AMH level was 2.8 ng/ml in SSc pts, and 3.1 ng/ml in the control group, showing no statistical difference. A decrease in ovarian reserve (AMH less than 1.0 ng/ml) was significantly more common in SSc pts compared to controls (45,8% vs. 13%, p<0,05).

Table 1. AMH and forms of SSc

form	diffuse, n=20	limited, n=20	overlap, n= 8	p
Mean AMH	1,1 [0,06-1,5]*	3,3 [0,4-5,6]*	2,3 [0,7;3,4]	* 0,03
AMH >1 ng /ml, n (%)	13 (65%)*	7 (35%)*	2 (25%)	*0,05

Mean AMH levels was significantly lower in the diffuse SSc in comparison with the limited SSc. A redaction of ovarian reserve (AMH less than 1.0 ng / ml) was more often observed in diffuse form of SSc compared to limited form (65% vs 35%), p=0.05.

Table 2. AMH and course of SSc

course	acute, n=5	subacute, n=19	chronic, n= 25	p
Mean AMH	1,2 [0,01-1,7]	0,9 [0,05-1,3]	3,5 [0,7;5,6]	0,01
AMH >1 ng /ml, n (%)	3 (60%)	13 (68,4%)*	6 (24%)*	*0,03

Mean AMH levels was significantly lower in acute and subacute course of SSc. A decrease of ovarian reserve was significantly more often observed in subacute course compared to chronic course of SSc (68% vs 24%, p=0,03).

CYC	CYC (+), n=14	CYC (-), n=34	p
Mean AMH	0,8 [0,08-1,07]	2,8 [0,4;3,6]	0,01
AMH >1 ng /ml, n	9 (64,3)	13 (32,2)	ns

Mean AMH levels was significantly lower in pts with SSc receiving CYC. Correlation analysis revealed a negative correlation between AMH and cyclophosphamide (CYC) therapy (r=-0.33, p>0.05), with erythrocyte sedimentation rate (r=-0.36), heart damage (r=-0.32) and gastrointestinal involvement (r=-0.31), digital ulcers (r=-0.33) and digital pitting scars (r=-0.28). Correlation with other clinical manifestations, immunological markers and immunosuppressive therapy of SSc wasn't found. In five patients who receivied CYC earlier, the levels of AMH was within normal values (the total dose of CYC did not exceed 4 g).

Conclusion: Ovarian reserve was significantly more often reduced in women with SSc compared to healthy controls. Mean AMH levels was significantly lower in the diffuse SSc compared to the limited SSc. Reduction of ovarian reserve was more often observed in diffuse form SSc. Mean AMH level was significantly lower in acute and subacute course of SSc. A decrease of ovarian reserve was significantly more often observed in subacute course SSc compared to chronic course. The levels AMH negatively correlated with CYC therapy, erythrocyte sedimentation rate, heart and gastrointestinal tract involvement, digital ulcers and digital scars. CYC therapy negatively affected the ovarian function, and most likely in a dose-dependent manner.
Disclosure of Interests: None declared
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AB0665 TURKISH VALIDATION OF THE 'COCHIN (DURUOZ) HAND FUNCTION SCALE' IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Hand impairment is the main challenge for patients with systemic sclerosis (SSc) and may arise from inflammatory arthritis, joint contractures, tendon friction rubs (TFRs), Raynaud's phenomenon (RP), digital ulcers (DU), puffy hands, skin sclerosis, acro-osteolysis, or calcinosis. There is not yet a tool which can objectively measure hand functions in scleroderma patients both in daily practice and for research purposes.
Objectives: To adapt and validate the Turkish version of Cochin (Duruoz) hand function scale (CHFS) and contribute to the development of outcome measures with good metric properties assessing hand disability in SSc (1).
Methods: Ninety one consecutive patients who fulfilled the 2013 ACR/ EULAR SSc classification criteria for SSc were enrolled in the study. Disease

related involvements and physical examination findings of the patients were recorded. Participants filled out the self-administered questionnaire of the Turkish version of the CHFS. Modified Rodnan skin scores of the patients were calculated, bilateral hand extension and fingertip-palm distances were measured, grip strength was evaluated with hydrolic hand dynamometer. We evaluated convergent validity by testing the correlation between CHFS and related components of Short Form 36 version 2 (SF-36v2) and Scleroderma Health Assessment Questionnaire (sHAQ). Discriminant validity was evaluated by stratifying patients according to hand related involvements and disease subtypes. Thirty of the patients re-filled the CHFS questionnaire two weeks after the first visit.

Results: Demographic data and disease characteristics of the patients shown in Table 1. For the convergent validity, the CHFS significantly correlated with the sHAQ, Raynaud visual analog scale (VAS), digital ulser VAS, overall disease severity VAS, hand grip, hand extension measurements and fingertip-palm distances (Table 2). The instruments could discriminate between disease subtypes (10[0-24] / 2[0-19], p=0,038) and between the patients with and without contractures (11[0-24] / 2[0-9], p=0,023) for the discriminant validity. We demonstrated high reproducibility for CHFS (ICC = 0,894, 95% confidence interval = 0,779-0,949).

Table 1. Demographic data and disease characteristics of the patients

Age (years)	**55.4±10.7**	**Total mRSS**	**6 ±5.1**
Sex (female)	79 (%86.8)	Right hand total mRSS	2.2±1.7
Diseasesubtype (diffuse)	25(%27.5)	Left hand total mRSS	2.2±1.7
PAH	6 (%6.7)	Right hand fingertip-palm distance (cm)	1.3±1
ILD	41 (%45.6)	Left hand fingertip-palm distance (cm)	1.2±1.2
ANA positivity	88 (%96.7)	Right hand extension (cm)	17.7±2.5
Arthritis	1 (%1.1)	Left hand extension (cm)	18±2.3
Sclerodactly	79 (%86.8)	Right hand hydrolic dynomometer pressure (kg)	21.7±8.6
Contracture	26 (%28.6)	Left hand hydrolic dynomometer pressure (kg)	20.4±7.6
Amputation	12 (%13.2)	SF 36 physical function	51.7 ±24
Active digitalulcer	3 (%3.2)	SF 36 role limitations due to physical health	52±42
Digitalulcerscar	23 (%25.3)	SF 36 role limitations due to emotional problems	57.3±33.4
Calcinosis	10 (%11)	SF 36 energy/fatigue	46±23.3
CHFS score	3 [0-13]	SF 36 emotional well-being	60.4±21.2
Raynaud's phenomenon VAS	0.8±0.9	SF 36 social functioning	70±26
Digital ulcer VAS	0.5±0.9	SF 36 pain	64±30
Overall disease severity VAS	0.9±0.9	SF 36 general health	44.3±21.7

PAH: Pulmoner arterial hypertension, ILD: Interstitial lung disease, ANA: Anti nuclear antibody, CHFS: Cochin hand function scale, mRSS: Modified Rodnan skin score, VAS: visual analog scale, SF36: short form 36

Table-2 Correlation of CHFC with hand measurements, scleroderma specific VAS's and sHAQ

	Cochin hand function scale	
	r	p
Right hand fingertip-palm distance	0,302	**0,004**
Left hand fingertip-palm distance	0,302	**0,004**
Right hand extension distance	-0,300	**0,004**
Left hand extension distance	-0,279	0,007
Right hand hydrolic dynamometer pressure	-0,462	**<0,001**
Left hand hydrolic dynamometer pressure	-0,511	**<0,001**
sHAQ global	0,703	**<0,001**
Raynaud's phenomenon VAS	0,302	**0,004**
Digital ulcer VAS	0,287	0,006
Overall disease severity VAS	0,432	**<0,001**
Right hand total modified Rodnan skin score	0,041	0,7
Left hand total modified Rodnan skin score	0,078	0,463

Conclusion: The Turkish version of the CHFS met the requirements of validity and reproducibility. With this study, we validated a scale which will contribute to the development of outcome measures with good metric properties assessing hand disability, disease evolution and treatment efficacy in our SSc patients.

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AB0666 BODY COMPOSITION AND PHYSICAL FUNCTION AS POTENTIAL PROGNOSTIC BIOMARKERS IN PATIENTS WITH SIBM

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Background: Sporadic inclusion body myositis (sIBM) is an acquired disease within the idiopathic inflammatory myopathy (IIM) spectrum, characterized clinically by progressive muscle atrophy, weakness and often severely impaired physical function leading to Sarcopenia. Despite of this, muscle mass and physical function is not routinely assessed in patients with sIBM.

Objectives: To investigate muscle mass, muscle power and physical function in patients with sIBM compared to healthy controls.

Methods: The study was a retrospective analysis of patients with sIBM (sIBM) and healthy age and gender matched controls (CON) from The Copenhagen Sarcopenia Study[1]. Appendicular lean mass (ALM) and skeletal muscle index (ALM/h^2) was assessed by DXA (iDXA, GE). Muscle strength and physical function was evaluated by maximal horizontal gait speed (GS), 30-s sit-to-stand test (30s STS) and maximal leg extensor power (LEP) (PowerRig). A linear mixed-effect model for all outcome variables was used for the statistical analysis. A linear mixed-effect model for all outcome variables was used for the statistical analysis, including sex and health condition as fixed factors, and performed using SPSS v20 (Inc., Chicago, Illinois, USA), and the level of significance was set at $\alpha = 0.05$ using two-tailed testing.

Results: In total, 22 patients with sIBM (18 men, age 69.8±4.6; 4 women, age 65.0±8.4) and 414 healthy age-matched controls (237 men, age 70.2±4.9; 177 women, age 65.5±5.4) were included. In men, ALM (sIBM: 21.4±3.1; CON: 25.3±3.6) and ALM/h^2 (sIBM: 6.9±0.9; CON: 8.0±1.0) was reduced in sIBM compared to CON ($p < 0.05$), while there was no differences in ALM (sIBM: 17.4±1.4; CON: 18.0±2.5) and ALM/h^2 (sIBM: 6.8±0.4; CON: 6.6±0.9) in women with sIBM compared to CON. In men, GS (sIBM: 1.05±0.23; CON: 2.20±0.50), 30s STS (sIBM: 6.1±3.8; CON: 17.8± 5.9) and LEP (sIBM: 79.4±57.3; CON: 255.8±81.3) was reduced in sIBM compared CON, respectively ($p < 0.05$). Likewise in women, GS (sIBM: 1.27±0.42; CON: 2.16±0.51), 30s STS (sIBM: 7.0±4.8; CON: 18.5±5.9) and LEP (sIBM: 76.5±23.4; CON: 163.7±51.6) was reduced compared CON, respectively ($p < 0.05$).

Conclusion: The present data demonstrate that muscle mass and physical function are reduced in patients with sIBM compared to healthy counterparts. Although data from larger studies are warranted, it may indicate that assessment body composition and physical function can be used as prognostic tools in these patients.

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AB0667 EFFECT OF TEMPERATURE VARIATION ON SERUM KL-6 LEVELS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Serum Krebs von den Lungen-6 (KL-6) levels has much evidence as a biomarker about the progression and prognosis of interstitial lung disease (ILD), including systemic sclerosis (SSc)-associated ILD[1-4]. However, serum KL-6

levels often fluctuate regardless of the progression of ILD. This sometimes mislead the evaluation of the disease activity, however, the reason for the fluctuation has not been clarified.

Objectives: We tested the hypothesis that serum KL-6 levels are affected by ambient temperature in patients with SSc.

Methods: We defined the warm season (May–October) as the period when the ambient temperature was above the Tokyo metropolitan average ambient temperature announced by the Japan Meteorological Agency, and the cold season (November–April) as the period when the ambient temperature was below the average. ILD was classified based on chest CT findings. Among SSc patients who had visited our department since May 2018, we selected those who had data of serum KL-6 levels at least 3 times in warm and cold seasons from October 2014 to September 2021, respectively. Patients having malignancy were excluded after confirmation of the onset of malignancy using medical record retrospectively. The difference in serum KL-6 levels between warm and cold seasons was evaluated by Wilcoxon's rank-sum test.

Results: In total, 252 patients with SSc were included. Median age was 66.3 years, with median disease duration of 13.5 (8.9–19.2) years, diffuse cutaneous type of 94 (37.3%) patients, and concomitant ILD of 120 (47.6%) patients (Table 1). The median follow-up was 6.4 (4.4–6.8) years, with median KL-6 measurement of 24 (14–39) times. Serum KL-6 levels were significantly higher in the cold season than that in the warm season, with a greater difference in the group with ILD (536 IU/L vs. 492 IU/L, p = 0.0012) in the group with ILD, 364 IU/L vs. 345 IU/L in the group without ILD, p = 0.0028) .

Table 1. Patients characteristics

	With ILD (n=120)	Without ILD (n=132)	*P* value
Female, n (%)	110 (43.7)	128 (52.4)	0.1
Age, years (IQR)	65.8(56.1–73.4)	66.4(56.0–72.5)	0.77
Disease duration, years (IQR)	14.0 (9.8-21.0)	13.0 (8.7-18.0)	0.23
Modified Rodnan skin score (IQR)	10 (4-15)	6 (2-11)	0.0017
Diffuse SSc, n (%)	53 (40.2)	27 (20.5)	<0.001
Pulmonary hypertension, n (%)	4 (3.3)	3 (2.3)	0.71
ANA positive, n (%)	98 (81.7)	112 (84.8)	0.50
SSc-related autoantibody, n (%)	98 (81.7)	112 (84.8)	0.50
Anti-centromere antibody, n (%)	17 (14.2)	86 (71.7)	<0.0001
Anti-topoisomeraseI antibody, n (%)	63 (52.5)	8 (6.1)	<0.0001
Anti-RNA polymerase III antibody, n (%)	7 (5.8)	11 (8.3)	0.62
Anti-U1-RNP antibody, n (%)	15 (12.5)	13 (9.8)	0.54
KL-6, IU/L (IQR)	548 (384–876.8)	233 (191.3–302)	<0.0001
KL-6 measurement, times (IQR)	33.5(20-45)	18.5(12.3-28)	<0.0001
Steroid use, n (%)	68 (56.7)	22 (16.7)	<0.0001
Cyclophosphamide, n (%)	44 (36.7)	12 (9.1)	<0.0001
Other Immunosuppressive agents, n (%)	31 (25.8)		0.002

Conclusion: Our results suggest that cold ambient temperature may affect serum KL-6 levels in patients with SSc.

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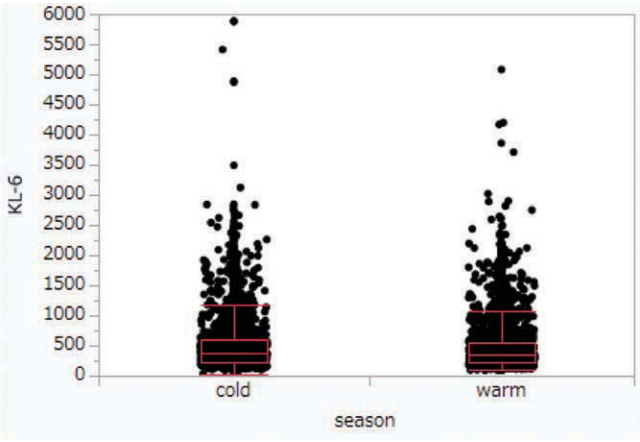

Figure 1.

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AB0668

ASYMMETRICAL DIMETHYLARGININE CORRELATES WITH WORSENING PERIPHERAL MICROANGIOPATHY IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a connective tissue disease characterized primarily by, micro-angiopathy and endothelial dysfunction stimulate fibrotic process. Asymmetrical dimethylarginine (ADMA) is an endogenous nitric oxide (NO) inhibitor and represents a novel risk factor for vascular dysfunction. Nailfold Video Capillaroscopy (NVC) is a non-invasive and reliable technique for the evaluation of microvasculopathy in SSc.

Objectives: The aim of this study was to examine the possible association between ADMA and microvascular involvement in patients with SSc.

Methods: This was a cross-sectional study including consecutive SSc patients attending the Scleroderma Outpatient Clinic. ADMA was measured in serum samples by using commercial enzyme immunoassay ELISA kit (Aviva Systems Biology ADMA ELISA Kit). Participants underwent NVC with qualitative and semi-quantitative assessment and all parameters were measured in the distal row of each finger. The findings were classified in one of the three qualitative NVC patterns: early, active, and late.

Results: Eighty-one (92,6% women) SSc individuals with mean age 55.44±13.4 years and disease duration 6.78 [9.22] years were included in this analysis. Within-groups comparisons revealed a trend between higher ADMA levels and progressive micro-vasculopathy (1,29 [2,1]vs 1,57 [1,95] vs 2,41 [3,87]; for early, active and late patterns respectively, p=0.039) (Figure 1). Furthermore, ADMA concentration was significantly associated with the number of capillaries/mm (r= -0.235; p=0.035).

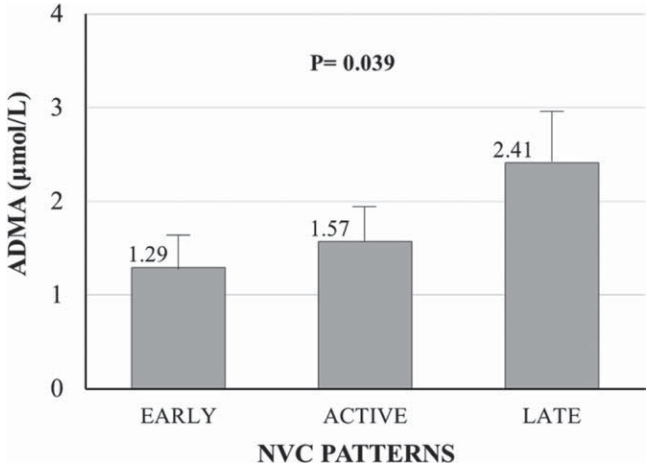

Figure 1. Serum ADMA levels in the early, active, and late NVC patterns

Conclusion: Serum ADMA levels were significantly associated with advancing stages of microcirculatory abnormalities suggesting that ADMA may have a role in promoting microvascular endothelial dysfunction in SSc individuals.

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AB0669 **PREGNANCY OUTCOMES IN SYSTEMIC SCLEROSIS, SYSTEMIC LUPUS ERITHEMATOSUS AND BEHCET'S DISEASE**

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Objectives: To clarify pregnancy outcomes in patients with systemic sclerosis (SSc), systemic lupus erythematosus (SLE) and Behcet's disease (BD) using retrospective analysis.
Methods: The study group included 48 women with SSc, 47 with SLE 45 with BD aged 20-40 years, and the control group - 15 age-matching healthy women. SSc pts' mean age was 32,9 [28;37] years, SLE pts' 32,3 [29;36] years, BD pts' 31,3 [27;35] years, disease duration 6,3 [3;10], 9,8 [3;16] and 6,0 [3;8] years respectively. Completed by all women issue-specific questionnaire covered clinical symptoms of SLE, SSc, BD and details of obstetric history (characteristics of menstrual and reproductive function, presence of genital and extragenital pathology, previous pregnancies outcomes; previous intrauterine interventions, a history of coagulopathy).
Results: Retrospective analysis of thematic maps of 48 patients with SSc revealed: 28 patients had 77 pregnancies, 44 of which ended with the birth of children (13 by caesarean section in 9 patients); 3 women had 4 premature births at 28-35 weeks, one of which ended with perinatal death of the baby; 33 incomplete pregnancies in 19 patients: 28 medical abortions up to 12 weeks of gestation at the woman's request; 5 pregnancy complications had 5 patients, spontaneous abortion - 3, undeveloped pregnancy - 2. The frequency of unfavorable pregnancy outcome was similar in patients with SSc and in the control group. Analysis of thematic maps of 47 patients with SLE: 27 patients had 68 pregnancies, 31 of which ended with the birth of children on time (12 by caesarean section in 9 patients); 3 women had 4 premature births at 27-33 weeks, two of which ended with perinatal death of the baby; 33 incomplete pregnancies in 18 patients: 15 medical abortions up to 12 weeks of gestation at the woman's request, two women had 3 abortions for medical reasons (high activity of SLE); 15 pregnancy complications had 9 patients, spontaneous abortion had 8 pts, undeveloped pregnancy was observed in 7 women. The frequency of unfavorable pregnancy outcome was similar in patients with SLE and in the control group. 118 pregnancies in 35 pts with BD resulted in 75 live birth (6 cesarean section in 3 pts). Thirty-nine incomplete pregnancies were observed in 26 patients. Ten patients had 20 medical abortions on request before 12 weeks of gestation, one patient had an abortion due to medical reasons (rubella on the 7 th week of gestation), two patients had premature birth at 28 and 32 weeks with subsequent perinatal death of the baby. Fifteen out of 35 pts had 20 adverse pregnancy outcomes: 8 spontaneous abortion, 12 missed miscarriage. Nine patients had 12 Missed miscarriage at 6-11 weeks of gestation, one patient had 3 missed miscarriage, two had 2, and the others had 1 missed miscarriage. Six patients had 8 spontaneous abortions (early miscarriage). In the control group of 15 women, 7 had 15 pregnancies, 13 live birth of healthy children on time.

Table 1. Pregnancy outcomes

Pregnancy, n	SSc, n=77 (%)	SLE, n=68 (%)	BD, n=118(%)	Control, n=15	*p*
Birth	44 (57,1)*	35 (51,5)*	77 (65)	13 (87)*	0,03
Abortion	28 (36,4)*	18 (26,5)*	21 (18)	0 *	0,01
Unfavorable pregnancy outcome	5 (6,4)	15 (22)	20 (17)	2 (13)	ns
Missed miscarriage	2 (2,6)	7 (10,3)	12 (10)	0	ns
Spontaneous abortion	3 (3,9)	8 (11,8)	8 (7)	2 (13)	ns

Patients with SSc and SLE were more likely to terminate pregnancy of their own volition compared to the control group.

Conclusion: Patients with SSc and SLE were more likely to terminate pregnancy on their own volition compared to the control group. Unfavorable pregnancy outcomes were similar in groups.
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AB0670 **MIXED CONNECTIVE TISSUE DISEASE IN A TERTIARY CARE HOSPITAL**

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Background: Mixed connective tissue disease is a rare syndrome characterized by the appearance of Raynaud's phenomenon, arthritis and edema in the hands, muscle weakness, dysphagia and dyspnea;It consists of the mixture of symptoms present in other collagen diseases such as erythematosus systemic lupus, scleroderma, polymyositis and rheumatoid arthritis, but without meeting diagnostic criteria for any of them.
Objectives: -Describe the clinical characteristics of a cohort of patients diagnosed with mixed connective tissue disease. -Study the evolution of these patients to other inflammatory autoimmune diseases. Disease conversion was defined as the appearance of new symptoms and autoantibodies compatible with another rheumatic disease.
Methods: Retrospective descriptive study of patients treated at our Hospital (2010-2020) by the Rheumatology and Internal Medicine service with a diagnosis of mixed connective tissue disease. The data was obtained through the review of medical records.
Results: 63 patients were included, of whom 56 were women (88%) and 7 men (12%). The average age of diagnosis is 37 +/- 13 years. At the end of the period, only 36.5% (23 patients) met criteria for mixed connective tissue disease. Of the 40 patients (65.5%) who underwent conversion to another autoimmune collagen disease, 65% (26 patients) met the criteria for systemic lupus erythematosus, 22.5% (9 patients) met the criteria for systemic sclerosis, 5% (2 patients) met criteria for rheumatoid arthritis and 7.5% (3 patients) for other systemic collagen pathologies. Of the initial sample of patients, 15 patients (23.8%) developed secondary Sjögren's disease. Regarding symptoms, in order of frequency, 50 patients (79.3%) of the sample presented myalgia, 39 patients (61.9%) sclerodactyly, 30 patients (47.61%) presented Raynaud's phenomenon, 10 patients (15.87%) esophageal alterations and 4 patients (6.3%) presented interstitial lung disease. Regarding treatment, 60% of the sample used corticosteroids, 52% hydroxychloroquine, 31.7% methotrexate, 23.8% mycophenolate, and 1.6% required rituximab. In the analyzed period, 2 patients died (3.17%), none as a result of their rheumatic disease.
Conclusion: The results obtained are consistent with those reported in the medical literature. The majority of patients with mixed connective tissue disease ended up progressing to another autoimmune collagen disease, mainly systemic lupus erythematosus and systemic sclerosis. According to our studies, stricter classification criteria would be convenient. However, more powerful and longer-term studies are needed to be able to draw conclusive conclusions.
Disclosure of Interests: None declared
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AB0671 **HISTOPATHOLOGICAL, CLINICAL AND SEROLOGICAL FEATURES IN IIM PATIENTS FROM A SINGLE CENTER COHORT**

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Background: Idiopathic inflammatory myositis (IIM) is a group of heterogeneous autoimmune diseases, characterized by myositis-specific (MSA) or myositis-associated autoantibodies (MAA). Muscle biopsy is the diagnostic gold standard, but correlations with elevated creatine level (CK) or MSA/MAA are unclear.
Objectives: To evaluate the association between specific histological findings and clinical and/or serological features in IIM patients from a single tertiary Rheumatology referral center.
Methods: We retrospectively analyzed demographic and clinical data from medical charts, of 184 patients affected by IIM followed-up for >1 year. Muscle biopsies of 89 IIM patients were retrieved from deltoid, biceps or quadriceps muscle, snap-frozen and stored at -80°C and processed for routine histology and histochemistry.
Results: The majority of our muscle biopsy cohort was represented by Dermatomyositis (DM) (39.3%), Polymyositis (PM) (29.2%) and Anti-synthetase syndrome (ASS) (13.5%), whereas the rest was composed of Overlap Syndrome (OS), Immune-Mediated Necrotizing Myopathy (IMNM) and Inclusion-Body Myositis (IMB) (13.5%, 2.2% and 2.2% respectively). DM presented perifascicular atrophy in 85% of cases and perivascular and perifascicular infiltration in only 40% of cases, similar to other types of IIMs. The overall histology finding was characterized by minimal inflammation and/or necrosis but major atrophy. In comparison, Polymyositis showed more endomysial infiltration and necrosis (Table 1). ASS was characterized by atrophy and perifascicular necrosis in 83% of cases, with perimysial and perivascular infiltration in 67% of cases. Those characteristics were observed both in anti-Jo-1+ (13.9%) as well as non-Jo-1+ ASS patients (13.2%). Non-Jo-1+ ASS patients presented endomysial infiltration, invading or enveloping the muscle fibers (not present in anti Jo-1+) (p: 0.036), with addition of rimmed vacuoles and aspecific clinical presentation. Moreover, in DM, anti-Mi2+ antibodies (9.3%) were significantly associated with perifascicular regeneration and endomysial infiltration, in comparison to both anti-TIF1γ+ (5.8%) and anti-NXP2+ patients (4.6%). No significant histopathological features were found in patients with anti-Ro52 autoantibodies (37.2%), that represented the most frequent MAA in our cohort.

Table 1.

BIOPSY CHARACTERISTICS	ASS 12 (%)	PM 35 (%)	DM 26 (%)	p [OR] ASS vs PM	p [OR] PM vs DM
diffuse atrophy	3 (25)	34 (97.1)	8 (30.8)	<0.0001 [0.010 (0.001-0.106)]	<0.0001 [76.5 (8.8-660.6)]
perifascicolar degeneration	----	29 (82.9)	15 (57.7)	----	0.044 [3.544 (1.09-11.5)]
prevalent necrosis	----	10 (28.6)	1 (3.8)	----	0.017 [10 (1.19-84)]
	Jo1 12 (%)	**PL7/PL12 5 (%)**	**p [OR]**		
endomysial infiltration (invading fibers)	0	3 (60)	0.015 [inf]		
	Mi2 8 (%)	**TIF1γ 5 (%)**	**NXP2 4 (%)**	**p [OR] Mi2 vs TIF1γ**	**p [OR] Mi2 vs NXP2**
perifascicolar regeneration	8 (100)	1 (20)	0	0.007 [inf]	0.002 [inf]
endomysial infiltrate (surrounding fibers)	6 (75)	----	0	----	0.061

Conclusion: No significant associations emerged between CK levels, different types of IIM and MSA. Some histological features seem to define subtypes of DM. A precise definition of autoantibody profile in IIM could define not only a clinical phenotype but also the muscle damage distribution.

Disclosure of Interests: None declared

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AB0672 FUNCTIONAL CAPACITY AND QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS – DATA FROM MOSCOW REGISTER OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a multisystem, connective tissue disease characterized by fibrosis of the skin and internal organ involvement, which can influence quality of life and functional capacity. SSc patients show some problems associated with reduced quality of life.

Objectives: Systemic sclerosis (SSc) is a multisystem, connective tissue disease characterized by fibrosis of the skin and internal organ involvement, which can influence quality of life and functional capacity. SSc patients show some problems associated with reduced quality of life.

Methods: In total, 51 patients with SSc were included: 50 women and 1 man (mean age: 63,2 ± 10,1 year, limited SSc 28/diffuse SSc 23, median duration since first non-Raynaud symptom: 10,1 years) who fulfilled the ACR/EULAR classification criteria (2013), filled in questionnaires assessing disability (HAQ, Health Assessment Questionnaire) and quality of life (SF-36, Medical outcomes study Short Form 36 - Physical Component Summary and Mental Component Summary).

Results: Average HAQ in patients with limited and diffuse SSc was 0,66±0,58 and 0,9±0,59. Data analysis showed that 59% of the patients were in the mild to moderate HAQ disability category ($0 \leqslant HAQ < 1$), 39% in the moderate to severe disability category ($1 \leqslant HAQ < 2$), and 2% in the severe to very severe disability category ($2 \leqslant HAQ \geqslant 3$). The SF36 mean scores of the total group were 34,8±8,7 on the Mental Component Summary and 37,0±13,1 on the Physical Component Summary.

Conclusion: Ssc and its complications decrease quality of life and functional capacity. Although validated in SSc, the HAQ disability index underestimates respiratory failure due to interstitial lung disease, gastrointestinal symptoms, cardiovascular complications and severity of Raynaud phenomenon. Alternative measures of functional impairment should be examined. Health-related quality of life, which was assessed by the SF-36 is reduced in both physical and mental domains. It should be taken into account by clinicians for further improvement of treatment and development rehabilitation program.

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AB0673 OVARIAN RESERVE IN SYSTEMIC SCLEROSIS, SYSTEMIC LUPUS ERYTHEMATOSUS AND BEHCET'S DISEASE

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Background: Anti-Mullerian hormone (AMH) is one of the key parameters for assessing reproductive function and ovarian reserve. The levels of AMH correlates with the residual follicular pool in women of reproductive age.

Objectives: To assess AMH levels in female patients of child-bearing potential with systemic sclerosis (SSc), systemic lupus erythematosus (SLE) and Behcet's disease (BD), and analyze the relationship between AMH levels and disease severity, as well as relationship between serum AMH levels and different therapeutic regimens.

Methods: The study group included 48 women with SSc, 47 with SLE 45 with BD aged 20-40 years, and the control group included 15 age-matched healthy women. SSc pts' mean age was 32,9 [28;37] years, SLE pts' 32,3 [29;36] years, BD pts' 31,3 [27;35] years, disease duration was 6,3 [3;10], 9,8 [3;16] and 6,0 [3;8] years respectively. AMH levels was measured using ELISA. AMH reference values ranged within 1.0-10.6 ng / ml. Values <1.0 were interpreted as a decreased ovarian reserve.

Results: Mean AMH levels were 3.4 ng/ml in SLE pts, 2.5 ng/ml in BD pts and 3.1 ng/ml in controls, showing no statistical difference. However, in patients with SSc mean AMH was significantly lower compared to control (2.2 ng/ml vs. 3.1 ng/ml, p=0,03).

Table 1. AMH in patients and control group

form	SSc, n=48	SLE, n=47	BD, n= 45	Controls,n=15	p
Mean AMH	2,2 [0,29-3,06]*	3,4 [0,64-5,4]	2,5 [1,1;3,7]	3,1 [1,9;4,9]*	0,03
AMH >1 ng /ml,n(%)	21 (43,7)*	13 (27,7)	8 (17,7)	2 (13,3)*	0,03

A redaction of ovarian reserve (AMH less than 1.0 ng / ml) was more often observed in SSc pts compared to controls (44% vs 13%), p=0,03. The mean AMH levels were significantly lower in pts with SSc receiving cyclophosphamide (CYC). Correlation analysis revealed a negative correlation between levels AMH and CYC therapy (r=-0.33, p<0.05), with erythrocyte sedimentation rate (r=-0.36), heart involvement (r=-0.32) and gastrointestinal involvement (r=-0.31), digital ulcers (r=-0.33) and digital pitting scars (r=-0.28). Correlation with other clinical manifestations, immunological markers and immunosuppressive therapy of SSc wasn't found. In five patients receiving CYC earlier, the level of AMH was within normal values, the total dose of CYC at them did not exceed 4g.

No correlation was found between AMH and activity SLE (SLEDAI 2K), disease duration, and clinical course. Correlation analysis of levels AMH and SLE therapy revealed a negative correlation between AMH and CYC therapy (r=-0.32, p<0.05), a positive correlation with hydroxychloroquine therapy (r=0.34, p<0.05). Correlations of AMH with the clinical picture of SLE and therapy with other immunosuppressive drugs have not been obtained. In patients with SLE, previously or currently received CYC, a significant decrease in average AMH was revealed 2,4 [0,4-4,3] vs 4,2 [1,3;5,7], and they also significantly more often had a low levels of AMH (<1 ng/ml), 47,4% vs 14,3% pts, p<0.05. In three patients who had received CYC earlier, the level of AMH was within normal values, the total dose of CYC did not exceed 5.6 g. When analyzing the levels of AMH with the clinical picture and BD therapy, no correlations were found.

Conclusion: Mean levels AMH and ovarian reduction of reserve was significantly lower in women with SSc pts compared to healthy controls. The levels of AMH negatively correlated in SSc pts with CYC therapy, erythrocyte sedimentation rate, heart damage and gastrointestinal tract involvement, digital ulcers and digital scars. The levels of AMH negatively correlated in SLE pts with CYC therapy. CYC therapy negatively affected ovarian function, and most likely in a dose-dependent manner. Behcet's disease does not seem to have much effect on the ovarian reserve.

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AB0674

PROVIDING PATIENTS WITH SYSTEMIC SCLEROSIS BY MEDICAL CARE IN RUSSIA: THE FIRST DATA FROM MOSCOW REGISTER OF SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a multisystem, connective tissue disease characterized by fibrosis of the skin and internal organ involvement, which can influence quality-of-life and functional capacity. [1] The mortality rate is increasing in the United States and Europe; as many as 3.08 persons are affected per 1 million. Changes in lungs and heart, pulmonary hypertension are the most significant reasons of death in patients with systemic sclerosis.[2]
Objectives: To estimate quality and completeness of medical care in patients with systemic sclerosis in Russia.
Methods: 66 patients included in the study. 61 female and 5 male (mean age: 62,48 ± 10,1), among which there were 24 limited SSc (lSSc) and 42 diffuse SSc (dSSc). All patients fulfilled the ACR/EULAR classification criteria. We estimated percentage of patients, who were examined by basic studies: capillaroscopy, functional lung tests, echocardiography, HRCT, fully immunologic study and right heart catheterization etc. and try to understand reasons of incompleteness of these assessments.
Results: Despite the presence of Raynaud's phenomenon in 85% of patients, capillaroscopy was performed only in 65.21% of them, examination of the esophagus was performed in only 22.92% of patients, with development of dysphagia in 50% of patients. HRCT was performed in 54.71% (25.76% NSIP, 9.09% UIP), right heart catheterization in 4.17% (signs of pulmonary hypertension according to ECHO detected in 42.86% of patients). FLT were performed in mostly patients (86.34%), but it wasn`t fully: measuring of DLCO was realized only in patients with severe desease (22.92% of patients). That explains its low mean level (61.37% from normal) as opposed to mean FEV1 (90.7% from normal) and FVC (89.47% from normal) level. Fully immunologic study was performed in 35.42% of patients, despite the fact that different autoantibodies showed up in 72.92% of patients (the most common were: antiScl70 41,67%, ACA 22,92%, ANF 52,08%).
Conclusion: According to the results of the study, we have identified a significant decrease in the quality of medical care despite the clinical recommendations and generally accepted standards. We suppose. that the main reasons for this situation are the complex healthcare problems: insufficient competence of doctors, lack of collaboration between related specialties, unavailability of a number of studies within the framework of free medicine and high cost of these studies for the patients themselves, and the lack of time for communication between the doctor and the patient to explain the seriousness of the disease and the nescessity of all parts of examination and treatment.

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AB0675

HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE: A COMPARISON WITH MATCHED SYSTEMIC SCLEROSIS PATIENTS

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Background: Mixed connective tissue disease (MCTD) is a systemic auto-immune disorder, being probably the least common among the connective tissue diseases. Symptoms can be severe and could affect health-related quality of life (HRQoL). Identification of the burden of MCTD patients is of key importance to provide appropriate pharmacological and non-pharmacological care. No reports on HRQoL have been published in adult patients with MCTD.
Objectives: To perform an explorative study to evaluate HRQoL and its main determinants in MCTD patients, and compare HRQoL between MCTD and matched systemic sclerosis (SSc) patients.
Methods: MCTD patients fulfilling the Kahn criteria and participating in the MCTD prospective follow-up cohort of the Leiden University Medical Center were included. In addition, SSc patients matched for age, gender and disease duration were included for comparison. Data on disease characteristics, functional disability and HRQoL were collected annually for both disease groups. HRQoL was evaluated using the 36-Item Short Form Health Survey (SF36) and EuroQol (EQ5D). At baseline, HRQoL, as reflected by SF36 mental component score (MCS), SF 36 physical component score (PCS) and EQ5D were compared between MCTD and SSc patients. For MCTD patients, factors associated with HRQoL at baseline were identified using linear regression and change in HRQoL over 3 years was evaluated using linear mixed models. In addition, characteristics of MCTD patients who showed worsening of MCS and/or had PCS superior to the minimal clinical important difference of three points were identified.
Results: Thirty-four MCTD patients (121 visits; 82% female, mean age 42 years, median disease duration 45 months) and 102 SSc patients (424 visits; 82% female, mean age 45 years, median disease duration 49 months) were included. At baseline, MCTD-patients more often had ILD (47% vs. 34%, p=0.027), cardiac involvement (30% vs. 2%, p<0.001), synovitis (26% vs. 11%, p=0.004) and myositis (15% vs. 1%, p=0.001) compared to SSc patients, whereas SSc patients more often used immunosuppressive treatments except for hydroxychloroquine (MCTD:18% vs. SSc:7%, p=0.007).
Baseline HRQoL in MCTD was comparable to HRQoL in SSc, with mean SF36-PCS of 40.2 (SD:9.1) and mean SF36-MCS of 44.9 (SD:9.9), which is (nearly) one standard deviation lower than the general Dutch population. The SF36 subscore "general health perception" was the most impacted in both groups (MCTD: 38.5 [SD:7.0], SSc: 39.9 [SD:8.9]). The median EQ5DNL was 0.38 (IQR:0.14 – 0.54) and comparable between SSc and MCTD.
At baseline, in MCTD, ILD was significantly associated with SF36-PCS (β:6.98, 95% CI: 1.10 to 12.86) and SF36-MCS (β:-8.10, 95% CI:-14.93 to -1.26). Sclerodactyly was significantly associated with EQ5DNL (β:0.006; 95% CI:0.002 to 0.010) and SF36-PCS (β:0.12, 95% CI:0.03 to 0.21). No other significant associations were identified.
Over time, in MCTD, both the SF36-MCS and SF36-PCS improved significantly (MCS: β:2.35/year [95% CI:0.58 to 4.13], PCS: β:1.34/year [95% CI:0.03 to 2.65), whereas EQ5DNL was stable. Explorative analyses did not reveal a specific clinical characteristic with significant impact on the change of HRQoL over time. With an MCID of 3 points on the MCS and PCS, 7 MCTD-patients worsened on the MCS and 3 on the PCS. Patients who showed worsening of MCS over time tended to be older, more often had ILD, sclerodactyly and GI complaints, and had worse exercise tolerance. All these differences did not reach statistical significance. The patients who decreased PCS more often had ILD (100% vs. 41%, p=0.015), and used glucocorticoids more often (33% vs. 0%, p=0.046), were slightly older and had a worse exercise tolerance as compared to those who showed a stable/improving PCS over time.
Conclusion: Like in SSc, HRQoL is significantly impaired in MCTD, especially the general health perception of patients. Cardiac involvement, ILD, age and worse functional disability might specifically impact HRQoL in MCTD. However, these associations need further evaluations in larger cohorts.

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AB0676

ONE YEAR PROGRESSION OF INTERSTITIAL LUNG DISEASE IN CONNECTIVE TISSUE DISEASES. A DESCRIPTIVE STUDY IN A SINGLE TERTIARY CENTER.

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Background: Interstitial lung disease (ILD) in connective tissue diseases (CTD) is an important cause of morbidity and mortalitiy.
Objectives: To evaluate ILD in CTD (systemic sclerosis, myositis, Sjögren syndrome, rheumatoid arthritis, mixed connective tissue disease), sarcoidosis and interstitial pneumonia with autoimmune features and its progression in 12 months evaluated through high resolution computed tomography (HRCT) and pulmonary function test (PFT).
Methods: A retrospective single tertiary center cohort study in CTD-ILD outpatients seen between 2012 and 2021. Clinical, serological data, PFT and HRCT results were collected. ILD patterns were classified into: usual interstitial pneumonia (UIP), inconsistent UIP, nonspecific interstitial pneumonia (NSIP), fibrosing NSIP, organizing pneumonia, interstitial lymphoid pneumonia and associated to sarcoidosis. Progression of ILD was defined as:
->10% decline in FVC in PFT.
->15% decline in DLCO in PFT.
-Progression of fibrosis in HRCT.
IBM SPSS v23 was used for statistical analysis.
Results: 51 patients were collected. Baseline characteristics are shown in Table 1. Figure 1 shows ILD progression in 1 year.

Table 1. Baseline characteristics.

Sociodemographic characteristics		**Clinical features/affection–** *n (%)*	
Total	51	Raynaud	23 (45,1%)
Female-n (%)	42 (82,4%)	Skin	23 (45,1%)
Age- years (mean) IQR)	56 (27-82)	Ocular	13 (25,5%)
		Arthritis	16 (31,4%)
		Myositis	7 (13,7%)
		Renal	1 (2%)
		Esophagus	7 (13,7%)
		Hematological	3 (5,9%)
		PHT	7 (13,7%)
Smoking status- n (%)		**Symptoms at ILD diagnosis- N (41) %**	
Current	9 (17,6%)	Cough	31,4%
Former	13 (25,5%)	Toracic pain	11,8%
Never	29 (56,9%)	Dyspnea	47,1%
Comorbidities- n (%)		**Pattern HRCT- n (%)**	
Diabetes mellitus	5 (9,8%)	UIP	11 (21,6%)
Ischaemic cardiopathy	3 (5,9%)	Fib-NSIP	5 (9,8%)
Hypertension	15 (29,4%)	UIPincons	13 (25,5%)
POCD	3 (5,9%)	NSIP	15 (29,4%)
		OP	2 (3,9%)
		LIP	2 (3,9%)
		Sarcoidosis	3 (5,9%)
Type of disease associated to ILD - n (%)		**Immunosupression- n (%)**	
Systemic Sclerosis	14(27,5%)	Methotrexate	20(39,2%)
Sjögren's Syndrome	7 (13,7%)	Mycophenolate mofetil	16 (31,4%)
Sarcoidosis	3 (5,9%)	Hydroxychloroquine	19(37,3%
Myositis	8 (15,7%)	Cyclophosphamide	4 (7,8%)
SLE	1 (2%)	Etanercept	6 (11,8%)
MCTD	3 (5,9%)	TNF inhibitors	4 (7,8%)
RA	12(23,5%)	Tocilizumab	2 (3,9%)
IPAF	4 (7,8%)	Azathioprine	10 (19,6%)
		Leflunomide	3 (5,9%)
		MP pulses	15 (29,4%)
		Rituximab	12 (23,5%)
		Abatacept	5 (9,8%)
		Tacrolimus	5 (9,8%)
Antibodies- n (%)			
Anti-myositis	6 (11,8%)		
Anti-sclerosis	15(29,4%)		
Anti- Ro	25 (49%)		
Anti- RNP	3 (5,9%)		
ANA	35(68,6%)		
RF	21(41,2%)		
Anti- Synt	6 (11,8%)		

Note.
POCD = Pulmonary Obstructive Chronic Disease
SLE = Systemic Lupus Erythematosus
MCTD = Mixed Connective Tissue Disease
RA = Rheumatoid Arthritis
IPAF = Insterstitial Pneumonia with Autoimmune Features
Anti RNP = Anti RiboNucleoProtein
ANA = Antinuclear Antibodies
RF = Rheumatoid Factor
Anti Synt =Anti-synthetase
PHT= Pulmonary Hypertension
UIP = Usual Interstitial Pneumonia
Incons-UIP = Inconsistent Usual Interstitial Pneumonia
NSIP = Nonspecific Interstitial Pneumonia
Fib-NSIP = Fibrosing Nonspecific Interstitial Pneumonia
OP = Organizing Pneumonia
LIP = Lymphoid Interstitial Pneumonia
TNF inhibitor = Tumor Necrosis Factor inhibitor
MP = Metyhprednisolone

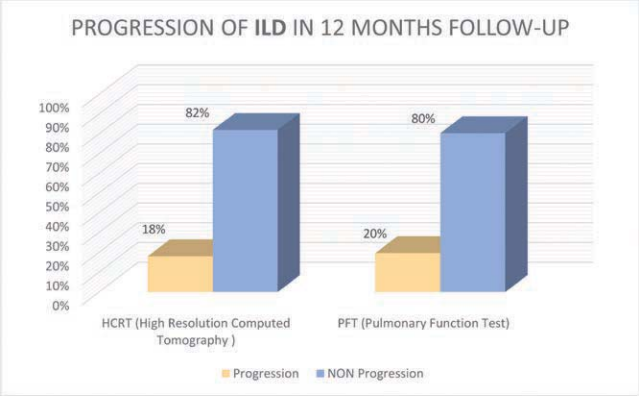

Figure 1.

During follow up, 1 patient with sarcoidosis died of COVID19 bilateral pneumonia.
Conclusion: In our series most patients were middle aged women. Anti-Ro antibodies and smoking status (former or current) were common among patients. Common clinical features were Raynaud (45%), skin affection (45%) and arthritis (40%). 47% of the patients expressed dyspnea at ILD diagnosis. 29,4% were treated with MP pulses, 23,5% with rituximab, 31,4% with mycofenolate mophetil. Fibrosing pattern in HRCT (UIP and fib-NSIP) was the most prevalent. 20% of the patients had progressive fibrosis under PFT criteria and 18% under HCRT. More studies of ILD-CTD are necessary to identify factors for progression and response to treatment and throw out more conclusions of prediction and prognosis of disease.
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AB0677

FREQUENCY AND RISK FACTORS OF OSTEOPOROSIS IN FERTILE WOMEN WITH SYSTEMIC SCLERODERMA

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Objectives: To determine the frequency and risk factors of osteoporosis (OP) in fertile women with systemic scleroderma (SSc)
Methods: 64 women (36,0 [31,5; 43,5] years old) with SSc were enrolled in the study: 35 (54,7%) with limited and 29 (45,3%) with diffuse cutaneous subtype without overlap rheumatic syndromes. The median disease duration was 5,0 [2,0; 9,0] years. Glucocorticoids (GC) were taken by 49 (76,6%) patients with the median duration of treatment 5,0 [2,0; 10,0] years. Dual energy X–ray absorptiometry (DXA) of the lumbar spine, the femoral neck and the total hip was performed. To estimate the value of the BMD the Z-score was used. Low BMD was considered at a Z-score < -2.0 SD. A univariate logistic regression analysis was performed to analyze the factors associated with OP.
Results: Low BMD was detected in 8 (12.5%) patients. 5 (7,8%) women had a history of low-trauma fracture, among them only 1 (1,6%) patient had low BMD and 4 (6,2%) persons - normal BMD.
A univariate logistic regression was performed to identify OP risk factors. Among traditional risk factors, low body mass index (BMI) associated with OP (OR 1,39 [1.04; 1.88], p=0,03) and falls during the past year (OR 5,25 [1.04; 26.36], p=0,04). Among specific ones – duration of SSc (OR 1,19 [1.02; 1.39], p=0,02), duration of GC using (OR 1,11 [1.00; 1.23], p=0,04), hand joint contractures (OR 8,54 [1.41; 51.63], p=0,02). There was no effect of smoking, treatment with proton pump inhibitors, family history of osteoporosis, age, subtype SSc, modified Rodnan score, digital ulcer, cutaneous calcification, esophageal hypotension, interstitial lung disease, diffusing capacity of the lung for carbon monoxide, force vital capacity, CRP, erythrocyte sedimentation rate, creatinine, presence of antinuclear antibody, anticentromere antibody or antitopoisomerase I antibody on the development of OP in fertile women with SSc.
Conclusion: Low BMD was detected in 12.5% of fertile women with SSc. Low BMI, falls during the past year, duration of SSs and GC taking, hand joint contractures associated with OP.
Disclosure of Interests: None declared
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AB0678

SUBCLINICAL ATHEROSCLEROSIS AND CARDIOVASCULAR RISK IN MYOSITIS PATIENTS AND HEALTHY CONTROLS: PRELIMINARY DATA FROM A SINGLE-CENTER CROSS-SECTIONAL STUDY

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Background: Idiopathic inflammatory myopathies (IIM) are associated with systemic inflammation, limited mobility, and glucocorticoid (GC) therapy, which can negatively impact metabolic disorders, atherogenesis, and increase the cardiovascular (CV) risk.
Objectives: This study aimed to evaluate CV risk in IIM patients compared to healthy controls (HC) and explore its associations with disease-specific features.
Methods: 39 patients with IIM (32 females; mean age 56; mean disease duration 4.8 years; dermatomyositis 16, polymyositis 7, immune-mediated necrotizing myopathy 8, antisynthetase syndrome 8) and 39 age-/sex-matched HC (32 females, mean age 56) were included. Subjects with a history of CV disease (angina pectoris, myocardial infarction, cerebrovascular, and peripheral arterial vascular events) were excluded in both groups. Disease activity, damage, and muscle involvement (Manual Muscle Test (MMT)-8, Myositis Intention to Treat Activity Index (MITAX), Myositis Damage Index (MDI)) were assessed. Comorbidities and current treatment were recorded. All participants underwent examinations of carotid intima-media thickness (CIMT), pulse wave velocity (PWV), ankle-brachial index (ABI), and body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA2000-M). The risk of fatal CV events was evaluated by the Systematic COronary Risk Evaluation (SCORE and SCORE2, charts for the European population; modified mSCORE according to the 2015 EULAR recommendation for inflammatory arthritis - only in IIM patients).
Results: In IIM, disease activity and damage were predominantly mild (MITAX 0.13, MDI 0.05). Compared to HC, there was no significant difference in the prevalence of traditional risk factors. Only PWV was significantly increased in IIM compared to HC (p=0.015). No other significant difference was observed between the IIM and HC regarding the CV examinations (CIMT, ABI, carotid plaques) and calculated SCORE and SCORE2 (p>0.05 for all). In IIM, age and mean arterial pressure were the most significant parameters that correlated positively with SCORE, SCORE2, and mSCORE; arterial hypertension was significantly associated with a higher SCORE, carotid plaque count/thickness, and PWV. Lipid profile parameters, body composition, and disease activity were significantly associated with CIMT and carotid plaques (p<0.05 for all). Antihypertensive treatment was associated with an increase in carotid plaque count (p=0.020), higher (favorable) ABI (p=0.004), while hypolipidemic treatment was associated with an increase in carotid plaque count/thickness (p=0.009, p=0.008). Diabetes was associated with lower (worse) ABI values (p=0.034), prediabetes with a higher carotid plaque count (p=0.036) and thickness (p=0.011), and a worse ultrasound examination related CV risk (p=0.006). Anti-Jo-1 positivity was associated with a lower (better) CIMT and lower SCORE (p<0.05 for all). There were no significant associations of CV risk with clinical manifestations, immunosuppressive treatment, and GC cumulative dose. However, exposure time to GC therapy was significantly associated with the carotid plaques count (p<0.001) and the carotid plaque thickness (p=0.003). In multivariate analysis, the age of the patients was the most significant factor affecting most of the parameters analyzed (SCORE and its modifications, PVW, CIMT, and the total count of carotid plaques). Other significant predictors were total cholesterol and atherogenic index of plasma (for ABI), mean arterial pressure (for PWV), and disease duration (for the total count of carotid plaques).
Conclusion: No significant differences in CV risk factors between IIM patients and HC were observed.In IIM, CV risk was associated with age, disease duration, duration of glucocorticoid therapy, lipid profile, and body composition, but not with clinical manifestations and disease activity.
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AB0679

INTRAVENOUS INMUNOGLOBULIN IN INFLAMMATORY MYOPATHIES: EXPERIENCE OF A SINGLE REFERRAL CENTER

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Background: Treatment of inflammatory idiopathic myopathies (IIM) is not well-stablished. Although the mechanism of action of intravenous immunoglobulins (IVIG) is not completely understood, they may be useful in rheumatic diseases, including IIM.
Objectives: To assess the efficacy and safety of IVIG in IIM.
Methods: Observational Single University study of IIM requiring therapy with at least one cycle of IVIG from January 2000 to December 2021. IIM, was diagnosed according to EULAR/ACR classification criteria **(1).** Efficacy outcomes were **a)** clinical features (muscular strength and cutaneous involvement), **b)** analytical parameters (Creatine Kinase) and, **c)** glucocorticoid-sparing effect. All of them were measured at 2-4 weeks, 3 months, 6 months, 1 year and 2 years after IVIG onset. Muscular Strength was measured in three muscle areas (upper limbs, lower limbs and neck flexor muscles) by using Medical Research Council Grading System. We classified clinical outcomes (muscular strength and dermatological) improvement in 3 categories: Complete improvement, Partial improvement and No improvement. IVIG schedule was a total of 2 g/kg administered in 1-5 days.
Results: We included 28 patients (22 females, mean age; 47.07±26.71 years) with IIM. The main clinical features are summarized in Table 1. Muscular weakness was present in 18 patients and cutaneous manifestations in 18 patients at baseline.

Table 1. General features of 28 patients with inflammatory idiopathic myopathies with IVIG treatment

GENERAL FEATURES		GENERAL FEATURES (continuation)	
Gender female / male, n (%)	22(78.6) / 6 (21.4)	**Clinical manifestations at IVIG onset;** n (%)	
Age (mean±SD)	47.07±26.71	Upper limbs involvement	17 (60.71)
Underlying IIM; n (%)		Lower limbs involvement	17 (60.71)
Dermatomyositis	12 (46.42)	Neck flexors muscular involvement	14 (50.00)
Amyopathic Dermatomyositis	1 (3.57)	Cutaneous involvement	18 (64.28)
Juvenile Dermatomyositis	6 (21.42)	Dysphagia	8 (28.57)
Polymiositis	2 (7.14)	Constitutional symptoms	9 (3.14)
Inmune-mediated necrotizing miopathy	5 (17.85)	Malignancy	2 (7.14)
Systemic sclerosis/myositis overlap syndrome	1 (3.57)	Respiratory disease	3 (10.71)
Toxic myopathy	1 (3.57)	Articular involvement	4 (14.28)
IIM duration, months (mean±SD)	28.74±38.75	Cutaneous vasculitis	2 (7.14)
Previous immunosupressants before IVIG; n (%)			
Methotrexate	9 (32.14)	**Concomitant Therapy with IVIG**; n (%)	
Azathioprine	4 (14.28)	Oral Corticosteroids at IVIG onset	18 (64.28)
Cyclophosphamide	1 (3.57)	Methotrexate	10 (35.71)
Mycophenolate mofetil	2 (7.14)	Azathioprine	4 (14.28)
Hydroxychloroquine	5 (17.85)	Mycophenolate mofetil	1 (3.57)
Rituximab	1 (3.57)	Hydroxychloroquine	5 (17.85)
Plasmapheresis	1 (3.57)		

An early and maintained improvement was observed in all outcomes: clinical (muscular strength (a) and cutaneous manifestations (b)), Creatine Kinase (c) and glucocorticoid-sparing effect (d) (Figure 1).

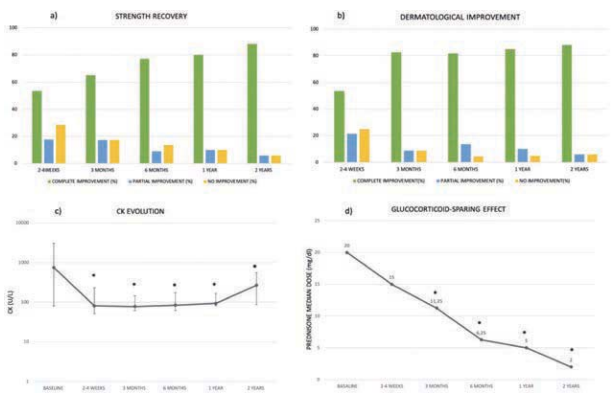

Figure 1. Efficacy Outcome.Figure 1. *p< 0.05 (Wilcoxon test).

After two years of follow-up, we observed the following adverse effects: headache (n=6), pruritus (n=3), allergic reaction (n=2) and arterial hypertension (n=1). No heart failure, renal insufficiency or thrombotic events were found.
Conclusion: IVIG seems effective and safety in IIM treatment.
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Disclosure of Interests: None declared
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AB0680 PSYCHOLOGICAL IMPACT OF AUTOLOGOUS STEM CELL TRANSPLANTATION IN SYSTEMIC SCLEROSIS PATIENTS AND INFLUENCE OF SUPPORT AND COPING STRATEGIES.

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Background: In severe cases of systemic sclerosis (SSc), autologous hematopoietic stem cell transplantation (aHSCT) is superior compared to cyclophosphamide with respect to effect on skin and lung manifestations, survival and quality of life. Nevertheless, major physical and psychological impacts have been found in a first qualitative study by Spierings et al. (2020) [1].
Objectives: Assessment of subjectively experienced physical and psychological impacts of aHSCT and exploration of potential interrelations of those impacts.
Methods: A SSc sample was assessed retrospectively after aHSCT in a two-step-approach. In the first step, 6 questionnaires were used: Global physical and mental health (SF-36 and Scleroderma Health Assessment Questionnaire = SHAQ), body image (Adapted Satisfaction with Appearance Scale = ASWAP), coping strategies (Freiburger Fragebogen zur Krankheitsverarbeitung = FKV-15), resilience (Resilienzskala = RS-11), and control beliefs (Fragebogen zur Erfassung von Kontrollüberzeugung zu Krankheit und Gesundheit = KKG). In the second step, semi-structured interviews based on Spierings et al. (2020) [1] were conducted and analysed via mixed methods qualitative content analysis following Mayring (2014).
Results: 19 patients (12 female, 7 male, mean age 53.47 years (SD = 9.50)) completed all questionnaires and interviews in a mean time of 6.56 years after aHSCT (SD = 3.90, range 1-12 years). A strong correlation was found between perceived physical impairment (SHAQ) and body image dissatisfaction (ASWAP) (Pearson's r = .63, p < .001). There was also a strong negative correlation between body image dissatisfaction (ASWAP) and the physical component of SF-36 (pcSF-36; r = -.59, p = .004) and a smaller correlation for the mental component of SF-36 (mcSF-36: r = -.38, p = .054). Depressive coping was negatively associated with SF-36 (pcSF-3: r = -.605, p = .003; mcSF-36: r = -.808, p < .001) (see Figure 1), whereas resilience was associated with a positive impact (pcSF-36: r = .622, p = .002; mcSF-36 r = .595, p = .004). In the qualitative content analysis of the interviews, all patients reported symptom improvements (mainly skin), which were associated with their coping strategies (depressive coping with fewer improvements, active coping with more improvements). Describing their emotional state during aHSCT, 7 patients verbalized "despair", 6 "loss of control", 5 "emotional instability", 4 "distress due to distance from home", 4 "loneliness", 3 "listlessness", 2 "concern for feelings of relatives", and 2 "depersonalisation". As valuable professional emotional support during aHSCT, 6 patients named nurses and 8 named physicians, while the crucial role of daily ward rounds of the specialised transplant team rather than the primary care team was emphasised. The additional support by a psychology team was not deemed necessary by 7 patients, while 4 patients would have wished such a support. 7 patients rated their physical and mental recovery after aHSCT as satisfying, 4 as better than expected, 4 as disappointing, and 3 as causing impatience.

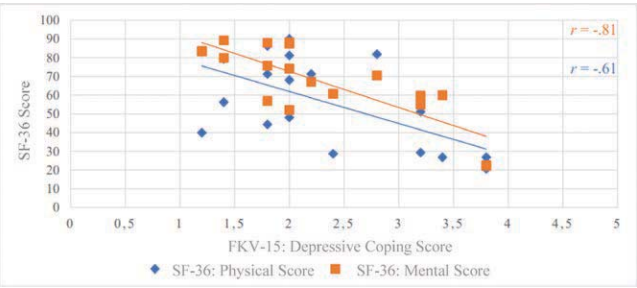

Figure 1. Correlation of SF-36 (physical and mental component) and FVK-15 (Depressive Coping Score) by Pearson's Correlation Coefficient

Conclusion: A transient negative impact of aHSCT on mental wellbeing of the majority of SSc patients is evident, but can be relieved by professional teams highly specialised in this particular treatment option.
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AB0681 THE 2-YEAR IMPACT OF COVID-19 PANDEMIC ON MUSCLE STRENGTH AND PHYSICAL PERFORMANCE IN PATIENTS WITH SYSTEMIC SCLEROSIS: A COHORT STUDY

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Background: Systemic sclerosis (SSc) patients are particularly prone to developing loss of muscle strength and worsening of physical performance due to decreased physical activity[1]. The lifestyle changes imposed by the SARS-CoV-2 outbreak have increased the incidence of sarcopenia in at-risk individuals[2]. However, the literature is scarce on the impacts of the COVID-19 pandemic on muscle strength and physical performance of SSc patients.
Objectives: (1) To assess the impact of the COVID-19 pandemic on muscle strength and physical performance of SSc patients and (2) to verify the associations of muscle strength and physical performance with inflammatory markers in a cohort study.
Methods: SSc patients who met the ACR / EULAR 2013 classification criteria were included. Patients followed between 2019 and 2021. Muscle strength was measured by handgrip strength (kg) and sit and stand (SST, seconds) tests. Physical performance was measured by timed up and go (TUG, seconds) and short physical performance battery (SPPB, points). Inflammatory markers were measured by C-reactive protein (CRP). T test for independent samples, Mann-Whitney U test of independent samples and Spearman's correlation coefficients were explored. The significance level was set at $p \leq 0.05$ for all analyses.
Results: Forty SSc patients concluded this study. At baseline, the mean age was 59 ±11.1 years old and the median disease duration was 13.1 (6.4-19.2) years. Patients had a median of 4.5 clinic visits (3.0-6.0) over the 2 years. The majority of patients were women (37, 92.5%). Ten patients (25%) had diffuse cutaneous disease, 30 patients (75%) non-diffuse cutaneous disease [25 patients (62.5%) had limited cutaneous disease, and 5 (12.5%) had *sine scleroderma* SSc]. The median of CRP was 2.9 (1.2-5.3). The median of handgrip strength was 20.0 (10.3-25.8) kg to the right hand and 19.0 (12.0-22.8) kg to the left hand. The median of SST was 14.4 (11.9-18.7) seconds. The median of TUG was 8.6 (7.7-9.5) seconds and the median of SPPB was 9.8 (9.0-11.0) points. The CRP was positively associated with SST (r=0.3, p=0.047) and TUG (r=0.3, p=0.029), and negatively with SPPB (r=-0.4, p=0.016). After 2 years of follow-up, the patients showed improvement in the left handgrip strength test (p=0.049) and SST (p=0.001). In physical performance, they showed improvement in the TUG test (p=0.005) and SPPB (p=0.001). The CRP was associated positively with TUG (r=0.4, p=0.033), no other associations were found.
Conclusion: Despite the COVID-19 pandemic and the restrictions imposed, in this population of patients with SSc, we did not detect any worsening in muscle strength and physical performance. Some of these parameters of muscle strength and physical performance were associated with the inflammatory marker CRP. More investigations are needed to assess the actual impact and possible associations.

Table 1. Baseline comparison and after 2 years of patients with SSc

		Baseline	After 2 years	*p*
CRP (mg/L),	median (IQR)	2.9 (1.2-5.3)	2.3 (1.0-5.1)	0.361
Handgrip (kg),	right, median (IQR)	20.0 (10.3-25.8)	20.5 (14.3-27.0)	0.072
	left, median (IQR)	19.0 (12.0-22.8)	19.0 (14.0-26.0)	0.049*
SST (seconds),	median (IQR)	14.4 (11.9-18.7)	11.6 (9.9-13.1)	0.001*
TUG (seconds),	median (IQR)	8.6 (7.7-9.5)	7.9 (7.1-9.2)	0.005*
SPPB (points),	median (IQR)	9.8 (9.0-11.0)	11.0 (10.0-12.0)	0.001*

SSc: systemic sclerosis; IQR: interquartile range; mg: milligram; L: liter; kg: kilograms grams; TUG: timed and up go; SST: sit and stand test; SPPB: short physical performance battery; PCR: C-reactive protein; and * significant difference of ≤0.05.

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AB0682 FREQUENCY OF SEXUAL DYSFUNCTION IN SYSTEMIC SCLEROSIS, SANTO DOMINGO, DOMINICAN REPUBLIC

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease.[1] Sexual function has been associated with a high prevalence of dissatisfaction.[2,3,4] Various factors have been implicated as causes of impaired sexual function.5 CSFQ-14 (Changes in Sexual Functioning Questionnaire) assesses changes in sexual functioning due to disease and/or treatment in [5] domains with a score range of 14-70; cut-off point indicating sexual dysfunction < 41 men and < 47 women.[6]
Objectives: To evaluate the frequency and degree of sexual dysfunction in patients with systemic sclerosis.
Methods: Prospective, observational, cross-sectional study of the cohort of the Rheumatology service at Hospital Docente Padre Billini. Patients were interviewed in November 2021. Inclusion criteria: > 18 years, diagnosis of SSc by ACR/EULAR 2013 classification criteria, at least 1 sexual relationship. Exclusion criteria: previous diagnosis of another autoimmune disease, depression, diabetes, treatment with antidepressants, antiepileptics, narcotics. Measurement of CSFQ-14, mRSS. Statistical analysis was performed with the Pearson correlation (r_p) with p=>0.05. The data was analyzed by SPSS V23.
Results: Of 63 patients, 54 met the inclusion criteria. 100% female, mean age 53+15.07 years, mean duration 11.3 years, lSSc 24.1% (13), dSSc 75.9% (41), single 50% (27), married 44.4% (24), widowed 5.6% (3). Frequency of sexual dysfunction 81.5% (44). Domains: pleasure 79.6% (43), desire/interest 37% (20), frequency desire 81.5% (44), arousal 46.3% (25), orgasm/completion 75.9% (41). Correlation CSFQ-14 with mRSS: Pleasure dysfunction: normal mRSS 2.3% (1), mild 23.3% (10), moderate 20.9% (9), severe 32.6% (14), terminal 20.9% (9). Desire/interest dysfunction: mild mRSS 35% (7), moderate 20% (4), severe 35% (7), terminal 10% (2). Frequency desire dysfunction: normal mRSS 2.3% (1), mild 25% (11), moderate 15.7% (12), severe 36.4% (16), terminal 20.5% (9). Arousal dysfunction: normal mRSS 4% (1), mild 16% (4), moderate 16% (4), severe 36% (9), terminal 28% (7). Orgasm/completion dysfunction: normal mRSS 2.4% (1), mild 22% (9), moderate 22% (9), severe 26.8% (11), terminal 26.8% (11). r_p=. 065 p> 0.05.
Conclusion: The study demonstrated a high frequency of sexual dysfunction in most of the population studied. The desire/frequency dysfunction domain turned out to be the one with the highest presentation, followed by the orgasm/completion domain. A statistically significant linear association between sexual dysfunction and cutaneous activity of the disease was evidenced.
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Disclosure of Interests: None declared
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AB0683 POLYNEUROPATHY IMPACT ON DISABILITY IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is one of the most severe autoimmune rheumatic diseases with high morbidity and mortality rates [1]. Peripheral neuropathy in SSc is reported with a broad prevalence variable between 0.01% to 28% [2]. Developed in 1978, the Health Assessment Questionnaire Disability Index (HAQ-DI) for rheumatoid arthritis, nowadays is widely used to measure functional status in patients with SSc as well, but data are lacking in SSc patients with polyneuropathy (PN) [3].
Objectives: To determinate the impact of PN on disability in SSc patients.
Methods: This was cross-section study in patients with SSc. Study was conducted in two University hospitals in Latvia for adults. Study included patients diagnosed with SSc that met the ACR / EULAR 2013 accepted classification criteria and have been consulted by rheumatologists between 1st January 2016 and 31st July 2021. Patients who agreed to comply in the study were evaluated by one rheumatologist and were surveyed and clinically evaluated according to The European Scleroderma Trials and Research group accepted domains. Disease duration was defined as time from first non-Raynaud SSc symptom to date of examination. SSc subtype was evaluated in each patient by clinical presentation that included modified Rodnan score (mRSS) as well: limited cutaneous systemic sclerosis (lcSSc) with skin thickening distal to the elbow/knee and diffuse cutaneous systemic sclerosis (dcSSc) with skin thickening proximal to the elbow/knee. For neuropathic pain assessment, the Neuropathic Pain Diagnostic Questionnaire (DN4) was used. Peripheral neuropathy symptoms were assessed using total neuropathy score (TNS). Peripheral nerve conduction study (NCS) and quantitative sensory testing (QST) was used to detect PN.
Functioning and disability were assessed using HAQ-DI. All patients completed the HAQ-DI form in the same day as they were evaluated, filling the form in native language.
Results: From 109 acknowledged patients, 67 were able to come for a visit, 54 females, 13 males. Mean age for females 62.54±12.02 years, for males 58.69±14.50 years.
After assessment by rheumatologist, 50 were classified as lcSSc, 17 were classified as dcSSc. The overall ratio of lcSSC and dcSSc was 50:17, in females 41:13, in males 9:4. Disease duration ranges from 1 to 39 years (mean 15.49±10.18), 16.61±10.47 years for females, 10.85±7.55 years for males. Large fiber PN was diagnosed in 47.8% of subjects by NCS (n=32/67) and small fiber PN in 40.3% of subjects by QST (n=27/67), while 11.9% had neither (n=8/67). Mean HAQ-DI score was 1.22. There was no statistically significant difference in HAQ-DI score between males (1.08±0.89) and females (1.26±1.01), (p=0.13). As well there was no difference between HAQ-DI score in patients with large fiber/small fiber neuropathy and without neuropathy symptoms (p=0.6817). But we found that neuropathy symptoms (assessed by TNS) have moderately strong and statistically significant correlation with HAQ-DI (r=0.39, p=0.0012). As well we found moderately strong correlation between HAQ-DI and neuropathic pain (assessed by DN4) (r=0.45, p=0.00015).
Conclusion: PN is more common complication in SSc that was previously reported, with significant impact on QoL.
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AB0684 FATIGUE ASSESSMENT IN SYSTEMIC SCLEROSIS, SANTO DOMINGO, DOMINICAN REPUBLIC

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease.[1] Fatigue has been reported in 75% of SSc patients, and is the most problematic symptom due to impact on quality of life. Despite its high prevalence, origin is unknown.[2] Some studies associate it with the degree of disease activity and decreased quality of life. Fatigue is defined as a feeling of exhaustion, also as a reduction in physical and mental capacity,[3] scales such as FACIT-F (Functional

Assessment of Chronic Illness Therapy-Fatigue) are used, which evaluates the last 7 days, with a score of 0-52. For the severity analysis, 4 grades are used: no or mild fatigue (40-52), moderate (27-39), severe (14-26) and extreme (0-13).[4,5]

Objectives: To evaluate the frequency and degree of fatigue in systemic sclerosis.

Methods: Prospective, longitudinal, observational study of the cohort of patients of the Rheumatology service of the Hospital Docente Padre Billini. Patients were interviewed in November 2021. Inclusion criteria: ≥18 years, diagnosis of SSc according ACR/EULAR 2013 classification criteria. Exclusion criteria: previous diagnosis of fibromyalgia, depression or anxiety, treatment with antidepressants, antihistamines, beta-blockers. Measurement of FACIT-F, HAQ-DI, mRSS scales. Statistical analysis was performed with the Pearson correlation (r_p) with p=>0.05. The data was analyzed by SPSS V23.

Results: 54 met inclusion criteria. 100% female, mean age 53.3±15.1 years, mean disease duration 11.3 years, SScd 75.9% (41), SScl 24.1% (13), interstitial pneumonia 33.3% (18), gastrointestinal reflux disease 27.8% (15), HAP 20.37% (11). Frequency of fatigue 100% (54): moderate FACIT-F: 29.6% (16), severe FACIT-F 38.8% (21), extreme 31.5% (17). Correlation FACIT-F with mRSS and HAQ-DI: Moderate FACIT-F: mRSS mild 43.8% (7), moderate 12.5% (2), severe 18.8% (3), terminal 25% (4), HAQ-DI mild 25% (4), moderate 37.5% (6), severe 18.8% (3). Severe FACIT-F: mRSS normal 4.8% (1), mild 19% (4), moderate 91% (4), severe 33.3 % (7), terminal 23.8% (5), HAQ-DI mild 4.8% (1), moderate 19% (4), severe 47.6% (10). FACIT-F extreme: mRSS mild 7.61% (3), moderate 29.4% (5), severe 35.3% (6), terminal 17.6% (3), HAQ-DI moderate 11.8% (2), severe 52.9% (9). r_p=. 246 p>0.05

Conclusion: The study demonstrated a high frequency of fatigue. The most frequent degree was severe. A statistically significant linear association was observed between skin involvement and the degree of functional limitation.

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AB0685 OXYGENATED HEMOGLOBIN AS PROGNOSTIC MARKER AMONG PATIENTS WITH SYSTEMIC SCLEROSIS SCREENED FOR PULMONARY HYPERTENSION

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Background: Oxygenated hemoglobin (OxyHem)[1] in arterial blood may reflect disease severity in patients with systemic sclerosis (SSc), particularly among those with pulmonary manifestations such as pulmonary hypertension (PH).

Objectives: Hence, the aim of this study was to analyze the predictive value of OxyHem in SSc patients screened for PH.

Methods: SSc patients were screened for PH including right heart catheterisation, laboratory and clinical assessment. They were followed for 3.2±2.6 (median 3.0) years. OxyHem was measured by multiplying the concentration of hemoglobin with oxygen saturation assessed in arterialized capillary blood. Kaplan-Meier analysis was performed using the defined threshold from Receiver Operating characteristic. Prognostic power was compared with known parameters of prognostic significance in SSc using uni- and multivariable analysis. Clinical parameters of patients with high and low OxyHem were compared by student's t-test.

Results: A total of 280 SSc patients were screened, 267 were included in the analysis (82% female, 59.8±13.4 years, 73.8% limited cutaneous SSc), 56 patients had manifest PH and 112 interstitial lung disease (ILD). Low OxyHem ≤12.5g/dl at baseline was significantly associated with a worse survival (p=0.046) among SSc patients. In the multivariable analysis the presence of ILD, age ≥60 years and diffusion capacity (DLCO) ≤65% were associated with worse survival among SSc patients. The combination of low DLCO and low OxyHem at baseline could predict the development of early pulmonary vascular disease at follow- up (sensitivity 79.6%).

Conclusion: This study detected for the first time that an OxyHem level ≤12.5 g/dl is a prognostic predictor in SSc- patients. Further studies are needed to confirm these results.

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AB0686 THE IMPACT OF SYSTEMIC SCLEROSIS (SSC) ON WOMEN'S HEALTH EVALUATED WITH A NEW SSC-SPECIFIC PATIENT-REPORTED QUESTIONNAIRE.

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Background: Systemic Sclerosis (SSc) can strongly affect the quality of life of affected women. We aimed at designing a SSc-specific, patient-reported questionnaire to explore different aspects of women's health.

Objectives: The questionnaire was created together with Obstetricians-Gynecologists (70 questions, 5 sections) and administered to consecutive patients with SSc (2013 ACR/EULAR classification criteria) regularly attending our Clinic in May-December 2021. The Female Sexual Function Index (FSFI) questionnaire was also administered.

Methods: The questionnaire was created together with Obstetricians-Gynecologists (70 questions, 5 sections) and administered to consecutive patients with SSc (2013 ACR/EULAR criteria) regularly attending our Clinic in the period May-December 2021. The Female Sexual Function Index (FSFI) questionnaire was also administered.

Results: Questionnaires were proposed to 114 patients; among 100 who accepted to participate (median age 59.0 [43.0-67.0], median disease duration 11.0 [6.0-17.0] years), 48% had received SSc diagnosis during reproductive age (<45 years). The cutaneous involvement was limited in 75% and anti-centromere were positive in 44%. A regular gynecological follow-up was not declared by 60% of the patients. Considering patients with SSc-diagnosis in reproductive age: 73% never discussed contraceptive methods with their SSc-Clinicians; 63% desired a pregnancy after diagnosis, but 30% did not satisfied the desired family size; about 50% reported they did not know whether a woman with SSc could experience

disease worsening or take safe medications during pregnancy, and have children also affected by SSc. 77% of patients declared improvement or stability of SSc manifestations during pregnancy. Table 1 shows the comparison of pregnancies before and after SSc diagnosis, based on data reported by the patients. Regarding sexuality, 59% reported that SSc negatively affected it by vaginal dryness (67%), digital ulcers (37%), gastro-intestinal disease (37%) and dyspnea (20%). Among 39 patients completing FSFI, 67% had sexual dysfunction.

Table 1. Results are presented as median [IQR] or number/number available data (%) based on patients answering the question. Continuous variables were compared with Mann-Whitney test; categorical variables with Fisher's exact test.

	Total pregnancies (n= 189)	Pregnancies after diagnosis (n= 42)	Pregnancies before diagnosis (n= 147)	p-value OR [95% CI]
Maternal age at conception, years	28.0 [24.0-32.0]	32.0 [28.0-39.0]	27.0 [23.0-30.0]	*< 0.001*
Live births	152/189 (80.4)	31/42 (73.8)	121/147 (82.3)	*0.221*
Cesarean sections	36/135 (26.7)	17/31 (54.8)	19/104 (18.3)	*< 0.001 5.43 [2.30-12.9]*
Preterm births <37 weeks	32/109 (29.4)	7/32 (21.9)	25/77 (32.5)	*0.269*
Preterm births <34weeks	7/32 (21.8)	2/7 (28.6)	5/25 (20.0)	*0.632*
Birth weight, kilograms	3.3 [2.8-3.6]	3.1 [2.5-3.5]	3.3 [3.0-3.7]	*0.049*
≥ 1 Adverse Pregnancy Outcomes	15/113 (13.3)	8/31 (25.8)	7/82 (8.5)	*0.016 3.73 [1.22-11.39]*
Gestational hypertension	4/113 (3.5)	3/31 (9.7)	1/82 (1.2)	*0.062*
Preeclampsia	1/113 (0.9)	1/31 (3.2)	0/82 (0.0)	*0.274*
Eclampsia	0/113 (0.0)	0/31 (0.0)	0/82 (0.0)	*1.000*
HELLP syndrome	1/113 (0.9)	0/31 (0.0)	1/82 (1.2)	*1.000*
Gestational diabetes	3/113 (2.7)	2/31 (6.5)	1/82 (1.2)	*0.182*
Intra Uterine Growth Restriction	4/113 (3.5)	2/31 (6.5)	2/82 (2.4)	*0.302*
Perinatal deaths	2/134 (1.5)	0/32 (0.0)	2/102 (1.9)	*1.000*
Neonatal Intensive Care Unit Admission	11/134 (8.2)	6/32 (18.8)	5/102 (4.9)	*0.022 4.48 [1.27-15.84]*
Perinatal infections	8/134 (8.2)	3/32 (9.4)	5/102 (4.9)	*0.396*
Breastfeeding	92/132 (69.7)	22/32 (68.8)	70/100 (70.0)	*0.893*

Conclusion: The newly created specific questionnaire was instrumental to facilitate physician-patient communication about 'women's health', particularly in the field of sexuality which is characterized by a high frequency of dysfunction. Adverse outcomes are possible during SSc pregnancies and should be discussed during the multidisciplinary preconception counselling, along with measures to possibly reduce their risk.

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AB0687 PROGNOSTIC MEANING OF RIGHT VENTRICULAR FUNCTION AND RESERVE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: The delay of the diagnosis of pulmonary hypertension (PH) in patients with systemic sclerosis (SSc) leads to severe impairment of survival.

Objectives: The objective of this study was to investigate the prognostic impact of right ventricular (RV) function at rest and during exercise on survival in patients with SSc presenting for screening for PH.

Methods: Data from SSc patients who underwent routinely performed examinations for PH screening including echocardiography and right heart catheterization at rest and during exercise were analyzed. Uni- and multivariable analyses were performed to identify prognostic parameters in SSc and to compare them to known prognostic predictors.

Results: Out of 285 SSc patients screened for PH, 225 patients (81.3% female, mean age 58.1±13.0 years, 68% limited cutaneous SSc, WHO-FC II-III 74%, 24 manifest PH) were included in the analysis. During an observation period of 3.2±2.7 (median 2.6) years 35 patients died. Tricuspid annular plane systolic excursion ≤18 mm (p=0.0004), increase of cardiac index (CI) during exercise ≤ 2 l/min (p=0.0002), RV output reserve >3 mmHg/l/min (p=0.001), peak CI ≤ 5.5l/min (p=0.01), pulmonary arterial compliance >2 ml/mmHg (p=0.0005) and qualitative RV function at rest (p<0.0001) significantly predicted survival. In the multivariable analysis, RV function at rest, diffusion capacity for carbon monoxide < 65% predicted and CI increase <2 l/min/m^2 were identified as independent prognostic predictors and had >70% sensitivity and specificity to predict development of pulmonary vascular disease (PVD) during follow-up.

Conclusion: This study demonstrates that assessment of RV function at rest and during exercise may provide crucial information to identify SSc patients who are at a high risk of an impaired survival and development of PVD.

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AB0688 PREDICTORS OF MUSCLE INVOLVEMENT IN PORTUGUESE PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE

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Background: Mixed connective tissue disease (MCTD) is a rare heterogeneous disease, characterized by overlapping features of classic connective tissue diseases. Myositis may be present in up to two-thirds of patients with MCTD and it is included in all diagnostic criteria available. Although some possible associations have been reported, to the best of our knowledge, no independent predictors of MCTD-related myositis have been described.

Objectives: To identify clinical and laboratorial predictors for muscular involvement in a cohort of Portuguese patients with MCTD.
Methods: Multicentre retrospective cohort study including adult-onset patients with a clinical diagnosis of MCTD and fulfilling at least one of the following diagnostic criteria: Sharp, Kasukawa, Alarcón-Segovia or Kahn criteria. Myositis was defined as proximal muscle weakness, creatine kinase elevation, electromyography (EMG) suggestive changes or a positive muscular biopsy. Univariate analysis was performed using Chi-Square, Fischer's Exact Test and Mann-Whitney Test, as appropriate. Multivariate analysis was performed using binary logistic regression modelling. The linearity of the continuous variables concerning the logit of the dependent variable was assessed via the Box-Tidwell procedure. Cases with missing information and outliers were excluded from the multivariate analysis to fulfil all assumptions necessary to assure the validity of the regression.
Results: A total of 98 patients were included, 43 (44.3%) of whom had muscular involvement at any time of the disease course. Concerning patients with MCTD-related myositis, the mean age at diagnosis was 34.8±12.5 years and the mean disease duration of 4.1±4.9 years. The majority of patients were female (90.7%) and of European ancestry (66.7%). EMG was performed in 24 patients, of whom 10 (41.7%) had a myopathic pattern. Seventeen patients were submitted to a muscular biopsy, of whom 8 (47.1%) had histological myositis features. Capillaroscopy was performed in 24 patients and 12 (50%) had a scleroderma pattern. African ancestry and leukopenia were positively associated with myositis at disease onset. Furthermore, fever at the onset of disease, younger age at diagnosis and shorter disease duration were positively associated with the occurrence of myositis at any phase of the disease. The multivariate analyses predicting myositis at diagnosis included 54 patients and at any time of the disease included 90 patients. These models explained 37.8% and 26.9% (Nagelkerke R2) of the variance in myositis and correctly classified 79.6% and 73.3% of all cases, respectively. African ancestry (OR 8.39, 95%CI: 1.43-49.37, p=0.019), leukopenia (OR 6.24, 95%CI: 1.32-29.48, p=0.021) and younger age at diagnosis (OR 1.07/year, 95%CI: 1.01-1.14, p=0.035) were identified as independent predictors of myositis at diagnosis. Fever (OR 6.51, 95%CI: 1.23-34.37, p=0.027) was an independent predictor of muscular involvement at any time of the disease in MCDT patients.
Conclusion: African ancestry, leukopenia and younger age at diagnosis are independent predictors of myositis at presentation in MCTD patients, while fever is an independent predictor of myositis at any time of the disease. While evaluating patients with MCTD, these predictive factors should be considered.
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AB0689 CLINICAL COURSES AND PREGNANCY OUTCOMES OF EIGHT CASES COMPLICATED WITH POLYMYOSITIS/DERMATOMYOSITIS (PM/DM) IN SINGLE CENTER

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Background: Pregnancies complicated by a number of rheumatic diseases are known to be at high risk for the occurrence of adverse pregnancy outcomes (APOs). There have been several reports on the risk of APOs in systemic lupus erythematosus and rheumatoid arthritis, but few reports on polymyositis (PM)/dermatomyositis (DM) pregnancies. There are also insufficient reports on changes in the activity of PM/DM during pregnancy. Based on the findings reported in other rheumatic diseases, it is suggested that increased activity during pregnancy is associated with APOs in PM/DM (1-3). However, the risk factors for pregnancy outcome in pregnancies complicated by PM/DM, including the presence or absence of worsening of disease activity, have not been clarified.
Objectives: The purpose of this study was to analyze a case series of PM/DM complicated pregnancies in a single center to determine the changes in disease activity during pregnancy and pregnancy outcomes.
Methods: PM/DM patients who were managed from pregnancy to delivery at Kagawa University Hospital from March 2006 to May 2021 were included in this study. Clinical indices including duration of illness, disease activity, and treatment were extracted from medical records and retrospectively analyzed for association with pregnancy outcome.
Results: Eight PM/DM pregnancies were included in the analysis. The mean age at delivery was 28.3±3.8 years and the mean duration of disease was 6.3±3.2 years. Treatment at the time of pregnancy included glucocorticoids (GC) in 7 cases and immunosuppressive drugs in 5 cases. Creatinine phosphokinase (CK) levels were normal in all patients at the time of pregnancy, but increased during pregnancy in 4 (50%) patients. These 4 patients with elevated CK required treatment with increasing doses of GC, and the mean GC dose during pregnancy was 10.9 ± 6.0 mg/day. Table 1 shows the pregnancy outcomes of the 8 patients. There was one spontaneous abortion and seven live births. Among the live births, 2 were preterm and 4 were low birth weight. The mean gestational age at delivery was 35.3±5.2 weeks and the mean birth weight was 2297.7±1041.4g.

Table 1. Pregnancy outcomes of eight cases

Case no.	Outcome	Mode of delivery	Gestational age at delivery (weeks)	Birth weight of the newborn (grams)	Adverse pregnancy outcomes
1	Live birth	Cesarean section	26	590	Preterm birth, LFD, HELLP syndrome
2	Spontaneous abortion				
3	Live birth	Transvaginal delivery	30	1,299	Preterm birth, LBW
4	Live birth	Cesarean section	38	2,765	Hypertensive disorder
5	Live birth	Transvaginal delivery	37	3,290	–
6	Live birth	Transvaginal delivery	37	2,492	LBW
7	Live birth	Transvaginal delivery	39	3,456	–
8	Live birth	Transvaginal delivery	40	2,192	LBW
	7 live births 1 abortion		35.3±5.2	2,297.7±1,041.4	

The birth outcomes of the 2 patients who received continuous immunosuppressive therapy were full-term and normal weight infants. APOs, such as preterm delivery and low birth weight, occurred in cases with increased CK levels and increased GC doses.
Conclusion: In pregnancies of PM/DM patients, pregnancy outcome was less than favorable. An association between disease activity and the development of APOs during pregnancy in PM/DM was suggested. An association was also suggested between GC dose and the risk of developing APOs. As in other rheumatic disease pregnancies, continued use of pregnancy-appropriate immunosuppressive drugs and control of disease activity with lower glucocorticoid doses in PM/DM pregnancies may be important to achieve good pregnancy outcomes.
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AB0690 CALCINOSIS CUTIS IN SYSTEMIC SCLEROSIS: CLINICAL AND BIOLOGICAL ASSOCIATIONS

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Background: Calcinosis cutis (CC) is a rare disorder characterized by the abnormal deposition of calcium salts in the subcutaneous tissues of patients with normal calcium metabolism. Dystrophic calcinosis is a common and potentially debilitating manifestation in systemic sclerosis (SSc) patients. The CC was described to appear more frequently in newly diagnosed SSc patients with Raynaud's phenomenon, with ischemic ulcer or telangiectasia and in areas related to repeated trauma, but current data remains inconclusive [1,2].

Objectives: Our objective was to analyze the prevalence, clinical features, and biological associations of CC in SSc patients.
Methods: A retrospective analysis of patients hospitalized in the Rheumatology Department of the Colentina Clinical Hospital, Bucharest, Romania. Data of the patients fulfilling the 2013 American College of Rheumatology/ European League Against Rheumatism (ACR/EULAR) SSc classification criteria were collected. In all patients, clinical examination, including evaluation of the cutaneous involvement by the modified Rodnan skin score (mRSS) was performed. A CC diagnosis was sustained by radiographic and/ or ultrasound imaging.
Results: 44 SSc patients were included with female predominance (39 patients - 88.6%), and with mean (SD) age 58.8±11.3 years old, CC was found in 11(25.0%) of these patients, all feminine gender. Elbow (36.4%), hands and forearms (27.3%) were the most frequent sites affected by CC.
Overall, CC was not related to the SSc subtype, when comparing limited (lc) with diffuse cutaneous (dc) involvement (27.3% *vs.* 48.5%, p=0.219). However, patients with CC had more often lc SSc, 72.7% *vs.* 27.3%. Accordingly, SSc patients with CC had a significant lower mRSS score, 6 (1;7) *vs*. 9 (5; 15.5) points, p=0.001 and more frequently expressed positives anti-centromere antibodies (ACA), 72.7% *vs.* 57.1%, p=0.036. CC was also found not to be related to sclerodactyly, 54.5% *vs.* 75.8%, p=0.038. Regarding the nailfold capillaroscopy (NFC) exam, the CC was more often described in patients with late NFC pattern, 45.5% of cases.
In SSc patients with CC, there was reported more often intestinal transit disturbances 45.5% *vs*. 3.0%, p=0.015, even if overall there was no gastrointestinal involvement, 72.7% *vs.* 63.6%, p=0.582.
Regarding inflammation, the level of erythrocyte sedimentation rate (ESR) was lower in patients with CC 18 (13;33) *vs.* 33 (17.0; 58.5) mm/h, p=0.040, but not the C-reactive protein level 2.4 (1.7; 6.7) *vs.* 3.3 (1.2; 8.5) mg/L, p=0.866.
When comparing SSc patients with or without CC we did not found any significant difference regarding the presence of anti-Scl70 antibodies, p=0.432, rheumatoid factor, p=0.067, lupus anticoagulant or antiphospholipid antibodies, p=0.835. Also, no significant correlations were identified for CC in SSc and the following parameters: smoking, p=0.162, obesity, p=0.812, hypertension, p=0.371, diabetes, p=0.403, Raynaud phenomenon, p=0.539, telangiectasia, p=0.28, pulmonary hypertension, p=0.777, lung interstitial disease, p=0.315, digital ulcers, p=0.723, or digital starry scars, p=0.223.
Conclusion: The CC prevalence in SSc consecutive patients was 25.0%, more frequently with elbow localization. We've also found more frequent CC in patients with positive ACA serology and defined relations with many other SSc-related parameters.
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AB0691 SYSTEMIC SCLEROSIS AT THE TIME OF COVID-19 PANDEMIC: A BIBLIOMETRIC STUDY

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Background: The Coronavirus disease 2019 (COVID-19) affects different organs and systems of the human organism. However, the main target remains the respiratory system and lungs in particular. Systemic sclerosis (SSc) is one of the systemic autoimmune diseases that can cause severe lung impairment. Considering the existence of common points of influence on the human organism, the overlapping of these two pathologies can significantly increase the negative impact on the patient's health.
Objectives: This study was aimed to analyze the common features of articles covering the link between COVID-19 and systemic sclerosis.
Methods: We retrieved the literature items in the scientific bibliometric database Scopus conducting our search on the 26th of January. We didn't set any time limits and did use the following keywords: "systemic sclerosis" OR "scleroderma" AND "Covid-19" OR "COVID-19" OR "coronavirus". The exclusion criteria were: absence of an abstract, literature items in form of conference papers, and articles dedicated to the rheumatological pathology in general with scarce mention of SSc. All selected papers were analyzed in view of the following characteristics: documents' type, authorship, journal, citations score, the origin of an article, language, and keywords. For data visualization, we have used software tool VOSviewer version 1.6.15 which make possible to build authors' and keywords' network (Figure 1 A and B) (the minimum keywords' threshold was 3 and the minimum author occurrence was 5).

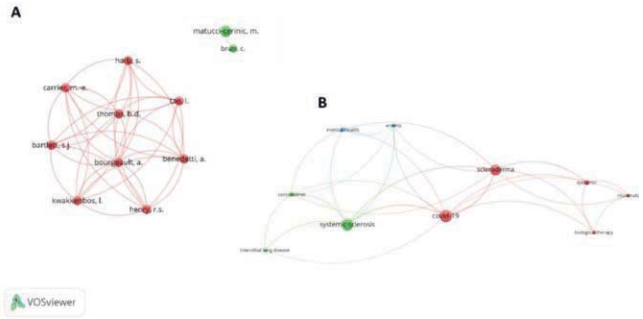

Figure 1.

Results: In the result of our comprehensive literature search only 206 items were obtained. After screening of title, abstract and keywords we omitted 166 articles as they met our exclusion criteria and were irrelevant for our study. The most (87.5%) of remained 40 articles were open access publications, which improves the articles' visibility and simplifies data sharing. The top journals covering this topic were: Annals Of The Rheumatic Diseases (n=7), Journal of Psychosomatic Research (n=4), Journal Of Scleroderma And Related Disorders (n=4), Clinical Rheumatology (n=3), Lancet Rheumatology (n=3) and Scandinavian Journal Of Rheumatology (n=3). The post productive authors originated from Italy (n of articles = 20); other countries with highest number of publications were: UK – 10; USA – 7; France – 7 and Netherlands – 6). The majority of papers were written in English and just one was in Chinese. The most prevalent research type among analyzed articles was Letter (47.5%), about a third of the articles were designed as Original Articles (35%), 7.5% were Notes, the number of Reviews and Editorials was 5% for each type. Based on the citations score, the most relevant article was dedicated to COVID-19 course in patients with SSc associated interstitial lung disease (SSC-ILD) using tocilizumab. The second highly cited paper highlighted a disease course of COVID-19 pneumonia in SSc patients treated with rituximab and the third actively cited article was World Scleroderma Foundation preliminary advice for patient management. It should also be noted that a lot of articles (n=7, 17.5%) were dedicated to the emotional wellbeing of SSc patients in time of COVID-19 pandemic.
Conclusion: Based on our literature analysis, it is the first attempt to overview comprehensively the papers focusing on SSc and COVID-19 overlap. The bibliometric studies offer an essential opportunity to emphasize the main features and trends in the particular topic and could be used by scientists as a guidance for forthcoming research.
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AB0692 PREDICTORS OF ILOPROST INFUSION TOLERANCE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is an autoimmune disease characterized by vasospasm and microvascular involvement. Iloprost (ILO), a prostaglandin analogous, is used for the treatment of SSc-related Raynaud's Phenomenon and digital ulcers. The indicated dosage is 0-5-2 ng/kg/min for 6-8 hours and the maximum dose is decided upon the patient's tolerance.
Objectives: Our study aims to analyse ILO infusion tolerance and possible predictive factors in patients with SSc.
Methods: We evaluated patients with SSc beginning ILO iv treatment between 2004 and 2021. We assessed the maximum tolerated ILO iv infusion rate, the incidence of adverse events (AEs) and the need for symptomatic therapy during the dose-finding sessions. We collected relevant demographic and medical data at the beginning of ILO iv treatment. Statistical

analysis were performed to assess possible predictors of maximum tolerated ILO infusion rate and AEs.
Results: We retrospectively analysed 113 patients. The median ILO infusion rate at the end of the dose-finding process was 0.88 ng/kg/min (IQR 0.37). We found a significant inverse correlation between ILO infusion rate and body mass index (BMI) at the beginning of treatment. BMI was negatively associated with ILO infusion rate (β -0.29, p = 0.001) after correction for relevant confounding factors. Subjects in the upper BMI tertile (BMI above 25) had a lower tolerance to ILO compared with subjects in the lower BMI tertile BMI below 22 (p=0.002). Disease pattern, disease duration, age at the onset of disease, mean blood pressure, gender, smoking habits, combination therapy with calcium channel blocker or endothelin inhibitors were not predictors of ILO tolerance. AEs during ILO titration occurred in 47.8% of patients, of whom 22.2% presented concomitant hypotension. The most common AEs were headache, nausea, vomiting, diarrhoea, oedema, hypotension, and symptomatic therapy was needed in half of the patients at least once. Overweight patients (BMI >26) presented a 13-fold increased risk of developing AEs during ILO titration (adjusted odd ratio 13.979 95% CI 2.359-82.845).
Conclusion: Our study showed that only a higher BMI was associated with lower ILO infusion rate tolerance and higher AEs rate, underlying a possible BMI-dependent endothelial dysfunction possibly mediated by endothelin receptor expression. Individual ILO regimens still need to be tailored to the patient.
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AB0693 EFFECTIVENESS OF RITUXIMAB IN PATIENTS WITH SYSTEMIC SCLEROSIS – EXPERIENCE IN A TERTIARY MEDICAL CENTER

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Background: There is ample evidence of B cell involvement in the pathogenesis of fibrosis in systemic sclerosis (SSc), making it a promising target for the treatment of skin and lung fibrosis in SSc. However, data regarding the long-term use of B cell depletion in the treatment of this life-threatening connective tissue disease is scarce.
Objectives: The primary aim of this study was to evaluate the safety and efficacy of long-term B cell depletion and to define the changes on both cutaneous and visceral organ involvement after rituximab (RTX) therapy in SSc patients over time, in a tertiary hospital.
Methods: A prospective observational case-control study, conducted between 2016 and 2021, enrolled 10 SSc patients, who fulfilled the ACR/EULAR 2013 classification criteria for scleroderma and who had received RTX infusions at least once. All patients had been taking immunosuppressive therapy previously. The following clinical data were included into the analysis: disease activity by the EUSTAR activity index, skin fibrosis by the modified Rodnan Skin Score (mRSS), interstitial lung disease by lung function tests including forced vital capacity (FVC), diffusing capacity of the lung for carbon monoxide (DLCO) and high-resolution CT (HRCT). For the comparison of non-parametric data at two time points, Wilcoxon matched paired Student's t-test was used.
Results: The study included 10 patients (all female), with a mean age of 52.9 years, most of them with diffuse subset (9/10), treated with RTX between 2016 and 2021. Average duration of disease before the RTX therapy was 27.6 months. Mean baseline mRSS was 19.3 and mean EUSTAR activity index was 4.48. Seven patients received 2 courses of RTX for at least 6 months, four of which were evaluated 1 year after the beginning of RTX therapy. We found a statistically significant improvement in mRSS (p=0.02) and EUSTAR activity index values (p=0.02), when comparing baseline levels with those found at each follow-up visit. Furthermore, all the patients who were treated with RTX early in the disease course achieved better results at 6 months follow-up. There was no significant change in PFT's, DLCO and chest HRCT lesions in all patients, neither in the subgroup with early disease, nor in the subgroup with worsening, progressing pulmonary function, during the follow up period.
Conclusion: Our results suggest that B cell depletion, in patients with SSc, leads mainly to a clinically relevant decrease in skin involvement and to a stabilization of disease activity after 6 and 12 months of use. The study did not find a clear beneficial effect on pulmonary function during short-term follow-up. Despite these considerations, our results indicate that the course of lung disease did not worsen in our patients. At 6-year follow-up the safety of single and repeated courses of the drug was confirmed. While the study provides important insights into the use of RTX in SSc, it is limited by the low number of patients, the lack of a sufficient control arm and the single center design.
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AB0694 VITAMIN D LEVELS IN SERUM OF PATIENTS WITH SYSTEMIC SCLEROSIS AND VERY-EARLY SYSTEMIC SCLEROSIS (VEDOSS)

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Background: Systemic sclerosis (SSc) is a chronic disease characterized by autoimmunity, vasculopathy, and visceral and cutaneous fibrosis and very-early systemic sclerosis VEDOSS is characterized by Raynaud's phenomenon with SSc marker autoantibodies and typical capillaroscopic finding. Vitamin D has several functions in the immunological system, and different studies have suggested a potential role in triggering autoimmune diseases. (1,2)
Objectives: Our goal was to verify the difference of Vitamin D levels causal in SSC definite and VEDOSS population, and relationship between hypovitaminosis D and SSc characteristics
Methods: 42 adults with SSc were recruited: 24 with American College of Rheumatology criteria were affected by diffuse systemic sclerosis (4) and limited systemic sclerosis (20); 18 with VEDOSS criteria. Patients were evaluated from medical history and physical examination (modified Rodnan skin score and the presence / number of ulcers), biohumoral evaluation of routine, electrocardiogram, echocardiogram, pulmonary function tests, high resolution computed tomography of the chest, capillaroscopy. For the determination of total vitamin D levels (25-OH), the serum samples were suitably centrifuged at 4 ° C at 3500g. Vitamin D levels were then determined by a two-step chemiluminescence enzyme immunoassay (CLIA), with a maximum limit of 100 ng / ml.
Results: The 42 subjects recruited (4 men and 38 women); age 48.2 ± 11.5 years (mean ± SD). All subjects were ANA positive, with anti-Scl70 positivity in dcSSc patients (4) and anti-centromere lcSSc patients (18). Patients with VEDOSS showed optimal serum levels of vitamin D (33.93 ± 3.5 ng / ml). Conversely, patients with systemic sclerosis showed serum levels of vitamin D at the limit of sufficiency (21.75 ± 4.0 ng / ml). (Figure 1) In particular, in the group of patients with systemic sclerosis, vitamin D levels were significantly reduced by 1.5 times (P <0.05) compared to VEDOSS group. In patients with SSc the serum levels of vitamin D were inversely proportional to the presence of mega capillaries. Furthermore, a directly proportional correlation of the serum levels of vitamin D with the age of the patient. It is therefore possible to assume that higher levels of vitamin D delay the onset of the disease, while lower levels of vitamin D favor the onset of the same.
Conclusion: Considering our findings from this work, it is possible to consider the Vitamin D supplement in patients suffering from sclerosis, especially as an adjuvant in the initial phase of the disease, thus hypothesizing a slowdown in the progression of the disease and an improvement in prognosis.
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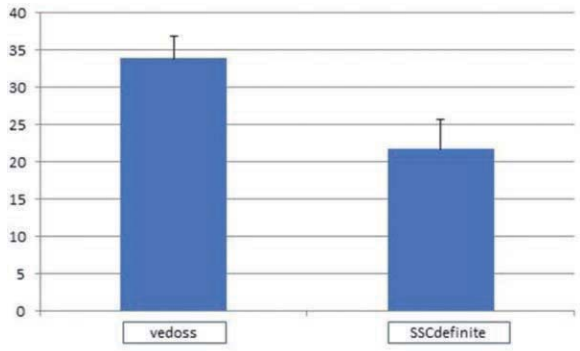

Figure 1.
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AB0695

ANTI-TH/TO POSITIVITY IN SYSTEMIC SCLEROSIS: ANALYSIS OF PULMONARY INVOLVEMENT, ORGAN DAMAGE ACCRUAL AND MORTALITY IN AN ITALIAN MONOCENTRIC COHORT

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Background: Anti-Th/To antibodies, detected in 2-5% Systemic Sclerosis (SSc) patients, are associated to interstitial lung disease (ILD)[1] in half of the cases. However, long-term data on ILD as well as on organ damage accrual are lacking.
Objectives: To describe the clinical associations of anti-Th/To SSc patients, focusing on ILD, organ damage and mortality.
Methods: Monocentric retrospective study. 1) Description of clinical associations of anti-Th/To SSc patients (2013 ACR/EULAR criteria). 2) Case-control study: anti-Th/To vs anti-Topoisomerase (anti-Topo)1 patients (1:3; matched for sex and age at SSc onset) regarding a) ILD b) organ damage c) survival. ILD progression was assessed through pulmonary function tests (PFTs) at baseline (T0) and after 1 (T1), 5 (T5), 10 (T10) and 20 (T20) years. Organ damage was evaluated with SCTD-Damage Index (SCTD-DI)[2]. Continuous data are expressed as median [IQR].
Results: We identified 13 anti-Th/To patients (all Caucasians, F/M=10/3, median age at SSc onset: 50 [37-67] years). Anti-Th/To were assayed by RNA immunoprecipitation in 8/13 and by immunoblotting in 5/13 cases.
1) 2/13 patients had SSc/myositis overlap syndrome: 1 associated to anti-SRP, 1 negative for myositis specific antibodies and affected by a synchronous (±3 years from onset) cancer. All presented lcSSc, 77% esophageal symptoms, 46% digital ulcers (DUs), 40% ILD, 39% telangiectasias, 39% heart involvement (3 pericarditis, 1 myocarditis in patient anti-SRP+, 1 arrhythmia), 15% gastrointestinal symptoms, 15% myositis and 8% calcinosis. No patients presented synovitis, joint contractures, pulmonary arterial hypertension nor scleroderma renal crisis.
2a) Anti-Th/To ILD patients, as compared to 39 anti-Topo 1, less frequently required immunosuppression and never required antifibrotic or O_2 therapy (Table 1); ILD progression (%pFVC decline ≥10% or %pFVC decline 5-10% and %pDLCO decline ≥15%) was shown for 3/13, albeit, after a longer interval than in 8/39 anti-Topo 1 progressors (15 [10-15] vs 1 [1-6.3] years, p:0.05); none died because of ILD.

Table 1.

	anti-Th/To+ n=13	anti-Topo 1+ n=39	p-value
ILD on HRTC	4/10 (40)	28/33 (85)	**0.01**
Immunosuppressants	1/13 (8)	16/39 (41)	**0.04**
Antifibrotic and/or O_2	0/13 (0)	8/39 (21)	0.18
PH secondary to ILD	0/13 (0)	6/39 (15)	0.32
SSc-ILD related death	0/13 (0)	6/39 (15)	0.32
%pFVC T0	105 [85-114]	90 [81-114]	0.26
%pFVC T1	107 [97-112]	88 [80-108]	0.09
%pFVC T5	97 [84-114]	99 [83-111]	0.88
%pFVC T10	103 [91-114]	88 [80-112]	0.23
%pFVC T20	104 [83-111]	81 [74-103]	0.35
%pFVC <70% T0	0/13 (0)	3/39 (8)	0.56
%pFVC <70% T1	0/12 (0)	3/39 (8)	1.00
%pFVC <70% T5	0/10 (0)	3/33 (9)	1.00
%pFVC <70% T10	0/7 (0)	3/25 (12)	1.00
%pFVC <70% T20	0/5 (0)	1/8 (13)	1.00
Progressive fibrosis (PF)* [T1-T0]	0/12 (0)	5/39 (13)	0.32
PF* [T5-T0]	1/10 (10)	5/33 (15)	1.00
PF* [T10-T0]	1/7 (14)	4/25 (16)	1.00
PF* [T20-T0]	2/5 (40)	0/8 (0)	0.20

Continuous data are presented as median [IQR] and compared with Mann-Whitney test; categorical data are presented as number/number available data (%) and compared with Chi-square test/Fisher's exact test. *Progressive fibrosis= %pFVC decline ≥10% or 5-10% %pFVC decline and %pDLCO decline ≥15%.

2b) During 16 [6-20] years of follow-up, SCTD-DI score progressively increased, but remained low in all patients (SCTD-DI ≤5) and was significantly lower than in anti-Topo 1 (Figure 1*a*), mainly due to ILD, joint contractures and DUs in the latter group (85% vs 40%, p:0.01; 39% vs 0%, p:0.01; 77% vs 46%, p:0.08).

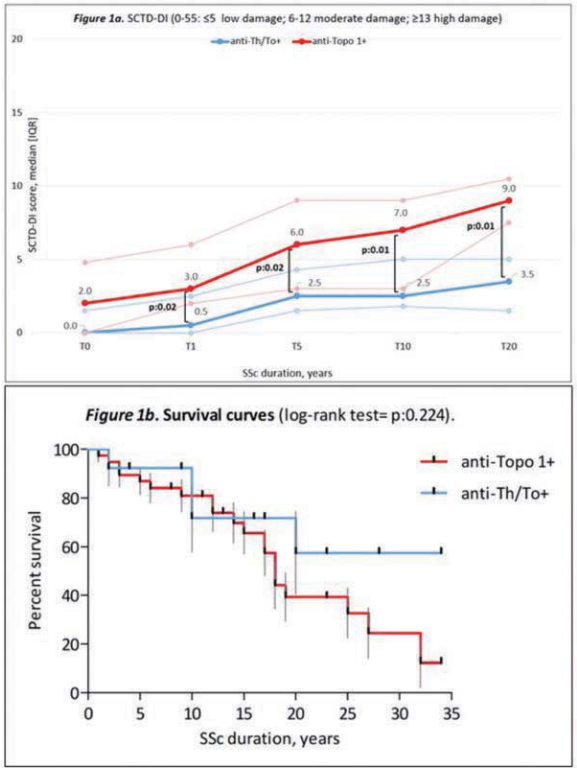

Figure 1.

2c) 4/13 patients died at 81 [75-86] years after 10 [8-13] years of disease duration, none due to SSc. The survival curves of the two groups are showed in Figure 1*b*.
Conclusion: In this cohort anti-Th/To patients showed a mild SSc phenotype, characterized by lower organ damage, more favorable long-term ILD functional outcome (although detectable in 40% of patients) and higher survival, as compared to matched anti-Topo 1 patients. Larger multicenter studies are needed to confirm these data.
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AB0696

PREVALENCE AND CLINICAL ASSOCIATIONS OF DIFFERENT AUTOANTIBODIES IN THE REUMA.PT SYSTEMIC SCLEROSIS COHORT: IS IT ALL REALLY SET IN STONE?

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Background: Different autoantibodies (Ab) have been associated with distinct systemic sclerosis (SSc) phenotypes. Most of these associations have not been confirmed in Portuguese patients.

Objectives: To evaluate SSc immuno-clinical associations in the Rheumatic Diseases Portuguese Register (Reuma.pt) cohort.
Methods: Multicentre open cohort study including adult SSc patients registered in Reuma.pt up to February 2021. The associations between Ab expression and clinical data were established using Chi-Square, Fischer's Exact or Mann-Whitney U tests. The Bonferroni correction for multiple comparisons was applied to get $\alpha \leq 0.05$. Definite associations were defined by $p \leq 0.002$, and likely associations by $p \leq 0.05$.
Results: 1080 patients were included, with a mean age and disease duration of 60.2±14.6 and 12.4±10.0 years, respectively. Most were females (87.5%) and had white European ancestry (WEA, 93.2%). The most common disease subtypes were limited cutaneous (lcSSc, 57.4%), diffuse cutaneous (dcSSc, 17.7%), and very early diagnosis of SSc (VEDOSS, 12.3%). Most patients expressed antinuclear Ab (ANA, 93.4%), and the most frequent were anti-centromere (ACA, 54.6%), anti-topoisomerase I (Scl70, 21.8%), and anti-Pm/Scl Ab (PmScl, 4.7%).
ACA had definite positive associations with female sex, older age at diagnosis, lcSSc, lower modified Rodnan skin score (mRSS, median 0 vs 4), and isolated sclerodactyly, and likely associations with a higher diagnosis delay, WEA and VEDOSS. ACA had definite inverse associations with flexion contractures (FC), myositis, digital ulcers (DU), and interstitial lung disease (ILD), and likely inverse associations with pitting scars (PS) and oesophageal involvement (OI).
Scl70 had definite positive associations with male sex, dcSSc, higher mRSS, FC, DU, PS, ILD, and OI, and likely associations with younger age at diagnosis, tendon friction rubs, active scleroderma pattern in capillaroscopy, and heart involvement.
PmScl had a definite association with myositis and likely associations with male sex, calcinosis, joints involvement, and ILD. Anti-U1RNP Ab had definite associations with younger age at diagnosis, MCTD and myositis, and likely associations with a lower diagnosis delay, African ancestry and joint involvement. Anti-RNA polymerase III Ab (RP3) had likely associations with higher mRSS and renal involvement. Anti-U3RNP Ab had a definite association with dcSSc and likely associations with calcinosis and renal involvement. Anti-Th/To Ab had likely associations with male sex and myositis. Anti-Ku Ab had likely associations with systemic lupus erythematosus and mixed connective tissue disease (MCTD) overlap syndromes.
Conclusion: There was a higher prevalence of ACA and PmScl compared to other cohorts, most likely due to the high proportion of WEA patients. Most immuno-clinical associations described in the literature apply, including ACA with lcSSc and Scl70 with dcSSc, DU, PS and ILD. However, Scl70+ patients did not have an increased risk of renal involvement, and ACA+ patients did not have an increased risk for calcinosis, PAH or OI, contrary to what was described in the literature. New findings included the association of PmScl with ILD and Scl70 with an active pattern in capillaroscopy. Also, anti-U3RNP+ and Th/To+ patients did not have an increased risk of ILD or PAH, contrarily to what was previously reported. These nuances may be specific to the Portuguese SSc population or signal previously reported associations as geographically specific.
Disclosure of Interests: None declared
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AB0697 DRAMATIC REDUCTION OF MORTALITY RATE BY TOFACITINIB IN ANTI-MDA-5 ANTIBODY-POSITIVE PATIENTS WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE

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Background: Rapidly progressive interstitial lung disease (RP-ILD) is often seen in dermatomyositis patients with anti-melanoma differentiation-associated gene 5 (anti-MDA-5) antibody. They often have a poor prognosis with rapid decline in pulmonary function, leading to respiratory failure (1). Aggressive immunosuppressive therapy has been reported with improved prognosis, however; it may lead to opportunistic infections, including cytomegalovirus (CMV) or Pneumocystis pneumonia (PCP) infection (2, 3).
Objectives: This study aimed to evaluate the effectiveness of tofacitinib (TOF) in combination with CMV and PCP prophylaxis in anti-MDA-5-positive patients.
Methods: Medical records of 17 anti-MDA-5-positive RP-ILD patients enrolled during Mar 2017 to May 2021 were reviewed. RP-ILD was defined by the presence of deteriorated dyspnea, with a decrease in PaO2 levels and emerging radiographic anomalies within 4 weeks without evidence of infection (4). Chest CT was scored using Ichikado score (5). Clinical parameters including ferritin levels, white counts (WBC), Lactate dehydrogenase (LDH) levels, GAP scores (Gender, Age, and Physiology score for idiopathic pulmonary fibrosis) were recorded. Medications included cyclophosphamide (CyP), intravenous immunoglobulin (IVIG), mycophenolic acid derivatives (MPA), rituximab (RTX), and calcineurin inhibitor (CNI). Kaplan-Meier survival analysis and Log-rank test were used to evaluate one-year mortality differences (MedCalc version 19.6). The Ethics Committee approved our study (CE17038B).
Results: Six anti-MDA-5-positive RP-ILD patients were treated with tofacitinib; five had concomitant CMV prophylaxis with valganciclovir (VGCV); 4 had PCP prophylaxis with trimethoprim/sulfamethoxazole (TMP-SMX). Patients' demographic data are shown in Table 1. The median age, clinical manifestations, laboratory data, and chest CT scores were comparable between tofacitinib and non-tofacitinib groups. Prevalence of MPA use was higher in the non-TOF group. Kaplan-Meier survival analysis (Figure 1) indicated that patients with tofacitinib treatment (p=0.001), valganciclovir (p=0.003), and TMP-SMX (p=0.028) prophylaxis exhibited better 1-year survival rates compared with those without TOF therapy, VGCV, and TMP-SMX prophylaxis.

Table 1. Clinical characteristics of anti-MDA-5 antibody-positive patients with RP-ILD receiving tofacitinib vs non-tofacitinib treatment.

	Tofacitinib (n=6)	Non-tofacitinib (n=11)	*p* value
Age (years)	58 (42.3-77)	57 (50.0-62.0)	0.884
Female sex, n (%)	2 (33.3)	6 (54.5)	0.620
Diabetes mellitus, n (%)	0 (0)	5 (45.5)	0.102
Fever, n (%)	5 (83.3)	10 (90.9)	1.000
Mechanic's hands, n (%)	4 (66.7)	5 (45.5)	0.620
Ferritin (n=16, ng/ml))	2670.9 (719.7-4209.7)	1563.5 (967.8-3169.0)	0.635
WBC (x1000µl)	8.7 (6.5-9.9)	8.7 (6.0-12.9)	0.884
LDH (n=16, U/l)	367.0 (218.0-557.5)	433.0 (331.0-625.3)	0.313
GAP score	5 (2.5-8)	5 (2-6)	0.808
CT score	200.0 (124.2-214.2)	196.7 (153.3-273.3)	0.733
TMP-SMX, n (%)	4 (66.7)	0 (0)	0.006**
VGCV, n (%)	5 (83.3)	0 (0)	0.001**
CyP, n (%)	1 (16.7)	4 (36.4)	0.600
IVIG, n (%)	1 (16.7)	6 (54.5)	0.304
MPA, n (%)	0 (0)	7 (63.6)	0.035*
RTX, n (%)	3 (50.0)	5 (45.5)	1.000
CNI, n (%)	2 (33.3)	6 (54.5)	0.620

Continuous variables were expressed as median (inter-quartile range).*$p<0.05$, **$p<0.01$ by Mann–Whitney U test or Fisher's Exact test.

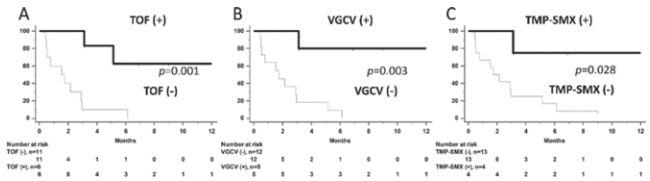

Figure 1.

Conclusion: The study demonstrated the efficacy of tofacitinib treatment in anti-MDA-5-positive RP-ILD. In addition, CMV and PCP prophylaxis appeared to improve in 1-year survival. Rheumatologists might consider TOF with prophylaxis as an option for anti-MDA-5-positive patients in daily practice.
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AB0698 IMPACT OF ILOPROST WITHDRAWAL IN SCLERODERMA PATIENTS DUE TO COVID-19 PANDEMIC

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Background: Intravenous iloprost is currently recommended in the treatment of Raynaud's phenomenon (RP) refractory to oral therapy and of digital ulcers (DUs) related to systemic sclerosis (SSc). In real-life practice there is a huge heterogeneity about the Iloprost regimens used, because of a lack of specific recommendations. Coronavirus pandemic resulted in an unexpected emergency leading to sudden and synchronous withdrawal of programmed iloprost infusions for most SSc patients in March 2020, in order to limit virus dissemination. At the same time, lockdown forced people to stay at home, thus reducing the exposure to coldness. Both these unavoidable circumstances were close to an experimental condition, clearly non-replicable in routine conditions.
Objectives: The aim of the survey was to evaluate the consequences related to a sudden and simultaneous iloprost discontinuation in a cohort of SSc patients.
Methods: A telephone survey was carried out on SSc patients that interrupted Iloprost infusion at our centre. They were specifically asked to compare acral vascular symptoms just before Iloprost withdrawal, in February and just after the missed infusion in March (0-10 scale). Demographic and disease characteristics, severity and frequency of RP, new DUs onset or aggravation of those pre-existing were reported for each patient. Last available capillaroscopic images were also evaluated to assess the pattern.
Results: The analysis included 50 patients. After iloprost withdrawal, 11 patients reported a RP worsening because of enhanced intensity (4.6±2.1 vs 5.2±2.3, p=0.007). Only 8 patients of them also complained of an increased frequency (4.5±2.3 vs 5.0±2.4, p=0.07). None of the patients experienced digital ulcers for the first time during quarantine. Among the 27 patients with a history of digital ulcers, 9 reported worsening and 7 recurrences of DUs. Overall, 17 patients (34.0%) complained of a worsening of SSc vascular acral manifestations, namely RP or DUs. Disease and general features did not statistically correlate with worsening of RP except for reduced capillary density. Of note, each unit increase of capillary density corresponds to an average 44% decrease in the odds of RP worsening (OR 0.56, CI 95% 0.36-0.97, p=0.037). History of DUs - either active or former at the time of iloprost discontinuation - was the only clinical predictor of worsening of DU severity. As for RP worsening, the worsening of DU was associated with a lower capillary density.
Conclusion: Low capillary density can predict a worsening of both RP and DUs within a month after iloprost discontinuation in SSc patients. Further studies are needed to assess whether the capillaroscopy should be used to personalize iloprost regimen in SSc patients.
Disclosure of Interests: None declared
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AB0699 DESCRIPTIVE STUDY OF A COHORT OF PATIENTS WITH DERMATOMYOSITIS IN A TERTIARY HOSPITAL.

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Background: Idiopathic chronic inflammatory myopathies (IICM) are a heterogeneous group of rare diseases characterized by skeletal muscle inflammation. The incidence ranges from 1 to 60 new cases per 1,000,000 habitants/year and the prevalence between 2.4 and 34 per 100,000 habitants.The main symptoms are muscle weakness, which may be accompanied by contractures, pain, cramps or stiffness and symptoms related to localized disease in skin, lungs and other organs. Increased muscle enzymes and a myopathic pattern are seen on electromyography. Definitive diagnosis is made by muscle biopsy with lymphocyte infiltrates, necrosis and regeneration of muscle fibers.
Objectives: Description of the clinical characteristics of a cohort of patients diagnosed with dermatomyositis together with the study of the evolution: organic involvement, specific autoantibody profile and treatments performed in this population.
Methods: Descriptive study of a cohort of patients diagnosed with dermatomyositis at the Rocio Virgin University Hospital (Seville), during 2010-2022, obtained from medical records.
Results: Sixty patients were included, including 17 (28.3%), 43 (71.7%) women, whose mean age 58 +/-12 years, and mean time of diagnosis was 5 years. Among the types of inflammatory myopathies: dermatomyositis 37 (61.6%), amyopathic DM 6 (10%), antisynthetase syndrome 5 (8.3%), paraneoplastic 1 (1.6%) and rapidly progressive MDA5 7 (11.6%) Among the most frequent affections: pulmonary 20 (34%) being the most frequent NINE pattern 9 (45%), NIU 8 (40%); esophageal 20 (34%), cardiological 12 (20%).
Among the specific antibodies: ANA positive 24(40%), Ro 3(5%), La4(6.6%),JO1 6(10%),PL7 1(1.6%)PL12 1(1.6%),Mi2 1(,1.6%),SAE 3(5%),NXP2 2(3.3%),SRP 1(1.6%),MDA5 7(11.6%) and HMG-CoA 3(5%). Among the diagnostic tests MRI/electromyogram were positive 63% and 56.6% respectively. Biopsy was positive in 72%(42) of cases. The drugs used to induce remission were: cyclophosphamide 36 (60%), rituximab 12 (20%), immunoglobulins 6 (10%) and mycophenolate mofetil 6 (10%). As for the maintenance of remission: mycophenolate 54 (90%), methotrexate 3 (5%) and azathioprine 3 (5%). There was only one exitus caused by cardiac arrhythmia.
Conclusion: The results obtained have been in accordance with the published literature, with a clear association between specific autoantibodies and the different muscular and extramuscular manifestations. Among the remission inducers, the most frequent regimen used in our setting is the use of cyclophosphosmide/rituximab and maintenance of remission with azathioprine and mycophenonate. More studies on new therapeutic options are needed.
Disclosure of Interests: None declared
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AB0700 HIGH BRONCHOALVEOLAR FLUID NEUTROPHILS INDEPENDENTLY PREDICT 15-YEAR MORTALITY IN SCLERODERMA PATIENTS WITH INTERSTITIAL LUNG DISEASE NAIVE TO IMMUNOSUPPRESSANTS

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Background: Scleroderma interstitial lung disease (SSc-ILD) has a variable and poorly predictable course. Data about the role of bronchoalveolar lavage fluid (BALF) analysis in prognostic stratification of SSc-ILD patients (pts) are conflicting.
Objectives: To assess BALF analysis role in prognostic stratification of SSc-ILD pts.
Methods: Forty SSc-ILD pts naive to immunosuppressants underwent comprehensive clinical evaluation, BALF analysis with total and differential leukocyte count, pulmonary function tests (PFTs), high-resolution computed tomography (HRCT) of the chest. All pts had fibrosing lung disease affecting more than 10% of lung volume on HRCT. Baseline alveolar and interstitial scores were computed. The 15-year crude mortality rate was retrospectively assessed.
Results: The enrolled pts (male 20%, aged 53.9±13 years) had a disease duration of4.3±3.4 years. Diffuse cutaneous involvement LeRoy variant was present in 47.5% of pts, while anti-Scl70 and anti-centromere antibodies were detected in 57.5% and 12.5% of pts, respectively. The average alveolar and interstitial scores were 6.5±4.8 and 6.2±2.7, respectively; 25% of the pts had FVC less than or equal to 80% and 35% had DLco less than or equal to 80%. During the follow-up, 18 pts (45%) received immunosuppressants. BALF neutrophilia (> 3%), eosinophilia (>1%) and lymphocytosis (>15%) were reported in 40%, 16% and 5% of pts, respectively. Twenty-five pts (62.5%) died within 15 years after bronchoscopy. Fifteen-year mortality was predicted by neutrophilia (HR 5.5, 95% IC 1.9-15.7), log-transformed total cell count (HR 2.5, 95% IC 1.1-5.7), absolute neutrophil (HR 1.8, 95% IC 1.3-2.5) and eosinophil (HR 1.3, 95% IC 1.1-1-6) cell counts, and macrophage (HR 0.1, 95% IC 0-0.6), neutrophil (HR 1.9, 95% IC 1.3-2.7), and eosinophil (HR1.3, 95% IC 1-1.7) percentages. Only absolute and relative neutrophil counts were independently associated with mortality also in regression models adjusted for demographics (age, gender), main disease traits (diffuse cutaneous variant, anti-Scl70 positivity), pulmonary function tests (FVC, DLco), HRCT involvement (alveolar and interstitial scores) and vascular complications (presence of pulmonary hypertension, digital ulcers).
Conclusion: High BALF neutrophils were associated with high 15-year mortality independently from established clinical risk factors. BALF analysis could improve prognosis prediction in SSc-ILD pts.
Disclosure of Interests: None declared
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AB0701 FREQUENCY AND RISK FACTORS OF OSTEOPOROSIS IN MEN WITH SYSTEMIC SCLERODERMA

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Objectives: To identify the frequency and risk factors of osteoporosis (OP) in men with systemic scleroderma (SSc).
Methods: 37 men with SSc were enrolled in the study: 19 (51,4%) with limited and 18 (48,6%) with diffuse cutaneous subtype. Patients with overlap rheumatic syndromes were not included. The median age was 56,0 [46,0; 61,0] years, the median duration of the disease was 6,0 [3,0; 9,0] years. 31 (83,8%) patients were treated with glucocorticoids (GC) > 3 months, the median duration of GC use was 3,7 [2,0; 7,0] years. Dual energy X–ray absorptiometry (DXA) of the lumbar spine (LS), the femoral neck (FN) and the total hip (TH) was performed. Osteoporosis (OP) was diagnosed with a T-score < -2.5 SD and osteopenia – with a T-score from -1SD to -2.5 SD at any region of interest. Z-score < -2 SD was used for diagnosis of OP in men < 50 years old. Spearman correlation between BMD and different factors was performed. Traditional and specific risk factors for OP were analyzed using univariate logistic regression analysis.
Results: The median LS BMD was 1,13 [1,03; 1,26] g/cm2, the FN BMD 0,95 [0,84; 0,99] г g/cm2 and the TH BMD - 0,99 [0,93; 1,06] g/cm2. Low BMD at least in one region of interest was detected in 19 (51,4%) patients: OP – in 8 (21,6%) (6 persons

50 years and older and 2 men < 50 years); osteopenia – in 11 (29,7%) men, without significant difference between the subtypes of the disease (p>0,05). 9 (24,3%) men had a history of low-trauma fracture, among them 2 (22,2%) patients had OP, 3 (33,3%) - osteopenia and 4 (44,4%) persons - normal BMD. 5 (27,8%) men with diffuse form and 3 (15,8%) - with limited cutaneous subtype had OP (p>0,05).
BMD in the LS correlated with uric acid (UA) (Rs = 0,59, p<0.05), BMD in the FN and BMD in the TH - with duration of the disease (Rs = -0,39, p<0.05 and Rs = -0,42, p<0.05, respectively), with duration of GC intake (Rs = -0,46, p<0.05 and Rs = -0,51, p<0.05, respectively), with the level of alkaline phosphatase (AP) (Rs = -0,54, p<0.05 and Rs = -0,46, p<0.05). In univariate logistic regression analysis, we found out that only the force vital capacity (FVC) was associated with OP (OR 15,19 [1.15; 199.79], p=0,04). There was no association between OP and other factors such as the duration of the disease or GC intake, the level of UC and AP.
Conclusion: OP was found in 21.6% of men with SSc. There was no statistically significant difference in the frequency of OP depending on the subtype of the disease. Among analyzed factors, only the FVC was positive associated with OP. Further research is needed.
Disclosure of Interests: None declared
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AB0702 COEXISTENCE OF SYSTEMIC SCLEROSIS AND MICROSCOPIC POLYANGITIS ASSOCIATED WITH PULMONARY RENAL SYNDROME: A CASE REPORT AND LITERATURE REVIEW

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Background: Systemic sclerosis is a chronic immune disease characterized by varying degrees of fibrosis of skin and internal organs. Microscopic polyangitis, as a subtype of ANCA associated vasculitis, mainly involves small blood vessels, often manifested as necrotizing glomerulonephritis and pulmonary capillary vasculitis. Pulmonary renal syndrome is characterized by diffuse alveolar hemorrhage based on pulmonary capillary vasculitis and rapidly progressive glomerulonephritis, which can be derived from a variety of autoimmune diseases, of which ANCA associated vasculitis accounts for about 60%[1]. The cases of coexistence of systemic sclerosis and microscopic polyangitis associated with pulmonary renal syndrome in clinic are rare, which is often dangerous and is easy to miss diagnosis or misdiagnosis.
Objectives: To investigate the clinical characteristics, diagnosis and treatment of coexistence of systemic sclerosis (SSC) and microscopic polyangitis (M-PA) associated with pulmonary renal syndrome (PRS).
Methods: The clinical data, diagnosis and treatment process of a patient who has SSC combined with MPA and PRS were summarized and analyzed. And the literature was reviewed to explore the correlation of the pathogenesis and clinical experience of SSC complicated with MPA and PRS.
Results: The case is a middle-aged male who was diagnosed as SSc due to the hardening of the skin of both hands , Reynolds phenomenon, the anti-scl-70 antibody are positive. The patient suffered from repeated hemoptysis, progressive dyspnea, severe anemia and renal insufficiency, so he was diagnosed as MPA with PRS. After giving glucocorticoid, immunosuppressant and anti-infection treatment, his condition has improved. A total of 7 case reports were retrieved by reviewing the relevant literature.A total of 7 patients were reported.They were first diagnosed as SSc and then MPA with PRS, of which 4 cases improved after treatment and 3 cases died. Among the dead patients, 1 case was treated with penicillamine for 3 years, and the remaining 2 cases were only treated with steroids without immunosuppressants.In SSc, P-ANCA is closely related to vasculitis, and the prognosis of PRS secondary to P-ANCA may be very poor. Most of the diagnosis of MPA is only after patients have kidney or lung diseases.There is a certain correlation between them in pathogenesis. Glucocorticoids, immunosuppressants, biological agents, hemodialysis and plasma exchange are the main treatments.
Conclusion: Although the cases of SSc combined with MPA and PRS are rare, there are still many cases reported,which reminds us: ①When SSc patients have new symptoms such as renal insufficiency or lungs, they should be alert to new entities that may be combined with other autoimmune diseases to avoid missed diagnosis or misdiagnosis.②ANCA should be detected in SSc patients at baseline, which may be related to disease activity.③PRS has rapid progress and high mortality, whcih is an emergency that needs urgent treatment. Such patients should be treated with glucocorticoid, immunosuppression and plasma exchange immediately. However, if patients are complicated with SSc, they need to be extra careful when using high-dose steroids, which increases the risk of renal crisis.
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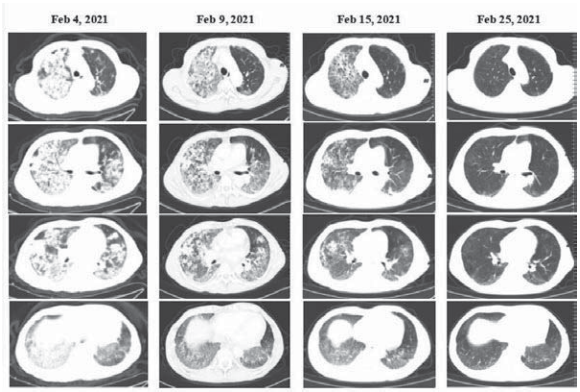

Figure 1. The contrast of chest CT before and after treatment showed that the exudative lesions of both lungs were significantly absorbed

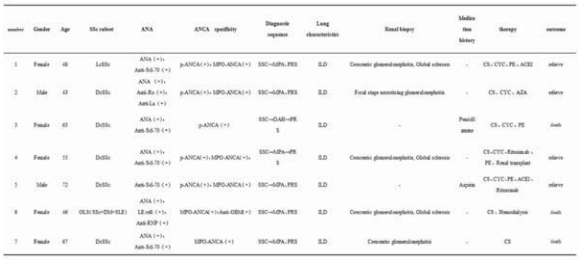

Figure 2. Clinical data of systemic sclerosis combined with microscopic polyangitis and pulmonary renal syndrome

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AB0703 THE NEED FOR ANTI-OSTEOPOROTIC THERAPY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Objectives: To determine the need for anti-osteoporotic therapy in postmenopausal women and men over 50 years of age with systemic sclerosis (SSc).
Methods: The study included 150 patients with SSc who met the ACR/EULAR 2013 criteria: 124 (82,7%) postmenopausal women and 26 (17.3%) men over 50 years of age. Median age was 59,0 [54,0; 64,0] years. The duration of the disease was 8,0 [5,0; 14,5] years. A history of fragility fractures was collected. FRAX was calculated in patients without prior fractures to identify patients at high risk of low-energy fractures. Dual-energy X-ray densitometry (DXA) was performed in persons at moderate risk of fractures, and 10-year probability of major osteoporotic fractures was recalculated with the inclusion of a hip neck T-score. DXA was also performed on all patients from the low-risk group who had 2 or more risk factors of OP.
Results: 36 (24%) patients had a history of fragility fractures: 21 (16.9%) women and 6 (4.3%) men - vertebrae fracture, 8 (6.5%) women - peripheral fractures, 1 (3.8%) man – hip fracture.
The calculation of the 10-year probability of fractures by FRAX showed that 21 (16,9%) women had a high risk, and another 60 women and 3 men had moderate risk of fractures. After the FRAX recalculation with the inclusion of the femoral neck T-score, only 26 (21,0%) women moved from the moderate-risk group to the high-risk group. All men and 48 women had a low risk of osteoporotic fractures according to FRAX, among them 12 (8,0%) people (4 men and 8 women) had osteoporosis by DXA.
Thus, among SSc patients 84 (67.7%) women and 11 (42,3%) men needed anti-osteoporotic treatment.
Conclusion: As a result of a comprehensive assessment of the risk of fractures and OP, it was found that 63.3% of patients with SSc needed anti-osteoporotic treatment.
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AB0704

LOW BODY MASS INDEX IN PATIENTS WITH RAYNAUD PHENOMENON IS ASSOCIATED WITH ENLARGED CAPILLARIES AND REDUCTION IN CAPILLARY DENSITY AT NAILFOLD VIDEOCAPILLAROSCOPY

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Background: Increased prevalence of peripheral vascular symptoms like Raynaud's phenomenon (RP) and acrocianosis is reported in anorexia nervosa (AN) and correlates with a more severe malnutrition.
Objectives: We aimed to characterize nailfold video capillaroscopy (NVC) abnormalities in patients with RP and BMI<18.5 kg/m2, according to adipokine levels, compared to subjects with RP and normal BMI.
Methods: We performed NVC in 21 female patients with primary RP with BMI<18.5 kg/m2, in 18 patients with primary RP and normal BMI, and in 18 patients classifiable as VEDOSS (Very Early Diagnosis of Systemic Sclerosis) and normal BMI, using a video-capillaroscope. Fingers two to four were evaluated bilaterally. Mean and minimum capillary density were registered for each patient, as well as maximum diameter and number of enlarged and giant capillaries, number of micro-haemorrhages and micro-thrombosis. We scored the frequency of enlarged capillaries considering the percentage of dilated capillaries out of the total. Demographic and clinical features of all patients were recorded.
Results: Patients with RP and low BMI presented a great number of elementary alterations on NVC; some of these modifications were typical of the scleroderma pattern. The percentage of enlarged capillaries was more than 33% of the total in 17(81%) patients with RP and low BMI with respect to 9(50%) of patients with RP and normal BMI (p=0.041). Furthermore, the number of megacapillaries was higher in patients with RP and low BMI compared to patients with normal BMI, while the maximum diameter of capillaries was comparable. Eight patients with low BMI presented a picture resembling an early scleroderma pattern (44%). The frequency of micro-thrombosis, micro-hemorrhages and microaneurysms were comparable in the twogroups. Patients with RP and low BMI presented a lower mean capillary and minimum capillary density compared to patients with RP and normal BMI (mean density: 7.4±1.4vs8.2±1.4,p=0.031; minimum density:4.8±1.0 vs5.4±1.0,p=0.05). Patients with RP and low BMI presented a comparable frequency of enlarged capillaries, number of megacapillaries when compared with patients with VEDOSS. Leptin and chemerin levels were lower in patients with low BMI with respect to patients with normal BMI (57.5±35.6vs124.2±92.0pg/mL, p<0.001; 46.9±11.9vs58.3±17.2 ng/mL, p=0.017, respectively); adiponectin levels were comparable.
Conclusion: Patients with low BMI and primary RP presented a great frequency of enlarged capillaries and a reduction of capillary density when compared with patients with normal BMI. The increased number of microvascular abnormalities on NVC in patients with low BMI reminds the NVC findings typical of early scleroderma, supporting the hypothesis of an endothelial dysfunction in such patients
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AB0705

CHANGES OF LUNG FUNCTION AND SKIN FIBROSIS IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS ON RITUXIMAB THERAPY - COMPARISON OF THE EFFICACY OF BIOSIMILAR ACELLBIA AND MABTHERA

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Background: Rituximab (RTX) has shown itself as an effective option in treatment of interstitial lung disease associated with systemic sclerosis (ILD-SSc). However, there is not enough data on the effect of rituximab biosimilars in patients (pts) with SSc. Biosimilars could reduce price and increase pts access to expensive, but more efficient biologic therapy. The RTX biosimilar Acellbia (ACB) was registered in Russian Federation for all indications consistent with RTX.
Objectives: To study changes of lung function and skin fibrosis in pts with ILD-SSc on ACB therapy in comparison with original RTX (Mabthera (MBT) during 1 year of follow-up.
Methods: This prospective study included 62 pts received RTX as an addition to previous therapy, when it was ineffective. The mean follow-up period was 12.9±2.2 months. 31 pts received MBT (group 1) and 31 pts received ACB (group 2). All pts had ILD. In group 1 the mean age was 42.2±12.3 years, female-25 pts (81%), the diffuse cutaneous subset of the disease had 21 pts (68%). The mean disease duration was 5.3±3.5years. 91% of pts were positive for ANA and 77% of them were positive for antitopoisomerase-1. All pts received prednisolone at a dose of 11.2±3.9 mg/day, immunosupressants (IS) at inclusion received 39% of them. The cumulative mean dose of RTX was 1.5±0.5g. In group 2 the mean age was 48.7±11.3 years, female-23 pts (74%), the diffuse cutaneous subset of the disease had 16 pts (52%). The mean disease duration was 6.2±7.1years. 88% of pts were positive for ANA, 36% of them were positive for antitopoisomerase-1. All pts received prednisolone at a dose of 10.6±4.5mg/day, IS at inclusion received 42% of them. The cumulative mean dose of RTX was 1.4±0.5g. The results are presented in the form of mean values and standard deviations, delta(Δ)-difference between the baseline parameter and follow up point, median, lower quartile and upper quartile.
Results: There was an improvement of all evaluated parameters in both groups: decrease of Rodnan skin score (mRSS) and activity index(EScSG-AI), increase of forced vital capacity % predicted (FVC), diffusion capacity for carbon monoxide % predicted (DLCO) and 6-minute walk distance (Table 1). Both groups managed to reduce the mean dose of prednisolone. B-lymphocyte depletion persisted in both groups. When we compared changes (Δ) of the parameters between groups - no significant difference was obtained (Table 1).

Table 1. Changes of the main parameters at RXT therapy in delta (Δ); median; lower quartile; upper quartile.

Parameters	Group 1	P for Group 1 (between baseline and follow-up point)	Group 2	P for Group 2 (between baseline and follow-up point)	P between group 1 and 2
Δ mRSS	4.7±5.6 [2; 0; 10]	0.0001	4.3±4.1 [3; 0; 8]	0.0001	NS
Δ FVC, % pred	4.9±5.6 [5.8; 1.8; 7.8]	0.0001	4.7±5.5 [3.1; 0.9; 7]	0.0002	NS
Δ DLCO, % pred	2.3±5.1 [1.4; -0.6; 5.5]	0.03	2.5±3.8 [2; 0.8; 4.9]	0.001	NS
Δ Activity Index (EScSG-AI)	2±1.9 [2; 0; 3.5]	0.0001	1.8±1.5 [2; 1; 2]	0.0001	NS
Δ B-lymphocyte, absolute count	0,221±0,16 [0.185; 0.09; 0.33]	0.0001	0,216±0,17 [0.135; 0.09; 0.34]	0.0001	NS
Δ 6-minute walk distance, m	60.4±67.5 [42.5; 10; 91]	0.008	55.1±42.6 [52.5; 13; 90]	0.0003	NS
Δ Prednisolone, mg/day	2.03±2.1 [2.5; 0; 5]	0.0006	2.1±2.7 [2.5; 0; 5]	0.0004	NS
Cumulative mean dose of RTX, g, M±σ	1.5±0.5	-	1.4±0.5	-	NS

Conclusion: Our prospective study showed the similar effectiveness of ACB in comparison with MBT in ILD-SSc. There was a significant improvement of lung function tests and decrease of skin fibrosis. RTX has been shown the positive effect even at low doses (less than 2 g). ACB has shown a good efficacy for therapy ILD-SSc, but studies with a large number of patients are required.
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AB0706

DEMOGRAPHIC, CLINICAL AND SEROLOGICAL CHARACTERISTICS IN IDIOPATHIC INFLAMMATORY MYOPATHIES. THE ROLE OF SPECIFIC ANTIBODIES

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Background: Idiopathic Inflammatory myopathies are a heterogenous group of diseases which main common characteristic is muscle injury. Specific autoantibodies related with different phenotypes have become an important diagnostic and prognostic tool. These antibodies may be associated with different histopathological features in muscle biopsies.
Objectives: To describe the demographic, clinical and serological characteristics of Idiopathic Inflammatory Myopathies (IIM); the most frequent corticoid sparing agents used and the frequency of associated neoplasms in a sample of patients with a compatible biopsy result. To compare these characteristics in patients with positive and negative ANA and the association of different biopsy patterns with specific myositis antibodies.

Methods: Muscle biopsies results that were compatible with inflammatory myopathy were collected from the Pathology Unit database of Leon´s hospital between January 2010 and March 2021.Demographic, clinical and serological characteristics, associated malignancies and treatments used were collected from clinical records.
Results: We included 30 patients in the study. Patient`s characteristics are shown in Table 1. Median age of diagnosis was 59 years. Arthritis and lung disease were found in 20% of patients. The patterns of lung involvement found in HRCT were NSIP in 2, UIP in 1, and bronchiectasis in 3 patients. Associated collagenopathies were found in 26,7%, being vasculitis the most frequent (2 patients). Associated Malignancies were found in 13,3%: lung carcinoma in 1, Urothelial carcinoma in 1, cervix carcinoma in 1 and prostate carcinoma 1 patient. Specific myositis antibodies were negative in 56,7%; positive ANA was found in 60%.

Table 1. Demographic, clinical, serological characteristics and treatment in the sample studied

Characteristics	Patients (n=30) Median; IQR or n(%)
Age at diagnosis (years)	59; 18,5
Sex F/M	17(56,7)/13(43,3)
Artralgias	11(36,7)
Arthritis	6(20)
Raynaud	3(10)
Lung disease	6 (20)
Skin disease	7 (23,3)
Autoimmunity biomarkers (+/-/ not done)	
ACPA	2(6,7) /3 (10) /25(83,3)
Positive Rheumatoid Factor	4(13,3) /13 (43,3) /13(43,3)
ANA	18 (60%) /12(40%)
Specific Myositis Antibodies	
Anti SRP	1(3,3)
Anti-HMG CoA reductase	5 (16,7)
Anti Jo1	2(6,7)
Negative	17 (56,7)
Not done	5 (16,4)
Biopsy pattern	
necrotizing	8 (26,7)
inflammatory	15(50)
Inclusion Bodies	4 (13,3)
dermatomyositis	3 (10)
Diagnosis	
Dermatomyositis	3 (10)
Statin Myopathy	5(16,7)
Inclusion body myopathy	3(10)
Polymyositis	8(26,7)
Immune-mediated necrotizing myopathy	2 (6,7)
Antisynthetase syndrome	1(3,3)
Other collagenopathies	8(26,7)
Treatment	
Methotrexate	11(36,7)
Azathioprine	3(10)
immunoglobulins	5(16,7)
Rituximab	5(16,7)
Mycophenolate	4(13,3)
Cyclophosphamide	2 (6,7)
None	11 (36,7)
2 or more treatments	8(26,7)
Associated malignancies	4 (13,3)

The median of levels at diagnosis of CK was: 1181; IQR:6252,5; aldolase 14,4; IQR: 34,65; AST 62; IQR:181,25; ALT 55,5; IQR:119,25; CRP 7,6; IQR 13,55. When compared, CK and ALT levels in patients with negative and positive ANA, this were higher in negative patients (6365; IQR:9592vs888;3045; P=0.044) and (182; IQR:287vs43; 85; P=0,035) respectively. Anti HMGCoA reductase antibodies were more frequently found in patients with necrotizing pattern in biopsies 5/8 patients; (62,5%); p=0.002. Methotrexate was the corticoid sparing agent most frequently used (36,7% of patients), 36,7% of patients were treated only with corticoids and 26,7% needed more than one treatment.
Conclusion: Specific myositis antibodies are helpful tools in the diagnosis when present, meanwhile biopsy can be an important tool when antibodies are negative. ANA positivity seems to be associated with milder disease at the muscular domain.
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AB0707 CHANGES OF IMMUNOGLOBULIN G AND FREQUENCY OF INFECTIONS IN SYSTEMIC SCLEROSIS PATIENTS DURING LONG-TERM RITUXIMAB THERAPY

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Background: Decrease of immunoglobulin G (IgG) could often be observed during rutuximab (RTX) therapy in systemic sclerosis (SSc) and other autoimmune diseases. Lower lever of IgG could be associated with an increased risk of secondary infectious complications. However, there are very few data on changes of IgG in SSc during long-term RTX therapy.
Objectives: To evaluate changes of Ig G and the frequency of infectious adverse events (AE) in SSc patients (pts) on RTX therapy during long-term follow-up.
Methods: Our prospective study included 78 pts with SSc received RTX therapy. The mean follow-up period was 50.2±23 months. The mean age was 48.2±13.7 years, female-64 pts (82%), the diffuse cutaneous subset of the disease had 48 pts (62%), limited - 24 (31%), overlap - 6 (7%). The mean disease duration was 5.4±3.4 years. 92% of pts were positive for ANA and 71% of them were positive for antitopoisomerase-1. All pts received prednisolone at a dose of 11.8±4.1 mg/day, immunosupressants at inclusion received 40% of them. The IgG was evaluated over the periods: at baseline (point 0), 12-18 mo (point 1), 24-60 mo (point 2) and 66-84 mo (point 3) after initiation of RTX therapy. IgG levels was measured using ELISA. Normal IgG reference values ranged within 7.0-16.0 g/l. AE were assessed and recorded by a physician at a hospital immediately after the infusion of RTX, then by patient reported outcome during the observation period. Severe AE were defined as those that required hospitalization for more than 24 hours and life-threatening situations. The results are presented in the form of mean values and standard deviations.
Results: There was a significant decrease of IgG during RTX therapy (Table 1). However, the level of IgG remained within normal limits. Initially lower level of IgG had 6 pts (8%). And further at point 1 there was 12 pts (15%) with decrease of IgG below normal limits, at point 2 - 12 pts (15%) and at point 3 - 5 pts (6%). When we compared the level of IgG between point 2 and 3 - no significant differences were found.

Table 1. Changes of IgG level during RTX treatment.

Parameters	Point 0 (n=78)	Point 1 (n=78)	Point 2 (n=76)	Point 3 (n=27)	P Point 0-1	P Point 0-2	P Point 0-3
IgG, g/l, M±σ	12.3±4.2	10.6±3.4	9.6±2.8	9.6±2.6	0.0001	0.0001	0.01
Cumulative mean dose of RTX, g, M±σ	-	1.8±0.5	3.9±1.3	4.8±2.1	-	-	-

AE was evaluated over the period of 335.4 patient-years (PY). Infectious AE were reported in 34 patients (44%), the overall frequency was 10.2/100 PY (95% Confidence Interval (CI) 7.1-13.8). No serious opportunistic infections were reported. The highest frequency of infectious AE was observed in the first 2-6 months after the first infusion of RTX, however these were mainly mild AE (82%). The frequency of serious infections was 1.8/100 PY (95% CI 0.7-3.8). There was a decrease of infectious AE in the follow-up period (4.4/100 PY, 95% CI 2.5-7.2 – at period from 24 month of RTX therapy).
Conclusion: In our study, a significant decrease of IgG was noted in SSc pts during the first 5 years of RTX therapy, but later its level stabilized and remained within normal limits. A decrease of IgG in the first year after the initiation of RTX therapy was accompanied by an increase in the frequency of infectious AE. However, with an increase of the cumulative dose of RTX, there was no increase in infectious AE. Monitoring of IgG levels may be useful for SSc pts on RTX therapy for early identification of the risk for developing infectious complications.
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AB0708 ANALYSIS OF THE PERFORMANCE OF COMMERCIAL TESTS IN THE DETERMINATION OF MYOSITIS-SPECIFIC AND MYOSITIS-ASSOCIATED AUTOANTIBODIES: PREVALENCE AND CORRELATION WITH DIAGNOSIS OF IIM

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Background: Idiopathic Inflammatory Myopathies (IIM) are a group of disorders sharing the common feature of immune-mediated muscle injury. In IIM autoantibodies specific for (MSA) or associated to (MAA) myositis are present in 60-65% of cases (1). Although only anti-Jo-1 (2) are included in the EULAR 2017 criteria, the presence of MSA allows to identify clinical and prognostic phenotypes.

Objectives: Aim of the work is to evaluate the positivity rate on sera analyzed by a line blot (LB) immunoassay able to detect MSA or MAA, the associated clinical diagnoses and the consistency with the antibody specificity.
Methods: 267 sera were analyzed using a commercial LB (Autoimmune Inflammatory Myopathies 16 Ag Profile EUROLINE) between March 2017 and March 2021. The diagnosis was identified by analyzing the medical records.
Results: A positivity for at least one MSA/MAA was found in 118/267 sera (44.2%); MAA isolated in 22% of cases and a double/multiple positivity for MSA in 12.7%. The distribution of antibody positivity and the associated clinical diagnoses are shown in Table 1.

Table 1. Autoantibody distribution and associated clinical diagnosis; for some patients there are multiple positivity

	Autoantibody specificity				Consistent diagnosis	
	Total positivity n. (%)	Isolated positivity n. (%)	Concomitant presence of at least one MAA n. (%)	Concomitant presence of MSA +/- MAA n. (%)	n. (%)	Type of IIM
MSA						
Mi-2	27 (22.9)	16 (59.3)	2 (7.4)	9 (33.3)	5 (18.6)	2 DM/2 PM/1 ASS
Tif-1γ	12 (10.2)	4 (33.3)	4 (33.3)	4 (33.3)	9 (75)	5 CAM/4 DM
PL-7	11 (9.4)	4 (36.4)	3 (27.3)	4 (36.4)	5 (45.5)	ASS
NXP-2	8 (6.8)	3 (37.5)	1 (12.5)	4 (50)	3 (37.5)	DM
SRP	8 (6.8)	3 (37.5)	1 (12.5)	4 (50)	1 (12.5)	PM
Jo-1	8 (6.8)	2 (25)	3 (37.5)	3 (37.5)	6 (75)	ASS
PL-12	7 (5.9)	3 (42.9)	0	4 (57.1)	4 (57.1)	ASS
MDA5	5 (4.2)	3 (60)	0	2 (40)	4 (80)	2 CADM/1 DM/1 ASS
Oj	4 (3.4)	3 (75)	0	1 (25)	3 (75)	ILD
SAE	3 (2.5)	2 (66.7)	1 (33.3)	0	2 (66.7)	DM
Ej	2 (1.7)	1 (50)	1 (50)	0	1 (50)	ASS
MAA						
Ro-52	33 (28)	12 (36.3)	2 (6.1)	19 (57.6)	-	
PM-Scl	19 (16.1)	11 (57.9)	3 (15.8)	5 (26.3)	-	
Ku	6 (5.1)	3 (50)	1 (16.7)	2 (33.3)	-	

DM: Dermatoyositis, PM: Polymiositis, ASS: Antisynthetase Syndrome, CAM: Cancer-Associated Myositis, CADM: Clinical Amyopatic Dermatomyositis, ILD: Interstitial Lung Disease

In our cohort, the most common antibodies were anti-Ro52kD, positive in 33 sera (28%), while the most frequent MSA were anti-Mi-2, positive in 27 sera (22.9%). MSA most frequently found as an isolated positivity were anti-Oj (75%), while anti-Jo-1 as an isolated positivity were present only in 25% of cases. Considering the 118 sera with at least one MSA/MAA a diagnosis of IIM was made in 52 cases (44%); in 11 cases others systemic autoimmune diseases were identified. The consistency between antibody specificity with the clinical diagnoses was analyzed: for some antibodies, as anti-Jo-1 (80%), anti-MDA5 (75%) and anti-Tif-1gamma (75%), LB results were consistent with clinical diagnoses; while for others, as anti-Mi-2 (18,6%) and anti-SRP (12,5%), the agreement was lower.
Conclusion: The use of LB in the diagnostic workout of IIM allowed the detection of MSA previously not found with routine methods. In our court low prevalence of anti-Jo-1 was found. This may be justified by the fact that anti-Jo-1 are included in the assays routinely used to identify anti-ENA antibodies, therefore these sera were not tested with an additional LB. With LB, a higher prevalence of double/multiple MSA positivity was found, compared to the 0.1% described with immunoprecipitation (IP) (3). LB give a semiquantitative result: low, medium or high titer, so the analysis of different titers, according with clinical data or IP, could be helpful in the interpretation of the co-existence of multiple MSA (4).
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AB0709 SLEEP DISTURBANCES AND RHEUMATIC DISEASES – A CASE-CONTROLLED CROSS-SECTIONAL STUDY

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Background: Rheumatic diseases may affect all aspects of life, including sleep[1]. Sleep disorders are common and potentially debilitating in these diseases, and the reason for this disturbance seems to be multifactorial.
Objectives: Evaluate the prevalence of sleep disturbance and its association with demographic-clinical factors in patients with Systemic Sclerosis (SSc) and Rheumatoid Arthritis (RA).
Methods: We conducted a cross-sectional study on patients, aged ≥18, who fulfilled the ACR/EULAR 2013 classification criteria for SSc and ACR/EULAR 2010 classification criteria for RA. Socio-demographic and clinical data was collected. Patients answered the Health Assessment Questionnaire (HAQ), Hospital Anxiety and Depression Scale (HADS), Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale and Pittsburgh Sleep Quality Index (PSQI) questionnaires. Sleep disorders were considered when PSQI was >5[2]. Differences between groups were assessed and variables with statistical significance in the univariate analysis were included in a multivariate logistic regression model, adjusted to age and sex. $p \leq 0.05$ was considered significant in all analysis.
Results: Fifty-six patients (28 with SSc and 28 with RA) agreed to participate in this study, of which 47 (83.9%) were female, with a median age of 61 years old (IQR 14). Most of our patients (73.2%) had a sleep disturbance, fatigue (80.4%) and disability (89.3%). Twenty patients (35.7%) suffered from anxiety and 10 (17.9%) from depression. A statistically significant association was found between sleep disturbances and the disease, its duration and body mass index (BMI). FACIT, HAQ and HADS-A, but not with HADS-D, were also associated (Table 1). When comparing diseases, there was no differences between gender, age, and BMI, however duration of disease was superior in RA patients (p<0.001) (Table 1). On the other hand, the SSc group showed worse mean scores in HAQ and PSQI compared with RA group (Table 1). Though, sleep disturbance was not associated with any clinical feature of SSc. Although SSc [3.882 (1.056-14.276), p=0.041], FACIT [0.883 (0.812-0.960), p=0.004], HAQ [4.223 (1.204-14.818), p=0.024] and HADS-A [1.257 (1.057-1.495), p=0.010] were predictors of sleep disorder in the univariate analysis, their effect disappeared in the multivariate logistic model.

Table 1. *Differences between sleep disorders and between Systemic Sclerosis and Rheumatoid Arthritis*

Characteristics	Without sleep disorder (n=15)	Sleep disorder (n=41)	P value	SSc group (n=28)	RA group (n=28)	P value
Age (year) Median (IQR)	55 (16)	61.50 (13)	0.059	60.50 (14)	61 (15)	0.941
Female gender N (%)	13 (86.7%)	34 (82.9%)	0.736	24 (85.7%)	23 (82.1%)	0.716
Disease duration (months) Median (IQR)	144.00 (156.00)	66.00 (60.00)	0.007*	60 (60)	120 (126)	<0.001*
BMI Median (IQR)	22.51 (6.47)	27.26 (6.95)	0.054	27.26 (7.92)	24.65 (6.06)	0.440
FACIT Median (IQR)	40.50 (12.25)	31.50 (18.00)	0.001*	33.00 (22.75)	36.00 (12.50)	0.522
HAQ Median (IQR)	0.438 (0.563)	0.813 (1.50)	0.022*	0.875 (1.625)	0.500 (0.563)	0.037*
HADS-A Median (IQR)	6.50 (5.50)	10.00 (5.00)	0.008*	9.50 (5.00)	8.00 (7.50)	0.229
HADS-D Median (IQR)	6.50 (5.00)	7.50 (5.00)	0.100	8.00 (4.75)	6.00 (5.00)	0.105
PSQI Median (IQR)				12.00 (7.25)	7.00 (7.50)	0.021*
Sleep disorder N (%)				24 (85.7%)	17 (60.7%)	0.035*

Legend: IQR - Interquartile Range.

Conclusion: In our cohort, sleep disturbances were highly prevalent, and we found a significant association between those and SSc, FACIT, HAQ and HADS-A. However, we didn't find a predictor of this disturbance in the multivariate analysis. New studies with large number of patients are warranted.
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AB0710 STUDY OF THE GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is a systemic autoimmune disease in which the gastrointestinal (GI) manifestation is one of the most frequent complications (90%), being esophagus and anorectal the most affected regions. The set of GI symptoms poses a diagnostic and therapeutic challenge, and the "Patient Reported Outcomes" (PRO) are good tools to address them. The UCLA GIT 2.0 validated questionnaire can be used as an instrument to measure the presence and severity of these symptoms, allowing screening, and improving subsequent management.
Objectives: To describe gastrointestinal (GI) involvement in patients with SSc.
Methods: Descriptive cross-sectional study conducted in a cohort of patients with SSc in a tertiary hospital. Sociodemographic, clinical, complementary tests and treatment variables were collected. Patients with established GI involvement needed to have urdergone some previous diagnostic test. The UCLA GIT 2.0 questionnaire was applied to all included patients, considering the presence of mild symptoms with a score of 0-0.49, moderate 0.49-1, and severe 1-3.
Results: 88 patients (90% women) were recruited, with a mean age of 61.3 years. They presented the subtypes of limited and diffuse SSc in 63.3% and 13.6%, respectively. The most frequent antibodies were anticentromere (ACA) in 52.3% of the patients, anti-Ro52 in 20.5% and anti-topoisomerase I in 14.8%. The most frequent manifestations were Raynaud's phenomenon in 98.8% of the patients followed by GI in 37.5% (gastro-esophageal reflux in 88.2%), diffuse interstitial lung disease in 18% and pulmonary hypertension in 10.22%. The most used treatment was proton pump inhibitors (PPI) in 47.7% of the patients. Patients with GI involvement presented the limited SSc subtype (72.7%) and ACA (60.6%) as main characteristics. Patients without digestive involvement had similar characteristics, but did not show a greater association with any specific antibody (p=0.321). 67% of the total number of patients presented a score greater than 0 in the UCLA GIT 2.0 questionnaire, with the reflux section being the most frequent (52.27%). In relation to the total score, they presented mild, moderate, and severe symptoms in 77.3%, 21.6% and 1.1% of the patients respectively. The rest of the results by categories are summarized in Table 1.

Table 1.

	Gastrointestinal involvement (n= 34)	Without gastrointestinal involvement (n= 54)
Subtype and antibodies		
Limited	24 (70,58%)	32 (59,25%)
Diffuse	5 (14,70%)	7 (12,96%)
ACA	20 (58,82%)	26 (48,14%)
ATA	5 (14,70%)	8 (14,81%)
Manifestations and treatment		
ILD	5 (14,70%)	11 (20,37%)
PAH	3 (8,82%)	6 (11,11%)
PPI	31 (91,17%)	11 (20,37%)
UCLA GIT 2.0 (median)		
Total score	0,30	0,05
Reflux	0,35	0
Swelling	0,62	0
Stain	0	0
Diarrhea*	0	0
Social functioning	0	0
Emotional well-being	0,22	0
Constipation ǂ	0	0

ILD (intersticial lung disease), PAH (pulmonary arterial hypertension), ACA (anti-centromere), ATA (anti-topoisomerase), PPI (proton pump inhibitors). *In the "diarrhea" subcategory the maximum score is 2. ǂ In the "constipation" subcategory the maximum score is 2,5.

Patients with GI pathology presented higher scores (moderate-severe) compared to those without pathology (p=0.009). In this last group, 34.5% of the patients presented GI symptoms according to the test, observing high scores in the bloating, reflux, and constipation sections in 25.2%, 16.6% and 14.8% of the patients respectively.
Conclusion: GI involvement tends to be one of the most frequent manifestations in our cohort and occurs more frequently in patients with limited skin involvement and ACA +. Patients with established GI pathology had higher scores on the UCLA test. The questionnaire may be useful in detecting undiagnosed patients, but more studies are necessary to establish this possible correlation.
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AB0711 THE IMPACT OF ANEMIA ON SYSTEMIC ORGAN DAMAGE IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease with multiple organ damage. Scleroderma Clinical Trials Consortium (SCTC) has developed the Damage Index (DI) in SSc to quantify organ damage in SSc[1]. Anemia has been implicated as an independent prognosis factor for mortality and organ complications in systemic sclerosis (SSc), while the relationship between anemia and the weighted organ damage index has not been reported.
Objectives: To determine the degree and feature of organ damage in SSc patients with or without anemia in a population of patients from Peking University Third Hospital SSc cohort (PKUTH-SSc).
Methods: Patients were recruited from PKUTH-SSc between January, 2010 and December, 2021. The diagnosis of anemia was based on the reduced hemoglobin (Hb) concentrations (<120g/L for female and <135g/L for male). The demographics, clinical characteristics, laboratory parameters, autoantibodies medication and SCTC-DI were collected. Student's t-test and Chi-square were used.
Results: As shown in Table 1, a total of 155 patients were enrolled in PKUTH-SSc cohort, 70 (45.2%) patients developed anemia, older and lower BMI than non-anemia patients. The inflammatory indices, ESR and CRP, were higher in anemia patients, indicating anemia was more common in patients with active disease. Consistent with the result that the positive rate of anti-SSA and anti-SSB antibody was higher in anemia patient, the sicca symptoms were also reported in nearly half of anemia patients. In anemia patients, the Gastrointestinal system related damage, Oesophageal dysmotility, Pseudo-obstruction and weight loss, and renal damage were more frequently discovered. Moreover, anemia patients were more likely to develop moderate to high organ damage risk, demonstrating the necessary of regular organ damage follow-up for anemia patients.

Table 1. Clinical parameters and SCTC-DI of SSc patients with or without anemia

	Anemia N=72	Non-anemia N=83	*p* value
Age at baseline (years)	54.43±1.88	49.64±1.32	0.034*
BMI (kg/m2) (meanyear	20.49±0.40	22.46±0.39	<0.001*
ESR	32.48±3.06	16.67±1.83	<0.001
CRP	1.20±0.22	0.64±0.11	0.014*
Anti-SSA	22 (31.4%)	13 (15.3%)	0.017*
Anti-SSB	8 (11.4%)	1 (1.2%)	0.018*
Musculoskeletal and skin	2.22±.22u	1.11±.11u	<0.001*
Sicca symptoms	31 (44.3%)	22 (25.9%)	0.016*
Vascular	0.67±.67u	0.59±.59u	0.628
Gastrointestinal	2.09±.09r	1.31±.31r	<0.001*
Oesophageal dysmotility	27 (38.6%)	18 (21.2%)	0.018*
Pseudo-obstruction	5 (7.1%)	0 (0.0%)	0.017*
BMI<18.5 kg/m^2 or weight loss >10% in the last 12 months	40 (57.1%)	31 (36.5%)	0.010*
Respiratory	2.24±.24i	1.59±.59i	0.132
Cardiovascular	0.94±.94i	0.66±.66i	0.468
Renal	0.21±.21l	0.00±.00l	0.027*
History of SRC	4 (5.7%)	0 (0.0%)	0.040*
SCTC-DI	8.37±.37-	5.25±.25-	<0.001*
Moderate to high damage score	48 (68.6%)	31 (36.5%)	<0.001*

Conclusion: Anemia is associated with distinct organ damage behaviors and higher disease progression risk in SSc. Specifically Sicca symptoms and gastrointestinal, renal system were more common in SSc patients with anemia.
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AB0712 DIGITAL ISCHEMIC COMPLICATIONS IN SYSTEMIC SCLEROSIS ASSOCIATED RAYNAUD'S: PREVALENCE, RISK FACTORS AND TREATMENT PATTERNS FROM A SINGLE CENTER COHORT

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Table 1.

	Overall (N=273)	DICs (N=217)	No DICs (N=56)	p-value
Demographics				
Age at procedure(y); mean (SD)	57.5 (13.3)	56.9 (13.6)	59.4 (11.8)	0.25
Sex (Female)	220 (81%)	173 (80%)	47 (84%)	0.48
Race (White)	253 (93%)	199 (92%)	54 (96%)	0.73
BMI (kg/m^2) at study; mean (SD)	26.6 (6.1)	26.3 (6.1)	27.4 (6.1)	0.14
Smoking status				
Never	154 (56%)	120 (55%)	34 (61%)	0.76
Former	102 (37%)	83 (38%)	19 (34%)	
Current	17 (6%)	14 (6%)	3 (5%)	
Disease characteristics				
SSc subtype:				
Limited	211 (77%)	166 (76%)	45 (80%)	0.18
Diffuse	59 (22%)	49 (23%)	10 (18%)	
Time from SSc diagnosis to duplex US (months) mean (SD)	57.9 (85.7)	63.5 (91.5)	36.1 (52.9)	0.04
Digital occlusive arterial disease	223 (82%)	193 (89%)	30 (54%)	<0.001
Macrovascular disease	74 (27%)	69 (32%)	5 (9%)	<0.001
Ulnar Occlusive disease	68 (25%)	63 (29%)	5 (9%)	0.002
Telangiectasias	239 (88%)	192 (89%)	47 (84%)	0.27
Calcinosis	102 (43%)	95 (49%)	7 (16%)	<0.001
Interstitial lung disease	105 (38%)	90 (41%)	15 (27%)	0.04
Pulmonary hypertension	50 (18%)	43 (20%)	7 (12%)	0.21
Pericardial effusion	61 (22%)	54 (25%)	7 (12%)	0.047
Gastrointestinal dysmotility	194 (71%)	159 (73%)	35 (62%)	0.11
Renal crisis	17 (6%)	12 (6%)	5 (9%)	0.35
SSc specific antibodies:	175 (68%)	138 (67%)	38 (69%)	0.77
Centromere	116 (63%)	95 (63%)	21 (64%)	0.97
Scl-70	48 (19%)	36 (18%)	12 (22%)	0.57
RNA-Polymerase	19 (20%)	14 (19%)	5 (22%)	0.79

Background: A significant number of Systemic sclerosis (SSc) patients with Raynaud's phenomenon (RP) experience digital ischemic complications (DICs-digital ulcers, digital pitting/scars, gangrene and/or amputation).
Objectives: We reviewed the prevalence & risk factors for DICs in SSc-RP and compared treatment patterns among patients with & without DICs.
Methods: SSc patients meeting ACR/EULAR 2013 classification criteria that underwent an upper extremity arterial study between 2001-2018 were included. Clinical characteristics, treatment for RP, use of antiplatelet (aspirin 81 mg), statin therapy & occurrence of DICs, digital occlusive arterial disease (DOAD) on laser doppler flowmetry (LDF) and macrovascular disease (MVD) on duplex US were abstracted. Risk factors for DICs and their associations with therapy were evaluated.

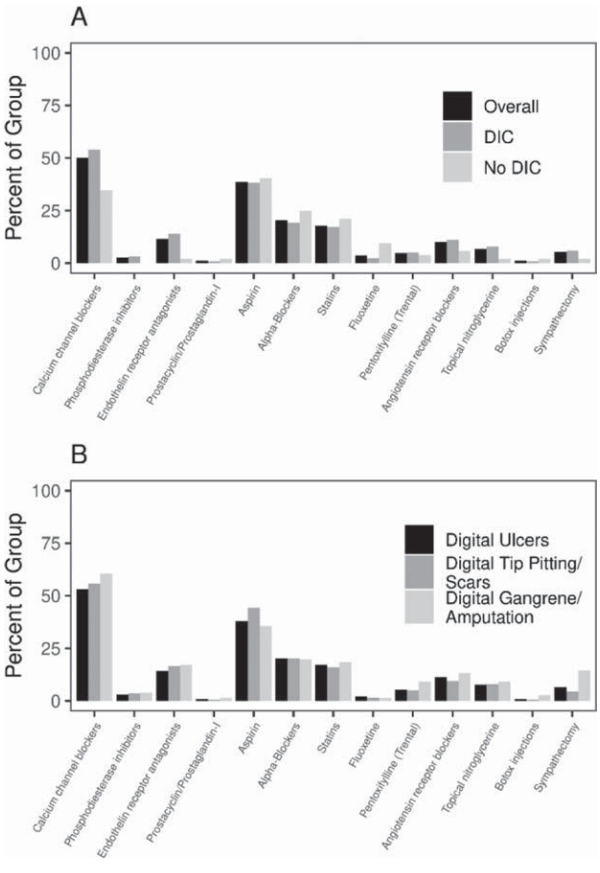

Figure 1.

Results: We identified 273 SSc patients (mean age 57±13 y, 81% F, 93% Caucasian, mean disease duration 4.8 ± 7.1 y). Cohort characteristics are described in Table 1. 79% (217/273) patients experienced DICs (digital ulcers 203, digital pitting/scar 138, digital gangrene 76). Patients with DICs had a higher prevalence of DOAD (89% vs 54%, p <0.001), MVD (32% vs 9%, p <0.001), ILD (41% vs. 27%, p=0.04), calcinosis (95/192 (49%) vs. 7/44 (16%), p<0.001), and pericardial effusion (25% vs. 12%, p=0.047), compared to those without DICs. No difference was noted between the 2 groups in regard to skin severity, smoking, BMI, hypertension, hyperlipidemia, diabetes, coronary artery disease, telangiectasias, pulmonary hypertension, renal crisis, GI dysmotility or myositis. Treatment patterns are described in Figure 1. Calcium channel blocker (CCB) and phosphodiesterase 5 inhibitor (PDE5I) use was higher among SSc patients with DICs than in those without DICs (CCBs: 53% vs. 34%, p=0.01; PDE5: 29% vs. 2%, p=0.01) likely due to confounding by indication. The use of aspirin or statins was not associated with DICs, even after adjusting for CV risk factors (ASA: OR 0.83, 95% CI 0.45-1.54; statin OR 0.67, 95% CI 0.28-1.62).
Conclusion: Our study confirms a high prevalence of DICs in SSc, with digital ulcers occurring in nearly 75% patients. A higher risk of DICs is associated with DOAD, MVD, ILD, calcinosis and pericardial effusion. While there is a significantly higher utilization of vasodilators among patients with DICs, the utilization of antiplatelet therapy and statins was not different among these groups. Whether this suggests a lack of evidence supporting their use in clinical practice, or inefficacy in preventing DICs remains unclear and warrants further study.
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AB0713 **CALCINOSIS CUTIS - INDEPENDENT RISK FACTOR FOR ALL-CAUSE MORTALITY IN SSC PATIENTS**

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Background: Calcinosis is a common and disabling complication of systemic sclerosis (SSc) with poorly understood pathogenesis and no effective treatment. Little is known about the etiology of this condition and management is essentially based on case studies and series.
Objectives: The objectives of this study were to describe the prevalence and characteristics of calcifications, and to investigate the relationships between calcinosis and clinical features in a population of patients with SSc.
Methods: This was a single center descriptive and retrospective study of patients treated at "Saint Mary" Clinical Hospital in Bucharest since January 2000 for SSc. Demographic and clinical features, including duration of disease progression, symptoms and parameters related to a specific organ involvement according to MEDS evaluation sheets, were evaluated in all patients. For testing

the association between nominal variables chi-square test was performed while independent t test was used to compare the differences between subgropus. Logistic regression analysis was used to predict the risk of all-cause mortality.
Results: 154 SSc patients were selected in the database, from which we identified a final group of 31 (20%) patients with calcinosis related to systemic sclerosis. The calcinosis cohort comprised 25 females and 6 males, with a mean age of 52.6 (±14.3) years, most of them with diffuse subset (16/31). Mean disease duration was 5.6 years (±3.1). Mean modified Rodnan skin score (mRSS) was 9.46 (±3.4) and mean adjusted EScSG activity index in the subgroup with calcinosis was 3.6 (±1.9). 45.16% (14/31) patients from the calcinosis subgroup developed interstitial lung disease (ILD) vs 43.9%; pulmonary hypertension was seen in 51.6% (16/31) cases vs 10.5% (13/123). As expected, calcifications were closely associated with vascular (p=0.004) and gastrointestinal (p=0.001) involvement and pulmonary hypertension (p=0.049). Moreover, associations were stronger for severe gastrointestinal involvement defined as chronic intestinal pseudo-obstruction (p=0.001). Females (p=0.024), patients with digital ulcers (p=0.004), those with disease duration longer than 10 years (p=0.001), those with pulmonary hypertension (p=0.049) and patients with gastrointestinal involvement (p=0.044) presented significantly more calcinosis. There were no significant associations between calcinosis and disease activity, myositis, interstitial lung disease, type of scleroderma or autoantibodies. Furthermore, in the logistic regression equation we identified calcinosis as a risk factor for all-cause mortality in SSc patients [OR:2.607 (CI:1.062,6,397), p=0.037].
Conclusion: Calcinosis cutis is a common manifestation is patients with SSc regardless of skin subset and type of autoantibodies. It seems to occur more often in patients with long-standing disease and is more commonly associated with vascular involvement such as digital ulcers and pulmonary hypertension. Furthermore, the present study has demonstrated that calcinosis could be an important prognostic factor when it comes to predict mortality. Given the fact that the management of calcinosis in scleroderma is an unmet need in almost half of patients with long-standing disease duration, systematic clinical trials are required to find effective measures to prevent this complication.
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AB0714 LOW BONE MINERAL DENSITY AND INCREASED FREQUENCY OF OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS – A CASE-CONTROL STUDY

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Background: Systemic sclerosis is an autoimmune disease characterized by fibrosis and vascular involvement. Osteoporosis, as a comorbidity among patients with systemic sclerosis is poorly described.
Objectives: The aim of this cross sectional case-control study was to investigate bone mineral density and prevalence of osteoporosis in patients with systemic sclerosis compared to controls.
Methods: We included 211 patients, 182 females and 29 males, with systemic sclerosis and 506 controls, individually matched for age and sex and from the same catchment area in the very south of Sweden. All participants underwent dual-energy X-ray absorptiometry (DXA). Bone mineral density (BMD, g/cm^2) and T-score were measured in lumbar spine L1-L4 and total hip. For patients, disease characteristics were obtained. Students T-test, one-way ANOVA or Chi-square test were used to compare groups and Pearson´s test for correlations. Osteoporosis (T-score ≤ -2.5) and osteopenia (T-score -1.0– -2.5) were defined using WHOs definitions.
Results: Systemic sclerosis patients had a mean (SD) age of 61.5 (13.5) and a mean (SD) disease duration from diagnosis of 9.2 (8.0) years. BMD (g/cm^2) was significantly lower in patients compared to controls: Total hip (SD) 0.874 (0.147) vs 0.941 (0.145) (p=<0.0001); lumbar spine 1.089 (0.170) vs 1.126 (0.195) (p=0.015). Total hip mean T-score difference between groups was -0.52 (95 % CI -0.67– -0.34). The frequency of osteoporosis was 14.7% vs 9.7% and of osteopenia 51.2% vs 41.2% in patients compared with controls (p=0.001). Only one (3.4%) of the male patients had osteoporosis but nearly half of them had osteopenia. In patients, we evaluated vascular features. Those with telangiectasias had lower total hip BMD than those without (p=0.026). Among patients with early disease (<2 years), a higher total hip BMD was observed compared to patients with longer disease duration (p=0.001). The difference was not seen in spine BMD. Features of fibrosis were not associated with BMD, ie there were no difference in BMD between patients with diffuse or limited disease or antibody status.
Conclusion: Patients with systemic sclerosis have lower BMD and osteoporosis is more frequent than among controls matched for age and sex.
Disclosure of Interests: None declared
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AB0715 ANTI-MDA5 DERMATOMYOSITIS AFTER BNT162B2 VACCINATION

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Background: Background: Anti-Melanoma Differentiation-Associated gene 5 (MDA-5) Dermatomyositis (MDA5, DM) is a rare systemic autoimmune disease, characteristically associated with Rapidly Progressive Interstitial Lung Disease (RP-ILD) and cutaneous manifestations. Anti-MDA5 dermatomyositis may develop in genetically predisposed subjects after environmental exposure such as vaccines, infections and neoplasms (1). Myalgia is one of the main symptoms related to SARS-COV2 infection and sometimes may occurs after COVID-19 vaccine administration (2). However, only few cases have reported the occurrence of severe inflammatory myopathies after COVID19 vaccine administration (3)
Objectives: To describe a case of Anti-MDA5 Dermatomyositis occurred after BNT162b2 vaccine administration
Methods: This is a case of a 44 year-old-patient affected by Anti-MDA5 Dermatomyositis occurred after BNT162b2 vaccination referred at the Center for Rheumatic Diseases in Venice, Italy
Results: A 44 year-old-woman presented to the Center for Rheumatic Diseases in Venice, suffering from a cutaneus rash on her face, upper limbs, décolleté, gluteus and lower limbs occurred two days after the first dose BNT162b2 vaccination (Figure 1). A few days after the second dose of the vaccine the rash got worse and myalgias, strength deficiency and fatigue occurred. Elevated inflammatory and myocytolysis parameters were detected (Table 1). After chest HRCT a mild ILD was diagnosed. Muscle edema was detected with whole-body short tau inversion recovery (STIR)-MRI (Figure 1).The Skyn biopsy showed features of dermatomyositis with perivascular inflammatory infiltrates. 1 mg/Kg/die of prednisone was administered and then cyclosporine 3mg/kg/die was associated with clinical benefit.

Table 1. Clinical and laboratory characteristics of the patient

Age (years)	44
Sex	Female
Previous Rheumatological diagnosis	-
Previous Vaccination reaction	-
Time to onset COVID 19 vaccination	2 days
MMT-8*	124/150 (150/150)
Blood Tests	
Hb* (12-16 g/dl)	11,5 g/dl
CRP* (< 5 mg/L)	23,4 mg/L
AST* (31 U/L)	98 U/L
ALT* (1-34 U/L)	63 U/L
CPK * (10-145 U/L)	1085 U/L
Aldolase (0-7,6)	13,2 U/L
SARS-CoV-2 RT PCR	negative
Autoantibodies	
ANA*	1:1280 nucleolar
Myositis antibodies	Anti-MDA5
HLA- DRB1	03-04
HLA-DQB	02-03

MMT-8 MANUAL MUSCLE TESTING; Hb Hemoglobin; WBC withe blood cells count; CRP C-reactive proteine; AST Aspartate amino transferase; ALT Alanine amino transferase; CPK creatinine phosphokinase; ANA anti nuclear antibodies, ENA extractable nuclear antigens; HLA HumanLeukocyte Antigen

Conclusion: In rare cases COVID-19 vaccination could induce inflammatory myopathies (3). COVID-19 vaccine administration may have acted as a trigger for the myopathy driven by an autoimmune-mechanism. In such cases, it could be useful to investigate inflammatory myopathies, requiring blood tests (e.g. myocytolysis indices and anti myositis antibodies) and medical instrumental insights, in patients affected by skin manifestation and muscle pain occurred after vaccine administration. Although the association between vaccination and inflammatory

myopathies is presumptive, the temporal proximity of the BNT162b2 vaccine to the onset of the signs and symptoms related to the inflammatory miopathies may suggest a possible relationship between these two events. To the best of our knowledge this is the first case of Anti-MDA5 Dermatomyositis occurred after BNT162b2 vaccination.

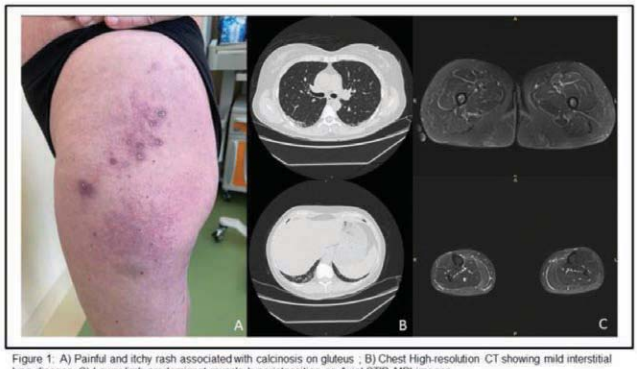

Figure 1: A) Painful and itchy rash associated with calcinosis on gluteus ; B) Chest High-resolution CT showing mild interstitial lung disease; C) Lower limb predominant muscle hyperintensities on Axial STIR MRI images

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Disclosure of Interests: None declared

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AB0716 CHARACTERISTICS OF 4 CASES OF PL - 7 POSITIVE ANTISYNTHATASE SYNDROME: INTERSTITIAL LUNG DISEASE BEING A MORE COMMON FEATURE THEN MYOSITIS

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Background: Anti synthetase syndrome is a heterogeneous group of auto immune diseases characterised by antibodies against aminoacyl t RNA synthetase, associated with interstitial lung disease, myositis, arthritis and Raynaud's phenomenon. Anti PL 7 antibody is rare, present in only 1-4% patients with anti synthetase syndrome.

Objectives: To describe clinical characteristics PL – 7 positive patients with anti-synthatase syndrome.

Methods: In this retrospective study, cohort of patients with inflammatory myositis were screened for anti PL-7 antibody positivity and 4 cases were detected. Diagnosis was made based on either 2017 EULAR/ ACR classification criteria and/ or Bohan and Peter criteria. [1, 2] Clinical manifestations, investigations including antibody profile, treatment and treatment response were described.

Results: Of the 4 patients, 3 were female and age of onset varied from 36 to 69 years. Only 1 patient presented with proximal muscle weakness while three patients with dyspnoea. Joint involvement and Raynaud's phenomenon was present in 2 patients. Two patients had scleroderma spectrum manifestations. Three patients had elevated CK during the disease course with maximum values being 228, 594 and 1200 with only one having muscle weakness. One patient had dermatomyositis and 2 patients had mechanic's hand. HRCT patterns were usual interstitial pneumonia(UIP), nonspecific interstitial pneumonia(NSIP) and fibrosing NSIP with organising pneumonia. Three patients had anti Ro antibodies. All patients were treated with steroids, one each received Cyclophosphamide and Azathioprine initially however all the patients ended up with Mycophenolate mofetil—which controlled disease effectively without flare.

Conclusion: In Anti PL – 7 positive patients, interstitial lung disease is much more common than myositis. Mechanic's hands and scleroderma overlap appear to be a common association. Additionally, antibody positivity with Anti Ro/Ro52 was also noted. One patient had features of dermatomyositis including facial rash which is extremely rare for PL7. All of these patients responded very well to Mycophenolate.

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Disclosure of Interests: None declared

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AB0717 DEVELOPING A DEEP LEARNING MODEL ON CONVENTIONAL X-RAYS IN THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS

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Table 1.

	Patient 1	Patient 2	Patient 3	Patient 4
Age at onset	69 years	52 years	36 years	55 years
Gender	Male	Female	Female	Female
Presentation	Shortness of breath	Shoulder weakness	Arthritis and shortness of breath	Shortness of breath
Muscle	No weakness		No weakness	No weakness
Maximum CK (U/L)	228	594	1200	105
Raynaud's	Present	Absent	Present	
Joint	Arthritis - present	Absent	Present	Absent
Skin	Skin tightness Scelrodactyly Nail fold capillaries dilation	Absent	Skin tightness Scelrodactyly Nail fold capillaries dilation Mechanic's hands, facial pigmentation	Mechanic's hand
Lung	Present	Absent	Present	Present
Antibodies	ANA+ Anti Ro+ PL - 7 +	ANA+, anti Ro & La +, anti Ro52+ PL – 7+	ANA negative anti Ro52+ PL – 7+	ANA negative PL – 7 +
HRCT	UIP	No ILD	NSIP	Fibrosing NSIP, COP
Lung function	FEV1 53% FVC 47% FEV1/FVC 113% DLCO 34%	Not available	FEV1 36% FVC 35% FEV1/FVC 103% DLCO 49%	FEV1 65% FVC 82% FEV1/FVC 83% DLCO 50%
EMG	Not done	Chronic myopathy	Not done	Not done
Muscle biopsy	Not done	Not available	Not done	Not done
Treatment	Prednisolone and IV cyclophosphamide initially (side effects) Later on Mycophenolate Mofetil Stable disease	Prednisolone Initially Azathioprine Later MMF due to relapsing disease while of AZA	MMF and Prednisolone—clinical response	Prednisolone and Mycophenolate-response with normalisation of PFT
Pulmonary hypertension	Present	Absent	Present	Absent

Background: Plain pelvic radiographs are the most common imaging modality used in the first line for diagnosis of axial Spondyloarthritis (axSpA). However, evaluation of the sacroiliac joint on two-dimensional plain radiographs may lead to misinterpretation among the evaluators.
Objectives: To investigate the diagnostic power of deep learning models in conventional radiographs of the patients with axSpA.
Methods: The study included 320 axSpA patients and 348 healthy controls (age; 34.5±15.3/38.2±10.6, p=0.072; gender (male) 53.8%/46.3%, p=0.064). Sacroiliitis was confirmed on sacroiliac MRI according to the Assessment of Spondyloarthritis International Society (ASAS) definition. The contrast equalization was preprocessed with the Clahel (Contrast-Limited Adaptive Histogram Equalization) filter. Then, classification was performed with Alexnet, VGG16, resnet101 and resnet50 models. As a result of the trials, the best result was achieved with resnet50. Four different filtering scenarios were applied (Clahel filter cliplimit 0.25, Clahel filter cliplimit 0.50, clahel filter 1.00 and no filter).Two different cropping processes were performed on the direct radiographs, and uncropped, cropped at pelvic borders, cropped images close to the sacroiliac joint were applied to the deep learning model. Meanwhile, all images were also evaluated by 3 rheumatologists for the presence of sacroiliitis.
Results: According to the results of 4 different scenarios studied with the Resnet50 model, the best result was obtained with the RESNET50 Model + Clahel filter clipLimit 0.50. With this model, after applying the clahel filter with a coefficient of 0.5 to the full resolution data, we achieved 0.8135 success in the separation of AS and normal. A kappa error of 0.0561, Cohen's Kappa Error = 0.6267, Fscore 0.8022 (AS), 0.8253 (normal) were obtained. After applying the clahel filter with a coefficient of 0.5 with Resnet50 to the pelvic data, we achieved 0.625 success in separation of AS and normal. Kappa error 0.0694, Cohen's Kappa Error=0.2400, Fscore 0.5399 (AS), 0.6838 (normal) values were obtained. After applying the Clahel filter with a coefficient of 0.5 with Resnet50 to the sacroiliac data, we achieved 0.61 success in the separation of AS and normal. Kappa error 0.0696, Cohen's Kappa Error=0.2131, Fscore 0.5517 (AS), 0.6549 (normal) values were obtained. As a result of the evaluation of the radiographs by the clinician, Cohen's kappa was 0.452 and accuracy was 0.73 for the first rheumatologist; Cohen's kappa 0.132 and accuracy 0.56 for the second rheumatologist and Cohen's kappa 0.362 and accuracy 0.68 for the third rheumatologist were found.
Conclusion: Application of RESNET50 Model + Clahel filter ('clipLimit', 0.5, 'Distribution', 'rayleigh') on uncropped images showed higher precision in diagnosing sacroiliitis from conventional radiographs compared to other filtering scenarios. Our results were found to have higher accuracy than the evaluation of three rheumatologists.

Table 1. Precision and kappa values of Resnet50 model, 4 different filtering scenarios and 2 different clipping operations

	Accuracy	Cohen's kappa (CI)
*RESNET50+no filter	0.7306	0.4509 (0.3234-0.5785)
*RESNET50 Model+ Clahel filter (0,25)	0.6943	0.3889 (0.2590-0.5189)
*RESNET50 Model+ Clahel filter (0,50)	0.8135	0.6267 (0.4186-0.7555)
*RESNET50 Model+ Clahel filter (1,00)	0.6839	0.3552 (0.2213-0.4890)
**RESNET50 Model+ Clahel filter (0,50)	0.625	0.2400 (0.1523-0.3245)
***RESNET50 Model+ Clahel filter (0,50)	0.610	0.2131 (0.1121-0.3430)

* Uncropped sacroiliac X-Rays; ** Cropped X-Rays at the pelvic margins; *** Cropped X-Rays close to the sacroiliac joints

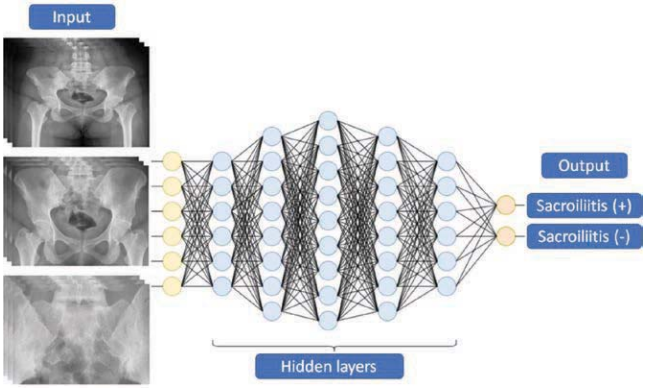

Figure 1. Steps of deep learning model in X-Ray images

Disclosure of Interests: None declared
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AB0718 **IMMUNE-APHERESIS IN PATIENTS WITH INFLAMMATORY MYOPATHIES, A CASE SERIES.**

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Background: Idiopathic inflammatory myopathies (IIM) comprise a heterogenous group of autoimmune diseases characterised by inflammation of muscle and affection of other organs, such as lung or skin. Some cases of IIM non-responsive to conventional treatment with glucocorticoids and DMARDs require treatment escalation. There are only limited data on efficacy and safety of immune-apheresis (IA) in IIM patients.
Objectives: This retrospective cohort study aims to determine whether IA is effective in treating therapy-refractory IIM.
Methods: Patients with active IIM undergoing IA (either plasma-exchange or immunoadsorption) at the Medical University Vienna were included in this explorative study. Patient characteristics and clinical data including serum levels of creatine kinase and concomitant medication were extracted from electronic medical records. As a primary endpoint, efficacy of IA was evaluated four weeks after initiation of IA, calculating absolute and relative change of CK-values as well as changes in steroid dose. Secondary endpoints included absolute and relative changes of CK-values at week 8 and week 12.
Results: From 2000 to 2021 25 IIM patients treated with IA were identified, 24 could be used for further analyses. Patient characteristics at start of IA are displayed in Table 1. Subtypes of IIM included dermatomyositis (DM 54.2%), polymyositis (PM 8.3%), Overlap-Myositis (20.8%), mmune-mediated-necrotising-myositis (IMNM 8.3 %), and antisynthetase syndrome (ASS 8.3 %). The majority of patients received concomitant steroid therapy (87.5 %) and DMARD therapy (62.5 %).

Table 1. Cohort descriptives:

Population, n (n= female%)	24 (n=19;79.2 %)	
Age at Baseline (years; mean [SD];)	42.5 [11.5]	
Subtyp Myositis (%,n)		
-Dermatomyositis	54.2 % (13)	
-Polymyositis	8.3 % (2)	
-Overlap-Myositis	20.8 % (5)	
-Immune mediated necrotising myositis	8.3 % (2)	
-Anti-Synthetase-Syndrom	8.3 % (2)	
Immune Apharesis within 4 weeks (number of cycles)	mean: 9.54, median: 9.5, [IQR: 8; 11.5]	
Previous DMARDs (%,n)		
-Any DMARDs		
-Mean number of previous DMARDs amongst all 24 patients	62.5% (15)	
-Azathioprin	33.3% (8)	
-Methotrexat	45.8% (11)	
-Rituximab	16.7% (4)	
-Mycophenolat mofetil	16.7% (4)	
-Cyclophosphamid	8.3% (2)	
-Ciclosporin	8.3% (2)	
-(Hydroxy)-Chloroquin	20.8% (5)	
-Etanercept	4.2% (1)	
-Infliximab	4.2% (1)	
Concomitant DMARDs (%,n)		
-Any DMARDs	62.5% (15)	
-Azathioprin	20.8% (5)	
-Methotrexat	20.8% (5)	
-Rituximab	4.2% (1)	
-Cyclophosphamid	4.2% (1)	
-Ciclosporin	4.2% (1)	
-(Hydroxy)-Chloroquin	8.3% (2)	
Concomitant Steroids % (n)	87.5% (21)	
-Dose prednisone at Baseline (mg/day; median [IQR])	25 [12.5; 50] (21)	
-Dose prednisone at week 4 (mg/day; median [IQR]	12.5 [0; 37.5] (22)	
CK-level at baseline (U/ml; median [IQR])	970.5 [157.5; 3795.5]	
Change in CK-values from baseline	*Absolute change*	*Relative change*
-to week 4 (n=24)	*median [IQR] U/ml*	*% [IQR]*
-to week 8 (n=16)	304.5 [28.8;2051]	49.1 [22.4; 79.3] %
-to week 12 (n=15)	648.5 [25.8; 3939.3]	70.0 [13.6; 87.7] %
	559 [-7; 3988]	63.8 [-5.8; 98.1] %

Until week 4 significant decrease in CK-values was observed in 21/24 patients (p<0.01; Figure 1), from median 970.5 [157.5; 3795.5] to 347[63; 1010] U/ml. Median [IQR] dose reduction of steroids was 12.5 [0; 12.5] mg/day absolute and 25% [0%, 100%] relative. No differences were observed within patients of different myositis subtypes. One patient died after 4 weeks, in 15 patients IA was maintained until week 12. Significant reduction in CK-values was observed from baseline to week 8 and 12 respectively (141 [78; 460], 111 [57;338]. Median and relative changes from baseline until week 12 are displayed in Table 1.

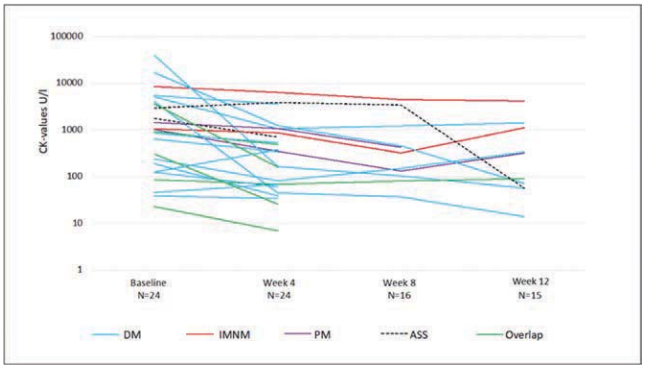

Figure 1. Individual response in CK-levels from baseline to week 12

Conclusion: Immune-apheresis seems an effective therapeutic option in refractory IIM, leading to decrease of CK-values and steroid dose.

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Disclosure of Interests: None declared

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AB0719 ECONOMIC BURDEN IN SCLERODERMA

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Background: Scleroderma (SSc) is a multi-system autoimmune disease, characterized by vasculopathy and fibrosis of the skin and internal organs, associated with substantial morbidity and disability. Patients with SSc commonly require considerable healthcare resources resulting in significant economic impact.

Objectives: The purpose of this systematic review is to provide a narrative summary of the economic impact and healthcare resource utilization associated with SSc.

Methods: MEDLINE and EMBASE were searched without language restriction from inception to January 20th, 2021. Studies were included if they provided information regarding total, direct, and indirect medical costs including medication, diagnostic test, and assistive devices costs. The cost of SSc complications was additionally collected. Included observational studies had risk of bias assessments through the Joanna Briggs Institute cross-sectional and case series checklists, and the Newcastle-Ottawa Cohort and Case-Control study scales.

Results: The search retrieved 1777 studies, of which 33 were included representing 20 cross-sectional, 10 cohort, and 3 case-control studies. Studies used various methods of calculating cost including prevalence-based cost-of-illness approach, bottom-up cost analysis, humanistic approach, and health resource units cost analyses. Overall scleroderma total annual medical cost ranged from USD $14,959-$23,268 in USA, CAD$10,673-$18,453 in Canada, €4,607-€30,797 in Europe, and AUD $7,060 to $11,607 in Oceania. Annual cost for SSc associated with interstitial lung disease and pulmonary arterial hypertension was USD $31,285-$55,446 and $44,454-$63,320, respectively.

Conclusion: Globally, SSc represents high patient and systemic economic burden. SSc-associated complications increase economic burden and are variable depending on geographical location, and access.

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Disclosure of Interests: None declared

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AB0720 ADULT ONSET STILL'S DISEASE: POINTS TO CONSIDER

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Background: Adult-onset Still's disease (AOSD) is a rare and complex autoinflammatory disease of unknown etiology. AOSD has a heterogeneous presentation which can lead to diagnostic uncertainty with prolonged time prior to treatment. NSAIDs, glucocorticoids, conventional DMARDs, and biologics are used in the management of AOSD with varying results. Furthermore, factors associated with de-escalation of therapies remain unclear.

Objectives: To review the literature and create a consensus on points to consider in the diagnosis, prognosis, and treatment of AOSD.

Methods: A scoping review of the AOSD literature over the last 15 years was performed. MEDLINE and EMBASE were searched and studies included if they provided information regarding the epidemiology, differential diagnosis, diagnostic criteria, complications, prognosis, and initial, chronic, and refractory treatment approaches in AOSD. Following narrative information synthesis, a meeting was held with experienced clinicians across Canada for the creation of a consensus on points to consider in AOSD.

Results: The annual incidence and prevalence of AOSD is observed to be between 0.16 to 0.62 per 100,000 and 3.9 to 6.9 per 100,000, respectively. AOSD most commonly affects young adults and women. Women are more likely to have severe complications from AOSD including macrophage activation syndrome, disseminated intravascular coagulation, or thrombotic thrombocytopenic purpura. The Yamaguchi criteria remains the most widely used diagnostic tool with a sensitivity of 96.2% and specificity of 92.1%. Common presentation manifestations include intermittent high fevers (>39.0 degrees Celsius), arthralgias/arthritis, pharyngitis, lymphadenopathy, and a maculopapular rash. Other manifestations can variably involve the cardiovascular, respiratory, and GI systems. Common laboratory abnormalities include leukocytosis with neutrophilia, elevated ESR and CRP, elevated ferritin, and transaminitis. AOSD patients are most commonly ANA and Rf negative. Initial treatment includes NSAIDs, glucocorticoids, and conventional DMARDs. Disease refractory to initial therapy is managed through IL-1 and IL-6 inhibitors such as Anakinra or Tocilizumab. Elevated ESR, pericarditis, and non-response to corticosteroids are some of the factors associated with refractory and chronic disease requiring advanced therapies and long term follow-up.

Conclusion: AOSD is a multi-faceted autoinflammatory disease with a diverse presentation profile. Clinicians are recommended to consider AOSD, following exclusion of infections, malignancies, and autoimmune diseases, as a cause for fever of unknown etiology. Our review provides points to consider in the diagnosis and management of AOSD following expert consensus.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2022-eular.4240

AB0721 FROM UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE TO IDENTIFIABLE DISEASE: PRECURSORS OF SYSTEMIC SCLEROSIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The pathogenesis of systemic lupus erythematosus and systemic sclerosis is characterized by derangements of the innate and adaptive immune systems, and inflammatory pathways leading to autoimmunity, chronic cytokine production, and chronic inflammation. Diagnosis is rooted in meeting established criteria. However, in pre-clinical states criteria is not fulfilled but biochemical and autoimmune derangements are present. Understanding the underlying processes responsible for disease pathogenesis in pre-clinical states, which place patients at increased risk for the development of established connective tissue diseases, presents a prognostic opportunity, and could enable timely treatment leading to limiting disease progression.

Objectives: We aim to describe the role of the innate and adaptive immune system in the pre-clinical states of UCTD-risk-SSc and prescleroderma, the underlying immune dysregulation in these pre-clinical states, and the evolution of antibodies from nonspecific antinuclear antibodies to specific prior to SLE development.

Methods: Our search strategy was developed alongside an experienced information specialist. We searched the databases EMBASE and MEDLINE with restrictions for the English language. Reference lists of all primary studies and review articles were searched for additional references. Studies reported in full-text and abstract formats were included.

Results: Multiple cytokines are observed to increase along a disease spectrum from UCTD-risk-SSc to classified SSc and include sICAM-1, CCL2, CXCL8, ang-2, CXCL16, e-selectin, and IL-13. The mechanism of action of these cytokines includes transmigration of lymphocytes endothelium, innate immune cell activation and signal propagation, and extracellular matrix deposition. The progressive nature of cytokine increase through a spectrum from pre-clinical to clinical emphasizes disease evolution and enables the discernment of patients who may warrant early intervention. Furthermore, there are disease markers which are observed to be predictive of established SSc and include sIL-2Rα, PIIINP, CXCL4, CXCL10, and CXCL11. Pre-clinical SLE is characterized by an evolving IFN signature and progressive SLE-specific antibody formation prior to disease classification.

Conclusion: The coordinated dysregulation of the innate and adaptive immune systems, and inflammatory signalling pathways leads to the pathogenesis of connective tissue disease. Our improved understanding of these underlying aberrations in pre-clinical stages of disease will serve to better identify patients at increased risk.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2022-eular.4241

AB0722 ONE-YEAR CLINICAL EXPERIENCE ON THE USE OF NINTEDANIB IN SYSTEMIC SCLEROSIS: SAFETY PROFILE.

L. Magnani[1], A. Spinella[2], S. Testoni[2], G. Bajocchi[1], L. Dardani[1], C. Salvarani[1,2], D. Giuggioli[2]on behalf of Scleroderma Unit - MORE. *[1]ASMN-IRCCS Santa Maria Nuova, Rheumatology, Reggio Emilia, Italy; [2]University of Modena and Reggio Emilia, Rheumatology, Modena, Italy*

Background: Systemic Sclerosis (SSc) is a complex autoimmune disease characterized by vascular damage, immune activation and fibrosis of skin and internal organs (1,2). One of the most common and severe SSc manifestations is interstitial lung disease (ILD) (3).

Objectives: Evaluate tolerability and safety profile of Nintedanib in patients with SSc-related ILD.

Methods: We enrolled 11 consecutive patients (6 female, 5 male, Mean age 62.7 ± 8 SD, disease duration (from the first Non-Raynaud symptom) 8 years (± 7SD) who referred to our Scleroderma Units during the last twelve months. Patients fulfilled EULAR/ACR classification criteria (4) for SSc. Patient was assessed by means of clinical evaluation (baseline and every three months), High Resolution computed tomography (every six month, or sooner), respiratory function test (every three to six months), laboratory work up, nailfold videocapillaroscopy, echocardiogram, and clinical questionnaires (BORG and mMRC).

Results: NSIP was the most frequent HRCT pattern (5 pts, 45%), followed by UIP and UIP/NSIP pattern (respectively 3 pts & 3 pts, 27%). 9 patients showed more than 20% of HRCT pulmonary fibrosis involvement. Only 1 patient had a history of smoking. mRSS was 9.23 (±10SD) points with any significant improvement during the twelve months follow-up (10 ±10SD). 8 pts were on Micophenolate Mophetil (MMF) (7 of them on MMF + steroids), 8 patients were on steroids (mean dose 5 mg/day of Prednisone or equivalent), 3 on rituximab. Main FVC was 2347 ml [+/- 1051 ml] (61.3% predicted) remaining stable. The mmRC decrased from 2.36 at baseline to 2.27 at the end of the follow up and Borg ameliorated from 7.27 at baseline to 6. Two patients were on oxygen therapy (O2 3l/min) with any significant airflow adjustment. Three patients reported irrepressible diarrhea, one patient had a partial intestinal obstruction, one had pulmonary arterial hypertension worsening with an immediate drug withdraw, one patient presented nausea, one irritability. Three patients had a clinical irrelevant weight loss (less than 2 Kg).

Conclusion: we report a preliminary real-life experience on the use of Nintedanib in SSc-related patients, focusing in particular to its tolerability and safety profile. Nintedanib is well tolerated with a low rate of definitive discontinuation due to SAE. Diarrhea is a very frequent adverse event (approximately 5 episodes a day) and had led to dose reduction and/or treatment re-challenge in the majority of patients. Diarrhea seems to ameliorate reducing daily dose of MMF (1 gram/day) or precribing loperamide along with diosmectite and probiotics. FVC, mRSS, HRCT and capilalroscopy pattern remained stable. Further studies are desirable to confirm the usefulness of Nintedanib in progressive ILD, but based on our experience we support the combined use of the anti-fibrotic therapy plus immunomodulatory drugs in early stages of SSc-related ILD

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AB0723 ANTI-TIF1-BETA AUTOANTIBODIES IN A PATIENT WITH CANCER-ASSOCIATED DERMATOMYOSITIS

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Background: Anti-transcriptional intermediary factor 1-gamma (TIF1-gamma) autoantibodies are strongly linked to cancer-associated dermatomyositis (DM). In addition to anti-TIF1-gamma autoantibodies, autoantibodies to TIF1-alpha and TIF1-beta have been described, often coexisting with TIF1-gamma or other known autoantibodies [1,2]. Thus far, anti-TIF1-beta autoantibodies without other known autoantibodies have been identified in only 3 patients with dermatomyositis, of which none had cancer [1,2].

Objectives: To report on a patient with cancer-associated dermatomyositis and isolated anti-TIF1-beta autoantibodies.

Methods: Serum of a patient with cancer-associated dermatomyositis without known autoantibody specificity was evaluated by immunoprecipitation combined with liquid chromatography-tandem mass spectrometry (IP + LC-MS/MS). Mass spectrometry data were matched against the Uniprot Homo Sapiens database with the Mascot search engine using Proteome Discoverer. Additional immunoprecipitation of radiolabeled cell extract followed by autoradiography were performed. Clinical and laboratory data were retrieved from the electronic health record.

Results: TIF1-beta was identified in the immunoprecipitate of the serum of the patient by IP + LC-MS/MS, but not TIF1-gamma or TIF1-alpha. These results were confirmed by immunoprecipitation of radiolabeled cell extract (Figure 1A). The HEp-2 indirect immunofluorescence assay showed a nuclear fine speckled pattern (AC-4, maximum titre > 1/1280, Figure 1B), which corresponds to the subcellular localization of TIF1-beta [3]. The patient, a 64-year old male, presented with dermatomyositis with classical cutaneous and muscular involvement (max. serum creatine kinase level 370 U/l). A renal cell carcinoma was found during the diagnostic work-up for which a partial nephrectomy was performed. There was a good response of both cutaneous and muscular disease activity to treatment with hydroxychloroquine and methylprednisolone.

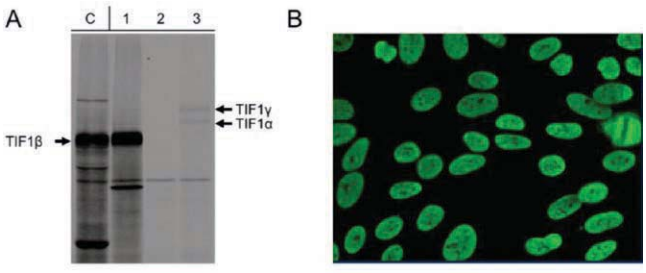

Figure 1. A Immunoprecipitation with ^{35}S-methionine labeled K562 cells with subsequent radiography. C Positive control with anti-TIF1-beta and anti-U1-RNP autoantibodies, 1 anti-TIF1-beta-positive patient (patient here described), 2 negative patient, 3 anti-TIF1-gamma/alpha-positive patient **B** Nuclear fine speckled pattern on HEp-2 indirect immunofluorescence assay, 40X magnification

Conclusion: Isolated anti-TIF1-beta autoantibodies should be considered in patients with dermatomyositis without known myositis-specific autoantibodies and can be associated with cancer.

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AB0724 TO ASSESS THE SCLERODERMA CLINICAL TRIALS CONSORTIUM DAMAGE INDEX (SCTC-DI) IN PATIENTS WITH SYSTEMIC SCLEROSIS IN RUSSIAN COHORT PATIENTS.

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Background: Systemic sclerosis (SSc) is a multiorgan disease wherein the pathogenic processes of inflammation, vasculopathy and fibrosis lead to multiple disease manifestations. The course of SSc is often one of progressive damage to multiple organs including the skin, joints, heart, lungs, gastrointestinal tract and kidneys. The scleroderma clinical trials consortium damage index (SCTC-DI): a new instrument to quantify organ damage in systemic sclerosis [1].

Objectives: To assess the scleroderma clinical trials consortium damage index (SCTC-DI) in patients with systemic sclerosis in Russian cohort patients.

Methods: Data from 104 patients with systemic sclerosis (mean age was 51,7±12,5;64% have limited subset of the disease; 88% were female) all fulfilling the ACR criteria for SSc. Functional lung tests, high-resolution CT (HRCT), echocardiography, SSc activity (by the European Scleroderma Study Group (EScSG) activity index), HAQ, SHAQ, the six minute walk test (6MWT), scleroderma clinical trials consortium damage index (SCTC-DI) were evaluated. Other data collected including biological results (high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR). Statistical analysis: descriptive data are presented as means (±SD) or medians (with interquartile range [IQR]) for continuous variables, while categorical variables are expressed as counts and percentages. Univariate comparisons were made with 2-sample t tests. we used the Spearman's rank-order (Spearman's p) correlations coefficients.

Results: A significant positive correlations were found between the SCTC-DI values and HAQ (r=0.31, p=0.003), SHAQ (r=0.28, p=0.0087), and values of EScSG activity index (r=0.31, p=0.0066) accordingly. The SCTC-DI values inversely correlated to values of 6MWT (r=-0.246, p=0.003). Moreover, the SCTC-DI values correlated inversely with forced vital capacity (r=-0.543, p<0.00000), forced expiratory volume in 1s (r=-0.487, p<0.00000) and diffusion capacity for carbon monoxide (r=-0.484, p<0.000001). A significant positive correlations the SCTC-DI values were found with pulmonary arterial pressure (PAP) (r=0.232, p=0.022), but didn't found any correlation with left ventriculi injection fraction (r=-0.104, p>0.05). Also we didn't find any correlations the SCTC-DI values with ESR levels and hsCRP levels (r=0.18, p>0.05 and r=0.15, p>0.05).

Conclusion: the SCTC-DI values correlate with dates of HAQ, SHAQ, EScSG activity index, values of 6MWT pulmonary function tests, supporting their use as measures of SSc severity.

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AB0725 SCLERODERMA STUDY GROUP EMILIA ROMAGNA (SCLERO-RER): REAL LIFE USE OF PROSTACYCLIN ANALOG. PRELIMINARY DATA FROM A MULTICENTRIC SURVEY.

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Background: Systemic Sclerosis (SSc) is a complex autoimmune disease characterized by vascular damage, immune activation and fibrosis of skin and internal organs [1]. Raynaud phenomenon (RP) is frequently the first symptom of the disease and growing evidences are supporting the hypothesis the SSc may be a vascular disease, with a pivotal role of endothelial cells, particularly in the very early phase[2,3]. Robust data support the use of vascular active drug to treat RP and to prevent vascular complication[4–7].

Objectives: The use of prostacyclin analog (PA) is evertything but standardized, with different regimen used all around the Country. We report data on the use of PA in a multicentric regional reality to understand which regimen are prevalent (and why) and if there is the opportunity to standardized them.

Methods: We collected data from an online survey exploring different items related to the use of PA.

Results: Survey was fullfilled by 12 sites: 5 university hospital and 7 local hospitals, 7 driven by Rheumatologist and 5 from internal medicine specialists with/without concomitant rheumatologists. PA are ubiquitarly used for SSc-related digital ulcers (SSc-DU) and secondary RP but only a half of sites use it for primary RP. Seventy-five percent of sites (9/12) dispense PA at least once a month, but some other (1 each one respectively) on weekly basis, every other month or every 7 weeks. Drug administration may last from 2 to 5 consecutive days (mean 1.91+/- 1.5SD) with drug dose ranging from 0.5 to 2 ng/Kg/min with a minimum variability from site to site. Our regional hospitals may count on overall 68 spots, some available as beds (outpatient or inpatient), some as reclining chair or chair (outpatients only). University centers have usually more assigned personnel than local hospital (on average: 2 versus 1.5 physicians, 2 versus 1.2 nurse). Sites are able to offer meals (except one) and are able to accomodate from 1 to 12 patients at the same time (mean 3.45, +/- 3.2SD).

Conclusion: PA has known benefit in vascular involvement in SSc patients. Despite a multicenter palcebo-control study[8] defining time and dose of this drugs and subsequent data based on the same regimen[9], there is no homogeneity in treatment administration. The unequal treatment, based on our data, seems due to limited resources and personnel. High variability has been found in regimen duration and administration frequency.

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AB0726 STUDY OF THE ASSOCIATION OF VARIOUS X-RAY SYMPTOMS OF INTERSTITIAL LUNG DISEASE (ILD) IN PATIENTS WITH SYSTEMIC SCLERODERMA(SSC) WITH INDICES OF LUNG FUNCTIONAL TESTS.

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Background: HRCT is the gold standard for confirming the presence of ILD. According to the literature data,there is an association between the prevalence of pulmonary involvement and the severity of PFTs.However,it remains unclear whether the nature of interstitial changes affects the degree of PFTs.
Objectives: To study the clinical significance of various X-ray symptoms in SSc-ILD during long-term follow-up.
Methods: The study included 37 pts with a SSc-ILD(average age-53.1±11.5 yrs, m/w- ¼, and d/l–1/1.8, SSc duration-10.9±9 yrs).For all pts at the time of inclusion in the study and after an average of 34±2.3 months,there were examined FVC,DLC,HRCT.All pts received immunosuppressive therapy-(IST). The analysis of HRCT data was conducted at 5 levels.The severity of changes by type of ground-glass,reticular changes,traction bronchiectases,and honeycombs were evaluated(0–3 points).The dynamics of X-ray changes and PFTs was assessed in the general group and in pts with the prevalence of ILD up to 20%(group A,n=23) and more than 20%(group B, n=14).
Results: At the time of inclusion in the study,the total CT score of ILD on average for the group was 9.6±8.2.FVC was normal(94±19.5%);a moderate decrease in DLC was detected(57.3±20.2%).The prevalence of ILD significantly correlated only with the DLC(R=-0.35, p<0.05). When included in the study,reticular changes were most often observed(the score was 4.6±3.5). Alterations by type of ground-glass were somewhat less common(the score was 3.2±3.1).The score of traction bronchiectases was 1.68±2.3.Changes by type of honeycombs were found in only 5 patients,of which only 1 patient was from the group A. Against the background of IST,values of FVC and DLC remained stable in the group as well as in the groups A and B,and the total CT score did not change.In patients of the group B,both the total CT score and the average score of ground-glass and reticular changes,and traction bronchiectases score were significantly higher. To assess the clinical significance of various X-ray symptoms,a correlation analysis of the total score of each of them with the PFTs data in groups A and B was executed. No significant correlation between the score of X-ray signs and values of FVC was detected. DLC significantly inversely correlated with the total score of each HRCT symptom, with the exception of ground-glass.At the same time,strength of the correlation was approximately the same for reticular changes, bronchiectases, and honeycombs in both groups.
Conclusion: The severity of the alveolar-capillary membrane functional disorders is primarily due to the prevalence of fibrotic changes.The variant of fibrotic changes has no significant importance.Changes by type of ground-glass to a lesser extent affect the degree of reduction in DLC.The best surrogate indicator reflecting the prevalence of interstitial changes was DLC.
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AB0727 STUDY OF THE INDICATORS DYNAMICS OF THE PULMONARY FUNCTIONAL TESTS (PFTS) AND X-RAY PICTURE AGAINST DURING THE 36-MONTH IMMUNOSUPPRESSIVE THERAPY (IST) OF INTERSTITIAL LUNG DISEASE (ILD) IN PATIENTS WITH SYSTEMIC SCLEROSIS (SSC)

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Background: HRCT is the gold standard for confirming ILD.However,the role of HRCT for estimating the effectiveness of therapy is not determined in full.
Objectives: To assess the dynamics of X-ray changes and PFTs during IST in pts with SSc and different prevalence of ILD according to HRCT.
Methods: The study included 37 pts with signs of ILD(the average age-53.1±11.5 yrs,the ratio of m/w- ¼, d/l–1/1.8,the SSc-duration-10.9±9 yrs).For all pts at the time of inclusion in the study and after an average of 34±2.3 months were studied FVC,DLC and HRCT.The pts received IST during the follow-up period.The ILD dynamics was assessed as follows:improvement,deterioration and no dynamics. The analysis of HRCT data was conducted at 5 levels.The severity of changes by type of ground-glass,reticular changes,traction bronchiectasis,and honeycombs were evaluated(0–3 points).The dynamics of X-ray changes and PFTs was separately assessed in pts with the prevalence of interstitial changes up to 20%(group A,n=23) and more than 20%(group B,n=14) of the total area of lung tissue.
Results: In the general group during the IST CT-improvement was noticed in 13(34.2%),deterioration–in 9(24.3%) pts.There was no dynamics in 15(40.5%) pts. On average,values of FVC and DLC remained stable.None of the pts with improvement of HRCT showed a deterioration of FVC.Among pts with the X-ray picture deterioration,in 2 cases,there was a decrease in FVC by 5% or more;in other cases,indicator stabilized.The mean CT score did not change during the therapy.In group B,the total CT score and the average score of ground-glass,reticular changes,and traction bronchiectasis were significantly higher.Changes by type of “honeycombs” were mainly revealed in group B.During the IST,positive X-ray was detected in 6(42.9%) pts of group A, in 7(30.4%) pts of group B(p=0.06),and negative X-ray dynamics–in 4(17.4%) pts of group A, in 5(35.7%) pts of group B(p>0.05).During the IST,the mean values of DLC and FVC did not significantly change in both groups.
Conclusion: Semi-quantitative evaluation according to HRCT in pts with SSc-ILD did not reveal any dynamics in the total score of structural changes during IST,which coincided with stable indices of PFTs.Pts with less common pulmonary involvement during therapy were more likely to demonstrate positive CT-dynamics. With an increase in the prevalence of ILD,signs of fibrosis increased.Most pts had unidirectional dynamics of values of FVC and CT-changes,which confirmed the possibility of effective use of HRCT to assess the conducted therapy.
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Table 1.

	Group A			Group B			p
Correlation DLC with CT score	DLC	CT score	R	DLC	CT score	R	<0.05
DLC1 with total CT score 1	60.6±19.6	4.5±4.4	-0.5	47.6±11.4	18.1±5.6	-0.35	
DLC2 with total CT score 2	62.6±19.1	4.1±3.9	-0.57	45.2±13.5	18.1±6.1	-0.47	
DLC1 with reticular changes score 1	60.6±19.6	2.6±2.4	-0.44	47.6±11.4	7.9±2.4	-0.43	
DLC2 with reticular changes score 2	62.6±19.1	2.7±2.3	-0.46	45.2±13.5	7.6±1.98	-0.51	
DLC1 with bronchiectases score 1	60.6±19.6	0.5±1.2 (median-0 [0;0])	-0.54	47.6±11.4	7.8±2.0	-0.49	
DLC2 with bronchiectases score 2	62.6±19.1	0.7±1.3(median-0 [0;1])	-0.6	45.2±13.5	7.6±2.0	-0.56	
DLC1 with honeycomb score 1	-			47.6±11.4	1.3±2.3 (median-0 [0;1])	-0.34	
DLC2 with honeycomb score 2	-			45.2±13.5	1.7±3.3(median-0 [0;1])	-0.34	

“1”–at the time of inclusion in the study“2”–at the time of the last examination.

Parameters	All group (n=37) point "1"	All group (n=37) point "2"	p	Group A (n=23) point "1"	Group A (n=23) point "2"	p	Group B (n=14) point "1"	Group B (n=14) point "2"	p	P Between groups A and B
Negative CT-dynamics, n/%		9/24.3			4/17.4			5/35.7		0.008
Positive CT-dynamics, n/%		13/34.2			6/42.9			7/30.4		0.06
Mean CT-score, points (M±σ)	9.6±8.2	9.4±8.3		0.7	4.1±3.9	0.5	18.07±5.6	18.1±6.1	1	p1=0.000038 p2=0.000001
"Ground-glass" score, points (M±σ)	5.1±3.3	4.95±3.3	0.6	1.9±2.6 (median-0 [0;3])	1.3±2.1 (median-0 [0;2])	0.12	5.4±2.6	4.6±3.2	0.3	p1=0.018 p2=0.013
Reticular changes score, points (M±σ)	7.4±3.7	7±3.4	0.4	2.6±2.4	2.7±2.3	0.7	7.9±2.4	7.6±1.98	0.3	p1=0.0007 p2=0.0004
Traction bronchiectasis index, points (M±σ)	1.67±2.3 (median-0 [0;3])	2.0±2.6 (median-1 [0;3])	0.02	0.5±1.2 (median-0 [0;0])	0.7±1.3 (median-0 [0;1])	0.1	7.8±2.0	7.6±2.0	0.7	p1=0.000000 p2=0.000000
FVC, % of proper values (M±σ)	94.2±19.5	94.6±16	1	92±18.9	91.9±19.6	0.95	89.2±21.5	90.3±14.2	0.23	p1=0.7 p2=0.8
DCL, % of proper values (M±σ)	57.3±20.2	57.9±20.7	0.6	60.6±19.6	62.6±19.1	0.3	47.6±11.4	45.2±13.5	0.22	p1=0.13 p2=0.02

** Between groups A and B*. Point "1"–at the time of inclusion in the study; point "2"–at the time of the last examination.

AB0728

COMPARATIVE RESULTS OF LONG-TERM (FOR 36 MONTHS) USE OF RITUXIMAB AND IMMUNOSUPPRESSANTS IN PATIENTS WITH SYSTEMIC SCLERODERMA WITH INTERSTITIAL LUNG DISEASE IN REAL CLINICAL PRACTICE

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Background: Immunosuppressants (IS) is considered as a drug of choice for the treatment of interstitial lung disease (ILD) in the patients with systemic sclerosis (SSc). However, the IS use leads to rather limited and transient improvement of the pulmonary fibrosis. In this context the search for novel, more efficacious agents have been continued, such as attracting much attention rituximab (RTM).

Objectives: To compare the dynamics of pulmonary function parameters and skin fibrosis in patients with SSc associated with ILD, who received RTM and IS for 3 years in real clinical practice.

Methods: 158 pts with the SSc-ILD were enrolled into the study. All pts received low- and moderate-dose glucocorticoids regimens. **Group A** (n=100) **received IS's** (31/31% mycophenolate mofetil, 27/27% cyclophosphamide, 15/15% methotrexate; 27/27% other drugs; the patient's average age was 49.5±12.2 years, with female proportion 87%; SSc duration 8.6±7.2 years; diffused/localized forms 1/ 2.8). **Group B (n=58) received RTM a total dose** 3.0±1.2 g, 22 patients received RTM in combination with ISs (11/19% mycophenolate mofetil, 11/19% cyclophosphamide; average age 48.0±13.2 years, female proportion 86%, SSc duration 6.4±4.9 years, diffused/localized forms 1.5/1). The therapy duration in both groups was 36 months. The time courses of forced vital capacity (FVC), diffusive lung capacity (DLC), modified skin count (mRss, points), activity index (EScSG, points), HAQ were assessed in the study.

Table 1.

Parameters	Group A n=100		Group B n=58		p
FVC1 M ± SD	95.2±17.0	P=0.3	76.8±20.7	P=0.0003	
FVC1 M ± SD	96.5±18.9		83.8±22.2		
Δ FVC %, SD'S [25%'S; 75%'S]	-0.7 [-5.8; 7,9]		5.6 [-1.9;14.8]		0.008
DLCO 1, M ± SD	62.6±19.9	P=0.08	46.4±18.3	P=0.6	
DLCO 2, M ± SD	60.1±17.4		47.1±17.6		
Δ DLCO %	-1.7 [-5.9;3.3]		1.25 [-4; 7.05]		0.15
mRss, 1 M ± SD	5.6±5.3	P=0.003	11.3±10.2	P=0.000013	
mRss, 2 M ± SD	4.3±3.7		5.5±4.8		
Δ mRss, SD'S [25%'S; 75%'S]	0 [-2;0]		-3 [-11;0]		0.000031
HAQ1	0.86±0.5	P=0.9	1.14±0.8	P=0.01	
HAQ2	0.86±0.6		0.9±0.8		
EScSG 1, M ± SD	1.64±1.2	P=0.4	2.6±	P=0.0005	
EScSG 2,M ± SD	1.8±1.3		1.4±		
Dose of glucocorticoids 1, mg	8.8±4.8	P=0.16	11.4±4.0	P=0.002	
Dose of glucocorticoids 2, mg	8.1±3.7		9.1±2.9		
FVC increment by ≥10%, n/%	16/16		17/29.3		0.04
FVC decrement by ≥10% n/%	14/14		4/6.7		0.18
DLCO increment by ≥10%, n/%	6/6		5/8.6		0.5
DLCO decrement by ≥10% n/%	14/14		5/8.6		0.3

*1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the vales measured before and after the treatment*

Results: In Groups A and B the therapy was associated with significant decrease in mRss and stabilization of the diffusive lung capacity. During the follow-up period in Groups A no change of the other studied parameters was observed.
In Groups B the therapy was associated with significant decrease in HAQ and EScSG. Evaluation of FVC time course in Group B revealed significant FVC increase with median increment about 5.6%. In Group B 10% FVC increase was found in the third of the patients thus exceeding respective parameter in Group B (16%). The patient percentage with FVC decrease by ≥10% in group B was less common compared to group A. During RTM therapy it was possible to significantly reduce the dose of glucocorticoids. RTM and immunosuppressants administration for 36 months in the patients with SSc and ILD effectively alleviated skin induration and stabilized DLCO.

Conclusion: Only RTM significantly improved FVC and the patient's quality of life and decreased of the activity index. RTM demonstrated a steroid-saving effect. The study findings substantiate potential use of RTM as a first-line agent for the treatment ILD progressive phenotype in SSc. The immunosuppressants use as a single-agent therapy is more preferable in patients with less pronounced ILD.

Disclosure of Interests: None declared

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AB0729

CLINICAL AND INSTRUMENTAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC SCLEROSIS IN DIFFERENT INTERVAL SEPARATED BY SCLERODERMA CLINICAL TRIALS CONSORTIUM DAMAGE INDEX (SCTC-DI) IN RUSSIAN COHORT PATIENTS.

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Background: Systemic sclerosis (SSc) is a complex disease having an incidence of 1-2 cases per 100,000. In SSc, inflammation leads to organ failure due to severe fibrosis of the skin and internal organs. At late stages, this disease is characterized by a profound decline in the quality of life and premature death [1]. The course of SSc is often one of progressive damage to multiple organs including the skin, joints, heart, lungs, gastrointestinal tract and kidneys. The scleroderma clinical trials consortium damage index (SCTC-DI): a new instrument to quantify organ damage in systemic sclerosis [2].

Objectives: To use the scleroderma clinical trials consortium damage index (SCTC-DI) for pts with systemic sclerosis and highlight pts with different disease severity in Russian cohort patients.

Methods: Data from 96 patients with systemic sclerosis (mean age was 51,3±12,2; 63% have limited subset of the disease; 88% were female) all fulfilling the ACR criteria for SSc. Functional lung tests, high-resolution CT (HRCT), echocardiography, SSc activity (by the European Scleroderma Study Group (EScSG) activity index), HAQ, SHAQ, the six minute walk test (6MWT), scleroderma clinical trials consortium damage index (SCTC-DI) were evaluated. Total scores of SCTC-DI were categorized into groups (low damage score<5, moderate damage score 6-12, high damage score ≥13). Other data collected including biological results (high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR). Statistical analysis: descriptive data are presented as means (±SD) or medians (with interquartile range [IQR]) for continuous variables, while categorical variables are expressed as counts and percentages. Univariate comparisons were made with 2-sample t tests.

Results: pts were divided into 3 groups in depend on total score of SCTC-DI. 77pts (80%) were into group 1 (with low damage score); 17 pts (18%) were into group 2 (with moderate damage score) and 2 pts (2%) were into group 3 (with high damage score). Baseline characteristics of the groups are presented in Table 1

Table 1.

parameters	Group1(n=77) (M±SD)	Group2 (n=17) (M±SD)	Group3 (n=2) (M±SD)	P
Age (months)	51.7±12.3	54.1±12.2	47±11.3	>0.05
SSc forms	43 (55%)	12 (70%)	1 (50%)	>0.05
Lim				
Gender: fem	69 (88%)	14 (82%)	2 (100%)	
Duration of dis.(years)	8.9±7.6	12.4±7.1	15±7	>0.05
HAQ	0.83±0.68	1.14±0.653	1.62	>0.05
SHAQ	1.174±0.704	1.3±0.76	1.5	>0.05
6MWT	412±170	358±187	108	>0.05
EScSG	1.81±1.44	2.14±1.44	0.5	>0.05
hsCRP	6.63±14.8	3.7±2.57	20.7±18.1	>0.05
MED[25;75‰]	2.93 [1.2;5.62]			
ESR	16.7±21.4	20±31.6	71.5±92.6.8	>0.05
MED[25;75‰]	12 [7;19]	14 [12;23]	71.5 [6;137]	
PAP	34.7±10.8	38±13.1	40±19.75	>0.05
Left ventriculi infection fraction	69.9±7.3	66.7±5.7	64.5±3.5	>0.05
FVC	97.3±14.68	64.7±17.3	43.3±5.8	Gr1 vsGr2 Gr1vs Gr3 p<0.0001
DLco	60.9±16	36.4±9.5.3	44.3	Gr1 vsGr2 p<0.0001
FEV1	96.8±14.9	66.3±20.1	46.7±7.2	Gr1 vsGr2 Gr1vs Gr3 p<0.0001

We didn't find a lot of significant differences in between groups, but it could be noted that group 3 was younger and the severity of the parameters increased in groups moderate and high damage. We found that mean value of FVC, DLco and FEV1 were significant increased in group1.

Conclusion: the pts with moderate and high damage scores of SCTC-DI had worse clinical and instrumental characteristics than pts with low damage score. We could try to use scores of SCTC-DI as measures of SSc severity.

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AB0730 SCCA-IGM AS A PREDICTOR OF INTERSTITIAL LUNG DISEASE PROGRESSION IN SYSTEMIC SCLEROSIS

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Background: Interstitial Lung Disease (ILD) is the major determinant of morbidity and mortality in patients with systemic sclerosis (SSc). The course of lung involvement is extremely variable in SSc-ILD. Squamous Cell Carcinoma Antigen 1 (SCCA1) is a cysteine protease inhibitor that plays a crucial role in inflammation and fibrosis. It may be detected in serum in the form of an IgM-linked immune complex (SCCA-IgM), and we previously demonstrated that it is increased in patients with SSc-ILD (1).

Objectives: We aimed to investigate the association between SCCA-IgM serum levels and ILD progression in a cohort of SSc patients.

Methods: Ninety-seven patients with SSc (2013 ACR/EULAR criteria) from the Rheumatology Unit of Padua University Hospital were consecutively enrolled in the study. Clinical, serological indices and organ involvement (pulmonary, cardiac, gastrointestinal and articular) were evaluated at the time of the SCCA-IgM assay. Pulmonary involvement was investigated by high-resolution CT (HRCT) and respiratory function tests (PFTs). Serum immune complex levels were measured by a validated ELISA assay (Hepa-IC, Xeptagen, Venice, Italy) and expressed in arbitrary units/mL (AU/mL). Follow-up period was defined as the time between baseline (i.e. SCCA-IgM blood sampling) and last PFTs and/or HRCT performed at least after 24 months. SSc-ILD progression was defined by HRCT and/or PFTs worsening. Progression on PFTs: FVC decline ≥ 10% from baseline or FVC ≥ 5-9% decline plus DLCO decline ≥ 15%; radiological progression: ILD worsening on HRCT evaluated by the same experienced thoracic radiologist.

Results: Among the 97 SSc enrolled patients (mean age 55.4±12.5 yrs), 82 (84.5%) were female, 35 (36%) affected by diffuse cutaneous form of SSc (dcSSc) and 41 (42.3%) had ILD diagnosed by HRCT. The mean follow-up was 34.6 ± 1.8 months, with PFTs and/or HRCT data available in 86 patients, 37 (43%) of whom had ILD at baseline. Patients with ILD who progressed during follow-up were more frequently affected by dcSSc (p = 0.003), and tended to have lower values of total lung capacity (p=0,091). The median SCCA-IgM values were significantly higher in patients with progressive ILD vs. those with stable ILD: 301 (57-526) vs. 45 (34-236), respectively (p = 0.017), Figure 1. At Cox regression multivariate analysis, SCCA-IgM serum levels was the only variable independently associated with ILD progression [HR 1,003 95% CI 1,000-1,006, p=0.02].

Conclusion: In conclusion, our preliminary data support SCCA-IgM as a potential candidate biomarker for progressive ILD in patients with scleroderma.

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AB0731 THYROID DISORDERS ASSESSMENT: AN UNMET NEED IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES?

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Background: Thyroid diseases (TD) might compromise health status of patients, in particular owing to their possible impact on cardiovascular risk, bone mineral density (BMD) and muscle function. The prevalences of Hashimoto thyroiditis (HT), multinodular goiter (MNG) and Graves' disease (GD) in general population correspond respectively to about 12%, 10% and 1.3%; it is well known HT represents a risk factor for the development of thyroid papillary cancer (TPC). Idiopathic inflammatory myopathies (IIMs) are rare systemic autoimmune disorders, with a pleiotropic clinical picture. TD are a known comorbidity of patients with connective tissue diseases; in particular, they might increase the risk of osteoporosis (OP) and fragility fractures (FF) in patients with SLE[1]. A recent study described the association between IIMs and both hyper- and hypo-thyroidism[2].

Objectives: To evaluate the prevalence of TD in a monocentric cohort of patients with IIMs, exploring possible correlations with serology, organ involvement and comorbidities.

Methods: We retrospectively analyzed medical records of consecutive patients diagnosed with IIM according the EULAR/ACR 2017 criteria and regularly followed at our specialistic outpatient Myositis Clinic from January 2018 to December 2021. We collected data about demography, subset and duration of disease, organ involvement, serology, thyroid dysfunction and other comorbidities. As TD, we took into account the occurrence of HT, MNG and GD. Intergroups comparisons were assessed by using Chi-square, t-test and ANOVA. P values <0.05 were considered significant.

Results: The clinical charts of 151 patients were examined: 101 (66,9%) were female, the mean age was 65,1±14,0 years and the mean disease duration was 8,5±6,5 years. Clinical diagnosis were the following: 69 (45.7%) polymyositis, 59 (39.1%) dermatomyositis, 11 (7.3%) clinically amyopathic dermatomyositis, 10 (6.6%) inclusion body myositis, 2 (1.3%) juvenile dermatomyositis. Seventy-five patients (49.7%) had a TD; in particular, 39/151 (25.8%) had MNG, 34/151 (22.6%) had HT and 2/151 (1.3%) GD. The presence of a TD was significantly related with esophagus' involvement (p=0.037), Raynaud's phenomenon (RP) (p=0.045), sicca syndrome (SiS) (p<0,001), OP (p<0,001) and cataract (p=0,017). In particular, HT and MNG occurrence was respectively associated with a higher risk of OP (p<0,001) and of sicca syndrome (p<0,001). Interestingly, TD were significantly less frequent in patients with anti-Mi2beta autoantibodies (p=0,003) and anti-Jo1 autoantibodies (p=0,026). No further significant correlations emerged.

Conclusion: Our study showed nearly half of our IIMs patients had a TD, with a prevalence of both MNG and HT significantly higher than in general population; besides, owing to the retrospective nature of our study, these data could be underestimated. In addition to correlating with RP and SiS, TD showed a significant association with esophagus involvement; this result should be confirmed and clarified with future analyses. Moreover, in our cohort, TD were confirmed as a risk factor for a compromised BMD; in particular, HT was significantly associated with the occurrence of OP. Further studies are needed to corroborated our data in other cohorts of IIM patients

and to explore if TD represent a risk factor for FF also in IIM; finally, since HT is a risk factor for TPC, an evaluation of its occurrence in our cohort should be designed. However, our data seem sufficient to underline the need to regularly screen IIM patients for thyroid function, aiming at optimizing their quality of care, both for activity and damage domains of their autoimmune disease.

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AB0732 ABATACEPT AS THERAPY OPTION IN SYSTEMIC SCLEROSIS (SSC) PATIENTS AFTER YEARS OF GRAZER- PROTOCOL TREATMENT- OUR EXPERIENCE

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Background: Previous studies have provided evidence that T cells may play a significant role in the pathogenesis of systemic sclerosis (SSc) and observational studies reported that Abatacept, which interferes with T cells activation, appeared to be safe and effective in SSc-patients with skin and muscle involvement. So far, there was no significant effective treatment for SSC-ILD. We have recently demonstrated the effectiveness of intensified –RTX- long term treatment ("Grazerprotocol" with 500 mg RTX in week 0 and 2, every 3 months +/- MMF) in SSc patients with severe organ involvement and/or progressive form non responding to methotrexate or cyclophosphamide. However, no data are available concerning how long Patients with a stable disease need to be treated. B-cell-depletion therapy over years for SSC in remission might represent a risk factor for infections. Additionally, the parenteral administration is associated with an increase in health care and patients are bound to regular hospital visits, which is a limiting factor for life quality.

Objectives: We aimed to investigate if subcutaneous Abatacept could be used as a maintenance treatment in SSc-patients reaching a stable disease activity after a treatment with RTX administered according to our Grazer protocol over several years.

Methods: In this retrospective analysis, we retrieved data from 20 patients who fulfilled the diagnosis criteria for systemic sclerosis (SSc) according to the European League Against Rheumatism Scleroderma Trial and Research standards, who started a treatment with abatacept (ABA) after years of 500 mg RTX therapy every three months +/- MMF (Grazer protocol). The following clinical parameter were evaluated: modified Rodnan Skin Score (mRSS), Systemic Sclerosis Activity Score (SScAS), Systemic Sclerosis Severity Score (SScSS) and lung diffusing capacity for carbon monoxide (DLCO). Lab parameters like IgG, ANA, ENA and inflammation parameters were routinely assessed. Clinical data from baseline visit (BSL) (before ABA treatment start) and follow-up visit (FU) (after 6 months of treatment) were collected.

Results: We included 20 SSc patients in this retrospective analysis who changed from RTX to Abatacept. The majority were female (n=16; 94.1%), with a mean age ±SD of 54.8 years ±11 and an average disease duration of 7.7 years ±4.5. In 17.9% (n=4) treatment needed to be stopped due to disease flare after three months (lung n=2, skin and tendons n=2).

However, interestingly, Abatacept further decreased significantly mRSS between baseline visit and follow-up visit regarding the affected skin of the fingers. Thus, the mRSS went from 3.9±3.4 to 2.5±1.8 ($p<0.05$). As expected, no significant difference in the EUSTAR-SScAS, or ScSS or DLCO was found. No infections were observed during the abatacept follow-up period and Immunoglobulins remained within the normal range.

Conclusion: Abatacept might be a feasible option as a maintenance therapy after intensive immunomodulation with RTX and may give our patients the possibility to further improve their quality of life.

The fact that 4 patients experienced a relapse after switching to Abatacept warrants further studies to find prognostic factors.

Disclosure of Interests: None declared

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AB0733 MUSCULO-ARTICULAR SYNDROME IN PATIENTS WITH SYSTEMIC SCLEROSIS-POLYMYOSITIS/ DERMATOMYOSITIS OVERLAP SYNDROME.

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Background: Systemic Sclerosis-polymyositis/dermatomyositis overlap syndrome (SSc-PM/DM) occurs in 10 to 37% of cases and has great differential diagnostic difficulties. Muscle damage in SSc-PM/DM is represented by myositis with primary inflammatory and necrotic alterations in muscle fibers by type of PM/DM.

Objectives: To evaluate joint and muscle damage in patients with SSc-PM/DM.

Methods: 112 pts had idiopathic inflammatory myopathies, of which 73 pts with SSc-PM/DM (51 pts with lSSc and 22 pts with dSSc, male/female 24/49, mean age 44±14,5 years, average disease's duration 7 (2;9) years) had the standard clinical examination, intramuscular electromyography (IM-EMG) and manual muscle testing (MMT-8).

Results: All pts had polyarthralgia, 40% pts - arthritis. Damage to periarticular tissues with the formation of flexion contractures was observed in 70% pts, of which 16% - contractures of large joints (knee and elbow). X-ray changes in the hands and feet (distal osteoporosis, narrowing of the joint spaces, and smoothness of the phalangettes) were observed in all pts, 13% of pts had erosions associated with osteoarthritis. There was noticed significantly frequent development of flexion contractures in pts with dSSc ($p<0.05$) and high skin score ($p<0.05$). Osteolysis peculiar to SSc was detected in 23.5% of pts, and soft tissue calcinosis in the area of the phalangettes, and metacarpophalangeal joints – in 32% pts. Calcifications, specifically associated with PM/DM, in the soft tissues of the shoulder and pelvic girdle, large joints were revealed in 6% pts. A direct correlation was revealed between the duration of the disease and the development of calcinosis and osteolysis ($p<0.05$). Myalgia and proximal muscle weakness was in all pts, dysphagia – in 43% pts, and dysphonia – in 19% pts. Patients with a moderate degree of muscle weakness (MMT-8 76-115 points) prevailed and topped 41% and patients with severe disabling functional disorders (MMT-8 ≤75 points) showed 37%, of which 4% of pts were completely immobilized. In 18% of pts, PM was detected during physical and/or laboratory examination (MMT-8 ≥ 116 points). Analysis of IM-EMG of changes confirmed the presence of primary muscle inflammatory process (all patients had a decrease in motor unit action potential (MUAP) and spontaneous activity, polyphasia – in 93% of pts. A correlation was observed with laboratory and immunological signs of disease activity: between ESR and spontaneous activity ($p<0.02$), CPK titers and polyphasia ($p<0.01$), the presence of a-Pm-Scl and a decrease in MUAP ($p<0.03$).

Conclusion: Muscular syndrome in SSc-PM/DM has clear clinical symptoms, and the underlying symptom of involvement is sharp muscle weakness with movement disorders intrinsic to PM/DM. However, such disorders do not lead to complete immobility, as in PM/DM, and they are combined with other manifestations of SSc. Articular syndrome in pts with SSc-PM/DM is mainly represented by periarticular changes, in some pts with osteolysis and calcinosis common to SSc.

Disclosure of Interests: None declared

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AB0734 **THE DYNAMICS OF LUNG FUNCTION IN PATIENTS WITH SYSTEMIC SCLERODERMA ASSOCIATED WITH INTERSTITIAL LUNG DISEASE DURING A THREE-YEAR FOLLOW-UP PERIOD.**

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Background: Nowadays ILD is one of the most common manifestations of SSc and the leading cause of death of patients. 25% to 30% of patients develop progressive ILD.
Objectives: To assess the course and outcomes of interstitial lung disease (ILD) in systemic sclerosis (SSc) based on lung function after three years of follow-up.
Methods: The study included 82 patients with SSc associated with ILD. There were 70 (85%) women and 12 (15%) men, whose average age was 49.86±12.30 years, 49 (60%) patients with limited SSc, 24 (29%) patients with diffuse SSD, 7 (9%) patients with overlap syndrome; median disease duration was 7 (4;11) years. The great majority of patients had a chronic course of the disease. The patients had systemic manifestations, vascular disorders and lesions of the musculoskeletal system. According to the results of CT scan of the thoracic organs, 28% of patients had more than 20% of pulmonary involvement. All patients took glucocorticoids (GCs); the average dose of prednisone was 8.6±4.6 mg. 50 (61%) patients took immunosuppressants (IS).
The diagnosis was set according to ACR/EULAR criteria. The patients were examined twice in accordance with generally accepted approaches. To identify and assess the dynamics of ILD, there was used high-resolution computed tomography (HRCT) Their lung function was assessed by data obtained due to spirometry (in particular, forced vital capacity, FVC) and diffusing capacity of the lungs (DCL); Doppler echocardiography was also conducted.
Results: In the group of patients with SSc, a significant improvement was noticed in some indicators demonstrating the peculiar manifestations of the disease. Therefore, skin induration (a decrease in skin score) decreased from the initial 5.8±5.2 to an average of 4.6±3.9 points after three years, p=0.0001. Functional capacities of the lungs and heart did not deteriorate. There was a trend towards an increase in FVC by 5.7% (from 91.8±19.1 to 96.15±18.26, respectively). However, these data were not clinically significant. Systolic pulmonary artery pressure (sPAP) also remained stable, mm Hg (31.83±8.10 and 33.57±9.03, respectively), indirectly indicating the absence of progression in pulmonary involvement. These positive alterations were the basis for reducing the daily dose of GCs in some patients. The reduction in dose of GCs was small but statistically significant (8.64±4.58 and 7.86±3.33, respectively, p=0.007).
Conclusion: Therefore, due to the study, stabilization of lung function and the absence of progression in the SSc-ILD group were noticed, which emphasizes the importance of continuous monitoring and follow-up of patients and continuation of therapy.
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AB0735 **INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC CONNECTIVE TISSUE DISEASES: DYNAMICS OF LUNG FUNCTION AFTER THREE YEARS OF FOLLOW-UP**

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Background: Interstitial lung disease (ILD) is one of the most common and severe manifestations of connective tissue diseases, such as systemic scleroderma (SSc), dermato- and polymyositis (DM/PM), mixed connective tissue disease (MCTD), etc.
Objectives: To compare the course and outcomes of ILD in SSD, MCTD and DM/PM, immunoinflammatory myopathies (IIM) after three years of follow-up.
Methods: The SSc group consisted of 82 patients, the IIM group – 61 patients, and the MCTD group – 20 patients. In all the studied groups, women predominated. The oldest patients were found in the IIM group, and the average age was 51±12.88 years. The duration of the disease varied from 0.5 to 18.5 years. A longer course of the disease was observed among patients with MCTD, the median was 10.6 (6.9; 18.5) years. When assessing the initial parameters of lung function tests, significantly lower values of FVC and DCL were recorded in the IIM group (on average, 82±21.5 and 51.1±16.2, respectively), and higher values in the MCTD group (95.4± 20 and 67.5±15). All patients took GCs, the highest doses were taken by patients with IIM. The great majority of patients received immunosuppressants, of which 100% of patients were in the MCTD group.
Results: Despite the fact that the indices of FVC and DCL in the SSc group were initially lower (on average 91.8±19.1 and 59.2±19.5, respectively) than in the MCTD group. The dynamics of Δ FVC over three years against the background of ongoing therapy was discordant: Δ FVC in the SSc group significantly increased [0.6 (-8; 4.9)], in the MCTD group, it decreased [-5.7 (-10.3; 10.9)]. The mean value of DCL over the follow-up period remained practically the same; the dynamics between the groups was also discordant: it slightly increased in patients with SSc [1.1 (-3.8; 4.6)] and decreased in patients with MCTD [-1.6 (-11.2; 12.6)]. FEV1 decreased in both SSD and MCTD groups, but the alterations were not significant. In the group of patients with IIM during the follow-up period, there was a significant increase in the mean values of Δ DCL, FVC and FEV1 [9.8 (4-16), 13.9 (3.2-28.5), 10.2 (2-26.8)].
Conclusion: Therefore, due to the study, positive dynamics in lung function in patients with ILD was noticed in the IIM group, stabilization of the pathological process and the absence of progression in the SSc group were achieved, and, despite the initially higher values of FVC and DCL, negative dynamics was detected in the group of patients with MCTD. It is likely that the positive dynamics of lung function in patients with IIM is due not only to an improvement in the condition of the lungs, but also to an increase in muscle strength. A peculiarity of the group of patients with IIM is the high frequency of intake of rituximab in this group (40 patients).
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AB0736 **ASSOCIATION BETWEEN ERYTHROCYTE DISTRIBUTION WIDTH AND SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE**

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Background: Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) account for 60% of deaths related to scleroderma (SSc). The erythrocyte distribution width (RDW) has been used as a marker of poor prognosis in different pathologies. In SSc, RDW has been found to be elevated in PAH and has been proposed as a predictor of cardiorespiratory compromise.
Objectives: The aim of this study is to evaluate the association between increased RDW and the presence of EPI in patients with SSc.
Methods: This is a multicenter, retrospective, cross-sectional study of patients diagnosed with SSc (ACR/EULAR 2013) from January 2011 to August 2021. Other concomitant autoimmune diseases, malignancy, active infections, iron-deficiency or pernicious anaemia and transfused patients were excluded. The diagnosis of PID was made by high-resolution computed tomography (HR-CT) and the extension evaluated by Goh criteria. A review of medical records was conducted, collecting clinical and demographic characteristics, interstitial pattern by HR-CT, assessed, acute phase reactants, capillaroscopy, functional respiratory tests (PFT) and echocardiographic resolution. Patients diagnosed with PAH by right heart catheterization were not excluded in this study but recorded.
Results: Seventy-five patients were included, with a mean age of 59.4 (SD 14.1 CI95% 56-6), from which 67 (89%) were women. A median of 8 years of disease evolution was observed RIC 8). Limited SS was observed in 50 (66%) and diffuse SS in 24 (32%). EPI was observed in 50 (66%) of which NSIP 25 (33%), NSIP-f 15 (20%) and UIP 10 (13%). The extension of the disease was limited in 25 (33%) and extensive in 19 (25%). Capillaroscopic findings were normal in 2 (3.4%), nonspecific in 1 (1.7%), early SD in 9 (15.3%), active SD in 22 (37.3%), and late SD in 25 (42.4%); in sixteen patients there was no capillaroscopy.
We observed an increase in RDW in the EPI group with a statistically significant difference OR 6.06 CI95% 2-17 (p 0.001). The median RDW is higher in patients with ILD and PAH than in healthy people (p<0.0001). We found a low negative correlation between RDW / FVC r (63) -.25 p 0.042 and RDW / FEV1 r (63) .30 p 0.015.
Conclusion: In the present study we have been able to evidence that there is a statistically significant relationship between the percentage of RDW and the presence of PID. When analysing the association between patients without pulmonary compromise, ILD and PAH and the percentage of RDW, we were able to find a statistically significant difference between the three groups. It is necessary to continue with studies with a larger number of patients to grant robustness to the results.
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AB0737 CAPILLAROSCOPIC PATTERNS IN PATIENTS WITH SYSTEMIC SCLEROSIS- RHEUMATOID ARTHRITIS (SSC-RA) OVERLAP SYNDROME.

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Background: Nailfold capillaroscopy is useful for the diagnosis and follow-up of autoimmune rheumatic diseases. Impaired microcirculation is one of the leading factors in local and general pathogenesis of SSc. Nail-fold video-capillaroscopy (NFVC) stands as the most informative and at the same time simple method used for evaluation of capillary circulation.
Objectives: To identify characteristic and specific for SSc-RA capillaroscopic features.
Methods: Both hand II – V fingers of 32 pts with SSc-RA were subjected to widefield NFC, evaluated using a binocular 20x magnification Olympus microscope and analyzed in view of specific skin lesions discriminating diffuse and limited SSc forms.
Results: SSc-specific dilatations of capillary loops were the most common for SSc-RA and were found in all pts SSc-RA. 1/3 pts had signs of active scleroderma pattern, such as capillary loss or “avascular areas” (37,5%) and hemorrhages (28%). The morphological capillary abnormalities such as varying degrees of capillary loops tortuosity/vascular inhomogeneity were present in 69% of examined nailfolds, branching bushy behavior of capillary loops predominated. Architectural disorientation/disarrangement of capillary loops was seen in 37,5% of them. Mega-capillaries and formation of subcutaneous plexus were presented infrequently in 16%. Ramified/bushy capillaries ($p<0.04$) were significantly more frequent in patients with lab signs of inflammatory ($p<0.03$).
Conclusion: Thus, widefield NFVC revealed a “mixed” nature of capillaroscopic changes, combining features specific for SSc (capillary dilation, avascular areas, hemorrhages) and for RA (various changes in capillary loops).
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AB0738 DO COSMETIC SILICONE IMPLANTS TRIGGER SYSTEMIC SCLEROSIS?

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Background: The pathogenesis of systemic sclerosis (SSc) is thought to result from interactions between epigenetic features and environmental factors, leading to the onset and progression of the disease in genetically susceptible patients (1). Case reports of women with silicone breast implants who developed SSc have been published, but case-control and prospective studies in connective tissue diseases often failed to find an increased risk of SSc associated with silicone cosmetic surgery (2,3). These studies have several limitations, including heterogeneous cohorts of enrolled patients not selective for SSc, non-homogeneous disease duration or disease stage at study entry. For these reasons, the possible effect of silicone implants as immune adjuvants is highly suspected but remains unclear (4).
Objectives: Retrospective study of SSc patients, to find out who developed SSc after silicone cosmetic surgery.
Methods: The clinical files of 140 female patients with systemic sclerosis were retrospectively evaluated and clinical data collected.
Results: Five patients showing a history of silicone cosmetic surgery (3.6%) before SSc development were identified. The brief clinical histories of the five patients are below reported, showing very similar outcomes after silicone implant. 1. TC 47-year-old female underwent cosmetic breast prosthesis: twelve months later she experienced Raynaud’s phenomenon (RP) and diffuse cutaneous SSc after 10 further months; antinuclear antibodies were positive with a speckled and nucleolar pattern, but specific SSc-related autoantibodies negative. 2. LS 28-year-old female underwent cosmetic breast prosthesis: twenty-two months later RP appeared and anticentromere antibodies (ACA) positive aggressive diffuse SSc was diagnosed one year later. 3. PJ 38-year-old female underwent cosmetic breast prosthesis: eleven months later she experienced RP and after 10 further months, aggressive diffuse cutaneous SSc; antinuclear antibodies were positive with a speckled patter, but specific SSc-related autoantibodies were negative. 4. CM 58-year-old female who underwent cosmetic lip silicone application: one year later she complained of simultaneous onset of RP and very aggressive diffuse cutaneous SSc with anti-topoisomerase positivity; she died during follow-up. 5. BS 33-year-old female who underwent cosmetic breast prosthesis: twenty months later she complained of RP and after ten further months, limited cutaneous SSc with ACA positivity; SSc clinical condition partially improved and its progression stopped after prosthesis removal. Globally, after silicone implant, RP occurred in a mean time of 15±5 months and SSc in 23±8 months.
Conclusion: This study reports a prevalence of 3.6% of silicone cosmetic surgery before SSc onset, interestingly with a close and similar temporal association between silicone implant and disease development. This finding suggests a possible role of silicone in SSc pathogenesis (ASIA syndrome). Specifically addressed large clinical studies or big-data studies need to rule out this matter.
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AB0739 AMINAPHTONE TOLERABILITY AND SAFETY IN SCLERODERMA PATIENTS: A FOUR-YEAR FOLLOW-UP

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Background: Recent studies show that Aminaphtone is effective in the treatment of Raynaud’s phenomenon (RP) symptoms in patients with systemic sclerosis (SSc), and an increase in peripheral blood perfusion was demonstrated by Laser speckle contrast analysis in treated patients (1,2). Unfortunately, the drug is only available in a few countries.
Objectives: To evaluate long-term tolerability and safety of Aminaphtone in SSc patients with secondary RP.
Methods: Seventy SSc patients (EULAR/ACR criteria) (mean disease duration 8±7 years, mean age 61±10 years) who started Aminaphtone treatment due to active RP were enrolled and followed for at least 4 years. Patients were also taking various concomitant treatments, including immunomodulators, cyclic intravenous iloprost, endothelin receptor antagonists and aspirin. None was taking sildenafil or selexipag. Survival of Aminaphtone in therapy was assessed along with possible drug-related side effect. The Raynaud condition score (RCS) to asses disease severity and blood examinations were routinely performed.
Results: The mean follow-up of patients was 49±11 months. Aminaphtone was orally administered at 75 mg twice daily, as standard initial posology in our clinical practice. During the follow-up, six patients (8,6%) referred headache as side effect and had to reduce Aminaphtone posology to 75 mg per day, while maintaining clinical benefits. No other side effect related to the drug was observed during the follow-up. Seven patients increased the posology to 75 mg three times daily due to poor effectiveness, and further seven patients increased the posology to 75 mg three times daily only during the colder months of the year. Conversely, thirty-five patients reduced the dosage to 75 mg once daily only during the hottest months of the year, due to partial remission of the RP. During follow-up, blood tests did not reveal any significant alteration ascribable to Aminaphtone. A subjective improvement of Raynaud’s symptoms (assessed by the RCS) was already evident after 1-2 months of treatment in fifty-six patients (80%). Globally, the patients referred a sustained improvement followed by stabilization of Raynaud’s symptoms during the follow-up.

Conclusion: During an average observation period of four years, Aminaphtone showed a good tolerability and safety profile along with sustained efficacy in patients with SSc-related RP, without disabling or serious side effects. A randomized controlled trial for Aminaphtone use in the management of SSc-related RP is desirable to better assess the clinical efficacy of the drug over time.

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AB0740 INTERSTITIAL LUNG DISEASE SYSTEMIC SCLEROSIS: AN EAST-EUROPEAN EUSTAR CENTER EXPERIENCE

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Background: Systemic sclerosis (SSc) is a complex autoimmune connective tissue disorder defined by multifaceted visceral involvement. Still considered the leading cause of morbidity and mortality, interstitial lung disease (ILD) remains one the most common complication of SSc that involves vascular, immunological, and fibrotic processes.

Objectives: We aimed to assess the relationship between demographic, clinical features and risk factors for the development of lung fibrosis in patients with SSc as well as the specific management.

Methods: We performed a retrospective observational study in a series of 45 patients with SSc and ILD followed-up in East-European EUSTAR center (Department of Rheumatology 2, Clinical Rehabilitation Hospital, Iasi, Romania). We analyzed the frequency of known risk factors associated with progressive interstitial lung disease such as diffuse cutaneous SSc, male sex, presence of anti-topoisomerase I and absence of anti-centromere antibodies as well as risk factors for mortality in SSc-ILD including older age, male sex, extent of disease on high-resolution computed tomography (HRCT), lower pulmonary function tests (PFTs), lower diffusing capacity of the lung for carbon monoxide (DLCO).

Results: The study included 35 females, 10 males, with the mean age of 55.5 years. The diagnosis of interstitial lung disease was based on HRCT findings (bibasilar ground glass opacities, crazy-paving pattern, nodules, honeycombing and traction bronchiectasis, mosaic pattern, air trapping, pulmonary artery and lymph node enlargement). Symptoms of the ILD (dry cough, different stages of dyspnea, VELCRO crackles) were reported in 14 cases (25.45%). Furthermore, 25 patients had a significant decline in PFTs and DLCO, being associated with extensive pulmonary fibrosis on HRCT ($p<0.05\%$). Almost all patients with SSc-ILD had diffuse cutaneous involvement and anti-Scl-70 antibodies positivity. Despite identifying a higher percentage of women with ILD (35/45, 63.63%), the extent and progression of pulmonary fibrosis was more significant in males. The treatment for SSc-ILD with ongoing evidence of disease progression based on PFT decline or radiographic deterioration has focused on immunosuppressive therapies, particularly cyclophosphamide and only in selected cases on antifibrotic agents.

Conclusion: It is important to identify the risk factors for developing ILD, in order to complete the diagnostic and staging parameters early so that the treatment can be initiated as soon as possible in progressive pattern. Our data showed that the extent of pulmonary fibrosis in HRCT was associated with low values of PFTs and DLCO, and men had a more severe prognostic than women. ILD-SSc was more frequent in patients with diffuse cutaneous involvement than limited cutaneous subtype, and in those with anti-Scl-70 positivity.

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AB0741 LUNG FUNCTIONS IN IDIOPATHIC INFLAMMATORY MYOPATHIES PATIENTS WITH INTERSTITIAL LUNG DISEASE DURING ≥ 3 YEAR OF FOLLOW-UP.

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Background: Interstitial lung disease (ILD) is the most common internal organ manifestation of idiopathic inflammatory myopathies (IIM) that can severely affect the course of the disease.

Objectives: To describe lung functions in IIM patients with ILD during ≥ 3 year of follow-up.

Methods: Our prospective study included 44 pts with IIM fulfilling Bohan and Peter criteria and having ILD. The mean follow-up period was 46.2±11.2 months. The mean age was 52.3±11.7 years, 34 (77.3%) pts were female. The median disease duration was 1.125 [0.16-18] years, 24 (54%) of pts were positive for a-Jo-1 antibody. All pts had the standard examination including anti-Jo-1 antibodies (anti-Jo-1) assay; forced vital capacity (FVC) and carbon monoxide diffusion capacity (DLCO) evaluation as well as high-resolution computed tomography (HRCT) scanning of the chest were performed at baseline, and 36 and more months.

Results: 61% with antisynthetase syndrome, 17% dermatomyositis (DM), 5% amyopathic DM, 15% with overlap myositis and 2 % with necrotizing myopathy were included. 70% patients had nonspecific interstitial pneumonia, 23% organizing pneumonia (OP) and 7% OP, transformed to diffuse alveolar damage.

All pts received prednisolone at a dose of 11.8±4.1 mg/day, immunosupressants at inclusion received 75% pts: cyclophosphamide 54%, mycophenolate mofetil 16.9% and combination 4.54%; Rituximab was administered in case of intolerance or inadequate response to GC and other immunosuppressive drugs in 37 pts (84%)(1-8 courses). 7 patients died, ILD progression was the cause of death in 4 cases

Table 1. Changes of the main parameters at the baseline and in 3 years

parameters	pts	baseline	in ≥ 3 years	p
a-Jo-1	23	177.2 ±41.7	90.5±76.7	0.000003
FVC	37	83.3±21.7	96.7±21	0.0001
DLCO %	37	52.4±14.9	60.8±17,3	0.001
Prednison, mg/day	37	23.04±12.8	5.9±2.3	0,000000001

Conclusion: Active immunosuppressive therapy improves lung function in IIM patients. However, some forms of ILD have a fatal course.

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AB0742 THE DYNAMICS OF LUNG FUNCTION IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE ASSOCIATED WITH INTERSTITIAL LUNG DISEASE DURING A THREE-YEAR FOLLOW-UP PERIOD

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Background: Nowadays ILD is one of the most common manifestations of systemic rheumatic diseases and one of the leading cause of death of patients.

Objectives: To assess the course and outcomes of interstitial lung disease (ILD) in mixed connective tissue disease (MCTD) based on lung function after three years of follow-up.

Methods: The study included 20 patients with MCTD associated with ILD. The diagnosis was set according to Kasukawa criteria (1987). There were 19 (95%) women and 1 (5%) men; average age was 44.73±15.26 years; mean disease duration was 13.7±9 years. All patients took glucocorticoids (GCs) and immunosuppressants (IS); the average dose of prednisone was 10.2±5mg. To identify and assess the dynamics of ILD, there was used high-resolution computed tomography (HRCT). Their lung function was assessed by data obtained due to spirometry (in particular, forced vital capacity, FVC) and diffusing capacity of the lungs (DCL); Doppler echocardiography was also conducted.

Results: In the group of patients with MCTD there was a chronic course of the disease with a gradual addition of symptoms, musculoskeletal pathology prevailed. After three-year follow-up period there was a decrease in clinical manifestations (arthritis, myositis, proximal muscle weakness). Functional capacities of the lungs and heart did not deteriorate. DCL remained stable 67.5±15 and 66.9±13.8, respectively. Systolic pulmonary artery pressure also remained stable (31.4±4.5 and 32.8±5.2, respectively), indirectly indicating the absence of progression in pulmonary involvement. These positive alterations were the basis for reducing the daily dose of GCs in some patients. The reduction in dose of GCs was small but statistically significant (8.64±4.58 and 7.86±3.33, respectively, $p=0.007$). There was a trend towards a decrease in dose of prednisone (from 10.2±5 to 8±4,5, respectively). However, these data were not clinically significant.

Conclusion: Due to the study,there were no significant changes in the main indicators in patients with MCTD. All indicators remained stable, indicating the absence of clinically significant progression of lung damage on the background of therapy with GCs and IS. There was no significant change in the daily dose of GCs, but there was a decreasetendency
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AB0743 BIOMARKERS IN SYSTEMIC SCLEROSIS: A 23-PLEX CYTOKINE/CHEMOKINE ANALYSIS

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Background: Systemic Sclerosis (SSc) is a rare inflammatory disease of unknown etiology associated with multi-organ involvement. Biomarkers remain urgently needed as tools for differential diagnosis, prognosis, disease progression, and as therapeutic response predictors in SSc. Ideally, for widespread utility, biomarkers should be easy to sample and analyse.
Objectives: We aimed at evaluating potentially pathogenic circulating key cytokines/chemokines in a monocentric cohort of SSc patients.
Methods: Sera were drawn from SSc patients and 23 cytokines/chemokines (CCL2/MCP-1, IP-10/CXCL10, Flt3 Ligand, IFNa2, IL6, IL7, IL12, IL13, IL15, IL17A, TNFa, IL-1Ra, CXCL13, IL21, IL23, IL33, TSLP, IL-2RA, IL1RII, TNFRII, BAFF, CCL19/MIP-3B 66, MMP-8) were quantified using Luminex multiplex immunoassay (Bio-Rad-BioPlex 200 System-Lumine x-Map technology R&D Systems, USA) following the manufacturer's instructions and customized procedures. Data were acquired using Bioplex manager v 6.1. P value ≤ 0.05 was considered to be significant. Data were analyzed using GraphPad Prism V.8 (GraphPad Software, Inc.) software.
Results: Clinical and demographic features of 17 SSc (5 dcSSc, 12 lcSSc) patients are reported in Table 1. Mean±SD age was 55±14.68 years, mean±SD disease duration was 89.47±95.34 months. We found that MCP-1 levels inversely correlated with PAPs (r=-0.55, P=0.03) and IP10 with anti-Scl70 (r=-0.561, P=0.004), Figure 1. No other associations were found

Table 1.

	N	%
Sex	2M/15F	11.8/88.32
Age (years, mean±SD)	55±14.68	
Disease duration (months, mean±SD)	89.47±95.34	
Cigarette smoke	8	47
Raynaud's phenomenon	17	100
Skin thickening	14	82.4
Ulcers	2	11.8
Rodnan's Skin Score (mean±SD)	5.9±6.6	
Articular involvement	2	11.8
Heart involvement	0	0
Paps max (mmhg, mean±SD)	28.3±5.9	
Pulmonary involvement	5	29.4
DLCO min (%, mean±SD)	90.24±21.2	
Gastrointestinal involvement	3	17.6
ANA	17	100
Rheumatoid factor	4	23.5
Anti-Scl70 (U/ml, mean±SD)	33.2±59.3	
Anti-CENP(U/ml, mean±SD)	55.9±48.9	
Anti-SSA	2	11.8
Anti-SSB	1	5.9
Anti-Sm	1	5.9
Anti-RNP	1	5.9
Elevated Blood Pressure	4	23.5
Obesity	1	5.8
Any DMARD	5	29.4

Conclusion: We confirm a potential pathogenic role for MCP-1 in SSc. The -2518 promotor polymorphism in the MCP-1 gene has been already associated with disease susceptibility and an increased expression of the molecule both in peripheral blood and in the skin has been described. Intriguingly, MCP-1 seems to drive skin fibrosis while the role played in pulmonary involvement is more controversial. Indeed, similarly to our results, Scala et al. found an inverse correlation between pulmonary fibrosis and MCP-1 from T cell lines (1). At the same extent, the observation that IP-10 has an inverse correlation with anti-Scl70 levels is not novel and the usage of this chemokine as a marker of lcSSc has been already suggested. In this view, Zhu et al. found that Scl-70 negative patients have a higher expression of IP-10 than Scl-70 positive (1,878 (2,964) ng/L vs 1,030 (2,196.6) ng/L, P<0.05) (2). Finally, this is the first report on MMP8 in SSc and we suggest that MMP8 - a collagenase and marker of idiopathic pulmonary fibrosis involved in the migration of fibroblasts - can represent a promising biomarker for SSc diagnosis.
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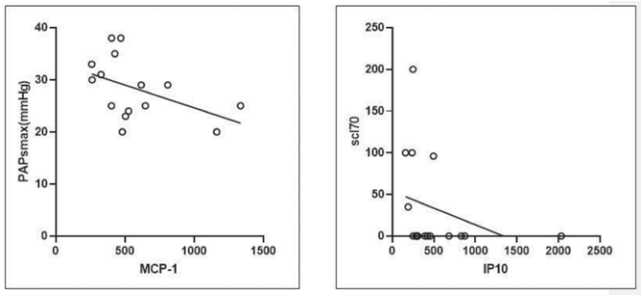

Figure 1.
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AB0744 "REACTIVE" MYOSITIS FOLLOWING ANTI-SARS-2 VACCINATION IN TWO PATIENTS CARRYING HLA-B*35 HAPLOTYPE

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Background: The anti-SARS2 vaccination is considered the best way to reduce the frequency and the subsequent effects of COVID19 pandemic. To this aim, the most used in western countries are mRNA vaccines BNT16162b2 (Pfizer-BioNT) and mRNA-1273 (Moderna). With both these vaccines the risk/benefits balance is largely favorable and severe adverse effects are almost rare. In keeping, although transient myalgia and arthralgia are frequently seen, myositis have been until now rarely reported.
Objectives: To report two cases of myositis occurring in two patients after BNT16162b2 vaccine administration evaluated at the Center for Rheumatic Diseases in Venice, Italy.
Methods: In these patients clinical examination, blood and instrumental investigations for myositis and, in addition HLA typing, were performed. Patients were followed for at least six months after the onset of symptoms.
Results: The first patient, a 54-year-old male, complained of high-grade fever 4 days after the I dose of BNT16162b2 (Pfizer-BioNT) followed, by mild fatigue, muscle soreness and increasing weakness. He was sent to the emergency department of the local Hospital. The physical examination confirmed the muscle weakness. Blood investigation revealed an increase of AST: 509 U/L (NV< 37), ALT:189 U/L (NV <78), LDH 609, CPK 11394 U/L (NV<, 309), Myoglobin 3571 ng/ml (VN <96), CRP 1.6 mg/dl. Prednisone (PN) was started (50 mg orally day) and tapered to 5 mg in two weeks. At high doses, the symptoms slightly improved, but when < 10 mg, all the symptoms reappeared. Thus, he was hospitalized again. The new examination confirmed the increase of all indices of myositis; antinuclear antibodies and myositis antibodies were absent and PN was restarted at 10 mg/day without benefit; echocardiography and TC scan were negative. He was then sent to our observation. We increased the dose of PN at 1 mg/PN/kg and we required HLA typing. Two weeks later symptoms disappared almost completely and then we tapered PN 5 mg/day weekly. At present the patients is completely well and muscle indices negative since two months. HLA typing revealed the presence of B*35 and DRB1*15.
The second case was a 29-year-old female presented with a history of complaints appeared two days after the vaccination with BNT16162b2 administration (Pfizer-BioNT) characterized by three days of high-degree fever, followed by sever weakness, especially in the arms. The family doctor decide to hear our advise. At the initial presentation arm strenght was very decrease and the patient was accompanied. We required a serie of investigations which revealed: CPK 8950 U/L (NV 250), CRP 3.5 mg/dl increased; antinuclear and anti-myositis antibodies absent; cardiac (Ultrasound) and thoracic (CT) investigation and electromyography negative. HLA typing revealed the presence of haplotypes B*35 and DRB1*15. PN (50 mg orally day) was started; two weeks later she improved and both muscle indices and CRP negative. Thus, we reduce the dosage at 25 mg/day with tapering 5 mg weekly. She was completely remitted at end of PN cycle. At present, three month later she is well.
Conclusion: The rare occurrence of some particular side effects is not predictable. Our cases of severe myositis which in both cases completely remitted in some months are associated with haplotypes HLA-B*35 and DRB1*15. These are both binding sites linked to high-affinity interactions to S-protein T-cell epitope which account for high potentials to trigger immunogenic responses to the S protein of SARS-CoV-2 (1). Furthermore classically, HLA-B35 is associated with reactive arthritis and self-limiting, unclassified rheumatism (2).

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AB0745 SYMPTOMS OF GASTROINTESTINAL DISORDERS IN SYSTEMIC SCLEROSIS PATIENTS WITH DIFFERENT DISEASE SUBTYPES AND ANTIBODIES

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Background: Gastrointestinal tract is the second most commonly affected organ system in approximately 90% of patients with systemic sclerosis (SSc) and has a negative impact on health-related quality of life (1,2).
Objectives: This study aims to analyze frequency and severity of gastrointestinal symptoms, their impact on social functioning and emotional wellbeing and compare results among patients with limited cutaneous (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc), as well as in patients with anti-centromere antibodies (ACA) and anti-topoisomerase I antibodies (ATA).
Methods: 42 patients with SSc were included in this study, 31 of them with lcSSc and 11 patients with dcSSc. ACA were detected in 26, and ATA in 16 patients. The *UCLA-SCTC-GIT 2.0 self-assessment questionnaire* (3,4) was used to assess presence and severity of gastrointestinal symptoms in our patients. It consists of seven scales: reflux, distension/bloating, diarrhea, fecal soilage, constipation, social functioning and emotional wellbeing.
Results: There was no difference in percentage of patients with lcSSc and dcSSc who used proton pump inhibitors (27.27%: 32.25%), as well as in patients with ACA and ATA (34.61%: 25%). Symptoms of gastroesophageal reflux (lcSSc: dcSSc = 64.5%: 81.8%), distension/bloating (lcSS: dcSSc = 61.3%: 81.8%), constipation (lcSSc: dcSSc = 45.2%: 45.5%) and fecal soilage (lcSSc: dcSSc = 6.4%: 18.2%) were found equally frequent ($p>0.05$) in patients with lcSSc and dcSSc. However, symptoms of diarrhea were found significantly more frequent in patients with dcSSc (lcSSc: dcSSc = 16.1%: 45.5%, $p=0.04$). The mean index value for diarrhea was significantly higher in patients with dcSSc (dcSSc: lcSSc = 0.45: 0.11, $p=0.02$), indicating more severe symptoms in diffuse form of disease. We did not notice a significant difference in frequency or severity of gastrointestinal symptoms in patients with ACA and ATA. Mean index values of social functioning and emotional wellbeing did not differ significantly in patients with lcSSc and dcSSc, as well as in patients with ACA and ATA.
Conclusion: Unlike other gastrointestinal manifestations, diarrhea is significantly more common and more severe in patients with dcSSc. No significant difference in frequency and severity of gastrointestinal symptoms was found in patients with ACA and ATA. Impact of gastrointestinal tract symptoms on social functioning and emotional wellbeing was similar in both forms of disease and antibodies.
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AB0746 MALIGNANCY IN DERMATOMYOSITIS

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Background: Link between dermatomyositis (DM) and malignancy is well established. Compared with general population, the incidence of cancer is estimated to be 5 to 7 times higher in patients with DM. However, criteria suggestive of associated malignancy still lack.
Objectives: The aim of our study was to describe clinical, biological, therapeutic features and outcomes of DM associated with malignancy.
Methods: We conducted a retrospective study of patients with DM diagnosed in an internal medicine department over a period time of 12 years. Cases of DM associated with malignancy were retained.
Results: Among 38 patients diagnosed with DM, malignancy was found in 10 (26.3%). Sex-ratio M/F was 0.3. The mean age at DM diagnosis was 40,22 years (range: 30-75 years) and the mean age at malignancy diagnosis was 43,19. In five cases the diagnosis of neoplasia was concomitant to the DM diagnosis. In the other 5 cases, the diagnosis of DM preceeded the neoplasia with a mean delay of 26 months [9-82 months].
The main clinical manifestations were: Gottron's papules (n=8), skin ulcers (n=7), periungual erythema (n=7), erythredema of the face with orbital rim (n=5), impaired general condition (n=4),Raynaud's with mega capillaries (n=2), skin necrosis(n=1) and subcutaneous calcinosis(n=1)., Muscular damage was found in 7 patients. Signs of severity such as swallowing disorders and false deglutition routes were found in 4 patients. Biological data showed acceleration of erythrocyte sedimentation rate (ESR) (n=4) and elevated muscle enzymes (n=7). Immunological features showed positivity of anti-Mi-2 antibodies in two cases, anti-transcription intermediary factor 1-gamma (TIF1-γ) antibodies in one case, simultaneous positivity of anti Jo1 and anti SRP in one other case. Associated cancers were: Breast cancer (n=5),Colon carcinoma (n=2), Lung cancer(n=1), Cancer of the cervix(n=1) and T-cell lymphoma(n=1). In addition to specific oncological treatment, all patients received high doses of corticosteroids. It was associated with methotrexate in 4 cases. Two patients received intravenous immunoglobulin. A relapse was observed in 4 cases although a durable remission of associated neoplasia. Outcomes were fatal in 3 cases due to the underlying cancer. Three patients were lost to follow-up.
Conclusion: In our series, breast neoplasm was the most frequent cancer associated with DM. Despite oncological treatment, DM can remain progressive.
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AB0747 ORAL MICROBIOME IN RHEUMATIC DISEASES.WHAT INVOLVEMENT?

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Background: The concept of core-microbiome in health is useful for investigating the possible role of the oral microbiome in autoimmune disease, such as Rheumatoid Arthritis, Spondyloarthritis, Sjogren Syndrome or Systemic Sclerosis (SSc), whose pathogenesis has not been fully understood. Environmental factors and certain genetic backgrounds have been proposed. Among the various environmental factors, the microbiota stands out, the entire composition of microorganisms, mainly bacteria but also fungi and viruses, which populate the human body.
Objectives: The aim of the study was to verify whether there were quantitative differences between the microorganisms present in the oral cavity, in particular between the *lactobacillus* spp., of patients with SSc compared to those present in the oral cavity of healthy subjects taken as controls.
Methods: Twenty-nine SSc female patients (mean age 62.) classified according to the ACR/EULAR2013 criteria and twenty-three female healthy subjects (HS, mean age 57.6) were enrolled and underwent tongue and gum swab sampling. Quantitative PCR was conducted in triplicates using *Lactobacillus* specific primers *rpo*B1, *rpo*B1o and *rpo*B2 for RNA-polymerase β subunit gene.
Results: Our data showed *Lactobacillus*spp.*rpo*B sequences significantly lower in the tongue of SSc patients than in HS ***(p=0.0211)***.The statistical analysis in HS highlighted a significant lower amount of *rpo*B on the gums than on the tongue.
Conclusion: Our preliminary data show that the number of *Lactobacillus* on the tongue in SSc patients is about half that of HS. These data make it more likely that *Lactobacillus* in SSc patients may play a protective role. Further investigations will also be needed in other autoimmune diseases.
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AB0748

ANTI-FIBROTIC THERAPY IN PROGRESSIVE PULMONARY FIBROSIS ASSOCIATED WITH SYTEMIC SCLEROSIS: CHARACTERISTICS OF SSC-ÎAH PATIENTS RECEIVING NINTEDANIB AND ADVERS EVENTS DURING TREATMENT

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Background: Nintedanib, an intracellular inhibitor of tyrosine kinases, has been recently approved for interstitial lung disease associated with systemic sclerosis (SSc-ILD). Nintedanib has shown antifibrotic and antiinflammtory effects in animal models of fibrosing ILDs.

Objectives: We aimed to evaluate clinical charcteristics of progressive SSc-ILD patients receiving anti-fibrotic therapy who were resistant to standart immunosuppressives (ISs) and adverse events during treatment period in this cohort.

Methods: Fifteen patients fulfilling ACR/EULAR (2013) classification criteria for SSc and receiving nintedanib for progressive ILD despite standart ISs included into this retrespective analysis.

Results: Demographics and clinical characteristics of SSc patients were summarised in Table 1. Median age, duration of Raynaud's and duration of non-Raynaud symptom were 49 (35-72), 8 (1-30) and 4 years (1-21), respectively. ILD was evident median 2 years (0.5-20) after onset of Raynaud's and 1 years (0.5-11) after onset of non-Raynaud symptom. Before pulmonary involvement, 7 patients received methotrexate and 1 patient cyclophosphamide (CYC) for diffuse cutaneous involvement. After evident ILD, 6 patients received CYC, 5 patients mycophenolate mofetil (MMF) and 4 patients azathioprine as first ISs for SSc-ILD. Median FVC(%) and DLCO(%) were 56 (39-67) and 44 (20-67) before antifibrotic therapy. Thirteen patients (%92,8) received ≥2 ISs before nintedanib. Duration of evident ILD to onset of antifibrotic therapy was median 5.5 years (2-11). Nintedanib was prescribed concomitantly with MMF in 8 or rituksimab-MMF in 6 patients. Median follow-up of antifibrotic treatment period was 7 months (2-18). Advers events during nintedanib were summarised in Table 2. One patient was deceased due to small cell lung cancer at 9.month of nintedanib.

Table 1. Characteristics of SSc-ILD Patients Receiving Nintedanib

	n (%)
Females	12 (80)
Clinical Characteristics	
Diffuse Cutaneous SSc	13 (86.7)
Limited Cutaneous SSc	2 (13.3)
Synovitis	3 (20)
Digital ulsers	8 (53.3)
Pulmonary arterial pressure >30 mmHg (echo)	5 (30)
Gastrointestinal involvement	10 (76.9)
Serology	
ANA	13(86.7)
Anti-Scl70	10 (66.7)
Immunosuppressives	
CYC	8 (53.3)
MMF	14 (93.3)
AZA	7 (46.7)
MTX	6 (40)
RTX	6 (40)
Low dose steroids	15 (100)

Table 2. Advers Events during Nintedanib Treatment inSSc-ILD patients

	SSc-ILD (n=15)
Any advers events n(%)	8 (53.3)
Diarrhoea	5 (30)
Nausea/ vomiting	1 (6.7)
Abdominal pain	3 (20)
Weight decreased	3 (20)
Yorgunluk	2 (13.3)
Cough	3 (20)
Infections (pneumonia)	3 (20)
Liver test abnormalities	4 (26.7)
Malignancy	1 (7.1)
Dose reduction and reescalation	7 (46.7)
Dose interruption	2 (13.3)

Conclusion: Nintedanib was prescribed in progressive SSc-ILD patients who had predominatly diffuse cutaneous involvement, anti-SCL70 positivity and exposed to multiple standart ISs. Duration of ISs were higher than 5 years before antifibrotic therapy. Gastrointestinal (GI) advers events were frequent during nintedanib requiring dose reduction in half of the patients. Nintetanib can be used in progressive SSc-ILD patients considering some difficulties in such a disease with GI involvement. Efficacy analysis of the antifibrotic therapy needs further studies including long term follow-up.

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AB0749

ANTI-PM/SCL 75 AND ANTI-PM/SCL 100 ANTIBODIES: DOES THE NUMBER MATTER?

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Background: Anti-polymyositis/Scl (PM/Scl) antibodies have been associated to systemic sclerosis (SSc), PM and PM-SSc overlap syndrome. Although not specific and with some uncertainty about their true prevalence, they have been linked to the clinical presentation and prognosis of SSc rather than traditionally related impact of the extent of the cutaneous involvement[12].

Objectives: The aim of this study is to describe the demographic, clinical and laboratorial data associated with the presence of anti-PM/Scl and to compare the differences against the two major antigenic components: 100 and 75 kDa proteins (anti-PM/Scl-75 and anti-PM/Scl-100).

Methods: A retrospective study including patients with positive anti-PM/Scl antibody followed in rheumatology department from January 2017 to December 2021 were analyzed. Demographic, clinical, immunological and nailfold capillaroscopy data at presentation and during follow-up were collected. Descriptive, Student's t and Fisher test were estimated.

Results: Fifty six patients were positive for anti-PM/Scl antibodies. Of these, 38 (68%) were female with a median age at presentation of symptoms was 47 ± 16 years. Asymptomatic carrier of anti-PM/Scl75 and anti-PM/Scl100 were present in 15 (27%) and 7 (13%) of the patients, respectively. SSc and PM were the diagnosis most found, 34% and 9%, respectively. Arthralgias/Arthritis and Raynaud phenomenon (RP) were the first clinical features most presented followed by respiratory symptoms and constitutional symptoms. Relating to cumulative organ complications, peripheral vascular involvement was the most affected (RP, 30%) followed by musculoskeletal (MSK) and lung (interstitial lung disease - ILD, 21%) and skin involvement (limited cutaneous form, 20%). All patients were positive to antinuclear antibodies by indirect immunofluorescence.

Comparing patients with positive anti-PM-Scl75 and anti-PM-Scl100 showed a statistically significant difference at the presence of RP (as first or cumulative manifestation) and early pattern on nailfold capillaroscopy (p= 0.049 and p=0.039, respectively). A statistically significant difference was also found in an asymptomatic patient (p<0.001) – Table 1.

Table 1. Demographic, clinical and immunological comparison between PM/Scl75 and PM/Scl100 antibody profile

	Anti-PM-Scl75 N = 37	Anti-PM-Scl100 N = 25	*p*-value
Sex, male/female*	11 (29.7)/26 (70.3)	7 (28.0)/18 (72.0)	0.558
Age (start of symptoms)*	46 ± 16	48 ± 18	0.759
Age (at diagnosis)*	49 ± 17	50 ± 19	0.872
Diagnosis			
Asymptomatic	15 (40.5)	7 (28.0)	**<0.001**
Systemic sclerosis	10 (27)	12 (48)	0.078
Myositis	3 (8.1)	3 (12.0)	0.463
Overlap Syndrome	1 (2.7)	2 (4)	0.648
Manifestation			
Raynaud phenomenon	9 (24.3)	13 (48.0)	**0.049**
Arthralgias/arthritis	20 (54.1)	14 (56)	0.544
Limited cutaneous	6 (16.2)	5 (20.0)	0.477
Diffuse cutaneous	0 (0.0)	2 (8)	0.159
Myositis	4 (10.8)	4 (16.0)	0.410
ILD	6 (16.2)	6 (24.0)	0.329
Nailfold capillaroscopy pattern			
Normal pattern	28 (75.7)	12 (48)	**0.025**
Early pattern	5 (13.5)	9 (36.0)	**0.039**
Active pattern	3 (8.1)	5 (20.0)	0.163

All values are presented as number (percentage) and those with * are presented as mean ± SD. ILD, interstitial lung disease.

Conclusion: Anti-PM/Scl antibodies are frequently associated to MSK and RP symptoms as first and cumulative clinical manifestations followed by ILD and limited cutaneous form of SSc. Between anti-PM/Scl 75 and 100 serological profile, anti-PM/Scl100 is more associated to RP and abnormal nailfold capillaroscopy pattern.

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Spondyloarthritis - treatment

AB0750

BACK PAIN AND MORNING STIFFNESS AS MEDIATORS OF TOFACITINIB TREATMENT EFFECT ON FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A MEDIATION ANALYSIS

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Background: Fatigue is a prevalent symptom of ankylosing spondylitis (AS)[1] and can contribute to higher levels of disease, disability and poor health-related quality of life.[2] Back pain and morning stiffness are also commonly reported symptoms.[3] Tofacitinib is an oral Janus kinase inhibitor for the treatment of adult patients (pts) with AS. In randomised studies, pts with active AS treated with tofacitinib experienced greater improvements in fatigue, back pain and morning stiffness at Week 12 and 16 of treatment compared with placebo (PBO).[4,5] Treatment of these symptoms is a priority for pts with AS and their healthcare providers, however, the mechanisms underlying the interrelationships between fatigue, back pain, morning stiffness and treatment are unclear.

Objectives: To describe the interrelationships between fatigue, back pain, morning stiffness and tofacitinib treatment in pts with AS, using mediation modelling.

Methods: Data from Phase 2 (NCT01786668)[4] and Phase 3 (NCT03502616)[5] studies of pts with active AS treated with tofacitinib 5 mg twice daily (BID) or PBO were used. Mediation modelling, a statistical method to assess the extent to which the effect of an independent variable on a dependent variable is indirect, via identified mediators, or direct, capturing all other (unmeasured) effects, was applied.[6,7] The initial model included: treatment as the independent binary variable (tofacitinib 5 mg BID vs PBO); fatigue (measured by Functional Assessment of Chronic Illness Therapy-Fatigue) as the dependent variable; mediators included back pain (measured by total back pain/nocturnal spinal pain [numerical rating scale, 0–10]) and morning stiffness (represented by the mean of Bath Ankylosing Spondylitis Disease Activity Index questions 5 and 6).

Results: Pooled data from 370 pts were included in the analysis. The initial model showed that 57.5% ($p<0.001$) of the tofacitinib treatment effect on fatigue was mediated via back pain and morning stiffness (indirect effect); mediation via morning stiffness alone was 49.7% ($p<0.01$), and 21.2% ($p=0.02$) via back pain alone. The effect of treatment attributable to factors other than back pain and morning stiffness (ie, direct effect) was not statistically significant (-28.4%; $p=0.33$). As a result, the initial model was re-specified to exclude the direct treatment effect on fatigue. In the re-specified model (Figure 1), 44.0% ($p<0.0001$) of the indirect effect of tofacitinib on fatigue was mediated via back pain and morning stiffness; mediation via morning stiffness alone was 40.0% ($p<0.001$), and 16.0% ($p<0.01$) via back pain alone. Analyses of the individual study data gave results generally consistent with those from the pooled data.

Conclusion: Overall, indirect pathways via morning stiffness accounted for ~84% of the effect of tofacitinib treatment on fatigue: (1) treatment affects morning stiffness, which impacts fatigue; and (2) treatment affects morning stiffness, which affects back pain and, ultimately, back pain affects fatigue. The indirect pathway via back pain alone accounted for ~16% of treatment effect on fatigue. These results suggest that in tofacitinib-treated pts with AS, improvements in fatigue are fully mediated through combined treatment effects on morning stiffness and back pain.

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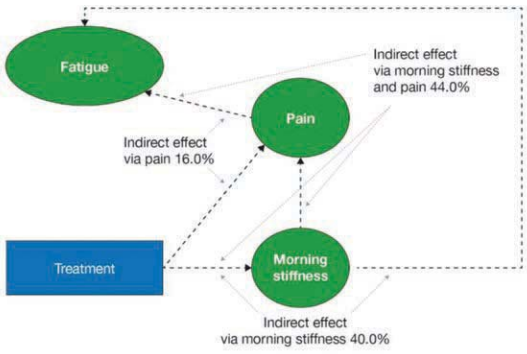
Figure. Re-specified mediation model results



- - ► Indirect effect of treatment on fatigue via back pain and morning stiffness

The mediation models were based on pooled data from Phase 2 (NCT01786668) and Phase 3 (NCT03502616) studies. Treatment is represented by a binary variable (tofacitinib 5 mg BID vs placebo). Pain is represented by total back pain due to AS on average during last week and pain at night due to AS on average during last week.
AS, ankylosing spondylitis; BID, twice daily

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AB0751

HOW DOES BODY MASS INDEX AFFECT SECUKINUMAB TREATMENT OUTCOMES AND SAFETY IN PATIENTS WITH ANKYLOSING SPONDYLITIS? – REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

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Background: Obesity is a risk factor for worse overall health in people with ankylosing spondylitis (AS)[1]. The German non-interventional study AQUILA provides real-world data in AS on the influence of body mass index (BMI) on therapeutic effectiveness and safety under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits IL-17A.

Objectives: The aims of this interim analysis are to describe selected baseline (BL) demographics and to evaluate secukinumab treatment outcomes on disease activity and global functioning and health and to report safety profile depending on the BMI of AS patients (pts).

Methods: AQUILA is an ongoing, multi-center, non-interventional study including up to 3000 pts with active AS or psoriatic arthritis. Pts were observed from BL up to week (w) 52 according to clinical routine. Real-world data were assessed prospectively and analyzed as observed. Validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI) and global functioning and health (Assessment of SpondyloArthritis-Health Index,

ASAS-HI). For calculation of proportion of pts that experienced (serious) adverse events ((S)AEs), all AS pts were included that received at least one dose of secukinumab. This interim analysis focuses on BMI subgroups ≤*25* kg/m^2 (normal weight), >*25 to* ≤*30* kg/m^2 (overweight) and >*30* kg/m^2 (obese) in AS pts.

Results: At BL, BMI data were available for 667 AS pts: 33.6% (n=224) normal weight, 39.9% (n=266) overweight and 26.5% (n=177) obese AS pts (Table 1). In all BMI subgroups the proportion of men was higher, even doubled among overweight AS pts. As BMI increased, so did age and comorbidities/extraarticular manifestations (EAMs, Table 1).

Table 1. Overview of baseline characteristics in AS pts depending on BMI

Demographics	BMI ≤25 kg/m^2 (N=224)	BMI >25 to ≤30 kg/m^2 (N=266)	BMI >30 kg/m^2 (N=177)
Male*	123 (54.9)	178 (66.9)	94 (53.1)
Age, years**	43.3 (12.1)	47.5 (12.3)	49.2 (11.0)
BASDAI**	4.8 (2.0)	5.5 (1.8)	5.5 (2.0)
ASAS-HI**	7.4 (3.7)	7.7 (3.3)	8.1 (3.6)
Comorbidities/EAMs*			
Heart-related disease	4 (1.8)	12 (4.5)	12 (6.8)
Coronary heart disease	4 (1.8)	10 (3.8)	8 (4.5)
Stroke	1 (0.4)	0 (0.0)	2 (1.1)
Heart insufficiency	1 (0.4)	4 (1.5)	8 (4.5)
Uveitis	11 (4.9)	17 (6.4)	13 (7.3)
Depression	88 (55.3)	121 (58.2)	73 (54.9)

*variables are given as n (%); **variables given as mean (SD)

Mean BASDAI developed similarly over time with lowest scores for normal weight and highest scores for obese AS pts (Figure 1A). Mean improvement from BL to w52 was 1.3 (27.1%) for normal weight, 1.5 (27.2%) for overweight, and 1.2 (21.8%) for obese AS pts.

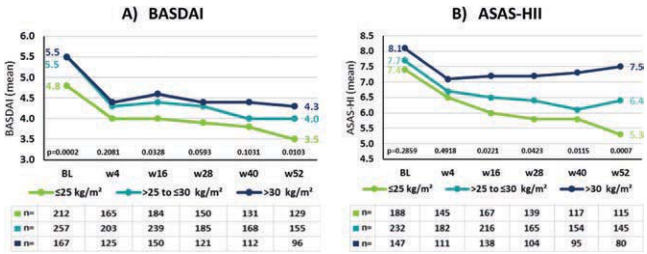

Figure 1. Disease activity and global functioning under secukinumab treatment in AS pts stratified by BMI

Mean ASAS-HI at BL was similar for all BMI subgroups (≤*25*: 7.4; >*25*-≤*30*: 7.7; >*30*: 8.1); the best improvement was observed in normal weight, the least in obese AS pts (Figure 1B). Mean improvement from BL to w52 was 2.1 (28.4%) for normal weight, 1.3 (16.9%) for overweight, and 0.6 (7.4%) for obese AS pts.

The occurrence of AEs/SAEs with or without suspected relationship to secukinumab increased with increasing BMI. For example, the percentage of SAEs in normal weight was 21%, in overweight 26.7% and in obese AS pts 30.9% (data not shown). There were no events with fatal outcome or unexpected safety signals in either subgroup.

Conclusion: In a real-world setting, secukinumab improved disease activity and global functioning and health in all BMI subgroups of AS pts; normal weight AS pts had numerically better ASAS-HI and BASDAI scores than obese AS pts. Altogether, real-world data of this interim analysis show that secukinumab is an effective treatment with a favorable safety profile up to 52 weeks in AS pts in all BMI subgroups.

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AB0752

HOW DOES TIME TO DIAGNOSIS AND GENDER AFFECT TREATMENT OUTCOMES IN PATIENTS WITH ANKYLOSING SPONDYLITIS OR PSORIATIC ARTHRITIS? – REAL WORLD DATA FROM THE GERMAN AQUILA STUDY WITH SECUKINUMAB

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Background: In both, ankylosing spondylitis (AS) and psoriatic arthritis (PsA), women typically have a longer delay in diagnosis.[1,2] There is scientific evidence that prognosis for AS and PsA improves when diagnosed early. The German non-interventional study AQUILA provides real-world data on the influence of time to diagnosis and gender on treatment outcomes under secukinumab, a fully human monoclonal antibody that selectively inhibits interleukin-17A.

Objectives: The aims of this interim analysis are to describe selected baseline (BL) demographics of AS and PsA patients (pts) and to evaluate the impact of time to diagnosis and gender on secukinumab treatment outcomes, such as disease activity and global functioning and health.

Methods: AQUILA is an ongoing, multi-center, non-interventional study including up to 3000 pts with AS or PsA. Pts were observed from BL up to week (w) 52 according to clinical routine. Real-world data were assessed prospectively and analyzed as observed. Validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI), global functioning and health (Assessment of SpondyloArthritis-Health Index, ASAS-HI) in AS, and skin and joint-related disease activity (Psoriasis Area and Severity Index, PASI; tender/swollen joint counts, TJC/SJC) and impact of disease (Psoriatic Arthritis Impact of Disease - 12 items, PsAID-12 score) in PsA pts. This interim analysis focused on the subgroups of male and female AS and PsA pts stratified by time to diagnosis after disease onset (˂1 year [y] and ≥1y for early and late diagnosis, respectively).

Results: At BL, 609 AS and 1145 PsA pts were included with information on time to diagnosis (Table 1); only 18.7% of AS and 25.8% of PsA pts were diagnosed within one year. Of interest, both female AS and PsA pts as well as male PsA pts with increased BMI tended to be diagnosed later (Table 1). Regarding BASDAI scores, male AS pts diagnosed late had increased disease activity at BL and throughout the study (Figure 1A); female AS pts diagnosed late showed reduced total treatment effect with increasing time to diagnosis (Figure 1B). Similarly, both male and female AS pts diagnosed late had slightly increased ASAS-HI at BL and throughout the study (Table 1). For PsA pts, there was no difference in skin- (PASI, Figure 1C/D) and joint-related (Figure 1E/F) disease activity with respect to time to diagnosis. Furthermore, there was no difference in PsAID scores (data not shown) between early- and late-diagnosed PsA pts.

Table 1. Overview of selected BL characteristics in AS and PsA pts stratified by time to diagnosis

	AS (N=609)			
	Time to diagnosis ˂1 year (n=114)		**Time to diagnosis ≥1 year (n=495)**	
	Male (n=63)	**Female (n=51)**	**Male (n=301)**	**Female (n=194)**
Age, years	43.1	46.3	45.9	47.7
BMI	27.7	25.9	27.3	27.8
BASDAI	4.7	5.0	5.3	5.2
ASAS-HI	6.7	8.0	7.4	8.2
	PsA (N=1145)			
	Time to diagnosis ˂1 year (n=295)		**Time to diagnosis ≥1 year (n=850)**	
	Male (n=126)	**Female (n=169)**	**Male (n=363)**	**Female (n=487)**
Age, years	50.1	51.8	52.3	53.1
BMI	28.7	29.4	29.3	28.8
PASI	6.5	6.2	7.0	7.2
PsAID	4.6	5.2	4.8	5.3
TJC/SJC	5.9/3.3	7.3/3.2	7.0/3.7	7.3/3.8

All variables given as mean

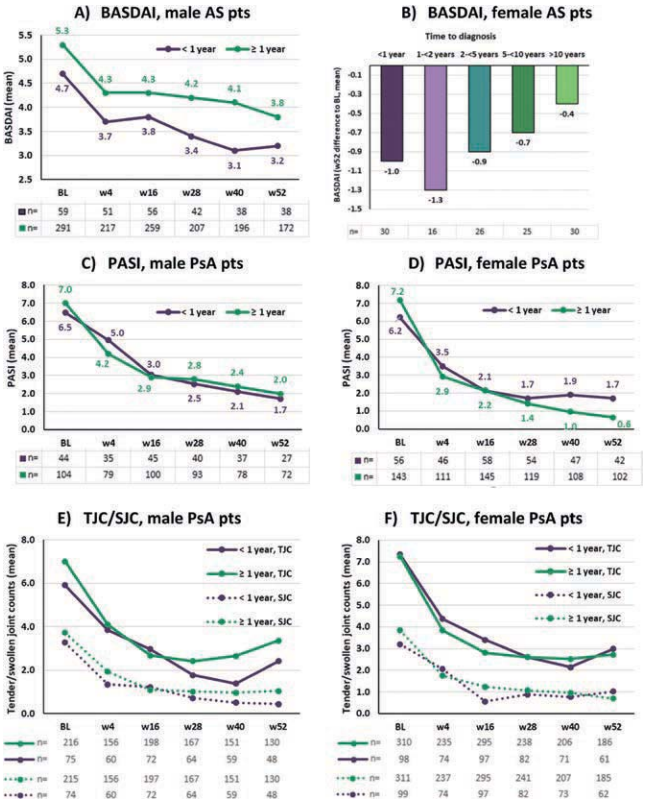

Figure 1. Disease activity in early- and late-diagnosed AS and PsA pts

Conclusion: In a real-world setting, secukinumab improved disease activity and global functioning in both AS and PsA pts. Both, male and female AS pts had a higher treatment response when diagnosed early. Interestingly, delay in diagnosis appeared to be BMI-dependent in female AS pts and PsA pts of both genders. However, in contrast to AS, treatment response of early- and late-diagnosed PsA pts did not differ in the further course.

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AB0753 REAL LIFE DOSE REDUCTION OF BIOLOGICAL THERAPY IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES. UTILITY OF THE REDOSER TOOL

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Background: The long-term use of standard dosing of TNFi therapy is costly and not without side effects, including infections, tuberculosis and potential malignancies(1,2,). Hence, we undertook this study to determine whether dose reduction of TNFi therapy may be possible in a realworld setting and if REDOSER tool(3) is an appropriateness criteria for reducing the dose of BT.

Objectives: Describe the percentage of patients with inflammatory rheumatic diseases (IRD) who continue with dose reduction of biological therapy (BT). Evaluate relapse in clinical practice after 2 years of follow-up. Identify factors associated with relapse.

Methods: Retrospective observational study. Patients with axial spondyloarthritis (axial SpA), psoriatic arthritis (PSA) and rheumatoid arthritis (RA) in BT dose reduction. Inclusion criteria: Axial SpA according to ASAS criteria, APS according to CASPAR criteria and RA according to ACR2010 criteria, who have started reducing the dose of BT treatment between 2009-2019 at the Hospital Regional Universitario de Málaga, Spain. Protocol: patients with TB are followed prospectively in a monographic consultation with a pre-established protocol. The day of dose reduction = baseline visit (v0). *Variables:* **Maintained dose reduction:** % of patients who maintained dose reduction from the start of optimization to the index date (data collection). **Relapse at 12 and 24 months**: % of patients who, after starting dose reduction, returned to the previous or usual dose. Other variables: Demographic, time to diagnosis and evolution of the disease, clinical-analytical: disease activity (DAS28, DAPSA and BASDAI) and physical function (HAQ, BASFI). Previous treatments. Appropriateness criteria for reducing the dose of BT according to REDOSER (1): 1.appropriate, 2. inappropiate, 3. uncertain. Statistical analysis: Descriptive, bivariate, multivariate logistic regression (VD: relapse).

Results: One hundred twenty-nine patients with axial SpA, PSA and RA in BT dose reduction were included. The mean time from the start of BT to dose reduction was 38.1 months (16.6-73.1). The mean time in dose optimization was 19.5(±15.7) months. At the end of follow-up, 70.2% of the patients (87pts) achieved a sustained dose reduction. At 12 months and 24 months, 12.4% and 11.6% of patients relapsed, respectively. At the end of follow-up, there were no differences between baseline inflammatory activity and after 24 months in dose reduction measured by the different indexes: DAS28 (1.9[0.7] Vs 2.1[1, 7], p=0.323; DAPSA (5.4[4.9] Vs 4.8[4. 7], p=0.718, and BASDAI (1.5[1.1] Vs 1.4[1.3], p=0.867). Retrospectively, we evaluated the appropriateness of optimization according to the REDOSER tool (1) at the end of follow-up and it was observed that 85% of patients who maintained the dose reduction had an appropriate REDOSER and 14.5% uncertain and none inappropriate p<0.001.

Conclusion: Dose reduction of BT in IRD is possible in most patients, maintaining low disease activity or remission at 24 months, compared to baseline.
Relapse was associated with a longer evolution time of the IRD, a longer diagnostic delay, a higher inflammatory activity measured by the respective indices and a uncertain or inappropriate result of the REDOSER tool. This tool can be very useful used prior to the assessment of TB dose reduction

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AB0754 REAL WORLD EVIDENCE ON DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TUMOUR NECROSIS FACTOR INHIBITORS AND/OR NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN ROUTINE CARE: RESULTS FROM THE "INVISIBLE" STUDY

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Background: Ankylosing Spondylitis (AS) is an inflammatory rheumatic disease affecting the axial skeleton (1), with a prevalence of up to 0.5% in Europe (2; 3), and occurs in men twice as often than in women (4). 80% develop AS symptoms before the age of 30 (4). Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and biological Disease-Modifying Antirheumatic Drugs (DMARDs) such as Tumour Necrosis Factor inhibitors (TNFi) are the first choice in pharmacological

treatments for AS patients (5; 6). Data on disease activity and disease control in AS patients treated in real life settings are limited.

Objectives: To evaluate the average disease activity status in the study population and assess the percentage of AS patients with a suboptimal treatment response following at least 12 weeks of treatment with TNFi and/or NSAIDs.

Methods: INVISIBLE was a real-world evidence study in Germany, Austria and Belgium. Adult patients with confirmed diagnosis of AS for at least 6 months and ongoing treatment with TNFi and/or NSAIDs for at least 12 weeks prior to enrolment were included. Primary data were collected at a single visit and medical history data from available patient files.

Results: 747 adult AS patients were included. 67% of patients were male, mean symptom duration 18.2 years. 77% of 696 patients were HLA-B27 positive. Appr. 23% of patients received NSAIDs, 42% received TNFi, 30% received both NSAIDs and TNFi, 5% received other treatment for at least 12 weeks prior to enrolment. Mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) scores were 3.4 and 2.2, respectively. Appr. 40% of patients achieved a BASDAI score ≥4 and appr. 50% an ASDAS ≥2.1. Patients with a BASDAI score ≥4 achieved higher scores in most physician and patient reported outcomes. Overall appr. 35% of patients were not satisfied with their current symptom state according to Patient Acceptable Symptom State (PASS). Of patients with a BASDAI score ≥4 appr. 61% were not satisfied according to PASS.

Conclusion: Results from the non-interventional study INVISIBLE showed that a high proportion of AS patients receiving NSAIDs and/or TNFi have high disease activity according to BASDAI and ASDAS in real life settings. These results suggest that in some patients, disease control and treatment response are suboptimal under current treatment strategy.

Table 1. Demographics and Disease Characteristics

	Total (N=747)		BASDAI <4 (N=445)		BASDAI ≥4 (N=292)	
	N	Result	N	Result	N	Result
Age in years, mean (±SD)	746	47.9 (±13.1)	445	46.7 (±13.4)	292	49.6 (±12.3)*
Male, n (%)	746	500 (67.0)	445	318 (71.5)	292	176 (60.3)
Age at AS diagnosis in years, mean (±SD)	745	35.2 (±12.3)	445	34.1 (±12.0)	292	36.8 (±12.5)*
Treatment with NSAIDs, n (%)	744	171 (23.0)	445	85 (19.1)	290	85 (29.3)
Treatment with TNFi, n (%)	744	311 (41.8)	445	208 (46.7)	290	100 (34.5)
Treatment with NSAIDs and TNFi, n (%)	744	222 (29.8)	445	126 (28.3)	290	92 (31.7)
Treatment with other, n (%)	744	40 (5.4)	445	26 (5.8)	290	13 (4.5)
Patient disease activity assessment (VAS 0-100), mean (±SD)	735	35.8 (±27.5)	444	20.7 (±19.7)	286	59.1 (±20.7)***
BASDAI Score, mean (±SD)	737	3.4 (±2.3)	445	1.8 (±1.1)	292	5.8 (±1.3)***
ASDAS Score, mean (±SD)	599	2.2 (±1.0)	363	1.7 (±0.6)	236	3.1 (±0.7)***
ASDAS ≥2.1, n (%)	599	297 (49.6)	363	73 (20.1)	236	224 (94.9)***
PASS: current state not satisfactory, n (%)	679	240 (35.3)	403	72 (17.9)	271	166 (61.3)***

SD – Standard Deviation; Level of significance: *< 0.05; ** < 0.01 *** < 0.001 (analyses refer to differences between BASDAI <4 and ≥4 and to respective available patient number).

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AB0755 HIP DENERVATION AND INTRA-ARTICULAR HYDRATION IN AXIAL SPONDYLOARTHRITIS PATIENTS WITH HIP DAMAGE

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Background: The hip joint is frequently affected in axial spondyloarhritis (SpA) of the adults with destructive effect in untreated patients. About 35% of axial SpA patients had either unilateral or bilateral hip arthritis. Destruction is more common with early-onset, active disease, or enthesitis [1, 2].

Objectives: The aim of this study is to evaluate the effect of hip denervation (HD) and intra-articular hydration (IAH) on pain, function score, hip mobility scores in a cohort of axial SpA patients with grade 3 and 4 hip BASRI score.

Methods: We enrolled 40 patients who fulfilled ASAS criteria for axial SpA. All had hip involvement with grade 3 or 4 BASRI score at baseline.

They were divided into 4 groups; group one received placebo, group 2 HD, group 3 IAH, and group 4 received HD and IAH. They all were assessed at baseline and after 4 weeks and 12 weeks. Outcome measures included; VAS, semi-quantitative scores of tenderness for the hip, range of motion, and Harris functional hip score (HHS).

Results: A significant improvement of VAS pain, tenderness score, ROM, HHS were detected in group 4 versus other groups ($p < 0.05$). Group 2 had significantly lower scores of tenderness and pain compared to group 3 ($p < 0.05$). In contrast, the patients of group 3 show better ROM and HHS than the patients of group 2 ($p < 0.05$). At 4- and 12-week, all therapeutic groups (2, 3, and 4) show considerable improvement in comparison to placebo (group 1) ($p < 0.05$).

Conclusion: HD and IAH can improve pain and function in damaged hip of axial SpA patients, especially when concurrently used.

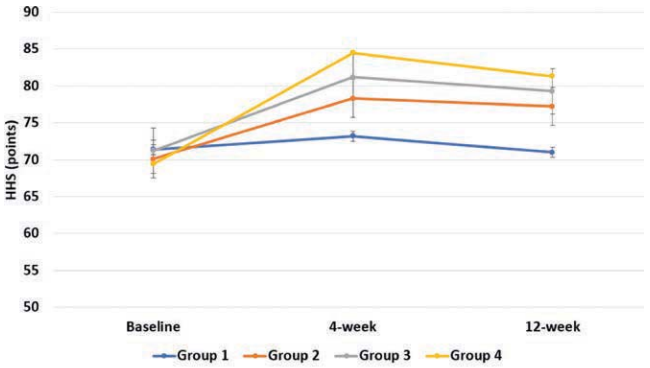

Fig. 1 HHS in all the studied groups during follow up.

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AB0756 FIRST SPANISH STUDY ON THE EFFECTIVENESS OF ULTRASOUND-GUIDED INJECTION OF CORTICOSTEROIDS INTO THE SACROILIAC JOINT OF PATIENTS WITH SPONDYLOARTHRITIS.

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Background: Sacroiliitis may be the main manifestation or a complication of any of the variants of spondyloarthritis. The few studies performed in patients with spondyloarthritis mainly evaluate the improvement in pain using a visual analog scale (VAS) and are limited by the need for an operating room and guidance based on fluoroscopy, tomography, or magnetic resonance. The advent of new ultrasound devices has meant that during the last decade, alternative approaches have been proposed for ultrasound-guided injection of the sacroiliac joint.

Objectives: To determine clinical improvement (Bath Ankylosing Spondylitis Activity Index [BASDAI], Ankylosing Spondylitis Disease Activity Score [ASDAS], acute-phase reactants, and the VAS score) after ultrasound-guided injection of corticosteroids into the sacroiliac joint of patients with spondyloarthritis.

Methods: We performed an observational, descriptive, and retrospective study at Ciudad Real General University Hospital (HGUCR), Ciudad Real, Spain. We reviewed the register of procedures carried out between June 1, 2020 and May 31,

2021 and included all patients with spondyloarthritis and inflammatory low back pain despite treatment with nonsteroidal anti-inflammatory drugs, biologics, or both. All patients underwent ultrasound-guided injection of the sacroiliac joint with corticosteroids (betamethasone chronodose 6/6 mg in each joint). We excluded patients whose clinical history did not contain the study variables and in whom modifications to pharmacologic treatment could have reduced the effectiveness of the injection. The outcome measures were presence of adverse effects/complications, reduction in the VAS score for inflammatory pain (>0=3 points), reduction of ≥1.1 points in the ASDAS score, reduction of ≥2 points in the BASDAI score, and reduced CRP and ESR values. These data were analyzed by comparing means (*t* test) for the variables VAS, BASDAI, ASDAS, CRP, and ESR. The potential association between the variables and a favorable clinical response was evaluated by calculating the odds ratio. The protocol was approved by the Research and Ethics Committee of Integrated Care Management, Ciudad Real, Spain.

Results: We analyzed 32 patients with spondyloarthritis (age 42.69±8.19 years; female sex, 56.25%) with a VAS score of 7.88±0.79, BASDAI of 5.43±1.48, and ASDAS of 3.27±0.86 before the procedure. At 2-3 months, 75% of patients had improved: VAS 3.81±2.33 (–4.07, p<0.0001) and BASDAI 3.24 ± 1.6 (–2.19, p<0.0001). At 5-6 months, 59.37% had improved: VAS 4.63±2.31 (–3.25, p<0.0001), BASDAI 3.57±1.67 (–1.86, p<0.0001), and ASDAS 2.27±0.71 (–1.0, p<0.0001). Bone marrow edema resolved in 87.5% of cases compared with the previous magnetic resonance scan. Analysis of factors potentially associated with improved clinical response as measured using the VAS, BASDAI, and ASDAS did not reveal a significant association with the variables analyzed (age, time since diagnosis, grade of sacroiliitis by radiography, presence of HLA B27 (+), peripheral and extra-articular manifestations, type of treatment). However, all the patients whose symptoms improved (EVA, BASDAI, and ASDAS) had had bone marrow edema on their magnetic resonance scan <1 year before the treatment. Only 5 patients experienced injection site pain, which lasted 1-2 days. No other adverse effects were reported.

Conclusion: Ultrasound-guided injection of corticosteroids into the sacroiliac joint of patients with spondyloarthritis and active sacroiliitis leads to an improvement in symptoms that is maintained at 5-6 months. The procedure is effective, safe, inexpensive, and easy to apply.

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Disclosure of Interests: None declared

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AB0757 THREE-YEAR DYNAMICS OF INFLAMMATORY CHANGES IN THE HIP JOINTS IN AXIAL SPONDYLOARTHRITIS.

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Background: Almost half of the patients with axial spondyloarthritis (axSpA) in Russia diagnosed hip joint lesions (HJ), but the causes and rates of progression are not studied. Until now, it remains unclear whether synovitis detected on MRI and ultrasound of hip joint is a predictor of radiological progression of coxitis.

Objectives: To assess the dynamics of inflammatory changes in the hip joint using instrumental research methods during 3-years observation and their relationship with the activity of axSpA.

Methods: 45 patients (mean age 30,07±7,1 years) with a diagnosed with axSpA (ASAS criteria 2009), which were observed for at least 3 years. Among them, AS according to the modified New York criteria (1984) - 40 (89%) patients and 5 (11%) were diagnosed with nr-axSpA. The median duration of the disease was 36 [19;108] moth, BASDAI 4,3 [3,1;6,8], BASFI 2,0 [0,6;4,7]. All patients underwent clinical, X-ray, ultrasound and MRI examination of the hip joint during the entire observation period. For ultrasound, coxitis was considered an increase in the cervical-capsular distance (CCD) of more than 7 mm. For MRI inflammatory changes were taken as osteitis of the acetabulum and / or femoral head and synovitis in STIR mode.

Results: At the time of inclusion of 45 patients, clinical signs of hip joint lesions were present in 66 (86%) patients, and after 36 months in 36 (80%) (p>0,05). The median CCD at the time of inclusion was 7,3 [6,6;7,9] mm, and after three years 6,6 [5,9;8,6] mm (p> 0.005). According to ultrasound, at the time of inclusion, 36 (80%) of 45 patients had coxitis, and after 3 years, 26 (58%) (p <0,005). Analysis of MRI changes initially showed the presence of synovitis in 42 (93%), and osteitis in 13 (29%) patients, and after 3 years synovitis persisted in y 25 (56%) (p <0,05), osteitis in 12 (27%) (p>0,005) and in 19 (42%) MRI patients, signs of active inflammation were arrested. Among all examined patients at the beginning of the study, the coincidence of signs of synovitis according to ultrasound and MRI data was noted in 35 (78%) cases. X-ray coxitis at the time of inclusion was detected in 11 (24%) patients, and after 2 years in 32 (68%) (p<0,05). The patients were divided into two groups ΔBASRI hip> 0 and ΔBASRI hip = 0. (Table 1)

Table 1. Characteristics of patients with axSpA at the time of inclusion in the study who had X-ray progression of coxitis after 36 months of observation.

Parametrs	ΔBASRI hip=0 n=15	ΔBASRI hip >0 n = 30	p
The duration of the disease, m., Me [25;75‰]	48 [12;120]	30 [24;108]	>0,05
Age, years, Me [25;75 ‰]	30,5 [23;34]	30,5 [25;35]	>0,05
BASDAI, Me [25;75 ‰]	6,7 [4,2;8,6]	4,2 [2,4;5,9]	<0,05
BASFI, Me [25;75 ‰]	4,4 [1,8;8,1]	1,7 [0,6;3,1]	>0,05
ASDAS (SRP), Me [25;75 ‰]	2,6 [1,6;3,9]	2,8 [2,1;4,2]	>0,05
ESR, mm/h, Me [25;75 ‰]	15 [7;30]	14,0 [7;27]	>0,05
SRP, mg/l, Me [25;75 ‰]	14,8 [10;56,0]	22,8 [3,7; 31,8]	>0,05
Peripheral arthritis, n %	11 (73%)	20 (67%)	>0,05
US synovitis n%	9 (60%)	23 (77%)	>0,05
Pain in HJ n%	28 (85%)	38 (86%)	>0,05
Synovitis in MRI, n%	15 (100%)	27 (90%)	>0,05
Osteitis in MRI, n%	3 (20%)	10 (34%)	>0,05
Therapy bDMARDs	9 (60%)	9 (30%)	<0,05

Conclusion: X-ray progression of coxitis in axSpA practically does not depend on the activity of the disease, nor on local signs of inflammation in the HJ, detected by ultrasound and MRI. X-ray progression of HJ lesions is less common in patients receiving bDMARDs therapy.

Disclosure of Interests: None declared

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AB0758 GOLIMUMAB AFTER DISCONTINUATION OF NON-TNF INHIBITORS IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: FOUR-YEAR RETENTION RATE IN THE SPANISH BIOBADASER REGISTRY

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Background: Treatment options for rheumatic diseases have evolved to include mechanisms of action beyond tumor necrosis factor inhibitors (TNFi). While non-TNFi biologics and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDS) have been studied as first-line therapy or after TNFi discontinuation, data on the use of TNFis after discontinuation of these drugs is scarce.

Objectives: We assessed the probability of retention (persistence or drug survival) of golimumab in patients with rheumatic diseases when used after discontinuation of non-TNFi biologicals or tsDMARDs.

Methods: Characteristics of all adults with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (SpA) who had initiated golimumab after discontinuation of non-TNFi biologicals or tsDMARDs in the BIOBADASER database were analyzed. The probability of golimumab retention was assessed with the Kaplan-Meier method, and differences between groups with the log-rank test. Patients were right-censored if they were still treated with golimumab at the last observation for data analysis. We also compared the probability of retention of patients who initiated golimumab after discontinuation of non-TNFi biologicals or tsDMARDs with that of patients who initiated it after discontinuation of TNFis.

Results: A total of 125 patients (85 [68%] women) with RA (n=72), axSpA (n=23), or PsA (n=30) had initiated golimumab after discontinuation of non-TNFi biologicals or tsDMARD. Golimumab had been initiated as second line of therapy (i.e., after discontinuation of a first non-TNFi biological or tsDMARD) in 26 patients (21%), as third in 29 (23%) and as fourth/subsequent line of therapy in 70 patients (56%). Upon golimumab initiation, the median disease duration was 10.0 years. The most common previously discontinued therapies were secukinumab (n=34) and abatacept (n=23). The retention rates of golimumab were 61% (95% confidence interval [CI]: 51-69) at year 1 (number at risk: 66), 46% (95% CI: 36-55) at year 2 (number at risk: 39), 40% (95% CI: 30-50) at year 3 (number at risk: 23) and 33% (95% CI: 23-44) at year 4 (number at risk: 13). There were no differences in retention rates over 4 years when golimumab was used as the second, third, or fourth/subsequent line of therapy (p=0.462). Retention rate was lower in

RA patients (26% at year 3) than in axial SpA (68%) or PsA (49%) (p=0.002) (Figure 1). As second line therapy, the 3-year retention rate of golimumab was slightly lower when it was initiated after non-TNFi biologicals/tsDMARD than when the previously discontinued therapy was a TNFi (32% vs 55%, p=0.119), but the figures were similar when it was initiated as third (52% after non-TNFi biologicals/tsDMARD vs 50% after TNFi, p=0.838) or as fourth/subsequent line of therapy (37% vs 44% respectively, p=0.554).

Conclusion: We present, for the first time, 4-year retention rates for golimumab in patients who discontinued non-TNFi biologicals or tsDMARDs, most of them in third and fourth/subsequent line of therapy. In this difficult-to-treat rheumatic population, overall golimumab retention rates were favorable through 4 years of treatment, with higher rates in SpA and PsA compared to RA patients.

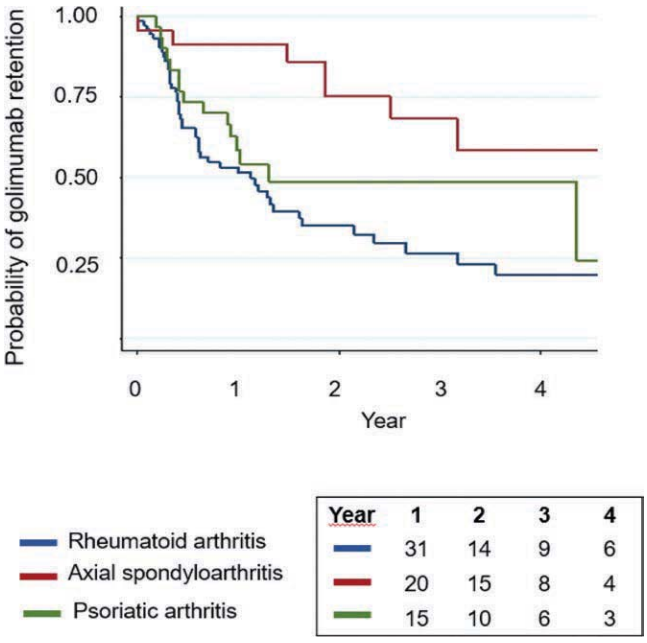

Figure 1.

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AB0759

EFFICACY OF SECUKINUMAB IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: ANALYSIS BY SYMPTOM DURATION AND AGE

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Background: Patients (pts) with axial spondyloarthritis (axSpA) often experience delayed diagnosis, which can lead to treatment delay[1]. However, earlier diagnosis and treatment of axSpA pts can lead to a greater clinical response[2]. Secukinumab (SEC) 150 mg has demonstrated sustained improvement in signs and symptoms over 2 years in non-radiographic (nr)-axSpA pts[3].

Objectives: To assess the efficacy of SEC in pts with nr-axSpA [tumour necrosis factor (TNF) naïve] by subgroups of younger versus (vs) older pts and early vs late symptom duration of back pain.

Methods: PREVENT (NCT02696031) is a phase 3, randomised study in pts with nr-axSpA and detailed study design is reported previously4. In this post hoc analysis, efficacy outcomes including Assessment of SpondyloArthritis international Society 40 (ASAS40), ASAS partial remission (ASAS PR), Ankylosing Spondylitis Disease Activity Score-C-reactive protein (ASDAS-CRP) inactive disease (ID) and low disease activity (LDA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and the proportion of pts meeting the minimal clinically important difference criteria for total back pain (improvement of ≥50%) were assessed in the TNF naïve population. Age categories included 4 approximately equally distributed age groups (18 to 33, 34 to 42, 43 to 51 and ≥52 years). The categories for time since onset of back pain as a surrogate of disease symptoms and sign, was based on patients' distribution and the hypothesis that patients with shorter disease duration will present better results (≤2, >2 to 5, >5 to 10 and >10 years). Missing responses were imputed as non-response up to Week (Wk) 16 and reported as observed at Wks 52 and 104. Data is presented here for categories 18-33 vs ≥52 years and patients with symptom duration ≤2 vs >10 years.

Results: At Wk 104, greater improvements in ASAS40 scores were reported in younger (18-33 years) vs older age categories (>52 years) treated with SEC and also in patients with shorter disease duration (≤2 years) when compared to long term disease (Figure 1 and Table 1).

Conclusion: Efficacy responses were numerically higher with SEC in patients with nr-axSpA with shorter symptom duration and in younger age. These data suggest that earlier treatment improves patient outcomes in nr-axSpA.

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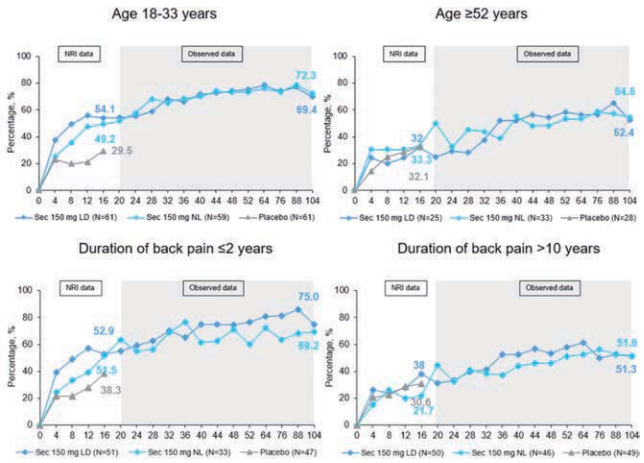
Table 1. Efficacy responses with SEC up to Week 104 based on age and symptom duration

Age 18-33 years			Age >52 years			≤2 years of back pain			>10 years of back pain		
SEC 150 mg LD (N=61)	SEC 150 mg NL (N=59)	PBO (N=61)	SEC 150 mg LD (N=25)	SEC 150 mg NL (N=33)	PBO (N=28)	SEC 150mg LD (N=51)	SEC 150 mg NL (N=33)	PBO (N=47)	SEC 150 mg LD (N=50)	SEC 150 mg NL (N=46)	PBO (N=49)
ASDAS-CRP ID and LDA											
50.8*	55.9*	34.4*	36.0*	39.4*	21.4*	51.0*	48.5*	40.4*	44.0*	30.4*	26.5*
77.4#	81.1#	72.2#	45.8#	46.7#	33.3#	77.3#	60.0#	77.3#	53.3#	48.7#	37.2#
71.7†	70.2†	77.6†	50.0†	57.1†	60.9†	74.4†	69.2†	82.1†	55.3†	53.3†	53.8†
BASDAI 50											
45.9*	47.5*	27.9*	28.0*	36.4*	17.9*	45.1*	51.5*	29.8*	34.0*	23.9*	20.4*
77.8#	71.7#	72.2#	37.5#	53.3#	37.0#	75.6#	60.0#	75.0#	46.7#	46.2#	43.2#
73.5†	72.3†	77.6†	47.6†	60.9†	52.2†	78.0†	65.4†	76.9†	53.8†	53.1†	51.3†
ASAS PR											
29.5*	32.2*	8.2*	12.0*	12.1*	7.1*	27.5*	24.2*	8.5*	18.0*	10.9*	12.2*
41.5#	50.9#	38.9#	12.5#	20.0#	22.2#	45.5#	40.0#	38.6#	22.2#	23.1#	20.5#
46.9†	44.7†	59.2†	23.8†	31.8†	21.7†	56.1†	34.6†	46.2†	25.6†	25.8†	23.1†
Total back pain											
50.8*	50.8*	27.9*	24.0*	30.3*	32.1*	51.0*	48.5*	36.2*	32.0*	23.9*	32.7*
74.1#	75.5#	72.2#	58.3#	46.7#	44.4#	73.3#	63.3#	72.7#	53.3#	48.7#	47.7#
71.4†	68.1†	79.6†	61.9†	52.2†	52.2†	75.6†	69.2†	74.4†	61.5†	50.0†	59.0†

Data is presented as % of responders. Symbols are used to denote the Weeks. *Week 16; #Week 52; †Week 104. All patients received open-label SEC 150 mg treatment after Week 52 up to Week 104. ASDAS-CRP ID and LDA (ASDAS-CRP <2.1); Total back pain improvement ≥50%. LD, loading dose; NL, without loading; PBO, placebo

Figure: ASAS40 response in different age categories and duration of back pain



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AB0760

FACTORS ASSOCIATED WITH THE RETENTION OF SECUKINUMAB (SEC) IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA) IN REAL WORLD PRACTICE: RESULTS FROM THE RETROSPECTIVE FORSYA STUDY

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Background: While data on real-life retention of SEC in patients (pts) with PsA is accumulating, there are no data on predictive factors for this retention.
Objectives: The primary objective of FORSYA study was to assess whether objective signs of inflammation (OSI) were predictive of SEC retention at 1 year.
Methods: French retrospective study collecting between October 2019 and September 2020 data from axSpA pts a) having initiated and received at least one dose of SEC between August 11th 2016 and August 31st 2018, b)with at least a one year follow-up period. Retention of SEC at 1 year was estimated by the Kaplan Meier (KM) method. OSI were defined by at least one of the following within the 3 months before initiation of SEC: CRP> N, confirmed clinical dactylitis, confirmed clinical synovitis or ultrasonography power-Doppler positive synovitis except on MTP of first toe. Preselected factors at initiation of SEC retention at 1 year (≥1 OSI, age, sex, BMI, smoking status, axial feature, past or present psoriasis / uveitis / Inflammatory Bowel Disease (IBD) / active arthritis or synovitis, diagnostic delay, disease duration, SEC line of biologic therapy, SEC maintenance dose, concomitant csDMARD, concomitant oral corticosteroids, ≥1 comorbidity) were analyzed by multivariate cox model regression. Only variables with <20% missing data were included in the model after imputation and stepwise selection (significance level for entering variables = 20%; for removing variables = 10%). OSI was forced into the model whatever its significance level or rate of missing data.
Results: In total, 475 pts (male: 40.2%, mean age: 51.9 ± 12.2 years, mean disease duration: 9.3 ± 8.6 years) from 48 centers were included in the analysis. At initiation of SEC, 62.2% of pts had ≥ 1 OSI and respectively 11.0%, 19.5% and 69.6% were in 1st, 2nd and ≥ 3rd line (L) of biologic/targeted synthetic DMARD. The overall 1 year KM survival rate for SEC was 63% [95%CI: 59%-68%] and was numerically greater in 1st L vs 2nd and ≥3rd L (82% [72%-93%], 62% [52-72%], 61% [56%-66%] respectively). The overall survival rates for PsA pts with or without OSI were 62% [56%-68%] and 71% [62%-80%]. In multivariate analysis, absence of OSI, longer disease duration and lack of prior exposure to anti-TNF inhibitors were associated with a better SEC retention at 1 year (Table 1).

Table 1. Predictive factors of SEC 1 year retention of SEC identified by multivariate cox regression analysis (multiple imputation + Stepwise selection)

Predictive factors (* reference)		HR [95% CI]	p vs refp type III	
At least one objective sign of inflammation	No (N=175)*			
	Yes (N=295)	1.46 [1.05; 2.02]	0.023	
Disease duration (years)	≤ 7.2 years (N=241)*			
	> 7.2 years (N=229)	0.69 [0.51; 0.94]	0.017	
Secukinumab treatment line	1st L (N=50)*			0.015
	2nd L (N=92)	2.43 [1.17; 5.05]	0.018	
	≥ 3rd L (N=328)	2.72 [1.38; 5.36]	0.004	

Interpretation for predictor: HR> 1: the hazard of discontinuation at 1 year is X times higher in category vs reference.

Conclusion: The overall retention of SEC at 1 year in daily practice at the time of its launch in France was 63% for PsA patients and OSI, disease duration and prior exposure to TNF inhibitors were identified as predictive factors of SEC retention.
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AB0761

ARE WE TREATING-TO-TARGET IN SPONDYLOARTHRITIS (SPA)? A CROSS SECTIONAL ANALYSIS FROM THE ASIA PACIFIC LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (APLAR) SPA REGISTRY

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Background: Data on the extent of treat-to-target (T2T) recommendations application in SpA patients across Asia Pacific region is lacking. APLAR SpA Registry aimed to assess the utility of T2T on long term clinical outcomes, and to improve disease management and inform health care policy.
Objectives: To provide a snapshot of the registry including demographics, disease activity and medication use.

Methods: Patients fulfill the CASPAR 2006 for psoriatic arthritis (PsA) and 2009 ASAS criteria for axial spondylitis (AxSpA) were recruited. This cross sectional analysis included the first 188 patients recruited across 7 Asia Pacific regions (Hong Kong, Singapore, Korea, Thailand, India, Qatar & Pakistan).

Results: 83 patients PsA and 115 AxSpA patients were included. They had moderate inflammation (DAPSA: 19.61±14.29, ASDAS: 2.32±1.07). Majority of PsA patients received conventional synthetic disease-modifying drug (csDMARDs, 81%) with relatively low prevalence of biologic DMARDs (bDMARDs) (24%). Most AxSpA patients used NSAIDs (79%) while nearly half of them received bDMARDs (49%). Other details listed in Table 1. Prevalence of bDMARDs use in our registry was lower than that from the USA (Corrona PsA Registry, 59%), Turkey & Canada (PsArt-ID, 40%) and the Netherlands AxSpA registry (56%) (1-3). Regarding T2T, 28% and 44% of PsA patient achieved minimal disease activity (MDA) and Disease Activity in Psoriatic Arthritis low disease activity (DAPSA LDA) respectively. The proportion of patients achieving target in other cohorts were 46% for MDA (PsArt-ID) and 46% for DAPSA LDA (Corrona) (1, 2). 37% and 47% of AxSpA patient achieved Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)<4 and Ankylosing Spondylitis Disease Activity Score (ASDAS) LDA. Proportion of patients achieving ASDAS LDA were similar to the Netherlands registry for patients with ASDAS LDA or BASDAI<4 (Figure 1A)(3). Patient on bDMARD were more likely to achieve treatment target (Figure 1B). There were no significant difference between socio-economic status and disease features between bDMARD user and non-user.

Table 1. Demographics, clinical features and disease activity of patients

	PsA (n=83)		AxSpA (n=115)	
Age	50.0	12.8	36.5	12.4
Male n, %	42	51%	85	83%
Asian n, %	83	100%	101	96%
Disease duration, years	7.1	7.3	5.2	7.6
Any sacroiliitis n, %			102	99%
HLA B27, positive n, %			91	89%
Duration of early morning stiffness, min	30	39	25	29
Tender joint count	7	9	0	1
Swollen joint count	3	4	0	0
No. of dactylitis digit	1	1	0	0
PASI	4.0	5.0		
SPRACC	1	2	0	1
BASDAI			2.8	2.0
ESR, mm/h	31	26	20	16
CRP, mg/L	10	15	11	27
HAQ-DI	0.61	0.61	0.39	0.51
DAPSA	19.61	14.29		
ASDAS CRP			2.32	1.07

Data given in mean SD unless stated. No. of case from Hong Kong 40; Singapore 46; Korea 24; Thailand 20, India 15; Qatar 10; Pakistan 33; HLA - human leucucyte antigen; PASI - psoriasis area and severity index; SPRACC - Spondyloarthritis Research Consortium of Canada Enthesitis Index; BASDAI - Bath Ankylosing Spondylitis Disease Activity Index; ESR - erythrocyte sedimentation rate; CRP - C-reactive protein; HAQ-DI - Health assessment questionnaire disability index; DAPSA - Disease activity in Psoriatic Arthritis; ASDAS - Ankylosing Spondylitis Disease Activity Score

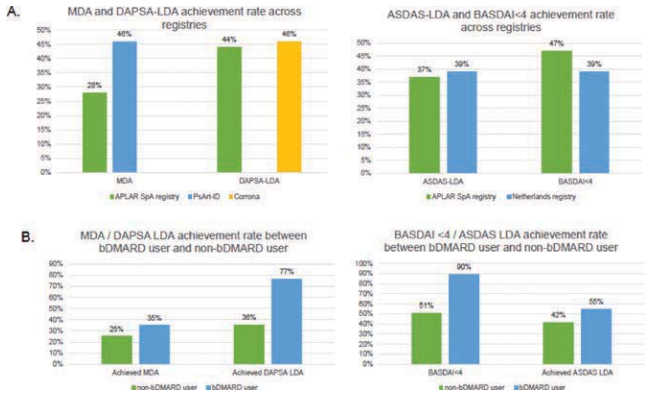

Figure 1. (A) Achievement of LDA in APLAR SpA registry and other registry and (B) use of bDMARDs among patients in APLAR SpA registry with or without achieving LDA

Conclusion: Patient using bDMARDs were more likely to achieve treatment target. We expect that when T2T is widely applied, better outcomes will be reported in future.

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AB0762

INCIDENCE OF ANTERIOR UVEITIS IN AXIAL SPONDYLOARTHRITIS DURING SECUKINUMAB TREATMENT: TWO YEARS REAL LIFE EXPERIENCE FROM TURKBIO REGISTRY

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Background: Secukinumab (SEC), a human anti-IL-17A monoclonal antibody, has similar treatment response rates to tumor necrosis factor (TNF) inhibitors in patients with axial spondyloarthritis (SpA). However, the efficacy of SEC on anterior uveitis (AU) is unclear.

Objectives: This study aimed to evaluate the risk of new-onset or relapsing AU in axial SpA patients treated with SEC.

Methods: In this prospective cohort study, 130 axial SpA patients receiving SEC at the TURKBIO registry between 2019 and 2021 were evaluated. Demographic and clinical characteristics and data about the presence of AU pre or post-treatment were collected. The univariate and multivariate logistic regression analyses were performed to evaluate the predictors of AU development.

Results: The mean age of the patients (F/M: 59/71) was 47.4±10.9 years. The median follow-up time was 540 days (IQR: 330-630). SEC was the first biological agent in 50 (38.4%) patients and 35 (26.9%) patients were using at least one concomitant conventional synthetic DMARD (Table 1). While continued SEC therapy was in 93 (71.5%) patients, treatment withdrawal was in 37 cases (in 26 due to ineffectiveness, two adverse events and nine other reasons). Overall, 15(11.5%) patients had a history of AU before the SEC. During follow-up, AU attacks were seen in the 6 cases (4 were new-onset and 2 were flare) and 5 of these patients have a history of inadequate response to TNF inhibitors. The frequency of AU was

calculated as 3.42 per 100 patient-years during SEC treatment. The only significant predictor of AU development was the baseline high C-reactive protein (CRP) level on multivariate analysis (p=0.003, OR: 1.063 [95% CI 1.021-1.107]).

Table 1. Demographics and clinical characteristics of the patients

	Total (n:191)
Gender (F/M)	59/71
Age (years) (mean±SD)	47.4±10.9
Diagnosis; n (%)	
AS	125 (96.2)
nr-axSpA	5 (3.8)
BASDAI (mean±SD)	47.2±20.48
Missing n (%)	4 (3.07)
ASDAS (mean±SD)	3.32±0.92
Missing n (%)	14 (10.7)
C-reactive protein (mg/L) median (IQR)	12.6 (4.67-22.62)
Sedimentation (mm/h) median (IQR)	22 (9-42)
Concomitant csDMARDs n (%)	35 (26.9)
Secukinumab dose n (%)	
150 mg	120 (92.3)
300 mg	10 (7.7)
TNFi-naive patients n (%)	50 (38.5)
Number of previous bDMARDs n (%)	
1	36 (27.7)
2	23 (17.7)
≥ 3	21 (16.1)
History of previous TNFi n (%)	
Monoclonal TNFi	64
Etanercept	16

AS; Ankylosing spondylitis, *nr-axSpA;* Non radiographic axial spondyloarthritis, BASDAI; Bath Ankylosing Spondylitis Disease Activity Index, *ASDAS;* Ankylosing Spondylitis Disease Activity Score, *csDMARD;* conventional synthetic disease modifying anti-rheumatic drug, *TNFi*; Tumor necrosis factor inhibitors, *bDMARD*; biological DMARD. Datas were expressed as number (%), mean±SD or median (IQR).

Conclusion: In this real-life data from the TURKBIO registry, the incidence of AU in axial SpA patients treated with SEC was calculated as 3.42 per 100 patient-years. A high baseline CRP level was an independent factor for developing AU.
Disclosure of Interests: None declared
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AB0763 PERSONAL APPROACH IN AXIAL SPONDYLOARTHROPATHY MANAGEMENT

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Background: Spondyloarthropathies (SpAs) are a group of diseases characterized by arthritis in the spine (axialSpA - axSpA) and peripheral joints, and extra-articular symptoms like uveitis, psoriasis or inflammatory bowel diseases. The onset of the disease is difficult to observe. Due to the lack of a pathognomonic test, diagnosis is based on a combination of physical examination, laboratory test and imaging results. The pathogenesis of SpAs is not fully understood, and genetic, environmental and immunological factors are assumed to play a pivotal role.
Objectives: The study aimed to evaluate selected polymorphisms (ERAP1 rs2287987, ERAP2 rs2549782, TNF rs1800629, TNFRSF1B rs1061622, FCGR2A rs1801274) as prognostic factors of clinical presentations, and response predictors of anti-TNF treatment in axSpA patients.
Methods: The study enrolled 216 Caucasians: 106 axSpA patients and 110 healthy controls. AS patients were diagnosed according to modified New York criteria, while nr-axSpA patients were diagnosed according to ASAS criteria. Genotyping was performed using LightSNiP assays on the Real-Time PCR Instrument. Clinical data were assessed at baseline, as well as after three and six months of anti-TNF treatment. In addition, information's about extra-articular symptoms were collected.
Results: The statistical analysis revealed that TNFRSF1B rs1061622-GG was significantly associated with a higher VAS score at baseline (TT + TG vs GG, p = 0.001), and a higher BASDAI score corrected for the first therapy cycle (X1C BASDAI: TT + TG vs GG, p = 0.005). Moreover, homozygotes were more frequently observed with a lack of BASDAI improvement after six months (X1C BASDAI: TT+GG vs TG, p = 0.045, OR = 2.46, 95%CI 1.00-6.12). ERAP1 rs2287987- GG was more frequently observed with enthesitis (AA vs G+, p = 0.049, OR = 4.636, 95%CI 1.101-21.24). The GG genotype of TNFRSF1B rs1061622 was more common in patients with uveitis than TT variant (GG vs TT, p =0.042, OR = 5, 95%CI 1.08-20). Associations between genetic variants and clinical outcomes were evaluated using laboratory parameters. A lack of the ESR improvement after six months of treatment was more frequently observed within ERAP1 rs2287987-AG (AG vs AA + GG, p = 0.027, OR = 2.72, 95%CI 1.115-6.137) and TNFRSF1B rs1061622- TT (TT vs G+, p = 0.020, OR = 3, 95%CI 1.27-6.9) compared to other genotypes. After three months of therapy, the GG variant of ERAP2 rs2549782 polymorphism was more common among individuals with the lack of ESR improvement than T allele carriers (GG vs T+, p = 0.037, OR = 2.76, 95%CI 1.13-6.72). Differences were also detected between the FCGR2A rs1801274 polymorphism and X1CBASDAI score after six months. The low disease activity (BASDAI < 3) and BASDAI improvement was more frequently observed in patients carrying the A allele than the GG genotype (AA+AG vs GG, p = 0.028, OR = 4.545, 95%CI 1.337-16 and p = 0.012, OR = 6.212, 95%CI 1.683-20.47, respectively). The AG genotype was more common among patients with remission (BASDAI < 2) compared to homozygotes (AG vs AA+GG, p = 0.046, OR = 2.36, 95%CI 1.05-5.13).
Conclusion: Genetic profiling of patients will help to identify those at risk of high initial disease activity or the presence of extra-articular symptoms. Identifying patients less responsive to treatment may allow selecting a drug with an appropriate efficacy profile.
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AB0764 FACTORS ASSOCIATED WITH REMISSION AFTER GRADUAL DECLINE OF TNFI IN SPONDYLOARTHRITIS

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Background: The natural history of axial spondyloarthritis (axSpA) includes periods of remission interspersed with flares. It is recommended to target remission during the disease management, the 2 most used definitions are ASAS partial remission and inactive disease (ASDAS <1.3 and / or BASDAI score <3.6). The factors associated with the gradual decline of biologics after achieving remission have been little explored.
Objectives: The objective of this work was to assess the proportion of patients with axSpA treated with TNFi in whom remission was maintained concomitantly with tapering at 3 years of follow-up and to identify the factors associated with this remission.
Methods: Single-center prospective descriptive study. A total of 44 patients included who attempted to space TNFi injections (etanercept, infliximab, adalimumab) among the 192 patients treated with bDMARDs, all of the patients fulfilled the ASAS criteria for SpA. Data collected: socio-demographic, clinical-biological and imaging data up to 3 years of follow-up.
Results: At the 3-year visit, a biologic decrease was achieved in 22.9% (86.4% maintenance of remission and 9.1% with relapse). That is a total of 19.8% (38/192) of patients (mean age 34.2 ± 8.1 years; 71% of men with HLAB27 positive 63.2% with low BMI in 68.4%) maintained clinical remission with TNFi tapering at the 3-year visit There was a significant association between ASDAS (p <0.001), BASDAI (p <0.001) and CRP (p = 0.004) per visit and maintenance of remission. Likewise, patients in remission more often presented strictly axial damage without enthesitic or peripheral damage and minimal structural on concomitant radiography (p = 0.03). They reported low smoking and stopping use of NSAIDs. Factors associated with successful 3-year TNFi spacing were a shorter delay between diagnosis and initiation of the biologic (0.9 [0.64-1.3]) and initial presentation of acute illness according to patient examination (2.37 [1.06-5.26]), a lower BASDAI and BASFI (respectively 1.3 [0.84-1.6] and 0, 9 [0.74-1.4]) and a lower NSAID score (0.715 [0.43-0.9]).
Conclusion: AxSpA patients in remission as defined by ASAS had significantly fewer objective signs of inflammation concomitantly but also over time. It is possible to maintain this remission after gradual decline in the biologics at 3 years in axSpA. Low activity and functional scores, as well as low consumption of NSAIDs are predictive of the success of tapering. Discontinuation treatment is not recommended due to the high risk of relapse.
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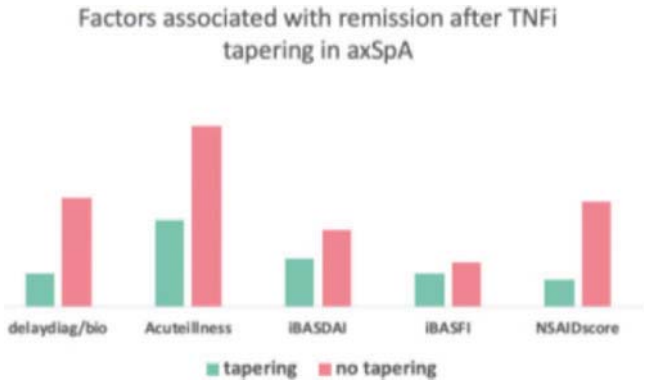

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AB0765

ANALYSIS OF THERAPY IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS WHO ACHIEVED THE ASAS PARTIAL REMISSION AND THE CLINICAL-LABORATORY REMISSION AT THE 3RD YEAR OF FOLLOW-UP

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Background: The main goal of "T2T" strategy for spondyloarthritis (SpA) is to achieve clinical remission or inactive disease. In 2001, the ASAS formulated criteria for partial remission [1], and the Russian Expert Group for Study of SpA (ExSpA) in 2018 identified clinical-laboratory remission (absence of clinical manifestations of the disease that persists for 6 months with normal values of CRP and ESR) [2].
Objectives: to analyze the therapy in patients with early axial spondyloarthritis who achieved the ASAS partial remission and the clinical-laboratory remission at the 3rd year of follow-up.
Methods: The study included patients with early axSpA (ASAS criteria 2009 with inflammation back pain duration less than 5 years) from the CORSAR cohort (Cohort of Early SpondyloArthritis), formed at the V.A. Nasonova Research Institute of Rheumatology. The cohort includes 175 patients with axSpA. The analysis included 66 patients followed for at least 3 years, of which 37 (56%) were men. The average age of patients was 31.5 (5.7) years, the average duration of the disease was 22.1 (17.0) months, 63 (95.4%) patients were HLA B27 positive. The criteria for clinical-laboratory remission include the following indicators (at least during 6 month): ASDAS≤1,3, BASDAI ≤1,0, morning stiffness<30 min., absence of swollen joints, absence of enthesitis, nocturnal pain ≤1,0 (NRS), spinal pain≤1,0 (NRS), no active extra-articular manifestations, normal levels of CRP and ESR [2]. The criteria for ASAS partial remission include a value not above 2 units in each of the 4 domains: patient global, pain, function, inflammation [1].
Results: Initially, no patients met the ASAS partial remission and the clinical-laboratory remission criteria. By the 3rd year of follow-up, the clinical-laboratory remission was achieved by 21 (31.8%) patients; the ASAS partial remission - 29 (44.0%) patients. When analyzing therapy at the 3rd year of follow-up of patients with early axSpA who achieved the clinical-laboratory and the ASAS partial remission, it was revealed that patients more often achieved remission when taking NSAIDs, a quarter of patients achieved remission on combined therapy with biologics and NSAIDs (Table 1). It is noting that a quarter of patients canceled therapy on their own.

Table 1. Therapy of patients with axSpA who achieved the clinical-laboratory and the ASAS partial remission at 3 years of follow-up.

	The ASAS partial remission (n=29)	The clinical-laboratory remission (n=21)	p
NSAIDs, n (%)	14 (48,2%)	9 (42,8%)	p>0,05
NSAIDs+sulfasalazine, n (%)	0	1 (4,7%)	p>0,05
Biologics, n (%)	2 (6,8%)	0	p>0,05
Biologics+NSAIDs, n (%)	6 (20,6%)	5 (23,8%)	p>0,05
Biologics+sulfasalazine, n (%)	0	1 (4,7%)	p>0,05
Biologics+sulfasalazine+NSAIDs, n (%)	1 (3,4%)	0	p>0,05
Without therapy, n (%)	6 (20,6%)	5 (23,8%)	p>0,05

Conclusion: 1. In the 3d year of follow-up 32% of patients with early axSpA achieved the clinical-laboratory remission and 44% - of the ASAS partial remission.
2. More than 40% of patients with early axSpA achieved remission while taking NSAIDs.

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AB0766

BIOLOGIC DRUG PREFERENCES OF TURKISH RHEUMATOLOGISTS IN SPONDILOARTROPATHY PATIENTS WITH ADVANCED CHRONIC RENAL DISEASE

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Background: Biological therapies are the main treatment options for patients with active spondyloarthropathy (SpA) who do not respond to nonsteroidal anti-inflammatory drugs or conventional synthetic disease-modifying drugs. Kidney diseases are not a contraindication to biologic therapies. However, there are some safety concerns for these drugs for patients with advanced chronic kidney disease. De novo infection or recurrence of infections are the main challenges in patients with multiple comorbidities during biologic treatments. Neverthless, physicans should initiate these treatments in active and resistant diseases.
Objectives: Here, we evaluated which biologic therapies clinicians' first option to initiate in SpA patients with advanced chronic kidney disease (CRD).
Methods: Total 140 patients of TREASURE database who fullfield axial and/or peripheral ASAS SpA criteria with glomerular filtration rate < 60 ml/dk (stage 3,4 or 5 CRD according to The National Kidney Foundation classification) were included to the study. Renal stages of the patients were evaluated when biologic therapy was initiated. Five anti-TNF (adalimumab, certolizumab, etanercept, golimumab, infliximab) and an interleukin-17A blocker (secukinumab) were on the market during the study. We evaluated physicans' first choice for biologic therapy for patients with stage 3,4 and 5 CRD respectively.
Results: More than two thirds of the patients had stage 3 CRD. Anti-TNF drugs were the first choice of biologic treatment in the patients with advanced CRD. Etanercept was started at most to the patients in general, in stage 3 and in stage 5 CRD groups. However, adalimumab was the first choise in stage 4 CRD. Both etanercept and adalimumab were the first drug of choise in three fourth of the stage 4 and stage 5 patients. All two patients on Il-17A blocker had stage 3 CRD (Table 1).

Table 1. Drug of choise in the SpA patients with advanced chronic renal diseases

	N	Total n (%)	N	Stage 3 n (%)	N	Stage 4 n (%)	N	Stage 5 n (%)
Adalimumab	140	44 (31.4)	108	30 (27.8)	20	9 (45.0)	12	5 (41.6)
Etanersept		52 (37.1)		41 (38.0)		5 (25.0)		6 (50.0)
Golimumab		9 (6.0)		7 (6.5)		2 (10.0)		0 (0)
Infliksimab		28 (20.0)		23 (21.3)		4 (20.0)		1 (8.4)
Secukinumab		3 (2.1)		3 (2.8)		0 (0)		0 (0)
Sertolizumab		4 (2.8)		4 (3.7)		0 (0)		0 (0)

Conclusion: We show that rheumatologists in the TREASURE group prefer to initiate anti-TNF drugs first in all advanced CRD stages. Etanercept was the first choice in these patients.

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AB0767 COMPARISON OF THE CLINICAL-LABORATORY REMISSION AND THE ASAS PARTIAL REMISSION IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS

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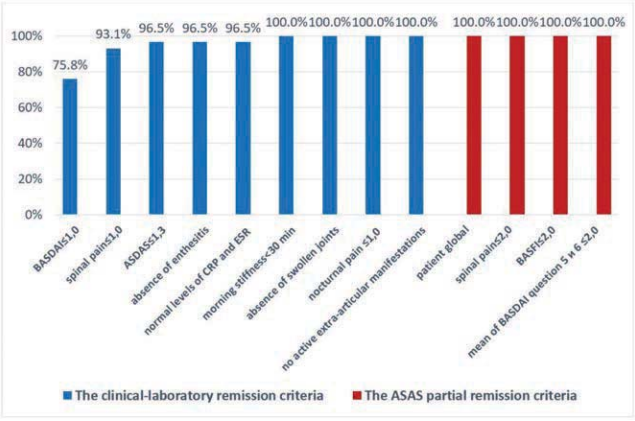
Background: The main goal of "T2T" strategy for spondyloarthritis (SpA) is to achieve clinical remission or inactive disease. In 2001, the ASAS formulated criteria for partial remission [1], and the Russian Expert Group for Study of SpA (ExSpA) in 2018 identified clinical-laboratory remission (absence of clinical manifestations of the disease that persists for 6 months with normal values of CRP and ESR), MRI remission and complete remission (a combination of clinical-laboratory and MRI remission) [2].

Objectives: to compare the ASAS criteria for partial remission and the clinical-laboratory remission in patients with early axial SpA (axSpA) at 3rd year of follow-up.

Methods: The study included patients with early axSpA (ASAS criteria 2009 with inflammation back pain duration less than 5 years) from the CORSAR cohort (Early SpondyloArthritis Cohort), formed at the V.A. Nasonova Research Institute of Rheumatology. The cohort includes 175 patients with axSpA. The analysis included 66 patients followed for at least 3 years, of which 37 (56%) were men and 29 (44%) - women. The average age of patients was 31.5 (5.7) years, the average duration of the disease was 22.1 (17.0) months, 63 (95.4%) patients were HLA B27 positive. The criteria for clinical-laboratory remission include the following indicators (at least during 6 month): ASDAS≤1,3, BASDAI ≤1,0, morning stiffness<30 min., absence of swollen joints, absence of enthesitis, nocturnal pain ≤1,0 (NRS), spinal pain≤1,0 (NRS), no active extra-articular manifestations, normal levels of CRP and ESR [2]. The criteria for ASAS partial remission include a value not above 2 units in each of the 4 domains: patient global, pain, function, inflammation [1].

Results: Initially, no patients met the ASAS partial remission clinical-laboratory criteria. At 3 year of follow-up, the clinical-laboratory remission was achieved by 21 (31.8%) patients; the ASAS partial remission - 29 (44.0%) patients.

We matched patients who achieved the ASAS partial remission (n=29) to criteria for clinical-laboratory remission and, conversely, patients who achieved the clinical-laboratory remission (n=21) to criteria for ASAS partial remission. When comparing the criteria for clinical-laboratory remission to the group of patients who achieved the ASAS partial remission, it turned out that the criteria were achievable (more than 93%), the fewest patients with ASAS partial remission achieved BASDAI≤1.0 (75.8%) (graph 1). All patients with early axSpA who achieved clinical-laboratory remission met the ASAS criteria for partial remission (graph 1).



Graph 1. Comparison of the clinical-laboratory remission and the ASAS partial remission in patients with axSpA at 3 y. of follow-up.

Conclusion: The criteria for clinical-laboratory remission are comparable to the ASAS criteria for partial remission in patients with early axSpA and can be used in a practice of rheumatologists. Further research is needed to analyze the various remission criteria for axSpA and their applicability in a practice.

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AB0768 INFLUENCE OF CONTINUOUS NON-STEROIDAL ANTI-INFLAMMATORY DRUGS INTAKE ON BONE MARROW EDEMA IN NON-RADIOGRAPHIC SPONDYLOARTHRITIS

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Background: The concept of non-radiographic axial spondyloarthritis (nr-axSpA) has revolutionized the classical understanding of axSpA. Indeed, it facilitated the classification of patients with axSpA who did not present substantial structural damage as it was only detectable on magnetic resonance imaging of the sacroiliac joints (MRI-SIJ) [1]. Continuous non-steroidal anti-inflammatory (NSAIDs) intake has been reported as a potential factor reducing the sensitivity of MRI-SIJ to detect bone marrow edema (BME).

Objectives: The aim of the study was to investigate the effect of continuous NSAIDs intake on BME in nr-axSpA.

Methods: We undertook a cross-sectional study including nr-SpA according to the ASAS criteria and treated with NSAIDs at baseline. Socio demographic data as well disease characteristics were recorded. Disease activity parameters were also collected including the duration of morning stiffness, night awakenings, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). MRI-SIJ was performed for all the patients. All the images were screened for bone marrow edema with the corresponding sequence (short tau inversion). Patients were grouped according to NSAIDs intake: G1: continuous versus G2 occasional. The level of significance was fixed for $p<0.05$.

Results: The study included 43 nr-axSpA patients. There was a female predominance with a sex ratio of 0.43. The mean age of the patients was 42±12 years [20-71] and the mean disease duration was 17±9.7 years [4-38]. The mean morning stiffness duration was 47.3±45.6 [15-240] minutes. The mean spinal VAS was 5.9±2.6 [0-10]. Nearly 41% of the patients had an active disease with a mean BASDAI of 4.7± 2.1 [0-8.6]. The prescribed NSAIDs were as follows: Diclofenac (44 %), Indomethacin (8%), Ketoprofen (18%), Meloxicam (3%), Celecoxib (3%), Piroxicam (3%) and Naproxen (21%). Nearly half of the patients were continuously taking NSAIDs (52.6%) versus occasional intake (47.4%). Four patients failed two NSAIDs and were treated with a third one. Both groups were comparable for age (p=0.193), sex (p=0.386), and disease duration (p=0.4). Similarly, there were no statistically significant differences regarding disease activity parameters between both groups: numerical rating scale of pain (p=0.713), ESR (p=0.314), CRP (p=0.644), morning stiffness (p=0.428), night awakening (p=1), as well as BASDAI (p=0.514). Regarding MRI-SIJ findings, hyper signal in STIR sequence was comparable between both groups (G1: 35% vs G2:33%, p=0.914). Moreover, the increased signal with Gadolinium injection on T1-weighted images was similar between both groups (p=0.113).

Conclusion: Our study showed that continuous NSAIDs intake was not associated with significant changes in MRI-SIJ features. This study suggests that a NSAID-free period is not necessary before assessing bone marrow edema on MRI-SIJ.

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AB0769

TREATMENT OUTCOMES OF PATIENTS WITH BIOLOGICAL THERAPY DURING PREGNANCY AND EFFECT OF PREGNANCY PLANNING ON TREATMENT PREFERANCE OF RHEUMATOLOGISTS

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Background: Rheumatic diseases occur mostly in adults at reproductive age. In addition to the impact of disease course on fetal and maternal health, safety concerns regarding the effects of biological drugs on the course of pregnancy have come to the fore with the introduction and widespread use of them. Unlike other biological treatments, all tumor necrosis factor (TNF) antagonists can be used during pregnancy.
Objectives: To investigate clinical features, treatment characteristics and pregnancy outcomes of patients with biological treatment and evaluate impact of planning pregnancy on treatment preferance.
Methods: The study was planned between January 2015 and December 2021. Patients who received biological treatment at conception were determined retrospectively. Demographycal data, clinical features, treatment characteristics and pregnancy outcomes were recorded.
Results: 15 patients (mean age 37.2±4) were included. Mean age at diagnosis was 25.6±5.4 and age at gestational was 33±3.9. Mean follow-up duration was 96±55 months. Median period of biological therapy was found 37 (1-156) months. Six (40%) patients were diagnosed with Axial Spondyloarthritis, 6 (40%) Psoriatic Arthritis, 1 (6.6%) Rheumatoid arthritis. While 12 (80%) patients had planned (wanted) pregnancies, 10 (66%) patients were evaluated as eligible for pregnancy in terms of rheumatological disease by rheumatologists. 13 (86.6%) patients were in remission/partial remission before pregnancy. 5 (33.3%) patients were using steroid and *disease modifying anti-rheumatic drugs (DMARDs)* were stopped before conception. 10 (66.6%) patients were receiving certolizumab, 4 (26.7%) patients were receiving adalimumab. It was found that the treatment of the patient who received rituximab was interrupted due to the pregnancy planning. While certolizumab treatment continued in 6 (60%) patients during pregnancy, the treatment of patients receiving adalimumab was discontinued within first trimester. Activation of disease was occurred in 2 patients whose therapy interrupted. Biological treatment was restarted during pregnancy in 3 of 9 patients whose biological treatment was discontinued. No perinatal complication was developed except premature rupture of membranes in one patient. It was observed that all infants were healthy at birth, but baby of the mother who received certolizumab was diagnosed mental retardation in early childhood.
Conclusion: In this study, it was established that the majority of patients using TNF antagonist during pregnancy;
1-Having wanted/planned pregnancy,
2-Being in remission or low disease activity before pregnancy,
3-Not experiencing disease activation during pregnancy.
In this study, it was concluded that having a pregnancy plan may be an important factor for rheumatologists to decide type of TNF antagonist, and physicians tend to prefer certolizumab in patients with pregnancy plan.

Table 1. Baseline clinical and treatment characteristics

Age, years	**37.2±4**
Age, at diagnosis	25.6±5.4
Age, at gestation	33±3.9
Follow-up duration, months	96±55
Biologic treatment duration, months	37 (1-156)
Rheumatologic disease	**n (%)**
-Spondyloarthritis	6 (40)
-Psoriatic arthritis	6 (40)
-Rheumatoid arthritis	1 (6.6)
-Behcet disease	1 (6.6)
-Systemic lupus eritematosus	1 (6.6)
Biologic treatment	**n (%)**
-Certolizumab*	10 (66.6)
-Adalimumab*	4 (26.7)
Discontinuation of treatment	9 (60)
Restart	3 (33.3)
Disease activity	
Remission/partial remission*	13 (86.6)
Activation during pregnancy	3 (20)

**At conception*

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AB0770

TREATMENT OF ANKYLOSING SPONDYLITIS (AS) WITHIN 1 YEAR AFTER DELIVERY.

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Background: Prescribing therapy to women after childbirth is still a difficult task in Russia due to the well-established ideas among patients and pediatricians of the incompatibility of lactation and treatment. Monitoring AS activity in patients without lactation is also important: maintaining physical and mental health are necessary for full-fledged care of the newborn and the joy of motherhood.
Objectives: To describe the frequency of drug use in women with AS within 1 year after childbirth, to determine the relationship with AS activity, to compare the incidence of diseases in children under one year whose mothers received and did not receive AS therapy during breastfeeding.
Methods: 44 pts with confirmed AS (modified New York criteria, 1984) were followed within 1 year after childbirth. The average age of the pts was 32,5 ± 5,8 years. BASDAI at 1, 6 and 12 months after delivery was: 2,4 [1,4;4,2]; 2,6 [1,4; 4,4]; 2,7 [1,5; 4,1], respectively. ASDAS-CPR was: 2,0 [1,2; 2,7]; 1,9 [1,4; 2,5]; 1,7[1,3; 2,3], respectively. AS activity in pts with and without lactation did not differ. 41 pts (93,2%) had been continuing lactation during 1 month after delivery, 27 (61,4%) pts – during 1 month after delivery, 17 (38,6%) pts – during 1 month. Adherence to nonsteroidal anti-inflammatory drugs (NSAID) therapy was defined as the ratio of the actual dose taken to the prescribed dose. The total dose of NSAIDs was determined by the NSAID intake index (M. Dougados, 2001).
Results: NSAIDs. Ibuprofen was the drug of choice in pts with lactation, 51,2%, 74,1% and 88,2% of pts received it after 1, 6 and 12 months after delivery. Women without lactation received various NSAIDs in 100% of cases. The index of NSAID intake in pts with lactation increased during the first six months after delivery and after 1, 6 and 12 months after delivery and was 0 [0; 25], 33,3 [12; 42,1] and 33,3 [17; 50], respectively ($p < 0,05$ compared to 1 month after delivery). The index of NSAID intake at 1 and 12 months after delivery in pts without lactation was higher than in pts with lactation ($p < 0,05$). Adherence to NSAID therapy in pts with lactation increased during follow-up and after 1, 6 and 12 months after delivery was 10 [0; 100], 71 [30; 100] and 100 [50; 100], respectively ($p < 0,05$ compared to 1 month after delivery). There was no effect of NSAIDs intake on the AS activity.
Sulfasalazine (SSZ) because of arthritis in the 3rd trimester of pregnancy was received by 5 pts (11,4%); 2 of them independently canceled SSZ after childbirth due to fear of its negative effect on the baby during breastfeeding, both had recurrent arthritis within a year after childbirth. Against the background of lactation, only 1 woman received SSZ at a dose of 1,5 g per day.
bDMARD. During the year after childbirth, 17 (38,6%) pts had a need for bDMARD, however, for insufficient availability only 11 pts (25%) received bDMARD: 1 (certolizumab pegol, CZP) within 1 month after childbirth, 8 (CZP– 4, ADA – 4) within 2 – 6 months, 11 (CZP – 4, adalimumab – 4, infliximab – 1, golimumab – 1, etanercept – 1) within 7 – 12 months. Of these, 4 pts (all pf them intake CZP) received TNF inhibitors during lactation. AS activity in pts with and without lactation on the background of iTNF-alpha therapy did not differ. There was a clear trend of AS activity decreasing against the background of iTNF therapy: ASDACRP 6 and 12 months after delivery was 2,7 ± 0,6 and 2,4 ± 0,5, respectively. In pts with lactation, the same trend was noted: ASDACRP was 2,8 ± 0,5 and 2,1 ± 0,3, respectively.
There were no differences in the frequency of acute respiratory viral infections, atopic dermatitis, the need for antibiotics, and the frequency of hospitalizations in breastfed children whose mothers received and did not receive AS therapy during lactation.
Conclusion: NSAIDs in low doses do not affect AS activity. According to our data performed on a small group of patients with AS, the effectiveness of TNF-alpha therapy does not differ against the background of lactation and without it. It is necessary to increase the knowledge of patients and pediatricians about therapeutic possibilities during lactation to avoid unjustified drug cancellation.
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AB0771

EVALUATION OF THE EFFICACY OF INHIBITORS OF TUMOR NECROSIS FACTOR ALPHA FOR PATIENTS WITH ANKYLOSING SPONDYLITIS IN REAL CLINICAL PRACTICE.

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Background: The question of the comparative efficacy of tumor necrosis factor-alpha (TNF-α) inhibitors is topical today, because the research data that were distributed in random sequence mainly reflect the efficacy of the only specific drug, and the available data obtained in the ankylosing spondylitis (AS) treatment use of a network meta-analysis are limited.
Objectives: To make a comparative evaluation of the efficacy of various TNF-α inhibitors for patients with AS in real clinical practice.
Methods: The study involved patients with a reliable diagnosis of AS (according to the 1984 New York criteria) who received TNF-α inhibitor during the 12-month

course of therapy, from 2018 to 2022. The efficacy of the drugs was evaluated by the ASDAS (CRP) (Ankylosing Spondylitis Disease Activity Score) and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) – disease activity indices obtained 6 and 12 months after the start of therapy. Comparison of indicators between drugs was carried out using a non-parametric Kruskal-Wallis test, designed to test the equality of the medians of several samples.

Results: The study involved 257 patients with AS who were treated with various TNF-α inhibitors, among which Adalimumab was taken by 77 patients (29.96%), Golimumab - 20 (7.78%), Infliximab - 15 (5.84%), Certolizumab pegol - 27 (10.51%) and Etanercept - 118 (45.91%). The mean age of the involved patients was 46.1 ± 11.4 years old, the mean age at the onset of the disease was 28.7 ± 11.7 years old. The majority of patients were males - 167 (64.98%), 143 (55.64%) had Higher education, 163 (63.42%) were married, 103 (40.08%) have been working and - 150 patients (58.37%) had never smoked before the study. Mean ASAS (CRP) and BASDAI, disease activity indices, values for each drug before therapy, 6 and 12 months after the start of therapy are presented in Table 1. «Head-to-head» comparison of medical preparations revealed no significant differences between TNF-α inhibitors in terms of the studied parameters (p > 0.05).

Table 1.

	Months since start of therapy	BASDAI	ASDAS (CRP)
Adalimumab	0	5,84	3,38
	6	3,52	1,91
	12	4,11	2,24
Golimumab	0	5,91	3,29
	6	5,17	2,91
	12	4,61	2,68
Infliximab	0	3,56	2,25
	6	2,59	1,08
	12	2,20	1,39
Certolizumab pegol	0	6,57	3,80
	6	3,38	2,17
	12	3,50	2,81
Etanercept	0	6,13	3,79
	6	3,75	2,20
	12	3,80	2,28

ASDAS - Ankylosing Spondylitis Disease Activity Score; BASDAI - Bath Ankylosing Spondylitis Disease Activity Index; CRP - C-reactive protein

Conclusion: The studied TNF-α inhibitors demonstrate similar clinical efficacy in real clinical practice. A direct comparison of drugs didn't reveal significant differences between TNF-α inhibitors.

Disclosure of Interests: None declared

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AB0772 SAFETY AND SURVIVAL ANALYSIS OF SECUKINUMAB TREATMENT IN A COHORT OF RHEUMATIC PATIENTS NAÏVE TO BIOLOGICAL THERAPY

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Background: Secukinumab is a fully human monoclonal antibody that selectively binds to IL-17A and inhibits the interaction with the IL-17 receptor. IL-17A plays a key role in the pathogenesis of plaque psoriasis, psoriatic arthritis (PsA), ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (SpA).

Objectives: To describe the safety and survival profile of treatment with Secukinumab in a cohort of patients (pac) with PsA, AS and non-radiographic SpA naïve to biological therapy.

Methods: Descriptive observational study. Patients: Cohort of patients with PsA, AS and non-radiographic SpA from the Rheumatology Service of the H.U.V. del Rocío of Seville who undergo treatment with Secukinumab 150mg sc/m as the first line of biological treatment. Main variable: Secukinumab suspension due to adverse event (AE) (mild: requires suspension, serious: hospital admission or death), inefficacy (primary or secondary failure), decision of the pac, clinical remission or other reasons.

Secondary variables: age, sex, type of disease (PsA, AS or non-radiographic SpA), clinical manifestations (axial, peripheral affectation and both) other clinical manifestations (cutaneous affectation, enthesis and/or dactylitis). Time from diagnosis to start of biological therapy (months) and exposure time to Secukinumab (months). Concomitant treatment with DMARDs. Statistical analysis: The statistical package SPSS v21 was used. Qualitative variables were analyzed using the Chi2 and Fisher tests, as required. It was considered statistically significant, p values <0.05. Survival analysis was performed using Kaplan-Meier survival curves, compared using the Log-Rank test.

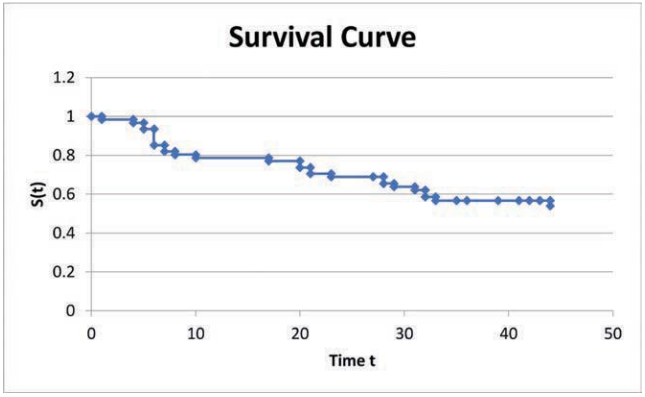
Results: 171 patients who underwent treatment with Secukinumab during their disease were analyzed. A total of 61 patients naïve to biological therapy were included. The baseline characteristics of the sample are shown in Table 1. The patients received treatment with Secukinumab for a median of 35m (SD +/- 17.5m). The drug was suspended in 27 patients; In 19 patients (70%) due to inefficiency (11 due to primary failure and 8 due to secondary failure); in 5 patients due to mild AD (1 patient with mucocutaneous candidiasis); 3 patients due to loss of follow-up and 1 patient for their own decision. There were no serious AEs. The average exposure time of the drug was 32.7 months. Drug survival was 85%, 76%, 68%, and 56%, at 6 months, 1, 2, and 3 years, respectively, with an overall survival of 69%.

Table 1. Basal features

Gender, men	36 (59%)
Age, years (average, SD)	47,8 (+/- 13,3)
Disease:	
-Psoriatic arthritis	36 (59%)
-Ankylosing spondylitis	22 (36%)
-Non-radiographic axial spondyloarthritis	3 (5%)
Disease time of evolution, years (average, SD)	12,6 (+/- 8)
Time from diagnosis to start of biological therapy with Secukinumab, years (median)	6
Clinical manifestations (%):	
-Axial involvement	32 (52%)
-Peripherical involvement	43 (70%)
-Axial and peripherical involvement.	31 (50,8%)
Other manifestations:	
-Enthesis	18 (29%)
-Dactylitis	17 (27%)
Concomitant treatment with DMARDs after 6 months of treatment with Secukinumab (n, %):	
-Methotrexate	19 (31%)
-Leflunomide	7 (11,5%)
-Sulfasalazine	6 (9,8%)

There was no association between the different diagnoses and drug suspension, both variables were independent (p=0.702) with a 5% significance level. There was also no evidence of a significative relationship between the type of involvement (axial/peripheral/both), and the suspension of treatment (p=0.743).

Conclusion: The suspension of the drug due to AEs was small in our sample (8,2%) and the AEs detected were mild (including a mucocutaneous candidiasis). No serious AEs were observed. We found an overall drug survival of 70% in our study. These data are consistent with those published in the different clinical trials of the drug (FUTURE I, II and V, MEASURE I, II and III, PREVENT...). Therefore, we can conclude that Secukinumab constitutes a drug with a good security profile.



Disclosure of Interests: None declared

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AB0773 SERUM VEGF LEVEL MAY BE HAVE A ROLE IN THE EVALUATION OF TREATMENT RESPONSE AND DISEASE ACTIVITY DURING TNFI THERAPY IN PATIENTS WITH AXSPA

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Background: Patient reported outcomes (BASDAI and BASFI) are used to evaluate disease activity in axial spondylarthritis (axSpA), however, apart from C-reactive protein (CRP) there are no widely used serum biomarkers to assess disease activity and treatment responce.

Table 1. The factors associated with serum VEGF levels longitudinally

	Univariate analiz		BASDAİ+CRP Model		ASDAS -CRP Model	
	B (%95 CI)	**p**	**B (%95 CI)**	**p**	**B (%95 CI)**	**p**
Hip involvement	181.74 (12.71- 350.77)	**0.035**	357.04(112.35- 601.73)	**0.04**	338.36 (102.40-574.3)	**0.005**
Duration of delay in diagnosis	-6.91 (-14.05- 0.24)	**0.058**	-13.93 (-24.56 to -3.31)	**0.01**	-14.36 (-24.68 to -4.03)	**0.006**
Gender	-216.88 (-390.6 to -43.2)	**0.014**	-154.23 (-336.94- 28.48)	**0.09**	-162.6(-336.70- 11.4)	**0.006**
HLA-B27 positivity	-233.4 (-440.67 to -26.11)	**0.027**	-135.78(-326.08- 54.52)	0.16	-126.54(-309.2- 56.1)	0.17
BASDAI	4.12 (1.06- 7.18)	**0.008**	5.60 (2.16- 9.05)	**0.001**		
ASDAS-CRP	110.04 (58.18- 161.88)	**<0.001**			132.31(74.70- 189.92)	**<0.001**
Serum CRP level	5.86 (1.02- 10.7)	**0.018**	4.09 (-0.99- 9.183)	0.11		

Objectives: In this study, we aimed to evaluate the relationship between serum biomarkers (serum leptin, VEGF, MMP-3) and disease activity as well as the changes of those biomarker levels during TNFi treatment.

Methods: Patients with axSpA who put on their first TNFi and had serum samples at baseline and 6th month of therapy were included in the analysis The demographic, clinical and laboratory characteristics disease activity and function parameters (BASDAI, BASFI, ASDAS-CRP, serum CRP levels) at baseline and 6th months were recorded. Levels of serum leptin, VEGF and MMP-3 were studied by ELISA method. The relationship between serum biomarkers and disease activity scales in addition CRP levels were tested by correlation analysis. The factors affecting the change in seruml biomarkers level in 6th month were also analyzed by GEE which is a longitudanal analysis method.

Results: A total of 74 patients (mean age (SD) 48.7 (12.8) years, 54.1% male, 68.9% with AS) were included in this study. Baseline median BASDAI scores (IQR) were 5.8 (2.4), ASDAS scores (IQR) 3.7 (1.5) and median CRP levels (IQR) 12 (23). Disease activity parameters (BASDAI, BASFI, ASDAS-CRP) were significantly decreased at 6th month of therapy (p<0,001, p<0,001, p<0,001, respectively). The correlation between baseline serum biomarker levels (leptin, MMP3, VEGF) and between biomarkers level and disease activity were eveluated and only serum MMP-3 levels were found to be associated with baseline ASDAS-CRP (p=0.02). Serum VEGF level decreased significantly compared to the baseline at the 6 th month of TNFi treatment (p<0.001), however, serum leptin and MMP-3 levels were not associated with disease activity and affected by biologic treatment (p=0.89, p=0.50, respectively). In the longitudinal analysis, serum VEGF level were significantly associated with gender, hip involvement, delay in diagnosis in addition to disease activity (Table 1).

Conclusion: TNFi treatment is not only effectively control disease activity but also cause significant decrease in serum VEGF levels in patients with axSpA. Considering the role of VEGF in radiographic progression it could be a promising biomarker in axSpA

Disclosure of Interests: None declared

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AB0774

PARADOXICAL REACTIONS, ESPECIALLY PSORIASIS IN RHEUMATOLOGY PATIENTS RECEIVING BIOLOGIC THERAPY FROM THE TREASURE DATABASE: A 5-YEAR FOLLOW-UP STUDY

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Background: Biologic agents have altered our ability to treat chronic inflammatory diseases effectively. Although paradoxical reactions (PRs) were initially described with TNF-α inhibitors, they have been reported with newly developed biologic agents or classes too (1). Due to the potential consequences of PRs, it is critical to identify and treat these drug class side effects as soon as possible.

Objectives: The aim of this study was to characterize PRs, especially psoriasis, in a large cohort of patients treated with biologic agents and to investigate their clinical implications.

Methods: TReasure database, which was launched in 2017, is a web-based prospective observational cohort comprised of patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA) from 17 centers located throughout Turkey. Characteristics of patients with PRs and clinicians' treatment approaches and outcomes were evaluated using descriptive statistics.

Results: 3147 RA and 6071 SpA patients were evaluated. 139 (1.5%) patients (40 (28.8%) with RA and 99 (71.29%) with SpA) developed a PRs (Table 1). The rate of paradoxical psoriasis was 90.6% and 9.7% of the patients had a family history of psoriasis. Females constituted 64% of the patients. The mean age was 46±12 years and the disease duration were 146±92 months. Mean time interval between the PRs and diagnosis was 99,6±86 months, whereas median 12 (1-132) months between the PRs and the biological agent. Adalimumab (30.9 %), etanercept (20.1 %), and infliximab (18.7 %) were the three most frequently used agents during the PRs. However, 8.6% of the patients developed PRs with non-TNF agents. Only seven patients (5.1%) who had PRs discontinued the drug, while 28 patients (20.6%) continued to receive the agent that caused the PRs. Majority of patients were switched to other TNF-α inhibitors (48.5%) and non-TNF agents (25.7%). When we limited our analysis to paradoxical psoriasis patients, we observed complete remission in 43.5% of patients and progression in only six (4.7 %) of patients. (Figure 1).

Table 1. Characteristics of RA and SpA patients who developed paradoxical reactions

	N	Patients (N, %)
Paradoxical reactions (PRs)	139	
Psoriasis		126 (90.6%)
Uveitis		6 (4.3%)
Sarcoidosis		2 (1.4%)
IBD		1 (0.7%)
Other*		4 (4.3%)
Primary disease	139	
RA		40 (28.8%)
SpA		99 (71.29%)
Time interval between PRs-diagnosis of RA/SpA (months)	124	99,6±86† 72 (3-420) ††
Time interval between PRs-biological onset (months)	126	22±25† 12 (1-132) ††
BMI, kg/m^2	123	28±5† 27,8 (17,3-49,7) ††
Smokers (Current/ex)	131	61 (46.6%) / 10 (8.5%)
Biological agents used during PRs	139	
TNF-α inhibitor used**		127 (91.3%)
Secukinumab		2 (1.4%)
Abatacept		6 (4.3%)
Rituximab		4 (2.9%)
Biological agents used after PRs	101	
Etanercept		31 (22.8%)
Adalimumab		15 (11%)
Secukinumab		12 (8.8%)
Other***		43 (57.5%)

PRs: Paradoxical reactions IBD: Inflammatory bowel disease. *Drug-induced lupus:3 Vasculitis:1. ** Adalimumab: 43 (30.9%), Etanercept: 28 (20.1%), Infliximab: 26 (18.7%), Certolizumab: 20 (14.4%), Golimumab: 10 (7.2%). *** Certolizumab: 9 (6.6%), Tofacitinib: 9 (6.6%), Infliximab: 7 (5.1%), Tocilizumab: 5 (3.7%), Golimumab: 4 (2.9%), Ustekinumab: 4 (2.9%), Rituximab:3 (2.2%), Abatacept: 1 (0.7%), Anakinra: 1 (0.7%). † mean ± standard deviation. †† median (min-max)

Conclusion: Clinicians should be aware that PRs may develop with biologic agents other than TNF-α inhibitors. Additionally, it is important to keep in mind that the development time of PRs could be variable. The mechanism(s) behind PRs remain unknown, and there is no currently available diagnostic or therapeutic protocol (2). The decision whether to continue or discontinue biologic agents should be individualized. We found that the majority of patients can be managed without discontinuing biologic agents. Finally, we believe that the experience of our large cohort can help physicians in clinical practice where sufficient protocol is lacking.

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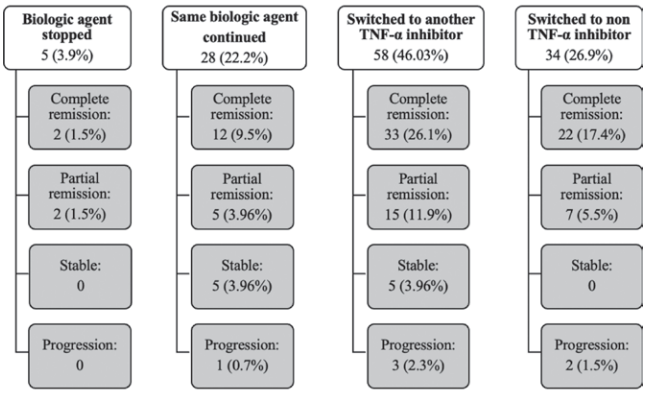
Figure. Management and outcomes of patients with **paradoxical psoriasis (N (%))** *



* The total number was not matched because the data of some patients could not be accessed.

Disclosure of Interests: None declared
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AB0775 EFFICACY, SAFETY AND SURVIVAL OF SECUKINUMAB IN SPONDYLOARTHRITIS.

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Background: Secukinumab (SCK) is a fully human monoclonal antibody that selectively inhibits IL-17A indicated for both axial and peripheral spondyloarthritis (SpA) and psoriatic arthritis (PsA). In this paper we present our experience with SCK since its approval, in a tertiary hospital.
Objectives: To describe the efficacy, survival and safety of SCK treatment in real clinical practice in patients with SpA and PsA.
Methods: We performed a descriptive, retrospective analysis of patients diagnosed with SpA according to ASAS criteria and PsA according to CASPAR criteria. For this purpose, data were collected from the medical records of 75 patients treated with SCK in the rheumatology service.
To evaluate efficacy in the Spa group, analytical variables (C-reactive protein (CRP)), the Ankylosing Spondylitis Disease Activity Score (ASDAS) scale and the patient's visual analog scale (VAS) were analyzed. In the PA group, VAS and CRP were assessed at baseline and at 12 months. Survival was evaluated with respect to the causes of drug discontinuation and its association with individual baseline characteristics, such as metabolic syndrome. Safety was evaluated by analyzing intercurrent infections or neoplasms requiring discontinuation.
Results: Seventy-five patients with spondyloarthritis included in treatment with SCK were analyzed, 40 had Spa and 34 had PAs. The mean age at diagnosis was 45.1 years (SD 11.3) and the median time from diagnosis to onset of SCK was 4.5 years (IQR 1-10) (Table 1).

Table 1. Baseline characteristics

	SpA	APs	Total
Age at diagnosis	45.1 (SD11.8)	44.9 (SD10.9)	45.1 (SD11.3)
Age at begging of SCK	53.5 (SD 9.3)	52.2 (SD 10)	52.9 (9.6DE)
Hypertension	10 (25.0%)	10 (29.4%)	20 (27.0%)
Dyslipidaemia	17 (42.5%)	17 (51.5%)	34 (46.6%)
Diabetes mellitus	5 (12.5%)	6 (17.6%)	11 (14.9%)
Body Mass Index	27.9 (SD4.4)	30.5 (SD8.4)	29.2 (SD6.7)
Tobacco	14 (35.0%)	10 (29.4%)	24 (32.4%)
Cardiovascular disease	5 (12.5%)	2 (5.9%)	7 (9.5%)
Previous sDMARD			
-Methotrexate	13 (32.5%)	24 (70.6%)	37 (50%)
-Leflunomide	1.7% (15%)	12 (35.3%)	18 (24.2%)
Initial corticosteroids	7 (18.4%)	15 (44.1%)	22 (30.6%)

Fifty-seven patients (76%) were on treatment with anti-TNF prior to SCK initiation. The mean number of anti-TNF prior to SCK was 1.8 (SD 1.2). Twenty-six patients (35.1%) received were on treatment with SCK at a dose of 150 mg and 48 (64.9%) with 300 mg every 4 wk. The mean CRP before starting SCK was 8.46 mg/L (SD 18.38) and VAS 4.83 (SD 2.99).
Statistically significant improvement was observed in both pathologies in VAS (-2.1 SD 3.1) (p 0.003). Despite the improvement in CRP, in both groups of -3.7 mg/L (SD 15) was not statistically significant. Regarding ASDAS, in the Spa group, 2 patients (5.3%) showed great improvement (>3.1), 9 patients (23.7%) clinical improvement (>1.1), 17 patients (42.5%) improvement (<1.1), 6 patients (15%) showed no improvement and 4 patients (10.5%) worsening.
The overall drug survival to date is 19.41 months (SD 13.76), 20.6 months (SD 14.8) in the Spa group and 18 (SD 12.6) in the AP group (Figure 1).

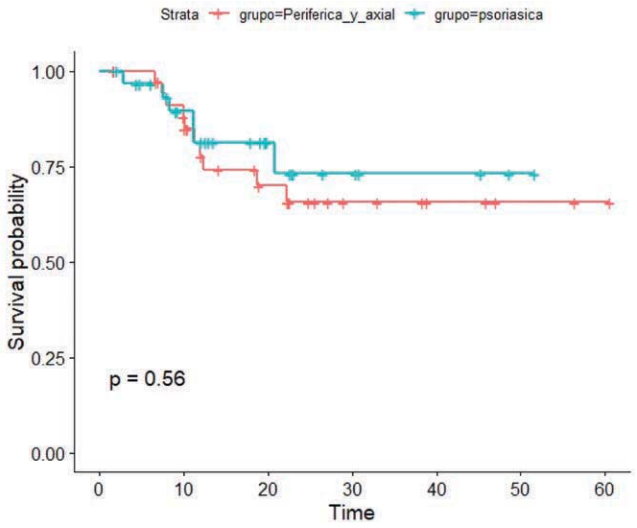

Figure 1. Secukinumab survival in both groups

17 patients (23%) discontinued treatment, with a median duration of 12 months (SD 4.66). 12 (70.6%) due to ineffectiveness, 1 (5.9%) by their own decision, 3 (17.6%) due to persistent mechanical pain and 1 (5.9%) due to neoplasia (gastric adenocarcinoma). The clinical variables of metabolic syndrome were evaluated (Table 1) none of these characteristics had a statistically significant association as a cause of drug discontinuation. No patient presented infections that required discontinuation of the drug. No association was detected between drug discontinuation or the development of metabolic syndrome.
Conclusion: In our cohort, SCK showed a statistically significant improvement in the VAS scale in both groups. A 23.7% of patients with Spa showed clinical improvement according to ASDAS values, 5.3% showed great improvement and 42.5% showed mild improvement. The overall drug survival to date is 19.41 months (SD 13.76) slightly longer in the SpA group than in APs. SCK seems to be a safe drug as none of our patients presented infections during its use.
Disclosure of Interests: None declared
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AB0776 CLINICAL AND LABORATORY PECULIARITIES OF TREATMENT-REFRACTORY ANKYLOSING SPONDYLITIS.

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Background: Despite the availability of newest guidelines for the treatment of ankylosing spondylitis and various groups of genetically engineered biological drugs, there are still patients with refractory, i.e., resistant to therapy (with two or more genetically engineered drugs), AS, maintaining high clinical and laboratory activity.
Objectives: To analyze the clinical peculiarities of patients with refractory AS and to identify markers for early detection of such cases.
Methods: Patients who received 2 or more GEBDs and demonstrated a primary or secondary failure were considered cases of refractory ankylosing spondylitis. Twenty-four (16 %) patients with refractory AS (mNYC 1984) were enrolled, including 14 males, 10 females. This group was selected from 150 successive AS patients admitted to the clinic of the Scientific Research Institute of Rheumatology in 2020–2021. Ninety-three per cent of patients had HLA B 27, the mean age was 39 [31.5;49] years, the age of onset of the disease was 21.7 [15.5;29] years, the duration of the disease was 17.3 [11;24]. They were treated with drugs of various groups (i-TNF-α, IL-17, 6 and Janus kinase inhibitors). The refractory AS patients were compared to a control group with the corresponding gender, age of onset and duration of the disease admitted successively to the Institute during the same period.
The examination followed the ASAS recommendations. All patients had additional nephelometric assay of SAA level using commercial reagent kits, reference value < 5 mg\L.

Results: Median SAA, CRP, ESR levels, BASDAI, ASDAS scores and correlation indicators are shown in Table 1.

Parameters	Refractory AS	Control	p
Median			
SAA, Me [25th; 75th percentiles]	53.6 [15.75;205.5]	10.7 [4.9;31.1]	p = 0.001
CRP, Me [25th; 75th percentiles]	16.35 [3.55;63.1]	11 [4.9;29.3]	p = 0.001
ESR, Me [25th; 75th percentiles]	35 [20.5;110]	29.1 [13.9;48.1]	p = 0.001
BASDAI, Me [25th; 75th percentiles]	5.95 [4.85;6.6]	5.2 [4.8;6.1]	p = 0.126
ASDAS-CRP, Me [25th; 75th percentiles]	3.8 [3.11;4.49]	2.8 [2.2;3.2]	p = 0.020
Peripheral arthritis, %	87.5	79.2	
Enthesitis, %	66.6	70	
Coxitis, %	75	71.5	
Knee and hip replacement, %	20.8	8.3	
The onset of the disease			
- urogenital infection, %	54	8.3	
- juvenile onset, %	30	30	
Correlation			
SAA and CRP	r = 0.82	r = 0.55	p < 0.001 and p < 0.001
SAA and ESR	r = 0.8	r = 0.5	p < 0.001 and p < 0.001
SAA and BASDAI	r = 0.2	r = 0.3	p = 0.330 and p = 0.421
SAA and ASDAS	r = 0.3	r = 0.4	p = 0.006 and p < 0.001
CRP and ESR	r = 0.8	r = 0.56	p < 0.001 and p < 0.001
CRP and ASDAS	r = 0.3	r = 0.4	p = 0.295 and p < 0.125

The refractory AS group had a higher SAA level compared to that of the control group (53.6 and 10.7, p = 0.001). There was no significant difference in the SAA, CRP levels, BASDAI and ASDAS scores. There was a strong association between SAA level and CRP level, ESR; correlation with BASDAI and ASDAS was non-significant and moderate.

The clinical presentation was dominated by peripheral arthritises 87.5% and coxitises 75%, followed by enthesopathies 66.6%. No significant differences from the control group were observed. At the onset of the disease, a urogenital infection was detected in 54% of patients with refractory AS.

Conclusion: Patients with refractory AS demonstrate higher levels of SAA in the clinical presentations. Patients with the onset of reactive arthritis prevail. A study of new markers, including genetic ones, is required to identify a refractory disease at an early stage.

Disclosure of Interests: None declared

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AB0777 INFLUENCE OF TNF INHIBITORS ON SUBCLINICAL ATHEROSCLEROSIS IN SPONDYLOARTHRITIS PATIENTS

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Background: Spondyloarthritis is a chronic inflammatory disease associated with increased cardiovascular morbidity and mortality due to accelerated atherosclerosis. Recent studies have reported the benefit of TNF inhibitors in reducing the risk of cardiovascular events and its association with changes in lipid profile. Nevertheless, it remains controversial.

Objectives: We aimed to investigate the effect of TNF inhibitors on subclinical atherosclerosis assessed with carotid intima-media thickness (CIMT) and flow mediated dilatation (FMD) in patients with spondyloarthritis (SpA).

Methods: We performed a cross sectional study including 47 patients meeting ASAS 2009 criteria for SpA. Patients with traditional cardiovascular risk factors were excluded. We collected clinical data, therapeutic modalities and biological tests including total cholesterol, HDL, LDL and triglyceride after 12 hours of fasting. FMD and mean CIMT (mean value of right and left carotid artery) were measured with a Mindray Resona 7 ZST+ ultrasound machine by an experienced radiologist.

Results: Among the 47 subjects, 18 patients (38%) were receiving TNF inhibitors for a median duration of 36 months (IQR 25-75%: 24-72) (9 were on Etanercept, 7 were on Adalimumab, one patient was on Infliximab and one was on Golimumab). The group treated with TNF inhibitors had a median age of 43 years (IQR 25-75%: 36-46.5) and a median duration of the disease of 12 years (IQR 25-75%: 9.5-22). Median ASDAS and BASDAI scores were 2.40 (IQR 25-75%: 1.48-3.1) and 2.60 (IQR 25-75%: 1.55-3.75) respectively. On the other hand, patients naïve to TNF inhibitors had a median age of 32 years (IQR 25-75%: 55-42), median disease duration of 7 years (IQR 25-75%: 3-12.5), median ASDAS of 2.13 (IQR 25-75%: 1.61-2.91), and median BASDAI of 2.40 (IQR 25-75%: 1.55-3.75). When comparing the two groups, there was no significant difference regarding disease activity scores ASDAS (p=0.431) and BASDAI (p=0.793) as well as biochemical variables; total cholesterol (p=0.483), HDL (p=0.395), LDL (p=0.263) and triglyceride (0.092). In contrast, patients on TNF inhibitors were significantly more aged (p=0.009) and had a significantly higher duration of the disease (p=0.004). Doppler ultrasound examination showed a median CIMT of 0.56 mm (0.48-0.64) in patients treated with TNF inhibitors versus 0.55 mm (0.48-0.60) in patients naïve to TNF inhibitors with no significant difference (p=0.238). Patients on TNF inhibitors had lower values of FMD (with a median of 12.5 (6.7-16) versus 15.5 (10-24.5)). However this difference was not significant (p=0.182).

Conclusion: In our study, biological treatment with TNF inhibitors did not affect endothelial function and subclinical atherosclerosis in patients with spondyloarthritis. Given the small size of our study population and its heterogeneity in terms of age and duration of the disease, no conclusions can be drawn. Further longitudinal studies that involve larger samples are necessary.

Disclosure of Interests: None declared

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AB0778 BASELINE CRP LEVEL AND RESPONSE TO INFLIXIMAB TREATMENT IN SPONDYLOARTHRITIS

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Background: The treatment of spondyloarthritis (SpA) is based on cDMARDS (Conventional disease-modifying anti-rheumatic drugs) and bDMARDS (Biologic disease-modifying anti-rheumatic drugs) and aims at remission or low disease activity. Elevated C-reactive protein (CRP) is a good marker of inflammation [1].

Objectives: Our goal was to find a link between the CRP level and the response to infliximab.

Methods: Retrospective study was conducted in the rheumatology department at the University Hospital of Fez from January 2011 to January 2021. The patients were recruited according to the ASAS 2009 criteria (Assessment of Spondyloarthritis International Society). A negative CRP is defined as less than or equal to 6mg / L and the ESR (Erythrocyte Sedimentation Rate) according to age. The main criteria for evaluating the response to the biological at 3, 6 and 12 months are: BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and ASDASCRP (Ankylosing Spondylitis Disease Activity Score). The secondary criteria are: global evaluation (EVA) and ESR. They were divided into 2 groups according to the CRP while seeking its link with the response to infliximab and with the other epidemiological, clinical and biological parameters.

Results: 375 SpA patients including 65 on infliximab: 50.8% men and 49.2% women. Mean age was 43.40(±1.86) years. Average duration of evolution was 7.71(±6.33) years. Mean baseline CRP was 35.1(±42.7) mg/L. Mean baseline ASDASCRP was 4.04(±1.49). 77.4% had a good ASDAS CRP response to treatment and 22.6% had no response. 59.7% had a good answer according to BASDAI. The bivariate analysis did not find a significant relationship between the initial CRP and the main treatment response criteria: ASDASCRP (p=1) BASDAI (p=0.14), nor with ESR (p= 0.09) and overall EVA (p=0.1).

Conclusion: No relationship was found between baseline CRP and disease remission. Further studies with a larger sample would be needed to discuss these results.

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AB0779

COMPARISON OF TNF-α INHIBITORS EFFICACY BETWEEN RHEUMATIC DISEASES AND INFLAMMATORY BOWEL DISEASES

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Background: The features of the underlying immune-mediated disease can affect the efficacy of TNF-α inhibitors (TNFi). No previous studies compared head-to-head the efficacy of TNFi between rheumatic diseases (RD) and inflammatory bowel diseases (IBD).
Objectives: To compare the efficacy of TNFi in the treatment of RD (ankylosing spondylitis (AS) and rheumatoid arthritis (RA)) and IBD (Crohn's disease (CD) and ulcerative colitis (UC)).
Methods: 123 patients were included into the study. 70 of them had RD (50 (40.7%) patients with AS, 20 (16.3%) with RA) and 53 patients had IBD (38 (30.9%) with CD and 15 (12.2%) with UC). The patients received infliximab (INX, 13 (18.6%) with RD and 23 (43.4%) with IBD), adalimumab (ADM, 36 (51.4%) with RD and 13 (24.5%) with IBD) or certolizumab pegol (CZP, 21 (30%) with RD, 17 (32.1%) with IBD). The response to the treatment was evaluated by ASAS20 for AS, EULAR criteria for RA, decrease in CDAI of ≥100 points for CD and Mayo Score decrease for UC. Statistical analysis was performed using the standard methods of descriptive statistics, Chi-squared test and Fisher's exact test for categorical variables, incidence rate and incidence rate ratio calculation, Student t test for continuous variables. Survival analysis was performed using Kaplan–Meier method and Cox proportional hazards regression. Log rank test was used to statistically compare the curves and p value was calculated.
Results: 95 (77.2%) patients were still responding to TNFα inhibitor after 23 [8; 24] months of observation. 10 (14.3%) patients in RD group and 18 (33.96%) patients in IBD group had loss of response to the treatment. Thus, the response rate of TNF inhibitor in RD patients was 1.3 times higher than among IBD patients (OR 1.298, 95%CI 1.046 to 1.61, p=0.016). Similarly, patients with AS responded to the treatment 1.3 times more often than patients with CD (86% vs 65.79%, OR=1.307, 95%CI 1.013 to 1.687, p=0.025). The efficacy rate of INX and ADM was comparable between the RD and IBD groups (23.1% vs 34.8%, for INX and 16.7% vs 30.8% for ADM, p>0.05) while loss of response to CZP developed more frequently among patients with IBD that with RD (35.3% vs 4.8%, OR 1.472, 95%CI 1.023 to 2.0, p=0.031). Incidence rate (number of cases of inefficacy per 100 patient-years) of TNFα inhibitor inefficacy was much higher in IBD than in RD (5.43 vs 17.02 cases per 100 patient-years, IRR 3.13, 95%CI 1.37 to 7.59, p=0.0033). The same ratio was observed between CD and AS patients (16.92 vs 5.29 cases per 100 patient-years, IRR 3.19, 95%ДИ 1.19 to 9.46, p=0.012). Median time to loss of response was 28.00±8.08 months in RD patients and 21.11±2.63 months in IBD patients (p>0.05). Only among patients taking INX the duration of therapy at the time of loss of response was significantly shorter in IBD group than in RD group (26.0±4.62 vs 53.67±13.37 months, p=0.03, Student t test 2.575). Event-free survival of the treatment (maintenance of efficacy during the whole period of observation) was significantly higher among RD patients than IBD patients (Log-rank test=8.1, plog-rank=0.0044). Cox proportional hazards regression was used to analyze the time to inefficacy, and a hazard ratio of 2.999 (95%CI 1.35 to 6.61, p=0.0052) was reported for IBD patients. This means that at any random time point patients with IBD have 74.9% probability of developing loss of response ealier than patients with RD.
Conclusion: TNFi are more efficient for the treatment of AS and RA than for IBD (CD and UC).
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AB0780

ASSOCIATION OF LOW TROUGH LEVEL OF TNFI AND THEIR IMMUNOGENICITY WITH EFFICACY IN RHEUMATIC DISEASES AND INFLAMMATORY BOWEL DISEASES

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Background: The immunogenicity of TNF-α inhibitors (TNFi) is known to affect the efficacy of these biologic drugs. No previous studies compared this effect head-to-head between different groups of immune-mediated diseases.
Objectives: To compare the effect of immunogenicity of TNFi and their trough level on their efficacy in rheumatic diseases (RD) (ankylosing spondylitis (AS) and rheumatoid arthritis (RA)) and inflammatory bowel diseases (IBD) (Crohn's disease (CD) and ulcerative colitis (UC)).
Methods: 123 patients receiving infliximab (INX) (n=36, 29.3%), adalimumab (ADM) (n=49, 39.8%) and certolizumab pegol (CZP) (n=38, 30.9%) were included into the study. 70 (56.9%) of them had RD (50 (40.7%) with AS and 20 (16.3%) with RA) and 53 (43.1%) of them had IBD (38 (30.9%) with CD and 15 (12.2%) with UC). The specific criteria were used to assess the response to the treatment (ASAS20 for AS, EULAR for RA, CDAI for CD and Mayo Score for UC). Measurement of trough level of TNFi and the level of anti-drug antibodies (ADAb) was performed with the use of commercially available ELISA kits. The threshold of low trough level depended on the diseases based on the guidelines: 1 μg/mL for INX[1] in RD group and 5 μg/mL for INX[2] in IBD group, 5 μg/ml for ADM[3], and 20 μg/l for CZP[4].
Results: Efficacy of TNFi was 1.3 times more prevalent among patients with RD than among IBD patients (n=60, 85.7% vs n=35, 66%, OR 1.3, 95%CI 1.0 to 1.6, p=0.01). Rate of response to INX and ADM was comparable between the diseases while CZP was more efficient in RD (4.8% vs 35.3%, OR 1.5, 95%CI 1.0 to 2.0, p=0.031). Median trough levels of TNFi did not differ between the groups (p>0.05). Low level was determined in 26 (40.6%) patients with RD and 27 (45.8%) patients with IBD. Low level of TNFi most often was found in patients with UC (n=12, 80%, OR 5.6, 95%CI 1.493 to 20.999, p=0.006). Only INX low level was more prevalent in IBD patients than in RD (87% vs 46.2%, OR 5.7, 95%CI 1.1 to 29.2, p=0.046). The rate of low level of other TNFi was comparable between the groups (p>0.05). In RD group low level was associated with loss of response (80%, OR 6.0, 95%CI 1.2 to 30.7, p=0.036) while in IBD group no relation was found (51.4% vs 50%, p>0.05). Positive ADAb were determined in 22 (17.9%) patients: 14 (20%) in RD group and 8 (15.1%) in IBD group. TNFi did not differ significantly by the rate of ADAb-positivity (p>0.05). Association of loss of response with ADAb was observed in 4 (40%) patients with RD and 2 (11.1%) patients with IBD. Inefficacy of TNFi due to immunogenicity was 6 times more frequent in RA than in IBD (p>0.05). ADAb to INX (a chimeric antibody) were found only in patients with inefficacy (n=2, 66.7%, p=0.067). After exclusion of patients receiving ADM (a humanized antibody) 3 (75%) non-responders to INX or CZP with RD had positive ADAb while significantly less non-responders among IBD patients were ADAb-positive (n=2, 14.3%; OR 0.06, 95%CI 0.004 to 0.84, p=0.044).
Conclusion: Most of non-responders with RD had either low trough level of TNFi or ADAb, while in IBD group only half of cases of non-response could be attributed to the effect of ADAb or low trough level of TNFi.
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Spondyloarthritis - clinical aspects (other than treatment)

AB0781 MALAYSIA SPONDYLARTHRITIS ACCELERATED MANAGEMENT (SAM) MODEL: EXPEDITING AXSPA PATIENT JOURNEY FROM EARLY REFERRAL, DIAGNOSIS AND ACCESS TO OPTIMAL CARE

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Background: Axial spondyloarthritis (axSpA) is an important cause of inflammatory back pain (IBP). It is under-recognized, leading to significant delays in diagnosis. Early recognition and diagnosis are crucial to achieve the best outcomes for patients and in Malaysia, significant gaps in the clinical management of axSpA remain. Therefore, we sought to implement a strategy to improve the time to diagnosis and management of axSpA in Malaysia by collaborating and adopting guidance from an international axSpA expert.
Objectives: The objectives were to improve disease recognition among healthcare practitioners (HCPs), reducing time to specialist referral and diagnosis whilst improving disease management by developing and implementing a new patient care model called the Spondyloarthritis Accelerated Management (SAM) and measure its effectiveness in 3 Rheumatology centers in Malaysia.
Methods: The SAM initiative was developed by the Malaysian SpA Consortium Working Group involving 8 Malaysian rheumatologists from 3 local centers and 1 international axSpA expert from the UK as part of the steering committee. Selections were based on clinical expertise. The first local alignment meeting on model structure was held in July 2020 with subsequent meetings held to address key barriers to early axSpA diagnosis and timely access to quality care. A care model with feasible key performance indicators (KPIs) was established, adapted and tracked monthly in the 3 rheumatology centers (Figure 1). Referral tools were developed to facilitate early referrals to rheumatologists. These included a QR-coded '3-R' referral guide[1] and a patient self-screening tool with a patient self-referral letter all hosted on the Malaysian Society of Rheumatology (MSR) website, educational talks to HCPs and public awareness forums on IBP and axSpA. Data were collected on referral source, duration of referrals, knowledge on IBP in HCPs by surveys and imaging accessibility at baseline and at 1 year after the initiative was launched. Baseline data collected were from August to October 2020 and 1 year data were from November 2020 to November 2021.

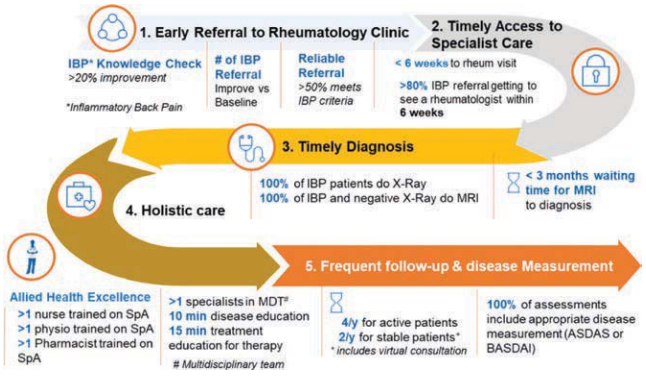

Figure 1. Summary of optimal Key performance indicators (KPIs) for Malaysia SAM

Results: At 1 year, the SAM initiative showed a 44.4% (Median: 1.33 [IQR 1-1.7] vs 1.92 [IQR 1.6-2.1]) increase in IBP referrals, a reducing trend from 9.5 (IQR 8-11.1) to 5.9 (IQR 5.1-6.8) weeks of waiting time to a first Rheumatology visit and an increase of 37.2% (34% vs 71%) in IBP patients who were seen at the rheumatology clinic within 6 weeks. All patients with IBP had x-rays (sacroiliac joints or pelvis). MRI requests in x-ray negative patients suspected of axSpA was increased by 13.9% (77.8% vs 91.7%) and waiting time for MRI was reduced by 3.1 weeks (12 vs 8.9 weeks). The IBP knowledge among 224 HCPs improved by 40.6% (45.7% vs 86.3%). The number of patients newly diagnosed with axSpA increased by 40% (Median: 5 [IQR 4-9.5] vs 7 [IQR 6.5-7]) despite the COVID-19 pandemic.
Conclusion: The SAM initiative has shown promising initial results in improving referrals of patients with IBP, promoting earlier diagnosis and establishing the importance of having timely access to optimal care. A nationwide implementation is being planned to improve the recognition of the axSpA in Malaysia.
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AB0782 SERUM PENTRAXIN 3 AS A BIOMARKER IN PATIENTS WITH SPONDYLOARTHRITIS.

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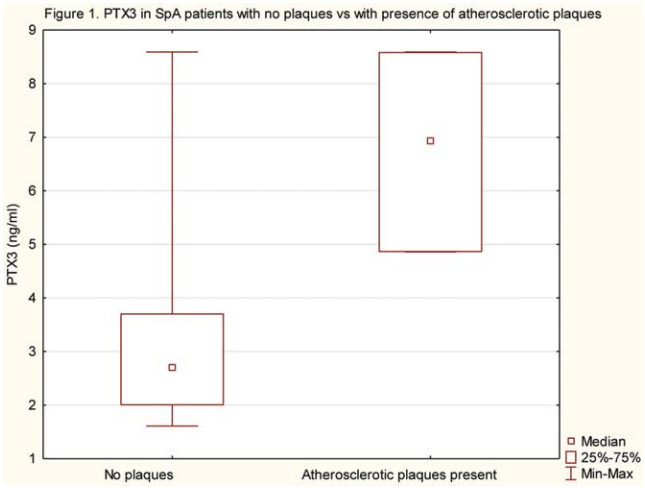
Background: A proper evaluation and management of patients with spondyloarthritis (SpA) requires the use of biomarkers, facilitating early diagnosis, reflecting disease activity and clinical response to therapies. The chronic, systemic inflammatory process is responsible for increased CV risk in SpA patients. Pentraxin 3 (PTX3) is an inflammatory marker, a member of long pentraxin superfamily, argued to be involved in pathogenesis of both inflammation and atherosclerosis. PTX3 is produced locally in the inflamed tissue, by different cell types including macrophages, endothelial cells, synoviocytes, but not hepatocytes. PTX3 is produced in walls of blood vessels, in atherosclerotic plaques, as a response to pro-inflammatory cytokines.
Objectives: The aim of the study was to assess the role of PTX3 as a biomarker in patients with SpA and to evaluate the relationship between PTX3 and CV risk markers (carotid intima-media thickness (cIMT), lipid profile).
Methods: The study group consisted of 40 consecutive patients with SpA: 29 patients with psoriatic arthritis (PsA) and 11 patients with ankylosing spondylitis (AS). The group consisted of 16 (40%) women and 24 (60%) men, with the mean (SD) age 43.9 (12.0) (range 25–68) and disease duration 7,8 (7,6) years (range 1–32). An assessment of the disease activity included: laboratory inflammatory parameters (erythrocyte sedimentation rate (ESR), C-reactive protein, CRP) and clinical assessment (in patients with peripheral SpA (pSpA) joints counts and disease activity score in 28 joints (DAS28); in patients with axial SpA (axSpA) Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and pain of the spine according to the patient in visual analogue scale (VAS). A measurement of carotid intima-media thickness (cIMT) was performed using high-resolution B-mode ultrasonography to estimate features of atherosclerosis (cIMT> 0.9 mm and/or presence of atherosclerotic plaques).
Results: The median (IQR) PTX3 concentration in SpA patients was 3.39 (2.22-3.88) ng/ml. The mean (SD) value of ESR was 27.7 (28.3) mm/h and CRP concentration 13.6 (19.9) mg/l. The mean values of clinical indices were as follows: DAS28 3.8 (1.1), BASDAI 4.02 (2.1), BASFI 4.22 (2.2), VAS spine pain 41.4 (24.0). The mean (SD) cIMT value was 0.77 (0.23) mm (range 0.48-1.33). The features of atherosclerosis were detected in 7 (17.5%) patients. No significant correlations were found between PTX3 and other inflammatory markers (ESR, CRP). There were no correlations between PTX3 concentration the clinical indices of the disease activity (DAS28, BASDAI, BASFI, VAS spine pain). No differences of PTX3 concentrations were detected between pSpA and axSpA patients. The PTX3 concentrations were significantly higher in patients with definite atherosclerosis (cIMT > 0.9 mm) than in patients with subclinical or no atherosclerosis (cIMT=< 0.9) (5.79 (3.84-8.59) vs 3.06 (2.0-3.52) ng/ml, p=0.01), as well as in patients with atherosclerotic plaques in comparison with no plaques (6.79 (4.86-8.59) vs 3.26 (2.0-3.71) ng/ml, p=0.02) (Figure 1).



Conclusion: The results of our study suggest that in patients with SpA, PTX3 could be regarded as a biomarker indicating intensity of atherosclerosis. However PTX3 was not associated with parameters of disease activity in patients with SpA.

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AB0783 BARRIERS DELAYING THE EARLY DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: DOES SEX MAKE A DIFFERENCE?

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Background: The diagnostic delay in patients with axial spondyloarthritis (axSpA) in Spain is almost 9 years, being about 2 years longer in women (1). MIRADDAS is an educational project focused on raising awareness among different specialties involved in the diagnostic journey of patients with axSpA (e.g. Primary Care, Rehabilitation, Orthopedic Surgery, etc.), with the objective of achieving an earlier referral and diagnosis, especially in women.

Objectives: To identify the present barriers hindering a correct and earlier diagnosis of patients with axSpA in Spain.

Methods: Rheumatologists with a broad experience in axSpA prepared a survey addressed to rheumatologists participating in an educational project (MIRADDAS). First, the participants answered a survey, then they received training that was disseminated locally afterwards.

Results: A total of 80 rheumatologists from different Spanish regions answered the survey. Almost all rheumatologists (94%) recognized that there is a diagnostic delay and that this is higher in women (85%). Participants stated that the most significant factors are: 1. the presence of generalized pain in women (83%) and 2. the historical assumption of a higher prevalence of axSpA in men. Most of the rheumatologists (65%) do not have referral protocols for axSpA, though more than half participate in multidisciplinary clinics with Ophthalmology and Dermatology. Of the patients referred due to suspected axSpA from other specialties, from 20% to 50% were finally diagnosed with axSpA, the majority coming from Primary Care. Regarding the diagnostic delay of axSpA, the barriers most frequently identified by rheumatologists are: lack of knowledge about the disease and sex and gender differences by other specialties and hence a tendency not to refer women with suspected axSpA. Other important barriers are the delayed referral to rheumatologist, lack of communication between different specialties, lack of time during the visits and the delay to perform the imaging tests.

Conclusion: Sex and gender differences of patients with axSpA seem to contribute significantly to the diagnostic delay. The lack of knowledge by other specialties about sex and gender differences in axSpA presentation was identified as one of the most important barriers for an early diagnosis of these patients. Targeted educational projects such as MIRADDAS could contribute to reducing and improving the diagnostic journey of women with axSpA, ensuring equal access to health care for men and women.

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Table 1. ***Barriers detected related to the diagnostic delay in axSpA***

	Score (mean)*
Lack of knowledge by other specialties about sex and gender differences in patients with axSpA	4.2
Lack of knowledge by other specialties about axSpA in general	3.7
Lack of knowledge about axSpA in Primary Care	3.6
Other specialists do not usually refer women with suspected axSpA	3.3
Delay in the first visit with Rheumatology	3.2
Lack of time for the visits	3.2
Delay in performing imaging tests	3.2
Lack of communication with Primary Care	3.1
Lack of multidisciplinary communication with other specialties	3
Lack of nursing staff	2.7
Limitation by Primary Care to request HLA-B27 or MRI	2.7
Difficulty in interpreting sacroiliac lesions on MRI	2.7
Difficulty in interpreting sacroiliac lesions on X-rays	2.6
Delay in performing the HLA-B27 test	1.7

**Measured on a scale from 0 to 5; axSpA: axial spondyloarthritis; HLA-B27: Human leukocyte antigen B27; MRI: magnetic resonance imaging; X-rays: radiography.*

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AB0784 SYMPTOMS COMPATIBLE WITH ROME IV FUNCTIONAL BOWEL DISORDER IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Clinical manifestations of gut problems except for inflammatory bowel disease (IBD) have not been well-established in patients with ankylosing spondylitis (AS). One study investigated that 30% patients with axial spondyloarthritis (axSpA) had irritable bowel syndrome (IBS) symptoms meeting Rome III criteria.[1]

Objectives: To determine the frequency of symptoms meeting Rome IV functional bowel disorder (FBD) in patients with AS, investigate factors associated with FBD symptoms, and assess whether having FBD symptoms might influence AS disease activity.

Methods: In this cross-sectional study, we consecutively enrolled 153 AS patients without known colonic ulcer and 56 sex- and age-matched controls to evaluate FBD (or its subtypes) symptoms.[2] In AS group, logistic regression models were used to explore whether demographic data, disease activity, level of gut inflammation, drug use, and fibromyalgia [3] were associated with presence of gut symptoms. Finally, potential impacts of gut symptoms on AS disease status were assessed in linear regression models.

Results: Sixty (39.2%) of 153 AS patients had FBD symptoms, which was more prevalent than controls (23.2%). Besides, symptoms compatible with IBS and chronic diarrhea were detected in 18 and 43 AS patients respectively. For AS group, multivariable logistic regression analyses showed that symptoms of FBD, IBS, and chronic diarrhea were negatively associated with using non-steroidal anti-inflammatory drug (NSAID), and positively associated with comorbid fibromyalgia, respectively. In exploration about effects of FBD (or its subtypes) symptoms on AS disease activity by multivariable linear regression analyses, FBD symptoms and chronic diarrhea had positive associations with assessments of AS respectively.

Conclusion: Patients with AS had frequent symptoms compatible with FBD, IBS, and chronic diarrhea, proportions of which were lower in those with NSAID-use. The improvement of FBD symptoms, especially chronic diarrhea, might be conducive to disease status of AS patients.

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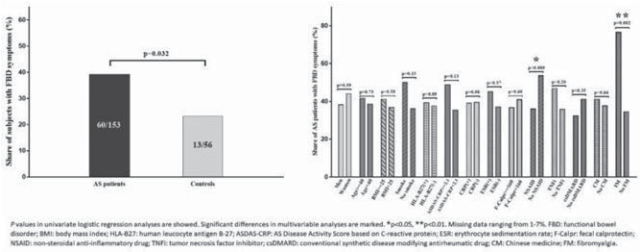

Figure 1. Frequencies with symptoms meeting FBD criteria

Table 1. Univariable and multivariable associations between gut symptoms and assessments of AS

		Univariable		Multivariable	
	Gut symptoms	β	p	β	p
ASDAS-CRP[a]	FBD symptoms	0.234	0.112	0.294	< 0.001
	IBS symptoms	0.039	0.863		
	Chronic diarrhea	0.217	0.172	0.301	0.002
BASDAI[b]	FBD symptoms	0.747	< 0.001	0.764	< 0.001
	IBS symptoms	0.202	0.560		
	Chronic diarrhea	0.761	0.002	0.845	< 0.001
BAS-G[c]	FBD symptoms	0.936	< 0.001	0.979	< 0.001
	IBS symptoms	0.059	0.889		
	Chronic diarrhea	0.903	0.003	0.949	0.001
ASAS HI[d]	FBD symptoms	1.941	< 0.001	1.673	0.003
	IBS symptoms	2.263	0.008	1.769	0.046
	Chronic diarrhea	1.500	0.015	1.343	0.030
BASFI[e]	FBD symptoms	0.433	0.049	0.428	0.048
	IBS symptoms	0.296	0.376		
	Chronic diarrhea	0.448	0.060	0.425	0.069
BASMI[f]	FBD symptoms	-0.373	0.190	-0.493	0.075
	IBS symptoms	-0.442	0.304		
	Chronic diarrhea	-0.179	0.564		

Besides gut symptoms, other clinical variables (Block-1) being chosen into hierarchical multivariable models were as follows: [a]HLA-B27, lnCRP, and lnESR; [b]HLA-B27 and lnESR; [c]HLA-B27 and lnCRP; [d]sex and TNFi; [e]HLA-B27, lnESR, and TNFi; [f]age and lnESR. Missing data ranging from 1-7%.

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AB0785

ROLE OF PATIENT ORGANIZATIONS IN IMPLEMENTATION OF RECOMMENDED NON-PHARMACOLOGICAL TREATMENT MODALITIES IN SPONDYLOARTHRITIS: EVIDENCE FOR THE EFFECTIVENESS OF SELF-MANAGEMENT STRATEGIES

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Background: EULAR recommends participation in patient (pt) organizations to improve pt self-management of axial spondyloarthritis (axSpA)[1]. Non-pharmacological treatment modalities (NPTM)[2] are recommended in axSpA treatment guidelines.[3]

Objectives: To characterize the impact of pt advocacy group membership and its association with NPTM frequency and clinical parameters in axSpA.

Methods: Pts with a confirmed axSpA diagnosis were enrolled in the multicenter, observational ATTENTUS-axSpA survey conducted across Germany (11/2019–07/2020). Demographics, clinical and pt-related data were collected electronically.

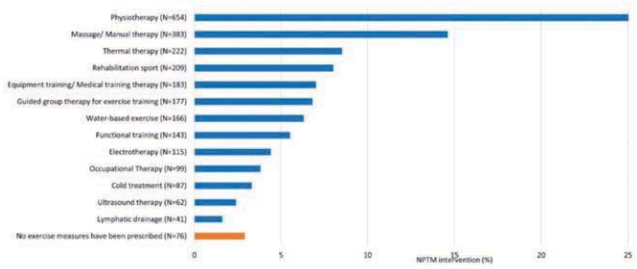
Results: Of the 787 enrolled axSpA pts, this analysis was conducted on the working population (n=695)[4]. Overall, 12.2% (n=85) pts were members of a pt advocacy group and 87.8% (n=610) were not. Pt advocacy group members had higher Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores, increased functional impairment (BASFI, Bath Ankylosing Spondylitis Functional Index) and higher impact of axSpA on health (ASAS-HI, Assessment of SpondyloArthritis International Society-Health Index; Table 1). Despite worse prognostic factors, there was no significant difference in Work Productivity and Activity Impairment (WPAI) score [40.6 (27.0) for pt advocacy group members vs 36.8 (29.9) for non-members; p=0.380]. Membership in a pt advocacy group was associated with increased prescribed, supervised NPTM (57.6% [n=49] vs 34.4% [n=210]). Pts reported to have ever received 2.6 rehabilitation measures, and ≥3.0 different rehabilitation NPTM measures. Cumulatively, 25.0% (N=654) of rehabilitation measures were physiotherapy (Figure 1).

Table 1. Descriptive characteristics and impact of membership in pt advocacy group

Characteristic	Patient advocacy group member (n=85)	Not patient advocacy group member (n=610)	Total (n=695)	p-value
Age (yrs), mean (SD)	50.2 (7.7)	44.6 (11.1)	45.3 (10.9)	**<0.001**
BMI (kg/m2) mean (SD)	27.5 (5.0)	28.0 (12.7)	28.0 (12.0)	0.713
Male, n (%)	45 (52.9)	378 (62.0)	423 (60.9)	0.128
Disease duration (yrs) mean (SD)	13.7 (10.3)	12.5 (11.1)	12.6 (11.0)	0.303
ASAS-HI, 0-17	7.3 (3.4)	6.4 (3.9)	6.5 (3.8)	**0.045**
BASDAI, 0-10	4.3 (1.9)	3.8 (2.2)	3.9 (2.2)	**0.044**
BASDAI ≥4, n (%)	49 (57.6)	275 (45.1)	324 (46.6)	**0.025**
BASFI, 0-10	3.9 (2.3)	3.2 (2.5)	3.3 (2.4)	**0.015**
Biologic treatment, n (%)	52 (61.2)	312 (51.1)	364 (52.4)	0.072
Full time employment, n (%)	48 (56.5)	410 (67.2)	458 (65.9)	0.06
Absenteeism*, mean (SD)	8.4 (21.2)	10.9 (26.8)	10.6 (26.2)	-
Presenteeism*, mean (SD)	38.4 (24.6)	31.8 (25.7)	32.6 (25.6)	-
Overall work impairment score*, mean (SD)	40.6 (27.0)	36.8 (29.9)	37.2 (29.6)	0.380
Activity impairment, mean (SD)	46.7 (21.7)	40.5 (26.8)	41.3 (26.4)	0.058
Pts having ever received medicinal rehabilitation measures, mean (SD)	67 (78.8)	328 (53.8)	395 (56.8)	**<0.001**
Prescribed supervised group NPTM[#], mean (SD)	49 (57.6)	210 (34.4)	259 (37.3)	**<0.001**
Regular physical training[†], mean (SD)	76 (89.4)	515 (84.4)	591 (85.0)	0.231

*Work-related questions of WPAI-score have been calculated for pts in employment (N=340); [†]regular physical training in the context of axSpA; [#]rehabilitation sport and/or functional training. ASAS-HI, Assessment of SpondyloArthritis International Society-Health Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, Body Mass Index; n, number of pts; pts, patients; SD, Standard Deviation; WPAI, Work Productivity and Activity Impairment; yrs, years.

Figure 1. NPTM measures ever received in patients with axSpA (2617 answers from 770 pts)



Multiple answers were permitted. A total of 2617 answers were submitted from 770 patients. N, total number of pts. NPTM, non-pharmacological treatment modalities.

Conclusion: Pt advocacy group membership was associated with increased prescribed NPTM in axSpA. Pt organizations may support the implementation of guidelines and improvement of self-management strategies in pts with axSpA, which may influence work participation.

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AB0786

SELF-REPORTED DISEASE BURDEN IS GREATER IN SPONDYLOARTHRITIS THAN IN RHEUMATOID ARTHRITIS PATIENTS ACCORDING TO MULTIDIMENSIONAL QUESTIONNAIRE (MDHAQ / RAPID3) SCORES, DESPITE FEWER FEMALES, WHO GENERALLY HAVE HIGHER SCORES ON PATIENT QUESTIONNAIRES

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Background: Female patients generally have higher scores than males on most items on self-report questionnaires, including MDHAQ/RAPID3 (multi-dimensional health assessment questionnaire/routine assessment of patient index data)[1]. MDHAQ/RAPID3 was validated in patients with rheumatoid arthritis (RA), but is informative in all diseases studied, including spondyloarthritis (SpA)[2]. More SpA patients are men than RA patients, suggesting lower scores, but MDHAQ scores are higher in SpA than RA.

Objectives: We compared self-report MDHAQ/RAPID3 scores in RA vs SpA patients according to gender.

Methods: Patients who met classification criteria for RA or SpA (axial SpA and psoriatic arthritis) completed MDHAQ at a routine rheumatology visit. The MDHAQ includes 10 activities for physical function (FN) (8 identical to HAQ), scored 0-3, total 0-30, divided by 3 for a 0-10 score, 3 0-10 visual numeric scales (VNS) for pain (PN), patient global assessment (PATGL), and fatigue (FT), a 60-symptom checklist (ROS60) and a RADAI self-report of painful joints (0-48). RAPID3 is a 0-30 index of FN + PN + PATGL. Means and standard deviations (SDs) of age, education, and 7 MDHAQ scores were computed in patients with RA versus SpA, and in subsets of female versus male patients with either RA or SpA. Unadjusted differences were evaluated using Student's t and chi-square tests; mean differences were adjusted for age, gender and education using analysis of covariance.

Results: 170 patients were studied, 102 with RA and 68 with SpA. 82% of patients with RA and 47% of patients with SpA were female (p<0.001); age and education did not differ between the 2 groups (Table 1). All 7 mean MDHAQ scores analyzed were higher in patients with SpA than in those with RA, although only differences for FN were statistically significant (Table 1). Within both the RA and SpA groups, however, all 7 scores were higher in women than in men, statistically significant for PN, PATGL, RAPID3 and fatigue in RA, and only for fatigue in SpA. In analyses adjusted for gender, FN, PATGL, FT, and RAPID3 were statistically significantly higher in SpA than in RA (Table 1).

Conclusion: The self-reported disease burden measured by MDHAQ / RAPID3 was higher in patients with SpA than in those with RA, despite having a lower proportion of women, who generally have higher scores on all patient self-report questionnaires, including MDHAQ/RAPID3, within both the RA and SpA groups. Gender differences may lead to underestimation of the greater disease burden in SpA compared to RA.

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AB0787

EXPLORATION OF PAIN SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS WITH ANXIETY-DEPRESSIVE SPECTRUM DISORDERS

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Background: To date, it has been established that anxiety-depressive spectrum disorders (ADSD) increase the perception of chronic pain. ADSD, as well as immuno-inflammatory diseases, in particular ankylosing spondylitis (AS), are caused by increased production of pro-inflammatory cytokines. Cytokines activate the hypothalamic-pituitary-adrenal system, and chronic stress factors provide a new release of cytokines with its subsequent sensitization, impairing the adaptive capabilities of the body, thereby exacerbating endocrine dysfunction that regulates stress and immune response in the body, which increases the level of proinflammatory cytokines, and is clinically manifested by a decrease in mood, chronic pain, fatigue, sleep disorders.

Objectives: To study the features of pain syndrome in patients with ankylosing spondylitis with anxiety-depressive spectrum disorders.

Methods: The exploration involved 112 patients with AS, aged 25 to 58 years (43.7±7.9 years), the average duration of the disease was 9.5±4.4 years. 67 of them (group 1) showed signs of ADSD, established by the Spielberger anxiety and Hamilton depression scales. The remaining 45 patients without ADSD were included in the 2nd observation group. The patients in the groups did not differ in age (p=0.67), however, they differed in the duration of the disease (p=0.035) - in the 1st group 10.2±4.5, in the 2nd group 8.4±4.0 years. In addition, patients of the 1st and 2nd groups did not differ in the frequency of occurrence of chronic fatigue (p=0.2) and decreased mood (p=0.08). However, sleep disorders (difficulty falling asleep, shallow sleep, early awakening) were significantly more frequent in-group 1 (p=0.046). Quantitative indicators of pain syndrome (PS) were studied using the McGill Pain Questionnaire (MGPQ). The severity of pain in the spine, morning stiffness, the patient's state of health (PSH) were studied using visual analog scales (VAS); BASDAI and BASFI indices, ESR and CRP indices were also recorded.

Results: Patients in the groups did not differ in BASDAI indices - in group 1, 4.04±1.24, in group 2, 3.83±0.98 and BASFI - 4.21±0.99 and 4.24±0.84, respectively; there were also no differences in the level of CRP and ESR. Spinal pain in group 1 (67.8±17.5 mm) was significantly stronger (p=0.02) than in group 2 (60.2±15.9 mm), morning stiffness was also significantly (p=0.028) more pronounced in group 1 (67.4±15.9 mm) than in group 2 (60.3±17.2 mm). According to the indicator of SPP, a more negative tendency to its increase should be noted in the 1st group (68.7±15.2 mm) than in the 2nd (63.7±14.4 mm), but without significant differences (p=0.084). All quantitative indicators of BS according to the ICD in the groups had significant differences (p<0.05), reaching maximum significance for the sensory and affective components of pain, the index of the number of selected descriptors (INSD). Namely: in group 1, the number of sensory and affective class descriptors was 5.9±0.8 and 4.5±0.7, the evaluative component of pain was 2.9±0.5, INSD was 11.9±1.4 points, the pain rank index (PRI) was 26.3±5.5 points; in group 2, the number of sensory and affective descriptors was 5.0±0.9 and 3.75±0.6, evaluative - 2.6±0.6, INSD - 10.3±1.5, RIB - 21.2±5.1 points. A higher number of affective class descriptors and ICPD in group 1 indicates the emotional lability of patients with ADSD and to a certain extent explains the significantly more significant negative indicators of BS recorded during the survey using VAS.

Conclusion: Significantly higher quantitative indicators of BS in patients with AS with ADSD confirm the presence in this category of patients of a pronounced emotional-affective component of pain, which has a central origin, and contributes to the growth of its somatic perception.

Disclosure of Interests: None declared

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Table 1. Mean differences in the MDHAQ scores between RA and SpA patients.

Total, n=170 patients	RA, n=102	SpA, n=68	RA: Female (n=84)/ Male (n=18)	SpA: Female (n=32)/ Male n=36)	Mean difference: RA–SpA (95% CIs) Unadjusted	Mean difference: RA–SpA (95% CIs) Adjusted for age, gender, and education
Age, mean (SD)	58.8 (12.2)	55.7 (12.2)				
Gender, female (%)	84 (82.4%)	32 (47.1%)*				
Years of education, mean (SD)	11.8 (4.3)	11.4 (3.7)				
MDHAQ variables, mean (SD)						
Physical function (0-10)	2.4 (1.8)	3.0 (2.1)	2.5 (1.8)/ 1.9 (1.6)	3.1 (2.0)/ 2.9 (2.2)	-0.6 (-1.2, -0.02)	-0.7 (-1.3, -0.05)
Pain (0-10 VNS)	4.5 (2.8)	4.9 (3.0)	4.8 (2.8)/ 3.3 (2.4)*	5.5 (2.9)/ 4.4 (3.0)	-0.4 (-1.3, 0.5)	-0.8 (-1.7, 0.1)
Patient global assessment (0-10 VNS)	4.6 (2.8)	5.3 (2.9)	4.9 (2.8)/ 3.4 (2.6)*	5.9 (2.8)/ 4.7 (3.0)	-0.6 (-1.5, 0.2)	-1.1 (-2.0, -0.2)
RAPID3 (0-30)	11.6 (6.8)	13.3 (7.3)	12.3 (6.8)/ 8.5 (6.1)*	14.6 (7.2)/ 12.2 (7.3)	-1.7 (-3.8, 0.4)	-2.7 (-4.9, -0.5)
Fatigue (0-10 VNS)	4.2 (2.9)	4.5 (3.1)	4.7 (2.9)/ 2.0 (2.1)*	5.5 (3.1)/ 3.6 (2.9)*	-0.3 (-1.2, 0.6)	-1.0 (-1.9, -0.04)
Self-report RADAI painful joint count (0-48)	12.4 (11.0)	13.4 (11.9)	13.2 (11.4)/ 8.6 (8.5)	15.6 (13.1)/ 11.5 (10.6)	-1.0 (-4.5, 2.4)	-2.2 (-5.8, 1.4)
60-symptom checklist (0-60)	12.6 (10.0)	15.2 (10.9)	13.3 (10.3)/ 9.4 (7.8)	16.0 (10.3)/ 14.6 (11.6)	-2.6 (-5.8, 0.6)	-2.5 (-5.8, 0.7)

*= p<0.05.

AB0788

THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRITIS (IMAS): A US PATIENT PERSPECTIVE ON DIAGNOSIS AND BURDEN OF DISEASE

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease encompassing radiographic (traditionally known as ankylosing spondylitis) and non-radiographic forms that lead to chronic pain, structural damage, and disability.[1] The International Map of Axial Spondyloarthritis (IMAS) survey is an initiative developed to generate insights into the real-life experiences of people living with axSpA to ultimately improve quality of life.[2]
Objectives: To assess the burden and daily experience of patients with axSpA in the United States.
Methods: The IMAS survey generates a report on patient-reported aspects of disease burden and experience with axSpA using adaptations of the original Atlas of axSpA questionnaire developed in collaboration with patients, the Axial Spondyloarthritis International Federation, and clinical academic experts. In this US adaptation of the IMAS survey, a 30-minute quantitative online survey was administered to US patients aged ≥18 years who completed screening questions, self-reported having been diagnosed with axSpA by a healthcare provider, and were under the care of a healthcare provider between July 22, 2021, and November 10, 2021. Survey questions were tailored to reflect differences in the US healthcare systems and the availability of treatments. This analysis presents a portion of the US data describing patient demographics, clinical characteristics, journey to axSpA diagnosis, and the emotional impact and overall burden of disease on quality of life using the General Health Questionnaire 12 (GHQ-12), the Assessment of SpondyloArthritis international Society – Health Index (ASAS-HI), and a global limitation index of 18 activities of daily living. All results were reported descriptively using summary statistics.
Results: Survey data from 228 US patients with axSpA were collected in this analysis. The mean age was 45 years, 60% of patients were female, and the mean BMI was 27.7 kg/m2 (Table 1). Participating patients had an average of 5.6 comorbidities, with anxiety (43%), depression (41%), and hypertension (32%) as the most commonly reported comorbidities. Among all patients, the mean age at onset of first symptoms was 26 years and the mean age at diagnosis was 35 years; overall, mean diagnostic delay was greater in female than in male patients (11.2 vs 5.2 years; Figure 1**A**). According to the validated GHQ-12, over half of the patients (57%) were at risk for psychological distress (GHQ-12 score ≥3; Figure 1**B**). Patients who were older (>40 years old), physically inactive, or who had active disease (BASDAI ≥4) were at risk for psychological distress. Most patients (82%) suffered from a high degree of impairment (ASAS-HI ≥6), 47% had a medium or high limitation in activities of daily living, and 46% of patients were not employed at the time of the survey.

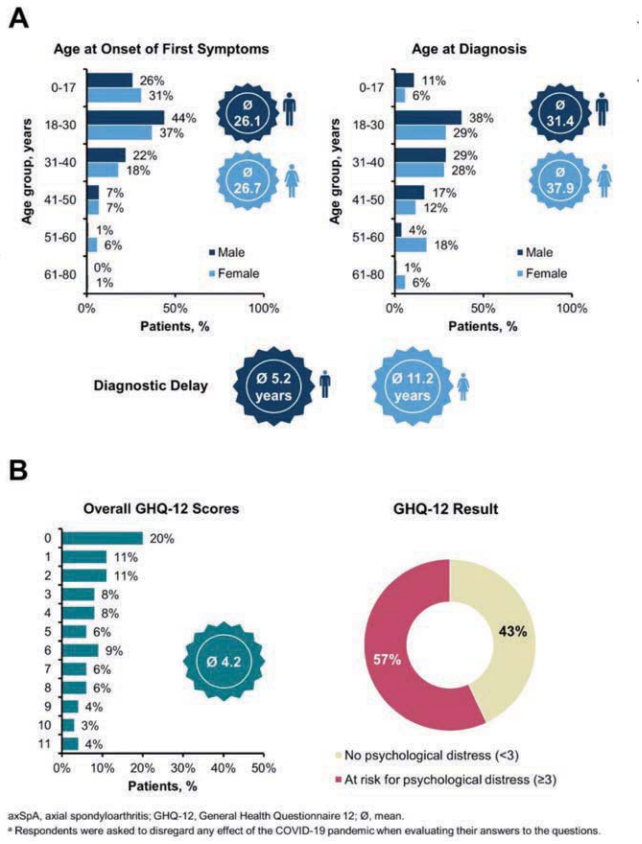
Table 1. Patient Demographic and Clinical Characteristics

Characteristic	Patients with axSpA (N=228)
Mean age, years	45
Female, %	60
White, %	86
Mean body mass index, kg/m^2	27.7
Nonsmoker, %	62
Alcohol consumption behavior, %	
Never	19
Every day	9
Mean number of comorbidities	5.6
Common comorbidities (≥20% of patients), %[a]	
Anxiety	43
Depression	41
Hypertension	32
Obesity/overweight	31
Sleep disorders	30
Hypercholesterolemia	29
Uveitis	24
Psoriatic arthritis	23
Fibromyalgia	20
Spinal or other fractures	20
Psoriasis	20
Employed, %	54

axSpA, axial spondyloarthritis. [a]Respondents could have selected ≥1 answer.

Conclusion: This study showed that a high proportion of US patients with axSpA report impaired function and are at risk for psychological distress. Patients also experienced a substantial delay in the time to axSpA diagnosis, with longer delays than those reported in the European Union. Delays were twice as long in women compared to men. These findings highlight the large impact of disease on daily activities and mental distress in US patients with axSpA.

Figure 1. (A) Age of First Symptom Onset and Diagnosis By Sex and **(B)** Burden of Disease on Psychological Distress Among Patients With AxSpA[a] (N=228)



axSpA, axial spondyloarthritis; GHQ-12, General Health Questionnaire 12; Ø, mean.
[a] Respondents were asked to disregard any effect of the COVID-19 pandemic when evaluating their answers to the questions.

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AB0789

WHAT DRIVES THE BASDAI IN PREGNANT PATIENTS WITH AXIAL SPONDYLOARTHRITIS? A POOLED ANALYSIS OF FOUR EUROPEAN PREGNANCY REGISTRIES.

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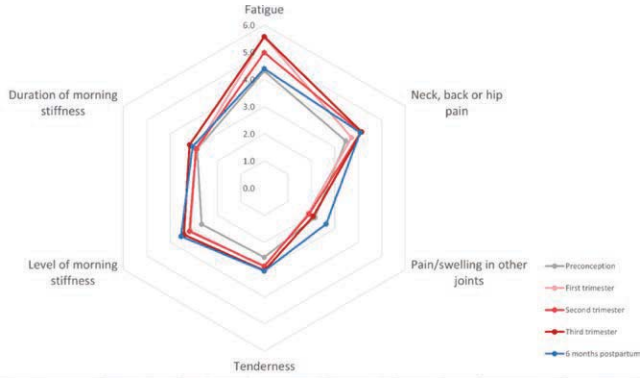
Background: The patient reported Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) includes the six components fatigue, neck, back or hip pain, pain or swelling in other joints, tenderness, morning stiffness severity and duration on a 0-10 scale.
Objectives: To explore the driving factors for the BASDAI in pregnant patients with axial spondyloarthritis (axSpA).
Methods: Anonymized pooled data of the European Network of Pregnancy Registries in Rheumatology (EuNeP) were used. The four participating registries are located in France, Germany, Norway and Switzerland, and collect data of women with child wish, during and after pregnancy prospectively and nationwide on regular time points. For the analysis, women who fulfilled ASAS classification criteria for axSpA and for whom a pregnancy outcome was reported until 12/2019 or 07/2020, depending on the registry, were selected. Mean BASDAI and its components were analysed descriptively.
Results: A total of 332 pregnancies from 304 women with axSpA were eligible. The Norwegian registry contributed half of the pregnancies (50.3%), followed by Germany (26.2%), France (15.4%) and Switzerland (8.1%). Mean maternal age was 31 years, the average disease duration 5 years. Mean BASDAI was 3.0 before conception, 3.4, 3.4 and 3.5 in the 1st, 2nd and 3rd trimester, and 3.4 within 6 months postpartum. The figure shows mean values of the BASDAI and its individual components in the different time periods. Fatigue was higher than the mean score during all phases, and especially elevated in the 1st and 3rd trimester. Furthermore, values for neck, back or hip pain were higher than the mean score, especially from 2nd trimester on. All other components were lower than the mean score. Data were not reported for all pregnancies and all time periods. Availability was highest in the 2nd and 3rd trimester with reported BASDAI in 60% and 62% of the pregnancies, respectively. Lowest reporting was 24% in the preconception period because only a part of the women was also observed before pregnancy.
Conclusion: The BASDAI is a validated instrument for assessing disease activity in patients with axSpA. Since the calculation of the score also includes factors that can be influenced by pregnancy, it may only be of limited value for measuring disease activity in pregnancy. This analysis shows that mainly fatigue and back pain in particular have an impact on the mean BASDAI. A limitation of this analysis is that data were not available for all measured time points of the individual pregnancies. Therefore, the results should be confirmed by other studies.



	Fatigue	Neck, back or hip pain	Pain/swelling in other joints	Tenderness	Level of morning stiffness	Duration of morning stiffness	BASDAI
Preconception	4.3 ± 3.2	3.5 ± 2.6	2.2 ± 2.6	2.5 ± 2.7	2.7 ± 2.6	2.9 ± 2.9	**3.0 ± 2.1**
1st trimester	5.6 ± 2.8	3.7 ± 2.9	1.9 ± 2.3	2.9 ± 3.0	3.1 ± 3.1	2.9 ± 2.6	**3.4 ± 2.2**
2nd trimester	5.0 ± 2.6	4.1 ± 2.6	1.9 ± 2.4	2.9 ± 2.8	3.2 ± 3.0	2.9 ± 2.8	**3.4 ± 2.2**
3rd trimester	**5.6 ± 2.7**	**4.1 ± 3.0**	**2.1 ± 2.5**	**3.0 ± 2.9**	**3.4 ± 3.2**	**3.2 ± 2.9**	**3.5 ± 2.3**
6 months postpartum	4.4 ± 2.8	4.1 ± 2.8	2.6 ± 2.7	3.0 ± 2.9	3.5 ± 3.0	3.1 ± 2.9	**3.4 ± 2.3**

Figure 1. Means of BASDAI components before, during and after pregnancy (the table presents means ± standard deviation).

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AB0790 EFFECTS OF PHYSICAL ACTIVITY ON DISEASE ACTIVITY AND CLINICAL ENTHESITIS SCORES IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Regular physical activity (PA) highly recommended for patients with inflammatory diseases [1]. It was shown to significantly improve disease activity [1]. However, data regarding the effects of physical activity on disease activity and clinical enthesitis scores in patients with SA are scarce.
Objectives: We aim to assess the effects of performing PA on disease activity and clinical enthesitis scores in patients with SA.
Methods: We performed a cross-sectional study including patients with axial spondyloarthritis. Each patient was asked if he performed regular physical activity. Clinical disease activity scores were calculated: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score using C-Reactive Protein (ASDAS-CRP). Clinical enthesitis scores were calculated: Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) [2], Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC) [3] and Leeds Enthesitis Index (LEI) [4].
Results: Thirty-seven patients were included: 29 males and 8 females. The mean age was 44.51±12.08 years. The mean disease duration of 9±7.8 years. Regular PA was reported by 51% patients (19). Aerobic exercise was performed by 48.6% of patients (walking: 27%, jogging: 8.1%, football: 5.4%, biking: 2.7%, handball: 2.7% and fitness exercise: 2.7%). Anaerobic exercise was performed by only one patient (2.7%) and consists of weightlifting. The mean weekly duration of PA was of 4.32±3.4 hours. Means BASDAI, ASDAS-CRP, and ASDAS-ESR were of 4.74±2.2, 3.02±1.2 and 3.26±1.3, respectively. Mean MASES was of 2.95±2.86, LEI of 1.51±1.72 and SPARCC of 2.97±3.42. Patients who performed regular PA had significantly lower disease activity evaluated with BASDAI (3.53 vs 5.45, p=0.007), ASDAS-CRP (2.64 vs 3.44, p=0.045) and ASDAS-ESR (2.84 vs 3.7, p=0.44). Clinical enthesitis scores were also significantly lower in physically active patients (MASES: 1.74 vs 4.22, p=0.007, LEI: 0.95 vs 2.11, p=0.038, SPARCC: 1.79 vs 4.22, p=0.029). However, no significative difference was found between the two groups regarding CRP (16.11 mg/L vs 39.67 mg/L, p=0.107). No correlation was found between the weekly number of hours of PA and the evaluated scores.
Conclusion: Physical activity was associated with lower disease activity scores and lower clinical enthesitis score. This highlights the importance of physical activity as a non-pharmacologic treatment in SA for the management of disease activity and entheseal involvement.
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AB0791 MADRID SONOGRAPHIC ENTHESIS INDEX: USEFUL OUTCOME IN THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS

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Background: Madrid Sonographic Enthesis Index (MASEI) is an ultrasound (US) score for the evaluation of enthesis including inflammatory abnormalities and chronic damage in spondyloarthritis (SpA) [1]. This score includes bilaterally: plantar aponeurosis, Achilles tendon, distal and proximal patellar ligament, distal quadriceps, and brachial triceps tendons.
Objectives: We aimed to study the diagnosis value of MASEI score in axial spondyloarthritis.

Methods: We conducted a case-control study including 74 subjects divided into 2 groups: -G1: 37 patients fulfilling the Assessment of SpondyloArthritis international Society (ASAS) criteria for axial SA. -G0: 37 healthy controls matched for age and sex. Eight hundred eighty-eight entheses were assessed by a musculoskeletal experienced sonographer who was blinded to the clinical data concerning patients and controls. The MASEI was calculated for the 2 groups. For G1, we collected the following parameters: disease activity using Bath Ankylosing Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS-ESR). Statistical analysis was performed using "IBM SPASS Statistics" software version 21. A Receiver Operator Curve (ROC) analysis was performed to determine the cutoff of MASEI able to discriminate G0 from G1.

Results: The study included 29 men (78%) and 8 women (22%) in each group. The mean age was 44.51 ± 12.08 years. The mean age of onset was 38.06 ± 11.36 years. The mean disease evolution of 9.02 ± 7.83 years. The mean BASDAI and ASDAS-ESR were 4.47 ± 2.21 and 3.26 ± 1.31. MASEI score was significantly higher in patients compared to healthy controls (25.76 ± 9.8 versus 8.32 ± 6.65, p <0.0001). A cutoff of 18 of the MASEI was able to distinguish G1 from G0 with a sensitivity of 81.1% and specificity of 91.9%. The air under curve (AUC) value was 0.920 (p<0.0001). No correlation was found between MASEI and BASDAI, and ASDAS-ESR.

Conclusion: Our study showed that MASEI score is significantly higher in SpA patients and seems to have a diagnostic accuracy. Besides, MASEI was able to distinguish between SpA patients and healthy controls with a cut-off of 18. Those results agree with the findings of other researchers in the field [2].

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AB0792 HIP INVOLVEMENT IN SPONDYLOARTHRITIS: ANALYSIS OF ASSOCIATED FACTORS

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Background: Hip involvement occurs in about one-third of patients with spondyloarthritis (SA) [1]. It can be responsible for significant disability and functional impairment.

Objectives: This study aimed to assess the associated factors with hip involvement in SA.

Methods: We conducted a cross-sectional study, including 165 patients with SA diagnosed according to Assessment of SpondyloArthritis international Society (ASAS) criteria over a period from 2017 to 2021. Demographic, clinical, biological and radiographic data were collected. We compared following parameters assessed at the time of diagnosis of coxitis: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP), modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), Bath Ankylosing Spondylitis Radiology Index (BASRI), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). We used logistic regression analysis to identify factors associated with hip involvement in SA.

Results: A total of 165 Patients were enrolled (121 men and 44 women), the mean age was 46.13 ± 13.07 years. The mean age of disease onset was 35.01 ± 12.55 years. The average diagnostic delay was 37.54 ± 50.51 months. The average disease duration was 10.91 ± 6.94 years. Eighty seven percent of patients had axial spondyloarthritis, 72% had extra-articular manifestations. Mean ESR and CRP values were 37.49 ± 28.1 mm and 30.14 ± 43.55 mg/L, respectively. Mean BASDAI and ASDAS-CRP values were 4 ± 1.8 and 3.09 ± 1.13, respectively. Hip involvement was noted in 60 patients (36.4%). It was bilateral in 75% of cases (n=45). A total number of affected hips was 105. Following parameters were significantly higher in patients with hip involvement: age over 40 years old (73.3 vs 56.3%, p=0.030), symptoms duration over 10 years (60% vs 40.2%, p=0.015), elevated CRP (87.9% vs 73.7%, p=0.036), radiographic sacroiliitis (95% vs 82.7%, p=0.023), frequency of pulmonary involvement (25.0% vs 11.4%, p:0.023), frequency of osteoporosis (20.0% vs 8.6%, p:0.034), BASMI (3.71 vs 1.65, p<0.001), BASRI spine (5.97 vs 2.91, p<0.001), and mSASSS (16.24 vs 5.80, p:0.001). However, no association was found between HLA-B27 and hip involvement (50% vs 28.6%, p=0.099). A multivariable logistic regression model showed that age over 40 years (OR=2.688 [1.020 - 7.083], p=0.045), radiographic sacroiliitis (OR=5.656 [1.007 - 31.769], p=0.049), and very high disease activity (ASDAS-CRP≥3.5) (OR=5.328 [1.774 - 16.002], p=0.003) were independently associated with hip involvement in SA.

Conclusion: Our study showed that age, symptoms duration, radiographic sacroiliitis, extra-articular manifestations, axial structural damage, elevated CRP, and very high disease activity were associated with hip involvement. These finding suggest that the control of disease activity and inflammation may prevent the onset of hip involvement. There are controversial findings regarding the association between HLA B27 gene and hip involvement [2].

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AB0793 FACET JOINT DISEASE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A RETROSPECTIVE CONVENTIONAL COMPUTED TOMOGRAPHY STUDY

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Background: Facet joints' (FJ) ankylosis was reported to occur frequently in patients with ankylosing spondylitis (AS). However, a detailed FJ evaluation was not reported in patients over the spectrum of axial spondyloarthritis (AxSpA).

Objectives: To analyze structural lesions in the FJ of patients with different forms of AxSpA, using computed tomography (CT).

Methods: All available conventional CT studies of the cervical, thoracic, lumbar spine, or studies of the chest or abdomen of patients with AS or non-radiographic AxSpA (nrAxSpA) from a single medical center cohort were analyzed for the presence of erosions, ankylosis, joint-space narrowing, osteophytes, subchondral sclerosis, subchondral cysts and vacuum phenomenon by 2 experienced readers. All patients, as well as age and gender matched control group, who performed conventional CT of the spine for any cause, but did not have a known rheumatic disease, had to be at the age of 50 years or less at the time of the study. The findings were binarically scored as present/absent. Several types of changes could be noted in the same FJ. All FJ findings were compared between groups of AxSpA patients and controls, separately for the cervical, thoracic and lumbar spine. Further, AxSpA patients were subdivided into three groups of which FJ findings were compared: AS patients with (AS+) or without (AS-) syndesmophytes on the cervical or lumbar radiographs, and patients with nrAxSpA as per pelvic radiograph. Fisher's exact test or Chi-Square test at < http://vassarstats.net >, were used to compare between groups.

Results: 959/666 FJs (49/44 patients) were assessed in the AxSpA/control group patients, respectively. The study group consisted of 16 AS+ patients, 22 AS- patients, and 11 nrAxSpA patients. FJ ankylosis was significantly more prevalent in all spinal segments of the AS + group compared to the two other groups. Erosions were seen almost exclusively in patients with AS. Joint-space narrowing and osteophytes were noted in all segments and all subgroups of AxSpA patients, including those with nrAxSpA.

Conclusion: FJ involvement is prevalent in all forms of AxSpA, including its non-radiographic form. Facet joints of all spinal segments are involved in AxSpA patients

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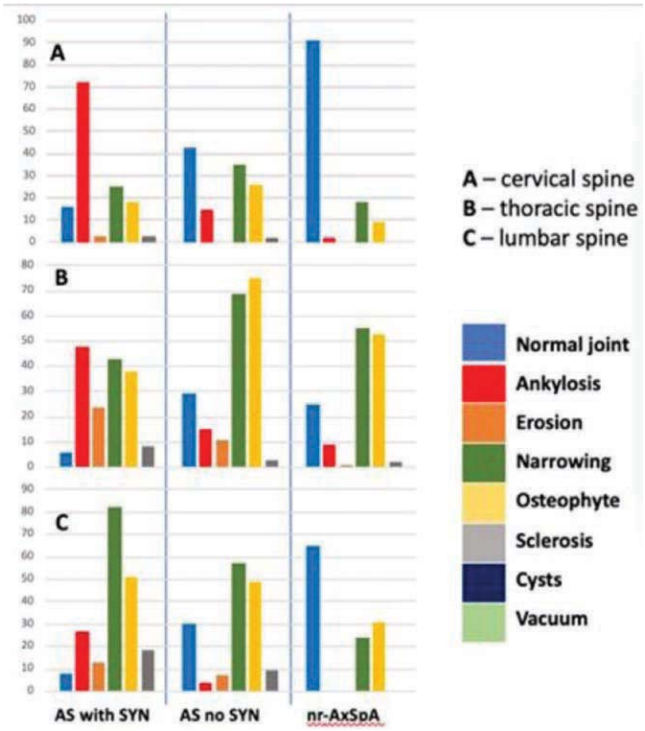

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AB0794 **HOPELESSNESS IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease leading to loss of function that is strongly related to impaired psychological status. Therefore, depression and anxiety are frequently investigated in these patients (1). However, hopelessness, regarded as a valuable psychological factor characterized by negative expectations and negative emotional states, was not well studied in AS patients(2).
Objectives: The aim of the study is to investigate the frequency of hopelessness in patients with AS and its relationship with clinical parameters and disease activity indices.
Methods: The study was designed as a prospective cross-sectional study. 113 AS patients were included in the study. Demographic data, clinical variables, laboratory results were recorded. Disease activity (ASDAS-CRP and ASDAS-ESR), patients' functionality (BASFI, BASMI), enthesitis (Leeds enthesitis index) and quality of life (SF-36) were assessed. Hopelessness was evaluated by Beck hopelessness scale (BHS). The relation of BHS scores with the clinical variables was assessed. The strength of the correlations were regarded as very weak(0–0.19), weak(0.2–0.39), moderate(0.40–0.59), strong(0.6–0.79) and very strong(0.8-1). Multiple linear regression analysis was performed to find the association between BHS scores and other clinical variables.
Results: Minimal, mild, moderate, and severe hopelessness were observed in 46 (40.7%), 36 (31.9%), 22 (19.5%), and 9 (8.0%) patients, respectively. Disease duration (p=0.025), ASDAS-CRP (p=0.033), ASDAS-ESR (p=0.015), visual analogue scale (p=0.030), all SF-36 subscales (all p<0.025), BASFI (p=0.024), and BASMI (p=0.009) were statistically different among the groups. BHS scores were higher in patients with high and very high disease activity (p=0.027) (in pairwise comparison, inactive disease vs. high disease activity, p=0.035) (Figure 1). BHS scores showed weak correlation with ASDAS-CRP, ASDAS-ESR, visual analogue scale, BASMI, Leeds enthesitis index, and BASFI. Moreover, negative moderate correlations were detected between BHS scores and SF-36 subscales except social functioning and body pain, which were found weak correlation. In multiple linear regression analysis, BASMI-maximal intermalleolar distance, SF-36 energy, SF-36 mental health, and SF-36 general health were found associated with BHS scores (Table 1).

Table 1. Multiple linear regression analysis to find predictors related to the Beck hopelessness scale scores

		B	95% CI	p
ASDAS-CRP		-0.063	(-1.939) to 1.282	0.687
VAS		-0.085	(-0.722) to 0.396	0.564
BASMI	Lateral spinal flexion	0.311	(-0.299) to 1.479	0.191
	Tragus to wall distance	0.157	(-0.404) to 1.602	0.239
	Modified Schober	0.298	(-0.114) to 1.368	0.096
	Maximal intermalleolar distance	0.228	0.076 to 0.557	0.010
	Cervical rotation	0.092	(-0.665) to 1.085	0.635
	Total	-0.730	(-5.572) to 1.042	0.177
SF-36	Physical function	-0.024	(-0.056) to 0.046	0.840
	Role physical	-0.114	(-0.046) to 0.017	0.364
	Role emotional	-0.019	(-0.029) to 0.024	0.870
	Energy/fatigue	-0.283	(-0.125) to (-0.005)	0.035
	Mental health	-0.306	(-0.142) to (-0.022)	0.008
	Social functioning	0.022	(-0.033) to 0.041	0.822
	Body pain	0.182	(-0.018) to 0.086	0.192
	General health	-0.344	(-0.125) to (-0.030)	0.002
BASFI		-0.085	(-0.606) to 0.248	0.408

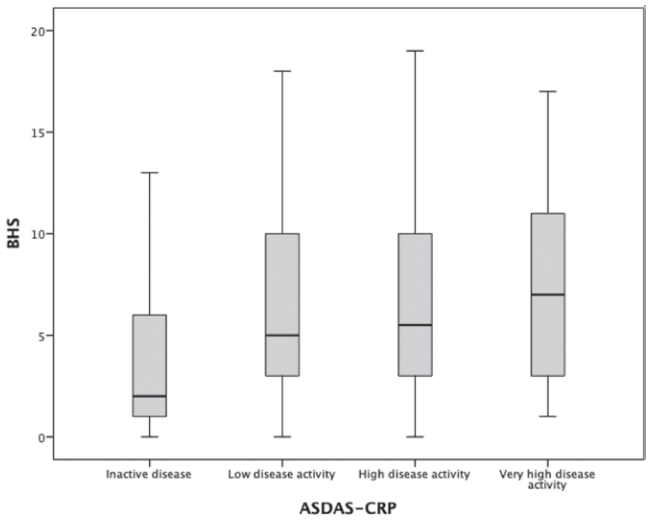

Figure 1. Beck hopelessness scale scores according to disease activity subgroups

Conclusion: Higher level of hopelessness is strongly related to higher disease activity in AS patients. Furthermore, higher BHS scores are negatively correlated with SF-36 subscales. Especially, lower energy and impaired mental health are associated with higher level of hopelessness.

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AB0795 **ARE PATIENTS WITH ANKYLOSING SPONDYLITIS AFRAID OF FALLING COMPARED TO HEALTHY CONTROLS?: THE ROLE OF BALANCE AND POSTURE**

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Background: Fear of falling is a low perception of self-efficacy in avoiding falling during basic, non-hazardous activities of daily life, and concern about falling. It is a risk factor for falls and individuals without a history of falls may have fear of falling. Although it has been shown that the risk of falls is increased in patients with ankylosing spondylitis (AS), there is a lack of sufficient data on the fear of falling in AS patients and the relation of falls with spinal mobility and balance in these patients is controversial.
Objectives: The aims of this study were to compare the fear of falling and balance parameters of AS patients with healthy controls and to evaluate the relation of fear of falling with spinal mobility, balance parameters, pain, disease activity, and functional capacity in patients with AS.
Methods: Forty patients diagnosed with AS and 50 gender-age matched healthy controls were included. Demographic data and the number of falls within the last one year were questioned for all participants. Fear of falling by Falls Efficacy

Scale-International (FES-I), balance with the Berg Balance Scale (BBS) and Short Physical Performance Battery (SPPB) were assessed in all participants. In patients; spinal mobility by Bath AS Metrology Index (BASMI), pain by visual analog scale (VAS), disease activity by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), functional capacity by Bath Ankylosing Spondylitis Functional Index (BASFI) were evaluated. Kolmogorov Smirnov test, chi-square test, Student t test, Pearson correlation analysis, and Multivariate linear regression analysis were used for statistical analyses.

Results: The mean ages of the patient and control groups were 45.73 ± 9.5 (18-63) and 42.28 ± 8.1 (26-56), respectively. Patients' fear of falling scores were significantly higher, and BBS and SPPB scores were significantly lower compared to the controls (p<0.001). In the patients FES-I scores were positively correlated with VAS pain, BASFI and BASDAI scores, and negatively correlated with BBS and SPPB scores (SPPB p<0.05, others p<0.001). BASMI scores were only correlated with BBS scores negatively (p<0.05). In the regression analysis, positive correlation with FES-I was BASFI scores (p<0.05).

Conclusion: In this study, patients with AS had more fear of falling than healthy individuals. Patients' balance parameters were worse than controls and fear of falling was associated with poor balance in AS patients. Functional limitation, increased pain and disease activity were also associated with fear of falling in AS patients. Since AS sample in this study had a good mobility, no correlation might not have been found between fear of falling and spinal mobility. According the results of this study AS patients may have fear of falling even if there is no history of falls; and balance exercises, reducing disease activity, preserving functions may help to reduce fear of falling in these patients. Future studies including patients with mobility restriction may clarify the relationship between fear of falling and mobility in AS patients.

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AB0796

QUANTITATIVE BONE MARROW LESION CHARACTERIZATION AT THE SACROILIAC JOINT WITH T1-MAPPING

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Background: Conventional magnetic resonance imaging (MRI) uses T1-weighted and short-tau inversion recovery (STIR) sequences to characterize bone marrow lesions in axial spondyloarthritis. However, quantification is restricted to the extent of marrow lesions because signal intensities are highly variable within and across patients and scanners. Furthermore, some marrow lesions are less visible in MRI and need further characterization with computed tomography (CT), e.g. sclerosis. Quantitative MRI in form of mapping sequences might help to better characterize bone marrow lesions.

Objectives: To evaluate the performance of T1-mapping for differentiating different bone marrow lesions at the sacroiliac joints in patients with suspected axial spondyloarthritis.

Methods: Sixty-two patients (mean age 41±12.5; thirty-two were finally diagnosed with axial spondyloarthritis and 30 with another condition) underwent CT and MRI of the sacroiliac joints. Besides standard oblique coronal T1 and STIR sequences a T1-mapping sequence (Modified Look-Locker Inversion Recovery) was added to the protocol. Bone marrow lesions (maximum 4 lesions per patient, 1 lesion of the same type per joint) were characterized by an expert radiologist into four groups, namely sclerosis (lesion type (LT) 1), osteitis (LT2), fat lesion (LT3) and mixed marrow lesions (LTm). Relaxation times on T1-maps were compared using Kruskal-Wallis test correcting for multiple comparisons and correlated to quantitative measures from conventional MRI sequences and CT.

Results: 119 lesions were selected (LT1: 38, LT2: 27, LT3: 40; LTm: 14). T1-map showed highly significant differences between LT1-3 with the lowest values for sclerosis (1522±227 ms), followed by osteitis (1906±82 ms) and fat lesions (2391±200 ms); p<0.0005. However, mixed lesions showed a broad distribution of values (1869±670), irrespective of their characteristics. T1-map correlated to a high degree with conventional T1-values (r = 0.74) and Hounsfield units in CT (r = -0.69) with p < 0.0001, respectively, but not with STIR (p = 0.8).

Conclusion: T1-Mapping allows for accurately characterizing lesions at the sacroiliac joint in patients with suspected axial spondyloarthritis and, thus, may combine information from two conventional sequences and CT into one in the future while providing superior capacity for quantification. However, in our study mixed lesions and inhomogeneous bone marrow remained problematic. Thus, further sequence development is needed before its implementation in clinical routine.

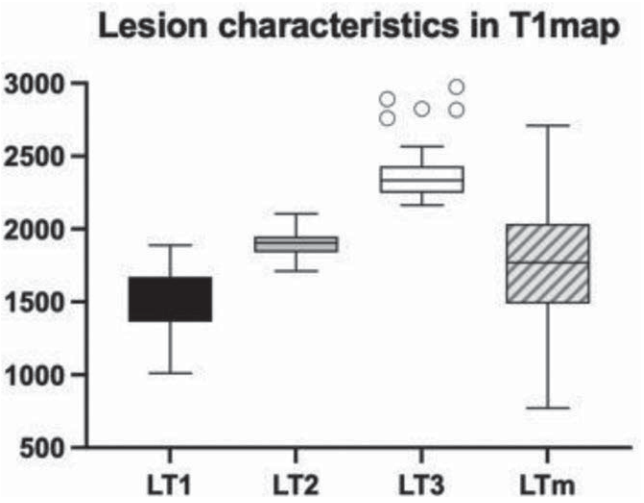

Figure 1. T1-mapping values of the different lesions, LT1: Sclerosis, LT2: Osteitis, LT3: Fat lesion, LTm: Mixed lesion. Differences are highly significant, which allows T1-mapping to characterize those different lesions in one sequence.

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AB0797

FACTORS ASSOCIATED WITH ADVERSE OUTCOMES IN UVEITIS RELATED TO SPONDYLARTHRITIS (SPA-U)- DEVELOPMENT OF A PROGNOSTIC OUTCOME SCORE IN PATIENTS WITH SPA-U

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Background: Uveitis is the most frequent extra-articular manifestation of spondylarthritis (SpA), characterized by a sudden onset, often unilateral, anterior and recurrent and may be the first clinical manifestation of the disease. The lack of standardized and validated outcome measures in uveitis makes it difficult to evaluate the efficacy and refractoriness to treatment and determine factors associated with adverse outcomes.

Objectives: To develop a prognostic outcome score for patients with uveitis associated with spondylarthritis (SpA-U) and determine factors associated with adverse outcomes in uveitis associated to SpA-U in patients under systemic treatment.

Methods: Clinical records of patients with SpA-U from 1990 to 2020 were retrospectively reviewed, including sociodemographic features, factors related to articular involvement, therapeutic choices and data related to uveitis outbreaks. The prognostic outcome score was defined by visual acuity, inflammation in anterior chamber (anterior chamber cells, hypopyon, presence of fibrin, active posterior keratic precipitates), presence of synechia, pupilar membrane, epiretinal membrane or any complications (macular oedema, vitritis, panuveitis, peripheral ulcerative keratitis), and refractoriness to 2 or more d/csDMARDs (conventional synthetical disease-modifying anti-rheumatic drug) or 1 or more bDMARD (biological disease-modifying anti-rheumatic drug) treatment. The prognostic outcome score ranked from 0 (good) to 5 (bad). Factors associated with adverse outcomes in uveitis were studied using linear regression. For categorical factors, marginal averages and their standard errors are displayed together with linear regression coefficients with 95% confidence intervals (CI). For continuous factors, averages and standard deviations are reported in addition to linear regression coefficients with 95% CI. For each variable, two regression coefficients are reported: unadjusted and adjusted for age at diagnosis and sex.

Results: 42 patients were included, 59.5% were male, with a mean age at diagnosis of 36.6±11.9 years and with a total of 190 uveitis outbreaks. Time since diagnosis was 12.5±7.9 years. 64.4% of patients had uveitis as disease onset. 52.4% were overweight (BMI≥30 kg/m2), 16.7% were former/active smokers.

28.6% of patients had a family history of SpA. 14.3% had 1-2 uveitis outbreaks, 47.6% had 3-5 uveitis outbreaks and 38.1% had 6-11 uveitis outbreaks. 102 (53.7%) uveitis outbreaks fulfilled 1 criterion, 38 (20%) uveitis outbreaks fulfilled 2 criteria, 19 (10%) uveitis outbreaks fulfilled 3 criteria and 5 (2.6%) uveitis outbreaks fulfilled 4 or more. The results of the linear regression model revealed that the uveitis was more severe in patients with smoking history (β=0.34), axial and peripheral involvement (β=0.43), a BASDAI (Bath Ankylosing Spondylitis Disease Activity Index)>4 (β=0.32), positive HLA-B27 (β=0.29), female sex (β=0.19), patients with CRP (C-reactive protein) elevation (β=0.002) and a history of bilateral ocular involvement (β=0.32) while shorter disease evolution (β=-0.02) and normal vitamin D levels (β= -0.03) were associated with a better outcome.

Conclusion: We identified factors associated with adverse outcomes in SpA-U by developing a prognostic outcome score that integrates ocular inflammatory activity, ocular complications and refractoriness to treatment.

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AB0798 THE PRESENCE OF HEEL ENTHESITIS DURING PHYSICAL EXPLORATION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IS ASSOCIATED WITH POORER OUTCOMES AFTER 2 YEARS OF FOLLOW-UP. DATA FROM REGISPONSER-AS

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Background: Enthesitis represents one of the most important peripheral musculoskeletal manifestation in patients with axial Spondyloarthritis (axSpA). The prevalence and the burden of the disease associated with this symptom have been widely studied in axSpA and Psoriatic Arthritis (PsA). However, studies evaluating specifically the heel enthesitis and its impact over time are scarce.

Objectives: A) to evaluate the prevalence of patients with heel enthesitis during physical exploration in patients with radiographic axSpA (r-axSpA); b) to evaluate the association of heel enthesitis with higher Patient Reported Outcomes (PROs); c) to assess the impact of the heel enthesitis on the outcome measures after two years of follow-up in these patients.

Methods: Observational and prospective study during 2 years of follow-up that included patients with r-axSpA from the REGISPONSER-AS study (Spanish Rheumatology Spondyloarthritis Registry). The patients were divided into two groups according to the presence on heel enthesitis on physical exploration during the study visit. The PROs evaluated were the Global VAS, BASDAI, ASDAS, BASFI and the mental and physical components from the SF12 questionnaire. Linear regression models were performed using the PROs as the dependent variable and the presence of heel enthesitis as the explanatory variable, adjusting for bDMARDs intake and age. The impact of the heel enthesitis on PROs over two years of follow-up was evaluated using mixed models for repeated measures adjusting for confounders. Finally, the achievement of ASDAS Low Disease Activity (ASDAS-LDA) and ASDAS Inactive Disease (ASDAS-ID) after 2 years of follow-up between the two groups were evaluated.

Results: 749 patients were included (mean age 48.4 years; 75.3% men). 46 (6.1%) patients suffered from heel enthesitis on the study visit. Patients with heel enthesitis showed an increase (β coefficient, 95%CI) in Global VAS (1.32, 0.52-2.12), BASDAI (1.49, 0.81-2.18), ASDAS (0.45, 0.12-0.77) and BASFI (9.54, 1.78-17.30) compared with patients without heel enthesitis after adjusting for confounders. The impact of the presence of enthesitis on the PROs after two years of follow-up is shown in [Table 1]. Patients with heel enthesitis showed higher scores during the two years of follow-up in Global VAS, BASDAI, ASDAS and BASFI. In addition, the percentage of patients who achieved ASDAS-LDA after 2 years of follow up was lower in patients with heel enthesitis (15.9% vs. 31.5%, p=0.030) in comparison with patients without enthesitis. No differences were found regarding ASDAS-ID.

Table 1. Impact of the presence of heel enthesitis on PROs over two years of follow-up: mixed models for repeated measures.

	Current heel enthesitis N = 46 Mean (SD)	No current heel enthesitis N = 703 Mean (SD)	p-value	p-value age and bDMARDs adjusted
Global VAS	5.1 (2.8)	4.3 (2.6)	0.015	0.010
BASDAI	4.8 (2.7)	3.9 (2.7)	<0.001	<0.001
ASDAS	2.9 (1.1)	2.6 (1.0)	0.007	0.005
BASFI	43.8 (29.7)	40.0 (27.4)	0.245	0.161
PC-SF12	33.3 (11.4)	35.3 (10.7)	0.128	0.110
MC-SF12	47.4 (14.2)	48.2 (12.2)	0.547	0.281

Conclusion: In patients with r-axSpA, the presence of heel enthesitis on physical exploration was associated with poorer scores on the outcome measures after two years of follow-up, in comparison with patients without heel enthesitis. The achievement of a low disease activity is less likely in patients with this manifestation.

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AB0799 ANATOMICAL ABNORMALITIES OF THE LOWER LUMBAR SPINE DO NOT CHANGE THE COURSE OF NON-RADIOLOGICAL AXIAL SPONDYLOARTHRITIS

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Background: Diagnosing early spondyloarthritis (SpA) is crucial for effective therapeutic intervention. Magnetic resonance imaging (MRI) helps us to diagnose non-radiographic SpA (nr-ax SpA) in an early stage according to the criteria of the imaging arm of the Assessment of Spondyloarthritis International Society (ASAS) classification. Diagnosis of sacroiliitis using MRI has limitations because of the lack of specificity and sensitivity. Several differential diagnoses are well known and should be considered[1]. In our daily practice, anomalies of the lower lumbar spine and the sacrum, such as spondylolysis, dysraphia, or assimilation joints, are often found to be accompanied by changes in the sacroiliac joints (SIG) corresponding to sacroiliitis.

Objectives: To investigate the presence of anatomical anomalies of the lower lumbar spine in our cohort of early diagnosed nr-ax SpA patients fulfilling the criteria of ax SpA and show if they cause a difference in the outcome.

Methods: Patients (n = 56, age < 45 years, symptom duration 3– 24 months) recently diagnosed with sacroiliitis using MRI and meeting the ASAS criteria for axial SpA were followed-up for 2 years[2]. We retrospectively analyzed the anatomic anomalies of the lower lumbar spine on MRI and, if available, on radiograph images.

Results: MRI on t0 revealed that 15 (26.7%, one female and 14 males) of 56 patients had anatomical anomalies of the lower lumbar spine, indicating bone marrow edema with clinical ax SpA according to the ASAS classification criteria. Spondylolysis, assimilation joints, and dysraphia were found in 4 (7.1%), 7 (12,5%), and 7 (12.5%) patients, respectively. The presence of HLA-B-27 and assessment results (CRP-ASDAS and BASDAI, BASMI) were similar to patients without the mentioned anatomical anomalies. Patients with spondylolysis and dysraphia of the lower spine and those without anomalies displayed similar progression of MRI findings between t0 and t2.

Conclusion: In addition to the well-known noninflammatory causes of sacroiliitis, such as pregnancies or intensive sporting activity, anatomical peculiarities could not be considered noninflammatory reasons. Contrary to the latest literature[3], they are not responsible for non-specific sacroiliitis. No difference in the development to axial SpA was observed when patients with and without anatomical changes were compared.

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AB0800 ULTRASONOGRAPHY OF SUPRASPINATUS ENTHESES IN AXIAL SPONDYLOARTHRITIS

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Background: Several scoring systems have been developed to quantify ultrasound (US) abnormalities of the entheses in patients with spondyloarthritis (SpA). These scores included entheses of the lower limb, triceps tendon, and lateral epicondylar tendon [1] [2].

Studies regarding the involvement of supraspinatus enthesis in patients with SpA are scarce.

Objectives: This study aimed to assess the supraspinatus enthesis in patients with axial SpA using ultrasonography.

Methods: We performed a cross-sectional case-control study including 74 subjects (148 entheses):

- G1: 37 patients with axial radiographic SpA diagnosed according to Assessment of SpondyloArthritis International Society (ASAS) criteria.
- G0: 37 age and sex-matched healthy controls.

All subjects underwent the US by a qualified-US rheumatologist. The long axis of the supraspinatus was assessed with the patient's hand placed near the ipsilateral hip and the elbow directed posteriorly. Following parameters were evaluated at the bone attachment supraspinatus tendon: thickness, echogenicity, loss of normal fibrillar structure, calcifications, enthesophytes, erosions, cortical irregularities, bursitis, and vascularity at power Doppler. Statistical analysis was performed using SPSS Statistics software version 21.

Results: The mean age was 44.62 + 12.31 years. There were 29 men and 8 women for each group. In G1, the mean disease activity using ASDAS-CRP was 3.03 with levels ranging from 0.10 to 5.66. The mean thickness of supraspinatus tendon at its bone attachment was 4.54 ± 0.84 mm in G1 versus 4.02 ± 0.57 mm in G0 (p=0.03). Receiver Operator Curve (ROC) analysis showed the cutoff point with the best accuracy in distinguishing patients of controls to be 4.65 mm, with a sensitivity of 45.9% and specificity of 86.5% (air under the curve (AUC) value: 0.666 (p=0.014). Hypo-echogenicity and loss of normal fibrillar structure were noted in 27% (n =10 patients) and 5% (n = 2), respectively, in G1. Structural damage lesions were found in 3 % in G0 (n= 1) and 51 % in G1 (n=19), p< 0.0001. In G1, structural damage lesions included: calcifications (38%, n=14), erosions (30%, n = 11), cortical irregularities (16%, n=6), and enthesophytes (8%, n=3). In G0, structural damage lesions comprised: calcifications (3%, n=1) and cortical irregularities (3%, n=1). Vascularity at power Doppler was found in 11% in G1 (n= 4) and 0 % in G0. Subacromial-subdeltoid bursitis was noted in 3% in G1 (n=1) and in 0% in G0.

Conclusion: Our study showed that structural damage lesions of supraspinatus enthesis were frequent in patients with SpA compared to healthy controls. A cut-off of 4.65mm supraspinatus's thickness was able to discriminate patients with SpA from healthy controls. This finding suggests that supraspinatus enthesis evaluation can be added in entheses US scores.

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AB0801 THE ASAS HEALTH INDEX (HI): CONSTRUCT VALIDITY AND RESPONSIVENESS IN RELATION TO TNF INHIBITOR (TNFI) TREATMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA).

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Background: The Assessment of Spondyloarthritis International Society (ASAS) has developed the ASAS HI aiming to capture the full range of functioning and disability in patients with axSpA.

Objectives: To examine the construct validity and responsiveness of ASAS HI in relation to TNFi treatment.

Methods: In this investigator-initiated 52-week prospective observational study (MANGO study; NCT02011386)(3) axSpA patients initiated sc. Golimumab 50 mg every month. Key inclusion criteria were BASDAI >4.0 and sacroiliitis on radiography and/or MRI.

Results: 45 of 53 TNFi naïve patients completed ASAS HI at weeks 0, 4, 16 and 52. 55.6% were male, 75.6% HLA-B27 positive, median age 34.6 yrs (IQR 28.3;46.1) and symptom duration 5.1 yrs. (2;13)(Table 1A). ASAS HI decreased from week 0 to weeks 4, 16 and 52, from median 10.0 (IQR 8;11)) to 7.0 (2.3;10), 5.5 (1.3;8) and 4.0 (1;7.5)(Wilcoxon-Pratt; all p<0.001). Patients with low ASAS HI (score 0-5, good heath state(4)) at week 16 and 52 had significantly lower ASDAS, BASDAI, BASFI, pain, pt. global and CRP than patients with moderate to high ASAS HI (6-17) (Table 1B). Patients with a decrease of >3 (clinically meaningful change(3)) or >30%(5) in ASAS HI from week 0-16 had significantly larger reductions in ASDAS, BASDAI, BASFI, pain, pt. global and SPARCC MRI spine inflammation score (Table 1C). At baseline, ASAS HI correlated with BASFI and SPARCC SIJ inflammation score (rho: 0.37-0.38, p<0.05), and changes in ASAS HI from week 0-16 correlated with changes in ASDAS, BASDAI, BASFI, pain, pt. global (0.51-0.67, p<0.001) and change in MRI SIJ inflammation score (0.30, p<0.05). ASAS HI had high responsiveness (Table 1D).

Conclusion: ASAS HI showed good construct validity and responsiveness.

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AB0802 PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE IN RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS, AND PSORIATIC ARTHRITIS.

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Background: Non-alcoholic fatty liver disease (NAFLD), the most common cause of liver disease, has a prevalence of about 25% in the general population.

Table 1. Diseases measures at baseline (Table 1A), stratified according to ASAS HI states at week 16 and 52 (Table 1B), changes from week 0 to 16 and 52 (Table 1C) and responsiveness (Table 1D).

	Table 1A	Table 1B				Table 1C				Table 1D	
	Baseline	ASAS HI at week 16		ASAS HI at week 52		Absolute change in ASAS HI week 0 to 16		Percentage change in ASAS HI week 0 to 16		Responsiveness week 0-16	
		0-5	6-17	0-5	6-17	<3	≥3	<30%	≥30%	SRM	ES
	n=45	n=22	n=22	n=26	n=16	n=18	n=26	n=16	n=28	n=45	n=45
ASAS HI	10.0 (8;11)	1.5*** (1;4)	8.0 (7;10)	2.0*** (0.8;3.3)	9.5 (7;10.8)	-1.5*** (-2;2)	-6.0 (-12;-3)	-1*** (-2;2)	-5.5 (-12;-2)	1.6	1.3
ASDAS	3.7 (3.1;4.2)	1*** (0.9;1.5)	2.1 (1.1;3.1)	1.2*** (0.8;1.5)	2.2 (1.8;3.3)	-1.3*** (-2.5;1)	-2.2 (-4.6;-1.3)	-1.2*** (-2.5;1)	-2.2 (-4.6;-1.3)	2.5	1.7
BASDAI	6.1 (5;7.2	0.9*** (0.5;2.3)	3.2 (1.8;5.1)	1.3*** (0.3;2.3)	3.8 (2.9;5.7)	-1.7*** (-5.3;0.9)	-4.9 (-6.7;-1.9)	-1.6*** (-5.3;0.9)	-4.8 (-6.7;-1.9)	2.7	1.8
BASFI	4.4 (3;5.9	0.6*** (0.3;1.4)	2.3 (1.4;4)	0.3*** (0.1;1.4)	2.5 (1.5;3.3)	-1.2*** (-4.4;1.2)	-3.5 (-6.7;-0.2)	-1.1*** (-3.9;1.2)	-3.5 (-6.7;-0.15)	1.4	1.4
BASMI	2;0 (1;3)	1.0 (0;2)	1.0 (0;2)	1.0 (0;2)	1.0 (0;3)	0 (-3;2)	-1.0 (-4;2)	0 (-3;2)	-1.0 (-4;2)	0.4	0.6
Pain	7.0 (5.6;8.1)	0.8*** (0.3;1.2)	2.9 (1.3;5.5)	0.7** (0.3;2.6)	3.3 (1.1;6.3)	-2.6** (-8.8;1.9)	-5.6 (-8.6;-1.1)	-1.8*** (-6.8;1.9)	-5.6 (-8.8;-1.1)	2.7	1.8
Pt. global	7.5 (6.4;8.4)	1.0*** (0.4;1.9)	3.0 (1.3;6.7)	0.6*** (0.2;2.1)	4.4 (2.3;6.9)	-3.4*** (-6.5;0.8)	-6.7 (-8.8;-1.1)	-2.8*** (-6.3;0.8)	-6.5 (-8.8;-1.1)	3.3	1.8
CRP (mg/l)	7.7 (0.9;22)	0.3* (0.3;2.2)	1.3 (0.3;8.5)	0.3** (0.3;2.5)	1.0 (0.3;5)	-1.7 (-39.6;6.9)	-5.2 (-79.7;19)	-1.7 (-39.6;6.9)	-5.2 (-79.7;19)	0.5	0.6
SPARCC MRI SIJ inflammation	14 (4;24.5)	4.0 (0;6.5)	2.0 (0;7.8)	2.0 (0;4.3)	2.0 (1;6)	-5.5 (-30;2)	-12.5 (-36;0)	-5.5 (-30;2)	-12.5 (-36;0)	0.9	1.1
SPARCC MRI spine infl.	8 (4;15)	0 (0;3.5)	1.0 (0;4.3)	0(0;2)	1.0 (0;3)	-2.5** (-98;2)	-8 (-55;0)	-2.5* (-98;2)	-8 (-55;0)	0.5	0.7

Median (IQR). Mann-Whitney test. * p<0.05. ** p<0.01. *** p<0.001. Standardized response mean (SRM) and effect size (ES) ≥0.50 to <0.80 and ≥0.80 represents moderate and high responsiveness.

It increases mortality and comorbidity in patients with immune-mediated inflammatory diseases.
Objectives: The main objective is to estimate the prevalence of NAFLD in three of the most common rheumatologic pathologies: rheumatoid arthritis (RA), axial spondyloarthritis (SpA-ax) and psoriatic arthritis (PsA). As a secondary objective, the possibility of finding associated risk factors in this group of subjects that may imply a higher risk of developing NAFLD is proposed.
Methods: We conducted a prospective single center observational study which included patients diagnosed with RA, EspA-ax, and PsA attended in the Rheumatology department of a tertiary hospital from January to April 2021. Anthropometric parameters, history related to cardiovascular risk factors and disease activity at the time of the visit were collected. Additionally, blood tests and transitional elastography were performed in all patients and the presence of NAFLD was assessed by the fatty liver index (FLI) scale. Different variables were considered to study their association with NAFLD.
Results: 90 patients were included: 28 diagnosed with RA, 36 with EspA-ax and 26 with PAs. 41.1% were male (age range: 27-79 years). Patients with previous liver disease were excluded from the study. 22 (27.2%) patients had NAFLD measured by FLI ≥ 60. No significant differences in prevalence of hepatic steatosis were found between the 3 groups, although values were higher in patients with PsA.
The variables that were significantly associated with the development of NAFLD in our cohort were: body mass index (BMI), abdominal perimeter, blood glucose level, HOMA-IR (Homeostatic Model Assessment for Insulin Resistance), HDL, TG, GGT, ferritin and uric acid levels. The rest of the variables studied did not show statistically significant differences (Table 1).

Table 1.

	NO STEATOSIS (FLI<60) n=59		STEATOSIS (FLI>60) n=22		
	Mean	Standard deviation	Mean	Standard deviation	p
BMI	24,52	3,00	30,29	2,77	< 0,001
Abdominal perimeter	86,34	10,01	106,82	8,55	< 0,001
Age	52,93	12,87	57,59	8,24	0,1185
Glucose	78,64	8,37	90,64	19,69	0,0002
Insulin	8,83	10,12	12,40	6,66	0,1302
HOMA	1,75	2,02	2,76	1,70	0,0500
HbA1c	5,35	0,45	5,69	0,64	0,0096
Total cholesterol	190,98	29,46	201,41	38,53	0,1977
HDL	64,88	17,66	55,59	11,55	0,0249
LDL	110,44	28,45	120,00	36,21	0,2163
TG	81,12	32,42	128,50	55,52	< 0,001
GPT	25,83	30,73	37,18	19,82	0,1116
GOT	27,20	23,49	26,82	10,69	0,9413
GGT	20,80	17,66	49,95	38,46	< 0,001
Creatinin	0,75	0,19	0,84	0,18	0,0583
Uric acid	4,78	1,30	5,91	1,14	0,0007
Ferritina	121,75	111,30	208,00	140,17	0,0050
PCR	2,89	4,55	2,67	2,33	0,8307

Conclusion: Hepatic steatosis was present in 27.2% of patients vs 25% estimated prevalence in the general population. Identification of risk factors involved would allow better control of the comorbidities associated with NAFLD.
The fact that the prevalence found in our sample population is so close to that of the general population, may be related to a good inflammatory control of the underlying disease.
Further prospective studies with larger sample sizes are needed to find additional predictive factors for the development of NAFLD in this group of diseases.
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AB0803

ACCURACY OF "HOSPITAL MILITAR CENTRAL" ADMINISTRATIVE DATA BASE FOR PSORIATIC ARTHRITIS DIAGNOSIS IN PATIENTS AT A HIGH COMPLEXITY CENTER.

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Background: Psoriatic Arthritis (PsA) is a chronic inflammatory musculoeskeletal disease highly associated with Psoriasis (Pso), with a substantial morbidity and disability. (1,2) Initially considered as a type of Rheumatoid arthritis but afterwards was defined as a distinct entity (3). PsA can cause damage to joints which lead patients to great impairment.(4)The estimated prevalence is variable according to the geographical zone, but it has been established in general population between 0,2-1%, meanwhile in Pso patients could be as frequent as 6-42% (5,6). Patients with PsA present pain and stiffness in the affected joints, they even can have axial skeleton compromise, peripheral arthritis, several nail changes, enthesitis and dactylitis (5,6). A delay in diagnosis as much as 6 months is associated with a much lower treatment response, meanwhile early treatment with anti-inflamatory or immune-modulating drugs improves clinical and radiological outcomes (7). There are several useful tools which allow us to establish easily prevalence, incidence or even chronic associations or acute diseases in public healthcare, these tools are known as administrative databases. (8) In the last few years, there has been developed multiple algorithms for the diagnosis of different pathologies using the information gathered from diagnostic codes, pharmacy reports and surgical procedures in order to identify relevant information for example a disease prevalence of an specific population.(9)
Objectives: Determine the accuracy of the 10th International Classification of diseases (CIE-10) for Psoriatic Arthritis (PsA) diagnosis in the hospital Militar of Bogotá administrative database and to examine the effects of adding specific pharmacy data to CIE 10 on accuracy of PsA diagnosis.
Methods: We drew a random sample of patients from all ambulatory patients who had at least 1 clinic visit to the hospital between January 1 2015 and February 1 2020 who are 18 years or older. Charts of 972 patients were reviewed. The gold standard for PsA diagnosis was chart documentation of PsA diagnosis by a Rheumatologist. The data definitions of PsA diagnosis included presence of CIE-10 alone or various combinations of CIE-10 an the addition of specific pharmacy data to the algorithm. Accuracy of data definitions of PsA was assessed by calculating sensitivity, specificity, positive and negative predictive values, plausibility reasons and area under the receiver operator characteristics curve (ROC). We used Python and R studio software for the database analysis.
Results: From the administrative database we had a prevalence of 5.2% patients with PsA, and was determined the diagnosis algorithm using CIE-10 code L40.5 had a correct classification rate by the algorithm of 97.9%, with 84.3% sensitivity CI 95% (71.4-93), and a higher specificity of 99.3% CI 95% (98.7-99,8). Evaluating positive predictive value of the test was 89.6% CI 95% (77.3 -96.5), while the negative predictive value was 99.1% CI 95% (98.3-99.6). In these results the number of false negatives are higher than the number of false positives, when compared with the gold standard (physician diagnosis in clinical chart). Through a statistical analysis we calculate the ROC curve and the area under the curve which was 0.92 CI 95% (0.868-0.969) when used the CIE-10 code L40.5 for PsA diagnosis. Indicating that the test, taking into account the CIE-10 code L40.5, has a very good performance classifying correctly the PsA patients.
Conclusion: CIE-10 code L40.5 in the administrative database is a very sensitive and specific screening tool for identifying patients with PsA in the general clinic population. This can be used to evaluate large population samples and classified them for public health research using this kind of databases.

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AB0804

ASSOCIATIONS BETWEEN ULTRASOUND CHRONIC LESIONS IN PERIPHERAL ENTHESES AND RADIOGRAPHIC STRUCTURAL SPINAL CHANGES IN MEN AND WOMEN WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is characterised by spinal bone formation and enthesitis. Whether patients with spinal bone formation have a

generalised bone formation phenotype also involving the peripheral entheses is not fully known.

Objectives: To assess in cross-sectional analyses the association between chronic ultrasound (US) lesions in peripheral entheses with spinal bone formation and factors associated with spinal bone formation, overall and by sex.

Methods: The entheses at 14 sites at the extremities were examined in 173 patients (54 % men, mean age (SD) 55 (13) years and symptom duration 29 (13) years) with AS (modified NY criteria) using US. Entheses were assessed for structural components (enthesophytes, calcifications and erosions) according to the OMERACT definition [1]. Each lesion was evaluated 0 or 1 and summarised to a damage score (0-42). Spinal radiographs from the same time point were graded according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) and presence of syndesmophytes were determined. The associations between US damage score and mSASSS and factors associated with spinal bone formation were analysed with Spearman´s correlation analysis overall and by sex. Also, Mann Whitney´s test and multivariable logistic regression analysis with presence of ≥ 1 syndesmophyte as dependent variable and age, sex, BMI, smoking status, CRP, and US damage score as independent variables were used.

Results: Presence of any US structural component was found in 158 (91 %) of the patients with no significant difference between men and women (95 % vs 87 % respectively, p = 0.15). The US damage score was median (IQR) 4 (2 to 6) in the total group with a higher score in men compared to women, 4.5 (2 to 7) vs 3 (2 to 5), p = 0.002. In analogy, more men had presence of syndesmophytes in the spine compared to women, 63 % vs 35 %, p <0.001 and men had higher mSASSS compared to women; median (IQR) mSASSS in men 14 (3 to 43) compared to 2 (0 to 11.5), p<0.001. Men had higher body mass index (BMI), but there were no sex differences for age, symptom duration, CRP, and smoking status.

The results from correlation analyses for US damage score and mSASSS, age, symptom duration, CRP, smoking status, and BMI are presented in the Table 1. Spinal bone formation (mSASSS) was positively correlated with the US damage score in the total group and in men. In both men and women, higher age was associated with higher US damage score. A comparison between patients with and without syndesmophytes showed that patients with syndesmophytes had higher US damage score than patients without syndesmophytes, median (IQR) 5 (3 to 7) and 3 (1 to 5) respectively, p<0.001. In the multivariable logistic regression analyses the US damage score was not independently associated with presence of syndesmophyte in the total group or in men. If age was excluded from the analyses though, the US damage score was significantly associated with presence of syndesmophyte, odds ratio (95 % CI) for total group 1.20 (1.05 to 1.37) and for men 1.26 (1.05 to 1.51).

Table 1.

	Ultrasound damage score					
	Total group (n=173)		Men (n = 94)		Women (n = 79)	
	rs	p-value	rs	p-value	rs	p-value
Age, years	**0.44**	**<0.001**	**0.43**	**<0.001**	**0.51**	**<0.001**
Symptom duration, years	**0.28**	**<0.001**	**0.34**	**<0.001**	**0.27**	**0.015**
BMI, kg/m^2	**0.21**	**0.006**	0.11	0.28	0.19	0.10
Current or past smoking	0.039	0.61	0.18	0.090	-0.10	0.37
CRP, mg/L	0.12	0.13	0.028	0.79	0.20	0.073
mSASSS, score	**0.31**	**<0.001**	**0.27**	**0.010**	0.20	0.084

r_s: Spearman´s correlations coefficient

Conclusion: Structural lesions were common in the entheses in patients with long-standing AS. Men had more severe bone formation in the spine and the peripheral entheses compared to women. Chronic lesions at the entheses accumulate with increasing age and US damage score could not independently identify patients with syndesmophytes in this cohort with long-standing AS. However, if age was not considered, there was an association between bone formation in the peripheral entheses and the spine in men with AS.

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AB0805

LEVELS OF NATURAL KILLER CELLS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A META-ANALYSIS

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Background: Ankylosing Spondylitis(AS) is a complex chronic inflammatory autoimmune disease that mainly affects the spine. Natural Killer (NK) cells are classified among the recently discovered innate lymphoid cell subsets and have capacity to influence both innate and adaptive immune responses. However, the status of NK cells remains debated in AS.

Objectives: This study aims to clarify the level of peripheral NK cells in AS patient.

Methods: We used CNKI, CBM, Wanfang data and Chinese science, scientific and technological journal data, PubMed, Embase, Web of science, Cochrane library and Medline to collect relevant literature data, and sorted out the proportion of NK cells in AS patients. Random effects were selected to assess pooled data, inconsistency was assessed using I-squared index (I^2), and Egger's test was used to assess potential publication bias (STATA v.12.0).

Results: A total of 11 case-control studies involving 561 AS patients and 592 healthy controls (HC) were included in this study. AS patients had a significantly lower proportion of $CD16^+CD19^+$NK cells compared with HCs [SMD=-0.41, 95%CI (-0.71,-0.11), P<0.05,] (Figure 1), with no publication bias according to Egg's test[t=0.50, P=0.63].

Conclusion: The proportion of of $CD16^+CD19^+$ NK cells in AS patients was significantly reduced, suggesting disturbance of NK closely involved in the pathogenesis of AS.

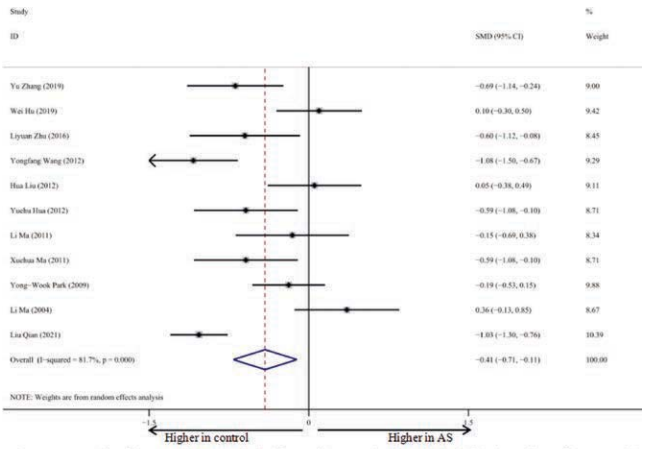

Figure1: Forest plot of the overall meta-analysis of NK cells proportions in peripheral blood,regardless of the NK cells definitions used, between AS patients and healthy controls.

Table 1. Summary of study characteristics of included records.

Author	Publish year	EI[a]	Q[b]	Case numbers AS	HC	NK cell's definition	Data Type	Mean % of NK cell (mean(or median)±SD)
Qian Liu	2021	4	7	121	120	CD16+CD56+	Original	AS:17.6 HC:138.9
Yu Zhang	2019	4	6	39	41	CD16+CD56+	Original	AS:22.78 HC:61.12
Wei Hu	2019	4	6	60	40	CD16+CD56+	Original	AS:13.3 HC:48.1
Liyuan Zhu	2016	4	7	30	30	CD16+CD56+	Original	AS:16.23 HC:44.58
Hua Liu	2012	4	5	60	30	CD16+CD56+	Original	AS:29.99 HC:49.5
Yongfang Wang	2012	4	6	60	44	CD16+CD56+	Original	AS:14.04 HC:60.12
Yuehu Hua	2012	4	7	36	32	CD16+CD56+	Original	AS:31.1 HC:59.8
Li Ma	2011	4	6	43	20	CD16+CD56+	Original	AS:24.98 HC:38.15
Xuehua Ma	2011	4	6	36	32	CD16+CD56+	Original	AS:31.1 HC:59.8
Yong-Wook Park	2009	4	7	41	173	CD16+CD56+	Calculated	AS:25.4 HC:190.4
Li Ma	2004	4	7	35	30	CD16+CD56+	Original	AS:33.48 HC:52.37

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AB0806

GENDER AND IMAGING PROGRESSION IN EARLY AXIAL SPONDYLOARTHRITIS: RESULTS FROM A 48-MONTH FOLLOW-UP (ITALIAN ARM OF SPACE STUDY).

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Background: Gender differences in disease presentation and imaging features of early axial-spondyloarthritis (axSpA) have not been thoroughly investigated.
Objectives: To assess the influence of gender on spinal/pelvic radiographic progression and magnetic-resonance-imaging (MRI) features in early-stage axSpA.
Methods: Baseline data from the Italian arm of SPondyloArthritis-Caught-Early-cohort, including patients with chronic-back-pain (CBP;duration≥3 months and ≤2 years;onset<45 years) were analyzed.Patients underwent a diagnostic work-up, including MRI and X-rays of the sacroiliac joints (SIJ), to establish a diagnosis of axSpA (according ASAS criteria). Clinical features, disease-activity and functional indices, imaging were collected at baseline (T0) and yearly during 48-months.Spinal and SIJ X-rays and MRIs were performed every 2-years and scored independently by 2 readers following *Stoke Ankylosing Spondylitis Spinal Score System modified by Creemers* (mSASSS) (score 0-72),*modified New York criteria grading system* (mNY-criteria) (score 0-4 per each joint) and *Spondyloarthritis Research Consortium of Canada* (SPARCC) (score of 0–40 for SIJ and of 0-92 for the spine). Characteristics of axSpA patients according the gender (male/female) were compared over-time with descriptive-statistics; multivariate-logistic-regression model was constructed to assess predictors of spinal and SIJ radiographic progression at 48-months.
Results: Out of 98 CBP patients, 91 had axSpA (83.5% non-radiographic;16.5% radiographic);47.3% were male. At T0 males were younger with less axial symptoms duration (p=0.04);had more frequently human-leukocyte-antigen (HLA)-B27+ (p=0.02),radiographic sacroiliitis with bilateral/symmetric pattern (p<0.02) and more signs of spondylitis (p=0.03).Females presented more frequently an associated peripheral/entheseal involvement (p=0.04) and a non-radiographic form (p=0.03). Functional and disease-activity indices decreased with slightly higher *Maastricht Ankylosing Spondylitis Enthesitis Score* (MASES),*Visual Analogue Scale of pain* (VAS),*Bath Ankylosing Spondylitis Disease Activity Index* (BASDAI) and *Bath Ankylosing Spondylitis Functional Index* (BASFI) values in females (p<0.04). Males showed a slight increased for both pelvic and spinal radiographic progression than females (Figure 1 **A-E**).At T0, 62 (68.1%) axSpA patients presented inflammatory lesions on MRI-SIJ, with more signs of active sacroiliitis in males (83.7% vs. 54.2%;p<0.05).Fifty-seven (62.6%) patients showed inflammatory-corner-lesions on MRI-spine: the frequency of these lesions no differed between males and females, while the localization varied:prevalently cervical/thoracic lesions were observed in females, instead lumbar lesions in males (p<0.05).We also found a higher prevalence of signs of active anterior spondylitis without active sacroiliitis on MRI in females (29.2% vs. 14.0%;p=0.03).Signs of enthesitis were found in 68.1% patients, with slightly higher prevalence of these lesions in thoracic area in females (p=0.04).Significant downtrend of SPARCC SIJ/spine scores was found, regardless the gender. More fat lesions were observed on MRI-spine in females, while more fat lesions were observed on MRI-SIJ in males (Figure 1**F-G**).Skin psoriasis was a predictor of spinal progression in all patients (OR=0.18; 95%CI:0.04-0.78).
Conclusion: The gender was associated with distinct axSpA features.Males had an increased pelvic and spinal radiographic progression and more frequently active sacroiliitis on MRI.Female axSpA showed a higher prevalence of cervical and thoracic spine-MRI signs (inflammatory-corner-lesions and fat lesions).

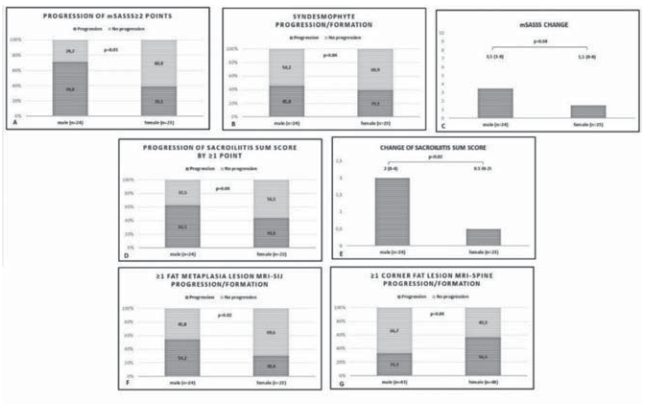

Figure 1 A-G: Association of gender with spinal and SIJ radiographic progression and fat lesions on MRI in axSpA after 48-months of follow-up.

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AB0807

RELAPSE INCIDENCE ACCORDING TO HLA-B*27 IN PATIENTS WITH SPONDYLOARTHRITIS IN A SPECIALIZED CENTER IN COLOMBIA

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Background: Spondyloarthritis (SpA) is a group of inflamatory diseases with multiple clinical manifestations (axial, peripheral, skin, eye, and intestine) including ankylosing spondylitis (AS), reactive arthritis, psoriatic arthritis (PsA), arthritis associated with inflammatory bowel disease, and non-radiographic axial spondyloarthritis. SpA is genetically related to HLA-B*27 as more tan 95% of the cases have it, while in general population its frequency is below 10%. The etiology and pathogenesis of this disease are unknown. Notwithstanding, the misfolding hypothesis suggests that it may be triggered by the formation of HLA-B*27 homodimers. The risk of developing SpA is 5-7% in positive HLA-B*27 individuals (1,2).
Objectives: Explore the relapse incidence and its associations with HLA-B*27 in SpA patients.
Methods: SpA patient cohort in a specialized multicentric health institution in Colombia (November 2011 to June 2021). Relapse was defined as the BASDAI increment ≥1+2≤ final BASDAI ≤4. A stratified analysis was performed for HLA-B*27 between diagnosis, current medication, and relapse. For group comparisons χ^2 and Wilcoxon tests were used, according to variable distribution. A logistic regression model was run in order to explain relapse incidence.
Results: 515 patients were included, among whom 60.9% were HLA-B*27 positive. 87.0% had an AS diagnosis (53.3% of men), 11.4% (64.4% of women) non-radiographic axial spondyloarthritis and 1.55% PsA (62.5% of women). Table 1 shows demographic and clinical characteristics. The relapse incidence was associated with positive HLA (Odss Ratio-OR 2.14 CI95% 0.982-4.674, p=0.055) and with time of disease evolution (OR 1.05 IC95% 1.02-1.091, p= 0.001) adjusting for sex.

Table 1. Demographic and clinical characteristics

	HLA-B*27				
	Negative (n=201)		Positive (n=314)		
Characteristics	Median	IQR	Median	IQR	p value*
Age	49	40 to 58	46	37 to 55	0.020
Time of disease evolution	6.6	4.6 to 10.6	8.6	5.6 to 14.6	0.000
Treatment time	3.2	2.1 to 6.4	3.3	2 to 5.6	0.648
BASDAI at entry	4.10	1.1 to 6.5	4.20	1.6 to 6.3	0.510
Current BASDAI	1.2	0 to 3.3	0.4	0 to 2.0	0.113
	n	%	n	%	
Sex					
Women	133	66.17	119	37.9	0.000
Men	68	33.83	195	62.1	
Diagnosis					
Non-radiographic axial spondyloarthritis	32	15.92	27	8.6	0.013
Psoriatic arthritis	5	2.49	3	0.96	
Ankylosing spondylitis	164	81.59	284	90.45	
Current medication					
Synthetic DMARD	13	6.47	19	6.05	0.780
Anti-TNF	154	76.62	251	79.94	
Anti-IL17	24	11.94	29	9.24	
Without treatment	10	4.98	15	4.78	
Relapse					
Yes	10	4.98	31	9.87	0.045

* p value for the difference between HLA-B*27 positive and negative groups. IQR: interquartile range

Conclusion: In SpA patients, HLA-B*27 frequency is higher in AS patients compared to other SpA forms. Furthermore, this is associated with a higher relapse risk and longer time of disease evolution.
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AB0808 COSTOVERTEBRAL, COSTOTRANSVERSE, STERNOCLAVICULAR AND MANUBRIOSTERNAL JOINT INVOLVEMENT IN SPONDYLOARTHRITIS: PRELIMINARY RESULTS OF SINGLE CENTRE EXPERIENCE

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Background: Costovertebral (CV), costotransverse (CTr), sternoclavicular (SC) and manubriosternal (MS) joint involvements may be in spondyloarthritis (SpA). However, the radiological and clinical characteristics of these involvements need further assessment.
Objectives: In this study, we aimed to determine the characteristics of CV, CTr, SC, and MS joint involvements in SpA patients.
Methods: SpA patients (searched from the hospital data-processing system according to ICD-10 system to determine the patients having M07 (enteropathic arthropathies), M45 (ankylosing spondylitis (AS)), M46 (other inflammatory spondylopathies) and/or M48 (other spondylopathies) codes) who have been requested a chest computed tomography (CT) for any reason between January 2010 and December 2020 included in this retrospective cross-sectional analysis. Chest CT reports were reviewed, and any CV, CTr, SC or MS joint involvement attributed to SpA accepted as positive CT for SpA involvement. Demographic/clinic data including smoking status, disease characteristics (duration, drug history, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI) and other related parameters) at the time of CT scan were collected and analyzed.
Results: After the confirmation of the diagnoses among 1700 patients, total of 339 SpA patients were included in the study. 244 were diagnosed with ankylosing spondylitis (AS), 66 with psoriatic arthritis (PsA), 14 with enteropathic arthritis, 13 with peripheral SpA, and 2 with non-radiographic axial SpA. According to CT reports, the number of patients with inflammatory changes in any of the CV, CTr, SC or MS joints on thoracic CT were 44. Of these patients, 42 were diagnosed with AS (95,5%), 1 with PsA (2,3%), and 1 (2,3%) with peripheral SpA. 39 CV, 9 SC, 5 MS joints, and 3 CTr joints were affected. Joint involvements (17%) were higher in patients with AS than in other patient groups (p<0.001). In the chest CT positive group, Schober's test, and chest expansion were significantly lower than chest CT negative group. Smoking history, C-reactive protein (CRP) value at diagnosis and at CT evaluation, and disease duration were associated with joint involvement. Demographic and clinical characteristics of patients with and without chest CT involvement were shown in Table 1.

Table 1. Demographic and clinical characteristics of patients with and without involvement on chest CT

	n	Without involvement	n	With involvement	P value	Odds Ratio
Age of diagnosis	295	41 (31-50)	44	39 (28-47)	0.23	
Gender (male) n (%)	295	142 (48.1 %)	44	37 (86%)	**<0.001**	**5.70 (2.46-13.19)**
Weight (kg)	96	71 (65-80)	18	72 (63-79)	0.73	
Height (cm)	96	165 (160-170)	18	171 (167-176)	**0.01**	**1.07 (1.01-1.14)**
BMI (kg/m²)	96	25,1 (23.7-29.9)	18	24,5 (22.5-25.5)	0.17	
Smoking ever n (%)	178	101 (56.7%)	31	26 (83.9%)	**0.004**	**3.96 (1.46-10.80)**
Smoking (pack x years)	101	20 (10-30)	26	30 (20-33)	0.04	
Disease duration (years)	295	4.9 (1.2-11.9)	44	13.5 (4.5-25.9)	**0.001**	**1.09 (1.05-1.12)**
ESR at diagnosis (mm/h)	194	16 (8-32)	19	26 (9-43)	0.13	
CRP at diagnosis (mg/dL)	193	0.80 (0.33-1.67)	19	1.99 (0.98-3.49)	0.004	
ESR at CT imaging (mm/h)	286	17 (10-35)	43	25 (10-40)	0.46	
CRP at CT imaging (mg/dL)	287	0.80 (0.40 -2.45)	43	1.56 (0.70-3.15)	0.04	
HLA B27 positivity n (%)	95	36 (37.9%)	14	8 (57.1%)	0.17	
Ever use biologic drugs n (%)	295	176 (59.7%)	44	26 (59.1%)	0.94	
BASDAI	37	3.5 (2.0-5.6)	10	2.2 (0.0-4.2)	0.16	
BASMI	2	5.5 (5.0-6.0)	6	5.5 (4.0-6.0)	0.86	
BASFI	20	1.7 (0.4-4.0)	9	1.2 (0.0-1.9)	0.36	
Tragus to wall distance (cm)	6	18.0 (15.5-23.0)	7	18.0 (16.0-27.0)	0.72	
Occiput to wall distance (cm)	17	7.0 (5.0-9.0)	9	12.0 (6.0-20.0)	0.07	
Schober's test (cm)	64	5.0 (3.4-6.0)	17	2.0 (1.0-3.0)	**0.002**	**0.67 (0.50-0.91)**
Lateral lumbar flexion (cm)	7	10.0 (7.0-17.5)	8	11.5 (6.0-17.0)	0.95	
Cervical rotation (°)	8	60.0 (40.0-70.0)	9	40.0 (30.0-60.0)	0.35	
Maximal intermalleolar distance (cm)	4	85.0 (64.5-105.5)	6	78.0 (66.0-115.0)	1.0	
Chest expansion (cm)	31	4.0 (2.5-5.0)	10	2.0 (1.0-3.0)	**0.001**	**0.35 (0.16-0.75)**
Morning stiffness at CT n (%)	188	119 (63.3%)	24	16 (66.7%)	0.75	
Morning stiffness (min)	178	20 (10-30)	26	22.5 (10-30)	0.84	

Data are presented as median (25-75 percentile) or number (%) CT; computerized tomography, BMI; body mass index, ESR; erythrocyte sedimentation rate, CRP; C-reactive protein, BASDAI; Bath Ankylosing Spondylitis. Disease Activity Index, BASMI; Bath Ankylosing Spondylitis Metrology Index, BASFI; Bath Ankylosing Spondylitis Functional Index
Conclusion: In this study, we have found that CV, CTr, SC, and MS joint involvement on thorax CT were more common in men and smokers and were associated with disease duration and appears to affect chest expansion and Schober's tests. In previous studies, CV and CTr joint involvement in AS patients with chest pain were 80-82% and 60%, respectively [1,2]. Our study showed that 17% of AS patients had involvement regardless of pain symptoms. As this is the preliminary data and the CTs will be re-evaluated by our radiologist, we will be capable to report more unbiased results.
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AB0809 ASSESSMENT OF THE IMPACT OF AXIAL SPONDYLOARTHRITIS ON PATIENT'S SOCIAL LIFE. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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Background: As spinal mobility becomes progressively impaired and pain levels escalate, difficulty in performing simple physical routines places a huge burden on axial spondyloarthritis (axSpA).
Objectives: The aim is to evaluate the impact of axSpA on patients' social life and to identify the factors associated with this.
Methods: Data from 2,846 unselected patients participating in EMAS, an online survey (2017-2018) across 13 European countries, were analysed. Impact of axSpA on social life was assessed by: "Score your relationships since you have been affected by Spondylitis / Spondyloarthritis" [Much worse to much better relationships with spouse, family, friend, and neighbours], and "Please indicate the frequency with which you do the following activities since you became affected by Spondylitis/ Spondyloarthritis?" [Much less frequent to much more frequent engagement in restaurants, cultural outings, travel, and sports]. Patients who rated at least one relationship as "worse/much worse" and at least one of social activity as "less/much less frequent" were considered to have a negatively impacted social life. BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and mental health via the General Health Questionnaire GHQ-12 (0-12) were assessed. Univariable and multivariable binary logistic regression were used to identify variables possibly explaining negative impact on social life (n= 2,120).
Results: Mean age was 43.8±12.3 years, 61.5% female, 49.2% had a university degree, and 68.2% married. 44.9% (n= 1,205) patients had their social life negatively impacted since the onset of axSpA. Those experiencing a negative impact on their social life were more frequently females (49.5% vs. 37.5% males, p<0.001), divorced/separated (59.5% vs. 34.4% widowed, p<0.001), and on sick leave (temporary and permanent) or unemployed (63.9%, 60.9% and 57.0% vs. 36.8% employed, p<0.001). Furthermore, those whose social life was negatively impacted reported greater BASDAI (6.2 vs. 5.0), functional limitation (24.4 vs. 17.4), spinal stiffness (8.4 vs. 7.3), longer diagnostic delay (9.7 vs. 7.4), poorer mental health (6.7 vs. 3.6), anxiety (62.6% vs. 37.1% no anxiety), depression (61.9% vs. 38.5% no depression), or sleep disorders (55.7% vs. 37.5% no sleep disorders), all p<0.001. The variables associated with negative impact on social life in the multivariable logistic regression were higher disease activity (OR=1.15),

poor mental health (OR=1.14), being on a sick leave/unemployed (OR=1.49), divorced/separated (OR=1.46), anxiety (OR= 1.41) and female gender (OR= 1.30; Table 1).

Table 1. Factors associated with a worsening social life (n= 2,120)

	Univariable logistic analysis		Multivariable logistic analysis	
	OR	CI 95%	OR	CI 95%
Age	0.99	**0.98, 0.99**	1.00	0.99, 1.01
Gender. Female[1]	1.63	**1.39, 1.91**	1.30	**1.06, 1.60**
Marital status. Divorced/separated[2]	1.93	**1.48, 2.50**	1.46	1.05, 2.04
Employment status. Sick Leave/Unemployed[3]	2.66	**2.24, 3.17**	1.49	**1.20, 1.85**
BASDAI (0-10)	1.41	**1.35, 1.48**	1.15	**1.08, 1.22**
Functional Limitation (0-54)	1.03	**1.02, 1.03**	1.02	**1.09, 1.02**
Spinal Stiffness (3-12)	1.20	**1.16, 1.24**	1.06	**1.01, 1.11**
Diagnostic delay	1.02	**1.01, 1.03**	1.01	0.99, 1.02
GHQ-12 (0-12)	1.22	**1.19, 1.24**	1.14	**1.11, 1.17**
Anxiety	2.84	**2.39, 3.37**	1.41	**1.08, 1.83**
Depression	2.59	**2.17, 3.10**	1.14	0.87, 1.49
Sleep disorders	2.10	**1.79, 2.46**	1.02	0.81, 1.27

[1]Female vs. male; [2]Divorced/separated vs. single/married/widow; [3]Sick leave/unemployed vs. other employment status.

Conclusion: Almost half of the axSpA patients reported to have negatively impacted their social life. Being female, divorced/separated, on sick leave/unemployed, with higher disease activity, poor mental health, and anxiety increase the likelihood of worsening social life. As relationships with others and engagement in social or community activities influence quality of life, greater attention to enabling individuals to participate socially through controlling disease activity and addressing mental health comorbidity in the management of axSpA.

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AB0810

ASSESSING HEALTHCARE UTILIZATION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE SPANISH ATLAS

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Background: Healthcare utilization by patients with axial spondyloarthritis (axSpA) is substantial, leading to a considerable social and economic burden[1]. Understanding patients' characteristics and the main determinants of healthcare utilization is essential to reduce this burden.

Objectives: The aim of the present study is to assess healthcare utilization in patients with axSpA in Spain.

Methods: Data from an online survey of 680 unselected axSpA patients pertaining to the Spanish Atlas of Axial Spondyloarthritis were analysed. Total healthcare utilization was assessed as the sum of number of healthcare visits, medical tests, hospital admissions, and emergency visits, all relying on the last 12 months prior to the survey. Mann-Whitney and Pearson's $\chi 2$ tests were used to analyse possible associations between sociodemographic (age, gender, educational level, marital status, and patient organizations membership) and patient-reported outcomes (disease activity measured by BASDAI [0-10], mental health measured by GHQ-12 [0-12], functional limitation index (0-54), spinal stiffness index (3-12), and diagnostic delay) with respect to total healthcare utilization. Simple and multiple linear regression was used to analyse its possible associated factors.

Results: A total of 530 axSpA patients participated in this study: the mean age was 45.3 years, 51.1% were female, 39.6% had a university degree, and 70.6% were married. In the previous 12 months, 77.9% (n= 530) used at least one healthcare source, of which 75.3% visited at least once a rheumatologist (n= 512, mean= 4.4), 55.6% GP (n= 378, mean= 9.4) and 33.5% physiotherapist (n= 228, mean= 20.1). With respect to medical tests performed in the last 12 months, 75.3% performed at least one x-rays test (n= 512, mean= 4.4) and 71.2% blood test (n= 484, mean= 4.5). Furthermore, 7.9% of patients were hospitalised (n= 54, mean= 2.2 and 23.1% of patients visited outpatient centre (n= 157, mean= 5.5).

Younger patients (r= -0.195) and females (52.0 vs 32.2 of males) showed higher healthcare utilization (p<0.001). In addition, a low positive correlation was found between healthcare utilization and disease activity (r= 0.290), mental health (r= 0.257), functional limitation (r= 0.283) and diagnostic delay (r= 0.151), all p-values <0.001.

In the multiple linear regression, the qualitative factors associated with higher healthcare utilization was female gender (B= 12.854), while the quantitative factors associated with high healthcare utilization were younger age (B= -0.737), higher disease activity (B= 3.378), greater functional limitation (B= 0.576), and longer diagnostic delay (B= 0.959; Table 1).

Table 1. Linear regression analysis of socio-demographic and patient-reported outcomes according to healthcare utilization (N= 402)

	Simple linear regression		Multiple linear regression	
	Beta	95% CI	Beta	95% CI
Age	-0.884	**-1,266, -0.503**	-0.737	**-1.190, -0.283**
Gender. Female	19.792	**11.600, 27.984**	12.854	**3.502, 22.207**
BASDAI (0-10)	7.260	**4.934, 9.586**	3.378	**0,571, 6.185**
GHQ-12 (0-12)	2.724	**1.786, 3.663**	1.126	-0.048, 2.300
Functional Limitation (0-54)	1.418	**1.007, 1.828**	0.576	**0.007, 1.145**
Diagnostic Delay	0.966	**0.419, 1.512**	0.959	**0.374, 1.544**

Conclusion: Higher healthcare utilization was associated with higher disease activity, greater functional limitation, and longer diagnostic delay, in younger and females axSpA patients. Optimal monitoring of axSpA patients may help to minimise healthcare utilisation in patients with axSpA.

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AB0811

RESPIRATORY TRACT INFECTIONS AND RISK FACTORS FOR INFECTION IN A SPONDYLOARTHRITIS COHORT: IS THERE A DIFFERENCE BETWEEN PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS?

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Background: Respiratory tract infections (RTIs) are the most common infections in patients with rheumatic diseases under immunosuppressive treatment. RTIs may cause significant morbidity with reduced quality of life (QOL), increased healthcare costs and may lead to interruption of DMARD therapy. However, to date only limited data on infection risk in spondyloarthritis (SpA) patients are available.

Objectives: To assess the occurrence of respiratory tract infections in a real-world SpA cohort and determine associated factors.

Methods: Questionnaire-based screening and retrospective medical chart analysis of a monocentric cohort of 314 SpA patients comprising 168 psoriatic arthritis (PsA) and 146 axial spondyloarthritis (axSpA) patients.

Results: Out of 314 SpA patients, 89% had a history of upper respiratory tract infections (URTI) and 31.1% of lower respiratory tract infections (LRTI) within the last two years (Table 1). In a linear regression model LRTIs were associated with glucocorticoid (GC) therapy (p=0.015), CRP level (p=0.018), previous history of severe respiratory infections (p=0.007) as well as absence of HLA B27 (p=0.024). In general, patients with LRTIs were significantly older (p=0.007), had increased functional impairment (p<0.001), a reduced health-related QOL (p<0.001), poorer sleep quality (p=0.001) and more depression (p=0.001). 46% of patients had required antibiotics for RTIs within the last two years. Antibiotic therapy was associated with smoking (p=0.006), biologic therapy (p=0.005) and poor sleep quality (p=0.005). Smoking was associated with LRTI (p=0.009), but not URTI. Female patients reported a significantly higher frequency of LRTI (p=0.003), sinusitis (p=0.001), pharyngitis/laryngitis (p=0.009) and had received more courses of antibiotics than male patients (p=0.032).

Table 1. ***Patient characteristics and infections***

	axSpA (n=146)	PsA (n=168)	Total (n=314)
Age, years, mean (SD)	49.6 (14.2)	57.4 (12.4)	53.8 (13.9)
Male / Female, %	56.8 / 43.2	53.0 / 47.0	54.8 / 45.2
BMI, kg/m^2, mean (SD)	27.1 (7.2)	27.4 (5.4)	27.3 (6.2)
Smokers, n (%)	41 (31.8)	27 (16.3)	68 (23.1)
HLA B27, n (%) (n=230)	97 (71.9)	23 (24)	120 (52.2)
Therapy:			
n (%)			
csDMARD	29 (19.6)	84 (50.6)	113 (36.2)
bDMARD	109 (75.2)	102 (60.7)	211 (67.4)
Glucocorticoids	14 (9.9)	15 (8.9)	29 (9.4)
Hypogammaglobulinemia (IgG<7g/l), n (%)	5 (3.5)	6 (3.6)	11 (3.6)
Polyclonal IgA (>4g/l) elevation, n (%)	15 (10.9)	29 (17.8)	44 (14.7)
URTI: n (%)	114 (88.4)	148 (90.2)	262 (89.4)
Rhinitis, %	87.1	87.5	87.3
Laryngitis/pharyngitis, %	37	36.9	36.9
Sinusitis, %	40.5	30.2	34.7
Otitis media, %	14.3	6.8	10.1
LRTI: n (%)	39 (30.5)	52 (32.1)	91 (31.1)
Bronchitis, %	28.0	30.6	29.6
Pneumonia, %	3.9	3.1	3.4
Pleuritis, %	2.4	1.2	1.7

There were no significant differences between PsA and axSpA regarding frequency of URTI or LRTI, though PsA patients had tendentially more overall RTIs. Biological therapy did not lead to a significantly increased occurrence of infections, but was associated with increased antibiotic therapy (p=0.039). Patients with a history of pneumonia had received anti-IL17 therapy more frequently (p=0.002), while there was no significant association with anti-TNF therapy (p=0.156). Patients on GC had a relative risk for LRTIs of 2.04.

Hypogammaglobulinemia was rare in SpA patients (3.6%) despite continuous immunosuppressive treatment, occurred with equal frequency in axSpa and PsA patients and was associated with pneumonia (p=0.007) and increased antibiotic use (p=0.016). Polyclonal IgA elevation was observed in 14.7% of patients (mean 4.98g/l) and was associated with fewer episodes of rhinitis (p=0.027), whereas LRTIs and antibiotic use did not differ significantly.

Conclusion: This study quantifies the incidence and effects of RTIs in a real-world SpA cohort. While infections constitute significant adverse events of biologicals, and URTI were common, severe respiratory tract infections were rare. Differences in infection risk between SpA and PsA need to be studied more closely.

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AB0812

EFFECT OF PRO-INFLAMMATORY CYTOKINE-INTERLEUKIN 6 ON THE COURSE OF ANKYLOSING SPONDYLITIS IN PATIENTS AFTER COVID-19

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Background: Everyone knows that COVID-19 not only has a severe effect on the pulmonary system, but also triggers a whole cascade of autoimmune reactions. The study of the effect of the pro-inflammatory cytokine - interleukin 6 (IL6) on the clinical course of patients with ankylosing spondylitis (AS) undergoing COVID-19 is an important problem in rheumatology..

Objectives: To study the significance of the pro-inflammatory cytokine-IL-6 on the clinical features of the course of AS in patients who have undergone COVID-19.

Methods: In the period from 2020-2021, 44 patients with a diagnosis (AS) were hospitalized in the City Clinical Hospital # 3 of Tashkent city. The patients were divided into two groups: Group I - 20 patients with AS who underwent COVID-19 and Group II of 24 patients with no history of AS who had COVID-19 infection. The average age of patients in group I was 32 ± 4.1 years and in group II - 36.5 ± 5.2 years. All patients underwent clinical and laboratory studies, including studies of serum IL-6 levels. Disease activity was assessed using the BASDAI and ASDAS scales, pain was assessed using a numerical rating scale (NRS), and peripheral joint damage was assessed by the presence of pain and swelling in 44 joints. All patients underwent PCR, as well as ELISA-IHLA tests for the presence of antibodies to COVID-19.

Results: Clinical examination of the patients revealed the presence of pain in the spine, which was assessed using the numerical rating scale – (NRS) in group I it was 8.5 ± 1.2 points and 5.9 ± 2.3 points in patients of group II. Examination of peripheral joints showed an average number of painful joints (PJ) of 16.9 ± 3.2 in group I and 8.6 ± 2.7 in group II, the number of swollen joints (NSJ) 8.8 ± 2.1 in group I and 4.2 ± 1.7 in group II. group. The study of AS activity using the BASDAI scale showed an average level of 5.1 ± 1.7 points in group I and 4.4 ± 2.1 points in group II. And the study of activity on the ASDAS scale showed an average level of 4.0 ± 1.7 points in group I and 2.5 ± 0.8 points in group II, which indicates a very high activity of the pathological process in group I and medium-high activity in group II. The IL-6 level in group I was 10.2 ± pg / mL, 4.2 pg / mL in group II and 1.39 pg / mL in the control group.

Conclusion: 1. The clinical course of AS in patients who have undergone COVID-19 is characterized by a more pronounced disease activity according to the BASDAI and ASDAS scales, a high intensity of pain syndrome according to a NRS, as well as a high level of IL-6.

2. A high level of IL-6 in group I indicates the impact of COVID-19 on the course, activity and severity of the autoimmune process in patients with AS, which is many times higher than in patients of group II, which allows us to consider it as a biomarker of damage to the articular and connective tissue in this infection.

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AB0813

CORRESPONDENCE BETWEEN PATIENT-REPORTED FLARE AND DISEASE ACTIVITY SCORE VARIATION IN AXIAL SPONDYLOARTHRITIS

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Background: There is currently no consensual definition of flare in axial spondyloarthritis (axSpA).
Objectives: The aims of this study were to determine thresholds of variations of BASDAI associated with patient-reported flare and to test performance of ASAS preliminary definitions of flare[1].
Methods: This prospective study was proposed to all patients registered on the Spondy+ platform, a secure e-health platform for SpA patients. Every week during one year, patients were invited to connect to the platform to fill a BASDAI questionnaire, a 0-10 pain visual analogic scale and to answer to the following question: "has your disease flared up since last week?". Variations of BASDAI and pain between connections were assessed and associated to the change of perception of flare. ROC curves were built to assess performances of BASDAI and VAS to identify patient-reported occurrence and resolution of flare. Performance of ASAS preliminary definitions of flare was also assessed.
Results: 99 patients participated to this study for an average duration of 309 ± 148 days. 92% of them reported at least one episode of flare over follow-up. Area under the ROC curve (AUC) was significantly higher for ΔBASDAI than for Δpain, to predict outbreak of flare (0.81 vs 0.77, p=0.02). In contrast, ΔBASDAI and Δpain were comparably accurate to predict flare resolution with no significant difference of AUC (0.78 vs 0.80, p=0.4). Best performance was obtained for an increase of 0.2 points of BASDAI (sensitivity=70%; specificity=79%) and 0.5 of pain VAS to predict outbreak of flare and a decrease of 0.4 points of BASDAI and 0.5 of pain VAS to predict flare resolution (Figure 1). None of the ASAS definitions yielded sensitivity values higher than 37% whereas specificity was higher than 95% for all of them.

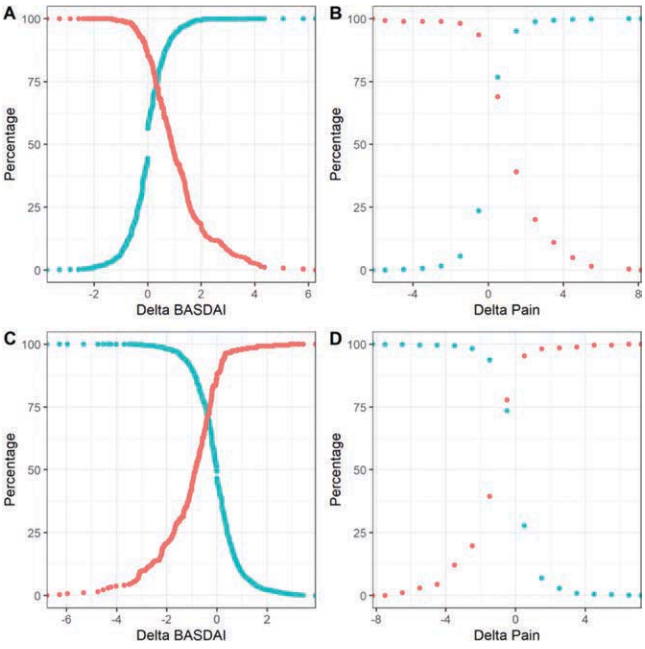

Figure 1. Sensitivity (red dots) and specificity (blue dots) according to ΔBASDAI (panels A,C) and Δpain (panels B,D) threshold as predictors of outbreak (panels A,B) or resolution (panels C,D) of flare.

Conclusion: ΔBASDAI appeared as a suitable variable to monitor both occurrence and resolution of SpA flare, as reported by patient.
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AB0814

ASSOCIATION BETWEEN UVEITIS AND OTHER CLINICAL MANIFESTATIONS OF ANKYLOSING SPONDYLITIS

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Background: Uveitis is a frequent extra-skeletal manifestation of ankylosing spondylitis (AS).
Data on the association of uveitis with other clinical manifestations of AS are contradictory and require further study.
Objectives: To assess the association of uveitis in AS with demographics and genetics, spine lesions, peripheral disease, coxitis, enthesitis.
Methods: 402 AS pts (New York criteria, 1984), were observed in V.A. Nasonova Research Institute of Rheumatology. 168 pts had at least 1 episode of uveitis (group 1), 234 pts did not have uveitis (group 2). The patients underwent standard clinical, laboratory and instrumental examination, including HLA-27- testing, X-ray examinaiton of joints and spine, ultrasonography of joints and entheses. Two groups were compared by gender, onset age and AS duration, presence of HLA-B27, damage of the spine, hip and peripheral joints and enthesitis.
Results: Both groups were dominated by men: 117 of 168 in group 1 and 189 of 234 in group 2. However, among patients with uveitis, the proportion of women was significantly higher: 51/168 (30.3%) and 45/234 (19.2%), p=0.01. The average duration of the disease was comparable in both groups – 14.9±10.2 and 12.8±9.9 years, respectively. The number of patients with AS onset before the age of 16 also did not significantly differ: 22/168 (13.1%) in the group with uveitis, 35/234 (14.9%) in the group without uveitis, p=0.6. HLA-B27 in the group with uveitis was in 166/168 patients (98.8%) and in 221/234 (94.4%) in the group without uveitis, p=0.04. Syndesmophytes were observed in both groups with similar frequency: in the cervical spine - in 49/168 (29.1%) in group 1 and in 78/234 (33.3%) in group 2, p>0.05; in the lumbar spine – in 87 /168 (51.8%) and in 139/234 (59.4%), respectively, p>0.05. Hip joint lesion (coxitis) was present in 75/168 (44.6%) and in 112/234 (53.8%) respectively, p=0.52; enthesitis – in 114/168 (67,9%) and in 168/234(71,8%), p>0.05. Peripheral arthritis was observed significantly more often in the group with uveitis: in 113/168 (67.2%) and in 70/234 (33.2%) respectively, p<0.001; its predominant localization was knee - 71/113 (62.8%) and ankle - 54/113 (47.8%).
Conclusion: AS with uveitis is characterized by a greater proportion of women and stronger association with HLA-B27, compared with patients without uveitis. Peripheral arthritis with predominant involvement of the knee and ankle joints is significantly more common in AS pts with uveitis compared with pts without uveitis.
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AB0815

SLEEP DISORDERS ARE FREQUENT IN SPONDYLOARTHRITIS, ASSOCIATED WITH REDUCED QUALITY OF LIFE AND DEPRESSION AND MORE PREVALENT IN FEMALE PATIENTS

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Background: Axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) may have a profound impact on health-related quality of life (HRQoL) and sleep despite effective treatment.
Objectives: To assess sleep and HRQoL in SpA and determine associated factors.
Methods: Monocentric questionnaire-based assessment of HRQoL, function, sleep and depression in 314 SpA patients (n=168 PsA, n=146 axSpA).
Results: Under effective treatment 138 SpA patients (46.5%) demonstrated abnormal sleep behaviour. 49.3% reported not being able to sleep through the night, with 6.1 % needing sleeping pills. 11.9% indicated feeling unrefreshed most mornings. Abnormal sleep behaviour was associated with female sex (p=0.005),

HLAB27 (p=0.034), functional impairment (p=0.001) and depression (p<0.001). Patients reporting unrestful sleep had significantly more depressive symptoms (p<0.001) and highly reduced physical and mental HRQoL (p<0.001). Satisfaction with health was rated significantly lower (p<0.001). Patients with axial involvement (axSpA/axPsA) reported worse sleep quality (p=0.002) and waking too early (p=0.038) despite 73.7% receiving biologics. Sleep quality and early awakening correlated with BASDAI (p<0.001). Smokers had a reduced HRQoL (p=0.018) despite younger age (p=0.008). Female patients had worse sleep quality (p<0.001), needing more time to fall asleep (p=0.022), not being able to sleep through the night (p=0.026) and feeling unrefreshed in the morning (p<0.001). They had a reduced physical (p=0.019) and mental HRQoL (p=0.003), more depressive symptoms (p=0.040) and lower functional capacity (p=0.002). Functional capacity was associated with younger age (p<0.001), sex (p=0.042), smoking (p=0.008), sleep quality (p<0.001) and depression (p<0.001). 66.2% of patients have been assessed longitudinally, before and 3y later during COVID19 pandemic. Physical and mental HRQoL were stable over time. Functional capacity had decreased slightly. Subjective QoL during the COVID19 pandemic was not reduced compared to before. Regarding depressive symptoms, there was a mild but significant improvement over time (p=0.019). Furthermore, we observed an improvement of environmental QoL (p=0.034) during COVID pandemic. Overall subjective QoL as well as satisfaction with health did not change significantly. Patients who had changed therapy (37% of the cohort) still had a reduced physical HRQoL (p=0.022) as well as significantly more depressive symptoms (p=0.010) and perceived their overall QoL as being worse (p=0.016).

Conclusion: Despite treatment many SpA patients have a reduced HRQoL and impaired sleep quality with significant differences between male and female patients. Impact of COVID19 pandemic was low.

Table 1. ***Patient characteristics***

	Total (n=314)	Women n=142 (45.2%)	Men n=172 (54.8%)	p-value
Age, years, mean (SD)	53.8 (13.9)	53.7 (14.5)	53.8 (13.4)	0.983
BMI, kg/m^2, mean (SD)	27.3 (6.3)	27.1 (6.5)	27.4 (6.1)	0.706
Smokers, n (%)	68 (23.1)	34 (24.6)	34 (21.7)	0.544
HLA B27, n (%) (n=230)	120 (52.2)	46 (45.1)	54 (54.9)	0.055
CRP, mg/l, mean (SD)	6.14 (11.9)	5.88 (6.0)	6.37 (15.2)	0.721
Significant functional impairment, n (%)	54 (17.5)	29 (20.6)	25 (15.0)	0.198
Therapy, n (%)				
csDMARD	113 (36.2)	56 (39.7)	57 (33.3)	0.243
bDMARD	211 (67.4)	91 (64.1)	120 (70.2)	0.252
Depressive symptoms, n (%)				
Mild	109 (37.5)	53 (39.3)	56 (35.9)	0.040
Moderate/severe	48 (16.5)	27 (20.0)	21 (13.5)	
WHO-QOL mean (SD)				
Physical	60.2 (19.4)	57.4 (19.7)	62.6 (19.0)	0.019
Mental	67.7 (17.2)	64.5 (17.8)	70.3 (16.2)	0.003
Social	67.8 (20.0)	67.4 (19.6)	68.2 (20.3)	0.703
Environmental	77.3 (13.3)	76.6 (13.6)	78.0 (13.1)	0.363
Sleep, n (%)				
Abnormal sleep behaviour	138 (46.5)	76 (55.1)	62 (39.0)	0.006
Inability to sleep through the night	145 (49.4)	76 (55.1)	69 (44.2)	0.024
Waking too early	89 (30.4)	43 (31.4)	46 (29.5)	0.459
Need for sleeping pills	18 (6.1)	11 (8.0)	7 (4.4)	0.133
Unrefreshing sleep most or all nights	35 (11.9)	24 (17.5)	11 (7.0)	<0.001

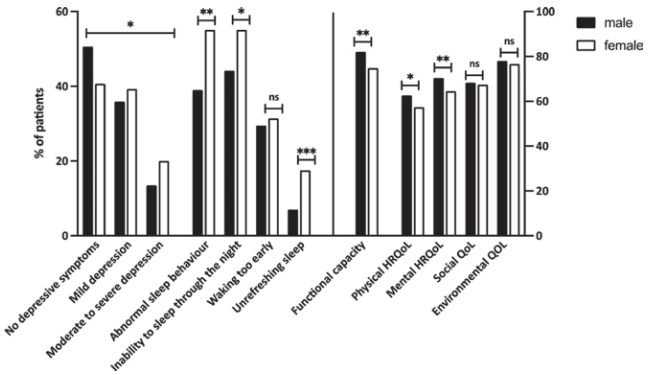

Figure 1. Female SpA patients have increased depressive symptoms and a reduced HRQoL.

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AB0816 COMORBIDITY AND THE USE OF BIOLOGICAL THERAPY IN AXIAL SPONDYLOARTHRITIS, IS THERE ANY IMPACT?

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Background: Spondyloarthritis (SpA) is a chronic inflammatory rheumatism that can be associated with a lot of comorbidities. Comorbidity seems to be a factor that is can influence the treatment tactics.

Objectives: The aims of our study were to describe the prevalence of commonly reported comorbidities in spondyloarthritis and to study the influence of comorbidity on the prescription of biological therapies in patients with SpA.

Methods: A retrospective study was conducted in a single rheumatology hospital in Morocco, including patients diagnosed as having SpA according to ASAS criteria 2010, during a period of 9 years. Comorbidity data were obtained through careful examination of the history and medical records. The Charlson comorbidity index [1] calculated for every patient.

Results: 375 patients were included in the study. 206 (54,9%) women, mean age 46.8±14,0 years. 105 patients were treated with biologic therapy (28%), in majority with TNF alpha inhibitors (99 patients). 188 (50,1%) patients had Charlson comorbidity index =1. The most common comorbidities were type 2 diabetes (12% patients), cancer (4,5%), chronic liver disease (2,9%), chronic kidney disease (2,1%), peptic ulcer (1,6%), ischemic heart disease (1,3%). Mean Charlson index was 1,14 ± 1,56 in total group; it was significantly lower in patients who were treated with biological therapy (0,6 ± 1,03) than in biologic naïve SpA (1,35 ± 1,68), p=0,0001. Biologics were prescribed in 66,7% of patients without comorbidities, in comparison with 17,1% of patients with Charlson comorbidity index = 1, 8,6% with Charlson comorbidity index = 2 and 6,8% of patients with Charlson index = 3 or more.

Conclusion: Comorbidities are common in SpA and have a direct impact on the use of biological therapy. The development of therapeutic strategy for treating comorbid conditions is a must to achieve therapeutic goals in SpA.

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Disclosure of Interests: None declared

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AB0817 COMORBIDITIES IN ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: ARE THERE ANY DIFFERENCES?

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Background: While comorbidity is increasingly being recognized and examined within patients with Axial spondyloarthritis (axSpA), few studies have investigated the occurrence of comorbidities in patients with non-radiographic axial spondyloarthritis (nr-axSpA) in relation to ankylosing spondylitis (AS).

Objectives: The aims of our study were to compare characteristics, comorbidities and medications between AS and nr-axSpA patients and to compare comorbidities between the two groups.

Methods: A cross-sectional study was conducted in a single rheumatology hospital in Morocco, including patients diagnosed as having axSpA according to ASAS criteria 2010, during a period of 9 years. The comorbidities studied were hypertension, diabetes, dyslipidemia, cardiac, digestive and pulmonary disorders, osteoporosis, renal insufficiency and neoplastic pathologies. Demographic, clinical, laboratory, comorbidities and treatment data were compared between AS and the nr-axSpA subgroups.

Results: 375 patients were included in the study. The cohort was predominantly female (54,9%) with a mean age of 46,83 years (± 14,00). 129 (50,2%) had at least one comorbidity. The mean number of comorbidities was 0,8 (± 1,05). We compared 257 AS to 118 with nr-axSpA.

AS patients were significantly young (45 vs 50 years; p=0,0001), more frequently male (55% vs 22%; p=0001) and had higher serum inflammatory markers than those with nr-axSpA. The mean number of comorbidities was similar between AS and nr-axSpA groups. 31,1% of patients SA have a history of biologics

DMARD-use (p=0,046) and less use NSAID (89,5 % vs 96,6 %; p=0,02). There were no statistically significant differences in prevalence of comorbidities between AS and nr-axSpA groups except hypertension which was higher in nr-SpA patients (24,6% vs. 14,4%, p=0,016) and digestive disorders which was most frequently detected in patients with AS (12,5 % vs 5,9%, p=0,05). The prevalence of cardiac disorders (p =0,068) and diabetes (p = 0,09) was nearly statistically significant. The multivariate analysis showed that hypertension is associated to AS form (OR: 1,976; IC [1,088-3,589])

Conclusion: Comorbidities were common in both axSpA populations with small differences between AS and nr-axSpA. These results highlight the importance of identifying and managing comorbidities.

Disclosure of Interests: None declared

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AB0818 PREDICTORS OF REMISSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Achievement of remission is a desirable outcome in axSpA, and the identification of remission predictors may further aid in the clinical and personalised management of the disease.

Objectives: To systematically review and summarize the predictors of remission in patients with axSpA.

Methods: A comprehensive search was performed in MEDLINE, EMBASE, Cochrane CENTRAL, and 2020-2021 abstracts of ACR and the EULAR annual meetings. To identify the relevant studies, medical subject headings and keywords related to "axial spondyloarthritis", "remission," and "prognostic study" were used. Studies were included if: patients were diagnosed with axSpA by a physician; age ≥18 years; the study assessed the potential predictive or prognostic factors related to remission, according to any definition; and the statistical analysis included multivariable analysis. The methodological quality of the included studies was assessed using the *Quality* of *Prognosis Studies* in Systematic Reviews tool.

Results: The systematic literature review (SLR) comprised 22 articles from 4245 citations identified in our search (Figure 1). Two studies investigated "sustained remission" (at least in 3 consecutive follow-up visits), while the others assessed "point remission" (at single points in time). The most commonly used remission criteria were Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (14 studies) and Assessment of SpondyloArthritis international Society partial remission (ASAS-PR; 11 studies) criteria. However, other non-validated definitions, most of them including Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) cut-offs, were also used. In 19 studies, subjects were treated with biological disease-modifying antirheumatic drugs (bDMARDs) with or without concomitant conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or non-steroidal anti-inflammatory drugs (NSAIDs), while in one study patients were treated with a Janus kinase inhibitor, upadacitinib. Study duration ranged from 12 weeks to 8 years. Younger age, HLA-B27 positivity, male gender, lower baseline BASDAI, lower baseline Bath Ankylosing Spondylitis Functional Index (BASFI) and treatment with tumour necrosis factor inhibitor (TNFi), were the most consistent predictors of remission. Additionally, lower baseline ASDAS-CRP, lower body mass index (BMI), shorter disease duration, TNFi naivety, and concomitant use of csDMARDs were found to be predictors of remission in two studies each. Other predictors were only found to be associated with remission in single studies, namely: higher education level, more intense morning stiffness, lower baseline total back pain score, history of peripheral arthritis, no smoking, higher pain catastrophizing, lower modified Rheumatic Disease Comorbidity Index, fulfilment of ASAS clinical arm criteria, fulfilment of European Spondyloarthropathy Study Group criteria, lower erythrocyte sedimentation rate, higher Spondyloarthritis Research Consortium of Canada magnetic resonance imaging (MRI) sacroiliac joint (SIJ) and spinal inflammation score, positive MRI of the SIJ, lower Bath Ankylosing Spondylitis Metrology Index, lower Health Assessment Questionnaire for the Spondyloarthropaties, lower global pain, lower back pain score and lower enthesitis index. Of note, contradictory data were found regarding CRP and NSAIDs usage.

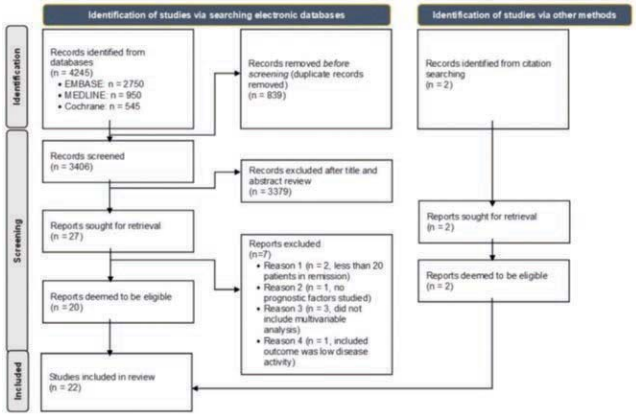

Figure 1. Flow chart of study selection

Conclusion: Thirty-four predictors of remission in axSpA were identified. However, many of these predictors were only identified in one or two studies. Considering the differences in study design, particularly characteristics of the population, duration of remission and remission criteria, further well-designed studies are needed to allow generalisation of the identified predictors to the general axSpA population.

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AB0819 IMPACT OF CHILDBIRTH ON THE SACROILIAC JOINTS IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Background: The era of magnetic resonance imaging (MRI) has contributed to a better assessment of patients with early disease stages of axial spondyloarhtis (ax-SpA), to the extent that a new entity has emerged. Indeed, the spectrum of SpA has broaden to include non-radiographic axial spondyloarthritis (nr-axSpA). Childbirth has been found to be associated with bone marrow edema (BME) in the sacroiliac joints (SIJ) [1], yet the extent of these lesions is inadequately described, which complicates the distinction with nr-axSpA.

Objectives: This study aimed to explore the impact of childbirth on MRI findings and BME in nr-axSpA.

Methods: We conducted a cross-sectional study including women diagnosed with nr-axSpA according to the ASAS (Assessment of SpondyloArthritis international Society) criteria. Socio-demographic data as well as childbirth history were recorded. The sacroiliac joints manoeuvers' examination were also transcribed. Ultrasound of the SIJ as well MRI-SIJ was performed in all the women. The sequence protocol included the following: T1-weighted, T2-weighted and axial STIR and were scored for BMO. We investigated an association between the number of children and MRI abnormalities mainly the presence of BME. The level of significance was fixed for $p<0.05$.

Results: The study included 30 women. The mean age at diagnosis was 40±9.8 years old [21-59] and the mean age at inclusion was 49±11 years old [26-74]. The median number of children was 2 [0-7]. Half of the patients were multiparous. Doppler ultrasound of the SIJ was found in 59.1% of cases. Overall, 36.7% of the women fulfilled the ASAS definition of a positive MRI. BME was displayed on STIR MRI sequence in 26.5% of cases and was equally present at the right SIJ compared with the left (26.7% vs 23.3%). Gadolinium enhancement was found in 16.7% of cases and subchondral erosions were found in 36.7% of cases.

There was no association between the different sacroiliac maneuvers on physical examination and the number of children: distraction test (p=0. 145), compression test (p=0.088), Gaenslen test (p=0.475), and Mennel test (p=0.088). BME was more frequent among multiparous women (33% vs 29%) without reaching a statistically significant difference (p=0.635). There was no association between the number of children and Hyper T1 (p=0.608), T1 gadolinium (p=0.55) as well as sclerosis (p=0.55). Similarly, there was no association between the presence of Doppler signal on ultrasound and multiparity (p=0.5).

Conclusion: Our study showed that MRI-SIJ findings were similar in nr-axSpA women regardless of the number of children, mainly BME. More trials are needed to evaluate the discriminatory capacity of MRI abnormalities and to palliate to the lack of specificities of the ASAS MRI criteria.

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AB0820 REMISSION CRITERIA IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: DON'T MISS SUBCLINICAL INFLAMMATION

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Background: With the advent of the treat-to-target strategy (T2T), clinical remission has become the main objective to achieve in patients with rheumatic diseases. Contrary to rheumatoid arthritis, the T2T strategy is less codified in axial spondyloarthritis, even more in non-radiographic SpA (nr-axSpA) [1]. More importantly, T2T based on imaging remission and guidance for tapering medication has not been extensively studied.

Objectives: The objective of this study was to investigate the prevalence of bone marrow edema in the sacroiliac joint of nr-axSpA patients in remission.

Methods: We undertook a cross-sectional study including nr-axSpA patients according to the ASAS criteria, treated with NSAIDs. Socio demographic data as well disease characteristics were recorded. Disease activity parameters were also collected including the duration of morning stiffness, the number night awakening, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). MRI-SIJ was performed for all the patients. All the images were screened for bone marrow edema with the corresponding sequence (short tau inversion). To define remission, we used in addition to BASDAI<4, more stringent criteria: BASDAI<4 and CRP<6 mg/l and ESR<20 mm/h and EGM<4 [2]. The level of significance was fixed for p<0.05.

Results: The study included 43 nr-axSpA patients. There was a female predominance with a sex ratio of 0.43. The mean age of the patients was 42±12 years [20-71] and the mean disease duration was 17±9.7 years [4-38]. The mean ESR and CRP were 2.2 mg/L [2-65] and 6.4mm/h [1-47], respectively. A higher level of acute phase reactants was found in 40.5% of cases (ESR: 35.7%, CRP: 11.9%). Forty percent of the patients had high CRP or ESR despite BASDAI<4. According to BADSAI<4, of the 15 patients in remission, BME was displayed in 43.5% of the cases. According to the used criteria, 25.6% of the patients were in remission, of which 45.4% exhibited BME in the sacroiliac joint. There was no statistically significant association between disease activity according to the used definition and the presence of BME (p=0.473). Nr-axSpa patients in remission without BME had more durable morning stiffness and articular involvement without reaching a statistically significant difference (p=0.361, p=0.08 respectively). Similarly, we did not find an association between this subgroup and sex, age, night awakenings, the presence of HLAB27 (p>0.05).

Conclusion: Our study showed that even when using stringent criteria, subclinical remission evidenced by BME was not achieved in nr-ax SpA. Nevertheless, imaging remains one important parameter to consider in therapeutic decision making. More studies are needed to identify the best criteria for an optimal remission in this population.

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AB0821 THE FREQUENCY OF LUMBOSACRAL TRANSITIONAL VERTEBRAS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Lumbosacral transitional vertebras (LSTVs) are anatomic variations observed at L5-S1 junction (1). The prevalence of LSVT ranges from 3.9% to 35.6%, indicating that this congenital anomaly is common in general population. LSVTs are well-defined anatomical differences causing low back pain and pelvic trauma (2). However, the studies assessing the influence of abnormal lumbosacral anatomy on low back pain and sacroiliac joints in patients with ankylosing spondylitis (AS) are scarce (3).

Objectives: The current study aimed to investigate the frequency of LSVTs and the their effects on clinical variables in AS patients.

Methods: The study was designed as a prospective cross-sectional study. 113 patients were included in the study. Demographic data, clinical variables, laboratory results were recorded. Disease activity (ASDAS-CRP and ASDAS-ESR), patients' functionality (BASFI, BASMI), enthesitis (Leeds enthesitis index) and quality of life (SF-36, visual analogue scale) were evaluated. The baseline pelvic conventional radiographs and the sacroiliac magnetic resonance imaginings at the diagnosis were screened and assessed by two independent physicians. LSTVs were classified via Castellvi classification. Kappa coefficient was used to find the interobserver reliability.

Results: LSVTs were observed in 38 (33.6%) patients. Castellvi type Ia, Ib, IIa, IIb, IIIa, IIIb, and IV were found in 10 (8.8%), 7 (6.2%), 7 (6.2%), 6 (5.3%), 4 (3.5%), 1 (0.9%), and 3 (2.7%) patients, respectively. The kappa value for interobserver reliability was 0.69. There were not any differences between AS patients with and without LSVTs in terms of disease activity, functionality, and quality of life (Table 1). No statistically significant correlation was found between LSVTs identified by conventional radiography and sacroiliitis determined by MRI. When compared the patients according to Castellvi classification, visual analogue scale was higher in patients with IIIa than in patients with IV (p=0.013). Disease duration was longer in patients with Ib than in patients with Ia (p=0.029). ASDAS-CRP and ASDAS-ESR were higher in patients with IIIa than in patients with IV (p=0.008 and p=0.007).

Table 1. The comparison of clinical characteristics between patients with and without LSVTs

	Patients without LSVTs (n=75)	Patients with LSVTs (n=38)	p
VAS	3.0 (2.0–5.0)	3.4 (1.0–6.0)	0.734
Disease duration (month)	122.0 (60.0–180.0)	120.0 (57.0–183.0)	0.834
ASDAS-CRP	1.8 (1.2–2.5)	1.8 (1.2–2.9)	0.855
ASDAS-ESR	1.6 (1.2–2.5)	1.6 (1.0–2.7)	0.976
CRP	1.8 (0.8–5.3)	2.5 (1.0–6.1)	0.471
BASMI	2.9 (2.0–4.4)	3.0 (2.1–4.0)	0.796
BASFI	1.8 (0.7–4.6)	2.1 (0.7–3.0)	0.768
SF-36 Physical function	80.0 (55.0–95.0)	80.0 (63.8–95.0)	0.765
Role physical	45.6 (0–100.0)	50.0 (25.0–100.0)	0.280
Role emotional	66.7 (0–100.0)	33.0 (0–100.0)	0.267
Energy/fatigue	50.0 (35.0–70.0)	60.0 (38.8–71.3)	0.201
Mental health	64.0 (48.0–76.0)	68.0 (52.0–80.0)	0.330
Social functioning	62.5 (50.0–87.5)	75.0 (50.0–100.0)	0.252
Body pain	67.5 (45.0–80.0)	67.5 (45.0–90.0)	0.751
General health	45.0 (35.0–65.0)	50.0 (40.0–71.3)	0.411

Values are given as median (interquartile range)

Conclusion: In AS patients, the frequency of LSVT is 33.6%, which is consistent with the general population. Type I, also known as a dysplastic transverse process, is the most observed type of LSVT. The presence of LSVTs is associated neither with clinical variables nor with sacroiliitis.

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AB0822 **FACTORS ASSOCIATED WITH A DELAYED DIAGNOSIS OF SPONDYLOARTHRITIS IN A POPULATION OF THE SOUTH OF MOROCCO**

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Background: Spondyloarthropathies are chronic inflammatory diseases with predominant axial involvement. Early diagnosis is a major challenge for physicians. Misdiagnosis and diagnostic delays lead to unnecessary paraclinical investigations, inadequate treatment and to poor outcomes including functional impairment and quality of life.
Objectives: We assess the diagnostic delay in spondyloarthritis and identify factors associated with it.
Methods: A retrospective study including patients diagnosed with spondyloarthritis between 2004 and 2020 according to ASAS 2010 criteria.Diagnostic delay was defined as period between the first symptom and diagnosis establishment. The potential factors predicting the diagnostic delay were explored through univariable and multivariable linear regression analysis, included epidemiological characteristics (age, gender, educational level, socio-economic level), clinical and biological presentation and sacroiliitis (radiographic or in MRI). Events occurring before the diagnostic were also analyzed.
Results: The study included 276 patients: 146 males (53%) and 130 females (47%) with a sex ratio of 1.1 and the mean age at the diagnostic was 38.87 years. Comorbidities included smoking (33 patients), cardiopathy (3 patients), hypertension (19 patients), diabetes (14 patients) and peptic ulcer (5 patients). The mean duration of symptoms was 2.6 years, and average diagnostic delay was 6.5 years with a median of 2.1 years. In univariable and multivariable linear regression analysis, low socio-economic level (p =0.023) and low educational level (p=0.042) were statistically significant parameters associated with a delayed diagnosis. There was no statistically significant association between the delay of diagnosis and age, clinical presentation or sacroiliitis (radiographic or in MRI). The use of traditional and herbal treatments before consulting a rheumatologist was also associated with a longer delayed diagnosis.
Conclusion: Spondyloarthropathies have a delayed diagnosis. This delay, also found in other studies, is responsible for persistent disease activity and important functional consequences. In our context, low socio-economic level, low educational level, and the use of traditional unconventional treatment are factors associated with a delayed diagnosis.
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AB0823 **DUAL ENERGY X-RAY ABSORPTIOMETRY IN PATIENTS WITH SPONDYLOARTHRITIS. CORRELATION WITH DISEASE DURATION, ACTIVITY AND CHANGES IN SACROILIAC JOINTS ON MAGNETIC RESONANCE IMAGING**

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Background: Bone loss (osteopenia or osteoporosis) and osteoporotic vertebral fractures are well-known complications of spondyloarthritis (SpA), and their prevalence in SpA patients (pts) is higher than in patients with mechanical low back pain [1, 2]. Osteopenia and osteoporosis can develop in both the late and early stages of SpA. The presence of bone marrow edema at the lumbar spine and sacroiliac joints (SIJ) on magnetic resonance imaging (MRI) was more common among pts with low BMD (bone mineral density) than normal BMD [3, 4]. At the same time, the dynamics of osteoporotic and osteosclerotic changes in the spine during the progression of SpA makes the assessment of DEXA results ambiguous.
Objectives: To determine the presence of osteopenia/osteoporosis in pts with SpA and to establish its correlations with disease duration, disease activity, active changes in SIJ on MRI.
Methods: 40 patients with SpA (55% – male, mean age 39.87±9.79, mean disease duration – 6.75±7.43 years) underwent DEXA. Spondyloarthritis Research Consortium of Canada (SPARCC) MRI SIJ score (0-72) was utilized for evaluation of the active inflammatory lesions in SIJ, Danish MRI scoring method (0-48) – for chronic changes. Disease activity was measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI, cm), Ankylosing Spondylitis Disease Activity Score (ASDAS), C-reactive protein (CRP, mg/l), and erythrocyte sedimentation rate (ESR, mm/hr). For correlation, the Spearman correlation coefficient was calculated.
Results: The mean value of DEXA parameters were: BMD – 0.72±0.15, T-score – -0.16±0.88, Z-score – 0.17±0.89 (forearm); BMD – 0.96±0.17, T-score – -1.13±1.35, Z-score – -0.88±1.31 (spine); BMD – 0.85±0.14, T-score – -0.85±0.93, Z-score – -0.56±0.97 (hip). Mean value (M±σ) of indices and laboratory parameters were: BASDAI – 4.44±1.76, ESR – 30.2±24.1, CRP – 17.9±19.7, ASDAS-CRP – 3.07±1.13, ASDAS-ESR – 3.14±1.14. SPARCC score was 12.3±11.8, Danish score – 15.2±7.77. Osteoporosis was present in 7 (17.5%), osteopenia - in 24 (60%) SpA pts. There was positive correlation between BMD at forearm and Danish MRI score (r=0.331, p=0.02). The CRP level showed negative correlation with BMD at hip (r=-0.322, p=0.02), BMD at spine (r=-0,288, p=0,038) and T-score at spine (r=-0.301, p=0.031). Patient's age showed negative correlation with BMD at hip (r=-0.268, p=0.05). Disease duration negatively correlated with BMD (r=-0.343, p=0.016) and T-score (r=-0.310, p=0.027) at hip. All correlations were weak. No other correlations were found.
Conclusion: Among disease activity parameters, only high CRP was associated with a decrease in BMD for both the back and hip. A decrease in hip BMD was also associated with the patient's age and disease duration. Regarding MRI indicators, only chronic changes in SIJ, measured by MRI, positively correlated with BMD at forearm only.
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AB0824 **BREASTFEEDING IN WOMEN WITH ANKYLOSING SPONDYLITIS (AS)**

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Background: Breast milk is the natural and most physiological nutrition for a child from the first days of life. The benefits of breastfeeding are numerous, including psychological aspects. However, some women with rheumatic diseases are afraid that their disease or therapy is not compatible with breastfeeding.
Objectives: To describe frequency, duration and reasons for stopping lactation in women with AS, to compare the activity of AS in women with and without lactation.
Methods: 44 women with confirmed AS (modified New York criteria, 1984) were followed within 1 year after childbirth. Visits were carried out in 1, 6 and 12 months after delivery. The average age of patients was 32,5 ± 5,8 years, the duration of the disease was 149,0 ± 96,3 months. BASDAI at 1, 6 and 12 months after giving birth was: 2,4 [1,4; 4,2]; 2,6 [1,4; 4,4]; 2,7 [1,5; 4,1], respectively. ASDAS-CPR was: 2,0 [1,2; 2,7]; 1,9 [1,4; 2,5]; 1,7[1,3; 2,3], respectively.
Results: Lactation was established in 41 women (93,2%), duration – 10 [4; 12] months; in 17 patients (41,5%) lactation persisted for 12 months. Lactation was unreasonably medically suppressed in 3 women in an obstetric unit due to therapy of AS (sulfasalazine – 2, certolizumab pegol – 1); in 1 woman lactation was not established for organizational reasons. Lactation lasted less than 6 months in 16 patients (39%), 13 of them had a natural attenuation of lactation, and in 3 cases, drug-induced suppression of lactation was carried out on the recommendation of pediatricians in connection with onset of AS therapy (adalimumab).
During lactation, 51,2%, 74,1% and 88,2% of women received nonsteroidal anti-inflammatory drugs for 1, 6 and 12 months after delivery, respectively; adherence to NSAID therapy did not differ in women with and without lactation. TNF-α

inhibitors (certolizumab pegol) were received by 4 women (7,3%), while the need for iTNF-α was in 13 patients (not received due to medicine unavailability).
In women who retained lactation, the severity of back pain was: 3,0 [2,0; 6,0], 3,0 [2,0; 5,0] and 3,0 [2,0; 4,5] according to NRS (numerical rating scale) after 1, 6 and 12 months since delivery, respectively; severity of night pain - 3,0 [2,0; 5,0], 3,0 [2,0; 5,0] and 2,0 [2,0; 4,0] according to NRS, respectively. BASDAI activity at 1, 6 and 12 months after delivery was 2,3 [1,0; 4,2], 2,1 [1,4; 4,1] and 2,2 [1,6; 2,8], respectively. Activity on ASDAScrp was 1,9 [1,2; 2,7], 1,6 [1,4; 2,6] and 1,6 [1,3; 1,7], respectively. CRP level was 3,4 [1,9; 8,2], 4,5 [2,0; 12,5] and 2,0 [0,8; 5,6] mg/l, respectively. The severity of back pain, BASDAI and ASDAS values of CRP did not differ in women with and without lactation.
Women with high AS activity (BASDAI≥4) maintained lactation at 1, 6 and 12 months after delivery in 84,6%, 50% and 8,3%, respectively; while patients with low activity did it in 93,6%, 66,7% and 51,6%, respectively ($p < 0,05$ 12 months after delivery).
Conclusion: The vast majority of women with AS are set up for lactation. High AS activity becomes a risk factor for termination of lactation more than 6 months after delivery. It is necessary to conduct training for obstetricians-gynecologists and pediatricians on issues related to medicine capabilities during lactation, in order to exclude unjustified cancellation of medicines compatible with breastfeeding.

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AB0825 A SOLUTION PROPOSAL TO THE INTRAOBSERVER DISAGREEMENT PROBLEM IN THE EVALUATION OF SACROILIAC JOINT RADIOGRAPHY: "IMAGE PROCESSING METHOD"

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Background: Ankylosing spondylitis (AS) is a rheumatological disease that causes low back pain. The diagnosis of ankylosing spondylitis is delayed for an average of 8 years due to the insidious course of the disease. Late diagnosis of AS can cause functional and physical disabilities. Radiographic sacroiliitis can be graded in the range of 0-4 and these classes may not be sharply separated from each other. Interpretation of the sacroiliac joint radiography may differ from physician to physician. In fact, the same physician may interpret it differently at different times (1). The reason for such confusion is the presence of blur or illumination and contrast problems leading to difficulties to detect pathological areas. This paper has developed a simple image processing technique that adjusts the contrast of such images by modifying their intensity distribution using the histogram information. This transformation gives a linear trend to the cumulative probability function associated with the image and makes the images better for human vision. The common characteristic of low contrast images is the concentration of the histogram values of the image intensity near a narrow range (2).
Objectives: Changing the contrast range into a wider range changes the image value distribution that leads to better image vision.
Methods: Rheumatologist scored 260 x-ray scans grade 0 to 4. One day later, the same rheumatologist scored again the same scans randomly. It has been noticed that most of the answers were closed to the first-day decision but not all of them. We processed all the x-ray images with histogram equalization. Then the rheumatologist scored the scans randomly and answered two times in two consecutive days. To compare the agreement in radiography interpretation Kappa test was used. We use IBM SPSS 21 for the statistical analysis (kappa test) and Matlab R2021a for the image processing part.
Results: Severe improvement before and after the image processing application by increasing the Kappa value from 0.55 ($p<0.001$) [moderate agreement] to 0.71($p<0.001$) [substantial agreement] which is a substantial agreement.
Conclusion: Multidisciplinary approach can be helpful in solving the intraobserver disagreement problem. The use of image processing techniques can be used for the benefit of the patient in radiographs whose standardization is difficult due to multifactorial reasons. The histogram equalization method was found to be statistically significant in finding the optimum contrast for interpreting the sacroiliac joint radiography. The output of this work indicates and motivates our team into deeper research and more analyses on how to further improve our results.

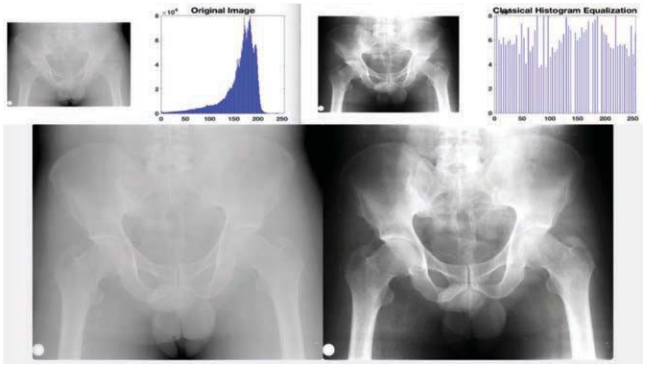

Figure 1. The original graph on the left, the classical histogram equalization method on the right and their histogram tables.

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AB0826 KEEP AN EYE ON THE BACK: SPONDYLOARTHRITIS IN PATIENTS WITH ACUTE ANTERIOR UVEITIS

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Background: Patients with acute anterior uveitis (AAU) have an increased risk for concomitant spondyloarthritis (SpA). Different referral strategies have been proposed to identify AAU patients with high probability of SpA, among them an Assessment of SpondyloArthritis international Society(ASAS)-based referral strategy focusing on patients with chronic back pain starting before the age of 45 years and the Dublin Uveitis Evaluation Tool (DUET) also including psoriasis, HLA-B27 and arthralgia (*Poddubnyy et al., Haroon et al., both ARD 2015*).
Objectives: To analyse the prevalence of SpA in patients with AAU, to identify parameters associated with SpA presence, and to evaluate referral algorithms.
Methods: Patients with non-infectious AAU underwent structured rheumatologic assessment including magnetic resonance imaging of sacroiliac joints allowing a definitive diagnosis/exclusion of concomitant SpA. Fisher's exact test and Mann–Whitney U test were used to compare AAU patients with and without SpA. Furthermore, logistic regression analyses were performed. Sensitivity, specificity, positive predictive value, positive and negative likelihood ratios were analysed for referral strategies.
Results: The 189 AAU patients with complete rheumatologic assessment and SIJ imaging were 40.8 years old, and 55% were males. SpA was diagnosed in 106 AAU patients (56%). The majority (93%) had predominantly axial SpA, 7 patients peripheral SpA. In 74 patients (70%), the SpA diagnosis was established for the first time. Pelvic X-rays were available for 88 (89%) of the axSpA patients, 66% of whom were classified as having radiographic axSpA.
SpA was equally frequent in patients experiencing the first episode of AAU and in patients with recurrent disease. In our cohort, AAU patients with and without underlying SpA showed no differences in their ophthalmologic examination. In multivariable logistic regression analysis, psoriasis (OR 12.5 [95%CI 1.3-120.2]), HLA-B27 positivity (OR 6.3 [95%CI 2.4-16.4]), elevated CRP (OR 4.8 [95%CI 1.9-12.4]) and male sex (OR 2.1 [95%CI 1.1-4.2]) were associated with SpA presence.

Table 1. Parameters associated with the presence of spondyloarthritis in patients with acute anterior uveitis.

	univariable		multivariable	
	OR	95%CI	OR	95%CI
Psoriasis (ever)	14.6	(1.9; 112.4)	12.5	(1.3; 120.2)
HLA-B27 positivity	6.2	(2.7; 14.6)	6.3	(2.4; 16.4)
Elevated CRP (≥ 5 mg/l)	4.1	(1.8; 9.0)	4.8	(1.9; 12.4)
Male sex	2.2	(1.2; 4.0)	2.1	(1.1; 4.2)
Inflammatory back pain (ASAS definition)	2.1	(1.2; 3.9)	1.9	(0.9; 4.0)
Any peripheral manifestation (ever)	1.9	(1.1; 3.5)	1.9	(0.9; 3.8)
Age in years	1.0	(1.0; 1.0)	1.0	(1.0; 1.0)

Univariable and multivariable logistic regression analyses. ASAS Assessment of SpondyloArthritis international Society; CRP C-reactive protein; OR odds ratio; CI confidence interval.

The Dublin Uveitis Evaluation Tool showed higher specificity for SpA recognition than the ASAS referral tool (42% vs. 28%), which had slightly higher sensitivity (78% vs. 80%). However, both referral strategies would have missed more than 20% of SpA patients.

Conclusion: We revealed a high prevalence of overall and previously undiagnosed SpA in AAU patients. Therefore, we propose rheumatologic evaluation for all AAU patients with musculoskeletal symptoms. Rheumatologists should consider that SpA in AAU patients might present "atypically" with back pain starting after 45 years and lasting shorter than 3 months.

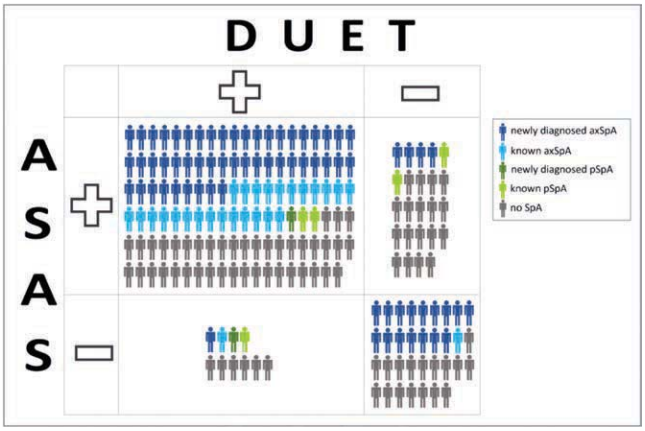

Figure 1. Performance of Referral Strategies in Patients with Acute Anterior Uveitis. Dublin Uveitis Evaluation Tool (DUET) and an ASAS-based referral tool (ASAS). + respective tool fulfilled, - not fulfilled. ASAS Assessment of SpondyloArthritis international Society; AxSpA axial spondyloarthritis, pSpA peripheral spondyloarthritis.

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AB0827 FREQUENCY OF SEXUAL DYSFUNCTION AXIAL SPONDYLOARTHRITIS, SANTO DOMINGO, DOMINICAN REPUBLIC

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Background: Axial spondyloarthritis (SpAa) is a chronic inflammatory disease of unknown etiology that affects the axial skeleton, affecting peripheral joints, entheses and extra-articular structures, with a prevalence of 0.5-1% associated with HLA-B27+.[1] The impact of Chronic disease is often multifactorial that affects physical, hormonal and psychological alterations, leading to problems of sexuality.[2] The CSFQ-14 (Changes in Sexual Functioning Questionnaire), evaluates changes in sexual functioning due to disease and/or or treatment in 5 domains with a score range of 14-70; cut-off point indicating sexual dysfunction <41 men and <47 women.[3,4]

Objectives: To evaluate the frequency and degree of sexual dysfunction in patients with axial spondyloarthritis.

Methods: Prospective, observational, cross-sectional study. of the SpAa cohort of the Hospital Docente Padre Billini rheumatology service Patients were interviewed in July 2021. Inclusion criteria: > 18 years, diagnosis of SpAa according to the ASAS 2009 classification criteria, at least 1 sexual. Exclusion criteria: previous diagnosis of another autoimmune disease, depression, diabetes mellitus (DM), treatment with antidepressants, antiepileptics, narcotics. Measurement of: CSFQ-14, BASDAI. Statistical analysis was performed with the Pearson correlation (r_P) with p>0.05. The data was analyzed by SPSS V23.

Results: Of the SpAa cohort, 87 met the inclusion criteria. Male 67.8% (59), female 32.2% (28), mean age 45.7±8 years, mean diagnosis 7, married 67.8%(59), single 24.1%(21), widowed 8%(7), HLA-B27+51.1 %, hypertension 8% (7), diabetes 6.8% (6), dyslipidemia 10.3%(9), smokers 4.5%(4), 100% (87) bDMARD´s, 13.6% (12) combined with csDMARD´s, Frequency of sexual dysfunction 24.1%(21). Sexual dysfunction in women 6.9% (6) and men 17.2% (15) by CSFQ-14. Global domains: Desire/Interest 2.3% (2), Desire/Frequency 2.3% (2), Pleasure 5.7% (5), Arousal 2.3% (2), Orgasm/Completion 2.3% (2). Female: Desire/interest 6.8% (4), desire/Frequency 3.4% (2), pleasure 8.5% (5). Male: Desire/interest 3.4% (2), desire/Frequency 3.4% (2), pleasure 8.5% (5), arousal 6.8% (4), orgasm/completion 3.4% (2). Correlation CSFQ-14 domains with BASDAI: r_p =. -0.088 p>0.05: Desire/interest dysfunction: inactive BASDAI 71.4% (15). Desire/frequency: inactive BASDAI 90.5% (20). Pleasure: inactive BASDAI 23.8% (5), active 23.8% (5). Excitation: inactive BASDAI 14.3% (3). Orgasm/completion> inactive BASDAI 90.5% (20)

Conclusion: The study showed a low frequency of sexual dysfunction, being more frequent in males. The greatest dysfunction was found in the pleasure domain in both sexes. A statistically significant inverse linear association was found between sexual dysfunction and disease activity.

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AB0828 DIFFERENCES IN EARLY-ONSET VS. LATE-ONSET PSORIATIC ARTHRITIS: DATA FROM THE RESPONDIA AND REGISPONSER STUDIES.

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Background: The prevalence of late-onset psoriatic arthritis (PsA) is increasing in parallel with the progressive aging of the population. The elderly population presents a greater functional deterioration and a greater number of comorbidities than the young people. With this study we aim to find clinically relevant differences to predict the evolution and prognosis of the disease depending on the onset of the symptoms to carry out a more exhaustive follow-up.

Objectives: To evaluate the association of the age at onset of PsA symptoms with the characteristics and burden of the disease.
Methods: Observational study that includes a subgroup of 231 patients with Psoriatic Arthritis (PsA) from the REGISPONSER study (Registry of Spondyloarthritis of Spanish Rheumatology) and the RESPONDIA study (Ibero-American Registry of Spondyloarthropathies). Patients with less than 10 years of disease duration (since the first symptom) were selected so that the sample was homogeneous. Patients were divided into two groups according to the age of PsA onset (early-onset: ≤40 years old and late-onset: ≥60 years old). The characteristics and burden of the disease were compared using the Student's t-test/ Mann-Whitney U test for quantitative variables or using the chi-square/Fisher test for qualitative variables.
Results: 411 patients were included [early-onset 179 (77.5%); late-onset 52 (22.5%)]. There was a higher percentage of men in the late-onset group compared to the early-onset group [94 (62.3%) vs. 38 (86.4%), p = 0.003]. The diagnostic delay was shorter in those whose onset of the disease was late [1.5 (2.7) vs 4 (7.7), p=0.036], as well as the duration of the disease [2.9 (2.4) vs 4.2 (2.7), p= 0.012]. A lower presence of sacroiliitis was found in patients with late-onset PsA [6 (12.2%) vs 58 (32.6%), p=0.005] as well as enthesitis [5 (9.8%) vs 44 (24.6%), p =0.023]. Regarding the comorbidities, there was a higher frequency of heart disease among patients with late-onset PsA [4 (7.8) vs 0 (0), p=0.000]. No statistically significant differences were found between kidney and lung disease. Regarding the outcome measures, the BASFI score was higher in the late-onset group [3.3 (2.5) vs. 2.2 (2.2), p=0.002]. The late-onset group had a lower FSF12 component [34.6 (8.7) vs. 38.7 (10.5), p = 0.001]. The radiographic indices measured by BASRI showed worse results in those patients with late-onset disease both in the spine [2.9 (3) vs 1.6 (2), p=0.020] and in the total BASRI [3.4 (3 .4) vs 1.9 (2.4), p=0.012].
Conclusion: Our study suggests that the age of onset of PsA was associated with the different characteristics of the disease. Patients with late-onset PsA were more frequently males, showed worse functionality and more structural damage in comparison with early-onset PsA. Sacroiliitis and enthesitis were found less frequently in the late-onset group. Quality of life, disease activity and treatments taken were not associated significantly with age of onset.

Table 1. Description of different characteristics across two groups: early and late onset

	Early-onset N=179 n (%)=77.5	Late-onset N=52 n (%)=22.5	p-value
Sex (male)	94 (62.3)	38 (86.4)	0.003
Age (SD)	38.7 (9.3)	71.3 (7.5)	0.000
Enthesitis	44 (24.6)	5 (9.8)	0.023
Dactilytis	36 (20.1)	9 (17.6)	0.695
Sacroiliitis	58 (32.6)	6 (12.2)	0.005
Diagnostic Delay, mean (SD)	4 (7.7)	1.5 (2.7)	0.036
Disease Duration, mean (SD)	4.2 (2.7)	2.9 (2.4)	0.012
Arthritis (lower limbs)	118 (65.9)	33 (64.7)	0.872
Arthritis (upper limbs)	82 (45.8)	31 (60.8)	0.059
BASDAI, mean (SD)	3.9 (2.5)	3.8 (2.4)	0.932
BASFI, mean (SD)	2.2 (2.2)	3.3 (2.5)	0.002
ASDAS, mean (SD)	2.3 (1.1)	2.3 (0.9)	0.894
FSF12, mean (SD)	38.7 (10.5)	34.6 (8.7)	0.001
MSF12, mean (SD)	47.7 (10.6)	49.3 (9.2)	0.341
BASRI spine	1.6 (2)	2.9 (3)	0.020
BASRI total	1.9 (2.4)	3.4 (3.4)	0.012
ESR mm/h, mean (SD)	17.2 (14.2)	23.9 (19.1)	0.005
csDMARDs (ever)	111 (62.7)	31 (63.3)	0.943
bDMARDs (ever)	21 (11.9)	3 (6)	0.234

Disclosure of Interests: None declared
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AB0829 BODY COMPOSITION IN SPONDYLOARTHRITIS: IS THERE ANY IMPACT ON DISEASE ACTIVITY?

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Background: The relationship between obesity and inflammation is bidirectional. Thus, obesity may influence clinical response to biological treatment.
Objectives: To investigate the association of obesity and body composition with disease activity in patients with spondyloarthritis (SA).
Methods: This is a cross-sectional study designed on spondyloarthritis patients diagnosed according to ASAS 2009 classification. Bath ankylosing spondylitis disease activity index (BASDAI), ankylosing spondylitis disease activity score (ASDAS), Bath ankylosing spondylitis functional index (BASFI), and Bath ankylosing spondylitis metrology index (BASMI) were assessed. Obesity was evaluated clinically by body mass index (BMI) and waist circumference (WC). Total body composition, total and regional fat and lean mass, android/gynoid ratio (A/G), fat mass index (FMI), fat-free mass index (FFMI) were measured by dual-energy X-ray absorptiometry (DXA) and reported as absolute values. Blood samples were collected to determine C-reactive protein serum (CRP) levels for each patient. Socio-demographic data, comorbidities, physical activity, disease-related variables (duration, characteristics, and drugs) were also collected. Correlations and regressions were made by SPSS.20.
Results: Forty-four SA participants (65.9% male) were enrolled. Their mean age was 39.82 ± 14.20 years and the mean ASDAS CRP was 1.42 ± 0.86. Patients under biologic disease-modifying antirheumatic drugs (bDMARDs) showed lower FMI (p = 0.011), percentage of fat mass (p = 0.008), and gynoid fat mass (p = 0.01). Correlations between ASDAS using CRP, total body fat mass, FMI, FFMI, visceral adipose tissue (VAT), appendicular lean height, and the A/G ratio were not statistically significant. Nevertheless, ASDAS CRP was positively correlated to total body mass (r = 0.352; p = 0.019), gynoid fat mass (r = 0.329, p = 0.029), and android fat mass (r = 0.323, p = 0.032). The association of disease activity and gynoid fat mass persisted after adjustment on disease duration and age (ß = 0.355, 95%IC [0.00003; 0.0003], p = 0.021).
Conclusion: Gynoid and android fat mass affected disease activity in our SA patients. However, FMI, visceral fat, and skeletal muscle mass showed no significant association with disease activity.
Disclosure of Interests: None declared
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AB0830 TURKISH TRANSLATION AND CROSS-CULTURAL ADAPTATION OF THE MODIFIED SHORT QUESTIONNAIRE TO ASSESS HEALTH-ENHANCING PHYSICAL ACTIVITY (MSQUASH).

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Background: The Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) is a validated tool measuring the duration, frequency, and intensity of physical activity. The modified version of the SQUASH (mSQUASH) has been developed, in collaboration between spondyloarthritis (SpA) experts and axial (ax)SpA patients, to better address the needs of these patients in the assessment physical activity (1).
Objectives: To translate and cross-cultural adapt the mSQUASH into Turkish as well as its cognitive debriefing to test the conceptual equivalence of the translated version among patients with axSpA.
Methods: The mSQUASH was translated into Turkish by 2 bilingual translators, native speakers of Turkish one from medical (informed) and the other is without medical background (uninformed). The consensus on forward-translation was reached by the team included two rheumatologist (GA and LK) and the translators. Backward-translation into Dutch was performed by 2 bilingual translators, native speakers of Dutch and who were blinded to the original mSQUASH version. After the review of the Turkish version by an expert committee that included translators, two patients and the research team a pre-final version was prepared. This version was used in a field-test with cognitive debriefing and involved a sample of 10 axSpA patients (7 radiographic- and 3 non-radiographic axSpA patients) with variation in gender, age, disease duration, and educational background. The final Turkish mSQUASH version was reached after the patients were interviewed to check understandability, interpretation and cultural relevance of the translation. The whole process was performed according to the Beaton method (Figure 1) (2).

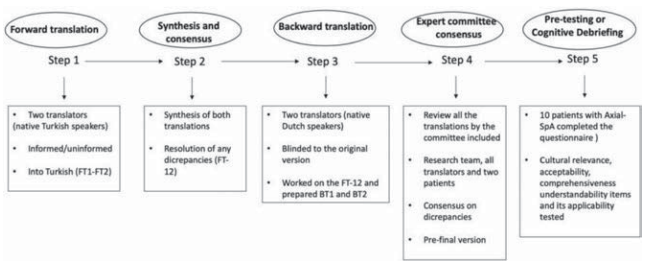

Figure 1. Flow-chart of the translation and cross-cultural adaptation process

Results: After the forward-backward translation process, small incompatibilities were resolved during the expert committee meeting. For example: `Ander transport (heen en terug)` was translated as `Diğer hedeflere (gidip gelmek)`. The meaning in English is `Other transport (round trip)'. This item questions the way of going to other places and the discrepancy raised whether to use `transportation` or the `target` as the title. To make it culturally adaptable consensus reached to use a word equivalent to `the target` which is semantically equal to the Dutch version. A total of 10 patients with axSpA [7 females, mean (SD) age of 38 (10)] participated in the field test. Mean (SD) time to complete the mSQUASH was 6.1 (2.4) minutes. Cognitive debriefing showed that items of the mSQUASH are clear, relevant, understandable, and easy to complete. None of the patients indicate any important aspect of physical activity that is missing from the questionnaire items. During the cognitive debriefing, 2 patients suggested a change in the wording of one item to make it more suitable to the Turkish culture. This item inquires after sport activities and patients raised the concern that the example activities, ice-skating, tennis, handball are not culturally suitable. According to their comments these items were replaced by other examples such as football.

Conclusion: The final Turkish version of the mSQUASH showed acceptable linguistic validity and can be used in both clinical practice and for research purposes. However, to implement the Turkish version of the mSQUASH, further assessment of its psychometric properties (validity and reliability) is needed.

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AB0831 THE QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS EVALUATED UNDER SF-36 QUESTIONNAIRE, ITS CONNECTION WITH THE DISORDER OF BONE MINERAL DENSITY

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Background: In recent time, the peculiarities of the quality of life in patients with many chronic diseases, which progress unaffectedly and lead to the restriction of all components of normal life, are being actively studied. Ankylosing spondylitis (AS) is no exception, it is the second most common inflammatory rheumatic disease, characterized by predominant lesions of the spine and sacroiliac joints. Rapid progression of the disease, constant pain in the joints, as well as in the periarticular tissues and muscles lead to significant functional limitations, gradual loss of mobility of the spine and deterioration of the quality of life. However, impaired quality of life can be caused not only by the manifestations of the underlying disease, but also by the presence of complications observed in the early stages of the disease. Thus, it is the decrease in bone mineral density and the development of osteoporosis that cause pathological fractures and, as a result, lead to early disability, reduced duration and quality of life. However, clear data on the peculiarities of the quality of life in patients with AS suffering from impaired bone mineral density have not been found to date.

Objectives: To investigate quality of life indicators using the SF-36 questionnaire in men with AS and to assess their relationship with the structural and functional state of bone tissue.

Methods: 105 patients with AS aged 40,7 ± 0,8 years were examined, the average duration of the disease was 8,7 ± 0,5 years. The control group included 25 healthy individuals of appropriate age and sex. All patients were diagnosed with AS according to ASAS criteria (2009). The SF-36 questionnaire was used to characterize the quality of life. Bone mineral density was measured by dual-energy X-ray absorptiometry on a Hologic Discovery Wi apparatus (S/N 87227).

Results: The analysis of quality of life according to the SF-36 questionnaire showed that patients with AS had significantly lower indicators of both physical (37,3 ± 1,5 points) and mental (44,2 ± 1,7 points) components of health in comparison with the control group (99,1 ± 0,3; 97,4 ± 0,7 points, respectively). Among the subscales that form the total physical component, the lowest indicators were recorded in role physical functioning (RP) (14,0 ± 3,1 vs. 99,0 ± 0,6 points) and pain (P) (37,2 ± 1,6 vs. 100,0 ± 0,0 points). And according to the subscales assessing the mental component of health, the most significant differences were found for the indicator of role emotional functioning (RE), which was 4,5 times lower than in the control group (22,2 ± 3,9 vs. 98,2 ± 0,7 points respectively).

The study did not reveal significant differences in quality of life in case of low bone mineral density (BMD). The average levels of total physical and mental components of health in patients with BMD (35,2 ± 2,4; 42,2 ± 3,2 points) were only 12,2 – 7,1% lower than in patients with preserved BMD (40,8 ± 2,7; 46,4 ± 2,8 points, respectively). In the group of patients with osteoporosis (Z-score -2,7 ± 0,1) there was a tendency to reduce the physical component due to the indicator of general health (GH), which was significantly lower (35,8 ± 2,1 points) than in patients with preserved BMD (43,4 ± 2,7 points).

Conclusion: In men with AS, there is a significant decrease in the total physical and mental components of health according to the SF-36 questionnaire which do not have a clear relationship with structural and functional state of bone tissue.

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AB0832 NONINFECTIOUS UVEITIS FROM THE RHEUMATOLOGIST'S PERSPECTIVE: PATTERNS FROM A SINGLE TERTIARY REFERRAL RHEUMATOLOGIC CLINIC IN ITALY

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Background: The noninfectious uveitis (NIU) is the intraocular inflammation that can be the first or one of extra-articular manifestations of systemic inflammatory rheumatic diseases mainly including spondyloarthritis (SpA), Behcet's disease (BD) and juvenile idiopathic arthritis (JIA)[1]. Rheumatologists are often asked to help in diagnostic assessment and relatively targeted treatment of particular subsets of NIU[2].

Objectives: To explore patterns and treatments of NIU from a population-based single-center study carried out in a Tertiary Referral Rheumatologic Clinic.

Methods: Selection criteria of this cross-sectional descriptive study consisted of having a diagnosis of NIU in an age of onset ≥16 years old regardless of its etiology among patients who were admitted (February 2018-December 2021) to Rheumatologic Clinic of Tor Vergata University Hospital (Rome, Italy). Clinical data were collected from medical records: gender, age of onset and admission, recurrence and anatomic patterns, HLA-B27 susceptibility, associated rheumatologic diagnosis and treatments were investigated.

Results: We included 100 patients with 58% women. Median age at NIU onset was 39.6±15 years whereas patients were 44±14 years old at the first referral, without gender-difference. NIU represented the main reason of referral in 22% of cases. Anterior uveitis occurred in 73% of patients and posterior in 25%; intermediate (IU) and panuveitis (PanU) were isolated cases. The prevalent course was acute (57%) followed by recurrent (31%) and chronic (12%); both eyes were involved in 39 patients. Almost half of NIU was associated with SpA including IBD-SpA (20%), ankylosing spondylitis (AS, 18%), and Psoriatic Arthritis (12%). A diagnosis of BD was reported in 14% of NIU while Rheumatoid Arthritis and other systemic autoimmune diseases occurred in 11% and 12%, respectively. Idiopathic NIU and JIA-NIU constituted the lowest prevalence (8% and 5%, respectively). A higher prevalence of BD-NIU and AS-NIU resulted in males than females ($p<0.01$ and $p<0.05$, respectively). One-third of the NIU cohort (34.3%) showed $B27^+$: a higher percentage of unilateral ($p=0.09$) and acute course ($p=0.02$) occurred in $B27^+$ than $B27^-$. AS was prevalent in $B27^+$ NIU than $B27^-$ ($p<0.00001$) while IBD-SpA and BD were mainly present in $B27^-$ NIU than $B27^+$ ($p=0.09$ and $p=0.04$ respectively). The only two cases of IU and PanU were both idiopathic $B27^-$ NIU. At the onset of NIU, most patients were not on systemic treatment (68%): remaining cases were on cDMARDs (22%) and bDMARDs (10%). During rheumatologic follow-up, 80% of patients changed therapies: cDMARDs were added in 43.7% patients while bDMARDs were started in 40%. Systemic steroids were added in the remaining 16.3% of patients. At the latest follow-up (follow-up-time 33±28 months), 86% of patients had achieved remission of NIU while 14% had recurrence of active uveitis.

Conclusion: Findings from this population-based study describe a representative estimate of extent and patterns of NIU in an Italian adult cohort from a single Rheumatologic Clinic and document that Rheumatologic referral might dramatically impact treatment strategies in NIU.

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AB0833 **EPICARDIAL FAT THICKNESS: A NOVEL MARKER OF SUBCLINICAL ATHEROSCLEROSIS IN SPONDYLOARTHRITIS PATIENTS**

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Background: Chronic inflammatory process seems to be the underlying cause contributing to atherosclerosis in spondyloarthritis. Epicardial adipose tissue (EAT) which is the accumulation of visceral fat between the myocardium and the visceral layer of pericardium, is actually considered a novel cardiometabolic risk predictor (1). Recent studies have shown its association with the development of coronary atherosclerosis.
Objectives: The aim of our study was to assess the epicardial fat thickness (EFT) in patients with spondyloarthritis (SpA) in comparaison with healthy subjects.
Methods: We performed a prospective study including 47 patients meeting ASAS 2009 criteria for SpA compared to 47 healthy controls matched for age, gender and body mass index (BMI). Patients with history of cardiovascular risk factors or diseases were not included. Sociodemographic, clinical, biological and radiographic features related to the disease were recorded. All subjects underwent transthoracic echocardiography with measurement of EFT.
Results: SpA group included 33 men and 14 women, with a median age of 36 years (IQR: 28-46). Median BMI was 24.5 kg/m^2 (IQR: 20.7-26.8). Median systolic (SBP) and diastolic (DBP) blood pressure were respectively 121 mmHg (IQR: 110-130) and 71 mmHg (IQR: 67-78). Median disease duration was 11 years (IQR: 5-16). Median disease activity scores BASDAI and ASDAS-CRP were 2.6 (IQR: 1.8-3.8) and 2.18 (IQR: 1.62-2.91) respectively. Median CRP level was 6.45 mg/l (IQR: 1.5-19.9). Median BASFI and BASMI were 3 (IQR: 1.5-5.1) and 1.5 (IQR: 0-4) respectively. Coxitis was found in 53% of patients. SpA patients received: NSAIDs (92%), csDMARDs (51%) and TNF inhibitors (38 %). EFT was significantly increased in SpA patients compared with healthy controls; median EFT value was 3.1 mm (IQR: 2.5-4) versus 2.4 mm (IQR: 2-3) (p=0.001).
Conclusion: As an early marker of atherosclerosis, EFT was significantly higher in SpA patients, supporting clinical evidence of increased cardiovascular risk in SpA. Thus, more studies that involve larger samples should be conducted, using EFT to cardiovascular risk stratification in SpA.
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AB0834 **EPICARDIAL FAT THICKNESS IS ASSOCIATED WITH PATIENT-REPORTED OUTCOMES IN SPONDYLOARTHRITIS**

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Background: Epicardial adipose tissue (EAT) is a metabolically active visceral fat located between the myocardium and the visceral pericardium. Increased epicardial fat thickness (EFT) has been shown as a novel cardiovascular risk factor in some recent studies (1), (2) and have been suggested as a marker for cardiovascular risk stratification. Few studies have studied EFT in patients with SpA.
Objectives: The aim of our study was to assess the relationship between EFT and Patient-Reported Outcomes (PROs) in SpA patients.
Methods: We conducted a case control study over a 12 months period. Patients diagnosed with SpA according to ASAS 2009 criteria and age and sex matched controls were included. All subjects were aged less than 50 years old and without cardiovascular risk factors. Clinical data related to the disease were collected. Patient-Reported Outcomes (PROs): morning stiffness duration, nocturnal awakenings, pain visual analog scale (VAS) and patient global assessment (PGA) were recorded. BASG-s (Bath Ankylosing Spondylitis-Global score) was also raised. All patients underwent echocardiographic examination with measurement of EFT.
Results: We included 94 subjects (47 patients and 47 controls), sex ratio was 2.35, and median age was 36 years (IQR: 18-32). Median disease duration was 11 years (IQR: 5-16). Median disease activity scores BASDAI and ASDAS-CRP were 2.6 (IQR: 1.8-3.8) and 2.18 (IQR: 1.62-2.91) respectively. Regarding Patient-Reported Outcomes (PROs); median duration of morning stiffness was 5 minutes (IQR: 0-180) and median number of nocturnal awakenings was 0 (IQR: 0-2). Median VAS pain and median PGA were 50 (IQR: 30-60) and 40 (IQR: 30-60), respectively. Median EFT was significantly increased in SpA patients 3.1 mm (IQR: 2.5-4) compared with healthy controls 2.4 mm (IQR: 2-3) (p=0.001). EFT was positively correlated with VAS pain (p=0.012; r=0.363) and BASG-s (p=0.025; r=0.327). No significant association was found between EFT and Morning stiffness duration (p=0.164; r=0.206), Nocturnal awakenings (p=0.463; r=0.11) and PGA (p=0.07; r=0.267). In multivariate linear regression analysis, pain visual analog scale was found to be independently associated with EFT (B=0.126; 95% Confidence Interval: 0.017-0.236; p=0.025).
Conclusion: EFT measurement as an early marker of atherosclerosis was associated with pain and BASG score.
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AB0835 **INFLUENCE OF SOCIODEMOGRAPHIC PARAMETERS ON ATHEROSCLEROSIS IN SPONDYLOARTHRITIS PATIENTS**

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Background: The increased risk of atherosclerosis is most likely multifactorial in patients with Spondyloarthritis (SpA). Ultrasound measurements of Intima Media Thickness and (IMT) Flow Mediated Dilation (FMD) can be used to investigate infra-clinical atherosclerosis [1].
Objectives: We aimed to investigate the relationship between socio-demographic parameters in SpA patients with the IMT and FMD.
Methods: It was a case control study conducted over a period of 12 months and including patients with SpA, aged less than 50 years old and without cardiovascular disease, and age and sex matched healthy controls. Sociodemographic and clinical features were recorded in our patients. All subjects had Doppler ultrasound with measurement of carotid IMT and FMD.
Results: There were 47 SpA patients and 47 controls. The median age was 36 years for patients group (18-50) and 32 years for controls (18-50). For the patients group: there were 14 female (28.8%) and 33 male (70.2%). The median duration of the disease was 11 years (1-32). For the marital status, 55.32% were single, 40.43% were married, and 4.26% were divorced. Thirty seven patients (79%) were living in an urban area. For the education level, 17% had a primary education, 64% a secondary education, and 19% were university graduates. Occupational status was recorded as follows: 17% unemployed, 11% students, and 72% employed. The median IMT was 0.55 millimeters (mm)(0.32 -0.83). We found a higher mean, right and left IMT (p<0.0001) in SpA patients compared with controls. Carotid IMT was positively correlated with age (p<0.0001; r=**0,578**). The analysis by 10-year age group showed a statistically significant difference in the IMT between patients (p=0.004). Median IMT increased significantly with age (every 10 years). IMT was significantly associated with occupational status (p=0.036); unemployed patients had the higher IMT (0.58 mm). The median FMD was 14.6% (2-32%). A significantly lower FMD (p=0.008) was noted in SpA patients compared with controls. FMD were negatively correlated with age (p=0.017; r=**-0,347**). FMD was also associated with sex (p=0.036), and with the marital status (p=0.013). The median FMD was significantly lower in male 13.8% (IQR;8-17.5) vs 22.5% (IQR; 10-25), and married patients (10%; 6-18). There was no significant difference with the other sociodemographic variables (living environment, educational level, occupation). In multiple regression analysis, age was an independent predictor of increased carotid IMT (B=0.004; T=3.146; p=0.003; CI 95% 0.001-0.006].
Conclusion: Our study showed that subclinical atherosclerosis in patients with SpA was strongly associated with age, although we included young patients with a limit age at 50 years.
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AB0836

MICRONUTRIENTS DEFICIENCIES IN ENTEROPATHIC SPONDYLOARTHRITIS: THE INTERPLAY WITH METABOLISM AND HLA-B27 IN DISEASE PHENOTYPE

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Background: Micronutrients play immunomodulatory roles through interactions with innate and adaptive immunity influencing the pro/anti-inflammatory balance. Serum levels depend on multiple factors such as gender, nutrition, and gut microbiome. Micronutrient deficiencies (MNDs) are associated with a pro-inflammatory status and co-morbidities in patients with chronic inflammatory diseases. No studies focused on potential interplay between MNDs and disease phenotype in Enteropathic Spondyloarthritis (ESpA) in which the combination of SpA with inflammatory bowel diseases (IBD) might dramatically affect micronutrients status.
Objectives: We analysed the occurrence of anemia (Hb ≤12 g/dl) and deficiencies of ferritin (Fe, ≤15 ng/dL), vitamin D [25(OH)D, ≤20 ng/ml], vitamin B12 (VB12, ≤200 pg/ml), and folic acid (FA, ≤ 4ng/mL) in ESpA patients. The interplay of MNDs with gender, metabolic parameters, HLA-B27 susceptibility, type of SpA and IBD, disease activity, and treatments was also explored.
Methods: Selection criteria of this cross-sectional descriptive study consisted of having a diagnosis of ESpA, regardless of its type, in an age of ESpA onset ≥18 and ≤80 years, among patients who were admitted to a combined Gastro-Intestinal and RHEumatologic "GI–Rhe" clinic (Tor Vergata University Hospital, Rome, Italy). Exclusion criteria were represented by active IBD, pregnancy or lactation, kidney and/or liver failure, alcohol abuse, neoplasia, ongoing supplementations. SpA disease activity was assessed by ASDAS-CRP and functional status by HAQ-S. All the enrolled patients underwent blood chemistry analysis to determine parameters including CRP, uric acid (SUA), Fe, 25(OH)D, VB12, FA, and HLA-B27 typing.
Results: We included 164 patients comprising 109 females and 55 age-matched males. A diagnosis of Crohn's Disease (CD) occurred in 70% of patients while Ulcerative Colitis (UC) represented a third of the cohort. Peripheral (per) and axial (ax) SpA were equally distributed (50%*vs*50%). Patients with ax-SpA displayed a greater prevalence of CD than UC (p=0.02) while UC was prevalent in per-SpA (p=0.02). $B27^+$ was revealed in 19% of our cohort: $B27^+$ patients had a higher prevalence of ax-SpA (p=0.016) and a more severe disease activity (p=0.02) than $B27^-$. Moreover, B27 positivity and uveitis were prevalent in ax-SpA compared to per-SpA (p=0.009 and p=0.01, respectively). According to univariate analysis, males showed higher SUA (P=0.004) and BMI (p=0.03) than females. Conversely, females showed a higher prevalence of anemia than males (p=0.002). A third of ESpA cohort showed FA (31.6%) and 25(OH)D (27.8%) deficiency while VB12 defect was less frequent (18.2%) and was registered almost entirely in $B27^-$ ESpA (p=0.02). CD-ESpA showed a lower mean VB12 (p=0.04) and a higher prevalence of ocular/skin co-morbidities (p=0.02) and ax-SpA (p=0.04) than UC-ESpA. Accordingly, CD-ESpA were on bDMARDs more than UC-ESpA (p=0.04).
Conclusion: Our findings document that FA and 25(OH)D deficiencies represent the main MNDs among ESpA patients while VB12 seems to be deficient mostly in patients with CD and almost exclusively in $B27^-$ patients. Otherwise, $B27^+$ in ESpA results to be associated mainly with disease phenotype and treatments. In ESpA, the gender of patients appears to impact principally on dysmetabolism highlighting the role for nutritional interventions particularly in males. The interplay of MNDs with B27 and dysmetabolism in ESpA deserves further investigations also taking into account CD/UC localization and behavior.
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AB0837

NEUROPATHIC PAIN COMPONENT AND ITS RELATIONSHIP WITH QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic systemic inflammatory disease of the connective tissue[1]. AS often affects men aged 20-40 years and characterized by a progressive affect with rapid loss of work ability, deteriorating quality of life and reducing its duration. Quality of life is one of the markers of disease progression and evaluation of the treatment efficacy. The leading clinical symptom of AS is chronic pain, which may have not only nociceptive but also neuropathic component, which is not taken into account in the treatment of this category of patients, while pain is one of the main factors in reducing quality of life.
Objectives: To investigate the prevalence of the neuropathic pain component (NPC) and its relationship with the quality of life in patients with AS.
Methods: AS patients was diagnosed according to the New York 1984 classification criteria. The NPC was assessed by the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) and The Douleur Neuropathique 4 (DN4). Quality of life was assessed by the Ankylosing Spondylitis Quality of Life (ASQoL). We examined 142 patients with AS (79.5% of men) in the rheumatology center from 2016 to 2021. The mean age was (M±SD) 41.9 ± 9.7 years, the disease duration was 5.7 ± 4.6. Statistical analysis performed by the Microsoft Excel and IBM Statistics SPSS 20.
Results: NPC assessed by the LANSS (≥ 12) was found in 31% of patients, by the DN4 (> 4) in 38%. ASQoL in patients with AS with NPC by the LANSS was 12.27 ± 4.27, by the DN4 - 11.64 ± 4.19, which was significantly higher than in patients with AS without NPC: LANSS (7.97 ± 3.76), DN4 (7.86 ± 3.88). ASQoL had a strong direct correlation with LANSS (0.561; p <0.01) and DN4 (0.478; p <0.01) that means - presence of neuropathic pain substantially effects quality of life in patients with AS.
Conclusion: NPC is found in 31% - 38% of patients with AS. It is established that the presence of the neuropathic pain component significantly reduces the quality of life in patients with AS, which should be taken into account during the treatment.
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AB0838

THE IMPACT OF COMORBIDITIES ON PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A CLUSTER ANALYSIS

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Background: Previous study using cluster analysis technique analyzed the association between comorbidities and various outcome measures in patients with axial spondyloarthritis (axSpA). Due to the cross-sectional nature of the study, however, prognostic information about each group were not provided.
Objectives: This study aims to perform cluster analysis to differentiate axSpA patients in terms of comorbidities and to examine the differential treatment outcomes of these groups using the data retrieved from Korean College of Rheumatology Biologics (KOBIO) registry which includes longitudinal data of axSpA patients using anti-TNF agents.
Methods: Clinical characteristics and demographic data of axSpA patients in KOBIO registry were analyzed using an agglomerative hierarchical cluster analysis. The optimum number of clusters was determined by the pseudo-F statistic. After clustering, baseline clinical characteristics and treatment outcomes were compared between isolated axSpA and classified comorbidity groups using multivariable linear models and mixed linear models, respectively.
Results: 1,207 patients were included in the study. At least one comorbidity was seen in 464 (38%) axSpA patients. Compared with those with isolated axSpA, patients with comorbidity were older, longer disease duration, and reported higher PtGA (p = 0.019), and BASFI (p <0.001), but did not have significantly different BASDAI, ESR, and CRP levels. The most common comorbidities were hypertension (14.4%), hyperlipidemia (13.0%), and obesity (4.5%). The hierarchical cluster analysis classified patients in 21 groups. We combined clusters 17-21 for further evaluation due to the small size of clusters (<5 patients). In multivariable linear models for baseline clinical characteristics, we found that patients in the hypothyroidism, asthma, and headache clusters reported poorer PtGA, BASDAI, or BASFI, and the weight loss cluster had higher level of CRP, compared with patients with isolated axSpA even after adjustment of patient demographic data. After 1-year treatment of anti-TNF agents, the patients in the hypothyroidism and weight loss clusters decreased greater amounts of BASDAI and BASFI scores and ESR/CRP levels, respectively, compared with patients with isolated axSpA (Table 1). However, the degree of improvement in asthma and headache clusters, which had higher disease activities at baseline, was similar with isolated axSpA. Therefore, they still had higher disease activity scores at the 1-year follow-up.

Table 1. Comparing each cluster to patients with isolated axSpA (i.e. no comorbidity) using multivariable linear mixed models for each treatment outcome measure at 1-year follow-up as the dependent variable.

Cluster/description	PtGA	BASDAI	BASFI	ESR	CRP
2 isolated axSpA	-	-	-	-	-
3 Obesity	0.233 (-0.57 - 1.036)	0.098 (-0.648 - 0.844)	-0.078 (-0.811 - 0.656)	**9.005 (0.481 - 17.529)†**	0.358 (-0.553 - 1.269)
10 Hypothyroidism	-1.243 (-3.139 - 0.653)	**-2.147 (-3.908 - -0.385)†**	**-2.38 (-4.076 - -0.684)†**	2.234 (-18.11 - 22.578)	-0.087 (-2.123 - 1.95)
11 Weight loss	-0.618 (-2.804 - 1.568)	-0.901 (-2.932 - 1.131)	-1.93 (-3.886 - 0.026)	**-26.891 (-50.351 - -3.431)†**	**-4.197 (-6.544 - -1.849)†**
15 Asthma	0.049 (-2.138 - 2.235)	0.833 (-1.199 - 2.864)	0.254 (-1.702 - 2.209)	-1.058 (-24.517 - 22.402)	2.018 (-0.552 - 4.589)
16 Headache	-0.103 (-1.052 - 0.846)	0.169 (-0.713 - 1.051)	0.463 (-0.387 - 1.312)	0.344 (-9.693 - 10.382)	-0.046 (-1.132 - 1.04)

† p-value < 0.05. Only clusters including significant results were shown due to the limitation oft he number of characters.

Conclusion: Comorbidity could affect the treatment outcomes in patients with axSpA in certain subgroups. Thus, we should also pay attention to the comorbidities when treating axSpA.

Disclosure of Interests: None declared

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AB0839 EXTRA-ARTICULAR MANIFESTATIONS IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Background: Spondyloarthritis (SpA) is a chronic inflammatory arthritis that combines joint involvement and extra-articular manifestations such as inflammatory bowel disease (IBD), uveitis and psoriasis.

Objectives: The aim of our study was to compare extra-articular manifestations in patients with ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA).

Methods: A retrospective study was conducted in a single rheumatology hospital in Morocco, including patients diagnosed as having SpA according to ASAS criteria 2010, during a period of 9 years. The patients were classified as AS by the presence of radiographic sacroiliitis according to the modified New York criteria and nr-axSpA defined by the presence of sacroiliitis on MRI. Extra-articular manifestations are compared between the two groups

Results: 375 patients were analyzed. 206 were female (54,9%). The mean age were 46,8 ± 14 years [16-84]. The mean duration of disease progression were 13.38 ± 8.44 years. The mean BASDAI were 4.20 ± 1.60 and the mean BASFI were 4.40 ± 2.24. 68,5% of patients had AS and 31.5% patients had nr-axSpA. Extra-articular manifestations were found in 109 (29,1%) of the patients, 72 (19,2 %) had IBD, 49 (13,1%) had uveitis and 9 (2,4%) had psoriasis. In bivariate analysis, IBD was noted in 23 % of patients with AS versus 11 % of patients with nr-axSpA (p= 0.006), psoriasis was present in 3.5% of patients with AS (p = 0.040), uveitis was present in 15.6% of AS (p = 0.034).

Conclusion: Extra articular manifestations are frequent in SpA. They are more frequent in patient with AS. Physicians need to screen carefully for extra articular manifestations at diagnosis and over follow-up.

Disclosure of Interests: None declared

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AB0840 COMPARATIVE ANALYSIS OF MACROSCOPIC CHANGES IN BONE TISSUE OF HEADS AND ACETABULUMS OF THE HIP JOINTS (HJ) IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS): DATA FROM A RETROSPECTIVE ANALYSIS

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Background: According to the results of Russian studies, coxitis occurs in 56% of patients (pts) with AS. At the same time, the need for total hip arthroplasty (THA) is only 8%, which is associated with the use of biologic disease-modifying anti-rheumatic drugs (bDMARDs).

Objectives: The aim of the study was to compare macroscopic changes in bone tissue of femoral heads (FH) and acetabulums in pts with AS who received and did not receive bDMARDs.

Methods: The retrospective study included 170 pts with a verified diagnosis of AS, who met the modified New York criteria of 1984, who were treated in the traumatological and orthopedic department in the period from 1998 to 2020, THA was routinely performed to all pts. Most of them were male (80.6%). The average age was 38.1±11.3 yrs. 82.9% of pts had low activity of the disease according to the BASDAI index at the time of surgical treatment and 17.1% of them had high activity. Nonsteroidal anti-inflammatory drugs were received by 61.7% of pts, sulfasalazine - 20.6%, methotrexate - 7.7%, systemic glucocorticoids - 8.8%, bDMARDs -53 (31.1%).

Results:

Parameter	All patients (n=170)	bDMARDs (+) n=53	bDMARDs (-) n=117
Average duration of the disease, years, M±σ	17,0±8,5	16,2±8,0	17,5±8,7
Age at the time of diagnosis, years, M±σ	27,6±9,1	27,6±10,0	27,6±8,9
Necessity of THA, years, M±σ	7,4±4,8	6,0±2,8	8,0±5,4
Osteophytes (Yes/No),%	90/10	96/4	88/12
Protrusion (Yes/No),%	75/25	68/32	78/12
Granulation (Yes/No),%	91/9	95/5	89/11
Ankylosis (Yes/No),%	47/53	48/52	37/53
Ankylosis (Fibrous/Osseous),%	77/23	80/20	75/25
Cysts of femoral heads (Yes/No),%	39/61	36/64	39/61
Cysts of femoral heads (Single/multiple),%	78/22	70/30	71/29
Erosion of femoral heads,%	47	39	50
Osteonecrosis of femoral heads,%	75,5	75*	45

***p<0,05**

The vast majority (85.9%) of pts had III grade of secondary coxarthrosis and 14.1% - had IV grade before THA. Complete absence of cartilage on the surface of acetabulum was revealed in 71.7% of cases, and there were either partial abrasions of the cartilage in the places of maximal load (6.5%), or chondromalacia (21.8%) in rest of the pts. Deformity of the FH was detected in 98.2% of pts, while as a result of osteonecrosis of FH (ONFH) in 75.5%. Complete absence of cartilage on FH was in 130 (76.5%) pts, and there were either partial abrasions of the cartilage in the places of maximal load (11.2%), or chondromalacia (12.3%) in rest of the pts. There were no significant differences in the macroscopic picture of the lesion of FH and acetabulums of HJ in pts with and without intake of bDMARDs, except for a higher frequency of ONFH in pts receiving bDMARDs.

Conclusion: The need for THA arose on average after 7.4±4.8 yrs from the appearance of pain in the hip joint (HJ). Macroscopic picture of HJ lesion in pts with AS was characterized as ONFH in 75.5% of cases, in almost half of cases - ankylosis of HJ, mainly fibrous (77.2%) with complete or partial absence of cartilage in acetabular surface and FH. According to the majority of macroscopic changes in the bone tissue of HF and acetabulums of HJ, pts with and without bDAMRDs did not differ, but the frequency of ONFH was significantly higher in the group of pts who was receiving bDAMRDs.

Disclosure of Interests: None declared.

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AB0841

ANALYSIS OF THE FUNCTIONAL STATE OF HIP JOINTS (HJ) BEFORE TOTAL HIP ARTHROPLASTY (THA) IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS): DATA OF A RETROSPECTIVE ANALYSIS

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Background: Injury of hip joint (HJ) in patients (pts) with ankylosing spondylitis (AS) is considered as a factor of unfavorable prognosis, which can lead to rapid disability of pts.
Objectives: To assess the functional state of HJ before performing THA in patients with AS.
Methods: This retrospective study included 170 pts with a verified diagnosis of AS, who met the modified New York criteria of 1984, who were treated in the traumatological and orthopedic department in the period from 1998 to 2020, THA was routinely performed to all pts. Most of the pts were male (80.6%). 64% of them did not work due to the disease. Functional insufficiency of the joints at the time of surgical treatment in 64.1% of all the cases corresponded to III grade, in 26.5% - to IV grade, in 9.4% - to II grade. 82.9% of pts had low activity of the disease according to the BASDAI index at the time of surgical treatment and 17.1% of them had high activity. 53 (31.1%) pts were receiving bDMARDs and 87% of them were TNF-alpha inhibitors. The Harris quantitative scale was used to assess the functional state of HJ.
Results:

Parameter	All patients (n=170)	bDMARDs (+) n=53	bDMARDs (-) n=117
Age, years, Me±δ	38,1±11,3	37,5±12,3	38,3±10,8
Age of AS debut, years, Me± δ	20,7±8,4	21,2±8,4	20,5±8,4
Age at the time of diagnosis, years, Me± δ	27,6±9,1	27,6±9,9	27,6±8,9
Average delay in diagnosis, years, Me± δ	6,8±5,8	6,4±4,3	7,1±6,4
Average duration of the disease, years, Me± δ	17,0±8,5	16,2±8,0	17,5±8,7
Average duration of pain in HJ, years, Me± δ	7,4±4,8	6,1±2,2*	8,0±5,4
Average level of pain in HJ, VAS, Me± δ	72,3±14,0	69,9±12,9	73,4±14,5
Average overall score on the Harris scale before surgery	38,0±15,4	42,1±15,0	36,1±15,3*
The average level of pain on the Harris scale, VAS,, Me± δ	15,6±8,4	17,5±8,3	14,7±5,5
Antalgic Gait (absent/mild/moderate/severe), %	42,9/42,9/11,8/2,4	41,5/35,8/18,9/3,8	43,6/46,2/8,5/1,7
Walking a distance (unlimited /1500 meters /500 meters/in the apartment/unable to walk), %	2,4/21,2/0,6/44, 7/27,1/4,1	2,4/21,7/44, 7/27,1/4,1	3,4/21,6/45, 2/26,4/3,4
Additional support (missing/ walking stick for long distances/ walking stick permanently/one crutch/two walking sticks/two crutches), %	30,6/5,3/4,1/29, 5/4,1/26,4	22,6/7,5/3,8/24,5/ 7,5/34,0	34,2/4,3/4,3/31, 6/2,6/23,0
Putting on shoes (without difficulty/ with difficulty/ impossible)	4,2/65,8/30,0	7,4/67,9/24,5	3,4/64,9/33,3
Fixed adduction (<10°/>10°), %	30,0/70,0	26,4/73,6	31,6/68,4
Fixed internal rotation (<10°/>10°)	22,9/77,1	26,4/73,6	21,4/78,6
Flexion contracture (<15°/>15°), %	39,4/60,6	41,5/58,5	38,5/61,5

***p<0,05**

Conclusion: The vast majority of pts with AS had pronounced severe disorders of HJ before THA - the average score on the Harris scale was 38.0±15.4. Most of the patients (85.9%) had severe and moderate lameness, with the need for additional support in 69.4% of cases. Objective signs of functional disorders (fixed inward rotation and reduction, flexion contracture) of HJ were detected in more than half of the cases. According to the assessment of most parameters of the Harris scale, there were no significant differences between pts with AS on bDMARDs and without bDMARDs, except for the average duration of pain in HJ and the overall value of the scale (6.1±2.2 vs 8.0±5.4 and 42 vs 36, respectively, p<0.05 in both cases).
Disclosure of Interests: None declared

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AB0842

FOOT ENTHESES ULTRASOUND IN SPONDYLOARTHRITIS: A CASE CONTROL STUDY

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Background: Foot entheses involvement is a common manifestation of spondyloarthritis (SpA). It can be responsible for functional impairment. The superiority of ultrasound (US) examination in foot entheses damages detection has been reported [1].
Objectives: We aimed to compare the US findings of foot entheses between SpA patients and asymptomatic healthy control subjects.
Methods: We conducted a cross-sectional study including 37 SpA patients (G1) fulfilling ASAS criteria for Axial SpA and 37 healthy subjects (G0) matched by age and gender. Demographic and clinical characteristics were collected. A blind US of foot entheses was performed by Mindray DC-70 equipment with a 6-16 MHz linear probe. Calcaneal enthesis (CT) and plantar fascia (PF) were examined bilaterally. A total of 296 entheses were assessed. In G1, disease activity was evaluated using the Bath Ankylosing Spondylitis Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS). Statistical Package for Social Sciences (SPSS) was used for analysis.
Results: The study included 58 men and 16 women. The mean age was 44.6 ± 12.3 years. In G1, the mean disease duration was 108.2±94 months. The average BASDAI was 4.5±2.2. The average $ASDAS_{CRP}$ was 3.2±1.3. In G1, clinical examination showed tenderness at the posterior insertion of the CT or inferior insertion of PF in 16.2% of patients. However, US lesions of the CT were found in 97% of cases in G1 and 67.6% in G0, p:0.001. US lesions are presented in Table 1.

Table 1. Elementary US lesions in SpA and healthy control groups

Enthesis		G1 (n (%))	G0 (n (%))	p
Calcaneal tendon	Thickness	15 (40.5)	6 (16.2)	0.02
	Erosion	9 (24.3)	1 (2.7)	0.007
	Enthesophyte	29 (78.4)	20 (54)	0.03
	Calcification	14 (37.8)	10 (27)	0.32
	Bursitis	4 (10.8)	3 (8.1)	1
	PD signal	10 (27)	0	0.001
Plantar fascia	Thickness	30 (81.1)	27 (73)	0.4
	Erosion	11 (30)	1 (3)	0.002
	Enthesophyte	12 (32.4)	2 (5.4)	0.003
	Calcification	18 (48.6)	6 (16.2)	0.003
	PD signal	11 (30)	0	<0.001

G0: control group, G1: Spondyloarthritis group, PD: power doppler

Calcaneal tendon thickness was noted in 40.5% in G1 and 16.2% in G2 (p=0.02). Hypo-echogenicity and loss of normal fibrillar structure were more frequent in G1 (86.5% versus 29.7%, p<0.001). Structural damage lesions were found in 89.6 % in G0 (n= 33) and 64.9% in G1 (n=24), p=0.01. In the PF, US structural damage lesions were significantly more frequent in the SpA patients (70% versus 21.6%, p<0.001). Vascularity at power Doppler was significantly more frequent in G1 (p=0.001 in CT and p<0.001 in PF). In G1, the disease activity was higher in patients with structural damage lesions of the CT ($ASDAS_{CRP}$: 3.2 versus 1.9; p=0.01). However, there was no associations between vascularity at power Doppler and high disease activity (p=0.47).
Conclusion: Our study showed that the US lesions of the heel entheses were frequent in SpA patients compared to healthy control. Moreover, US can reveal enthesitis even in asymptomatic patients.
The disease activity was higher in patients with US structural damage lesions of the CT.
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AB0843

OSTEOPOROSIS IN PATIENTS WITH SPONDYLOARTHRITIS: DO WE NEED TO DO MORE?

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Background: Data regarding the prevalence and especially incidence of osteoporosis in Spondylarthritis (SPA) is scarce and very divergent among studies from different patient populations (1).
Objectives: In this study, we aimed to compare demographic, disease and laboratory characteristics of SpA patients regarding their bone mineral densitometry (BMD) categories and find out incidence of osteoporosis in the follow-up BMD of patients who were not found to have osteoporosis at baseline.
Methods: Between 2010-2021, patients with a SPA diagnosis in the HUR-BIO database were searched. HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a single center biological disease modifying anti-rheumatic drug (DMARD) registry since 2010. Patients with BMD measurement were included in the study. Follow-up BMD scores were also documented. The patients were divided into 3 groups as normal, osteopenia and osteoporosis in accordance with the WHO criteria (2). Demographic characteristics, comorbidities, laboratory data and drugs in each group were documented.
Results: 3245 patients were reviewed. BMD was measured at least once in 118 patients out of 3245 (3.6%) patients. When the groups classified, 34 patients (28.8%) were included in the normal, 49 (41.5%) osteopenia and 35 (29.7%) osteoporosis groups. Patients with normal BMD was younger than both groups. Diabetes and hypertension were more prevalent in patients with osteopenia. The BMI was significantly lower in the osteoporosis group. 25 patients with normal and osteopenia in baseline BMD measurement had at least 1 follow-up BMD measurement. During the total follow-up of 91 patient-years, 3 patients had osteoporosis, revealing a the incidence of 3.3% in 100 patient-years.
Conclusion: In our study, the incidence of OP development in SPA patients was found to be 3.3%. Frequency of osteoporosis was 29.7% among SpA patients with BMD measurement (118/3245; 3.6%), however; only 40% of them had appropriate treatment. Osteoporosis seems as an overlooked and undertreated comorbidity of SpA.

Table 1. Comparison of spondyloarthritis patients according to BMD scores (normal, osteopenia and osteoporosis) according to baseline BMD assessment

	NORMAL Number, (%)	OSTEOPENIA Number, (%)	OSTEOPOROSIS Number, (%)	P VALUE
Number of Patients	34 (28.8)	49 (41.5)	35(29.7)	
Age	47,5 (27-70)	63 (45-79)	58 (20-75)	0.00*
Gender (Female)	24 (70.6)	34 (69.4)	23 (65.7)	
Diabetes Mellitus	3 (8.8)	14 (29.2)	1 (2.9)	0.00*
Hypertension	11 (32.4)	28 (58.3)	5 (14.3)	0.00*
Chronic Renal Failure	2 (6.9)	1 (2.7)	1 (5.3)	0.81
Chronic Ostructive Pulmonary Disease	4 (13.8)	4 (10.8)	1 (5.3)	0.30
Coronary Artery Disease	0 (0)	5 (12.5)	3 (15)	0.27
Malignancy	1 (3.6)	1 (2.9)	1 (4.2)	1.0
Smoking	21 (61.8)	23 (47.9)	21 (63.6)	0.37
	9 (26.5)	13 (27.1)	5 (15.2)	
	4 (11.8)	12 (25)	7 (21.2)	
Calcium mg/dl	9.4 (8.2-10.2)	9.5 (8.7-10.4)	9.7 (8.1-10.4)	0.49
Phosphorus mg/dl	3.5 (3-4.4)	3.4 (2.6-5)	3.8 (2.9-4.9)	0.25
Vitamin D ng/ml	16 (7.4-64.4)	21.2 (5-69.6)	15.8 (5.8-49.1)	0.66
ALP IU/ml	89.5 (54-137)	89.5(53-169)	80 (50-239)	0.43
Albumin g/dl	4.2 (1.7-4.7)	4.2 (3.3-8.4)	4.2 (2-4.8)	0.43
TSH mU/ml	1.5 (0.8-4.1)	2.3 (0.1-9.7)	2 (0.7-3.3)	0.71
Body Mass Index (BMI) kg/m2	29 (17-41.2)	28.3 (20-44.6)	25.1(15.8-43.2)	0,06*
Steroids	4 (11.8)	8 (16.3)	2 (5.7)	0.33
Anti-TNF	25 (73.5)	35 (71.4)	26 (74.3)	0,95
D Vitamin	7 (20.6)	14 (28.6)	10 (28.6)	0.67
Calcium	4 (11.8)	5 (10.2)	6 (17.1)	0.63
Bisphosphonate	0 (0)	4 (8.2)	14 (40)	0,00*

Data was represented as median (minimum-maximum) or n(%)

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AB0844

CHARACTERIZING GUT MICROBIAL ENTEROTYPES IN UNDIFFERENTIATED SPONDYLOARTHRITIS

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Background: The presence of dysbiosis in the gut microbiome is responsible for the initiation of autoinflammatory and autoimmune diseases. However, such dysbiosis is difficult to characterize in sweeping generalization owing to the high dimensional complexity of the gut microbiota.
Objectives: This study designed to characterize the gut microbial enterotype in patients with undifferentiated spondyloarthritis (USpA) from lower dimensionality and describe the dysbiosis.
Methods: The Fecal samples of 105 patients were diagnosed with USpA and gender- and age- matched 105 healthy controls (HC) were included in the intestinal microbiota composition analyses via Illumina sequencing of bacterial 16S rRNA genes. Microbiota-derived clustering was performed using Dirichlet multinomial mixtures (DMM) modeling. To identify discriminative features in abundance between enterotypes, the Linear Discriminant Analysis Effect Size (LEfSe) algorithm was used with the online interface Galaxy (Log10 LDA score > 4.0). The phyloseq R package to compute alpha diversity (ACE, Chao1, Shannon and Simpson indices), beta diversity (Bray-Curtis dissimilarity) and the microbial composition (at the genus level) to describe the richness and diversity of the microbiota between two enterotypes.
Results: As showed in Figure 1A and C, by evaluating the Laplace approximation to the negative log mode, 2 distinctly enterotypes were identified in the USpA and HC microbiota dataset. LEfSe Analysis indicated the distinctive abundant microbial clades between the 2 enterotypes (LDA score >4) in both the USpA and HC group respectively. At the genus level, Faecalibacterium and Prevotella

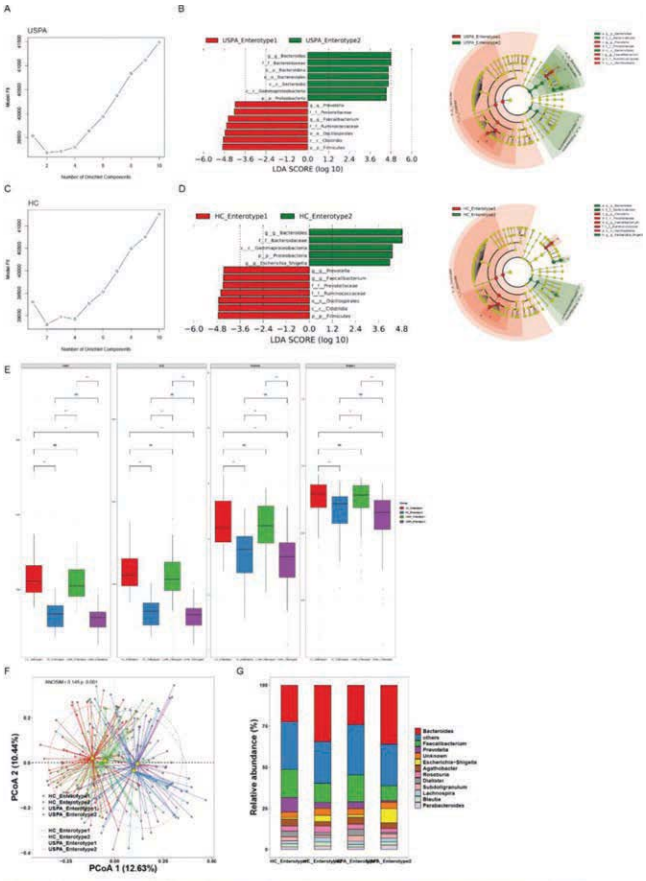

Figure 1 (A, C) Evaluates model fit for increasing number of K using the Laplace approximation to the negative log model evidence. (B, D) LEfSe-derived taxonomic cladogram; LDA score of enriched bacterial taxa (LDA >4 of LEfSe). Significantly enriched bacterial taxa in fecal samples in distinct enterotypes are indicated by different colors. Red bars indicate taxa enriched enterotype 1, and green bars indicate taxa enriched enterotype 2. (E) Comparison of alpha diversity indices between enterotype 1 and enterotype 1. (F) Comparison of beta diversity indices between enterotype 1 and enterotype 1, Principal coordinate analysis plot generated from the bray distance analyses. (G)The composition of gut microbiota between enterotype 1 and enterotype 2 in USpA and HC.

was the driving genus of enterotype 1 and Bacteroides contributed to enterotype 2 (Figure 1B, D). The alpha-diversity and beta diversity between the distinctive enterotypes was highly significantly different (P < 0.01, Figure 1E, F). Distinct bacterial profiles were also observed in enterotype 1 and 2 (Figure 1G). Interestingly, no significant differences were found between USpA patients and HC for the corresponding same intestinal type. This may be because USpA was at a comparatively early stage of spondyloarthritis (SpA).

Conclusion: Two significantly distinct bacterial microbiota structures existed in the USpA patients which was consistent with the general healthy population.

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AB0845 IMPORTANCE OF WEIGHT MANAGEMENT ON ENDOTHELIAL FUNCTION IN SPONDYLOARTHRITIS

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Background: Subclinical atherosclerosis is not rare in spndyloarthritis (SpA) patients. Endothelial dysfunction is the first step of atherosclerosis process. Obesity is a major traditional cardiovascular risk factor.

Objectives: The purpose of our study was to determine the association of anthropometric measures with endothelial dysfunction in non-obese SpA patients.

Methods: This was a prospective study conducted over 12 months and including 47 SpA free cardiovascular disease patients and aged less than 50 years. The following anthropometric parameters were collected for each patient: weight, height, Body Mass Index (BMI), hip and waist circumferences. Endothelial dysfunction was assessed by the ultrasound evaluation of the Flow Mediated Dilatation (FMD).

Results: There were 14 female (28.8%) and 33 male (70.2%). The median age was 36 years (IQR; 18-50). The median disease duration was 11 years (IQR; 1-32). The median weight, height and BMI were 69 (IQR; 43-95), 170 cm (IQR; 144-193) and 24.5 kg/m^2 (IQR; 16.33 - 29.41), respectively. Overweight (BMI: 25-29 kg/m^2) was noted in 40% of patients. The median hip and waist circumferences were respectively 100 cm (IQR; 84-116) and 88 cm (IQR; 70-114). Median FMD was 18.18% (IQR; 12.8-23.1). We didn't found correlation between anthropometric parameters and FMD: weight (p=0.225; r=-0.180); height (p=0.273; r=-0.163), BMI (p=0.437; r=-0.116); waist circumference (p=0.22; r=-0.182) and hip circumferences (p=0.142; r=-0.217).

Conclusion: Our study showed that anthropometric parameters do not influence endothelial function in non-obese and young SpA patients. This highlights the importance of weight management and maintaining a healthy weight in SpA patients.

Disclosure of Interests: None declared

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AB0846 HLA-B51 PREVALENCE IN PATIENTS WITH SPONDYLOARTHRITIS AND IMPACT ON DISEASE PHENOTYPE: A CASE-CONTROL STUDY

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Background: Spondyloarthritis (SpA) is a group of rheumatic diseases with a heritable component associated with Human Leucocyte Antigen B27 (HLA-B27). Although many studies have reported an overlap between the clinical features of SpA and Behcet's disease (BD), as well as an increased prevalence of HLA-B27 in BD, the prevalence of HLA-B5 (namely B51 and B52, the split antigens of B5) in SpA, have been scarcely examined, particularly in countries with a low HLA-B27 prevalence.

Objectives: To estimate the prevalence of HLA-B51 and HLA-B52 in patients with SpA compared to healthy controls (HC), to identify the alleles found in HLA-B locus in patients with SpA compared to HC, and to evaluate the impact of HLA-B51 on SpA disease phenotype.

Methods: A case-control study included consecutive patients with a diagnosis of SpA (axial SpA (axSpA), peripheral SpA (pSpA), and psoriatic arthritis (PsA)) from three rheumatology clinics. HC were recruited among blood donors and medical students. Demographic data, as well as SpA and BD disease features, were collected through an interview with a trained medical student and file review (low back pain, peripheral joint disease, enthesitis, dactylitis, psoriasis, uveitis, inflammatory bowel disease, family history, oral and genital ulcerations, skin, vascular and neurologic manifestations, CRP, BASDAI, imaging of the spine and sacroiliac joints). The entire B locus was tested using molecular biology technique on Luminex with the possibility of precise B51/B52 differentiation. The prevalence of HLA-B51/B52 was calculated in patients and compared to HC using the Chi-square test. A complete HLA-B mapping was performed for patients and HC. A binary logistic regression identified factors associated with HLA-B51 in patients with axSpA.

Results: Data from 119 HC and 89 patients with SpA were available (66 axSpA, 16 pSpA, and 7 PsA). Mean age of the patients was 44.8 years [SD 13.5], 66.3% were males, disease duration was 12 years [SD 12.7], 72.4% had a history of elevated CRP, 30.3% were positive for HLA-B27, 53.9% had sacroiliitis on MRI, 47.2% had radiographic sacroiliitis, and 23.6% had syndesmophytes. Oral ulcerations were reported in 38.2% of patients, genital ulcerations in 3.4%, uveitis in 5.6%, skin lesions in 18%, and vascular lesions in 3.4%. Patients with SpA fulfilled the classification criteria for BD in 2.9% (International Study Group criteria for BD) and 38.2% (International Criteria for BD). HLA-B51/B52 were found more frequently in patients with SpA (20.2%/ 7.9%) compared to HC (11.8%/4.2%), although the difference was not statistically significant. The difference was mainly driven by ant association between HLA-B51 and axSpA (27.2% versus 11.8%, OR 2.8 [95%CI 1.3-6.1], p=0.008) (Table 1). The most frequent allele in SpA and HC was HLA-B35; complete HLA-B mapping is shown in Figure 1. In patients with axSpA, HLA-B51 was associated with radiographic damage in peripheral joints, while it was negatively associated with sacroiliitis. Uveitis was numerically associated with HLA-B51, but the association did not reach statistical significance.

Table 1. Prevalence of HLA-B5 genes in patients with spondyloarthritis (SpA) and healthy controls

	Controls	SpA	Axial SpA	Peripheral SpA	Psoriatic Arthritis	p-value (SpA vs. Controls)	p-value (axSpA vs controls)
N	119	89	66	16	7		
HLA-B51+, N (%)	14 (11.8)	18 (20.2)	18 (27.3)	0 (0.0)	0 (0.0)	0.094	**0.008**
HLA-B52+, N (%)	5 (4.2)	7 (7.9)	5 (7.6)	2 (12.5)	0 (0.0)	0.262	0.331
HLA-B51 or HLA-B52+, N (%)	19 (16)	21 (23.6)	19 (28.8)	2 (12.5)	0 (0.0)	0.167	**0.039**

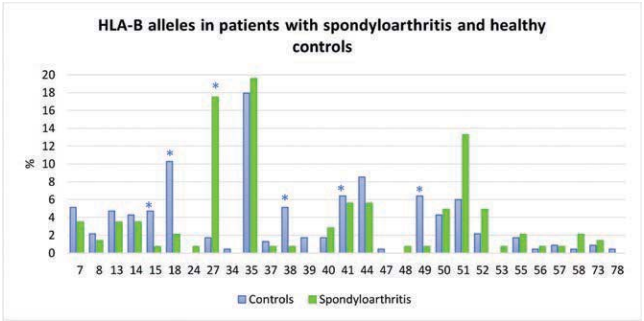

Figure 1. Distribution of the HLA-B alleles in patients with spondyloarthritis and healthy controls (Statistically significant differences between patients and controls indicated with*)

Conclusion: HLA-B51/B52 were more numerically more prevalent in patients with SpA compared to HC. A statistically significant association was found between HLA-B51 and axSpA and correlated with more peripheral and less axial radiographic involvement.

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AB0847

PROFILE OF SPONDYLOARTHRITIS IN THE MOROCCAN POPULATION: RESULTS OF A MULTICENTER STUDY

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Background: Spondyloarthritis (SpA) is a frequent group of chronic inflammatory rheumatic diseases, their epidemiology varies considerably in different regions of the world.
Objectives: The aim of our study was to describe the epidemiological, clinical, paraclinical and therapeutic profile of SpA in the Moroccan population.
Methods: This is a multicenter descriptive study, including patients followed for SpA. 8 hospital centers participated in this study. All data were measured by standard instruments.
Results: Seven hundred patients were included, 54% were men, the mean age was 40.42±14.19 years at the time of diagnosis [14 years-90 years]. The patients lived in urban and rural areas in 83.5% and 13.8% of cases, respectively. 38.4% were without occupation. A history of tuberculosis was noted in 5.9% of cases. Associated pathologies were autoimmune in 2.3% and neoplasia in 1.5% of cases. 15.6% of patients were smokers. A family history of SpA was noted in 11.7%, psoriasis in 1% and Inflammatory bowel disease (IBD) in 0.6% of cases. The average diagnostic delay was 59.76 months [0-444 months]. The revealing symptomatology was axial in 19%, peripheral in 10.1%, enthesitis in 0.4%, and a combination of the 3 forms in 22.1% of cases. Dactylitis was noted in 2.3% of cases. SpA was non-radiographic in 14% of cases. The forms of SpA were: ankylosing spondylitis (80.1%), IBD associated with SpA (9.4%), psoriatic arthritis (6%), and undifferentiated SpA (4%). Juvenile SpA accounted for 15.5% of cases. The prevalence of HLA-B27 was 65.51%. The mean BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) was 4.42 ± 1.67 and the mean ASDAS (Ankylosing Spondylitis Disease Activity Score) was 3.19 ± 1.24. Systemic involvement was dominated by uveitis (11.3%), followed by IBD (9.4%), restrictive syndrome (2.7%), renal involvement (0.6%) including amyloidosis (0.1%), IgA nephropathy (0.4%), interstitial nephropathy (0.1%), and aortic insufficiency in 0.2% of cases. The most commonly used treatments were non-steroidal anti-inflammatory drugs (81.7%), sulfasalazine (24.2%), methotrexate (22.9%) and 31.8% of patients were on biotherapy. Surgery for arthroplasty was necessary in 5.6% of patients.
Conclusion: This is a study of the clinical and demographic characteristics of Spondyloarthritis in a population in Morocco, on which a large scale data base could be initiated, in order to better determine the role of genetic and environmental factors in the pathogenesis of the disease.
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AB0848

ATHEROGENIC INDEX IS THE BEST DETERMINANT OF SUBCLINICAL ATHEROSCLEROSIS IN SPONDYLOARTHRITIS PATIENTS

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Background: Blood lipid levels particularly total cholesterol (CT), low-density lipoprotein cholesterol (C-LDL), high-density lipoprotein cholesterol (C-HDL), and triglycerides (TG), are commonly used to predict cardiovascular risk. However, it has been demonstrated that atherogenic index (CT/HDL, C-LDL/C-HDL) are prognostic indicators of atherosclerosis [1].
Objectives: The purpose of our study was to determine the role of lipid indicators in predicting subclinical atherosclerosis among SpA patients.
Methods: It was a cross sectional study over a period of 12 months including patients with established SpA (ASAS Criteria). They were cardiovascular disease free. Lipid analyses were performed for all patients including the determination of: C-LDL, C-HDL, CT, and TG. The ratios CT/C-HDL, C-LDL/C-HDL were calculated. Atherosclerosis was assessed by Doppler ultrasound with measurement of the carotid Intima-Media Thickness (cIMT).
Results: There were 47 SpA patients: 14 female (28.8%) and 33 male (70.2%). The median age was 36 years (18-50). The median disease duration was 11 years (1-32). The median lipid factors levels were respectively 3.66 mmol/l (2.27-6.34) for CT, 0.84 mmol/l (0.43-2.88) for TG, 2.17 mmol/l (0.93-3.9) for C-LDL, and 1.08 mmol/l (0.63-1.49) for C-HDL. The median CT/C-HDL, C-LDL/C-HDL ratios were respectively 3.48 (2.21-6.79) and 1.99 (0.86-3.77). There were 17% of patients with a high ratio CT/C-HDL (>4.5) and 9.3% of patients with high ratio C-LDL/C-HDL (>3.22).
The median cIMT was 0.55 millimeters (0.32-0.83). cIMT was positively correlated with low linearity with CT (p=0.007; r=0.404) and with the CT/C-HDL ratio (p=0,028; r=0.34).
Conclusion: In our study, CT/HDL ratio and CT were the best determinant of subclinical atherosclerosis in SpA patients.
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AB0849

ASSESSMENT OF CAROTID INTIMA-MEDIA THICKNESS IN SPONDYLOARTHRITIS PATIENTS

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Background: Cardiovascular morbidity and mortality are increased in spondyloarthritis (SpA) (1), which is attributed to accelerated atherosclerosis. Recognition of subclinical atherosclerosis in asymptomatic population is important for risk stratification and optimal management. Due to its simplicity and non-invasive nature, carotid intima-media thickness (cIMT) is actually widely used for identifying subclinical atherosclerosis.
Objectives: The aim of our study was to investigate the presence of subclinical atherosclerosis in SpA patients compared with healthy controls, by evaluating cIMT.
Methods: We performed a case control study including 47 patients and 47 age and gender matched healthy controls. All subjects were included without history of cardiovascular disease or cardiovascular risk factors. Sociodemographic features, disease characteristics, radiographic structural damage and therapeutics were recorded. cIMT was measured with Mindray Resona 7 ZST+ ultrasound machine, from the right and the left carotid artery; than mean cIMT was calculated. We considered that cIMT was increased if the measurements were between 0.7 mm and 1.5 mm. Measurements higher than 1.5 were defined as an atherosclerotic plaque.
Results: Fourty seven patients with a sex ratio of 2.35 were included in our study. Median age was 36 years (IQR: 28-46) and median duration of the disease was 11 years (IQR: 5-16). Median BASDAI and ASDAS-CRP scores were 2.6 (IQR: 1.8-3.8) and 2.18 (IQR: 1.62-2.91) respectively. Of the 47 patients, 10 (21%) had an active disease according to BASDAI and 19 (40%) had an active disease according to ASDAS. Median BASFI score for functional impairment was 3 (IQR: 1.5-5.1). Median BASRI and mSASSS scores were 3 (IQR: 2-4) and 10 (IQR: 4-15) respectively. Regarding treatment, 92% of patients were using non-steroidal anti-inflammatory drugs (NSAIDs), 51% were on csDMARDs and 38% were on anti-TNF alpha drugs. Median right, left and mean cIMT were respectively 0.54 mm (IQR: 0.50-0.63), 0.55 mm (IQR: 0.49-0.61) and 0.55 mm (IQR: 0.48-0.62) respectively. Increased cIMT values were found in 8 patients (17%). No patient had atherosclerotic plaque. Median values of cIMT were significantly higher in patients with spondyloarthritis than the control subjects (p<0.0001) as shown in Table 1.

Table 1. Comparaison of carotid intima-media thickness values between spondyloarthritis patients and control subjects.

	Spondyloarthritis Patients	Control group	p
Right cIMT (mm)*	0,54 (0,50-0,63)	0,45 (0,42-0,50)	< 0.0001**
Left cIMT (mm)*	0,55 (0,49-0,61)	0,47 (0,45-0,50)	<0.0001**
Mean cIMT (mm)*	0,55 (0,48-0,62)	0,46 (0,43-0,50)	<0.0001**

cIMT: carotid intima-media thickness; mm: millimeters; *: median value (IQR 25-75%); **: p < 0.05 denotes statistical significance.

Conclusion: Our study demonstrated increased cIMT in patients with SpA compared with healthy population; which attests higher risk for subclinical atherosclerosis and cardiovascular atherosclerotic events.

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AB0850 ENTHESITIS, FEMALE GENDER AND VITALITY PERCEPTION AS FATIGUE DETERMINANTS IN SPONDYLOARTHRITIS PATIENTS UNDER BDMARD

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Background: Fatigue is an important domain in quality of life of spondyloarthritis patients, not always directly associated with disease course. The explanatory factors of fatigue in these patients are still not clearly understood.

Objectives: To assess the determinants of fatigue in patients with SpA under biologic disease modifying anti-rheumatic drugs (bDMARDs).

Methods: A retrospective observational study was performed using registry data of patients with SpA under bDMARD therapy followed at a tertiary level hospital. Data regarding disease activity, response criteria measures, analytic markers, function, metrology, pain, general health and fatigue (using FACIT score) was gathered at baseline, 6 months (t6) and 12 months (t12) after introduction of bDMARD. Statistical analysis (significance at p < 0.05) was performed using paired T-test, Wilcoxon test and McNemar tests for paired samples, Mann Whitney-U, Kruskall-Walis and One Way ANOVA for independent samples. Linear and logistic regression models were performed to assess direction and strength of association.

Results: A total of 46 SpA patients were analysed; most were male (24, 52.2%) with a predominantly axial involvement (31, 68.9%) and 74.4% of them were positive for HLA-B27. Most patients had high school or lower education (29, 69.1%), never smoked (26, 61.9%), never drank (34, 79.1%) and had a full-time job (38, 88.4%). All patients were under TNF inhibitors, mostly adalimumab (23, 50%). There was a significant decrease in inflammatory markers (p<0.001), disease activity scores (ASDAS-CRP and BASDAI) (p<0.001), function index BASFI (p< 0.001), metrology indexes (p<0.05) and MASES enthesitis score (p< 0.01). Patient, physician and night pain VAS were significantly lower (p< 0.001) at t6 and t12, but spine VAS only varied significantly between t0 - t6 (p = 0.021) and not t0 - t12 (p= 0.405). FACIT didn't vary significantly after bDMARD initiation, and among the domains of SF36 questionnaire, only SF36 vitality score varied significantly (p<0.05). No significant changes in EQ5D, HADs anxiety or depression scores were observed.

At baseline, there was a strong negative correlation between fatigue, expressed by FACIT score, and pain VAS (R = 0.9, p=0.037), without other significant associations. Several positive correlations with fatigue at t6 were observed, the strongest with anxiety and depression HADs (p < 0.001), BASFI (p < 0.001) and ASDAS-CRP (p< 0.001). Other positive associations were seen with 66 TJC (p <0.01), patient VAS (p<0.001, pain VAS (p = 0.001), nocturnal pain VAS (p <0.001), BASDAI (p <0.001) and MASES (p <0.001). Fatigue at t6 had a negative correlation with increased ASAS response measures mean value (p = 0.014), all domains of SF36 (p < 0.001), the strongest correlation of which was with the general health domain (R=-0.811), and EQ5D (p<0.001). When comparing subgroups at t6, there was more fatigue in the female group (p=0.01) and in patient with higher ASDAS disease activity score (p < 0.05), with no differences according to work status, alcohol consumption or tobacco use, educational level, TNF inhibitor exposure or ASAS response.

Prediction analysis showed univariable association between several baseline variables and fatigue (lower FACIT scoring) at t6: age at bDMARD introduction (B = - 0,405, p = 0.02), age at diagnosis (B = -0.43, p = 0.02), physician VAS (B = 0.149, p < 0.05), MASES (B = -1.732, p <0.001), SPARCC (p < 0.05) and female gender (B = -7.95, p = 0.01). Multivariate linear regression analysis allowed for creation of a predictive model for FACIT scoring at t6 (R2 = 0.900, p = 0.019): (-3.426) x MASES t0 + (-24.074) x female gender + 0.949 x SF36 vitality score.

Conclusion: Enthesitis, female gender and subjective assessment of vitality seem to be determinants of fatigue in SpA patients under bDMARD. Fatigue in this population is associated with diverse factors that should be optimized in a holistic approach to the patient.

Disclosure of Interests: None declared

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AB0851 APPLICABILITY OF THE MASEI INDEX IN ENTHESIS AND ITS ASSOCIATION WITH OTHER INDICES / SEROLOGICAL MARKERS OF ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Spondyloarthritis (SpA) are a group of chronic inflammatory diseases with affectation, mainly of the axial skeleton and, also, of peripheral joints. The enthesis is one of the target organs, since an inflammation of it, known as enthesitis, can be observed, which in many patients with spondyloarthritis could be unnoticed.

Objectives: Find the relation between the MASEI index (Madrid Sonographic Enthesitis Index) in entheses and other indices/serological activity markers (such as BASDAI, DAPSA or ASDAS and ESR, CRP) in spondyloarthritis patients.

Methods: Observational, descriptive and cross-sectional study. Data were collected from patients with SpA who underwent musculoskeletal ultrasound using the Madrid Sonographic Enthesitis Index (MASEI) and who were treated in our clinics from May 2021 to September 2021 and under the approval of the CEICm of our center. The variables evaluated were described using measures of frequency and measures of central tendency/dispersion, as appropriate. First, we tested the normality of all the variables, using a Shapiro-Wilk test. We studied the correlation of parametric numerical variables (such as MASEI-Vitamin D, MASEI-ASDAS), using the Pearson coefficient. On the other hand, for non-parametric numerical variables (such as MASEI-BASDAI) we use Spearman's coefficient. For parametric numeric and categorical variables (such as MASEI-VITAMINA D, ASDAS-VITAMINA D) we constrast the mean of differences using the T-Student test, while for non-parametric numerical and categorical variables, we contast the difference of means with the Mann-Whitney U test (MASEI-PCR, MASEI_VSG). Finally, to find out the correlation between categorical variables (such as VITAMIN D-PCR), we used a chi-square test. Finally, we have done a curve-fitting study with Matlab, obtaining the functions that better adjust the data avoiding overfitting. We have done this parametric optimization with the following pairings: MASEI-ASDAS, MASEI-BASDAI and MASEI DAPSA.

Results: We analyze twenty four patients with SpA (with mean age 50.50 ± 10.63 years) 8 women and 16 men. They present: radiographic axial spondyloarthritis (5 patients), non-radiographic axial spondyloarthritis (4 patients), psoriatic arthritis (10 patients), spondyloarthritis associated with inflammatory bowel disease (2 patients), reactive arthritis (2 patients), and, finally, one patient has undifferentiated peripheral spondyloarthritis. The variables have the following average levels: ASDAS, 2.35 (±1.09); BASDAI (for those with axial involvement) 4.54 (±2.93); DAPSA (for psoriatic arthritis) 10.98 (± 6.85) and total MASEI 19.88 (± 14.77). We have found a correlation between the total MASEI and the following variables: ASDAS (Pearson coefficient=0.696), BASDAI (Spearman coefficient=0.823) and DAPSA (Pearson coefficient=0.823). The mean vitamin D levels were 25.98 (±12.05), and it has a negative correlation with the MASEI equal to -0.317. As far as curve fitting is concern, a couple of sinusoidal functions were obtained for the MASEI-ASDAS and MASEI DAPSA pairings (see Figure 1 and Figure 3) and a linear regression for MASEI-BASDAI (see Figure 2). These three curves have an R-squared fit of 0.77, 0.87 and 0.52, respectively.

Conclusion: Patients with spondyloarthritis who present greater activity of the disease measured by ASDAS, BASDAI/DAPSA and by the serological markers of inflammation CRP and ESR, present a higher total MASEI than patients who are controlled. In addition, it has been observed that patients with low levels of vitamin D have higher disease activity and a higher total MASEI.

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AB0852 ASSESSMENT OF ENDOTHELIAL DYSFUNCTION IN SPONDYLOARTHRITIS

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Background: Endothelial dysfunction is the earliest step in the pathogenesis of atherosclerosis, preceding structural vascular alterations. Few studies have focused on the endothelial dysfunction in spondyloarthritis.
Objectives: The aim of our study was to assess endothelial dysfunction using Flow-Mediated dilatation (FMD) in patients with spondyloarthritis.
Methods: Forty-seven consecutive patients meeting ASAS 2009 criteria for spondyloarthritis and 47 matched healthy subjects were included in the study. Subjects with traditional cardiovascular risk factors were excluded. Sociodemographic, clinical, biological and radiological features related to the disease as well as therapeutics were recorded. FMD was assessed ultrasonographically according to guidelines of American college of cardiology (ACC) (1).
Results: Spondyloarthritis group included 47 patients with a sex ratio of 2.35 and a median age of 36 years (IQR: 28-46). Median body mass index (BMI) was 24.5 kg/m2 (IQR 25-75%: 20.7-26.8) with no significant difference compared with the control group (p=0.238). Physical examination showed normal values of blood pressure (BP) with a median systolic BP of 121 mmHg (IQR 25-75%: 110-130) and a median diastolic BP of 71 mmHg (IQR 25-75%: 67-78). In laboratory findings, total cholesterol and triglyceride levels were increased in 2 and 3 patients respectively.
Median age at onset of SpA was 20 years (IQR 25-75%; 18-32). For disease activity, median CRP level was 6.45 mg (IQR 25-75%: 1.45-19.9) and median ASDAS-CRP and BASDAI were respectively 2.18 (IQR 25-75%: 1.62-2.91) and 2.6 (IQR 25-75%: 1.8-3.8). Median MASES score was 0 (IQR 25-75%; 0-0). Median BASFI and BASMI were 3 (IQR 25-75%; 1.5-5.1) and 1.5 (IQR 25-75%: 0-4). Regarding treatment, 92% of patients were using NSAIDs, csDMARDs (51%) and 38% were on TNF inhibitors.
Patients with spondyloarthritis exhibited significantly lower FMD values than healthy age and gender matched controls with a median value of FMD 14.6% (IQR; 9-24) versus 18.8% (IQR; 12.8-23.1%); p=0.008.
Conclusion: Our study demonstrates impairment of endothelial function in patients with spondyloarthritis compared with healthy population, confirming the accelerated atherosclerosis in spondyloarthritis.
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AB0853 THE ROLE OF IL-17, IL-23 SERUM LEVELS IN PATIENTS WITH ANKYLOSING SPONDYLITIS WITH INFLAMMATORY BOWEL DISEASES

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Background: Currently, there is a lot of interest in the frequency and risks of developing of inflammatory bowel diseases (IBD) in patients with ankylosing spondylitis (AS) [1]. IL-17 and IL-23 are one of the key pathogenetic markers of AS [2]. A lot of studies also showed that the average number of IL-17 cells was significantly increased in active Ulcerative colitis (UC) and Crohn disease (CD) patients [3]. According to some studies cytokines, such as IL-17 and IL-23, play crucial role in intestinal protection and homeostasis [4].
Objectives: The aim of this study was to evaluate IL-17 and IL-23 serum levels in patients with AS without IBD and with AS and IBD.
Methods: In the analysis were included 50 patients with AS, fulfilling the modified New York criteria, among them man-36 (72%), woman-14 (28%), mean age of patients was 42.5±9.9, mean disease duration – 13.4±8.7 years. All patients were examined with ESR, CRP, esophagogastroduodenoscopy, colonoscopy, IL-17 and IL-23, using enzyme-linked immunosorbent assay for the quantitative measurement of IL-17 and IL-23 in serum ELISA kit. IL-17 and IL-23 levels were also studied in control group (13 healthy donors), mean IL-17 was 1.16±1.02 pg/mL, mean IL-23 was 33.03±18.02 pg/mL.
Results: All patients had a high disease activity, mean BASDAI was 5.3± 1.8, mean ASDAS CRP 3.7±1.01, mean ASDAS ESR 3.6±1.01. IBD were diagnosed in 11 cases: 6 patients (12%) with CD and 5 patients (10%) - UC, in the remaining cases (78%-39 patients) was no intestinal pathology. Patiens with AS had higher levels of IL-17(10.4±9.1 pg/ml) and IL-23(188±156 pg/ml), than the group of healthy donors. Patients with AS and IBD had slightly lower IL-17(6.7±4.5 pg/ml) and IL-23(155.5±97 pg/ml) levels than patients with AS without IBD(p=0.03). IL-23 was positively correlated with ESR (r=0.5) and CRP (r=0.5) (p <0.001) levels, however IL-17 level had negative correlation with ESR and CRP level (r=-0.2) (p<0.001).
Conclusion: IL-23 and IL 17 serum levels in patients with AS and IBD was lower than in patients with AS without IBD. There is a significant association between the CRP, ESR and IL-23 level, but not with IL-17.
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AB0854 DESCRIPTIVE AND RETROSPECTIVE STUDY OF DIFFERENT TYPES OF SPONDYLOARTHRITIS AND REFERRAL AND DIAGNOSIS TIMES

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Background: Spondyloarthritis (SpA) is a group of inflammatory arthropathies of unknown aetiology that share several clinical, pathophysiological, serological and radiological features. In many cases the initial symptoms are insidious, leading to a delay in diagnosis and initiation of treatment. The time between the onset of symptoms and treatment is of vital importance for the prognosis of the disease.
Objectives: To describe the clinical characteristics of the SpA cohort, to analyse the number of months from symptom onset to referral to the rheumatology department and diagnosis of SpA, as well as differences according to the referring department.
Methods: Retrospective descriptive study of patients with a diagnosis of PsA according to the ASAS criteria and CASPAR criteria for the psoriatic arthritis subgroup (PsA), in a single hospital centre.
We collected demographic variables separated by subgroups of peripheral and axial SpA and PsA, age at diagnosis, time from symptom onset to referral to the rheumatology department and to diagnosis, as well as differences according to the department making the referral.
Results: Seventy-five patients with SpA were analysed, 40 had peripheral and axial SpA and 35 (46.66%) PsA. Thirty-six patients (49.3%) were female (Table 1). Patients with peripheral and axial SpA had a higher mean age at diagnosis than patients with PsA. 45.1 years (SD 11.3) was the mean age at diagnosis. 73.6% of patients were referred from primary care (PC), 9.4% from traumatology, 9.4% from rehabilitation (RH), 3.8% from dermatology and 3.8% from the emergency department. The median time from first symptom to referral to rheumatology was 31.4 (SD 57.2), 7.1 (SD 38.5), 21.7 (SD 51.4) months in peripheral and axial SpA, PsA and total respectively (Table 2). The service with the longest time between symptom onset and referral to rheumatology is PC and rehabilitation for all groups. The median time from first symptom to diagnosis was 43.1 (SD 55.1), 34.4 (SD 65.8) and 39.2 (SD 59.7) months for peripheral and axial SpA, PsA and total respectively (Table 2). The time from referral to rheumatology to diagnosis of peripheral and axial SpA was 12.2 (SD 19.4), PsA 17 (SD 39.3) and total 14.3(SD 29.5) months.

Table 1. Demographic characteristics and time in months according to type of SpA.

	Peripheral and axial SpA	PsA	Total
Age at diagnosis	45.1 (SD11.8)	44.9 (SD10.9)	45.1 (SD11.3)
Female	20 (51.3%)	16 (47.1%)	36 (49.3%)
Hypertension	10 (25.0%)	10 (29.4%)	20 (27.0%)
Dyslipidaemia	17 (42.5%)	17 (51.5%)	34 (46.6%)
Diabetes mellitus	5 (12.5%)	6 (17.6%)	11 (14.9%)
Body Mass Index	27.9 (SD4.4)	30.5 (SD8.4)	29.2 (SD6.7)
Cardiovascular disease	5 (12.5%)	2 (5.9%)	7 (9.5%)
Cerebrovascular disease	2 (5.0%)	2 (5.9%)	4 (5.4%)
Depression	1 (2.5%)	1 (2.9%)	2 (2.7%)
Renal insufficiency	1 (2.5%)	1 (3.0%)	2 (2.7%)
Liver failure	3 (7.5%)	5 (14.7%)	8 (10.8%)
Time in months from 1st symptom to referral	31.4 (SD57.2)	7.1 (SD38.5)	21.7 (SD51.4)
1Primary care	30.9(SD10.9)	7.01(SD34.1)	21.07(SD35.2)
1Traumatology	5 (SD1.25)	5 (SD2.82)	5 (SD1.48)
Rehabilitation	36 (SD29.14)	19	27.5 (SD24.75)
7Dermatology		13 (SD1.41)	13 (SD1.41)
3Emergency service	1	1	1
Time from referral to diagnosis	12.2 (SD19.4)	17.0 (SD39.3)	14.3 (SD29.5)
Time from 1st symptom to diagnosis	43.1 (SD55.1)	34.4 (SD65.8)	39.2 (SD59.7)

Conclusion: In our cohort, patients are referred to rheumatology mainly from PC, which in turn is the service with the longest delay, especially in the peripheral and axial SpA group. Patients with PsA take less time to be referred than patients with peripheral and axial SpA. Once referred to rheumatology, peripheral and axial SpA patients take less time to be diagnosed than those in the PsA group.

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AB0855 COMPARISON OF CARDIAC INVOLVEMENT BETWEEN ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLITIS

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Background: While cardiac involvement is increasingly recognized and investigated in patients with axial spondyloarthritis (axSpA), few studies have investigated the occurrence of cardiac involvement in patients with non-radiographic axial spondyloarthritis (nr- axSpA) in relation to ankylosing spondylitis (AS).
Objectives: The objectives of the present study are to describe and compare the characteristics of cardiac involvement between AS and axSpA nr patients.
Methods: A cross-sectional study was conducted in the rheumatology department of the University Hospital of Fes in Morocco, including patients diagnosed as having axial spondyloarthritis according to the ASAS 2010 criteria, for a period of 9 years. Patients were classified as r-axSpA by the presence of radiographic sacroiliitis according to the modified New York criteria and nr-axSpA defined by the presence of sacroiliitis on MRI.
Results: 375 patients were included in the study. We compared 257 AS to 118 with nr-axSpA. The cohort was predominantly female (54.9%) with a mean age of 46.83 years (S.D. 14.00). AS patients were significantly young (45 vs 50 years), more frequently male (55% vs 22%) and had higher serum inflammatory markers than those with nr-axSpA. Between AS and nr-axSpA groups, arterial hypertension was higher in nr-SpA patients (24.6% versus 14.4%, p = 0.016). While valvulopathy, myocardial infarction, pericarditis and heart failure were higher in AS patients with respectively (8.6% vs 3.4%, p=0.067) (1.6% vs 0.8%, p=0.578) (1.2% versus 0.8%, p = 0.779) (0.4% versus 0%, p = 0.497). However, arrhythmias were similar in AS patients and nr-SpA patients (0.8% versus 0.8%, p = 0.571).
Conclusion: Cardiac involvement was common in both axSpA populations and similar between AS and nraxSpA except in hypertension where there is a significant difference between the two groups. These results highlight the importance of identifying and managing cardiac involvement in these patients

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AB0856 PREVALENCE OF HLAB27 ANTIGEN IN MOROCCAN PATIENTS WITH SPONDYLOARTHRITIS (SPA): A MULTICENTER STUDY

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Background: Spondyloarthritis includes an heterogeneous group of rheumatisms characterized by their strong association with HLA-B27 (1). The association between SpA and HLA-B 27 is one of the strongest known associations between an HLA allele and disease (2). Several studies have highlighted the importance of this association for diagnosis, predicting disease phenotype and prognosis of spondyloarthritis (SpA) (1.2).
Objectives: The aim of the present study is to determine the prevalence of HLAB27 in Moroccan SpA patients and to analyze the correlation between HLAB27 status and different disease parameters.
Methods: It is a multicenter cross-sectional study including 256 SpA patients. Demographic, clinical, paraclinical and therapeutic parameters of the disease were collected. Disease activity was assessed by BASDAI and ASDAS-CRP scores. Patients were classified into two groups: HLAB27(+) and HLAB27(-). A comparison regarding HLA-B27 status was performed using the Mann-Whitney and Chi2 T-student tests. The significance threshold was set at p<0.05.
Results: 256 SpA patients were included in the study, 241 patients have HLAB27 status of which 114 (44.5%) were HLAB27-positive. 46.6% of men and 40.9% of women were HLAB27-positive. 233 patients had axial SpA of which 110 patients (47.21%) were HLAB27-positive. The mean age was 39.58 ±12.89 years. The HLAB27-positive group had a longer diagnostic delay (p= 0.008) with a mean of 4 years. 46 patients had a family history of SpA of which 25.4% were HLAB27-positive and 11.8% HLAB27-negative (p=0.007). The HLAB27-positive patients had more axial manifestations (96.5% vs. 85.9%; p=0.01). While peripheral involvement was more noted in the HLAB27-negative group (90.6% vs 35.1%; p<0.001). Enthesopathy was more observed in the HLAb27-positive group (78% vs 62.2%; p=0.001). HLAB27-positive patients had more active disease defined by ASDAS-CRP (3.13±1.23 vs. 2.24±1.14; p<0.001). Only one case of uveitis was noted in the HLAb27-negative group versus 27 cases in the HLAB27-positive group (p<0.001). 33 HLAB27-positive patients had radiographic coxitis (33 vs16, p=0.002). The bDMARDS were more prescribed in the HLAB27-positive patients (58.8% vs 35.4%; p=0.009).
Conclusion: In our study, the prevalence of HLAB27 was close to the MENA region (3). The presence of HLAB27 is related to an earlier disease onset, higher activity, to the presence of coxitis and uveitis and consequently more use of biotherapy in this group (HLAB27-positive).

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AB0857 INCREASED CAROTID INTIMA-MEDIA THICKNESS IS CORRELATED WITH RENAL FUNCTION IN SPONDYLOARTHRITIS

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Background: Cardiovascular diseases are the main cause of mortality in spondyloarthritis and seem to be multifactorial. Due to its easy application and reproductibility, carotid intima-media thickness (CIMT) is increasingly used for assessment of subclinical atherosclerosis and cardiovascular risk stratification.
Objectives: The aim of our study was to investigate the relationship between CIMT and renal function in patients with spondyloarthritis (SpA).
Methods: We performed a cross sectional study including 47 patients with SpA and no history of cardiovascular disease. Clinical and biological data were recorded. Data related to renal involvement and creatinine level were extracted. CIMT was measured in the right and the left common carotid artery by an experienced radiologist; than mean CIMT was calculated.
Results: Our study included 33 men and 14 women with a sex ratio of 2.35, a median age of 36 years (IQR 25-75%: 28-46) and a median duration of the disease of 11 years (IQR 25-75%: 5-16). Renal involvement was found in 6 patients (13%): kidney stones (n=2), tubulo-interstitial nephritis (TIN) (n=2), IgA nephropathy (n=1) and AA amyloidosis (n=1). Median creatinine level was 63 µmol/l (IQR 25-75%: 58.5 - 64). No patient had kidney failure.
Ultrasound examination found median right, left and mean (CIMT) of 0.54 mm (IQR 25-75%: 0.50-0.63), 0.55 mm (IQR 25-75%: 0.49-0.61) and 0.55 mm (IQR 25-75%: 0.48-0.62) respectively. Increased CIMT values were found in 8 patients (17%). No patient had atherosclerotic plaque.

Patients with renal involvement had significantly higher values of CIMT (0.64 mm (IQR 25-75%: 0.56-0.70) vs 0.53 mm (IQR 25-75%: 0.47-0.59); p= 0.045). Significant positive correlation was also detected between CIMT values and creatinine level (p=0.002; r=0.445).

In multivariate linear regression, creatinine level was identified as independent predictor of increased CIMT (B=0.002; 95% confidence interval=0.000-0.005; p=0.035).

Conclusion: Although all patients included have normal creatinine level, we identified creatinine level as independent predictor of subclinical atherosclerosis in SpA patients. This finding highlights the monitoring of this parameter.

Disclosure of Interests: None declared

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AB0858 CLINICAL CHARACTERISTICS OF PATIENTS WITH SPONDYLOARTHRITIS WITH COVID-19 IN ANAMNESIS IN THE REPUBLIC OF TATARSTAN

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Background: The management of patients with spondyloarthritis (SpA) during the period of the novel coronavirus infection (NCI) pandemic is a significant problem due to insufficient evidence base.

Objectives: To study the features of the course NCI and its influence on the course of SpA.

Methods: From March 2020 to January 2022, 55 patients with SpA who underwent NCI (with a confirmed result of SarsCoV2 PCR and / or using X-ray computed tomography (CT) of the lungs): ankylosing spondylitis (AS) 37 people, with psoriatic arthritis (PsA) 18 people. Of these 32 (58.2%) were men, 23 (41.8%) - women, the average age of patients was 49 [37.5; 57.5] years. The duration of SpA at the time of NCI was 11 [7; 16] years. SpA activity before NCI was low in 15 (34.8%) patients, moderate in 25 (58.1%), and high in 3 (6.9%) patients. The results of clinical and laboratory examinations were evaluated during the NCI and after 1, 3, 6 months.

Results: Symptoms of NCI in patients with SpA were comparable in frequency and severity to the course of infection in the population. 47.3% had a mild course of NCI, and 52.7% of those observed had a moderate course, which is comparable with the general population data. Lung involvement was detected in 29 (52.7%) patients. The outcome of COVID-19 in all patients is recovery. Analysis of the course of SpA showed an increase in activity 1 and 3 months after NCI: BASDAI from baseline to COVID-19 4.3±1.57 to 4.9±1.7 points after 3 months, similar to ASDAS_CRP from 2.6±1, 2 to 3.7±0.2, BASFI from 3.0±1.9 to 3.8±1.8. A positive correlation was found between the severity of NCI and the BASFI index after 3 months (0.870). Analysis of the course of PsA showed an increase in activity 1 and 3 months after NCI: DAS28 from the baseline 2.78±0.98 to 4.15±1.16 points after 3 months. Of the total number of recoveries, 72.2% of patients showed an increase in activity due to clinical and laboratory parameters.

78.1% of patients noted the presence of post-COVID symptoms after NCI, 56.3% had a combination of more than 3 different symptoms. Most often there was an increase/appearance of pain in the joints - in 78.1%: significant - in 61.8%, insignificant - in 16.3% of respondents. Strengthening/appearance of muscle pain and/or headache and/or dysautonomia occurred in 72.7%. This can be assessed as an exacerbation of the underlying disease, or, conversely, the appearance of arthralgia and myalgia could have an impact on the increase in AS and PsA activity indices. The second most frequent were a decrease in the quality of life (QOL) and working capacity in 69.0% of patients: significant in 36.3% of patients, insignificant in 32.7%.

The appearance/intensification of shortness of breath and a decrease in exercise tolerance were noted by 60% of the respondents. Among them, 34.5% of patients with moderate severity, 25.4% - with mild NCI. Appearance/intensification of chest pain and/or palpitations was noted by 16.3% of patients

Conclusion: The prevalence and course of the NCI in patients with SpA did not differ from that in the population. However, coronavirus infection has led to increased pain and an increase in AS activity, long-term persistence of post-COVID manifestations in the form of musculoskeletal pain and asthenic symptoms in the form of a decrease in the quality of life. At the same time, specific respiratory symptoms occurred in a third of patients and were not associated with the severity of the NCI.

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AB0859 ASSESSMENT OF SELF-ESTEEM AND REINTEGRATION TO NORMAL LIVING IN SPONDYLOARTHRITIS PATIENTS

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Background: Spondyloarthritis is a chronic inflammatory disease involving sacroiliac joints and spine. It mainly affects young patients typically of working age. Pain, reduced spinal mobility and deformities may lead to psychological distress.

Objectives: The aim of our study was to assess self-esteem and social reintegration in spondyloarthritis patients in comparaison with healthy controls.

Methods: Fifty patients diagnosed with spondyloarthritis and 50 healthy controls aged less than 50 years old, were included in our study. Clinical, biological and radiological data related to disease were recorded. All subjects completed Reintegration to Normal Living Index (RNLI) and Rosenberg self-esteem scale (SES) questionnaires.

Results: Our study population included 39 men (78%) and 11 women (22%) with a mean age of 36.8 years [17-50]. Mean disease duration was 11.3 ± 8.2. Mean disease activity scores BASDAI, ASDAS-CRP and ASDAS-ESR were respectively 4.45 ± 1.84, 3.03± 1.06 and 2.74 ± 1. For inflammatory markers, mean CRP and ESR levels were respectively 29.3 ± 41.8 mg/l and 46.5 ± 35.3. Mean BASFI and BASRI scores were respectively 5.21 ± 2.24 and 5.5 ± 2.38. Forty eight pour cent of patients had an extra-articular feature and 47% had coxitis. Regarding treatment, 47% were on TNF inhibitors.

Mean SES was 30.6 [25-36]. Fifty six per cent of patients had a low self-esteem (SES<31) and 12% had high self-esteem (SES>34). Self-esteem was within the normal ranges (SES between 31 and 34) in 32% of patients. Mean reintegration to normal life (RNL) adjusted score was 72.8 ± 9.3.

Significant association was found between RNL adjusted score and BASDAI (p=0.02, r=0.126) and BASFI (p=0.034, r=0.235). There was no significant association between RNL adjusted score and disease duration (p=0.747), CRP (p=0.213), ESR (p=0.818), ASDAS-ESR (0.747) and ASDAS-CRP (p=0.330) and BASRI scores (p=0.413). No association was found between SES score and disease duration (p=0.447), activity scores BASDAI (p=0.178), ASDAS-ESR (p=0.929) and ASDAS-CRP (p=0.940), ESR (p=0.417) and CRP levels (p=0.828), as well as BASFI (p=0.295) and BASRI (p=0.470).

In comparaison with healthy controls, adjusted RNL score was significantly lower in patients with spondyloarthritis (72.8 versus 77.65; p=0,017). In contrast, no significant difference was found between the two groups when comparing SES score (31.4 in spondyloarthritis patients versus 30.6 in healthy controls, p=0.283).

Conclusion: In our study, spondyloarthritis patients had lower RNL score in comparaison with healthy subjects. Reintegration to normal living was associated with disease activity and functional impairment. In contrast, self-esteem was similar between the two groups.

Disclosure of Interests: None declared

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AB0860 REPERCUSSIONS OF TOBACCO ON SPONDYLOARTHRITIS: THE ICEBERG EFFECT!

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Background: The deleterious effect of smoking is frequently studied in inflammatory diseases such as spondyloarthritis (SA) [1].

Objectives: The objective of our study was to identify the consequences of smoking during AS.

Methods: We conducted a cross sectional study including patients followed for spondyloarthritis meeting the ASAS 2009 criteria. For each patient we collected the following parameters: age, age at onset of the disease, duration of progression, disease activity using BASDAI and ASDAS-CRP scores and structural damage using BASRI and mSASSS scores. We also measured sedimentation rate (ESR) and C-reactive protein (CRP).

Statistical analysis was performed using SPSS software.

Results: We included 140 patients. Seventy-three percent were male (n=102). The mean age was 43 ± 12.9 years. The age of onset of the disease was 34.28 ± 12 years. The mean disease duration was 110 ± 107.8 months.

Sixty patients were smokers (43%) at an average of 20.75 ± 16.09 pack-years.

Mean ESR and CRP were 36.49 ± 27.22 mm and 29 ± 44.27 mg/L, respectively.

The mean BASDAI and ASDAS-CRP were 3.68 ± 1.86 and 2.99 ± 0.98, respectively.

The mean BASRI and mSASSS were 4.12 ± 3 and 10.26 ± 15.41, respectively.

Smokers had significantly higher BASRI and mSASSS scores (BASRI: 5.02 ± 3.32 vs 3.47 ± 2.6; p=0.005 and mSASSS: 14.07 ± 17.56 vs 7.02 ± 12 .62; p=0.03). In addition, the number of packets year was correlated to mSASSS (r=0.399; p=0.01).

On the other hand, we did not find any association between smoking and the following parameters: ESR, CRP, BASDAI or ASDAS-CRP.

Conclusion: As reported in other studies, ours' showed that structural damage was correlated with the number of pack-years [2]. Smoking was associated with this structural damage in SA regardless the inflammatory biomarkers and the disease activity. This suggests that control of structural damage in SA requires smoking cessation.

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AB0861 INCREASED SERUM INTERLEUKIN 8 LEVELS IN SPONDYLOARTHRITIS

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Background: Physipathological mechanisms of spondyloarthritis (SA) are very complex. The role of the interleukin (IL)- 8, which is an angiogenic chemokine, has been suggested [1].

Objectives: We aimed to evaluate the discriminative value of interleukin 8 in SA.

Methods: We conducted a cross-sectional study during two years (2019-2020) including 144 subjects divided into two groups: a group G1 that included 72 patients followed for spondyloarthritis meeting the Assessement of SpondyloArthritis international Society (ASAS) criteria and a group (G2) including 72 healthy controls. The two groups were matched by age and sex.

IL-8 was measured for each participant using chemiluminescence.

We performed a ROC analysis and computed the air under the curve (AUC) at IL-8 to assess the ability of this chemokine to diagnose SA and to distinguish between SA patients from healthy controls. Statistical analysis was performed using SPSS.

Results: We included 57 men and 15 females in each group. The mean age was 44.84 ± 13.42 years. In G1, the mean disease duration was 10.25 ±7.7 years. Axial and peripheral involvements were found in 85% of cases (n=65) and 50% of cases, respectively.

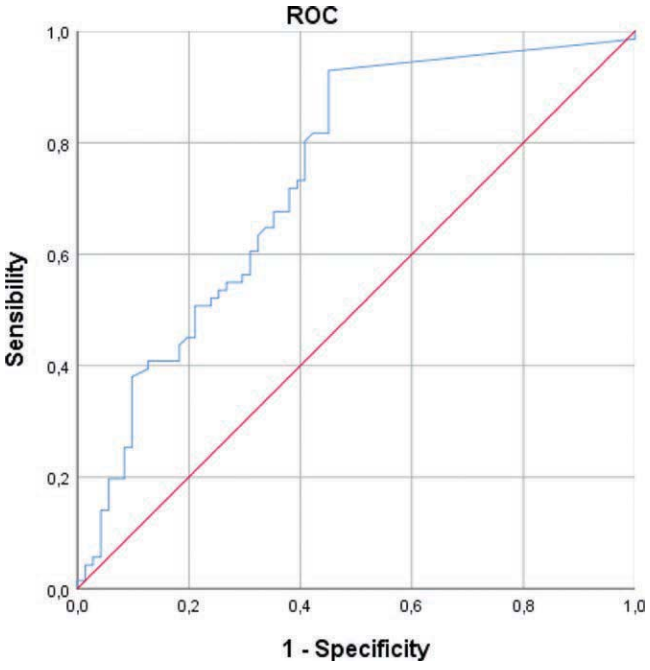

Figure 1. AUC at IL-8 between SA patients and healthy controls 0.855 (p<0.0001)

The mean BASDAI and ASDAS-CRP were 3.21 ± 1.87 and 2.92 ±1.55, respectively.

IL-8 was able to distinguish SA patients from healthy controls with a cutoff of 4.5 pg/mL. The AUC was good at 0.855 (p<0.0001). The sensibility and the specificity were 92.8% and 81.6% (Figure 1).

Conclusion: Several studies have found that IL-8 was significantly higher in SA patients comparing to controls [2,3]. Our study showed that IL-8 could distinguish SA patients from controls with a cutoff of 4.5 pg/mL. This suggests that IL-8 could play a role in the pathophysiology of SA.

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AB0862 ASSOCIATION OF EMOTIONAL DYSFUNCTION WITH GASTROINTESTINAL SYMPTOMS AND DISEASE ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Spondyloarthritis (SpA) is a heterogeneous condition characterized by chronic back pain, fatigue and progressive loss of mobility, associated to decreasing quality of life, physical and mental health. SpA patients may have a presence of non-specific gastrointestinal symptoms or subclinical intestinal inflammation. Although the association between SpA and high levels of distress has been investigated, few studies have included gastrointestinal involvement among the factors associated with mental health.

Objectives: To evaluate emotional functionality of patients with SpA, and their association with the presence of gastrointestinal symptoms and disease activity.

Methods: In total, 98 patients with SpA (fulfilling ASAS criteria) were assessed by rheumatologists. Patients with two or more gastrointestinal symptoms were referred to gastroenterology. Furthermore, those patients with SpA and concomitant IBD were excluded. BASDAI, BASFI, ASDAS-CRP, ASDAS-ESR were performed. Patient Health Questionnaire (PQH9) for depression and Perceived Stress Scale-10 (PSS10 for Distress and confrontation) were used to assess clinical and psychological status. Fecal Calprotectin, CRP, ESR, and HLA-B*27:05 were assessed. The associations were evaluated using the Chi-square or Fisher's exact test and U de Mann-Whitney. Spearman and Pearson test were made to explore correlations (Ethical/Code. 2017-023).

Results: The average age of patients was 42.3±10.5 years, 58.2% were men and 42.9% presented the HLA-B*27:05 allele. Axial involvement (77.60%), peripheral involvement (46.90%), and ≥2 gastrointestinal symptoms in the last month (65.30%) were found. With regard to outcome measures of disease activity, BASDAI 4.75±2.74 and ASDAS-CRP 2.44 ±0.95 was observed.

In total, 72.4% of patients had some degree of depression: 22.4% mild, 20.4% moderate, 12.2% high moderate and 11.2% severe. Male gender was associated with higher frequency of depression, 51% of them presented with moderate to severe involvement (p=0.036). The presence of ≥2 gastrointestinal symptoms was associated with a higher frequency of depression (p=0.013), taking importance the presence of abdominal pain in 57.2% (p=0.007), it is also associated with fatigue (p < 0.001) and with higher scores of disease activity BASDAI (CC 0.696), ASDAS-CRP (CC 0.590) ASDAS-ESR (CC 0.519) and BASFI (CC 0.737) (p < 0.001 respectively).

Considering the PSS-10 assessment, 21.4% of patients had higher levels of distress, which were associated with the presence of abdominal pain (p=0.038), BASDAI>4 (p=0.047), ASDAS-CPR > 3.5 (p=0.013). Additionally, 57.1% of patients reported more frequency of decreased confrontation capacity which was related with fatigue (p=0.013), BASFI>4 (p=0.028), ASDAS-CRP >2.1 (p=0.03) and HLA-B*27:05 (p=0.06). These variables were simultaneously associated with higher levels of distress (p=0.035, p=0.004, p=0.03 and p=0.06 respectively).

Conclusion: Disease activity and gastrointestinal symptoms in SpA patients without IBD, are associated with emotional dysfunctional outcome related to poor

quality of life. These findings highlight the importance of a holistic monitoring towards remission of SpA patients ensuring an emotional functional balance.
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AB0863 EMERGENCE OF SPONDYLOARTHRITIS FOLLOWING B CELL-DEPLETING MONOCLONAL ANTIBODY THERAPY FOR MULTIPLE SCLEROSIS

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Background: Anti-CD20 B-cell-depleting therapies, including rituximab and ocrelizumab, have demonstrated their efficacy in patients with relapsing–remitting multiple sclerosis (RRMS).
Objectives: Herein we report a series of patients with RRMS treated with anti-CD20 monoclonal antibodies (mAb) who developed a de novo spondyloarthritis (SpA).
Methods: Following the presentation of an index case, we collected all cases of de novo SpA in the anti-CD20-treated RRMS cohort of our institution's referral center. Clinical, biochemical, and imaging characteristics of the cases were identified through a clinical assessment. Information was collected via a standardized form to obtain key characteristics on the onset and type of disease development at baseline and on outcomes up to 12 months. All patients had a magnetic resonance imaging (MRI) of the sacroiliac joints and, depending on the clinical presentation, a spine MRI and/or a musculoskeletal grayscale and power Doppler (PD) ultrasound (US) examination.
Results: De novo SpA developed in 6 of 480 patients with RRMS treated with anti-CD20 mAb, accounting for an incidence of 1.25%. All but one received rituximab treatment. The median time from the last anti-CD20 mAb infusion to SpA onset was 1.5 months [IQR: 1-4]. At the time of SpA emergence, the RRMS activity was controlled. The most frequent clinical SpA phenotype identified was peripheral SpA (4/6), with Power Doppler ultrasound-detected synovitis. The 2 patients with axial SpA phenotype had bilateral sacroiliitis on MRI. Five of the 6 patients had a personal or family history of psoriasis, whereas the prevalence of psoriasis in the entire RRMS cohort was 3.33% (16/480). No other extra-articular manifestation was observed. All patients were HLA B27 negative and fulfilled at least one classification criteria of SpA. None required hospitalization and the SpA onset did not affect the management of MS. The 2 patients with axial SpA were successfully treated with NSAIDs. Among the patients with peripheral SpA, 3 of four had inadequate response to NSAIDs, 2 were treated with methotrexate and 1 with leflunomide. Only one patient required initiation of an IL-17 inhibitor to control the SpA activity.
Conclusion: We report a pattern of patients with MS successfully treated with B cell-depleting drug developing axial or peripheral SpA, predominantly HLA-B27 negativity and associated with psoriasis.
Disclosure of Interests: None declared
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AB0864 A NOMOGRAM MODEL COMBINING INFLAMMATORY FACTORS AND MRI RADIOMICS TO ASSESS THE DISEASE ACTIVITY OF THE PATIENTS WITH AXSPA IN A PROSPECTIVE STUDY

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Background: Clinical and magnetic resonance imaging (MRI) disease activity score (DAS) are measuring different aspects of axial spondyloarthritis (axSpA), they are essential in disease activity assessment. The radiomics was on facilitating readings by clinical specialists via enhancing the medical images in which subtle data differences could be distinguished.
Objectives: If the additional information of MRI imaging can be considered as a predictor for axSpA disease activity? In this study, we sought to construct a nomogram integrating the sacroiliac joint (SIJ)- MRI radiomics features and the inflammatory biomarkers to assess disease activity and compare it with clinical disease acitivity index in axSpA patients.
Methods: 203 patients data were collected prospectively and confirmed as axSpA were randomly divided into training (n = 143) and validation cohorts (n = 60). 1316 radiomics features were extracted from the 3.0T SIJ-MRI. A Nomogram model was constructed using multivariate logistic regression analysis Incorporating independent clinical factors and radiomics features score (Rad-score). The performance of clinics, Rad-score and nomogram models were evaluated by ROC analysis, calibration curve and decision curve analysis (DCA), and compared with the disease activity index(Ankylosing Spondylitis DAS (ASDAS)-C reactive protein (CRP), ASDAS-erythrocyte sedimentation rate (ESR), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI)) and Spondyloarthritis Research Consortium of Canada (SPARCC) MRI scoring system.
Results: The Rad-score allowed a good discrimination in the training (AUC, 0.91; 95% CI, 0.85-0.96) and the validation cohort (AUC, 0.84; 95% CI, 0.73-0.96). The CRP-radiomics nomogram model also showed favorable discrimination in the training (AUC, 0.96; 95% CI, 0.93-0.99) and the validation cohort (AUC, 0.89; 95% CI, 0.80-0.98), better than BASDAI(AUC, 0.58), ASDAS-CRP(AUC, 0.72), ASDAS-ESR(AUC, 0.77), ESR(AUC, 0.72), CRP(AUC, 0.77) and BASFI(AUC, 0.73), had no statistical difference with SPARCC(AUC, 0.87). Calibration curves and DCA demonstrated the nomogram fit well ($p > 0.05$) and was useful for activity evaluation.
Conclusion: Rad-score showed good discriminative ability to assess disease activity in axSpA. The nomogram can increase the efficacy for assessment axSpA disease activity, which might simplify clinical evaluation.

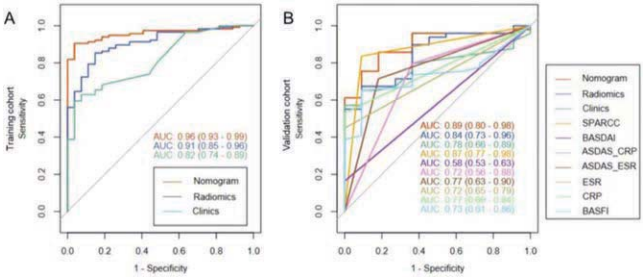

Figure 1. Comparison of ROC curve analyses in prediction models. ROC curves of the clinical features (green curve), radiomics signature model (blue curve), and hybrid model (gold curve) of axSpA in the training cohort (A) and validation cohort (B), respectively. In addition, there are AUC of ASDAS-CRP(pink curve), ASDAS-ESR(brown curve), BASDAI(purple curve), BASFI(azure curve) and SPARCC scoring system(yellow curve) in the validation cohort (B), respectively. AUC: area under the curve; ROC: receiver operating characteristic; SPARCC: Spondyloarthritis Research Consortium of Canada; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: C reactive protein; ESR: erythrocyte sedimentation rate; BASFI: Bath Ankylosing Spondylitis Disease Activity Index.

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Disclosure of Interests: None declared
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AB0865 THE FACTORS AFFECTING PATIENT GLOBAL ASSESMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: The BASDAI is one of the basic scales used in the measurement of disease activity in patients with spondyloarthritis and allows the evalution of various aspects of the disease (axial and peripheral disease as well as

inflammation). The patient global assesment (PGA) is a one-dimensional scale in which patients evaluate how their illness affects their health.

Objectives: In this study, we planned to test and review the possible determinants of PGA and its relation with BASDAI components, BASFI scores and disease-related features both at first visit and at the 2 year follow-up.

Methods: Patients with axSpA whose baseline BASDAI and PGA scores were complated, were included in the analysis. The demographic, clinical and laboratory characteristics of the patients were recorded. The relation between PGA scores and BASDAI sub-score, BASFI score and other patient and disease characteristics were tested both univariate and multivariate analysis methods. The factors affecting the change in the PGA score over 2-year follow-up were also analyzed with GEE analysis method.

Results: In total 313 patients (56.5% of male, 61.7% AS, mean age at diagnosis 34.3±11 years) were included in the analysis. Sperman's rho test was used for correlation analysis. Baseline PGA scores were in correlation with the BASDAI total score (rho:0.71, p<0.001). PGA scores of female patients were found to be significantly higher (p=0.037) and each BASDAI indivual score and BASFI scores were moderately/well correlated with PGA (Table 1). Multivariate analysis revealed that spinal pain (BASDAI Q2), the severity of morning stiffness (BASDAI Q5) and BASFI scores were the main determinants in the global health assesments of patients with axSpA (Table 1). GEE analysis was performed to evaluate the factors affecting the 2 year change in the PGA of the patients, fatigue (BASDAI Q1) (B:1.575, CI%95: [0.241- 2.922]; p=0.021), enthesis (BASDAI Q4) (B:0.888, CI95% [0.049-1.727]; p=0.038) severity of morning stiffness (BASDAI Q5) (B: 2.663, CI%95 [1.447-3.878]; p<0.001),and BASFI scores (B: 2.909, CI95% [1.806-4.011]; p<0.001) were independent determinants of PGA in longitudinal analysis.

Table 1. Baseline PGA related factors

	Sperman Analysis		Model 1		Model 2	
	rho	**p**	**B (%95 CI)**	**p**	**B (%95 CI)**	**p**
sex	0.12	**0.037**	-3.183 (-8.903; 2.538)	0.27	-3.612 (-9.372; 2.148)	0.22
BASDAI Q1	0.59	**<0.001**	0.614 (-0.936;2.175)	0.44	0.861 (-0.686; 2.406)	0.27
BASDAI Q2	0.66	**<0.001**	3.168 (1.536; 4.800)	**<0.001**	3.231 (1.587; 4.874)	**<0.001**
BASDAI Q3	0.43	**<0.001**	0.619 (-0.613; 1852)	0.32	0.538 (-0.703; 1.779)	0.39
BASDAI Q4	0.43	**<0.001**	0.374 (-0.741;1.489)	0.51	0.529 (-0.587; 1.645)	0.35
BASDAI Q5	0.60	**<0.001**	2.088 (0.542; 3.634)	**0.008**		
BASDAI Q6	0.43	**<0.001**	-0.697(-2.053;0.660)	0.31		
BASDAI (Q5+Q6)/2	0.56	**<0.001**			1.195 (-0.218; 2.608)	0.097
BASFI	0.62	**<0.001**	2.097 (0.273-3.921)	**0.02**	2.263 (0.433; 4.094)	**0.016**
BASMI	0.28	**<0.001**	-0.321 (-1.879;1.237)	0.69	-0.319(-1.891; 1.253)	0.69
Serum CRP level	0.23	**<0.001**	0.066 (-0.100;0.233)	0.43	0.073 (-0.094; 0.241)	0.39

Conclusion: The study shows that the patients with axSpA mainly rely on morning stiffness and spinal pain in deciding their global health status. Fatigue, enthesis and morning stiffness were found to be effective factors in the PGA changes of the patients under treatment. Although PGA is unidimentional, its well correlation with the BASDAI total score may be another proof of the validity of both scales.

Disclosure of Interests: None declared

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AB0866 WOMEN SPONDYLOARTHRITIS: EPIDEMIOLOGICAL, CLINICAL AND PARACLINICAL CHARACTERISTICS

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Background: Spondyloarthritis (SPA) is a chronic inflammatory rheumatism characterized by sacroiliitis and spinal involvement, affecting both genders but more frequent in males.

Objectives: The aim of this study is to analyze the epidemiological, clinical and paraclinical characteristics of Spondyloarthritis in women.

Methods: Retrospective study included 333 patients followed up for SPA at the Rheumatology Department between 2004 and 2021.

Results: Our study involved 153 women and 180 men. In the female population, the mean age was 45.1 years, 12.4% had high blood pressure, 4.8% had a psychiatric comorbidity and none of the patients were smokers, versus a mean age of 36.4 years, 5% of high blood pressure's patients, 1.7% having a psychic comorbidity and 25% of the smokers for the male with SPA. The age of onset of symptoms was 36.5 years for women versus 28 years for men (p =0.001). Axial involvement was 84.3% in women and 85% in men, while peripheral and enthesial involvement was present in 73.8% and 56.8% of female subjects and 58.8% and 46.6% of male subjects (p at 0.004 and 0.064 respectively). Coxitis was present in 13.1% and syndesmophytis in 15.3% of females versus 36.1% and 18.3% of males (p at 0.001 and 0.4 respectively). Mean erythrocyte sedimentation rate was 45.7, mean CRP 28.5 and mean calcemia 92 in the 1st group versus 43, 40.6 and 93.4 in the 2nd (p at 0.4; 0.03 and 0.03 respectively). Relapse was 26.8% in female with SPA and 12.6% in male (p =0.025)

Conclusion: In our study, females SPA patients developed symptoms later than did males, peripheral and enthesial involvement is more common in females while coxitis is more common in males with statistically significant higher CRP and calcemia.

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AB0867 PARTICULARITIES OF UVEITIS ASSOCIATED WITH SPONDYLOARTHRITIS: DATA FROM THE MOROCCAN RBSMR REGISTRY

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Background: Acute anterior uveitis is the most frequent extra-articular manifestation in spondyloarthritis (SpA). [1]

Objectives: The purpose of this study is to assess the prevalence of uveitis during SpA and to identify associated factors with its presence.

Methods: A cross-sectional multicentric observational study was conducted; the main data source was the Moroccan registry of biological therapies in rheumatic diseases (RBSMR registry). Patients, included from May 2017 to January 2019, were all adult patients (age > 18 years old), presenting SpA, according to ASAS (Assessment of Spondyloarthritis International Society) classification criteria for SpA 2010.

Demographic and clinical characteristics, disease activity, radiographic damage and functional ability have been compared between two groups of patients: Patients with SpA suffering from uveitis and patients without uveitis. General and specific data regarding uveitis were collected.

Results: 194 patients were included in the study. The mean age was 40.22 ± 13.68 years. The sex ratio was 1, 7 (man/woman). The mean duration of disease was 615.90 ± 349.12 weeks.

96.4 % of the patients had axial involvement, 70 % had peripheral involvement and 61.5 % had enthesic involvement. SpA was radiographic in 88.1 % of the cases and coxitis was found in 40.9 %. The mean erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) was 39.04 ± 27.16 mm/h and 32.87 ± 38.77 mg/l, respectively. HLA B27 was positive in 34 % of patients. The mean ASDAS (Ankylosing Spondylitis Disease Activity Score) ESR, BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and BASFI (Bath Ankylosing Spondylitis Functional Index) was 3, 19 ± 2,118; 4.8 ± 1.8 and 5.29 ± 2.21, respectively. Uveitis was seen in 14.5% of cases.

The bi-variate analysis did not reveal any statistically significant difference between the two groups regarding demographic and clinical characteristics, disease activity and radiographic damage.

Conclusion: Acute anterior uveitis is the most frequent extra-articular manifestation in spondyloarthritis (SpA). The presence of uveitis in Moroccan patients diagnosed with SpA wasn't associated with specific characteristics. Even though, its screening is systematic because it conditions the treatment.

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AB0868

PREVALENCE AND RISK FOR BUNDLE BRANCH BLOCK, ATRIOVENTRICULAR BLOCK AND PACEMAKER IMPLANTATION IN SPONDYLOARTHRITIS. A SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Inflammation of the valve attachment site may produce tissue degeneration near the atrioventricular node, which may lead to electrical conduction disturbances, that is to say atrioventricular block (AVB) and bundle branch block (BBB).
Objectives: To evaluate the evidence regarding the prevalence and risk of BB, AVB and pacemaker implantation (PMI) in patients with spondyloarthritis (SpA) compared to a control group without SpA.
Methods: A systematic review of the literature was performed using Pubmed (Medline), EMBASE (Elsevier) and Cochrane Library (Wiley) databases until December 2021. The risk for AVB, BBB and PMI were analyzed. Cohort, case control and cross-sectional studies in patients ≥18 years meeting the classification criteria for SpA were included. The Odds ratio (OR), risk ratio (RR) or Hazard ratio (HR) were considered as outcomes. Data was synthesized in a previously defined extraction form. The risk of bias was assessed by the Newcastle-Ottawa Scale.
Results: In total, eight out of 374 studies were included. As for low grade AVB and BBB, only indirect results comparing prevalences from low to medium quality studies were found. According to population based registries, the sex and age adjusted HR of AVB was 2.3 (95% CI 1.6 - 3.3) in ankylosing spondylitis, 2.9 (95% CI 1.8 - 4.7) in undifferentiated spondyloarthritis and 1.5 (95% CI 1.1 a 1.9) in psoriatic arthritis. The RR for PMI was 1.3 (95% CI 1.16 - 1.46) for groups aged between 65-69 years, 1.33 (95% CI 1.22 - 1.44) for 70-75 years, 1.24 (95% CI 1.55 - 1.33) for 75-79 years and 1.11 (95% CI 1.06 - 1.17) for groups older than 80 years.
Conclusion: The differences of prevalence in AVB and BBB were similar in SpA and control groups even though studies lacked the power. According to population registries there was an two fold-increased risk of high grade AVB in SpA patients. RR for PMI was higher in younger age groups.
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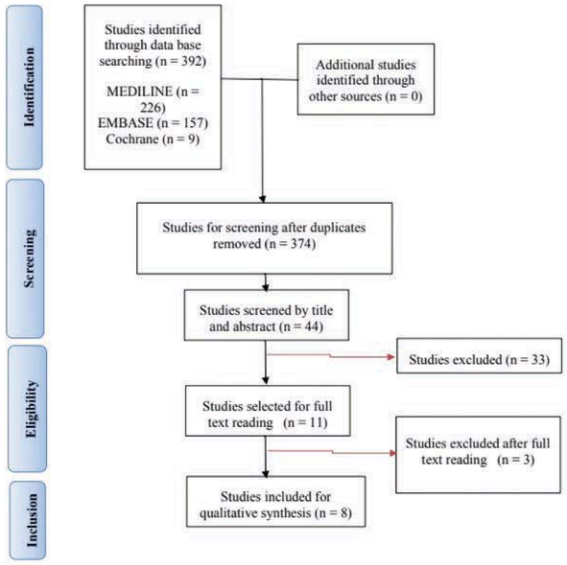
Figure 1. PRISMA flow chart



AB0869

IMPORTANCE OF SCREENING OF TRADITIONAL CARDIOVASCULAR RISK FACTORS IN SPONDYLOARTHRITIS

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Background: Epicardial adipose tissue has been associated with the development of coronary artery disease and recently suggested as a novel marker for evaluating subclinical atherosclerosis.
Objectives: The aim of our study was to assess the relationship between EFT and cardiovascular risk parameters in patients with spondyloarthritis (SpA).
Methods: We performed a case control study including patients meeting ASAS 2009 criteria for SpA, and healthy controls. Subjects were aged less than 50years old and without traditional cardiovascular risk factors. Clinical features related to the disease were recorded. Anthropometric data (body mass index (BMI), waist circumference and hip circumference) and arterial blood pressure of the patients were also recorded. Blood specimens were collected after 12 hours of fasting and total cholesterol, HDL, LDL, triglyceride and fasting glucose were measured. Total cholesterol to HDL ratio and LDL to HDL ratio were calculated. All subjects underwent Doppler echocardiography with measurement of EFT by an experienced cardiologist.
Results: We enrolled 47 SpA patients and 47 controls. Subjects were age, sex and BMI matched (p=0.267, p=0.589 and p=0.238 repectively). Median disease activity scores BASDAI and ASDAS-CRP were 2.6 (IQR 25-75%: 1.8-3.8) and 2.18 (IQR 25-75%: 1.62-2.91) respectively. Median waist and hip circumference

Author	Study design	Population	Sample number	Test	Outcomes	Adjustment
Baniaamam 2021[6]	Cross sectional	AS and osteoarthritis between 50-75 years	267	ECG	Prevalence of AVB, BBB and PMI	Controls matched for age, sex and smoking status
Bengtsson 2017[12]	Cohort	AS, uSpA, PsA, GP from the Swedish national registry	294136	ICD-10	Prevalence, Incidence, HR, for AVB and PMI compared to GP	Age, sex
Dik 2010[9]	Cross sectional	AS	131	ECG	Prevalence of AVB and BBB Association of PR interval with AS disease related variables	Age, sex, disease duration
Feld 2008[10]	Case control	PsA compared to non psoriatic nor arthritic patients	184	ECG	Prevalence of AVB, BBB Correlation of PR interval with AS disease related variables	None
Fu 2016[8]	Cross sectional	AS between 18-50y without cardiac disease	122	ECG	Prevalence of AVB, BBB	None
Goulenok 2010[13]	Cross sectional	SpA, RA and control group without known CV disease	288	ECG	AS without kyphosis Prevalence AVB, BB	None
Ward 2018[7]	Cohort	AS from Medicare database older than 65	42,327	ICD-9	Prevalence, incidence, OR of PMI	Age, sex, race
Yildrir 1999[11]	Case control	AS	88	Holter and ECG	Prevalence of AVB	None

were 88 cm (IQR 25-75%: 82-97) and 100 cm (IQR 25-75%: 91-97), respectively. Median systolic (SBP) and diastolic (DBP) blood pressure were respectively 121 mmHg (IQR 25-75%: 110-130) and 71 mmHg (IQR 25-75%: 67-78). Laboratory findings showed a median fasting glucose level (FG) of 4.93 mmol/l (IQR 25-75%; 4.55-5.1). Median total cholesterol (CT), HDL, LDL and triglyceride levels were respectively 3.66 mmol/l (IQR 25-75%: 3.18-4.28), 1.08 mmol/l (IQR 25-75%: 0.92-1.2), 2.17 mmol/l (IQR 25-75%: 1.78-2.6) and 0.84 mmol/l (IQR 25-75%: 0.79-1.15). CT/HDL ratio and LDL/HDL ratio were 3.48 (IQR 25-75%: 2.95-3.97) and 1.99 (IQR 25-75%: 1.54-2.48), respectively.

Median EFT was significantly increased in patients compared to controls (3.1 mm (IQR: 2.5-4) versus 2.4 mm (IQR: 2-3), p=0.001).

A positive correlation was found between EFT and SBP (p=0.028; r=0.323) and triglyceride level (p=0.022, r=0.349). In contrast, EFT was not associated with DBP (p=0.069, r=0.270), BMI (p= 0.223, r=0.181), waist circumference (p=0.114, r=0.234), hip circumference (p=0.451, r=0.113), CT (p=0.127; r=0.236), HDL (p=0.587; r=0.085), LDL (p=0.342; r=0.149), FG (p=0.104, r=0.248), CT/HDL ratio (p=418; r=0.128) and LDL/HDL ratio (p=0.683;r=0.064).

In multivariate linear regression, triglyceride level was identified as an independently predictor of increased EFT (B=0.676; 95% confidence interval = 0.209-1.143; p= 0.006).

Conclusion: The importance of our results that we identified a traditional cardiovascular risk factor as a predictor of subclinical atherosclerosis in SpA without cardiovascular risk factor and with normal triglyceride level. This finding highlights the importance of regular screening for traditional cardiovascular risk parameters even if the disease in low activity.

Disclosure of Interests: None declared

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AB0870 ASSESSMENT OF FRACTURE RISK IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Background: Spondyloarthritis (SpA) is a chronic inflammatory disease that predominantly affects the sacroiliac joints and the spine. Patients with SpA have an increased risk of osteoporosis and fracture resulting from a combination of inflammation and immobility. The non-radiographic form for SpA (nr-axSpA) has the same predictors factors of bone fragility however the real fracture risk is unknown in this phenotype.

Objectives: This study aims to investigate BMD and the Fracture Risk Assessment Tool (FRAX) in patients with nr-axSpA.

Methods: We conducted a retrospective study including 40 patients with nr-axSpA, according to the ASAS criteria. For the enrolled patient, we collected the clinical and biological data. We calculated the disease activity using the Bath Ankylosing Spondylitis disease activity (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS). Functional impairment was assessed by the Ankylosing Spondylitis Functional Index (BASFI). We measured the bone mineral density using the dual-energy X-ray absorptiometry (DXA) in the anteroposterior lumbar, lateral spine, and hip neck. The ten-year probability of major osteoporotic fracture was calculated using the Tunisian version of Fracture Risk Assessment Tool (FRAX).

Results: Twenty-seven women (67.5%) and thirteen men (32.5%) were enrolled. The mean age was 41.5 years (±11.2), and the mean disease duration was 3,1 years (±2.7). The mean BASDAI and ASDAS CRP was 4.7 ± 2.2 and 3.27 ± 1.29, respectively. The mean BASFI was 3.6 ± 2.5. According to World Health Organization (WHO) criteria, 45% of patients displayed osteopenia and 30% osteoporosis. The mean major osteoporotic fracture (MOF) score was 0,09 ± 0,25 [0-1,3]. The MOF was significantly associated with BMD (p=0.000). The variables associated with MOF were a high physician's global assessment score, a high BASFI, and female gender, but without significant relation. However, no correlation was found between the MOF and the disease duration, the presence of peripheral arthritis or enthesitis, and the ASDAS.

Conclusion: In nr-axSpA, patients with low BMD had a higher calculated 10-year fracture risk. FRAX score is related to functional impairment and gender. Disease activity does not affect the probability of fracture.

Disclosure of Interests: None declared

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AB0871 FACTORS ASSOCIATED WITH RADIOGRAPHIC HIP INVOLVEMENT IN ANKYLOSING SPONDYLITIS

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Background: Hip involvement is a classic feature of ankylosing spondylitis (AS). It causes functional impairement and disability in patients with AS. Although, many studies have looked at factors associated with radiographic hip involvement, these remain debated.

Objectives: To define the factors associated with radiographic hip involvement in patients with AS.

Methods: A cross-sectional comparative study of 105 patients was performed. Hip involvement was defined as hip pain considered related to AS inflammation and confirmed radiographically. The patients were classified into two categories: (1) no hip involvement, (2) hip involvement according to a Bath Ankylosing Spondylitis Radiology Index (BASRI)-hip score ≥2. Multivariate logistic regression analyses were used to identify the factors associated with radiographic hip involvement.

Results: Fifty-three patients had radiological hip involvement and 52 patients were whithout hip involvement. Multivariate logistic regression analyses showed male sex (OR 6.383 IC 1.553-26.29, p=0.010), Bath Ankylosing Spondylitis Functional Index (BASFI) score (OR 1.436, IC 1.079-1.913, p=0.013), and BASRI-spine score (OR 1.456, IC 1.190-1.783, p<0.001) to be significantly associated with radiographic hip involvement, and an inverse relation-ship with age at onset (OR 0.955, IC 0.995-0.998, p=0.038) was seen.

Conclusion: Male sex, younger age at onset, worse BASFI score and worse BASRI-spine score are associated with radiographic hip involvement. AS patients with risk factors for radiographic hip involvement should be diagnosed at an early stage to improve their quality of life.

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AB0872 INFLUENCE OF JOINT AND ENTHESIS DAMAGE ON THE QUALITY OF LIFE OF PATIENTS WITH INFLAMMATORY BOWEL DISEASES.

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Background: Inflammatory bowel diseases (IBD) are chronic immune-inflammatory diseases that are often associated with various extraintestinal manifestations [1]. Among them, joint involvement is the most common, occurring in 5–20% of patients with IBD [1], while the prevalence of enthesitis varies in studies from 12.5% to 90% of cases [2].

Objectives: To assess the relationship between the state of peripheral joints and entheses in patients with IBD and their quality of life.

Methods: 95 pts with IBD were prospectively enrolled into the study: 55 of them with ulcerative colitis (UC) and 40 with Crohn's disease (CD). The average age of the pts was 32 (26; 37) years. The average duration of the disease was 44 (12; 95) months. The severity of UC exacerbation was assessed by the Mayo index, in CD – by Harvey-Bradshaw index. In UC, moderate and severe exacerbation was revealed in 40 pts (73%), in CD - in 17 (43%). Among 95 pts with IBD, extraintestinal manifestations occurred in 67 pts (71%), of which 34 (62%) pts with UC and 33 (82%) pts with CD. 14 joints and 68 enthesis were evaluated clinically and by US in each pt. The clinical examination included tenderness of enthesis. US examination with power Doppler detected synovitis with / without vascularization, inflammatory (hypoechogenicity of enthesis, thickening of enthesis, presence of vascularization) and structural (erosion, enthesophyte) changes in enthesis. The quality of life was assessed using the SF-36 questionnaire that covers eight health domains. Scores for each domain range from 0 to 100, with a higher score defining a more favorable health state. Spearman coefficient used to calculate correlations.

Results: 61 pts with IBD (64%) complained of pain in the joints, 49 pts (52%) noted pain on palpation of entheses. As a result of ultrasound examination, synovitis were detected in 41 pts (43%), including synovitis with vascularization in 29 pts (31%). Enthesitis were found in 72 pts (76%), while vascularized enthesitis was detected in 35 pts (37%). Erosions were identified in 76 pts (80%), and enthesophytes were identified in 37 pts (39%). The average level of physical health was 43.53 (35.67; 51.66), mental health 38.53 (31.13; 48.37).

An inverse correlation was observed between the number of extraintestinal manifestations and physical functioning (SR=-0.22; p=0.03). The number of painful joints was inversely correlated with physical functioning (SR=

-0.22; p=0.03), pain intensity (SR= -0.23; p=0.02), vital activity (SR= -0.23; p=0.027), as well as with physical health (SR= -0.21; p=0.04). The number of painful entheses was inversely correlated with physical functioning (SR = -0.21; p = 0.03), pain intensity (SR = -0.3; p = 0.003) and physical health (SR = -0, 21; p=0.03). An inverse correlation was observed between the number of synovitis with vascularization and physical functioning (SR= -0.26; p=0.01), vital activity (SR= -0.29; p=0.005), physical health (SR=-0.23; p=0.024). The number of enthesitis was inversely correlated with the pain intensity (SR = -0.22; p = 0.036).

Conclusion: With an increase in the number of affected joints and enthesis, the physical health of pts decreases, due to physical functioning and pain intensity, as well as their vital activity.

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Disclosure of Interests: None declared

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AB0873 ETHNICITY AND PATIENT REPORTED OUTCOME BASDAI IN THE MONITORING OF AXIAL SPONDYLOARTHROPATHY: DOES IT MATTER?

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Background: The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is a patient reported outcome (PRO) used in the monitoring of axial spondyloarthropathy (axSpA). It is completed by the patient and based on their assessment of disease severity and therefore quite a subjective measure of disease (1). There has been research around the relationship between ethnicity and patient perception in Rheumatology. Many studies have demonstrated that non-Caucasian patients especially South Asians are less likely to engage with patient education, abandon their disease modifying therapy early and have more mistrust with the medical establishment (2). Quite a large population study in America examining axSpA severity in Caucasians, Afro-Caribbean's and Latinos found Afro-Caribbean and Latino patients to score themselves higher on BASDAI compared to Caucasians (3). With Leicester being such a diverse area, with a particularly high South Asian population we took this opportunity to investigate whether there were ethnic variations in disease severity.

Objectives: The aim was to investigate whether there is a relationship between patient-reported outcome BASDAI and ethnicity. The secondary aim was to investigate the relationship between ethnicity and radiographic findings and extra-articular manifestations.

Methods: Data was collected by retrospective analysis of axSpA patients attending University of Leicester (UHL) axSpA services. Inclusion criteria entailed a diagnosis of axSpA with a documented BASDAI within a year of MRI spine + sacroiliac joints, prior to starting any biological treatment. Data of 149 patients was collected on demographic characteristics, extra-articular manifestations (uveitis, inflammatory back pain, enthesitis, peripheral arthritis, dactylitis, psoriasis, and inflammatory bowel disease), family history, response to NSAIDs, and HLA-B27 status. Data was analysed using Statistical Package for the Social Sciences (SPSS) software to assess the relationship between ethnicity and collected data using Pearson's chi squared.

Results: Of the 149 patients 68% were White Caucasian, 30% Asian and 1% Black. The average age was 43 and 66% were male and 34% female. The mean BASDAI was 6.5, there was no observable correlation between BASDAI and ethnicity (p=0.668). There was no significant relationship between ethnicity and active sacroiliitis (p=0.926), chronic sacroiliitis (p= 0.218) or axial disease (p=0.307). 64 Caucasian patients were HLA-B27 positive compared with 27 Asian and no Black patients were positive however there was no statistical correlation between ethnicity and HLA-B27 (p=0.383). Overall, Caucasians consistently had a greater incidence of extra-articular manifestations compared with non-Caucasians however no significant p values were observed here or with response to NSAIDs, family history or familial HLA-B27 and BASDAI scores, results are summarised in Table 1.

Table 1. Correlation with ethnicity and extra-articular manifestations, family history and HLA-B27.

	Number of patients	Correlation with ethnicity
Uveitis	36	p=0.470
Peripheral arthritis	24	p=0.304
Enthesitis	22	p=0.959
Psoriasis	7	p=0.062
Inflammatory bowel disease	7	P=0.947
Dactylitis	6	P=0.173
HLA-B27	103	p=0.383
Inflammatory back pain	139	p=0.062
Response to NSAIDs	46	p=0.718
Family history of axSpA	20	p=0.800
HLA-B27 in family	10	p=0.221

HLA-B27= Human leukocyte antigen B27, NSAIDs= non-steroidal anti-inflammatory drugs, axSpA= Axial Spondyloarthropathy.

Conclusion: This study did not demonstrate statistically significant finding of ethnic variations in BASDAI. There was also no relationship between ethnicity and other data sets. However, the main limitation of this study is the sample size and unequal representation of ethnicities with there being far more Caucasians than non-Caucasian patients. Though this study provides an insight into quite a limited area of research, a larger study with equal ethnic patient population samples is required to obtain more meaningful results.

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AB0874 TARSITIS IN MEXICAN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Spondyloarthritis (SpA) is a set of auto-immune and auto-inflammatory diseases that share similar manifestations of axial spine and sacroiliac, peripheral joint including oligoarthritis predominantly of lower limbs, dactylitis, enthesitis and fasciitis, and extraarticular manifestations involvement eyes, skin, nails, bowel and the presence of high c-reactive protein (CRP) levels and Human Leucocyte Antigen (HLA)-B27 seropositivity. Peripheral manifestations such tarsitis (mid-foot arthritis) has been reported associated to ankle arthritis, Achilles tendon enthesitis and plantar fasciitis, besides linked mainly to juvenile-onset forms of SpA (18.1%) in contrast with peripheral adult form (13.6%) [1,2]. Tarsitis occurs more frequently in SpA patients of Latin American (23.6%), Asia (9.1%) and less commonly in SpA patients of Europe and North America (5%) and middle-East and North Africa (3.5%) [1,2]. This mid-foot inflammation has not been completely well described in the adult population with SpA, specifically in Mexican adult population [3]. Here is presented the frequency and factors associated to tarsitis in Mexican adult patients with SpA.

Objectives: To determinate the frequency and factors associated to tarsitis in Mexican SpA patients.

Methods: That is a cross-sectional, comparative a retrospective study including 211 (≥18 years) Mexican SpA patients recruited from 2012 to 2021 that fulfilled ASAS criteria. Patients with or without presence of tarsitis are included. This work explores demographic factors, clinical features, c-reactive protein levels and pharmacologic treatments in Spa patients with or without tarsitis. It use Chi-square, Student´s-t, U Mann-Whitney tests to univariate analysis and logistic regression to multivariate analysis adjusted for age and gender. The level of significance of statistical tests is less of 5%.

Results: The present investigation involves 211 patients with SpA and 62.6% of them are men. The mean age [standard deviation (SD)] is 43.72 (13.5) years. The mean of age at onset of SpA (SD) is 31.93 (11.3) years. The SpA distribution is axial (42.2%), peripheral (27%) and both (30.8%). A total of 63 (29.9%) patients has tarsitis; of them

63.5% are men and the mean age at onset of tarsitis (SD) is 26.52 (10.2) years. The seronegative spondyloarhtropathies associated to tarsitis are ankylosing spondylitis (81%), psoriatic arthritis (9.5%), undifferentiated spondyloarthropathy (7.9%), and reactive arthritis (1.6%). In the univariate analysis SpA patients with tarsitis are likely younger at onset of manifestations and diagnosis of disease, present peripheral distribution and unilateral tarsitis, show more frequently knee and ankle arthritis, Achilles and calcaneus tendon enthesitis and plantar fasciitis, have more probably HLA-B27 seropositivity and higher c-reactive protein levels, and use more often oral and intraarticular corticosteroids. On the other hand, SpA patients with tarsitis are less frequently smokers and exhibit less probably cervical and lumbar involvement, dactylitis and family history of SpA. In multivariate analysis, use of intraarticular corticosteroids (OR 61.75, 95% CI 8.46–450, p=<0.001) and calcaneus tendon enthesitis (OR 31.40, 95% CI 4.42–223, p=0.001) remain significant in SpA patients with tarsitis.

Conclusion: This study suggests that SpA patients from Mexico have high prevalence of the tarsitis (29.9%) compare to other populations. Those with tarsitis use more intraarticular corticosteroids and present more often calcaneus tendon enthesitis. However, these observations must be confirmed in larger and prospective studies.

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AB0875 ASSESSMENT OF CLINICAL SIGNS OF SPONDYLOARTHRITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Patients with inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC), commonly face the presence of extraintestinal manifestations (EIMs). Spondyloarthritis (SpA) is present in about 10-39% of patients with IBD, being the most frequent EIM [1]. Diagnosis of axial SpA (axSpA) in IBD represents a clinical challenge. The diagnostic value of Ankylosing Spondylitis Assessment Society (ASAS) criteria that are used for defining inflammatory back pain (IBP) in axSpA, in patients with the association of axSpA and IBD is not clear.

Objectives: To determine the diagnostic value of ASAS criteria for IBP (2009) and to evaluate factors that are associated with a higher risk of axial SpA in patients with IBD.

Methods: The study included 91 patients with IBD (UC - 52 patients (57.1%), CD - 39 (42.9%), males – 47 (51.6%), mean age 40.2±11.7 years, duration of IBD – 7.7±7.6 years). IPB was defined by ASAS criteria (2009). AxSpA in patients with IBD is recommended to be diagnosed by the combination of Inflammatory Back Pain (IBP), and imaging (MRI and X-ray) [2]. Imaging of lumbar spine and sacroiliac joints was performed to patients, who fulfilled the ASAS criteria for IBP: X-ray - 55 patients; MRI (T1, STIR) - 41 patients. Imaging was considered positive when patients had at least unilateral sacroiliitis stage 2 or higher according to the accepted grading system on X-Ray, or MRI-verified sacroiliitis.

Results: Low back pain was observed in 84 (92.3%) patients with IBD, 39 (42.9%) patients fulfilled the criteria ASAS for IBP. MRI-verified sacroiliitis was present in 26 patients. Changes on X-ray were present in 40 patients. After imaging, 26 patients were diagnosed with axSpA, 14 of them fulfilled the modified New York criteria for the ankylosing spondylitis. Diagnostic value of the ASAS criteria was the following: sensitivity 76.9%, specificity 67.2%, PPV 0.51, NPV 0.87, LR+ 2.3, and LR- 0.3 (ECCO consensus definition used as the "gold standard"). Presence of arthritis - OR 10.77 [95% CI 2.26-44.2], p=0.005, arthralgia - OR 4.12 [95% CI 1.55-10.95], p=0.005, CD - OR 2.92 [95% CI 1.14-7.48], p=0.025 and IBP – OR 8.07 [95% CI 2.8-23.23], p=0.001 was associated with a higher risk of axSpA diagnosis in the univariate logistic regression model. The associations remained statistically significant when multivariate logistic regression model was constructed – arthritis 20.03 [95% CI 3.05 -131.69], CD – 3.51 [95% CI 1.04-11.82], IBP – 8.72 [95% CI 2.64-28.79], R^2=0.486.

Conclusion: The ASAS criteria for IBP had a good diagnostic value in patients with IBD. The diagnostic value of the ASAS criteria for IBP (2009) in patients with IBD was comparable to the following in the patients with chronic back pain. Clinicians should pay attention to the presence of arthritis, arthralgia, IBP and CD, as these factors were associated with a higher risk of being diagnosed with axSpA in patients with IBD.

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AB0876 CAN ULTRASONOGRAPHIC PERIPHERAL ENTHESITIS MIRROR SPINAL RADIOGRAPHIC ABNORMALITIES AND OTHER DISEASE PARAMETERS IN PATIENTS RADIOGRAPHIC AXIAL SPA?

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Background: Although enthesitis is the hallmark of spondyloarthritides, the association between peripheral enthesitis, radiographic spinal affection and disease assessment parameters is still underestimated.

Objectives: In this cross-sectional prospective study, we aimed to evaluate the relation of US pattern of peripheral enthesitis with the spinal radiographic changes and other disease parameters in patients with radiographic axial spondyloarthritis (SpA).

Methods: Fifty-eight patients with radiographic axial SpA (ASAS criteria) were studied for the presence and pattern of peripheral lower limb enthesitis according to the Outcome Measures in Rheumatology (OMERACT) US definitions: Achilles tendon, plantar fascia, proximal and distal patellar ligaments, and quadriceps tendon insertions. The findings then were correlated with the radiographic spinal abnormalities, Bath AS radiographic index (BASRI), Bath AS disease activity index (BASDAI), Bath AS functional index (BASFI), and Bath AS metrology index (BASMI) together with the HLA-B27 status and inflammatory markers using Spearmann rho correlation co-efficient.

Results: The mean age was 37.96 (±13.1) years, 75.86% were males. Thirty-six patients (62%) had US enthesitis (USE) with a mean age of 39.2 (±12.8). HLA-B27 was positive in 61% of patients with USE and 54.5% in those without. There was no difference between patients with and without USE regarding the disease duration, age at onset but those with USE showed less diagnostic delay (p = 0.03). Clinical enthesitis and peripheral arthritis were more frequent in those with USE (50% vs 22.7% and 25% vs 13.6% respectively). No statistical significant difference has been found between the inflammatory, structural and total scores of USE and BASRI, BASFI and BASDAI (p > 0.05). No correlation could be detected between BASRI and USE scores (rs= 0.12, p =0.45 for inflammatory, rs=0.25, p=0.11 for structural and rs=0.18, p=0.28 for total score). There was a positive correlation between BASMI and both inflammatory and total scores of USE (rs= 0.485, p=0.003). No significant association between BASDAI, CRP or ESR and USE scores.

Conclusion: Ultrasonographic peripheral entheseal abnormalities couldn't reflect the spinal radiographic changes or disease assessment parameters in patients with radiographic axial SpA. However, these results can be considered preliminary and more studies on wider scales are needed to support our findings.

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AB0877 QUANTIFICATION OF THE ENTHESIC RESPONSE TO BIOLOGICAL THERAPIES IN PATIENTS WITH SPONDYLOARTHRITIS BY COMPUTER ANALYSIS OF ULTRASOUND IMAGES.

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Background: Enthesitis is the base of the pathophysiology of spondyloarthritis. Recently, our group has shown that computer analysis of static images can be used in the evaluation of patients with enthesic inflammatory diseases with good intra-patient and intra-observer validity and sensitivity to change.

Objectives: To determine the enthesic evolution in patients with spondyloarthritis (SpA) treated with three different biological therapies through the computer analysis of ultrasound images.

Methods: We selected patients diagnosed with SpA and enthesitis followed by imaging, who started biological therapy with a TNF inhibitor, an IL17 inhibitor or an IL12/23 inhibitor. For the records to be included, it was necessary to have clinical information from the period of perfoming the ultrasound. All images were obtained from the Achilles tendon, with the same ultrasound equipment, grayscale and settings for each patient. To homogenize the results of the analysis, the gray intensity mean index (iMIG) was used, which has been shown to appropriately discriminate the inflammatory pathology from the mechanical or healthy controls as well as being sensitive to change.

Results: 14 patients were included: 6 treated with a TNF inhibitor, 4 with an IL17 inhibitor and 4 with an IL12/23 inhibitor. Patients 2, 3, 5, 7, 10, 11, and 12 had enthesophytes.

Table 1. List of patients included in the analysis. After the final ultrasound examination, the follow-up time up to the present is recorded in the case of continued treatment (m: months).

	Treatment	Enthesophytes	Basal MIG	Basal iMIG	Intermediate examination	Intermediate iMIG	Final examination	Final iMIG	Treatment follow-up
1	TNFi		71,424	0,85	+6m	0,89	+6m	0,94	Continues +24m
2	TNFi	+	156,415	1,48	+5m	1,51	+6m	1,52	Suspended for inefficacy (enthesitis)
3	TNFi	+	164,323	1,32	+6m	1,34	+6m	1,35	Suspended for inefficacy (enthesitis)
4	TNFi		69,321	0,78	+4m	0,80	+6m	0,94	Suspended for inefficacy (axial pain)
5	TNFi	+	141,473	1,14	+6m	1,19	+4m	1,18	Suspended for inefficacy (enthesitis)
6	TNFi		68,483	0,85	+3m	1,03	+5m	1,05	Continues +20m
7	iIL17	+	135,432	1,34	+5m	1,26	+4m	1,15	Continues +22m
8	iIL17		72,225	0,90	+6m	1,02	+4m	1,06	Continues +20m
9	iIL17		80,465	0,89	+3m	1,03	+6m	1,03	Suspended for inefficacy (arthritis).
10	iIL17	+	122,254	1,16	+6m	1,11	+4m	1,04	Continues +24m
11	iIL12/23		71,401	0,79	+8m	1,01	+4m	1,1	Suspended for inefficacy (axial pain)
12	iIL12/23	+	134,41	1,12	+6m	1,08	+6m	1,07	Continues +18m
13	iIL12/23		75,42	0,94	+4m	1,12	+6m	1,16	Continues +20m
14	iIL12/23		69,112	0,84	+3m	0,9	+8m	1,12	Continues +18m

In the global analysis, the iMIG did not show statistically significant differences between the treatment groups at the start of the treatment, at the intermediate and at the final evaluation (P=.588, .739 and .674, respectively). Patients with enthesophytes presented significantly higher baseline, intermediate and final iMIG than patients without them: 1.26 SD 0.14 vs 0.85 SD 0.05 (t=7.407, P=.001), 1.24 SD 0.15 vs 0.97 SD 0.1 (t=3.659, P=.006); and 1.21 SD 0.12 vs 1.05 SD 0.07 (t=2.342, P=.037), respectively. Analyzing only the patients without enthesophytosis, the final iMIG showed statistically significant differences between the 3 administered treatments (ANOVA, F=8.142, P=.027), being relevant between the use of IL12/23 and TNF inhibitor in favor of the former (Bonferroni, P=.03). In the same subgroup of patients without enthesophytosis, iMIG analysis over time showed statistically significant differences between final and baseline iMIG (Friedman -1.938 P=.000).

Conclusion: Computer analysis of ultrasound images using the iMIG distinguishes therapeutic response in patients without enthesophytosis.

The interposition of enthesophytes impede the correct visualization of the enthesis and does not allow ultrasound changes to be detected in some areas of the image. Although there are indications that the use of this analysis could also predict the behavior of certain therapies, it is convenient to propose prospective studies with homogeneous ultrasound controls.

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AB0878

HIGHER VITAMIN D SERUM LEVEL IS ASSOCIATED WITH A BETTER CLINICAL RESPONSE TO BDMARDS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS.

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Background: Vitamin D deficiency has been shown to be associated with higher disease activity and severity of several inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease and spondyloarthritis (SpA). It is, however, unknown if vitamin D level might affect the response to treatment with biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients with SpA.

Objectives: To investigate the association between vitamin D serum levels and the response to a bDMARD therapy in patients with axial SpA.

Methods: Patients with a radiographic axial SpA (r-axSpA), fulfilling the modified New York criteria and starting a bDMARD therapy were recruited between 2015 and 2019 in an extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC-AS). All patients were required to have at inclusion high disease activity (BASDAI >=4 and/or ASDAS >=2.1) despite previous treatment with nonsteroidal anti-inflammatory drugs. Demographics, patient clinical characteristics and vitamin D serum levels were collected at baseline. Disease activity measures (BASDAI, CRP, ASDAS) were assessed at baseline and after 6 months of bDMARD treatment. Vitamin D deficiency was defined as serum level of 25-hydroxyvitamin D < 20 ng/mL. A multivariable regression analysis was performed to determine the association between vitamin D serum level at baseline and the treatment response as defined by BASDAI and ASDAS change scores at month 6 as compared to baseline.

Results: A total of 129 patients with r-axSpA were included in the study. No patient took supplements of vitamin D at baseline. Patients had an average age (mean±SD) of 36.5±10.5 years, 64.3% were males and 86.6% were HLA-B27 positive. The prevalence of vitamin D deficiency in our cohort was 54.3%. Patient characteristics and disease activity were comparable with regard to the presence of vitamin D at baseline (Table 1); with the exception of body mass index (BMI), which was higher in patients with vitamin D deficiency. In the multivariable linear regression analysis, baseline serum level of vitamin D was independently and significantly associated with higher change in BASDAI and ASDAS (Figure 1).

Table 1. Baseline characteristics of patients with radiographic axial SpA (n=129) according to vitamin D levels at baseline.

	Patients with vitamin D deficiency (<20 ng/mL) n=70	Patients with normal levels of vitamin D n=59
Age, years	36.6±11.0	36.3±10.0
Male sex	46 (65.7)	37 (62.7)
BMI, kg/m^2	26.0±4.5*	24.0±3.8
Smoking, ever	41 (58.6)	29 (49.2)
Winter and Spring, n (%)	33 (47.1)	23 (39.0)
Symptom duration, years	11.5±11.3	10.3±7.1
HLA-B27 positive	62 (88.6)	50 (84.7)
Uveitis ever	17 (24.3)	12 (20.3)
Psoriasis ever	11 (15.7)	7 (11.9)
IBD ever, n (%)	2 (2.9)	7 (11.9)
CRP, mg/L	12.9±19.3	13.9±15.3
BASDAI	5.7±1.4	5.4±1.4
ASDAS	3.4±0.8	3.5±0.8
BASFI	4.6±2.2	4.4±1.9
BASMI	3.1±1.5	2.7±1.3
NSAID intake, current	50 (71.4)	45 (76.3)
DMARDs intake, ever	9 (12.9)	6 (10.2)
TNFi naive	55 (78.6)	47 (79.7)
Corticoids intake, current	5 (7.1)	2 (3.4)

*p value <0.05. All numerical variables were presented as mean±SD, all categorical variables were presented as n (%). BMI, body mass index; CRP, C-reactive protein; DMARD, disease-modifying antirheumatic drug; IBD, inflammatory bowel disease; NSAID, nonsteroidal anti-inflammatory drug; TNFi, tumor necrosis factor inhibitor.

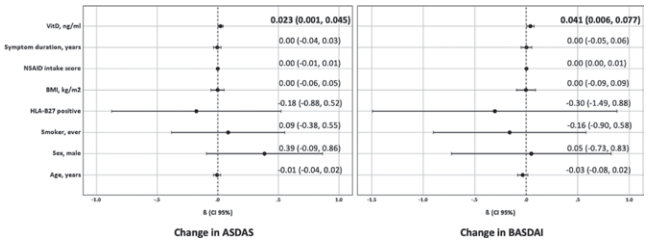

Figure 1. Association between the response to bDMARDs (change in BASDAI and ASDAS after 6 months) and level of vitamin D at baseline in patients with radiographic axial SpA in the multivariable regression analysis.

Conclusion: Higher vitamin D levels at baseline may predict a better treatment response to bDMARDs in patients with r-axSpA. It has to be shown, however, if vitamin D supplementation might result in a better treatment response in axial SpA.

Disclosure of Interests: None declared

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Psoriatic arthritis - treatment

AB0879

INTERIM ANALYSIS OF BASELINE CHARACTERISTICS AND 12-WEEK OUTCOMES FOR A SUBSET OF PATIENTS WITH MODERATE-TO-SEVERE PLAQUE PSORIASIS AND PSORIATIC ARTHRITIS FROM THE PSORIASIS STUDY OF HEALTH OUTCOMES

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Background: Approximately 30% of patients (pts) with plaque psoriasis (PsO) develop psoriatic arthritis (PsA)[1], which is associated with high Psoriasis Area and Severity Index (PASI) and nail involvement. The Psoriasis Study of Health Outcomes (PSoHO) is a 3-year (yr), international, prospective, observational cohort study comparing the effectiveness of anti-IL-17A biologics to all other approved biologics in pts with moderate-to-severe PsO.

Objectives: This interim subset analysis describes the baseline characteristics and Week 12 (W12) effectiveness in pts with moderate-to-severe PsO and PsA in PSoHO.

Methods: Adults with moderate-to-severe PsO for ≥6 months who initiated/switched biologic treatment during routine medical care were enrolled. PsA diagnosis was recorded by the dermatologists based on the medical history and/or information provided by the patient. W12 effectiveness was assessed by the proportion of pts achieving almost clear or clear skin defined by ≥90% improvement in PASI, affected Body Surface Area (BSA), Dermatology Life Quality Index (DLQI), and Patient Global Assessment of Disease Severity (PatGA). Musculoskeletal endpoints were not collected. Data were analysed descriptively, using mean (standard deviation [SD]) or median ([Q1/Q3]) for continuous variables and n, % and 95% confidence limits for categorical variables.

Results: Overall, 1981 pts were enrolled in this study, of whom 461 (23.3%) had a PsA diagnosis and received either anti-IL-17A (n=227; 49.2%) or other biologics (n=234; 50.8%). This subset of pts had a mean age of 48.7 yrs and a median disease duration of 18.9 yrs for PsO and 5.6 yrs for PsA (Table 1).

Table 1. Baseline characteristics for PsO patients with PsA. Mean (SD) reported for all available data for that measure, unless stated otherwise.

	Overall (n=461)	Anti-IL-17A (n=227)	Other Biologics (n=234)
Age, yrs	48.7 (12.9)	50.9 (12.9)	46.6 (12.6)
Male, n (%)	232 (50.3)	112 (49.3)	120 (51.3)
BMI (kg/m^2)	29.7 (6.2)	29.8 (5.9)	29.6 (6.4)
Smoking status – Current, n (%)	100 (25.4)	41 (21.1)	59 (29.5)
Disease duration (PsA), yrs, median (Q1/Q3)	5.6 (2.2/13.1)	5.6 (2.0 / 13.8)	5.5 (2.3 / 12.8)
Disease duration (PsO), yrs, median (Q1/Q3)	18.9 (9.7 / 28.6)	18.9 (9.2 / 30.3)	18.7 (10.1 / 27.3)
Any previous biologic therapy, n (%)	249 (54.0)	123 (54.2)	126 (53.8)
PASI	14.3 (9.3)	13.6 (8.1)	15.0 (10.3)
BSA, %	21.7 (19.4)	19.8 (17.3)	23.5 (21.1)
mNAPSI	16.6 (22.8)	16.5 (25.5)	16.7 (20.1)
Presence of nail PsO, n (%)	217 (47.2)	103 (45.4)	114 (48.9)
PatGA	3.5 (1.2)	3.5 (1.3)	3.6 (1.2)
DLQI	13.6 (7.9)	13.4 (7.8)	13.7 (8.0)
HADS Depression score >10, n (%)	73 (19.3)	38 (20.5)	35 (18.1)
HADS Anxiety score >10, n (%)	124 (32.8)	62 (33.5)	62 (32.1)

BMI = Body Mass Index; BSA = Body Surface Area; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS >10 indicates significant symptoms of depression/anxiety; mNAPSI = Modified Nail Psoriasis Severity Index; PASI = Psoriasis Area and Severity Index; PatGA = Patient Global Assessment of Disease Severity; Q1/Q3 = Quartile 1/3.

At W12, 62.4% and 42.6% of anti-IL-17A-treated pts achieved PASI90 and PASI100, respectively, compared with 34.2% and 16.8% in the other biologics cohort, respectively (Figure 1). BSA <3% was reached by 70.9% of anti-IL-17A-treated pts and 49.5% in the other biologics cohort, while 71.2% and 44.8%, respectively, reached PatGA 0/1. Among pts with baseline DLQI ≥2, 38.0% and 27.1% of the anti-IL-17A and other biologics cohorts, respectively, reached DLQI 0/1.

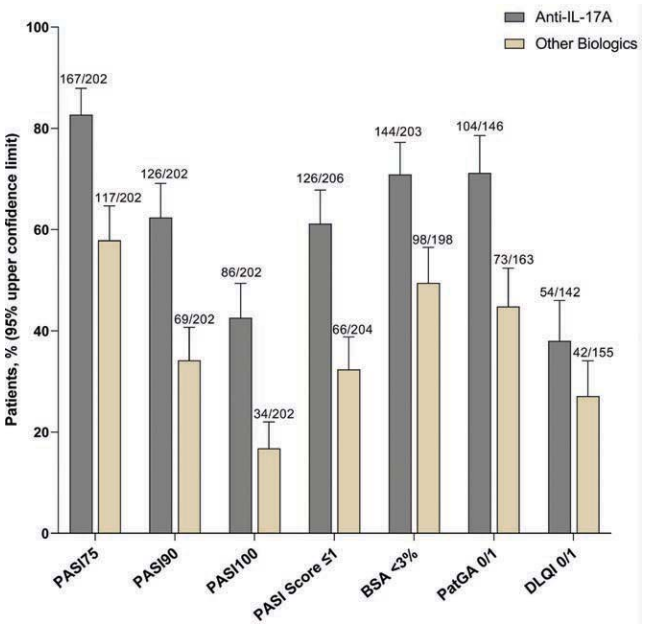

Figure 1. Percentage of patients receiving anti-IL-17A or other biologics who achieved PASI75/90/100, absolute PASI ≤1, BSA <3%, PatGA 0/1 and DLQI 0/1 (baseline DLQI ≥2) at Week 12. Bars represent upper 95% confidence limits.

Conclusion: The effectiveness of blocking IL-17A on skin manifestations and on quality-of-life improvements in pts with PsO and PsA in the real-world study was consistent with observations from clinical trials.

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Disclosure of Interests: Lars Erik Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals., Consultant of: Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals., Grant/research support from: IIT research grants from Pfizer, AbbVie, UCB, Gilead, Biogen, Novartis, Eli Lilly, and Janssen pharmaceuticals., Frank Behrens Speakers bureau: Amgen, AbbVie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Boehringer and Sandoz, Consultant of: Amgen, AbbVie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Boehringer and Sandoz, Grant/research support from: AbbVie, Pfizer, Roche, Chugai, GSK and Janssen, Luis Puig Speakers bureau: Celgene, Janssen, Eli Lilly, Novartis, Pfizer, Consultant of: Abbvie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Fresenius-Kabi, Janssen, JS BIOCAD, Leo-Pharma, Eli Lilly, Mylan, Novartis, Pfizer, Regeneron, Roche, Sandoz, Samsung-Bioepis, Sanofi, UCB, Grant/research support from: Abbvie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, Leo-Pharma, Eli Lilly, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, Adam Reich Speakers bureau: Abbvie, Novartis, Janssen, Pfizer, Sandoz, Galderma, Eli Lilly, Consultant of: Abbvie, Novartis, Janssen, Pfizer, Sandoz, Galderma, Eli Lilly, Thorsten Holzkaemper Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Alan Brnabic Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Khai Ng Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Soyi Liu Leage Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Christopher Schuster Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Andreas Pinter Speakers bureau: AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Biontec, Boehringer-Ingelheim, Celgene, GSK, Eli Lilly, Galderma, Hexal, Janssen, LEO-Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi-Genzyme, Schering-Plough and UCB Pharma, Consultant of: AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Biontec, Boehringer-Ingelheim, Celgene, GSK, Eli Lilly, Galderma, Hexal, Janssen, LEO-Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi-Genzyme, Schering-Plough and UCB Pharma

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AB0880 **OPTIPSA: NATIONWIDE SURVEY ON CLINICAL/ THERAPEUTIC INERTIA IN PSORIATIC ARTHRITIS**

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Background: Therapeutic inertia (TI), or clinical inertia, is the medical behavior of not initiating or intensifying treatment when recommended by clinical recommendations (1). TI was established in diabetes and then studied in hypertension, multiple sclerosis and psoriasis, and is estimated to affect 30 to 70% of physicians managing patients with chronic diseases (2-4). To our knowledge, no data have reported TI in the setting of psoriatic arthritis (PsA).
Objectives: The OPTI PSA survey was conducted to assess therapeutic inertia around PsA in France.
Methods: 825 French rheumatologists were contacted by e-mail between January and March 2021 and asked to complete an online questionnaire, consisting of 7 clinical vignettes illustrating common situations and reflecting the polymorphic character of PsA: five clinical cases (oligoarthritis, enthesitis, polyarthritis, neoplastic history, cardiovascular risk) requiring treatment optimization in accordance with the latest SFR/EULAR recommendations (5, 6,7) and two "control" clinical cases (DIP arthritis, atypical axial) not requiring any change of treatment. The rheumatologists were also questioned about their routine practice and perception of PsA.
Results: 101 (12%) of the rheumatologists contacted completed the questionnaire. Sixty percent of respondents were men, and 45% of rheumatologists were aged between 46 and 60 years; most practiced exclusively in hospitals (34%), private practice (33%) or in both (34%); the mean duration of clinical practice was 23 years. Almost all of the respondents stated that they were comfortable with the management of PsA (99%) and familiar with French and EULAR recommendations (90%). There was general consensus regarding the difficulties inherent in PsA: therapeutic objectives difficult to achieve (74% of respondents); polymorphism making it difficult to evaluate the effectiveness of a treatment (72%). Almost half the respondents (47%) demonstrated TI on at least one of the 5 vignettes that warranted treatment optimization. The clinical cases that induced the most TI were "oligoarthritis" and "enthesitis" with 20% and 19% of respondents not modifying treatment, respectively. Conversely, the vignettes "polyarthritis in relapse", "neoplastic history" and "cardiovascular risk" generated fewer TIs with 11%, 8% and 6% of respondents, respectively, choosing not to change the current treatment.
Conclusion: Despite a good knowledge of PsA and associated clinical recommendations, almost half of the rheumatologists we surveyed demonstrated at least one TI. The rate of TI we observed for PsA is similar to published data for other chronic diseases (1-4). The clinical profiles for which there was the least uncertainty (comorbidities and polyarticular involvement) generated the least inertia; the more complex profiles oligoarthritis and enthesitis generated more inertia. Our study is the first to show the existence of clinical inertia in PsA and further research is warranted to ascertain the reasons behind this inertia.

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AB0881 **GUSELKUMAB PROVIDES SUSTAINED IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH 2 YEARS OF DISCOVER-2**

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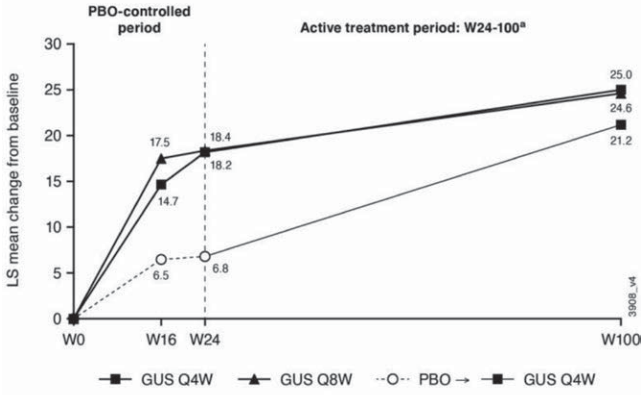
Background: Psoriatic arthritis (PsA), a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis, and skin/nail psoriasis, is associated with reduced health-related quality of life (HRQoL).
Objectives: To assess long-term effect of guselkumab (GUS), a human monoclonal antibody that selectively targets the interleukin (IL)-23p19 subunit, on HRQoL of bio-naïve PsA patients (pts) who participated in the Phase 3 2-year DISCOVER-2 trial.[1]
Methods: Pts with active PsA despite nonbiologic disease-modifying antirheumatic drugs (DMARDs) and/or nonsteroidal anti-inflammatory drugs (NSAIDs) received GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). At W24, PBO pts crossed over to GUS 100 mg Q4W. HRQoL was assessed using the pt-reported EuroQoL-5 Dimension-5 Level (EQ-5D-5L) questionnaire index and EuroQol Visual Analog Scale (EQ-VAS), widely used and complimentary tools that allow pts to provide a global assessment of their HRQoL. The EQ-5D-5L index assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression; an index score is derived ranging from 0 (death) to 1 (perfect health).[2] EQ-VAS assesses pt health state on a scale of 0-100, with higher scores indicating better health. Using mixed effects models for repeated measures (MMRM), least squares (LS) mean changes from baseline in the EQ-5D-5L index and EQ-VAS through W100 were assessed. Observed changes from baseline were evaluated; in pts who met treatment failure rules before W24 and in pts who discontinued with missing data after W24, changes from baseline were imputed as 0.
Results: GUS-treated pts achieved greater improvements in pt-reported health status than PBO at both W16 and W24 when evaluated using both the EQ-5D-5L index score and the EQ-VAS. The improvements by GUS in EQ-5D-5L index scores through W24 (0.12 for GUS Q4W/Q8W vs 0.05 for PBO; each nominal $p<0.0001$) were maintained with continued GUS through 2 years (0.15 for GUS Q4W/Q8W) (Table 1). PBO-treated pts who started GUS at W24 reported comparable improvements in their HRQoL by W52 (0.12), with maintenance though W100 (0.14). Similar results were observed with EQ-VAS (Figure 1). W24 improvements in EQ-VAS scores were greater following GUS treatment (18.2/18.4 GUS Q4W/Q8W) vs PBO (6.8; nominal $p<0.0001$). EQ-VAS scores continued to improve with GUS through 2 years (25.0/24.6 GUS Q4W/Q8W). Likewise, PBO-treated pts who crossed over to GUS at W24 experienced improvements in HRQoL by W52 (18.8), with maintenance through W100 (21.2).

Table 1. LS mean change from baseline through W100 in EQ-5D-5L index

	GUS 100mg Q4W (W0-100)			GUS 100mg Q8W (W0-100)			PBO → GUS 100 mg Q4W		
							PBO (W0-24)		GUS (W24-100)
Week	16	24	100	16	24	100	16	24	100
N	243	244	243	247	246	248	244	244	244
LS mean change (95% CI)	0.10 (0.09,0.12)	0.12 (0.1,0.13)	0.15 (0.13,0.16)	0.11 (0.1,0.13)	0.12 (0.1,0.13)	0.15 (0.13,0.17)	0.06 (0.04,0.07)	0.05 (0.04,0.07)	0.14 (0.12,0.16)
Diff vs. PBO	0.04 (0.02,0.06)	0.06 (0.04,0.09)	--	0.05 (0.03,0.07)	0.06 (0.04,0.08)	--	--	--	--
Nominal p-value	<0.0001	<0.0001	--	<0.0001	<0.0001	--	--	--	--

CI=Confidence interval; Diff=Difference

Figure. LS mean change from baseline in EQ-VAS Scores (W0-100)



[a] Pts receiving PBO crossed over to GUS 100 mg Q4W at W24

Conclusion: In bio-naïve pts with active PsA receiving GUS, earlier improvements (at the first timepoint assessed) in self-reported HRQoL measures were sustained through 2 years.

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AB0882 GUSELKUMAB: DESCRIPTION OF CARDIOVASCULAR RISK AND EFFICACY IN PSORIASIS AND PSORIATIC ARTHRITIS IN REAL CLINICAL PRACTICE

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Background: Guselkumab is the first human monoclonal antibody that binds selectively to the p19 subunit of IL23. It's approved for the treatment of moderate to severe psoriasis and psoriatic arthritis.

Objectives: We present a case series of patients with psoriasis and / or psoriatic arthritis who had a good response to Guselkumab and theirs cardiovascular risk factors.

Methods: An observational and retrospective study of patients with psoriasis and / or psoriatic arthritis under treatment with Guselkumab in the Dermatology and Rheumatology consultation at our hospital. A total of 11 patients were included. Baseline characteristics, comorbidities, and cardiovascular risk were collected. The SCORE (European High Risk Chart) and cardiovascular risk categories (European Society of Cardiology, European Atherosclerosis Society 2019) were used. Disease severity and treatment response were assessed by PASI, DLQI, DAPSA and ASDAS at baseline and after 12, 24 and 36 weeks.

Results: Our cases had a mean age of 52.45 years, 63.6% of them were women. A total of 45.5% had polyarticular psoriatic arthritis. 90.9% were obese, 45.45% were type 2 obesity, with a mean BMI of 34.88. Dyslipidemia and hypertension were observed in 54.5% and 72.7% of the patients, respectively. They all had varying degrees of Non-alcoholic fatty liver disease (NAFLD). A total of 45.5% had SCORE >1% and 90.9% were in moderate category of cardiovascular risk. At baseline their disease parameters were: PASI=11.09 (± 7.01), DLQI=15.09 (± 7.33), DAPSA=19.11 (± 9.95) and ASDAS=2.12 (± 0.43). After 12 weeks of treatment, the mean reduction of PASI and DLQI was 7.09 and 6.45, which continued improving at week 36. None of them were naive. There were no adverse effects, with a treatment survival of 76.73 weeks (± 42.93).

Conclusion: Guselkumab showed excellent results in our clinical practice in the control of psoriasis and / or psoriatic arthritis in non-naive patients with cardiovascular risk factors, with a good safety profile.

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AB0883 REAL-WORLD TREATMENT PATTERNS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a complex inflammatory disease with manifestations that play an important role in treatment selection.[1] Treatments include oral agents, biologic therapies (inhibitors of tumor necrosis factor [TNFi], interleukin [IL-17Ai, IL-12/23i], cytotoxic T lymphocyte–associated antigen 4 inhibitor [CTLA-4i]), and new targeted oral agents (inhibitors of phosphodiesterase-4 [PDE-4i] and Janus kinase [JAKi]).[1] Few studies have examined real-world treatment patterns of recently approved therapies.
Objectives: Evaluate real-world treatment patterns for branded systemic therapy in patients with PsA.
Methods: In this retrospective study, medical and pharmacy claims from the US IBM MarketScan Commercial and Medicare databases (1/1/2012–12/31/2019) were used to identify patients with PsA who initiated treatment with a TNFi (adalimumab, etanercept, infliximab, golimumab, or certolizumab), IL-17Ai (secukinumab, ixekizumab), IL-12/23p40i (ustekinumab), IL-23p19i (guselkumab), CTLA-4i (abatacept), JAKi (tofacitinib), or PDE-4i (apremilast). Patients (≥18 years) with ≥1 prescription, ≥2 PsA claims separated by ≥1 day on or before the index date (first prescription date [1/1/13–12/31/2018]), and 1-year continuous enrollment before and after the index date were eligible. Treatment patterns were grouped into continuers, discontinuers, and patients with treatment modification (switchers [without a treatment gap], reinitiators [same drug with a treatment gap], and restarters [different drug with a treatment gap]) (Table 1). Patients were followed for 1 year or until treatment modification, whichever came first. Descriptive statistics were used.

Table 1. Terminology

Cohort	Definition	n/N (%)
Continuers	On index treatment during 1-year follow-up with no treatment gaps*	1910/6455 (29.6)
Discontinuers	No prescription claims for any therapy during 1-year follow-up	1614/6455 (25.0)
Patients with treatment modifications	All patients with a change in treatment during 1-year follow-up	2908/6455 (45.1)
Switchers	Prescription claims for treatments different than index therapy before permissible treatment gaps*	794/6455 (12.3)
Reinitiators	Prescription claims for treatments SAME as index therapy AFTER treatment gaps*	1686/6455 (26.1)
Restarters	Prescription claims for DIFFERENT therapy AFTER treatment gap*	428/6455 (6.6)

Note: All terminology applies to cohorts within the first year of treatment.*Treatment gap: gap of 200% of recommended dosing schedule from end of previous prescription's days' supply.

Results: A total of 6455 patients were included (mean age, 50.5 years; 55.5% female; mean Charlson Comorbidity Index score, 0.54). At baseline, the most commonly used therapies were immunosuppressants (58.5%), corticosteroids (52.2%), and nonsteroidal anti-inflammatory drugs (45.9%). Treatments most used at index were TNFi (72.5%; including adalimumab [41.6%] and etanercept [23.8%]) and the PDE-4i apremilast (21.1%). During the 1-year study period, 29.6% of patients maintained their index therapy and 25.0% discontinued. Treatment modification was observed in 45.1% of patients; 12.3% switched to a new therapy without a treatment gap, 26.1% restarted their index therapy, and 6.6% started a new therapy after a treatment gap.
Conclusion: Among patients with PsA, there is substantial variability, including high rates of discontinuation within the first year and after index therapy. Further studies are warranted to understand reasons for these treatment patterns.
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AB0884 DISEASE OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS COMPLETING 12 MONTHS OF APREMILAST TREATMENT - REAL-WORLD DATA FROM THE REWARD STUDY

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Background: Patients with moderately active psoriatic arthritis (PsA) and limited joint involvement have considerable disease burden[1,2]. Recent data shows these patients have a high likelihood of achieving treatment goals if treated with apremilast[3]. This is the first report of outcomes in patients with PsA who received apremilast for 12 months in Dutch clinical practice.
Objectives: We report disease outcomes, including the PsA Impact of Disease (PsAID) 12-item questionnaire, swollen joint count (SJC), tender joint count (TJC), dactylitis and enthesitis, among patients in the prospective, multicenter, observational REWARD study who completed 12 months of apremilast treatment.
Methods: The ongoing REWARD study enrolled patients who had initiated apremilast for the treatment of PsA in the Netherlands between 13 April 2017 and 24 March 2021, and includes up to 12 months follow-up[1,4]. We report interim data from patients with data available as of 16 September 2021. Baseline data are summarized separately for patients who discontinued apremilast before their month 12 study visit (stoppers) and patients still receiving apremilast at their month 12 visit (completers). Post baseline data are summarized for completers. Continuous data are summarized using mean and SD, categorical data are summarized using n and percent.
Results: 98 patients were included in this interim analysis; 32 had completed 12 months of apremilast treatment (completers), 54 had discontinued apremilast before month 12 (stoppers), 12 were ongoing in the study. Compared with stoppers, completers were more likely to be biologic naïve and have dactylitis, and had lower BSA. All other baseline characteristics were similar (Table 1). Among completers, all PsAID domains improved after 3 months of apremilast treatment and these improvements were maintained through month 12 (Figure 1). Mean SJC and TJC decreased between baseline and month 12 (SJC, 4.2 and 1.0 at baseline and month 12, respectively; TJC, 7.1 and 3.3, respectively). The proportion of completers with SJC, TJC, enthesitis and dactylitis scores of 0 increased from baseline to month 12 (Figure 1B). The proportion of completers reporting at least one adverse event (AE) was comparable to the overall study population (14/32 [44%] and 48/98 [49%], respectively); the reported adverse events were similar to the known safety profile of apremilast.

Table 1. Baseline characteristics

Baseline Characteristics		All (n=98) N(%)	Completers (n=32) N(%)	Stoppers (n=54) N(%)
Gender	Male	50 (51.0)	18 (56.3)	26 (48.2)
	Female	48 (49.0)	14 (43.8)	28 (51.9)
Age (Years)	Mean (SD)	53.0 (11.6)	52.8 (12.1)	53.2 (12.1)
BMI (kg/m²)	Mean (SD)	28.7 (5.8)	28.9 (4.8)	28.5 (6.5)
Prior Biologicals Given?	Yes	25 (25.8)	1 (3.1)	23 (43.4)
PsO	Yes	77 (78.6)	25 (78.1)	42 (77.8)
BSA PsO (%)	Mean (SD)	5.6 (11.2)	2.2 (4.0)	8.0 (14.2)
SJC (0-66)	Mean (SD)	3.7 (5.2)	4.2 (6.1)	4.0 (5.0)
TJC (0-68)	Mean (SD)	6.9 (9.3)	7.1 (9.8)	7.6 (9.8)
PSAID12 (0-10)	Mean (SD)	4.5 (1.9)	4.3 (1.9)	4.6 (2.1)
VAS Pain	Mean (SD)	43.3 (27.6)	45.3 (25.3)	43.0 (29.8)
CRP (mg/L)	Mean (SD)	7.6 (9.8)	6.0 (7.3)	7.3 (8.6)
Dactylitis (Yes)	(%)	35	53	29
Enthesitis (yes)	(%)	43	47	48
cDAPSA	Mean (SD)	19.8 (15.2)	20.3 (15.5)	20.8 (16.1)
	Rem-Low-Mod	73 (21.5)	24 (77.4)	39 (75.0)
	High	20 (78.5)	7 (22.6)	13 (25.0)
PsA Duration (Years)	Mean (SD)	7.6 (8.0)	7.7 (8.3)	7.5 (7.3)

All=all patients included in this interim analysis; Completers= patients that received apremilast for 12 months; Stoppers= patients that stopped apremilast treatment prior to 12 months.BMI=Body Mass Index, PsO=Psoriasis, BSA PsO= Body Surface Area Psoriasis, SJC=Swollen Joint Count, TJC=Tender Joint Count, PsAID=Psoriatic Arthritis Impact of Disease, VAS=Visual Analog Scale, CRP= C-reactive protein, cDAPSA=Clinical Disease Activity in Psoriatic Arthritis, Rem=Remission, Mod=Moderate, PsA= Psoriatic Arthritis

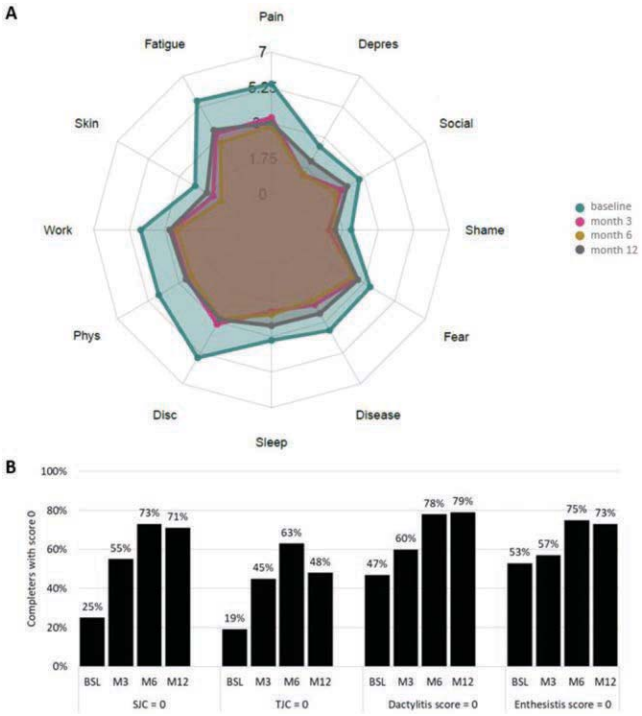

Figure 1. (A) PSAID scores in completers and (B) percentage of completers with no swollen joints, no tender joints, no dactylitis and no enthesitis at baseline (BSL), month 3, 6 and 12 (M3, M6, M12).

Conclusion: In this interim analysis of the REWARD study, patients completing 12 months of apremilast treatment were more likely to be biologic naïve than patients who discontinued apremilast within 12 months of initiation, and had significant decreases in TJC, SJC, dactylitis and enthesis during apremilast treatment. Completed patients also reported decreased PsAID scores during apremilast treatment, indicating improvements in their quality of life.

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AB0885

REFRACTORY CHRONIC SYNOVITIS OF THE COMMON FLEXOR SYNOVIAL SHEATH IN PSORIATIC ARTHRITIS PATIENT SUCCESSFULLY TREATED BY ULTRASOUND GUIDED LOCAL METHOTREXATE INJECTION.

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Background: Psoriatic arthritis (PsA) is a variant of inflammatory musculoskeletal conditions that usually associated with skin psoriasis. PsA is typically heterogenous in comparison to other rheumatic diseases, It affects multiple musculoskeletal domains including synovitis of peripheral and axial joints, entheses, and tendons with tenosynovitis. [1,2]

Persistent cases of arthritis or tenosynovitis usually controlled by local injection with corticosteroids, though some refractory cases of chronic synovitis still not sufficiently controlled by corticosteroid local injection with some case series shows a significant response to local DMARDs and even local Biologics. [3-6]

Objectives: To describe a case of psoriatic arthritis with chronic synovitis of the common flexor synovial sheath successfully treated by ultrasound guided local Methotrexate injection.

Methods: 31 Years old female with psoriatic arthritis in the form of symmetrical hand arthritis for the last 10 years, and extensive nail disease shows partial control under treatment with Methotrexate after failure of sulfasalazine. Her DAPSA score usually ranges between 16 to 18 with tender persistent fluctuating cystic swelling overlying her right palm extending proximally to the distal third of the forearm that becomes more tens on fingers flexion. Ultrasound examination shows hypoechoic distension of the right common flexor synovial sheath, that is partially compressible and partially displaceable with highly positive Doppler signals indicating active synovitis. Figure 1

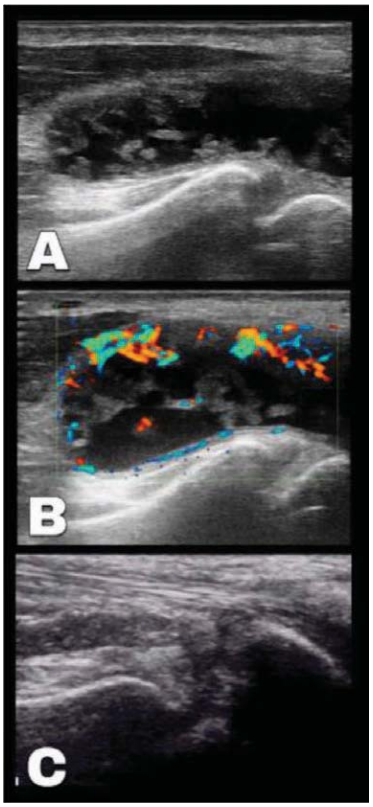

Figure 1. palmar longitudinal ultrasound scan over the radio-carpal region, A: Synovitis with effusion in the common flexor Sheath, B: Positive Color Doppler denoting active synovitis, C: Follow up ultrasound scan showing resolution of synovitis and effusion.

October 2019, ultrasound guided aspiration and local corticosteroid injection applied for the common flexor sheath with escalation of her treatment to Ixekizumab plus Methotrexate to achieve clinical remission. January 2020, patient achieve DAPSA 8 with resolution of have nail lesions, though her right hand function was still significantly impaired due to the refractory persistent synovitis of the Common flexor sheath. Two doses 15mg Methotrexate one week apart inserted into the common flexor sheath under ultrasound imaging.

Results: April 2020, on regular follow up patient achieve DAPSA remission <4, with complete resolution of the right palm swelling and she reports complete recovery of her hand function which is maintained up to January 2022 in her last

follow up visit. Follow up ultrasound scan shows normalization of the common flexor sheath with disappearance of the mixed picture of synovitis and effusion. Figure 1

Conclusion: Refractory synovitis of the common flexor sheath in PsA successfully treated with ultrasound guided local methotrexate injection with persistence of improvement for one year.

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Disclosure of Interests: None declared
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AB0886 THE IMPACT OF DEUCRAVACITINIB ON HEALTH-RELATED QUALITY OF LIFE MEASURED BY THE SHORT FORM HEALTH SURVEY 36-ITEM QUESTIONNAIRE: ANALYSIS OF A PHASE 2 TRIAL IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Patients (pts) with psoriatic arthritis (PsA) experience pain, loss of physical function, joint damage, and significant impairments in social and emotional well-being. The Short Form Health Survey 36-item questionnaire (SF-36v2), a generic measure of pt-reported health-related quality of life (HRQOL), includes 36 items and measures 8 domains—physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH)—that contribute to both physical component summary (PCS) and mental component summary (MCS) scores. Deucravacitinib (DEUC) is a novel, oral, selective, allosteric inhibitor of tyrosine kinase 2 (TYK2), an intracellular kinase that mediates cytokine signalling pathways implicated in PsA pathogenesis. In a Phase 2 trial in pts with active PsA, DEUC was well tolerated and significantly more efficacious than placebo (PBO) after 16 weeks (wks) of treatment.[1]

Objectives: To further evaluate the effect of DEUC treatment on SF-36 scores.

Methods: This double-blind Phase 2 trial (NCT03881059) enrolled pts with a PsA diagnosis ≥6 months who fulfilled Classification Criteria for Psoriatic Arthritis at screening and had active joint disease (≥3 tender and ≥3 swollen joints), high-sensitivity CRP ≥3 mg/L, and ≥1 plaque psoriasis lesion (≥2 cm). Pts failed or were intolerant to ≥1 nonsteroidal anti-inflammatory, conventional synthetic DMARD, and/or 1 TNF inhibitor (≤30%). Pts were randomised 1:1:1 to DEUC 6 mg once daily (QD) or 12 mg QD, or PBO. Changes from baseline (BL) in SF-36 PCS and MCS scores at Wk 16 were prespecified key secondary and additional endpoints, respectively. The 8 SF-36 domain scores were evaluated at Wk 16. The proportions of pts reporting improvements ≥2.5 and ≥5 points (the minimum clinically important difference [MCID]) in SF-36 summary and domain scores, respectively, were evaluated.

Results: Of 203 pts randomised, 180 (89%) completed 16 wks of treatment (DEUC 6 mg QD, 63/70 [90%]; DEUC 12 mg QD, 59/67 [88%]; PBO, 58/66 [88%]). Demographic and BL disease characteristics were similar across groups. BL mean SF-36 PCS and MCS scores were similar among DEUC 6 mg QD, 12 mg QD, and PBO groups (PCS: 34.0, 34.5, and 33.4; MCS: 45.4, 46.9, and 47.5, respectively). At Wk 16, adjusted mean changes from BL in SF-36 PCS and MCS scores were significantly improved with DEUC 6 and 12 mg QD treatment vs PBO (PCS: 5.6, 5.8, and 2.3; MCS: 3.6, 3.5, and 0.7, respectively; $P<0.05$). Reported improvements in domain scores with both doses exceeded MCID and were significant in 5 of 8 domains with DEUC 6 mg QD (PF, RP, BP, VT, and SF) and 6 of 8 domains with DEUC 12 mg QD (RE in addition; Figure 1 **and** Table 1).

Table 1. Improvements reported in SF-36 domains with deucravacitinib 6 mg QD and 12 mg QD vs placebo at Week 16

	PF	RP	BP	GH	VT	SF	RE	MH
Deucravacitinib 6 mg – BL	41.9	42.9	32.5	39.6	39.0	57.0	69.5	58.4
Deucravacitinib 12 mg – BL	44.1	46.0	33.4	38.5	43.0	65.5	71.5	59.2
Placebo – BL	42.4	42.8	31.7	40.3	38.8	63.8	75.1	59.9
Deucravacitinib 6 mg – LSM Wk 16	14.6	12.3	15.9	9.5	11.7	13.2	6.9	8.1
Deucravacitinib 12 mg – LSM Wk 16	13.3	13.5	19.5	8.4	12.1	10.5	8.7	8.2
Placebo – LSM Wk 16	3.3	5.3	7.0	6.2	4.2	-0.2	1.6	3.6
Protocol A/G norms	81.1	81.9	72.5	70.2	59.1	85.1	88.0	76.2

Domain scores range from 0-100, with higher scores indicating better health status.A/G, age/gender; BL, baseline; BP, bodily pain; GH, general health; LSM, least square mean change; MH, mental health; PF, physical functioning; QD, once daily; RE, role-emotional; RP-role-physical; SF, social functioning; SF-36, Short Form-36; VT, vitality; Wk, week.

Conclusion: Pts with PsA treated with DEUC reported clinically meaningful and significant improvements in HRQOL, including fatigue, social functioning and role emotional in addition to physical functioning, role physical and pain, at Wk 16.

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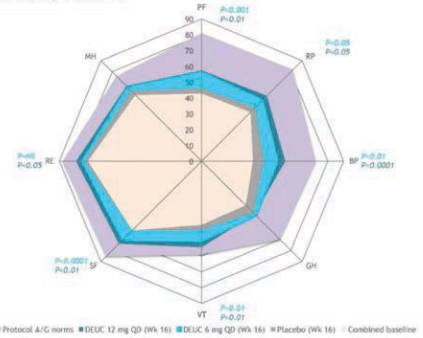
Figure. Improvements reported in SF-36 domains with deucravacitinib 6 mg QD and 12 mg QD vs placebo at Week 16



Scores for each domain range from 0-100, with higher scores indicating better health status.
A/G, age/gender; BP, bodily pain; DEUC, deucravacitinib; GH, general health; MH, mental health; PF, physical functioning; QD, once daily; NS, not significant; RE, role-emotional; RP, role-physical; SF, social functioning; SF-36, Short Form-36; VT, vitality; Wk, week.

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AB0887 DESIGNING A PHASE 3B, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO INVESTIGATE THE EFFECT OF GUSELKUMAB DOSING INTERVAL IN PSORIATIC ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO TUMOR NECROSIS FACTOR INHIBITION

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Background: Tumor necrosis factor inhibitors (TNFi) are frequently chosen as the first biologic therapy for patients (pts) with psoriatic arthritis (PsA), though a sizeable proportion of pts have an inadequate response (IR), and some may also have intolerance. Guselkumab (GUS), a human mAb that targets the IL-23 p19 subunit, provides an alternative mechanism of action to treat PsA. In the Phase 3 (Ph3) DISCOVER-1 study of GUS in active PsA, GUS every 4 weeks (Q4W) and Q8W clinical response rates were generally consistent between TNFi-naïve (263 pts) and TNFi-experienced (118 pts) cohorts. In the TNFi-experienced cohort and the limited number of DISCOVER-1 pts with IR to their prior TNFi (N=44), American College of Rheumatology 50% improvement (ACR50) and ACR70 response rates at W24 were numerically higher in GUS Q4W- than Q8W-treated pts.[1]
Objectives: To further investigate whether GUS Q4W could provide incremental benefit to some TNFi-IR PsA pts by analyzing the existing DISCOVER-1 dataset to facilitate the design of a new clinical trial.
Methods: Study feasibility assessments included comparison of key efficacy endpoints by treatment group at W24 among TNFi-experienced pts receiving GUS Q8W and Q4W in DISCOVER-1. Results from the DISCOVER-1 study also informed sample size power calculations for a primary endpoint of ACR20 response at W24 in a future study in a TNFi-IR PsA pt population.
Results: Comparison of several efficacy endpoints (ACR70 response, minimal disease activity, Investigator's Global Assessment [IGA] of psoriasis 0/1 response) across treatment groups in the TNFi-experienced DISCOVER-1 cohort supports a potential dose response, with more frequent GUS administration eliciting numerically higher response rates (Table 1). A similar trend was observed for ACR20/50/70 responses in the smaller TNFi-IR population[1], though these findings should be interpreted with caution due to limited sample size. ACR20 response rates at W24 of DISCOVER-1 were employed to estimate sample size requirements for a new study. Assuming comparable rates of GUS treatment effect seen in DISCOVER-1, a sample size of 150 randomized pts per group for PBO, GUS Q8W, and GUS Q4W would provide >90% power to detect a significant difference between each GUS group and PBO for ACR20 response at W24. Based on these findings, a new Ph3b, multicenter, randomized, double-blind, PBO-controlled study, SOLSTICE, was designed to further evaluate the efficacy and safety of GUS in approximately 450 pts with active PsA who had IR to one prior TNFi, and to investigate the effect of GUS dosing interval in this important cohort of pts with PsA (Figure 1).

Table 1. Clinical efficacy at W24 among DISCOVER-1 TNFi-experienced pts

	Placebo	GUS Q8W	GUS Q4W
ACR20	17.9% (7/39)	56.1% (23/41)	57.9% (22/38)
ACR50	5.1% (2/39)	26.8% (11/41)	34.2% (13/38)
ACR70	2.6% (1/39)	2.4% (1/41)	21.1% (8/38)
MDA	2.6% (1/39)	17.1% (7/41)	26.3% (10/38)
IGA 0/1[a]	7.7% (2/26)	48.3% (14/29)	67.9% (19/28)

[a]IGA score of 0 (clear) or 1 (almost clear) among pts with ≥3% body surface area of psoriatic involvement and an IGA score ≥2 (mild-to-severe psoriasis) at baseline.ACR20/50/70, American College of Rheumatology 20%/50%/70% improvement; GUS, guselkumab; IGA, Investigator's Global Assessment; MDA, minimal disease activity; Q4W, every 4 weeks; Q8W, every 8 weeks; TNFi, tumor necrosis factor inhibitor; W, week

Conclusion: PsA pts with TNFi-IR are typically difficult to treat. Overall data from the pivotal DISCOVER-1 study of GUS in pts with active PsA showed consistent clinical response between doses and between TNFi-naïve and TNFi-experienced pts. Analyses based on limited numbers of TNFi-experienced pts from DISCOVER-1 demonstrated potential incremental benefit for achievement of higher response criteria with more frequent dosing in some TNFi-IR pts. SOLSTICE, a Ph3b, randomized, placebo-controlled study, will test this hypothesis.
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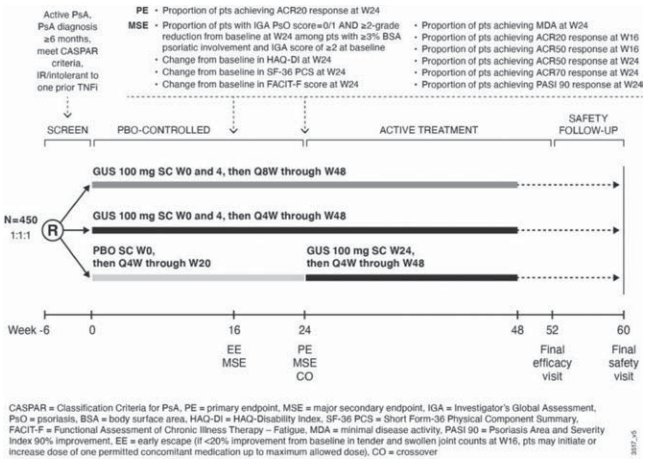

Figure 1.

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AB0888 GUSELKUMAB PROVIDES SUSTAINED IMPROVEMENTS IN WORK PRODUCTIVITY AND DAILY ACTIVITY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH 2 YEARS OF DISCOVER-2

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Background: Psoriatic arthritis (PsA) impacts patients' (pts) work productivity (WP) and daily activity.[1] DISCOVER-2 (D2), a Phase 3 trial of the selective interleukin-23 p19-subunit inhibitor guselkumab (GUS) in biologic-naïve pts with PsA,[2] demonstrated significant improvements in pt-reported WP and daily activity following 1 year (Y) of GUS treatment.[3]

Objectives: Assess WP and daily activity impairment in D2 pts through 2Y. Estimate indirect savings associated with GUS treatment and assess changes in employment status.

Methods: Pts with active PsA received GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). At W24, PBO pts crossed over to GUS 100 mg Q4W. WPAI-PsA assesses PsA-related work time missed (absenteeism), impairment while working (presenteeism), and impaired overall WP (absenteeism + presenteeism) for pts employed at baseline (EBL) and daily activity for all pts, including those unemployed at baseline (UBL) during the previous week. Mean changes in WPAI-PsA domains were calculated for each multiple imputation (MI) dataset using an analysis of covariance (ANCOVA); the reported LS mean is the average of all MI datasets. Significance was defined as $p<0.05$. Among pts EBL, potential indirect savings from improved overall WP were estimated using 2020 European Union mean yearly wage estimate (all occupations) combined with LS mean change from BL in WPAI-PsA overall work impairment.[4] A shift analysis evaluated proportions of pts employed vs unemployed by treatment group using observed data over time.

Results: Pts EBL comprised 64% of the analysis cohort. Significant improvements in WP in pts EBL and in daily activity among all pts were observed with GUS Q4W/Q8W vs PBO at W24;[3] mean improvements in WP and daily activity increased with continued GUS through 2Y (Table 1). Potential annual indirect savings from improved overall WP in pts EBL were *€10,826* GUS Q4W, *€12,712* GUS Q8W, and *€10,948* PBO→ GUS Q4W at 2Y. Shift analysis showed relatively stable employment in pts EBL with GUS up to 2Y (>83% continued to work). Among pts UBL (36% of cohort), the proportion of pts employed increased by >20% through 2Y of GUS (Figure 1).

Conclusion: In GUS-treated bio-naïve PsA pts, robust improvements in WP and daily activity seen at W24 were maintained and increased through 2Y of GUS. Long-term improvements in WP achieved may result in substantial indirect cost savings for GUS-treated pts. Rates of employment remained stable in pts employed and increased in those unemployed at BL.

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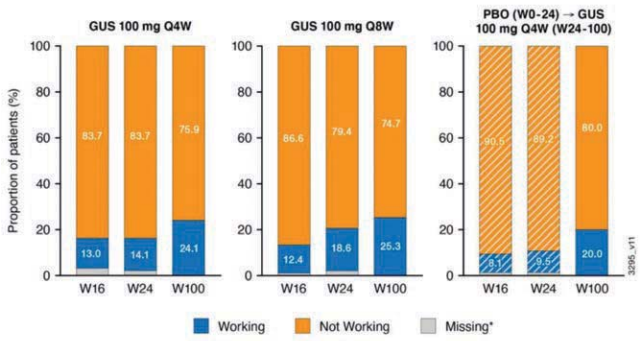
Figure. Change in Employment Status Among Pts UBL



GUS 100 mg Q4W (N = 92), GUS 100 mg Q8W (N = 97), PBO (W0-24) → GUS 100 mg Q4W (W24-100) (N = 74)
* GUS 100 mg Q4W: W16, 3.3%; W24, 2.2%. GUS 100 mg Q8W: W16, 1.0%; W24, 2.1%. PBO (W0-24) → GUS 100 mg Q4W (W24-100): W16, 1.4%; W24, 1.4%.

Table 1. Model-Based Estimates of Change From BL in WPAI-PsA Domains[1]

	GUS 100mg Q4W		GUS 100mg Q8W		PBO (W0-24) → GUS 100 mg Q4W (W24-100)	
Visit	W24	W100	W24	W100	W24	W100
Absenteeism, N	145	147	147	149	162	166
LS Mean (95% CI)	-3.4 (-6.5, -0.3)	-1.8 (-4.5, 0.9)	-3.0 (-6.0, 0.1)	-4.2 (-6.8,-1.5)	-3.0 (-6.0, 0.04)	-4.2 (-6.8,-1.6)
Diff vs. PBO	-0.4 (-4.6, 3.8)	-	-0.01 (-4.2, 4.2)	-	-	-
Presenteeism, N	145	147	147	149	162	166
LS Mean (95% CI)	-20.1 (-23.7, -16.6)	-26.3 (-30.1,-22.5)	-19.6 (-23.2, -16.1)	-28.0 (-31.8, -24.2)	-10.5 (-13.9, -7.0)	-24.2 (-27.9, -20.5)
Diff vs PBO	-9.7* (-14.4, -5.0)	-	-9.2* (-13.9, -4.5)	-	-	-
Work productivity, N	145	147	147	149	162	166
LS Mean (95% CI)	-20.1 (-24.1, -16.1)	-23.8 (-28.0, -19.6)	-19.2 (-23.1, -15.2)	-28.0 (-32.1, -23.8)	-10.6 (-14.4, -6.8)	-24.1 (-28.1, -20.1)
Diff vs PBO	-9.5* (-14.8, -4.2)	-	-8.6* (-13.9, -3.3)	-	-	-
Daily Activity, N	242	242	246	246	245	245
LS Mean (95% CI)	-20.5 (-23.3, -17.7)	-29.2 (-32.2, -26.1)	-21.2 (-23.9, -18.4)	-28.0 (-31.0, -24.9)	-9.9 (-12.6, -7.1)	-26.6 (-29.6, -23.6)
Diff vs PBO	-10.6* (-14.4, -6.8)	-	-11.3* (-15.1, -7.5)	-		

[1]Mean changes in WPAI-PsA domains were calculated for each MI dataset using an ANCOVA; reported LS mean (95% confidence interval [CI]) = average of all MI datasets.*p<0.002

AB0889

ASSOCIATION BETWEEN CLINICALLY MEANINGFUL IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES AND STRINGENT MEASURES OF DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH UPADACITINIB VERSUS PLACEBO OR ADALIMUMAB: RESULTS FROM A PHASE 3 TRIAL

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Background: The achievement of disease control has been shown to be associated with improved prognosis in PsA, though no single measure of low disease activity or remission is currently universally accepted. Patient-reported outcomes

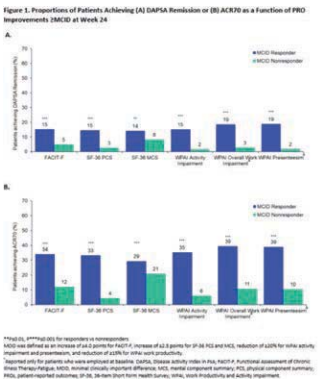
(PROs) have been well-established in PsA and are important indicators of patient improvement while on treatment. To date, the association between PROs and disease control in PsA has not been fully characterized.

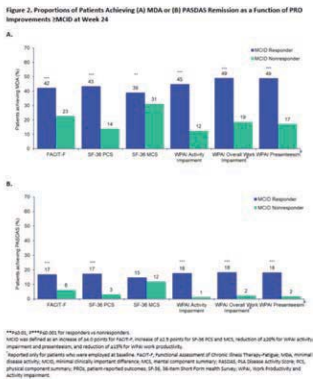
Objectives: We examined the association between clinically meaningful improvement in PROs and stringent measures of disease control among patients with PsA enrolled in the Phase 3 SELECT-PsA 1 trial.

Methods: Patients with active PsA and an inadequate response to ≥1 non-biologic DMARDs were randomized to receive upadacitinib (UPA) 15 mg once daily (QD), UPA 30 mg QD, adalimumab (ADA) 40 mg every other week, or PBO for 24 weeks. PROs included: Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), 36-Item Short-Form Health Survey (SF-36), and Work Productivity and Activity Impairment (WPAI). Measures of stringent disease control included achievement of minimal disease activity (MDA), ACR70 response, and remission based on Disease Activity Index in PsA (DAPSA ≤4.0) or PsA Disease Activity Score (PASDAS ≤1.9). The percentage of patients achieving stringent disease control was determined among patients reporting vs not reporting PRO improvements ≥ minimal clinically important differences (MCID) in the combined active treatment and PBO group at Week 24.

Results: A total of 1704 patients were included in the SELECT PsA 1 trial, of whom 59.2%, 72.4%, 51.3%, 62.3%, 64.6%, and 63.9% reported improvements ≥ MCID (MCID responders) in FACIT-F, SF-36 physical component summary score, SF-36 mental component summary (MCS) score, WPAI activity impairment, WPAI overall work impairment, and WPAI presenteeism, respectively, at week 24. The percentage of patients achieving MDA, ACR70 or DAPSA remission at week 24 was significantly higher (nominal $P \leq 0.01$) among patients who reported improvements ≥ MCID for all PROs vs those who did not (Figures 1, 2). Similar results were seen in patients achieving PASDAS remission except for SF-36 MCS score (Figure 2). Among patients reporting improvements ≥ MCID across all PROs, more patients achieved ACR70 and MDA responses (29%-49%) with fewer patients achieving DAPSA or PASDAS remission (14%-19%).

Conclusion: PsA patients who reported clinically meaningful improvements in key PROs: fatigue, quality of life, and work productivity were more likely to achieve stringent measures of disease control. These results suggest a close association between meaningful improvements in patient-centric outcomes and achievement of stringent disease control.





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AB0890

DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 INHIBITOR, IN MODERATE TO SEVERE PLAQUE PSORIASIS: 52-WEEK EFFICACY RESULTS FROM THE PHASE 3 POETYK PSO-1 AND POETYK PSO-2 TRIALS

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Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling of key cytokines (eg, interleukin [IL]-23 and Type I interferons) involved in the pathogenesis of immune-mediated diseases including plaque psoriasis and psoriatic arthritis (PsA). Deucravacitinib is a novel, oral, selective, allosteric inhibitor of TYK2 that achieves high selectivity by uniquely binding to the regulatory domain of the enzyme, rather than to the more conserved active domain. Deucravacitinib showed superior efficacy compared with placebo at 16 weeks in a Phase 2 trial in patients with PsA (NCT03881059). Results from the 16-week, placebo-controlled periods of two 52-week, Phase 3 trials in psoriasis (POETYK PSO-1 and POETYK PSO-2) previously showed that deucravacitinib was significantly more efficacious than placebo and apremilast based on the coprimary endpoints of ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and a static Physician's Global Assessment (sPGA) score of 0 or 1 (clear or almost clear) at Week 16.

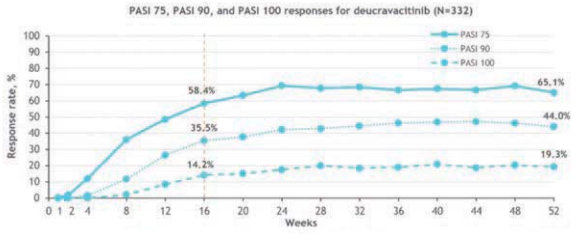
Objectives: To evaluate the efficacy of deucravacitinib over 52 weeks in the POETYK PSO-1 and POETYK PSO-2 trials.

Methods: POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) were double-blinded trials that randomised patients with moderate to severe plaque psoriasis (body surface area involvement ≥10%, PASI ≥12, sPGA score ≥3) 2:1:1 to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily. Patients receiving placebo were switched to deucravacitinib at Week 16 in both trials. Patients randomised to deucravacitinib in PSO-1 received deucravacitinib continuously through Week 52. PSO-2 included a randomised withdrawal phase in which patients originally randomised to deucravacitinib who had achieved PASI 75 response at Week 24 were rerandomised 1:1 to placebo or deucravacitinib, whereas those who did not achieve PASI 75 response at Week 24 continued receiving deucravacitinib. The proportions of patients achieving PASI 75 and sPGA 0/1 responses were evaluated up to Week 52. Secondary efficacy endpoints evaluated over this period included PASI 90, PASI 100, percentage change from baseline in PASI, sPGA 0 (clear), change from baseline in the Psoriasis Symptoms and Signs Diary (PSSD) symptom score, and Dermatology Life Quality Index (DLQI) 0/1 (no impact on patient's life).

Results: A total of 666 and 1020 patients were randomised in PSO-1 and PSO-2, respectively. Demographic and baseline disease characteristics were balanced across treatment groups; mean age was 46.6 years, mean disease duration was 18.6 years, 18.4% of patients had PsA, and 34.8% had previously used biologic therapy. PASI 75, PASI 90, and PASI 100 responses were maintained from Week 16 to Week 52 in PSO-1 (Figure 1). Additionally, sPGA responses were maintained during this period (sPGA 0/1: 53.6% to 52.7%; sPGA 0: 17.5% to 23.5%, respectively). Patients who switched from placebo to deucravacitinib at Week 16 demonstrated PASI 75 and sPGA 0/1 responses at Week 52 (68.3% and 53.8%, respectively) comparable to those observed in patients who received continuous deucravacitinib treatment from Day 1 (65.1% and 52.7%, respectively). In PSO-2, among deucravacitinib-treated patients who achieved PASI 75 at Week 24 and were rerandomised to continue treatment, responses were maintained at Week 52 in the majority of patients (PASI 75, 80.4% [119/148]; sPGA 0/1, 70.3% [83/118]). Results for percentage change from baseline in PASI, change from baseline in the PSSD symptom score, and DLQI 0/1 were consistent with those reported for PASI and sPGA responses.

Conclusion: Results from the Phase 3 POETYK PSO-1 and PSO-2 trials demonstrated that deucravacitinib was efficacious through 52 weeks in patients with moderate to severe plaque psoriasis. Clinical responses were maintained in patients who received continuous deucravacitinib treatment and were improved in patients who switched from placebo at Week 16 to deucravacitinib treatment.

Figure. PASI responses with deucravacitinib 6 mg QD through Week 52 - POETYK PSO-1 (NRI)



NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; PASI 90, ≥90% reduction from baseline in PASI; PASI 100, 100% reduction from baseline in PASI; QD, once daily.

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Warren Consultant of: Consulting fees: AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, DiCE, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, UCB, Biogen, and UNION., Grant/research support from: Research grants: AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, and UCB;, April Armstrong Grant/research support from: Grants and personal fees: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Parexel, Celgene, Dermavant, Genentech, GlaxoSmithKline, Menlo Therapeutics, Merck, Modernizing Medicine, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Science 37, Sun Pharma, and Valeant; Grants: Dermira, Kyowa Hakko Kirin, and UCB, outside the submitted work., Melinda Gooderham Consultant of: Advisory board, principal investigator, and lecture fees: Arcutis, Galderma, Leo Pharma, Pfizer, and Regeneron; Principal investigator and consulting fees: Akros Pharma and Kyowa Kirin; 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AB0891

DEUCRAVACITINIB EFFICACY IN PSORIATIC ARTHRITIS BY BASELINE DMARD USE: EXPLORATORY ANALYSIS FROM A PHASE 2 STUDY

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Background: Psoriatic arthritis (PsA) treatment guidelines recommend that patients (pts) inadequately responding to conventional synthetic DMARDs (csDMARDs) can be treated with targeted synthetic DMARDs with or without background use of csDMARDs. Deucravacitinib (DEUC) is a novel, oral, selective, allosteric inhibitor of tyrosine kinase 2 (TYK2) that binds to the unique TYK2 regulatory domain, thereby suppressing signaling of key cytokines (eg, IL-23) involved in PsA pathogenesis. In a Phase 2 trial in pts with active PsA, DEUC was well tolerated and significantly more efficacious than placebo (PBO) after 16 weeks of treatment.[1]

Objectives: This analysis further evaluated the effect of DEUC in this Phase 2 trial in pts treated with and without background csDMARDs for 16 weeks.

Methods: This double-blind trial (NCT03881059) enrolled pts with active PsA who had either failed or were intolerant to ≥1 nonsteroidal anti-inflammatory drug, corticosteroid, csDMARD, and/or 1 TNF inhibitor (TNFi; up to 30%). Pts were randomised 1:1:1 to DEUC 6 mg once daily (QD) or 12 mg QD, or PBO. A post hoc subgroup analysis in pts with and without background csDMARD use assessed improvements in select clinical outcomes (ACR 20 response, and change from baseline in ACR components, Psoriasis Area and Severity Index total score, and Psoriatic Arthritis Disease Activity Score) at Week 16.

Results: Baseline (BL) demographics, clinical characteristics, and disease activity were generally similar among pts with and without background csDMARD use. At BL, background csDMARD use was 64.3%, 64.2%, and 66.7% and methotrexate use was 50.0%, 55.2%, and 59.1% in the DEUC 6 mg QD, 12 mg QD, and PBO groups, respectively. Pts with and without background csDMARD use showed similar improvements at Week 16 with DEUC treatment versus PBO

on most clinical measures, pt-reported outcomes, and composite measures (Table 1 **and** Figure 1). No clinically meaningful differences in adverse events (AEs) were observed in pts with or without background csDMARD use.

Table 1. Adjusted mean (SE) change from baseline at Week 16 in clinical outcomes by csDMARD use

	PBO w/o csDMARD (n=22)	PBO w csDMARD (n=44)	DEUC 6 mg QD w/o csDMARD (n=25)	DEUC 6 mg QD w csDMARD (n=45)	DEUC 12 mg QD w/o csDMARD (n=24)	DEUC 12 mg QD w csDMARD (n=43)
Swollen joint count	-4.7 (1.4)	-5.0 (0.9)	-7.4 (1.4)	-6.8 (0.9)	-8.4 (1.3)	-7.7 (1.0)
Tender joint count	-5.3 (2.2)	-6.6 (1.3)	-6.4 (2.2)	-11.3 (1.3)	-11.5 (2.0)	-11.6 (1.4)
Physician's Global Assessment of Disease Activity	-20.6 (5.6)	-20.6 (3.7)	-29.1 (5.8)	-32.6 (3.5)	-30.1 (5.3)	-32.1 (3.9)
Patients' Global Assessment of Disease Activity	-14.9 (5.8)	-13.4 (3.9)	-23.0 (5.9)	-28.4 (3.8)	-28.2 (5.4)	-24.9 (4.2)
Pain	-14.7 (5.6)	-14.6 (3.9)	-22.7 (5.7)	-26.2 (3.7)	-25.5 (5.3)	-25.5 (4.2)
HAQ-DI	-0.23 (0.11)	-0.04 (0.09)	-0.31 (0.11)	-0.38 (0.08)	-0.48 (0.10)	-0.34 (0.09)
hsCRP	12.0 (5.3)	-4.4 (2.1)	-10.1 (5.3)	-13.3 (2.0)	-4.9 (4.9)	-10.0 (2.2)
PASI total score	2.5 (1.4)	-2.3 (0.7)	-3.7 (1.4)	-4.0 (0.6)	-4.0 (1.3)	-4.9 (0.7)
PASDAS	-0.9 (0.4)	-1.2 (0.3)	-1.8 (0.4)	-2.1 (0.2)	-2.2 (0.3)	-2.1 (0.3)

The number of patients with data available for individual endpoints may vary.csDMARD, conventional synthetic disease-modifying antirheumatic drug; DEUC, deucravacitinib; HAQ-DI, Health Assessment Questionnaire-Disability Index; hsCRP, high-sensitivity C-reactive protein; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; PBO, placebo; QD, once daily; SE, standard error; w, with; w/o, without.

Conclusion: These analyses demonstrate that the efficacy of DEUC for the treatment of PsA was similar in pts with and without background csDMARD use. The AE profile of DEUC treatment with and without csDMARD use was consistent with findings from the overall Phase 2 PsA trial population.

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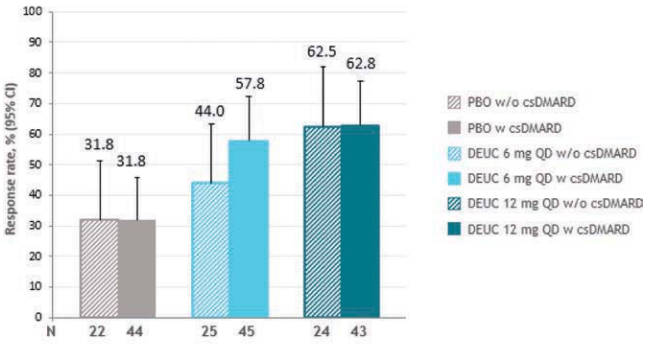
Figure. ACR 20 response at Week 16 by csDMARD use



Analyses were performed using NRI for patients with missing data. Difference and 95% CI are obtained using a stratified Cochran-Mantel Haenszel test with body weight and TNFi use history.
ACR, American College of Rheumatology; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DEUC, deucravacitinib; NRI, non-responder imputation; PBO, placebo; QD, daily; TNFi, tumor necrosis factor inhibitor; w, with; w/o, without.

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AB0892

TARGETED SAFETY ANALYSES OF GUSELKUMAB: LONG-TERM RESULTS FROM RANDOMIZED CLINICAL TRIALS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND MODERATE TO SEVERE PSORIASIS

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Background: Guselkumab (GUS) demonstrated efficacy and a favorable safety profile in active PsA in the Phase (Ph) 2[1] and Ph3 DISCOVER-1&2 trials[2,3] and in moderate-to-severe plaque psoriasis (PsO) in the Ph3 VOYAGE-1&2 trials.[4,5]

Objectives: To assess long-term safety of GUS across PsA/PsO trials.

Methods: Using pooled safety data through 2 years (yrs) from PsA trials (N=1229; GUS 100 mg every 4/8 weeks [Q4W/Q8W])[1-3] and through 5 yrs from PsO trials (N=1721; GUS 100 mg Q8W),[4,5] incidences of serious adverse events (SAEs); gastrointestinal (GI)-related SAEs and other targeted AEs; including candidiasis, uveitis, and opportunistic infections (OIs) were evaluated. Incidence rates (IRs) were calculated as the number of events per 100 pt-yrs (PY) of follow-up with 95% CI. Patients (pts) with an IBD history were not excluded in PsA/PsO trials. Max exposure duration was W100 for PsA trials and W252 for PsO trials.

Results: The PsA and PsO populations had comparable mean age and BMI. IRs of SAEs and GI-related SAEs were generally similar between GUS- and PBO-treated pts during PBO-controlled periods, and between PsA pts receiving GUS Q4W/Q8W for up to 2 yrs and PsO pts receiving GUS Q8W for up to 5 yrs (Table 1). IRs of other targeted AEs of interest were low. OIs did not occur in PsO pts and were infrequent in PsA pts (Table 1). Candidal infections were infrequent and non-serious. Iridocyclitis was reported in 1 PBO- and 1 GUS Q8W-treated PsA pt. No exacerbations or new onset of IBD or active tuberculosis was reported in GUS-treated PsA/PsO pts.

Conclusion: IRs of SAEs; GI-related SAEs; and AEs of interest including candidiasis, uveitis, and OIs were low, or no cases were reported. No new safety concerns were identified with GUS treatment through 2 yrs and 5 yrs of follow-up in the pooled PsA and PsO trials, respectively, supporting a durable and favorable GUS safety profile consistent between pts with active PsA and moderate-to-severe PsO.

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Table 1. Targeted AEs of Interest

	Pooled PsA*					Pooled PsO		
	Through 2 Yrs					Through 5 Yrs		
	GUS 100 mg Q4W (N=373)	GUS 100 mg Q8W (N=475)	PBO→GUS 100 mg Q4W (N=352)[a]	PBO→GUS 100 mg Q8W (N=29)[a]	GUS Combined (N=1229)	GUS 100 mg Q8W (N=1221)[b]	ADA→GUS 100 mg Q8W (N=500)[c]	GUS Combined (N=1721)
Total PY	645	748	461	17	1871	5254	1912	7166
Mean PY	1.7	1.6	1.3	0.6	1.5	4.3	3.8	4.2
Events/100 PY (95% CI)								
Overall SAEs	4.65 (3.14, 6.64)	6.42 (4.73, 8.51)	5.86 (3.86, 8.52)	0.00 (0.00, 17.24)	5.61 (4.59, 6.79)	5.18 (4.58, 5.83)	4.55 (3.64, 5.61)	5.01 (4.50, 5.56)
GI-related SAEs	0.46 (0.10, 1.36)	0.27 (0.03, 0.97)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.27 (0.09, 0.62)	0.44 (0.28, 0.66)	0.42 (0.18, 0.82)	0.43 (0.29, 0.61)
OIs[d]	0.00 (0.00, 0.46)	0.27 (0.03, 0.97)	0.22 (0.01, 1.21)	0.00 (0.00, 17.24)	0.16 (0.03, 0.47)	0.00 (0.00, 0.06)	0.00 (0.00, 0.16)	0.00 (0.00, 0.04)
Candida infections	0.31 (0.04, 1.12)	0.00 (0.00, 0.40)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.11 (0.01, 0.39)	0.49 (0.32, 0.73)	0.52 (0.25, 0.96)	0.50 (0.35, 0.70)
Non-pathogen specific fungal infections, suspicious for candida	0.00 (0.00, 0.46)	0.27 (0.03, 0.97)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.11 (0.01, 0.39)	0.11 (0.04, 0.25)	0.16 (0.03, 0.46)	0.13 (0.06, 0.24)
Uveitis/ Iridocyclitis	0.00 (0.00, 0.46)	0.13 (0.00, 0.75)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.05 (0.00, 0.30)	0.00 (0.00, 0.06)	0.00 (0.00, 0.16)	0.00 (0.00, 0.04)

*In PsA Ph2, data after early escape at W16 were excluded. AEs are coded using MedDRA Version 23.1[a]For PBO→GUS, data on/after 1st GUS administration were included[b]PBO crossover pts were included in GUS column after crossover to GUS[c]Events prior to GUS (ADA events) were excluded. Only includes pts randomized to ADA at W0 and crossed over to GUS at/after W52 for VOYAGE-1 & W28 for VOYAGE-2[d]Herpes zoster disseminated, fungal oesophagitis, and meningitis listeria (1 each)ADA=Adalimumab

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AB0893

AN ANALYSIS OF FATIGUE IN PATIENTS WITH PSORIATIC DISEASE UTILIZING SF-36 VITALITY SCORES: RESULTS THROUGH WEEK 24 IN PHASE 3 TRIALS OF GUSELKUMAB IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS

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Background: Patients with chronic inflammatory diseases can experience significant fatigue, negatively impacting health-related quality-of-life.[1,2]

Objectives: This post-hoc analysis evaluated baseline fatigue severity among patients with psoriasis and/or psoriatic arthritis (PsA) and the effect of guselkumab treatment on patient-reported fatigue.

Methods: VOYAGE-2 evaluated guselkumab every 8 weeks (Q8W) versus placebo (W16→guselkumab) and adalimumab in treating moderate-to-severe psoriasis.[3] DISCOVER-1[4] and DISCOVER-2[5] evaluated guselkumab Q4W and Q8W versus placebo in treating active PsA. Fatigue was assessed using 36-item Short Form (SF-36) vitality scale score (includes 4 questions on fatigue/energy level); the US population norm=50±10; 5-10-point decrements are typically observed in conditions known to cause fatigue[2]; scores ≤35 indicate clinically important fatigue[1]; increases ≥5 indicate clinically meaningful improvement.[2]

Results: Across randomized groups at baseline, mean SF-36 vitality scores were 47.7-48.5 in psoriasis and 42.2-44.0 in PsA patients; 11%-15% of psoriasis and 20%-28% of PsA patients had scores <35. In psoriasis patients, mean increases in SF-36 vitality score at W16 were: placebo, 1.1; adalimumab, 3.9 (p<0.001 versus placebo); guselkumab, 5.6 (p<0.001 versus placebo); at W24: placebo→guselkumab, 4.6; adalimumab, 3.9; guselkumab, 5.8 (p=0.0148 versus adalimumab). In PsA patients, mean increases at W24 were: placebo, 2.3-4.0; guselkumab, 5.5-7.5 (p≤0.001 versus placebo). Through the placebo-controlled periods, significantly greater proportions of guselkumab-treated patients achieved clinically meaningful improvement in fatigue versus placebo (W16 psoriasis: guselkumab, 48%; placebo, 32%; p<0.001; W24 PsA: guselkumab, 53%-55%; placebo, 34%-44%; p<0.05).

Conclusion: At baseline, patients with psoriatic disease experienced clinically important fatigue, more so with PsA (20%-28%) than psoriasis (11%-15%). In guselkumab-treated psoriasis and PsA patients, clinically meaningful improvements in fatigue were achieved at W16 and W24, respectively.

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AB0894 EFFICACY AND SAFETY OF GUSELKUMAB IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE AXIAL PSORIATIC ARTHRITIS: STUDY DESIGN OF A PHASE 4, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Background: Established criteria for classifying axial psoriatic arthritis (PsA) are lacking, and assessments of disease activity often rely on measures developed for ankylosing spondylitis (AS). There is an unmet need to systematically identify and measure efficacy of treatments for axial PsA patients (pts). Guselkumab (GUS), a selective interleukin (IL)-23p19 inhibitor, was efficacious in improving signs and symptoms of active PsA in 2 phase 3, randomized, placebo (PBO)-controlled studies: DISCOVER-1 and DISCOVER-2. In a post-hoc pooled analysis of DISCOVER-1&2 pts with investigator-confirmed sacroiliitis, GUS-treated pts had greater improvements in axial symptoms compared with PBO.[1] Imaging in DISCOVER-1&2 was restricted to the sacroiliac (SI) joints, occurring prior to/at screening as confirmed by the investigator, and locally read.

Objectives: To design a new, dedicated study to evaluate the effects of GUS on axial PsA prospectively.

Methods: Cumulative evidence from DISCOVER-1&2, including exposure–response relationship, covariate adjustment for modest baseline imbalances across treatment groups, subgroup analyses, and comparisons within and across these studies, was considered in designing a new trial. Data from the pivotal registrational studies suggest similar efficacy with GUS every-4-weeks (Q4W) and Q8W regimens in treating PsA signs and symptoms, including symptoms of axial involvement. Power calculations were based on mean changes in Bath AS Disease Activity Index (BASDAI) scores in DISCOVER-1&2.

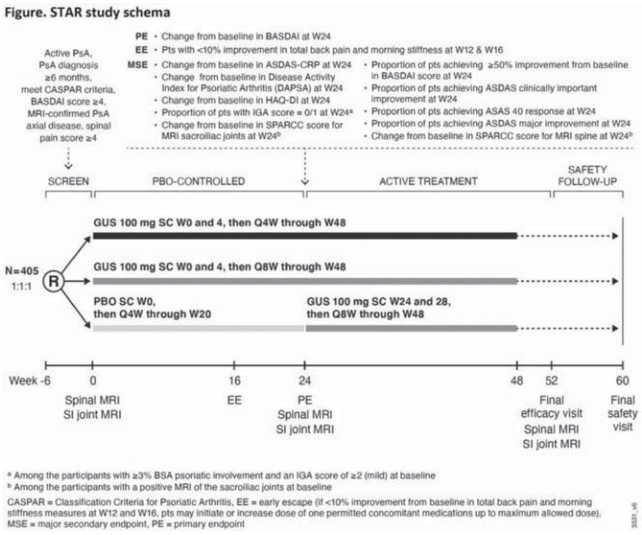
Results: The phase 4, randomized, PBO-controlled STAR study is specifically designed to prospectively assess efficacy outcomes in PsA pts with magnetic resonance imaging (MRI)-confirmed axial inflammation. Based on observed mean (SD) changes from baseline in BASDAI score from DISCOVER-1&2 (Table 1), 405 pts, randomized (1:1:1) to GUS Q4W, GUS at W0, W4, then Q8W, or PBO →GUS Q8W at W24, are planned for enrollment (Figure 1). STAR eligibility criteria include PsA ≥6 months and active disease (≥3 swollen & ≥3 tender joints, C-reactive protein [CRP] ≥0.3 mg/dL) despite prior non-biologic disease-modifying antirheumatic drugs, apremilast, and/or non-steroidal anti-inflammatory drugs. Pts will be naïve to biologics and Janus kinase inhibitors and have BASDAI ≥4, spinal pain score (visual analog scale [VAS]) ≥4, and screening MRI-confirmed axial disease (positive spine and/or SI joints defined as centrally read Spondyloarthritis Research Consortium of Canada [SPARCC] score ≥3). Follow-up MRIs of spine and SI joints will be obtained at W0, W24, and W52 and also centrally read, with readers blinded to treatment group and timepoint. Spinal/SI joint inflammation will be scored using the SPARCC method, with the former also assessed using the CAN-DEN method. The primary endpoint is mean change in BASDAI at W24; controlled (hierarchical) secondary endpoints, all at W24, include AS Disease Activity Score (ASDAS-CRP), Disease Activity Index for PsA (DAPSA), ≥40% improvement in Assessment in AS criteria (ASAS40), and mean changes in spine/SI joint SPARCC scores.

Table 1. Power calculations for the primary endpoint in the Phase 4 STAR study.

Historical trial data*	Observed mean (SD) change in BASDAI from W0-24	Effect size	Power (N=135; α=0.05)**
PBO	-1.28 (2.24)		
GUS 100 mg Q4W	-2.51 (2.00)	1.23	>99%
GUS 100 mg Q8W	-2.61 (2.47)	1.33	>99%

* From the pooled DISCOVER-1&2 trials**Power calculations based on N=135 per study group (1:1:1 randomization) and 2-sided significance of 0.05 using a 2-sample T-test assuming equal variancesBASDAI, Bath Ankylosing Spondylitis Disease Activity Index; GUS, guselkumab; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; SD, standard deviation; W, week

Figure. STAR study schema



Conclusion: The phase 4 STAR study will allow for an in-depth, prospective evaluation of the effects of selectively inhibiting the IL-23p19 subunit with GUS in pts with MRI-confirmed axial PsA.

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[1] Mease, et al. *Lancet Rheum*. 2021;3(10):e715-e723.

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RESIDUAL BURDEN AND DISEASE ACTIVITY OF CANADIAN PSA PATIENTS TREATED WITH ADVANCED THERAPIES: PRELIMINARY RESULTS FROM A MULTIPLE REGISTRY ANALYSIS (UNISON-PSA)

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Background: Given the availability of advanced therapies in PsA with different modes of action, it is of interest to characterize their impact on overall clinical outcomes.

Objectives: To describe residual disease activity in Canadians with PsA treated with advanced therapies.

Methods: Multi-region, observational, retrospective analysis of data from Rhumadata (Quebec) and International Psoriasis and Arthritis Research Team (IPART) Canadian registries was performed. Data from each registry and region were analyzed separately using a common statistical analysis plan to generate descriptive statistics. Patients included in the registries were eligible if they were adults at the time of PsA diagnosis and were treated with an advanced therapy for ≥6 months initiated between January 2010 and December 2019. Residual disease activity was defined as failing to achieve MDA (defined as achieving ≥5 of: TJC ≤1; SJC ≤1; PASI ≤1 or BSA ≤3%; patient pain VAS score of ≤15 mm; patient global disease activity VAS score of ≤20 mm; HAQ score ≤0.5; and tender entheseal points ≤1) (primary endpoint), or DAPSA score ≥14 (secondary endpoint) within 6 months of initiation of an advanced therapy (TNFi, IL-12/23i, IL-17i, PDE4i, CTLA4i or JAKi).

Results: 1,866 subjects (Atlantic [IPART; Newfoundland]: N=83; Quebec [Rhumadata]: N=687; Ontario [IPART]: N=966; West [IPART; British Columbia, Manitoba]: N=130) were included in this preliminary analysis. Baseline characteristics are presented in Table 1. Overall, 899 were receiving their 1st advanced therapy, 464 were receiving their 2nd, and 264 had received ≥3. The most common therapy class was TNFi, followed by IL-17i. 18/21 (85.7%) subjects in the Atlantic region with an assessment, 184/246 (74.8%) in Quebec, 391/571 (68.1%) in Ontario, and 30/43 (69.8%) in Western Canada failed to achieve MDA within 6 months following advanced therapy initiation. Failure to achieve MDA within the allotted period was higher among patients receiving an IL-17i compared with a TNFi. There was no appreciable effect of lines of therapy. Also, 74 of 110 (67.3%) patients with an assessment in Quebec, 201/365 (55.1%) in Ontario and 3/3 (100%) in the West failed to achieve at least low disease activity (LDA; DAPSA ≤14) within 6 months following initiation of an advanced therapy. Data were not available for the Atlantic region. The proportion of patients not achieving LDA by advanced therapy was similar for those receiving a TNFi and IL-17i but increased with line of therapy.

Conclusion: Preliminary data show approximately three quarters of Canadians with PsA failed to achieve MDA or LDA within 6 months of initiating an advanced therapy. Disease duration is a possible explanation for not achieving MDA or LDA; better therapeutic approaches are needed to achieve these outcomes in patients with PsA.

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Table 1. Patient demographic and baseline characteristics, and response to treatment

	Atlantic (N=83)	Quebec (N=687)	Ontario (N=966)	West (N=130)
Age (years, mean [SD])	50.3 (11.1)	50.7 (12.1)	49.1 (12.9)	46.7 (12.1)
Female (n [%])	44/83 (53.0)	346/687 (50.4)	427/966 (44.2)	81/128 (62.3)
BMI (kg/m^2, n, mean [SD])	15, 30.8 (3.6)	553, 29.6 (6.6)	579, 30.6 (6.9)	45, 32.8 (10.6)
Time since diagnosis (years, N, mean [SD])	83, 8.7 (8.7)	687, 7.1 (7.9)	895, 11.7 (11.1)	74, 11.7 (8.9)
HLA-B27 positive (n/N [%])	N/A	58/335 (17.3)	86/648 (13.3)	N/A
Presence of EAMs (n/N [%])	4/44 (9.1)	27/687 (3.9)	65/693 (9.4)	2/33 (6.1%)
Fulfillment of CASPAR (n/N [%])	N/A	391/687 (56.9)	100/100 (100)	N/A
Therapy class (n [%]):*				
TNFi	66 (79.5)	478 (69.6)	651 (67.3)	104 (80.0)
IL-17i	11 (13.3)	106 (15.4)	191 (19.9)	21 (16.2)
IL-12/23i	6 (7.2)	33 (4.8)	124 (12.9)	5 (3.9)
PDE4i		48 (7.0)		
Other		22 (3.2)		
Failure to achieve MDA within 6 months of starting therapy (n/N [%])**	18/21 (87.5)	184/246 (74.8)	391/571 (68.1)	30/43 (69.8)
Failure to achieve DAPSA ≤14 within 6 months of starting therapy (n/N [%])**	N/A	74/110 (67.3)	201/365 (55.1)	3/3 (100.0)

*Patients may be taking >1 advanced therapy, **Not all patients had assessments of disease activity.

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AB0896 COMPARATIVE EFFECTIVENESS OF GUSELKUMAB IN PSORIATIC ARTHRITIS: UPDATES TO A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS

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Background: The efficacy of guselkumab (GUS), an interleukin (IL)-23 p19-subunit inhibitor, has been demonstrated for psoriatic arthritis (PsA) in two pivotal phase 3 trials (DISCOVER-1&2). A third phase 3b trial (COSMOS) evaluated GUS in patients with PsA who had an inadequate response (IR) to tumor necrosis factor inhibitors (TNFi). GUS has previously been compared to targeted PsA therapies through network meta-analysis (NMA).
Objectives: This NMA update was to include data for GUS in TNFi-IR patients from COSMOS, as well as two additional key comparators, risankizumab (RIS), an IL-23 inhibitor, and upadacitinib (UPA), a Janus kinase inhibitor (JAKi).
Methods: A systematic literature review identified PsA randomized controlled trials up to February 2021. A subsequent hand-search identified data for newer agents, including congresses up to July 2021. Bayesian NMAs were performed to compare treatments on American College of Rheumatology (ACR) response, Psoriasis Area and Severity Index (PASI) response, modified van der Heijde-Sharp (vdH-S) score, and serious adverse events (SAEs). Analyses used fixed or random effects models and adjusted for placebo response via meta-regression on baseline risk when feasible. Multinomial models were used for ACR and PASI. Results were summarized by ranking treatments in league tables according to results derived from NMAs. Conclusions (ie, comparable or better/worse) for GUS 100 mg every 8/4 weeks (Q8W/Q4W) versus comparators were based on overlap of pairwise 95% credible intervals (CrIs) (ie, treatments are comparable if CrIs overlap 1 [dichotomous outcomes] or 0 [continuous outcomes]).
Results: Thirty-three phase 3 studies were included in the NMAs. Studies were placebo-controlled up to 24 weeks except for 2 head-to-head studies, and evaluated 15 targeted PsA therapies in TNFi naïve, IR, or mixed populations. For ACR 20 response, GUS Q8W and Q4W ranked 14th and 12th among 23 treatments and were comparable to most other active agents, including RIS and UPA, subcutaneous (SC) TNFi, and most IL-17A inhibitors (IL-17Ai), as demonstrated by overlap in pairwise 95% CrIs with unity. Results were similar for ACR 50 and 70 responses. For PASI 90, GUS Q8W and Q4W ranked 2nd and 1st among 23 treatments and were better than multiple agents, including all SC TNFi, JAKi, including UPA, and other small molecules, as demonstrated by nonoverlap in pairwise 95% CrIs with unity. GUS Q8W and Q4W were similar to RIS and most IL-17Ai for PASI 90, but point estimates consistently favored GUS. For vdH-S score, GUS Q8W and Q4W ranked 8th and 3rd among 18 treatments; GUS Q4W was better than RIS, and both GUS Q8W and Q4W were comparable to most other agents, including UPA. SAEs were comparable across most agents.
Conclusion: GUS demonstrated better skin efficacy than most other targeted PsA therapies, including UPA. For vdH-S, both GUS dose regimens were comparable to most treatments, with both GUS dose regimens ranking higher than most, including UPA and RIS. Both GUS dose regimens demonstrated ACR responses that were comparable to most other agents, including UPA and RIS, and ranked favorably in the network for SAEs.
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AB0897 IMPACT OF RISANKIZUMAB ON IMPROVING SYMPTOMS AND HEALTH-RELATED QUALITY OF LIFE AND REDUCING FATIGUE AND PAIN AMONG PSORIATIC ARTHRITIS PATIENTS WITH MODERATE-TO-SEVERE SKIN INVOLVEMENT: EVIDENCE FROM TWO PHASE III TRIALS

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Background: Psoriatic arthritis (PsA) greatly affects patient-reported health-related quality of life (HRQoL).
Objectives: To assess the impact of risankizumab (RZB) on patient-reported outcomes (PROs) in patients with high skin burden using integrated efficacy data from two Phase III clinical trials (KEEPsAKE-1 and KEEPsAKE-2).
Methods: Adult patients with PsA with inadequate response or intolerance to disease-modifying antirheumatic drugs were randomized 1:1 to receive RZB (150 mg) or placebo (PBO). Improvement from baseline in PROs (Patient's Global Assessment of Disease Activity [PtGA] by visual analog scale [VAS], Short-Form 36 Health Questionnaire physical and mental component summary scores [SF-36 PCS and MCS], Health Assessment Questionnaire – Disability Index [HAQ-DI], EQ-5D 5-Level questionnaire [EQ-5D-5L] index and by VAS, Functional Assessment of Chronic Illness Therapy – Fatigue [FACIT-Fatigue], and pain by VAS) were assessed at Week 24 in patients with high skin burden (body surface area involvement ≥3% and Psoriasis Area Severity Index >10). Least squares mean (LSM) difference (95% confidence interval [CI]) between RZB and PBO groups based on mixed-model repeated measures regression is reported.
Results: RZB- vs PBO-treated patients demonstrated greater improvements in PROs with notable LSM differences (95% CI) between groups ($P<0.01$) in PtGA (-18.7 [-25.1, -12.2]), SF-36 PCS (6.3 [4.2, 8.4]) and MCS (4.4 [2.3, 6.6]), HAQ-DI (-0.4 [-0.5, -0.3]), EQ-5D-5L index (0.1 [0.1, 0.2]) and VAS (8.2 [2.5,13.9]), FACIT-Fatigue (4.9 [2.7, 7.2]), and pain (-18.9 [-25.1, -12.7]).
Conclusion: In patients with PsA with high skin burden, 24 weeks of RZB treatment, as compared with PBO, improved patients' HRQoL, including fatigue and pain.
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AB0898

GUSELKUMAB IMPROVES DACTYLITIS IN PSA PATIENTS WITH INADEQUATE RESPONSE TO TNFI: DATA FROM THE PHASE 3B COSMOS TRIAL

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Background: Dactylitis is a biomarker of disease severity in psoriatic arthritis (PsA) associated with functional disability, impaired quality of life and radiographic progression. The COSMOS study demonstrated the efficacy and safety of guselkumab (GUS), an IL-23 p19 subunit inhibitor (i), in patients (pts) with PsA who had inadequate response (IR; insufficient efficacy or intolerance) to 1–2 TNFi.[1]

Objectives: Evaluate the effect of GUS 100 mg Q8W on dactylitis, and assess the relationship between dactylitis resolution and improvement in other clinical outcomes, through 1 year in TNFi-IR PsA pts.

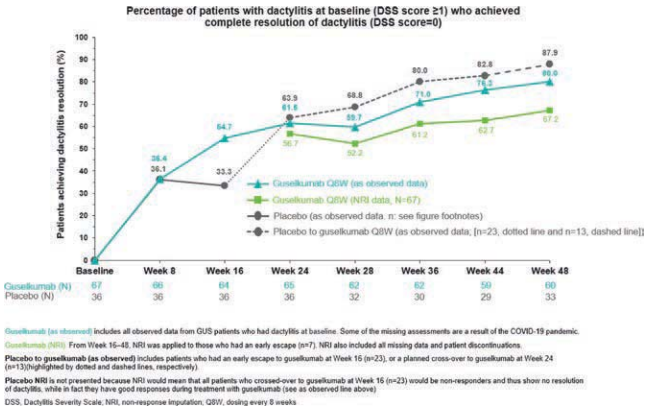
Methods: Pts received GUS or placebo (PBO); PBO pts crossed over to GUS at either Week (W) 16 (early escape [EE], n=45/96) or W24 (planned, n=51/96). Each of 20 digits was determined by the investigator to have no (0) to severe (3) dactylitis (Dactylitis Severity Scale [DSS]; total score: 0–60). Presence of dactylitis was defined by DSS score ≥1; complete or partial resolution was defined as a DSS score=0, or lower than baseline (BL), respectively. Change in DSS from BL at W24 was a secondary endpoint. Other clinical response outcomes including DAPSA LDA/remission, MDA and enthesitis resolution (Leeds Enthesitis Index score=0) were assessed by dactylitis resolution status. Both as observed and non-responder imputation (NRI; for missing data or EE) data are presented.

Results: Of 285 pts, 103 (36%; 67 GUS, 36 PBO) had dactylitis and 190 (67%) had enthesitis at BL. The majority of pts with dactylitis (76%) also had enthesitis. Pts with dactylitis had more severe joint and skin disease than those without (Table 1).

Table 1. BL characteristics for TNFi-IR PsA pts with/without dactylitis

	With dactylitis	Without dactylitis
N	103	182
Age, mean years (SD)	48.3 (11.8)	49.6 (12.5)
Sex: male, %	50	48
Years since PsA diagnosis; mean (SD)	8.1 (7.2)	8.6 (7.8)
BMI, mean kg/m^2 (SD)	28.5 (5.8)	30.1 (6.6)
PsA characteristics		
Swollen joint count, 0–66; mean (SD)	12.3 (8.1)	8.5 (4.8)
Tender Joint count, 0–68; mean (SD)	22.0 (12.9)	19.1 (12.2)
DAPSA score; mean (SD)	48.6 (20.9)	41.2 (16.8)
Spondylitis with peripheral arthritis, %	28	24
Enthesitis, %	76	62
Psoriasis characteristics, mean (SD)		
PASI score, 0–72	14.5 (12.7)	8.8 (9.6)
BSA, %	23.4 (23.6)	12.4 (17.1)
DLQI score, 0–30	14.1 (7.0)	12.6 (6.9)

In an as-observed analysis of pts with BL dactylitis, numerically more GUS- (55%) than PBO- (33%) treated pts achieved complete dactylitis resolution at W16. By W48, 80% of GUS-randomized pts achieved complete resolution (NRI: 57% at W24, 67% at W48; Figure 1).



Among 12 GUS pts with persistent dactylitis at W48, 9 (75%) had partial resolution. The 36 PBO pts with dactylitis crossed over to GUS at W16 (n=23; EE) or W24 (n=13; planned). As observed, 88% of these PBO→GUS pts had complete resolution of dactylitis at W48 (Figure 1). Of 105 dactylitis-free pts at BL in the GUS arm, 8 (8%) developed dactylitis before W48: 4 at W4, 2 at W8 and 1 each at W16 and 36. Complete resolution was seen in 6 (75%) of the 8 pts by W48, when 1 further new-onset case occurred. Utilizing observed data among GUS-randomized pts with and without BL dactylitis, 32% and 34%, respectively, achieved MDA at W48. Respective response rates were 59% and 55% for DAPSA LDA, and 28% and 15% for DAPSA remission. In those who did and did not achieve complete dactylitis resolution at W48, respective response rates were 38% and 0% for MDA, 68% and 13% for DAPSA LDA, and 31% and 0% for DAPSA remission. Of 69 pts with both enthesitis and dactylitis at BL who continued to receive GUS through W48, GUS resolved both manifestations in 72%, neither in 16%, only enthesitis in 4%, and only dactylitis in 7% of pts.

Conclusion: Complete dactylitis resolution was achieved in ≥80% of pts who continued to receive GUS at W48, with partial resolution seen in most remaining pts in an as-observed analysis. Response rates increased through W48. Dactylitis resolution in this difficult-to-treat TNFi-IR PsA population was frequently associated with enthesitis resolution and achievement of clinical outcomes representing low levels of disease activity.

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[1] Coates LC *et al. Ann Rheum Dis* 2021

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AB0899 A 24-MONTH PROSPECTIVE PSORIATIC ARTHRITIS OBSERVATIONAL STUDY OF PERSISTENCE OF TREATMENT (PRO-SPIRIT) - INTERIM ANALYSIS OF BASELINE CHARACTERISTICS

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Background: Ixekizumab (ixe), a highly selective interleukin (IL)-17A monoclonal antibody, has been approved for treatment of psoriatic arthritis (PsA). However, there is limited real-world evidence (RWE) available for ixe. PRO-SPIRIT is the first large-sample prospective observational study to provide RWE for ixe in patients (pts) with PsA.

Objectives: PRO-SPIRIT's primary objective is to describe treatment persistence at 24 months (M) among pts with PsA who initiate or switch to a new biologic Disease Modifying Arthritis Rheumatic Drugs (bDMARDs) or targeted synthetic (tsDMARDs), including ixe. This abstract describes the interim baseline (BL) characteristics.

Methods: PRO-SPIRIT is a prospective observational study, conducted in FR, ES, IT, DE, UK, and CA, enrolling adults with PsA (≥6M) to be initiated or switched to a new b/tsDMARD, locally approved for PsA. Treatment groups include ixe, secukinumab, IL-12/IL-23 inhibitors (i) (ustekinumab) or IL-23i (guselkumab), tumour necrosis factor (TNFi) (adalimumab, etanercept, infliximab or biosimilar), Janus kinase (JAKi) (tofacitinib or upadacitinib). Pt demographic, disease activity and therapy characteristics are collected at BL; clinical and patient-reported outcomes measures are collected at BL and at a routine post-BL visit. BL descriptive statistics are reported.

Results: From December 2019 until this interim data cut (June 2021), a total of 477 pts (305 female; mean age 52) were enrolled. Mean age ranged from 48 (IL-12/23i and IL-23i) to 55 (JAKi), with a majority of female pts in each group (Table 1). Pts in the IL-12/23i and IL-23i and TNFi groups showed the shortest time since PsA diagnosis (5.2±4.5; 6.5±7.9), while pts in the JAKi group showed the longest time (10.6±9.4). The lowest proportion of pts with a prior b/tsDMARDs use was observed in the TNFi group (31%), the highest in the IL-12/23i and IL-23i group (71%). Pts in the ixe and IL-12/23i and IL-23i groups were more likely to be on monotherapy. Tender Joint Count (9.1-11.3) and Swollen Joint Count (3.3-5.8) were comparable across groups, with the highest values in the ixe and JAKi groups, respectively. Pt proportion with enthesitis and dactylitis was higher in the ixe, secukinumab and JAKi groups. Percentage of Body Surface Area affected by psoriasis was higher in the ixe, secukinumab and IL-12/23i and IL-23i groups. Pt proportion with nail psoriasis was higher in the ixe and secukinumab groups. Physician's Global Assessment Visual Analog Scale (VAS), Patient's Global Assessment VAS and Patient's Assessment of Joint Pain VAS reflected a high burden of illness.

Table 1. Baseline characteristics

	bDMARDs				tsDMARDs
	Ixekizumab	**Secukinumab**	**IL-12/23 and IL-23 inhibitors**	**TNF inhibitors**	**JAK Inhibitors**
	N=137	N=46	N=24	N=211	N=40
Age	52.8±12.2	52.8±13.1	47.6±13.4	50.3±11.7	55.3±9.9
Female, n (%)	86 (62.8)	31 (67.4)	16 (66.7)	135 (64.0)	25 (62.5)
Years since diagnosis	8.4±7.5	7.6±8.0	5.2±4.5	6.5±7.9	10.6±9.4
Prior b/tsDMARD, n (%)	87 (63.5)	27 (58.7)	17 (70.8)	66 (31.3)	26 (65.0)
Concomitant csDMARD, n (%)	47 (34.3)	19 (41.3)	5 (20.8)	108 (51.2)	19 (47.5)
Tender Joint Count	11.3±10.2	9.1±10.8	9.1±9.3	10.9±10.6	11.1±8.8
Swollen Joint Count	5.7±6.6	3.3±3.8	3.4±6.4	4.8±5.6	5.8±6.6
Body Surface Area % affected by psoriasis	6.1±10.5	7.6±14.2	7.0±9.7	4.6±11.0	2.2±3.1
Presence of enthesitis, n (%)	58 (42.3)	16 (34.8)	4 (16.7)	67 (31.8)	16 (40.0)
Presence of dactylitis, n (%)	33 (24.1)	10 (21.7)	3 (12.5)	26 (12.3)	10 (25.0)
Presence of nail psoriasis, n (%)	57 (41.6)	20 (43.5)	7 (29.2)	71 (33.6)	11 (27.5)
Physician's Global assessment VAS	62.6±18.1	59.5±20.5	55.7±24.6	61.7±18.0	63.0±20.5
Patient's Global Assessment VAS	60.5±20.4	56.8±25.1	56.2±25.7	57.5±22.9	55.4±22.5
Patient's Assessment of Joint Pain VAS	62.7±21.3	58.4±27.1	55.7±28.3	59.4±22.9	57.5±24.0

Mean±SD, unless otherwise stated

Conclusion: The reported BL characteristics offer preliminary information about which pts initiate or switch to a b/tsDMARD in a real life-setting. Future disclosures (at 12 and 24M) will provide RWE regarding persistence, effectiveness, and health care resource use of available treatments for PsA, which will help pts and physicians to make better informed treatment decisions.

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AB0900 A TEMPORARY ANTIRHEUMATIC DRUGS WITHDRAWAL DOES NOT CAUSE AN EXCESS OF DISEASE FLARES IN PATIENTS WITH PSORIATIC ARTHRITIS UNDERGOING COVID-19 MRNA VACCINATION

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Background: The best way to manage disease-modifying antirheumatic drugs (DMARDs) in patients with rheumatic and musculoskeletal diseases (RMDs) undergoing the Coronavirus disease (Covid)-19 vaccination and the recommendations regarding the use and timing of immunomodulatory therapies around the time of vaccination are still a matter of debate, due to the difficulties in balancing the vaccination efficacy and safety.

Objectives: To assess the impact of different strategies of antirheumatic treatment management on disease activity around the time of vaccination for Coronavirus disease (Covid)-19 in patients with psoriatic arthritis (PsA).
Methods: We prospectively evaluated patients with PsA in remission or low-disease activity candidate to receive Covid-19 vaccination with mRNA vaccines. Methotrexate (MTX) and leflunomide were withheld 7 days after each dose, whilst biological DMARDs (bDMARDs), were either continued (46.8% of the patients) or withheld (53.2%) from the day of the first dose until 7 days after the second dose. Patients were reassessed after 3 months from enrollment or in case of disease flare.
Results: After the second dose of Covid-19 vaccination 7 patients (5.6%) (6 females) had an articular disease flare each (mean involved joints: 1.29), one patient presented a concomitant worsening of psoriasis, and four patients had an isolated worsening of their psoriasis. All patients received additional treatments with oral GC (n=2) or non-steroidal anti-inflammatory drugs (n=5). Two flares lasted more than one week and required a modification of the ongoing bDMARD. Articular flare incidence (6.8% vs 3%, p=0.259), involved joints (1.4 vs 1.5, p=0.846), disease flare severity, and changes in antirheumatic therapies (1 vs 1, p=0.928) did not differ significantly between the two different bDMARD management strategy groups (continued vs temporary withheld). There was no significant difference in disease activity score for psoriatic arthritis (DAPSA) and C-reactive protein (CRP) after vaccination, but patients who flared up had a higher mean basal DAPSA (7.3 vs 4.1, p=0.046). On binomial logistic regression analysis, we did not find any significant association with gender, age, basal CRP, basal DAPSA, active psoriasis, conventional synthetic DMARDs, or bDMARDs and disease flare.
Conclusion: Our findings suggest that a temporary short halt of bDMARDs could be a viable option in patients with well-controlled PsA undergoing Covid-19 vaccination without increasing the risk of flares, which could be useful to increase T cell response and antibody titres after Covid-19 vaccination.
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AB0901 EFFECTS OF TREATMENT WITH RISANKIZUMAB ON REDUCING PAIN AND INFLAMMATION IN PATIENTS WITH PSORIATIC ARTHRITIS: AN ANALYSIS OF THE KEEPSAKE -1 AND -2 TRIALS

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Background: Risankizumab (RZB), a monoclonal antibody that specifically inhibits interleukin 23, is being investigated as a treatment for adults with psoriatic arthritis (PsA).
Objectives: Evaluate the efficacy of RZB treatment on the reduction in pain and inflammation in patients with active PsA
Methods: KEEPsAKE-1 and -2, double-blind, phase 3 trials, evaluated the efficacy of RZB versus placebo (PBO) for the treatment of adult patients with active PsA. Patients were randomized (1:1) to receive subcutaneous RZB 150 mg or PBO at weeks 0, 4, and 16. A reduction in pain visual analogue (VAS) score of 30% (meaningful), 50% (substantial) from baseline, and achievement of a minimal clinically important difference (MCID) in pain VAS was analyzed using NRI. High-sensitivity C reactive protein (hsCRP) was analyzed using mixed-effect model repeated measurement. Results are reported from the 24-week timepoint.
Results: A total of 1407 patients were included in the 24-week assessment (KEEPsAKE-1 RZB=483, PBO=481; KEEPsAKE-2 RZB=224, PBO=219). Patients receiving RZB achieved significantly higher levels of meaningful pain reduction than did patients receiving placebo (KEEPsAKE-1 54.7% vs 31.1%, P<0.001; KEEPsAKE-2 43.3% vs 22.2%, P<0.001). Similar trends were noted for substantial pain reduction (KEEPsAKE-1 37.7% vs 18.5%, P<0.001; KEEPsAKE-2 31.9% vs 15.2%, P<0.001). Patients receiving RZB were also significantly more likely to achieve a MCID than patients receiving PBO in both KEEPsAKE-1 (72.9% vs 56.2%, P<0.001) and KEEPsAKE-2 (64.6% vs 46.0%, P<0.001). A numerically greater reduction in hs-CRP was demonstrated in both studies for patients receiving RZB compared to PBO (KEEPsAKE-1 -4.32 vs -0.20; KEEPsAKE-2 -1.14 vs 0.25).
Conclusion: RZB treatment resulted in clinically meaningful improvements in pain and inflammation for patients with active PsA.
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AB0902 EFFICACY OF IL-17 INHIBITORS IN PSORIATIC ARHTRITIS. SISTEMATIC REVIEW OF SCIENTIFIC LITERATURE AND META-ANALYSIS

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Background: Psoriatic arthritis is a chronic inflammatory joint disease with a great heterogeneity of manifestations both at the musculoskeletal (arthritis, enthesitis, dactylitis, axial skeleton involvement) and dermatological (skin, nail involvement) domain. The main goal of treatment is to maximize quality of life by controlling symptoms and preventing structural damage. For this, multidisciplinary management must be carried out without forgetting non-musculoskeletal manifestations and considering comorbidities. Regarding pharmacological therapy to control arthritis, non-steroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular corticosteroid injections are proposed as initial therapy. When symptoms are not controlled or there are associated poor prognostic factors, conventional disease-modifying antirheumatic drugs (DMARDs) are recommended, especially methotrexate. When the classic DMARDs do not achieve good control of the disease, the next step will be the biological DMARDs, among which are TNF-alpha inhibitors, interleukin-17 inhibitors or inhibitors of the IL12/IL23 axis. Other molecules such as janus kinase (JAK) inhibitors or phosphodiesterase-4 inhibitors such as Apremilast also continue to be incorporated into treatment alternatives. Although these drugs provide a promising result, the scarcity of direct comparative studies implies a need for more research to determine better treatment strategies.
Objectives: To analyze the efficacy of IL-17 inhibitors (Secukinumab, Ixekizumab, Brodalumab and Bimekizumab) in the treatment of patients diagnosed with psoriatic arthritis based on data published in randomised clinical trials (RCTs).

Methods: We perform a systematic review of the scientific literature using the Pubmed, Cochrane Library, Embase and Web of Science electronic databases, selecting RCTs evaluating the efficacy of IL-17 inhibitors for the treatment of psoriatic arthritis. A meta-analysis was performed using the random-effects model for each efficacy measure evaluated at different weeks.

Results: 23 studies met the selection criteria from a total of 2198 references identified in the search. 14 references contained data on the use of Secukinumab from 7 RCTs. Ixekizumab was the second IL-17 inhibitor most identified with 6 references with data from 5 RCTs. Bimekizumab with 2 references and Brodalumab with 1 reference completed the review. Despite extracting efficacy data in nail, enthesitic and PROs manifestations. We were only able to perform meta-analyses of the ACR 20, AC50, ACR70 and PASI75 response rates at week 12 of treatment, due to the lack of statistically comparable data. The meta-analysis performed demonstrated that IL-17 inhibitors are effective in psoriatic arthritis, compared to placebo in the different efficacy outcomes evaluated (ACR20 12 wk (OR: 3.60 [95%CI: 2.85-4. 55]), ACR50 12 wk (OR: 10.85 [95%CI: 6.20-18.94]), ACR70 12 wk (OR: 7.94 [95%CI: 4.23-14.91]) and PASI75 12 wk (OR: 21.26 [95%CI: 13.72-32.95])

Conclusion: Our review concluded that IL-17 inhibitors are effective in the treatment of patients who have shown intolerance or had an unsatisfactory response to other lines of treatment in Psoriatic arthritis.

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Disclosure of Interests: None declared

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AB0903 DUAL IMMUNOMODULATORY THERAPIES IN PSORIATIC DISEASE

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Background: Since the advent of numerous biologic therapies and small molecular drugs targeting specific cytokines and signalling pathways; the management of patients with psoriatic arthritis (PsA) has significantly improved. However, at least 40% of PsA patients exhibit an incomplete or failure to respond to these treatments. While the outcomes of patients with psoriasis (Pso) has dramatically improved with monoclonal antibody therapies targeting IL-23 and IL-17A; achieving a measurable low disease activity state such as minimal disease activity (MDA) for musculoskeletal manifestations of psoriatic disease is infrequent. Given the complex and heterogeneity of signalling pathways, cytokines and cell types resulting in synovio-entheseal disease in PsA; new treatment strategies must be evaluated to induce deep and sustainable clinical responses in all the phenotypic domains of psoriatic disease (cutaneous, synovium, entheseal and axial). (1) In patients who do not achieve remission in all clinical domains on a biologic monotherapy or combination of a biologic therapy with an oral synthetic agent; dual targeted anti-cytokines strategies or combined biologic with a targeted oral small molecule are a possible treatment option.

Objectives: To describe a series of four patients with recalcitrant psoriatic disease and failure to respond to previous treatment regimens who were successfully treated with dual immunomodulatory therapies.

Methods: Patients on dual immunomodulatory therapies attending our department were prospectively followed and clinical response monitored.

Results:

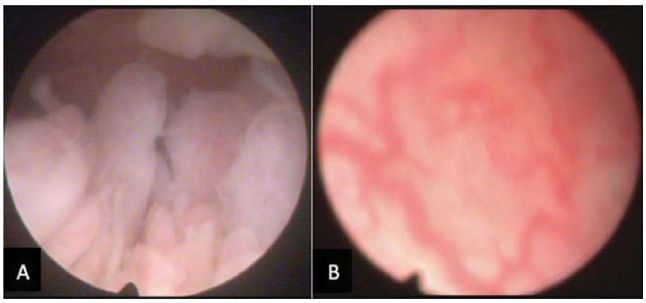

Figure 1. Mini-Arthroscopy of left knee for Case 3 prior to starting dual immunomodulator therapy.**(A)** Macroscopic aspects of synovitis **(B)** Synovium vascularization

Conclusion: Multiple pathways and mediators are responsible for the initiation of and sustained joint inflammation and damage seen in PsA. A phase II trial of ABT-122, a biologic engineered to target both TNF and IL-17A showed statistically significant superior efficacy outcomes at multiple time points based on ACR50, ACR70 and psoriasis outcome measures (PASI75/PASI90) when compared to adalimumab, with similar safety profile.(2)

Safety concerns such as infectious risks are important considerations with such strategies; however, the targeted second-generation anti-cytokine biologics and targeted JAK-I have exhibited improved safety profiles.(3) In our small case series, patients have not, to date, experienced adverse events of combination therapy.

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AB0904 EVALUATING NUMERIC RATING SCALE VERSIONS OF THE 3 AND 4 VISUAL ANALOG SCALE (3/4-VAS) COMPOSITE MEASURES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS FROM THE SELECT-PSA PROGRAM

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Background: The multifaceted nature of psoriatic arthritis (PsA) can make it challenging to evaluate treatment targets and disease activity. Moreover, most existing assessment tools are time-consuming and not always feasible in routine clinical care, indicating a need for new disease measures that are easy to perform and calculate. Composite measures using 3-visual analog scale (VAS;

Table 1.

	Age/gender	Diagnosis	prior therapies	combination therapy	dose	adverse events
Case 1	49/ Male	PsA + PsO	Methotrexate, adalimumab, etanercept, infliximab, golimumab, certolizumab, ustekinumab, secukinumab, ixekizumab	Baracitinib + infliximab	4mg OD + 5mg/kg Q8W	None
Case 2	51/ Male	PsA + PsO	Methotrexate, etanercept, adalimumab, ustekinumab, infliximab, secukinumab, apremilast, ixekizumab, brodalumab, guselkumab	Adalimumab + guselkumab	40mg QoW +100mg Q8W	None
Case 3	51/ Female	PsA + PsO	Methotrexate, sulphasalazine, etarnercept, certolizumab, leflunomide, infliximab, adalimumab, secukinumab, ustekinumab, tofacitinib, abatacept, baracitinib	Adalimumab + tofacinitib	40mg QoW + 5mg BD	None
Case 4	39/ Male	PsA +PsO	Methotrexate, etanercept, ustekinumab, adalimumab, secukinumab, ixekizumab, sulphasalazine	Ixekizumab + baracitinib	80mg Q4W+ 4mg OD	None

physician's global assessment, patient's global assessment, and skin) or 4-VAS (physician's global assessment, joints, skin, and pain) have been proposed as simpler alternatives.[1] Given potential advantages of numeric rating scales (NRS) over VAS, we here adapted 3/4-VAS for use with NRS components and tested its validity via post hoc analysis of the upadacitinib (UPA) SELECT-PsA program.

Objectives: Evaluate the ability of 3/4-NRS scores to assess treatment response in SELECT-PsA 1 and 2, as well as the correlation of 3/4-NRS with other common disease activity measures.

Methods: Data are from the SELECT-PsA 1 and 2 phase 3 trials in patients with prior inadequate response or intolerance to ≥1 non-biologic DMARD or ≥1 biologic DMARD, respectively. In both trials, patients received once daily UPA 15 mg, UPA 30 mg, or placebo (PBO); SELECT-PsA 1 also included the active comparator adalimumab (ADA) 40 mg every other week (wk). 3-NRS scores were determined using the mean of SAPS questions 1–10, physician's global assessment of disease activity, and patient's global assessment of disease activity; 4-NRS scores were determined using the mean of SAPS questions 1–10, physician's global assessment of disease activity, patient's assessment of pain, and BASDAI question 3 related to joint pain and swelling. The 3/4-NRS scale ranges from 0 (no disease activity) to 10 (severe activity). 3/4-NRS and cDAPSA (DAPSA without the CRP component) were assessed at all available visits through wk 56. Correlations between 3/4-NRS with PsA disease activity score (PASDAS), routine assessment of patient index data 3 (RAPID3), DAPSA, cDAPSA, and other disease activity measures were determined using the nonparametric Spearman rank correlation coefficient for UPA 15 mg patients from both trials and ADA for SELECT-PsA 1. All data are shown as observed; nominal p-values are provided throughout.

Results: A total of 1281 and 423 patients were included from SELECT-PsA 1 and 2, respectively. For both cDAPSA and 3/4-NRS scores, patients receiving UPA 15 mg showed clear numerical improvements compared with PBO at wk 24 in both trials (Table 1). 3/4-NRS scores were highly correlated with RAPID3 and PASDAS measures (r >0.6, *P* <0.0001) for UPA 15 mg patients at baseline (Figure 1). Moderate correlations were observed between 3/4-NRS and DAPSA/cDAPSA (r = ~0.4, *P* <0.0001), as well as physical function (HAQ-DI) and quality of life measures (SF-36). Nominally significant but weaker correlations were detected for joints, skin, and other disease activity assessments. Similar overall results were observed for patients receiving ADA.

Table 1. 3/4-NRS and cDAPSA Disease Activity Scores at Week 24 and 56 (As Observed)

SELECT-PsA 1

	Wk 24			Wk 56	
Mean score [n]	PBO	UPA 15 mg	ADA	UPA 15 mg	ADA
3-NRS	3.7 [370]	2.2 [398]	2.4 [398]	1.8 [372]	2.0 [359]
4-NRS	3.8 [367]	2.3 [392]	2.6 [395]	1.9 [367]	2.2 [357]
cDAPSA	24.0 [372]	14.9 [399]	16.6 [400]	10.2 [372]	11.3 [358]
SELECT-PsA 2					
	Wk 24			**Wk 56**	
Mean score [n]	**PBO**	**UPA 15 mg**		**UPA 15 mg**	
3-NRS	4.7 [172]	2.9 [190]		2.4 [164]	
4-NRS	4.9 [170]	3.1 [188]		2.7 [162]	
cDAPSA	37.1 [172]	21.6 [190]		15.3 [166]	

3/4-NRS ranges from 0–10; cDAPSA ranges from 0–154. Lower scores indicate decreased disease activity.

Conclusion: 3/4-NRS was able to successfully discriminate between PBO and therapeutic groups in SELECT-PsA 1 and 2. 3/4-NRS scores correlated well with other clinical and patient reported outcome measures, including those focused on joints (DAPSA) or multiple manifestations (PASDAS), supporting 3/4-NRS as a viable and easy to use tool in daily clinical practice.

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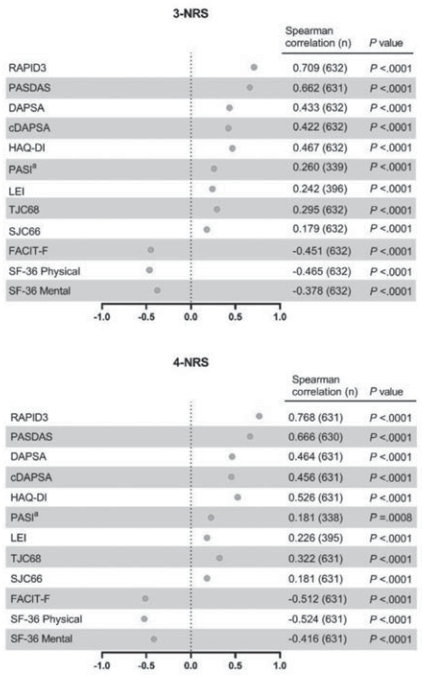
Figure. Correlation of 3/4-NRS With Other Disease Activity Measures at Baseline Among Patients Receiving UPA 15 mg



[a]PASI for BSA-Ps ≥3%. Higher FACIT-F and SF-36 scores indicate better health status. For all other disease activity measures, higher values are indicative of poorer health outcomes.
BSA, body surface area; DAPSA, disease activity in psoriatic arthritis; FACIT-F, functional assessment of chronic illness therapy-fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; NRS, numeric rating scale; PASDAS, psoriatic arthritis disease activity score; PASI, psoriasis area and severity index; RAPID3, routine assessment of patient index data 3; SF-36, Short Form 36 Health Survey; SJC66, swollen joint count based on 66 joints; TJC68, tender joint count based on 68 joints; UPA, upadacitinib.

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AB0905

ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3 (RAPID3) IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS (PSA) AFTER INADEQUATE RESPONSE OR INTOLERANCE TO DMARDS: POOLED RESULTS FROM THE PHASE 3, RANDOMIZED, DOUBLE-BLIND KEEPSAKE 1 AND 2 TRIALS

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Background: PsA is a chronic, systemic inflammatory disease with diverse clinical manifestations that can impact a patients' quality of life. Risankizumab (RZB), a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits interleukin 23 by binding to its p19 subunit, is approved for the treatment of active PsA in adults. In the phase 3 KEEPsAKE 1 and 2 studies, RZB treatment resulted in significantly greater improvements in signs and symptoms of active PsA compared with placebo (PBO).[1,2] RAPID3 is frequently used in clinical practice to evaluate PsA disease activity and consists of 3 key patient-reported measures (physical function, pain, and patient's global assessment of disease activity [PtGA]).[3]

Objectives: To evaluate short- (24 week) and long-term (52 week) improvements in RAPID3 scores and achievement of RAPID3 minimal clinically important difference (MCID) across the RZB KEEPsAKE 1 and 2 clinical program.

Methods: In KEEPsAKE 1 (NCT03675308) and KEEPsAKE 2 (NCT03671148), patients with active PsA who experienced inadequate response or intolerance to ≥ 1 csDMARD (KEEPsAKE 1) and/or ≤ 2 biological therapies (KEEPsAKE 2) were randomized to PBO or RZB 150 mg from baseline to week (W) 24; from W28–W52, all patients received open-label RZB 150 mg. At W16, nonresponders could add or modify rescue therapy. This post hoc analysis assessed the mean change from baseline to W24 and W52 in RAPID3 scores and the proportion of patients who achieved a RAPID3 MCID (defined as a decrease of ≥3.8 points[4]). Modified RAPID3 scores (range: 0–30) were calculated using pain scores, PtGA, and HAQ-DI, each rescaled to 0–10 and summed together.[3]

Results: A total of 961 and 443 patients were included from KEEPsAKE 1 and 2, respectively. At baseline, mean RAPID3 scores were 15.3 in both treatment arms of KEEPsAKE 1 (PBO n = 479, RZB n = 482) and 15.1 (PBO n = 219) and 14.8 (RZB n = 224) in KEEPsAKE 2. From W4 to W24, RAPID3 scores were significantly reduced with RZB treatment compared with PBO in both KEEPsAKE 1 (mean change from baseline at W24 of –5.3 vs –2.4, respectively, *P* <.001) and KEEPsAKE 2 (–3.8 vs –1.6, *P* <.001; Figure 1 **A, B**), and a significantly greater proportion of patients achieved MCID at W24 with RZB than with PBO in KEEPsAKE 1 (57.0% vs 36.4%, *P* <.001) and KEEPsAKE 2 (48.8% vs 32.8%, *P* <.001; Table 1). At W52 among patients who received RZB from W0–W52, mean change from baseline was –7.0 (KEEPsAKE 1) and –5.2 (KEEPsAKE 2; Figure 1 **C, D**), and MCID was achieved by 67.5% (KEEPsAKE 1) and 56.5% (KEEPsAKE 2) of patients. Patients who switched from PBO to RZB at W24 experienced similar and substantial improvements in RAPID3 scores by W52.

Table 1. Proportion of Patients Achieving a Minimal Clinically Important Difference From Baseline in RAPID3 (AO).

Patients, % (n/N) [95% CI]	KEEPsAKE 1		KEEPsAKE 2	
	PBO	RZB 150 mg	PBO	RZB 150 mg
W24	36.4 (166/456) [32.0, 40.8]	57.0 (262/460) [52.4, 61.5]***	32.8 (64/195) [26.2, 39.4]	48.8 (104/213) [42.1, 55.5]***
	PBO to RZB 150 mg[a]	**RZB 150 mg**	**PBO to RZB 150 mg[a]**	**RZB 150 mg**
W52	59.8 (260/435) [55.2, 64.4]	67.5 (297/440) [63.1, 71.9]	57.4 (105/183) [50.2, 64.5]	56.5 (109/193) [49.5, 63.5]

[a]Patients randomized to PBO at W0 switched to open-label RZB 150 mg at W24.***, *P* < .001 vs PBO.AO, as observed; PBO, placebo; RAPID3, Routine Assessment of Patient Index Data 3; RZB, risankizumab; W, week.

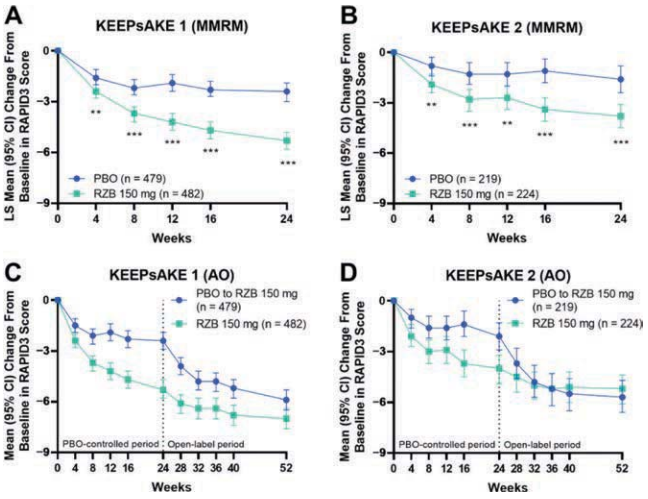

Figure 1. Mean Change From Baseline in RAPID3 Scores During KEEPsAKE 1 and 2.**, *P* < .01; ***, *P* < .001 vs PBO.AO, as observed; LS, least squares; MMRM, mixed-effect model repeated measurement; PBO, placebo; RAPID3, Routine Assessment of Patient Index Data 3; RZB, risankizumab.

Conclusion: RZB 150 mg was associated with improvement in RAPID3 total scores over 24–52 weeks of treatment in patients with active PsA in KEEPsAKE 1 and 2.

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AB0907

TREATMENT WITH UPADACINITIB IN REFRACTORY PSORIATIC ARTHRITIS. MULTICENTER STUDY OF FIRST PATIENTS OF CLINICAL PRACTICE

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Background: Upadacitinib (UPA) is an inhibitor of JAK kinases recently approved by EMA for the treatment of psoriatic arthritis (PsA) in Europe (January 2021) [1]. UPA has shown efficacy in refractory patients to anti-TNF [2].

Objectives: A) to assess efficacy and safety of UPA in the first cases in Spain in clinical practice. **B)** to compare the profile of clinical practice patients with clinical trial of UPA in PsA refractory to biologics [2].

Methods: Study of 39 patients of clinical practice with PsA treated with UPA in Spain. The diagnosis of PsA was made using CASPAR criteria. Patients who received at least one dose of UPA were included. Results are expressed as percentage, mean±SD or median [IRQ].

Results: 39 patients (29♀/10♂), mean age of 51.5 ± 11.4 years (Table 1**).** Pattern joint involvement was as follows: peripheral (n=19), axial (3) and mixed (17) During the PsA evolution, patients also presented enthesitis (59%) nail involvement (28.2%) and dactylitis (35.9%).

Table 1.

	CLINICAL PRACTICE N=39	CLINICAL TRIAL N=211	p
Baseline demographic parameters			
Age, years (mean±SD)	51.5±11.4	53.0 ± 12.0	0.4706
Sex, n (%) female	29 (74.4)	113 (53.6)	0.016
Disease Characteristics			
Duration of psoriatic arthritis, year (mean±SD)	12.41±8.68	9.5 ± 8.4	0.0499
HAQ-DI	1.10± 0.42	1.10 ± 0.6	1.000
Swollen joint count, mean±SD	6±7.29	11.3 ± 8.2	< 0.001
Painful joint count, mean±SD	7.48±7.58	24.9 ± 17.3	< 0.001
Enthesitis, n (%)	23 (59.0) MASES	172 (81.5) SPARCC	
Dactylitis, n (%)	14 (35.9)	55(26.1)	0.217
PASI score, mean±SD	2.72±2.32	10.1 ± 9.2	< 0.001
CRP (mg/L)	11.1±18.86	11.2 ± 18.5	1.000
Oral glucocorticoid use, n (%)	17 (43.6)	22 (10.4)	< 0.001
Concomitant synthetic DMARDs, n (%)	16(41)	98 (46,4)	0.532
Previous use of biological DMARDs, n (%)	39(100)	195 (92.4)	0.075
Number of prior failed biologic DMARDs, n(%)			
1	3(7.7)	135 (63.7)	<0.001
2	4(10.3)	35 (16.5)	0.383
≥3	32(82)	24 (11.3)	<0.001
UPA in monotherapy, n (%)	23(59)	113 (53.6)	0.531

HAQ-DI Health Assessment Questionnaire-Disability Index, PASI Psoriasis Area Severity Index, CRP C-reactive protein, DMARD disease-modifying antirheumatic drug

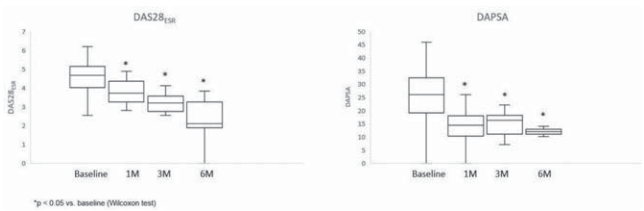

Figure 1.

Prior to UPA, most patients (59%) had received oral prednisone or equivalent (max 9.03±12.12mg/d), synthetic immunosuppressants (mean1.8±0.9) and biological therapy (TB) (4.5±2.1). TB were as follows: etanercept (25), adalimumab (28), infliximab (12), golimumab (16), certolizumab (15), secukinumab (29), ustekinumab (21) Abatacept (2), brodalumab (1) and ixekizumab (17). Apremilast was used in 13, Tofacitinib in 11 and filgotinib in 1. After a mean follow-up of 12.41± 8.68.3 years after the PsA diagnosis, UPA was started (15 mg/24 h), 43.6% associated prednisone (7.35±3.36 mg/d). In 16 (41%) UPA was started in combined therapy: methotrexate (9), salazopyrin (3) and leflunomide (4); in the remaining 23 (59%), monotherapy was prescribed. At UPA onset patients presented peripheral arthritis (76.9%), axial involvement (35.8%), skin involvement (25.6%), enthesitis (41%), and dactylitis (10.3%). Patients of clinical practice compared with clinical trial there were more women, have a longer duration of PsA, and received a higher proportion of previous TB (Table 1**).** After a median follow-up of 4.28 ± 2.6 months, patients showed prompt improvement in activity indexes (DAS28, DAPSA) (Figure 1) and laboratory test (CRP mg/L decreased from 4.00 [1.5;10.0] to 0.40 [0.30;4.00] (p 0.024) at the sixth month. Extra-articular manifestations also improved: dactylitis in 25% patients, enthesitis (43.8%), skin involvement (40%) and onychopathy (50%). No serious events were reported. Minor side effects were reported in 7 patients (17.9%), and UPA was discontinued in 9 due to inefficiency.

Conclusion: In this preliminary study, first patients of clinical practice in Spain with UPA in PsA had a longer evolution and received a greater number of TB than those of clinical trial. As in the UPA clinical trial, it seems effective, rapid and relatively safe in daily clinical practice for refractory PsA.

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AB0908

TREATING TO TARGET OF PSORIASIS: AN EVIDENCE-BASED CONSENSUS ON CLINICAL PRACTICE RECOMMENDATIONS

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Background: The Tight Control of psoriatic arthritis (TICOPA) trial revealed a treat to target (T2T) strategy has led to improved clinical outcomes in psoriatic arthritis (PsA). The heterogeneity of the disease, the feasibility of therapy and the associated comorbidities made the implementation of such strategy in routine care a real challenge. There is a high need for establish real world recommendations for the T2T approach in PsA tailored to the disease activity status, the Psoriasis manifestations as well as the individual patient's requirements.

Objectives: to provide up-to-date, evidence-based and consensus-based recommendations for Treat-to-Target management of psoriatic arthritis (PsA) and its associated clinical manifestations.

Methods: 14 key clinical questions were identified by scientific committee according to the Patient/ Population, Intervention, Comparison, Outcomes and Timing (PICOT) approach. Literature Review team performed a systematic review to summarize evidence advocating the benefits and harms of available pharmacologic and nonpharmacologic therapies for PsA. Subsequently, recommendations were formulated. The level of evidence was determined for each section using the Oxford Centre for Evidence-based Medicine (CEBM) system. A 3-round Delphi process was conducted with 19 experts. All rounds were conducted online. A consensus was achieved on the direction and the strength of the recommendations.

Results: An online questionnaire were sent to expert panel who participated in the three rounds (response rate 100%). At the end of round 3, a total of fifty-one recommendation items, categorized into 6 sections to address the main 6 PsA categories, were obtained. Agreement with the recommendations (rank 7-9) ranged from 89.5-100%. Consensus was reached (i.e.≥75%of respondents strongly agreed or agreed) on the wording of all the 51 clinical standards identified by the scientific committee. Algorithms for the management of PsA have been suggested.

Conclusion: These recommendations provide an updated consensus on the pharmacological treatment of PsA and strategies to reach optimal treat to target outcomes

in in common clinical scenarios, based on a combination of evidence and expert opinion. Best treatment decisions should be tailored to each individual patient situation.
Disclosure of Interests: None declared
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AB0909 RETENTION RATE OF APREMILAST AND RISK FACTORS FOR INADEQUATE RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM AN ITALIAN MONOCENTRIC COHORT

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Background: Apremilast (APR) is an oral PDE4 inhibitor approved for the treatment of Psoriatic Arthritis (PsA). Its effectiveness has been assessed in clinical trials[1,2], but real-life data are still scarce.
Objectives: To evaluate the retention rate (RR) of APR in PsA patients and the risk factors associated to APR inadequate response.
Methods: Retrospective monocentric analysis of PsA patients (CASPAR criteria 2006) treated with APR between 2017 and 2021. Disease activity was evaluated at baseline (T0) and after 6 (T6), 12 (T12) and 24 (T24) months of therapy using DAPSA score. Data are expressed as median [IQR].
Results: The cohort included 79 patients (41% males; age at PsA onset: 47 [37-58] years). PsA domains were: oligoarticular involvement (58%), enthesitis (42%), dactylitis (6%), axial involvement (13%), psoriasis (62%). Half patients presented dysmetabolic traits: 47% overweight/obesity, 34% arterial hypertension, 20% dyslipidemia. APR was prescribed mainly as first-line targeted therapy; in 42% APR was administered after the failure of ≥1 bDMARD. Contraindications to bDMARDs (47%) especially increased infectious risk (19/37) and current/previous malignancy (15/37), and mild PsA phenotype (27%) were the main reasons for APR choice. APR was discontinued in 61% after 4 [1-10] months because of inefficacy (25/48) or adverse events (AEs) (21/48; 81% gastrointestinal complaints). Patients who discontinued APR were compared with patients who continued APR (Table 1).

Table 1.

	APR WITHDRAWAL n=48	APR CONTINUATION n=31	p value
Females	28 (58)	19 (61)	0.79
Age at T0, years	51 [44-58]	57 [53-71]	**0.03**
PsA duration at T0, years	5 [2-11]	5 [0-12]	0.81
Oligoarticular involvement	24 (50)	20 (65)	0.21
Axial involvement	6 (13)	4 (13)	1.00
Enthesitis / dactylitis	26 (54)	11 (36)	0.10
DAPSA at T0	22 [16-28]	18 [13-26]	0.27
APR in monotherapy	26 (54)	23 (74)	0.07
bDMARDs naïve	24 (50)	22 (71)	0.07

Results are presented as median [IQR] or number (%). Continuous variables were compared with Mann-Whitney test; categorical variables were compared with Chi Squared/exact Fisher test.

The RR of APR was 62% at T6, 51% at T12 and 38% at T24 (Figure 1*a*).

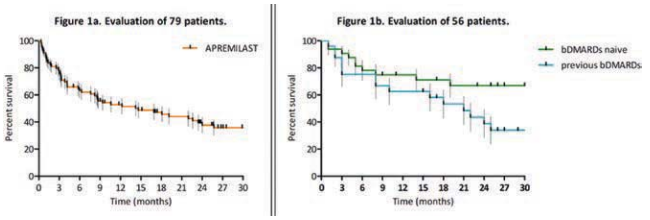

Figure 1. a) Overall RR of APR b) RR of APR in bDMARDs naïve vs previously treated with bDMARDs patients (exclusion of withdrawals for intolerance).

In patients continuing therapy, APR showed a good efficacy, with a significant reduction of DAPSA score observed at T6 (13 [9-19]), T12 (11 [4-18]) and T24 (8 [3-10]) as compared to T0 (21 [14-28]) (p<0.01). An overall trend of reduction of the BMI (kg/m^2) was observed (T0: 25 [22-28], T6: 24 [21-27], T12: 23 [21-26]); in overweight patients the BMI decreased significantly (28 [26-31] at T0 vs 27 [26-29] at last evaluation; p<0.01). Because of the high rate of discontinuations due to intolerance in the first months of therapy, we conducted a sub analysis: patients who continued APR (n=31) vs patients who discontinued it for inefficacy (n=25). A higher frequency of APR withdrawal was registered in younger patients (51 [47-57] vs 57 [53-71] years; p:0.01) previously treated with bDMARDs (71% vs 40%; p:0.02). Multivariate analysis confirmed these associations (OR [95% CI]: 0.1 [0.89-0.99], p:0.03 and 2.3 [1.70-59.17], p:0.01; respectively). The RR was higher in bDMARDs naïve patients compared with patients previously treated with bDMARDs (T6: 75% vs 67%, T12: 71% vs 63%, T24: 67% vs 34%; log-rank test= p:0.05) (Figure 1*b*).
Conclusion: This study confirms the safety and effectiveness of APR in a real-life scenario. We experienced a higher APR withdrawal rate for AEs (44%) in the first months of therapy, compared to registration studies in which APR was suspended in (8%). However, when tolerated, APR maintained efficacy over time, as demonstrated by progressive DAPSA reduction. The higher RR in bDMARDs naïve patients suggests the early use of APR. Moreover, the reduction of BMI could favor APR use in dysmetabolic patients. These data need to be confirmed in larger studies.
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AB0910 EVALUATION OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH PSORIASIC ARTHRITIS UNDER TREATMENT WITH METHOTREXATE

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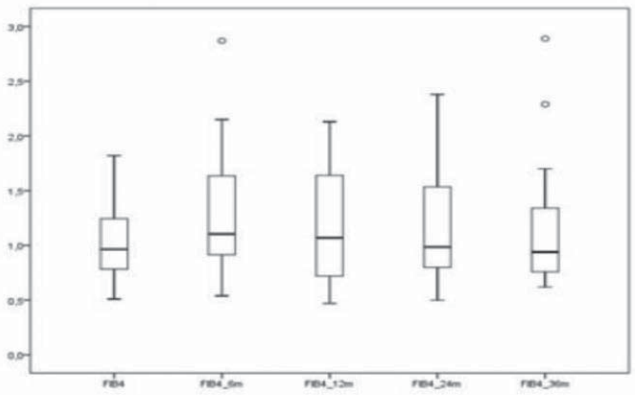
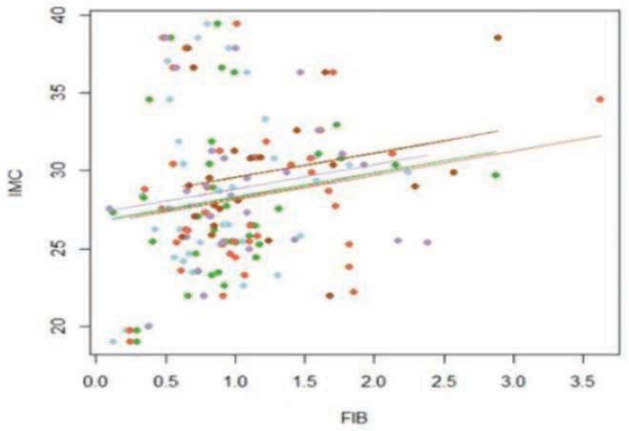
Background: Nowadays, non-alcoholic fatty liver is the most common hepatic disease. In patients with psoriatic arthritis with metabolic syndrome or obesity, there is a state of inflammation that produces the existence of a replacement of normal hepatic tissue by connective tissue, creating a non-alcoholic fatty liver disease (NAFLD). Disease Modifying Anti- Rheumatic Drugs (DMARDs) are widely used in the treatment of psoriatic arthritis. Among these drugs, we find methotrexate, chosen as the primary treatment for such pathologies. This DMARD must be administrated cautiously in patients with risk of developing fatty liver since it is hepatotoxic and it might cause the development of a hepatic disease.
Objectives: Measure the risk of developing hepatic fibrosis in patients with psoriatic arthritis under methotrexate.
Methods: It is a study of retrospective cohorts to determine the existence of NAFLD in patients with psoriatic arthritis under methotrexate through fatty index biomarkers (FIB-4). 41 patients have been studied for more than a year. Demographical & clinical variables have been collected (sex & gender) and (BMI, tobacco, use of alcohol, dyslipidemia and AHT), scales of disease activity and the FIB-4 (transaminases, age, platelets). A baseline evaluation was made at 6 and 12 months with a 3 years extension of the treatment.
Results: A total of 41 patients (17 women & 24 men), with an average age of 50.3 years (minimum 18 and maximum 80) and a BMI of 28.16 has been studied. 4.9% consumed alcohol habitually, 17.1% were smokers, 39% had hypertension, 41.5% had hypercholesterolaemia and 17.1% hypertriglyceridemia. Most patients had a moderate disease (DAPSA 20.9) at the beginning of treatment and kept a low activity in posterior months (DAPSA 6-8). The results of the Friedman's test indicate that there are no significant statistic differences on the different measurements of FIB-4 (P=0.575). In the study can be seen an increasing evolution of the FIB-4 values through the first months that is later stabilized through time. When studying if the evolution of FIB-4 is related to the evolution of BMI, it can be observed that exists a significant statistic relation in the evolution of both measures but being such relation quite weak. The evolution of the classification of the patients' FIB-4 at the beginning, at 6 months, at 1 year and at 3 years of treatment with methotrexate does not present significant statistic differences.
Conclusion: In patients with psoriatic arthritis, the treatment with methotrexate does not seem to increase the risk of developing a non alcoholic fatty liver disease.
Graphics
FIB-4 evolution



Relation of the BMI and FIB-4



Disclosure of Interests: None declared
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AB0911 **SHORT-TERM RESULTS OF GUSELKUMAB EFFICACY FOR PSORIATIC ARTHRITIS IN REAL LIFE.**

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Background: Psoriatic arthritis is a chronic immune-mediated disease that mainly affect joints, but is associated with a significant increase in cardiovascular risk and other comorbidities. In the last decades, some pathogenic pathways of these diseases have been identified and have led to the development of new therapeutic strategies such as biologic drugs. Early treatment and treat-to-target strategies have achieved a great improvement in the management of the disease, but there are still many refractory cases and further research is needed. Guselkumab is a human IgG1λ monoclonal antibody that selectively binds to interleukin 23, a regulatory cytokine that affects the activity of T lymphocyte subsets. In this way, blockade of IL-23 normalizes the production of pro-inflammatory cytokines. Guselkumab was approved by FDA to psoriatic arthritis treatment in 2020.
Objectives: To analyze the real-life effectiveness of guselkumab in a cohort of patients with psoriatic arthritis.
Methods: A prospective observational study was conducted in psoriatic arthritis patients who received treatment with guselkumab in a hospital center in the southeastern area of Spain, from April 2020. Patient demographic and baseline data were recorded and response variables such as DAPSA index, presence of enthesitis and dactylitis, skin affection by BSA, and drug persistence at 12 and 24 weeks of treatment were analyzed. In addition, adverse events were recorded.
Results: Twenty-nine psoriatic arthritis patients, 20 women, mean age at entry 52 ± 2.47 years, were included in this analysis. The mean of years since psoriatic arthritis diagnosis was 10.14 ± 1.68 years. Demographic and baseline variables of the patients are detailed in Table 1. The mean DAPSA value at the start of treatment was 25.02 ± 2.446. After 12 weeks, it was 17.51 ± 2.855, and after 24 weeks of treatment, it had dropped to 12.37 ± 3.547 points, this difference was statistically significant with p<0.01. The percentage of enthesitis presented a significant reduction, from 37.93% at baseline to 3.84% at 24 weeks of treatment. BSA index had a mean of 12.54 ± 5.94 at baseline, with a significant reduction at 12 weeks (2.136 ± 1.214) and at 24 weeks (0.4167 ± 0.4167). According to their DAPSA index score, patients were classified into remission, low activity disease, and active disease categories. One third of patients achieved complete remission, and another third achieved low disease activity at 24 weeks, as reflected in Figure 1. Treatment persistence was 89.65% at both 12- and 24-week reviews, as only 3 patients dropped out of treatment at 12 weeks. No drug-related adverse events, including local injection site reactions, were recorded.

Table 1. Demographics and baseline patient characteristics.

Baseline Patient Characteristics	guselkumab 100 mg/8 W (n = 29)
Age at inclusion, mean (95% CI), years	52 ± 2.47
Sex	
Female, *n* (%)	20, 68.9 %
Male, *n* (%)	9, 31.1 %
Disease duration of PsA mean [95% CI], years	10.14 ± 1.68
DAPSA mean [95% CI]	25.02 ± 2.44
Enthesitis, *n* (%)	11, (37.93 %)
Dactylitis, *n* (%)	
BSA mean [95% CI]	3, (10.34 %)
Line of treatment	12.54 ± 5.94
Second, *n* (%)	2, (6.89 %)
Third, *n* (%)	8, (27.58 %)
Fourth, *n* (%)	8, (27.58 %)
Fifth, *n* (%)	2, (6.89 %)
Sixthh, *n* (%)	3, (10.34 %)
Seventh, *n* (%)	5, (17.24 %)
Eighth, *n* (%)	1, (3.44 %)

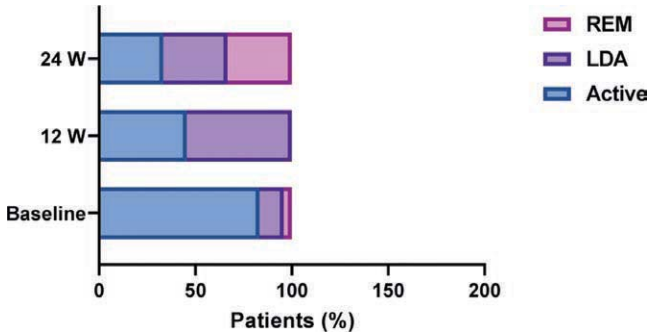

Figure 1. Percentage of patients reaching remission (REM), low disease activity (LDA) or active disease at baseline, 12 and 24 weeks after guselkumab treatment.

Conclusion: Guselkumab is effective and safe for the manifestations of psoriatic arthritis in a real-life cohort of patients.
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AB0912 **SWOLLEN AND TENDER JOINTS IMPROVEMENT IN THE RANDOMIZED CONTROLLED TRIALS OF PSORIATIC ARTHRITIS**

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Background: The ACR response is used to evaluate peripheral joints in psoriatic arthritis. However the main component in ACR treatment response is swollen (SJ) and tender joints (TJ), therewithal patient and physician global assessment, acute phase response, pain and function are included in this treatment response. Therefore, it can be thought that peripheral arthritis can best evaluated over SJ and TJ. Although ACR treatment responses are generally found to be similar between anti-TNF and anti-IL17/anti-IL23 in PsA, there is a general opinion that anti-TNF treatments may be more effective on the peripheral joint. (1).
Objectives: In this study, it was aimed to evaluate the efficacy on SJ and TJ in RCTs performed in PsA.
Methods: We was searched with the keywords 'psoriatric arthritis' and 'randomized controlled trial' in Pubmed. All studies between 1975 and 31.10.2021 were screened for TJ count (SD) and SJ count (SD) values at treatment initiation and primary endpoint. The 2 studies with anti-TNFs and the SPIRIT-1 study comparing ixekizumab with placebo and adalimumab showed the number of SJ and TJ at baseline and primary endpoint. Effect size calculated separately according to Morris and Klauer formula. (2,3) We can interpret the effect size according to Cohen as follows: 0-0,1 no effect; 0,2-0,4 small effect; 0,5-0,7 intermediate effect; 0,8-≥1 large effect. (4)
Results: Certolizumab study, ES was found at a good level in the number of TJ and SJ at 200 and 400 mg doses. (ES 0.84 for SJ). The study comparing ixekizumab with adalimumab and placebo, it was observed that administration of ixekizumab every 4 weeks was minimally more effective in the number of TJ (ES 0.16) and SJ (ES 0.13) than adalimumab. The effect of ixekizumab over placebo is also slightly better than that of Adalimumab over placebo. (0.51 vs 0.36 in TJ, 0.38 vs 0.29 in SJ)
Conclusion: Changes in the number of SJ and TJ that directly assess the peripheral joint have not been reported enough in RCTs in PsA patients. According to a limited number of reports, Anti-TNFs (eg, certolizumab) cause significant improvement in the number of SJ and TJ in the primary endpoint. On the other hand, Ixekizumab has as much effect on SJ and TJ as Adalimumab. The effect of anti-IL 17 treatments on the peripheral joint is not less than that of anti-TNFs, as thought.
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Table 1. Effect size analysis of studies

Tender Joint Count						
Reference	Week (w)	Intervention	Control	Baseline (Intervention vs Control)	ES (Morris)	ES (Klauer)
Spirit-1	12	Ixekizumab 4 w (n=107)	Adalimumab (n=101)	20,5 (13,7) vs 19,3 (13,0)	0.16	0.91
	12	Ixekizumab 2 w (n=103)	Adalimumab (n=101)	21,5 (14,1) vs 19,3 (13,0)	0.12	0.29
	12	Ixekizumab 4 w (n=107)	Plasebo (n=106)	20,5 (13,7) vs 19,2 (13,0)	0.51	5.1
	12	Ixekizumab 2 w (n=103)	Plasebo (n=106)	21,5 (14,1) vs 19,2 (13,0)	0.47	3.9
	12	Adalimumab (n=101)	Plasebo (n=106)	19,3 (13,0) vs 19,2 (13,0)	0.36	4.1
GENOVESE, Mark C., et al. M02-570 Study Group	12	Adalimumab (n=51)	Plasebo (n=49)	25,3 (18,3) vs 29,3 (18,1)	0.19	0.30
RAPID-PsA	24	Certolizumab 200 mg (n=138)	Plasebo (n=136)	21,5 (15,3) vs 19,9 (14,7)	0.67	0.75
	24	Certolizumab 400 mg (n=135)	Plasebo (n=136)	19,6 (14,8) vs 19,9 (14,7)	0.49	0.61
Swollen Joint Count						
Spirit-1	12	Ixekizumab 4 w (n=107)	Adalimumab (n=101)	11.4 (8.2) vs 9.9 (6.5)	0.13	0.63
	12	Ixekizumab 2 w (n=103)	Adalimumab (n=101)	12,1 (7,2) vs 9,9 (4,7)	0.19	1.18
	12	Ixekizumab 4 w (n=107)	Plasebo (n=106)	11,4 (8,2) vs 10,6 (7,3)	0.38	3.8
	12	Ixekizumab 2 w (n=103)	Plasebo (n=106)	12,1 (7,2) vs 10,6 (7,3)	0.45	3.2
	12	Adalimumab (n=101)	Plasebo (n=106)	9.9 (6.5) vs 10.6 (7.3)	0.29	4.4
GENOVESE, Mark C., et al. M02-570 Study Group	12	Adalimumab (n=51)	Plasebo (n=49)	18.2 (10.9) vs 18.4 (12.1)	0.33	0.29
RAPID-PsA	24	Certolizumab 200 mg (n=138)	Plasebo (n=136)	11.0 (8.8) vs 11.0 (8.8)	0.84	0.83
	24	Certolizumab 400 mg (n=135)	Plasebo (n=136)	10.5 (7.5) vs 11.0 (8.8)	0.84	0.87

AB0913

EFFICACY AND SAFETY OF SWITCHING FROM FILGOTINIB TO TOFACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS AFTER 6 MONTHS OF FOLLOW-UP

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Background: Phase 2 studies have shown that Filgotinib (FIL), a JAK-inhibitor (JAKi), significantly improves signs and symptoms of psoriatic arthritis (PsA) in patients with active disease. PENGUIN 1 and 2 were two phase III trials of FIL in PsA that were stopped. We considered Tofacitinib (TOFA) the best alternative drug for these patients because TOFA is the only JAKi approved so far in Spain for PsA. However, data in clinical practice about switching from FIL to TOFA have not been reported.

Objectives: To assess the efficacy and safety of switching FIL to TOFA in patients with PsA.

Methods: Prospective Single-University-hospital study of PsA patients diagnosed according to CASPAR criteria, and previously treated with FIL 100 mg and 200 mg/day in two clinical trials (PENGUIN 1 and 2). Based on a shared decision between the patient and the physician, once the trial was finished, patients receiving FIL were switched to TOFA (5 mg/12h) with a 7 days wash-up period. PsA activity, analytical and ultrasound outcomes were assessed at baseline and after 1, 3 and 6 months of treatment with TOFA. A power doppler ultrasound score (PDUS) was obtained using a scoring system which assessed bilateral midline wrists, metacarpophalangeal joints 1-5, proximal and distal interphalangeal joints 2–5 in hands and feet, bilateral knees, ankles and metatarsophalangeal joints 2-5 (apart from any other painful joint). Each image was scored semi-quantitatively on a scale of 0-3. We used MASEI index for the enthesis US evaluation (that includes entheses at 6 sites: proximal plantar fascia, distal Achilles tendon, distal and proximal patellar tendon insertion, distal quadriceps tendon and distal brachial triceps tendon). We also evaluated in these enthesis the presence/absence (0/1) of PD signal as it is the main activity signal.

Table 1. Psoriatic Arthritis activity, ultrasound and analytical outcomes at baseline, month 1, 3 and 6.

	Baseline	Month 1	Month 3	Month 6	p
Musculoskeletal activity scores, median [IQR]					
TJC – no.	2 [0-3]	3 [1.5-16]	1 [0-12]	2 [0-5]	0.22
SJC – no.	0 [0-0]	0 [0-5]	0 [0-6]	0 [0-2]	0.09
Ultrasound exam, median [IQR]					
PDUS score (0-90)	2 [1-9]	3 [1-6]	2 [0-4]	2 [2-9]	0.99
Enthesitis according to PDUS (n)	1 [0-2]	1 [0-2]	0 [0-2]	1 [0-1]	0.85
MASEI index	16.5 ±10.5	19.6 ± 14.5	15.5 ± 4.8	17.5 ± 11.8	0.82
Laboratory values					
Hemoglobin (g/dl) - mean±SD	13.96 ± 1.40	13.54 ± 1.38	13.79 ±1.60	14.40 ± 1.75	0.64
Leucocytes (x103/µL) - mean±SD	7.10 ± 3.40	7.27 ± 2.96	7.14 ± 2.89	8.20 ± 2.87	0.89
Lymphocytes (x103/µL) - mean±SD	2.03 ± 1.01	1.94 ± 0.95	2.16 ± 0.86	1.96 ± 0.45	0.94
Neutrophils (x103/µL) - mean±SD	4.24 ± 2.92	4.54 ± 1.97	4.18 ± 1.84	5.30 ± 2.37	0.85
Platelet count (x103/µL) - mean±SD	266.44 ± 57.35	250.67 ± 53.29	264.90 ± 56.78	287.20 ± 25.58	0.69
CRP (mg/dl) - median [IQR]	0.00 [0.00-1.70]	0.00 [0.00-0.00]	0.00 [0.00-0.00]	0.00 [0.00-0.00]	0.12
ESR (mm/h) - median [IQR]	15 [6-19]	9 [5-15]	12 [4-15]	13 [5-45]	0.12

CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; MASEI: Madrid Sonographic Enthesis Index; TJC: Tender joint count; PDUS: Power doppler ultrasound; SJC: Swollen joint count.

Results: We included 11 patients (6 women/5 men) with a mean age of 52.5±6.5 years who had received FIL during a mean time of 16.0±9.3 weeks. JAKi was used in monotherapy or combined with sulfasalazine (n=2), methotrexate (n=1) and apremilast (n=1). Disease activity, US scores and laboratory values during the follow-up are shown in Table 1. No significant changes were observed in any case. No adverse events were reported during the 6 month of follow-up except for 1 patient with lymphopenia (500/µL). TOFA was discontinued after 1 month in 1 patient because of lypmphopenia and inefficacy and after 3 months in 4 patients for worsening of the joint pain. It was remarkable that in some of the patients who reported a worsening of painful joints we did not observed a higher inflammatory activity in the SJC or US exam, and this incongruity could be due to the role that JAK/STAT inhibition plays in pain signaling pathways.

Conclusion: Switching from FIL to TOFA appears to be an effective and safe therapeutic option.

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AB0914

IS TENDER TO SWOLLEN JOINT COUNT RATIO A USEFUL CLINICAL MARKER OF RESPONSE TO BIOLOGICAL TREATMENT IN PSORIATIC ARTHRITIS PATIENTS?

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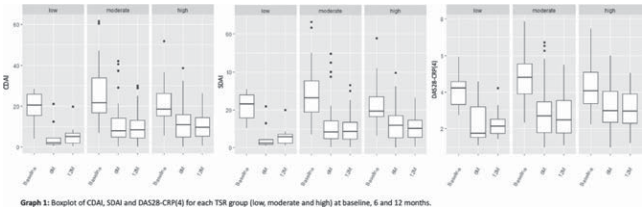
Background: Chronic inflammation in psoriatic arthritis (PsA) may trigger both peripheral and central sensitization via central modifications of pain pathways that can lead to disconnection between tender and swollen joint count. This can result in increased difficulties for the clinician in the assessment of the disease and response to treatment.

Objectives: To study the impact of tender to swollen joint count ratio (TSR) on treatment response to a first course of biologic disease-modifying antirheumatic drug (bDMARD) therapy in PsA patients.

Methods: Observational study including PsA patients under bDMARD, followed with clinical and laboratory examination at baseline, 6 and 12 months of treatment. All patients meet the CASPAR classification criteria. TSR was defined as the tender joint count divided by the swollen joint count, using the 68/66 joint assessment. Patients with no tender nor swollen joints at baseline were excluded. TSR was categorized into 3 groups, based on the empirical distribution, with cuts corresponding to the 20th and 70th percentiles. Disease activity was assessed using the *Clinical Disease Activity Index* (CDAI), the *Simplified Disease Activity Index* (SDAI) and *Disease Activity Score based on 28 joints* (DAS28-CRP(4)). Individual time profiles were plotted within each TSR group. CDAI, SDAI and DAS28-CRP(4) individual time profiles within each TSR group were modelled by mixed-effects linear regression using the TSR group and time as fixed factors and a random factor at the intercept level (accounting for the intra-individual correlation structure). The identification of the statistically significant pairwise differences was obtained from the Tukey's method for multiple comparisons.

Results: We included 113 patients, 62 (54.0% females) with a mean age of 48.1±10.8 years-old at the start of the first bDMARD. Sixty-four patients (56.6%) had symmetric polyarthritis, 19 (16.8%) spondyloarthritis, 25 (22.1%) asymmetric oligoarthritis, 2 (1.8%) distal arthritis and 1 (0.9%) arthritis mutilans. Forty-three percent were under corticosteroid therapy and 57.5% under conventional synthetic DMARD (csDMARD) therapy at baseline (mostly methotrexate, in 45.1% of patients under csDMARD). Etanercept (n=35, 31.0%), adalimumab (n=34, 30.1%), golimumab (n=25, 22.1%), infliximab (n=6, 5.3%), certolizumab (5, 4.4%), secukinumab (n=8, 7.1%) were the bDMARD started in these patients. TSR was categorized into 3 groups, namely low [TSR < 1], moderate [1 ≤ TSR ≤ 2.2] and high [TSR > 2.2], with frequencies 15 (13.3%), 66 (58.4%) and 32 (28.3%), respectively. Whenever the number of tender joints was different from 0 and that of swollen joints equal to 0, patients were included in the group high TSR. All TSR groups, with initiation of bDMARD, showed significantly decreases at 6 months in CDAI (low: p=0.006, moderate: p<0.001, high: p<0.001), SDAI (low: p<0.001, moderate: p<0,001, high: p<0.001) and DAS28-CRP(4) (low: p<0.001, moderate: p<0.001, high: p<0.001). From 6 to 12 months of treatment, the differences were not significant in any of the groups (p>0.05). At baseline, CDAI, SDAI and DAS28-CRP(4) means did not differ between groups (p>0.05). There were also no differences in the means of outcome measures at 6 months as well as at 12 months of treatment (p>0.05). Despite this, patients with low baseline TSR had lower mean values of CDAI, SDAI and DAS28-CRP(4) at 6 and 12 months of treatment, consistent with a low disease activity.

Conclusion: To our knowledge this is the first study exploring the TSR on treatment response in samples of patients exclusively with PsA. All patients benefited from bDMARD therapy, regardless of the group, suggesting that TSR might not be a good predictor of treatment response in patients with PsA.



Graph 1: Boxplot of CDAI, SDAI and DAS28-CRP(4) for each TSR group (low, moderate and high) at baseline, 6 and 12 months.

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AB0915 GUSELKUMAB REAL WORD DATA: EFFICACY AND SAFETY IN A COHORT OF 69 PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriasis (PSO) is a systemic immune-mediated disorder, characterized by inflammation skin and joint manifestations: it is known that up to 30% of PsO patients develop PsA. PsO and PsA share common etiopathogenetic pathways, as IL-23/IL-17 axis. In Italy, Guselkumab (GUS), a selective IL-23 inhibitor, was approved in 2018 for the treatment of PsO, and recently it was also approved for PsA therapy. Today, there are few "real-world" studies regarding the use of GUS in PsA patients.

Objectives: A multicenter Italian study group of dermatologists and rheumatologists aimed at evaluate GUS efficacy and safety in patients with concomitant PsO and PsA in real word setting on both skin and joint domains.

Methods: An observational retrospective, multicentric study was performed in 69 PsO patients with a confirmed diagnosis of moderate to severe PsA. PASI and DLQI were used for the evaluation of skin response, and the number swollen/tender joints, presence or absence of dactylitis or enthesitis or axial involvement and painVAS were evaluated for the articular and periarticular efficacy. These analyses were performed at baseline T0 (beginning of the therapy), T1 (12 weeks) and T2 (24 weeks).

Results: 38/69 patients (55,1%) presented oligoarthritis, 31/69 (44,9%) showed polyarthritis, none of the patients had enthesitis or axial involvement. Moreover, co-morbidities were diagnosed: hypertension (52,2%), hypercholesterolemia (34,8%), Hypertriglyceridemia (29%), diabetes (24,6%), obesity (23,2%), HIV-positive (20,3%), psychiatric disorders (17,4%), cardiopathies (15,9%), inflammatory bowel disease (7,3%), Latent Tubercolosis (4,4%), Chronic B-Hepatitis (2,9%), Chronic C-Hepatitis (1,5%). In all these patients, skin and joint responses were evaluated at week 12 and week 24.

Concerning skin efficacy, PASI 90 was achieved at week 24. Concerning Joint response: painVAS progressively improved till T2, tender joint count decreased in patients with oligo and polyarthritis at T1 and maintained at T2, while swollen joint count decreased in polyarthritis patients at T1 and maintained at T2. In oligo-arthritis patients, this parameter was not improved. The number of dactylitis did not decrease during the period of study (see Table 1). No safety concerns were reported in this population.

Conclusion: Efficacy and safety of GUS was confirmed in this study group of PsO patients with concomitant PsA and several comorbidities in a real-life setting.

	Male	Female	Total
Time point 0 (T_0): beginning of the therapy			
PASI	15,5	16,8	13,1
DLQI	15,8	16,9	15,3
Oligo-arthritis: number of tender joints (mean)	1,8	1,9	1,85
Oligo-arthritis: number of swollen joints (mean)	0,5	0,6	0,55
Poly-arthritis: number of tender joints (mean)	5,5	8,5	6,9
Poly-arthritis: number of swollen joints (mean)	2,1	2,5	2,3
Dactylitis	0,5	0,5	0,5
painVAS	5,5	7	6,3
Time point 1 (T_1): week 12			
PASI	4,9	5	4,9
DLQI	4,1	4,3	3,7
Oligo-arthritis: number of tender joints (mean)	1,03	0,45	0,8
Oligo-arthritis: number of swollen joints (mean)	0,6	0,6	0,6
Poly-arthritis: number of tender joints (mean)	1,4	2,2	1,8
Poly-arthritis: number of swollen joints (mean)	0,8	0,5	0,7
Dactylitis	0,4	0,4	0,4
VAS	2,7	2,3	2,6
Time point 2 (T_2): week 24			
PASI	1,5	1,6	1,5
DLQI	1	1,2	0,5
Oligo-arthritis: number of tender joints (mean)	0,7	0,4	0,5
Oligo-arthritis: number of swollen joints (mean)	0,6	0,5	0,6
Poly-arthritis: number of tender joints (mean)	0,8	0,5	1,3
Poly-arthritis: number of swollen joints (mean)	0,8	0,2	0,7
Dactylitis	0,4	0,4	0,4
VAS	1,4	1	1,2

Table 1: PsO & PsA parameters evaluated at each time points.

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AB0916 ASSESSMENT OF PSORIATIC ARTHRITIS IMPACT OF DISEASE (PSAID-12) QUESTIONNAIRE FOR EVALUATIONS OF 6-YEARS TREAT-TO-TARGET STRATEGY OUTCOMES

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Background: The 12-item psoriatic arthritis impact of disease questionnaire (PSAID-12) have been found to be a reliable instrument to specifically assess the impact of psoriatic arthritis (PsA) for the patients (pts) as well as predictive of long-term outcomes [1]. There are no data about use of the PsAID-12 for evaluation of long-term outcomes of treat to target (T2T) strategy in PsA pts.

Objectives: to assess the PSAID-12 for evaluations of 6-years outcomes of T2T strategy in PsA.

Methods: 50 (M/F–24/26) PsA pts fulfilling CASPAR criteria were included. Mean age 45±12.1 yrs, median (Me) PsA duration 82 [66;97] month (mos), Me follow-up 72 [58;89] mos. At the early stage (PsA duration≤2 yrs) all pts were treated according to T2T study within 24 mos. At 6 years follow-up all pts underwent standard clinical examination (tender joint count (TJS), swollen joint count (SJC), patient global assessment disease activity (PtGA), CRP (mg/l), skin psoriasis (PsO) by BSA (%), presence of nail PsO, enthesitis dactylitis, DAPSA and completed PsAID-12. PsAID-12 score≤ 4 is considered as a "patient-acceptable status symptoms" (PASS). PsAID-12 > 4 is considered as worse quality of life. DAPSA remission (REM-DAPSA) ≤4 and low disease activity (LDA) ≤14, moderate activity (Mo)≤28, high activity >28 were calculated. Me [Q25-Q75], M±SD, Spearman's correlation, Mann-Whitney test were performed. All p<0.05 were considered to indicate statistical significance.

Results: At 6 yrs follow-up REM-DAPSA were seen in 17 out of 50 pts (34%), LDA in 15 out of 50 (30%) pts. Mean total PsAID-12 score was 2.62±2.1. PASS was seen in 38 out of 50 pts (76%). PsAID-12 significantly associated with the PsA activity parameters: TJC (r=0.73, p<0.05), SJC (r=0.55, p<0.05), PtGA (r=0.77, p<0.05), CRP (r=0.55, p<0.05) and DAPSA (r=0.75, p<0.05). PsAID>4 significantly correlated with presence of dactylitis (r=0.33, p<0.05), skin severity (BSA>3) and presence nails PsO (r=0.41/r=0.38) accordingly. In pts with REM/LDA by DAPSA total PsAID score was significantly lower compare to pts with Mo/High activity - 1.34±0.99 and 4.89±1.84, accordingly (p<0.0001). All pts with REM/LDA status is achieved PASS by PsAID.

Conclusion: In our clinical practice PsAID-12 associated with joint and skin severity in PsA pts. PsAID-12 is useful instrument for evaluating of the long-term T2T outcomes, including REM/LDA by DAPSA.

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AB0917 A RANDOMIZED, USUAL CARE CONTROLLED, PARALLEL-GROUP PRAGMATIC CLINICAL TRIAL IN AN INTERDISCIPLINARY COMBINED DERMATOLOGY–GASTROENTEROLOGY–RHEUMATOLOGY CLINIC; PRELIMINARY DATA ON BASELINE CHARACTERISTICS OF 128 PATIENTS AND QUESTIONNAIRE-BASED QUALITATIVE DATA FROM 30 PATIENTS AND 15 HCPS

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Background: Immune-Mediated Inflammatory Diseases (IMIDs), including psoriatic arthritis (PsA), axial spondyloarthritis (AxSpA), psoriasis, hidradenitis suppurativa, and inflammatory bowel disease share both pathophysiological and environmental factors, individuals with one IMID have an increased risk for developing other IMIDs, and are associated with reduced health-related quality of life, increased risk of comorbidities, and reduced socioeconomic status.

Unmet needs in care of patients with IMIDs may result from lack of patient-centricity in the usual mono-disciplinary siloed approach to these diseases.

Objectives: The overall aim of this study is to determine the effectiveness of an interdisciplinary combined clinic intervention compared to usual care in patients with the aforementioned IMIDs.

Table 1. Advantages and challenges on feedback from 15 HCPs and feedback from 30 patients.

Advantages - HCP	Challenges - HCP	Themes mentioned by the patients
Professional development	Culture -Old habits from regular departments -"This is how we usually do this"	Communication between HCOs improved treatment
Satisfying to work on a high professional level	Create a new culture takes time and patience -Large differences between specialties and subject areas	Collaboration between HCPs improved treatment
Improved perspective on diseases and patients	Logistics, physical requirements	Holistic approach –patients felt HCPs cared for all health aspects
Collaboration – professional, personal, team spirit	Shared goals	Confidence in living with diseases
Meaning full to work with all aspects of disease	Time and patience	Coherence
Effective communication	Optimal use of time and resources	Treatment optimization
Learning can be brought back to "monodisciplinary" work (improved treatment in respective departments)		Clarification about diet, mastering fatigue and work-related problems
Broader disease focus		Avoid patient being information carrier
Reflection		

Methods: This is a randomized, usual care controlled, parallel-group pragmatic clinical trial. 300 consecutively enrolled participants with co-occurrence of at least two IMIDs are randomly assigned 2:1 to either treatment in the interdisciplinary combined clinic or usual care. The study consists of a 6-month active intervention period and a 6-month follow-up period. Primary outcome is change from baseline to 24-Weeks on the Short-Form Health Survey (SF-36). Additional questionnaire-based qualitative date from 30 patients and 15 health-care professional (HCP)s involved in the center are reported.

Results: Here we report baseline characteristics of the first 128 patients (mean age: 45.4y, 18–74.2, females (83, 64.8%)). All patients had ≥2 IMIDs: Psoriasis (99, 77.3%), PsA (peripheral) (72, 56.3%), AxSpA (34, 26.6%), Hidradenitis (16, 12.5%), Crohn (35, 27.3%), Colitis (20, 15.6%), AxPsA (9, 7.0%), IBD-associated arthritis (10, 7.8%), HS-associated arthritis (1, 0.8%). HLA-B27 was positive in 24 (22.2%) patients. Advantages, challenges and themes mentioned by the patients are listed in Table 1.

A statement from a patient: "It gave me much more peace of mind that I should not "split" my health problems and run errands between different departments. Didn't have to tell the same issues in several places or even try to figure out who to say what to, or who can answer a given question."

Conclusion: In conclusion, an interdisciplinary combined clinic based on an inflammation medicine holistic concept has been successfully established. Preliminary results indicate a high value of an interdisciplinary combined clinic in patients with IMIDs, and HCPs find both advantages and challenges in establishing a combined clinic.

Disclosure of Interests: None declared

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AB0918 EVALUATION OF X-RAY PROGRESSION AT 6 YEARS FOLLOW-UP OF TREAT-TO-TARGET STRATEGY IN EARLY PSORIATIC ARTHRITIS

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Background: In Psoriatic arthritis (PsA) patients (pts) persistence inflammation in the peripheral joins leading bone erosions, joint space narrowing and new bone formation. Tight control of PsA disease improved joint and skin outcomes, but the number of pts with erosions increased [1]. Despite of clinical improvement no long-term treat to target (T2T) strategy data on radiographs progression yet [2].

Objectives: To study X-ray progression in PsA pts treated according to T2Tstrategy at the early stage of disease at 6 years (yrs) follow-up.

Methods: 30 (M/F–17/13) PsA pts fulfilling CASPAR criteria, mean age 44.7±11.4 yrs, median (Me) PsA duration 78.5 [66;95] month (mos), Me follow-up 71 [60;86] mos, Me DAPSA 24 [7;45]. All pts was treated according to T2T strategy at the early stage with MTX alone or in combination with iTNF within 2 yrs. When T2T study was ended all pts were treated according to standard care. All pts underwent standard clinical examination of PsA activity, DAPSA was calculated. Radiographs of the hands and feet were available for 30 pts at baseline and 26 (86.6%) at 6-yrs follow-up. Radiographs of the hands and feet were scored using the modified van der Heijde-Sharp (m-v-d-HS) scoring method for PsA assessing both erosion, joint space narrowing (JSN) and total score (TS) m-v-d-HS. Scoring was done by two readers. The number of pts with erosions was calculated at baseline and 6 yrs later. M±SD, Me [Q25; Q75], Me (Min-Max), Mann-Whitney test were performed. All p<0.05 were considered to indicate statistical significance.

Results: At 6 yrs follow-up Me TS m-v-d-HS and JSN significantly increased from 34 (0-104) to 50 (6-253) and from 34 (0-97) to 50 (6-127) accordingly (p=0.006 and p=0.011); count of erosion from 0 (0-13) to 4 (0-128), p=0.002. In 19 out of 26 pts significantly negative X-Ray progression in the feet and hands by TS m-v-d-HS, count erosion, joint space narrowing was seen (for all p<0.05). In 7 out of 26 pts no X-Ray progression was found. PsA activity by DAPSA was significantly higher in pts with X-ray progression compare to those without progression 14.1 [5.19;33.67] and 2.22 [0.55;13.54] accordingly (p=0.04). 6 yrs later the number of pts with erosions significantly increased from 12 out of 26 (46%) at baseline to 22 out of 26 (85%) pts accordingly (p=0.002).

Conclusion: At 6 yrs follow-up negative radiographic progressions in the hand and feet found in mostly early PsA pts despite of tight control treatment strategy within 2 yrs.

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AB0919 PSORIATIC ARTHRITIS: FACTORS ASSOCIATED WITH THE USE OF BIOTHERAPY

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Background: The use of biological treatment in psoriatic arthritis has revolutionized its management with both joint and skin efficacy [1].
Objectives: The goal of our study was to evaluate the use of biological treatment in these patients and to assess the factors associated with it.
Methods: Retrospective study conducted within the rheumatology department of the University Hospital of Fez. Patients were recruited from January 2011 to January 2021. We included patients with psoriatic arthritis according to CASPAR criteria and assessed the use of biotherapy as well as the epidemiological, clinical and biological factors associated with it.
Results: There were a total of 98 patients with psoriatic arthritis, 21 of whom had been put on biological treatment. Of the total of 21 patients, there were 42.9% women and 57.1% men, the average age was 51.1 (± 9.92) years. 20% of patients had a history of tuberculosis, 14.3% had diabetes, 10% had hypertension and 30% had dyslipidemia. 60% of patients had an inflammatory syndrome, 73% had radiographic sacroiliitis and 63.2% had functional repercussions. In bivariate analysis, the value of the initial C-reactive protein CRP (p = 0.04), the initial disease activity score DAS 28 CRP (p = 0.0001) and the value of the initial erythrocyte sedimentation rate ESR (p = 0.02) were significantly associated with the use of biotherapy, there was no significant association with the other parameters. In multivariate analysis, no factor was significant.
Conclusion: An active psoriatic arthritis predicts the prescription of a biological treatment, other studies with a larger sample would be necessary to confirm our results.
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AB0920 SAFETY OF APREMILAST IN PSA PATIENTS WITH HISTORY OF MALIGNANCIES OR ACTIVE CANCER: A RETROSPECTIVE STUDY

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Background: One of the most intriguing aspects in the management of patients with inflammatory arthritis is the safety of novel therapies in those with a recent history of malignancy or active neoplasm. In this regard, apremilast (APR), an oral PDE4 inhibitor, is emerging as one of the safest therapeutic options in patients with PsA with comorbid cancer.
Objectives: This retrospective study aims to assess the effectiveness and safety of APR in PsA patients with a recent history of malignancy or active cancer.
Methods: We retrospectively observed patients with a history of neoplasm diagnosed from 1997 to 2021, who underwent apremilast treatment from 2017 to 2021 in a tertiary care centre. We recorded demographic and clinical characteristics at APR baseline and last visit. Furthermore, we recorded the eventual recurrence of primary cancer or the onset of new neoplasms. Paired t-test was used to assess the difference of continuous variables at different follow-ups.
Results: Thirteen patients (sex: female 6/13, 46,15%; mean age (mean ± 63,7 years sd ± 9,9 years)) started Apremilast between 2017 to 2021 in a tertiary care center. We assessed their clinical condition using DAPSA, LEI and PASI score in the baseline and in the last visit. Mean follow-up time was 32,02 ± 18,92 months. Mean DAPSA at baseline 20,55 ± 9,15 decreased to 16,21 ± 1,73 at last visit. Similarly mean LEI at baseline was 1,23 ± 1,58 and decreased to 0,61 ± 0,35 at last visit, even in absence of statistical significance (p=0,15). Conversely mean PASI at baseline (1,76 ± 2,57) did not show a decrease (1,61 ± 0,93);
Ten patients were still treated with apremilast at last available follow-up. Patient 6 (Table 1) experienced the relapse of Ductal Breast Papilloma. For patient 8, a relapse of primary cancer occurred. Patient 9 had the onset of a new neoplasm. The APR was not discontinued as such malignancies were not considered as treatment associated. Three patients (4, 6, 10) discontinued APR due to intolerance or lack of efficacy.

Table 1.

	DIAGNOSIS OF NEOPLASM	YEAR OF DIAGNOSIS	TREATMENT	RELAPSES/NEW OCCURRENCES
1	MENINGIOMA	2019	FOLLOW-UP	N
2	PROSTATE ADENOCARCINOMA	2017	PROSTATECTOMY (2017) RADIOTHERAPY	N
3	DUCTAL BREAST CANCER	2019	RADICAL MASTECTOMY (2019) CHEMOTHERAPY	N
4	DUCTAL BREAST PAPILLOMA	1997	FOLLOW-UP	Y
5	BLADDER CARCINOMA	2012	RESECTED (2013)	N
6	FOLLICULAR LYMPHOMA	2014	STEM CELLS (2014)	N
7	OSTEOID OSTEOMA	2017	FOLLOW-UP	N
8	FOLLICULAR LYMPHOMA IIIA	2017	CHEMOTHERAPY	Y
9	PULMONARY NODULE	2019	CHEMOTHERAPY, RESECTED	Y
10	BLADDER CARCINOMA	2017	RESECTED (2017)	N
11	ONCOCITOMA	2016	RESECTED (2016)	N
12	COLON CARCINOMA	2020	RESECTED (2020), CHEMOTHERAPY (2021)	N
13	BREAST CANCER	2018	RESECTED (2018)	N

Ten patients were still treated with apremilast at last available follow-up. Patient 6 (Table 1) experienced the relapse of Ductal Breast Papilloma. For patient 8, a relapse of primary cancer occurred. Patient 9 had the onset of a new neoplasm. The APR was not discontinued as such malignancies were not considered as treatment associated. Three patients (4, 6, 10) discontinued APR due to intolerance or lack of efficacy.
Conclusion: APR seems a safe option in PsA patients with a recent history of malignancy or active cancer, improving articular involvement.
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AB0921 EFFECTIVENESS OF GUSELKUMAB IN PSORIATIC ARTHRITIS IN DAILY CLINICAL PRACTISE

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Background: Guselkumab is a monoclonal antibody against interleukin-23, biological agent approved for the treatment of plaque psoriasis and psoriatic arthritis. There are two randomised, double-blind, placebo-controlled phase III studies (DISCOVER 1 and DISCOVER 2) that evaluated the efficacy and safety of guselkumab versus placebo. Treatment with guselkumab resulted in significant improvements in the measures of disease activity compared to placebo at Week 24. [1]
Objectives: To evaluate the response to Guselkumab in patients with Psoriatic Arthritis, according to CASPAR criteria, undergoing treatment by dermatology indication.
Methods: This is an observational descriptive retrospective study that includes patients with Psoriatic Arthritis (acording to CASPAR criteria) who are being treated with Guselkumab under dermatology indication due to skin involvement. In this study, the epidemiological and clinical characteristics of the patients are assessed: IMC, affected domains, previous treatments, concomitant treatments, PASI before begining the treatment, at 12 week and 24 week, and joint activity mesured by DAPSA at the beggining, after 12 and 24 week.
Results: There are 7 patients included, 5 women and 2 men, the mean age were 50 ± 7.9 years old, with a BMI (body mass index) average of 33.13 ± 6.26. All the patients presented skin involvement: 4 of 7 with plaque psoriasis (2 of them with scalp psoriasis, and one of those two with inverse psoriasis), 3 of 7 with psoriasis in palms and soles (one with scalp psoriasis and inverse psoriasis), and 2 of 7 pacients with nail involvement. Regarding joint damage, all the patients presented peripheral joint involvement, 2 of 7 with axial too. For the other domains: 2 of 7 have had recurring uveitis, 1 of 7 one episode of dactylitis, and none of them any episode of enthensitis nor inflammatory bowel disease. All the patients had received at least 1 bDMARD (average of 2.8 ± 2.23, but one of them have used 7 before). All the patients received the standard dose of Guselkumab 100mg sc (week 0 and 4) and later each 2 months, with a duration of treatment in months with an average of 6.3 ± 2.88. At the same time, 1 of 7 patient used Methotrexate concomitantly, 2 of 7 with leflunomide, and 1 of 7 with NSAIDs. The PASI average at the beggining of the treatment with Guselkumab was 9.25 ± 4.99, at 12 week all the patients had obtain a PASI 0, and remained in remission. Regarding joint damage measured with DAPSA, at the beggining of Guselkumab treatment the average was 24.15 ± 22.02, at 12 week 12.19 ± 5.56, at the 24 week 8.86 ± 1.6, all of the patients improved, without any inflammatory flares. Any of them presented uveitis, enthensitis nor dactylitis. Drug retention rate of 100%, all the patients are still in treatment with Guselkumab, any side effect was detected.
Conclusion: Guselkumab is a very effective drug for the treatment of psoriasis, but also for the joint involvement in patients with failure to bDMARD. We need more real life studies to determinate the effectiveness in daily clinical practise.
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Psoriatic arthritis - clinical aspects (other than treatment)

AB0922 PSORIATIC ARTHRITIS DISEASE ACTIVITY DIFFERS BY RACE/ETHNICITY

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Background: Psoriatic arthritis (PsA) affects up to 30% of individuals with psoriasis. Studies have demonstrated that the presenting disease severity and quality of life impact of psoriasis differs by race/ethnicity in patients with and without PsA, but little is known about disease activity among different racial/ethnic groups [1-3].
Objectives: The objective of our study was to evaluate disease activity by race/ethnicity among patients with PsA.
Methods: We performed a cross-sectional study of adult (≥18 years old) patients with PsA who had at least one outpatient visit within the University of Pennsylvania health system between 2010 and 2019. Patients with PsA were identified by the presence of at least two International Classification of Diseases (ICD)-9 or ICD-10 codes for PsA associated with two different healthcare encounters. The primary outcome was disease activity as measured by the Routine Assessment of Patient Index Data 3 (RAPID3) assessment. The RAPID3 score is a validated patient-reported measure of physical function, pain, and global status [4]. RAPID3 scores range from 0 to 30, with higher scores indicating greater disease activity. Patients were included if they had at least one documented RAPID3 score. For patients with multiple RAPID3 scores, the median value was used. The primary independent variable was race/ethnicity categorized as White (reference), Black, Asian, Hispanic, or other race. Multivariable linear regression was used to assess the relationship between race/ethnicity and RAPID 3 score.
Results: The study population included 742 patients. Mean (standard deviation [SD]) age was 47.2 (13.3) years and 57.4% were female. The racial/ethnic distribution was 79.4% White, 7.0% Black, 5.0% Asian, 3.1% Hispanic, 2.6% other race, and 3.0% missing race/ethnicity. The means of the median Rapid3 scores were statistically significantly different across racial/ethnic groups (p<.001): White mean (SD) 9.79 (6.02), Black mean (SD) 14.86 (14.86), Asian mean (SD) 9.79 (5.44), Hispanic mean (SD) 15.09 (7.11), other race mean (SD) 10.57 (6.91). In an adjusted multivariable model controlling for other sociodemographic factors, body mass index, treatment history, and medical comorbidity, Hispanic patients had higher RAPID3 scores compared to White patients, indicating greater disease activity (β 3.36; 95% confidence interval [CI] 1.04 – 5.67, p <.005). In exploratory stratified analyses to evaluate effect modification by sex, among males, Black (β 3.43; 95% CI 0.23 – 6.63, p=.04) and Hispanic (β 5.94; 95% CI 2.18 – 9.70, p <.005) patients had higher RAPID3 scores than White patients. Among females, no significant racial/ethnic differences in RAPID3 scores were identified.
Conclusion: Black and Hispanic patients report greater disease activity as indicated by higher RAPID3 scores compared to White patients. Larger studies are necessary to confirm our findings and understand the causes of racial/ethnic differences in disease activity among patients with PsA.
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AB0923 ASSESSMENT OF FOUR SCREENING TOOLS AND RETRIEVAL OF KEY QUESTIONS TO DETECT UNDIAGNOSED PSORIATIC ARTHRITIS IN CHINESE PATIENTS WITH PSORIASIS: A MULTICENTER STUDY

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Background: The available data showed great discrepancies in the performance of screening tools in detecting psoriatic arthritis (PsA) in patients with psoriasis, and those including the diagnosed PsA in the validation might exaggerate/overestimate the performance. The key questions in each tool were unclear and their contributions were not systematically assessed. Here the performance of four different screening tools were validated and compared in detecting undiagnosed PsA, and the key questions with different weights of them were retrieved and evaluated.
Objectives: To compare and validate the performance of the four screening tools in detecting undiagnosed psoriatic arthritis (PsA) in Chinese patients with psoriasis, and to determine the key questions and their weights.
Methods: Consecutive patients with psoriasis but no prior diagnosis of PsA from dermatology clinics and patients with newly diagnosed PsA from rheumatology clinics who were blind to the diagnosis were recruited to complete questionnaires, including early psoriatic arthritis screening questionnaire (EARP), psoriatic arthritis screening and evaluation questionnaire (PASE), psoriasis and arthritis screening questionnaire (PASQ), and psoriasis epidemiology screening tool (PEST). The receiver operator characteristic (ROC) curve with area under curve (AUC) was used to determine sensitivity, specificity and accuracy. The LASSO and logistic regression were utilized to retrieve key questions, and a nomogram was utilized to visualize their weights.
Results: Of 482 psoriasis patients from dermatology clinics, 77 patients were newly diagnosed with PsA. Another 68 patients with newly diagnosed PsA from rheumatology clinics were incorporated in the analysis. ROC analysis indicated that the optimal cut-off values for EARP, PASE, PASQ and PEST were 3, 40, 7 and 3, with corresponding sensitivities of 91.4%, 88.6%, 86.2% and 88.5%, and specificities of 88.6%, 75.2%, 80.2%, and 83.6%, respectively. The AUC of EARP (0.925) was higher than those of PASE (0.885), PASQ (0.905) and PEST (0.827). A total of twelve key questions were retrieved from these four tools, and their relative weights were scored as 5~100 individually with a nomogram.
Conclusion: To screen undiagnosed PsA, EARP have slightly better balanced sensitivities and specificities. The retrieved twelve key questions may be helpful in proposing a new questionnaire with different scores of each question to screen PsA more efficiently.
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AB0924 INDIVIDUAL DIGIT LEVEL NAIL INVOLVEMENT AND JOINT ASSESSMENT IN PATIENTS WITH NAIL PSORIASIS

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Background: The relationship between the evolution of nail disease and the articular features of Psoriatic Arthritis (PsA) is poorly understood. There is a lack of data on the relationship between nail and joint disease, important clinical parameters of disease activity, specifically at the individual digit level.
Objectives: To evaluate the level of association, at digit level, between nail involvement and joint disease at baseline, with a special focus on distal interphalangeal joint (DIP) assessment.
Methods: SPIRIT-H2H (NCT03151551) was a 52 week, multicenter, randomised, open-label, parallel-group, assessor-blinded study evaluating the efficacy and safety of IXE vs ADA in PsA.[1] Nail psoriasis was measured using Nail Psoriasis Severity Index (NAPSI). Joint involvement was measured by tender/swollen joint count (TJC/SJC) scores. Here we examine both baseline tenderness and swollenness at the DIP joint, proximal interphalangeal (PIP) joint and metacarpophalangeal (MCP) joint level for each digit and evaluate the level of association

between nail involvement (NAPSI>0 vs NAPSI=0) and joint assessment using Chi-square tests and/or Fisher's exact test where relevant.

Results: Overall, 368 patients (IXE N=191, ADA N=177) out of 566 had a baseline NAPSI >0. The overall level of nail involvement ranged from 52.7% (n=194) (right 5th finger) to 67.9% (n=250) (right 1st finger). When considering a digit-wide assessment of joints (DIP, PIP, and MCP), in general, no clear association was found between NAPSI >0 and joint involvement. However, there was more frequent DIP joint involvement in patients with nail involvement compared to patients without nail involvement. When taking only the DIP joint into account, nail involvement was found to be statistically associated with tenderness and/or swelling at the DIP level (Figure 1), with differences between patients with nail involvement vs. without nail involvement ranging from 7.9% (p=0.023) (right 5th finger) to 19.4% (p<0.001) (left 3rd finger). These differences are mostly driven by tenderness rather than swelling, irrespective of digit. For tenderness, differences (with vs. without nail involvement) ranged from 7.0% (right 2nd finger) to 18.0% (left 3rd finger). Differences due to swelling ranged from 5.0% (left 1st finger) to 12.2% (left 3rd finger).

Conclusion: In SPIRIT-H2H, tenderness and/or swelling at the DIP joint was significantly associated with nail involvement in individual digits.

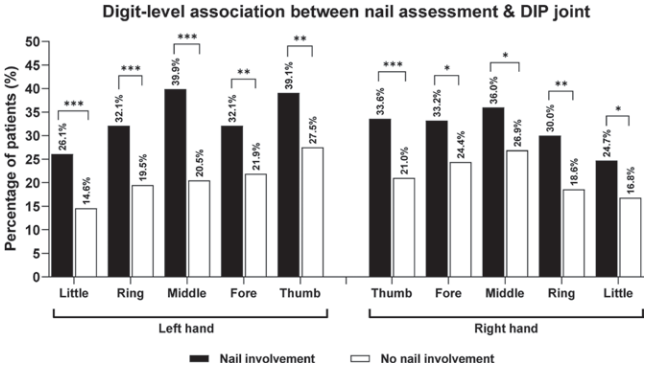

Figure 1. Digit level association between nail assessment and DIP joint.Significant difference between nail involvement and no nail involvement denotated by * (p≤0.05), ** (p≤0.01), *** (p≤0.001). Abbreviation: DIP= Distal interphalangeal joint.

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AB0925 ADVANTAGES OF COMBINED DERMA-RHEUMATOLOGICAL EVALUATION IN EARLY PSORIATIC ARTHRITIS

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Background: Psoriatic Arthritis (PsA) is a challenging diagnosis both for the absence of specific biomarkers and for its clinical heterogeneity, especially in its initial phases. Early onset of PsA is mostly characterized by mono-oligoarthritis, enthesitis, dactylitis, onychopathy, modest cutaneous involvement. At least 50% of early-PsA patients initially come at dermatologist's attention because they carry only few musculoskeletal symptoms such as enthesitis and dactylitis. Rheumatological evaluation and ultrasound (US) demonstration of articular and entheseal inflammation allows to augment the probability of an early diagnosis in a short period of time.

Objectives: We described patients referred to our derma-rheumatological clinic. We focused our attention on the main affected domain and on the advantages of a combined evaluation in terms of diagnosis, access to advanced therapies and short-term outcome.

Methods: All patients referred to our derma-rheumatological clinic by dermatologists from July 2017 to July 2019 for suspected PsA were considered in the present study. 55% of them were studied with US, according to clinical necessity. All the suspected domains were studied using both B-mode and Power Doppler.

Results: 81 patients, sent to our attention for suspected PsA, were included. In 18 (37%) of them diagnosis was confirmed (Caspar criteria were satisfied). In these patients oligoarthritis (80%), enthesitis (40%), dactylitis (23%), sometimes in combination, were the most frequent presentations. In 25% of cases enthesitis was the only clinical feature. Articular disease activity was low to moderate in most of patients (DAPSA 14,83 ± 10,08). Disease duration at the diagnosis was 12 months in 90% of cases and the time occurring between symptoms and the first advanced therapy was 18 months in 50% of cases. US study allowed to redefine disease status in 30% of cases. Arthritis and enthesitis were the main domains where US evaluation gave more diagnostic value.

Conclusion: Literature reports a mean time to diagnosis and to start advanced pharmacological therapy respectively of 1,5 and 5 years. In our report, time to start advanced therapy was much lower than expected, falling in the so-called window of opportunity. US study importantly contributed to reach this target, allowing us to identify as soon as possible sub-clinical and pauci-symptomatic forms (low disease activity, prevailing entheseal domain), which could otherwise be misdiagnosed or have an important diagnostic delay. The attention of dermatologist and integrated evaluation allowed us to optimize our diagnostic-therapeutic work-up in patients affected by early PsA, allowing them to receive sooner advanced therapies, according to recent EULAR and GRAPPA recommendations.

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AB0926 ENTHESITIS OF THE HAND IS A DOMINANT LESION IN PSORIATIC ARTHRITIS AND MAY HELP DISTINGUISH IT FROM RHEUMATOID ARTHRITIS: CASE-CONTROL, SINGLE-CENTRE, ULTRASOUND STUDY

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Background: Enthesitis is the hallmark of psoriatic arthritis (PsA) and may assist in distinguishing PsA from other forms of arthritis (1,2). Its clinical evaluation is hampered by lack of specificity of physical examination (3). Ultrasound (US) may provide information about its presence and response to treatment. Although some previous works have shown that enthesitis of the hand is important in PsA (4), most US studies and scores focused on greater size entheses.

Objectives: To explore the prevalence of enthesitis of the hand in PsA patients as evaluated by US, and compare it with other inflammatory arthritides, namely rheumatoid arthritis (RA).

Methods: Cross-sectional study in which consecutive patients with PsA and RA were recruited for an US protocol evaluating 4 entheses of the hand including: 1. measurement of the extensor digitorum tendon central slip at its insertion at the middle phalanx of the 2nd and 3rd finger bilaterally; 2. search for the presence of power-Doppler (PD) sign; 3. identification of structural lesions. Linear regression models were built to test if diagnosis (PsA vs RA) explained part of the variance of the thickness of tendons insertion while controlling possible influences of age, type of work and body surface area. A ROC curve was built to find a mean thickness cut-off allowing distinction between PsA and RA. The prevalence of PD sign and structural lesions of the entheses was compared between groups.

Results: Fifty-eight patients were recruited (29 with PsA and 29 with RA) and a total of 232 entheses were evaluated. Mean thickness of the interest entheses was superior in PsA patients compared to RA patients (2nd finger – 0.96 ± 0.16mm vs. 0.74 ± 0.09mm; 3rd finger – 0.96 ± 0.20mm vs. 0.76 ± 0.11mm). Linear regression models including diagnosis and potential confounders significantly explained mean thickness of both entheses (2nd finger – R^2=0.56, p<.001; 3rd finger – R^2=0.41, p<.001), with the diagnosis group being the most important predictor (Table 1). ROC curve (AUC 0.897, p<.001) showed a cut-off value of 0.925mm for the mean of the 4 entheses had a specificity of 93.1% for the identification of PsA patients.

Table 1. Multiple linear regression models explaining thickness of the entheses.

	2nd finger (mean of both sides)	3rd finger (mean of both sides)
Linear regression model	R^2=0.56 p<.001***	R^2=0.39 p<.001***
Diagnosis (PsA vs RA)	β=0.587; B=0.203mm p<.001***	β=0.483; B = 0.182mm p<.001***

In our sample, 8 (3.5%) entheses had a measured thickness above mean + 2 SD, all belonging to PsA patients; 6 (75%) had signs of ongoing inflammatory process as proved by the presence of PD sign (Figure 1). Regarding structural lesions, enthesophytes or bone irregularities/erosions were found in 13.8% of PsA entheses, which compared to 1.7% of RA entheses.

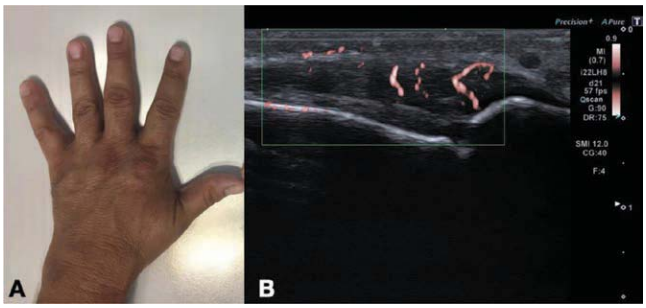

Figure 1. Enthesitis of the central slip of extensor digitorum of the 3rd finger in a patient with PsA: swelling of the 3rd proximal interphalangeal joint (A) due to inflammatory process originating in the enthesis, with no signs of synovitis, as evaluated by US (B).

Conclusion: This work reinforces enthesitis as a key lesion in PsA. It also shows enthesitis occurs significantly in small entheses, like the ones of the hand and that, in some instances, it may be the dominant lesion in a swollen joint. US may be valuable for establishing a diagnosis in the setting of inflammatory arthritis of unknown etiology.

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AB0927 CLINICAL AND RADIOGRAPHIC PHENOTYPE OF AXIAL PSORIATIC ARTHRITIS

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Background: The latest data show that axial psoriatic arthritis (PsA) is less symptomatic, as compared with ankylosing spondylitis, and is associated with distinct radiographic features (1).
Objectives: To analyze clinical characteristics of PsA patients (pts) with axial involvement, using data from a real-life outpatient cohort.
Methods: 50 pts (M/F–30 /20) with PsA according to CASPAR criteria were included. All pts had either a present or past history of back pain, which rheumatologist suspected to be axial involvement. Pts' age 42.0 [34.0; 54.0], disease duration 3.5 [0.3; 32.5] years. Pts underwent standard clinical examination of PsA activity: Me BASDAI was 6.2 [3.8; 8.0], ASDAS-CRP 3.5 [2.5; 4.8], DAPSA 38,1 [20,2; 52,2], CRP 12.4 [0.3; 94.6] mg/L. All pts were evaluated for presence of inflammatory back pain (IBP) by ASAS criteria. HLA B27 antigen status was observed. Physical examination included Bath Ankylosing Spondylitis Metrology Index (BASMI). Pts underwent X-ray of sacroiliac joints (pelvic radiographs), cervical and lumbar spine, and hands and feet. Radiographic sacroiliitis (rSI) was defined as bilateral grade ≥ 2 or unilateral grade ≥ 3. All radiographs were interpreted by two experienced musculoskeletal radiologists. Me [Q25; Q75], Pierson-χ2 tests were performed. All p<0.05 were considered to indicate statistical significance.
Results: IBP was detected in 31 (62.0%) pts, while 19 (38.0%) pts didn't meet IBP criteria – they had chronic back pain (CBP); 12 (24.0%) of all pts had episodic mild back pain. In 15 (30.0%) pts back pain started at age of above 40. RSI was found in 29 (58.0%) pts, while mostly symmetrical in 23/29 (79.3%) cases. Unilateral grade 2 sacroiliitis was found in 4 (8.0%) pts. 13/29 (44.8%) pts developed rSI without IBP. 38 (76%) pts had erosive arthritis, 18 (36%) pts had numerous erosions. HLA-B27 antigen was positive in 16 (32.0%) of pts. A correlation was revealed between the presence of rSI and limited spine mobility by BASMI (r=0.347). Association was found between rSI and numerous erosions (p=0.003), as well as between rSI and juxtaarticular new bone formation on hands and feet X-rays (p = 0.02). Syndesmophytes were found in 28 (56%) cases. 11 (22%) pts developed syndesmophytes without rSI. Asymmetrical syndesmophytes in the lumbar spine were found in 7/13 (53.8%) pts, vertebral non-bridging syndesmophytes in the lumbar and/or cervical spine in 16 (57.1%) pts. Restricted neck rotation was found in 85% of cases. Syndesmophytes in the cervical spine were found twice as often (26 pts) as in the lumbar spine (13 pts); 14 (28%) pts had isolated involvement of the cervical spine. An association was detected between asymmetrical syndesmophytes and radiographic changes on hands and feet X-rays such as osteolysis (p = 0.005) and juxtaarticular new bone formation (p = 0.05).
Conclusion: Axial PsA is often asymptomatic, one third of pts develop back pain at age above 40. HLA-B27 positivity was found in only 32% of pts. Pts with rSI are more likely to have severe peripheral arthritis with multiple joint erosions. Radiographic SI is associated with juxtaarticular new bone formation, which may indicate common mechanisms of bone formation in axial and peripheral skeleton. Syndesmophytes may occur in absence of sacroiliitis. Cervical spine involvement is more frequent in axial PsA pts. Asymmetrical syndesmophytes characteristic of PsA, are associated with typical, for PsA, radiographic changes on hands and feet X-rays, such as osteolysis and juxtaarticular new bone formation.

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AB0928 CHARACTERISTICS OF AXIAL PSORIATIC ARTHRITIS PATIENTS WITH SYMMETRICAL AND ASYMMETRICAL SACROILIITIS

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Background: The latest data show that psoriatic arthritis (PsA) patients (pts) with asymmetrical sacroiliitis (SI) have clinical and genetic features which are considered typical for PsA (1).
Objectives: To analyze comparative clinical characteristics of PsA pts with symmetrical and asymmetrical SI.
Methods: 287 pts (M/F–147/140) with PsA according to CASPAR criteria were examined. Data was collected from 6 rheumatology clinics of the Russian Federation. Pts' age 45.6±12.2 years (yrs), disease duration 10.9±6.7 yrs. Pts underwent standard clinical examination of PsA activity. Disease activity was measured by DAPSA, BASDAI, ASDAS-CRP. The examination involved

determining HLA B27 antigen status and X-rays of sacroiliac joints (SIJs) (pelvic radiographs), hands and feet. Bilateral changes in SIJs of grades 2-2, 3-3 and 4-4 were defined as symmetrical SI (sym-SI). Changes in SIJs of grades 2-1, 2-3, 3-1, 1-4, 2-4 and 3-4 were defined as asymmetrical SI (asym-SI). Skin lesion severity was evaluated in terms of body surface area (BSA) affected and Psoriasis Area Severity Index (PASI). When BSA was ≥ 3%, PASI was calculated. Me [Q25; Q75], Pierson-$\chi 2$ tests were performed. All $p<0.05$ were considered to indicate statistical significance.

Results: Sym-SI was found in 187 (65.1%) pts, asym-SI – in 100 (34.8%) pts. In group (gr) of pts with asym-SI there were more females than in the sym-SI gr: 63 (63.0%) vs 77 (41.2%; p = 0.0004). Pts with asym-SI had more severe peripheral arthritis as measured by Tender Joint Count (TJC68) and Swollen Joint Count (SJC66). These values were higher in asym-SI gr: 9 (4-16) vs 6 (2-14; p = 0.007) and 5 (2-12) vs 3 (0-9; p = 0.004), respectively. High activity according to DAPSA was found in 53 (54.6%) pts in the asym-SI gr vs 71 (38.8%) in the sym-SI gr (p = 0.01); low activity and remission by DAPSA– in 16 (16.5%) pts vs 51 (28.3%; p = 0.028), respectively. The frequency of enthesitis was higher in the asym-SI gr: 50 (57.5%) pts vs 57 (38.5%) pts (p = 0.005). Pts' functional capacity as measured by Health Assessment Questionnaire (HAQ) was worse in the asym-SI gr: HAQ>0.5 values were found in 83 (84.7%) pts vs 130 (72.6%) pts (p = 0.023). No significant differences were found between HLA B27 positivities in sym-SI and asym-SI groups (which were 54.2% and 44.0%, respectively; p = 0.23).

Conclusion: Asym-SI in PsA pts is associated with female gender, more severe peripheral arthritis, higher activity according to DAPSA, more frequency of enthesitis and reduction of pts' functional capacity.

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AB0929 IS THERE A CORRELATION BETWEEN SKIN SEVERITY AND JOINT ACTIVITY IN PSORIATIC ARTHRITIS (PSA)?

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Background: The majority if patients with PsA present with skin manifestations first. Few studies have examined the relationship between severity of skin and joint manifestations, but the results have been variable.

Objectives: To assess the correlation between the extent and severity of skin psoriasis and musculoskeletal manifestations of PsA over time.

Methods: This study is a retrospective analysis of prospectively collected data at a single center cohort study of patients who enrolled within 12 months of PsA diagnosis from 2000-2020. Patients are assessed according to a standard protocol which includes demographics, clinical assessment including skin and joint assessments, laboratory evaluation at 6–12-month intervals and radiographs every 2 years. Skin severity is measured by the PASI score, joint disease severity is measured by the number of tender and swollen joints. Axial disease was defined by the presence of bilateral grade sacroiliitis or unilateral grade 3 or 4. The Bath Ankylosing Spondylitis Metrology Index (BASMI) was also measured. Spearman correlations were calculated between PASI scores and joint counts and BASMI (in patients with axial disease). Multivariable analysis was done using negative binomial model for the joint counts and a linear regression for BASMI. This preliminary analysis includes only the baseline information.

Table 1. Baseline characteristics of 397 patients

Variable	Mean (SD)*, Number (%)** N=397
Age (years)	44.97 (13.01)*
PsA duration (years)	0.43 (0.66)*
Psoriasis duration (years)	14.64 (13.65)*
Married	236 (60.5)**
Smoker ever	193 (48.7)**
Alcohol intake	246 (62.3)**
Employed	309 (78.4)**
Post secondary education	277 (71.0)**
BMI	29.21 (8.85)*
PASI	6.11 (9.03)*
Nail	238 (61.2)**
Active joint count (tender ± swollen)	7.3 (13/15)*
Swollen joint count	2.96 (4.93)*
Axial disease	53 (17.8%)**
Treatment level	
None/NSAIDS only	272 (68.2)**
DMARDS ± NSAIDs	98 (24.7)**
Biologics ± DMARDs	27 (6.80)**

Results: 397 patients were included. Characteristics are shown in the Table 1. There was a correlation significant correlation between PASI score and the active joint count (AJC) (ρ 0.14, p=0.0095), swollen joint count (ρ 0.15, p=0.0071). Among the patients with axial disease there was a strong correlation between the PASI and BASMI scores ((ρ 0.58, p=0.0001). Multivariable analysis for AJC revealed traditional DMARDs (0.85 p=0.000). PASI score when patients were on no therapy (0.02 p=0.01) and those on biologics 0.04 p<0.05) were associated with higher AJC. Similarly for swollen joints the use of traditional DMARDs (0.85 P0.00), and the PASI score in those taking biologic DMARDs (0.07 p=0.003) were associated with higher swollen joint count. In patients with axial disease Age (0/05, p=0.004), PASI score in patients on no treatment (0.06 p=0.000) or those taking biologics (0.28 p=0.000) were associated with higher BASMI scores.

Conclusion: In patients presenting within 12 months of diagnosis of PsA, there is a correlation between the severity of skin and joint disease. Further studies will assess whether this correlation persists over time.

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AB0930 PSORIATIC ARTHRITIS DISEASE FLARES: IS COVID-19 VACCINATION JUST AN INNOCENT BYSTANDER?

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Background: So far, few studies provided detailed data for the incidence of disease flare after the vaccination against Coronavirus (Covid)-19 in patients with psoriatic arthritis (PsA). Results from small cohorts report an incidence of flares after Covid-19 vaccination of 0-7.7% and disease activity does not seems to be influenced by Covid-19 vaccination in patients with PsA. However, since PsA is a highly fluctuating disease with prolonged remission and irregular reactivation, it is difficult to establish a causal relationship between the Covid-19 vaccination and disease flares.

Objectives: To define the impact of Covid-19 vaccination and disease activity on the incidence of disease flare in patients with psoriatic arthritis (PsA).

Methods: We prospectively evaluated patients with PsA in remission or low-disease activity candidate to receive Covid-19 vaccination with mRNA vaccines, collecting demographic, clinical, and therapeutic data and assessing DAPSA 28, PCR before and after vaccination. We assessed flares using patients and clinician concordance. We retrospectively evaluated flare incidence in the same timeframe of the previous year. We performed statistical analysis to find possible predictors of flares after vaccination.

Results: A total of 57 patients with PsA were prospectively evaluated, and retrospective analysis was possible for 53 of them. DAPSA 28 and CRP did not differ significantly before and after the vaccination. The incidence of flares in the two periods (2020 vs 2021) did not differ significantly (18.8% vs 8.8%, p=0.166). We found a higher basal mean DAPSA 28 in patients who flared up after vaccination (7.3 vs 4.1, p-value 0.046). Only having a flare in the previous year was associated with a higher chance of recurrence after Covid-19 vaccination (p=0.02) in the logistic regression analysis, while other predictors (age, gender, disease activity, ongoing DMARD therapy, ongoing bDMARD therapy) did not.

Conclusion: Our findings suggest that, in patients with PsA, disease activity could be the main driver of disease flares rather than Covid-19 vaccination.

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AB0931 CHARACTERISTICS ASSOCIATED WITH THE PERCEPTION OF HIGH-IMPACT DISEASE (PSAID ≥4) IN PATIENTS WITH RECENT-ONSET PSORIATIC ARTHRITIS. MODEL BASED ON MACHINE LEARNING

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Background: The Psoriatic Arthritis Impact of Disease (PsAID) questionnaire is the standard tool for evaluating the impact of psoriatic arthritis (PsA) on quality of life [1]. Variables associated with high disease impact were studied in patients with long-standing established disease. The characteristics associated with high-impact PsAID in recent-onset PsA remain unknown.
Objectives: To evaluate which patient and disease characteristics are associated with the perception of high-impact disease (PsAID ≥4) in recent-onset PsA. All patients gave their informed consent. The study was approved by the Clinical Research Ethics Committee of the Principality of Asturias. We conducted a cross-sectional analysis. The dataset was generated using data for the independent variables at the 3 visits (baseline, first year, and second year of follow-up) matched with the PsAID values at each of the 3 visits. PsAID was categorized into two groups, namely, <4 and ≥4 [1]. We trained logistic regression models and a random forest–type machine learning algorithm to analyze the association between the outcome measure and the variables selected in the bivariate analysis (statistical significance defined as p value <0.05). We used a confusion matrix to visualize the performance of the final model. This matrix shows the real class of the data items, together with the class predicted by the machine learning algorithm, and records the number of hits and misses.
Results: The sample comprised 158 patients. 20.9% were lost to follow-up. Of the patients who attended the clinic, 45.8% scored PsAID ≥4 at baseline; 27.1%, at the first follow-up visit, and 23.0%, at the second follow-up visit. The variables associated with PsAID ≥4 selected in the logistic regression analysis were HAQ, patient global pain during the previous week, educational level, and level of physical activity in the previous week. The association was positive for the first 2 variables and for level of physical activity and negative for educational level. When physical activity was introduced as a categorical variable, a possible negative association was observed for a moderate level (although this was not statistically significant) and a positive association was observed for a high level (Table 1).

Table 1. Variables associated with PsAID ≥4: Logistic regression analysis.

Variable	Regression coefficient	95% CI	p value (Wald test)
HAQ	10.394	[7.777, 13.011]	<0.001
Patient global pain in the previous week	5.668	[4.016, 7.320]	<0.001
Educational level	-2.064	[-3.515, -0.613]	0.005
Moderate level of physical activity in the previous week	-0.341	[-1.255, 0.573]	0.465
High level of physical activity in the previous week	1.221	[0.158, 2.283]	0.024

When the random forest–type machine learning algorithm was trained with these 4 variables, the order of importance (from more to less) attributed by the model was: patient global pain, HAQ, educational level, and physical activity. The percentage of hits in the confusion matrix was 86.14%.
Conclusion: Pain control and control of the disease as a whole, preventing patients from suffering a decrease in their functional capacity, are first-order treatment objectives. PsA patients should take regular physical exercise, but with a moderate or low impact on their joints and entheses.
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Disclosure of Interests: None declared
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AB0932 PATIENT AND LEARNER EXPERIENCE IN A NEW SET UP OF A RHEUM-DERM COMBINED CARE MODEL FOR PSORIATIC ARTHRITIS

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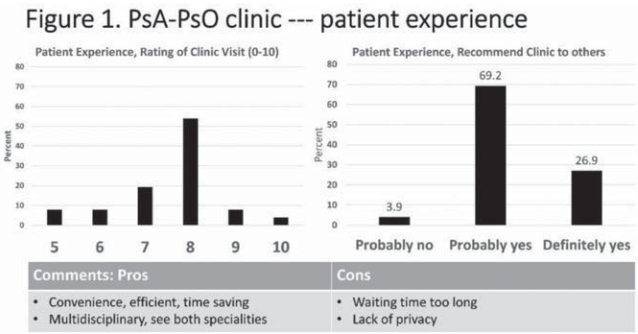
Background: Psoriasis (PsO) and musculoskeletal manifestations are common among patients with psoriatic arthritis (PsA). A shared-care model between rheumatologists and dermatologists has been advocated to promote early diagnosis and improve management care. Data from Asia is scanty. Patients' and learners' experience of shared-care models are seldom explored.
Objectives: We described the set-up of a new shared-cared PsA-PsO clinic incorporating service, education and research between rheumatologist and dermatologist for PsA. We describe the patients' and learners' experience of this shared-care model.
Methods: A combined care clinic was newly set up in 2019. Referrals were internal through either specialty. Each patient was first seen by a trainee, followed by both a dermatologist and rheumatologist simultaneously in the same consultation room. We collected patients' and learners' experience through self-administered survey.
Results: From May 2019 to January 2020, data from 44 visits (55% new referrals, 45% follow-up) from 28 patients were captured in the PsA-PsO clinic. 50% of cases were referred from either specialty. 34% were referred for diagnostic doubts, 66% were for therapeutic issues. 61% of patients continued follow-up in the PsA-PsO clinic, and 39% discharged back to respective care. From patients' experience rated on scale from 0-10, median (interquartile range, IQR) rating of the care was 8 (7, 8). 69.2% and 96% of patients would recommend the care to others. Free text comments included enhanced convenience, time saving, and having both specialties input on management. From 20 learners (3 medial students, 12 residents, 4 senior residents and one scientist), 95% reported extremely or very beneficial to training, 77.8% reported improved confidence in care for PsA and/or PsO patients. The PsA-PsO clinic was temporally suspended during the Covid-19 viral pandemic since February 2020 due to lack of manpower and not fulfilling the spacing out requirement for infectious control. The service was resumed gradually from May 2021.
Conclusion: Despite challenges, we report the setup of a new care model between dermatologists and rheumatologists for care of patients with psoriatic disease. The care model was well received by patients. Learners from various levels reported benefit from the learning experience.



Disclosure of Interests: Cassandra Hong: None declared, Liwen Fang: None declared, Yi-Wei Yeo: None declared, Haur Yueh Lee: None declared, Andrea Low: None declared, Ying Ying Leung Speakers bureau: Received honorarium from Abbvie, DKSH, Janssen, Novartis and Pfizer.
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AB0933

DEVELOPMENT AND VALIDATION OF A NOMOGRAM FOR PREDICTION OF NONALCOHOLIC FATTY LIVER DISEASE IN PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) has been linked to an increased risk of metabolic syndrome (MetS). Non-alcoholic fatty liver disease (NAFLD), the hepatic manifestation of MetS, is now the commonest liver disease worldwide. About 65% of PsA patients suffer from NAFLD, and chronic systemic inflammation may be an important predisposing factor.
Objectives: The purpose of this study was to establish and validate a diagnostic model nomogram for predicting the occurrence of NAFLD in patients with PsA.
Methods: A total of 127 PsA patients (46 had NAFLD and 81 had no NAFLD) were enrolled in this study. Retrospectively collected clinical and serological parameters of these patients. The percentage and absolute number of lymphocytes and CD4+T cells were determined by Flow cytometry. The independent risk factors for NAFLD were screened in the PsA patients using univariate and multivariate binary logistic regression analyses and were used for construction of the nomogram prediction model. The AUROC (C index) was used to verify the model discrimination; the calibration curve and Hosmer-Lemeshow test were used to verify the model calibration; and the DCA curve was used to verify the clinical validity of the model.
Results: Univariate and multivariate logistic regression analyses showed that Body Mass Index (BMI) (OR=1.25, *P*=0.001), serum triglyceride (TG) (OR=3.51 , *P*=0.015) and peripheral blood Th1 cell percentage (OR=1.12, *P* < 0.001) is an independent risk factor for NAFLD in PsA patients, and an individualized nomogram prediction model was successfully established. The prediction model had a good discrimination power with AUROC (C-index) of 0.83 (95% *CI*: 0.76-0.90); the P value in the Hosmer-Lemeshow test was 0.683, suggesting a high reliability of the predicted probability by the model; the DCA curve indicating a good clinical efficiency of the model.
Conclusion: Our study shows that the establishment of a nomogram prediction model of PsA complicated with NAFLD patients is helpful for early clinical screening and identification of such high-risk patients.

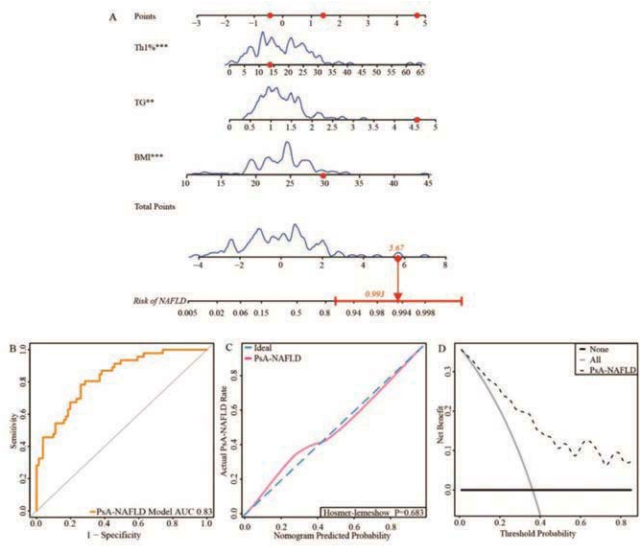

Figure 1. A. Example of prediction nomogram for risk of PsA complicated with NAFLD patients; B. The ROC curve of the prediction model; C. The calibration curve of the prediction model; D. The decision curve analysis of the prediction model.

Disclosure of Interests: None declared
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AB0934

DOES THE SEVERITY OF PSORIASIS IMPACT ON PSORIATIC ARTHRITIS ACTIVITY? DATA FROM RHEUMATOLOGICAL CLINICAL PRACTICE

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Background: Psoriatic arthritis (PsA) is a chronic, musculoskeletal inflammatory disease that develops in up to 30% of patients (pts) with psoriasis (PsO). There are conflicting data about correlations between skin and joint severity from the observational cohort [1, 2]. But it's very important for clinical phenotyping and treatment PsA pts.
Objectives: to evaluate association between PsO severity and PsA activity.
Methods: 778 (M/F=357/421) PsA pts fulfilling the CASPAR criteria were included into Russian rheumatological observational cohort. Mean age 46.7±13 years (yrs), DAPSA 29.05±19.7, CRP - 15.3±23 mg/l, SJC/66 - 6.6±7.5, TJC/68 – 10.6±10.2, LEI – 1.06±1.4. All pts underwent standard clinical examination: tender joins count (TJC)/68, swelling joints count (SJC)/66, CRP (mg/l), DAPSA, dactylitis, enthesitis by LEI, nail/skin PsO was evaluated. All pts were divided in two groups based on BSA≤3% (mild PsO) and BSA>3% (moderate/severe). M±SD, Me [Q25; Q75], Min-Max, %, t-test, Pierson-χ2, Manna-Whitney tests, ORs with 95% CI were performed. All p<0.05 were considered to indicate statistical significance.
Results: BSA≤3% was found in 427 out of 778 pts (54.9%), BSA>3% in 352 pts out of 778 (45.2%). Nail PsO were seen in 258 out of 778 (33.2%). Among these pts with BSA>3% nail PsO were seen in significantly more cases - 135 out of 258 pts (52.3%) (p=0.03). In pts with BSA>3% all parameters of PsA activity (DAPSA, SJC, TJC, CRP) was significantly higher compare to pts with BSA≤3% (for all p<0.0001). The one-factor model of logistic regression shown that PsO severity significantly associated with nail PsO, higher PsA activity by DAPSA, CRP, SJC, TJC and smoking (OR analysis with CI 95% for all parametres are shown on Figure 1).

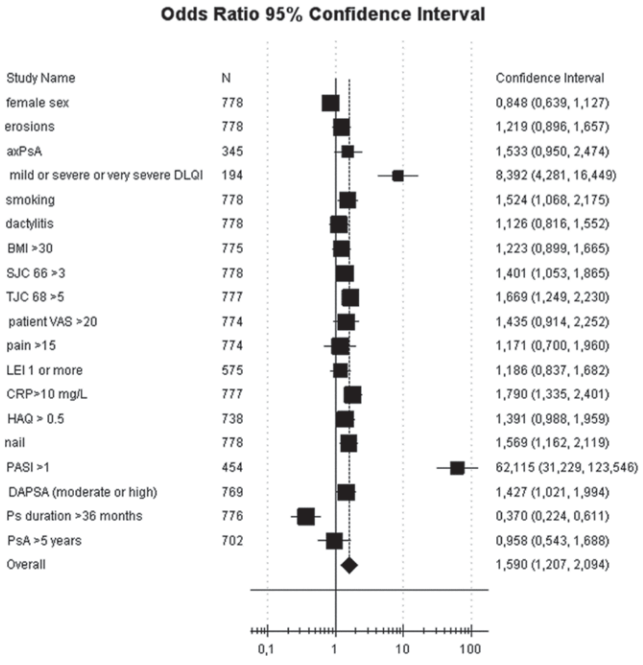

Figure 1. Forest plot of factors associated with psoriasis severity in PsA pts.

Conclusion: In our observational cohort about half of PsA pts had severe PsO. Skin severity associated with higher PsA activity. It should be taken into account for choice of properly treatment both for skin and joint in clinical practice.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.2304

AB0935

NUMBER OF PATIENTS WITH PSORIATRIC ARTHRITIS (PSA) IN GERMANY UNTIL 2040: PROJECTION BASED ON DATA FROM 65 MILLION PEOPLE IN THE GERMAN STATUTORY HEALTH INSURANCE

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Background: Recently, we have reported an increase in the incidence and prevalence of patients with PsA in Germany based on claim data from 65 million people in statutory health insurance during 2009 to 2012 [1].
Objectives: Population-based estimation of long-term projection for incidence and prevalence of patients with diagnosis of PsA until the year 2040.
Methods: Based on prevalence and incidence of PsA, the number of men and women diagnosed with PsA until 2040 is projected using the illness-death model [2]. The mortality and age distribution of the general population is taken from the official population forecasts of the German Federal Statistical Office. Mortality of patients with PsA was considered by using estimates of the mortality rate ratios [3]. Percent change in projected case numbers refer to 2012 (base year).
Results: Starting from 2012, three scenarios about the incidence of PsA after 2012 were found (Graph 1): (A) increase of 5% per year as observed in [1], (B) no trend in incidence and (C) decrease of a similar 5% per year due to a theoretically anticipated early treatment effect. In scenario C, the number of men and women peaks at about 2028 and decreases slightly afterwards. The graph shows the projected numbers of men (left panel) and women (right) with PsA until 2040 in the three incidence scenarios. The projected numbers and the percent changes are given in the Table 1.
Conclusion: Different scenario may be considered based on recent population data for the incidence course of PsA until 2040. The most optimistic scenario showed a trend of stabilization of incidence including the anticipated population mortality rates. Thus, it is likely that substantially more medical resources for treating patients with PsA are necessary in the next two decades, whereby approaches to the potential prevention of PsA, for example by very early treatment of psoriasis patients, should be further pursued.
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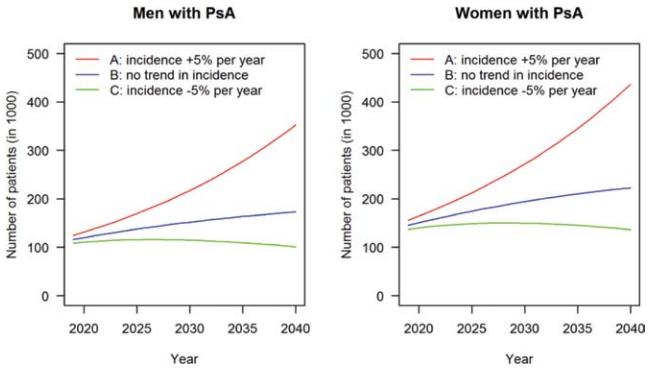
[2] DOI 10.1016/j.tpb.2013.11.006
[3] DOI 10.1111/j.1365-2796.2010.02310.x



Graph 1.

Table 1.

Scenario	Sex	Projected number 2019 (in 1000)	Projected number 2040 (in 1000)	Change 2040 compared to 2019
A	Male	125	353	+183%
	Female	156	437	+180%
B	Male	116	173	+49.0%
	Female	146	223	+53.2%
C	Male	109	101	-6.9%
	Female	137	136	-0.5%

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AB0936

NEUROPATHIC PAIN IN PSORIATIC ARTHRITIS: ANALYSIS OF POPULATIONS TREATED WITH ANTI TNF AND ANTI IL17

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Background: Psoriatic arthritis (PsA) is a disease characterized by chronic pain and it is often associated with the presence of fibromyalgia (FMS) with an estimated prevalence of 18%. Several studies demonstrated the central role of neuropathic pain in FMS. However, patients with inflammatory diseases such as PsA frequently complain of complex pain symptoms, with neuropathic characteristics. Therefore, in PsA we can recognize both an inflammatory pain and a neuropathic pain that can be exacerbated both by the concomitant fibromyalgia or depending only on the PsA itself. In fact, In the context of PsA, the presence of neuropathic pain features has been documented in 28% of patients. This could be a reason why the low remission rate in these patients. Finally, Studies on murin models revealed a possible role of IL17, key cytokine of PsA pathogenesis, in mechanism of neuropathic pain.
Objectives: To evaluate the role of anti-TNF and antiIL-17 in neuropathic pain in PsA patients treated with the first biological drug (bDMARDS).
Methods: A cross-sectional evaluation was conducted on 38 PsA patients classified by Classification criteria for Psoriatic Arthritis (CASPAR), referred to the PsA outpatient clinic of "University of Campania Luigi Vanvitelli". Thirty patients were treated with anti-TNF (mean age 53 years, 17F, 13M), 8 were treated with anti-IL17 (mean age 50 years, 5F, 3M), for almost 6 months. For each patient, an assessment of disease activity using DAPSA and physical function was carried out. The presence of comorbid fibromyalgia syndrome (FMS) was evaluated according to ACR 2016 criteria. We investigated neuropathic pain features through the PainDETECT Questionnaire (PDQ).
Results: Nine patients treated with anti TNF were in DAPSA remission; 18 patients had low disease activity, 3 had High disease activity, FMS was detected in 11 of 30 patients, no one in DAPSA remission for PsA. Characteristics of neuropathic pain (PDQ ≥ 19) were found in 13 (43.3%) patients overall; unlikely neuropathic pain (PDQ < 12) in 16 (53.3%) patients. In the first group 7 patients had FMS, in the second group 3 had FMS. So, our analysis revealed the presence of neuropathic pain in 6 patients (54,5%) with PsA treated with antiTNF with no FMS; all of them were in low disease activity. The same analysis was conducted on anti IL17 treated population: 4 patients were in DAPSA remission, 2 patients in low disease activity, 2 patients in high, disease activity. FMS was diagnosed in 3 patients, 1 of them was in DAPSA remission for PsA. PDQ>19 was found only in 1 patient, who had FMS in comorbidity; the others had no neuropathic pain. So, we had no PsA patient treated with antiIL17, that manifested symptoms of neuropathic pain.
Conclusion: The contribute of IL-17 in developing of neuropathic pain suggests the possible role of anti IL17 as therapy; our results support this tesis suggesting a possible role of anti IL17 in treatment of neuropathic pain. A limit to our work is given by the low sample size for which further studies are necessary to confirm this data.
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Disclosure of Interests: None declared
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AB0937

IMPROVEMENT IN CLINICAL DISEASE ACTIVITY AND NO DETERIORATION IN QUALITY OF LIFE IN PSORIATIC ARTHRITIS PATIENTS FOLLOWED FOR 5 YEARS IN A NORWEGIAN OUTPATIENT CLINIC.

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of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Trondheim, Norway

Background: Recent years of progress in conventional and biologic disease-modifying anti-rheumatic drugs development and improved treatment strategies (treat to target) have yield in improved outcome in psoriatic arthritis (PsA) patients. [1,2]. Still, despite modern treatment and clinical monitoring methods, we might miss dimensions of disease burden outside our main focus including quality of life (QoL), which are of high importance from patients' perspective.
Objectives: Main objective of this study was to explore how clinical aspects of disease activity and QoL measures will change in PsA patients in an ordinary outpatient clinic in Norway, followed for 5 years, in the biological treatment era.
Methods: PsA patients fulfilling the CASPAR criteria visiting an outpatient clinic in Norway between January 2013 and February 2020 were consecutively included in the study. Data collection included variables for demographics, treatment, laboratory assessment of ESR and CRP, joint counts, disease activity score in psoriatic arthritis (DAPSA), global assessments – patient's (PGA) and investigator's (IGA), reported joint and global pain, patient reported outcomes (PROMs) regarding different aspects of quality of life (QoL), (MHAQ, RAID, QoL15D and reported fatigue level). Patients were analyzed at baseline and after 5-year follow-up period. Statistics included paired sample t test and McNemar test.
Results: Among 140 PsA patients included at baseline, 114 (81.4%) were re-examined after 5 years. Mean age at baseline was 52 years (95%CI 50.3-53.7) and percentage of women was 50.7%. Proportion of patients treated with biologics increased from 32.9% to 39.5%, but the difference wasn't statistically significant. During the 5 year follow up period most clinical disease activity measures decreased and QoL was maintained (Table 1).

Table 1. Demographic data, clinical activity measures and patient reported outcomes regarding quality of life in PsA patients followed for 5 years. Values are mean (95CI) or number (%).

	Baseline (140)	5-years follow up (114)	p
Age (years)	52.0 (50.3, 53.7)	56.3 (54.4, 58.3)	
Women	71 (50.7%)	56 (49.1%)	
Exercise >1h week	62 (44.3%)	59 (51.8%)	0.28
BMI (kg/m2)	28.4 (27.5, 29.2)	28.2 (27.3, 29.1)	0.89
Current smoker	24 (17.1%)	17 (14.9%)	0.90
Current bDMARD treatment	46 (32.9%)	45 (39.5%)	0.65
DAPSA	18.6 (16.2, 21.0)	12.8 (10.8, 14.8)	<0.01
TJC68	4.1 (3.2, 5.0)	1.8 (1.3, 2.4)	<0.01
SJC66	0.7 (0.5, 0.9)	0.3 (0.2, 0.4)	<0.01
ESR	15.9 (13.9, 18.0)	10.7 (7.8, 13.5)	<0.01
CRP	4.9 (3.5, 6.3)	5.3 (2.5, 8.2)	0.41
IGA (VAS 0-100)	4.1 (3.2, 5.0)	1.8 (1.3, 2.4)	<0.01
PGA (VAS 0-100)	36.6 (32.5, 40.8)	29.3 (25.0, 33.6)	0.12
Global pain (VAS 0-100)	35.1 (31.2, 39.0)	28.9 (24.4, 33.5)	0.42
Joint pain (VAS 0-100)	33.8 (29.9, 37.8)	27.5 (23.2, 31.9)	0.31
MHAQ (0-3)	0.4 (0.4, 0.5)	0.3 (0.3, 0.4)	0.72
RAID (0-10)	3.5 (3.1, 3.9)	3.2 (2.9, 3.6)	0.41
QoL15D (15-75)	24.2 (23.1, 25.2)	22.7 (21.6, 23.9)	0.85
Fatigue (VAS 0-100)	47.8 (41.5, 54.2)	39.1 (32.8, 45.4)	0.16

Conclusion: In our cohort of PsA patients after 5 years follow up disease activity was reduced and QoL maintained. Our data adds to the evidence that the burden of disease in PsA patients has decreased in the biologic treatment era however is still significant. Further improvement in pharmacological and non-pharmacological treatments in PsA patients is still needed.

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AB0938

A NEW SCREENING TOOL FOR PSORIATIC ARTHRITIS IN PSORIASIS PATIENTS: TURPAS

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Background: Psoriatic arthritis (PsA) is a heterogenous disease with different disease manifestations. Several tools have been developed for screening of PsA in patients with psoriasis with variable performances. An optimal screening tool for PsA is still an unmet need.
Objectives: We aimed to develop a new screening tool in Turkish which could detect different domains involved.
Methods: A core group was determined including 11 rheumatologists/10 dermatologist and a systematic literature review on PubMed until 15 August 2020 using the keyword 'psoriatic arthritis` was performed. The review revealed tools named PEST, PASE, EARP, STRIPP, SIPAS, SIPAT, TOPAS-II, GEPARD, PASQ, CONTEST, A novel, short, and simple screening questionnaire. Each item of those tools were included in the Delphi set. After the 3 rounds of Delphi, a new set of screening questionss was developed.
Results: Overall 85 items were inquired, including questions on joint, dactylitis, enthesitis, back, skin-nail domains as well as morning stiffness, function, treatment and others for the fırst round of Delphi. Seventeen experts (9 dermatologists/ 8 rheumatologists from the core group) and fifteen patients (Female/Male= 9/6) answered the Delphi (mean (SD) age of 39.3 (10.9) participated to the first round. The involvemet types were peripheral (73.4%), axial (40%), entheseal (33.4) and dactylitis was present in 14% of the patients. As a result of this first evaluation, 44 out of 85 questions were selected and carried to second round The distribution of these questions was as follows; joint question n=13, skin and nail involvement n=6, dactylitis n=5, morning stiffness n=5, axial n=3, enthesitis n=2, general questions n=5. These questions were sent to the members through rheumatology and dermatology societies. In total, 85 rheumatology specialists

Table 1. The new screening tool

Domain	Turkish version	English version
Joint	El/ayak parmaklarınızda ya da herhangi bir ekleminizde hiç şişlik veya ağrı oldu mu?	Have you ever had swelling or pain in your fingers/toes or any of your joints?
Dactylitis	Resimde gösterildiği gibi el veya ayak parmağınızda sosis şeklinde şişlik oldu mu?	Have you had a sausage-shaped swelling on your fingers or toes as shown in the picture?
Enthesitis	Topuk ağrınız olur mu?	Do you have heel pain?
Axial involvement and morning stiffness	Belinizde, sırtınızda veya boynunuzda istirahatle artan, özellikle sabaha karşı kötüleşen veya sabahları hareketinizi kısıtlayan ağrınız olur mu?	Do you have pain in your lower back, back, or neck that increases with rest, worsens especially in the morning, or restricts your movement in the morning?
Drug use	Eklem şikayetleriniz için zaman zaman ilaç kullanır mısınız?	Do you take medication for your joint complaints from time to time?
History of rheumatic disease	Size daha önce iltihaplı romatizma tanısı konuldu mu?	Have you ever been diagnosed with a rheumatic disease before?

and 48 dermatology specialists answered the questions in the second round. At the second tour, the number of questions was reduced from 44 to 22. The distribution of the questions was as follows; Skin and nail involvement n=5, dactylitis n=3, joint question n=2, axial involvement n=2, morning stiffness n=2, axial involvement and morning stiffness n=2, enthesitis n=1, general questions n=5. A consensus meeting was held to discuss 22 questions determined at the end of the second round within the initial core group. Each question was handled one by one, some of the questions were combined, if necessary, adapted to Turkish. The tool was given its final form. The final version of the questionnaire consists of 6 questions. (Table 1).

Conclusion: A new screening tool targeting different domains in Psoriatic disease was developed in Turkish. While cultural differences play an important role in screening, we believe that the first tool developed in Turkish will be helpful in clinical practice and research settings. Further assessments will be done to understand its validity and reliability within a large cohort of psoriatic patients.

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AB0939 PSORIATIC ARTHRITIS RELATED FATIGUE: WHAT IS THE MAGNITUDE OF THIS PROBLEM AND WHAT ARE THE CORRELATED FACTORS? A CROSS-SECTIONAL STUDY.

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Background: Fatigue is a common constitutional feature and has a significant impact on *quality of life* in patients with chronic inflammatory rheumatic diseases, such as psoriatic arthritis (PsA). It is a complex phenomenon and its pathogenesis remains unclear. Despite being a common symptom, it is largely ignored and rarely assessed in clinical practice.

Objectives: This study aims to evaluate the incidence and severity of fatigue in PsA patients under biological agents and to assess the influence of several clinical and demographic features on PsA related fatigue.

Methods: We conducted a cross-sectional study including patients with PsA, according to CASPAR criteria, treated with biological agents, from our University Hospital and registered in the national database (reuma.pt). Fatigue was assessed by a 13-item self-administered questionnaire (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F]). Data collected and analyzed included: demographic data, disease activity data, functional status, comorbidities and therapies. Student's t-test, ANOVA and Pearson's correlation were performed to compare data, as appropriate. A p-value <0.05 was considered statistically significant.

Results: 60 PsA patients were included, 61.7% were males, with a mean age at diagnosis of 38.1±10.5 years and a median disease duration of 13.0 (8.75-19.25) years. Most of the included patients had a predominant polyarticular pattern (n=33, 55.0%). The mean FACIT-F score was 34.48±11.61. No differences were found in the FACIT-F score according to gender, *pattern* of *joint involvement*, presence or absence of cutaneous involvement, nail dystrophy and/ or dactylitis. Patients with depression and enthesitis exhibited a lower FACIT-F score (p=0.017 and p=0.007, respectively). Patients treated with tofacitinib had a lower FACIT-F score than patients treated with adalimumab (p=0.025). No differences were found among the other biological agents. Patients in remission (according to EULAR response criteria) had a higher FACIT-T score than patients with moderate disease activity (p=0.032). In patients with a predominant axial involvement, inactive disease (according to ASDAS) was associated with a higher FACIT-T score, when compared to very high disease activity (p=0.02). Also, patients with moderate disease activity had a higher FACIT-T score than patients with very high (p=0.003) and high (p=0.008) disease activity.

FACIT-F showed a significant correlation with disease activity scores as BASDAI (r=-0.546, p<0.001), DAS 28 CRP (r=-0.506, p<0.001), CDAI (r=-0.672, p<0.001), SDAI (r=-0.641, p<0.001) and ASDAS CRP (r=-0.500, p<0.001). FACIT-F was also correlated with BASFI (r=-0.598, p<0.001), HAQ (r=-0.701, p<0.001), BASMI (r=-0.431, p<0.001) and MASES (r=-0.401, p<0.001). The authors found strong correlations between FACIT-F and HADS domains (Depression and Anxiety domains; r=-0.850, p<0.001 and r=-0.748, p<0.001, respectively). A strong correlation was also found between the FACIT-F and the 8 domains of health of the SF36 (p<0.001).

Conclusion: Fatigue was a common symptom in our sample of PsA patients and, its magnitude was closely related with disease activity, physical function, depression and anxiety status, indicating its multifactorial nature. We can speculate that achieving disease remission could significantly alleviate the fatigue intensity and vice versa. As recommended by EULAR/ACR task force in 2008, fatigue should be measured in clinical practice and should be part of the multidisciplinary approach, in addition to controlling disease activity.

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AB0940 IS PSORIATIC ARTHRITIS REALLY SERONEGATIVE?

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Background: Psoriatic Arthritis (PsA) is a heterogeneous disease classified as a seronegative group of inflammatory arthritis.

Objectives: Our aim was to understand the real-life seropositivity rates for commonly used autoantibodies in rheumatology practice in a cohort of PsA patients treated with biologic agents.

Methods: PsA patients from the Hacettepe University biological database (HUR-BIO) were assessed for the anti-nuclear antibody (ANA), rheumatoid factor (RF), and anti-cyclic citrullinated peptide (CCP) before and after the initiation of biologic agents. Demographic characteristics, the interval between the test and biologic initiation, and the rates of seropositivity for individual tests, autoantibody titers, and subtypes for ANA were determined.

Results: From 520 PsA patients registered, results of 419 patients with at least one autoantibody tested either before or after biologic treatment is presented in Table 1. From the patients tested, 69% of them had at least one autoantibody positive and 30.8 % of them were triple negative before the biologic treatment. The rates reached to 78.7% of seropositivity for at least

Table 1. Demographics and ANA, RF, Anti-CCP test results of patients before and after biologic treatment

	ANA		RF		Anti-CCP	
bDMARDs initiation	Before	After	Before	After	Before	After
Number of patients	104	132	310	278	144	97
Age	43.5 (12.7)	46.7 (11.6)	43.3 (12.5)	47.9 (11.9)	44.3 (12)	48.6 (12.1)
Female sex, n (%)	84 (80.7)	97 (73.5)	225 (72.5)	211 (75.8)	110 (76.3)	75 (77.3)
Time interval between test and bDMARD initiation, months, median (IQR)	7.4 (0.84-17.83)	32.6 (14.93-72.33)	4.1 (0.35-16.75)	31.63 (13.10-64.08)	3.23 (0.30-11.5)	35.13 (12.40-75.43)
Positivity, n (%)	42 (40.4)	73 (55.3)	30 (9.6)	32 (11.5)	12 (8.3)	11 (11.3)
Titer IU/ml, median (IQR)	NA	NA	28.7 (22.35-98.5)	28.9 (21.9-110)	139.1 (20.38-250)	67.5 (16.77-139)
Titer, n (%) *	28 (66.6)	38 (52)	N/A	N/A	N/A	N/A
1/100	7 (16.7)	14 (19.1)				
1/160	7 (16.7)	20 (27.3)				
≥1/320						

bDMARD: Biologic Disease Modifying Anti-Rheumatic Drugs, ANA: Anti-nuclear antibody, RF: Rheumatoid factor, Anti-CCP: Anti- Cyclic citrullinated peptide, F:Female, M:Male, IQR: Interquartile range, IU/ml: International units per milliliter, N/A: Not available *Subtype is not given for one patient in patients with positive ANA after biologic treatment

one autoantibody and 21.2 %triple negativity after treatment. ANA showed the highest rates of seropositivity among autoantibodies with a rate of 40% before and 55.3 % after biologic treatment. Concomitant seropositivity for RF and CCP autoantibodies showed rates of 2.8% and 6.3% before and after treatment, respectively. The most common subtype was AC4-5 before and AC1-4-5 after biologic agent treatment. ANA was tested in 31 patients both before and after biologic treatment showing 6 negative patients became positive after treatment and from 12 positive patients at the baseline 6 of them became negative (p=0.452). The most common biologic agents used in patients with ANA tested after treatment, were adalimumab (ADA) (42.4%), etanercept (ETN) (18.9%), and infliximab (IFX) (18.9%). The only difference was observed in IFX treated patients (n=25) with significantly higher rates of IFX usage in ANA-positive patients (p=0.001).

Conclusion: Synovial lymphoid neogenesis rates in PsA are similar to the frequency seen in rheumatoid arthritis (1). Nevertheless, PsA is classified under the group of "seronegative diseases". On the other hand, current reports have started to define specific autoantibodies particularly in psoriasis patients (2). The real-life experience in serology results of PsA patients showed that only 20-30 % of the patients were seronegative for all three tests commonly used in practice.

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AB0941

DISCRIMINATION OF ENTHESIC INFLAMMATORY INVOLVEMENT IN PATIENTS WITH SPONDYLOARTHRITIS THROUGH THE USE OF COMPUTER ANALYSIS OF STATIC ULTRASOUND IMAGES

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Background: One of the weaknesses of the ultrasound study of the entheses is the absence of a universal, recognized and replicable ordinal evaluation scale that allows quantifying or semi-quantifying the degree of involvement of these structures.

Objectives: To analyze computer analysis of static images of patients with inflammatory enthesopathies differentiation capacity.

To determine its ability to discriminate between an affected and a healthy contralateral enthesis in the same individual.

Methods: Static images of the Achilles and epicondylar entheses of patients who consulted regarding enthesis pain associated with spondyloarthritis (ASAS/CASPAR criteria) were analyzed. We picked patients between 2016 and 2020. Images were obtained by the same observer under clinical practice routine circumstances and with the same ultrasound equipment (Logiq 8e, General Electric, USA). The same settings for each of the two enthesic examinations were used. Image analysis was performed using the ImageJ 1.53e program (Wayne Rasband & contributors – NIH, USA). Imaging records with contralateral studies in patients with recently diagnosed asymmetric enthesopathies (before the start of treatment) were selected. A repository of images from healthy controls, matched by age and sex of the patients, was used as control.

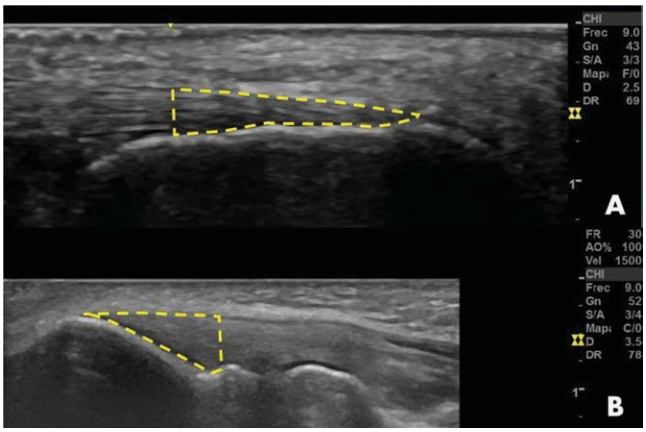

Figure 1. Scheme to obtain the analysis area of the Achilles (A) and epicondylar enthesis (B). The enthesic area was considered from the most distal point of the enthesis to the point of emergence or separation of the tendon from the cortex. Case A corresponds to a healthy control. Case B corresponds to a patient with psoriatic arthritis and severe epicondylar pain.

We compared the mean gray intensity (MGI), its dispersion (DGI) and the mode (MoGI) of the studied entheses. Figure 1 explains how to acquire the image for the study of both entheses.

Results: We included image records of 9 patients with axial spondyloarthritis (34.1 ±9.5 years, 7 males) and 10 with psoriatic arthritis (34.0 ±5.7 years, 8 males) with asymmetric involvement of 15 Achilles and 10 epicondylar entheses (LEI/MASES/ SPARCC). The distribution of the MGI, DGI, and MoGI variables was normal for both enthesis, contralateral patient controls and healthy subjects controls. In the records with Achilles involvement, the MGI on the affected side was 76.69 ±25.14, the DGI 24 ±3.48, and the MoGI 76.6 ±30.1. In the non-painful Achilles enthesis, the measurements were 83.99 ±27.29, 22.72 ±3.14 and 78.7 ±32.5, respectively. Statistically significant differences were detected in all pairwise comparisons (t -9.522, P=.000; t=3.393, P=.004; and t=-2.247, P=.041, respectively). In the epicondylar involvement records, the MGI on the affected side was 75.3 ±14.71, the DGI 25.93 ±2.52, and the MoGI 72.7 ±15.4. In the non-painful Achilles enthesis the measurements were 82.57 ±16.06, 25.7 ±2.99 and 74.9 ±16.5, respectively. Statistically significant differences between MGI and MoGI were identified (t=-9.849, P=.000; and t=-2.752, P=.022, respectively). The MIN ratio of the affected side and healthy side among patients was 1.18 ±0.047 while the MIN ratio between the dominant and non-dominant sides of the healthy athletes was 0.91 ±0.022 (t=25.81, P=.000).

Conclusion: Computer analysis of entheses static images correctly discriminates symptomatic from non-symptomatic entheses in early ultrasound studies. Even in non-symptomatic entheses, it detects differences compared to healthy subjects. This discriminatory capacity could be useful in updating ultrasound enthesis count indices. It may also be interesting as a criterion for evaluating changes over time. As a weakness, it is worth highlighting the potential confounding effect that enthesophytoses could have in this type of analysis if specific demarcations of the area studied are not made.

Disclosure of Interests: Carlos Guillén-Astete Speakers bureau: Novartis, Janssen, Abbvie, Grunenthal, UCB, Gebro, Paid instructor for: Roche, Novartis, Janssen, Esteve, Menarini, Consultant of: Janssen, Novartis, Roche, Grant/research support from: Pfizer, Grunenthal, Gebro, Novartis, África Andreu-Suárez: None declared, Marina Tortosa-Cabañas: None declared, Miguel Martinez Aznar: None declared

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Psoriatic arthritis - clinical aspects (other than treatment)

AB0942 INVOLVEMENT OF THE FOOT IN PSORIATIC ARTHRITIS. A REVIEW OF 55 CASES.

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory rheumatic disease belonging to the spondyloarthritis family with which it shares many clinical and radiographic features. The involvement of the feet with an asymmetric distribution of arthritis is very specific to Psoriasis.
Objectives: The objective of our study is to determine the frequency of foot involvement in a population of psoriatic arthritis by detailing the clinico-radiological aspect of the foot.
Methods: Retrospective descriptive study carried out on the files of patients hospitalized for psoriatic arthritis over a period of 9 years from January 2013 to December 2021. For each file, we collected epidemiological, clinical and radiological data.
Results: 55 patients were included: 41 women (74.5%) and 14 men (25.5%). The mean age was 48.81 ±17.08 years [20-85 years]. Personal and family history of skin psoriasis was noted in twenty and one patients, respectively. The average duration of evolution was about 5.5 years. Inflammatory talalgia was noted in 34 patients (61.8%) and forefoot involvement was found in 13 cases (23.6%). Sausage toe was noted in three cases (5.5%). None of the patients had Bauer's toe or psoriatic onychopachydermoperiostitis of the great toe. The radiographic workup showed calcaneitis in 34.5% (n=30), osteoperiostitis of the great toe in 6 patients (10.9%). According to the radiological criteria fingers-toes or (CRDO), 3 patients had juxta articular periostitis (5.5%), two cases of phalangeal tuft resorption (3.6%) and one case of osteolysis of an interphalangeal joint (1.8%).
Conclusion: In our context, the involvement of the foot during psoriatic arthritis is dominated clinically and radiologically by the involvement of the hindfoot. The importance of the classification criteria for Psoriasis cannot be undermind, and aim is improving their sensitivity and specificity.

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AB0943 ASSOCIATION BETWEEN PULSE PRESSURE AND ATHEROSCLEROSIS IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) is associated with an increased prevalence of cardiovascular events due to accelerated atherosclerosis that seems to depend on traditional and non-traditional risk factors(1). There is a positive correlation between pulse pressure (PP) and the progression of atherosclerosis in general population (2). Currently, there are no studies linking PP as an independent risk factor of atherosclerosis in PsA patients.
Objectives: To compare PP between PsA patients with and without carotid plaque (CP).
Methods: This was a cross-sectional study that included patients aged 40 to 75 years with PsA diagnosis according to the 2006 CASPAR criteria. A carotid ultrasound was performed in all patients, and they were divided into two groups, 27 patients with the presence of CP and 27 patients without CP matched by age, gender, and comorbidities. Blood pressure and PP was measured according to current guidelines. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done with Chi-square test for qualitative variables and Student´s t test for quantitative variables. A p value <0.05 was considered statistically significant.
Results: There were no differences regarding demographic characteristics between groups. When comparing the arterial measures, a statistically significant difference was found in the PP, which was higher in patients with CP (48.66 ± 12.04 mmHg vs 41.51 ± 9.10 mmHg, p=0.017) (Table 1). A binary logistic regression was performed, and we found that PP was the only independent factor for the presence of CP in patients with PsA, OR 6.638 (95% CI 0.453- 12.823, *p*=0.036).

Table 1. Demographic characteristics of the patients.

Characteristics	PsA patients with CP (n=27)	PsA patients without CP (n=27)	*P* Value
Age, mean ± SD	51.55±8.24	50.74±8.68	NS
Female gender, n (%)	16 (59.25)	15 (55.55)	NS
Obesity, n (%)	16 (59.25)	17 (62.96)	NS
T2DM, n (%)	20 (74.07)	23 (85.18)	NS
Hypertension, n (%)	19 (70.37)	22 (81.48)	NS
Dyslipidemia, n (%)	12 (44.44)	17 (62.96)	NS
Active smoking, n (%)	17 (62.96)	16 (59.25)	NS
Methotrexate, n (%)	9 (33.33)	11 (40.74)	NS
Glucocorticoid, n (%)	23 (85.18)	22 (81.48)	NS
bDMARD, n (%)	14 (51.85)	18 (66.66)	NS
SAP, mean ± SD	132.44±14.40	123.44±13.80	**0.023**
DAP, mean ± SD	83.77±10.71	81.92±10.95	NS
PP, mean ± SD	48.66±12.04	41.51±9.10	**0.017**

PsA, psoriatic arthritis; NS, non-significant; T2DM, type 2 diabetes mellitus; bDMARD, biologic disease-modifying anti-rheumatic drugs; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; PP, pulse pressure.

Conclusion: PsA patients with CP presented higher measures of PP compared with PsA patients without CP. This suggests that PP could be related with an increased risk of subclinical atherosclerosis in PsA patients. It is recommended to consider PP as an important parameter when evaluating cardiovascular risk in PsA patients.

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AB0944 HIGHER PREVALENCE OF PULSE PRESSURE IN PSORIATIC ARTHRITIS PATIENTS

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Background: There is an increased risk of cardiovascular diseases in patients with psoriatic arthritis (PsA) compared with the general population due to higher prevalence of cardiovascular risk (CVR) factors (1). Pulse pressure (PP) is an independent risk factor for cardiovascular morbidity and mortality (2). Currently, there are no studies about PP in PsA patients.
Objectives: To compare PP between PsA patients and healthy controls.
Methods: This was a cross-sectional, observational, and comparative study. A total of 74 PsA patients aged 40-75 years old, who fulfilled the 2006 CASPAR criteria were recruited and matched to 74 controls by age (±5 years), gender and comorbidities. Patients with history of a previous cardiovascular event or pregnancy were excluded from this study. Blood pressure and PP was measured according to current guidelines. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done with Chi-square test for qualitative variables and Student´s t test and Mann-Whitney's U test for quantitative variables. A p value <0.05 was considered statistically significant.
Results: There were no differences regarding demographic characteristics between groups. When comparing the arterial measures, a statistically significant difference was found in the PP, which was higher in the PsA group [45.00 mmHg (40.00-56.50) vs 42.50 mmHg (38.00-50.00), p=0.024], and in the systolic

arterial pressure, higher in PsA patients (131.06 ± 18.27 mmHg vs 123.02 ± 14.27 mmHg, p=0.003) (Table 1).

Table 1. Demographic characteristics of the patients.

Characteristics	PsA patients (n=74)	Controls (n=74)	*P* Value
Age, mean ± SD	55.08±7.61	54.94±7.45	NS
Female gender, n (%)	41 (55.40)	41 (55.40)	NS
Obesity, n (%)	47 (63.51)	48 (64.86)	NS
T2DM, n (%)	58 (78.37)	56 (75.67)	NS
Hypertension, n (%)	48 (64.86)	44 (59.45)	NS
Dyslipidemia, n (%)	44 (59.45)	46 (62.16)	NS
Active smoking, n (%)	49 (66.21)	53 (71.62)	NS
SAP, mean ± SD	131.06±18.27	123.02±14.27	**0.003**
DAP, mean ± SD	81.06±11.12	79.13±9.69	NS
PP, median (p25-p75)	45.00 (40.00-56.50)	42.50 (38.00-50.00)	**0.024**

PsA, psoriatic arthritis; NS, non-significant; T2DM, type 2 diabetes mellitus; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; PP, pulse pressure.

Conclusion: PsA patients presented higher measures of PP compared to healthy controls. This suggests that PsA patients could have a higher risk of cardiovascular disease. It is recommended to consider PP as an important parameter when evaluating CVR in PsA patients. Further studies are necessary to validate these results.

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AB0945 SPECIAL FEATURES OF THE LIPID PROFILE IN PATIENTS WITH THE INFLAMMATORY ARTHROPATHIES

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Background: The main cause of death in patients with the inflammatory arthropathies is involvement of the cardiovascular system, and primarily atherosclerotic lesion with its complications. Initiation and progression of these arthropathies are underlied with similar immune and inflammatory mechanisms and associated with highly atherogenic changes of blood lipoproteins.

Objectives: Identification of particular qualities of the lipid profile in rheumatoid (RA) and psoriatic (PsA) arthritis, ankylosing spondylitis (AS) and their relationship with essential predisposing factors.

Methods: We enrolled 20 patients with RA, 15 with PsA, and 15 with AS, receiving basic anti-inflammatory therapy with methotrexate 10 to 20 mg per week for 6 months, in combination with various non-steroidal anti-inflammatory drugs. These diagnoses were verified according to the ACR/EULAR 2010, CASPAR 2006, ASAS 2009 criteria, respectively. The single exclusion criterion was the presence of a concomitant disease that could affect lipid metabolism. Total cholesterol (TC), HDL cholesterol, and triglycerides (TG) were measured in the plasma samples of all the patients, LDL cholesterol was calculated using Friedewald's formula: TC – (HDL + (TG/2.2)). The atherogenic index was taken as (TC – HDL)/HDL. Results were expressed as arithmetic means ± standard deviations. Differences were considered significant when $p<0.05$.

Results: The age of all patients ranged from 30 to 67 years, disease duration range was 1.5 to 12 years. All the patients with chronic arthritis had moderate or high disease activity grades. In the subgroup of RA patients average TC value was 5.63±1.6 mmol/l, HDL – 1.09±0.2 mmol/l, LDL – 3.74±1.16 mmol/l. Increased TC levels were detected in 80% of cases, TG - in 40%, LDL - in 80%, and decreased HDL - in 60% patients. There were strong relationships of TC with age, menopause, or overweight. The duration of RA also positively correlated with TC ($r=0.189$, $p<0.05$) and LDL ($r=0.159$, $p<0.05$). RA (C-reactive protein level) activity was negatively associated with HDL ($r=-0.169$, $p<0.05$). 80% of PsA patients had increased TC levels, but TG or HDL levels were within reference intervals. Mean TC in this subgroup was 6.04±1.55 mmol/l. TC values of PsA patients also positively correlated with age, BMI, and duration of PsA. There was an increase in TC, LDL, and the atherogenic coefficient in AS patients. Mean values of TC, TG, LDL, and HDL in this subgroup were 5.65±0.28, 1.28±0.12, 3.86±0.23 and 1.09±0.06 mmol/l, respectively.

Conclusion: Lipid disorders in patients with chronic inflammatory joint diseases may be a source of increased risk of early atherosclerosis and the cardiovascular events. Increased TC and LDL were most pronounced changes in lipid profiles of RA, PsA and AS patients. All these markers were revealed to be associated with both common cardiovascular (age, increased BMI) and the disease-associated factors (arthritis duration, activity of the underlying disease).

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AB0946 PELVIS RADIOGRAPHY FINDINGS AND PROGRESSION RATES IN PATIENTS WITH PSORIATIC ARTHRITIS UNDER BIOLOGIC TREATMENT

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Background: Psoriatic arthritis (PsA) is a heterogenous disease that can present with various musculokeletal manifestations. Several studies have assessed the rate of sacroileitis in PsA population, however data on the involvement of other pelvic structures that may cause symptoms, such as major entheseal or hip involvevement, and progression rates during follow-up is scarce.

Objectives: This study aimed to understand overall pelvis radiography findings and progression rates during follow-up in a cohort of patients with PsA under biologic treatment.

Methods: PsA patients from the Hacettepe University biological database (HUR-BIO), were retreospectively analyzed for their pelvis radiographs. All radiographs for individual patient were consecutively scored. Modified New York (mNY) criteria was used to assess sacroileitis and ischium/ iliac wing/ greater-lesser trochanteric enthesopathy and symphysis pubis osteitis assessments were done using a grade 0, no changes, 1, minimal changes and grade 2 and more counted as significant changes (1). Hip involvement was scored using BASRI-hip score and data on prosthesis were noted (2). All of the assessments were done by an experienced rheumatologis (UK) and in cases with suspicion, another experienced rheumatologist reviewed the cases (LK) and a consensus was reached.

Results: Overall 273 patients (69.6% of females) with the mean (SD) age at the time of first radiography 43.3 (12) years were included. At their initial radiographic assessment, the median (IQR) PsA duration was 2 (7) years. Baseline radiographs showed 10 (%3.7) of the patients had transitional vertebra and 137 (50.2%) patients had sacroiletis according to mNY criteria. From patients without sacroileitis (n=136), 67 patients had following radiographs. After a mean (SD) 47.1 (37) months, 16 (23.8%) of them progressed to sacroiletitis according to mNY criteria. Regarding the major enthesopathies, Regarding significant changes, 26.8 % of the patients had ischium enthesopathy, 19.3% of the patients ad symphysis pubis involvement and 13.2% of the patients had iliac

Table 1. Distribution of major entheseal involvement and BASRI-hip socres and progression rates

Location	Grades	First assessment N (%)	Progression rate*
Ischium (n=164)	4	0	9/65 (13.8)
	3	11 (6.7)	
	2	33 (20.1)	
	1	74 (45.1)	
	0	46 (28)	
Symphysis Pubis	4	0	8/78 (10.2)
(n=191)	3	5 (2.6)	
	2	32(16.8)	
	1	60 (31.4)	
	0	94 (49.2)	
Iliac wing	4	0	3/72 (4.1)
(n=174)	3	9 (5.2)	
	2	14 (8.0)	
	1	28 (16.1)	
	0	124 (71.3)	
BASRI score	4	3 (1.4)	0
(right)	3	2 (0.9)	
(n=220)	2	1 (0.5)	
	1	0	
	0	214 (97.3)	
BASRI score	4	0	0
(left)	3	4 (1.8)	
(n=219)	2	2 (0.9)	
	1	0	
	0	213 (97.3)	

*Defined as one unit increase in the grade

wing enthesopathy. Trochantor major enthesopathy rates were 2.4% and 1.4 % at right and left sites respectively. Only one patient had trochanter minor enthesitis on the left site (Table 1). Prosthesis requirement was observed in 4 hip joints and 4 hip joints had prosthesis. There was no correlation between meeting mNY criteria and having iliac, ischium, and pubis involvement ≥ 2. On the other hand, patients with when there is ischium enthesopathy ≥2 (17/46 (36.9%) vs 18/96 (18.7%), p=0.013) or iliac wing enthesopathy ≥2 above (10/18 (55.5%) vs. 26/129 (20.1%), p=0.001), any syndesmophyte in the spine is more commonly seen.

Conclusion: Half of the patients with PsA requiring advanced treatment modalities, had sacroileitis in a median 2 years of disease duration and the rest may progress to sacroileitis during the follow-up period. Major enthesopathy involvement was also seen in more than half of the patients. Ischium, iliac wing enthesopathies and spinal syndesmophytes may be all a part of the osteoproliferative process. Further assessment is needed to correlate those radiographic changes to clinical symptoms.

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AB0947 CORRELATION BETWEEN ENTHESITIS AND CLINICAL PHENOTYPE PSORIASIS, NAIL PSORIASIS AND DURATION PSORIASIS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a disease with multidimentional manifestations in patients who have psoriasis (PsO). Enthesitis is an important component of PsA and may be a primary pathological feature driving other manifestations of the disease. [1] Psoriasis and psoriatic nail dystrophy are also important predictors of PsA. Skin and joint disease may indeed arise from the same underlying process at the same time, with patients developing similar inflammatory lesions in the skin and entheses, while the speed of detection of these lesions is different and allows skin changes to be detected earlier. [2]

Objectives: to evaluate correlation between enthesitis and clinical phenotype psoriasis, nail psoriasis and duration psoriasis in patients with psoriatic arthritis.

Methods: 187 (M/F=97 (50.2%)/90(48.8%) PsA pts fulfilling the CASPAR criteria were included. Mean age 45.6±11.7 years (yrs), DAPSA 21.05±21.03, median (Me) PsA duration 88 [16;421] mo. All pts underwent standard clinical examinations. Analysis were performed in 2 groups: enthesitis positive (42.3%) and enthesitis negative (57.7%), for assess enthesitis in PsA pts used Leeds Enthesitis Index (LEI), modified LEI (LEI and plantar fascia), Maastricht Ankylosing Spondylitis Enthesitis Score (MASES).

Results: When 79 (42.3%) pts with enthesitis and 108 pts (57.7%) without enthesitis were compared. In pts with enthesitis had more duration PsO – 275,6±153,4 vs 227,4±139,5, p=0,03. The duration of PsA, both groups were comparable (p=0,9). Also in pts with enthesitis had more nail PsO - 66,6% vs 45% (p=0,005). BSA in both group were comparable, but in pts with enthesitis had more inverse PsO – 6,94% vs 3%, gluttate PsO – 4% in pts without enthesitis with phenotype PsO did not have, and combination plaque and inverse PsO – 51,3% vs 31% (p=0,0056). Moreover, significant but weak positive correlations between the LEI score and duration PsO and nail PsO. Assessment of the correlation modified LEI score and MASES score showed significant positive correlations with duration PsO, nail PsO and phenotype PsO. (Table 1).

Table 1. Correlation between LEI, modified LEI, MASES and parameters PsO.

Parameters	LEI		Modified LEI		MASES	
	r	p	r	p	r	p
Duration psoriasis	0,3	0,001	0,3	0,01	0,34	0,03
BSA	0,05	0,4	0,06	0,4	0,07	0,3
Nail psoriasis	0,3	0,001	0,35	<0,0001	0,32	0,01
Phenotype psoriasis						
Plaque psoriasis	-	-	0,53	0,001	0,61	0,001
Plaque+inverse psoriasis	-	-	0,65	0,001	0,62	0,001
Inverse psoriasis	-	-	0,70	0,02	0,66	0,03
Gluttate psoriasis	-	-	0,63	0,001	0,63	0,001

Conclusion: In our cohort PsA pts reported that with enthesitis is associated with duration PsO, nail psoriasis and phenotype PsO. These finding should be considered in the turn of improved screening, earlier diagnosis, timely treatment initiation and, eventually, should improve overall disease outcomes.

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AB0948 OSTEOPOROTIC SCREENING AND PREVALENCE OF SEVERE OSTEOPOROTIC FRACTURES IN A POPULATION OF PSORIATIC ARTHRITIS INITIATING A BIOLOGIC TREATMENT

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Background: Osteoporosis is a common complication of Rheumatic diseases. The association between osteoporosis and rheumatoid arthritis is clearly demonstrated while this association is still debated as well as for the screening of osteoporosis by Dual-Energy X-Ray Absorptiometry (DEXA) or to demonstrate an increased risk of fracture on radiography in a population of Psoriatic Arthritis (PsA). The prevalence of fragility fractures reported on medical reports ranged between 12% and 40% in PsA patients. Only a few studies evaluated the prevalence of vertebral fracture (VF) on spine radiographs. To our knowledge no study has evaluated the contribution of radiographic or CT assessment of the spine on the prevalence of fragility fracture reported in medical records.

Objectives: To determine Psoriatic Arthritis patient's characteristics screened for osteoporosis by DEXA in a population initiating a biologic treatment (bDMARD) and to estimate the prevalence of severe osteoporotic fractures on medical reports and after imaging modalities scoring (X-ray or CT-scan).

Methods: Patients with psoriasis should satisfy the CASPAR or ASAS criteria and have been screened during their follow up for a bDMARD. Osteoporotic screening was defined by a BMD testing (DEXA). Vertebral fractures were scored according to Genant's method on spine X-ray or sagittal CT-scan images. Clinical and demographic data and the presence of previous severe osteoporotic fracture reported in the medical records were collected.

Results: On 417 PsA patients screened for bDMARDs during 2008-2019, 89 patients (21.3%) were assessed for osteoporosis by DEXA. Increased age, female sex, menopause, previous severe fracture, disease duration, presence of inflammatory bowel disease, current and previous corticosteroid and bDMARDs uses were significantly associated with osteoporotic screening. On DEXA, 7 patients (7.9%) were classified as osteoporotic. The prevalence of severe osteoporotic fracture was 6.7% in medical reports and increased to 23.6% after scoring spine radiographies or TAP-CT images. In univariate analysis the presence of severe osteoporotic fractures was associated with age (p=0.013), scanographic bone attenuation coefficient (p=0.005) and Lumbar T-score (p=0.039).

Conclusion: Less than a quarter of PsA patients initiating a bDMARD is screened for osteoporosis. The prevalence of osteoporosis on DEXA and severe osteoporotic fractures on medical records are inferior to 10%. After systematic imaging evaluation, this prevalence increases at 23.6%.

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AB0949 PSORIASIS IN SPECIAL LOCALIZATIONS IN PATIENTS WITH PSORIASIS VERSUS PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriasis and psoriatic arthritis (PsA) are chronic immune-mediated diseases that primarily affect the skin and joints, respectively. A large proportion of patients with plaque psoriasis suffer from psoriatic lesions on the scalp, nails, palmoplantar area and genitals. These locations can also be soley or predominantly affected. Psoriasis in special localizations are often perceived as particularly stigmatizing and significantly reduce quality of life. Involvement of these body parts is associated with an increased risk of PsA.
Objectives: To provide a descriptive analysis of psoriasis in special localizations in patients with psoriasis versus patients with PsA.
Methods: This cross-sectional study was performed in Vega-Baja Hospital (Orihuela-Spain) from May2021 to December 2021. We prospectively enrolled 77 consecutive psoriasis patients and 76 consecutive patients affected by PsA and followed at the Vega-Baja Hospital (Orihuela-Spain). Sociodemographic data and clinical characteristics were analysed.
Results: One hundred and fifty-three patients were included (77 psoriasis patients and 76 patients affected by PsA). The registry variables used in this study are detailed in Table 1.

Table 1. Patients' data variables recorded

	Psoriasis	PsA	p-value
Sex, n (%)			
Male	35 (45.5)	31 (40.8)	0.625
Female	42 (54.5)	45 (59.2)	
Age (years), mean (SD)	50.27 (15.3)	53.83 (10.2)	0.094
Weight (kg), mean (SD)	86.1 (21.3)	78.8 (17.7)	**0.022**
Height (m), mean (SD)	1.66 (0.1)	1.65 (0.1)	0.76
BMI (kg/m2), mean (SD)	31.3 (7.6)	28.7 (5.5)	**0.017**
HTA, n (%)	20 (26.0)	19 (25.0)	0.89
DM, n (%)	12 (15.6)	14 (18.4)	0.64
DLP, n (%)	25 (32.5)	29 (38.2)	0.46
Metabolic syndrome, n (%)	36 (46.8)	42 (55.3)	0.29
Smoker, n (%)			
No	31 (40.3)	23 (30.3)	**0.012**
Yes	29 (37.7)	19 (25.0)	
Ex-smoker	17 (22.1)	34 (447)	
Psoriasis in special localizations, n (%)	67 (87.0)	74 (97.4)	**0.031**
Scalp	52 (67.5)	51 (67.1)	0.96
Genital	30 (39.0)	31 (40.8)	0.817
Palmoplantar	19 (24.7)	18 (23.7)	0.886
Nails	30 (39.0)	42 (55.3)	**0.043**

BMI, body mass index; DLP, dyslipidemia; DM, diabetes mellitus; HTA, hypertension; PsA, psoriatic arthritis.

There was a significant difference in weight and body mass index between the groups. PsA patients have more frequent psoriasis in special locations.
Conclusion: We have found that patients with PsA have more frequent psoriasis in special locations.
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AB0950 DETECTION OF ASYMPTOMATIC ENTHESEAL INVOLVEMENT IN PATIENTS WITH PSORIASIS: A CASE-CONTROL ULTRASOUND STUDY

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Background: Enthesopathy is one of the major features of psoriatic arthritis (PsA). The clinical screening for enthesopathies and synovitis in patients with psoriasis is nonspecific during the subclinical phase. Ultrasonography (US) has already demonstrated its ability to study entheses and joints in early stages of PsA.
Objectives: To evaluate the prevalence of ultrasonographic subclinical synovitis and enthesopathies in psoriasis patients with no clinical evidence of PsA compared with controls.
Methods: A cross-sectional study conducted on 40 patients with psoriasis and 40 healthy sex- and age- matched controls. The Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada (SPARCC) were used to evaluate entheseal involvement. US examination of 18 joints (wrists, metacarpophalangeal, and proximal interphalangeal joints) was performed along with 22 entheseal sites (deep flexor of the fingers, lateral epincondyle, triceps, quadriceps, patellar and calcaneal tendons and plantar fascia). Inflammatory-score (thickening, hypoechogenocity, bursitis and Doppler signal) and damage-score (calcifications, enthesophytes and erosions) were calculated (0= absent, 1=present for each abnormality). A total-score was obtained by adding these two scores.
Results: The mean age of psoriatic patients 51,90±15,90 [19 -76] and the sex ratio of males to females was 3:2. US synovitis were more frequent in psoriatic patients 7/1040 (0,68%) than in controls 3/1040 (0,29%) but this was not significant (p= 0,420). Patients with psoriasis had more US enthesopathies 37 (92,5%) comparing to controls 16 (40%) (p < 0,001). The total number of enthesopathies was higher in the psoriatic group 184/880 (20,90%) comparing to controls 42/880 (4,78%) (p < 0,001). Entheses with more US abnormalities in the psoriasis group comparing to controls were deep flexor tendons of the fingers entheses (p<0,001), distal patellar tendon entheses (p<0,001) and calcaneal tendon entheses (p<0,001). LEI and SPARCC scores were positively correlated to higher number of US enthesopathies (p=0,046, p=0,006). SPARCC was positively correlated to inflammatory-score and damage-score (p=0,009, p=0,024). The mean C-reactive protein level was higher in psoriatic arthritis 5,77±10,10 mg/L than in controls 2,15±3,26mg/L (p=0,037).
Conclusion: Our results confirm that US enthesopathies and synovitis are more frequent in patients with psoriasis comparing to healthy population. The US screening for subclinical enthesopathies should be the object of longitudinal investigations to define its value in predicting the clinical onset of PsA.
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AB0951 ENTHESEAL INVOLVEMENT IN HEALTHY SUBJECTS: WHAT CAN LOWER LIMB ULTRASONOGRAPHY TELL US?

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Background: Over the past few years, ultrasonography (US) has been a very useful tool in the detection of subclinical enthesopathy especially in spondyloarthritis patients. However, could US entheseal involvement detection by US in healthy subjects be predictive of evolution to an inflammatory rheumatic disease?
Objectives: To identify by US the prevalence of entheseal abnormalities at the lower limb of healthy subjects and associated risk factors.
Methods: US assessment was performed on 400 entheses of 40 healthy volunteer subjects along with clinical examination. Exclusion criteria: Enthesitis on the physical examination, personal of family history of inflammatory rheumatic disease and previous surgery or procedural interventions in the knees and/or ankles. Quadriceps, patellar and calcaneal tendons, and plantar fascia entheses were scanned. Depending on lesion type, inflammation (thickening, hypoechogenecity, bursitis and Doppler signal) and chronic damage (calcifications, enthesophytes and erosions) scores (0= absent, 1=present) were calculated per entheseal site and per participant. Total score was obtained by adding these two scores. Data about age, gender, body mass index (BMI) and physical activity according to the short form of the International Physical Activity Questionnaire score (IPAQ-SF) were collected.
Results: The mean age of participants was 52.3±14.83 [20-78] and the ratio of males to females was 3:2. Fourteen participants had US subclinical enthesopathy (35%). Among 400 scanned entheses, thickening was the most frequent

inflammatory lesion observed in 4 % (n=16) of the entheses, followed by hypoechogenecity (0.5 %, n=2). Enthesophytes were the most frequent chronic damage lesions detected in 1.25% (n=5) of the entheses followed by erosions (0.5%, n=2). The highest total US scores per entheseal site were observed at the calcaneal enthesis [mean (SD) 0.27(0.59)], followed by plantar fascia [0.18(0.50)] and distal patellar tendon origins [0.10 (0.37)]. Age was not associated to higher scores (total, inflammation, chronic damage; p=0.339, p=0.412, p=0.531). Female participants had higher inflammation scores than males (mean inflammation scores (SD) 0.69 (1.44) versus 0.39 (0.71), p=0.044). The BMI was correlated to higher inflammation score (p=0.020, r=0.368) but not to chronic damage nor to total scores (p=0.478, p=0.104). Intense physical activity was associated to higher chronic damage score comparing to moderate physical activity (mean chronic damage scores (SD) 0.30(0.67) versus 0.003(0.00), p=0.058) and to low physical activity (mean chronic damage scores (SD) 0.30(0.67) versus 0.0018(0.00), p=0.043). No association between physical activity and inflammation score had been observed.

Conclusion: Our study demonstrates that US changes within the enthesis are associated with higher BMI and physical activity. These results support the effect of biomechanical forces on the entheses that should be considered when differentiating by US pathological from healthy entheses.

Disclosure of Interests: None declared

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AB0952 CHARACTERIZATION OF PATIENTS WITH PSORIATIC ARTHRITIS IN DERMATOLOGIC AND RHEUMATOLOGIC CARE: AN ANALYSIS OF TWO DISEASE REGISTRIES

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease affecting the musculoskeletal system, skin and nails. Therapeutic management in Germany is usually provided by a dermatologist or rheumatologist.

Objectives: The aim is to characterize the socioeconomic and clinical patient profiles in dermatologic and rheumatologic settings.

Methods: Baseline data of patients with PsA from [1] the dermatological German Psoriasis Registry PsoBest (PB) and [2] the rheumatological German disease register RABBIT-SpA (RS) [2] were analyzed. For this purpose, comparable anamnestic and clinical variables collected in the period 10/2017 to 12/2020 were identified and descriptively analyzed. The analysis was carried out in each of the data-holding registers.

Results: 1066 RS patients and 704 PB patients were included in the analysis (Table 1). The proportion of women was higher in the rheumatology setting (RS) (60% vs. 49%). Disease duration of psoriasis was longer in the dermatology setting (PB). Cutaneous severity was higher in PB, including affected body surface area and nail psoriasis. However, more patients in RS had tender joints and swollen joints. The physician-reported global disease activity was higher in RS. The mean DLQI (Dermatology Life Quality Index) was higher in PB and the mean HAQ (Health Assessment Questionnaire) was higher in RS. Patient reported global disease activity and pain were lower in PB. Most of the patients received biologics at inclusion (RS: 71% and PB: 73%). In the dermatology setting IL23 inhibitors were used more frequently, whereas TNF inhibitors were used more frequently in the rheumatology setting.

Table 1. Baseline data of patients with PsA from the registers PsoBest and RABBIT-SpA included 10/2017 to 12/2020.

	RABBIT-SpA (Rheumatology setting)	PsoBest (Dermatology setting)
N	1066	704
Age, mean (SD)	51.9 (12.2)	51.7 (13.2)
Female, n (%)	637 (60)	346 (49)
Disease duration skin, mean (SD)	14.3 (13.9)	21.6 (16.0)
Body surface area, mean (SD)	8.5 (15.0)	20.8 (19.8)
Nail psoriasis, n (%)	434 (41)	407 (58)
Tender joints, n (%)	905 (85)	498 (71)
Swollen joints, n (%)	708 (67)	387 (55)
Physician reported disease activity, mean (SD)	5.2 (1.9)	4.6 (2.7)
DLQI, mean (SD)	5.6 (6.2)	12.2 (7.6)
HAQ, mean (SD)	0.9 (0.7)	0.7 (0.6)
Patient reported disease activity, mean (SD)	5.7 (2.4)	4.9 (2.9)
Patient reported pain, mean (SD)	5.5 (2.4)	5.2 (2.8)
bDMARD, n (%)	751 (71)	514 (73)
TNF, n (%)	346 (46)	117 (23)
IL17, n (%)	351 (47)	246 (48)
IL23, n (%)	54 (7)	151 (29)
tsDMARD, n (%)	109 (10)	47 (7)
csDMARD, n (%)	195 (18)	142 (20)

Conclusion: The clinical specialization of the treating physician was associated with a different treatment and clinical status of patients with PsA. Our analysis showed that patients in the rheumatology setting more frequently had joint affections and lower functional status, whereas skin severity was worse in the dermatology setting, indicating selection effects of health care access. We hypothesize out that these differences may be biased due to different diagnostic and therapeutic routines in the specialized health care settings. Psoriatic arthritis should be treated in a multidisciplinary approach to take into account all facets of this complex disease.

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[1] PMID: 24393314

[2] PMID: 30874933

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AB0953 LACK OF RACIAL DIVERSITY IN CLINICAL TRIALS OF PSORIATIC ARTHRITIS

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Background: Participant diversity in clinical trials of therapeutics in rheumatology is important to understand how persons of different races and ethnicities might respond differently to therapeutics. Specifically, for psoriatic arthritis (PsA), although people of color (POC) have lower disease prevalence, prevalence still ranges from 0.04-0.19% in Blacks, 0.13-0.19% in Asians, and 0.09-0.30% in Hispanics versus 0.19-0.34% in Whites in the insured population of the US[1]. Literature on the diversity of PsA clinical trials remains limited, though data suggest that minorities are underrepresented in clinical trials[2]. This analysis aims to evaluate the diversity of participants in randomized clinical trials (RCTs) of US Food and Drug Administration approved targeted therapies for PsA.

Objectives: To evaluate the reporting of race and ethnicity in published RCTs of targeted therapeutics approved for the treatment of PsA in the US.

Methods: Targeted therapies approved for use in the treatment of PsA in the US were identified. Package inserts and ClinicalTrials.gov (CT.gov) were used to

identify the pivotal double blind, RCTs in PsA which supported the approval of the identified therapeutics in the US. The articles reporting the primary endpoint data were obtained. Race and ethnicity data were extracted from the published data. Countries in which the studies were conducted were identified from the publications or CT.gov. Descriptive analyses were performed.

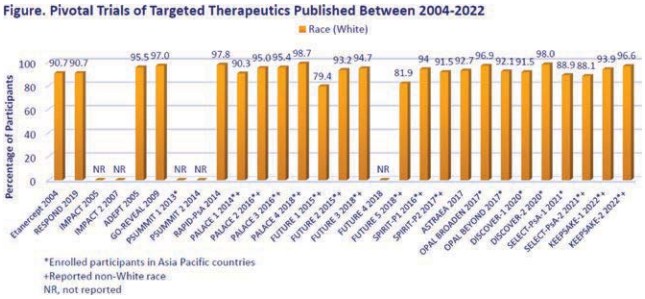
Results: Twenty-nine pivotal RCTs in PsA evaluating targeted therapeutics, published from 2002 – 2022, were identified; 24 reported race; non-White race was reported in only 13 (45%) (Table 1 and Figure 1). In the latter, people of Black race comprised <1% of the overall population in 12 RCTs and 2.7% in the remaining RCT. People of Asian race comprised 6.1% of the overall population reflecting <10% of the population in 11 studies and 11.3% and 19.0% in the remaining 2 studies. Overall, 19 (65.6%) trials recruited participants from Asia Pacific countries. Hispanic/Latinx ethnicity was not reported in any study. Studies published from 2017-2022 reported non-White race (n=7 of 15 [47%]) no more frequently than studies published from 2004-2016 (n=6 of 14 [43%]). Although the 13 RCTs reporting non-White race may not reflect unique individuals, the total number of people included across these RCTs was 7261, of which 48 (0.7%), 441 (6.1%), and 6598 (90.9%) were Black, Asian, and White, respectively.

Table 1. Race Reporting in Psoriatic Arthritis Pivotal Clinical Trials of Targeted Therapeutics

Race Reporting Status	Total Trials (N)	Trials which recruited in AP countries (n [% of N])	Total Participants (N)	White (n [% of N])	Black (n [% of N])	Asian (n [% of N])	Other* (n [% of N])
Not reported	5	1 (20.0)	1572	-	-	-	-
Non-White race reported	13	13 (44.8)	7261	6598 (90.9)	48 (0.7)	441 (6.1)	172 (2.4)
Non-White race not reported	11	5 (45.5)	6588	5803 (88.1)	-	-	-
Total (N)	29	19 (65.5)	15421	-	-	-	-

Abbreviations: AP, Asia Pacific; N and n, number.*Other also includes American Indian/Alaskan Native, mixed race, unknown raceNote: Numbers across rows may not add up to 0, and the total number of individuals reported in any one group may not be unique. Dashes reflect data not provided or able to be calculated.

Figure. Pivotal Trials of Targeted Therapeutics Published Between 2004-2022



Conclusion: Our data show under-reporting of race and ethnicity in publications of pivotal PsA RCTs, and no evidence of improved reporting over time. Whites were overrepresented in pivotal trials of PsA, especially when considering 72 and 62% of the US population was White in 2010 and 2020 (US Census data), respectively, and the reported prevalence of PsA by race in the insured population of the US[1]. Improved reporting of race/ethnicity and increased representation of racial/ethnic minorities in PsA RCTs are needed.

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Disclosure of Interests: Niti Goel Shareholder of: UCB, Abcuro, Employee of: Abcuro

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AB0954

CONCORDANCE BETWEEN DIFFERENT COMORBIDITIES SCORES IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Patients with psoriatic arthritis (PA) are more likely to suffer from other chronic medical conditions, associated comorbidities having significant impact upon both quality of life and survival. As disorders like the cardiovascular disease, metabolic syndrome, hepatic or renal pathologies were shown to be more prevalent in PA [1], assessment of comorbidities is important in these patients [2].

Objectives: To investigate the concordance of different comorbidities scores in patients with PA.

Methods: Prospective inclusion of patients diagnosed with PA according to the CASPAR (CIASsification criteria for Psoriatic ARthritis) criteria. Associated comorbidities were prospectively assessed using the Psoriatic arthritis comorbidity index (PsACI) with a cut-off of 8 points as previously defined [2]. Also, the following comorbidities scores were completed in all patients: Charlson comorbidity index (CCI), Rheumatoid Arthritis Comorbidity Index (RACI), Rheumatic Diseases comorbidity index (RDCI), Functional comorbidity index (FCI).

Results: A total of 56 patients were included: 27 (48.2%) were female, with a med (q1;q3) disease duration of 17.5 (12.7; 26.5) years for the cutaneous disease and 6.0 (4.0; 13.0) years for the articular one. At inclusion, the results of the comorbidities scores assessed were as follow: PsACI 3.2 (2.0; 6.5), CCI 1.0 (0.0; 2.0), RACI 3.5 (1.5; 6.5), RDCI 1.0 (0.0; 2.0), and FCI 2.0 (0.0; 2.0), respectively. According to PsACI, hypertension, hyperlipidemia, osteoarthritis, liver disease, and diabetes mellitus were the most frequent associated comorbidities in PA patients, in 53.6%, 44.6%, 41.1%, 37.5%, and 28.6% cases, respectively (see Table 1).

Table 1. Comorbidities according to the Psoriatic Arthritis Comorbidity Index

Parameter	n (%)	Parameter	n (%)
Diabetes mellitus	16 (28.6)	Cerebrovascular disease	1 (1.8)
Metabolic syndrome	8 (14.3)	Peripheral vascular disease	2 (3.6)
Ischemic heart disease	9 (16.1)	Osteoporosis	4 (7.1)
Myocardial infarction	1 (1.8)	Fracture	3 (5.4)
Hypertension	30 (53.6)	Fall	1 (1.8)
Hyperlipidemia	25 (44.6)	Liver disease	21 (37.5)
Arrhythmia	2 (3.6)	Renal disease	2 (3.6)
Depression	6 (10.7)	Pulmonary disease	6 (10.7)
Anxiety	10 (17.9)	Gastrointestinal tract	2 (3.6)
Endocrine	7 (12.5)	Osteoarthritis	23 (41.1)
Periodontitis	1 (1.8)	Fibromyalgia	3 (5.4)
Smoking	6 (10.7)	Amyloidosis	1 (1.8)
Infection	0 (0.0)	Eyes inflame/ uveitis	0 (0.0)
Vasculitis	0 (0.0)	Tumor	3 (5.4)

In bivariate analysis, we found significant correlations between the results of PsACI and those of the other comorbidities scores used: CCI (p<0.001, rho=0.668), RACI (p<0.001, rho=0.792), RDCI (p<0.001, rho=0.691), and FCI (p<0.001, rho=0.697), respectively. The ability of the comorbidities scores assessed to discriminate a PsACI high value is presented in Figure 1, AUC (95%CI): CCI 0.743 (0.601- 0.886) p=0.017, RACI 0.815 (0.634 - 0.996) p=0.002, RDCI 0.818 (0.657-0.980) p=0.002, and FCI 0.837 (0.725-0.948) p=0.001, respectively.

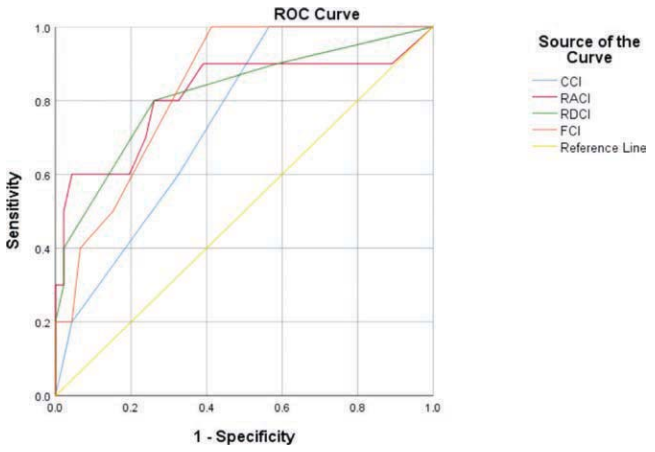

Figure 1. The Area Under the curve of the Receiver Operating Characteristic (AUROC) for high PsACI results (PsACI > 8)

Conclusion: The composite indexes offer the advantage of reducing all associated comorbidities as long with their severity into a single score. We herein

identified good correlations between the results of the comorbidities scores analyzed, PsACI, CCI, RDCI, RACI, and FCI, respectively.

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AB0955 DISEASE ACTIVITY IMPACT OVER THE ANXIETY LEVEL IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PA) is a complex, systemic, chronic inflammatory condition with substantial multisystemic detrimental effects on patients' health status. In PA patients there was reported increased anxiety occurrence when compared to general population, even if specific predictors are not defined yet [1].

Objectives: To characterize disease-related predictors of anxiety in patients with PA.

Methods: Cross-sectional study with prospective, successive inclusion of patients fulfilling the CASPAR (CIASsification criteria for Psoriatic ARthritis) classification criteria for PA. Anxiety level was assessed using the General Anxiety Disorder-7 (GAD-7) with a cut-off of 10 points as previous defined [2]. Moreover, disease activity status for PA was defined using also validated scores, namely the Disease Activity Index for Psoriatic Arthritis (DAPSA), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Ankylosing Spondylitis Disease Activity Score (ASDAS), cutaneous involvement by the Psoriasis Area Severity Index (PASI), and comorbidities by Psoriatic arthritis comorbidity index (PsACI).

Results: 56 PA patients were included, 29 (51.8%) males, with mean±SD age at inclusion of 54.1±13.2years. Regarding the tools for disease activity assessment, the probability of impact over a high anxiety level as estimated by area under curve (AUC) was high (> 0.800) for BASDAI [AUC(95%CI) 0.859 (0.738-0.979)], especially in relation with the last 3 items about inflammation of other than neck, back or hip joints and morning stiffness (see Figure 1).

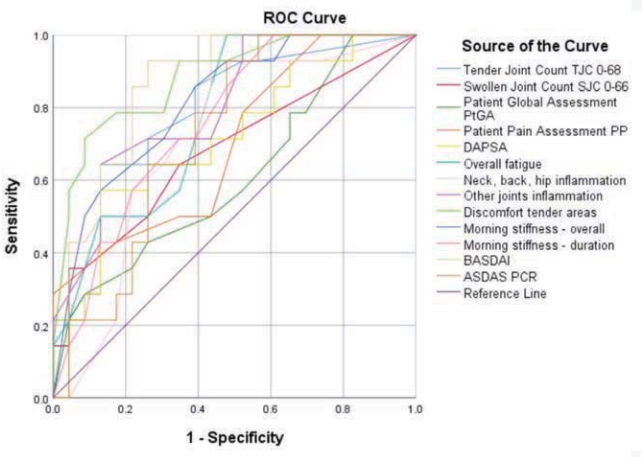

Figure 1. The Area Under the curve of the Receiver Operating Characteristic (AUROC) for high anxiety level (GAD-7 > 10)

In bivariate analysis, we found a significant difference regarding a higher anxiety level as assessed by GAD-7 for female gender (28.6% vs. 78.9%, p=0.001), concomitance of peripheral and axial articular involvement (25.7% vs. 52.6%, p=0.034), DAPSA (14.8 (7.1; 22.8) vs. 24.6 (12.2; 36.8), p=0.035), BASDAI (3.1 (1.3; 4.1) vs. 7.1 (5.0; 8.0), p<0.001), and ASDAS-CRP (2.5 (1.1; 3.7) vs. 3.5 (2.7; 4.0), p=0.038), but not for the other parameters search, namely age, smoking, alcohol intake, home settle (urban/ rural, living alone, kids), disease duration, HLA-B27 status, PASI, PsACI, Patient (PtGA) or Physician (PGA) Global Assessment, ongoing corticosteroid treatment, or inflammation status (ESR, CRP).In multivariate analysis, the PA disease-related predictor for increased anxiety was the auto-evaluation by BASDAI, OR (95%CI) 1.844 (1.198 - 2.839) (see Table 1).

Table 1. Independent predictors for anxiety in psoriatic arthritis patients

Parameter		95% CI		p-value
		lower	upper	
Gender, F/M (%F)	0.106	0.023	0.498	0.004
Articular axial and peripheric, Y/N (%Y)	0.289	0.055	1.503	0.140
DAPSA	1.017	0.973	1.063	0.460
BASDAI	1.844	1.198	2.839	0.005
ASDAS-CRP	1.312	0.877	1.964	0.186

Conclusion: Therefore, higher BASDAI results were associated with increased anxiety in PA and so such results should raise awareness about the need of search for associated anxiety disorders. On the contrary, the extension of the cutaneous involvement, the systemic inflammation level or the comorbidities degree were not identified as predictors for the anxiety occurrence.

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Disclosure of Interests: None declared

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AB0956 TO WHAT EXTEND IS NAIL ULTRASOUND DISCRIMINATIVE BETWEEN PSORIATIC ARTHRITIS AND HEALTHY SUBJECTS?

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Background: Clinical physical examination can detect superficial nail changes in psoriatic patients. However, the nail matrix and bed are not accessible for clinical assessment. Recently, ultrasonography (US) has emerged as a useful tool to assess nail involvement in psoriatic arthritis (PsA) patients.

Objectives: To assess the discriminative utility of nail features detected by B-mode (BM) and color Doppler (CD) ultrasound (US) between patients with psoriatic arthritis (PsA) and healthy controls (HC).

Methods: This was a cross-sectional study including PsA patients and HC.

All patients and controls underwent an US assessment of the fingernails that included the study of morphological changes based on Wortsman's description [1]: focal hyperechoic involvement of the ventral plate without involvement of the dorsal plate (type I), loosening of the borders of the ventral plate (type II), appearance of wavy plates (type III) and loss of definition on both plates (type IV), blood flow disturbances and measurement of the thickness of nail bed (NBT), nail plate (TNP) and adjacent skin.

Results: A total of 536 nails were examined (PsA:326 nails, HC:210). Patients with PsA had significantly more morphological changes of the nails than healthy controls (23% vs 3.33%, p = 0.006). In PsA patients, the most frequently observed aspect was type III (47 nails, 14.4%), followed by type II (40 nails,12.3%) and type IV (38 nails, 11.6%). In HC, the only observed type was type (type II). US detected subclinical nail involvement in 37 healthy nails among PsA patients (11.34%). On the other hand, seven nails with clinical involvement did not demonstrate US changes: perionyxis (n=1), pitting (n=2), onycholyses (n=3), hemorrhage (n=1). The power Doppler signal of the nail bed and matrix was comparable between the groups (54% vs 61%, p= 0.603 and 41% vs 37.1%, p=0.432, respectively). NBT and skin thickness were higher in the HC group than the PsA group (1.90±0.22 mm vs 2.07±0.34 mm, p=0.047 and 2.25±0.69 vs 2.59±0.31 mm, p=0.002, respectively). While NPT was similar between the groups (0.38±0.09 vs 0.36±0.07mm, p=0.239).

Conclusion: Us detected morphological changes in clinically healthy fingernails in both PsA patients and healthy controls. However subclinical involvement was more common in PsA patients. Loosening of the borders of the ventral plate (type II) was the only aspect observed in HC. This would suggest that this type is not

a specific feature of psoriatic nail. With regards to nail plate thickness, the measurements were similar between PsA patients and HC as previously reported by Mondal et al [2].
However, unlike previous studies, we showed that the nail bed and skin thickness were significantly higher in healthy controls than PsA patients [3].

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Disclosure of Interests: None declared

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AB0957 LIMITED GENDER-RELATED DIFFERENCES CHARACTERIZE PSORIATIC ARTHRITIS: DATA FROM A MONOCENTRIC ANALYSIS OF 306 PATIENTS

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Background: Psoriatic Arthritis (PsA) is characterised by a wide spectrum of clinical phenotypes which are ultimately driving therapeutic choices. The male-to-female ratio of the disease is approximately even but in the last decades some gender differences have been proposed in terms of clinical expression and therapeutic responses.
Objectives: The aim of this study is to confirm these differences in a real-life cohort of PsA patients.
Methods: A retrospective data collection has been conducted on a cohort of outpatients with PsA attending our Rheumatology Clinics at Humanitas Research Hospital between January 1st and December 31st 2021. All patients were ≥ 18 years old and fulfilled the CASPAR criteria for PsA. For each patient we obtained demographic, laboratory and clinical parameters and registered which domains (peripheral arthritis, axial PsA, skin and/or nail disease, enthesitis, dactylitis) have been involved in the course of the disease. We also collected data regarding any concomitant comorbidities and previous and current therapies. To investigate possible gender specific differences a cross-sectional univariate descriptive analysis was performed.
Results: Our cohort included 306 patients (169 - 55% - women) with PsA. The median age of disease onset was the same for men and women, also when separately considering skin (median 38 years) and articular presentation (median 48 years). No statistically significant differences were observed when comparing the two groups in terms of clinical phenotypes. In both groups peripheral arthritis was referred by the vast majority of patients (95% of women vs. 93% of men) and similar rates of axial involvement (34% in women vs. 37% in men). Considering current or previous therapies, we found a comparable use of non steroidal anti-inflammatory drugs (43% in both groups), systemic glucocorticoids (9% in men vs 10% in women), conventional synthetic DMARDs and biologic DMARDs and in each group the percentages of patients with a history of bDMARDs targeting TNFalfa, IL12-23 or IL17 failure (women vs men: 11%vs 11%, 9% vs 6% and 4% vs 5% respectively) were essentially the same. A higher proportion of women received apremilast (13% vs. 4% of men, P= 0.003). We also observed differences in terms of comorbidities: in our cohort women were more frequently affected by hypothyroidism (6/137 vs. 23/149 in men, P=0.006), fibromyalgia (2/137 vs 33/149, P<0.001) and neurologic disorders (13/137 vs. 41/149, P=0.001) compared to men.
Conclusion: Our cohort demonstrated limited gender-related differences in PsA course and therapeutic choices or duration, reporting only higher prevalence of hypothyroidism, fibromyalgia and neurologic disorders in women.
Disclosure of Interests: Nicoletta Luciano Speakers bureau: Eli-Lilly, Galapagos, Consultant of: Eli-Lilly, Galapagos, Gianmarco Roselli: None declared, Lorenzo Canziani: None declared, Giacomo Maria Guidelli Speakers bureau: Amgen, Eli-Lilly, Galapagos, UCB, Consultant of: Amgen, Eli-Lilly, Galapagos, UCB, Marta Caprioli: None declared, Maria De Santis Grant/research support from: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme, Actelion, Boehringer, Italfarmaco, Grunenthal, Roche, Angela Ceribelli Speakers bureau: Amgen, Grant/research support from: Novartis, Lilly, Pfizer, Grunenthal, GSK, Carlo Selmi Speakers bureau: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme, Paid instructor for: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme, Consultant of: AbbVie, Amgen, Alfa-Wassermann, Biogen, Celgene, Eli-Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme, Grant/research support from: AbbVie, Amgen, Janssen, Pfizer

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AB0958 THE RELATIONSHIP BETWEEN THE EXTENSOR TENDON ENTHESIS AND THE NAIL IN DISTAL INTERPHALANGEAL JOINT DISEASE IN PSORIATIC ARTHRITIS: ULTRASOUND STUDY

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Background: It has been shown that there is an anatomical link between the distal interphalangeal joint (DIP) extensor tendon enthesitis and the nail changes in psoriatic arthritis (PsA) [1].
Objectives: To evaluate the relationship between nail involvement and enthesopathy at DIP level in PsA patients using ultrasonography (US).
Methods: We included patients with PsA. According to OMERACT, the following elemental lesions were dichotomously (presence/absence) evaluated on greyscale US assessment at extensor tendon insertion at distal phalanx of DIP joints: abnormally hypoechoic, enthesophytes, and erosions. We also measured the tendon thickness. Increased abnormal vascularization at entheseal level was also assessed using PD technique. We also performed an US assessment of the finger nails that included the study of morphological changes and measurement of the thickness of nail bed (NBT), nail plate (NPT) and adjacent skin (ST).
Results: We included 33 PsA patients (323 DIP). Eleven patients (34 %) presented psoriatic onychopathy (45 fingernails) with a mean NAPSI 7 (IQR (25,75)) [2 -18]. US study of the nails revealed dystrophy in 75 nails (23%). At patient level, the mean NPT, NBT and SK were 1.90±0.22, 0.38±0.09, and 2.33±0.62, respectively. None of the patients had clinical involvement of DIP. Using US, we examined 325 extensor tendon. The mean thickness of the tendon was 0.63mm ±0.1 mm. The tendon was abnormally hypoechoic in two fingers (0.61%). Erosions were present in 16 DIP (4.9%). We found enthesophytes in 82 DIP joints at insertion of extensor digitorum tendon (25.23%). We did not observe increased abnormal vascularization at entheseal level. At finger level, the extensor tendon thickness was higher in the presence of US nail dystrophy (0.70 mm vs 0.60, p=0.01). Erosions were more common in fingers with US nail involvement (14.6 % vs 1.9%, p=0.00). Osteophytes were present in 20% of fingers with US nail involvement and 26.3% of fingers without US nail involvement (p=0.166). The thickness of DIP digital extensor tendons was correlated with the NBT(r = 0.412, p = 0.00), the NPT (r = 0.310, p = 0.00), and the thickness of the adjacent skin (r = 0.509, p = 0.00).
Conclusion: The presence of US nail dystrophy was associated with thicker extensor tendon and more erosions. The thickness of the tendon was correlated with the thickness of the nail parts. This might be explained by the close relationship between nail and enthesis and supports the theory of the enthesis as an extended organ beyond the tendon bony attachment.

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AB0959 THE ACTIVITY OF PSORIATIC ARTHRITIS WITH AXIAL INVOLVEMENT CORRELATES WITH PSAID12.

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Background: Patients with psoriatic arthritis (PsA) show an impact on the physical and psychological aspect of the disease and it can be measured with the PsA Impact of Disease (PsAID) questionnaire, and it is expected that the impact of the disease improves when the patient is in remission or low disease activity.
Objectives: To determine the rate of low impact of the disease in patients with PsA in daily clinical practice, and to evaluate its relationship with its axial activity.
Methods: A cross-sectional study was conducted in consecutive patients who met the CASPAR criteria, with positive clinical (DLI) and positive axial radiology, with or without peripheral involvement, and who were treated according to standard clinical practice (EULAR recommendations). Demographic, clinical, analytical data, HAQ index (0-3) and PsAID12 (0-10) were also collected. Patients were divided into 2 groups: those with a PsAID above 4 (high impact) or below 4 (low

impact). Continuous variables are shown as median (Q1-Q3) and categorical variables as percentages and frequencies. The analyzes were performed using SPSS23 software. Differences were considered statistically significant if $p < 0.05$.
Results: Of the 269 patients evaluated with PsA, 72 patients with axial involvement were included, 40 men (55.6%), with a median age of 54.1 years (45.0-62.0) and disease duration of 7 years (2-11). Obesity (BMI>29.99) affected 28.3% and serum CRP level was 0.45 mgr/dl (0.08-1.10). The treatments of the patients were: NSAIDs 43.1%, corticosteroids 21.6%, csDMARD 52.9% and biological therapy 51.9%. The BASDAI was 4.2 (2.0-6.2) and the ASDAS-PCR was 2.4 (1.5-3.2), with 39.6% being in low activity or remission. The median PsAID total score was 3.9 (1.6-5.4), evaluated in 61 patients. The patients who achieved a PsAID12 ≤4 was 63% (see Table 1), more men and with a lower CRP. In addition, the low impact measured by the PsAID12 was associated with a lower BASDAI and ASDAS-PCR.
Conclusion: Almost two thirds of patients with PsA with axial involvement in daily clinical practice had a low impact of the disease measured by PsAID12 and correlated with low activity in the BASDAI and ASDAS-PCR.

	PsAID≤4 n=39	PsAID>4 n=22	p
Age, years	54 (42-62)	54 (49-66)	0.284
Male gender, n %	28 (70)	10 (43.5)	0.038
Disease duration, years	7 (3-10)	5 (1.2-9.5)	0.432
CRP, mgr/dl	0.30 (0.04-0.79)	1.04 (0.07-2.44)	0.03
BSA, %	0.2 (0-1)	0.5 (0-1.5)	0.594
BASDAI	2.1 (0.8-4.0)	6.1 (4.4-6.9)	<0.001
ASDAS-PCR	1.5 (1.1-2-4)	3.1 (2.3-3.4)	<0.001

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AB0960 ULTRASONOGRAPHIC ASSESSMENT OF DISTAL INTERPHALANGEAL JOINTS IN PSORIATIC ARTHRITIS

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Background: Distal interphalangeal (DIP) joint involvement is frequent in Psoriatic arthritis (PsA). Ultraousnd (US) may help identify subclinal DIP arthritis.
Objectives: We aimed to assess by US the DIP joint involvement in PsA in comparison with healthy controls (HC).
Methods: This was a cross-sectional study including 33 PsA patients and 21 matched-healthy controls (HC). An US scan of all DIP joints was performed in order to look for erosions, synovitis (B-mode and doppler) and extensor tendon enthesopathy.
Results: We included 33 patients with PsA and 21 HC. There was no difference between the two groups regarding the age (51.2 ±12.5 vs 53±11.8 years, p=0.5), sex-ratio (0.65 vs 0.61, p=1), manual activity (p=1) and smoking status (23.8% vs 18%, p=0.433).On clinical examination,we did not find any tender nor swollen DIP joints in both groups. Eleven PsA patients (34 %) had psoriatic onychopathy (45 fingernails) with a mean NAPSI 7 (IQR (25,75)) [2 -18]. In the PsA group, a total of 323 DIP joints were examined by US, synovitis of the DIP joints was detected in ten DIP joints (3.1%) (right hand: seven, left hand:three), six of them had PD (right hand:four, left hand:two). Eosions were found in 16 DIP joints (4.95%) (right hand:seven, left hand: nine). Enthesophytes were seen in 82 DIP joints (25,2%). At patient level, six PsA patients had at least one US synovitis (18.1%), seven had at least one erosion (21.2%) and 22 had at least one DIP joint with enthesophytes (66.6%) Compared to HC, PsA patients had more synovitis (3.1% vs 0, p=0.001),more erosions (4.95% vs 0.4%, p=0,03), and more enthesophytes (25.2% vs, 17%, p=0,002) The was no difference between the two groups regarding the thickness of the extensor tendon (0.63 mm vs 0.61 mm, p=0.594).
In the PsA group, the patients with nail dystrophy had more osteophytes (24% vs 10%, p<0,001), more erosions (14.6% vs 1.96%, p=0.000), and more synovitis (6%, vs 1.9%, p=0.037).
Conclusion: Subclinical involvement of DIP joints is common in PsA patients, notably in the presence of nail dystrophy.
Disclosure of Interests: None declared
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AB0961 UVEITIS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a common disease in Departments of rheumatology. PsA affects from 5 % to 30 % of patients with psoriasis. The arthritis associated with psoriasis follows different patterns, including oligoarticular disease, polyarticular disease, distal interphalangeal disease, arthritis mutilans and axial disease. The axial disease often overlaps with the other four groups. Psoriatic arthritis belongs to the group of spondyloarthropathies in which uveitis is an associated disease. The prevalence of uveitis among PsA patients is not well established.
Objectives: The aim of this study is to describe the clinical characteristics of uveitis related to psoriatic arthritis.
Methods: Uveitis is described as an inflammation of the tissues that comprise the uveal tract (i.e., iris, ciliary body, and choroid). It can be classified either according to the anatomic parts of uvea that are involved or according to its underlying etiological cause. Anterior uveitis involves the iris and/or the ciliary body, intermediate uveitis involves the vitreous humor, while posterior uveitis is characterized by inflammation of the uvea and the choroid. A retrospective database study was conducted on 164 (96 female, 68 male, mean age 52,36±16,14 years) adult PsA patients with ocular symptoms. Demographic variables, smoking status, socioeconomic status (SES), body mass index (BMI), presence of selected chronic comorbidities, and medication use, including conventional and biologic disease modifying anti-rheumatic drugs (c/b DMARD) were extracted. We collected data about psoriasis type, uveitis laterality, onset type, human leukocyte antigen types, visual acuity, ocular inflammation localization, anterior segment findings, funduscopy findings, complications, recurrence, intraocular pressure, visual acuity, comorbidities, and medical treatments and outcomes for uveitis and psoriasis, and medical treatments for uveitis and skin diseases. Descriptive statistics was applied as appropriate. Cox proportional hazard regression time dependent models were used to calculate the risk of uveitis given demographic variables, SES, smoking, selected comorbidities, and c/bDMARD. P values of ≤ 0.05 were considered statistically significant.
Results: This study included a broad spectrum of ocular inflammation associated with PsA. We found that conjunctivitis was the most common problem, affecting 53 patients (32,32 %). Iritis (anterior uveitis) was found in 10 (6,1%), episcleritis - in 3 (1,83 %) and keratoconjunctivitis sicca - in 5 (3,05 %) patients. 14 patients were with axial involvement, seven of them with anterior uveitis. Patients with PsA and uveitis were more often female (7), of a younger age (48,25±15,4 years). In our cohort of patients uveitis is bilateral in 7 patients, all cases had acute non-granulomatous anterior uveitis. Anterior uveitis is usually accompanied by pain and redness of the eye without vision loss, while intermediate (1 patients) and posterior (2 patients) uveitis are mainly associated with visual symptoms such as floaters or blind spots and may affect central vision. Patients with uveitis had a previous history of uveitis and were more often treated with cDMARDS, monoclonal anti-Tumor Necrosis Factor-a (antiTNF-a) agents and etanercept. No difference in uveitis occurrence was noted regarding demographic characteristics and comorbidities.
Conclusion: Uveitis, in particular, is being considered as a relatively rare but very serious ocular complication of psoriasis. Patients with psoriasis should be educated about the increased risk and manifestations of uveitis. An ophthalmological consultation is needed when patients present with eye symptoms.
Disclosure of Interests: None declared
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AB0962 PSORIATIC ARTHRITIS WITH POSITIVE ACPA, WHICH FEATURES?

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Background: Anti-cyclic citrullinated peptide antibodies (ACPA) have been detected in several patients with psoriatic arthritis (PsA). It is possible that these autoantibodies are associated with particular features of PsA.

Objectives: The objective of our study was to assess the frequency of anti-CCP antibody positivity in psoriatic arthritis, and to identify the factors associated with this positivity in PsA.
Methods: Observational cross-sectional study, carried out in the rheumatology department of the CHU Hassan II of FES between January 2012 and October 2021. Including 67 patients with RP fulfilling the CASPAR criteria. ACPA positivity threshold was >20Ui/ml.
Results: Our study included 67 patients, the mean age was 55.3 +/- 15 years, the sex ratio was 0.36 M/F, the mean disease duration was 6.61 +/- 9 years. ACPA were positive in 16.4% of cases (11 patients), and negative in 83.6% of cases (56 patients). In bivariate analysis, PsA with positive ACPA was more common in men (27.8% versus 12% p=0.049), PsA patients with positive ACPA presented less inflammatory back pain (14% versus 86%) (p=0.049), developed more frequently pulmonary complications (60%) (P=0.001, and presented more often a positive rheumatoid factor (32% versus 7%) (P=0.019). In multivariate analysis, male gender was significantly related to ACPA positivity (p=0.049, OR=22.702, IC=1.05-505). Likewise for lung involvement (p=0.010, OR=67.903, IC=2.6 -1709.8). Also, ACPA positivity during PsA was significantly related to that of rheumatoid factor (RF) (p=0.05 OR=61.375 IC=0.994-3789). In addition, no statistically significant difference was found between the two groups concerning the activity of the disease, the structural impact, the biological inflammatory syndrome and the use of biotherapy.
Conclusion: In our study, PsA is characterized by a low predominance of a positive ACPA form. This form with positive ACPA is found in our context to be more frequent among men, more often associated with positive RF, and is more complicated by pulmonary damage.
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AB0963 FREQUENCY OF SEXUAL DYSFUNCTION IN PSORIATIC ARTHRITIS, SANTO DOMINGO, DOMINICAN REPUBLIC

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Background: Psoriatic arthritis (PsA) is an inflammatory joint disease that cause structural damage, disability, and an impairment of quality of life.[1]Sexual function is a neglected area of quality of life in patients with PsA, with a high prevalence of dissatisfaction.[2] It has been described that there is no relationship between the activity of the disease and the degree of joint dysfunction.[3] In 1 out of 5 patients consider that the disease negatively impacts their sexuality.[4] CSFQ-14 (Changes in Sexual Functioning Questionnaire), evaluates changes in sexual functioning due to an illness or treatment in 5 domains with a score range 14-70; cut-off point indicating sexual dysfunction -41 men and -47 women.[5]
Objectives: To evaluate the frequency and degree of sexual dysfunction in patients with psoriatic arthritis.
Methods: Prospective, observational, cross-sectional study. The patients of the outpatient clinic of the rheumatology service of the Padre Billini teaching hospital were interviewed during November 2021. Inclusion criteria: ≥18 years, PsA diagnosis according to CASPAR classification criteria 2006. Exclusion criteria: diagnosis of another autoimmune disease, depression, treatment with antidepressants. We analyzed the data in SPSS23 and used the Pearson correlation coefficient with a statistical significance p=<0.05 (rp) to relate the data.
Results: 58 met inclusion criteria. 63.8% (37) female, male 36.2% (21), mean age 54.8 + 11.75 y, mean diagnosis 7.9 y, married 55.2% (32), unmarried 39.7% (23), widowed 5.2% (3). Frequency of sexual dysfunction 39.7% (23), CSFQ-14 indicative of dysfunction in women 35.1% (23), men 47.6% (10). Female Domains: Pleasure dysfunction 35.1% (13), desire/interest 32.4% (12), desire/frequency 32.4% (12), arousal 24.3% (9), orgasm/completion 43.2% (16). Male Domains: Pleasure dysfunction 38.1% (8), desire/interest 47.6% (10), desire/frequency 33.3% (7), arousal 23.8% (5), orgasm/completion 42.9% (9). Correlation CSFQ-14/DAPSA28 domains: Pleasure dysfunction: DAPSA remission 19.2% (5), low 32.1% (9), moderate 50% (2). Desire/interest: DAPSA remission 34.6% (9), low 32.1% (9), moderate 100% (4). Desire/frequency: DAPSA remission 30.8% (8), low 37.5% (10), moderate 25% (1). Excitation: DAPSA remission 30.8% (8), low 17.9% (5), moderate 25% (1). Orgasm/completion: DAPSA remission 50% (13), low 37.5% (10), moderate 50% (2). r_p=. 042 p<0.05.
Conclusion: The study showed a modest frequency of global sexual dysfunction. In men it was superior. The orgasm/completion domain proved to be the most dysfunctional in both sexes. A statistically significant linear association of sexual dysfunction and disease activity was evident.
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AB0964 PSORIATIC ARTHRITIS (PSA) WITH POSITIVE RHEUMATOID FACTOR (RF) VERSUS PSORIATIC ARTHRITIS WITH NEGATIVE RF

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Background: Rheumatoid factor (RF) has been detected in several patients with psoriatic arthritis (PS). It is likely that its positivity is linked to a very specific clinical, biological and/or evolutionary profile of PsA.
Objectives: The objective of our study was to evaluate the frequency of positive rheumatoid factor during PsA, and to define the characteristics and factors related to this positivity.
Methods: Monocentric observational cross-sectional study including 84 patients with PsA, fulfilling the CASPAR criteria, and hospitalized in our rheumatology department in University Hospital Hassan II of Fez, on the period lying between January 2012 and October 2021. A threshold greater than 20Ui/ml of defines RF positivity.
Results: Our study included 84 patients, the average age was 57 +/- 13 years. The sex ratio was 0.35 M/F, the average duration of disease progression was 6 years +/- 8 years. 47.6% of patients had a positive RF (40 patients) while 52.4% of patients had a negative RF (44 patients). In bivariate analysis, PsA with positive RF had an earlier age of the disease onset (p=0.017), was more frequent in chronic smokers (p=0.045), and showed more enthesis damage (p=0.046). Also, patients with PsA and a positive RF had a higher biological inflammatory syndrome (p=0.013) in particular CRP (p=0.007), higher Basdai and DAPSA (p=0.021) (p=0.021) respectively In multivariate analysis, enthesis damage involvement was significantly linked to RF positivity (p=0.039, OR=3, IC=1.059-8.495), as was the biological inflammatory syndrome (p=0.010, OR=3.875, IC=1.382 -10.766).
Conclusion: In our study, PsA with positive RF is found to be earlier and more severe in comparison with PsA with negative RF, and more frequently adopts the peripheral enthesitic form.
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Disclosure of Interests: None declared
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AB0965 SERIAL SEROLOGY TESTING IN PATIENTS WITH PSORIATIC ARTHRITIS- SHOULD IT BE DONE?

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Background: The diagnosis of psoriatic arthritis (PsA) is largely based on clinical phenotype due to the heterogeneity of the presenting features, which can include synovio-entheseal disease, dactylitis, skin and nail disease, uveitis and axial involvement. (1) In contrast to rheumatoid arthritis (RA), PsA is a seronegative inflammatory arthropathy. Rheumatoid factor (RF) and Anti-CCP antibodies are usually absent in PsA, and if patients do have positive serological findings for RF or CCP, the titres tend to be low. (2) Seronegativity for RF has a significantly high discriminant value in the Classification Criteria for Psoriatic arthritis (CASPAR), such that a negative RF forms one of the five possible criteria; thus serological testing is often done once at the initial diagnostic appointment. (3) A previous study in the context of RA has shown that there is a tendency for

repeated serological testing with as much as 70% of patients having RF tested more than once.(4) Repeated testing amounts to additional expense and is rarely needed in PsA. The literature on the frequency of repeated serology testing in PsA patients is absent.

Objectives: To determine how often was serology for RF and anti-CCP antibodies repeated in a PsA cohort.

Methods: A cohort of consecutive patients attending the rheumatology clinic at our centre with a diagnosis of PsA were included. We reviewed the laboratory results of individual patients to determine how many times each patient had been tested for RF and anti-CCP antibodies.

Results: 118 patients with a diagnosis of PsA were included. 117 patients had RF antibody testing at least once and all 118 patients had a minimum of one anti-CCP antibody test. 59/117 (50.4%) patients had RF checked more than once and 28/117 (23.9%) had testing at least 3 times. 3 patients had an initial positive RF which was negative on subsequent testing. Anti-CCP antibody was checked on all 118 patients. 41/118 (34.7%) patients had anti-CCP checked more than once and 13/118 (11.0%) patients had testing at least 2 times. One patient had an initial equivocal anti-CCP antibody titre which was subsequently negative on repeat testing.

Conclusion: As opposed to RA, PsA has not been associated with the presence of circulating antibodies. The presence or absence of RF in PsA patients has for long been a subject of debate. (3) In cases of peripheral polyarticular PsA, which may be difficult to distinguish from RA, serological testing can be useful to identify RA. However, studies have found that RF can be present in 5-13% of PsA patients. (5) In the context of RA, serological conversion from negative to positive is infrequent and repeat testing is not recommended. (6) Over half of the patients in our PsA cohort had repeated RF testing. Certainly this is unlikely to be helpful or cost effective and serial serology measurements in PsA patients should be avoided.

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AB0966

ARE CURRENT PATIENT REPORTED OUTCOMES TOOLS OPTIMIZED TO CAPTURE THE ENTIRE PATIENT EXPERIENCE?

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Background: Psoriatic Arthritis (PsA) affects multiple attributes of patient health; to assess treatment effectiveness a compilation of Patient Reported Outcomes (PRO) have been utilized. While useful, most of these were originally created for other diseases and only later validated or adapted for use in PsA. More recent efforts have focused on development of PsA specific PRO tools, with inclusion of patient input and relevance for use in both clinical research and clinical care (1).

Objectives: To subject a broad set of currently used PROs to patient assessment, giving insight into usefulness in the clinic and informing efforts for optimization of PsA PROs.

Methods: Four focus groups were conducted across three regionally-diverse areas in the United States from March 2016 to October 2016. Patients represented a range of disease history, symptoms, and severity. After trained facilitators encouraged open conversation about PsA, including symptoms, challenges and feelings about disease and treatment, patients reviewed 13 currently utilized PROs and rated relevance of these instruments to reporting their disease experiences on a 3 point scale of Relevant, Somewhat Relevant, and Irrelevant. Verbal discussion followed on the merits and challenges of each rated PRO

Results: PRO instruments ranged from overall global assessments to disease specific assessments (Table 1). The PROs received a variety of ratings, with Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) and Psoriatic Arthritis Impact of Disease (PsAID) judged as Very Relevant by the largest number of patients, followed by Health Assessment Questionnaire-Spondyloarthropathies (HAQ-S) and Pain VAS (Figure 1). Instruments receiving the most assessments of Not Really Relevant were Pt Global and PsA Quality of Life (PsAQOL). In the qualitative portion of the research, major patient critiques across PROs were the time frames listed on the questionnaires; some were too restrictive and disallowed reporting important recent disease activity. Preferences were for questions asked as '.since your last visit..' Multiple participants also agreed that a visual tool allowing patients to circle specific joints to indicate pain would be useful.

Table 1. Outcomes Instruments Assessed in the Study

Tool	Abbreviation	Time Period Queried
Patient Global	Pt GA	None Specified
Pain Visual Analog Scale	Pain VAS	In the past week
Health Assessment Questionnaire-Spondyloarthropathies	HAQ-S	Over the past week
Short Form - 36	SF-36	Different periods queried for different questions: Compared to a year ago; None Specified; Over the past 4 weeks
Functional Assessment of Chronic Illness Therapy - Fatigue	FACIT-F	Past 7 Days
EQ-5D and EQ Visual Analog Scale	EQ-5D-5L	Today
Psoriatic Arthritis Quality of Life	PsAQOL	None specified
Psoriatic Arthritis Impact of Disease	PsAID	During the last week
Dermatology Life Quality Index	DLQI	Over the last Week
Psoriasis Symptom Inventory	PSI	Last 7 days
Work Productivity and Activity Impairment: General Health	WPAI:GH	During the past 7 days
Work Productivity Survey - PsA	WPS-PsA	Last month
Beck Depression Inventory	BDI-II	During the past 2 weeks

Conclusion: Currently utilized PROs in PsA evaluating domains of fatigue, function, pain, and disease specific manifestations were all important regarding new therapeutic agents. However, some are more relevant than others to patients, most notably FACIT-F and PsAID, the latter being an important example of a patient-led and disease-specific development effort. Allowing reporting of items of concern without restrictive time periods is important to patients. These preferences and comments can be utilized to better understand the value of PROs in clinical settings to optimize patient-clinician communications.

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Osteoarthritis

AB0967 IMPACT OF CARPAL TUNNEL SYNDROME ON SYMPTOMS AND STRUCTURAL SEVERITY OF HAND OSTEOARTHRITIS: RESULTS FROM THE DIGICOD COHORT.

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Background: Carpal tunnel syndrome (CTS) and hand osteoarthritis (HOA) are common diseases that can coexist in the same patient. Only one recent study showed that CTS was associated with a significant decrease in strength and performance of the OA-affected hand [1]. This observation suggested that CTS-induced neuropathic disorders may have effects on the surrounding joints symptomatically supporting the role of nerve-joint axis in OA pain.
Objectives: Our work aimed to study the impact of CTS on the symptoms and structural severity of HOA in the DIGICOD (DIGItal Cohort Design) cohort.
Methods: DIGICOD is a single-center prospective hospital cohort which includes 426 patients over 35 years of age with symptomatic HOA [2]. Patients in our study were those in the DIGICOD cohort at inclusion for whom the dominant hand and laterality in case of CTS involvement were known. The analysis was based on the study of the dominant hand. We compared the demographic, clinical and radiographic characteristics (notably by the sum of the Kellgren Lawrence (KL) score) between patients with CTS and those without CTS. In case of comparison test, Chi-square or Fisher exact test were performed. Then, we investigated whether CTS was associated with grips strength, pinch strength and KL score by linear regression model and with number of joints painful pressure with negative-binomial model, after adjustment for age and sex.
Results: 417 patients including 39 with CTS were included in our study. Obesity and metabolic syndrome were more frequent in patients with CTS than in those without CTS (obesity: 29.7% vs 10.2%, p<0.01; metabolic syndrome: 51.4% vs 35.1%, p<0.05). The same was true for dysthyroidism (38.5% vs 18.5%, p<0.01) and thyroid hormone replacement therapy (30.8% vs 15.4%, p<0.05). At the level of the dominant hand, clinical signs of HOA (painful, swollen, or nodal joints), sum of Kellgren Lawrence (KL) score, number of joints with a KL score ≥ 2, and the presence of erosive HOA (defined by the presence of at least 1 erosive joint defined as phase "E" or "R" in the Verbruggen scoring) were comparable between HOA patients with and without CTS. After adjustment for age and sex, the presence of CTS in the dominant hand was not statistically associated with grip strength disturbances (measured with the Jamar dynamometer), pinch strength (thumb index finger pinch), number of joints painful to pressure, and KL score.
Conclusion: The risk factors for CTS in HOA are those known in the general population (hypothyroidism, obesity and metabolic syndrome). However, our study did not find any impact of CTS on the clinical signs and structural severity of HOA.

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AB0968 ACUTE EFFECT OF A SINGLE BOUT OF BICYCLE ERGOMETRY EXERCISE ON AFFECT, MOOD AND PAIN IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS

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Background: Exercise provokes psychological responses that results in an increase in positive affect and mood, and a reduction in negative affect in patients with musculoskeletal problems including knee osteoarthritis (KOA) (Hoffman and Hoffman, 2007; Ekkekakis and Petruzzello, 1999). However, there is no consensus on the optimum duration of exercise that will bring about such positive effects among individuals with KOA.
Objectives: The objective of this study was to compare the acute effects of 10- and 15- minute bicycle ergometry exercise on affect, mood and pain in patients with KOA.
Methods: A quasi-experimental study with a follow-up arm. Forty-six participants with KOA were randomly assigned to either a 10-minute bicycle ergometer (10BE) exercise group or a 15-minute bicycle ergometer (10BE) exercise group. Participants' affect, mood and pain were assessed at baseline, pre-exercise, immediately after the exercise, 10 minutes post-exercise, and 20 minutes post-exercise using the International Positive and Negative Affect Scale, Visual Analogue Mood Scale, and Visual Analogue Scale, respectively. Descriptive statistics, Friedman's ANOVA, Mann-Whitney-U and generalised estimating equation were used to analyse the data with P-value at 0.05.
Results: Participants' (94.23% females) age ranged from 40-79 years for the two groups. The mean age for 10BE and 15BE groups was 67.09±1.85 and 66.96±2.03 years, respectively. At baseline, the median scores for positive (19.00; interquartile range (IQR=18.00-20.00 vs. 20.00; IQR=18.00-21.00) and negative (8.00; IQR=7.00-11.00 vs. 9.00; 5.00-14.00) affect, mood (6.00; IQR= 3.00-8.00 vs. 7.00; IQR=4.75-8.00) and pain (5.00; IQR=5.00-8.00 vs. 5.50; IQR=5.00-7.00) were not significantly different between10BE and 15BE. Ten minutes of aerobic exercise significantly improved PA (*P*=0.001; Effect size (Es)=0.25)) and mood (*P*=0.001; Es=0.58), and reduced NA (*P*=0.001; Es=0.44) and pain (*P*=0.001; Es=0.73) of participants across the time points of the study. A 15-minute aerobic exercise also significantly improved PA (*P*=0.001; Es=0.25), mood (*P*=0.001; Es=0.45) and reduced NA (*P*=0.001; Es=0.49) and pain (*P*=0.001; Es=0.84) of participants across the time points of the study. There was no significant difference between groups and group-time interactions regarding effect of aerobic exercise on the outcomes (p>0.05).
Conclusion: Both 10- and 15-minutes single bouts of bicycle ergometry exercise had positive effects on affect and mood in individuals with KOA. Ten and 15- minutes single bout of bicycle ergometry exercise had comparable effects on affect and mood improvements in individuals with KOA.

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AB0969 FACTORS INFLUENCING THE RESULT OF LOCAL INJECTION THERAPY WITH HYALURONIC ACID PREPARATIONS IN OSTEOARTHRITIS OF THE KNEE JOINT

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Background: Local injection therapy (LIT) with hyaluronic acid (HA) preparations is one of the methods of conservative treatment of the knee joint osteoarthritis (KOA). However, the factors affecting the effectiveness of such treatment require clarification.
Objectives: to study the influence of age, body mass index (BMI), stage of KOA, the presence of deformity of the knee joint and enthesitis on the results of LIT with HA preparations in KOA.
Methods: from September 2017 to June 2019, intra-articular injections of HA were performed in 160 patients with primary and posttraumatic KOA stage I-III. For the analysis, the patients were divided into groups depending on the factor studied: by age into young - 36 (22.5%), middle age - 51 (31.3%), elderly - 61 (38.7%) and old age - 12 (7.5%); by BMI: on patients with normal values - 32 (20%), preobesity - 56 (35%), I - 43 (26.9%), II - 16 (10%) and III - 13 (8.1%) degrees of obesity; by stages of KOA: I - 37 (23.1%), II - 91 (56.8%), III - 32 (20.1%); by the presence of deformity: varus deformity <10° - 83 (51.8%), >10° - 23 (14.4%), valgus deformity - 22 (13.8%), no deformity - 32 (20%); and also depending on the presence (44 (27.5%)) or absence (116 (72.5%)) of enthesites. To assess the results, the pain intensity was determined using a visual analogue scale and the knee injury and osteoarthritis outcome score before treatment, 1, 3, and 6 months after the course of LIT.
Results: 1 month after the course of LIT, the best results were obtained in young patients (p=0.001), as well as stage I of KOA (p=0.0001) and normal BMI values

(p=0.034), the worst in elderly patients (p=0.006), at stage III of KOA (p=0.01), varus deformity >10° (p=0.006), obesity degree 3 (p=0.015) and the presence of concomitant enthesitis (p=0.003). 3 months after the course of LIT, the previously identified differences persisted, so the best results were again revealed in young people (p=0.0001), in stage I of KOA (p=0.0001), in the absence of deformity (p=0.002) and in normal BMI values (p=0.002), while lack of improvement or deterioration in elderly patients (p=0.001), in stage III KOA (p=0.0001), varus deformity >10° (p=0.001), obesity degree 3 (p=0.022) and the presence of concomitant enthesitis (p=0.001). 6 months after the course of LIT, the improvement remained as before in young patients (p=0.0001), as well as stage I of KOA (p=0.0001), in the absence of deformity (p=0.001) and with normal BMI values (p=0.0001). Lack of improvement or deterioration of knee joint function 6 months after the course of LIT was found in the elderly (p=0.03) and old age patients (p=0.06), in stage II (p=0.045) and III of KOA (p=0.007), varus deformity >10° (p=0.015), obesity degree 2 (p=0.025) and the presence of concomitant enthesitis (p=0.02).

Conclusion: The best LIT results with HA preparations can be obtained in young patients with normal BMI values, at the initial stage of KOA, in the absence of deformity and enthesitis. The elderly age of patients, the presence of stage III KOA, varus deformity of the knee joint >10°, BMI >40 kg/m^2, and the presence of enthesitis are associated with the lack of effect from intra-articular injections of HA preparations. Performing LIT with HA preparations in patients with stage II KOA and degree 2 obesity allows maintaining improvement for up to 6 months.

Disclosure of Interests: None declared

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AB0970 WHAT IS THE EFFECT OF INTRA-ARTICULAR INJECTIONS OF GLUCOCORTICOIDS IN REAL CLINICAL PRACTICE?

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Background: Intra-articular injections of glucocorticoids (IAI GC) are widely used in the complex therapy of rheumatic diseases (RD). However, there are relatively few modern data on their efficacy and safety in real clinical practice.

Objectives: To evaluate the effectiveness of IAI HA in RD in clinical practice.

Methods: The study group consisted of 290 patients with RD, mainly osteoarthritis (OA) and rheumatoid arthritis (RA) (69.0% of women, age 55.6 ± 12.6 years), who underwent IAI GC in the knee joint. The indications for IAI were determined by the attending physicians. The control consisted of 112 patients with OA (71.4% of women, age 59.3 ± 14.6 years), who underwent a course of IAI of hyaluronic acid (HA). The result of treatment was assessed after 2 weeks, 1 and 3 months. according to a telephone survey.

Results: After 2 weeks, 1 month. and 3 months. after IAI GC, the severity of pain during movement decreased (numerical rating scale, NRS 0-10, Me [25%; 75%]) from 6.0 [4.0; 8.0] to 1.0 [0; 2.0], 2.0 [1.0; 4.0] and 2.5 [1.0; 4.0], respectively (p <0.001). After 3 months. the number of patients with no / mild pain (<4 according to the NRS) was 63.8%, with a complete / almost complete absence of pain (≤1 by the NRS) - 30.3%. The effect of HSI HA was higher in RA than in OA: the dynamics of pain after 3 months. -4.0 [-2.0; -6.0] and -2.0 [-1.0; -5.0], p = 0.003. In OA, the effect of HAI HA and HA did not differ: the dynamics of pain after 3 months. was -2.0 [-1.0; -5.0] and -3.0 [-1.0; -5.0] p = 0.869. There were no serious adverse reactions in IAI.

Conclusion: IAI GC are an effective and fairly safe method of short-term treatment of synovitis in RD.

Disclosure of Interests: None declared

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AB0971 RELATIONSHIP BETWEEN WALKING SPEED AND LOWER LIMB SKELETAL MUSCLE MASS IN PATIENTS WITH KNEE JOINT DISORDERS.

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Background: Knee joint disorder is one of the factors causing frailty in the elderly, which is associated with a decrease in walking speed.

Objectives: We measured the walking speed of patients scheduled to undergo primary total knee arthroplasty (TKA) and examined factors correlated with walking speed.

Factor	Group	
disease (n)	osteoarthritis	78 (94%)
	rheumatoid arthritis	5 (6.0%)
body mass index (kg/m^2)		25.54 (4.11)
pain VAS on walking		37.08 (26.35)
total Knee Society Score		77.66 (27.85)
range of motion (degree)	flexion	119.46 (12.88)
	extension	-9.58 (6.59)
quadriceps power (N)		122.00 [53.00, 350.00]
waling speed (m/sec)		0.95 (0.33)
grip power (kg)		20.24 (6.97)
skeletal muscle mass index (kg/m^2)	appendicular	6.50 [4.92, 9.85]
	lower limb	5.06 [3.76, 7.56]
Frailty (n)	none	10 (12.5%)
	Pre-frail	41 (51.2%)
	frail	29 (36.2%)
Sarcopenia (n)	none	76 (92.7%)
	sarcopenia	4 (4.9%)
	severe sarcopenia	2 (2.4%)

mean (standard deviation); median [min max]

Methods: The patients with knee disorders scheduled to undergo knee arthroplasty at our hospital between July 2020 and May 2021 were included. They were assessed for basic attributes, clinical assessment including Kness Society Score (KSS), degree of pain on walking by visual analogue scale (VAS), range of motion (ROM), and also leg skeletal muscle mass index (SMI; whole-body mode DXA), quadriceps strength by dynamometer with written consent (UMIN ID: 000040940). And Japanese Cardiovascular Health Study criteria for frailty, and sarcopenia by Asian Working Group for Sarcopenia 2019 criteria were evaluated.

Results: Demographic data of 83 patients (65 women, mean age 74.9 years) included in this study was shown in Table 1. The distribution in frailty is 36.2% and that in sarcopenia is 7.3%. Most of the patients with frailty with knee disorder did not suffer from sarcopenia. A multivariate analysis was conducted with walking speed as the objective variable and the dependent variables as age, gender, pain VAS on walking, KSS, leg SMI, quadriceps strength, and ROM. The results showed that age and ROM in flexion were significantly and independently associated with walking speed (P=0.01, 0.03). Gender, pain VAS on walking, KSS, leg SMI, quadriceps strength, and ROM in extension were not significantly associated with walking speed (P=0.92, 0.11, 0.11, 0.52, 0.85, 0.52).

Conclusion: Among the patients with knee disorders immediately before arthroplasty, frailty was not caused by sarcopenia. Age was found to be the most correlated factor with walking speed, and walking speed became slower with age. In addition, poor flexion angle was also the factor for delayed walking speed, but it did not correlate with lower limb skeletal muscle mass or quadriceps strength. In this study pain on walking was not significant factor for walking speed, because it was observed in most of all cases.

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AB0972 IMPACT OF OBESITY ON CLINICAL MANIFESTATIONS IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

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Objectives: To determine the influence of obesity on clinical parameters in patients with knee osteoarthritis (OA) in comparison with patients with OA with normal body weight.

Methods: Overall 72 patients with OA were studied, 28 (39.8%) male and 44 (61.1%) female; mean age was 51.3±7.5 years and the duration of disease was 11.2±5,3 years. The diagnosis of OA was made according to the ACR criteria. Anthropometric data were assessed by height, body weight, waist and hip circumference, body mass index (BMI). Clinical and instrumental studies of OA revealed monoarthrosis in 2 (2.8%), oligoarthrosis in 32 (44.4%) and polyosteoarthrosis in 38 (52.8%) patients. Visual analogue scale (VAS) in centimetres (cm) was used to assess pain, Lequesne and WOMAC indices were determined. Synovitis was documented on the basis of an ultrasound examination of the joints.

Patients were divided into 2 groups according to BMI: BMI<24.9 kg/m^2, n=22 (no obesity); BMI>30kg/m^2, with signs of grade 1-2-3 obesity, n=50.
Results: OA patients with obesity had higher WOMAC and Lequesne index values than OA patients with normal weight (5.8±1.2 cm and 13.8±1.1 points versus 1.75±0.7 cm and 2.9±0.5 points, respectively, p<0.05). WOMAC parameters in overweight patients were significantly higher than in non-obese patients (31.2±5.9 vs. 9.7±2.7, respectively, p<0.05 for the above parameters). There was a direct correlation (p<0.05) between the severity of OA and increased BMI. Radiological changes of the joints in patients without obesity were stage I (60.6%) in 14 (60.6%), stage II in 7 (34.8%) and stage III in 1 (4.5%) patient. Grade I obesity was noted in 8 (16.0%), Grade II in 22 (44.0%), Grade III in 18 (36.0%), Grade IV in 2 (4.0%) patients. Inadequate joint function (NFS) grade I was in 16 (72.7%), II in 4 (18.2%), III in 2 (19.1%) patients with normal body weight, with NFS grade II (26 - 52%) and III (18-36%) predominating with obesity, grade I in 6 (12.0%). Synovitis was diagnosed in 37 (74.0%) with elevated BMI, significantly higher than in non-obese patients in 7 (31.8%). On the course: rapid progressive OA was seen more frequently in 11 obese patients (22. 0%) than in non-obese patients (4.5%); there was a direct correlation between the VAS pain index, Lequesne index and WOMAC index (r=0.5, p<0.05; r=0.4, p<0.05; r=0.45 p<0.05 respectively).
Conclusion: Overweight in patients with OA was associated with greater joint destruction and functional impairment of the joints, progressive course and pain syndrome, including secondary synovitis.
Disclosure of Interests: None declared
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AB0973 LONG TERM EFFICACY OF INTRA-ARTICULAR VISCOSUPPLEMENTATION WITH HYALURONIC ACID IN HIP OSTEOARTHRITIS SECONDARY TO SYSTEMIC RHEUMATIC DISEASES: A PRELIMINARY EVALUATION

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Background: Few studies have assessed response to intra-articular HA viscosupplementation in patients affected by hip osteoarthirtis secondary to systemic rheumatic diseases (SOA). From in vitro studies we know that the synovial environment in these diseases presents different molecular characteristics in comparison to primary osteoarthritis (POA) in terms of pro-inflammatory activity and therefore in degradation of hyaluronic acid.
Objectives: To evaluate differences in efficacy and safety of treatment with US-guided intra-articular HA viscosupplementation between a cohort affected by POA and one affected by SOA, with regard to pain assessment and time to arthroplasty.
Methods: We conducted this observational retrospective study on consecutive patients treated with US-guided hip intra-articular injections with Hylan G-F 20 2 ml at the Rheumatology Unit of ASST-Pini-CTO (Milan, Italy) from 2013 to 2021. Joints with active synovitis detected by US examination weren't treated. VAS pain at baseline and at the end of October 2021 was registered as well as time to the event of hip arthroplasty and adverse reactions. Patients treated had hip pain at least 6 months before treatment and radiological OA assessed by standard hip X-rays no more than 6 months before baseline. Patients included in the SOA group had a diagnosis of rheumatic systemic disease, POA patients had osteoarthritis and any further rheumatological condition was ruled out. Additional clinical features recorded for the SOA patients were clinimetric assessment of disease activity according to SDAI for RA, clinical judgment for PMR, DAPSA for PsA, ASDAS for SpA and medical treatment at baseline.
Results: We included 55 primary OA patients and 16 systemic rheumatic diseases patients (5 JIA, 5 peripheral SpA, 2 PMR, 1 Axial-Spa, 1 PsA, 2 RA) who had received hip intra-articular HA injection with Hylan G-F 20 2 ml once a month for three consecutive months and then every six month. Mean duration of follow up was 51.1 (± 27.1) months. We observed significant longer treatment survival and lower VAS pain in POA patients at follow up (in absence of significant difference of VAS pain at baseline). In both cohorts we observed a reduction in VAS pain similar to that reported in literature: in the POA a mean reduction of 29.7 (95% CI 23.8-35.6), while in the SOA was noticed a mean reduction of 12.8 (95% CI 1.8-23.7) in absence of significant clinimetric variations over time. We observed higher incidence of local adverse reactions in SOA group (2 cases of post-injection synovitis in the SOA cohort only (12.5%), p 0.04).

	POA Hips (N=62)	SOA Hips (N=16)	p-value
Treatment duration, m	46.8±30.2	22.4±22.4	0.0038
HA injections, (N)	9.9±5.1	5.3±3.2	0.0011
3 or more HA injections, % (N)	85% (53)	81% (13)	0.70
Adverse reactions, % (N)	0	12.5% (2)	0.040
VAS Pain	3.25±1.73	4.3±1.4	0.029
Total Hip arthroplasty during follow up, % (N)	11.2 (7)	6.2 (1)	1.00
Time to arthroplasty, m	46.8±30.2	26	0.28

Conclusion: According to our results symptomatic hip SOA patients respond less and with a slightly higher degree of adverse reactions to intra-articular viscosupplementation when compared to POA patients, even if the incidence of these adverse events was similar to that observed in previous studies. We can infere that synovial pro-inflammatory enviroment in rheumatic systemic diseases can reduce efficacy of intra-articular viscosupplementation with hyaluronic acid.
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AB0974 ASSOCIATION BETWEEN DIABETES MELLITUS AS PART OF METABOLIC SYNDROME AND OSTEOARTHRITIS (PRELIMINARY DATA)

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Background: There are more evidence that diabetes mellitus (DM) aggravates the course of osteoarthritis (OA).
Objectives: At multicenter study to evaluate impact of DM as part of metabolic syndrome on course of knee OA.
Methods: The enrolled patients had knee OA based on ACR criteria with x-ray confirmation with stage I-III (Kellgren and Lawrence (K&L). Mean disease duration was 5 (2-10) years. Patients were evaluated by report form, using the anthropometric parameters, questionnaires, disease history and comorbidity, clinical examination data, assessment of knee joints pain, standard X-ray, ultrasound signs of OA, DXA three sites the L1-L4 lumbar spine, femoral neck, and total hip. All participants were signed an informed consent form.
Results: At prospective study were enrolled 253 women with mean age 58.3 ± 9.5 years (40-75) years, with knee OA. Compensated DM type 2 was diagnosed in 26 (10.3%) patients with knee OA. All patients with knee OA were divided into two groups:1st group was with DM and 2nd group without DM (Table 1). Patients with DM were older, had higher weight and BMI. In patients with DM was harder course of OA based on clinical and instrumental data: higher pain by WOMAC score; at X-ray were more frequent confirmed III stage (K&L) (OR=3.1, 95%CI 1.1-8.7, p= 0.01). At X-ray investigation narrow of medial joint space and at ultrasound thickness of the cartilage were also smaller at 1st group (p<0.05). Bone mineral density (BMD) in site total hip was also higher at DXA at 1st group. More often comorbidity at 1st group was hypertension (OR=3.5 (95%CI 1.2-10.6), p= 0.01), metabolic syndrome (MS) (OR=10.2 (95%CI 2.3-44), p=0.0002) and nonalcoholic steatohepatitis as part of MS (OR=33.9 (95%CI 3.22-356.8), p=0.003).

Table 1. Comparative characteristics of patients with OA with or without DM.

Parameters	1 group (n=26)	2 group (n=227)	p
Age, years, Me	65.5 (60- 68)	59 (52- 65)	0.002
BMI, кg/m2, Me	33.5 (29.4- 35.8)	28.7 (25.6- 32.3)	0.0006
OA duration, years, Me	11 (7- 18)	4 (2-10)	0.0032
Generalized OA, %	50	24.5	0.009
WOMAC pain, mm, Me	199 (158- 230)	120 (45- 190)	0.005
X-ray stage (K&L), %			
I	8.7	32.5	0.04
II	65.2	57.3	
III	26.1	10.2	
Medial knee joint space, mm, Me	2 (0.6- 3.1)	3.4 (2.2- 4.5)	0.03
Cartilage thickness in posterior-lateralis area of knee joint, mm, Me	1.5 (1.4-1.7)	1.7 (1.6- 1.9)	0.05
HbA1c, %; Me	7.2 (5.4-7.7)	5.4 (5-5.7)	0.01
Glucosae, mmol/l, Me	6.6 (5.1-6,9)	5.3 (4.9- 5.7)	0.003
Hypertension, %	84.6	60.8	0.01
Metabolic syndrome, %	92.3	54.2	0.0002
Medial knee joint space, mm, Me	2 (0.6- 3.1)	3.4 (2.2- 4.5)	0.03
Cartilage thickness in posterior-lateralis area of knee joint, mm, Me	1.5 (1.4-1.7)	1.7 (1.6- 1.9)	0.05
BMD total hip, g/cm2, Me	0.966 (0.955-1.054)	0.878 (0.801-0.944)	0,04
Number of components of MS, %			
0	0	21.1	0.0009
I	10.5	32.8	
II	47.4	36.7	
III and more	41.2	9.4	
Nonalcoholic steatohepatitis, %	18.8	0.8	0.003

In the Spearman correlation analysis are confirmed positive associations between DM and more difficult and prolonged course of OA. We found out that higher WOMAC pain subscale (r=0.18), total hip BMD at DXA (r=0.25), smaller size of medial joint space (r=-0.24) and thickness of the cartilage at ultrasound (r= -0.13) are associated with DM (p<0.05 for all parameters). Positive relationships also are indicated with BMI (r=0.21), hypertension (r=0.15), MS (r=0.24), type, such as nonalcoholic steatohepatitis (r=0.26) and number of components of MS (r=0.39).

Conclusion: The patients with OA are high frequent comorbidity with DM (10.3%). Association OA and DM lead to severe OA and higher comorbidity.

REFERENCES: None

Disclosure of Interests: None declared

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AB0975 MINIMAL CLINICALLY IMPORTANT DIFFERENCE OF TOTAL KNEE ARTROPLASTY PATIENT-REPORTED OUTCOME MEASURES

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Background: Total knee arthroplasty (TKA) is one of the commonest operations performed for end-stage osteoarthritis. Patient-reported outcome scales (PROMs) are optimal measures of the patient' aspects of their current condition and response to treatment. However, a statistically significant change does not always mean or create an effect that clinically meaningful. Clinicians can use a greater change than minimal clinically important difference (MCID) value as a meaningful change in patients with TKA [1]. Nevertheless, there are variations in MCID values in studies analyzing the same outcome measures or patient populations.

Objectives: The aim of this study is to create a global summary of literature of the MCID for PROMs for TKA.

Methods: A comprehensive literature search administered using PubMed database from their years of inception to January 2022. Original articles calculating MCID of PROMs for TKA were identified, and the full texts of these publications, as well as their bibliographies were reviewed. Keywords included "outcome scale," "TKA," and "MCID."

Results: This review examined 43 studies, in which 15 different outcome scales were administered to patients with TKA. MCIDs of the PROMs had distinct value or measurement process depending on the patients and clinical context. Distribution-based and anchor-based approaches were the most commonly used methods for calculating MCID. According to the analysis'; the WOMAC, KOOS, SF-12 and KSS were the most commonly used scales and there were so little research regarding the MCID of outcome instruments for TKA.

Conclusion: The reporting of outcomes in TKA were traditionally focused on implant survivorship and objective outcomes such as radiographic alignment, range of motion and, knee stability. However, patients and clinicans can have different perceptions of outcome, especially in the domains of subjective quality of life [2]. Therefore, it is recommended to use a combination of both objective and subjective measures to assess outcomes after TKA. In general, a wide range of MCID values was observed according to the scales. This can be due to the heterogenity in patient' clinical conditions recruited for the studies. Apart from the differences, MCIDs of the Oxford Knee Score and KOOS were lower than the WOMAC score therefore we can interpret that they are more sensitive as an outcome scale. However, the MCID values must be interpreted in light of all variables, including the participants which were administered to. Each method for determining MCID has advantages and disadvantages, and the best way to calculate an MCID is to combine the results of both methods. The MCID is not flawless in detecting a clinically significant change, as sensitivity and specificity play a role.

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AB0976 DETERMINATION AND CHARACTERIZATION OF PATIENT SUBGROUPS WITH DIFFERENT PAIN PROGRESSION IN HAND OSTEOARTHRITIS

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Background: Hand pain is common in hand osteoarthritis (OA). Previous cohort studies reported stable average pain levels on the short to midterm. Subgroups with different pain trajectories have been found in knee OA. Similar subgroups of hand OA patients may exist. Knowledge of such subgroups in hand OA patients may help inform decisions for pain treatment.

Objectives: To determine and characterize subgroups with different hand pain trajectories over four years in hand OA patients.

Methods: Data from the ongoing HOSTAS (Hand OSTeoArthritis in Secondary care) cohort were used, collected from consecutive patients at the LUMC Rheumatology outpatient clinic with primary hand OA followed for four years. Hand pain measurements were collected annually starting at baseline with the AUSCAN pain questionnaire (range 0-20). Development of pain over time was modelled using latent class growth analysis (LCGA), dividing the cohort into subgroups based on differences in pain development. The optimal model was selected based on the AIC, BIC, entropy and likelihood ratio test for models with n vs n-1 classes. LCGA requires ≥2 measurements per case, so patients with less were excluded. Associations of LCGA classes with baseline demographics and factors associated with hand pain were analyzed using multinomial logistic regression.

Results: Of 538 participants, 484 completed the AUSCAN at ≥2 timepoints. Data of excluded patients were missing at random. Included and excluded patients were comparable. Of included participants 86% were women, mean (SD) age was 60.8 (8.5), 29% had erosive disease, median (IQR) symptom

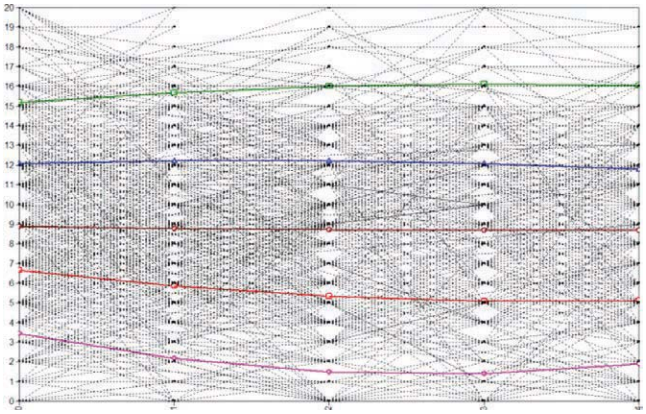

Figure 1. LCGA trajectories. *Trajectories of AUSCAN pain identified by latent class growth analysis.* Least pain to most pain, named class 1 (pink), class 2 (red), class 3 (brown), class 4 (blue) and class 5 (green).

duration was 5.2 (1.9-12.2), 91% fulfilled the ACR criteria for hand OA. Mean AUSCAN pain score was 9.3 (4.3). LCGA yielded five classes (Figure 1). Classes were characterized by different pain levels at baseline; mean level of pain remained stable over time. Classes with more pain were associated with more erosive disease, higher tender joint count, longer symptom duration, more comorbidities, worse AUSCAN function scores and worse SF-36 and HADS scores (Table 1).

Table 1. Multinomial logistic regression for associations with 5 LCGA classes

		OR (95% CI)			
Baseline	1 (N=37)	2 (N=104)	3 (N=171)	4 (N=131)	5 (N=41)
Erosive disease	1	1.20 (0.45-3.18)	1.48 (0.55-4.03)	1.23 (0.41-3.70)	1.21 (0.30-4.87)
Symptom duration, years;	1	1.05 (0.97-1.13)	1.09 (1.01-1.18)	1.13 (1.04-1.22)	1.12 (1.03-1.23)
KL sum score	1	1.01 (0.98-1.05)	1.01 (0.98-1.05)	1.02 (0.99-1.06)	1.03 (0.99-1.08)
Tender joint count	1	1.17 (0.98-1.39)	1.20 (1.00-1.44)	1.28 (1.07-1.54)	1.29 (1.06-1.57)
AUSCAN function	1	0.98 (0.90-1.08)	1.08 (0.99-1.18)	1.17 (1.06-1.30)	1.31 (1.13-1.51)
SF-36					
-PCS	1	0.95 (0.89-1.02)	0.90 (0.84-0.97)	0.84 (0.77-0.91)	0.81 (0.73-0.89)
-MCS	1	0.98 (0.90-1.06)	0.96 (0.89-1.04)	0.95 (0.87-1.03)	0.90 (0.82-0.99)
HADS					
-Depression	1	1.28 (0.91-1.82)	1.46 (1.02-2.09)	1.50 (1.04-2.16)	1.54 (1.04-2.28)
-Anxiety	1	1.09 (0.85-1.38)	1.19 (0.93-1.54)	1.19 (0.91-1.54)	1.24 (0.92-1.65)
No. Comorbidities	1	1.64 (0.77-3.47)	1.84 (0.86-3.90)	2.22 (1.01-4.88)	2.12 (0.89-5.06)

Multinomial logistic regression of variables associated with LCGA classes adjusted for baseline AUSCAN pain, age, sex and BMI. Class 1 = least pain, class 5 = most pain. SF-36 = Short Form-36. MCS = Mental component scale. PCS = Physical component scale. HADS = Hospital anxiety and depression scale. SF-36 scores are standardized on age, sex and nationality with mean 50 and SD 10.

Conclusion: Latent class growth analysis showed five subgroups with different pain trajectories in hand OA patients, with differing baseline pain and stable pain over time. These subgroups were associated with disease characteristics, number of comorbidities, psychological distress and health-related quality of life. This knowledge can help develop treatment for hand OA patients and inform them about the disease course.

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AB0977 THE RELATIONSHIP OF OVERWEIGHT AND CONCOMITANT METABOLIC DISORDERS WITH THE FEATURES OF THE COURSE OF PRIMARY OSTEOARTHRITIS OF THE KNEE JOINTS

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Background: There are two theories of the relationship between osteoarthritis (OA) and obesity: biomechanical and metabolic.
Objectives: To study the prevalence of overweight and obesity and concomitant metabolic disorders in patients with OA and to assess their impact on the features of the course of primary OA of the knee joints.
Methods: Patients with primary OA with a lesion of the knee joints (n = 90, including 22 men) were examined. The age of the patients is 29-69 years, the duration of the disease is 1.5-20 years. The control group (n = 114, including 26 men) was formed by random sampling of the population from practically healthy people, it is representative by gender and age. Anthropometric examination, determination of lipid metabolism parameters, levels of dehydroepiandrosterone sulfate (DHEA-C) and cortisol in the blood, X-ray and arthrosonographic examination of joints were performed. The functional state of the knee joints was analyzed by the Lequesne gonarthrosis severity index and the WOMAC algofunctional index.
Results: Average Body Mass Index (BMI) in patients, OA was 28.6±5.8 kg/m^2 and was slightly higher than in the control group (27.6±4.5 kg/m^2, p>0.05). Overweight and obesity were detected, respectively, in 40.7% and 33.0% of patients with OA, and in 43.0% and 28.9% of the control group. An increase in BMI in patients with OA, despite the absence of a significant difference in age and duration of the disease, is accompanied by an increase in the total values of the WOMAC index (p=0.042) and Lequesne (p=0.038). According to arthrosonography, the increase in BMI is directly related to an increase in the size of osteophytes (r=+0.43, p=0.003) and inversely correlates with the width of the articular gap of the medial knee joints (r=-0.37, p=0.014). Knee synovitis was detected in 5 patients out of 24 people (20.8%) with normal body weight, in 11 patients out of 37 people (29.7%) who are overweight, and in 13 patients out of 30 people (43.3%) who are obese of varying severity (p>0.05). Synovitis of the knee joints in most cases was detected in patients with OA with an abdominal type of fat distribution. The negative influence of the abdominal type of fat distribution on the course of knee joint OA was revealed: positive correlations between waist circumference and the total Lequesne index (r=+0.443, p=0.027), and the radiological stage of OA (r=+0.467, p=0.019). In patients with OA with abdominal type of fat distribution, the severity of joint pain during exercise was 33.3% higher than in patients with gluteofemoral type (p<0.001), the total Lequesne and WOMAC indices were 27.2% (p=0.028) and 20.1% (p=0.041), respectively. In patients with OA, a significant increase in the blood content of cholesterol (HC) of low-density lipoproteins (LDL) was found (p=0.039) and a decrease in high-density lipoprotein (HDL) cholesterol (p=0.046). Disorders of lipid metabolism of atherogenic orientation were more pronounced in patients with III-IV radiological stages of gonarthrosis. In patients with OA who are overweight or obese, the serum DHEA-C content was lower than in patients with OA with normal body weight (2.31±0.98 mcg/ml vs 2.63±1.68 mcg/ml, p>0.05). As the radiological changes in the joints progress, there is a clear decrease in the concentration of DHEA-C. In women with OA, a significant relationship was found between waist circumference and the concentration of DHEA-C in the blood (r=-0.321, p=0.045). There was an increase in the concentration of cortisol in the blood of patients with OA. The inverse correlation relationship between the number of swollen joints with the blood content of DHEA-C (r=-0.269, p=0.012) and cortisol (r=-0.232, p=0.028) was revealed.
Conclusion: The mechanisms of the negative effect of overweight and obesity on the course of OA are lipid disorders (high concentrations of LDL cholesterol, low HDL cholesterol), hormonal changes (low DHEA-C, elevated cortisol levels) and the production of proinflammatory cytokines by adipose tissue.

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AB0978 EFFECT OF ATORVASTATIN ON SKELETAL MUSCLES OF PATIENTS WITH KNEE OSTEOARTHRITIS: POST-HOC ANALYSIS OF A RANDOMISED CONTROLLED TRIAL

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Background: Statins are often discontinued due to muscle-related side effects. The effect of statin on skeletal muscles in populations with osteoarthritis is unknown.
Objectives: This study aims to examine the effect of atorvastatin on skeletal muscle biochemistry, strength, size and symptoms in patients with symptomatic knee osteoarthritis.
Methods: This is a post-hoc analysis of a multicentre randomised, double-blind, placebo-controlled trial over 2 years in which participants with knee osteoarthritis who met the American College of Rheumatology clinical criteria received atorvastatin 40mg daily (n=151) or placebo (n=153). Outcomes included levels of creatinine kinase (CK), aspartate transaminases (AST) and alanine transaminases (ALT) at baseline, 4 weeks, 6, 12 and 24 months; muscle strength measured by dynamometry at baseline, 12 and 24 months; vastus medialis cross-sectional area (CSA) on magnetic resonance imaging at baseline and 24 months; and self-reported myalgia during the trial.
Results: 304 participants [mean age 55.7 (SD 7.6) years, 55.6% female] were randomised. There were no significant differences in CK and AST levels between atorvastatin and placebo groups at 4 weeks (CK median 107 vs 110, p=0.76; AST 22 vs 21, p=0.14), 6 (CK 109 vs 101.5, p=0.37; AST 21 vs 20, p=0.45), 12 (CK 103 vs 103, p=0.93; AST 22 vs 21, p=0.99), and 24 (CK 103 vs 93.5, p=0.17; AST 22 vs 21, p=0.34) months. The atorvastatin group had higher ALT levels than the placebo group at 4 weeks [26 vs 21, p=0.0004] and 6 months [25 vs 22, p=0.007] but no between-group differences at 12 [24 vs 21, p=0.08] and 24 [24 vs 21, p=0.053] months. Muscle strength significantly increased in the atorvastatin group but not the placebo group over 24 months with no between-group differences [mean 8.5 (95% CI 2.6,14.4) vs 5.6 (-0.3,11.5), p=0.50]. Change in vastus medialis CSA over 24 months showed between-group differences favouring the atorvastatin group [+0.12 (-0.09,0.34) vs

-0.24 (-0.48,0.01), p=0.03] but of uncertain clinical significance. There was a trend for more myalgia in the atorvastatin group over 2 years (8/151 vs 2/153, p=0.06), mostly occurring within 6 months (7/151 vs 1/153, p=0.04). Of the 10 participants with myalgia, there was no relationship between the incidence of myalgia and CK levels.
Conclusion: In those with symptomatic knee osteoarthritis, despite a trend for more myalgia, there was no clear evidence of an adverse effect of atorvastatin on skeletal muscles, including those most relevant to knee joint health.
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AB0979 RECOMMENDATIONS FOR WEIGHT MANAGEMENT IN OSTEOARTHRITIS: A SYSTEMATIC REVIEW OF CLINICAL PRACTICE GUIDELINES

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Background: Weight loss interventions are often recommended to target overweight and obesity in the clinical practice guidelines (CPGs) for the management of osteoarthritis. This is despite evidence from meta-analyses of clinical trials that significant weight loss results in modest improvements in symptoms and minimal effects on disease progression[1,2]. There is evidence that weight gain is associated with increase in knee pain[3,4]. In countries such as USA, adults gain on average 0.5 to 1 kilogram per year from early to middle adulthood Preventing weight gain is easier to achieve and sustain than losing weight.
Objectives: Given that weight loss is accepted as fundamental to osteoarthritis management, we systematically reviewed the recommendations and approaches for weight management in all current osteoarthritis CPGs.
Methods: Nine databases were searched (1st January 2010 to 30th September 2021) to identify guidelines informing the non-pharmacological management of osteoarthritis. Three reviewers appraised guidelines according to the AGREE II instrument, and independently extracted data on their characteristics. One author extracted and summarised guideline recommendations on weight management. This systematic review is registered on PROSPERO (CRD42021274195).
Results: Fifteen CPGs from developed and developing countries were included. Weight loss was recommended for knee (12 of 13 guidelines) and hip (10 of 11 guidelines) but not hand osteoarthritis (0 of 4 guidelines). Combination approaches of diet and/or exercise were recommended for overweight or obese individuals (knee: 8 of 12; hip: 4 of 10), with 2 guidelines specifying ≥5% weight loss for knee and hip osteoarthritis. One of 15 guidelines specified strategies for weight loss and maintenance of lost weight. Two of 15 guidelines recommended controlling body weight for osteoarthritis, regardless of obesity status.
Conclusion: Most CPGs for knee and hip osteoarthritis include recommendations for weight loss in those with overweight or obesity as key to managing osteoarthritis, despite evidence of modest at best effect of weight loss on symptoms and no effect on joint structure[1,2]. Given obesity is a major risk factors for osteoarthritis, the prevention of weight gain may be more effective and practical in improving clinical outcomes for osteoarthritis, and hence should be considered as part of the key management in osteoarthritis.
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AB0980 HAND OSTEOARTHRITIS: INVESTIGATING PAIN EFFECTS IN A RANDOMISED PLACEBO-CONTROLLED FEASIBILITY STUDY OF ESTROGEN-CONTAINING THERAPY (HOPE-E): REPORT ON THE PRIMARY FEASIBILITY OUTCOMES

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Background: There is an unmet need for new treatments for hand osteoarthritis (OA). Symptomatic hand OA is more common in women and its incidence increases round the age of menopause. Pre-clinical, epidemiological and post hoc studies in Hormone Replacement Therapy (HRT) trials implicate estrogen deficiency as of likely importance in OA aetiopathogenesis. No clinical trials of HRT have been carried out in hand OA to date. The licensed HRT Duavive (conjugated estrogens + SERM bazedoxifene) was selected on its potential for efficacy and tolerability.
Objectives: We set out to determine the feasibility and acceptability of this form of HRT in post-menopausal women with hand OA, to generate proof of concept data and refine methods for a full study.
Methods: ISRCTN12196200. Females aged 40-65 yrs and 1-10yrs after final menstrual period with hand OA fulfilling ACR criteria and 2+ painful hand joints were recruited. Eligibility incorporated best practice for HRT prescription but did not require menopausal symptoms. Recruitment was at 3 sites in primary/secondary care, including directly from the community. Design was parallel group, double-blind 1:1 randomisation of Duavive or placebo, orally once daily for 24 weeks, then weaning for 4 weeks before stopping. Routes and rates of recruitment and the acceptability of randomisation, medication (compliance, retention), and proposed outcomes were measured, and the likelihood of unblinding. Measures related to hand pain and function, menopause symptoms and joint appearance. Patient and Public Involvement actively informed study rationale, design and materials. An end of study questionnaire and 2 participant focus groups provided further acceptability data.
Results: Recruitment was for 12/possible 18 months, interrupted due to COVID-19. Some study procedures were modified to allow reopening whilst collecting all primary outcomes. 434 enquiries/referrals were received, leading to 96 telephone pre-screens, of which 33 gave written informed consent and attended face to face screening. 28/33 screened (85%) were eligible and randomised. The highest number of randomisations was from study web presence (n=7) followed by SMS text from GP surgeries (n=5). Of 401 not proceeding, 250 (62%) were ineligible, most commonly due to contraindicated medication, followed by medical contraindication, whilst 55 (14%) decided not to take part, for reasons including not wanting to take a hormone-based drug or difficulty attending study visits. Retention and compliance were excellent. All 28 participants completed all study follow ups, with only 3 withdrawals from treatment due to AEs, 2 of these at week 24 and all in the placebo arm. There were no serious AEs. High levels of completeness of all study outcome measures were achieved. Bang's blinding index suggested that participants/investigators were well blinded. There were overall high/good levels of satisfaction with taking part in the study. 26/28 (92%) would recommend taking part to others with hand OA (irrespective of study arm). Many found the flexibility

offered by a combination of remote and face to face visits (due to the pandemic) attractive. Additional insights from focus groups were to include hand stiffness as well as pain measures but to reduce the overall number of questions.
Conclusion: Despite COVID-19 and a reduced recruitment period, this study recruited sufficient numbers to assess feasibility outcomes. Randomisation of eligible people and retention rates were high. A mixture of remote and face to face visits due to COVID-19 probably improved recruitment and retention and was supported by participants, who were generally satisfied with the study design and medication. The study provided useful insight and improvements that would be incorporated into a future study. Overall, this feasibility study showed that with clear messaging on eligibility and a defined recruitment strategy, recruitment and retention to a study testing this treatment is possible.
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AB0981 DYNAMICS OF PAIN ACCORDING TO THE VAS SCALE, FUNCTIONAL ACTIVITY ACCORDING TO THE WOMAC INDEX AND QUALITY OF LIFE ACCORDING TO THE EQ-5D QUESTIONNAIRE IN ELDERLY AND SENILE PATIENTS WITH KNEE JOINT OSTEOARTHRITIS AFTER COVID-19

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Objectives: To evaluate the dynamics of pain on the VAS scale, functional activity according to the WOMAC index and quality of life according to the EQ-5D questionnaire in elderly and senile patients with knee joint osteoarthritis (OA) after COVID-19.
Methods: A total of 32 elderly and senile male patients with an established diagnosis of knee joint OA (according to the criteria of ACR, 1986) of stage II–III according to Kellgren–Lawrence, with pain ≥40 mm on a visual analog scale (VAS), who needed to take nonsteroidal anti-inflammatory drugs (NSAIDs), were included in the study. The median age of the patients included in this study was 72.6 (66.0; 79.3) years. All patients have been ill with COVID-19 for the last 6 months. Pain dynamics was assessed on the VAS scale, functional activity - on the WOMAC index, quality of life - on the EQ-5D questionnaire.
Results: When analyzing the clinical picture, it was found that the majority of patients - 22 people (68.8%) - had moderate COVID–19, 4 people (12.5%) – in mild form, 6 patients (18.7%) - in severe. The average duration of hospitalization was 14.0 (9.0; 17.0) days. The majority of patients were discharged with recovery - 30 people (93.75%), 2 people died (6.25%). The most frequent manifestations of postcovid syndrome in elderly and senile patients with OA: weakness – in 18 (56.2%) patients, arthralgia – in 17 (53.1%) and memory loss – in 14 (43.8%). There was a significant increase in the pain index on the VAS scale and the total WOMAC index after COVID-19. Pain on the VAS scale before COVID-19 was 45.9 (34.8; 72.4), after the disease - 60.9 (51.4; 68.5) ($p<0.001$); the total WOMAC index was 46.3 (38.5; 51.2) and 63.1 (48.9; 76.2), respectively ($p=0.007$). There were no differences in the need for NSAIDs before and after the disease. When filling out the EQ-5D questionnaire, all the interviewed patients indicated health problems to one degree or another. When calculating the quantitative index after COVID-19, there was a deterioration in the health index, but the changes were unreliable. The "health thermometer" also changed in a similar way.
Conclusion: COVID-19 in elderly and senile patients with OA occurred in a variant of moderate severity in 22 (68.8%), severe - in 6 (18.7%), mild - in 4 (12.5%). The most frequent manifestations of postcovid syndrome in elderly and senile patients with OA: weakness, arthralgia and memory loss. Negative dynamics of indicators of functional activity according to the WOMAC index and pain on the scale VAS after COVID-19 was registered.
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AB0982 RISK OF OSTEOPORTIC FRACTURES IN POST-MENOPAUSE WOMEN WITH KNEE OSTEOARTHRITIS

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Background: Osteoporosis is an interdisciplinary problem, the medical and social significance of which is determined by its consequences: fractures of the vertebrae and bones of the peripheral skeleton.
Objectives: To estimate the 10-year probability of developing osteoporotic fractures in postmenopausal women with knee osteoarthritis (OA).
Methods: The study included 36 postmenopausal women (mean age 65.7±1.01 years). The main group consisted of 21 women with knee OA, the control group consisted of 15 women without OA. Bone mineral density (BMD) (g/cm2) and T-score (standard deviation, SD) of the femoral neck and lumbar spine (LI-LIV) were assessed by dual-energy X-ray absorptiometry (DXA) (Lunar Prodigy Primo, USA). The 10-year probability of developing major osteoporotic fractures (clinically significant vertebral fracture, distal forearm fracture, proximal femur fracture or shoulder fracture) and proximal femoral fracture was calculated using the FRAX calculator.
Results: Osteopenic syndrome in the study cohort was detected in 33 (91.7%) patients, including osteopenia in 18 (50.0%) women and osteoporosis in 15 (41.7%) women. Normal BMD was registered in 3 (8.3%) patients. In patients with knee OA osteopenic syndrome was registered in 19 (90.5%) patients: osteopenia - in 11 (52.4%), osteoporosis - in 8 (38.1%). In the control group, osteopenic syndrome was diagnosed in 13 (86.6%) people: osteopenia - in 6 (40.0%), osteoporosis - in 7 (46.7%). Normal BMD in both studied groups was determined only in 2 women (9.5% and 13.3%, respectively). There were no statistically significant differences in the structure of osteopenic syndrome among the studied groups ($p=0.961$). When analyzing the 10-year probability of developing major osteoporotic fractures, it was found that in women with OA of the knee, this probability was 12.4±0.91, in the control group it was 15.2±1.06 ($p=0.085$). The 10-year probability of a fracture of the proximal femur in women with knee OA was statistically significantly less than in the control group: 1.53(0.70;1.98) and 2.11(1.20;2.95), ($p =0.031$) respectively.
Conclusion: The overall incidence of osteopenic syndrome in the study cohort was 91.7%, with no statistically significant differences between the groups. The probability of developing a fracture of the proximal femur in women with knee OA was statistically significantly less than in the control group, while the risk of a 10-year fracture of the main localizations was comparable in the study groups.
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AB0983 RESULTS OF A PROSPECTIVE 6-YEAR OBSERVATIONAL STUDY OF THE EFFICACY AND SAFETY OF A BIOACTIVE CONCENTRATE OF SMALL MARINE FISH IN SENILE PATIENTS WITH KNEE OSTEOARTHRITIS AND MULTIMORBIDITY

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Background: According to the updated ESCEO, 2019 guidelines for the management of the knee osteoarthritis (OA), SYSADOA, which includes bioactive concentrate small sea fish (BCSSF), is a mandatory component of OA therapy. There are few studies evaluating the efficacy and safety of BCSSF in elderly patients with knee OA and a high level of multimorbidity, which served as the basis for this work.
Objectives: To evaluate the efficacy and safety of BCSSF therapy in elderly patients (75–90 years old) with knee osteoarthritis (OA) and multimorbidity based on the results of a prospective 6-year follow-up.
Methods: The study included 38 elderly women with OA of the knee (according to the criteria of ACR, 1986) stage II-III according to Kellgren-Lawrence, with pain ≥40 mm on the visual analog scale (VAS), who needed non-steroidal anti-inflammatory drugs (NSAIDs). BCSSF was administered as 1 ml intramuscular injections 20 consecutive days with a 6-month interval (12 courses). The impact of comorbidity on long-term prognosis was assessed using the Charlson comorbidity index. The effectiveness of therapy was assessed by VAS and WOMAC index. All patients during V0, V4 (36 months), V5 (72 months) underwent radiography of the knee joint. The safety of therapy was monitored throughout the observation period. The duration of the study was 6 years, the number of visits (V) - 6: V0 - day 1 (inclusion in the study and initiation of therapy); V1 - 21st day of therapy, V2, V3, V4, V5 - 12, 24, 36 and 72 months after the start of treatment, respectively.
Results: The 29 (76.3%) patients completed the full course of BCSSF treatment. 9 (23.7%) patients withdrew from the study due to the inability to visit the treatment site (for reasons not related to the study). Elderly patients with OA of the knee showed a

high level of multimorbidity - an average of 5 comorbidities. The prognosis of 10-year mortality according to the Charlson index was 1–2 points (26%) in 2 (5.3%) patients, 3–4 points (52%) in 26 (68.4%) patients, ≥5 points (85 %) - in 10 (26.3%) respectively. There was a significant decrease in pain according to VAS (≥20%): by V1 - in 76.3%, by V2 - in 71.0%, by V3 - in 68.4%, by V4 - in 63.1% and V5 - in 55.2% of patients. There was a significant decrease in the total WOMAC index at all visits compared with baseline: V0 - 1125±135.0 mm, V1 - 647±229.0 mm, V2 - 642±224.0 mm, V3 - 594±216.0 mm, VB4 - 609±183.0 mm, V5 - 669±141.0 mm ($p \leq 0.001$ for all cases). The reduction in OA symptoms resulted in a significant reduction in the need for NSAIDs. By V1, 31.6% of patients refused to take NSAIDs, by V2 - 47.4%, by V3 - 44.7%, by V4 - 50.0% and by V5 - 44.7%. After 12 months of therapy, the number of days of taking NSAIDs significantly decreased to 5 (0; 10) days per month versus 14 (7; 15) days per month at the beginning of the study ($p = 0.005$). This rate remained relatively stable throughout the follow-up. X-ray progression of OA ≥1 stage according to Kellgren-Lawrence during BCSSF therapy after 36 months was recorded in 10.5% of patients, after 72 months - in 50.0%. During the entire period of observation, no serious adverse events were registered, including new cardiovascular accidents and allergic reactions.

Conclusion: The results of a 6-year prospective study demonstrate the high efficacy and safety of BCSSF in elderly patients with knee OA and high multimorbidity.

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AB0984 CHANGES IN PLASMA VOLUME WHEN MEASURING BIOCHEMICAL MARKERS OF JOINT TISSUE TURNOVER IN RELATION TO ACUTE PHYSICAL ACTIVITY

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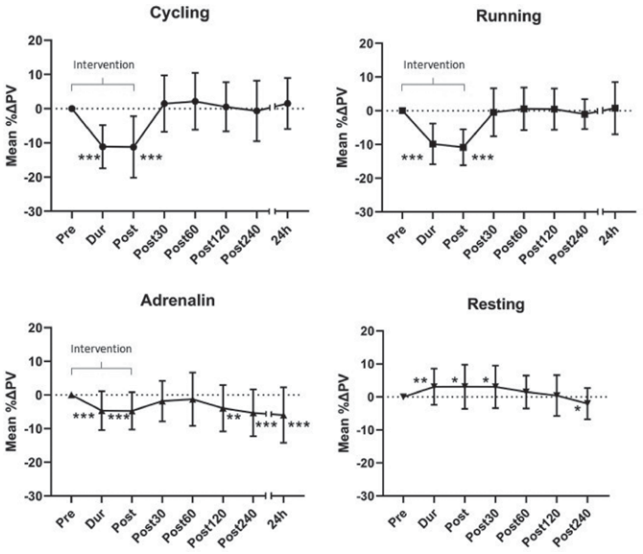
Background: Physical activity can induce acute changes in plasma volume (PV) and thereby influence concentration of plasma constituents, such as biochemical markers[1,2]. However, it remains undocumented to what extent PV changes occur during physical exercise in osteoarthritis (OA) patients.

Objectives: Investigating the direct course and magnitude of PV changes during and after weight-bearing (WB) and non-weight-bearing (NWB) exercise, adrenaline-induced cardiovascular stress and resting in an OA population.

Methods: Data originates from the EFEX-OA-02 study (Reg. no.: NCT04542668), which explored biomarker changes in knee OA patients during and after running, cycling, adrenaline infusion and resting on separate days. Blood samples were obtained before, during, at five time points after and again 24 hours post exercise/infusion. Hemoglobin (Hgb) and derived hematocrit (Hct) were measured at all time-points to monitor PV fluctuations. Main inclusion criteria: Cumulative Kellgren-Lawrence (KL) radiographic grade of the left and right knee of ≥ 2, 40-75 years of age, bodyweight 50-100 kg and BMI 18.5-35.0 kg/m^2. Active interventions consisted of 4x5-minute intervals each progressing from low intensity and peaking at ≥80% of the heart rate reserve (HRR). For the adrenaline infusion, 0.06 mg/kg of adrenalin was prepared in 50 mL saline and administered intravenously. At rest, blood samples were collected at time points similar to the other study interventions, however the 24-hour follow-up sample was omitted. Hgb was measured on a ABL800 FLEX blood gas analyzer and converted to Hct using the formula: Hct (%) = (0.0485 × ctHb (mmol/L) + 0.0083) × 100. Estimated PV change (% ΔPV) was calculated as: % $\Delta PV = [100 / (100 - Hct_{pre})] \times [100 (Hct_{pre} - Hct_{post}) / Hct_{post}]$, where: ΔPV % = Percentage change in PV: Hct_{pre} = Hct before exercise, Hct_{post} = Hct after exercise. A repeated measures linear mixed-model and 1-way ANOVA was used to assess PV changes and compare interventions, respectively.

Results: Forty subjects were included. Mean age was 60.4 years (Standard deviation (SD): 8.7), 16 (40%) were male, mean BMI was 27.0 kg/m^2 (SD: 3.5), and mean score in the nine item pain domain of the Knee Injury and Osteoarthritis Outcome Score (KOOS) at baseline was 67.5 (SD: 15.2) out of 100 (0 and 100 corresponding to max pain and no pain, respectively). Baseline Hgb was 9.05 mmol/L (SD: 0.68) and Hct was 44.7% (SD: 2.9%). All subjects were able to reach the defined peak cardiovascular intensity or higher during exercise, while reaching on average 70% (SD: 8.7%) of that during the adrenaline infusion.

Cycling, running and adrenaline infusion led to acute reductions in PV compared to rest: Cycling -14.3% (95%CI: -10.0 to -18.7%), running -13.9% (95%CI: -10.9 to -17.0%), adrenaline -7.8% (95%CI: -4.2 to -11.5%). The reductions in PV induced by both cycling and running were greater compared to adrenaline ($p<0.001$). There was no difference in PV changes after cycling vs. running ($p=0.99$). Thirty minutes after both modes of exercise, PV had returned to baseline. After completion of the adrenaline infusion, PV returned to baseline at 30-60 minutes, but was lower than baseline levels at 120 minutes by -3.9% (95%CI: -0.7 to -7.1%), at 240 minutes by -5.3% (95%CI: -2.1 to -8.6%), and at 24-hour by -5.9% (-2.0 to -9.9%). During seated rest, PV initially increased (3.1%, 95%CI: 0.7-5.4%) (Figure 1).



Conclusion: Moderate-high intensity running, cycling and cardiovascular stress led to rapid reductions in PV of knee OA patients. Adjustment for PV changes should be considered when measuring biochemical markers in relation to physical activity.

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AB0985 PREDICTIVE VALUE OF ULTRASOUND IN HAND OSTEOARTHRITIS

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Background: Hand osteoarthritis (HOA) is a complex degenerative pathology with sometimes noisy joint manifestations that can mimic inflammatory rheumatism. The osteoarticular ultrasound, is a valuable addition to the clinical examination, remains little used for diagnosis and monitoring HOA.

Objectives: The objective of our study is to analyze the ultrasound characteristics of arthritic hands OA in order to know the lesions and to better correlate the clinical data with the sonographic results.

Methods: We performed an ultrasound study of 38 patients (76 osteoarthritis hands) suffering from finger osteoarthritis meeting the ACR criteria. SPSS.20 Software was performed to data analysis

Results: There were 38 patients: 84% women and 16% men, mean age was 61 years. 47.36% had had a manual profession, 39.47% had associated osteoporosis, 66% had reported the presence of finger nodules in the mother in family history. 60.52% of patients presented with Heberden's nodules, 34.21% with Bouchard nodules, 63.15%an adductus inch and 13.15% an inch in "M" deformation. Impairment of Metacarpo-phalangeal (MP), Proximal inter-phalangeal (PIP), Distal Inter-phalangeal (DIP) and Trapeziometacarpal (TM) were found respectively: clinically in 24%, 58%, 87% and 76% of cases, and in 8%, 37%, 74% and 92% after ultrasound examination. The impairment was more severe from side of the dominant hand in 39.47% of cases clinically vs 52.63% after an ultrasound analysis. Regarding "erosive" HOA, 36.84% of patients presented at least one clinical and / or sonographic criterion suggesting an erosive form. 7.89% of patients had rigidity, 13.15% erythema, 34.21% swelling and 60.52% paresthesia. According to ultrasound, 28.94% showed an erosion / reconstruction aspect. 26.31% of the patients had presented an effusion of the PIP, 47.36% an effusion of the DIP, grade 1 Doppler signal was found in 15.78% with a strong clinical correlation and positive ultrasound signs in 65,78% of cases, no synovitis was reported.

Conclusion: Hand osteoarthritis is a very heterogeneous disease, the added value of ultrasound appears to be of interest in the diagnosis and monitoring patients with this pathology.

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AB0986 RISK OF SARCOPENIA IN THE WOMEN WITH OSTEOARTHRITIS

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Background: Recently, physicians all over the world have been focusing on the relationship between sarcopenia and osteoarthritis (OA) [1, 2]. This connection is considered from different positions: as coexisting conditions, sarcopenia as a risk factor for the progression of OA, or OA as a risk factor for sarcopenia.

Objectives: The aim of this study was to determine the risk of sarcopenia (according to the SARC-F Questionnaire) and the level of probable sarcopenia in Ukrainian women with (hip and knee) OA.

Methods: The study included 271 women aged 50-84 years old (mean age 65.6 ±8.0 years, mean height 162.2±5.6, mean body weight 76.7±14.2, mean BMI 29.1±5.1). All subjects were divided into 2 groups: the group of healthy women (group I, n=176), a group of patients with hip or knee osteoarthritis (OA) (group II, n=95). The risk of sarcopenia was determined by the SARC-F Questionnaire. The probable sarcopenia was determined due to muscles strength (handgrip strength using spring hand dynamometer ≤ 16(kg)) and physical performance (5-time chair stand test > 15 s), the fall risk – by Desmond Fall Risk Questionnaires and function – according to the assessment of IADL scale.

Results: In 20.3% of females without musculoskeletal pathology and in 34.7% of women with OA was detected high risk of sarcopenia. The probable sarcopenia was practically 2 times higher in patients with OA and was equal to 42.1% compared to 21.5% in healthy women. According to the Desmond Fall Risk Questionnaire, 27.5% of healthy subjects and 49.3% with OA had increased fall risk. Low function (according to the assessment of the IADL scale) was detected in 36.4% of females without pathology of the musculoskeletal system and in 57.2% of women with OA.

Conclusion: Our results demonstrated that the incidence of probable sarcopenia was 2 times higher in women with hip and knee OA, as well as the risk of sarcopenia – 34.7%, compared to healthy subjects – 20.3%. Also, the risk of falls and the need for outside help were higher in patients with hip and knee OA but their function (by IADL scale) was significantly lower.

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AB0987 KNEE RESERVE: ULTRASONOGRAPHIC FEATURES OF KNEES IN PATIENTS WITH ASYMPTOMATIC KNEE OSTEOARTHRITIS

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Background: Symptoms of knee osteoarthritis (KOA) vary according to many factors mainly degree of KOA and degree of inflammatory features.The primary goal of treatment the patients with KOA is to maximize long-term health-related quality of life through control of symptoms. Understanding ultrasonographic characteristics of KOA in asymptomatic patients may help in management of knee osteoarthritis. Zagazig scale is a new validated and feasible tool for KOA assessment.

Objectives: To understand the ultrasonographic features of thepatients with asymptomatic knee osteoarthritis

Methods: Among 245 patients with knee OA diagnosed according to ACR criteria and recruited in a previous ultrasonographic study (1), data of patients with no or mild pain (VAS ≤ 2) was recorded and studied in a separate section. All patients were subjected to clinical assessment WOMAC scaleWestern Ontario and McMaster Universities Index of Osteoarthritis), global visual analogue scaleVAS, and functional assessment through the use of health assessment questionnaire-II (HAQ-II). Ultrasonographic assessment was conducted following ZAGAZIG scale comprising five domains: (1) Severity ofknee OA 6 grades (0-5) according to severity scale published by Mortadaet al 2016, (2) Effusion: 4 grades (0-3) no, mild moderate and severeeffusion respectively, (3) synovitis: 4 grades (0-3) using the combinedEULAR/OMERACT score of grey scale synovitis and Doppler activity, (4) Pes Anserine tendonitis /bursitis: 3 grades (0-2) normal, mild inflammation and severe inflammation (5) Baker cyst: 3 grades (0-2),grade0: normal no cyst, grade 1:small and simple cyst and grade 2: largeand/or complicated cyst. Each grade in all domains take one point in thescore with the total sore of all domains ranged from 0 to 15.

Results: At cut-off point of >5, total US score distinguishes between knee osteoarthritis patients with no or mild pain87.2% sensitivity and 87.2% specificity.

Table 1. Demonstrate demographic and ultrasonographic features of patients with KOA andVAS ≤ 2.

Variables	
Age	(47.9±7.1)
	33-58
Sex	
Females	32(71.2%)
Males	13(28.8%)
VAS (mean±SD)	(1.7±0.5)
HAQ-II	2(1.7±1.1)
median(mean±SD)	
WOMAC pain subscale	
median(mean±SD)	1(0.62±1.1)
WOMAC stiffness subscale	
median(mean±SD)	0(0.31±0.75)
WOMAC function subscale	
median(mean±SD)	3(4.9±2.1)
WOMAC Total scale	
median(mean±SD)	4(5.9±3.9)
Osteophyte grades:	
1	10(45.5%)
2	4(18.2%)
3	3(13.6%)
4	5(22.7%)
5	0(0.0%)
Effusion	
0	11(50.0%)
1	10(45.5%)
2	1(4.5%)
Synovitis	
0	15(68.2%)
1	6(27.3%)
2	1(4.5%)
Baker cyst	
0	22(100%)
1	0(0%)
PesAnseinebursits	
0	20(90.9%)
1	2(9.1%)
Total score	
median(mean±SD)	3(3.9±2.4)

22 patients had no to mild pain according to Universal pain assessment, may have different combinations of wide range of degenerative changes (severity score (0-5) and inflammatory changes [effusion (0-3), synovitis (0-3), Pes Anserine (0-2) andBaker cyst (0-2)]but the total score of Zagazig scale ranged from 1 to 4. This may refer that patients can accommodate any combinations of degenerative and inflammatory changes with total score less than 5 on Zagazig scale with no or mild pain. Score less than 5 on Zagazig scale may consider as knee reserve in KOA.

Conclusion: The present study confirm that patients with KOA and asymptomatic or with mild pain may have awide range of degenerative changes and inflammatory changes. Score of less than 5on Zagazig scale are associated with no or mild pain. Score less than 5 may be considered as a marker of knee reserve in KOA.

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AB0988 FREQUENCY OF OSTEOPENIC SYNDROME AND LOW-ENERGY FRACTURES IN POSTMENOPAUSAL WOMEN WITH OSTEOARTHRITIS OF THE KNEE JOINT

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Background: The impact of knee osteoarthritis on the risk of low-energy fractures remains an open question in recent times. Some cohort studies show that OA of the knee joint is associated with increased risk of fractures [1-3]. Other studies do not support this link [4-5].
Objectives: to compare the incidence of osteopenic syndrome and low-energy fractures in postmenopausal women with osteoarthritis (OA) of the knee joint.
Methods: The study includes 98 women, of whom: 51 (median age 63.0 [59.3;69.8] years) are diagnosed with OA of the knee joint according to the ACR criteria (1991) and 47 without OA of the knee joint (median age 65.0[61.8;71.0] years). The bone mineral density (BMD) (g/cm2) and the T-criterion (standard deviation, CO) of the femur neck and lumbar spine (LI-LIV) were evaluated by the two-energy X-ray absorption (DXA) method (Lunar Prodigy Primo, USA). The DXA data of the femoral neck and the lumbar spine were interpreted using the following reference intervals: normal BMD - T-criterion -1 CO, osteopenia - T-criterion from -1 or less CO. Low-energy fractures were considered to have occurred with minimal trauma (falling from a height of own height to the same surface or an even smaller injury) and were found in the anamnesis.
Results: In the group of patients with OA of the knee joint, normal BMD was found to be statistically significantly more frequent than the control group (15.7% vs. 4.3%) p=0.033. It is shown that in women with OA of the knee joint, low-energy fractures were statistically less recorded than in the control group: in 29.4% and 51.0% of women respectively (p=0.002). The chances of having low-energy fractures in the group of patients with OA of the knee joint were statistically lower by a factor of 2.64 compared to the control group (OR = 0.378; 95%CI: 0.203 - 0.703).
Conclusion: The low frequency of low-energy fractures and the lower the chances of them in women with OA of the knee joint compared to the control group are probably associated with lower prevalence of the osteopenic syndrome among these patients.
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AB0989 PLANTAR FASCIITIS IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis (OA) is a highly prevalent disease, it shares with plantar fasciitis similar risk factors including aging, occupation, obesity, and inappropriate shoe wear. The association between knee OA and heel pain caused by plantar fasciitis has received limited attention to date.
Objectives: The aim of our study was to detect plantar fasciitis using ultrasound in patients with confirmed knee OA.
Methods: We conducted a cross-sectional study including 30 patients with symptomatic knee OA. Health status was evaluated using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index. The functional impairment of knee OA was determined by the Lequesne index. Ultrasound evaluation of heels was performed in all patients searching signs of plantar fasciitis (measure thickness, echogenicity, enthesopathy, calcification, erosion, doppler).
Results: The study included 30 patients. Mean age was 62.09 +/- 6.7 years. Patients reported lower back pain and heel pain in 67% (n=20) and 47% (n=14) respectively. Knee symptoms were evaluated by the WOMAC index: mean score for pain, stiffness, and physical function was 9.68 +/- 4.25, 4,18 +/- 7.55 and 27.27 +/- 16.39, respectively. Mean Lequesne index for the knee OA was 11,4 +/- 4,57. Physical examination revealed limited range of motion in knees in 33 % (n=10) with a genu flexum in two patients. Patella tap was positive in 20 % (n=6). Heel ultrasound revealed thickening of the plantar fascia in 50% (n=15). Other sonographic abnormalities found were loss of fibrillar structure in 26.7% (n=8), perifascial collections in 13.3% (n=4), calcifications in 16.7 % (n=5) and erosions in 33.3% (n=10). No correlation was found between health status attested by WOMAC index and the presence of plantar fasciitis.
Conclusion: Our study showed that half of our knee OA patients have plantar fasciitis confirmed with ultrasound. More studies with larger cohorts are needed to explain the correlation between the two lesions.
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AB0990 CORRELATION OF CLINICAL PARAMETERS WITH URINARY COLLAGEN TYPE II C-TELOPEPTIDE AND KNEE CARTILAGE THICKNESS MEASURED WITH ULTRASOUND IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Although knee osteoarthritis (KOA) incidence is one of the highest among chronic diseases, no effective biomarkers are known for its management [1].
Objectives: To estimate the relationship between the sensitive marker of matrix metalloproteinase-dependent cartilage degradation - urinary collagen type II C-telopeptide (uCTX-II) levels, patient-reported outcomes (PRO), and knee cartilage thickness measured with ultrasound (US) in patients (pts) with KOA.
Methods: WOMAC questionnaire and Leken`s functional index, VAS pain by pts, knee joints US, uCTX-II levels (ng/ml; ELISA) were evaluated in 46 pts (71.7% female) with KOA, who haven`t received any medical treatment except paracetamol or NSAIDs the last 12 weeks. The mean age was 62.6±6.2, mean disease duration – 10.2±6.3 years; 63% and 27% of pts had Kellgren-Lawrence grade II and III, respectively. The knee cartilage thickness (mm) in three compartments (medial, middle, lateral) of the patellofemoral region was evaluated using a linear L50 sensor in standard sensor positions, frequency 5–12 MHz. Calculation of average thickness for each knee joint and both joints was performed. The Spearman correlation coefficient was utilized to detect the association of uCTX-II, PROs and knee cartilage thickness.
Results: The mean values (M±σ) of WOMAC and Leken`s indices were 39±13,65 and 12±4,18, respectively. The mean value of VAS pain by pts was 57.7±16.5. The mean concentration of uCTX-II was 0.18±0.12. The means of cartilage thickness were: 1.7±0.33 for the right, 1.7±0.36 for the left, and 1.7±0.31 for both knee joints. The mean value of both knee joints cartilage thickness had significant negative moderate correlation with Leken`s index (r=-0.354, p<0.01). Leken`s and WOMAC indices significantly correlated with each other (r=0.354, p<0.01). According to VAS following tertile groups were detected: 1 group: means interval less than 50 mm; 2 group: means interval 50-64 mm; 3 group: more than 64 mm. There were negative moderate correlations between cartilage thickness of the left knee joint and Leken`s index (r=-0.513, p=0.03) and WOMAC (r=-0.535, p=0.024) only in group 1. Also, pts were divided into three groups according to disease duration: 1 group: means interval less than 7 years; 2 group: means interval 7-10 years; 3 group: more than 10 years. There were negative correlations between uCTX-II and medial, middle compartments of left knee cartilage thickness (r=-0.474, p=0.03; r=-0.592, p<0.01, respectively). WOMAC negatively correlated with cartilage thickness of the left (r=-0.517, p=0.02) and right (r=-0.435, p=0.046) knee joints. Leken`s index negatively correlated with cartilage thickness of the left knee joint (r=-0.590, p<0.01). All correlations were moderate and found in group 2. There were negative moderate correlation between uCTX-II and the mean value of middle compartments of both knee joints cartilage thickness (r=-0.538, p=0.04) and positive moderate correlation between uCTX-II and Leken`s index (r=0.561, p=0.036) in men. There were no correlations between uCTX-II and cartilage thickness of each knee joint and both joints in all pts.
Conclusion: Cartilage thickness measured with US associated with PROs in KOA pts. At the same time, the association between uCTX-II and cartilage thickness was less pronounced, only in men and in pts with disease duration 7-10 years. In pts with VAS pain less than 50 mm and in the group of pts with 7-10 years disease duration - WOMAC and Leken`s indices negatively correlated with the thickness of the cartilage of the knee joints. In other cases, correlations didn`t represent the expected relationship between uCTX-II level and clinical, instrumental characteristics of KOA. This may be because the current level of uCTX-II characterizes only the state of cartilage metabolism at the time of examination of the patient and doesn`t show the cumulative results of previous anabolic/catabolic changes in articular cartilage.
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AB0991

DECREASE LEVEL OF PRO-INFLAMMATORY CYTOKINES ASSOCIATED WITH REDUCTION OF BODY WEIGHT IN PATIENTS WITH OSTEOARTHRITIS

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Background: Recently, much attention has been paid to the problems of comorbidity of rheumatic diseases. Patients with osteoarthritis (OA) have a high risk of developing cardiovascular disease (CVD) [1]. Common risk factors for them are metabolic disorders, overweight and an increase in the level of pro-inflammatory cytokines [2,3]. To study the effect of weight loss on leptin levels in patients with OA and metabolic syndrome.
Objectives: We examined 130 patients with OA and 45 practically healthy individuals aged 49.26±3.89 years. Average BMI = 30.49 kg/m^2. Cardiovascular pathology was revealed in 121 (93%) patients.
Methods: Serum leptin levels were determined by ELISA-test (DBC Inc., cat no. CAN-L-4260) before and after treatment.
Results: The average level of leptin in healthy men was 3.8±0.21 ng/ml (M±m); no increase in leptin level was detected in them. The level of normal leptin in men, defined as M±2d, ranged from 2.0 to 5.6 ng/ml. The average level of leptin in healthy women was 7.4±0.37 ng/ml (M±m). The level of normal leptin in women ranged from 3.7 to 11.1 ng/ml. An increase in leptin levels in healthy women was detected in 4% of cases (1 person). The level of leptin significantly correlated with the sex of patients (t=7.91, p<0.001). Elevated levels of leptin in patients with OA were found in 42 patients out of 130 (32.3%), which is significantly more common than in healthy individuals (p<0.001). Elevated leptin levels were also found in 33 out of 78 women with OA (42.3%), which is significantly more common than in healthy women (p<0.001). The average level of leptin in women with OA was 14.4±0.32 ng/ml, which is significantly higher than in healthy females (p<0.001). Elevated leptin levels were found in 9 out of 28 men with OA (21.4%), which is significantly more common than in healthy men (p<0.001). The level of leptin in men with OA was 6.2±0.25 ng/ml (p<0.001). In patients with elevated leptin levels, the following were more often detected: secondary synovitis, radiographic stage of OA - III-IV, functional insufficiency of joints II-III and disease duration of more than 5-10 years. A significant relationship was found between high levels of leptin and higher levels of C-reactive protein (t=2.31, p<0.05) and ESR (t=2.06, p<0.05), both in men and women. and in women with OA. We found that weight loss by more than 5 kilograms in 3 months improves the clinical condition of patients, lowering blood pressure, pulse rate, lowering leptin concentration (t=3.43, p<0.001), and reducing postprandial glycemia (t=2, 53, p<0.005), by increasing the concentration of stimulated C-peptide (t=5.00, p<0.001).
Conclusion: A high level of leptin is associated with a high atherogenic coefficient, the severity of the metabolic syndrome, and a severe course of osteoarthritis with secondary synovitis. Weight loss contributes to a decrease in leptin levels, a decrease in the manifestations of insulin resistance, stabilization of blood pressure and pulse rates, and an improvement in the clinical course of OA.
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AB0992

PROGNOSTIC FACTORS RELATED TO CLINICAL RESPONSE IN 197 PATIENTS WITH KNEE OSTEOARTHRITIS TREATED BY PLATELET RICH PLASMA (PRP)

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Background: The European League Against Rheumatism (EULAR) [1] and the Osteoarthritis Research Society International (OARSI) [2] recommend a combination of non-pharmacological and pharmacological treatment in the management of knee osteoarthritis. New therapies have emerged such as Platelet Rich Plasma (PRP) injections. Many studies have shown the effectiveness of this treatment, and even its superiority over Hyaluronic Acid.
Objectives: The aim of this study was to determine the prognostic factors related to clinical response to PRP injections in knee osteoarthritis, in order to better select candidates for this therapy.
Methods: This was a single-center, prospective observational study including patients treated by PRP injections for knee osteoarthritis, from a university hospital. The PRP was leukocyte-poor, obtained by an ARTHREX kit, and was injected twice, at one-month intervals. They were assessed at 4 months (M4) and 7 months (M7) after the first injection. Pains on a Visual Analog Scale (VAS) and function with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Knee injury and Osteoarthritis Outcome Score (KOOS) – Physical Function Shortform (KOOS-PS) were collected. Patients were then classified as responders if they met the OMERACT-OARSI criteria at M7. Univariate and multivariate analysis was performed to compare the two groups.
Results: Among 197 patients, 210 knees were treated. The mean age was 59.8±10.8 years, Body mass index (BMI) was 31.0±6.5. Patellofemoral osteoarthritis was found in 34.3% of the patients, the distribution according to Kellgren and Lawrence stages I, II, III, IV was 11.8%, 33.5%, 40.4% and 14.3% respectively. A majority of patients had failed viscosupplementation (62.4%). At 7 months, 43.8% were classified as responders. Total WOMAC was 49.4±16.1 at M0, 43.6±17.9 at M1, 31.1±19.0 at M4 and 31.9±19.8 at M7, with significant improvement at M4 and M7 versus baseline (p<0.0001). The VAS was 58.5±19.7, 51.6±21.7, 43.7±23.2 and 43.5±23.5 at M0, M1, M4 and M7 respectively (p<0.0001 at all 3 times versus baseline). Regarding treatment satisfaction, 70% of patients considered the treatment effective or very effective at M7. Physical therapy and a heel-buttock distance greater than 35 centimeters were the two criteria associated with a poorer response at M7 on multivariate analysis. The pain VAS at M7 appeared to be lower in patients whose osteoarthritis had been evolving for less than 24 months. Tolerance was good. There was an increase in joint effusions between M0 and M1 (17% vs. 41%, p<0.0001), but no increase in pain.
Conclusion: PRP treatment in knee osteoarthrisis appeared to be effective and well tolerated, and this response was not associated with the radiographic stage or the type of knee osteoarthritis. In accordance with the recommendations of a group of French experts, this treatment should be proposed in case of failure of drug and rehabilitation treatment, at the same level as hyaluronic acid injections.
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AB0993

INDICATORS OF BONE MINERAL DENSITY IN ELDERLY AND SENILE MALE PATIENTS WITH OSTEOARTHRITIS OF THE KNEE JOINT, DEPENDING ON THE STATE OF THE MUSCULAR APPARATUS

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Objectives: To evaluate bone mineral density (BMD) indicators in elderly and senile male patients with osteoarthritis (OA) of the knee joint, depending on the state of the muscular apparatus.
Methods: The study included 32 patients with an established diagnosis of knee joint OA. The average age of patients was 68.7 (66.1; 70.3) years. The diagnosis of knee joint OA was established according to the diagnostic criteria of the American College of Rheumatology (ACR, 1991). For comparative analysis, all patients were divided into 3 groups depending on the state of the muscular apparatus (EWGSOP, 2010: muscle mass was assessed by multispiral computed tomography, muscle strength was measured using a wrist dynamometer, muscle function was examined using a battery of short tests): 1st – 9 patients without sarcopenia, 2nd - 11 patients with presarcopenia and 3rd - 12 patients with sarcopenia. BMD was assessed by two-energy X-ray absorptiometry in the neck and proximal femur as a whole and in the lumbar spine.
Results: Osteopenic syndrome in the study cohort was diagnosed in 23 (71.9%) patients: osteopenia - in 19 (59.4%) patients, osteoporosis – in 4 (12.5%). Normal BMD values were observed in 9 (28.1%) patients. Osteopenic syndrome was detected in patients with sarcopenia significantly more often than in patients without sarcopenia (p>0.05) and with presarcopenia (p=0.05). Thus, in the group of patients without sarcopenia, normal BMD indicators were noted in 6 (18.8%) patients, OPe – in 3 (9.4%), no cases of OP were detected. In patients with presarcopenia, normal BMD indicators were determined in 3 (9.4%) patients, OPe - in 8 (25%) patients, no cases of OP were also detected. In patients with sarcopenia, normal BMD indicators were not registered, OPS was detected in 12 (37.5%) patients, while OPe – in 8 (25.0%) and OP – in 4 (12.5%). BMD in patients with sarcopenia in the neck and proximal femur as a whole were statistically significantly lower than in patients without sarcopenia and with

presarcopenia (p<0.050). The BMD in the femoral neck in patients with sarcopenia was 0.908 [0.817; 0.977] g/cm2, which corresponds to -0.95 [-1.35; 0.425] CO according to the T-criterion, while in the groups of patients without sarcopenia and with presarcopenia, statistically significantly higher BMD values were recorded: 0.998 [0.935; 1.09] g/cm2 and 0.995 [0.94; 1.04] g/cm2 (p=0.009 and p=0.027), which corresponds to -0.30 [-0.80; 0.225] and -0.30 [-0.70; 0] CO according to the T-criterion (p= 0.013 and p=0.024), respectively. When comparing the BMD and T-test in the lumbar spine, there were no statistically significant differences in the studied groups of patients.

Conclusion: Sarcopenia is associated with low BMD in the neck and proximal femur in general in elderly and senile male patients with knee joint OA.

Disclosure of Interests: None declared

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AB0994 EXPLORING KNEE OSTEOARTHRITIS PAIN TRAJECTORIES AND MOVEMENT-EVOKED PAIN CHANGES DURING A 24-WEEK OUTDOOR WALKING PROGRAM (WALK)

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Background: Exercise therapy is recommended as first line treatment for knee osteoarthritis (OA), but it remains to be sub-optimally applied (1). Movement-evoked pain is a potential barrier to exercise adherence, but recent evidence suggests that such pain can be improved by training (2). Walking programs are low-cost, easily adopted and can be performed outdoors which can minimize the risk of SARS-CoV-2 transmission when in a group (3).

Objectives: To explore the acute pain trajectories of individuals with knee OA during a 24-week outdoor walking intervention. In addition, to explore the effect of pain trajectories and/or baseline characteristics on retention and adherence.

Methods: Individuals with clinical knee OA and bone marrow lesions (BMLs) on magnetic resonance imaging (MRI) were asked to follow a 24-week walking program. Every week consisted of two one hour supervised group sessions at various outdoor locations and one unsupervised session. At the start and end of every supervised group walk, knee pain was self-reported by participants to their trainer using a numerical rating scale (NRS) (0-10). The difference between the NRS pain values was considered as an acute pain change evoked by that walk. At baseline, the most affected knee of each participant was assessed using the Visual Analogue Scale (VAS) pain, the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) pain, stiffness and function, wellbeing (3 questionnaires) and the Osteoarthritis Research Society International (OARSI) recommended strength and performance measures.

Results: In total, N = 24 participants started the program of whom N = 7 (29%) withdrew. Pain at the start of each walk decreased from NRS 2.5 (SD 1.6) at the first walk (N = 24) to NRS 0.9 (SD 0.8) at the final walk (N = 17). This pain was estimated to decrease on NRS by -0.04 (95% CI -0.05 to -0.02) per supervised session, p < 0.001 during the first 12 weeks and -0.01 (95% CI -0.02 to -0.004), p = 0.004 during the second twelve weeks of the program. The number (%) of participants who experienced an acute increase in pain decreased from 11 (45.8%) at the first walk to 4 (23.5%) at the last walk. At baseline, non-adherent participants (<70% of group sessions) (N = 11) had lower physical performance scores, including the 30s Chair Stand Test (mean 10 (SD 1.7) stands versus mean 12.0 (SD 1.7) stands, p = 0.011), Fast Past Walk Test (1.23 (SD 0.14) meter per seconds (m/s) vs 1.50 (SD 0.20) m/s, p = 0.001), Six Minute Walk Test (418.8 (SD 75.9) m vs 529 (SD 72.6) m, p = 0.002), compared to adherent participants (N = 13). Non-adherent participants also had less severe self-reported symptoms including WOMAC stiffness (90.7 (SD 44.5) mm vs 121.5 (SD 17.0) mm, p = 0.031), compared to adherent participants. During the first two weeks of walking, acute increases in pain on average (mean ≥0.5 NRS) were reported by a greater number of non-adherent (N = 5 (45.5%)) than adherent participants (n = 4 (30.8%)).

Conclusion: This was an exploratory study and results need to be interpreted with caution due to the small sample size. The walking program resulted in clinically important improvements (MCIIs) (≥ 1 on NRS) (4) in start pain and acute pain changes. Improvements in start pain during the first 12-weeks were comparable to improvements measured in the NEMEX program (2) and may suggest that 12 weeks of exercise is sufficient to achieve MCIIs in pain. Improvements in acute changes in pain were smaller, which may have been related to a floor effect (5). Lower physical performance scores at baseline and more acute increases in pain during the first two weeks was associated with non-adherence. Participants with these characteristics may benefit from a lighter introduction to exercise.

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AB0995 METABOLIC PHENOTYPE OF KNEE OSTEOARTHRITIS: CHARACTERISTIC BIOCHEMICAL AND IMAGING FEATURES

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Objectives: to outline specific biochemical and imaging features of metabolic phenotype of knee osteoarthritis (OA) in a multicenter prospective study.

Methods: 284 female patients with knee OA (according to the ACR criteria) aged 40-78 were included in this prospective multicenter study. OA radiologic stages in the study group varied from I to III (Kellgren & Lawrence) and all the patients signed an informed consent. Mean age was 58.5 ± 9.5 years, disease duration was 5 (2-10) years. BMI was 29.6 ± 5.6 kg/m^2, with hip (HC) – 109.3 ± 10.4 cm and waist circumference (WC) – 92.5 ± 12.5 cm. Physicians filled out individual case report forms, which included anthropometric information, history and physical assessment data. All patients performed lab tests, ultrasonography and x-ray of the knee, as well as proximal femur and lumbar spine DEXA.

Results: Metabolic phenotype was diagnosed in 52.4% of patients. Participants were then divided in two groups. Patients with metabolic phenotype of osteoarthritis were older (61 (57-68) vs 52 (43-58), respectively, p<0.0001), had higher BMI (31.6 (28.6-35.4) vs 26.4 (23.4-30.3), p<0.0001) and had more intense VAS knee pain while walking on flat surface (50 (40-60) vs 35 (10-50), p<0.0001). There were also statistically significant differences when we analyzed the imaging results (Table 1). Patients with metabolic phenotype of knee OA had higher chances of grade III K&L (OR=4.4, 95% CI 1.3-14.2, p=0.01) and more significant medial joint space narrowing, bigger tibial osteophytes; knee ultrasound revealed thinner cartilage and thicker synovium. DEXA showed higher total hip BMD. Patients with metabolic phenotype had higher levels of CRP, HbA1c, uric acid, cholesterol, LDL, triglycerides, ALT, AST, glucose, leptin and COMP.

Table 1. Comparison of patients depending on phenotype

Index	Metabolic phenotype (n=149)	No metabolic phenotype (n=135)	p
K&L radiologic grade			0.01
I grade	13.6%	56.7%	
II grade	62.7%	36.7%	
III grade	23.7%	6.6%	
Posterior lateral tibial cartilage, mm, Me	1.5 (1.4-1.8)	1.7 [1.6;1.8]	0.05
Posterior medial tibial cartilage, mm, Me	1.6 (1.3-1.8)	1.7 [1.6;1.8]	0.014
Medial knee joint space, mm, Me	2.6 (1-4.6)	3.6 [3;4.3]	0.023
Osteophytes of the medial tibial condyle, mm, Me	1 (1-2)	0 [0;0]	0.025
Osteophytes of the lateral tibial condyle, mm, Me	1 (1-2)	0[0;1]	0.042
Synovium thickness, mm, Me	3.1 (2.9-3.5)	2.9 (2.6-3.1)	0.02
Total hip BMD, (g/cm^2), mm, Me	0.95 (0.87-1.02)	0.87 (0.77-0.99)	0.03
CRP, mg/l, Me	2.8 (1.4-5.1)	1.1 (0.49-2.0)	0.0001
HbA1c, %, Me	5.7 (5.4-5.9)	5.2 (4.9-5.6)	0.0001
Uric acid, mcmol/l, Me	312 (268-391)	269.7 (233.9-324.5)	0.0002
Cholesterol, mmol/l, Me	6.4 (5.33-6.85)	5.4 (4.78-5.82)	0.002
LDL, mmol/l, Me	4 (3.38-4.59)	3.1 (2.6-3.89)	0.0009
Triglycerides, mmol/l, Me	1.6 (1.19-2.44)	1.1 (0.76-1.48)	<0.0001
ALT/AST, units/l, Me	21 (17.15-28.9)/ 20.6 (17.6-25)	15.9 (11.4-19.8)/ 18.1(14.9-21.6)	0.0006
Glucose, mmol/l, Me	5.6 (5.1-6,155)	5.2 (4.97-5.53)	0.001
Leptin, ng/ml, Me	35.6 (25.5-55.6)	20 (14.7-31)	<0.001
COMP, ng/ml, Me	1415 (1115-2100)	712.2 (484.5-1015)	<0.001
IL-6, pg/ml, Me	0.55 (0.25-0.8)	0.03 (0.01-0.4)	<0.005

Spearman correlation analysis showed positive correlations (p <0.05) between the metabolic phenotype and OA radiologic stage (r=0.44), size of tibial osteophytes (r=0.31), synovium thickness (r=0.28), hsCRP (r=0.44), HbA1c (r=0.45), cholesterol (r=0.29), LDL (0.3), triglycerides (r=0.36), uric acid (r=0.3), leptin (r=0.46), IL-6 (r=0.38), COMP (r=0.51). Negative correlations (p <0.05) were established with medial joint space (via X-ray): (r=-0.24) and cartilage thickness (via ultrasound) (r=-0.25).

Conclusion: Comprehensive examination of patients with the use of imaging and biochemical methods showed that metabolic phenotype of osteoarthritis is more severe (with correction for age taken into account). Patients with metabolic phenotype showed higher levels of hsCRP, leptin, IL-6, COMP, which possibly demonstrate a more active form of low-grade inflammation (the underlying mechanism of OA pathogenesis) and more significant cartilage damage

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AB0996 THE POSSIBILITY OF LONG-TERM PAIN CONTROL IN PATIENTS WITH OSTEOARTHRITIS

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Background: In some patients with osteoarthritis (OA), moderate or severe joint pain may persist for a long time and functional limitations may increase, which requires long-term administration of nonsteroidal anti-inflammatory drugs (NSAIDs).

Objectives: To evaluate the efficacy and safety of long-term use of NSAIDs in patients with OA in real clinical practice.

Methods: 611 patients with OA (knee or hip) were included in an open observational study. 64.5% were female, mean age 58.3±11.0years. All patients received aceclofenac at a dose of 200 mg / day. Pain at movement was determined on a 10-cm visual analog scale (VAS). The number of patients with severe pain (≥6 cm by VAS) and the number of patients with pain reduction ≥50% were evaluated. The assessment was carried out 2 weeks, 3, 6, 9 and 12 months after the start of therapy. Adverse events were noted at each visit.

Results: By 12 months of follow-up, 53.3% of patients had completed the study. The mean pain severity at baseline, after 2 weeks, 3, 6, 9 and 12 months was 6,5±1,2; 4,8±1,4; 3,2±1,4; 2,6±1,4; 2,2±1,1; 1,4±1,1 cm VAS (p<0.05). The number of patients with severe pain decreased from 77.8% to 24,9%, 2,9%, 2,3%, 0,9% and 0%. The number of patients with pain reduction ≥50% was 12,0%, 65,1%, 81,0%, 88,5% and 84.0%. Adverse events were observed in about 30% of patients, mainly mild or moderate dyspepsia (11.1%- 23.3%) and arterial hypertension (7.1% - 10.9%). No serious complications were recorded.

Conclusion: Taking into account the large number of drop-outs from the study (46.7%), approximately half of the patients can have long-term pain control with NSAIDs in real clinical practice. Aceclofenac is effective and well tolerated and can be used for long-term pain control in patients with OA.

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AB0997 NEW EPIGENETIC PREDICTORS OF THE VARIOUS LOCALIZATIONS OSTEOARTHRITIS DEVELOPMENT

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Background: Osteoarthritis (OA) is one of the most common joint diseases, often causing persistent pain and immobilization [1]. The genetic contribution to OA varies from 40% to 65%, depending on the presence of the pathology in the immediate family, the location of the affected joint, sex, and ethnicity of the patients [2]. The study of miRNA target sites is a new promising direction in molecular diagnostics [3].

Objectives: The aim of our work was to study the microRNA binding sites of COL1A1, COL11A1, ADAMTS5, MMP1, MMP13, SOX9, GDF5, FGF2, FGFR1, FGFRL1 genes in patients with OA of different localization.

Methods: A total of 417 women (mean age 51.67±11.5) from Ufa (Republic of Bashkortostan, Russia) participated in the study between January 2013 and August 2017. The patients were examined to diagnose for osteoarthritis according to the criteria of the American College of Rheumatologists (1995) with X-ray confirmation. Overall, 356 women with OA were recruited and divided into 3 groups as follows: subgroup 1 included 84 women affected by generalized OA, subgroup 2 included 197 women affected by knee OA, subgroup 3 included 75 women affected by hip OA. For genotyping, RT-PCR analysis using KASP@ technology was used. Selection of the miRNA target loci was carried out using the database of the National Center for Biotechnological Information (https://www.ncbi.nlm.nih.gov), Ensemble Ge-nome-Browser (www.ensembl.org), and the base of polymorphisms of microRNA target sites (http: // compbio. uthsc.edu/miRSNP). As a calculation tool, Statistica v.6.2 (StatSoft) software packages were used. Considering the type I error caused by multiple testing, p values were adjusted by calculating the FDR value using the Benjamini-Hochberg method (https://tools.carbocation.com/FDR).

Results: The T allele of the rs9659030 (COL11A1) was associated with the generalized OA (p = 0.019; OR = 2.0; 95% CI 1.11 to 3.62), the TT genotype was associated with total patients (p = 0.026; OR = 1.59; 95% CI 1.05 to 2.42), generalized OA (p = 0.003; OR = 2.75; 95% CI 1.39 to 5.46) and OA of the hip (p = 0.016; OR = 2.3; 95% CI 1.14 to 4.36). With respect to rs229069 (ADAMTS5), a significant association was found between the C allele and the incidence of total OA (p = 0.018; OR = 1.43; 95% CI 1.06 to 1.93), as well as with the knee OA (p = 0.042; OR = 1.43; 95% CI 1.01 to 2.03) and hip OA (p = 0.026; OR = 2.039; 95% CI 1.08 to 3.85). The CC genotype was also found to be associated with total OA (p = 0.037; OR = 1.53; 95% CI 1.02 to 2.28) and hip OA (p = 0.026; OR = 2.039; 95% CI 1.08 to 3.85). The T allele of rs13317 (FGFR1) was strongly associated with the total OA (p = 0.001; OR = 1.67; 95% CI 1.2 to 2.3), knee OA (p = 0.003; OR = 1.74; 95% CI 1.19 to 2.55) and generalized OA (p = 0.044; OR = 1.67; 95% CI 1.01 to 2.75) After Benjamini-Hochberg correction, rs13317 remained statistically significant in the following groups: the T allele in control vs total patients (adjusted p*= 0.01) and in control vs OA of the knee (adjusted p* = 0.03). Neither the genotype nor the allele frequencies of rs1061347 (COL1A1), rs229077, rs9978597 (ADAMTS5), rs5854, rs470215 (MMP1), rs1042840 (MMP13), rs1042673 (SOX9), rs4647940 (FGFRL1) were significantly different between the affected individuals and normal controls.

Conclusion: The current study demonstrated an association between the T allele of rs13317 in FGFR1 and incidence of the total OA and knee OA in women from Volga-Ural region of Russia.

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AB0998 DIET AND JOINT SYMPTOMS: A SURVEY OF MOROCCAN PATIENTS WITH OSTEOARTHRITIS

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Background: The question of diet is frequently asked by patients with osteoarthritis. Beyond the effect of weight on the aggravation of their symptoms, patients

often ask whether certain foods, described as inflammatory or anti-inflammatory, can improve or worsen their disease.
Objectives: The objective of our study is to investigate whether Moroccan patients report a relationship between certain foods and their symptoms and also to study whether they adopt specific dietary behaviors in an effort to alleviate their symptoms.
Methods: This is a survey based on a questionnaire, that included any patient followed for osteoarthritis who presented to the rheumatology department.
The questionnaire consisted of 3 parts:
1) Socio-demographic data, co-morbidities, and information on osteoarthritis (location, duration of evolution, functional impact and treatments).
2) Beliefs and attitudes of patients regarding diet in relation to osteoarthritis.
3) A list of 24 foods for which patients were asked to indicate whether they aggravated, improved or left their joint symptoms unchanged.
Results: At this time we included 120 patients. The mean age was 57.1 ± 11.8, 88.3% of the patients were women, 41.2% had comorbidities, 62.5% were illiterate. The median duration of osteoarthritis was 4 years [2; 7]. 64.2% of the patients were followed for gonarthrosis, 25% for discarthrosis and 10.8% for digital osteoarthritis. The average BMI was 27.8 ± 5.2. 8.3% of the patients thought that diet influenced their osteoarthritis. 9.5% of the subjects stated that food had an effect on their symptoms, 9.2% of them reporting an improvement and 8.3% an aggravation. Fish (1.7%), garlic (1.7%), and olive oil (1.7%) were the foods most often cited as improving joint symptoms, while red meat (3.3%), and sweetened soft drinks (2.5%) were the most often cited as worsening symptoms. 6.7% of the patients had food avoidance behaviors, 10.8% adopted certain diets and 5.8% had tried fasting in order to relieve joint symptoms. In univariate and multivariate analysis, education level (OR: 0.165; 95% CI [0.046-0.592]; p=0.006) and experience with a food that improves symptoms (OR: 46.8; 95% CI [1.798-1222.5]; p=0.021) were associated with reporting that food influences OA symptoms.
Conclusion: Our study showed that associations between certain foods and worsening or improving joint symptoms were reported by a minority of patients and appeared to be mostly associated with patients' education level and experience of a food improving symptoms.
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AB0999 OSTEOARTHRITIS. PHARMACOECONOMICS ASPECTS OF SYMPTOM-MODIFYING THERAPY IN REAL CLINICAL PRACTICE.

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Background: Treatment of osteoarthritis (OA) is a significant medical and social problem worldwide. Modern therapeutic approaches include a combination of pharmacological and non-pharmacological methods aimed at reducing pain, improving joint function, and preventing disease progression. A wide variety of symptomatic slow-acting drugs for osteoarthritis and their usage dictate the necessity for a clinical and economic analysis to select the most economically feasible treatment regimen for OA.
Objectives: To conduct a clinical and economic assessment of OA therapy using drugs of the SYSADOA group.
Methods: The search for publications for the period 2011-2022 on the clinical efficacy and safety of SYSADOA (bioactive concentrate of small marine fish containing chondroitin sulfate, amino acids, peptides, sodium, potassium, calcium, magnesium, iron, copper and zinc ions) was conducted using available sources (Medline, eLIBRARY.ru). The research selection methodology was in compliance with the PRISMA criteria(Preferred Reporting Items for Systematic reviews and Meta-analysis), 124 sources were analyzed. To collect data on the costs for managing patients in real clinical practice, a survey of 15 rheumatology experts was conducted with an assessment of the frequency and average duration of SYSADOA drugs usage. The direct medical costs paid from budgetary funds and/or funds of the compulsory medical insurance system related to the treatment of OA were assessed. Cost minimization analysis was carried out for 10 SYSADOA drugs; the average course cost of treatment was calculated according to the dosage regimens and duration of admission, as well as the cost of providing medical services.
Results: Analysis of the literature data showed that bioactive concentrate of small marine fish, produced by Biotehnos S.A. is a modern original SYSADOA for the initial therapy of knee joint OA with proven efficacy and safety. The estimated course cost of SYSADOA therapy ranges from 36.961 to 92 euros. The median exchange rate of all drugs in the sample was 50.2 euros; for SYSADOA drugs with oral administration - 85.82 euros; injectable drugs - 47.76 euros. The median amount of direct costs for injectable SYSADOA was 388,012 euros. Cost minimization analysis showed that the use of an alternating mode of administration of the drug (2 ml every other day intramuscularly - 10 injections) in patients with knee joint OA is the most cost-effective method for the treatment of OA and allows to reduce direct costs up to 64% per patient by reducing the number of medical services provided.
Conclusion: The analysis proved rationality of the established medical practice in prescribing of the injectable SYSADOA (bioactive concentrate of small marine fish was a leader among injectable SYSADOA according to HWC and IQVIA marketing analytical data for the period 2020-2021). Choosing the most economically feasible drug for the treatment of patients with OA will reduce the costs of the healthcare system and reduce the overall economic burden of OA.
Disclosure of Interests: None declared
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AB1000 RELIABILITY AND VALIDITY OF THE CONE EVASION WALK TEST IN PATIENTS WITH TOTAL KNEE ARTHROPLASTY: A PILOT STUDY

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Background: Total knee arthroplasty (TKA) is the gold-standard procedure for end-stage knee osteoarthritis, however, some residuel problems may still continue and cause a variety of dysfunctions, such as impaired strength, proprioception, gait, balance, postural instability, and, impaired ability to avoid obstacles while walking. Tripping over an obstacle is the most frequent cause of falls 1 and falls can limit daily activities and induce post-fall syndromes, such as dependence, loss of autonomy, immobilization, and depression 2. The Cone Evasion Walk test (CEW) to assess fall risk by the ability to evade obstacles, (ICF-code d455), which requires attentional, perceptual, and several neuromusculoskeletal and movement related functions 3. However, there is no study investigating the reliability and validity of the CEW in TKA patients.
Objectives: The aim of the study is to investigate the reliability and validity of the CEW in patients with TKA.
Methods: Twenty patients with TKA included in the study. The CEW, the Timed Up And Go Test (TUG) and the Hospital for Special Surgery (HSS) Knee Score administered to the patients. Patients rested between the tests for an hour.
Results: Mean age was 68.1 ± 2.59 years and the mean HSS Knee Score was 85.43± 3.47. The relative (ICC coefficient) and absolute (SEM and SRD95) reliability values were 0.98, 1.01, and 2.75 respectively. The Spearman correlation coefficient of the CEW with the TUG was 0.72.
Conclusion: Based on the current findings, the CEW has excellent reliability, high validity and responsiveness in evaluating dynamic balance and obstacle avoidance in patients with TKA. The minimal clinically important difference of CEW in TKA patients is 2.75 and it may be concluded that the fact that this value is low, indicates the sensitivity of the test. Therefore, the CEW can identify even small alterations in the functional status, can be reliably used for post-operative surveillance of TKA to observe patient results, and the usage of the CEW for assessing the fall risk and mobility in the community may be a better predictor of the patients' current condition.
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AB1001 OSTEOARTHRITIS AND OBESITY: RELATIONSHIPS AND EFFICACY OF THERAPY.

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Background: Osteoarthritis (OA) is the most common joint disease. The most important factor not only in the development but also in the progression of OA is obesity. Higher incidence of OA in obese patients is associated with several factors. One of them is a large volume of fat mass, which increases the mechanical load on the joints. On the other hand, in obesity, hyperexpression of pro-inflammatory mediators (cytokines, adipokines) is observed, which negatively affect joint tissues, as well as provoke the development of low-level metabolic inflammation. Thus, the problem of OA and obesity is very relevant in modern rheumatology.
Objectives: To determine features of clinical manifestations of OA in obesity and evaluate the effectiveness of obesity therapy in OA.
Methods: The study included 73 patients (women) with knee OA (according to the ACR criteria) II-III X-ray stage by Kellgren-Lawrence: obese 50 (body mass index (BMI) > 30 kg/m2) and non-obese 23 (control group). Obese patients were divided into 2 groups: 1 group (n = 25) - received orlistat 120mg 3 times a day for 6 months in combination with non-medicamentous methods of controlling excess body weight and 2 group (n = 25), whose patients were recommended a diet and dosed exercise for 6 months. Monthly visits evaluated anthropometric measures, articular status, WOMAC. Initially and after 6 months, laboratory scores were evaluated in obese patients (determination of leptin, TNF-α, IL-6, CRP in peripheral blood).
Results: In patients with OA and obesity, a more severe course of OA is determined compared to the control group (Table 1).

Table 1. Comparative characteristics of obese and non-obese knee OA patients

Parameters	Obese patients (n = 50), BMI > 30 kg/m^2	Non-obese patients (n = 23), BMI < 30 kg/m^2	p
The mean age, y.o.,(M ± δ)	56.5 ± 5.86	58.69 ± 5.43	0,13
The mean age of OA onset, y.o., (M ± δ)	49.33 ± 6.14	55.17 ± 4.88	**< 0.001**
Average duration of OA, years, (M ± δ)	7.43 ± 3.93	3.52 ± 1.47	**< 0.001**
BMI of onset OA, kg/m^2, (M ± δ)	36.53 ± 4.35	25.8 ± 2.0	**< 0.001**
The mean body weight, kg, (M ± δ)	102.97 ± 14.57	70.87 ± 8.84	**< 0.001**
WOMAC pain, mm, (M ± δ)	227.9 ± 85.15	168.35 ± 49.17	**0.006**
WOMAC stiffness, mm, (M ± δ)	94.44 ± 49.4	71.52 ± 25.71	**0.039**
WOMAC functional insufficiency, mm, (M ± δ)	846.8 ± 337.57	692.69 ± 121.99	**0.037**
Total WOMAC, mm, (M ± δ)	1170.28 ± 437.85	932.61 ± 159.09	**0.014**

After 6 months of drug therapy of obesity in patients of group 1, a significant decrease in body weight by 10.07% ($p < 0.05$) was achieved. In patients of group 2, body weight decreased by 0.84% ($p > 0.05$). In patients of group 1, the indicators of the WOMAC index improved: pain decreased by 52.5% ($p < 0.05$), stiffness by 47.98% ($p < 0.05$), functional insufficiency by 51.55% ($p < 0.05$). In patients of group 2, there was also a decrease in the WOMAC index, however, these changes were worse than in patients with greater body weight loss. Analyzing laboratory data, in group 1 there was a significant decrease in the level of leptin ($p = 0.05$) and IL-6 ($p < 0.05$), in contrast to patients of group 2 ($p = 0.64$; $p = 1.0$, respectively). In the study of TNF-α, no significant changes in the two groups were determined. CRP level in 1 group of patients decreased by 23.74% ($p > 0.05$) compared to baseline data, in 2 group of CRP increased by 24.54% ($p > 0.05$). Correlation analysis revealed a direct relationship between a decrease in leptin level and a decrease in body weight ($r = 0.5$, $p = 0.02$) in patients with greater weight loss. Direct correlations of leptin reduction and WOMAC index decline (pain, stiffness, functional insufficiency, total WOMAC) ($r = 0.5$, $p = 0.01$; $r = 0.4$, $p = 0.04$; $r = 0.4$, $p = 0.03$; $r = 0.5$, $p = 0.01$, respectively).
Conclusion: The results of our study demonstrated a more severe clinical course of OA in obese patients. Drug therapy for obesity in patients with knee OA and obesity not only leads to a decrease in the presentation of clinical symptoms of OA, but also entails changes at the metabolic level: a decrease in leptin, IL-6 and CRP, which indicates a decrease in the intensity of metainflammation in obese patients. Thus, therapeutic interventions aimed at reducing body weight should be an integral part of knee OA therapy.
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AB1002 CLASSIC VERSUS AQUATIC REHABILITATION IN GONARTHROSIS: WOMAC SCORE

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Background: Gonarthrosis is the most frequent and common condition of the lower limb, responsible for gonalgia, stiffness, leading sometimes to major functional impotence. The WOMAC with its three domains (pain, stiffness and function) is a valid index for the evaluation of lower limb osteoarthritis [1]. The management of gonarthrosis is multidisciplinary with rehabilitation as the mainstay. Currently, aquatic gymnastics is more and more prescribed in the management of this pathology.
Objectives: The objective of our work was to compare the contribution of aquatic rehabilitation to classical one in patients with gonarthrosis through the WOMAC score.
Methods: This is a prospective, comparative study conducted over a period of 15 months, between September 2016 and December 2017, including 120 patients recruited at the Physical Medicine and Functional Rehabilitation Department of The HMPIT, in whom the diagnosis of gonarthrosis was made according to the ACR criteria. The patients were randomly divided into 2 groups of 60 patients each. The first group, called G1, received a conventional rehabilitation program. The second group, called G2, received aquatic rehabilitation. Two evaluations were made, the first (T1) before the beginning of the rehabilitation and the second (T2) at the end of the eight weeks of treatment.
Results: The average age of the general population was 54.85 ± 9.5 years [40- 81 years]. The average age of G1 was 59.07 ± 10.2 years versus 50.63 ± 6.4 years for G2. Among the 120 patients, 28 were male (23%) and 92 were female(77%) There were 6 males and 54 females in group 1 versus 22 males and 38 females in group 2. Initially, the average WOMAC pain was 15.1 ± 3.9 in G1 and 12.3 ± 1.22 in G2. There was a statistically significant difference between the 2 groups ($p=0.01$). After rehabilitation, there was an improvement in the WOMAC pain score of 17% in G1 and 50% in G2 with a statistically significant difference between the 2 groups ($p<0.001$). The average WOMAC score for stiffness was initially 5.1 ± 2 in G1 and 3.2 ± 2 in G2 with no statistically significant difference between the 2 groups ($p=0.076$). After rehabilitation, an improvement of this score was noted in both groups, it was 19% in G1 and 50% in G2 with a statistically significant difference between the 2 groups ($p<0.001$). The average initial WOMAC function score was 42.32 ±15.7 in G1 and 33 ± 11 in G2 with a statistically significant difference between the 2 groups ($p=0.002$). After conventional rehabilitation, this score had improved by 10% and after hydrotherapy, the improvement was 46% with a statistically significant difference between the 2 groups ($p<0.001$).
Conclusion: These results were aligned with the literature and confirmed the effectiveness of functional treatment whether aquatic or classic with better outcome for aquatic rehabilitation. The best would be to combine the different methods according to the needs of the patient and their functional capacities in order to ensure a better adherence.
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AB1003 EFFECTIVENESS OF CLASSIC VERSUS AQUATIC REHABILITATION IN GONARTHROSIS: LEQUESNE SCORE

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Background: Gonarthrosis is a benign knee condition, but it can become disabling if poorly managed. The evaluation of the functional impact of gonarthrosis is based on Lequesne's algofunctional index [1], thus judging the effectiveness or failure of the proposed treatment. Water gymnastics is increasingly prescribed in the management of this pathology.

Objectives: The main aim of our work was to compare the efficacy of aquatic gymnastics with conventional rehabilitation in patients with gonarthrosis using Lequesne's algofunctional index.
Methods: This is a prospective, comparative study conducted over a period of 15 months, between September 2016 december 2017, including 120 patients recruited at the outpatient clinic of the Physical Medicine and Functional Rehabilitation Department of The HMPIT, in whom the diagnosis of gonarthrosis was made according to the ACR criteria. The patients were randomly divided into 2 groups of 60 patients each. The first group, called G1, received a conventional rehabilitation program. The second group, called G2, received water gymnastics. Two evaluations were made, the first (T1) before the beginning of the rehabilitation and the second (T2) at the end of the eight weeks of treatment.
Results: The mean age of the general population was 54.85 ± 9.501 years [40-81 years]. The mean age of G1 was 59.07 ± 10.275 years versus 50.63 ± 6.425 years for G2. Thus, there was a female predominance with a sex ratio M/F of 0.11 in G1 and 0.57 in G2. Lequesne's algofunctional index was initially 11.46 ± 3.2 in G1 patients and 8.7 ± 1 in G2 patients with a statistically significant difference between the 2 groups (p<0.001). The discomfort according to the Lequesne algofunctional index was very important and unbearable in 69% of the cases in G1 against 41% of the cases in G2. The Lequesne index was ≥ 10 in 46 patients in G1 (i.e. 77%) versus 32 patients in G2 (i.e. 53%). After conventional rehabilitation, there was a 10% improvement in this index compared with a 28% improvement after water gymnastics with a statistically significant difference between the 2 groups (p<0.001).
Conclusion: The effectiveness of functional treatment whether aquatic or classic was well demonstrated by Lequesne's algofunctional index, with better result for aquatic rehabilitation. The best would be to combine the two according to the initial functional capacities of the patient to ensure his adherence to the rehabilitation program.
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AB1004 CONTRIBUTION OF DRY REHABILITATION VERSUS BALNEOTHERAPY IN THE CONTROL OF PAIN TRIGGERS IN GONARTHROSIS

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Background: Gonarthrosis is a very common condition and a real public health problem [1]. One of the pillars of its management is pain management. In addition to drug treatment, rehabilitation is part of the therapeutic arsenal.
Objectives: The main objective of our work was to compare the contribution of balneotherapy versus dry rehabilitation in the control of pain triggers.
Methods: We carried out a prospective, comparative study carried out over a period of 15 months, (September 2016- December 2017), in 120 patients recruited from the outpatient department of the Physical Medicine and Functional Rehabilitation Department of HMPIT in whom the diagnosis of knee osteoarthritis (KOA) was made according to the criteria of the ACR [2]. The patients were randomly divided into 2 groups of 60 patients each. The first group, called G1, received a standard rehabilitation program. The second group, called G2, received water gymnastics. Two evaluations were made, the first (T1) before the beginning of the rehabilitation and the second (T2) at the end of the eight weeks of treatment.
Results: The mean age of our patients was 57.2 ± 12.5 years in G1 vs 54.3 ± 7.1 years in G2 (p = 0.012). The sex ratio was 0.2 in G1 versus 0.37 in G2 (p = 0.011). The duration of KOA was 63.4 ± 4.5 months in G1 vs 56.2±7.5 months in G2 (p=0.172). Pain was triggered by standing in 92% of cases in G1 versus 98% in G2 with a mean delay of 17.2 min for G1 and 20.1 min for G2. There was no statistically significant difference between the two groups (p=0.452). After rehabilitation, 22% of the patients in G1 and 43% in G2 noted an improvement in pain with a statistically significant difference between the 2 groups (p=0.001).Prolonged sitting in 62% of cases in G1 versus 38% in G2 with a mean delay of 6.2 min for G1 and 52.3 min for G2 awakened pain. There was a statistically significant difference between the two groups (p=0.02). After rehabilitation, 23% of the patients in G1 and 30% in G2 noted an improvement in pain with a statistically significant difference between the 2 groups (p=0.001). Pain was awakened by squatting in 93% of cases in G1 versus 97% of G2. There was no statistically significant difference between the 2 groups (p=0.554). After rehabilitation, 13% of the patients in G1 and 30% in G2 had noted a complete disappearance of pain with a statistically significant difference between the 2 groups (p=0.001). All patients in G1 and 92% of patients in G2 reported pain when climbing/descending stairs. There was no statistically significant difference between the 2 groups. An improvement in symptomatology was noted in both groups with disappearance of pain in 18% of G1 and 27% of G2. An adjustment on the parameters by which the 2 groups differed was made without impact on the results obtained.
Conclusion: Rehabilitation has an important role in the control of pain triggers by ensuring, in addition to analgesic means, good muscle balance, joint gain and good proprioception. Balneotherapy has proven to be more effective.
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AB1005 EFFICACY AND SAFETY OF GARCINIA KOLA (CLUSIACEAE) IN KNEE OSTEOARTHRITIS: A PILOT STUDY

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Background: Administration of supplements to strengthen the joint cartilage matrix have become popular not only for pain relief but also for joint preservation. Reports have suggested anti-inflammatory and analgesic properties of *Garcinia kola* (GK) extracts in knee osteoarthritis (KOA)[1,2].
Objectives: To evaluate the non-inferiority of GK compared to Diclofenac in patients with KOA.
Methods: Randomized, double-blind, controlled trial (1:1) in outpatients aged 18 to 70 years followed at the Douala General Hospital, Cameroon for KOA with Kellgren-Lawrence grade ≥ 2. Patients with pain on the visual analog scale (VAS) > 5 and who had not taken non-steroidal anti-inflammatory drugs or corticosteroids in the previous 15 days were included. Paracetamol, tramadol, and codeine were accepted as analgesics. The trial was approved by the institutional ethics committee. Patients were divided into 2 groups: Garcinia kola (400 mg/12hours *per os*) and Diclofenac (50 mg/8hours *per os*). The primary endpoint was the per-protocol change in ultrasensitive CRP (CRP_{us}) measured at D0 and D15. Secondary endpoints were the decrease in VAS pain with clinical relevance if decrease ≥ 20%, and safety. Statistical significance was set at p<0.05.
Results: Forty-seven patients (33 women) were randomized (GK, n = 24 and Diclofenac, n = 23). There were no differences ($p > 0.05$) in sociodemographic, clinical, and radiographic characteristics between the two groups [Table 2]. Between D0 and D15, there was no difference in CRP_{us} variation between patients in the GK and Diclofenac groups ($p > 0.05$) [Table 2]. The same was true for pain VAS ($p > 0.05$), with an effect considered clinically relevant. Adverse events were mild to moderate in severity, including 2 cases of epigastralgia (Diclofenac) and 3 cases of increased libido (GK). No significant changes in seric level of liver transaminases, creatinine, and fasting blood sugar were observed.

Table 1. Main baseline patient characteristics

Variables	*Garcinia kola*, n = 24	Diclofenac, n = 23
Age, years	57 ± 12	58 ± 11
Female gender, n (%)	19 (79.1)	17 (73.9)
BMI, Kg/m2	27 ± 10	27 ± 12
Duration of osteoarthritis, years	4 ± 2	4 ± 1
Kellgren-Lawrence ≥ 2, n (%)	20 (83.3)	20 (86.9)
VAS pain, mm, mean	72 ± 17	70 ± 15
CRPus, mg/L	4.8 ± 0.7	4.2 ± 0.5

Table 2. Assessment of the evaluation criteria: CRP_{us} and VAS pain

	Garcinia kola (G.K)	Diclofenac
CRP_{us}*		
Day 0	4.8	4.2
Day 15	3.1	2.6
Variation, n (%)	-1.7 (35,4)	-1.6 (38,1)
p-Value	$p = 0.003$	$p < 0.001$
VAS pain**		
Day 0	72	70
Day 15	54	53
Variation, n (%)	-1.8 (25.0)	-1.7 (24.3)
p-Value	$p < 0.001$	$p < 0.001$

*GK *vs*. Diclofenac: $p > 0.05$; **GK *vs*. Diclofenac: $p > 0.05$

Conclusion: *Garcinia kola* (GK) was non-inferior to Diclofenac in reducing CRP_{us} and VAS pain in patients with KOA. The safety was good. GK would be a promising alternative to explore in the future management of osteoarthritis.

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AB1006 IMPACT OF OSTEOARTHRITIS ON THE QUALITY OF LIFE IN PATIENTS WITH KNEE PAIN

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Background: Knee osteoarthritis is a common disease which mainly concerns aged population and impairs the quality of life in all aspects. Apart from causing pain or other related biomechanical comorbidities, osteoarthritis might affect phychological and social aspects of life.

Objectives: The purpose of the study was to investigate the impact of knee osteoarthritis on the quality of life and whether certain factors are related to this impact.

Methods: In a cross-sectional study, performed in our Hospital from January 2016 to December 2016, 150 patients (127 females and 23 males) with a mean age of 61.8 ± 8.07 years were examined. The sample included outpatients of the Rheumatology Department diagnosed with osteoarthritis and patients displaying knee pain. Individuals who had undergone previous knee surgery, and those with other osteometabolic, rheumatic diseases or chronic degenerative disorders that could interfere with the quality of life, were excluded from the study. All participants, who gave their informed consent, answered the identification questionnaire and were interviewed with the Western Ontario and McMaster Universities Arthritis Index (WOMAC), The World Health Organization Quality of life (WHO QoL) questionnaire, the IPQ and the PHQ-9. All instruments used, were standardized in the Greek context.

Results: The effect of certain variables including patient associated characteristics, demographics, medical history, drug intake and symptomatology related to osteoarthritis, were evaluated with each of the WHO QoL measurements, the IPQ total score and the WOMAC scale. The regression analysis results demonstrated common significant correlations regarding the presence of injuries, the depression, the increased body mass index (BMI) and occasional crepitus. However, no significant difference was observed between patients with osteoarthritis and patients without osteoarthritis, concerning any of the examined parameters.

Conclusion: It was demonstrated that quality of life indices were related to agents that are not exclusively met in patients with osteoarthritis which implies that patients` quality of life does not depend on the specific diagnosis but on patient`s psychological aspect (depression), presence of pain (injury) and overall health status (BMI).

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Osteoporosis

AB1007 CLINICAL SIGNIFICANCE OF SERUM CREATININE-TO-CYSTATIN C RATIO AS A SURROGATE MARKER FOR INCIDENT OSTEOPOROTIC FRACTURE

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Background: In a previous article, we introduced a novel index of osteoporosis that represented as T-score ≤ -2.5, which constituted the combined criteria of age, serum creatinine-to-cystatin C ratio (Cr/CysC), and tartrate-resistant acid phosphatase-5b.

Objectives: We hypothesized that serum cystine C to creatine ratio (CysC/Cr), that is the reciprocal of Cr/CysC, might function as a predictive marker of incident osteoporotic fractures in elderly population and tested this hypothesis in a retrospective cohort study.

Methods: Subjects were 50 years of age or older who had their lumbar spine and femoral neck bone mineral density (BMD) measured by dual-energy X-ray absorptiometry, and simultaneously had their CysC/Cr measured. The dates of BMD and CysC/Cr measurements were set as baseline. The primary outcomes were incidental major osteoporotic fractures (MOF), including vertebral fractures, proximal femur fractures, proximal humerus fractures, and distal radius fractures. Follow-up was continued until the first fracture occurred, was terminated at death, was lost to follow-up, or was completed. In these patients, the relationship between baseline developmental MOF and variants was investigated using Cox regression analysis. The variants were candidate risk factors for MOF for positivity and negativity. After identifying risk factors using univariate models, multivariate model was undergone in order to relative higher risk in the factors. Receivers operating characteristic analyses (ROC) were conducted in order to determine cut-off index (COI) of these factors. Kaplan-Meier survival analysis was tested in order to determine hazard ratio for presenting these risk factors.

Results: A total of 175 patients, 38 men and 137 women, were included in the dataset. The mean age at baseline was 70.2 years, ranged from 50 to 98 years, and the mean follow-up was 30.4 months. Mean BMD at baseline was 0.734 and 0.659 g/cm^2 (T-score: -2.21 and -2.04) in lumbar spine and femoral neck, respectively, and mean CysC/Cr at baseline was 1.49. fall-ability, LSD, and pr-MOF, were present in, 59, 113, and 77, respectively. Administration of OPD, vitamin-D, GCS, and polypharmacy were present in 92, 170, 12, and 47, respectively (Table 1).

Table 1. Results of receiver operation characteristics and Kaplan-Meier survival analysis for each factor

Factor	cut-off index	area under the curve	p-value	Hazard ratio (95%CI)	p-value
CysC/Cr	> 1.345	0.614	< 0.01	6.32 (2.87 – 13.92)	< 0.01
LSD	present	0.626	< 0.01	3.60 (1.67 – 7.73)	< 0.05
Fall-ability	present	0.703	< 0.001	4.83 (2.16 – 10.21)	< 0.001
CKD	present	0.612	< 0.05	2.56 (1.06 – 6.20)	< 0.05
pr-MOF	present	0.685	< 0.001	4.81 (2.08 – 9.39)	< 0.001

In Cox regression analysis, the presence of prevalent MOF (pr-MOF), fall-ability, lifestyle-related diseases (LSD), chronic kidney diseases (CKD) ≥ Grade3a, and higher CysC/Cr had significant higher risk ratios with univariate models. In these, the presence of LSD and fall-ability had significant higher risk ratios with multivariate model. All the binary factors had COI as the presence of each event such with 0.626, 0.703, 0.612, and 0.685 of area under the curve for LSD, Fall-ability, CKD, and pr-MOF, respectively. CysC/Cr also had COI (1.345) with 0.614 of the area under the curve. In the Kaplan-Meier survival analysis, CysC/Cr > COI, Fall-ability, pr-MOF, LSD, CKD ≥ Grade 3 b was significantly higher in descending order of Hazard ratio (6.32, 4.83, 4.81, 3.60, 2.56, respectively) (Table 1).

Conclusion: These results suggest that CysC/Cr may be a predictor of MOF or a risk factor if it exceeds the COI. This value is the reciprocal of Cr/CysC, and if Cr/CysC reflects muscle mass, CysC/Cr is assumed to reflect low relative muscle mass. It is supposed that this is also affected by sex difference and age. There seems to be a correlation between MOF and CysC/Cr. Early measurement of CysC/Cr facilitates screening for fractures. As a result, it may be easier to implement fracture prevention programs such as drug interventions such as OPD and exercise habit guidance.

Disclosure of Interests: None declared

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AB1008

CHARACTERIZATION OF THE RISK OF OSTEOPOROSIS IN A COHORT OF RHEUMATIC PATIENTS DURING 10 YEARS OF FOLLOW-UP.

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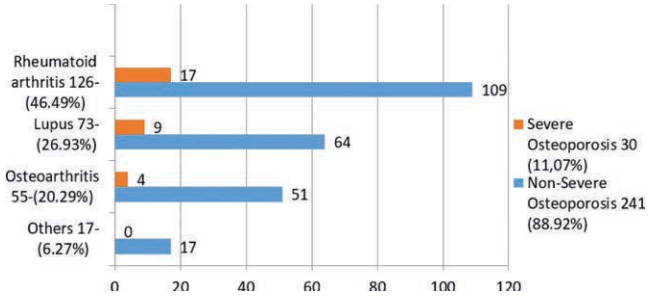
Background: Osteoporosis is the most common cause of fractures. The lifetime risk of fracture after age 50 is 40% for women and 13% for men.
Objectives: Patients with rheumatological diseases are at greater risk for the development of osteoporosis, either due to the natural history of their disease or due to the side effects of the medications used. We proposed to carry out this study.
Methods: Retrospective study aimed at determining the presence of risk factors in patients over 50 years of age who attend the Rheumatology service of a hospital in Venezuela during a follow-up from January 2010 to December 2020 in order to know these risk factors and thus generate strategies that allow better orienting the care of these patients.
Results: The main group of patients was constituted by the female gender and the ages between 50 and 65 years. The main rheumatological pathology was rheumatoid arthritis, followed by Lupus, Osteoarthritis in 3 place and finally in the last box other entities other than those indicated.



Graph 1. Prevalence of Osteoporosis due to rheumatological pathologies.

Conclusion: The 2 main risk factors for the development of osteoporosis were the use of steroids and obesity. The main type of osteoporosis of the 2 categories described was non-severe. The main group of rheumatological patients most associated with osteoporosis were those with rheumatoid arthritis. 12% of the patients with rheumatic disease and osteoporosis did not have appropriate therapy.

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Disclosure of Interests: None declared
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AB1009

EXERCISE IS ASSOCIATED WITH HIGHER BONE MINERAL DENSITY IN PATIENTS WITH POLYMYALGIA RHEUMATICA AND VASCULITIDES

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Background: Exercise is an effective non-pharmaceutical intervention for osteoporosis (OP). However, it has not yet been explicitly validated whether it is associated with bone mineral density (BMD) in patients suffering from polymyalgia rheumatica (PMR) and vasculitides.

Objectives: To assess whether exercise is associated with BMD in PMR and vasculitis patients.
Methods: We evaluated baseline visits of patients enrolled in the monocentric, prospective "Rh-GIOP" cohort. Patients were included when having PMR or any kind of vasculitis. Simple and multiple linear regression models with minimum T-score (lumbar spine or hip, whichever was lowest) as the dependant variable were constructed. A dose-response analysis (frequency of exercise per week) was conducted in patients who were doing any kind of exercise. In multiple regression, we adjusted for potential confounders associated with minimum T-scores in an analysis of the overall cohort (*manuscript in preparation*): age, sex, menopause, body mass index, bisphosphonate use, denosumab use, current glucocorticoid dose, proton-pump inhibitor use, history of vertebral fractures, health assessment questionnaire scores, alkaline phosphatase levels, and gamma-glutamyltransferase levels. Multiple imputation by chained equations was used to handle missing data.
Results: 198 patients were included. The mean age was 68 ± 11 years, 68% were females, and the most common diseases were PMR (36%), giant cell arteritis (26%), and granulomatosis with polyangiitis (17%). The mean minimum T-score was -1.74 ± 0.9. Five patients had a disease duration of less than three months. In both unadjusted (Figure 1) and adjusted analysis, exercise was positively associated with minimum T-scores (unadjusted: $\beta = 0.36$; 97.5% CI 0.09 to 0.63; $p = 0.01$; adjusted: $\beta = 0.30$; 0.04 to 0.56; $p = 0.02$). In exercising patients, there was no association between frequency and minimum T-scores (p(ANOVA) = 0.66.
Conclusion: In PMR and vasculitis, exercise is positively associated with BMD. We adjusted for several covariates, including health assessment questionnaire scores, so it is unlikely that the association between exercise and BMD is only caused because generally healthier patients have a higher likelihood of exercising. However, we found no dose-response relationship by looking at exercise frequency. This is probably due to confounding caused by different kinds of exercises. E.g., weight-bearing exercise is thought to be more effective in elevating BMD. Furthermore, our analysis might have been underpowered (too few patients) to assess differences within the group of exercising patients. Our findings underpin the general advice given to most patients suffering from low bone mass or OP irrespective of their underlying disease, which is to start or to continue exercising within the scope of personal possibilities. Of note, this study is of cross-sectional nature and must be interpreted accordingly as residual confounding cannot be fully ruled out. We plan for the future longitudinal analyses.

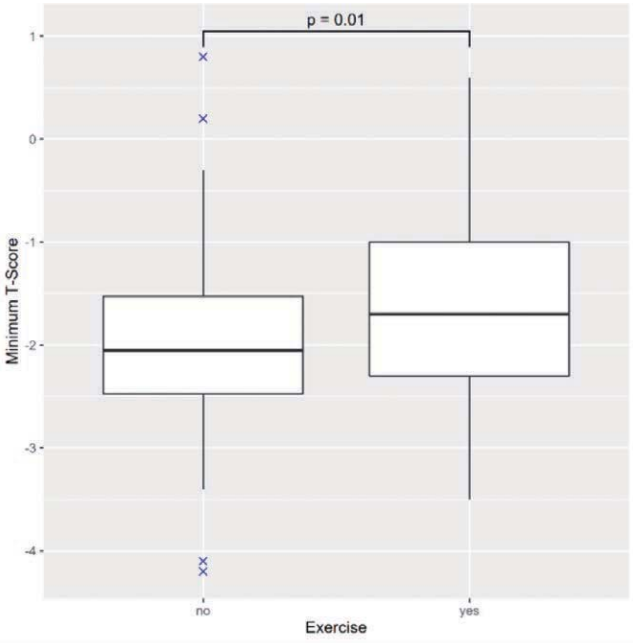

Figure 1.

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Disclosure of Interests: Andriko Palmowski: None declared, Edgar Wiebe Grant/research support from: Travel expenses from Medac, Sandra Hermann Paid instructor for: Lecture fees from AbbVie, Burkhard Muche Speakers bureau: consultancy or speaker fees and/or conference expenses from Amgen, Gilead, Galapagos, UCB and Stadapharm, Paid instructor for: consultancy or speaker

fees and/or conference expenses from Amgen, Gilead, Galapagos, UCB and Stadapharm, Consultant of: consultancy or speaker fees and/or conference expenses from Amgen, Gilead, Galapagos, UCB and Stadapharm, Frank Buttgereit Speakers bureau: consultancy fees, honoraria and travel expenses from Abbvie, AstraZeneca, Grünenthal, Pfizer, and Roche, and grant support from Abbvie, Pfizer and Roche, Paid instructor for: consultancy fees, honoraria and travel expenses from Abbvie, AstraZeneca, Grünenthal, Pfizer, and Roche, and grant support from Abbvie, Pfizer and Roche, Consultant of: consultancy fees, honoraria and travel expenses from Abbvie, AstraZeneca, Grünenthal, Pfizer, and Roche, and grant support from Abbvie, Pfizer and Roche, Grant/research support from: consultancy fees, honoraria and travel expenses from Abbvie, AstraZeneca, Grünenthal, Pfizer, and Roche, and grant support from Abbvie, Pfizer and Roche

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AB1010 FACTORS ASSOCIATED WITH LONGITUDINAL BONE MINERAL DENSITY CHANGES IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is a long-term inflammatory disorder affecting the joints. It is associated with osteoporosis, possibly linked to inflammation around affected joints and glucocorticoid medication. To our knowledge, longitudinal analysis of a UK based cohort of patients with RA has not been carried out. The impact of average tissue thickness on bone mineral density (BMD) has not been studied longitudinally in RA.

Objectives: This study aimed to identify factors that affect the rate of BMD change in patients with RA in a UK based cohort.

Methods: RA patients referred for multiple routine DEXA scans at the Royal Lancaster Infirmary from 2004-2019 were studied. Demographic and physical data such as age, sex, weight and height were collected. BMD in grams/centimetre2 and average tissue thickness were collected from DEXA images of the left and right hip (femoral neck and total femur), and the spine (L1-L4). BMD was modelled at the regions of the hip and spine using mixed-effects linear models. Age, sex, average tissue thickness and weight were used as explanatory variables.

Results: 1135 scans from 496 patients (80.4% female) with more than one scan were included, mean age was 64.1 (standard deviation 12.5). Fixed effect size and confidence intervals for each variable are shown in the Table 1. Female sex had a negative fixed effect at the hip but no significant effect on BMD change at the spine. Average tissue thickness had a significant positive fixed effect at all regions of the left and right hip, but no significant effect at the spine. Weight showed a significant positive fixed effect with BMD at the hip but no significant effect at the spine.

Conclusion: This study demonstrates that in RA patients, sex is associated with an increased rate of BMD loss at the hip but not at the spine. It also shows that weight and average tissue thickness are associated with lower BMD loss over time. This could be due to increased inflammation at the hip compared to the spine leading to osteoporosis. This study supports longitudinal data from other countries suggesting that factors associated with the rate of BMD change are different at the hip and the spine in RA (1). Average tissue thickness is associated with a reduced rate of BMD loss at the hip in RA patients, which is a novel finding. Average tissue thickness could be used in conjunction with other risk factors to help identify RA patients at risk of osteoporosis. This study may have been underpowered to detect changes at the spine. There may have been selection bias not all patients were routinely referred for repeat DEXA scans.

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Disclosure of Interests: None declared

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AB1011 FACTORS RELATED TO GLUCOCORTICOID-INDUCED OSTEOPOROSIS AND FRAGILITY FRACTURES IN YOUNG SUBJECTS.

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Background: Glucocorticoid (GC) treatment is the most frequent cause of osteoporosis (OP) in young subjects. However, the factors related to the development of glucocorticoid-induced osteoporosis (GIOP) and fragility fractures (FF), and consequently, the therapeutic approach to GIOP in young populations is not well established.

Objectives: Analyze the prevalence of GIOP and FF in GC-treated patients and compare the risk factors related to their development according to age (< and ≥50 years).

Methods: 127 patients (62±18 years) receiving chronic GC treatment were included (≥5 mg/day of prednisone, >3 months). The clinical data collected included: dose and duration of GC treatment, disease activity, previous FF, anthropometric data, bone metabolism parameters (including bone turnover markers and the presence of hypogonadism), bone mineral density (by DXA; defining densitometric OP: T-score ≤-2.5 or Z-score ≤-2, depending on the age of the patient), trabecular bone score (by DXA), and vertebral fractures (X-ray). GIOP was defined as densitometric OP and/or FF. Results were compared between subjects < and ≥50 years old.

Results: The prevalence of GIOP was similar in both age groups: <50 (n=36) 44.4% vs. 46.1% ≥50 years (n=91). Five subjects <50 (13.8%) and 30 ≥50 years (33%) presented FF (p=0.05). Young subjects with FF tended to be >40 years, have a higher body mass index (BMI) (25.4 *vs.* 23.3, p=n.s.), and inflammatory disease activity (CRP 0.90 *vs.* 0.06mg/dL, p=0.06). When analyzing the differential risk factors related to FF depending on age, a higher body mass index (BMI) (29.63 *vs.* 26.95, p=0.048) and inflammatory disease activity (PCR -0.87 *vs.* -2.51 [log scale], p=0.03) were observed in young subjects, while low lumbar T-scores (-1.08 *vs.*-0.06 DE, p=0.003) and higher cumulative GC-doses (9.11 *vs.* 8.56 g, p=0.03) were differential factors in subjects over 50. Hypogonadism was a risk factor independent of age (OR 4.89; 95%CI 1.36-17.59), being associated with the presence of FF in both age groups.

Conclusion: More than 40% of the patients receiving GC developed GIOP, with a similar prevalence in both age groups (< and ≥50 years); however, FF are less common in young subjects. Hypogonadism is a determining risk factor for FF independent of age. In addition, young subjects with FF tend to be older, with a higher BMI and disease activity, and, thus, evaluation of these risk factors can improve the identification of subjects at increased risk of fracture.

Disclosure of Interests: None declared

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AB1012 MANAGEMENT OF BREAST CANCER TREATMENT INDUCED BONE LOSS- RE-AUDIT

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Background: Breast cancer treatment therapies (aromatase inhibitors (AI)) are associated with early menopause and adverse effect on bone density. Identifying high-risk patients and managing them appropriately will help reduce their fracture risk.

Table 1

	Effect size estimate (95% confidence interval)		
Location	Sex	Weight	Average Tissue Thickness
Left femur	-0.104(-0.135,-0.074)*	0.004(0.004,0.005)*	0.022(0.018,0.025)*
Left neck	-0.088(-0.115,-0.061)*	0.003(0.002,0.003)*	0.015(0.012,0.019)*
Right femur	-0.136(-0.165,-0.106)*	0.004(0.004,0.005)*	0.022(0.018,0.026)*
Right neck	-0.06 (-0.094,-0.026)*	0.003(0.002,0.003)*	0.016(0.012,0.019)*
L1	-0.001(-0.038,0.036)	0(-0.001,0.001)	0.003(-0.001,0.006)
L2	0.007(-0.037,0.05)	-0.001(-0.001,0)	0(-0.003,0.004)
L3	0.021(-0.022,0.065)	-0.001(-0.002,0)	-0.001(-0.005,0.002)
L4	0.01(-0.035,0.054)	0(-0.001,0.001)	0.001(-0.003,0.005)

Objectives: We wanted to ascertain whether our management of breast cancer patients on aromatase inhibitors (AI) referred to osteoporosis clinic were as per guidelines. A consensus position statement from a UK expert group regarding breast cancer treatment induced bone loss, published with the support of the National Osteoporosis Society, the National Cancer Research Institute, Breast Cancer Study Group and the International Foundation.
The guideline recommend lifestyle advice for low risk patients; calcium plus vitamin D supplementation and lifestyle advice for medium risk; bisphosphonate, calcium plus vitamin D supplementation and lifestyle advice for high risk.
Methods: This is a re-audit cycle conducted for all patients referred to the osteoporosis clinic who were treated with aromatase inhibitors for breast cancer between 2016-2020. Patients were divided into two algorithms: Algorithm 1: women who had experienced premature menopause associated with ovarian suppression with or without AI. Algorithm 2: Postmenopausal women receiving treatment with an AI. T-scores were used to stratify patients in algorithm 1 into high risk (HR- T score <-2), medium risk (MR-T score -1 to -2) and low risk (LR- T score >-1). Algorithm 2 into high risk (HR-T score <-1) medium risk (MR -T score >-1).
Results:

Table 1. Showing the results of Audit 1 and Re-audit

	Audit 1		Re-audit	
Total Patients	54		72	
Data collected	2014-2016		2016-2020	
Gender	Female 100 (%)		Female 100 (%)	
Age in years	45-96		38-92	
Median age	77		68	
No of Osteoporotic patients	31		41	
No of Osteopenic patients	23		31	
Algorithm 1:	Total patients= 23	• 18 HR • 5MR • LR nil	Total patients = 20	• 19HR • 1 MR
Algorithm 2:	Total patients =31	• 31 HR • MR-nil • LR nil	Total patients =52	• 45HR • 5MR • 2LR
Drug therapy	45		63	
Bisphosphonates	21		49	
Denosumab	23		14	
Teriparatide	1		0	
Declined treatment	0		1	
Lifestyle/Vit D & Cal	9		6	
Lifestyle advice only	0		2	

Conclusion: Re-audit showed all patients were on AI and treated appropriately. As compare to audit 1, all high risk group patients were treated with drug therapy and bisphosphonate was the first line therapy as per guidelines. It was recommended that patients with risk of osteoporosis should be referred and treated according to their risk stratification. It is a collective responsibility of Breast surgeons, Geriatrician, Frailty team, Oncologist, Rheumatology and General Practitioners).All patients should have repeat bone density scan in 2 years' time after initial bisphosphonate therapy. The next audit cycle will be conducted in five years' time.
Disclosure of Interests: None declared
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AB1013 SCHOOL FOR DOCTORS ON THE PROBLEM OF OSTEOPOROSIS - "START WITH YOURSELF".

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Background: Observing in practice the attitude of the medical community to the problem of OP, we decided to conduct a course of training lectures for doctors within the framework of the program "Start with yourself" on the basics of diagnosis and treatment of this disease. After the lecture material, the fracture risk was calculated using the FRAX (Fracture Risk Assessment Tool) in the audience before and after the two-energy X-ray absorptiometry (DXA). If necessary, additional examination and treatment were prescribed.
Objectives: To evaluate the frequency of decrease in bone mineral density in doctors, to raise awareness about the frequency of decrease in bone mineral density (BMD), to assess the attitude to therapy.
Methods: The risk of fractures according to FRAX was calculated for doctors of therapeutic specialties, DXA was performed at the Center for Osteoporosis of the A. B. Zborovsky Research Institute of KIER, Volgograd. Bone mineral density (BMD) was determined on the Lunar DPX (GE) apparatus.
Results: The average age of 59 trainees was 54 ± 10.55 (M±σ) years, 36 women were aged 50 years and older, 23 were under the age of 50, the average body mass index –BMI) was 26.51 ± 4.8 kg/m2. 47 (79.6%) of 59 showed a decrease in bone mineral density (BMD) below the norm (according to the T/Z criterion, according to age) in at least two positions. 15 (25.4%) of them showed a decrease in BMD according to the T criterion by -2.5 SD or lower, which corresponds to the diagnosis of "Osteoporosis". Of these 15 people, 9 had previously undergone DXA, were diagnosed with OP, and drug therapy was prescribed. Only 3 students are constantly taking medications. Another 6 people were previously treated, but for the last 2-3 years they have not been examined and have not taken anything. OP was detected for the first time in 6 listeners, for 2 listeners the diagnosis of OP was a complete surprise, 4 guessed about a possible decrease in BMD, but did not expect to detect such low indicators (T criterion -2.5 and -2.6 SD for the lowest values). Out of 5 students under 50 years of age with a decrease in BMD by the Z criterion of less than -2.0 SD, 4 had significant risk factors. No obvious risk factors were identified in 1 listener. The average values of TL1-L4 were -1.26 ± 1.06 SD [0.8 to -3.1], ZL1-L4 = -0.68 ± 0.9 [+1 to -2.7], the average values for TNeck were -1.14 ± 1.04 [1.5 to -2.7], Z Neck -0.26 ± 0.88 [1.9 to -1.7]. An additional result of the educational event was a change in the structure of patients referred to DXA. The proportion of patients with osteoporosis and osteopenia among the surveyed increased from 65% to 88% after a month after the schools.
Conclusion: As a result of the study, a high percentage of detection of a decrease in BMD in female doctors was found. Low compliance to treatment was found in doctors over 50 years of age, a positive attitude to preventive measures in younger doctors. Considering that we have just started the educational program, the first students sought to get examined for personal reasons, which probably overestimates the detectability of reduced BMD. At the same time, it should be noted that doctors with an existing history of low-traumatic fractures did not come for examination, citing high employment. It is necessary to further study the problem of the prevalence of BMD reduction among doctors, increase awareness of the problem of OP and the need for early preventive measures to prevent the development of OP. Conducting theoretical and practical classes in small groups based on the assessment of their own survey data makes it possible to increase the interest of practitioners in studying the problem of OP. The greatest interest on the part of listeners is caused by the DXA procedure itself with the decryption of protocols. When creating motivation for doctors' personal interest in maintaining personal bone health, the likelihood of a more attentive attitude of doctors to the prevalence of OP among the population increases.
Disclosure of Interests: None declared
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AB1014 FRACTURES REDUCTION WITH OSTEOPOROTIC TREATMENTS IN PATIENTS OVER 75-YEAR-OLD: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Osteoporosis consists in the reduction of bone mineral density and increased fracture risk. Age is a risk factor for osteoporosis. Although many treatments are available in osteoporosis, there is limited data regarding their efficacity in older people.
Objectives: We aimed to evaluate the efficacy of osteoporosis treatments in patients over 75 years old.
Methods: we reviewed all published studies in MEDLINE, COCHRANE and EMBASE including patients over 75-year-old treated by osteoporosis drugs and focused on vertebral fractures or hip fractures.
Results: we identified 4393 records for review. 4216 were excluded after title/abstract review. After full text review, 19 records were included in systematic review. Most of the studies showed a reduction of vertebral fracture with osteoporosis treatments but non-significant results were observed for hip fractures. Meta-analysis of 10 studies showed that osteoporosis treatments significantly reduced the occurrence of vertebral fractures at one (OR=3.67; 95%CI=2.50-5.38) and three years (OR=2.19; 95%CI= 1.44-3.34) as well as those of hip fractures at one (OR=2.14; 95%CI=1.09-4.22) and three years (OR=1.31, 95%IC=1.12-1.53).
Conclusion: osteoporotic treatments showed to be effective in the reduction of vertebral and hip fractures in older people. However, majority of data derived from *post hoc* and pre-planned analyses or observational studies.
Disclosure of Interests: None declared
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AB1015

SUSTAINED SYNERGISTIC EFFECT ON BONE MINERAL DENSITY TREND WITH SHORT TERM COMBINATION OF TERIPARATIDE AND DENOSUMAB FOLLOWED BY DENOSUMAB ALONE IN POSTMENOPAUSAL WOMEN - A SINGLE INDIAN CENTRE EXPERIENCE.

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Background: Use of Teriparatide (PTH) with Denosumab (Dmab) have shown to have a synergistic effect on the bone mineral density (BMD) of both Hip and Spine[1] because Dmab completely inhibits the PTH induced bone resorption and does not interfere with the bone formation.
Objectives: Since PTH has a limited period of approved use, a short term (6 months) use of PTH in combination with Dmab followed by continued use of Dmab may show a sustained synergistic effect of the combination.
Methods: The BMD trends from real time data from a central dual-energy x-ray absorptiometry (DXA) at our centre in India was studied retrospectively to see if the effect was sustained. Women with postmenopausal osteoporosis who were treated with a combination of Dmab 60 mg via subcutaneous injection (sc) at 6 monthly interval along with PTH 20 mcg sc daily for the first 6 months (Combo), followed by Dmab alone for the next six months were inculded in the study group. Average BMD at L2, L3 and L4 (sp BMD), and Right and Left Hip (hip BMD) were studied from before treatment (a BMD), after the Combo treatment (b BMD) and after 6 months of the second injection of Dmab (c BMD). The mean percentage trend change between a-b BMD and b-c BMD were evaluated. Out of the patients treated with the protocol, 25 were randomly chosen for the retrospective analysis. The least significant change (LSC)[2] from a single centre DXA was used to validate the findings.
Results: The percentage change after the treatment for 6 months with the Combo was found to be 5.22% in the Spine (LSC= 2.6%)[2] and 4.13% in the hip (LSC=3.6%)[2]. The trend after use of Dmab alone was 5.39% in the spine and 2.93% in the hip showing sustained synergistic effect of the Combo for at least 6 months with the use of Dmab alone. The effect was more profound in the spine than the hip. A $p>0.05$ was considered statistically significant. Table 1 shows the percentage BMD changes.

Table 1. Percentage BMD changes

BMD trend (n=25)	sp BMD (LSC – 2.6%)	hip BMD (LSC – 3.6%)
a-b BMD	5.22%	4.13%
b-c BMD	5.39%	2.93%

sp BMD - Mean of L2,L3 & L4 Spine BMD, hip BMD - Mean of Right and Left Hip BMD, a-b BMD - Percent change in BMD from before treatment to 6 months of PTH & Dmab, b-c BMD -Percentage change in BMD form after 6 of Dmab & PTH to next 6 mths Dmab alone and LSC – Least significant change from a single DXA machine.

Conclusion: These findings suggest that a short term combination of Dmab and PTH for 6 months followed by Dmab alone shows sustained synergistic effect on the BMD trend which was more profound in the spine than the hip. This would help in judicious and cost effective utilisation of the limited period of PTH use.

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AB1016

ROMOSOZUMAB AS A TREATMENT FOR OSTEOPOROSIS: PREDICTORS OF EFFICACY AT 12 MONTHS

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Background: Romosozumab (ROMO) is an antisclerostin antibody that is used in the treatment of severe osteoporosis (OP). In March 2019, ROMO was approved for use in Japan for treating severe OP in clinical practice, causing an increase in its prescription in our institute. Although efficacy data for ROMO have been presented in clinical trials, there is a lack of real-world data. In our experience, ROMO treatment results in significant bone mineral density (BMD) gain in some patients, but not all. Therefore, understanding the predictors that enhance the efficacy of ROMO treatments to achieve BMD gain is essential.
Objectives: This study investigated the efficacy of a 12-month ROMO treatment in patients with OP and explored the efficacy predictors of increased BMD.
Methods: Our study included 52 patients with OP, who were started on ROMO treatment between June 2019 and August 2020. The following information was collected: 1) baseline characteristics, 2) time-course of BMD (lumbar spine [LS] and total hip [TH]) and bone turnover markers (BTM; bone-specific alkaline phosphatase [BAP], type I procollagen-N-propeptide [P1NP], type I procollagen-N-propeptide[NTX], and tartrate-resistant acid phosphatase-5b [TRACP-5b]), 3) multiple regression analysis results following Spearman's correlation analysis of increased BMD values (%) at 12 months and BL characteristics, including BTM change (%) at one month, to investigate the efficacy predictors of ROMO.
Results: 1) The mean age of the participants was 72.9 years (48 female and four male). Of the 52 understudied patients, 78.8% had past insufficiency fractures, whereas 21.2% had been treated with concomitant prednisolone. Furthermore, 21 patients had primary OP, 20 had rheumatoid arthritis, nine had glucocorticoid-induced OP, and two had other conditions. Pretreatments for OP were bisphosphonate (33 patients), vitamin D (6), none (5), selective estrogen receptor modulator (4), and denosumab (3). 2) Both mean LS- and TH-BMD significantly increased in the patients for whom ROMO administration was continued for 12 months. The average percentage changes of LS- and TH-BMD were 7.1% and 1.6% at six months and 11.7% and 3.0% at 12 months, respectively (Figure 1). However, BAP and P1NP increased steeply at one month, followed by a gradual decrease. As observed, the average percentage changes of BAP and P1NP were +70.1% and +166.8% at one month, +50.3% and +91.7% at six months, and +24.4% and +41.5% at 12 months, respectively. The results also showed that TRACP-5b decreased from one to 12 months, with the average percentage changes being –22.9% at one month, –13.8% at six months, and –17.7% at 12 months. Moreover, NTX, a bone-resorptive marker, was slightly increased during ROMO treatment. 3) Multiple regression analysis results revealed that the baseline BAP and percentage calcium changes at 12 months were significant factors positively correlated with the percentage change of LS-BMD at 12 months. As observed, the baseline T-score of LS-BMD was a significant factor negatively correlated with the percentage change of LS-BMD at 12 months. The standardized partial regression coefficient values were +0.68, +0.26, and –0.40, respectively. Moreover, the multiple regression analysis results revealed no significant factor that was correlated with the percentage changes of TH-BMD at 12 months.

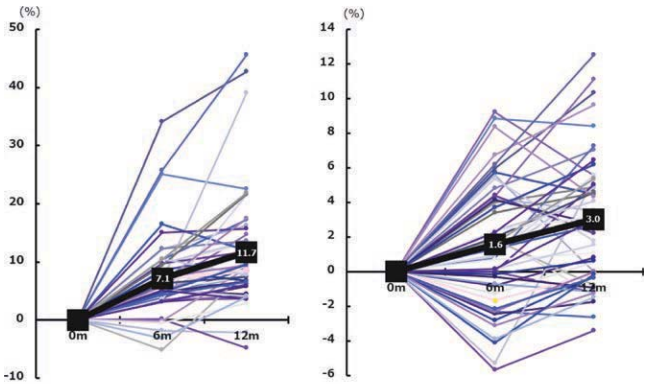

Figure: Time-course of % Change of Bone Mineral Density (Left: lumbar spine, Right: total hip)
Bold lines indicated averaged values. Thin lines indicated individual values of each patient.

Figure 1.

Conclusion: ROMO treatments rapidly increased BMD, especially LS-BMD, and changed BTM after one month. Baseline BAP were correlated with increased LS-BMD but not with TH-BMD. The factors correlated with increased BMD may differ between LS-BMD and TH-BMD.

Disclosure of Interests: None declared
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AB1017

RADIOFREQUENCY ECHOGRAPHIC MULTI-SPECTROMETRY (REMS) AND DUAL-ENERGY X-RAYS ABSORPTIOMETRY FOR THE EVALUATION OF BONE MINERAL DENSITY IN A PERITONEAL DIALYSIS SETTING

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Background: Radiofrequency echographic multi-spectrometry (REMS) is a novel ultrasound-based technique that has shown good reliability in the assessment of bone mineral density (BMD).

Objectives: The aim of this study was to compare the performance of the REMS BMD assessment with dual-energy X-rays absorptiometry (DXA) in a cohort of patients affected by end-stage renal disease undergoing peritoneal dialysis (PD).
Methods: Consecutive patients referring to the PD clinic of our hospital were enrolled. Lumbar spine and proximal femur REMS scans were performed, and lumbar spine (anteroposterior and laterolateral) and proximal femur DXA scans were performed as well. Clinical data were extracted from medical records. The risk assessment outputs of two fracture risk algorithms (FRAX and DeFRA), calculated upon the worst BMD obtained from either technique were compared as well. Analysis of variance (ANOVA) with post hoc analysis (Bonferroni) and a two-sided Student's t-test were used to estimate the absolute differences between groups. Written informed consent was obtained from all participants included (protocol 1483 CESC).
Results: 41 total patients were enrolled (Table 1). No significant differences were documented between the BMD T-scores measured through DXA or REMS at the proximal femur. At the lumbar spine, the DXA laterolateral T-score was not significantly different from that of REMS, while the DXA anteroposterior T-score was significantly higher than both the anteroposterior DXA and the REMS measurements (Figure 1, panel A and B). When either DXA or REMS was adopted, no significant difference in the fracture risk estimate was found for both algorithms (Figure 1, panel C and D).

Table 1. anthropometrics, clinical and biochemical characteristics of the enrolled sample. CKD, chronic kidney disease; PTH, parathyroid hormone; ALP, alkaline phosphatase; IQR, interquartile range; VFA, vertebral fracture assessment.

Sample size (M)	41 (29)
Age (y)	
Median [IQR]	62 [52-73]
Height (cm)	
Median [IQR]	170 [165-176]
Body weight (Kg)	
Median [IQR]	74 [61-83]
Body mass index (Kg/m2)	
Median [IQR]	25 [22-27.8]
Disease duration – CKD (months)	
Median [IQR]	132 [48-140]
Dialysis duration (months)	
Median [IQR]	10 [3-24]
S-calcium (mg/dL)	
Median [IQR]	9.1 [8.6-9.4]
S-phosphorous (mg/dL)	
Median [IQR]	5.4 [4.6-6.4]
PTH (pg/mL)	
Median [IQR]	31.4 [22.8-46.8]
25OH Vitamin D (nmol/L)	
Median [IQR]	53 [36-72]
Patients with morphometric fractures (VFA)	15%
Patients with femoral fractures	2.4%
Total n° of morphometric fractures	12

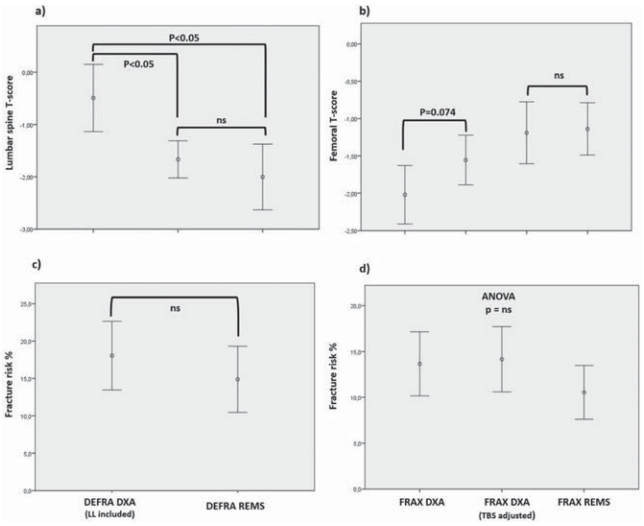

Figure 1. comparison of the mean T-scores (error bars represent 95%CI) measured with DXA and REMS at the lumbar spine (panel A), and at the femur (panel B). Comparison between the DeFRA DXA and REMS-derived outputs (panel C) and FRAX DXA and REMS-derived outputs (panel D) raw and after correction for TBS. DeFRA, FRAX-derived risk assessment tool; FRAX, Fracture Risk Assessment tool; AP, anteroposterior; LL, latero-lateral; TH, total hip; FN, femoral neck; TBS, trabecular bone score.

Conclusion: Our data showed a good agreement, in a real-life PD setting, between the DXA and REMS-derived BMDs and in the consequent fracture risk assessment obtained with the FRAX or DeFRA tools.
Disclosure of Interests: Angelo Fassio: None declared, Stefano Andreola: None declared, Davide Gatti Paid instructor for: Amgen, Celgene Eli-Lilly, MSD-Italia, Organon, UCB., Consultant of: Amgen, Celgene Eli-Lilly, MSD-Italia, Organon, UCB., Matteo Gatti: None declared, Giovanni Gambaro Speakers bureau: Vifor Pharma, Maurizio Rossini Speakers bureau: Abiogen, Amgen, Abbvie, BMS, Celgene, Eli-Lilly, Galapagos, Grunenthal, MSD, Novartis, Pfizer, Sanofi, Sandoz, Theramex, UCB., Ombretta Viapiana: None declared, Giulia Zanetti: None declared, Francesca Pistillo: None declared, Valeri Messina: None declared, Giovanni Adami: None declared
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AB1018

RELATIONSHIP BETWEEN AORTIC CALCIFICATIONS AND DXA AND RADIOFREQUENCY ECHOGRAPHIC MULTI-SPECTROMETRY (REMS) ACQUISITIONS

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Background: Data on the relationship between peritoneal dialysis (PD), BMD and aortic calcifications (AOC) are lacking.
Objectives: to study the relationship between the degree of AOC and DXA and Radiofrequency Echographic Multi-Spectrometry (REMS) acquisitions.
Methods: Consecutive patients referring to the PD our clinic were enrolled. Lumbar spine (LS) and proximal femur REMS scans were performed, and LS (anteroposterior and laterolateral) and proximal femur DXA scans were performed as well. The degree of AOC was assessed through the semiquantitative score described by Kauppila et al, and applied to the laterolateral LS DXA scans. To test for correlations between different variables, we used the Pearson's correlation for continuous variables and Spearman's rho for discrete variables. Multiple regression analysis was performed to adjust for age and body mass index (BMI) the correlation between BMD and the CKD duration. Written informed consent was obtained from all participants (protocol 1483CESC).
Results: 41 total patients were enrolled (29 males, 19 females). Median disease duration of CKD [IQR]: 132 months [48-140]. 15% had vertebral fractures at the DXA Vertebral Fracture Assessment (VFA). The median calcification score [IQR] was 2 [0-6] (min-max 0-20). We found a statistically significant positive correlation of moderate strength between the total calcification score and the difference between the DXA AP T-score and the DXA LL T-score at the LS (p<0.01, Spearman's rho = 0.402), Figure 1.

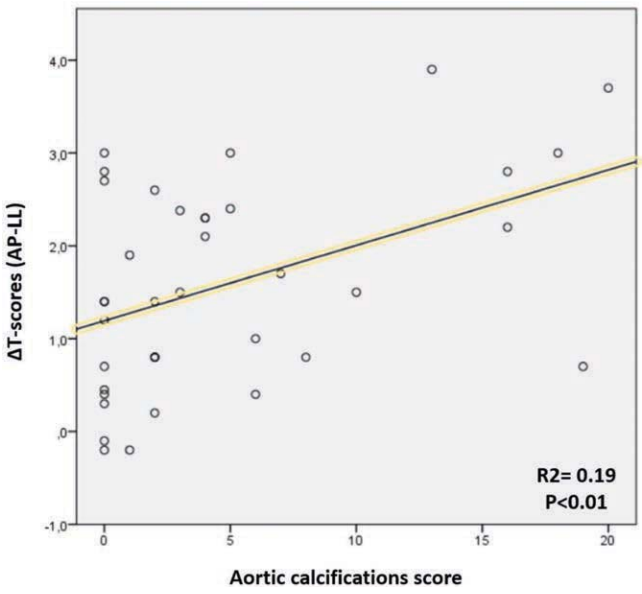

Figure 1. scatter plot reporting the relationship between the difference between the AP and LL T-scores and the aortic calcifications score.

After adjustment for confounders, we found a significant negative between the LS and femoral neck BMD measured through REMS and CKD duration (Table 1). The same correlation was not significant then BMD was assessed with DXA.

Table 1. multiple linear regression analysis for REMS T-score at each site after adjustment for age and BMI. BMI, body mass index; β, standardised coefficient.

REMS lumbar spine T-score		
	β	p
CKD duration (months)	-0.228	0.035
Age (years)	-0.511	<0.01
BMI (kg/m2)	0.566	<0.01
REMS femoral neck T-score		
	β	p
CKD duration (months)	-0.210	0.04
Age (years)	-0.612	<0.01
BMI (kg/m2)	0.484	<0.01
REMS total hip T-score		
	β	p
CKD duration (months)	-0.153	0.219
Age (years)	-0.523	<0.01
BMI (kg/m2)	0.560	<0.01

Conclusion: Our study confirmed that the overestimation of DXA BMD assessed with the anteroposterior scan is indeed influenced by AOC. Furthermore, our data suggest that REMS might be an interesting tool for the investigation of bone changes in CKD.

Disclosure of Interests: Angelo Fassio: None declared, Stefano Andreola: None declared, Davide Gatti Speakers bureau: Amgen, Celgene Eli-Lilly, MSD-Italia, Organon, UCB, Paid instructor for: Amgen, Celgene Eli-Lilly, MSD-Italia, Organon, UCB, Matteo Gatti: None declared, Giovanni Gambaro Speakers bureau: Vitor Pharma, Ombretta Viapiana: None declared, Valeri Messina: None declared, Giulia Zanetti: None declared, Francesca Pistillo: None declared, Maurizio Rossini Speakers bureau: Abiogen, Amgen, Abbvie, BMS, Celgene, Eli-Lilly, Galapagos, Grunenthal, MSD, Novartis, Pfizer, Sanofi, Sandoz, Theramex, UCB., Giovanni Adami: None declared

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AB1019 THE EFFECTS OF THREE DIFFERENT VITAMIN D3 SUPPLEMENTATION REGIMENS IN DEFICIENT SUBJECTS ON INFLAMMATORY CYTOKINES – A RANDOMISED OPEN-LABEL PARALLEL GROUPS STUDY

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Background: The effects of cholecalciferol supplementation on the regulation of inflammatory cytokines are still unclear.

Objectives: This is a preliminary analysis on exploratory outcomes the DIBA/11 RCT [1,2] and aimed to compare the effects on serum inflammatory cytokines of three different regimes of cholecalciferol supplementation in vitamin D-deficient subjects.

Methods: We evaluated, in healthy subjects affected by vitamin D deficiency (defined as 25OHD<20 ng/mL), 18 to 60 years of age, the efficacy of three different oral supplementation regimens: daily 10,000Iu administered for 8 weeks (group A), weekly 50,000Iu (group B) for 12 weeks and biweekly 100,000Iu (group C) for 12 weeks. Serum TNFα, interleukin-6 (IL6), interleukin-17 (IL17) and interleukin-10 (IL10) were dosed at baseline, Day 28, 53, 84 and 112. This study was approved by the institutional research committee (protocol identification: DIBA/11,EudraCT Number:2017-000194-36). Supported by Abiogen Pharma, Italy).

Results: A total of 75 subjects were randomized to receive one supplementation regimen. The descriptive of the sample at baseline and relative cytokines levels at the various observation points are reported in Table 1. The absolute changes of IL6, IL17 and IL10 are depicted in Figure 1. No significant differences were found among the three groups. TNFα was undetectable at baseline and at any time point.

Table 1. anthropometrics and laboratory parameters at baseline (mean values ± standard deviation)

Parameter	All patients (N=75)	Daily 10.000 Ui (N = 25)	Weekly 50.000 Ui (n = 25)	Biweekly 100.000 Ui (N = 25)	p-value (ANOVA)
M:F	31:44	12:13	7:18	12:13	NS
Age (years)	34.1 ± 10.2	30.2 ± 9.9	36.7 ± 8.7	35.4 ± 11.0	0.059
Body Weight (kg)	66.7 ± 12.4	65.8 ± 13.2	67.8 ± 10.8	66.6 ± 13.7	NS
BMI	23.1 ± 2.6	22.55 ± 2.7	23.8 ± 2.2	22.8 ± 2.7	NS
Baseline 25OHD (ng/mL)	13.5 ± 3.7	14.6 ± 3.9	12.8 ± 3	13.5 ± 4.1	NS
Baseline IL-6 (pg/mL)	1.3 ± 1.2	0.9 ± 0.6	1.4 ± 1.6	1.6 ± 1.3	NS
Baseline IL-17 (pg/mL)	0.4 ± 1.8	0.7 ± 3	0.2 ± 1.1	0.2 ± 0.7	NS
Baseline IL-10 (pg/mL)	0.9 ± 0.9	0.8 ± 0.7	1.2 ± 1.2	0.8 ± 0.7	NS

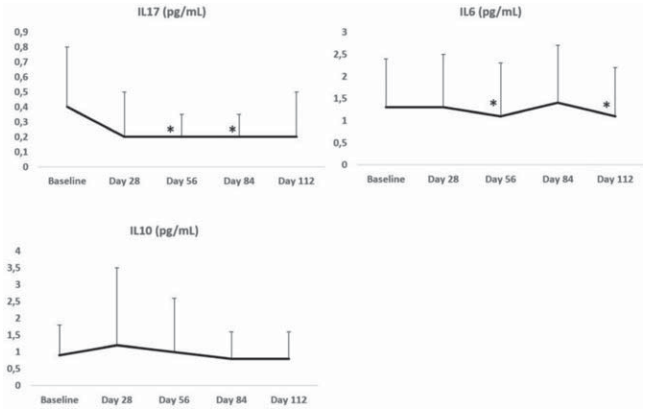

Figure 1. absolute changes of IL17, IL6 and IL10. *p<0.05 vs baseline.

Conclusion: In the overall cohort we found slight decreases in serum IL6 and IL17 serum levels. No differences were found among groups.

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Disclosure of Interests: Angelo Fassio: None declared, Davide Gatti Speakers bureau: Amgen, Celgene Eli-Lilly, MSD-Italia, Organon, UCB., Paid instructor for: Amgen, Celgene Eli-Lilly, MSD-Italia, Organon, UCB., Matteo Gatti: None declared, Maurizio Rossini Speakers bureau: Abiogen, Amgen, Abbvie, BMS, Celgene, Eli-Lilly, Galapagos, Grunenthal, MSD, Novartis, Pfizer, Sanofi, Sandoz, Theramex, UCB., Eugenia Bertoldo: None declared, Giovanni Adami: None declared

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AB1020 OSTEOPOROSIS'S PARTICULARITIES IN BREAST CANCER PATIENTS UNDER AROMATASE-INHIBITORS

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Background: Breast cancer is the first female cancer, especially after menopause. In Morocco its prevalence is estimated at 35.8%. Its hormone-dependent aspect requires the use of hormone-modulating treatments, in particular aromatase-inhibitors responsible for hypogonadism, bone loss and osteoporosis (OP) with increased fracture risk.

Objectives: The aim of this study is to determine the epidemiological, clinical and densitometric profile of osteoporotic patients with breast cancer under aromatase-inhibitors and to evaluate the factors associated with bone gain in this population.

Methods: This is a descriptive and analytical retrospective study of 126 osteoporotic patients with breast cancer under aromatase-inhibitors, collected during a period of 4 years (2017 to 2021). Statistical data analysis was performed using SPSS version 20 software. The bivariate study was performed by ANOVA test.

Results: All the patients were treated for breast cancer and received systemic hormone-modulating anti-aromatase type therapy. All the patients had densitometric osteoporosis confirmed by a T score < or equal to –2.5, of which 31.7% had a T-score < or equal to -3.5. The average age was 62.29 (40–92) years. 1.6% had an osteoporosis family history and 0.8% had an osteoporosis's fracture family history, 77% had a personal history of fracture. 54.8% were overweight, 14.3% had a metastasis. 88.1% had insufficient vitamin D levels (<20 ng/L). 15.9% had high blood pressure. The average duration of anti-osteoporotic treatment was 2.31 years. 77% of patients were on Residronate, 8.7% on Zoledronate, and 14.3% on Alandronate. The study of bone gain involved patients who had an evaluation of osteodensitometry whithin 2 years, the average spine bone gain was 0.011 and 0.018 for femur bone gain. In bivariate analysis, they were a statistically significant association between the presence of a T-Score value <-3.5 and spine bone gain (p=0.035), the absence of metastasis with femur bone gain (p<0.0001), the absence of hypertension and femur bone gain (p=0.015), concerning the therapeutic means used there were an association between the use of zoledronic acid and spine bone gain (p =0.021).

Conclusion: Breast cancer patients under aromatase-inhibitors are particularly prone to osteoporosis, hence the interest of paying close attention to this population and intervening on the associated modifiable factors for better management.

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Disclosure of Interests: None declared

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AB1021 FACTORS ASSOCIATED WITH FRAGILITY FRACTURE IN PATIENTS WITH SYSTEMIC MASTOCYTOSIS: DATA FROM AN INCEPTION COHORT IN A SINGLE CENTRE

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Background: Systemic Mastocytosis (SM) is a very rare disease. Most common manifestations are skin related or anaphylaxis, however almost one third of patients may present with concomitant osteoporosis (OP) resulting in fragility fracture (FF) in around 5 -37% of patients affecting lumbar spine (LS) in young men. Alcohol consumption, high serum tryptase level, and low femoral T score have been described as risk factors but there are some discrepancies between studies. [1-2]

Objectives: Our primary objective was to identify factors associated with FF in patients with SM.

Methods: We analysed all consecutive patients attending a multidisciplinary clinic up to April 2021 with SM diagnosis according to the 2001 WHO criteria. We collected demographic data, general risk factors for OP, cutaneous, bone involvement and laboratory data as serum tryptase level. Bone involvement is defined as densitometric OP (T score ≤ - 2.5) or FF. Normally distributed variables are described as means (SD) and dichotomous variables as number and frequencies. Comparison between patients with and without FF is performed using t-test and Chi^2 when needed.

Results: Seventeen patients with SM are included in this preliminary analysis. Four patients (24%) presented a FF, all of them vertebral fractures identified by plain radiographies.Two men and two women presented FF, they were older versus patients without FF (Table 1), and without general risk factors for OP. All of them have a high basal serum tryptase and most of them presented other MS symptoms (cutaneous, anaphylaxia). FRAX tool was useful in only one patient to predict FF risk. The two men with FF diagnosis do not met criteria for densitometric OP, specific characteristics for these patients are presented in Table 2.

Table 2. Characteristics of Fragility Fracture in four patients with Systemic Mastocytosis.

Patient	Age	Gender	Localization of FF	Severity of Fracture	Time to fracture diagnosis
Patient 1	65	Male	D6,D8,D10,D11, L1	3 Mild 2 Moderate	2 years prior SM diagnosis
Patient 2	81	Female	D4,D8,D12, L1	1 Mild 3 Severe	2 years after SM diagnosis
Patient 3	65	Female	D4,D11	Unknown	2 years prior SM diagnosis
Patient 4	42	Male	D7,D8,D9,D11,D12, L1,L2,L3,L5	3 Mild 3 Moderate 3 Severe	At time of SM diagnosis

Conclusion: Twenty five percent of patients present FF (multiple, located in dorsal spine, and without densitometric diagnosis of OP). SM should always be considered in differential diagnosis in the presence of FF, especially in men with no OP or another risk factor associated.

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Disclosure of Interests: None declared

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AB1022 PLACE OF BONE MINERAL DENSITY MEASUREMENT IN THE DIAGNOSIS OF ASYMPTOMATIC VERTEBRAL FRACTURES

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Background: Vertebral fracture (VF) is the most common fragility fracture. The majority of them are asymptomatic and only third of VFs are clinically recognized. Screening of osteoporosis may increase early detection of these fractures.

Objectives: to emphasize on the routine practice the lateral and frontal X-rays of dorso-lumbar spine each time that the diagnosis of osteoporosis has been made.

Methods: This is a cross-sectional study which includes patients followed for a well-defined rheumatological disease in the rheumatology department at TAHER SFAR University Hospital, Mahdia, Tunisia. All patients had a bone mineral density (BMD) measurement whenever there is an indication according to the HAS 2006 recommendation with a systematic radiography of the dorso-lumbar spine (face and profile incidences).

Results: Thirty seven female patients were enrolled, with a mean age of 59.8 ± 9.9 years. The average body mass index was 30.85 ± 5.7kg/m2 and 83.7% of them were overweight (BMI>25kg/m2). 86.5% of patients had a history of back pain and 16.2% of them had a family history of fracture of the femoral upper extremity. The reasons for performing BMD were dominated by corticosteroid therapy ≥7.5mg/d for more than 3 months and a history of vertebral fracture in 37.8% of cases each and treatment with anti-aromatases in 16.2% of cases .18 patients had a Spinal T-score ≥-2.5 DS. 12 patients had a spinal Tscore between -2.5 DS and -1 DS. 6 patients had a femoral Tscore ≥-2.5 DS and 12 had a femoral Tscore between -2.5 DS and -1DS. 19/37 patients (51.4% of cases) had osteoporosis. 9/19 (47.3%) had a vertebral fracture

Table 1

	Population (N = 17)	Without fragility fracture (N = 13)	With fragility fracture (N=4)	P
Male, n (%)	9 (53%)	7 (54%)	2 (50%)	0.89
Age at first symptoms, years, mean (SD)	37.6 (21.1)	33.0 (20.2)	58.1 (10.1)	0.05
Age at diagnosis, years, mean (SD)	47.7 (21.1)	38.8 (20.9)	59.7 (13.1)	0.08
Ever smoker, n (%)	6 (35%)	4 (30.8%)	2 (50%)	0.48
Alcohol, n (%)	2 (11.76%)	1 (7.69%)	1 (25%)	0.34
BMI, mean (SD)	26.5 (4.3)	25.3 (4.0)	30.6 (2.0)	0.02
BMI<19kg/m2, n (%)	1 (6%)	1 (7%)	0 (0%)	0.56
Cutaneous mastocytosis, n (%)	8 (47%)	5 (38.5%)	3 (75%)	0.20
Anaphylaxia, n (%)	8 (47%)	6 (46.1%)	2 (50%)	0.89
Digestive symptoms, n (%)	8 (47%)	7 (53.5%)	1 (25%)	0.31
Basal serum tryptase >11,4	12 (70.6%)	8 (61.5%)	4 (100%)	0.14
Basal serum tryptase, mean (SD)	20.20 (18.33)	10.68 (20.75)	22.85 (7.64)	0.75
General risk factors for OP present, n (%)	5 (29%)	5 (38.5%)	0 (100%)	0.14
Femoral T score, mean (SD)	-1.03 (1.22)	-3.82 (1.36)	-1.86 (1.23)	0.12
Lumbar T score, mean (SD)	-1.06 (1.57)	-5.27 (1.36)	-1.95 (2.08)	0.20
Femoral Z score, mean (SD)	-0.34 (1.05)	-1.79 (1.44)	-0.75 (0.65)	0.39
Lumbar Z score, mean (SD)	-0.30 (1.88)	-5,38 (1.57)	-0.67 (2.96)	0.66
FRAX global fracture, mean (SD)	2.27 (2.52)	2.34 (1.57)	6.83 (7.82)	0.11
FRAX hip fracture, mean (SD)	0.23 (1.01)	0.48 (0.27)	2.1 (1.92)	0.18

among which 12% were previously unknown and in women who were fully symptom-free. The vertebral fractures were mainly located at the dorsal-lumbar region: the L1 and T11 vertebrae were fractured in 3 patients and the T12 vertebrae in 3 patients.
Conclusion: Our study showed that nearly half of patients with BMD-objectified osteoporosis had a VF detected on standard X-rays, most of which were previously unknown. It is plausible to speculate the place of this method combining BMD with spinal X-rays in the diagnosis of asymptomatic VFs.
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AB1023 CHARACTERISTICS OF PATIENTS REFERRED FOR FIRST BONE DENSITOMETRY TO A RHEUMATOLOGY FLS, WITH NORMAL RESULTS IN THE LUMBAR SPINE

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Objectives: To analyze the characteristics of postmenopausal women referred for the first bone densitometry (BMD), with normal results in the lumbar spine.
Methods: Retrospective study of postmenopausal women, for a first BMD, at a rheumatology FLS, during February/2010-December/2021. General patient data (age, gender), osteoporosis (OP) risk factors were collected: age at menopause, parental hip fracture, body mass index (BMI), smoking and alcohol habit, drugs and potentially osteopenizing diseases, low-impact fractures in adulthood (fractures of osteoporotic origin included: vertebral, hip, humeral head and distal radius and pelvis), current treatment for OP and FRAX index.
Results: 2.930 postmenopausal women with normal lumbar BMD are included: 505 (17%) had suffered an OP fracture: mean age (SD): 63.2 years (8.5) and of menopause 48 years (10). Among the OP risk factors: early menopause: 818 (28%) women, active smoking: 521 (18%), alcohol > 3 units: 84 (2%), parents hip fracture: 310 (11%). Among osteopenizing diseases: rheumatoid arthritis/chronic arthritis: 112 (4%) patients, inflammatory bowel disease: 44 (2%), arteritis/polymyalgia rheumatica: 35 (1%) and the rest <1%. Among the osteopenizing drugs: omeprazole: 967 (33%) patients, thyroxine: 354 (12%), oral or inhaled corticosteroids: 261 (9%) and aromatase inhibitors: 168 (6%). 427 (15%) patients had had a previous OP fracture: distal radius: 188 (6%), vertebral: 146 (5%), humeral head: 46 (2%) and hip: 47 (2%). 808 (28%) patients were receiving treatment for OP: oral bisphosphonates: 518 (18%), SERM: 136 (5%), strontium ranelate: 75 (3%), denosumab: 51 (2%), teriparatide: 16 (0.7%) and zoledronate: 12 (0.5%) (Table 1).

Table 1. Characteristics of patients with normal lumbar spine BMD.

	TOTAL BMD LS Normal N: 2.930	Normal BMD LS WITH fracture N: 505 (17%)	Normal BMD LS WITHOUT fracture N: 2.425 (83%)	p
Age in BMD, years, mean (SD)	63,2	70.5 (7.78)	60.6 (26)	**0.0001**
Menopausal age, years, mean (SD)	48 (8.4)	45 (5.46)	48 (8.48)	**0.0001**
Early menopause, n (%)	814 (28)	171 (34)	643 (27)	**0.07**
BMI, kg/m^2, media (SD)	29,1 (10.3)	29.5 (17.03)	28,9 (10.3)	**0.44**
Active tobacco, n (%)	521 (18)	40 (8)	481 (20)	**0.06**
Alcohol ≥ 3 units, n (%)	84 (2)	10 (2)	74 (3)	0.85
Parent hip fracture, n (%)	310 (11)	60 (12)	250 (10)	0.65
Ostepenizing drug, n (%):	1.750	289 (57)	1.461 (60)	0.34
Omeprazole	967 (33)	178 (35)	789 (33)	0.60
Thyroxine	354 (12)	53 (10)	301 (12)	0.67
Corticosteroids	261 (9)	42 (8)	219 (9)	0.83
Aromatasa Inhibitor	168 (6)	16 (3)	152 (6)	0.62
Treatment, n (%):	808 (34)	226 (48)	582 (24)	**0.0001**
Oral bisphosphonate	518 (18)	127 (25)	391 (16)	
SERM	136 (5)	24 (5)	112 (5)	**0.02**
Strontium ranelate	75 (3)	20 (4)	55 (2)	1
Denosumab	51 (2)	31 (6)	20 (0.8)	0.35
Zoledronate	12 (0.5)	10 (2)	2 (<0.1)	0.84
Teriparatide	16 (0.7)	14 (3)	2 (<0.1)	0.84
BMD, mean Tscore (SD):				
Lumbar spine	0.89	0.04 (1.49)	0.05 (1.49)	0.89
Femoral neck	0.70	-1.3 (1.06)	-0.54 (1.06)	**0.0001**
Osteoporosis, n (%)	108 (4)	51 (10)	57 (2)	**0.07**
Osteopenia, n (%)	981 (33)	247 (49)	734 (30)	**0.0001**
Total hip	-0.31	-0.8 (1.12)	-0.17 (1.12)	**0,0001**
FRAX with BMD, mean (SD):				
Mean fracture	5.23	10.6 (5.79)	3.99 (5.78)	**0.0001**
Hip fracture	1.54	3.7 (3.58)	1.09 (3.58)	**0.0001**

The group with OP fractures, are significantly (Table 1): older (p<0.0001), with lower mean age of menopause (p<0.0001), receive more treatment (p<0.0001), especially oral bisphosphonates (p=0.02), have worse results in hip BMD (p<0.0001), with a higher percentage of osteopenia (50% vs 30%, p<0.0001) and worse result in FRAX of major fracture (p<0.0001) and of hip (p<0.001).
Conclusion: Among the patients referred to BMD, although the result of lumbar spine is normal, 17% have suffered an OP fracture, presenting this group: 1) Older age, 2) Osteopenia in hip BMD 50%, with high risk of fracture due to FRAX and they followed treatment for OP, especially oral bisphosphonates. 3) It is advisable to simultaneously perform BMD at the lumbar and hip levels, especially in older subjects
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AB1024 SECONDARY PREVENTION OF VERTEBRAL FRACTURES SUSTAINED EFFICACY OVER TIME

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Background: Vertebral fractures entail a notorious social and health problem, and their presence is the greatest risk factor for the appearance of a new vertebral fracture. Despite the availability of different drugs for secondary prevention, there are few comparative studies in real clinical practice.
Objectives: Our aim is to evaluate the appearance of new vertebral fractures depending on the strategy chosen as secondary prevention.
Methods: We performed a retrospective descriptive study with patients who had suffered their first vertebral fracture between 2010 and 2018, in whom we checked the subsequent appearance of new vertebral fractures.
We selected only those patients who had completed a minimum of 18 months of secondary prevention with antiresorptive drugs, or a sequential scheme (anabolic treatment followed by at least 1 year with an antiresorptive drug). Those patients who had presented new fractures in the first 6 months of treatment were excluded. Finally, we adjusted efficacy by treatment time.
Results: A total of 452 patients were included, out of an initial baseline pool of 1184 patients. We found female predominance (83% of the total). The mean age of the first vertebral fracture was 69.2 years, with a mean latency to fracture of 51.4 months. A new vertebral fracture happened in 4.7% of these patients. The different secondary prevention strategies were classified according to the different therapeutic options, as we can see in Table 1.

Table 1.

Treatment	Patients (%)	New fractures (%)
Denosumab	205 (45.35%)	10 (4.87%)
Oral bisphosphonate	75 (16.59%)	5 (6.66%)
(alendronate, risedronate or ibandronate)		
Zoledronate	38 (8.41%)	3 (7.89%)
Teriparatide followed by Denosumab	94 (20.8%)	0 (0%)
Teriparatide followed by Oral bisphosphonate	36 (7.96%)	3 (8.33%)
Teriparatide followed by Zoledronate	4 (0.89%)	0 (0%)

No statistically significant differences between different treatments were observed, but we found a lower probability of a new fracture in patients treated with sequential treatment with teriparatide followed by denosumab. Finally, the Kapplan-Meier survival analysis showed a lower probability per year of new fractures in patients treated with teriparatide followed by denosumab, being this probability greater in patients treated with teriparatide followed by oral bisphosphonate.
Conclusion: A lower probability of refracture was observed in patients who received sequential treatment with teriparatide followed by denosumab.
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AB1025 TRABECULAR BONE SCORE IN PATIENTS WITH AXIAL-SPONDYLOARTHRITIS

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Background: In axial spondyloarthritis, the bone mineral density (BMD) is usually overestimated due to syndesmophytes. Hence, the trabecular bone score

(TBS) could be suggested as a complementary tool that provides additional information on bone microarchitecture (1).

Objectives: The aim of this study was to explore the trabecular bone score (TBS) association with disease parameters and vertebral fractures in axial spondyloarthritis.

Methods: We designed a cross-sectional study of patients with axial spondyloarthritis diagnosed according to the ASAS 2009 classification, recruited from December 1st, 2021. SA patients excluded were those with a history of cancer, hyperparathyroidism, hyperthyroidism, chronic kidney disease, cirrhosis, and those using osteoporosis and steroid drugs or having a body mass index (BMI) of more than 36kg/m ^{2}. BMD (of lumbar, hip, femoral neck, 33% distal radius of non-dominant hand) and TBS were measured with Dual-energy X-ray absorptiometry (DXA). Vertebral fractures (VF) were assessed by vertebral fracture assessment (VFA). They were defined as grade 2 or 3 according to Genant criteria. Clinical data and laboratory tests collected simultaneously with the DXA scan were analyzed. The associations between TBS and disease parameters: Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI), and the Modified stoke ankylosing spondylitis spinal score (mSASSS) were studied by correlations and multiple linear regressions using SPSS 20.

Results: Forty-three patients were included with a mean age of 36.42 ± 13.10 years and a mean disease duration of 12.88 ± 7.69 years. The mean TBS was 1.370 ± 0.098 and the mean lumbar BMD was 0.937 ± 0.210. The mean TBS was significantly lower in patients with comorbidities (high blood pressure and diabetes). TBS was also positively associated with lumbar BMD (r = 0.386; p = 0.011), hip BMD (r = 0.621; p < 0.001), but not forearm BMD (r = 0.276; p = 0.073). Moreover, TBS was negatively associated with age (r = - 0.525; p < 0.001), BMI (r = - 0.440; p = 0.001), and waist circumference (r = - 0.558; p < 0.001). TBS was also negatively correlated with the ASDAS score (r = - 0.378; p = 0.014), while there was no correlation with the BASDAI, BASMI, BASFI, and mSASSS. The association of TBS and ASDAS CRP was significant at adjustment on disease duration and mSASSS (p = 0.017; β = - 0.363; [- 0.056; - 0.006]). However, there was no association between TBS and VF.

Conclusion: In SA patients, TBS was negatively associated with disease activity score and positively associated with axial bone loss. This result may explain bone fragility in active spondyloarthritis. No clear association was found between TBS and VF in the present study.

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AB1026 ASSOCIATION BETWEEN TRABECULAR BONE SCORE, 10-YEAR PROBABILITY RISK FOR FRACTURE, AND VERTEBRAL FRACTURES IN RHEUMATOID ARTHRITIS

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Background: Trabecular bone score (TBS) utility in vertebral fracture prediction is still questionable.

Objectives: To evaluate the association of trabecular bone score (TBS), the fracture risk assessment tool (FRAX), and TBS adjusted FRAX with prevalent vertebral fractures (VFs) in Rheumatoid Arthritis (RA).

Methods: This is a cross-sectional study of RA patients diagnosed according to ACR/EULAR 2010 criteria and recruited in our rheumatology department. Patients with an age under 40 or above 90, diabetes, thyroid disease, hyperparathyroidism, cancer, cirrhosis, renal clearance < 70 mL/min, and those using osteoporosis drugs or having a body mass index (BMI) of more than 36kg/m^2 were excluded. TBS, bone mineral density (BMD), and vertebral fracture assessment (VFA) were obtained using dual-energy X-ray absorptiometry (DXA). We used the FRAX tool to assess the 10-year probability of major osteoporotic fracture (MOF-FRAX) and hip fracture (HF-FRAX) with and without BMD. These parameters were further adjusted for TBS (FRAX/TBS-MOF and FRAX/TBS-HF). Prevalent VF was evaluated by two readers using VFA. We defined patients with prevalent VFs as patients who had moderate-to-severe degree VFs of the thoracic and lumbar spine (T4 to L4) according to Genant criteria. Osteoporosis was defined as a T-score < -2.5 in the lumbar spine, femoral neck, or 1/3 of the non-dominant forearm location. Clinical data, results of radiological and laboratory tests performed on the same day of the DXA scan were collected. Receiver operating characteristic curves were generated by SPSS.20 to study the predictability of each parameter for VF.

Results: Sixty-nine patients were enrolled, and 66.7% of them were menopausal. Their mean lumbar spine, hip, and forearm BMD were 0.817 ± 0.155, 0.681 ± 0.676, and 0.572 ± 0.119, respectively. The mean TBS was 1.328 ± 1.041. Thirty-nine patients (56.5 %) had osteoporosis. Nine patients (13%) had moderate to severe VFs with predominance at the thoracic spine (77.8%). There was a negative correlation between MOF-FRAX score and lumbar spine BMD (r = -0.473; p < 0.001), and also hip BMD (r = - 0.530; p < 0.001), while there was no correlation between MOF-FRAX score, HF-FRAX and TBS. The areas under curves were 0.824, 0.800, 0.792, and 0.443 for the FRAX-MOF score with BMD, FRAX-MOF score, FRAX-MOF score adjusted for TBS, and TBS, respectively.

Conclusion: In this study, MOF-FRAX score showed a better correlation with BMD than TBS. It was also superior to TBS and TBS adjusted FRAX in identifying prevalent VFs in RA patients.

Disclosure of Interests: None declared

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AB1027 CLINICLAL EFFICACY OF SEQUENTIAL TREATMENT AFTER ROMOSOZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS FOR 18 MONTHS

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Background: Romosozumab (ROMO), a monoclonal antibody that binds sclerostin, increases bone formation and decreases bone resorption. And although it is a novel therapeutic agent for osteoporosis, which has shown high effects of increasing bone density and inhibiting fragile fracture in overseas clinical trials. However the clinical efficacy for rheumatoid arthritis complicated with osteoporosis (RA-OP) is unknown.

Objectives: To evaluate the clinical efficacy of ROMO for 12months and denosumab (DMB) 6months in patients with RA-OP for 18 months.

Methods: RA patients diagnosed according to the 2010 ACR/EULAR criteria. All patients met at least one of the following criteria were eligible; a bone mineral density T score of -2.5 or less at the lumber spine or total hip and either one or more moderate or severe vertebral fractures or two or more mild vertebral fractures. All patients were initiated ROMO from between April, 2019 and March, 2020. The total number of patients was 12 cases. The ROMO dose was 210mg at once every 1 months. After 12 months of ROMO, all cases were changed to DMB. In all cases native or activated vitamin D has been used. We reviewed the results for 12 months about the increase and decrease of bone mineral density (BMD) of lumbar spine(LS) and total hip(TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen(PINP) and tartrate-resistant acid phopshatate form 5b(TRACP-5b).

Results: he gender was all female. The mean age was 72.8 ± 7.0; disease duration was 17.7 ± 16.5 years; the body mass index was 19.4 ± 3.1 and the FRAX was 36.0 ± 14.9. Clinical findings related to RA-OP at baseline were as follows; CRP 1.25 ± 1.75; DAS28-CRP 3.45 ± 0.99; HAQ 1.56 ± 0.99 and, bone turnover markers and bone mineral density at baseline were as follows; P1NP 62.4 ± 36.2; TRACP-5b 485 ± 252; LS-BMD and T-score 0.79 ± 0.14 g/cm^2 and -2.82 ± 0.99 and TH-BMD 0.55 ± 0.07 g/cm^2 and -3.14 ± 0.53 g/cm^2. The rate of increased P1NP from baseline to 1, 3, 6, 12 and 18 months were each 116.3 ± 68.7% at 1 month, 135.0 ± 131.3% at 3 month, 126.1 ± 177.0% at 6 month, 83.7 ± 179.1% at 12 month and -45.1 ± 35.7% at 18 month and decreased TRAC-5b were -13.0 ± 91.4% at 1 month, 6.9 ± 38.8% at 3 month, 20.0 ± 63.4% at 6 month, 14.8 ± 64.5% at 12 month and -11.4 ± 95.9% at 18 month. The rate of increased LS-BMD from baseline to 6, 12 and 18 months were 10.8 ± 8.0%, 15.2 ± 9.5% and 18.9 ± 10.4% and TH-BMD were 4.1 ± 4.5%, 5.7 ± 6.3% and 8.4 ± 8.1% (Figure 1, 2).

Conclusion: Clinical efficacy of treatment with ROMO for 12months and DMB for 6months for RA-OP was extremely effective and has the high potential to be an important option in the treatment of RA-OP.

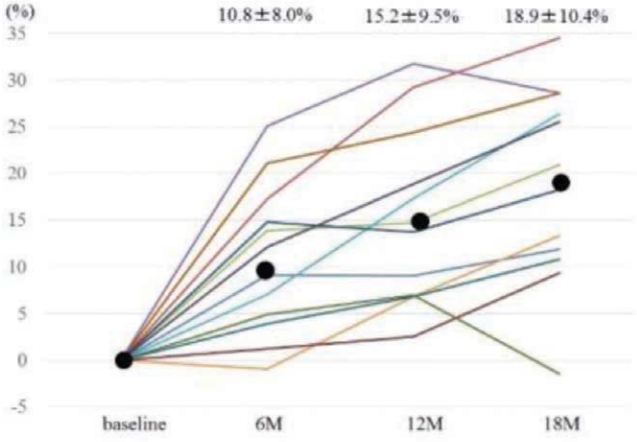

Fig.1: The rate of increased LS-BMD from baseline to 18 month

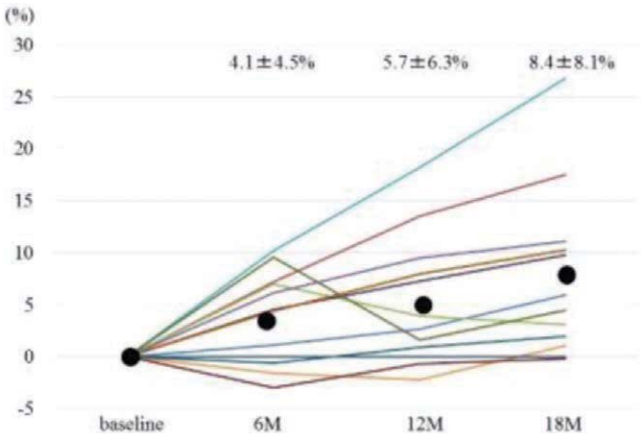

Fig.2: The rate of increased TH-BMD from baseline to 18 month

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AB1028

REGRESSIVE BONE MINERAL DENSITY TRENDS SEEN WITH DELAY IN FOLLOW UP OF DENOSUMAB TREATMENT DUE TO THE PANDEMIC INDUCED LOCKDOWN - A SINGLE CENTRE INDIAN EXPERIENCE.

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Background: Denosumab (Dmab), a fully human monoclonal antibody that inhibits receptor activator of nuclear factor kappa-β ligand (RANKL), which selectively inhibits osteoclastogenesis can be used for a long period unlike the relatively short period with Teriparatide.[1-2] However the effects of Dmab can quickly regress if the treatment is delayed.[3]
Objectives: The pandemic led to multiple prolonged lockdowns since March 2020 to Jan 2022 in India. This resulted in follow up Dmab treatment delays. The retrospective study was aimed to look for the effect of the delays.
Methods: The bone mineral density (BMD) trends from the central dual-energy x-ray absorptiometry (DXA) at our centre were studied. The trends of patients under Dmab for one year and delay in follow up for 10 - 12 months for the forth dose were evaluated. 21 postmenopausal women who had been under treatment with Dmab 60 mg subcutaneous injection at 6 monthly interval for one year followed up with such delays. 6 were excluded because of history of sars-cov-2 infection and glucocorticoid use. In the study group of 15 (n=15), the mean BMD at L2, L3 & L4 (sp BMD) and Right and Left Hip (hip BMD) were studied from before treatment (a BMD), 6 months after 1st and at the time of 2nd injection (b BMD), 6 months of the 2nd and at the time of 3 rd injection of Dmab (c BMD), and that due to delay in follow up of 10-12 months (d BMD). The mean percentage trend change between a-b, b-c, and c-d BMDs was evaluated. The least significant change (LSC) [4] from a single centre DXA was used to validate the findings.
Results: The mean percentage change after the treatment for the 1st 6 months of Dmab (a-b BMD) was 4.08% and 3.60% and the second injection resulted in a further change (b-c BMD) of 5.98% and 4.52% in the sp BMD & hip BMD respectively. The delay in follow up of 10-12 months resulted in a change (c-d BMD) of -7.81% in the sp BMD and -2.96% in the hip BMD. The LSC from a single centre DXA is 2.6% and 3.6% for sp BMD and hip BMD respectively. A p>0.05 was considered statistically significant. Table 1 shows the BMD changes.

Table 1. Percentage BMD changes

BMD trend (n=15)	sp BMD (LSC – 2.6%)	hip BMD (LSC – 3.6%)
a-b BMD	4.08%	3.60%
b-c BMD	5.98%	4.52%
c-d BMD	-7.81%	-2.96%

sp BMD - Mean of L2,L3 & L4 Spine BMD, hip BMD - Mean of Right and Left Hip BMD, a-b BMD - Percent change in BMD from before to 6 months after Ist & at the time of 2nd Dmab, b-c BMD - Percentage change in BMD 6 months after 2nd & at the time of 3rd Dmab, c-d BMD - Percentage change in BMD after 3rd Dmab & follow up after delay of 10-12 months and LSC – Least significant change.

Conclusion: These findings suggest that regressive trend in BMD are seen when the treatment with Dmab is delayed even as early as 10 to 12 months. It was seen much faster in the spine compared to the hip. It is therefore advised that short term treatment with Dmab without follow up could lead to loss of all gains and may also worsen the osteoporosis.
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AB1029

CLINICAL AND RADIOLOGICAL OUTCOMES AFTER VERTEBROPLASTY AND KYPHOPLASTY FOR OSTEOPOROTIC VERTEBRAL FRACTURES

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Background: Vertebral Fractures are among the most frequent osteoporotic fractures. Pain and spinal deformation cause loss of autonomy and predispose to a higher risk of morbidity and mortality. Vertebroplasty and Kyphoplasty are an efficient therapeutic alternative in the management of these fractures [1,2].
Objectives: The aim of our study was to evaluate functional and radiological outcomes of Vertebroplasty and Kyphoplasty for osteoporotic vertebral fractures.
Methods: It was a retrospective study including patients treated with Vertebroplasty or Kyphoplasty for osteoporotic vertebral fractures with no spinal cord injuries. Clinical, functional, and radiological data were collected. Pain assessment was evaluated by the Visual Analogue Scale (VAS) and the Denis pain scale. Oswestry Disability Index (ODI) was used to evaluate the functional impairment. The measurement of the vertebral height pre and postoperatively was assessed by the Beck's index on the spine lateral X-ray.
Results: There were 36 patients: 26 female and 10 male. The mean age was 65 years (41-74). The follow-up period was about 17 months. The thoracolumbar hinge was the most affected region (70%). Twenty two patients were treated by kyphoplasty and 14 by Vertebroplasty. The

mean VAS pain improved from 5.28 preoperatively to 2.92 postoperatively (delta VAS pain was 2.36, $p<10^{-3}$). The improvement in the VAS pain was by 3.42 ($p<10^{-3}$) in the last follow-up. There was no difference between the two technics regarding the pain improvement (p=0.06). On preoperatively, the mean Denis pain scale was 4. It was 2.19 after kyphoplastyand and 2.27 after Vertebroplasty with no significant difference between the two technics (p=0.6). The mean ODI at the last setback was fourteen: 95 % of patients had minimal to moderate disability, 5% had severe disability. There was no difference between Kyphoplasty and Vertebroplasty regarding the functional impairment (14.87 vs 12.36, p=0.5). Kyphosis on the level of the fractured vertebra improved from 16.8° preoperatively to 9.5° postoperatively with a significantly mean reduction of 7.3° ($p<10^{-3}$). Regional kyphosis improved from 12.1° to 7.4° with a significantly mean reduction of 4.3° ($p<10^{-3}$). Beck's index went up from 0.66 to 0.8 post-operatively (p<0.05). The improvement of kyphosis on the level of the fractured vertebra (angulair gain) was more important for the group treated with Kyphoplasty (8.45° vs 5.5, p=0.01). A significant association was found between the Beck's index losses with the ODI at the last setback (p=0.02). Complications were cement leakage in five patients without clinical symptoms. We had noted one anterior vascular leak without any clinical implication. Surgical site infection was noted in one case and was managed by medical treatment without any general complication.

Conclusion: Our study showed that Vertebroplasty and kyphoplasty were both effectively for the pain reduction and for restoration of autonomy in osteoporotic patients. They also allowed an improvement of the kyphosis necessary for an appropriate spinal static's.

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AB1030

PATIENT CARE AT THE FRACTURE LIAISON SERVICE REDUCE THE GAP IN THE TREATMENT OF OSTEOPOROSIS BETWEEN MEN AND WOMEN.

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Background: Osteoporosis (OP) between men and women is different,and the way it is treated also differs. In men, the gap in clinical care, especially diagnosis and treatment, is worse.

Objectives: To analyze the differences in the clinical characteristics of OP (demographics, comorbidities, diagnosis, and treatment) in an gold star Fracture Liaison Service (FLS).

Methods: Design: Observational, prospective, analytical study of usual clinical practice. All patients treated from an FLS from May 2018 to August 2021 were prospectively included. Of each patient, 160 clinical variables were introduced in a real time database, and they were followed for 2 years.

Results: 557 patients were analyzed, 472 (83%) women and 100 (17%) men. The main features are summarized in the table. In women the vertebral fracture predominated followed by the hip fracture, in men the hip followed by the vertebral ones. Men had higher rates of smoking and alcoholism. The frequency of secondary OP and exercise was different between sexes. Weight, height, and BMI were different, due to different body composition. The frequency of specific treatment for OP (bisphosphonate, denosumab, teripatide, SERM) before fracture was very low, lower in men. The most remarkable result was the low percentage of patients with OP receiving treatment before the FLS, and the differences between sex; 77 (16%) women versus 6 (6%) men had received it at some point in their lives, p=0.008. The probability of a man not receiving prior treatment was 2. 70 (95%CI 1.13- 7.81); p=0,008. After the FLS all the patients were treated. Treatment adherence in the first two years after the FLS was 84% in both sexes.

Table 1

Variable	Hip n, % 239, 43		Vertebral n, % 159, 28		DER n, % 96, 17		Humerus n, % 41, 7		Other n, % 37, 6		p
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	0.0001
Number	179, 75	60, 25	129, 81	30, 19	93, 97	3, 3	40, 98	1, 2	31, 84	6, 16	0.06
Current smoker	13, 8 *	19, 32	20, 16 *	14, 48	16, 17 *	1, 33	3, 8	0, 0	8,	1	0.3
Drinker >3 cups/day	5, 3 *	14, 24	9, 7 *	11, 38	6, 6	1, 33	2, 5	0, 0	2, 6	0	0.001
Secondary causes of OP	24, 16	10, 21	24, 22	14, 56	14, 18	0, 0	11, 32	0, 0	9, 32	1, 20	0,03
Exercise											0,0001
Bed to armchair	35, 28 *	12, 21	10, 8*	8, 28	1, 1	0, 0	3, 8		1, 3*	2, 33	
Wanders at home	64, 0	13, 23	36, 30*	5, 17	7, 8	0, 0	5, 13		11, 38	1, 17	
Walk in the street	58, 36	26, 46	53, 43	15, 52	59, 68	2, 67	25, 64		10, 34	3, 50	
Daily exercise	4, 2	5, 9	22, 18	1, 3	20, 23		6, 15		7, 24	0, 0	
Total	161, 74	56, 26	121, 81	29, 19	87, 97	1, 33	39, 100		29, 82	6, 17	
						3, 3					
BMI ≥ 30	53, 32	14, 25	51, 43	13, 46	38, 43*	3, 7	17, 45	1, 5	9, 29	2, 40	0.01
OP treatment before FF	26, 15 *	2, 3	28, 23 *	3, 10 *	13, 15	0, 0	6, 16	0, 0	4, 14	1, 20	0,008
Re-fracture (one year)	11, 9	4, 8	6, 7	0, 0	5, 8	0, 0	2, 8	1, 100	0, 0	0, 0	0.9
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age, Years	79 ±8.7*	75.5 ±10.3	70.4 ±9.0	69.3 ±10.0	69 ±9.2	73.6±6.5	71.3 ± 8.7*	76	68.6 ±11.3	82.6 ±8.3	0.6
Weight, Kg	65.3 ±14,3*	72.1 ±12.9	67.2 ±13.4	78.5 ±14.9	70.7 ±12.1	85.5 ±13.4	71.7 ±11.8	90	68.6 ±18.6*	77.7 ±19.4	0.00001
Size, m	1.5 ±0.06*	1.64 ±0.06	1.51 ±0.01	1.63 ±0.06	1.54 ±0.06	1.6 ±0.06	1.54 ±0.06	1,63	1.54 ±0.06*	1.61 ±0.09	0.00001
BMI	28.4 ±5.1*	26.7 ±4.1	29.2 ±6.3	29.1 ±4.8	29.9 ±5.4	33.2 ±2.6	30.1 ±4.9	33.8	28.9 ±6.7	29.4 ± 6.2	0,04

DER= distal end of radius, Others included ribs, tibia and fibula, distal end of femur. BMI Body mass index. *p value between women and men in each group of fragility fractures.

Conclusion: OP is different between women and men. The probability of not receiving treatment in men was higher among men, these differences disappeared after care in FLS.
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AB1031 PREVALENCE OF GLUCOCORTICOID INDUCED OSTEOPOROSIS IN AFRICAN ADULT PATIENTS WITH CHRONIC RHEUMATIC DISEASES. A SYSTEMATIC REVIEW AND META-ANALYSIS.

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Background: Glucocorticoid (GC) use is well established in the treatment of rheumatics diseases, particularly rheumatoid arthritis (RA). The use of low dose GC has been endorsed by EULAR recommendations for the management of rheumatic and musculoskeletal diseases even if in the context of SARS-CoV-2, but long-term use is generally discouraged.
Objectives: To estimate the prevalence of glucocorticosteroids induced osteoporosis (GIOP) on bone mineral density (BMD) in African adult patients with inflammatory rheumatic diseases.
Methods: For this systematic review and meta-analysis, PubMed, Google Scholar, Scopus and African index medicus were systematically searched up to December 2020 without language restrictions. We included studies as follows: population-based or hospital-based study, study with sufficient information to estimate the prevalence of GIOP and osteoporotic fractures in African patients with rheumatic disease. Searches were limited to peer-reviewed full text articles. A standardized data extraction form was used to collect information from eligible studies. A random-effects meta-analysis was conducted to obtain the pooled prevalence of GIOP in these studies. The meta-analysis was stratified by geographical region. The study is registered with PROSPERO, number CRD42021256252.
Results: Our search identified 8571 studies, of which 8 studies were included in the systematic review from only four African countries and 7 studies in the meta-analysis. The pooled prevalence of osteoporotic fractures in our study was 47.7% (95% CI 32.9–62.8) with 52.2% (95% CI 36.5-67.6) in North Africa and 15.4% (95% 1.9-45.4%) in South Africa (SA). There was no evidence of publication bias, although heterogeneity was high (p=0.018). There was no data from sub-Saharan Africa apart from the two studies from SA.
Conclusion: The overall prevalence of GIOP in African adult patients with inflammatory rheumatic diseases was high at 47.7% (95% CI 32.9–62.8). Meta-analysis calculation revealed patient geographic origin as possible confounding factors of the proportion outcomes and further studies are required.
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AB1032 PREDICTORS OF INCREASING NUMBER OF FRACTURES IN A LARGE COHORT OF PATIENTS PRESENTING FOR DUAL-ENERGY X-RAY ABSORPTIOMETRY SCAN

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Background: Osteoporosis has been described as a global epidemic(1), it is the most common disease affecting bones (2). Incidence of osteoporosis is estimated to double by 2034(2) and osteoporotic fractures are expected to cost the US healthcare system around $50 billion by 2040(1), this is more than that for either chronic lung disease, breast cancer, diabetes, or stroke (1). Thus, it is vital to define the risk factors and characteristics associated with fractures to aid early prophylaxis.
Objectives: 1.Identify risk factors and predictors associated with fractures.
Methods: 31546 patients presented to a district general hospital in North West England for dual energy X-ray absorptiometry scan between 1996 and 2017. Demographics, risk factors and incidence of fractures were recorded. This data was retrospectively analysed to identify patients who had sustained at least one fracture. Patients were divided into three groups – group 1 had one fracture, group 2 had two fractures and group 3 had three or more fractures. *STATA* was used for statistical analysis. One way ANOVA with a Tukey post-hoc test and chi-squared test were used to compare the three groups.
Results: 11839 patients were identified to have sustained at least one fracture, this included 9993 females and 1846 males (Table 1). Group 1 contained 9390, group 2 contained 2050 and group 3 contained 399 patients. A statistically significant increase in the proportion of females within in each group was observed as the number of fractures increased (chi squared=13.99, p=0.001). There was a significant reduction in average height, weight and BMI between the 3 fracture groups with an increasing number of fractures (f(2)=31.67, p=0.0000, f(2)=23.71, p=0.0000 and f(2)=8.14, p=0.0003 respectively). Group 3 had the oldest mean age and group 1 the youngest (f(2)=44.36, p=0.0000). A significant reduction in fat percentage of the spine was identified as number of fractures increased (f(2)=4.92, p=0.0073). A significant increase in the proportion of patients with a history of smoking and alcohol excess within each group was observed as number of fractures increased (chi squared=7.48, p=0.024 and chi squared = 23.12, p=0.000 respectively). Mean T score in the lumbar spine, total femur and femoral neck were significantly lower between the 3 fracture groups with increasing fractures (f(2)=60.54, p=0.0000, f(2)=156.44, p=0.0000 and f(2)=115.86, p=0.0000 respectively).

Table 1. No. of fractures vs patient characteristics.

Characteristic	1 Fracture	2 Fractures	≥3 Fractures
Mean height, cm (SD)	161.49 (8.33)	160.45 (8.45)	158.70 (8.73)
Mean weight, kg (SD)	70.77 (15.93)	69.70 (15.42)	65.51 (14.69)
Mean BMI, kg/m2 (SD)	27.09 (5.54)	27.01 (5.27)	25.96 (5.22)
Mean age (SD)	67.45 (11.85)	69.76 (11.76)	70.84 (11.62)
Mean spine fat, % (SD)	30.61 (10.92)	30.58 (10.52)	28.87 (11.36)
Mean lumbar spine T-score (SD)	-1.23 (1.60)	-1.55 (1.52)	-1.86 (1.47)
Mean total femur T-score (SD)	-1.28 (1.22)	-1.69 (1.15)	-2.07 (1.13)
Mean femoral neck T-score (SD)	-1.47 (1.10)	-1.80 (1.00)	-2.04 (0.97)
Proportion of females (%)	83.84	86.00	89.47
Proportion of pts with smoking history (%)	37.42	39.41	43.11
Proportion of pts with excess alcohol history (%)	7.96	9.90	13.78

Conclusion: Some important risk factors and characteristics in patients sustaining fractures have been identified. Increased height, weight and BMI are associated with sustaining fewer fractures. Increasing age is associated with having sustained more fractures, in line with what is expected with the reducing T-scores and the ageing process. A reduced spine fat percentage is associated with higher number of fractures suggesting that fat provides a protective effect to bone. Finally, a history of smoking and excess alcohol consumption are shown to be important risk factors in sustaining increasing numbers of fractures.
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AB1033

RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS) FOR THE ASSESSMENT OF FEMORAL BONE HEALTH IN A MALE POPULATION

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Background: Bone mass reaches the peak during the third decade of life. By this age, men reach an increased bone mass that starts declining in their fifties, however less rapidly than women after menopause. However, men and women lose bone mass at the same rate by age 65-70, becoming fragile and more likely to have fracture.

Objectives: This study aimed to evaluate the diagnostic accuracy in osteoporosis diagnosis of Radiofrequency Echographic Multi Spectrometry (REMS) technology applied on the proximal femur in an adult male population in comparison with the Dual-energy X-ray Absorptiometry (DXA).

Methods: A cohort of Caucasian males was enrolled in the study. Inclusion criteria were: age between 30 and 90 years, body mass index (BMI) less than 40 kg/m^2, no significant walking impairments and proximal femur DXA medical prescription. All the enrolled patients underwent proximal femur scans with both DXA and REMS. The agreement between REMS and DXA-measured BMD was expressed by Pearson correlation coefficient and Bland-Altman method. The classification into patients "with osteoporosis" or "without osteoporosis" was carried out considering the conventional threshold of T-score (-2.5) for both techniques independently. The accuracy was evaluated by the assessment of sensitivity and specificity considering the DXA outcome as reference [1].

Results: A total of 219 men were included in the analysis, with mean age of 55.5 (± 15.3) years. The Pearson correlation coefficient between REMS- and DXA-measured BMD values was r=0.94. At Bland-Altman analysis, Bias ± 1.96 Standard Deviation were -0.004 ± 0.04 g/cm^2. The REMS capability to discriminate osteoporotic patients from non-osteoporotic ones was very high: a sensitivity of 90.0% and specificity of 91.8% was detected.

Conclusion: REMS, applied to the proximal femur site, is a reliable technology for the diagnosis of osteoporosis also in men, thus confirming the diagnostic performance already observed in studies carried out in female populations [1, 2].

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AB1034

FRACTURE RISK BY FRAX WITH AND WITHOUT BONE MINERAL DENSITY, COMPARISON OF FACTORS AFFECTING CONCORDANCE

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Background: The Fracture Risk Assessment Tool (FRAX) estimates the 10-year probability of hip (FXC) and major osteoporotic (FXOM) fractures in patients aged 40 to 90 years using important clinical factors, such as bone mineral density (BMD), optional input variables. (1) There is convincing evidence that with or without the use of BMD it provides a well-validated instrument and may be useful in clinical practice for identifying patients at high risk of fracture and informing treatment decisions. (2)

Objectives: This study aims to determine the concordance between the treatment decision, calculated using FRAX scores with and without BMD, and to identify the risk factors associated with the discordance in patients with autoimmune rheumatic diseases.

Methods: A cross-sectional study was carried out in patients with autoimmune rheumatic diseases who had undergone osteoporosis detection (OP) using dual bone densitometry in the Rheumatology service of the University Hospital "Dr. José Eleuterio González" during the period August 2020 - August 2021. The FRAX questionnaire was applied to determine risk factors for OP and the results of the instrument with and without BMD were calculated, the patients were classified as low, intermediate, and high risk.

A Student's t-test, a Wilcoxon rank-sum test, and a Chi-square or Fisher's exact test were used to compare variables between groups and calculate P-values.

Results: A total of 88 patients were included. Based on FRAX questionnaire responses, 82 (93.18%) patients had at least one risk factor for OP. The FRAX result with or without densitometry resulted in a treatment decision in 48 (54.5%) and 28 (31.8%) patients, respectively. The results were concordant in 65 (73.9%) of the cases. It was found that patients with osteopenia due to BMD had a greater agreement between both measurements (93.3%, p 0.003) than patients with normal BMD (62.5% p 0.001). Likewise, patients with secondary osteoporosis had lower concordance than patients without this diagnosis (25% and 72.5%, respectively, p 0.006).

Conclusion: The results of FRAX with and without densitometry were mostly agreeable in predicting the need for treatment according to the 10-year probability of hip fracture, however, this concordance decreased in patients with a previous diagnosis of secondary osteoporosis, no significant difference was found between the risk factors for the concordant and discordant groups. More studies are required to determine the variables that cause a decrease in the concordance of the tests.

Table 1. Factors that affect the results between the discordant groups.

Variables	Concordant n=65	No concordant n=23	P value
Sex (%)			0.078
Men	8 (12.3%)	0 (0%)	
Women	57 (87.7%)	23 (100%)	
Age (years)	57.85 ± (11.66)	59.2 ± (8.36)	0.13
<50	12 (18.4%)	4 (17.3%)	
50-59	24 (36.9%)	8 (34.6%)	
60-69	17 (26.1%)	9 (39.1%)	
70-79	10 (15.3%)	2 (8.7%)	
>80	2 (3%)	0 (0%)	
Height (meters)	1.52 ± (0.08)	1.52 ± (1.06)	0.042
Weight (kilograms)	68.5 (59.5-80.5)	68 (64-74)	
BMI (kg/m^2)	28.2 (24.9-33.1)	30.9 (29.2-32.5)	0.002
Normal weight (%)	16 (24.6%)	3 (13%)	0.136
Overweight (%)	22 (33.8%)	5 (21.7%)	0.150
Obesity (%)	27 (41.5%)	15 (65.2%)	0.051
Normal BMD	35 (53.84%)	21 (93%)	0.001
Osteopenia	28 (43.07%)	2 (8.69%)	0.003
Osteoporosis	2 (3.07%)	0 (0%)	0.395
	With BMD	***Without BMD***	
Hip Fracture FRAX Score	5.3 (3.62-9.77)	1 (0.42-2.67)	
Major osteoporotic fracture	6.2 (4.02-9.85)	0.75 (0.3-1.77)	
Treatment suggested by FRAX	48 (54.5%)	28 (31.8%)	

BMI= Body mass index, BMD= Bone mineral density, FRAX= Fracture risk assessment tool

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Crystal diseases, metabolic bone diseases other than osteoporosis

AB1035 END STAGE RENAL DISEASE IN PATIENTS WITH GOUT AND CONTROLS, ETIOLOGICAL DIFFERENCES?

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Background: The association between gout and renal disease is well known. However, whether hyperuricemia causes renal disease, or if the association is explained by comorbidities, is still up for debate. Studies on the effects of urate and gout on chronic kidney disease (CKD) show conflicting results. There is a lack of data on the underlying causes of CKD in gout patients.
Objectives: To compare causes of end stage renal disease (ESRD) in patients with gout and population controls.
Methods: This is a population-based and register-based case-control study. Gout cases, aged 18 years or older, were identified by at least one visit to a physician either an in- or outpatient clinic with a registered ICD-10 code for gout (M10) in the Western Regional Healthcare Contact Register (VEGA), between January 1st 2001 through December 31st 2018. For each case five controls without gout were matched by sex, age, and county/place of residence at year of first diagnosis. Cases and controls were excluded if they prior to the first recorded ICD-10 code for gout, had a record of end stage renal disease, defined as codes for renal transplantation or dialysis either in VEGA or the Swedish Kidney Register (SNR). In this cohort, all cases and controls developing ESRD during the follow-up period (2001 to 2018) were identified, and the registered causes of ESRD were compared across the groups.
Results: In total, 48594 gout cases (mean age 68.4 years; 67% male), and their 150618 matched controls (mean age 63.3 years; 67% male) were included. Of the cases and controls, 529 (1.1%) and 128 (0.1%) developed ESRD, respectively. At the time-point of active uremia treatment start (as in start of dialysis or kidney transplantation), the cardiovascular comorbidity burden was higher for the gout patients (Table 1). There was no significant difference in the distribution of ESRD-causes between patients with gout and their controls (Figure 1).

Table 1. Baseline data

	Gout	Controls
Number (% of total)	529 (80.5)	128 (19.5)
Age at gout diagnosis, mean (median)	64.2 (65)	63.3 (65)
Age at ESRD, mean (median)	69.2 (72)	68.9 (71)
Male sex, n (%)	389 (73.5)	109 (85.2)
No renal failure at baseline, n (%)	239 (44.6)	77 (60.2)
Diabetes, n (%)	215 (40.6)	44 (34.4)
Hypertension, n (%)	473 (89.4)	110 (85.9)
Ischemic heart disease, n (%)*	206 (38.9)	26 (20.3)
Cerebrovascular disease, n (%)	89 (16.8)	15 (11.7)
Hematologic malignancy, n (%)	11 (2.1)	6 (4.7)
Dermatologic malignancy, n (%)	12 (2.3)	3 (2.3)
Other malignancy, n (%)	65 (12.3)	16 (12.5)

*p<0,001

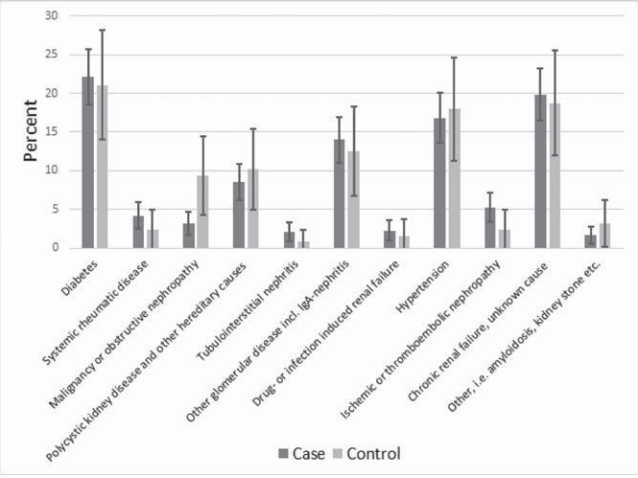

Figure 1.

Conclusion: In this study, including 48594 cases with gout, of which 529 developed ESRD, there was no apparent difference in the cause of ESRD compared to matched controls. This suggests similar pathophysiological mechanisms of ESRD development in patients with gout and the general population.
Disclosure of Interests: None declared
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AB1036 IS HEMODIALYSIS ENOUGH TO CONTROL GOUT IN CHRONIC TERMINAL RENAL DEFICIENCY PATIENTS? A TEN YEARS RETROSPECTIVE STUDY

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Background: Gout is the most common inflammatory rheumatism of industrials countries and chronic renal deficiency is one of the most usual risk factor(1). Uncontrolled gout can cause articular impairment but is also associated with a global and cardiovascular excess mortality, especially in dialysis population(2). International guidelines on gout management remain currently unclear for this particular population(3,4) and current literature data are contradictory on the effectiveness of hemodialysis alone in stemming gout flares.
Objectives: The objective of this study was to analyze the rate of gout flares, during 5 years on gouty patients who starts hemodialysis, treated or not by hypouricemic drugs.
Methods: We performed an observational, retrospective and multicentric study on gouty patients who started hemodialysis between 2005 and 2015 in two nephrology unit. We recorded demographic, clinical and therapeutic data at the start of hemodialysis and throughout 5 years of follow up. A gout flare was defined as presence of uric acid crystal in articular punction when it was performed, or clinical diagnosed as such with a colchicine prescription. The effectiveness of dialysis was measured by the KT/V ratio measured during gout flares and 3 times per year for each patient correlated with the serum uric acid level. According to the French legislation, no ethics committee approval was requested for such a retrospective survey. Survival analysis by Kaplan - Meier method and bivariate analysis have been performed to study gout flares and their association with clinical or biological factor.
Results: One hundred eighty two patients have been included, 98/182 (53, 8%) had long term hypouricemic treatment: 88/98 (89%) by allopurinol and 10/98 (11%) by febuxostat. Mean age at dialysis initiation was 68.6 years with a male/female sex ratio of 2.7:1. Sixty-four/182 patients (35.16%) presented at least one gout flare during the follow-up: 42 patients (65%) without hypouricemic treatment and 22 patients (45%) with hypouricemic treatment. Patients on hypouricemic treatment since hemodialysis beginning had significantly less gout flares compared to those without (p = 0.0009) **(graphic 1).** There was no significant KT/V ratios difference between the 2 populations at the time of gout flares. Hypouricemic treatment was a protective factor for the occurrence of gout attacks (HR: 0.42, 95% CI 0.25 – 0.71) (Table 1**).**

Table 1. Associated factor of gout flares after the beginning of hemodialysis on gouty patients

	HR	95% CI
Current or active smoking	0.92	0.46-1.86
Male	0.82	1.48-1.42
Caucasian ethnic	0.83	0.64-1.75
Hypouricemic treatment	**0.42**	**0.25-0.71**
High Blood Pressure	1.21	0.44-3.36
Obesity	0.84	0.47-1.51
Dyslipidemia	0.79	0.47-1.30
Diabetes	1.28	0.78-2.11
Cardiac failure	1.42	0.73-2.81

HR: Hazard Ratio; CI: Confidence interval

Conclusion: Therefore hypouricemic treatment at the initiation of hemodialysis seems to be a protective factor against gout flares, which may persist in dialysis patients. Prospectives studies should be performed to confirm these results for this particular gouty population.
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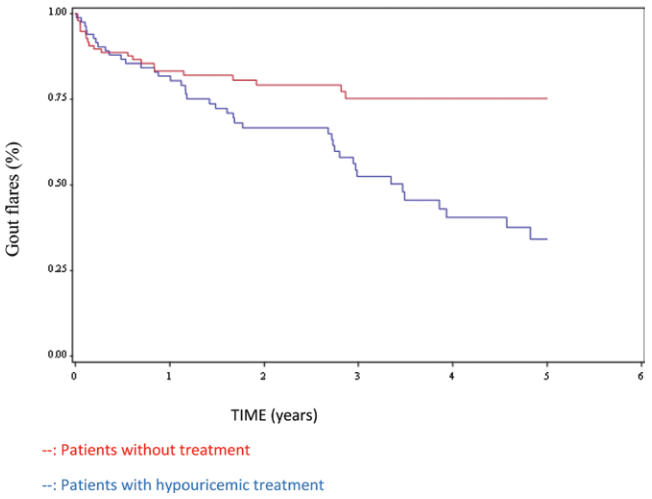

Graphic 1. Survival analysis of gout flaresTIME (years)--: Patients without treatment--: Patients with hypouricemic treatment

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AB1037 CRYSTAL DEPOSITS IN PRIMARY SYNOVIAL CHONDROMATOSIS

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Background: Primary synovial chondromatosis (**prSynCh**) is a metaplastic disorder of the synovial membrane, characterized by chondrocyte differentiation of synovial pluripotent stem cells, and chondroid tissue production. The **prSynCh** may be accompanied with amorphous calcium phosphate or carbonate deposition and bone formation, with or without true medullary spaces. The cause of stem cell differentiation is unknown; different irritative agents (infective, toxic, mechanic, etc.) are mentioned, but the condition may occur spontaneously as well [1, 2]. Crystal deposits as irritative agents of primary synovial chondromatosis due to a clinically latent metabolic disorder are not mentioned.
Objectives: The **aim** of this study was to determine the formal pathogenesis of synovial chondromatosis, and to detect crystal deposits in synovial membrane in order to explore the possible role of metabolic diseases in transformation of stem cells into chondrocytes, i.e., to demonstrate the metabolic origin of **prSynCh**.
Methods: Surgical specimens (synovial membranes of 14 knees, 4 hips and 2 elbows) of 20 patients (females 13. mean age of 50.17 years, range 40 – 74; males 7, mean age of 40.64 years, range 30 – 76years) with primary synovial chondromatosis were studied histologically. Cases of secondary synovial chondromatosis, i.e., due to osteoarthritis, rheumatoid arthritis, aseptic (avascular) bone necrosis, osteochondral traumatic injury, etc. were excluded. Serial sections (5 microns) of tissue samples were stained with **H-E**, **Alizarin red S** (specific for calcium), and **von Kossa**'s reaction (specific for phosphate and/or carbonate), and were compared with unstained sections according to **Bély** and **Apáthy** (2013). The non-staining technique is a very sensitive method to detect small crystals with weak birefringence viewed under polarized light [3-5].
Results: Chondromatosis (chondroid formation without osteoid or bone formation) was found in **8**, osteochondromatosis (chondroid with osteoid and bone formation) in **11**, and only bone formation in **1** of 20 patients. True medullary spaces accompanied bone formation in **8** of 12 cases. Different stages of chondroid and/or bone formation existed side by side in the same histologic section. In non-stained sections **HA** [$Ca_5(PO_4)_3(OH)$], **CPPD** [$Ca_2P_2O_7.2H_2O$] crystals, and/or unidentified crystal fragments were detected in all cases. Amorphous calcium phosphate and/or carbonate deposits were present in 12 of 20 patients.
Conclusion: The formal pathogenesis of primary synovial chondromatosis corresponded to the descriptions of the pertinent literature characterized by clean chondromatosis, mixed osteochondromatosis, and pure osteomatosis. We assume that the pre chondromatous phase of **prSynCh** starts with hydroxyapatite (**HA**) crystal deposition with or without calcium pyrophosphate dihydrate (**CPPD**) deposits, and the **prSynCh** may be regarded essentially a metabolic disease, like chondrocalcinosis or apatite rheumatism. The difference between these diseases is only in the prevalence and amount of **HA** and/or **CPPD** crystals, accompanied with or without amorphous calcium phosphate and/or carbonate deposits. In our opinion the chondrocalcinosis, apatite rheumatisms and **prSynCh** represent the same group of metabolic diseases.
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AB1038 PEGLOTICASE URATE-LOWERING RESPONSE FOLLOWING COVID-RELATED GAP IN THERAPY: EXPERIENCES OF ONE RHEUMATOLOGIST

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Background: When uncontrolled gout cannot be managed with oral urate-lowering therapies, pegloticase is one of the few remaining treatment options. Patients receiving infusion therapies experienced treatment interruptions due to the COVID-19 pandemic. As with other biologic therapies, patients can develop anti-drug antibodies (ADAs) against pegloticase, and longer infusion intervals can result in higher rates of pegloticase immunogenicity.[1] The literature suggests that co-administering an immunomodulator with pegloticase can markedly decrease the proportion of patients who develop ADAs,[2] increasing the proportion with sustained urate-lowering response.[3]
Objectives: This case series reports one rheumatologists' experience with a gap in pegloticase therapy during the COVID-19 pandemic.
Methods: Uncontrolled gout patients who underwent pegloticase treatment during 2019/2020 and had a gap in therapy of ≥28 days were identified. Patient, clinical, and treatment (number post-gap infusions, immunomodulation co-therapy) characteristics were retrospectively examined, along with urate-lowering response following therapy interruption. Patients who had a serum urate (SU) <6 mg/dL after the last post-gap pegloticase infusion were considered to have recaptured response.
Results: 7 patients (5 men, 64.3±13.5 years, pretherapy sUA: 7.76±2.47 mg/dL, 6 had tophi) were included with 2 remaining on therapy at data collection. Eleven gaps were noted with an average gap duration of 11.4±9.3 weeks (median: 9 weeks). For the last gap in therapy, patients received 13.9±7.0 infusions (range: 4-22) before the gap and 7.0±4.1 infusions (range: 2-14) after (Figure 1). Four patients (57%; Patients 1, 2, 5, 7) had recaptured urate-lowering at last pegloticase infusion, all of whom began immunomodulation (3 methotrexate, 1 mycophenolate mofetil/hydroxychloroquine) prior to resuming pegloticase. Of the 3 patients without response recapture, 2 initiated MTX after resuming pegloticase. 4 patients (57%) experienced ≥1 AE, including mild infusion reaction (n=1), acute gout flare (n=2), clinically meaningful decrease in eGFR (14.8 ml/min/1.73m^2, n=1), heart attack (n=1), and anemia (n=1).
Conclusion: These cases suggest that it may be possible to recapture urate-lowering response to pegloticase in some patients, particularly in the presence of immunomodulation. These preliminary findings are important to this vulnerable patient population, particularly during the COVID-19 pandemic. Further study is needed to confirm our findings.
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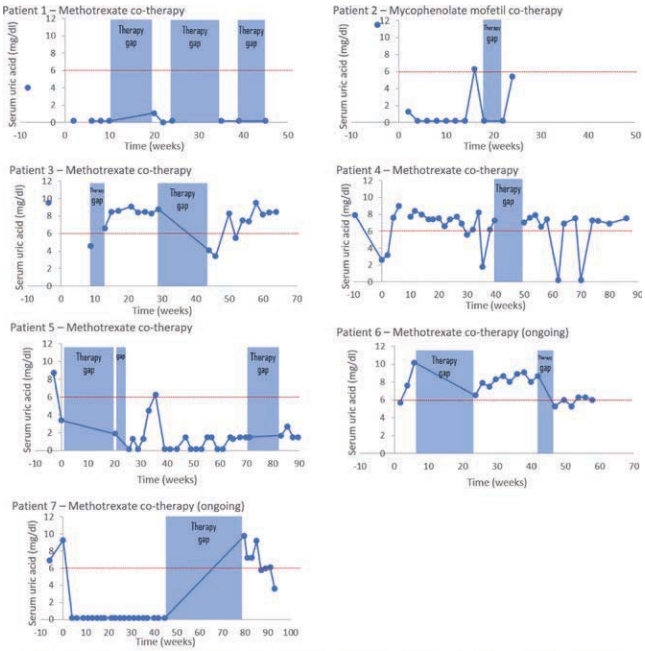

Figure. Serum uric acid over time in patients with pegloticase therapy gaps longer than 28 days. Data points represent pre-infusion serum uric acid levels. All patients were also co-treated with an immunomodulator as noted. "Ongoing" denotes patients who remained on therapy at the time of data collection.

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AB1039 PATIENT REPORTED OUTCOMES AMONG PATIENTS RECEIVING TREATMENT FROM THE PEGLOTICASE PHASE 3 CLINICAL TRIALS FOR UNCONTROLLED GOUT

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Background: Gout affects more than 9 million Americans,[1] with some suffering so severely that everyday life becomes painful and difficult.[2] Pegloticase is an infused uricase-based medicine that significantly reduces serum uric acid (sUA) levels in patients suffering from treatment-resistant gout,[3] but the direct effect of treatment on quality of life (QoL) by response status has not yet been reported.[4]

Objectives: To determine if the effect of pegloticase treatment on QoL and other patient-reported outcomes is significant compared to placebo, regardless of treatment response status.

Methods: This analysis utilized results from two parallel 6-month randomized phase 3 registrational clinical trials in which subjects were treated with 8 mg of pegloticase or placebo biweekly. Responders were those who maintained sUA levels <6 mg/dL for ≥80% of the time during Months 3 and 6 combined. Multiple QoL measurements were taken throughout the 6-month treatment period, including the Health Assessment Questionnaire (HAQ; Pain, Disability Index [DI], and Health), the 36-Item Short Form Health Survey Questionnaire (SF-36), and the number of swollen and/or tender joints. This analysis assessed the differences between three groups: treatment responders, treatment non-responders, and placebo-treated patients. The change from baseline to Week 25 in each assessment was analyzed using a mixed model for repeated measures adjusting for age, visit, presence of tophi at baseline, and the interaction between visit and group.

Results: A total of 36, 49, and 43 patients were included in the treatment responder, treatment non-responder, and placebo-treated groups, respectively. Significant differences in the change from baseline to Week 25 in HAQ-Pain, HAQ-DI, HAQ-Health, and SF-36 Physical Component Score (PCS) between treatment responders and placebo-treated patients were observed (all $P \leq 0.006$, Figure 1). The reduction in the number of swollen or tender joints was also significantly greater in treatment responders compared to placebo-treated patients ($P < 0.001$). Between treatment responders and treatment non-responders, there were no significant differences in the change from baseline in HAQ-Pain, HAQ-DI, HAQ-Health, and SF-36 PCS. Significant differences were observed between treatment non-responders and placebo-treated patients in the change in HAQ-Pain, HAQ-DI, HAQ-Health, and SF-36 PCS (all $P \leq 0.003$), as well as the number of swollen or tender joints ($P = 0.049$, Figure 1). The change in SF-36 Mental Component Score was not significantly different between any of the 3 groups examined.

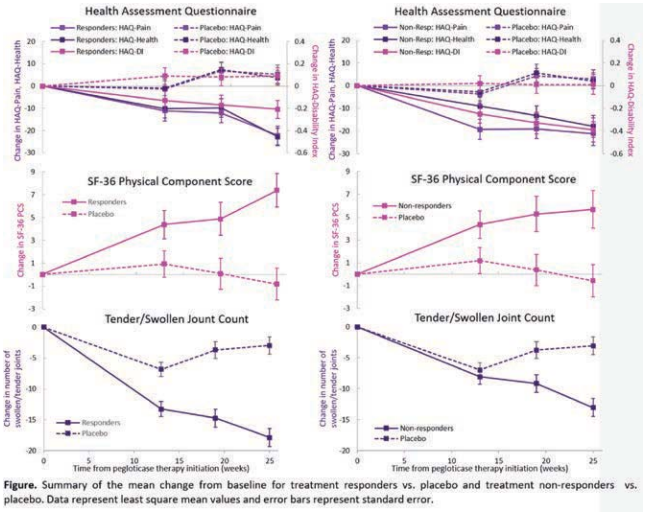

Figure. Summary of the mean change from baseline for treatment responders vs. placebo and treatment non-responders vs. placebo. Data represent least square mean values and error bars represent standard error.

Conclusion: In the Phase 3 registration trials of pegloticase used as monotherapy for uncontrolled gout, QoL parameters improved among pegloticase-treated patients regardless of response status.

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AB1040 ASSOCIATION OF Q141K POLYMORPHISM OF ABCG2 GENE WITH THE EFFECTIVENESS OF URATE-LOWERING THERAPY IN PATIENTS WITH GOUT (PILOT STUDY)

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Background: The effectiveness of allopurinol in pts with gout depends on genetic factors (GF) [1]. How GF works on probability of the target serum uric acid (sUA) level achievement is not studied.

Objectives: To study the opportunity of the target sUA level achievement in pts with gout while taking allopurinol or febuxostat, depending on the polymorphism (rs2231142) of the *ABCG2* gene.

Methods: The study included 82 pts with gout aged ≥18 yrs who did not take urate-lowering drugs (ULD) and had sUA level >360 μmol/l. Initially all patients were prescribed allopurinol 100 mg/day, than the dose was up-titrared to achieve the target sUA level (<360 μmol/l or <300 μmol/l in pts with chronic tophaceous gout). Maximum dosage was 900 mg/day; in pts with glomerular filtration rate (GFR) <60 ml/min/1.73 m^2 - 300 mg/day. Pts who did not achieve the target sUA level while using allopurinol were prescribed febuxostat 80 mg/day, which, if necessary, was increased to 120 mg/day. Each patient was followed up until the target sUA level was achieved. All pts underwent genotyping of the C>A (rs2231142) polymorphism of the *ABCG2* gene. During the study we compared: the probability of achieving the target sUA level, the average values of the sUA level decline, the average doses of ULD in pts with different genotypes (CC, CA, AA) of the *ABCG2* gene. Statistical analysis was carried out using the Statistica 12.0 software package, and descriptive statistics methods.

Results: The target sUA level was defined as <300 μmol/l in 45 (55%) of 82 pts, as <360 μmol/l in 37 (45%) pts. In 26 pts, the dose of allopurinol did not exceed 300 mg/day. In 28 (34%) pts on allopurinol therapy, the target level of sUA was achived. In 54 (66%) pts allopurinol was replaced with febuxostat, while in 22 (41%) of them, the level of sUA decreased and was below the target. The CC genotype of the *ABCG2* gene was found in 51 (62%) pts, the CA genotype in 30 (37%) pts, and the minor AA genotype in 1 (1%) pt. The opportunity of the target sUA level achievement during the allopurinol therapy in carriers of the

homozygous CC genotype and CA or AA genotypes did not differ: 17 (33%) and 11 (35%) cases, respectively. It turned out that CA and AA pts required a significantly higher dose of allopurinol (365±102 mg/day) than CC pts (290±85 mg/day), p=0.002. Of 54 pts treated with febuxostat who did not achieve the target sUA level, 30 (56%) pts had the CC genotype and 24 (44%) pts had the CA genotype. The opportunity of the target sUA level achievement was comparable (p=0.22).

Conclusion: The opportunity of achieving the target sUA level in pts with gout taking allopurinol is not associated with the C>A polymorphism of the *ABCG2* gene, but the presence of the CA and AA genotypes is associated with the need to prescribe large doses of allopurinol.

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AB1041 REAL-WORLD REPORTING OF GOUT FLARES IN UNCONTROLLED GOUT PATIENTS CO-TREATED WITH PEGLOTICASE AND METHOTREXATE

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Background: Acute gout flares are a known result of urate-lowering in gout patients[1] and are the most common adverse event in patients treated with pegloticase.[2] Fortunately, the proportion of pegloticase-treated patients who experience flares and the number of flares/patient decrease over time.[3] Though well-studied in the clinical trial setting, little has been published on the rate of acute gout flares during pegloticase therapy in a real-world, rheumatology setting. This retrospective study examined one community practice's findings on gout flares in uncontrolled gout patients co-treated with pegloticase and methotrexate.

Objectives: This retrospective chart review examined acute gout flare occurrence and characteristics in patients undergoing pegloticase-methotrexate co-therapy. Patients with and without gout flares were also compared to investigate potential factors that may have influenced gout flare.

Methods: All patients who underwent pegloticase plus methotrexate co-therapy between January 2017 and March 2021 at a community rheumatology practice were included. Patient, treatment, and flare characteristics were extracted from the medical record and compiled into a de-identified data set.

Results: 29 patients treated with pegloticase and methotrexate (28 subcutaneous, 1 oral) were included. Mean patient age was 59.9±17.0 years and 79% were male. Gout duration was 11.7±10.8 years, pre-therapy serum uric acid (sUA) averaged 9.4±1.8 mg/dL, and 97% had visible tophi. Patients had received 12.8±14.3 pegloticase infusions over 25.1±9.7 weeks, with pre-infusion sUA<6 mg/dL in 27/29 patients (93%) at last pegloticase dosing. 23 gout flares were noted in 12 patients (41%, 1.9±1.8 flares/patient), 59% of which were noted as severe and 50% involved a single joint. Acute gout flare was most common in the first 4 weeks of therapy, with first flare occurring a mean of 3.4±2.1 weeks after first pegloticase infusion. Demographic and treatment characteristics were similar between flaring and non-flaring patients. However, patients with ≥1 flare were older (65.8±15.4 years vs. 55.6±17.8 years), more often obese (83% vs. 47%), and had an overall higher comorbidity burden.

Conclusion: This retrospective study of real-world pegloticase use suggests that gout flare rates may be lower in a real-world setting (41%) than that reported in clinical trials (76–86%[2,3]), which have different gout flare criteria. Consistent with clinical trials,[2,3] flare rate was highest during the first 4 weeks of pegloticase treatment, progressively decreasing over time. Interestingly, these data suggest that patients who experience gout flares on pegloticase may have more obesity and a higher comorbidity burden than those who do not experience flares. Further examination of gout flares during real-world pegloticase use is warranted.

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Disclosure of Interests: John Albert Speakers bureau: Horizon Therapeutics, Consultant of: Horizon Therapeutics, Lissa Padnick-Silver Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Brian LaMoreaux Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics

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AB1042 PEGLOTICASE USE IN RENAL TRANSPLANT RECIPIENTS WITH GOUT: AN INSURANCE CLAIMS STUDY

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Background: Kidney transplant (KT) recipients have a high gout incidence due to reduced eGFR and medication use associated with hyperuricemia.[1] Oral urate-lowering therapies in KT patients are further limited by residual chronic kidney disease and potential drug-drug interactions. Pegloticase rapidly lowers serum urate in uncontrolled gout patients,[2-3] but efficacy for monotherapy is limited in ≥50% of treated patients by anti-drug antibodies that cause loss of urate-lowering effect and can lead to infusion reactions in some patients.[4-5] Anti-rejection medications are ubiquitously used after organ transplantation and are known to reduce the development of anti-drug antibodies,[6] but published data of pegloticase use in KT recipients is limited.

Objectives: This claims-based analysis examined real-world pegloticase use in KT patients to determine the number of administered infusions compared to non-transplanted patients.

Methods: Patients in the IQVIA database (2015-2020) who had ≥1 CPT or ICD9/10 code for KT and ≥1 pegloticase claim following KT were identified. Patients who returned to dialysis due to graft failure/rejection prior to pegloticase use were excluded. Patient characteristics and pegloticase therapy parameters were examined.

Results: 91 KT recipients with pegloticase use were identified. Of 85 patients with demographics, 81% were male, mean(±SD) age at first transplant was 55.0±10.7 years, and 67% had tophaceous gout. The most common comorbidities were hypertension (84%), hyperlipidemia (48%), anemia (46%), type 2 diabetes (40%), and heart failure (34%). First transplant and gout codes occurred 2.6±1.7 and 2.1±1.7 years, respectively, before first pegloticase claim. Among 67 patients with medication codes, immunosuppressive medications used <3 months before and/or during pegloticase included tacrolimus (51%), mycophenolate mofetil (49%), and/or cyclosporine (37%). Patients received 13±16 pegloticase infusions (median: 8 [Q1, Q3: 4, 15]), with 38% receiving ≥12 and 20% receiving ≥20 infusions.

Conclusion: This study showed a higher median number of pegloticase infusions than reported in prior claims-based studies of non-KT patients.[7] Real world data from KT patients support the hypothesis that transplant immunosuppression may allow more patients to receive a longer course of pegloticase therapy, presumably via anti-drug antibody attenuation. This is of particular importance for this vulnerable patient group that is at a high risk for developing uncontrolled gout.

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AB1043 IDENTIFICATION OF UNUSUAL TOPHI ANTERIOR TO THE THYROID CARTILAGE USING DIFFERENT IMAGING METHODS

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Background: Inadequately treated gout patients could develop tophi. However, tophi could appear as atypical mass, leading to difficulty in differential diagnosis.

Objectives: The objectives of the study were to describe an unusual case with tophi anterior to the Thyroid Cartilage using different imaging methods.

Methods: Clinical information of the case was presented. Ultrasound, dual energy Computed Tomography (DECT) and CT scan were compared to describe the tophi.

Results: A 66-year-old man with a 30-year history of gout was admitted. He had received urate-lowering drugs intermittently over the past few years. Physical examination revealed multiple tophi on the hands, feet, and other auricular surfaces. Moreover, there was a subcutaneous mass above the thyroid cartilage (Figure 1A). Ultrasound revealed hyperechoic nodule anterior to the thyroid cartilage, 11*7cm in size, with uneven internal echo, no blood flow signal inside, and a close relationship between the barrier of the nodule and the thyroid cartilage (Figure 1B). DECT of the neck confirmed that the mass anterior to the thyroid cartilage were tophi (Figure 1C-D). A plain radiographic evaluation demonstrated

soft-tissue swellings and para-articular erosions involving hands (Figure 1E-F). The serum creatinine and uric acid levels were elevated as follows, creatinine, 562 µmol per liter (normal range, 31.8 to 116); and uric acid, 621 µmol per liter (normal range, 90 to 420).

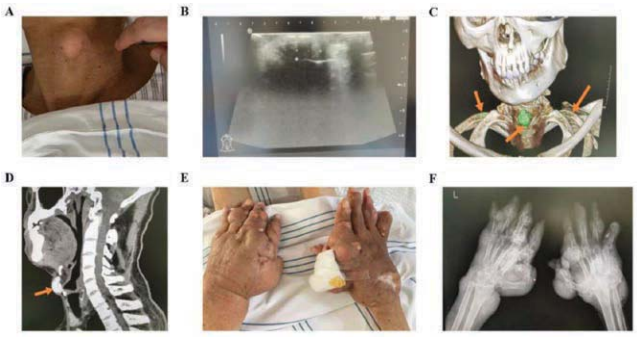

Figure 1. Tophi detected by different imaging methods. A.A picture of the mass anterior to the thyroid cartilage; B. A mass anterior to the thyroid cartilage detected by ultrasound; C. The mass anterior to the thyroid cartilage detected by dual energy CT; D. The mass anterior to the thyroid cartilage detected by CT scan; E. a picture of tophi in the hands; F. a plain radiograph of tophi in the hands.

Conclusion: DECT has more advantages over ultrasound and CT for detection of atypical tophi in gout patients.
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AB1044 RISK FACTORS OF DIABETES MELLITUS IN PATIENTS WITH GOUT (RESULTS OF A PROSPECTIVE STUDY)

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Background: It is assumed that the risk of developing diabetes mellitus (DM) is due not only to generally accepted risk factors (RF), but also to RF related to gout.
Objectives: To evaluate the influence of various RF for DM in pts with gout.
Methods: 444 pts aged ≥18 years with a crystal-verified diagnosis of gout without DM were included in the study. The average duration of observation was 5.66 [2.69; 7.4] yrs. To identify the RF associated with developing of DM in patients with gout, multivariate logistic regression was used. There were included: gender; DM in relatives; insufficient physical activity; unbalanced diet; age ≥45 yrs; ≥ 4 exacerbation of arthritis per yr; presence of tophi; BMI ≥ 30 kg/m^2; presence of hypertension; allopurinol, febuxostat, GC, diuretics, metformin or colchicine intake; GFR <60 ml/min/1.73 m^2; serum uric acid (sUA) level ≥420 µmol/l; UA ≥480 µmol/l. Statistica 12.0 package was used for statistical data processing.
Results: DM was developed in 108 (24.3%) pts. Pts who developed DM were older than those who did not develop (52.84±10.96 vs 49.72±11.95 respectively, p=0.02); they were more likely to have heredity for DM of the first and second kinship lines (49.1% vs 25.6% respectively, p=0.0001); they took antihypertensive drugs more often (73.1% vs 50.5%, p=0.0001), also diuretics (27.7% vs 14.8%, p =0.003) and GC (47.2% vs 36.4%, p=0.047). There were more pts with subcutaneous tophi (59.3% vs 29.9%, p=0.001), those who had ≥ 4 attacks of arthritis per yr (67.6% vs 31.6%, p=0.001), sUA ≥480 µmol/l (71.3% vs 50.8%, p=0.0002), sUA≥600 µmol/l (34.3% vs 11.8%, p=0.0002). According to a multivariable logistic regression, the risk of DM is increased in case of: ≥ 4 arthritis attacks per yr (odds ratio [OR] 5.231, 95% confidence interval [CI] 2.978-9.187, p=0.0001); presence of subcutaneous tophi (OR 2.609, 95% CI 1.500-4.537, p=0.001); sUA level ≥480 µmol/l (OR 2.261, 95% CI 1.022-5.004, p=0.144); hypertension (OR 2.577, 95% CI 1.348-4.926, p=0.004); taking diuretics (OR 2.353, 95% CI 1.193-4.64, p=0.014). The risk of developing DM was reduced by taking febuxostat (OR 0.309, 95% CI 0.113-0.844, p=0.022) and metformin (OR 0.49 (95% CI 0.21; 1.16), p=0.107).
Conclusion: The risk of developing DM in pts with gout is associated with the frequency of arthritis attacks, sUA level ≥480 µmol/l, hypertension and diuretics intake. Therapy with febuxostat or metformin is associated with descended risk of DM.
Disclosure of Interests: Olga Sheliabina Speakers bureau: Berlin Chemie Menarini Group, Maxim Eliseev Speakers bureau: Berlin Chemie Menarini Group, Sobi, EGIS, CSC, MosFarma, Alium Group, Svetlana Glukhova: None declared
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AB1045 QUALITY OF LIFE IN PATIENTS WITH GOUT TAKING URATE-LOWERING DRUGS, DEPENDING ON THE ACHIEVEMENT OF THE TARGET LEVEL OF SERUM URIC ACID

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Background: Intake of urate-lowering drugs (ULD) leads to an improvement in the quality of life (QoL) in pts with gout. However, it is not clear to what extend the QoL is changed in pts who did not achieve the target level of serum uric acid (sUA).
Objectives: to evaluate the dynamics of the QoL in pts, taking ULD, who have achieved and have not achieved the target sUA level.
Methods: 98 pts with gout were included in the prospective study. The follow-up period was 24 months, allopurinol or febuxostat at doses sufficient to achieve the target sUA level (<360 µmol/l) were used. The maximum daily dose of allopurinol was 900 mg/day, febuxostat - 120 mg/day. Pts who did not achieve the target sUA level continued taking ULD at the maximum dosages. The values of the Qol in dynamics were calculated using the SF-36v2 questionnaire. The assessment of the QoL was carried out separately in pts who achieved and did not achieve the target level of sUA. The frequency of exacerbations of arthritis was also assessed. Statistica 12.0 package was used for statistical data processing.
Results: 69 of 98 (70%) pts achieved the target sUA level, wherein allopurinol was taken by 46 pts, febuxostat – 34 pts. Pts who achieved the target level of sUA after 6 mo. of ULD usage, demonstrated a significant improvement in the physical health (PH), including physical functioning (PF), role limitations due to physical functioning (RP), general health (GH), as well as vitality (VT) (p<0.05 for all). After 12 and 24 mo. improvement was achieved in RH, GH and PF (p<0.01), RP, bodily pain intensity (BP) and VT (p<0.05). General mental health (MH), role-emotional functioning (RE) and social functioning (SF) were unchanged throughout the study. Pts who did not achieve the target sUA level after 6 and 12 mo. significantly improved: PF, RP (p<0.05 for all). After 24 months, for all QoL parameters, the values did not differ from the initial ones. The frequency of arthritis exacerbation in pts who achieved the target sUA level decreased from 3.1±1.6 cases per year to 0.9±1.1 cases per year (p=0.0013); in those who did not achieve - from 3.1±1.9 cases per year to 2.4±1.6 cases per year (p=0.047).
Conclusion: : The QoL in gout pts who achieved target sUA level continues to improve during the first year of ULD intake. Even if the target sUA level is not achieved, the QoL of patients with gout treated with ULD remains stable for at least 2 years of therapy. This predetermines the need to use maximum daily doses of ULD, even if the target serum UA level is not achieved.
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AB1046 EFFICACY OF FEBUXOSTAT IN PATIENTS WITH GOUT STRATIFIED BY BASELINE RENAL FUNCTION

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Background: The opportunity of achievement of the target serum UA (sUA) level in pts with gout, stratified by renal function, is not studied.
Objectives: To compare the probability of the sUA level achievement during therapy with febuxostat in patients with gout, stratified according to renal function.
Methods: The prospective study included 136 pts aged ≥18 years with a crystal-verified diagnosis of gout and sUA level >360 µmol/L who had never taken febuxostat or other urate-lowering drugs (at least 2 weeks before the start of the study). All pts were prescribed febuxostat 80 mg/day; if the target sUA level (<360 µmol/l) was not achieved, the dose was increased to 120 mg/day. Prophylactic anti-inflammatory drugs (AIDs) were taken: colchicine in 59 (43.4%) pts, NSAIDs - 51 (37.58%) pts, GC - 12 (98.8%) pts. 14 (10.3%) pts did not take AIDs. Laboratory tests (serum levels of glucose, creatinine, UA) before and after 26 weeks of therapy were collected. GFR was calculated using CKD-EPI formula before and after therapy. The pts were initially divided into groups depending on the CKD stages according to the level of GFR (CKD-EPI): C1 – normal or high renal function (>90 ml/min/1.73 m^2), C2 – mildly decreased (60-89 ml/min/1.73 m^2), C3 - moderately decreased (30-59 ml/min/1.73 m^2), C4 – severely decreased (15-29 ml/min/1.73 m^2). The observation period covered at least 26 weeks, the primary end point was the achievement of the target sUA level. The dynamics of GFR was also assessed. Statistica 12.0 package was used for statistical data processing.
Results: It was found that 30 (22.12%) pts had CKD stage 0-1, 28 (66-20.6%) pts - C2, 62 (45.6%) pts – C3, 16 (11.8%) – C4. 98 (72.1%) pts received febuxostat 80 mg/day, 38 (27.9%) pts - 120 mg/day. Pts with CKD C4 were older than ones with CKD C2 (p=0.00001) and CKD C0-1 (p=0.002); had a longer duration

Table 1. Levels of UA, eGFR in patients with gout, stratified by the level of eGFR at baseline and after 26 weeks of febuxostat therapy.

Parameters	All patients, n=136	CKD C0-1, n=30	CKD C2, n=28	CKD C3, n=62	CKD C4, n=16
UA baseline, μmol/l	472,4±99,3	451,9±102,8	486,9±103,8	476,9±86,7	468,3±109,8
UA after 26 weeks, μmol/l	306,27±104,4	298,6±104,8*	282,2±95,8*	318,9±97,6*	313,5±106,9*
Δ UA, μmol/l	166±10,2	153,3±10,7	204,7±12,4	157,9±17,8	154,8±14,9
UA<360 μmol/l, n (%)	117 (84)	25 (83)	25 (89)	51 (82)	13 (81)
GFR baseline, ml/min/1.73 m^2	63,98±15,3	101,3±18,1	75,9±9,7	50,2±5,5	26,5±2,6
GFR after 26 weeks, ml/min/1.73 m^2	64,74±26,9	102,8±28,6*	76,7±9,3	50,9±6,9	27,3±4,9

* - p<0.05 between baseline and 26 weeks

of gout (p=0.003); they were more likely to have subcutaneous tophi than pts with CKD C2 (p=0.007). The frequency of diagnosing DM, hypertension, as well as the sUA level in the groups did not differ. The levels of sUA, GFR in patients with gout, stratified by the level of GFR at baseline and after 26 weeks of febuxostat therapy, are given below (Table 1). The target sUA level was achieved in 33 (87%) patients with DM (the probability did not depend on the initial GFR value). Achievement of target sUA level was registered in 84% of general sample: in 83% of pts with CKD C0-1, 89% - CKD C2, 82% - CKD C3, 81% of pts with CKD C4. Mean GFR values increased in all groups, but significant differences registered in patients with CKD C0-1 (p=0.002) only.

Conclusion: The ability to achieve the target sUA level while taking febuxostat in patients with gout does not depend on renal function, exceeding 80% in patients with CKD C4. The drug is well tolerated regardless of renal function.

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AB1047 EFFECT OF THERAPY ON SUBCLINICAL CAROTID ATHEROSCLEROSIS IN PATIENTS WITH CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (PILOT STUDY)

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Background: Supposedly, anti-inflammatory therapy in calcium pyrophosphate deposition disease (CPPD) pts may reduce the progression of atherosclerosis.

Objectives: Assessment of the dynamics of atherosclerosis development based on changes of carotid artery intima-media thickness (caIMT) in pts with CPPD receiving anti-inflammatory therapy (colchicine, methotrexate, hydroxychloroquine).

Methods: The prospective study included 26 pts aged ≥18 years with a crystal-verified diagnosis of CPPD and osteoarthritis (OA). Exclusion criteria were age >65 years, presence of cardiovascular disease, carotid artery (CA) atherosclerosis according to ultrasound results, high or very high SCORE (Systematic Coronary Risk Evaluation) index. The examination included anthropometric parameters, information about the affected joints and the time of onset of symptoms. Laboratory tests included determination of the following in blood serum: hs-CRP, lipid levels; SCORE index was calculated for all pts; CA Doppler ultrasonography (DU) was performed using the Esaote MyLab Twice ultrasound system (Italy). The manifestation of subclinical atherosclerosis was diagnosed in case of caIMT increase >0.9 mm. The criteria for the presence of an atherosclerotic plaque in the CA was a local caIMT increase of more than 50% compared to the surrounding areas or an caIMT increase >1.3 mm. CaIMT was measured at the first visit, then, pts with CPPD were administered methotrexate 15 mg/week or hydroxychloroquine 200 mg/day or colchicine 0.5 mg twice daily. Pts could take NSAIDs to relieve pain. After 26-28 weeks, a second examination was carried out. Statistica 12.0 package was used for statistical data processing.

Results: The baseline values of caIMT in pts with CPPD and OA did not differ. 22 pts with CPPD and 19 with OA were examined in dynamics. Baseline caIMT >0.9 mm was detected in 11 of 22 (50%) pts with CPPD and in 8 of 19 (42%) pts with OA (p=0.39). CaIMT >0.9 mm was associated with an increase in hs-CRP levels >0.2 mg/l in 8 pts with CPPD. 9 of 19 (47%) pts with OA demonstrated an increase in caIMT averages, the values in other pts remained unchanged. By the end of the study, 14 of 22 (64%) pts with CPPD had a decrease in the average values of caIMT, in 2 (9%) pts - an increase, in 6 pts the average values of caIMT did not change. 7 of 11 pts with CPPD showed normalization of caIMT, 5 of them (45.5%) had a decrease in serum hs-CRP <2 mg/l. A decrease in the number of pts with CPPD and caIMT >0.9 mm from 11 (42%) to 4 (18%) pts was found. At the same time, in 8 pts with CPPD the serum hs-CRP level significantly decreased: baseline 6.02 [0.69; 6.4] mg/l vs at the end of study period 1.71 [0.78; 2.25] mg/l, p=0.043. Pts with OA demonstrated the constant level: baseline 2.13[0.22; 2.8] mg/l vs at th end of study period 3.06 [0.39; 6.38] mg/l, p=0.627. A decrease in mean values of caIMT was noted in 5 of 6 (83%) pts took hydroxychloroquine, in 6 of 9 (67%) pts took colchicine, in 4 of 7 (57%) pts – methotrexate.

Conclusion: Therapy with colchicine, methotrexate and hydroxychloroquine in pts with CPPD leads to regression of early signs of atherosclerosis. This result can be achieved by suppressing chronic inflammation.

Disclosure of Interests: Maxim Eliseev Speakers bureau: Berlin Chemie Menarini Group, Sobi, EGIS, CSC, MosFarma, Alium Group, Olga Sheliabina Speakers bureau: Berlin Chemie Menarini Group, Maria Chikina: None declared, Eugenia Markelova: None declared, Irina Kirillova: None declared

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AB1048 ESTIMATED GLOMERULAR FILTRATION RATE CHANGES IN UNCONTROLLED GOUT PATIENTS CO-TREATED WITH PEGLOTICASE AND METHOTREXATE: A RETROSPECTIVE CASE SERIES

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Background: Gout patients are at increased risk for developing chronic kidney disease (CKD)[1] and hyperuricemia is an independent risk factor for CKD worsening,[2,3] particularly in women.[3] As a result, renal function is of concern in uncontrolled gout patients. Pegloticase, a recombinant PEGylated uricase, can rapidly decrease serum uric acid levels (sUA) in uncontrolled gout patients, but with pegloticase monotherapy <50% have sustained urate-lowering during Month 6 of treatment.[4] Pegloticase treatment response rate is markedly higher when immunomodulating therapies such as methotrexate (MTX) are co-administered,[5,6] but MTX use can be limited by renal impairment. Clinical trials excluded CKD patients, but real-world published cases of immunomodulation-pegloticase co-therapy have included patients with a pre-therapy eGFR <60 ml/min/1.73 m^2.

Objectives: This study examined pooled case data from prior studies, focusing on renal function changes during MTX-pegloticase co-treatment in patients with and without pre-therapy CKD.

Methods: This retrospective study examined deidentified case data collected for prior retrospective studies.[7-9] All patients who underwent MTX-pegloticase co-therapy were included and categorized as CKD (baseline eGFR <60 ml/min/1.73 m^2) or non-CKD (baseline eGFR ≥60 ml/min/1.73 m^2). sUA, renal function, blood cell counts, and liver function were closely monitored during therapy. Patient characteristics, pegloticase treatment parameters, proportion of treatment responders (≥12 infusions received and sUA <6 mg/dL at infusion 12 [ongoing patients with <12 infusions excluded]), renal function changes (eGFR, CKD stage), and adverse events were examined.

Results: 15 uncontrolled gout patients with CKD (9 stage 3a, 4 stage 3b, 2 stage 4; pre-therapy mean[±SD] eGFR: 43.2±11.3 ml/min/1.73 m^2, sUA: 8.5±2.2 mg/dL) and 27 without CKD (pre-therapy eGFR: 82.9±19.0 ml/min/1.73 m^2; sUA: 9.5±1.7 mg/dL) were included. Patient characteristics and comorbidity profiles were similar, but CKD patients were older (72.0±9.9 vs. 52.3±14.3 yrs) and more often female (33% vs. 7%). On average, MTX was initiated ~4 wks before pegloticase in both CKD status groups. MTX dose was lower in CKD patients (14.8±5.8 vs. 19.3±4.9 mg/wk). Pegloticase treatment was similar between groups (CKD: 14.7±8.1 infusions over 28.5±17.1 wks, non-CKD: 14.1±7.1 infusions over 27.9±15.1 wks), with similar urate-lowering response rate (92% vs. 86%). eGFR increased during therapy in 60% and 44% of CKD and non-CKD patients, respectively, with mean eGFR increase of 11.5±20.9 and 4.2±15.0 ml/min/1.73m^2, respectively. In the CKD group, CKD stage either improved or was stable in 13/15 patients (87%). The 2 patients with CKD progression both moved from stage 3a to 3b, and both stage 4 CKD patients had an eGFR increase, improving to stage 3a. In the non-CKD group, 3 patients developed stage 3 CKD (2 stage 3a, 1 stage 3b). 7/15 (47%) CKD and 13/27 (48%) non-CKD patients had ≥1 AE noted, with gout flare most reported (47% vs. 41%). A mild infusion reaction and pancytopenia occurred in 1 non-CKD patient each.

Conclusion: In this retrospective real-world review of a limited number of cases, MTX-pegloticase co-therapy resulted in sustained sUA lowering in uncontrolled gout patients with and without CKD. Close monitoring of renal function indicated stability or improvement during therapy in 86% of uncontrolled gout patients with CKD. Further study is needed to better understand therapy tolerance and treatment response rates of uncontrolled gout patients with CKD undergoing MTX-pegloticase co-therapy.

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AB1049 PECULIARITIES AND COMPARISON OF 24-HOUR BLOOD PRESSURE MONITORING IN PATIENTS WITH GOUT AND OTHER FORMS OF ARTHRITIS

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Background: The leading cause of death in patients with gout is cardiovascular diseases (CVD), with the mortality rate being higher as compared to that in the general population. Hypertension (HT) occurring early with gout is considered among other reasons. Current studies demonstrate a number of features of HT in gout (in contrast to patients with essential HT), which determine an unfavourable prognosis for gout.

Objectives: To compare the indicators of 24-hour blood pressure monitoring (24hBPM) in patients with gout and these in a group of patients with other forms of arthritis, as well as in the group of patients with essential HT.

Methods: The retrospective study included 162 patients hospitalized at the Rheumatology Department of the City Clinical Hospital № 11 (Minsk) from 2014 to 2021. The study group 1 (n=90) consisted of patients with gout (AKP, 1977). The comparison group 2 (n=39) included patients with other forms of arthritis different from gouty (rheumatoid arthritis – 25.6%, osteoarthritis – 60.7%, reactive arthritis – 13.7%); group 3 (n=33) – patients with essential HT. Patients from all groups were comparable in terms of gender and age (p>0.05). All patients underwent 24hBPM.

Results: In the study group, significantly higher average systolic blood pressure (SBP) (p˂0.05) and diastolic blood pressure (DBP) values were determined during night hours than in group 2 (p˂0.05). In the main group, there was also a higher time index of HT in SBP (p˂0.05) and DBP (p˂0.05) during the day and SBP during night hours (p˂0.01). The same group was characterized by a high DBP variability during the day (p˂0.01) and night hours (p˂0.01). In addition, in patients with gout, increased values (p˂0.01) and rate (p˂0.01) of the morning rise in DBP were more common. When compared to group 3, patients with gout had higher daytime SBP profiles (p˂0.01) and DBP (p˂0.01), nocturnal SBP profiles (p˂0.05), as well as high hypertensive time index (HTI) at the day (SBP, DBP, p˂0.01) and night hours (SBP, p˂0.01). The variability of BP in patients of the compared groups did not differ (p>0.05). When assessing the degree of nocturnal decline (DND) in all studied groups, impaired daily SBP and DBP profile was revealed. The proportion of patients with normal DND in SBP (dippers) in all three groups was comparable (p>0.05). In turn, the number of DBP dippers in the main group was less than in group 2 (x^2=6.66; p˂0.01). Thus, DND disorders according to DBP were more common (x^2=7.56; p˂0.01) in the study group. In the gout group, the following features were significantly more common than in group 2: obesity (x^2=15.3; OR=2.92; CI95% 2.30-3.70 p˂0.001), CKD with GFR<60 ml/min/1.73 m^2 (CKD-EPI) (x^2=4,93; OR=2.31; CI 95% 1.87-2.86; p˂0.05), and hyperuricemia (x^2=68.08; OR=41.7; CI 95%;23.2-74.4 p<0.001).

Conclusion: In patients with gout, 24hBPM parameters testify to a more severe course of HT than that in other forms of arthritis and essential HT. Contributing factors may include obesity, CKD with GFR<60 ml/min and hyperuricemia. All this requires more active strategy in the treatment of early detected HT in patients with gout and rational hypouricemic therapy already at the first gout attack in patients with concomitant HT.

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AB1050 CHARACTERISTICS OF PATIENTS WITH COINCIDENT GOUT AND ADVANCED CHRONIC KIDNEY DISEASE

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Background: Patients with chronic kidney disease (CKD) are at increased risk for developing gout[1] and vice versa.[2] Those with both gout and CKD present distinct challenges for patients and physicians because of the high prevalence of other comorbidities and restrictions on gout medication use, including non-steroidal anti-inflammatories[3,4] and some oral urate-lowering therapies (ULTs).[5] This unique patient population has not been well characterized using real-world data.

Objectives: This retrospective chart review study of patients with coincident gout and CKD was conducted to better understand patient characteristics and treatment patterns of this population. This study is unique in that patient data were obtained from nephrologists, allowing a glimpse of how they view gout and its management.

Methods: 111 nephrologists provided de-identified medical record data of their most-recently seen advanced (stage 3–5) CKD patients. Patients met study criteria for gout if any of the following were true: gout listed as a comorbidity, ULT use, or visible tophi or gout flares documented. A patient's gout was determined to be uncontrolled if they had serum uric acid >6 mg/dL in addition to ≥1 visible tophus, ≥2 gout flares in the past year, or gouty arthritis (≥1 tender or swollen joint). Characteristics of this unique population were examined, along with gout management patterns. Differences between patients with controlled and uncontrolled gout were also investigated using data from patients' most recent evaluation.

Results: 173 patients with stages 3-5 CKD and who met study criteria for gout were included. Mean age was 58.3±18.1 years and BMI averaged 32.0 ± 11.8 kg/m^2. A higher than expected proportion of patients were female (47%). The most common comorbidities were hypertension (85%), diabetes mellitus (47%), anemia of CKD (42%), CKD-mineral bone disorder (41%), ischemic heart disease (23%), and congestive heart failure (21%). Mean CKD duration was 4.1 ± 5.5 years, mean estimated glomerular filtration rate (eGFR) at most recent visit was 32.3 ± 13.9 ml/min/1.73 m^2, and 62% were using a ULT. 23 patients (13%) had uncontrolled gout (48% female, 63.1 ± 16.4 years, mean eGFR 32.0 ± 14.6 ml/min/1.73 m^2), all of whom had been prescribed a ULT. Compared with controlled gout patients, uncontrolled patients had higher rates of pulmonary hypertension (14% vs. 4%), gout-related chronic pain in the 12-months prior to data collection (63% vs. 42%), and joint involvement (joint swelling, tenderness, flexibility loss, and/or damage/lesions on x-ray; 26% vs. 9%). Colchicine was also used more frequently in uncontrolled gout patients (26% vs. 7%).

Conclusion: The coincident gout with advanced CKD population described here shows unique differences from the general gout population, including a high proportion of females (47%). Given that women have a lower likelihood of developing gout at the same serum uric acid level,[6] this finding was particularly surprising (general gout population: 67% male[7]). Importantly, nearly 40% of included patients were not utilizing a ULT, leaving them susceptible to developing the painful and debilitating sequalae of uncontrolled gout. Additionally, 41% of the study population had a CKD-related mineral bone disorder, indicating that patients with coincident gout and CKD may have bones that are more vulnerable to gout-related bone damage. Our study confirms a high prevalence of gout and its associated comorbidities in patients with advanced CKD and suggests another nephrology education opportunity to highlight the potential benefits of gout monitoring, earlier intervention, and management.

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Therapeutics, Brad Marder Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Sreedhar Mandayam Shareholder of: Medingenii Capital LLC and Prosalus Capital LLC, Speakers bureau: Otsuka and Alexion, Consultant of: US Renal Care and Aurinia, Grant/research support from: Travere, Norvartis, Omeros, Roche, Vertex, Equillium, Goldfinch Bio, and Pfizer
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AB1051 CLINICAL OUTCOMES AND HEALTHCARE RESOURCE UTILIZATION OF UNCONTROLLED GOUT PRIOR TO PEGLOTICASE THERAPY

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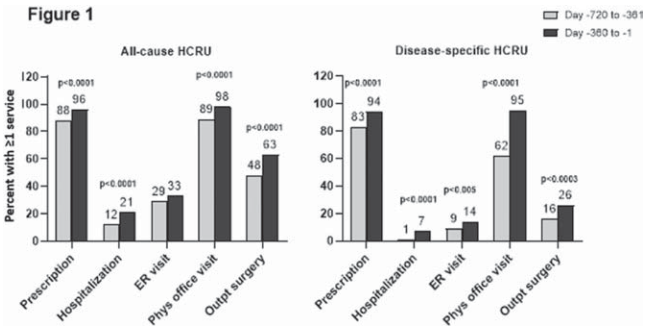
Background: By definition, uncontrolled gout (UG) cannot be managed with oral urate lowering therapies (ULTs) and is associated with substantial morbidity. UG, also known as refractory gout, results in escalated treatment and management. Recent American College of Rheumatology guidelines recommend treating gout to serum uric acid targets; if targets are not achieved or patients continue to have symptoms, pegloticase is recommended. There is a paucity of data documenting the clinical and economic burden of UG patients.
Objectives: Assess clinical outcomes and healthcare resource utilization (HCRU) of UG prior to pegloticase initiation.
Methods: A retrospective observational database analysis was conducted among patients initiating pegloticase between April 1, 2011 and August 31, 2020 using the PharMetrics Plus database. Eligible subjects had ≥1 pegloticase claim (first claim = index date) and continuous enrollment for 24 months prior to index. Relevant clinical and economic (HCRU) outcomes were evaluated over a 24-month pre-index period and compared between two different time intervals prior to index: time interval 1 (Day -720 to Day -361) and time interval 2 (Day -360 to Day -1). Assessment of comorbid disease burden included Charlson Comorbidity Index (CCI) and relevant health conditions. Dependent pairwise comparisons were conducted to compare clinical and economic outcomes between time intervals prior to pegloticase initiation. To assess statistical differences, paired t-tests (continuous variables) or McNemar's tests (categorical variables) were used.
Results: Of the 408 eligible subjects, most were male (88.5%), with an average age (SD) of 55.2 (11.3) years, 66.9% were between the ages of 45-64 years and 78.2% had a preferred provider organization (PPO) health plan. Most often (34.8% of patients), a rheumatologist was associated with initiation of pegloticase therapy, while primary care physicians accounted for 23.8% of initiations. Mean (SD) CCI score was 2.4 (2.4) with 37.3% of subjects having a CCI score of >3. Prevalence of relevant health conditions over the 24-month pre-index period included tophi (62.5%), urolithiasis (8.6%), chronic kidney disease (34.6%) and chronic pain/fibromyalgia (76.5%), all of which significantly increased from time interval 1 (Day -720 to Day -361) to time interval 2 (Day -360 to Day -1) prior to pegloticase initiation (Table 1). Of patients initiating pegloticase, 57.4% had 1 ULT (excluding probenecid), 11.3% had >2 ULT (excluding probenecid), and 10.3% UG patients had ≥1 probenecid claim over the 24-month pre-index period. Most patients (98.3%) had ≥1 physician office visit, 27.2% had ≥1 hospitalization and 45.3% had ≥1 emergency room (ER) visit over the 24-month pre-index period. HCRU significantly increased from time interval 1 to time interval 2, prior to pegloticase (Figure 1).

Table 1. Relevant Health Conditions and Disease-specific Health Care Resource Utilization (HCRU)

	Overall N= 408	Time Interval 1	Time Interval 2
Tophi	62.5%	15.4%	61.5%***
Urolithiasis	8.6%	4.2%	6.9%*
Chronic kidney disease	34.6%	22.5%	31.6%***
Cardiovascular disease	32.6%	21.3%	28.4%**
Type 2 diabetes mellitus	31.4%	23.3%	28.9%**
Hypertension	76.2%	58.1%	70.3%***
≥1 gout flare	87.7%	48.5%	83.8%***
Mean number of gout flare (SD)	3.5 (2.4)	1.0	2.1***
Gout-related medications	56%	39.5%	63.7%***
≥1 claim for colchicine			
≥1 claim for opioids	71%	52.9%	60.3%*
≥1 claim for oral corticosteroids	80%	50.2%	75.7%***
≥1 claim for injectable corticosteroids	64%	38.5%	53.7%***

†Time Interval 1: Day -720 to Day -361 prior to pegloticase initiation; ††Time Interval 2: Day -360 to Day -1 prior to pegloticase initiation***, p<0.0001; **, p<0.001; *, p<0.05

Figure 1



Conclusion: Overall, these data demonstrate the progressive nature of UG as confirmed by significant increases in gout-related conditions and healthcare resource utilization prior to pegloticase initiation. Further research is needed on healthcare resource utilization among patients with UG post-pegloticase use.
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AB1052 ASSOCIATION BETWEEN BODY MASS INDEX AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH GOUT

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Background: Gout is an inflammatory disease that may cause decreased function and health-related quality of life (HRQoL) [1]. In a few studies, it was demonstrated a negative relationship between body mass index (BMI) and HRQoL in individuals with gout; in the others, it was not confirmed.
Objectives: This study aimed to assess the BMI and quality of life in patients with gout and to value the association between these variables.
Methods: All 151 patients were male with mean age (M±SD) 52.4±9.2 years. Diagnosis of gout was based on the ACR/EULAR 2015 criteria [2]. Tophi was present in 51 (33.7%), and the median duration of gout was 7 years (25th to 75th interquartile range (IQR), 4 to 14.0). The mean uric acid in serum was (sUA) (M±SD) 477.2±120.5 μmol/l. HRQoL was evaluated by the SF-36 and calculated summary physical (PCS) and mental component (MCS) scores of the SF-36.
Results: About 67.5% of the surveyed patients had BMI > 30 kg/m2, while the average index was 31.9±3.4. The overall median SF-36 PCS score was 33.9 (IQR 28.8 to 38.4), and the overall median SF-36 MCS score was 41.1 (IQR 34.2 to 47.4). Among the eight subscales of SF-36, there was a correlation between BMI and role physical functioning (RP) r = -0.22 (p<0.01), general health (GH) r = -0.17 (p<0.05), but others were statistically not significant (P>0.05). Our analysis showed negative associations between BMI and physical and mental HRQoL. BMI correlated with PCS r = -0.19 (p<0.05) and MCS r = -0.17(p<0.05).
Conclusion: This analysis provides further evidence to support the injurious effects of obesity on different aspects of health patients with gout and underline the importance of weight loss.
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AB1053 CARDIOVASCULAR RISKS AND MORTALITY IN KOREAN PATIENTS WITH GOUT

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Background: Gout is associated with an increased risk of cardiovascular comorbidities and premature mortality. Many epidemiologic studies support an association between gout and increased risk of diverse cardiovascular diseases. There has been no study on cardiovascular risks and mortality in Korean patients with gout with large scale data. Therefore, we intended to investigate the risk of each specific cardiovascular disease and mortality in Korean patient with gout with the national insurance database. The purpose of this study is to investigate cardiovascular risks and mortality in Korean patient with gout.
Objectives: The purpose of this study is to investigate cardiovascular risks and mortality in Korean patient with gout.
Methods: Using Korean National Health Insurance Service data, we conducted a cohort study on gout patients. Gout patients were defined as those aged ≥ 20 years who were diagnosed as gout between 2009 and 2010, and control patients were matched with gout patients (1:1 ratio) after frequency matching for age, sex and index year. Primary outcomes were ischemic heart disease (IHD), acute myocardial infarction (AMI), congestive heart failure (CHF), cerebrovascular disease (CVD), cerebral infarction, cerebral hemorrhage, or transient ischemic attack (TIA). Secondary outcomes were all-cause mortality and cardiovascular mortality. We calculated hazard ratio (HR) in Cox regression, adjusting potential confounders.
Results: This study included 3,306 gout patients and an equal number of matched controls. Multivariate Cox regression analysis showed that gout patients showed increased risks of IHD (HR 1.860, 95% CI 1.446-2.392), AMI (HR 3.246, 95% CI 1.460-7.217), CVD (HR 1.552, 95% CI 1.177-2.036) after adjusting age, sex, laboratory findings, comorbidities, and medication (Table 1). However, statistical differences were not found in the risks of CHF, cerebral infarction, cerebral hemorrhage, TIA, all-cause mortality, and cardiovascular mortality.

Table 1. Multivariate Cox proportional HRs for cardiovascular risks of gout patients

Outcome	HR	95% CI	P-value
Ischemic heart disease	1.860	1.446-2.392	<0.001
Acute myocardial infarction	3.246	1.460-7.217	0.004
Congestive heart failure	1.399	0.853-2.295	0.183
Cerebrovascular disease	1.552	1.177-2.046	0.002
Cerebral infarction	1.061	0.687-1.637	0.790
Cerebral hemorrhage	0.779	0.283-2.145	0.629
Transient ischemic attack	1.233	0.651-2.336	0.521
All-cause mortality	1.199	0.737-1.952	0.465
Cardiovascular mortality	1.377	0.452-4.188	0.573

HR, hazard ratio; CI, confidence interval.

Conclusion: Our study showed that cardiovascular risks of Korean patients with gout were increased, especially IHD, AMI and CVD.
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AB1054 FERRITIN LEVELS IN PATIENTS WITH GOUT AND COMORBID PATHOLOGY

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Background: Gouty arthritis is the most common type of inflammatory arthritis among the working-age population. In patients with gout, the following comorbidities are often recorded: hypertension, diabetes mellitus, and heart failure. The issue of the relationship between ferritin levels in patients with gout and comorbid pathology remains relevant, as well as establishing the nature of this relationship.
Objectives: The aim of this study was to determine the frequency of hyperferritinemia in patients with gout and comorbid hypertension.
Methods: 122 patients with hypertension, middle age of whom amounted to 56.0 (10.29) years, had been surveyed, 104 (85.2 %) men and 18 (14.8 %) women. All patients were divided into three groups: the main group – 72 patients with hypertension in combination with gout, comparison group – 50 patients with hypertension without gout, control group – 20 patients with gout. Standard clinical examination and laboratory evaluation including ferritin, uric acid levels were performed.
Results: The following ferritin values were determined in the main group 344.0 (196.5; 389.0) ng/ml, comparison group 130.9 (68.0; 143.3) ng/ml, control group 276.5 (257.0; 354.5). The ferritin level were significantly higher in the main group - 2.6 ($p < 0.01$) times than in the comparison group. The ferritin level were significantly higher in the control group - 2.1 ($p < 0.01$) times than in the comparison group. There is no significant difference the ferritin levels between main and control groups ($p > 0.05$), which indicates the important role of this marker in gout and requires further study of hyperferritinemia in gout and comorbid pathology.
Conclusion: The combination of hypertension with gout in patients was associated with a higher ferritin levels, which should be considered not only in the context of chronic inflammation, but as part of the disease with the possibility of further determining the cause and diagnostic value of hyperferritinemia in this category of patients.
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Disclosure of Interests: None declared
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AB1055 GENDER DIFFERENCES IN TAKING XANTHIOXIDASE INHIBITORS IN GOUT

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Background: There is little evidence of a possible difference between men and women in response to urate-lowering therapy (ULT).
Objectives: To compare the clinical characteristics of the gout course and evaluate the differences in response to ULT with allopurinol and febuxostat in men and women.
Methods: The retrospective cohort study included 279 men and 83 women diagnosed with gout (ACR/EULAR, 2015). The comparative analysis of the clinical characteristics of gout and responses to taking xanthioxidase (XO) inhibitors in representatives of different genders was conducted. We compared the gender characteristics of obtaining a positive response to ULT, defined as achieving a target serum uric acid (sUA) level of <360 μmol/l within 6 months of treatment with allopurinol and febuxostat.
Results: By the age when gout manifistated women were older than men, the duration of their disease was shorter. Men showed a shorter duration of the first arthritis attack. Chronic arthritis was diagnosed in 56% of men and 35% of women ($p < 0,05$). The process involved the joints of the lower and upper extremities. More often the joints of the lower extremities were affected in men, and in the upper extremities in women. Tophus were detected in 35% of patients: 30,3% – men, 4,7% – women ($p < 0,05$). Allopurinol was prescribed to 216 men and 54 women, febuxostat – to 63 men and 29 women. After six months the proportion of women who achieved the target sUA was 57,5% and 65,8%, the proportion of men – 60,4% and 76,2% for allopurinol and febuxostat, respectively.
Conclusion: The clinical manifestations of gout in men and women differ. Due to the marked increase in the uric acid level, men develop more severe joint damage because of the tendency to chronicity. However, the study did not reveal gender differences in the response to XO inhibitors, which indicates that there is no need to choose therapy depending on the patient's gender.
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AB1056 CHARACTERISTICS OF METABOLIC SYNDROME IN PATIENTS WITH GOUTY ARTHRITIS AND NON-ALCOHOLIC FATTY LIVER DISEASE

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Background: Gouty is an inflammatory and metabolic disease. Hyperuricemia can contribute to inflammation, hypertension and cardiovascular disease, adipogenesis and lipogenesis, impaired insulin and glucose metabolism, and liver disease. In turn, non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide; is closely associated with obesity, type 2 diabetes mellitus, dyslipidemia, and other metabolic risk factors included in the metabolic syndrome (MS). Problem of MS exists for many years, due to its extremely rapid spread in the world.
Objectives: To study the frequency and structure of MS in patients with gouty arthritis in combination with NAFLD, to identify the main traditional and disease-associated risk factors.
Methods: The study included 70 patients with gouty arthritis. The diagnosis was made based on the criteria of S. Wallace et al. All patients were examined with general clinical and biochemical blood tests (determination of uric acid, transaminases, glucose, glycosylated hemoglobin, insulin, lipid spectrum), physical examination (measurement of blood pressure, body mass index in kg/m2), calculation of the HOMA index. An ultrasound examination of the liver was performed as the instrumental diagnostic method.
Results: Among the surveyed, men and women accounted for 60% and 40%, respectively, with an average age of 52 years, with an average disease duration of 8.2±3.5 years. The debut of gouty arthritis was observed at 35.6 years. 25 patients had a family history of gouty arthritis. 64 patients had arterial hypertension. The patients were divided into two groups: the first group included 50 patients with primary gouty arthritis and signs of NAFLD (signs of steatosis in 64%, non-alcoholic steatohepatitis in 36%), the second group included 20 patients with gouty arthritis without signs of NAFLD. In group 1, 20 patients (40%) had arterial hypertension of the 1st degree, 30 (60%) patients of the 2nd degree. The uricemia level varied from 390.8 to 612.2 μmol/l. Dyslipidemia was diagnosed in 72% of patients (mainly type IIa and IIb). The average level of fasting glycemia was 7.8±3.0 mmol/l, and glycosylated hemoglobin was 7.0±1.5%. The average level of insulin in the blood serum of patients of the 1st group is 7.9 mIU/l, the 2nd group is 2.2 mIU/l, and the average HOMA index is 18.0. The body mass index ranged from 29.05 to 49.39 kg/m2 (70% were obese, the rest were overweight). All indicators of the metabolic syndrome in patients of the 1st group were significantly different from those of the 2nd group of patients (p<0.005).
Conclusion: Thus, a high prevalence of metabolic syndrome was revealed in patients with gouty arthritis and signs of NAFLD. In this group of patients, there are higher risks of developing insulin resistance and dyslipidemia, abdominal obesity and arterial hypertension, as well as hyperuricemia. All identified factors of the metabolic syndrome directly correlated with the duration of gouty arthritis.
Disclosure of Interests: None declared
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AB1057 EFFICACY AND SAFETY OF LOW-DOSE RASBURICASE IN COMBINATION WITH CONVENTIONAL URATE-LOWERING THERAPY FOR REFRACTORY CHRONIC GOUTY ARTHRITIS: A PILOT STUDY IN

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Background: Recombinant uricase such as pegloticase are indicated for chronic gouty arthritis who have failed to achieve serum urate level <300μmol/L even though receiving conventional urate-lowering drugs. Rasburicase which is currently approved at a dosage of 0.2 mg/(kg.d) for 5 days for the prevention of tumor lysis syndrome in pediatric patients with hematological tumors, is the only available uricase in China at present.
Objectives: To evaluate the efficacy and safety of low-dose rasburicase in refractory chronic gouty arthritis.
Methods: We retrospectively collected data of 17 patients with refractory chronic gouty arthritis who were treated with rasburicase from January 2021 to September 2021 at Sun Yat-sen Memorial Hospital, Sun Yat-sen University. The refractory chronic gouty arthritis was defined as serum urate level was still more than 300μmol/L and dual-energy CT showed the volume of urate more than 10 cm^3, even though the allopurinol, febuxostat, and/or benzbromarone of the maximum tolerable amount were received for more than 3 months. Rasburicase was added every four weeks (week 0, week 4, and week 8) with a dosage of 1.5 mg/d for three consecutive days, on the basis of daily oral urate-lowering drugs of the maximum tolerable amount. The serum urate level was monitored. The primary outcome was the change in urate volume at week 12 compared to week 0 by dual-energy CT.
Results: ① Seventeen patients were recruited with 16 males (94%) and mean age 47±15 years old. The median gout course was 11 (6.5, 15) years with gout flares number 20 (11, 36) times in the previous year. At week 0 before the rasburicase add-on treatment, the mean serum urate was 652±94μmol/L and the median urate volume was 44 (21, 215) cm^3 (Table 1). ② Urate level after the rasburicase add-on treatment was significantly decreased than that before the treatment either at week 0, week 4, or week 8 (Figure 1A, all $p< 0.001$). The median reduction of serum urate were 565 (446, 621) at week 4, 214 (57, 373) at week 8, and 118 (21, 185) at week 12 (all $p<0.017$). Five cases (29%) showed serum urate lower than 300μmol/L at week 12. ③ The urate volume decreased at week 12 compared to week 0 in all patients (Figure 1B~D). The median volume of urate reduction was 24 (12, 60) cm^3 ($p<0.001$) and the median percentage of urate reduction 42% (25%, 66%). Urate reduction volume was positively correlated with baseline urate volume (r=0.890, $p<0.001$), while the percentage of urate reduction volume negatively correlated with baseline urate volume (r=-0.689, p=0.002). ④ Rasburicase was generally well tolerated. No gout attack occurred on the basis of intravenous methylprednisone 20mg before each rasburicase add-on treatment and oral colchicine 0.5mg/d to 1mg/d. No hypersensitive reaction occurred during the treatment. Phlebitis occurred in a patient (6%), while dizziness and nausea occurred in two patients (13%). One patient (6%) who was suffering chronic kidney disease of stage 3 developed acute kidney injury after rasburicase injection at week 0 and week 8, but the serum creatinine spontaneously returned to the baseline level during follow-up.

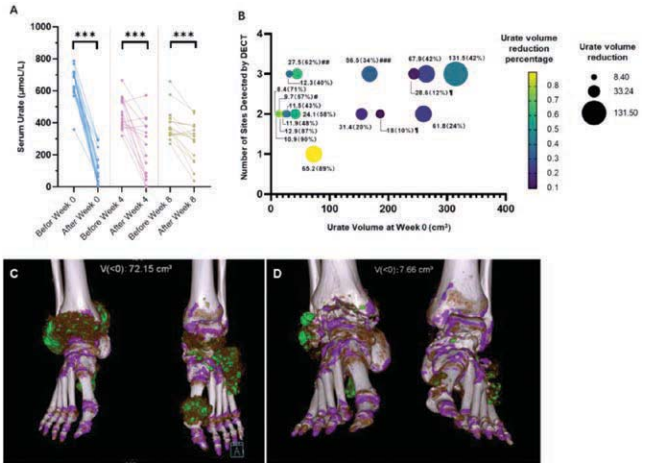

Figure 1. The serum urate and urate volume before and after rasburicase add-on treatment. A: Paired comparison of serum urate level before and after each time of rasburicase administration; B. Reduction value and percentage of urate volume at week 12 for each patient. C&D: Dual-energy CT (DECT) showed a dramatical reduction in urate volume from week 0 (C, urate volume: 72.15 cm3) to week 12 (D, urate volume: 7.66 cm3). ***: p< 0.001; #: Received rasburicase at week 0 only; ##&###: Received rasburicase 7.5mg at week 0.

Conclusion: This pilot study shows rasburicase is well tolerated in patients with refractory chronic gouty arthritis and may be a reasonable option to effectively lower the urate burden of these patients, although this is an off-label use. Further prospective randomized controlled studies to verify the efficacy and safety are needed.
Funding: This study was funded by Yat-sen Clinical Research Project.
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AB1058 IS HYPERURICEMIA ASSOCIATED WITH TYPE 2 DIABETES DEGENERATIVE COMPLICATIONS?

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Background: Prevalence of hyperuricemia (HU) is constantly increasing around the world and HU is now identified as an independant cardiovascular risk factor.
Objectives: To determine the prevalence of HU in patients with type 2 diabetes (T2D) and to identify degenerative complications of T2D associated with HU.
Methods: A cross-sectional descriptive study was conducted in the rheumatology and endocrinology departments of Farhat Hached University Hospital of Tunisia over a period of 6 months. Patients diagnosed with T2D according to the 2021 guidelines of the American Diabetes Association were included. A cut-off of uric acid ≥ 360 μmol/L in females and ≥ 420 μmol/L in males was used to define HU.
Results: One hundred fifty-one patients were included. Sex ratio F/M was 1.4. The median of age was 61 years. The prevalence of HU was 17.2%. Only 6 % of patients had gout. Degenerative complications of T2D were encountered in 74.2% of cases. Diabetic neuropathy was the most common (51.7%) and was significantly associated with HU (p=0.049). Diabetic nephropathy was reported in 38.4% of patients and was also associated with HU (p= 0.008). HU was associated with renal failure (p < 0.01), microalbuminuria (<0.01), proteinuria (p=0.001) and history of ischemic stroke (p=0.048). Diabetic feet problems were reported in 15.9 % of patients and were associated with HU (p=0.008). Nevertheless,

diabetic retinopathy (39.7%), peripheral arteriopathy of lower limbs (27.2%) and myocardiopathy (15.2%) were not associated with HU.
Conclusion: HU is common in patients with T2D. Our study raises the question whether HU could be a risk factor for the development of degenerative complications in T2D patients. Screening for HU could be recommended in T2D patients for a holistic assessment of the disease.
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AB1059 POSSIBILITIES OF COMBINED THERAPY FOR TREATMENT OF HYPERURICEMIA AND ARTICULAR SYNDROME EXACERBATIONS IN PATIENTS WITH GOUT

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Background: Throughout the year 69 per cent of patients with gout experienced repeated exacerbations during therapy aimed at reducing urate levels. Prevention of arthritis exacerbations with low-dose NSAIDs should be done in the first 3-6 months of urate-reducing therapy.
Objectives: To assess the frequency of exacerbations and quality of life in patients with gout after a 12 weeks course of urate-reducing therapy with allopurinol in combination with the anti-inflammatory drug meloxicam for the prevention of gout exacerbations.
Methods: Physical examination, clinical blood, urine tests, biochemical blood tests, instrumental diagnostics were performed in all patients. Information about concomitant diseases was entered, drug therapy was recorded at the time of observation. Allopurinol was administered orally, once a day. Every 3 weeks under the control of serum uric acid levels (sUA), the allopurinol dosage was increased by 50 mg, up to 300 mg per day. The total daily dose of meloxicam administered in different dosage forms was 7.5-15 mg. After 3, 6, 9 and 12 weeks, the clinical effeciency of treatment was assessed using the EuroQol-5D-5L questionnaire, physical examination, joint pain dynamics at rest, during movement and palpation, as well as the Likert scale and visual analog scale (VAS) in mm. Factors such as the presence of anxiety or depression, self-care ability, normal daily activities of daily living were taken into account, as well as their rating of their level of satisfaction with the treatment on a scale of 1 to 5, where 1 is not an improvement but a deterioration and 5 is a very good result. Both the period of remission and the time before the onset of a recurrence of gouty arthritis were taken into account, as well as adverse events (AEs) were recorded.
Results: 143 patients with an established diagnosis of gout (ACR/EULAR, 2015) were examined at an outpatient appointment. Against the background of treatment with meloxicam 7.5 mg per day, more than two-thirds of the patients did not experience a worsening of the joint syndrome with an increase in the dose of allopurinol to 300 mg per day. By the 12th week of follow-up, it was found that the characteristic features of gouty arthritis significantly began to differ in improving mobility, self-care, habitual daily activities, reducing soreness, reducing anxiety and depression ($p < 0.05$). Moreover, the initial ESR and sUA levels were significantly different from the follow-up endpoint ($p < 0.05$), indicating a positive effect on the inflammatory process. A three-month course of combination therapy did not cause a significant increase in blood pressure or change in serum creatinine clearance in the patients. From the gastrointestinal tract there were no adverse events. 90.9% of patients assessed the treatment efficiency as very good. AEs in the form of an allergic skin rash were observed in one patient. But there was no need to interrupt the treatment, as the rash completely disappeared without consequences after completing the course of treatment with allopurinol and meloxicam.
Conclusion: A 12-week combination therapy with allopurinol, a urate-reducing drug, and meloxicam, an anti-inflammatory drug, prevents exacerbation of joint syndrome and improves quality of life in patients with gout.
Disclosure of Interests: None declared
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AB1060 LONG-TERM DISABILITY SECONDARY TO CRPS-1. RETROSPECTIVE MONOCENTRIC STUDY ON 106 CASES.

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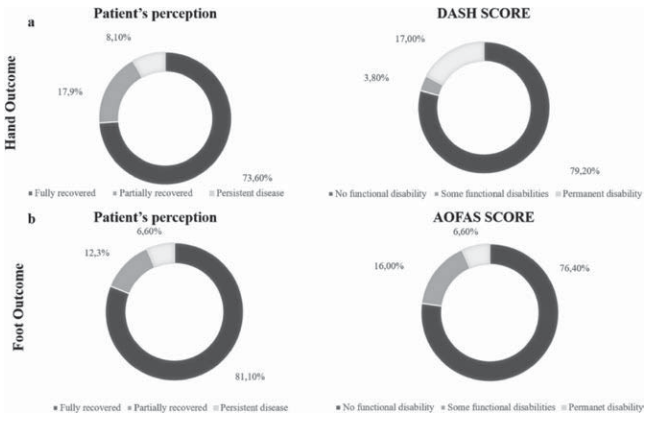
Background: Complex regional pain syndrome type-1 (CRPS-1) is a severely disabling pain syndrome characterized by sensory and vasomotor disturbance, swelling, and functional impairment. Persistence of signs and symptoms has been observed in up to 64% of cases until 5.8 yrs after the onset of manifestations. Long-term disability, such as irreversible functional limitation, has been reported in up to 28% of cases with severe consequences on workability. No scores are validated to evaluate residual disability. Bisphosphonates have the best efficacy profile, compared with other therapeutic approaches, but data on long-term effectiveness are lacking.
Objectives: To retrospectively evaluate long-term residual disability in patients with CRPS-1 of hand or foot after treatment with IV Neridronate (IVNer). To identify predictors of residual disability. To quantify disease outcomes, such as patient's subjective perception and residual pain. To assess long-term safety profile.
Methods: We retrospectively collected data of patients affected by CRPS-1, treated with IVNer, referred to a tertiary Rheumatology Centre between Feb 2013 and Dec 2020. Visual analogue scale (VAS) and McGill Questionnaire (McGQ) were used for pain assessment. Disabilities of the Arm, Shoulder and Hand (DASH) and American Orthopaedic Foot and Ankle Society's (AOFAS) ankle-hindfoot scale for hand and foot involvement, respectively, were administered to explore disability through a phone survey. This kind of investigation was preferred for Covid pandemic.
Results: 106 patients with definite diagnosis of CRPS-1 were included, mean age±standard deviation 55.6±13 yrs, 67% females, mean follow up duration 56.3 months (range 14-94), 46.2% with hand involvement. The mean VAS score before treatment onset was 55.8±23.4mm, while the McGQ was 12.9±6.7 in the sensory domain, 4.9±3.3 in the affective domain and 17.8±9.2 on the total score. Based on the patient's subjective perception and the proposed semi-quantitative scale, 77.4% described themselves as fully recovered (FR), 15% partially recovered (PR), and 7.6% with persistent disease (PD). Comparison between baseline and follow-up VAS shows a significant reduction (55.8±23.4 vs 15.1±26.4, $p<0.00001$). Pain assessment by McGQ showed a significant improvement in global score (baseline vs follow-up 17.8±9.2 vs 3.9±7.8, $p<0.00001$), sensory (12.9±6.7 vs 2.7±5.7, $p<0.00001$) and affective (4.9±3.3 vs 1.2±2.3, $p<0.00001$) domains. According to DASH score, 79.2% of the patients were FR, 3.8% had some difficulties, but with overall preserved use of the upper limb, and 17.0% had permanent functional disability. According to AOFAS ankle-hindfoot scale 76.4% of patients were FR, 16.0% had partial recovery, and 7.6% had severe functional impairment. Percentages of DASH and AOFAS scores showed a complete accordance with patients' subjective perception (Figure 1a and b). The only predictor of long-term functional impairment for CRPS-1 in the hand was a delayed treatment compared to symptoms onset ($p=0.02$). No predictors were found for foot localization. No patients reported the occurrence of osteonecrosis of the jaw or atraumatic fractures/atypical fracture features.

Figure 1.



Conclusion: IVNer maintained a good long-term effectiveness and safety profile in the treatment of CRPS-1. The effectiveness of IVNer is maintained on both pain symptoms and function, in terms of reductions in the VAS, McGQ and in hand and foot disability scores.
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Disclosure of Interests: None declared
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AB1061 THE ROLE OF PROSTAGLANDIN E2 IN HYPERTROPHIC OSTEOARTHROPATHY AND/OR CLUBBING OF DIFFERENT CAUSES.

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Background: Hypertrophic osteoarthropathy (HOA) is characterized by several clinical findings, including arthralgia/arthritis, periostosis, and digital clubbing. It can occur as a congenital condition called pachydermoperiostosis, and more commonly, as a secondary manifestation of pulmonary or extrapulmonary diseases or malignancy. Genomic studies support the role of prostaglandin E2 (PGE2) in the pathogenesis of primary HOA, with mutations in the 15-hydroxyprostaglandin dehydrogenase encoding gene resulting in increased PGE2 levels.
Objectives: To analyse the clinical characteristics, comorbidities, and the potential role of PGE2 in primary and secondary forms of HOA and/or clubbing and also evaluate the clinical evolution of these patients.
Methods: Eighteen patients (10 men/8 women) aged 15 to 78 years (49,9 ± 15,6) diagnosed with clubbing and/or HOA were attended in our Rheumatology Department over an 11-year period. We reviewed the clinical characteristics of the patients, including associated comorbidities, image findings, bone turnover markers (BTM), and serum and urinary levels of PGE2, among others. Additionally, we evaluated the treatment and the clinical evolution of these subjects.
Results: Most patients presented associated clinical conditions for HOA and/or clubbing, with only one, the youngest (15 years old), having primary HOA (pachydermoperiostosis). Pulmonary disorders were the most frequent associated conditions, with interstitial lung disease (4 cases), COPD (3 cases), and lung cancer (4 cases) being the most frequent, followed by liver diseases including primary biliary cirrhosis (1 patient), liver cirrhosis (2 patients) and chronic hepatitis C virus (2 patients). All the subjects evaluated (15/18) presented increased urinary PGE2 levels (the highest being observed in primary HOA), with most also presenting increased serum PGE2 values. BTM were evaluated in most subjects (17/18) showing increased values in most (11/17), particularly in PINP and CTx. 4 patients were treated with selective inhibitors of cyclooxygenase-2 (COX-2) presenting, when evaluated, a small decrease in urinary PGE2 titers and partly improving their symptoms, which clearly improved after treating the associated cause when possible.
Conclusion: In the present series, all subjects with primary or secondary HOA and/or clubbing presented markedly increased PGE2values, particularly in urine, supporting the role of this agent in the etiopathogenesis of this disorder. Pulmonary disorders, including malignancy and liver diseases, constituted the most frequent associated conditions. The use of COX-2 seems to be an effective symptomatic therapeutic approach in this entity.
Disclosure of Interests: None declared
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AB1062 EVALUATION OF THE EFFECTIVENESS OF GOUT THERAPY IN OUTPATIENT PRACTICE

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Background: gout is a socially significant pathology, as it affects men of working age and is associated with the development of cardiovascular diseases. Meanwhile, according to studies, most patients with gout do not reach the target values of uric acid (UA).
Objectives: to evaluate the effectiveness of gout therapy in real clinical practice and to identify factors that improve this indicator.
Methods: The study included patients with an established diagnosis of gout (according to ACR/EULAR criteria). Depending on the stage of the disease, patients were prescribed symptomatic anti-inflammatory therapy, and urate-lowering therapy (UST) - allopurinol or febuxostat - to reduce the level of UA. The dosage of allopurinol in the first 2 months of admission was 300 mg / day and then adjusted depending on the level of UA, the dosage of febuxostat was 80 mg, adjusted to 120 mg if necessary. To prevent exacerbation, all patients were prescribed colchicine 0.5-1.0 mg/day for up to 6 months. After 2 and 6 months of therapy, the effectiveness of it was assessed. All patients had a conversation about the correction of risk factors (diet, alcohol intake) and recommendation to watch online educational school for patients with gout.
Results: the average age of 60 patients included in the study was 46.9±9.9 years, the duration of the disease was 8.5±3.4 years, of which 96.7% were men. The mean number of exacerbation per year prior to therapy was 7.8±3.5. After 6 months of therapy, 46.7% of patients noted the absence of gout attacks, the rest - a decrease in the duration of attacks (from 10.4 to 1.6 days on average) and their intensity (the average pain during an attack on the VAS scale decreased from 7.8 points up to 3.9). The average level of UA decreased over 2 months from 541.3±146.8 to 387.4±146.9 μmol/l, and after six months of admission it was 299.6±56.5 μmol/l. The creatinine level did not change significantly and amounted to 104.7±34.9 μmol/l before therapy and 97.5±26.7 μmol/l after 6 months. None of the patients discontinued therapy due to intolerance; one of the patients experienced a slight leukopenia while taking febuxostat, which did not lead to discontinuation of the drug. It should be noted that the majority of the subjects - 56.7% - had previously consulted a rheumatologist, but most of them did not receive permanent therapy. Patients highlighted qualitative information and the effect of treatment as the most important reasons for continuing therapy.
Conclusion: This study proves that achieving the target level of UA is possible in most patients with gout, leads to a significant reduction in the number of attacks and their severity, requires educational work and patient monitoring. It is important that this work is part of a planned 2-year follow-up of patients with gout in order to determine the long-term effectiveness of therapy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3943

AB1063 POSSIBILITIES OF RENOPROTECTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND HYPERURICEMIA

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Background: the number of patients with progressive chronic kidney disease (CKD) and the costs of their treatment is constantly increasing. Possibly, control of serum uric acid (sUA) levels with urate lowering therapy (ULT) drugs can slow the progression of kidney function deterioration.
Objectives: to determine the efficacy and safety of allopurinol and febuxostat in treatment of patients with CKD to reduce the level of sUA and to analyze the effect of such treatment on glomerular filtration rate (GFR).
Methods: the study included 45 patients with CKD (stages 3b-5). Patients with recent acute kidney injury, acute glomerulonephritis, advanced heart failure, with kidney transplant, other severe/decompensated diseases; contraindications to the use of allopurinol/febuxostat – were not included. The target level of sUA for patients with pre-dialysis stages of CKD was set at 300 μmol/l, for patients on hemodialysis target was not set. All patients underwent a comprehensive clinical and laboratory examination, laboratory tests (full blood count, creatinine, sUA, ALT, AST, GFR calculation (CKD- EPI). All patients were divided into one of the study groups for the treatment of HU: Group I (28 patients, 61,3±3,2 y.o., CKD3b-12, CKD4-10, on hemodialysis-6 patients) received febuxostat (40-120 mg/day), Group II (24 patients, 60,7±4,1y.o., CKD3b-9, CKD4-10, on hemodialysis -5 patients) took allopurinol (50-300 mg/day – for patients with pre-dialysis CKD and up to 800 mg/day - for patients on hemodialysis). Clinical and laboratory examination was repeated after 1, 3 and 6 months; sUA levels were determined with individual frequency, with correction of of ULT drugs doses, taking into account GFR (for allopurinol).
Results: The majority of participants showed a significant decrease in the level of sUA under the influence of ULT drugs, however, the achievement of the target level of sUA was significantly more often registered in Group I: after 1 month – in 45.5% (in group II – in 15.9%, p<0.001); after 3 months - in 67.5% (in group II - 21.2% p<0.01); after 6 months, these figures were 90% and 37.1%, respectively (p<0.01). The achievement of sUA levels of less than 300 μmol/l was accompanied by significant positive GFR dynamics in most patients (in 90% of patients, GFR increased compared with the baseline, on average - in group I - by 3.1±0.51 ml/min, while in group II there was a gradual progression of GFR deterioration - in 31.8% of patients. During the study period, no serious adverse events (AE) were noted in study patients, mild and moderate adverse events (totally - 8 events) were registered in 5 patients (2 patients took febuxostat and 3 - allopurinol). Development of AEs did not lead to the discontinuation in study participation in any cases, but made impossible to increase the dose of allopurinol in 3 patients.
Conclusion: In patients with pre-dialysis stages of CKD, the use of febuxostat is accompanied by stabilization or increase in GFR. Use of febuxostat in patients with CKD stage 3b-4 and in patients on hemodialysis is safe and more effective for target sUA level achievement than the use of allopurinol.
Disclosure of Interests: None declared
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AB1064 **HYPERURICEMIA IN PATIENTS WITH PRIMARY HYPERTENSION: PREVALENCE AND ASSOCIATED FACTORS**

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Background: Hypertension and hyperuricemia (HU) are both cardivascular risk factors. HU is frequently associated with hypertension even without the use of treatments that potentially cause elevations of uric acid levels.
Objectives: To determine the prevalence of HU in patients diagnosed with primary hypertension and its associated factors.
Methods: A cross-sectional study was conducted in the rheumatology and endocrinology departments of Farhat Hached Hospital of Tunisia over a period of 6 months. Patients diagnosed with primary hypertension were included. HU was defined by uric acid levels ≥ 360 µmol/L in women and ≥ 420 µmol/L in men.
Results: One hundred patients were included. Study population was mainly made of women (65%). The median of age was 63 years [min:34, max:89]. The prevalence of HU was 26%. HU was more common in women (19%) compared to men (7%) without statistical significance (p= 0.315). The median values of systolic and diastolic blood pressure values were 140 mmHg and 80 mmhg, respectively. Elevated diastolic blood pressure was associated with HU (p=0.043). All patients presented other comorbidities. Type 2 diabetes was the most common one (83%) followed by obesity (56.7%). Forty three percent of patients had dyslipidema, 21% renal failure, 16.9% proteinuria, 9% gout, 8% hypothyroidism and 30% osteoarthritis. HU was significantly associated with hypothyroidism (p=0.027), renal failure (p= 0.000), obesity (p=0.038) and proteinuria (p=0.02). HU was not associated with disturbance of lipid and glycemic status. High uric acid levels were associated with the use of thiazide diuretics (p= 0.048) and ACE inhibitors (p= 0.037). Nonetheless, no association was found with the use of low dose aspirin (p= 0.412) nor other antihypertensive treatments.
Conclusion: Prevalence of HU is high in patients diagnosed with primary hypertension and is associated with hypothyroidism, obesity, renal failure, proteinuria and diastolic hypertension. HU is also associated with the use of thiazide diuretics and ACE inhibitors.

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AB1065 **EARLIER ONSET OF ARTERIAL HYPERTENSION IS A RISK FACTORS FOR SEVERE COURSES OF GOUT**

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Background: Comorbidities cardiovascular disease such as arterial hypertension (AH) are common in people with gout and complicate its management and disease outcomes.
Objectives: Our purpose was to evaluate the effect of AH on the severity of gout.
Methods: We included data of 286 male patients with gout: median (Me) age 51.2 [interquartile range (IR) 42.8;59.4] years (ys), disease duration – Me 6.2 [IR 3.8;12.1] ys, number of joints involved during disease course – Me 7 [IR 4;12], subcutaneous tophi – in 35% pts, intraosseous tophi – in 44% pts. All pts underwent standard clinical examination. AH was defined using by 2018 ESC/ESH Guidelines for the management of arterial hypertension criteria: elevated blood pressure (BP) (systolic BP≥140 or diastolic BP≥90 mm Hg or treatment for hypertension).
Results: AH was found in 244 out of the 286 pts (85 %). AH was diagnosed before gout in 129 (52.9%) pts, and after gout - in 115 (47.1%) pts. The 1st degree of AH was found in 27 (11%), the 2nd degree – in 62 (25%), the 3rd degree – in 155 (64%) pts. AH developed at a younger age in patients with 3rd degree AH compared to patients with 2nd and 3rd degree AH, but did not reach statistical significance. Patients with 3rd degree of AH had longer gout and AH duration compared to patients with 1st and 2nd degree of AH. They had higher prevalence of subcutaneous and intraosseous tofuses, nephrolithiasis compared with the 1st and 2nd degree of AH, p<0.05 (Table 1).

Table 1.

Parameters	Grade 1 hypertension	Grade 2 hypertension	Grade 3 hypertension
Age of gout onset,ys	41.6[34.4; 53.5]	39.6[35.6; 48.0]•	44.1[36.9; 52.6]
Age of AH onset,ys	44.9[37.4; 55.4]	43.6[36.9; 49.9]	40.4[29.9; 49.9]
Gout duration,ys	3.8[1.6; 5.8]	5.6[3.8; 13.5]	8.0[4.8; 14.6]*
AH duration,ys	0.1[0; 2.0]	3.3[0.2; 9.8]	11.3[4.7; 22.8]*
Number of joints involved,n	4.0[2.0; 6.0]	7.0[4.0; 10.0]	9,0[5,0; 14.0]*
Subcutaneous tophi,%	4(14.8%)	16(26%)	69(44.5%)*
Intraosseous tophi,%	5(18.5%)	29(47%)	83(53.5%)*
Nephrolithiasis,%	16(59%)	34(55%)	124(80%)*

Data are presented in median values and IR (unless otherwise noted), •p<0,05 reliability of differences for trend, *p<0,05 compared vs group 3 (Mann -Whitney).

AH preceded the development of gout in 26% pts with 1st degree of AH, in 42% pts with 2nd degree of AH, in 62% pts with 3rd degree of AH.
Conclusion: Hypertension preceded the development of gout in 62% patients with 3rd degree of AH. They had a more severe course of gout compared to patients with 1st and 2nd degree of AH. It can be assumed that an earlier onset of AH is a risk factor for severe courses of gout.

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AB1066 **TREATMENT OF ACUTE CALCIUM DEPOSITS IN HAND AND WRIST WITH ANAKINRA**

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Background: Acute calcium deposits (ACD) of hydroxyapatite in hand and wrist are a rare cause of acute pain due to crystal-induced soft tissue inflammation. There are no standard management guidelines for this condition, which is frequently treated with non-steroid anti-inflammatory drugs or steroid infiltrations with variable efficacy, some patients presenting symptoms for several months[1]. Anakinra, an interleukin-1 receptor antagonist, showed non-inferiority compared to usual care in the treatment of acute gout arthritis in a randomized controlled study[2] and demonstrated effectiveness in comorbid patients with recurrent crystal-related arthritis. Due to our local experience with anakinra to treat calcific periarthritis[3], we started using anakinra in the treatment of selected patients with ACD in hand and wrist with severe pain.
Objectives: To report our experience with anakinra to treat ACD in hand and wrist in terms of efficacy and safety.
Methods: We retrospectively included all patients treated with anakinra for ACD in hand or wrist in our department in 2020. We extracted data on treatment duration, pain, range of motion, skin erythema, hypervascularization, oedema and X-ray findings when available.
Results: Ten patients (mean age 45, SD 11) were treated for ACD in hand or wrist with anakinra 100 mg per day for a mean duration of 2.7 days. We observed a fast and significant improvement of pain at rest on a 0-10 VAS scale (mean pain reduction at day 2 (SD): -3.9 (2.8), p=0.01). All patients were free of pain at rest after day 6 and at motion after day 21. Range of motion significantly improved at day 2 (+41° (24), mean (SD), p=0.03). We observed local erythema and oedema improvement from day 2 and a decrease in skin temperature from day 3. Calcifications decreased in size or disappeared in the majority of the patients. We did not observe any adverse events. Patients did not report recurrence after phone contact, 12 months after treatment.
Conclusion: Anakinra was associated with a significant clinical improvement after only two days of treatment of ACD in hand or wrist and may be considered to treat patients with this condition, especially those with contraindication to NSAIDs or glucocorticoids. Further controlled studies are needed to confirm our observations.

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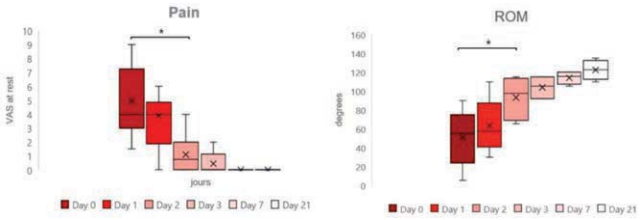

Figure 1: Graph 1. Box plot of pain at rest (0-10 VAS scale) and range of motion (ROM) at day 0, 1, 2, 3, 7 and 21 after treatment with anakinra 100 mg per day.

Disclosure of Interests: None declared
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AB1067 ASYMPTOMATIC HYPERURICEMIA AND ASSOCIATED FACTORS IN MALE PATIENTS VISITED HANOI MEDICAL UNIVERSITY HOSPITAL

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Background: Asymptomatic hyperuricemia prevalence in Vietnamese men has rose over the past several years. This leads to gout and increase cardiovascular risk.
Objectives: To assess the prevalence of asymptomatic hyperuricemia and associated factors in male patients who had medical check-ups in Hanoi Medical University Hospital.
Methods: All asymptomatic hyperuricemia male patients over 18 years old, had medical check-ups in outpatient clinics from January 2020 to May 2021. Exclude criteria included patients having medicine which affected serum uric acid (allopurinol, probenecid, sulfinpyrazone, salicylate, phenylbutazone, ascorbic acid, ethambutol, pyrazinamide, ect.), had acute diseases, diabetes type 1, chronic kidney disease and malignancies. All patients were tested for serum uric acid, total Cholesterol, Triglyceride, HDL-C, LDL-C and fasting serum glucose using Roche Cobas 6000 analyzer. Age, body mass index, alcohol consuming, physical activities and comorbidities were identified.
Results: 798 male patients over 18 years old were included in the study. Mean age was 39.5 ± 11.2, overweight and obesity rate was 31.5% and 29.8%, respectively. 41.4% patients had hyperuricemia with mean serum uric acid was 405.2 ± 81.2 µmol/l (highest was 820 µmol/l). We found that the factors associated to hyperuricemia in men were: the presence of hypertension (OR 1.64, 95% CI 1.1 -2.34), dyslipidemia (OR 2.37, 95% CI 1.73-3.24) and alcohol consuming (OR 2.16, 95% CI 1.6-2.8). We did not find association between smoking, physical activities, impaired glucose tolerance with hyperuricemia.
Conclusion: Alcohol consuming, dyslipidemia and hypertension were associated with higher risk of incident asymptomatic hyperuricemia in Vietnamese men.
Disclosure of Interests: None declared
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AB1068 HIGH FREQUENCY OF STRUCTURAL DAMAGE IN THE LOWER SPINE OF PATIENTS WITH CHONDROCALCINOSIS

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Background: Calcium pyrophosphate dihydrate crystal deposition disease (CPPD, chondrocalcinosis) is known to affect fibrocartilaginous tissue in the large and smaller peripheral joints. The affection of similar structures in the axial skeleton is unclear.
Objectives: To assess the frequency and severity of structural changes in the lower spine in patients with established CPPD in comparison to degenerative disc disease (DDD).
Methods: In a retrospective study, patients with CPPD or DDD as a main diagnosis with available spinal conventional radiographs (CR) performed during 2014 – 2020 were included. Definite other inflammatory conditions affecting the spine were excluded. The CR segments T7/8-L5/S1 were evaluated for the occurrence of disc calcification, intradiscal vacuum phenomenon, disc height (normal, narrowing, complete loss), endplate erosion, osteophytes and spondylolisthesis. When lumbar spine MRIs of the same time point were available, discovertebral units were evaluated for the occurrence of vacuum phenomena, endplate erosion, Modic changes and disc dehydration (Pfirrmann). Follow up CR were assessed if available. All available images were evaluated by 2 independent readers and discrepancies were solved by consensus.
Results: CR of 140 patients (1.171 discovertebral units) with CPPD and 99 DDD (803 discovertebral units) were evaluated (mean age 74.4±9.9 and 71±6.2, 20% vs. 20.2% males, respectively). MRIs of the spine were available from 48 CPPD and 44 DDD patients. Vacuum phenomena, disc calcification, osteophytes and erosion were significantly more frequently seen in patients with CPPD compared to DDD (Table 1) with no differences between the thoracic and the lumbar spine. Follow-up CR were available for 29 patients with CPPD and 46 DDD. Both groups presented statistically significant progression of endplate erosions and osteophytes (p 0.001 - 0.02 for both groups). Notably, even though CR follow-up times in the CPPD group were, compared to DDD (median (IQR) 1.9 (2.4) *vs* 3.0 (3.1) years, p=0.033, respectively), shorter, radiographic progression was noted more frequently in CPPD vs. DDD for erosive changes (6.8% vs. 0.6%, p=0.018) and disc calcification (5.8% vs. 0.6%, p=0.007), respectively. When comparing MRIs, a higher number of discovertebral units was affected by vacuum phenomena (34 *vs* 13, p=0.04) and endplate erosions (L4/5 (45.5% *vs* 24.4%, p=0.04), L5/S1(40.4% *vs* 19.5%, p=0.03) in patients with CPPD vs. DDD, respectively.

Table 1. Frequency of affected discovertebral units on conventional radiographs

	CPPD	DDD	p
Vacuum phenomenon	156 (13.3%)	44 (5.5%)	<0.001
Disc calcification	193 (16.5%)	42 (5.2%)	<0.001
Endplate erosion	159 (13.6%)	26 (3.2%)	<0.001
Osteophytes	861 (73.5%)	480 (59.8%)	<0.001
Spondylolisthesis	126 (10.8%)	69 (8.6%)	0.264

CPPD: calcium pyrophosphate dihydrate crystal deposition disease DDD: degenerative disc disease

Conclusion: Patients with chondrocalcinosis showed more severe and progressive degenerative findings in the lower spine as assessed by both, CR and MRI, even more in comparison to established DDD. This data shows that disease manifestations of CPPD in the axial skeleton are clinically relevant.
Disclosure of Interests: None declared
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AB1069 URIC ACID LEVELS IN RELATION TO FASTING BLOOD GLUCOSE AND HBA1C

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Background: Hyperuricemia is reported to be a risk factor for the development of type 2 diabetes (T2D) and prediabetes.
Objectives: To determine the prevalence of HU and gout in T2D and prediabetes and to study the relationship between HU, gout, T2D and prediabetes.
Methods: A cross-sectional study was conducted beween January 2021 and June 2021 in the Rheumatology and endocrinology departments of Farhat Hached Hospital. Patients who fulfilled the diagnosis of diabetes or prediabetes according to the American Diabetes Association guidelines of 2021 were included. Uric acid levels were also assessed and HU was defined as uric acid levels ≥ 360 µmol/l in women and ≥ 420 µmol/l in men. Diagnosis of gout was based on the ACR/EULAR 2015 classification.
Results: One hundred fifty-one patients having T2D and 46 prediabetic patients were included. The mean of age in both groups was 61 and 54 years respectively. Prevalence of HU was 26.1% in prediabetic while it was 17.2% in the group of T2D with no statistical relevance (p=0.182). No difference related to gender was observed in both groups. The prevalence of gout was higher in the prediabetes group (15.2%) compared to the T2DM group (6%) but without significant difference (p=0.062). Uric acid levels were remarkably higher in prediabetic patients (mean=324,3 µmol/l) compared to patients having T2D (median=278 µmol/l) with a significant statistical difference (p=0.022). No association was identified between HU, fasting blood glucose and HbA1C in the two groups. However, uric acid levels are inversely proportional to fasting blood glucose (p=0,001) and HBA1C (p=0.001) in all patients.
Conclusion: Individuals with moderately elevated HbA1c and fasting glucose levels (prediabetes) may be at a higher risk of HU, whereas individuals with diabetes or elevated HbA1c levels may have a normal uricemia. This could be explained by the GLUT-9 transporter regulation in the renal proximal tubule that blocks the absorption of uric acid when glycosuria is present.
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Infection-related rheumatic diseases

AB1070 INFECTIOUS SACROILIITIS: A RARE ENTITY IN RHEUMATOLOGY!

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Background: Infectious sacroiliitis (ISI) is a rare disease, with misleading clinical symptoms that often delay the diagnosis.
Objectives: The aim of this study was to describe the clinical, microbiological, therapeutic and radiological characteristics of ISI.
Methods: This descriptive, retrospective study included all ISI patients that were hospitalized in our rheumatology department over an 11-year period [2010 - 2021].
Results: Overall, 25 cases of ISI were identified, comprising 15 men (60%) and 10 women (40%), with a mean age of 48.7±10.5 years [21-67]. ISI was caused by pyogenic microorganisms in 12 cases (70.5%), mycobacterium tuberculosis in 7 cases (41.2%), and brucella spp in 6 cases (35.3%). The mean symptoms duration in pyogenic, brucellar and tuberculous ISI was 42 days, 67 days, and 255 days, respectively. The onset was brutal in 88% of pyogenic ISI, while it was progressive in 68% of brucellar ISI and in all cases of tuberculous ISI. Lumbogluteal pain was the most common symptom (80%). The involvement of the sacroiliac joint was always unilateral, and inflammatory in 92% of cases. The other most common symptoms included: fever (80%), impotence (68%), and lumbago (52%). An infectious source was found in 17 patients: 41.2% pulmonary (tuberculosis, n=7), 29.4% urinary, 17.6% gynecological (postpartum, n=3), and 11.7% septicemic (n=2). Fifteen patients (60%) had a biological inflammatory syndrome. Leukocytosis was found in 11 cases (64.7%). Pelvic x-ray showed a narrowing of the sacroiliac joints in 52% of cases. CT of the sacroiliac joints showed erosions in 60% of cases. Sacroiliac MRI showed erosions (45%), joint effusion (32%), and psoas abscess (14%). A second infectious site was found in 20% of cases: psoas abscess (n=2), and a collection of the soft tissues facing the joint (n=1). A pathogenic agent was isolated by means of blood culture (48%; staphylococcus aureus 56%, streptococcus 28%, and staphylococcus with negative coagulase 16%), articular biopsy (40%), cytobacteriological examination of urine (20%), Wright serology (20%), and Tuberculin skin test (6.2%). All patients received germ-adapted antibiotics. No patients have had surgical treatment. Evolution was favorable in most cases (n=11). Four patients complained of residual pain in the sacroiliac region. None of the patients relapsed.
Conclusion: Although IS is rare, it remains an emergency diagnosis. A rigorous physical examination is essential in order to detect this infection early. Antibiotics often lead to clinical improvement, making thus the need for surgery exceptional.
Disclosure of Interests: None declared
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AB1071 INFECTIONS IN RHEUMATOLOGIC PATIENTS IN A LATIN AMERICAN HOSPITAL, A 10-YEAR COHORT STUDY.

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Background: Infections have been indicated to be the cause and / or consequence of the calving and decompensation of some Connective Tissue Diseases and, in principle, both the immunological disorder and the immunosuppressive action of medications contribute to this.
Objectives: To describe the frequency of infections associated with the various rheumatological pathologies in patients admitted to hospitalization and to know their associated factors.
Methods: A descriptive study was carried out in which 3328 medical records belonging to the patients of the Rheumatology service were reviewed during a follow-up period from January 2010 to December 2020, measures of central tendency such as mean, mode, median and applied the Chi square test to appreciate statistical value between the various variables to be correlated.
Results: Most of the patients were female. The main rheumatological pathology was Rheumatoid Arthritis, followed by Systemic Lupus Erythematosus, Osteoarthritis in 3 place and finally in the last box other entities other than those indicated. The main infectious were those of the urinary tract, in the second instance those of skin and soft tissues, in third place the respiratory ones and lastly those not included in the previous categories. The 2 main therapies related to infections were the use of steroids followed by biological therapy (p 0.001).

Table 1. Medications received, categories of infections and reason for hospitalization presented by patients in frequencies and percentages.

	Reumathoid Arthritis	Lupus	Osteoarthritis	others
	n=1 296 (43,9%)	n=347 (11,7%)	n=259 (8,7%)	n= 1 045 (35,4%)
Treatments				
Corticosteroids	829 (64)	220 (63,4)	165 (63,8)	545 (52,2%)
Non-steroidal immunomodulator	184 (14,2)	71 (20,6)	57 (22,2)	312 (29%)
TNF Inhibitors.	195 (15)	0 (0)	0 (0)	130 (12,5%)
No treatment	88 (6,7)	56 (16)	37 (14)	58 (6,4%)
Infections				
Urinary	773 (59,6)	215 (62)	165 (63,6)	648 (62,1%)
Skin	257 (19,8)	71 (20,6)	47 (18,3)	210 (20,1%)
Pneumonia	162 (12,5)	38 (10,8)	30 (11,5)	103 (9,8%)
Others	104 (8,1)	23 (6,5)	17 (6,6)	84 (8%)
Hospitalized				
Variable	Total Hospitalized (n_216)	Total Hospitalized (n_347)	Total Hospitalized (n_24)	Total (n_79)
Not infectious	71 (32,87%)	39 (11,2%)	3 (12,2%)	11 (13,8%)
Infections	145 (67,12%)	308 (88,8%)	21 (87,8%)	68 (86,2%)

Conclusion: In the present study it was found that infections were the main cause of decompensation and hospitalization in these patients. Infection is the cause of significant morbidity and mortality in rheumatology patients. Conclusions: Based on the observations obtained in the present study, it is recommended that the risks for the development of infections in rheumatology patients be evaluated through stratification systems and thus generate strategies that reduce their frequency.
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AB1072 HERPES ZOSTER IN INDIVIDUALS WITH AUTOIMMUNE DISEASES AND RECOMBINANT HERPES ZOSTER VACCINE AS A PREVENTATIVE STRATEGY

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Background: Individuals with autoimmune diseases (AIDs) are particularly vulnerable to herpes zoster (HZ) and its related complications. Although the live attenuated HZ vaccine is contraindicated in many of these individuals, the two-dose non-live recombinant zoster vaccine (RZV) can be used in immunosuppressed individuals. Based on accumulating data from RZV studies within specific immunosuppressive conditions, recently updated guidelines recommend RZV not only in immunocompetent adults aged ≥50 years, but also in adults aged ≥18 years (EU)/≥19 years (USA) at risk of HZ due to immunodeficiency or immunosuppression.[1–3]

Objectives: To evaluate the burden of HZ in individuals with AIDs and the use of RZV as a preventative strategy.

Methods: We reviewed PubMed for available data on HZ incidence, summarised RZV data (effectiveness and safety) and the current recommendations for RZV in individuals with AIDs. The latest search was conducted in September 2021.

Results: HZ incidence in the general population is 4–7/1000 person-years (increases with age) and 8–15/1000 person-years in individuals with AIDs. Common immunosuppressive and immunomodulatory therapies can predispose individuals to HZ, as shown by large meta-analyses of interventional and observational studies. No published randomised controlled trial data of RZV in AID populations were found in our search. In two retrospective cohort studies in patients with inflammatory bowel disease (IBD), [4,5] RZV demonstrated high vaccine effectiveness (OR 0.64; 95% CI 0.44, 0.77).[4] In a real-world observational study investigating RZV in beneficiaries of the Medicare national health insurance program in the USA, individuals with AIDs achieved vaccine effectiveness of 68.0% (95% CI 62.3%, 72.8%), which was similar to the overall population (70.1% [95% CI 68.6%, 71.5%]).[6] In two single-centre, retrospective studies of RZV in individuals with AIDs, including rheumatoid arthritis (RA), adverse events after the first RZV dose were mild[7,8]. Disease flares were uncommon, mild and self-limiting, although a flare at the first RZV dose was significantly associated with an increased risk of a flare at the second dose (hazard ratio 3.9; P=0.0015)[7]. In addition, glucocorticoid use during vaccination was significantly associated with flares (odds ratio [OR] 2.31; P=0.004; Lenfant, 2021)[7]. In a study of individuals with IBD, receiving ≥1 RZV dose was associated with a low flare rate[9]. Current RZV guidelines vary by country and will be revised as new data emerge. Ongoing studies include phase 4 studies of individuals with RA and IBD receiving immunotherapies, and a study investigating the immunogenicity and safety of RZV in individuals with stable systemic lupus erythematosus.

Conclusion: Individuals with AIDs are at increased risk of HZ and its related complications, which may be due to either or both of their underlying condition and the treatment(s) they are receiving. The developing collective scientific evidence from the published literature on RZV in individuals with AIDs demonstrates a favourable benefit:risk profile for RZV in this population which contributed to the recent USA ACIP recommendation. Further studies are warranted to evaluate potential effects of individual conditions and immunotherapies on vaccine efficacy and methods to optimise vaccine use.

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AB1073 HIGH INCIDENCE OF VIRUSES INFECTION IN CONNECTIVE TISSUE DISEASES PATIENTS

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Background: Connective tissue diseases (CTDs) are a group of diseases with a variety of clinical manifestations. The main drug was glucocorticoids and immunosuppressive drugs, but the results are not satisfactory and the side effects are obvious, increased the incidence of infection, especially opportunistic infections. Infections becomes important causes of morbidity and mortality in CTD patients.

Objectives: To evaluate the incidence of infection in CTD patients who were clinically considered for co-infection by a combination of metagenomic next-generation sequencing (mNGS) and conventional diagnostic testing methods.

Methods: We analyzed 126 connective tissue diseases (CTD)patients with suspected infections admitted to The Second Hospital of Shanxi Medical University. All patients with CTD were diagnosed according to relevant diagnostic criteria, including 34 systemic lupus erythematosus (SLE), 24 dermatomyositis and polymyositis (DM/PM), 19 rheumatoid arthritis (RA), 10 undifferentiated connective tissue disease(UCTD),16 Sjogren syndrome (SS), 5 mixed connective tissue disease (MCTD), 5 ANCA associated systemtc vasculitis (AAV), 5 adult onset Stillystemtc isease disease(tic criteria, including 34nfections admitted to The Second Hospital of Shanxi (TA), 1 systemic sclerosis (SSC), 1retroperitoneal fibrosis (RPF). All enrolled patients were tested for conventional diagnostic testing methods(CDT) and mNGS.

Results: Among the 126 patients with CTD who were clinically considered for co-infection, 31 patients were negative for mNGS, and pathogens were detected in 99 of them. In our results, the mNGS and CDT were both positive for pathogens detection in 28 individuals.Of both positive individuals, 2 cases were perfect matches,12 cases were partly matched, 14 cases were totally mismatched. A total of 23 cases were negative for both mNGS and CDT. 70 cases were positive for mNGS only.There were only 5 cases positive for pathogens detection by CDT only. In addition, the results of mNGS showed that 131 patients were virus-positive(54%), 78 patients were prokaryotes-positive (37%) inculding bacteria, mycoplasma and 14 patients were eukaryotes-positive (9%). Of course, someones have mixed infections among these patinets some of these patients, with two or more pathogens. In the mixed infection, 5 cases have no viruses infection, 38 cases with virus infection, including 20 cases of bacteria and viruses infection, 4 cases of bacteria,fungi and viruses infection, 9 cases of viruses mixed infection, 1 case of bacteria,viruses,fungi and mycoplasma infection, 1 case of bacteria,viruses and mycoplasma infection, 1 case of viruses and mycoplasma infection, 1 case of viruses and fungi infection. According to the results, viruses were the most common pathogens identified, followed by prokaryotes and eukaryotes. It is noteworthy that the incidence of Human gammaherpesvirus 4(EBV), Human betaherpesvirus 5(CMV) and Human alphaherpesvirus 1 are more common in virus-positive. The most frequently detected prokaryotes were Acinetobacter baumannii, Mycobacterium tuberculosis complex, followed by Staphylococcus aureus, Prevotella melaninogenica,Staphylococcus homini and Helicobacter pylori. The major pathogens were Pneumocystis jirovecii and Candida albicans among eukaryotes-positive individuals.

Conclusion: As a complementary approach to conventional methods, mNGS could help improving the identification of infection in CTD patients.The incidence of viral infection is high in patients with connective tissue disease and close attention should be paid to it in clinical works.

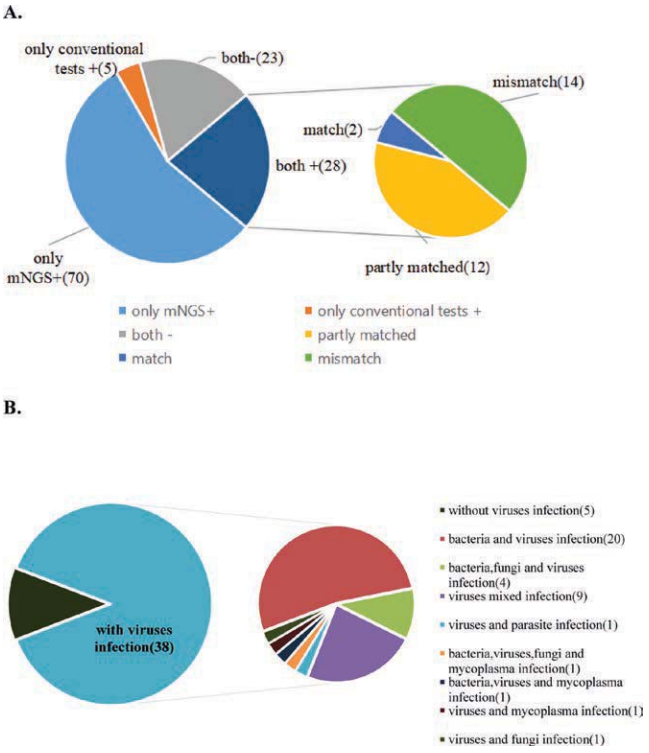

Figure 1. A. Comparison of test results between mNGS and conventional diagnostic testing methods(CDT) in CTD patients. B. The classification of mixed infections with or without viruses infection detected by mNGS and conventional diagnostic testing methods(CDT).

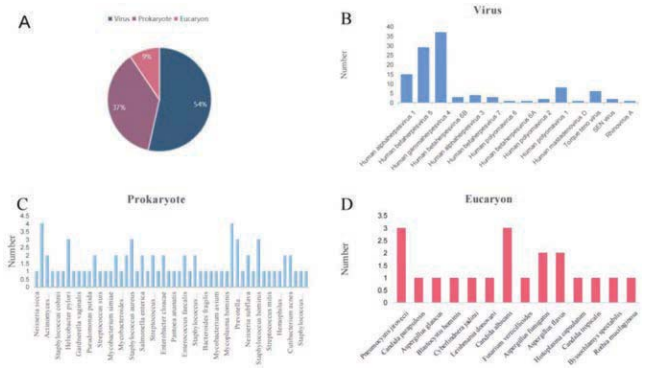

Figure 2. Distribution of pathogens detected by mNGS. A. Type distribution of pathogens identified by mNGS. Species distribution of viruses of B.viruses, C.Prokayote, D. Eucayon detected by mNGS.

Disclosure of Interests: None declared
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AB1074

FATAL BUT PREVENTABLE - SINGLE CENTRE SERIES OF 6 CASES OF PNEUMOCYSTIS JIROVECII PNEUMONIA (PJP) IN PATIENTS WITH AUTO-IMMUNE INFLAMMATORY RHEUMATIC DISEASE (AIIRD) IN ONE YEAR.

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Background: Pneumocystis jirovecii pneumonia (PJP) is an uncommon but frequently fatal fungal infection, which can affect patients with rheumatic diseases treated with immunosuppressants or high doses of steroids. There are no clear guidelines on when to prescribe primary prophylaxis and available agreements differ depending on the disease or immunosuppressant.
Objectives: To raise awareness about this preventable infection and to highlight the urgent need to create a tailored probability scoring, before starting any immunosuppression so that the risk benefit of prophylaxis can be objectively assessed.
Methods: This is a retrospective case series of six patients who developed definite or probable PJP known to the Rheumatology Department at Oxford University Hospitals NHS FT since the beginning of 2021. These patients were identified through the microbiology and infectious disease teams, and notes were reviewed to collate data regarding the clinical characteristics. Of these, five were being treated for large vessels vasculitis (LVV) whilst the other one had seropositive rheumatoid arthritis (RA). The diagnosis of PJP was made on clinical picture, laboratory results, bronchoscopy and CT findings.
Results: In this series, the median age was 78 years (range 55-93) with equal gender distribution. In three LVV patients, the diagnosis was confirmed on ultrasound, one had a positive PET-CT whilst the other case had a high probability clinical diagnosis. Comorbidities included chronic kidney disease and hypertension in three patients, diabetes, or previous underlying malignancy in other two. Smoking history was present in four patients, while five patients had lymphopenia with counts <1x10^9/L. Four of the six cases were on combined therapy with disease modifying anti-rheumatic therapy drugs (DMARDs) and prednisolone, only one was exclusively on prednisolone and the patient with RA was on Methotrexate and Humira. The chronology of the infection was variable, still most of the patients developed PJP infection during the first three months of starting either a biologic or corticosteroids. The median steroids dose by the time of PJP infection was 30 mg and unfortunately three of the patients died. None of the patients who developed PJP had been given antibiotic prophylaxis prior to infection. Some proposed scoring systems for serious infection risk in patients with AIIRD exist, however they focused on RA or biologics use rather than patients with vasculitis or connective tissue disorders who might be on high dose corticosteroids. Additionally, PJP prophylaxis is not recommended in any of the current guidelines for LVV management (BSR, EULAR, ACR). Cochrane review suggests reduction of risk by 85% in patients given prophylaxis.
Conclusion: Pneumocystis Jirovecii pneumonia (PJP) prophylaxis is not current practice for patients with large vessel vasculitis. Consideration needs to be given to PJP prophylaxis for patients on high dose steroids for a prolonged period, particularly in the presence of other risk factors. More data will be needed to help establish guidelines on PJP primary prophylaxis.

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Table 1. Baseline characteristics of the cases (*n)

Male gender	3		
Age, year Median	78		
Underlying disease			
Large vessels vasculitis	5	Confirmed on imaging (n)	4
Seropositive Rheumatoid arthritis	1		
Smoking	4		
Lymphopenia	5		
Steroid dose ≥ 30 mg by the time of PJP infection	4		
Concomitant DMARDs used	4		
Numbers of deaths	3		

*n = numbers

Disclosure of Interests: None declared
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AB1075

KNEE ARTHRITIS BY PARACOCCIDIOIDES BRASILIENSIS IN A LONG-STANDING RHEUMATOID ARTHRITIS PATIENT

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Background: Arthritis by *Paracoccidioides brasiliensis* is a remarkably unusual etiology of infectious joint disease. While osseous lesions can be present in systemic disease, intra-articular-restricted disease without typical lung or lymph node involvement is mostly anecdotal[1,2].
Objectives: We hereby describe a case of this fungal arthritis in a patient with rheumatoid arthritis (RA) without significant immunosuppression.
Methods: Patient records review. Written informed consent was obtained.
Results: A 65-year-old female Brazilian patient with a 35-year history of seropositive RA complained of a painful knee edema for the last three weeks. Skin surrounding the joint was erythematous, warm, and tender to the touch, which initially raised the suspicion of cellulitis. She had already received a 10-day course of amoxicillin-clavulanate, with no improvement. C-reactive protein was 17.8 mg/L, rest of blood chemistry panel was within reference range. Point-of-care ultrasound revealed joint effusion, and a diagnostic arthrocentesis was performed. Synovial fluid was slightly turbid, with 10,100 cells per mm^3, of which 80% were lymphocytes. Cultures for bacteria and mycobacteria yielded negative results, but culture for fungi detected growth of *P. brasiliensis*. The patient had been solely on prednisone 5 mg once daily for the last year, given that, due to covid-19 pandemics, she lost regular follow-up and abandoned treatment with immunosuppressants. Aside from mild RA-related interstitial lung disease, she had no other comorbidity. She denied local trauma to the knee, which made hematogenous dissemination of the fungi the most probable source. Comprehensive work-up to search for organic involvement of paracoccidioidomycosis, including chest computed tomography and transthoracic echocardiogram, did not evidence any visceral compromise. Voriconazole 200mg t.i.d. was started, with good response. Three months after the beginning of the azole, tofacitinib was started for moderate RA disease activity, which also responded satisfactorily. Repeat arthrocentesis and synovial biopsy were performed eight months after the start of antifungal treatment, the former being normal (770 cells per mm^3, negative cultures), and the later only demonstrating non-specific chronic synovitis with fibrosis.
Conclusion: We reported an exceedingly rare presentation of *P. brasiliensis* infection with exclusive joint involvement.
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Disclosure of Interests: None declared
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AB1076

IS THERE AN ADDITIONAL IMPACT OF STIMULATING CD8+ LYMPHOCYTES TO DETECT LATENT TUBERCULOSIS IN PATIENTS WITH RHEUMATIC DISEASES?

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Background: Purified protein derivative skin test (PPD) or interferon gamma release assays (IGRAs) are used as diagnostic tools to detect latent tuberculosis. QuantiFERON-TB Gold Plus (QFT-Plus) is a new test that detects latent tuberculosis. Antigens of *Mycobacterium tuberculosis* (ESAT-6 and CFP-10) are used. The test contains two tubes: TB1 and TB2. TB1 tube contains peptides of these antigens that induce CD4+T cell response while TB2 tube contains peptides designed to stimulate both CD4+ and CD8+ T cells. The amount of interferon gamma releases from those cells are determined by ELISA method. In patients with recent exposure to tuberculosis, there is an increased amount of CD8+ expression in comparison to patients with past exposure to tuberculosis.
Objectives: To investigate the additional impact of stimulating CD8+ lymphocytes with QFT-Plus test in order to detect latent tuberculosis in patients with inflammatory rheumatic diseases.
Methods: Hacettepe University Rheumatology Biologic Registry Database (HURBIO) database was used in this study. QFT-Plus test of patients with rheumatoid arthritis (RA) and spondyloarthritis (SPA) between January 2018 and March 2021 during work up before biologic/targeted therapy were analysed, retrospectively. Positivity of any of tubes has been reported as QFT (+). The impact of each tube on QFT positivity is analysed.
Results: 1480 patients (946 (64%) SPA, 534 (36%) RA) were enrolled. 957 patients were women. The median age was 45 (min-max:18-82). Totally 12.2% of patients had been reported as QFT(+). In 6% of QFT (+) patients only TB2 tube is positive (Table 1).

Table 1. The impact of each tube on QFT-Plus positivity

		QFT-Plus test (n=1480)	
Negative			86.2%
Indeterminate			1.5%
Positive	Only TB1 tube positivity	8% of positively reported patients	12.2% of all patients
	Only TB2 tube positivity	6% of positively reported patients	
	TB1 and TB2 positivity	86% of positively reported patients	

Conclusion: Disease inflammatory cascades along with ongoing usage of immunosuppressive agents could affect results of QFT-plus assay in rheumatic diseases. TB2 tubes stimulating CD8(+) T lymphocytes have additional impact in detecting latent TB infection in patients with RA and SpA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3924

AB1077

INFECTIOUS SPONDYLODISCITIS IN ELDERLY: IS IT MORE SEVERE DISEASE?

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Background: Spondylodiscitis is a chameleon among infectious diseases due to the lack of specific symptoms. In older patients, there are often difficulties in diagnosis and management.
Objectives: This retrospective study aimed to assess the characteristics of infectious spondylodiscitis in patients over 65 years of age.
Methods: This retrospective, monocentric study included patients aged over 65 years olds hospitalized in our department of rheumatology for spondylodiscitis.
Results: A total of 20 consecutive patients (10 males, 10 females) aged over 65 years were analyzed. The mean age of patients was 74 years (65-85). The most common comorbidities included diabetes (20%), chronic renal failure (5%). A history of nodal tuberculosis (10%), a tuberculosis contagion (30%), and raw milk ingestion (15%) were reported. The average delay for diagnosis was 10 months. The most common symptom was axial back pain (100% patients), then worsening health status (34%), and one patient had a significant neurological deficit. C-reactive protein was elevated in 95%. The most common involvement was in the lumbar vertebrae (13 patients, 65%), followed by thoracic and cervical level disease respectively in 3 patients (15%) and 2 patients (10%). Two patients (10%) had a multifocal spondylodiscitis. All patients underwent an MRI exam that confirmed the diagnosis. A percutaneous spine biopsy was performed in 80%. Pyogenic spondylodiscitis was the most common etiology (50%), followed by tuberculosis (35%) and brucellosis (15%). Antibiotic therapy was indicated to all patients with spinal immobilization in 65% of cases. Two patients underwent percutaneous drainage of paravertebral abscesses. The outcome was favorable in almost all cases until 12 months of following-up after completion of treatment. One patient died of septic shock and multi-visceral failure.

Conclusion: Elderly patients with infectious spondylodiscitis have fewer clinical symptoms leading to a delayed presentation. Increasing morbidity and mortality make rigorous monitoring necessary.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.4658

AB1078 SPECTRUM OF INFECTIONS DURING RHEUMATOID ARTHRITIS

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Background: Immunosuppression during rheumatoid arthritis (RA) induced by the disease but especially immunomodulatory treatments, is responsible for an increased frequency of infections in these patients.
Objectives: The purpose of this study is to assess the incidence of infections during RA and to determine their nature and management.
Methods: A retrospective study over a period of 10 years, including 150 patients with RA. We identified 33 patients who had at least one infectious episode during their follow-up.
Results: There were 19 women and 14 men. The mean age was 51 years old [39-63]. RA was immunopositive and erosive in all cases. The average disease duration was 8 years. A comorbidity was associated with RA in 14 patients (42%): diabetes in 7 cases, hypertension in 3 cases, ethylism in 2 cases and history of pulmonary tuberculosis in 2 cases. As an extra-articular manifestation, 15% of patients had Sjogren's syndrome and 18% had pulmonary interstitial fibrosis (3 cases) or pulmonary nodules (3 cases). The most prescribed DMARDs was Methotrexate, prescribed in monotherapy at the average dose of 17.5 mg/week [10-25mg] in 18 cases. The other patients received Methotrexate associated to Hydroxychloroquine in 4 cases, Sulfasalazine in 3 cases and biotherapy in 8 cases. Corticosteroid therapy at an average dose of 7.5 to 15 mg/day was received in 16 cases (48.5%). All infections noted in our population were community acquired. Urinary tract infection was the most common infection noted in 15 cases: pyelonephritis in 3 cases and cystitis in 12 cases. Other infection sites were ENT in 4 cases, bronchopulmonary in 6 cases including 2 cases of tuberculous infection and viral hepatitis (B and C) in 4 cases. Osteo-articular infections were noted in 3 cases: one cervical spondylodiscitis and two septic arthritis. Finally, one case of RA treated with rituximab was complicated by staphylococcal sepsis. Germs causing these infections were identified in 14 cases (42%).
Conclusion: The risk of infections is increased during RA, this is due to lymphocyte and autoimmune abnormalities but also to treatments and comorbidities that predispose to the emergence of infectious agents.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.4816

AB1079 INFECTIOUS SACROILIITIS ACCORDING TO THE GERM: ABOUT 42 CASES

S. Rekik[1], S. Boussaid[1], H. Tbini[1], S. Jemmali[1], S. Rahmouni[1], K. Zouaoui[1], H. Sahli[1], M. Elleuch[1]. [1]*Tunis, Department of Rheumatology, La Rabta hospital, Tunis, Tunisia*

Background: Infectious sacroiliitis is a rare rheumatological emergency. Its semiology is misleading due to the deep location of the joint. The responsible germs play an important role in its semiology.
Objectives: The objective of this work was to identify the germs responsible for infectious sacroiliitis and their effect in the sacroiliac joint.
Methods: We conducted a retrospective study, including 42 patients hospitalized for infectious sacroiliitis over a period from 2000 to 2020. Demographic, clinical, biological and radiographic data were collected.
Results: A total of 42 Patients were enrolled (11 men and 31 women). The mean age was 36,7 years [29-76]. Low back pain with difficulty walking were the most common manifestations (88%). The inflammatory syndrome was present in 70% of cases. Standard radiographs showed loss of cortical margins with erosion of the sacroiliac joints in 34 cases and were normal for the rest of the patients. MRI and CT scan were performed to confirm the diagnosis in 28 and 13 cases respectively. A puncture guided by ultrasound or scanner was performed in 24 patients. In the cases of absence of germ on the conventional examinations, we performed a sacroiliac biopsy and histological examinations. Pyogenic germs were responsible for 46% of infectious sacroiliitis: Staphylococcus Aureus in 11 cases (28%), Escherichia Coli in 7 cases (16 %) and Streptococcus in one case (2%). Tuberculosis and Brucella were responsible for 38% and 7% of the cases respectively. A subcutaneous abscess was associated with tuberculous sacroiliitis in 4 patients. The outcome was favorable in 36 cases (86%) under appropriate antibiotic therapy. Eight patients presented a treatment-related complication. Progression to multifocal bone tuberculosis and chronic brucellosis was noted in one case each. In 3 cases, rapid ankylosis was found on radiological control. Unfortunately, one patient died from septic shock.
Conclusion: Common germs are most responsible for infectious sacroiliitis and seem to have the best prognosis. Tuberculosis is responsible for various complications and its treatment has a high iatrogenic risk. Chronicity is the most feared development, mainly during Brucella sacroiliitis and would be related to a loss of antibiotic efficacy.
Disclosure of Interests: None declared
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AB1080 BRUCELLAR SPONDYLODISCITIS: EPIDEMIOLOGICAL, CLINICAL AND BIOLOGICAL ASPECTS

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Background: Brucellosis is a systemic infection characterized by significant clinical polymorphism and non-specific manifestations. The spine is a common location for brucellosis.
Objectives: The aim of this study was to describe the epidemiological, clinical and biological characteristics of brucellar spondylodiscitis.
Methods: A retrospective study over a period of 15 years, including 18 patients diagnosed with brucellar spondylodiscitis on clinical, biological and/or imaging data.
Results: Eighteen cases were collected (13 men and 5 woman). The mean age was 52 years [19-76]. The main symptom was unifocal or diffuse spinal pain associated or not with radiculalgia. Inflammatory pain was reported in 12 cases. Thirteen patients consumed raw milk, eleven had contact with farm animals or professional exposure. The average duration of symptoms was 5.7 months [0.5-12], the disease had a progressive onset in 13 patients. The general signs were frequent: deterioration of general condition (13 cases), fever (12 cases) and night sweats (6 cases). All patients had a biological inflammatory syndrome. Wright's serology, performed in 17 patients, was positive in 15 cases. The Rose Bengal test was positive in 13 of the 15 patients tested. Diagnosis by indirect immunofluorescence, performed in 11 patients, was positive in nine cases. However, the blood cultures, carried out in 13 patients and the disco-vertebral biopsy, carried out in 9 patients, did not find the causal agent.
Conclusion: The diagnosis of brucellar spondylodiscitis must be based on epidemiological, clinical arguments and biological examinations. Immunological examinations, however, seem to be more contributory and should be performed in case of diagnostic doubt and negative bacteriological investigation.
Disclosure of Interests: None declared
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COVID-19

AB1081 FLARES OF RHEUMATOID ARTHRITIS FOLLOWING CORONAVIRUS VACCINATION

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Background: With the emergence of the Coronavirus vaccine and the clear and important role it provides in maintaining the health of individuals and the population (1), it is important that our patients receive or are recommended the vaccine. We here document a case series of patients who have long-term quiescent rheumatoid arthritis who then experienced a flare of disease activity after receiving a vaccine. This information is important to understand as it allows informed discussions regarding the side effect profile of the vaccine and also the influence this may have on the patient's disease control and future management options.

Objectives: To understand the changes to control of rheumatoid arthritis in those experiencing a flare of disease after receiving the coronavirus vaccine.

Methods: Patients were reviewed in clinic as part of standard care. Individuals with Rheumatoid Arthritis who had experienced a flare defined as a self-reported disease activity score of >5.1 in otherwise stable disease were noted and their response to treatment reviewed. This was a review of usual clinical practice and did not alter the treatment undertaken or monitoring of the patent. Information obtained was through the consultation with a rheumatologist and the data was collected retrospectively through review of clinical notes and clinic letters.

Results: The table below outlines the patient details and treatment responses. All flares occurred within two weeks of receiving the vaccine. Of the patients who flared, two required short term steroid treatment; three an increase in the usual medications and one who had been in disease remission to re-start previous therapy. More patients in the Pfizer vaccine group required an escalation of usual care compared to the AstraZeneca vaccine group.

Table 1

Antibody status	Vaccine brand	Time since diagnosis	Time since last flare	Flare after 1st or 2nd dose	Usual treatment	Flare management
Seropositive, anti-CCP positive	AstraZeneca	13 years	3 years	1st	Etanercept, Methotrexate	Intramuscular Methylprednisolone
Seropositive, anti-CCP positive	AstraZeneca	11 years	4 years	1st	Etanercept, Sulfasalazine	Intramuscular Methylprednisolone, local joint injection
Seronegative, anti-CCP negative	AstraZenica	13 years	2 years	1st	Methotrexate	Increase methotrexate dose
Seronegative, anti-CCP positive	Pfizer	23 years	11 years	1st	Infliximab	Local joint injection, reduce interval of infusions
Seronegative, anti-CCP positive	Pfizer	7 years	3 years	2nd	Sulfasalazine, hydroxychloroquine	Increase Sulfasalazine dose
Seropositive, anti-CCP positive	Pfizer	7 years	4 years	2nd	nil	Re-start methotrexate, hydroxychloroquine

Conclusion: We report 6 cases of rheumatoid arthritis flare soon after receipt of the coronavirus vaccine. In all, disease control was returned with minimal changes to treatment, 42% of those requiring either no treatment or an intramuscular steroid injection alone. Therefore, we recommend that clinicians should counsel patients of this potential effect, but continue to advocate the vaccine, as the risk of complications to their underlying arthritis is very low and seemingly easily treatable.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2022-eular.38

AB1082 FREQUENCY AND SEVERITY OF COVID-19 IN PATIENTS WITH VARIOUS RHEUMATIC DISEASES TREATED REGULARLY WITH COLCHICINE OR HYDROXYCHLOROQUINE

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Background: Several anti-inflammatory drugs which were targeted different mechanisms and investigated for both prevention and treatment for COVID-19.

Objectives: The current study aimed to investigate whether patients regularly using colchicine or hydroxychloroquine (HCQ) have an advantage of protection from COVID-19 or developing less severe disease.

Methods: Patients who were taking colchicine or HCQ regularly for a rheumatic disease including Familial Mediterranean Fever, Behçet's syndrome, Systemic Lupus Erythematosus, Rheumatoid Arthritis and Sjogren's syndrome as well as their healthy household contacts as the control group were included into the study. The clinical data regarding COVID-19 were collected using a standard form, and serum samples were analyzed for anti-SARS-COV-2 nucleocapsid IgG. Patients treated with any biologic or immunosuppressive treatments were not included into the study.

Results: A total of 635 regular colchicine users with their 643 household contacts and 317 regular HCQ users with their 333 household contacts were analyzed. Anti-SARS-Cov2 IgG was positive in 43 (6.8%) regular colchicine users and 35 (5.4%) household contacts (OR=1.3; 95% CI:0.8-2; p=0.3) (Table 1). COVID-19 related symptoms were described by 29 (67.4%) of the patients and 17 (48.6%) household contacts (OR=2.2; 95% CI:0.9-5.5; p=0.09), and hospital admission was observed in five (11.6%) and one (2.9%) of these subjects (OR=4.5; 95% CI:0.5-40.2; p=0.1), respectively (Figure 1). Seropositive subjects were observed in 22 (6.9%) regular HCQ users and 24 (7.2%) household contacts (OR=1.1; CI:0.6-1.9; p=0.8) (Table 1). COVID-19-related symptoms occurred in 16 (72.7%) of the 22 patients and 12 (50%) of 24 household contacts (OR=2.7; 95% CI:0.8-9.1; p=0.1). Three patients (13.6%) were admitted to hospital, while one household contact (4.2%) was hospitalized (OR=3.6; 95% CI:0.3-37.8; p=0.2) (Figure 1). Disease-specific analyses disclosed that there was no significant difference in terms of COVID-19 frequency and severity between a particular disease subset and household contacts (Table 1). Univariate logistic regression analysis showed no effect of age and gender on the SARS-CoV-2 seroprevalence rate among regular colchicine or HCQ users and household contacts (p=0.2 and p=0.7, respectively for colchicine users versus contacts, p=0.7 and p=0.3, respectively for HCQ users versus contacts).

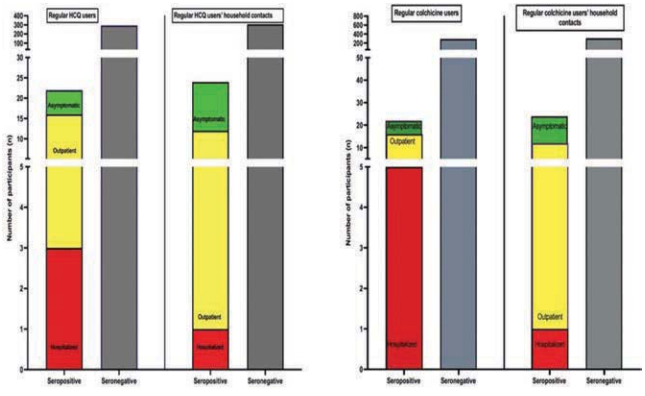

Figure 1. Severity of COVID-19 in regular colchicine or HCQ users and these patients' household contacts

Table 1. Disease specific outcomes of the entire cohort

Variable	FMF (n=373)	FMF HHC* (n=386)	P	Behcet Patients (n=262)	Behcet HHC (N=257)	P	SLE Patients (N=197)	SLE HH (n=221)	p	RA Patients (n=79)	RA HH (n=73)	P	Sjögren patients (N=41)	Sjögren HH (N=39)	p
Age, mean ± SD years	36.4 ± 13.2	36.3 ± 16.1	0.9	42.9 ± 11.4	38.1 ± 15.2	0.001	44.2 ± 12.6	39.4 ± 17	0.002	53.9 ± 10.3	40.3 ± 16.6	0.001	57.1 ± 11.2	46.2 ± 16.1	0.001
Gender, n (%) Female	249 (66.8)	173 (44.8)	0.001	160 (61.1)	118 (45.9)	0.001	184 (93.4)	75 (33.9)	0.001	73 (61.1)	20 (27.4)	0.001	41 (100)	10 (25.1)	0.001
Positive antibody to SARS-COV-2, n (%)	25 (6.7)	23 (5.9)	0.6	18 (6.9)	12 (4.7)	0.3	14 (7.1)	19 (8.6)	0.6	4 (5.1)	2 (2.7)	0.5	4 (9.8)	3 (7.7)	0.9
Symptomatic COVID-19 in seropositive cases, n (%)	18 (72)	10 (43.4)	0.04	11 (61.1)	7 (58.3)	0.6	11 (78.6)	9 (47.3)	0.07	3 (75)	0 (0)	0.4	2 (50)	3 (100)	0.4
Hospital admission in seropositive cases, n (%)	1 (3.8)	0 (0)	-	4 (22.2)	1 (8.3)	0.3	2 (14.3)	0 (0)	0.2	1 (25)	0 (0)	-	1 (25)	1 (33.3)	0.3
Mean colchicine dose, mg/day ± SD	1.5 ± 0.4	-	-	1.4 ±0.4	-	-	-	-	-	-	-	-	-	-	-
Mean duration of colchicine usage, years ± SD	11.3 ± 8.3	-	-	10.4 ± 7.7	-	-	-	-	-	-	-	-	-	-	-
Mean HCQ dose, mg/day ± SD	-	-	-	-	-	-	263.6 ± 95.1	-	-	255 ± 90.8	-	-	273.7 ± 132.5	-	-
Mean duration of HCQ usage, years ± SD	-	-	-	-	-	-	10.1 ± 6.6	-	-	7.3 ± 5.2	-	-	9 ± 6.3	-	-

HCQ hydroxychloroquine*, FMF familial mediterranean fever, HHC* household contacts, *RA* rheumatoid arthritis, *SLE* systemic lupus erythematosus

Conclusion: Being on a regular treatment of colchicine or HCQ was not resulted in the prevention of COVID-19 or amelioration of its manifestations.

Disclosure of Interests: None declared

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AB1083 MUSCULOSKELETAL MANIFESTATIONS AND POSTCOVID SYNDROME IN HOSPITALIZED PATIENTS INFECTED WITH COVID-19

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Background: Covid-19 may cause musculoskeletal manifestations or postcovid syndrome (1-3). Molecular mimicry, precursor activation, continue immune activation are held responsible for the development of autoimmunity (4). It has been suggested that SARSCoV-2 infection can cause blockage of lymph vessels since the virüs can infect lymph endothelial cells branching tot he nasal cavity and may cause postcovid syndrome (5).

Objectives: The aim of this study was to characterise the prevalence of musculoskeletal complaints, postcovid syndrome in hospitalized COVID-19 patients and relationship between clinical features and labaratory parameters.

Methods: A single-centre retrospective cohort study was conducted of patients at Baskent University between March 1 and December 31, 2020. The study protocol was approved by the Ethics Committee. Hospitalized patients aged above 18 years, diagnosed with COVID-19 via RT-PCR are included the study. Pregnant patients, those with severe end-stage disease or with missing documentation were excluded. Data were obtained from electronic health records. Information was collected about patient demographics, history and duration of complaints, history of postcovid syndrome, fever or anosmia, respiratory problems, length of stay, history of intensive care and COVID- 19-related biochemical parameters and rheumatologic tests. The corelation between musculoskeletal manifestations, postcovid syndrome and clinical and labaratory parameters were observed. P value<0,05 was considered statistically significiant.

Results: Totaly 109 patiensts included to the study. %39,45 of patients were female (n=66), %60,55 of patients were male (n=43). %34,86 (n=38)of patiens complained about athralgia, %1.83 (n=2) had arthritis and %41,28 (n=45) described fatigue. Postcovid syndrome was determined in %32.11 (n=35) of patients. Positive otoantibody was determined in one patient and arthritis due to paraneoplastic syndrome was detected in a case. There was significiant corelation between fever, length of stay and control CRP (p<0,05). There was significiant corelation between basal CRP and control CRP, length of stay, history of intensive care, oxygen support (p<0,05). There was significiant corelation between postcovid syndrome and arthritis, arthralgia, fatigue (p<0.05) but there was no corelation between postcovid syndrome and basal or control CRP, fever, anosmia, length of stay, intenssive care or oxygen support (p>0.05).

Conclusion: As there was no corelation between musculoskeletal manifestations, postcovid syndrome and labaratory and clinical findings. There should be further studies for understanding mechanisms of musculoskeletal manifestations and postcovid syndrome in SARSCoV-2 infection.

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Table 1. Corelation between musculoskeletal complaints (arthralgia, arhtritis, fatigue), postcovid syndrome and labaratory and clinical parameters

	Basal CRP	Control CRP	Fever	Length of stay
*Arhritis (n=2) P value	0,19	0,28	0,39	0,09
*Arthralgia (n=38) P value	0,57	0,81	0,17	0,89
*Fatigue (n=45) P value	0,73	0,56	0,24	0,35
*Postcovid syndrome (n=35) P value	0,39	0,56	0,11	0,35

* Spearman's corelation test ** Statistically significiant p<0,05

Disclosure of Interests: None declared

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AB1085 COVID-19 VACCINATION INTENTION AMONG TUNISIAN HEALTH CARE WORKERS

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Background: Health care workers (HCW) are the soldiers in the forefront of the fight against the coronavirus (COVID-19) pandemic. It is therefore a priority target group in the COVID-19 vaccination process.

Objectives: Our purpose was to assess the COVID-19 vaccination intentions of Tunisian HCW and the reason for fear in case of hesitancy.

Methods: We conducted an anonymous online questionnaire in the months of May and June 2021among HCW via social networks. The data collected included demographic characteristics, vaccination intentions, and reasons of hesitancy.

Results: Five- hundred HCW were included in the study. Participants were divided as follows: 74% doctors (15% seniors, 37% juniors, 22% interns), and 26% nurses. The mean age was 34 ± 5 years [24 – 58]. Seventy-three percent of participants were female. A history of chronic illness was noted 150 HCW (30%). A psychiatric disease was noted in 105 participants (21%): anxiety disorder (62%), depression (33%), and bipolar disorder (5%). A treatment was prescribed in 63% of cases: anxiolytics (84.2%), antidepressants (16.6%), and neuroleptics (10%). Psychotherapy was prescribed in 47% of cases. A personal and family history of COVID-19 infection was noted in 50.4 and 55% of cases, respectively. The infection was mild in 91.2% of cases. Four-hundred and five HCW (81%) had the intention to get vaccinated against COVID-19. Twenty participants (4%) refused the vaccine, and 75 (15%) were still hesitant. Vaccination hesitancy was linked to concerns about the safety of a rapidly-developed vaccine in 92% of cases: adverse reactions (95.8%), tolerance (75%), and efficacy (25%). Sixteen percent of hesitant respondents expressed

concerns about the involvement of policy in vaccine development. Vaccines to avoid according to participants were: Astra Zeneca (62%), Synovac (26%), Sputnik (8%), and Pfizer (4%).
Conclusion: The intention to be vaccinated against COVID-19 reached 81% among Tunisian HCW. Acceptance of the vaccine, even among medically informed individuals, is based on a personal perception of the risks and benefits of vaccine safety. Hence the need for campaigns targeting both the general population and the HCW.
Disclosure of Interests: None declared

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AB1086 VACCINE HESITANCY AGAINST COVID-19 VACCINES IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES AND EFFECT OF SPECIALIST COUNSELLING ON VACCINE HESITANT PATIENTS WILLINGNESS TO TAKE VACCINE

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Background: Vaccination is one of the most significant public health achievements; however, the success has been marred with vaccine hesitancy. The reasons for vaccine hesitancy are neither singular nor straightforward and arise from a complex interplay between scientific, religious and political beliefs. This study aims to understand the possible reasons for vaccine hesitancy in patients with autoimmune rheumatic diseases and the effectiveness of Specialist counselling on vaccine-hesitant patients willingness to take the vaccine.
Objectives: 1. To assess causes of Vaccine hesitancy against COVID-19 vaccines in patients with autoimmune rheumatic diseases.
2. To study the effect of specialist counselling on vaccine-hesitant patients willingness to take vaccine.
Methods: Study design: We conducted an observational survey-based in person cross-sectional study. Patients attending a tertiary care hospital's outpatient department were asked about their vaccination status. Those unvaccinated were asked reasons for vaccine hesitancy The vaccine-hesitant patients were counselled by the treating rheumatologist and asked regarding their willingness to take the vaccine after the counselling. The patient responses were recorded. Sample: Convenience sampling was used, so the sample size was not calculated. Inclusion and exclusion criteria: All adults(>18yrs) with AIRD coming to the rheumatology OPD. Those vaccinated, recently infected(within 6 weeks), and non-AIRD patients were excluded. Data collection: The questionnaire included patients' demographic details, Diagnosis, medication details, and response to the reason for vaccine hesitancy. Statistical analysis: Descriptive statistics were performed by calculating measures of central tendency for quantitative variables and using counts and percentages for qualitative and nominal variables.
Results: A total of 322 patients participated in the study with a mean age of 40 years(18-76), with 73%(234) females and 27%(88) males. Most patients had Rheumatoid Arthritis(40%) followed by SPA (27%), SLE(13%) and others and may were on immunosuppressive medications(95%). A significant proportion of patients(60%) had more than one reason for vaccine hesitancy. Almost 60% of the respondents feared their disease might flare post-vaccination, while almost half(44.4%) were hesitant to take the vaccine due to the fear of vaccine side effects and more than one third (35%) feared vaccine may not be effective on them as they were on immunosuppressive medications. Other major causes of vaccine hesitancy were the inability to get a chance to get vaccinated (18%), doubts about vaccine efficacy (15%), and fear of injections (10%).Most patients(91%) were willing to take the vaccine after specialist counselling and only 28 of the 322 (9%) were unwilling even after specialist counselling.
Conclusion: Vaccine hesitancy can be multifactorial. Major reasons for vaccine hesitancy in patients with autoimmune rheumatic diseases were fear of flare of disease post-vaccination, fear of vaccine side effects and doubts whether the vaccine would work in patients taking immunosuppressive medications. Most patients were willing to take vaccine after counselling by a rheumatologist.
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AB1087 COVID-19 IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS

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Background: In patients with ANCA associated vasculitis (AAV) a higher mortality rate due to COVID-19 has been observed compared to general population[1].
Objectives: We aimed to evaluate the frequency and severity of COVID-19 in a well-defined AAV cohort.
Methods: Medical records of AAV cases diagnosed at our secondary/tertiary rheumatology center between January 2010 and February 2020 and followed during the COVID-19 pandemic between March 2020 and November 2021 were analyzed.
Results: During the 122-month period, AAV was newly diagnosed in 117 patients. Fifteen patients died before the beginning of COVID-19 pandemic. Of the remaining 102 patients (68.8% females, 42 (41.2%) GPA; 32 (31.4%) MPA; 19 (18.6%) EGPA and 8 (7.8%) not further clinically subclassified AAV), SARS-CoV-2 infection was documented by PCR test in 11 (10.8%) patients (9 (81.8%) females; mean (SD) patient age at COVID-19 65.3 (±20.4) years; 7 GPA and 4 MPA). Five patients had mild COVID-19 symptomatically treated at home, and 6 patients had severe infection. Clinical features of COVID-19 are presented in Table 1. Three patients (27.3%) died due to COVID-19. There were 5 additional deaths of AAV patients during pandemic period, all these related to cancer progression. At the time of diagnosed COVID-19, AAV was in remission in 10 patients and relapsed 2 months prior in one patient. All patients except one were receiving immunomodulatory treatment (steroids only 2; DMARDs only 4; steroids + DMARDs 4). Of the 97 patients eligible for vaccination against COVID-19 (5 AAV patients died before vaccines against SARS-CoV-2 were available), 79 (81.4%) received by the end of November 2021 at least one dose, including 2 patients that later developed COVID-19 (both fully vaccinated; 2.5% breakthrough rate).

Table 1. Presentation of COVID-19 in AAV patients

Characteristics (11 patients)	No.	Characteristics (11 patients)	No.
COVID duration (days)	18(±9)	Respiratory insufficiency	4
Fever	6	Chest pain	5
Headache	6	Abdominal pain	1
Rhinitis	2	Diarrhoea	1
Smell loss	4	Malaise/fatigue	7
Taste loss	4	Myalgia	4
Cough	6	Arthralgia	4
Dyspnoea	7		

Conclusion: Our study shows that COVID-19 heralds a poor prognosis in AAV, with over 50% patients having severe disease and 25% deaths.
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Disclosure of Interests: None declared

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AB1088 COVID-19 VACCINATION OF SPONDYLOARTHRITIS PATIENTS RECEIVING BIOLOGICAL THERAPY: REAL-LIFE DATA

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Background: Considering the concerns regarding COVID-19 vaccine safety among patients with rheumatic diseases due to a lack of data, an urgent need for studies evaluating safety profiles of vaccines emerged.
Objectives: Vaccination against the coronavirus disease-2019 (COVID-19) started in March 2021 in the group using biological therapy in our country. In this study, post-vaccine real-life data of patients with spondyloarthritis (SpA) followed up with biological therapy were analyzed.
Methods: Adult patients diagnosed with SpA who were followed up under biological therapy and vaccinated by CoronaVac inactive SARS-CoV-2 orBNT162b2 messenger RNA (mRNA) COVID-19 (Pfizer-BioNTech) vaccine were included in our observational, multicenter, prospective study.
Results: A total of 287 patients (58.2% male; mean age: 47) were included in the study. 202 (%70,4) of patients were being followed up with the diagnosis of AS, 40 (%13,9) of them with PsA, 32 (%11,1) of them with nr-axSpA, 11 (%3,8) of them with enteropathic arthritis, and 2 (%0,7) of them with uSpA. The

most common comorbidities were found to be HT (n:65; 22.6%) and DM (n:38; 13.2%). While 221 (77%) of the patients were receiving biological therapy alone, 27 (9.4%) patients were using methotrexate, 25 (8.7%) patients were using sulfasalazine, and 12 (4.2%) patients were using leflunomide. The median duration of biological therapy was 40 weeks (19-75 IQR). The most commonly used treatment was infliximab (26.8%), adalimumab (23.3%) was the second (Table 1). It was determined that 207 (72.1%) of the patients preferred inactivated virus vaccine, while 80 (27.9%) preferred mRNA vaccine. When the time between the biological treatment and the day of vaccination is examined, detected median time between biological treatment and the first dose of vaccination is 11.5 days (5-19 IQR), between the first dose of vaccination and biological treatment is 14 days (7-21 IQR), between treatment and the second dose of vaccine is 14 days (5-23.5 IQR), and between the second dose of vaccine and the next biological treatment is 12.5 days (7-15 IQR). While 25 (8.7%) of the patients had COVID-19 infection before vaccination, 7 (2.4%) patients were found to have COVID-19 after vaccination (p<0.001). While two of the patients who had COVID-19 infection in the pre-vaccination period required hospitalization, none of the patients who had COVID-19 in the post-vaccination period required hospitalization. The rate of patients who developed side effects after the first dose of the vaccine was 20.6%. The side effects seen, respectively, were detected as pain-redness at the injection site (16%), fatigue (11.8%), headache (8.4%), muscle-joint pain (7.3%) and fever (5.6%). The rate of patients reporting side effects after the second dose of the vaccine was 17.1%. The incidence of side effects after mRNA vaccine was found to be statistically significant compared to inactivated virus vaccine in terms of both doses (p=0.011, p<0.001). Major side effects such as myocarditis, anaphylaxis-angioedema, myocardial infarction, and thrombosis were not observed in any of the patients included in the study. There was no evidence of disease activation in the median follow-up of 209 days (145-280 IQR) after vaccination.

Conclusion: During the follow-up of the patients during the study, no major vaccine-related side effects, post-vaccine disease activation and the need for treatment change were not detected. In order to more accurately evaluate the efficacy of the vaccination program in the patient population using biologic agents, larger-scale studies including unvaccinated individuals are needed.

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AB1089 PSYCHOSOCIAL IMPACTS OF THE COVID-19 PANDEMIC ON ETHIOPIAN AND CANADIAN RHEUMATOLOGY PATIENTS

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Background: The Coronavirus-2019 (COVID-19) pandemic increased psychosocial distress in the general population and in patients with rheumatic disease. Limited data exists on the impact of COVID-19 in rheumatology patients living in Africa.

Objectives: To describe COVID-19 related illness and psychosocial impact in Ethiopian (ET) rheumatology patients attending the only public rheumatology clinic in Ethiopia (Tikur Anbessa Specialized Hospital (TAH) in Addis Ababa). To compare findings in ET with findings in Canadian (CA) rheumatology patients.

Methods: Between May 1 and Oct 31 2021, 130 patients attending the TAH rheumatology clinic answered questions related to COVID-19 infection, symptoms and testing, and psychosocial impacts of the COVID-19 pandemic. We assessed depression (Patient Health Questionnaire- 9), anxiety (General Anxiety Disorder-7; GAD7), COVID-19 stress factors and coping measures, Resilience (Brief Resilience Scale-BRS) and medication compliance (Morisky medication adherence scale – 4 item; MAS4). Rheumatic disease severity was assessed with the Routine Assessment of Patient Index Data-3 (RAPID-3). Questionnaires were translated to Amharic. Descriptive statistics are reported [mean (standard deviation), median (25%, 75%) number and percent.)] and compared to data of 97 CA patients with rheumatoid arthritis (RA) and lupus patients from Quebec[1].

Results: ET patients were mainly female (71%) with a mean (SD) age of 47 (16), and resided in the capital city (Addis Ababa) (72%). Half had RA or lupus. A quarter of patients had moderate to severe rheumatic disease severity desite good medication adherence [MAS4 score of 3(2,4)]. Most (89%) reported no COVID-19 symptoms since the beginning of the pandemic, were not tested for COVID-19 and reported few risk factors for COVID-19 exposure. Eight (6%) ETs were diagnosed with COVID-19; 2 required hospitalization. Diagnosed patients reported a median of 2 COVID-19 symptoms (range 0-8; mainly cough, fever and malaise). Within the entire cohort, depression (PHQ9= 10 or above) and anxiety (GAD7=10 or above) were more frequent in ETs than CAs (depression 30% vs 3%; anxiety 16% vs 1%) yet nearly half (47%) of ETs had normal or high resilience levels. The most common COVID-19 stressors were risk of contracting COVID illness personally [ETs vs CAs risk ratio(95% confidence limits- CL); 0.67 (0.5, 0.99)] or of loved one [0.56 (0.36, 0.86)]. More ETs reported COVID-19 related stress related to difficulty obtaining food, medicine or other essentials [1.74, (1.00-3.0)], and getting needed supports [1.97 (1.03, 3.77)] (Table 1). CAs and ETs used similar levels of problem solving [median (25%,75%) CA 3.3 (2.8, 3.3), ET 3.5 (3.0, 3.7)] and emotion-focus [CA 2.5 (2.2, 3.1); ET 3.3 (2.8, 3.7)] coping strategies.

Table 1. COVID-19 related stressors reported by Ethiopian and Canadian rheumatology patients

Common stressors from the coronavirus pandemic reported as severe †	ET % reported	CA % reported	RR (95% CI) ET vs CA
Getting sick	28	41	0.67 (0.5, 0.99)
Having a loved one who becomes ill	23	41	0.56 (0.36, 0.86)
Difficulty getting food, medicine and other essentials	29	16	1.74 (1.0-3.0)
Difficulty getting support or help	24	12	1.97 (1.03-3.77)
Postponement or cancellation of tests	8	20	0.42 (0.18, 0.95)
Losing a job or experiencing a drop in income	19	10	0.185 (0.90, 3.81)
Having more responsibilities at home	21	20	1.06 (0.59, 1.87)
Having to work in a place likely to expose you to the coronavirus	20	27	0.73 (0.42, 1.24)
Postponement or cancellation of medical visits	19	15	1.2 (0.63, 2.28)
Changes in treatments	7	15	0.43 (0.17, 1.06)

†Severe stress = score 2 (moderately) to 5 (extremely)

Conclusion: During the COVID-19 pandemic, depression was more common in ETs compared to CAs with rheumatic disease. COVID-19-related stressors due to insecurity in obtaining the basic essentials and support were more pronounced in ETs. Differences between ETs and CA in these stressors may reflect local public health and economic supports. There were no differences in coping strategies.

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AB1090 IMPACT OF THE COVID19 PANDEMIC ON THE SOCIAL BEHAVIOR OF PATIENTS WITH RHEUMATIC DISEASES

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Background: Depression in rheumatic diseases negatively influences the support network and the perception of company of these patients (1).

Objectives: To describe how the COVID-19 pandemic affects the social activitiesn patients with chronic rheumatic diseases such as Rheumatoid arthritis (RA), Systemic Lupus Erithematosus (SLE) and Spondyloarthritis (SpA).

Methods: Design: Observational, longitudinal study of a series of patients. Patients: RA (ACR/EULAR 2010 classification), SpA (ASAS/EULAR 2010 criteria), and SLE (ACR 1997 criteria) patients, age ≥ 18 years. Questionaries for the evaluation of participation in social activities is the Patient Reported Outcomes Measurement Information Systems (PROMIS) v2.0 Short-Form (8 items, PROMIS-APS) at baseline (OCT to DEC 2019) and after 18 months of pandemic (SEP to DEC 2021) were performed. Variables evaluated were: social activities in terms of various factors, such as satisfaction with social roles mobility, depression, companiony social isolation, emotional support, instrumental support, support via information and ability to participate in social activities. All the variables were evaluated using the PROMIS questionnaire with quantitative scores. We also recorded demographic, clinical, and comorbidity data. Statistical analysis: Multivariate Linear Regression (Dependent variable: PROMIS ability to participate in social activities 18 months COVID19) was performed.

Results: We recruited 91 patients, 31 (34.1%) RA, 30 (33%) SpA y 30 (33%) SLE. The 3 groups were well balanced in terms of clinical-epidemiological characteristics, except that patients with SLE were younger (mean 45 years) than patients with RA (53 years) and SpA (55 years) (p = 0.004) and because most of the patients with RA and SLE were women (97%) compared to those with SpA (60%) (p <0.001). There was a worsening after 18 months of the COVID19 pandemic in the mean scores of the PROMIS for: satisfaction of the social role (26.9 ± 8.7 vs 25.3 ± 8.4; 0.046), depression (14.7 ± 7, 6 vs 16.1 ± 8.4; p = 0.044) and for the ability to participate in social activities (27.7 ± 7.2 *vs* 26.1 ± 6.8; *p* = 0.020). By diagnoses, the ability to participate in social activities was very similarbetween the different groups except for worse mobility in patients with RA and SpA compared to SLE, both at baseline and at 18 months of the pandemic. SLE patients worsened more after 18 months of the COVID19 pandemic in social role satisfaction, depression, instrumental support and ability to participate in social activities. In the multivariate analysis, the ability to participate in social activities at 18 months of the COVID19 pandemic was inversely associated with the diagnosis of SLE compared to the rest (ß [95% CI], -2.60 [-4.62 - 0.58]; p = 0.012) and depression (ß [95% CI], -0.23 [-0.39, -0.08]; p = 0.004); and directly with social role satisfaction (ß [95% CI], 0.18 [0.10-0.35]; p = 0.031), mobility (ß [95% CI], 0.13 [0.07-0.20]; p = 0.001) and company (ß [95% CI], 0.32 [0.11-0.60]; p = 0.023).

Conclusion: At baseline evaluation, social activities were affected by the impact of rheumatic disease. After 18 months of the pandemic-COVID19, patients with RA and SPA remain stable but SLE patients significantly worsened their social role and depression.

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AB1091 THE IMPACT OF COVID-19 PANDEMIC ON DISEASE MONITORING AND MONITORING FOR ADVERSE CLINICAL OUTCOMES IN THOSE ON BIOLOGIC THERAPY.

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Background: The coronavirus pandemic, is an ongoing global pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2.[1] The pandemic has posed major challenges to the National Health Service, with implications for patients with rheumatological diseases. [2] In order to try and prevent transmission of the virus, the delivery of patient care has adapted, involving more telephone and virtual review of patients. The British Society of Rheumatology (BSR) has highlighted the importance of adopting a 'treat-to-target' [3] approach in managing these patients to facilitate early treatment escalation in the presence of active disease. Close monitoring of disease is an integral approach to managing these patients. Disruption to previous patterns of care and disease monitoring of biologic patients theoretically may increase the risk of disease flare and adverse clinical outcomes. [4]

Objectives: The BSR recommends all patients receiving biologic therapy should be reviewed for drug safety every 6 months. It recommends that patients prescribed a biologic should have monitoring blood tests every 3–6 months.[3, 5] The BSR has published mitigating guidance outlined within the COVID-19 rapid guideline.[5] This suggests it's safe to increase time intervals between blood tests for drug monitoring, particularly if 3-monthly blood tests have been stable for over 2 years. Our aims are to evaluate whether altering our delivery of care has impacted on the 'treat-to-target' approach and the frequency of blood monitoring in those on biologic therapy, despite the challenges of an ongoing global pandemic.

Methods: Over a period of 1 month a total of 51 patients receiving biologic therapy case notes were reviewed. Data was collected relating to underlying diagnosis, choice of biologic, whether a disease activity score was performed, method of consult and compliance with drug monitoring.

Results: Of the 51 patients 24 patients were receiving adalimumab, 20 baricitinib, 2 filgotinib, 2 upadacitinib and 3 on entarcept. Diagnoses ranged from 33 patients with rheumatoid arthritis, 7 psoriatic arthritis, 5 ankylosing spondylitis, 5 spondyloarthropathy and 1 enteropathic arthritis. Disease activity scores were documented in the majority of patients (75%). In those where disease activity scores were not documented, 11 had rheumatoid arthritis and the remaining 2 psoriatic arthritis. The majority of the patients who didn't have disease activity scores documented were reviewed via telephone consult (84%). All patients had undergone adequate blood monitoring with 100% compliance with blood tests performed within 6 months.

Conclusion: The COVID-19 pandemic has presented an extraordinary necessity for change in how we manage patients suffering from rheumatic disease. The impact of this global pandemic will be long-lasting and thorough analysis of patient outcomes is needed. However, this period presents an exciting opportunity to embrace new ways of working, which may improve efficiency and efficacy of patient care.

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AB1092 INFLAMMATORY ARTHRITIDES IN POST-COVID-19 PATIENTS: AN ALBANIAN EXPERIENCE.

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Background: COVID-19 is a disease caused by the new pathogen SARS-CoV2 (severe acute respiratory syndrome coronavirus 2) typically presenting with pneumonia but also other systemic manifestation has been reported worldwide [1]. Different reports have described the appearance of inflammatory arthritis (IA) after resolution of acute infection from COVID-19 [2].

Objectives: To observe the frequency of Inflammatory Arthritis in an Albanian cohort of post-COVID-19 patients.

Methods: Post-Covid-19 patients, having two consecutive negative PCR (real-time reverse transcription polymerase chain reaction), discharged from the Pulmonology Department (January – July 2021) were invited to enter in a 6 (six) month multidisciplinary observational study. Data regarding post-COVID-19 inflammatory arthritis are presented in this study. Descriptive statistical analysis was used to express data.

Results: From 154 post-COVID-19 patients (F/M = 62/92) enrolled, 14 (9.09%) patients didn't follow regularly the dedicated ambulatory thus were excluded from this study. Considering the remaining 140 patients (F/M = 58/82), only 21 (15%) patients were diagnosed with IA where the most common were, respectively: Reactive Arthritis (ReA) 11 (52.3%) patients; Rheumatoid Arthritis (RA) 4 (19.09%) patients; Ankylosing Spondylitis (AS) 3 (14.2%) patients; Gout Arthritis (GA) 3 (14.2%) patients. All rheumatic conditions were more frequent in male than in female post-COVID-19 patients. Data summarized in Table 1. All patients that developed a post COVID-19 IA, had fever during the period of SARS-CoV2 infection. Arthralgia was a typical symptom that have been reported by patients that have developed RA and AS. All RA post-Covid-19 patients reported having had even symptoms like cough, dispnea and fatigue. None of the AS patients neither GA reported symptoms of dysguesia or anosmia. Only 9% of ReA patients reported having had abdominal pain during acute infection with SARS-Cov2. Data summarized in Figure 1.

Table 1.

Inflammatory Arthritis	Patients (N, %)	Age (mean ± SD)	Male (N, %)	Days after COVID-19 (mean ± SD)
ReA	11 (52.3)	48.2 ± 12.5	7 (63.6)	15.8 ± 9.9
RA	4 (19,09)	55.7 ± 8.7	2 (50)	32.3 ± 11.3
AS	3 (14.2)	50.5 ± 9.7	2 (14.2)	18.8 ± 5.5
GA	3 (14.2)	55.3 ± 1.2	3 (100)	10.6 ± 0.9

Conclusion: IA is another manifestation that follows acute infection from COVID-19. In this regard increased awareness and further investigations are needed

in order to better understand weather SARS-Cov2 infection can accelerate the development of a rheumatic autoimmune disease.

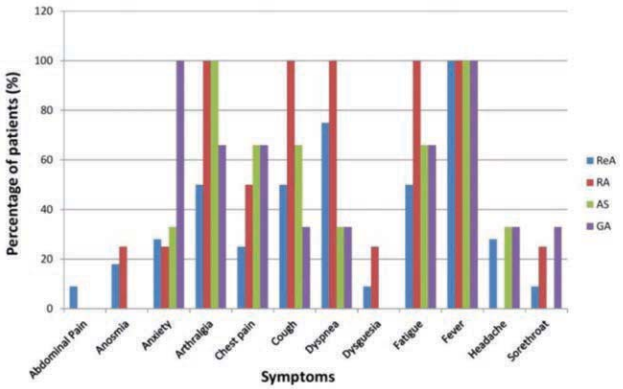

Figure 1. Most frequent symptoms during infection period for each post-COVID - IA.

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AB1093 SAFETY OF COVID-19 VACCINES IN PATIENTS WITH RHEUMATOID ARTHRITIS (PRELIMINARY DATA).

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Background: Patients with rheumatoid arthritis (RA) are at high risk of developing COVID-19. Vaccination should be an effective method of preventing this disease. However, vaccination may be unsafe in RA patients. At present, data on the safety of vaccines against COVID-19 in RA patients are few and relate to foreign vaccines that are not licensed in Russia.

Objectives: To study the safety of COVID-19 vaccines in patients with RA in real clinical practice.

Methods: The study included 131 RA patients (120 women, 11 men, age 53.8±13.9 years, duration of disease 11.5±9.2 years) - the main group and 121 people without any immuno-inflammatory rheumatic diseases (87 women, 34 men, age 39.8±14.2 years) - the control group. 103 patients received disease-modifying antirheumatic drugs (54 - methotrexate, 30 - leflunomide, 10 - hydroxychloroquine, 8 - sulfasalazine, 1 - mofetil mycophenolate), 68 - biological drugs (58 - rituximab, 5 – TNF-α inhibitors, 4 - abatacept, 1 - tocilizumab), 64 - glucocorticoids, 10 - did not receive therapy. In the main group, 92 patients were vaccinated with Gam-COVID-Vac (Sputnik V), 21 with Sputnik Light, 16 with CoviVac, 2 with EpiVacCorona (110 patients received two components of the vaccine). In the control group, 91 were vaccinated with Sputnik V, 16 with CoviVac, 6 with BNT162b2, 5 with Sputnik Light, 2 with EpiVacCorona, 1 with mRNA-1273 (114 participants received two components of the vaccine). All participants were interviewed by a research doctor with a unified questionnaire, additional information was obtained from medical documentation.

Results: Local and systemic adverse events (AEs) were observed both in the main group and in the control group. After the introduction of the first component of the vaccine, local AEs (pain/hyperemia/edema) were noted in 12.2% of RA patients and in 10.7% of the control group, after the introduction of the second component of the vaccine - in 9.1% and 11.4% of respondents, respectively (in both groups p>0.05). There was a significant difference between the main group and the control group in the frequency of pain at the injection site without restriction of movements both after the first (24.4% and 40.5%, p=0.007) and after the second component (18.2% and 31.6%, p=0.021). The most frequent systemic AEs were weakness, fever, muscle or joint pain, headache, chills, which were observed in both groups after administration of both the first and second components of the vaccine. There was a significant difference between the main group and the control group in the frequency of fever (16.8% and 39.7%, p<0.001), weakness (26.0% and 38.8%, p=0.029), muscle and joint pain (9.2% and 25.6%, p<0.001) after administration of the first (but not the second) component of the vaccine. A significant difference was revealed between the main group and the control group in the number of patients with local and systemic AEs both after the introduction of the first component of the vaccine (19.1% and 43%, p<0.001) and after the second (15.5% and 30.7%, p=0.007). After administration of the two components of the vaccine, a higher number of patients without any AEs were detected in the main group compared to the control group (32.7% and 18.4%, p=0.014). Exacerbation of RA and the emergence of new autoimmune phenomena in main group are not marked.

Conclusion: According to preliminary data, the tolerance of vaccines against COVID-19 in RA patients is satisfactory. Further studies are needed to study the safety, immunogenicity and clinical efficacy of immunization against COVID-19 in patients of this cohort.

Disclosure of Interests: None declared

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AB1094 SAFETY AND EFFICACY OF VACCINES FOR SARS-COV-2 IN PATIENTS WITH RHEUMATIC AND IMMUNE-MEDIATED INFLAMMATORY DISEASES: DATA FROM THE ARGENTINEAN REGISTRY SAR-COVAC

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Background: Currently there is little information on the efficacy and safety of SARS-CoV-2 vaccination in patients with immune-mediated diseases and/or under immunosuppressive treatment in our country, where different types of vaccines and mix regimens are used. For this reason, the Argentine Society of Rheumatology (SAR) with the Argentine Society of Psoriasis (SOARPSO) set out to develop a national register of patients with rheumatic and immune-mediated inflammatory diseases (IMIDs) who have received a SARS-CoV-2 vaccine in order to assess their efficacy and safety in this population.

Objectives: To assess SARS-CoV-2 vaccine efficacy and safety in patients with rheumatic and IMIDs.

Methods: SAR-CoVAC is a national, multicenter and observational registry. Adult patients with a diagnosis of rheumatic or IMIDs who have been vaccinated for SARS-CoV-2 were consecutively included between June 1st and September 17th, 2021. Sociodemographic data, comorbidities, underlying rheumatic or IMIDs, treatments received and their modification prior to vaccination and history of SARS-CoV-2 infection were recorded. In addition, the date and place of vaccination, type of vaccine applied, scheme and indication will be registered. Finally, adverse events (AE), as well as SARS-CoV-2 infection after the application of the vaccine were documented

Results: A total of 1234 patients were included, 79% were female, with a mean age of 57.8 (SD 14.1) years. The most frequent diseases were rheumatoid arthritis (41.2%), osteoarthritis (14.5%), psoriasis (12.7%) and spondyloarthritis (12.3%). Most of them were in remission (28.5%) and low disease activity (41.4%). At the time of vaccination, 21% were receiving glucocorticoid treatment, 35.7% methotrexate, 29.7% biological (b) Disease Modifying Anti-Rheumatic Drugs (DMARDs) and 5.4% JAK inhibitors. Before vaccine application 16.9% had had a SARS-CoV-2 infection. Regarding the first dose of the vaccine, the most of the patients (51.1%) received Gam-COVID-Vac, followed by ChAdOx1 nCoV-19 (32.8%) and BBIBP-CorV (14.5%). In a lesser proportion, BNT162b2 (0.6%), Ad26.COV2.S (0.2%) and CoronaVac (0.2%) vaccines were used. Almost half of them (48.8%) completed the scheme, 12.5% were mix regimenes, the most frequent being Gam-COVID-Vac / mRNA-1273. The median time between doses was 51days (IQR 53). More than a quarter (25.9%) of the patients reported at least one AE after the first dose and 15.9% after the second. The flu-like syndrome and local hypersensitivity were the most frequent manifestations. There was one case of mild anaphylaxis. No patient was hospitalized. Altogether, the incidence of AE was 246.5 events/1000 doses. BBIBP-CorV presented significantly lower incidence of AE in comparison with the other types of vaccines. (118.5 events/1000 doses, p<0.002 in all cases) Regarding efficacy, 63 events of SARS-CoV-2 infection were reported after vaccination, 19% occurred before 14 days post-vaccination, 57.1% after the first dose (>14 days) and 23.8%

after the second. In most cases (85.9%) the infection was asymptomatic or had an outpatient course and 2 died due to COVID-19.
Conclusion: In this national cohort of patients with rheumatic and IMIDs vaccinated for SARS-CoV-2, the most widely used vaccines were Gam-COVID-Vac and ChAdOx1 nCoV-19, approximately half completed the schedule and in most cases homologously. A quarter of the patients presented some AE, while 5.1% presented SARS-CoV-2 infection after vaccination, in most cases mild.
Disclosure of Interests: None declared

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AB1095 POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS AFTER COVID-19 VACCINATION: A CASE REPORT

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Background: The COVID-19 pandemic has infected millions of people around the world and there has been a new surge of virulent strains in many parts of the world[2]. Patients with Systemic Lupus Erythematosus (SLE) were reported to be at higher risk of SARS-CoV-2 infection and worse outcomes from COVID-19, possibly due to their intrinsic immune dysfunction, demographics, disease activity, medications, associated organ damage, comorbidities and as such, have been among the first to receive the vaccines [3]. The most common reason for vaccine refusal in patients with SLE is fear of SLE disease flare. Additionally, SARS-CoV-2 mRNA vaccines could potentially induce interferon production, associated with increased SLE disease activity[1].
Objectives: we report a case of SLE presented with lupus flare after receiving the 1st dose of phizer vaccine.
Methods: A 30-year-old female patient, kown case of SLE since 2011 well controlled on low dose steroids, hydroxychloroquine and azathioprine. Upon receiving her 1st shot of Pfizer-BioNTech COVID-19 Vaccine, she developed high grade fever associated with generalized tender papulovesicular skin eruption mainly on the back of the trunk and the outer surface of both thighs, then she developed generalized tonic-clonic convulsions and transferred for Intensive Care Unit (ICU), intubated, mechanically ventilated and received intravenous anti-epileptic medications. During her admission, Cerebrospinal fluid (CSF) examination and Magnetic Resonance Imaging (MRI) brain were done.she regained her consciousness, extubated after 48 hours.
Results: The initial laboratory invwstigations revealed COVID19-PCR: negative,ESR: 35 mm/hr,CRP: 78,C3: 70 mg/dL (90 – 180) and C4: 8 mg/dL (10 – 40). CSF examination revealed proteins: 116.9 mg/dL (15 – 45),glucose: 46.3 mg/dL (50-60% of serum),LDH: 49.1 U/L (10% of serum) and no cells.Emergency MRI brain was performed revealed multiple bilateral symmetrical mainly cortical and subcortical abnormal signal with cortical swelling are seen mainly involving both occipito-temporo-parietal lobes with patchy enhancement of left cerebellar hemisphere, cerebellar vermis, both thalami, medulla and pons,Picture suggestive of Posterior Reversible Encephalopathy Syndrome (PRES).Accordingly the patient received received pulse steroid therapy for 3 days under cover of oral acyclovir.She also received levetiracetam and Oxcarbazepine.the condition markedly improved and discharged from the hospital for follow up after one month.
Conclusion: 1)The mRNA COVID Vaccine may rarely cause CNS affection, or even SLE flare so, SLE patients must be well controlled before giving the Vaccine. 2) SLE patients must be monitored closely by clinical examination and laboratory investigations after taking mRNA COVID Vaccine.
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AB1096 THE INFLUENCE OF THE BEHAVIORAL RESTRICTION OF COVID-19 PANDEMIC FOR THE FRAILTY OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: We previously reported the prevalence of frailty and relation of disease activity at patients with rheumatoid arthritis (RA)[1]. The behavioral restriction of COVID-19 pandemic influenced for the lifestyle of people included patients with RA.
Objectives: The relationship between the behavioral restriction of COVID-19 pandemic and frailty was investigated.
Methods: We used the date from prospective observational study (CHIKARA study: UMIN000023744). 70 from 100 patients with RA were followed-up and evaluated the frailty and subcategories (social, physical, mental, nutrition, and cognitive) by frailty checklist. The prevalence of frailty and the change of exercise and daily life activities by visual analog scale were investigated at pre- and post-behavioral restriction. The correlation of frailty and change of amount of exercise and daily life activity examined by univariate analysis.
Results: Mean age was 69.7 years (women n=57, men n=13). The prevalence of frailty at post-behavioral restriction increased compared that at pre-behavioral restriction (post:35.8% vs pre:30.0%). Especially, cognitive and total score at post-behavioral restriction increased significantly. The rate of decrease of exercise by <25%, 26~50%, and 51%< were 70%, 21%, and 9%, respectively (mean:20% decrease). Whereas, the rate of decrease of daily life activities by <25%, 26~50%, and 51%< were 37%, 27%, and 36%, respectively (mean:44% decrease). The change of exercise was significantly negatively correlated with the change of nutrition (R=-0.245, P=0.041) at Table 1. There was no correlation between the change of daily life activities and subcategories.

Table 1. Univariate analysis of the changes in daily living activities or exercise and those in frailty and subcategories

	Change of daily living activities		Change of exercise	
	R value	P value	R value	P value
Δ Social	0.099	0.417	-0.006	0.962
Δ Physical	0.182	0.130	-0.005	0.965
Δ Mental	-0.200	0.097	-0.234	0.051
Δ Nutrition	-0.204	0.091	-0.245	0.041
Δ Cognitive	-0.087	0.476	-0.034	0.778
Δ Total	-0.091	0.454	-0.178	0.140

Δ, change from pre- to post-behavioral restriction. Analyzed by Spearman's rank correlation coefficient

Conclusion: The exercise slightly decreased and the daily life activities decreased almost 50% by the behavioral restriction of COVID-19 pandemic. The prevalence of frailty increased 5.8%, and cognitive and total score were significantly high at post-behavioral restriction of COVID-19 pandemic. The decrease of exercise correlated with the worse of nutrition.
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AB1097 FEATURES OF THE COURSE AND CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO UNDERWENT COVID-19

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Background: COVID-19 remains a serious problem almost two years later, despite the ongoing active search for effective tools to control it. To date, it is known that COVID-19 not only proceeds as an acute respiratory illness, but also leads to a systemic inflammatory response and hypercoagulability through activation of both the innate and adaptive immune systems. Patients with rheumatic and musculoskeletal diseases appear to be more vulnerable to the development of severe forms of COVID-19 due to the impaired immune response associated with RMD. In addition, immunosuppressants prescribed to control RMD increase the risk of infections. And finally, RMD is often combined with comorbid conditions from the group of risk factors for severe forms of COVID-19 such as arterial hypertension, diabetes mellitus and obesity.
Objectives: to characterize the features of the course of COVID-19 in patients with rheumatoid arthritis.
Methods: We studied the material of questionnaires filled out by patients of the hospital of the V.A. Nasonova Research Institute of Rheumatology who underwent COVID-19, verified by RT-PCR to SARS-CoV-2 RNA, for the period from 05/15/2020 to 12/15/2021. The information was supplemented with data from discharge reports after inpatient treatment of COVID-19. Statistica software (version 12) was used for statistical processing. The results of the correlation analysis were considered reliable at $p \leq 0.05$.

Results: The study included 32 adult (over 18 years old) patients (29 women, 90%) with a reliable diagnosis of rheumatoid arthritis (ACR / EULAR). The average age of patients is 50.75 ± 16.48 years. In the study group, 29 (90.6%) patients never smoked, 2 smoked in the past and 1 was an active smoker. The duration of the course of RA (median) was 8 [4; 14.5] years. The most common comorbidities were diseases of the cardiovascular system (in 20 patients), diseases of the gastrointestinal tract (in 7 patients), diabetes (in 4 patients) and obesity (in 5 patients). The median number of comorbid diseases was 1 [0; 3]. At the time of the development of COVID-19, the severity of RA symptoms, assessed by the VAS, was 4.78 ± 3.06. As antirheumatic therapy, 10 (31.25%) patients took glucocorticoids at an average dose of 5 ± 3.9 mg / day. (prednisolone equivalent), 22 (68.75%) - DMARDs. 19 patients received bDMARDs, incl. 12 - rituximab (37.5%, of which 7 received the last infusion within 6 months or less before the first symptoms of COVID-19 appeared). Among the clinical manifestations of COVID-19, weakness was most often noted, fatigue - in 29 (90.6%), fever - in 23 (71.9%), anosmia - in 20 (62.5%), dysgeusia - in 19 (59.4%), increased arthralgia - in 17 (53.1%), shortness of breath during exercise - in 16 (50%), cough - in 15 (46.9%). There was a significant positive correlation between increased arthralgia during COVID-19 and RA activity. On average (median), each patient reported 13.5 [9.75; 19.25] symptoms associated with COVID-19. There was no significant correlation between the number of COVID-19 symptoms and RA activity. During COVID-19, CT scan was performed in 19 patients: CT-0 - in 1 patient (5.3%), CT-1 - in 9 (47.4%), CT-2 - in 5 (26.3%), CT-3 - in 3 (15.7%), CT-4 - in 1 (5.3%). There was no correlation between the CT stage and RA activity. 12 patients (37.5%) were hospitalized, of which 8 needed oxygen support. Rituximab treatment was not associated with hospitalization rates. Complications were reported in 4 cases (12.5%): venous thrombosis in 2 patients and acute respiratory failure in 2 more patients.
Conclusion: 37.5% of COVID-19 patients in the study group required inpatient treatment. In 12.5% - COVID-19 proceeded with complications. The number of symptoms associated with COVID-19 did not correlate with RA activity. However, patients with higher RA activity more often noted increased arthralgia.
Disclosure of Interests: None declared

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AB1098 DEVELOPMENT OF INFLAMMATORY MYOPATHY AFTER COVID-19

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Background: It has been more than a year and a half since the WHO announced a pandemic of a new coronavirus infection caused by SARS-CoV-2. The virus belongs to the respiratory group, but it it can damage various organs and tissues of the body. COVID-19 infection is characterized by pathological activation of immunity, violated synthesis of pro-inflammatory, immunoregulatory, anti-inflammatory cytokines, such as interleukins-1 and -6, tumor necrosis factor α and others. These features contribute to the development of rheumatic diseases and syndromes in people who have had COVID-19. Cellular and humoral immune responses are also of primary importance in the pathogenesis of inflammatory myopathies.
Objectives: Description of a case of severe dermatomyositis after COVID-19.
Methods: The 34-year-old female patient complained of pain and weakness in the proximal muscles of the upper and lower extremities, difficulty swallowing solid and liquid food, rash on the face, neck, chest and arms. In August 2020 she had a mild case of COVID-19. A month later, flaky erythematous papules like Gottron's sign appeared on the extensor surfaces of the metacarpophalangeal joints and proximal interphalangeal joints of the hands. Six months later, sore throats, hoarseness of voice, belching of air, choking on solid food and episodes of subfebrility joined. Reflux esophagitis, duodenitis was detected by fibrogastroduodenoscopy. After 9 months, there were muscle pains and muscle weakness, erythema on the face, neck and chest, the patient lost 11 kg. She was hospitalized in the rheumatology department with suspected dermatomyositis.
Results: On objective examination: proximal myopathy, erythematous rashes on the face, neck, chest, Gottron's erythema on the hands. In the analyses: clinical analysis of blood and urine without pathology, ANA 1:1280, creatinkinase 5370 IU/l, with an increase in dynamics up to 9260 IU/l, CRP 0.03 mg /dl, LDH 1023 IU/l, rheumatoid factor and anti-ds DNA were negative. Nasal regurgitation was detected during radiography of the pharynx with contrast. Instrumental examination revealed no signs of a tumor process. Fibrogastroduodenoscopy - superficial reflux-esophagitis, duodenitis, Chest CT - interstitial pneumonitis, abdominal ultrasound without pathology, ECG - sinus rhythm, normal EOS position, accelerated A-V conduction, echocardiography - minor separation of pericardial leaves (up to 5 mm), colonoscopy - dolichosigma. The patient was diagnosed with idiopathic dermatomyositis of high activity. Because of progressive myopathy and increasing dysphagia, pulse therapy with methylprednisolone500 mg for 3 days and rituximab 1000 mg was performed. She also received metipred 48 mg per day orally, methotrexate 15 mg per week subcutaneously and folic acid 5 mg per week. Against the background of therapy, positive dynamics was noted: swallowing normalized, the severity of myopathy decreased, after 10 days CKdecreased to 2049 IU/l. After 6 months during the control examination: there are no skin rashes, muscle strength is restored, CK 300 IU/l. The dose of methylprednisolone is reduced to 10 mg per day, the patient continues injections of methotrexate 15 mg per week.
Conclusion: COVID-19 may be a trigger for the development of inflammatory myopathy. In this clinical case there are features of the course and therapy of inflammatory myopathies in patients after coronavirus infection.
Disclosure of Interests: None declared

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AB1099 CORONAVIRUS INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (CASE SERIES).

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Background: SARS -CoV 2 infection (Covid -19) has a wide range of Clinical and laboratpry symptoms typical for rheumatic diseases, in particular systemic lupus erythematosus (SLE).
Objectives: Analysis of the course of Covid-19 in patients with SLE and the influence of antirheumatic drugs on its outcomes.
Methods: A retrospective analysis of 12 patients with SLE previously observed in the rheumatology department and had Covid-19 in 2020-2021. Average age of patients (83% women) is 41 years (24-59 years old), duration of SLE - 11 years (3-25 years). 10 patients had low SLE activity, 1 - moderate, 1 - high. In anamnesis 8 patients had hematological disorders, 4 - secondary antiphospholipid syndrome (APS) with thrombosis, 3 - cerebrovasculitis, 5 - lung damage, 3 - lupus nephritis. All patients were treated with glucocorticosteroids (GCs) (the average dose 2 1/4 tablets per day), 10 (66,7%) - with hydroxychloroquine (HCQ), 4 (33,3%) – with immunosuppressants: 2 - mycophenolate mofetil, 1 - methotrexate, 1 – cyclophosphamide. 3 (25%) patients received rituximab (RTM) 2-3 months before the onset of COVID-19. 9 (75%) patients received outpatient treatment, 5 of them had a mild infection (3 - without lung damage, 2 - with lung damage - CT 1), 4 - had a moderate course, 3 (25%) - were admitted to the hospital,1 - to the intensive care unit.
Results: Patients were divided into 3 groups for SLE therapy. The first group (6 patients) was treated with GCs (average dose of 1 1/2 tab.) and HCQ (200-400 mg). All of them had mild to moderate course of infection without complications. Exacerbation of SLE was noted in 3 (50%) patients: 2 had capillarities, psycho-emotional lability, deterioration of laboratory parameters, 1 (with secondary APS) developed deep vein thrombosis of the legs and an exacerbation of lupus nephritis a month after. The second group (3 patients) received GCs (average dose 2 1/4 tab.) and immunosuppressants. In 2 patients the course of Covid-19 was mild, in 1 - moderate. Exacerbation of SLE was noted in 2 patients: 1 had headaches, high titers of ANA and anti-DNA, 2nd - a severe exacerbation (hematological disorders, lupus nephritis with impaired renal function). The third group (3 patients) received GCS (average dose 5 tab.) and rituximab. 2 patients received RTM for 2 years, the last infusion was carried out for 3 months before the onset of an infection. Their course of Covid-19 was moderate with CT-2 lung damage and mild respiratory failure. There were no exacerbations of SLE after recovery. The 3rd patient initially had a high activity of SLE with nephrotic syndrome, arterial hypertension, batterfly rash, arthritis, fever, which required high doses of GCs and 2 rituximab infusions of 500 and 1000 mg. A month later, a severe COVID-19 developed with 70% lung damage, severe respiratory failure (SpO2 - 80%), and cytokine storm syndrome. He was treated with GCS, anticoagulants, tocilizumab, immunoglobulin, followed by recovery. Mild and moderate course of COVID-19 was observed in 92% of patients with SLE, in 8% - severe. Exacerbation of SLE after infection occurred in 41% of cases with no lethal outcomes.
Conclusion: Patients with low activity SLE on small doses of GCs and HCQ tolerate COVID-19 relatively easily. The high activity of SLE and the use of rituximab contribute to the severe course of COVID-19 with damage to the lungs and respiratory failure, so the use of anti-B-cell therapy during a pandemic is undesirable. The effect of immunosuppressants is controversal. Exacerbation of SLE after COVID-19 in 41% of all patients requires monitoring of laboratory parameters and observation by a rheumatologist for at least six months after recovery from infection.
Disclosure of Interests: None declared

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AB1100 COVID-19 VACCINATION IN A REAL-LIFE SETTING OF A RHEUMATOLOGICAL OUTPATIENT CENTER

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Background: Since approvement of the first vaccines against COVID-19 in European in 12/2020, a large vaccination (VAC) campaign was started. Patients with inflammatory diseases (ID) were graded as higher risk. Many of our patients used the possibility and got vaccinated. Until know, there is few knowledge about the efficacy and safety of VAC in patients with ID. There are some reports of less VAC response in patients with ID (1). Many antibody (AB) studies are ongoing but monitoring of AB status is not recommended by official recommendations (1,2). Nevertheless, AB testing is commonly used in daily care in outpatient centers (OC).
Objectives: To evaluate in a real life setting of a single rheumatological OC how many patients have been vaccinated against COVID-19, how many of these did not develop AB and search for possible explanations.
Methods: All consecutive patients of the routine follow up visits from 03/2021 to 12/2021 were retrospectively evaluated if VAC and an AB testing (e.g. ELISA-tests) was done ≥4 weeks after the 2nd VAC was documented. All AB tests were classified for AB levels (Ratio <0,8 negative, >0,8 Ratio < 4,5 low to moderate, Ratio ≥ 4,5 high level). The group of patients without AB was specified.
Results: N=1206 persons were questioned. N=23/1206 (1.9%) patients refused a VAC. N=1183/1206 (98.1%) have got a VAC. N=984/1183 (83.2%) were had an ID, n=199/1183 (16.8%) were healthy persons (HP). In n=608/1138 (51%) an AB status after ≥4 weeks after VAC was available. N=14/608 (20%) HP developed all but one high AB levels. 1 HP had a low to moderate AB level. In n=595/1183 (50%) patients with ID an AB status was available. N=438/595 (74%) patients developed high AB levels, n=126/595 (21%) low to moderate, n=30/595 (5%) had no AB. Mean age in the group without any AB was 69years (range 38-95). N=27/30 (90%) patients received ≥1 DMARD (disease modifying antirheumatic drug), n=3/30 patients were not treated with DMARD, n=2/3 of these patients received Prednisolone (P) instead. N=4/30 received Rituximab (RTX), n=1/30 Abatacept (ABA), n=1/30 MMF (3g), n=1/30 Azathioprine in combination with high P (55mg), n=15(50%) MTX alone or in combination, n=24/30(80%) P (range mg 1-55, mean 5,7). One 52y old patient without any AB did receive nether a DMARD nor P. N=3/30 patients got both vaccinations with Vaxzevira (V), n=25/30 (83,3%) Comirnaty (C), n=1/30 Spikevax, n=1/30 first V, second C. 1 patient, treated with ABA has been vaccinated with 2 doses of C. A AB testing 4 months later did not reveal any antibodies. This patient came down with COVID-19 5 months after complete VAC and died.
Conclusion: There is very high number of VAC (98,1%) in a real life setting of a rheumatological OC. Many patients (95%) developed low to high AB levels after 2 VAC, independently which agent was used. Otherwise, we must be aware of the small group of patients (5%) without developing any AB. Unfortunately, our group was too small to find significant risk factors (RF). But RF seems to be the age, therapy with RTX, ABA and P. This is in line with reported RF in clinical studies (1). Furthermore, we see lower levels in elderly patients who get vaccinated with C. This could be biased by the fact that, in the first months of the VAC campaign, C was used in patients with higher age and the 2nd C-VAC was given 3 weeks after 1st VAC. Retrospectively, this interval seems to be too short. Thus now, the 2nd VAC is given 4-6 weeks after 1st VAC. In conclusion it is still unclear, which levels of AB make VAC effective and which patients will develop AB levels. AB levels should be evaluated to pick out patients with VAC gap, since the high risk of fatal course of COVID-19-disease. The booster campaign and 3rd VAC will change the current state again, therefore revaluation will be necessary.

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AB1101

PREVALENCE OF LONG COVID IN RHEUMATIC DISEASE PATIENTS: ANALYSIS OF SAR COVID REGISTRY

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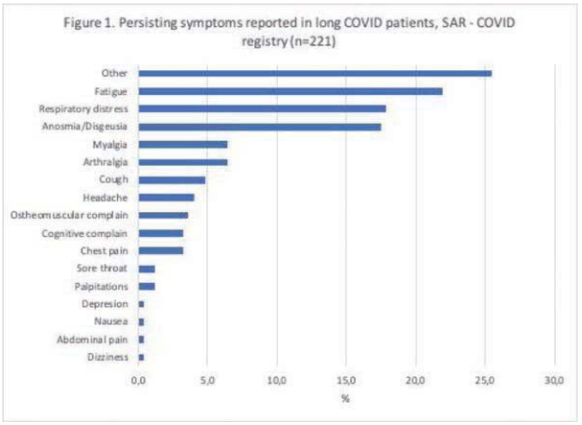
Background: Persistent symptoms after acute COVID have been described previously. Main symptoms reported are fatigue, arthralgias, myalgias and mental sickness. Definition and methods vary widely.[1]
Objectives: To asses prevalence and related factors to long COVID in a retrospective cohort of patients with rheumatic diseases from Argentina.
Methods: A total of 1915 patients were registered from August 18th, 2020 to July 29th, 2021. Patients > 18 years old, with rheumatic disease and confirmed infection by SARS-CoV-2 (antigen or RT-PCR) were included. Those dead, with unknown outcome, wrong date or missing data were excluded. Demographic data, comorbidities, rheumatic disease, and characteristics of SARS-CoV-2 infection were recorded. Long COVID was defined according to NICE guidelines (persistent symptoms for more than 4 weeks, without alternative diagnosis). Long COVID symptoms were defined by rheumatologist. Severity of infection was classified according to WHO ordinal scale. We used descriptive statistics, univariate model (Student's test, chi square test, ANOVA) and multivariate logistic regression analysis.
Results: 230 (12%) had long COVID. Median age was 51 (IQR 40-61]) years, 82% were females, 51% were not caucasian. Median of education was 13.3 years (IQR 12 – 16), 79 % had private health insurance and 55 % were employed. Nearly half (n=762, 46%) had comorbidities, the most prevalent was hypertension (n=396, 24%). The most frequent rheumatic diseases were rheumatoid arthritis (n=719, 42%) and systemic lupus erythematosus (n=280, 16 %). Most were in low activity/remission (79%), used Conventional DMARD (n=773 patients, 45%) and steroids (n=588, 34%) at low dose (n=415, 71%). Main laboratory findings were abnormal D-dimer (n=94, 28%) and leukopenia (n=93, 26%). Most patients had a WHO ordinal scale < 5 (n=1472, 86%). Median of hospitalization at intensive care unit (ICU) was 8 days [IQR 5, 13]. Treatment for SARS-CoV-2 infection (steroids, anticoagulation, azithromycin, convalescent plasma) was used in 461 (27%) patients. Most of long COVID (n= 152, 69%) reported 1 symptom, the most frequent was fatigue (n= 55, 22%). Figure 1. Univariate analysis is presented in Table 1. In multivariate logistic regression analysis non-caucasian ethnicity OR 1.44 (1.07-1.95), years of education OR 1.05 (1-1.09), treatment with cyclophosphamide OR 11.35 (1.56-112.97), symptoms of COVID – 19 OR 13.26 (2.75-242.08), severity scale WHO ≥ 5 OR 2.46 (1.68-3.57), and ICU hospitalization days OR 1.09 (1.05-1.14) were factors associated to long COVID.

Table 1. Univariate analysis of long COVID syndrome in SAR – COVID registry

Variable	Acute COVID n=1486	Long COVID n=221	P value
Age, years, median [IQR]	**51 [40, 60]**	**54 [42, 62]**	**0.032**
Caucasian, n (%)	744 (48)	132 (53)	0.227
Female sex, n (%)	1242 (80)	215 (86)	0.066
Education, years, median [IQR]	12 [10, 17]	13 [12, 16]	-
Private health insurance, n (%)	1161 (79)	181 (82)	0.325
Smoking, n (%)	381 (25)	71 (29)	0.224
Comorbidities, n (%)	650 (45)	108 (52)	0.066
Dyslipidemia, n (%)	**173 (12)**	**39 (19)**	**0.008**
Hypertension, n (%)	**332 (23)**	**60 (29)**	**0.053**
Low activity/remission disease, n (%)	1140 (80)	179 (77)	1
Rheumatoid arthritis, n (%)	623 (42)	96 (42)	1
Systemic lupus erythematosus, n (%)	243 (16)	37 (16)	0.996
DMARD, n (%)	664 (45)	109 (47)	0.486
Cyclophosphamide, n (%)	**3 (0.2)**	**3 (1)**	**0.035**
Rituximab, n (%)	**19 (1)**	**9 (34)**	**0.008**
Lymphocyte <1.500 / mm3, n (%)	**66 (23)**	**19 (30)**	**0.011**
Ferritin > 2000 ng/ml, n (%)	**32 (11)**	**16 (25)**	**0.011**
ICU hospitalization, days, median [IQR]	**7 [4, 10]**	**10 [8, 24]**	**<0.001**
Treatment for COVID-19, n (%)	**394 (27)**	**91 (41)**	**<0.001**



Conclusion: Prevalence of long COVID was 12%. Non-caucasian ethnicity, higher education, treatment with cyclophosphamide, symptoms of COVID – 19, severe disease and ICU hospitalization days were related to long COVID.

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AB1102 A RARE CASE OF ACUTE INFLAMMATORY DEMYELINATING POLYRADICULOPATHY FOLLOWING THE SECOND DOSE OF PFIZER COVID-19 VACCINE

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Background: We present a case of a 36 year-old female who developed Acute Immune-mediated Demyelinating Polyneuropathy (AIDP) after receiving the second dose of Pfizer COVID-19 vaccine.

Objectives: To report a rare auto-immune complication of COIVD-19 vaccination. To educate and inform physicians about the approach to diagnosing AIDP and narrowing down its etiology.

Methods: Case report and literature review

Results: A 36 year-old female with no significant past medical history presented to the hospital with progressive bilateral paresthesia. She started to experience numbness and tingling sensation in her extremities 1 week after receiving the second dose of Pfizer COVID-19 vaccine. Following 5 days of symptoms onset, she was no longer able to hold onto objects and experienced difficulty ambulating without assistance. Physical exam was notable for decreased distal sensation to touch and pain in all 4 limbs, otherwise, the rest of her neurological and musculoskeletal evaluation was normal. MRI-head showed small scattered foci of increased FLAIR signal in the white matter, suggesting an underlying inflammatory process. Electromyography (EMG) was performed and showed evidence of acute diffuse sensorimotor neuropathy with mixed axonal and demyelinating features. These results along with the clinical features allowed us to diagnose our patient with Acute Immune-mediated Demyelinating Polyneuropathy (AIDP). Extensive autoimmune workup, including anti-GM1, GD1b, Gq1b, ANA, DS-DNA, RF, CCP, and C/P ANCA, were unremarkable. She had positive anti-Ro atb but did not have any clinical or physical features that would suggest Sjogren's Syndrome. Vitamin levels (B12, folate, thiamine) were found to be normal. Infectious workup of serum and CSF which included hepatitis serologies, Campylobacter jejuni serology, Lyme atb, CMV atb, EBV atb were all negative. The possible etiology of her disease was attributed to Pfizer COVID-19 vaccine given the temporal correlation. She was subsequently treated with 6 cycles of IVIG which resulted in moderate symptomatic improvement.

Conclusion: AIDP is an autoimmune-guided inflammatory neuropathy which result in axonal degeneration of myelinated nerves [1]. In some extremely rare cases, molecular mimicry following vaccination may lead to this disease [1]. There have been reports of AIDP linked to Johnson & Johnson and AstraZeneca COVID-19 vaccines [2]. Recently, a few cases have also been observed with Pfizer COVID-19 vaccine [2-3]. Interestingly, the majority of these cases occurred after the first dose of the vaccine, making our case even more peculiar [2]. We report this case as physicians should be made aware that AIDP is a potential complication of COVID-19 vaccination. Given the extreme rarity of these cases, it is also important to note that more common infectious and autoimmune etiology of AIDP should be investigated before attributing any potential causal relationship to COVID-19 vaccines.

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Disclosure of Interests: None declared

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AB1103 THE EFFECT OF COVID-19 PANDEMIC IN A LARGE SERIES OF PATIENTS WITH TAKAYASU ARTERITIS

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Background: Patients with inflammatory rheumatic diseases faced several challenges during the COVID-19 pandemic. Uncertainties such as the lack of evidence regarding the use of immunosuppressive (IS) therapies and deferred patient care because of limited health resources impacted negatively on many aspects of treatment decisions and routine follow-up of the patients (1).

Objectives: We aimed to investigate the prevalence and severity of SARS-CoV-2 infection, the impact of the pandemic on delays in routine clinical follow-up, changes in IS treatment, and COVID-19 vaccination status of patients with Takayasu arteritis (TAK).

Methods: The study was performed between July and September 2021. TAK patients who registered in our database were investigated with regards to the COVID-19 infection and vaccination status, delays in routine clinical visits, changes in their IS treatments, and flares during the pandemic. Physical examination, laboratory tests, and imaging of the patients were performed and ITAS2010 scores were calculated.

Results: There were 56 adult TAK patients (87.5% female and median age 47 years). 44 (78.6%) patients experienced a delay with routine follow-up visits to their physicians and about 20% of patients stopped their antirheumatic treatments without consulting their physicians. Compared to the pre-COVID-19 pandemic, 16 (28.5%) patients were flared. 13 (23.2%) patients had a mild COVID-19 infection. Pneumonia was reported in five patients, two of them required hospitalization, and all patients recovered completely. In the total group, about 90% of the patients had received the COVID-19 vaccine (Table 1).

Table 1. Effects of COVID-19 pandemic on patients with Takayasu arteritis

Patients with a delay regarding to the routine follow-up visits, n (%)	44 (78.6)
Average delay in routine follow-up visits since the beginning of COVID-19 pandemic (months), median, Q1-Q3	3.5 (2.25-9)
Patients who don't receive their treatment regularly due to COVID-19 concern, n (%)	11 (19.6)
Disease relapse compared to the pre-pandemic time, n (%)	16 (28.6)
Progression in acute phase reactants, n (%)	14 (25)
Progression in vascular involvement (according to MR angiography or Doppler ultrasound findings) n (%)	15 (26.8)
Patients diagnosed with COVID-19 disease, n (%), pre-vaccination / post-vaccination	13 (23.2), 8/5
Vaccination status, n (%)	50 (90.9)

Continuous data is presented with median (interquartile range, Q1-Q3) values and categorical data are presented as counts (n) and percentages (%)

Conclusion: COVID-19 disease in TAK patients were in mild severity and IS therapy seem not affecting the COVID-19 course. A substantial number of patients who stopped their medications flared and its long-term consequences need to be assessed by large-scale studies. New approaches are required to maximize healthcare access for patients who have chronic diseases during pandemic.

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AB1104 CHARACTERISTICS OF POST-COVID SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Almost two years after the start of the pandemic, it has become clear that the severity of COVID-19 is not limited to the manifestations of the acute phase of SARS-CoV-2 infection. The so-called post-covid syndrome (PCS) can

occur even in patients who have experienced mild or moderate COVID-19 and includes long-term symptoms that may be associated with residual inflammation, organ damage, non-specific effects of hospitalization or prolonged ventilation, social isolation, or comorbid diseases. In October 2021, the WHO defined PCS as a condition that occurs in individuals with a history of probable or confirmed infection with the SARS-CoV-2 virus, usually within 3 months of the onset of COVID-19, and is characterized by the presence of symptoms for at least 2 months, as well as the impossibility of explaining them with an alternative diagnosis.

Objectives: To conduct a comparative assessment of clinical and demographic indicators in groups of patients with rheumatoid arthritis who underwent COVID-19, with and without PCS.

Methods: The material of the questionnaires filled in by patients of the V.A. Nasonova Research Institute of Rheumatology, who underwent COVID-19, verified by RT-PCR for SARS-CoV-2 RNA. The information was supplemented with data from discharge records after inpatient treatment for COVID-19. Statistica program (version 12) was used for statistical processing. The results of correlation analysis were considered significant at $p<0.05$.

Results: The study included 23 adult patients (over 18 years of age) with a reliable diagnosis of rheumatoid arthritis (ACR/EULAR). Of these, 11 (47.8%) patients noted the development of PCS (Group 1), and 12 patients underwent COVID-19 without consequences (Group 2). Both groups were represented predominantly by women (90.9% and 91.7%, respectively). The average age in both groups did not differ significantly and amounted to 56.73±14.79 years in group 1, and 48.17±19.59 years in group 2. The median number of comorbid diseases was 2 [1;4] in group 1 and 0.5 [0;2.5] in group 2. PCS was presented by the following symptoms: weakness, increased fatigue - in 6 patients, problems with attention, concentration - in 7, memory impairment - in 6, sleep disturbances - in 7, increased pain in the joints - in 7, shortness of breath during exercise - in 6, fluctuations in blood pressure - in 5, tachycardia - in 4. On average (median), each patient noted 10 [6.5;12] symptoms of PCS at a time. When assessing the number of symptoms in the infectious phase, in group 1, patients reported 20 [16;23], and in group 2, 10 [7;12] symptoms of COVID-19. At the time of development of COVID-19, the severity of RA symptoms, assessed by VAS, was 5.64±3.26 in group 1 and 4.75±2.99 in group 2. In group 1, 5 (45.5%) patients needed hospitalization, 3 of them needed oxygen support. In group 2, 4 (33.3%) patients were hospitalized, two of them needed oxygen support. 3 patients in group 1 suffered COVID-19 again on average 9.33±2.52 months after the first illness. One of them has been vaccinated. All patients in this group were treated as outpatients, while the first case of COVID-19 required one hospitalization and oxygen support. Statistical assessment of significant differences ($p<0.05$) between groups in terms of sex, age, number of comorbid diseases, number of COVID-19 symptoms in the infectious phase, severity of RA symptoms, and hospitalization rate was not revealed.

Conclusion: Even though when assessing the socio-demographic characteristics, no statistically significant differences were found between the study groups, the average age, the number of comorbid diseases, and the severity of RA symptoms at the time of COVID-19 were higher in the group of patients with RA and PCS. Patients with PCS reported higher rates of hospitalizations and more severe COVID-19. There were also repeated cases of COVID-19 in this group. It is necessary to continue the study on a larger cohort.

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AB1105 PSEUDOPERNIOSIS AS A Llate MANIFESTATION AFTER SARS2-COD19 INFECTION. A PURPOSE OF A SERIES OF 19 CASES

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Background: In winter, you can usually see a picture of Perniosis and / or chilblains. Painful, often itchy, red-to-purple lesions that affect the acrid surfaces of the fingers and toes after contact with the cold, resembling vasculitis, characterize them. Chilblains can be idiopathic and self-limiting or associated with systemic diseases. The diagnosis is usually clinical, but in some circumstances, analytical and microscopic studies of a biopsy sample may be necessary. We present a series of 19 consecutive cases of Pseudoperniosis associated with probable past INFECTION by SARS-CoV-2.

Methods: During the winter 2020-21, an unexpected number of cases referred as "acute arthritis/vasculitis" have been received in our rheumatology section and associated consultations. In the pathochrony of patients, exposure to cold was referred to as the main triggering factor. Initially qualified as PERNIOSIS. Given the appearance in the current situation of Pandemic by covid-19, we began to request the serology SARS2-COVID19 IgG / IgM. Appreciating an approximate rate of 70% of IgG+ positivity in which it was performed.

Results: Characteristics of the clinical data collected evolutionarily in the 19 patients: These are preferably young people, without any other pathology, although there are also people of all ages, with a clinical picture of edema of soft parts preferably of the hands, but also in the feet, with pain and some hemorrhage infusions, including ulcerations in the areas of the knuckles or pressure (PHOTO1-2-3). Despite the overwhelming nature of the picture, they do not associate any other symptoms and the analyses are normal, including acute phase reactants (ESR and PCR), and serological markers of autoimmune disease. Approximately 1/4 of them reported having passed clinical compatible with the covid19 infection and / or having been isolated with some minor symptom, but they had not been performed PCR. The others did not report any symptoms associated with COD19 infection. From the initial diagnosis, about 40 days passed on average. Many of them were being treated with corticosteroids/NSAIDs without improvement. In the ultrasounds performed, only edema of periarticular and paratendinous tissue is appreciated, such as that which can occur after a momentary ischemic picture. All evolved favorably avoiding cold (probable triggering factor), and with antiplatelet agent (infant aspirin).

Conclusion: This picture of Pseudoperniosis lacks the typical pruritus of perniosis and the main problem is pain along with edema of the tissues of the hand that leads to make it impossible to use. Similarly, asymmetric lesions similar to perniosis were observed in patients who presented skin manifestations of SARS-CoV-2 infection in a study conducted in Spain (1). We are following these patients to assess if there is any relationship with any other factor that facilitates this unusual incidence, and at the same time indicate the transience of the clinical picture that evolves favorably in a few weeks.

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AB1106 HOW HAS THE COVID-19 PANDEMIC AFFECTED OUR RHEUMATOLOGY PATIENTS USING BIOLOGICAL/ TARGETED DMARDS?

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Background: Bioinformatics data, which are becoming more detailed day by day, show that male gender, advanced age, smoking, and comorbidities are associated with poor outcome of COVID-19. However, it is well known that the active disease state that may occur as a result of discontinuing the drugs also increases the susceptibility to infection.

Objectives: It was aimed to investigate the effects of the COVID-19 pandemic on the course and treatment of rheumatic disease in patients with inflammatory rheumatic musculoskeletal disease (iRMD) using biological or targeted synthetic DMARDs (b/tsDMARDs).

Methods: The study was carried out in two stages: while investigating the delay of b/tsDMARD treatment in the first 3 months of the pandemic with the fear of infected by SARS-Cov-2 in the first stage, in the second stage, it was investigated whether all patients who decided to continue treatment after interruption in the 12-month period.

Results: A total of 521 patients were included in the study. It was seen that the iRMD diagnosis were listed as SpA (54.3%), RA (25.7%), PsA (8.4%), vasculitis (6.1%), and others (5.4%). The overall 12-month drug retention rate was 92.3%. Concurrent use of hydroxychloroquine (HCQ) (HR=1.49), iv bDMARD use (HR=1.34), and a history of discontinuation of drug in the first 3 months of the pandemic (HR=1.19) were determined as factors that reduced 12-month drug retention rates. During a total of 12 months, 34 (6.5%) of patients had COVID-19. COVID-19 was severe in 7 patients and 5 of these patients died.The use of GC (HR=3.81) and having a diagnosis of ILD/COPD (HR=4.96) were found to increase the risk of infected by SARS-CoV-2.

Table 1. Comparison of demographic and clinical characteristics of patients with COVID-19

	COVID-19 (-) (n=487)	COVID-19 (+) (n=34)	
Demographics	**Median (Min./Max.)**	**Median (Min./Max.)**	**P**
Age	48 (18-86)	48 (18-82)	0.615
Disease Duration	130 (22-478)	144 (48-519)	0.573
b/ts DMARD Duration	45 (12-192)	26 (14-170)	0.253
GC dose, mg	4 (1-16)	4 (2-16)	0.863
	n (%)	**n (%)**	
Gender, F	259	19	0.909
COVID-19 diagnosis and outcome			
Hospitalization	–	**11 (32.3)**	–
Mortality	–	**5 (14.7)**	–
Active disease (anytime during the pandemic)	82 (16.4)	9 (26.5)	0.246
ILD and/or COPD	14 (2.9)	**4 (8.9)**	**0.002**
	n (%)	**n (%)**	
b/tsDMARD type			**0.049**
TNFi	**382 (78.4)**	15 (44.1)	0.243
Tocilizumab	19 (3.9)	2 (5.9)	0.684
Abatacept	13 (2.7)	1 (2.9)	0.886
Rituximab	9 (1.8)	**6 (17.6)**	**0.001**
GC	83 (17.0)	**17 (50.1)**	**0.001**

Conclusion: The results of this study with a long follow-up period suggest that the retention rates of b/tsDMARD treatment increased with good communication with iRMD patients during the COVID-19 pandemic.

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AB1107 COVID-19 INFECTION MAY BE TRIGGER FOR DEVELOPMENT OF IMMUNE-MEDIATED DISEASES (IMDS)

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Background: As considerable evidence indicates viruses play an important role in the pathogenesis of inflammatory rheumatic diseases as environmental factors. The most prominent pathogenic viruses which have been proposed in the triggering and initiation of autoimmune diseases include Parvovirus B19, Epstein-Barr-virus (EBV), Cytomegalovirus (CMV), Herpes virus-6, HTLV-1, Hepatitis A and C virus, and Rubella virus[1]. It is possible that COVID-19 infection is also a trigger. Because SARS-CoV-2 infection can break immune tolerance and trigger autoimmune responses, it is also likely to induce clinical autoimmunity[2].

Objectives: Find out a possible association between Covid-19 infection and development of IMDs.

Methods: We analyzed data of 21 patients (Male 4 /19 %/, female 17 /81%/, mean age 45.5 ± 13,9 years), who were admitted to Rheumatology department of "Mikayelyan" University Hospital after Covid -19 infection with newly diagnosed IMDs from June till December 2021. All of included had never had such kind of disorder before. EULAR/ACR criteria were used for diagnosis and assessment of disease activity.

Results: After SARS-CoV-2 infection some patients presented with preserved fever, high levels of CRP and ESR, had rash and arthritis. Particularly, 3 (14.3%) developed systemic lupus erythematosus, 3(14.3%) – antiphospholipid syndrome, 4 (19%) – rheumatoid arthritis, 2(9.5%) - spondyloarthritis, 3 (14.3%) - sarcoidosis, 4 (19%) - erythema nodosum, 1 (4.8%) - small-vessel vasculitis, 1 (4.8%) - undifferentiated arthritis, and 1(4.8%) - Tietze syndrome. 11 (52.4%) experienced severe course of Covid-19 with pneumonia and respiratory failure, in 10 (47.6%) patients the course of disease was mild. We've found a significant association between severe course of Covid-19 and development of erythema nodosum. ($p < 0.05$). Also an association between female gender and severe course of Covid-19 was determined ($p<0,05$).

Conclusion: In acute progression of the COVID-19 along with development of antiviral immunity, a dysregulated response of immune system may occur, represented by the marked cytokine release syndrome, macrophage activation, and systemic hyperinflammation.[3] We analyzed the data of patients who didn't have any typical symptom of rheumatic diseases before coronavirus infection, therefor, on our opinion, virus played an important role to induce clinical autoimmunity and autoinflammation and subsequently – IMDs. Possibly, Covid-19 infection may be included in the group of trigger viruses for

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AB1108 IMPACT OF THE FIRST WAVE OF THE COVID 19 PANDEMIC ON HEALTHCARE ACCESSIBILITY, DISEASE BEHAVIOUR, ANXIETY, AND PHYSICAL ACTIVITY IN RHEUMATIC DISEASE PATIENTS: AN ONLINE SURVEY AND POTENTIAL SOLUTIONS

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Background: Coronavirus Disease (covid 19) negatively impacted psychosocial health, health care accessibility and exercise regimen but problem's scope and potential solutions remain elusive. We conducted a patient based online survey to understand these impacts and discussed potential solutions.

Objectives: Assess impact of Covid 19 on rheumatological disease status, accessibility to health care, patient anxiety and behavior and continuation of physical activity during pandemic.

Methods: Google form (18-question) based questionnaire was sent via SMS/WhatsApp in Aug 2020, at height of first pandemic and responses were collected over next month.

Results: Only 339 /2700 patients (12.5 %) responded to the survey. Other authors (1)(2) have observed a similar low response rate to online surveys. We recognise questionnaires with fewer questions tend to generate more responses, which should be considered critical in constructing future health-related surveys. Patients' global assessment of their disease score was 7/10, with 0 representing the worst disease status and10 representing best disease status, also 1/3 patients not felt need for rheumatological consultation during six months (March 2020- Aug 2020) of lockdown. These may imply adequate rheumatic disease control over long periods and during subsequent waves of pandemic, rheumatology patients can be shielded by avoiding non-urgent hospital follow up visits. Significant number of patients (20%) were unable to contact their rheumatologist, implying a significant impact of covid 19 and lockdown on rheumatology care, as suggested by other authors (1). As expected, there was switch to tele consultancy mode of communication, with 22 per cent of patients already using it within 3 months of its introduction, which appears to be a good indicator of future adaptability and feasibility of teleconsultation. Identifying specific profile of patients during physical consultation who can be easily managed via teleconsultation, may reduce unnecessary hospital visits while also improving healthcare delivery. 1/3 of our patients had anxiety about disease flare, and 41 %were concerned about increased risk of covid 19 infection as they were on immunosuppressive medications as noted by other authors (3). Improving access to health care and increasing public awareness could help alleviate this anxiety. Reaching out to isolated rheumatology patients through SMS / educational video may improve the sense of health security. Contrary to our expectations, overall medication adherence was reasonable, likely due to be management of supply chains by local authorities .15% completely stopped exercising and 25% reduced their exercise regimen by 50%. Shifting to home-based exercise, educational videos on physical therapy and online teleconsultation with physiotherapists could overall have positive impact.

Conclusion: Covid 19 has significantly impacted rheumatological patients in terms of increased anxiety, decreased healthcare accessibility and decreased exercise and physical activities. Modifications in teleconsultation methodology are needed in the future. Patients' anxiety can be alleviated by educating them through digital and social media platforms and enrolling them in online patient support groups.

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AB1109 EVALUATION OF THE POTENTIAL INDUCTION OF AUTOANTIBODIES AFTER THE ANTI-SARS-COV2-VACCINATION IN A COHORT OF PATIENTS WITH TRIPLE POSITIVITY FOR ANTIPHOSPHOLIPID ANTIBODIES

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Background: Anti-SARS-CoV2 vaccines showed a good efficacy in prevention of severe COVID-19[1]. Their potential in induction of autoantibodies (abs) has not been well established[1]. One recent study demonstrated an increase of abs' titre after anti-SARS-CoV2 vaccination only in patients with already pre-existing positivity[2].

Objectives: To evaluate the potential induction of abs after anti-SARS-CoV2 vaccination in a triple positive antiphospholipid antibodies (aPL) cohort.

Methods: 18 subjects were enrolled [M/F= 17/1; median age=52 years; 5 Primary Antiphospholipid Syndrome (PAPS), 5 Systemic Lupus Erythematosus

Table 1. Autoantibodies' titre pre (T0) and post (T1) anti-SARS-CoV2 vaccination.

Autoantibodies	Level at T0	Level at T1	p-value*	Patients positive at T0	Patients positive at T1	p-value°
Anti-dsDNA (n.v. <27 IU/ml)	28.7 (21.8-64.5)	25.8 (15.9-68.5)	0.163	7/18 (38.9%)	6/18 (33.3%)	0.729
aCL IgG (n.v. <20 CU)	88.1 (27.1-218.9)	68.2 (18.8-181.3)	0.118	15/18 (83.3%)	13/18 (72.2%)	0.691
aCL IgG (n.v. <12 IU/ml)	11.9 (11.2-77.2)	11.2 (11.2-24.5)	0.432	9/18 (50%)	7/18 (38.9%)	0.502
aCL IgM (n.v. <20 CU)	20.8 (5.9-35.9)	8.9 (3.3-21.6)	**0.006**	9/18 (50%)	5/18 (27.8%)	0.171
aCL IgM (n.v. <12 IU/ml)	30.4 (18.1-170.8)	23.8 (11.2-82.3)	**0.029**	14/18 (77.8%)	12/18 (66.7%)	0.457
aCL IgA (n.v. <12 IU/ml)	11.7 (11.2-30.9)	11.2 (11.2-17.6)	**0.029**	8/18 (44.4%)	6/18 (33.3%)	0.494
aβ2GPI IgG (n.v. <20 CU)	230.4 (110.1-971.1)	242.3 (33.7-652.9)	0.083	16/18 (88.9%)	14/18 (77.8%)	0.658
aβ2GPI IgG (n.v. <20 IU/ml)	9.3 (9.3-128.1)	19.4 (9.3-126.9)	0.844	8/18 (44.4%)	9/18 (50%)	0.738
aβ2GPI IgM (n.v. <20 CU)	16.9 (3.6-51.3)	6.8 (1.5-23.1)	**0.041**	7/18 (38.9%)	5/18 (27.8%)	0.480
aβ2GPI IgM (n.v. <20 IU/ml)	19.8 (11.1-78.8)	9.9 (9.3-52.4)	0.109	8/18 (44.4%)	7/18 (38.9)	0.735
aβ2GPI IgA (n.v. <20 IU/ml)	20.8 (9.3-39.9)	9.3 (9.3-37.8)	0.080	10/18 (55.6%)	7/18 (38.9%)	0.317

Antiphospholipid antibodies were determined with chemiluminescence (CU) and home-made ELISA (IU/ml) methods of detection. Pre and post-vaccine values are expressed as median (IQR). In bold, statistically significant comparisons. *Wilcoxon signed-rank test for paired variables was applied. °Chi-square test or Fisher's exact test were applied. dsDNA=double-stranded DNA; aCL: anti-cardiolipin; aβ2GPI: anti-beta2-glycoprotein I; n.v.: normal value.

(SLE) with associated APS and 8 aPL carriers (1 Behçet Disease, 1 SLE, 4 Undifferentiated Connective Tissue Disease, 2 with no diagnosis of systemic autoimmune disease)]. Serum samples were collected before the first (T0) and at least one month after the second administration (T1) of the anti-SARS-CoV2 vaccine (16 BNT162b2, 1 mRNA-1273, 1 Gam-COVID-Vac). A wide panel of abs were evaluated through routinely methods.

Results: None developed any additional sign of autoimmune diseases upon vaccination. Patients majority did not display any new autoantibody positivity (Table 1). Changes were observed in 3 patients: 1) one aPL carrier patient who was antinuclear antibodies (ANA) negative at T0 was found to be ANA positive at T1 [negative anti-double stranded DNA and anti-extractable nuclear antigen (ENA)]; this patient was actually ANA positive in her clinical history; 2) one aPL carrier patient affected by SLE, who was IgM and IgG aCL and IgG aB2GPI positive at T0, turned positive for IgM and IgA aB2GPI; 3) one aPL carrier patient affected by Behçet Disease, who was positive for IgM aCL and for IgM aB2GPI at T0, turned positive for IgA aCL and IgA aB2GPI. All emerging aPL were low titre. None of the patients displayed raising aPL titres from low to medium-high.

Conclusion: Anti-SARS-CoV2 vaccination did not induce any clinical signs of autoimmunity in a cohort of patients with triple aPL positivity. Serology for autoantibodies remained stable in the majority of patients. Few patients experienced the emergence of low titre aPL, possibly as an expected inter-assay variation rather than an evolving "serological flare".

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AB1110 **COVID19 IN SPONDYLOARTHRITIS PATIENTS UNDER BDMARD – A COMPREHENSIVE ASSESSMENT**

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Background: SARS-Cov-2 infection had a major impact on patients with inflammatory rheumatic diseases. Spondyloarthritis (SpA) patients were one of the most affected groups of these patients.

Objectives: To assess the impact of Covid19 in spondyloarthritis patients under biological disease modifying anti-rheumatic drugs (bDMARDs).

Methods: A retrospective observational study was conducted using registry data of patients with SpA under bDMARD therapy, followed at a tertiary level hospital, that have been diagnosed with COVID19 from March 2019 to December 2021. At least one evaluation previous (t0) and two evaluations after SARS-CoV-2 infection (t1, t2) were included in our analysis. Sociodemographic, clinical, disease activity, therapeutic response, function and general health status data were collected. Statistical analysis (significance at $p < 0.05$) was performed using paired T-test, Wilcoxon test and McNemar tests for paired samples. Linear and logistic regression models were performed to assess direction and strength of association

Results: Thirty-two patients with SpA under bDMARD had COVID19, mostly women (20, 62.5%), with a disease course time averaged 18.65 (± 9.69) years, mainly with axial involvement (19, 59.4%) and positive for HLA-B27 antigen (11, 64.7%). The majority were under TNF inhibitors (30, 93.75%), with golimumab being the most common (9, 28.1%), and with a median bDMARD persistence of 2.63 (5.09) years. Seven (21.9%) were under a cDMARD, 3 (9.4%) under NSAID and 18 (56.3%) under corticosteroids. Three (9.4%) were already vaccinated against SARS-CoV-2, 2 (66.6%) with the mRNA-1273 vaccine, presenting a medium time since inoculation of 240 (± 234.01) days. Arterial hypertension was the most common comorbidity (5, 15.6%) and one patient (3.1%) had a previous diagnosis of type 2 diabetes. Most were never-smokers (17, 53.1%) and never-drinkers (29, 90.6%). The average age at infection was 40.97 (± 6.15) years and the most common symptom was cough (22, 68.8%), followed by headache (20, 62.5%) and myalgia (19, 59.4%). Event tree analysis didn't show association with SpA subtype, education level, work status, tobacco or alcohol consumption. Only one patient needed hospital admission but without needing of oxygen, therapy, ventilator or ECMO. Only one patient had an overlaid bacterial infection and no thromboembolic complications were observed. Two patients needed specific SARS CoV-2 infection treatment, one with hydroxychloroquine and another with azithromycin. Twelve (37.5%) patients suspended bDMARD at the time of infection, with only 2 (6.3%) maintaining suspension at the time of the first post-infection visit. When comparing clinical variables, higher disease activity was seen at t1 only for BASDAI mean values, without statistical significance. Higher all domains VAS scores were also observed at t1, but not at t2, also without statistical significance; moreover, physical function didn't change significantly. No differences were observed according to gender or SpA subtype, nor with the use of cDMARDs, NSAIDs or corticosteroids. The only statistically significant difference concerned MASES score between t0 and t1 (1 ± 4 vs. 2 ± 6, p=0.04), but not between t0 and t2. Higher baseline tender joint score ($p < 0.01$) and higher baseline LEI (p=0.03) negatively correlated with MASES score variation. Several baseline variables correlated positively with MASES at t1, including female gender ($p < 0.01$), corticosteroid use (p = 0.04), BASDAI ($p < 0.01$), ASDAS-ESR ($p < 0.01$), ASDAS-CRP ($p < 0.01$), DAS28 ($p < 0.01$), SPARCC (p = 0.04), physician VAS (p = 0.03) and total spine VAS (p = 0.01). Working status varied significantly after SARS-Cov-2 infection (at least part-time - 29, 90.6% vs. 22, 68.8%, p= 0.016).

Conclusion: SpA patients on bDMARD had a mild course of SARS-CoV-2 infection, with slight changes in enthesitis score in the short term, the latter particularly in those with higher disease activity in the pre-infection period. Long-term effects on work status could represent confounding factors related to the economic constraints of the pandemic.

Disclosure of Interests: None declared

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AB1111

NO INCREASED RISK OF ADVERSE EVENTS OF THE WHO-VALIDATED COVID-19 VACCINES IN PATIENTS WITH RHEUMATIC DISEASES TREATED WITH BIOLOGICS

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Background: The COVID-19 pandemic is a major concern for the management of patients with rheumatic diseases (RD). Indeed, an increasing risk of coronavirus infection has been demonstrated in these patients, explained on the one hand by the chronic inflammation and on the other hand by the immuno-modulating treatments used [1]. In this context, vaccination represent an efficient mean to prevent infections and should be included in the management of these patients.

Objectives: The objective of our study was to determine the peculiarity of vaccination against SARS-COV2 in patients with RD treated with biologic therapies.

Methods: We conducted a cross-sectional study during August 2021, including patients with RD: rheumatoid arthritis (RA) and spondyloarthritis (SpA). Sociodemographic data as well as disease characteristics were recorded. Patients were asked to answer a self-questionnaire about SARS-COV2 vaccination: modalities, time between doses, type of vaccine, adverse events, and time to biologic injection. We compared these results between the two groups: group 1 patients on biologics and patients on conventional disease-modifying antirheumatic drugs (DMARDs). A significance level was set for p<0.05.

Results: The study included 102 patients with RD: RA (65.3%) and SpA (34.7%). The mean age was 52.4 ± 13 years [19-77]. There was a female predominance (71 women and 31 men) with a gender ratio of 0.4. The mean duration of disease progression was 7.8 ± 5 years [1-35]. Fifteen percent of patients were on corticosteroids with a mean dose of 6.7 mg [2-20] of prednisone equivalent. A CsDMARD was prescribed alone in 36.3% of cases and combined with a biologic in 18% of cases. SARS-COV2 infection was found in 27.3% of cases, of which 19% had a severe form. Sixty percent of patients received the SARS-COV2 vaccine, and 25% of them received only the first dose. The mean time between the two injections was 27 ± 7.6 days [23-67 days]. The most common type of vaccine was Pfizer (54.4%), Moderna (5.5%), followed by AstraZeneca (20%), Sinovac (16.4%), Johnson (1.8%) and Sputnik (1.8%). Three patients deferred their biotherapy injection by one week. Only one patient discontinued methotrexate therapy for one month. Sixteen patients reported adverse events such as injection site pain (62.5%), disease flare (12.5%) and fatigue and fever (25%). Patients receiving biologics were not at greater risk of SARS-COV2 infection (p=0.076) or hospitalization (p=0.131) compared to patients receiving conventional therapy. Similarly, patients on conventional therapy did not report more adverse events (p=0.678). The vaccination rate was significantly higher in patients on biologics compared to patients on CsDMARD: 72% versus 43%, p=0.004.

Conclusion: Our work demonstrated that patients treated with biologics adhered to vaccination and did not have more SARS-COV2 infections or adverse events compared to patients on conventional treatment.

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AB1112

SARS-COV-2 INFECTION AND IT VACCINATION IN AUTOINMUNE DISEASE-ASSOCIATED INTERSTICIAL LUNG DISEASE

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Background: Intersticial lung disease (ILD) is a common condition in patients with systemic autoinmune diseases (SAI) that is characterized by increased morbility and mortality. Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, has posed huge challenges worldwide and previous studies suggest that ILD patients experience a more severe clinical course.

Objectives: To analyze COVID-19 infection effects in patients with ILD associated systemic autoinmune disease (ILD-SAI) and to describe their vaccination status.

Methods: Design We performed a multicenter, retrospective, observational study from 6 teaching hospitals in Andalusia, Spain. **Study protocol** We included ILD-SAI patients: rheumatoid arthritis (RA), systemic sclerosis (SS) and inflammatory myopathies (IM), assisted in reumatology consultations in 2021. **Variables** COVID-19 infection was the main variable that we collected and it was confirmed by a positive result on a PCR test. Secondary variables: (1) COVID-19 severity defined as hospitalization or death; (2) vaccination status; (3) temporary relationship between infection and vaccination. Other variables included: clinical, epidemiological characteristics, treatments received, type of ILD (UIP/NSIP), pulmonary function testing and high-resolution computed tomography. **Statistic analysis** Two multivariable logistic regression analysis to indentify the "COVID-19" and "severe COVID-19" associated factors.

Results: We included 176 ILD-SAI, of whom: 105 (59.7%) had RA, 49 (27.8%) had SS and 22 (12.54%) had IM. The main baseline characteristics for the oversall simple and te 3 subgroups are shown in Table 1.

Table 1. Clinical and epidemiological characteristics of 171 ILD-SAI patients.

Variable	Rheumatoid artritis n=105	Systemic sclerosis n=49	Inflammatory myopathies n=22	p-value
Sex, women, n (%)	58 (55.2)	42 (85.7)	17 (77.3)	<0.001
Age in years, mean (SD)	67.9 (9.6)	60.9 (12.5)	55.7 (18.9)	<0.001
SAI evolution time, month, median (IQR)	46.2 (25.4-79.0)	67.1 (52.2-88.2)	39.1 (25.1-72.5)	0.010
Radiological patterns				<0.001
UIP, n (%)	66 (62.9)	8 (16.3)	1 (4.5)	
NSIP n (%)	32 (30.5)	39 (79.6)	20 (90.9)	
Last PFT				
FVC, mean (SD)	70.7 (19.9)	71.3 (21.4)	73.1 (16.6)	0.471
FEV1, mean (SD)	71.2 (19.3)	72.2 (17.3)	74.4 (17.9)	0.345
SB-DLCO, mean (DS)	54.3 (16.5)	52.4 (15.9)	60.8 (15.2)	0.140
Treatment				
sDMARD, n (%)	88 (86.3)	10 (20.4)	11 (50.0)	<0.001
Biologic DMARD, n (%)	47 (46.1)	14 (28.6)	6 (27.3)	0.590
Immunosuppressants, n (%)	37 (36.3)	33 (67.3)	17 (77.3)	<0.001
Corticosteroid, n (%)	72 (71.3)	24 (49.0)	18 (81.8)	0.007
COVID-19				
COVID-19 infection, n (%)	14 (13.3)	4 (8.2)	4 (18.2)	0.460
Severe COVID-19 infection, n (%)	7 (50.0)	0 (0.0)	0 (0.0)	0.085
Complete COVID-19 vaccination, n (%)	94 (89.5)	47 (95.9)	22 (100.0)	0.135

We recorded 22/179 (12.5%) SARS-CoV-2 infections, 7/22 (31.8%) of them were severe and 3/7 (42.85%) died. As to the vaccination, 163/176 (92.6%) patients received the complete dosis. Among those correctly vaccinated 18/163 (11%) had the SARS-CoV-2 infection, 4/18 (22.2%) after the vaccinated date and 14/18 (77.7%) when they still dint´t have the complete vaccination. From the 13 not vaccinated patients, 4/13 (30.7%) had COVID-19. As to frequency, COVID-19 severity and vaccination, there were no difference between subgroups of CTD-ILD patients. The risk factors associated with the COVID-19 infection were the last FVC (OR [CI 95%], 0.971 [0.944-0.998]; p=0.048), the vaccination (OR [CI 95%], 0.185 [0.049-0.691]; p=0.012) and the Rituximab treatment(OR [CI 95%], 3.172 [1.028-6.785]; p=0.045). Moreover, the only variable associated independently with the severe COVID-19 was the protective effect of vaccination (OR [CI 95%], 0.020 [0.003-0.119]; p<0.001).

Conclusion: A total of 12.5% ILD-SAI patients were COVID-19 infected, most of them without the complete vaccine. Rituximab and a deterioration of FVC were risk factors for the COVID-19 wehreas the vaccination was a protective factor for the mild and severe infection.

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AB1113

THE IMPACT OF SARS-COV-2 INFECTION ON DISEASE ACTIVITY AND CLINICAL RESPONSE TO BIOLOGICAL DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Infections are a known trigger for Rheumatoid Arthritis (RA) flares.[1] It is still unclear whether SARS-Cov-2 infection affects RA disease activity and the clinical response to biological disease-modifying antirheumatic drugs (bDMARDs).
Objectives: To evaluate the effect of SARS-Cov-2 infection on disease activity and bDMARD responses in patients with RA.
Methods: A retrospective study was carried out in a cohort of RA patients treated with bDMARDs from a tertiary hospital centre. Demographic and clinical data, including occurrence of SARS-Cov-2 infection, were obtained through medical records. Disease activity (DAS28, DAS28-CRP, CDAI and SDAI) and ACR and EULAR bDMARD responses were evaluated at four time points: baseline (t1 - last evaluation before Covid-19 pandemic), before (t2) and after (t3) SARS-Cov-2 infection and at the end of follow-up (t4 - last appointment of 2021). In patients with no record of SARS-Cov-2 infection the middle evaluations were obtained from two random consecutive appointments during Covid-19 pandemic. Statistical analysis (significance at $p<0.05$) was performed using paired t-test, Wilcoxon and McNemar tests for paired samples and unpaired t-test, Mann-Whitney, Fisher and χ^2 tests for independent samples according to the type of variable and the presence of normal distribution.
Results: Of the 237 patients included, most of them was women [n = 195 (82.3%)], with a mean age of 59.6 ± 10.1 years old and a median [min, max] disease duration of 18 [2, 50] years. The majority presented rheumatoid factor (RF) and/or anti-citrullinated protein antibodies (ACPA) positivity [n = 204 (87.9%)] and radiographic erosions [n = 119 (72.6%)]. The prevalence of SARS-Cov-2 infection was 11.4% (n=27). Mean disease activity was lower after SARS-Cov-2 infection compared to the previous evaluation on all scores used; however, this difference was not statistically significant. Nevertheless, when compared to the mean disease activity at the end of follow-up, there were statistically significant differences in DAS28-CRP (t2 3.2±1.0 vs. t4 2.8±1.1, p=0.017) and CDAI (t2 11.1±8.1 vs. t4 8.7±6.2, p=0.05) scores. The relative number of patients with no ACR or EULAR bDMARD responses before SARS-Cov-2 infection wasn't different from post infection and at the end of follow-up. At baseline, the infected and uninfected groups were similar regarding gender, age, RF and/or ACPA positivity, erosive disease, disease and biologic treatment durations, baseline disease activity and ACR and EULAR response. The variation in disease activity and the relative number of patients with worsening or improving EULAR and ACR bDMARD responses between t2 and t3 were not significantly different in the two groups, as well as between t2 and t4. The prevalence of patients who switched to another bDMARD was significantly higher in the group of patients who had Covid-19 [n=4 (14.8%) vs. 9 (4.3%), p=0.047]. The main reason for switching was the ineffectiveness of the therapy (n=11).
Conclusion: No worsening of disease activity or ACR and EULAR bDMARD responses was found after SARS-Cov-2 infection in RA patients under bDMARD. However, the later can be explained by the small sample size. Indeed, these patients exhibited a higher rate of switch due to ineffectiveness of therapy, suggesting a negative impact of SARS-Cov2 infection on the disease course.
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AB1114

VACCINATION OF PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: AN ANALYSIS OF BARRIERS AND FACILITATORS IN A PROSPECTIVE COHORT

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Background: Patients (pts.) with chronic inflammatory rheumatic diseases (CIRD) are often not adequately protected against infectious diseases. As shown in an earlier study, less than 50% of CIRD pts. were vaccinated against pneumococci and influenza before the SARS-CoV2 pandemic started [1]. High vaccination rates are critical to achieve herd immunity. Knowledge on barriers and facilitators of vaccine uptake in CIRD pts. is limited.
Objectives: The aim of this study was to characterize barriers and facilitators towards vaccines in general and specifically against pneumococci, influenza and SARS-CoV-2 in adult CIRD pts.
Methods: In early 2021, consecutive CIRD pts. completed a structured questionnaire including knowledge on vaccination, attitudes, and perceived barriers and facilitators towards vaccination. A total of 12 facilitators and 11 barriers towards vaccination was assessed in general, and specifically for vaccination against pneumococci, influenza and SARS-CoV2. The Likert scales had 4 response options, ranging from 1 (completely disagree) to 4 (completely agree). Patient and disease characteristics, their vaccination history and attitudes towards vaccination against SARS-CoV-2 were assessed.
Results: Of 514 prospectively recruited pts., 441 responded (85.8%) to the questionnaire (table 1). Self-reported vaccine uptake was 48.8% against pneumococci and 66.2% against seasonal influenza. The majority (82.2%) was willing to be vaccinated against SARS-CoV-2. The majority (≥70%) had decent knowledge about vaccination, and only <10% doubted its effectiveness. The level of knowledge did not differ between the studied 3 vaccinations. Pts. were more likely to rate statements about facilitators favorably compared to statements about barriers. Facilitators for SARS-CoV-2 vaccination did not different from vaccination in general (Figure 1). Societal and organizational facilitators such as public vaccine campaigns or protection for high-risk pts. were more commonly named compared to inter- or intrapersonal facilitators. Protection of high-risk pts. was by far the most frequently cited facilitator. Most pts. indicated that they were likely to receive a vaccine if their health care professional would recommend it – without preference for GP or rheumatologist. The frequency of barriers was much lower compared to facilitators and more barriers towards SARS-CoV-2 vaccination were reported in comparison to vaccination in general or pneumococci and influenza, respectively. However, pts. frequently cited intrapersonal issues as barriers against vaccination. Importantly, the major barrier was an inadequate risk perception between the severity of COVID-19 and the potential adverse events of the vaccine.

Table 1. Patient and disease characteristics

Age, y	54.1 (12.6)
Women, No. (%)	272 (61.7)
Rheumatoid Arthritis, No. (%)	156 (35.4)
Axial Spondyloarthritis, No. (%)	120 (27.2)
Psoriatic Arthritis, No. (%)	61 (13.8)
Other diagnoses, No. (%)	104 (23.6))
Treatment, csDMARD, No. (%)	121 (27.4)
Treatment, bDMARD, No. (%)	280 (63.5)
Treatment, tsDMARD, No. (%)	24 (5.4)
CDAI, n=194	11.1 (9.0)
CRP, mg/L, n=440	0.4 (0.7)
HAQ score, n=317	1.1 (0.7)
BASDAI, n=118	3.8 (2.2)
BASFI, n=118	3.8 (2.3)
Patient global, NRS 0-10	4.1 (2.5)
HADS-A, n=436	6.6 (4.0)
HADS-D, n=436	5.8 (4.3)

variables as mean (SD)

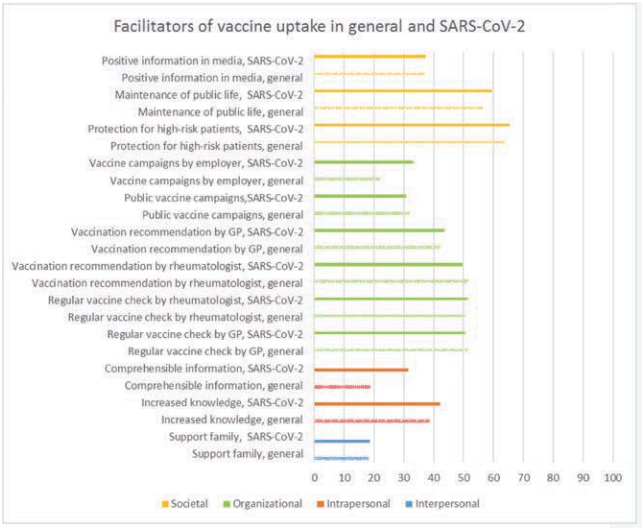

Figure 1. Facilitators of vaccine uptake in general and for SARS-CoV-2

Conclusion: A relatively high number of pts. was vaccinated against pneumococci and influenza, – a probable campaign success during the last years. In addition, more than 80% of pts. were willing to be vaccinated against SARS-CoV2. Facilitators were of greater significance than barriers in this scenario. The high number of societal and organizational facilitators enables the implementation of effective strategies to increase future vaccination rates.

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Disclosure of Interests: Ioana Andreica Speakers bureau: UCB, MSD, Novartis, Abbvie, Lilly, Janssen, Sobi, Consultant of: Novartis, Lilly, Sobi, Galapagos, Amgen, Takeda, Grant/research support from: Lilly, Iulia Roman: None declared, Xenofon Baraliakos Speakers bureau: Abbvie, Lilly, Pfizer, UCB, MSD, Novartis, Galapagos, Hexal, Paid instructor for: Abbvie, Lilly, Pfizer, UCB, MSD, Novartis, Galapagos, Hexal, Consultant of: Abbvie, Lilly, Pfizer, UCB, MSD, Novartis, Galapagos, Hexal, Grant/research support from: Abbvie, MSD; Novartis, Lilly, Juergen Braun Speakers bureau: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, FResenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Pfizer, UCB, Novartis, Consultant of: Abbvie, Amgen, Biogen, BMS, Boehringer, Celltrion, Chugai, FResenius, Hexal, Janssen, Lilly, Medac, MSD, Mylan, Mundipharma, Pfizer, UCB, Novartis, Grant/research support from: Abbvie, Amgen, Biogen, Fresenius, Hexal, Janssen, Lilly, MSD, Pfizer, UCB, Novartis, Uta Kiltz Consultant of: AbbVie, Chugai, Eli Lilly, Fresenius, Hexal, Janssen, MSD, Novartis, onkowissen.de, Pfizer, Roche and UCB, Grant/research support from: Abbvie, Amgen, Hexal, Fresenius, Novartis und Pfizer.
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AB1115 COVID-19 VACCINE HESITANCY AMONG RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGICS

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Background: Vaccine hesitancy is defined by the OMS as "a delay in acceptance or refusal of vaccines despite availability of vaccination services" [1], and it is considered as one of threats to global health. This hesitancy emerges around Covid-19 vaccination. Patients on biologic Disease-Modifying Anti-Rheumatic Drug (bDMARD) are vulnerable to Covid-19 infection and their perception to vaccination is unknown.
Objectives: The aim of our study was to identify Covid-19 vaccine hesitancy among rheumatoid arthritis (RA) patient on bDMARD.
Methods: We conducted a monocentric, cross-sectional study, including patients with RA who met the ACR/EULAR 2010 criteria. All patients were on bDMARD with or without conventional synthetic (Cs) DMARD for at least 3 months. Disease activity was assessed using the Disease Activity Score (DAS) 28 (CRP) and the functional impairment using the Health Assessment Questionnaire (HAQ). A structured interview was done using a prepared questionnaire evaluating their vaccine hesitancy behavior.
Results: We enrolled 60 patients: 10 male (16.7%) and 50 females (83.3%). Their average age was 58.16±9.04 years [34-80]. For the education level; 38.5% of patients were illiterate, 34.6% had primary education, 23.1% had secondary education, and 3.8% have a university degree. Forty-four patients (73.3%) had no occupation, 13 patients (21.7%) were employed, and 5% were retired. The majority of patients lived in urban areas (85%) and 98.2% with their families. The average duration of RA was 15.23±8.92 years [2-39]. The average DAS28 (CRP) and the average HAQ were 4.05±1.22 [1.5-7.2] and 0.7±0.4 [0-2.4], respectively. Fifteen patients (25%) had a high disease activity and seven (11.7%) were in remission. When asking patients about their Covid19 infection and vaccination status; 15% had caught the virus and 61.7% have already received the vaccine. One third (35.6%) believed that they had enough information about vaccination. Their main sources were their family, friends, and the media. More than half of the asked patients (68.3%) reported vaccine hesitancy. Reasons of vaccine hesitancy were divided into three categories: lack of confidence (66.7%, p<0.005) (63.3% fear related to side effects, 10% conspiracy theory, 6.7% lack of confidence in the provider), complacency problem (16.7%, p=0.01) and lack of convenience (8.6%). There was no association between vaccine hesitancy and sociodemographic data. The existence of comorbidities had no influence on vaccine hesitancy (p=0.4). This hesitancy was not associated with DAS28 (CRP) (p=0.6) and with HAQ (p=0.7). Patients with moderate to high disease activity were more likely to deny the usefulness of Covid-19 vaccination (p=0.09). Regarding to the therapeutic data, there was no association between corticotherapy and vaccine hesitancy (p=0.1). There was no influence on the type of the current bDMARD (p=0.3) or of the rate of administration (p=0.4). The route of administration was associated with hesitation (53.65% intravenous vs 46.34% subcutaneous, p=0.04).
Conclusion: Our study showed that Covid-19 vaccination coverage among RA patients on bDMARDs was not optimal with a high percentage of hesitancy. The reasons are complex and they may be related to a lack of awareness. Rheumatologists should play a key role in the vaccine company.
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Disclosure of Interests: None declared
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AB1116 RESULTS OF PRESCRIBING BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS AND JANUS KINASE INHIBITORS FOR RHEUMATOID ARTHRITIS DURING THE COVID-19 PANDEMIC: DATA FROM A TELEPHONE SURVEY OF 254 PATIENTS.

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Background: Prescribing biologic disease-modifying antirheumatic drugs (bDMARDs) and Janus kinase (JAK) inhibitors during the global pandemic of coronavirus disease 2019 (COVID-19) requires a balanced approach and rigorous monitoring of patients' condition.
Objectives: To evaluate the effect of bDMARDs and JAK inhibitors on the condition of patients with rheumatoid arthritis (RA), taking into account the outcomes assessed by the patients themselves, as well as the incidence of COVID-19 in these patients.
Methods: A telephone survey was conducted of 254 patients with RA (age 49.8 ± 13.7 years, 83.5% women, RF + 64.4%, DAS28 5.4 ± 1.6), who in the period from January 2020 to June 2021 by decision of the medical commission of the V.A. Nasonova Research institute was first prescribed bDMARDs or JAK inhibitors: rituximab (RTX) - 148 (58.3%), TNF-a inhibitors - 57 (22.4%), JAK inhibitors - 20 (7.9%), IL 6 inhibitors - 17 (6 .7%), abatacept - 12 (4.7%).
Results: At the time of the survey, 204 (80.3%) patients continued to take the prescribed drugs. The main cause discontinuation of treatment was for non-medical reasons. Synthetic DMARDs (mainly methotrexate and leflunomide) were received by 68.0%, glucocorticoids - 45.3%, non-steroidal anti-inflammatory drugs - 44.5% of respondents. Among the patients who took bDMARDs or JAK inhibitors, 68.1% noted the "state of symptoms acceptable to the patient", the absence of frequent joint pain - 65.3%, increased fatigue - 14.3%. The incidence of COVID-19 and hospitalization associated with this disease didn't differ between individuals who continued and discontinued the use of bDMARDs or JAK inhibitors: 41.2% and 44.6; 13.7% and 14.0% respectively, p=0.80884. There was no significant difference in the incidence of COVID-19 and hospitalization associated with this disease in patients taking various biologics or JAK inhibitors.
Conclusion: Despite the COVID-19 pandemic, rituximab remains one of the most popular bDMARD. About a third of patients receiving bDMARDs and JAK inhibitors aren't satisfied with their condition. More than 40% of patients treated with these drugs experienced COVID-19, and 14.0% required hospitalization.
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AB1117 THE IMPACT OF THE COVID-19 PANDEMIC ON HEALTH AND LIFESTYLE IN INDIVIDUALS WITH KNEE PAIN, A HALLOA STUDY

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Background: Covid-19 has affected everyday life, health and lifestyle among the general population and vulnerable groups. Individuals with knee pain are recommended an active lifestyle to reveal pain but find it difficult to maintain health and lifestyle compared to the general population due to the cause of chronic pain, impaired physical function and a diminishes quality of life. This adds to the importance of exploring how to preserve health and lifestyle among individuals with knee pain during the pandemic.
Objectives: The aim of this study was to explore the impact of the covid-19 pandemic on the health and lifestyle in individuals with knee pain.
Methods: Nineteen participants with current knee pain, and with no earlier diagnosed radiographic osteoarthritis, and no rheumatologic disorder or cruciate ligament injury, were recruited from The Halland Osteoarthritis (HALLOA) Cohort Study, twelve female and seven males, between 41-62 (median 51) years of age. Data were collected through individual interviews with open-ended questions: "What impact have you experienced with your health and lifestyle during covid-19?", and "What activities or strategies have you changed to maintain your health and lifestyle during covid-19? ". Qualitative content analysis was used, where two categories and five sub-categories emerged (Table 1).

Table 1. Categories, and sub-categories exploring the impact of the covid-19 pandemic on health and lifestyle in individuals with knee pain

Categories	Sub-categories
Adjusting behaviours due to covid-19	Spending time at home Becoming digitally Spending time outdoors
Valuing life due to covid-19	Having a positive outlook on life Sharing responsibility

Results: The result from this study explored how behaviour and attitude towards valuing life have been adjusted to maintain health and lifestyle among individuals with knee pain during covid-19. The category adjusted behaviours emerged with the sub-categories: spending more time at home, becoming digitally, and spending more time outdoors. These sub-categories determine how a more reclusive behaviour have appeared due to the pandemic, where digital platforms and outdoor activities have facilitated companionship and togetherness when feelings of loneliness and isolation were present. The category valuing life emerged with the sub-categories: having a positive outlook of life and sharing responsibility. These sub-categories establish the importance of trying to be grateful for maintaining health and lifestyle and trying to be solution-oriented to find the best possible outcomes to continue with everyday life, despite the pandemic. While having a responsibility towards others arose as a facility to manage to keep social distance during the pandemic.
Conclusion: In conclusion, the behaviour was adjusted to continue with everyday life and maintain health and lifestyle among individuals with knee pain during covid-19. Valuing life was also considered important to maintain health and lifestyle as well as supporting others maintain their health and lifestyle. The result may in the future contribute to alternative ways of maintaining health and lifestyle in different vulnerable groups and may be used in situations other than the pandemic.
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AB1118 INVESTIGATION OF THE EFFECT OF THE HISTORY OF COVID-19 ON COGNITIVE LEVEL, PAIN CATASTROPHIZATION, AND PHYSICAL ACTIVITY LEVEL IN INDIVIDUALS WITH CHRONIC LOW BACK AND NECK PAIN

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Background: Low back and neck pain is one of the most common health problems in society and one of the top reasons for admission to the hospital (1). Studies show that the level of physical activity decreases in individuals with chronic pain, and the cognitive level and quality of life are negatively affected (2). There are studies examining the effects of the Covid-19 pandemic process on the level of physical activity and cognitive level in various groups. However, the number of studies on how the history of Covid-19 affects individuals with low back and neck pain is limited.
Objectives: The aim of this study is to examine the effect of Covid-19 history on cognitive level, pain catastrophe and physical activity level in individuals with chronic low back and neck pain in individuals.
Methods: A total of 25 individuals with chronic pain, including 16 with low back pain and 9 with neck pain, were included in the study. Demographic data such as age, gender and body mass index (BMI) were obtained from all individuals. The education levels of the individuals were recorded. Cognitive level was assessed by the Montreal Cognitive Assessment (MoCA)[3], pain severity was assessed by the Visual Analog Scale (VAS), pain catastrophization was assessed by the Pain Catastrophizing Scale (PCS)[4], and physical activity level was assessed by the International Physical Activity Questionnaire-Short Form (IPAQ- SF)[5].
Results:
Table 1.

		WITH A HISTORY OF COVID-19		WITHOUT A HISTORY OF COVID-19	
n(%)		7(28%)		18(72%)	
		FEMALE	MALE	FEMALE	MALE
Gender (%)		57	43	87	13
		X±SD		**X±SD**	
Age (year)		33.14±14.58		46.06±13.26	
BMI (kg/m$^{2)}$		22.38± 4.52		28.98 ±18.85	
Education level					
Primary school n (%)		0 (0%)		3 (16.7%)	
Secondary school n (%)		1 (14.3%)		7 (38.9%)	
High school n (%)		1(14.3%)		6 (33.2%)	
Bachelor's degree n (%)		5 (71.4%)		2 (11.2%)	
Education Level	**p**	**Median (IQR)**		**Median (IQR)**	
	0.01*	4 (4-5)		2 (2-3)	
Moca	**0.014***	30 (27-30)		25 (19.75-28.5)	
VAS	0.313	6 (4-8)		5 (2-7)	
PSC	0.671	13 (5-32)		13 (9.75-22.75)	
IPAQ-SF	0.326	924 (297-3684)		981.5 (577.5-3312)	

Demographic data, VAS, MoCA, PCS, and IPAQ-SF scores are given in Table 1. 7 of the participants had history of Covid-19, 18 did not. The MoCA scores and education levels of individuals with Covid-19 were higher than individuals without history of Covid-19 ($p<0.05$). There was no difference in physical activity, pain and pain catastrophization levels between the 2 groups ($p> 0.05$).
Conclusion: Surprisingly, individuals who had a history of Covid-19 had higher cognitive levels than individuals without a history of Covid-19. In addition, there was no difference between physical activity and pain catastrophization levels. This may be due to the higher education level of individuals with a history of Covid-19. There is a need for further studies in which education levels are similar, and hospitalization and the Covid-19 positivity process are examined in more detail.
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AB1119 GLUCOCORTICOIDS' TREATMENT IMPAIRS THE MEDIUM-TERM IMMUNOGENIC RESPONSE TO SARS-COV-2 MRNA VACCINES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS.

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Background: Patients with rheumatic diseases are at an increased risk for community infections (1,2). There still exists lack of data regarding SARS-CoV-2 vaccines' efficacy in vulnerable collectives with a compromised immune system, either due to a chronic pathology or to therapies targeting an autoimmune disease (3).
Objectives: To evaluate neutralizing antibodies (nAB) to SARS-CoV-2 vaccine after 3 to 5 months from administration in Systemic Lupus Erythematosus (SLE) patients, as a surrogate of sustained-immunological response.
Methods: This cross-sectional study compared nAB titre of 39 SLE patients and 37 Healthy individuals with no previous SARS-CoV-2 infection, who had all received two doses of a mRNA SARS-CoV-2 vaccine within the last 3 to 6 months. SLE patients included 10 Not-treated subjects, 10 patients with Hydroxychloroquine (First-Line), 10 subjects with immunosuppressive drugs (Second-Line) and 9 patients under biological treatment (Third-Line). Glucocorticoids were permitted in all patient groups. Neutralization assay were used to determine nAB titre according previously validated protocol (4).
Results: Neutralizing antibody titres were assessed for a total of 76 serum samples from 39 (51%) Lupus patients and 37 (49%) healthy Controls. Healthy individuals showed the highest levels of nAB (1638.0 titre median), which were like not treated SLE subjects (1361.5 titre median). Treated patients presented substantially lower nAB titres compared to Healthy subjects: a 73% decrease for First-Line patients (p-value = 0.0135), 56% for patients received a Second-Line treatment (p-value = 0.2218) and 72% for Third-Line treated patients (p-value = 0.0104). A multivariate analysis pointed to Glucocorticoids as the most associated factor with declining nAB levels (75% decrease, p-value = 0.0037), and the one explaining, to a large extent, the lower acquired response in treated SLE patients. Furthermore, a significant reduction in nAB titres was observed for patients treated with Rituximab compared to Healthy subjects (89% decrease, p-value= 0.0008) (Figure 1).

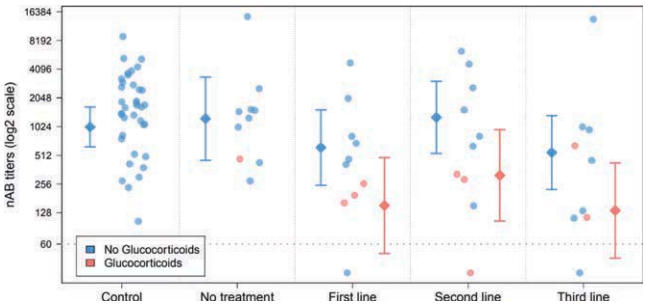

Figure 1. Neutralizing antibody (nAB) titre after SARS-CoV-2 vaccination in Healthy individuals (Controls) and Systemic Lupus Erythematosus (SLE) patients under different therapy regimes. Estimations are derived from a linear model in which sex, age, time from vaccination, vaccine type and corticoids therapy were included as covariates for statistical control.

Conclusion: Medium-term response of SLE patients to SARS-CoV-2 vaccination, as measured by the titre of nABs, may be compromised by Glucocorticoids and Rituximab users. This reduced response likely translates into a higher probability of COVID-19 infection These findings might help to inform recommendations in vaccination protocols for SLE patients.

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AB1120 PSYCHOLOGICAL ASSESSMENT IN PATIENTS WITH CHRONIC RHEUMATIC, SYSTEMIC AUTOIMMUNE, OR AUTOINFLAMMATORY DISEASES PRESENTED WITH COVID-19: THE MENTCOVRMD STUDY.

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Background: The COVID-19 pandemic has raised concerns about its psychological effects. Sleep disturbances, anxiety and/or depressive symptoms, post-traumatic stress symptoms have been reported in general population. Patients with chronic rheumatism, systemic autoimmune disease or auto-inflammatory disease, due to immunosuppression, are at risk of severe forms of infection. Currently, there is little information on psychological impact of the pandemic on the mental health of these more vulnerable patients.

Objectives: To compare psychological assessment between patients with chronic rheumatic, autoimmune and/or autoinflammatory diseases who presented with COVID-19 infection between March and September 2020, first wave of French pandemic, and patients with same diseases who did not presented with infection to date.

Methods: The MentCOVRMD study was a multicenter descriptive study. Cases were patients with chronic rheumatic, autoimmune and/or autoinflammatory diseases from the French RMD cohort who presented COVID-19 infection between March and September 2020. Controls were patients with same diseases who did not develop infection. The study is registered in Clinical Trials under number 2020-A02058-31. For participants, following criteria were collected: demographics (age, gender, smoking status); psychological assessment questionnaires: Insomnia Severity Index (ISI); Post-traumatic stress disorder (PTSD) checklist; Patient Health Questionnaire (PHQ9) Depression; Generalized Anxiety Disorder (GAD7) Anxiety; Patient Health Questionnaire-15 (PHQ-15) and Somatic Symptom Disorder (SSD)-12.

Results: Between February and December 2021, 60 cases (46 (76.7%) women), median age 52.0 (39.0; 63.0) were included, of which 15 (25%) had been hospitalized during infection, and 169 controls (148 (87.6%) women), median age of 52.0 (38.0; 63.0). There were more smokers in the group of cases 12 (20%) than controls 14 (9.1%) (p=0.028) as well as more cases on ARA2 treatment (8 (13.3%)) than controls (7 (4.5%)) (p=0.035) with no statistically significant difference in others comorbidities or treatments. There was no statistically difference concerning the ISI scores between cases (11.83 ± 7.31) of which 60% had sleep disorders and controls (11.64 ± 6.82) of which 70.4% had sleep disorders. There was no statistically significant difference in PTSD scores of 15.5 (5.0 to 28.0) for cases and 18.0 (8.0 to 35.0) for controls, of which respectively 12 (20%) had values indicating possible PTSD for cases and 50 (29.6%) for controls. There was no statistically significant difference in PHQ-9 scores (5.5 (1.5 to 11.0)) of which 50% had depressive symptoms and controls (6.0 (2.0 to 11.0)) of which 54.5% had symptoms. There was no statistically significant difference in GAD-7 scores (3.5 (0.0 to 8.0)) of which 40% had anxiety symptoms and controls (4.0 (0.0 to 8.0)) of which 43.2% had symptoms. There was no statistically significant difference in PHQ-15 scores (11.4 ± 6.7), 85% of whom reported presence of symptoms, and controls (10.9 ± 6.2), 82.3% of whom reported symptoms. There was no statistically significant difference in SSD scores between cases (17.7 ± 10.9) and controls (18.4 ± 10.9). There was a statistically significant difference in reported VAS scores of pain related to inflammatory rheumatism in cases with a median of 4.5 (3.0 to 6. 0) compared to controls with a median of 4.0 (1.0 to 6.0) (p=0.011). There was no statistically significant difference in any of the psychological assessment scores between the inpatient and outpatient COVID cases.

Conclusion: There was no statistically significant difference between COVID cases and controls in the evaluation of these psychological parameters. Prevalence of all these variables were high in the whole study population, testifying to the need to manage these psychological aspects for patients with chronic rheumatisms, autoimmune and/or autoinflammatory diseases.

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AB1121 HOW FEARS AND HOPES HAVE EVOLVED IN PATIENTS WITH RMDS THROUGHOUT THE COVID-19 PANDEMIC? RESULTS FROM THE REUMAVID STUDY (PHASE 1 AND 2)

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Background: The COVID-19 pandemic has generated uncertainties and concerns along with expectations and hopes that may be of relevance to patients with rheumatic diseases.
Objectives: The aim of this study is to assess changes in the fears and hopes of patients with rheumatic diseases throughout the two phases of REUMAVID.
Methods: REUMAVID is an international cross-sectional study collecting data through an online survey in seven European countries led by the Health & Territory Research group of the University of Seville, together with a multidisciplinary team including patient representatives, rheumatologists, and health researchers. Data were collected in two phases: Phase 1 (P1) between April-July 2020 and Phase 2 (P2) between February-April 2021. Demographics, health behaviours, employment status, access to healthcare services, disease characteristics, WHO-5 Well-Being Index and Hospital Anxiety and Depression Scale (HADS). Participants rated a series of fears (infection, medication consequences, lack of medication, impact on healthcare, lost job, civil disorder) on a scale from zero ("no concern at all") to five ("extremely concerned") and hopes (treatment/vaccine availability, going outside, travel, economic situation, treatment continuation, health status) on a scale from zero ("no hopeful at all") to five ("extremely hopeful"). Descriptive analysis and Mann-Whitney test were used to explore fears and hopes in both phases of REUMAVID.
Results: A total of 3,802 participants were recruited across both phases in REUMAVID with comparable demographic characteristics: mean age 52.6 (P1) vs. 55.0 years (P2), 80.2% female (P1) vs. 83.7% (P2), 69.6% married (P1) vs. 68.3% (P2), and 48.6% university educated (P1) vs. 47.8% (P2). Most prevalent RMD was axial spondyloarthritis in P1 (37.2%), and rheumatoid arthritis in P2 (53.1%). In P1 and P2 the major concern was the impact on healthcare in the future (3.1 and 3.2 out of 5, p=0.051). Compared to P1, patients in P2 had less fears about RMD medications not reaching the country (2.4 vs. 1.9, p<0.001), civil disorders (2.0 vs. 1.8, p=0.001), or losing their jobs (1.4 vs. 1.5, p=0.003). Comparing hopes with P1, patients in P2 had greater hopes about availability of treatments or vaccines suitable for COVID-19 (3.2 vs. 3.9, p<0.001), to be able to go out as before the pandemic (3.1 vs. 3.5, p<0.001), to be able to travel as before the pandemic (2.8 vs. 3.3, p<0.001), maintain and even improve the current economic situation after the pandemic (2.6 vs. 3.0, p<0.001), and to be able to continue their treatment as usual (3.8 vs. 3.8, p=0.049; Table 1)

Table 1. Bivariate analysis of patients' fears and hopes in both phases of REUMAVID (N= 3,802, unless specify)

	Mean ± SD		
	First Phase n= 1,800	Second phase n= 2,002	P-value
Fears			
Impact on healthcare in the future, n= 3,653	3.1 ± 1.6	3.2 ± 1.6	0.051
Treatment taken could make you more likely to get serious illness from COVID-19 infection, n= 3,651	2.8 ± 1.8	2.9 ± 1.8	0.160
More likely to be infected due to the condition, n= 3,649	2.8 ± 1.7	2.9 ± 1.7	**0.040**
Lack of medication, n= 3,656	2.4 ± 1.8	1.9 ± 1.8	**<0.001**
Civil disorder, n= 3,634	2.0 ± 1.6	1.8 ± 1.7	**0.001**
Lost job, n= 3,566	1.5 ± 1.9	1.4 ± 1.9	**0.003**
Hopes			
Availability of a treatment or vaccine suitable for COVID-19, n= 3,318	3.2 ± 1.5	3.9 ± 1.3	**<0.001***
Continue treatment as usual, n= 3,306	3.7 ± 1.4	3.8 ± 1.3	**0.049***
Go out as before the COVID-19 pandemic, n= 3,318	3.1 ± 1.5	3.5 ± 1.4	**<0.001***
Don't get infected with COVID-19 and continue in the same health, n= 3,280	3.5 ± 1.5	3.5 ± 1.5	0.696
Travel as before the COVID-19 pandemic, n= 3,311	2.8 ± 1.6	3.3 ± 1.5	**<0.001***
Maintain or improve economic situation after the COVID-19 pandemic, n= 3,310	2.6 ± 1.7	3.0 ± 1.7	**<0.001***

Conclusion: During the first phase of REUMAVID at the beginning of the pandemic, patients with RMDs were more fearful and less hopeful compared to the second phase. These fears were notable in terms of lack of medication for their RMD, while during the second phase, patients were hopeful of a treatment or vaccine against COVID-19, and of being able to go out and travel as before.
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AB1122

HAVE TREATMENTS FOR AUTOIMMUNE DISEASES WORSENED THE PROGNOSIS OF COVID-19 INFECTION?

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Background: According to the literature patients with autoimmune diseases (AID) have a high risk of develop serious infections due to the use of immunosuppressive treatment. In published clinical trials neither the risk nor the severity of COVID-19 infection in patients with AID seem to be higher than in the general population.
Objectives: The objective of our study is to analyse the clinical course in patients with AID undergoing immunosuppressive treatments and infected by COVID-19.
Methods: Patients were included after reviewing four rheumatology outpatient clinics from Ciudad Real University General Hospital between November 2020 and February 2021. The inclusion criteria were being older than 18 years and being positive for COVID-19 by epidemiological (positive molecular and/or antigen test) or clinical criteria (symptoms compatible between March and May 2020). We collected demographic data, cardiovascular comorbidities, AID, treatment with synthetic or biological DMARDs, immunomodulators or glucocorticoids; and progression of infection COVID-19.
Results: We found a total of 210 patients that had suffered from SARS-COV2 of which 95 patients were affected by AID. The most prevalent pathology in our sample was spondylarthritis followed by arthritis rheumatoid and systemic lupus erythematosus of which 81.82%, 100% and one 92.86% respectively were receiving treatment to control the disease. Among the 95 patients suffering from COVID and AID a small number of patients did not follow any immunosuppressive treatment regimen (n=25) but most of our patients were undergoing immunosuppressors (n=70); the most used drugs were prednisone and methotrexate. No statistically significant differences were found between the treated versus untreated group in the studied variables, being similar the results relative to mean age, sex, presence of cardiovascular risk factors, absence of symptoms, number of admissions to hospital ward or in Intensive Care Unit, or complications during COVID-19 infection (Table 1).

Table 1. Baseline characteristics of patient with AID undergoing or not immunosuppressors.

	Treated	Untreated	p
	n=70 (73,68%)	n=25 (26,32%)	
Medium age (SD)	51,74 (+/- 2,18)	55,74 (+/-3,36)	0,467
Female sex, n (%)	49 (70%)	17 (68%)	0,852
HTA, n (%)	22 (31,4%)	5 (20%)	0,277
DM, n (%)	8 (11,4%)	2 (8%)	0,632
DL, n (%)	13 (18,6%)	1 (4%)	0,078
Tobacco, n (%)	7 (10%)	3 (12%)	0,78
Asymptomatic, n (%)	13 (18,6%)	4 (16%)	0,773
Admitted, n (%)	11 (15,7%)	5 (20%)	0,623
ICU, n (%)	2 (2,9%)	0 (0%)	0,393
ARDS, n (%)	7 (10%)	2 (8%)	0,769
Overinfection, n (%)	4 (5,7%)	0 (0%)	0,222
Thrombosis, n (%)	1 (1,4%)	0(0%)	0,548
Death, n (%)	6 (8,6%)	2 (8%)	0,930

SD, standard deviation; n, absolute numbers; %, percentages; p, p-value; AID, autoimmune diseases; HTA, arterial hypertension; DM, diabetes mellitus; DL, dyslipidaemia; ICU: intensive care unit; ARDS: Acute respiratory distress syndrome

Conclusion: Patients treated with synthetic or biologicals DMARDs, immunomodulators or glucocorticoids do not seem have a higher rate of death or hospital admission respect to patients diagnosed of AID without such treatments.

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AB1123 EFFICACY AND SAFETY OF SARS-COV-2 THIRD VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO DID NOT RESPOND AFTER PRIMARY TWO-DOSE REGIMEN

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Background: Vaccination for COVID-19 is an essential tool to fight the pandemic. Evidence suggests that patients with immune mediated inflammatory diseases (IMIDs) have less response. The application of a booster shot is a strategy that has been implemented in this population, however there is scarce information about its efficacy.

Objectives: To assess the humoral and cellular immune response after a third dose of SARS-CoV-2 vaccine in patients with rheumatoid arthritis (RA) with undetectable antibodies titles after primary regimen of two doses.

Methods: Observational study. Patients with RA (ACR/EULAR 2010 criteria) from two rheumatology centers, ≥18 years old, with no seroconversion after two doses of SARS-CoV-2 vaccine, who received a third dose of either mRNA or vector-based vaccines (BNT162b2 or ChAdOx1 nCoV-19) were included. Anti-SARS-CoV-2 IgG antibodies, neutralising activity and T cell responses were assessed between 21 and 40 days after the third dose. Sociodemographic data, comorbidities, treatment, vaccine applied and the presence of adverse events (AE) were recorded. Statistical analysis: descriptive analysis. Chi^2 or Fischer test and T test.

Results: A total of 21 non-responder patients were included, all of them females with a mean age of 63.7 years (SD 11,6) and mean disease duration of 15.8 years (SD 8). Most of them (81%) reported comorbidities, being the most frequent arterial hypertension, obesity and dyslipidemia. At vaccination time, 6 (28.6%) were receiving glucocorticoids, 3 of them ≥10 mg/day, 17 c-DMARDs (methotrexate 57.1%) and 18 (85.1%) b-DMARDs, 6 abatacept (ABT) and 4 rituximab (RTX). Regarding the primary vaccination regimen, 13 (61.9%) received two doses of BBIBP-CorV, 3 (14.3%) Gam-COVID-Vac, 3 (14.3%) ChAdOx1 nCoV-19 and 2 (9.5%) a mix regimen of Gam-COVID-Vac/mRNA-1273. The majority (95.2%) received BNT162b2 vaccine and only one of them ChAdOx1 nCoV-19, with a mean time between the second and third dose of 151,4 days (SD 46,4). After the third dose, 90.5% of the patients presented detectable anti-SARS-CoV-2 IgG and 76.2% presented neutralizing activity. The median of neutralizing antibodies titers was 1/12 (IQR 1/7-1/48). Both patients who did not present detectable antibodies were obese, recieved BBIBP-CorV during the primary regimen and BNT162b2 as the third dose, one of them was taking methotrexate and ABT and the other one RTX. Compared to other treatments, ABT and RTX was associated with no neutralizing activity in 4 (80%) patients and lower titers of neutralizing antibodies [median 1/3 (IQR 0-1/20) vs median 1/8 (IQR 1/4-1/128), p=0.197]. A T-cell response was present in 41.2% of all patients after the second dose, increasing to 75% after the third dose. The use of ABT was associated with a lower frequency of T-cell response (80% vs 20%, p=0.014). Sixteen (76.1%) patients reported at least one AE, 66.7% injection site reaction and 25% flu-like syndrome.

Conclusion: In this RA cohort who failed to seroconvert after two doses of SARS-CoV-2 vaccine, 90.5% presented detectable anti-SARS-CoV-2 IgG and 75% T-cell responce after a third dose. The use of ABT was associated with a lower frequency of T-cell response. This data highlights the importance of a third vaccine in this group of patients.

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AB1124 IMPACT OF COVID-19 ON PATIENTS WITH RHEUMATIC DISEASES IN A SECOND LEVEL HOSPITAL

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Background: Covid-19 has generated a change in society and in people's daily lives. Patients with rheumatic diseases have suffered physically and mentally, both due to mobility restrictions and to the impact on personal, family, work and social life that COVID-19 has brought [1-4].

Objectives: To examine the impact of the pandemic COVID-19 on patients with rheumatic diseases.

Methods: Cross-sectional descriptive study in patients with rheumatic diseases. Data collection was done through an online questionnaire to assess the impact of COVID-19, adapted for this purpose and made up of 5 scales of the 9 of the Coronavirus Psychological Impact Questionnaire [3]. This instrument is divided into two parts: 1) sociodemographic variables and 2) Experience with Coronavirus(ECOVI); Preventive Behaviour Use(UCP); Fear against coronavirus Scale(EMC); Interference with the coronavirus Scale(EIC) and positive psychological aspects(EEPA). This questionnaire was accessed through a QR code (provided to all patients both in consultations and in the day hospital) by the rheumatology team for two weeks between November-December 2021. In addition, this code was sent by the nurse via WhatsApp to all patients registered in our database. Statistical analysis: SPSS 24.0 and Pearson Chi-square, T-Student and ANOVA tests.

Results: n=362 online surveys; 72% women with a mean age of 63 years ± 14.21 (22-70 years). The most frequent rheumatic diseases were Rheumatoid Arthritis (50%) and Spondyloarthritis (31%). 83.2% had only one rheumatic disease (mean 1.26 ± 0.66) and 90% self-completed survey. In experience with the Coronavirus (ECOVI), 89% patients had not had symptoms or confirmed diagnosis of coronavirus, 98% were not hospitalized, 91% had confidence in our health system; Regarding the Use of Preventive Behaviors (UCP), 98% used a mask outside the house and 78.5% kept a safe distance; In relation to the most common fears associated with the Coronavirus (EMC), 40% were a little afraid of getting infected (34% quite a bit) and 50% were almost nothing afraid of losing their job; Regarding the interference that the coronavirus has caused in these patients (EIC), 73% had not had serious work problems and 74% had not had difficulties in their studies. In reference to the positive psychological aspects (EEPA), 48% had discovered new hobbies, 19% had become more religious,83% had learned to value personal relationships more. It was significant that women were more afraid of infecting themselves or a loved one or family member and/or dying from coronavirus than men (p=0.02; p=0.011 and p=0.002 respectively). Regarding age, younger patients (45y) were more concerned that they could lose their job compared to older patients (61y), p=0.

Conclusion: The COVID-19 disease has impacted patients with rheumatic diseases. In our sample, women have been more concerned about being infected and dying themselves and their closest relatives/friends, and younger people more concerned about job loss and economic income than older people. It has to be considered that the majority of this population has not been hospitalized or diagnosed with COVID-19 and also has great confidence in our health care system. More studies are necessary to examine the impact of the COVID-19 after the 6th wave of the pandemic.

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AB1125 SAFETY OF BIOLOGIC-DMARDS DURING COVID-19 OUTBREAK: FOLLOW-UP STUDY IN 1051 RHEUMATIC PATIENTS OVER THE FIRST TWO WAVES.

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Background: A novel viral infection known as COVID-19 (Coronavirus-19 disease) spread up in Wuhan (China) in December 2019, but rapidly diffused worldwide and nowadays it remains an international health problem. Because of its impact on immunologic system, immunomodulating therapies have been studied as possible treatments for severe cases of COVID-19. In that context, patients affected by from rheumatic musculoskeletal disorders (RMD) under disease modifying anti-rheumatic drugs (DMARDs) have been observed in several studies to evaluate the impact of COVID-19 on these subjects, well known to be at higher risk of infection.
Objectives: The primary objective of this study is to assess prevalence and severity of COVID-19 in patients with RMD under treatment with biologic (b-DMARDs) or targeted synthetic (ts-DMARDs) DMARDs, before the vaccination campaign. The second aim is to compare those data with that in general population of the same Area (Province of Udine, Friuli Venezia Giulia Region, Italy,).
Methods: A cohort of RMD patients treated with b-DMARDs or ts-DMARDs was observed from September 2019 to November 2020. Both pandemic waves have been considered, until the start of vaccination (since current variants can overcome vaccine protection), between February 2020 and April 2020 (first wave) and between September 2020 and November 2020 (second one).
Results: Among 1051 RMD patients treated with b- or ts-DMARDs COVID-19 prevalence was 3.5% (37 cases) without significant differences compared to general population of the same Region (Table 1). Infected patients were 18 men and 19 women, with a median age of 60 years (IQR 49-68). Notably, the infection rate of RMD patients was significantly lower compared to the general population of the same province, particularly during the second wave (p<0.001, Table 1). Almost all patients reported fever (70%). Gastro-intestinal symptoms (nausea, vomit and diarrhoea) have been recorded in 10 subjects (27%) and resulted significantly associated with longer swab positivity (p<0.05) (Figure 1). Only a small percentage of patients with COVID-19 infection was receiving corticosteroids (8%), and the doses were low (3.5 or 5 mg per day of prednisone equivalents). The most used b-DMARDs were anti-TNFs (24/37, 65%), while just 4/37 (11%) employed JAK inhibitors. A small percentage of patients (6/37, 16%) continued ongoing treatment, with no worsened outcomes, while none preventively suspended the immunosuppressant. The course of infection was generally benign with a mortality rate of 2.6% (1 patient, with several risk factors) and only 9 patients needed to be hospitalized (24%). After COVID-19 infection, 12 subjects (32%) had RMD flare and 5 of them subsequently needed to change the immunosuppressive drug.

Table 1. Cases and proportion of COVID-19 among different populations. *p<0.001, patients vs province population; °p<0.05 patients vs province population.

	Cases (proportions)		
Periods	**RMD patients**	**Province population**	**Region population**
Overall wave	37 (0.0352)*	14437 (0.1441)	32970 (0.0273)
First wave	5 (0.0048)°	1190 (0.0119)	3769 (0.0031)
Second wave	32 (0.0304)*	13247 (0.1322)	29201 (0.0242)

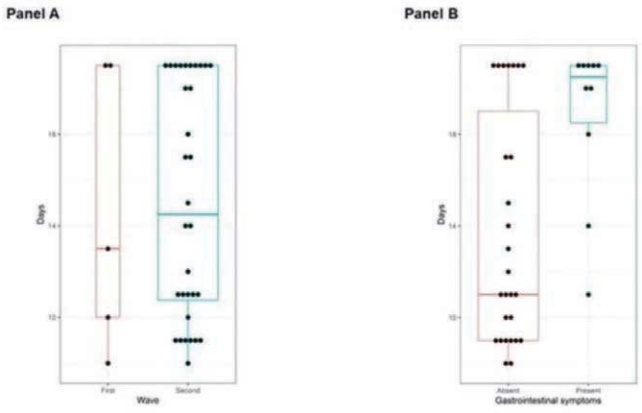

Figure 1.

Conclusion: The prevalence of COVID-19 in RMD patients has been confirmed low in both waves and it could be partially explained by the great awareness about preventive strategies by the patients. The benign course of COVID-19 in our patients may be linked to the very low amount of chronic corticosteroids used and the possible protective effect of anti-TNF agents, which were the main class of biologics herein employed. Gastro-intestinal symptoms might be a predictor of viral persistence in immunosuppressed patients. This finding could be useful to identify earlier COVID-19 carriers with uncommon symptoms (without respiratory manifestations), eventually eligible for antiviral drugs.
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AB1126 CHARACTERISTICS AND OUTCOMES OF COVID-19 IN PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES: EXPERIENCE FROM A TERTIARY RHEUMATOLOGY CENTER IN MALAYSIA

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Background: South East Asia was one of the first regions affected by the SARS-CoV-2 virus causing COVID-19 however data on the impact of COVID-19 infection in patients with systemic rheumatic diseases (SRD) in South East Asia remains scarce.
Objectives: To evaluate basic demographics, clinical features and outcomes of COVID-19 infection in patients with SRD from a tertiary rheumatology centre in West Malaysia.
Methods: A retrospective observational study of 77 patients with SRD diagnosed with COVID-19 between 1st December 2020 to the 31st of December 2021 was performed. Demographic details, type of SRD, number and type of disease-modifying antirheumatic drugs (DMARD), dose of glucocorticoid, comorbidities, SARS-CoV-2 vaccine (type and number of doses) hospitalisation, oxygen requirement, type of COVID-19 related complication and death were recorded.
Results: A total of 55 (71%) patients were hospitalised and 9 (12%) died. Mean age at time of COVID-19 diagnosis was 51 ± 14. Amongst these patients, 32 (42%) were Chinese, 30 (39%) Malays and 15 (19%) Indians. Majority of these patients had inflammatory arthritis (58%) which included rheumatoid arthritis and seronegative spondyloarthropathy. The most common DMARDs used was methotrexate (51%), hydroxychloroquine (46%), sulfasalazine (22%), leflunomide (13%), azathioprine and mycophenolate mofetil (5% each). Two patients were on Janus Kinase (JAK) inhibitors and 3 on biologic DMARDS (tumour necrosis factor inhibitor, IL-6 inhibitors and IL-17 inhibitors). There were 38 patients (49%) vaccinated with two doses of SARS-CoV-2 vaccine (Pfizer n=29, CoronoVac n=7 and AstraZeneca n=2) prior to admission and amongst those unvaccinated, 15 (20%) contracted COVID-19 before the vaccine was released in Malaysia. Among hospitalised patients, those more than 60 years and those with more than one comorbid had a higher chance of admission (n= 21, 88%; p=0.036 and n=28, 88%; p=0.001) and death (n=8, 33%; p<0.001 and n=7, 22%; p<0.001). Comorbidities associated with higher risk of hospitalisation was diabetes mellitus (85%, p=0.06), hypertension (92%, p<0.001) and coronary artery disease (100%, p=0.03) and those associated with death was obesity (33%, p=0.01) and hypertension (22%, p=0.007). Use of conventional DMARD, JAK, biologics and glucocorticoid were not associated with hospitalisation or morbidity. However, we found that patients who developed acute respiratory distress syndrome secondary to COVID-19 were mostly on sulfasalazine compared to other DMARDS (35%, p=0.01).

Conclusion: In our multiethnic cohort of patients with SRD we found that age and multiple comorbidities such as diabetes mellitus, hypertension, obesity and coronary artery disease were associated with hospitalisation and morbidity. Disease activity and glucocorticoid use which have been shown to be associated with morbidity [1] was not seen in our cohort. The association between sulfasalazine and poor outcomes have been reported [2] however further studies are still needed to investigate the causal relationship between the two.

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AB1127 ANTIOSTEOPOROTIC TREATMENT AND COVID-19 RISK: IS THERE AN ASSOCIATION?

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Background: Nowadays, the COVID-19 and its complications are considered an important medical issue with aggravated medico-social outcomes, both at the worldwide scale, and in terms of various individual countries. Despite the recent ASBMR, AACE, Endocrine Society, ECTS and NOF recommendations according to osteoporosis management in the era of COVID-19 the influence of antiosteoporotic drugs on disease incidence and severity continue to be studied [1, 2].

Objectives: The purpose of this study was to assess the COVID-19 risk for the patients receiving the parenteral bisphosphonate or Denosumab treatment, and the severity of its course in the systemic osteoporosis patients.

Methods: We performed the phone survey and studied the results of 195 patients (92 % women; mean age – 62.7±10.8 years, height – 161.0±8.0 cm, body weight – 68.9±12.3 kg) with systemic osteoporosis depending on the current use of parenteral antiresorptive drugs (Zoledronic acid, Ibandronic acid, or Denosumab, n=125) and compared the results with patients with osteoporosis who did not use any antiosteoporotic drugs previously (n=70). The mean duration of antiosteoporotic treatment did not vary across the groups, accounting for 15 [9-27] months. Prior to the beginning of the antiosteoporotic therapy, all the patients had a confirmed diagnosis of osteoporosis at the Ukrainian scientific-medical Center of osteoporosis.

Results: We did not reveal any significant differences in the COVID-19 frequency and severity depending on the presence and type of parenteral antiosteoporotic therapy. Additionally, there were no differences depending on patients' age of sex, obesity presence, and other osteoporosis risk factors. The risk of COVID-19 in the patients with systemic osteoporosis did not differ depending on antiresorptive drug use, amounting (Odd Ratio (OR) 95 % CI) to 1.1 (0.6-2.0), or on the use of the definite antiosteoporotic drug (for the Zoledronic acid - 0.9 (0.4-2.0), the Ibandronic acid - 1.1 (0.5-2.3), and for the Denosumab - 1.6 (0.5-5.2).

Conclusion: Our study did not reveal any significant differences in the COVID-19 frequency and severity depending on the presence and type of parenteral antiosteoporotic therapy. We conclude that parenteral antiosteoporotic drugs (Zoledronic acid, Ibandronic acid, or Denosumab) do not have an influence on COVID-19 frequency and severity and can be recommended for the continuation of treatment of patients with osteoporosis.

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AB1128 MAINTENANCE THERAPY FOR PATIENTS WITH RHEUMATIC DISEASES DURING THE COVID-19

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Background: The Covid-19 pandemic has been raging for more than a year in a pandemic mode. Since then, many questions have been raised regarding the management of patients with rheumatic diseases (RD). In this context, the maintenance therapy of conventional, biologic and targeted synthetic disease-modifying antirheumatic drugs (Cs DMARDs, bDMARDs and tsDMARDs respectively) during the Covid-19 infection remains a subject of debate given their immunosuppressive effects as well as their potential generation of lung fibrosis. While the EULAR 2020 guidelines emphasize that discontinuation or maintenance should be discussed on a case-by-case basis, the ACR guidelines advocate discontinuation of all therapies except for the anti-interleukin-6 [1,2].

Objectives: The objective of our work was to report our real-life experience of therapeutic maintenance during the covid-19 pandemic.

Methods: We conducted a cross-sectional study of patients with RD: rheumatoid arthritis (RA) and spondyloarthritis (SpA) recruited from the rheumatology department of the Kassab Institute of Orthopedics. All the patients were asked to complete a questionnaire about their disease management in the era of the Covid-19. The questionnaire included sociodemographic data, treatment modalities, as well as data related to the infection with the Covid-19 (severe forms defined by the need for oxygen therapy or hospitalization), and changes in treatment during the infection.

Results: The study included 102 patients with RA (65.3%) and SpA (34.7%). The mean age was 52.4 ± 13 [19-77] years. There was a female predominance with a sex ratio of 0.4. The mean duration of the disease was 7.8 ± 5 years [1-35]. Fifteen percent of patients were on corticosteroids with a mean dose of 6.7±4.5 mg/L [2-20] of prednisone equivalent. A CsDMARD was prescribed alone in 36.3% of cases and combined with a biologic in 18% of cases. A Covid-19 infection was occurred at least once in 25.5% of cases, of which 19.2% had a severe form (hospitalization (15.4%), oxygen therapy (19.2%)). No deaths were observed. The treatments received during the covid-19 infection were: corticosteroids (n=5), heparin therapy (n=6) and antibiotic therapy (n=10). No patient tapered treatment dosage of DMARDs but discontinuation was reported by 4 patients with a mean time between discontinuation and resumption of 2.1 ± 2 months [0.5-5 months]. The cessation of the treatment was dictated by the treating physician in 2 cases and involved csDMARD in 3 cases (Methotrexate (n=2), Leflunomide (n=1)) and biologics in only one patient. There were no cases of clinical pulmonary worsening upon resumption of the treatments. We found no statistically significant association between severe forms of the infection and the type of RD (p=0.925), as well as the presence of comorbidities (p=0.825). Similarly, the presence of severe forms was not associated with the use of long-term NSAIDs (p=0.29), corticosteroids (p=0.85), or biological treatment (p=0.7). However, maintenance therapy was significantly associated with a lower risk of severe forms (p=0.013).

Conclusion: Our work showed that the maintenance of conventional treatment during Covid-19 infection was associated with a lower risk of severe forms. Our results, along with those of other studies in the literature, support the maintenance of antirheumatic treatments.

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AB1129 SAFETY OF VACCINES AGAINST COVID-19 IN PATIENTS WITH SPONDYLOARTHRITIS (PRELIMINARY DATA).

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Background: Patients with spondyloarthritis (SpA) probably have a high incidence of COVID-19. Vaccination remains one of the most effective methods of preventing infectious diseases. However, data on the safety of vaccines against COVID-19 in patients with SpA are few and relate to foreign vaccines that are not licensed in Russia.

Objectives: To study the safety of COVID-19 vaccines in patients with SpA in real clinical practice.

Methods: The study included 47 SpA patients (25 - ankylosing spondylitis, 13 - psoriatic arthritis, 9 - undifferentiated SpA, 19 women, 28 men, age 42.3±11.6 years, duration of the disease 11.8±9.2 years) - the main group and 97 people without any immuno-inflammatory rheumatic diseases (67 women, 30 men, age 43.7±13.1 years) - the control group. 20 patients received disease-modifying antirheumatic drugs (12 - methotrexate, 8 - sulfasalazine), 10 - biological drugs (8 – TNF-α inhibitors, 2 - IL-17 inhibitors), 6 - glucocorticoids, 1 - tofacitinib, 12 - only nonsteroidal anti-inflammatory drugs, 8 - did not receive therapy. In the main group, 40 patients were vaccinated with Gam-COVID-Vac (Sputnik V), 3 – CoviVac and Sputnik Light, 1 – EpiVacCorona (both components of the vaccine were received by 44 patients). In the control group 69 were vaccinated with Sputnik V, 15 - CoviVac, 5 - Sputnik Light and BNT162b2, 2 - EpiVacCorona, 1 - mRNA-1273. (91 participants received both components of the vaccine). All participants

were interviewed by a research doctor with a unified questionnaire, additional information was obtained from medical documentation.

Results: The data obtained are reflected in the Table 1. Local adverse events (AEs) occurred relatively less frequently in patients with SpA than in the control group. After the introduction of the first component of the vaccine, there was a significant increase in the frequency of pain without restriction of movement and edema/hyperemia in the control group (p<0.001 and p=0.049, respectively), while after the introduction of the second component, a significant difference was registered only for the first indicated symptom (p<0.001). The most frequent systemic AEs were weakness, fever, arthralgia or myalgia, headache, and chills, which were significantly less common (p=0.008) in the main group after immunization with the first component. The proportion of SpA patients without any reactions was significantly higher after the introduction of the first component of the vaccine (59.6% and 29.9%, p<0.001), while after immunity with the second component there were no differences (59.1% and 44.0%, p>0.05). After complete immunization, the percentage of patients without any AEs was significantly higher in the main group than in the control (50.0% and 17.6%, p<0.001). There was no exacerbation of SpA or development of new autoimmune phenomena in the main group after full vaccination.

Table 1. The frequency of AEs in SpA patients and in control

	The first component					The second component				
	SpA, n=47		Control, n=97			SpA, n=44		Control, n=91		
	n	%	n	%	p	n	%	n	%	p
Local AEs										
Pain w/r movement*	2	4.3	38	39.2	<0.001	2	4.5	32	35.2	<0.001
Pain w/r movement**	5	10.6	10	10.3	>0.05	4	9.1	4	4.4	>0.05
Edema or hyperemia	1	2.1	14	14.4	0.049	3	6.8	13	14.3	>0.05
Systemic AEs										
Weakness	13	27.7	36	37.1	>0.05	11	25.0	23	25.3	>0.05
Temperature >37.0ºC	13	27.7	33	34.0	>0.05	9	20.5	21	23.1	>0.05
Myalgia/Arthralgia	6	12.8	22	22.7	>0.05	6	13.6	14	15.4	>0.05
Headache	5	10.6	11	11.3	>0.05	6	13.6	6	6.6	>0.05
Chills	1	2.1	20	20.6	0.008	3	6.8	5	5.5	>0.05
Nausea/vomiting	1	2.1	2	2.1	>0.05	0	0	1	1.1	-
Other	1	2.1	10	10.3	>0.05	0	0	4	4.4	-

Notes: * - pain at the injection site **without** restriction of limb movement, ** - pain at the injection site **with** restriction of limb movement

Conclusion: According to preliminary data, the tolerability of vaccines against COVID-19 in patients with SpA is satisfactory. Further studies with an increased sample are needed to study the safety, immunogenicity and clinical efficacy of immunization against COVID-19 in patients of this cohort.

Disclosure of Interests: None declared

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AB1130 A REDUCTION IN NEW REFERRALS FOR RHEUMATOID ARTHRITIS, OSTEOARTHRITIS AND CRYSTAL ARTHRITIS COMPARED TO GCA DURING COVID19 PANDEMIC

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Background: The COVID-19 pandemic has had profound effects on the Rheumatology department; we wanted to see if consequently referrals for Rheumatoid arthritis (RA), Crystal Arthritis (CA), Osteoarthritis (OA) and Giant cell arteritis (GCA) were affected. A greater understanding of the impact may enable adequate number of clinics and resources to be made available where needed.

Objectives: To evaluate the impact of COVID-19 pandemic on volume of new referrals to the Rheumatology department for RA, CA, OA and GCA.

Methods: A retrospective analysis of data was conducted from the period of January 2016 to December 2021. The Rheumatology department database was closely analysed and information about new referrals for GCA, RA, OA and CA were evaluated. Statistical analysis was conducted using t-test to compare the mean value pre and during the COVID19 outbreak (2020).

Results: From 2016 to 2021 a total number of 9998 new patients were referred to the Rheumatology department. There were 2768 new referrals for GCA (15%), RA (34%), OA (40%) and CA (11%) made during this period. In 2020, there was a significant decrease in OA, RA and CA referrals (p value 0.000004, 0.00017, 0.0042 respectively) but an insignificant decrease in GCA referrals (p value 0.243).

	Number of referrals		
Diagnoses	**Mean nº 2016-2019**	**2020**	**p value**
GCA	79.75 (14%)	63 (33%)	0.24334236
RA	204 (36%)	55 (28%)	0.000175427
OA	219.7 (39%)	59 (30%)	4.26975E-06
CA	64.5(11%)	18 (9%)	0.004278881
	100%	100%	

Conclusion: During COVID19 pandemic in 2020 there was a significant reduction in the number of new referrals for RA, OA, and CA in contrast to GCA where the referrals have been constant. This may be due to the detrimental consequences of untreated GCA with regards to risk of sight loss. However, with less RA referrals, this may result in a delayed diagnosis with an impact on the disease course.

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AB1131 IDENTIFICATION OF FACTORS ASSOCIATED WITH THE OCCURRENCE OF SEVERE FORMS OF COVID-19 INFECTION IN PATIENTS WITH AUTOIMMUNE/ INFLAMMATORY RHEUMATIC DISEASES

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Background: Patients with autoimmune/inflammatory rheumatic diseases (AIRD) were suspected to be an at-risk population of severe COVID-19. However, whether this higher risk is linked to the disease or to its treatment is difficult to determine.

Objectives: To identify, among AIRD patients, factors associated with occurrence of moderate-to-severe COVID19 infection and to evaluate if having an AIRD was associated with an increased risk of severe form of COVID19 infection (defined by hospitalization in ICU or death), compared to general population.

Methods: Data source: The "Entrepôt des Données de Santé (EDS)" collect data from electronic health records of all patients hospitalized or followed in the AP-HP (39 hospitals in Paris area, France). The French RMD COVID19 cohort is a national multi-center cohort that included patients with confirmed AIRD and diagnosed with COVID-19. All AIRD patients diagnosed with COVID-19 before September 2020 from both cohorts were included.

-We Identified factors associated with severe COVID-19 was made in a combined analysis of the 2 cohorts.

-Then, we compared COVID-19 infection severity in the EDS-COVID database in AIRD patients and controls, by a propensity score (PS)-matched case-control (1:4) study

Results: Among 1213 patients (334 in EDS and 879 in RMD cohort), 195 (16.1%) experienced a severe COVID19. In multivariate analysis, greater age, history of interstitial lung disease, arterial hypertension, obesity, sarcoidosis, vasculitis, auto-inflammatory disease and treatment with corticosteroids or rituximab were associated with severe COVID-19 (Table 1).

Table 1. AIRD patient's characteristics associated with severity of COVID-19

	Patients with mild or moderate infection	Patients with severe infection	OR ajustés	
	(N = 1018)	(N = 195)	95%CI	p-value
Patients characteristics				
Age	55.9 (16.7%)	70.3 (14.3%)	1.05 [1.03;1.07]	<0.001
Gender: Female	695 (68.3%)	105 (54.1%)	0.59 [0.38;0.94]	0.025
Interstitial pneumonia	38 (3.7%)	20 (10.3%)	2.94 [1.34;6.34]	0.008
Obesity	143 (17.8%)	38 (27.7%)	2.09 [1.26;3.43]	0.004
Hypertension	268 (26.3%)	114 (58.5%)	1.81 [1.13;2.89]	0.013
Underlying Disease:				
Chronic inflammatory arthritis	618 (60.8%)	72 (36.9%)	Ref.	
Auto-inflammatory disease	29 (2.9%)	5 (2.6%)	3.91 [1.2;11.32]	0.025
Other	29 (2.9%)	4 (2.1%)	0.35 [0.06;1.41]	0.15
Connectivitis	190 (18.7%)	34 (17.4%)	1.13 [0.62;2.01]	0.69
Sarcoidosis	40 (3.9%)	24 (12.3%)	5.19 [2.15;12.3]	<0.001
Vasculitis	111 (10.9%)	56 (28.7%)	1.8 [1.02;3.16]	0.044
Treatments				
Corticosteroid	318 (31.2%)	117 (60.0%)	2.47 [1.58;3.87]	<0.001
Leflunomide	44 (4.3%)	2 (1.0%)	0.13 [0;0.97]	0.045
Rituximab	37 (3.7%)	22 (11.5%)	4.05 [1.96;8.27]	<0.001
Not significant in multivariate analysis	COPD, Asthma, Coronary heart diseases, stroke, diabetes, smoking, cancer, non-steroidal anti-inflammatory drugs, colchicine, hydroxychloroquine, methotrexate, salazopyrine, mycophenolate mofetil, azathioprine, intravenous immunoglobulins, anti-TNFα, anti-IL1, -IL6, -IL17, Abatacept, JAK inhibitor			

Among 35741 COVID-19 patients in EDS, 316 with AIRD were compared to 1264 PS-matched controls. Severe form occurred in 118 (37,3%) AIRD cases and 384 (30.4%) controls (Adjusted OR (aOR) for severe form= 1.43 [1.1;1.9], p=0,01). In analysis restricted to rheumatoid arthritis (RA) and spondylarthritis (SpA), no increased risk of severe form (aOR=1.11 [0.68;1.81]) form or death (aOR=1.00 [0.55;1.81]) was observed.

Conclusion: In this multicenter study we confirmed that AIRD patients treated with rituximab or corticosteroids were at increased risk of severe COVID-19, as were those with vasculitis, auto-inflammatory disease, and sarcoidosis. Also, when compared to controls from the same cohort of hospitalized patients, AIRD patients had, overall, an increased risk of severe COVID-19, increased risk not observed in an analysis restricted to patients with RA or SpA.

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All clinicians/physicians implicated in COVID-19 patient care in APHP hospital and generated EDS patient data

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AB1132 FEATURES OF THE COURSE OF COVID-19 IN ELDERLY PATIENTS WITH IMMUNO-INFLAMMATORY RHEUMATIC DISEASES (PRELIMINARY DATA).

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Background: It is assumed that patients with immuno-inflammatory rheumatic diseases (IIRDs) in old age are susceptible to a more severe course of COVID-19 both due immunological disorders (autoimmune disease and its activity, immunosuppressive therapy, immunosenescence leading to systemic subclinical chronic inflammation with increased secretion of IL-6, IL-1, IL-18, TNF-α) and due to the presence of comorbid pathology. There are no Russian data on the course of COVID-19 in elderly patients with IIRDs.

Objectives: To study the features of the course of COVID-19 in elderly patients with IIRDs.

Methods: The study included 93 patients with IIRDs: 72 women, 21 men, average age 67.5±6.1 years. Of them, 62 patients suffered from rheumatoid arthritis, 9 - systemic sclerosis, 5 - ankylosing spondylitis, 4 - Sjogren's disease, 4 - systemic vasculitis, 3 - psoriatic arthritis, 2 - osteoarthritis, 1 - systemic lupus erythematosus, 1 - polymyositis, 1 - rheumatic polymyalgia, 1 - gout. At the moment of COVID-19, 10 patients had high activity of IIRDs, 26 - moderate, 40 - low, 17 - remission. 69 patients were treated with disease-modifying antirheumatic drugs-DMARDs (40 - methotrexate, 12 - leflunomide, 8 - sulfasalazine, 7 - hydroxychloroquine), 45 - glucocorticoids (34 - low doses, 11 - medium or high doses). 36 patients received biologic or target DMARDs: 24 - rituximab (the interval from the last administration to the development of COVID-19 symptoms averaged 7 months), 4 – TNF-α inhibitors, 3 - abatacept, 2 - secukinumab, 1 - tofacitinib, 1 - baricitinib, 1 - ustekinumab. Comorbidities included hypertension (n=74), coronary artery disease (n=27), obesity (n=17), diabetes mellitus (n=8), bronchial asthma (n=5), chronic obstructive pulmonary disease (n=4), chronic kidney disease (n=3). The patients were interviewed by a research doctor, additional information was obtained from medical documentation.

Results: The most common symptoms of COVID-19 were fever - 67.7%, weakness/drowsiness - 53.7%, cough - 48.4%, as well as anosmia and dyspnea - 35.5% each, headache - 20.4%, body aches - 16.1%, congestion nose - 8.6%, chest pain - 7.5%, dysgeusia - 5.4%, diarrhea/vomiting - 3.2%. According to CT chest scan, 8 patients had 0% of lung damage, 31 - 25%, 32 - 50%, 12 - 75%, in other cases the study was not carried out (n=9) or data are not available (n=1). In 2 patients the course of COVID-19 was complicated by bacterial pneumonia, in 1 - bacterial-fungal. An asymptomatic course was noted only in 2 patients (PCR+/IgM +, CT 0, close contact with a confirmed case of COVID-19). Recovery was noted in 90 patients, fatal outcome - in 3. Exacerbation of IIRDs after COVID-19 was noted in 48.4% of patients, which required intensifying antirheumatic therapy.

Conclusion: Preliminary data indicate that COVID-19 is characterized by moderate and severe course in elderly patients with IIRDs. Further studies are required to identify risk factors for severe course and complications in order to provide timely qualified care.

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AB1133 MUSCULOSKELETAL MANIFESTATIONS AMONG PATIENTS WITH COVID-19 INFECTION

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Background: Coronavirus disease-2019 (COVID-19) is declared as a global pandemic [1]. It is caused by a novel coronavirus with structural similarities to the virus that causes severe acute respiratory syndrome (SARS) [2].While the pulmonary consequences have received a lot of attention, the impact of the disease extends far beyond the respiratory system and affects other organs of the body such as heart,kidney or liver [3]. Although different musculoskeletal (MSK) manifestations have been linked to COVID-19 infection, a systematic approach to outline these manifestations is still lacking [4].

Objectives: The aim of this study was to determine the prevalence, distribution and determinants of MSK manifestations in patients with COVID-19 infection.

Methods: Patients with a history of confirmed COVID-19 infection were asked to answer a web-based survey. The survey consisted of multiple questions centered around demographic, clinical and COVID-19 infection data in addition to MSK discomfort form based on the Nordic MSK Questionnaire. The inclusion criteria included age of ≥18 years. Patients who had malignancies or any chronic rheumatic, MSK, neurological disease were excluded.

Results: There was a total of 110 participants, mostly females (72.7%), with mean age 37.7 years, only 9 (8.2%) were current smokers while 31 (28.2%) had associated comorbid conditions. Headache (75.5%), loss of smell (61.8%) and fever were the most main COVID-19 presenting symptoms. The MSK manifestations reported during or shortly after COVID-19 infection were myalgia (95.5%), arthralgia (81.8%) and facial muscle pain (7.3%). The severity of COVID-19 related arthralgia ranged from mild (18.2%), moderate (32.7%), severe (23.6%) and very severe (7.3%). The most affected part was low back (60%), neck (33.3%), and upper back (30%) (Figure 1). MSK manifestations were significantly associated with shortness of breath (p=0.004), fever (p=0.004), loss of taste (p<0.001), diarrhea (p=0.018), fatigue (p<0.001), higher severity of COVID-19 infection (p<0.001), and longer duration of COVID-19 symptoms (from the first day until symptoms resolved) (p<0.001).

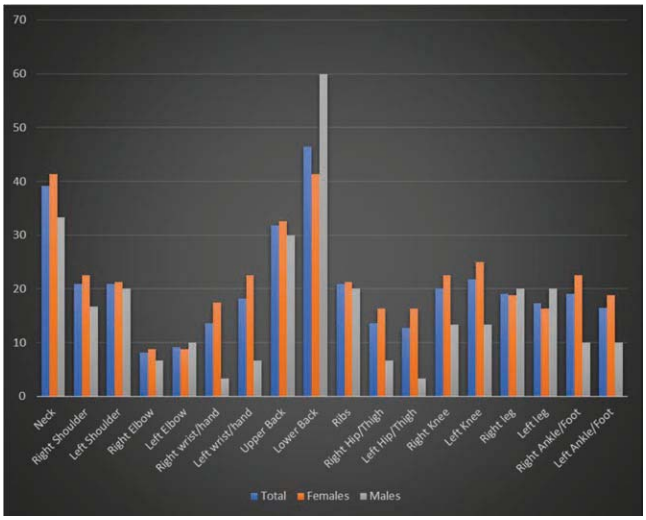

Figure 1. Distribution of MSK manifestations (ache, pain, discomfort, numbness) associated with COVID-19 infection

Conclusion: MSK manifestations are prevalent among patients with COVID-19 infection. They are usually associated with more severe COVID-19 infection and longer disease duration.

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AB1134 BIBLIOMETRIC NETWORK ANALYSIS ON TOCILIZUMAB TREATMENT FOR COVID-19 PATIENTS

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Background: Tocilizumab is a humanized monoclonal antibody. It provokes inhibition of the proinflammatory signals by binding to IL-6 receptors [1]. Due to these properties, it is used in inflammatory arthritis conditions and in cytokine release syndromes [2]. Notably, given its ability to intercept proinflammatory cascades, tocilizumab is an important option for patients with critical forms of COVID-19 [3]. Nevertheless, several aspects about the use of tocilizumab in this clinical setting should be better explained [4].

Objectives: This bibliometric analysis is aimed at dissecting the developed research in the subject. It could provide useful findings for predicting the direction of future studies, implementing corrective measures, and enhancing research networks.

Methods: The global literature on tocilizumab treatment for COVID-19 was scanned in the Web of Science (WOS) online database. The search terms applied to identify the closest matching articles included "tocilizumab" and "COVID-19". All data were acquired on January 29, 2022. The information for the documents that met the requirements were extracted. The source was Journal Citation Reports™ 2020 (Clarivate Analytics). The literature analysis and knowledge visualization software tool VOSviewer (version 1.6.17) was used to analyze the co-occurrence of keywords (interconnection), co-citation (bibliographic coupling), co-citation analysis for sources, and countries, and analysis of the most productive organizations and networks.

Results: A total of 1019 articles on tocilizumab treatment for COVID-19 patients were published from 2020 to January 2022, in WOS. Of those: 462 in 2020, 546 in 2021, 11 on January 29, 2022. About article types, 697 were research articles, 322 reviews. The analysis of keywords provided by authors showed that of 50 keywords, 17 met the threshold (interconnection 2). The most frequent keywords were EFFICACY, and OFF-LABEL USE (Figure 1)

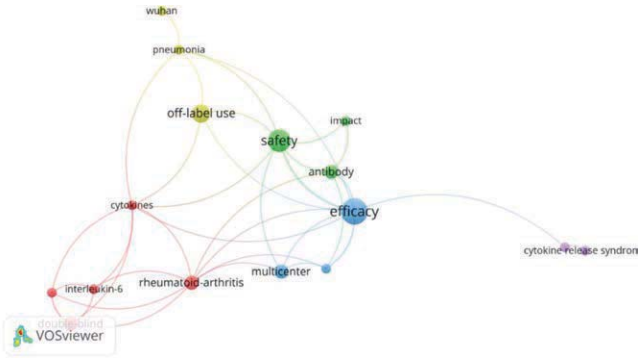

Figure 1. Co-occurrence of keywords

For the co-citation study, we used cited sources (journals) as unit (minimum numbers of citations of a source 1, maximum 3). Of 45 sources, 27 met the threshold. For each source, the total strength of the co-citation links with other sources was rated. The minimum number of documents per country was 2. Thus, 23 countries met the threshold. The largest number of partnerships regarded the US, and Italy. The analysis of affiliations was conducted by considering the cut-off 1 and 5 as the minimum and maximum number of documents. Out of 151 organizations, 94 met the threshold.

Conclusion: This bibliometric network analysis on tocilizumab treatment for COVID-19 patients can be useful for planning future research. It highlights the strength of representative scholars and core research teams. Additional networks should be built, and high-value clinical studies are needed.

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AB1135 RESPONSE TO SARS-COV-2 VACCINATION IN SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASE DEPENDS ON IMMUNOSUPPRESSIVE REGIMEN: A MATCHED, PROSPECTIVE COHORT STUDY

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Background: Vaccination efficiency has been demonstrated to be reduced in patients with systemic autoimmune rheumatic disease (SARD) compared with the general population.

Objectives: To assess the humoral response to mRNA vaccine in patients with (SARD) and the effect of immunosuppressive medication in a matched cohort study.

Methods: Patients with SARD were enrolled and matched 1:1 for gender and age with healthy control subjects (HC). Differences in the humoral response to two doses of mRNA vaccine BNT162b2 in terms of seroconversion rate and SARS-COV-2 antibody titer between the two groups and impact of treatment within SARD patients was assessed using Fisher's exact test, Student's t-test, Mann-Whitney test and Kruskal-Wallis test, adjusting for multiple testing.

Results: We enrolled 82 patients with SARD and 82 matched HC (Table 1). Among patients the seroconversion rate was significantly lower after the 1st dose (65% compared to 100% in HC, p<0.0001) but levelled up after the 2nd dose (94% vs. 100%). While the difference in seroconversion rate was independent of treatment regime (no disease modifying anti-rheumatic drug (DMARD), DMARD monotherapy, DMARD combination therapy), the seroconversion rate of SARD patients on mono- or combination DMARD therapy was also significantly lower as compared to those receiving no DMARD therapy (56% for monotherapy and 57% for combination therapy compared to 77% for no DMARD therapy, p=0.002 and p=0.004 respectively; Figure 1A). Seroconversion rate after the 2nd dose was significantly

lower for patients on combination DMARD therapy compared to all other groups (81% compared to 95% for monotherapy, and 100% for both no DMARD therapy and HC respectively, all p<0.0001); also antibody titers after the 2nd dose were lower when comparing patients on combination DMARD therapy to all other groups (49 binding antibody units (BAU)/ml versus 1673 BAU/ml in HC, p<0.0001; 2500 BAU/ml in those on no DMARD therapy, p<0.0001; and 687 BAU/ml in those on DMARD monotherapy, p=0.0072; Figure 1B). Considering effects of individual compounds, mycophenolate mofetil in mono- or combination therapy led to lower antibody titers after the 2nd dose as compared to HC or patients receiving no DMARDs (2 BAU/ml versus 1673 BAU/ml and 2500 BAU/ml respectively, both p<0.0001).

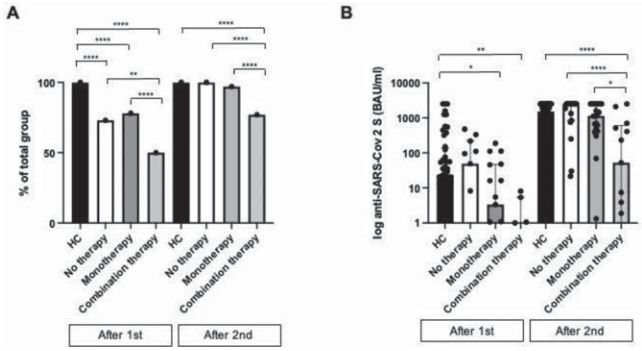

Figure 1. Seroconversion rate (A) and anti-SARS-Cov 2 S antibody levels (B) after the 1st and 2nd vaccination between the healthy control (HC) group and patients according to therapy

Table 1. Study subject characteristics

	SARD (n=82)	HC (n=82)
Age, mean (±SD)	52.05 (±14.06)	52.15 (±13.42)
Female, n (%)	65 (79%)	65 (79%)
Different disease entity, n (%):		
Systemic lupus erythematosus	33 (40%)	
Systemic sclerosis	13 (16%)	
Other connective tissue diseases*	15 (18%)	
Vasculitides#	17 (21%)	
Miscellaneous$	4 (5%)	
Treatment groups, n (%):		
csDMARD or b/tsDMARD monotherapy	43 (52%)	
csDMARD and/or b/tsDMARD combination therapy	16 (20%)	
No therapy	23 (28%)	
Treatment agents, n (%):		
Methotrexate	13 (16%)	
Mycophenolate	14 (17%)	
Hydroxychloroquine	28 (34%)	
Azathioprine	13 (10%)	
Belimumab	3 (4%)	
Tocilizumab	3 (4%)	
Tacrolimus	2 (2%)	
Olumiant	1 (1%)	

*dermato-/polymyositis (n=4), mixed connective tissue disease (n=2), primary Sjögren's syndrome (n=6), undifferentiated connective tissue disease (n=3)#antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (n=3), Behcet's disease (n=1), large-vessel vasculitis (n=3), polymyalgia rheumatica (n=10)$ adult-onset Still's disease (n=1), immune deficiency (n=2), sarcoidosis (n=1)b/tsDMARD: biological/targeted synthetic disease modifying antirheumatic drug; csDMARD: conventional synthetic disease modifying antirheumatic drug; HC: healthy control; n: number; SARD: systemic autoimmune rheumatic disease; SD: standard deviation;

Conclusion: Patients with SARD showed a good response after the 2nd vaccination with the mRNA vaccine. However, the choice of immunosuppressive regimen has a marked effect on both seroconversion rate and overall antibody titer.

Acknowledgements: We thank Sylvia Taxer and Zoltan Vass for their support.

Disclosure of Interests: Peter Mandl Speakers bureau: AbbVie, Janssen, Novartis, Consultant of: AbbVie, Janssen, Novartis, Grant/research support from: AbbVie, BMS, Lilly, Novartis, MSD, UCB, Selma Tobudic: None declared, Helmut Haslacher: None declared, Daniel Mrak: None declared, Thomas Nothnagl: None declared, Thomas Perkmann: None declared, Helga Radner Speakers bureau: Gilead, Merck Sharp, Pfizer, Abbvie, Consultant of: Gilead, Merck Sharp, Pfizer, Abbvie, Judith Sautner Speakers bureau: Otsuka, Novartis, Consultant of: Lilly, Astro Pharma, UCB, Abbvie, Elisabeth Simader Grant/research support from: Pfizer, Bristol-Myers Squibb, Florian Winkler: None declared, Heinz Burgmann: None declared, Daniel Aletaha Speakers bureau: Abbvie, Amgen, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Consultant of: Abbvie, Amgen, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz , Grant/research support from: Abbvie, Amgen, Lilly, Novartis, Roche, SoBi, Sanofi, Stefan Winkler: None declared, Stephan Blüml Speakers bureau: Novartis, Abbvie, Consultant of: Gilead, Merck, Novartis, Abbvie

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AB1136 **PREVALENCE OF COVID-19 IN SYSTEMIC LUPUS ERYTHEMATOSUS: A META-ANALYSIS**

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Background: Novel Coronavirus pneumonia 2019 (COVID-19) is a systemic infectious disease with prominent involvement of the respiratory tract, due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. Systemic lupus erythematosus is charcterized by an aberrant immune response with the presence of circulating autoantibodies, lymphopenia, and proinflammatory[2]. They are immune-compromised and vulnerable to infections with immune-suppressants treatment. However, data regarding the impact of COVID-19 pandemic in patients with SLE and drug use were relatively scarce.

Objectives: The prevalence of COVID-19 in SLE patients was estimated by means of meta-analysis, and the effect of the use of anti-rheumatic drugs on the clinical outcome of SLE patients with COVID-19 was investigated.

Methods: Cross-sectional investigations and case series on SLE and COVID-19 published by CBM, CNKI, China Science and Technology Journal Database, Wan Fang Data, PubMed, Embase, Web of Science, Cochrane Library and Medline from its establishment to November 10, 2021 were searched. Random effects model was used to pool data. Heterogeneity and risk of bias was examined with I-squared index (I^2) statistic. Inconsistency was evaluated by using the I^2. Egger tests were used for the evaluation of potential publication bias (STATA v.12.0).

Results: A total of 14 studies comprising 5365 patients were identified (Table 1). Overall prevalence of COVID-19 in SLE patients was 1.5% (95%CI: 1.2%-1.8%). Eight of the studies included patients who used hydroxychloroquine as part of their treatment regimen, with 29.8% (95%CI: 25.8%-33.8%) hospitalization rates and 14.6% (95%CI: 11.5%-17.8%) adverse outcome rates. Among patients treated with hydroxychloroquine throughout the course of disease, the prevalence was 0.7% (95%CI: 0.4%-1.0%, Figure 1).

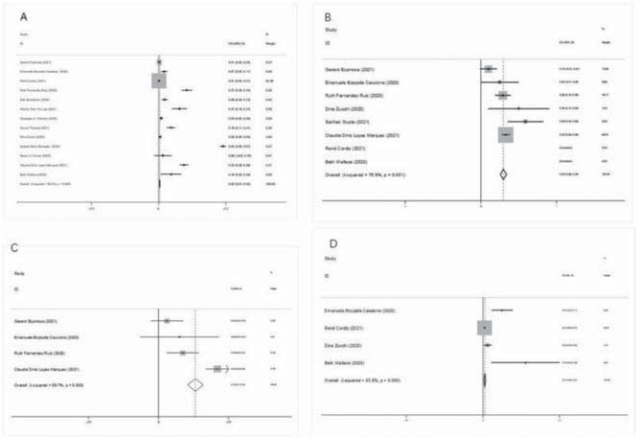

Figure 1. A:Forest map of a meta-analysis of COVID-19 prevalence in SLE patients.B: Forest map of a meta-analysis of hospitalization rates among patients treated with hydroxychloroquine.C:Forest map of meta-analysis of the rate of adverse outcomes in patients using hydroxychloroquine as part of a treatment regimen.D:Forest map of a meta-analysis of the prevalence of patients treated with hydroxychloroquine throughout the course.

Conclusion: Patients with SLE had a higher risk of COVID-19. Hydroxychloroquine might benefit to reduce the overall hospitalization rate and prevalence rate of COVID-19, and alleviate inflammatory damage in the chronic stage of viral infection by inhibiting over activation of the immune system.

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Disclosure of Interests: None declared

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Table 1. Summary of study characteristics of included records.

Author	Total number of patients	Mean/ Median Age	HCQ	Other therapeutic drugs	Number of COVID19 (n)	Mean/Median Age	HCQ	Other therapeutic drugs	Hospitalization (n)	supplemental oxyge (n)	Combined poor outcomes
Gerard Espinosa	400	50.7		GCs:47	4	47.9	22	GCs:12,T-DMARD:28,others:13	3	3	4
Emanuele Bozzalla Cassione	165	52.5	127	T-DMARD:12,others:41	12	52.5	3	GCs:1,others:3			1
Ren: Cordtz	2533	55.4	1170	GCs:685,B-DMARD:42,T-DMARD:374,others:926	16	69.1	5	GCs:4	16		
Ruth Fernandez-Ruiz	226				83	43	32	GCs:18,T-DMARD: 5,others:50	24	19	8
Zos Gendebien	225	51.7	152	GCs:92,T-DMARD:25,others:52	32				2		2
Wendy Wan Hui Lee	85	38.28	58	GCs:54,others:50	23				1		1
Giuseppe A. Ramirez, MD	417			others:389,combination:289	14				1		1
Samar Tharwat	200	30.1	140	GCs:174,B-DMARD:4,T-DMARD:310,others:184	32						
Dina Zucchi	332	47	267	GCs:176,B-DMARD:41,T-DMARD: 118,others:118,combination:112	6	40.3	6	GCs:6,T-DMARD:1, others:6	3	1	1
Sarthak Gupta	17		7	GCs:8	17	46.1	1	GCs:12,T-DMARD:3	10	2	2
Seow Lin Chuah	18				18	38uah			6		7
Claudia Diniz Lopes Marques	110				334	45 (31ques	118	GCs:134,T-DMARD:110,others:284	110	35	78
Beth Wallace	31	61	6	GCs:12,others:4	5	54 (26-67)	4	GCs:4,others:3	5		5
Isabela Maria Bertoglio	382	45.1			382	45.5				206	173

AB1137

USE OF TOCILIZUMAB IN CRITICALLY ILL SARS-COV-2 PATIENTS CARE- PROGNOSTIC FACTORS OF TREATMENT EFFECTIVENESS AND TREATMENT RESULTS

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Background: The treatment of COVID-19 caused by SARS-CoV-2 posed serious challenges to health care systems. In 8-10% of patients with severe COVID-19 have a cytokine storm syndrome, highlighting the importance of host immune response in pathogenesis.

Objectives: Our aim was to evaluate the effect of tocilizumab treatment in COVID-19 patients with severe cytokine storm who were refractory to standard of care therapy. To determine the prognostic factors that indicate the success of treatment in these patients.

Methods: Fifty-three patients were treated with tocilizumab during waves 2 and 3 of the pandemic due to a cytokine storm associated with SARS-CoV-2 infection. All patients underwent physical examination, saturation monitoring, laboratory examination, blood gas analysis and chest CT examination. Deteriorating clinical status, elevated IL-6 and other acute phase protein levels observed in patients treated with standard therapy suggest cytokine storm syndrome. The treatment of these patients was supplemented with 8 mg/kg (max. 800 mg) tocilizumab (1 or 2 times within 24 hours). We assessed the clinical and laboratory response of these patients to IL-6-R inhibitor therapy, the need for ventilation, the need for intensive care and mortality.

Results: Immunological consultations were performed in 31 patients, of whom 21 (68%) were successfully treated. Eleven patients of them (22%) died. In the 22 non-consulted patients, this rate was reversed: 7 (22%) were successful and 15 (68%) were treatment failures. The success of the treatment was mainly influenced by the well-established indication, the recognition of contraindications, and the condition that did not require invasive ventilation method. The 29 tocilizumab therapies initiated in the non-intensive care unit avoided intensive care unit treatment in 18 patients. Eleven patients were admitted to the intensive care unit, but 7 patients required temporary respiratory support and recovered, 4 patients required invasive mechanical ventilation and later died (14%). In contrast, 24 treatments initiated in the intensive care unit saved the lives of only 3 patients, and 21 patients were lost (87.5%). The effectiveness of treatment was not affected by age, with survival rates of 40%, 44%, 57% and 55% for the 40-49, 50-59, 60-69, 70-79 age groups, respectively. Interestingly, the extent of lung involvement also did not show a significant difference. Although it was a prerequisite for initiating tocilizumab treatment to have fresh alveolitis on the CT image of the chest.

Conclusion: Use of tocilizumab is most effective in patients with COVID-19 who have high levels of inflammatory activity and IL-6, who are at an early stage of lung involvement and who do not respond to high-dose corticosteroid therapy, who have no bacterial superinfection and require not invasive mechanical ventilation. It is also important that specialist who has immunological approach and routine with biological treatment be also involved in the care of patients with severe COVID-19 disease.

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Disclosure of Interests: None declared
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AB1138

SAFETY OF SARS - COV- 2 VACCINES IN PATIENTS WITH AUTOIMMUNE DISEASES

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Background: Patients (pts) with autoimmune diseases are at higher risk of infections, including those by SARS-COV-2. There is no general agreement regarding priority criteria for anti-COVID vaccine access for pts with autoimmune rheumatic diseases (ARD). Few studies have addressed the issue of anti-COVID vaccination in these pts, but many are available on the safety, immunogenicity, efficacy, and possible contraindications of traditional vaccines in pts with ARD. These studies may represent the basis on which to recommend the anti-COVID-19 vaccines.

Objectives: Patients (pts) with autoimmune diseases are at higher risk of infections, including those by SARS-COV-2. There is no general agreement regarding priority criteria for anti-COVID vaccine access for pts with autoimmune rheumatic diseases (ARD). Few studies have addressed the issue of anti-COVID vaccination in these pts, but many are available on the safety, immunogenicity, efficacy, and possible contraindications of traditional vaccines in pts with ARD. These studies may represent the basis on which to recommend the anti-COVID-19 vaccines.

Methods: A telephone survey investigating the AE of SARS-CoV-2 vaccinations on pts with systemic lupus erythematosus, systemic sclerosis, inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis), idiopathic inflammatory myopathies, ANCA-associated vasculitis was administered. Data extraction included diagnosis, disease activity status, demographics, disease duration, therapy, comorbidities, and laboratory tests. Vaccinated participants are asked to report whether they experienced any local or systemic AE following vaccination, and if so, to report on the severity and duration of the AE. Mild AE were defined as unpleasant reactions that did not limit daily activities, moderate AE as those that limited daily activities, and severe AE - required medical attention. Serious AE were defined as reactions that resulted in hospital admission.

Results: ChAdOx1 nCoV-19 and BNT162b2 are the most common vaccines in our pts. 98 (39,84 %) of 246 pts received the BNT162b2 vaccine, 95 (38,62 %) - ChAdOx1 nCoV-19 vaccine, 47 (19,10%) - CX-024414 and 6 (2,44 %) were vaccinated with Ad26.COV2-S. 127 (51,63%) pts had at least one mild AE and 51 (20,73 %) pts reported moderate AE. Severe AE were rare - 4 (1,63 %) pts and no serious AE were reported. The most commonly reported AE is pain (40,24 %), redness (30,49 %), swelling (18,7 %) at the injection site, which was consistent across all vaccines for both first and second doses. Systemic AE occurred in 104 (43,27 %) pts, most frequently fatigue (29,67 %), headache (27,13 %) and muscle ache (24,39 %). The symptoms started mostly during the first day post-vaccination and lasted for no more than two days. Joint complaints were reported in 8,94 %, but only a small proportion of pts (2,84 %) reported a deterioration of their autoimmune disease up to 3 months after COVID-19 vaccination. Age was a significant effect modifier in the association between autoimmune status and the risk of moderate or severe AE. Vaccination with ChAdOx1 nCoV-19, female sex, age between 35 - 50 years were independently associated with an increased likelihood of reporting any AE. The current results

support the safety of different COVID-19 vaccines in pts with ARD. This information can help fight vaccine hesitancy in this population.
Conclusion: Our data indicated that COVID-19 vaccines are well tolerated by pts with ARD. We did not observe any serious AE, but the number of pts included in our study is too low to draw conclusions about rare serious events. Additionally, our data suggest that COVID-19 vaccinations do not seem to trigger autoimmune disease flares, which is in accordance with data from previous small studies that assessed consequences of vaccines in pts with ARD.
Disclosure of Interests: None declared
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AB1139 SARS-COV2- INFECTION AFTER VACCINATION AGAINST COVID-19 IN PATIENTS WITH RHEUMATIC DISORDERS IN A REAL LIFE SETTING OF A RHEUMATOLOGICAL OUTPATIENT CENTER

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Background: Coronavirus SARS-CoV-2 and its associated disease COVID-19 have become a worldwide pandemic since its first case in 12/2019. Since approvement of the first vaccines against COVID-19 in Europe in 12/2020 a large vaccination campaign was started. Our patients with inflammatory diseases (ID) were graded as higher risk, thus an early vaccination was possible. Many of our patients used the possibility and got vaccinated. Until now, there is few knowledge about the efficacy and safety of vaccination in patients with rheumatic disorders. There are some reports of less vaccination response in patients with ID (1). First reports of those patients with rheumatological disorder and infection with SARS-CoV2 are available (1,2). Nevertheless, there is few knowledge about SARS-CoV2-infection in patients with ID after vaccination against COVID-19, yet.
Objectives: The aim of our study was to evaluate, how many patients got infected with SARS-CoV2 after vaccination against COVID-19 and the course of the disease.
Methods: All consecutive patients of the routine follow up visits from 07/2021 to 01/2022 in our rheumatological outpatient center were questioned for SARS-CoV2-infection. In case of infection, they were questioned for vaccination status and the course of the disease.
Results: N=1206 patients could be evaluated. N=1183/1206 (98.1%) vaccinations were documented. N=12/1183 (1%) patients got infected with SARS-CoV2 after at least 2 doses of vaccination against COVID-19. N=1/12 (8.3%) patient got infected after 3 doses of vaccination. N=3/12 (25%) received 2 doses Vaxzevira (AstraZeneca), n=2/12 (16,7) patients 1st dose Vaxzevira, 2nd dose Comirnaty (Biontech), n=7 /58.3%) patients two doses Comirnaty. In n=8/12 (66.7%) patients antibody levels were available. N=7/8 (87,5%) patients developed high antibody levels after 2 vaccinations. N=1/8 (21,5%) patient developed any antibodies against SARS-CoV2 after 2 doses of Comirnaty, measured ≥4 months after 2nd vaccination dose. This patient was treated with Abatacept. This patient came down with COVID-19 5 months after complete vaccination and died after long-standing highly intensive care. All other patients developed a mild to moderate course of COVID-19, without need of hospitalizing.
Conclusion: There is a very high number of patients (98,1%), who got vaccinated in a real life setting of our rheumatological outpatient center. We have seen only a low number of SARS-CoV2-infections (1%). Most patients developed high antibody levels after vaccination and fortunately had a mild to moderate course of COVID-19 in case of SARS-CoV2-infection, independently from the different vaccination agents. Nevertheless, 1 patient came down with COVID-19 5 months after complete vaccination and died after long-standing highly intensive care. This patient did not develop any antibodies after vaccination. In conclusion, vaccination seems to be effective in patients with rheumatological disorders. However, we must be aware of the small group of patients without antibody development, since they are at risk to have a fatal course. Yet, antibody testing is not recommended in routine clinical care by official recommendations, largely because it is still unknown which level of antibodies predicts protection (3). The booster campaign and 3rd vaccinations will change the current state again, but a revaluation and further studies will be necessary.
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Disclosure of Interests: Stephanie Gabriele Werner Speakers bureau: Pfizer, Abbvie, Janssen, Grant/research support from: Pfizer, Leander Moll: None declared, Antje Uhlenberg-Moll: None declared, Sabine Mettler: None declared, Hans-Eckhard Langer Speakers bureau: Pfizer, Abbvie, Medac, Janssen, Bristol
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AB1140 IMPACT OF COVID-19 NEWS SOURCES ON RHEUMATOID ARTHRITIS PATIENTS' LIFESTYLE AND THEIR DISEASE ACTIVITY FROM NINJA 2020 COHORT STUDY

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Background: One of the problems with the COVID-19 epidemic is infodemic. Insufficient and inaccurate information can be confusing and hinder treatment. In Japan, tabloid TV show might be an easily accessible source of information, but its reliability is low and it has a harmful effect on patients' mental status and lifestyle. There are no reports to examine what is the source of COVID-19 news for patients with rheumatoid arthritis and how these information affect patients' daily lives and disease activity. By using NinJa, Japanese largest database of rheumatoid arthritis, it may be possible to examine them in detail.
Objectives: To investigate the impact of the COVID—19 news sources on rheumatoid arthritis patients' lifestyle and their disease activity using NinJa 2020 cohort study.
Methods: At the timing of collection of patients' data of NinJa2020, questionnaire about their lifestyle and news source of COVID-19 was given. Questionnaire includes questions about frequency of scheduled visit, going out and exercise, weakness and news source.
Results: 6677 patients out of 15553 patients answered questionnaire. Most patients did not change the interval of scheduled visit. The frequency of hospital visits was "unchanged" in 85.8%, "longer" in 13.6%, and "shortened" in 0.6%. The chances of going out were "unchanged" at 14.4%, "significantly decreased" at 57.5%, "slightly decreased" at 27.8%, and "increased" at 0.3%. 42.6% answered that the amount of exercise did not change, 30.2% answered that it decreased considerably, 26.1% answered that it decreased a little, and 1.1% answered that it increased. Regarding muscular strength and physical strength, 46.0% answered "no change", 19.9% answered "significantly dropped", 33.5% answered "slightly dropped", and 0.6% answered "increased". The media used as information sources are "newspaper (86.4%)", "tabloid show (54.5%)", "family, acquaintances and friends (43.7%)", and "official web of Ministry of Health, Labor and Welfare and academic societies (9.4. %)". Respondents often referred to multiple media and 30.6% of them listed three sources (Figure 1). There was a positive correlation between the decrease in frequency of going out and the number of information sources, and a negative correlation between age and the number of information sources. We also found a negative correlation with age for muscle weakness. No correlation was found between the number of information sources and SDAI, CDAI, HAQ-DI, EQ-5D, HADS (A), HADS (D).

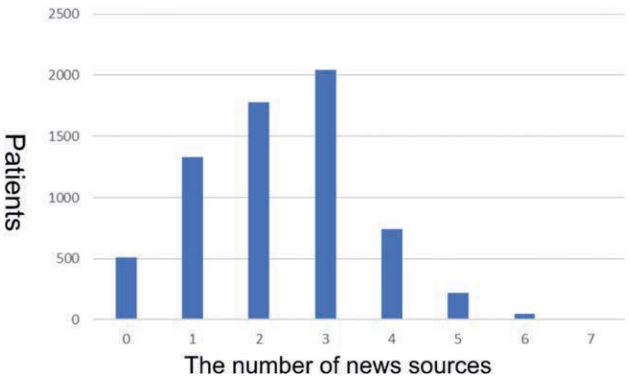

Figure 1.

Conclusion: The more sources of information, the less chance of going out. About 80% of the patients refrained from going out, the opportunity for exercise decreased in more than 50% of the patients, and the decrease in physical fitness was also noticed in nearly 50% of the patients. Newspapers, tabloid shows, and acquaintances were the most common sources of medical information, and relatively few patients used official sources. He provision of accurate information about COVID-19 was important to avoid infodemic. From this questionnaire, more practical information delivery system was required in Japan.
Disclosure of Interests: None declared
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AB1141 **THE PATTERN OF POST COVID-19 REACTIVE ARTHRITIS**

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Background: According to the recent medical literature, COVID-19 disease can lead to a constellation of clinical syndromes lasting well beyond the first 30 days of infection. The most common post COVID sequalae includes pulmonary, nervous system and neurocognitive, mental, metabolic, cardiovascular, gastrointestinal and several other clinical manifestations. Regarding joint involvement and particularly reactive arthritis (ReA), literature data is limited and describes case reports or series of cases of patients diagnosed with this condition following COVID-19 disease.
Objectives: To describe the pattern and the management of post-COVID reactive arthritis.
Methods: We have conducted a descriptive study of consecutive adult patients who presented to rheumatology outpatient clinic for joint or peri-articular pain/swelling/stiffness and received a diagnosis of post-COVID 19 reactive arthritis, by excluding other types of rheumatological conditions. The assessed clinical variables were: visual analogue scale (VAS) pain, swollen joint count (SJC), tender joint count (TJC), duration of morning stiffness, presence of enthesitis/tendinitis and axial involvement. Biochemistry and serology was performed: rheumatoid factor, ACPA, ANA, HLA B27, antiChlamydia Trachomatis, Ureaplasma Urealyticum and Mycoplasma Hominis Ab, anti HBs and HBc Ab, and anti HCV. COVID-19 disease prior to diagnosis of ReA was confirmed by PCR test.
Results: In the study were included 16 patients with confirmed post COVID-19 ReA. The mean age of the study group was 43.5±10.8 (range 21-60), the female: male ratio was 4:1 and the duration of joint symptoms was 10.4±11.8 (range 1-42) weeks. The severity of COVID-19 disease was mild in 68.7% cases, moderate in 18.7% and severe in only 6.2% of the cases. The duration between COVID-19 diagnosis and ReA varied between cases, with a mean value of 4.3±4.2 (range 1-12) weeks. In 43.7% of the cases patients had peripheral joint involvement (synovitis), in 37.5% - periarticular involvement (enthesitis), 6.25% - isolate axial involvement (sacroiliac joints), 6.25% enthesitis and axial involvement (cervical spine) and 6.25% synovitis and enthesitis. In patients with peripheral joint pattern, the distribution of pain was symmetric (71.4%). The pattern of synovitis was determined by a TJC of 6.25±5.2 (range 1-16) joints and SJC 1.6±2.4 (range 0-7) joints. Both TJC and SJC correlated positively with the duration of morning stiffness (r=0.9 and r=0.6), but did not correlate with the VAS pain scale. In most of the cases synovitis affected the hand (wrist, MCP and PIP) 62.5% and the knee, feet and ankles – 50%. Two patients presented with monoarthritis, 1 with oligoarthritis and 5 with polyarthritis, in the majority of cases, involvement being symmetric (75%). Periarticular pattern was determined by enthesitis, affecting the elbow and shoulder (50%), costo-sternal enthesitis (25%) and trochanteritis (25%). From the entire study group, 31.2% had elevated serum inflammatory markers (ESR and/or CRP). Patients responded well to NSAIDs alone in 68.7% cases, local (intra-articular or peri-articular infiltrations) or and systemic corticoids (5 mg Prednisolone equivalent) were administered in 5.3% and 12.5% cases respectively, in 12.5% cases (two patients) Methotrexate was administered.
Conclusion: Reactive arthritis represents a post COVID-19 sequelae. The time of onset of ReA varied between 1 and 12 weeks after COVID-19 diagnosis. The clinical pattern of the disease was expressed by joint or periarticular involvement, mainly affecting the hand, feet and knee symmetrically. Cases of axial manifestations were less common. Most of the patients responded well to NSAIDs, only in a few particular cases, low doses of corticoids and/or Methotrexate were recommended.
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AB1142 **EFFECTS OF SULFASALAZINE USED IN AXIAL SPONDYLOARTHRITIS ON COVID-19 OUTCOMES: REAL-LIFE DATA FROM A SINGLE CENTER**

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Background: Compared to biologic-agents, little is known about effects of sulfasalazine used for axial spondyloarthritis(AxSpA) on COVID-19 outcomes.
Objectives: So, we aimed to understand the impact of sulfasalazine on COVID-19 in AxSpA patients.
Methods: This was a retrospective study from a single center which included 2344 AxSpA patients. We analyzed 219 of 406 confirmed COVID-19 patients from March 2020 to July 2021. The primary outcome was COVID-19 severity in terms of COVID-19 pneumonia, hospitalization rate and length of hospitalization. Analyses were stratified according to use of sulfasalazine and/or biologic-agents.
Results: Most of the patients were male(59%) with a mean age of 45.0 years. Peripheral arthritis was present in 35% and uveitis in 15%. In total, sulfasalazine was used in 42% and biologic-agent in 42%. COVID-19 pneumonia detected in 16%, hospitalization required in 14% and median(IQR) duration of hospitalization was 10(8) days. Two patients died due to COVID-19. The sulfasalazine users had higher age, more frequent COVID-19 pneumonia, hospitalization and longer hospitalization. After biologic-agent users were excluded, the sulfasalazine group had again longer hospitalization. When patients regrouped as sulfasalazine monotherapy, sulfasalazine+biologic and biologic monotherapy, in pairwise comparisons, sulfasalazine monotherapy group had a higher frequency of COVID-19 pneumonia than biologic monotherapy group(p=0.008).
Conclusion: Although sulfasalazine seemed to be related with increased rates of COVID-19 pneumonia and hospitalization, this impact diminished after exclusion of biologic-agent users. Sulfasalazine monotherapy and sulfasalazine+biologic therapy might be associated with development of COVID-19 pneumonia, compared to biologic monotherapy. Our results imply sulfasalazine may be related with worse disease course AxSpA patients with COVID-19.
Disclosure of Interests: None declared
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AB1143 **MUSCULOSKELETAL PAIN AS A PART OF THE RHEUMATIC SPECTRUM IN COVID-19**

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Background: Since the outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for the coronavirus disease 2019 (COVID-19) (1), our understanding of the underlying pathophysiology is constantly evolving in order to explain the wide range of heterogenic clinical manifestations (2). Nevertheless, limited data are available for the severity and multifactorial causality of musculoskeletal pain in COVID-19 patients (3).
Objectives: This study aimed to evaluate the prevalence and intensity of rheumatic pain symptoms – arthralgia and myalgia and their association with anxiety and depression in a cohort of COVID-19 patients, hospitalized at the COVID-19 rheumatology department of the University Hospital St. Marina, Varna, Bulgaria.
Methods: In the present single-center cohort study, a prospective analysis was performed among COVID-19 patients who were hospitalized from 1 Oct 2021 to 20 Jan 2022 and self-reported for new-onset of musculoskeletal pain. All 226 patients (age 26 - 91 years) were treated for moderate or severe SARS-CoV-2 infection confirmed by laboratory tests, including positive antigen test or polymerase chain reaction (PCR) test, and imaging modality. Detailed disease history and clinical examination were carried out by a fully certified rheumatologist. All patients who reported new-onset of musculoskeletal pain during the acute phase of the infection, participated on a voluntary basis in a questionnaire survey, by completed Zung self-rating anxiety scale (SAS), Zung self-rating depression scale (SDS) and visual analogue scale (VAS) for arthralgia and myalgia. The questionnaire form also elicited information on sociodemographic characteristics of the patients. In all patients, inflammation and thrombotic biomarkers were assessed. The level of significance was set to 0.05.
Results: Among all 226 COVID-19 patients with musculoskeletal pain, 46.5% (n =105) were women and 53.5% (n = 121), were men. Mean age was 65.6 years. We found a significant correlation of depression and anxiety scales scores with pain intensity (both arthralgia and myalgia), all < 0.001. A multiple regression analysis found that SDS and SAS accounted for significant variance in the prediction of muscle pain ($\beta = 0.441$, $p < 0.001$; $\beta = 0.293$, $p = 0.003$, respectively) while SDS significantly predicted joint pain ($\beta = 0.341$, $p = 0.043$). On the other hand, musculoskeletal pain does not correlate with any of inflammation and thrombotic biomarkers assessed in SARS-CoV-2 patients ($p > 0.05$).
Conclusion: Rheumatic pain manifestations are part of the heterogeneous spectrum of COVID-19 disease. The pain intensity is significantly associated with

anxiety and depression symptoms and does not correlate with inflammation and thrombotic biomarkers.

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AB1144 COGNITIVE AND PSYCHOSOCIAL OUTCOME IN CHILDREN WITH MULTISYSTEM INFLAMMATORY SYNDROME FOLLOWING SARS-COV-2 INFECTION

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Background: Despite the low rate of neurological deficits following the SARS-COV-2 infection in the pediatric population, children and adolescents who develop multisystem inflammatory syndrome (MIS-C) after being infected with SARS-COV-2 are at a higher risk for neurological abnormalities and brain injury, increasing the risk of adverse cognitive and psychiatric outcome.

Objectives: Given the increased risk of central nervous system impairment we chose to conduct a prospective study looking at the cognitive and psychosocial outcome of patients with MIS-C.

Methods: Our study included 27 of the 29 patients between 2 to 18 years of age (M = 11.1, SD = 4.4) who were treated for MIS-C from the onset of the SARS-COV-2 pandemic until the beginning of May 2021 at the only tertiary care pediatric immunology center in Slovenia. We assessed these patients 6 months after diagnosis using the age-appropriate Wechsler intelligence scales and a battery of neuropsychological test measuring attention, executive function, memory and fine motor skills. We also asked parents to report on patients' psychosocial outcome using the Achenbach Child Behavior Checklist.

Results: By using Bayesian statistics to take into account parental education and any potential pre-morbid learning difficulties we found no evidence of impairment on measures of intelligence. However, the posterior distribution of scores on neuropsychological measures indicated that a significant proportion of patients scored 1SD bellow expected levels on measures of attention (31%), executive function (28%) and visual memory (35%). Increased symptoms of depression, anxiety and attention difficulties were also reported by parents, although their extent did not rise to a clinically significant level.

Conclusion: The findings from our cohort suggest that the cognitive and psychosocial outcome of patients with MIS-C is generally favorable, although up to 35% may experience specific neuropsychological deficits more than 6 months after diagnosis. The most commonly impaired cognitive domains seem to be attention, executive function and visual memory.

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Disclosure of Interests: David Gosar Speakers bureau: Biogen, Novartis, Mojca Zajc Avramovič: None declared, Nina Emersic: None declared, Mateja Šušterič: None declared, Maja Maša Šömen: None declared, Damjan Osredkar: None declared, Tadej Avcin: None declared

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AB1145 EVALUATION OF THE HUMORAL IMMUNE RESPONSE SECONDARY TO VACCINATION AGAINST SARS-COV2 IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES

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Background: Several trials have reported lower seroconversion rates in patients with autoimmune rheumatic diseases than in healthy patients. In Argentina, the vaccines that were available during the development of this study were: Sputnik V (Gam-COVID-Vac), AstraZeneca (ChAdOx1 nCov-19), Sinopharm (BBIBP-CorV) and Moderna (mRNA-1273). Limited information is available about vaccines against SARS-CoV2 with inactivated virus or viral vector in autoimmune patients.

Objectives: To evaluate the humoral immune response to vaccines against SARS-CoV2 in patients with autoimmune rheumatic diseases; to compare the humoral response among patients with Systemic Lupus Erythematosus (SLE) and other autoimmune diseases and to analyse the variables associated.

Methods: We included patients with autoimmune rheumatic diseases (Rheumatology Unit of Padilla Hospital, Tucumán, Argentina), who received vaccination against SARS-CoV2 from June 2021. Sociodemographic, comorbidities, related to rheumatic disease, vaccination and SARS-CoV2 infection were the variables recorded. To evaluate the humoral immune response, the neutralizing anti-S-RBD IgG antibody titres were determined by ELISA "In House" test with a cut-off titre of 200 (IMMCA). The times established for the serological determinations were: T0 or baseline: 1st vaccine dose, T1: 14 ± 2 days after the 1st dose, T2: 2nd dose, T3: 21- 45 days after the 2nd dose, T4: 30 days after the 3rd dose, T5: 6 months and T6: 12 months after the 3rd dose.

Results: 66 patients were included, 91% women and 92.4% Amerindians. The mean age was 40.7 ± 11.4 years; 53% with SLE, 15.2% Rheumatoid Arthritis, 7.6% Systemic Sclerosis, 7.6% Juvenile Idiopathic Arthritis, 7.6% Systemic Vasculitis and 9% other diagnoses; mean disease duration was 12.05 ± 7.5 years; 63.6% had at least one comorbidity (57% HBP, 31% overweight or obesity). At baseline, the treatments received were: corticosteroids (37.9%, prednisone mean dose 4.12 ± 8 mg/day), cDMARDs (75.7%), bDMARDs (18.2%): Rituximab (58.3%) and anti TNF (25%). Sixteen patients (24.2%) had previous COVID19 (75% mild symptoms). The vaccines applied were: AstraZeneca 38.2%, Sinopharm 31.7%, Sputnik V 19%, and combined schedule Sputnik V/ Moderna in 11%. At baseline, 28.8% had detectable anti-S-RBD IgG antibodies. This frequency increased to 48.4% at 1st dose and 70.2% at 2nd dose. The variables that were associated with lower seroconversion rates and lower antibody titre were vaccination with Sinopharm (p 0.028) and treatment with bDMARDs (p 0.02), none of the 5 patients with Rituximab showed seroconversion. There were no significant differences in the levels of anti-S-RBD IgG antibodies between patients with SLE and the other rheumatic diseases. Patients who had SARS-CoV2 infection prior to vaccination had higher antibody titres in both T1 (p 0.006) and T2 (p 0.002) but after the two doses this difference was not significant (p 0.67). In the regression analysis, the variables that were independently associated with seroconversion were the type of vaccine applied at the 1st dose and the hypertensive disease. The chance of responding to vaccination was 13 and 9 times higher for those who received Sputnik V (OR 12.78; 95% CI 1.46 - 315.9) or AstraZeneca (OR 8.61; 95% CI 1.63 - 72.5) respectively, than Sinopharm in the 1st dose. The chance of being a responder was 88% lower for hypertensive patients (OR 0.12; 95% CI 0.02 - 0.58).

Conclusion: In this preliminary analysis, a seroconversion rate of 70.2% was associated with two-dose vaccination for SARS-CoV2 in patients with autoimmune rheumatic diseases. There were no differences in the serological response between patients with SLE and other rheumatic diseases. The humoral immune response was lower in patients with bDMARDs and null in those who received Rituximab. Seroconversion and antibody titres levels were associated with the type of vaccine applied, being Sinopharm who presented the lowest response. The follow-up will provide more knowledge about the behaviour of the humoral response in our patients.

Disclosure of Interests: None declared

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AB1146 SARS-COV-2 VIRAL LOAD IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASE, A RETROSPECTIVE COMPARATIVE STUDY

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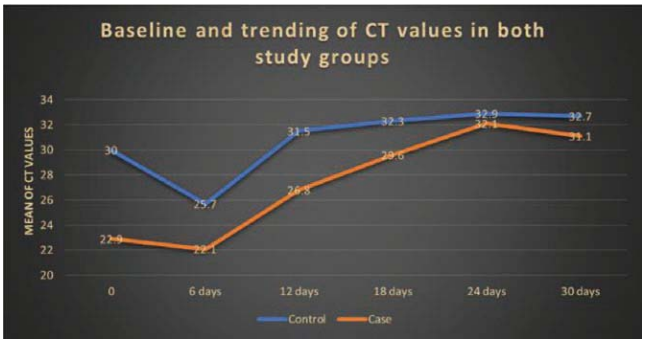
Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral load and its impact on disease outcome in patients with autoimmune rheumatic disease (ARD) are lacking. Also, whether patients with ARD receiving immunomodulators have different viral loads compared to the general population is unknown.

Objectives: To compare the viral load of SARS-CoV-2 and its trending between patients without and with ARD.

Methods: Retrospectively, patients with ARD infected with SARS-CoV-2 were matched by age and sex at a ratio of 1:2 to patients without ARD and not receiving immunosuppression or immunomodulator drugs. Viral load was determined by the cycle threshold (CT) value measured by a number of platforms: (a) Automated Platforms - the Roche Cobas 6800 system using the Cobas SARS-CoV-2 Test targeting the E and orf1a/b genes (Roche, Switzerland) and the Xpert Xpress SARS-CoV-2 targeting the E and N genes (Cepheid, USA); (b) Manual platforms - EZ1 (QIAGEN, USA), QIAsymphony (QIAGEN, USA), and Bioneer ExiPrepTM 96 Virus DNA/RNA kits Catalogue No K4614 (Bioneer, South Korea) extraction with thermal cycling using TaqPath™ PCR COVID-19 Combo Kit targeting the N, S and orf1a/b genes (Thermo Fisher Scientific, USA) on ABI 7500 thermal cyclers. Independent samples t-test was used to compare the mean CT values of the study groups at baseline and at 5 subsequent intervals (1 – 5.9, 6 – 11.9, 12 – 17.9, 18 – 23.9 and 24 – 30 days).
Results: Mean age (SD) of 197 cases and 420 controls were 45.2 (11.8) and 44.1 (12.3) years, respectively. Females were predominant in both groups 60% vs. 52%, P=0.053. The most common ARD was rheumatoid arthritis in 82 cases (41.6%), followed by spondyloarthropathy in 33 (16.8%) and systemic lupus erythematosus in 31 (15.7%). Of the cases, 67% were on conventional synthetic disease modifying anti-rheumatic drugs (DMARDs), 15.2% on biological DMARDs and 4.6% patients were on rituximab. The mean CT values was significantly lower in the ARD group at baseline and persisted till day 24.

Table 1. demographic characteristics and comparison of the mean CT values in the study groups at baseline and at different intervals with the corresponding OR (95% CI)

	Case (N=197)	Control (N=420)	OR (95% CI)
Mean (SD) age, years	45.2 (11.8)	44.1 (12.3)	1.008 (0.994–1.022)
Sex, female N (%)	120 (60.9%)	221 (52.6)	0.713 (0.505–1.006)
Mean (SD) CT values at Baseline	22.9 (5.5)	30 (5.2)	**0.799 (0.745–0.858)**
1 – 5.9 days	22.1 (4.6)	25.7 (6.3)	**0.901 (0.842–0.963)**
6 – 11.9 days	26.9 (4.9)	31.5 (3.9)	**0.802 (0.724–0.888)**
12 – 17.9 days	29.6 (4.1)	32.3 (3.2)	**0.827 (0.743–0.921)**
18 – 23.9 days	32.1 (4)	32.9 (2.5)	0.903 (0.728–1.119)
24 – 30 days	31.2 (1.2)	32.7 (2.6)	0.824 (0.589–1.151)



Conclusion: Compared to patients without ARD, the viral load of SARS-CoV-2 in patients with ARD is significantly higher at baseline testing and persists till day 24. This finding may indicate that patients with ARD are at higher risk of severe SARS-CoV-2 infection and prolonged potential transmission. Clinical outcome correlation is needed.
REFERENCES: None
Disclosure of Interests: None declared
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AB1147

COVID 19 INFECTION IN PATIENTS WITH RHEUMATIC IMMUNE-MEDIATED DISEASES IN A SINGLE UNIVERSITY HOSPITAL. MATCHED CASE-CONTROL STUDY.

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Background: COVID19 may present different degrees of severity. It is generally thought that viral infections in patients with rheumatic inflammatory diseases (R-IMID) or receiving immunosuppressive treatment tend to present more severe disease. However, data comparing the severity of the disease between R-IMID and the general population are scarce.
Objectives: To assess the predisposing factors, clinical-analytical features and severity of COVID-19 infection in R-IMID compare to patients without R-IMID.
Methods: Case-control study in a single University Hospital. We included all consecutive patients with a diagnosis of a R-IMID and a positive test for COVID-19 up to March 31st, 2021. A total of 274 controls were selected for each case, and matched by sex, age (± 5 years), and without previous diagnosis of R-IMID or use of immunosuppresive therapy. Confirmed infection was defined if the patient had a positive nasopharyngeal swab for SARS-CoV-2. COVID-19 case severity was divided into mild, moderate, severe and critical according to the United States National Institute of Health (NIH) COVID-19 guidelines **(1).** Mild/moderate COVID19 was compared with critical.
Results: We included 274 patients (185 women/89 men), mean age 59.1 18 years. More frequent R-IMID were: Rheumatoid arthritis (RA) (n=87, 31.8%), Axial spondyloarthritis/ Psoriatic arthritis (SpA/PsA) (n=90, 32.8%), Polymyalgia Rheumatica (PMR) (n=22, 8%) and Systemic Lupus Erythematosus (SLE) (n=22, 8%) We also included 274 age and matched controls. Main characteristics of patients with R-IMID and controls are shown in **Table 1**.

Table 1. Main clinical and analytical features of patients with R-IMID and matched controls

	R-IMID patients (n=274)	Controls (n=274)	P
Age	59.1±18	58.8±17.3	0.842
Sex F/M, n, (%)	185/89 (67.5/32.5)	185/89 (67.5/32.5)	1
Comorbidities (n,%)			
Hypertension	119 (43.4)	84 (30.7)	**0.0026***
Dyslipidemia	119 (43.4)	79 (28.8)	**0.0005***
Diabetes mellitus	36 (13.1)	37 (13.5)	1
Pulmonary disease	29 (10.6)	32 (11.7)	0.79
Cardiovascular disease	45 (16.4)	33 (12)	0.18
Severity of the disease (n, %)			
Mild	209 (76.3)	204 (74.5)	0.69
Moderate	35 (12.8)	47 (17.2)	0.19
Severe	9 (3.3)	14 (5.1)	0.39
Critical	21 (7.7)	9 (3.3)	**0.04***
Deaths	17 (6.2)	7 (2.6)	**0.0076***
Analytical values, median [25-75th IQR]			
CRP	4.7 [2-9.3]	3.9 [1-7.3]	0.176
Lymphocytes (x103 /µL)	1 [0.6-1.5]	1.1 [0.8-2.5]	0.711
Platelets (x103 /µL)	179 [141-237]	174 [155-211]	0.722
D-Dimer (ng/mL)	999 [342-1417]	548 [336-997]	**0.032***

CRP: C-reactive protein.

Concerning comorbidities, hypertension and dyslipidemia were more frequent in patients with R-IMID (p< 0.05). COVID-19 symptoms' distribution is shown in Figure 1.

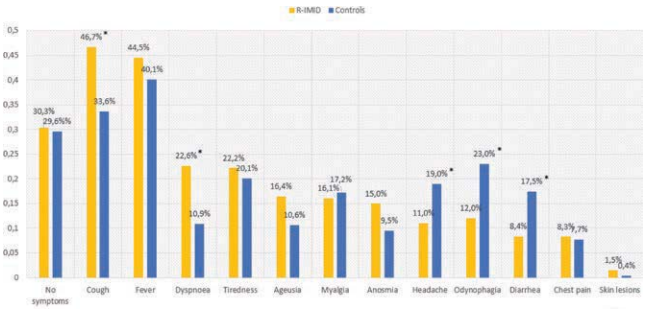

Figure 1. Symptoms in R-IMID patients and matched controls

*: p < 0.05

Cough and dyspnoea were more frequent and headache, odynophagia and diarrhea were less frequent in the R-IMID group. The only analytical difference was D-Dimer that was significantly higher in patients with R-IMID. Although most of the cases were mild, critical cases and deaths were more frequent in R-IMID (p <0.05).
Conclusion: Most of the patients present a mild COVID-19. However, a more severe syndrome was observed in R-IMID

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AB1148 POST COVID-19 RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Recent data suggests that SARS-Cov-2 can alter self-tolerance and trigger autoimmune responses through cross-reactivity with host cells; therefore it can lead to late autoimmune and inflammatory manifestations. With regard to rheumatic and musculoskeletal diseases (RMDs), medical literature displays sporadic case reports describing a variety of conditions diagnosed after COVID-19, but it remains still unclear what are the most common problems in patients presenting to rheumatology clinic following COVID-19 disease.
Objectives: To describe the pattern of post-COVID-19 RMDs in a consecutive group of patients from rheumatology outpatient clinic.
Methods: We have performed an observational descriptive study of a group of adult patients who received a new diagnosis of RMD within a timeframe of 12 weeks after the confirmation of COVID-19. Data was collected based on clinical presentation, paraclinical pattern and radiological examinations.
Results: The study included 23 patients who were consulted in rheumatology outpatient clinic and had post COVID-19 new onset joint, periarticular, bone or inflammatory syndrome manifestations. The general characteristics of the study group were as follows: mean age 45.5±11.3 (range 21-63) years and female to male ratio of 1.8:1. The majority of subjects consulted for joint symptoms (91.4%), in other cases reason for consultation was persistent low grade fever and fatigue (4.3%) and skin rash with dyspnea (4.3%). The mean duration of symptoms was 9.8±10.5 (range 1-42) weeks, and the time of onset after COVID-19 diagnosis was 4.9±4.1 (range 0-12) weeks. Concerning COVID-19 severity, it was established that in 60.9% it was mild, 17.4 % - moderate and 21.7% - severe. After clinical and paraclinical examination, the following diseases were diagnosed: ReA, lupus like syndromes, avascular necrosis, new onset RA and new onset PsA. In 69.7% of patients were diagnosed with ReA, the clinical pattern being joint or periarticular involvement of the hand, knee and feet. In 13.0% cases patients had multisystemic involvement (myocarditis, pericarditis, skin rash, inflammatory arthritis and/or low grade fever) and positive ANA and or dsDNA Ab, these cases were diagnosed as lupus like syndromes and followed a severe form of COVID-19. In 8.7% of patients who presented with non-inflammatory hip pain, avascular necrosis was diagnosed, in both cases femoral head being the affected part. No be noted that patients with avascular necrosis had a severe form of COVID-19 disease and joint pain started later after COVID-19 diagnosis (10-12 weeks). In 4.3% of cases each, new onset RA and PsA were identified.
Conclusion: In the present study we have found that COVID-19 can be followed by a variety of RMDs. The most common symptom of patients presenting with RMD was joint pain. The most common disease was post-COVID ReA (69.7%). Avascular necrosis (8.7%) and lupus like syndromes (13.0%) were found in patients who experienced a severe form of COVID-19. More rarely, patients had new onset of rheumatoid arthritis (4.3%) or psoriatic arthritis (4.3%). Our findings suggest that during the COVID-19 recovery period patients might experience onset of RDMs; therefore, in the presence of joint symptoms or other manifestations suggesting an autoimmune disease, patients should be referred to a rheumatologist for careful clinical examination.
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AB1149 EVALUATION OF THE EFFICACY AND SAFETY OF THE SARS-COV-2 VACCINE IN PATIENTS WITH CHRONIC INFLAMMATORY DISEASES TREATED WITH BIOLOGICAL THERAPY.

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Background: In the current situation of the SARS-CoV-2 pandemic, the Spanish Society of Rheumatology recommends vaccination of patients with chronic inflammatory diseases (CID) under treatment with biological DMARDs (bDMARDs). However, the data regarding the generation of protective antibody titers after mRNA vaccines in patients with CID is limited.
Objectives: To determine the seroconversion rate and safety after the SARS-CoV-2 vaccine in patients with CID under treatment with bDMARDs
Methods: Cross-sectional observational study of 81 patients with CID from the HURS in Córdoba, who have received full vaccination for SARS-CoV-2 (without having previously suffered from COVID-19 disease) according to national guidelines. A determination of specific IgG-type antibodies against the trimeric spike protein of SARS-CoV2 was performed on all of them. The chemiluminescence technique with the kit was used in serum samples taken 4-5 weeks after administration of the second dose of the vaccine. Information about sociodemographic characteristics, disease, type of bDMARDs, concomitant treatments and adverse effects after the second dose of the vaccine were collected in each patient.
Results: 81 patients were included (mean age 59.5, 72.8% females). 50.6% of patients had RA, 17.3% SpA, 11% PsoA and 18.5% other CID. 23.5% were under treatment with Rituximab, 38.8% antiTNF, 13.6% Tocilizumab, 9.9% abatacept, 5% anti-JAK and 14.2% under other treatments. Anti-SARS-CoV-2 antibodies and neutralizing activity were detected in 80% of study participants. Rituximab treatment was significantly associated with negative seroconversion in comparison with patients under antiTNF treatment (OR 84.0 (95%CI 12.9-1709.2)). No interaction was found between the bDMARDs treatment and the type of vaccine with regard to the seroconversion, nor between bDMARDs and concomitant synthetic DMARD. When we evaluated IgG titers against the spike protein of SARS-CoV2, we found that patients under treatment with Rituximab showed the lowest titers levels in comparison with patients with other treatments (Figure 1, Table 1). In addition, patients who received AstraZeneca vaccine developed lower titers of antibodies in comparison with patients who received Pfizer (Table 1).

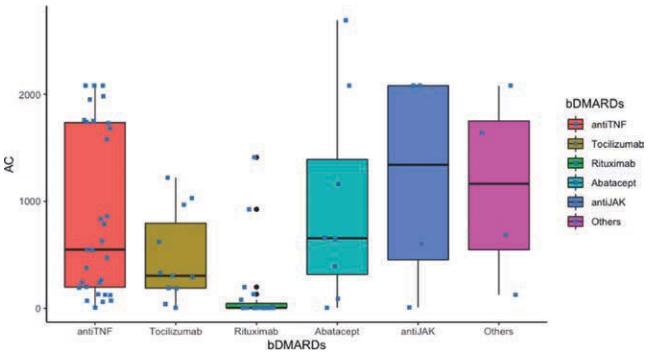

Figure 1. IgG titers against the spike protein of SARS-CoV2 with regard to the bDMARD

Table 1. Linear regressions to evaluate the IgG titers and their association with the bDMARD and the type of vaccine.

	Beta Coefficient (95% CI) IgG titers	p-value
bDMARD	Reference	
- Anti-TNF	-405.6 (-893.7 to 82.4)	
- Anti-IL6	-728.7 (-1133.8 to -323.5)	0.102
- Rituximab	88.7 (-462.8 to 640.1)	**<0.001**
- Abatacept	315.6 (-423.2 to 1054.4)	0.749
- Anti-JAK	256.3 (-482.5 to 995.1)	0.397
- Otros		0.491
Vaccine		
- Pfizer	Reference	
- AstraZeneca	-408.6 (-804.6 to-12.6)	**0.043**
- Janssen	- 783.4 (-1662.1 to 95.3)	0.08
- Moderna	130.6 (-407.5 to 668.7)	0.63
Methotrexate* bDMARD	27.3 (-215.3 to 269.9)	0.823
Leflunomide* bDMARD	208.0 (-188.9 to 604.9)	0.300
Corticosteroides* bDMARD	32.9 (-259.4 to 325.2)	0.823
Vaccine* bDMARD	4.2 (-106.1 to114.6)	0.939

Interestingly, among patients with antiTNF treatment, AstraZeneca was associated with lower IgG titers in comparison with Pfizer and Moderna [405.9 (553.0) vs. 1084.1 (791.2) vs. 1264.0 (1012.6), p=0.016, respectively]. No differences between vaccines were found in patients with the other type of bDMARDs.
Only 18.9% presented mild adverse effects. No serious adverse effects were observed and no patient experienced a disease flare after vaccination.
Conclusion: Our results show that SARS-CoV-2 mRNA vaccines produce seroconversion in most patients with CID, except in the case of patients with rituximab. No severe adverse effects or CID reactivation were found. Despite the small number of patients included, this study suggests the need for revaccination in the group of patients treated with rituximab or vaccinated with Astrazeneca.
Disclosure of Interests: None declared
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AB1150 IMMUNOGENICITY AND SAFETY OF THE CORONOVAC AND BNT162B2 COVID-19 VACCINE IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES AND HEALTHY ADULTS: COMPARISON OF DIFFERENT VACCINES

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Background: Having an autoimmune disease was an exclusion criterion in the efficacy and safety phase studies of vaccines against Covid-19 (1-2). In Turkey vaccination first started with the inactivated CoronaVac, then with the mRNA BNT162b2 vaccine. Although there are studies on vaccine efficacy and safety in adults with inflammatory rheumatic disease (IRD), there are still many unknowns (3-4).
Objectives: Primary outcome of this study is to determine the seroconversion (SC) rate after CoronaVac and BNT162b2 vaccines in adults with IRD and to compare it with a healthy control group. Secondary outcomes are to evaluate whether there are efficacy differences in the two vaccine types, and to investigate the effects of the biologic agent used in the patient group on the vaccine immunogenicity.
Methods: This prospective observational single center study was conducted at the Gazi University Hospital. Patients who were followed up in our outpatient clinic with IRD and who received two doses of either CoronaVac or BNT162b2 vaccines were included. Subjects with two doses one of these vaccine without IRD were included in the healthy control group. Patients who had Covid-19 infection before or during vaccination were excluded. The demographic characters were recorded. The interval between the two doses was 4 weeks. The blood samples of the patient and control groups were taken a minimum of two and a maximum of 12 weeks after the second dose. Anti-S antibodies against SARS-CoV-2 spike proteins were evaluated with the IgG Abbott kit, and a value above 50 arbitrary unit/ml was considered as positive SC. The neutralizing antibody titers were evaluated with the DIA.PRO kit, and cut-off value was above 1 Co/S.
Results: The SC rate was slightly lower among patients with IRD versus controls (84% vs 97%, p:0.002). The SC rate was 100% in all participants who received BNT162b2 both in the patient and control group. The IgG antibody level after CoronaVac was significantly lower than that of BNT162b2 vaccine (p:0.031) in both patient and healthy controls (p:0.001). Among patients with IRD, those on rituximab (RTX)(12/81, %14.8) had significantly less SC rate (5/12, 41.7%) compared to patients on other biologicals (63/69, 91.3%) (p<0.001).
Conclusion: This study showed that all patients with BNT162b2 vaccine developed immunogenicity in patients with IRD, while there was a decreased antibody response with CoronaVac vaccine compared to the healthy control group. In particular, the use of RTX significantly reduces the SC rate.
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Table 1.

	Patients with IRD n:81	Healthy controls n:100	P value
Age (mean±SD)	50.65±1.37	50.65±1.37	
Female	58	65	
-RA	35	N/A	
-SpA	14		
-CTD	20		
-FMF	4		
-Vasculitis	8		
-CoronaVac	61	70	
-BNT162b2	20	30	
Seroconvertion rate (%)	68/81 (84%)	97/100 (97%)	0.002
-CoronaVac	48/61	67/70	
-BNT162b2	20/20	30/30	
IgG (median) (IR)			0.001
-CoronaVac	275.8 (68.95-916.70)	1116.7 (477.70-2074.18)	
-BNT162b2	4007.20 (1904.65-10415.25)	5792.30 (3696.42-9419.85)	
Neutralization (median) (IR)	p: 0.031	p: 0.552	
-CoronaVac	1.97 (0.92-6.82)	N/A	
-BNT162b2	16.34 (13.85-16.67)		
bDMARD/Seroconvertion rate (%)	p: 0.001	N/A	
-naive	52/58		
-RTX	5/12		
-Anti-cytokine	11/11		

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AB1151 DOES PREDNISONE AFFECT COVID19 VACCINE T CELL RESPONSE? A STUDY OF VACCINE RESPONSE IN PATIENTS WITH IMMUNE SYSTEM DISEASES

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Background: A whole blood interferon gamma release assay (IGRA) based on the stimulation of SARS-Cov2-specific memory T cells using purified and full-lenght Spike and Nucleocapsid recombinant proteins was developed, together with anti-Spike antibody detection.
Objectives: To study COVID19 vaccine cellular and humoral responses in patients with immune system diseases (ISD) and healthy controls.
Methods: Non-vaccinated healthy individuals (n=103), SARS-Cov-2 infected individuals (n=9), and 104 samples from individuals having received COVID19 vaccine including 28 non-sars-cov2 infected patients with ISD diseases were included. Preliminary experiments were initiated using different platforms (ELISpot, IGRA, recombinant proteins or peptides) in order to evaluate Spike T cell

response in volunteers vaccinated with BNT162b2 showing a S2>S1 poly-epitopic response.

Results: Twenty-eight patients (25 women, 3 men; mean age 59.1(±17,8)) with various ISD were investigated. These patients suffered from lupus (n=14), vasculitis (n=4), myositis (n=2), sarcoidosis (n=2), primary immunodeficiency (n=3), Sjögren's syndrome (n=2) and pericarditis (n=1). Three patients had received 4 doses, 16 three doses, and 8 two doses of vaccine (Pfizer: n=25; Moderna n=1, Astra-Zeneca n=1). One patient refused the vaccination. The tests were performed 86.7 (±60.5) days after last vaccine dose. Ten patients were on prednisone (mean dose: 11,8 mg, median 7.5 mg, range: 5-40). Among those patients, 6 had only prednisone, 1 was also treated with belimumab, 3 with methotrexate (MTX) and 1 with azathioprine (AZA). Following COVID19 vaccination, humoral (100% in healthy vs 84.6% in ISD patients) and IGRA-Spike T cell (96% in healthy vs 59.7% in AI patients) responses took place with lower response reported among the ISD disease group (Figure 1). Humoral and cellular COVID19 vaccine responses significantly decrease after 100 days post vaccine.

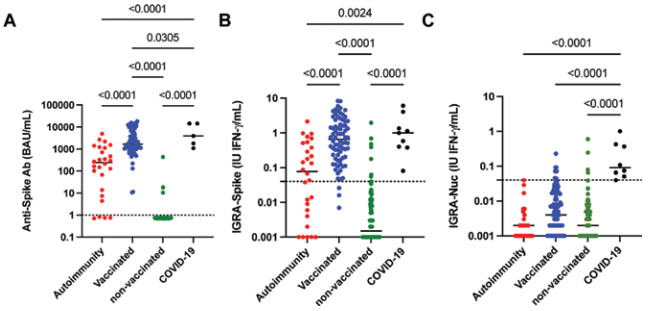

Figure 1. SARS-Cov2 humoral and T cell responses in non-vaccinated healthy individuals (n=103), SARS-Cov-2 infected individuals (n=9), and 104 samples from individuals having received COVID19 vaccine including 28 non-Sars-cov2 infected patients with ISD diseases. A- Anti-SARS-Cov2 Spike total IgM/IgG/IgA antibody (Ab) titers (BAU/mL) tested by ELISA. B- Whole blood IFN-γ release assay (IGRA) response to the full-length Spike recombinant protein (IGRA-Spike). C- Whole blood IGRA response to the nucleocapsid recombinant protein (IGRA-Nuc). Positivity cut-off (dot line) p values <0.05 are indicated when significant (ANOVA).

5/5 vaccinated patients on CS alone, 2/5 vaccinated patients on corticosteroids with MTX/AZA/Belimumab and 3/17 other vaccinated patients (all being primary immunodeficiency patients) had no cellular response. Humoral and T cell responses were independent from sex and age.

Conclusion: Altogether, this ongoing study confirms the utility of the IGRA-Spike/-nucleocapsid assay coupled with serology in COVID19 vaccinated individuals and in particular in ISD patients treated with steroids, who may be at risk when the humoral protection decreases.

References: none

Disclosure of Interests: None declared

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AB1152 COVID-19 MRNA VACCINE BOOSTER IN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES

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Background: Patients with systemic autoimmune diseases (SADs) are often treated with drugs that interfere with the immune system and previous data showed a reduced seroconversion rate after anti-SARS-CoV2 vaccine in these subjects compared to healthy controls[1]. Administration of a booster dose of the vaccine could be particularly important in these patients, but data available to date are still scarce.

Objectives: To evaluate the antibody response to the booster dose of mRNA SARS-CoV2 vaccine in patients with SADs and to compare it to the response after completion of the first vaccination course. Secondly, to find possible correlations between a low antibody titre and patients' clinical features, with special regard to ongoing immunosuppressive therapies.

Methods: Consecutive patients with an established diagnosis of SADs undergoing SARS-CoV2 vaccine were prospectively enrolled from January 2021; among them, we selected the patients who received the third vaccination dose between September and December 2021. Demographic and clinical data were collected at enrolment (sex, age, diagnosis, disease duration, ongoing therapies, previous SARS-CoV2 infection, presence of hypogammaglobulinemia); the last three elements were reassessed at each follow-up visit. Blood samples were collected 4 weeks both after the second (W4a) and the third (W4b) dose of the vaccine; a minority of patients was also tested 12 weeks after the second dose (W12). IgG antibodies to SARS-CoV2 receptor-binding domain (RBD) and neutralizing antibodies inhibiting the interaction between RBD and angiotensin converting enzyme 2 were evaluated. IgG anti-RBD were detected by solid phase assay on plates coated with recombinant RBD, while neutralising antibodies by using the kit SPIA (Spike Protein Inhibition Assay). Cut-off values were defined as the 97.5th percentile of a pre-vaccine healthy population. Statistical analysis was performed using IBM SPSS Statistics 20 and GraphPad Prism statistical packages. P values <0.05 were considered significant.

Results: Forty-five patients (95.6% female; mean age ±SD 55.6±14.1 years; mean disease duration 12.9±10.6 years) were enrolled. Diagnosis was in most cases connective tissue disease (31/45, 68.9%), followed by inflammatory arthritis (11/45, 24.4%) and systemic vasculitis (3/45, 6.7%). Two patients (4.4%) had a previous SARS-CoV2 infection and three had hypogammaglobulinemia (6.7%). At the time of the second dose, 18/45 patients were treated with glucocorticoids (GCs) [mean daily 6-methylprednisolone (6MP) dose 3.9 mg (min. 2, max. 14)], 17/45 with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and 12/45 with biologic DMARDs (bDMARDs). At the third dose administration, 19/45 patients were treated with GCs [mean daily 6MP dose 4.1 mg (min. 1.5, max. 10)], 18/45 with csDMARDs and 13/45 with bDMARDs. Anti-RBD IgG were positive in 42/45 patients (93.3%) at W4a, in 16/18 (88.9%) at W12 and in 42/45 (93.3%) at W4b. Neutralizing antibodies were present in 38/45 patients (84.4%) at W4a, in 14/18 (77.8%) at W12 and in 42/45 (93.3%) at W4b. Both anti-RBD IgG titers and neutralizing antibody titers significantly increased after the third dose if compared to W4a (p<0.0001 both) (Figure 1). Interestingly, of the 7 patients who had not developed an adequate neutralizing antibody response after the first vaccination course, 5 mounted an adequate titer after the booster. Two non-responder patients were both on combination therapy (one with low dose of GCs plus mycophenolate mofetil, the other with methotrexate and infliximab).

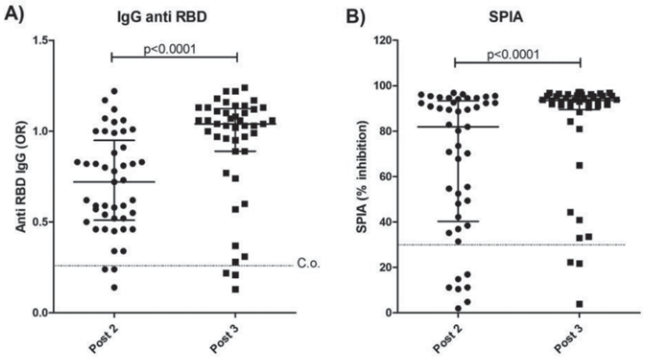

Fig. 1: levels (A) and neutralizing ability (B) of anti-RBD antibodies.

Conclusion: Our data suggest that in patients with SADs there is a decline in the antibody titers developed after COVID-19 vaccination, however the booster dose is effective in restoring an adequate antibody titre. These data consolidate the importance of a booster dose of COVID-19 vaccination in patients with SADs to aid in the generation of an immune response.

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Disclosure of Interests: None declared

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AB1153 HYPEREOSINOPHILIC SYNDROME FOLLOWING THE BNT162B2 (BIONTECH / PFIZER) VACCINATION

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Background: Some reports of small vessel vasculitis following nSARS-CoV2 vaccination are reported in the literature (1, 2).

Objectives: We purpose to report the case of small-medium vessel vasculitis after BNT162b2 (BioNTech/Pfizer) vaccination.

Methods: We present the case of a 48 years old man with an unremarkable history who underwent BNT162b2 vaccination.
Results: Five days after the first shot of BNT162b2 vaccine, the patient refer the onset of left inguinal adenopathy, and erythematous dermatitis of the trunk. Ultrasound of the groin found increase bilateral inguinal lymph nodes with reactive characters. Contextually, erythematous, itchy and painful nodular lesions appear in the lower and upper limbs as well as acrocyanosis and paresthesia in the right hand and foot. The tests performed showed thrombocytopenia and eosinophilia. While, CRP, search for fecal parasites, pANCA, cANCA, ANA, RAST test, serum tryptase were all absent. Haematological evaluation, bone marrow biopsy, karyotype and molecular biology (FIP1L1/PDGFRa), were performed, all results negative. The patient was admitted in Internal Medicine ward for worsening of skin lesions and of acrocyanosis with gangrenous lesions at the tips of the fourth finger of the right hand. An angio-CT showed an occlusion of the right ulnar artery. At electromyography an axonal sensory neuropathy was found. The skin biopsy showed fibrinoid necrosis of venules of the superficial vascular plexus associated with numerous eosinophils, lymphocytes and karyorrhetic debris (Figure 1). High-resolution CT scan described diffuse minimal accentuation of the interstitial texture with micronodular aspects and some ground glass appearance. The diagnosis of hypereosinophilic syndrome was made. Therapy with Methylprednisolone 500 mg/daily for 3 days then Prednisone 1 mg/ kg daily in association with IL-5 inhibitor (mepolizumab) with good clinical response, in addition to anticoagulation with warfarin was started.

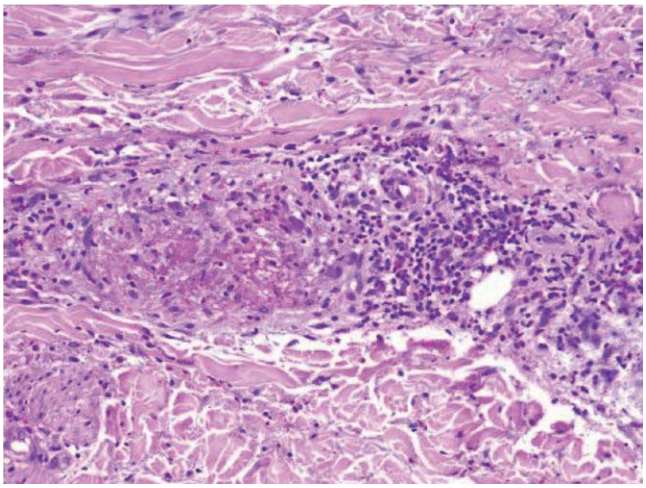

Figure 1.

Conclusion: To our knowledge this might be the first case of (HES) following COVID vaccine. As our experience, due to the short commercialization of antinSARs-CoV2 vaccines, is limited further studies are needed to explore the possible effect on small-medium vessels.
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AB1154 HUMORAL AND CELLULAR RESPONSE TO A THIRD BOOSTER DOSE SARS-COV- 2 VACCINATION IN PATIENTS WITH AUTOIMMUNE DISEASE: A CASE SERIES

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Background: Patients with systemic rheumatic diseases (SRD) are at increased risk for viral infections and successful vaccination is crucial to combat COVID-19 pandemic in this population. However, reduced antibody responses have been described in a proportion of SRD individuals on immunosuppressant agents including mycophenolate (MMF).
Objectives: We aimed to assess humoral and cellular response of SRD patients who received a booster SARS-CoV- 2 vaccination.
Methods: Twenty patients without history of COVID-19 infection (11 men, median age 58 years (range:38-74), 12 on treatment with MMF (2gr daily) due to systemic sclerosis (n= 6), inflammatory myositis (n=4) and systemic lupus erythematosus (n=2) and 8 on tumor necrosis factor-alpha inhibitors (anti-TNF) due to spondyloarthritis (n=5), rheumatoid arthritis (n=2) and Bechet disease (n=1) were included. All were on monotherapy with anti-TNF except patient with Bechet. Patients on MMF discontinued treatment for 1 week after the booster dose whistle no treatment modification was implemented in anti-TNF group. Serological response to vaccination was assessed using the Abbott SARS-CoV-2 IgG II Quant assay. Cellular immunity was estimated via interferon-γ produced by CD4+ and CD8+ T-lymphocytes in response to a SARS-CoV-2 peptide cocktail, with the SARS-CoV-2 ELISA Kit.
Results: Nineteen patients (95%) demonstrated positive serological response following booster vaccine dose (Table 1). Only one female patient in MMF group failed to develop adequate levels of antibodies. The median antibody titers of patients under MMF and anti-TNF was 647.90 BAU/mL (range: 0.71-4795.32 BAU/mL) and 542.98 BAU/mL (range: 4.32-1391.33 BAU/mL) respectively. No statistically significant difference was found between the two groups. Regarding cellular immunity a T-cell response was present in all patients on monotherapy with anti-TNF but only in 7/12 under MMF including the one with negative humoral response.
Conclusion: We report sufficient immunogenicity following a third booster vaccine in patients with RSD on immunossupresive medications coupled by a strong cellular immune response particularly in patients on anti-TNF monotherapy. Perrivaccination management of immunosuppressive therapy represents an important parameter of vaccine administration in patients with RSD.
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AB1155 PAUSING METHOTREXATE IMPROVES IMMUNOGENICITY OF COVID-19 VACCINATION IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Several research groups have recently described a reduced vaccination response to COVID-19 vaccination under methotrexate (MTX) (1,2). The increase in humoral immune response when pausing MTX two weeks after vaccination has already been described for influenza vaccination (3). However, data regarding MTX-hold during COVID-19 vaccination are still lacking.
Objectives: To study the effect of MTX and its discontinuation on the humoral immune response after COVID-19 vaccination in patients with autoimmune rheumatic diseases (AIRD).
Methods: In this retrospective study, neutralising SARS-CoV-2 antibodies were measured after second vaccination in 64 rheumatic patients on methotrexate therapy, 31 of whom temporarily paused medication without a fixed regimen. The control group consisted of 21 AIRD patients without immunosuppressive medication.
Results: MTX patients showed a significantly lower mean antibody response compared to AIRD patients without immunosuppressive therapy (71.8 % vs 92.4 %, $p<0.001$). For patients taking MTX, age correlated negatively with immune response ($r=-0.49$; $p<0.001$). All nine patients with antibody levels below the cut-off were older than 60 years. Patients who held MTX during at least one vaccination showed significantly higher mean neutralising antibody levels after second vaccination, compared to patients who continued MTX therapy during both vaccinations (83.1 % vs 61.2 %, $p=0.001$). This effect was particularly pronounced in patients older than 60 years (80.8 % vs 51.9 %, $p=0.001$). The impact of the time

period after vaccination was greater than of the time before vaccination with the critical cut-off being 10 days.

Conclusion: MTX reduces the immunogenicity of SARS-CoV-2 vaccination in an age-dependent manner. Our data further suggest that holding MTX for at least 10 days after vaccination significantly improves the antibody response in patients over 60 years of age.

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AB1156 COVID19 CLINICAL COURSE AND OUTCOMES IN PATIENTS WITH RHEUMATIC DISEASES: DATA FROM SINGLE INPATIENT CLINIC

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Background: Considerations regarding clinical manifestations and outcomes of COVID19 in patients (pts) with autoimmune rheumatic diseases (ARD) still remain ambiguous.

Objectives: This study aims to assess the clinical course of moderate and sever COVID19 and its outcomes in hospitalized pts with ARD in comparing with osteoarthritis (OA) pts.

Methods: We have analyzed clinical picture and outcomes of COVID19 in 84 pts with RD admitted to inpatient clinic. 36 ARD pts and 48 OA pts were observed during whole period of hospitalization. Clinical, laboratory and instrumental data characteristic of COVID19 were monitored in both groups. The following COVID19 outcomes: ICU admission, mechanical or non-invasive ventilation and death were registered. The impact of concomitant diseases and antirheumatic therapy on adverse outcome was taken into account.

Results: The ARD group preferably consisted of SLE pts (10 pts - 27.78%), RA pts (12 pts - 33.33 %), and systemic vasculitis – SV (12 pts - 33.33%), there were only 2 pts with psoriatic arthritis -PsA (5.56%). In OA group there were 23 pts with knee lesion, 14 pts with hip lesion and 11 pts with both. The structure of ARD and OA groups were similar on demography and associated conditions (CVD, T2DM, obesity). Severe coronovirus pneumonia (CT≥3) was diagnosed in 27.78% pts from ARD group and 35.42% pts from OA group ($p>0.05$, χ^2-criterion). Prevalence of leucopenia, elevated CRP and ferritin in compared groups was comparable, but lymphopenia and elevated IL6 levels>1000 pg/ml were detected oftener in ARD group (77.78% vs 41.46%, $p< 0.05$; 44.44% vs 18.75%, $p<0.05$ respectively). There were no significant differences in mean indexes of WBC (6.55±2.41 vs 6.93±1.84, $p>0.05$), CRP (69.48±9.32 vs 62.19±7.35, $p>0.05$), ferritin (471.03±26.18 vs 428.14±19.02, $p>0.05$). However ICU admission and non-invasive ventilation was oftener in ARD group than in OA group: 38.89% vs 18.75% ($p<0.05$ χ^2-criterion). Fatal outcome was registered in 3 pts (8.33%) from ARD group (SLE -2, ANCA-vasculitis-1) and in 3 pts (6.25%) with concomitant CVD, T2DM and/or obesity from OA group. All deceased pts from ARD group had been treated with GC≥ 8mg, csDMARD and biological agents (rituximab in 2 cases).

Conclusion: The severity of COVID19 clinical course in general was identical in pts with ARD and in OA pts. At the same time lymphopenia and significantly elevated IL6 levels were detected in ARD group oftener than in OA group. Despite the comparable mortality rate in observed groups, more pts from ARD even without concomitant conditions required ICU admission and non-invasive ventilation. Deceased pts with ARD received moderate dose of GC, conventional and biological DMARDs, preferentially rituximab. In OA mortality from COVID19 was associated with CVD and/or metabolic disorders.

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AB1157 CLINICAL CHARACTERISTICS OF PATIENTS WITH RHEUMATIC DISEASES AFTER COVID-19 IN THE REPUBLIC OF TATARSTAN

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Background: The management of patients with rheumatic diseases (RD) who have undergone a new coronovirus infection (NCI) is an urgent and significant problem.

Objectives: To study the course of the NCI and its influence on the course of RD in the Republic of Tatarstan.

Methods: From June 2020 to January 2022, 159 cases of NCI with a confirmed SarsCoV2 PCR result and/or X-ray computed tomography (CT) of the lungs in patients with RD were analyzed. The study included 104 patients with RA, 36 patients with AS, 18 patients with PsA. RD activity before NCI was low in 56 (35.2%) patients, moderate in 91 (57.3%), and high in 12 (7.5%) patients. Distribution by gender: 113 (71.0%) females, 46 (28.9%) males, mean age 58 [46; 64]. 56 patients (49.5%) were hospitalized, the average age of those hospitalized was 61 [49; 67] year. The average duration of RD at the time of NCI was 11 [7; 16.75] years. The results of clinical and laboratory examinations were evaluated before and 1-3 months after the NCI.

Results: Manifestations of infection in patients with RD in terms of frequency and severity were comparable to the course of NCI in the population: intoxication with fever above 38C, respiratory symptoms, ageusia, anosmia, pneumonia. 27.1% (43) of patients had asymptomatic or mild course of COVID-19, 64.1% (102) had moderate course, 8.8% (14) of patients - severe NCI. Lung involvement was detected in 116 (72.9%) patients. Patients received NCI therapy according to national guidelines. The outcome of COVID-19 in 154 (96.9%) patients was recovery, in 5 (3.1%) patients it was fatal, 3 of them were on rituximab therapy. A total of 8 patients received rituximab. After undergoing NCI, 26 (16.4%) patients did not develop an increase in activity, in 76 (47.7%) patients RD corresponded to a moderate degree of activity. In 57 (35.9%) patients RD activity became high, 3 months after the NCI, a significant ($p<0.05$) increase in the activity of the main RD was observed due to clinical and laboratory (C-reactive protein) parameters, which required intensification of antirheumatic therapy.

Conclusion: The prevalence and course of COVID-19 in patients with RD did not generally differ from those in the population. The most unfavorable course of NCI in terms of life prognosis was observed in patients receiving rituximab for underlying RD. The COVID-19 contributes to an increase in the activity of the main RD.

Disclosure of Interests: None declared

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AB1158 CLINICAL CHARACTERISTICS OF POST-COVID SYNDROME IN PATIENTS WITH RHEUMATIC DISEASES IN THE REPUBLIC OF TATARSTAN

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Background: The management of patients with rheumatic diseases (RD) after a new coronavirus infection (NCI) is an urgent and significant problem.

Objectives: To study post-COVID manifestations in patients with RD in the Republic of Tatarstan.

Methods: From June 2020 to January 2022, 154 cases of NCI with confirmed SarsCoV2 PCR and/or X-ray computed tomography (CT) of the lungs in patients with

RD were followed up. The study included 100 patients with RA, 36 patients with AS, 18 patients with PsA. RD activity before NCI was low in 56 (36.4%) patients, moderate in 90 (58.4%) patients, and high in 8 (5.2%) patients. Among the patients, 110 (71.5%) were female, 44 (28.5%) were male, the average age was 58 [46; 64]. 28% (43) of patients had asymptomatic or mild NCI, 66.2% (102) had moderate NCI, and 5.8% (9) of people had severe NCI. Bilateral polysegmental pneumonia was detected in 111 (72.0%) patients. The results of clinical and laboratory examinations for RD were assessed before and 3 and 6 months after NCI. Patients underwent an in-depth survey 3 and 6 months after undergoing NCI for the presence of various symptoms, including manifestations of asthenia. Additionally, the severity of depression and anxiety was assessed using the Hospital Anxiety and Depression Scale (HADS) and the Hamilton Scale.

Results: 90.3% of patients noted the persistence or appearance of symptoms after undergoing NCI, and all of them had a combination of at least 3 different groups of symptoms. The most common asthenic manifestations were in the form of a decrease in the quality of life and working capacity in 85% of patients: significant in 47.9% of people, insignificant - in 38.7% of people. The second most frequent was the intensification/appearance of pain in the joints - 80.5% of the respondents. Strengthening/appearance of muscle pain and/or headache and/or dysautonomia occurred in 47.4%. The appearance/intensification of shortness of breath and a decrease in exercise tolerance were noted by 30.5% of the respondents, while there was no connection with the severity of NCI, and half of the patients had a mild course of COVID 19. The appearance/intensification of chest pain and/or palpitations was noted by 20.8% of people. After 3 months, a decrease in the quality of life, manifestations of depression and anxiety were revealed: 32.2% of people had a mild depressive disorder of moderate severity, 22.3% had clinically expressed anxiety and depression. Six months after the NCI, no abnormalities were detected on the Hamilton scale, and subclinically expressed anxiety/depression on the HADS scale.

Conclusion: In most patients with RD, post-covid manifestations persist, primarily due to general constitutional, articular and cognitive symptoms. Manifestations of NCI itself in the form of respiratory and cardiovascular manifestations persist in less than a third of patients.

Disclosure of Interests: None declared

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AB1159 HYDROXYCHLOROQUINE SHORTAGE AND ITS RELATION TO ANXIETY LEVEL AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS DURING COVID-19 PANDEMIC

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Background: Concerns of hydroxychloroquine (HCQ) shortage for patients with rheumatic diseases are growing during the era of COVID-19 pandemic as it was assigned in some treatment protocols. Its nonavailability may impact the disease management especially in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

Objectives: To evaluate the shortage of HCQ in patients with RA and SLE and its impact on patients anxiety and disease activity.

Methods: 219 RA patients (according to 2010 ACR/EULAR criteria) and 200 SLE patients (according to 2012 SLICC criteria) were recruited in the study. Demographic and clinical features of the patients together with the current disease activity parameters (CDAI and SELENA/SLEADI) were prospectively collected. previous disease activity measures were collected from the patients records before hydroxychloroquine shortage. Patient's anxiety was measured using Hamilton anxiety rating scale.

Results: A total of 419 patients divided into two groups, Group (1); 219 RA patients with mean age 45.6±9.6 years, disease duration 45.5±32.8 months with female predominance (63 %). Group (2): 200 SLE patients with mean age 33.8±7.9 years, disease duration 61.2±39.2 months with female predominance (84%). 168 (76.7%) of the RA patients and 128 (64%) of SLE patients reduced or stopped the dose of HCQ due to unavailability. Despite HCQ shortage, there was no significant change in disease activity in RA or SLE patients (P=0.063 and 0.064 respectively). All participants suffered from different levels of anxiety which was positively correlated with HCQ shortage (p= 0.001 and 0.005 for RA and SLE respectively).

Conclusion: COVID 19 pandemic caused hydroxychloroquine shortage in the majority of patients with RA and SLE with no significant impact on their disease activity. Anxiety was found correlating to HCQ shortage in both diseases more significantly in SLE patients.

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AB1160 IMPACT OF COVID-19 TREATMENTS ON PERIPHERAL CAPILLARY DENSITY EVALUATED BY NAILFOLD VIDEOCAPILLAROSCOPY

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Background: Human SARS-CoV-2 infection can induce a wide spectrum of organ dysfunctions, including microvascular impairment [1]. S_1 subunit of viral receptor-binding domain binds to the angiotensin-converting enzyme 2 receptor on endothelium and S_2 subunit allows the virus to enter endothelial cells. The resulting breakdown of barrier integrity drives a cascade of inflammatory and thrombotic events, that aggravate the course of COVID-19 together with other risk factors [2-4]. Up to date, a lower capillary density has been reported in several distinct body districts, using sublingual video microscopy, ocular optical coherence tomography angiography, skin functional laser Doppler perfusion imaging and nailfold videocapillaroscopy (NVC) [5-8]. NVC examination has been performed in adult COVID-19 patients, however, without a control group [8].

Objectives: To confirm the statistical significance of the reduction in capillary density per linear millimeter evaluated by NVC in comparison with primary Raynaud's phenomenon (PRP) patients and control subjects (CNT) and to evaluate the impact of an aggressive therapy against COVID-19 on the sparing in the number of capillaries.

Methods: Sixty-one COVID-19 survivors, thirty-one PRP patients and thirty CNT age and sex-matched underwent NVC analysis. Demographic and clinical data of COVID-19 survivors were collected with special regard to concomitant therapies, that included antivirals, antibiotics, anticoagulants and anti-inflammatory/immunomodulant drugs (glucocorticoids, hydroxychloroquine, IL-6 receptor antagonist). COVID-19 survivors were divided in two subgroups according to the severity of the active infection: thirty-four survivors with past mild-moderate disease (either unneedy for oxygen supplementation or need for Venturi mask) and twenty-seven survivors with past severe disease (need for Continuous Positive Airways Pressure and/or mechanical ventilation). The same Rheumatologist performed NVC evaluations in all patients and controls, using an optical probe, equipped with a 200x magnification lens and connected to a picture analysis software (Videocap, DS Medica, Milan, Italy). Absolute capillary number per linear millimeter was counted.

Results: COVID-19 survivors underwent NVC examination after a mean period of 126±53 days from the disease onset. Multivariate analysis showed differences in absolute capillary number per linear millimeter ($p<0.001$) after adjusting for age, sex, body mass index, comorbidities and concomitant drugs. The mean (± standard deviation) absolute nailfold capillary number per linear millimeter was significantly lower in severe (8.2±1.15) and mild-moderate (8.4±0.75) COVID-19 survivors than in both PRP (8.7±0.68) and CNT subjects (9.3±0.53) ($p<0.001$). The analysis of the impact of treatments on capillary density in the severe COVID-19 patients showed a positive trend (preservation of the capillary number) with antivirals (no: 7.8±1.53; yes: 8.5±0.64; p=0.35) and anti-IL-6 receptor antagonist administration (no: 7.8±1.36; yes: 8.6±0.74; p=0.16), while none of the other drugs was shown to be effective (glucocorticoids p = 0.46; antibiotics = 0.52; anticoagulants not evaluable as they were used in all COVID-19 patients).

Conclusion: SARS-CoV-2 infection seems associated to a significant capillary loss as distinctive NVC feature and data concerning the comparison of capillary density pre COVID-19 and post COVID-19 are desirable to reinforce this observation. The positive trend in saving the number of capillaries induced by aggressive anti-inflammatory therapies in COVID-19 survivors needs larger cohorts of patients.

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AB1161 COVID-19 IN MY RA CLINIC: DATA FROM QUESTIONNAIRE, VACCINATION, INFECTION AND FLARES FROM THE RA LOUVAIN BRUSSELS COHORT

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Background: Over 5 million deaths from the COVID-19 disease have been reported in the world. Patients (pts) living with rheumatoid arthritis (RA) affecting the immune system or under immunosuppressive agent are considered as a high risk population for a SARS-CoV-2 infection. Since no antiviral treatment is available, the vaccination is a major option.
Objectives: The aim of this study is to evaluate in our RA cohort a questionnaire about the COVID-19 vaccination willingness, to analyse the vaccination rate, the number of COVID infection, the RA flares and the side effects.
Methods: We included pts with RA from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria. A simple and standard questionnaire about the vaccine willingness was distributed in 2020 before the vaccination. From January to December 21, the rate of vaccination was calculated. The number of Covid infections, RA flares, therapy switches and side effects were also collected. All patient and RA characteristics were analyzed.
Results: 605 eligible RA pts were included. The average age of the population is 58.21 years. 72% of the patients are women. 21% are smokers and 65% are positive for anti-citrullinated protein antibody (ACPA) with a mean DAS28-CRP of 2.39 and a mean HAQ of 0.821. In 2020, 460 pts filled the questionnaire and 61% indicated they would receive the vaccine as soon as it is available. For the 179 pts (39%) who decline, the reasons for not having vaccine were no trust in the vaccine at this time (53%), fear of side effects (28%), opposition to vaccine (4%), previous SARS-CoV-2 infection (2%) and unknown (5%). Pts under the age of 50, women, low education grade, smokers, presence of RF/ACPA and treatment with a bioDMARD were less willing to receive the vaccine. In 2021, 538 pts were vaccinated and only 67 pts (11.1%) not. The majority received a mRNA vaccine (81.8%). 72 and 21 pts developed a SARS-CoV-2 infection before and after the vaccination, respectively. Among them, 5 were admitted to intensive care unit leading to 4 deaths. Only, 7 RA flares were observed and 17 pts switched the therapy. 101 adverse events were reported. All of them were mild and transient except 2 cases with pulmonary embolism and one case with Herpes Zooster infection.
Conclusion: The SARS-COV-2 global pandemic is responsible of many medical dramas. In our RA cohort, we observed first hesitation followed by a high rate of vaccination. The safety was reassuring with a minimal number of RA flares and serious adverse events including only 4 deaths.
Acknowledgements: This work was supported by CAP48/RTBF.
Disclosure of Interests: None declared
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AB1162 THE LINK BETWEEN INFLAMMATION AND THROMBOSIS: CLINICAL AND IMMUNOHISTOCHEMICAL CHARACTERIZATION OF PULMONARY ARTERIAL THROMBOSIS IN COVID-19 PATIENTS

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Background: Coronavirus-19 disease (COVID-19) has been responsible, to date, for more than 5 million of deaths. Immunothrombosis may be a major factor contributing to mortality in COVID-19 and pulmonary arterial tree involvement that mimics multiple pulmonary embolism could be a major contributor to disease course. Immunomodulatory drugs are of some benefit but mechanism not completely clear. We investigated pulmonary arterial tree clots to better appreciate their immunothrombotic nature, in contrast to the pathological characteristics of non-inflammatory thrombi (1).
Objectives: The primary objective was to study in depth the arterial thrombosis in COVID-19, by characterizing the immunohistochemical nature of thrombi, performing macroscopic and microscopic analyses, and by comparing clinical, laboratory and anatomical-pathological data of these patients with other patients died for COVID-19 but without evidence of pulmonary arterial thrombosis.
Methods: Autopsies were performed in patients (cases) who died for COVID-19 with evidence of pulmonary arterial thrombosis at autopsy finding but without pathological signs of bronchopneumonia or peripheral venous thrombosis. COVID-19 positive patients without pulmonary arterial thrombosis were selected as control group. Hematoxylin and eosin stained slides were reviewed choosing those with visible pulmonary thrombi. Further histochemical and immunohistochemical staining were performed in selected paraffin blocks. Each component of the thrombus was evaluated with the software application QuPath in terms of fibrin, red blood cells, platelets and immune cells percentage after scanning the slides with Aperio System. Laboratory tests were recorded at 2 points: at hospital admission and at Intensive Care Unit transfer.
Results: We included 13 patients (cases) and 14 controls, matched for age, gender and time from diagnosis to death. Twenty arterial thrombi were studied. By immunohistochemistry, arterial thrombi were composed by white blood cells (WBC) [median, IQR range: 10% (5-12.25)], mainly neutrophils [58% (35.2-64.5)], red blood cells [12%, (6-34.25)], fibrin [19% (14.5-42.25)], platelets [39%, (31.75-48)] (Figure 1). Three cases had a history of previous thrombosis. All cases had received anticoagulant treatment during hospitalization, low molecular weight heparin in 12/13 (therapeutic regimen in 4/12, prophylactic in 8/12) while 1/13 continued oral anticoagulants for comorbidity. By comparing laboratory findings between cases and controls, cases showed significantly higher levels of platelet count [median, IQR range: 195000/mmc (157750-274500) vs 143500 (113000-175250), p=0.011], LDH [854 U/l (731-1315) vs 539 (391.5-660), p=0.003)] at hospital admission, and D-dimer at ICU transfer [25072 FEU (6951-50531) vs 1024 (620-5501), p=0.003)].

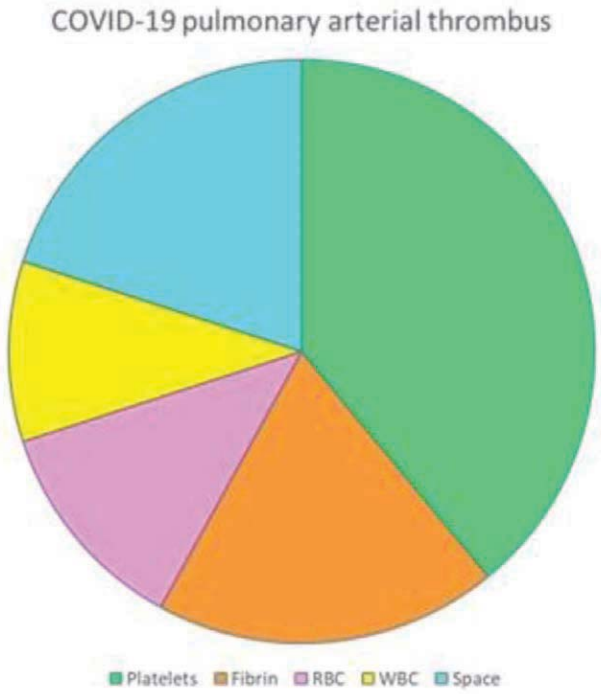

Figure 1.

Conclusion: Pulmonary arterial thrombosis in COVID-19 is a type of immune-mediated inflammatory thrombosis, since the amount of WBC is 6-times more than normal value seen in non-inflammatory thrombi. Some markers of inflammation, necrosis and coagulation are much more increased in this subset of patients. Chest CT angiography rather than simple CT scan at hospital admission could be more useful in this setting, and treatments with antiplatelet agents or anticoagulants, eventually in combination with immunotherapy, might positively affect the outcome.
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AB1163 ATTITUDES AND HESITANCY IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES TOWARDS SARS-COV-2 VACCINATION: A SINGLE-CENTER STUDY FROM BULGARIA

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Background: Bulgaria is among the countries with the lowest vaccination rate of adult population in Europe. The presence of autoimmune rheumatic disease could further contribute to vaccine hesitancy and skepticism and influence patients' attitudes towards vaccination [1, 2]. However, little is still known about the willingness and particular causes of hesitancy in patients with inflammatory joint diseases in the skeptical part of adult population across Europe.
Objectives: Our goal was to assess the rate of SARS-CoV-2 vaccination among patients with immune-mediated rheumatic joint diseases receiving biological and targeted synthetic disease-modifying antirheumatic drugs (DMARDs) and to determine the modifiable predictors of vaccination hesitancy.
Methods: Patients with rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis undergoing biological or targeted synthetic DMARDs therapy were consecutively selected and included in this single-center cross-sectional study. Excluding criteria in patients were psychiatric or neurological disease preventing understanding or responding to the questions, being illiterate, or not willing to participate in the study. Various demographic, anthropometric, and clinical data were collected. Disease activity was determined using DAS28-CRP for rheumatoid arthritis and peripheral psoriatic arthritis and ASDAS for ankylosing spondylitis and psoriatic spondylitis. All patients were given a questionnaire assessing their vaccination status, hesitancy, and attitude towards vaccination. Binary logistic regression analysis was used to analyze the relationship between self-reported modifiable parameters and vaccination status for SARS-CoV-2.
Results: Two hundred and one participants were eligible for participating in the study with mean age and BMI of 54.6 years and 28.2, respectively. Of these, 40.3% were women; 30.3% had rheumatoid arthritis, 17.9% - psoriatic arthritis, and 51.7% - ankylosing spondylitis. 29.4 % of all participants had already survived a COVID-19 infection with a mean time of 8.4 months since the COVID-19 onset. Only slightly above 1/3 (35.8%) of the study group was fully vaccinated and the majority of them were vaccinated with BNT162b2 (68.1%). Among the modifiable factors, we identified preceding discussion with a rheumatologist, hesitancy due to autoimmune disease presence and (un)awareness of vaccine safety and efficacy as significant predictors of vaccination status
Conclusion: Our data suggest that there are still possibilities to influence rheumatic patients on their decision to vaccinate against SARS-CoV-2 in Bulgaria. Raising the awareness of the safety and efficacy of the SARS-CoV-2 vaccines and spending more time on the education of patients with rheumatic diseases may positively affect their attitude towards vaccination.
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Disclosure of Interests: None declared
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AB1164 EFFICACY AND TOLERABILITY OF THE VACCINE AGAINST SARS- COV-2 IN PATIENTS WITH SJOGREN'S SYNDROME RECEIVING VARIOUS TYPES OF THERAPY.

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Background: there are some concerns among patients (pts) with rheumatic diseases regarding the tolerability and efficacy of SARS-CoV-2 vaccination. The impact effect of vaccination on the course of Sjogren`s syndrome (SjS) is not entirely clear.
Objectives: to evaluate the efficacy and tolerability of the heterologous recombinant adenovirus (rAd)-based vaccine Sputnik in pts with SjS receiving various types of therapy.
Methods: single center observational retrospective study. Diagnosis of SjS was based on ACR/EULAR 2016 criteria. Rituximab (RTM) was administered in two 1000 mg infusions 14 days apart for the 1 st course, then 500 mg every 6 months.
Results: 70 pts with a definite diagnosis of SjS were included in the study. Four out of 70 were women. The mean age was 52.5±14.6 years, the average duration of the SjS was 72 (36-120) months. Three pts had concomitant RA, 3 pts - SLE, 2 pts - Systemic sclerosis. Extraglandular manifestations of SjS were detected in 35 cases. Five pts received single-dose rAd26 vector-based COVID-19 vaccine "Sputnik Light", other 65 pts received 2 doses of Gam-COVID-Vac (Sputnik V). Eighteen pts did not receive any immunosuppressive therapy and were vaccinated before RTM therapy. One patient of them just diagnosed with lymphoma, 8 pts had extraglandular manifestations of the SjS (hypergammaglobulinemic purpura, cryoglobulinemic vasculitis with polyneuropathy, interstitial lung disease). 20 pts at the time of vaccination received various immunosuppressive drugs: 1 – cyclophosphamide (CYC), 1 – leflunomide, 1 – Azathioprine, 3 – methotrexate, 2 - mycophenolate mofetil (MMF), 10 – hydroxychloroquine, 13 - low doses of methylprednisolone. Thirty-two pts received anti B-cells therapy with RTM. The duration of RTM therapy before vaccination was 18 (12-36) months, the period of time between the last injection of the RTM and the vaccine was on average 6 (5-8) months. B-cells level was determined in 18 pts immediately before vaccination and it was normal only in 10 pts. The level of neutralizing antibodies after vaccination was monitored in 44 pts. The level of IgG antibodies against SARS-CoV-2 was positive in 15 of 22 pts who did not receive RTM and in 10 of 22 pts who received the RTM ($p>0.05$). Neutralizing antibodies did not develop in 4 pts despite complete recovery of B cells. It is important that none of the vaccinated pts was infected COVID-19 within at least 6 months after vaccination. Various types of adverse reactions were observed in 8 pts. The most common was flu-like syndrome. In one case this syndrome required the prescription of dexamethasone. In 3 cases disease exacerbation occurred after vaccination. These pts had extraglandular manifestations of SjS and received immunosuppressants (CYC, MMF or RTM), 2 of them required treatment intensification, in one case the exacerbation was self-limiting.
Conclusion: vaccination against SARS-CoV-2 infection was well tolerated by pts with SjS even in the absence of immunosuppressive therapy. In most cases, there were no exacerbation of the SjS and pts could continue immunosuppressive therapy without becoming infected COVID-19.
Disclosure of Interests: None declared
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AB1165 THE ROLE OF MOLECULAR MIMICRY IN SARS-COV-2 RELATED AUTOIMMUNE RHEUMATIC DISEASES

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Background: Several studies suggested that SARS-CoV-2 infection may induce autoantibodies related to autoimmune rheumatic diseases (ARD).
Objectives: To determine whether polyclonal antibodies from SARS-CoV-2 uninfected patients with ARDs cross-react with SARS-CoV-2 and vice versa.
Methods: 90 sera positive at high-titres for 23 common autoantibodies (all sera stored before 2018), were tested for reactivity against proteins of SARS-CoV-2 (spike protein S1, nucleocapsid NC etc) by ELISA and CMIA. Vice versa, 10 monoclonal antibodies against S1 protein (most of them against RBD) were tested for autoantibody reactivity by indirect immunofluorescence, ELISA, immunoblot and dot/line immunoassays coated with different antigens. Ten post-COVID sera with high titers of anti-Spike abs were tested by ELISAs for reactivity against various autoantigens related to ARDs.
Results: 88 out of 90 samples (%), were totally unreactive to SARS-CoV-2 proteins; 2 sera, one anti-CCP and one anti-CENP reacted against S protein. All sera tested negative for neutralized abs against SARS-CoV-2. None of 10 sera from SARS-CoV-2 infected patients reacted with different autoantigens by molecular assays. None of the 10 monoclonal abs against S1 protein reacted with 23 different self-antigens. On HEp2 cells as substrate for IIF, 3 of the 10 monoclonal abs gave a low-titre coarse speckled pattern. No reactivity was found by IIFL using tissue substrates.
Conclusion: Our data do not suggest a dominant role for molecular mimicry and immunological cross reactivity as a trigger of autoantibodies related to ARDs.
Disclosure of Interests: Christos Liaskos: None declared, Eleni Patrikiou: None declared, Lars Komorowski Employee of: emploee of EUROIMMUN Medizinische Labordiagnostika, Christina Tsigalou: None declared, Alexandra Tsirogianni: None declared, Lazaros Sakkas: None declared, Dimitrios Bogdanos: None declared
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AB1166 MYOCARDITIS FOLLOWING MRNA COVID VACCINE COMPARED TO PAEDIATRIC MULTISYSTEM INFLAMMATORY SYNDROME MULTICENTER RETROSPECTIVE STUDY

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Background: Since the development of COVID 19 vaccines, more than 300 million people have been immunized worldwide. Soon after vaccinations were initiated, reports on cases of myocarditis following the second vaccine dose have emerged.
Objectives: This study aims to report our experience with nine patients with post COVID-19 vaccine myocarditis, and to compare them to a cohort of patients who presented with paediatric inflammatory multisystem syndrome (PIMS / PIMS-TS) post COVID 19 infection.
Methods: We collected all reported cases of patients who developed myocarditis following COVID 19 vaccination (Pfizer mRNA BNT162b2), from all pediatric rheumatology centers in Israel, and compared them to the cohort of patients previously diagnosed with PIMS.
Results: Nine patients with myocarditis post-vaccination were identified and compared to 78 patients diagnosed with PIMS. All patients with post-vaccination myocarditis were males who developed symptoms following their second dose of the vaccine. Patients with myocarditis post-vaccination had a shorter duration of stay at the hospital (4.4±1.9 vs. 8.7±4.7 days), less myocardial dysfunction (11.1% vs. 61.5%), and all had excellent outcomes as compared to chronic changes among 9.2% of patients with PIMS.
Conclusion: The clinical course of vaccine-associated myocarditis appears favorable, with resolution of symptoms in all the patients in our cohort. The risk–benefit decision for vaccination remains highly favorable, given the potential morbidity of patients with COVID-19, especially those with PIMS.
Disclosure of Interests: None declared
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AB1167 THE USE OF ORAL AMINO-BISPHOSPHONATES AND CORONAVIRUS DISEASE 2019 (COVID-19) OUTCOMES

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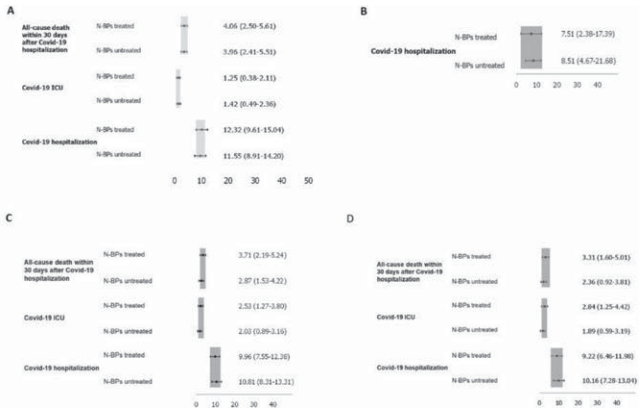
Background: The determinants of the susceptibility to SARS-CoV-2 infection and severe Coronavirus Disease 19 (COVID-19) manifestations are yet not fully understood. Amino-bisphosphonates (N-BPs) have anti-inflammatory properties and have been shown to reduce the incidence of lower respiratory infections, cardiovascular events and cancer.
Objectives: We conducted a population-based retrospective observational case control study with the primary objective of determining if oral N-BPs treatment can play a role in thesusceptibility to the development of severe COVID-19.
Methods: Administrative ICD-9-CM and ATC data, representative of Italian population (9% sample of the overallpopulation), were analyzed. Oral N-BPs (mainly alendronate and risedronate) were included in the analysis. Patients treated with bisphosphonates (cases) were randomly matched (1:1 ratio) for age, sex and for other clinically relevant variables (presence of treatments other than bisphosphonates and hospitalizations) with all the health-assisted population without this treatment (controls).
Results: Incidence of Covid-19 hospitalization was 12.32 [95%CI 9.61-15.04] and 11.55 [95%CI 8.91-14.20], of ICU utilization due to COVID-19 was 1.25 [95%CI 0.38-2.11] and 1.42 [95%CI 0.49-2.36] and of all-cause death was4.06 [95%CI 2.50-5.61] and 3.96 [95%CI 2.41-5.51] for oral N-BPs users and non-users, respectively (Figure 1A). Figure 1B Incidence and 95% CI of COVID-19 related events in N-BPs treated and untreated subjects with anti-osteoporotic drugs and without corticosteroids. C. Incidence and 95% CI of COVID-19 related events in N-BPs treated and untreated without previous vertebral or hip fragility fractures. D. Incidence of COVID-19related events in bisphosphonates treated and untreated patients without previous vertebral or hip fracture without corticosteroid prescriptions.
Conclusion: In conclusion, we found that the incidence of COVID-19 hospitalization, intensive care unit (ICU) utilization and COVID-19 potentially related mortality were similar in N-BPs treated and non-treated subjects. Similar results were found in N-BPs versus other anti-osteoporotic drugs. We provided real-life data on the safety of oral N-BPs in terms of severe COVID-19 risk on a population-based cohort. Our results strongly support national and international guidelines that advocate against the discontinuation of oral bisphosphonates only for the fear of COVID-19.



Disclosure of Interests: None declared
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AB1168 CLINICAL AND SEROLOGICAL EVOLUTION OF RHEUMATIC PATIENTS INFECTED BY SARS-COV-2

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Background: SARS-CoV-2 infection is a public health problem due to its high contagiousness and mortality. Spectrum of symptoms ranges from no symptoms to interstitial pneumonia. Patients with rheumatic disease present an increased infectious risk, especially those treated with immunosuppressants or biologic therapy. Since the beginning of the pandemic, risk of contagion and development of complications in these patients has been questioned.
Objectives: To describe hospitalization prevalence, seroconversion, and symptoms in patients under follow-up by the rheumatology department of a tertiary hospital.
Methods: Observational, cross-sectional study conducted by phone interview including patients with different diagnosis of rhematic diseases. Data about symptoms, hospital admission, serology by ELISA (when >15 days of evolution), diagnosis and baseline treatment, from March 2020 to February 2021 were collected.
Results: Eighty-six patients with different rheumatic diseases and positive COVID-19 PCR were included (82.35% women) in Table 1. Mean age was 49.30 years (16.16). The 48.71% received biological therapy, JAK inhibitors or apremilast, with a median of 3.11 years (Q1 1,08; Q3 3,17). Secukinumab was the biological therapy most often used (24,32%), followed by Tocilizumab (13,51%). The 34,18% received DMARDs or immunosuppressors, with a median of 5.09 years (Q1 12,25; Q3 11.09). The most frequent symptoms were asthenia (72.15%), headache (66.23%) and cough (59.49%). Nine patients (11.25%) were admitted to hospital, eight of them (10%) for pneumonia. Three of them were admitted to intensive care and one died.

Table 1.

Diagnosis	Number (%)
Rheumatoid arthritis	24%
Psoriasic arthritis	16%
Ankylosing espondilitis	16%
Systemic erythematosus lupus	8%
Juvenile idiopathic arthritis	8%
Systemic sclerosis	7%
Behçet disease	5%
Sjögren syndrome	3%
Mediterranean fever	3%
Sarcoidosis	1%
Granulomatosis with polyangitis	1%
Mixed connective tissue disease	1%
Leucocitoclastic vasculitis	1%
Rhupus	1%
Rheumatic polymyalgia	1%
Dermatomyositis	1%
Cutaneous panarteritis	1%

Seroconversion occurred in 53.25%. low IgG titers were present in 2.94% and IgM persisted positive in 56.25% of this group. In 6.45% the result was indeterminate.
Conclusion: Hospitalization and mortality rate obtained was low and the most frequent symptoms were mild. Seroconversion occurred in more than 50% of patients and the result of 6.45% was indeterminate. It's important to highlight that since March 2020 to May 2020 IgG positive prevalence was 25%, while since September 2021 to February 2021, this prevalence increased until 57,45%. This difference is due to a modification of autoantibody detection technique since summer 2020.
Disclosure of Interests: None declared
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AB1169 IMMUNOMODULATORY EFFECTS OF SARS-COV-2 VACCINATION: INCREASE OF REGULATORY T CELLS AFTER MRNA VACCINE

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Background: Besides the ability to induce antigen-specific responses, vaccines can be endowed with immunomodulatory properties including the capacity to induce or downregulate regulatory T cells (Treg) that suppress adaptative and autoreactive immune responses (1).
Objectives: We asked if an anti-SARS-CoV-2 mRNA vaccine could also induce an accumulation of Treg cells in patients with mixed cryoglobulinemia vasculitis (MCV), who have a deficiency of Treg cells (2) and in healthy individuals. We also investigated immunologic variables possibly associated with a low immunogenicity of SARS-CoV-2 mRNA vaccine in patients with MCV (3).
Methods: We analyzed peripheral blood lymphocyte subpopulations and anti-SARS-CoV-2 serological response in 24 patients with MCV and 9 Healthy donors (HD) before and after 2 weeks after the second dose of the Pfizer/BioNTech vaccine.
Results: Among MCV patients we found 15 serological responders and 9 non-responders. All 5 seronegative patients treated recently with rituximab had <5 B cells/μL, whereas the absolute B cell count was increased in 2 of 4 untreated patients due to monoclonal B cell lymphocytosis, with monoclonal cells representing more than 90% of B cells, associated with non-Hodgkin lymphoma. The percentage of pathologic $CD21^{low}$ B cells was significantly increased in seronegative patients. Before receiving the Pfizer/BioNTech vaccine, patients with MCV had a significantly reduced frequency of Treg cells among $CD4^+$ T cells compared to HD. After the second dose of the vaccine, there was in MCV patients a significant increase in the percent and absolute count of Treg among CD4+ T cells Concerning the pre-vaccination distribution of T cells subpopulations, including the percentages and absolute counts of total $CD3^+$, $CD4^+$, $CD8^+$, HLA-DR^+ activated, Treg or $CD56^+$ natural killer T cells, we could not reveal any pattern significantly associated with lack of serological response to vaccine.
Conclusion: Our findings show that lack of immunoreactivity in patients with MCV may be associated with expansion of pathologic B cells and that anti-SARS-CoV2 mRNA vaccine may induce an increase of Treg cells.
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Disclosure of Interests: None declared
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AB1170 IMPACT IN PRENATAL EVALUATION OF PREGNANT WOMEN WITH RHEUMATIC DISEASES BY THE SARS-COV2 PANDEMIC

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Background: Due to the SARS-CoV-2 pandemic, an increase in stress, anxiety, and depression has been seen, as well as greater use of substances and a decrease in prenatal care in pregnant women. (1) Women of childbearing age with autoimmune rheumatic diseases (ARDs) experience greater psychological stress, which can negatively influence behavior. (2)
Objectives: This study aims to compare changes in prenatal laboratory and ultrasound tests by trimester, as well as the detection of anxiety and depression in pregnant women with ARDs due to the SARS CoV-2 pandemic.
Methods: This study was carried out on pregnant patients with ARDs from the Pregnancy and Rheumatic Diseases clinic of the rheumatology department of the University Hospital "Dr. José Eleuterio González" during the period from February 2018 to August 2021. Two standardized evaluations of anxiety and depression were carried out using the Inventory of Trait and State Anxiety (IDARE) and the Edinburgh Postpartum Depression Scale (EPDS) respectively in the third trimester of pregnancy. Maternal report of alcohol consumption during any trimester of pregnancy, as well as adherence to routine laboratory studies such as structural ultrasound and gestational diabetes screening, was addressed. Positive COVID-19 nasopharynx PCR results were evaluated during pregnancy beginning in the pandemic period (March 2020). The pre-pandemic recruited group was compared with the pandemic group. The comparison of the groups was carried out using the Chi-Square and Fisher tests. A significant value of $p < 0.05$ was considered. Statistical analysis was performed using the IBM SPSS v.25 program.
Results: 50 pregnant patients with ARDs were recruited, of which 24 were included in the pre-pandemic group and 26 in the pandemic group. Compared with the pre-pandemic group, pregnant women recruited during the pandemic had a statistically significant higher positivity for state anxiety (p=0.023), likewise trait anxiety, depression, and suicidal ideation were detected more frequently, but the difference was not statistically significant, a higher rate of adherence to laboratory and cabinet studies was found, being significant for laboratories performed in the 1st and 2nd trimesters (0.005 and 0.025 respectively). See Table 1.

Table 1. Characteristics of pregnant women with autoimmune rheumatic diseases before and during the SARS-CoV-2 pandemic.

Measure	Before pandemic n=24	During pandemic Covid Negative n=22	During pandemic Covid Positive n=4	P value[a]
EPDS Positive depression detection (≥10)	**16.7%**	**36.4%**	**50%**	**.197**
suicidal ideation	**16.7%**	**0%**	**25%**	**.099**
IDARE Positive state anxiety detection (>45)	**12.5%**	**27.3%**	**75%**	**.023**
IDARE Positive trait anxiety detection (>45)	**8.3%**	**13.6%**	**50%**	**.204**
Any alcohol consumption during pregnancy	**20.8%**	**4.5%**	**0%**	**.176**
Structural Ultrasound – Mid-Pregnancy	**66.7%**	**95.5%**	**100%**	**.025**
Gestational diabetes screening	**75%**	**86.4%**	**100%**	**.376**
Laboratories				
First trimester	**20.8%**	**50%**	**0%**	**0.005**
Second quarter	**45.8%**	**77.3%**	**100%**	**0.025**
Third trimester	**58.3%**	**81.8%**	**75%**	**0.216**

IDARE= State and Trait Anxiety Inventory, EPDS= Edinburgh Postpartum Depression Scale.A Chi-square test for categorical variables or Fisher's exact test where the expected cell n

Conclusion: A higher frequency of positivity for state anxiety was demonstrated in pregnant women with ARDs recruited during the pandemic, as well as higher trait anxiety, depression, and suicidal ideation, although this increase was not statistically significant. On the other hand, concern about the pandemic and health status could positively influence better adherence to screening and routine studies during pregnancy.
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AB1171 **PERSISTENT POST-DISCHARGE SYMPTOMS AFTER COVID-19 IN RHEUMATIC AND MUSCULOSKELETAL DISEASES**

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Background: The COVID-19 pandemic continues worldwide and has had a strong impact on public health. As the pandemic evolves, efforts have been intensified to identify persistent symptoms associated with the infection once resolved have intensified.

Objectives: We aimed to describe persistent symptoms and sequelae in patients with rheumatic and musculoskeletal diseases (RMD) after admission due to Covid-19. We also compared the role of autoimmune rheumatic diseases (ARD) with that of non–autoimmune rheumatic and musculoskeletal diseases (NARD) in persistent symptoms and sequelae.

Methods: We performed an observational study of patients with RMD who attended a rheumatology outpatient clinic in Madrid and required admission to hospital due to Covid-19 (1st March-30th May 2020) and survived. The study began at discharge and ran until 1st October 2020. The main outcomes were persistence of symptoms and sequelae related to Covid19. The independent variable was the RMD group (ARD and NARD). The covariates were sociodemographic data, clinical findings, and treatment. We ran a multivariate logistic regression model to assess the risk of the main outcomes by RMD group.

Results: We included 105 patients, of whom 51.5% had ARD and 68.57% reported at least 1 persistent symptom. The most frequent were dyspnea, fatigue, and chest pain. Sequelae were recorded in 31 patients. These included lung damage in 10.4% of patients, lymphopenia in 10%, central retinal vein occlusion (1 patient), and optic neuritis (1 patient). Two patients died. Eleven patients required readmission owing to Covid-19 problems (16.7% ARD vs 3.9% NARD; p=0.053). No statistically significant differences were found between RMD groups in the final models.

Conclusion: Many RMD patients have persistent symptoms, as in other populations. Lung damage is the most frequent sequela. Compared to NARD patients, ARD patients do not seem to differ in terms of persistent symptoms or sequelae, although ARD patients might generate more readmissions due to Covid-19.

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AB1172 **POSTER: SARS-COV 2 INFECTION AND ANTI TNF THERAPY IN RHEUMATOID ARTHRITIS PATIENTS**

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Background: High levels of tumor necrosis factor (TNF), a key proinflammatory cytokine, is associated with SARS-CoV-2 infection. In rheumatoid arthritis patients with SARS-CoV-2 infection, anti TNF therapy reduces not only TNF but other cytokines responsible for high morbidity and mortality. The severe systemic inflammation in COVID-19 causes respiratory symptoms, fever, fatigue, neurological and gastrointestinal manifestations.

Objectives: We followed the evolution of SARS-CoV-2 infection in rheumatoid arthritis patients who received anti TNF blockers.

Methods: Our study included 95 rheumatoid arthritis patients who were diagnosed with SARS CoV-2 infection through a positive RT-PCR-SARS-CoV2 test. 21 patients were men and 74 were women. Mean age was 58 ±11,5. 24 patients received monotheraphy with anti TNF blockers (Adalimumab/ Infliximab), 48 received TNF blockers in combination with Methotrexate (10 mg per week) and 23 received TNF blockers in combination with Leflunomide (20 mg per day).

We followed serum ferritin, C reactive protein and D-dimer in all patients. 59 patients were vaccinated with two doses of Pfizer-BioNtech (64.1 %).

The study group was analyzed from 30th December 2021 to 1st of January 2022. From 95 patients, 35 (36,8%) were hospitalized and 60 received ambulatory care.

Results: Our patients with COVID-19 presented with asimptomatic forms, forms with mild symptoms and complicated forms that required hospitalization. No patients had died. Milder forms were associated with the use of TNF blockers and Methotrexate and patients with monotherapy – TNF blockers. They presented with mild symptoms (fever, arthralgia, odynophagia, dysgeusia/ageusia, anosmia). Hospitalization rate in patients who received monotheraphy with TNF blockers was 29,1%, 31,2% in patients who received TNF blockers and Methotrexate and 56,5% in patients with TNF blockers and Leflunomide (69,3%). Factors associated with higher odds of hospitalization included older age (p=0,001), active disease (p=0,02), obesity (p=0,005), pulmonary chronic disease (p=0,02), diabetes (p=0,001) and concomitent dose of Leflunomide (p=0,0006). Female sex was associated with milder forms of the disease. Patients with high levels of D-dimer had a higher odd of hospitalization (p<0,001). Strong positive correlation was observed between elevated D-dimers and hospitalization odds.

Conclusion: TNF blockers in monotheraphy or associated with Methotrexate were correlated with lower odds of hospitalization and milder forms of COVID-19. No significant difference of hospitalization odd was observed between vaccinated and unvaccinated patients.

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AB1173 **INCIDENT CASES OF COVID-19 AND VACCINATION ADHERENCE IN A MULTICENTRIC COHORT OF INFLAMMATORY ARTHRITIS IN BRAZIL**

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Background: The SARS-CoV-2 virus has caused a worldwide health crisis. Patients with inflammatory arthritis are at higher risk of hospitalization and death by COVID-19 due to comorbidities or immunosuppressive treatments. Vaccination is one the most important strategies to control the pandemic.

Objectives: To evaluate the incident cases of SARS-CoV-2 infection in a multicentric cohort of inflammatory arthritis in Brazil.

Methods: BiobadaBrasil is a multicentric registry-based cohort study of Brazilian patients with rheumatic diseases starting their first bDMARD or tsDMARD (1). The present analysis is a retrospective evaluation of adult patients with inflammatory arthritis (rheumatoid arthritis – RA, spondylarthritis -SpA and psoriatic arthritis-PsA) that were alive since the beginning of the COVID-19 pandemics in Brazil in February 2020. We evaluated the incidence and severity of COVID-19 infection and the adherence to anti- SARS-CoV-2 vaccines schedules, up to January 2022.

Results: A total of 300 patients were interviewed and 69 (23.0%) reported confirmed anti-SARS-CoV infection and 5 (1.7%) had a second infection. Among known infected patients, 18.8% need hospitalization and oxygen support, 7.2% were admitted at ICU, and 5.8% died. After COVID-19 infection, 31.8% reported worsening of disease activity but only 6.1% had modification in medication due to disease activity. Distribution of cases followed the pattern of waves observed in Brazil (Figure 1). Regarding vaccination, 285 (95%) reported to have received at least one dose of any anti-SARS-CoV-2 vaccine: 43% received the first with the adenovirus ChAdOx1 nCoV-19 (AstraZeneca) adenovirus vaccine, 32% received the Sinovac-CoronaVac inactivated vaccine, 22% received the BNT162b2 (Pfizer-BioNtech) mRNA vaccine and 3% received the BNT162b2 (Pfizer-BioNtech) adenovirus vaccine. Almost all (98.1%) of these patients had already received the second dose of vaccine and after the first and second vaccine doses, 6% and 4% of patients, respectively, reported worsening of articular disease activity, while, after the third dose, no patient reported disease activity worsening.

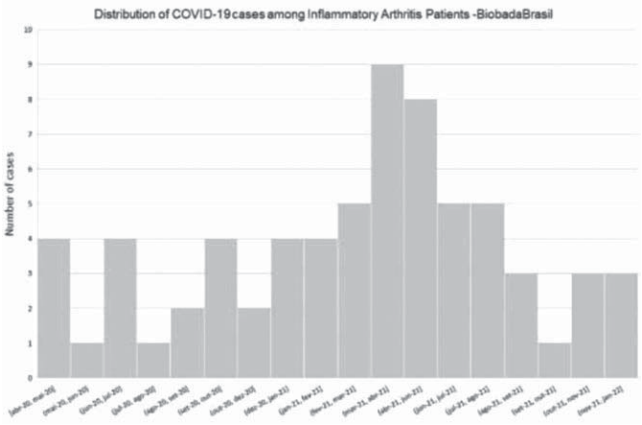

Figure 1.

Conclusion: During the pandemics, patients with inflammatory arthritis had a pattern of distribution of cases very similar to general population. Adherence to vaccination is high and well tolerated.

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AB1174 ADVERSE EVENTS AFTER TWO DOSES OF BNT162B2 ANTI-SARS-COV-2 VACCINE IN PATIENTS WITH RHEUMATIC MUSCULOSKELETAL DISEASES: RESULTS FROM A SINGLE CENTER ITALIAN STUDY

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Background: Vaccination against COVID19 is the most important prevention tool against the current pandemic. However, since the approval of anti-COVID19 mRNA vaccines by EMA, safety and tolerability in patients with rheumatic musculoskeletal diseases has always been a much-discussed topic, given their novel, unprecedented mechanism of action and the concern for potential disease flares.

Objectives: To assess the safety and type of adverse events after two doses of BNT162b2 anti-SARS-CoV-2 vaccine in patients affected by rheumatologic diseases.

Methods: 241 patients who received two doses of BNT162b2 were invited to take part to a follow-up live visit 2 months after completion of the primary vaccination cycle. Data regarding age, sex, diagnosis, treatment and adverse events after vaccination were collected for each patient during the visit. Pearson chi-square and Fisher exact tests were used to compare the distribution of each type of adverse event between male and female and among Rheumatoid Arthritis, Spondyloarthritis and Connective Tissue Disease patients.

Results: Mean age of recruited patients was 57 years (IQR 49-65) and F:M ratio was 2.49:1 (172 F/69 M). Number and percentage of individuals for each disease category were represented as follows: Rheumatoid Arthritis 87 (36,10%), Spondyloarthritides 72 (29,88%), Connective Tissue Diseases 65 (26,97%), Autoinflammatory Diseases 4 (1,66%), Vasculitides 13 (5,39%). 42 subjects (17,42%) reported no adverse events, whereas local reactions such as pain and swelling at injection site were the most commonly reported side effect, (154 subjects, 63,9%, Table 1). Constitutional symptoms, comprising fatigue, muscle and joint pain, fever, chills and headache, were described in 54,77% of the interviews (132 subjects, Table 1). No patient experienced severe allergic reactions after vaccination. Statistical comparison among disease categories showed no differences in the distribution of adverse events. When analysing for sex, joint pain appeared to be reported significantly more frequently in male patients (p=0.002), while chills were more present in female patients (p=0.033). None of the interviewed subjects reported any sign or symptom relatable to disease flares.

Table 1

	All pts n (%)	Female n (%)	Male n (%)	RA n (%)	SpA n (%)	CTD n (%)
	241	172	69	87	72	65
Local reactions	154 (63,90)	110 (63,95)	44 (63,77)	53 (60,92)	46 (63,89)	43 (66,15)
-Pain	152 (63,07)	108 (62,79)	44 (63,77)	53 (60,92)	45 (62,50)	42 (64,62)
-Swelling	4 (1,66)	3 (1,74)	1 (1,45)	1 (1,15)	2 (2,78)	1 (1,54)
Constitutional symptoms	132 (54,77)	98 (56,98)	34 (49,28)	46 (52,87)	38 (52,78)	37 (56,92)
-Fatigue	75 (31,12)	58 (33,72)	17 (24,64)	25 (28,74)	21 (29,17)	22 (33,85)
-Headache	35 (14,52)	29 (16,86)	6 (8,70)	10 (11,49)	10 (13,89)	14 (21,54)
-Muscle pain	37 (15,35)	28 (16,28)	9 (13,04)	14 (16,09)	10 (13,89)	12 (18,46)
-Joint pain	14 (5,81)	5 (2,91)	9 (13,04)	7 (8,05)	4 (5,56)	1 (1,54)
-Fever	35 (14,52)	24 (13,95)	11 (15,94)	15 (17,24)	5 (6,94)	11 (16,92)
-Chills	22 (9,13)	20 (11,63)	2 (2,90)	7 (8,05)	8 (11,11)	6 (9,23)
Gastrointestinal symptoms	19 (7,88)	14 (8,14)	5 (7,25)	7 (8,05)	5 (6,94)	5 (7,69)
-Nausea	17 (7,05)	13 (7,56)	4 (5,80)	5 (5,75)	5 (6,94)	5 (7,69)
-Vomiting	1 (0,41)	1 (0,58)	0 (0,00)	0 (0,00)	0 (0,00)	1 (1,54)
-Diarrhea	3 (1,24)	2 (1,16)	1 (1,45)	2 (2,30)	0 (0,00)	1 (1,54)
Lymphoadenopathy	2 (0,83)	2 (1,16)	0 (0,00)	0 (0,00)	0 (0,00)	2 (3,08)
Severe allergic reactions	0 (0,00)	0 (0,00)	0 (0,00)	0 (0,00)	0 (0,00)	0 (0,00)
Other	5 (2,07)	4 (2,33)	1 (1,45)	2 (2,30)	1 (1,39)	2 (3,08)
None	42 (17,43)	29 (16,86)	13,00 (18,84)	19 (21,84)	12 (16,67)	9 (13,85)

Table notes. RA: Rheumatoid Arthritis; **SpA**: Spondyloarthritides; **CTD**: Connective Tissue Diseases; **Other**: comprising reports of increased heart rate, visual disturbances, conjunctival hyperaemia, transient hyperglycaemia.

Conclusion: Vaccination with two doses of BNT162b2 was safe and generally well tolerated. No reports of signs or symptoms of disease reactivation were found in our cohort.

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AB1175 EFFECTS OF THE COVID-19 DISEASE ON AXIAL SPONDYLOARTHRITIS DISEASE FLARE

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Background: Rheumatological disease flares may be seen after many infections. However, our knowledge for the post-COVID axial spondyloarthritis (SpA) flares and its related factors is limited.

Objectives: We aimed to evaluate disease activity and factors that may be associated with disease activity in axial SpA patients in post-COVID period.

Methods: We retrospectively assessed the axial SpA patients who have had COVID-19 disease confirmed by a positive SARS-CoV-2 polymerized chain reaction (PCR) test result. Demographics, comorbid diseases, active medical treatments for SpA and information regarding COVID-19 clinical courses were collected from medical records. PCR positive patients were reached via telephone and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scored for pre- and post-COVID SpA symptoms. An increase of ≥2 points in the BASDAI score was defined as flare, and SpA groups with and without flare were compared. Factors predicting SpA flare were also analyzed by the logistic regression analysis.

Results: A total of 48 axial SpA patients were included in our study, 65% of them male and the mean±SD age was 42.3±8.6 years. Post-COVID SpA flare was seen in 38% patients. Demographic, clinical, medical features of the SpA patients and COVID-19 disease severity were similar between Flare and No flare groups. In comparison of the COVID-19 symptoms, although most of the

COVID-19 related symptoms were similar between two groups, the frequency of the back pain and diarrhea were higher in the Flare group than No flare group. But in multivariate analysis, only history of the inflammatory bowel disease had an increased risk for post-COVID SpA flare (Table 1).

Table 1. Results from adjusted logistic regression model of the spondyloarthritis flare

Variables	Enter Method			Backward:Conditional Method		
	OR	95% CI	p	OR	95% CI	p
Smoking	0.125	0.013-1.233	0.075			
Multimorbidity	0.244	0.047-1.256	0.091			
Inflammatory bowel disease	33.221	1.236-892.720	0.037	34.382	1.571-752.462	0.025
Fever	1.582	0.334-7.486	0.563			
Arthralgia	3.438	0.233-50.630	0.368			
Back pain	1.054	0.080-13.895	0.968			

OR: Odds ratio, CI: Confidence Interval

Conclusion: The presence of inflammatory bowel disease statistically significant related post-COVID SpA flares. In addition, diarrhea and back pain symptoms in COVID-19 disease may be stimulating factors for SpA flares but we found no effect of rheumatological therapies.

Disclosure of Interests: None declared

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AB1176 DOES VACCINATION AND VARIANTS AFFECT THE COURSE OF THE COVID-19 IN INFLAMMATORY RHEUMATIC DISEASE?

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Background: Although there have been expansion of knowledge about the course of COVID-19 in rheumatologic diseases, it still remains unclear the effect of vaccination status and variants on the disease course.

Objectives: We aimed to investigate the general clinical characteristics of our patients with inflammatory rheumatic disease (IRD) who had COVID-19 disease, their vaccination status and the time periods in which different variants were dominant during the disease.

Methods: During the routine follow-up of our patient's with IRD, whether the patients had COVID-19 disease, when they were vaccinated (Pfizer/Biontech or Sinovac in our Country) and main clinical characteristics and their comorbid diseases were recorded. The last patient was included in the study on January 25, 2022. They were divided into those who received insufficient or no vaccine and those who received a full dose of vaccine. The patients were divided into 3 groups according to the period they had the disease: Those who had the disease between March 2020 and June 2021accepted as "1st period patietns", the period when the Alpha and Beta variants, the initial forms of the disease, were dominant variants in populations; those who had the disease between July 2021 and November 2021, when the Delta variant dominated the World and in our country accepted as "2nd period patients"; and those who had the disease in December 2021 and later, when the Omicron variant was dominant throughout the world and in our country, was accepted as " 3rd period" patients.

Results: Total 463 (294 woman) IRD patients enrolled to the study. Distrubution of these patients included Behcet's syndrome:15; familial mediterranean fever: 57, rheumatoid arthritis:134, Sjogren's syndrome:24, systemic lupus erythematosus:26, Spondyloarthritis:141, necrotising vasculitis:6 and Others:50 cases. Mean age of patients were 46±13,2 (18-83) years. 354 (77%) of our patients got sick in the 1st period, 80 (17%) in the 2nd period and 28 (6%) in the 3rd period. When patients were compared in terms of their clinical complaints in these periods, dyspnea was significantly higher in patients in the 1st period (1st. period 36% vs 3rd period 18%; p:0.039), but there was no difference between other complaints including lung involvement and the frequency of hospitalization (p>0.05). 53% of patients had received at least 2 doses of mRNA vaccine. 84% of the patient has had COVID19 before full vaccination with any valid vaccine. When the patients who were full vaccinated and those who were not vaccinated or inadequately vaccinated at the time of illness were compared in terms of clinical features, lung involvement frequency and hospitalization frequency, no difference was found between them. (p>0.05, for all). However, hospitalization and lung involvement were less in those who received a booster dose of any valid vaccine (p: 0.03). While the average hospitalization rate was 17% for all groups, this rate was 50% for necrotizing vasculitis and was significantly higher (p:0,005). The probability of lung involvement and hospitalization were found to be significantly higher in patients using prednisolone 5mg (or equivalents) or more; (p:0.008 and p:0.000, respectively). Pulmonary involvement was significantly higher among patients receiving sulphasalasine (p:0.008). Among the patients on Rituximab, the probability of hospitalization was higher than those who did not (p: 0.01). There was no statistical difference in terms of hospitalization and pulmonary involvement between patients who took other drugs (p>0.05, for all). A total of 5 cases died, including 2 GPA, 1 EGPA, 1 RA and 1 FMF patients. Only 8 patients had a second history of COVID19.

Conclusion: The frequency of COVID-19 among IRD cases seems to decrease over time. Full vaccination seems effective for the prevention of COVID-19. It should be recommended that IRD patients have the full dose of vaccines and boosters. The risk of lung involvement and hospitalization increases in patients using certain drugs, such as corticosteroids, sulphasalasine and rituximab. These patients should be followed more closely.

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AB1177 SEXUALITY, FAMILY PLANNING AND MENTAL HEALTH AMONG REPRODUCTIVE-AGE WOMEN WITH RHEUMATIC DISEASE DURING THE COVID-19 PANDEMIC

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Background: Women with rheumatic disease are more likely to suffer from sexual dysfunction, infertility, depression, and anxiety. The pandemic may have affected these constraints.

Objectives: To investigate the effect of the Covid-19 pandemic on sexuality, family planning and mental health in a sample of women with rheumatic disease.

Methods: Women aged 18-50 with a rheumatic disease and women in an age-matched healthy control group received questionnaires featuring: 1) demographic information, sexual frequency, family planning; 2) the Female Sexual Function Index (FSFI); 3) the Depression, Anxiety and Stress Scale (DASS-21); and 4) the Coronavirus Anxiety Scale (CAS). Recruitment took place 3/21-12/21. Patients with rheumatic conditions were recruited at the Vienna University Clinic (AKH) and the control group through social media. Parameters were compared between the patients and the healthy control group, and with data on sexuality from women with rheumatic disease from 2019.

Results: A preliminary analysis was conducted with 83 patients with rheumatic disease and 124 healthy controls. The rheumatic disease group exhibited lower levels of stress (6.46 vs. 8.36 p<0.01) and Coronavirus Anxiety (6.27 vs 7.50 p<0.01) than the control group and was less likely to report that the pandemic led to a reduction of their sexual frequency (p<0.01). The control group cited "stress" frequently the decrease of sexual frequency. The FSFI analysis revealed that patients with rheumatic disease experienced higher levels of pain (p<0.001) during sex than the control group but were more satisfied with their relationships (p<0.05). In comparison to 58 patients with rheumatic conditions, whose data was collected in 2019, the 2021 cohort reported reduced FSFI values in the domains of desire (p<0.01), arousal (p<0.05), lubrication (p<0.05), and orgasms (p<0.01).

Conclusion: Consistent with research on female sexuality during the pandemic among healthy women, we found that patients with rheumatic conditions reported lower FSFI values in 2021, in comparison to 2019. Our finding that the pandemic had less impact on the patient group than a healthy control group, is consistent with research on MS and IBD patients, who showed surprising resilience in the face of the Covid-19 pandemic.

Disclosure of Interests: None declared

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AB1178 THE COMPARISON OF EXECUTIVE FUNCTIONS OF RECOVERED COVID-19 PATIENTS WITH HEALTHY CONTROLS

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Background: The epidemiological and clinical features of COVID-19 patients are currently well characterized. However the subacute and long-term effects of COVID-19 are not clear. Cognitive disturbance is one of the residual effects of COVID-19 infection besides fatigue, dyspnea, chest pain, arthralgia, and decline in quality of life. It has been stated that patients with COVID-19 may have cognitive dysfunction, but it still remains unknown whether the COVID-19 infection is associated with cognitive impairment.

Objectives: The aims of this study were to compare the executive functions of recovered COVID-19 patients with healthy controls, and to evaluate the relation of the executive functions with sleep quality, emotional status, disease severity, and post COVID-19 duration in these patients.
Methods: Twenty-five patients aged 18-60 with a previous diagnosis of COVID-19 infection and 25 gender-age matched healthy individuals as a control group participated this study. The executive functions of participants were evaluated by the Wisconsin Card Sorting Task (WCST), Stroop Test-TBAG Form, and N-back test. Data on sleep quality by Pittsburgh Sleep Quality-Index (PSQI), depression by Beck Depression-Inventory (BDI), anxiety by Worry and Anxiety Questionnaire were collected in all participants. In patients, disease severity, COVID symptoms, and post-covid duration were noted. Data were analyzed by SPSS using Kolmogorov Smirnov test, chi-square test, Student-t test, and Pearson correlation analysis.
Results: In terms of WCST; patients' number of trials administered, total errors, and nonperseverative-errors scores were statistically higher; categories achieved and percentage of conceptual-level responses scores were statistically lower than controls ($p<0.05$). Patients' N-back test scores were statistically lower than controls ($p=0.012$). BDI, PSQI total, sleep quality, sleep latency, duration of sleep scores were significantly different in patients and controls ($p<0.05$). Patients were divided into three groups according to the severity of the disease and there was no significant difference between the three groups in terms of WCST, Stroop test, and N-back test ($p>0.05$). There were negative correlations between WCST-total errors and duration of sleep, WCST-number of trials administered and sleep efficiency, Stroop-number of errors and total PSQI scores. No correlation was found between the executive functions and emotional status of the patients ($p>0.05$).
Conclusion: According to the results of this study, executive functions may be effected in the patients recovered from COVID-19. After COVID-19 infection patients may have sleep problems, and executive dysfunctions may be correlated with sleep disorders in these patients. Since the executive functions were not associated with clinical findings of COVID-19 infection in this study, we suggest that it is not predicted in which patients executive functions will be impaired. Regardless of the COVID-19 infection severity, executive functions should be considered in the follow-up of these patients.
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AB1179 CLINICAL CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO UNDERWENT COVID-19 IN THE REPUBLIC OF TATARSTAN

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Background: The management of patients with rheumatoid arthritis (RA) and novel coronavirus infection (NCI) is a significant problem due to the insufficient evidence base on this topic.
Objectives: To study the features of the transferred NCI in patients with RA and its influence on the course of RA.
Methods: From March 2020 to January 2022, 105 patients with RA who underwent NCI with a confirmed SarsCoV2 PCR result and/or X-ray computed tomography (CT) of the lungs were followed up. The age of the patients was 62 [55; 68] years, among them females - 84.7% (89 patients). The duration of RA at the time of NCI was 11 [6.5; 17.5] years. RA activity before NCI was low in 14 (13.3%) patients, moderate in 70 (66.6%), and high in 21 (20%) patients. The results of clinical and laboratory examinations were evaluated during the COVID-19, 1 and 3 months after it.
Results: The symptoms of NCI in patients with RA were comparable in frequency and severity to the course of infection in the population. 30 (28.6%) patients had a mild course of COVID-19, 74 (70.5%) had a moderate course, and 1 had a severe course. Bilateral polysegmental pneumonia was detected in 75 (71.4%) patients. The outcome of COVID-19 in all patients is recovery. Analysis of the course of RA showed a significant increase in activity 1 and 3 months after NCI: DAS28 from baseline to COVID-19 3.59±1.13 to 4.87±1.27 points after 3 months, respectively. Of the total number of recovered patients, 38.0% of patients showed an increase in activity due to clinical and laboratory parameters. 90.4% of patients noted the persistence or appearance of symptoms after undergoing NCI after 3 months, 45.7% had a combination of more than 3 different symptoms. The most common manifestations of asthenia in the form of a decrease in the quality of life (QOL) and working capacity. in 90.4% of patients: significant in 58.0% of people, insignificant in 32.4% of people. There was no significant correlation between RA activity and NCI severity. The second most frequent was the increase/appearance of pain in the joints - in 86.6% of respondents: significant in 72.3%, insignificant - 14.2%. Strengthening/appearance of muscle pain and/or headache and/or dysautonomia occurred in 44.7%. Appearance/intensification of shortness of breath and a decrease in exercise tolerance were noted by 36.1% of respondents: significant in 19.0% of people, insignificant in 17.1% of people. Among them, 64.8% (24) people with moderate severity, 35.2% (13) people with asymptomatic or mild NCI. Appearance/intensification of chest pain and/or palpitations was noted by 44.7% of people.
Conclusion: The prevalence and course of COVID-19 in patients with RA did not differ from that in the general population. However, coronavirus infection has led to an increase in pain and an increase in RA activity, a long-term persistence of post-COVID manifestations in the form of musculoskeletal pain and asthenic symptoms with a deterioration in the quality of life. There was no significant correlation between RA activity and NCI severity. At the same time, specific respiratory symptoms occurred only in a third of patients.
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AB1180 COVID-19 HAD DISPROPORTIONATE IMPACTS ON RA SYMPTOMS AND FUNCTION BY SEX AND AGE: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT (CATCH)

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Background: During the COVID-19 pandemic, Canadians with RA faced considerable uncertainty due to greater risk of infection, hospitalization, changing access to RA medications, and very limited access to in-person RA care. Further, to reduce transmission of the virus and COVID-related hospitalizations, stringent mitigation measures were implemented across the country to greatly reduce social contacts including curfews, limits on private gatherings and business closures. Little is known about the impact of the COVID-19 pandemic and associated mitigation efforts in RA. We hypothesized that women and younger adults with RA would report greater impairments in HRQL.
Objectives: To compare changes in HRQL prior-to and during the COVID-19 pandemic by sex and age groups in real-world RA patients seen in routine practice settings.
Methods: Data were from patients in the Canadian Early Arthritis Cohort (CATCH) who completed a study visit in the year prior to the COVID-19 pandemic (Mar 2019 through Feb 2020) and a repeat assessment during the pandemic period (Mar 2020 – Jan 2022). RA disease activity was assessed using the RA Flare Questionnaire, a validated patient-reported measure of current RA disease symptoms (pain, stiffness, fatigue) and function (physical, participation). An RA-FQ score ≥ 20 was used to classify RA symptoms consistent with an RA inflammatory flare. HRQL was assessed using PROMIS-29 Adult Profiles. We compared changes in mean Physical (PHS) and Mental Health (MHS) scores, and the proportion of patients with impairments in each domain (i.e., scores ≥ 55 for pain interference, fatigue, anxiety, depression, and sleep and ≤45 for physical function and participation) before and during the COVID-19 pandemic across sex and age groups (<40, 40-64, ≥65 years).
Results: The 938 CATCH participants in the analytic sample with data available at both time periods had a mean (SD) age of 60 (13) and RA symptom duration of 5.8 (3.7) years; 72% were women, 88% were white, and 64% reported >high school education. Most (80%) were in CDAI REM/LDA at the most recent visit prior to start of pandemic. The proportion of patients with RA-FQ ≥20 were similar at both time periods. While physical and emotional RA symptom impacts

remained stable in men prior to and during the COVID-19 pandemic, women reported significant increases in anxiety and depression during the pandemic period. Younger RA patients <40 reported increases in depression, and older RA patients (65+) reported increases in anxiety and greater impacts on participation.
Conclusion: Our results illustrate that while the proportions of patients with high inflammatory disease activity were similar prior to and during the COVID-19 pandemic, we observed disproportionate impacts on HRQL by sex and age with a higher proportion of women, adults <40, and those ≥65 years of age experiencing greater impairments in several HRQL domains.

Table 1.

	Women (N = 673)		Men (N=265)		Age <40 (N=84)		Age 45-64 (N=492)		Age 65+ (N= 362)	
Domain	Before	During	Before	During	Before	During	Before	During	Before	During
RA Flare >20%	17%	21%	19%	18%	13%	7%	18%	21%	18%	21%
Anxiety	**34%***	**42%***	23%	23%	42%	55%	32%	35%	**28%***	**35%***
Depression	**28%***	**34%***	22%	20%	**25%***	**42%***	28%	28%	24%	30%
Fatigue	36%	38%	24%	23%	43%	43%	36%	33%	26%	32%
Pain	47%	52%	48%	45%	39%	48%	46%	49%	49%	54%
Physical function	54%	57%	46%	46%	40%	40%	49%	50%	59%	62%
Participation	42%	47%	34%	36%	37%	38%	40%	41%	**40%***	**49%***
Sleep	30%	34%	18%	22%	26%	29%	29%	33%	23%	28%

*p <0.05

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AB1181 THE BURDEN OF POST-SARS-COV2 VACCINE COMPLICATIONS AND NEWLY DIAGNOSED IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Background: Local and systemic reactions have been observed after all vaccines for SARS-CoV-2 but in the majority of cases, symptoms are mild and self-limiting. However, evidence on more severe clinical scenarios, requiring admission to hospital or referral to outpatient clinics after the administration of SARS-CoV-2 vaccines has accrued. This also includes newly diagnosed diseases, such as cardiovascular and immune-mediated inflammatory diseases (IMID).
Objectives: We aimed at quantifying the burden of post-vaccine hospital admissions/referrals and of newly diagnosed IMID.
Methods: Clinical records of patients referred to our Internal Medicine institution (both inpatients and outpatients) between February and June 2021 were retrospectively assessed. Subjects having received one or more doses of any of the EMA-approved SARS-CoV-2 vaccines within the previous 30 days were included. Subjects with a previous diagnosis of IMID were excluded.
Results: Our cohort included 99 patients, 45 females and 54 males, with a mean age of 64 years and a median of 3 comorbities (range 0-7). Eighty-eight patients (89%) required admission to the Internal Medicine ward while 11 were referred to the outpatient clinic. 68 (69%) of patients received the vaccine BNT162b2, 16 (16%) the ChAdOx1 nCoV-19, 9 (9%) the mRNA-1273 and 6 (6%) the Ad26.COV2.S. Twenty-seven (27%) subjects developed symptoms after the first vaccine dose with a mean latency of 2 days (median=0 indicating symptom onset on the day of the vaccine administration). Twenty-four (24%) subjects developed symptoms after the second dose with a mean latency of 4 days (median 1 day). All the other subjects did not develop symptoms within the week after the vaccine and were admitted for reasons apparently unrelated to vaccine administration. The number of presenting complaints ranged between 1 and 4 with 87% of subjects presenting with 1 or two coexisting complaints. Gastrointestinal manifestations were the most frequent being the presenting complaint in 31 (31%) of patients followed by severe fatigue/appetite loss in 19 (19%) of subjects, fever in 18 (18.2%) and neurological manifestation in 16 (16%) of subjects. A temporal and causal association with the SARS-CoV-2 vaccine was identified since all other known causes for these manifestations were ruled out. No in-hospital deaths were observed and 19 (19%) patients were diagnosed with a new onset IMID (Table 1). The clinical picture of these subjects was not significantly different from that of patients without a confirmed IMID and neither were demographic features. No association with the type of vaccine was observed.

Table 1. Immune-mediated inflammatory diseases diagnosed after SARS-CoV2 vaccination (N=19)

Disease	Number of patients
Rheumatoid arthritis	5
Psoriatic arthritis	2
IgA vasculitis	2
Spondyloarthritis	1
Giant cell arteritis	1
Polymyalgia rheumatica	1
Gout	1
Primary biliary cholangitis	1
Antiphospholipid syndrome	1
Graves' disease	1
Ulcerative colitis	1
Autoimmune thrombocytopenia	1
Leukocytoclastic vasculitis	1

Conclusion: Our data show that post-vaccine newly diagnosed IMID may represent a challenge in clinical practice and it seems that no demographic or clinical feature is able to predict their onset. A multidisciplinary cooperation and registry data are needed in order to reliably estimate and define the impact of SARS-CoV-2 vaccinations on new onset IMID.
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AB1182 SPECIALIZED PRO-RESOLVING MEDIATORS (SPMS) AND INFLAMMATORY NETWORKS IN PATIENTS AFFECTED BY ADULT ONSET STILL'S DISEASE (AOSD) AND COVID-19

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Background: Uncontrolled systemic inflammation characterizes COVID-19 and autoinflammatory diseases such as adult-onset Still's disease (AOSD). Biosynthesis of pro-resolving mediators (SPMs), i.e. lipoxins (LX), resolvins (Rv), protectins (PD), and maresins (MaR), ensures inflammation shutdown and tissue repair, limiting neutrophils recruitment and stimulating macrophages to remove apoptotic cells. Among protectins, reduction of PD1 was found in the lungs of mice infected with the H5N1 influenza virus and experimental treatment with PD1 resulted in increased animals' survival (Morita M et al 2013).
Objectives: We investigated the effects of SPMs in pathogenesis and clinical evolution of AOSD and compared these data with mild and severe COVID-19. Finally, we analyzed the potential role of PD1 in modulating the inflammatory response of macrophages obtained from AOSD patients, COVID-19 patients and healthy donors (HDs).
Methods: 21 patients hospitalized for COVID-19 (10 ICU and 11 hospitalized in medical clinical unit) and 13 patients with AOSD were enrolled. Plasma PD1 levels from patients and controls were analyzed by ELISA, and monocytes-derived macrophages were polarized into M1 and M2 phenotype. We analyzed the effect of PD-1 on macrophages differentiation. At 10 days, macrophages were analyzed for surface expression of subtypes markers by flow cytometry. Cytokines production was measured in supernatants by Bio-Plex Assays. Peripheral blood mononuclear cells (PBMCS) from 3 AOSD patients, 2 COVID-19 patients and 3 HDs were obtained. Next-generation deep sequencing was then performed to identify the differences in PBMCs transcripts profiles.
Results: AOSD patients with systemic scored (SS) ≥1 showed an increase of PD1 levels compared to AOSD patients with lower systemic score (p=0.04) (Figure 1A). Similarly, plasma levels of PD1 were increased in COVID-19 patients independently from their clinical subsets, compared to HDs (p=0.02). I*n vitro* treatment with PD1 of monocytes-derived macrophages from AOSD and COVID-19 patients induced a significant increase of M2 polarization vs control (p<0.05) (Figure 1B). Furthermore, a significant release of IL-10 and

CCL4 from M2 macrophages was observed when compared to control (p<0.05) (Figure 1C). In the transcriptomes from 3 AOSD patients (2 mild and 1 severe), 2 COVID-19 patients (1 mild and 1 ICU) and 2 HDs, we observed that genes involved in inflammation, lipid catabolism and monocytes activation were specifically dysregulated in AOSD and COVID-19 patients when compared to HDs. Among them *pla2g15, pla2g12a, pla2g2d,* involved in mobilization of SPMs precursors, were significant upregulated in patients compared to HDs (p<.01, |log2FoldChange|>1.2) (Figure 1D). The largest part of the genes involved in inflammation, lipid catabolism, and monocytes activation are less expressed in AOSD patients when compared to COVID19 patients, as reported in Table 1.

Table 1.

Gene symbol	Log2 fold change	p	Adjusted p	Counts COVID19	Counts AOSD
Inflammation-related genes					
ALOX5	0.98	0.024	0.21	16861.61	8562.92
IL13RA1	1.28	0.002	0.053	7154.78	2938.95
RTN3	0.72	0.002	0.0069	9948.37	6045.92
SSH2	1.05	6,78 E-7	0.00016	18343.86	8848.67
Lipid catabolism genes					
PLBD1	1.68	0.00011	0.0082	28051.88	8671.3
CYP4F3	2.85	0.00034	0.017	1996.63	277.13
STS	1.53	0.010	0.036	1798.5	623.9
HADHA	0.74	0.00014	0.0097	12766.44	7625.38
Monocytes-related genes					
ALDH2	1.46	2.48E-10	1.85E-07	9186.55	3340.87
CD163	2.37	9,99E-06	0.0014	66499.45	12870.59
MGST1	1.13	0.0026	0.063	1385.54	631.67
RNASE4	2.48	0.0001	0.0092	86.66	15.42

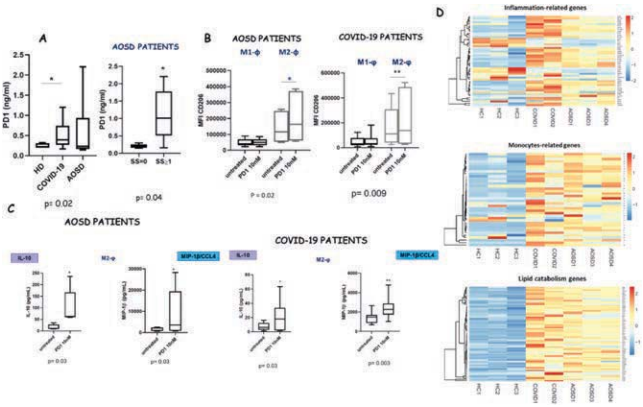

Figure 1.

Conclusion: The counterbalance by SPMs during inflammation is still a largely unexplored pathway. Our study suggests that an imbalance of SPMs in autoinflammatory diseases as well as COVID-19. The modulation of SPMs as observed in our experiments, might represent a new possible therapeutic strategy during AOSD and COVID-19.

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Disclosure of Interests: luca navarini Speakers bureau: AbbVie, Pfizer, MSD, UCB, GSK, BMS, Roche, Sanofi Aventis, Novartis, Janssen, Galapagos, Eli Lilly, Paid instructor for: AbbVie, Eli Lilly, Consultant of: Philogen, Grant/research support from: AbbVie, Marta Vomero: None declared, Onorina Berardiucrti: None declared, Damiano Currado: None declared, Annalisa Marino: None declared, Alice Biaggi: None declared, Stefano Di Donato: None declared, Francesco Ursini: None declared, Piero Ruscitti: None declared, Riccardo Meliconi: None declared, Paola Cipriani: None declared, Annamaria Iagnocco Speakers bureau: AbbVie, Pfizer, MSD, UCB, GSK, BMS, Roche, Sanofi Aventis, Novartis, Janssen, Galapagos, Eli Lilly, Antonella Afeltra Speakers bureau: AbbVie, Pfizer, MSD, UCB, GSK, BMS, Roche, Sanofi Aventis, Novartis, Janssen, Galapagos, Eli Lilly, Roberto Giacomelli Speakers bureau: AbbVie, Pfizer, MSD, UCB, GSK, BMS, Roche, Sanofi Aventis, Novartis, Janssen, Galapagos, Eli Lilly, SOBI, Consultant of: Philogen, Grant/research support from: AbbVie, SOBI

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AB1183 COVID-19 VACCINE: HESITANCY, ACCEPTANCE AND TOLERANCE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) are considered a high-risk population to develop severe COVID-19 [1] and therefore vaccination is strongly recommended. Previous reports have shown a high hesitancy rate to receive a COVID-19 vaccine among RA.

Objectives: This study aimed to evaluate the attitude of patients with RA to vaccination against SARS-CoV-2, explore the factors which may influence it, and assess adverse events of SARS-CoV-2 vaccines.

Methods: This is a cross-sectional study including 106 patients with RA diagnosed according to the ACR/EULAR 2010 classification criteria and followed in the Rheumatology Department, over a period of 10 months from March to December 2021.Demographic and disease parameters were collected: age, gender, educational status, disease duration, erythrocyte sedimentation rate (ESR), disease activity score (DAS28), and treatments being used. All patients responded to a questionnaire on their perceptions and concerns about the covid-19 vaccine, and the adverse effects for those who got vaccinated.

Results: Among the 106 patients, 90 (84,9%) were females and 16 (15,1%) were males. The mean age was 54 ±13 years old [23-77]. Sixty-four percent were from urban areas and 36 % were from rural areas. Thirty-three percent of patients were illiterate. The mean disease duration was 9.54 ±5.76 years [2-22]. The mean DAS28 ESR was 3,88 ±1.34 [1.2-7.58]. All of our patients were taking conventional synthetic DMARDs. Seventeen percent of patients were on biological DMARDs. The majority of the patients (90%) reported that they respected the preventive measures. Twenty-two percent of patients had stopped their treatment because they were afraid of the covid-19. Twenty-eight patients had contracted the SARS- CoV-2. Seventeen percent of the patients reported that they didn't get vaccinated against covid-19. The reasons given by these patients were: presumed adverse events (53,3%), presumed inefficiency (25%), no recommendation from their doctor (46,7%), fear that the vaccine would make RA worse (64,7%). For the vaccinated patients, the vaccines administered were: 63,6 % Pfizer BioNTech, 6,8% Oxford/AstraZeneca, 5,7% Moderna, 4,5% Janssen/Johnson & Johnson, 2,3% Sinovac-CoronaVac and 17% unspecified. The majority of the patients (72,7 %) received two doses,14,8 % one dose and 12,5% 3 doses. After vaccination, 73,9% of patients reported adverse events, such as pain at the site of injection (88,1%), fatigue (35,8%), headache (14,9%), fever (13,4%) and muscle/joint pains (4,5%). Only 1 patient had experienced rheumatic disease flare. Hesitancy about the COVID-19 vaccination was associated with low intellectual level (p=0.004) and rural origin (p=0.001).RA disease duration, DAS28-ESR, and treatments have no influence on the attitude of patients towards COVID-19 Vaccination (p > 0,05).

Conclusion: The acceptance of COVID-19 vaccination by RA patients in our study is quite promising. The majority of patients tolerated their vaccination well, with rare RA flares up. These results should reassure rheumatologists and patients. Education and outreach efforts need to be continued, especially for illiterate people and those who live in rural areas.

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Disclosure of Interests: None declared

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AB1184 SAFETY PROFILE OF SARS COV-2 VACCINES IN PATIENTS WITH CONNECTIVE TISSUE DISEASE, VASCULITIS AND POLYMYALGIA RHEUMATICA. BI-CENTRIC STUDY.

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Background: In recent times, safety and potential adverse effects (AEs) of Sars-CoV-2 vaccines have gained great relevance and have been a central topic in scientific discussion.

Objectives: The aim of this study was to evaluate the incidence of AEs after Sars-CoV-2 vaccine administration in patients affected by Connective Tissue Disease, Vasculitis or Polymyalgia Rheumatica. Moreover, we assessed patients' adherence to the American College of Rheumatology (ACR)[1] or Italian Rheumatology Society (SIR)[2] recommendations.
Methods: 139 patients affected by Connective Tissue Disease, Vasculitis or Polymyalgia Rheumatica were enrolled at the Rheumatology Units of University Hospitals of Bari and Foggia. All patients were given a questionnaire to evaluate vaccine type and dose number, AEs, potential pre-vaccine prophylaxis, immunosuppressive therapy and its possible suspension according to the clinical guidance summary proposed by ACR or SIR.
Results: Among the 139 enrolled patients (120 females and 19 males, mean age 54 ± 14,7 year, mean disease duration 8,6 ± 7,4 years), 31 subjects (19%) received anti Sars-CoV-2 vaccination. 5 patients received the AstraZeneca COVID-19 vaccine, 23 the BioNTech-Pfizer COVID-19 vaccine and 3 the Moderna vaccine. Only 48% of subjects received two doses. 42% of patients reported non-severe AEs after the first dose of vaccine, specifically 45% of patients who received the BioNTech-Pfizer COVID-19 vaccine, 40% of those who were administered the AstraZeneca vaccine and 33% of those who received the Moderna vaccine. Most frequent AEs were site injection pain (19%), fatigue (13%), headache (13%), myalgia (6%), fever (6%), nausea (3%), rheumatic disease flare (3%) (the latest was reported only among the Polymyalgia Rheumatica patients). Considering the different diseases, the highest trend of AEs was observed in Polymialgya Rheumatica (66%), Systemic Sclerosis (57%), Sjogren Syndrome (40%) and undifferentiated connective tissue disease (23%) patients. 30% of patients who received the second vaccine dose reported AEs. All of them were administered the BioNTech-Pfizer COVID-19 vaccine. Most reported AEs after the second vaccine dose were site injection pain (6%), headache (3%), myalgia (6%), fever (6%). The highest trend of AEs was observed in undifferentiated connective tissue disease (60%) and Sjogren Syndrome (33%) patients. Only 13 % of subjects who reported AEs after the first vaccine administration, reported AEs also after the second dose. Only 9,7% of patients did not comply with the COVID-19 vaccine clinical guidance prosed by ACR or SIR regarding immunosuppressive treatment management before and after immunization.
Conclusion: Patients enrolled in this study developed mild AEs. Only among Polymyalgia Rheumatica patients were described disease flares and higher trend of AEs. Although patients affected by Systemic Lupus Erythematosus, Antiphospholipid Syndrome and Vasculitis were enrolled, none of them reported severe AEs, included the extensively discussed post-vaccine thrombosis. We found no significant dissimilarity of AEs relating to different types of vaccine and good patient compliance to physician recommendations about treatment management.
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Disclosure of Interests: None declared

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AB1185 PATIENT-REPORTED EXPERIENCE IN IMMUNE MEDIATED INFLAMMATORY DISEASES (IMID) IN THECONTEXT OF THE COVID-19 PANDEMIC: ACCESSIBILITY AND CONTINUITY OF CARE.

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Background: The lockdown and mobility restrictions in early COVID19 pandemic had a great impact in chronic patient care due to limited access and scheduled visits. In our hospital, coordinated non-pharmacological interventions (NPI) were designed in Rheumatology and Pharmacy services to maintain the accessibility and continuity of care for patients with IMID.
Objectives: To evaluate the patient reported experience (PRE), health status and quality of life in Rheumatology outpatient IMID subjects since March 14, 2020 when lockdown was imposed and during subsequent restrictions, related to the healthcare team and medications accessibility, and continuity of care.
Methods: Observational study, using a patient survey. Adult patients attending the rheumatology outpatient clinic between Nov 2, 2020 to Feb 13, 2021, with rheumatoid arthritis (RA), psoriatic arthritis (PsA), spondylarthritis (SpA) or systemic autoimmune diseases (SAD), with at least 1 year from diagnosis and 1 month of treatment with conventional synthetic (cs) targeted synthetic (ts) or biological (b) disease modifying antirheumatic drugs (DMARD). Face to face or phone interviews were conducted using an ad hoc designed questionnaire that included COVID19 related questions, the 11 IEXPAC scale items (5 point Likert scale ranging from never to always) (www.iexpac.org), and 4 items (5 points, very good to very bad) of the global scale PROMIS 10 (Patient-Reported Outcomes, PRO). All questions refer to the patient's experience during the 6 months prior to data collection.
Results: From 174 screening patients, 158 completed the survey, mainly woman (66.5%) with a median age of 60 (IQR 47-69,3) years. The most frequent diagnosis was RA (43%) followed by ESAP (35%), EAS (22%) and PsA (13%). 46.8% of the patients have been prescribed b or ts DMARD and 53.2% sc DMARD, 32.9% in combination. From 158, 39 persons requested healthcare for COVID-19 related symptoms and diagnosis was confirmed in 17 (10,8%). Just 2 patients required hospital admission. Clinical control and continuity of care for COVID19+ patients were carried out from their primary care center and by phone consultation. Some key results of the survey are displayed in Table 1.

Table 1. PRO and Patients' perception during COVID19 lockdown and restrictions.

During confinement and restrictions due to covid-19, in the last 6 months …	Responses (%) N= 158
Your degree of concern about the COVID19 crisis is.	High + Quite high (86.7)
PRO (PROMIS 10)	
How good was your health …?	Very good (11.4), Good: (43.7)
and your emotional/mental health, including mood and ability to think?	Very good (10.1) Good (41.1)
your quality of life was.	Very good (8.25) Good (49,4)
Your satisfaction in performing daily tasks (home, work, family) was.	Very good (7.8) Good (55.1)
Accessibility to care and medications	
I could contact my rheumatologist whenever I needed (email, phone).	Always (79.9)
My rheumatologist changed my face-to-face visit for a phone call	Yes (53)
I received my medication at home from the hospital pharmacy	Yes (16)
I picked up my medication from the hospital pharmacy, without incident.	Yes (21)
I maintained the prescribed dose medication…	Always + almost always (96,2)
At some point I modify a medication by my own decision	Yes (6)
My doctor changed the dose or route of administration	Yes (7)
Your satisfaction with the care provided from all professionals in the team was	Very + Quite satisfied (75)
PREMS (IEXPAC)	
Item 2. The professionals … are coordinated to offer me good healthcare	Always (34.18)
Item 8. They make sure that I take my medication correctly	Always (73.42)
Item 9. They worry about my welfare	Always (74.68)

Conclusion: Lessons have learned during the COVID19 lockdown and restrictions by assessing patients' health status and patients-reported experience. Coordinated NPI such as medication monitoring and home delivery, appointment reorganization and protocolized phone visits can result in a good patient perception and medication adherence whilst receiving care in a challenging situation.
Disclosure of Interests: None declared

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AB1186 ACUTE PERICARDITIS IN TIMES OF COVID

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Background: The most common etiology of acute pericarditis is usually infectious, especially viral. When its cause is inflammatory (up to 7% of cases), it can be presented as an isolated process or be a clinical manifestation in the context of multiple systemic autoimmune diseases (SAD), therefore it is necessary to make a broad differential diagnosis. Nowadays, an increased incidence has been described in relation to SARS-CoV-2 infection, and especially in global vaccination against this one. This represents a clinical challenge when we have to identify the cause of this pathology with a not insignificant comorbidity.

Table 1.

	Age	Sex	Underlying rheumatological disease	Previous treatment	Treatment performed	Pericardial effusion	Evolution
Case1	23	Male	Seronegative oligoarthritis and vasculitis	Hydroxychloroquine	Colchicine Steroids Azathioprine Anakinra	Moderate	Resolution
Case2	48	Woman	No	No	Colchicine Steroids Hydroxychloroquine	No	Resolution
Case3	68	Woman	Seropositive RA and Sjögren syndrome	Leflunomide Rituximab	Steroids Hydroxychloroquine Leflunomide Tocilizumab	Mild	Resolution
Case4	47	Woman	No	No	Colchicine Steroids Hydroxychloroquine	Moderate	Resolution
Case5	27	Male	No	No	Colchicine Steroids	Severe	Resolution
Case6	61	Woman	lcSSc	D-penicillamine	Steroids Azathioprine	Severe	Resolution
Case7	68	Woman	SLE	Steroids	Steroids Azathioprine Rituximab	No	Resolution
Case8	71	Male	ANA+ polyarthritis	Steroids	Steroids Hydroxychloroquine	No	Resolution

Objectives: To describe the characteristics of a series of patients with acute pericarditis and its association with SAD.

Methods: Retrospective and descriptive observational study. Digitalised records of patients with acute pericarditis evaluated in the Rheumatology unit of a tertiary hospital in Seville during 2021 were reviewed. Demographic, epidemiological, clinical and therapeutic variables were analysed.

Results: Eight cases of acute pericarditis were detected. The average age of the patients was 51.50 ± 18.601 years. 62.5% were women. 50% had previous rheumatological pathology: two rheumatoid arthritis (RA), one systemic lupus erythematosus (SLE) and one limited systemic sclerosis (LSS); with an average disease duration of 8.63 ± 2.387 months. Of these, 3 were on treatment with steroids and DMARDs (leflunomide or hydroxychloroquine) and 1 had previously received rituximab. Pericardial effusion was moderate in 50% of cases, severe in 33.3% and mild in 16.7%. One patient had cardiac tamponade. Five patients had pleural effusion, which was moderate in 80%, and in one case associated with pneumonia. As complications, one patient developed heart failure and the patient with ESL was diagnosed with pulmonary arterial hypertension. Two patients had previous COVID19 and 7 were vaccinated against Sars-CoV2. Treatment was colchicine in 57.15% of cases, steroids in 85.7%, DMARDsc in 85.8% (3 hydroxychloroquine and 3 azathioprine) and DMARDsb in 42.9% (1 anakinra, 1 tocilizumab and 1 rituximab). Pericarditis resolved in all patients. Table 1.

Conclusion: In the previous year, an increase in consultations from other departments for acute pericarditis with suspected inflammatory origin was observed. The possibility of a correlation with COVID19 or vaccination against COVID was initially considered, but it could not be demonstrated, since vaccination was later in vaccinated patients, and in those who had been infected, the time interval until the development of pericarditis was too long for it in order to be attributed to COVID19. Finally, in 5 of the 8 patients, pericarditis was related to SAD, in particular with the rheumatic pathologies most associated with this clinical manifestation (RA and SLE). Therefore, in the middle of the COVID pandemic, in addition to considering COVID19 or its vaccine in the differential diagnosis of acute pericarditis, we must not forget to include SAD in this diagnosis.

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AB1187

AUTOIMMUNITY PROFILE AND LUNG INVOLVEMENT IN ITALIAN PATIENTS WITH DERMATOMYOSITIS DURING COVID-19 PANDEMIA

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Background: Dermatomyositis (DM) is a rare idiopathic inflammatory myopathy that can present with a variable spectrum of cutaneous and systemic manifestations[1]. Correlations between myositis-specific autoantibodies (MSAs) and disease phenotype have been documented in DM in particular in association with the development of interstitial lung disease (ILD). Ongoing studies focus on the potential role of MSAs in similarities of the pathophysiological mechanisms of COVID-19 associated ILD and that related to DM suggesting an intriguing cross talk between autoimmunity and COVID-19[2].

Objectives: To explore clinical patterns including ILD and MSAs profile in DM patients from a population-based single-center study carried out in a Tertiary Referral Rheumatologic Clinic. SARS-CoV-2 infections and vaccination were also analysed.

Methods: We enrolled patients affected by DM classified according to 2017 EULAR/ACR criteria[1] with a disease onset at ≥18 years referring to the Rheumatologic Clinic of Tor Vergata University Hospital in Rome (Italy). Clinical data were collected from medical records: gender, age of onset of symptoms and diagnosis, clinical features, auto-antibodies patterns (ANA, MSAs including anti-tRNA synthetase, -Jo1, -PL7, -EJ, - MDA5, -NXP2, SAE, Mi2, and myositis-associated antibodies comprising anti-PM/Scl, -Ro-52, -Ku, U1RNP), pattern of lung abnormalities at thoracic CT scans, and treatments. The prevalence of SARS-CoV-2 infection and vaccination profile were also investigated.

Results: Among eligible cases (n=30), patients who completed the study (n=19) included almost entirely women (F=73.7%). The median age at disease onset was 57.4±12.4 yrs while the mean diagnostic delay resulted as 12±10 months. Skin manifestations and myalgia were the prevalent symptoms (79% and 63%, respectively) whereas dyspnea and cough occurred in a third of the cohort at DM onset. Besides the skin involvement, the decrease in pulmonary function was the main clinical manifestation at the first rheumatological referral (52.6% of cases) followed by joint pain (36.8%) and cardiovascular events (10.6%). ANA titer≥1:160 occurred in 79% of patients. All patients showed MSAs positivity with a similar distribution: a single case of double positivity was registered in a man with anti-MDA5 and -NXP2. The most common CT findings were ground-glass opacity and parenchymal band in a third of patients (32%). The entire cohort had undergone cycles of steroids from the onset of DM and during the follow-up, according to disease severity. The main used therapies were methotrexate (47%), intravenous immunoglobulin (42%) and mofetil micofenolate (31.6%). None of patients had SARS-CoV-2 infection (until December 2021). The 63% of the cohort received at least one dose of the anti- SARS-CoV-2 mRNA vaccine (BNT162b2), of which 10% had completed with the booster dose. No adverse reactions or post-vaccination DM flare were registered. A third of the cohort had not been vaccinated due to concomitant disease activity or therapies. No cases of post-COVID19 new-onset DM were diagnosed.

Conclusion: Our preliminary findings support the relevant impact of lung involvement in DM. The availability of MSAs can help to stratify patients with

DM for outcome and risk of potential disease complications. The impact of MSAs on ILD associated or not to COVID-19 deserve further investigations in a larger DM cohort and for a longer post-COVID-19 pandemia follow-up time.

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Disclosure of Interests: None declared

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AB1188 SARS-COV-2 VACCINATION WILLINGNESS AND PREDICTORS IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES (CIRD) AND WITHOUT CIRD

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Background: Recent surveys in chronic inflammatory rheumatic diseases (CIRD) showed a high degree of vaccine hesitancy. Current knowledge about patients' attitudes towards vaccination against SARS-CoV-2 is limited.

Objectives: To assess the willingness of CIRD patients to be vaccinated against SARS-CoV-2 and to identify influencing factors compared to non-CIRD patients.

Methods: In this cross-sectional study, two cohorts of consecutively in parallel recruited patients with and without CIRD presenting to our tertiary hospital answered questions of a structured interview to assess vaccination willingness to SARS-CoV-2, experience with SARS-CoV2 in their environment and their personal history of infections and vaccinations. Vaccination willingness was assessed by a numerical rating scale (0: fully disagree; 10: fully agree). Arbitrarily defined cut-offs were used to define definite (score ≥7) and probable willingness (scores of 5 or 6) to be vaccinated. Statistical analyses were performed with appropriate tests such as Kendall-tau b.

Results: A total of 514 CIRD and 100 non-CIRD patients, mean age 54.7±12.8 and 55.6±9.8 years, were included. Definite and probable willingness to be vaccinated against SARS-CoV-2 was declared by 79.6% and 90.7% vs. 76.0% and 85.0% of CIRD and non-CIRD patients, respectively. Only 60% of CIRD patients believed that the vaccines against SARS-CoV-2 were safe, and 42% indicated to be afraid of side effects. Vaccination willingness correlated significantly with the degree of education, age, identification with a risk group for COVID-19 disease, hypertension, and the degree of information about preventable diseases. There was no correlation with the history of infections or with immunosuppressive therapy.

Conclusion: Although our results show a high willingness for vaccination against SARS-CoV-2 in both groups, there was quite some uncertainty regarding the safety and efficacy of the vaccines. Since major influencing factors were education and information about SARS-CoV-2 and COVID-19, patient education should be immediately improved.

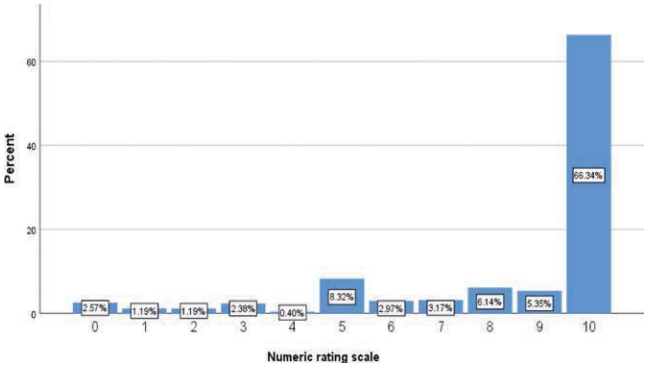

Figure 1. Vaccination willingness of CIRD patients

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Disclosure of Interests: None declared

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AB1189 THE RISK OF FLARE UP FOLLOWING NSARS-COV2 VACCINE IN INFLAMMATORY ARTHRITIS

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Background: As autoimmune phenomena following anti-nSARS-CoV2 vaccine was reported in the healthy population, there is increasing concern in patients with inflammatory joint diseases regarding possible side effects and disease flare-ups.

Objectives: We set out to evaluate the possible risk of disease exacerbation and the predisposing risk factors for the flare up.

Methods: This is a single center prospective cohort study, enrolling patients attending Arthritis Clinic at San Bortolo Hospital, during a follow-up of 12 months. All patients, after obtaining informed consent, answered a 24-item questionnaire including information about nSARS-CoV2 infection, vaccination, disease activity, ongoing treatment, vaccine side effects, disease flare up and need to change therapy.

Results: A total of 109 patients, 60 (55.1%) females and 49 (44.9%) males with a mean age of 60.1 years ±12.6 SD were enrolled. Forty-three (39.5%) were affected by rheumatoid arthritis, 43 (39.5%) from psoriatic arthritis and 23 from anchylosing spondylitis. There were 19 (17.43%) nSARS-CoV2 infection, of them 3 (15.8%) need hospitalization. Ninety-five (87.2%) receive at least one shot of nSARS-CoV2 vaccine, of these 78 (82.1%) got three shots of vaccine. Vaccine-related side effects were reported in 36 (37.9%), of these 15 (41.7%) have fever, 14 (38.8%) arthralgia and 29 (80.5%) fatigue. No patients required

Table 1. Patient demographics, disease characteristics and infection history

	CIRD patients	Non-CIRD patients	Missing values of CIRD and non-CIRD patients No. (%)		Group differences p-value
Age (years), mean (SD)	54.7 ± 12.8	55.6 ± 9.8	0	0	
Women, No. (%)	315 (61.3)	83 (83)	0	0	
Body mass index (BMI, kg/m^2), mean (SD)	27.9 ± 5.9	30.4 ± 7.8	0	0	
CIRD, No. (%)	192 (37.3)		0		
Rheumatoid arthritis	134 (26)				
Axial spondyloarthritis	72 (14)				
Psoriatic arthritis	116 (22.6)				
Connective tissue disease/vasculitis					
Disease duration (years), mean (SD)	9.8 ± 8.9	4.0 ± 6.5	0	0	
Therapy, No. (%)	316 (61.5)		0		
bDMARDs	147 (28.6)				
csDMARDs	33 (6.4)				
tsDMARDs	18 (3.5)				
no DMARDs					
History of a positive SARS-CoV-2 PCR test No. (%)	22 (4.3)	5 (5.0)	3 (0,6)	5 (5)	0.79
History of recurrent infection No. (%)	54 (10.5)	16 (16.0)	1 (0.2)	0	0.12
History of severe infection No. (%)	23 (4.5)	13 (13.0)	3 (0.6)	0	0.004
Educational level, No. (%)		9 (9.3)	35 (6.8)	3 (3)	0.13
low (< 8 years)	50 (10.4)	67 (69.1)			
moderate (8 to 12 years)	275 (57.4)	21 (21.6)			
high (> 12 years)	154 (32.2)				

BMI body mass index, SD standard deviation, no number, DMRD Disease Modifying Anti-Rheumatic Drugs, b biological, ts targeted synthetic, cs conventional synthetic

medical attention. Twenty (21.05%) of patients who receive at least one vaccine shot experienced a flare up. Nine (45%) need to change therapy. The risk of flare up was significantly associated with low disease activity/active disease in the last 12 months, p=0.009; OD 4.0; 95% CI: 1.5-11.3.

Conclusion: Overall, the nSARS-CoV2 vaccine is well tolerated in patients with inflammatory arthritis. The risk of disease flare is associated with active disease within the past 12 months. According to our results, the patients affected by inflammatory arthritis in sustained remission have no reason to hesitate to get the nSARS-CoV2 vaccination.

Disclosure of Interests: None declared

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AB1190 SOURCES OF INFORMATION ABOUT SARS-COV-2 USED BY PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES (CIRD)

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Background: Patients with chronic inflammatory rheumatic diseases (CIRD) may be at increased risk of Corona Virus Disease 2019 (COVID-19).[1] The quality of information obtained plays a crucial role for patients' decision to be vaccinated. Knowing patients' needs for information and which sources are used is important for the management of CIRD patients by rheumatologists and other physicians.

Objectives: To identify main sources of information on SARS-CoV-2 used by patients with CIRD and to analyze their influence on opinions and willingness to be vaccinated.

Methods: CIRD patients presenting to our tertiary rheumatology hospital were, after informed consent, consecutively included in the study once the vaccination campaign in Germany had started, to fill out a questionnaire. Next to sociodemographic and disease-specific data, vaccination willingness and knowledge regarding SARS-CoV-2 were assessed. Furthermore, patients' sources of information and their concerns about accuracy of information were evaluated. A numerical rating scale (NRS) ranging from 0 (completely disagree) to 10 (completely agree) was used. Values between ≥7 were taken as positive answer. Nonparametric tests and multivariate linear regression analyses were performed.

Results: In early 2021, a total of 514 patients were interviewed (Table 1). The majority (63.9 %) reported to be well-informed (NRS ≥7), whereas 18% had doubts regarding information on SARS-CoV-2. The most often used source of information was television, and only 8.6% reported to have been informed by a rheumatologist (Figure 1). About 20% of patients were no longer interested in receiving any information on SARS-CoV-2 through media. Information from rheumatologists, general practitioners, public health authorities or health related web sites did not reach 30.5% of patients. Of interest, 16% of subjectively well-informed patients were hesitant towards vaccination. As many as 43.6% of patients with doubts regarding information about SARS-CoV-2 indicated that they were not willing to be vaccinated. No source of information showed a strong correlation with SARS-CoV-2 vaccination willingness or with knowledge on SARS-CoV-2. Weak positive correlations were found between age and education level on the one hand and information sources about SARS-CoV-2 on the other hand. A weak negative correlation was found between doubts about information and health authorities, whereas positive correlations were found with social networks, friends and family.

Table 1. Sociodemographic and disease characteristics

Age (years)	54.7 ± 12.8
Women, No.* (%)	315 (61.3%)
Educational level, No.* (%)	
< 8 years	50 (10.4 %)
8-12 years	275 (57.4 %)
>12 years	154 (32.2 %)
Occupation, No.* (%)	
Full time	198 (38.5 %)
Pensioner	157 (30.5 %)
Part-time	80 (15.6 %)
Housewife/husband	37 (7.2 %)
Occupational incapacity	29 (5.6 %)
In training	7 (1.4 %)
Healthcare	5 (1 %)
CIRD, No.* (%)	
Rheumatoid arthritis	192 (37.3 %)
Axial spondyloarthritis	134 (26.1 %)
Connective tissue disease and vasculitis	106 (22.6 %)
Psoriatic arthritis	72 (14.0 %)
Disease duration, mean (years)	
Therapy, No.* (%)	9.8 ± 8.9
bDMARD	316(61.5 %)
csDMARD	147(28.6 %)
tsDMARD	33 (6.4 %)
no DMARDs	18 (3.5 %)

*Number of patients

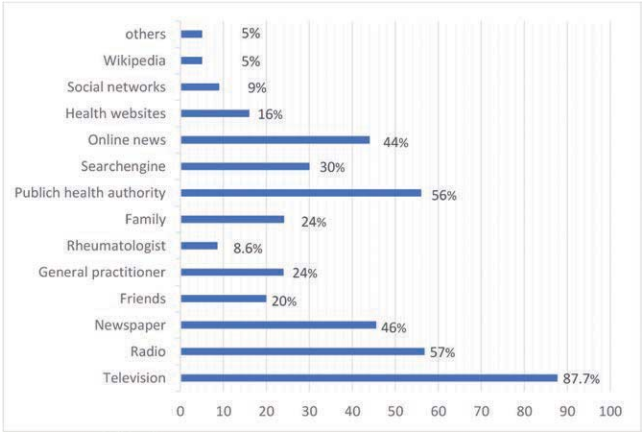

Figure 1. Sources of information of CIRD patients about SARS-CoV-2

Conclusion: Most CIRD patients think that they are well-informed about SARS-CoV-2. However, their information rarely comes from expert-based sources and rarely from rheumatologists. Thus, there is an unmet need for CIRD patients to receive appropriate and comprehensive information about SARS-CoV-2, its influence on rheumatic diseases, and about vaccination of patients with CIRD.

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Disclosure of Interests: None declared

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AB1191 SAFETY PROFILE OF COVID VACCINES IN ARTHRITIS PATIENTS. A TWO-CENTERS STUDY.

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Background: Coronavirus 19 disease (COVID-19) represents the most important pandemic of the last century. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection has produced more than 170 million cases and more than 3 million deaths. Due to the easy spread of the infection and the possibility of serious clinical manifestations, the role of anti-COVID 19 vaccination is essential. Vaccines with different mechanisms of action have been developed: mRNA-based, such as Biontech-Pfizer and Moderna, and viral vectored, such as AstraZeneca and Janssen. Despite possible adverse events, benefits afforded by these vaccines significantly outweigh potential risks associated with their administration in the general population.

Objectives: This study aimed to evaluate incidence and severity of adverse events (AEs), secondary to vaccination, in patients with Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Spondyloarthritis (SpA), immune-mediated diseases treated with immunomodulating drugs, by administering a questionnaire.

Methods: 294 patients (201 f and 93 m) were enrolled with a diagnosis of arthritis (RA 28%, PsA 43%, SpA 28%).

Results: Of the 294 enrolled patients, 107 underwent COVID vaccination, 73% with Biontech-Pfizer vaccine, 20% Astrazeneca and 6% Moderna. 50% of patients completed the entire vaccination cycle. 46% of patients presented AEs after the first dose of vaccine (45% of vaccinated with Biontech-Pfizer; 48% of vaccinated with Astrazeneca, 33% of vaccinated with Moderna). The most frequently observed AEs are: pain at the injection site (17%), fever (13%), headache (12%), myalgia (12%), fatigue (7.5%). Only 2.9% of patients had arthritis flares. The greatest trend of AEs was observed in patients with PsA (48%), and RA (26%). 32% of patients receiving the second dose of vaccine presented AEs (40% Moderna, 32% Biontech-Pfizer). The most frequently observed AEs after the second dose are: pain at the injection site (4.7%), fever (9%), headache (2.8%), myalgia (6%). No patient had arthritis flare after the second dose. The greatest trend of AEs was observed in patients with SpA (66%). Only 11% of patients presented AEs after the administration of both doses. Thirteen percent of patients did not follow the clinician's recommendations for immunomodulatory drug management, provided as per ACR or SIR recommendations.

Conclusion: The incidence of adverse events in arthritis patients was in line with that of the general population, without presenting serious manifestations, such as thrombosis, and without indicating a preference on the type of vaccine.

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AB1192 SARS-COV-2 VACCINE IN SPONDYLOARTHRITIS PATIENTS: OVERALL MODERATE/ HIGH IMMUNOGENICITY IMPAIRED BY IMMUNOSUPPRESSANTS AND BIOLOGICAL THERAPY

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Background: We recently reported an attenuate immunogenicity in patients with autoimmune rheumatic diseases. However, the effect of spondyloarthritis (SpA) and its treatment on COVID-19 vaccine immunogenicity remains to be determined for this group of patients. We therefore aimed to evaluate humoral immune responses to inactivated SARS-CoV-2 vaccine (CoronaVac) in patients with SpA (axial spondyloarthritis and psoriatic arthritis) taking DMARDs and commonly used targeted biological therapies, compared with a control group(CG).
Objectives: Evaluate immunogenicity and safety of CORONAVAC (Sninovac, Beijing) in Spondyloarthritis (SpA) patients.
Methods: Prospective observational cohort patients diagnosed with 194 SpA and 183 CG were vaccinated with CoronaVac in two doses with a 28-days interval. 194 patients completed the study and could be paired with CG for immunogenicity analysis. Blood samples were collected in the days 0, 28 and 69 (D69) to evaluate anti-SARS-CoV-2 IgG seroconversion(SC) and presence of neutralizing antibodies (NAb) in participants with negative IgG and NAb at baseline.
Results: Patients and GC were comparable regarding age (p=0.93) and sex (p=1.00). Immunogenicity at D69 showed a moderate/high SC (80.2% vs. 95.7%, p<0.0001) and Nab positivity (61.6% vs. 82.7%, p<0.0001) in SpA but lower than CG. Factors associated with lower immunogenicity were older age (56.8 vs. 51.4;p=0.03318) and higher frequencies of prednisone (25.7% vs 4.2%; p=0.0004), methotrexate (51.4% vs 40.1%, p=0.0016) and TNF inhibitor (TNFi) (62.9% vs 34.5%, p=0.0035). Likewise, prednisone (17.6% vs. 2.8%, p=0.0013) and TNFi (50% vs 33.9%; p=0.0408) were associated with diminished NAb positivity. Sulfasalazine was associated with higher SC rates (8.6% vs. 26.8%, p=0.0246) and NAb positivity (13.2% vs. 29.4%, p=0.0168). The multivariate analysis revealed that older age (p=0.037), prednisone (p=0.001), TNFi (p=0.016), and methotrexate(p=0.017) were independently associated with lower SC while prednisone (p=0.006) and TNFi (p=0.027) were also associated with reduced NAb response.
Conclusion: Our finding of an excellent safety and moderate/high SC rate in SpA supports the recommendation of CoronaVac vaccination. The impaired immune response in the minority of patients under immunosuppressive and biological therapy requires novel strategies to enhance antibody response in this subgroup of patients.
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AB1193 THE COURSE OF COVID-19 INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING VARIOUS BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: With the ongoing COVID-19 pandemic, the safety of biologic disease-modifying antirheumatic drugs in patients with rheumatic disease remains an important issue.
Objectives: to assess the course of COVID-19 infection in patients with rheumatoid arthritis receiving various biological disease-modifying antirheumatic drugs.
Methods: An analysis was made of the course of COVID-19 in patients with rheumatic diseases who were under observation at the North-Western State Medical University. I.I. Mechnikov in the period from March 2020 to November 2021. During this period, 198 (14.04%) cases of COVID-19 were registered out of 1389 patients included in the registries of the anticytokine therapy center. Among patients with rheumatoid arthritis who recovered from COVID-19 infection, 105 cases were registered, of which 53 patients received outpatient treatment, and 52 patients received inpatient treatment. In 76% of cases, patients received biological DMARDs in combination with synthetic DMARDs.
Results: Exacerbation of the articular syndrome was observed only in 12 (11.4%) patients with RA during COVID-19. The low percentage of exacerbations in patients with RD on the background of COVID-19 was probably associated with the use of dexamethasone at a dose of 16-32 mg, which has the ability to reduce the activity of the immune-inflammatory process in rheumatic diseases. This statement is confirmed by the fact that out of 52 patients with RA who were hospitalized for COVID-19, 16 patients (30.8%) received dexamethasone intramuscularly or intravenously, and 8 patients (15.4%) continued oral administration of this drug.

Table 1. The course of COVID-19 infection in RA patients treated with various biological DMARDs.

Severity and outcomes of COVID-19	All patients (n=105) N (%)	Abatacept (n=11) N (%)	Rituximab (n=56) N (%)	IL-6 inhibitors (n=9) N (%)	TNF-alpha inhibitors n=15 N (%)	JAK inhibitors n=17 N (%)
No hospitalization required	53 (50,5)	3 (27,3)	19 (33,9)	8 (88,9)	12 (80)	11 (64,7)
Hospitalization without oxygen support	31 (29,5)	5 (45,5)	18 (32,1)	1 (11,1)	3 (20)	4 (23,5)
Hospitalization with oxygenation or mechanical ventilation	24 (22,8)	3 (27,3)	19 (33,9)	0	0	2 (11,8)
Death	5 (4,8)	1 (9,1)	4 (7,1)	0	0	0

Conclusion: The use of rituximab was associated with a more severe course of COVID-19, which required hospitalization in 66% of cases, compared with the group of patients treated with TNF-α inhibitors, in which hospital treatment was carried out only in 20% of cases. The introduction of blockers of co-stimulation of T-cells, IL-6 inhibitors, targeted synthetic drugs did not affect the severity of COVID-19.
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Pain in rheumatic diseases, including fibromyalgia_

AB1194 PREVALENCE OF FIBROMYALGIA IN THE RHEUMATOLOGY OPDS DURING COVID19 LOCKDOWN: A CROSS-SECTIONAL STUDY

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Background: In the challenging times of Covid 19, anxiety increased among the general population. Fibromyalgia patients are more at risk of developing anxiety in these difficult times. This might result in more frequent visits to the rheumatology clinics with an exacerbation of their chronic pain syndrome.
Objectives: The main objective of this study is to compare the prevalence of FM in the rheumatology outpatients' clinics during the Covid 19 lockdown period (2020) and during the same period in the previous year (2019).
Methods: A cross-sectional study is conducted through 5 rheumatology clinics located in the 3 biggest emirates of the country (3 in Dubai, 1 in Abu Dhabi and 1 in Sharjah) to detect the number and charachteristics of fibromyalgia from March 15 to May 15th2019, and March 15 to May 15th2020.
Results: Total number of patients seen from march to May 2019 was 3480 out of them 55 were fibromyalgia patients with frequency 0.0158%. While from march to May 2020 total number of patients seen were 1355 out of them 66 were fibromyalgia patients with frequency 0.0487%. Figure 1

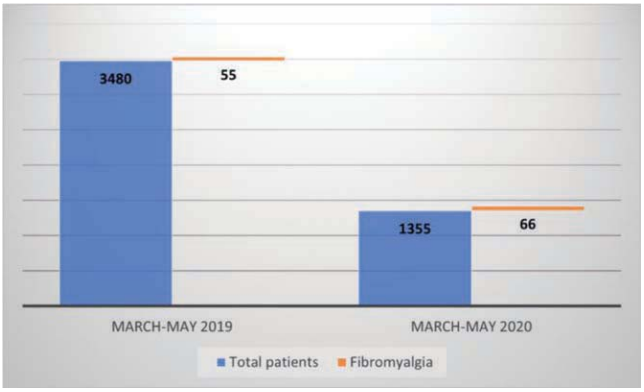

Figure 1. Total and fibromyalgia patients in March-May 2019 and March-May 2020

Descriptive analysis of fibromyalgia patients seen in the lockdown time March to May 2020 shows that; gender was 64 females 97%, 2 males 3%, profession 36 unemployed 54.5%, 28 white collar 42.4%, 2 blue collar 3%, Age minimum was 25 years, maximum 77 years, with mean 48.3±13 years. Table 1

Table 1. Descriptive analysis of the fibromyalgia paients

Gender *(Frequency)*	*Female*	64 (97%)
	Male	2 (3%)
Profession *(Frequency)*	*unemployed*	36 (54.5%)
	White collar	28 (42.4)
	Blue collar	2 (3%)
Fibromyalgia severity *(Mean±SD)*	*Tender Points*	15.7±3
	Pain	6.5±2.1
Fibromyalgia associates *(Frequency)*	*Headache*	32 (48.5%)
	Sleep Disturbance	47 (71.2%)
	Fatigue	65 (98.5%)
	IBS	26 (39.4%)
	Anxiety	43 (65.2%)
	Depression	37 (56.1%)

Tender points were 15.7±3, VAS for pain 6.5±2.1, sleep disturbance was present in 47 patients 71.2%, fatigue 65 patients 98.5%, irritable bowel syndrome in 26 patients 39.4%, headache in 32 patients 48.5%, anxiety in 43 patients 65.2%, and Depression in 37 patients 56.1 %. Comparing frequencies of fibromyalgia between March to May 2019 and 2020 shows a significantly higher frequency of fibromyalgia in March to May 2020, 3.1-fold more than 2019.

Conclusion: The prevalence of patients with fibromyalgia seen in the Rheumatology clinics significantly increased during the lockdown time in comparison to the same period of 2019.

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AB1195 FIBROMYALGIA AND SOCIODEMOGRAPHIC FACTORS: DATA FROM THE ITALIAN FIBROMYALGIA REGISTRY

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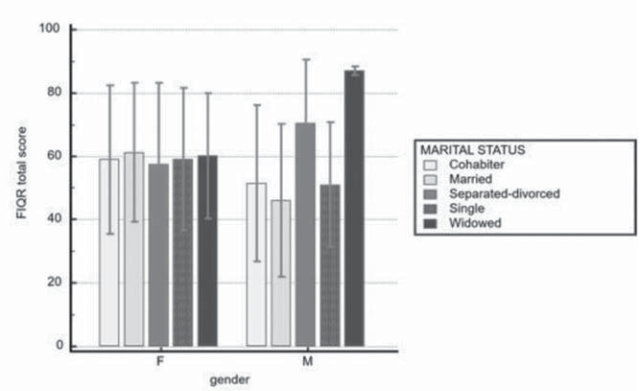
Background: Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome of unknown etiopathogenesis. Its development and maintenance are related to a complex interplay of biological, psychological, and contextual factors. Among the contextual factors, sociodemographic aspects are poorly elucidated.
Objectives: This study aimed to evaluate the relationships between sociodemographic/clinical factors and symptom severity measures using a web-based registry of patients with FM.
Methods: The study included adult patients recruited between November 2018 and April 2019 at 19 Italian rheumatology centers. All the patients underwent a complete physical examination and those laboratory tests specified in the revised European League Against Rheumatism (EULAR) recommendations for the management of FM. The inclusion criteria were (a) age from 18 to 80 years and (b) diagnosis of FM based on the 2010/2011 criteria of the American College of Rheumatology (ACR), made by a rheumatologist with at least 10 years of experience. All patients were asked to complete a package of questionnaires about their sociodemographic data (age, sex, marital status, education and BMI), disease-related variables, their quality of life, and the type(s) of pharmacological and non-pharmacological treatments currently received. The data and measures were electronically entered into the web-based Italian Fibromyalgia Registry (IFR) by physicians working at those 19 Italian rheumatology centers. Two disease-specific questionnaires were used for the clinical evaluation in this study: the Revised Fibromyalgia Impact Questionnaire (FIQR) and the Polysymptomatic Distress Scale (PDS).
Results: Data relating to 3,221 patients (3001 women and 220 men) was collected. The ANOVA showed significant difference in mean FIQR scores when the five marital conditions (cohabiter, married, separated/divorced, single, widowed) were compared (F 3.321, p <0.01). While males and females were found to have comparable FIQR scores, the interaction between gender and marital status indicated that separated/divorced males have higher FIQR scores (F 5,684, p = 0,617) (Figure 1). The multiple regression analysis demonstrated that patients who reported lower educational level experienced more severe FM symptoms, as scored with FIQR (p <0.0001).
Conclusion: Our results indicated that being male and separated/divorced is associated to higher severity of FM symptoms, as rated with FIQR. Furthermore, a relationship between educational level and FIQR scores has been detected. This study supports the importance of collecting simple SES measures to identify environmental risk factors for FM severity.

Figure 1. Interaction between marital status and gender



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AB1196 INFLUENCE OF NEUROPATHIC PAIN ON THE FUNCTIONAL STATUS OF ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Objectives: The aim of the study was to study the influence of neuropathic pain on functional status in elderly patients with rheumatoid arthritis (RA) with moderate disease activity.

Methods: Methods. The study included 115 geriatric patients who were divided into two groups. Group G1 included 80 patients (mean age 76.9 ± 9.6 years) with neuropathic pain, group G2 - 35 persons of comparable age (77.1 ± 8.6 years) without signs of neuropathic pain. Neuropathic pain was identified using the DN4 questionnaire. The RA activity in patients of both groups did not differ statistically significantly. All patients underwent a comprehensive geriatric assessment (CGA) to determine the functional status and diagnose geriatric syndromes [1]. All patients received basic anti-inflammatory drugs. Patients G1 and G2 were compared in terms of the following parameters, such as pain intensity according to a visual analogue scale (VAS, 0-100 mm), Rivermead Mobility Index (0-15), functional disorders according to International Classification of Function (ICF) (0-4), signs of anxiety and depression (HADS).

Results: According to the CGA data, senile asthenia syndrome was detected in 32 (40.2%) patients with neuropathic pain and in 10 (28.6%) patients without neuropathic pain (p = 0.035). The average number of geriatric syndromes in G1 was 6.06 ± 1.03, in group B - 4.5 ± 1.0 (p <0.05). Patients with G1 showed higher indices of pain severity according to VAS than in patients of the control group: 68.2 ± 10.1 and 52.1 ± 4.1 mm, respectively (p <0.001). In G1, patients had a significant decrease in mobility, in the domain «Activity and participation» in the ICF categories d450 (walking), d 540 (dressing), the indicator of dysfunction was 2.9 ± 0.3 versus 2.2 ± 0.2 (p = 0.049), there were more symptoms of anxiety and depression 56.5% and 35.2% (HADS ≥7; p <0.001), respectively.

Conclusion: Elderly patients with chronic neuropathic pain have higher signs of senile asthenia and decreased mobility and physical functioning in daily life. It is necessary to include the help of a psychologist and occupational therapist in planning the most effective comprehensive strategies for the treatment and prevention of exacerbations of neuropathic pain.

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AB1197 ANTIDEPRESSANTS TREATMENT AND SEVERITY OF PAIN IN RHEUMATOID ARTHRITIS PATIENTS WITH ANXIETY AND DEPRESSIVE DISORDERS

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Background: Anxiety and depressive disorders (ADD) significantly affect disease activity and pain modulation in rheumatoid arthritis (RA) patients. Psychopharmacotherapy (PPT) of ADD attempts to improve RA disease activity and manage pain in RA patients.

Objectives: To determine factors associated with intensive pain syndrome in antidepressants-treated RA-patients at five years endpoint.

Methods: 128 RA-patients (pts) were enrolled, 86% were women with a mean age of 47,4±11,3 (M±SD) yrs. All patients met the full ACR/EULAR 2010 criteria for RA. Disease activity was assessed using DAS28, pain severity – using Brief Pain Inventory scale (BPI). Severe Pain was defined as BPI Worst Pain Score (BPImax) from 7 to 10. 69,4% RA-pts were already taking prednisone (9 [5; 10] mg/day (Me (25%; 75%)), 84,4% - cDMARDs, 7,8% - bDMARDs (anti-TNF-α – 6,3%, rituximab – 1,6%). Biologics treatment duration varied from 1 to 6 years, antidepressants – from 6 to 96 weeks. ADD were diagnosed by psychiatrist in 123 (96,1%) of RA-pts in accordance with ICD-10 in semi-structured interview. Severity of depression and anxiety was evaluated with Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A). RA-pts with ADD were divided into the following treatment groups: 1 – cDMARDs (n=39), 2 – cDMARDs + PPT (sertraline or mianserine) (n=43), 3 – cDMARDs + bDMARDs (n=32), 4 – cDMARDs + bDMARDs + PPT (sertraline or mianserine) (n=9). Baseline BPImax by groups was as follows: 4,82±2,1, 5,85±2,06, 5,5±2,1, 7,57±2,17, respectively (p1-4<0,001; p2-4=0,048; p3-4=0,013). Multivariate logistic regression was used to determine predictors of severe pain.

Results: At five-years follow-up pain severity was assessed in 74 out of a total of 83 patient. By univariate logistic regression, baseline age, HAQ, CRP, DAS28 and BPImax, presence of extraarticular manifestations, cardiovascular diseases, cognitive impairments and schizotypal personality disorder, lower HADS for anxiety, no remission of anxiety or depression at five years and no history of glucocorticoids usage were significantly (p≤0,3) associated with severe pain at five-years follow-up (Table 1). These variables were subjected to multivariate stepwise logistic regression. Only extraarticular manifestations at baseline (OR 4,01 (95%CI 0,96 – 16,77), p=0,057), no history of glucocorticoids usage (OR 0,15 (95%CI 0,04 – 0,56), p=0,005) and nonremission of anxiety and depressive symptoms at 5-yrs (OR 0,11 (95%CI 0,019 – 0,668), p=0,016) were independently associated with severe pain at 5-years follow-up (R2=0,406, sensitivity 38,5%, specificity 92,7%).

Table 1. Factors associated with severe pain at 5 years (univariate logistic regression).

Factor	p	OR	95%CI	
			low	up
Baseline age	,129	1,047	,987	1,112
Baseline HAQ	,056	2,155	,981	4,734
Baseline DAS28	,075	1,361	,969	1,911
Baseline CRP	,151	1,011	,996	1,026
Baseline BPImax	,083	1,269	,970	1,662
Extraarticular manifestations at baseline (yes/no)	,027	4,278	1,179	15,517
Cardiovascular diseases at baseline (yes/no)	,259	2,111	,577	7,718
Cognitive impairments at baseline (yes/no)	,218	2,758	,549	13,860
Schizotypal personality disorder	,085	3,733	,834	16,715
HADS anxiety	,259	,904	,758	1,077
Anxiety and depressive symptoms remission at 5-yrs endpoint	,102	,313	,077	1,261
History of glucocorticoids usage (yes/no)	,025	,234	,066	,833

Conclusion: RA patients with severe pain should be routinely screened for anxiety and depression, and in patients with probable ADD consultation with a psychiatrist and prescription of antidepressants should be considered.
Disclosure of Interests: None declared
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AB1198 PREVALENCE AND PSYCHOPATHOLOGICAL CHARACTERISTICS OF ANXIETY AND DEPRESSIVE SYMPTOMS IN FIBROMYALGIA PATIENTS

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Background: Several studies reported higher depression and anxiety rates in fibromyalgia (FM) patients compared to the general population. Furthermore, dysfunctional coping strategies have been pointed to as intrinsic parts of the pathogenesis of FM.
Objectives: Our study aimed to verify the prevalence of anxiety and depressive symptoms and explore their correlation with physical symptoms as fatigue, sleep, and widespread pain in a cohort of patients diagnosed with FM. We also aimed to determine whether dysfunctional coping strategies might increase the depression and anxiety burden, besides worsening the core symptoms of FM.
Methods: We analyzed a cohort of 105 patients (median age of 53 years 6 M, 99 F) with a diagnosis of FM according to the ACR 2016 criteria. The participants were consecutively recruited from the Fibromyalgia clinic of the University of Campania "Luigi Vanvitelli". All patients underwent a psychiatric evaluation. We assessed widespread pain by the Widespread Pain Index (WPI) and the presence of fatigue by the Symptom Severity score (SS). Sleep disorders were investigated through Pittsburgh Sleep Quality Index (PSQI). We analyzed mental alterations by Hamilton Depression and Anxiety Rating Scales (HAM-D, HAM-A), and coping strategies by Coping Orientation to Problems Experienced (COPE) Inventory.
The Statistical Package for Social Sciences (SPSS) 22.0 was used; the level of significance was set at $p < 0.05$.
Results: All patients showed fatigue and widespread pain (100%); sleep disturbances were found in 90.5% of patients and overlapped with all sleep phases. The prevalence of anxiety associated with depression was 75.2%. We found isolated anxiety in 14.3% and isolated depression in 4.8% of patients. We further evidenced a different degree of depression: mild (50.7%), moderate (24.3%), and severe (6.5%). All patients showed depressed mood only if questioned (low tendency to spontaneous verbalization). COPE analysis showed no significant differences in the use of the three coping strategies (Problem-focused, emotion-focused, avoidance-focused). Pearson's correlation analysis highlighted a negative relationship between problem-focused strategies and the severity of anxiety ($r = -0.31$, $p = .001$) and depression ($r = -0.32$, $p = .001$). Our analysis also highlighted a positive correlation between fatigue, sleep disturbances, widespread pain, and both anxiety and depression. The analysis of the characteristics of anxiety and depressive symptoms showed a scarce tendency to spontaneous verbalization of depressed mood and ideas of guilt, mostly limited to family relationships, and a sense of ineffectiveness conditioned by the physical symptoms of the disease. Most patients showed psychomotor agitation, psychic and somatic anxiety, poor insight. The analysis of coping strategies adopted showed a negative correlation between problem-focused strategies and anxiety-depressive symptoms, suggesting that such strategies are less frequent in FM patients with comorbid anxiety and depressive symptoms.
Conclusion: Our study confirms the high prevalence of anxiety and depressive symptoms in FM patients. A positive correlation between the pivotal symptoms and anxiety and depressive symptoms may suggest, without implying a cause-and-effect relationship, that psychiatric intervention should be considered along with rheumatologic treatment, to improve both physical symptoms and quality of life. Potentiating problem-focused coping strategies may represent a target to improve anxiety and depressive symptoms.
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Table 1. Correlation analysis between coping strategies and HAM-D and HAM-A total scores

	HAM-D	HAM- A
Problem-focused Coping	- 0,32**	- 0,31**
Avoidant Coping	0,80	0,92
Emotion Coping	0,14	0,13

**$p<0.01$

Disclosure of Interests: None declared
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AB1199 THE ROLE OF THORACOLUMBAR FASCIA ULTRASOUND IN LOW BACK PAIN - IMPLICATION FOR GUIDED DRY NEEDLING

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Background: Dry needling under ultrasound guidance (DN-US) is a crucial therapeutic for treatment myofascial pain [1], restore muscle function and motion [2], is among priotized methods for treatment low back pain (LBP), can be effective in rheumatic diseases. The definition `myo-fascial` calls for searching trigger points (TrPs) in fascia to improve the treatment effectiveness [3]. Ultrasound examination and guided dry needling can help understanding the role of the thoracolumbar fascia (TLF), its layers function and role in development of low back pain.
Objectives: Aim was to evaluate the relevance of fascial ultrasound and guided dry needling in low back pain in particular for thoracolumbar fascia (TLF).
Methods: We included 32 patients (20 females, 21-63 years old) with myofascial low back pain, postural imbalance; did DN-US protocol according to R. Bubnov [1]: muscle TrPs were identified, fine (28G) steel needle DN-US was applied. Additionally considered fascial structures for detecting areas of abnormalities (hypervascularity, heterogeinity, hypomotility, adhesions) aka `trigger points`. We did separate re-evaluating after stage of fascia and muscle needling.
Results: In all patients movement restored and pain decreased after muscles DN; in 24 patients additionally we detected changes in the major fascial points as follows: TLF, its layers (thickness increased up to 5-10 mm, local and diffuse calcification), sacroiliac joint (SIJ); and did successful DN-US to affected areas (increased thickness and stiffness according to SWE). During procedure we revealed places of stiff areas in fascia (TrPs), did precise dry needling to place the top of needle in the affected area in fascia. The strong `needle grasp`, low level of sensation during needling, local twitch response was not seen in fascia. TFL TrPs were associated with quadratus lumborum muscle. We noted fair improvement of motion in lumbar level after TFL needling alone, decreased hyperechoic lamina to 2-4 mm after DN. We detected higher rates of motility, improvement postural balance and pain decrease, fewer sessions needed in patients after extensive protocol.
Conclusion: Fascia dry needling is accessible and effective method for myo-fascial low back pain treatment, can provide additional mechanical benefit and help to maintain treatment effect. Affected fascia can be considered as relevant TrPs, specific ultrasound symptoms should be validated.
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AB1200 THE IMPACT OF THE PRESENCE OF FIBROMYALGIA ON ILLNESS PERCEPTIONS AND COPING STRATEGIES IN HIV INFECTED PATIENTS: PRELIMINARY STUDY

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Background: Coexisting fibromyalgia syndrome (FMS) to the chronic diseases and its negative impact on global health status in these diseases has been identified. Recent treatment strategies have changed HIV from a terminal disease to a chronic condition that requires great effort because of regular treatment and periodic medical screenings. The prevalence of fibromyalgia has been reported in HIV patients as 1-17%. It was reported that greater illness perceptions are associated with dysfunctional coping strategies in HIV patients with detectable or high viral load. There are no data on illness perceptions and coping strategies in HIV patients with FMS.
Objectives: The aim of this study was to evaluate the impact of the presence of fibromyalgia on illness perceptions and coping strategies in HIV infected patients.
Methods: Data about illness perceptions by The Brief Illness Perception Questionnaire (Brief-IPQ) and coping strategies by the COPE questionnaire were collected from 79 HIV patients. FMS was determined according to 2010 American College of Rheumatology criteria. CD4+ cell counts, viral load, and disease

duration were also noted. Kolmogorov Smirnov test, chi-square test, Mann Whitney-*U* test, Spearman correlation analysis, and Univariate analysis of variance were used for statistical analyses.

Results: Patients were aged between 22 and 77 years, with a mean age of 44.63±10.7 years. Thirteen patients (16.5%) were diagnosed with FMS and of those 4 (30.8%) were women. Cognitive illness representations and emotional representations scores were higher in HIV patients with FMS than those without FMS ($p<0.05$). Disease duration, HIV-progression biomarkers (CD4+ and viral load), COPE questionnaire scores, and illness comprehensibility sub scores of Brief-IPQ were not different between the HIV patients with and without FMS ($p>0.05$). The significant effect of the presence of FMS on cognitive illness representations ($p<0.001$) and emotional representations ($p<0.05$) was found by univariate analysis of variance in patients with HIV.

Conclusion: According to the preliminary results of this study, FMS was detected 16.3% of 79 HIV patients and coexisting FMS was associated with increased cognitive and emotional representations in patients with HIV. Coping strategies were not affected by the comorbid FMS. The presence of FMS may adversely affect perceptions of the disease in HIV infected patients. Since the patients' beliefs about their illness have great importance in the patients' health outcomes and the understanding of the disease, physicians should be aware of the possibility of concomitant FMS in patients with HIV.

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AB1201

PAIN DESCRIPTORS AND DETERMINANTS OF PAIN SENSITIVITY IN KNEE OSTEOARTHRITIS: A COMMUNITY-BASED CROSS-SECTIONAL STUDY

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Background: The phenomenon of heightened pain sensitivity is implicated in the pain experiences of people with OA[1]. Limited research show that pain sensitivity is associated with poor health and treatment outcomes. However, epidemiological research investigating the extent and determinants of pain sensitivity in OA is scarce. In addition, the quality of pain is poorly described. Both the assessment of quality of pain and pain sensitivity can be important to inform clinical decision-making and treatment.

Objectives: To explore pain characteristics in individuals with knee osteoarthritis (KOA), to compare pain sensitivity across individuals with KOA, chronic back pain (CBP) and pain-free individuals (NP), and to examine the relationship between clinical and pain characteristics with pain sensitivity in KOA.

Methods: Cross-sectional, community-based online survey. Two datasets were combined comprising Dutch individuals of ≥ 40 years of age, experiencing chronic knee pain (KOA, N=445; dataset 1), chronic back pain (CLP, N=504; dataset 2), or no pain (NP, N=256; dataset 2). Demographic and clinical characteristics, global health, physical activity/exercise, and pain characteristics including intensity, spreading, duration, quality (SF-MPQ), and sensitivity (PSQ) were assessed. Differences between (sub)groups were examined using analyses of variance or Chi-square tests. Regression analyses were performed to examine determinants of pain sensitivity in the KOA group.

Results: Quality of pain was most commonly described as aching, tender, and tiring-exhausting in the KOA group (Figure 1). Overall, the KOA group had higher levels of pain sensitivity compared to NP group, but lower levels than the CBP group (Table 1). Univariately, pain intensity, its temporality and spreading, global health, doing exercise, and having comorbidities were weakly related to pain sensitivity (standardized beta's: 0.12-0.27). Symptom duration was not related to pain sensitivity. Older age, higher levels of continuous pain, lower levels of global health, and doing exercise uniquely contributed, albeit modest, to pain sensitivity ($P<0.05$).

Table 1. Mean (SD) pain sensitivity scores across three groups

	KOA	CBP	NP	KOA vs CBP¥		KOA vs NP¥	
	N=445	N=504	N=256	Difference#	95% CI	Difference#	95% CI
PSQ-total, mean (SD)	4.4 (1.5)	4.7 (1.8)	3.6 (1.4)	-0.23	-0.49, 0.03	0.68	0.36, 1.01
PSQ-minor, mean (SD)	3.2 (1.6)	3.7 (2.0)	2.4 (1.3)	-0.32	-0.60, -0.05	0.70	0.36, 1.05

Abbreviations: PSQ=Pain Sensitivity Questionnaire, KOA=Knee OA pain group, CBP=Chronic Back Pain group, NP=Non-pain group. ¥CBP: N = 487, NP: N=242. #Mean differences adjusted for sex and age.

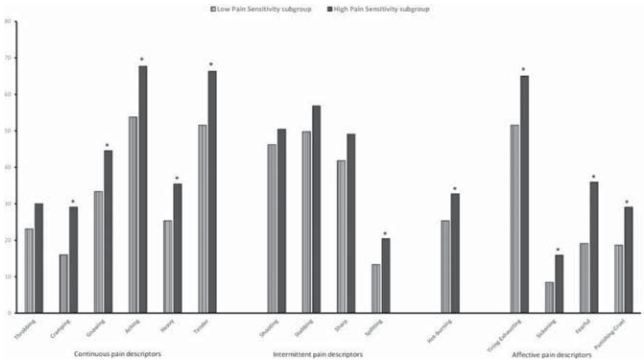

Figure 1. Percentage of individuals with self-reported knee OA who rated pain descriptors as moderate to severeNote: Subgroups based on median split total score Pain Sensitivity Questionnaire. *P<0.05

Conclusion: Continuous pain such as aching and tenderness in combination with decreased physical activity may be indicative for individuals at risk for widespread pain and, ultimately, poor treatment outcomes.

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Disclosure of Interests: None declared

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AB1202

ASSESSMENT OF PAIN THRESHOLDS TO VERIFY CENTRAL SENSITIZATION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS OF THE KNEE

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Background: Central sensitization in patients with rheumatoid arthritis, osteoarthritis of the knees increases the risk of comorbid disorders, the most frequent of which are depression, cognitive impairment and insomnia. Verification and timely diagnosis of central sensitization will help to improve pain control in rheumatic diseases. (1,2)

Objectives: to study pressure pain thresholds in patients with rheumatoid arthritis (RA) and osteoarthritis of the knee (OAk) with chronic pain.

Methods: All patients had pain intensity scores according to the VAS scale, neuropathic/nocytoplastic pain severity according to the DN4 and Pain DETET questionnaires, central sensitization severity was assessed using the CSI scale. To verify the presence of central sensitization instrumentally and to confirm the presence of secondary hyperalgesia detected clinically, algometry was performed in 42 female patients with OAk and 42 patients with RA. A comparison group of 42 healthy volunteers comparable in gender and age with the patients was also selected. Using a Wagner FDK20 algometer, pressure pain thresholds for OAk in the knee joints were studied (4 points: 1st point located 2.5 cm medial to the patella, 2nd point in the center of the patella, 3rd 2.5 cm distal to the patella, 4th in the goosefoot area) and m. Trapezius (5th reference point) in all patients with OAC and controls. In the group with RA, pain thresholds were studied at 4 points: 1st - nail bed of the 1st finger, 2nd - wrist (above the extensor tendon retention), 3rd - 2.5 cm lateral to the kneecap and 4th m. trapezius (reference point) in all patients and controls.

Results: The mean age of patients with RA and OAk was 53.0 [41.0;61.0] and 61.0[57.0;63.0] years, with disease duration at the time of study of 9.0 [4.0;13.0] and 13.0[7.0;15.0] years, respectively. The DN4 questionnaire scores were 2.0 [1.0;4.0] for RA and 5.0[5.0;6.0] for OAk, and the Pain DETECT scores were

9.0[4.0;15.0] for RA and 17.0[14.0;19.0] for OAk. Pain intensity on VAS in patients was 60.0[40.0;70.0] for RA and 70.0[60.0;80.0] for OAk.
The results of algometry are shown in Figure 1.

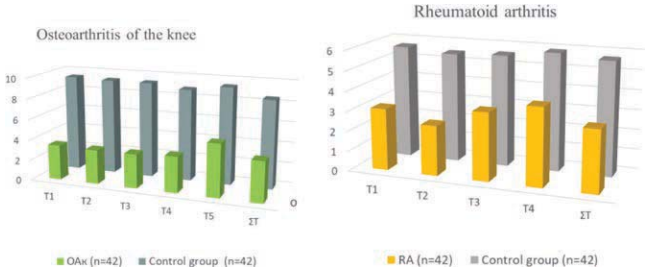

Figure 1.

Lower pain thresholds in patients with RA and OAk were noted not only in the area of the affected joints, but also in the distant reference point, indicating the presence of secondary hyperalgesia in these patients, which is a neurophysiological sign of central sensitization. A significant decrease in the pain threshold index was also noted in patients with central sensitization compared to those in the control groups.
Conclusion: The study of pain thresholds is one of the tools for verification of CS in patients with RA and OAk, but requires further study.
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AB1203 DAS28 (DISEASE ACTIVITY SCORE) ELEVATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) WHO HAVE COMORBID FIBROMYALGIA ARE EXPLAINED BY ELEVATED TENDER JOINT COUNTS AS MUCH AS BY ELEVATED PATIENT GLOBAL ASSESSMENT

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Background: DAS28 (disease activity score 28) is elevated in the 20-30% of patients with rheumatoid arthritis (RA) who have comorbid fibromyalgia (FM), largely on the basis of tender joint count (TJC) and patient global assessment (PATGL) [rather than swollen joint count (SJC) or erythrocyte sedimentation rate (ESR)].[1] High DAS28 in the absence of clinical inflammatory activity may suggest inappropriate treatment escalation and/or changes in a treat-to-target approach. Some reports suggest removal of PATGL from criteria for remission[2].
Objectives: We analyzed the 4 DAS28-ESR component measures in reports of FM+ or FM- RA patients, to recognize the possible contribution of each to elevated DAS28 in patients with FM.
Methods: We reviewed reports from a meta-analysis of elevated DAS28 in RA patients with comorbid FM,[1] and conducted a PubMed search for further reports of DAS28-ESR in FM+ or FM- RA patients in routine care. We analyzed reports that presented the 4 individual DAS-28-ESR components in FM+ vs FM- RA patients, calculated overall medians of published mean or median results, and calculated ratios of each component measure in FM+ and FM- patients.
Results: Eleven reports were identified. Mean disease duration was 5-12.8 years. Median DAS28-ESR of means/medians in FM+ RA patients was 5.3, and >5.1 in 9 of 11 studies, suggesting high disease activity (moderate in 2 studies) (Table 1). By contrast, median DAS28-ESR of means/medians in FM- RA patients was 4.1, moderate (3.2–5.1) in all 11 studies (Table 1). Medians of individual DAS28-ESR components were 28.5 vs 26 for ESR, 3.25 vs 3 for SJC, 12.3 vs 5.5 for TJC, and 62.7 vs 40 for PATGL in FM+ vs FM- RA patients, respectively. Ratios of DAS28 components in FM +/FM - patients were 2.7 for TJC, 1.6 for PATGL, 1.1 for ESR, and 1.0 for SJC.
Conclusion: Mean DAS28-ESR indicated high vs moderate disease activity in 9 of 11 FM+ RA patient groups vs all 11 FM- RA groups, respectively. Among the 4 DAS28 component measures, TJC differed most in FM+ vs FM- RA patients followed by PATGL, while SJC and ESR were similar in both groups. The impact of TJC likely is underestimated as the DAS28 formula weights TJC twice as SJC. Elevated DAS28 in the absence of inflammation in RA FM+ patients may result as much or more from TJC as from PATGL.
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Disclosure of Interests: None declared
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AB1204 MUSCULOSKELETAL MANIFESTATIONS IN PATIENTS WITH ENDOCRINE DISORDERS IN AN AMAZON OUTPATIENT CLINIC

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Background: Chronic pain is frequently associated with these conditions and is an important cause of care in the health service. This pain is among the main manifestations of the musculoskeletal system, and 40% of individuals can manifest this type of pain at some point in their lives. That is why it is important to have doctors prepared to make an adequate approach to the symptomatology and especially to the underlying diseases. Rheumatic manifestations are part of the manifestation of systemic diseases, in which include diseases of the endocrine

Table 1. DAS28 and component measures In RA patients who have or do not have comorbid fibromyalgia and ratio of means in the two groups (FM+/FM-)

MEASURES	DAS28		ESR		SJC		TJC		PATGL	
STUDY	FM+/ FM-	FM+/ FM-	FM+/ FM-	FM+/ FM-	FM+/ FM-	FM+/ FM-	FM+/ FM-	FM+/ FM-	FM+/ FM-	FM+/ FM-
Ranzolin 2009	5.4, 4.0	1.3	29*,25	1.16	3.5*,2.0*	1.7	9.5*,3*	3.2	76*,40*	1.9
Pollard 2010	6, 4.3	1.4	39,27	1.4	4.0,4.0	1	17,6	2.8	66,40	1.6
Toms 2010	5.3, 3.7	1.4	39.4,28.5	1.4	4.9,3.0	1.6	14.1,2.9	4.9	60.4,32.6	1.8
Zammurrad 2013	5.3, 3.9	1.3	38.9,31	1.2	2.8,1.7	1.6	13.1,4.1	3.2	62.7,38	1.6
Nawito 2013	5.6, 4.5	1.2	38.2,41.8	0.9	2.8,3.0	0.9	12.3,4.5	2.7	38.2,41.8	0.9
Ghib 2015*	5.6, 4.6	1.2	23,22	1.1	5.0,6.0	0.8	15,5.5	2.7	66,44.5	1.5
Joharatnam 2015*	4.8, 4.4	1.1	19,17	1.1	1.0,1.0	1	11,6	1.8	70,42	1.6
Mian 2016	5.2, 4.1	1.3	20.5,19.1	1.1	1.8,2.8	0.6	15.6,7.3	2.1	57,49.5	1.1
Chakr 2017	5.3, 3.9	1.3	28.5,26	1.1	3.9,2.4*	1.6	10*,3*	3.3	56.5*,31.5*	1.8
Salaffi 2018*	4.5, 3.8	1.2	24,32	0.7	3.0,4.0	0.7	12,6	2	80,70	1.1
Provan 2019	5.2, 4.2	1.2	23,21	1.1	8.4,6.4	1.3	10.7,6.4	1.7	55,30	1.8
Median-11 Studies	5.3, 4.1	1.3	28.5,26	1.1	3.2,5.3	1	12.3,5.5	2.7	62.7,40	1.6

* All values were reported means other than medians noted by asterisk (*).

system, which can mimic rheumatic conditions. Despite the ignorance of some, endocrine diseases are underlying diseases linked to musculoskeletal manifestations. Thus, secondary arthropathies of non-rheumatologic origin or osteoarticular complaints that simulate or show rheumatic diseases can be found in patients with endocrine diseases during their evolution or in the initial phase along with other systemic symptoms. Based on this concept, we carried out the follow-up and evaluation of musculoskeletal manifestations presented by patients with endocrine disorders in a tertiary health service.

Objectives: The aim of this study is to characterize the musculoskeletal manifestations in patients with endocrine diseases: type 1 and type 2 Diabetes Mellitus; hypothyroidism; hyperthyroidism and pituitary diseases and to clinically classify the patients based on physical examination and imaging findings.

Methods: A cross-sectional and descriptive study, where clinical screening was performed at the endocrinology outpatient clinic, in which patients with musculoskeletal complaints were identified. These patients were referred for evaluation with a rheumatologist with clinical, laboratory and imaging investigation for the diagnosis of rheumatic disease. A questionnaire with epidemiological and clinical data was applied.

Results: To date, 466 patients diagnosed with endocrine diseases have been interviewed, 53.4 ± 14.7 years old, 371 (79.6%) were female and 95 (20.4%) were male. Of the patients interviewed, 326 (70.1%) reported musculoskeletal pain. In relation to endocrine diseases, the most frequent one was type 2 DM with 212 patients (45.5%), and 77.25% of these people have chronic musculoskeletal pain, most of them 5 to 7 times a week, showing an intrinsic character of this disease with pain complaints from a great part of this population. The prevalence of 27.3% of hypothyroidism, 10.7% of DM type 1, 7.1% of hyperthyroidism, and less expressive amounts of other endocrine diseases such as acromegaly (1.7%), giantism (0.4%), and the like were also identified. About 59.6% of those who have pains are not followed up in the rheumatology service, 41.3% of these have already indicated these pains to their endocrinologist, however they did not have their complaint properly signaled. Of those interviewed, 94 (37.5%) take antihypertensives and 32.7% oral anti-diabetics. The most commonly found diagnoses in rheumatic diseases: Rheumatoid Arthritis (39%); Osteoarthritis 22.9% and Fibromyalgia 20%; Osteoporosis 19%, Tendinitis calcaria, Psoriatic Arthritis and GOTA with 5.7%. The main joints affected were: Hands (54.4%); Knees (45.3%) and feet (41.8%).

Conclusion: Our research with pre liminal results has demonstrated the mutuality between endocrine diseases and musculoskeletal manifestations and, therefore, that rheumatologic diagnoses are increasingly frequent in this population. The high prevalence of these symptoms secondary to endocrine diseases raises serious questions to improve the quality of life of these patients, and also to increase the number of investigations in this field, because the pathophysiological mechanisms of this association are not well elucidated and, from there, to expand this information to professionals who may not be aware of this relationship.

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Disclosure of Interests: None declared

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AB1205

MEDICAL AND PSYCHOLOGICAL COMORBIDITIES IN FIBROMYALGIA: A CROSS SECTIONAL STUDY

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Background: Psychological disorders are commonly observed in fibromyalgia (FMS). Medical comorbidities are less well characterised in FMS. We sought to assess the prevalence of these disorders in an observational cohort of patients in a tertiary hospital in North India.

Objectives: The prevalence of medical and psychological comorbidities in FMS and the prevalence of these disorders in FMS subgroups classified according to different ACR classification criteria were assessed.

Methods: Patients satisfying either the 1990 ACR or the 2016 ACR Fibromyalgia criteria were included in a cross-sectional study between October'19 and December'21. All patients were assessed for prevalence of chronic fatigue syndrome (CFS), post-traumatic stress syndrome (PTSD), restless leg syndrome (RLS) and medical comorbidities including obesity, obstructive sleep apnoea, anemia, diabetes mellitus, hypertension and hypothyroidism.

Results: A total of 98 patients of median age 39 years (34 – 47) were included, of which 9 met only the 1990 ACR criteria (100% females), 30 met only 2016 ACR criteria (86% females) and 59 met both criteria (89% females). Widespread Pain index was significantly higher in the 1990+2016 group compared to subgroups which met only either of the criteria. Hypothyroidism (subclinical or clinical) was similarly higher in the 1990+2016 subgroup. At least one psychological comorbidity was seen in 41%, with CFS present in 30% and PTSD in 14%. The median systolic blood pressure was in the hypertensive range (146 mm Hg) in the 1990-only group, with hypertension being present in 1/3rd of the total cohort. Obesity was present in 59% and Diabetes in 11%. Iron deficiency anemia was seen in 20%.

Table 1. Prevalence of comorbidities in different subgroups of Fibromyalgia

Clinical features	FMS Cohort (N-98)	ACR 1990 (N-9)	ACR 1990+2016 (N-59)	ACR 2016 (N-30)	p-value
F:M	**88:10**	9:0	53:6	26:4	0.6
Age (years)	**39 (34 – 47)**	38 (32 – 46)	38 (34 – 45)	44 (35 – 50)	0.2
Duration of symptoms (months)	**48 (24 – 84)**	48 (36 – 84)	48 (24 – 78)	60 (27 – 84)	0.6
WPI	**15 (12 – 17)**	14 (8 – 15)	16 (14 – 18)	13 (10 – 16)	0.001
SSS	**8 (6 – 10)**	3 (1 – 4)	6 (7 – 10)	8 (6 – 9)	<0.000
TP	**13 (9-16)**	13 (12 – 15)	15 (13 – 16.5)	6 (4 – 8)	<0.000
BMI (kg/m2)	**26 (23 – 28)**	23 (22 – 25)	26 (24 – 28)	26 (23 – 29)	0.2
Obese (BMI ≥ 25 kg/m2)	**58 (59%)**	3 (33%)	37 (62%)	18 (60%)	0.08
Prediabetes (HbA1c 5.7 – 6.5)	**21 (21%)**	0	16 (27%)	5 (16%)	0.8
Diabetes (HbA1C ≥6.5)	**11 (11%)**	1(11%)	9 (15%)	1 (3%)	0.2
Systolic BP	**125(115–143)**	146 (117–148)	120(114–137)	127(116–143)	0.1
Diastolic BP	**80 (76 – 88)**	80 (76 – 83)	82 (75 - 88)	79 (76 – 88)	0.8
Hypertension (≥140/90 cm)	**37 (37%)**	6 (66%)	20 (33%)	11 (36%)	0.2
Hypothyroidism (TSH > 5 mIU/L)	**12 (12%)**	0	11 (22%)	1 (3%)	0.04
Iron deficiency anemia (Serum Ferritin < 12 ng/ml)	**14 (20%) (n-67)**	3 (42%)	9 (23%)	2 (9%)	0.1
OSA (intermediate to high risk by STOPBANG questionnaire)	**32 (32%)**	1 (11%)	17 (28%)	14	0.1
CFS	**30 (30%)**	1 (11%)	22 (37%)	7 (23%)	0.1
PTSD	**14 (14%)**	0	11 (18%)	3 (10%)	0.2
RLS	**9 (9%)**	0	5 (8%)	4 (13%)	0.4

F female, M male, WPI widespread pain index, SSS symptoms severity score, TP tender points, BMI body mass index, BP blood pressure, OSA obstructive sleep apnoea, CFS chronic fatigue syndrome, PTSD post traumatic stress disorder, RLS restless leg syndrome

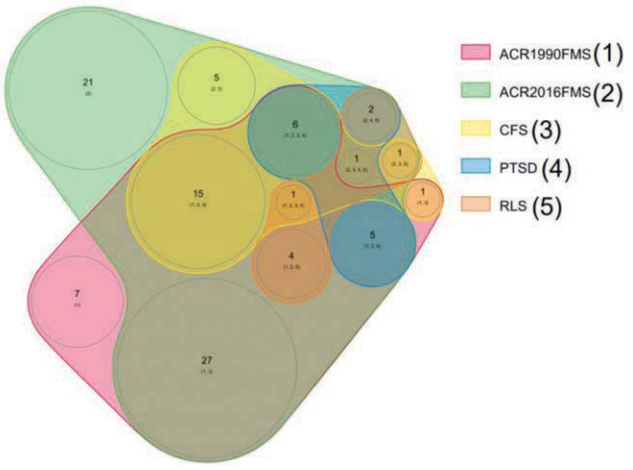

Figure 1. Venn Diagram depicting Fibromyalgia subgroups having psychological comorbidities

Conclusion: There is a high prevalence of comorbidities in patients with fibromyalgia with nearly half having atleast one psychological comorbidity, and obesity, hypertension and iron deficiency anaemia being the common medical comorbidities. Those who met only the 1990 ACR criteria formed less than 10%.

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AB1206 JUVENILE PRIMARY FIBROMYALGIA SYNDROME. RESULTS FROM A VOSVIEWER-BASED BIBLIOMETRIC NETWORK ANALYSIS.

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Background: In 1985, Yunus and Masi described the juvenile primary fibromyalgia syndrome (JPFS). It is a chronic musculoskeletal pain syndrome that affects children and adolescents [2] with an estimated prevalence that varies from 1.2 to 6.2% [3]. Clinical features are widespread persistent pain, sleep disturbance, fatigue, and the presence of multiple discrete tender points on physical examination. Notably, this syndrome can impact the quality of life status and psychosocial development of children and adolescents [4]. Despite a lot of research being conducted, several aspects on etiology and pathogenesis, clinical characteristics, and evaluation, as well as therapy should be better explained.
Objectives: This bibliometric analysis is aimed at dissecting the developed research in the subject. It could provide helpful findings for predicting the direction of future studies, implementing corrective measures, and improving research networks.
Methods: The global literature on JPFS was scanned in the Web of Science (WOS) online database. The search string applied to identify the closest matching articles was "Juvenile primary Fibromyalgia Syndrome (all field)".All data were acquired on January 30, 2022. The information for the documents that met the requirements were extracted. The source was Journal Citation Reports™ 2020 (Clarivate Analytics). The literature analysis and knowledge visualization software tool VOSviewer (version 1.6.17) was used to analyze the co-occurrence of keywords (interconnection), co-citation (bibliographic coupling), co-citation analysis for sources, and countries, and analysis of the most productive organizations and networks.
Results: A total of 66 articles on JPFS were published from 1985 to January 2022, in WOS (n=24; median 2). About article types, 38 were research articles, 16 reviews, 8 meeting abstracts, 2 letters, 1 book chapters, 1 correction, 1 proceeding papers.
The analysis of keywords provided by authors showed that of 235 keywords, 38 met the threshold (interconnection 3). The most frequent keywords were Children (n=14); Adolescent (n=13), and Functional disability (n=10) (Figure 1)

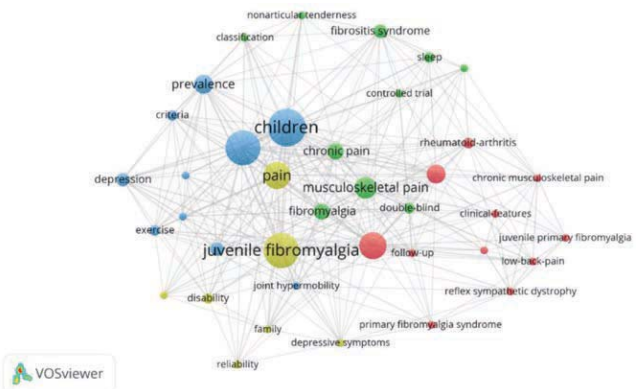

Figure 1. Co-occurrence of keywords

For the co-citation study, we used cited sources (journals) as unit (minimum numbers of citations of a source 15). Of 563 sources, 23 met the threshold. For each source, the total strength of the co-citation links with other sources was rated. The JOURNAL OF RHEUMATOLOGY (IF 4.66; Q2) obtained 22 links and 173 citations.
Most documents came fro the US (n=40; links=5), and Israel.
The analysis of affiliations was conducted by considering the cut-off 2 as the minimum number of documents of an organization. Out of 59 organizations, 23 met the threshold. The University of Cincinnati produced a total length strength of 3675 (11 documents).

Conclusion: This bibliometric network analysis on JPFS can be helpful for planning future research. It highlights the strength of representative scietists and core research teams. Research networks should be built, and high-value investigations are warranted.
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AB1207 RISK FACTORS FOR HIGHER RELAPSE RATE AND/OR PROLONGED GLUCOCORTICOID THERAPY IN POLYMYALGIA RHEUMATICA: MULTICENTRE STUDY IN 185 PATIENTS

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Background: Glucocorticoids (GC) are the therapeutic mainstay in polymyalgia rheumatica (PMR). However, their adverse effects are of particular concern in elderly patients. Relapses and long-term GC dependency are common.
Objectives: Assess the risk factors for higher relapse rate and/or prolonged glucocorticoid therapy in 185 PMR patients from Argentina.
Methods: A multicenter observational study of PMR patients diagnosed according to the Chuang criteria seen at the outpatient clinics at 12 public or private rheumatology units from Argentina between 2006 and 2021 was performed. Patients were followed until permanent remission, lost to follow up, or a maximum of 2 years after diagnosis. Relapse was defined as an exacerbation of PMR symptoms requiring an adjustment of GC dose (≥ 4 mg) occurring at least 1 month after diagnosis. Time to relapse was modeled using the Kaplan-Meier method. Cox regression models were used to evaluate predictors of time to first and subsequent relapses.
Results: A total of 185 patients were included (69.1% female) with a median age of 71 years (IQR 65-78 years). The median follow-up time was 17.1 months (IQR 6.8-34.7) and the incidence of relapses was 1.2 per 100 persons/month. The median time to relapse was 70.5 months (25th percentile = 14 months). Pain and/or stiffness in shoulder girdle and pelvic girdle together more common (p = 0.02) in the clinical presentation of patients who relapsed. In univariate analysis, PMR patients with a previous history of dyslipidemia had a lower risk of relapse (HR = 0.55, 95% CI = 0.33-0.94, p = 0.03). Laboratory at time of diagnosis showed that an ESR > 50 mm was found as a risk factor for relapse (HR = 2.50, 95% CI = 1.23-5.10, p = 0.011). Regarding therapy, meprednisone (HR = 2.38, 95% CI = 1.31-4.31, p = 0.004) and high dose GC (HR = 2.35, 95% CI = 1.42-3.87, p = 0.001) had higher risk of relapse. In multivariate analysis, only meprednisone (HR = 2.59, 95% CI = 1.28-5.23, p = 0.008) and high dose of GC (HR = 2.41, 95% CI = 1.19-4.89, p = 0.014) remained the only risk factors for relapse.
Conclusion: A lower relapse rate than that reported in the literature was observed. Meprednisone and high dose of GC are significant predictors of future relapses. Our results suggest that efforts should be made to minimize initial GC dose and avoid the use of meprednisone as GC of first choice in order to prevent disease relapses.
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AB1208

FREQUENCY OF MUSCULOSKELETAL AND OTHER EXTRA-INTESTINAL SYMPTOMS IN PATIENTS WITH CELIAC DISEASE

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Background: Celiac disease (CD) is one of the most common gastrointestinal tract diseases, in adults and children. Prevalence of CD is 1-3% [2]. The most common symptoms of CD are gastrointestinal symptoms. At the same time, celiac disease may manifest with extraintestinal symptoms, including the musculoskeletal, nervous, reproductive system, and skin, especially when it debuts at a late age [1,2]. However, data about musculoskeletal manifestations of CD are limited.

Objectives: To show the frequency of musculoskeletal complaints and their peculiarities in patients with CD.

Methods: Data from 94 patients with diagnosed by gastroenterologist celiac disease were collected with the on-lain survey. All the patients were positive in CD-related immunological and genetic tests and had biopsy established CD.

Results: The average age of respondents is 37,52 ± 11,2 years, women 79 (84,1%), men 15 (15,9%). Among 94 respondents 0.1% do not follow a gluten-free diet, 10.6% <1 year, 25.5% from 1 to 3 years, 11.7% – 4-5 years, 28.7% are on a gluten-free diet >5 years, 14.9% – 10-15 years, 8.5% > 15 years. Gastrointestinal symptoms have started at the age < 10 years old in 59.6% of patients, in 4.2% in 11-16 years old, 13.8% at the age 17-25 years old, 12.8% at the age 26-40 years old, 9.6% had late CD onset (>40 years old).

Extraintestinal symptoms such as drowsiness were noted by 46.8 %, headaches by 40.4%, weakness by 59.6%, irritability by 57.4% of respondents. Lack of coordination was noticed in 18.1% of cases, dizziness in 22.3%, 57.4% have numbness, decreased sensitivity, and tingling feeling in the limbs. Joint pain had 54.3% of the patients with CD (Figure 1).

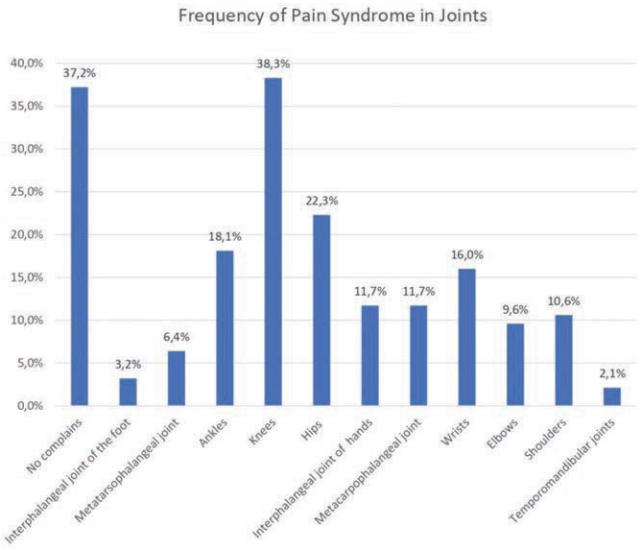

Figure 1. Frequency of pain in different joints

The maximal intensity of pain was noticed in the morning (8.5%) or late night (13.8%) times and fulfilled inflammatory pain criteria (ASAS). In 17% was noticed interrelation between gluten-free diet violation and the appearance of joint pain. In 26.6% was noticed signs of enthesitis. Weakness of arms was noticed by 39.4% of respondents. Non-steroidal anti-inflammatory drugs (NSAIDs) were started by 35.1% of patients, without any improvement in 66% of cases.

Conclusion: Patients' surveys showed that musculoskeletal symptoms in patients with celiac disease are not a rare problem and they are comparable with the frequency of neurological symptoms. Additional research is necessary for a better understanding of the nature of musculoskeletal involvement in celiac disease.

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AB1209

MECHANISTIC FACTORS CONTRIBUTING TO PAIN AND FATIGUE IN FIBROMYALGIA AND ME/CFS: AUTONOMIC AND INFLAMMATORY INSIGHTS FROM AN EXPERIMENTAL MEDICINE STUDY

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Background: Fibromyalgia and ME/CFS are multifaceted conditions with overlapping symptoms(1); the pathoaetiological mechanisms are complex and debated(2), however there is a strong association with features of hereditary disorders of connective tissue (hypermobility) and autonomic and inflammatory abnormalities (1,2).

Objectives: To determine potential autonomic and inflammatory mechanisms of pain and fatigue in fibromyalgia and ME/CFS

Methods: After excluding participants with WCC higher than 10 (suggesting acute infection) baseline markers of inflammation (CRP and ESR) were available for 60 patients with confirmed diagnoses of Fibromyalgia and/ or ME/CFS and 23 matched controls. Participants then underwent full research diagnostic evaluation including a hypermobility assessment(1) and autonomic challenge (60 degree head up tilt, ISRCTN78820481). Subjective pain and fatigue were assessed before and after challenge (VAS). Linear regression models were used to explore predictors, with adjustment for confounders as appropriate. Mediation analyses (looking for mechanistic effects) were conducted according to the method of Hayes (3) and mediation considered significant if bootstrapped confidence intervals of the estimated indirect effect did not cross zero. In these mediation analyses predictor variable was group membership (patient or control), outcome variable was change in 1)pain and 2)fatigue induced by challenge and mediatiors 1)no of connective tissue features in hypermobility diagnostic criteria endorsed by participant; 2)baseline inflammatory markers.

Results: ESR and CRP were significantly higher in patients rather than controls, even after correcting for BMI, age and sex (B=5.15, t=2.05, p=0.044; B=1.77, t=2.15, p=0.044 respectively). Adjusted ESR and CRP correlated with both subjective fatigue (B=0.44, t=2.09, p=0.04; B=1.63, t=2.60, p=0.011) and pain severity (B=0.13, t=2.51, p=0.014; B=0.45, t=3.01, p=0.004) at baseline. Autonomic challenge amplified pain (B=14.20, t=2.87, p=0.005) and fatigue (B=31.48, t=5.95, p=<0.001) in patients to a significantly greater degree than controls, controlling for baseline levels. Baseline ESR and CRP also predicted challenge-induced increase in fatigue (B=0.78, t=370, p=<0.001; B=1.91, t=3.36, p=<0.001) and ESR challenge-induced increases in pain (B=0.46, t=2.35, p=0.021).

Mediation analysis demonstrated that number of connective tissue features expressed in hypermobility criteria mediated the degree to which subjective pain was increased by the autonomic challenge (Bootstraped 95% CI of indirect effect do not cross zero, 0.1572 – 6.8171). ESR mediated the degree to which subjective fatigue was increased by the autonomic challenge (Bootstraped 95% CI of indirect effect do not cross zero,0.7541 – 7.3888).

Conclusion: To our knowledge this is the first study to directly explore autonomic and inflammatory mechanisms of pain and fatigue in a combined population of Fibromyalgia and ME/CFS. This study this adds to the evidence-base of baseline inflammatory abnormalities in fibromyalgia and ME/CFS. It highlights their potential role in predicting symptom severity and their potential mechanistic role in autonomic induced pain and fatigue, suggesting future treatment strategies.

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AB1210

FIBROMYALGIA AND BODY MASS COMPOSITION IN POST-MENOPAUSAL WOMEN: PRELIMINARY RESULTS FROM A CROSS-SECTIONAL MONOCENTRIC STUDY

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Background: Fibromyalgia (FM) is characterized by chronic musculoskeletal widespread pain, fatigue, sleep disturbances and functional symptoms.
Objectives: Our study aimed to determine if FM could affect body composition of post-menopausal women and to investigated potential correlations between disease severity and body mass variables.
Methods: Thirty post-menopausal FM female patients (median age 58 years, BMI = 25.8) were diagnosed according to either ACR 1990 fibromyalgia classification criteria or ACR 2010 preliminary diagnostic criteria. They underwent Dual-energy X-ray absorptiometry (DEXA) for clinical purposes (i.e. screening for osteoporosis). The parameters analyzed by a dedicated software (GE Lunar, USA) were the spine and femoral bone mineral density (BMD), the total lean mass and the total body fat (TBF), quantitative variables of bone, muscle and fat composition. Additionally, qualitative analysis of the bone was indexed by the trabecular bone score (TBS). All the variables were compared with the parameters of 30 healthy controls (median age 59 years, BMI = 24.4) matched for sex and age. For each patient, data on disease duration, comorbidities, current treatment and disease severity self-reported scores were collected. The last ones derived from the Italian Fibromyalgia Impact Questionnaire Revised (FIQ-R) version that each patient independently compiled before the medical visit: widespread pain index (WPI), symptom severity scale (SSS), polysymptomatic distress scale (PDS), modified fibromyalgia assessment status (modFAS) and the FIQ-R total score.
Results: The clinical features of the FM patients included in our cohort are reported in Table 1. No statistically significant differences were observed between femoral/spine BMD, TBS and muscle mass between patients and controls (p = 0.3, p = 0.06, p = 0.16, p = 0.8 respectively). Conversely, both total and central body fat were significantly higher in patients compared with healthy controls (29.4 kg vs 25.2 kg, 15.7 kg vs 13.2 kg, p = 0.006 and p = 0.01 respectively). No significant correlations were observed between body mass composition indexes with scores of disease severity. Body mass composition variables did not statistically differ when patients were sub-analyzed according to pharmacological treatment and comorbidities.

Table 1. Clinical features of FM patients included in present cohort (please see text for explanations of terminology)

	Patients, N = 30
Age (range)	58.0 [53.8, 69.2]
BMI (range)	25.8 [23.0, 28.4]
Disease duration (years), Median [IQR]	4.5 [2.2, 9.2]
ModFAS, Median [IQR]	24.5 [20.0, 29.2]
PDS, Median [IQR]	17.5 [16.0, 23.2]
SSS, Median [IQR]	8.0 [6.0, 9.0]
WPI, Median [IQR]	12.0 [7.8, 15.0]
FIQ-R, Median [IQR]	57.9 [32.4, 68.8]
Current pharmacological treatment	
Cyclobenzaprine N (%)	24 (80)
Fluoxetine N (%)	5 (16.6)
Duloxetine N (%)	4 (13.3)
Gabapentinoids N (%)	2 (6.6)
Tizanidine N (%)	2 (6.6)
Benzodiazepines N (%)	2 (6.6)
Cannabinoids N (%)	3 (10)
Nson-pharmacological treatment	
Aerobic physical activity N (%)	5 (16)
Comorbidities	
Hypertension N (%)	10 (33.3)
Diabetes N (%)	3 (10)
Osteoarthritis N (%)	10 (33.3)
Anxiety/depression N (%)	3 (10)
Psoriasis N (%)	3 (10)

Conclusion: Our preliminary results suggest that FM seems not associated with impaired bone mass and bone quality in post-menopausal women compared to matched healthy controls, in line with the majority of literature evidences [1]. However, total and central adipose tissue mass resulted higher in this cohort of FM patients compared with controls but not correlate with disease severity. This might be due to a disease-induced sedentary lifestyle and might reinforce the concept that physical activity represents the best preventive method of overweight and obesity, one of most reported comorbidities for FM patients[2].

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AB1211

DOES BODY MASS INDEX AND METABOLIC SYNDROME IMPACT ON FIBROMYALGIA?

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Background: Fibromyalgia (FBM), obesity and the metabolic syndrome (MTB) are common conditions with significant impact on health and quality of life, producing relevant economic burden for healthcare systems. Although obesity represents a negative prognostic factor for FBM, the relation between body mass index (BMI) or MTB and FBM severity is still unclear.
Objectives: The aim of our ongoing study was to evaluate the relationship between BMI or prevalent MTB and FBM severity, estimated with 3 different severity scores.
Methods: We included the first 100 women presenting with FBM, defined according to the ACR2016 diagnostic criteria, consecutively evaluated during the period of 1 year in 2 Clinic in Italy. On enrolment were assessed/recorded demographic, clinical and pharmacological characteristics, weight, height, physical activity, tenderness, pain and symptoms. The following scores were calculated: tender points count (TP), Widespread Pain Index (WPI), Polysymptomatic Distress Scale (PDS), Fibromyalgia Impact Questionnaire (FIQ) and modified Fibromyalgia Assessment Status (mFAS). BMI was calculated, and the presence of MTB was evaluated according to current definition. Patients were categorized as presenting with severe disease or moderate/mild disease according to recent definition validated in an Italian population. The prevalence of MTB and the mean ± standard deviation (SD) BMI in subgroups defined according to severity were estimated.
Results: Mean age ±SD was 57.5±12.7 years, mean BMI ±SD was 25.3±5.1, and 9.5% presented with MTB. FBM severity (mean±SD) calculated by PDS, FIQ and mFAS was respectively 25.3±9.3, 63.2±23.1, and 30.1±7.7. Patients with the highest FBM severity according to PDS (>25) were less likely to present with MTB (2.4%) compared to those with a PDS of 0-25 (20.0%, P=.026), with an adjusted (age and BMI) OR (95%CI) for presenting with MTB in patients with less severe FBM of 8.2 (0.962-69.925, P=.054). Similar results were found when the specific conditions characterizing the MTB were considered separately, except for excessive body fat around the waist (not related to severity). The BMI ±SD was comparable between patients with severe disease (25.8±5.8) according to PDS and those with less severe FBM (24.8±4.4, P=.388), with no correlation between BMI and PDS (Rho: 0.083, P=.454). Considering all other characteristics of the two groups defined according to PDS categories (PDS >25 versus PDS 0-25) a significant difference was found in mean age ±SD, greater in patients with less severe FBM (60.2±13.2) compared to those with highest FBM severity (54.8±11.6, P=.046). Similar but less significant findings were found also with FIQ and mFAS. The prevalence of MTB according to the FIQ was 7.3% for highest severity versus 14.3% for less severe FBM (P=.200), with a comparable BMI ±SD between the two groups (respectively 26.2±6.1 versus 24.4±3.7, P=.125). Corresponding figures for MTB or BMI and FBM severity according to the mFAS were respectively: prevalence of MTB in highest severity 3.0% versus 16.3% in the less severe FBM (P=.078); mean ±SD BMI in highest severity 26.4±6.2 versus 24.6±4.2 in less severe patients (P=.121).
Conclusion: The preliminary results of our ongoing analysis demonstrated a slightly inverse relationship between FBM severity and the prevalence of MTB, trending to significance, while no relationship was found between severity and BMI.

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AB1212 GENDER DIFFERENCES IN FIBROMYALGIA PATIENTS IN VIEW OF THE 1990, 2011, AND 2016 ACR CRITERIA

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Background: Fibromyalgia (FM) is a common rheumatic illness distinguished by chronic pain, headache, fatigue, cognitive problems, and functional disability. However, the differences between men and women have not yet been comprehensively studied, especially after the development of the last 2016 American College of Rheumatology (ACR) criteria.
Objectives: The aim of this study was to evaluate the gender differences in symptom characteristics, cognitive dysfunction, and disease severity in Egyptian FM patients considering both the ACR 1990, 2011, and the last 2016 ACR diagnostic criteria
Methods: In this cross-sectional study, 352 individuals with fibromyalgia were interviewed from January 1, 2020, to June 1, 2021. In addition to the number of tender points (TPC), data was collected on age, gender, body mass index (BMI), marital status, disease onset, duration, and diagnostic delay. The Widespread Pain Index (WPI), the Symptom Severity Scale (SSS), fatigue, cognitive dysfunction, sleep disturbance, awakening unrefreshed, headache, abdominal pain, and depression were evaluated and scored according to 2010 and 2016 ACR criteria. The questionnaire includes a visual analog scale (VAS) for pain, fatigue, stiffness, anxiety, and depression. Total score ranges were calculated with total score ranges between 0 and 80 (without job items), where higher scores indicated a greater negative impact and/or severity of symptoms. The Polysymptomatic distress scale (PDS) has been calculated by the summation of the SSS with the WPI. The Revised FM impact questionnaire (FIQR) has also been evaluated.
Results: The study shows that females have a significantly higher prevalence of fatigue, cognitive dysfunction, sleep disturbance, headache, and abdominal pain ($p < 0.05$). Also, females showed significantly higher scores than males regarding WPI, SSS, and mean TPC ($p = 0.004$, 0.027, and 0.001, respectively). While there was no difference regarding the FIQR ($p=0.93$), PDS was significantly higher in women ($p= 0.001$).
Conclusion: Female patients with FM had greater disease severity scores, symptomatology, and number of tender points. Whatever the criteria applied, the prevalence and intensity of the disease features are higher in females, which may underestimate the disease in male patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.5146

AB1213 EFFECTIVENESS OF A ONE-WEEK INPATIENT MULTIMODAL PAIN TREATMENT PROGRAM FOR PATIENTS WITH RHEUMATOLOGIC DISEASES AND MUSCULOSKELETAL PAIN – A SINGLE CENTER OBSERVATIONAL STUDY

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Background: Multimodal rheumatologic complex treatment (MRCT) is a treatment concept for patients with rheumatologic diseases requiring acute inpatient care suffering from exacerbated pain and/or functional impairment. A rheumatologist directs the treatment program including multimodal assessments and treatment from three of the following: ergotherapy, physiotherapy, pain medicine and cognitive behavioural treatment. Most studies evaluated data from a two-week inpatient MRCT program.[1] Available data on the effectiveness of a one-week inpatient multimodal treatment program are scarce. However, whether a shorter program might also be effective has not been studied so far.
Objectives: To evaluate the effectiveness of a one-week inpatient multimodal and interprofessional treatment program on musculoskeletal pain and function of patients with rheumatologic disorders.
Methods: 59 consecutive patients were entered into a program of multimodal treatment courses (MRCT) from January 2021 until December 2021. All patients completed a total of 11 hours of therapy in one week. Two patients were excluded for evaluation (one patient acquired COVID 19 during hospitalization and one patient was excluded due to missing data).
Pain was assessed via visual analogue scale (VAS) and functional impairment via the "Funktionsfragebogen Hanover (FFbH)" and the "Health Assessment Questionnaire (HAQ)" at admission, at discharge and at 12 weeks of follow up. Paired t-test analyses for all treatment episodes were performed.
Results: The mean treatment duration (days, ±SD) was 8.1 ± 0.8. Mean age (years, ±SD) of the 57 patients treated in the MRCT program was 57.2 ± 12.5, with 72% female and 28% male patients. Of all patients, 40% had an underlying inflammatory disorder, 60% a non - inflammatory rheumatic disease. 23% of all patients had "back pain", 14% "spondyloarthritis" and 11% "rheumatoid arthritis". Overall, VAS (pain) mean at admission was 6.9 ± 1.0 (SD), HAQ mean 0.57 ± 0.23 (SD) and FFbH mean 81.44 ± 7.95 (SD), respectively. Significant improvements in VAS, HAQ and FFbH were demonstrated at discharge (day 8), with a mean improvement of VAS of -2.86 (95% CI: -3.07 to -2.64, P value: <0.0001), a mean improvement of HAQ of -0.24 (95% CI: -0.28 to -0.20, P value: <0.0001) and a mean improvement of FFbH of 5.38 (95% CI: 3.78 to 6.98, P value: <0.0001). Follow up assessment at week 12 was recorded in 22 patients (39%) with a significant mean improvement in VAS of -2.23 (95% CI: -2.98 to -1.48), P value < 0.0001) (Table 1 and Figure 1).

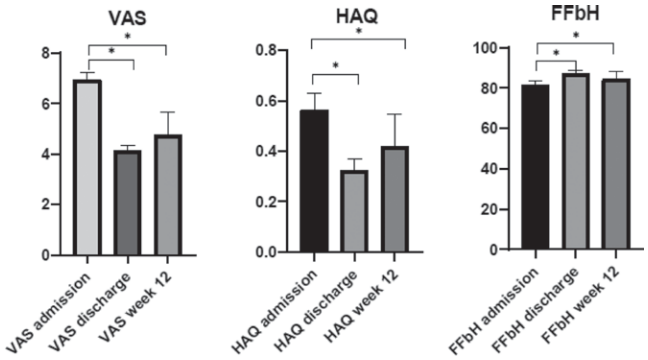

Figure 1.

Table 1.

VAS mean difference admission/discharge	**-2.86 (95% CI: -3.07 to -2.64, P value: <0.0001), n= 55**
HAQ mean difference admission/discharge	**-0.24 (95% CI: -0.28 to -0.20, P value: <0.0001), n= 57**
FFbH mean difference admission/discharge	**5.38 (95% CI: 3.78 to 6.98, P value: <0.0001), n= 56**
VAS mean difference admission/12 weeks follow up	**-2.23 (95% CI: -2.98 to -1.48, P value: <0.0001), n= 22**
HAQ mean difference admission/ 12 weeks follow up	**-0.16 (95% CI: -0.29 to -0.04, P value: 0.01), n= 22**
FFbH mean difference admission/12 weeks follow up	**3.96 (95% CI: 1.18 to 6.74, P value: 0.01), n= 22**

Conclusion: Significant improvement of pain and function was demonstrated at discharge and at week 12 in patients with rheumatologic diseases and musculoskeletal pain completing a one-week inpatient multimodal interprofessional treatment program. A multimodal therapeutic approach may provide an effective treatment strategy superior to unimodal standard management.
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AB1214 VITAMIN D SUPPLEMENTATION IN FIBROMYALGIA: A SYSTEMATIC REVIEW

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Background: Fibromyalgia (FM) is a chronic disease characterized by diffuse pain associated with high levels of fatigue whose intensity is very variable. Similar symptoms are found in patients with low levels of vitamin D, a vitamin that behaves like a hormone with multiple receptors spread in several tissues. Although its role in the pathophysiology of FM remains unclear many studies point to a correlation between vitamin D deficiency and FM symptoms severity. (1)

Objectives: Conduct a systematic review of the literature to determine the value of vitamin D supplementation in fibromyalgia.
Methods: Medline, EMBASE, and Cochrane databases were searched, from January 2000 to January 2022, using the descriptors "Fibromyalgia", "Fatigue" and "Vitamin D." Randomized and clinical control trials including FM patients in whom supplementation of vitamin D was made were selected. Data comprised sociodemographic description, diagnosis criteria, fibromyalgia symptoms, Fibromyalgia Impact Questionnaire (FIQ), short-form 36 (SF36), and vitamin D supplementation protocol was collected.
Results: Of the initial 2480 articles, 4 were eligible for final analysis. One did not observe any significant improvement in FIQ scores with vitamin D supplementation. The remaining three observed significant improvements in SF-36 and FIQ scores but to different extents. One only demonstrated improvements in specific components of the SF-36, also demonstrating improvements concerning morning fatigue. Another demonstrates improvements in all SF-36parameters, except for pain level. Lastly, other observed improvements in the scores of both FIQ and SF-36 scales.
Conclusion: Our review shows conflicting results regarding the role of using vitamin D supplementation in the quality of life of patients with FM(S). These results can be explained by different supplementations protocols and also different baseline levels of vitamin D for which it was decided to supplement. Nevertheless, vitamin D supplementation appears to have a benefit in fatigue and quality of life in FM patients. Larger studies, which last longer and have a more uniform supplementation protocol, are needed to confirm the results of this review.
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Spine, mechanical musculoskeletal problems, local soft tissue disorders

AB1215 A COMPARATIVE ANALYSIS OF RADIOLOGICAL FINDING BETWEEN TUBERCULOUS, BRUCELLAR AND PYOGENIC SPONDYLODISCITIS

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Background: Infection spondylodiscitis (IS) is a serious infectious disease which involves intervertebral disc and its adjacent vertebral bodies but later may also extend into the the adjacent neural structures. The clinical picture of IS is rather non specific but there are significant radiological differences that permit a presumptive aetiological diagnosis and orient the initial empirical treatment.
Objectives: This study aimed to compare the radiological features of of tuberculous (TS), brucellar (BS) and pyogenic spondylodiscitis (PS).
Methods: A retrospective monocentric study involving 70 cases of infectious spondylodiscitis admitted between January 2009 and August 2019 at our rheumatology department. Clinical, laboratory and radiological data of the patients were collected.
Results: Of these 70 patients, 18 (25.7%) had TS, 8 (11.4%) BS and 44(62.9%) PS. There were 37 women (52.9%) and 33 men (47.1%). The age of the patients ranged from 12 to 82 years, with a mean of (SD±) 54± 15,23 years. Standard X-rays showed abnormalities suggestive of spondylodiscitis in 78.6% of cases. A great majority of the patients had involvement at only one vertebrae level (70%). The most frequently affected level, were the thoracic (33.3%), the lombosacral (100%) and the lombar (38.6%) segment in the TS, BS and PS respectively. In BS the lombosacral segment was significantly the most frequently affected level (p<0.0037). Computed tomography was performed in 52.9% of cases and showed that the epidural and paravertebral abscess were characteristic of tuberculous involvement (p=0.013 and 0.05). Magnetic resonnance imaging was performed in 63% of cases. The intervertebral disc narrowing was observed in 87.3% of patients. Paravertebral or epidural masses were present respectively in 53.5% and 86.7% of TS, versus 14.3% and 71.4% of BS, and 46.3% and 80.5% of PS, there were no significant differences between the groups.The enhancement was rather heterogeneous in the SDT and homogeneous in the two other groups, but these differences were not statistically significant.
Conclusion: There are significant radiological differences between TS, BS and PS. A better understanding of typical and atypical manifestations on imaging can be an excellent diagnostic tool for every attending physician.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.819

AB1216 TUBERCULOUS, BRUCELLAR AND PYOGENIC SPONDYLODISCITIS: A DESCRIPTIVE AND COMPARATIVE STUDY OF 70 CASES

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Background: Infection spondylodiscitis is a serious infectious disease which involves intervertebral disc and its adjacent vertebral bodies but later may also extend into the the adjacent neural structures. Early diagnosis and identifing the causative agent seem critical in term of prognosis.
Objectives: To describe and to compare the clinical, biological and radiological features of tuberculous (TS), brucellar (BS) and pyogenic spondylodiscitis (PS).
Methods: A retrospective monocentric study involving 70 cases of infectious spondylodiscitis admitted between January 2009 and August 2019 at our rheumatology department. Clinical, laboratory and radiological data of the patients were collected.
Results: Of these 70 patients, 18 (25.7%) had TS, 8 (11.4%) BS and 44(62.9%) PS. There were 37 women (52.9%) and 33 men (47.1%). The age of the patients ranged from 12 to 82 years, with a mean of (SD±) 54± 15,23 years. The patients with TS were younger than those with PS (p=0.0016). Of our cases, 67.1% had comorbid chronic diseases such as predominantly renal failure and diabetes. The median diagnostic delay (MDD) in our series was 120,180 and 30 days for TS, BS and PS respectively (p=0.004).All of the patients included in this study suffered from pain, 30 of these had fever and 19 had night sweats. Radiculalgia was found in 50% of cases and 8.6% of them had a neurological deficit. There were no significant differences those clinical features between the groups. In view of laboratory findings, increased erytrocyte sedimentation rate (ESR) was detected in 82.9%, C-reactive protein(CRP) positivity in 84.3% and hyperleukocytosis in 33.3% of patients. ESR and CRP levels were significantly higher in PS patients when compared with TS cases (p=0.005; P=0.006, respectively). Standard X-rays showed abnormalities suggestive of spondylodiscitis in 78.6% of cases. Computed tomography and Spinal magnetic resonance imaging were performed respectively in 52.9% and 63% of cases and were pathological in all cases. A great majority of the patients had involvement at only one vertebrae level (70%). The most frequently affected level, were the thoracic (33.3%), the lombosacral (100%) and the lombar (38.6%) segment in the TS, BS and PS respectively. In BS the lombosacral segment was significantly the most frequently affected level (p<0.0037). The intervertebral disc narrowing was observed in 87.3% of patients. Paravertebral or epidural masses were present respectively in 53.5% and 86.7% of TS, versus 14.3% and 71.4% of BS, and 46.3% and 80.5% of PS, there were no significant differences between the groups.
Conclusion: There are significant clinical, biological and radiological differences between TS, BS and PS. The presence of back pain, fever, moderate elevation of inflammatory markers with thoracic radiological involvement was suggestive of tuberculous spinal infection.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.823

AB1217 CHRONIC LOW BACK PAIN AND MUSCULAR HYDATIDOSIS: THE TREE THAT HIDES THE FOREST

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Background: Hydatid cyst disease is a zoonosis caused by *Echinococcus granulosus*. The parasite implants most commonly in the liver and lung. Musculoskeletal involvement is rare.
Objectives: To describe clinical and imaging presentation of spinal and muscular hydatidosis.
Methods: We report two cases of chronic low back pain caused by hydatid cyst.
Results: Case 1: A 36-year-old woman living in a rural area presented with a three-years history of lumbar back pain complicated with right-sided sciatica and intermittent episodes of urinary retention. The pain was gradually worsening and resisting conventional analgesics and physiotherapy. On physical examination, she had tenderness of the lumbar back and left sacroiliac joint with limited mobility. Biological findings were normal and X-ray features showed osteolytic lesions of L5 left side. The magnetic resonance imaging (MRI) results revealed septated multilocular hydatic cysts with high signal intensity in T2-weighted images and low signal intensity in T1-weighted images along L5 and the sacrum left side. Serological test for hydatid disease was positive. The treatment was wide surgical resection combined with Albendazole (400 mg/day) for one year postoperatively. Case 2: A 62-year-old woman presented with a one-year history of lumbar back pain with gait instability and right flank swelling. Biological findings and X-ray features were normal. The patient first was explored by uro-CT to assess for nephrolithiasis and it revealed retro and sub-peritoneal two multilocular hydatic

cysts (60x80mm, 36x35mm) along right iliopsoas and adductor muscles. MRI showed same cystes described on the CT (Figure 1). No other localizations were detected. The diagnosis of hydatidosis was confirmed perioperatively after visualization of the cyst. Wide resection was performed but signs of recurrence were detected by MRI at the 3-month follow-up.

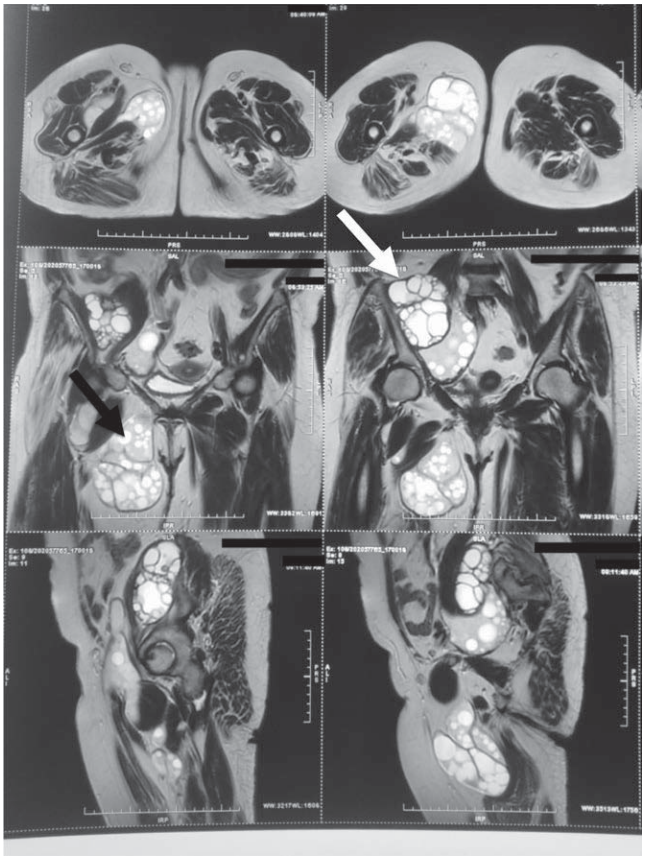

Figure 1. MRI showing two multilocular cysts along right iliopsoas (white arrow) and adductor muscles (black arrow).

Conclusion: In endemic areas, bone and muscle involvement from echinococcosis should be considered during clinical investigation of chronic lumbar pain.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.2405

AB1218 AURICULOTHERAPY AS A TREATMENT FOR CHRONIC NECK PAIN: AN INTERVENTIONAL COMPARATIVE STUDY

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Background: Data indicates promising benefits of auriculotherapy (AT) in pain management of several pathologies. Common cervical pain (CCP) is recurrent plaint often resistant to standard treatment. And use of auriculotherapy as a therapeutic solution in neck pain has not been well explored.
Objectives: The aim of our study is to evaluate efficacy of a single session of AT in the management of CCP's pain and disability.
Methods: We conducted an interventional comparative study. Fifty patients with CCP consulting were divided in two group of 25: group A underwent a session of AT, group P had a placebo treatment using a detuned ultrasound machine. Evaluation of the patients was performed before, and right after the intervention. The Neck and Pain Disability Scale (NPDS) questionnaire. It includes 3 areas: F1 for functional disability, F2 for movement-induced pain and F3 for pain in static position.
Results: We enrolled 32 women and 18 men with an average age of 47. Epidemiological, clinical and radiographic features were comparable for both groups, except for the standard of living and the consumption of analgesics, which were significantly higher in the group A (p=0.027and p<0.001, respectively). Initially, NPDS total score and F1, F2, F3 sub scores were comparable in both groups.
After the intervention, all scores had decreased significantly. In the A group: NPDS total went from 34.3 to 22.9 (p<0.001), F1 went from 9.5 to 6.2 (p<0.001), F2 went from 16.5 to 11.9 (p<0.001), F3 from 8 to 5.4 (p<0.001). In the P group: NPDS total decreased from 28.9 to 26 (p=0.001), F1 from 6.3 to 5.7 (p= 0.001), F2 going from 14.4 to 13.3 (p =0.013), F3 went from 8 to 7.3 (p=0.006).
When we compared the scores after the intervention, the improvement was statistically higher in the A group for all scores (p<0.001 for total, F1 and F2, and p=0.002 for F3 sub score).
Conclusion: Our study revealed that a single session of auriculotherapy is effective on short term in the treatment of pain and disability related to CCP. This alternative technique may gain its place in the therapeutic management protocol to overcome disability of chronic neck pain.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.2843

AB1219 ASSOCIATION OF CAROTID ATHEROSCLEROSIS WITH SARCOPENIA IN MALE PATIENTS WITH CORONARY ARTERY DISEASE

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Objectives: To investigate the association between sarcopenia and carotid atherosclerosis in male patients with coronary artery disease (CAD).
Methods: Here we enrolled 79 male patients with CAD verified by coronary angiography (median age = 63 (57; 66) years). Sarcopenia was diagnosed according to the recommendations of the European Working Group on Sarcopenia in Older People (EWGSOP, 2010) by examining muscle strength, muscle mass, and muscle function. Severity of carotid atherosclerosis was assessed by color duplex scanning by measuring intima-media thickness and percent stenosis. Patients were then divided into those without sarcopenia (n = 31), with pre-sarcopenia (n = 21), and sarcopenia (n = 27).
Results: Patients with sarcopenia had significantly higher intima-media thickness than those without sarcopenia (p = 0.005). Multiple carotid plaques and > 50% stenosis were significantly more frequent in patients with sarcopenia compared with those with pre-sarcopenia (48.15% versus 9.50%, p = 0.015) and without sarcopenia (48.15 % versus 12.90%, p = 0.013). Severity of carotid atherosclerosis negatively correlated with musculoskeletal index (r = -0.227, p = 0.047).
Conclusion: Severe carotid atherosclerosis was associated with a decrease in muscle mass, suggesting a link between atherosclerosis and sarcopenia and potentially elevated risk of adverse outcomes in patients with a sarcopenia comorbidity.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3744

AB1220 CHARACTERISTICS OF INFECTIOUS SPONDYLODISCITIS IN ELDERLY

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Background: Infectious spondylodiscitis is a rare but growing disease. It is a serious infection that can compromise both the functional and vital prognosis especially on elderly subjects.
Objectives: The purpose of this study was to compare the clinical, bacteriological and evolutionary characteristics of elderly patients admitted for management of infectious spondylodiscitis with a case-control group of young subjects.
Methods: Retrospective, descriptive study carried out in the rheumatology department of the Charles Nicolle Hospital from 2010 to 2019. Adult patients hospitalized for infectious spondylodiscitis were included. Clinical, bacteriological and evolutionary data were analysed and comparing those over 65 years of age with young case-control subjects.
Results: Of the 78 patients included, 33 patients belonged to the elderly group and 45 to the control group. The duration of evolution was shorter for the control group (123 vs. 181 months for the elderly; p=0,71). The progressive mode of onset characterised the elderly group (P<0.05). Spinal pain was constant. Neurological abnormalities, night sweats, and altered general condition were more present in the elderly (p<0.05). Spinal stiffness was more present in the control group (p<0.05). There was no difference between the two groups in terms of the presence of fever and radiculalgia. Spinal biopsy was performed in 72% of the elderly subjects and in 80% of the control group. The most common germ in the elderly group was tuberculosis and brucellosis in the control group (p<0.05). A favorable evolution was noted in 75% of the cases in the control group compared to 66% of the elderly subjects (p<0.05). Neurological complications and mortality were more common in the elderly (p<0.05).
Conclusion: Infectious spondylodiscitis on elderly is characterised by an insidious onset, a confusing clinical picture and a more severe presentation than young people with significant complications and mortality.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3923

AB1221

START BACK TOOL RISK SCORE: WHAT GUIDANCE TO GIVE IN A MILITARY LOW BACK PAIN POPULATION?

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Background: The Keele start back Tool (SBT) is a 9-item self-reported questionnaire validated to identify individuals with non-specific low back pain (LBP) who have prognostic factors for persistent disabling pain. Thus, it is a useful component of stratified care, where patients' prognostic subgroups are matched with appropriate treatment.
Objectives: The aim of our study was to report the prevalence of SBT-calculated risk for back pain disability in Tunisian military patients.
Methods: It was a cross sectional study. The SBT questionnaire was administered to patients > 18 years presenting with common low back pain in outpatient Military teaching hospital in Tunis, Tunisia (from January to Mars 2021). The normality of data distribution was checked by the Kolmogorov-Smirnov test. Quantitative variables were presented as mean ± standard deviation (SD) or median (interquartile range), as appropriate. The categorical variables were expressed as percentages.
Results: Out of 114 participants; the mean age at diagnosis was 79 +/- 12 years old, sex ratio was equal to 1, the median of symptom duration was 22 (6-36) months, 83 (72.8%) were employed, 54 (47.4%) were on active military duty. Comorbidities reported in our patients were distributed as followed: 52 (45.6%) cases of overweight, 21 (18.4%) cases of obesity, 17 (14.9%) had hypertension, 13 (11.4%) suffered from type 2 diabetes, 10 (8.8%) had dyslipidemia, 6 (5.3%) cases of hypothyroidism and 3 (2.6%) cases of auto-immune diseases. Seventy (61.4%) participants reported anxious thoughts, 75 (65.8%) patients expressed avoidance beliefs, 59 (51.8%) patients mentioned catastrophizing thoughts and 50 (43.9%) were dealing with low mood. Mean SBT psychological score was at 2.68 +/-1.5. Patients reported a mean SBT score of 5.31+/-2.1 with the following risk stratification: 27 (23.7%) scored low-risk, 47 (41.2%) medium risk, and 40 (35.1%) high-risk.
Conclusion: This is the first study to report the prevalence of SBT-designated risk subgroups among Tunisian population. Medium or high-risk scores for back pain disability were more prevalent the surveyed sample. Also, rates of low mood and anxious thoughts indicate a need for future research to explore psychosocial factors in non-specific low back pain.
Disclosure of Interests: None declared
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AB1222

POSITIVE DIAGNOSIS OF TUBERCULOUS SPONDYLODISCITIS: CT-GUIDED PERCUTANEOUS BIOPSY OF SPINAL LESIONS VERSUS CLINICAL, BIOLOGICAL AND IMAGING ARGUMENTS

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Background: Tuberculosis is still endemic in Tunisia. Although pulmonary localization is the most common, other localizations, including osteo-articular involvement, are increasingly diagnosed. Spinal or «Pott's Disease» is the most common expression. A bundle of clinical, paraclinical and evolutionary arguments or a disco-vertebral biopsy puncture (DVBP) contribute to the positive diagnosis.
Objectives: Our aim was to assess the real contribution of DVBP compared to clinical-biological and imaging arguments for the diagnosis of tuberculous spondylodiscitis (SPDT).
Methods: We conduct a retrospective and descriptive study in a single rheumatology department. Data were collected from files of patients hospitalized in the past 20 years (2000-2020) who have been diagnosed with SPDT.
Results: Fifty-two cases of SPDT were collected (37F/15M). The mean age of the population was 55.21 years ± 17.79 [19-91]. Diagnosis SPDT was retained based on the results of the DVBP in 15 patients (28.8%); and it was strongly suspected in front of the presence of clinico-biological and imaging arguments in 37 patients (71.2%). Among the clinical arguments suggestive of SPDT were: progressive onset of symptoms in 47 patients (90.4%), segmental spinal stiffness in 37 patients (71.2%), spinal pain with general signs of tuberculosis such as impaired general condition, fever, night sweats and weight loss in 32 patients (61.5%). Lumbar spine involvement was the most common in tuberculous SPD (57.7%). A biological inflammatory syndrome has been objectified in 38 patients (73.1%). Imaging was contributive to positive diagnosis using standard X-rays, computed tomography and magnetic resonance imaging (MRI). Disc pinch, erosion of vertebral plateaus and vertebral collapse were the major signs. Once the diagnosis was retained for these patients, the first week noted a most significant clinical improvement (56.8%) in patients diagnosed with a range of suggestive arguments (p = 0.002). During the second week, clinical improvement was most marked in patients diagnosed with suggestive clinical and paraclinical arguments (70.3%) but with no statistically significant difference (p = 0.1). The improvement was statistically greater during the fourth week (66.7%) and the third month (60%) in patients diagnosed with histological examination (p < 0.001).

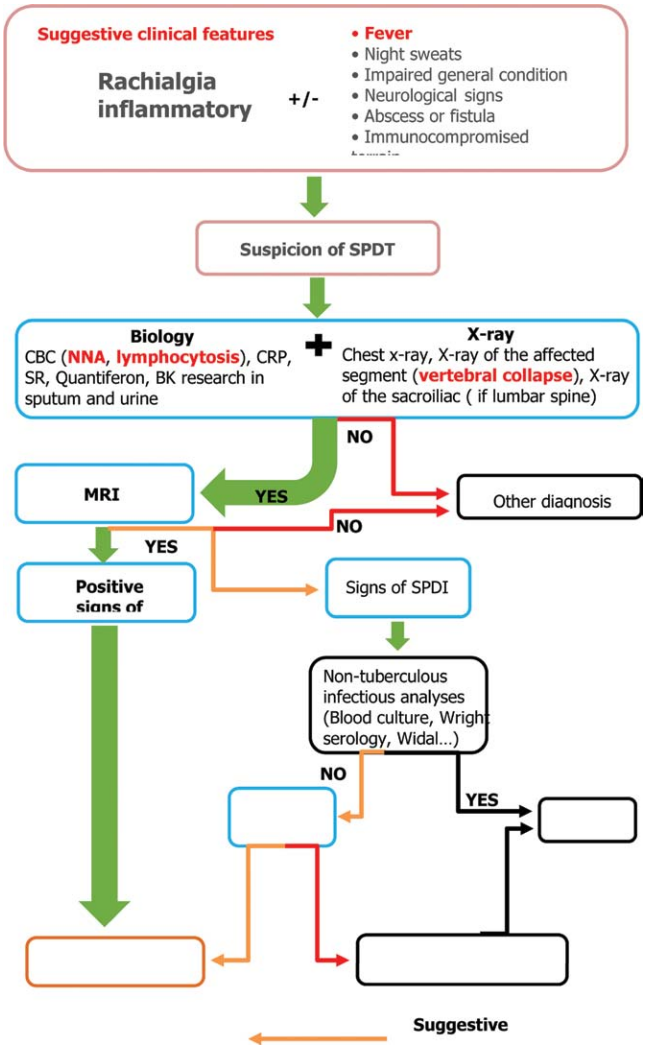

Figure 1. *SPDT Diagnostic Strategy*SPDT= Tuberculous spondylodiscitis, CBC= Cell blood count, NNA= Normochromic normocytic anemia, CRP= C reactive protein, SR= Sedimentation rate, BK= koch's bacillus, SPDI= infectious spondylodiscitis, SPDNT= Non-tuberculous spondylodiscitis

Conclusion: Tuberculous spondylodiscitis is a frequent condition that needs to be treated rapidly. A range of highly suggestive clinical, paraclinical and evolutionary arguments contribute in the majority of cases to the positive diagnosis with a comparative clinical evolution to that of the DVBP which remains an invasive exam with variable sensitivity depending on studies.
Disclosure of Interests: None declared
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AB1223

ACTIVE MILITARY ARE AT HIGHER RISK OF CHRONICITY IN LOW BACK PAIN: A CROSS SECTIONAL COMPARATIVE STUDY

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Background: The incidence of low back pain (LBP) was 40.5 per 1,000 person-years in active military population and thus was comparable to the general population. Other than pain and disability, chronicity of LBP has a significant impact on work through the high rates of resulting sick leave. The Start Back

Tool (SBT) questionnaire is a well-known tool used to detect patients with prognostic factors for persistent and disabling back pain. The risk of chronicity in individuals on active military duty suffering from acute back pain is yet to be explored.

Objectives: The aim of our study was to assess the risk of chronicity in active Tunisian military population compared to non-military controls using the SBT questionnaire.

Methods: Cross sectional study in which we enrolled adult patients suffering from acute back pain, who consulted the outpatient department of rheumatology in the military hospital of Tunis from January 2021 to Mars 2021. All patients had a standardized clinical examination. They completed the SBT questionnaire in the validated Arabic language version. Patients were stratified in two groups, active military group (AMG) and non-military group (NMG). Categorical variables were compared with the $\chi 2$ -test. Comparisons of the differences of continuous variables were performed by Student's T-test.

Results: We included 54 patients in the active military group and 60 patients in the non-military group, epidemiologic characteristics were distributed respectively as followed: mean age was at 43+/-8 versus 53+/-13 years old (p<0.001), sex ratios (F/H) were 0.23 versus 3.62 (p<0.001), 54% versus 73% (p=0.033) of patients were overweight or obese, 4% versus 18% (p=0.014) of patients had type 2 diabetes, 4% versus 13% (p=0.099) of patients had dyslipidaemia while 9% versus 20% (p=0.108) of patients had hypertension. Active military group patients had significantly higher proportions of high risk SBT scores than non-military patients 50% versus 22% (2.27 risk ratio 95% CI 1.47 to 3.08; p=0.002), with total mean of scores significantly higher in the active military group 5.81 (95% CI 5.33 to 6.29) versus 4.85 (95% CI 4.43 to 5.27), p=0.014. Active military group patients scored significantly higher on the psychological SBT sub-score with a mean of 3.02 (95% CI 2.8 to 3.24) versus 2.38 (95% CI 2.07 to 2.7) p=0.032, they were more susceptible to express low mood 53% versus 35% (1.51 risk ratio 95%CI 1.13 to 1.89; p=0.044). There was no significant difference in expressed anxiety 69% versus 55% (p=0.139), catastrophizing thoughts 57% versus 47% (p=0.252) and avoidance beliefs 72% versus 60% (p=0.170) though all of these parameters were more prevalent in the active military group.

Conclusion: Though NMG patients had more classic low back pain risk factors such as age and obesity, this did not prevent the AMG to show higher trends toward chronicity via SBT scores. This is to our knowledge the first study to assess the high risk of persistent disabling back pain using the SBT in a Tunisian military population. The implementation of risk stratification for patients with low back pain in routine military health may improve physical function and time off work, sickness certification rates and reductions in healthcare costs compared to usual non-stratified care.

Disclosure of Interests: None declared

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AB1224 NON-CONTIGUOUS MULTIFOCAL SPONDYLODISCITIS: A RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Non-contiguous multifocal spondylodiscitis (mSpD) is a serious infection. Although literature data highlight the opportunity to miss a non-contiguous spondylodiscitis (SpD), recommendations for which cases an MRI of the entire spine should be performed are missing.

Objectives: The aim of the study was to assess the clinical features of mSpD to reveal risk factors underlining the need for screening a multifocal spine involvement

Methods: We retrospectively evaluated the data of patients with confirmed non-contiguous multifocal spondylodiscitis

Results: Twelve patients suffered from mSpD were included (6 males, 6 females). The mean age was 60 years. Four patients had underlying chronic comorbidity, Diabetes (n=3), hepatitis C virus (n=1). Most patients had spine pain (11 patients,), radiculalgia in one patient, neurologic deficit (3 patients), worsening health status (7 patients). Symptoms onset was acute (n=1) or sub-acute (n=3) or long term (n=8) before admission. The mean duration between the diagnosis and the onset on symptoms was 9,6 months. Tubercular spondylodiscitis was the most detected etiology (n=8), confirmed by histological analysis (n=3) then brucellar, confirmed by serlology lab test, and pyogenic SpD in two patients each. Non-contiguous multi-level involvement in the lumbar, thoracic, and cervical spine was detected in one patient for each region. Seven patients suffered from a lumbar and thoracic spine involvement and SpD occurs in the three regions in two patients. Elevated inflammatory biomarkers (CRP and ESR) were present in all cases. Entire spine MRI was performed for almost all patients, confirmed the diagnosis, showed para-vertebral abscess (n=3), epidural inflammation (n=6), and spinal cord compression (n=3). The majority of cases showed a favorable evolution with appropriate antibiotic therapy. One patient maintain a neurologic deficit, and one suffered from a severe degree of pain. Surgical approach was not indicated.

Conclusion: In our study, mSpD did not appear to be associated with a particular pattern. Tuberculosis was the dominant etiology. That suggests, an MRI of the entire spinal column should be performed for each patient with suspicious SpD, especially when tuberculosis is evocated

Disclosure of Interests: None declared

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AB1225 TUBERCULOUS SPONDYLODISCITIS: DIAGNOSTIC DELAY AND OUTCOMES

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Background: Tuberculous spondylodiscitis (SPDT) is a serious clinical condition that must be treated promptly. Despite the actual availability of more effective diagnostic tools, early diagnosis of SPDT remains difficult and a high index of suspicion is needed due to the chronic nature of the disease and its insidious and variable clinical presentation.

Objectives: Our aim was to study the correlation between the diagnostic delay of SPDT and its outcomes.

Methods: We conduct a monocentric retrospective and descriptive study in a rheumatology department. Data were collected from observations of patients hospitalized in the past 20 years (2001-2021) who have been diagnosed with SPDT. An early diagnosis is defined by a diagnosis within the first six months versus a late diagnosis that is retained after 6 months of symptoms.

Results: Fifty-two cases of SPDT were collected (37F/15M). The mean age of the population was 55.21±17.79 years [19-91]. Late diagnosis was more common: 41 patients (78.8%) versus 11 patients (21.2%) diagnosed early. Complications were more frequent (61%) in patients diagnosed late, but with no statistically significant difference (p=0.1). Disease-related complications, such as spinal compression, spinal deformation and recurrence of the disease, was statistically higher (45.5%) in early diagnosed patients (p < 0.001). Drug complications, such as disruption of liver balance, hyperuricemia and major intolerance to anti-tuberculosis, were more frequent (36.6%) in patients diagnosed late (p = 0).

Conclusion: Despite highly sensitive imaging techniques, the diagnosis of tuberculous spondylodiscitis is often late, which may lead to severe deformity and early or late neurological complications.

Disclosure of Interests: None declared

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AB1226 AUTOLOGOUS MOSAIC OSTEOCHONDROPLASTY IN THE TREATMENT OF TALAR OSTEOCHONDRAL DEFECTS

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Background: Osteochondral defects of the talus (ODT) is a relatively rare, mostly traumatic pathology, in 6.5 % of cases complicate the course of inversion and eversion injuries of the foot and ankle [1].

Objectives: To conduct a clinical analysis of the effectiveness of autologous mosaic osteochondroplasty in the treatment of patients with osteochondral defects of the talus on the basis of determining the dynamics of pain and restoring the amplitude of ankle movements.

Methods: The study included 34 patients with post-traumatic osteochondral defects of the talus (27 men, 7 women, mean age 24.8 ± 2.1 years) who underwent osteochondroplasty. The duration of painful clinical symptoms before osteochondroplasty ranged from 4 to 18 months. Functional treatment outcomes were assessed over a period of 12 to 36 months using the International Foot and Ankle Surgery Scale (AOFAS), pain dynamics were assessed using the Visual Analog Scale (VAS), and ankle movement recovery dynamics were determined.

Results: Osteochondral autologic grafts were removed from the lateral condyle of the ipsilateral femur. Defect sizes: square from 82 to 129 mm^2 (110,3 ± 0.8 mm^2), depth from 7 to 16 mm (12 ± 0,8 mm). Incorporation of the graft in the recipient bed occurred within 1,5 – 3 months. Long-term follow-up was 12 – 36 months (22,8 ± 3,8 months). The level of pain was decreased from 5,7 ± 0,3 before to 0,9 ± 0,3 after the operation (p < 0.001; paired t-test). Improving of foot function according to AOFAS scale (hindfoot section) was established from 64,9

± 1,4 to 95,9 ± 1,1 (p < 0.001; paired t-test). Extension increasing from 15,0 ± 0,9 to 18,4 ± 0,7 and flexion increasing from 22,9 ± 1,2 to 30,7 ± 1,1 was registered. There were no cases of implants failure or their instability neither the increasing of degenerative changes in the ankle joint.

Conclusion: Osteochondroplasty is the effective method of congruity restoration in cases of post-traumatic talus osteochondral defects, promotes a significant reduction in pain syndrome and an improvement in the function of the ankle. The unknown mechanism of the analgesic effect of osteochondroplasty requires further research.

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Disclosure of Interests: None declared

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AB1227 ATTITUDES AND BELIEFS ABOUT LOW BACK PAIN OF TUNISIAN PATIENTS: A KEY PREDICTOR OF RECOVERY

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Background: Low back pain (LBP) is a common problem related with significant disability and psychosocial dysfunction. Unhelpful beliefs about it are associated with higher levels of pain and may cause a delay in recovery due to unsuitable behaviours. Therefore, studies targeting these beliefs are necessary to modulate messages delivered to the population in order to decrease the burden of LBP.

Objectives: The aim of the present study was to assess the attitudes and beliefs in the management of patients with LBP.

Methods: We applied a cross sectional study including Tunisian patients with LBP. The arabic version of Back Pain Attitudes Questionnaire (10-item Back-PAQ) was used to evaluate back beliefs as a clinical screening tool. We analysed patients' attitudes in 5 domains: vulnerability of the back (items 1 and 2), relationship between back pain and injury (items 3 and 4), activity participation during back pain (items 5 and 6), psychological influences on back pain (items 7 and 8), prognosis of back pain (items 9 and 10). For each item, the scale ranges from "False" to "True" which is the option that represents unhelpful beliefs for recovery. Intermediate labels are: "Possibly False", "Unsure", "Possibly True". Responses were scored from –2 ("True") to +2 ("False"). Unhelpful beliefs attract negative scores and vice versa.

Results: The questionnaire was completed by 32 participants (27 women and 5 men) with a mean age of 56.6 years [45-69]. The mean LBP's duration was 9.1 years [2-28]. The mean Body Mass Index (BMI) was 29.4 [25.5-46.8]. The mean Schober's Test and Fingertip-to-floor (FTF) were respectively 2.8 [1.5-4] and 13.2 [0-50]. The mean Visual Analogue Scale of pain (VAS pain) was estimated at 69 [40-100]. The mean Oswestry Disability Index (ODI) and Short form Health Survey (SF36) were 42.4 [28-66] and 48.3 [20-80] respectively. Unhelpful beliefs were widespread. The mean Back-PAQ-10 score was -4 [-13 -3]. Women had significantly a lower score compared to men (-4.1 [-13-2] versus -1.6 [-5-3]) (p=0.01). Vulnerability of the back had an average score of -2[-3-1]. The relationship between back pain and injury had a mean score of –2.4 [-4-0]. The activity participation during back pain had a mean score of -4 [-4-1]. The psychological influences and prognosis of back pain had an average score of -2[-3-0] and -1.6[-2-3] respectively.

Conclusion: The results of this survey reveal that Tunisian patients have high levels of negative beliefs about LBP. As beliefs and attitudes have been recognised as significant predictors of recovery from LBP, we should promote cognitive behavioural therapy aiming at coping with unhelpful beliefs.

Disclosure of Interests: None declared

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AB1228 MEDICAL CARE CONSUMPTION BY TUNISIAN DOCTORS SUFFERING FROM LOW BACK PAIN

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Background: Common low back pain (LBP) is a real public health problem. Indeed, LBP is associated with important socio-professional consequences and involves a raised cost for society due to absenteeism and medical consumption. Various studies show that it is also a major problem in workplace especially in hospitals.

Objectives: The aim of this study was to evaluate LBP medical consequences among doctors.

Methods: We performed a cross-sectional study including the medical staff of a Tunisian hospital. A standardized questionnaire was distributed to all departments and collected the following day. Doctors who had not responded to the questionnaire received two reminders before considering their exclusion. We defined two groups: Group 1 with acute LBP (<3 months) and Group 2 with chronic LBP (≥3 months). The following parameters were collected: consultation with a physician, self-medication, treatments used, hospitalization, use of imaging methods and objectified spinal abnormalities. A *p* value inferior to 0.05 was considered statistically significant.

Results: Of the 217 questionnaires distributed to physicians, 107 (49.3%) were completed. The participants were composed of 85 women and 22 men. The mean age was 31.8 ± 7.7 years [25-57]. The mean BMI was 23.2±3.7 kg/m^2 [16.6-36.7]. Consumption of tobacco and alcohol was noted in 16.7% and 20.4% of cases respectively. Five participants (4.6%) reported consumption of cannabinoids. Depression, anxiety and sleep disturbances were reported in 25.3%, 57.3% and 46.7% of cases respectively. Among the participants, 84.3% reported having had LBP at least once in their life, and 71.3% reported LBP in the past 12 months. The mean duration of low back pain was greater than 3 months in 11.9% of cases. The mean pain intensity was 4.4 ± 1.9 [2-10]. Twenty participants (26%) consulted a doctor. It was a rheumatologist in 13 cases, an orthopedist in 7 cases, a neurosurgeon in 1 case and a family doctor in 1 case. More than half of the participants (57.5%) self-medicated. Standard radiography was performed in 18 cases, computed tomography (CT) in 5 cases and magnetic resonance imaging (MRI) in 8 cases. The following abnormalities were objectified: degenerative disc disease (13.6%), herniated disc (22.7%) and posterior inter-apophyseal osteoarthritis (9%). Medication use was noted in 56 cases (72.7%), functional rehabilitation in 9 cases (11.7%), back support belt in 3 cases (3.9%), epidural corticosteroid injection in 1 case (1.3%), thermal treatment in 1 case (1.3%), and surgery in 1 case (1.3%). Three doctors required hospitalization ranging from 2 to 15 days. Medical care consumption was significantly more important in patients with chronic LBP: functional rehabilitation (6,8% in group 1 vs 50% in group 2, p<0.001), back support belt (1,6% vs 20%, p=0.046), epidural corticosteroid injection (0% vs 10%, p=0.035), thermal treatment (0% vs 10%, p=0.035), surgery (0% vs 10%, p=0.035) and hospitalization (0% vs 30%, p<0.001).

Conclusion: Medical care consumption was important among LBP and chronic LBP sufferers. Thus, a prevention strategy must be established in hospitals in order to reduce the socio-economic cost of LBP among caregivers.

Disclosure of Interests: None declared

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AB1229 FRÉQUENCE ET ÉTIOLOGIES DES LOMBOSCIATIQUES SECONDAIRES: EXPÉRIENCE D'UN SERVICE DE RHUMATOLOGIE

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Background: Secondary lumbosciatica (LS) is a rare clinical situation, but which must be eliminated in the event of any radiculopathy for better therapeutic management.

Objectives: The objective of our study was to determine the frequency and etiologies of secondary LS among patients hospitalized in the rheumatology department for exploration of lumbosciatica.

Methods: This is a retrospective, single-center study including patients hospitalized in the Rheumatology department of the Taher Sfar hospital in Mahdia for treatment of lumbosciatica, during the period between January 2014 and November 2021.

Results: We included in this study 357 patients hospitalized in our department for exploration of LS. After an etiological assessment, we retained the diagnosis of secondary LS in only 11 patients among our study population, ie 3.1% of cases. Among them, 8 patients were men (72.72%) and the other 3 were women (27.27%) with a sex ratio (M / F) of 2.66. The average age was 65 years with extremes between 55 and 88 years. The mean duration of symptomatology evolution was 6 months with extremes ranging from 15 days to 02 years. The mean pain VAS was 6.8 [2-8], and the majority (81.81% of cases) had inflammatory sciatica. 36.36% of patients (4 cases) had an L5 path, one patient had S1 irradiation and 54.54% (6 cases) had a truncated LS The general deterioration with weight loss was noted in 5 patients (45, 45% of cases) and vesico-sphincteric disorders in 2 patients (18.18%). Physical examination revealed spinal syndrome in 63.63% of cases (7 patients), radicular syndrome in 45.45% of cases (5 patients) and neurological signs of cauda equina syndrome in two patients (18, 18% of cases). Biologically, 81.81% of

patients (9cas) had a biological inflammatory syndrome, 36.36% (4cas) had impaired protein electrophoresis (hypo-gamma peak) and 27.27% (3cas) had hypercalcemia. Recourse to CT or lumbar MRI made it possible to objectify tumor bone lesions in 72.72% (8 cases) of patients, of which 3 cases (37.5%) were of prostatic origin, 2 cases (18,18 %) multiple myeloma, one case of small cell carcinoma, one case of squamous cell carcinoma and one case of bladder tumor. For the other three patients (27.27% of cases), LS was caused by infectious spondylodiscitis in the lumbar stages.

Conclusion: As evidenced by our study, secondary sciatica is a very rare clinical situation, more encountered in the elderly with often an alteration of the general condition. But in front of its seriousness and its functional repercussions, arises the need to eliminate it systematically whatever the ground before starting the treatment.

Disclosure of Interests: None declared

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AB1230 EVALUATION OF THE STRUCTURAL MODIFICATION OF THE SUPRASPINATUS TENDON BY COMPUTER ANALYSIS OF ULTRASOUND IMAGES THROUGHOUT THE EVOLUTION OF TENDINOSIS.

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Background: In subacromial pain syndrome, the supraspinatus tendon is the most frequently injured. Supraspinatus tendinosis is a structural lesion of the tendon stroma whose ultrasound diagnosis depends largely on the observer. Due to this, the follow-up is mainly clinical, based on ordinal scales of pain or mobility. The computer analysis of the image has been recently integrated into the musculoskeletal pathology, but the evidence in ultrasound is very limited.

Objectives: To evaluate the computer analysis of the ultrasound image of the supraspinatus tendon at diagnosis and during evolution depending on the treatment administered.

Methods: A retrospective study was carried out based on the ultrasound records of patients diagnosed with supraspinatus tendinosis between 2014 and 2020. All images were obtained with the same ultrasound equipment. The records had to fulfill the following characteristics: (i) Absence of direct or indirect ultrasound signs of fibrillar continuity solution, (ii) absence of calcifying lesions and (iii) availability of an ultrasound study 5-7 months after diagnosis with the same frequency, gain, and depth parameters for each case. The ultrasound images showing tendinosis were analyzed using the ImageJ 1.53e program. The means and modes of the grayscale signal intensities were determined in longitudinal and transverse projection for each image. For the statistical analysis, paired before-after comparisons based on the normal distribution were used, grouping the patients according to the injured tendon area (lateral, central, medial) and the treatment administered. To determine the weight of the variables analyzed in the probability of resolution, a forward modeled binary logistic regression was performed using the Wald method.

Results: Records of 35 patients were included: 10 treated with immobilization, 12 with corticosteroid injections and 13 with physical therapy. Table 1 summarizes the demographic and clinical characteristics of the population. The changes observed in the mean gray intensity in the longitudinal projection of the tendon did not correlate with the fact that the patients were discharged (0.006 SD 10.47) or not (2.231 SD 7.8835) after the second evaluation (t=-0.708, P=.484). In contrast, the gradient of the mean gray intensity in the transverse projection of the tendon showed significant differences between patients discharged (9.268 SD 3.752) or not (-0.2054 SD 5.26), (t=6.162, P=.000). On the other hand, in the group of patients discharged, a greater reduction was observed in the dispersion of the mean gray intensities (-11.08 SD 5.843) compared to the group that was not discharged (1.178 SD 1.859), (t=-8.458, P=.000). In the multivariate logistic regression analysis, only the final dispersion of gray intensity was associated with the discharge condition with Coef. B=-0.096, P=.027, HR 0.908 (95% CI: 0.834-0.989).

Conclusion: Computer analysis of ultrasound images of the supraspinatus tendon in patients with pure structural tendinosis distinguishes a favorable clinical course only in the study of the cross-sectional projection, probably due to the more flattened shape of the tendon. Clinical resolution, understood as medical discharge after the second evaluation, is associated with an increase in the mean intensity of grays but especially with a reduction in the dispersion of grays.

Disclosure of Interests: Marina Tortosa-Cabañas: None declared, Carlos Guillén-Astete Speakers bureau: Novartis, Janssen, Abbvie, Grunenthal, UCB and Gebro, Paid instructor for: Roche, Novartis, Janssen, Esteve and Menarini, Consultant of: Janssen, Novartis and Roche, Grant/research support from: Pfizer, Grunenthal, Gebro and Novartis, África Andreu-Suárez: None declared

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AB1231 ULTRASOUND-GUIDED INJECTION OF LOW MOLECULAR WEIGHT HYALURONIC ACID VERSUS STEROID FOR INFLAMMATORY AND DEGENERATIVE SACROILIITIS: A RANDOMIZED CONTROLLED TRIAL

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Background: Sacroiliitis may be degenerative (DSI) or inflammatory (ISI) and the latter is one of the clinical features of spondyloarthropathies.

Objectives: To determine the effect of hyaluronic acid versus corticosteroid injection for chronic sacroiliac joint arthropathy.

Methods: forty patients with sacroiliitis either degenerative (DSI: 20 patients) or inflammatory (ISI: 20 patients) based on the New York criteria. Each group was allocated into 2 subgroups; 10 patients received 2ml Betamethasone dipropionate plus 2 ml lidocaine 2% (A) and 10 patients received 2 ml hyaluronic acid plus 2 ml lidocaine 2% (B). All sacroiliac joint injections were done under ultrasonographic guidance using a 22-gauge needle. Visual analogue scale was used for pain assessment at base line, 1, 2 and 4 week post injection.

Results: there was no significant difference between main groups (ISI & DSI) regarding VAS score before injection, 1, 2 and 4 weeks after injection while there was a significant difference between subgroups A&B in ISI group at 2 and 4 weeks (P= 0.012 and 0.008 respectively). Also, there was a significant difference between subgroups A & B in DSI group at 1, 2 and 4 weeks after injection (P= 0.04, 0.006, and 0.005 respectively). There was a high significant difference before and after injection in the main groups and all subgroups. However, there was no significant difference between the subgroups of ISI and DSI.

Conclusion: both steroid and hyaluronic acid were effective in relieving pain in treatment of inflammatory and degenerative sacroiliitis but steroid was more efficacious than the hyaluronic acid.

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Table 1. Demographic and clinical characteristics of the population. GI: gray intensity according to longitudinal or transverse axis. SD: standard deviation.

		Treatment group								
		Physical therapy			Immobilization			Injections		
		Mean	SD	N (%)	Mean	SD	N (%)	Mean	SD	N (%)
Age		55	8		54	10		56	10	
Sex	Women			11 (84,6%)			7 (70%)			9 (75%)
	Men			2 (15,4%)			3 (30%)			3 (25%)
Injured area	Central			1 (7,7%)	0 (0%)		1 (10%)			0 (0%)
	Lateral			5 (38,5%)			3 (30%)			3 (25%)
	Medial			7 (53,8%)			6 (60%)			9 (75%)
GI Long axis.		79,209	20,127		69,953	14,815		82,213	33,638	
GI Trans axis		81,840	17,291		74,091	19,639	3 (25%)	85,991	34,520	

Paediatric rheumatology

AB1232 RELATIONSHIP BETWEEN NEW BIOMARKER (IL18 AND IFN GAMMA) WITH DISEASE ACTIVITY SCORES (DAS71 ESR AND DAS71 CRP) IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: Juvenile idiopathic arthritis (JIA) is a chronic inflammatory condition lasting ≥6 weeks in children ≤ 16-year-old and characterized by pro-inflammatory cytokines (IL1B, IL6, IL18, and IFN- gamma) as a key cytokine in inflammation. The pathogenesis of JIA are still poorly understood and different theories are implicated. Different disease activity scores aimed at guiding the treatment strategies.

Objectives: Correlation between new biomarker (IL18 and IFN gamma) with disease activity scores (DAS71 ESR and DAS71 CRP) and how much these biomarkers change with treatment.

Methods: Prospective nonrandomized study carried on 45 child diagnosed as Juvenile Idiopathic Arthritis (JIA) fulfilling (ILAR)1997 where assessment of the level of IL18, IFN gamma and IL18, IFN-gamma decrement with correlation to disease activity (Juvenile Arthritis Disease Activity Score (JADAS)) and their role as prognostic markers.

Results:

- Serum IL18 and IFN gamma show significant decrease with the end of the study (Figure 1).
- The disease activity (JDAS71 ESR), (JDAS71 CRP) has decreased significantly with the end of the study (Table 1).
- Serum IL18 show negative correlation with ESR, CRP, JDAS71ESR, JDAS-71CRP and IFN gamma level.
- Poor response groups show higher level of ESR, JDAS71ESR and IL18 than good response groups. IL18 and IFN-gamma decrement level was statistically significant higher in good response than poor response.

Conclusion: IL18 and IFN-gamma cytokine and level of decrement are a useful biomarker in predicating the disease activity and response to therapy.

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AB1233 CHARACTERISTICS OF PEDIATRIC MPO AND PR-3 ANCA ASSOCIATED VASCULITIS- SINGLE CENTER EXPERIENCE FROM CENTRAL CALIFORNIA

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Background: ANCA-associated vasculitides (AAV) are rare in childhood and characterized by necrotizing inflammation in small to medium sized vessels. Most of the available literature in children focuses on clinical subtypes Granulomatosis with Polyangiitis (GPA), Microscopic Polyangiitis (MPA), and Eosinophilic Granulomatosis with Polyangiitis (EGPA). Adult studies have demonstrated differences in clinical outcomes based on myeloperoxidase (MPO) and proteinase 3 (PR3) ANCA specificity (1). There is limited information about the characteristics of MPO- AAV and PR3-AAV in children.

Objectives: The objective of this study was to review the characteristics of MPO-AAV and PR3-AAV at a children's hospital in multi-ethnic Central California, United States.

Methods: We performed a retrospective case review of patients less than 18 years of age diagnosed with AAV at a tertiary care children's hospital in Central California in United States from January 1, 2010 to March 31, 2021. Cases were identified from electronic health records using ICD-9 and ICD-10 codes for vasculitis. Records were reviewed for a diagnosis of AAV based on ACR/EULAR classification criteria. Demographic and clinical data including laboratory parameters including ANCA specificity, treatment, and outcomes were collected. Continuous data were expressed as a median and interquartile range, categorical data as frequency and percentages. Chi-square and Mann-Whitney U tests were used for statistical comparison as appropriate.

Results: Eighteen cases of pediatric AAV were identified, of which 10 (55.5%) patients had MPO-AAV and 8 (44.4%) had PR3-AAV. All patients who were MPO positive were diagnosed with MPA. Among PR3-AAV cohort, 7 patients were diagnosed with GPA and 1 patient received diagnosis of MPA. The median age at diagnosis was 12.6 years (IQR 10.1-15.4) in patients with MPO-AAV and 14.8 years (13.8-16.7) in children with PR3-AAV. In MPO-AAV cohort, 90% (n=9) were female, meanwhile 37.5% (n= 3) of patients diagnosed with PR3-AAV were female (p=0.02). Significantly higher proportion of patients diagnosed with MPO-AAV were from racial and ethnic minority groups (n=10, 100%) which included Hispanic (8), Asian (1) and other (1). In comparison, patients with PR3-AAV were predominantly white (n= 7, 87.5%; p <0.01). Median length of hospital stay was 19 days (IQR=12.8-41) in patients with MPO-AAV and 14 days (IQR=9.5-21.8) in patients with PR3-AAV. Rate of ICU admission was 60% in MPO-AAV cohort and 37.5% in PR-3 cohort, although this was not statistically significant. 50% (n=5) of patients in MPO-AAV cohort required dialysis and 25% (n=2) in PR3-AAV cohort. Peak creatinine was higher in MPO-AAV cohort (7.4, IQR 1-13.4 versus 2, IQR 0.7-3.7 mg/dL), although it did not reach statistical significance (p=0.1). PR3-AAV group had significantly higher levels of C-reactive protein (22.9, IQR=7.05-26.3) compared to MPO-AAV cohort (2.25, IQR=0.3-6.2; P=0.02). ENT involvement was more frequent in PR3-AAV cohort (87.5% versus 10%). All patients received treatment with high dose corticosteroids at diagnosis. Other immunosuppressive therapy included cyclophosphamide (40% in MPO-AAV cohort and 75% in PR-3 AAV cohort), rituximab (40% MPO-AAV cohort and 0% in PR-3 AAV cohort), cyclophosphamide and rituximab (10% in MPO-AAV cohort and 25% in PR-3 AAV cohort). Two deaths were reported in MPO-AAV cohort, related to Aspergillus pneumonia and pulmonary hemorrhage.

Conclusion: Our study reviews characteristics of pediatric MPO-AAV and PR3-AAV in the Central California of United States. We observed a more frequent diagnosis of MPO-AAV in racial/ethnic minority children. Limitations of our study include small sample size. This study highlights the need for further research to understand the impact of ethnicity and MPO and PR3 positivity on pediatric AAV presentation, disease activity and outcomes.

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AB1234 RHEUMATIC MASKS OF ONCOLOGICAL DISEASES IN CHILDREN

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Background: Early diagnosis of oncological pathology, which can occur under the guise of other diseases, including rheumatic diseases, is relevant.

Objectives: To analyze the features of the course of rheumatic masks of oncological diseases in children.

Methods: An analysis was made of the features of the course of oncological diseases in 15 children (5 girls and 10 boys) aged 3 to 15 years, hospitalized in the rheumatology department of the Republican Children's Clinical Hospital for the period from 2012 to 2021.

Results: The disease was manifested by fever in 11 of 15 patients. Complaints when contacting a rheumatologist: pain and limitation of movement in the joints (15/15), in the lumbar region (2/15), weakness (8/15), abdominal pain (3/15), vomiting (2/15), myalgia (3/15), hair loss (1/15), nosebleeds (1/15). On physical examination: peripheral lymphadenopathy (4/15), periorbital shadows, pallor (10/15), lupus-like erythema on the face (1/15), joint tenderness on palpation and movement (11/15), joint deformity (2/15). 15), spinal rigidity (3/15), hepatosplenomegaly (5/15). On laboratory examination: anemia (7/15), leukopenia (3/15), leukocytosis (4/15), thrombocytopenia (3/15), thrombocytosis (1/15), pancytopenia (1/15), hypoalbuminemia (2/15). 15), increase in ESR (11/15), CRP (11/15), LDH (4/15), AST, ALT (3/15). Established preliminary clinical diagnoses: juvenile rheumatoid arthritis (10/15), systemic lupus erythematosus (2/15), dermatomyositis (1/15), reactive arthropathy (1/15), fever of unknown origin (1/17). Appointed: NSAIDs (8/16), glucocorticoids (9/15), methotrexate (5/15), cyclophosphamide

(1/15). An oncological search was carried out. The following diagnoses were verified: stage 4 neuroblastoma (4/15), acute lymphoblastic leukemia (5/15), stage 4 B-large cell lymphosarcoma (1/15), stage 4 B-lymphoblastic lymphoma/leukemia (1/15), T-cell lymphoma (1/15), stage 3 glioma (1/15), malignant histiocytoma (1/15), brain tumor (1/15).

Conclusion: Oncological diseases in children can occur under the guise of rheumatic diseases. Immunosuppressants and glucocorticoids mask the true clinical picture of the neoplasm and prevent early diagnosis.

Disclosure of Interests: None declared

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AB1235 MULTISYSTEM INFLAMMATORY DISEASE IN CHILDREN (MIS-C) IN SINGAPORE CHILDREN: ARE WE DIFFERENT?

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Background: Multisystem Inflammatory Syndrome in Children (MISC) is a hyper-inflammatory state with similarities to Kawasaki Disease, 4 to 6 weeks after Covid-19 infection[1]. Literature describes a 11:1 Relative Risk for Asian children versus Caucasians[2]. Since the start of the pandemic, 17,699 children under 12 years were infected with Covid-19[3].

Objectives: To describe presentation and short term outcomes, for a cohort of children with MIS-C at the sole Children's Hospital in Singapore.

Methods: Demographic and clinical/lab data were collected from children diagnosed with MIS-C accrording to the WHO criteria[4] at KK Woman's and Children's Hospital, Singapore. Nonparametric descriptive statistics were used to describe and analyse data.

Results: Eleven patients were diagnosed with MIS-C between October 2021 and Jan 2022. Seven (64%) were male and 4 (36%) were Chinese, with median age at presentation was 8.08 years (IQR 4.54 - 9.79). All patients had positive COVID-19 serology at the time of diagnosis. Median duration of fever prior to diagnosis was 5 days (IQR 4 - 5); Nine (82%) had gastrointestinal symptoms and median number of Kawasaki Disease (KD) features were 2 (IQR 2 - 3.5); common manifestations were conjunctivitis (90%), red lips (55%) and rash (36%). Of note, 8 (70%) patients had KD type peeling on follow-up. No BCGitis was found during acute phase. Seven (64%) were admitted to higher dependency care.

Table 1, all patient received IVIG and IV steroids; 6 (55%) as pulse (30mg/kg/day) therapy. Patient 8, additionally received Anakinra. Median duration of admission was 6 days (IQR 5-13). One patient developed complications post therapy and was re-admitted to hospital for hematochezia. Treatment involved stopping Enoxaparin and Prednisone. Aspirin was resumed as soon as bleeding ceased. Laboratory characteristics and outcomes are denoted in Table 1. All patients had a monophasic course during the median of 10 weeks (IQR 8 - 11.5) of follow-up.

Conclusion: 1.Asian prevalence of MIS-C is not as high as that reported from the West. Similarities in presentation as to age and gender were noted.

2.Most of our MIS-c patients developed periungual peeling at follow up, similarly to Kawasaki Disease.

3.Different from our typical KD population, no BCG site inflammation was found.

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AB1236 CLINICAL CHARACTERISTICS OF JUVENILE ONSET SYSTEMIC SCLEROSIS PATIENTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT COMPARED TO ADULT AGE JUVENILE-ONSET PATIENTS FROM EUSTAR. ARE THESE DIFFERENCES SUGGESTING RISK FOR MORTALITY?

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Background: Juvenile systemic sclerosis (jSSc) is an orphan autoimmune disease with a prevalence of 3 in 1 000 000 children. Information on long-term development of organ involvement and clinical characteristics of jSSc patients in adulthood are lacking. It was believed that patients in adult cohorts may represent a survival biased population.

Objectives: To assess differences in clinical characteristics of jSSc-onset patients from the pediatric age group, with a mean disease duration of 3 years, compared to the adult age jSSc-onset group, with a mean disease duration of 18.5 years.

Methods: We extracted clinical data at time of inclusion into the cohorts from the Juvenile Scleroderma Inception Cohort (jSScC) and data from juvenile-onset adult SSc patients from the European Trials and Research Group (EUSTAR) cohort. We compared the clinical characteristics of the patients by descriptive statistics.

Table 1.

No	Age (yr)	GI symptoms	KD features	Hemoglobin (g/DL)	Absolute Lymphocyte (10x9/L)	Platelet (10x9/L)	CRP (mg/L)	D-Dimer (mg/L FEU)	Ferritin (ug/L)	Enoxaparin started	Peeling	Abnormal echo
1	10	YES	2	12.2	0.23	67	173.2	32	3179.1	YES	YES	YES
2	11	NO	2	14.8	1	166	94.9	2.51	350	NO	YES	YES
3	4.25	YES	2	10.4	1.02	241	134.6	6.05	277.2	YES	NO	YES
4	7.67	YES	5	11	0.41	102	250.6	9.32	3607.6	YES	YES	NO
5	8.58	YES	4	11.4	0.56	93	105.6	1.31	846.6	NO	YES	NO
6	4.58	YES	2	10.3	3.09	198	137.4	1.87	291	NO	NO	NO
7	9.58	YES	3	12.2	1.31	119	184	2.51	244.3	NO	YES	NO
8	4.5	YES	4	11.9	0.45	102	181.8	11.12	1798.4	YES	NO	YES
9	11	YES	1	10.1	1.23	59	74.2	4.53	1445.8	YES	YES	NO
10	3.42	NO	2	9.1	1.09	138	153.9	8.66	609.4	YES	YES	NO
11	8.08	YES	2	11.4	1.25	101	66.8	1.31	521.8	NO	YES	YES

Results: We extracted data of 187 jSSc patients from the jSScC and 236 patients from EUSTAR. The mean age at time of assessment was 13.4 years old in the jSScC and 32.4 years old in EUSTAR. The mean disease duration since first non-Raynaud was 3.0 years in jSScC and 18.5 years in the EUSTAR (Table 1). We found significant differences between the cohorts. There were more female patients in EUSTAR (87.7% versus 80.2%, p=0.04). More patients had diffuse subtype in jSScC (72.2% versus 40%, p<0.001). The modified Rodnan skin score (mRSS) was significantly higher in jSScC (14.2 versus 12.1, p=0.02). Active digital ulceration occurred more often in EUSTAR (26.6%, versus 17.8% p=0.01), but history of active ulceration was more frequent in jSScC (54.1% versus 43%, p<0.001). Mean DLCO was lower in jSScC (75.4 versus 86.3, p<0.001). Intestinal involvement was significantly more common in jSSc (33.2% versus 23.8%, p=0.04). Esophageal involvement was more common in EUSTAR (63.7% versus 33.7%, p<0.001). (Table 1).

Table 1. Clinical characteristics of juvenile onset SSc patients at time point of the inclusion into the juvenile scleroderma inception (jSScC) cohort and in the adult EUSTAR- cohort

	jSScC	EUSTAR Cohort	P value
Number of patients	187	236	0.04
Age in years, mean (SD)	13.4 (3.6)	32.4 (15.4)	
Female patients, n (%)	150 (80.2%)	207 (87.7%)	
jSSC Subtype, n (%)			
diffuse	135 (72.2%)	87 (38.1%)	<0.001
limited	52 (27.8%)	121 (53.3%)	
Age at Raynaud onset in years, mean (SD)	10.0 (3.9)	13.7 (9.1)	
Age at non-Raynaud onset in years, mean (SD)	10.3 (3.9)	11.7 (3.7)	
Duration since first Raynaud symptoms in years, mean (SD)	3.4 (2.7)	20.6 (15.9)	
Duration since first non-Raynaud symptoms in years, mean (SD)	3.0 (2.7)	18.5 (15.6)	
Raynaud´s, n (%)	170 (90.9%)	222 (94.9%)	
ANA positive, n (%)	166 (91.7%)	210 (92.9%)	0.99
Anti-Scl 70 positive, n (%)	62 (34.4%)	73 (33.3%)	0.68
Modified Rodnan Skin Score, mean (SD)	5%	*Data missing*	
Modified Rodnan Skin Score, mean (SD)	14.2 (11.7)	12.1 (14.5)	0.02
Digital ulceration, n (%)			
At the time of inclusion	33 (17.8)	21 (26.6%)	0.01
In the past history	100 (54.1%)	34 (43%)	<0.001
Telangiectasia	*62 (37.4%)*	*42 (53.2%)*	*0.04*
FVC, mean (SD)	84.1 (18.6)	84 (22.4)	0.96
DLCO, mean (SD)	75.4 (19.2)	86.3 (19.9)	<0.001
Arterial hypertension, n (%)	10 (5.4%)	20 (8.5%)	0.26
Renal crisis, n (%)	0	3 (1.3%)	0.26
Esophageal involvement, n (%)	63 (33.7%)	149 (63.7%)	<0.001
Intestinal involvement, n (%)	62 (33.2%)	56 (23.8%)	0.04
Articular involvement, n (%)	34 (18.3%)	27 (11.6%)	0.06
Muscular involvement, n (%)	31 (19.3%)	46 (19.8%)	0.45

Conclusion: Patients with jSSc-onset who are currently adult age (defined as >18 years of age) are less frequently male and from the diffuse subset, have lower mRSS, less digital ulcers and intestinal involvement. This might represent a combination of both survival bias and/or be explained by the longer observation time with less active disease (i.e. natural progression decreased mRSS over time). Further long-term observational studies with jSSc patients are required to address this issue.

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AB1237

COMPARISON BETWEEN ENZYME IMMUNOASSAY AND CHEMILUMINESCENCE TO DETERMINE THE CONCENTRATION OF SERUM CALPROTECTIN AND ITS ASSOCIATION WITH CLINICAL VARIABLES IN PEDIATRIC RHEUMATOLOGY.

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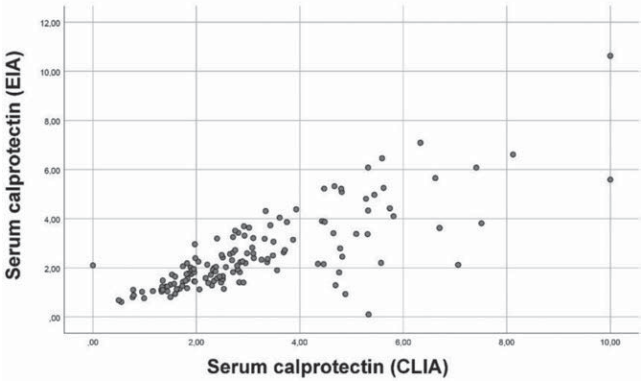
Background: Serum calprotectin (SC) is an emerging biomarker in the measurement of inflammation. It can be determined by different techniques, such as enzyme immunoassay (EIA) or chemiluminescence (CLIA). However, there are no studies comparing whether there is a correlation between the two diagnostic methods in paediatric rheumatologic diseases.
Objectives: (i) To assess whether there are differences between serum calprotectin (SC) levels determined by EIA (Bühlmann) method and CLIA (QUANTA Flash) in pediatric age patients with systemic autoimmune rheumatic disease (SARD). (ii) To evaluate which clinical and analytical variables are associated with an increase of SC in each method.
Methods: Analytical cross-sectional study that included patients from a pediatric rheumatology specialized unit between 02/2017 and 05/2021. We included 41 patients with SARD who had at least one SC analysis determined by EIA in their routine controls (144 serum) and afterwards had SC determined again, this time using the CLIA method. The collected variables were sex, age, remission according to clinical judgment, swollen joint count according to physical examination (PE Count) and ultrasound (US Count), Juvenile Arthritis Disease Activity Score according to physical examination (PE JADAS-27) and ultrasound (US JADAS-27), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). As for the statistical analysis, intraclass correlation (ICC) and paired samples t-test were performed to compare the two methods. Univariate linear regression was performed to study the association between EIA, CLIA and both clinical and analytical variables.
Results: We included 41 patients, 50.1% were women with a mean age (± SD) of 13.1 (± 3.8) years. The details of their descriptive characteristics were: mean SC (EIA) of 3.1 (±1.8) µg/ml, mean SC (CLIA) of 2.5 (±1.6) µg/ml, mean CRP of 2.6 (± 6.5) mg/l, mean ESR of 10.1 (± 11) mm/h, and mean PE JADAS-27 of 2.8 (± 8). Most frequent diagnosis was oligoarticular juvenile idiopathic arthritis (JIA) (24.4%), followed by enthesitis-related (ERA) JIA (12.2%) and polyarticular JIA (12.2%), familial Mediterranean fever (FMF) (9.8%), psoriatic JIA (4.9%), systemic JIA (4.9%) and syndrome of periodic fever, aphtous stomatitis, pharyngitis, and cervical adenitis (PFAPA) (4.9%), vasculitis (4.8%), and undifferentiated JIA (2.4%). Clinical diagnosis was unspecific in 9.8% of the patients. In our sample, 66.7% were in clinical remission at the discretion of the specialist. A statistically significant Pearson's CCI of 0.77 (95%CI 0.70-0.83; p=0.00) was observed as a single measure between EIA and CLIA and with an average of 0.87 (95%CI=0.82-0.91; p=0.000). Figure 1 shows the dispersion of this correlation.

Figure 1. Dispersion diagram representing the correlation between EIA and CLIA.



On the other hand, we observed a statistically significant difference in the mean between both methods of 0.58 (95%CI=0.40-0.77; p=0.000), observing a greater difference in SC (EIA) > 4 µg/ml.
A significant association was observed between EIA and clinical remission, joint count, JADAS and CRP; and also between CLIA and clinical remission, JADAS and CRP. The analysis performed is shown in Table 1.

Table 1. Association between EIA and CLIA with clinical and analytical variables.

	Remission		PE Count		US Count		PE JADAS		US JADAS	
	b	**p**	**b**	**p**	**b**	**p**	**b**	**p**	**b**	**p**
SC(EIA)	0.43	**0.011**	0.14	**0.027**	0.08	**0.024**	0.09	**0.000**	0.06	**0.000**
SC(CLIA)	0.53	**0.000**	-0.00	0.945	0.31	0.320	0.05	**0.021**	0.04	**0.015**
	Sex		**Gender**			**ESR**		**CRP**		
	b	**p**	**b**	**p**		**b**	**p**	**b**	**p**	
SC(EIA)	0.00	0.997	0.05	0.207		0.00	0.487	0.05	**0.027**	
SC(CLIA)	-0.24	0.362	0.01	0.795		0.02	0.105	0.08	**0.000**	

b, regression coefficient; p, statistical significance.

Conclusion: There is a good correlation between EIA and CLIA methods to determine SC in pediatric patients with SARD. Significant differences were observed between both methods above the value of 4 µg/ml. This fact could be explained by methodological differences, since CLIA discriminates better at higher values than EIA.

An association was observed between both methods and variables of remission or disease activity.
Disclosure of Interests: None declared
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AB1238 THE EFFECT OF DRUG THERAPY IN JUVENILE IDIOPATHIC ARTHRITIS ON THE LEVEL OF CYSTATIN C AS A MARKER OF RENAL DYSFUNCTION

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Background: Juvenile idiopathic arthritis (JIA) is a chronic disease requiring years of therapy with non-steroidal anti-inflammatory drugs (NSAIDs), immunosuppressant's, cytostatics, immunobiological agents. The aforementioned drugs, namely NSAIDs and cytostatics are potentially nephrotoxic [1]. The above drugs, namely NSAIDs and cytostatics, are potentially nephrotoxic. About 8% of children with JIA have kidney damage, which develops on average 5 years after the onset of the disease. It has been established that the main risk factor for the development of kidney damage is the long-term exposure to NSAIDs and methotrexate in children with active forms of JIA [2]. Early diagnosis of kidney damage will allow timely correction in the dosage of drugs and avoid their nephrotoxic effects [3].
Objectives: To determine the effect of drug therapy in children with JIA on eGFR by using the Cystatin C-based equation and the Hoek formula based on the serum cystatin C study.
Methods: 80 children with JIA participated in the study. The age of subjects was 10.4±4.41 (10.6-15.0) years. All children received methotrexate as a base drug. At the moment of examination 22 children received NSAIDs, 25 children received immunobiological preparations. Serum cystatin C content was determined by enzyme immunoassay. The Cystatin C-based equation 2012 and Hoek formulas were used to set the GFR by serum cystatin C levels.
Results: Non-steroidal anti-inflammatory drugs led to a decrease in GFR as found by both the Cystatin C-based equation 2012 and the Hoek formula. The incidence of GFR reduction in patients treated with NSAIDs using the Cystatin C-based equation 2012 was 100%, and using the Hoek formula was 81.8%.
The use of NSAIDs in children with JIA is a risk factor for the development of reduced GFR calculated by the Hoek formula. The incidence of reduced GFR in children with NSAID use was 54.5%, 6.7 times greater than in those without NSAIDs (OR = 12.9; CI: 3.76-44.25; p<0.001). There was a low chance of a Hoek formula decrease in GFR in children with JIA who received immunobiological therapy 9.1% vs 46.8% (OR = 0.11; CI: 0.03-0.42; p<0.001).
Conclusion: Use of NSAIDs in children with JIA was more often associated with a reduction in GFR: by Cystatin C - based equation 2012 in 100% of cases p<0.01, by Hoek in 81.8%, p<0.001. The average of GFR was significantly lower in children treated with NSAIDs than in children without NSAIDs. Immunobiological therapy had a positive effect on the GFR value. The frequency of a decrease in GFR was significantly lower in the children treated with immunobiological therapy compared with those without immunobiological therapy 9.1% vs 46.8% (OR = 0.11; CI: 0.03-0.42; p<0.001).
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AB1239 PRIMARY SJÖGREN'S SYNDROME WITH JUVENILE ONSET: REPORT OF 15 CASES

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Background: Primary Sjögren's syndrome (pSS) is a chronic and progressive multisystem autoimmune disease which rarely onset in children and adolescents. Diagnostic delay in large part of patients are common due to the non-specific and variable symptoms and the slow progression of disease.
Objectives: To analyse demographic data, specific extraglandular, salivary and ocular manifestations, laboratory parameters and therapy of pSS with juvenile onset.
Methods: Retrospective study of all patients (pts) with pSS in single center.
Results: pSS was verified in 15 pts (6.7% were boys), which amounted to 23.8% of all pts with SS in our pediatric rheumatologic department. The median age of pSS onset was 8.0 y.o. [IQR 7.0; 10.2]. The median of disease duration at the time of pSS verification was 2.75 years [2.2; 5.6]. All patients had systemic manifestations at onset: constitutional abnormalities – 33.3%, nonerosive polyarthritis – 64.3%, polyarthralgias – 26.7%, lymphadenopathy – 73.3%, cutaneous involvement – 53.3% (2 – xerosis, 2 - annular erythema, 1 - erythema nodosum, 2 – Raynaud phenomenon, 2 – nonspecific spotty rashes, 1 – hemorrhagic rash). At the time of diagnosis 7 pts (46.7%) had isolated involvement of salivary glands, 8 pts (53.3%) – combined with involvement of lacrimal glands. The decrease in salivary gland function was recorded in 80% of cases, hypolacrimia – in 46.7%, 1 patient had isolated hypolacrimia. Recurrent parotitis was present in 6 pts (40.0%). At time of diagnosis pulmonary involvement had 20.0% of pts, 1 patient had renal tubular acidosis. 8 pts (53.3%) had various hematological disorders: anemia – in 3 pts (20.0%), leukopenia – in 6 (40.0%). ANA Hep-2 were detected in 100% pts (in titer 1/640 – 4, 1/1280 – 7, 1/2560 – 3, 1/20480 - 1, with mixed patterns in all pts: speckled + homogeneous – 9 pts, speckled + homogeneous+cytoplasmic – 6 pts), anti-Ro - in 12 pts (80.0%), anti-La - in 8 pts (53.3%), RF+ - in 9 pts (60.0%). 6 pts (40.0%) had polyclonal hypergammaglobulinemia, max 42%. 2 pts (13.3%) had concomitant autoimmune non-rheumatic disease; 1 – cutaneous psoriasis, 1 - autoimmune thyroiditis. The treatment of each patient was justified by the main individual manifestations: 93.3% received glucocorticoids, 26.7% - methotrexate, 33.3% - hydroxychloroquine, 6.7% - mycophenolate mofetil. Treatment with biologics (B) was received by 13 (93.3%) pts (7 – rituximab (RTM), 6 – abatacept (ABA)) with a good response in 10 pts, including improvement in the function of the salivary and lacrimal glands in 7 pts. 1 patient received 2B - RTM and ABA sequentially due to the development of MAS 7 days after 1st RTM infusion. B was discontinued in 3 pts: 1 due to development of hemorrhagic vasculitis 2 days after the 1st RTM infusion, 1 – COVID-19 with lung involvement (CT 3-4) 2 weeks after the 1st RTM infusion, 1 – inefficiency of ABA during 15 months.
Conclusion: In our pediatric rheumatologic department pts with pSS made up less than a quarter of all pts with SS. The diagnosis was verified delayed in all pts, which can be explained by a wide range of nonspecific manifestations at the onset. However, the manifestations of SS that were present at the time of diagnosis were brought under control on the background of complex therapy, including the prescription of B, with a good efficacy and safety profile of therapy.
Disclosure of Interests: None declared
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AB1240 PROSPECTIVE EVALUATION OF COGNITIVE FUNCTION IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Objectives: Prospectively evaluate changes in the cognitive function of patients with juvenile idiopathic arthritis (JIA) and associated factors.
Methods: Design and protocol: We performed a prospective cohort study with JIA patients that participated in a previous cross-sectional study (2019) to evaluate cognitive function. After 24 months, the patients were administered the same test battery previously used through an established protocol, and data was collected from their clinical histories. The neuropsychological tests were corrected by a neurologist and neuropsychologist. Study population: Inclusion criteria: Patients aged ≥16 years with JIA classified according to the criteria of ILAR 2001. Patients with inflammatory or rheumatic diseases other than JIA, previous neurological disease not associated with the course of JIA, and patients with scores lower than the normal in the manual skill test were excluded. Outcomes: The main variable was cognitive impairment, defined as worsening of ≥2 scaled points after 24 months (V24) in any of the subtests used to evaluate each cognitive area in the Wechsler Adult Intelligence Scale (WAIS). The evaluated cognitive domains and their respective subtests were: Attention/concentration (Digit Span); verbal function (Vocabulary); visuospatial organization (Block Design); working memory (Letter-Number Sequencing); problem-solving (Similarities). Depression was evaluated by The Beck Depression Inventory-II (BDI-II): minimal (0-13), mild (14-19), moderate (20-28), and severe (29-63). Other variables: Clinical-epidemiological characteristics; treatments; and inflammatory activity evaluated as the C-reactive protein average (CRP) and JADAS-27 along the 2 years of follow-up. Statistical analysis: Descriptive analysis, followed by $\chi 2$ and paired T-test. Multivariate analysis to identify independent variables associated with impairment of cognitive function in JIA.

Results: Thirty patients with JIA were included. The clinical characteristics in V24 are shown in Table 1. Thirteen patients (43%) showed impairment in one or more cognitive functions. The most frequent impaired cognitive functions were verbal function (13.3%), visuospatial organization (13.3%) and problem solving (13.3%); followed by attention/concentration (10.0%) and working memory (6.7%). The variables independently associated with cognitive impairment were the mean CRP along the follow-up (OR [IC 95%], 1.510 [1.012-2.254]; p=0.044) and depression (OR [IC 95%], 1.358 [1.028-1.794]; p=0.031). This model would explain the 47% of the cognitive impairment in JIA (R2=0.470).

Table 1. Clinical, laboratory, and treatment characteristics of 30 patients with JIA

Variable	JIA n=30
Age in years, mean (SD)	2.4 (7.0)
Sex, woman, n (%)	19 (63.3%)
Cultural level	
Basic studies, n (%)	3 (12.5%)
Secondary education, n (%)	8 (33.3%)
University studies, n (%)	13 (54.2%)
Dyslipidaemia, n (%)	2 (6.6%)
BMI, mean (±SD)	22.6 (3.3)
Evolution time JIA, months, mean (±SD)	158.1 (88.4)
Rheumatoid factor >10 U/mL., n (%)	2 (6.6%)
Anticitrullinated peptide antibodies >20 U/mL., n (%)	1 (4.5%)
HLA B27, n (%)	6 (20.0%)
ANA, n (%)	12 (40.0%)
RCP average, mean (±SD)	4,9 (6.6)
JADAS27, mean (±SD)	8,1 (10.5)
Uveitis, n (%)	9 (30.0%)
Current synthetic DMARDs, n (%)	18 (60.0%)
Previous biologic DMARDs, n (%)	12 (40.0%)
Corticosteroid, n (%)	5 (16.6%)

BMI: Body Mass Index, JIA: Juvenile Idiopathic Arthritis, ANA: Antinuclear antibodies, CRP: C-Reactive Protein, DMARD: Disease-Modifying Antirheumatic Drugs.

Conclusion: Forty percent of the patients with JIA showed cognitive impairment after 24 months of follow-up. Cognitive impairment was associated with higher inflammatory activity and depression.

Disclosure of Interests: None declared

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AB1241 BONA MINERAL DENSITY IN JUVENILE ONSET MIXED CONNECTIVE TISSUE DISEASE AFTER LONG-TERM DISEASE DURATION - A CASE-CONTROL STUDY

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Background: Rheumatic diseases are associated with reduced bone mineral density (BMD) as measured by Dual Energy x-ray absorptiometry (DXA). Mixed connective tissue disease (MCTD) is a rare connective tissue disease, and about 25% of all cases have a pediatric presentation. One study implies that osteoporosis is common in postmenopausal women with MCTD (1), but data regarding BMD and osteopenia are lacking in younger patients with the disease.

Objectives: To assess the BMD in a cohort of juvenile mixed connective tissue disease (JMCTD) patients compared to a matched control group.

Methods: BMD was measured in a cohort of 52 JMCTD patients with mean age 28.2 years (SD 10.3) and mean disease duration 16.2 years (SD 10.3), and 52 controls matched for age and gender. Inclusion criteria were fulfilment of the Kasukawa- or the Alarcon-Segovia criteria and symptom debut before the age of 18 years.

Results: Patients and controls did not differ in age, body mass index, smoking habits, level of physical activity or vitamin D status (Table 1). Forty-four (85%) were female. Patients were shorter and had lower body weight compared to controls. None had had osteoporotic fractures. Patients over 20 years of age at examination had significantly lower BMD in the spine, femoral neck, proximal- and distal radius. Patients also had lower T-score compared to matched controls.

Table 1.

Variable	JMCTD patients (n=52)	Controls (n=52)	P value
BMI, kg/m^2	22.7 (3.5)	23.4 (3.0)	0.239
Height, cm	166.0 (7.5)	170.1 (8.5)	**0.016**
Weight, kg	63.0 (12.1)	68.1 (12.1)	**0.033**
Never smokers, n (%)	35 (67)	34 (65)	0.83
Moderate physical activity (hours/week), median (range)	2.0 (0-28)	1.2 (0-30.0)	0.278
Vitamin D*, nmol/l, median (range)	50.0 (27-106)	51.5 (23-115)	0.829
BMD, gm/cm^2			
Spine L2-L4	1.19 (0.13)	1.25 (0.10)	0.110
< 20 years (n = 14, 27%)	1.14 (0.21)	1.17 (0.11)	0.496
>20 years (n = 38, 73%)	1.19 (0.12)	1.26 (0.10)	**0.018**
Femoral neck	0.97 (0.12)	1.04 (0.09)	**0.006**
>20 years	0.97 (0.12)	1.04 (0.09)	**0.002**
Proximal radius	0.79 (0.12)	0.86 (0.09)	**0.007**
>20 years	0.79 (0.12)	0.86 (0.09)	**0.013**
Distal radius	0.40 (0.07)	0.50 (0.10)	**<0.001**
>20 years	0.41 (0.07)	0.51 (0.10)	**<0.001**
T-score >20 years			
Spine L2-L4, median (range)	-0.40 (-2.3 to 2.0)	0.29 (-1.4 to 1.8)	**0.006**
Femoral neck, median (range)	-0.50 (-2.2 to 2.1)	0.40 (-1.7 to 1.6)	**0.007**
Proximal radius, median (range)	-0.90 (-0.2 to 1.6)	-0.30 (-0.2 to 1.3)	**0.044**
Distal radius, median (range)	-1.0 (-3.0 to 1.3)	0.20 (-2.6 to 3.8)	**<0.001**

All values are mean (SD) unless otherwise stated

Conclusion: Bone mineral density was impaired in JMCTD patients after 16 years disease duration compared to matched controls.

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Disclosure of Interests: None declared

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AB1242 RETROSPECTIVE SINGLE CENTER STUDY OF BIOLOGICAL THERAPY IN CHILDREN WITH RHEUMATOID FACTOR-POSITIVE SUBTYPE OF JUVENILE IDIOPATHIC ARTHRITIS

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Background: Rheumatoid factor-positive subtype of juvenile idiopathic arthritis (RF+ JIA) is a relatively rare condition (5-7% of all cases of JIA), but is associated with a poor prognosis. For these patients (pts), it is extremely important to timely prescribe adequate therapy, including biologics (B), to prevent rapid progression and early disability.

Objectives: To analyze in retrospective study the rate of usage, efficacy and safety of B in pts with RF+ JIA.

Methods: Pts with RF+ JIA were identified from clinical database. Diagnosis of RF+ JIA was reviewed based on New Classification Criteria for JIA, PRINTO, 2019 [1]. Demographic and clinical data, therapy, efficacy and adverse effects observed under B were analysed.

Results: The diagnose RF+ JIA was verified in 81 pts (11,1% boys). The median age at onset of JIA was 12.0 y.o. (7.4; 14.0). The median age at time of diagnosis – 13.0 y.o. [9.3; 15]. In total, RF+ were detected in 93.8% of pts (median 71.4 IU/ml [IQR 28.8; 218.5]), anti-cyclic citrullinated peptide antibodies-positive (ACCP+) - in 70.4% of pts (median 164.9 EU/ml [97.4; 300]). 64.2% of pts had combination RF+ and ACCP+, 29.6% - only RF+, 6.2% - only ACCP+. The therapy included NSAIDs in 97.5% of pts, steroids – in 48.1%, DMARDs in all pts (methotrexate (MTX) alone – 80.2%, 2 DMARDs – 13.6%, 3 DMARDs consecutive – 6.2%), B - in 85.2 % of pts. 2 pts received JAK-inhibitors (1 - tofacitinib, 1 – baricitinib). The median of the number of active joints at start of B was 16 [10; 23]. The median of ESR was 26 [18;43] mm/h, CRP - 14.7 [5.3;31.8] mg/l. We observed extra-articular manifestations in 29.0% of pts: 24.6% - lymphadenopathy, 4.3% - rheumatoid lung disease, 2.9% - rheumatoid nodules, 4.3% - distal polyneuropathy. Secondary Sjögren's syndrome (SS) was diagnosed in 27.5% of pts. The experience of using B included from 1 to 4 prescriptions sequentially: 83.3% of pts received only 1 B, 20.3% - 2 B, 8.7% - 3 B, 4.3% - 4 B. B was started during the 1st year of disease in 82.7% of pts due to the rapid progression of the erosive process. As the 1st B used: abatacept (ABA) – 47.8%, etanercept (ETA) – 20.3%, adalimumab (ADA) – 10.1%, rituximab (RTM) – 7.2%, infliximab (INF) – 5.8%, tocilizumab (TCZ) – 4.3%, golimumab (GLM) – 1.4%, sarilumab – 2.9%. As the 2nd B used: 26.1% - RTM, 21.7% - ADA, 17.4% each - ETA and ABA, 13.0% - TCZ, 4.3% - GLM. As the 3d B used: 33.3 % each – TCZ and ADA, 22.2% - PTM, 11.1% - ETA. 3 pts received successively 4 B (ABA-ETA-ADA-TCZ, ABA-ETA-ADA-RTM, TCZ-ABA-ADA-RTM). Adverse events (AE) were observed in 24.6% of pts as recurrent uncomplicated upper respiratory tract infections being the most common. The reasons for substitution therapy were serious AE, subsequent loss of effect. The frequency of ACCP+ was not statistically different in groups with the effective use of only 1 B and, if necessary, replacement. In the presence of systemic manifestations, preference was given to TCZ or RTM, with secondary SS - RTM or ABA.

Conclusion: Most pts with RF+ JIA needs to require B in the first year of the disease. Application B has good efficacy and an acceptable safety profile. The presence of systemic manifestations/secondary SS influence on choice of B. Our data didn't reveal the effect of ACCP+ on preferred choice or frequency of replacement B.

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AB1243 EFFICACY OF ABATACEPT IN THE TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in pediatric age, uveitis IS the most frequent extra-articular complication (1). Uveitis, if not properly treated, can lead to potentially irreversible ocular complications such as blindness.
The treatment of uveitis associated with JIA (U-JIA) remains a challenge due to the aggressiveness of the disease and the frequency of complications.
Following the current guidelines for screening and treatment of uveitis, the use of topical and sistemic corticosteroids, Methotrexate, cyclosporine or some biological drugs such as Adalimumab constitute the mainstay of treatment in this manifestation.
In some refractory cases, the use of Abatacept has been reported
Objectives: To analyze the efficacy of Abatacept in the treatment of U-JIA from the data avaliable in the scientific literature.
Methods: We perform a systematic review of the scientific literature, following the PRISMA statement, using the following electronic databases: *Medline, Embase, Cochrane Library and Web of Science*.
Results: An overall of 89 bibliographic references fulfill the inclusion criteria. A total of 64 patients from 6 studies were followed for a mean time per patient of 11.5 months. The mean age of onset of JIA was 5.25 years, with a time of evolution of the disease of 7 and 11.85 years.
In all the series included, a high percentage of patients showed complications secondary to ocular inflammation (synechia, band keratopathy, cataracts, macular cystic edema and/or ocular hypertension) as well as visual deficits secondary to JIA-U.
All patients, fhave shown refractoriness to conventional DMARDs, as well as anti-TNF biological drugs.
In all the studies, the best correct visual activity (BCVA) is used as main outcome measure. Another outcome measures were used: number of uveitis flares, the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), or the number of cells present in the anterior eye chamber.
Four series of cases showed an improvement or stabilization of visual acuity after Abatacept treatment. Two studies provided variations in visual acuity that are not statistically significant.
Regarding the efficacy of Abatacept, we can observe improvement, in the most of the studies we observed a decrease in the severity of the ocular inflammation and/or its complete remission.
Due to the lack of comparable data, a meta-analysis could not be performed. However the data suggest a clear recovery of t JIA-U patients refractory to conventional treatment.
Conclusion: Abatacept is shown as a promising drug in the treatment of U-JIA, considering its efficacy in improving visual acuity, as well as in the control of flare-ups and the decrease in inflammatory eye symptoms. However, more studies are necessary to corroborate the efficacy of Abatacept
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Disclosure of Interests: None declared
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AB1244 TOTAL KNEE ARTHROPLASTY IN PATIENTS UNDER 21 YEARS OF AGE: A U.S. NATIONWIDE ANALYSIS

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Background: Total knee arthroplasty (TKA) is a procedure rarely performed in patients under 21 years old. However, the number of patients <21 undergoing TKA in the United States (US) is unknown. In one of the largest US studies of an institutional arthroplasty registry, only 19 TKAs were performed in patients <21 out of ~30,000 primary TKAs over 34 years[1]. While a few national or multi-national studies have been performed outside the US, these studies have small cohorts (~100), making it difficult to determine the indications for TKA in this age group.
Objectives: We identified the number of patients <21 years of age who underwent TKA in a US nationwide dataset. Additionally, we determined the epidemiological characteristics of patients undergoing TKA, including their age, sex, race, indications for surgery, and in-hospital mortality.
Methods: We analyzed the Kids' Inpatient Database, which is a national weighted sample of all inpatient hospital admissions in the US in patients <21 years old from ~4,200 hospitals in 46 states. We included all admissions from 2000-2016 with a primary procedural code of TKA determined by ICD-9 and 10 codes. Descriptive statistics such as means and percentages, along with 95% confidence intervals were calculated using appropriate sample weights.
Results: The total number of TKAs performed in patients <21 years old from 2000 to 2016 was 1,331 (Table 1). The majority of TKAs performed (n=936; 70.3%) were for treatment of an oncologic disease. The most common diagnosis was malignant tumor (68.7%), followed by osteoarthritis (7.3%) and inflammatory arthritis or juvenile idiopathic arthritis (JIA) (7.0%) (Figure 1). Osteonecrosis accounted for 3.9% of cases, while mechanical complications accounted for 3.3%. Fewer than 2% of cases had an indication of either benign or uncertain tumor, infection, or trauma. The mean age was 14.8 years, and 48.4% of the cohort was female. A higher proportion of the non-tumor cohort was female (57.1%) than the tumor cohort (44.7%). 57.1% of patients in the overall cohort were White, and this proportion was smaller in the tumor group (53.8%) than the non-tumor group (64.9%). No patients died during the inpatient event. 87.8% of TKAs were performed in urban teaching hospitals.

Table 1. Characteristics of patients <21 undergoing TKA by diagnosis type

Variable	Overall N = 1331	Non-tumor N = 395	Tumor N = 936
Age, mean (95% CI)	14.8 (14.4, 15.2)	15.9 (14.7, 17.1)	14.3 (14.1, 14.6)
Sex: Female, % (95% CI)	48.4 (44.9, 51.9)	57.1 (49.1, 64.8)	44.7 (41.1, 48.3)
Race, % (95% CI)			
White	57.1 (52.3, 61.8)	64.9 (55.5, 73.3)	53.8 (48.4, 59.2)
Black	13.1 (10.1, 16.9)	16.9 (10.1, 27.2)	11.5 (8.7, 14.9)
Hispanic	19.7 (16.6, 23.3)	14.3 (9.9, 20.2)	22.0 (18.1, 26.6)
Asian or Pacific Islander	3.4 (2.1, 5.4)	**	4.6 (2.9, 7.4)
Native American	0.9 (0.4, 1.9)	**	**
Other	5.8 (4.1, 8.1)	2.9 (1.3, 6.4)	7.0 (4.8, 10.0)
Payor, % (95% CI)			
Medicare	1.4 (0.7, 2.9)	4.7 (2.2, 9.7)	—
Medicaid	31.1 (27.5, 35.0)	28.0 (21.0, 36.3)	32.4 (28.3, 36.7)
Private	57.8 (53.7, 61.7)	60.2 (52.1, 67.8)	56.7 (52.2, 61.1)
Self-pay	3.3 (2.3, 4.9)	**	4.2 (2.7, 6.2)
Other	6.1 (4.4, 8.3)	5.1 (3.0, 8.6)	6.6 (4.5, 9.4)
Admission type: elective, % (95% CI)	85.9 (81.1, 89.6)	81.6 (72.6, 88.2)	87.7 (82.2, 91.6)

N represents weighted estimateCI = Confidence Interval** Per HCUP guidelines, cell sizes ≤10 have been omitted to protect patient confidentiality

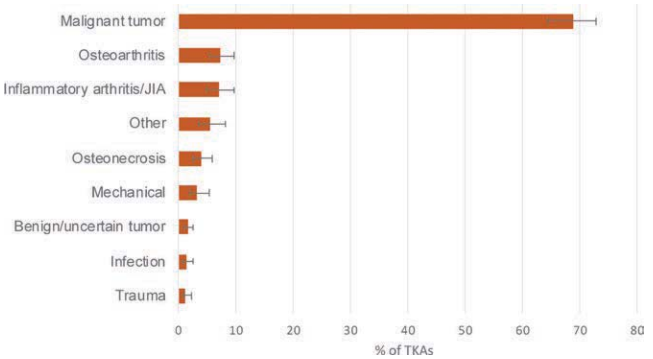

Figure 1. Most common primary diagnoses for TKA in patients <21 years oldThe most common primary diagnosis of 1,331 patients <21 undergoing TKA. Bars represent 95% Confidence Intervals. JIA = juvenile idiopathic arthritis.

Conclusion: TKA is a rarely-performed procedure for patients <21 years old in the US; it is mainly performed in urban teaching centers and has excellent in-hospital survival rates. 70.3% of these procedures are performed for tumors—the vast majority of which are malignant. Also, even with the advent of better treatment options for JIA and inflammatory arthritis, TKA is still performed frequently in this population indicating that better clinical management is needed.

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AB1245 HOSPITAL ADMISSION RATES FOR JUVENILE IDIOPATHIC ARTHRITIS IN WESTERN AUSTRALIA HAVE NOT CHANGED FOLLOWING THE INTRODUCTION OF BIOLOGICAL DRUG THERAPY.

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Background: Aggressive treatment with disease modifying drugs to reach early disease remission has become standard of care for juvenile idiopathic arthritis (JIA) in Australia this millennium (1,2).

Objectives: We examined whether this modern approach including the availability of subsidised TNF inhibitor treatment has led to a change in the rate of first hospitalisation for JIA patients in Western Australia (WA). Hospital data were also used to estimate a minimum prevalence of JIA in WA.

Methods: State-wide hospital data were used to identify patients aged 15 years and younger with a first hospitalisation for JIA between 1990 and 2012. Changes in the hospitalisation rate over time were examined using join-point regression. State-wide PBS prescription data on TNFi (available for JIA since 2004) were obtained from Services Australia and expressed as defined daily dose /1000/day (DDD).

Results: We identified 786 unique cases of JIA in WA hospital records. At the time of the index hospitalisation, patients were on average 7.6 (± 4.4) years of age and female patients made up the majority of cases (n=465, 59.2%). The overall rate for a first hospitalization for JIA was 7.9 (95%CI: 7.3, 8.4) per 100,000 children ≤15 years, and did not change significantly over the study period (annual percentage change (APC): 1.3, 95%CI -0.3, 2.8), although TNFi usage increased linearly and DDD reached 0.3 at the end of study. The hospital-based prevalence of JIA in 2012 reached 114.5/100.000 for girls (0.12%) and 52.9/100.000 for boys (0.05%).

Conclusion: The hospital based (i.e. minimum) prevalence of JIA in WA aligns with international data. Rates for a first hospitalization for JIA have not decreased during a time when early aggressive therapy became common practice and TNFi use for JIA reached 30/100.000. This unexpected finding requires further investigation.

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AB1246 ANALYSIS OF 38 CYTOKINES PROFILE IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: systemic lupus erythematosus (SLE) as "the disease of thousand faces" has multiple pathogenic mechanisms with disturbance in different parts of immune system. A variety of cytokines have been found as a biomarker of active disease and a candidate for targeting treatment [1].

Objectives: to analyze 38 cytokines profile in juvenile SLE (jSLE) and compare them with disease activity and clinical manifestations.

Methods: 29 patients with SLE under 18 years (3 boys, 26 girls, median age – 16.0 (13.0; 16.9) and 28 health control patients (14 boys, 14 girls, median age 16.0 (11.0; 17.0) were included in the study. Cytokine levels in the serum were measured by multiplex analysis using the MILLIPLEX MAP Human Cytokine/Chemokine/Growth Factor Panel A 41 plex kit (MilliporeSigma, USA) on the Luminex MAGPIX System (Luminex, USA).

Results: significant differences between jSLE patients and health control have observed in 10 cytokines (Table 1). Interestingly upregulation in jSLE compared to HC was found only in IP10 and IL1RA, while other cytokines were lower. MCP1 was associated with disease activity measured by SLEDAI (p=0.0073), while activity measured by ECLAM correlated with TGFa (p=0.049), MCP3 (p=0.025), IL-15 (0.038), IL-7 (p=0.002), IL-8 (0.043), MCP1 (p=0.014), MIP1b (p=0.014). Positive correlation was found between skin involvement and IL-6 (p=0.43), carditis and FLT-3L (p=0.018), IL1RA (p=0.03), IL-8 (p=0.019), TNFa (p=0.05), lung involvement and FLT3-3L (p=0.014), IL-15 (p=0.047), IL1RA (p=0.034), IL-5 (p=0.005), TNFa (p=0.004), myositis and TGFa (p=0.011), MCP3 (p=0.000), IL-13 (p=0.000), IL1a (p=0.000), IL-9 (p=0.000), IL1b (p=0.03), IL-4 (p=0.000) TNFb (p=0.000), anti-dsDNA levels and MDC (p=0.016), anemia and GRO (p=0.030), IL-1b (p=0.050), IL-3 (p=0.022). There's no correlation between nephritis, CNS involvement and cytokines levels.

Table 1.

Cytokines	jSLE (n=29)	HC (n=28)	p-value
EGF	28.4 (15.3-133.3)	122.0 (25.8-218.5)	0.032
TGFa	1.4 (0.0-2.6)	4.6 (3.2-7.7)	0.00001
IL-10	3.8 (2.8-8.7)	2.4 (2.0-3.6)	0.034
MDC	461.3 (297.8-663.3)	1042.5 (808.9-1277.5)	0.00000
sCD40L	945.6 (126.5-1322.0)	1991.5 (1275.0-2395.0)	0.00003
IL1RA	21.9 (12.3-38.7)	12.3 (8.6-19.4)	0.013
IL1b	0.9 (0.6-1.2)	1.0 (0.9-1.9)	0.010
IL4	17.3 (11.1-32.2)	35.2 (19.6-87.8)	0.003
IL5	1.0 (0.8-1.4)	1.6 (1.0-3.0)	0.038
IL8	9.1 (7.4-21.3)	30.1 (11.5-46.5)	0.010
IP10	310.9 (215.6-472.1)	118.0 (89.3-143.7)	0.000009

Conclusion: we identified differences in cytokines levels between jSLE patients and HC and found multiple correlation between manifestations and different cytokines levels. Most of them were in FLT-3L, MIP-1b, TNFa, IL1RA, IL-3, IL-5, IL-8, IL-15, MCP1 and MCP3.

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AB1247 **ASSESSMENT OF ARTICULAR AND EXTRA-ARTICULAR DAMAGE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS**

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Background: Juvenile idiopathic arthritis (JIA) affects patients' well-being and can lead to disability and long-term damage. Evaluating damage in patients can be beneficial to make therapeutic decisions and take rehabilitation measures.
Objectives: To assess articular and extra articular damage in patients with JIA by the use of the Juvenile Arthritis Damage Index (JADI)[1] and to identify variables that correlate with disease damage.
Methods: We conducted a cross-sectional study among patients with JIA who met the ILAR classification criteria and had a disease duration more than 12 months. Early clinical data was obtained from medical files. It included socio-demographic features, biological and radiological parameters, subtype of JIA, disease duration and ongoing treatments. Damage was assessed in the last clinical visit using articular and extra-articular damage index[1] (JADI-A and JADI-E).
Results: Thirty-two patients were enrolled in this study with a mean age of 23.8 ±11.6 years. Sex ratio was 0.6 (12 males and 20 females). The mean age of disease onset was 8.3 years [3-15], and the mean disease duration was 183.7 months [12-624]. At the last clinical examination, 71.9% of patients had joint damage with a mean JADI-A score of 5.09 ±5.4 and 40.6% of patients had extra-articular damage with a mean JADI-E score of 0.75±1.2. The most affected joints were: the elbows (43.8%), the hips (37.5%) and the wrists (25%). Extra articular damage was mainly: a growth failure (25%), osteoporosis (18.8%) and ocular damage (12.5%). Patients with polyarticular arthritis without rheumatoid factor had the highest JADI-A score with a mean of 7.83 while patients with systemic arthritis had the highest JADI-E score with a mean of 3. Mean JADI-A score was significantly different between patients who received corticosteroids and those who did not receive them (8.5 Versus 3.4, p=0.004). Damage scores correlated with disease duration (p<0.001 for JADI-A score and p=0.034 for JADI-E score). Damage scores were not significantly different between different classes of treatment (conventional dmards and biologic dmards).
Conclusion: Articular damage is frequent in patients with JIA. It is higher for patients on corticosteroids. Articular and extra articular damage correlate with disease duration, but they were not significantly different between classes of treatment.
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AB1248 **CONTRIBUTION OF IMAGING IN THE DIAGNOSIS OF ATRAUMATIC HIP**

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Background: Joint pain of the hip in children and adolescents is one of the most frequent symptoms seen by pediatricians, orthopedists, and pediatric rheumatologists, with an annual incidence of 148.1/100 000 [1]. The identification of an etiology for atraumatic hip pain is challenging. Even though imaging findings are often various and nonspecific, they are necessary for an accurate diagnosis.
Objectives: The main goal of this study is to investigate the contribution of the different imaging techniques in the diagnosis of the hip main in children.
Methods: We conducted a retrospective study including children and adolescents with atraumatic hip pain recruited from the Kassab institute of orthopedics. Transcribed data included age, sex, and the etiology of the hip disease. We also recorded different imaging techniques performed for the diagnosis: plain radiography, ultrasound (US), Computed tomography (CT) as well as magnetic resonance imaging (MRI).
Results: The study included 81 patients. There was a male predominance (59.3% boys versus 40.7% girls) with a sex ratio of 1.45. The mean age at diagnosis was 9.9 years [1-16]. The mean disease duration was eight months [0.1-156]. Hip disorders were distributed as follows: Legg-Calvé-Perthes disease (n=3), epiphysiolysis of the femoral head (n=30), transient synovitis of the hip (n=7), septic hip (n=10), tumor (n=4), hip dislocation (n=8), hip dysplasia (n=4), juvenile idiopathic arthritis with coxitis (n=15). The hip X-ray was abnormal in 75.6% of cases. The hip US was performed in 34.2% of the patients and showed abnormalities in most of the cases (88.5%). US findings were as follows: joint effusion (n=26), synovial thickening (n=18), synovitis (n=12), and a positive power Doppler signal (n=7). Seven patients underwent pelvic CT scans. The main findings were joint effusion (n=2), synovial thickening (n=1), and hip dysplasia (n=4). MRI of the hip was carried out in 23 children and was contributive in 91.3% of the cases. The main findings were as follows: joint effusion (n=12), synovitis (n=10), bone marrow edema (n=8), synovial thickening (n=7), nidus (n=3) and tumoral process (n=1).
Conclusion: Our study showed that hip X-ray and US are the first-line imaging modalities in an atraumatic hip diagnosis. However, in other cases, further investigations may be needed to make an early diagnosis and avoid adverse sequelae.
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Disclosure of Interests: None declared
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AB1249 **IMPACT OF OVERWEIGHT AND OBESITY ON HIP INVOLVEMENT IN JUVENILE IDIOPATHIC ARTHRITIS**

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Background: The prevalence of obesity among children is on the rise, becoming a worldwide epidemic. The overweight is also associated with mechanical stress in the weight-bearing joint especially in the hip joint. Previous studies showed that increased Body mass index was a predicting factor of a poor outcomes [1].
Objectives: In this regard, we proposed to evaluate the effect of obesity on hip involvement in JIA patients.
Methods: We conducted a cross-sectional study including children with JIA according to the International League of Associations for Rheumatology (ILAR)). Transcribed data included age, sex and the characteristics of the disease (subtype of JIA, disease duration). Data on hip involvement was also collected. Weight and height of each patient was recorded. The body mass index (BMI) was calculated (Kg/m^2). We compared these parameters between two groups: G1: presence of coxitis and G2: absence of coxitis.
Results: The study included 62 patients with a male perdominance: sex ratio was 2.3. The mean age of onset of the disease was 11.4 years [3-16].The frequency of each JIA subset was at follows: polyarticular with rheumatoid factor (n=2), polyarticular without rheumatoid factor (n=4), systemic (n= 1), enthesitis-related arthritis (n=44), oligoarthritis (n=8), psoriatic arthritis (n=3). Hip involvement was reported in 71 % of cases and was bilateral in 81% of patients. The mean weight (Kg) and height (meter) was similar between the two groups (57.4 in G1 vs 53.6 in G2, p=0.486) and (1.61 in G1 vs 1.58 in G2, p=0.483) respectively. The prevalence of overweight patients was higher in G1 than G2 without reaching a statistically significant correlation (23% vs 12.5%, p=0.518). Similarly, there was no statistically significant correlation between the body mass index (Kg/m^2) and coxitis (22.2 vs 21, p=0.45). Moreover, a higher BMI was not associated with a limited range of motion as well as hip replacement (p=0.7, p=0.1 respectively).
Conclusion: Our study showed that BMI did not impact hip involvement in juvenile idiopathic arthritis patients. As obesity confers an additional health risk, addressing this co-morbidity should be a health priority in these patients.
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AB1250 **TOFACITINIB IS A SAFE AND EFFECTIVE TREATMENT OPTION FOR JUVENILE IDIOPATHIC ARTHRITIS**

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Background: The management of juvenile idiopathic arthritis(JIA) is often constrained by the limited number of oral drugs available. Whether JAK inhibitors would add a much needed therapeutic armamentarium in this regard needs to be explored.
Objectives: To assess the safety and efficacy of tofacitinib in juvenile idiopathic arthritis (JIA) patient who were prescribed during the period January 2021 to December 2021.
Methods: It's a retrospective study of JIA patients who were prescribed tofacitinib during the period Jan 21 to Dec 21 with minimum of 3 months' follow-up after prescribing tofacitinib. The demographics,details of medications,investigations parameters and any adverse events were noted.

Results: There were a total of 35 patients who were given tofacitinib during this period. Male is to female ratio is 25:10, mean age of 12.91(4.81) yrs., the mean disease duration was 58.6 months. Enthesitis related arthritis(ERA) was the commonest seen in 12, followed by oligo articular in 10, polyarticular in 7 and systemic onset in 6. In the ERA group 10 were HLA B27 +VE, of the oligo articular 6 were ANA +VE, in the polyarticular one was RF +ve. Out of the 35,14 were already on biologicals (tocilizumab and anti TNFs). Tofacitinib was stopped in 8 patients during this period, 5 as they achieved remission, 2 with no response and one because of itching and abdominal pain. There were no documented infections. There was significant reduction in the inflammatory markers (ESR, CRP), leucocyte count and platelet count.

	Before tofa	After tofa	p value
Methotrexate in mg (week) mean(stdev)	9.64(1.94)	8.88(3.34)	0.66
Steroid in mg mean (stdev)	3(2.35)	2.8(1.8)	0.91
Leucocyte count mean(stdev)	11242(1858)	7884(1471)	0.005
Platelet count in lakhs Mean(stdev)	4.51(0.48)	3.37(0.82)	0.017
ESR mm/1hr	57.75(17.25)	30.83(11.48)	0.009
CRP mg/L	25.36(10.9)	12.36(7.97)	0.05

Conclusion: Tofacitinib seems to be a promising drug in the management of JIA with good safety profile and efficacy.

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AB1251 LATE ONSET PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN AN INDIAN ADOLESCENT BOY DURING A PEAK OF POST COVID-19 MULTISYSTEM INFLAMMATORY SYNDROME

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Background: Familial Hemophagocytic lymphohistiocytosis (fHLH) categorized as FHL2 (*PRF1)*, FHL3 (*UNC13D)*, FHL4 (*STX11)*, and **FHL5 (*STXBP2)*** encoding for Perforin, Munc13-4, Syntaxin11, and Syntaxin binding protein 2, respectively. There is limited information available about the clinical and mutational spectrum of FHL patients in Indian population.

Objectives: To delineate clinical and laboratory features of late onset familial Hemophagocytic Lymphohistiocytosis.

Methods: A **12-years**-old well nourished sick looking boy, born to a non-consanguineous parents with normal birth, development and immunization history with uneventful past presented to us with 6 days history of high fever, cough, breathing difficulty and severe headache. He had occasional vomiting, abdominal pain, polyarthragia & chest pain from last 10 days. Mother also had given history of throat pain, backache & some non-specific papular rashes over face before the onset of fever. His vitals were normal. Examination revealed faint diffuse fixed erythematous rash all over the body, pallor, icterus and hepatosplenomegaly. Musculoskeletal examination was unremarkable. Lab evaluation revealed HB 8.9gm%, TLC 4700/cumm with neutrophils 40% and lymphocytes 56% with 8-9% activated lympocytes. Further evaluation showed low ESR 6mm/hr, fibrinogen 97mg% and albumin 2.2 gm% with elevated CRP 40mg/L, ferritin 2000ng/ml, LDH 658IU/L, SGPT 110IU/L, SGOT 221 IU/L, total bilirubin 6mg%, D-dimer 4355 ng:EFU/ml and Triglycerides 441mg%. His blood, urine, CSF and bone marrow cultures were sterile for endemic bacterial and viral infections in our area. **His EBV PCR, CoVID RT PCR and CoVID antibody (Total & IgG) test were negative**. His immunoglobulin leves were normal. HRCT Chest showed bilateral mild-moderate plural effusions, mild interstitial thickening in both the lower lobes, few fibrotic opacities & old areas of consolidation bilaterally. 2D echo showed mild pericardial effusion. Bone marrow examination showed Hypercellular marrow with iron depletion and occasional hemophagocytosis with CD8 T lymphocytes proliferation (55.2%) and double positive CD4 & CD8 (1.2%). He was initially commenced on supportive therapy, oxygen & intravenous antibiotics. In view of most probable non-infectious, non-malignant hemophagocytic lymphohistiocytosis, he was finally given intravenous immunoglobulin (2gm/kg) and intravenous pulse methylprednisolone (30mg/kg). He responded well to above regimen within 3 days. He was discharged with tapering steroids over few weeks. Clinical exome by NGS revealed Homozygous Mutation in **STXBP2 gene** Intron 14, c.1280-1G>C (3' Splice Site) His parents has been counselled for hematopoietic stem cell transplantation and their decision is still pending.

Results: We compared our patietnt with a reference to the largest Indian series of pediatric HLH[1].

Table 1.

	Snehal Shabrish et al*	Index Patient
Age > 4 years	56%	Yes
Male Sex	89%	Yes
Family History	20%	No
Consanguinity	57%	No
Fever	100%	Yes
Organomegaly	100%	Yes
Bicytopenia	78%	Yes
Hyperferritinemia	86%	Yes
Hemophagocytosis	100%	Yes
Hypertriglyceridemia	100%	Yes
Hypofibrinogenemia	40%	Yes
Splice Site Intronic Mutation	38%	Yes
Expired during presentation	55%	No
Remission under protocol and awaiting transplantation	22%	Yes

Conclusion: Primary HLH type 5 can present first time during childhood and adolescence. Any child presenting with unexplained HLH features should undergo genetic analysis irrespective of person's past and family history.

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AB1252 RETROSPECTIVE SINGLE CENTER STUDY OF THE PREDICTIVE ROLE OF CERTAIN BIOMARKERS IN MACROPHAGE ACTIVATION SYNDROME RELATED TO SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Systemic juvenile idiopathic arthritis (sJIA) is a childhood arthritis with signs of autoinflammation and high risk of macrophage activation syndrome (MAS). Immunopathogenesis of sJIA is based on excessive activation of innate immunity, which is characterized by hyperproduction of pro-inflammatory cytokines - interleukin (IL)-1 and IL-18, which play a key role in induction of synthesis of other pro-inflammatory mediators. Macrophage activation mediates the evidence of hyperferritinemia, which stimulates a pathological immune response with the development of MAS. In clinical practice, the study of the cytokine profile and its comparison with the acute-phase inflammatory response markers in patients (pts) with sJIA can make possible assessment the nature of the course process and predict the possibility of MAS.

Objectives: To study distinctive features of some biomarkers in pts with sJA in relation with history of MAS.

Methods: Total IL-18, IP-10, IL1RA, IL1b, IL6, CRP and ferritin levels were determined in pts with sJIA and compared between between groups regarding to disease activity and history of MAS. Serum levels of cytokines, ferritin were measured using standard commercial enzyme-linked immuno-sorbent assay. CRP were estimated by commercial nephelometric method.

Results: A total of 39 pts were included to study, the ratio of boys and girls was 1:1.4. Median age of sJIA onset was 4.4 years [2.9; 6.5], age at the time of examination - 11.4 years [7.35; 13.5]. The pts were divided into 3 groups: group I - with MAS (8 pts), group II - with active sJIA without MAS (16 pts), group III - with inactive sJIA (15 pts). Total IL-18 levels were significantly higher in pts with MAS (group I) (median 6036.5 pg/ml [IQR 1932.5; 9160.3], and remained persistently elevated even in the majority of pts with inactive disease (group III) (median 1625.25 pg/ml [IQR 634.1; 2451.6]. CRP was higher in group I (CRP: median 60.6 mg/l [IQR 41.2; 109.4]), than in group II (CRP: median 15.65 mg/l; IQR 10.4; 38.4), without a statistically significant difference (p=0.5), but the level of ferritin was significantly higher in group I (median 893.25 ng/ml [IQR 253.9; 7725.25]), than in group II (median 62.1 ng/ml [IQR 19.8; 211.8], p=0.009). Generally, we observed positive correlation between CRP and ferritine (r=0.629, p<0.05), CRP and IL-18 (r=0.352, p<0.05), CRP and IL1RA (r=0.693, p<0.05); between ferritin and IL-18 (r=0.566, p<0.05), between ferritin and IL1RA (r=0.545, p<0.05). The strongest correlation was for ferritin and overall for groups I and II. We didn't observe significantly difference between IP-10, IL1b, IL6 between groups.

Conclusion: Serum levels of IL-18 were elevated in the majority of pts with sJIA regardless of activity, but were significantly higher in pts with active disease and, especially, in pts with MAS. Increased level of IL-18 may reflect increased disease activity or

development of MAS, that confirms the key role of IL-18 in sJIA and MAS. According to our data, in clinical practice the measure of serum level of ferritin more useful for early detecting MAS in pts with sJIA due to more stronger correlation between the levels of proinflammatory cytokines and ferritin, than between proinflammatory cytokines and CRP. We were unable to identify a statistically significant difference in the level of IL1RA in active sJIA and MAS, despite a significant correlation between the level of CRP and IL1RA, ferritin and IL1RA, which may be associated with small number of pts.

Disclosure of Interests: None declared

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AB1253 DISEASE PERCEPTION ASSESSMENT IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS AND THEIR PARENTS.

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Background: Juvenile Idiopathic Arthritis (JIA) has an impact on the quality of life of the patient and his family. Parent/patient reported outcomes have shown an increasing interest in the management of JIA because it reflects the perception of the disease course and the effectiveness of the therapeutic interventions.

Objectives: To determine the level of agreement between patients with JIA and their parents for the five quantitative items in Juvenile Arthritis Multidimensional Assessment Report (JAMAR) questionnaire.

Methods: We included children aged between 7 and 18 years old with AJI (ILAR criteria) and their parents. Demographic data and disease related parameters were collected. We asked both parent and child to complete the five quantitative items of JAMAR questionnaire. Were measured on a 21-numbered circle visual analogue scale (VAS) for pain (0 =no pain; 10 =very severe pain), disease activity (DA): (0 =no activity; 10 =maximum activity) and well-being (WB): (0 =very well; 10 =very poorly). Physical function was assessed by Juvenile Arthritis Functional Score (JAFS) [0-45] and health-related quality of life (HRQoL) [0-30] through the Physical Health (PhH) and Psychosocial Health (PsH) subscales. We calculated children and parents median scores for the five items. Intra class correlation coefficient ICC was used for analysis (ICC below 0.50: poor; between 0.50 and 0.75: moderate; between 0.75 and 0.90: good; above 0.90: excellent).

Results: A total of 21 patients/parent (12 girls and 9 boys) were included in the study. Forty percent belong to rural enviroment. Majority of patients were in secondary school (77%), 23% were in primary school. Seven patients had oligoarticular JIA, 13 had polyarticular JIA and one had systemic JIA. Median age at diagnosis was 11.4 ± 1.2 years [6-13]. Median age at disease onset was 9.5 ± 1.9 years [2-13]. Median disease duration was 4.3 years [0-7]. Median JADAS was 10 [8-18]. Uveitis was noted in 30% of cases. Comparison of parent proxy-reported and child self-reported data revealed a striking similarity for all items ($p<0.001$). The results of the five quantitative items of JAMAR questionnaire are represented in Table1. Good correlation was noted in JAFS, DA VAS, well-being VAS and HRQoL. Excellent correlation was noted in VAS pain.

Table 1. Assessement of quantitative items of Juvenile Arthritis Multidimensional Assessment Report by patients and parents.

Items	Patients	Parents	ICC
Mean pain VAS (0-10)	4.2 [4-6]	4.3[4-6]	0.97
Mean disease activity VAS (0-10)	4.1 [4-5]	4.2 [4-5]	0.81
Mean well-being VAS (0-10)	4.4 [4-6]	4.3 [4-5]	0.9
Mean Juvenile Arthritis Functional Score (JAFS)	10.0 [1-20]	10.2 [2-21]	0.81
Mean HRQoL score	14.1 [7-17]	14.8 [6-14]	0.88

ICC: Intraclass Correlation Coefficient; HRQoL: Health-Related Quality of Life; VAS: Visual Analogue Scale.

Conclusion: Our study showed high level of agreement between patients and parents. The JAMAR provides a promising approach to quantitative measurement in standard pediatric rheumatology care. Availability of this new instrument may enhance regular use of parent/patient questionnaires in routine practice and improve disease management.

Disclosure of Interests: None declared

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AB1254 CHALLENGES FACED BY FAMILIES OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common inflammatory rheumatism of childhood. Diagnostic and therapeutic approaches are difficult for families to sustain with significant psychological and social effect.

Objectives: The aim of this study is to understand the different challenges faced by families with children suffering from JIA.

Methods: Parents of children with JIA (according to the International League of Associations for Rheumatology (ILAR)) followed in rheumatology department were asked to complete a survey in order to screen the impact of their children's disease on their family life. Open-ended questions and directed questions were included. General demographic and clinical information (family history of chronic inflammatory disease, child's current age, diagnosis and type of JIA and, duration of disease progression) were also collected.

Results: The study included 24 children with a gender-ratio of 1. The mean age was 12.4 years old [4-16]. The mean duration disease was 4 years with extremes varying from 3 months to 13 years. The frequency of each JIA subset was at follows: polyarticular with rheumatoid factor (n= 2), polyarticular without rheumatoid factor (n=5), psoriatic arthritis (n= 1), enthesitis-related arthritis (n=10) and oligoarthritis (n= 6). Twenty-four parents completed the survey. The mother was the one who answered the questions in 83% of the cases. Other family members with a chronic rheumatic disease were reported in 40% of the families. Parents noted negative impact on their work in 50% of cases (40% missing time from work, 10% changing work schedule) and, significant parental stress, anxiety, and fatigue in 75% of the cases. In 33% of the cases, parents had difficulty getting the required medical care and attention for their child's illness because of financial issues and 37.5% of them were feeling anxiety regarding diagnosis uncertainty. Parents reported worry about their child's daily functioning and future in 75% of the cases. They noted psychological impact on the child itself in 58% of the cases and child missing school in 41% of the cases. The most common resources parents used for information were health care professionals in 54.2 % of the cases and 45.8% of them got additional information from online research.

Conclusion: Parents of children with JIA share common challenges due to their child's illness including a substantial impact on their work and personal wellness in addition to the psychosocial impact of the disease on the child. Support groups or educational sessions may be needed to provide guidance for these families to cope with disease.

Disclosure of Interests: None declared

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AB1255 ASSESSMENT OF SLEEP DISTURBANCES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Sleep problems are common among children with chronic illnesses such as Juvenile Idiopathic Arthritis (JIA), which is one of the most common rheumatic diseases in childhood. Sleep disturbances collectively refer to impairments in the ability to initiate or maintain sleep. They can be measured by parent or child self-report and by objective measures such as actigraphy and polysomnography.

Objectives: The aim of this study was to assess sleep disorders in children with JIA.

Methods: Parents of children suffering from JIA (according to the International League of Associations for Rheumatology (ILAR)), followed in rheumatology department were asked to complete a specific specialized scale for children (HIBOU) [1] to screen sleep disorders. This scale assesses five aspects of sleep: irregular schedule and daytime drowsiness, insomnia, moves in sleep, nose obstruction and ultra-vigilance. Parents were asked to answer 8 questions rated from 1 to 3 according to the frequency of the problem, 1: rarely, 2: 3 to 4 times a week and 3 if 5 to 7 times a week. If the sum is ≤ 9, only sleep hygiene is recommended. If the sum is between 10 and 15 the child requires regular supervision. If the sum is between 16 and 24, the child needs to be referred to a specialist. General demographic and clinical information (family history of chronic inflammatory disease, child's current age, diagnosis and type of JIA, duration of disease progression and activity of the disease) were also collected.

Results: Twenty-four children with a mean age of 12 years [4-16] were included in the study. The gender ratio was 1. The mean duration of the disease was 4 years with extremes from three months to thirteen years. The frequency of each JIA subset was as follows: polyarticular with rheumatoid factor (n= 2), polyarticular without rheumatoid factor (n=5), psoriatic arthritis (n= 1), enthesitis-related arthritis (n=10) and oligoarthritis (n= 6). Irregular sleep schedule and daytime drowsiness were reported at least 3 times a week by 58.3% of the children. Insomnia and inability to initiate sleep were reported in 29.3% of the children at least 3 times a week. Parents reported exaggerated moves during sleep in 50% of the cases and airway obstruction or snoring in 58.3% more than 3 times a week. Difficulties to maintain a good night of sleep more than three times a week were reported in 25% of cases. To sum up, 29.2% of the children had a score above 15 and needed to be referred to a specialist and 58.3% of them need a regular supervision of their sleep and may need to be referred to a specialist. Only three children had a score under 9 and don't have concerning sleep disorders according to this scale.

Conclusion: This study showed that sleep disorders are a common challenge in children and adolescents with JIA which could have a huge impact on their physical and psychosocial health-related quality of life. This study highlights the need for assessment of sleep disorders in JIA patients.

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AB1256 TRANSITIONAL CARE IN JUVENILE IDIOPATHIC ARTHRITIS: TIMING, PREVALENCE OF SUBTYPES AND TREATMENT PROFILE IN A SPANISH TERTIARY HOSPITAL.

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Background: Juvenile Idiopathic Arthritis (JIA) is the leading cause of chronic inflammatory rheumatic disease in children. It's classified into subtypes with different relative prevalences depending on geographical area (Oligarticular subtype predominates in Western Europe/North America. Enthesitis-related arthritis subtype predominates in Eastern Europe/Asia). To ensure continuity of care in adult rheumatology services, a systematic transition process is recommended. Various authors recommend that the process, of which pediatric and adult rheumatology teams should be part, begins around 14 years and ends around 18 years of age.
Objectives: We aim to study the age, relative prevalence and treatment profile in JIA subtypes at the beginning of the transitional care.
Methods: Descriptive and cross-sectional study of patients with JIA (according to ILAR criteria), diagnosed and treated in the pediatric rheumatology service and seen in the transitional care unit of the adult rheumatology service within the same tertiary hospital between January 2013 and December 2018. Demographic, clinical, analytical and treatment data were collected at the first visit to the transitional care unit.
Results: 72 patients were included (46 women) mean age at diagnosis of 9.5 ± 4.6y and mean of 11.3 ± 4.36y from diagnosis to the first visit at the transitional care unit. 27.7% were diagnosed with oligoarticular JIA, 20.8% with arthritis-enthesitis JIA, 19.4% with Rheumatoid Factor negative (RF-) polyarticular JIA, 11.1% with systemic JIA, x9.7% with undifferentiated JIA, 5.5% with Rheumatoid Factor positive (RF+) polyarticular JIA and 5.5% of psoriatic arthritis. The mean age at the first visit to the transitional care unit was 20.81 ± 2.96y (no differences between subtypes). Oral ulcers (20.8%), anterior uveitis (13.8%) and enthesitis (13.8%) were the most frequent extra-articular manifestations. 56.9% had antinuclear antibodies (ANA) titers >1/160 at some point in course of disease (Table 1). 43% were treated with methotrexate, 38% with biological therapies, 11.% with glucocorticoids (GC) and 22.% had no treatment.
Conclusion: The oligoarticular form was the most prevalent subtype of JIA, similar to previously published series from Western Europe. The first visit at the transition care unit occurred significantly later than recommended by various authors. The most frequent treatment was methotrexate. The use of biological therapies was high, with TNF alpha inhibitors being the most widely used, especially etanercept. The use of glucocorticoids was low. A non-negligible number of patients were treatment free.
Disclosure of Interests: None declared
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AB1257 INVESTIGATING THE ASSOCIATIONS BETWEEN THE MAXIMAL RESPIRATORY PRESSURES AND CARDIORESPIRATORY FITNESS PARAMETERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The most prominent symptom of juvenile idiopathic arthritis (JIA) is joint involvement; however, the effect of the disease is not limited to the joints. Evidence suggests that cardiopulmonary fitness is affected in children with JIA compared to their healthy peers [1].
Objectives: This study aimed to investigate the associations between the maximal respiratory pressures and cardiorespiratory fitness parameters.
Methods: Seventeen children with JIA (mean age: 15.4±2.2 years, 11 male) who have been using biological agents for at least three months were included in the study. Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were evaluated with a portable device (Cosmed Pony FX Desktop Spirometer, USA). The Quark Cardiopulmonary Exercise Test Treadmill System (COSMED, Rome, Italy) was employed to analyze cardiorespiratory fitness parameters by using expired gas collection and analysis.
Results: Significant moderate correlations were detected between MIP and maximum oxygen consumption ($VO_{2max)}$ values (r=0.519, p=0.033) and MEP and VO_{2max} values (r=0.507, p=0.038), (Table 1). No other significant correlations were observed between maximal respiratory pressures and other parameters.

Table 1. The associations between maximal respiratory pressures and cardiorespiratory fitness parameters

n:17	MIP (cmH_2O) (r)	*p*	MEP (cmH_2O) (r)	*P*
VO_{2max}(ml/kg/min)	0.519	**0.033***	0.507	**0.038***
METs (ml/kg/min)	0.276	0.283	0.298	0.246
HR (bpm)	0.285	0.268	0.184	0.479
VO2/HR	0.456	0.066	0.479	0.052
$PETCO_{2max}$ (mmHg)	0.416	0.097	0.358	0.158
$PETO_{2max}$ (mmHg)	-0.284	0.269	-0.158	0.544

***:** $p<0.05$, Pearson Correlation Coefficients**,** **VO_{2max}**: Maximum oxygen consumption, **ml:** milliliters**,** **kg**: kilograms, min: minute, **METs:** Metabolic equivalent **HR:** Heart rate, **bpm:** beats per minute, **VO_2/HR:** Oxygen consumption/heart rate, **$PETCO_2$**: Tidal partial pressure for carbon dioxide, **$PETO_2$**: Tidal partial pressure for oxygen.

Conclusion: The results of the study suggest that maximal respiratory pressures are associated with maximal oxygen consumption. Evaluating maximal respiratory pressures might be helpful when prescribing exercise programs for JIA patients with diminished cardiorespiratory fitness.
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Table 1.

JIA subtypes	Gender	Age at diagnosis	Age at first visit transicion care unit	ANA positivity	TNF alfa inhibitors	Tocilizumab	Abatacept	Methotrexate	Leflunomide	GC	NSADs	No treatment
n (%)	*(% woman)*	*Mean (SD)*	*Mean (SD)*									
Oligoarticular (n=20)	77%	7,35 (4,88)	20,55 (2,91)	85%	Etanercept: 3 (15%) Adalimumab: 2 (10%)	1 (5%)	0	11 (55%)	1 (5%)	3 (15%)	5 (25%)	5 (25%)
Arthritis/ Enthesitis (n=15)	27%	10,07 (4,3)	19,67 (2,38)	33,33%	Etanercept: 4 (26,66%) Adalimumab: 1 (6,66%)	0	0	6 (40%)	1 (6,67%)	0	5 (33.33%)	2 (13,33%)
RF- Polyarticular (n=14)	77%	10,64 (4,99)	22,14 (2,48)	57,14%	Etanercept: 2 (14,28%) Adalimumab: 2 (14,28%) Infliximab: 1 (7,14%)	1 (7,14%)	0	7 (50%)	0	1 (7,14%)	7 (50%)	2 (14,28%)
Systemic (n=8)	56%	9,12 (4,88)	20,75 (3,58)	12,5%	Etanercept: 1 (12,5%) Adalimumab: 1 (12,5%) Infliximab: 1 (12,5%)	1 (12,5%)	0	2 (25%)	0	2 (25%)	0	3 (37,5%)
Undifferenciated (n=7)	61%	11 (2,24)	19,57 (3,46)	57,14%	Etanercept: 1 (14,29%)	0	0	1 (14,29%)	0	1 (14,29%)	2 (28,57%)	3 (20%)
RF+ Polyarticular (n=4)	100%	14,5 (1,29)	22,5 (4,04)	75%	0	1 (25%)	1 (25%)	3 (75%)	0	0	2 (50%)	1 (25%)
Psoriatic Arthritis (n=4)	50%	7,5 (σ: 3,7)	22,25 (σ: 2,2)	75%	Etanercept: 1 (25%) Golimumab: 1 (25%)	2 (50%)	0	1 (25%)	0	0	0	0

AB1258

THE PREDICTED VERSUS MEASURED RESPIRATORY PRESSURES, PULMONARY FUNCTIONS, CARDIOPULMONARY FITNESS PARAMETERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Although musculoskeletal system-related symptoms are the most common problems in children with Juvenile Idiopathic Arthritis (JIA), cardiac and pulmonary manifestations are observed in more than half of these children. However, the available research on the extent of cardiorespiratory involvement is very limited [1].

Objectives: The aim of this study was to compare the predicted respiratory pressures, pulmonary functions, cardiopulmonary exercise test (CPET) values to objectively measured ones in children with JIA.

Methods: Twenty-two children with JIA (mean age: 15.5±2.3, 14 male) who were under biological agents for at least three months were included in the study. Maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP), and pulmonary functions were measured by using a portable automated testing device (Cosmed Pony FX Desktop Spirometer, USA). Cardiorespiratory fitness parameters were measured with the Quark CPET Treadmill System (COSMED, Rome, Italy). The values calculated by the softwares of the Cosmed Pony FX Desktop Spirometer and Quark CPET Treadmill System according to the healthy children's normative data were used as predictive values.

Results: Within-group analyses demonstrated statistically significant differences between all measured and predicted parameters ($p<0.05$), (Table 1), except for MIP and forced vital capacity/forced expiratory volume values.

Table 1. The comparison of predicted versus measured respiratory pressures, pulmonary functions, cardiopulmonary fitness parameters

	Measured	Predicted	*p*
	(Mean±SD)	(Mean±SD)	
FVC (l)	3.82±0.92	4.20±1.04	**<0.001***
FEV_1 (l)	3.31±0.80	3.59±0.86	**0.004***
FEV_1/FVC (%)	86.13±7.74	83.91±0.41	0.179
MIP (cmH_2O)	101.90±37.45	104.31±21.92	0.686
MEP (cmH_2O)	95.13±47.84	134.36±30.22	**<0.001***
VO_{2max} (ml/kg/min)	2109.83±732.95	3159.94±745.87	**<0.001***
METs (ml/kg/min)	9.71±2.180	14.88±2.39	**<0.001***
HR (bpm)	187.88±20.28	205.0±2.37	**0.02***
VO_2/HR (ratio)	11.20	15.42±3.75	**<0.001***

***:** $p<0.05$, Student's t-test, **FVC:** Forced vital capacity, **FEV_1**: Forced expiratory volume, **FEV_1/FVC:** Forced expiration volume/forced vital capacity, **VO_{2max}**: Maximum oxygen consumption, **ml:** milliliters, **kg**: kilograms, **min:** minute, **METs:** Metabolic equivalent **HR:** Heart rate, **bpm:** beats per minute, **VO_2/HR:** Oxygen consumption/heart rate.

Conclusion: The present study's findings indicate that the respiratory pressures, pulmonary functions, and cardiopulmonary fitness parameters of the children with JIA are diminished compared to predicted values.

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AB1259

THE NEUTROPHIL-TO-LYMPHOCYTE AND THE PLATELET-TO-LYMPHOCYTE RATIOS AS INFLAMMATORY MARKERS IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: The neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) have recently emerged as potential indicators of systemic inflammation in chronic rheumatic diseases such as polymyalgia rheumatica, rheumatoid arthritis, and spondyloarthritis.

Objectives: To investigate the value of NLR and PLR as inflammatory markers in juvenile idiopathic arthritis (JIA) and to explore possible associations with disease activity parameters.

Methods: We enrolled 29 patients with JIA according to International League of Associations for Rheumatology (ILAR) criteria. Tender joint count (TJC), swollen joint count (SJC) and laboratory tests were retrospectively collected from medical records. Disease activity was also assessed by the Juvenile Arthritis Disease Activity Score (JADAS). All data were checked for normality by the Kolmogorov-Smirnov test. The Spearman correlation was used for data analysis and *p* values less than 0.05 were considered statistically significant.

Results: A total of 54 consultations (29 at baseline and 25 at the last follow-up consultations) of 29 patients were included in our study. The mean age was 13.1±4.2 years [4-21] and the sex ratio of males to females was 1.07. JIA subtypes were: enthesis-related arthritis (n=12), polyarthritis (n=7), oligoarthritis (n=6), undifferentiated (n=3) and psoriatic arthritis (n=1). At baseline 51,73% of the patients were not under treatment, 34.49% were under non-steroidal anti-inflammatory drugs (NSAIDs) and 13.8% under methotrexate (MTX). At the last follow-up consultation 41.38% of the patients were under MTX, 34.49% under NSAIDS and 10.35% under Etanercept. At baseline, NLR1 was positively correlated with TJC1 (p=0.022, r=0.424) and SJC1 (p=0.014, r=0.453) but not with C-reactive protein CRP1 (p=0.512) neither erythrocyte sedimentation rate ESR1 (0.096) nor disease activity scores JADAS-CRP1 (p=0.063) and JADAS-ESR1 (p=0.091). PLR1 was positively correlated with SJC1 (p=0.004, r=0.521) and both disease activity scores JADAS-CRP1 (p=0.026, r=0.462) and JADAS-ESR1 (p=0.052, r=0.364). At the follow-up consultations only PLR2 was positively correlated to CRP2 (p=0.045, r=0.404). No correlation was noted between NLR2 and PLR2 and JADAS-CRP2 (p=0.281, p=0.063) and JADAS-ESR2 (p=0.324, p=0.082).

Conclusion: Our study suggests that NLR and PLR may be used as assessment tools of disease activity in patients with JIA. Further studies with larger sample sizes are needed to confirm these results and to explore the value of these ratios in the follow-up and the prognosis of JIA.

Disclosure of Interests: None declared

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AB1260

SIGNIFICANCE OF WHOLE-BODY MRI IN CHILDREN WITH RHEUMATIC DISEASES

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Background: Whole-body MRI (WB-MRI) has the potential to detect early or hidden signs of inflammation and seems to be more informative test than X-ray and ultrasound methods for bone and joints diseases. WB-MRI is important for identification of asymptomatic inflammation areas that are not available for clinical examination methods (sacroiliitis, TMJ). WB-MRI can become a tool for monitoring the progression of the disease and the efficacy of therapy. There is not enough data of knowledge about the role of WB-MRI in children with JIA.

Objectives: To evaluate the results of WB-MRI in children with rheumatic diseases (RD) in a single-center retrospective study.

Methods: 57 WB-MRI studies performed in children with RD in our center as a part of real-life diagnostic procedures.

Results: Among 57 children there are 22 boys and 35 girls, the average age is 13 years [11; 16]. 33 patients were examined once, 20 children twice after the initial course of therapy, two children underwent WB-MRI three times to evaluate the dynamics. It was most important to detect inflammatory lesions in multifocal non-bacterial osteomyelitis (mf-NBO). The structure of diagnosis and therapy before and after WB-MRI is present in Table 1.

Table 1. The effect of MRI on changes in the structure of diagnoses and approaches to therapy

	Before WB-MRI	After WB-MRI
Diagnosis:		
Juvenile idiopathic arthritis (JIA)	22	12
JIA+ mf-NBO	22	30
JIA+ mf-NBO +Psoriasis	5	8
JIA+ mf-NBO +FMF	1	1
JIA+ Psoriasis	2	0
JIA+IBD	1	1 (JIA+IBD+ mf-NBO)
Fibrodisplasia ossificans progressive (FOP) +JIA	1	1
Systemic JIA	1	1
Juvenile dermatomyositis (JDM)	1	1
Systemic lupus erythematosus (SLE)	1	1
SLE+ mf-NBO	0	1
Therapy:		
NSAIDs mono	17	12
DMARDs	26	29
Biologics: / bDMARDs:	12	27
anti-TNFα	10	21
Tofacitinib	1	5
Abatacept	1	1
Bisphosphonates	4	5
No current therapy	3	0

11 patients have multimorbidity (in addition to RD, one girl has Down syndrome). 5 pts had severe hypermobility syndrome patients making it difficult to identify inflammation due to the discrepancy between objective signs and the absence of limitation of joint mobility. 2 patients had multiple ankylosis. 7 patients underwent surgical interventions: 5 because of vertebral fracture, 2 because of osteomyelitis. The WB-MRI revealed: 48 polyarthritis signs, 33 osteitis, 3 osteonecrosis, 11 sacroiliitis, 1 sequestration, 1 epiphyseolysis, 1 initial signs of myositis. Surgical intervention was recommended to two patients after the diagnosis of WB-MRI (sequestration of the osteomyelitis focus and vertebral fracture).

Figure 1. WB-MRI 10-yrs old girl with JIA+ mf-NBO +Psoriasis. Than WB-MRI picture 4 months after the Etanercept administration. Positive dynamics in the sacroiliac joints, but the persistence of osteitis in the right radius, calcaneus, femur with the forming lytic destruction.

The principal significance and purpose of the performance of WB-MRI were disease control (continuation of therapy) - 22 (39%), the onset of DMARDs/bDMARDs – 17 (30%), the change of bDMARDs - 2 (3%), differential diagnosis – 16 (28%).
Conclusion: WB-MRI is useful for detecting asymptomatic and radiologically hidden lesions in JIA. Early diagnosis leading to appropriate treatment can prevent long-term structural damage to the joint. WB-MRI is a important tool for the diagnosis and diseases control in children with RD.
Disclosure of Interests: None declared
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AB1261 THE ANALYSIS OF THE ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS IN PEDIATRIC POPULATION

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Background: Systemic lupus erythematosus (SLE) is characterized by multiple autoantibodies associated with a multisystem illness where any organ can be targeted. There are different classification criteria for SLE. Sensitivity and specificity of three criteria have been debated and may vary in different populations and clinical settings.
Objectives: We aim to evaluate the clinical and laboratory symptoms of the onset of systemic lupus erythematosus in pediatric population.
Methods: A total of 116 SLE patients (female –92, male-24) were included into the study. We analyzed the primary diagnosis, the time before identification the SLE, clinical and laboratory symptoms, their combination, and fulfilling the classification criteria of SLE. All data is presented as Me (IQR).
Results: The age of the onset of SLE was 13.3 (10.7, 15.2) years. 55/116 patients had other diagnosis before the verification of SLE, the time before the verification was 10 (5, 26) months. The loss of weigh was in 63(54%) of patients, fever – in 83(72%) (febrile – 57, subfebrile -26), adenopathy in 55(47%), malar rash – in 45(39%), discoid rash – in 19(16%), alopecia – in 19 (16%), photosensitivity – in 39(34%), oral ulcers – in 38 (33%), nazal ulcers – in 11(9.5%), arthritis – in 31(27%), pleuritis- in 18(16%), pericarditis- in 20(17%), renal disorder – in 52(47%), seizures- in 7(6%), psychosis – in 1(0.9%), myelitis – in 2(1.7%), peripheral neuropathy – in 3(2.6%), cranial neuropathy – in 2(1.7%), hemolytic anemia – in 59(51%), leukopenia- in 62(53%), thrombocytopenia- in 27(23%), ANA positivity – in 100(86%), anti-dsDNA antibody positivity – in 91(78%), antiphospholipid antibody positivity– in 27 (25%), direct Coombs' test- in 22(19%). SELENA–SLEDAI Score was 13 (9, 20): low activity- in 14(12%) patients, moderate activity- in 23(20%), high activity – in 42(36%), very high activity – in 37(32%).
96 (83%) patients met the eligibility criteria ELAR/ACR 2019, 112(97%) – ACR criteria modified in 1997, 106(91%) – SLICC in 2012.
Conclusion: In this cohort, although all three criteria have sufficient. Some SLE patients with a clinical diagnosis lacked sufficient number of criteria.
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AB1262 PERFORMANCE OF JADAS-ESR AND JADAS-CRP IN THE ASSESSMENT OF DISEASE ACTIVITY IN TUNISIAN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The Juvenile Arthritis Disease Activity Score (JADAS) is a feasible tool which consists of four items: tender (TJC) or swollen joint count (SJC), the physician and the patient's/parent's global assessment and the erythrocyte sedimentation rate (ESR). C-reactive protein (CRP) has also been suggested as an alternative inflammatory marker.
Objectives: To compare the performance of JADAS-ESR and JADAS-CRP in the evaluation of JIA activity.
Methods: Twenty nine patients who met the International League of Associations for Rheumatology (ILAR) criteria for JIA were enrolled in the study. Disease activity was assessed by the JADAS-ESR and JADAS-CRP scores at 54 consultations, 29 at baseline and 25 during the last follow-up consultation. Data of JIA subtypes, disease duration and treatment were retrospectively collected from medical records. All data were checked for normality by the Kolmogorov-Smirnov test. The Spearman correlation was used for data analysis and p values less than 0.05 were considered statistically significant.
Results: The mean age of our population was 13.1±4.2 years [4-21] and the sex ratio of males to females was 1.07. The mean disease duration was 4.69±3.26 years [0.3-13]. JIA subtypes were: enthesis-related arthritis (n=12), polyarthritis (n=7), oligoarthritis (n=6), undifferentiated (n=3) and psoriatic arthritis (n=1). At baseline most of our patients (51,73%) were not under treatment, 34.49% were under non-steroidal anti-inflammatory drugs (NSAIDs) and 13.8% under methotrexate (MTX). At the last follow-up consultation 41.38% of the patients were under MTX, 34.49% under NSAIDS and 10.35% under TNF inhibitor (Etanercept). At baseline JADAS-ESR1 was correlated to JADAS-CRP1 ($p<0.001$, $r=0.808$) in all AIJ subtypes. JADAS-ESR1 and JADAS-CRP1 were not correlated to ESR1 ($p=0.416$, $p=0.661$) nor to CRP1 ($p=0.376$, $p=0.058$). Both JADAS-ESR1 and JADAS-CRP1 were correlated to TJC1 ($p<0.0001$, $r=0.643$; $p=0.015$, $r=0.502$) and only JADAS-ESR1 was correlated to SJC1 ($p=0.012$, $r=0.461$). At the last follow-up consultation, correlations were observed between JADAS-ESR2 and JADAS-CRP2 ($p<0.001$, $r=0.992$) in all AIJ subtypes. JADAS-ESR2 and JADAS-CRP2 were both correlated to CRP2 ($p=0.015$, $p=0.003$) but not to SJC ($p=0.175$, $p=.119$), nor to ESR2 ($p=0.535$, $p=0.426$).
Conclusion: Our study suggests that both JADAS-ESR and JADAS-CRP correlate closely during the follow-up of JIA. JADAS-CRP could be recommended for assessing disease activity in JIA.
Disclosure of Interests: None declared
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AB1263 CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS IN CHILDREN: A SINGLE CENTER 10-YEAR EXPERIENCE.

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Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a chronic autoinflammatory disease that primarily affects the skeleton in the absence of an infectious etiology in children and adolescents. It is an orphan disease with many unclear aspects in terms of diagnosis, treatment and follow-up.
Objectives: To report demographic, clinical and laboratory characteristics of a single center cohort of CRMO patients in Morozovskaya Children's City Clinical Hospital in Moscow, Russia.
Methods: We retrospectively and prospectively reviewed clinical records of 33 CRMO patients diagnosed between 2011 and 2021 and admitted to Rheumatology Department of Morozovskaya Children's City Clinical Hospital.
Results: We identified 33 patients with CRMO. Twenty-five (75%) were female. Median age of symptoms onset was 9 [6;12] years. Median delay in diagnosis was 12 month. All patients had bone pain as an initial symptom; fever has been present in 12 patients (63%). Joints involvement was observed in 22 patients (67%) – 39%, 18%, 12%, and 3% of patients had ankle, hip, knee, and shoulder and wrist joints involvement, respectively. All patients had multifocal bone lesions, which were confirmed by radiological methods (CT scan, MRI, scintigraphy). Vertebrae (42.4%) and femur (48.5%) were the most commonly affected bones. One child had a skull lesion (os parietale). Eleven patients (33%) also had sacroiliitis. Other organs involvement was observed 7 patients presented with palmoplantar pustulosis and psoriasis. Histopathological examination has been performed in 24 (73%) patients to confirm the diagnosis. Mean ECR was 43 [28;80] mm/h and CRP – 27 [15;61] mg/L. Twenty-three (69,6%) patients had immunological activity.
Conclusion: From our experience, most of the patients had delay in diagnosis. Laboratory tests showed mild elevation of inflammatory parameters. Seven (21%) patients had psoriasis.
Disclosure of Interests: None declared
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AB1264 CLINICAL, DEMOGRAPHIC CHARACTERISTICS AND TREATMENT RESPONSES OF PATIENTS WITH CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME

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Background: Cryopyrin-associated periodic syndrome (CAPS) is a rare autoinflammatory disease that inherited autosomal dominantly. The disease occurs as a result of mutations in the NLRP3 gene, which encodes cryopyrin (1). It has three clinical presentations called familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS) and neonatal-onset multisystem inflammatory disorder (NOMID) or chronic infantile neurologic, cutaneous and articular (CINCA) syndrome (2). FCAS is the mildest form of this spectrum, characterized by cold-induced fever, urticarial rash, joint complaints, conjunctivitis, and systemic inflammation.
Objectives: In our study, we aimed to evaluate the clinical and demographic characteristics and treatment responses of CAPS patients.
Methods: We retrospectively enrolled 44 pediatric patients who were diagnosed with CAPS admitted to Umraniye Training and Research Hospital, Pediatric Rheumatology Clinic, Istanbul, Turkey, June 2016 - December 2021. Medical records were analyzed for clinical presentation, disease associations, physical examination, and laboratory findings.
Results: A total of 44 patients (41 FCAS, 3 MWS) were included in the study. Of the patients, 19 were girls and 25 were boys. The median age of the patients was 10.5 (1.4-20.6) years. The median age of onset of attack was 3 years (1 month-14.6 year), age at diagnosis was 7.9 years (13 months-18 years), and the follow-up period was 2.2 years (4 months-5.2 years). There were a history of consanguinity in 9 (20.4%) patients. Twelve (27.2%) patients had the autoinflammatory disease in their families. The most common clinical findings were fever (100%), joint pain (86.4%), and abdominal pain (79.5%). Afterward, rash (56.8%), myalgia (45.5%), conjunctivitis (31.8%), arthritis (31.8%), diarrhea (31.8%), chest pain (27.3%), headache (25%), and vomiting (22.7%) were other findings accompanying the attacks. Thirty-nine (88.6%) patients had mutations in the NLRP3 gene. No mutation was detected in five (11.4%) patients. The most common Q705K mutation was detected in 28 (71.4%) patients. Forty-two (95.4%) patients were started on colchicine treatment. Biological therapy was started in 9 (21.4%) patients whose attacks continued despite colchicine. Anakinra and canakinumab, which are anti-interleukin 1 agents, were used as biologic therapy. FCAS patients had an adequate response to standard doses of canakinumab therapy, while MWS patients required significantly higher doses of canakinumab therapy.
Conclusion: Although familial Mediterranean fever and PFAPA are the most frequent periodic fever syndromes in our country, CAPS should be included in the differential diagnosis in patients with recurrent fever complaints and accompanying urticaria-like rash and conjunctivitis. In our clinical experience, some FCAS patients show significant clinical benefits with colchicine treatment. We think that it would be beneficial to try colchicine treatment before starting biologic therapy in FCAS patients.
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AB1265 BIOTECHNOLOGICAL AGENTS IN PEDIATRIC-ONSET SCLERITIS

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Background: the term scleritis refers to the inflammation of the sclera, the white outer type I collagen tunic of the eye (1). It may be rarely found in pediatric patients, with the incidence of pediatric scleritis accounting for about 1.2% of all scleritis cases (2). An early diagnosis and an adequate treatment are mandatory to avoid irreversible ocular sequelae (3). In this regard, the experience of biotechnological agents in patients with pediatric scleritis is quite limited at current.
Objectives: To assess the effectiveness of biotechnological agents in terms of scleritis control and glucocorticoid dosage tapering in patients with pediatric-onset scleritis; b) to assess the safety of the biotechnological agents employed and their ability in avoiding new ocular disease complications.
Methods: patients with pediatric-onset scleritis resistant to the conventional therapy and treated with biotechnological agents were retrospectively enrolled and prospectively followed-up. Demographic, clinical, ophthalmologic and therapeutic data were collected. The endpoints of the study consisted in the description of the therapeutic details gathered at the start of the biotechnological agents compared to what was observed at the 6-month, 12-month and last follow-up visits.
Results: 5 patients (3 males; 2 females) treated with adalimumab, infliximab, abatacept secukinumab were consecutively enrolled. A remarkable clinical efficacy was observed in 5/5 cases during a 10-to-54 months follow-up period; complete and persistent suppression of ocular inflammation was pointed out in 2/2 patients with active disease at the start of the treatment, while a clinically relevant decrease of scleritis relapses was observed in 5/5 patients after the start of biotechnological treatment, compared to the past years of scleritis activity. In particular, the 5 patients suffered from a total number of 17 scleritis relapses during the 12 months preceding the start of the biologic treatment; the same patients suffered from 2 scleritis relapses within the first 12 months from the start of the treatment and 4 scleritis relapses during the entire follow-up period (median time of 28 months, interquartile range=118 months). These results were obtained despite the progressive and persistent glucocorticoid sparing effect, with a median daily dosage of prednisone or equivalent ranging from 15 (interquartile range =21.75) mg/day at the start of treatment to 2.5 (interquartile range =8.75) mg/day at the 3-month assessment, 2.5 (interquartile range=0) mg/day at 6 month visit, and 0.0 (interquartile range =2.5) mg/day at the last assessment. Regarding the safety profile, one out of five patients experienced an adverse event represented by oral candidiasis, presumably related to the concomitant use of glucocorticoids.
Conclusion: biotechnological agents have shown to be highly effective in controlling pediatric-onset scleritis, allowing a remarkable glucocorticoids sparing effect in patients previously resistant to conventional treatment and recalcitrant to a glucocorticoid-sparing approach. The safety profile was excellent.
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AB1266 ANGIOTENSIN-CONVERTING ENZYME LEVEL IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: One of the most common comorbid conditions accompanying rheumatoid arthritis is atherosclerosis and arterial hypertension. Previous studies have shown a change in the blood lipid spectrum with an increase in the atherogenic index in children with juvenile idiopathic arthritis. The next link in the development of this pathology is a change in the endothelial function of the vessels.
Objectives: To study the level of angiotensin-converting enzyme in children with JIA and establish its interdependence with the blood lipid spectrum of sick children.
Methods: The level of angiotensin-converting enzyme (ACE) was studied in 46 children (28 girls and 18 boys) from 11 to 17 years old by enzyme immunoassay as well as indicators of the lipid spectrum: low density lipoprotein cholesterol (LDL), very low-density lipoprotein cholesterol (VLDL) and atherogenic coefficient. The results obtained were compared with the data of children in the control group, which consisted of 34 people. Data were analyzed depending on patients' gender, age, and age of JIA onset, its variant, duration, activity, and presence of methotrexate (MTX).
Results: The results of the study are presented in the Table 1.

Table 1.

Lipid spectrum indicators	Children's groups	M+m	Me	Min	Max	p
LDL	JIA, n=46	2,33±0,09	2,18	0,97	4,31	0,001
	Control, n=34	2,5±0,09	2,55	1,39	4,13	
VLDL	JIA, n=46	0,36±0,09	0,35	0,13	1,1	0,001
	Control, n=34	0,14±0,01	0,13	0,06	0,27	
KA	JIA, n=46	2,04±0,09	1,83	0,82	3,5	0,4
	Control, n=34	2,03±0,09	2,02	0,83	3,8	
ACE	JIA, n=46	41,23±3,9	35,59	14,4	101,2	0,2
	Control, n=34	40,22±6,37	46,75	17,97	63,78	

There were no significant differences in the ACE level in children with JIA in comparison with the control group. Analysis of the data obtained did not reveal significant changes in the obtained ACE parameters depending on the gender and age of patients, JIA activity, and the presence of MTX in complex treatment. At the same time, a direct correlation of ACE values and low-density lipoprotein levels ($r=0.5$, $p<0.05$) was obtained, which confirms the relationship between the ACE level and the development of dyslipoproteinemia in children with JIA.
Conclusion: The obtained results illustrate the stages of development of atherogenic changes in children with JIA. Data were obtained that against the background of an increase in the level of VLDL and a decrease in LDL, the level of ACE remains preserved, which reflects the absence of changes in the endothelium. Research into these changes is ongoing.
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AB1267 LONG-TERM SINGLE CENTER EXPERIENCE OF THE THERAPY WITH BIOLOGICS IN MULTIFOCAL NON-BACTERIAL OSTEOMYELITIS

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Background: Children and adolescents who suffered from the rare polygenic autoinflammatory disease such as multifocal non-bacterial osteomyelitis (NBO) can stay without specialized care for the long time. Currently we don't have standardized treatment for these patients. Administration of Biologics (B) established on opportunity to diagnose juvenile idiopathic arthritis (JIA) or juvenile ankylosing spondylitis (JAS) in relation to combination of bone lesions with arthritis and/or axial skeleton damage.
Objectives: To describe clinical/laboratory findings and therapy approaches in patients with NBO who was treated by BA.
Methods: We analyzed a single center retrospective nine-year study, which includes cohort of 56 patients (pts) with multifocal NBO. 22 pts of them were treated by different B (TNF-inhibitors mostly) in our pediatric department. Standard rheumatological assessment were included for all pts. X-ray, whole-body MRI and/or scintigraphy were done for revealing all localizations of bone lesion. Infection, oncology and other reasons of bone damage were excluded at the time of B administration.
Results: In total we identified 22 pts (10-boys; 12-girls) treated by B (TNF-inhibitors as first-line) among the whole group (n=56). The median age at the disease onset was 10 years (Me 10, range 1.3;16,5). Classifying diagnosis according to rheumatological nosology as JIA or JAS we were able for legal administration of targeted agents. 12 pts had JIA (7 girls), 10 pts had JAS (5 girls). JIA was presented by poly- (7 pts) and oligoarticular (5 pts) types. MRI evidence of axial involvement that was established on active erosive sacroiliitis with deep bone marrow edema had 15 pts (68%), on active spondylitis in thoracic spine – 3 pts, on erosive arthritis with partial ankyloses of facet joints of neck – 3 pts; multiple syndesmophytes had 1 girl. According to our findings, axial damage associated with NBO had developed much earlier (at 2 y.o. as minimum) than in case of «idiopathic» JAS. HLA-B27 positive was 11 pts, high levels of ANA had 5 pts (all of them HLA-B27 negative). Extraskeletal manifestations were observed in 8 pts (acne conglobate, uveitis, inflammatory bowel disease – one in each condition, psoriasis pustulosus – 5). High laboratory markers were revealed before biologics in 14 pts. Non-biological therapy was based on worldwide practice and included NSAIDs (all pts), methotrexate (10 pts), sulfasalazine (10 pts, in 9 pts it was withdrawal), bisphosphonates (2 pts), glucocorticoids (7 pts). Persistent arthritis, severe course of NBO, appearance of new bone lesions, refractory to treatment were determinant factors for administrate the TNF-inhibitors. Among first line of B etanercept (ETN) was used in 14 pts (63%), adalimumab (ADA) – in 5 pts (23%), golimumab – in 2 pts (9%), infliximab (IFX) – in 1 pts (4,5%). At the start of B the average age was 13.7 years (range 7.2-17.9); mean disease duration was 3,4 years (range 0.3-8.1). There were 4 cases of withdrawals: 1 for IFX (to ETN) due to development of skin involvement (chalazion,streptoderma), 3 for ETN. In 2 pts due to ineffi-cacy ETN was switched to ADA. Decreasing of disease activity was detected in the most of patients. Among them 2 pts developed the whole remission with resolving of active arthritis and bone marrow edema spots. Skin lesions (acne, psoriasis) were significantly improved. There weren't fixed adverse events during TNF-therapy except of the development of staphylococcus sepsis under ETN in a patient with rare genetic comorbidity (congenital indifference to pain). ETN was withdrawn immediately. The patient was treated for a long time by the surgery methods and antibiotics. A year later because of flares of arthritis JAK-inhibitors tofacitinib was administrated and marked improvement achieved.
Conclusion: Established on our experience, we can suggest that treatment with TNF-inhibitors is a good therapy approach for patients with high activity of NBO. It's expected that option of prescribing BA can prevent progression and bone destruction.
Disclosure of Interests: None declared
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AB1268 CLINICAL ASPECT AND THERAPEUTIC MANAGEMENT OF SUBACUTE OSTEOMYELITIS IN CHILDREN

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Background: Subacute osteomyelitis in children is a distinct entity encompassing primary localized osteomyelitis. It poses a diagnostic problem related to its few or no constitutional symptoms, misleading radiological manifestations and often a negative bacteriological investigations. The treatment remains very controversial.
Objectives: The aim of this study was to identify the main epidemiological, clinical, histological and evolutionary characteristics of this affection and to propose an adequate therapeutic attitude.
Methods: It was a retrospective longitudinal study, carried out over a period of 25 years from January 1995 to December 2019 in the orthopedic department of Taher Sfar Hospital,Mahdia, that included 37 cases of subacute osteomyelitis in children.
Results: The mean age of the patients was seven years nine months with a male predominance (sex ratio: 2.27). The average time to hospitalization was 41 days. A diagnostic delay was very likely because of delay in consultation which was related to clinical latency, reported in all cases. The imaging showed osteolysis in all cases, setting in long bones in 54% of cases and in 46% other cases in short and flat ones. The lesion was multiple in two different bones only in one case and was found in pure epiphyseal location in seven cases. The bacteriological investigation allowed the isolation of a germ only in eight cases. In all cases, it was a Staphylococcus aureus. Surgical treatment was performed in 21 cases (60% of patients). The outcome was favorable in 35 cases (95% of cases). An infectious awakening was noted in 2 cases.
Conclusion: Subacute osteomyelitis poses a diagnosis and therapeutic problem. Magnetic resonance imaging is a valuable examination. Surgical treatment combined with appropriate antibiotic therapy is indicated for any suspicious lesion. It can be useful in taking samples for diagnosis, improve distribution of the antibiotic in injury and accelerate healing radiation.
Disclosure of Interests: None declared
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Other orphan diseases

AB1269 SHULMAN'S DISEASE OR EOSINOPHILIC FASCIITIS, A RARE FIBROSING DISORDER: A CASE REPORT TREATED WITH TOCILIZUMAB

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Background: Schulman eosinophilic fasciitis (EF) is a rare fibrosing disorder, typified by erythema, edema, and symmetric induration of the distal bilateral extremities (only proximal to the wrists and ankles) or/and trunk**(1).**The "groove sign" and/or a pseudocellulite appearance of the involved skin may be present**(1),** followed by joint contractures **(1).**Fascial biopsy is the gold standard for making a diagnosis.Systemic corticosteroids are first-line treatment**(2).**The use of c/bDMARDs is described in literature with clinical improvements**(2).**
Objectives: to evaluate efficacy of Tocilizumab in a patient affected by Shulman's disease
Methods: A 54-year-old woman went to our observation for appearance of abrupt-onset simmetric edema followed by induration of the bilateral extremities and trunk. She has been feverish for about 2 weeks associated with diffuse arthromyalgia. On rheumatological examination: non-liftable skin in folds on the bilateral arms and forearms and lower limbs; absence of frank synovitis or lymphoglandular swellings. The blood tests performed showed an increase in acute phase reactants. The ferritin and electrophoretic picture, complement and immunoglobulin dosage were normal. The blood count showed a marked absolute eosinophilia accompanied by modest monocytosis and modest platelet disease. There was a slight increase in LDH and in serum beta2microglobulin. Serology for viral infections and autoimmunity were negative. Screening for celiac disease was negative. Coprocultures, parasitology and the search for the fecal H. pylori antigen are negative. Excluded lymphadenopathy or hepatosplenomegaly to the total body computed tomography. Modest non-buffering pericardial effusion was reported in CT scan. Nailfold capillary changes were absent. Chronic inflammatory bowel diseases were excluded. A skin biopsy of the left forearm confirmed the clinical diagnosis of EF. In particular, it documented thickening of the fascia, site of an inflammatory process that included small lymphocytes, plasma cells, histiocytes and some eosinophils, distributed both diffusely and around blood vessels.The underlying muscle tissue and the supra-fascial skin were free from alterations. Secondary fasciitis was excluded by 18 fluorodeoxyglucose (FDG)-positron emission tomography; this showed a diffusely accumulation of the radiopharmaceutical in the muscles of the forearms and of both lower limbs, compatible with eosinophilic fasciitis and confirmed the pericardial effusion. Immunophenotypic analysis on peripheral blood excluded the presence of a monoclonal cell population. Diagnosis of primary eosinophilic fasciitis was made and therapy was started with methylprednisolone 1 g intravenously for 3 days followed by another 3 boluses of methylprednisolon of 500 mg iv. Given the poor response, it was decided to set up therapy with Methotrexate 15 mg up to a dose of 20 mg intramuscularly per week associated with prednisone 25 mg/day. The rheumatological re-evaluation at 3 months showed a worsening of the fibrosis and diffuse skin edema with an obligatory kyphosis of the spine and limitation in the patient's movements. Therefore it was decided to start off label infusion therapy with Tocilizumab 8 mg/kg/month.
Results: A complete resolution of the skin picture with disappearance of the pericardial effusion was documented 12 months after the start of the biological drug
Conclusion: There are currently no guidelines for the treatment of eosinophilic fasciitis. Tocilizumab has been shown to be effective when introduced in the early inflammatory stages of the disease, as in the case described.
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AB1270 EFFICACY AND SAFETY OF THE OPTIMISATION OF BIOLOGICAL THERAPY IN NON-INFECTIOUS UVEITIS: SYSTEMATIC REVIEW

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Background: In other rheumatic diseases it is possible to optimize biological therapy, maintaining its effectiveness and without risk in its safety. But this aspect has not been studied in the field of non-infectious uveitis.
Objectives: In other rheumatic diseases it is possible to optimize biological therapy, maintaining its effectiveness and without risk in its safety. But this aspect has not been studied in the field of non-infectious uveitis.
Methods: A search strategy (Pubmed, Embase and Cochrane) was carried out on UNI up to Jan-22 with Mesh vocabulary and free text (human beings, English or Spanish). Review last 2 years of International Congresses Rheumat/Oft. We included meta-analyses, systematic reviews, clinical trials, prospective and retrospective longitudinal observational studies (OA). Secondary manual search and quality assessment with the Oxford scale by 2 independent researchers. The population included were UNI in ophthalmological remission after TB use. Articles with TB optimization strategies and whether there is a comparison with those that maintain the smPC dose are examined. The main measures being evaluated are efficacy and safety. Data are collected on eye activity, number of outbreaks, GC (glucorticoid) doses and adverse effects.
Results: 11 articles of low or moderate quality. They were mostly retrospective EO (n=7), and to a lesser extent prospective (n=4), and included 513 patients. With a variable follow-up from a minimum of 12 months, up to 17 years of evolution. There was a predominance of males, of average age of 36 years, the most represented disease was Bechet's disease. There was no homogeneous criterion when trying to optimize, since the minimum required time of remission maintained with TB, varied from 3 to 12 months. The use of FAME and GC was allowed. The intervention is described in 7 articles with Infliximab, 2 with Adalimumab and 2 with Etanercept. Other TB other than anti-TNF, have not performed optimization so they are not included in this systematic review. They included patients treated with DMARD and even with previous anti-TNF. Many articles did not have a comparison group. Studies suggest that after 3-6 months in remission, it could be a time to assess optimization. The remission maintained after discontinuation of the drug, is maintained from 7.5 months, up to 2 years. GC reduction and suspension up to 74% and even 40% FAME are described. But there are also relapses in 25-50%, but they are controlled in general with the increase in doses and in some cases with change of TB. There were no relevant security issues.
Conclusion: 1. Low quality of the evidence. 2. Great variability in patients, pathologies, definitions or outcome variables. 3. There is no consensus at the time of starting the optimization, the data suggest that after 3-6 months in remission it could be assessed. 4. Articles with a limited number of cases (some without a control group) or retrospective are included. There is great heterogeneity in the optimization and protocols used. But despite all this, these results suggest that optimization and/or suspension (in selected cases) can be carried out safely and planned for anti-TNF TB, with a low probability of short-term recurrences. 5. In case of reactivation of uveitis, it seems that it is usually controlled in most cases, using again the standard doses. 6. There were no relevant security issues. 7. More studies with homogeneous criteria and established protocols are needed to determine the duration of the ideal treatment and see if there are differences in the etiology of uveitis or TB used.
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AB1271 PREVALENCE OF RHEUMATOLOGIC DISEASES IN PATIENTS PRESENTING WITH UVEITIS

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Background: Uveitis may occur in the course of systemic inflammatory rheumatic diseases, or it may be the first clinical presentation of these diseases.
Objectives: To determine the prevalence of systemic inflammatory rheumatic disease in patients whose initial clinical manifestation is non-infectious uveitis.
Methods: Adult patients diagnosed with non-infectious uveitis in Dokuz Eylul University Ophthalmology Department and referred to investigate the

etiology of rheumatological disease were included in the study. Demographic and clinical features, laboratory and imaging findings of the patients were examined.

Results: 106 patients diagnosed with uveitis (42.4% anterior uveitis, 2.8% intermediate uveitis, 19.8% posterior uveitis, 34.9% panuveitis) were included in the study. 52.8% of the patients were male and the mean age was 40.19±14.82 years. The mean age of uveitis attack was 38.7±15.02 years. 33% of the patients were diagnosed with rheumatologic disease (10 SpA, 17 Behçet's Disease, two vasculitis, two sarcoidosis, three undifferentiated connective tissue disease, one rheumatoid arthritis). SpA was diagnosed in 20% of patients presenting with anterior uveitis. Behçet's disease was detected in 27% of patients referred with panuveitis and in 33.3% of patients whose first clinical finding was posterior chamber involvement. Bilateral uveitis was detected in two-thirds of patients with posterior chamber affected, and it tends to recur more (p=0.014).

Conclusion: A rheumatological disease was detected in approximately one-third of the patients presenting with uveitis. Investigation of patients referred for uveitis in terms of systemic rheumatological diseases is very important as it may change the diagnosis and treatment process.

Disclosure of Interests: None declared

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AB1272 FACTORS AFFECTING PATIENT-ACCEPTABLE SYMPTOM STATES IN FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by recurrent attacks of fever, serositis, and musculoskeletal symptoms (1, 2). Arthritis is the most common musculoskeletal symptom of attacks and also included in diagnostic criteria of FMF (3). If it is specifically queried, myalgia may be detected in up to 20-25% of the patients with FMF. (4,5).

Objectives: In our study, we aim to assess the localization of attack-related myalgia and associated parameters in patients with FMF.

Methods: A total of 349 consecutive patients followed by FMF in our clinic were enrolled in the study and asked for attack-induced myalgia and if present, localization of muscle groups on the mannequin body parts diagram.

Attack frequency, duration, and disease activity were evaluated with the Auto-Inflammatory Diseases Activity Index (AIDAI) scoring system (6). Patients were also asked for work/study day loss during attacks and patient acceptable symptom state (PASS) status (7).

Results: 126 patients showed attack myalgia (36%); attack duration, frequency, severity were significantly higher in patients with attack-myalgia (p<0,005). Most common muscle groups were calves, lower back, and latissimus dorsi muscles in order. Myalgia was most commonly accompanied by arthritis (p<0,002). Patients with myalgia have a higher frequency of colchicine resistance and work/study day loss due to attacks.

Conclusion: Our results conclude that myalgia is an important domain of attacks and causes absenteeism and uncontrolled disease activity. Treatment of myalgia attacks may provide controlled disease act**iv**ity, and prevent absenteeism from work/school.

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Table 1. Comparison of clinical and laboratory parameters between patients with /without myalgia attacks

	Patients with myalgia attack	Patients without myalgia attack	p value
Age (years)	36,33 ±10, 68	37,9±11, 48	>0,05
Sex (female/male)	78/43	138/87	>0,05
Follow-up time (years)	16,1	17,6	>0,05
Dominant attack(number)			
Peritonitis	42	55	>0,05
Arthritis	11	39	**0,012**
Pleuritis	13	10	>0,05
Only fever	4	7	>0,05
AIDAI score (mean, 0-175)	127,40	80,68	**<0,05**
VAS score for pain (median score, during attack. 0-10)	8	5	**<0,05**
Colchicine resistance (number of patients)	69	25	**0,003**
Colchicine-resistant	29	84	**0,002**
Colchicine-sensitive			
PASS status (number)			
Need additional treatment	41	6	**0,016**
Satisfied from treatment	34	74	**0,010**
Work/study day loss (number)	48	6	**0,003**

Acknowledgements: All study population signed informed consent for both participation and publication. Local Ethical Committee of the university approved the study.

Disclosure of Interests: None declared

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AB1273 MACROPHAGE ACTIVATION SYNDROME IN RHEUMATIC DISEASE: CLINICAL CHARACTERISTICS AND PROGNOSIS OF 20 PATIENTS

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Background: Macrophage activation syndrome (MAS) is a hyperinflammatory condition that is known to be secondary hemophagocytic lymphohistiocytosis (HLH) in patients with rheumatic disease.

Objectives: The aim of study was to evaluate the clinical manifestations and outcomes in patients with MAS with rheumatic disease.

Methods: We performed a retrospective study of 20 adult patients who were diagnosed with MAS from 2012 to 2020. MAS was classified according to the HLH-2004 criteria. Patients' information, including clinical features, laboratory findings, and treatment regimens, was collected, and the overall survival rate was estimated by the Kaplan–Meier method.

Results: Twenty patients (18 women, 35.6 ± 18.3 years) who met the HLH-2004 criteria also fulfilled the 2016 EULAR/ACR/PRINTO classification criteria for MAS, and HScore was higher than 169 (median, 238.5). Fourteen patients with systemic lupus erythematosus and 6 patients with adult-onset Still's disease were included. All patients were treated initially with corticosteroids, and 16 patients required additional immunosuppressants. The overall survival at 3 and 6 months was 75.2% and 64.3%. In survivors, renal impairment was less common (23.1% versus 42.9%, p = 0.007), the levels of AST (202.0 versus 72.0 IU/L, p = 0.006) and LDH (1144.0 versus 343.0IU/L, p = 0.001), and platelet count (90.0 versus 46.0 × 10^9/L, p = 0.016) were higher in compared to non-survivors. Nine patients had opportunistic infections, five of whom died during admission.

Conclusion: The mortality of patients with MAS remains high. Renal impairment, levels of AST and LDH, and platelet count might be associated with prognosis.

Table 1. Treatments and management characteristics of patients with MAS

No.	Age/sex	Disease	Disease duration (months)	1st Treatment (corticosteroids)	2nd Treatment	3rd Treatment	Combined infection	Alive/dead
1	19/F	SLE	1	1 mg/kg	IVIG + PP	TCZ, RTX	Bacteremia	Dead
2	20/M	SLE	0	1 mg/kg	-	-	-	Alive
3	20/F	AOSD	1	1 mg/kg	VP16	-	-	Alive
4	22/F	SLE	1	100 mg	IVIG + PP	-	Pneumonia	Dead
5	22/F	AOSD	0	500 mg	IVIG	-	-	Alive
6	23/F	SLE	182	1 mg/kg	-	-	-	Alive
7	23/F	SLE	41	1 mg/kg	-	-	-	Alive
8	30/F	SLE	146	1 mg/kg	IVIG	CsA	-	Alive
9	32/F	SLE	127	1 mg/kg	IVIG + PP	CsA, TCZ	Pneumonia	Alive
10	35/F	AOSD	0	1 mg/kg	CsA	-	Viral infection	Alive
11	37/F	SLE	65	1 mg/kg	CsA, VP16	-	Bacteremia	Alive
12	38/F	SLE	0	1 mg/kg	IVIG + PP	RTX	-	Dead
13	40/F	AOSD	0	0.5 mg/kg	CsA	-	-	Alive
14	43/F	SLE	60	1 mg/kg	IVIG + PP	TCZ, RTX, CsA, VP16, IFX	PCP, Viral infection	Dead
15	49/F	SLE	0	1 mg/kg	CYC	-	Bacteremia	Alive
16	51/F	AOSD	0	1 mg/kg	-	-	-	Alive
17	57/F	SLE	0	1 mg/kg	IVIG + PP	CsA, VP16	Fungal infection	Dead
18	61/F	SLE	2	1 mg/kg	IVIG + PP	TCZ	-	Dead
19	68/F	SLE	2	1 mg/kg	IVIG + PP	CsA	Fungal infection	Alive
20	70/M	AOSD	0	1 mg/kg	IVIG + PP	CsA, VP16	Fungal infection	Dead

SLE: Systemic lupus erythematosus, IVIG: Intravenous immunoglobulin, PP: Plasmapheresis, TCZ: Tocilizumab, RTX: Rituximab, AOSD: Adult-onset still's disease, VP16: Etoposide, PCP: Pneumocystis pneumonia, CsA: Cyclosporin, IFX: Infliximab, MCTD: Mixed connective tissue disease.

Disclosure of Interests: None declared

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AB1274 ADULT-ONSET STILL'S DISEASE IN WESTERN AUSTRALIA: EPIDEMIOLOGY, COMORBIDITY AND LONG-TERM OUTCOME.

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Background: Adult-onset Stills disease (AOSD) is a rare, potentially life-threatening autoinflammatory condition for which the reported prevalence shows regional variation and where comparative long-term outcome data are scarce (1).

Objectives: To investigate annual incidence and point prevalence of AOSD in Western Australia (WA) and compare long-term health-related outcomes between AOSD patients and hospital-based controls.

Methods: Population-based cohort study using longitudinally linked administrative health data from all hospitals in WA between 1999 and 2013. ASD patients (ICD-10-AM code M06.1) were matched to controls for age and gender. Rate and odds ratios (RR/OR) with 95% confidence intervals (CI) were used to compare ASD patients and controls for serious infections (SI), osteoporosis, joint replacement and the modified Charlson Comorbidity (mCCI).

Results: In total 52 patients had incident AOSD for an average period incidence of 0.22/100,000 and a point prevalence of 2.4 /100.000 (per 30/12/2013). Compared to controls, ASD patients (median age 41.5 years, 59.6% females) had higher odds of prior liver disease (OR 2.67, 95%CI: 1.31-5.45), fever (OR 54.1, 95%CI: 6.6-43), rash (OR 15.7, 95%CI: 4.08-60.8) and SI (OR 4.36, 95%CI: 2.11-22.8). During 49 months of follow up, crude mortality (11.5% vs 7.5%; p=0.34), survival at one and five years (p=0.78) and m-CCI score at last observation (median 2 vs 2) were similar for ASD patients and controls. However, the odds for subsequent joint replacement (in 7 patients; 13.5%) (OR 45.5, 95%CI: 4.57-93), osteoporosis (OR 31.3, 95%CI: 3.43-97) and SI (RR 5.68, 95%CI: 6.61-8.74) were significantly higher in ASD patients.

Conclusion: The epidemiology and demographics of AOSD in Western Australia fall within the internationally reported range. Compared to controls, AOSD patients presented higher rates of liver disease, rash and SI before disease onset. Mortality following AOSD was not increased for five years despite high rates of chronic arthritis requiring joint replacement, SI, and osteoporosis.

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AB1275 SUGGESTED APPROACH TO UBA1 GENE MUTATION TESTING IN PATIENTS WITH SUSPECTED VEXAS SYNDROME

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Background: VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is a recently identified autoinflammatory disease caused by *de novo* somatic mutations in the X-linked gene *UBA1* (1). This disease is clinically characterized by inflammatory symptoms and bone marrow failure (2).

Objectives: The aim of our study was to identify genetic variants associated with VEXAS syndrome and to design an algorithm for detection of *UBA1* gene mutations in patients with suspected VEXAS syndrome, which could be used for diagnosis.

Methods: We examined the UBA1 gene in 9 patients with clinically suspected VEXAS syndrome. We first focused on variants p.Met41Val, p.Met41Thr and p.Met41Leu with a known association with this disease (1). Samples of individual blood cell populations obtained by magnetic isolation were evaluated using RFLP, tetra-primer ARMS-PCR and Sanger sequencing. Subsequently, we analyzed the remaining exons of the *UBA1* gene by Sanger sequencing.

Results: Using the above described method we have identified the previously described variants p.Met41Thr in two and p.Met41Leu in another two patients. In one patient, we discovered a new mutation p.Gly477Ala (c.1430G>C) in exon 14 that has not yet been identified. The presence of these variants and their allelic forms (heterozygous / homozygous) varied between cell populations in individual patients.

Conclusion: The increasing number of reports suggests that VEXAS syndrome is not rare. In patients with clinical suspicion, typically UBA1 sequencing analysis of haematopoietic cells is performed in hot spot sites of p.Met41 in exon 3 only. Our results suggest that other variants, such as the newly identified p.Gly477Ala variant, may also be associated with clinical features of VEXAS syndrome. We propose that an extended analysis of all coding regions of the *UBA1* gene may uncover other mutations with putative functional consequences.

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AB1276 EVALUATION OF DRUG-FREE REMISSION RATES IN IDIOPATHIC GRANULOMATOUS MASTITIS

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Background: Idiopathic granulomatous mastitis (IGM) is a rare inflammatory breast disease. There is no clear consensus on its treatment yet (1).
Objectives: The aim of the study was to evaluate the rates of drug-free remission of the patients with IGM in a period of three-year follow-up.
Methods: A total of 76 patients who were followed-up with biopsy proven IGM, between February 2011 and November 2021 in rheumatology outpatient clinic of Gulhane Training and Research Hospital, were evaluated retrospectively. To analyze long-term outcomes, 55 patients who were followed up for 3 years were included in the study. Data regarding the demographic and clinical characteristics of the patients were obtained from patients' files.
Results: The study included 55 female patients with a mean age of 36.8 ± 6.3 years. Forty-nine (89.1%) patients received immunosuppressive treatment, one (1.8%) patient received postoperative immunosuppressive treatment, 3 (5.4%) patients had immunosuppressive treatment due to recurrence after surgery, and 1 (1.8%) patient underwent only surgery. One (1.8%) patient had no treatment for IGM. Patients who received immunosuppressive drugs for initial treatment, 38 (69.1%) received methotrexate (MTX) and corticosteroids (CS), 7 (13.2%) received azathioprine (AZA) and CS, 3 (5.6%) received only CS and 1 (1.8%) received cyclosporine A (CsA) and CS. Four (7.2 %) patients had received MTX after surgery. At 3-year follow-up 54 (98.1%) patients were in drug-free remission. The median duration of drug-free remission in patients receiving MTX plus CS, CS, and azathioprine plus CS was 19.7, 32.9, and 14.7 months, respectively. One patient who received CsA plus CS was in drug-free remission for 28.3 months. The median duration of treatment with combination of CS and other immunosuppressives was 6.7 months. The median duration of immunosuppressive treatment was 15.8 months (Table 1). Recurrence was observed in 4 (80%) patients who did not receive immunosuppressive therapy after surgery. Three (75%) of these patients received MTX due to recurrence, and remission was achieved.

Table 1. Duration of immunosuppressive treatment and drug-free remission of the patients

Treatment	Duration of immunosuppressives, (n=53)	Duration of drug-free remission, (n=54)
Only corticosteroids (month)*	4.6 (2.9-5.8)	32.9 (32.4-33.4)
Methotrexate (month)*	19.7 (2.8-32.4)	19.7 (2.7-32.4)
Azathioprine (month)*	16.2 (11.0-30.1)	14.7 (8.8-22.9)
Cyclosporine (month)	7.6	28.3
Total (month)*	15.8 (2.9-34.3)	21.2 (2.7-36.6)

* Variables as median, (minimum - maximum)

Conclusion: Immunosuppressives provide a remarkably high sustained remission and maintain a longer drug-free remission in patients with IGM.
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AB1277 POOR LONG-TERM OUTCOMES AND SUBSTANTIAL BURDEN OF COMORBIDITIES IN EUROPEAN PATIENTS WITH DERMATOMYOSITIS/POLYMYOSITIS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

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Background: Dermatomyositis (DM) and polymyositis (PM) are rare heterogenous systemic autoimmune disorders of the skin, muscles and other organs that may have a devastating impact on patients' lives. Despite various therapies used in clinical practice, a notable proportion of patients seem not to achieve sustainable remission. There is a need to better understand long-term outcomes and comorbidities in patients with DM/PM in Europe.
Objectives: To systematically review and summarize evidence on clinical burden of disease in patients with DM/PM in Europe.
Methods: A systematic literature review (SLR) was conducted in MEDLINE and Embase databases to identify studies in children and adults with DM/PM, published in the English language between 2011 and 2021. Primary studies enrolling 10 or more patients were included, irrespective of country or region. Each eligible article was independently reviewed by two reviewers. The title and study abstracts were reviewed to assess eligibility for full-text review. The current abstract summarizes SLR results on the long-term outcomes and comorbidities in patients with DM/PM in Europe.
Results: A total of 2,967 non-duplicated publications were retrieved from medical databases and analyzed against pre-defined study selection criteria. There were 2,574 records excluded at title and abstract screening. Remaining 393 records were analyzed in the full text with 208 papers considered relevant. Additional 21 papers were identified from searching reference list of relevant studies and conference proceedings. In total, 222 studies (229 publications) were included in data abstraction. Among 43 studies conducted across 14 European countries, 23 studies evaluated long-term outcomes of disease and burden of comorbidities. There were 14 longitudinal cohort studies, 7 cross-sectional analyses and 2 case-control studies. Only 29-44% of DM/PM adults achieved remission. Between 38% and 62% of adults with DM/PM required at least 3 different medications, suggesting inadequate response to initial and subsequent regimens. During a mean follow-up of 13.9 years, 69% patients with JDM had polycyclic or chronic disease characterized by periods of remission and recurrence or by permanently active disease for more than 2 years after diagnosis. A notable proportion of children (60.4%) showed evidence of damage in at least one body organ and 13-20% of patients had complications such as calcinosis, lipodystrophy, or muscle atrophy. Adults with DM/PM often suffered from interstitial lung disease (16-66%), serious infections leading to hospitalization or death (21-26.7%), and cardiovascular disorders (CVDs) (19-71%). Compared to age and gender matched controls without DM, patients with DM had 16-times higher risk of venous thromboembolism (HR=16.44, 95% CI: 7.54-35.86). Incidence of coronary heart disease, hemorrhagic stroke, or ischemic stroke during 10-year follow-up was approximately 1.5- to 2-times higher in DM/PM adults relative to general population. Multiple studies reported high rates of any malignancy in DM adults (7.5-33%) and in PM adults (8-11.7%). During approximately 24,000 patient-years of follow-up, adults with DM/PM had more than 4-times higher incidence of lung cancer compared to general population that also was one of the highest incidences among multiple other autoimmune diseases. Long-term prognosis in DM/PM was poor with 20-year survival below 70%. The most common causes of deaths were pulmonary-related, malignancies, and cardiac complications. Mortality due to lung cancer was more than 4-times higher than in general population (standardized mortality ratio=4.17, 95% CI: 3.03-5.60).
Conclusion: European patients with DM/PM suffer from substantial burden of comorbidities including serious infections, malignancies and CVDs that lead to poor long-term outcomes. A notable proportion of adult and juvenile patients do not achieve sustainable remission or experience relapse indicating high unmet need.
Disclosure of Interests: Jiří Vencovský Speakers bureau: Abbvie, Biogen, Boehringer, Eli Lilly, Gilead, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Werfen, Consultant of: Abbvie, Argenx, Boehringer, Eli Lilly, Gilead, Octapharma, Pfizer, UCB, Grant/research support from: Abbvie, Konrad Pisarczyk Consultant of: Kezar Life Sciences, Richard Leff Shareholder of: Kezar Life Sciences, Consultant of: Kezar Life Sciences, Eunmi Park Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Kiruthi Palaniswamy Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Li Long Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences.

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AB1278 INCIDENCE OF ENDOCRINE AND EXOCRINE INSUFFICIENCY IN PATIENTS WITH AUTOIMMUNE PANCREATITIS AT DIAGNOSIS AND AFTER TREATMENT

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Background: Autoimmune pancreatitis (AIP) is a rare form of chronic pancreatitis that may lead to endocrine and exocrine insufficiency if left untreated. AIP clinically responds to glucocorticoids (GCs) therapy, but multiple GCs courses are often required to maintain remission with potential detrimental effects on glycaemic control. To date, data on pancreatic function in AIP are scanty and heterogeneous.
Objectives: We aimed to assess the rate of endocrine and of exocrine insufficiency at diagnosis and at follow up in patients with AIP as well as the impact of GC therapy on pancreatic function in the long term.

Methods: The MEDLINE, SCOPUS, and EMBASE databases were searched from inception to August 2021 to identify studies reporting data on endocrine and exocrine insufficiency in patients with type 1or type 2 AIP. Studies involving ≥ 3 patients were selected. In case of duplicated studies, the most recent or the one with the largest sample were included. The study was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Pooled events were calculated using a random-effect model and expressed in terms of pooled prevalence rates.
Results: A total of 6522 AIP patients and sixty-two studies were included in the analysis. The pooled estimate rate for the overall prevalence of diabetes in AIP at baseline (combined type 1 and type 2 AIP) was 36.9% (95% CI 31.9-41.9, I^2 96.1%). The pooled estimate for the prevalence of diabetes was 44.3% (95%CI 39.1-49.4, I^2 91.9%) in type 1 AIP and 11.3% (95%CI 6.1-16.6, I^2 42.5%) in type 2 AIP ($p < 0.01$), respectively. The pooled prevalence rate of exocrine insufficiency was 45.2% (95%CI 32.9-57.4; I^2 97.4%). The pooled estimate rate of diabetes at follow-up was 44.2% (95%CI 26.1-62.4) in studies where GCs were given to 100% of patients and 41.8% (95%CI 30.6-52.9) in studies where GCs were given to less than 100% of patients. The pooled prevalence of pancreatic exocrine insufficiency was 36.2% (95%CI 20.4-52.0, I^2 96.4%).
Conclusion: A large proportion of patients with AIP displays concomitant exocrine and endocrine insufficiency at the time of diagnosis. The incidence of diabetes at the longest available follow up tends to increase in patients treated with GCs. Further long-term studies are warranted to assess the impact of GCs and immunosuppressive treatments on glycaemic control and on exocrine pancreatic function.
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AB1279 POOR QUALITY OF LIFE AND REDUCED WORK PRODUCTIVITY IN EUROPEAN PATIENTS WITH DERMATOMYOSITIS AND POLYMYOSITIS: FINDINGS FROM A SYSTEMATIC LITERATURE REVIEW

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Background: Dermatomyositis (DM) and polymyositis (PM) are rare heterogenous systemic autoimmune disorders of the skin, muscles, and other organs with few effective treatment options available. They are described as devastating diseases but the full impact on patients' lives in Europe is not well understood.
Objectives: To systematically review and summarize evidence on humanistic burden of disease in patients with DM and PM in Europe to better understand patient-relevant aspects of disease and key domains of life impacted by DM and PM in the European setting.
Methods: A systematic literature review (SLR) was conducted in MEDLINE and Embase databases to identify studies in children and adults with DM and PM, published in the English language between Jan 1, 2011, and Apr 28, 2021. Only primary studies enrolling 10 or more patients were included, irrespective of country or region. Each eligible article was independently reviewed by two reviewers. The title and study abstracts were reviewed to assess eligibility for full-text review. The topics of interest were clinical, humanistic, and economic burden of disease, as well as current management and unmet needs in DM and PM. Information on geographic scope was extracted from the papers of included studies. The current abstract summarizes SLR results on humanistic burden of DM and PM in European patients.
Results: A total of 2,967 non-duplicated publications were retrieved from medical databases and analyzed against pre-defined study selection criteria. There were 2,574 records excluded at title and abstract screening. Remaining 393 records were analyzed in the full text with 208 papers considered relevant. Additional 21 papers were identified from searching reference list of relevant studies and conference proceedings. In total, 222 studies described in 229 publications were included in data abstraction. Among 43 studies conducted across 14 European countries, 12 studies evaluated health-related quality of life (HRQoL) and work productivity in patients with DM and PM. In 6 studies, patients received standard of care therapy. Six studies enrolled adults with DM and PM and 6 were conducted in patients with juvenile onset of DM. There were 6 cross-sectional analyses, 4 longitudinal cohort studies, 2 case-control studies, with sample size ranging from 11 to 246 patients. Adults with DM and PM had significantly worse HRQoL across multiple domains of 36-Item Short Form Survey (SF-36) compared to controls from general population, with a strong negative impact of muscle weakness on physical functioning. Patients reported high difficulties in performing leisure time activities, moving around and work as indicated by median scores of 4-5 points in a 7-point Myositis Activity Profile (MAP). Reduced grip force in DM and PM adults was significantly associated with worse performance in domestic activities in the MAP assessment ($p<0.05$). In women with DM and PM, poor grip force additionally impacted vitality and mental health as measured by SF-36 ($p<0.05$). There were no associations between grip force and any SF-36 domain in men. Approximately 60% of adult patients rated their ability to work as "poor" or "less good" according to the Work Ability Index, 68% of patients had more than one week of sick leave in the past year, and 20.8% of them were permanently not able to work for at least 2 years. Children and adolescents with DM had impaired physical and psychosocial functioning compared to healthy norms with 40% of individuals showing increased emotional distress requiring in-depth psychological assessment.
Conclusion: European patients with DM and PM experience a muscle weakness that has a detrimental impact on HRQoL, daily activities and ability to work. Similar disease impact on HRQoL was reported in patients in North America. These findings suggest a need for a novel therapy that will restore physical functioning in patients with DM and PM.
Disclosure of Interests: Jens Schmidt Speakers bureau: Euroimmun, CSL Behring, Consultant of: Alnylam, Argenx, Biotest, CSL Behring, Kezar Life Sciences, LFB, Novartis, Octapharma, UCB, Grant/research support from: CSL Behring, Novartis, Konrad Pisarczyk Consultant of: Kezar Life Sciences, Richard Leff Shareholder of: Kezar Life Sciences, Consultant of: Kezar Life Sciences, Kiruthi Palaniswamy Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Eunmi Park Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Li Long Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences

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AB1280 IGG4 RELATED DISEASE WITH ATYPICAL SCALENE MUSCLES INVOLVEMENT

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Background: IgG4 related disease is a chronic, immune-mediated, fibro-inflammatory condition that may affect nearly any organ, but most common presentations include salivary glands and lacrimal enlargement, orbital disease, pancreatitis, retroperitoneal fibrosis and tubulointerstitial nephritis. Even as IgG4-related disease is increasingly associated with head and neck manifestations, the involvement of scalene muscles hasn't been previously described.
Objectives: Describe an interesting case of IgG4 related disease presenting with scalene muscle and ocular manifestations.
Methods: Case report and clinical imaging
Results: 79-year-old female, with a history of Sjogren syndrome treated with hydroxychloroquine 200mg twice a week, presented with unilateral right blepharoptosis. Physical examination confirmed right eye ptosis, supraorbital soft tissue enlargement, diplopia and limited ocular movement. CT Scan revealed right and left orbit with diffuse enlargement of the right superior rectus, suggesting bilateral dacryoadenitis, and most important it described a pseudotumor of 5.7 cm x 3.2 cm x 6.2 cm infiltrating asymmetrically the lower portion of the left scalene muscle. Lacrimal biopsy and immunohistochemistry revealed IgG4 related disease (dense lymphocytic infiltrate, IgG4+:IgG+ ratio 53% and more than 10 cells/hpf). Serum IgG4 concentration 633 mg/dl (more than 5 times upper limit of normal). Pulmonary embolism was also detected. The patients received treatment with a tapering regime of oral prednisone and mycophenolate mofetil for long term immunosuppression, with adequate response and complete remission of symptoms.
Conclusion: The multiorgan involvement and recently recognized nature of IgG4 related disease, may cause confusion among physicians; leading to misdiagnosis, unnecessary procedures and delay in treatment. It requires a high degree of clinical suspicion to diagnose a IgG4 RD, when presenting with ocular involvement, and even more when it affects organs that are not usually associated with this condition, such as scalene muscles. The diagnosis is supported by pathognomonic histopathological findings, and even as treatment strategies are constantly evolving, glucocorticoids remain as first line treatment.
Whether this finding is related with those observed in the paravertebral band – like soft tissue in the thorax, has to be defined. Also interesting is that in this case, this pseudotumor is in the left side.

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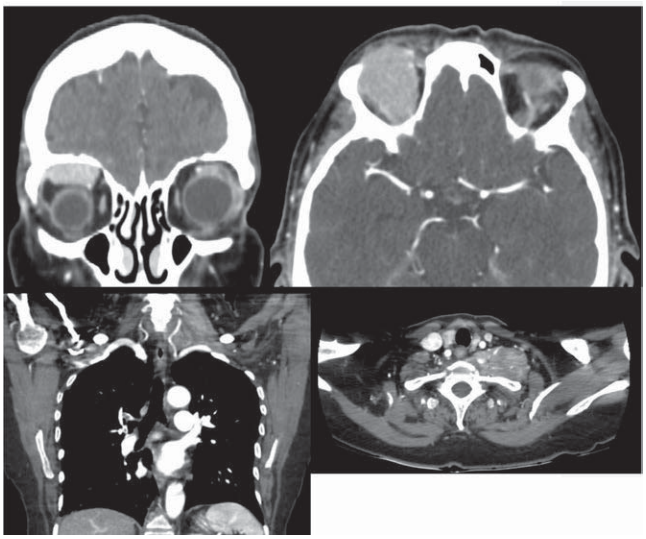

Figure 1.

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AB1281 PRESENTATION, TREATMENT AND PROGNOSIS OF SARCOIDOSIS IN A COHORT OF SPANISH PATIENTS

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Background: Sarcoidosis is usually a benign disease, but it is described that the lung is the most frequently affected organ and in some cases the disease can progress to pulmonary fibrosis. Systemic corticosteroids, immunosuppressants and/or monoclonal antibodies are used for its treatment. The mortality rate without treatment is 1% to 6%.
Objectives: To establish the frequency of appearance of the stages of radiological involvement in patients diagnosed with sarcoidosis at Ciudad Real University General Hospital (CRUGH) for 4 years, describe the treatment guidelines used and investigate the causes of death.
Methods: Retrospective descriptive study that includes patients treated at Pneumology, Rheumatology and Internal Medicine Services of CRUGH from January 2017 to January 2021. Sarcoidosis diagnosis has been established according to ATS/ERS/WASOG (1999) criteria: compatible clinical and radiological presentation, evidence of non-caseating granulomas and exclusion of other granulomatous disease. The variables have been collected in an anonymized database analyzed by SPSS program.
Results: We have included 47 patients, 24 men and 23 women, with 52.0 ± 14.3 years of age. All presented radiological pulmonary involvement and in 26 cases (55.3%) there were also extrapulmonary manifestations. The most frequent radiological pattern is stage II in 29 cases (67.7%, hilar adenopathies and pulmonary infiltrates); followed by stage I in 16 (34.1%, hilar adenopathies) and only 2 cases presented stage IV (4.2%, fibrosis). Currently, 20 patients (42.5%) are without treatment: 9 (19.1%) have not required it due to hyliomediastinal lymph node involvement without associated symptoms, and 11 (23.4%) achieve remission with oral glucocorticoids [OCG] at doses recommended in clinical guidelines. The other 27 (57.5%) receive these regimens: 10 (21.3%) OCG at usual doses; 11 (23.4%) OCG and conventional immunosuppressants -metrotexate 9 (19.1%), azathioprine 1 (2.1%) and cyclophosphamide 1 (2.1%)-; 3 (6.4%) OCG and antimalarials (hydroxychloroquine); 2 (4.2%) monotherapy with azathioprine; and 1 (2.1%) biological treatment with infliximab. Three patients died (6.4%): one aged 71 due to progression to pulmonary fibrosis (2.1%), another 2 due to pulmonary adenocarcinoma (47 years old) and due to adenocarcinoma of the rectum (81 years old).
Conclusion: The predominant radiological pattern in our cohort is stage II with hilar adenopathies and pulmonary infiltrates. The most used treatment is OCG, as monotherapy (44.7%) or combined (29.4%). The high frequency of cancer mortality stands out.

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AB1282 OVARIAN RESERVE IN BEHCET'S DISEASE

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Background: Behcet's disease (BD) is a multisystemic disease of unknown cause. Anti-Mullerian hormone (AMH) is one of the key parameters for assessing reproductive function and ovarian reserve. The levels of AMH correlates with the residual follicular pool in women of reproductive age.
Objectives: To assess AMH levels in BD female patients of child-bearing potential, and analyze the relationship between AMH levels and disease severity, as well as relationship between serum AMH levels and different therapeutic regimens.
Methods: The study group included 45 women with BD (according to ISGBD 1990 and ICBD 2014) aged 20-40 years, and the control group icluded 15 age-matching healthy women. Pts' mean age was 31,3 [27;35] yrs, disease duration 6 [3;8] yrs. 17,8% pts had severe BD according to Ch.Zouboulis classification (due to generalized uveitis, retinal vasculitis and parenchymatous CNS lesions), 37,8% pts had a moderate disease, 44,4% pts had a mild disease with mainly dermal-mucous manifestations. AMH levels was measured using ELISA. AMH reference values ranged within 1.0-10.6 ng / ml. Values <1.0 were interpreted as a decreased ovarian reserve.
Results: The mean levels AMH was 2.5 ng/ml in BD pts, and 3.1 ng/ml in control group, showing no statistical difference. A decrease in ovarian reserve (AMH less than 1.0 ng/ml) was observed with the same frequency 18% in patient's vs. in control group 13%. In the analysis of AMH, depending on the severity of BD, a decrease in ovarian reserve was more often observed in patients with moderate and severe forms of BD.

Table 1. AMH and severe BD

severe	mild, n=20	moderate disease, n=17	severe, n= 8	p
AMH	2,7 [1,6-3,5]	2,5 [1,0-3,7]	1,9 [0,8;6,7]	ns
AMH >1 ng/ml, %	10	23	25	0,02

There are no correlations of levels AMH with treatment of BD.

A decrease in ovarian reserve was noted in two patients under 30 years old, one was 29 years old woman with "Neurobehcet" with two children, and the patient with BB+AS was not married, had no pregnancies, and received colchicine therapy for a long time. Two BD patients with low AMH had no pregnancies - unmarried, all other patients with reduced ovarian reserve had from 1 to 6 children. When analyzing the levels of AMH with the clinical picture and BD therapy, no correlations were found.

Conclusion: The average levels of AMH in women with BD and in the control group did not differ. A decrease in ovarian reserve (AMH less than 1.0 ng/ml) occurred with the same frequency in patients with BD and controls. A decrease in ovarian reserve was more often observed in patients with moderate and severe BD.

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AB1283 HOW TO COUNSEL A WOMAN WITH BEHÇET'S DISEASE: RESULTS FROM A MONOCENTRIC COHORT OF WOMEN DIAGNOSED DURING CHILDBEARING AGE

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Background: Patients with autoimmune diseases require appropriate pregnancy counceling, as their disease can negatively impact both maternal and fetal outcomes. In regards to Behçet's disease (BD), although commonly diagnosed during the childbearing age, only few studies focused on its impact on gestation, with contradictory results.

Objectives: We aimed to collect new data on BD and its impact on pregnancy by designing a single-center cohort study, reporting the pregnancy and maternal outcomes in BD patients attending the Multidisciplinary Centre for Immunopathology and Rare Diseases at Giovanni Bosco Hospital (Turin, Italy).

Methods: We retrospectively included 26 women diagnosed with BD followed at our center. Out of 26 patients, data from 33 pregnancies in 16 women were collected. Ten patients were never pregnant. Table 1 shows the demographical and clinical characteristics and the pregnancy outcomes of the enrolled patients.

Table 1. Clinical characteristics and pregnancy outcome of the Behçet's disease patients enrolled in the study.

	Patients (tot=31)
Nulliparous; n (%)	10/26 (38,46%)
Primigravida; n (%)	16/26 (61,54%)
Demographics	
Age at BD diagnosis; mean± S.D.	40,56±11,42
Age at first pregnancy; mean ± S:D.	24,86 ± 6,56
Clinical characteristics of BD	
Oral ulcers; n (%)	26/26 (100 %)
Genital ulcers; n (%)	21/26 (80,76%)
Folliculitis; n (%)	15/26 (57,69%)
Erythema nodosum; n (%)	6/26 (23,08%)
Ocular manifestations; n (%)	11/26 (42,31%)
HLA B-51+; n (%)	13/26 (50%)
Pregnancy outcome	
Rate of live births; n (%)	27/33 (81,81%)
Any complications; n (%)	12/33(36,36%)
Early miscarriage before 10 weeks of gestation; n (%)	6/33 (18,18%)
Gestational diabetes; n (%)	3/33 (9,09%)
Placental abruption; n (%)	2/33 (6,06%)
Vaginal bleeding before 20 weeks of gestation; n (%)	1/33 (3,03%)
Worsening of oral and genital ulcerations; n (%) *	2/ 11 (18%)

* This information was available only for 11/33 pregnancies.BD – Behçet's diseaseS.D – Standard deviation

Results: All included patients fulfilled the international criteria for BD (1), with a median age at the time of diagnosis of BD and first pregnancy of 40,56±11,42 and 24,86±6,86 respectively. The frequency of clinical manifestations was oral ulcers (100%), genital ulcers (80,76%), erythema nodosum (23,08%), folliculitis (57,69%), ocular manifestations (42,31%) and HLA B-51+ (50%), respectively. The overall rate of live births was 81,81% (27/33). Twelve women experienced pregnancy complications (36,36%), in particular we report one case of vaginal bleeding before 20 weeks of gestation, six miscarriages before the 10th week of gestation, three cases of gestational diabetes and two placental abruptions. Among the analyzed pregnancies, a worsening of oral and genital ulcerations was observed in the 18% of them, while in the remaining cases a subjective amelioration of aphtosis and other concurrent symptoms was reported by the patients. No systemic flare, worsening of ocular complications and VTE was reported during pregnancy and in the post-partum period.

Conclusion: The results of our study highlight an overall favorable rate of life births in BD women and a positive rate of disease remission in pregnancy. Currently, the studies focusing on pregnancy outcomes in BD are scarce, however it might be appropriate to give a specialized counseling to a BD woman planning for a pregnancy and follow these patients with a multidisciplinary approach.

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AB1284 GENDER CHARACTERISTICS OF IDIOPATHIC LOBULAR PANNICULITIS

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Background: Idiopathic lobular panniculitis (ILP) (Weber-Christian disease) is the least studied disease from the group of "systemic lesions of the connective tissue" and is characterized by a multifaceted lesion of the subcutaneous adipose tissue (SAT) of organs.

Objectives: to compare the incidence of clinical and laboratory manifestations of ILP in patients of different sexes in the Russian cohort.

Methods: We examined 67 patients (9 men and 58 women) aged 20 to 76 years with an average duration of the disease 78.91 months [48; 540] with a verified diagnosis of ILP, who were observed at the V.A. Nasonova Research Institute of Rheumatology in 2010-2021. In addition to general clinical examination, determination of the titer of α-1 antitrypsin, liver fractions, amylase, lipase, trypsin, ferritin, creatine phosphokinase, leptin, TNF-α, computed tomography of the chest and pathomorphological studies of induration were carried out.

Results: The peak of the disease in men (55.55%) was detected at 35–45 years old, while in women (38.5%) from 50 to 60 years old. In 55.2% of women, two periods of the development of the disease were identified – from 16 to 25 in 12 patients (32.4%) and from 46 to 60 in 25 patients (67.5%). When analyzing the demographic indicators in patients with ILP, 86.3% were residents of the European part of Russia, no gender differences were found. In 3 men (33.3%) and 22 women (37.9%), ILP was diagnosed within a year. With the disease duration of 1 to 5 years, the diagnosis was confirmed in 44.4% of men and in every third woman. The duration of more than 5 years from the onset of the first symptom to the establishment of a reliable diagnosis of ILP in women was 32.7%, while in men – 11.1% ($p < 0.03$). The nodular form (Nf; 55.5%) and the mesenteric form (Mf; 33.3%) were observed somewhat more often in men than in women, with a tendency to a higher body temperature and a greater number of painful (according to VAS) indurations. In women, Nf was found in 43.1% of cases, plaque form and Mf – in 15.5% each. The infiltrative form (25.8%) was found only in women. Indurations were characterized by a subfebrile temperature, mainly with localization on the thighs (75.8%), upper limbs (51.7%) and trunk (43.1%). Later, in 31 patients (46.2%) (93.5% of them were women), a combination or transition from one form to another was detected, indicating a mixed nature of the disease. Body temperature indices in men were inversely correlated with the duration of the disease ($r = –0.73$; $p < 0.05$). In women, there was a significant association of an increase in body temperature with pain (according to VAS) of the nodes ($p < 0.05$), as well as with the form of the disease ($p < 0.03$). Average ESR data were higher in women (24.50 ± 15.99 mm/h). In men, a high level of CRP (46.2 ± 21.7 pg/ml) was significantly more often observed with Mf ($p < 0.0176$), which correlated with the concentration of TNF-α ($r = 0.72$; $p < 0.05$). Women had a 2.3 times higher leptin content than men ($r = 0.46$; $p < 0.05$). Pathomorphological examination of a biopsy of the skin and SAT confirmed lobular panniculitis (ILP) in all cases.

Conclusion: In the Russian cohort of patients, male gender is associated with a progressive course of the disease, which is the basis for prescribing immunosuppressive therapy for men with ILP at early stages of the disease.

Disclosure of Interests: None declared

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AB1285

BEHCET'S DISEASE IN RUSSIAN FEDERATION: GENDER RELATED CLINICAL FEATURES

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Background: In Behcet's Disease (BD) some major organs are more involved in men and have worse outcomes. Gender related clinical features of BD are different in various countries.
Objectives: to describe the gender related clinical features of Russian Federation's cohort of BD patient's.
Methods: This single center cohort study was carried out at the V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia from 1990 to 2021. 560 of BD patients (351 men (62,7%) and 209 (37,3%) women were consecutively enrolled in the study. All the patients met the ICBD (2014). The activity of the disease was determined using a Behcet's Disease Current Activity Form (BDCAF). Clinical features of the BD were compared according to the patient's gender.
Results: Female to male ratio was 1,0: 1,7. The majority of patients were natives of the North and South Caucasus (66,0%) and ethnic Russians (21,6%). Mean (M±SD) age of male and female did not differed at the study inclusion (32,4±9,65 vs 33,8±10,5 years) and at disease onset (22,1±9,67 vs 22,6±10,8 years). The most frequent clinical manifestations were oral and genital aphthosis, skin, ocular and joints involvements. Men had higher BD-activity score (BDCAF) (p<0,001), prevalence of skin (91,1% vs 79,4%, OR=1,57, 95% CI=0,95-2,58, p<0,001), ocular (68,4% vs 48,8%, OR=1,38, 95% CI=0,96-1,96, p<0,001), vascular (venous and arterial thrombosis) involvement (21,4% vs 11,5%, OR=1,26, 95% CI=0,77-2,07, p=0,002), pathergy test (33,3% vs 22,9%, OR=1,19, 95% CI=0,80-1,77, p=0,004) and HLA-B51 (65,0% vs 40,6%, OR=1,53, 95% CI=1,02-2,29, p<0,001) positivity. Male and female did not differ in prevalence of oral and genital aphthosis, joint, neurological, gastrointestinal manifestations (Table 1).

Table 1. BD manifestations in the Russian Federation depending on gender

Characteristics, M±SD; n (%)	Male, n=351	Female, n=209	p
Mean age, yrs	32,4±9,65	33,8±10,5	n/s
Mean age at disease onset, yrs	22,1±9,67	22,6±10,8	n/s
BDCAF, point	7,43±2,23	6,62±2,11	<0,001
Oral aphthosis	338 (96,3%)	204 (97,6%)	n/s
Genital ulcers	245 (69,8%)	146 (69,8%)	n/s
Ocular involvement	240 (68,4%)	102 (48,8%)	<0,001
Skin involvement	320 (91,1%)	166 (79,4%)	<0,001
Positive pathergy test	117 (33,3%)	48 (22,9%)	0,005
Gastro-intestinal involvement	67 (19,1%)	37 (17,7%)	n/s
Neurological involvement	52 (14,8%)	21 (10,0%)	n/s
Vascular involvement	75 (21,4%)	24 (11,5%)	0,002
Joints involvement	230 (65,5%)	137 (65,6%)	n/s
HLA-B5(51) positivity	158 from 243 (65,0%)	71 from 175 (40,6%)	<0,001

Conclusion: Russian Federation's cohort of BD patients did not differ in clinical characteristics from other world regions. Ocular, skin, vascular lesions, positive pathergy test and HLA-B51 positivity are more frequent in men than in women.
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AB1286

BEHCET'S DISEASE IN RUSSIAN FEDERATION: ETHNICITY RELATED CLINICAL FEATURES

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Background: clinical manifestations of Behcet's Disease (BD) determine the prognosis and differ in patients of different ethnicity.
Objectives: to describe the ethnicity related clinical features of Russian Federation's cohort of BD patient's.
Methods: This single center cohort study was carried out at the V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia from 1990 to 2021. 560 of BD patients (351 men (62,7%) and 209 (37,3%) women) were consecutively enrolled in the study. All the patients met the ICBD criteria (2014). The activity of the disease was determined using a Behcet's Disease Current Activity Form (BDCAF). Clinical features of the BD were compared according to the patient's ethnicities.
Results: The majority of patients were natives of the North and South Caucasus (370 (66,0%)) and ethnic Russians (121 (21,6%)), 48 (8,57%) - natives of Central Asia, 12 (2,14%) – Ukrainians/ Moldovans, 6 (1,07%) – Yakuts/ Evenks and 3 (0,53%) - Jews. Mean age of Caucasus and Russians patients did not differ; the Russian were significantly older than Central Asia patients. Patients of different ethnicities did not differ in the BDCAF score. The most frequent clinical manifestations were oral aphthosis and skin involvements for all groups. Joints involvement occurred with a similar frequency in all groups. Genital ulcers were significantly more common in Russians and Caucasus compared to Central Asia patients. Ocular and vascular involvement was more typical for the Central Asia and the Caucasus natives. Gastrointestinal and neurological manifestations were more common for Russians. HLA-B51 positivity was less frequent in the Russians (Table 1).

Table 1. BD manifestations in the Russian Federation depending on ethnicity

Characteristics,	North and South Caucasus, n=370	Russians, n=121	Central Asia, n=48	p
M±SD; n (%)	1	2	3	
Mean age, yrs	32,7±9,74	34,5±11,0	29,9±9,15	P_{2-3}=0,012
Mean age at disease onset, yrs	22,5±9,74	22,8±11,5	18,5±8,98	p_{1-3}=0,011 p_{2-3}=0,027
BDCAF, point	7,27±2,34	6,90±1,85	6,93±1,98	n/s
Oral aphthosis	360 (97,3%)	117 (96,7%)	46 (95,8%)	n/s
Genital ulcers	263 (71,0%)	88 (72,7%)	26 (54,2%)	P_{1-3}=0,015; P_{2-3}=0,017
Skin involvement	324 (87,6%)	101 (83,5%)	40 (83,3%)	n/s
Positive pathergy test	99 (26,7%)	45 (37,2%)	16 (33,3%)	p_{1-2}=0,020
Ocular involvement	232 (62,7%)	58 (47,9%)	34 (70,8%)	p_{1-2}=0,003, p_{2-3}=0,005
Gastrointestinal involvement	59 (15,9%)	33 (27,3%)	7 (14,6%)	p_{1-2}=0,005
Neurological involvement	44 (11,9%)	21 (17,3%)	3 (6,3%)	P_{2-3}=0,046
Vascular involvement	72 (19,5%)	18 (14,8%)	10 (20,8%)	n/s
Joints involvement	246 (66,5%)	83 (68,6%)	27 (56,2%)	n/s
HLA-B5(51) positivity	179 from 251 (71,3%)	28 from 79 (35,4%)	20 from 36 (55,5%)	P_{1-2}<0,001, P_{1-3}=0,044, P_{2-3}=0,034

Conclusion: Behcet's disease is most often detected in natives of the North and South Caucasus, Russians and natives of Central Asia in the Russian Federation's cohort. Differences in the frequency of various clinical manifestations depending on the ethnicity of patients were revealed.
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AB1287

DESIGN OF A GLOBAL PHASE 2/3 RANDOMIZED, PLACEBO-CONTROLLED TRIAL EVALUATING THE EFFICACY AND SAFETY OF RAVULIZUMAB IN ADULTS WITH DERMATOMYOSITIS

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Background: Dermatomyositis (DM) is a rare and life-altering chronic immune-mediated disease characterized by distinct skin rash and/or progressive muscle weakness and other systemic manifestations. Many patients are refractory and/or experience serious adverse effects when treated with currently prescribed medications, including high-dose systemic steroids and immunosuppressive therapies[1-3], which are often prescribed off-label. Therefore, there is a need for new DM treatment options that offer more favorable risk-benefit profiles. The classical complement pathway is implicated in DM pathophysiology, including a close correlation between endothelial deposition of the C5b-9 membrane attack complex (MAC) and organ damage.[4] Treatment with the long-acting anti-C5 monoclonal antibody ravulizumab is associated with immediate, complete, and sustained inhibition of the complement protein C5, which prevents its cleavage to form MAC, and it has proven to be a safe and effective therapeutic approach for multiple complement-mediated diseases.[5]
Objectives: Given the continued unmet need in DM and the evidence implicating the terminal complement pathway in the disease pathophysiology, a global, multi-center double-blind, randomized, placebo-controlled Phase 2 (Part A)/Phase 3 (Part B) trial was designed to evaluate the efficacy and safety of the C5 inhibitor ravulizumab compared with placebo in adults with DM (ALXN1210-DM-310; NCT04999020; EudraCT2021-001200-15).
Methods: A total of 180 adult patients with DM[6] who have active disease with muscle weakness and inadequate responses or intolerances to two or more DM treatments including glucocorticoids will be randomized to receive either intravenous

ravulizumab or placebo, delivered as loading dose followed by maintenance administration once every eight weeks. Different patients will be enrolled in Parts A and B, which each consist of a screening period, a randomized, controlled period (Part A; 26 weeks; Part B: 50 weeks), and an open-label extension period. The primary endpoints are the proportion of patients with a minimal improvement from baseline on the ACR/EULAR Myositis Response Criteria Total Improvement Score (TIS20) at 26 weeks (Part A) and 50 weeks (Part B). In addition, a wide range of key secondary and exploratory outcome measures will be evaluated, including the mean change from baseline in the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score and a novel participant-reported outcome measure, the Dermatomyositis-Disease Symptoms Questionnaire (DM-DSQ). Safety will be assessed by analyzing the incidence of treatment-related adverse events (TEAEs), including those classified as serious and/or leading to intervention discontinuation.

Results: The ALXN1210-DM-310 trial is currently enrolling patients.

Conclusion: ALXN1210-DM-310 is the first global, multi-center, randomized, placebo-controlled Phase 2/3 interventional trial designed to evaluate the safety and efficacy of a C5 inhibitor in adult patients with DM who continue to have active disease despite treatment with standard medications.

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AB1288 FIRST USE OF ETORICOXIB FOR LOBULAR PANNICULITIS

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are the primary means of controlling chronic pain in many rheumatic diseases and, in particular, in lobular panniculitis (LPn).

Objectives: to evaluate a possibility of effective and safe control of patients with LPn during long-term use of NSAIDs in clinical practice.

Methods: We studied 21 patients (15 women and 6 men, average age 41.2±9.3 years) with LPn who were treated with etoricoxib in a dose of 60 mg/day. Patients' condition was assessed at the time of prescription, after 2 and 4 weeks of therapy, and 4 weeks after discontinuation of treatment (8 weeks from baseline). Localization, prevalence, color and number of affected skin areas and subcutaneous fat were determined during clinical examination. Pain intensity in motion was evaluated by 10-cm Visual Analog Scale (VAS), as well as general health score (GHS) on a 10-cm VAS, pain intensity on the Likert Verbal Rating Scale (VRS) (0-4), number of patients with pain reduction ≥50% from baseline, and patients' assessment of therapy outcome on the Likert VRS (1-5). Adverse reactions (ARs) were evaluated at each visit. General clinical examination included standard diagnostic methods.

Results: In 90% of cases, the affected areas of skin and subcutaneous fat were located on the tibia, mainly on the anterior and medial surface, in 33% – on the hips, in 24% – on the upper extremities, and in 5% – on the torso. Symmetrical rashes occurred in 62% of patients. In 48% of patients the nodes merged into a conglomerate. The fact that more than 50% of the lower leg surface (67%) was affected was directly associated with the number of nodules ($p < 0.001$; $r = 0.60$) and C-reactive protein level ($p = 0.006$; $r = 0.38$). There was a direct correlation between the number of nodules and the duration of LPn ($p = 0.04$; $r = 0.20$) and their tendency to merging ($p < 0.001$; $r = 0.39$). Signs of joint involvement were detected in 14 patients (67%), with predominant involvement of the ankle (67%) and knee (38%) joints. In 29% of the patients, the affected joints were asymmetrical. All patients took Etorax for 4 weeks. Mean pain severity (according to VAS) at baseline, after 2, 4 and 8 weeks was 6.5±1.2; 4.8±1.4; 2.6±1.4; 2.2±1.1 cm (significant difference from baseline in all points, $p<0.05$). Similarly, there was a statistically significant difference in VAS values. The number of patients with moderate/severe pain (Likert scale) decreased from 77.8% to 24.9%, 2.9%, and 2.3%. The number of patients with pain reduction ≥50% from baseline were 12.0%, 65.1%, 81.0%, and 78.5%. A good or excellent rating of the treatment results after 2 weeks was demonstrated by 57.1% and after 4 weeks by 76.1% of patients. ARs were registered in approximately 14.2% of patients, mostly mild dyspepsia (in 5%) and arterial hypertension (in 10%). No severe ARs were reported

Conclusion: Etoricoxib is effective and relatively safe for long-term control of chronic pain in LPn.

Disclosure of Interests: None declared

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AB1289 STUDY DESIGN OF A PHASE 2/3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF NIPOCALIMAB, AN FCRN ANTAGONIST, IN WARM AUTOIMMUNE HEMOLYTIC ANEMIA (WAIHA)

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Background: Warm autoimmune hemolytic anemia (wAIHA) is characterized by the destruction of red blood cells (RBCs) by pathogenic autoantibodies which bind to RBCs and lead to their clearance in the spleen and liver. Patients with wAIHA can experience acute worsening of anemia, which can be a medical emergency, and have an increased risk of thromboembolic events and premature death. Nipocalimab is a fully human, aglycosylated, effectorless IgG1 monoclonal antibody that targets the IgG binding site on the neonatal Fc receptor (FcRn) with high affinity. FcRn, which is expressed in endothelial cells, is responsible for recycling IgG into the circulation and for the relatively long half-life of IgG antibodies compared to other Igs. It is expected that nipocalimab, by inhibiting IgG binding to FcRn, will prevent IgG recycling and lower pathogenic IgG autoantibodies that cause many autoimmune diseases including warm autoimmune hemolytic anemia (wAIHA). Nipocalimab has been studied in multiple phase 1 studies in healthy subjects and in a recently completed phase 2 study in subjects with Generalized Myasthenia Gravis (gMG). In the gMG phase 2 study, nipocalimab was well tolerated at doses from 5 mg/kg every 4 weeks to 60 mg/kg every 2 weeks. Treatment with nipocalimab was associated with rapid and durable total serum IgG and pathogenic IgG autoantibody reduction and meaningful clinical response. A statistically significant relationship between IgG autoantibody reduction and clinical benefit was observed. This study provided proof-of-concept evidence that lowering pathogenic IgG autoantibodies can ameliorate the autoimmune condition these antibodies cause.

Objectives: To share the rationale and study design for an adaptive, phase 2/3 multicenter, randomized, double-blind, placebo-controlled study in patients with wAIHA whose aim is to evaluate the efficacy, safety, tolerability, PK, and PD of nipocalimab compared with placebo[1].

Methods: Male or female patients ≥18 years of age who have been diagnosed with primary or secondary wAIHA and have not experienced a sufficient response or have not tolerated currently available treatments will be included in the study. Patients with cold antibody AIHA, cold agglutinin syndrome, mixed type (i.e., warm and cold) AIHA, or paroxysmal cold hemoglobinuria will be excluded. Patients will be randomized 1:1:1 to receive nipocalimab at two different dose schedules or placebo. Following completion of 24 weeks of double-blind treatment, patients may enter an open-label extension period to receive nipocalimab.

Results: The following endpoints will be analyzed:

Primary endpoint: Percentage of participants achieving durable response of improvement in hemoglobin (Hgb).

Main secondary endpoints: Change from baseline in the total score from the Functional Assessment of Chronic Illness Therapy-Fatigue Scale at the end of the double-blind period. Number of participants who attain normal lactate dehydrogenase, normal haptoglobin, and normal indirect bilirubin levels at a minimum of 3 consecutive visits after baseline.

Conclusion: A phase 2 study investigating nipocalimab in patients with gMG provided proof of concept for a phase 2/3 interventional study with nipocalimab in patients with wAIHA. This phase 2/3 study is currently enrolling in the USA and Europe.

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AB1290 SOMETIMES IT IS ALL IN THE HEART; CARDIAC INVOLVEMENT IN BEHCET'S SYNDROME

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Background: Cardiac involvement is an uncommonly seen but might be a fatal clinical manifestation of Behcet's syndrome (BS), if not recognized early and treated aggressively.
Objectives: Our aim was to retrospectively evaluate the characteristics of cardiac involvement in Behcet's syndrome and investigate possible risk factors.
Methods: 800 patients with BS diagnosis according to International Study Group for Behcet's Disease (ISG) criterias in our center were screened. 14 patients with cardiac involvement were included in this study.
Results: All the patients were male with positive smoking history. The age at the onset cardiac involvement was 32.5 ± 7.8 years. In 3 patients, diagnosis of BS was made simultaneously with cardiac involvement. Types of cardiac involvement were as following; intracardiac thrombosis (ICT) in 8, right coronary artery aneurysm in 2, and myocardial infarction in 4 patients. The majority of ICT was seen in right ventricle followed by right atrium (75% vs 25%). Deep vein thrombosis (DVT) was the most common accompanying other vascular involvement (57%).Thrombophilic factors were studied in 8 patients, whom only 2 cases were found positive for heterozygous factor V Leiden mutation. Cyclophosphamide was the most common used immunosuppressive agent and anticoagulation was used in 9 patients (Table 1).

Table 1. Characteristics of cardiac involvement in BS patients

Male/female, (n), (%)	14 (100%)
Diagnosis age, years (Mean ± SD)	30 ± 7
Age of cardiac involvement, years, (Mean ± SD)	32.5 ±7.8
Smoking history, (n), (%)	14 (100%)
Other vascular involvement, (n), (%)	12 (85%)
-Deep vein thrombosis, (n)	8
-Pulmonary involvement, (n)	4
-Peripheral artery aneurysm, (n)	1
Cardiac involvement patterns	
-ICT, (n), (%)	
• RV	6
• RA	2
-CAA, (n), (%)	2(14.3%)
-AMI, (n), (%)	4(28.6%)
Immunosuppression, (n)	
-Steroid	14
-CYC	9
-AZA	3
-IFN	1
Anticoagulation, (n)	9

ICT; intracardiac thrombosis, RV; right ventricle, RA; right atrium, CAA; coronary artery aneurysm, AMI; acute myocardial infarction, CYC; cyclophopshamide, AZA; azathioprine, IFN; interferon

Conclusion: Most common type of cardiac involvement is pericarditis, whereas intracardiac thrombosis has its unique characteristics (1). Male gender and smoking seems to be major significant risk factors.
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AB1291 AGE OF ONSET AND DIAGNOSTIC DELAY IN PATIENTS WITH MONOGENIC AUTOINFLAMMATORY DISEASES AND SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS - DATA FROM THE FEDERAL CENTER IN RUSSIAN FEDERATION

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Background: Autoinflammatory diseases (AIDS) are a group of rare monogenic and multifactorial diseases manifested by systemic inflammation, organ disorders, the development of complications, primarily amyloidosis, and possible death without timely targeted therapy. Rapid diagnosis contributes to the early appointment of treatment, prevention of the development of organ damage and improvement of prognosis in such patients.
Objectives: To establish the age of the onset and the duration of the delay of diagnosis in patients (pts) with monogenic AIDS (m AIDS) and systemic juvenile idiopathic arthritis (sJIA) according to the Federal Rheumatology Center.
Methods: 273 pts were included in the study for the period from 2007 to 2021, 158 of them with mAIDS: FMF - 75, CAPS - 50, TRAPS - 28, HIDS/MKD - 5; 115 pts with sJIA.
Results: The age of pts with mAIDS ranged from 6 months to 65 y.o. (120 children and 38 adults), among pts with sJIA there were only children aged 12 months to 17 y.o. Most of the pts with CAPS, TRAPS, HIDS/MKD were female (62.4%), as with sJIA (57.4%). FMF was more often affected by male persons (56.6%). The age of the onset of mAIDS ranged from 0 to 53 y.o., sJIA - from 4 months to 15 y.o., was the smallest in pts with CAPS and HIDS/MKD. 33.5% pts with mAIDS had the onset of the disease from birth or within the first year of life, more often with CAPS and HIDS /MKD, in the first decade of life in half of the pts (52.5%), more often in FMF and TRAPS, from 10 to 18 years - 8.2%, in adulthood - 5.7%. In pts with sJIA, the onset of the disease was mainly in the first 5 years of life – 69 (60%), from 5-10 years – 38 (33%), rarely in the first year of life and after 10 years of age (6.95%). The duration of the disease at the time of diagnosis ranged from 1 month to 48 years in FMF pts, from 1 month to 46 years with CAPS, from 3 months to 59 years with TRAPS, from 3.5 to 16.5 years with HIDS/MKD, from 3 weeks to 7.8 years with sJIA. Within 1 year the diagnosis was established in 15.2% of children with mAIDS, in 12.2% with sJIA, in the first 5 years of the disease in 35.4% and 15.6% respectively. The delay in diagnosis for more than 5 and 10 years was observed in 24.1% and 25.9% of pts with mAIDS, practically did not occur in sJIA. The least delay in diagnosis was noted in pts with FMF.
Conclusion: Most of the pts with mAIDS had the onset of the disease in the first 5-10 years of life, an earlier age of onset was noted in pts with CAPS and HIDS/MKD. To date, the delay in diagnosis in pts with mAIDS remains very long and reaches decades, especially with CAPS, TRAPS and HIDS/MKD. In pts with sJIA, the diagnosis was established faster, according our opinion a later diagnosis is associated with a polycyclic course of the disease. Earlier diagnosis and the appointment of targeted therapy are needed, which will help to avoid complications, improve the prognosis and quality of life of pts.
Disclosure of Interests: None declared
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AB1292 CHARACTERISTICS OF UVEITIS IN BEHCET'S SYNDROME; A RETROSPECTIVE ANALYSIS OF 109 PATIENTS

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Background: Uveitis is still an important cause of morbidity leading to vision loss in Behcet's syndrome (BS).
Objectives: Our aim in this study was to retrospectively evaluate characteristics of uveitis, long term complications, and its association with the other components of BS.
Methods: 800 patients with BS diagnosis according to International Study Group for Behcet's Disease (ISG) criterias in our center were screened and among those, data of 109 patients with BS-related uveitis were included in this study.
Results: The overall prevalence of uveitis was found 13% among all BS population. Majority of BS-related uveitis were male (65,1%/34,9%). Mean age for BS diagnosis and onset of uveitis were found 28 ± 8,48 and 27 ± 8,42 years. In this group, uveitis developed before BS diagnosis in 33% of patients,

Table 1.

	FMF	CAPS	TRAPS	HIDS/MKD	sJIA
Age (me, IQR) y	10,5[6,0;15,4]	13[7,0;31,5]	9,0[7,9;14,5]	9,0[5,0;17]	4,5[2,8;7,6]
Age of onset	3[1,5;5]	1,0[0,15;7,0]	4,0[1,0;7,1]	0,5[0,4;1,5]	4,2[2,1;6,75]
(me, IQR), y	18 (24%)	24(48%)	8 (28,6%)	3 (60%)	8 (6,95%)
≤1y	46 (61,3%)	18 (36%)	17 (60,7%)	2 (40%)	99 (86,1%)
>1-10y	7 (9,3%)	5 (10%)	1 (3,6%)	-	8 (6,95%)
>10-18y	4 (5,3%)	3 (6%)	2 (7,1%)	-	-
>18y					
Delayed diagnosis (me, IQR), y	10,5[6,0;15,4]	13[7,0;31,5]	9,0[7,9;14,5]	9,0[5,0;17]	0,25[0,1;0,5]
≤1y	11 (14,7%)	9 (18%)	4 (14,3%)	-	14 (12,2%)
>1-5y	30 (40%)	12 (24%)	12 (42,9%)	2 (40%)	18 (15,6%)
>5-10y	20 (26,7%)	11 (22%)	6 (21,4%)	1 (20%)	1 (0,9%)
>10y	13 (17,3%)	18 (36%)	8 (28,6%)	2 (40%)	-

whereas 44% were diagnosed at onset of uveitis.The frequency of this population was estimated 6% among all BS patients,. Characteristics of uveitis were as following; unilateral (45/99), bilateral (54/99), anterior (12), posterior (30), panuveitis (30), retinal vasculitis (9) and not defined (9). 25 patients experienced only one attack, whereas more than one attack was seen in 45 patients during follow up. 74 patients whose complications data was available, cataract, maculopathy, glaucoma, and optic atrophy developed in 10, 7, 6 and 3 patients, respectively. Vision loss was seen in 8 patients as partial, in 28 as total (Table 1).

Table 1. Characteristics of uveitis, complications and other components of BS patients

Male/female, (n), (%)	71/28 (%65,1/%34,9)
Age at diagnosis, years (Mean± SD)	28 ±8,48
Age at uveitis, years (Mean± SD)	27 ±8,42
Uveitis-Behcet's diagnosis relationship, (n)	109
-Before, (n), (%)	36 (%33)
-At the time of, (n), (%)	48 (%44)
-After, (n), (%)	25 (%23)
Characteristics of uveitis, (n)	99/109
-Unilateral/Bilateral	45/54
-Anterior	12
-Posterior	30
-Panuveitis	30
-Retinal vasculitis	9
Complications, (n)	26/74
-Maculopathy	7
-Glaucoma	6
-Cataract	10
-Optic atrophy	5
-Vision loss (partial/total)	8/28

BS; Behcet's syndrome

Conclusion: Male gender and onset at young age are important risk factors for uveitis development. Uveitis is seen as a critical component for diagnosis. Complications, despite declining in the era of biologics use, are still a major concern. Retrospective design and missing data are limitations of this study.

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AB1293 INTRATHECAL INJECTION OF METHOTREXATE COMBINED WITH DEXAMETHASONE FOR COGAN SYNDROME WITH NEUROLOGICAL INVOLVEMENT: A CASE REPORT

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Background: Cogan syndrome (CS) is a rare autoimmune disease, mainly occurring among young people, with an incidence rate of <0.11/100000 (100000). CS is mainly characterized by interstitial keratitis, visual loss associated with cochlear vestibular involvement and Meniere type vertigo. It usually involves all systems of the body, and about 10% to 13% of cases have nervous system involvement. Fewer than 400 cases have been reported worldwide (*1*). Glucocorticoid is mainly used in acute attack as the basis of treatment, the effect was not satisfactory(*2*). Here, we report a case of CS with nerve injury as the main manifestation, which was successfully treated by intrathecal injection of methotrexate combined with dexamethasone.

Objectives: CS often involves multiple systems throughout the body and has a poor clinical prognosis. From a review of our patient's treatment experience, intrathecal methotrexate combined with dexamethasone may be an effective treatment modality for CNS involvement in patients with refractory recurrent Cogan syndrome.

Methods: The clinical manifestation, laboratory test, treatment, and outcome were described.

Results: A 31-year-old man presented with recurrent bimanual joint pain for 2 years, after which the patient developed interstitial keratitis, hearing loss and was diagnosed with CS. The patient received treatment with glucocorticoid, cyclophosphamide, methotrexate, tacrolimus, leflunomide, mycophenolate mofetil, hydroxychloroquine, adalimumab. The joint pain was improved, but the headache, dizziness, tinnitus and hearing impairment were significantly aggravated, and syncope occurred. Cerebrospinal fluid examination for lumbar puncture on admission of the patient showed CSF pressure > 185 mmH_2O, CSF microprotein 1.10 g/l, and CSF nucleated cell count 120x10^6 /L. At the beginning, we successively treated the patient with methylprednisolone (40 mg, QD), gamma globulin (10 g, QD), methotrexate (20 mg, QW) and cyclophosphamide (100 mg, QOD), but the effect was not satisfactory. After excluding infection, we treated this patient with intrathecal methotrexate 10 mg combined with dexamethasone 10 mg, and the patient's symptoms of dizziness, headache, and tinnitus improved significantly, and his hearing did not decline significantly any more. The patient received a total of seven intrathecal injections (cumulative methotrexate 60 mg + dexamethasone 65 mg) during the subsequent 6 months. His dizziness, headache, tinnitus and other neurological symptoms improved significantly, no further syncope, fever. CSF protein quantification and the number of CSF nucleated cells decreased significantly.

Conclusion: CS patients are often accompanied by multisystem injuries, so it is essential to correctly identify CS and provide appropriate treatment as soon as possible. For patients with neurological involvement who do not respond to treatment with glucocorticoids and immunosuppression, intrathecal methotrexate combined with dexamethasone may be considered as a treatment option for CS in the future.

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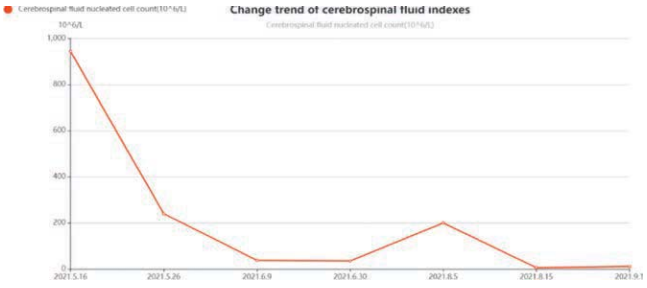

Figure 1. Change trend of nucleated cell count in cerebrospinal fluid during treatment

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AB1294 CO-OCCURRENCE OF IGG4 RELATED DISEASE AND OTHER SYSTEMIC IMMUNO-MEDIATED DISORDERS.

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Background: IgG4-related disease (IgG4RD) is a fibroinflammatory disease with unique clinical and pathophysiological features. According to the recently released Classification Criteria, the presence of other concomitant immunological disorders (OID) represents an exclusion criterion for the classification of IgG4RD (1). Rigorous application of the Classification Criteria, however, can lead to misdiagnosis because our increasing appraisal of IgG4RD indicates that this condition may coexists with OID (2).

Objectives: To describe IgG4RD presentation in the context of OID.

Methods: IgG4RD was diagnosed based on definitive histological findings. OID were diagnosed based on specific classification/diagnostic criteria.

Results: In six out of 234 (3%) patients IgG4RD occurred in accompaniment with OID, including two patients with sarcoidosis (33%), two with granulomatosis with polyangiitis (33%) one with eosinophilic granulomatosis with polyangiitis (16%) and one with Takayasu arteritis (16%). In three cases IgG4RD preceded OID (Table 1).

Conclusion: Our data demonstrate that IgG4RD can occur in overlap with OID, especially granulomatous diseases. Further research is needed to define whether this clinical scenario is associated with different pathological bases and long-term outcomes.

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Table 1. *ACR / EULAR 2017 provisional classification criteria for GPA **ACR 1990 Classification criteria for EGPA ***Modified diagnostic criteria for Takayasu arteritis. Shanna et al. 1995. Abbreviations: AZA: Azathioprine; CYC: Cyclophosphamide; EGPA: Eosinophilic Granulomatosis with Polyangiitis; ENG: electroneurography; GPA: Granulomatosis with Polyangiitis; IgG4RD: IgG4 Related Disease; INFX: Infliximab; F: female; M: male; MPDN: Methylprednisolone; MTX: Methotrexate; N: No; PDN: Prednisone; RTX: Rituximab; TCZ: Tocilizumab; Y: Yes

GENDER (Age at IgG4RD diagnosis^)		M (56)	M (69)	F (47)	F (51)	M (65)	F (16)
IgG4RD	Organs involved	pancreas, biliary tract, lymphnodes, nasal cavities, skin, ascending aorta	salivary glands, pancreas, biliary tract, lung	eyelid	periorbital region, lacrimal gland	meninges, abdominal aorta	peritoneum
	ACR/EULAR score	34	36	20	21	24	26
	Definite histological diagnosis	Y (pancreas, lymphnodes)	Y (salivar glands, lung)	Y (eyelid)	Y (periorbiatl tissue, lacrimal gland)	Y (meninges)	Y (peritoneal lesion?)
	Induction of remission therapy	PDN + AZA	PDN	AZA	PDN	PDN + MTX	PDN + MTX
	Response	Y	Y	Y	Y	Y	Y
	Relapse (years after treatment)	Y (6)	Y (10)	N	Y (0,5)	Y (5)	N
	Second line therapy	RTX	RTX	-	MPDN + RTX	PDN	-
OTHER IMMUNOLOGICAL DISEASE	Diagnosis	Sarcoidosis	Sarcoidosis	GPA	GPA	EGPA	Takayasu
	Organs involved	lymphnodes over and infra diaphragmatic, axillary, laterocervical, lumboaortic, inguinal, hepatic	pulmonary and over and infra-diafragmatic lymphnodes	tracheal cartilage	pulmonary nodules, scleritis	respiratory tract (asthma), skin, peripheral nervous system, blood eosinophilia	left subclavian artery, left common carotid, anonymous artery, thoracic aorta, suprarenal abdominal aorta, right pulmonary artery
	Classification criteria fulfilled?	not available	not available	Y*	Y*	Y**	Y***
	Autoantibody	none	none	c-ANCA	c-ANCA	p-ANCA	none
	Definite histological diagnosis	Y (lymphnode)	Y (paratracheal lymphnodes)	not available	Y (pulmonary nodule)	Y (skin biopsy)	not available
	Timing of diagnosis vs IgG4RD	subsequent	previous	previous	contemporary	previous	contemporary
	Years after/before IgG4RD diagnosis	2	1	12	0	3	0
	Treatment	PDN	PDN + MTX	PDN + AZA	PDN	PDN + CYC	INFX
	Response to treatment	Y	Y	Y	Y	Y	N

AB1295

TREATMENT OUTCOMES OF ADULT-ONSET STILL'S DISEASE PATIENTS WITH BIOLOGICAL THERAPY

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Background: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder with heterogeneous distrubition (1). Due to rarity of AOSD and limited controlled study about efficacy of biologic treatment in AOSD, management of refractory AOSD patients poses several challenges.

Objectives: The aim of this study to investigate clinical characteristics and treatment outcomes of AOSD patients who receive biological therapy.

Methods: Patients were identified who met Yamaguchi classification criteria between January 2010 and December 2021 from our database. AOSD patients treated with biologic treatment were included in this study. Demographic data, clinical features and treatment characteristics were recorded.

Results: 49 AOSD patients were identified from database. 9 AOSD patients with biologic therapy (7 female, mean age 42.3±19) were included in this study. Mean age at diagnosis was 31.5± 16.7 and mean follow-up period was 9.3± 5.5 years. Median drug retention duration was found 95 (5-150) months. It was established that all patients used high dose steroid at diagnosis and 3 (33.3%) out of them received pulse steroid therapy. Initial therapy was methotrexate for all patients and leflunomid was used secondly as monotherapy or combination therapy after methotrexate inefficacy. It was observed that indication for biologic therapy was arthritis and systemic inflammatuar symptoms in 5 patients. 4 patients was initiated biologic therapy for refractory arthritis without systemic inflammation findings. First biologic agents were tocilizumab and etanercept in 3 patients, infliximab and anakinra in 2 patients. It was shown that biological therapy was switched in 3 patients due to inefficacy and 2 patients because of side effects. Allergic reaction developed in 2 patients treated with infliximab and infliximab switched to adalimumab and etanercept. Biological therapy was discontinued in 2 patients due to remission, and patients remained in remission after cessation of biological agent. None of patients had serious infection. Hemophagocytic syndrome was developed in only one patient during disease course.

Conclusion: According to our cohort, one of five AOSD patients received biological therapy during follow-up. Our results revealed that the need for biologic therapy during the course of the disease is not uncommon in AOSD, and that biologic therapy is essential for maintaining remission in resistant patients.

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Table 1. Baseline clinical and treatment characteristics (n=9)

Female, n (%)	7 (77.7)
Age, years	42.3±19
Age at diagnosis, years	31.5± 16.7
Smokers, n (%)	6 (66.6)
Drug retantion duration, months	95 (5-150)
Follow-up time, years	9.3± 5.5
Treatment characteristic	n (%)
Biologic therapy indication	
-Systemic inflammation findings	5 (55.5)
-Refractory arthritis	4 (44.4)
İnitial biologic therapy	
Etanercept	3 (33.3)
Tocilizumab	3 (33.3)
Infliximab	2 (22.2)
Anakinra	2 (22.2)
Switching agent	5 (55.5)
Cessation of biologic therapy	3 (33.3)

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AB1296

LONG-TERM EXPERIENCE OF THE THERAPY WITH INTERLEUKIN-1 INHIBITORS IN MONOGENIC AUTOINFLAMMATORY SYNDROMES AND SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN REAL-LIFE PRACTICE OF RHEUMATOLOGISTS IN SINGLE FEDERAL CENTER

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Background: Autoinflammatory diseases (AIDs) are a heterogeneous group of rare genetically determined conditions. Biologics (B) are used, especially inhibitors of interleukin 1 (iIL-1), in the treatment of the most common monogenic AIDs (mAID) – FMF, TRAPS, HIDS/MKD, CAPS. IIL-1 has shown high efficiency and led to significant progress in the treatment of these patients (pts). Currently, iIL1 are the first-line drugs for mAIDs therapy, primarily CAPS. In pts with systemic juvenile idiopathic arthritis (sJIA) IL-1 inhibitors are also successfully used in the first or second line of therapy along with IL-6 inhibitors.

Objectives: To evaluate in the real clinical practice the frequency of prescribing, efficacy and safety of IL-1 therapy in pts with mAIDS and sJIA according to the Federal Rheumatology Center.
Methods: A retrospective study from 2013 to 2021 included 66 pts who were prescribed iIL-1. Among them 45 pts with mAIDS: FMF - 8, CAPS - 25, TRAPS - 10, HIDS/MKD – 2, 21 pts had sJIA. Canakinumab (CAN) was administered subcutaneously at the dose of 2-5mg/ kg or 150mg every 4-8 weeks, anakinra (ANA) - subcutaneously at the dose of 1-5mg/ kg or 100mg daily.
Results: Among pts with mAIDS 45 received iIL-1. The age of pts ranged from 1.5 to 44 years, the median (Me) age was 9.5[6.9;17] years. Female pts predominated (60%). The median age at onset was 0.5 [0;4] years (0 - 35 y). The median duration of the disease was 7.5 [3.9;15.1] years (3 months to 44 years). 35 pts received CAN, 10 - ANA. Both drugs showed significant positive dynamics with a complete response in 40 (88.9%), a partial response in 5 (11.1%), mainly due to serious neurological and cognitive impairments in 2 pts with CINCA/NOMID, sensorineural hearing loss in 3 adult pts with MWS, as well as amyloidosis in 1. In 7 pts with CAPS who received ANA as first biologic treatment, after achieving a reliable positive response, switching to CAN was performed while maintaining full efficacy. It was possible to discontinue the glucocorticoids (GC) in all pts. In 2 pts with CINCA/NOMID (1), MWS (1) due to insufficient efficiency the interval between injections of CAN was reduced from 8 to 4 weeks. The duration of use of CAN in pts with mAIDS ranged from 6 months to 12 years, ANA – 2 months to 12 years, 13 pts (28.9%) have been receiving therapy for 5 years or more. The age of pts with sJIA ranged from 3 to 17 years, Me 8,15 [5,3; 12,7] years. The age of the onset varied from 4 months to 12 years, Me 3,1 [1,8; 5,7] years. Female pts predominated (61,9%). 20 pts received CAN (18 after secondary inefficiency/infusion reaction of tocilizumab (TCZ), 2 had previous experience of 3 B: TCZ-etanercept-adalimumab, TCZ-abatacept-adalimumab). 1 patient received ANA. The duration of CAN treatment was from 5 months to 4.5 years. Among pts with sJIA who received CAN, secondary inefficiency with discontinuation was observed in 6 (28,6%) (10-25 months after treatment initiation), and in 1patient who received anakinra for 8 months. The tolerability of therapy was generally good. We have not observed any SAE in the treatment of iIL-1. All pts are continue taking medications.
Conclusion: Among the B iIL-1 are used in most pts with mAIDS, these are currently first-line drugs, especially for CAPS and TRAPS. They have high efficiency and good tolerance for long-term use. While among pts with sJIA there is a high frequency of secondary inefficiency and discontinuation, which, however, may be due to the late timing of iIL-1 treatment initiation. As a test of administration, and base on the concept of window of opportunity in treatment sJIA pts it is possible to use short-acting iIL-1 (ANA) with switch to CAN as a drug with a prolonged duration of action.
Disclosure of Interests: Svetlana Salugina Speakers bureau: Novartis, Sobi, Maria Kaleda Speakers bureau: Pfizer, Roche, Novartis, Evgeny Fedorov Speakers bureau: Novartis, Sobi, MEDAC, Irina Nikishina Speakers bureau: Pfizer, MSD, Roche, Novartis, Sobi, Anna Torgashina Speakers bureau: Novartis
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AB1297 EVALUATION OF POSSIBLE RISK FACTOR OF PULMONARY EMBOLISM IN SARCOIDOSIS PATIENTS

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Background: Some studies reported a correlation between sarcoidosis and an increased risk of pulmonary embolism (PE) [1,2].
Objectives: To assess possible risk factors of PE in sarcoidosis patients.
Methods: We enrolled 260 sarcoidosis patients (170 females and 90 males; mean age at diagnosis 46 ± 9), after giving written informed consent. We perform clinical evaluations, laboratory tests and radiology features.
Results: Our study population included 20 sarcoidosis patients with PE (14 females and 6 males; mean age at diagnosis 45 ± 10), diagnosed by lung scintigraphy and 240 sarcoidosis patients without PE (170 females and 70 males; mean age at diagnosis 46 ± 11). There was a significant increase of the presence of antiphospholipid antibodies in the sarcoidosis group with pulmonary embolism (55%) than in group without PE (9%) (p-value<0.01). There was no statistically significant difference between the two groups on smoking habit, obesity, treatments and hereditary thrombophilia frequency (p > 0.05, respectively).
Conclusion: This study demonstrated an increased of antiphospholipid antibodies positivity in sarcoidosis patients with pulmonary embolism. Furthermore, we propose screening for these antibodies
in all sarcoidosis patients.
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AB1298 AL-AMYLOIDOSIS MIMICKING IGG4-RELATED DISEASE

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Background: Hematological diseases such as multiple myeloma (MM) and POEMS-syndrome can be accompanied by high serum IgG4 level and thus mimic an IgG4-related disease (IgG4-RD) [1, 2]. However, there are no descriptions of AL-amyloidosis with increased secretion of IgG4 in the literature.
Objectives: to present a clinical case of AL-amyloidosis mimicking IgG4-RD.
Methods: At the age of 42, patient S. developed nasal congestion, and 2 years later bilateral symmetrical swelling of submandibular salivary glands developed. Chest CT scan revealed hydrothorax and pericarditis, interstitial changes in both lungs and intrathoracic lymphadenopathy. According to blood tests, ANF, RF and CRP were within normal values, an increase in the serum IgG4 (32.9 g/l) and IgG (34.1 g/l) levels was detected, and the patient was admitted to our clinic with suspicion of IgG4-RD.
Results: On examination, we noticed a symmetrical enlargement of submandibular salivary glands and macroglossia. The patient also complained of tingling in the fingers, we performed electroneuromyography and revealed bilateral carpal tunnel syndrome. According to the immunofixation of blood and urine proteins, IgG-lambda paraproteinemia (18,3 g/l) and a trace amount of Bence-Jones-lambda protein in the urine were detected. AL-amyloidosis was suspected and a biopsy of the submandibular salivary gland was performed, followed by Congo red staining and darkfield microscopy that confirmed amyloidosis (Figure 1). There were no signs of IgG4-RD (storiform fibrosis or obliterative phlebitis) in the biopsy specimens. Echocardiography revealed thickening of the interventricular septum and hypertrophy of the ventricular myocardium. MM and other malignancies were excluded on the basis of bone marrow trephine biopsy and PET-CT (also revealed severe hepatomegaly). The diagnosis of IgG4-secreting AL-amyloidosis affecting salivary glands, tongue, heart, lungs, liver, nervous system was made and polychemotherapy was started, the patient's further life remained unknown.

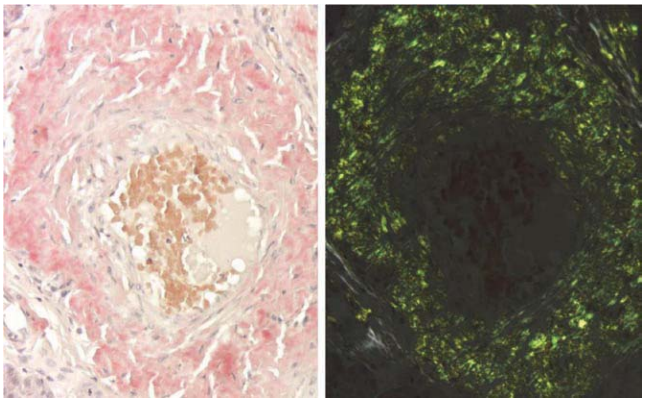

Figure 1. Congo red staining and darkfield microscopy demonstrating amyloid deposits.

Conclusion: AL-amyloidosis can be accompanied by high serum IgG4 level and mimic IgG4-RD. The serum level of IgG4 should not be used as a criterion for IgG4-RD, and in all cases of suspected IgG4-RD the diagnosis should be confirmed morphologically.
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Other orphan diseases

AB1299 DIFFERENCES IN THE CLINICAL SPECTRUM OF HAPLOINSUFFICIENCY OF A20 (HA20) CASES DIAGNOSED DURING ADULTHOOD

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Background: Haploinsufficiency of A20 (HA20) is a monogenic autoinflammatory disease caused by heterozygous loss-of-function mutations in *TNFAIP3* gene and characterized by Behçet disease (BD)-like manifestations such as mucocutaneous, articular, gastrointestinal, ocular symptoms as well as recurrent fever, elevated acute-phase reactants during relapses; and it usually starts during early childhood. Autoimmunity is another component of HA20 with autoantibodies and variable clinical features resembling systemic lupus erythematosus (SLE) and other autoimmune diseases.
Objectives: We herein present three cases of HA20 with different clinical features and diagnosed during adulthood.
Methods: We used the Ion Torrent platform for deep sequencing.
Results: Case 1: A 51-year old woman diagnosed with BD because of oral and genital aphthous ulcers, arthralgias, erythema nodosum, and pathergy positivity starting from age of 40 in 2012. She developed sudden vision loss (diagnosed with bilateral optic neuropathy), sixth nerve palsy, and entrapment neuropathies in the lower limbs in 2014; and she had flares of neurologic findings between 2014-2020. The only laboratory abnormality was elevated acute-phase reactants, and no pathologic finding was reported for cranial MRI. Pathological examination of sural nerve biopsy revealed chronic inflammatory demyelinating polyneuropathy (CIDP). She received adalimumab and then tofacitinib, and her treatment was switched to certolizumab and IVIG (30 g/6 weeks) in 2020. At the last visit, she was asymptomatic with normal acute phase response, and her examination revealed normal eye movements.
Case 2: A 33-year old woman was followed for 12 years with the diagnosis of SLE, based on fever, photosensitivity, alopecia, polyarthritis, serositis, positive anti-nuclear antibody (ANA) at a titer of 1:1280 with a homogeneous pattern, positive anti-dsDNA, anti-Sm, anti-Sm/RNP, and lupus anticoagulant test, and leukopenia, lymphopenia, hypocomplementemia in 2008. She developed shrinking lung syndrome and Jaccoud arthropathy during the disease course. She received several drugs including corticosteroids, hydroxychloroquine, cyclophosphamide, mycophenolate mofetil, belimumab, rituximab, tocilizumab, abatacept, tofacitinib because of fever, arthritis, skin rash, increased acute-phase reactants, pancytopenia, anti-dsDNA positivity. Her fever, red arthritis attacks with high CRP values did not respond, and after the genetic diagnosis of HA20, anakinra was added to treatment. Due to the high dose anakinra requirement, her treatment was switched to canakinumab (150 mg/2 week), and at the last visit, her attacks were significantly reduced.
Case 3: A 44-year old woman was evaluated because of recurrent prolonged >38°C fever attacks (2 days-2 weeks duration), arthritis of the elbow, wrist, knee joints, and high acute phase reactant in 2004. She did not have a history of recurrent oral and genital aphthous ulcers, intermittent periorbital edema, rash, any ocular symptoms, or sensorineural hearing loss. ANA, RF, anti-CCP, and MEFV gene mutation were negative on admission. PET-CT demonstrated FDG uptake in the wall of the ascending aorta, aortic arch, and descending aorta in 2011. She had used colchicine in 2004, etanercept between 2009 and 2010, anakinra in 2011, tocilizumab in 2012, and canakinumab in 2013. She repeatedly received IV methylprednisolone pulse therapy, but she experienced a relapse of fever when she reduced the dose of methylprednisolone to <8 mg/day. Her knee arthritis did not respond to adalimumab, and she is currently on infliximab treatment since 2019 with a Daily methylprednisolone dose of 8-12 mg.
Conclusion: HA20 can be diagnosed even in adult patients, and the clinical picture of presented cases suggests that monogenic autoinflammatory disorders including HA20 should be suspected in any patient with flares of described manifestations along with strong acute phase response even in adults. Response to corticosteroids and targeted treatments may also be variable.
Disclosure of Interests: None declared
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Table 1: Characteristics of patients with A20 haploinsufficiency

	Case 1	Case 2	Case 3
Gender	Female	Female	Female
Family history	None	None	None
Systemic findings	Yes	Yes	Yes
Autoantibodies	None	Yes	None
High acute-phase reactants	Yes	Yes	Yes
Oral ulcers	Yes	Yes	No
Erythema nodosum	Yes	None	None
Genital ulcers	Yes	None	None
Uveitis	None	None	None
Arthritis	Yes	Yes	Yes
Neurologic involvement	Yes	None	None
Parenchymal involvement	None	None	None
Peripheral neuropathies	Yes	None	None
Current treatment	Certolizumab	Canakinumab	Infliximab
TNFAIP mutation	Arg697Lys	Thr647Pro	p.Phe40LeufsTer56

AB1300 AA AMYLOIDOSIS IN A PATIENT WITH MUTATIONS IN BOTH ADA2 AND A20 GENES

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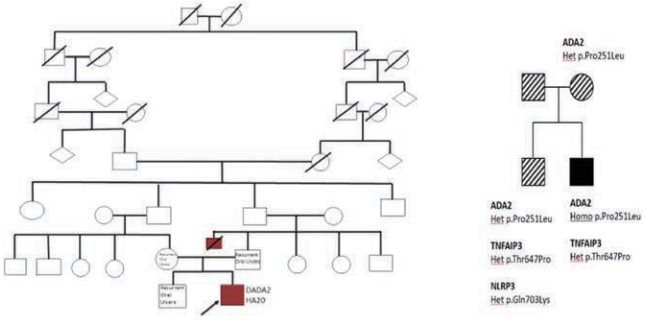
Background: Adenosine Deaminase 2 Deficiency (DADA2) and Haploinsufficiency of A20 (HA20) are two recently described monogenic autoinflammatory diseases (AID). The uncontrolled inflammatory response has been associated with an increased risk of AA amyloidosis in other AID, but there are only two reported patients with DADA2-related amyloidosis so far.[1,2]
Objectives: We herein report a patient with AA amyloidosis and AID associated with both DADA2 and HA20.
Methods: We used the Ion Torrent platform for deep sequencing.
Results: Case: A 20-year-old male patient born to consanguineous parents (Figure 1), was admitted to our hospital with fever and abdominal pain in June 2014. Peritonitis, hepatomegaly, and a palpable non-tender mass in the right axillary cavity were detected in physical examination, and his laboratory investigations revealed neutrophilic leukocytosis, high acute phase reactants (APR), and nephrotic range proteinuria. CT angiography showed multiple thrombotic microaneurysms in celiac, splenic, superior, and inferior mesenteric and bilateral renal arteries; and MRI documented an additional aneurysm in anterior communicating artery. No finding was detected in hepatitis serology. He had been diagnosed with polyarteritis nodosa, and prednisolone and azathioprine were started. Renal histopathology confirmed the AA amyloidosis. Genetic analysis revealed no pathogenic *MEFV* variant. Colchicine and anakinra 100 mg/day were added to his treatment. He experienced 1-2 abdominal episodes annually between 2014-2019, and APR were normal between attacks. In March 2019, he was admitted to the hospital because of abdominal pain, high APR, and iron deficiency anemia. No gross pathology was observed in endoscopic examination of gastrointestinal tract, but histopathological investigation of the gastric mucosa and terminal ileum showed AA amyloidosis. Multiple aneurysms were detected in renal arteries with angiography. Deep sequencing of the targeted genes revealed homozygous p.Pro251Leu in ADA2 gene and heterozygous p.Thr647Pro in TNFAIP3 gene encoding A20, confirming the molecular diagnosis of DADA2 and HA20. The patient described oral recurrent aphthous ulcers starting from his childhood, but he had no uveitis or genital ulcers. His mother and brother also had recurrent oral aphthous ulcers. Genetic analyses showed heterozygous p.Pro251Leu variant in ADA2 gene in his mother, and heterozygous p.Gln703Lys variant in NLRP3 gene as well as heterozygous p.Thr647Pro TNFAIP3 variant and heterozygous p.Pro251Leu ADA2 in his brother. An improvement in his findings was observed within 2 weeks after switching his anakinra to adalimumab 40 mg every other week. At his last visit in February 2021, the patient had no complaints with normal APR, and urinalysis analysis showed 200 mg/day proteinuria, which was regressed from 3 g/day.
Conclusion: This is the first case of AA amyloidosis associated with ADA2 and TNFAIP3 (A20) variants. ADA2 p.Pro251Leu variant has previously been validated as likely pathogenic, and our patient's clinical findings were mainly compatible with DADA2. On the other hand, TNFAIP3 gene p.Thr647Pro mutation has been reported as

Figure1: Pedigree of family and results of genetic analyses



variant of unknown significance, but it may have contributed to the DADA2 associated increased risk of amyloidosis. A better response of proteinuria to adalimumab treatment indicates superiority of anti-TNFs in DADA2 patients compared to anti-IL-1 drugs.

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AB1301 DETERMINING THE RELATIONSHIP BETWEEN SERUM INTERLEUKIN 33 LEVELS AND CLINICAL FEATURES OF THE DISEASE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by recurrent fever, serositis, arthritis and erysipelas-like erythema caused by mutations over activating caspase-1. As Interleukin (IL)-1 beta, IL-33 is a nuclear cytokine from IL-1 family which is activated by caspase-1. IL-33 is known to take part in pathogenesis of several rheumatic diseases.
Objectives: The aim of this research is determining the relationship between serum IL-33 levels and clinical features of the disease in patients with FMF disease.
Methods: The research involved 54 FMF patients and 29 healthy volunteers. Serum IL-33 levels were evaluated in both patients and healthy individuals, and its relationship between clinical and laboratory features of FMF.
Results: 28 out of 54 patients (%51.8) had favorable response to colchicine while 26 patients (%48.2) had colchicine resistant disease. FMF patients had lower IL-33 levels compared to healthy control group (p= 0.06). There were no difference between colchicine responsive and resistant patients (p=0.12) and no association was found between clinical features and serum IL-33 levels. Additionally, IL-33 did not correlated with C-reactive protein and disease activity assessed by autoinflammatory disease activity index.
Conclusion: No association was found between serum IL-33 levels and FMF disease features and laboratory findings. This may be due to the small size of our patient group, the involvement of IL-33 in tissue homeostasis as well as inflammation, and the use of higher doses of colchicine in the resistant disease group than in the remission group. Additional research is needed to determine IL-33's role in FMF pathogenesis and its relationship with clinical and laboratory features.

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AB1302 EVALUATING THE CLINICAL UTILITY OF PATIENT ACCEPTABLE SYMPTOM STATE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by recurrent attacks of fever, serositis, arthritis and erysipelas-like erythema. Patient acceptable symptom state (PASS) is a disease evaluation method to assess disease activity with a simple question especially in rheumatic diseases.
Objectives: We aimed to investigate clinical utility of PASS in FMF patients.
Methods: The research involved 54 FMF patients. Patient acceptable symptom state was applied to all patients in the study. The answers to PASS were compared with the patients clinical and laboratory features.
Results: 28 out of 54 patients (51.8%) were colchicine responsive whereas, 26 patients (48.2%) had colchicine resistant disease. The number of patients who answered yes to PASS (I'm happy with my current disease condition) was 32 (59%), while answered no (I need further treatment options) was 22 (41%). Considering the disease severity assessed with International severity scoring FMF (ISSF) of those who answered yes, 22 (68%) patients had mild disease, 10 patients had moderate (32%) disease, and there was no patient with severe disease in this group. Among those who answered no, 3 (14%) had mild disease, 14 (63%) had moderate disease, and 5 (23%) had severe disease (p <0.001). When the CRP levels of the patients were compared, the median CRP value of those who answered yes was found to be 4.45 mg/L, and the median value of CRP for those who answered no was 11.25 mg/L (p= 0.04).
Sensitivity and specificity of PASS for detecting patients in remission was 78% and 61% respectively. Moreover, PASS had a positive and negative predictive value of %68 and %72 respectively, for determining patients in remission. If cut off level of CRP was chosen as 6.5 mg/L for answering "yes" to PASS, sensitivity of test has been found to be 62.5% while the specificity is 59.1%. On the other hand, if cut off level of CRP is selected as 9.35 mg/L; sensitivity and specificity of the test was found as 75% and 72.7% respectively (p=0.045).
Conclusion: Patient acceptable symptom state is found beneficial in evulation these patients simply and swiftly especially in terms of distinguishing severe FMF disease. In FMF, laboratory remission is as important as clinical remission, therefore, PASS by alone, is not sufficient for making treatment decisions and should be supported by inflammatory markers.

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AB1303 VACCINATION PRACTICES OF ADULT FAMILIAL MEDITERRANEAN FEVER PATIENTS IN TURKEY.

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Background: Vaccines are the safest and most effective method to prevent invasive and life-threatening infections. Vaccines against influenza, pneumococcal disease, herpes zoster, and human papillomavirus are the main recommended vaccines for adults. In addition, rheumatology patients are advised to receive adult vaccinations according to the vaccines available in their country and local guidelines. In Turkey, both influenza and pneumococcal disease vaccines are commercially available. In addition, these vaccines are strongly recommended for rheumatology patients in local guidelines. Although familial Mediterranean fever (FMF) is one of the most common rheumatological diseases in Turkey, it is often neglected in vaccination recommendations.
Objectives: In this study, we surveyed the vaccination practice against influenza or pneumococcal diseases of adult FMF patients in our cohort. In addition, we evaluated the factors related to favorable vaccination practice.
Methods: We included 360 FMF patients over 18 years of age. All patients fulfilled the Tel-Hashomer criteria for FMF. We asked them if they had ever been vaccinated against pneumococcal or influenza, and how often they received them. In addition, we dichotomised patients in terms of vaccinated against at least one of influenza or pneumococcal diseases. We then compared the groups for demographic (age gender and comorbidities) and disease related characteristics (disease duration, disease activity calculated by ISSF and colchicine dose). We used qi-square test to compare categorial variables and Mann-Whitney U test to compare continuous variables. P<0.05 was accepted as significant.
Results: Of 360 FMF patients, 238 (66.1%) were female. The mean age of the patients was 34.5±10.7 years. Disease duration of the patients was 9.38±0.7 years. In addition, the mean ISSF score of the patients was 1.83±1.5. The mean dose of colchicine received by the patient was 1.23 ± 0.47 mg. Only 54 (15.0%) of the patients had at least one comorbidity. In our cohort, 22 (6.1%) patients were vaccinated against influenza or pneumococcal disease. Only 18 (5.0%) of the patients have been vaccinated against influenza at least once so far. Half of these patients (9/18) were vaccinated against influenza each year. In addition, 8/360 (2.2%) patients were fully vaccinated against pneumococcal diseases. Here, six of them received the pneumococcal vaccine after the start of the COVID-19 outbreak. There was no statistically significant difference between the groups in terms of demographic and disease related characteristics.
Conclusion: We found that vaccination practice of FMF patients in our cohort was unsatisfactory. Few patients follow adult vaccination recommendations. In addition, clinicians should be concerned about the importance of vaccination and guide their patients to get the adult vaccines available in their country.

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Disclosure of Interests: None declared
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AB1304 COMPARISON OF CHARACTERISTICS OF PATIENTS WITH IDIOPATHIC GRANULOMATOSIS MASTITIS IN REMISSION AND NON-REMISSION: RESULTS FROM A TERTIARY REFERRAL CENTRE

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Background: Idiopathic granulomatous mastitis (IGM) is an uncommon, benign, chronic inflammatory disease of the breast of unknown etiology. Although an ideal treatment regimen is controversial in IGM, the ultimate goal is remission.
Objectives: To compare the clinical, radiological, laboratory and treatment features of patients in remission and non-remission, and assess predictor factors of remission.
Methods: The data of patients who were histopathological diagnosed with IGM between 2010 and 2020 were evaluated retrospectively. The patients were divided into 2 groups as those in complete remission and non-remission. Complete improvement in clinical and physical examination with medical and/or surgical intervention findings at 2 consecutive visits was defined as complete remission. Patients who were not in complete remission including partial remission and refractory to treatment, were defined as non-remission group.
Results: In this study, there were a total of 103 patients with a diagnosis of IGM followed-up in the rheumatology clinic. Of these, 39 (38%) were in remission and 64 (62%) were non-remission. Age, age at symptom onset, comorbidity, pregnancy (ever), disease localization, clinical signs and symptoms, imaging classification, and baseline acute phase reactants and autoimmune markers were similar in the remission and non-remission groups. The use of antibiotics and azathioprine was significantly higher in the remission group than in the non-remission group. However, there was no difference between the groups in terms of breast surgery, use of corticosteroids and methotrexate (Table 1). In the univariable analysis, antibiotic use [OR: 2.55 (95% CI 1.07-6.11)] was found to be a predictor factor of remission.
Conclusion: Patients with in remission did not have the distinctive baseline demographic, clinical, laboratory and radiological features that distinguish them from patients with in non-remission. Patients in remission used more antibiotics and azathioprine. Antibiotic use seems to be associated with remission in univariable analysis. However, further studies are needed to evaluate the factors associated with remission in IGM.
Disclosure of Interests: None declared
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AB1305 A SYSTEMATIC REVIEW OF AA AMYLOIDOSIS AMONG PATIENTS WITH BEHÇET'S SYNDROME

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Background: Data on patients with Behçet's syndrome (BS) complicated with AA amyloidosis is limited to case reports or case series with a small number of patients.
Objectives: In this study, we aimed to perform a systematic review (SR) of published reports on BS patients with AA amyloidosis.
Methods: PubMed and EMBASE were searched with the keywords "Behcet* AND amyloidosis", without date and language restriction, until May 2020. Two independent reviewers (SNE, GK) performed title/abstract and full text screening and data extraction. A third reviewer (GH) made the final decision in case of disagreement between the two reviewers. Studies that reported patients who were reported by authors as having BS and AA amyloidosis were included. The risk of bias assessment was done using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool.
Results: The systematic literature search yielded 760 articles of which 703 were excluded after title and abstract review. After full-text review, we further excluded 15 duplicate articles and 1 article was added after handsearching the reference lists of the full texts. Finally, we included 43 articles reporting 96 cases. Among these articles, 38 were case reports and 5 were case series reporting between 6 and 14 patients. All patients but 8 were reported from Mediterranean countries.

Table 1. Characteristics of patients in remission and non-remission

	All patients	Patients in remission	Patients not in remission	p value
	n= 103	n = 39	n= 64	
Age, years	38.1 ± 7.1	39.6 ± 7.8	37.2 ± 6.5	0.07
Age at symptom onset, years	33.5 ± 6.6	34.4 ± 7.3	33 ± 6.1	0.30
Comorbidity, n (%)				
Thyroid disorders	4 (3.9)	1 (2.6)	3 (4.7)	1.00
Hypertension	2 (2)	2 (5)	0	0.14
Diabetes mellitus	1 (1)	1 (2.6)	0	0.38
Pregnancy (ever), positive/total (%)	75/77 (97.4)	31/32 (97)	44/45 (98)	1.00
Breast localization, n (%)				
Left	47 (45.6)	19 (48.7)	28 (43.8)	0.88
Right	36 (35)	13 (33.3)	23 (35.9)	
Bilateral	20 (19.4)	7 (17.9)	13 (20.3)	
Clinical signs and symptoms, n (%)				
Palpabl mass	94 (91.3)	35 (89.7)	59 (92.2)	0.72
Fistula formation	37 (38.1)	16 (42.1)	21 (35.6)	0.52
Erythema	61 (65.6)	23 (65.7)	38 (65.5)	0.98
Nipple inversion	11 (12)	2 (5.4)	9 (16.4)	0.19
Axillary lymph node	45 (48)	17 (47.2)	28 (48.3)	1.00
Erythema nodosum	10 (9.9)	4 (10.3)	6 (9.7)	1.00
Arthralgia	13 (12.6)	3 (7.7)	10 (15.6)	0.36
BI-RADS classification*, n (%)				
2	13 (25)	7 (35)	6 (18.8)	0.12
3	31 (59.6)	9 (45)	22 (68.8)	
4	6 (11.5)	2 (10)	4 (12.5)	
5	2 (3.8)	2 (10)	0	
Baseline laboratory				
-CRP (mg/dL)	0.75 (1.4)	0.75 (1.4)	0.73 (1.4)	0.77
- ESR (mm/h)	23 (28)	21.5 (28)	25.5 (28)	0.39
-ANA (more than or equal 1/100), n$^{\alpha}$ (%)	37/69 (53.6)	12/25 (48)	25/44 (56.8)	0.48
-RF, n$^{\alpha}$ (%)	12/30 (40)	5 /16 (45.5)	7/19 (36.8)	0.71
-anti-CCP, n$^{\alpha}$ (%)	3/12 (25)	2/5 (40)	1/7 (14)	0.52
Treatment, n (%)				
Surgical intervention	38 (36.9)	16 (41)	22 (34.4)	0.49
Antibiotics	63 (61.2)	29 (74.4)	34 (53.1)	0.03
Corticosteroids	93 (90.3)	34 (87.2)	59 (92.2)	0.49
Methotrexate	66 (64.1)	26 (66.7)	40 (62.5)	0.67
Azathioprine	19 (18.4)	11 (28.2)	8 (12.5)	0.04

* 52 patients with data were evaluated.$^{\alpha}$ positive/total
Results are given as mean ± SD or median (IQR).
ANA: Antinuclear antibody; anti-CCP: Anti-cyclic citrullinated peptides; BI-RADS: Breast imaging-reporting and data system; RF: Rheumatoid factor

The quality of all articles according to GRADE was very low due to the lack of a control group.

The main features of the patients were male predominance (81/96, 84%), a high frequency of major organ involvement (62/80, 77.5%) especially vascular involvement (60%), a low frequency of comorbidities predisposing to AA amyloidosis (11/96, 11.5%), and a very low frequency of gastrointestinal involvement (3/72, 4%). All but 8 patients were diagnosed with BS and AA amyloidosis simultaneously. The most common presentation was nephrotic syndrome (60/81, 74%). Presenting symptoms other than proteinuria were diarrhea (n=2), acute renal failure (n=2), upper gastrointestinal bleeding (n=1), end stage renal disease (ESRD) (n=1), cardiac symptoms due to cor pulmonale (n=1), and hypertension (n=1). Renal biopsy (72%) and rectal biopsy (17%) were the most commonly used procedures to diagnose AA amyloidosis.

After diagnosing AA amyloidosis, colchicine was initiated in 58 patients, cyclophosphamide in 16, and biologics in 3 (1 anakinra and 2 tocilizumab). In the 67 patients with available data on follow-up, 43% of the patients were followed-up for ≤1 year and median follow-up duration was 20 months (IQR: 4-48). Among the 64 patients with available data, 30 (47%) had developed ESRD. Among the 72 patients with available data on survival status, 30 patients (42%) had died. Ten patients (33%) had died within 6 months, 15 had died after a median follow-up of 48 months (IQR: 24-150), and follow-up duration was not available in the remaining 5 patients including 3 patients whose diagnoses were made by autopsy. Reasons for death were infection (n=7), ESRD (n=6), intractable diarrhea (n=3), pulmonary embolism (n=1), cor pulmonale (n=1), hemorrhage due to pulmonary artery aneurysm (n=1), liver cirrhosis (n=1), gastric cancer (n=1), subarachnoid hemorrhage (n=1), and not reported (n=8).

Conclusion: Male gender and major organ involvement, especially vascular involvement, appear to be risk factors for the development of AA amyloidosis in BS patients. While BS patients complicated with AA amyloidosis have been reported rarely, it is a fatal complication of BS. One third of the patients had died within 6 months after AA amyloidosis diagnosis.

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AB1306 AA AMYLOIDOSIS IN CHRONIC RHEUMATIC DISEASES: ABOUT 20 CASES

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Background: Secondary AA amyloidosis is a complication of certain uncontrolled chronic inflammatory rheumatic diseases. The diagnosis of AA amyloidosis is anatomo-pathological based on the detection of amyloid deposits within a biopsy specimen.

Objectives: The aim of this study is to determine the clinical, biological, therapeutic and evolutionary aspects of amyloidosis during these diseases.

Methods: This is a retrospective descriptive study conducted in the rheumatology department in Monastir, Tunisia, including patients followed for chronic inflammatory rheumatism complicated by AA amyloidosis.

Results: Our study included 20 patients (13 women and 7 men). Their mean age at the time of diagnosis of amyloidosis was 55.4 years [18-76]. The rheumatic diseases were: Rheumatoid Arthritis (RA) in 13 cases (65%), Ankylosing Spondylitis in 3 cases (15 %), Behçet's disease in 2 cases and Juvenile idiopathic arthritis in its systemic form in 2 cases (10% for both). Amyloidosis occurred after a mean duration of rheumatic disease of 11.5 years [3-27]. The mean sedimentation rate at diagnosis of amyloidosis was 100.5 mm per hour [21-131]. The mean C-reactive protein at diagnosis was 38.35 mg/L [1.4-135]. Inaugural manifestations of amyloidosis were: edema of lower limbs in 8 cases, nephrotic syndrome in 7 cases, renal failure in 4 cases and an abdominal clinical presentation (diarrhea and abdominal pain) associated with proteinuria in 2 cases. Proteinuria was constant, with a mean level of 7.5 g/24 h [3.5-20]. It was isolated in 5 cases. Amyloidosis was subclinical in 2 cases and was discovered by an abdominal fat biopsy performed during a research protocol. The diagnosis was confirmed by: renal biopsy (n=9), rectal biopsy (n=5), salivary gland biopsy (n=4) and abdominal fat biopsy (n=2). Amyloidosis extension was assessed for 50% of our patients. Cardiac involvement was the most frequent, revealed in 5 patients. Concentric left ventricular hypertrophy was found in 4 patients. Pulmonary arterial hypertension and pericardial effusion were found in 1 case. Hepatic involvement was detected in 2 cases in the form of hepatomegaly without disturbance of liver function tests. Adrenal gland involvement was detected in 1 case with homogeneous hypertrophy of the adrenal glands associated with adrenal dysfunction. Only 1 patient had peripheral nerve damage in the form of bilateral carpal tunnel syndrome. Concerning the treatment; 12 patients received Colchicine. Chloraminophen was tried for 4 patients with amyloidosis secondary to RA and Azathioprine for one patient with RA. The evolution was unfavorable in 6 cases marked by death within a mean time of 3.4 years.

Conclusion: Although its prevalence is decreasing, owing to therapeutic progress in chronic rheumatic diseases, AA amyloidosis remains a not exceptional complication. It has a poor prognosis, particularly because of renal disease and cardiac involvement.

Disclosure of Interests: None declared

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AB1307 RHEUMATIC SYNDROMES INDUCED BY ONCOLOGIC AND HEMATOLOGIC TARGETED THERAPIES

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Background: Targeted therapy has gradually become the first-line clinical therapy for solid tumors and hematologic disorders (1). Immune related adverse side effects (irAE) due to checkpoint inhibitors are well recognized side effects in patients with underlying oncologic disorders; however, information regarding rheumatic side effects due to several targeted therapies are rarely reported.

Objectives: Our aim was to describe the main rheumatic syndromes induced by targeted therapies.

Methods: This observational study included patients from 2 referral University centers in Barcelona. We included patients referred from Oncology and Hematology departments visited from January 2017 to January 2022 at Hospital Clinic and Hospital de Bellvitge, Barcelona, Spain.

Results: Fifteen patients were included (Female 60%), with a mean age 63.3± 10.8 years. Nine patients had hematological disorders and 8 solid tumors. Main diagnosis included Multiple Myeloma in 3 (20%) patients, Non-Hodgkin Lymphoma 2 (13%), Acute Myeloid Leukemia 2 (13%), Melanoma 2 (13%), Colon carcinoma 1 (6.7%), Breast carcinoma 1 (6.7%), Glioblastoma multiforme 1 (6.7%), Chronic lymphatic leukemia 1 (6.7%), Renal cell carcinoma 1 (6.7%) and Sésary Syndrome in 1 (6.7%) patient. Targeted therapies included MAP kinases in 4 (26.7%) patients, Anti CD-38 in 3 (20%), Anti BRAF in 2 (13.3%), and anti STAT-3, anti VEGF, BTK inhibitor, anti CCR4, Isocitrate dehydrogenase 2 inhibitor and Halichondrin B analoge in 1 (6.7%) patient each. Treatment was administrated as monotherapy in 9 (60%) and as combined therapy in 6 (40%). Mean time from the initiation of targeted therapies and rheumatic syndrome onset was 5.0 ± 3.8 months. Main rheumatic syndrome were: Polymyalgia rheumatica (PMR) in 4 (26%) patients, Raynaud's phenomenon in 2 (13%), Tenosynovitis in 2 (13%), RA-like 2 (13%), cutaneous vasculitis, amyopathic dermatomyositis, oligoarthritis, spondyloarthropathy-like and non-inflammatory arthralgias in 1 (6.7%) case each. Main clinical characteristics are summarized in Table 1. In 8 (53%) cases, targeted therapies were stopped due side effects. Rheumatic syndrome were treated with, glucocorticoids (GC) 12 (80%), calcium antagonist 2 (13%), Hydroxychloroquine in 2 (13%), Methotrexate in 1 (6.7%), Sulfasalazine in 1 (6.7%) and NSAID in 1 (6.7%) patient. Mean follow-up were 15.4± 20 months. Most of the patients remain alive (86%). According oncologic prognosis, 4 (26%) had complete response, 6 (40%) had partial response and 5 (33%) had disease progression. At the time of the last visit, 6 (40%) patients remain on GC (mean dose 6.7 ± 4.7 mg/d) and 4 (26%) patients on DMARD therapy.

Conclusion: In this heterogeneous group of patients treated with targeted therapies, we described a variety of induced rheumatic syndromes including PMR, arthritis, and even vasculitis or dermatomyositis. An important proportion of patients stopped the treatment due to side effects and some of them required sustained treatment including GC and DMARD.

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Table 1. Main clinical rheumatic syndromes induced by targeted therapies

Case	Age/ Gender	Underlying diagnosis	Type of targeted therapy	Treatment	Rheumatic presentation	Rheumatic Diagnosis	Treatment for side effect	Withdrawal of targeted therapy	Time from targeted therapy and side effects (months)	Follow-up (months)	Oncologic/ Hematologic prognosis
1	70/F	Melanoma	Anti BRAF	Vemurafenib + Cobimitinib	Polyarthritis	Tenosynovitis	PDN	Yes	0.5	5	Complete response
2	80/M	Colon adenocarcinoma	Anti-STAT-3	Napabucasin	PMR-Like	PMR	PDN	Yes	7	36	Progression
3	72/F	Acute myeloid leukemia	IDH2	Enasidenib	PMR-Like	PMR	PDN	Yes	12	6	Progression
4	64/M	MM	Anti CD38	Daratumumab	PMR-Like	PMR	PDN	Yes	11	3	Progression
5	72/F	Sésary syndrome	CCR4	Mogamulizumab	PMR-Like	PMR	PDN	No	5	7	Complete response
6	46/M	Chronic lymphatic leukemia	BTK inhibitor	Acalabrutinib	Polyarthralgias	Non-inflammatory poliarthralgias	NSAID	No	2	1	Progression
7	64/M	MM	Anti CD 38 + anti CD3	Daratumumab + Teclistamab	Polyarthralgias	Tenosynovitis	PDN	Yes	2	0	Partial response
8	52/F	NH lymphoma	MAP kinases	Ibrutinib	Oliogoarthritis	Spa	PDN + SFZ	Yes	6	19	Complete response
9	53/F	NH lymphoma	MAP kinases	Ibrutinib	Cutaneous vasculitis	Leukocytoclastic vasculitis	PDN	Yes	7	18	Complete response
10	70 /F	Melanoma	Anti BRAF	Dabrafenib	Polyarthritis	RA-like	PDN + MTX	No	10	80	Partial response
11	76/F	Breast cancer	Halichondrin B Analog	Eribulin	Raynaud 's phenomenon	Raynaud's phenomenon	Calcium antagonist	No	1	6	Partial response
12	68/F	Acute myeloid leukemia	MAP kinases	Sofarenib	Hand skin lesions	Amyopathic DM	PDN + HCQ	Yes	0.5	22	Partial response
13	58/M	Gliobastoma multiforme	Anti-VEGF	Bevacizumab	Polyarthritis	RA-like	PDN + HCQ	No	2	5	Partial response
14	44/M	Renal cell carcinoma	MAP kinases	Sunitinib	Oliogoartritis	Oliogoartritis	PDN	No	2	19	Partial response
15	61/F	MM	Anti CD-38	Isatuximab	Raynaud's phenomenon	Raynaud's phenomenon	Calcium antagonist	No	3	15	Complete response

DM: dermatomyositis, HCQ: Hydroxychloroquine, IDH2: Isocitrate dehydrogenase type 2, MM: Multiple myeloma, NSAID: Nonsteroidal anti-inflammatory drugs, PMR: Polymyalgia rheumatica, SFZ: Sulfasalazine

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AB1308

MYCOPHENOLATE FOR THE TREATMENT OF EYE INVOLVEMENT IN PATIENTS WITH BEHÇET'S SYNDROME

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Background: Experience with mycophenolate in uveitis associated with Behçet's syndrome (BS) is limited.

Objectives: We aimed to report the efficacy and safety of mycophenolate mofetil (MMF) and mycophenolate sodium (MPA) in the treatment of BS uveitis.

Methods: All patients with panuveitis or posterior uveitis who used mycophenolate for eye involvement between 2016 and 2018 were included. Patient charts were reviewed and data on demographic features, previous immunosuppressives, concomitant therapies, ocular attacks and outcome, and adverse events were extracted. Follow up was ended on October 2021.

Results: We included 12 BS patients (M/W: 8/4, mean age: 35±7 years) treated with mycophenolate during a mean follow-up of 42±19 months (Table 1). All but 3 patients had bilateral eye involvement. IFX and INF-α had been discontinued due to adverse events in all patients, AZA in 10/12, and Cy-A in 7/10. Seven patients were prescribed mycophenolate for remission induction. One of these patients had had his first uveitis attack while on AZA treatment due to gastrointestinal involvement. The remaining 6 patients were using other immunosuppressives and experienced relapses that led to mycophenolate use. MMF was added to a biologic agent in 2 patients (IFX and ADA) and was initiated in combination with IFX in 1 patient. These 3 patients did not experience further ocular attacks and IFX was stopped due to remission in 1 patient. In the fourth patient, MMF was switched to MPA due to numbness in hands and feet and MPA was stopped due to arthralgia. This patient did not experience ocular attacks during 5 months of MPA therapy. The remaining 3 patients had further uveitis attacks without decrease in visual acuity 2, 6, and 12 months after MMF initiation, and IFX was added in 2 patients, and ADA in 1 patient. Two of these patients were switched to INF-α due to uveitis relapses. MMF was switched to MPA for diarrhea in 1 patient. Five patients had received MMF for maintenance. One of these was using IFX when MMF was started and these 2 agents were used together. This patient discontinued MMF due to remission 17 months after MMF initiation and is still on IFX monotherapy. The second patient is still on MMF for 39 months without further ocular attacks. ADA, IFX and Cy-A were added in the remaining 3 patients due to ocular attacks 2, 5 and 31 months after MMF initiation. One of these 3 patients stopped IFX and MMF due to remission and is off treatment for 2 years.

Conclusion: Mycophenolate may be an alternative treatment modality in addition to biologics for patients with eye involvement who are intolerant to conventional therapies. Further data is needed to show whether it would be effective when used alone.

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Table 1. Demographic, treatment and outcome of the 12 patients

Age / gender	Previous therapies	Remission induction or Maintenance therapy	Concomitant biologic	Time to ocular attack (months)	Treatment after ocular attack	At the end of the follow-up	MMF duration (months)
25/M	AZA, Cy-A	Remission induction	None	2	ADA was added	ADA and MPA[a] were switched to INF due to further ocular attacks	38
42/W	AZA, Cy-A, INF, IFX	Remission induction	IFX	N/A	N/A	Still on IFX and MMF	72
37/M	AZA, Cy-A, INF, IFX, ADA	Remission induction	ADA	N/A	N/A	Still on ADA and MMF	27
32/M	AZA	Remission induction	None	12	IFX was added	Still on IFX and MMF	52
33/W	AZA, Cy-A, INF, ADA, IFX	Remission induction	None	N/A	N/A	MPA[b] was switched to certolizumab and MTX	5
24/M	AZA	Remission induction	IFX	N/A	N/A	Still on MMF and IFX was stopped due to remission	63
37/M	AZA, Cy-A	Remission induction	None	6	IFX was added	IFX and MMF were switched to INF due to further ocular attacks	41
36/W	AZA, Cy-A, INF	Maintenance	None	2	ADA was added	Still on ADA and MMF	50
36/M	AZA, Cy-A, INF, IFX	Maintenance	IFX	N/A	N/A	Still on IFX and MMF was stopped due to remission	17
49/W	AZA, Cy-A, INF	Maintenance	None	N/A	N/A	Still on MMF	39
37/M	AZA, INF	Maintenance	None	31	Cy-A was added	Still on MMF and Cy-A	38 d
31/M	AZA, Cy-A, INF	Maintenance	None	5	IFX was added	Off treatment for 2 years	38

a MMF was switched to MPA due to numbness in hands and feet, and MPA was stopped due to arthralgia.b MMF was switched to MPA due to diarrhea

AB1309

ANALYSIS OF A MONOCENTRIC COHORT OF IGG4-RELATED DISEASE PATIENTS: GREATER REDUCTION OF THE RESPONDER INDEX IN PHARMACOLOGICALLY-TREATED PATIENTS AS COMPARED TO UNTREATED ONES

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Background: IgG4-related disease (IgG4-RD) is a systemic disease characterized by lymphoplasmocellular infiltration and storiform fibrosis. Pancreas, biliary tract, lacrimal and salivary glands, lymph nodes and retroperitoneum are frequently involved, although the clinical presentation may vary [1].
Objectives: The aim of this study is to retrospectively describe the clinical manifestations of a monocentric cohort of patients with IgG4-RD and analyze their clinical course by applying the validated IgG4-Related Disease Responder Index (RI) [2].
Methods: We enrolled 22 IgG4-RD patients classified with 2011 diagnostic criteria [3] and/or 2019 classification criteria [4].
Results: 22 IgG4-RD patients (M/F=3.4/1), mostly Caucasian (91%), were diagnosed at a mean age of 59 years (44-74) with a median IgG4 concentration at diagnosis of 239 mg/dl (IQR 106-391 mg/dL). 14/22 (64%) patients fulfilled the 2011 classification criteria, while 8/22 (36%) were classified as possible (2), probable (5) or definitive (1) according to the diagnostic criteria of 2011. Organ involvement at diagnosis (T0) is described in Table 1. The organs most involved were lymph nodes, salivary glands and retroperitoneum. Patients were followed for a median of 49 months (IQR 16-88). Three patients were lost to follow-up. One patient died for pneumonia 96 months after diagnosis. During the follow-up 5 (23%) patients didn't receive specific treatment, 1 (5%) was treated surgically, 6 (27%) with steroid only, 10 (45%) with steroid and immunosuppressants (with methotrexate and/or rituximab, tocilizumab, mycophenolate, cyclosporine, hydroxychloroquine, azathioprine) and/or surgical resection. A statistically significant reduction in RI between T0 and last follow-up (TLF) was observed in all the patients [from 6 (3-6) to 3 (1-4) p=0.010]. A significant reduction was also observed in the group of pharmacologically treated patients [from 6 (3-6) to 3 (1-4) p=0.035] but not in the group of patients without drug treatment (p = 0.174).

Table 1. Organ involvement at diagnosis

Organ involvement T0	N. Patients (%)
Pancreas	2 (9)
Lymph nodes	14 (64)
Salivary glands	13 (59)
Lungs	1 (5)
Aorta and large blood vessels	4 (18)
Retroperitoneum, mediastinum, mesentery	6 (27)
Bile duct and liver	3 (14)
Kidneys	2 (9)
Pachymeninges	1 (5)
Orbits and lacrimal glands	3 (14)
Paranasal sinuses and / or nasal mucosa	5 (23)

Conclusion: In our cohort, patients were predominantly male with mean age at diagnosis of 59 years, consistent with literature data [1]. A statistically significant reduction in disease activity defined by reduction of RI was observed in patients who received immunosuppressive therapy. No significant reduction was observed in patients not pharmacologically treated.

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AB1310

JANUS KINASE INHIBITORS IN SEVERE AND REFRACTORY INFLAMMATORY OCULAR PATHOLOGY. CASES REPORTS AND LITERATURE REVIEW

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Background: Inflammatory ocular pathology (IOP) includes internal and external involvement. IOP may be severe ocular conditions refractory to conventional immunosuppressants and even biological therapy. Janus Kinase inhibitors (JAKINIB) had shown efficacy in refractory cases of different immune-mediated inflammatory diseases (IMID).
Objectives: In patients with refractory IOP treated with JAKINIB our aims were **a)** to assess the patients of Spanish referral centers, **b)** Literature review.
Methods: Multicenter study of 6 patients with refractory IOP treated with JAKINIB. For Literature review a search was conducted in PubMed, Embase and the Cochrane library from their inception to 1st January 2022, and conference proceedings from four major rheumatology conferences. In addition, a therapeutical approach of refractory IOP is proposed.
Results: We have identified 6 cases in five University Hospitals and 11 cases in the literature review. These 17 patients (14 women/ 3 men) (24 affected eyes), mean age 35.5±23.4 years had different refractory IOP (uveitis=11; scleritis= 3, PUK= 3). Most of IOP were associated with IMID (n=13, 76.5%). The main underlying IMID were juvenile idiopathic arthritis (n=5, 29.4%), rheumatoid arthritis (n=2, 11.8%) and spondyloarthritis (n=2; 11.8%) (Table 1**).**
Uveitis (n=11) followed by ocular surface pathology (n=6) were the most frequent subtypes of IOP. Patterns of uveitis were panuveitis (n=6), anterior uveitis (n=4; 2 of them with Cystoid macular edema) and posterior (n=1). Ocular surface pathology was due to scleritis (n=3) and PUK (n=3).
Besides systemic corticosteroids, before JAKINIB, conventional (n= 16; 94.1%) and biological immunosuppressive drugs (n=13; 76.5%) were required. The JAKINIB most widely used was tofacitinib (n= 10; 58.8%) followed by baricitinib (n=7; 41.2%). In only one patient with Blau Syndrome and uveitis, tofacitinib was switched to baricitinib due to severe lymphopenia.
After starting JAKINIB treatment, all patients presented clinical improvement, complete (n=15, 88.2%) or partial (n= 2; 11.8%).

Table 1. Cases reports and Literature review

Study, year (Ref)	Cases	Age/ Sex	Underlying IMID	JAKINIB	Ocular involvement	Previous immunosuppressive treatment	Ocular Improvement
Meadow et al. 2014 (1)	1	59, F	RA	TOFA	PUK	MTX, ABA, ivMP	Partial (PI)
Bauermann et al. 2018 (2)	1	22, F	JIA	TOFA	A. uveitis, CME	MTX, ADA, RTX, GOLI, IFX, CsA, TCZ, MMF	Complete (CI)
Paley et al. 2019 (3)	2	1.40, F 2.45, F	1.Idiopathic 2.Idiopathic	1.TOFA 2.TOFA	1.Scleritis 2.A. uveitis, CME	1.MTX, MMF, AZA, CYP 2.MTX, LFN, AZA, MMF, ADA, IFX, CZP, intravitreal fluocinolone ac.	1.CI 2.CI
Liu J et al. 2020 (4)	1	30, M	Behçet dis	TOFA	Scleritis	SSZ, MTX, AZA, LFN, THD, COL, GLM	PI
Majumder et al. 2020 (5)	1	26, F	Vogt-Koyanagi-Harada dis	TOFA	P. uveitis	ivMP	CI
Miserocchi et al. 2020 (6)	4	1. 9, F 2. 1, F 3. 2, F 4. 10, M	JIA	1. TOFA 2. BARI 3. BARI 4. BARI	1. Panuv 2. Panuv 3. Panuv 4. Panuv	1. IFX, ADA, LFN, ABA, RTX, TCZ. 2. MTX, ADA, IFX, RTX, ABA. 3. MTX, AZA, IFX, ADA, TCZ. 4. ETN, MTX, CsA, IFX, ADA, ABA, TCZ, RTX.	1. CI 2. CI 3. CI 4. CI
Pyare et al. 2020 (7)	1	45, F	Idiopathic	TOFA	Necrotizing scleritis	MMF	CI
Present study, 2022	6	1. 25, F 2. 85, F 3. 41, F 4. 65, F 5. 59, M 6. 40, F	1. Blau Syndrome 2. RA 3. Relapsing polychondritis 4. Idiopathic 5. AS 6. SpA and ulcerative colitis	1. TOFA/BARI 2. BARI 3. BARI 4. BARI 5. UPA 6. TOFA	1. Panuv 2. PUK 3. PUK 4. Panuv 5. A. uveitis 6. A. uveitis	1.MTX, ETN, ANA, ABA 2.MTX, LFN, CZP, ADA, iv MP. 3. MTX, CsA, SSZ, MMF, AZA, IFX, TCZ, CZP, ABA, ADA. 4. MTX, AZA 5. MTX, ADA 6. MTX, AZA, ADA	1. CI 2. CI 3. CI 4. CI 5. CI 6. CI

Based on these data a therapeutical approach of refractory IOP was proposed (Figure 1**).**

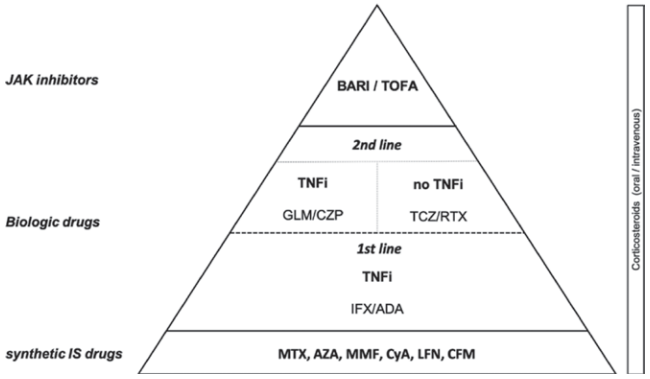

Figure 1. Therapeutical approach

Conclusion: JAKINIB may be an effective and safe therapy in IOP refractory to conventional or even biological immunosuppressive therapy.

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AB1311

INCREASED RISK OF HEPATOTOXICITY WITH DMARDS IN PATIENTS WITH PREVIOUS LIVER TOXICITY WITH ISONIAZID. STUDY IN A SINGLE UNIVERSITY HOSPITAL

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Background: Isoniazid (INH) is used to treat latent tuberculosis infection (LTBI), and hepatotoxicity is one of the most frequent adverse effect. Several Disease-modifying drugs (DMARDs) can also cause hepatotoxicity. Many patients with rheumatic immune mediated diseases (R-IMID) receive INH prior to DMARDs for prophylaxis of LTBI. This risk of hepatotoxicity with DMARDs after hepatotoxicity with INH is unknown.

Objectives: To assess the risk of hepatotoxicity with DMARDs in patients who have presented hepatotoxicity with INH.

Methods: Study of all consecutive R-IMID patients evaluated in the last five years (2016-2020) in a University Hospital, who presented hepatotoxicity after INH and later received DMARDs. We study if they also presented hepatotoxicity with DMARDs. Hepatotoxicity was defined as an elevation of liver enzymes (ALT and/or AST) upper the high limit after the introduction of the treatment.

Results: INH was used in 232 of 7218 patients with R-IMID. We finally included 64 patients (45 women; 70.3%; mean age 53.4±10.5 years), who had hepatotoxicity due to INH (Table 1).

Table 1. Main characteristics of 64 patients with rheumatic immune-mediated diseases (R-IMID) that presented hepatotoxicity after receiving isoniazid (INH).

Variables	Patients (n=64)
Age (years), mean ±SD	53.4±10.5
Sex (women), n (%)	45 (70.3)
R-IMID	
- SpA / PsA	36 (56.3%)
- RA	21 (32.8%)
- SSc	3 (4.7%)
- Conectivopathies	3 (4.7%)
- Other	2 (3.2%)
Liver enzyme elevation over baseline (INH)*	
- x2	64 (100)
- x3	22 (34.4)
- x4 or higher	13 (20.3)
csDMARDs	
- MTX	34 (53.1%)
- HCQ	15 (23.4)
- LFN	13 (20.3)
- SSZ	10 (15.6)
bDMARDs	47 (73.4%)
Targeted synthetic DMARDs (Jakinib)	8 (12.5)

ABA: Abatacept; AZA: Azathioprine, HCQ: Hydroxychloroquine; INH: Isoniazid; LFN: Leflunomide; MMF: Mycophenolate mofetil, MTX: Methotrexate; PsA: Psoriatic arthritis, RA: Rheumatoid arthritis, RTX: Rituximab; SpA: Axial spondyloarthritis; SSc: Systemic sclerosis; TCZ: Tocilizumab; TNFi: TNF inhibitors* Patients with higher liver enzyme elevation are included in the previous groups.

The most frequent R-IMIDs were rheumatoid arthritis, axial spondyloarthritis and psoriatic arthritis. Methotrexate (MTX) (n=34, 53.1%) and TNF inhibitors (n=27, 42.2%) were the conventional and biologic-DMARD more frequently used, respectively. Hepatotoxicity was higher with MTX (14 of 34, 41.2%), and lower with the other DMARDs (Figure 1). Hepatotoxicity was not observed with hydroxychloroquine, azathioprine, mycophenolate mofetil, secukinumab, abatacept or rituximab.

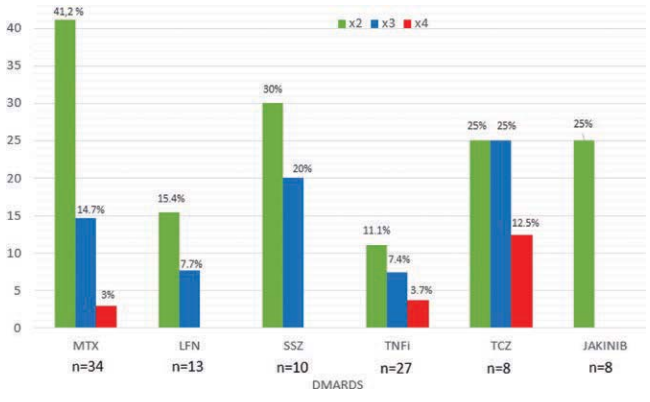

Figure 1. Hepatotoxicity with different DMARDs in 64 patients with previous hepatotoxicity with INH* Patients with higher liver enzyme elevation are included in the previous groups.

Conclusion: In patients with previous hepatotoxicity with INH, we observed an increased risk with different DMARDs, especially with MTX.

Disclosure of Interests: David Martínez-López: None declared, Joy Osorio-Chavez: None declared, Virginia Portilla: None declared, Carmen Álvarez-Reguera: None declared, Alba Herrero-Morant: None declared, Lara Sanchez-Bilbao: None declared, Iñigo Gonzalez-Mazon: None declared, Miguel A González-Gay Speakers bureau: Consultation fees/participation in company-sponsored speaker´s bureau from Abbvie, Pfizer, Roche, and MSD, Grant/research support from: Dr. Miguel A. Gonzalez-Gay received grants/research supports from Abbvie, MSD, and Roche, Ricardo Blanco Speakers bureau: Consultation fees/participation in company-sponsored speaker´s bureau from Abbvie, Lilly, Pfizer, Roche, Bristol-Myers, Janssen, and MSD., Grant/research support from: Dr. Ricardo Blanco received grants/research supports from Abbvie, MSD, and Roche

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AB1312 HIGH PREVALENCE OF IRMD IN SARCOIDOSIS PATIENTS

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Background: Sarcoidosis is a chronic granulomatous disease that primarily affects the lungs and lymph nodes, and can affect any organ and system (1). The incidence of concomitant iRMD is increased in patients with sarcoidosis. Anti-nuclear antibody (ANA) test are frequently used markers for inflammatory rheumatic diseases (iRMDs) (2). The relationship of this association with ANA is not clear.

Objectives: We aimed to determine the frequency of ANA in sarcoidosis patients and its possible correlation with clinical and laboratory data, and also to reveal the severity of osteoporosis in patients with sarcoidosis.

Methods: Ninety sarcoidosis patients, who were followed up in rheumatology clinic were included in this study. ANA were determined with indirect immunofluorescent method and 1/160 titration was accepted as positive. Demographic, clinical, serological, and bone mineral densitometry (BMD) results of all patients were recorded. BMD results were obtained from the images taken before the last date or osteoporotic fracture of the patients.

Results: Average age of the 90 patients (79 females) with sarcoidosis was 57.5 (IQR: 51–66) years, and median disease duration was 7.6 (IQR: 4-19) years. 28 (31.1%) patients had a diagnosis of extrapulmonary sarcoidosis (Most commonly skin, n=20, 71.4%). 21 patients had BMD values consistent with osteoporosis, while 9 patients had osteoporotic fractures. In 18 (20%) patients, rheumatologic autoimmune disease combined with sarcoidosis was found. SpA was diagnosed in 6 patients, RA in 2 patients, Lofgren Syndrome in 2 patients, SjS in 2 patients, systemic sclerosis in 1 patient, and morphea in 1 patient. Other rheumatological diseases were found as uBDH, polymyositis, Gout, Behçet's Disease and FMF. ANA test was performed in a total of 83 patients. ANA positivity was found in 30 (36.1%) patients with sarcoidosis (1/100-1/320 in 12 patients; >1/320 in 18 patients). There was no significant relationship between ANA positivity and gender distribution, age, disease duration, development of extrapulmonary sarcoidosis, refractory disease status, and laboratory findings at the time of diagnosis. It was found that ANA positivity at diagnosis time for sarcoidosis increased the risk of developing iRMD 4.8 times in patients [HR: 4.8, CI 95% (1.455-15.833), p=0.009].

Conclusion: In sarcoidosis, ANA positivity is of great importance in the determination of accompanying iRMDs. It was found that ANA positivity at the time of diagnosis in sarcoidosis patients increased the risk of developing rheumatological autoimmune disease 4.8 fold. Since these patients receive long-term moderate-high-dose steroid-based treatments, they should be closely monitored and screened for osteoporosis.

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Table 1. Distribution of clinical features of patients with sarcoidosis according to ANA results

		ANA (-) (n=53)	ANA (+) (n=30)	
		n (%)	n (%)	p value
Gender	**Female**	46 (86.8)	27 (90)	>0.05
	Male	7 (13.2)	3 (10)	
Rheumatic Disease	**No**	48 (90.6)	20 (66.7)	**0.009 (HR: 4.8, CI 95% (1.455-15.833)***
	Yes	5 (9.4)	10 (33.3)	
Refractory Disease	**No**	35 (66)	19 (63.3)	
	Yes	18 (34)	11 (9.1)	
BMD-DEXA	**Normal**	16 (43.2)	12 (60)	0.630
	Osteopenia	14 (37.8)	4 (20)	
	Osteoporosis	7 (18.9)	4 (20)	
Osteoporotic Fracture	**No**	46 (86.8)	28 (93.3)	0.477
	Yes	7 (13.2)	2 (6.7)	
		Median (IQR)	**Median (IQR)**	**p value**
Age (year)		56.5 (51/64)	58 (51/66)	0.836
Follow-up duration (year)		6 (4/10)	6 (2/9)	0.718
Age at diagnosis (year)		45.5 (38/55)	49 (36/55)	0.861
Calcium (mg/dL)		9.585 (9.25/9.9)	9.4 (9.17/9.76)	0.138
25 (OH)D (pg/ml)		15.5 (10.1/24)	8 (6/12)	0.005
Phosphorus (mg/dL)		3.65 (3.245/3.98)	3.75 (3.3/4.1)	0.17
ACE (mcg/L)		60 (32/87)	59.595 (34/88.225)	0.876
ESR (mm/h)		23 (15/39)	29 (22/48)	0.171
CRP (mg/dL)		4.8 (2.3/17)	5.4 (2.7/24)	0.343

*Multivariate regression analysis

Disclosure of Interests: None declared

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AB1313 THE RATIONAL USE OF BIOLOGICS IN REFRACTORY IMMUNE-MEDIATED INFLAMMATORY DISEASES CONSORTIUM (RUBRIC) NATIONAL REGISTRY: RESULTS ON GLUCOCORTICOID USE AND WORK PRODUCTIVITY

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Background: Rare therapy-refractory immune-mediated inflammatory diseases (IMIDs) are increasingly treated with new targeted therapies such as biological (b) or targeted synthetic (ts) DMARDs. However, in the Dutch healthcare system these treatments are not reimbursed for off-label use unless there is sufficient evidence of efficacy. Currently, no official guidelines or treatment protocols exist for many of these rare diseases. To overcome this issue we set up a national registry to document off-label use of b/tsDMARDs in patients with rare therapy-refractory IMIDs and to document efficacy and safety of these therapies.

Objectives: To report results on glucocorticoid use and work productivity of patients with rare therapy-refractory IMIDs treated off-label with b/tsDMARDs.

Methods: Using the web-based RUBRIC registry patients with rare therapy-refractory IMIDs treated off-label with b/tsDMARDs were prospectively followed to document efficacy and safety. Physicians supplied data on disease activity (i.e. VAS physician and ESR/CRP) and concomitant medication, including glucocorticoid use. Patients filled out questionnaires on patient reported outcomes (PROs; i.e. HAQ, WPAI-GH, SF-36, PASS, EQ-5D) prior to starting off-label treatment and at regular intervals afterwards. Any potential serious adverse events were also recorded.

Results: Many different diagnosis-treatment combinations were recorded (i.e. undifferentiated vasculitis, TRAPS, Hyper-IgD syndrome, auto-inflammatory diseases treated with various b/tsDMARDs). Of the 82 patients currently followed in RUBRIC, for 61 patients multiple questionnaires over a time period of > 1 year were available for analysis. Glucocorticoid use was documented accurately in 55 patients. Analysis of glucocorticoid use demonstrated that the majority of patients (38/55; 69.1%) used glucocorticoids prior to off-label treatment and all patients remained at a stable dose (10/55; 18.2%) or could reduce the dose (23/55; 41.8%), whereas (5/55; 9.1%) could eventually even stop glucocorticoids completely. Of the patients that did not use glucocorticoids prior to off-label b/tsDMARD therapy, no glucocorticoids were initiated. Analysis of WPAI-GH over time revealed that off-label treatment resulted in a significant gain in work productivity in all working patients and 15% of patients who were not employed prior to initiating off-label treatment were able to resume work again, whereas none of the patients became unemployed during off-label treatment. No serious adverse events associated with off-label b/tsDMARD therapy were reported.

Conclusion: Off-label treatment of rare therapy-refractory IMIDs with b/tsDMARDs results in a clear beneficial effect as glucocorticoid use could be reduced or stopped in the majority of patients and a clear increase in work productivity/

employment was observed. Despite these positive outcomes, at present not enough patients per diagnosis-treatment combination have been included in the registry to draw definitive conclusions on efficacy and safety of specific off-label treatments or to formulate treatment recommendations for certain diseases. Consequently, it is important to continue the registry and include more patients or link various (inter)national registries to obtain sufficient data and promote evidence-based and effective use of biologics in rare therapy-refractory IMIDs. This may eventually also help to facilitate reimbursement of these therapies.

Disclosure of Interests: Anne Musters: None declared, Marjolijne Kleijn-de Graaf: None declared, Sander Tas Consultant of: Gebro, GSK, AbbVie, Galvani, Arthrogen/MeiraGTx, Galapagos, Grant/research support from: Pfizer, GSK, Celgene, BMS, Sanofi, AstraZeneca

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AB1314 JANUS KINASE INHIBITORS IN REFRACTORY AUTOINFLAMMATORY SYNDROMES. TWO CASE REPORTS AND LITERATURE REVIEW.

C. Álvarez-Reguera[1], D. Prieto-Peña[1], L. Sanchez-Bilbao[1], A. Herrero-Morant[1], D. Martínez-López[1], M. Á. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*

Background: Autoinflammatory syndromes are characterized by dysregulation of innate immunity and recurrent episodes of fever, cutaneous and other. Janus Kinase inhibitors (JAKINIB) may inhibit innate and acquired immunity. They have been approved in several immune mediated diseases, but not in autoinflammatory syndromes.

Objectives: To assess the efficacy and safety of JAKINIB in refractory autoinflammatory syndromes.

Methods: Study of patients from a single University Hospital and Literature review of refractory autoinflammatory syndromes treated with JAKINIB.

Results: We have identified 2 cases in our hospital. One of them was a 25-year-old girl diagnosed with Blau syndrome refractory to different conventional and biological therapies. Tofacitinib (TOFA) had a good clinical response but was switched to Bariticitinib (BARI) due to severe lymphopenia. The 2nd patient was a 65-year-old man, diagnosed with an autoinflammatory syndrome (WDR1 mutation) and policytemia vera (positive JAK-2; V617F mutation). Based on the JAK2 mutation, BARI was started with complete improvement. In literature review, we found 59 patients (41 women/ 18 men), mean age 38.1±13 years. TOFA (n=23) was the most used JAKINIB, followed by BARI (n=20) and Ruxolitinib (RUXO) (n=16). After starting JAKINIB treatment, most patients presented clinical complete (n=45, 76.3%) or partial (n=11; 18.6%) improvement, only 3 (5.1%) did not respond. (Table 1)

Conclusion: JAKINIB may be an effective therapy in autoinflammatory syndromes refractory to conventional and/or biologic therapy.

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AB1315 SARILUMAB IN PATIENTS WITH REFRACTORY GRAVES' ORBITOPATHY. EFFECTIVENESS AND SAFETY IN A SERIES OF CASES IN CLINICAL PRACTICE.

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Background: Graves' orbitopathy (GO) is an autoimmune disease of the retroocular tissues that occurs in patients with Graves' disease. Tocilizumab (TCZ), an interleukin (IL)-6 inhibitor has been used in patients with glucocorticoid (GC)-resistant Graves' orbitopathy with good results. We have previously reported results obtained in 15 OG patients treated with TCZ where a decrease in mean CAS from 4.9 to 1.7 was observed. Sarilumab, another IL-6 inhibitor, is indicated for the treatment of rheumatoid arthritis and has been used in other pathologies as an off-label use, similar to TCZ, on the grounds that they share a common mechanism of action.

Objectives: To analyse the effectiveness of Sarilumab treatment in patients with GC-resistant OG in routine clinical practice.

Methods: A descriptive retrospective observational study of a series of patients with moderate-severe active OG on Sarilumab treatment was performed. Medical records of patients who had received at least 1 cycle of Sarilumab treatment were reviewed. Demographic and disease data were collected. Effectiveness was assessed by CAS (Clinical Activity Score) reduction before and at 3-6 months of treatment. A reduction of CAS≥ 2 points together with obtaining inactivity (CAS < 3) was considered a favourable response. The study was approved by Research Ethics Committee.

Results: In the rheumatology department of the Hospital Virgen Macarena, 25 patients were treated with IL-6 inhibitors, 20 with tocilizumab and 5 with Sarilumab. Five patients were included, 2 women and 3 men, with a mean age of 43 years. All but one had bilateral ocular involvement. 2 patients were active smokers, 1 ex-smoker and 2 non-smokers. Two patients were diabetic, none of them had retinopathy. The mean time of disease until their evaluation in Rheumatology was 3.5 years. All had been treated with antithyroid drugs, 1 with Radioiodine and one patient had undergone thyroidectomy. 100% of patients had an active moderate-severe orbitopathy, all had been treated with local measures, 3 with selenium and none had undergone rehabilitative surgery. Three patients had been on at least one course of intravenous steroids. Patients received Sarilumab at a dose of 200 mg subcutaneous injection every 15 days for a mean of 11 months (range 7-21 months), 100% in monotherapy. The mean initial CAS was 5/7 and the final CAS was 2.75/10. The CAS score was reduced by 3 points on average. 100% had a favourable response and achieved inactivity, also reducing the severity of the disease. Furthermore, there was an improvement in thyroid function parameters

Table 1. Case reports and literature review of patients with refractory autoinflammatory syndromes treated with Janus Kinase Inhibitors.

Study, year (Ref)	Cases, n	Age/Sex	Underlying Disease	JAKINIB	Previous immunosuppressive treatment	Clinical Evolution
García-Robledo et al, 2022 (1)	1	16, F	FMF	TOFA	MTX, TCZ, CANA	C.I.
Gök K et al, 2017 (2)	1	27, F	FMF	TOFA	MTX	C.I.
Forbes et al, 2018 (3)	17	12.4±7.5*, F=9	STAT1 and TAT3 GOF	RUXO (n=16) TOFA (n=1)	AZA(n=1), iv immunoglobulins (n=3), CsA (n=2), RTX (n=2) ECU (n=1), ANA (n=1), MTX (n=2), CYC (n=2), MMF (n=1)	C.I. (n=14) N.R. (n=3)
Landhari et al, 2020 (4)	1	43, F	AOSD	BARI	MTX, SSZ, ANA, IFX, TCZ, ABA	C.I.
Sánchez et al, 2018 (5)	18	12.5 (1.2-24.1) ** (F=12)	CANDLE n=10 CANDLE-related n=4 SAVI n=4	BARI	Immunomodulators (n=17) Biologics (n=13)	C.I. (n=16) P.I. (n=2)
Karadeniz et al, 2020 (6)	4	1. 28, M 2. 58, F 3. 64, F 4. 43, F	FMF	TOFA	1. AZA, MTX, ANA, CANA, IFX, TCZ 2. SSZ, MTX, LEF, ANA, ADA, TCZ 3. SSZ, MTX, LEF, HCQ, CsA, ADA, ABA, ANA 4. SSZ, ADA, ETA, ANA	1. C.I. 2. C.I. 3. P.I. 4. C.I.
Hu et al, 2020 (7)	14	34,8±14* F=12	AOSD	TOFA	MTX (n= 8), HCQ (n=5), CsA (n=5), TCZ (n=2), ANA (n=1)	C.I. (n=7) P.I. (n=7)
Honda et al, 2020 (8)	1	68, F	AOSD	TOFA	TCZ, Tacrolimus, CYC	P.I.
Present study, 2022	2	1.25, F 2. 64, M	1. Blau Syndrome 2. Autoinflammatory syndrome (WDR1 mutation)	1.TOFA/BARI 2.BARI	1. MTX, ETN, ANA, ABA 2. ANA	1. C.I. 2. C.I.

*Mean±Standard deviation, **Median (range)

Abbreviations: ABA: abatacept, ADA: adalimumab, ANA: anakinra, AOSD: adult onset Still disease, AZA: azathioprine, BARI: baricitinib, CANA: canakinumab, CANDLE: Cronichle atypical neutrophilic dermatosis with lypodistrophy and elevated temperature, C.I.: Complete improvement, CsA: cyclosporine A, ECU: eculizumamb, ETN: etanercept, FMF: familial mediterranean fever, HCQ: hydroxychloroquine, IFX: infliximab, LEF: leflunomide, MMF: mycophenolate mofetil, MTX: methotrexate, N.R: no response, P.I.: partial improvement, RUXO: ruxolitinib, SAVI: STING-associated vasculopathy with onset in infancy, SSZ: sulfasalazine, STAT1 and STAT3 GOF: STAT1 and STAT 3 gain of function, TCZ: tocilizumab, TOFA: tofacitinib.

and a reduction in antibody titters against TSH receptor and anti-thyroid peroxidase. All patients were continuing treatment except for one patient who had discontinued treatment due to clinical remission. No adverse events were recorded except for mild neutropenia in one patient, which did not require dose reduction. No patient required subsequent immunosuppressive treatment or surgery.

Conclusion: Sarilumab treatment in patients with moderate-severe active OG appears to be an effective and safe therapeutic alternative, clinically similar to that obtained with TCZ in our series. This is the first published series of Sarilumab use in OG patients.

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AB1316 PREVALENCE, DIAGNOSTIC DELAY AND TREATMENT PROFILE OF PATIENTS WITH MONOGENIC AUTOINFLAMMATORY DISEASES IN AN ADULT RHEUMATOLOGY SERVICE OF A TERTIARY HOSPITAL.

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Background: Monogenic autoinflammatory diseases (MAISs) have a low prevalence and a delay in their diagnosis, with the risk of complications being AA amyloidosis the most serious. Biological therapy has been a fundamental pillar in improving the prognosis of these diseases, reducing said risk.

Objectives: We aim to study the prevalence, diagnostic delay and treatment profile of MAISs patients in an adult rheumatology service of a tertiary hospital.

Methods: Observational and retrospective study of patients with MAISs, excluding those without genetic test or negative genetic test, with a follow-up period of 17 years (2005-2021). Demographic, clinical and therapeutic variables were collected.

Results: 24 patients (50% men) were included with a mean age of 27,88 ± 11.57y. The prevalence of MAISs was 0.34%, from a total of 7,032 patients followed up in the Rheumatology service during 2020. Familial Mediterranean Fever (FMF) was the most frequent (70.83%). FMF, Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), and Hyperimmunoglobulin D Syndrome (HIDS) had a median age at symptom onset of 6, 8.5 and 2 years, a median diagnostic delay of 6, 8.75 and 11 years and a mean duration of the bouts of 4.47 (2.87), 12.25 (7.59) and 6 (2.65) days, respectively. The most frequent symptoms were: fever (79.17%), arthralgia/arthritis (79.17%) and abdominal pain (75%). During follow up 20.83% received glucocorticoids (GC) chronically (more than 3 months), 79.16% colchicine, 16.66% methotrexate and 41.66% biological therapies (Table 1). At the end of follow up 4.17% were receiving GC, 79.16% colchicine, 4.16% methotrexate and 33.33% biological therapies (Table 1). No AA amyloidosis or deaths were reported.

Table 1.

MAISs	Gender (men %)	Biological therapies prescribed during follow up (n)	Patients under biological therapies at the end of follow up (n)
FMF (n=17)	41.17%	Anakinra: 2 Canakinumab: 2 Etanercept: 1 Tocilizumab: 1	Anakinra: 3 Canakinumab: 2
TRAPS (n=4)	100%	Anakinra: 1 Canakinumab: 1 Etanercept: Tocilizumab:	Canakinumab: 1
HIDS (=3)	66.66%	Anakinra: 3 Canakinumab: 3 Etanercept. 1	Canakinumab: 2

Conclusion: MAISs prevalence was 0.34%. The diagnostic delay was of years, more than a decade for HIDS. Colchicine was widely used and well tolerated. Synthetic DMARDs had little role in treatment. Biological therapies were prescribed in a third of patients, anti IL-1 being the most used.

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AB1317 SERUM INTERLEUKIN 37 LEVELS IN FAMILIAL MEDITERRANEAN FEVER PATIENTS AND ASSOCIATION WITH CLINICAL FEATURES

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Background: Familial Mediterranean Fever (FMF) is the most common form of autoinflammatory diseases that is characterized by febrile episodes of serositis, arthritis and skin rash (1). Mutations in MEFV gene causes dysfunction of pyrin inflammasome, ultimately resulting in over-activation of Caspase-1 which is responsible for catalytic activation of interleukin (IL)-1 beta and gasdermin-D (2). IL-37 is also one of the IL-1 cytokines activated by caspase-1 acting as natural inhibitor of inflammation (3).

Objectives: IL-37 has pathogenetic roles for certain inflammatory diseases. We aimed to investigate serum IL-37 levels and its relationship with clinical and laboratory features of disease.

Methods: 58 adult patients diagnosed with FMF according to Tel Hashomer criteria were included. Thirty subjects were served as healthy control subjects. Demographic, genetic, clinical and laboratory features and treatment responses of patients were recorded. Twenty-nine patients were colchicine responsive whereas 29 were colchicine refractory. Serum IL-37 levels were measured by ELISA from blood samples obtained at attack free periods.

Results: Peritonitis was the most common attack type (81%) followed by fever (80%) and arthritis (67%). There was no difference between FMF patients and healthy subjects for their serum IL-37 levels. A negative correlation was found between IL-37 values and erythrocyte sedimentation rate in FMF patients (r: -0,31; p:0.015). IL -37 level was found to be significantly lower in patients who suffer from arthritis (median [IQR] 119 [396] ng/L vs 53 [164] ng/L, p= 0.03), myalgia (147 [364] ng/L vs 53 [84] ng/L, p= 0.05) or skin rash (102 [360] ng/L vs 54 [130] ng/L, p= 0.05) compared to those who did not have these attacks.

Conclusion: Although there was no difference in serum IL-37 levels between FMF patients and healthy subjects, IL-37 seem to be associated with musculoskeletal and skin attacks of FMF. Further research is needed to determine whether IL-37 have relationships with other features of FMF such as spondyloarthritis and febril myalgia.

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AB1318 ULTRASOUND EVALUATION OF ACHILLES ENTHESIS AND GASTROCNEMIUS ARCHITECTURE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: PRELIMINARY RESULTS FROM A CROSS-SECTIONAL STUDY

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Background: Exertional leg pain and Achilles enthesitis are two musculoskeletal manifestations which have been described in familial Mediterranean fever (FMF) patients. Muscle performance is related both with mass and architecture. Measurements of muscle thickness and pennation angle in muscles with pennate structure, such as gastrocnemius, are representative of muscle mass and architecture, both of which can easily be measured via musculoskeletal ultrasound.

Objectives: Aim of this study is to evaluate thickness and pennation angle of medial gastrocnemius via ultrasound to evaluate muscle structure in FMF patients in order to detect implications of altered muscle condition and search for any relations with exertional leg pain/Achilles enthesitis. To our best knowledge this is the first study on the subject.

Methods: Consecutive FMF patients meeting Tel-Hashomer criteria between the ages of 18-65 were enrolled. A control group was formed from healthy volunteers

with similar demographics. All ultrasound evaluations were performed by the same observer. Thickness and pennation angle of medial gastrocnemius was measured. Achilles tendon findings were scored according to OMERACT suggestions and total inflammation and structural damage scores recorded.

Results: A total of 40 FMF patients and 17 controls were enrolled. Clinical characteristics and ultrasound findings of subjects were presented in Table 1. All FMF patients were under colchicine treatment and 10% was also under anti-interleukin 1 treatment. Demographics were similar between groups. Right gastrocnemius pennation angle was significantly reduced in FMF group (degree, median(IQR): 20.8 (3.6) vs 22.7 (4.5), p=0.048). OMERACT ultrasound inflammation total scores were incresed on both sides in FMF group. When gastrocnemius and enthesis ultrasound findings were compared between FMF patients with and without exertional myalgia, no significant differences were observed. When FMF patients with and without enthesis findings in ultrasound examination were compared, again no significant differences in pennation angles and muscle thicknesses were observed.

Table 1. Clinical characteristics and ultrasound findings in subjects

	FMF group	Control group	
	N =40	N=17	p
Age, years, median (IQR)	42.8 (23.0)	38.0 (15.0)	0.447
Gender, female, number (%)	29 (72.5)	10 (58.8)	0.310
BMI, median (IQR)	24.6 (5.3)	24.8 (5.7)	0.485
Presence of exertional myalgia, number (%)	22 (55)		
Gastrocnemius thickness, mm, median (IQR)			
Right	19.7 (2.9)	20.7 (5.6)	0.303
Left	19.6 (2.7)	20.7 (4.6)	0.321
Gastrocnemius pennation angle, degrees, median (IQR)			
Right	20.8 (3.6)	22.7 (4.5)	**0.048**
Left	21.0 (3.3)	21.8 (4.7)	0.417
OMERACT ultrasound tissue damage total score, median (IQR)			
Right	2.0 (2.0)	2.0 (2.0)	0.659
Left	2.0 (2.0)	2.0 (2.0)	0.280
OMERACT ultrasound inflammation total score, median (IQR)			
Right	0 (2.0)	0 (0)	**0.005**
Left	0 (2.0)	0 (0)	**0.023**

Conclusion: Our preliminary results imply altered right gastrocnemius structure in FMF patients regardless of Achilles tendon involvement and exertional myalgia, which may imply altered muscle function. By increasing the number of subjects we plan to achieve more accurate results.

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AB1319 MUSCULOSKELETAL IMMUNE-RELATED ADVERSE EVENTS IN PATIENTS WITH SOLID CANCER TREATED WITH CHECKPOINT INHIBITORS: A CASE SERIES

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Background: Immune-related adverse events (irAE) are common in cancer patients treated with checkpoint inhibitors. irAE can affect any organs and systems including musculoskeletal. The characteristics of immune-related musculoskeletal disorders (MD) still remain incomplete.

Objectives: to determine the characteristics of MD manifested during the treatment of solid cancer with check-point inhibitors in case series.

Methods: We identified 13 patients with inflammatory MD manifested during treatment with check-point inhibitors. Mean age of patients was 59±10 (ranged 43-74) years, 7 (54%) of them were female. Patients were treated with anti-PD-1 (77%) and anti-PD-L1 (33%) drugs (nivolumab [n=6], pembrolizumab [n=3], atezolizumab [n=3], prolgolimab [n=1]). Cancer types include melanoma (n=5), renal cell carcinoma (n=3), bladder cancer (n=2), non-small cell lung cancer (n=1), breast cancer (n=1), cervical cancer (n=1). 7 (54%) patients had another irAE also including thyroiditis (n=3), neuropathy (n=2), rash (n=1), sicca syndrome (n=1), hepatitis (n=1). The median time of musculoskeletal manifestation after the treatment`s onset was 20 [9-48] weeks.

Results: Musculoskeletal manifestations were performed by synovitis in 9 (69%) cases, tenosynovitis in 11 (85%), entesitis in 4 (31%), morning stiffness(>30min) in 4 (31%). The most commonly affected areas were knees (77%) shoulders (69%), hands (69%) and feets (46%). Bilateral involvement was in 9 (69%) cases. MD was transient in 2 cases and persistent in 11 (9 patients with inflammatory arthritis and 2 patients with periarthritis). Clinical characteristic of inflammatory arthritis was represented by tenosynovitis more than synovitis in 3 cases (2 patients with symmetrical inflammatory polyarthritis and severe tenosynovitis, 1 patient with RS3PE-syndrome). In 6 cases inflammatory arthritis was represented by synovitis primarily (3 patients with symmetrical polyarthritis, 2 patients with oligoarthritis, 1 patient with monoarthritis). Severity of MD was assessed according to Common Terminology Criteria for Adverse Events V5.0. Grade 1 was in 2 cases (15.5%), grade 2 in 9 (69%), grade 3 in 2 (15.5%). Laboratory findings include ESR ≥30 mm/h in 7/12 (58%) cases (the median of ESR was 34 [14-42] mm/h); CRP >5 mg/l in 7/10 (70%) cases (the median of CRP was 7.2 [4.6-12.9] mg/l). RF, ACPA were negative in all cases. ANA test was positive without any specificities in 7/10 (70%) cases in dilution 1:160 (n=2), 1:320 (n=3), 1:640 (n=2). Treatment of these conditions include NSAIDs (n=10), oral systemic corticosteroids (n=5), intra-articular corticosteroids (n=1), and csDMARDs (hydroxychloroquine [n=5] methotrexate [n=1]) as corticosteroid-sparing agents. 2 patients with polyarthritis and generalized tenosynovitis and 1 patient with symmetrical polyarthritis required treatment with ≤20 mg daily of prednisone. 2 patients with poly- and oligoarthritis were treated with 5-10 mg daily of prednisone. 5 patients with arthritis required long-term treatment with NSAIDs, corticosteroids and csDMARDs (the median of follow-up was 12 [3-12] months). 1 case of the inflammatory polyarthritis with severe tenosynovitis required to suspend the anticancer treatment with checkpoint inhibitor.

Conclusion: Our data demonstrated that the musculoskeletal irAE may be represented by heterogeneous manifestation and required long-term treatment. In rare cases musculoskeletal irAE can lead to suspension of the anticancer treatment with checkpoint inhibitors.

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AB1320 JAK2 (V617F) MUTATION AND ASSOCIATION TO RHEUMATOLOGICAL DISEASES TREATMENT. STUDY OF 130 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL.

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Background: Janus Kinases (JAK) can promote cytokine production in immune and hematopoietic cells. The JAK-2 (V617F) mutation is the most frequently detected mutation in myeloproliferative neoplasms (MPN) which include essential thrombocythemia (ET), polycythemia vera (PV), primary myelofibrosis (PMF) and undifferenciated MPN. JAK-2 (V617F) mutation displays a pro-inflammatory phenotype that may be associated to a higher risk of immune mediated diseases (IMID).

Objectives: In a wide series of JAK2 (V617F) mutation, we assess the presence of a) IMID (rheumatic and non-rheumatic), b) treatment of rheumatic IMID.

Methods: We studied all the patients diagnosed with a positive JAK-2 (V16F) mutation in a single University Hospital from January 2004 to December 2019. JAK-2 (V16F) mutation was detected by using both peripheral blood and bone marrow samples. Associated IMID and treatment of rheumatic IMID were evaluated.

Results: We included 130 patients (73 men/57 women; mean age, 70.1±14.5 years). All of them were diagnosed of MPN; ET (n=64, 49.2%), PV 46 (35.4%), undifferentiated MPN (n=12, 9.2%) and PMF (n=8, 6.1%). In 10 of these 130 patients (7.7%) a rheumatic IMID was diagnosed: rheumatoid arthritis (RA) (n=4; 40%), polymyalgia rheumatica (PMR) (n=3; 30%), Sjögren syndrome (SS) (n=1; 10%), antiphospholipid syndrome (APS) (n=1; 10%) and autoinflammatory syndrome (WDR1 mutation) (n=1; 10%). Patients with RA, SS, PmR, and APS were clinically mild. RA patients were seronegative, non-erosive and without extraarticular involvement. Treatment and response are summarized in Table 1. All patients diagnosed with PMR were treated with glucocorticoids (prednisone 5 mg/12 hours), SS with hydroxychloroquine (HCQ) (200 mg/day), APS was anticoagulated with acenocumarol and one autoinflammatory syndrome was finally treated with baritinib (4 mg/day) after failure to anakinra (100 mg/day).

Conclusion: Except in autoinflammatory syndrome, most rheumatic IMID associated to JAK-2 (V16F) mutation are clinically mild, and treatment and response of patients seems similar or even better than those without this mutation.

Table 1. Treatment of 10 patients with rheumatic IMIDs and JAK-2 (V16F) mutation.

Cases, n	Underlying Disease	Age/Sex	Treatment	Clinical Evo
4	RA	67/M 87/F 93/M 82/M	NSAIDs PDN/MTX PDN/MTX HCQ	Improveme Improveme Improveme Improveme
3	PMR	68/M 89/M 82/M	PDN PDN PDN	Improveme Improveme Improveme
1	APS	76/F	Acenocumarol	No Improve
1	SS	78/F	HCQ	Improveme

Abbreviation: ANA: anakinra, BARI: baricitinib, NSAIDs: Non-Steroidal Anti-inflammatory Drugs, PDN: prdnisone, RA: Rheumatoid arthritis, SS: Sjögren syndrome, PMR: polymyalgia rheumatica.

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AB1321 THE DIAGNOSTIC DELAY IN PATIENTS WITH SCHNITZLER SYNDROME: A CASE SERIES

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Background: Schnitzler syndrome is a rare syndrome associated with recurrent whealing and monoclonal gammopathy. Since its first description in 1972 by the French dermatologist Prof. Liliane Schnitzler, around 500 cases have been described in Europe. The diagnostic delay in Schnitzler syndrome of 5 years was previously reported [Lipsker et al, 2001]. Despite a growing clinical experience [de Koning et al, 2014], Schnitzler syndrome presents a diagnostic challenge in clinical practice. The variation in the diagnostic delay in Europe is a subject of an ongoing systematic review by our multidisciplinary team.

Objectives: In this work, we would like to analyze a diagnostic delay in the patients with Schnitzler syndrome followed up at tertiary clinical and research setting.

Methods: We present the data from the patients with Schnitzler syndrome that have been under our care by a multidisciplinary team over a period from 2015 to 2021. All patients were analyzed for the age of disease onset and a diagnostic delay for Schnitzler syndrome.

Results: There are currently 14 patients with Schnitzler syndrome under our care. Of these, there were eight men and six women. The median age at the disease onset was 50.5 years, with the range from 25 to 79 years. The median diagnostic delay in our patient series was 3 years, ranging from 1 to 22 years. Noteworthy, in three patients the diagnostic delay for Schnitzler syndrome was over 5 years [6, 12 and 22 years]. Nine patients were treated with IL-1 inhibitors (iIL-1) (canakinumab and anakinra).

Conclusion: Our analysis suggest that the diagnostic delay remains considerable even 50 years after the initial description of this syndrome. Our data on the diagnostic delay in Schnitzler syndrome is in keeping with the clinical experience in most countries with over 5 published cases, including France, Germany, Spain, Portugal and Italy. An early recognition of Schnitzler syndrome is crucial for prompt treatment targeting IL-1. The rarity of this syndrome and a wide range of initial signs and symptoms in these patients delay the correct diagnosis and a start of the biological therapy in these patients. An increased awareness of Schnitzler syndrome may reduce the diagnostic delay in these patients. A multidisciplinary approach is essential for an early diagnosis of Schnitzler syndrome.

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AB1322 APPENDICITIS STILL A MISDIAGNOSIS FOR FMF PATIENTS

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Background: Familial Mediterranean Fever(FMF) is an autoinflammatory disease characterized by recurrent polyserositis attacks. Attacks typically consist of fever and/or abdominal pain and/or chest pain and/or arthritis. The disease is caused by mutations in the MEFV gene. Abdominal pain during the attacks is frequently misdiagnosed as acute abdomen and these patients go undersurgical intervention is not uncommon [1].

Objectives: Severe abdominal pain during FMF attacks is frequently misdiagnosed as acute abdomen and patients receive surgical intervention. In this study, we aim to compare the clinical and genetic characteristics of FMF patients with appendectomies to those without appendectomies.

Methods: We reviewed 176 patients with FMF who went under appendectomy. We randomly matched these patients with 176 FMF patients without appendectomy for comparison. We compared clinical manifestations, MEFV mutations, and treatment modalities.

Results: In this study, 176 patients with FMF went under appendectomy. Only 2 of these appendectomies were performed after FMF diagnosis. In the appendectomy group fever(84% vs 68%), abdominal pain(91% vs 79%), pathogenic exon 10 mutations(65% vs 59%), lower leg pain(0.5% vs 0%) and orchitis(0.5% vs 0%) were more common but only the abdominal pain and fever was statistically significant. In the control group chest pain(18% vs 19%), arthralgia(46% vs 53%), arthritis(29% vs 37%), anti IL-1 usage(3% vs 5%), amyloidosis (0% vs 3%) and erysipelas(1% vs 3%) were more common but none of them were statistically significant. Myalgia(3%) was the same in both groups[Table 1]. Median diagnostic delay was 8(IQR 2-15) years in the appendectomy group and 3.5(IQR1-10) years in the control group.

Table 1. Characteristics of the patients

	No Of Patients(%) Appendicitis	No Of Patients(%) Control Group	P value
Patients	176(100)	176(100)	
Fever	148(84)	120(68)	0.0007
Abdominal Pain	160(91)	139(79)	0.0029
Chest Pain	32(18)	33(19)	1
Arthralgia	81(46)	94(53)	0.20
Arthritis	51(29)	65(37)	0.12
Myalgia	5(3)	5(3)	1
Erysipelas	2(1)	5(3)	0.45
Lower Leg Pain	1(0.5)	0(0)	-
Orchitis	1(0.5)	0(0)	-
Anti IL-1 usage	6(3)	9(5)	0.6
Amyloidosis	0(0)	6(3)	-
Diagnostic Delay	8.5(IQR2-15) years	3.5(IQR1-10) years	0.0002
Pathogenic Exon 10 Mutations	114(65)	103(59)	0.27
Appendectomy Before FMF diagnosis	174(99)	0(0)	

Conclusion: Even after the discovery of colchicine and identification of the MEFV gene diagnosis of FMF remains a challenge. Previous studies reported a median diagnostic delay of 8.2-11 years. In these studies, 28%-32% of the patients went under abdominal surgical intervention before the diagnosis of the FMF[2,3]. The most common symptoms of FMF(fever and abdominal pain) are also the most common symptoms of acute abdomen. Thus distinguishing between FMF and acute abdomen in undiagnosed FMF patients represents an understated problem. These patients have a longer diagnostic delay[8(IQR 2-15) vs 3.5(IQR1-10) years], worse control of attacks, poorer quality of life. In our study, most of the appendectomies were unnecessary in the FMF patients. Thus we recommend investigating the patient for FMF if the evidence of the acute abdomen does not expand beyond the symptoms.

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AB1323 THE MYSTERY OF FAMILIAL MEDITERRANEAN FEVER: IS THERE ANY FACTOR TRIGGERING THE ATTACKS?

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by recurrent episodes of fever and serositis. Although it is known that the attack frequency differs among patients carrying different mutant genotypes [1], whether physical and environmental factors play a role in triggering attacks or whether they have an influence on timing of attacks remains to be elucidated.
Objectives: We aimed to identify different conditions causing flare-ups in FMF course and to investigate if there is a significant difference between patients carrying distinct mutations, regarding the distribution of the factors mentioned.
Methods: Two hundred patients were randomly selected among individuals who were routinely followed-up with FMF diagnosis in our centre. Individuals carrying only a variant of unknown significance or polymorphism such as R202Q, according to Infevers database, were excluded in order to gather a cohort consisting of patients with definite FMF. An inquiry was made based upon triggering factors determined by the patients themselves. The patients were classified into subgroups by their sex and mutation genotype. Since M694V variant is responsible for pronounced FMF course [2], we sorted the patients according to their status for M694V mutant allele. Group A included patients carrying M694V homozygously. Group B included patients carrying at least one M694V mutant allele whereas Group C consisted of patients who were non-M694V carriers. Chi-square test was performed to assess distribution of the trigger factors in terms of establishing its significance.
Results: Detailed distribution of trigger factors is shown in Table 1. 144 out of 200 patients described a culprit condition. Patients usually stated more than one factor, however some patients reported only one. The most-reported trigger factors by the cohort are summarized as following: 76 emotional stress (38%), 60 menstruation (30%), 40 cold exposure (20%), 34 fatigue (17%), 13 seasonal changes (6.5%). The distribution of trigger factors between Group A, B, and C were non-significant (p=0.88).

Table 1. The distribution of triggering factors in subgroups.

Group	Total (%)	Reported trigger factor (%)	Menstruation (%)	Emotional stress (%)	Cold exposure (%)	Fatigue (%)	Seasonal changes (%)	Others (%)
Female	123	97 (78.8)	60 (48.8)	47 (38.2)	24 (19.5)	19 (15.4)	7 (5.7)	6 (4.9)
Male	77	47 (61)	-	29 (37.7)	16 (20.8)	15 (19.5)	6 (7.8)	7 (9.1)
Group A	61	44 (72.1)	14 (23)	24 (39.3)	13 (21.3)	12 (19.7)	4 (6.6)	6 (9.8)
Group B	165	120 (72.7)	49 (29.7)	66 (40)	34 (20.6)	29 (17.6)	13 (7.9)	11 (6.6)
Group C	35	24 (68.6)	11 (31.4)	10 (28.6)	6 (17.1)	5 (14.3)	0	1 (2.8)

Group A: M694V homozygous patients, Group B: patients with at least one M694V allele, Group C: non-M694V carriers

Conclusion: We concluded that trigger factors did not vary between distinct mutant genotypes. Although emotional stress is the most reported trigger factor by the participants, one should bear in mind that emotional stress influences most chronic diseases negatively. We also observed that menstruation overtly triggers an FMF attack. Additionally, cold exposure should be considered as a notable trigger factor. It is still unclear what triggers an FMF attack in 28% of the patients, remains a mystery.
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AB1324 DIFFERENCES IN PERIPHERAL BLOOD B-CELL SUBSETS IN PATIENTS WITH IGG4-RELATED DISEASE, PRIMARY SJOGREN'S SYNDROME AND HEALTHY DONORS

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Background: The level of circulating plasmablasts has been proposed as a good marker for diagnosing and monitoring IgG4-related disease (IgG4-RD) independent of serum IgG4 level [1]. However elevated plasmablasts can be seen in other rheumatologic conditions.
Objectives: To compare B-cell subsets in peripheral blood of IgG4-RD, Sjogren's syndrome (SjS) patients (pts) and healthy controls.
Methods: Twelve pts with clinically active IgG4-RD (7F/5M, mean age 50,25 years (range 33-62), 20 active SjS pts (19F/1M, mean age 42 years (range 32-54 years); median disease duration 3 (2-10) years; ESSDAI score ≥5 in 6 pts,) and 20 healthy donors were included. SS was diagnosed based on the ACR-EULAR 2016 criteria. IgG4-RD was diagnosed according to comprehensive diagnostic criteria (H. Umehara, 2011). CD19+ B cells, memory B-cells (CD19+CD27+), non-switched memory B-cells (CD19+IgD+CD27+), switched memory B-cells (CD19+IgD-CD27+), naïve (CD19+IgD+CD27-), double negative (CD19+IgD-CD27-), transitional (CD19+IgD+CD10+CD38+) B-cells, plasmablasts (CD19+CD38+++IgD-CD27+), and plasma cells (CD19+CD38+) were analyzed by multicolor flow cytometry using cytometer Navios (Beckman Coulter, USA). The nonparametric Mann-Whitney test was used for statistical analysis. Data were shown as median (Me) with an interquartile range of 25 - 75 percentile. The differences were considered statistically significant when $p < 0.05$. Statistica 10 for Windows (StatSoft Inc., USA) package was used for statistical data processing.
Results: There were no significant differences in the number of all studied B-cell subsets between pts with IgG4-RD and with SjS. But absolute numbers of plasmablasts, memory B-cells cells and transitional B-cells in IgG4-RD were significantly higher than in healthy donors: 4.5[1;9.8] $x10^3$/µl vs. 0.2 [0.09;0.4] $x10^3$/µl; 41 [33.5;57.5] $x10^3$/µl vs. 2.5 [1;6.3]; 12 [6.5;21] $x10^3$/µl vs. 0.1 [0;0.23] $x10^3$/µl respectively, $p<0.05$ for all cases.

Table 1. Peripheral blood B-cell subsets in patients with SS and healthy donors.

B-cell subsets, Abs. $x10^3$/µl	IgG4-RD	SjS	HD	P<0.05
B lymphocyte	166 [109.3;251.3]	164.5 [109.3;236.3]	150 [95;200]	
plasmablasts	4.5 [1;9.8]	2 [1;3.5]	0.2 [0.09;0.4]	*
transitional B-cells	12 [6.5;21]	8.5 [4;32.5]	0.1 [0;0.23]	*
switched cells	24.5 [20;41.8]	18.5 [11;29.8]	20 [9.75;40]	
non-switched cells	16.5 [10.5;21]	7 [3.75;15.5]	10 [4.75;20]	
memory B-cells	41 [33.5;57.5]	26 [14.8;40.8]	2.5 [1;6.3]	*
naïve B-cells	122 [63.3;176.5]	107.5 [49.5;193.8]	100 [57.5;100]	
double negative	13.5 [8.8;17]	10.5 [5.3;22.3]	20 [9.75;22.5]	

HD healthy donors
* IgG4-RD and HD groups compared, $p<0.05$

Conclusion: Immunophenotyping showed disturbed homeostasis of the B-cells subpopulations in IgG4-RD pts with a significant increase in plasmablasts compared to HD, but there were no differences between IgG4-RD and SjS pts. Further research is needed to evaluate the diagnostic utility of circulating plasmablasts in IgG4-RD.
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AB1325 DIAGNOSTIC DELAY IN FAMILIAL MEDITERRANEAN FEVER: IS IT STILL A PROBLEM?

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Background: Familial Mediterranean fever (FMF) is a rare hereditary autoinflammatory disease with disease onset in childhood in most cases. Although autoinflammatory disease awareness is increasing among physicians, delayed diagnosis is still prevalent as a cause of greater morbidity[1].
Objectives: We aimed to study the characteristics of FMF patients diagnosed between 2000-2010 and 2011-2021 and to see if there was a difference in diagnostic delay.
Methods: We retrospectively evaluated the medical records of the FMF patients followed up in our rheumatology clinic that were diagnosed between 2000-2021 and split them into two groups according to the year they received their diagnosis. There were 1151 patients diagnosed between 2000-2010 (Group 1) and 821 patients diagnosed between 2011-2021 (Group 2). The data studied included gender, age of onset, diagnostic delay, attack characteristics, MEFV mutation, and family history.
Results: The median current age of patients in Group 1 is 37 years (IQR:30-46) and the median current age of the patients in Group 2 is 36 years (IQR:29-44). The female to male ratio was 1.57 in Group 1 and 1.75 in Group 2, with no significant difference between the groups. Group 2 had later disease onset ($p<0.001$) and later diagnosis ($p<0.001$) than Group 1 as shown in the Table 1. The proportion of patients with at least one M694V mutation was higher in Group 2 ($p<0.001$). The attack durations did not vary between the groups. There was no significant difference in the prevalence of abdominal pain, fever, arthritis, and arthralgia between

Group 1 and Group 2. Chest pain (p=0.005), myalgia (p<0.001), and erysipelas-like erythema (p=0.041) were more common in Group 2 than Group 1. Patients with positive family history were more frequent in Group 2 than Group 1 (p=0.046).

Table 1.

	Group 1 (2000-2010, n=1151)	Group 2 (2011-2021, n=821)	p
Female/Male, n	704/447	522/299	0.275
Age at onset, median (IQR) years	13 (7-21)	18 (12-26)	**<0.001**
Delay in diagnosis, median (IQR) years	4 (1-11)	5,5(2-15)	**<0.001**
Attack duration, median (IQR) years	3(2-4)	3(2-4)	0.325
Presence of at least one M694V mutation (%)	526(46%)	390(60%)	**<0.001**
Presence of abdominal pain in the initial attack (%)	936(81%)	669(81%)	0.926
Presence of fever in the initial attack (%)	855(74%)	592(72%)	0.281
Presence of chest pain in the initial attack (%)	218(19%)	199(24%)	**0.005**
Presence of arthritis in the initial attack (%)	330(29%)	215(26%)	0.224
Presence of arthralgia in the initial attack (%)	213(19%)	170(21%)	0.223
Presence of myalgia in the initial attack (%)	45(4%)	65(8%)	**<0.001**
Presence of erysipelas like erythema in the initial attack (%)	31(3%)	36(4%)	**0.041**
Presence of positive family history (%)	652(57%)	502(61%)	**0.046**

Conclusion: There was some increase in the diagnostic delay in 2011-2021 compared to 2000-2010. This may be partly due to the later onset of symptoms in patients diagnosed in 2011-2021, which could have led the physicians to consider other differential diagnoses. Nevertheless, diagnostic delay in FMF still seems a prevalent problem that should be addressed to prevent excess morbidity and mortality.

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AB1326 EFFICACY AND SECURITY OF TNF-A INHIBITORS BIOSIMILARS IN NON INFECTIOUS UVEITIS

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Background: Biological drugs have become established as an effective therapeutic alternative to non infectious uveitis refractory to the usual treatment. In that sense, expiry of patents for tumor necrosis factor (TNF-a inhibitors) has allowed the development of biosimilars such as Infliximab and Adalimumab; both originals with years of experience in such pathology but with barely no evidence in real life case series of its biosimilars.

Objectives: To analyze the effectiveness and security of biosimilars of Infliximab and Adalimumab used in uveitis in a third level hospital.

Methods: Descriptive study based on a retrospective cohort of 40 patients suffering of non infectious uveitis who have received biological treatment with Infliximab and Adalimumab collected over the last 20 years (2000-2021), taking into account the complete substitution of the original for the biosimilar in our hospital in February 2015 and March 2019, respectively. The number of outbreaks during both the years before and after the start of the biological therapy, as well as the number of outbreaks during the year following the switch from the original to the biosimilar, have been analyzed. In that regard, we have studied variables such as visual acuity, presence of macular edema, vitritis and retinal vasculitis, as well as the need for systemic corticosteroids treatment. We have registered minor and major side effects associated with the treatment and the cases that have required a change of drug.

Results: The average duration of the immunosuppressive therapy previous to the introduction of the biological therapy was 3,15 years with an average frequency of 2,25 outbreaks during the previous years of the start of the biological therapy. Subsequently, 30 patients received treatment with Adalimumab and 10 with Infliximab showing an average of 0,35+- 0,73 outbreaks during the following year of its start. The switch from the original drug to the biosimilar was subsequently performed in 27 patients (25 for Adalimumab and 2 for Infliximab) with an average of 0,2 +-0,5 and 0,12+-0,44 outbreaks during the 12 months following the switch. Most of them (87%) stayed with the concomitant immunosuppressive treatment, being the Methotrexate the most frequently used (55%). No major side effect has been registered during the biological therapy; however a 25% of the patients showed minor side effects, mostly infections. In 11 cases (27,5%) the biosimilar drug had to be switched, in 7 cases due to inefficiency and 4 to poor tolerance, all of them corresponding to Adalimumab biosimilar. In 5 of those cases the switch was back to the original biological therapy while in the 5 remaining it was to Infliximab biosimilar (4) and Tocilizumab. Two cases of suspension of Adalimumab biosimilar due to disease remission should be highlighted.

Conclusion: According to our experience, the use of biosimilars of Infliximab and Adalimumab in non infectious uveitis is safe. The switch to biosimilars could be considered a feasible therapeutic choice in regards to keeping its effectiveness in patients previously treated with the original drug, even though studies featuring longer follow-up time and more population would be needed.

Table 1.

BASAL CHARACTERISTICS	
AGE, mean (SD)	36,8 (24)
Male n (%), Female n (%)	23 (57,5%), 17 (42,5%)
UVEITIS	
Primary n (%)	20 (50%)
Secundary n(%)	20 (50%)
***Systemic disease association**	JIA (30%); Behcet (15%); AS (10%); Others (45%)
Anterior Uveitis n (%)	22 (55%)
Posterior Uveitis n(%)	9 (22,5%)
Panuveitis n(%)	9 (22,5%)
Acute Uveitis n(%)	14 (35%)
Chronic Uveitis n(%)	26 (65%)
Bilateral Uveitis n(%)	28 (70%)
Unilateral Uveitis n(%)	12 (30%)
ANA	
Not Performed n(%)	1 (2,5%)
Negative n(%)	32 (80%)
Positive n(%)	7 (17,5%)
HLA	B27 4(10%), B51 7 (17,5%), negative 26 (65%)

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AB1327 PREVALENCE OF IMMUNORELATED MUSCULOSKELETAL ADVERSE EFFECTS IN PATIENTS WITH LUNG CANCER OR MELANOMA TREATED WITH IMMUNO-CHECKPOINT INHIBITORS

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Background: mmunotherapy in the field of medical oncology, consisting of inhibiting key immune checkpoints, is revolutionising the way patients with these pathologies are treated, being mainly used in skin and lung tumours. These molecules are aimed at controlling T-cell activation by interacting with cytotoxic T-lymphocyte antigen 4 (CTLA-4) protein (Ipilimumab); by acting on the programmed cell death receptor (PD-1) (Pembrolizumad, Nivolumab); or by binding to programmed cell death ligand 1 (PDL-1) such as Atezolizumad or durvalumad. Despite the improvement in survival in the management of cancers with poor prognosis, this type of therapy is characterised by a series of side effects, including dermatological, gastrointestinal, endocrine, rheumatological and other effects. In this study, we focused mainly on rheumatological adverse effects, ranging from mechanical and/or inflammatory musculoskeletal involvement to dry syndrome, vasculitis, polymyalgia rheumatica, inflammatory myopathy, among others.

Aims: To assess the prevalence of immuno-related adverse effects (Eair) in cancer patients with lung cancer or melanoma treated with immunotherapy targeting check-ponits, such as anti-CTLA-4, anti-PD-1, anti-PDL-1.

Objectives: To assess the prevalence of immuno-related adverse effects (Eair) in cancer patients with lung cancer or melanoma treated with immunotherapy targeting check-ponits, such as anti-CTLA-4, anti-PD-1, anti-PDL-1.

Methods: Observational study of a series of 115 patients diagnosed with lung cancer or melanoma, in treatment with checkpoint inhibitors (nivolumab, pembrolixumab, durvalumab, atezolizumab), from 2016 to 2021 at the Hospital Universitario Clínico San Cecilio. Patients who developed some type of rheumatological symptomatology after the start of immunotherapy were included. The clinical history of these patients was reviewed to confirm or rule out these adverse effects. The following musculoskeletal Eair were included: arthralgias, arthritis, generalised musculoskeletal pain, myalgias, osteoporosis and/or osteopenia. In the Eair registry, the following entities were not included: polymyalgia rheumatica, vasculitis and myositis.

Results: Out of a total of 115 patients who received immunotherapy, with age, type of tumour and treatment received (Table 1); 24 developed non-specific arthromyalgia, low back pain and/or neck pain, with no previous history of interest, and clearly related to the immunotherapy treatment. Five of the patients developed active arthritis with visible swelling; only one of them had previous RA with treatment, the others had no PA of interest. Of the patients with rheumatological involvement, x had underlying PsA, x had a family history of immune-mediated disease. Of the total patients, 2 had a gout flare-up (one of them with a previous diagnosis).

Conclusion: The most frequent rheumatological adverse effects related to immunotherapy are non-specific arthromyalgias considered to be grade 1 or 2 in severity, for which patients do not require specific treatment or suspension of treatment doses. However, several of the patients did develop active arthritis, requiring corticosteroid treatment and in some cases, the suspension of at least one treatment session. In our study, there is no clear relationship between one immunosuppressive drug or another for the development of Eair.

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Diagnostics and imaging procedures

AB1328 A FEASIBILITY STUDY ON A NOVEL COMBINED THERMAL IMAGING AND CLINICAL JOINT ASSESSMENT APPROACH USING ULTRASOUND DETECTED JOINT INFLAMMATION OUTCOMES IN RHEUMATOID ARTHRITIS

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Background: Thermal imaging (TI) is a portable, low cost imaging tool with high feasibility for use. Clinical joint assessment. Is routinely performed in rheumatoid arthritis (RA) patient care.
Objectives: To assess a combined TI and clinical joint assessment (CTCA) approach in comparison with TI alone using ultrasound (US) detected joint inflammation outcomes as a gold standard.
Methods: Bilateral (BL) hand and wrist (22 joint sites) were assessed in this cross-sectional study. For TI (performed in a draft free room with a controlled temperature of around 22°C), the adjusted maximum (Tmax), minimum (Tmin) and average (Tavg) temperatures were derived by subtracting a control temperature (lowest Tmin at the joints per subject) from the Tmax, Tmin and Tavg per joint. US power Doppler (PD) and greyscale (GS) joint inflammation were graded semi-quantitatively (0-3) using validated scoring methods. Joint swelling and tenderness were graded as yes = 1 or no = 0. To increase the relative weightage of CTCA-MAX, CTCA-MIN and CTCA-AVG on the CTCA scores, if the joint was swollen and/or tender, the adjusted Tmax, Tmin and Tavg at each joint were multiplied by a factor of 2; otherwise, they remained unchanged. Receiver operating characteristic (ROC) analysis assessed the performance of TI and CTCA in identifying joints with US PD score > 1 and GS score > 1. A parameter was selected as a univariate predictor if statistically significant (P < 0.05) with area under the ROC curve (AUC) ≥ 0.70.
Results: This study included 814 joints from 37 RA patients (mean disease duration, 30.9 months; mean DAS28, 4.43). For both TI and CTCA, out of the 22 joints sites, 3 joint sites were evaluated for PD score > 1 and 14 joint sites for GS score > 1; the remaining joint sites had AUC results unavailable due to small number of outcomes. For TI (Table 1), 3 joint sites had ≥ 1 predictive parameter for either PD score > 1 and/or GS score > 1 as follows: left (L) wrist and right (R) MCPJ 1, AUCs (0.813 to 0.897) for PD score > 1; L wrist and R MCPJs 1 and 3, AUCs (0.808 to 0.947) for GS score > 1. For CTCA (Table 1), 6 joint sites had ≥ 1 predictive parameter for either PD score > 1 and/or GS score > 1 as follows: BL wrists, AUCs (0.726 to 0.899) for PD score > 1; BL wrists, MCPJs 2 and 3, AUCs (0.739 to 0.931) for GS score > 1.

Table 1. Identifying joints with ultrasound PD score >1 & GS score >1

Thermal Imaging alone					CTCA					
Joint	US criterion	Parameter (AUC ≥ 0.7 & P <0.05)	AUC (95% CI)	Cut-off	Joint	US criterion	Parameter (AUC ≥ 0.7 & P <0.05)	AUC (95% CI)		Cut-off	
								L	R	L	R
L Wrist	PD score >1	Adjusted Tmax	**0.841 (0.691, 0.992)	4.7	L & R Wrist	PD score >1	CTCA-MAX	**0.899 (0.797, 1)	**0.776 (0.578, .973)	9.4	7.3
		Adjusted Tmin	**0.813 (0.669, 0.958)	2.85			CTCA-MIN	**0.861 (0.735, 0.987)	*0.726 (0.526, 0.926)	5.7	4.45
		Adjusted Tavg	**0.849 (0.714, 0.985)	3.9			CTCA-AVG	**0.889 (0.781, 0.997)	*0.761 (0.563, 0.959)	7.3	5.95
	GS score >1	Adjusted Tmax	**0.827 (0.687, 0.966)	4.7		GS score >1	CTCA-MAX	**0.918 (0.833, 1)	**0.813 (0.632, 0.994)	8	7.3
		Adjusted Tmin	**0.808 (0.67, 0.947)	2.85			CTCA-MIN	**0.873 (0.761, 0.986)	**0.766 (0.581, 0.951)	4.4	4.45
		Adjusted Tavg	**0.837 (0.707, 0.967)	3.9			CTCA-AVG	**0.913 (0.824, 1)	**0.802 (0.62, 0.985)	5.5	5.95
R MCPJ 1	PD score >1	Adjusted Tmax	*0.897 (0.726, 1)	5.7	L & R MCPJ 2	GS score >1	CTCA-MAX	-	*0.758 (0.494, 1)	-	9.8
	GS score >1	Adjusted Tmax	*0.936 (0.813, 1)	7.2			CTCA-MIN	*0.902 (0.775, 1)	*0.739 (0.443, 1)	2.75	3.9
		Adjusted Tmin	*0.932 (0.793, 1)	3.95			CTCA-AVG	*0.931 (0.835, 1)	**0.763 (0.474, 1)	4.7	5.5
		Adjusted Tavg	*0.947 (0.868, 1)	4.9	L & R MCPJ 3	GS score >1	CTCA-MAX	*0.914 (0.735, 1)	*0.873 (0.617, 1)	6.35	12.2
R MCPJ 3	GS score >1	Adjusted Tmax	*0.922 (0.76, 1)	4.6			CTCA-MIN	-	*0.902 (0.75, 1)	-	3.15
							CTCA-AVG	-	*0.902 (0.728, 1)	-	4.1

Corresponding P-value: statistically significance at *P <0.05, **P<0.01.

Conclusion: A novel CTCA approach helps discriminate the severity of US detected joint inflammation in RA at more joint sites when compared to TI alone; this includes the commonly affected BL wrists, MCPJs 2 and 3. Further validation work in a larger RA cohort will be required.
Disclosure of Interests: None declared
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AB1329 INTERAPOPHYSEAL JOINTS INJECTION UNDER ULTRASOUND GUIDANCE AN ALTERNATIVE TO FLUOROSCOPY GUIDANCE

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Background: Ultrasound-guided injections are an alternative to evaluate, it eliminates the risk of ionizing radiation for both the patient and the practitioner as fluoroscopic procedures require a radiology technician, increase the overall support time and cost, decrease accessibility.
Objectives: The main objective of the study was to compare the short-term efficacy of posterior inter-apophyseal joint infiltrations under ultrasound versus scopic guidance.
Methods: Observational, retrospective, single-centre study. Patients benefited from posterior zygapophysial joints injection(s) under fluoroscopy or ultrasound and a follow-up consultation at one month.
Results: Data from 54 patients was collected. The evolution of VAS at 1 month was on average - 31.4cm (p <0.001) in the ultrasound group and - 31.3cm (p <0.001) in the fluoroscopy group with no statistically significant difference between the two groups (p =0.835). There were no injection-related complications in either group during the follow-up. The decrease in the consumption of NSAIDs was no statistically significant difference between both groups (p = 1.00). Statistically significant differences in procedure time were observed between groups with a longer time recorded for the ultrasound group (p = 0.007).
Conclusion: A corticosteroid injection of the posterior zygapophysial joints under ultrasound allows for a significant reduction in pain after one month with no difference found between the two techniques. Injection under ultrasound are a reliable, accessible and safe alternative.
Disclosure of Interests: None declared
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AB1330 AUTOMATIC SUBPIXEL MEASUREMENT OF RADIOGRAPHIC FINGER JOINT SPACE NARROWING IN RHEUMATOID ARTHRITIS PATIENTS UNDER TOCILIZUMAB TREATMENT

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Background: The conventional scoring methods of radiographic joint space narrowing (JSN) in rheumatoid arthritis (RA) such as the Genant-modified Sharp score (GSS) are widely accepted but include subjective and time-consuming nature[1]. Therefore, we have developed an in-house software equipped with partial image phase-only correlation (PIPOC)[2] which can automatically quantify joint space width (JSW) change.
Objectives: The purpose of this study was to investigate whether the in-house software can predict the inhibitory effect of tocilizumab on joint destruction in a short period of time.
Methods: The study included 39 RA patients (35 female) who were treated with tocilizumab (Table 1). Radiological progression of the metacarpophalangeal and the proximal interphalangeal joints was evaluated according to the GSS at 0, 6, and 12 months. Automatic measurement was performed by the in-house software (Figure 1). We then validated in-house software in terms of accuracy in detecting the JSN.

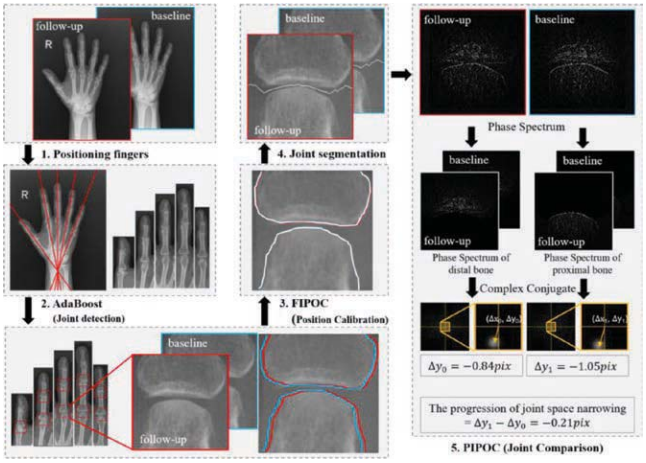

Figure 1. The algorithm flow of in-house software equipped with PIPOC

Table 1. Clinical characteristics of RA patients

variable	baseline	6 months	12 months
Total number of patients	39		
Sex, female/male	35/4		
Rheumatoid factor status, positive/negative	29/10		
Age, mean (SD) years	61.5 (14.6)		
Duration of disease, mean (SD) months	111.4 (85.0)		
Swollen joint count, mean (SD)	6.0 (4.7)	3.5 (3.5)	2.9 (4.0)
Tender joint count, mean (SD)	6.4 (3.5)	2.9 (2.2)	1.9 (2.0)
DAS28-ESR, mean (SD)	4.9 (1.2)	3.0 (1.1)	2.6 (1.0)
DAS28-CRP, mean (SD)	4.4 (1.1)	3.0 (0.9)	2.6 (0.8)

RA, rheumatoid arthritis; SD, standard deviation; DAS28, disease activity score with 28 joints; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

Results: To ensure homogeneity of the subjects, we targeted the joints with GSS = 0 at baseline in the software analysis. The success rate of the in-house software for JSW measurement was 96.8% (449/464). Here, the GSS (+)/PIPOC (+) were defined as joints with JSN progression according to the GSS and the software analysis, respectively. Otherwise, joints were defined as the GSS (-)/PIPOC (-) namely non-progressive JSN. The 0–12-month GSS with the 0–6-month GSS (+) group was significantly more JSN progression than the 0–6-month GSS (-) group (Mann-Whitney U test, $p < 0.001$). Similarly, the 0–12-month PIPOC with the 0–6-month PIPOC (+) group was significantly more JSN progression than the 0–6-month PIPOC (-) group ($p < 0.001$). The 0–12-month JSW change of finger joints with the 0–12-month GSS (+) detected by the in-house software was significantly greater than the 0–12-month GSS (-) ($p = 0.02$).
Conclusion: Our in-house software equipped with PIPOC might be able to predict the subsequent joint destruction with 6 months observations.

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AB1331 DIAGNOSTIC CAPABILITY OF ANESTHETIC INTRA-ARTICULAR INJECTIONS FOR FEMOROACETABULAR IMPINGEMENT

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Background: Femoroacetabular impingement syndrome (FAIS) is a highly prevalent painful disorder that is considered a risk factor for hip osteoarthritis. Confirming that FAIS is the main cause of a pain is a hard task. There are patients who have the typical morphological alterations of FAIS, but are asymptomatic. FAIS morphologies can represent a major confounding factor in patients with undiagnosed rheumatic diseases. On the other hand, surgery can significantly improve quality of life of patients with FAIS. Anesthetic intra-articular injections might constitute viable alternatives for diagnosing FAIS.
Objectives: This systematic review aimed to answer the following question: "What is the diagnostic capability of anesthetic intra-articular hip injections for the assessment of FAIS?".
Methods: This study was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement. Embase, CINAHL, LILACS, PubMed, SCOPUS, SPORTDiscuss, The Cochrane Library, and Web of Science databases were screened. All studies that assessed the diagnostic capability of anesthetic intra-articular hip injections for the assessment of FAIS were considered eligible. Study selection and data collection were performed by three independent reviewers. Risk of bias of the included studies was assessed through the QUADAS-2 tool.
Results: A total of 13 articles were selected for full-text reading, of which 5 were finally considered eligible and included for analysis [1-5]. A summary of the studies' descriptive characteristics can be found in the Table 1. Overall judgment was "at risk of bias" for all included studies (Figure 1). More detailed information regarding bias assessment at QUADAS-2 is available in the Figure 1. From 5 included studies, only 2 [2,5] indicated that anesthetic intra-articular injections can be useful as diagnostic tools for FAIS.
Figure 1.

Table 1.

Author	Mean Age	N (Female)	Injection Content	Injection Guidance	Time for pain assessment after injection (Way of assessment)	Threshold to consider FAIS diagnosis	Reference Standard	Findings
Kivlan	29.9 ± 10.4	72 (54)	Lidocaine + bupivacaine + triamcinolone	Fluoroscopy	2 hours (provocative activities)	Not established	Arthroscopy	No difference in pain relief after injection between individuals with and without FAIS (p=0.128)
Kraeutler	38.8 ± 14.2	161 (120)	Lidocaine + triamcinolone	Non-guided	10 minutes (physical tests and provocative activities)	>70% of pain relief after injection	Symptoms + physical tests + radiography	FAIS and dysplasia diagnosed in 76% of patients with >70% of pain relief after injection, and in 67% in patients presenting <70% (p=0.62)
Chinzei	36.7 ± 14.7	49 (27)	Lidocaine	Fluoroscopy	2 weeks (uninformed)	>50% of pain relief	Arthroscopy	No significant association between pain relief intensity after injection and the presence of FAIS (p>0.05)
Gao	36 (16-65)	78 (41)	Lidocaine + betamethasone	Ultrasound	10 minutes and 1 week (routine tasks)	> 50% of pain relief	Arthroscopy	Response to injection is 91.7% accurate for detecting FAIS
Perdikakis	33 (18-58)	34 (20)	Ropivacaine	Fluoroscopy	30 minutes (physical tests)	Uninformed	Arthroscopy	Response to injection presented 92% of PPV and 96,5% of accuracy for diagnosing FAIS, with NPV and sensitivity of 100%

Conclusion: Evidence regarding the diagnostic capability of anesthetic intra-articular hip injections for FAIS is sparse. In order to accurately answer our research question, future studies that use standardized and optimized protocols of injection and pain assessment after injection are still essential. Furthermore, the need to take into account the different biases surrounding diagnostic studies was highlighted in our study.

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AB1332

INSIGHTS INTO DISEASE ACTIVITY SCORE IN 28 JOINTS (DAS28) AND ITS COMPONENTS FROM AN ULTRASOUND PERSPECTIVE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Disease Activity Score in 28 Joints (DAS28) is a composite disease activity score commonly used to evaluate disease activity in rheumatoid arthritis (RA). Musculoskeletal ultrasound (US) allows visualization and assessment of joint inflammation and structural damage in RA.
Objectives: The aim of this study is to gain insights into DAS28 and its components through studying their relationship with US detected joint inflammation and bone erosion (BE).
Methods: At each joint recess, US power Doppler (PD) and greyscale (GS) joint inflammation were semi-quantitatively (0 to 3) graded using validated scoring methods while BE was scored as present=1 or absent=0 based on Outcome Measures in Rheumatology (OMERACT) consensus definition of BE. At the patient level, Pearson's correlation coefficient was used to correlate US PD, GS and Erosion scores with the following clinical variables: DAS28 and its components (including the erythrocyte sedimentation rate (ESR) in mm/hr; swollen joint count (SJC) ranging from 0 to 28; tender joint count (TJC) ranging from 0 to 28; and patient's global assessment (PGA) of disease activity ranging from 0 to 100). Bonferroni correction was used to account for the above multiple testing. Among associations which were statistically significant, simple linear regression was used to describe the relationship between variables.
Results: A total of 2520 joints and 2800 joint recesses from 36 joint sites (bilateral proximal interphalangeal joints, thumb interphalangeal joints, metacarpophalangeal joints, metatarsophalangeal joints, wrists, elbows and ankles) were scanned in 70 adult RA patients (baseline characteristics: 81.4% female; 74.3% Chinese; mean (SD) DAS28 3.99 (1.25); mean (SD) disease duration 75.3 (61.2) months). All 70 patients underwent US joint inflammation assessment with a subset of 30 patients assessed for US BE. Table 1 summarizes the correlation results between the US and clinical variables. US PD scores were correlated with DAS28 (r=0.34, p=0.02) and SJC (r=0.33, p=0.03). US GS scores were correlated with DAS28 (r=0.42, P=0.002). US Erosion scores were correlated with SJC (r=0.69, P<0.001). Simple linear regression (see scatter plots in Figure 1) demonstrated a statistically significant relationship between the following variables: US PD score versus DAS28 (R^2=0.13, p=0.004); US PD score versus SJC (R^2=0.11, p=0.008); US GS score versus DAS28 (R^2=0.18, P<0.001); US Erosion score versus SJC (R^2=0.48, p<0.001).
Conclusion: Both DAS28 and SJC have significant correlation with US detected joint inflammation. However, among the clinical variables, only SJC appears to be associated with structural damage and has significant correlation with US detected BE. Therefore, it appears that the results from both DAS28 and SJC can be more reflective of the RA disease status when compared to DAS28 alone. The role(s) of both DAS28 and SJC versus DAS28 alone as patient outcome measures in RA need to be further explored.

Figure 1. Scatter plots for ultrasound versus clinical variables

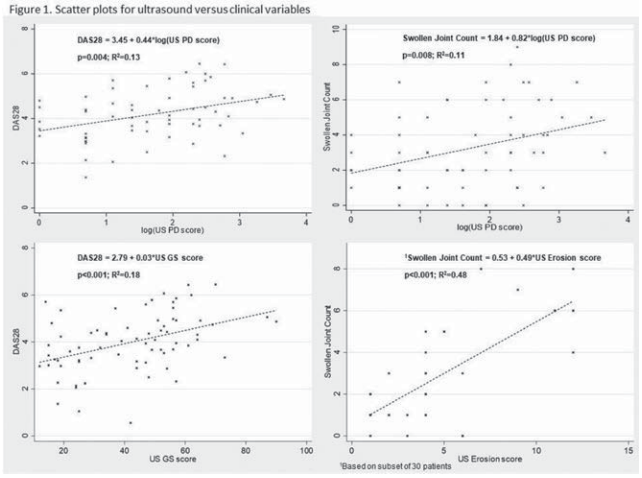

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Table 1. Pearson's correlation between the ultrasound and clinical variables

	DAS28		ESR (mm/hr)		Swollen Joint Count (0-28)		Tender Joint Count (0-28)		Patient's Global Assessment (0-100)	
	r	[2]p-value	r	[2]p-value	r	[2]p-value	r	[2]p-value	r	[2]p-value
US PD score	0.34	0.02*	0.29	0.08	0.33	0.03*	0.15	>0.99	0.16	>0.99
US GS score	0.42	0.002**	0.24	0.20	0.30	0.053	0.29	0.07	0.23	0.30
US Erosion score[1]	0.22	0.25	0.14	0.46	0.69	<0.001***	0.066	0.73	-0.11	0.55

[1] Based on subset of 30 patients. [2] Accounted for multiple testing. Statistically significant: *p<0.05; **p<0.01; ***p<0.001

AB1333 **ULTRASOUND FINDINGS IN NORMAL ANKLES – ULTRASOUND-MRI COMPARISON**

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Background: Although in recent years efforts have been made to standardize the protocols of ultrasound acquisition for each anatomical region, as well as the definitions and quantification of pathological findings, there is still an unanswered question: what should an ankle joint look like in a healthy subject?
Objectives: The study aims to describe ultrasound changes in the ankles of healthy subjects and to compare the ultrasound method with MRI.
Methods: The study included healthy volunteering adults, without any ankle symptoms or local pathological medical history. The right ankle was examined clinically, by ultrasound (by the same expert, using a Esaote MyLabTwice with a 12-18 MHz linear probe, with standard definition of imaging findings [1-4]) and by MRI without contrast (by the same expert, using a 1.5 T GE Optima 450 WGEM machine, with standardized definitions of finding [5-7]).
Results: The study included 25 healthy subjects, with a median age of 54.6 ± 11.8 years, mostly women (84%). Ultrasound identified minimal synovial effusion (SE) in the tibiotalar joint (TTJ) in 20% of subjects (24% on MRI, overall agreement - OA=88%, k=0.65, sensitivity=66.7%, specificity=94.7%), in equal proportions between the anterior and posterior recess (12% on ultrasound and 16% on MRI). One subject had SE in both TTJ's recesses. Ultrasound minimal SE was also found in the subtalar joint in 36% of subjects (44% on MRI, OA=92%, k=0.83, sensitivity=81.8%, specificity=100%), only in the posterior recess (8% in the anterior recess on MRI, with 2 subjects having SE in both recesses). A minimal amount of SE in tendon sheets, only in the medial ankle compartment (flexor tendons, retro and infra-malleolar segments), was also found and quantified in ultrasound mode B as grade 1 tenosynovitis: 20% in tibialis posterior (48% on MRI, OA=72%, k=0.43, sensitivity=41.7%, specificity=100%, mean MRI thickness of 1.28±0.26mm – grade 1), 16% in flexor digitorum longus (32% on MRI, OA=76%, k=0.36, sensitivity=37.5%, specificity=94.1%, 2.70±2.39mm, of which 24% grade 1 and 8% grade 3) and 20% flexor hallucis longus tendons (32% on MRI, OA=88%, k=0.69, sensitivity=62.5%, specificity=100%, 1.38±0.69mm, of which 28% grade 1 and 4% grade 3). There were no cases of articular or tendon sheath synovial hypertrophy and no cases of intra- or peri-articular power Doppler signals.
Conclusion: Ultrasound has proven to be an accurate imaging method for ankle examination. Healthy subjects may exhibit minimal ankle intra- and peri-articular SE, especially in the posterior recess, respectively in the medial compartment of the ankle, which may imply that these findings should not be of clinical relevance in the diagnostic evaluation or monitoring of rheumatoid arthritis disease activity.
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AB1334 **SCANOGRAPHIC EVALUATION OF BONE FRAGILITY 2 YEARS AFTER BARIATRIC SURGERY IN OBESE PATIENTS: AN OBSERVATIONAL STUDY**

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Background: Osteoporosis is a common disease whose prognosis can be seriously impacted by the development of fractures that lead to functional limitations and may even have life-threatening sequelae (1). CT is useful for diagnosing vertebral fracture (VF) and measuring the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC- L1). Obesity might be a protective factor against bone loss and osteoporosis (2). Nonetheless, epidemiological studies have reported an association between obesity and an increased risk of fragility fractures (3) and suggested that obesity may be a risk factor for fracture and decreased bone density (4,5). For bariatric surgery, the results are less controversial. According to many studies, malabsorptive procedures lead to a decrease in bone mineral density and sometimes an increased risk of fragility fractures (2,6,7,8). However, the kinetics of bone loss and its physiopathology are unclear.
Objectives: The primary objective was to evaluate bone fragility on computed tomography (CT) in obese patients before and 2 years after bariatric surgery. The secondary objectives were to identify risk factors for a decrease in the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1).
Methods: This descriptive study included obese patients who underwent bariatric surgery between January 2014 and December 2019 and CT before and two years (±6 months) after bariatric surgery. SBAC-L1 (in Hounsfield units (HU)) was measured on CT, and vertebral fracture (VF) was manually assessed. The SBAC-L1 fracture threshold was defined as below 145 HU.
Results: Among the 78 included patients, 85.9% were women, with a mean age of 48.5 years (±11.4); the mean body mass index (BMI) was 46.2 kg/m2 (±7) before surgery and 29.8 kg/m2 (±6.7) 2 years after surgery. There was a significant change in SBAC-L1 two years after surgery (p=0.037). In multivariate analysis, the risk factors for having an SBAC-L1 ≤ 145 HU 2 years after bariatric surgery in those with an SBAC-L1 > 145 HU before surgery were age and sex, with men and older patients having a higher risk (OR = 32.6, CI95% = [1.86-568.77], and OR = 0.85, CI95% = [0.74-0.98], respectively).
Conclusion: SBAC-L1 was significantly lower two years after bariatric surgery than before surgery. When the SBAC-L1 was over 145 HU before bariatric surgery, men sex and older patients were the risk factors for having an SBAC-L1 below the fracture threshold 2 years after surgery.
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AB1335 **BONE MARROW EDEMA SCORE IN HAND X-RAY FILM BY AI DEEP LEARNING ASSOCIATE WITH MRI BONE EDEMA IN RHEUMATOID ARTHRITIS.**

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Background: Rapid radiographic progression (RRP) was reported to be one of clinical symptom in difficult to treat RA(D2T RA) (1). Eular recommendation for imaging showed BME is strong and independent prognostic factor for bone destruction(2). We reported bone marrow edema (BME) in MRI image was most associated with RRP compared with bone erosion, synovitis in Adalimumab add-on therapy in MTX-IR RA patients(3). To rescue RRP, early detection of BME is important although cost of MRI is expensive and hard to repeat.
Objectives: To investigate the score of BME in hand X ray film by deep learning between X ray film and MRI BME information can discriminate the differences between BME and non-BME images.
Methods: In this work, we use a neural network consisted of convolutional layers and fully connected layers to classify X-ray images (Figure 1) In this paper, the output is the socre of BME which ranges from 0 to1(threshold = 0.4). We also

used an interpretation technique called the Grad-CAM for visual explanations. Hand MRI (1.5T) were used.

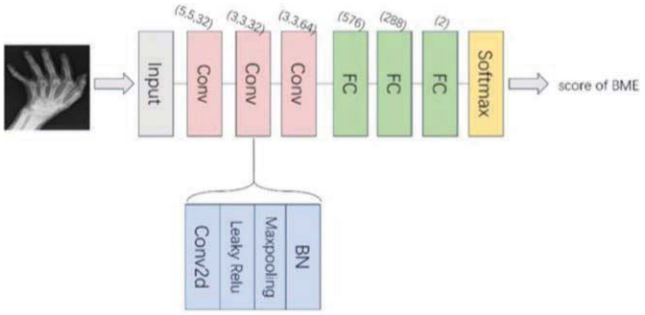

Figure 1. The convolutional neural network design. A red block "Conv" means a convolutional block. It contains a 2D convolution layer, a leaky relu activation function, a maxpooling layer and a batch normalization layer. The numbers above each "Conv" block are (kernal size, kernal size, kernal number). A green block "FC" is a fully connection layer. The number above it is (neuron number). After the last Softmax layer, the output becomes the probability of BME which ranges from 0 to 1.

Results: Regarding data split, 104 images including 79 non-BME images and 25 BME images are used as a hold-out test set. The rest of the images (473 images) are used as training data and validation data. Five fold cross-validation is used for these 473images. For each fold, there are about 378 images including 297 non-BME images and 81 BME images in the training set. There are about 95 images including 74 non-BME images and 21 BME images in the validation set. In order to fully utilize every image and unify the distribution of the training set and the validation set, the ratio of non-BME and BME is controlled to be the same which is about 3.66:1. The five folds showed similar performance on the hold-out test set. AUC is the area under the ROC curve. As the result, AUC which indicates the general performance of this model, ranged from 0.88 to 0.91. The average precision was 63% and the average recall rate was 87%. In this experiment, the initialization seed will greatly influence the final result. For example, AUC can be reduced to 0.73 from 0.89 because of a different initialization seed. It perhaps results from the shortage of data, which can easily make the neural network drop into a local minimum.We also utilized Grad-cam to visualize the result. The result of Grad-cam shows the importance of each part to the final prediction(Figure 2).

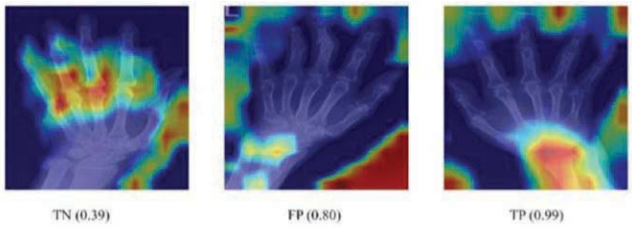

Figure 2. Result of Grad-cam. Numbers in the parenthesises are the possibilities of BME. The middle case is unexpected because red region is the surrounding of the hand. The left and right cases may indicate the evidence for prediction.

Conclusion: The preliminary result is much better than a random guess. According to this result, there should be a certain difference between BME and non-BME images. If it's the characteristic of BME that domains this difference, our classification algorithm will be feasible for BME. Our future work is to justify the evidence of the predictions and improve performance.

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AB1336 EFFECTS OF MUSLIM PRAYER ON LOWER LIMB ENTHESIS ULTRASOUND

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Background: Muslim prayer, also known as salat, includes a series of postures and movements, concomitant with a spiritual meditation and Quran recitations, performed at least 5 times a day by Muslim worshipers [1]. Each prayer includes a specific number of rakaa which consists of a single iteration of movements [2].
Objectives: We aim to assess the effects of the Muslim prayer movements on the lower limb entheses, using ultrasonography (US).
Methods: We performed a cross-sectional study including asymptomatic healthy individuals. Each subject was asked if they performed prayer (G1) or not (G0). People who performed prayer were asked about the age and year when they started praying, number of rakaa performed daily and duration of each rakaa. US of lower limb entheses was performed. We explored the entheses of quadricipital tendon (QT), proximal patellar tendon (PPT), distal patellar tendon (DPT), calcaneal tendon (CT), and plantar aponeurosis (PA) looking for thickening, hypoechogenicity, loss of fibrillar pattern, presence of doppler signal and structure damage lesions (calcifications, cortical irregularity, erosions and enthesophytes). The highest value of enthesis thickness of both sides was considered. Ultrasonographic enthesitis assessment tools were used: the Spanish Enthesitis Index (SEI) [3] and the Glasgow Ultrasound Enthesitis Scoring System (GUESS) [4]. Data analysis was performed using the IBM SPSS software version 26.
Results: A total number of 370 entheses was evaluated. There were 29 males (78%) and 8 females. The mean age was 44.73±12.7 years. Twenty-five subjects (68%) practice prayer. The mean prayer starting age of 28.58±13.345 years. The mean number of years since prayer was started of 20±16.32 years. The mean daily number of rakaa was 19.16±4.16. The mean total daily prayer duration was 35.28±65.58 minutes. The mean enthesis thickness was 5.98±0.72 mm (QT), 3.69±0.48 (PPT), 4.1±0.64 (DPT), 4.83±0.62 (CT) and 4.89±0.75 (PA). Structural damage lesions were found in 43.2% of subjects (QT), 8.1% (PPT), 13.5% (DPT), 64.9% (CT) and 21.6% (PA). Structure damage lesions of CT enthesis were significantly more frequently found in people who performed prayer (G0: 41.6%, G1: 76%, $\chi 2$=4.194, p=0.041). Furthermore, they are significantly more likely to have thickened PA enthesis (G0: 50%, G1: 84%, $\chi 2$=4.752, p=0.029). The mean SEI was 17.83 in G0 and 19.56 in G1, p=0.647. The mean GUESS was 18.29 in G0 and 19.34 in G1, p=0.781. A positive correlation was found between total daily duration of prayer and PPT enthesis thickness (r=0.575, p<10-3), DPT enthesis thickness (r=0.362, p=0.028), SEI (r=0.360, p=0.026) and GUESS (r=0.388, p=0.018). Thickness of PPT enthesis was also positively correlated to the number of years since prayer was started (r=0.036, p=0.026).
Conclusion: Our study showed that lower limb enthesis US abnormalities are frequent in asymptomatic and healthy subjects who perform Muslim prayer. This finding suggests that lower limb enthesis US should be carefully interpreted in these subjects.

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AB1337 EFFECT OF CONTRAST MEDIA IN BONE MINERAL DENSITY MEASUREMENTS AND THE POTENTIALS FOR OPPORTUNISTIC OSTEOPOROSIS SCREENING USING QUANTITATIVE COMPUTED TOMOGRAPHY – A SYSTEMATIC LITERATURE REVIEW

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Background: Quantitative computer tomography (QCT) has emerged as a screening tool for opportunistic measurements of volumetric bone mineral density (vBMD) from clinical CT scans, enabling early diagnosis of osteoporosis. However, intravenous contrast media administered during clinical CT examinations, calibration methods as well as different scan phases may influence vBMD and must be considered.[1] Calibration methods include synchronous and asynchronous CT phantoms as well as phantom-less internal calibration.
Objectives: To investigate the effect of intravenous contrast media on QCT-measured vBMD. Furthermore, to review the effects of different calibration methods and scan protocols on vBMD.
Methods: In this systematic literature review, two independent reviewers (AH and AC) conducted a blinded screening for articles involving human participants who had undergone a contrast and non-contrast CT scan to measure vBMD. A total of 1,981 studies, published between 01.01.2000 and 17.01.2021, were screened and 9 eligible studies were included. A meta-analysis was conducted and standard mean differences (SMD) with 95% confidence intervals (CI) were calculated and presented in a forest-plot. Quality of studies was rated by the preliminary ROBINS-E risk of bias tool.[2]
Results: In total, the 9 studies included 515 patients. On average the vBMD SMD changed 0.45 (95% CI: 0.24-0.67, *P < .0001)* from non-contrast to contrast-enhanced (CE) scans at the lumbar region (Figure 1). Phantom-based QCT had a SMD of 0.64 (95% CI: 0.33-0.94, *P < .0001*) and phantom-less QCT had a SMD of 0.20 (95% CI: -0.00-0.40, P = 0.05). Subgroup analyses showed a mean arterial phase vBMD SMD of 0.29 (95% CI: 0.12-0.45 P < .0008) and a venous phase vBMD of 0.56 (95% CI: 0.30-0.81, P < .0001). All studies were deemed to have moderate or serious risk of bias by the ROBINS-E tool.

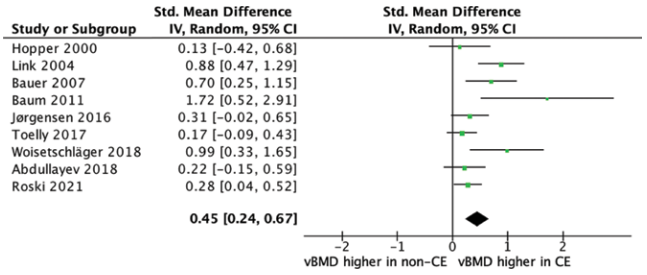

Figure 1. *Meta-analysis of standardized mean difference in lumbar spine vBMD (mg/cm^3) change from non-contrast enhanced (non-CE) CT scans and contrast enhanced (CE) CT scans.*

Conclusion: QCT-measured vBMD is higher in CE scans in both phantom-based and phantom-less scans compared to non-contrast CT. Our meta-analysis suggest that contrast has a larger impact on vBMD in phantombased vs. phantom-less and in venous phase scans vs. arterial phase scans, underlining not only the time-dependency but also the dependency of the calibration method. Arterial phase CT scans using internal calibration may be preferred when measuring vBMD in a clinical setting without an adjusting conversion factor. However, if CE scans are to be used in opportunistic vBMD screening, development of a universal calibration- and protocol specific conversion factor is of importance.
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AB1338 CALPROTECTIN, A SENSITIVE MARKER OF INFLAMMATION, IS ROBUSTLY ASSESSED IN PLASMA FROM PATIENTS WITH ESTABLISHED RA BY USE OF DIFFERENT LABORATORY METHODS

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Background: Calprotectin (S100A8/S100A9, MRP8/MRP14) in plasma has been shown to be more sensitive than C-Reactive Protein (CRP) or Erythrocyte Sedimentation Rate (ESR) in reflecting inflammatory activity in patients with rheumatoid arthritis (RA).[1,2]
Objectives: The present objective was to explore the robustness of laboratory examination of calprotectin by comparing the results from assessments by use of two different methods.
Methods: Frozen plasma samples from a study of 177 patients with established RA initiating biologic disease modifying drugs were analysed for calprotectin levels at baseline and after 1, 2, 3, 6 and 12 months by use of either enzyme-linked immunosorbent assay (ELISA) or fluoroenzyme immunoassay (FEIA). The ELISA technique used kits from Calpro AS (Oslo, Norway) and the samples were assessed in a semi-automatic analysis machine Dynex DS2 (Dynex Technologies, Virginia, USA) at Diakonhjemmet hospital. The Calpro AS kits included all necessary buffers, cleansing solutions, enzyme substrate, standards, and controls (high and low calprotectin levels) and their protocol was used for the calprotectin assessments. The standards and controls were used as the mean of two measures, while all the patient samples were analysed as single measures. As a sub-study in NORA (a study exploring personalized medicine in RA by including several study cohorts from the Nordic countries), the same plasma samples were additionally assessed by FEIA. The FEIA technology used the EliA™ calprotectin 2 wells in a Research Use Only setting on the PhadiaTM 2500 instrument (Phadia AB, Uppsala, Sweden) with a 1:50 dilution. Spearman was used for correlation assessments. To explore differences across concentration levels the baseline calprotectin levels were divided into 3 groups based on results from the Calpro AS assay (normal levels; ≤ 910 µg/L; moderately elevated; 911-2000 µg/L, highly elevated; > 2000 µg/L).
Results: A total of 917 samples from the 177 patients (mean (SD) age 52.9 (13) years, disease duration 10 years (ranging from a few months to 46 years), 81% women, 78% anti-CCP IgG positive and 81% RF IgM positive) were included. The median of the correlation coefficients between the two methods at the six visits was 0.96 (range 0.91-0.97). Correlations were very high for normal levels (0.91) but somewhat lower for moderate and highly elevated levels (0.85 and 0.79, respectively). There were no significant differences between the associations depending on age, sex, or disease duration, nor on the anti-CCP IgG and RF IgM status of the patient.
Conclusion: The present study supports the robustness of calprotectin analyses, showing similar results across two different analytical methods, and that the concentrations were not influenced by demographic or immunological variables. Being a robust and more sensitive marker of inflammation than the commonly used CRP and ESR, calprotectin analyses should be available for assessments of RA patients in routine clinical care.
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AB1339 MUSCLE ULTRASOUND FOR THE DIAGNOSIS OF SARCOPENIA IN RHEUMATOID ARTHRITIS (RA).

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Background: Sarcopenia is a muscular disease characterized by a loss of muscle mass and function. The condition is associated with chronic diseases and

ageing and predicts disability, hospitalization and death (1). Due to chronicity and disability produced by RA, it is convenient to see the relationship with sarcopenia.

Objectives: To assess the diagnostic utility of ultrasound (US) for sarcopenia.

Methods: Cases: Outpatients, 65 years old or more, with RA (ACR/EULAR 2010 criteria) from the rheumatology clinics of 4 Spanish University Hospitals were randomly selected consecutively from rheumatology consultation since May 2021 to September 2021. Controls: Control subjects without rheumatoid disease were selected from family members or friends of the cases, paired by age, gender and social status from May to September 2021. Variable and measures: The main evaluated outcome was sarcopenia as defined in 2019 by the European Working Group on Sarcopenia in Older People (EWGSOP). Crossectional Ultrasounds (US) of the third proximal forearm were evaluated for the perpendicular distance (milimetres) between superficial surface of subcutaneous celular tissue and the deep surface close to the ulnae with two different measures (66% and 75%). Crossectional US images were also obtained of lower limbs, at an equidistant point between anterosuperior iliac spine and the upper border of the patella for measuring the distance between superficial surface of subcutaneous celular tissue and the deep interface of the femur with vastus medialis muscle with two different measures (50% and 75%). Handheld dynamometer was used to measure the strength in upper limbs. Body composition was evaluated using dual-energy X-ray densitometry.

Statistics: A descriptive analysis, chi square y T-student tests were done to compare the main characteristics and results between patients and controls. Correlations between forearm US and strength and between thigh US and total DEXA were calculated by Pearson's test.

Results: 76 patients and 76 controls were included in the study, 120 were women (78,9%), with media ± SD of age 74,7 ±6,98 of media and 32 (21,1%) were men, with age 70,1 ±3,78 of media. In comparation with controls, RA patients presented more frequency of sarcopenia (30 [19,53%] vs 6 [3,94%]; p=0,005) according to EWGSOP criteria. From the point of view of ultrasound, RA patients presented less muscle mass in cubital forearm and thigh. Control group presented larger size of muscle (Table 1).

Table 1. ***Results measirements case-control in milimeters***

	Control (m±ds)	RA (m±ds)	p-valor
Right forearm 66% ulnar	42,92±8	38,72±9,33	0,003
Left forearm 66% ulnar	41,17±8,97	37,93±9,27	0,03
Left forearm 75% cubital	38,74±7,7	35,18±8,5	0,008
Right Thigh 50% FR+VI	30,9±7,46	28,09±6,31	0,011
Right Thigh 50%VI	14,5±4,26	13,08±4,27	0,042
Right Thigh 50% FR	15,26±3,6	13,5±3,28	0,002
Right Thigh 50% area FR	588±181,29	481,49±140,56	0,001
Lefth Thigh 50% FR+VI	27,67±8,9	22,37±8,26	<0,001

Ultrasound measurements in forearm which showed a positive correlation with strength were: right forearm: 66% ulnar (r=0,364, p=0,001), 75% ulnar (r=0,365, p=0,001); left forearm: 66% ulnar (r=0,348, p=0,002), 75% ulnar (r=0,337, p=0,003). In the other hand, ultrasound measurements in thigh which showed a positive correlation with DXA were: right thigh 50% femoral rectus (FR)-vastus intermedius (VI) (r=0,255, p=0,003), 50% VI (r=0,256,p=0,003), 50% FR (r=0,265, p=0,002), 50% area FR (r=0,280, p=0,003), 75% FR-VI (r=0,357,p<0,001), 75% VI (r=0,382,p<0,001), 75% FR (r=0,240, R2=0,006), 75% area FR (r=0,218,p=0,023); Left thigh: 50% FR-VI (r=0,251, p=0,004), 50% VI (r=0,293,p=0,001), 50% FR (r=0,214, p=0,015), 75% FR-VI (r=0,347,p<0,001), 75% VI (r=0,342, p<0,001), 75% FR (r=0,295, p=0,001).

Conclusion: Muscle Ultrasound is a useful diagnostic tool to detect sarcopenia. It can be cost-efficient and faster when compared with DEXA and the results correlate consistently with the strength in forearm. Patients with rheumatoid arthritis are in high risk of suffering sarcopenia and US could be used to control the evolution of this condition.

Disclosure of Interests: None declared

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AB1340 PREVALENCE OF THE WRISTS AND HANDS SYNOVITIS IN SUBGROUPS OF PATIENTS FOLLOWED FOR SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background: Joint damage is one of the most common manifestations of SLE. Represented by the presence of arthralgia or arthritis, with or without deformities or erosions. Musculoskeletal ultrasound allows evaluation of the inflammatory joint damage for more targeted therapeutic approach.

Objectives: The aim of this study was to estimate the prevalence of the wrists and hands synovitis (WHS) in subgroups of patients with systemic lupus erythematosus (SLE) and to compare them with each other.

Methods: One hundred and sixty-nine patients with SLE were consecutively recruited in the rheumatology unit (consultation or hospitalization) of the Ben Aknoun hospital, Algiers-Algeria. Stratification into subgroups was carried out: non-deforming non-destructive patients (NDND), rhupus patients (if coexistence of lupus and rheumatoid arthritis criteria), patients with moderate deforming arthropathy (MDA) or Jaccoud arthropathy according to the score of the Spronk index. For each patient, demographic data, duration of SLE evolution and joint involvement were collected, a standard inflammatory biology report and screening for rheumatoid factor (RF) and anti-CCP (ACPA) were requested. A musculoskeletal ultrasound of the wrists, MCP and PIP (from the 2nd to the 5th rays) was performed with a search for synovitis and erosions, the ultrasound examination was preceded by the calculation of the SLEDAI score and the HAQ score.

Results: 169 patients were recruited: 135 NDND, 18 rhupus, 10 Jaccoud, 6 MDA, respective mean age of 38.38 ± 11.79, 39.39 ± 11.74, 41.10 ± 9.5, 47 ± 9.35 years. The mean duration of lupus was 8.23 ± 6.97, 12.33 ± 8.71, 13.10 ± 6.6 and 15 ± 5.93 years, respectively. The mean duration of joint involvement was 7.38 ± 6.920, 12.22 ± 8.84, 13.10 ± 6.6, 15 ± 5.93 years. The positive CRP was found respectively in 20%, 38.9%, 20%, and 16.7%. The frequency of WHS, RF, ACPA and erosions was significantly higher in the rhupus group compared to that of NDND (p <0.001). No difference in mean SLEDAI scores between subgroups. The mean HAQ score was higher in patients in the rhupus and Jaccoud groups compared to the mean score in patients in the NDND and MDA group (p <0.0001).

Conclusion: Our results confirm that rhupus patients have more inflammatory and erosive involvement than other lupus subgroups. It represents an overlap between rheumatoid arthritis and lupus more than a separate entity. We have also shown that deforming arthropathies without structural damage correspond to a late course in a group of patients initially non-deforming non-destructive.

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AB1341 ASSESSMENT OF COMMON FEMORAL VEIN INTIMA-MEDIA THICKNESS BY ULTRASOUND IN BEHÇET'S DISEASE: COMPARATIVE STUDY OF PATIENTS WITH OR WITHOUT VASCULAR INVOLVEMENT IN A NATIONAL REFERRAL CENTER

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Background: Vascular manifestations are frequent in Behçet's disease (BD). However, they have been less studied than other manifestations, such as uveitis [1]. Increased venous wall thickness assessed with ultrasound (US) has been reported in BD [2]. However, it remains unclear if US findings correlate with vascular involvement in BD.

Objectives: To assess vascular Doppler US findings in patients with BD with and without clinical vascular manifestations.

Methods: Observational study of unselected consecutive patients with BD assessed in a national referral center, from March 2021 to May 2021. All patients fulfilled the 2014 ICBD criteria [3]. They were evaluated sequentially with a scheduled clinic visit after signing an informed consent. Demographic and clinical variables were collected. Patients were considered to have vascular involvement

Table 1.

	Vascular manifestations (n=17)	Without vascular manifestations (n=25)	P value
Sex *(men)*, n (%)	10 (41.2)	13 (48)	0.663
Age *(years)*, mean ± SD	51.24±12.8	45.56±12.88	0.133
HLA B51 positive, n/tested cases	4/17	14/25	-
Evolution time (years) from diagnosis, mean ± SD	13.35 ± 10.45	13.04 ± 8.52	0.891
Cardiovascular risk factors			
Hypertension, n (%)	7 (41.2)	1 (4)	**0.003**
Diabetes mellitus, n (%)	1 (5.9)	2 (8)	0.794
Dyslipidemia, n (%)	6 (35.3)	5 (20)	0.268
Smoking habit *(current or former smokers)*, n (%)	10 (58.8)	12 (48)	0.067
Clinical manifestations			
Oral ulcers, n (%)	16 (94.1)	25 (100)	0.220
Genital ulcers, n (%)	12 (70.6)	16 (64)	0.657
Erythema nodosum like, n (%)	9 (52.9)	6 (24)	0.055
Pseudofollicullitis, n (%)	9 (52.9)	19 (76)	0.120
Uveitis, n (%)	7 (41.2)	9 (36)	0.735
Arthralgia, n (%)	14 (82.4)	17 (68)	0.299
Neurological manifestations, n (%)	2 (11.8)	2 (8)	0.683
Ultrasound findings			
Femoral vein IMT (mm), median [IQR]	0.65 [0.45-0.82]	0.49 [0.39-0.55]	**0.028**

IMT: intima-media thickness. IQR: interquartile range.

if they had history of deep vein thrombosis, pulmonary thromboembolism, superficial thrombophlebitis, arterial thrombosis (peripheral arterial thrombosis, stroke, transient ischemic attack), aneurysms, acute myocardial infarction or Raynaud's disease. Wall thickness of bilateral common femoral vein was measured by assessing the intima-media thickness (IMT) with a high-resolution Doppler US [2]. Statistical analysis was performed with SPSS. Student´s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher´s exact test for categorical variables, as appropriate.

Results: We evaluated 17 BD patients with vascular manifestations and 25 BD patients without vascular manifestations. Main clinical and demographic characteristic are described in Table 1. The vascular manifestations were deep vein thrombosis (n=4), superficial thrombophlebitis (n=1), arterial aneurysms (n=2), acute myocardial infarction (n=3), arterial thrombosis (n=1) and Raynaud's disease (n=10). The median [IQR] value of the common femoral vein IMT was significantly higher in patients with vascular manifestations (0.65 [0.45-0.82] vs 0.49 [0.39-0.55]; p= 0.028). A significant increase in vascular manifestations was observed in patients with arterial hypertension (p=0.003). HLA B51 presence was more frequent in patients with no vascular manifestations.

Conclusion: Patients with BD and vascular involvement present higher values of common femoral vein IMT. The assessment of venous wall thickness with Doppler US constitutes a useful technique to evaluate clinical vascular involvement in BD patients.

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AB1342

THE EVALUATION OF 18F-PET-CT USE IN RHEUMATOLOGY CLINICAL PRACTICE WITH DEMOGRAPHIC AND CLINICAL FINDINGS

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Background: There is an increasing number of studies in the literature on the use of 18 F-FDG-PET/CT in the diagnosis and treatment follow-up of inflammatory rheumatic and musculoskeletal diseases (iRMD) (1). PET/CT do have an important place in the diagnosis of large-vessel vasculitis (LVV), which shows increased involvement in the walls of large vessels (2).

Objectives: In this study, the aim was to evaluate the demographic, clinical, and laboratory characteristics, compatibility of PET/CT with other imaging methods, and the role of PET/CT in treatment follow-up of the patients who underwent PET/CT at the Rheumatology Clinic between 01.01.2010 and 31.12.2020.

Methods: The patients' age, gender, comorbidities, iRMD types, medications, PET/CT, and ages at the time of iRMD diagnosis were collected. In addition, the compatibility of PET/CT with other imaging methods (MR angiography, Doppler US, and CT angiography) was evaluated in vasculitis subgroups. Control PET/CT images of the patients were evaluated by comparing them with previous imaging findings.

Results: A total of 280 patients, 179 (63.9%) women, with a mean age of 58±15 years, underwent PET/CT in the rheumatology department. 202 (72.1%) patients had a diagnosis of iRMD before PET/CT. After PET/CT, 40 (48.2%) patients were diagnosed with a new iRMD, and 43 (41.8%) were diagnosed with a non-iRMD. No rheumatic disease was detected in 33 (11.8%) patients. iRMD diagnosed by PET/CT are respectively; LVV (n=11), IgG4-RD (n=10), sarcoidosis (n=9), and other (n=10). It was determined that 22 (26.5%) of newly diagnosed patients other than iRMD had malignancy [Bronchial (n=8), lymphoma (n=3), breast (n=3), other (n=8) cancer]. PET/CT revealed lymphadenopathy (LAP) in 119 of 165 patients who underwent the scan to exclude malignancy, and 22 of 91 patients who underwent PET/CT for rheumatologic diagnosis. LAP was found in 45% of those diagnosed with iRMD and 74.4% of those diagnosed with non-iRMD (p=0.002). PET/CT imaging was performed on 18 patients for follow-up. The treatment of 4 out of 18 patients with follow-up PET/CT and 76 out of 280 total patients was changed after imaging. In patients with a diagnosis of giant cell arteritis (GCA), the compatibility of PET/CT with MRA was 62.5%, while its agreement with CTA was 100%, and with Doppler US was 40%. In patients diagnosed with Takayasu's arteritis, the compatibility of PET/CT with MRA was 40%, while its compatibility with CTA was 50% and with Doppler USG was 38%.

Conclusion: PET/CT imaging was found to be an important adjunctive examination in the diagnosis and follow-up of sarcoidosis, LVV, and IgG4-RD in patients evaluated in the rheumatology clinic. It has been observed that it is often used in the diagnosis and follow-up of RA, SpA, and autoinflammatory diseases, to investigate the malignancies accompanying rheumatic diseases and to evaluate the characteristics of LAP. PET/CT findings provide significant benefits to the clinician in the early diagnosis of iRMDs and differentiation of malignant and/or infectious etiologies.

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Table 1.

Demographics	**Age (mean±SD.)**	58±15
	Female/Male	179 (63.9)/101 (36.1)
	CRP (mg/L), median (Min.-Max.)	16.9 (0.2-431)
	ESR (mm/h), median (Min.-Max.)	43 (1-120)
iRMD Subgroups, n (%)	**Connective Tissue Disease**	70 (28.4)
	Vasculitis	63 (25.5)
	Rheumatoid Arthritis	28 (11.3)
	İgG4-RD and Retroperitoneal Fibrosis	22 (8.9)
	Spondyloarthropathies	21 (8.5)
	Sarcoidosis	16 (6.5)
	Polymyalgia Rheumatica	8 (3.2)
	Others (Autoinflammatory Fever Syndromes, Crystal Arthropathies, CVID)	19 (7.7)
Reason for PET/CT scan, n (%)	**For Rheumatologic Diagnosis**	91 (32.5)
	Scan to Exclude Malignancy	165 (58.9)
	Treatment Response Evaluation	24 (8.6)
PET/CT SUV_{max} Values	**iRMD SUV_{max}, median (Min.-Max.)**	4.6 (3.3-7.2)
	Malignancy SUV_{max}, median (Min.-Max.)	8 (6.1-10.6)

***iRMD:** inflammatory rheumatic and musculoskeletal diseases

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AB1343

ON THE DEVELOPMENT OF NEW DISEASE ACTIVITY SCORES FOR REMOTE ASSESSMENT OF PATIENT WITH RHEUMATOID ARTHRITIS USING THERMOGRAPHY AND MACHINE LEARNING.

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Background: Disease activity scores are used in the follow-up of patients with rheumatoid arthritis (RA). These scores include variables obtained through physical examination, such as the tender and swollen joint count. In telematic consultations it is not possible to determine these variables. Thermography is a safe and fast technique that measures heat through infrared imaging. Inflammation of the joints causes an increase in temperature and could therefore be detected by thermography. Machine learning methods are highly accurate in analyzing medical images, and could be used to analyze thermal images automatically. Thermography of hands, patient global health (PGH) and acute phase reactants could be combined to develop new activity scores that facilitate remote assessment of RA patients.
Objectives: To develop new disease activity scores based on the machine learning analysis of thermal images of the hands, PGH and acute phase reactants.
Methods: Multicenter observational study conducted in the rheumatology and radiology service of two hospitals. Patients with RA, psoriatic arthritis, undifferentiated arthritis and arthritis of hands secondary to other diseases that attended the follow-up visits were recruited. Companions of patients and healthcare professionals were also recruited as healthy subjects. In all cases, a thermographic image of the hands was taken using a Flir One Pro or a Thermal Expert TE-Q1 camera connected to a smartphone. Ultrasound (US) of both hands was performed. The degree of synovial hypertrophy (SH) and power doppler (PD) was assessed for each joint (score from 0 to 3). Machine learning was used to quantify joint inflammation from the thermal images using US (SH+PD) as ground truth. This score has been named ThermoJIS. RA patients whose thermal image was taken with the Thermal Expert TE-Q1 camera were used to evaluate the performance (test dataset). The other participants were used as training dataset. The PGH, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were also assessed in the test dataset. ThermoDAS (ThermoJIS + PGH), ThermoDAS-ESR (ThermoJIS + PGH + ESR) and ThermoDAS-CRP (ThermoJIS + PGH + CRP) activity scores were developed using a linear regression. The Spearman's correlation coefficient of ThermoJIS, ThermoDAS, ThermoDAS-ESR and ThermoDAS-CRP vs. SH, PD, PGH, ESR and CRP were used to characterize the new developed disease activity scores. The study was approved by the Clinical Ethics and Research Committee of both centers.
Results: The total number of recruited subjects were 616 (475 for the training and 141 for the testing dataset). The correlations obtained between the different activity scores (ThermoJIS, ThermoDAS, ThermoDAS-ESR and ThermoDAS-CRP) vs. SH, PD, PGH, ESR and CRP are shown in Table 1. All correlations are statistically significant.

Table 1. Spearman's correlations of the developed scores vs synovial hypertrophy (SH); vs power doppler (PD); vs patient global health (PGH); vs erythrocyte sedimentation rate (ESR) and vs C-reactive protein (CRP).

	SH	PD	PGH	ESR	CRP
ThermoJIS	0.42	0.43	0.18	0.16	0.12
ThermoDAS	0.50	0.53	0.87	0.16	0.19
ThermoDAS-ESR	0.54	0.53	0.79	0.49	0.33
ThermoDAS-CRP	0.60	0.60	0.77	0.49	0.54

Conclusion: ThermoJIS shows moderate correlation with US but weak correlation with PGH and acute phase reactants, suggesting that ThermoJIS is non-redundant with symptoms and laboratory assessment. Adding PGH and acute phase reactants to ThermoJIS improves all correlations, including correlation with US. These thermographic scores do not require a physical examination, opening an opportunity to facilitate remote consultations in RA patients.
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AB1344

THE ROLE OF ULTRASOUND CRITERIA IN PREDICTING THE OUTCOME OF EARLY UNDIFFERENTIATED ARTHRITIS OF THE SMALL JOINTS OF THE HAND

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Background: Arthritis of peripheral joints is among the most frequent manifestations in the onset of rheumatic diseases. Determining its nosological identity and rational therapy at an early stage is a complex clinical problem.
Objectives: To evaluate the possibility of using hand ultrasound to predict the outcome of early undifferentiated arthritis (EUA).
Methods: Since 2018, patients with a first-time diagnosis of early undifferentiated arthritis were consecutively included into the study. The final group consisted of 102 patients (women, 71.6%; mean age 44.8±17.2 years old) who were prospectively observed at baseline, after 3 months, and after 1 year. Ultrasound examination (ultrasound) of the hand joints was performed according to a standard technique using a 5-12 MHz linear transducer on an Accuvix V10 ultrasound diagnostic system (Samsung Medison, South Korea). Ultrasound was performed twice with the following criteria: 1) synovium thickness, 2) blood flow in synovium by Doppler, 3) presence of hyperechogenic inclusions in synovium, 4) cortical bone contour, 5) signs of tendon inflammation (flexors and extensors of the fingers). Synovium thickness in the hand joints over 3 mm was interpreted as synovial thickening [1]; appearance of blood flow from the contour of the cortical bone of the joint with tree branching — as "pannus", single loci of blood flow by Doppler — as synovitis in hyperemia stage.
Results: During 12 months of follow-up, 47 patients (46.1%) were diagnosed with early rheumatoid arthritis (based on clinical diagnosis according to 2010 criteria and/or prescription of basal anti-inflammatory drugs); 16 (15.7%) had reactive arthritis associated with urogenital infection; 7 (6.9%) had gouty arthritis; 3 (2.9%) had psoriatic arthritis; 2 (1.9%) had systemic lupus erythematosus; 1 patient (0.9%) was found to have a renal malignancy; 26 (25.5%) had no change in EUA diagnosis. Retrospective analysis of the data showed that initially patients with rheumatoid arthritis (RA) in 46.8% (22/47) were determined to have a tree-like blood flow in the synovium of the joint from the cortical contour of the bone ("pannus"); in patients with reactive arthritis associated with urogenital infection, axial tendon lesions were found most frequently (43.8%; 7/16); in patients with gouty arthritis, changes in the triangular cartilage and hyperechogenic inclusions in the synovium were more common (42.9%; 3/7). During the initial examination of patients with EUA who were subsequently diagnosed with RA, the ultrasound picture of the hand joints in the overwhelming percentage of cases (83%; 39/47) was characterized by the presence of extensor tenosynovitis and/or synovial thickening with Doppler blood flow (against the background of symmetrical arthritis of the metacarpophalangeal joints). The sensitivity of detection of these criteria to the development of RA in patients with small joint EUA was 56% with a positive prognostic value of 69%. It has been previously demonstrated that in EUA the presence of subclinical inflammation of the major joints and high titers of antibodies to cyclic citrullinated peptide are strong predictors of RA development [2]. Probably, the combination of clinical and serological tests with the presented ultrasound data of small joints can also increase the accuracy of diagnosis of early RA in patients with EUA.
Conclusion: Detection of subclinical inflammation in the small joints of the hand and synovial thickening with Doppler blood flow in patients with EUA at baseline can help in the stratification of patients at high risk of developing RA.
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AB1345

PREDICTIVE MODEL FOR THE DIAGNOSIS OF PSORIATIC ARTHRITIS IN DERMATOLOGY REFERRALS ACCORDING TO PURE-4 SCALE

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Background: The rate of psoriatic arthritis progression is increased in those patients presenting with established disease greater than 2 years duration, so it is necessary to find tools that allow early diagnosis to prevent joint damage[1]. Prevalence of psoriatic arthritis varies according to the screening strategies used. The COMPAQ study compared four screening questionnaires for psoriatic arthritis (PEST, ToPAS, PASE and EARP), whose sensitivities ranged from 44 to 91%, with the EARP questionnaire showing the highest sensitivity[2]. A new, shorter questionnaire, PURE-4 scale, has been developed, with a sensitivity of 85.7%[3].
Objectives: To evaluate the usefulness of PURE-4 scale in real clinical practice conditions to identify patients with psoriatic arthritis in patients with psoriasis referred from a dermatology department to a rheumatology department.
Methods: Retrospective descriptive study of patients diagnosed with psoriasis who have been referred from the Dermatology Department in the last 12 months for suspected joint domain according to PURE-4 scale used by this department. The following variables were collected: age, sex, obesity, dyslipidaemia, smoking, family history of psoriasis, form of psoriasis (plaque, palmoplantar, scalp, nail), previous treatment (topical, methotrexate, other, none), PASI index, compliance with CASPAR criteria, rheumatological diagnosis (psoriatic arthritis yes/no), PURE-4 score, morning stiffness in hands, Achilles enthesitis, inflammatory low back pain and need for anti-inflammatory drugs for joint pain in the last 3 months. Descriptive statistics was performed and Chi-square test was used to compare the diagnosis of psoriatic arthritis with PURE-4 values (at the response threshold ≥ 1 it has a sensitivity of 85.7% and a specificity of 83.6%).
Results: In the last 12 months the Dermatology Department of our hospital made 33 referrals for suspected psoriatic arthritis in patients diagnosed with psoriasis. Mean age was 46.4 ± 12.4 years, 51.5 % were men. Fifty-one percent of the patients had a BMI ≥25, 30.3% had dyslipidaemia and 45.5% were smokers; 10% of the patients had family history of psoriasis. The most prevalent form of psoriasis was plaque (18%) followed by nail (6%), palmoplantar (3%), scalp (3%) and droplet (3%) involvement; 51.5% of patients were on topical treatment, 9% on methotrexate and 39.4% on biologic treatments; mean PASI was 6.2 ± 7.5. Seventy-five percent of the referred patients did not meet CASPAR criteria; 33.3% were diagnosed with psoriatic arthritis by the rheumatologist. Of the 33 patients, 4 (12.1%) scored 0 points on PURE-4 scale; 21 (63.6%) scored 1 point; and 8 (24.3%) scored 2 points. Once assessed by a rheumatologist, 75.5% had no morning stiffness in the hands, 93.9% had no Achilles enthesitis and 87.9% had no inflammatory low back pain; only 24.2% of patients had required NSAIDs in the previous 3 months for joint pain. Finally, the diagnosis of psoriatic arthritis was analyzed against the PURE-4 cut-off point (Table 1).

Table 1. ***Psoriatic arthritis diagnosis based on total score on PURE-4 scale***

PURE-4 Score	Chi-squared test	p value
≧ 1	0.25	0.61
= 1	0.10	0.74
= 2	0.69	0.41

Conclusion: PURE-4 scale with a score ≥ 1 does not seem to improve the diagnosis of arthritis in psoriatic patients. It would be necessary to implement other questionnaires that are more complete, but at the same time affordable, when carried out during the dermatology consultation in order to increase the sensitivity to refer or not to the rheumatologist.

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AB1346 **ULTRASOUND ASSESSMENT OF SUB-CLINICAL HAND JOINT INFLAMMATION: A COMPARATIVE STUDY BETWEEN EARLY RHEUMATOID AND PSORIATIC ARTHRITIS**

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Background: Ultrasound (US) detected subclinical inflammation can be present in early psoriatic arthritis (PsA) and rheumatoid arthritis (RA), and also in patients fulfilling clinical remission criteria[1-2]. Numerous evidences support that the persistence of subclinical synovitis detected by US is associated with a high risk of disease progression [2-3].
Objectives: To evaluate sub-clinical inflammation of PsA and RA at the level of small joints of the hand and wrist by B-mode and Power Doppler US.
Methods: 30 patients of early PsA and 35 patients of early RA (no clinical evidence of hand joint involvement, PsA disease duration <2 years, and RA disease duration <1 year) were recruited. US [grey scale (GS) and power Doppler (PD)] was performed to assess synovitis, tenosynovitis, joint effusion, and bone erosion of bilateral wrists, metacarpophalangeal joints, proximal and distal interphalangeal joints, as well as the flexor tendons and extensor compartments.
Results: A total of 35 patients were included in the RA group, including 10 males and 25 females. A total of 30 patients were included in the PsA group, including 12 males and 18 females. There were no significant differences in gender composition, age, and duration of disease between the two groups (P>0.05) (Table 1). 19 (63.33%) PsA patients and 16 (45.71%) RA patients had sub-clinical hand joint synovitis. At the joint level, wrist joints were most commonly involved (23.08%), followed by MCP3 (15.38%) and DIP3 (13.46%) in PsA group. In RA group, wrist joints were most commonly involved (55.17%), followed by MCP3 (12.41%), and MCP2 (11.03%). Eight (26.67%) PsA patients and 16 (45.71%) RA patients were detected tenosynovitis. Tenosynovitis was most frequently presented at the extensor tendons in RA and at the flexor tendons in PsA patients (p<0.05). The two most commonly affected were the 4th and 1st extensor compartments in RA patients, and the flexor pollicis longus and flexor digitorum profundus in PsA patients. 81 (6.80%) joint recesses in the RA and 75 (7.35%) joint recesses in PsA were detected effusion. Joint effusion was most frequently detected at radiocarpal and midcarpal joints in RA (30.86%, 25.92%, respectively). Effusion in PsA was most commonly presented at the 3rd PIP joints (26.67%), followed by radiocarpal joints (24.00%). Bone erosions were uncommon, totally 2 (6.67%) PsA patients and 3 (8.57%) RA patients were detected bone erosions.

Table 1. Demographic characteristics of RA and PsA patients

	RA (n=35)	PsA (n=30)	*P*
Female, n(%)	25 (71.43%)	18 (60.00%)	0.33
Age, years, mean±SD	53.20±14.50	54.23±13.65	0.77
Disease duration, years, mean±SD	0.72±0.37	0.91±0.53	0.07

Conclusion: There are significant differences in the US findings of sub-clinical inflammation at the hand and wrist joints, such as the joint effusion and tenosynovitis, which may assist the identification between early RA and PsA. Simultaneously, it should be pointed out that there are some similarities in the joint involvement of sub-clinical synovitis between RA and PsA, physicians should take this into account in clinical work.

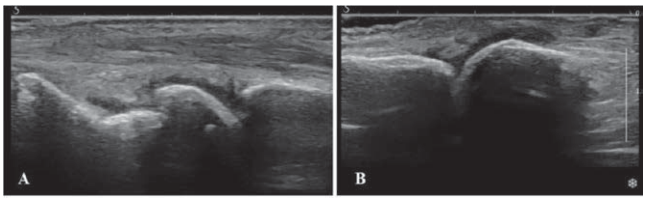

Figure 1. Gray scale ultrasound sagittal view shows synovitis at the wrist joint in an RA patient (A) and at MCP3 in a PsA patient.

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AB1347

ASYMPTOMATIC SACROILIITIS DETECTED BY MAGNETIC RESONANCE ENTEROGRAPHY IN PATIENTS AFFECTED BY CROHN'S DISEASE: PREVALENCE AND ASSOCIATION WITH CLINICAL DATA IN A MULTICENTER STUDY OF ADULT AND PEDIATRIC POPULATION

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Background: Magnetic resonance enterography (MRE) is usually performed in patients with Crohn's disease (CD) for evaluating small bowel involvement. Inflammatory bowel disease (IBD) mainly affect the gastrointestinal tract, although patients may present extraintestinal manifestations (1). Musculoskeletal symptoms are the most frequent extraintestinal manifestation in IBD, especially in CD. Furthermore, sacroiliitis at imaging occurs in about 6-46% of CD patients and may correlate with axial spondyloarthritis (2,3).

Objectives: The primary aim of our study was to assess the prevalence of sacroiliitis in adult and pediatric patients affected by CD who performed MRE. We also evaluated the inter-rater agreement for MRE sacroiliitis and the association between sacroiliitis and patients' clinical data.

Methods: We included consecutive patients with CD diagnosis (4), who underwent an MRE in the period between December 2012 and May 2020. We excluded patients with a known diagnosis of SpA; patients with confirmed or suspected inflammatory back pain; and patients treated at the time of MRE with systemic Disease-Modifying Antirheumatic Drugs (DMARDs), which influence both bowel and joint disease (i.e., conventional DMARDs, and biologic DMARDs).

Two radiologists assessed the prevalence of sacroiliitis at MRE. We evaluated the inter-rater agreement for sacroiliitis and assessed the correlation between sacroiliitis and demographic, clinical, and endoscopic data.

Results: We retrospectively identified 100 adult and 30 pediatric patients. The prevalence of sacroiliitis at MRE was 20% in adults and 6.7% in pediatric patients. The inter-rater agreement for sacroiliitis was substantial (k=0.62, p<0.001) in the adults, and moderate (k=0.46, p=0.011) in the pediatric cohort. Age ≥50 years and the time between CD diagnosis and MRE (≥86.5 months) were significantly associated with sacroiliitis in adult patients (p=0.049 and p=0.038, respectively).

Conclusion: Asymptomatic sacroiliitis at MRE is a frequent and reliable abnormality in adult patients with CD, associated with age of the patients ≥ 50 years and CD duration. Detecting sacroiliitis at MRE in patients affected by CD may help the appropriate and early referral to the rheumatologist.

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AB1348

COMPARISON OF SACROILIAC CT FINDINGS IN PATIENTS WITH AND WITHOUT PSORIATIC ARTHRITIS: RESULTS OF THE CASIPSA STUDY.

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Background: Psoriatic arthritis (PsA) is an inflammatory arthritis associated with various rheumatological manifestations, such as arthritis or enthesitis, predominantly in the peripheral skeleton. However, the axial skeleton may be affected, as shown clinically or by conventional radiographs in up to 70% of patients with peripheral involvement. While there are studies comparing joint damage on standard radiography between patients with PsA and patients with ankylosing spondylitis [1], to our knowledge, no study has specifically evaluated the extent of structural lesions of the sacroiliac joints (SIJs) on computed tomography (CT) in patients with PsA compared with healthy controls.

Objectives: To describe SIJ CT characteristics in patients with PsA and compare them with those of age- and sex-matched controls.

Methods: An observational, retrospective study was performed using medical records from Besançon and Dijon University Hospital's rheumatology departments, which were screened to identify patients with PsA, according to the CASPAR criteria. A search was then carried out for patients in the hospitals' imaging archiving system to identify those who had undergone a CT which included the SIJs in their entirety. Non-inclusion criteria were the existence of pelvic bone lesions and a history of pelvic radiotherapy. Each patient was then matched with a control of the same age and sex, recruited through the hospital's imaging archiving system. For each individual, CT was interpreted by two independent readers using a score previously used by Diekhoff et al. [2], dividing each SIJ into 12 regions, for each of which joint space narrowing (JSN), erosions, and sclerosis are assessed. For this study, we also observed the existence of intra-articular gas and diffuse idiopathic skeletal hyperostosis (DISH) lesions for each region. Quantitative variables were compared using Student's t-test. Qualitative variables were compared using the Chi-2 test.

Results: 48 patients and 48 controls were included. Mean (SD) age was 54.76 ± 12.91 in the PsA group and 54.74 + 12.87 in the control group. 26 (54.18%) were male in both groups. In PsA patients, mean (SD) disease duration was 22.87 ± 14.95 years, 10 (43.48 %) were HLA-B27 positive, and 1 (2.86%) had a bamboo spine. CT findings are described in Table 1. The only lesion found significantly more frequently in PsA patients was erosion, which appeared to be preferentially located on the anterior and middle regions of the SIJs (Figure 1). A positive CT scan (significant joint space narrowing, erosion and/or sclerosis) was found in 15 (32.61%) of the patients with peripheral involvement and 6 (30.00%) of the patients with axial involvement.

Table 1. Sacro-iliac CT findings using a score modified from Diekhoff et al.

Finding	PsA Patients	Controls	p-value
Mean (SD) total score (range 0-264)	26.37 ± 29.12	14.47 ± 10.85	0.01
Global positivity, n (%)	16 (33.33 %)	10 (20.83 %)	0.17
Bilateral ankylosis, n (%)	5 (10.42 %)	0 (0.00 %)	0.02
Positive joint space score, n (%)	15 (31.25 %)	10 (20.83 %)	0.25
Positive erosion score, n (%)	9 (18.75 %)	1 (2.08 %)	0.008
Significant sclerosis, n (%)	11 (22.92 %)	12 (25.00 %)	0.81
Intra-articular gas, n (%)	29 (60.42 %)	35 (72.92 %)	0.19
DISH, n (%)	9 (18.75%)	11 (22.92 %)	0.62

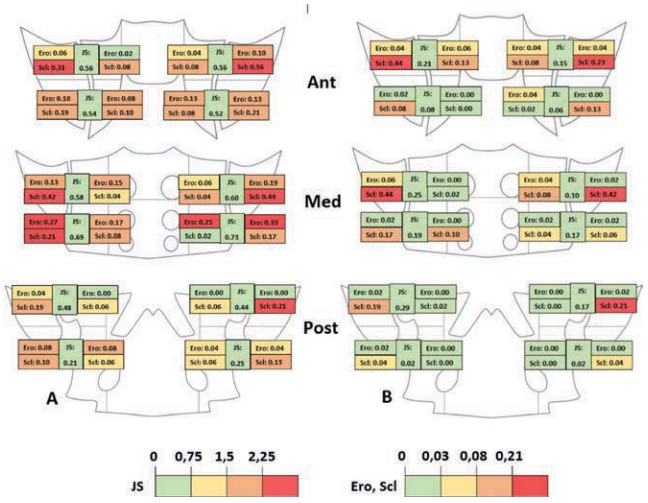

Figure 1. Mean scores by region on anterior, middle, and posterior slices (JS: joint space, Ero: erosions, Scl: sclerosis) in PsA patients (A) and controls (B).

Conclusion: The CT characteristics of SIJs from patients with PsA were similar to those of age- and sex-matched controls, but with a higher prevalence of erosions. Structural lesions of the SIJs were found in nearly one PsA patient out of three.

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AB1349 CORRELATION OF CHRONIC INFLAMMATION MARKERS WITH ULTRASOUND SIGNS OF ATHEROSCLEROTIC HEART DISEASE AND BRACHIOCEPHALIC ARTERIES LESIONS IN RHEUMATOID ARTHRITIS

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Background: Clinical and experimental data confirm the role of both systemic and arterial inflammation in potentiating atherosclerosis and increasing cardiovascular risk in patients with rheumatoid arthritis (RA) against the background of severe immunological disorders.

Objectives: To study the severity of ultrasound signs of atherosclerotic lesions of brachiocephalic arteries and heart valve apparatus in patients with rheumatoid arthritis (RA).

Methods: 57 patients with RA (50 women and 7 men; mean age 50,45±10,12 years old; mean duration of disease 9,2±6,8 years; DAS28 activity: low - 3,5%, medium - 86%, high - 10,5%) were examined. Laboratory examination included determination of serum IgG-RF, CRP, antibodies to cyclic citrullinated peptide (ACCP), antibodies to modified citrullinated vimentin (MCV), total antinuclear antibodies (ANA), and levels of proinflammatory cytokines (IL-1, IL-6, TNF-α, angiopoietin-like proteins types 2, 3, and 4 - ANGPTL 2, 3, 4) by enzyme immunoassay. Cardiac ultrasound examination was performed according to the traditional technique on an Accuvix V10 ultrasound diagnostic system (Samsung Medison, South Korea) equipped with a multifrequency microconvex transducer with a frequency of 2-4 MHz. All patients underwent duplex scanning of brachiocephalic arteries (BCA) with assessment of the severity of atherosclerotic changes (A0 - absence of BCA atherosclerosis, AI - isolated thickening of intima-media complex as a manifestation of non-stenotic BCA atherosclerosis, AII - presence of atherosclerotic plaques and artery stenosis as manifestation of stenotic BCA atherosclerosis). The following gradation was used to estimate the degree of cardiac valve calcification: 0 - no calcification, 1st degree - unexpressed calcification, 2nd degree - moderate calcification, 3rd degree - expressed calcification of cardiac valves.

Results: Signs of cardiovascular system lesions (pericarditis, heart valve lesions, cardiomyopathies, cardiac conduction pathway lesions, myocarditis, endocarditis, coronary arteritis etc.) were diagnosed in 28 (49,1%) RA patients. Heart valve dysfunction was manifested by mitral valve (MV) and/or aortic valve (AV) insufficiency in the majority of cases. In RA patients, ultrasound signs of cardiac valve calcification occurred in 40.4% (23/57) of cases; there was a high prevalence of aortic valve calcification of varying severity (19/23; 82.6%) and less detectable mitral valve calcification (12/23; 52.17%); patients with grade II-III cardiac valve calcification predominated (16/23; 69.6%); 5 patients (21.7%) had combined AV and MV lesions. In 25 (43.8%) patients with RA the signs of atherosclerosis of brachiocephalic arteries were determined: in 19 (33.3%) - non-stenotic (AI), in 6 (10.5%) - stenotic atherosclerosis (AII). No statistically significant correlations were found between changes of cardiac valve apparatus, BCA lesions and main clinical characteristics of RA (disease activity, erosions, RF and ACCP positivity). Increased levels of ANGPTL2 (χ2=4.6, p=0.032) were observed in the group of RA patients with cardiac valve lesions, and ANA (χ2=3.91, p=0.049) and elevated IL-6 (χ2=4.28, p=0.039) were detected more frequently in patients with signs of atherosclerotic lesions of BCA. The presence of autoimmune chronic inflammatory process is an independent sign of premature atherosclerosis development and causes the highest risk of atherosclerotic lesion of BCA and accelerates the processes of cardiac valve calcification in RA patients.

Conclusion: Regular echocardiography (with duplex scanning of BCA and heart valve examination) in RA patients can contribute to earlier identification of groups of patients possible requiring changes in therapeutic approaches to treatment and prevention of vascular accidents.

Disclosure of Interests: None declared

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AB1350 CAN DIFFUSION-WEIGHTED MRI REPLACE INTRAVENOUS GADOLINIUM CONTRAST-ENHANCED MRI FOR ASSESSMENT OF SYNOVITIS?

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Background: In clinical trials of rheumatoid arthritis (RA) patients, intravenous gadolinium contrast injection is the gold standard method for MRI assessment of synovitis, e.g. by the OMERACT RA MRI Scoring method (RAMRIS). It has been shown that diffusion-weighted MRI (DW-MRI) allows visualization of synovitis[1].

Objectives: To establish a method for measuring MRI-derived apparent diffusion coefficient (ADC) from DW-MRI and to test its correlation with RAMRIS synovitis scoring.

Methods: MRI including diffusion-weighting of the dominant hand was performed in a cohort of RA patients in clinical remission (disease activity score in 28 joints-C-reactive protein [DAS28-CRP] <3.2 and no swollen joints). ADC measurements of the synovium were assessed in 7 areas (3 wrist joint areas and 4 metacarpophalangeal (MCP) joints), similar to the RAMRIS. Intra-observer agreement for the ADC reading was determined using the intraclass correlation coefficient (ICC). Spearman's rho (ρ) was calculated for the correlation of ADC with RAMRIS Synovitis. Differences in mean ADC between the individual RAMRIS synovitis grades were examined using ANOVA with Bonferroni correction for multiple tests.

Results: In 63 patients (67% females, age mean 61.0 years (range 36-78 years), disease duration 11.9 years, 0-59 years), DAS28-CRP 2.1 (1.6-3.0) the total RAMRIS synovitis was mean 5.8 (range 0-18). The mean ADC was 0.98x10-3 mm^2/s (0.11-2.80). Correlations between RAMRIS synovitis and ADC in the 7 joint areas and mean differences in ADC between RAMRIS synovitis grades are presented in the Table 1. When all 7 joints were pooled the mean ADC and RAMRIS synovitis were moderately positively correlated, ρ=0.49; p<0.01. Statistically significant differences (p<0.01) in mean ADC were observed between all RAMRIS synovitis grades (0 vs 1, 0 vs 2, etc) except for the difference between grade 2 and 3. Good intra-observer (ICC = 0.62 (95%CI 0.49-0.72)) was found.

Conclusion: ADC, determined from DWI-MRI, may be used to grade synovitis without the use of gadolinium contrast injection.

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Disclosure of Interests: Jakob Møllenbach Møller: None declared, Karen Lind Gandrup: None declared, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Celgene, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Orion, Pfizer, Roche and UCB, Consultant of: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, Amgen, BMS, Merck, Celgene and Novartis, Daniel Glinatsi Speakers bureau: Eli Lilly, Consultant of: AbbVie, Ole Madsen: None declared, Kim Hørslev-Petersen: None declared, Signe Møller-Bisgaard: None declared

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Table 1.

	All joints	RUJ	RCJ	CMCJ	MCP2	MCP3	MCP4	MCP5
RAMRIS synovitis vs ADC correlation, (Spearman's rho)	**0.49; p<0.01**	**0.39; p<0.01**	**0.34; p=0.01**	**0.37; p<0.01**	**0.59; p<0.01**	**0.46; p<0.01**	**0.69; p<0.01**	**0.42; p<0.01**
Mean differences in ADC [x10-3 mm^2/s] between RAMRIS synovitis grades (ANOVA with Bonferroni correction)								
0-1	**-0.20, p<0.01**	-0.29, p=0.31	0.09, p=1.00	-0.14, p=1.00	-0.04, p=1.00	0.02, p=1.00	**-0.42, p<0.01**	n/a
0-2	**-0.55, p<0.01**	-0.28, p=0.91	-0.15, p=1.00	-0.27, p=0.43	-0.38, p=0.03	**-0.47, p<0.01**	**-0.62, p<0.01**	n/a
0-3	**-0.79, p<0.01**	**-0.87, p<0.01**	-0.20, p=1.00	-0.01, p=1.00	**-0.72, p<0.01**	**-0.57, p<0,01**	**-0.93, p<0.01**	n/a
1-2	**-0.34, p<0.01**	0.14, p=1.00	-0.25, p=0.70	-0.13, p=1.00	-0.34, p=0.1	**-0.49, p<0,01**	-0.19, p=1.00	n/a
1-3	**-0.59, p<0.01**	-0.58, p=0.26	-0.29, p=1.00	0.13, p=1.00	**-0.68, p<0.01**	**-0.59, p<0.01**	**-0.51, p=0.02**	n/a
2-3	-0.24, p=0.09	-0.60, p=0.24	-0.05, p=1.00	0.26, p=1.00	-0.34, p=0.12	0.10, p=1.00	-0.31, p=0.63	n/a
Intra-observer ICC (95%CI)	0,62 (0,49:0,72)	0.70 (0.34:0.89)	0.57 (0.14:0.82)	0.39 (0.14:0.74)	0.81 (0.53:0.93)	0.70 (0.34:0.89)	(0.81 (0.51:0.93)	0.40 (0.18:0.74)

ADC: Apparent diffusion coefficient, CI: confidence interval, CMCJ: carpo-metacarpal joint, ICC: intraclass correlation coefficient, MCP: metacarpo-phalangeal joint, RCJ: radio-carpal joint, RUJ: radio-ulnar joint

AB1351 FULL LONGITUDINAL NAILFOLD VIDEOCAPILLAROSCOPY ANALYSIS OF MICROVASCULAR CHANGES DURING NORMAL PREGNANCY

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Background: During pregnancy profound physiologic changes are required to ensure fetal development and meet maternal needs. Microvascular remodelling is one major responsible for pregnancy haemodynamic adaptation, still it is not routinely evaluated in the obstetric field [1–2].
Objectives: To investigate the role of nailfold capillaroscopy (NCV) as a gold-standard and safe technique in detecting microvascular changes during normal pregnancy and to explore its possible application in clinical obstetric setting.
Methods: A population of 30 healthy pregnant women was longitudinally followed performing clinical assessment and NVC evaluation at each trimester and post-partum. Thirty non-pregnant age-matched healthy women having received at least two NVCs with a minimum 9 to 12-month interval were selected as controls. All NVC images were evaluated by a qualitative and semi-quantitative assessment using current standardised approach [3]. Statistical analyses were conducted to explore NVC parameters trend throughout gestation and its possible association with pregnancy course and clinical macrovascular parameters (i.e., systemic blood pressure, umbilical artery Doppler ultrasound).
Results: A progressive significant increase of capillary neoangiogenesis and a specular reduction in capillary dilations was observed during pregnancy ($p<0.05$). These statistically significant variations were not found in age-matched controls, who showed stable NVC parameters over a similar time frame ($p<0.05$). Not any significant association was found between NVC changes and pregnancy course, delivery outcome or macrovascular parameters.
Conclusion: This first comprehensive longitudinal NVC evaluation during normal pregnancy reports significant physiological microvascular variations throughout gestation, suggesting NVC as a safe and promising technique for further investigate and define patterns of microvascular changes in pregnant patients with rheumatic diseases.
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Disclosure of Interests: None declared

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AB1352 VALIDATING DIAGNOSTIC GCA ULTRASONOGRAPHY SKILLS AGAINST AN EXPERT SONOGRAPHER

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Background: Ultrasonography has become the recommended first line investigation for suspected giant cell arteritis (GCA). However, it is still not yet widely available in the UK due to a paucity of skilled rheumatologists. Effective training programmes have been developed, but subsequent hands-on practice is needed to become truly proficient. There is no consensus on the logistics of gaining the 'appropriate' level of skill.
Objectives: This project demonstrates a potential mechanism for validation against an expert sonographer.
Methods: Over a 6-month period, 12 scans of patients referred with suspected GCA were sequentially performed by first a trainee (FC) and then an expert sonographer (CM) on the same day. FC had theoretical knowledge and supervised practical experience but had not scanned independently prior to this project. CM has performed >1000 scans. 6 vascular territories considered to be the core GCA US data set (common, frontal and parietal branches of the superficial temporal artery, and the 1st, 2nd and 3rd part of the axillary artery) were marked as either 'normal' or 'halo'. CM was blinded to FC's results. Inter-observer reliability was calculated for all vascular territories using Cohen's kappa.
Results: A total of 144 vascular territories were scanned in 12 patients. Table 1 details the inter-observer variation, with a near perfect level of agreement demonstrated, kappa=0.90 (95% CI 0.83 – 0.98).

Table 1. Matrix of inter-observer variation for all vascular territories in 12 patients, k=0.90 (95% CI 0.83 – 0.98)

	FC positive	FC negative	Total
CM positive	48	4	50
CM negative	2	90	92
Total	50	94	

Conclusion: This is the first study that demonstrates a mechanism for validation of ultrasonography skills which will allow GCA US to become a feasible reality in clinical practice. This project demonstrates that after acquiring supervised training, near perfect levels of agreement can be arrived between a trainee and expert.
Disclosure of Interests: None declared

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AB1353 VESSEL AFFECTION AND THE INFLUENCE OF GLUCOCORTICOIDS ON 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY IN GIANT CELL ARTERITIS

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Background: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) represents one of the standard imaging modalities in the detection of giant cell arteritis (GCA). Detailed data regarding the vessel involvement in GCA are not available.
Objectives: The aim of this study was to quantify arterial vessel involvement at the onset of GCA by ^{18}F-FDG PET/CT and to verify the influence of glucocorticoid treatment on the diagnostic performance of ^{18}F-FDG PET/CT.
Methods: This study included 60 patients (44 women and 16 men, mean age 72.8 ± 8.8 years) at the onset of GCA. All patients received a PET/CT. 44 patients were glucocorticoid naïve. 16 patient were treated with glucocorticoid (prednisone median dose 60 mg) 3.5 ± 4.4 days before the ^{18}F-FDG PET/CT was performed. All ^{18}F-FDG PET/CT scans were scored regarding the active inflammation of the large arteries.
Results: The most affected arteries were the aorta ascendens (72 %), followed by truncus brachiocephalicus (62 %), acrus aortae (60 %), aorta descendens (60 %), left and right arteria sublcavia (60 % and 58 %). The aorta and their outgoing arteries presented an involvement in 39 GCA patients (89 %). A singular affection of the aorta was shown in 9 patients (20 %). glucocorticoid naïve patients (89 %) showed affected arteries more frequently than glucocorticoid treated patients (38 %).
Conclusion: The study showed that the thoracic aorta (in particular aorta ascendens) is the most involved vascular segment in GCA. The use of glucocorticoids was associated with a marked decrease of vascular inflammation. Consequently,

the imaging of the thoracic aorta should be included in the diagnostic procedure of GCA. ^{18}F-FDG PET/CT should be performed without glucocorticoid treatment, if the clinical situation allowed this proceeding.

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AB1354 ULTRASOUND JOINT EXAMINATION BY AN AUTOMATED SYSTEM VERSUS BY A RHEUMATOLOGIST – FROM A PATIENT PERSPECTIVE

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Background: The Arthritis Ultrasound Robot (ARTHUR) is an automated system for ultrasound scanning of the joints of both hands and wrists, with subsequent disease activity scoring using artificial intelligence.
Objectives: To describe the patients' perspective of being examined by ARTHUR, compared to an ultrasound examination by a rheumatologist. Further, to register any safety issues in the use of ARTHUR.
Methods: Twenty-five patients with rheumatoid arthritis (RA) had both hands and wrists examined by ultrasound, first by a rheumatologist subsequently by ARTHUR (see Figure 1 A, B and C). Patient-reported outcomes (PRO) were obtained after the examination by the rheumatologist and then again after the examination by ARTHUR. PROs regarding pain, discomfort and overall experience were collected. In addition, willingness to be scanned again by ARTHUR as part of future clinical follow-up was also collected. All ARTHUR examinations were observed for safety issues.

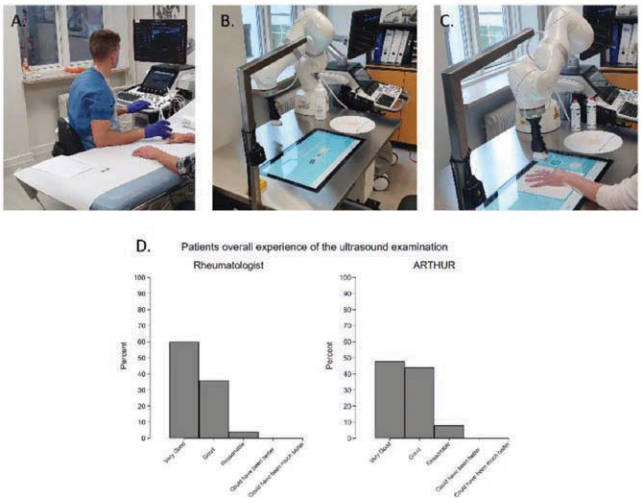

Figure 1. A. The rheumatologist is performing the ultrasound examination. B. The ARTHUR system used in this trial used a GE Logiq 10 ultrasound scanner. C. ARTHUR started ultrasound scanning a RA patient. The patient follows the instructions given on the touchscreen and by audio. D. Overall experience with ultrasound scanning by Rheumatologist and ARTHUR.

Results: For baseline characteristics of RA patients, see Table 1.

Table 1. Baseline Characteristics. CRP: C-reactive protein; DAS28CRP: Disease Activity Score in 28 joints combined with CRP value, RF: Rheumatoid factor antibody, CCP: cyclic citrullinated peptide antibodies.

Table 1	Patients
Patients, n	25
Age (SD)	63,7 (12,22)
Female, n (%)	17 (68 %)
Erosive disease, n (%)	10 (40%)
RF and/or CCP-positive, n (%)	17 (68%)
DAS28CRP (SD)	2.8 (1.2)

There was no difference in pain or discomfort between the examination by a rheumatologist and by ARTHUR (p=0.29 and p=0.20, respectively). The overall experience of an examination by ARTHUR (see Figure 1 D) was described as very good or good by 92% (n=23), with no difference compared to the examination by the rheumatologist (p=0.50). All (n=25) patients were willing to be examined by ARTHUR again, and 92% (n=23) would accept ARTHUR as a regular part of their RA clinical follow up. No safety issues were registered.
Conclusion: Joint ultrasound examination by ARTHUR was safe and well-received, with no difference in PRO components compared to ultrasound examination by a rheumatologist. Fully automated systems for joint disease activity assessment could be important in future strategies for RA management.

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AB1355 NAILFOLD CAPILLAROSCOPY CHANGES IN PATIENTS WITH PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: In psoriatic arthritis (PsA) and rheumatoid arthritis (RA) systemic inflammation is known to cause endothelial dysfunction[(1)]. Nailfold videocapillaroscopy (NVC) analyzes *in vivo* blood vessels, looking for alterations due to microvascular damage, and its application in these pathologies often highlights interesting abnormalities. PsA is characterized by lower mean capillary length and density and abnormal morphology, such as tight terminal convolutions. In RA typically elongated and dilated capillaries and prominent subpapillary plexus are described[(2, 3)]. Differences between RA and PsA NCV patterns are known but not well defined yet[(3)].
Objectives: Aim of our study was to evaluate the microvascular features circulation by NVC in patients affected by PsA and RA, looking for possible differences that may characterize the two diseases.
Methods: We recruited outpatients affected by PsA or RA classified according to standard criteria[(4, 5)] referring to the Rheumatology Unit at Sapienza University of Rome. Healthy controls (HCs) without known risk factors for nailfold capillary alterations[(6)] were also recruited. Patients and HCs underwent NVC with a 200x magnification lens. The following morphological parameters were considered: number of capillaries per square millimeter, alterations in length, dimension, morphology and distribution of the capillary; presence of ectatic loops, hemorrhages, flux abnormalities[(7, 8)]. A semi-quantitative rating scale was adopted to score these changes, according to previous studies[(9)]. The mean score for each subject was obtained by analyzing all fingers, except the thumbs. For the statistical analysis, Chi-square and Mann-Whitney tests were used. All tests were two-sided with a significance level set at p<0.05.
Results: We recruited 34 patients (20 with PsA and 14 with RA) and 30 HCs. For patients, the mean age was 61,7 years (SD 15,4), median disease duration was 184 months (SD 204) and males were 18 (53%). Active or past smokers were 11 (18%), 9 (15%) suffered from arterial hypertension and 2 (0.03%) from type 2 diabetes mellitus. Raynaud's phenomenon was present in 4 patients with PsA (20%) and 6 with RA (43%). The most frequent morphological changes were tortuous capillaries (90% in PsA and 100% in RA), single-crossing shape (90% and 86%) and bizarre capillaries (30% in both groups) while multiple crossing and ramified capillaries were present in 50% and 21 % RA patients only. With respect to HCs, we found significantly more frequent changes concerning morphology, ectatic loops, presence of hemorrhages and capillary plexus visibility in both PsA and RA patients. Moreover, patients with RA showed significantly more frequent abnormalities of the blood flow with respect to HCs. These results are shown in Table 1.

Table 1. Comparison of the main NVC changes in patients and HCs.

NVC Changes	HC	PsA		RA	
	N (%)	N (%)	P value vs HCs	N (%)	P value vs HCs
Morphology	3 (10%)	14 (70%)	**p<0.0001**	12 (86%)	**p<0.0001**
Ectatic loops	0 (0%)	11 (55%)	**p<0.0001**	8 (57%)	**p<0.0001**
Hemorrhages	2 (0.07%)	1 (5%)	**p<0.01**	6 (43%)	**p<0.0058**
Plexus	19 (63%)	10 (50%)	**p<0.02**	7 (50%)	**p<0.02**
Flux abnormalities	3 (10%)	6 (30%)	p>0.05	5 (36%)	**p<0.026**

The presence of hemorrhages was significantly higher in RA rather than in PsA patients (p<0.01). No significant differences were found in number, length, and distribution of capillaries between PsA/RA cases and HCs.

Conclusion: Our study confirms and completes the frame of NCV alterations in PsA and RA. We described for the first time alterations in the capillary morphology and the presence of hemorrhages in both groups of patients with respect to HCs. It remains to evaluate how these findings can reflect the microvascular environment of chronic arthritis.

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AB1356 QUANTITATIVE ANALYSIS BY SODIUM AND PROTON BASED 3-TESLA MR IMAGING OF THE ACHILLES TENDON

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Background: Decrease of proteoglycan is the initiating stage of post-inflammatory tissue degradation. Sodium MRI is promising great potential for identification and monitoring of proteoglycan changes in tendons and cartilage associated with inflammatory and degenerative musculoskeletal diseases, where the Achilles tendon is frequently affected.
Objectives: Proof-of-concept study to examine the usage of sodium MRI in quantifying sodium concentrations in the Achilles tendon in healthy volunteers.
Methods: Sodium (^{23}Na) MR imaging of the Achilles tendon together with established proton (^{1}H) MRI sequences were performed in 10 healthy volunteers (6 males, 4 females, age 29 ± 9 years) using a dual-tuned ^{23}Na/^{1}H surface coil (RAPID Biomedical GmbH, Würzburg-Rimpar, Germany). Imaging was performed using a 3D density adapted radial sequence [1] providing sufficient signal-to-noise ratio for sodium imaging. Reference tubes on the backside of the coil were used to enable assessment of sodium concentration from sodium signal-to-noise ratio maps. Sodium concentrations were determined for tendon insertion into calcaneus bone (INS), middle portion of the tendon (MID) and muscle-tendon junction (MTJ) and for the whole Achilles tendon. Statistical differences were analysed by Wilcoxon test.
Results: Sodium concentrations c [mM] of the Achilles tendon could be quantified in all 10 (exemplary selected volunteer is shown in Figure 1). Significantly higher sodium concentrations were obtained in INS compared to MID (p=0.002) and MTJ (p=0.002) and in MID compared to MTJ (p=0.037). The average sodium concentration of the whole Achilles tendon was 57.23±17.69 mM with only minor outliers in this healthy population.

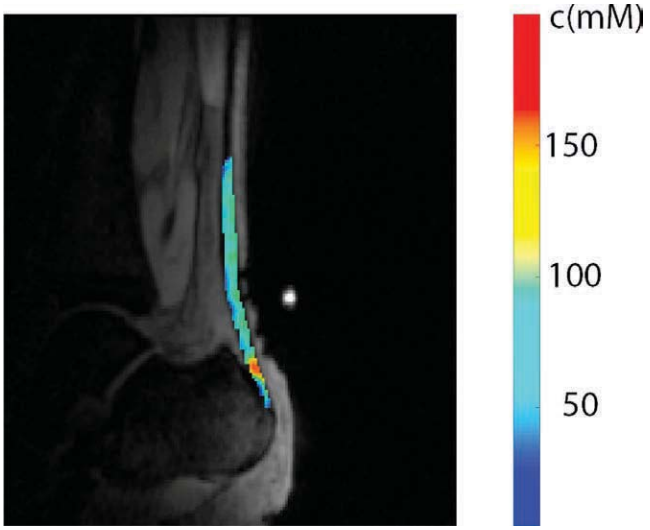

Figure 1. Sodium concentrations of the Achilles tendon. Highest sodium concentrations c(mM) were observed at the tendon insertion into calcaneus bone (INS), whereas lower concentrations were measured in the middle portion of the tendon (MID) and muscle-tendon junction (MTJ).

Conclusion: Performance of quantitative sodium imaging of the Achilles tendon in a high-field MRI machine is feasible for assessing sodium concentrations, a surrogate biomarker for proteoglycan content. Molecular MR studies investigating changes in the proteoglycan content of the Achilles tendon in patients with inflammatory and degenerative musculoskeletal diseases could support early diagnosis or therapy monitoring in the future.

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AB1357 THE BEST CUT-OFF POINT FOR MEDIAN NERVE CROSS SECTIONAL AREA AT THE LEVEL OF PISIFORM BONE

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Background: Carpal tunnel syndrome (CTS) is a focal neuropathy caused by compression of the median nerve (MN) at the wrist. Electromyography (EMG) is the gold standard for the diagnosis of CTS. Currently, the ultrasound (US) is frequently used as an initial screening exam by measuring the cross-sectional area (CSA) of the MN. The cut-off point of the CSA at the pisiform bone level to define CTS remains controversial with previous studies reporting values between 6.5mm^2 and 15mm^2 (1).
Objectives: The aim of this study is to determine the best cut-off point of the CSA for the diagnosis of CTS.
Methods: Cross-sectional study at a Tertiary Rheumatology Department including patients aged ≥ 18 years with symptoms compatible with CTS. Sociodemographic and clinical data, visual analogue scale for pain (VAS), Boston Questionnaire (BQ), and the results of EMG and US performed in each patient were collected. The EMG was performed according to the standardized protocol (sensory conduction velocity, sensory amplitude, distal sensory and motor latency), and the patients were categorized in 4 groups: normal, mild, moderate, and severe. A rheumatologist with expertise in imaging performed all the US evaluations by means of a 6–18-MHz (Siemens ACUSON S 2000) linear array transducer. The largest CSA of the MN was measured at the level of the pisiform bone. Receiver operating characteristic (ROC) curve was used to determine optimal cut-off values of the CSA taking the EMG result as the gold-standard. One-way ANOVA test was used to compare CSA between the 4 EMG groups.
Results: Fifty patients were included, 90% were female, mean age was 52.1 ± 10.8 years and median duration of symptoms was 28.0 (IQR 23.0-31.0) months. The mean VAS was 4.2 ± 2.9. In the BQ there was a mean symptom severity score of 2.4 ± 0.6 and a mean functional status score of 2.0 ± 0.9. One-way ANOVA showed that mean CSA values were significantly different in the 4 groups of patients. The Ryan-Einot-Gabriel-Welsch post hoc analysis showed that only the mean CSA of patients with severe STC is different from the remaining groups defined by EMG results. The best cut-off point for CSA at the pisiforme bone level for CTS diagnosis was 6.6 mm^2 with a sensitivity and specificity of 92.9% and 75.0% (AUC=0.9, P<0.001). The positive and negative predictive values were 95.1% and 66.7%, respectively. For severe CTS diagnosis the best cut-off point for CSA was 12.3mm^2 with a sensitivity of 82.4% and a specificity of 72.7% (AUC=0.8, P<0.001). The positive and negative predictive values were 60.9% and 88.9%, respectively.
Conclusion: In our study we found that the best cut-off point of the CSA was 6.6mm^2 for distinguishing patients with/without CTS based on EMG alterations, with a high sensitivity and moderate specificity. This is a lower cut-off value than usually used in clinical practice and could be explained by small sample and the greater number of patients with mild and moderate STC on EMG.

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Table 1. "Patient's characteristics"

	Sex	Age	RD	anti-TNF-α	Time doing anti-TNF-α	DMARD	GCS	PPD	Chest X-ray	TB prophylaxis
1	Male	66	PsA	adalimumab	6 years	methotrexate	No	5 mm	Normal	Isoniazid
2	Female	56	RA	adalimumab	10 years	methotrexate	No	5 mm	Normal	Isoniazid
3	Female	62	RA	adalimumab	5 years	methotrexate	Yes	10 mm	Normal	Isoniazid
4	Male	45	AS	certolizumab	1 year	No	No	20 mm	Normal	Isoniazid

AS, ankylosing spondylitis; DMARD, disease-modifying antirheumatic drugs; GCS, glucocorticosteroids; PPD, purified protein derivative; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RD, rheumatological disease; TB, tuberculosis.

AB1358

AN OLD METHOD FOR CURRENT CHALLENGES: SKIN TEST CONVERSION OF PURIFIED PROTEIN DERIVATIVE (PPD) IN RHEUMATOLOGICAL PATIENTS TREATED WITH ANTI-TNF-α

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Background: Anti-TNF-α are a cornerstone for the treatment of multiple rheumatic diseases. They are associated with an increased risk of developing tuberculosis (TB), which is endemic in several countries and an important burden across the globe. Purified protein derivative (PPD) is one of the tests used to demonstrate a latent TB infection (LTBI). Screening is recommended for TB prior to the onset of anti-TNF-α and monitoring evaluating possible conversion of PPD during treatment, defined as the change from a negative (<5 mm) to positive result (≥5 mm). Identification and treatment of LTBI can reduce the risk of disease development by up to 90%. Currently the results of PPD conversion and its interpretation during anti-TNF-α treatment are variable and that is why we set out to know the frequency of conversion of PPD in this group of patients in our environment.
Objectives: To identify PPD conversion in patients with rheumatological diseases undergoing anti-TNF-α treatment.
Methods: A descriptive, analytical, observational, retrospective study was conducted from January 1, 2018 to January 1, 2022. Inclusion criteria: Patients >18 years old, diagnosed with rheumatological diseases and treated with anti-TNF-α for more than 3 consecutive months, with a negative PPD (<5 mm diameter) previous starting anti-TNF-α and a normal chest X-ray.
Results: 62 patients (age 45.8 ± 12.5 years), with rheumatological diseases (41 rheumatoid arthritis, 7 juvenile idiopathic arthritis, 5 ankylosing spondylitis, 4 psoriatic arthritis, 4 uveitis and 1 interstitial keratitis) under anti-TNF-α therapy (35 adalimumab, 18 certolizumab, 9 etanercept) were included. Concomitant use of immunomodulators (52 methotrexate, 23 leflunomide, 10 hidroxicloroquine, 3 sulfasalazine, 2 azathioprine and 1 mycophenolate mofetil) and glucocorticoids (33/62) was observed. The conversion of PPD took place in 4 patients (6.5%) (Table 1).
Conclusion: Considering the prevalence of TB in our country, this research showed a lower PPD conversion percentage compared to previous reports. Anti-TNF-α have radically changed the evolution of rheumatological diseases, considerably improving the patient's quality of life. With the increase in the accessibility of anti-TNF-α worldwide, new challenges have arisen regarding infectious diseases such as TB, which is endemic in some countries. PPD is a well known, cheap, sensitive and widely available method, suitable for LTBI diagnosis. Although sensitivity could be increased using, in addition, other LTBI detection methods such as IGRAs (interferon gamma release assays), they are usually unavailable in developing countries (1-3).

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AB1359

DO LATERAL AND AP RADIOGRAPHS TELL DIFFERENT STORY IN PATIENTS WITH PSORIATIC ARTHRITIS?

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Background: The conventional radiography score that is frequently used in spondyloarthritis patients is mSSASS. This score was developed for Anylosing Spondylitis patients and is also frequently used in Psoriatic arthritis (PsA) (1). The mSSASS score takes into account lateral imaging of the lumbar and cervical radiographs. On the other hand, syndesmophytes can be detected on lumbar anterior-posterior (AP) radiographs, which may not be seen on lateral assessment.
Objectives: The aim of this study is to determine whether lumbar AP radiographs have an additional contribution to the evaluation of syndesmophytes in PsA patients.
Methods: Lumbar lateral radiographs and AP radiographs of 274 PsA patients receiving bDMARD therapy were evaluated. A total of 182 lateral lumbar radiographs and 144 AP radiographs were evaluated. On lateral lumbar radiographs each lumbar vertebral unit was evaluated between T12 lower and S1 upper ends. Areas between L1-L5 as AP, right-left, upper and lower vertebral units were evaluated. Syndesmophytes are classified as follows; corner and/or non-marginal syndesmophytes and bridging syndesmophytes. All of the assessments were done by an experienced rheumatologis (UK) and in cases with suspicion, another experienced rheumatologist reviewed the cases (LK) and a consensus was reached.
Results: 182 patients had lumbar radiographs with the mean (SD) age of 44.9 (12.7) years and the mean (SD) PsA duration of 4. 8(6.1) years at the time of the radiographs were taken. The rate of females was 70.3%. When the lateral lumbar radiographs were evaluated, 42/182 (23.1%) patients had at least one syndesmophyte. These 42 patients had a total of 80 syndesmophytes, 41 of which were bridging and 39 were corner syndesmophytes. The distribution of syndesmophytes is shown in the Table 1. The mean number of syndesmophytes in patients with at least one syndesmophyte on the lumbar lateral radiograph is 80/42 (1.9). In patients with at least one syndesmophyte, 14/42 (33.3%) patients had additional syndesmophytes not seen on lateral radiographs but on AP X-ray. Their distribution is as follows: L1 (4 patients), L2 (3 patients), L3 (2 patients), L4 (6 patients) and L5 (1 patient). In addition, 11 corner syndesmophytes and 5 bridging syndesmophytes were detected in the lumbar AP radiograph. When lumbar and AP radiographs are evaluated together, 44/182 (24.2%) patients have at least one syndesmophyte. When the lumbar lateral and AP radiographs are evaluated together, there are 96 syndesmophytes in 44 patients with syndesmophytes, 46 of which are bridging and 50 are corner syndesmophytes. Average number of syndesmophytes were 96 in 44 patients (2.2 per-patient).

Table 1. The distribution of syndesmophytes on lateral lumbar radiographs

Lateral Lumbar X-ray	Patients with syndesmophytes	Total syndesmophyte count n(%)	Number of bridging syndesmophyte	Number of corner syndesmophyte
	N (%)		n(%)	n(%)
L1 lower-L2 upper border	14	29	16	13
L2 lower-L3 upper border	14	21	12	9
L3 lower-L4 upper border	15	21	10	11
L4 lower-L5 upper border	4	6	2	4
L5 lower-S1 upper border	2	3	1	2

Conclusion: AP radiographs are not taken into account in conventional radiograph scores accepted as mSSASS. PsA patients have syndesmophytes in approximately one-quarter of patients on lateral radiograph, with an average syndesmophyte number of about 2. On the other hand, when AP radiographs are evaluated, new syndesmophytes that are not seen on lateral radiographs are seen in one-third of patients with at least one syndesmophyte. Although it does not cause a significant change in the number of patients with syndesmophytes, it should be kept in mind that the use of AP radiographs in PsA patients may cause an increase in the total score. Whether there is a difference between PsA and SpA patients should be investigated in further studies.

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AB1360 DISTRIBUTION OF INFLAMMATORY/DEGENERATIVE/ AMBIGUOUS LESIONS ON CONVENTIONAL LUMBAR LATERAL RADIOGRAPHS IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) patients are relatively older than spondyloarthritis patients, and accordingly, degenerative changes on spine are more frequent and confusing.
Objectives: The aim of this study is to determine the distribution, relation of different type of lesions on the lumbar spine in PsA patients receiving bDMARD therapy.
Methods: 182/274 (66.4%) patients had lateral lumbar radiographs. Two and three lumbar radiographs were present in 53 (19.3%) 14 (5.1%) patients respectively. The upper and lower regions of each vertebra were evaluated between T12, S1 (total of 2184 regions). Lesions were determined as osteophyte (O) (grade 0-3), vertebral corner erosion, sclerosis, squaring, corner syndesmophyte (SP), bridging SP. While osteophyte was determined according to the degenerative character of new bone formations, the definition of SP was made according to mSSASS. Lesions that the clear distinction of cannot be made were defined as ambigious. For patients with follow-up radiographs, the change of lesions defined as ambigious was also recorded. All of the assessments were done by an experienced rheumatologis (UK) and in cases with suspicion, another experienced rheumatologist reviewed the cases (LK) and a consensus was reached.
Results: The mean (SD) age of 182 PsA (69.2% female) patients was 47.6 (12.7), the age at diagnosis of PsA was 39.7 (12.7). Of the patients, 112 (61.5%) met the criteria for mNY. There was at least one abnormality in 111 (61.0%) patients with lumbar spine radiograph. O was the most frequently detected lesions (42.3%), with 18.1% of patients having O grade 2 and above. While SP was present in 24.2% of all patients, ambigious lesions were detected in 13 (4.7%) patients. While O were most frequently grouped between L2 upper and L4 upper regions, SPs were distributed in a similar ratio between L4 upper and T12 lower regions. Ambigious lesions were anywhere between T12 sub-L5. Patients with ambigious lesions were older (55.7 (9.8) vs 47.0 (12.7), p=0.017), lumbar mSSASS score was higher (5.4 (8.1) vs 1.6 (3.8), p=0.002) corner SPs (46.1% vs. %) 17.7, p=0.013) and bridging SPs (30.7% vs 7.7%, p=0.006) were more common, while no difference was found in terms of O grade 2 (23.1% vs 17.7%, p=0.63). Changes were observed in 5 ambigious lesions in patients with follow-up lumbar radiography, 4 of them transformed into corner SP at follow-up, and one was evaluated as osteophyte grade 2.
Conclusion: Approximately one-fifth of patients presenting with significant degenerative new bone formation and SP was found in one fourth. In approximately 5% of all patients, lesions in the lumbar vertebrae could not be differentiated. The frequency of SPs in other vertebral areas are more prominent in patients with ambigious lesions. It is seen that ambigious lesions turn into SPs in a small group of patients with follow-up data. The nature of these lesions needs to be evaluated in further imaging studies.

Table 1. The distribution of the lesions on lumbar spine

Location	Osteophyte	Osteophyte ≥ 2	Corner SP	Bridging SP	All SP	Erosion, Sclerosis, Squaring	Ambigious
T12L, n (%)	7 (3.8)	1 (0.5)	9 (4.9)	5 (2.7)	14 (7.7)	3 (1.6)	2 (1.1)
L1, U n (%)	6 (3.3)	0 (0)	10 (5.5)	5 (2.7)	15 (8.2)	2 (1.1)	2 (1.1)
L1, L, n (%)	10 (5.5)	6 (3.3)	8 (4.4)	6 (3.3)	14 (7.7)	4 (2.2)	0 (0)
L2, U, n (%)	15 (8.2)	8 (4.4)	8 (4.4)	7 (3.8)	15 (8.2)	4 (2.2)	4 (2.2)
L2, L n (%)	16 (8.8)	6 (3.3)	5 (2.7)	6 (3.3)	11 (6.0)	4 (2.2)	0 (0)
L3,U n (%)	31 (17.0)	13 (7.1)	4 (2.2)	6 (3.3)	10 (5.5)	10 (5.5)	2 (1.1)
L3,L n (%)	17 (9.3)	8 (4.4)	3 (1.6)	5 (2.7)	8 (4.4)	5 (2.7)	2 (1.1)
L4,U, n (%)	37 (20.3)	14 (7.7)	8 (4.4)	5 (2.1)	13 (7.1)	11 (6.0)	4 (2.2)
L4, L n (%)	10 (5.5)	1 (0.5)	3 (1.6)	1 (0.5)	4 (2.2)	6 (3.3)	4 (2.2)
L5, U n (%)	24 (13.2)	8 (4.4)	1 (0.5)	1 (0.5)	2 (1.1)	1 (0.5)	1 (0.5)
L5,L n (%)	8 (4.4)	3 (1.6)	1 (0.5)	1 (0.5)	2 (1.1)	0 (0)	0 (0)
S1, U, n (%)	3 (1.6)	3 (1.6)	0 (0)	1 (0.5)	1 (0.5)	0 (0)	0 (0)
All vertebral corners (n=2184)	184 (8.4)	75 (3.4)	60 (2.7)	49 (2.2)	109 (4.9)	50 (2.2)	21 (1.0)
All patients	77 (42.3)	33 (18.1)	36 (19.8)	17 (9.3)	44 (24.2)	22 (12.1)	13 (4.7)

SP:Syndesmophyte, L:Lower, U:Upper

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AB1361 PAIN MANAGEMENT IN METASTATIC BONE DISEASE

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Background: Bone metastases are the most common cause of pain in patients with malignant disease. Bone metastasis (BM) pain management is one of the greatest challenges for oncologists, due not only to safety issues, but also to the significant impairment of patients' quality of life and performance status.
Objectives: To provide an overview of the epidemiology, clinicopathological features and treatment approaches of painful BM in patients followed-up at the pain treatment center (PTC) of Tunisia.
Methods: We performed a retrospective review of the medical records of all patients with BM, seen at the PTC of Tunisia in 2019. The information collected included patient demographics, clinicopathological features and treatment approaches of the BM.
Results: A total of 117 patients, with male to female ratio of 2.5 and a mean age of 61,2± 12.5 years [22-93], were included. Primary cancers were mainly lung cancer (40%), breast cancer (13,7%), prostate cancer (11,1%), malignant hemopathies (5%) and kidney cancer (3,5%). Mean cancer duration was 10.5 months [0-84]. Mean duration from the diagnosis of cancer to the diagnosis of BM was 4.2± 1.7 months [0-11].The most common BM sites were the spine (83.6%), the pelvis (28.5%) and the ribs (22.4%). BM was painful in 97% of cases. The mean number of consultations at the PTC was 5.5±2.8 [1-18].Malignant bone pain was nociceptive in 73.3% of cases, neuropathic in 9.5% and mixed (both nociceptive and neuropathic) in 33%. Mean visual analogue scale (VAS) pain was 8.7±1,5 [2-10]. Most of the patients (84.5%) were treated by opioid analgesics which was morphine in 98% of cases. The route of administration of morphine was the oral in 85.3% of cases with a median dose of 60mg/j [10-240]. Laxatives and antiemetic therapy, in prevention of side effects of morphine, were prescribed in respectivly 87% and 28% of cases. The transdermal fentanyl patch was prescribed for three hepatically impaired patients. Only 15.5% of patients had a good response to pain killers palier II (Tramadol) and did not necessitate to switch to morphin. Mean dose of Tramadol was 178±75.1 mg [75-300]. Pregabalin was indicated in 25% of cases with a mean dose of 227.5± 127.7mg [150-600].Tricyclic antidepressants were prescribed for 9.5% of the patients and the mean dose was 16 ±10 mg [10-40]. Corticoisteroids were used in almost two-third of cases with a mean daily dose of 1mg/kg/j [0,5-1.5]. However, in 14% of cases, non-steroidal anti-inflammatory drugs were prescribed instead of corticosteroids. Bisphosphonates were used in 15% of cases. Antalgic radiotherapy was indicated in one-third of cases. By a median follow-up of 3 months [0-24], mean VAS pain was 3.7±1.7 [1-9].
Conclusion: Currently, the treatment of painful BM remains palliative at best with systemic therapy as well as local treatments especially when BMs become symptomatic or complicated. Consequently, a multidisciplinary approach to BM is essential, to ensure a proper integration of local and systemic therapies

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AB1362 LOCATION AND NUMBER OF SARCOIDOSIS GRANULOMA, A POSSIBLE DIAGNOSTIC ARGUMENT?

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Background: Sarcoidosis is a non-necrotizing granulomatous disease which diagnosis is often challenging and requires elimination of other causes of granulomatous lesions. Location and number of granulomatous lesions in patients are not yet established as arguments in diagnosing this disease.
Objectives: We therefor conducted a study aiming to compare locations and number of granulomas between patients with sarcoidosis and patients with other granulomatous diseases (OGD).
Methods: Cross sectional study in which were included patients in whom non-necrotizing granulomatous lesions have been identified via biopsy over a period of 11 years (2010 to 2021) then were stratified into two groups: sarcoidosis group and OGD group. Categorical variables were compared with the $\chi 2$ –test or Fisher's test. Comparisons of the differences of continuous variables were performed by the Mann–Whitney U test or Student's t-test. Pearson correlation ratio was used for linear correlation analysis.
Results: 30 patients were included in the sarcoidosis group and 32 in the OGD group. Aetiologies in the OGD group were: 10 tuberculosis cases, 5 lymphoma cases, 4 Primary biliary cholangitis cases, 1 Castleman's disease and 12 idiopathic granulomas.

Mean age was respectively in both groups 51+/-13 versus 57+/-17 years old (p=0.128), sex ratio (F/M) was 29/1 versus 27/5 (p=0.197). Associated signs were distributed in both groups as followed: 11(37%) versus 5(16%) general signs (p=0.085), 15(50%) versus 20(63%) lymphadenopathy (p=0.442), 4(13%) versus 6(19%) inflammatory arthralgias (p=0.733), 13(43%) versus 2(6%) cutaneous lesions (p=0.001), 4 versus no ocular manifestations (p=0.049), 20 (66%) versus 3(9%) pulmonary manifestations (p<0.001), 5 (17%) versus 10 (31%) abdominal manifestations (p=0.239). Cutaneous, salivary gland and ENT granulomas were significantly more frequent in patients with sarcoidosis with respectively 11(37%) versus 1 (3%) (12.3 risk ratio 95%CI 10.4 to 14.4)(p=0.001), 8 (27%) versus 0% (p=0.002), 8(27%) versus 2(6%) (4.5 risk ratio 95% CI 3.1 to 5.9) (p=0.025). Lymph node, hepatic and pulmonary granulomas prevalence was not significantly higher in sarcoidosis patients, 17 (57%) versus 24 (75%) (p=0.180), 2 (7%) versus 5 (16%)(p=0.427), 3(10%) versus 0%(p=0.308). Mean number of granulomas found in one patient was significantly higher in sarcoidosis patients with 1.7 (95% CI 1.5 to 2) versus 1.1 (95%CI 1 to 1.2) (p=0.001). There was also a significant correlation between the number of granulomas in one patient and the angiotensin converting enzyme titres (r=0.566, 95% CI 0.360 to 0.771); (p=004).
Conclusion: This study shows that sarcoidosis patients have more often granulomas in the skin, salivary gland and ENT regions, and that the number of granulomas is on average superior in sarcoidosis than in OGD, these findings could be considered when establishing future diagnostic algorithms, as taking into account these elements could ease this diagnostic challenge in clinical practice.
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AB1363 IMAGE PATTERN ANALYSIS IN FLUORESCENCE OPTICAL IMAGING FOR DIFFERENTIAL DIAGNOSIS IN RHEUMATIC JOINT DISEASES

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Background: As outlined in previous studies, different rheumatic joint diseases present specific characteristic patterns and features in fluorescence optical imaging (FOI) (1-4).
Objectives: We tested different features in FOI for their ability to differentiate various rheumatic joint diseases such as rheumatoid arthritis (RA), osteoarthritis (OA) and psoriatic arthritis (PsA) with the aim to identify clear FOI criteria for the diseases.
Methods: FOI images from patients with RA, OA, PsA and healthy volunteers were evaluated by two readers blinded for diagnosis and calibrated against each other, using the prima vista mode (PVM) and the 5-phase model. For the latter, the overall time course of FOI in each hand was divided into 5 phases with a computational algorithm. Phases 1 and 2 describe the inflow (start to 15% and 15%-90% on rising edge), phase 3 is the peak phase and phases 4 and 5 comprise the outflow (90%-36.8% and 36.8% to end on falling edge). Twenty-six different features were defined by an atlas, for example the streaky pattern feature (T) as a signal enhancement around the PIP area that appears streaky, whereby the stripes are orthogonal to the finger axis (Figure 1a). The cloudy pattern (W) is visible during the inflow on the back of the hand (Figure 1b). The enthesis feature (E) depicts a V shaped and filled pattern between nail and DIP (Figure 1c). The feature frequency in each patient and phase (PVM, 5-phase) was counted and statistically analysed.

Figure 1. Examples for FOI patterns and features: a) (T) Streaky pattern in PVM image (OA); b) (W) Cloudy pattern on the back of the hand in phase 1 (PsA); c) (E) Enthesis pattern in phase 3.

Results: In total, 128 patients (RA (age mean 54.2; SD 10.6; median 52.4), OA (58.0; 14.3; 60.1), and PsA (47.9; 12.7; 46.8)) and healthy volunteers (32 in each group) were included in the feature reading. In our analysis, OA can be differentiated from RA on the basis of the feature T. Feature T is found in phase 3 (χ^2: 4.61; diagnostic odds ratio (DOR): 7.49; sensitivity (TPR) 0.11; specificity (TNR): 0.98; positive predictive value (PPV): 0.87; negative predictive value (NPV): 0.52), phase 5 (χ^2: 18.5; DOR: 5.60; TPR 0.55; TNR: 0.82; PPV: 0.76; NPV: 0.64 and PVM (28.3; 12.1; 52%; 92% 87%; 65%). By means of the feature E, a distinction between RA and PsA is only limited possible (χ^2: 9.58; DOR: 3.65; TPR 0.40; TNR: 0.84; PPV: 0.71; NPV: 0.59). But PsA can well be distinguished from RA by the appearance of pattern W in phase 1 (χ^2: 7.68; DOR: 6.92; TPR 0.19; TNR: 0.97; PPV: 0.86; NPV: 0.54). Other significant features yield high specificity (70%-98%) while having low sensitivity (12%-52%).
Conclusion: This work demonstrates that FOI feature analysis has the potential for differential diagnosis with FOI, which could optimize the (early) diagnostic process of rheumatic joint diseases. A majority of features yield high specificity, but only low sensitivity. The combination of different features using artificial intelligence might lead to improved diagnostic accuracy.
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AB1364 IMAGING DIAGNOSIS OF BRUCELLAR SPONDYLODISCITIS

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Background: Spondylodiscitis is the most common location in the musculoskeletal involvement of brucellosis.
Objectives: The aim of this study is to describe magnetic resonance imaging (MRI) and computed tomography scan (CT) results in patients with brucellar spondylodiscitis.
Methods: A retrospective study over a period of 15 years, including 18 patients diagnosed with brucellar spondylodiscitis and having benefited from a CT scan and/or an MRI of the spine.
Results: Eighteen patients were included. In all cases spinal pain was reported, associated with radiculalgia in 8 patients. Low back pain was the most common symptom, present in 17 cases, associated with back pain in 3 cases including one case with neck pain. Isolated neck pain was noted in one patient. Neurologic examination was normal in all cases. Standard Radiographs showed disc narrowing in 14 cases, erosions in 9 cases and hazy changes of the vertebral end plate in 2 cases. A CT scan was performed in 11 cases. It showed disc narrowing in 6 cases, erosions in 3 cases and endplate destructions in 5 cases. Abscesses were found in 4 patients. Complementary MRI was performed in three of the patients who had already undergone CT. The MRI results were consistent with those of the CT scan, except for one patient in whom it revealed spondylodiscitis while the CT scan revealed degenerative lesions. Eleven patients underwent MRI in total. It showed unifocal and multifocal spondylodiscitis in 5 and 6 cases respectively, epiduritis in 6 cases, spinal cord compression in 2 cases and abscesses in 4 cases.
Conclusion: Our study showed that CT and spinal MRI allow early diagnosis of spondylodiscitis. They help to identify asymptomatic lesions and neurological complications.
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AB1365 PROPOSAL FOR A STANDARDIZED ULTRASOUND SCANNING PROTOCOL OF THE NAIL PLATE.

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Background: Ultrasonography of the nails with high frequency linear transducers can properly perform morphological images, achieving highly descriptive power but the lack of standardization may hesitate in lack of reproducibility and scarce usefulness.

Objectives: The aim of this study was to provide a detailed scan protocol of nail plate, including comparison of scan planes and probe positioning.
Methods: Transversal and longitudinal ultrasound scans were performed on each fingernail of both hands in healthy subjects. Nail plate thickness and Power Doppler of the nail bed were recorded. All the images were acquired using Canon Aplio i800 with a linear transducer of 22 MHz (i22LHB). Two different operators performed evaluation of thickness at distal, middle and proximal portion of nail in longitudinal view and at 0°, -45° and +45° for transverse view (Figure 1). ANOVA for repeated measures was used to determine differences between nail of the different digits.

Figure 1. Longitudinal and transverse view of the nail. In yellow the position and angles of the caliper used for acquiring the measures

Results: The study sample was composed of 27 healthy subjects between 25- and 40- year old with no rheumatological or dermatological nail issues. A total of 270 nails were scanned; none of them was excluded due to comorbidity, trauma or other conditions which can interfere in the evaluation. A decrease in nail thickness was observed from first to fifth digit, regardless the hand (dominant or not), that resulted significant for the ANOVA. No differences were found regarding the thickness in the different segments of nail plate and this occurred both for longitudinal and transverse scans.
Conclusion: We demonstrated the absence of a statistically significant difference between thickness at proximal, middle and distal portion of the nail in longitudinal view or at any different angle in transverse view, concluding the fastest and easiest way to measure the nail plate thickness is in the longitudinal view at the middle segment, avoiding potential issues in positioning the probe in the transverse view or in positioning the caliper at proximal or distal segment in longitudinal view. All the nails should be scanned per protocol, since the thickness is variable and the fifth may be the most interesting in order to consider its highest variance.
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Table 1. ANOVA for repeated measures of the nail plate thickness. A trend in decreasing P value is clearly visible from first to fifth. P considered statistically significant when ≤ 0.05

LONGITUDINAL					TRANSVERSE				
PROXIMAL					**-45°**				
Row-mean	1	2	3	4	Row-mean	1	2	3	4
2	1.000				2	0.731			
3	0.765	1.000			3	0.264	1.000		
4	0.028	0.888	1.000		4	0.000	0.056	0.187	
5	0.000	0.001	0.003	0.158	5	0.000	0.005	0.023	1.000
MIDDLE					**0°**				
Row-mean	1	2	3	4	Row-mean	1	2	3	4
2	1.000				2	0.719			
3	1.000	1.000			3	0.056	1.000		
4	0.070	1.000	1.000		4	0.000	0.158	1.000	
5	0.000	0.001	0.002	0.095	5	0.000	0.025	0.389	1.000
DISTAL					**+45°**				
Row-mean	1	2	3	4	Row-mean	1	2	3	4
2	1.000				2	1.000			
3	0.854	1.000			3	0.765	1.000		
4	0.006	0.093	0.754		4	0.050	0.583	1.000	
5	0.000	0.000	0.000	0.114	5	0.000	0.001	0.016	0.323

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AB1366

ULTRASOUND ASSESSMENT OF THE EFFECTIVENESS OF TOCILIZUMAB IN GIANT CELL ARTERITIS. STUDY OF 26 PATIENTS FROM CLINICAL PRACTICE

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Background: Large-vessel vasculitis are characterized by the wall inflammation of the involved vessels, which can be detected by imaging tools **(1-3)**. Ultrasound (US) is one of the most commonly used tools for the diagnosis of giant cell arteritis (GCA), especially in patients with a cranial phenotype. Tocilizumab (TCZ) has shown efficacy in large-vessel vasculitis (LVV) including GCA **(4,5)**. However, the improvement objectified by imaging techniques such as US after TCZ therapy is poorly documented.
Objectives: To assess the effectiveness of TCZ improving the wall vessel inflammation by US.
Methods: Observational, multicenter study of 26 GCA patients treated with TCZ. GCA was diagnosed according to: **a)** ACR criteria, and/or **b)** biopsy of temporal artery, and/or **c)** presence of signs of vessel wall inflammation by US, defined by the presence of halo sign. In all the cases a baseline US and in the follow-up was mandatory. Patients were divided into two subgroups: **a)** with, and **b)** without signs of improvement (partial or total) in the follow-up US.
Results: We studied 26 patients (19 women/7 men; mean age, 76.3±9.7 years). Main clinical features of GCA with and without US improvement are shown in Table 1. We found no significant differences in any of the variables studied between the two groups.

Table 1. Main features of 27 GCA patients treated with tocilizumab followed by Ultrasound (US).

	With US improvement (n=21)	Without US improvement (n=5)	p
Baseline characteristics at TCZ onset			
General characteristics			
Age(years), mean±SD	77.3±8.9	72.2±12.9	0.270
Sex, female/male (% female)	17/4 (80,95)	2/3 (40)	0.101
Time from GCA diagnosis to TCZ onset (months), median [IQR]	6 [3-9]	3 [1-6]	0.452
Systemic manifestations, n (%)			
Fever, n (%)	1/21 (4.76)	1/5 (20)	0.354
Constitutional syndrome, n (%)	10/21 (47.62)	2/5 (40)	0.999
PmR, n (%)	11/21 (52.38)	1/5 (20)	0.330
Ischaemic manifestations, n (%)			
Visual involvement, n (%)	1/21 (4.76)	1/5 (20)	0.354
Headache, n (%)	15/21 (71.43)	5/5 (100)	0.298
Jaw claudication, n (%)	4/15 (26.67)	¼ (25)	0.999
Laboratory data			
ESR, mm 1st hour, median [IQR]	33 [22-49]	55 [54-80]	0.216
CRP, mg/dL, median [IQR]	1.5 [0.7-6.7]	3.8 [1-4.2]	0.948
Prednisone dose, mg/day, median [IQR]	13.7 [10-30]	30 [12.5-30]	0.505
Time from TCZ onset and follow-up US (months)	3.9±3.6	3.1±2.1	0.456

After TCZ onset, 21 of 26 patients (80.7%) showed US signs of improvement (12 complete, 9 partial). In 4 out of 5 patients in whom there was no improvement in US findings, clinical improvement was observed at first month after starting TCZ.
Conclusion: TCZ seems to be effective controlling GCA including vascular involvement detected by US. This improvement can be seen by follow-up US, especially when performed at least 3 months after TCZ onset.
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AB1367

PET ASSESSMENT OF THE EFFECTIVENESS OF TOCILIZUMAB IN GIANT CELL ARTERITIS. STUDY OF 101 PATIENTS FROM CLINICAL PRACTICE

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Background: Positron emission tomography (PET) is one of the tools available for the diagnosis of extracranial large-vessel vasculitis **(1-5)**. Tocilizumab (TCZ) has shown efficacy in large-vessel vasculitis (LVV) including GCA. However, the improvement objectified by imaging techniques after TCZ therapy in extracranial GCA patients is controversial.

Objectives: To assess the effectiveness of TCZ improving the wall vessel inflammation by PET in GCA patients with large-vessel involvement.

Methods: Observational, multicenter study of 101 GCA patients treated with TCZ. GCA was diagnosed according to: **a)** ACR criteria, and/or **b)** biopsy of temporal artery, and/or **c)** presence of signs of vessel wall inflammation by PET, defined by the presence of vascular wall uptake of Fluorodeoxyglucose (FDG). Patients were divided into two subgroups: **a)** with, and **b)** without signs of improvement (partial or total) in the follow-up PET.

Results: We studied 101 patients (74 women/27 men; mean age 69.7±9.3 years). Main clinical features of GCA with and without PET improvement are shown in Table 1. The group of patients which experienced PET improvement was older and was receiving higher doses of corticosteroids at TCZ onset.

Table 1. Main features of 101 GCA patients treated with tocilizumab and with presence of signs of vessel wall inflammation by PET.

	With PET improvement (n=88)	Without PET improvement (n=13)	p
Baseline characteristics at TCZ onset			
General characteristics			
Age(years), mean±SD	70.6±9.1	63.8±9.2	**0.014**
Sex, female/male (% female)	67/21(76)	7/6 (54)	0.103
Time from GCA diagnosis to TCZ onset (months), median [IQR]	11 [4-24.2]	4 [2-6]	0.102
Systemic manifestations, n (%)			
Fever, n (%)	5 (6)	2 (15)	0.225
Constitutional syndrome, n (%)	36 (41)	4 (31)	0.466
PmR, n (%)	53 (60)	9 (10)	0.761
Ischaemic manifestations, n (%)			
Visual involvement, n (%)	2 (2)	1 (1)	0.342
Headache, n (%)	30 (34)	3 (23)	0.538
Jaw claudication, n (%)	8 (9)	0 (0)	0.592
Laboratory data			
ESR, mm 1st hour, median [IQR]	38.0 ± 26.2	13.54 ± 9.9	**0.001**
CRP, mg/dL, median [IQR]	1.5 [0.7-2.4]	1 [0.5-1.7]	0.179
Prednisone dose, mg/day, median [IQR]	40.3 ± 19.4	21.9 ± 12.7	**0.001**
Time from TCZ onset and follow-up PET (months)	13.1±8.0	10.1±5.3	0.446

Conclusion: TCZ seems to be effective controlling GCA including vascular involvement detected by PET. However, the improvement observed by PET is most often partial, and rarely complete.

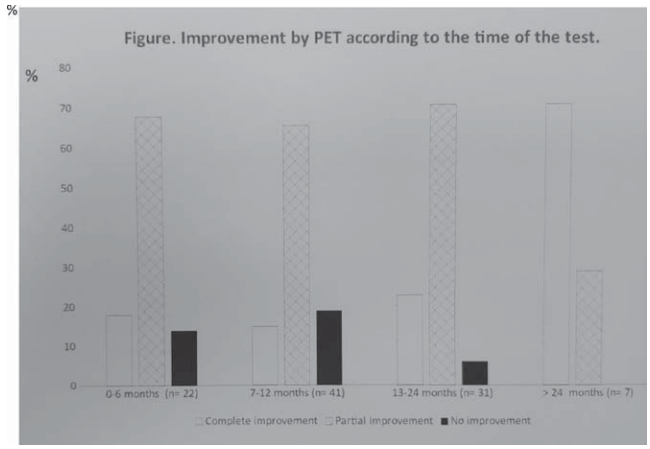

Figure 1. Improvement by PET according to the time of the test.

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AB1368 ULTRASONOGRAPHIC EVALUATION OF THE KNEE AND MUSCLE ARCHITECTURE IN OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: Involvement of lower extremity joints in both rheumatoid arthritis (RA) and osteoarthritis (OA) is an important cause of declined functional status. Deterioration of skeletal muscle performance further contributes to disability. Quadriceps muscle plays an important role in most daily activities. Measuring thickness and pennation angle of quadriceps compartments can provide knowledge regarding quadriceps condition.

Objectives: Aim is to investigate structural and inflammatory changes in knee joint and architecture of quadriceps muscle in RA, knee OA patients and a group of healthy subjects.

Methods: Twenty RA patients and 20 knee OA patients with radiographic disease meeting Kellgren-Lawrence grade 2 and above were consecutively recruited, in absence of exclusion criteria. 20 healthy volunteers with similar demographics were recruited as control group. Knee symptoms and disability were evaluated by Lequesne Knee Index (LKI). Disease activity was evaluated by DAS28-CRP in RA patients. Quadriceps muscle was evaluated by ultrasonographic measurements of muscle thickness, subcutaneous fat tissue thickness and pennation angle of vastus muscles. Suprapatellar, lateral and medial compartments of knee joint were examined for effusion, synovial hypertrophy, power Doppler (PD) activity and degenerative changes.

Results: Demographics and clinical features of subjects and results of ultrasonographic evaluation are presented in Table 1. LKI scores were significantly higher in OA patients when compared to RA patients (p=0.004). Rate of degenerative changes was increased in RA and OA groups in comparison to controls (p=0.013). None of the subjects had PD activity. No differences were observed in thickness of rectus femoris, vastus muscles and subcutaneous fat between groups. Vastus medialis and intermedius pennation angles were reduced in OA and RA groups when compared to controls, but reached statistical significance only in vastus intermedius (3.56 ± 6.37 vs 4.89 ± 7.14 vs 7.29 ± 4.93, p=0.038).

Table 1. Demographics, clinical features and ultrasonographic findings of subjects

	OA (n=20)	RA (n=20)	Control (n=20)	*p*
Age, years¶	58.44 ± 6.68	54.67 ± 7.15	55.11 ± 5.89	0.178
Gender, female$^{\mu}$	17 (85)	15 (75)	16 (80)	0.732
BMI¶	30.05 ± 3.88	28.29 ± 4.78	28.27 ± 3.34	0.343
Duration of diagnosis, months¶	11.95 ± 17.15	14.80 ± 8.50		**0.023**
LKI¶	9.37 ± 2.65	6.95 ± 3.38		**0.004**
DAS28-CRP¶		2.59 ± 1.10		
Presence of effusion $^{\mu}$	9 (45)	9 (45)	4 (20)	0.166
Presence of SH $^{\mu}$	9 (45)	11 (55)	8 (40)	0.626
Presence of degeneration $^{\mu}$	16 (80)	13 (65)	7 (35)	**0.013**
Muscle thickness, mm¶				
VM	14.09 ± 4.17	15.38 ± 5.15	14.57 ± 3.41	0.243
VL	17.17 ± 3.53	16.96 ± 4.98	16.66 ± 3.18	0.985
VI	10.54 ± 2.65	10.49 ± 3.32	10.67 ± 1.83	0.926
RF	13.01 ± 3.92	13.74 ± 3.78	13.63 ± 3.49	0.879
SFT thickness, mm¶	12.59 ± 5.79	13.81 ± 7.10	12.53 ± 5.20	0.969
Pennation angle, degree ¶				
VM	5.50 ± 7.01	6.94 ± 8.29	9.05 ± 5.10	0.244
VL	13.61 ± 5.15	13.44 ± 3.40	13.29 ± 3.25	0.703
VI	3.56 ± 6.37	4.89 ± 7.14	7.29 ± 4.93	**0.038**

¶: mean ± SD, μ: number (%),LKI: Lequesne Knee Index, KL: Kellgren – Lawrence grade, SH: synovial hypertrophy, VM: vastus medialis, VL: vastus lateralis, VI: vastus intermedius, RF: rectus femoris, SFT: subcutaneous fat tissue

Conclusion: In our study ultrasound evaluation findings of knee joint and quadriceps muscle were similar between knee OA and RA patients.VM and VI pennation were reduced when compared to healthy subjects in both groups. These findings may indicate a similar degree of functional impairment in OA and RA due to knee joint involvement.

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AB1369 DISCO-VERTEBRAL BIOPSY VERSUS INDIRECT DIAGNOSTIC TOOLS IN BRUCELLAR SPONDYLODISCITIS

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Background: The diagnosis of brucellar spondylodiscitis can be made by serological examinations or by isolating the germ on disco-vertebral biopsy (DVB).

Objectives: We aimed to study the interest of DVB and other less invasive diagnostic tools in brucellar spondylodiscitis.

Methods: A retrospective study over a period of 15 years, including 18 patients diagnosed with brucellar spondylodiscitis.

Results: Eighteen cases were collected (13 men and 5 woman).

Nine patients had a DVB. In all cases, microbiological study did not reveal the causative agent (Brucella). A case of superinfection with Staphylococus Xylosus was noted. Histopathological examination was performed in eight patients. It showed osteitis and chronic spondylodiscitis lesions in 4 cases, a non-specific inflammatory infiltrate in 3 cases, and a progressive infectious spondylitis in one case. Wright's serodiagnosis and the rose bengal test were positive in 7 out of 8 cases performed. As for the diagnosis by indirect immunofluorescence made in 6 cases, it was positive in 5 cases. For the other nine cases who did not undergo DVB, Wright's serodiagnosis and rose bengal test were positive in 9 and 6 patients respectively, indirect immunofluorescence made in 5 patients was positive in 4 cases.

Conclusion: Serological examinations in brucellar spondylodiscitis seem more profitable and less invasive than DVB. Other studies with a larger population seem to be necessary to compare the different methods and complete this preliminary study.

Disclosure of Interests: None declared

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AB1370

MICROVASCULAR CAPILLAROSCOPIC ABNORMALITIES AND AUTOANTIBODY OCCURRENCE IN SARCOIDOSIS PATIENTS.

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Background: Sarcoidosis (S) is a granulomatous disease with multi-organ involvement displaying a mixed immune-mediated pathophysiology. Raynaud's phenomenon (RP) has been occasionally reported in S patients [1] and serum positivity for autoantibodies has been detected in S patients but their significance is debated [2].
Objectives: We described nailfold videocapillaroscopy (NVC) findings and estimated the prevalence of serum anti-nuclear (ANA) and extractable nuclear antigen autoantibodies (ENA-Abs) in S patients, comparing them with age- and sex- matched healthy controls (HCs) and patients with primary Raynaud's phenomenon (PRP). Secondarily, we analysed potential correlations between NVC findings with the occurrence of autoantibodies, immunomodulatory treatment, laboratory parameters, variables of pulmonary function and whole-body imaging.
Methods: Twenty-seven (27) S patients, classified according to WASOG criteria[3], were assessed through NVC examination, laboratory parameters (including serum concentrations of angiotensin-converting enzyme [ACE], C-reactive protein [CRP], calcium, phosphorus, albumin, 25-hydroxyvitamin D, parathormone, ANA and ENA), pulmonary function tests (PFTs), chest-X ray and positron emission tomography/computerized tomography (PET/CT). Among NVC parameters, we analysed capillary dilations, giant capillaries, haemorrhages, nonspecific abnormalities, and capillary absolute number for mm [4]. Pulmonary involvement was classified by X-ray Scadding staging system (SSS) scoring S patients in 4 grades [5]. From PET data, the maximum standard uptake value (SUVmax) was quantified as a variable of tissue 18-fluorodeoxyglucose hyper-uptake: consequently, S patients were defined PET-positive when SUV value ≥ 2.5. NVC parameters and ANA/ENA dosage were recorded also in 30 PRPs and 30 HCs.
Results: We excluded, among the cohort of S patient, one participant having a systemic sclerosis in overlap with S. The remaining 26 S patients (mean age 56.5 ± 12.5 years, 53.8 % of females, disease duration 28.4 ± 55.1 months, 27% glucocorticoid-naïve) showed a significant higher rate of dilations and nonspecific abnormalities and a lower mean capillary absolute number than PRPs and HCs ($p < 0.01$ for all comparisons). (Figure 1) The prevalence of ANA positivity was significantly higher in S patients compared with PRPs and HCs ($p < 0.02$ for both). Among the whole cohort of patients only one S patient displayed a positive ENA-Ab (Ro52). In the analysis of S patients' subgroup, a significant negative correlation was detected between serum ACE levels with the presence of capillary dilations (rho = -0.45, p = 0.04), between CRP and mean capillary absolute number (rho = -0.49, p = 0.02) and a positive correlation was also detected between the mean capillary absolute number and the forced vital capacity percentage (FVC%) (rho = 0.40, p = 0.04).

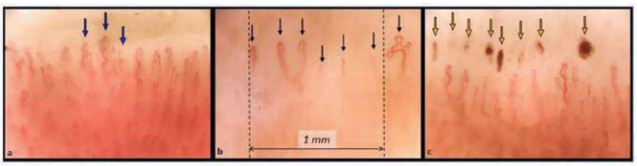

Figure 1 Examples of 3 nailfold videocapillaroscopy images recorded among 3 different sarcoidosis patients. (Magnification 200x).

a: blue arrows indicate the presence of "bushy" capillaries, sign of neoangiogenesis.
b: black arrows indicate the capillaries of the first row. The capillary number for linear mm is slightly reduced (6 capillaries/mm)
c: yellow arrows show the presence of hemosiderin deposits due to microhaemorrhages.

Conclusion: Our findings suggest a microvascular involvement in sarcoidosis whose investigation by NVC could be useful for the detection of an overlapping connective tissue disease and for the monitoring of the phenotypes of S patients displaying RP. The positivity for autoantibodies in S patients is in line with literature data suggesting, at least partially, autoimmune features of the disease or the production of autoantibodies reactive to tissue damage. The correlations between NVC findings with ACE levels and lung function variables generate hypotheses of a potential partial vascular impairment in sarcoidosis disease activity and lung involvement.

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AB1371

USE OF ULTRASOUND TO DIAGNOSE INTERSTITIAL LUNG DISEASE IN RHEUMATIC DISEASES ON RUSSIAN COHORTS OF PATIENTS.

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Background: Interstitial lung disease (ILD) is one of the most relevant extra-articular manifestations of rheumatic diseases resulting in a substantial increase in morbidity and mortality. High-resolution computed tomography (HRCT), which is the current gold standard for diagnosis and evolutionary control, is problematic owing to ionizing radiation, cost, and accessibility. In the last decade, the use of lung ultrasound (LUS) in clinical medicine has increased. LUS is an accurate tool for the diagnosis of pneumonia, pneumothorax, acute pulmonary edema, and pleural effusion. LUS may also be useful in detection of ILD by the evaluation of B-lines, the sonographic hallmark of the interstitial syndrome.
Objectives: To compare semi-quantitative scores of B lines in patients with rheumatic disease with different intensity of lung fibrosis.
Methods: 50 pts with ILD of rheumatic disease such as: vasculitis n=11 (mean age 40.7± 9.1, fem 5); dermatomyositis (DM), anti-synthetase syndrome (ASS), polymyositis (PM) n=20, (mean age 48.7± 11.9, fem 13); rheumatoid arthritis (RA) n=9 (mean age 56.5± 6.3, fem 7); Sjogren's syndrome (SSj) n=9 (mean age 59.6± 12.3, fem 8). To determine the intensity of fibrosis of ILD we used a limited/extensive classification for disease extent, integrating HRCT observation. According this scheme pts were divided into 2 groups: group 1 included 33 pts had "limited" lung disease (lung lesions less than 20%) and the group 2 included 17 pts had "extensive" lung disease (lung lesions greater than 20%). LUS examination protocol that include the anterior, lateral, and/or posterior thorax have been suggested The B-lines score denoting the extension of ILD was calculated by summing the number of B-lines on a total of 58 scanning sites. In each patient ULC score was obtained by summing the number of comets detected as previously recommended. The data were collected in protocols for statistical testing. Other data collected including biological results (high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR)).
Results: the mean score of B-lines in each groups were: vasculitis (n=11) 21,4 ±12,6; (DM, PM, ASS) (n=20) 41,3±20.8; RA (n=9) 56.5±6.3; SSj (n=9) 59 ± 11.8. The mean score of B-lines in groups pts with different intensity of fibrosis are presented in Table 1.

Table 1.

Groups	mean score of B-lines	Anterior chest Mean score of B-lines	Posterior chest Mean score of B-lines
Limited (n=33)	22±14	6.6 ±7.1 5 [1;10]	15.4±13.4
Extensive (n=17)	61.3±27.4	24.2±12.5	36.4±22.4
P	<0.001	<0.001	<0.001

The correlations in Table 1 may confirm the connection of B-lines score and extensity of ILD association with rheumatic disease. The mean score of ULCs determined in all 50 pts didn't correlate with dates of ESR (R = 0,188, p>0.05) and hsCRP (R= -0,07, p>0.05).
Conclusion: In Russian cohorts presence of LUS score is associates with more severe ILD. Echographic examination of the lung allows evaluating the severity of lung fibrosis and can be used as an additional simple and available method to assess the ILD of rheumatic disease, but we couldn't find correlation with hsCRP and ESR.

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AB1372

SPECIFICITY AND SENSITIVITY OF LUNG ULTRASOUND (LUS) IN RHEUMATIC DISEASES ON RUSSIAN COHORTS OF PATIENTS

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Background: Pulmonary disease is one of the most relevant with interstitial lung disease (ILD) being one of the most frequents forms of involvement with resultant worsening of morbidity and mortality in disorders such as systemic sclerosis (SSc), rheumatoid arthritis (RA), or inflammatory myopathies. High-resolution computed tomography (HRCT), which is the current gold standard for diagnosis and evolutionary control, is problematic owing to ionizing radiation, cost, and accessibility. In this context, lung ultrasound (LUS) is an attractive tool in a growing research and validation process.
Objectives: to assess specificity and sensitivity of LUS in rheumatic diseases on Russian cohorts of patients.
Methods: 110 pts with ILD of rheumatic disease such as: systemic sclerosis (n=60) (mean age 49.8±13.3, fem 57); vasculitis n=11 (mean age 40.7± 9.1, fem 5); dermatomyositis (DM), anti-synthetase syndrome (ASS), polymyositis (PM) n=20, (mean age 48.7± 11.9, fem 13); rheumatoid arthritis (RA) n=9 (mean age 56.5± 6.3, fem 7); Sjogren's syndrome (SSj) n=9 (mean age 59.6± 12.3, fem 8). Chest HRCT were evaluated. Control group (n=30) without rheumatic diseases and ILD (mean age 51.4± 15.4, fem 24); (chest X-ray (CXR) were evaluated). LUS examination protocol that include the anterior, lateral, and/or posterior thorax have been suggested. The B-lines score denoting the extension of ILD was calculated by summing the number of B-lines on a total of 58 scanning sites. In each patient ultrasound comets (ULC) score was obtained by summing the number of comets detected as previously recommended. The data were collected in protocols for statistical testing. The diagnostic accuracy LUS is expressed as sensitivity, specificity. ROC (receiver operating characteristic) curves and AUCs (areas under curve) were used of analyze the accuracy of B-lines in recognizing the presence of ILD on HRCT.
Results: the analysis included all the 110 patients enrolled in the study. ROC cure analysis the ULC score of anterior chest area was (AUC =0.876; 95% CI 0.82-0.96; p<0.0001); ROC cure analysis the ULC score of posterior chest area was (AUC =0.908; 95% CI 0.858-0.958; p<0.0001); ROC cure analysis for the total ULC score was (AUC =0.932; 95% CI 0.892-0.972; p<0.0001).
Accuracy of echographic signs (B-line) in the different chest areas in the detection of interstitial lung disease (Table 1).

Table 1.

	Total B-line Score (TBLS)	Sensitivity	Specificity
Anterior chest area	>5	61.8%	96%
	>10	48.2%	100%
Posterior chest area	>5	85.5%	83%
	>10	73.6%	90%
All chest areas	>5	89.1%	70%
	>10	81.8%	87%

Using the TBLS to identify a positive LUS examination, sensitivity and specificity were different depending on the area investigation. The best results were in the posterior area and all chest areas.
Conclusion: our research documented the high diagnostic accuracy of LUS in the detection of ILD. Our findings support the use of LUS a sensitive tool for ILD detection, especially considering that it's an inexpensive and nonionizing technique.
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AB1373

RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS) AS AN ALTERNATIVE APPROACH TO BIOELECTRICAL IMPEDANCE ANALYSIS (BIA) FOR THE ASSESSMENT OF BODY COMPOSITION

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Background: The evaluation of human body composition is crucial for body weight management, especially in pathological conditions. Patients whose body weight greatly exceeds or remain below the reference range, need regular monitoring in order to personalise the nutritional treatment plan. To this end, bioelectrical impedance analysis (BIA) is a widely accepted tool, along with ultrasound techniques. Among emerging ultrasound-based technologies, Radiofrequency Echographic Multi Spectrometry (REMS) is a powerful approach that can be effectively used for body composition analysis.
Objectives: The present study aims to assess the accuracy of REMS in comparison to BIA for body composition assessment.
Methods: The cohort included 141 males and females aged between 60 and 80 years. All subjects underwent body mass measurement by REMS and BIA and both body fat percentage (BFP) and basal metabolic rate (BMR) parameters were assessed.
Results: The estimation of BFP measured with BIA resulted in 40.4% (interquartile range [IQR]: 35.5% to 45.2%), which value did not differ from 41.1% (IQR: 36.5% to 47.1%) obtained with REMS (p=0.6). The BMR determined by BIA was 1329.0 kcal/day (IQR: 1270.5 to 1423.5 kcal/day), which was in a similar range as the value of 1323.5 kcal/day (IQR: 1266.0 to 1420.0 kcal/day) assessed by REMS (p=0.7).
Conclusion: The present study demonstrated the excellent ability of REMS to accurately determine the body composition, resulting as an alternative approach to conventional BIA.
Disclosure of Interests: Paola Pisani: None declared, Alessandra Natale: None declared, Fiorella Anna Lombardi: None declared, Francesco Conversano Shareholder of: Francesco Conversano owns stocks of Echolight Spa, Ernesto Casciaro Shareholder of: Ernesto Casciaro owns stocks of Echolight Spa, Maurizio Muratore: None declared, Sergio Casciaro Shareholder of: Sergio Casciaro owns stocks of Echolight Spa
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AB1374

INTERSTITIAL LUNG DISEASE IN ASYMPTOMATIC PATIENTS AT THE ONSET OF INFLAMMATORY RHEUMATIC DISEASES

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Background: Interstitial lung disease (ILD) in inflammatory rheumatic diseases (IRD) is associated with increased mortality. Moreover, the lung is one of the most effected organs on IRD, but the clinical manifestations and severity can vary from subclinical abnormality to dyspnoea, respiratory failure, and death.
Objectives: The objective of the following study is to evaluate the frequency and type of ILD in asymptomatic patients at the onset of IRD.
Methods: The study represents a sub-analysis of a case-control study performed earlier, and includes 126 patients with a newly diagnosed IRD. The study cohort was divided in two groups (ILD group: n = 63 and control group: n = 63). The patients were evaluated for respiratory symptoms (cough, sputum, dyspnea) and sclerosiphonia. If possible, all patients received a lung function test and optional a chest x-ray. Patients with pathological findings in the screening tests (chest x-ray or reduced diffusing capacity for carbon monoxide (DLCO) < 80 %) maintained a high-resolution computer tomography (HR-CT) of the lung. The sub-analysis includes 20 patients with asymptomatic ILD at the onset of IRD.
Results: The asymptomatic ILD group consists out of 75 % female (n = 15) and 25 % male (n = 5) patients, with median age of 51.8 years (SD ± 17.1 years). In comparison, asymptomatic ILD patients are significant younger ($t(27.4) = 2.36$, $p = 0.026$), but the distribution of gender is similar. The mean values in different pulmonary function parameter are: FVC: 89.9% ± 19.3%; DLCO: 69.9% ± 21.2%; FEV1: 87.9% ± 21.4%; TLC: 91.0% ± 16.5% and TLCO: 82.1% ± 20.6% (FVC = Forced Vital Capacity, FEV1 = Forced Expiratory Volume in 1 second, TLC = Total Lung Capacity, TLCO = Transfer factor of the Lung for carbon monoxide). The observed CT patterns are pure ground glass opacities (GGO) (50%, n = 10), non-specific interstitial pneumonia (NSIP) (25%, n = 5), granuloma/proliferations (15%, n = 3), usual interstitial pneumonia (UIP) (5%, n = 1) and lymphocytic interstitial pneumonia (LIP) (5%, n = 1). The distribution of CT pattern was not significant to the symptomatic ILD group ($\chi^2(6) = 10.224$, $p = 0.116$).

Conclusion: The study highlighted that also clinical asymptomatic patients have ILD in IRD at the onset of the IRD. Frequently, a reduced DLCO is detectable in PFT as a sign of early lung involvement, so this represents a potential screening parameter. Moreover, asymptomatic patients are often younger than symptomatic patients. No significant difference was found in CT pattern, but further research is needed as the number of patients is quite small.

Disclosure of Interests: None declared
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AB1375 PERFORMANCE OF ULTRASOUND EXAMINATION OF INSERTIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES.

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Background: Enthesitis is one of extraintestinal manifestation of inflammatory bowel diseases (IBD). US examination appears to be a useful imaging technique, specifically in identifying enthesis involvement in patients with inflammatory bowel diseases [1].
Objectives: The aim of the study was to perform the individual anatomical site analysis for the evaluation of enthesopathies in patients with inflammatory bowel diseases (IBD).
Methods: A total of 95 patients with IBD were prospectively enrolled, 55 with ulcerative colitis (UC) and 40 with Crohn's disease (CD). All patients underwent ultrasound in B-mode and PD-mode, to assess the presence of entesitis. Thirty four different anatomical sites (insertions of short head of the biceps brachii, coracoacromial ligament (2 sites), infrascapularis, supraspinatus, infraspinatus, triceps brachii, flexor carpi ulnaris, flexor carpi radialis, extensor carpi ulnaris, extensors carpi radialis (2), gluteus minimum, gluteus medium, spina iliaca anterior superior/inferior, ischiadicus tuberositas, medial collateral ligament of knee (2 sites), lateral collateral ligament of knee (2 sites), patellar ligament (2 sites), pes anserinus, biceps femoris, semimembranosus, quadriceps femoris, tibialis anterior, tibialis posterior, peroneus brevis, achille, plantar fascia, medial epicondyle, lateral epicondyle) were evaluated bilaterally with total count 6460. If typical ultrasound features, such as entheseal hypoechogenicity, entheseal thickening, presence of vascularization, were present, acute lesions was diagnosed. Bone erosions and enthesophytes were considered as chronic lesions. Fisher's exact test was used to calculate differences.
Results: The number of positive enthesitis sites was 293/6460 (4.5%), 177 positive sites in patients with UC versus 116 in patients CD (4,7% vs 4,2%). Most often involved sites were pes anserinus and proximal insertion of medial collateral ligament of knee (Figure 1). The number of positive vascularizated enthesitis sites was 62/6460 (1.0%), 40 in patients with UC versus 22 in patients with CD (1,0% vs 0,8%). Proximal insertion of medial collateral ligament of knee was involved more often then other sites. At least one positive enthesitis was detected in 72 (76%) patients, 42 (76%) patients with UC versus 30 (75%) patients with CD. Vascularizated enthesitis were detected in 35 (37%) patients, 21 (38%) patients with UC versus 14 (35%) patients with CD. There are not statistically significant differences between UC and CD. Signs of chronic lesion were often detected. The number of sites with erosions was 313/6460 (4.8%), 178 (4,8%) in patients with UC versus 135 (5,0%) in patients CD. Enthesophytes of insertion were detected in 91/6460 (1, 4%) sites, 41 (1,1%) in patients with UC versus 40 (1,5%) in patients CD. Most often erosion was detected in insertion of medial collateral ligament of knee (both sites) and enthesophyte was found in insertion of quadriceps femoris. There are not statistically significant differences between UC and CD.
Conclusion: Enthesis abnormalities are often features detected by ultrasound in patients with IBD. Most often involved site is medial collateral ligament of knee. There are not significant differences between UC and CD patients.
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AB1376 RELATIONSHIP BETWEEN INTRANEURAL HYPERVASCULARIZATION OF THE MEDIAN NERVE IN POWER DOPPLER AND ELECTROMYOGRAPHIC SEVERITY STAGES IN THE DIAGNOSIS OF SEVERITY OF CARPAL TUNNEL SYNDROME (PRELIMINARY RESULTS)

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Background: Carpal tunnel syndrome (CTS) is the most common tunnel syndrome in the upper limbs. Ultrasound has been increasingly used in recent years in the diagnosis of positive and severe CTS. Although the diagnosis of severity is essentially based on the ENMG, several studies have shown that ultrasound data can also constitute criteria for the severity of CTS.
Objectives: The objective of our study is to evaluate the relationship between intraneural hypervascularization of the median nerve in power Doppler and the severity of CTS measured by ENMG.
Methods: This is a descriptive cross-sectional study of patients with clinically retained CTS. We excluded from the study operated patients and patients who received cortisone infiltration in the previous six months. All patients underwent ultrasound examination (B mode and Doppler mode) and electromyography one week apart. The severity stages of CTS have been defined according to the classification of Stevens (1997). The study is still ongoing.
Results: To date we have included 14 patients with typical signs of CTS. 25 wrists were examined sonographically and by ENMG. The mean age of the patients was 54± 10 years. Bilateral SCC was present in 11 patients. Of the 25 affected wrists: 10, 7 and 8 were classified by the ENMG as mild, moderate and severe SCC respectively. On ultrasound, positive Doppler was found in 5 wrists (20% of wrists studied): Doppler was present in 10% of wrists with mild-stage SCC, 14.3% of wrists with moderate-stage SCC and in 37.5% of wrists with severe SCC. But this difference was not statistically significant (p=0.31) probably related to the small size of our current sample (study still ongoing).
Conclusion: The preliminary results of our study suggest that intraneural hypervascularization of the median nerve in power Doppler could provide additional information on the severity of carpal tunnel syndrome. Results to be confirmed by the final results.
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AB1377 FULLY AUTOMATIC ASSESSMENT OF NAIL FOLD CAPILLAROSCOPY SOFTWARE – PILOT STUDY

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Background: The nail fold capillaroscopy is one of the basic techniques used in diagnosis and monitoring the course of connective tissue diseases, primarily a systemic sclerosis. However, the assessment of the capillary image is time-consuming and subjective, this makes it difficult for a detailed comparison of studies assessed by various physicians.
Objectives: The aim of this study was to validate an automated software for classification the nail fold capillaroscopy as normal or pathological and counting the numerous of vessels on a millimetre.
Methods: 100 correct and 100 pathological images were selected from the capillaroscopic image database. The original examination was performed with Dinolite MEDL4N Pro. The classic, manual evaluation of the capillaroscopy was performed twice. The imagines was classified as correct or pathological and mean number of capillaries per millimetre was calculated. The photos were then exported to the training program created for the study, the region of interest (ROI) and individual capillaries were marked. The

calculation of the number of vessels was made at a magnification of about 50x (ensuring the maximum quality of the image obtained during a classic examination). The neural network was trained using the fast.ai library (based on PyTorch). The ResNet-34 deep residual neural network was chosen, 10-fold cross-validation with validation and test set was performed, using Darknet-YoloV3 state of the art neural network in a GPU-optimized (P5000 GPU) environment. For calculation of 1mm capillaries, additional detection mechanism was designed, in order to automatically detect the scale of the image and transform it into proper pixel dimensions.

Results: The results obtained under neural network training have been referred to the results obtained as part of a manual photo assessment. For the image classification correct vs pathological test sensitivity 89.0% and specificity 86.9% was obtained. For validation (20% of images have been drawn as a validating group), 89.0% and 89.4% respectively were noticed. For the average number of capillaries in 1mm, an average of three regions have been estimated (the first region with 1mm from the left, the second with 1mm from the right and the third with 1mm in the middle). The estimated number of capillars in each region has been compared with ground truth data. The RMSE (Root Mean Squared Error) for the test set was 2.81 and the accuracy was 76.2%.

Conclusion: The use of fully automatic Nail Fold Capillaroscopy Software can be a fast and easy method of the correct and changed capillaroscopy pattern classification, the possibility of counting gives a repetitive result regardless of the physician evaluating the capillaroscopy pattern. In the further course of work on the software, it will be possible to distinguish megacapillary, branched vessels, avascularisation and other pathological features, which will allow full automatic image evaluation and easy follow-up of patients.

Disclosure of Interests: None declared

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AB1378 RELATION BETWEEN SHARP SCORE AND RADIOLOGICAL PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE OBSERVATION

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Objectives: to analyse rheumatoid arthritis (RA)-patients depending on their individual peak radiographic progression.

Methods: 61 RA pts, mean age 50,0 [38,0; 59,0] yrs, mean disease duration 7 [4; 20] months were treated with MTX and biologics according to the Treat-To-Target concept. After first year of therapy management was following real clinical practice rules until the termination of the study (7 years FUP, median 7,7 [7,4;8,6]). The general characteristics of the group are presented in the Table 1. Hands and feet ultrasound (US) with grayscale (GS), power Doppler (PD), according to the criteria of OMERACT, were analyzed before initiation of treatment and in 3, 6, 9, and 12 months after. Radiographs were obtained at baseline, at 12 months, 4 years, and 7 years, radiographic changes were assessed using Sharp/van der Heijde modified scoring method. Structural damage progression was evaluated by change in the Sharp van der Heijde score (ΔSHS) between baseline and 1,4 and 7 year. We determined the individual peak radiographic progression (Δ SHS scores/time) in RA- patients.

Table 1. General characteristics

Characteristic	At baseline	After 1 year follow-up	After 4 years follow-up	After 7 years follow-up
Median age, years	50,0 [38,0; 59,0]			
Disease duration, months	7 [4; 20]			
GS	6 [4; 9]			
PD	2 [1; 6]			
DAS 28	5,6 [4,8; 6,5]	2,88 [2,02; 3,93]	3,76 [2,94; 5,09]	4,03 [3,42; 4,74]
ESR, mm/h	35,0 [13,0; 50,0]	12,0 [8,0; 28,0]	22,0 [14,0; 36,0]	22,0 [14,0; 36,0]
CRP, mg/l	10,6 [3,8; 32,3]	2,9 [1,1; 7,1]	3,0 [1,2; 8,8]	3,0 [1,2; 8,8]
Rheumatoid Factor, positive results	53 (87%)			
Anti-CPA, positive results	52 (85%)			
Erosion score	0 [0; 3]	1 [0; 4]	2 [0; 6]	3 [1; 11]
Joint-space narrowing score	57,0 [31,0; 88,0]	62,0 [31,0; 92,0]	93,0 [77,0; 106,0]	98,0 [77,0; 110,0]
Modified total Sharp score	70,0 [31,0; 88,0]	71,0 [31,0; 93,0]	97,0 [79,0; 112,0]	102,0 [78,0; 117,0]

Results: RA progression by 1 years FUP was identified in 10% (6 p) of pts, 4 years FUP was identified in 36% (22 p) of pts, by 7 years FUP was identified in 69% (42 p) of pts. All pts divided into groups based increase in erosions according to radiography (Rg +) and without it (Rg-). In the group Rg + GS at baseline was significantly higher than in Rg- group (6 [5; 10] and 5 [1; 8], respectively, p=0.04). We analyzed relation between SHS (erosion score and total Sharp score) 7 years FUP, individual peak radiographic progression and Δ erosion score and total Sharp score in the observation periods: 0-1 years, 1-4 years, 4-7 years and 0-7 years. The following correlations were identified of erosion score 7 years FUP with Δ erosion score in all observation periods (r=0,33 p=0,016, r=0,54 p=0,000, r=0,68 p=0,000, r=0,84 p=0,000, respectively) and with individual peak radiographic progression in the observation periods 1-4 years, 4-7 years, 0-7 years (r=0,54 p=0,000, r=0,49 p=0,000, r=0,84 p=0,000, respectively). The following correlations were identified of total Sharp score 7 years FUP with Δ total Sharp score in the observation periods 4-7 years, 0-7 years (r=0,43 p=0,000, r=0,34 p=0,007, respectively) and with individual peak radiographic progression in the observation periods 4-7 years, 0-7 years (r=0,43 p=0,000, r=0,34 p=0,007, respectively).

Conclusion: These data show that the radiological progression increases over time at different rates.

Disclosure of Interests: None declared

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AB1379 PREDICTORS OF RADIOLOGICAL PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE OBSERVATION

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Objectives: to identify the prognostic role of ultrasound signs (US) in radiologic progression in RA patients

Methods: 61 RA pts, mean age 50,0 [38,0; 59,0] yrs, mean disease duration 7 [4; 20] months were treated with MTX and biologics according to the Treat-To-Target concept. After first year of therapy management was following real clinical practice rules until the termination of the study (7 years FUP, median 7,7 [7,4;8,6]). Among them 40 patients with early RA, mean age 51,0 [43,0; 60,0], disease duration 5 [3; 6,5] months. The general characteristics of the group are presented in the Table 1. Hands and feet ultrasound (US) with grayscale (GS), power Doppler (PD), and destructive changes (erosion), according to the criteria of OMERACT, were analyzed before initiation of treatment and in 3, 6, 9, and 12 months after. Radiographs were obtained at baseline, at 12 months, 4 years, and 7 years, radiographic changes were assessed using Sharp/van der Heijde modified scoring method. Radiographic progression was documented based on Sharp/Van der Heijde modified score changes during the follow-up.

Table 1. General characteristics

Characteristic	At baseline	After 7 years follow up
Median age, years	50,0 [38,0; 59,0]	
Disease duration, months	7 [4; 20]	
GS	6 [4; 9]	
PD	2 [1; 6]	
DAS 28	5,6 [4,8; 6,5]	4,03 [3,42; 4,74]
ESR, mm/h	35,0 [13,0; 50,0]	22,0 [14,0; 36,0]
CRP, mg/l	10,6 [3,8; 32,3]	3,0 [1,2; 8,8]
Rheumatoid Factor, positive results	53 (87%)	
Anti-CPA, positive results	52 (85%)	
Mean erosion score	0 [0; 3]	3 [1; 11]
Mean joint-space narrowing score	57,0 [31,0; 88,0]	98,0 [77,0; 110,0]
Modified total Sharp score	70,0 [31,0; 88,0]	102,0 [78,0; 117,0]

Results: 52 ACPA+ (85%) and 9 ACPA– (15%) patients presented among the 61 patients with RA. RA progression by 4 years FUP was identified in 36% (22 p) of pts, by 7 years FUP was identified in 69% (42 p) of pts. During the 7 years FUP 42 of 61 patients had radiographic progression: the count of erosion increased from 0 [0; 3] to 3 [1; 11]. At the same time, on the background of therapy during the first year, a decrease in ultrasound signs of inflammation was determined according to the GS and PD: from 6 [4; 9] to 4 [2; 6] p = 0.000 and from 2 [1; 6] to 0 [0; 2] p = 0.000, respectively, and increase in the number of joints with erosions (from 1 [0; 2] to 2 [0; 3], p = 0.000).

All pts divided into groups based increase in erosions according to radiography (Rg +) and without it (Rg-). In the group Rg + GS at baseline was significantly higher than in Rg- group (6 [5; 10] and 5 [1; 8], respectively, p=0.04). CRP at 3 months and at 6 months was significantly higher in RG+ group than in RG- group (4,15 [1,2; 8,7] and 1,2 [0; 3,5], respectively, p=0.03 and 2,35 [0,8; 10,1] and 0,4 [0; 4,3], respectively, p=0.025).

Conclusion: Thus, we obtained the first data on the important prognostic role of ultrasound in assessing the progression of early RA in a prospective seven-year follow-up.

Disclosure of Interests: None declared

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AB1380 ULTRASONOGRAPHIC CHANGES OF PLANTAR FASCIA IN PATIENTS WITH PLANTAR FASCIITIS DUE TO ACQUIRED FLAT FOOT

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Background: Plantar fasciitis is a chronic degenerative process of the plantar fascia enthesis. It manifests by pain, predisposition to prolonged course and treatment resistance. In many cases, plantar fasciitis develops in patients with acquired flat feet. Taken into consideration above mentioned, the study of the plantar fascia changes in patients with acquired flat feet by sonography is relevant.

Objectives: To investigate the quantitative and qualitative sonographic changes of the plantar fascia in the case of plantar fasciitis in patients with acquired flat foot.

Methods: 190 patients with plantar fasciitis on the basis of acquired flat feet (133 females and 57 males). The average age of patients was 48 ± 0.97 years (18-81years). Unilateral pathology was noted in 117 patients and bilateral – in 73 patients. The average body mass index was 27.68±0.3. The average duration of pain syndrome was 101 ± 6.0 days (7-390 days). The pain syndrome lasted up from 1 to 6 months – in 152 patients, and more than 6 months – in 38 patients. The control group included 15 healthy volunteers (30 feet). Clinical radiological, sonographic, and statistical methods were used.

Results: The main sonographic features were significant reduction in echogenicity, erased or missing fibrous pattern, fuzzy contour of the aponeurosis; and modified contour of the calcaneus; small focal hyperechogenicity points in enthesis were detected. Loci of vascularization were detected using power Doppler sonography. The average thickness of plantar fascia in the study group was 6,14±1,5 mm (2,3-7,7 mm) and in control group – 3,5±0,1 mm (2,5-4,4 mm).

Conclusion: Sonographic signs of plantar fasciitis on the basis of acquired flat feet were changes in echogenicity and structure, changes in the contours of the cortical layer of enthesis and plantar fascia, the thickening of the enthesis of the plantar fascia of more than 4 mm.

Disclosure of Interests: None declared

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AB1381 DETECTION OF QUANTITATIVE ULTRASOUND CHANGES AFTER CORTICOID INFILTRATION OF THE PREACHILLEAL BURSA IN PATIENTS WITH INFLAMMATORY OR MECHANICAL ENTHESOPATHIES

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Background: It has recently been demonstrated that computer analysis of static ultrasound images can detect exercise-induced stromal changes in the body's load-bearing tendons.

Objectives: The purpose of this study is to determine if the same analysis can detect enthesic changes in patients who have undergone corticosteroid infiltration in the preachilles bursa.

Methods: Serial images of patients who received corticosteroid injections (around 40mg of triamcinolone acetonide) in the preachilles bursa were selected. For the records to be considered it was necessary at least one baseline ultrasound study, one between the first and second month after the injection and one between the third and sixth month after the injection. All images were obtained with the same ultrasound equipment, by the same operator and with the same gain and frequency settings.

The images were analyzed using the ImageJ 1.53e program, which allowed the recording of the mean intensity of gray (MIG), dispersion of gray intensities (DIG) and mode of gray intensities (MoIG).

Results: Eighteen image collections from the same number of patients were selected. Eight corresponded to mechanical enthesopathies (without any diagnosis of spondyloarthritis) and ten were patients with a diagnosis of axial spondyloarthritis (5) or psoriatic arthritis (5). The ratios of MIG, DIG and MoIG of the injured enthesis with respect to its control were, respectively, 1.12 SD 0.14, 0.88 SD 0.42 and 2.04 SD 1.54 for the mechanical pathology group and 0.89 SD 0.05, 1 SD 0.04 and 0.96 SD 0.03 for the inflammatory pathology group. Statistically significant differences in the MIG ratio were detected between patients with inflammatory diseases and patients with mechanical injuries (t=4.69, P=.000). Among patients with inflammatory pathology, the change between baseline and 3-6 months after infiltration MIG was statistically significant (82.59 SD 37.68 vs 92.02 SD 38.67; t=-5.69, P=.000). The changes between DIG and MoIG were not significant (t=0.899, P=.392 and t=-1.542, P=.158, respectively). Among patients with mechanical pathology, there were no significant differences between final and baseline MIG, DIG, or MoIG (t=1.921, P=.096; t=-1.533, P=0.169; and t=1.761, P=0.122, respectively). Figure 1 summarizes the changes in the mean gray intensity index (iMIG) in patients with mechanical and inflammatory pathology. In patients with inflammatory diseases, the changes between the final and basal iMIG tend to normalize (approaching the unit). In the mechanical pathology group, the iMIG variation shows a less defined behavior.

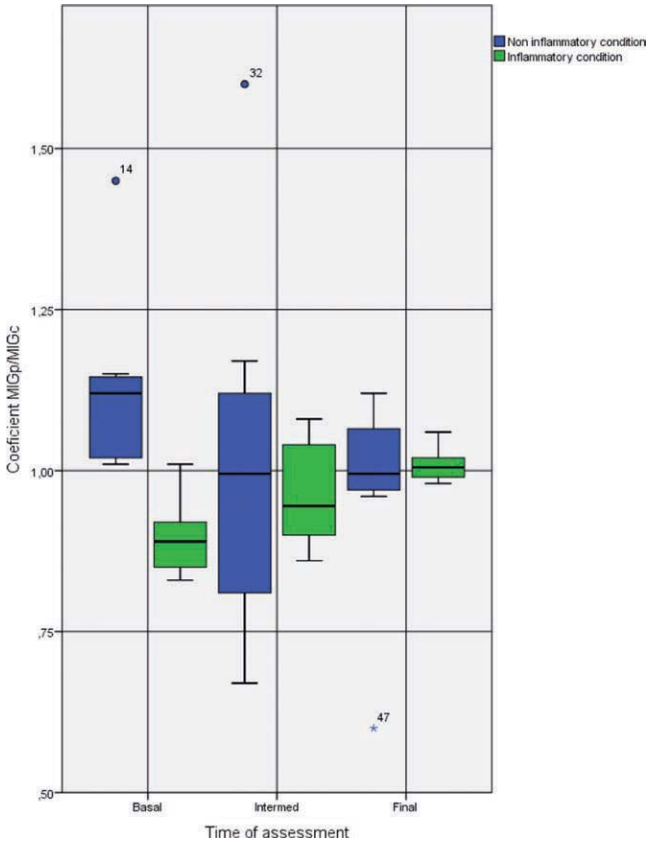

Figure 1. *Box and whisker plot showing the evolution over time of the pathological/healthy gray intensity mean coefficient. MIGp: Mean gray intensity in the pathological enthesis. MIGc: Mean gray intensity in the control enthesis of the same patient.*

Conclusion: The computer analysis of static images in gray scale can detect the changes observed in the Achilles enthesis of patients with inflammatory diseases such as spondyloarthritis. It is also demonstrated that in these patients the gray intensity change rate tends to be normalized (approaching the unit) after a steroid injection. Trend to normalization has not been evidenced in patients with mechanical pathology. Corticosteroids apparently do not act on the origin of the mechanical enthesopathies. Therefore, the study of the average, dispersion and fashion of gray intensities is erratic.

The capacity of MIG detecting evolutionary changes in inflammatory pathology shows a potential for the follow-up of patients with spondyloarthritis and enthesseal commitment.

Disclosure of Interests: Carlos Guillén-Astete Speakers bureau: Novartis, Janssen, Abbvie, Grunenthal, UCB and Gebro., Paid instructor for: Roche, Novartis, Janssen, Esteve and Menarini., Consultant of: Janssen, Novartis and Roche., Grant/research support from: Pfizer, Grunenthal, Gebro and Novartis., Marina Tortosa-Cabañas: None declared, África Andreu-Suárez: None declared

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AB1382 SCREENING OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS THROUGH AN ULTRASONOGRAPHY PROTOCOL

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Background: Interstitial Lung Disease (ILD) is a frequent complication in patients with autoimmune diseases. Rheumatoid arthritis (RA) does not escape this statement. Different protocols have been proposed for the ultrasound evaluation of this affectation showing very good correlation with high-resolution computed tomography.

Objectives: To determine the sensitivity and specificity of an ultrasound evaluation protocol as a screening method for interstitial lung disease in rheumatoid arthritis.

Methods: Consecutive patients diagnosed with RA, with and without ILD, will be included. High-resolution chest CT (HRCT) will be performed in all patients. The lung evaluation protocol by ultrasonography (US); evaluates 50 intercostal spaces (ICS) and will be performed by a rheumatologist and imaging specialist trained in the procedure. The presence of B lines and pleural alterations in the EICs explored will be evaluated. A semiquantitative scale will be used to assess each EIC: 0 = normal, (<10 B lines); 1 = mild (11 to 20 B lines); 2 = moderate (21 to 50 B lines) and 3 = marked (> 50 B lines). CT scan was considered the "gold standard" for the diagnosis of ILD and they were evaluated by experienced pulmonologists who were blind to the patient.

Results: 79 patients were included. Female sex 77% with a mean age of 55 (SD 11.4). The comorbidities observed were: hypertension 27%, dyslipidemia 15%, diabetes mellitus 10%, hypothyroidism 30%, smokers 14%, former smokers 18% and osteoporosis in 14% of patients. The patients had a median duration of the disease in years of 7.5 [IQR 9.2]. Erosive disease was seen in 20 (20%) and rheumatoid nodules in 9.1% of patients. 91% of the patients were under treatment with corticosteroids. Rheumatoid factor was observed in 87% of the patients and Anti-CCP in 71% of the patients, of which 70% had high titers. DILD was observed by HRCT in 21 (27%) patients. The tomographic patterns observed were UIP 7 (33%), probable UIP 2 (10%), cellular NSIP 6 (29%), fibrosing NSIP 3 (14%). An indeterminate pattern was observed in 3 patients. The extent of pulmonary involvement was extensive in 48% of patients and limited in 52%. A sensitivity of 63% (CI95% 44-78) and a specificity of 92% (CI95% 81-97) were observed for the ultrasound evaluation protocol with a PPV of 81% (CI95% 61-92) and NPV of 83 % (95% CI 71-90) and an LR+ 8.1 (95% CI 4.6-14.3) and LR- 0.4 (95% CI 0.3-0.48). AUC: 0.81 (p<0.0001).

Conclusion: We observed a moderate sensitivity and specificity of the method to assess interstitial lung involvement in RA with an acceptable AUC for a screening method. These findings are similar to what was found in other cohorts. We observe a high NPV. This means that in patients with a negative study result, the possibility of ILD would be removed. Studies in larger cohorts and comparison with other factors associated with ILD are necessary to improve our understanding of the method and give it the place it deserves.

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Disclosure of Interests: None declared

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AB1383 QUANTIFICATION OF THE PD SIGNAL BY COMPUTER ANALYSIS OF STATIC IMAGES: INTRA-OBSERVER, INTRA-PATIENT AND SENSITIVITY TO CHANGE VALIDATION.

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Background: The computerized assessment of ultrasound images is an alternative to the dichotomous subjective assessment often used in the study of entheses. Previously, our group has demonstrated its usefulness in assessing greyscale images; however, the evaluation of enthesial hyperemia using this technique remains a pending task.

Objectives: -To determine the intra-observer and intra-patient variability of the hyperemia study using computer analysis of static images.

Methods: Patients with a diagnosis of known spondyloarthritis and ultrasound enthesitis of the Achilles tendon -according to EULAR criteria (detection of hyperemia by power Doppler (PD) signal within 2mm of the cortex)- were selected. Longitudinal medial, central and lateral image sections were obtained. Hyperemia was assessed by PD signal detection, and the images with the highest signal intensity were recorded, maintaining the same doppler gain and PRF settings for each subject. For image analysis, recordings were coded and randomized so that the analyst did not know to which patient a given section corresponded. Intra-patient validity was assessed by comparing the results of sections from the same patient with each other at two different times. Intra-observer validity was evaluated by subjecting the same image to two computer analyses at different times. Finally, validation of sensitivity to change was performed by successive measurements. The software used was ImageJ 1.53e (NIH, USA).

Results: Images of 12 patients with Achilles enthesitis were included: 6 patients with SpA-nRx, four patients with PsA, and two patients with SpA-Rx. On intra-patient evaluation, significant differences in PD signal intensity were detected between medial, lateral, and central sections. In all cases, the measurement obtained in the central section was the highest (Friedman 15.500 P=.000; medial-central -1.500, P=.001; lateral-central -1.250, P=.007). The coefficient of variation in the first and second determinations without considering the sign of the variation was: 4.2% SD 5.5%. In the intra-observer evaluation of the PD signal evaluations at the central cut-off, the mean coefficient of variation, without considering the sign, was: 9.1% SD 7.2%. In assessing sensitivity to change, patients with 6-month ultrasound studies were grouped into those who maintained treatment and those who eventually discontinued treatment due to therapeutic failure. In the seven patients who maintained treatment, the mean change in hyperemic areas was -94.3% SD 4.4%, while in the five patients who discontinued treatment, it was -65.4% SD 6.3% (p=.000).

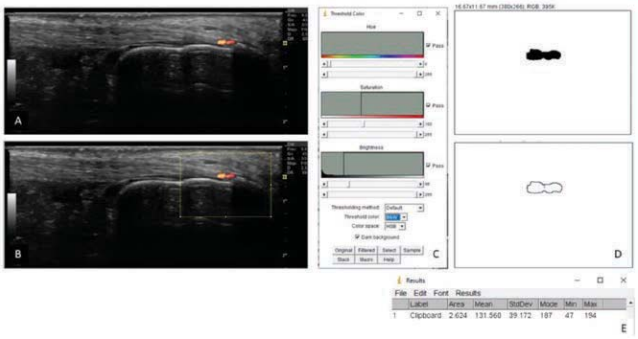

Figure 1. *Evaluation of the PD signal.*

Conclusion: Computer analysis of static Achilles tendon images conforms to the same ultrasound image acquisition recommendations. In addition, it demonstrates excellent intra-patient and inter-observer variability and sensitivity to change, at least when correlated with therapeutic success or failure from a clinical perspective.

Disclosure of Interests: Carlos Guillén-Astete Speakers bureau: Novartis, Janssen, Abbvie, Grunenthal, UCB, Gebro, Paid instructor for: Roche, Novartis, Janssen, Esteve, Menarini, Consultant of: Janssen, Novartis, Roche, Grant/research support from: Pfizer, Grunenthal, Gebro, Novartis, África Andreu-Suárez: None declared, Marina Tortosa-Cabañas: None declared

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AB1384 CLINICAL SIGNIFICANCE OF DENSE FINE SPECKLED PATTERN ANA

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Background: The clinical significance of Dense Fine Speckled (DFS) pattern Anti-nuclear antibodies (ANA) by indirect immunofluorescence method (IIF) is unclear and has been inversely associated with rheumatic disease [1 2].

Objectives: Our purpose was to determine associations between DFS pattern ANA and the disease categories of inflammatory arthritis, ANA associated rheumatic diseases (AARD), fibromyalgia/chronic pain syndrome/chronic fatigue syndrome and atopic disorder.

Methods: This retrospective study used data from patients tested for ANA by IIF between August 2017 to August 2019 at the University of Minnesota Medical Center. Comparisons between the diagnostic categories listed in objectives were made for patients with negative ANA, positive ANA (any pattern) and DFS pattern. Individual disease diagnoses belonging to the above categories were also analyzed. The inflammatory arthritis category included seropositive rheumatoid arthritis (RA), seronegative RA, RA with unknown serology, ankylosing spondylitis, and psoriatic arthritis. The disease category of AARD included systemic lupus erythematosus (SLE), systemic sclerosis, mixed connective tissue disease, idiopathic inflammatory myopathies, Sjogren's syndrome (SS), and undifferentiated connective tissue disorder (UCTD). Atopic disorders included atopic dermatitis, allergic rhinitis, urticaria, and asthma. Frequency of Raynaud's phenomenon (RP) was also calculated.

Results: 13,845 patients with an ANA during the study period were identified. 9106 (65.8%) had negative ANA and 4739 (34.2%) had positive ANA by IIF (including all patterns). 640 (4.6%) had ANA positive DFS patterns. Relative risk (RR) was calculated for diagnostic categories and individual diseases. For patients with positive ANA and DFS pattern, the RR for diagnostic codes of inflammatory arthritis categories [1.35 (1.07- 1.71), p=0.02] was higher when compared to the frequency of codes in ANA negative. RR for AARD among patients with DFS pattern was also higher [1.78 (1.44- 2.2), p <0.001]. There was no significant difference in the frequency of diagnostic codes of chronic pain/fibromyalgia/chronic fatigue syndrome [1.02 (0.9- 1.2), p=0.84] atopic disorder [0.68 (0.4- 1.15), p=0.16] for DFS+ compared to the ANA group. The frequency of AARD diagnostic codes was lower for patients with DFS pattern [0.64 (0.52-0.79), p<0.001] compared to ANA positive patients with all other patterns, consistent with published data. There was no significant difference of frequency of diagnostic codes for the rest of the disease categories when comparison was made between ANA positive DFS pattern and ANA positive with other patterns.

Individual disease diagnostic codes of RA were higher among DFS+ patients when compared to ANA- patients. The frequency of diagnostic codes of SLE, SS, UCTD, fibromyalgia, Raynaud's phenomenon, and autoimmune thyroid disease was also higher among patients with DFS pattern compared to ANA- patients. The frequency of diagnostic codes of seropositive RA was lower among patients with DFS pattern compared to ANA+ with all other patterns. The frequency of diagnostic codes of SLE, SSc, UCTD, and chronic pain was also lower among DFS+ patients, compared to those with ANA of all other patterns, consistent with prior reports.

Conclusion: The frequency of diagnostic codes of RA, SS and Raynaud's was higher among DFS pattern ANA compared to ANA negative group but was not significantly different from ANA positive with other patterns. This suggests that the presence of a DFS pattern should not be used to indiscriminately exclude the presence of a rheumatic disease.

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AB1385 CHARACTERISTICS OF MICROANGIOPATHY IN THE NAILFOLD AREA IN UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE

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Background: Undifferentiated connective tissue disease (UCTD) is characterized with presence of clinical signs and immunological findings suggestive of connective autoimmune disease, but the criteria for a definite rheumatic disease are not fulfilled. Duration of symptoms below 3 years defines UCTD as "early" pathological condition (1) that requires follow-up for assessment of possible disease progression. Raynaud's phenomenon could be found in approximately 50% of cases with UCTD and about half of patients with RP and UCTD exhibit "scleroderma-like" pattern.

Objectives: To assess the characteristics of capillaroscopic changes in early UCTD.

Methods: Inclusion criteria for the study were diagnosis UCTD made for the first time by rheumatologist in patients with RP. 14 patients were included in the study – 13 women, 1 men, mean age 37±14 years. Capillaroscopic examination was performed in all patients using USB microscope Dino-Lite. Follow-up was perfomed in 7 of the patients for a period between 1 and 2 years.

Results: At the time of the initial diagnosis "scleroderma-like" pattern, "early" phase (giant capillaries, presence of haemorrhages in some cases, preserved distribution, normal capillary density) was found in 8 patients. More advanced capillaroscopic changes with devascularization, derangement and neoangiogenesis were not observed. In 5 patients nonspecific capillaroscopic findings were present (dilated, tortuous capillaries, haemorrhages) and in 1 case – normal pattern. During 1-year follow-up in one patient the diagnosis was revised to systemic lupus erythematous due to newly appeared clinical, laboratory and immunological findings. The normal capillaroscopic pattern was changed to nonspecific findings in this case. In the rest 6 patients with available follow-up both clinical diagnosis and capillaroscopic findings remain unchanged.

Conclusion: In conclusion, the predominant finding in UCTD with capillaroscopic features of "scleroderma-like" microangiopathy is "early" pattern while more advanced microvascular pathology is not a characteristic finding. Stable capillaroscopic pattern during the follow-up correlates with stable clinical symptoms. Thus, capillaroscopy should be considered as a key technique for assessment of UCTD patients with manifestations of RP regarding vascular and overall disease progression.

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Public health, health services research, and health economics

AB1386 A SURVEY ON ACCEPTANCE OF COVID-19 VACCINATION AMONG PATIENTS WITH RHEUMATIC DISEASES -A SINGLE CENTER EXPERIENCE IN MALAYSIA

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Background: According to Statista, 78.5% of the population in Malaysia have completed their vaccination as of 6th january 2022 [1].The acceptance of patients with rheumatic diseases on Covid-19 vaccination is crucial in the long term protection against Covid-19 infection. We conducted a survey to determine the acceptance of Covid-19 vaccination amongst patients with underlying rheumatic disease.

Objectives: To find out the reasons of vaccination refusal amongst rheumatology patients.

Methods: This was an interview survey. All rheumatology patients who were follow up in rheumatology clinic Hospital Sultan Ismail, Malaysia from 26th April 2021 to 25th July 2021 (total 3 months) were interviewed. Demographic and diagnosis of the patients were collected.

Results: A total of 952 patients were identified. 83.7% of them were female patients (797/952) and majority of them were Malay (46.4%). This was followed by Chinese (36.1%), Indian (16.3%) and others (1.2%). The mean age group was 48 (range from 13 -85). 97.6% of the respondents were categorized as having inactive disease during the interview sessions. 36.6% of the patients were diagnosed to have rheumatoid arthritis and 29.1% of them were having systemic lupus erythematosus. These were followed by psoriatic arthritis (10.9%), mixed connective tissue disease (5.5%), systemic sclerosis (2.9%), gout (2.6%), Sjogren syndrome (1.9%), ankylosing spondylitis (1.6%), myositis (1.5%), vasculitis (1.3%), osteoarthritis (1.2%), antiphospholipid syndrome (0.9%), non-specific arthralgia (0.8%), juvenile idiopathic arthritis (0.8%), seronegative spondyloarthropathy (0.8%), undifferentiated connective tissue disease (0.7%), adult onset still's disease 0.5%) and others (< 0.5% each for Ig G 4 related disease, soft tissue rheumatism and fibromyalgia). 87.3% of them were keen or have already received Covid-19 vaccination. 12.7% of them were not keen for the vaccination with various reasons. 48.8% of them were worrying about worsening clinical condition, 12.4% of them were not keen as they concerned about side effects (3 worry about fever, 1 worry about hepatitis, 1 for nausea, 1 for dizziness, 1 for breathlessness, and 7 for non-specific reasons). 10.7% of them were not keen due to pregnancy, 5.79% of them were not keen as worried about allergic reactions, 4.9% of them were worrying about sudden cardiac death, 4% were not keen as on chemotherapy treatment, 3 % of them doubted the efficacy of vaccination, 2.5% were not keen as they worried about heart disease, 2.5% worried about increase risks of infection and others (2 for old age, 2 for thrombotic event, 2 for drug interaction and 1 patient due to hemodialysis).

Conclusion: The overall acceptance rate of Covid-19 vaccination amongst patients with rheumatic diseases is very encouraging with the percentage of >85% despite of lacking knowledge about vaccine Covid-19. This result can assist our Ministry of Health to plan for future battle to improve vaccine uptake that hopefully can lead to herd immunity against COVID-19 infection. More counseling sessions are required to clear up the doubts of vaccination and increase the vaccination rate amongst rheumatic patients.

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Disclosure of Interests: None declared

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AB1387 THE EFFECTS OF PREGNANCY AND FERTILITY ON DRUG USAGE AND PREFERENCES IN RHEUMATOLOGICAL DISEASES: A SINGLE CENTER EXPERIENCE

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Background: Rheumatological diseases usually affect women of reproductive age. Although the effects of these diseases on pregnancy vary; Joint and organ damage that may occur should be prevented, maternal and fetal effects of the treatment should be evaluated (1).

Objectives: The aim of this study to determine the effects of rheumatological diseases and drugs used on pregnancy and fertility.

Methods: Between January 2014 and January 2021, women between the ages of 18-45 who were diagnosed and treated at Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department were retrospectively analyzed.

Results: The median age of the patients is 37 (min 19-max 45) years. 517 patients (51,7%) were pregnant after diagnosis, 39 patients (3,9%) had abortion after diagnosis, 957 patients (95,7%) had live birth, 69 patients (6,9%) had curettage, 43 patients (4,3%) could not have children. The median of pregnancies before diagnosis is 2 (min 1-max 11) the median of pregnancies after diagnosis is 1 (min 1-max 6) the median of abortions before diagnosis is 2 (min 1-max 7) the median of abortions after diagnosis is 1 (min. 1-max 4) the median of curettage is 1 (min 1-max 3) the median of live births is 2 (min 1-max 5). The distribution of patients according to drug use and drug used during pregnancy is shown in Figure 1. The distribution of the patients according to the diagnosis and the factors affecting pregnancies after diagnosis, abortions after diagnosis, curettage and live birth is shown in Table 1.

Table 1. The distribution of the patients according to the diagnosis and the factors affecting pregnancies after diagnosis, abortions after diagnosis, curettage and live birth.

	†FMF	‡RA	¶AS	§PSA	Sarcoidosis	Granulomatous Mastitis	Myositis	Vasculitis	Behçet's Disease	Still's Syndrome	Gout	Fibromyalgia	††SLE	Sjögren's Syndrome	Systemic Sclerosis	‡‡APS
Avaliable (%n)	224 %22.4	197 %19.7	274 %27,4	59 %5,9	1 %0,1	1 %0,1	1 %0,1	7 %0,7	169 %16,9	3 %0,3	2 %0,2	146 %14,6	105 %10,5	60 %6	37 %3,7	29 %2,9
Not Avaliable (%n)	776 %77,6	803 %80,3	726 %72,6	941 %94,1	999 %99,9	999 %99,9	999 %99,9	993 %99,3	831 %83,1	997 %99,7	998 %99,8	854 %99,9	895 %89,5	940 %94	963 %96,3	971 %97,1
Total (%n)	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100	1000 %100
Number of pregnancy after diagnosis			Use of colchicine (*OR %95 confidence range) **p value *OR:1,58 (1,22-2,034) **p: ‹0,001			Use of anakinra (*OR %95 confidence range) **p value *OR:6,69 (1,51-29,60) **p: ‹0,004			Use of methorexate (*OR %95 confidence range) **p value *OR: - 0,73 (0,51-0,93) **p: 0,05				Use of leflunomide (*OR %95 confidence range) **p value *OR: - 0,53 (0,30-0,93) **p: 0,035		
Number of abortion after diagnosis					‡‡APS (*OR %95 confidence range) **p value *OR: 3,7 (1,68-8,43) **p: ‹0,001								††SLE (*OR %95 confidence range) **p value *OR: 7,5 (2,78-20,25) **p: 0,001			
Number of curettage									‡‡APS (*OR %95 confidence range) **p value *OR: 5,5 (1,94-15,84) **p: 0,001							
Number of live birth									*OR: - 0,20 (0,05-0,75) **p: 0,017							

*OR: Odds Ratio**p‹0,05 significant†FMF: Family Mediterranean Fever‡RA: Rheumatoid Arthritis¶AS: Ankylosing Spondylitis§PSA: Psoriatic Arthritis††SLE: Systemic Lupus Erythematosus‡‡APS: Anti Phospholipid Syndrome

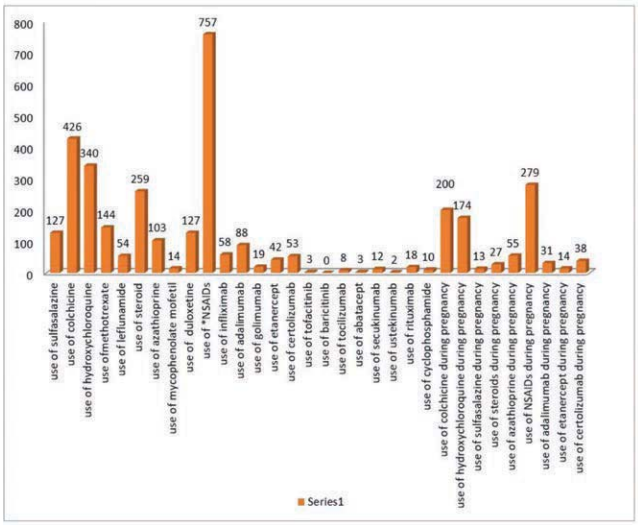

Figure 1. Distribution of patients according to drug use and drugs used during pregnancy

Conclusion: Women with rheumatic diseases should be in remission before pregnancy and should be followed closely throughout their pregnancy and treated with pregnancy-safe drugs. Preparations that can cause infertility in women during the reproductive period should not be used as much as possible. Patients should be informed in detail about the effects of their disease and the drugs used on pregnancy.

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AB1388 CHARACTERISTICS ASSOCIATED WITH MYCHART ACTIVATION AND REASONS FOR NON-USE AMONG RHEUMATOLOGY CLINIC PATIENTS

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Background: Electronic patient portals, such as MyChart by Epic, allow patients to view their medical records, request medication refills, and communicate with their health care providers. Factors associated with portal use include being younger, female, White, having private insurance, and having chronic illness.[1] The Hospital for Special Surgery (HSS) rheumatology clinic serves primarily patients with public insurance (Medicaid, which insures low-income adults, and Medicare, which insures adults >65 years old and those with eligible chronic illness/disability). These patients may be at increased risk for poor health outcomes due to clinical and socioeconomic factors and they are less likely to use MyChart than patients seen in HSS private practices. Increased MyChart use may benefit this high-risk group and improve health equity.

Objectives: This study aims to identify characteristics associated with MyChart activation and reasons for its underutilization among patients seen in the HSS rheumatology clinic.

Methods: We identified all patients aged ≥ 18 years seen in the HSS rheumatology clinic at least twice between January 15, 2019 and January 14, 2021, with at least one visit occurring between July 15, 2020 and January 14, 2021. MyChart status (active vs. inactive) and sociodemographic and clinical variables were extracted from the electronic health record (EHR). We used chi-square tests and t-tests to compare characteristics between patients with and without active MyChart; p-value <0.05 was considered significant (Table 1). In addition, 10 rheumatology fellows were prompted on 3 occasions over 6 weeks to informally survey their own clinic patients with inactive MyChart accounts by asking: "What is your primary reason for not using MyChart?"

Table 1. Baseline Characteristics of Hospital for Special Surgery Rheumatology Clinic Patients Stratified by MyChart Activation Status

	MyChart Active (N=726)	MyChart Inactive (N=501)	p-value
Age, yrs - Mean (SD)	50.3 (15.6)	60.0 (15.3)	*<0.01*
Female - N (%)	601 (82.8)	412 (82.2)	0.80
Race - N (%)			0.37
•White/Caucasian	275 (37.9)	184 (36.7)	
•Black/African American	185 (25.5)	135 (27.0)	
•Asian	58 (8.0)	25 (5.0)	
•Other	189 (26.0)	145 (28.9)	
•Unknown	18 (2.5)	11 (2.2)	
Ethnicity - N (%)			0.27
•Hispanic/Latino	294 (40.5)	226 (45.1)	
•Not Hispanic/Latino	422 (58.1)	268 (53.5)	
•Unknown	10 (1.4)	7 (1.4)	
Preferred language - N (%)			*<0.01*
•English	611 (84.2)	332 (66.3)	
•Spanish	72 (9.9)	134 (26.8)	
•Other	43 (5.9)	35 (7.0)	
Needs interpreter - N (%)	106 (14.6)	156 (31.1)	*<0.01*

Results: There were 1,227 patients included (93.2% with Medicaid and/or Medicare insurance). Compared to patients with inactive MyChart (42.9%), those with active MyChart (57.1%) were younger (50.3 ± 15.6 vs. 60.0 ± 15.3 years, p<0.01). The majority of patients in both groups was female. There was no significant difference in race or ethnicity between groups. Patients without active MyChart were less likely to identify English as their preferred language and more likely to require an interpreter for clinic visits (Table 1). The rheumatology fellows collectively asked 16 clinic patients with inactive MyChart their primary reason for non-use. The most commonly cited reason was difficulty using the technology (n=8; 50.0%); others included visual impairment (n=2; 12.5%), preference for using the telephone (n=2; 12.5%), concerns about security/spam (n=2; 12.5%), not having a smart phone/computer (n=1; 6.3%), and having a language barrier (n=1; 6.3%).

Conclusion: In the HSS rheumatology clinic, patients who did not have active MyChart were older and less likely to be English-speaking than those who did. The most common barrier to MyChart use reported by patients was difficulty with the technology. This pilot data suggests a need for interventions to facilitate patient-provider communication, specifically targeting older and non-English-speaking rheumatology clinic patients, with the goal of advancing patient engagement and health equity.

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AB1389 COST-MINIMIZATION ANALYSIS IN RHEUMATOID ARTHRITIS IN SPAIN

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Background: Rheumatoid Arthritis (RA) is a chronic condition causing fatigue, swelling and deformation of the joints. Together with its associated co-morbidities and high indirect costs represents a high humanistic and economic burden [1]. In Spain, RA has a prevalence around 1%[2], representing about 473.942 people. Since biological treatments were introduced, such as adalimumab (ADA), the clinical outcomes of RA's have improved[3]. Nevertheless, due to its high cost, biologics introduction was hurdled until biosimilars appeared[4]. At the moment, the available network meta-analyses[5,6] do not show a statistically significant difference in effectiveness between the different available treatment. Therefore, cost-minimization analysis can be a useful tool in this pathology.

Objectives: Our objective was to conduct a cost-minimization analysis for RA in Spain.

Methods: All the cost information for the therapeutic alternatives (certolizumab, etanercept, golimumab, infliximab, tocilizumab, tofacitinib, and upadacitinib)

was gathered from drug cost datasets[7], and a range of discounts were applied according to experts opinion obtained through a survey. Finally, non-pharmacological costs were obtained from literature review[8]. With all this information, a cost-minimization analysis between the suitable therapeutic alternatives was performed for a 1-year time horizone. Robustness of results was validated by a deterministic and probabilistic sensitivity analysis (PSA).

Results: ADA was the less expensive option with an annual cost of 4,529€ vs 4,650€ - 10,001€ for the alternative treatments. Infliximab had only a slightly higher cost than ADA (2,7% higher). Certolizumab, etanercept, and tofacitinib showed a higher cost profile, with an annual cost between 54% and 71% higher than ADA. Finally, golimumab, tocilizumab and upadacitinib had the highest cost, between 103% and 137% higher than ADA. Sensitivity analysis showed similar results. The deterministic sensitivity analysis showed ADA to be the best option with average and maximum discounts. In the PSA, only ADA and infliximab performed as the best alternative. ADA was the best option 63% of times.

Conclusion: According to our model, ADA was the most cost-effective biologic option for treating RA in Spain, and the sensitivity analysis validated the results.

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AB1390 COMPLEMENTARY DIGITAL THERAPY SAFELY IMPROVES QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: Self-management strategies play a central role in improving clinical outcomes in patients with inflammatory arthritis. EULAR recently highlighted the essential role of digital health to increase the self-management of patients. Evidence regarding these supporting digital tools, including mobile apps, is currently however very limited [1].

Objectives: To evaluate the efficacy and safety of a mobile app (Mida Rheuma App) in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA, including psoriatic arthritis [PsA]) in a prospective study.

Methods: Patients with RA, SpA/ PsA, stable on their antirheumatic therapy for ≥4 weeks, were eligible to use the Mida Rheuma App in addition to standard care treatment. The usage of the app targeted the optimization of non-medical treatment in a 4-step process: (1) collection of the information (HRQoL, disease activity, physical impairment, diet, mental health, physical activity, etc.) using standardized questionnaires via the conversational health coach Mida; (2) development of a patient profile that focuses on the patient's disease, well-being, and behavior; (3) creation of a personalized, evidence-based disease management program based on recommendations from medical guidelines, medical standards, and state-of-the-art clinical research; (4) implementation of personalized recommendations into the patient's daily life by providing short daily tasks that accelerate positive behavior change. Additionally, the health coach Mida supports the patient in coping with stress, sadness, depression, fatigue, and further disease-related symptoms. This is achieved by various cognitive behavioral techniques, meditation and relaxation methods.

Additionally, we assessed demographic parameters, treatment regimen, disease activity (e.g., SDAI, ASDAS), and other patient-reported outcomes (e.g., SF-36) at baseline and after 4 weeks. The study was approved by the Ethics Committee of the Medical Faculty of Mannheim, Heidelberg University.

Results: Of 20 patients screened after obtaining informed consent, 19 were enrolled in the study, and 17 patients (12 RA, SpA: 1 axSpA, 4 PsA) completed the study (2 drop-outs due to unwillingness to finish the study). 7 (41.2%) patients were male, and ages ranged from 19 to 63 (40.5±12.2) years). Patients were treated as follows: 7 NSAIDs (41.2%), 2 GC (>5 mg) (11.8%), 3 HCQ (17.6%), 10 MTX (58.8%), 1 LEF (5.9%), 1 SSZ (5.9%), 1 APR (5.9%), 3 JAKi (17.6%), 1 TNFi (5.9%), 2 IL-6i (11.8%), 1 IL-17i (5.9%). No significant change in antirheumatic treatment was observed during the study. At baseline, 29.4% of the RA and PsA patients were in remission, 25.2% had low, 29.4% had moderate, and none had high disease activity according to SDAI, one axSpA patient had low disease activity (ASDAS: 2.2). At the end of the study, slightly more RA and PsA patients were in remission and had low disease activity (58.8% and 23.5%, respectively) and less had moderate activity (11.8%); the axSpA patient had inactive disease (ASDAS: 1.8). Regarding patient-reported outcomes, statistically significant improvement was noted for the following parameters: SF-36 Total Score (relation of CI 90% and minimum clinically important difference of 2.5), increase of Physical Component Summary of SF-36 by 23.6% (p=0.024), 'role limitations due to physical health' by 76.9% (p=0.022), and 'general health' - by 17.1% (p=0.048); and evidence of potential clinical importance of their dynamics for Patient Health Questionnaire (PHQ)-9, 'emotional well-being' and RADAI-5. No negative changes were observed for assessed parameters. No adverse events were reported throughout the study.

Conclusion: This prospective study suggests that using an app-based personalized disease management program significantly quickly improves several measures of patient-reported outcomes and disease activity in patients with RA and PsA/SpA. These findings highlight the potential of complementary digital therapy in patients with inflammatory arthritis.

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AB1391 19% PATIENTS WITH CHRONIC RHEUMATIC INFLAMMATORY DISEASES PRESENT AN UNFAVORABLE PREGNANCY OUTCOME: A DESCRIPTIVE ANALYSIS OF THE NATIONAL FRENCH SOCIAL SECURITY DATABASE

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Background: patients with chronic rheumatic inflammatory diseases (CRID, i.e. rheumatoid arthritis (RA) or spondyloarthritis (SpA)) have been reported to have poorer pregnancy outcomes than the general population.
Objectives: to describe the pregnancy outcomes of singleton in patients with CRID in France in the past decade.
Methods: this is an analysis of the French Health Insurance claims database (SNDS), which represents 87% of the French population) from 2008 to 2016. To be included in the analysis patients had to be identified as RA or SpA according to existing diagnostic algorithms, to have at least one pregnancy declaration in the database, and to have continuous health insurance from 1-year before pregnancy onset to 1-year after end of the pregnancy or until death (if death occured before the 1-year-period after the end of pregnancy) to be included. Only the first singleton pregnancy occurring during the study period was included in this analysis. Both maternal and pregnancy outcomes were considered. Outcomes were identified either by ICM-10 codes or hospital discharge summaries discharge between 2008-2016.
Results: Among the 35 737 identified adult females with a CRID diagnosis (40.7% with RA and 59.3% with SpA), 27 722 (78%) had a pregnancy during the study period. 11 274 (42%) had received at least one DMARD prior to the pregnancy and were included in the analysis. Among them, only 4025 (36%) were exposed to DMARDs during pregnancy. Mean (SD) age of females at the start of the pregnancy was 32 (5) years, and mean (SD) disease duration was 4 (4) years. Pregnancy ended before 13 WG in 21% and after 37 WG in 70% cases. Live-birth represented the most frequent pregnancy outcome (76.9%), and overall 34.7% patients presented at least one unfavorable outcome (see Table 1).

Table 1.

	Unfavourable outcome	N(%)
Pregnancy outcomes	**Miscarriage (<22WG)**	579 (5.3%)
	Abortion	91 (0.8%)
	Stillbirth	48 (0.4%)
	Preterm delivery (>= 22WG and <37 WG)	779 (7.1%)
	Low weight at birth (<3th percentile)	287 (2.6%)
	Perinatal mortality (22WG to 6 days of life)	2 (0%)
Maternal outcomes	**Severe maternal infection***	211 (1.9%)
Newborn outcomes	**Hospitalisation in neonatal intensive care > 48h in full-term newborns (after 37 WG)**	95 (0.8%)
	Neonatal mortality (27 first days of life)	2 (0%)
	Severe infection * during first year	603 (5.3%)

Conclusion: More than 75% pregnancies in patients with CRID resulted in a live-birth. Prevalence of miscarriage was surprisingly low, probably related to under-coding. Maternal and infant outcomes seemed comparable to general population. Whether medications had an impact on such outcomes is currently under evaluation.
Disclosure of Interests: None declared
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AB1392 COVID-19 HAD AN ADVERSE IMPACT ON DENOSUMAB TREATMENT PROVISION - COMPARISON WITH PRE-PANDEMIC WAITING TIMES AT A UK-BASED RHEUMATOLOGY DEPARTMENT

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Background: Denosumab treatment is licensed for prevention of osteoporotic fractures. It can cause hypocalcaemia, so bone profile blood tests must be checked prior to treatment. In our department, we have a Standard that patients have blood tests within 1 month before their denosumab injection, and that they receive the injection within 1 month from its due date. A customized MS Access database to record this information and generate a date for the next dose was established in 2015 after a quality improvement project (QIP)1. At the onset of the COVID-19 pandemic, UK national guidance recommended continued provision of denosumab as an essential service.
Objectives: 1. To re-audit delay from due date to actual injection date after establishment of our database.
2. To compare delay from due date to actual injection date before and after onset of COVID-19.
3. To compare the time between blood tests and actual injection date, before and after onset of COVID-19.
Methods: Data for 2 time-periods were extracted from the database: Time Period 1 (pre-COVID-19) 01-03-2019 – 29-02-2020; Time Period 2 (post-COVID-19 onset) 01-03-2020 – 28-02-2021. For each patient attendance, dates of blood test, due date and actual injection date were extracted. All patient details were anonymised, with a decryption key to identifiers held on a secure server at the host Trust. It was manually determined whether blood tests and injections were within 1 month of when they were due. Statistical analyses were carried out in Stata v.14.0. The Kolmogorov-Smirnov test was used to compare distributions between Time Periods 1 and 2.
Results: TIME PERIOD 1: 100 appointments were audited from 68 patients. 20% of blood tests were within 1 month of actual injection date. Median time between blood tests and actual injection was 45 days [IQR 35 – 59]. 52% of actual injections were given within 1 month from due date. (This compares favourably with our 2015 QIP, when 40% of actual injections were within 1 month from due date1). Median time between due date and actual injection was 29.5 days [IQR 13 – 50.5]. TIME PERIOD 2: 77 appointments were audited from 66 individual patients. 24.7% of blood tests were within 1 month of actual injection. Median time between blood tests and actual injection was 45 days [IQR 35 – 59]. 16.6% of actual injections were given within 1 month of due date. Median time between due date and actual injection was 82 days [IQR 40 – 141]. There were no significant differences in time between blood tests and actual injection between Time Periods 1 and 2. However, the time between due date and actual injection date was significantly longer in Time Period 2 ($p<0.005$).
Conclusion: The introduction of our customized database promoted an improvement in time between due date and actual injection date of denosumab. However, this improvement significantly declined after the onset of the COVID-19 pandemic. Resources may need to be increased and processes adapted to minimise the impact of future emergencies on denosumab provision.
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AB1393 RHEUMABUDDY4.0 LEADING THE PATH TO A PATIENT-DRIVEN ELECTRONIC SUPPORT AND MONITORING TOOL

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Background: The use of health apps has become more popular in recent years, but it is still a small and rather unregulated market. Few apps have been designed in collaboration with patients and these mostly address patient reported symptoms. Some clinical registries have already developed patient apps to complete patient-reported outcome measures (PROMs) on smartphones, which normally would have been collected during an outpatient visit and have shown interchangeability. The next step would be providing a patient app offering possibilities not only of individual disease tracking, but to provide automated peer support, health information and behavioural advice.
Objectives: We aimed to further develop and validate RheumaBuddy, a health app for patients with rheumatoid arthritis (RA), from a standard monitoring app to an intelligent health app tailored to the needs of the user that provides transparency to all important stakeholders in Rheumatology care.
Methods: This is an international interdisciplinary project between Austrian and Danish partners funded by the EUREKA program. Rheumatologists, health scientists, digital data experts and patients with RA joined forces in a 4 phase-program, running from 2020 to 2023. Phase 1 continues to develop the app in a co-creation approach in several iterations with patients. Phase 2 concerns developing an automated learning algorithm based on user data to identify patient strata and connect these with helpful non-pharmacological interventions. Phase 3 connects healthcare system data on diagnosis, medication prescription, healthcare facility usage with a large clinical RA database. By that we develop patient pathways that correlate high granularity data with system resources to retrieve results on socioeconomic impact. In phase 4 a randomised clinical trial will evaluate the effect of the developed RB4.0 on clinical disease activity and quality of life.

Results: Currently, RB is regularly being used by more than 3100 patients in 35 countries and 8 languages throughout Europe. The current RheumaBuddy version offers logging of symptoms using Likert scale questions, a joint mannequin to mark painful body parts and a peer-support forum. Additionally, the user can anytime display his/her entries over time in a graphical report and also share data with the healthcare provider. This version is extended with tracking of sleep, working hours and other behaviours. A consultation compass function helps the patient to reflect on goals and issues before the rheumatologist visit. Within this project, we already established a first version of a Recommender System (RS), which computes correlations between user entries (e.g. between a user's mood and pain), thus providing individual feedback. Through integration of information obtained from the app with claims data and clinical data from a RA registry, patterns can be identified and translated into different case models that concern the impact of common RA symptoms. By mapping these scenarios with evidence based behaviour and lifestyle advice, the "virtual coach" (advanced RS) will be developed and integrated into the RB4.0 system. During continuous data collection on app users, similarities in user behaviour can be identified, and similar entry patterns can be grouped. This will allow users to exchange and learn from each other regarding certain difficult situations (ex. "life-hack") etc. We are creating a comprehensive system in providing feedback to both clinical and psychosocial aspects of coping and disease management, as well as everyday practicalities for living with a chronic disease. Figure 1 displays these aspects, contributing the empowerment of patients.

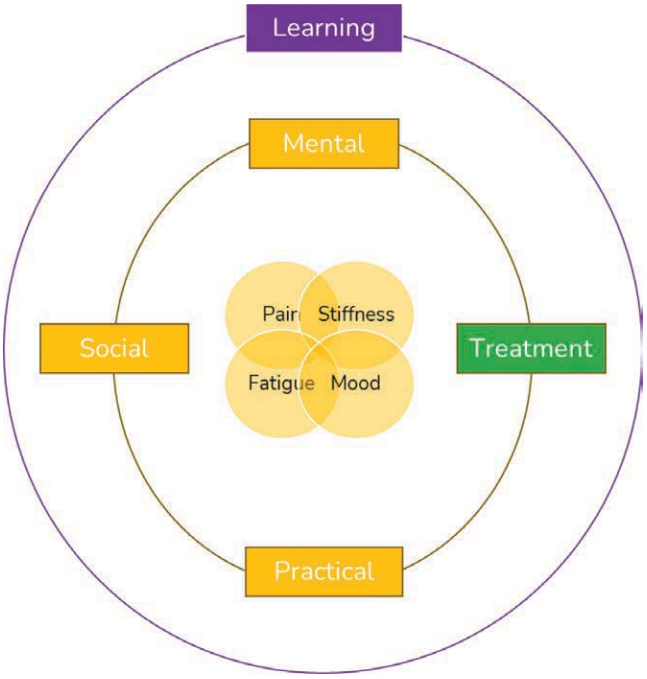

Figure 1. RB4.0 shall support people living with RA in dealing with disease impact

Conclusion: RheumaBuddy4.0 will provide RA patients the means to improve their quality of life on an individual level, better understand their needs and therapy which could support overcoming barriers of successful shared decision making to achieve better outcomes.

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AB1394

ON-FLARE RETREATMENT WITH RITUXIMAB IN RHEUMATOID ARTHRITIS: PATIENTS' AND RHEUMATOLOGISTS' PERCEPTIONS

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Background: Rituximab is an efficacious drug for the treatment of Rheumatoid Arthritis (RA). According to literature, administration of rituximab can be based on a fixed interval or on relapse of disease activity. In some countries, like Belgium, after the first rituximab cycle a flare is required for reimbursement of a subsequent cycle. A better understanding of the perceptions of patients and rheumatologists regarding this retreatment strategy would be informative in view of potential adjustments.
Objectives: The aim was to investigate patients' and rheumatologists' perceptions on the on-flare retreatment strategy of rituximab.
Methods: Patients with RA, who were currently or previously treated with rituximab, and rheumatologists were invited to participate in a qualitative study consisting of individual, in depth, face-to-face, semi-structured interviews. Participants were recruited based on purposive sampling to ensure diversity. Interviews were conducted via video or telephone call. Additional participants were interviewed until data saturation was achieved, meaning no new information emerged from the last 3 interviews. Interviews were audiotaped and transcribed verbatim, followed by analysis according to the Qualitative analysis guide of Leuven, which generated themes and subthemes. Patient experts were involved in this research.
Results: In total, 16 patients with RA and 13 rheumatologists were interviewed. Five overarching themes were generated from the interviews: flare definition, recognition, reaction, balance between benefits and barriers and suggestions (Figure 1). Patients and rheumatologists described how they perceive the on-flare retreatment strategy in daily practice, starting with the *FLARE DEFINITION* itself. Namely, what patients perceived as a flare and the impact of this flare. The second step was *RECOGNITION* of the flare. Both rheumatologists and patients indicated that patients are able to recognise a flare. However, the patient's ability to discriminate between inflammatory and other types of pain was perceived as a difficulty. Moreover, patients indicated that depending on the flare's intensity, they can cope with it themselves, delaying the need for a rituximab cycle. The next step after correctly recognising a flare, was the *REACTION*, from both the patient's and rheumatologist's side. It was stressed that patients must contact their treating rheumatologists in time. Furthermore, a swift response of the rheumatologists was perceived as important. After confirming eligibility, the shared decision to plan a new rituximab cycle can be made while keeping an eye on the organisation. Remarkably, it seemed that rheumatologists approached the retreatment strategy in different ways, meaning that not everyone adhered to the on-flare principle. Several perceived *BENEFITS* (e.g. lower safety risk, societal cost savings) and *BARRIERS* (e.g. disease activity fluctuations, slow working mechanism) were mentioned, making clear that the optimal retreatment strategy should be based on a *BALANCE* between both. Finally, some *SUGGESTIONS* (e.g. biomarkers for flare prediction, subcutaneous administration of rituximab) were brought up that could be helpful in applying the optimal retreatment strategy.

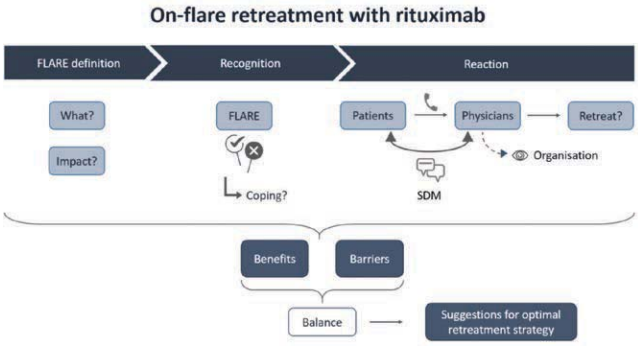

Figure 1. Conceptual framework of the perceptions of patients and rheumatologists regarding the on-flare retreatment strategy with rituximab. SDM = Shared decision making. (Icons: Iconfinder)

Conclusion: Patients play an important role in the recognition of flares and their reaction, in shared decision with the rheumatologist, contributes to the effectiveness of the rituximab on-flare retreatment strategy. Rheumatologists handle the on-flare retreatment strategy as pragmatically as possible, resulting in different approaches. Moreover, both benefits and barriers of on-flare retreatment were

perceived, making clear that a balance should be found to determine the optimal retreatment strategy.
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AB1395 PATIENTS' AND RHEUMATOLOGISTS' PERCEPTIONS REGARDING TAPERING OF RITUXIMAB

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Background: Rituximab is an efficacious drug for the treatment of Rheumatoid Arthritis (RA). The commonly used dose consists of two infusions of 1000 mg with a 2-week interval, but evidence is growing that a lower dose could be as effective. Before implementing a tapering strategy, understanding the perceptions of patients and rheumatologists in this regard is important.
Objectives: The aim was to investigate patients' and rheumatologists' perceptions on rituximab tapering.
Methods: Patients with RA, who were currently or previously treated with rituximab, and rheumatologists were invited to participate in a qualitative study consisting of individual, in depth, face-to-face, semi-structured interviews. Participants were recruited based on purposive sampling to ensure diversity. Interviews were conducted via video or telephone call. Additional participants were interviewed until data saturation was achieved, meaning no new information emerged from the last 3 interviews. Interviews were audiotaped and transcribed verbatim, followed by analysis according to the Qualitative analysis guide of Leuven, which generated themes. Patient experts were involved in this research.
Results: In total, 16 patients with RA and 13 rheumatologists were interviewed. Four themes were found: In favour/reluctant of tapering, shared decision making, implementation and evidence gap (Figure 1). Patients and rheumatologists were *IN FAVOUR* of rituximab tapering, for reasons of safety and economic benefit. Patients and rheumatologists mentioned that a lower dose could allow shorter retreatment intervals, which might avoid flares. Furthermore, rheumatologists referred to available evidence of the effectiveness of a lower rituximab dose. Additionally, patients and rheumatologists indicated that the dose could be tailored based on the patient's clinical manifestations, e.g. usual cycle interval and disease activity measures. However, some patients and rheumatologists felt *RELUCTANT* towards rituximab tapering. Patients and rheumatologists were concerned about potential loss of effectiveness and quality of life, next to more practical concerns. Rheumatologists mentioned that they had insufficient experience with rituximab in general to feel comfortable with tapering. Moreover, when applying an on-flare retreatment strategy, patients present with an active disease at the time of retreatment and therefore the option of tapering is less appealing. The next theme was *SHARED DECISION MAKING*. Patients and rheumatologists mentioned that patients have trust in their physician and thus leave the tapering decision in the hands of the rheumatologists. However, rheumatologists added that this should be combined with explanation of the tapering rationale. Another theme was *IMPLEMENTATION*. When asking participants about 2 possible dose reduction regimens, a cycle consisting of 2 infusions with a lower dose or a cycle of only 1 infusion with a higher dose, advantages were raised for both regimens (e.g. safety reasons and time savings, respectively). On the other hand, the on-flare retreatment regimen itself was already perceived as a kind of tapering, as the interval is prolonged as much as possible between the cycles. *EVIDENCE GAP* was the last theme, meaning that patients and rheumatologists felt there was a need of more research regarding rituximab tapering. For instance, predictive tools for flares, as well as the possibility of subcutaneous administration of rituximab, were mentioned as unmet needs by rheumatologists.

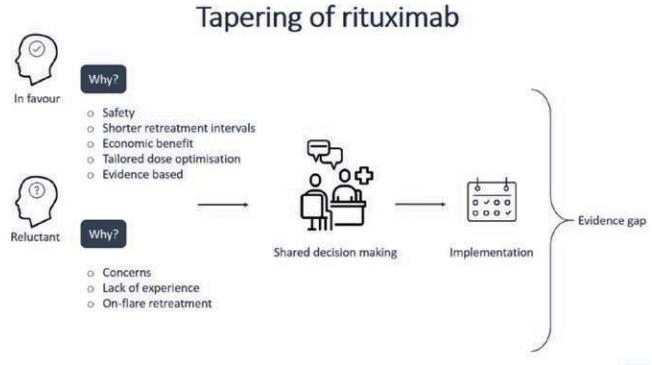

Figure 1. Conceptual framework of the patients' and rheumatologists' perceptions regarding tapering of rituximab. (Icons: Iconfinder)

Conclusion: It seems that rituximab tapering is not yet incorporated in daily practice as much as tapering of other antirheumatic drugs and this could potentially be related to a lack of experience with rituximab. However, with appropriate education and communication, rheumatologists and patients are willing to taper rituximab. Although, many questions remain, indicating an evidence gap and a need of more research.
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AB1396 MULTICENTER QUALITATIVE STUDY ON THE EXPERIENCE OF USE OF BIOLOGIC AND TARGETED SYNTHETIC DISEASE-MODIFYING DRUGS IN PATIENTS WITH RHEUMATIC DISEASES. WHAT DO OUR PATIENTS THINK?

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Background: The development of targeted biologic (bDMARDs) and targeted synthetic disease-modifying drugs (tsDMARDS) has made a substantial change in the control of our patients, and has allowed an increasing number of patients to achieve clinical remission.
Objectives: To gain understanding of patients' experiences of starting treatment with b/tsDMARDs, and explore their attitudes in order to improve the doctor-patient relationship, adherence to treatment, compliance, and knowledge about the experience of using b/tsDMARDs.
Methods: A qualitative study was carried out. A consecutive sample of 130 patients attended in the rheumatology units of four Madrid hospitals, from August 29th, 2021 to January 21st, 2022 completed a questionnaire that consisted of 31 questions, a subsequent qualitative analysis of discourse and content through focus groups with patients was carried out. Descriptive statistical analysis was performed. Chi-squared tests were applied to explore the dependency relationship between the different qualitative variables.
Results: One hundred and thirty questionnaires were collected (see general characteristics in the Table 1).

Table 1. Baseline demographics.

Sex, n (%)	96 female (73.85%), 34 male (26.15%)
Age, years, mean (SD)	51,62±12.31 years
Ethnicity/race, n(%)	74.6% White or Caucasian 22.3% Hispanic or Latino 2.3% Asiatic 0.8% Black or African American
Diagnosis, (%)	42.4% rheumatoid arthritis 25.3% axial spondyloarthritis 10% psoriatic arthritis 6.9% connective tissue diseases 15.4 % other
Time since diagnosis (years), mean (SD)	14,7 years (+/-11,43)
Time since initiation of treatment with b/tsDMARDs (years), mean (SD)	5,84 years (+/-4,28)

Most of the patients (68.46%) felt hope when they were informed that they were going to start treatment with b/tsDMARDs, 26.9% relief, 22.3% happiness and 27.7% fear and concern. 76% of the patients received information about why the treatment was modified, the advantages of b/tsDMARDs (60%), their mechanism of action (48.5%) and the precautions to be aware of (38.5 %). Fifty-two percent of the respondents searched for additional information on their own, with the most used sources being from internet search engines (34.2%), the corresponding drug insert (22.8%) and the page of the Spanish Society of Rheumatology (23.7%). 60% of the respondents were informed about the possible risks associated with the treatment, 49.4% reported being more concerned when they contracted an infection. Most of the patients were recommended to receive influenza (81.5%) and pneumococcal (69.2%) vaccination, of which 74.6% and 54.6% received those respectively. A statistically significant dependence was observed between the recommendation of the vaccine and vaccination, since most (91,5%) of those who received the recommendation were vaccinated ($p<0.001$). Most of the respondents kept their scheduled appointments (87.3%) and never forgot to take their medication (37.04%). 51% of the patients reported that with b/tsDMARDs they had experienced "considerable improvement", 38.5% indicated that "their life has changed", 10% reported little or no improvement. It was observed that men reported a maximum degree of improvement with a significantly higher frequency than women (77% vs 37% respectively), OR 5.79 ($p <0.009$, IC 95% 1.42, 23.67). To the question "In which

aspects have you noticed the greatest changes?" the respondents answered: reduction in outbreaks of the disease (67%), emotional improvement (38.6%) and regaining work activity (31.8%).

Conclusion: In our setting, education programs inform patients adequately, but it seems necessary to make a greater emphasis on therapeutic compliance, providing more safety information, and compliance to recommended vaccinations.

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AB1397 WORK SMARTER NOT HARDER

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Background: In 2014 we were a small team with only 1 WTE (Whole Time Equivalent) CNS (Clinical Nurse Specialist) and 2 WTE consultants for a population of 220,000. Most CNS clinic appointments were taken up for drug counselling. Waiting times were approx. 6 weeks for drug counselling. Consultants would often counsel for DMARDs. That year at a national meeting a virtual group MDT (multidisciplinary) was presented by the team at Manchester Royal infirmary (MRI). They used a good quality presentation for patients starting bDMARDs as a tool for drug counselling. After having to put on an extra clinic to counsel 5 patients, all for rituximab, frustratingly I asked why can't I get them all in the same room to save time? We needed to work smarter, not harder, utilise time & space to ensure best practice but also ensure gold standard, patient centered care continued. We modified the format used at MRI to a face to face group education and counselling of patients to improve waiting times and patient flow.

Objectives: Reduce the amount of clinic appointments used to counsel patients for sDMARDs (synthetic disease modifying anti-rheumatic drugs) and bDMARDs (biologic). Free up clinic appointments for follow up/ review and flares. Standardise information given out to ensure they are all given the same gold standard information and education.

Methods: We visited the team at MRI to view the format of their virtual clinic. It didn't meet the needs of our service so we modified and adapted the presentation.Set up a group education session to discuss the most common sDMARDs and bDMARDs used for Inflammatory Arthritis. I developed a power point presentation and booklet that can be used by CNS- ensuring the same information is given to every patient, both attending the group session and those not suitable for group session (ie Language barriers) who would be seen individually. We use a screening proforma to ensure safety of commencement for the individual prior to attending clinics which has a tick list for screening requirements. The session is undertaken in our education centre. Pre Covid the session could accommodate up to 10 patients per session per week, uptake on average 8-10 patients for sDMARDs and 5-6 for bDMARDs. We alternated biologic and sDMARD sessions, if demand required, we changed a session to accommodate. The room is booked for 1½ hours every week, the sDMARD presentation lasts approximately ½ an hour & bDMARD session 50 minutes, time is allowed for group & individual questions if required at the end. This contrasts with 25 minute appointment for sDMARD & 50 minute for bDMARD counselling 1:1. The booklet, along with information pack, is given at the group session to all patients. This includes all the information the patient requires (advice line information, blood forms). Prior to the group clinic admin team prepare the patient packs for the CNS to give to patients.

Results: We received 102 anonymous responses back from 136 patients asked. (75% response) Following these sessions we found less calls to the advice line regarding medication queries, able to add in further cDMARDs or switch to alternate due to S/Es over the telephone Feedback from patients.-120 comments received. Clear simple information about a number of possible drugs used to treat my condition not just the 1 I am prescribed. If my medication needs changing I already know about it. The lecture aspect of the types/contra-indications of meds was very useful & removed the 'fear' attached to these specialist drugs. The session with other patients present stopped me from feeling alone in this position. The booklet is brilliant as it includes everything that was in the session. Also it took away the 'fear' of the side effects.

Conclusion: 7 years on we feel that Group Counselling has been a huge success, we noticed how successful this was once we had to deal with the pandemic and cancel the group sessions. Patients feedback proves that they like the session and find them valuable. Whilst being beneficial and impoving work productivity and streamling the service.

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AB1398 CORRELATES OF CANCELLED HEALTHCARE APPOINTMENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS DURING THE COVID-19 PANDEMIC

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Background: Rheumatologists have noted challenges in treating patients with systemic sclerosis (SSc) during the COVID-19 pandemic, such as patients on immunosuppressants and those with preexisting pulmonary issues.[1] Also of potential concern was patients delaying treatment due to fears of COVID.

Objectives: This study examined to what extent patients with SSc cancelled health-care appointments due to fears of COVID, how this correlated with their mental and physical functioning, and their levels of anxiety and depression.

Methods: Participants were 60 people with SSc who had not had COVID-19 or been vaccinated for COVID. Participants had a mean age of 58 years (*SD*=11.5) and were primarily female (92%) and white (87%).

Participants completed an online survey after learning about it from a scleroderma organization newsletter or at their visit with a rheumatologist specializing in scleroderma in New York State, USA. Data were collected August 2020 through March 2021. Participants completed measures assessing health-related appointments attendance, Patient Reported Outcome Measurement Information System (PROMIS) measures (anxiety, depression, fatigue, sleep disturbance, pain intensity, physical function), coping strategies to deal with the pandemic, and reported functioning relevant to SSc (hand, gastrointestinal, dyspnea, and Raynaud's disease).

Results: Due to COVID-19 concerns, 28 respondents (47%) cancelled one or more appointments with their primary care physician, specialist, physical or occupational therapist, pulmonologist, or dentist. Compared to those who did not cancel appointments due to COVID concerns, participants who cancelled reported higher anxiety, $t(58) = 2.46$, $p = .02$, higher sleep disturbance, $t(56) = 3.31$, $p = .002$, worse physical functioning, $t(56) = 2.00$, $p = .05$, more constipation, $t(55) = 2.05$, $p = .045$, and lower positive reframing as a coping strategy, $t(56) = 2.08$, $p = .04$.

Many participants reported moderate or severe anxiety (36%), depression (22%), fatigue (32%), sleep disturbance (28%), and physical dysfunction (40%). As shown in Table 1, anxiety scores were positively correlated with scores on measures of fatigue, sleep disturbance, physical dysfunction, diarrhea, and the coping strategies of substance use, self-distraction, emotional support, behavioral disengagement, and venting. Depression scores were positively correlated with scores on measures of fatigue, sleep disturbance, physical dysfunction, pain intensity, dyspnea, diarrhea, and behavioral disengagement as a coping strategy.

Table 1. Correlations Between Anxiety and Depression with Patient-Reported Outcomes and Coping with the Pandemic

Measure	Anxiety	Depression
Fatigue	.38**	.43**
Sleep disturbance	.35**	.34**
Physical dysfunction	.28*	.49**
Pain intensity	.16	.36**
Reflux	.25	.15
Distention/bloating	.28*	.24
Fecal soilage	-.001	.07
Diarrhea	.34**	.28*
Constipation	.21	-.03
Dyspnea	.18	.32*
Raynaud's disease activity	-.08	-.02
Hand functioning	.06	.25
Coping strategy		
Substance use	.29*	.21
Self-distraction	.32*	.18
Behavioral disengagement	.37**	.41**
Using emotional support	.43**	.06
Venting	.34**	.14

Note. *$p < .05$; **$p < .01$

Conclusion: Almost half of participants cancelled one or more health appointments due to COVID fears. This subgroup reported significantly higher anxiety, sleep disturbance, constipation, worse physical functioning, and less coping with the pandemic by looking for the positive. Anxiety and/or depression also played a role in 42% of SSc patients and were related to a variety of worse mental and physical health correlates. Future research should examine the extent to which changes in health-related care during the pandemic have implications for disease progression in patients with SSc.

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AB1399 PEOPLE SUFFERING FROM RHEUMATIC AND MUSCULOSKELETAL DISEASES DESCRIBE THEIR OWN EXPERIENCES OF INTEGRATED CARE: FINDINGS FROM A CROSS-SECTIONAL STUDY AMONG ITALIAN PATIENTS

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Background: Integrated care is an approach to health care based on multidisciplinary working and the continuity and coordination of different levels of care (1). In an integrated care setting, health services are designed to go beyond fragmentation and isolation and delivered in response to chronic patient health needs. Integrated care has been proved to enhance patients' quality of life (2), as well as reduce hospital admission rates and length of stay (3). Furthermore, integrated care favors patients' access to care and improves their satisfaction (4). To evaluate the application and benefits of integrated care, patient experiences should be measured (5). However, while the patient experiences of integrated care have been documented for various chronic diseases, little is known in the context of rheumatic and musculoskeletal diseases (RMDs).

Objectives: This study aims at providing an overview of the patient experience of integrated care of RMDs patients in Italy and defining the experience profiles and priorities of different patient subgroups.

Methods: A cross-sectional online self-administered survey formulated following a scoping review of the literature was administered to a purposive sample of Italian RMDs patients (n=433). Respondents were asked to evaluate their patient experience and the importance attributed to different aspects of integrated care. Explorative factor analysis (EFA) was performed to determine the dimensions of integrated care investigated by the survey. The differences in the responses provided by different subgroups of the sample were assessed using the non-parametric versions of ANOVA and ANCOVA statistical tests with Scheffe's adjustment for multiple comparisons.

Results: Two factors ("person-centered care" and "health service delivery") were extracted in the EFA. Respondents attributed high importance to both of them. However, an overall positive experience was reported only for the dimension of person-centered care. The delivery of integrated care services was evaluated poorly, especially for digital ones. Women described both dimensions of integrated care as more important compared to men ($H(1)=45.292$, $p<.001$ and $H(1)=6.998$, $p=.008$). However, their experience of integrated care services was significantly worse ($H(1)=20.201$, $p<.001$). Older participants reported poorer health service delivery compared to younger ones ($H(3)=73.203$, $p=.009$), especially for digital and outpatient services. Person-centered care was especially important for patients with comorbidities ($F(1,431)=4.944$, $p=.027$). However, this subgroup reported markedly worse experiences of integrated care services ($F=(1,431)=4.187$, $p=.041$).

Conclusion: Italian RMDs patients identified integrated care as something important to them. They reported receiving positive person-centered care but the delivery of integrated care services was evaluated poorly. Different patient subgroups described different experience profiles and priorities. This diversification can inform the design of tailored interventions to address the specific concerns and needs of each patient subgroup.

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AB1400 ARE COMORBIDITIES IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES ASSOCIATED WITH TREATMENT NON-ADHERENCE TO BIOSIMILARS IN A NON-MEDICAL SWITCH SCENARIO?

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Background: The availability of biosimilars has created a financial incentive to encourage non-medical switching if cheaper products are on the market. In patients with chronic inflammatory rheumatic diseases (CIRD), we have previously reported a relatively high retention rate after switching from originator etanercept to its biosimilar. However, this has been different in other studies and the reasons for non-adherence are poorly understood. Comorbidity has recently gained much attention in patients with CIRD and might be a reason for non-adherence.

Objectives: The aim of this study was to analyse the effectiveness and safety of systematic non-medical switching from originator adalimumab (ADA) to ADA ABP501 biosimilar (ABP) over 6 months in patients with CIRD and to investigate the influence of comorbidities on retention rates.

Methods: Patients with CIRD on originator ADA who switched to ABP subsequently from October 2018 onwards were identified from a large routine database and then followed for 6 months. The presence of comorbidities and disease characteristics as well as measures of disease activity, physical function and changes in treatment were documented at baseline (the time of switching from originator ADA to ABP), and at months 3 and 6. Longitudinal data including information on the clinical efficacy and safety of ABP, and the reasons for discontinuation were documented.

Results: A total of 111 CIRD patients on treatment with originator ADA were switched to the biosimilar ABP (Table 1). More than half of the patients (62%) had a Charlson comorbidity score of 0, though there were differences between disease subtypes. RA patients were comparatively older (mean age 65 years) and had the highest mean Charlson score (1.8). Treatment retention varied only slightly between patients with a Charlson score of 0 and those with ≥0 (Figure 1). In both groups, the majority of patients (90% vs 95%) continued therapy with ABP, while only a small proportion either switched back to originator ADA (6% vs 5%), switched to a different biologic (3% vs 0%), or dropped out (1% vs 0%). The main reason for back switch was the occurrence of adverse events, mostly subjective complaints, most frequently pain. Patients with a Charlson comorbidity score > 0 tended to have poorer scores in trajectories of scores for disease activity and physical function stratified by disease subtype.

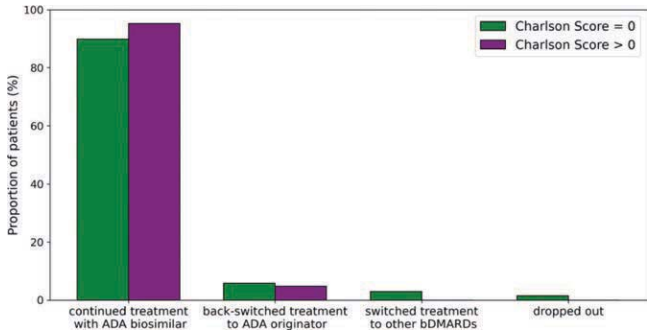

Figure 1. Treatment retention after 6 months stratified by the Charlson comorbidity score

Table 1. ***Patients and disease characteristics***

	RA	axSpA	PsA	Other
	N=23	N=68	N=15	N=5
Age (years), mean (SD)	65.1 (12.0)	47.3 (13.1)	51.1 (11.2)	41.8 (14.2)
Women	60.9% (14)	32.4% (22)	53.3% (8)	40.0% (2)
Disease duration (years), median (IQR)	4.0 (3.0-8.0)	5.0 (2.0-8.0)	4.0 (2.0-13.0)	7.0 (4.0-7.0)
Duration originator ADA therapy (month), mean (SD)	43.8 (28.6)	39.4 (26.9)	34.7 (29.0)	60.9 (27.7)
Charlson score, mean (SD)	1.8 (2.1)	0.6 (1.1)	0.7 (1.2)	0.2 (0.4)
Gastroenterological comorbidities	26.1% (6)	22.1% (15)	6.7% (1)	0
Hepatic comorbidities	17.4% (4)	2.9% (2)	13.3% (2)	0
Hematological conditions	8.7% (2)	2.9% (2)	13.3% (2)	0
Cardiovascular comorbidities	60.9% (14)	32.4% (22)	33.3% (5)	60.0% (3)
Neurological and psychological comorbidities	8.7% (2)	17.6% (12)	33.3% (5)	0
Metabolic comorbidities	21.7% (5)	7.4% (5)	26.7% (4)	40.0% (2)
Osteoporosis	43.5% (10)	11.9% (8)	6.7% (1)	20.0% (1)
Lung diseases	21.7% (5)	8.8% (6)	0	40.0% (2)
Skin diseases	26.1% (6)	26.5% (18)	80.0% (12)	20.0% (1)
Eye diseases	8.7% (2)	23.5% (16)	6.7% (1)	60.0% (3)
Kidney diseases	13.0% (3)	10.3% (7)	0	40.0% (2)

Conclusion: Comorbidity had no influence on the biosimilar retention rate after 6 months in this study but the majority of patients did not have Charlson scores > 0. However, disease activity and physical function tended to be worse among CIRD patients with comorbidity. Cardiovascular disease and osteoporosis were more often present in RA patients than in axSpA or PsA patients, while neurological and psychological comorbidities were more often observed in the latter.

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AB1401

IMPACT OF THE COVID-19 PANDEMIC ON HEALTHCARE UTILIZATIONS OF RMD PATIENTS IN EUROPE. RESULTS FROM THE REUMAVID STUDY (PHASE 1 AND 2)

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Background: The beginning of the COVID-19 pandemic led to a collapse of healthcare systems that was difficult to manage.
Objectives: The aim of this study was to assess the impact of the COVID-19 pandemic on RMD patients' healthcare utilization.
Methods: REUMAVID is an international cross-sectional study collecting data through an online survey on RMD in seven European countries led by the Health & Territory Research group of the University of Seville, together with a multidisciplinary team including patient representatives, rheumatologists, and health researchers. Data were collected in two phases, the first (P1) between April-July 2020 and the second (P2) between February-April 2021. Demographics, health behaviours, employment status, access to healthcare services, disease characteristics, WHO-5 Well-Being Index and Hospital Anxiety and Depression Scale (HADS) were collected in the survey. Healthcare utilization includes scheduled appointments and attendance at the rheumatologist, consultation of possible treatment effects if COVID-19 is contracted with the rheumatologist, primary health care and psychological care. Descriptive analysis and Mann-Whitney test was used to explore association with healthcare utilization in both phases of REUMAVID.
Results: There were a total of 2,002 participants across both phases with comparable demographic characteristics [mean age 52.6 (P1) vs. 55.0 years (P2); 80.2% female (P1) vs 83.7% (P2); 69.6% married (P1) vs 68.3% (P2), 48.6% university educated (P1) vs 47.8% (P2)]. Most prevalent RMD was axial spondyloarthritis in P1 (37.2%), and rheumatoid arthritis in P2 (53.1%). Only 39.2% could have a scheduled appointment with their rheumatologist during P1, compared to 72.5% of patients in P2 (p<0.001). In this sense, only 41.6% of participants in the P1 attended such an appointment while in P2 this figure was 61.5% (p<0.001). The majority of patients (83%) had their scheduled face-to-face appointment changed to an online or telephone phone in the P2, although this proportion was lower in the P1 (54.4%). The most frequent reason for canceling the face-to-face appointment was the alternative of making it by phone or online (54.4% in P1 vs. 83.0% in P2, p<0.001). Although, in P1, 38.1% of participants could contact with their rheumatologist by phone or online, this proportion was 64.3% in P2 (p<0.001). In P1, 64.0% of patients were able to consult with their rheumatologist about the possible effects of treatment in case of contracting COVID-19 (vs. 41.2% in P2; p<0.001). With respect to general practitioners, 57.6% of patients in P1 declared to had accessed primary care or general practitioner (vs. 77.5% in P2; p<0.001). Furthermore, in P2, a higher proportion of participants (63.2%) were able to continue their psychological or psychiatric therapy either online or by phone (vs. 48.3% in P1; p<0.001; Figure 1)
Conclusion: During the first year of COVID-19 pandemic, RMD patients had easier access to the healthcare system, specifically to their rheumatologist. This access was improved through phone and online care. In addition, access to primary care as well as psychological care improved during the second year of pandemic.

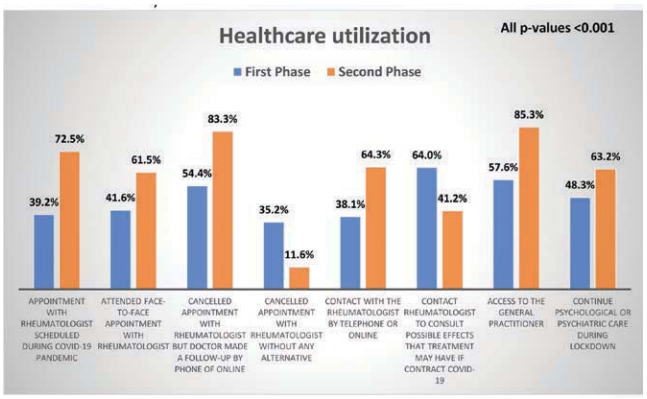

Figure 1. Bivariate analysis of healthcare utilization in P1 and P2 of REUMAVID

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AB1402

FACILITATORS AND BARRIERS OF VACCINE UPTAKE IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASE: A SCOPING REVIEW

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Background: Patients with chronic inflammatory rheumatic diseases (CIRD) remain underrepresented in receiving vaccinations despite being disproportionately affected by infectious complications.
Objectives: To systematically review the literature regarding vaccination willingness and vaccination hesitancy in CIRD patients with focus on the perspective of patients and physicians.
Methods: A scoping review was conducted in PUBMED, EMBASE and the Cochrane Library through 2021. Study selection was performed by two independent reviewers, data were extracted using a standardized form and risk of bias was assessed using instruments from the McMaster University. Identified barriers and hurdles were synthesized by categorizing them into the WHO's Measuring Behavioural and Social Drivers of Vaccination (BeSD) conceptual model.
Results: The search yielded 1,644 hits, of which 30 were included (cross-sectional studies (n=27) based on interviews and 3 intervention studies). The majority of studies reported barriers to influenza and pneumococcal vaccination (n=11), or influenza vaccination only (n=9) from the patients perspective. Two studies assessed the attitudes towards COVID-19 vaccinations. Only one study assessed the view of rheumatologists. Patients mainly mentioned behavioral and social factors that negatively influence their willingness to be vaccinated while physicians see deficits in the organization and lack of time as a major barrier. Coverage of domains matched to the BeSD model suggests a lack of awareness of infection risk by both patients and physicians (Figure 1).

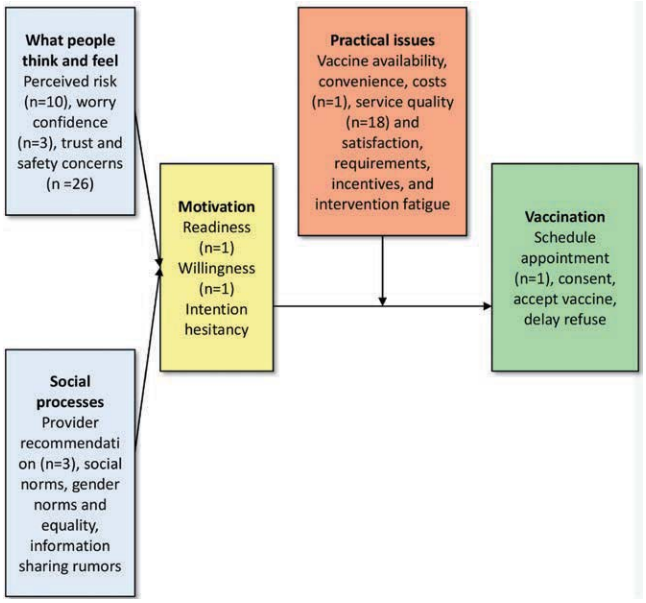

Figure 1. Coverage of domains matched to the WHO BeSD Model

Conclusion: The view of vaccination in CIRD patients diverges between patients and rheumatologists. Our results show that in-depth counseling on vaccines is important for patients, whereas physicians need support in implementing specific immunization recommendations. The themes identified provide a starting point for future interventions to improve vaccine rates in CIRD patients.
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AB1403

IMPACT OF THE SARS-COV 2 PANDEMIC AND RELATED EPIDEMIOLOGICAL RESTRICTIONS ON THE CARE OF PATIENTS WITH OSTEOPOROSIS – EXPERIENCES OF A HUNGARIAN CENTRE

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Background: Treatment of patients with osteoporosis was inadequate even before the COVID-19 pandemic. Not only patients without fracture, but only a small proportion of patients with osteoporotic fracture have treated. In Hungary only 30% of patients with osteoporosis received adequate antiporotic treatment before the pandemic. Almost 90% of whom were women, less than 10% of men. The incidence of fractures is increasing dramatically worldwide. In 2010, the vertebral fracture rate was 3.5 million in Europe but it is expected to reach 4.5 million by 2025. In 1990, osteoporosis caused 1.26 million hip fractures and by 2025 this is estimated at 2.6 million worldwide. The care for patients with osteoporosis was further aggravated by the restrictions necessarily imposed due to the coronavirus.
Objectives: The aim of the study was to explore the extent and consequences of diagnostic and therapeutic failure in patients with osteoporosis.
Methods: I determined the number of osteoporosis examinations performed in our centre in 2019-2021 from the medical database. I surveyed how many patients were discontinued the antiporotic treatment during the pandemic according to the different drug groups in Hungary and also in our centre as well as the prevalence of wrist and hip fractures due to minor trauma in our county in the pre- and post-pandemic period.
Results: In our centre an average of 30 DEXA examinations were performed daily in the pre-pandemic period. From the end of October 2021 to the end of May 2021 there was not perform any ODM examinations. It means 3.980 missed exams and at least 1.000 missed osteoporosis diagnoses and therapy starts. More than 20% of patient were lost from the antiporotic care in Hungary. Drop-out was mainly seen in patients treated with bisphosphonates. There were 20730 bisphosphonate-treated patient in 2019, 19813 in 2020 and 17315 in 2021. Antiporotic treatment was discontinued in 30% of patients treated with bisphosphonate+vitamin-D (7849 in 2019, 6950 in 2020, 5484 in 2021) or bisphosphonate+calcium+vitamin-D fixed combination products (3256-2876-2289). In our centre, the prescribing of bisphosphonates has also decreased more than half. Patients treated with iv. bisphosphonates were interrupted or switched to oral formulations. Denosumab therapy was continuous: 581 injections were prescribed in the 12 months before and 579 during the pandemic. However, no new treatment started. In case of teriparatide, the initiated therapies were continued and even the number of prescriptions increased. As a consequence, an increase in the occurrence of fractures due to minor trauma is expected. Although epidemiological restrictions in this regard, the curfew has had some positive effects. According to international data, the number of wrist fractures has almost halved, while the data for hip fractures are controversial. The decrease of wrist fractures can also be verified in our county. The number of wrist fractures was 598 in April-May 2019, 393 in the same period in 2020, and 372 in 2021. After a significant reduction in hip fractures in 2020, there is already an upward trend in 2021 (470 in 2019, 358 in 2020, 393 in 2021). The real consequences of failure to treat osteoporosis are expected only after years.
Conclusion: Missed doctor-patient appointments were associated with missed diagnoses and interruptions of ongoing treatments. Fear of the virus, immobilisation due to home office and curfews, lack of exercise, sun exposure, caused depressive symptoms, increased alcohol consumption and caloric intake are all increase the risk of osteoporosis. Thus, traditional risk factors for osteoporosis expanded with the direct effects and the introduced restrictions because of the pandemic.
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AB1404

ELECTRONIC CONSULTATION: A USEFUL TOOL TO OPTIMIZE THE ON-SITE MEDICAL CONSULTATION IN RHEUMATOLOGY

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Background: Electronic consultation (e-Consults) is a form of telemedicine. It permits communication between primary health care (PHC) and hospital care (HC). It is proving to be a helpful tool to reduce waiting times in consultations, to prioritize those pathologies that require an on-site consultation and also to avoid unnecessary travel for the patients (1).
Objectives: To evaluate the efficacy of e-Consults to avoid on-site consultations To evaluate the usefulness of e-Consults as a screening tool for on-site consultations To analyze the most frequent reasons for consultation To evaluate the evolution of e-Consults from the first to the second year of its implementation

Methods: Retrospective, observational study of all e-Consults carried out during 2021 in the hospital area *Virgen Macarena*, which includes 47 PHC centres. E-Consults were carried out by the tool "Plataforma de Teleconsultas del Servicio Andaluz de Salud" (teleconsultation platform of the Andalusian health service) as a clinical extension of the research project E-Hermes for the implementation of e-Consults. It collects information about the reason for the consultation, the suspected diagnosis of the rheumatologist, the response time of the TC and whether the consultation is completely resolved online (DISCHARGE), whether on-site consultation is required (CONSULTATION) or whether the patient needs further e-Consults in order to obtain more medical tests or to evaluate the treatment (FOLLOW-UP) The e-Consults of 2021 were compared to those of the previous year.
Results: Of the 733 e-Consults examined, 610 (83.2%) were fully resolved online and 123 (16.8%) required on-site consultation. Of those fully resolved online, 544 (89.2%) were resolved in the first consultation and 66 (11.8%) required more than one e-Consults. The most common reasons for consultation in this group of e-Consults were: suspected diagnoses of osteoporosis (19.1%), polyarthralgia (14.4%), questions about follow-up patients in Rheumatology (9.4%), joint swelling (7%), hand pain (6.8%) and questions about laboratory or imaging tests (3.9%). For 28% of patients, a rheumatic disease could be excluded, and for those patients who were diagnosed with a rheumatic disease, the most frequent diagnosis was: osteoarthritis 17.3%, osteoporosis 14.4%, fibromyalgia 8.3% and gout 3%. Of the patients that were recalled for an on-site evaluation, in 101 of the cases (90%) this decision was taken after the first e-Consults, while 11 patients (10%) were recalled after subsequent e-Consults. Among the patients recalled for an on-site visit, the most common reason was joint inflammation (23.4%), followed by polyarthralgia (22.1%), osteoporosis (18.2%) and hand pain (7.8%). The most frequent suspected diagnosis was inflammatory rheumatic disease (RA, PsA, SpA) in 49.4% of cases, followed by osteoporosis (24,4%) The average response time of the e-Consults was 82 hours (3 days and 10 hours) Compared to the e-Consults in 2020, it increased by 34%, 186 e-Consults more. The number of cases resolved without on-site consultation was 29% higher than in the previous year, while the e-Consults that required follow-up decreased by 7% and the number of patients that required further on-site consultation also decreased by 11%. The reasons for the consultation and suspected diagnosis were similar in both years.
Conclusion: E-Consults has proved efficacious, avoiding the necessity for on-site consultations in more than 80% of the patients. E-Consults helps to reduce on-site referrals to Rheumatology. E-Consults is effective in reducing waiting times before obtaining an evaluation from the rheumatologist and in prioritizing those patients who need on-site consultation. There are certain pathologies that are especially amenable to resolution without on-site consultation, like osteoarthritis, osteoporosis and fibromyalgia Over time, e-Consults is being integrated in the clinical practice of both the primary care physician and the rheumatologist and is becoming ever more efficient.

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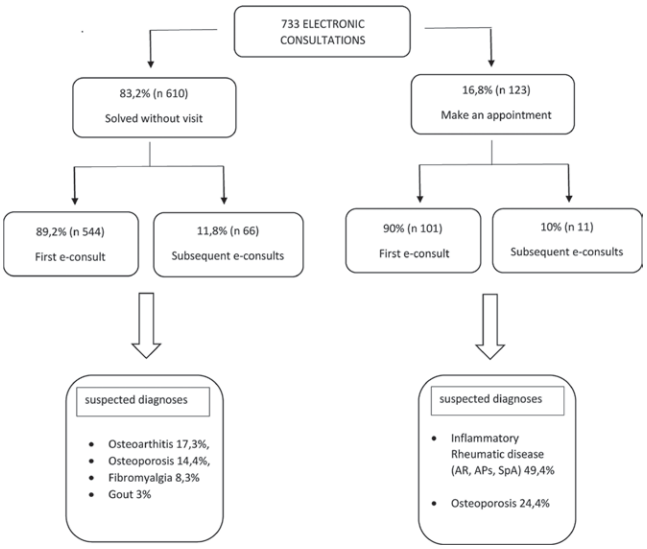

Figure 1.

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AB1405 THE USEFULNESS OF TELEMEDICINE IN RHEUMATOLOGY: POINTS OF VIEW OF PRACTITIONERS AND PATIENTS

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Background: The advent of COVID-19 has allowed a rapid expansion of telemedicine (TM) and its implementation in various specialties. Despite this extensive use of TM, its role in rheumatology is conflicting and much remains unknown about TM's acceptability and efficiency in rheumatology [1].
Objectives: Our study aimed to evaluate rheumatologists' and patients' willingness for TM and factors helping to adopt this alternative.
Methods: We conducted a cross-sectional study including patients attending our rheumatology department as well as rheumatologists. Patients were contacted by phone and rheumatologists were invited to answer a questionnaire via Google Form. We evaluated their points of view and suitability for TM by inquiring about their experience with tele-rheumatology, information technology supports, personal barriers to telemedicine, and reasons for adopting this alternative. Moreover, additional questions probed the clinician's perception of the appropriate clinical context for TM application as well as the corresponding legislation.
Results: Overall, 135 responses were collected including 60 rheumatologists and 75 patients. The distribution of diagnosis was as follows: rheumatoid arthritis (RA) (n=15), spondyloarthritis (SpA) (n=20), juvenile idiopathic arthritis (n=23), and osteoarthritis (n=17). Of the rheumatologists, 76.2 % were aged between 30 and 50 years old, 79.3% reported working at an academic center, and the majority were physician-level practitioners (71.2%), working for more than 5 years (61%). Afforded electronic devices were as follows: laptop (87.9%), smartphone (70.7%), afforded headset microphone (24.1%), camera (29.3%) for doctors. Forty-six percent of the rheumatologists estimate that they have a good internet connexion, 62.7% had an appropriate place for teleconsultation. Nearly, 40.7% of the rheumatologists were familiar with the concept of TM but only 39% reported experience with TM. Willingness to accept this model of care for rheumatologists and patients was found in 78% and 37.3% respectively. According to the doctors, the benefits of TM encompassed tele-training (61.7%), remote medical monitoring (61.7%) especially during the COVID-19 (70.2%), benefits for patients (74.5%), reduced inequalities in access to healthcare (46.8%), and improved quality of care (29.8%). The main barriers to TM were the lack of clear legislation (47.8%) and financial compensation (17.4%). Clinicians and patients identified common barriers to effective tele-rheumatology as the inability to perform a physical exam (91.3% vs 33.3%), the fear of trivializing the disease (34.8% vs 36%), and the lack of resources and infrastructures (43.5% vs 29.3%). The majority of the doctors (86.2%) expressed their willingness to attend training workshops. Reported areas to apply TM according to the doctors were mainly osteoarthritis (76.3%) and rheumatic diseases (64.4%), but also pediatric rheumatology (28.8%) and undiagnosed new patients (3.4%). Regarding legislation, most of practitioners estimated that it should be selective with specific authorizations (42.4%) or relaxed with the possibility of derogation (32.2%). Twenty-two percent of them reported that legislation should be strict with the possibility of sanctions, whereas a minority (3.4%) opted for a free practice without regulation at all. Factors associated with adherence to TM were age<40 years (p=0.036) for doctors and familiarity with the concept (p=0.006) and electronic devices afforded (p=0.000) for the patients.
Conclusion: Findings from this study showed the reluctance of the patients to adhere to TM compared to doctors. Concerns and risks may lessen for both sides, once remote consultations are applied. Nevertheless, patient education is required for the success of TM application.

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AB1406 TELERHEUMATOLOGY FOR IMPROVING FIRST ACCESS TO THE OUTPATIENT CLINIC: A PILOT PROSPECTIVE MONOCENTRIC ITALIAN STUDY

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Background: The COVID-19 public health emergency has amplified both the potential value and the challenges with healthcare providers deploying telehealth solutions. Furthermore, outpatients may wait up to several months for their first

appointment with specialists including rheumatologists for diseases other than COVID-19. In Italy it is now possible to get access to telemedicine services within the national healthcare systems, yet only follow-up visits are allowed for reimbursement purposes. Instead, it is not clear the role of telemedicine as a tool for improving first access and patient acceptance of this innovation.

Objectives: To investigate the feasibility of a '*teletriagerheum*' service before the first visit and to identify potential benefits and disadvantages of it by comparing first face-to-face visit preceded by '*teletriagerheum*' service to regular first visit without it.

Methods: A pilot prospective monocentric study was conducted. Consecutive patients were contacted by phone 30 days before the scheduled rheumatological first visit by administrative staff to investigate their willingness to receive 20 days before the first visit a phone call ('*teletriagerheum*' service) by a physician of the Rheumatology Unit. The '*teletriagerheum'* service aimed at investigating the reason for the visit and at prescribing additional exams or specialistic consultations before the face-to-face first visit to facilitate the diagnosis process or anticipate the appointment in case of urgency. Socio-demographic characteristics, reason for referral, face-to-face visit duration, number of additional exams prescribed, number of definite diagnosis at first visit in the '*teletriagerheum*' group were compared to the ones receiving regular first visit without '*teletriagerheum*' service.

Results: In October 2021 a total of 102 patients were phone called by administrative staff: 18 (17.6%) did not answer for a maximum of three times, 9 (8.8%) responded but refused the 'teletriagerheum' service (6 cancelled the visit, 1 postponed, 2 for unknown reason) and 75 (73.5%) accepted the service, but 21 were not real first visits and 8 patients did not answer the call of physician. Among the remaining 46 (45.1%) pts (the 'teletriagerheum' group) the median call time was 11.5 minutes (IQR 5-15 min), blood exams were prescribed to 34 (74%) and instrumental exams to 8 (17.4%). Further consultation was prescribed only to 1 patient and the visit was not anticipated in any case. A preliminary diagnosis was possible in 36 (78.2%). In most of the cases (33, 76%) no difficulties were reported by the physician, in 7 (16.3%) there were difficulties in communication, in 1 (2.3%) difficulty to get the history from a patient suffering from a psychiatric disorder. Socio-demographic characteristics, Information and communication technologies skills, face-to-face visit duration were not statistically different between the '*teletriagerheum*' group (46 pts) and the group receiving regular first visit without '*teletriagerheum*' service (52 pts). In the '*teletriagerheum*' group, a lower number of blood exams (14% vs 46%, p<0.005) and a lower number of instrumental exams (25% vs 45%, p=0.04) were prescribed during the face-to-face first visit; a higher percentage of definitive diagnosis (79% vs 67%, whilst not statistically significant p=0.2) and a lower number of patients requiring a visit before 6 months (26% vs 54%, p<0.05) were observed compared to the group without teletriagerheum service.

Conclusion: These preliminary data showed that telemedicine for the first rheumatological visit was well-accepted by patients searching for rheumatology consultations and had the potential to be a tool for improving clinical diagnosis and rheumatological follow up in everyday clinical practice. A larger cohort will let us to further explore the potential benefits of telemedicine to improve accessibility to rheumatological services.

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Disclosure of Interests: None declared

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AB1407 TELERHEUMATOLOGY AND WORKING VISIT: INITIAL MONOCENTRIC EXPERIENCE ON USE OF TELEVISIT IN THE REGULAR FOLLOW-UP.

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Background: The COVID-19 pandemic shifted most healthcare to remote delivery methods (telehealth technologies including clinical video televisit) to protect patients, clinicians, and hospital staff. Telerheumatology visits were found to be noninferior to in-person visits and are often more time and cost effective for patients.[1]

Objectives: Description of an initial integration of video televisit in regular follow-up.

Methods: In cooperation with the ALTEMS Operational Telemedicine Observatory, we built a procedural manual for televisit, whose phases were as much as possible similar to the usual visit scenario. Patients in remission or in mild disease activity at the time of enrolling visit were involved. Clinical characteristics, treatments and televisits' features were considered for all patients (Table 1). Patient overall satisfaction was evaluated (rating 1 to 5).

Table 1.

Patients (n.)	74
M/F	27/47
Age (y) median	46.2±13.5
RA n. (%)	19 (25.6)
PsA n. (%)	21 (28.3)
SpA (%)	13 (17.5)
CTD n. (%)	8 (10,4)
Vasculitis n. (%)	7 (9.4)
Other n. (%)	6 (8.1)
b or tsDMARDs n. (%)	20 (62.5)
Televisits n.	86
Mean duration (min.)	17±3.5
Satisfaction (1-5)	4.68
Device (PC/smartphone) %	62.5/37.5
Distance saved, mean (km)	77,5
Time travel saved, mean (min.)	66
CO2 saved (kg)	866.71
€ saved (per patient)	44,37
Working visit n. (%)	5 (15.6)

Results: 86 televisits were performed in 74 consecutive patients, with a mean age of 46.2 ± 13.5 years, diagnosed with the most common rheumatic diseases and on chronic immunosuppressive therapy (c-b-ts DMARDs mono or combination therapy). In 5 cases, in-person visit after televisit was required. the average duration of the televisit was 17 ± 3.5 minutes and the average overall satisfaction was 4.68 / 5. The average distance saved (round trip) was 77,5 km, equal to an avoided travel time of 66 minutes and with a total reduction in CO2 production of approximately 866 kg. 5 patients performed video visit from workplace, de facto inventing the "working visit."

Conclusion: Telemedicine is going to become an essential element of clinical practice in rheumatology,[2] especially for active, young, and working patients, helping to minimize the overall impact of the disease on QoL, as far as they are properly selected for clinical characteristics and informatic skills. The possibility to attend to televisit from the workplace will reduce the lost working-hours and the need of travel, thus acquiring undoubted social utility. In the near future, the use of televisit should be also extended to vulnerable patients lacking basic informatic resources, with the help of care-givers or dedicated territorial services.

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[2] https://www.salute.gov.it/imgs/C_17_pubblicazioni_2129_allegato.pdf ALTEMS = Alta Scuola di Economia e Management dei Sistemi Sanitari

Disclosure of Interests: None declared

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AB1408 WELL-BEING AND MENTAL HEALTH OF RHEUMATOLOGY AND FAMILY MEDICINE RESIDENTS

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Background: Burnouts and poor well-being among medical residents are becoming a global concern for health institutions. Its negative consequences are far-reaching, affecting patients, coworkers, family members, and healthcare organizations as well as the burned-out resident.

Objectives: The aim of the study was to measure the extent of burnout among rheumatology and family medicineresidents'and to elucidate wellness status as well as barriers to wellness.

Methods: An online questionnaire was issued to rheumatology and family medicine residents. We collected sociodemographic data (Age group, gender, marital status, children, smoking and alcohol status, Sport and other activities, Specialty, Weekly working Hours,Vacation) and mental health measurements. Participants were also requested to fill the 14-item Mental Health Continuum Short Form (MHC-SF) and the 5-item WHO-5 well-being form. Multivariable logistic regression analysis was used to explain the relationship between well-being and the work circumstances.

Results: A total of 64 residents with a 0,28 sex-ratio completed the online questionnaire. Sixty-nine percent (69%) of responders were in the [25-29] age group. Sixty three percent (63%) of responders were single and 14,1% had children. Most residents were not smokers (76,6%) nor alcohol users(68,8%). Eighty seven percent of responders were a family medicine resident. Thirty

four percent (34%) of responders practiced sports 2 to 4 times a year and 25% exercised 2 to 4 times a week. The average working hours per week was 30 hours [10-70] with an average of 3,38 weeks' vacation per year. Seventy eight percent (78%) of residents worked overnight shifts in hospitals with an average of 1,83 shift per month. Female sex (p=0,049), less physical activities (p=0,037) and long working hours (p=0,042) were associated with worst degree of quality of life (WHO5 Well-Being Index). Residents who practice art and had fewer overnight shifts showed a significantly flourishing mental health (p=0,032, p=0,014) according to the MHC-SF. Family medicine residents had more long working hours (p=0,039) and overnights shifts (p=0,047) than rheumatology residents.

Conclusion: Residents working more than 50 hours per week with more than 5 overnight shifts per month and those practicing fewer physical activities and art appear to be at high risk of developing languishing mental health according to the Who5 well-being index and the MHC-SF score. It is important to protect health care workers and to promote well-being to acquire a flourishing mental health.

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AB1409 EVALUATING HOW EFFECTIVELY PATIENTS WITH A NEW INFLAMMATORY ARTHRITIS ARE BEING TRIAGED INTO THE APPROPRIATE CLINIC AT A TERTIARY CARE HOSPITAL IN THE UK: A RETROSPECTIVE AUDIT.

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Background: Inflammatory arthritis is associated with significant morbidity and costs to the NHS, social care, and wider economy. Early diagnosis and treatment are essential to reduce the impact of the disease. Therefore, it is important that referrals for a new inflammatory arthritis are appropriately triaged to be seen in the early inflammatory arthritis (EIA) clinic so that they can be seen and started on disease modifying anti-rheumatoid drugs (DMARDs) without delay. The British Society of Rheumatology guidance for inflammatory arthritis states that patients must be seen within three weeks of referral and started on DMARDs within six weeks.

Objectives: To evaluate how effectively people referred with a new EIA are currently being triaged. To evaluate whether we are meeting the national standards.

Methods: We performed a retrospective review of the medical notes of all new patients who were seen in the EIA clinic from 01/09/21-31/11/21. During this same time period, we will also reviewed all the patients who had been newly diagnosed and started on a DMARD in the other Rheumatology clinics (e.g., general rheumatology, vasculitis). We collected data on referral date, referral source (e.g., GP), date of clinic assessment, clinic type (e.g., EIA clinic or other Rheumatology clinic), diagnoses made, days' wait from referral to assessment and days' wait from referral to commencing DMARD. We then calculated the conversion rate (percentage of referrals triaged to the EIA clinic that have an EIA) and detection rate (percentage of new EIA patients that are seen in the EIA clinic (as opposed to in non-urgent clinics)). The standard for conversation rate (CR) was 50% and for detection rate (DR) was 95%.

Results: Of all the patients seen in the EIA clinic (n=73), 36 had a new diagnosis of an EIA, giving a CR of 49%. Of all the new diagnoses of EIA made during that time-period (n=53), 36 were appropriately triaged to be seen in the EIA clinic, giving a detection rate 68%. Those new referrals who had been appropriately seen in the EIA clinic had an average of 5 weeks wait from referral to assessment/ commencement of DMARD. In contrast, those new referrals who had been seen in other clinics had an average of 10 weeks from referral to assessment/ commencement of DMARD. A previous audit performed before the COVID-19 pandemic (01/11/19- 01/01/20) showed a CR of 25% (115 patients seen in EIA clinic, 29 new diagnoses) and a DR of 69% (29 new diagnoses, 20 seen in EIA clinic). **Conclusion:** Those patients with a new EIA who are appropriately seen in the EIA clinic do not meet the national guidance for being seen within three weeks of referral but do meet the guidance for starting a DMARD withing six weeks. However, those new EIA who are seen outside the EIA clinic do not meet either of these standards, with a delay of 10 weeks to be seen/ started on a DMARD. Given that only 68% of people with a new EIA are being correctly triaged to be seen in the EIA clinics, it highlights that there is a need for an improvement in the triage process (currently being done manually by Rheumatologists). Interestingly, when comparing our findings to the audit done pre-COVID-19 pandemic, the CR has improved whilst the DR has stayed steady. The next steps include exploring using additional data collected from patients electronically to improve the CR/ DR rates, as well as artificial intelligence informed modelling.

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AB1410 IMPACT OF COVID-19 PANDEMIC ON HEALTHCARE RESOURCE USE AND CLINICAL OUTCOMES IN A COHORT OF PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES- AN INTERIM ANALYSIS FROM THE PER-MAS PROJECT.

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Background: Management of the health emergency caused by COVID-19 pandemic majorly disrupted the delivery of healthcare services to patients with chronic conditions like Systemic Autoimmune Diseases (SAD), both because resources were mainly channeled towards the care of infected patients, but also because patients tended to avoid seeking medical care for fear of becoming infected. PER-MAS is a 2-year project aimed at assessing the clinical, psychopathological, and socio-economic impact of COVID-19 in a cohort of patients with SAD.

Objectives: To assess the impact of COVID-19 pandemic on drug withdrawal, disease flares and hospitalizations for disease exacerbation in a cohort of patients with SAD through an interim analysis of data from the PER-MAS project.

Methods: A sample of 214 consecutive patients was recruited in a reference center for rare and complex autoimmune diseases from April 2021 to January 2022. Inclusion criteria were definite diagnosis of SAD (Connective Tissue Disease (CTD), Inflammatory Arthritis (IA) or Vasculitis), regular follow-up and at least 2 years of disease. Patients were asked to fill out an extensive self-administered questionnaire on disease activity and healthcare resource use during the pandemic (March 2020-moment of assessment). Pre-pandemic (March 2019-February 2020) and early pandemic (March 2020-February 2021) clinical data were recorded through retrospective chart review and patient interview.

Results: At enrolment, 119 patients were affected by CTDs (55.6%), 71 by IA (33.18%), 24 by vasculitis (11.21%), with mean age 50.44± 12.97, and mean disease duration 11.17 ± 8.94. 30.37% took steroids, 39.7% hydroxychloroquine, 61.68% DMARDs, and 9.3% vasoactive drugs. Overall, disease course was similar in pre-pandemic and early pandemic phase: in the first period, rheumatologic condition was stable in 57.35% of patients, persistently active in 27.3% and 35.61% had ≥ 1 episode of disease exacerbation (mean 0.665±1.15, range 0-6); in the second period, 60.56% of patients was stable, 24.88% persistently active, and 39.44% had ≥1 exacerbation (mean 0.49 ±0.77, range 0-4). Mean number of visits (2.56±2.57 and 2.61±2.79), hospitalizations (0.168±0.698 and 0.14±0.473, p=0.6), number of patients with outpatient visits=0 (7.47 vs 7%), and number of patients with ≥ 1 hospital admission (10.28 vs 11.6%) were also similar, while the number of patients with hospital admissions for disease exacerbation was significantly higher in the second period (6.1 vs 11.21%, p=0.001). 170 patients completed the survey: from March 2020 to enrolment, 18.2% suspended ≥*1* anti-rheumatic drug (6.25% of them for fear of contracting COVID-19 disease, 15.6% for difficulty in obtaining medications), 20% self-managed ≥ 1 disease exacerbation, and 40% had ≥ 1 telemedicine consult. From March to July 2020, 41.76% had their visit rescheduled (35.23% for hospital access restrictions, 5.3% for travel restrictions, 1.17% for fear). Conversely, only 14.7% of patients had their visit rescheduled (8.23% for hospital access restrictions, 4.7% for other reasons) from July 2020 to enrolment.

Conclusion: In the early pandemic phase, overall disease course was similar to the pre-pandemic phase, but we observed an increase in the number of patients with ≥ 1 hospitalization for disease. Moreover, despite our efforts, patients reported a non-negligible rate of drug discontinuation for non-medical indication and difficulty to get access to rheumatologic consultation, highlighting the need of alternative organizational models in case of future pandemics.

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AB1411 JOINT RHEUMA-DERMA CLINIC: FOUR YEARS OF EXPERIENCE AT THE SAN MARCO HOSPITAL IN CATANIA

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Background: Psoriatic arthritis (PsA) affects up to one-third of patients with psoriasis. Many recent works in literature have underline that the percentage of undiagnosed PsA is still high. A direct collaboration between dermatologists and rheumatologists appears fundamental for a better management of these patients, to reduce the risk of joint damage, disability, and comorbidities.
Objectives: The aim of this study is to highlight the benefits of a Rheuma-Derma clinic and a shared approach, focused to an early diagnosis and prompt therapeutic strategy of PsA.
Methods: Patients with psoriasis complaining joint symptoms or rheumatologic patients with cutaneous involvement, were simultaneously assessed by a dermatologist and a rheumatologist. The collected data included demographics, clinical characteristics as joint patterns (axial/peripheral), clinimetric index evaluated (DAS28, HAQ, BASDAI, DAPSA, PASI, PGA) family history of psoriasis or PsA, BMI (Mass Body Index), psoriasis, comorbidities and Charlson Index, gastrointestinal and ophthalmic involvement, and previous and current treatments with conventional (csDMARDS) and/or biological therapy (bDMARDs).
Results: During the period from 2012 to 2016 the Rheumatology Department registered 255 of patients under biological treatment, against 374 of patients during the Rheuma-Derma Clinic (2017-2021), with an increase of 47% in number. CsDMARDs therapy counted 367 patients before the Rheuma-Derma Clinic and 539 after the shared outpatient activity, with a raise of the 46%. Globally the number of patients with the diagnosis of PsA moved from 622 to 913, reaching an increase of 47% of patients. The joint pattern have shown a peripheral involvement in 69.3% of cases in comparison to 11% of cases with axial involvement and a mixed for the rest of population, 19.8%. In the group analyzed 539 patients were treated with csDMARDs, 76.5% methotrexate, 30.7% salazopyrine and only 6.7% with cyclosporine. 374 patients under treatment with bDMARD: the majority of patients (86.1%) were treated with TNFα inhibitors, 25.4% Secukinumab, 20.1% Ustekinumab, 16% Apremilast, 4.8% Ixekizumab, 1.1% Tofacitinib. The Charlson Comorbidity Index (CCI) assesses comorbidity level by taking into account the number, the severity of pre-defined comorbid conditions and the age of patients. It provides a weighted score in a range from 0 to 8, which can be used to predict short term and long-term outcomes such as function, hospital length of stay and mortality rates. In our study the majority of patients (27%) had a score of 2 while fortunately only 0.5% of population had a score of 8. The most frequent comorbidities registred in our cohort were hypertension (24.6%) and dyslipidemia (28.3%). Psoriasis was diagnosed in 41% of patients: in 80% of them the skin disease preceded the articular symptoms while 20% of patients developed psoriasis after the arthritis onset. History of family psoriasis was positive in 26% of patients. The nails involvement was observed only in 8% of patients, followed by gastrointestinal disorders (3%) and uveitis (7%). The value of BMI (Body Mass Index), the majority of patients (56%) have shown a normal weight, followed by over-weight patients (31.7%); only 10% of patients presented an obesity grade I and 1.1% an obesity grade II-III. For all the clinimetric index evaluated (DAS28, HAQ, BASDAI, DAPSA, PASI, PGA), there was an improvement over the twelve months under the Reuma-Derma clinic
Conclusion: In conclusion, the diagnosis of an Early PsA is essential, as an early treatment and management can alter the natural course of PsA and prevent irreversible joint damage. Our experience proved the increased number of patients since the Rheuma-Derma Clinic have started, such as an increased number of patients under treatment, leading to a significant improvement in the quality of life of PsA and Pso patients.
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AB1412 IMPORTANCE OF TELEMEDICINE IN THE SYSTEMIC SCLEROSIS DURING COVID-19 PANDEMIC

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Background: Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2), also called COVID-19 disease, was firstly reported in December 2019 in China and soon declared a pandemic by the World Health Organization (WHO) on March 11, 2020 (1). As a result, patients' visits to medical facilities are affected. Systemic sclerosis (SSc) is a chronic systemic autoimmune disease characterized by vascular damage, autoimmunity, and fibrosis. In these patients, a tight follow-up is crucial to verify the specific cases and clinical needs. In particular, the infection risk in SSc might also be related not only to disease activity but also to possible flares due to therapy discontinuation. Telemedicine has demonstrated as a valid alternative to improve the quality of rheumatic patients' care during COVID-19 pandemic, thus reducing hospitalizations only to urgent admissions (2)
Objectives: In december 2020 the Azienda Policlincio Vanvitelli approved telemedicine by IRPLUS platform as a particular measure in the face of the COVID-19 pandemic. In this study we examined the impact of the COVID-19 pandemic on visit status of SSc patients at our centre and the patient benefits of telemedicine
Methods: In this study, we retrospectively enrolled 480 SSc patients who visited in our centre between January and December 2021. Of the patients included in the study, 198 patients (18 males and 180 females) used telemedicine, while 282 patients (20 males and 262 females) did not use it
Results: During televisites, we assessed possible contacts with COVID-19 patients and/or potential risk of COVID-19, investigating about the occurrence of typical symptoms in the last 15 days. No significant differences in background data, such as the severity of the disease, type of treatment and frequency of complications were found between these two groups. In more detail, SSc is associated interstitial lung disease was complicated by 35.4% and 31.3% of patients in the telemedicine and non-telemedicine groups, respectively (p=0.9). Besides, 53.7% of patients in the telemedicine group and 49.9% of patients in the non-telemedicine group were treated with prednisone (p=0.344). 74.1% of patients in the telemedicine group were administered immunosuppressive drugs, compared to 78.5% of patients in the non-telemedicine group (p=1.000). The number of patients who discontinued treatment was significantly lower in the telemedicine group, with 14 patients (7%) compared to 30 patients (11.4%) in the non-telemedicine group (p=0.003). These patients who voluntarily discontinued treatment were finally resumed. However, the time required to resume treatment differed between the two groups. This means that the duration of treatment interruption was significantly shorter in the telemedicine group, with a mean (± standard deviation) of 1.85 (5.5) days compared to 7.5 (12.1) days in the non-telemedicine group (p=0.001). There was no difference in the amount of change in laboratory data between the groups receiving telemedicine and those not receiving telemedicine.
Conclusion: This study confirmed the data published by Norimatsu et al (3), as that telemedicine may help SSc patients to continue and/or resume treatment under the COVID-19 pandemic. SSc is associated to interstitial lung disease, cardiac involvement, vascular injury and prednisone and immunosuppressive agents have been used as treatment. Thus, disruptions in treatment can lead to worsening of symptoms and missed opportunities for early interventions for complications. Patients who use telemedicine may be more motivated to treat, and this retrospective study demonstered it. This study suggests that telemedicine can be useful in treating SSc and other diseases that require ongoing treatment in the COVID-19 infection.
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AB1413 SURVEY ON THE PRESCRIPTION OF GENERAL CORTICOSTEROID THERAPY BY MOROCCAN RHEUMATOLOGISTS IN RHEUMATOID ARTHRITIS

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Background: The prescription of glucocorticoids at the diagnosis of rheumatoid arthritis (RA) is no longer systematically recommended because of the difficulty of withdrawal and the occurrence of adverse effects. The expert groups currently insist on a short duration of corticosteroids to obtain a low cumulative dose (1, 2). The real-life applicability of the current recommendations may be difficult to achieve (3).
Objectives: Moroccan rheumatologists were interviewed about their experiences on prescription of general corticosteroid therapy during the diagnosis of RA.
Methods: We conducted a descriptive cross-sectional study of practice conducted with the Moroccan rheumatologists belonging to public and private sectors according to a questionnaire established on a declarative and anonymous mode. The questionnaire was validated by a committee of experts before submitting them to rheumatologists and consisted of 24 single or multiple-choice questions. These questions were divided into 5 items: general data (3 questions), initiation of corticosteroid therapy at diagnosis (7 questions), withdrawal modalities and problems of withdrawal (8 questions), self-medication and patient information (6 questions). The elaboration of the questionnaire was done in "Google Forms" then the collected data were analyzed with the Microsoft office software Excel 2013.
Results: A total of 100 Moroccan rheumatologists responded to the questionnaire. In the initial treatment of RA, 14% of the rheumatologists reported starting corticosteroid therapy in all patients, 41% in two-thirds of their patients, 23% in one-third, 20% in half and 2% in none. The initial oral dose of prednisone or equivalent was 7.5 to 10 mg/day for 52% of rheumatologists and between 5 and 7.5 mg/day for 38%. Flare-up of activity and accompanying conventional treatment were the two first indications for initiation of corticosteroid therapy. 46% of rheumatologists considered weaning after 3 to 6 months of treatment, 26% between 6 months and one year, 23% in less than 3 months and 5% in more than one year. 35% achieve withdrawal in two thirds of their patients. The main problems encountered during withdrawal are self-medication and rebound of the disease. 96% of rheumatologists were in favour of introducing therapeutic education sessions using different tools adapted to the context of the patient and the disease.
Conclusion: The prescription of corticosteroids in RA must be based on the evaluation of the risk-benefit balance. A collaboration between rheumatologist and patient is necessary to prevent the risk of toxicity of corticosteroids and to achieve the goal of withdrawing them.
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AB1414 THE COST OF PRENATAL CARE IN WOMEN WITH RHEUMATIC DISEASES.

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Background: In Mexico, over 60% of the population is uninsured and not able to afford private healthcare services. Women with autoimmune rheumatic diseases (ARDs) are a high-risk group during pregnancy. Morbidity associated with ARDs and pregnancy can include lower birth weight, increased preterm delivery, and more emergency cesarean sections than pregnant women without ARDs. Close monitoring and multidisciplinary care are necessary to prevent and timely treat complications, on the other hand these health interventions are not available to all women with ARDs because of the high prices that it represents.
Objectives: The aim of this study was to estimate the cost of prenatal care in women with ARDs without health insurance in Northeast Mexico.
Methods: To assess the costs of prenatal care of women with ARDs in the Northeast of Mexico from the perspective of a women without any health insurance, we estimated only the direct costs of the mandatory medical follow-up. Direct costs are all healthcare costs that are directly related to the consultations with a multidisciplinary team, serological and immune laboratory test, and ultrasounds per trimester. All costs and medical fees were obtained from a university hospital in Monterrey, Mexico. To assess the impact of prenatal care in real life, we compared the health expenditure per trimester reported by the pregnancy and rheumatic diseases clinic from the same institution. The data is presented in USD. We were not able to assess indirect costs related to health coverage (like transportation) and specific medical treatment (antirheumatic drugs or other interventions).
Results: The mean cost for medical consultations and ultrasounds per trimester was $184-277 USD. The average cost of immune test and general lab test ranges from $424-428 USD. The total cost per trimester was from $608 to 705 USD, and the direct cost per three trimesters was $1824-2115 USD.
The average family income per month was $614.23 USD and the average health expenditure (per month) was 105.71 USD; which represents 16.21% of the family income. The average family health expenditure per trimester was $317.13 USD.
Conclusion: The total cost for prenatal care per trimester was calculated in $608 to 705 USD. The cost of prenatal care per trimester is 193.69% higher than the average health expenditure per trimester for uninsured women with ARDs. More and new strategies are needed to solve and reduce inequalities in access to health.

Table 1. Average cost of prenatal care per trimester

Medical consultations and ultrasounds			
Medical Consultations	**Costs (USD)**	**Frecuency**	**COST PER TRIMESTER $184-277 USD**
Rheumatologist	$13	Monthly	
Genetics	$49	At least one	
Obtetrician	$14	Monthly	
US 1st Trimester	$54	Only one time	
US 2nd Trimester	$49	Only one time	
Psychologist	$39	If needed	
Nutritionist	$5	If needed	
Clinical test			
Clinical test	**Costs (USD)**	**Frecuency**	**COST PER TRIMESTER $188 USD**
Complete Blood Count	$9	One per trimester	
Blood Chemistry	$38	One per trimester	
Vitamin D (25-OH)	$59	One per trimester	
Thyroid profile test	$16	One per trimester	
PT, TTP	$36	One per trimester	
Protein C reactive	$20	One per trimester	
Erythrocyte sedimentation rate	$5	One per trimester	
Urine general test	$5	One per trimester	
Immune lab test (For patients with rheumatoid arthritis and spondylarthritis)			
Immune lab test	**Costs (USD)**	**Frecuency**	**COST PER TRIMESTER $240 USD**
Rheumatoid factor	$24	One per trimester	
Anti-CCP	$33	One per trimester	
Anti SS-A/RO	$19	One per trimester	
Anti-SS-B/LA	$19	One per trimester	
Anticardiolipins	$33	One per trimester	
Beta-2-glycoprotein	$66	One per trimester	
Lupus anticoagulant	$46	One per trimester	
Immune lab test (For patients with lupus, antiphospholipid syndrome, Sjogren's syndrome, vasculitis, and others) (Others: rheumatic skin and muscle diseases,)			
Immune lab test	**Costs (USD)**	**Frecuency**	**COST PER TRIMESTER $236 USD**
Anti-SS-A/RO	$21	One per trimester	
Anti-SS-B/LA	$21	One per trimester	
Anticardiolipins	$33	One per trimester	
Beta-2-glycoprotein	$66	One per trimester	
Lupus anticoagulant	$46	One per trimester	
Anti-DNA	$24	One per trimester	
Antinuclear antibodies	$25	One per trimester	

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AB1415

GENDER EQUITY IN RHEUMATOLOGY IN GERMANY, WHERE DO WE STAND? – PRELIMINARY RESULTS FROM A NATIONWIDE ONLINE SURVEY AMONG RHEUMATOLOGISTS IN GERMANY

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Background: Despite the increasing number of female medical students and fellows, women are still underrepresented in higher career and academic positions in rheumatology [1].
Objectives: To assess gender distribution in rheumatology in Germany and to analyze potential hurdles of flexible work opportunities with the overall aim to improve gender equity in future German rheumatology.
Methods: A web-based anonymous survey using QuestionPro was distributed among rheumatologists in Germany via newsletters, social media and personal contacts (12/2021-01/2022). The survey was developed based on a narrative literature review [1] and discussions among the commission members. It was composed of 29 questions, with single or multiple answers and/or free text. Non-demographic questions could be answered with "I do not know".
Results: Among the total of 170 respondents who fully completed the survey, 72% were female, 28% were male and 1% was third gender. 73% were employed at a rheumatology clinic with 79% working at an academic institution and 20% at a non-academic clinic, 1% did not specify their institution. Of those working at a clinic, 48% were rheumatologists in training, 35% trained rheumatologists and 7% were head of rheumatology departments. Regarding the gender-ratio in different hierarchical levels, only 17% reported more male than female rheumatologists in training at their workplace, in 32% the gender ratio was balanced. On higher levels, respondents reported more male than female rheumatologist at staff level in 44% (29% balanced) and in leading positions in 74% (12% balanced). 53% of female respondents were responsible for >50% of family and housework, compared to 11% of the male respondents. Most men covered 50% (49% of male respondents) or less than 50% (32% of male respondents) of family work. There were coworkers in part time in the work environment of 86% of respondents, with only women working part time in 56% of cases, both women and men in part time in 29% and only men in part time in 1%. Most respondents stated that men and women working part time did not have the same opportunities as coworkers working full time. (Table 1)

Table 1. Opportunities for advancements of part time working employees compared to full time coworkers with similar qualification in percent of all respondents.

Employees working part time have similar opportunities for advancements as employees of the same gender working full time.

	Yes	No	I do not know
Women	23%	65%	12%
Men	21%	54%	25%

Many respondents perceived a preference of either gender despite equal performance regarding different aspects with men more often perceived as preferred in terms of opportunities for advancements and staffing of positions. (Figure 1)

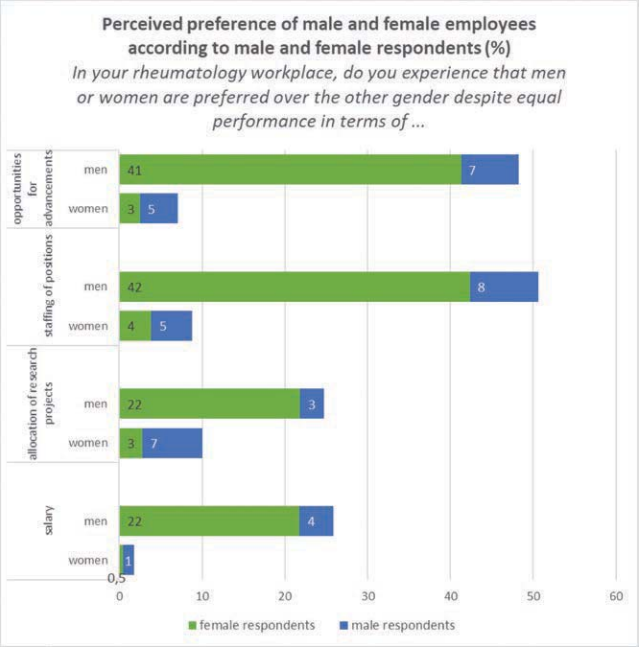

Figure 1. Perceived preference of employees in rheumatology with regards to opportunities for advancements, staffing of positions, allocation of research projects and salary according to gender by female and male survey-respondents. Perceived discrimination was not assessed.

66% of respondents agreed that activities to improve gender equity are necessary. The highest need was seen in the improvement of compatibility of care and work with adequate part time models, childcare options at work, and the higher acceptancy of part time working men and women by employers and persons in higher positions (freetext).
Conclusion: Gender misbalance is prevalent in rheumatology in Germany with lower numbers of women at higher hierarchical levels. Traditional role allocation is still common with a higher frequency of part time working females. Part time employment is perceived to decrease chances of advancement. The focus should be on promoting flexible job-sharing models, part time work among men and gender equity not only at work but also in private life ("care work"). Preference for one gender over the other is perceived differently between women and men.

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AB1416

WHAT IS THE FULL ECONOMIC COST OF DELAYED DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS IN THE UK?

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Background: Axial Spondyloarthritis (AS) is an umbrella term for both inflammatory conditions known as Ankylosing Spondylitis and Non-radiographic Axial Spondyloarthritis. AS generally develops in younger people. Symptoms typically start in the late teenage years to early twenties (with the average age of onset being 24). Hence this condition has a life-long impact, which could increase if left untreated. Average delay to diagnosis is over eight years after the appearance of symptoms. There are currently 220,000 people in the UK living with this painful and progressive form of inflammatory arthritis. While people wait for a diagnosis, many withdraw from socialising and find it harder to establish careers, form relationships, and start families. In addition to healthcare costs, that include multiple visits to GPs, prescription of unnecessary medication and extensive use of over the counter painkillers, there are intangible costs that have large impacts on patients and society. For example, quality of life for the patient, their earning and saving for retirement capacity, social care costs.

Objectives: To determine the full economic cost, including medical productively loss and other out of pocket related costs of delayed diagnosis for AS in the UK.

Methods: We are building an economic Markov model to determine a total cost per patient per year of delay. The model will project disease progression forward in time-steps with feedback loops to allow movement in states back and forth. Transition states within each time-step will be constructed according to the various stage of the disease and they will be used primarily to demonstrate an assessment of the costs in the time taken to a confirmed diagnosis. The model will capture symptoms and impacts of AS leading up to that diagnosis and before initiation of treatment. Assuming the one-year maximum 'gold standard' time to diagnosis that NASS would like to see to, the sum of costs prior to this in each consecutive cycle will be estimated. The inputs will consist of the average delay to diagnosis per gender and age group, the health resources utilisation, the cost of managing the symptoms, cost related to productivity losses and any other parameters and costs reflecting real resources required to diagnose, confirm, treat, cope with, manage and accommodate AS symptoms. Data include anonymised diagnosed patient data with the pathways they followed pre-diagnosis shared under strict confidentiality data sharing agreement from the secondary health units participating in the project. Cost data gathered from national sources and research into AS, NHS unit costs reports, productivity related reports and interviews with people with AS and clinicians providing valuable insight into the condition. The model will be validated by experts in the field and sufferers of AS to ensure accurate representation of actual events.

Results: The results will be provided at the conference and this is work in progress. A preliminary analysis of anonymised data of the pathway of 513 people towards an AS diagnosis show that the delay on female patients is slightly longer (mean of 9.85 years) compared to male patients (mean of 9.39 years). In both genders the delay is higher if the patient present symptom after the age of 31 years increasing the mean of previous age groups by 5 to 9 yrs.

Table 1.

	Female			Male		
Age Group	**Obs.**	**Mean**	**95% CI**	**Obs.**	**Mean**	**95% CI**
0-15	1	1	-	2	1.00	0.00, 13.71
16-30	49	3.59	2.69, 4.49	144.00	4.01	3.45, 4.57
31-45	50	11.72	9.64, 13.80	161.00	9.61	8.58, 10.65
46-60	24	18.17	13.05, 23.28	60.00	15.90	13.30, 18.50
61+	3	17.33	0.00, 52.58	19.00	28.58	21.14, 36.02

Conclusion: The results will help the National Axial Spondyloarthritis Society (NASS) to build an economic case for earlier diagnosis. The interactive model will support decision making in the future by allowing assumptions to be changed e.g., changing prices over time; varying wage rates depending on staff and skill mix; and the anticipated scale of savings in actual practice.

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AB1417 CORRELATION BETWEEN THE ATTITUDE OF PATIENTS SUFFERING FROM CHRONIC RHEUMATIC DISEASES TOWARDS REMOTE CONSULTATIONS BY RHEUMATOLOGIST AND THE HEALTH LOCUS OF CONTROL

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Background: During the COVID-19 pandemic telemedicine has become an important and safe means for patients suffering from chronic diseases to control their condition with the assistance of a physician [1]. In order to ensure that treatment of chronic rheumatic diseases is effective, it is important that patients develop a favorable attitude towards telerheumatology [2] as well as disease-related individual behavior, which significantly depends on the patients' health locus of control [3].

Objectives: To analyze the attitude of patients suffering from chronic rheumatic diseases towards peculiarities of remote consultations by a rheumatologist and their correlation with health locus of control.

Methods: To reveal the patients' attitude towards remote consultations by a rheumatologist, an original questionnaire has been prepared, which contains: reasons for choosing remote consultations, fears about such consultations and their advantages. Health locus of control was evaluated using a Multidimensional Health Locus of Control (MHLC) scale, which consists of three subscales: Internal, Chance, and Powerful Others. Demographical questions and questions related to health are also included in the questionnaire. 207 subjects participated in the study: 177 (85.5 %) women and 30 (14.5 %) men, (M_{age}=39.4, SD=11.76). The majority of subjects were diagnosed with spondyloarthritis (n=83), connective tissue diseases (n=53), rheumatoid arthritis (n=49), and osteoarthritis (n=20), 42 subjects were diagnosed with some other rheumatic diseases. 111 (53.6%) patients had the previous experience of remote consulting by a rheumatologist.

Results: It has been determined that the attitude of patients with rheumatic diseases is related to various demographic characteristics of patients, e.g., gender, etc., and the peculiarities of the disease, e.g., strength of the symptoms, etc. It has been found that patients without experience of remote consultations have more fears about such consultations (p=0.024). When comparing the average of statements revealing a positive attitude M=66.4% with the average of statements revealing a negative attitude M=27.3%, it becomes clear that the overall attitude of subjects toward remote consultations of a rheumatologist is favorable. To assess correlations between positive or negative attitude of patients with rheumatic diseases and health locus of control correlational analysis was performed. The results did not confirm the expected correlations between the positive attitude of patients with the internal locus of control. However, it has been obtained that negative attitude towards remote consultations by a rheumatologist positively correlates with two indicators of health locus of control – Chance (r=0.203, p≤0.0001) and Powerful Others (r=0.194, p=0.01), although the said correlation is not strong, but statistically significant.

Conclusion: The study has revealed the major fears and satisfaction sources related to remote consultations of Lithuanian patients with rheumatic diseases. In addition, it has shown that personal convictions of a patient that health depends on the circumstances and the influence of other people exacerbates the attitude towards remote consultations.

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AB1418 A SYSTEMATIC REVIEW OF CURRENT RHEUMATOLOGY GUIDELINES FOR GERIATRIC PERSPECTIVES

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Background: Geriatric population (GP) includes people over 65 years of age. GP can also be divided into the 65-75 age group and >75 age group. In the last 50 years, the proportion of the elderly in the society has increased (1). Meanwhile, GP has higher frequency of rheumatological disorders. While managing the treatment of this special patient group, some physiological differences of the elderly should be considered. Elderly patients are at increased risk for adverse drug reactions as a result of age-related changes in pharmacokinetics and pharmacodynamics. Polypharmacy is contributing to increased risk of clinically significant drug interactions. In addition, alterations in cognitive functions may impair drug compliance. On the other hand, clinicians may hesitate to apply more effective treatment due to safety concerns. (2).Rheumatologists should be aware of the problems they may encounter when planning the treatment of this privileged group.

Objectives: We reviewed rheumatology guidelines to assess rheumatology organizations' perspective on GP.

Methods: Guidelines published by EULAR, ACR and the British Society for Rheumatology (BSR) for adult patients from 1970-2022 were reviewed by two

rheumatologists to assess the existence of specific recommendations for the treatment of adult patients over 65 years of age.
Results: In total, 58 guidelines were reviewed. None of the guidelines grouped patients by age. Seven (12%) guidelines had recommendations or statements about elderly patients (Table 1). As we observe, there are no satisfactory recommendations for the GP with rheumatological diseases. The most propable reason for this result is the lack of studies in the rheumatology literature to lead to guideline recommendations.

Table 1. Characteristics of guidelines reviewed

	Number of guidelines (n)	Guidelines with specific recommandation for GP
EULAR	38	1-2-3-4-5-6
ACR	11	6
BSR	9	7

[1]EULAR points to consider for the management of difficult-to-treatrheumatoidarthritis(recommendation 6)[2]. Points to consider for the development, evaluation and implementation of mobile health applications for self-management in patients with rheumaticdiseases (points to consider 8)[3]. 2019 update of EULAR recommendations for Vaccination in AdultPatientswithAutoimmuneInflammatoryRheumatics[4]. EULAR Recommendations for prevention and management of osteoporoticfractures(recommendation 6)[5]. EULAR Points to consider for monitoring (detection/prevention) comorbidities in inflammatoryrheumaticdiseases (point to consider 10)[6]. 2015 Recommendations for the management of polymyalgiarheumatica: a European League AgainstRheumatism/American College of Rheumatologycollaborativeinitiative (recommendation 9)[7]. BSR guidelines for the management of polymyalgiarheumatica (recommendation 6)

Conclusion: Current prominent rheumatology guidelines have insufficiently addressed the management of rheumatological diseases in GP. Additional studies ares needed to delineate specific guidelines for the management of geriatric patients with rheumatological diseases.
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Disclosure of Interests: None declared
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AB1419 PERFORMANCE OF AN EARLY TRIAGE SYSTEM FOR IDENTIFICATION OF PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: The preselection of patients with suspicion of an inflammatory rheumatic disease is not easy for general practitioners and orthopedists. In countries with a limited number of practicing rheumatologists waiting lists are often long, since a full rheumatologic examination often needs a long consultation time.
Objectives: To test the performance of an early triage strategy for early identification of patients with inflammatory rheumatic diseases.
Methods: Prior to the SARS-CoV 2 pandemic, physicians caring for patients contacting a tertiary rheumatologic cente were first contacted by a health-care professional (HPR) who offered an appointment the timing of which was based on the symptoms reported (Step 1). Patients were then seen by a rheumatologist who, within a 10-minute consultation (Step 2), shortly examined the patient to determine the urgency of a planned full work up. The main outcome of the study was the comparison between the initial assessment and the final expert diagnosis (Step 3).
Results: Within 9 months, physicians caring for 1.180 patients contacted the hospital, 972 of whom kept their appointment (82.4%). Most patients were transferred by GPs (73.1%) and orthopedists (22.1%). The mean time between Step 1 and Step 2 was 10.4 days, while 6.2% of patients were seen within 4 days, 24.4% within 7 days and 69.3% within 12 weeks. Only 36 patients (3.7%) of patients had an already established rheumatic disease. Complaints lasting between 0-4 weeks were reported by 69 (7.1%), of > 4-12 weeks by 100 (10.3%), and of > 12 weeks by 973 (82.6%) patients. Almost 90% of patients reported a pain intensity >4/10 (NRS) for < 2 weeks. An elevated CRP was found in 207 patients (24.5%). Prior treatment with glucocorticoids was reported in 163 (16.8%) and with NSAIDs in 730 (75.1% of) patients. The confirmed diagnosis at Step 3 was rheumatoid arthritis in 127 (13.1%), spondyloarthritis including psoriatic arthritis in 72 (7.4%), systemic diseases including connective tissue diseases in 112 (11.5%), vasculitides in 41 (4.2%), and crystal arthropathy in 38 (3.9%) patients, while 38 (3.9%) had an infection, a malignancy or a differential diagnosis such as Raynaud's phenomenon or sicca syndrome. Degenerative joint diseases (n=254; 26.1%) and non-inflammatory soft tissue syndromes such as fibromyalgia (n=369; 38%) accounted for more than half of the patients.
Conclusion: This study describes the performance of a standardized triage system hereby confirming the need for an early identification and preselection of patients with rheumatic musculoskeletal symptoms, including involvement of HPRs in the initial phase of contact. Based on the results, three patients with musculoskeletal complaints had to be examined in order to identify one patient with an inflammatory rheumatic disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.5124

AB1420 CLINICIAN-RELATED FACTORS MAY INFLUENCE REMOTE CONSULTATIONS IN RHEUMATOLOGY – ANALYSIS OF SENIOR VS TRAINEE CLINICIANS' OUTCOMES FROM A COVID-19 INITIATIVE

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Background: Since COVID-19 pandemic started, there have been changes in clinical practice to limit transmission, such as switching from face-to-face to remote consultations. Our department switched to delivering remote consultations without suspending service. Patients were offered the preference of either video or telephone consultation. It is unclear what factors including clinician-related factors significantly influence remote consultations in Rheumatology.
Objectives: We aimed to study the influence of senior (substantively employed) vs trainee status of clinicians on remote consultations in our experience during the pandemic.
Methods: Between 15/10/2020 and 09/11/2020, 12 clinicians in our department completed data collection forms after each remote consultation, recording the technology used (video vs phone); technical problems encountered; discharge and subsequent appointment status; and technical aspects of the consultation itself using 11-point numerical rating scales (NRS) (Time Adequate; Relevant History; Physical Exam; Management Plan; and Communication Quality). Data were collated on an MS Access 2016 database, and transferred to SPSS version 25 for statistics.
Results: Nine senior clinicians (3 consultant rheumatologists, 3 Specialist Nurses, 1 Advanced Rheumatology Practitioner and 2 Senior Rheumatology Pharmacists) and 3 trainee clinicians (2 Specialty Trainee Registrars and 1 Foundation Year 2 doctor) completed forms. 285 forms were validated for analysis. The majority of consultations were completed by senior clinicians (266, 93.3% vs 19, 6.7%). Senior and trainee clinicians had a similar proportion of new patients compared to follow-up patients (18%, n=48 vs 15.8%, n=3; p=0.80); of female patients (68%, n=181 vs 63.2%, n=12; p=0.66); and video consultations (17.3%, n=43 vs 10.5%, n=2; p=0.45); and similar mean age of their patients (59.5 vs 56.7years; p=0.72) respectively. Senior clinicians accounted for all the technical issues reported (20%, n=48 vs 0%, n=0; p=0.03). Senior clinicians had lower mean scores compared to the trainee clinicians on NRS for Relevant History (8.68 vs 9.68; p<0.001), Physical Exam (1.49 vs 2.95; p=0.045), and Communication Quality (8.02 vs 9.37, p=0.002); and had no significant differences in scores for Time Adequate (8.46 vs 9.00; p=0.10) and Management Plan (7.17 vs 7.84; p=0.16). Senior and trainee clinicians and a similar proportion requests for subsequent face-to-face appointments (21.9%, n=51 vs 25%, n=4; p=0.77).
Conclusion: There were no significant differences between senior and trainee clinicians in distributions of patients and proportion of video consultations. While no technical issues were reported by the trainee clinicians, this may in part be a reflection of their smaller proportion of overall consultations. Although senior clinicians rated their consultations somewhat lower in some of the NRS, there was no significant difference in management plan scores and subsequent face-to-face appointment status compared to trainee clinicians. While the lower scores may partly reflect the technical issues reported by the senior clinicians, longer clinical experience and greater knowledge may also be an underlying factor for this. Further studies with larger numbers may clarify these issues.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.5311

Epidemiology, risk factors for disease or disease progression

AB1421 IMPACT OF HOSPITALIZATION ON CLINICAL OUTCOMES IN PATIENTS WITH CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASE (CTD-ILD) - A SINGLE CENTER OBSERVATIONAL STUDY

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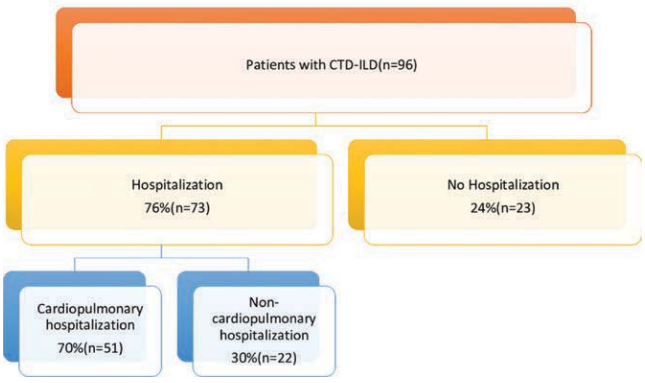
Background: Interstitial lung disease(ILD) is major cause of morbidity and mortality in patients with connective tissue disease (CTD). Hospitalization is being increasingly recognized as poor prognostic indicator in these patients.
Objectives: The objective of our study was to assess the impact of hospitalization on clinical outcomes in patients with CTD-ILD.
Methods: We conducted a retrospective chart review of patients with radiologically or biopsy proven ILD associated with rheumatologist diagnosed CTD who were seen at Montefiore Medical Center between January 2007 and December 2018. Patients with age>18 years who had either 2 CT scans of the chest and/or 2 sets of pulmonary function tests (PFT) atleast 6 months apart were included in the study. Clinical demographics, cause of hospitalization, length of stay, use of immunosuppression and mortality were identified. Patients were stratified into 2 cohorts; non-hospitalized and hospitalized patients. The latter cohort was further sub-stratified into patients with cardiopulmonary vs. non-cardiopulmonary hospitalization (Figure 1). Two-sample t-tests and Wilcoxon's rank sum tests were used for comparing the continuous variables. Chi-square tests and Fisher's exact tests were used for comparing the categorical variables as appropriate. Kaplan-Meier method was used for calculating the survival probabilities, and log-rank tests were used to compare differences between the groups.

Figure 1: Flow chart showing hospitalization pattern in CTD-ILD patients.



Results: During the study period, we identified 213 patients with CTD-ILD using ICD 9/10 code. Of the 213 patients, 96 met our inclusion criteria and 73 (76%) had at least 1 hospitalization (Figure 1). Both groups were similar in baseline clinical characteristics but we identified significantly higher transplant referrals in the hospitalized group(23.9%) vs. non-hospitalized group(0%) (Table 1). Overall rheumatoid arthritis (29.2%) was the most common CTD associated ILD followed by inflammatory myositis (21.9%) and scleroderma (14.6%). Median time from diagnosis of ILD to first hospitalization was 1.42 years. The patients hospitalized for cardiopulmonary cause were significantly older(57.2 ±13.1 years) than those admitted with non-cardiopulmonary cause(49.2±14.8 years)(Mean±SD). Older age (HR 1.95, p=0.02) and length of stay greater than 7 days for cardiopulmonary cause(HR 4.82,p=0.01) was associated with higher risk of mortality. Kaplan Meier curve analysis showed that hospitalization (p-value=0.02) was associated with statistically significant increased risk of death.
Conclusion: -Hospitalization in CTD-ILD patients especially length of stay more than 7 days due to cardiopulmonary causes was associated with statistically significant increased risk of death. Male gender and older age was associated with a worse prognosis in patients who were hospitalized.

Table 1. Baseline Characteristics of patients with CTD-ILD

Characteristic	Entire Cohort (n = 96)	Patients with CTD-ILD and hospitalization (n = 73)	Patients with CTD-ILD and no hospitalization (n = 23)	p-value
Age(mean ± SD)	54.15 ± 13.97	54.82 ± 13.77	52.00 ± 14.71	0.40
Female, n (%)	76 (79.2)	56 (76.7)	20 (87.0)	0.39
Race, % (n)				0.10
Black	38 (39.6)	31 (42.5)	7 (30.4)	
White	4 (4.2)	3 (4.1)	1 (4.4)	
Others	54 (56.2)	39(53.4)	15(65.3)	
Ethnicity, % (n) (Hispanic)	44 (53.7)	35 (53.0)	9 (56.3)	0.82
Former or active smoker, % (n)	41 (42.7)	34 (46.6)	7 (30.4)	0.17
Pulmonary hypertension, % (n)	28 (31.1)	24 (33.3)	4 (22.2)	0.36
FVC, n (%)				0.37
Moderately severe(47.1-64.2)	37 (44.6)	26 (40.6)	11 (57.9)	
Severe(24.3-47.0)	7 (8.4)	6 (9.4)	1 (5.3)	
DLCO, n(%)				0.30
Moderate	26(31.7)	23(37.1)	3(15.0)	
Severe	25(30.5)	17(27.4)	8(40.0)	
Immunosuppression, n(%)	78 (81.3)	59 (80.8)	19 (82.6)	1.00
Transplant referral, n(%)	17 (18.3)	17 (23.9)	0 (0)	**0.01**

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AB1422 PREVALENCE OF HYPERURICEMIA IN CHINESE ADULTS: DATA FROM A CROSS-SECTIONAL STUDY

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Background: Previous studies have observed an increasing trend in the prevalence of hyperuricemia which is linked to the physiological prerequisite for gout in recent years. However, the prevalence of hyperuricemia varies across different populations and different areas.
Objectives: The aim of this study was to explore the prevalence of hyperuricemia and influencing factors in Chinese adults.
Methods: The analysis was a part of a cross-sectional study in Guangdong Second Provincial General Hospital in Guangzhou City, China between January 2009 and December 2019. A total of 205922 participants (21401 with hyperuricemia) were included in this study. Hyperuricemia was defined as serum uric acid ≥416.0 μmol/L (7.0 mg/dl) for men and ≥357.0 μmol/L(6.0 mg/dl) for women. We calculated the prevalence of hyperuricemia and used the multivariate-adjusted logistic regression model to identify the risk factors associated with hyperuricemia.
Results: The overall estimated prevalence of HUA was 10.4% in China. Our study showed the prevalence of hyperuricemia in male (10.7%) was higher than that in female (9.9%) (P<0.05). The prevalence of HUA in the age group(≥75) subjects (13.3%) was higher than others. Multivariate logistic regression analysis revealed that sex (OR=1.75), age (OR=1.68), blood urea nitrogen (BUN) (OR=1.051), creatinine (Cr) (OR=1.045), high-density lipoprotein cholesterol (HDL-C) (OR=1.225), low-density lipoprotein cholesterol (LDL-C) (OR=1.466), systolic blood pressure (SBP) (OR=1.012),triglycerides (TG) (OR=1.460) and Body Mass Index (BMI) (OR=1.080) could increase the risk of hyperuricemia, while diastolic blood pressure (DBP) (OR=0.998), fasting plasma glucose (FPG) (OR=0.902) and total cholesterol (TC) (OR=0.704) were associated with a lower risk of hyperuricemia in all adults.
Conclusion: The latest prevalence of hyperuricemia is high in Chinese adults and is associated with multiple factors, indicating that prevention and control strategies for hyperuricemia are needed urgently.
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Table 1. The prevalence of hyperuricemia by gender and age groups

		Hyperuricemia	
Variable	Number	n	Prevalence (%)
Gender			
Male	124237	13330	10.7
Female	81685	8071	9.9
Age group			
< 30	48437	4965	10.3
30-44	84331	8989	10.7
45-59	52175	4976	9.5
60-74	14710	1640	11.1
≥75	6269	831	13.3
Overall	205922	21401	10.4

Disclosure of Interests: None declared
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AB1423 CLINICAL AND LABORATORY FEATURES OF PATIENTS WITH IDIOPATHIC GRANULOMATOUS MASTITIS AT A TERTIARY MEDICAL CENTER

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Background: Idiopathic granulomatous mastitis (IGM) is a benign, inflammatory disease of the breast. As per the literature review, etiopathogenesis of this disease is unclear. The gold standard of diagnosis is through breast biopsy and identification of non-caseating granulomas. **[1]** Until recently, there has been a lack of clinical, serological or histopathological criteria to guide physicians on management of IGM.
Objectives: The objective of our study is to identify distinguishing clinical and laboratory features amongst individuals with IGM based on serologic and histopathologic status. In this study, clinical and laboratory features were compared between patients with complete remission of IGM and those with relapse of IGM after three months of remission.
Methods: After institutional review board (IRB) approval, we queried pathology and clinical looking glass databases at Montefiore Medical Center between 1990-2021 to identify patients with the diagnosis of IGM. We identified 46 patients, and did a retrospective chart review to extract data. Clinical features were compared in patients with IGM who had complete resolution of disease and those who had relapse of disease using two-sample t-tests for continuous variables and chi-squared or Fisher's exact tests for categorical variables. In this study, we included females older than eighteen years of age. We excluded patients with breast cancer, lymphoproliferative disorders, solid organ malignancy, foreign body reaction in breast, plasma cell mastitis, and ductal ectasia.
Results: Of the 46 symptomatic patients with histopathological diagnosis of IGM, 27 female patients with sufficient clinical data were included in final analyses. All patients in our cohort had a mean age of 36 years (SD 9 years) and average body mass index of 31.5 kg/m^2 (SD 6.7 kg/m^2). Majority of patients were Hispanic, 11 patients (40.7%). Unilateral disease (96.3 %) was predominant in patients. Most patients had at least one previous full-term pregnancy prior to diagnosis, 25 patients (92.6%) and 8 patients were on hormonal oral contraceptives (29.6%).
Of the 27 patients, 18 patients (66.6%) had complete remission of disease. All of these patients were initially treated with antibiotic therapies until tissue cultures were reported negative. Six of these patients received steroid therapy after antibiotic therapy, while 5 patients were started on methotrexate therapy, starting with a dose of 15 milligrams (mg) orally once per week. Of the total cohort, 9 patients (33.3%) experienced relapse of the disease.
Conclusion: IGM is a relatively newer entity that is difficult to manage, due to lack of standard guidelines in literature. In this study, on comparing IGM patients with remission and relapse, there were no statistically significant differences in clinical and laboratory features. However, immunomodulating therapy with methotrexate can be considered in patients with relapsing IGM. Further studies are needed to evaluate patients with IGM and their disease evolution that can facilitate management to determine utility of methotrexate in improving relapse rates in these patients.

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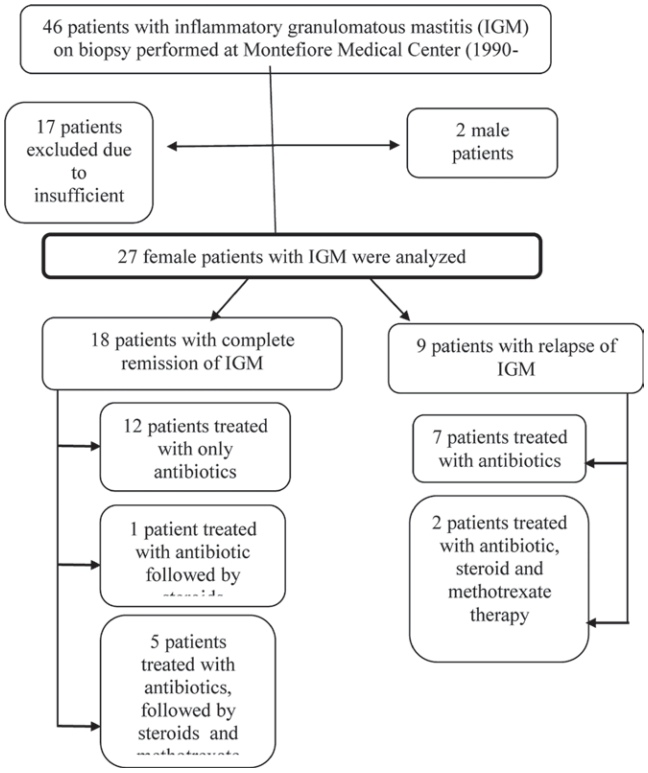

Figure 1. Study Population

Disclosure of Interests: Bhavna Abbi: None declared, Xianhong Xie: None declared, Susan Fineberg Consultant of: expert consultant /expert panel for AXDEV Group in 2021 and Genomic health (now exact Sciences) in 2017, Anjuli Gupta: None declared, Anand Kumthekar: None declared, Bibi Ayesha: None declared
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AB1424 INVESTIGATION OF THE TYPE AND FREQUENCY OF NEUROLOGICAL SIDE EFFECTS WITH BIOLOGICAL TREATMENT IN INFLAMMATORY RHEUMATIC DISEASES

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Background: With the increasing use of biological treatment in inflammatory rheumatic diseases, some neurological side effects, especially central and peripheral nervous system demyelinating disorders, are seen.
Objectives: To evaluate whether there is an increase in the frequency of neurological disorders with biological treatment compared to the normal population, and the relationship between discontinuation of biological agents and neurological symptoms.
Methods: Adult patients using biological treatment followed in the Rheumatology outpatient clinic of Dokuz Eylul University between January 2011 and January 2020 were included. The relationship between biological agents and type, severity and duration of neurological symptoms, and the laboratory, imaging (cranial CT, MRI) and electrophysiological findings of the patients were retrospectively reviewed. Current treatments for rheumatologic disease and neurological findings, and disease activity were investigated.
Results: In our study, neurological side effects were observed in 16 (1.8%) of 877 patients using biological drugs. The mean age of the patients was 51.8±12.53 years, and the duration of rheumatologic disease was 10.69±4.86 years. Nine patients had peripheral neuropathy, two had CNS demyelinating disease, two had peripheral demyelinating disease, two had intracranial mass and one had

headache syndrome. The neurological disease developed a mean of 51.31±44.26 months after the first biological agents. The demographic and clinical characteristics of the patients and the neurological side effects that developed during the follow-up period are summarized in Table 1. Biological treatment was discontinued in 68.8% of patients. There was no significant correlation between biological agents' continuation status and progression of neurological findings.

Table 1. Demographic and clinical characteristics of patients who developed neurological symptoms with biological treatment

		n=16 (%)
Gender	Male	8 (50)
Age of diagnosis (years)¶		41,13±12,02
Disease duration (years)¶		10,7±4,86
Smoking	active	7 (43,8)
	exmoker	2 (12,5)
CRP (mg/L)¶		5,03±6,28
bDMARD	Adalimumab	5 (31,3)
	İnfliximab	4 (25,0)
	Etanercept	2 (12,5)
	Certolizumab	1 (6,3)
	Tocilizumab	1 (6,3)
	Secukinumab	2 (12,5)
	Tofacitinib	1 (6,3)
Imaging (CT, MRI)	Presence of pathological findings	5 (31,3)
Electrophysiological study	Presence of pathological findings	8 (50,0)
Neurological Side Effect	Diabetic Amyotrophy	1 (6,3)
	Foot drop	1 (6,3)
	Grade 2 astrocytoma	1 (6,3)
	Meningioma	1 (6,3)
	Cauda equina syndrome	1 (6,3)
	Cubital Tunnel Syndrome	1 (6,3)
	Multiple sclerosis (de nova)	1 (6,3)
	Multiple sclerosis attack	1 (6,3)
	Myasthenia gravis attack	1 (6,3)
	Radicular neuropathy	1(6,3)
	Sensorimotor polyneuropathy	1 (6,3)
	Sensory neuropathy	1 (6,3)
	Pseudotumor cerebri worsening	1(6,3)
	Facial paralysis	1 (6,3)
	CIDP progression	1(6,3)
	Guillain Barre Syndrome	1 (6,3)
Time to development of adverse events after last bDMARD¶		26,37±29,58
Time after neurological adverse event (months)¶		23,75±20,86
bDMARD continuation status after adverse events	bDMARD discontinuation	11 (68,8)
Neurological symptoms at last visit	Stable	6 (37,5)
	Improvement	9 (56,3)
	Progression	1(6,3)

¶ mean±SD. CIDP:Chronic inflammatory demyelinating polyneuropathy

Conclusion: In this study, the prevalence of neurological diseases such as brain tumors, multiple sclerosis, and myasthenia gravis increased in patients receiving biological treatment compared to the normal population. Therefore, patients using biological agents should also be questioned and examined in terms of neurological symptoms, and further examination should be applied if necessary. No significant relationship was found between discontinuation of biological drugs and improvement/progression of neurological symptoms, and more comprehensive studies are needed.

Disclosure of Interests: None declared

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AB1425 MENTAL DISTRESS AND ITS CONTRIBUTING FACTORS AMONG ADOLESCENTS IN A RHEUMATOLOGY CENTER IN MALAYSIA

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Background: According to World Health Organization 2021, approximately 1 in 7 from the age group of 10-19 years old encountered mental health conditions [1]. Multiple factors can affect their mental health including their underlying medical conditions and depression may influence both reporting symptoms and response to treatment. This study is to investigate the prevalence of depression among adolescents diagnosed with rheumatic diseases by using CES-D questionnaire and to determine its contributing factors.

Objectives: To screen for depression by using center for epidemiologic studies depression (CES-D) among adolescents diagnosed with rheumatic diseases and to determine its contributing factors.

Methods: This was a survey interview. All rheumatology patients from the age group of 12-21 who followed up in rheumatology clinic Hospital Sultan Ismail from March 2020 to December 2021 were identified and interviewed. Demographic data, clinical data and disease duration were identified and the results were analysed by using IBM SPSS Statistics version 20.

Results: A total of 71 patients were identified. 93% of them were female (66/71) and majority of them were Malay (60.6%). This was followed by Chinese (23.9%), Indian (7%) and others (8.5%). The mean age group was 16 (range from 12 to 21). 85.9% of them were diagnosed to have systemic lupus erythematosus. 5.6% of them were having juvenile idiopathic arthritis followed by 2.8 % for each juvenile dermatomyositis and psoriatic arthritis. The rest of them were having mixed connective tissues disease and rheumatoid arthritis with the percentage of 1.4% for both diseases. 57 .7% of the respondents were having inactive disease during the interview session. From our survey, it showed that 53.5 % of the respondents were considered depressed with the score of 16 points and above according to the cut off point determined by CES-D questionnaire. The statistics showed association in between disease activity with the score of depression by using Chi Square ($p<0.015$). However, there was no association between the races and the score of depression ($p = 0.1$, using Chi Square). There was also no association between duration of disease with the score of depression. ($p= 0.485$, by using independent t-test).

Conclusion: Our study showed the prevalence of depression amongst adolescents diagnosed with rheumatic diseases are more than 50% and there was an association between depression score and disease activity. Hence, it is recommended to routinely screen for depression among adolescent as it helps to improve their response and compliant to treatment. Treat to target approach must always be implemented by treating physician to keep disease in remission and indirectly helps to reduce emotional distress among patients.

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Disclosure of Interests: None declared

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AB1426 PREDICTORS OF RHEUMATIC TOXICITIES OF IMMUNE CHECKPOINT INHIBITORS AND CANCER OUTCOMES IN PATIENTS WITH ADVANCED MELANOMA

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Background: Immune checkpoint inhibitors (ICIs) including monoclonal antibodies to PD-1 and CTLA-4 have activity across various cancers. Dedicated cohort studies have examined the epidemiology and clinical course of rheumatic toxicities (1–3) and the effect of pre-existing autoimmune disease has been explored (4), with limited assessment of the effect of non-immune mediated rheumatic disease (3). A positive association between ICI-induced rheumatic disease and favourable cancer outcomes has been suggested (1,2), although derived from heterogenous cancer populations.

Objectives: To identify risk factors for the development of ICI-induced rheumatic disease and predictors of cancer outcomes in patients with advanced melanoma.

Methods: A single-centre observational study of patients with stage III or IV melanoma receiving all available ICI therapies, who completed a for-purpose questionnaire to capture rheumatic symptoms and risk factors upon recruitment and at 12-months. Symptom severity was assessed according to patient reported measures such as visual analogue scale (VAS) scores for pain. Clinical details were extracted from patients' medical records. Predictors of rheumatic toxicities and cancer outcomes were identified through regression analysis.

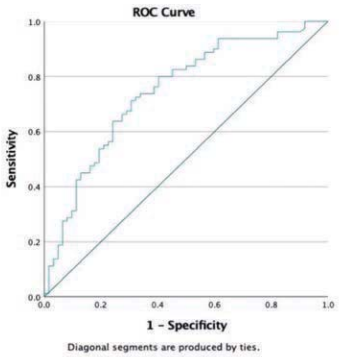
Results: Amongst 147 eligible patients, the prevalence of new or worsening rheumatic symptoms was 32.5% at recruitment and 21% at 12 months. The incidence of documented arthralgia, inflammatory arthritis and PMR-like syndrome was 39.5%, 5.4% and 3.4% respectively. Binary logistic regression identified pre-existing symptomatic rheumatic disease, including non-immune mediated rheumatic disease, as the primary risk factor for developing rheumatic toxicities (OR 3.161). Continuation of ICI therapy (OR 16.52), followed by rheumatic toxicities (OR = 4.368) were predictors of favourable tumour response.

Conclusion: Rheumatic toxicities of ICI therapy commonly affect patients with melanoma and are more likely to occur in patients with pre-existing autoimmune and non-immune mediated rheumatic disease. Continuation of ICI therapy improves cancer outcomes and can be facilitated by early detection of rheumatic symptoms using patient reported outcome measures.

Table 1. ***Bivariate logistic regression of predictors of patient-reported rheumatic toxicity. Sig., Significance; OR, Odds ratio; CI, confidence interval; BRAF/MEK, BRAF and MEK inhibitors; PD-1, Programmed Cell Death protein – 1; CTLA-4, Cytotoxic T-lymphocyte-associated protein.***

Variables	Sig.	OR	Lower 95% C.I.	Upper 95% C.I.
Age at initial questionnaire	0.95	0.999	0.969	1.03
Gender	0.153	0.566	0.259	1.236
Pre-existing autoimmune rheumatic disease	0.457	1.891	0.353	10.118
Symptomatic pre-existing rheumatic disease	0.007	3.161	1.362	7.338
Pre-existing musculoskeletal injury	0.078	0.479	0.211	1.085
Family history of rheumatic disease (1st degree)	0.4	1.555	0.556	4.352
Previous or current smoking	0.788	0.899	0.415	1.949
Skeletal metastases	0.218	0.523	0.186	1.467
Prior BRAF/MEK inhibitors	0.477	1.449	0.522	4.027
Combination PD1 and CTLA4 inhibitors	0.24	0.605	0.261	1.399
Constant	0.753	0.709		

A



B

AUROC	Std. Error(a)	Asymptotic Sig.(b)	Lower asymptotic 95% C.I.	Upper asymptotic 95% C.I.
0.745	0.042	0	0.663	0.827

Figure 1. *A) Receiver-operator curve for accuracy of binary logistic regression model clinician-recorded rheumatic disease. (B) Area under receiver-operator curve. Test result variable(s): predicted probability. AUROC, Area Under Receiver-Operator Curve; Std. Error, Standard Error; Sig., Significance.(a) Under the nonparametric assumption(b) Null hypothesis: true area = 0.5*

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AB1427

ASSOCIATION BETWEEN HYPERURICEMIA AND OSTEOPOROTIC IN CHINESE ADULTS, A CROSS-SECTIONAL STUDY

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Background: Hyperuricemia may have a protective role in diseases characterized by high levels of oxidative stress, such as osteoporosis. Previous studies have shown that hyperuricemia is associated with osteoporotic. However, this association is controversial and even yielded conflicting results.

Objectives: This study investigated the relationship between hyperuricemia and osteoporotic among Chinese adults.

Methods: The data of cross-sectional study was collected at Guangdong Second Provincial General Hospital in Guangzhou City, China between January 2009 and December 2019. Physical examinations and laboratory measurement variables were obtained from the medical check-up system. The multivariate-adjusted logistic regression model was performed to assess the association between hyperuricemia and osteoporotic.

Results: A total of 18917 participants (11334 males and 7579 females) were included in this study, with an average age of 46.23 years (SD: 11.67) at baseline. It included 5881 cases of hyperuricemia and 1587 osteoporotic. After adjusted for the confounding factors in logistic regression analysis, we observed a negative significant association between hyperuricemia and risk of osteoporotic (odds ratio [OR],0.852, 95%CI 0.795–0.967; P <0.05). Further stratified analyses showed a negative significant association with the risk of osteoporotic in women (OR,0.787, 95%CI 0.698–0.853; P <0.05), man (OR,0.897, 95%CI 0.786–0.954; P <0.05) and old adults (OR, 0.808, 95%CI, 0.759-0.894; P <0.05). No significant differences in other groups.

Conclusion: Our study observed participants with hyperuricemia had significantly less osteoporosis. More high-quality research is needed to further support these findings.

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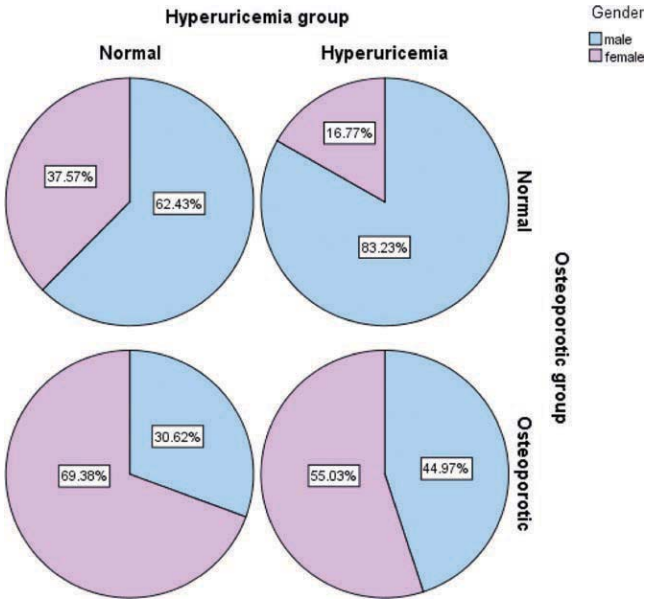

Figure 1. Distribution of hyperuricemia and osteoporotic by gender.

Disclosure of Interests: None declared
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AB1428 CONTRAINDICATIONS, BOXED WARNINGS AND SPECIAL WARNINGS OF BIOLOGICAL AND TARGETED SYNTHETIC DMARDS

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Background: The list of biological DMARDs (bDMARDS) and targeted synthetic DMARDs (tsDMARDs) approved to treat synovitis and extra-articular manifestations is long and constantly expanding. The choice of drug for the individual patient depends on multiple factors. 1) Among these, contraindications and warnings are pivotal to consider. 2), 3) However, a systematic collection of drug class specific warnings for the b/tsDMARDs based on regulatory drug approvals is lacking.
Objectives: Our aim was to make an overview of the different contraindications, boxed warnings and special warnings listed in the European Medicines Agency (EMA) summaries of product characteristics (SmPCs) and the U.S. Food and Drug Administration (FDA) Prescribing Information (PI) for b/tsDMARDs.
Methods: We included all b/tsDMARDs with an FDA and/or EMA approval for any of the diagnoses: rheumatoid arthritis (RA), psoriatic arthritis (PsA), spondylarthritis (SpA), juvenile idiopathic arthritis (JIA), uveitis, plaque psoriasis, inflammatory bowel diseases (IBD). The included drugs were tumor necrosis factor (TNF) inhibitors (inh), anti-CD20 (rituximab), inhibitors of interleukin (IL)-6 receptor (6R), IL-1, IL-17, IL-12/23, IL-23, CD80/86 (abatacept), janus kinase (JAK), the phosphodiesterase 4 (PDE4) (apremilast), and the $\alpha 4\beta 7$ antibody (vedolizumab) We used the most recent SmPCs and PIs for the reference products in case of existing biosimilar products and extracted the information listed in the categories; contraindications, boxed warnings, and special warnings.
Results: There was a big difference between the year of first approval of the drugs spanning from 1998 to 2017. All drug classes except apremilast had warnings about infection. A warning about herpes zoster was listed specifically for rituximab, inhibitors of IL-6R, IL-1, IL-12/23 and JAK, while warning about hepatitis was listed for TNF inhibitors, rituximab, IL-6R inh., IL-1 inh., abatacept and JAK inh. All drug classes except IL-17 inh., IL-12/23 inh. and apremilast had warnings about malignancy. A warning about demyelinating disease was listed for TNF inh., IL-6R inh., and abatacept. Heart failure was specific for TNF inh. and rituximab while risk of major adverse cardiac events and venous thromboembolism was listed only for JAK inh. A recommendation regarding monitoring lipids was listed for inhibitors of IL-6R and JAK, monitoring liver enzymes was listed for all drug classes except IL-17 inh., IL-12/23 inh., abatacept and apremilast. Development of IBD was listed for IL-17 inh. and risk of diverticulitis was listed for inhibitor of IL-6R and JAK. Cytopenia was listed for rituximab, inhibitors of TNF, IL-6R, IL-1 and JAK. Depression was listed for IL-17 inh. and apremilast.
Conclusion: We made a systematic description of contraindications, boxed warnings and special warnings for b/tsDMARDs with a focus on drugs approved for use in chronic inflammatory arthritis and related disease entities. There were some associations between time of first drug approval and number of listed concerns. This, we presume, is because some of the rare events will not be found before several years after marketing. Group effects and specific concerns for individual drugs were identified.
Based on the warnings, we made a figure with clinically relevant conditions to consider when choosing a drug.
This systematic data collection could prove to be a useful decision tool for clinical practice to ensure patient safety and improve personalized drug choices.
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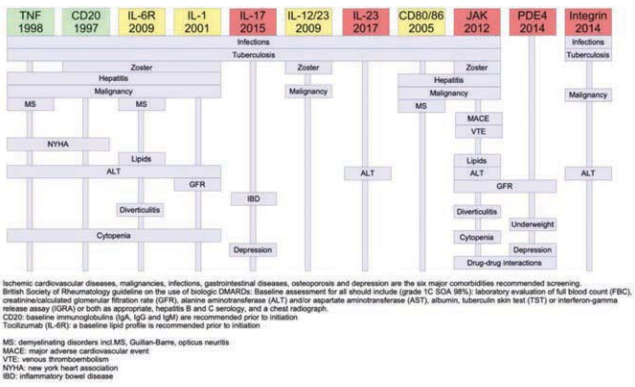

Figure 1.

Disclosure of Interests: Lykke Skaarup: None declared, Tue Wenzel Kragstrup Shareholder of: Co-founder and clinical developer in iBio tech ApS., Speakers bureau: Speaking fees from Pfizer, Bristol-Myers Squibb, Eli Lilly, Novartis, UCB, and Abbvie., Consultant of: Consultancy fees from Bristol-Myers Squibb and Gilead., Grant/research support from: Research grants from Gilead.
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AB1429 PERSISTENT INFLAMMATION AND PULMONARY FUNCTION CHANGES PREDICT PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASES DEVELOPMENT IN RHEUMATIC PATIENTS

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Background: The progressive fibrosing interstitial lung disease (PF-ILD) remains a challenge for clinical care. Studies reported that fibrosis-predominant pattern on high-resolution computed tomography (HRCT) and a worse baseline pulmonary function tests were associated with a progression to PF-ILD [1]. Whether the inflammatory marker changes predict PF-ILD development was unknown.
Objectives: To evaluate prognostic values of the early inflammatory markers and the pulmonary function tests of developing PF-ILD in patients with connective tissue disease-related interstitial lung disease (CTD-ILD) and interstitial pneumonia with autoimmune features (IPAF).
Methods: This was a retrospective, single-center study. The patients with CTD-ILD and IPAF were included. The PF-ILD was identified at two years after the ILD diagnosis, as according to the INBUILD study [2]. The ILD patterns on the HRCT and the pulmonary function tests at diagnosis and one year after ILD diagnosis were reviewed by three pulmonologists independently. The baseline demographics, autoimmune manifestations, and serology at diagnosis, three months, and one year after ILD diagnosis were collected. The data were analyzed using the R version 4.1.2.
Results: From 2010 to 2020, we enrolled 34 patients into the analysis. These included 11 patients with Sjogren's syndrome, 7 patients with idiopathic inflammatory myopathy, 3 patients with mixed connective tissue diseases, 1 patient with systemic sclerosis, and 14 patients with IPAF. The HRCT patterns were usual interstitial pneumonia in 13, non-specific interstitial pneumonia (NSIP) in 8, organizing pneumonia (OP) in 6, and lymphocytic interstitial pneumonia (LIP) in 1.
At 2 years, 15 patients developed PF-ILD. The CTD diagnoses and the radiographic patterns at diagnosis were not associated with the development of PF-ILD. The predicted functional vital capacity (FVC) at diagnosis (80% vs. 69%, p=0.047), diffusion capacity of the lung for carbon monoxide (DLCO) at diagnosis (76% vs. 44%, p = 0.021), FVC at one year (94% vs. 68%, p = 0.047), and DLCO at one year (68% vs. 36%, p = 0.018) were associated with the PF-ILD progression. Immunologically, the PF-ILD patients had a borderline higher 1-hour erythrocyte sediment rate (ESR) at baseline (36 vs. 22 mm/h, p = 0.051), but the difference became prominent after 3 months (38 vs. 10 mm/h, p = 0.023), and 12 months (28 vs. 8 mm/h, p = 0.005) after the ILD diagnosis. (Figure 1)

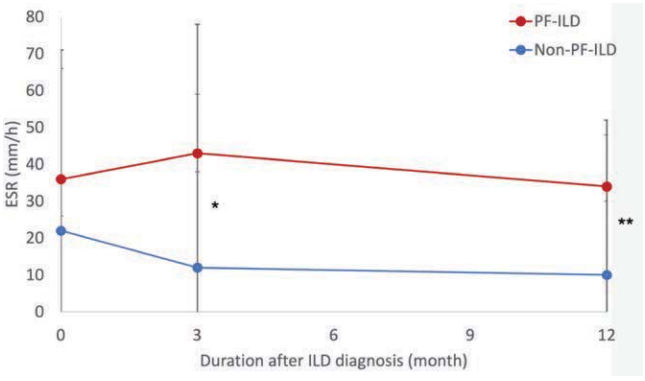

Figure 1. Change of erythrocyte sediment rate at 1 hour over time. ESR, erythrocyte sediment rate at 1 hour. ILD, interstitial lung disease. PF-ILD, progressive fibrosing interstitial lung disease. * $p < 0.05$, ** $p < 0.01$

Conclusion: The higher ESR during the first one year after ILD diagnosis was associated with the progression to PF-ILD. In serial pulmonary function tests, both the FVC and DLCO at baseline were associated with PF-ILD, and the between-group differences were more prominent at 1 year of follow up. The findings suggest that the persistent inflammation might contribute to the progressive worsening of pulmonary fibrosis and subsequent lung function decline. The immunology and pulmonary function parameters at one year predict the development of PF-ILD.

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AB1430 COMPARISON OF COGNITIVE ABILITY ACROSS THE IMMUNE MEDIATED INFLAMMATORY DISEASES: SYSTEMATIC REVIEW AND META-REGRESSION

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Background: Age strongly influences cognitive ability. Previous studies have tried to compare the cognitive ability of people with different immune mediated inflammatory diseases (IMIDS: systemic lupus erythematosus [SLE], rheumatoid arthritis [RA], axial spondyloarthritis [axSpA], psoriatic arthritis [PsA], psoriasis [PsO]) in age-matched analyses. However, given the varying age of onset of these conditions, within direct age-matched comparisons one of the disease groups is necessarily older/younger than typical.
Objectives: (i) To perform a systematic review of the cognitive ability of people with IMIDs compared with age-matched controls, and (ii) use meta-regression to indirectly compare the cognitive ability of people with different IMIDs.
Methods: A search strategy was implemented in the Medline, Embase and PsychInfo databases on 29.5.2021. Identified studies were screened by two reviewers, selecting observational studies comparing the cognitive ability of people with an IMID against healthy controls. This abstract only includes studies reporting overall cognition scores, memory scores and attention scores. The standardised mean differences (SMDs) of the cognitive assessments between people with IMIDs and controls were pooled using random-effects meta-analysis, stratified by IMID. The IMIDs were compared using meta-regression, to identify the IMID with the greatest impairment in cognitive ability compared with healthy people of a similar age (inclusion cut-off: ≥5 studies).
Results: In total, 62 studies (SLE: 37, RA: 18, axSpA: 1, PsA: 2, PsO: 4) were included in the meta-analyses. People with IMIDs had moderate impairments in overall cognition, memory and attention compared with controls (Table 1), with similar results seen when limiting analyses to studies which included age-matched controls (N=48 studies). People with SLE and RA had similar levels of impairment compared with controls of comparable age in terms of overall cognition (coef: -0.12 (95% CI -0.42, 0.19) and attention (coef: -0.35 (95% CI -0.73, 0.04)). Other IMIDs and cognition dimensions were not included in the meta-regression analysis due to lack of studies.
Conclusion: People with IMIDs have significant impairments in terms of overall cognition, memory and attention. Whilst this indirect analysis shows that people with SLE and RA have a similar magnitude of impairment compared with healthy controls of a similar age, a number of factors could be influencing this finding (e.g. selection bias, demographic differences).
Disclosure of Interests: None declared
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AB1431 EPIDEMIOLOGICAL AND GENETIC FEATURES OF ANTI-3-HYDROXY-3-METHYLGLUTARYL-COA REDUCTASE NECROTIZING MYOPATHY IN NORTHERN SPAIN: SINGLE-CENTER EXPERIENCE

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Background: Anti-3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) immune-mediated necrotizing myopathy (IMNM) is an entity of growing interest. However, data on epidemiology and clinical spectrum are still scarce and there is a need for the identification of its potential risk factors.
Objectives: To characterize the demographic, genetic, clinical, and serological features of patients with anti-HMGCR IMNM in a region of northern Spain.
Methods: Study of all patients diagnosed with anti-HMGCR IMNM during a 5-year period at a reference hospital in Northern Spain. Besides clinical and laboratory data, we analyzed the genetic influence of HLA genes and the rs4149056 (c.521T>C) single nucleotide polymorphism (SNP) in the *SLCO1B1* gene.
Results: 8 patients (5 women, 3 men) with a mean ± SD age of 64.9±7.3 years, fulfilled the criteria for anti-HMGCR IMNM. The incidence rate was 0.6 per 100.000 person-years and the prevalence 3 per 100.000 population. All patients had dyslipidemia and had been exposed to statins. Seven of the 8 of cases complained of myalgia. All of them had predominant lower limb proximal and symmetric muscle weakness that was severe in 2 of them. None of the patients had extra-muscular involvement. No evidence of malignancy was found. All patients had elevated serum CK levels with a median [IQR] of 4488 [2538-9194] IU/L. Serum 25-hydroxy vitamin D levels were decreased in all patients in whom it was determined. The 3 patients with a previous diagnosis of hypothyroidism had abnormal levels of TSH at the time of diagnosis. All patients experienced improvement with different schemes of immunosuppressive therapy. Noteworthy, 7 of 8 patients carried the HLA-DRB1*11 allele. The frequency of the rs4149056 C allele in the *SLCO1B1* gene (12.5%) was similar to that of the general population.
Conclusion: In northern Spain, the IMNM anti-HMGCR preferentially affects people over 50 years of age who are carriers of the HLA-DRB1*11 allele and take statins. Both low vitamin D levels and hypothyroidism may play a potential predisposing role in the development of this disease
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Table 1. Results of meta-analyses

		Standardised mean difference (95% Confidence Interval) [N studies]				
		Systemic lupus erythematosus	Rheumatoid arthritis	Axial spondyloarthritis	Psoriatic arthritis	Psoriasis
Overall cognition	All	-0.55 (-0.70. -0.39) [18]	-0.59 (-0.82, -0.35) [13]	-0.66 (-1.11, -0.21) [1]	-0.50 (-0.78, -0.21) [2]	-0.51 (-1.09, 0.07) [3]
	Age-matched	-0.55 (-0.72, -0.38) [14]	-0.66 (-0.92, -0.41) [11]	-0.66 (-0.11, -0.21) [1]	-0.61 (-1.08, -0.14) [1]	-0.77 (-1.39, -0.16) [2]
Attention	All	-0.51 (-0.63, -0.38) [27]	-0.79 (-1.10, -0.47) [9]	-0.58 (-1.03, -0.13) [1]	-	-0.14 (-0.42, 0.14) [2]
	Age-matched	-0.51 (-0.67, -0.36) [21]	-0.87 (-1.35, -0.39) [6]	-0.58 (-1.03, -0.14) [1]	-	-0.36 (-0.75, 0.04) [1]
Verbal memory (immediate)	All	-0.59 (-0.79, -0.38) [19]	-1.00 (-1.47, -0.53) [7]	-	-	-0.52 (-1.05, 0.02) [3]
	Age-matched	-0.61 (-0.90, -0.32) [12]	-1.42 (-1.73, -1.12) [4]	-	-	-0.72 (-1.42, -0.02) [2]
Verbal memory (delayed)	All	-0.44 (-0.57, -0.31) [18]	-0.93 (-1.48, -0.38) [5]	-0.23 (-0.67, 0.21) [1]	-	-0.52 (-1.52, 0.49) [2]
	Age-matched	-0.39 (-0.56, -0.21) [12]	-1.40 (-1.76, -1.03) [3]	-0.23 (-0.67, 0.21) [1]	-	-1.05 (-1.47, -0.63) [1]
Non-Verbal memory (immediate)	All	-0.41 (-0.57, -0.25) [15]	-0.32 (-1.23, 0.58) [1]	-0.21 (-0.62, 0.23) [1]	-	-
	Age-matched	-0.34 (-0.52, -0.16) [10]	-	-0.21 (-0.62, 0.23) [1]	-	-
Non-Verbal memory (delayed)	All	-0.45 (-0.63, -0.27) [16]	-0.41 (-0.91, 0.08) [1]	-0.14 (-0.58, 0.30) [1]	-	-
	Age-matched	-0.46 (-0.75, -0.17) [10]	-0.41 (-0.91, 0.08) [1]	-0.14 (-0.58, 0.30) [1]	-	-

Table 1.

Patient	Age/Sex	HLA DRB1*11	rs4149056 genotype	MRC at the weakest muscle group*	Dysphagia	CK (IU/L) at diagnosis	Anti-HMGCR titer (CU)	Induction therapy*	Maintenance therapy	Clinical improvement**	CK (IU/L) at last follow-up visit
1	56/M	Yes	TT	2	No	8963	277.8	GC. IVIG.MTX	GC. IVIG. MTX. RTX	Marked	134
2	69/F	Yes	TT	0	Yes	9271	235.9	GC iv bolus. IVIG.	GC. MTX. RTX.	Marked	890
3	64/F	Yes	TT	3	No	4000	242.6	IVIG.	IVIG.RTX	Marked	1284
4	79/M	Yes	TT	4	No	4977	145.6	GC. IVIG.	GC. IVIG.	Complete	92
5	62/F	No	TT	3	No	2116	210.0	GC	GC.MTX.	Marked	236
6	57/F	Yes	TC	4	No	2294	259.3	IGIV	IGIV	Complete	235
7	68/F	Yes	TT	3	No	3273	236.0	GC. IGIV. AZA.	GC. AZA	Complete	249
8	64/M	Yes	TC	4	Yes	11000	179.0	GC iv bolus. AZA.	GC. AZA	Complete	161

*AZA: azathioprine; CK: creatinine kinase; CU: chemiluminescence units; F: female; GC: glucocorticoids; IVIG: intravenous immunoglobulins; M: male; MRC: medical research council scale; MTX: methotrexate; RTX: rituximab; ** Induction therapy initiated within 3 months of diagnosis. **Clinical improvement: no improvement (no improvement in MRC grade), mild improvement (improvement of MRC grade but still requiring assistance for activities of daily living), marked improvement (persistence of mild weakness without functional limitation), and complete improvement (return to baseline with no symptoms or signs of weakness).*

AB1432 THE ASSOCIATION OF PAINFUL AND NON-PAINFUL COMORBIDITIES WITH CENTRAL MECHANISMS OF KNEE PAIN

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Background: Central mechanisms of knee pain occur in the central nervous system and may intensify and prolong pain. Central pain mechanisms might be facilitated by ongoing nociceptive input. A link between multimorbidity and central mechanisms of knee pain is proposed; ongoing sensory inputs due to comorbidities may trigger changes in pain processing by the CNS. This might be particularly expected with painful comorbidities.

Objectives: To investigate potential relationships of painful and non-painful multimorbidity with central mechanisms of knee pain.

Methods: Cross-sectional analysis of self-report data from participants of the Investigating Musculoskeletal Health and Wellbeing cohort, who reported knee as their most bothersome site of joint pain over the previous month, with pain rated ≥1/10, and who had completed FRAIL and CAP-Knee (1) questionnaires. Two indirect measures suggesting central mechanisms involvement in knee pain were used as dependent variables; pain intensity (0-10 numerical rating scale) and CAP-Knee score (0-16 scale). Comorbidities were assigned either "painful comorbidity" or "non-painful comorbidity" status based on IASP classification of chronic pain criteria (2). Multivariable linear regression models, adjusted for age and sex, were employed to explore associations of comorbidity counts with pain intensity and CAP-Knee score.

Results: 736 participants satisfied inclusion criteria. 55% were female, mean age 71 (range 40 to 95). Painful comorbidity count and non-painful comorbidity count each had positive associations with pain intensity (β=0.42, 95% CI=0.29 to 0.54, p<0.001; and β=0.31, 95%CI=0.16 to 0.45, p<0.001, respectively). Painful and non-painful comorbidity counts each also were associated with CAP-Knee score (β=0.80, 95% CI=0.59 to 1.01, p<0.001; and β=0.52, 95% CI=0.27 to 0.77, p<0.001, respectively). Painful and non-painful comorbidity counts each remained significantly associated both with pain intensity and with CAP-Knee scores when both types of comorbidity count were included in the same multivariable model.

Conclusion: Both painful and non-painful comorbidities were positively associated with central mechanisms of knee pain, providing further insight into the interconnectedness of pain processing systems and the rest of the body. The explanation behind these relationships may depend on more than just ongoing nociceptive input. Future work should address possible contributions from genetic, pathophysiological, psychological, and pharmacological factors associated with comorbid diagnosis.

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AB1433 ASSESSING THE CARDIOVASCULAR RISK IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: QRISK AND GAPSS SCORES HEAD TO HEAD

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Background: Cardiovascular diseases (CVDs) represent one of the most life-threatening conditions that can affect SLE patients. Assessing the potential CVD risk of these patients is still a challenge and an important aspect in the clinical practice. Recently the QRISK3 score has attempted to encompass for SLE augmented thrombotic risk by adding items (such as corticosteroid use) that are missing in traditional CVD risk scores.

Objectives: To apply and compare the QRISK3 and the adjusted Global AntiPhospholipid Syndrome Score (aGAPSS), a validated score to assess CVD and overall thrombotic risk in aPL positive patients, in a cohort of SLE patients with and without a concomitant diagnosis of APS.

Methods: 25-85 years old patients attending San Giovanni Bosco Hospital (Turin) during a period of 6 months (Sep 2019 – Feb 2020) with a confirmed diagnosis of SLE (2019 ACR/EULAR classification criteria) and/or a diagnosis of SAPS (Sidney criteria) were included in the study. QRISK3 has been calculated using the official online calculator (https://qrisk.org/). aGAPSS has been calculated using the validated point values based on aPL profile and independent risk factors: aCL=5, aβ2GPI=4, LA=4, aPS/PT=3, hyperlipidemia=3, hypertension=1.

Results: The analysis included a cohort of 142 SLE patients: 34 SAPS (23.9%) and 108 SLE patients without APS (76.1%), with a mean age of 48±12.9 (SAPS=51.6±12.8/SLE without APS=46.9±12.8). Table 1 summarizes patients characteristics. When focusing on cerebrovascular/coronary events, we found a statistical significance with respect to aGAPSS (pt with event =10.1±6.2 vs pt without event=5.8±6.1; p=0.007), but not QRISK3. Also, a significant association was observed between the occurrence of these events and high risk aGAPSS: p=0.03 for aGAPSS≥8, p=0.01 for aGAPSS ≥9, p=0.008 for aGAPSS ≥10. Moreover, the aGAPSS but not the QRISK3 resulted to strongly correlate with the occurrence of any thrombotic event, both at the uni- and multivariate analysis (univariate: pt with event =8.17±7.1 vs pt without event= 5.41±5.6; p=0.012 / multivariate: p=0.009). The same was observed for gender: male gender resulted to correlate with the occurrence of any thrombotic event at both uni- and multivariate analysis (p=0.017 and p=0.03, respectively). Finally, when focusing on aPL profile, regardless

the diagnosis, we found a statistical significance only with respect to aGAPSS (aPL+ =9.6±6.3 vs aPL- = 4.1±5.1; p<0.001).

Table 1. Demographic and clinical features of the patients included in the study.

PATIENTS CHARACTERISTICS	
Age (m±sd)	Tot=48±12.87
	SAPS=51.61±12.82
	SLE w/o APS=46.87±12.83
Females, n (%)	Tot=120/142 (84.5%)
	SAPS=22/34 (64.7%)
	SLE w/o APS=98/198 (90.74%)
THROMBOTIC EVENTS	
Thrombotic event, n (%)	Tot=48/142 (33.8%)
	SAPS=33/48 (68.75%)
	SLE w/o APS=15/48 (31.25%)
Arterial thrombosis, n (%)	Tot=22/142 (15.49%)
	SAPS=19/22 (86.36%)
	SLE w/o APS=3/22 (13.64%)
Venous thrombosis, n (%)	Tot=32/142 (22.53%)
	SAPS=18/32 (56.25%)
	SLE w/o APS=14/32 (43.75%)
Stroke, n (%)	Tot=13/142 (9.15%)
	SAPS=13/13 (100%)
	SLE w/o APS=0/13 (0%)
TIA, n (%)	Tot=6/142 (4.22%)
	SAPS=6/6 (100%)
	SLE w/o APS=0/6 (0%)

Conclusion: By encompassing factors that can contribute to CVD development in complex/autoimmune diseases, QRISK3 has been shown to be more accurate than traditional risk score in predicting SLE patients CVD risk. Nonetheless, the results of this analysis showed how the aGAPSS still seems to be the most valuable tool for this purpose when facing SLE patients. Moreover, the significance observed when focusing on patients' aPL profile, suggests that adding this item to the QRISK3 could be a useful strategy to improve the management.

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AB1434 PREGNANCY AND RHEUMATIC DISEASES – COMBINING BIOLOGICAL MATERIAL AND CLINICAL DATA FOR FUTURE RESEARCH

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Background: Rheumatic diseases affect women in fertile age. There is an increased risk for disease flares and pregnancy complications, especially for patients with systemic rheumatic diseases. Improving knowledge of immunological changes that happen during and after pregnancy in women with rheumatic diseases is of great importance. The Norwegian National Advisory Unit for Pregnancy and Rheumatic Diseases (NKSR) therefore established a biobank in 2012 with material from this patient group. NKSR also administers RevNatus, a nationwide pregnancy quality register including women with inflammatory rheumatic diseases, with comprehensive clinical data.

Objectives: To facilitate high quality research by developing a possibility to combine biobank material and comprehensive clinical data. We aim to increase current knowledge in this field, with the ultimate goal of making pregnancies safer for women with rheumatic diseases.

Methods: The RevNatus biobank is part of the Regional Biobank of Central Norway (Biobank[1]). Biobank[1] is a research facility established to provide an organizational framework for all research, which involves biological material from patients in any of the public hospitals of the region. The collection of biologic material is approved by the regional committees for medical and health research ethics. Patients are included after having signed a consent form. Blood samples are collected before pregnancy, in each trimester, 6 weeks, 6 months and 12 months postpartum. So far, serum, plasma, buffy-coat and Tempus Blood RNA tubes have been collected. At the same time points when blood samples are collected, clinical data is registered in RevNatus. Serum, plasma, buffy-coat and Tempus Blood RNA tubes from 32 healthy pregnant women have also been collected as control group material.

Results: 310 donors are so far included in the RevNatus biobank. These include systemic lupus erythematosus (36), rheumatoid arthritis (61), juvenile idiopathic arthritis (40), spondyloarthritis (96), Sjögren's syndrome (8), granulomatosis with polyangiitis (5), MCTD (5), healthy controls (32) and others (27).

Table 1. Number of donors in the biobank at each time point

Time point	Number of donors
Before pregnancy	135 donors
1st trimester	123 donors
2nd trimester	124 donors
3rd trimester	117 donors
6 weeks postpartum	175 donors
6 months postpartum	166 donors
12 months postpartum	129 donors

Conclusion: Collections of biological samples from pregnant women with rheumatic diseases are hard to come by, and therefore research is scarce. RevNatus with its biobank has the potential to make a substantial impact combining clinical and biological material, and take an important role in further molecular research in the field of rheumatic disease and pregnancy.

Disclosure of Interests: None declared

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AB1435 CLINICAL PREDICTION MODELS FOR METHOTREXATE OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS: SYSTEMATIC REVIEW AND CRITICAL APPRAISAL

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Background: Methotrexate (MTX) is the preferred first line therapy for rheumatoid arthritis (RA). MTX has several advantages over other treatments including effectiveness and low cost; however, around 40% of patients are classed as non-responders after 6 months (1). Therefore, there is a clinical need to identify patients at high-risk of poor outcomes, such that patients could potentially be fast tracked onto alternative therapies to improve their clinical outcomes and quality of life. Such risk stratification is possible through prognostic prediction models, although models which have previously been developed appear to have had little impact on practice. This may be in part due to methodological features of their development and validation but, to date, no review has collated the evidence in this field.

Objectives: This systematic review aimed to (i) identify and summarise multivariable prediction models of MTX treatment outcomes in biologic-naïve adult RA patients, and (ii) critically appraise their methodological properties.

Methods: The electronic databases Medline and Embase were searched to identify studies developing or validating prediction models of MTX outcomes in the population of interest, including demographic, disease-specific or treatment-related covariates, published after 2005. Models were stratified by outcome definition, and information on participants, predictors, model performance, handling of missing data and model validation were extracted. A risk of bias (ROB) assessment using PROBAST (prediction model risk of bias assessment tool) was carried out. Two reviewers were independently involved in screening, data extraction, and ROB stages.

Results: The included studies used three main outcome definitions: a state of disease activity, such as low disease activity or remission; the EULAR response criteria; or discontinuation due to adverse events (AEs). Some studies incorporated AEs into a composite outcome with disease activity and few accounted for potential competing risks, which are events that preclude the occurrence of the primary outcome of interest. Not handling competing risks may result in under-prediction, leading to potentially compromised risk stratification. There was a lack of internal validation using cross sampling techniques, which is critical for reducing overfitting, as well as external validation in new data, a process necessary to ensure reproducibility and generalisability of a prediction model to the larger patient population. Missing data was mostly handled using complete case analysis, leading to potentially biased risk estimates. The ROB assessment showed overall high ROB of the included studies.

Conclusion: This systematic review summarises current prediction models of MTX treatment outcomes in RA. It highlights several methodological shortcomings, such as poor handling of missing data and competing risks to the primary outcome, and a lack of internal and external validation. These should be addressed in future model development and validation to improve accuracy of predictions. Without tackling these issues, prediction of MTX treatment outcomes will remain at high risk of bias and should not be recommended for informing risk stratification for RA treatment decisions.

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AB1436 INFECTIONS IN PATIENTS WITH RHEUMATIC DISEASES IN TREATMENT WITH BIOLOGIC THERAPY

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Background: Patients with rheumatic diseases (RD) have a higher risk of developing infections due to disease and immunosupressor treatment factors[1]. Biologic disease -modifying antirheumatic drugs (bDMARD) have been associated with the development of opportunistic infections, nevertheless their impact on severe infections has not been consistent[2].

Objectives: To describe the sociodemographic and clinical characteristics of patients with RD on bDMARD treatment with and without infections, using data from the Mexican Adverse Events Registry (BIOBADAMEX), as well as to identify factors associated with the presence of infections.

Methods: BIOBADAMEX is a Mexican ongoing cohort of patients using bDMARDs. In this analysis we included all patients registered in Biobadamex from 2016 to 2021. We compared sociodemographic, clinical and treatment characteristics between patients who developed infections with to those who did not. We used descriptive statistics, Chi square and Kruskal Wallis tests to analyze differences between the groups.

Results: A total of 780 patients registered in Biobadamex were included in this study, among them 42 (5%) patients presented infections and 738 (95%) did not. At baseline, patients had a median (IQR) age of 50 (40-58) years and median disease duration of 7 (3-15) years. The most common diagnosis was rheumatoid arthritis with 512 (66%) patients, followed by ankylosing spondylitis in 115 (15%), psoriatic arthritis in 44 (6%), systemic lupus erythematosus in 30 (4%) and idiopathic juvenile arthritis in 27 (3%) patients. Comorbidities were present in 351 (45%) of the patients. Conventional DMARD (cDMARD) were used by 626 (80%) patients, and 290 (37%) used steroids. The most frequently used bDMARDs were adalimumab in 166 (21%) patients, certolizumab in 129 (16%), tocilizumab in 103 (13%) and abatacept 94 (12%). Table 1 shows baseline characteristics in the groups with and without infections. Patients with infections presented more severe adverse events 3 (7%) compared to those who did not 11 (2%), p=0.007, with a complete recovery without sequels. Most common infection site was skin (21%) followed by superior airways (12%). Most common infectious agents were gram negative bacteria. Only 2 patients presented bacteremia.

Table 1. Patients baseline characteristics

	Infection n=42	Without infection n=738	p
Female, n(%)	33 (79)	595 (80)	0.74
Age, median(IQR)	50.9 (43-59)	49.8 (40-58)	0.58
Disease duration (years), median (RIC)	7.5 (2-16)	7.0 (3-15)	0.9
Diagnostic, n(%):			
Rheumatoid arthritis	25 (59)	487 (66)	0.42
Idiopathic Juvenile Arthritis	0 (0)	27 (4)	
Ankylosing Spondylitis	6 (14)	109 (15)	
Others	11 (26)	115 (15)	
Comorbidities, n(%):	22 (52)	329 (44.6)	0.32
Previous bDMARD, n(%):	15 (36)	271 (37)	0.89
Use of steroids, n(%):	16 (38)	274 (37)	0.9
cDMARD, n(%)	33 (79)	593 (80)	0.77
Severe Adverse Events, n(%)	**3 (7)**	11 (2)	0.007
Outcome, n(%)			
Recovered without sequels	3 (100)	6 (55)	p=0.34*
Not recovered	0	3 (27)	
Unknown	0	2 (18)	
Infection site, n(%)			
Skin	9 (21)		
Superior airways	5 (12)		
Urinary tract	4 (10)		
Agent, n(%)			
Gram- bacteria	9 (21)		
Gram+ bacteria	0 (0)		
Virus	4 (14)		

*Chi2

Conclusion: The frequency of infections in patients using bDMARD in Biobadamex is low compared to the frequency reported in similar studies in other countries[3]. The presence of infections was associated with more severe adverse events in general, which recovered completely without sequels.

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AB1437 RHEUMATOLOGICAL IMMUNE-MEDIATED ADVERSE EVENTS OF IMMUNE CHECKPOINT INHIBITORS BASED ON THE FDA ADVERSE EVENTS REPORTING SYSTEM

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Background: Immune checkpoint inhibitors (ICIs) provide effective treatment for many cancers but, presumably due to persistent activation of the immune system, they cause a variety of immune-related adverse events (irAEs) in almost every organ. Rheumatological manifestations have been reported in ~5-10% of patients treated with ICIs.

Objectives: We aimed to analyze the rheumatological irAEs (rh-irAEs) reported to the FDA Adverse Event Reporting System (FAERS) from October 2012 through March 2021.

Methods: From October 1st, 2012, to March 31st, 2021, we studied all case reports found on the FAERS database when any of the following seven FDA-approved ICIs, nivolumab, pembrolizumab, ipilimumab, atezolizumab, durvalumab, avelumab, or cemiplimab, was the primary suspect of the reported adverse events (AEs). Of the 6,090 different AEs reported for the ICIs, we selected 186 irAEs, which were rheumatological manifestations, or were associated with rheumatological conditions. We calculated the frequencies of rh-irAEs for each ICI. RStudio v1.4.1106 was used for general data analysis and the R package

openEBGM v0.8.3 was used for the calculation of disproportionality scores such as the Empirical Bayes Geometric Mean (EBGM) with its 90% two-sided credibility interval, frequently used in safety signal detection models. Drug-event combinations with an EBGM 5% lower limit credibility interval ≥ 1 were considered significant.

Results: During the study period, 90,974 individual case safety reports (ICSR) included 236,239 AEs with one ICI as the primary suspect of the AE. The highest frequency of AEs was reported for nivolumab (49.6%), followed by pembrolizumab (23.4%), ipilimumab (12.6%), atezolizumab (8.6%), durvalumab (4.6%), avelumab (0.9%), and cemiplimab (0.3%). The AEs were more frequent in males (62.7%) than in females (37.3%). Of the total ICSRs, 84.2% were expedited because they reported serious, unexpected irAEs. Rh-irAEs were 11,203 (4.7%) out of the 236,239 AEs reported. These rh-irAEs were reported in 3,898 (4.3%) out of the 90,974 ICSRs. For the ICSRs containing rh-irAEs, 78.5% were expedited. Unspecific complains, such as arthralgia, myalgia or muscle weakness were among the most frequent rh-irAEs. Avelumab and atezolizumab were associated with Sjogren's syndrome and sarcoidosis. Durvalumab, avelumab, atezolimumab and cemiplimab were all associated with myositis. Twenty-one drug-event combinations were significant for EBGM. Of those, nivolumab and pembrolizumab were the two most frequent ICI, with 7 and 6 significant drug-event combinations, respectively.

Conclusion: Approximately 5% of the reported ICIs-associated AEs were rh-irAEs. The most frequent complaints were unspecific, such as arthralgia, myalgia, or muscle weakness. Arthritis, myositis, Sjogren's syndrome, and sarcoidosis were also relatively frequent. The improved understanding of the mechanism of action of the ICIs and the characteristics of the rh-irAEs may help to elucidate the pathogenesis of the rheumatological autoimmune diseases that they trigger.

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AB1438 CARDIOVASCULAR RISK STRATIFICATION FOR TOFACITINIB PATIENTS IN A LARGE TEACHING HOSPITAL

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Background: Tofacitinib is an oral JAK-Inhibitor often reserved for patients with treatment-resistant Rheumatoid Arthritis and Psoriatic Arthritis. Tofacitinib modulates cytokines crucial to the inflammatory response which characterises the above conditions, and inhibits certain pathways in the inflammatory response cascade. Rheumatoid and Psoriatic Arthritis are linked with an inherent increased risk for major cardiovascular events. Recent emerging data has evidenced increased cardiovascular risk associated with long-term use of tofacitinib.

Objectives: To identify all patients currently undergoing Tofacitinib treatment across all sites at King's College Hospital NHS Foundation Trust. To risk-stratify all patients into three categories; low risk of developing major cardiovascular events, moderate risk of developing MACE (patients with modifiable risk factors, eg. high cholesterol or a borderline blood pressure), and high risk of developing MACE (unmodifiable risk factors). To switch patients at high risk onto another treatment or alternative JAK-inhibitor.

Methods: Patient data was obtained through electronic patient records including age, blood pressure reading, full lipid profile, smoking status, and comorbidities (hypertension, diabetes, chronic kidney disease, previous cardiovascular history and history of malignancy). A QRISK3 score was calculated.

Modifiable risk factors with a lower QRISK3 score were categorised as moderate risk. Patients were considered at high risk if they had a previous cardiovascular event, or a QRISK3 score of more than 10%.

Results: A total of 40 patients were on tofacitinib; 64% with RA, 31% with PsA, and 5% for other reasons (interstitial lung disease and colitis). Of the rheumatoid arthritis cohort: 36% of patients were at high risk, 40% at moderate risk, and 24% low risk. Of the psoriatic arthritis cohort: 67% at high risk, 25% at moderate risk, 8% at low risk.

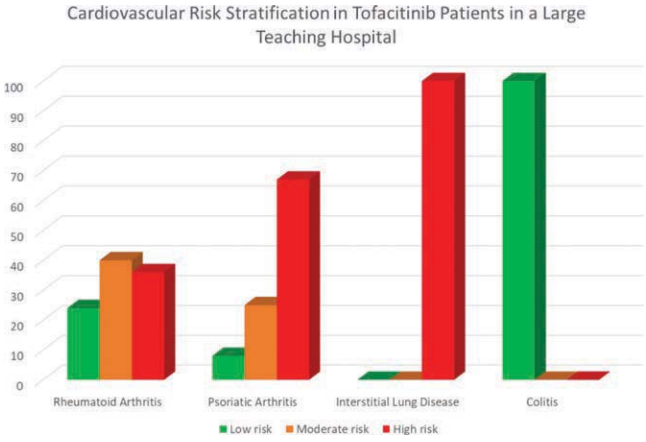

Figure 1.

Conclusion: A significant number of patients were deemed at moderate and high risk. Patients with moderate risk were advised to undergo lifestyle changes, like exercise and diet modification and smoking cessation.

Patients at high risk were discussed at the trust-wide Rheumatology local clinical governance meeting, and advised to switch onto an alternative treatment or alternative JAK-inhibitor.

A repeat audit will be made in a few months' time to assess the impact of lifestyle changes and alteration of drugs on cardiovascular risk.

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AB1439 IS THERE AN INCREASED PREVALENCE OF DIABETES MELLITUS IN THE AXIAL SPONDYLOARTHROPATHY PATIENT GROUP: A REVIEW FROM A UK TEACHING HOSPITAL SPONDYLOARTHROPATHY SERVICE

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Background: The prevalence of diabetes mellitus (DM) has often been found to be increased in patients with axial spondyloarthropathy (axSpA) compared to the general population. However, studies conducted in the United Kingdom (UK) have found varying results with regards to prevalence. One study[1] found that 5% of patients with axSpA had DM, compared to 4% of patients without axSpA and another UK study[2] reported that although findings showed a 1.8% increase in DM in patients with axSpA compared to controls, this result was not significant. There is also the influence of ethnicity to consider as DM is more prevalent in the Asian and Afro-Caribbean population. Therefore, it is evident that more research is required into the relationship between DM and axSpA.

Objectives: This study aims to investigate the correlation between DM and axSpA, and also explore the influence of ethnicity on DM and axSpA.

Methods: Retrospective analysis was carried out for axSpA patients attending University Hospitals of Leicester axSpA services. Inclusion criteria entailed an axSpA diagnosis and a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) within a year of MRI spine and sacroiliac joints before starting biological therapy. Patients were excluded if they had an active infection or malignancy, BASDAI was not documented before starting biological therapy or within a year of MRI, or if clinical information was not able to be obtained. Data was obtained from electronic medical records, including age, gender, ethnicity, date of diagnosis of axSpA and DM, and cardiovascular comorbidities.

Results: Of the 149 patients, 8 (5.37%) had a diagnosis of DM. 4 (50%) of these patients were diagnosed with DM prior to diagnosis of axSpA, and 4 (50%) were diagnosed with DM post diagnosis of axSpA. Differences in ethnicity were analysed. Of the 149 axSpA patients, 102 (68.46%) were Caucasian, 45 (30.20%) were Asian, and 2 (1.34%) were Afro-Caribbean. Of the 102 Caucasian patients, 3 (2.94%) had DM, of whom 1 was diagnosed with axSpA prior to diagnosis of DM. Of the 45 Asian patients, 5 (11.11%) had DM, of whom 3 were diagnosed with axSpA prior to diagnosis of DM. Looking at cardiovascular comorbidities, of the 8 patients with axSpA and DM, 2 (25%)

had hypertension, and were both diagnosed with axSpA prior to diagnosis of DM.

Conclusion: This small study has found a similar prevalence of DM in patients with axSpA (5.37%) compared to the general UK population (6%), which contrasts with published international studies which have found a higher prevalence of DM in the axSpA group. However, the study did find a higher prevalence in the Asian population (11.11%) which is in keeping with ethnic variation for DM. Larger epidemiological studies are needed to understand the reason for reported higher prevalence of DM in patients with axSpA in other countries compared to the UK.

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AB1440 ASSOCIATION BETWEEN GAMMA-GLUTAMYL TRANSFERASE (GGT) AND SERUM URATE: CROSS-SECTIONAL FINDINGS FROM THE 1993 PELOTAS (BRAZIL) BIRTH COHORT

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Background: Gout attack is associated with an abrupt increase or decrease on serum urate concentrations, which can precipitate urate crystals in tissues in and around the joints. Serum urate (SU) has been positively associated with cardiometabolic risk factors and subclinical inflammation in observational studies, but causal roles remain unclear. [1] Additionally, gamma-glutamyl transferase (GGT) has been linked to oxidative stress, metabolic syndrome, and nonalcoholic fatty liver disease (NAFLD).

Objectives: The aim of this study was to assess the association between GGT and SU in Brazilian young adults.

Methods: During 1993, all live born babies in the city of Pelotas (Brazil) were invited to take part in a prospective study. At the 22-year follow-up of this birth cohort, SU was evaluated by enzymatic-colorimetric assay. GGT was evaluated by kinetic assay and converted into logarithm for regression analysis. The co-variables taken into consideration were waist circumference (WC), systolic and diastolic blood pressures (SBP, DBP), glucose (G), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), creatinine (Scr), fasting period, smoking status, excessive alcohol consumption (>8 points in the Alcohol Use Disorders Identification Test-AUDIT), and physical activity (PA). For association analyses, serum concentration of urate was categorized into tertiles. Sex-stratified linear regressions have been performed due to the significant interaction between GGT, SU and sex (p<0.001). A p-value less than 0.05 was considered statistically significant.

Results: The sample comprised 1660 (47.7%) men and 1822 (52.3%) women aged 22.6 (±0.34) years old. Median (IQR) GGT (U/L) was 26 (20-35) in men and 21 (16-30) in women (p<0.001). Mean (±SD) SU (mg/dL) was also higher in men (5.2±1.2 *vs.* 3.9±1.1; p<0.001). No significant association between GGT and tertiles of SU was observed in men (between the 1st and 2nd tertiles, the p-value was 0.713; and between the 1st and 3rd, p = 0.185). In women, between the 1st and 2nd tertiles, the linear p-value was 0.251; and between the 1st and 3rd; p = 0.001. The corresponding exponential mean of GGT for each SU tertile is described in (Table 1).

Table 1. Exponential means (95%CI) of GGT (U/L) according to the SU tertiles in 22-year-old individuals from the 1993 Pelotas (Brazil) birth cohort

	Men (n=1638)		Women (n=1801)	
SU Tertile	**Mean**	**95%CI**	**Mean**	**95%CI**
	*p=0.231**		***p=0.005****	
1	26.8	(25.3; 28.5)	22.6	(21.8; 23.3)
2	27.1	(26.3; 28.2)	23.3	(22.4; 24.3)
3	28.2	(27.4; 29.1)	26	(24.1; 28)

Linear regression adjusted for WC, SBP, DBP, Glu, HDL-c, LDL-c, Scr, fasting, smoking status, alcohol consumption (>8 points AUDIT), and PA. ***heterogeneity p-value**

Conclusion: GGT was positively associated with SU in women, even after adjusting for potential confounders. This finding reinforces that uric acid is associated with cardiometabolic risk factors since early adult age. Nonetheless, further prospective studies are needed to understand the causality of this association especially observed in women.

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AB1441 LEARNING NEEDS ASSESSMENT FOR PATIENTS WITH CANCER AND A PRE-EXISTING AUTOIMMUNE DISEASE WHO ARE CANDIDATES TO RECEIVE IMMUNE CHECKPOINT INHIBITORS

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Background: Patients with autoimmune disorders and cancer are at risk of developing immune-related adverse events (irAEs) and increasing flares of their underlying disease with immune checkpoint inhibitors (ICI) and harms and benefits must be weighed.

Objectives: We conducted an assessment of learning needs.

Methods: We interviewed 19 patients who had received an ICI and 20 physicians who provide care for these patients. We asked what do cancer patients with pre-existing autoimmune diseases need to know in order to make an informed decision about whether to receive an ICI.

Results: Fifty-three percent of the patients were female, median age was 62.9 (±10.9). They had rheumatoid arthritis (47.4%), psoriasis (26.3%), Crohn's disease (10.5%), ankylosing spondylitis (5.3%), systemic lupus erythematosus (5.3%), or ulcerative colitis (5.3%). Half of the patients (52.6%) had a demonstrable disease activity of the autoimmune disease at the time of making the decision on whether to start ICI. Most (84%) of the patients had melanoma, and at the time of the interview 68.4% had completed or discontinued the ICI. Physicians were melanoma oncologists (30%), thoracic-head & neck medical oncologists (25%), rheumatologists (20%), gastroenterologists (10%), and dermatologists (15%) who treat patients with irAEs. Sixty percent were female. Key points mentioned by patients and physicians included information on probability of irAEs and flares of the autoimmune condition with discussion about severity, benefits of ICI, ICI mechanism of action in the context of the autoimmune disease, and management for flare-ups. Key topics raised only by patients included possible reasons for stopping or modifying treatment (for cancer or autoimmune disease), when to contact the provider, possibility of autoimmune disease progression or organ damage, sharing information with other providers, and lifestyle changes that can be done to help.

Conclusion: Although patients and physicians listed common learning points, patients also considered specific needs to increase their self-care. The information derived from this study will be used to develop a decision support tool.

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AB1442 A PREDICTIVE MODEL OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME: A RETROSPECTIVE COHORT STUDY

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Background: Catastrophic antiphospholipid syndrome (CAPS) is a life-threatening form of antiphospholipid syndrome (APS), with rarely occurrence but high mortality. Current classification diagnosis criteria require more than 3 organs involvement in 1-week time and pathological evidence in patient with persistent positive antiphospholipid antibodies (aPL), which could result the delaying

Table 1. Characteristics and predicting factors of CAPS in PUMCH-APS cohort

	CAPS (N=27)	Non-CAPS (N=199)	p	Odds ratio	p	Coefficient B	Score
Gender (M)	14(51.9)	64(32.2)	**0.043**				
Age (y)	36.3±15.2	36.2±12.5	0.975				
Disease duration (m)	49.7±77.7	53.9±72.3	0.777				
Secondary APS	14(51.9)	52(26.1)	**0.006**				
APS diagnosis							
Venous thrombosis	17(63.0)	106(53.3)	0.342				
Arterial thrombosis	22(81.5)	79(39.7)	**0.000**				
Pregnancy morbidity	5(18.5)	68(34.2)	0.103				
LA	22(81.5)	155(77.9)	0.671				
aCL	21(77.8)	123(61.8)	0.105				
a-β2GP1	23(85.2)	155(77.9)	0.384				
Precipitating factors	**24(88.9)**	**19(9.5)**	**0.000**	**108.961(23.299-509.572)**	**0.000**	**4.691**	**5**
WBC($\times10^9$/L)	9.0±6.3	6.6±2.9	0.067				
HGB(g/L)	82.7±20.4	130±23.8	**0.000**				
Hemolytic anemia	15(55.6)	20(10.1)	**0.000**				
PLT($\times10^9$/L)	61.1±67.1	132±84.0	**0.000**				
Thrombocytopenia	**24(88.9)**	**80(40.2)**	**0.000**	**14.765(3.088-70.612)**	**0.001**	**2.692**	**3**
Cr(μmol/L)	224.5±225.8	74.4±28.4	**0.002**				
Elevated Cr	**15(55.6)**	**34(17.1)**	**0.000**	**5.339(1.301-21.07)**	**0.020**	**1.675**	**2**
LDH(U/L)	476.4±227.0	226.9±92.3	**0.000**				
Elevated LDH	25(92.6)	54(27.1)	**0.000**				
Proteinuria	18(66.7)	28(14.1)	**0.000**				
Hematuria	15(55.6)	20(10.1)	**0.000**				

diagnosis and treatment. A predictive model could help identify CAPS patients earlier and initiate early intervention.

Objectives: To develop a predictive model of CAPS in APS patients in a single-center prospective APS cohort.

Methods: Data of consecutive APS patients referred into Peking Union Medical College Hospital from May 2013 to October 2021 was collected. A binary logistic regression method was used to identify predictors of CAPS, coefficient B was assigned with score value in the development of prediction model, and risk-stratification was based on the calculated score using the predictive model. The performance of the model was assessed by Nagelkerke's R^2, Hosmer-Lemeshow test, Omnibus test, and area under the receiver operating characteristic curve (AUC).

Results: A total of 27 CAPS (11.9%) occurred in 226 APS patients. CAPS were more likely to occur in male secondary APS patients with history of arterial thrombosis. Precipitating factors (OR 108.961, 95% CI 23.299 to 509.572), thrombocytopenia (OR 14.765, 95% CI 3.088 to 70.612) and elevated serum creatine (OR 5.339, 95% CI 1.301 to 21.907) were selected by the binary logistic regression. The scores of precipitating factors, thrombocytopenia and elevated serum creatine were 5, 3 and 2. The risk scores were divided into high-risk (7-10) and low-risk (0-6), the risk for CAPS were 73.3% and 2.6%, with sensitivity of 81.5% and specificity of 96%. The Nagelkerke's R^2 (0.696), the Hosmer-Lemeshow test ($\chi2$ =2.192, df=4, p=0.701) and the Omnibus test ($\chi2$ =101.307, df=3, p=0.000) indicated the logistic regression model has a good fit. The AUC was 0.969 (95% CI 0.947 to 0.991, SE=0.011, p=0.000) indicated the model has good discrimination.

Conclusion: A predictive model of CAPS was developed with precipitating factors, thrombocytopenia, and elevated serum creatine. This model helps physicians identify CAPS in high-risk patients, could achieve early intervention and improve prognosis.

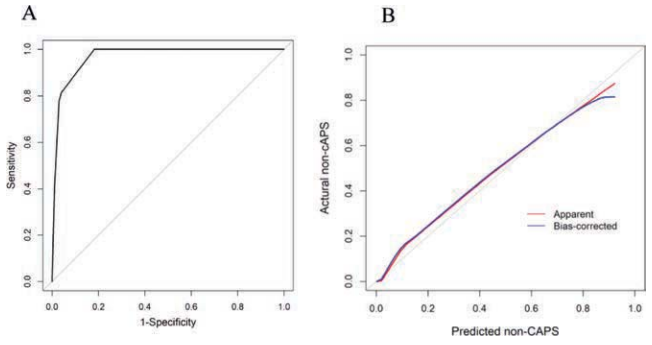

Figure 1. (A). Receiver Operating Characteristic (ROC) curve of the predictive model. Area under the receiver operating characteristic curve (AUC) was 0.969, the cut-off value of 7 were with sensitivity of 81.5% and specificity of 96%. (B). Calibration curve in internal validation.

Disclosure of Interests: None declared

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AB1443

INCIDENCE OF RHEUMATIC DISEASES DURING THE COVID-19 PANDEMIC IN KOREA: A NATIONWIDE CLAIMS STUDY

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Background: In Korea, it has been reported that the incidence of some respiratory diseases and Kawasaki diseases has decreased compared to the previous year along with active non-pharmaceutical interventions in the early stages of the COVID-19 pandemic. Autoimmune inflammatory rheumatic disease (AIIRD) is mainly affected musculoskeletal organs and connective tissues due to impaired immune regulation. Although gout and osteoarthritis are rheumatic diseases, they are not a disease of the immune system, and are not included in the AIIRD.

Objectives: In this study, we investigated the change and difference in the incidence rate of various rheumatic diseases during the COVID-19 pandemic after 2020.

Methods: The number of patients for each disease from January 2016 to December 2020 was obtained from the Korea Health Insurance Review and Assessment Service database. We compared the incidence of 9 rheumatic diseases [systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), ankylosing spondylitis (AS), Sjogren syndrome (SJS), Behcet's disease (BD), inflammatory myositis (IIM), scleroderma, polymyalgia rheumatica (PMR), and gout] and hypertension before and after the COVID-19 outbreak. The incidence rates of patients before and after the COVID-19 outbreak were compared using the Poisson test.

Results: From 2016 to 2019, the prevalence of rheumatic diseases showed gradually increased. In 2020, the incidence of SLE, AS, SJS, BD, and IIM were significantly decreased compared to the previous 4 years. In contrast, the incidences of gout and hypertension during the COVID-19 pandemic period were significantly increased from the predicted values.

Conclusion: In conclusion, we found that the incidence of many AIIRDs, including SLE, AS, SJS, BD, and IIM decreased despite the increased incidence of hypertension and gout during the COVID-19 pandemic.

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Table 1. Cumulative incidence of rheumatic diseases and HTN (by Poisson test)

	Mean (2016-2019)	Observed (2020.1~12)	Rate ratio (95%CI)	P value
SLE	5371.3	4541.0	0.844 (0.811, 0.878)	<0.001
BD	3598.3	3057.0	0.848 (0.808, 0.890)	<0.001
AS	11679.5	10934.0	0.935 (0.910, 0.959)	<0.001
SJS	7913.5	7280.0	0.918 (0.890, 0.948)	<0.001
IIM	839.8	397.0	0.472 (0.418, 0.532)	<0.001
RA	17490.3	17342.0	0.990 (0.969, 1.011)	0.343
SSc	592.8	557.0	0.938 (0.834, 1.054)	0.288
PMR	1072.0	1152.0	1.073 (0.986, 1.167)	0.098
Gout	129543.0	131133.0	1.011 (1.003, 1.018)	0.007
HTN	680943.2	696391.0	1.021 (1.018, 1.024)	<0.001

SLE; systemic lupus erythematosus, BD; Behçet disease, AS; ankylosing spondylitis, SSc; systemic sclerosis, IIM; idiopathic inflammatory myositis, RA; rheumatoid arthritis, SJS; Sjogren syndrome, PMR; polymyalgia rheuamtica, HTN; hypertension, CI; confidence interval.

Disclosure of Interests: None declared
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AB1444 ASSOCIATION BETWEEN THIOPURINE S-METHYLTRANSFERASE POLYMORPHISMS AND HEPATOTOXICITY IN AZATHIOPRINE-TREATED PATIENTS WITH AUTOIMMUNE DISEASES

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Background: Azathioprine(AZA) is widely used in patients with autoimmun diseases. Thiopurine methyltransferase (TPMT) is the rate-limiting enzyme in AZA metabolization. Although several studies have investigated the association between TPMT polymorphisms and AZA-induced bone marrow suppression, the relationship of TPMT genotypes and hepatoxicity in patients taking AZA remained unclear.
Objectives: This study aimed to investigate the correlation between TPMT polymorphisms and adverse reactions of AZA.
Methods: This retrospective case-control study enrolled patients with prior exposure to AZA at the Taichung Veterans General Hospital (TCVGH) using data extracted from the Taiwan Precision Medicine Initiative (TPMI) cohort. Drug-prescription profile, comorbidities, the occurence of leukopenia and hepatotoxicity following AZA treatment were extracted from hospital health records. Genetic variatns affecting TPMT activity were determined using SNP array. Participants were categorized into normal metabolizer (NM) and non-normal metabolizer (Non-NM) groups accordingly.
Results: From the 43,035 patients in the TCVGH-TPMI cohort, we identified 2,128 azathioprine users; 2.6% (57 out of 2,128) were classified as TPMT Non-NM group. After matching by age and sex, we included 50 TPMT Non-NM, including 1 poor metabolizers (PMs), 49 intermediate metabolizers (IMs), and 1,000 NM patients for further analysis. The Non-NM genotype was associated with hepatotoxicity compared with NM genotype (HR: 3.85, 95% CI: 1.83–8.10) after adjustment for gender, AZA dosage, and comorbidities(Table 1). In the Non-NM group, the 3-year cumulative incidence of hepatotoxicity was 6.6% for one year, 16.9% for two and three years, respectively, which was significantly higher than the NM group (p=0.003)(Figure 1).

Table 1. Cox regression analysis of risk factors for hepatotoxicity following AZA treatment

	Hepatotoxicity*			
	HR	95% CI		*p* value
Age	0.99	0.98	1.01	0.60
Male gender	1.77	1.07	2.91	0.03
TPMT non-NM genotype	3.85	1.83	8.10	0.0004
AZA dose (mg)	1.00	1.00	1.01	0.31
Medication				
MTX	1.62	1.03	2.57	0.04
Comorbidity				
Hepatitis B carrier	1.18	0.40	3.48	0.76

By Cox regression model with adjustment of all listed variables. *Development of GPT ≥ 150 U/L after AZA treatment; GPT, glutamic pyruvic Transaminase; TPMT, thiopurine S-methyltransferase; NM, normal metabolizer; AZA, azathioprine; MTX, Methotrexate; CI: confidence interval

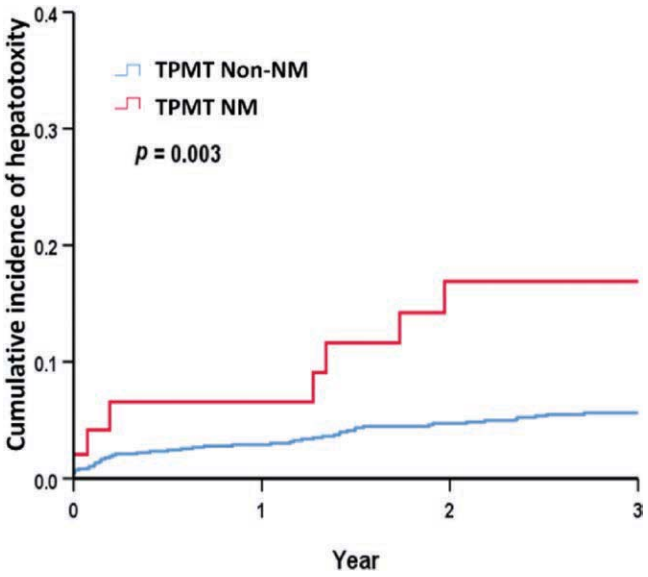

Figure 1. Cumulative incidence of hepatotoxicity

Conclusion: TPMT Non-NM genotype were associated with the developement of hepatotoxicity following AZA therapy. Prospective studies are needed to varify our results.

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Disclosure of Interests: None declared
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AB1445 SYNOVIAL FLUID ANALYSIS IN HOT SWOLLEN JOINTS – A QUALITY IMPROVEMENT PROJECT

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Background: Previous studies have reported delays in the investigation and suboptimal management of hot swollen joints, particularly crystal arthritis. In our hospital, it was noted that synovial fluid was inconsistently analysed for crystals which may lead to patients receiving delayed treatment.
Objectives: The aim of this quality improvement project was to 1) identify the number of synovial fluid samples that were not checked for crystals 2) implement changes to improve this process 3) re-audit and commitment to a continuous evaluation.
Methods: Retrospective review of synovial fluid analysis requested for adult patients presenting with hot swollen joints over a six month period. Following, the implementation of changes in the hospital, another comparison of pre-post intervention was performed.
Results: A total of 106 synovial fluid samples were sent for analysis between March and August 2021, of which only 69 (65%) of the samples were analysed for crystals. All samples were analysed for microscopy and culture. Following involvement with IT and laboratory departments we have introduced an intervention to make requesting crystal analysis easier. The request for synovial fluid analysis was grouped in a bundle (reflex test) so whenever a synovial fluid is collected, two forms are generated, one for microbiology (microscopy and culture), and the other for cytology (crystal analysis). Additional interventions included education and raising awareness. Post-interventions, another three month analysis of synovial fluid showed that compliance improved to 78%.
Conclusion: There was an improvement in the synovial fluid analysis requests of patients with hot, swollen joints. By implementing these changes and raising awareness, patients with acute crystal arthritis can be treated in a timely manner. We plan to continue our work with synovial fluid analysis following re-review and will continue to generate improvements.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3318

AB1446

TRANSLATION AND CROSS-CULTURAL ADAPTATION OF COPING WITH RHEUMATIC STRESSORS (CORS) INTO TURKISH LANGUAGE

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Background: Coping with Rheumatic Stressors (CORS) is a valid and reliable instrument that measures eight coping strategies directed at pain, limitations and dependency as the most prominent chronic stressors of Rheumatoid Arthritis (RA) (1). This questionnaire has also been used in axial Spondyloarthritis (ax-SpA) previously (2).
Objectives: To describe the translation and cross-cultural adaptation process of the CORS into Turkish as well as its cognitive debriefing to test the conceptual equivalence of the translated version among patients with RA, radiographic (r) and non-radiographic (nr) axSpA.
Methods: The CORS was firstly translated into Turkish (by 2 bilingual translators who are native speaker for Turkish) and then back-translated into Dutch (by 2 bilingual translators who are native speaker for Dutch) following the Beaton's method (Figure 1) (3). Back-translation procedure was done totally blinded to the original version. After the review of the Turkish version by an expert committee that included translators, two patients and the research team, a consensus was reached on the pre-final version. Using the pre-final version, the field test with cognitive debriefing involved a sample of 10 RA and 10 axSpA patients with different gender, age, disease duration, and educational background. After some small changes resulting from the feedback from patients the final version was obtained.
Results: The CORS was translated into Turkish following the forward-backward procedure. Minor incompatibilities arose from the translation process of CORS which have been easily resolved by the expert committee meetings. For example, `Ik concentreer me op iets anders` was translated as `Başka seylere odaklanırım` which is in English `I concentrate on something else`. The discrepancy was raised whether to use a word equivalent `to concentrate` or `to focus` and decision was made to use `to focus` while there was no exact Turkish word of `to concentrate`. A total of 10 patients with RA [9 females, mean (SD) age of 49 (13)] and 10 patients with axSpA [7 females, mean (SD) age of 38 (10), r-AxSpA, n=7, nr-AxSpA, n= 3] participated in the field test. Mean (SD) time to complete the CORS was 8.3 (3.4) minutes. Cognitive debriefing showed that items of the CORS are clear, relevant, understandable, and easy to complete. Cognitive debriefing revealed that the wording of one item had to be changed to provide better understanding (Section B, item 22 the word `stop` in Dutch and `stop` in English which was translated as `durdurmak` in Turkish changed to `sonlandırmak`.
Conclusion: The final Turkish version of the CORS showed acceptable linguistic validity and can be used in both clinical practice and for research purposes, in patients with RA and in patients with axSpA. However, to implement Turkish-CORS, further assessment is ongoing to test its psychometric properties (validity and reliability).

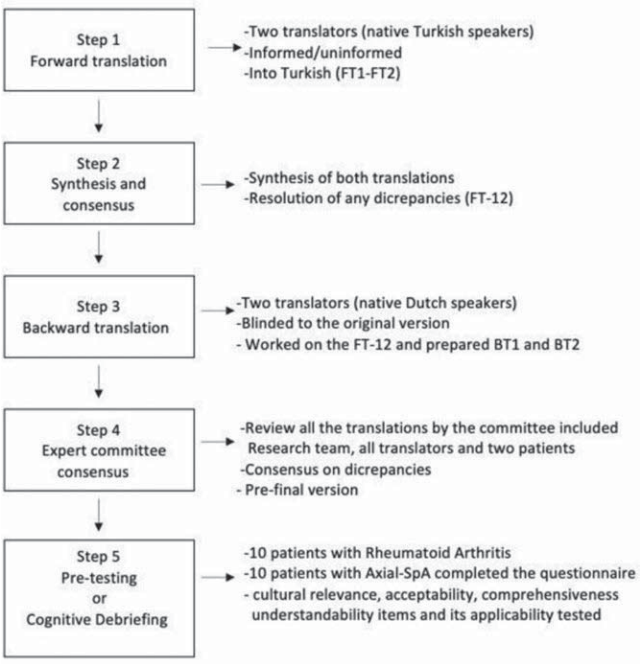

Figure 1. Flow-chart of the translation and cross-cultural adaptation process

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Disclosure of Interests: Gizem Ayan: None declared, Sofia Ramiro Speakers bureau: Eli Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB, Sanofi, Grant/research support from: AbbVie, Galapagos, Novartis, Pfizer, UCB, Fernando M Pimentel-Santos Speakers bureau: Abbvie, Novartis, UCB, Tecnimed, Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer, Tecnimed, UCB, Grant/research support from: AbbVie, Janssen, Novartis, Wim van Lankveld: None declared, Levent Kılıç: None declared
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AB1447

CATASTROPHISM IN MOROCCAN PATIENTS WITH CHRONIC RHEUMATIC DISEASES UNDER BIOLOGICS

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Background: Catastrophizing is a distortion of the perception of pain, both cognitively and emotionally, which leads patients to consider only the worst. There is a lack of knowledge about catastrophism in Moroccan patients with chronic rheumatic diseases under biologic DMARDs (disease-modifying anti-rheumatic drugs).
Objectives: To assess catastrophism and its associated factors in rheumatic patients under bDMARDs.
Methods: This is a cross-sectional study of patients admitted to a day hospital for biologic treatment evaluation. Patients included were all adults with SpA or RA diagnosed according to ASAS 2009 and ACR/EULAR 2010 classifications, respectively. The Pain Catastrophizing Scale (PCS) [1] was used to assess catastrophism. This scale is a self-report measure, consisting of 13 items scored from 0 to 4, resulting in a total possible score of 52. It is divided into three subscales: magnification, rumination and helplessness. A total score above 30 indicates a clinically relevant level of catastrophizing. Sociodemographic and treatment data were collected. Disease activity scores (DAS28, ASDAS) using C-reactive protein (CRP) dosage of the same day were calculated for each disease. Questionnaires were obtained for all patients for functional assessment (HAQ, BASFI), insomnia by the insomnia severity index (ISI), and depression by hospital anxiety and depression scale (HADS). Anxiety was evaluated by the generalized anxiety disorder-7 (GAD-7). Statistical analysis was done using regressions by SPSS.20.
Results: We included 75 patients with a mean age of 42.20 ± 16.206 years and a mean disease duration of 17.47 ± 8.758 years. Almost all patients (90.7%) had a disease lasting for more than 05 years. Twenty-nine patients (38.7%) had inactive disease. The average duration of bDMARDs use was 24.29 ± 18.96 months (27.83 ± 18.5 months in SpA patients and 19.53 ± 18.81 months in RA patients). Seventy-nine percent of these patients have received only one bDMARD, and 66.7% were currently taking a TNF inhibitor. The mean catastrophizing scores were 21.91 ± 11.38 for all patients, 22.05 ± 12.163 for SpA patients, and 21.72 ± 10.24 for RA patients. The prevalence of catastrophism was 25.3%, and the highest sub-score was helplessness (17.53 ± 3.95, p= 0). These scores were similar in RA and SpA patients. Catastrophizing was significantly associated with anxiety degree (p = 0.021, OR = 2.362, [1.211-4.607]), and swollen joints (p = 0.042, OR= 1.197, 95%IC [1.006-1.423]) using logistic regression analysis. Catastrophism scores were positively associated with the number of bDMARDs used (p = 0.044, ß = 0.233, 95%IC [0.095-7.211]). This association remained significant with anxiety (p<0.0001) and the number of bDMARDs received (p=0.04) at multivariate regression adjusted on swollen joints, ISI and HADS.
Conclusion: Catastrophizing scores were high despite biotherapy use. They were related to anxiety disorder, swollen joints, and bDMARDs rotation. It would therefore be interesting to detect catastrophism in clinical routine to ensure good patients care.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3515

AB1448 DEEP VENOUS THROMBOSIS IN YOUNG ADULTS: INCIDENCE AND RISK FACTORS

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Background: After a first venous thromboembolic (VTE) episode, recurrence is frequent and associated with significant morbidity and mortality.
Objectives: Our aim is to identify the risk factors for recurrent VTE in young subjects and to assess the risk-benefit ratio of continuing long-term anticoagulant treatment.
Methods: We carried out a retrospective study including 100 patients with deep vein thrombosis (DVT) admitted to the Internal Medicine Department at Fattouma Bourguiba University Hospital in Monastir between 2011 and 2020.
Results: In our study, the gender ratio was 1.17. The mean age was 34.49 years ± 9.19. Lower extremity deep venous thrombosis (LEDVT) was the most common location (90%). Pulmonary embolism (PE) was found in 8% of cases. The most frequent risk factors were obesity: BMI>30 (40%), bed rest (20%), personal history of DVT (18%), smoking (16%), recent surgery dating less than one month (14%), and recent trauma (12%). The etiological assessment had concluded to inherited thrombophilia in 41 cases: protein S deficiency (23%), protein C deficiency (8%), activated protein C resistance (8%), and antithrombin III deficiency (2%); acquired thrombophilia in 28 cases: hyperhomocysteinemia (HH) in 19 cases and antiphospholipid syndrome (APLS) in 9 cases; Behçet's disease in 10 cases and systemic lupus erythematosus in 5 cases. No cases of neoplasia were detected. The treatment was based on low molecular weight heparin (LMWH), relayed by vitamin k antagonists (VKAs), and physical therapy (graduated compression stockings and early mobilization). Duration of the treatment of DVT in the young adult depends on the nature and extent of the thrombosis, the underlying risk factors, and etiologies. Among the 100 hospitalized patients, recurrent DVT was detected in 20% of cases: 17% of patients reported a history of DVT with a mean number of previous episodes of 2, and only 3% developed DVT during their follow-up. The mean time to recurrence was three years. Recurrence was located on the same side in most cases (70%). In our study, only Behçet's disease was associated with an increased risk of DVT recurrence (p: 0.015, OR: 5.46, CI [1.38-21.56]). Gender, age, venous insufficiency, and bed rest had no significant influence on the risk of recurrence (p>0.05).
Conclusion: Young adults should be assessed for acquired and also genetic factors, which would suggest extending the duration of anticoagulant therapy in high-risk patients, reducing the incidence of post-thrombotic syndrome and VTE recurrence. Further studies are needed to evaluate the association of Behçet's disease with DVT recurrence.
Disclosure of Interests: None declared
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AB1449 ADHERENCE TO MTX AT INITIATION OF FIRST TARGETED THERAPY (PREVALENCE AND ASSOCIATED FACTORS): RESULTS OF THE STRATEGE2 STUDY.

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Background: Treatment adherence is a major challenge in chronic inflammatory rheumatic disease (CIRD). Mainly studied in rheumatoid arthritis (RA), this ranges from 30 to 80% [1]. Given the impact of non-adherence to disease-modifying therapy among RA patients, guidelines aiming to facilitate management of adherence were published in 2019 [2]. These guidelines highlight the multifactorial characteristics and importance of clarifying the factors determining non-adherence. In addition, treatment adherence was also listed as a point to consider for the management of difficult-to-treat RA by an EULAR task force [3].
Objectives: Based on inclusion results of STRATEGE 2 we explore the adherence to methotrexate (MTX) and its associated factors prior to initiation of a first targeted therapy.
Methods: The objective of STRATEGE2 is to describe the therapeutic strategy in RA patients treated with MTX for at least 3 months, naive of targeted biological (bDMARD) or synthetic (tsDMARD) therapy and who are candidates for initiation of first b/tsDMARD therapy due to RA activity. Patients were included prospectively in 2019-2020 and completed the Compliance Questionnaire for Rheumatology (CQR) [4], a self-administered questionnaire specific to rheumatology, measuring treatment adherence. They were then divided into 2 groups: adherence (Ad) (CQR19>80) *vs.* non-adherence (NAd) to investigate factors liable to be associated with adherence. Then, univariate and multivariate analysis was applied to identify potential predictors for adherence.
Results: Between Feb. 2019 and Dec. 2020, 230 patients were included, with 124 RA patients having an analysable CQR19: 73.4% females, mean age 56.6 years (±13.2), diagnosed 5.6 years (±7.4) previously, treatment with MTX for 4.4 years (±5.3) and a mean DAS of 4.3 (±1.2). The mean CQR score was 75.8. Patient distribution: 45.2% in the Ad group and 54.8% in the NAd group.

Table 1.

At baseline (before b/tsDMARD initiation)	Ad - N=56	NAd - N=68	*p*
Sex: female	73.2%	73.5%	-
Age (mean)	59.3 (±13.6)	54.4 (±12.4)	p < 0.05
BMI (mean)	27.2 (±7.0)	25.0 (±4.7)	p < 0.15
Still in work	39.3%	55.9%	p < 0.15
At least 1 comorbidity	60.7%	47.1%	p < 0.15
Positive anti-CCP	67.9%	80.6%	p < 0.15
Positive rheumatoid factor	69.8%	84.8%	p < 0.05
Radiological signs	57.1%	41.8%	p < 0.15
RA duration (years)	4.9 ±6.7	6.3 ±8.0	-
Average MTX initiation (years)	4.0 ±4.7	4.8 ±5.7	-
Per os MTX	28.6%	29.4%	-
→ mean dosage (mg/week)	16.4 ±4.5	15.6 ±4.6	
Subcutaneous MTX	69.6%	70.6%	-
→ mean dosage (mg/week)	20.1 ±4.6	19.4 ±3.3	-
Intramuscular MTX	1.8%	0%	-
Patients self-administration	30.0%	12.5%	P < 0.05
Corticosteroid therapy	53%	50.6%	-
→ mean dosage (mg/day)	8.1 ±4.1	9.5 ±5.8	
Mean DAS28	4.5 ± 1.3	4.2 ±1.2	-
Mean HAQ	1.1 ± 0.7	0.9 ±0.7	p < 0.15

In the multivariate analysis, no formal predictive factors to MTX adherence was identified except BMI>30kg/m^2 (odds ratio, OR (95% confidence interval, CI)=4.00, 1.08-14.86, p=0,038) and adherents who estimate having completely participate to the decision-making for the targeted therapy (OR (95% CI)=6.41, 2.32-17.65, p<0.001).
Conclusion: In this cohort, beyond the recently published guidelines, nearly half of patients do not show adherence to MTX (CQR19-based evaluation) before initiation of b/tsDMARD. As physicians tend to overestimate adherence to medication, clarification of the factors associated with non-adherence would help improve patient assessment and, therefore, management. Supplementary data on patients' adherence evolution and adherence predictors, might be observed on the follow-up data at 12 and 24 months of this cohort.
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Roche, Sandoz, Sanofi and UCB Pharma., Eric Senbel Speakers bureau: AbbVie, Amgen, Biogen, Janssen, Lilly, MSD, Nordic Pharma, Pfizer Roche-Chugai and Sandoz, Sanofi., Consultant of: AbbVie, Amgen, Biogen, Janssen, Lilly, MSD, Nordic Pharma, Pfizer Roche-Chugai and Sandoz, Sanofi., Hélène Herman-Demars Employee of: Nordic Pharma France, Jennifer Becker Employee of: Nordic Pharma France, René-Marc Flipo Speakers bureau: Abbvie, Bristol-Myers Squibb, Eli-Lilly, Janssen, Medac, MSD, Nordic-Pharma, Novartis, Pfizer, Roche-Chugaï, and Sanofi., Consultant of: Abbvie, Bristol-Myers Squibb, Eli-Lilly, Janssen, Medac, MSD, Nordic-Pharma, Novartis, Pfizer, Roche-Chugaï, and Sanofi.

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AB1450

CHARACTERISTICS, OUTCOME AND FACTORS ASSOCIATED WITH EVOLUTION TO MULTIPLE MYELOMA AND SURVIVAL IN PATIENTS WITH SOLITARY BONE PLASMACYTOMA.

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Background: Solitary bone plasmacytoma (SPB) is a rare malignancy whose main risk is progression to multiple myeloma (MM).

Objectives: To describe the characteristics and outcome of patients treated for SBP and to identify factors associated with progression to MM and death.

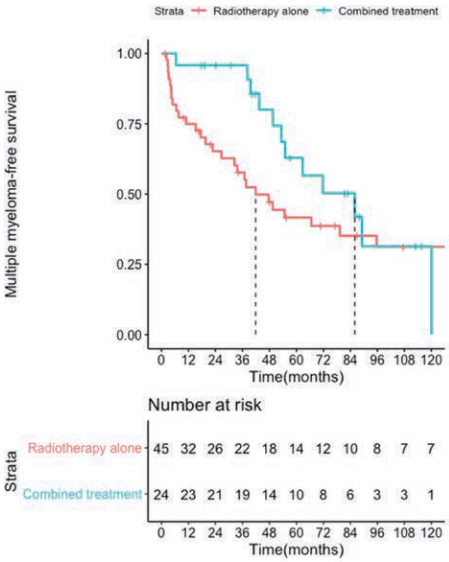

Figure 1. Myeloma-free survival in patients treated by radiotherapy alone compared to patients treated by radiotherapy followed by adjuvant chemotherapy (Combined treatment)

Methods: This retrospective study was conducted between 1992 and 2020. Patients were included if they met the International Myeloma Working Group (IMWG) criteria for the diagnosis of SBP (1). Treatment response was assessed according to the IMWG criteria (2) for patients with detectable monoclonal protein and according to radiological response only for non-secretory SBP. Hazard ratios (HR) and their 95% confidence intervals (CI) were estimated by Cox proportional hazards models, adjusted for potential confounders. When available, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) were reviewed by two experienced nuclear physicians.

Results: A total of 77 patients diagnosed with SBP were included. The median age was 59 years [range: 27-89]. Median follow-up duration was 87.1 months [range: 1.6-306.8]. At the end of the follow-up, 45 (58.4%) patients had developed a MM and 13 (16.9%) deaths occurred, including 10 patients with progression to MM. Five-year myeloma-free survival and overall survival were 47.9% and 86.8% respectively. All patients received radiotherapy with a median dose of 45 Grays [range: 30-55]. Chemotherapy was prescribed in 32 (41.6%) patients, concomitant to radiotherapy in 8, because of high risk of local extension, or adjuvant in 24 because of persistent disease after radiotherapy. Chemotherapy included mainly immunomodulatory drugs (28/32 (87.5%)) and/or proteasome inhibitors (11/32 (34.4%)) based combinations. Adjuvant chemotherapy after radiotherapy was associated with a reduced risk of MM compared to patients treated by radiotherapy alone, in a multivariate model adjusted for potential confounding factors, including response after radiotherapy alone (adjuvant chemotherapy *versus* no chemotherapy, HR 0.30, 95%CI [0.14-0.64]). Response to the first line of treatment (radiotherapy +/- chemotherapy) was the main factor associated with progression to MM (complete response *versus* partial response or progressive disease, HR 0.25, 95%CI [0.11-0.59]) and death (HR 0.22, 95%CI [0.05-0.99]). A non-significant trend between bone marrow plasmacytosis ≥ 5% at diagnosis and higher risk of MM was observed (≥ 5% *versus* <5%, HR 2.40, 95%CI [1.00-5.74]). ^{18}F-FDG PET/CT images were available for review in only 36/77 patients. A significant decrease of ^{18}F-FDG uptake after treatment was observed whereas the lesion size was unchanged. No association was observed with the risk of MM but the limited available images may have resulted in underpowered analyses.

Conclusion: In this large study of patients with SBP, we observed that even though mostly prescribed for insufficient response to radiotherapy alone, treatment with adjuvant chemotherapy was associated with a decreased risk of evolution to MM, suggesting that this treatment might be systematically prescribed in addition to radiotherapy alone. These observations need to be confirmed and justify conduction of a prospective trial evaluating adjuvant chemotherapy in patients with SBP.

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AB1451

MACHINE LEARNING MODEL OF THE ULTRASOUND INDEX OF MASEI ENTHESIS AND OTHER VARIABLES OF DISEASE ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS.

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Background: Spondyloarthritis (SpA) are a group of chronic inflammatory diseases with affectation, mainly of the axial skeleton, and also of peripheral joints. The enthesis is one of the target organs, and its inflammation known as enthesitis could be unnoticed. Machine Learning is a branch of artificial intelligence that studies the construction of a function y=f(x), from a finite set of observations D={x,y}, where y is an endogenous variable and x are explanatory variables. The objective of this method is to obtain a model that best fit to the data without overfitting, that could be useful to make predictions.
Objectives: We try to find Machine Learning models that relate the MASEI index (Madrid Sonographic Enthesitis Index) in entheses depending on the activity of the disease (ASDAS, BASDAI and DAPSA) and other variables in patients with spondyloarthritis.
Methods: Observational, descriptive and cross-sectional study. We have analyzed 24 patients with SpA who underwent musculoskeletal ultrasound using the MASEI index and who were treated in our clinics from May 2021 to September 2021 and under the approval of the CEICm of our center. First, we have done a feature selection of the variables most related to MASEI. To do so, we compute mutual information and chi-square test, using the scikit-learn (python) library and Matlab, respectively. Using Matlab Regression Learner package, we obtain the best Machine Learning model with the lowest RMSE for 5 fold cross-validation, which turned out to be a linear regression.
Results: To obtain regressive models that explain TOTAL MASEI, the following variables have been chosen: Type of SpA, BASDAI-DAPSA-ASDAS activity, Arthritis, Enthesophytes, Corticosteroids and CRP because they present a high degree of mutual information with MASEI and a high chi-square index. (See Figures 1 and 2). With these variables we have obtained the model that presents a lower RSME error for validated data, which has turned out to be a linear regression, given by the formula:
MASEI = -9.29-2,29* **type of SpA** + 10,42***ASDAS**+4,08***Corticoids** + 8,2***Arthritis/sinov**. + 4,46***Enthesithis**-8,6***CRP**
The basic statistical characteristics of the coefficients of this equation can be consulted in Figure 3. The characteristics of the model are specified in Figure 3. In Figure 4, we observe how the data fit the diagonal and in Figures 5 and 6, we have compute a prediction and confidence intervals of our model using ASDAS and MASEI as coordinate axes.
Conclusion: We have obtained a linear model, which explains the MASEI variable as an explicit linear combination of the variables: type of SpA, ASDAS, Corticoids, Arthritis/sinov, Enthesithis and CRP. Our model, not only is simple, but it is also optimal, in the sense that for 5-fold cross validation, it obtains the lowest RSME error, compared to other Machine Learning methods, such as: neural networks, SVM, Gaussian regression processes, etc. Our model is useful to build confidence intervals, make predictions and to understand the relation between the variables mentioned above.
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AB1452

EVALUATION OF HEPATITIS E VIRUS INFECTION DURING JAK INHIBITOR THERAPY IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES

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Background: Although impacting hundreds of thousands of people in Western nations each year, hepatitis E virus (HEV) is an under-reported health problem (1). HEV usually is a self-limiting disease, but especially immunocompromised individuals are at risk to develop a chronic course of infection, with rapid progression to fibrosis, cirrhosis or even the development of liver failure. Janus kinase (JAK) inhibitors are a novel drug class for the treatment of autoimmune inflammatory rheumatic disease (AIRD). As JAKs play a key role in innate immunity, viral infections and reactivation are frequently reported during JAK inhibitor treatment in AIRD patients (2).
Objectives: To characterize the influence of JAK inhibitors on HEV replication *ex vivo* and assess the risk for the development of symptomatic HEV infection during JAK Inhibitor therapy *in vivo*.
Methods: To determine the effect of JAK inhibitors on HEV replication we performed infection experiments with primary human hepatocytes (PHH) followed by immunofluorescence analysis and RNAseq. To evaluate the risk of HEV infection during JAK Inhibitor therapy, we monitored HEV RNA and HEV IgG/IgM of 111 AIRD patients, receiving JAK inhibitors. Moreover, we conducted a retrospective analysis of liver enzymes of patients which were anti-HEV IgG/IgM positive.
Results: Transcriptomic analysis of PHH revealed an upregulation of innate immunity components during HEV infection. This induction was perturbed in the presence of a JAK inhibitor, concomitant with strong elevation of HEV RNA levels. In line, infection experiments displayed an up to 50-fold increase of progeny virus production during JAK inhibitor treatment indicating that JAK signaling is critical to control HEV infection. Monitoring of seroprevalence identified 17 patients which were anti-HEV IgG and/or IgM positive, while no patient hat detectable HEV RNA levels. Five patients had detectable anti-HEV IgM levels suggesting a recent HEV infection. Three of 17 had a period with elevated liver enzymes (f.e. GGT> 200 U/L) during time of retrospective analysis (ranging from 10 to 23 months).
Conclusion: Obtained *ex vivo* data suggest that JAK inhibition facilitates HEV life cycle progression. Considering that JAK inhibitors are routinely applied for the treatment of AIRD, these patients may be at higher risk for a symptomatic course and outcome of HEV infection. In addition to established protocols, screening for HEV seroprevalence and HEV RNA should be considered prior starting JAK inhibitor treatment and in case of elevated liver enzymes during JAK inhibitor therapy.
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AB1453

TRADITIONAL AND NON-TRADITIONAL CARDIOVASCULAR RISK FACTORS IN THE DEVELOPMENT OF EARLY ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

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Background: It is known that patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are characterized with a variability of traditional and non-traditional cardiovascular risk factors for the early development of arthrosclerosis. The results of numerous studies, examining the significance of these factors for the development of atherosclerosis in patients with autoimmune rheumatic disease (ARD), are contradictory. Additionally the prevalence of these factors was compared between ARD patients and healthy persons. There are few data about comparison cardiovascular risk factors between patient with SLE, RA and ischemic heart disease (IHD).

Objectives: The aim of our study was to determine the frequency of occurrence of traditional and non-traditional cardiovascular risk factors in patients with SLE and RA in comparison to patients with IHD and to assess their role for the development of early atherosclerosis.
Methods: The study included 85 female patients with ARD (SLE (n=40), mean age 33,5 (27,5; 44,5) years old, disease duration 8,0 (5,0; 14,5) years, disease activity SLEDAI-2K 7,0 (4,0; 11,5) points and RA (n=45), mean age 43,0 (33,0; 52,0) years old, disease duration 9,0 (5,0; 13,0) years, disease activity (DAS28=5,37 (4,69;5,89) points. Fifty four healthy women of the same age formed the first control group (CG1), 22 women with IHD (mean age 50,0 (48,0; 51,0) years old) made the second control group (CG2). The presence of traditional (age, arterial hypertension (AH), smoking, obesity, dyslipidemia, low physical activity, family history of cardiovascular disease (CVD)) and non-traditional (menopause, hyperhomocysteinemia (HHC)) risk factors was assessed. The early development of atherosclerosis was confirmed with the help of common carotid artery sonography according to standard procedures.
Results: It was found that only AH and HHC were more in patients with SLE and RA in comparison to CG1 (AH: 65% vs. 0% (p<0,0001), HHC: 45% vs. 9% (p<0,0001), respectively for SLE patients and 27% vs. 0% (p<0,0001), 36% vs. 9% (p=0,001), respectively for RA patients). Age, smoking, obesity, dyslipidemia, low physical activity, family history of CVD, menopause were similar in both groups of patients and CG1. It was revealed that patients with SLE were 14 years younger (p<0,0001) than female patients with IHD. They had less often family history of CVD (18% vs. 41%, p=0,044), but HHC was revealed 2 times more often (45% vs. 22%, p=0,031) than in CG2. Patients with RA were 8 years younger than patients with IHD (p=0,007). Moreover the frequency of occurrence of AH, obesity, dyslipidemia, family history of CVD was less than in CG2 (27% vs. 73% (p=0,0003), 40% vs. 68% (p=0,030), 71% vs. 95% (p=0,025), 11% vs. 41% (p=0,005), respectively). HHC was detected 1,5 times more often in RA patients in comparison to patients with IHD, but without statistically difference (36% vs. 22%, p=0,288). Other risk factors were similar in both groups of patients with ARD and IHD. The presence of subclinical atherosclerosis was observed in 54% patients with ARD. Comparative analysis of the frequency of occurrence of investigated cardiovascular risk factors between these patients and those with IHD has shown the highest prevalence of HHC in patients with ARD (54% vs. 22%, p=0,014), what could be as a result of autoimmune inflammation in this group of patients.
Conclusion: Thus, we revealed a high prevalence of AH (as traditional risk factor) and HHC (as non-traditional risk factor) in patients with SLE and RA. More than half of patients with ARD had subclinical atherosclerosis. The presence of HHC in patients with SLE and RA may be associated with the development of early atherosclerosis.
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AB1454 CLINICAL AND BIOLOGICAL FACTORS CORRELATED WITH MAGNETIC RESONANCE IMAGING RESULTS IN TUBERCULOUS SPONDYLODISCITIS

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Background: Tuberculosis is still endemic in Tunisia. Although pulmonary localization is the most common, other localizations, including osteo-articular involvement, are increasingly diagnosed. Tuberculous spondylodiscitis (SPDT) or Pott's disease is an infectious involvement of the disc-vertebrate couple, caused by the tubercular bacillus (Mycobacterium tuberculosis). Magnetic resonance imaging (MRI) is the most sensitive (95-100%) and the most early abnormal exam.
Objectives: Our aim was to study the correlation of contributing factors, epidemiological, clinical, biological, radiological and therapeutic data with positive signs of spinal MRI.
Methods: We conduct a retrospective and descriptive study in a single rheumatology department. Data were collected from observations of patients hospitalized in the past 20 years (2000-2020) who have been diagnosed with SPDT. Epidemiological, clinical, biological, radiological, and therapeutic data were analyzed. Each patient had spinal MRI. Positive signs have been individualized, represented by intervertebral disc involvement, vertebral body involvement and visualization of a paravertebral abscess.
Results: Fifty-two cases of SPDT were collected (37F/15M). The mean age of the population was 55.21±17.79 years [19-91]. Thirty-three patients (69.2%) were classified as young versus 16 elderly patients (30.8%), with female predominance in both groups (69.4% and 75% respectively, p = 0.57). The positive diagnosis of tuberculous spondylodiscitis was facilitated by the spinal MRI. Positive signs were sought in our patients which are represented by: the achievement of the intervertebral disc with diffuse T2 hypersignal (56.5%) and diffuse or circumferential increase of the signal in sp T1 Gadolinium (50.9%), Involvement of the vertebral body with moderate and extensive condensation (60.4%), macrogeodes (60.4%) and heterogeneous increase in spT1 Gado signal (52.8%) and visualization of a paravertebral abscess (51.9%). Correlations made between the favouring factors, epidemiological, clinical, biological, radiological and therapeutic data and the positive signs of spinal MRI, objecting that six parameters had a statistically significant correlation with MRI signs strongly suggestive of the diagnosis of SPDT: Hospitalization duration was correlated with the diffuse T2 disk hypersignal (p= 0.02; r= - 0.38), Hemoglobin rate was correlated with the diffuse or circumferential increase in T1 disk sp signal (p= 0.03; r= - 0.34), the initial rate of lymphocytes was correlated with the paravertebral abscess (p= 0.04; r= - 0.47). The extra-vertebral tuberculosis location was correlated with the diffuse T2 disc hypersignal (p= 0.03; r= -0.96), the moderate condensation and the extent of vertebral body (p < 0.001) and vertebral body macrogeodes (p < 0.001). The neurological clinical signs were correlated with the heterogeneous increase in vertebral body T1 sp signal (p= 0.04; r= -0.33) and the surgical treatment (p < 0.001).
Conclusion: Tuberculous spondylodiscitis is a frequent condition that needs to be diagnosed and treated rapidly. Spinal MRI is the first-line exam in case of suspicion. Clinical, biological and therapeutic parameters were correlated with the MRI images highly suggestive of positive diagnosis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.4160

AB1455 VERY LOW FREQUENCY ANAS/DFS70 PATTERN POSITIVITY IN A LARGE COHORT OF AUTOIMMUNE/ AUTOINFLAMMATORY AND CONTROLS IN A SINGLE HOSPITAL FROM COLOMBIA

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Background: Antinuclear antibodies (ANA) have diagnostic significance in rheumatology. Anti-DFS70 (Dense Fine Speckle-70 kd) antibodies may be an exclusionary marker for systemic autoimmune rheumatic disease (SARD). Low frequency of this pattern has previously been described in healthy populations.
Objectives: To evaluate ANAS/DFS70 positivity and autoantibody profile in a large Colombian population with rheumatoid arthritis (RA), psoriasis (PsO), as well as, undifferentiated connective tissue diseases (UCTD), first degree relatives (FDR), and healthy controls (HC).
Methods: A cross-sectional study was conducted. We analyzed 531 individuals between 18-65 years, 101 RA patients (ACR/EULAR 2010 classification criteria), 137 relatives from RA, 60 PsO patients (Colombian classification consensus), 47 UCTD patients, and 186 HC matched by age and sex. The determination of ANAS-HEp2 antibodies, was carried out. The ANAS/DFS70 positive results used as a confirmatory test the determination by Knocked out, for the psip gen and CytoBead by indirect immunofluorescence-IFI technique. Absolute and relative frequencies were established and associations with chi square test.
Results: The distribution by diagnostic group was RA: 19%, PsO: 11,3%, UCTD: 8,9%, 25,8% RA relatives, and 35% healthy controls. RA was ANA test (+) in 42%, PsO 41,7%, UCTD 78,7%, FDR 26,3%, and HC 26,9%. The positive frequency of ANA/DFS70 in the total group was 2.3% and 1,4% in SARD (n=12; 2 FDR, 6 HC, 3 UCTD, and PsO 1), no RA patients were positive. These 12 participants were negative for rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA), one patient with UCTD were positive for Anti SSB/La, Anti Sm, Anti RNP, and anti DNAds, another was positive for anti Sm IgG and IgM B2GP, and IgG ACA. Most participants had negative acute phase reactants (erythrosedimentation rate ESR[-] 83,3% and C-reactive protein CRP[-] 66,6%). ANAS/DFS70 was associated with positivity for ANAS independently of ANAS titers, (p <0,001). None of the patients' positives ANAS DFS70 in the UCTD group in 5 years developed definitive autoimmune disease.
Conclusion: Despite the low frequency in the group in general, it has been shown that anti-DFS70 is more prevalent in healthy individuals than in patients with SARD, which was found in this group of individuals. ANAS/DFS70 autoantibodies were present in very low frequency in Colombian patients with SARD. Thus, patients with a positive result tend to have a mild or non-progressing phenotype of autoimmune or autoinflammatory diseases. This analysis reinforce evidence of ANA/DFS70 positivity as well as autoantibody negativity described abroad as a negative predictive marker of SARD.
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Table 1. Clinical and demographical variables for ANAS/DFS70 patients n=12.

	AGE	GENDER	ANAS	ESR	CRP	RF	ACPA	Ro	La	Sm	RNP	DNAds	ACA IgG	ACA IgM	ACA IgA	B2GP IgG	B2GP IgM
UCTD	30	F	1/160	-	-	-	-	-	-	+	-	-	+	-	-	+	+
UCTD	61	F	1/320	-	-	-	-	-	+	+	+	+	-	-	-	-	-
UCTD	42	F	1/160	-	+	-	-	-	-	-	-	+	-	-	-	-	-
PsO	43	F	1/320	-	-	-	-	-	-	-	-	-	-	-	-	-	-
FDR	31	M	1/80	-	-	-	-	-	-	-	-	-	-	-	-	-	-
FDR	32	F	1/160	+	-	-	-	-	-	-	-	-	-	-	-	-	-
HC	50	F	1/80	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HC	26	F	1/80	+	-	-	-	-	-	-	-	-	-	-	-	-	-
HC	27	F	1/160	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HC	54	F	1/320	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HC	32	F	1/160	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HC	53	F	1/320	-	+	-	-	-	-	-	-	-	-	-	-	-	-

Rheumatoid arthritis (RA), Psoriasis (PsO), as well as, Undifferentiated connective tissue diseases (UCTD), first degree relatives (FDR), healthy controls (HC), rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA), erythrosedimentation rate (ESR), and C-reactive protein (CRP).

AB1456 CLINICAL IMPACT OF THE INTERSTITIAL LUNG DISEASE MULTIDISCIPLINARY SERVICE

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Background: Interstitial lung diseases (ILD) are a diverse group of pulmonary diseases for which accurate diagnosis is critical for optimal management and outcomes. Diagnosing ILD, both idiopathic pulmonary fibrosis (IPF) and connective-tissue-disease-associated interstitial lung disease (CTD-ILD), has become critically important, as the disease has a devastating prognosis with poor survival. There are also management implications, as patients with ILD can now potentially be treated with new antifibrotic therapies such as pirfenidone and nintedanib, both of which have been approved. Certain types of CTD – ILD may benefit from systemic immunomodulatory therapies. Diagnosis of ILD can be challenging and a multidisciplinary team (MDT) approach is recommended in current guidelines. Several studies have reported that MDT diagnosis is associated with higher levels of diagnostic confidence and better interobserver agreement (1-3).

Objectives: We describe the benefits of an ILD multidisciplinary service on the diagnosis and management of patients with suspected ILD.

Methods: We performed a single-centre retrospective review of consecutive patients referred to the ILD clinic with subsequent discussions in ILD MDTs over a 36-month period from 2016 to 2019. We compared changes in ILD diagnosis and management at referral to those following the ILD-MDT. We collected data on the demographics, occupation, age at ILD onset, smoking status, imaging, blood tests including autoimmune serology, MDT recommendations, change in diagnosis after MDT, tertiary referral, serial PFTs, medications and outcomes. Cases of suspected ILD that were not fully characterised and those with complex management issues were presented at our monthly ILD MDT.

Results: A total of 208 patients were referred to the ILD clinic over a 36-month period. Of these, 106 cases were discussed at the ILD MDT and the remaining 102 cases did not require discussion at the MDT as these deemed to be clear cut, which included RA and CTD ILD. The mean age of the total cohort was 74 (min age 32, max age 97) and 120 (58 %) were males. Overall, evaluation by the ILD service (i.e. ILD clinic and MDT) resulted in a change in diagnosis in 106(51%) patients. Of those, 49(46%) didn't have ILD. In the remaining 57 patients with suspected ILD, the majority of the diagnoses were ILD with an uncertain classification (24, 23%). The other diagnoses included CTD-ILD (4, 3.7%), ILD with autoimmune serology 11(10.4%), IPF 10(9.4%), Drug-induced-ILD 3(2.8%), Hypersensitivity Pneumonitis 5(4.7%), Eosinophilic pneumonitis 1 (0.94%), Cryptogenic Pneumonitis 1(0.94%), PPFE with IPF 1 (0.94%), PPFE 1 (0.94%), CPFE 4 (0.94%), EAA 2 (0.94%), RB-ILD 2 (1.88%), Langerhans Histiocytosis 2 (1.88%).16/57(28%) were referred to a tertiary centre for further management. Serology was positive in 11 patients (ANA 6, CCP 3, and ANCA 2). Of the 57 patients with other diagnoses, the main recommendations included steroids (28), anti-fibrotic therapy (4), immunomodulatory therapy (6) and ambulatory Oxygen (1). Further analysis will be carried out on survival and treatment outcomes of the cohort.

Conclusion: Dedicated ILD-MDT service has an important clinical impact on the care of the ILD patient, with frequent changes in ILD diagnosis and subsequent management and outcomes. Multidisciplinary approach to the management of these patients should be standard of care for these patients.

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AB1457 OPALE: A PROSPECTIVE OBSERVATIONAL STUDY OF THE REAL-WORLD USE OF AN ADALIMUMAB BIOSIMILAR AND EVALUATION OF NUTRITIONAL STATUS ON THE THERAPEUTIC RESPONSE. PATIENTS NUTRITIONAL STATUS AT BASELINE

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Background: Chronic inflammatory diseases treatment has been greatly improved since the introduction of TNF inhibitors and later, of their biosimilars. In addition, epidemiological and interventional studies suggest a pathophysiological or therapeutic role, respectively, of nutrition in Inflammatory Rheumatic Diseases (IRDs).

Objectives: The objective of the OPALE observational study was to describe in real life the profile of patients treated with an adalimumab biosimilar and to assess the impact of nutrition on disease evolution and response to treatment.

Methods: The study planned a one-year follow-up of patients with at least three visits: inclusion, six months and one year. In this study, 754 patients treated with Fresenius-Kabi adalimumab were included: 54.4 % of patients with an IRD, 42.8 % with Inflammatory Bowel Disease (IBD) and 2.8 % patients with a psoriasis. Patients' condition was assessed using a Clinical Global Impression of disease scale (CGI, primary end point of the study). Nutritional status was assessed through clinical data (weight, BMI (Body Mass Index), abdominal circumference) and the available biological analyses results. Screening for sarcopenia was based on a SARC-F score ≥ 4. Nutritional behavior was assessed using a diet questionnaire with a list of 48 foods divided into 6 classes (Fruits & vegetables, meat, fish & eggs, dairy products & fats, starchy foods, sweet foods and drinks). Foods voluntarily withdrawn due to illness and those avoided at acute flare-ups were recommended to be reported. This analysis aims to describe IRD patients' nutritional status at baseline.

Results: From 754 included patients, 410 patients presented with an IRD (Psoriatic Arthritis (PsA), n= 80 / Rheumatoid Arthritis (RA), n=102 / SpondyloArthritis (SpA), n=228). Mean patients' age was 47.7± 14.1 years, 56% are female, mean BMI was 26.0 ± 5.4 kg/m^2. From this IRD population, 28.5% of patients have a family history of chronic inflammatory disease. Mean disease duration was of 6.4 ± 8.4 years. Concerning the previous IRD treatment, 47.4% of patients had previously been treated by methotrexate among them 58% were still receiving this treatment at inclusion. Among IRD patients recruited in OPALE study, 72.8% received Fresenius Kabi adalimumab as their first biotherapy. Most of patients were assessed on the CGI scale as markedly ill (50.7%) or moderately ill (29.9%) and 110 patients (37.3%) had a score ≥ 4 on the SARC-F questionnaire (mean age 48.9 ± 14.1 years and mean BMI 27.2 ±5.6 kg/m^2). Concerning the disease history at baseline, the descriptive analysis of self-administered questionnaire shows that 68.3% of patients may have changed their nutritional behavior because of their illness, by banishing several foods (mean number: 12.7 ± 10.1). These restrictions are increased during flare-ups: 32.7% of patients removed an average of 6.0 ± 5.8 additional foods number. These changes are in part based on the patients' own beliefs: 17% of them consider that certain foods can improve their illness, 35% of patients think they have identified the foods likely to make it worse (Table 1).

Table 1. Patient-reported influence of certain foods on disease

	PsA	RA	SpA	TOTAL IRD
	(n=60)	(n=72)	(n=177)	(n=309)
Patients identifying foods with negative influence	21 37.5% [24.9% - 51.5%]	22 32.4% [21.5% - 44.8%]	58 36.0% [28.6% - 44.0%]	101 35.4% [29.9% - 41.3%]
Patients identifying foods with positive influence	9 16.4% [7.8% - 28.8%]	12 17.6% [9.5% - 28.8%]	27 17.2% [11.7% - 24.0%]	48 17.1% [12.9% - 22.1%]

Conclusion: These preliminary baseline data from OPALE observational study confirm the risk of decreased muscle mass in IRD. Mean BMI of patients screened for sarcopenia is higher than that of non-sarcopenic patients (respectively 27.2 ± 5.6 kg/m^2 and 25.6 ± 4.8 kg/m^2; p=0.02). These results plead for a systematic screening for sarcopenia in IRD patients. The risk of sarcopenia could be further aggravated by inappropriate nutritional behaviors aimed at excluding food groups, which would justify dietary education of these IRD patients.

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AB1458 JAK INHIBITORS AND VENOUS THROMBOEMBOLISM EVENTS - REASSURING DATA FROM A LARGE SINGLE CENTRE RETROSPECTIVE STUDY

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Background: In March 2021, the European Medicines Agency (EMA) sent out a Medicine Alert related Xeljanz (tofacitinib): The Initial clinical trial results suggested an increased risk of major adverse cardiovascular events and malignancies with use of tofacitinib relative to TNF-alpha inhibitors. In light of these safety alerts, March 2021, the Rheumatology department at Portsmouth Hospitals University NHS Trust updated the Biologics Screening documents to include a cardiovascular and venous thromboembolism (VTE) risk assessment. We conducted a retrospective observational study to document the incidence of VTE in patients on Janus kinase (JAK) inhibitors admitted to our Venous thromboembolism Service from 14th April 2018 to 30th November 2021 (43 months). This includes patients who were suspected of having both deep vein thrombosis (DVT) and/or Pulomonary Thromboembolisim (PE). We were particularly interested to assess whether any patients with VTE events had been receiving JAK inhibitors given the potential association of JAK inhibitor usage and VTE.

Objectives: To establish whether patients exposed to JAK inhibitors had any increased incidence of VTE. This was done through a retrospective analysis for all patients presenting to Portsmouth Hospitals University NHS Trust.

Methods: We utilised the International Classification of Diseases (ICD10) diagnosis code of I82 (182.0, 182.1,182.2,128.3,182.8,1782.9). This includes; Budd Chiari syndrome, thrombophlebitis migrans, embolism and thrombosis of vena cava, embolism and thrombosis renal vein, embolism and thrombosis of other specified view and embolism and thrombosis unspecified vein. From this data set, we reviewed how many case of VTE were noted in patients on JAK inhibitors. The Data was confined to patients who underwent diagnostic tests for VTE at Portsmouth Hospials University NHS Trust.

Results: A total of 417 patients had been admitted to the VTE Service for diagnostic assessment between 14th April 2018 to 30th November 2021. A total of 261 patients had been on a JAK inhibitor during the period of observation. This included patients on Tofacitinib, Baricitinib, Filgotinib and Upadacitinib. This was for treatment in Rheumatoid Arthritis and Psoriatic Arthritis where liscenced indications were appropriate. None of these had a VTE event. The age range of the patients on active treatment was 18 to 86 years old with the average of 60.7 years. The majority of patients were female (72.7%) with male patients comprising the remainder (27.3%). 8 patients under the care of the Rheumatology service were identified as having VTE events.

Conclusion: From a total of 261 patients on JAK inhibitors during a 43 month period; 0 patients had a confirmed VTE event. After March 2021, the Rheumatology department soutght to address the concerns raised by the EMA alert. There were two key areas in addressing the concerns highlighted. Firstly, clinicians had an heightened awareness of the potnetial risk of VTE and JAK inhibitor useage. Additionally, there was also the introduction of a new screening process which focussed on highlighting and assessing risk facotrs for VTE in patients being screened for JAK inhibitors. This was a new departmental service innovation introduced following the potential patient safety alert. We would postulate that some of the highly encouraging data obtained may partly be influenced by this service development. Conversely, much of the data was gathered before these assocations were established and before any service changes were made. We acknowedge that this data set is from a single centre analysis. However, given the sample size and duration of retrosepctive review we hope this serves to reassure clinicians that JAK inhibitor usage should remain a valid treatment option in Rheumatology patients, for licenced indications.

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AB1459 IMPACT OF SOCIOECONOMIC FACTORS ON THE DISEASE ACTIVITY: DATA FROM THE TUNISIAN BINAR REGISTRY

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Background: Despite the considerable therapeutic progress of inflammatory rheumatic diseases, access to treatment still challenging in developing countries because of scarce health resources and low socioeconomic status.

Objectives: To determine the influence of socioeconomic factors on disease activity in a national registry cohort, the Biological National Registry (BINAR) in Tunisia.

Methods: We enrolled patients with inflammatory rheumatic diseases under the first received biological drug and included in the BINAR registry from 2016 to 2020. Data on the inflammatory rheumatic disease (rheumatoid arthritis (RA) and spondyloarthritis (SA)), disease activity of RA and SA (DAS28-CRP and ASDAS-CRP respectively) at baseline, gender, active smoking, marital and work status and educational attainment were collected. Two groups were identified: Groupe 1 (G1) for patients with remission or low disease activity and groupe 2 (G2) for moderate or high disease activity according to DAS28-CRP and ASDAS-CRP.

Results: The study included 298 patients with a mean age of 49.2 years [18-79]. The mean disease duration was 6.7 ± 3.5 years [1-14] in patients with RA and 6.5 ±3.6 years [1-12] in patients with SA. G1 was made of 13 patients and G2 of 285 patients. The were no significant difference between G1 and G2 for (49.5 ± 11.9 versus 49.5±14.2, p=0.93) gender (% of females, 46.2% versus 37.1%, p=0.51) and marital status (% of single patients, 30.8 % versus 33.7%,p=0.82). Patients of G1 had better employability than G2 (61.5% % versus 45.6%) but this difference was not significant (p=0.26). Smoker patients had better disease outcomes comparing to nonsmokers but this difference was not significant (23.1 % versus 13.7%, p=0.34). Illiterate patients had more active diseases, comparing to literate, but this difference was not significant (30.8% versus 40.4%, p=0.49).

Conclusion: Our results did not confirm any difference in disease activity according to the collected socioeconomic factors. Data on the personal income, health insurance type and geographic distribution of our population should be further studied.

Disclosure of Interests: None declared

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AB1460 ACCUMULATED ADVANCED GLYCATION ENDPRODUCTS ARE SIGNIFICANTLY HIGHER IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES THAN IN HEALTHY POPULATION.

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Background: Advanced glycation endproducts (AGEs) are the result of non-enzymatic glycation of proteins, lipids or nucleic acids. In circumstances characterized by increased oxidative and carbonyl stress, such as chronic inflammation, AGEs can be formed more rapidly1, generating reactive oxygen species and activating inflammatory signaling cascades through their chief signaling receptor (commonly abbreviated as RAGE)[2]. This positive feedback of inflammation can play a role in the etiology of immune-mediated inflammatory diseases, more specifically in rheumatoid arthritis (RA), ankylosing spondylitis (AS) and systemic lupus erythematosus (SLE).

Objectives: To investigate whether the accumulated concentrations of AGEs in patients with SLE, RA or AS are significantly higher than in healthy patients.

Methods: One hundred thirteen consecutive patients fulfilling ACR/EULAR criteria for RA, 60 patients fulfilling ASAS/OMERACT MRI criteria for AS, 97 patients fulfilling ACR/SLICC criteria for SLE and 527 sex-matched healthy controls were recruited.in cross-sectional study. Exclusion criteria were pregnancy, diabetes mellitus, corticosteroid treatment ≥ 20mg/day and malignant neoplasm.

Table 1. Descriptive characteristics of the cohorts

		SLE		RA		AS	
		Patients	**Controls**	**Patients**	**Controls**	**Patients**	**Controls**
		N=96	*N=189*	*N=113*	*N=240*	*N=60*	*N=99*
AGEs		2.57 (0.65)	1.98 (0.45)	2.59 (0.58)	2.00 (0.42)	2.26 (0.46)	1.90 (0.46)
Age		51.0 [43.0;61.0]	56.0 [52.0;62.0]	58.0 [54.0;65.0]	61.0 [56.0;66.0]	47.5 [41.0;55.0]	53.0 [49.0;57.0]
Smoker	**No**	76 (79.2%)	133 (70.4%)	86 (76.1%)	196 (81.7%)	42 (70.0%)	58 (58.6%)
	Yes	20 (20.8%)	56 (29.6%)	27 (23.9%)	44 (18.3%)	18 (30.0%)	41 (41.4%)
Packs/year		0.00 [0.00;10.8]	2.50 [0.00;18.8]	2.50 [0.00;18.0]	0.00 [0.00;12.6]	0.00 [0.00;7.88]	14.9 [2.00;30.6]
Hypertension	**No**	74 (77.1%)	116 (61.4%)	77 (68.1%)	146 (60.8%)	53 (88.3%)	75 (75.8%)
	Yes	22 (22.9%)	73 (38.6%)	36 (31.9%)	94 (39.2%)	7 (11.7%)	24 (24.2%)
Obesity	**No**	80 (83.3%)	128 (67.7%)	86 (76.1%)	163 (67.9%)	51 (85.0%)	81 (81.8%)
	Yes	16 (16.7%)	61 (32.3%)	27 (23.9%)	77 (32.1%)	9 (15.0%)	18 (18.2%)
Dyslipidemia	**No**	85 (88.5%)	104 (55.0%)	79 (69.9%)	108 (45.0%)	51 (85.0%)	55 (55.6%)
	Yes	11 (11.5%)	85 (45.0%)	34 (30.1%)	132 (55.0%)	9 (15.0%)	44 (44.4%)

Continuous normal: mean (SD); Continuous non-normal: median [IQR]; Categorical: absolute (relative frequency)

Accumulated AGEs were non-invasively measured by skin autofluorescence (Age Reader Mu Connect, Diagnostics Technologies B.V) and demographic and clinical data were collected. AGEs comparisons between patients and controls were performed by multiple linear regression analysis adjusted by confunders, previously described in literature (age, smoking habit and cardiovascular risk-factors). Age was centered at 55 years.

Results: Table 1 shows some descriptive characteristics of our cohorts. AGEs adjusted mean was significantly increased in SLE patients compared with matched controls (95% CI [2.27, 2.76] vs [1.66, 1.89], p<0.0001), RA patients and controls (95% CI [2.41, 2.61] vs [1.68, 1.88], p<0.0001) and AS patients and controls (95% CI [2.03, 2.6] vs [1.66, 1.93], p<0.0001). In all 3 models, AGEs were also significantly positive correlated with smoking habit measured by packs per year (p<0.001) and age (p<0.0001).

Conclusion: Accumulated AGEs in all 3 pathologies are significantly higher than in the healthy controls. The different means of AGEs in each of the diseases, being higher in SLE and lower in AS, may suggest a different participation of AGEs in the immune-mediated mechanisms of each pathology.

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AB1461

IMPACT OF BASELINE DISEASE ACTIVITY ON DISCONTINUATION OF BIOLOGICAL DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE MEXICAN ADVERSE EVENTS REGISTRY (BIOBADAMEX)

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Background: Decrease treatment persistence in rheumatoid arthritis (RA) patients has been associated with several factors, including number of previous biological DMARDs (bDMARDs), female gender and higher disease activity or lower function at baseline [1].

Objectives: Determine if drug discontinuation of bDMARDs differs by disease activity level at baseline in patients with RA in the Mexican Adverse Events Registry (BIOBADAMEX).

Methods: BIOBADAMEX is a Mexican ongoing cohort of patients using bDMARDs. In this analysis we included all patients with RA registered from 2016 to 2021 with at least two assessments. Survival on bDMARDs was estimated using Kaplan-Meier analysis. Predictors of discontinuation, including high disease activity defined as DAS28-ESR>5.1, were investigated by Cox regression analyses.

Results: Among 528 RA patients in the registry, 302 had at least two assessments. Of patients analyzed, 276 (91%) were women. At baseline, patients had a median (IQR) age of 52.7 (44-60) years old, median disease duration of 9.3 (4-16) months. A total of 142 (47%) had comorbidities, 34 (11%) had more than 2 morbidities. At baseline DAS28-ESR was 4.8 (4-6), 59 (20%) patients had low (DAS28-ESR<=3.2) and 130 (43%) had high disease activity. The most common bDMARDs received at baseline were abatacept 68 (23%), tocilizumab 59 (20%), adalimumab 50 (17%) and certolizumab 41 (14%). At the time of analysis, the median bDMARDs treatment duration was 17.2 (12-27) months. Overall, 130 (43%) patients had discontinued treatment, the most common causes of discontinuation were inefficacy in 64 patients, 15 for remission, 12 for adverse events and 26 for others. Figure 1 shows discontinuation rate curves in patients by disease activity. Cox proportional hazards demonstrated significant difference in bDMARD discontinuation between patients with baseline high disease activity (HR 1.3, 95% CI 1.1-1.7, p=0.03), but not differences were found regarding baseline age (HR 1.0, 95% CI 0.9-1.0, p=0.16), sex (HR 0.9, 95%CI 0.6-1.4), disease duration (HR 1.0, 95%CI 0.9-1.0, p=0.92), smoking (HR 1.2, 95% CI 0.7-2.1, p=0.44), number of comorbidities (HR 1.0, 95%CI 0.9-1.2, p=0.51) or other factors. The significant association of baseline high disease activity remained after adjusting by baseline age, sex, smoking, disease duration and number of comorbidities (HR 1.3, 95% CI 1.1-1.7, p=0.02).

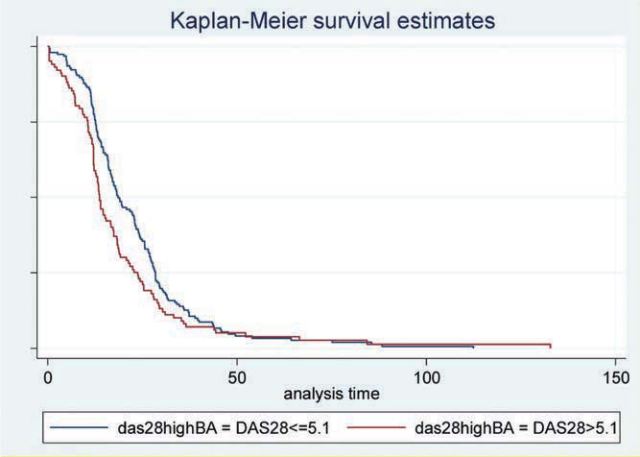

Figure 1. Discontinuation rate curves in RA patients with high disease activity (DAS28 >5.1) and DAS28<=5.1

Conclusion: In Mexican RA patients registered in BIOBADAMEX, we found that baseline high disease activity is associated with the discontinuation of bDMARDs. Further longitudinal analyses will be performed including more patients to assess retention rate of specific bDMARDs and identify predictive variables of discontinuation in Mexican population.

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AB1462

RHEUMATIC IMMUNE- AND NONIMMUNE-RELATED ADVERSE EVENTS IN PHASE 3 CLINICAL TRIALS ASSESSING PD-(L)1 CHECKPOINT INHIBITORS FOR LUNG CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Several adverse events (AEs) occurring during immune checkpoint inhibitors (ICIs) therapy are clearly related to their mechanisms of action, and in this case they are indicated as immune-related AEs (irAEs). Every organ may be affected, including the musculoskeletal system; myositis, polymyalgia rheumatica, arthritis or arthritis have been reported in several retrospective and prospective case series and cohorts, with an incidence between 1.5% and 22%. While arthritis, vasculitis, myositis, and polymyalgia rheumatica are usually defined as "irAE" in RCTs, other rheumatic musculoskeletal conditions such as arthralgia, myalgia, back pain and muscular pain are often reported under the umbrella of "general" AEs.
Objectives: We aimed to analyze rheumatic irAE and non-irAE due to immune-checkpoint inhibitors (ICIs) targeting programmed cell death-1 or its ligand PD-(L)1 in lung cancer patients from the available literature.
Methods: We performed a systematic review and meta-analysis of phase III randomized clinical trials (RCTs) assessing PD-(L)1 -ICIs in lung cancer patients, from inception until January 12th, 2021. We extracted data of each trial to estimate odds ratio (OR) for rheumatic ir or non-irAE as classified in RCTs safety data. Sensitivity analyses (by ICI, treatment group and histology) were performed.
Results: Eighteen RCTs met the inclusion criteria (n=12172 subjects). The OR [95%IC] for rheumatic irAE in ICIs versus controls (either placebo or chemotherapy) was 2.20 [0.85,5.72].
Among rheumatic non-irAEs, both overall (any grade, Figure 1A) and severe (grade≥3, Figure 1B) back pain were significantly more frequent in ICIs versus controls (2.01 [1.09;3.73] and 2.90 [1.18;7.08], respectively).

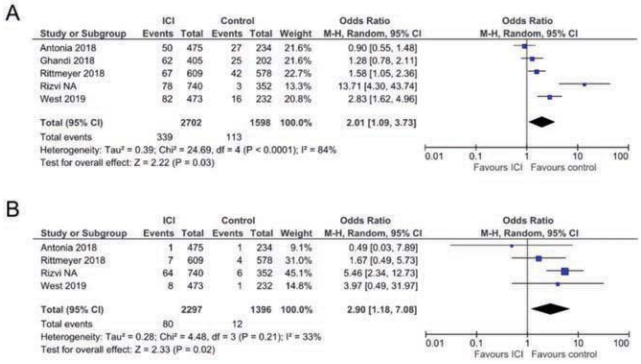

Figure 1. Forest plot showing pooled odds ratio (OR) for back pain (5 phase III trials) (A) and severe back pain (4 phase III trials) (B), respectively.

The overall frequency of arthralgia and severe arthralgia was similar between ICIs and controls (1.13 [0.86, 1.47] and 1.69 [0.68, 4.20], respectively). By sensitivity analysis RCTs assessing ICIs in combination with chemotherapy versus chemotherapy alone showed a significant association with arthralgia (1.55 [1.15;2.10]). Similarly, the frequency of myalgia did not differ between ICIs and controls, but was significantly lower in RCTs assessing ICIs alone versus chemotherapy (OR 0.32 [0.24;0.42]). Muscular pain was not significantly increased with ICI. **Conclusion:** Rheumatic irAEs are not increased in RCTs assessing PD-(L)1 inhibitors, not reflecting the real-life incidence, therefore likely underreported or misclassified. Back pain is significantly associated with PD-(L)1-ICIs regardless its severity, suggesting a possible implication of the PD-(L)1 axis in the development of inflammatory back pain in some patients. In addition, PD-(L)1-ICIs added on conventional chemotherapy are associated with a significantly higher frequency of arthralgia than ICI alone. This trend was seen in the other rheumatic AEs, suggesting that conventional chemotherapy might be a confounder in the interpretation of the occurrence of rheumatic AEs.
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AB1463

CHARACTERISTICS AND MORTALITY OF PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES ADMITTED TO THE INTENSIVE CARE UNIT.

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Background: Autoimmune rheumatic diseases (ARD) are associated with multiple organ dysfunction, which may require admission to Intensive Care Units (ICU), constituting a challenge for rheumatologists and intensivists. The new immunomodulatory treatments may be changing the characteristics and mortality of these patients.
Objectives: The primary objective of the study is to know the mortality and the characteristics related to this event of our patients admitted to the ICU in the last 5 years. The secondary objective is to compare the characteristics of our series with the series of our patients admitted to the ICU in the previous decade.
Methods: We conducted a retrospective transversal observational study using computerized medical records. A database was created with patients with ARD admitted to the ICU of the Princess University Hospital between October 1, 2015 and September 30, 2020, excluding those with a stay of less than 24 hours. Information was collected about the characteristics and treatments of the disease prior to their admission to the ICU, as well as the clinical characteristics and therapeutic measures established in the ICU during their stay. Statistical analysis was performed using SPSS.
Results: After ruling out admissions of less than 24 hours, a population of 45 patients with a mean age of 65.3 ± 12.2 years and 69% women were included. Connectivopathies (40%) and rheumatoid arthritis (37.8%) were the most prevalent ARDs that required admission to the ICU. Cardiovascular events (51%) were the main reason for ICU admission, followed by infectious processes (27%). The median ICU stay was 5 days. It is striking that 77% of the patients had received glucocorticoids prior to admission throughout their disease. The median score on the severity scales was 34 in SAPS II and 17 in APACHE II. Mortality during the ICU stay was 30.4% and in the multivariate analysis it was associated with the previous administration of glucocorticoid boluses and the APACHE II scale score. This mortality is higher compared to historical series of patients admitted to Spanish ICUs with similar APACHE II severity scores. In the comparative study with the previous period, similar mortality rates were observed, an increase in the mean age of those admitted, a decrease in patients with vasculitis and an increase in patients with rheumatoid arthritis. Likewise, an increase in cardiovascular events is observed as a fundamental reason for admission to the ICU.
Conclusion: The mortality of our patients with ARD admitted to the ICU in the last five years is 30.4%, similar to the previous decade but higher than the observed in other pathologies with similar severity characteristics. It is related to the APACHE II score and to the prior administration of glucocorticoid boluses. Connectivopathies and rheumatoid arthritis are the diseases that are most frequently admitted to the ICU and the fundamental reasons are cardiovascular events and infections.
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AB1464

THE ROLE OF EPSTEIN-BARR VIRUS ACTIVITY IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is one of the most common autoimmune diseases with a 1% worldwide prevalence (1) and still elusive etiology (2). Epstein-Barr virus (EBV) evidently plays an important role in the pathogenesis of autoimmune diseases by molecular mimicry, bystander activation effect or epitope-spreading (3). However, cause/effect relationship between EBV and RA is still missing.
Objectives: The aims of this study were to explore the association between EBV infection activity, findings of autoantibodies and markers of acute inflammation in patients with two most prevalent diseases of joints, autoimmune RA and degenerative osteoarthritis (OA).
Methods: A blood samples of 89 seropositive RA patients, 64 newly diagnosed (RAa) and 25 with poorly controlled disease (RAb) (unsuccessfully methotrexate treatment ≥ 6 months), and 50 OA were enrolled. The complete anti-EBV serological panel was detected by commercial ELISA kits. Nested-PCR was used for detection of EBV DNA. Clinical data, biochemical and immunological parameters were obtained from electronic medical records. Complete statistical analysis was performed in IBM SPSS ver. 21.

Results: The average age of all patients was 61.54±11.77 years (p=0.007) with predominant female gender in all groups, 81.3% (p=0.139). Anti-EBNA1 IgG antibodies were present in 95%, 92%, and 98% (p=0.474), anti-EBV-CA IgG antibodies in 98%, 60%, and 100% (p<0.001), anti-EBV-CA IgM antibodies in 25%, 40%, and 4% (p=0.008), anti-EBV-EA IgG antibodies in 14.1%, 20%, and 4% (p=0.084), and anti-EBV-EA IgM antibodies in 20%, 16%, and 6% (p=0.094) in RAa, RAb, and OA, respectively. There was statistically significant difference in the titer of anti-EBV-CA IgG and IgM antibodies between all three groups (p=0.001 and p=0.007, respectively). According to serology findings active EBV infection was present in 47.5%, 40%, and 12% in RAa, RAb, and OA, respectively (p<0.001). On the other hand, corresponding to PCR results only, active EBV infection was detected in 6.3%, 0%, and 20% in RAa, RAb, and OA, respectively (p=0.010). There was statistically significant difference in way of detecting active EBV infection based on serology or PCR only (p<0.001). Further analysis showed that over 80% of all RA patients (81% in RAa and 96% in RAb), whilst 48% of OA had elevated values of sedimentation (SE) (p<0.001). C-reactive protein (CRP) was raised in 83% RA (79% in RAa and 100% in RAb) and in 26.5% of OA patients (p<0.001). The majority of all RA patients had elevated rheumatoid factor (RF) and ACPA (84% and 92%) with no difference between RAa and RAb patients (p=0.361 and p=0.203, respectively). Among patients with active EBV infection (based on both serology and PCR results), there was a significantly higher level of anticardiolipin IgG (p=0.012) and anticardiolipin IgM (p=0.009) autoantibodies in RAa patients, while the level of SSA autoantibodies (p=0.024) was higher in RAb patients. On the other side, there was no significant difference in the level of any autoantibody or factors of acute inflammation (SE and CRP) in patients with past EBV infection.
Conclusion: This study demonstrated linkage between an active EBV infection and elevation of some autoantibodies in RA pathogenesis. As EBV DNA was not found only in a group of RA patients under immunosuppressive therapy, it's suggested that EBV clearing from blood could be direct consequence of methotrexate use. Collectively, these findings indicate that determining of EBV activity must be based on both serology and molecular methods in order not to oversee EBV reactivation during follow-up of these patients.

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AB1465 BLACK PATIENTS ARE LESS SATISFIED WITH THE PROCESS OF CARE FOLLOWING PRIMARY HIP AND KNEE ARTHROPLASTY: A RETROSPECTIVE STUDY

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Background: Patients' post-operative satisfaction with their hospital experience is important to patient care, hospital reimbursement, and comparison between hospitals. The Press Ganey (PG) inpatient survey is commonly administered to assess patient satisfaction with the process of care. However, whether patient PG survey scores following primary unilateral hip and knee arthroplasty are associated with a patient's race and socioeconomic status (SES) is unknown.
Objectives: We aimed to determine whether patient PG survey overall assessment scores differ by race and SES.
Methods: We linked data for patients in large institutional hip and knee arthroplasty registries consisting of surgeries from July 2010–February 2012 to their PG survey responses. Patients undergoing primary unilateral surgery of Black or White race who resided in New York, New Jersey, or Connecticut at the time of surgery were included in the analysis. The primary outcome variable was the PG overall assessment score, calculated as the mean of a patient's ratings for the three questions in the "Overall Assessment" section of the PG survey and dichotomized as either completely satisfied (score of 100) or not completely satisfied (score <100). Primary payor was used as a proxy for patient SES. Multivariable logistic regression was performed for the hip and knee cohorts separately to determine if patient race and primary payor were associated with not being completely satisfied, adjusting for age, sex, and American Society of Anesthesiology (ASA) score.
Results: There were 2,516 hip patients and 2,113 knee patients with PG overall assessment scores included in the analyses (Table 1). Black patients were more likely to be not completely satisfied compared to White patients in both cohorts [hip (odds ratio (OR)=1.64; 95% confidence interval (CI): 1.03, 2.61; p=0.04)]; [knee (OR=1.83; 95% CI: 1.16, 2.88; p=0.01). In the hip cohort, patients between 70-79 years old (OR=1.71; 95% CI: 1.09, 2.67; p=0.02) and older than 80 years (OR=2.00; 95% CI: 1.20, 3.32; p<0.01) were more likely to be not completely satisfied. In the knee cohort, patients 50-59 years old (OR=0.56; 95% CI: 0.33, 0.97; p=0.04) and 60-69 years old (OR=0.57; 95% CI: 0.33, 0.96; p=0.03) were less likely to be not completely satisfied compared to patients <50 years old.

Table 1. Likelihood of not being completely satisfied with the process of care (PG score <100)

			Hip Cohort (n = 2,516)			Knee Cohort (n = 2,113)		
Variable	Reference	Category	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Age Group	<50	50-59	1.02	(0.69, 1.50)	0.939	0.56	(0.32, 0.97)	**0.039**
	<50	60-69	1.04	(0.70, 1.54)	0.858	0.57	(0.33, 0.96)	**0.034**
	<50	70-79	1.71	(1.09, 2.67)	**0.019**	0.63	(0.36, 1.11)	0.113
	<50	80+	2.00	(1.20, 3.32)	**0.008**	0.97	(0.53, 1.77)	0.912
Sex	Female	Male	0.84	(0.69, 1.02)	0.082	1.03	(0.83, 1.26)	0.816
Race	White	Black	1.64	(1.03, 2.61)	**0.038**	1.83	(1.16, 2.88)	**0.010**
ASA status	1	2	1.04	(0.70, 1.55)	0.832	1.23	(0.60, 2.51)	0.580
	1	3	1.45	(0.91, 2.29)	0.116	1.36	(0.64, 2.87)	0.419
	1	4	<0.01	(0.00, ***)	0.968	<0.01	(0.00, ***)	0.977
Primary Payor	Medicare	Medicaid	1.35	(0.26, 7.01)	0.718	<0.01	(0.00, ***)	0.983
	Medicare	Other/ Unknown	1.24	(0.94, 1.64)	0.126	0.87	(0.65, 1.17)	0.362
	Medicare	Private	1.13	(0.61, 2.10)	0.688	1.01	(0.57, 1.78)	0.983

ASA = American Society of Anesthesiologist (ASA) physical status classification. PG = Press Ganey. CI = Confidence Interval. *** indicates >999.99. **Bold** indicates p < 0.05

Conclusion: Black patients were less likely to be completely satisfied compared to White patients following total hip and knee arthroplasty. More research is needed to investigate other factors such as perceived staff courtesy and baseline pain and function to understand why these disparities exist.
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AB1466 CORRELATION BETWEEN SALES OF CERTAIN BEVERAGES AND GOUT ATTACKS DURING THE COVID-19 CURFEW IN CAMEROON: A HOSPITAL-BASED STUDY

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Background: An unusual increase in the number of gout cases was observed in Cameroon in 2020. Was there a link with lifestyle changes during confinement, especially the consumption of certain types of beverages (beer, liquor, water, sweetened drinks)?
Objectives: To determine if there was a correlation with the consumption of different beverages (water, beer, liquor, sweetened drinks).
Methods: Cross-sectional study in the rheumatology consultation of the Douala General Hospital, from January 1 to December 31, 2020, including all patients with a diagnosis of gout (ACR/EULAR criteria of 2015). Pearson's correlation (r) was used to determine the effect of the consumption of the different beverages on the increase in the number of gout cases. A p<0.05 was significant.
Results: We included 1952 patients, including 111 gout cases (107 men; median age: 51 years [36-81]). Compared with the same period in 2018 and 2019, a peak in gout cases was observed between May and November 2020 (Figure 1). In the same period, a positive correlation existed between the number of gout cases and the increase in sales of liquor (r=0.8434, p=0.034) and sweetened beverages (r=0.8436, p=0.034). This correlation was not significant for beer sales (r=0.7980, p=0.057) [Table 1].

Table 1. Correlation between the number of gout cases and sales of different types of drinks

Variables	Correlation coefficient (r)	*p*
Beer	0.7980	0.0571
Liquor	0.8434	0.0349*
Sweetened beverages	0.8436	0.0348*
Water	-0.7569	0.0815

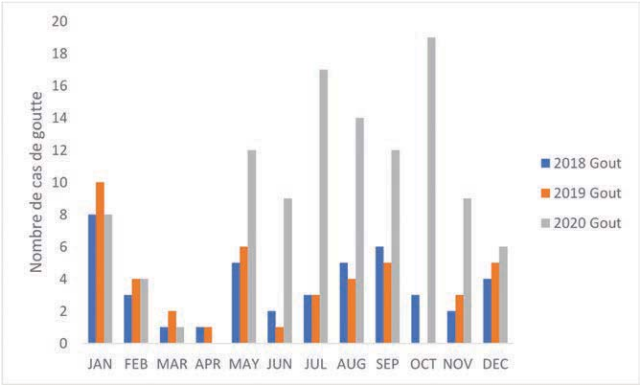

Figure 1. Evolution of Gout cases from 2018 to 2020

The COVID-19 PCR test was negative in all patients.
Conclusion: The real "outbreak" of gout observed during the curfew related to COVID-19 between May and November 2020 was favored by a punctual increase in the consumption of liquors and sweetened drinks.
Disclosure of Interests: None declared
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AB1467 EPIDEMIOLOGICAL DESCRIPTION OF JUVENILE IDIOPATHIC ARTHRITIS FROM A COLOMBIAN POPULATION

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood and presents predominantly with peripheral arthritis; this pathology is divided into subgroups. In Colombia there are few descriptive studies.
Objectives: The objective was to describe the sociodemographic, immunological and clinical characteristics of a cohort of patients with Juvenile Idiopathic Arthritis.
Methods: An observational cross-sectional study was conducted that included 171 JIA patients treated at a specialized rheumatology institution between 2010 and 2021. Univariate analyzes were performed to describe the sociodemographic, immunological, and clinical profile of the population. The epidemiological characteristics were obtained from the review of medical reports.
Results: 171 patients were analyzed. 58.48% were women; with a median age at diagnosis of 12.25 years (IQR=6.55), and a median duration of the disease of 3.71 years (IQR=5.52). According to the classification criteria of the International League of Associations for Rheumatism (ILAR), the most frequent were enthesitis related to JIA present in 61 patients (35.67%), oligoarticular 27 (15.79%), negative polyarticular rheumatoid factor (14.62%) and positive polyarticular rheumatoid factor (14.04%). JIA-enthesitis related was 17,85% ANAs positive, 16,66% rheumatoid factor positive and HLA-B27 en 22,72%. In JIA oligoarticular the auto-antibodies ANAS, FR was present in 26,32% and 16,66%. The JIA-polyarticular rheumatoid factor positive was positive for ANA in 76.47% and AntiCCP in 88.88%. JIA-polyarticular rheumatoid factor negative was positive for ANAs (40%) and AntiCCP (10%).
Conclusion: The epidemiological description of JIA in the Colombian population is similar to the current one in other populations, but we found differences in the subtypes of juvenile idiopathic arthritis and in the presence of autoantibodies. This is the first step to discover the characteristics of this autoimmune disease in this population.
Disclosure of Interests: Miguel Dario Canola Escobar: None declared, DANIEL RODRIGUEZ-ARIZA: None declared, LUIS AARON-INFANTE: None declared, DIANA CARDONA: None declared, YADITH HERNANDEZ-ARENAS: None declared, DIEGO MELO: None declared, JUAN PUENTES: None declared, PAULA ROZO-TELLEZ: None declared, Veronica Usuga-Graciano: None declared, OLGA ARIZA-QUINTERO Employee of: actual employee in Novartis Colombia as medical science liaison
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AB1468 ALL-CAUSE MORTALITY IN PATIENTS WITH PALINDROMIC RHEUMATISM: A POPULATION-BASED COHORT STUDY

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Background: Palindromic rheumatism (PR), is a clinical syndrome characterized by the intermittent acute arthritis or peri-arthritis involving one or several regions. It presents with pain with or without redness or swelling, lasting from a few hours to days with variable symptom-free periods. Different from rheumatoid arthritis (RA), PR does not lead to residual joint destruction. A recent study showed that RA patients had a mean loss of life expectancy of about 5 years [1]. However, whether all-cause mortality rate in PR patients differs from that in individuals without PR was still known.
Objectives: To compare the all-cause mortality rate between PR patients and non-PR individuals.
Methods: Usint a two-million representative cohort from the 2000-2018 Taiwan's National Health Insurance Research Database, we identified 2,791 incident adult (aged ≥ 20 years) PR patients. Matching for sex, age and year of index date at a 1:40 ratio, we selected 111,640 non-PR individuals for comparison. Then using the greedy algorithm, we further selected another comparison group of 5,582 non-PR individuals by propensity score (PS) matching for Charson comorbidity index (CCI) at a 1:2 ratio. Using the Cox proportional hazard model, we examined the risk of all-cause mortality in PR patients shown as adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs). Potential confounders included age, sex, CCI, a history of immune mediated inflammatory disease (IMID) including systemic lupus erythematosus erythematosus (SLE), RA, idiopathic inflammatory myopathies (IIM, including dermatomyositis and polymyositis), Sjögren's syndrome (SS), inflammatory bowel disease (IBD), psoriasis, and medication use including corticosteroid (0, 1-5, >5 mg/day prednisolone equivalent dose), methotrexate, sulfasalazine, leflunomide, hydroxychloroquine and nonsteroidal anti-inflammatory drugs within one year before the index date.
Results: In the 1:2 PS-matched popultion, the mean age was 48.4 years and female to male ratio was 1.54 in the PR group and non-PR group. Amon 2,791 PR patients, 226 (8.10%) died during a mean follow-up period of 8.29 years; while 11,958 (10.71%) of 111,640 non-PR individuals expired during a mean follow-up period of 8.13 years. The all-cause mortality rates in PR patients and non-PR individuals were 976.83 per 10^5 years and 1,317.93 per 10^5 years, respectively (incidence rate ratio, 0.74; 95% CI, 0.65-0.85, $p < 0.001$). After adjusting for potential confounders, the risk of all-cause mortality was significantly lower in PR patients compared with non-PR individuals (aHR, 0.70; 95% CI, 0.59–0.82). In the subgroup of subjects without IMID, the relative risk of all-cause mortality in PR patients compared with non-PR individuals was 0.68 (0.58–0.80), $p < 0.001$. In the subgroup of subjects with a history of any IMID, the relative mortality risk in PR patients compared with the non-PR group was 0.64 (0.30–1.34), $p = 0.236$. The top 3 causes of mortality with their proportions in the PR group (n = 226) were neoplasms (28.3%), diseases of circulatory system (23.5%) and diseases of the respiratory system (11.5%). While the top 3 causes of mortality in the non-PR group (n = 11,958) was neoplasms (32.3%), diseases of circulatory system (21.5%) and disease of respiratory system (9.6%).

	1:40 age and sex-matched population		1:2 age, sex and CCI-matched population	
	HR (95% C.I.)	P value	HR (95% C.I.)	P value
PR (ref: non-PR)	0.61 (0.57–0.74)	<0.001	0.70 (0.59–0.82)	<0.001

Conclusion: This population-based cohort study showed that the all-cause mortaltiy rate in PR patients was lower than that in non-PR individuals, in particular in subjects without a history of IMIDs.
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[1] Chiu YM, et al. Arthritis Rheumatol 2021 May;73(5):750-758
Disclosure of Interests: None declared
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Validation of outcome measures and biomarkers___

AB1469 SPANISH TRANSLATION AND CROSS-CULTURAL ADAPTATION OF THE MSQUASH

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Background: Regular physical activity is recommended for all patients in the ASAS/EULAR recommendations for the management of axial spondyloarthritis (axSpA). However, there is a lack of outcome measures that assess the amount and type of physical activity in patients with axSpA. For this matter, the modified Short QUestionnaire to Assess Health enhancing physical activity (mSQUASH) was developed and validated, originally in Dutch1.

Objectives: To translate and cross-culturally adapt the mSQUASH into Spanish and to test the equivalence of the translated version in patients with axSpA.

Methods: The mSQUASH was translated into Spanish and then back-translated into Dutch, following forward-backward procedure as described by Beaton[2] (Figure 1). Two bi-lingual translators (native speakers for European Spanish) produced independent forward translations of the item content, response options, and instructions of the mSQUASH into Spanish. Both versions were harmonized in a meeting among the Spanish translators, a methodologist and a rheumatologist into a consensual version. Another translator (native speaker for Dutch), blinded for the original version, back translated the synthesized version into Dutch. An expert committee, including all translators, one methodologist and a rheumatologist, reached consensus on discrepancies, ensuring equivalence between the Dutch and Spanish versions, and developed a pre-final version of the Spanish mSQUASH. The field test with cognitive debriefing involved a sample of 10 patients with axSpA covering the full spectrum of the disease -radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA)- with different gender, age, disease duration, and educational background. Each patient was interviewed to check understandability, interpretation and cultural relevance of the translation.

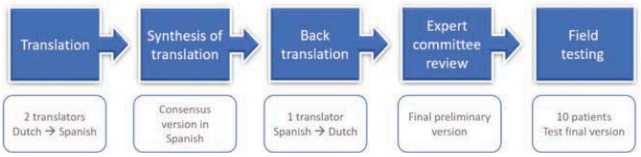

Figure 1. Cross-cultural adaptation of the mSQUASH

Results: The translation process of the mSQUASH was completed without major complications following the forward-backward procedure. The first translation needed several iterations due to small discrepancies in the wording. Back-translation was performed without difficulties, and the expert committee agreed upon a final version of the questionnaire. A total of 10 patients with axSpA participated in the field test (Table 1). Seven were male, mean age (SD) was 38.9 (14.4) years; 6 patients had r-axSpA, 9 were HLA-B27+. Cognitive debriefing showed the Spanish questionnaire to be, relevant, understandable and comprehensive. The preliminary version was accepted with minor modifications. As a result of the interviews, minor spelling errors were corrected, and the wording of the response categories was homogenized ("despacio/ligero"). Besides, the term "colegio"- translated literally from the Dutch "school"- was found not comprehensive enough to reflect possibilities on education (i.e. it does not include university), so it was adapted to "el lugar de estudio".

Conclusion: The resulting Spanish version of the mSQUASH showed good linguistic and face validity according to the field test, revealing potential for use in both clinical practice and research settings. In order to conclude the cross-cultural adaptation of the mSQUASH into Spanish, the next step is the assessment of psychometric properties of the Spanish version.

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[1] Beaton DE, et al. Spine. 2000; 25:3186-91

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Disclosure of Interests: Diego Benavent Speakers bureau: Jannsen, Roche, Grant/research support from: Novartis, Andrea Jochems: None declared, DORA PASCUAL-SALCEDO Speakers bureau: Pfizer, Menarini, Takeda, Abvvie., Grant/research support from: Pfizer, Menarini, Takeda, Abvvie., Gijs Jochems: None declared, Chamaida Plasencia Speakers bureau: Pfizer, Abbvie, Lilly, Sandoz, Sanofi, Biogen, Roche and Novartis, Grant/research support from: Pfizer and Abbvie, Sofia Ramiro Speakers bureau: Eli Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB, Sanofi, Grant/research support from: AbbVie, Galapagos, Novartis, Pfizer, UCB, Suzanne Arends: None declared, Anneke Spoorenberg Consultant of: AbbVie, Novartis, Pfizer; UCB, Lilly, Grant/research support from: AbbVie, Pfizer, Alejandro Balsa Speakers bureau: Pfizer, Abbvie, Lilly, Galapagos, BMS, Sandoz, Nordic Pharma, Gebro, Roche, Sanofi, UCB, Consultant of: Pfizer, Abbvie, Lilly, Galapagos, BMS, Nordic Pharma, Sanofi, UCB, Grant/research support from: Pfizer, Abbvie, BMS, Nordic Pharma, Gebro, Roche, UCB, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie and Novartis

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AB1470 DOES TESTING FOR SAA IS MORE BENEFICIAL THAN CRP FOR THE FOLLOW-UP OF PATIENTS WITH FMF?

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Background: In order to follow subclinical inflammation and adjust the therapy for an optimal disease control, clinicians seek for readily accessible, affordable and reproducible markers. C reactive protein (CRP) is widely used for this purpose. Some suggest that the Serum Amyloid A (SAA) is preferable to CRP as a biomarker of inflammation in FMF patients[1].

Objectives: To evaluate and to compare the sensitivity of the serum SAA and CRP levels in FMF patients.

Methods: Serum SAA and CRP levels were measured in 45 patients. 153 measurements from 28 patients with M694V homozygous mutation and 74 measurements from 17 patients with M694V heterozygous mutation were obtained during a mean follow-up of 1 year. For the analysis, the folds of normal CRP and SAA values were used for correlation. Serum levels of the given markers were measured with nephelometric kits (normal CRP levels < 5 mg/L and SAA levels < 6,8 mg/L). More than one and half fold increasement of CRP and SAA was defined as an active inflammation. The correlation coefficients and their significance were calculated using the Spearman test.

Results: Except a patient, all patients in whole cohort were on prophylactic colchicine. Among 28 patients with M694V homozygous mutation, a patient with adalimumab, 12 (42,8%) patients with anti-IL-1 regimens. Of the 17 patients with M694V heterozygous mutation, four (23,5%) were under anti-IL-1 treatment. There was a total of 227 measurements of CRP and SAA from 45 patients. Twenty-five (11%) measurements were obtained during the attack period in and the remaining 202 measurements were collected in attack free period. Figure 1 demonstrates the correlation between CRP and SAA levels (r=0.8, p< 0,001). Both acute phase reactants were increased in 72 (31,7%) measurements, while in 13 (5,7%) CRP level was high but SAA level was normal and in 31 (13,6%) SAA level was high however CRP level was within the normal limits. The vast majority (30:31) of high SAA with normal CRP levels were observed in patients with M694V homozgous mutation. The mean increase in CRP of the entire cohort was 2,06 ± 3,34-fold, whereas mean increase in SAA was 6,23 ± 15,04-fold of the normal levels.

Table 1. Patients' characteristics

#	Gender	Age	Working status	Education	axSpA subtype	Disease duration	HLA-B27	Drug	BASDAI
1	Male	63	Working	University	r-axSpA	35 y	+	NSAIDs	2.3
2	Male	24	Student	Secondary	r-axSpA	6 y	+	NSAIDs	0
3	Male	37	Working	University	r-axSpA	5 y	+	ADA	2.5
4	Male	66	Retired	University	r-axSpA	23 y	+	IFN	3.1
5	Male	29	Working	University	r-axSpA	11 y	+	ADA	0
6	Female	26	Working	University	nr-axSpA	2 y	+	NSAIDs	-
7	Male	24	Student	University	nr-axSpA	1 y	+	ETA	4.5
8	Male	35	Working	University	r-axSpA	12 y	+	GOL	0
9	Female	40	Working	Secondary	nr-axSpA	4 y	+	NSAIDs	-
10	Female	45	Unemployed	Primary	nr-axSpA	9 y	-	GOL	8.2

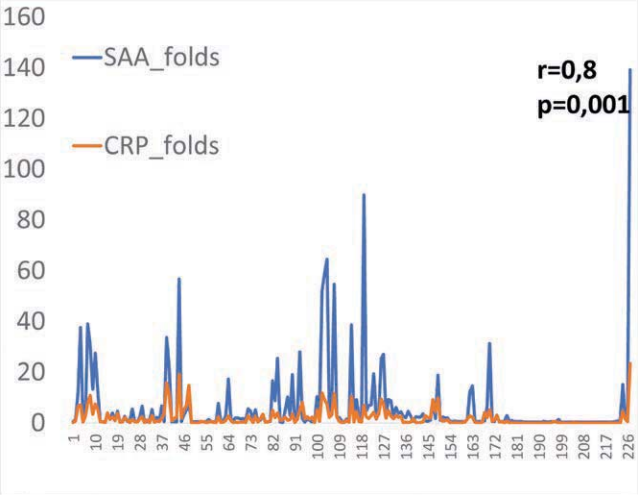

Figure 1. The folds of the serum CRP and SAA levels in the entire cohort.

Conclusion: According to our results, serial testing of SAA does not provide any additional advantages over CRP. Readily accessible and affordable bio-marker CRP seems to be sufficient for follow-up of patients with FMF.

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[1] DOI: 10.1038/nrrheum.2010.181

Disclosure of Interests: None declared

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AB1471 EVALUATION OF CXCL13 SERUM LEVELS IN A COHORT OF PATIENTS WITH PERIPHERAL PSORIATIC ARTHRITIS IN COMPARISON WITH RHEUMATOID ARTHRITIS.

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Background: The research of circulating biomarkers in the field of chronic arthritis is still an unmet need, especially for the subgroup of seronegative arthritis [e.g., negative for anti-citrullinated peptides autoantibodies (ACPA) and/or rheumatoid factors (RF)]. In fact, in this clinical subset, there is a lack of soluble molecules which could help for a diagnostic or prognostic purpose, and the differential diagnosis between psoriatic arthritis (PsA) and seronegative rheumatoid arthritis (RA) is still a challenge. C-X-C motif chemokine 13 (CXCL13) is one of the most promising biomarkers recently identified, because of its association with active synovitis (1) and with a poor prognosis in RA (2), although there are still inadequate results to justify its routine use. No data are available of the determination of CXCL13 serum levels in PsA.

Objectives: To analyze CXCL13 serum levels in a cohort of PsA patients with a history of peripheral involvement in comparison with RA.

Methods: Cross sectional analysis of consecutive patients with peripheral PsA [n:81; male/female=44/37; median age (25°-75° percentile)=54 (46-62) years; 28-joint Disease Activity Score-C Reactive Protein (CRP-DAS28)=1.9 (1.6-2.5); active psoriasis=43%; DAPSA (Disease Activity in PSoriatic Arthritis) score=8 (3-14)] and RA [n:143; male/female=30/113; age =62 (50-70) years; seropositive=67%; CRP-DAS28=2.1 (1.5-2.8)] was performed. 100 sex and age-matched healthy controls (HC) were enrolled. CXCL13 serum levels were assessed through commercial ELISA test (R&D).

Results: CXCL13 serum levels were higher in all the subgroups of patients [PsA: 50.9 (34.5-80.2) pg/mL, p<0.01; RA: 77.2 (52.9-107.7) pg/mL, p<0.01; RA ACPA+: 77.7 (55.9-110.7) pg/mL, p<0.01; RA ACPA-: 69.5 (49.3-104) pg/mL, p<0.01] than in HC (22.3 (17.7-33.8) pg/mL). No significant differences were found among RA patients according with their seropositivity (p=0.378). CXCL13 serum levels were lower in PsA patients than in RA patients, independently from their seropositivity [vs RA ACPA+, p<0.01; vs RA ACPA-, p=0.012]. CXCL13 serum levels were positively correlated with CRP in PsA patients (r=0.30; p=0.008), but not with DAPSA score.

Conclusion: These results confirm the value of CXCL13 as a biomarker in the field of chronic arthritis. Its higher levels in seronegative RA than in PsA suggests its possible value in the differential diagnosis of these two subsets of arthritis.

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[1] Bechman et al. BMC Rheumatology 2020;
[2] Bugatti et al. Rheumatology 2014.

Disclosure of Interests: None declared

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AB1472 TRANSLATION AND CROSS-CULTURAL ADAPTATION OF THE CORS INTO SPANISH

D. Benavent[1], A. Jochems[2], D. Pascual-Salcedo[2], G. Jochems[3], C. Plasencia[1], S. Ramiro[4,5], W. Van Lankveld[6], A. Balsa[1], V. Navarro-Compán[1]. [1]*Hospital Universitario La Paz, IdiPaz, Department of Rheumatology, Madrid, Spain*; [2]*Hospital Universitario La Paz, IdiPaz, Immuno-Rheumatology Group, Madrid, Spain*; [3]*Promega Biotech Ibérica, -, Madrid, Spain*; [4]*Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; [5]*Zuyderland Medical Center, Department of Rheumatology, Heerlen, Netherlands*; [6]*HAN Unitversity of Applied Sciences, Institute of Paramedic Studies, Nijmegen, Netherlands*

Background: Rheumatic diseases substantially affect the lives of patients, with complex associations between disease severity and self-perceived health status. In this regard, the Coping with Rheumatic Stressors (CORS) questionnaire was developed to measure how patients with rheumatoid arthritis cope with stressors such as pain or dependence. There is no validated instrument to measure coping in axial spondyloarthritis (axSpA) and therefore the adaptation of the CORS would be of great value.

Objectives: To cross-culturally adapt the CORS into Spanish and to test the conceptual equivalence of the translated version in patients with axSpA.

Methods: A translation of the CORS into Spanish was performed, followed by a back-translation into Dutch, following forward-backward procedure as described by Beaton[1](Figure 1). Two bi-lingual translators (native speakers for Spanish), one of them informed of the content of the questionnaire and the other not informed, produced independent forward translations of the item content, response options, and instructions of the CORS into Spanish. Both versions were harmonized in a consensual version. Another translator (native speaker for Dutch), not informed of the concepts used in the questionnaire, back translated the synthesized version into Dutch. An expert committee including all translators, one methodologist and a rheumatologist, held a meeting and reached consensus on discrepancies to develop a pre-final version of the Spanish CORS. The field test with cognitive debriefing involved a sample of 10 patients with axSpA covering the full spectrum of the disease and with different sociodemographic backgrounds.

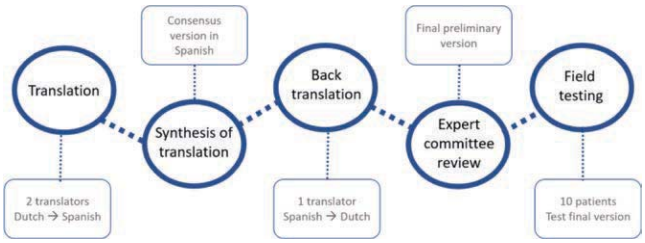

Figure 1. Cross-cultural adaptation of the CORS

Results: The translation process of the CORS was completed following the forward-backward procedure, after discussion of the discrepancies throughout the process. The first translation was done without major complications. However, several discrepancies appeared in the back-translation, in which there were minor modifications in the wording in one response option ("muchas veces" to "muy a menudo") and 15 questionnaire items. As an example, "Ik ga de deur uit", literally meaning "I go out by the door", was initially translated as such ("salgo por la puerta"); however, it conceptually represents "I go away", and it was adapted like this ("me voy a la calle"). Thus, a pre-final consensus version of the CORS was agreed by the expert committee. This pre-final version was field tested in 10 patients with axSpA: mean age (SD) was 38.9 (14.4) years, 7 patients were male, 6 had radiographic axSpA, and 9 were HLA-B27+. The Spanish questionnaire appeared clear and understandable to all patients. However, some minor modifications were proposed in some items (Table 1). As a result of the cognitive debriefing, two changes were implemented (one instruction and one item), whereas two other suggestions did not lead to any change due to minor wording discrepancies with similar conceptual equivalence. The final version of the Spanish CORS is shown at shorturl.at/cimC6.

Table 1. Cognitive debriefing queries and decisions from the expert committee

Original Dutch item	Spanish translation pre-final	# Patient queries	Queries	Final version
(….) aan te geven hoe vaak u het beschreven gedrag uitvoert.	*(…) indique cuán a menudo usted ha llevado a cabo dicho comportamiento.*	1	Literal discrepancies	*(…) indique la frecuencia con que usted ha tenido dicho comportamiento.*
Ik rust op tijd uit	*Me voy a tiempo a descansar*	1	Literal discrepancies	No changes
Ik probeer er het beste van te maken	*Intento aprovechar al máximo*	1	Literal discrepancies	No changes
Ik houd rekening met anderen	*Tengo en cuenta a los demás*	2	Meaning doubts	*Tengo en consideración a los que me ayudan/ cuidan*

Conclusion: The Spanish version of the CORS showed good cross-cultural validity and good face validity in patients with axSpA according to the field test. Before the Spanish CORS is implemented, further validation is in progress to test the psychometric properties of the instrument.

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[1] Beaton DE, et al. Spine. 2000; 25:3186-91

Disclosure of Interests: Diego Benavent Speakers bureau: Jannsen, Roche, Grant/research support from: Novartis, Andrea Jochems: None declared, DORA PASCUAL-SALCEDO Speakers bureau: Pfizer, Menarini, Takeda, Abvvie., Grant/ research support from: Pfizer, Menarini, Takeda, Abvvie., Gijs Jochems: None declared, Chamaida Plasencia Speakers bureau: Pfizer, Abvvie, Lilly, Sandoz, Sanofi, Biogen, Roche, Novartis., Grant/research support from: Pfizer, Abvvie., Sofia Ramiro Speakers bureau: Eli Lilly, MSD, Novartis, UC, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB, Sanofi, Grant/research support from: AbbVie, Galapagos, Novartis, Pfizer, UCB, Wim van Lankveld: None declared, Alejandro Balsa Speakers bureau: Pfizer, Abbvie, Lilly, Galapagos, BMS, Sandoz, Nordic Pharma, Gebro, Roche, Sanofi, UCB, Consultant of: Pfizer, Abbvie, Lilly, Galapagos, BMS, Nordic Pharma, Sanofi, UCB, Grant/research support from: Pfizer, Abbvie, BMS, Nordic Pharma, Gebro, Roche, UCB, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie and Novartis

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AB1473

EFFICACY RESPONSES ACROSS DISEASE SEVERITY AND TREATMENT HISTORY SUBGROUPS OF PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS TREATED WITH GUSELKUMAB: POOLED RESULTS FROM VOYAGE-1 AND VOYAGE-2 THROUGH 5 YEARS

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Background: The VOYAGE-1 and VOYAGE-2 phase 3 studies evaluated efficacy and safety of guselkumab (GUS) in patients with moderate-to-severe plaque psoriasis.

Objectives: To assess the five-year efficacy of GUS by baseline disease characteristics and treatment history.

Methods: This study evaluated 1829 patients randomized to GUS, placebo (PBO)→GUS, and adalimumab (ADA) →GUS from the VOYAGE-1 and VOYAGE-2 trials. All patients received open-label GUS 100 mg every 8 weeks (Q8W) during Week (W) 52 to W252 in VOYAGE-1 and during W76 to W252 in VOYAGE-2. The proportions of combined GUS patients (including PBO→GUS and ADA→GUS) achieving Investigator's Global Assessment of cleared or minimal (IGA-0/1) and Psoriasis Area and Severity Index (PASI) 90 response were evaluated from W100 to W252 by baseline PASI (<20/≥20) and IGA (<4/=4) scores, body surface area (BSA; <20%/≥20%), and prior psoriasis treatments. Analysis was performed using observed data after applying treatment failure rules.

Results: At W252, proportions of combined GUS patients achieving IGA 0/1 or PASI 90, respectively, were comparable or numerically greater for patients with baseline PASI < 20 (85.4%; 81.1%) vs PASI ≥ 20 (81.4%; 83.8%); IGA < 4 (85.1%; 82.7%) vs IGA = 4 (78.9%; 81.1%); BSA < 20% (85.1%; 82.7%) vs BSA ≥ 20% (82.6%; 82.0%); no prior phototherapy (83.3%; 84.0%) vs prior phototherapy (83.8%; 81.1%); no prior non-biologic systemic therapy (84.5%; 83.0%) vs prior non-biologic systemic therapy (83.2%; 82.0%); and no prior biologics (85.3%; 83.8%) vs prior biologics (76.7%; 76.3%). This trend was consistent at each timepoint evaluated from W100 to W252.

Conclusion: This analysis demonstrated that the high degree of efficacy of GUS treatment is durable through 5 years among broad subpopulations of patients with varying disease severity characteristics and previous psoriasis treatments.

References: None

Disclosure of Interests: Kenneth Gordon Grant/research support from: AbbVie, Almirall, Amgen, BMS, Celgene, Dermira, Dermavant, Eli Lilly, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Sun Pharma, and UCB Pharma, Joseph F. Merola Consultant of: AbbVie, Arena, Avotres, Biogen, Bristol-Myers Squibb, Celgene, Dermavant, Eli Lilly, EMD Sorono, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB pharma, Peter Foley Speakers bureau: AbbVie, Celgene, Eli Lilly, Galderma, GSK, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Roche, and Valeant, Consultant of: AbbVie, Amgen, Arcutis, Aslan, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Eli Lilly, Galderma, Genentech, GSK, Hexima, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals Inc, Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma, and Valeant, Grant/research support from: grant/research support from AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Sanofi, and Sun Pharma; and travel grants from AbbVie, Eli Lilly, Galderma, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Roche, Sanofi, and Sun Pharma, Olivia Choi Shareholder of: may own stock or stock options in Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Daphne Chan Shareholder of: may own stock or stock options in Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Megan Miller Shareholder of: may own stock or stock options in Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yin You Shareholder of: may own stock or stock options in Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yaung-Kaung Shen Shareholder of: may own stock or stock options in Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Ya-Wen Yang Shareholder of: may own stock or stock options in Johnson & Johnson, Employee of: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, Andrew Blauvelt Speakers bureau: AbbVie, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly, Evommune, Forte, Galderma, Incyte, Janssen, Leo Pharma, Novartis, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma, Consultant of: AbbVie, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly, Evommune, Forte, Galderma, Incyte, Janssen, Leo Pharma, Novartis, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma

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AB1474

LIPIDOMIC PROFILING IDENTIFIES SERUM LIPIDS ASSOCIATED WITH PERSISTENT MULTISITE MUSCULOSKELETAL PAIN

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Background: Lipid mediators have been suggested to have a role in pain sensitivity and response; however, longitudinal data on lipid metabolites and persistent multisite musculoskeletal pain (MSMP) are lacking.

Objectives: This study was to identify lipid metabolic markers for persistent MSMP.

Methods: Lipidomic profiling of 807 lipid species was performed on serum samples of 536 participants from a cohort study. MSMP was measured by a questionnaire and defined as painful sites ≥4. Persistent MSMP was defined as having MSMP at every visit. Logistic regression was used with adjustment for potential confounders. The Benjamini Hochberg method was used to control for multiple testing.

Results: A total of 530 samples with 807 lipid metabolites passed quality control. Mean age at baseline was 61.54±6.57 years and 50% were females. One hundred and twelve (21%) of the participants had persistent MSMP. Persistent MSMP was significantly associated with lower levels of monohexosylceramide (HexCer)(d18:1/22:0 and d18:1/24:0), acylcarnitine (AC)(26:0) and lysophosphatidylcholine (LPC)(18:1 [sn1], 18:2 [sn1], 18:2 [sn2], and 15-MHDA[sn1]

[104_sn1]) after controlling for multiple testing. After adjustment for age, sex, body mass index, diabetes status, and physical activity, HexCer(d18:1/22:0 and d18:1/24:0) and LPC(18:1 [sn1] and 15-MHDA [sn1] [104_sn1]) were significantly associated with persistent MSMP [Odds Ratio (OR) ranging from 0.24 - 0.32]. Two lipid classes -- HexCer and LPC were negatively associated with persistent MSMP after adjustment for covariates (OR=0.19 and 0.21, respectively).

Conclusion: This study identified four novel lipid signatures of persistent MSMP, suggesting that lipid metabolism is involved in the pathogenesis of persistent pain.

Disclosure of Interests: None declared

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AB1475 SERUM LEVELS OF INFLAMMATORY BOWEL DISEASE-SPECIFIC ANTIBODIES IN ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is an immune-mediated inflammatory disease of the musculoskeletal system, that is often accompanied with a subclinical intestinal inflammation. Inflammatory bowel diseases (IBD), including, Crohn's disease (CD) and ulcerative colitis (UC), are the most frequent extra-articular manifestation in patients (pts) with AS. Several autoantibodies and antimicrobial antibodies are used as additional non-invasive serological markers for the diagnosis of CD and UC [1]. The evaluation of IBD-associated antibodies in AS pts provided conflicting results [2, 3].

Objectives: The aim of the study was to determine the serum levels of IBD-specific antibodies in AS.

Methods: We studied 51 pts with AS fulfilled modified New York criteria (1984); (40M/11F); median and interquartile range (25th—75th percentile) of age 44.0; 34.0-49.0 years; disease duration 12.0; 5.0-20.0 years; BASDAI - 5.3; 4.5-6.4; ASDAS ESR - 3.6; 3.0-4.4; ASDAS CRP - 3.7; 2.8-4.5; 40% HLA-27 positive. In 22% of pts with AS, IBD (CD and UC) were diagnosed. The control group included 44 healthy donors (HC). Atypical perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) were detected using indirect immunofluorescence. The serum levels of IgA/IgG antibodies to *Saccharomyces cerevisiae* (ASCA), IgA/IgG antibodies to glycoprotein 2 (GP2), IgG antibodies to cathepsin G, lactoferrin, elastase and bactericidal permeability-increasing protein (BPI) were detected by ELISA.

Results: AS pts without signs of IBD and AS with IBD (AS/IBD) pts had significantly higher serum levels of IgA ASCA, IgA anti-GP2, anti-elastase antibodies than HC (4.5; 2.6-6.4 U/ml and 4.9; 3.7-7.3 U/ml vs 1.9; 0.6-2.6 U/ml, p=0.0008, p=0.001; 1.2; 0.8-5.5 U/ml and 1.2; 0.9-11.8 U/ml vs 0.7; 0.6-1.3 U/ml, p=0.007, p=0.02; 8.2; 5.9-9.9 U/ml and 9.1; 8.5-10.5 U/ml vs 5.6; 4.7-8.3 U/ml, p=0.01, p=0.003). The median concentration of anti-cathepsin G antibodies was greater for AS/IBD pts than AS pts (0.8; 0.5-1.0 U/ml vs 0.4; 0.3-0.6 U/ml, p=0.02). In AS and AS/IBD, the occurrence of anti-elastase antibodies (23.0%, 33.0%) was higher than for HC (0%, p=0.05, p=0.01). The positivity rate of IgA anti-GP2 in AS/IBD exceeded that in HC (27.0% vs 0%, p=0.025). AS/IBD pts demonstrated a higher prevalence of pANCA (36.0%), and anti-BPI antibodies (36.0%), when compared to AS alone (4.8%, p=0.005, and 8.0%, p=0.02) and HC (0%, p=0.0001, and 0%, p=0.008).

Conclusion: Our findings indicate that elevated serum levels of IgA ASCA, IgA anti-GP2, anti-elastase antibodies in AS did not differ from those in AS/IBD and may serve as potential biomarkers for predicting intestinal inflammation at an early stage. For AS/IBD, the most useful diagnostic markers were atypical pANCA, IgA ASCA, IgA anti-GP2, anti-elastase and anti-BPI antibodies.

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AB1477 MEDIAN 0-10 PATIENT GLOBAL ASSESSMENT WAS 2.5-5 POINTS HIGHER IN INFLAMMATORY ARTHRITIS PATIENTS POSITIVE VS NEGATIVE FOR FAST4 (FIBROMYALGIA ASSESSMENT SCREENING TOOL) AND/OR MSD2 (MDHAQ DEPRESSION SCREEN): 2 EASILY-SCORED MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE (MDHAQ) INDICES

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Background: Patient global assessment (PATGL) is included in DAS28, CDAI, ASDAS, DAPSA, and other indices to assess rheumatoid arthritis (RA) or spondyloarthropathy (SpA). PATGL reflects inflammatory activity in many patients, but may be elevated by comorbid fibromyalgia (FM) and/or depression (Dep), which are often unrecognized in others, complicating interpretation and use in treat-to-target. A 2-page multidimensional health assessment questionnaire (MDHAQ) includes PATGL and two easily scored cumulative indices, FAST4 (0-4 FM assessment screening tool) and MDS2 (0-2 MDHAQ Dep screen), which agree more than 80% with reference 2011 revised FM criteria, HADS-D and PHQ-9,[1-3] and may clarify interpretation of high PATGL and index scores, particularly in busy clinical settings.

Objectives: Analysis of PATGL in patients with RA or SpA according to MDHAQ FAST4 and/or MDS2 positivity (+) or negativity (-).

Methods: MDHAQ was completed at a routine care visit at 3 sites in Australia, Spain, and USA. Medians and interquartile ranges (IQRs) for PATGL were computed for RA and SpA, according to FAST4 + or – and/or MDS2 + or -. Differences between medians of PATGL with 95% confidence intervals (CIs) for FAST4 and/or MDS2 were estimated from median regression models that included FAST4 and MDS2 for each setting, and setting for pooled analyses.

Results: Among 393 RA and 175 SpA patients, 23.0%-32.7% were FAST4+ and 29.4%-36.7% MDS2+, with 41.1% positive for either FAST4 or MDS2 (data not shown). PATGL medians were 4.8-5.0 in all RA and 3.0-6.0 in SpA, 2.0-3.0 in FAST4-/MDS2-, 5.5-6.0 in FAST4-/MDS2+, 7.0-7.5 in FAST4+/MDS2-, and 7.0-8.0

Table 1. Median scores and interquartile ranges for PATGL according to positive or negative FAST4 and/or MDS2

Primary ICD10 diagnosis	Total	FAST4 NEG MDS2 NEG	FAST4 NEG MDS2 POS	FAST4 POS MDS2 NEG	FAST4 POS MDS2 POS	Adjusted median difference (95% CI) (FAST4 POS – FAST4 NEG)	Adjusted median difference (95% CI) (MDS2 POS – MDS2 NEG)
Three sites pooled	n=518	n=305 (58.9%)	n=71 (13.7%)	n=50 (9.7%)	n=92 (17.8%)		
RA	355	3.0 (1.0, 5.0)	5.5 (3.6, 6.5)	7.5 (6.5, 8.5)	8.0 (7.0, 9.0)	3.5 (2.8, 4.2)	2.0 (1.4, 2.6)
SpA	163	2.5 (1.0, 5.0)	6.0 (4.0, 6.5)	7.3 (6.8, 8.5)	8.0 (6.5, 10.0)	3.0 (2.1, 3.9)	2.5 (1.5, 3.5)
Australia	n=257	n=155 (60.3%)	n=35 (13.6%)	n=22 (8.6%)	n=45 (17.5%)		
RA	182	3.0 (1.0, 5.0)	5.5 (4.5, 6.5)	7.5 (7.0, 8.0)	8.0 (7.0, 9.0)	4.0 (3.0, 5.0)	1.5 (0.5, 2.5)
SpA	75	2.5 (1.0, 5.0)	4.5 (2.0, 6.8)	9.0 (7.0, 9.5)	8.0 (7.0, 8.5)	4.0 (2.2, 5.8)	1.0 (-0.8, 2.8)
Spain	n=169	n=90 (53.3%)	n=27 (16.0%)	n=18 (10.7%)	n=34 (20.1%)		
RA	101	3.0 (1.0, 4.5)	5.5 (3.6, 6.8)	6.0 (5.5, 7.0)	8.5 (8.0, 8.5)	3.0 (2.1, 3.9)	2.5 (1.7, 3.3)
SpA	68	3.0 (0.8, 5.0)	6.5 (6.0, 7.0)	7.3 (6.5, 8.0)	7.5 (6.5, 10.0)	3.0 (1.1, 4.9)	2.5 (0.9, 4.1)
USA	n=92	n=60 (65.2%)	n=9 (9.8%)	n=10 (10.9%)	n=13 (14.1%)		
RA	72	3.0 (1.0, 6.0)	6.0 (3.5, 7.0)	8.5 (8.0, 9.5)	7.0 (7.0, 9.0)	5.0 (2.7, 7.3)	1.0 (-1.3, 3.3)
SpA	20	2.0 (1.0, 4.5)	2.0 (1.0, 3.0)	7.0 (7.0, 7.0)*	8.5 (5.5, 10.0)	5.0 (0.5,10.5)	0 (-3.3, 3.3)*

NEG = negative, POS = positive, NA=Not available (No patients or the adjusted median differences cannot be estimated due to the small number of patients), *=Only one patient in category.

in FAST4+/MDS2+ patients, similar in RA and SpA at 3 settings in 3 continents (Table 1). Adjusted median differences were 3.0–3.5 for FAST4 + vs - (twice the level for FAST4 -, MDS2 -) and 2.0–2.5 for MDS2 + vs - groups (Table 1).

Conclusion: Median 0-10 PATGL was 2-3-fold higher in 41.1% of RA or SpA patients with positive MDHAQ FM and/or DEP screening indices vs 59% with 2 negative indices. Differences were greater according to FM than Dep. MDHAQ may clarify interpretation of PATGL and indices, including in treat–to–target, using a single, brief, feasible questionnaire in research and busy clinical settings.

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AB1478 RELIABILITY AND CONTENT VALIDITY OF THE PORTUGUESE VERSION OF THE COMMISSIONING FOR QUALITY IN RHEUMATOID ARTHRITIS PATIENT-REPORTED EXPERIENCE MEASURE (CQRA-PREM): PRELIMINARY RESULTS

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Background: The CQRA-PREM has been developed in the United Kingdom to evaluate the perspective of patients with rheumatoid arthritis (RA) about the care provided in rheumatology units of the National Health Service (1). This PREM might also be feasible to be used in Portugal, yet an adaptation and validation process is needed.

Objectives: We aimed to translate and cross-cultural adapt CQRA-PREM to Portuguese and evaluate the reliability and content validity of this version.

Methods: A study combining qualitative and quantitative approaches was conducted with patients with RA from a single rheumatology center. The translation and cultural adaptation of Portuguese CQRA-PREM included initial translation and cultural adaptation by 2 native Portuguese researchers, evaluation of this initial translation by a panel of 5 experts during an online meeting and back translation by 1 bilingual researcher. Authors of the original version approved this initial translation. CQRA-PREM includes 7 domains for patient-centered care: Needs and preferences (5 items); Coordination of care and communication (4 items); Information, education, and self-care (4 items); Daily living and physical comfort (2 items); Emotional support (2 items); Family and friends (1 item); Access to care (5 items) and 1 question for the overall experience with the care provided. Answers are given on a 5-point Likert scale (strongly disagree-1 to strongly agree-5). A total of 21 patients were invited to participate in online focus groups and 14 accepted. Patients were then asked to fill in a consent form and the preliminary version of the CQRA-PREM. The focus groups were transcribed and analyzed using thematic analysis. Questionnaire responses were analyzed with descriptive statistics and reliability (internal consistency) with the Cronbach´s alpha (α).

Results: A total of 12 patients (53±9y; 92% female) with a mean disease duration of 14±9 years participated in 2 focus groups (duration 95±7min). The focus groups revealed that patients considered CQRA-PREM "simple" and "objective" and that all questions were easy to understand. Nevertheless, patients suggested the addition of synonyms for certain terms and of daily living examples to clarify some items. The "Needs and preferences" and "Access to care" were the domains with better experience (Table 1). The Cronbach's alpha was 0.94 for the total questionnaire and between 0.71 and 0.91 for the domains.

Table 1. Median's responses and quartile (Q) for each domain (1-Strongly disagree; 2-Disagree; 3-Neither agree nor disagree; 4-Agree; 5- Strongly agree).

CQRA-PREM domains	Median (Q1-Q3)
1.Needs and preferences	4.5(4.25-4.5)
2.Coordination of care and communication	4(3.25-4.5)
3.Information, Education and Self-care	3(2-4)
4.Daily living and physical comfort	3.25
5.Emotional support	3.25
6.Family and friends	4(3-4)
7.Access to care	4.5(2.5-5)

Conclusion: Our findings suggest that both content validity and internal consistency of the Portuguese version of CQRA-PREM are acceptable. In future, a field-testing study to assess other psychometric properties (e.g., test-reliability and validity) should be conducted. We believe this PREM will contribute to optimize patient-centered care in Portugal.

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AB1479 VALIDATION OF RUSSIAN VERSION PSAID-12: ASSESSMENT OF THE RELIABILITY, CONSTRUCTIVE AND CONVERGENT VALIDITY OF THE QUESTIONNAIRE

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease of widely varying presentation, which determines functional and psychological impairment, with a high negative impact on patients' quality of life. Therefore, knowing the patient's perception of their health status is of fundamental importance for understanding the real impact of PsA. In recent years, a PsAID (Psoriatic Arthritis Impact of Disease) questionnaire has been developed for PsA EULAR, consisting of 9 or 12 questions related to the severity of pain, anxiety, fatigue, disability, sleep disorders, and social activity.

Objectives: To study, in a real-life setting, the construct and convergent validity, the reliability, and the interpretability of the Russian version PsAID-12 in patients with PsA.

Methods: 187 (M/F=97 (50.2%)/90(48.8%) PsA pts fulfilling the CASPAR criteria were included. Mean age 45.6±11.7 years (yrs), DAPSA 21.05±21.03, median (Me) PsA duration 88 [16;421] mo. All pts underwent standard clinical examinations and PROs (EQ-5D, PsAID12). Reliability was assessed by Cronbach's alpha coefficient and by the intraclass correlation coefficient (ICC) for each of the 12 scales. The construct validity was evaluated by exploratory factorial analysis and also by Spearman correlation with EQ-5D and measures of disease activity evaluation.

Results: The reliability of ICC (alpha-Cronbach = 0.8-0.9) and test-retest (ICC 95%CI 0.85-0.96) were good. Construct validity: Factor analysis revealed a 2-factor result defined as the PsAID-12: Phisical health score and Emotional health score. A strong correlation was also found for each of the 12 scales with the questionnaire EQ-5D was strong correlation (r= -0.52 to -0.78, p<0.001) In determining convergent validity, significant correlations were found between the PsAID-12 and TJC 68, SJC 66, DAPSA, VAS global assessments, VAS global pain, BASDAI. The high correlation was found between the BASDAI and the scale "Functional capacity" (r=0.8, p<0.001), as well as sufficiently high correlation coefficients with parameters were noted with the scales "Pain", "Fatigue", "Work and/or leisure activities", "Discomfort" and "Coping". The lowest was observed with scales "Skin problems" and "Depression" (Table 1).

Table 1. Convergent validity PsAID-12 with clinical parameters (r)

Scales	TJC 68	SJC 66	DAPSA	VAS global assess-ments	VAS global pain	BASDAI
Pain	**0,6**	**0,68**	**0,71**	**0,72**	**0,75**	**0,78**
Fatigue	**0,59**	**0,62**	**0,68**	**0,71**	**0,68**	**0,75**
Skin problems	0,35	0,36	0,41	0,47	0,37	0,46
Work and/or leisure activities	**0,57**	**0,62**	**0,68**	**0,75**	**0,71**	**0,67**
Functional capacity	**0,61**	**0,64**	**0,72**	**0,79**	**0,71**	**0,80**
Discomfort	**0,61**	**0,65**	**0,71**	**0,77**	**0,70**	**0,76**
Sleep disturbance	0,44	**0,50**	**0,54**	**0,55**	**0,60**	**0,61**
Coping	**0,59**	**0,63**	**0,67**	**0,66**	**0,65**	**0,76**
Anxiety, fear and uncertainty	0,46	0,48	**0,52**	**0,52**	**0,51**	**0,64**
Embarrasment	0,47	0,49	**0,51**	0,48	0,41	**0,52**
Social participant	**0,54**	**0,57**	**0,62**	**0,64**	**0,62**	**0,66**
Depression	0,43	0,43	0,49	**0,57**	**0,54**	0,47

Conclusion: The russian version of PsAID-12 has been shown to be a reliable and valid measure of the impact of the disease in patients with psoriatic arthritis.

Disclosure of Interests: None declared

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AB1480 ASSESSMENT OF THE SENSITIVITY OF THE RUSSIAN VERSION OF PSAID-12 QUESTIONNAIRE

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Table 1. Assessment the sensitivity of the russian version of PsAID-12

PsAID-12	I		p	II		p	III		p
	MDA			REM/LDA			No effect on therapy		
	(n=50)			(n=43)			(n=79)		
	Baseline	12 mo		Baseline	12 mo		Baseline	12 mo	
Pain	10,0±8,81	4,47±3,90	**0,0001**	12,4±10,7	5,86±6,8	**0,0001**	10,5±4,41	9,77±6,49	0,37
Fatigue	6,43±5,2	3,64±3,09	**0,003**	5,8±4,5	2,69±3,3	**0,002**	8,93±5,62	7,77±4,64	0,15
Skin problems	5,64±5,9	3,09±3,37	**0,003**	8,3±7,2	3,62±3,4	**0,0008**	7,51±5,40	6,5±5,19	0,23
Work and/or leisure activities	5,05±5,6	2,39±3,73	**0,007**	4,0±3,08	1,74±1,4	**0,0002**	7,51±5,40	5,92±4,6	0,056
Functional capacity	6,19±6,17	2,15±3,12	**0,00009**	7,06±6,02	3,39±3,11	**0,00008**	8,30±5,63	7,68±4,58	0,44
Discomfort	5,60±5,55	2,35±3,59	**0,0007**	3,48±4,0	2,04±2,01	**0,0006**	9,16±5,17	6,3±4,61	**0,0003**
Sleep disturbance	5,56±6,04	1,84±3,81	**0,0005**	7,93±7,3	3,04±2,95	**0,0002**	8,63±5,26	4,31±3,66	**0,0001**
Coping	2,39±2,75	0,84±1,25	**0,0002**	3,81±4,1	1,53±2,2	**0,001**	6,36±5,45	2,7±2,12	**0,0001**
Anxiety, fear and uncertainty	2,37±2,69	1,13±1,76	**0,014**	8,04±6,96	3,2±3,3	**0,0001**	3,88±2,75	2,7±2,18	**0,003**
Embarrasment	1,21±1,71	0,86±1,78	**0,01**	3,9±3,26	1,2±1,83	**0,0006**	4,21±3,27	2,7±2,84	**0,002**
Social participant	2,31±3,10	0,58±1,52	**0,0003**	9,1±8,38	2,79±2,9	**0,0008**	3,56±3,08	2,49±2,36	**0,01**
Depression	1,43±2,06	0,47±1,13s	**0,009**	4,41±4,1	1,46±1,6	**0,002**	3,68±2,90	2,1±2,23	**0,0001**

Background: The Psoriatic Arthritis Impact of Disease 12-item questionnaire (PsAID-12) has been developed to measure impact of Psoriatic Arthritis (PsA) for purposes of monitoring and clinical management.
Objectives: Assessment the sensitivity of the russian version of PsAID-12 against the background of ongoing therapy at baseline and after 12 month (mo).
Methods: 172 (M/F=90 (52.3%)/ 82(47.7%) PsA pts fulfilling the CASPAR criteria were included. Mean age 45.1±11.8 years (yrs), DAPSA 28±22.2 median (Me). All pts underwent standard clinical examinations and PROs (EQ-5D, VAS global assessments, VAS global pain, BASDAI, PsAID-12). All pts at the time of inclusion in the study and 12mo received DMARDs: NSAIDs-158 (91.8%), methotrexate -134 (77.9%), leflunomide- 11 (6.3%), sulfasalazine - 12 (6.9%), TNFα inhibitors - 72 (44.04%), sekukinumab -14 (8.1%), ustekinumab -3 (1.74%), ixekizumab - 1 (0.58%), apremilast- 16 (9.3%), tofacitinib - 51 (29.1%). To determine the sensitivity of PsAID-12, its changes were analyzed depending on: I group of patients in whom MDA was achieved - 50, II - 43 REM / LDA patients, III - 79 patients with no effect on therapy.
Results: By 12 mo of therapy significant improvement in all PsA clinical examination (DAPSA - 28±22.2 vs 15±14.1, TJC 68 – 10.5±10.1 vs 6.68±5.77, SJC 66 – 8.31±7.4 vs 4.62±3.17, CRP – 13.6±8.06 vs 13.6±8.06) and PROs (BASDAI – 3.93±2.56 vs 2.49±1.93, VAS global pain – 40.1±25.1 vs 24.7±20.0, VAS global assesments – 43.4±27.1 vs 27.6±19.5, EQ-5D – 0.68±0.21 vs 0.72±0.18) were observed (p<0.0001 for all). The sensitivity assessment of the PsAID-12 showed that in groups I and II there were statistically significant differences on all scales of the questionnaires, in group III with no effect on therapy, there were no significant improvements on the scales “Pain” (p = 0.37), “Fatigue” (p=0.15), “Skin problems” (p=0.23), “ Work and/or leisure activities “ (p=0.056), “ Functional capacity “ (p=0.44) (Table 1).
Conclusion: The russian version of the PsAID-12 questionnaire reflects the dynamics depending on the activity of the disease during treatment, which proves its good sensitivity.
Disclosure of Interests: None declared

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AB1481 REDOX HOMEOSTASIS AND ANTIOXIDANT RESPONSE DEFENSE IN SKELETAL MUSCLE PERFORMANCE IN THE ELDERLY

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Background: Aging is accompanied by a progressive decline in physical activity due to a loss of skeletal muscle mass and strength considered as a geriatric characteristic defined as sarcopenia. This latter may be associated with joint damage, all of which may predispose older people to the risk of falls. Few evidences suggest that oxidative stress plays a key role in the pathophysiology of sarcopenia.
Objectives: The aim of this study was to clarify the relationship between sarcopenia and oxidative stress. To this end, measurements of antioxidant enzyme activities as well as levels of lipid oxidation products were performed on plasma and/or red blood cells.
Methods: All the participants (age ≥ 65) were classified into two groups according to the SARC-F score: non-sarcopenic patients (SARC-F <4; n=50) and sarcopenic (SARC-F ≥4; n=50). Redox biomarkers: antioxidant enzymes (erythrocyte superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activities) as well as, lipid peroxidation products (plasma malondialdehyde (MDA), and conjugated dienes (CD) levels), were measured using spectrophotometric methods.
Results: SOD levels were significantly higher in the group of sarcopenic patients than in non- sarcopenic subjects (3.20 ± 1.00 U/mg Hb vs. 2.41 ± 0.88 U/mg Hb, respectively, p= 0.007). Similarly, catalase levels were significantly higher in sarcopenic patients compared with non sarcopenicsubjects (0.13 ± 0.04 U/mg Hb vs. 0.11 ± 0.03 U/mg Hb, respectively, p= 0.008). However, no significant differences in GPx levels were detected (p= 0.254). An accumulation of lipid oxidation biomarkers MDA (17.14 ± 3.13 nmol/mg protein vs. 10.39 ± 2.60 nmol/mg protein) and CD (0.24 ± 0.09 nmol/mg protein vs. 0.17 ± 0.06 nmol/mg protein) was observed in the plasma of sarcopenic patients compared with non- sarcopenic subjects(p< 0. 001 and p= 0.003, respectively).
Conclusion: Sarcopenia is associated with oxidative stress as shown by increased levels of antioxidant enzyme activities (SOD, GPx) and lipid peroxidation products (MDA, CD).
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AB1482 PROGNOSTIC FACTORS FOR TUBERCULOUS SPONDYLODISCITIS

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Background: Tuberculous spondylodiscitis (SPDT) or Pott’s disease is an infectious involvement of the disc-vertebrate couple, caused by the tubercular bacillus (Mycobacterium tuberculosis). It accounts for 46% to 64% of infectious spondylodiscitis and is the most common form of vertebral tuberculosis. Pott’s disease still poses a public health problem in Tunisia due to the endemicity of tuberculosis and the increase in extra-pulmonary forms.
Objectives: Our aim was to study factors impacting SPDT outcome.
Methods: We conduct a retrospective and descriptive study in a single rheumatology department. Data were collected from observations of patients hospitalized in the past 20 years (2000-2020) who have been diagnosed with SPDT. The diagnosis was based either on a range of highly evocative clinical, biological and radiological arguments or on the disco-vertebral biopsy puncture. The study included correlations of the promoting factors of SPDT (tuberculosis infection, history of tuberculosis, diabetes, corticosteroids and trauma), epidemiological, clinical, biological, radiological and therapeutic data with good clinical outcome in the fourth week of the anti-tuberculosis drugs treatment.
Results: Fifty-two cases of SPDT were collected (37F/15M). The mean age was 55.21±17.79 years [19-91]. Thirty-three patients (69.2%) were aged under 65 years versus 16 elderly patients (30.8%), with female predominance in both

groups (69.4% and 75% respectively, p = 0.57). The diagnosis of SPDT was based either on a range of highly evocative clinical, biological and radiological arguments (71.2%) or on the disco-vertebral biopsy puncture (28.8%). Among the clinical arguments suggestive of tuberculous SPD were: progressive onset of symptoms in 47 patients (90.4%), segmental spinal stiffness in 37 patients (71.2%), spinal pain with general signs of tuberculosis such as impaired general condition, fever, night sweats and weight loss in 32 patients (61.5%). Lumbar spine involvement was the most common in tuberculous SPD (57.7%). A biological inflammatory syndrome has been objectified in 38 patients (73.1%). Imaging was contibutive to positive diagnosis using standard X-rays, computed tomography and magnetic resonance imaging. Disc pinch, erosion of vertebral plateaus and vertebral collapse were the major signs. The treatment was based on anti-tuberculosis drugs for at least nine months. Only four factors had an unfavourable predictive value ($p \leq 0.05$): Normochromic normocytic anemia observed in 53.8% of our patients (p = 0.018; Odds Ratio = 6.66), initial lymphocytosis (p = 0.048), fever in 36.5% of our patients (p = 0.01; Odds Ratio = 9.6) and standard X-ray vertebral compression in 67.3% of our cases (p = 0.001; Odds Ratio = 13).
Conclusion: Tuberculous spondylodiscitis is a frequent condition that needs to be diagnosed and treated rapidly. Poor prognosis factors have been identified to provide insight into disease progression.
Disclosure of Interests: None declared
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AB1483 ASSOCIATION BETWEEN THE DECREASE OF CAPILLAR DENSITY IN THE CAPILLAROSCOPY AND THE DIAGNOSIS OF SYSTEMIC SCLEROSIS PATIENTS WITH RAYNAUD

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Background: Videocapillaroscopy (VC) has become a widely used tool due to its low cost, accessibility and no invasive nature. PANLAR study group proposes a semi-quantitative method to inform it, which includes four grades to categorize capillary density (methods). Previous studies found that capillary density is associated with microvascular damage, predicts disease progression and organ affection in systemic sclerosis (SSc) and can be useful as a follow-up tool (1-5).
Objectives: Describe the associations between the different patterns and grades of capillary density loss and the SSc diagnosis.
Methods: A cross sectional study was designed using clinical records, including outpatients attending to a VC consult between the March and October 2021. Descriptive data regarding patients demographics, presence of rheumatologic diagnosis and treatment was registered. The VC was performed by an experienced rheumatologist (RTR) (DinoLite), with a 200x amplification. Capillary density loss (CDL) was scored based on PANLAR recommendations: Grade 0 (no loss), Grade I (7-9 capillaries / lineal mm), Grade II (4-6 capillaries / lineal mm), Grade III (< 4 capillaries / lineal mm). Descriptive statistics were performed and data was compared using Student´s T test, Mann-Whitney, Chi2 or exact Fisher´s test depending on the type of data and its distribution. A p value < 0.05 was considered as significative.
Results: One hundred and one patients were included, 91 (91%) female, mean age 43 years (SD 13.9), 72 (71,3%) had raynaud phenomenon (RP), with a mean evolution of 1 year (IQR 0.5-3.5). Rheumatologic diagnosis was: 19 rheumatoid arthritis (RA), 16 SSc, 11 systemic lupus erythematosus (SLE) and 27 no diagnosis, including 2 with digital necrosis and one with endocarditis suspicion. VC was normal in 40 (39.6%) patients, 34 (33.7% had non-specific findings, and 26 (26%) SD pattern. In the latter, the pattern was 2 were early pattern, 11 active and 13 late. SD pattern was associated with SSc diagnosis, and the use RP medication (both p<0,001). Three patients with inflammatory idiopathic myopathy (IIM), 2 SLE, 2 primary sjögren syndrome (pSS) and 2 without diagnosis had also this pattern. LCD was found in 27% of the patients, and Grade III was associated with SSc diagnosis being 14 times more frequent compared with non-SSc. [Table 1]

Table 1. Capillary density loss presence and grades in SSc vs non-SSc

Variable	SSc	No-SSc	OR (95%CI)	p value
CDL – n (%)	12 (75)	15 (17.6)	14 (3.9-49.4)	0.0001
Grade I – n (%)	7 (8.2)	4 (25)	3.8 (0.9-14.6)	0.07
Grade II – n (%)	3 (18.8)	6 (7.1)	3 (0.6-13.8)	0.1
Grade III – n (%)	4 (25)	2 (2.4)	13.8 (2.2-83.8)	0.005

Ssc (systemic sclerosis), CDL (capillary density loss),

Conclusion: CDL was present in almost 1/3 of non selected patients attending to a VC study, and was strongly associated with SSc diagnosis. Future studies including this outcome can bring new data regarding microvascular damage and its implications.

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AB1484 THE SIGNIFICANCE OF ANTI-DFS70 ANTIBODIES IN HEALTHY POPULATION AS A MARKER OF EXCLUSION OF SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES

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Background: The prevalence of anti-DFS70 antibodies in healthy volunteers (HV) by various methods ranges from 0 to 22% [1]. This pattern, which is rare in patients with systemic autoimmune rheumatic diseases (SARDs), has been described as the second most common in serum HV [2].
Objectives: To study the frequency of detection of anti-DFS70 in HV, patients (pts) with undifferentiated SARDs and systemic lupus erythematosus (SLE).
Methods: A total of 45 HV, 17 undifferentiated SARDs pts and 81 SLE pts were included in the study. Groups were comparable in gender and age among themselves. The diagnosis of SLE was performed according to the ACR/EULAR 2019 classification criteria. Serum samples were tested for anti-DFS70 (ANA HEp-2 ELITE/DFS70 knock-out IFA, "Trinity Biotech", Ireland). Fluorescence titers ≥1:160 were considered as positive for ANA HEp-2 cell patterns.
Results: Positive results of the ANA study were found in 81 (100.0%) pts with SLE, in 16 (94.0%) pts with undifferentiated SARDs and 7 (15.6%) HV (Table 1). Abs to DFS70 were isolated, detected in 4 (57.1%) HV, in 9 (56.2%) undifferentiated SARDs, but were not detected in SLE pts. Classical HEp-2 cell patterns (homogeneous AC-1, speckled AC-4.5, homogeneous+speckled AC-1,4,5, cytoplasmic AC-19,20,21) without anti-DFS70 were deficient in 3 (42.9%) HV, in 7 (43.8%) patients with undifferentiated SARDs and in 81 (100%) patients with SLE (Table 2). Therefore, monospecific anti-DFS70 were detected in the HV and undifferentiated SARDs groups, but were not detected in patients with a reliable diagnosis of SLE.

Table 1.
ANA-HEp-2/DFS70 KO detection rate

Groups of pts	n	ANA-HEp-2/DFS70 KO ≥ 1:160, n (%)
HV	45	7 (15.6)
SLE	81	81 (100.0)
Undifferentiated SARDs	17	16 (94.0)

Table 2.
Detection rate of patterns in ANA-HEp-2-positive pts

HEp-2 cell patterns	HV, n=7	SLE, n=81	Undifferentiated SARDs, n=16
Nuclear dense fine speckled - DFS70 (AC-2), n (%)	4 (57.1)	0 (0.0)	9 (56.2)
Nuclear homogeneous (AC-1), n (%)	0 (0.0)	26 (32.1)	0 (0.0)
Speckled (AC-4,5), n (%)	1 (14.3)	14 (17.3)	1 (6.2)
Nuclear homogeneous+speckled (AC-1,4,5), n (%)	2 (28.6)	35 (43.2)	3 (18.8)
Cytoplasmic (AC-19,20,21), n (%)	0 (0.0)	6 (7.4)	3 (18.8)

Conclusion: Monospecific anti-DFS70 can potentially be considered as a possible marker for the exclusion of SARDs and a sign of benign autoimmunity.

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AB1485 PATIENT-REPORTED OUTCOMES AND BIOMARKERS ASSOCIATED WITH THE CUTANEOUS DERMATOMYOSITIS AREA AND SEVERITY ACTIVITY (CDASI-A) SCORE IN A PHASE 2 CLINICAL TRIAL IN DERMATOMYOSITIS

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Background: Retrospective reviews of clinical databases from two sites have identified strong relationships between patient-reported outcomes and skin activity in dermatomyositis (DM), as measured by CDASI-A.[1,2] No studies validate these associations in a controlled setting. Additionally, the relationship between the PROMIS-29 Short Form and skin activity in DM has not been assessed. Previous investigations have demonstrated a correlation between IL-31 and itch in DM.[3] IFN-β and IFN-γ are known type I and II interferons, which are critical drivers of DM pathogenesis.[4]

Objectives: To assess correlations between CDASI-A, quality of life (QoL), and biomarkers of disease activity in a double-blind, randomized, placebo-controlled clinical trial.

Methods: Data were retrospectively collected from five visits of a Phase 2 trial evaluating Lenabasum, a cannabinoid receptor type 2 agonist. Quality of life assessments extracted from the trial included Patient Global Assessment (PtGA) scores, PROMIS domains, and Skindex domains. Skindex question 10, regarding itch, was included in the analysis as a separate domain. Physician Global Assessment scores were also evaluated. Additionally, biomarkers derived from skin samples via IHC/PCR collected at visits 1 and 6 were assessed for predictors of CDASI-A response and association with disease activity. Analysis used linear mixed effect models to account for within subject-variability and repeated measures, where applicable. Analysis was performed without regard to treatment arm, as our goal was to correlate CDASI, QoL, and biomarkers among all subjects.

Results: Data from 22 subjects with DM and a combined total of 110 visits were included. Biopsies were collected from 12 subjects. Improvement in CDASI-A significantly correlated with Skindex-S, Skindex-E, Skindex-F, Skindex-Itch, PtGA global skin, PtGA global skin, PtGA global skin, and PtGA global skin, with $p < 0.001$. Improvement in PROMIS social role ($p = 0.046$) correlated with improvement in CDASI-A. Worsening of PROMIS fatigue ($p = 0.019$) and pain ($p < 0.001$) correlated with improvement in CDASI-A. Decreases in PGA overall disease, PGA skin activity, and PGA global skin all correlated with improvement of CDASI-A ($p < 0.001$). Change in IL-31 protein area positively correlated with change in disease activity ($p = 0.047$). A positive relationship between changes in IFN-β and IFN-γ protein area and disease activity trended towards significance.

Conclusion: In accordance with previous investigations from our group, well-established measures of QoL correlated significantly with CDASI-A. These findings support that CDASI-A reflects both clinical and patient-reported aspects of skin disease and is an appropriate outcome in DM clinical trials. Additionally, Skindex and PtGA scores may better relate to skin activity as measured by the CDASI compared to PROMIS domains. IL-31, a cytokine previously associated with itch in DM,[3] correlated significantly with CDASI-A in our study. Trends for IFN-β and IFN-γ reduction with disease improvement support their role in the pathogenesis of DM. This study helps define patient-reported outcomes and biomarkers that may be informative in DM trials.

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AB1486 ASSESSMENT OF GLUCOCORTICOID-RELATED ADVERSE EVENTS BY THE GLUCOCORTICOID TOXICITY INDEX (GTI) IN RHEUMATIC PATIENTS

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Background: Glucocorticoids (GCs) remain the mainstay treatment for several autoimmune and inflammatory diseases however, its long-term or high-dose usage also has many potential side effects. The glucocorticoid toxicity index (GTI) is a novel global monitoring tool (1) developed to systematically assess glucocorticoid-associated morbidity.

Objectives: To evaluate GC toxicity by using GTI in patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and vasculitis receiving glucocorticoids.

Methods: This descriptive, cross-sectional study included patients who were admitted to the rheumatology clinic between January 2021 and December 2021, were diagnosed with RA, SLE or vasculitis and treated with GCs. A single measurement of GC toxicity was performed using the GTI for each patient. Baseline GTI consists of twelve domains that related to commonly recognized adverse events that result of cumulative GCs exposure: body mass index (BMI), glucose metabolism, blood pressure, lipids, GC-induced myopathy, bone mineral density, skin toxicity, neuropsychiatric effects, infection, ocular, gastrointestinal and endocrine toxicity. The total GTI score ranges from 0 to 538 depending on the increase in toxicity burden.

Results: The study included 85 patients (55.3% male) with a mean age of 47.5 (±16.0) years (Table 1). Twenty (23.5%) patients had BMI values ≥30 kg/m2 and 63% of the patients were either hypertensive or receiving medications for hypertension. While HbA1c was ≥5.7% in 30 (35.3%) patients, 17 (20.0%) patients had glycated hemoglobin (HbA1c) value of ≥5.7% despite antidiabetic medication. Low density lipoprotein cholesterol (LDL-C) value of 33 (39%) patients was not on target. The median (IQR) GTI score of the study patients was 73 (81.5). Only 10 patients had a score of 0 in the GTI assessment. GTI scores were not correlated with the cumulative steroid doses ($r=0.145$, $p=0.198$) however, age was strongly associated with GTI scores ($r=0.605$, $p<0.001$).

Table 1. Demographics, disease characteristics, and glucocorticoid toxicities of the patients

Characteristic[¶]	All patients (n=85)		
	RA (n=21)	SLE (n=14)	Vasculitis* (n=50)
Age (years), mean (±SD)	47.3 (±17.2)	36.4 (±11.0)	50.6 (±15.5)
Duration of disease (months)	12 (12.5)	16 (17.8)	14 (13.3)
Damage and activity indices	DAS-28=2.66 (2.1) HAQ=0.07 (0.4)	SLEDAI=4.0 (6.5) SLICC=0 (1.5)	BVAS**=0 (1.0) VDI=1.0 (1.0)
Cumulative methylprednisolone dose (mg)	1458 (1496.9)	4646 (9053.5)	5604 (5281.5)
GTI toxicity domain, n (%)	9 (42.8)	6 (42.8)	24 (48.0)
✓ BMI ≥27 kg/m^2	8 (38.1)	6 (42.9)	33 (68.8)
✓ HbA1c ≥5.7%	7 (33.3)	4 (28.6)	26 (53.0)
✓ Blood pressure >120/85	6 (28.5)	2 (14.2)	25 (51.0)
✓ LDL-C >target	4 (20.0)	0	11 (24.5)
✓Osteoporosis	2 (10.0)	2 (14.3)	13 (26.5)
✓ Skin toxicity	2 (10.0)	3 (21.4)	8 (16.3)
✓ Neuropsychiatric toxicity	2 (10.0)	0	6 (12.2)
✓ Ocular toxicity	2 (10.0)	0	5 (10.0)
✓ Gastrointestinal toxicity			
GTI score	65 (104.5)	44 (48.0)	87 (76)

[¶] n (%), if otherwise specified; median (IQR) for numeric values other than ageGTI: Glucocorticoid toxicity index, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, BMI: Body mass index, HbA1c: Glycated hemoglobin, LDL-C: Low density lipoprotein cholesterol*Vasculitis patients include ANCA-associated vasculitis, Giant cell arteritis, Takayasu arteritis, Behcet's syndrome, Igg4-related disease, Polymyalgia rheumatica and Leukocytoplastic vasculitis patients.***BVAS value given only for ANCA-associated vasculitis (n=19)

Conclusion: Our study revealed the iceberg of glucocorticoid toxicities in patients with rheumatic disease. Usage of GTI would help management of these possible toxicities. Therefore, it is important to assess GC toxicity at regular intervals during ongoing treatment in order to detect potential differences in the GTI scores.

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AB1487

VALIDATION AND CULTURAL ADAPTATION OF THE QUALISEX QUESTIONNAIRE IN WOMEN WITH SJÖGREN'S SYNDROME IN ITALY

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Background: The quality of sexual life (QSL) is a complex and multimodal experience influenced by endogenous and external factors, including age, gender, and cultural environment. Rheumatic diseases, with their burden of pain, fatigue, organ damage, and disability, can severely impair sexual life and this is true also for Sjögren's Syndrome, where simple tools to assess the QSL in everyday clinical practice are needed.
Objectives: To translate ad adapt into Italian the Qualisex, a new brief questionnaire originally created for Rheumatoid Arthritis patients, for women with primary Sjögren's Syndrome (pSS) and evaluate the impact of the disease on their sexuality.
Methods: Consecutive sexually active pSS (according to ACR/EULAR 2016 criteria) patients aged >18 were asked to participate in this study approved by the local bioethics committee. With the permission of the developer, the French original version of the Qualisex questionnaire (consisting of 10 items, the higher the score, the greater the negative impact of the disease on the QSL) was translated and adapted into Italian according to current guidelines. In the absence of a gold standard assessment for sexuality in pSS, face and content validity was assessed cross-sectionally by correlations with other disease aspects such as anxiety and depression measured by Hospital Anxiety and Depression Scale (HADS), EULAR SS patient-reported index (ESSPRI), and quality of the relationship. As a measure of reliability, internal consistency was assessed through Cronbach's Alpha coefficient. A Cronbach's value >0.7 is generally regarded as satisfactory. The feasibility of the scale was indirectly assessed through missing data. To assess the factorial structure of the Italian version of the questionnaire an Exploratory Factor Analysis (EFA) was carried out. Moreover we also assessed the level of redundancy by means of intra-item correlation of the Qualisex questionnaire. ESSDAI (EULAR Sjögren's Syndrome Disease Activity Index), and SSDDI (Sjogren's Syndrome Disease Damage Index) were assessed as well. Analyses were carried out with IBM SPSS Statistics for Macintosh, version 22.0 (IBM Corp., Armonk, NY, USA).
Results: 40 sexually active women with pSS and a median age of 53 (IQR 45.25-57.25) were enrolled. The EFA showed that the model with a single factor appeared to be highly significant (Chi235= 2943.10; p<0.05); the average inter-item correlation was found to be 0.392 (Min -0.479; Max 0.834) which is an acceptable value as for redundancy. There were no missing answers. Cronbach's alpha coefficient resulted to be 0.86 which indicates an adequate internal consistency. The median Qualisex score was 4.65 (IQR 2.13–6.2). As far as correlations, age (Rho=0.39; p<0.05), menopause (Rho=0.41; p<0.05), relationship quality (Rho=0.55; p<0.05), anxiety (HADS-A; Rho=0.38; p<0.05), and depression (HADS-D; Rho=0.47; p<0.05) appeared to be positively correlated with Qualisex score. Also, a positive correlation with ESSPRI (Rho=0.43; p<0.05), and drug use (Rho=0.37; p<0.05) was demonstrated. On the contrary no significant correlation was found with education (Rho=-0.07; p=0.64), systemic disease activity (Rho=0.14; p=0.39), and damage (Rho=0.06; p=0,74).
Conclusion: The Italian version of the Qualisex questionnaire is a valid, reliable and useful tool to assess the quality of sexual life in pSS. QSL in pSS women has an inverse relationship with age, menopause, drug use, ESSPRI, mood disorders, and dissatisfaction with the partner, while, as previously reported, no correlation was found with disease activity, damage, and educational status. This further highlights the impact of subjective symptoms such as dryness, pain, fatigue, and the overall psychological well-being on patients' life. Thus, it is critical for the physician to consider patients' perspective.
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AB1488

GRAY INTENSITY RATIO INDICES AS A METHOD OF DISCRIMINATION BETWEEN CHANGES INDUCED BY SPORT AND BY SPONDYLOARTHRITIS IN LOAD-BEARING ENTHESES.

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Background: Computer analysis of radiological images has recently been introduced in the study of patients with musculoskeletal pathologies. In the field of ultrasound, baseline settings and differences between images obtained by different equipment pose a potential problem in the comparative study of patients. Our research group has shown that this type of ultrasound image analysis is sensitive to exercise-induced adaptive changes.
Objectives: The purpose of this study is to determine if the computer analysis of entheses ultrasound images can distinguish adaptive changes from those produced by spondyloarthritis.
Methods: A test validation study was carried out. Since the analysis of static ultrasound images strongly depends on the characteristics of the image and the ultrasound settings, three indices based on the findings in pathological territories and their counterpart in healthy entheses were defined. Gray Intensity Mean Index (iMIG): Mean gray intensity in the clinically affected enthesis/mean gray intensity in the same healthy enthesis. Gray intensity dispersion index (iDIG): Mean of the standard deviation of the gray intensity means in the clinically affected enthesis/mean of the standard deviation of the gray intensity means in the same healthy enthesis. Index of gray intensity modes (iMoG): Mean gray intensity modes in the affected enthesis/mean gray intensity in the same healthy enthesis. The same indices were used in the controls with the dominant side as the numerator and the non-dominant side as the denominator. All the studied entheses corresponded to the lower limb.
Results: Records of 49 patients (20 diagnosed with psoriatic arthritis, 19 with radiographic axial spondyloarthritis and 10 with non-radiographic axial spondyloarthritis) and 100 healthy controls were included. Of the 49 studies, 30 corresponded to the Achilles tendon, 10 to the distal patellar tendon and 9 to the proximal patellar tendon. In the patient group, iMIG was 0.917 SD 0.062, iDIG was 0.976 SD 0.042, and iMoIG was 0.962 SD 0.041. In the control group, iMIG 1 SD 0.020, iDIG was 1.001 SD 0.03, and iMoIG was 0.999 SD 0.03. The area under the curve (Figure 1) for the three indices was: iMIG 0.879 (95% CI 0.807 to 0.951), iDIG (95% CI 0.582 to 0.785), iMoIG 0.751 (95% CI 0.662 to 0.840). All areas demonstrated diagnostic validity with P<.0001. According to the matrix of coordinates of the receiver-operating-characteristic (ROC) curve, for an iMIG cut-off point less than or equal to 1.02, a sensitivity of 95.9% and a specificity of 71% would be achieved.

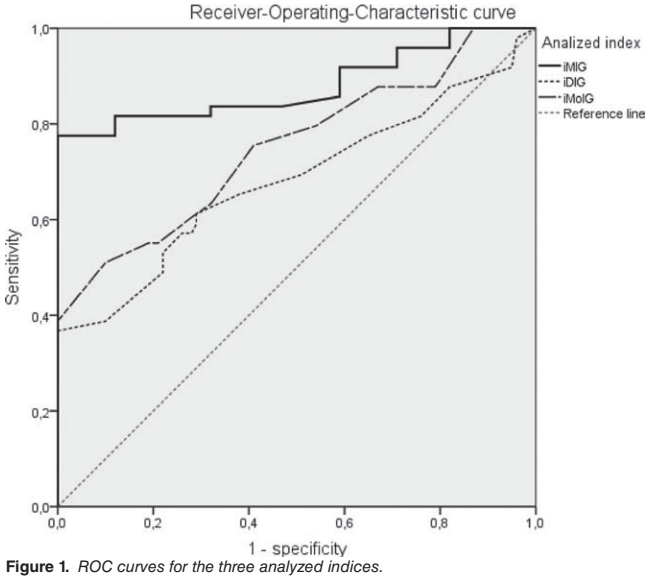

Figure 1. *ROC curves for the three analyzed indices.*

Conclusion: The indices that contrast the means, dispersion and mode of gray intensities are valid for discriminating between healthy subjects and patients with load-bearing enthesopathies related to spondyloarthritis. Of all of them, the iMIG seems the most reliable. A cut-off point of less than 1.02 is proposed to identify patients with inflammatory enthesopathies. In patients, the affected entheses have a lower mean gray than the healthy counterpart, so iMIG tends to be less than 1. In healthy subjects, the mean gray is slightly higher in the dominant enthesis, so iMIG tends to be greater than or equal to 1.
Disclosure of Interests: Marina Tortosa-Cabañas: None declared, Carlos Guillén-Astete Speakers bureau: Novartis, Janssen, Abbvie, Grunenthal, UCB and Gebro, Paid instructor for: Roche, Novartis, Janssen, Esteve and Menarini, Consultant of: Janssen, Novartis and Roche, Grant/research support from: Pfizer, Grunenthal, Gebro and Novartis, África Andreu-Suárez: None declared
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AB1489

VALIDATION OF QUANTITATIVE COMPUTER ANALYSIS OF ULTRASOUND IMAGES OF THE ACHILLES AND PATELLAR TENDONS IN HEALTHY SUBJECTS.

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Background: The ultrasound study of tendons is a component of the complementary evaluation of patients with different musculoskeletal pathologies, which include immune-mediated rheumatological diseases. Until now, the assessment

of the ultrasound status of the tendons largely depends on the subjectivity of the explorer, following specific guidelines such as the fibers structure, their global echogenicity and their thickness. This evaluation is of great interest for the diagnose, however its role for the follow-up is not so clear as the subjective evaluation may not perceive subtle changes. Computerized image analysis has recently been introduced to complement the echographic evaluation. Two of the most useful parameters in this analysis are the mean and mode of gray intensities. Both allow a global evaluation of the echostructure of an organ based on the distribution of shades of gray and the highest concentration of a particular shade, without evaluating the organization pattern of the image obtained.

Objectives: To determine if computer analysis of static images is valid and suitable for its use in the study of tendons.

Methods: The ultrasound images of healthy volunteers were analyzed. The analysed tendons were: the body of the patellar tendon in transverse approach and the longitudinal section of the Achilles tendon, both of them from the dominant side. Image processing was performed using the ImageJ 1.53e program (Wayne Rasband & contributors – NIH, USA). A gray spectrum analysis (0-255) was performed with the calculation of the mean, standard deviation (SD), range, median and mode. Two measurements of different cuts of the patellar tendon (at the point of emergence of the tibial plateau and 20 mm proximal to it) and three longitudinal cuts of 20 mm of the Achilles tendon (paramedial, central and paralateral) were used for the validation process of the analysis carried out by the software.

Results: Images from 44 healthy volunteers were analyzed: 20 men and 24 women. 44 Achilles tendon image trios and 44 patellar tendon image pairs were analyzed and their corresponding means and modes were compared as related variables. In the study of the Achilles tendon, according to the Shapiro-Wilk test, the distribution of the gray distribution means had a non-normal distribution while the modes had a normal distribution. The means ± standard deviation of gray intensity was: 80.15 ± 26.04, 80.05 ± 25.57 and 79.91 ± 25.83 for the medial, central and lateral slices, respectively (Friedman, P=.454; Bonferroni not applicable). The means of the modes of gray intensities for the same measures were 67.35 ± 31.60, 67.76 ± 32.18 and 68 ± 32.18, respectively (ANOVA paired data, P=.259; Bonferroni not applicable). In the patellar tendon study, all measurement distributions were non-normal. Mean gray intensity at the point of tendon emergence (P) was 81.35 ± 29.63 and at 20mm proximal to this point it was 80.97 ± 29.08 (Wilcoxon, P=.327). The means of the modes at the same locations were 82.71 ± 28.75 and at 20mm proximal to this point it was 64.44 ± 33.31 (Wilcoxon, P=.079).

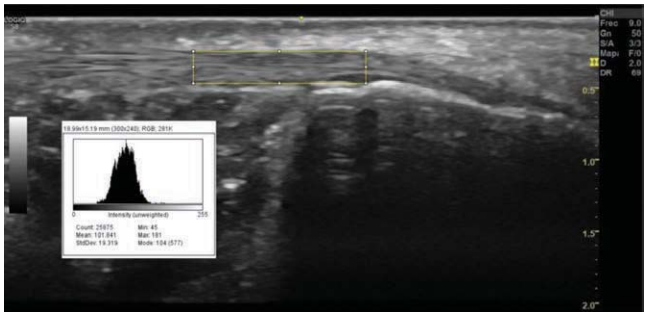

Figure 1. *Image analysis of an Achilles tendon in the central longitudinal plane.*

Conclusion: The quantitative analysis of static images of healthy tendons shows no differences between the same structures in longitudinal or transverse planes. Based on this validation test, the demonstration of sensitivity to change caused by any stimulus (sport, noxae or treatments) could allow its use as a complementary instrument for the assessment of tendinous structures over time.

Disclosure of Interests: África Andreu-Suárez: None declared, Carlos Guillén-Astete Speakers bureau: Novartis, Janssen, Abbvie, Grunenthal, UCB, Gebro, Paid instructor for: Roche, Novartis, Janssen, Esteve, Menarini, Consultant of: Janssen, Novartis, Roche, Grant/research support from: Pfizer, Grunenthal, Gebro, Novartis, Marina Tortosa-Cabañas: None declared

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AB1490 THE POLISH VALIDATION OF A DISEASE SPECIFIC PATIENT REPORTED OUTCOME MEASURE OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is a chronic multisystemic autoimmune disease with a very broad clinical picture. Due to its generalized nature, it affects all aspects of the patient's life, such as physical, psychological and social well-being. As a result, the quality of life in patients with SLE is substantially decreased. Therefore, it is recommended to introduce evaluation of quality of life in clinical trials and in the daily practice. LupusPRO is a disease-targeted, patient reported outcome measure developed for assessment of quality of life in patients with Systemic Lupus Erythematosus. Originally, the questionnaire was validated among US patients of varied ethnic background and both genders. What differs LupusPRO from previous disease-specific quality of life questionnaire used in SLE is its comprehensiveness. It comprises two constructs: health- related quality of life domains (HRQOL) and non- health - related quality of life domains.

Objectives: The aim of this study is to carry out a cross-cultural adaptation and validation of the Polish-translated version of LupusPRO.

Methods: The Polish version of LupusPRO was administrated along with the 36-Item Short Form Health Survey (SF-36) and EQ-5D-5L questionnaire and Hospital Anxiety and Depression Scale (HADS). At the same time, demographics and clinical characteristics were collected. Disease activity, damage and exacerbation were assessed using SELENA-SLEDAI, SLICC/ACR DI and LFA Flare. Internal consistency reliability, test-retest reliability, convergent validity (against corresponding domains of SF-36) and criterion validity (against disease activity and damage) and known group validity were tested.

Results: A total of 199 (91% females) patients with SLE with a mean age of 42.6 ⊥12.62 years participated in the study. The mean SELENA-SLEDAI reached 5.3(⊥ 5.9) points and SLICC/ACR DI was observed at 1.3(⊥ 2.0) points. The internal consistency reliability of LupusPRO domains ranged between 0.737-0.925 (except for Lupus Symptoms, Social Support, Coping and Satisfaction with care). For all domains, except Social Support, test-retest reliability exceeded 0.7. Convergent validity with corresponding domains of the SF-36 was good (r>0,5). All health-related quality of life domains performed well against disease activity and damage measure, establishing its criterion validity. Known group validity against disease activity was observed. Confirmatory factor analysis showed a good fit.

Conclusion: The Polish version of LupusPRO has proved to have fair psychometric properties among Polish patients with SLE. It is the first disease-specific quality of life questionnaire in Polish, validated among Polish patients with Systemic Lupus Erythematosus.

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Rehabilitation

AB1491

ACUTE EFFECTS OF AN INSTRUMENT ASSISTED SOFT TISSUE MOBILIZATION TECHNIQUE ON CHRONIC NECK PAIN: A DOUBLE-BLIND, RANDOMIZED CONTROLLED TRIAL

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Background: Individuals with chronic neck pain, proprioceptive afferent information from the cervical spine may be impaired due to the presence of pain. Instrument-assisted soft-tissue mobilization (IASTM) is used to reduce pain and improve range of motion (ROM) and function. Cervical sensorimotor control includes the central integration and processing of all afferent information and the execution of the motor program through the cervical muscles and contributes to the maintenance of head posture and balance(1). In individuals with chronic neck pain, proprioceptive afferent information from the cervical spine may be impaired due to the presence of this pain(2). Many treatment modalities such as instrument-assisted soft-tissue mobilization (IASTM) have been used to reduce pain and increase proprioception(3). IASTM is used to reduce pain, increase soft-tissue mobility, and improve range of motion (ROM) and function. These instruments cause microtrauma to restore normal elasticity and function in soft-tissue(4). Kivlan has shown that significant and rapid changes in muscle function can occur with only a single IASTM application and have suggested the following mechanisms of action: an increased fascial motility, a proliferation of extracellular matrix fibroblasts, and an increased blood flow to the area close to the injured tissue, with decreased cellular matrix adhesion and localized ischemia(5).
Objectives: Aim of this study, to determine the acute effects of single-session, IASTM on cervical joint position error (JPE) and pain in individuals with chronic neck pain.
Methods: A total of 39 individuals (mean age=40.18±11.10 years) with chronic neck pain were included in this study. We divided the participants into IASTM, sham, and control groups of 13 members each. In the IASTM group, intervention was applied to the sternocleidomastoid and trapezius muscles with an application time of 45 seconds and a frequency of 60 beats/min. In the sham group, IASTM was applied at a 90° angle without pressure. The control group received no intervention. The pain severity and joint position error were evaluated before and after the intervention, by using the visual analog scale (VAS) and a cervical range of motion device.
Results: The effects of time and treatment group on VAS score were statistically significant. The effect of time and treatment for VAS score was statistically significant (p=0.001). When the post-test was examined according to application, a statistically significant difference found in VAS scores (p=0.001), with the lowest pain score in the IASTM group and the highest pain score in the control group. The significant improvements found in JPE in all aspects of the cervical region in the IASTM group (p<0.05). In the sham group, significant improvements observed in cervical extension, left rotation, and left lateral flexion movements in JPE (p<0.05).
Conclusion: Single-session IASTM is effective for improving the acute pain and JPE in individuals with chronic neck pain.
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AB1492

COMPARISON OF TELEREHABILITATION METHODS FOR SYSTEMIC SCLEROSIS PATIENTS IN THE COVID-19 ERA: A RANDOMIZED CONTROLLED STUDY

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Background: Scleroderma (SSc) is an autoimmune connective tissue disease progressing with fibrosis. SSc patients need to be protected from epidemic diseases as well as rehabilitation needs. For this reason, it is important for them to continue their exercises in an environment where they can be both rehabilitated and protected from infectious diseases.
Objectives: In this study, it was aimed to reveal the effects of exercises performed by telerehabilitation on individuals with Scleroderma with hand involvement and to compare the effects of real-time telerehabilitation (RTT) and asynchronous telerehabilitation (AT).
Methods: Forty-two participants with a mean age of 44.17±11.05 years were included in the study. The patients were divided into three groups and followed for 8 weeks. RTT was applied to the 1st group and AT was applied to the 2nd group, and the 3rd group was the control group. Participants' finger and wrist joint range of motion (ROM) were evaluated with a goniometer, upper extremity functions were evaluated with Scleroderma Hand Mobility Test (HAMIS), Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire and 9Hole Peg Test (9HPT), grip strength was evaluated with a dynamometer, superficial sense of touch was evaluated with the Semmes Weinstein Monofilament test, activities of daily living (ADL) were evaluated with the Michigan Hand Outcomes Questionnaire (MHQ), and general health status was evaluated with the Scleroderma Health Assessment Questionnaire (SHAQ).
Results: There were improvements in finger and wrist ROM, upper extremity functions and ADL parameters in the RTT group; and there were improvement in finger ROM and hand functions in the AT group (p<0.05). Wrist radial deviation ROM decreased in the control group (p<0.05). Significant differences were noted between the groups in finger ROM and upper extremity functions after treatment (p<0.05).
Conclusion: Our study shows that exercises performed via RTT and AT are effective in individuals with Scleroderma with hand involvement, and RTT has additional benefits.
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AB1493

REHABILITATION OF PATIENTS WITH OSTEOARTHRITIS OF THE KNEE USING MAGNETIC THERAPY

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Background: Currently, along with the basic treatment at the outpatient stage of rehabilitation, methods using physical and balneological factors are successfully applied: magnetotherapy, electrotherapy, peloidtherapy.
Objectives: Evaluation of the effectiveness of rehabilitation using magnetotherapy for osteoarthritis of the knee joints at the second radiological stage.
Methods: The study included 75 patients with primary osteoarthritis of the knee joints of the II X-ray stage, who were on outpatient rehabilitation in the sanatorium "Chuvashiyakurort", including 45 women and 30 men aged 50 to 65 years with a disease duration of 15 to 20 years. Rehabilitation was carried out by a multiprofessional team led by a physical and rehabilitation doctor. All patients were divided into two groups by simple randomization. The main group (n = 50) received basic treatment (chondroprotectors) + non-steroidal anti-inflammatory drugs (NSAIDs on demand) and a course of apparatus magnetotherapy. Magnetic therapy was applied to the area of the knee joints using the «Polus-2» apparatus using solenoid inductors, mode - continuous, frequency - 50 Hz,

low-sinusoidal current, intensity 111-1V, procedure duration 20 minutes, daily, № = 10. The control group (n = 25) received basic treatment (chondroprotectors) and NSAIDs (on demand). When analyzing the results of treatment, the VAS and WOMAC scales were used, and the Bartel index was estimated.

Results: In both groups, from the 2nd week of treatment, there was a decrease in pain during movement and at rest according to the VAS data compared with the baseline level. In patients in the main group, there was a decrease in joint swelling, a decrease in the level of pain according to the VAS by 41.3% ($p < 0.05$). The range of motion in the joints increased by 19.5% ($p < 0.05$) in the study group. In the control group, a decrease in the level of pain by 20.1% ($p < 0.05$) was recorded, the range of motion in the joints did not change. The overall WOMAC index was also lower in the main group compared with the control group ($p = 0.03$). Patients in the main group differed from patients in the control group in a significantly higher degree of dependence in daily life (Bartel index) and a lower score on the battery of tests of physical functioning. According to the results of dynamic observation of patients, no side effects associated with the use of the device "Polyus-2" were registered.

Conclusion: Magnetic therapy relieves pain, improves motor and daily activity in patients with osteoarthritis of the knee joints and can be recommended for use in medical rehabilitation programs in addition to basic therapy.

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Disclosure of Interests: None declared

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AB1494 THE QUALITY OF REPORTING IN RANDOMIZED CONTROLLED TRIALS OF BALANCE EXERCISES IN TOTAL KNEE ARTHROPLASTY

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Background: Total knee arthroplasty (TKA) is used to treat patients with end-stage osteoarthritis who experience pain and struggle to perform activities of daily living owing to having degenerative knee joints. Although TKA can improve the quality of life of patients, some may experience a decrease in their proprioception and the ability to balance after surgery (1). Decreased balance ability makes it difficult to undertake daily life activities in patients after TKA, impairs walking capacity and increases the risk of falling (2). Almost all studies which investigate the risk of falling conclude that physical activity(PA) are effective methods in order to maintain an intact balance control and prevent falls(4). Today, however, measures aimed at controlling COVID-19 include quarantines that lead to PA restrictions (5). In these days when PA cannot be increased due to quarantines, the most effective way to prevent falls in TKA patients may be to apply balance exercises (3). The "gold standard" in clinical trials are randomized controlled trials(RCTs) in which healthcare professionals make decisions about the safety and efficacy of treatments. However, poorly designed and reported RCTs can give misleading results. Methodological quality (MQ) assessment of clinical trials is important because it can prevent erroneous results in clinical practice and improve the quality of medical care. (6) Although RCTs provide the highest quality clinical evidence selection of balance exercises(BE) to be applied, there is no study in the literature investigating the MQ of RCTs of BE in TKA patients.

Objectives: The aim was to investigate assess the reporting MQ of RCTs of BE in patients with TKA.

Methods: We analyzed 17 published full-text reports of RCTs using BE in patients who underwent TKA. RCTs were sourced from PubMed, the Cochrane Reviews and PEDro Database. The PEDro scale and the 9-item CONSORT (7) were used to evaluate the MQ of the studies.

Results: The mean PEDro score was 6,64 ± 1,57. Classification of RCTs according to total PEDro score revealed that 1 study was classified as excellent, 13 studies as good, and 3 as fair. The least fulfilled criteria in the PEDro scale were: Blinding of all therapists who administered the therapy (1[5.88%]), allocation was concealed (5[29.4%]) and blinding of all subjects (7[41.17%]). The adherence of the reports to CONSORT items ranged from 41.17 % to 100%. The most underreported CONSORT items were: funding sources (7[41.17%]), statistical adjustment for multiple primary outcomes (8[47.05%]), and number of primary outcomes (8[47.05%]).

Conclusion: Our findings show that the quality of reporting for RCTs of BE in TKA patients is not high quality. Since it is not possible to improve balance with PA today, when there are quarantine due to COVID-19, patients should be encouraged to participate in BE programs with telerehabilitation, home-based or web-based exercises, and high quality RCTs should be planned in these programs.

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AB1495 THE QUALITY OF REPORTING IN RANDOMIZED CONTROLLED TRIALS OF STRENGTHENING EXERCISES IN TOTAL KNEE ARTHROPLASTY

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Background: End-stage knee osteoarthritis (KOA) is a significant health issue worldwide resulting in severe pain and disability. Total knee arthroplasty (TKA) leads to significant improvements in pain and the performance of functional activities such as walking for patients with end-stage KOA. Although TKA reduces pain and improves perceived function, patients continue to exhibit reduced muscle strength, voluntary muscle activation, and functional performance even years after surgery (1). In addition, quarantine, and related social restrictions due to the current Covid-19 pandemic may have affected the recovery of patients undergoing TKA due to limited access to exercise, physiotherapy, face-to-face follow-up, and medical services (2).Limited recovery after TKA will require intensive rehabilitation programs in the future. Strengthening exercises(SE) are the most effective intervention for improving muscle strength and functionality and have been recommended in the guidelines for KOA management and in clinical reviews for TKA rehabilitation (3). Randomized controlled trials (RCTs) are the gold standard for assessing the effects of health care interventions. However, RCTs may yield misleading results if they lack methodological rigors(4). RCTs provide the highest quality clinical evidence in the selection of the SE method to be applied (5). However, there are no studies examining the quality of RCTs related to SE in patients with TKA.

Objectives: The aim of this study was to assess the reporting quality of RCTs of SE in patients with TKA.

Methods: RCTs published between 2002 and 2021 were sourced from clinical trial registers, PubMed, and the Cochrane Reviews. RCTs were included if they involved SE in patients who underwent TKA. Analysis was carried out with two assessment tools: PEDro scale and 9-items from CONSORT(6). In addition, we have identified some key methodological elements and examined their relationship to their methodological quality.

Results: We found 35 RCTs that included SE in individuals with TKA. The mean PEDro score was 6.40 ± 1, 73. The most common deficient PEDro Items were: Blinding of all therapists who administered the therapy (14,2 %: 5/35 trials), allocation was concealed (31,4 %; 11/35 trials), blinding of all subjects (31,4 %: 11/35 trials). The most common deficient CONSORT Criteria were: Statistical adjustment for multiple primary outcomes (40 %; 14/35 trials), funding sources (40 %; 14/35 trials) and identification as a randomized trial in the title (62,85%; 22/35 trials). Of the key methodological factors we identified, only exercise duration (weeks) was associated with PEDro score ($R^2 = .169$, $p<0.01$).

Conclusion: Our results show that the quality of reporting in the literature on RCTs of SE in patients with TKA is insufficient. In order to increase muscle strength after TKA, the lack of face-to-face programs due to COVID-19 should be eliminated with telerehabilitation methods, video conferencing platforms and virtual reality applications, and high-quality RCTs should be planned where these programs are examined.

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AB1496 THE EFFECTS OF TELEREHABILITATION BASED EXERCISE PROGRAM IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is a rare, systemic autoimmune disease characterized by skin fibrosis and vasculopathy [1]. Patients may experience a

decrease in their daily activities, physical activity levels and quality of life, while psychological problems such as anxiety and depression may increase. In order to eliminate or reduce these symptoms and the consequences of symptoms, exercise programs for the patient, as well as medical treatment, are an important part of the treatment [2, 3]. Telerehabilitation increases overall health awareness, treatment adherence, and satisfaction by enabling patients to take an active role in decision-making and disease management [4]. Telerehabilitation replaces the traditional face-to-face treatment approach, allowing patients to access treatment remotely [5, 6]. In addition Telerehabilitation enabled patients with chronic diseases to access exercise during the COVID 19 pandemic [7].

Objectives: The aim of the study was to investigate the effect of telerehabilitation-based exercise program in patients with SSc.

Methods: Forty-six SSc patients were included in the study. The patients were randomly divided into two groups as telerehabilitation and control group. Youtube videos consisting of clinical pilates-based exercises were uploaded to the system so that only the patients in the telerehabilitation group could see it. In the telerehabilitation group; An exercise program was applied for eight weeks, twice a day. Video interviews were conducted with the patients once a week. To the control group; the same exercises were given to the telerehabilitation group. An eight-week exercise program was given in the form of a home program. Brochure introducing the exercises was given and exercises were taught. Pain, dyspnea, fatigue, physical activity, anxiety-depression, sleep and quality of life levels were evaluated in all patients at the beginning of the study and at the end of the eight weeks.

Results: Demographic and clinical features of the patient groups were similar (p>0.05). After the exercise program, pain, fatigue, anxiety-depression levels decreased in the telerehabilitation group compared to the control group, while sleep quality and quality of life increased (p<0.05). The results of the study induced that both exercise programs improve pain, fatigue, anxiety-depression, physical activity, sleep quality and quality of life in SSc patients. The telerehabilitation-based treatment program are more and more effective than the home program.

Conclusion: Our study shows that this innovative treatment program should be applied especially in SSc patients and it will be beneficial.

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AB1497 THE EFFECT OF AQUATIC REHABILITATION ON QUALITY OF LIFE IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: In addition to its multiple functional, social and economic consequences, knee osteoarthritis is responsible for a significant deterioration in the quality of life (QOL)[1]. Studies examining the impact of osteoarthritis on quality of life have been made possible through the development of validated measurement questionnaires. The SF-12 score with its aspects (physical, mental and social) is a valid and reliable instrument for the assessment of QOL.

Objectives: The main aim of our study was to make a comparison between the contribution of aquatic rehabilitation and classic rehabilitation in patients with knee osteoarthritis using the SF-12 score.

Methods: We carried out a prospective, comparative study carried out over a period of 15 months, (September 2016- December 2017), in 120 patients recruited from the outpatient department of the Physical Medicine and Functional Rehabilitation Department of HMPIT in whom the diagnosis of knee osteoarthritis was made according to the criteria of the ACR.

The patients were randomly divided into 2 groups of 60 patients each. The first group called G1 received a classic rehabilitation program. The second group called G2 benefited from aquatic gymnastics. The study was based on the SF-12 quality of life assessment. Two evaluations were made, the first (T1) before the start of rehabilitation and the second (T2) at the end of the eight weeks of care.

Results: The mean age of our patients was 57.2 ± 12.5 years in G1 vs 54.3 ± 7.1 years in G2 (p = 0.012). The sex ratio was 0.2 in G1 versus 0.37 in G2 (p = 0.011). The duration of knee osteoarthritis was 63.4 ± 4.5 months in G1 vs 56.2±7.5 months in G2 (p=0.172). Initially, the mean of SF12-P in G1 patients was 31.2 ± 6.5 compared to 35.4±6.2 in G2 patients. In our patients, the SF12-P score was less than 50 in 100% of cases in G1 and in 98% of cases in G2. There was a statistically significant difference between the 2 groups (p = 0.04). After classical rehabilitation, the SF12-P had increased on average by 2.3 against 6.1 after aquatic gymnastics with a statistically significant difference between the 2 groups (p = 0.012). Initially, the mean of SF12-M in G1 patients was 32.5 ± 10.2 and 35.3 ± 8.9 in G2 patients. In our patients, the SF12-M score was less than 50 in 94% of cases in G1 and in 98% of cases in G2. There was no statistically significant difference between the 2 groups (p = 0.652). After classical rehabilitation, the SF12-M increased on average by 6.9 and 12.1 after aquatic gymnastics with a statistically significant difference between the 2 groups (p = 0.005).

Conclusion: The effectiveness of functional rehabilitation, whether aquatic or dry, has been well demonstrated by the study of quality of life, with better results for balneotherapy. The physical properties of water and heat have a positive short-term impact on quality of life by acting on several parameters, including pain, contractures and anxiety. Further studies evaluating this long-term effectiveness will be required.

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AB1498 THE BIOPSYCHOSOCIAL-BASED EXERCISE MODEL VIA TELEREHABILITATION IN PATIENTS WITH INFLAMMATORY AND NON-INFLAMMATORY RHEUMATIC DISEASES: A PROSPECTIVE COHORT STUDY DURING THE COVID-19 PANDEMIC

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Background: During the COVID-19 pandemic, the patients with rheumatic disease in the biopsychosocial perspective have been adversely affected by social isolation, uncertainty, and the thought that their chronic disease will worsen and increase in their symptoms. ACR/EULAR (American College of Rheumatology / European League Against Rheumatism) defines recommendations about continuing current pharmacotherapy and the significance of the biopsychosocial approach and exercise for patients with rheumatic diseases during a COVID-19 infection [1, 2].

Objectives: This study aims to investigate the effectiveness of the biopsychosocial exercise performed by telerehabilitation on biopsychosocial status, general health status, and anxiety-depression levels in the patients with inflammatory and non-inflammatory rheumatic diseases.

Methods: Fourteen patients with inflammatory rheumatic diseases (rheumatoid arthritis: 4; ankylosing spondylitis: 4; sjogren's syndrome: 3; polymyalgia rheumatica: 2; and vasculitis: 1) and eight patients with non-inflammatory rheumatic diseases (fibromyalgia: 6; and osteoarthritis: 2) performed a biopsychosocial-based exercise model (named as "Bilişsel Egzersiz Terapi Yaklaşımı"-(BETY) in original; "*Cognitive Exercise Therapy Approach*" in English) via telerehabilitation continued for three sessions per week for 12 months [3]. Outcome measures were Health Assessment Questionnaire (HAQ), Hospital Anxiety and Depression Scale (HADS), and BETY-Biopsychosocial Questionnaire (BETY-BQ) [4]. All outcomes were measured baseline and at the 12th month. The Wilcoxon's test was used for statistical analysis.

Results: All of the 22 patients were female. The mean age was 57.4 and 55.8 years in the inflammatory and non-inflammatory rheumatic diseases groups respectively, and they had a mean BMI of 25.9 and 25.3 kg/m^2. There was no significant difference by time for HAQ score (p = 0.125), HADS anxiety and depression (p = 0.916 and p = 0.663, respectively), and BETY-BQ score (p = 0.753) between the baseline and at the 12th month follow-up in the patients with inflammatory rheumatic diseases. Similarly, in the patients with non-inflammatory rheumatic diseases, there was no significant difference by time for HAQ score (p = 0.546), HADS anxiety and depression (p = 0.343 and p = 0.527, respectively), and BETY-BQ score (p = 0.068) between the baseline and at the 12th month follow-up.

Conclusion: This study showed that biopsychosocial-based exercise through real-time telerehabilitation was able to maintain their conditions before pandemic in biopsychosocial status, general health, and anxiety-depression levels on the patients with inflammatory and non-inflammatory rheumatic diseases during COVID-19 pandemic period in one-year follow-up.

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AB1499 **PAIN MANAGEMENT IN KNEE OSTEOARTHRITIS: BALNEOTHERAPY VERSUS CLASSIC REHABILITATION**

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Background: Knee osteoarthritis presents a heavy financial burden due to disability and supported care. Gonalgia is the main symptom leading patients to consult. For some clinicians, this is a warning signal that correlates with the extent of joint degradation [1]. The management of pain in knee osteoarthritis is multidisciplinary comprising pharmacological and non-pharmacological means including classical rehabilitation and aquatic gymnastics. The objective of our work was to study the contribution of aquatic gymnastics compared to conventional rehabilitation in the management of pain in patients with knee osteoarthritis.

Objectives: The objective of our work was to study the contribution of aquatic gymnastics compared to conventional rehabilitation in the management of pain in patients with knee osteoarthritis.

Methods: Prospective, evaluative and comparative study about 120 patients with knee osteoarthritis carried out over 15 months (September 2016- December 2017) in the Department of Physical Medicine and Functional Rehabilitation. The patients were divided into two groups of 60. The first group (G1) benefited from a classic rehabilitation program, the second group (G2) benefited from aquatic gymnastics. The 2 programs were carried out at the rate of three sessions per week for two months. The study was based on the assessment of pain by the following scales: VAS pain and the Western Ontario and McMaster Universities' Osteoarthritis Index (WOMAC) questionnaire for the lower limbs (pain section).

Results: The mean age of our patients was 57.2 ± 12.5 years in G1 vs 54.3 ± 7.1 years in G2 (p = 0.012). The sex ratio was 0.2 in G1 versus 0.37 in G2 (p = 0.011). The duration of knee osteoarthritis was 63.4 ± 4.5 months in G1 vs 56.2±7.5 months in G2 (p=0.172). The pain was mechanical in 89 % of cases. Positional nocturnal pain was noted in 72% of cases. Hydarthrosis was associated in 46% of cases. A daily intake of palliative I analgesics was noted in 56 % of patients. The mean pain VAS at rest of 33.4±18 in G1 vs 27.3±23.2 in G2 (p=0.13). On exertion, it was 72.3±19 in G1 vs 83.3±20 in G2 (p = 0.72). After the rehabilitation treatment, an improvement in the two groups was objectified, which was significantly more marked in G2: Resting VAS improved by 57 % for G1 and by 84% for G2 (p = 0.015). Exercise VAS improved 20% in G1 and 43% in G2 (p <0.001). The mean WOMAC pain score was 14.3 in G1 and 10.3 in G2 (p = 0.006). There was an improvement in the WOMAC pain score of 24% in G1 and 58% in G2 (p <0.001).

Conclusion: Functional rehabilitation in the water or in the dry has a marked effect on pain in gonarthrosis patients. The aquatic environment can also bring many benefits on pain by lightening the weight of the body and the analgesic effect of the heat.

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AB1500 **ASSESSMENT OF CLINICAL PARAMETERS AFTER CLASSIC REHABILITATION VERSUS BALNEOTHERAPY IN GONARTHROSIS**

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Background: Knee osteoarthritis (KOA) is the most common pathology of the lower limb. It is multifactorial and constitutes a real public health problem. Nowadays, in addition to the rehabilitation that is part of the multidisciplinary management of this affection, water gymnastics is increasingly finding its place [1].

Objectives: The main objective of our work was to compare the contribution of aquatic gymnastics compared to classical rehabilitation in patients with knee osteoarthritis through a clinical evaluation.

Methods: This is a prospective, comparative and evaluative study carried out in a department of Physical Medicine and Functional Rehabilitation over a period of 15 months between September 2016 and December 2017, including 60 patients with KOA. The patients were randomly divided into 2 groups of 60 patients each one. The first(G1) benefited from a classic rehabilitation program. The second(G2) benefited from water gymnastics. Two clinical evaluations were carried out: T1 before the start of rehabilitation and T2 at the end of the eight weeks of treatment.

Results: The mean age of our patients was 57.2 ± 12.5 years in G1 vs 54.3 ± 7.1 years in G2 (p = 0.012). The sex ratio was 0.2 in G1 versus 0.37 in G2 (p = 0.011). The duration of knee osteoarthritis was 63.4 ± 4.5 months in G1 vs 56.2±7.5 months in G2 (p=0.172). 55 patients presented with a misalignment of the lower limbs with a varus knee in 33% of cases (G1 25% and G2 42%). 5 patients in G1 and 7 patients in G2 had a valgus knee. In G1, one patient had recurvatum and two patient had knee flexum with no statistically significant difference between the two groups. After classic rehabilitation, Zohlen's sign had disappeared in 6 patients for the right knee and 3 patients for the left knee. However, after water gymnastics, this sign had disappeared in 12 patients for the right knee and in 16 patients for the left knee. A functional mobility sector (>90◦) was found in all patients with an average of 120◦ in G1 and 126◦ in G2. After rehabilitation, an improvement of 2% in G1 and 5% in G2 was noted with a statistically significant difference between the two groups (p<0.001). Thirty-sex percent of G1 patients had quadriceps amyotrophy versus 32 % of G2, which disappeared in 5 patients after classic rehabilitation and in 6 patients after hydrotherapy. 48 patients of G1 and 56 patients of G2 presented with quadriceps retraction which disappeared in 21 subjects of G1 after classic rehabilitation and in 45 subjects of G2 after hydrotherapy. A retraction of the hamstrings was noted in 13 and 18 patients respectively in G1 and G2 with a total improvement in the 2 groups.

Conclusion: Dry rehabilitation has its place in the management of knee osteoarthritis, but rehabilitation in water has better results. The aquatic environment makes it possible, by reducing the weight of the body, to reduce the stresses exerted on the knee joints, allowing better joint mobility with the added effect of heat on the reduction of pain and muscle relaxation.

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Education

AB1501 **EFFECT OF SARS-COV-19 PANDEMIC ON RHEUMATOLOGY TRAINING IN INDIA**

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Background: The current study aims to gauge the magnitude of the effect the pandemic has had on Rheumatology training (including the effect on clinical,

academic and research training) in India, their physical, mental and social well-being during the pandemic and the perceived changes in Rheumatology training and care during the pandemic from the trainee's view

Objectives: 1.To asses the Impact of COVID-19 Pandemic on the training of Rheumatology Residents (DM, DNB and Fellows)

2.Understand the issues faced by trainees and the extent of affection.

Methods: Study design: We conducted an observational cross-sectional study using an online survey sent to rheumatology trainees in India.

Sample: Convenience sampling was used, so the sample size was not calculated.

Inclusion and exclusion criteria: Rheumatology trainees from India including DM/DNB residents and fellows with the ability and desire to complete the survey were included.

Data collection and instruments: The link to the survey was sent to the rheumatology trainees through social media platforms like WhatsApp, Telegram and email.

Statistical analysis: Descriptive statistics were performed by calculating measures of central tendency for quantitative variables and using counts and percentages for qualitative and nominal variables.

Results: A total of 78 trainees from 24 institutes in 12 states participated in the study. Mean age of the participants was 31 with 70% of trainees being male and 30 % females. 56 (70%) participants were DM students, 15 (19%) participants were DNB students, 5 fellowship students and 2 Non- academic Senior Residents. An overwhelming majority of residents (84%) felt COVID-19 Pandemic Negatively impacted their residency and their Physical (65%), Mental(74%) and Social wellbeing (80%). 79% of trainees felt burnt-out due to the pandemic. Majority of trainee felt the pandemic negatively impacted their training with clinical teaching(91%), Clinical examination skill (74%), current(80%) and future(70%) research opportunities suffered during the pandemic. Most residents felt diminution and significant reduction of the overall footfall(99% & 72%) of patients in rheumatology including OPD(100% & 77%) and indoor(99% & 67%) admissions along with academics(85% & 35%), procedures(97% & 66%) and exposure to musculoskeletal ultrasound(96% & 71%). Almost 60% and 40% of trainees had their OPDs and indoor admissions stopped during COVID-19 pandemic of these 20% had their OPDs and Admissions closed for more than 6 months. 85% of the participants had one or the other psychological symptoms with almost half experiencing anxiety(44%), low mood(47%) or lack of sleep(41%); 85% were concerned about their family members being infected and 40% lost a close relative to COVID. 91% of the trainee were posted in COVID-duties 2/3rd of them in ICUs, 50% being posted for 1-3 months and 20% more than 3 months, a quarter of trainees got infected during their duties (COVID and Non-COVID) and though most had asymptomatic to mild COVID, 15% still had moderate to severe COVID. Teleconsultation was started by more than half of the respondents after COVID related lockdowns with greater than half not being happy with teleconsultations.

Conclusion: The COVID-19 Pandemic has completely altered the status quo for rheumatology trainees and has affected their physical, social and mental wellbeing. Academic and clinical training has reduced, Current and future Research has become difficult, disruptions in OPDs and Admissions, recurrent COVID postings and reduction in patient footfall, Procedures and MSK-US have been detrimental to trainees.

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AB1502 AWARENESS OF BIOLOGICAL AGENTS RELATED SIDE EFFECTS AMONG INTERNAL MEDICINE RESIDENTS IN A UNIVERSITY HOSPITAL

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Background: Biological agents have become a core component of therapeutic strategies in the last two decades. The number of patients treated with biological agents has been increasing with the expansion of these agents' indications among rheumatic disorders.

Objectives: Unfortunately, biological agents have varied side effect profiles, and rheumatic patients with possible side effects are commonly consulted with internal medicine physicians in emergency departments. We surveyed to assess the awareness of biological agents related side effects among internal medicine residents in our university hospital.

Methods: We conducted a web-based multiple-choice test with 10 questions in total. Monoclonal antibodies (anti-TNF, anti-CD20), anti-cytokines, and JAK inhibitors related side effects and management of these adverse events were assessed. Figure 1 depicted the topics and the correct answer rate of the related questions.

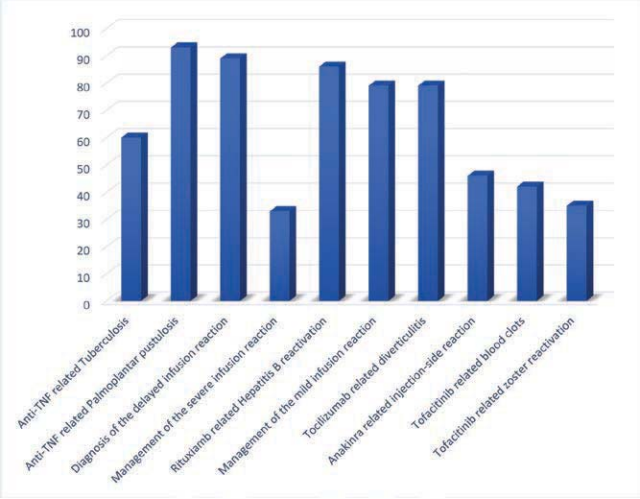

Figure 1. The topics and the correct answer rate of the related questions

Results: A total of 57 responses were collected and analyzed. The mean number of the correct answers was 6,4± 1,5. Fourteen (24,6%) out of the 57 participants scored below 5, whereas 58% of the participants scored ≥6 points. The majority of the participants have correctly answered the anti-TNF, rituximab and tocilizumab-related questions, however, less than half of the participants have accurately answered the anakinra and JAK inhibitors-related questions (Figure 1). Awareness of the JAK inhibitors related zoster reactivation and increased risk of serious cardiovascular events were 35% and 42%, respectively. The approach to the delayed and mild infusion reactions was adequate, however, 33% of the participants accurately approached the severe infusion reaction.

Conclusion: Our survey suggests that the awareness of biologic agents related side effects among the internal medicine residents is satisfactory. Poorer results were observed especially in JAK inhibitors related side effects and severe infusion reaction management which indicate the educational needs of the residents for these topics.

Disclosure of Interests: None declared

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AB1503 MOST MEDICINE RESIDENTS WOULD LIKE TO LEARN JOINT ASPIRATION PROCEDURES BUT 2/3 HAVE NEVER DONE IT: SURVEY OF COMMUNITY HOSPITAL TRAINEES IN NORTHEASTERN USA

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Background: Arthrocentesis is a procedure performed to aspirate synovial fluid from a joint cavity. It has both diagnostic and therapeutic utilization in outpatient and inpatient settings. While arthrocentesis is considered a minor surgical procedure, there is always potential to injure blood vessels, nerves, and tendons[1]. Although joint arthrocentesis is not an Accreditation Council for Graduate Medical Education procedural requirement for Internal Medicine (IM) residents in the United States, several studies have revealed that training on knee arthrocentesis and injection provided a solid foundation to medical residents toward increasing their confidence and refining motor skills[2].

Objectives: To evaluate the current Roger Williams Medical Center (RWMC) IM residents' confidence level in performing intra-articular injection. Results from this study will inform the design of resident-orientated quality improvement arthrocentesis teaching series in RWMC.

Methods: Project was incepted and designed by one rheumatology faculty, one fellow and five IM residents of RWMC. We selected the survey as a tool to elicit information from all current IM residents who filled out a 7-question survey regarding their residency experience and exposures to knee aspiration and injection. We used Survey Monkey as an anonymous survey tool (see Table 1). Data were collected between 1/14/22 until 1/27/22 and were verified by two members of the research team.

Results: A total of 47 IM residents within three classes in this community residency program were provided with the survey. The survey response rate was 82.9% (39 /47). 69.23% residents do not feel comfortable doing arthrocentesis. More than half of the resident population (51.28%) do not think they have adequate exposure to knee arthrocentesis. 73.68% respondents have never performed knee injections/arthrocentesis. According to the survey, 94.87% of the

Table 1. Survey from 39 total responses

Question	Responses
1.What post-graduate year are you?	PGY1:41.03% PGY2: 35.90% PGY3: 9%
2. Are you comfortable/confident with knee arthrocentesis/injection during residency?	Not Comfortable/confident: 69.23% Somewhat comfortable/confident: 28.21% Quite comfortable/confident: 2.56%
3. Do you think you have adequate exposure to knee procedures in residency?	Strongly Agree: 0% Agree: 0% Undecided: 5.13% Disagree: 51.28% Strongly Disagree: 43.59%
4. How many knee aspirations/injections have you done during residency?	0: 73.68% 1-4: 26.32% 5-10: 0% >10: 0%
5. Do you think our residency program is preparing you to do knee aspirations/ injections?	Strongly Agree: 0% Agree: 0% Undecided: 17.95% Disagree: 35.90% Strongly Disagree: 46.15%
6. Would you be interested in doing more knee aspirations/injections?	Yes: 94.87% No: 5.13%
7. Having exposure to arthrocentesis is very important for me to have in my residency program	Strongly Agree: 33.33% Agree: 35.90% Undecided: 23.08% Disagree: 5.13% Strongly Disagree: 2.56%

residents would be interested in learning to do knee procedures. Having exposure to knee arthrocentesis during residency was important to 36.84% and very important to 34.21% of the trainees.

Conclusion: The survey results demonstrate that most of the IM residents had no prior exposure and are uncomfortable with knee arthrocentesis. However we proved that there is high interest in learning this procedure. Literature review shows that structured training sessions have a long-term effect in competency and confidence with similar procedures. This survey provides us data to set up a system to improve the quality of joint procedures teaching in RWMC.

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AB1504 WILL YOU CHOOSE RHEUMATOLOGY? SURVEY ON THE ATTRACTIVENESS OF RHEUMATOLOGY AMONG MOROCCAN STUDENTS, INTERNS AND FRESHLY GRADUATED DOCTORS.

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Background: In several countries, studies have shown that fewer medical students choose rheumatology as specialty. In Morocco no study has yet focused on this subject.

Objectives: The aim of our study is to assess the attractiveness of rheumatology as a specialty among Moroccan medical students, recently graduates and interns, and to analyze the factors that may be associated with it.

Methods: An online survey was sent to 297 medical students who had started their hospital practice, to 100 medical interns (students in 6th and 7th year who successfully passed the internship competition) and to 280 freshly graduated doctors (residency program candidates before choosing a medical or surgical specialty). The survey covered three areas: anonymous social and demographic informations, data on clinical trainee in a rheumatology department, and the attitude toward rheumatology as a specialty. Descriptive data were collected and Chi 2 Tests were used to assess differences between groups, Logistic regression was performed to investigate associations between demographic and exposure variables and the choice of rheumatology as a career.

Results: We collected responses from 161 students (response rate: 54%), 68 interns (68%) and 89 freshly graduated doctors (32%). The demographic characteristics are presented in Table 1.

Table 1.

	Medical students (N=161)	Interns (N=68)	Freshly graduated doctors (N=89)
Age*	21.5 ±1	24.2 ±1.1	28.62.3
Gender (females) (%)+	93 (57.8)	30 (44.1)	64 (71.9)
level (%)+	Third year: 44 (27.3) Fourth year: 53 (32.9) Fifth year:64 (39.8)	First year: 44 (64.7) Second year: 24 (35.3)	-
Training in a rheumatology departement (%)+	118 (73.3)	28 (41.2)	37 (41.6)
Dduration of training (weeks)*	3.4 ± 0.7	5.3 ±1.4	6.3 ±2.6

(*) expressed as a number and percentage /(+) expressed as a mean and standard deviation

73% of students, 41.2% of interns and 41.6% of graduates said they had already completed a clinical trainee in a rheumatology department. While 41.6% of students and 43.8% of graduates consider the possibility of choosing rheumatology as their specialty, only 11.2% of students, 5.9% of interns and 7.9% of graduates said that rheumatology is their dream career specialty. In uni and multivariate analysis, clinical exposure to rheumatology is retained as the main statistically significant factor predicting the choice of rheumatology in all categories (Odds ratio (95% CI) = 0.191 (0.07- 0.497; p= 0.02)), to this is added the female sex among freshly graduated doctors (Odds ratio (95% CI) = 4.02 (1.251- 12.918; p= 0.001).

Conclusion: Our study showed that rheumatology is considered a fascinating specialty by Moroccan medical students and freshly graduated doctors. Clinical exposure to rheumatology is the strongest predictor factor for choosing rheumatology as a future career.

Disclosure of Interests: None declared

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AB1505 MOROCCAN MEDICAL STUDENTS SURVEY: WHAT ARE THE MOTIVATIONS AND BARRIERS TO CHOOSE RHEUMATOLOGY AS A CAREER?

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Background: Rheumatology has experienced a genuine progress in recent decades, especially with the development of new treatments and the use of ultrasound as a mean of exploring the musculoskeletal system, which has contributed to its attractiveness for medical students.

Objectives: The objective of this survey is to study the factors that motivate or discourage medical students to choose rheumatology as a career.

Methods: Web-based questionnaire was sent to 297 medical students who had begun their Hospital training, 100 medical interns, and 280 general practice graduates after passing the residency program's examinations and before choosing their specialty. This questionnaire covered three areas: anonymous demographic information, attitudes toward rheumatology as a specialty, and reasons behind choosing or not choosing rheumatology (multiple choice and open-ended questions).

Results: We collected responses from 161 students (answer rate: 54%), 68 interns (68%), and 89 (32%) medical school graduates. 41.6% of students and 43.8% of graduates consider that they can choose rheumatology as a specialty, whereas 11.2% of students, 5.9% of interns and 7.9% of graduates considered rheumatology as their dream career. The main motivation for students to choose rheumatology is "the diversity of the musculoskeletal pathology". According to interns and graduates, the benefit of choosing rheumatology is the quality of life

Table 1. Main motivations and barriers to choose rheumatology according to Moroccan medical students, interns and medical graduates.

	Students	Interns	Graduates
Motivations	N=67	N=4	N=39
-Wide-ranging specialty with diversity of musculoskeletal pathologies	48 (71,6 %) 24 (35,8 %) 19 (28,4 %)	2 (50 %) 2 (50 %) 3 (75 %)	11 (28,2 %) 10 (25,6 %) 28 (71,8 %)2
- - -Interventional aspect of rheumatology: ultrasound guided injections, biopsy, Hydrodilatation. - - -Relatively less time-consuming specialty			
Barriers	N=88	N=62	N=50
-I am interested in surgical specialties	44 (50 %) 21 (23,9 %) 22 (25 %)	32 (49,2 %) 12 (18,5 %) 18 (27,7 %)	23 (46 %) 21 (42 %) 26 (52 %)
- -Monotonous specialty - -Limited therapeutic aspects			

it can offer, given that it is a "relatively less time consuming specialty». The main barrier to choose rheumatology is "the interest in surgical specialties" for students and interns and "the limited therapeutic aspects" for graduates. Other commonly reported reasons are shown in Table 1.

Conclusion: Our study has shown that rheumatology fascinates Moroccan medical students by its clinical abundance and the diversity of musculoskeletal pathology and also by the quality of life it can offer. According to the students, the main barriers to choose rheumatology are the interest in a surgical specialty, and the limited therapeutic aspects of the specialty.

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AB1506 RHEUMATOLOGY TRAINING EXPERIENCE: ARE RHEUMATOLOGY RESIDENTS WELL-PREPARED NOWADAYS? A SELF-APPRAISAL

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Background: Rheumatology residence in Europe is a 4-year training program where Medical Doctors (MD) purchase all capacities for turning into Rheumatologists at each Hospital. European guidelines concerning which contents should be acquired and recommendations for its obtaining are available (UEMS, Union Européenne des Médecins Spécialistes).[1] Several researches have proven high self-reported abilities, but some deficiencies are displayed in deepen investigations: musculoskeletal ultrasound sonography, poorly crystal identification by optic microscopy and injection skills. As well, low clinical experience remains as one of the most self-reported deficiencies.[2,3]

Objectives: To assess the quality of one-year rheumatology trainee consultation at the outpatient clinic in a Spanish Hospital.

Methods: The last year during outpatient consultation of a resident training in Rheumatology in one Spanish hospital was assessed, from May 2021 to May 2022. All patients visited by the trainee were included, absent patients in the consultation date were excluded from the study. Main variables were collected, such as gender, main diagnosis, biological or targeted synthetic treatments and supplementary tests. The final resident's opinion about his training was also checked.

Results: During one-year period of the Resident's consultation, 1419 visits were performed. From those, 470 were the first visit of the patient and 119 of them were solved in the first visit and no follow-up was needed. 60.7% of patients were woman. Most frequent diagnosis were arthropaties: 21.8% psoriatic arthritis, 16.9% rheumatoid arthritis and 8.4% axial spondyloarthritis. Regarding collagenopathies, 3.4% of patients were diagnosed of systemic erythematosus lupus, 1.3% antiphospholipid syndrome, 2.3% systemic sclerosis and 1.3% myopathies. Bone-related diseases as Paget's disease and osteoporosis were also frequent (21 and 132 patients). The most prevalent vasculitis was giant cell arteritis with 51 patients, although patients with Behçet's disease, Takayasu artheritis and polyarteritis nodosa were also followed. A total of 207 musculoskeletal ultrasonography were made during daily clinical practice. As well, 67 articular injections were performed. Capillaroscopy and salivary gland biopsy were the least frequent procedures (21 and 18, respectively). Biological therapies most supervised by the resident were anti-TNF (76.9%), followed by anti-IL-6 (12.8%) and anti-IL-17 (10.3%).

Conclusion: Most of rheumatic diseases can be diagnosed and followed during one-year period in the resident's training program. Also, ultrasonography and injection skills are granted during this time. The most important self-reported deficiency is the low number of patients under biological/targeted synthetic treatments.

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AB1507 ATTRIBUTES INFLUENCING THE SELECTION OF FELLOWSHIP PROGRAMS BY RHEUMATOLOGY APPLICANTS: A PILOT WEB-BASED SURVEY

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Background: Recruitment of candidates is a cost- and effort-intensive aspect of rheumatology fellowship programs. For program leaders to efficiently use the available resources and improve recruitment outcomes, it is imperative to understand the attributes that influence the candidates' choice of a program. Previous studies have examined the type and relative importance of the factors that candidates use in selecting other fellowship programs (1, 2). However, no such studies have been conducted in the field of rheumatology.

Objectives: To examine the factors that influence the selection of fellowship programs by rheumatology applicants.

Methods: An anonymous, web-based survey comprised of 13 questions was shared with rheumatology fellowship applicants on messaging applications and online forums. The survey was open from 10/29/2021-11/06/2021. Participation was voluntary and informed consent was implied through the participants' response. Three reminders to complete the survey were sent. Four domains of the applicant's perception in relation to their preference of ranking rheumatology programs were assessed: (1) program prestige, (2) program structure, (3) interview day experience, and (4) career path of the alumni. The survey questions were devised in one of the following formats: (1) 5-point Likert scale, (2) rank order questions, (3) yes/no questions, (4) multiple choice questions, and (5) open-ended questions.

Results: Thirty-two rheumatology applicants responded to the survey. The prestige of the program was reported to be extremely important by 16%, very important by 19%, somewhat important by 44%, and little or not important by 21% responders. The opportunity to see a diverse patient population was reported to be important by 97% respondents. The call schedule and higher number of fellows were considered important by 88% of the respondents. 66% preferred programs with higher number of faculty members. 69% favored programs with an ultrasound curriculum. The availability of clinician-educator track (18%), MCR/MPH (14%), and T32 grand (4%) were considered less important. 69% reported that the opportunity to train at a Veterans Administration hospital did not influence their choice. Regarding interview day experience, interaction with the faculty (63%) and the fellows (17%) were considered important factors influencing program ranking. Respondents preferred programs with alumni in academic clinician track (45%) and private practice (43%) compared to programs with alumni in academic research (13%) or industry pathway (4%). The geographical location of the program including the cost of living and location of significant others also influenced the applicants' choice.

Conclusion: To the best of our knowledge, this is the first survey to assess the attributes that influence a candidate's choice of a rheumatology fellowship program. Our survey demonstrated that a positive interview day experience and program attributes including the opportunity to interact with a diverse patient population, relaxed call schedule, higher number of fellows and faculty, the presence of an ultrasound curriculum, and the location were the dominant factors influencing applicants' choice of a program. The main limitation of our study is the lack of generalizability due to selection bias. Understanding the factors involved in decision making of the rheumatology fellowship applicants can provide valuable information for both the applicants and the programs and therefore lead to a better match.

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Educational cases

AB1508 A NOVEL PATHOGENIC VARIANT IN ZNF462 GENE ASSOCIATED WITH WEISS-KRUSZKA SYNDROME AND SLE

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Background: Weiss-Kruszka syndrome (WSKA) is an autosomal dominant congenital anomaly syndrome due to mutations in the *ZNF462* gene and manifests with developmental delay and multiple craniofacial abnormalities with variable expressivity[1]. It is also characterized by cognitive impairment, whilst about a third of the affected individuals belong to the autism spectrum. Although the disease is inherited with the autosomal dominant manner, most of the described subjects (95%) had *de novo* variants with no affected family members[1]. WSKA has been recently described and only 26 (including our patient) affected individuals have been classified to date[2]. Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by the presence of autoantibodies and multi-organ inflammation. Genetic factors might play an important role in disease pathogenesis in patients with childhood-onset SLE.

Objectives: To describe the case of a SLE patient who was found to have WSKA related to a novel pathogenic autosomal dominant (AD) variant in the ZNF462 gene, and inform clinicians of a possible association between the 2 conditions.
Methods: A 25-year-old Caucasian female with a history of SLE, diagnosed at the age of 14, manifested with malar rash, Raynaud's phenomenon, arthritis, thrombocytopenia, positive ANA, ds-DNA antibody and hypocomplementemia. At the age of 17, she developed renal dysfunction due to lupus nephritis class IV, and she was treated with glucocorticoids (GCs), cyclophosphamide and hydroxychloroquine. In Oct 2020, she was admitted to the hospital for thrombotic thrombocytopenic purpura due to lupus exacerbation. She was successfully treated with GCs, plasma exchange and rituximab. During her hospitalization, the presence of various clinical features raised the suspicion of a genetic syndrome. First, the patient exhibited dysmorphic features such as hypertelorism, prognathism, arched eyebrows, flattened nasal bridge, small upper lip, mild intellectual disability, and a history of childhood-onset SLE. Whole exome sequencing (WES) by NGS was used for the genetic investigation of the patient.

Figure 1.

Results: The patient underwent genetic evaluation with WES and the novel heterozygous AD pathogenic variant c.4142delT (p.Ile1381ThrfsTer16) in *ZNF462* gene was identified. Confirmation of the identified variant was also verified by sanger sequencing. Pathogenic variants in the *ZNF462* gene were previously described in patients with the recently reported WSKA of which several characteristics are compatible with our patient's features. The ZFN462 encodes a zinc-finger transcription factor that plays a role in embryonic development, transcriptional regulation, and chromatin remodelling. Given that chromatin remodelling has been implicated in the pathogenesis of SLE, the association of this novel *ZNF462* variant in the development of SLE, needs to be determined[3].
Conclusion: This is the first report of a patient with coexisting SLE and WSKA due to a novel variant. It illustrates the need for further research in order to elucidate any possible pathophysiologic link among the 2 conditions.
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AB1509 OVARIAN CARCINOMA MIMICKING SYSTEMIC SMALL VESSEL VASCULITIS: CASE REPORT

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Background: Few cases of digital ischemia and gangrene associated with primary solid tumors have been described in literature[3]. The exact mechanism of severe occurrence has not been completely understood and the available treatment options have an extremely limited utility [1,2].In the most cases the patients were elderly women with adenocarcinomas of digestive or gynaecologic apparatuses [4].

Objectives: We describe a new case of digital gangrene as unusual presentation of ovarian cancer in a 36 years old woman.
Methods: 36 years old female was admitted to our Reheumatology deparment with blackish Blackish discoloration of the toes of one week duration. She had history of COVID -19 infection 8 months prior to the presentation then developed hemoptysis, picture suggestive of ILD, generalized anasarca and skin rash; accordingly an initial diagnosis of post COVID-19 vasculitis was made by dermatologist. The blood tests were ESR:21 mm/hr, CRP:25.7, D.Dimer:8.8, Ferritin:575 ng/ml, lymphopenia:0.9, S.Creatinine:2, 24 h urinary protein: 325 mg/24h and all autoimmune markers were negative except anti nuclear antibody (ANA) with titer:1/160. Further assessment revealed that she had multiple site coagulopathy; internal jugular vein thrombosis, bilateral lower limbs Deep Venous Thrombosis (DVT). Neck ultrasound surprisingly showed bilateral enlarged suspicious looking supraclavicular lymph node with lost hilum which was Biopsied for histopathological correlation which revealed focally necrotizing adenocarcinoma with significant signet ring differentiation. Searching for the primary malignancy, tumor markers were sent CA125: 584 u/ml (up to 35), Pelvi-abdominal Magnetic resonance imaging (MRI) revealed Left ovarian mass measuring 3.6 x 3.4 x 4.4 cm highly suspicious of malignant neoplastic growth for histopathological correlation, Suspicious looking pelviabdominal lymph nodes mostly representing malignant lymphadenopathy, Scattered peritoneal nodules suspicious of metastatic deposits.
Results: During admision the patient received full dose anticoagulation (Low Molecular Weight Heparin: 60 iu /12 h). Upon diagnosis we arrange the transferal to the oncology department to continue her management plan. Unfortunately; the case was terminal for palliative therapy and she died after 2 weeks.
Conclusion: Bluish discoloration of digits and toes may be a clue for diagnosis of many diseases not only vasculitis. Malignancy can disturb the immune system in a way that mimic any systemic connective tissue disease. Acute insult aggressive multiple site deep venous thrombosis (DVT) necessitate thinking outside the box and consider other causes of coagulopathy like visceral malignancy.
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Figure 1.

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AB1510 INFLAMMATORY MYOSITIS – FINAL ANSWER?

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Background: Motor neurone disease may mimic inflammatory myositis. There is an overlap in clinical symptoms (such as muscle weakness, dysphagia and respiratory involvement) which may pose a diagnostic challenge. Careful history, thorough clinical examination and appropriate investigations can help to distinguish between the two. Monitoring the response to treatment is also crucial. We present a case that presented to rheumatology with progressive muscle weakness, she was investigated and treated for inflammatory myositis but was later diagnosed with motor neurone disease.

Objectives: To illustrate the need for thorough clinical assessment and investigations in patients with suspected inflammatory myositis and consider alternative diagnoses as clinical picture evolves.

Methods: A 68 year old lady, presented with 6 months history of progressive proximal muscle weakness. She also reported weakness of grip, affecting activities of daily life. She was finding it difficult to get up from chair. There was no swallowing difficulty, respiratory symptoms and skin rash. She had no weight loss or constitutional symptoms. She did not have any joint pain or features of connective tissue disease. She had history of hypertension. On clinical examination, she did not have any features of connective tissue disease. There was no evidence of joint synovitis or skin rash. Proximal power in upper and lower limbs noted to be 4/5 with intact reflexes. Initial investigations revealed mildly raised CPK at 287 with normal thyroid function and inflammatory markers. Immunological tests including ANA and myositis panel were requested alongside EMG, MRI thighs and CT chest/abdomen/pelvis. Myositis panel was positive for anti-MDA-5 antibodies (in the absence of any skin or respiratory symptoms). There was no evidence of malignancy on CT imaging. MRI thighs revealed fluid in the trochanteric bursae. She was trialled on oral prednisolone in view of her clinical features and positive anti-MDA5 antibody. However, there was no improvement in her symptoms or functional status. EMG revealed widespread neurogenic process affecting upper and lower limbs on both sides, without significant evidence of acute myopathy. The progressive nature of symptoms with the upper motor neurone signs raised the possibility of an evolving anterior horn cell disorder. She was referred to neurology and was subsequently diagnosed to have Motor Neurone Disease. The steroids were rapidly tapered off and stopped.

Results: Motor neurone disease is an important differential when considering inflammatory myopathy, particularly inclusion body myositis which causes more progressive muscle weakness. It is a neurological disorder characterised by degeneration of neurons. There is no clear cause identified. MND causes both upper and lower motor neurone signs. Symptoms include limb weakness, bulbar weakness that can affect speech and swallowing, muscle twitching and fasciculation. Respiratory weakness may occur. Thorough clinical examination and EMG findings help identify the diagnosis. Imaging may be needed. There is no cure. Management requires an MDT approach, primarily guided by neurology, including physiotherapy, occupational therapy, speech and language therapy and respiratory support.

Conclusion: This lady was initially treated for inflammatory myositis based on her symptoms, mildly raised CK and positive anti-MDA5 antibodies. On review of her clinical progress, we noted poor response to steroids and EMG results pointing at an alternative diagnosis of MND. This case highlights the importance of EMG in the assessment and management of patients with suspected inflammatory myositis as well as the need to closely monitor progress and re-evaluation where needed. Although she had anti-MDA-5 antibodies and mildly raised CK, she did not have any skin disease or other systemic features, inflammatory markers and muscle imaging was normal. Response to steroids was inadequate.

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AB1511 SLE ONSET POST COVID-19 VACCINATION: COINCIDENTAL OR ASSOCIATION?

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Background: Numerous immune-mediated diseases flare or new disease onset after SARS-CoV2-vaccination have been reported. There were case reports showed the immune-mediated disease flare post vaccination but study on new disease occurs post Covid-19 vaccination is still lacking.

Objectives: To describe two SLE cases that diagnosed post Covid-19 vaccination.

Methods: Case report

Results: 14 years old girl, post Covid-19 vaccination 1st dose 3 weeks ago presented with 2 day history of giddiness, breathlessness, vomiting and diarrhea prior to admission. She also complained of frothy urine for the past 1 week associated with lower limbs swelling and facial puffiness. Clinical examination noted she had sparse hair, oral ulcers and discoid lupus at the ear concha. She also noted to have periorbital puffiness with pedal edema. Lung auscultation noted bi-basal crepitations. Blood investigation noted ANA positive (1:640, speckled) with low complement 3 (0.1g/L). Her full blood count showed leucopenia (3100 UL) with low lymphocyte count of 810UL. UFEME noted protein of 3 + and red blood cell of 2+ with normal renal profile. Her serum albumin was 22g/L. Chest x ray showed clear lung field with no cardiomegaly. Her 24-hour urine protein showed proteinuria of 2.345g/dl and her renal biopsy showed mesangial proliferative lupus nephritis class ii. She was given intravenous methylprednisolone 500mg OD for 3 days and discharged with tapering dose of prednisolone, hydroxychloroquine, calcium supplements, perindopril and frusemide. Another case was a 17 year-old female, post covid-19 vaccination 10 weeks, presented with 3 weeks history of bilateral lower limbs weakness with difficulty in getting up from chair. She also had fever on and off with cough for 1 week. There was no alopecia, oral ulcer, facial rash or photosensitivity. No joints pain. Clinical examination noted presence of proximal myopathy with stable vital signs. Other systemic examinations were unremarkable. Blood investigation noted ANA positive (1:640, homogenous and speckled) with low complements level (C3 0.19g/L and C4 0.049 g/L).Her creatine kinase was 2367U/L and EMG showed evidence of irritable myopathic process which is consistent with inflammatory myositis. Her TFT was normal. Myositis panel showed anti-Ku and anti-Ro 52 were positive. She was treated as SLE with myositis and intravenous methylprednisolone was given. She discharge well with tapering dose of prednisolone and azathioprine. Her creatine kinase showed improvement with immunosuppression therapy and she was advised on intensive physiotherapy.

Conclusion: The onset of these two SLE cases were occurred within the 2 month of post covid-19 vaccination. Whether Covid-19 vaccination direct contribute to the occurrence of SLE remained inconclusive. More studies are required to show its correlation between onset of SLE and Covid-19 vaccination.

References: NIL

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AB1512 CENTRAL RETINAL ARTERY OCCLUSION (CRAO) LEADING TO BILATERAL BLINDNESS; DUE TO BOTH ARTERITIC AND NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY

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Background: Giant cell arteritis (GCA) is a large vessel vasculitis which is common in the elderly. It affects the cranial branches of the aorta, commonly superficial temporal, posterior ciliary and retinal arteries. Hence blindness can be one of the dreaded complications of the disease which makes prompt diagnosis and treatment of utmost importance. Sometimes atypical presentations and concurrent pathologies can make the timely diagnosis of the disease difficult. Therefore it is very important for clinicians to be vigilant of the varied presentations of the GCA and coexisting vascular risk factors.

Objectives: A 78-year-old Caucasian male was presented with acute onset blindness of the left eye. It started as few blotchy patches in the peripheral visual field and gradually became diffuse visual loss over a few days. He denied any headache, temporal tenderness, tongue or jaw claudication or symptoms of polymyalgia rheumatica. Following ophthalmology review he was diagnosed to have CRAO with marked disc pallor without any evidence of retinal emboli. He was in sinus rhythm, no carotid bruits or cardiac murmurs were noted. His comorbidities were hypertension and hypercholesterolemia. He was assessed in the transient ischemic attack clinic for screening for vascular risk factors and started on anti platelets.

Methods: Three months later he re-presented with visual loss in the right eye. Apart from the mild tenderness of the right temporal region noticed when trimming his hair he had no symptoms of GCA. He was started on dual antiplatelets and urgently referred to ophthalmologist who diagnosed central retinal artery occlusion of right eye with clear demonstration of emboli in all the arcades of the central retinal artery. A temporal arterial biopsy was performed.

Results: His CRP was 19mg/l & ESR was 18mm/hr initially. During the second presentation both ESR (35) and CRP (40) were further elevated. His carotid doppler did not show significant stenosis in internal carotid arteries. ECG at presentation was in sinus rhythm however 24 hour holter monitoring after involvement of both eyes showed paroxysmal atrial fibrillation (PAF). Transthoracic echocardiogram was normal. His temporal arterial biopsy showed destruction of the internal elastic lamina with lymphohistiocytic infiltration and occasional giant cells in keeping with a diagnosis of GCA. Patient was started on prednisolone 60 mg daily followed by a tailing off regime and antiplatelets were changed to anticoagulation due to PAF. His vision improved mildly, only in the right eye in the way of perception of hand movements.

Conclusion: CRAO is an ocular emergency and is the ocular manifestation of a stroke. The usual presentation is a painless unilateral visual loss leading to profound blindness and is commonly due to non arteritic causes like carotid artery stenosis, cardiogenic embolism, small vessel disease and rarely due to arteritic causes like GCA. Accurate identification of the aetiology is very important to avoid further recurrence. By consensus multiple retinal emboli usually excludes a diagnosis of GCA[(1).] However considering, the patient's age and recurrence of CRAO while on antiplatelets led us to consider occult GCA. 21.2% of patients with GCA induced vision loss do not have any systemic symptoms of the disease[(2)]. Hence there should be a high index of suspicion when an elderly person presents with ischaemic ocular manifestations especially optic nerve and retinal ischaemia even in the presence of another plausible explanation like PAF.

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AB1513 SIROLIMUS INDUCED INFLAMMATORY ARTHROPATHY

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Background: Sirolimus is a non-calcineurin immunosuppressant commonly used in patients with organ transplantation to prevent rejection. While various inflammatory syndromes have been described post-sirolimus use, it is uncommon to have inflammatory arthritis to sirolimus[1]. We present a patient who developed significant joint inflammation following sirolimus use.

Results: Our patient is a 39 year old gentleman who had a heart transplant in 1992 following dilated cardiomyopathy. He was switched to sirolimus after concerns about chronic kidney disease and graft vascular disease. Six weeks later, he developed bilateral foot pain and swelling which prevented him from weight bearing. He had an MRI which showed significant bone marrow oedema in the midfoot tarsal bone and basal metatarsals. He then had a nuclear scan which showed highly increased and symmetrical uptake in both mid feet affecting the cuneiform and second, third and fourth bases of the metatarsals. The appearances showed increased osteoblastic activity with increased vascularity which was more in keeping with bone inflammation/infection and no osteonecrosis. His C-reactive protein was elevated at 148. This improved to 30 after cessation of the sirolimus. Blood cultures were negative. Of significance in his history, he also suffers from gout and has had previous monoarthritic flares involving his wrist, elbow and index finger. However, he was placed on febuxostat 80 mg in 2018 with excellent response. His serology was negative for anti-CCP and Rheumatoid factor. His urate levels were controlled at 374. He was also found to be HLA-B27 positive, but there was no evidence of inflammatory back pain.

He was placed on a tapering course of prednisolone and coupled with the cessation of the Sirolimus, his pain and swelling resolved. In follow-up clinic appointments, he remained in remission from his inflammatory arthritis and did not require any additional treatment but continued on Mycophenolate Mofetil and Ciclosporin for his cardiac transplant.

Conclusion: There are many studies investigating the use of sirolimus as an anti-inflammatory agent in autoimmune conditions such as rheumatoid arthritis[2] and inflammatory bowel disease[3]. The mechanisms include down regulation of IL-17 and IL-6[3]. However, the induction of an inflammatory arthritis by sirolimus can paradoxically occur as sirolimus causes a reduction in the STAT 3 and the anti-inflammatory cytokine IL-10[3]. There has been raised levels of IL-6 and TNFα in serum of patients with inflammatory sequelae post sirolimus therapy[1]. This disequilibrium of inflammatory cascade is related to the ability of Sirolimus to inhibit mammalian target of rapamycin (mTOR) which then subsequently modulates these effects[4]. In general, these pro-inflammatory sequelae are mild and tend to resolve after cessation of the drug[1]. Although our patient had severe arthritic manifestations which required steroid therapy, his symptoms were transient after removal of Sirolimus.

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AB1514 AN UNUSUAL ASSOCIATION BETWEEN THROMBOTIC THROMBOCYTOPENIC PURPURA AND PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: Thrombotic thrombocytopenic purpura (TTP) is a rare and life-threatening thrombotic microangiopathy characterized by microangiopathic haemolytic anemia, consumption thrombocytopenia and organ injury, particularly kidney failure and neurological manifestation[1]. Two forms are distinguished: the hereditary one, caused by a deficit of the metalloprotease ADAMTS13, and the idiopathic one characterized by the presence of antibodies directed against ADAMTS13. The second one is the most common. There are various subgroups of acquired TTP associated with HIV infection, sepsis, pregnancy, autoimmune disease, disseminated malignancies and drugs. Antiphospholipid syndrome (APS) is a clinical immunological condition characterized by thromboembolic events, repetead miscarriages or stillbirth and thrombocytopenia; it can be a primary disorder or due to connective tissue disease, in particular systemic lupus erythematosus[2].

Objectives: We describe a case of TTP associated with a primary APS. The real clinical challenge lies in the differential diagnosis between TTP and anti-phospholipid antibody syndrome.

Methods: A 37-year-old man presented to the emergency department for short-term episodes of anesthesia of the right upper limb and face with spontaneous resolution. In his past medical history, he suffered of antiphospholipid syndrome treated with warfarin. Upon admission, blood tests revealed severe thrombocytopenia, haemolytic anemia with schistocytes on peripheral blood smear, low thrombin time and prolongation in the prothrombin time. Neurological symptoms were assessed by electroencephalogram and CT brain, resulted negative, while a brain MRI revealed acute-subacute ischemic stroke. Based on these findings we suspected a diagnosis of TTP, subsequently confirmed by reduced activity of ADAMTS-13 with borderline ADAMTS-13 inhibitory antibodies. Immunological testing confirmed positivity of antiphospholipid antibodies and antinuclear antibodies.

Results: According to the last guidelines3 about management of acute episode of TTP, immediate therapy with high-dose corticosteroids (prednisone 1 mg/kg) and plasmapheresis was started and then we added infusion of rituximab (375 mg/m2/week for 4 times). Efficacy of treatment was evaluated by weekly dosage of ADAMTS13 activity, with a gradual rise in values (3 → 78%) and improvement in symptoms and laboratory examination. After persistent remission, we gradually reduced steroid therapy. Few months later, in February 2021, patient developed a bilateral comunitary pneumonia, that required hospitalization, oxygen - therapy (also with C-PAP) and endovenous antibiotics. After two weeks patient was discharged from hospital in good clinical health and he was subjected to periodic outpatients visits. Disease activity was in remission, so steroid therapy was reduced and recently we added hydroxychloroquine for APS. Some days ago patient developed covid – 19 infection, despite vaccination, and he was treated with monoclonal antibodies, with good clinical response.

Conclusion: We have described a rare clinical case of TTP, despite concomitant warfarin treatment for primary anti-phospholipid syndrome. A careful follow-up of these medical conditions is recommended for patient's fragility and for the risk of related serious clinical complications.

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AB1515 ANCA-NEGATIVE PAUCI-IMMUNE GLOMERULONEPHRITIS AS A PARANEOPLASTIC MANIFESTATION OF SARCOMATOID MALIGNANCY

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Background: Pauci-immune glomerulonephritis (PIGN) is a type of small vessel vasculitis associated with anti-neutrophilic cytoplasmic antibodies (ANCA). However, about 10-20% of PIGN patients have negative ANCA serologies. PIGN as a paraneoplastic syndrome is rarely described in literature with a few cases reporting an association with lung cancer.

Objectives: We describe a case of ANCA negative glomerulonephritis in a patient with underlying malignant sarcoma responsive to rituximab.

Methods: An 80-year-old female was admitted with complaints of upper abdominal pain and new onset hematuria for 2 days. Vital signs were stable, and physical exam was remarkable for mild tenderness on deep epigastric palpation. Initial laboratory workup was significant for acute kidney injury with serum creatinine of 2.1 mg/dl (creatinine two months ago at outpatient visit was 1.0 mg/dl). Urinalysis showed 4+ proteinuria and dysmorphic red blood cells. CT scan of the abdomen revealed a soft tissue mass surrounding celiac artery and a right adrenal hypodense mass. Further serologies to elucidate the cause of kidney injury revealed normal perinuclear-ANCA and cytoplasmic-ANCA levels. Renal biopsy was positive for focal segmental necrotizing and crescentic glomerulonephritis consistent with pauci-immune vasculitis. She also underwent right adrenal and celiac mass biopsy; both revealing malignant spindle and epithelioid cell neoplasm consistent with undifferentiated pleomorphic sarcoma (UPS). Our patient was treated with four rounds of plasmapheresis followed by 600mg rituximab infusion which decreased her creatinine to 1.7 mg/dl and resolved hematuria within 10 days of admission. She was followed up in rheumatology clinic two weeks later where she denied further hematuria and was given another round of 600mg rituximab infusion.

Results: UPS is a rare soft tissue cancer with a 5-year survival rate as low as 15% in metastatic disease. Paraneoplastic manifestations of UPS are seldom described in literature due to poor prognosis of the disease and low annual incidence. PIGN is scarcely reported in association with lung carcinoma in a few case reports[1, 2]. It is interesting to note that in these cases there was antecedent chemotherapy raising suspicion of vasculitis induced by adjuvant agents. As our patient did not receive chemotherapy, PIGN was deemed to be a paraneoplastic phenomenon secondary to malignant sarcoma.

Conclusion: This case underscores the importance of recognizing sarcoma as a possible etiology of paraneoplastic ANCA-negative PIGN. We also explain how plasmapheresis and rituximab may play a role in the treatment of renal dysfunction in these patients.

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AB1516 A CASE OF SEVERE ANCA ASSOCIATED VASCULITIS AFTER COVID-19 VACCINATION

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Background: The world is currently rocking to and fro in the midst of the COVID-19 viral storm and vaccinations have played a pivotal role in calming this.Although COVID-19 vaccines have been thoroughly assessed and studied before being rolled out to the general population, there have been reports of post vaccination complications in limited number of subjects strongly associated with COVID-19 vaccinations[1].

Objectives: To report a case of severe ANCA associated vasculitis after COVID-19 vaccination.

Methods: A case report and discussion.

Results: In view of this, we report the case of a 77 year old caucasian male who developed severe ANCA associated vasculitis (AAV) after two doses of Astra-Zeneca vaccine and one booster dose of Pfizer COVID-19 booster. He presented with acute onset inflammatory arthritis with mononeuritis multiplex with bilateral foot drop and left radial and ulnar nerve forearm weakness in typical asymmetrical pattern two weeks after the Pfizer vaccination. He had a raised MPO-ANCA titre of 66 IU/ml, C-reactive protein of 131mg/L and reactive thrombocytosis of 458 X 10 ^{9}/L. Nerve conduction study confirmed mononeuritis multiplex in the bilateral peroneal nerves and left radial and ulnar nerve. A total body CT had excluded malignancy and paraneoplastic associations and Gullian-Barre diagnosis was also excluded. The patient was treated with 3 days of intravenous methylprednisolone 1g daily then given intravenous Rituximab 1g, two weeks apart. He is currently undergoing rehabilitation in view of the vasculitic neuropathy from his diagnosis.

Conclusion: Diagnosis of AAV is often delayed or missed by other medical specialties due to its varied presentation. AAV should be suspected in a patient with paraesthesia/weakness in keeping with mononeuritis multiplex or other peripheral neuropathy in the absence of an alternative explanation (e.g. diabetes,B12 deficiency) and in particular with a wrist or foot drop.Exposure to certain drugs and substances of abuse such as cocaine, hydralazine and propylthiouracil has been implicated with AAV.While short-term side effects of COVID-19 vaccine resemble those of other vaccines, long-term side effects remain unknown[2]. Rare side effects continue to surface as millions of people receive COVID-19 vaccines around the world.

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[2] **https://doi.org/10.1136/bmj.m1070**

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AB1517 SYNOVITIS COMPLICATING THE COURSE OF COMMON VARIABLE IMMUNODEFICIENCY: CAUSAL OR COINCIDENTAL?

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Background: Common variable immunodeficiency (CVID) is a heterogeneous disorder characterized by hypogammaglobulinemia and an increased susceptibility to recurrent bacterial infections. Even though several immunological defects are involved in the pathogenesis of CVID, the genetic background of the disease

remains unidentified [1]. Autoimmunity in CVID is not restricted to hematologic cells, as rheumatologic complications occur in perhaps 10% of patients, with females being more affected [1].

Objectives: Here by we report a case of a CVID complicated with RF negative synovitis.

Methods: We report a case of a 36-year-old woman who was referred to our department for oligoarthritis. She had a history of primary immune deficiency revealed at the age of 30 with recurrent pulmonary infections. The disease was complicated with type 1 diabetes and bronchiectasis and was treated with annual infusion of immunoglobulin. The patient presented with pain and swelling in both knees evolving for two months. On physical examination, she had synovitis in both knees. Laboratory investigations revealed normal blood count with elevated C-reactive protein (CRP) and erythrocyte sedimentation rate: 36.2mg/l, and 32 mm/h respectively. Synovial fluid aspiration analysis of the knee revealed an inflammatory liquid without crystals. Bacterial culture was negative. Her serum was negative for Rheumatoid Factor (RF), anti-cyclic citrullinated peptide (anti-CCP) antibody and antinuclear Antibodies (ANA). Knee ultrasound revealed synovitis in both knees with Doppler signal. The Magnetic resonance imaging (MRI) of the knees showed active synovitis without any erosion. Ophthalmological assessment showed severe dry eye syndrome. As Sjögren's syndrome was suspected, we performed a salivary gland biopsy that was normal.

Results: The patient did not fulfill criteria for auto-immune rheumatic related disease. She was treated with intraarticular glucocorticoids injections, with complete resolution of symptoms and disappearance of effusion on ultrasound. A follow-up was scheduled after one month. The synovitis has been attributed to rheumatologic involvement in the context of immune deficiency.

Conclusion: We report a rare case of RF negative synovitis complicating the course of CVID. Even though the symptoms could be mild compared to a typical RF+RA, it is important to educate clinicians as to the importance of maintaining a high index of suspicion about this rare, yet potentially treatable disease. Future research is indicated to understand the etiopathogenesis of rheumatologic manifestations in CVID.

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AB1518 CASE REPORT OF A HARD TO TREAT DERMATOMYOSITIS AFTER A COVID-19 INFECTION AND SUBSEQUENT VACCINATION

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Background: A 50 years old woman, a medical doctor, came to our department with symmetrical proximal muscular weakness, several months after Covid-19 infection and three weeks after a second dose of Covid-19 mRNA vaccine. The patient had no prior or family history of autoimmune diseases and take no medicines. In the past she undergone an operation for double-kidney with frequent urinary infections. Objective findings have shown symmetrical proximal muscular weakness and classic sings of dermatomyositis - Gottron's papules, shawl and holster signs, periungual vasculitis.

Objectives: We present a case of a 50 old woman with clinical and laboratory proven dermatomyositis, starting three weeks after a second dose of a Covid1-19 mRNA vaccine without other reasons.

Methods: The laboratory tests showed elevated CPK, lactate dehydrogenase, aspartate aminotransferase and alanine aminotransferase, high ANA – 1:1280 and myositis specific autoantibodies- anti-NXP2 and anti-Mi-2-beta. The electromyography showed myopathic changes and the muscle MRI – symmetrical edema of mm.obturator and mm.adductor brevis. We exclude diseases that may mimic inflammatory myopathies. We made a cancer screening – whole body MRI, colonoscopy, gastroscopy, mammography and gynecological exam, immunoblot for detection of paraneoplastic syndrome-associated neuronal antibodies, with no detection of cancer. Muscle biopsy of m.vastus lateralis showed attenuating muscle inflammation with advancing muscle atrophy and fibrosis.

Results: The diagnose dermatomyositis was made according Bohan and Peter criteria and we start a high dose (1mg/kg/day) glucocorticoid therapy with good initial clinical and laboratory effect. Two months after starting a therapy muscle weakness worsened together with difficulty of swallowing. We excluded steroid myopathy after second EMG and lack of improvement when tapering the GS dose. Methotrexate 20 mg/weekly was added as a steroid sparing drug with good response, but was stopped because flare of pyelonephritis. Accordning to the opinion of dermatologist hydroxychloroquine was started for a couple of weeks, because of active skin manifestations. Muscle weakness worsened on the background of treatment, which was stopped. We started a therapy with intravenous immunoglobulins and considered therapy with cyclophosphamide or azathioprine after urinary infection. Because the patient was infected for a second time with covid-19, although vaccine, we continued only with glucocorticoids and anti-osteoporotic therapy.

Conclusion: The etiology and pathogenesis of inflammatory myopathies are not fully clarified so far. We speculate that the infection with Covid-19 as well as mRNA vaccine trigger inflammatory myopathy and compromise the patient's immunity for poor treatment response with glucocorticoids and immunosuppressives. On the other hand advanced muscle atrophy and fibrosis within a short period show that suspected triggering factors could be a reason for difficult to treat such type of dermatomyiositis.

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AB1519 STEROID FREE REMISSION IN ORGAN THREATENING ANCA ASSOCIATED VASCULITIS: WITHOUT AVACOPAN

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Background: Steroid free remission in organ threatening ANCA associated vasculitis is currently described only with Avacopan, a C5a receptor inhibitor. However, this drug is not yet available for use in the third world.(1)

Objectives: To describe a clinical case of granulomatous polyangiitis with orbital pseudotumor right eye with optic atrophy, who developed steroid induced central serous retinopathy in the other eye, necessitating a steroid free treatment regime.

Methods: A 45year old man was admitted to the department of clinical immunology, JIPMER in January 2021 with Orbital pseudotumor Rt eye since 2019 causing optic atrophy, treated with high dose steroids for more than a year. He developed steroid induced central serous retinopathy of left eye, necessitating withdrawal of steroids, leading to disease flare in the form of painful right orbital inflammation, acute glomerulonephritis, vasculitic ulcers over leg and lung nodules. His PR3 ANCA titers were elevated at the time of disease flare. His sputum infectious workup was negative for bacteria/fungus/tuberculosis. He was treated with 10 cycles of radiotherapy to right eye for debulking followed by exenteration. As he had pseudomonal infection in the post operative orbital cavity at the time of flare, 2 monthly

Table 1. Investigations:

	Week 0	Week 28	Week 48
Hemoglobin(g/dl)	5.5	7.8	10.7
Creatine (mg/dl)	1.43	1.35	1.0
Albumin (mg/dl)	1.9	2.5	3.8
Urine analysis	Protein:2+ RBCs:50 -100/hpf	Protein:1+ RBCs: 10-15/hpf	Protein: trace RBCs: <10/hpf
CECT Thorax	Left upper lobe solitary nodule	Resolved	
MRI orbit	RT orbital pseudotumor with optic atrophy	S/P exenteration	
Renal Biopsy	Focal proliferative sclerosing glomerulonephritis; No crescents.		
Orbital tissue biopsy	Palisading granuloma		
PR3 ANCA(ELISA)	57.63		
MPO ANCA(ELISA)	negative		
ANA	Negative		
C3/C4	1.61/0.32 (normal)		
ACE levels	25.3 (normal)		
IgG4	2.73		
BVAS	20	5	0
VDI	3	3	3

Abbreviations: hpf: high power field, CECT: Contrast enhanced computed tomography, PR3: proteinase3, MPO: Myeloperoxidase, ANA: Antinuclear antibodies, ACE: Angiotensin converting enzyme, BVAS: Birmingham vasculitis activity score, VDI: Vasculitis damage index

doses of IVIG 2g/kg was given; infection treated with antibiotics and regular dressing. After resolution of infection 6 doses of cyclophosphamide as per EUVAS protocol and Rituximab 2 gm was given along with the first dose of Cyclophosphamide.

Results: At 48 weeks of follow up, he continues to be in sustained clinical remission without steroids. He has received additional 500 mg of rituximab at 28 weeks. His lung nodules and vasculitic ulcers of leg healed over 34 weeks. He has developed saddle nose deformity for which reconstruction is planned.

Conclusion: Steroid free remission in GPA may be possible without Avacopan.

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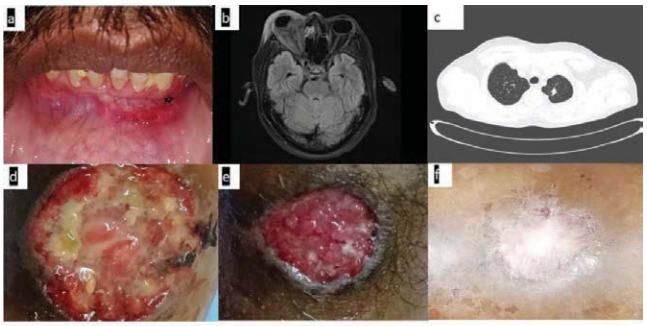

a: Gingivitis , b: Right orbital pseudotumor compressing optic nerve, c: left lung nodule
d: leg ulcer at week 0, e: leg ulcer at week 20, f: leg ulcer at week 34

Figure 1. Clinical features of GPA

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AB1520 EFFECTIVE TREATMENT OF TOCILIZUMAB IN PATIENTS WITH REFRACTORY ADULT-ONSET STILL'S DISEASE

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Background: Pro-inflammatory cytokines such as interleukin 6 (IL-6) are involved in the pathogenesis of adult-onset Still's disease (AOSD). Anti-IL-6 agents such as tocilizumab have been tried to treat AOSD successfully.

Objectives: To access the efficacy of tocilizumab in the treatment of AOSD patient refractory to,or with initial treatment.

Methods: We reviewed three cases with refractory AOSD treated with tocilizumab. All patients fulfill the Cush criteria for AOSD. All patients performed blood culture, auto-antibodies test and bone marrow test to exclude infectious diseases, other rheumatic diseases and tumors. All patients received broad-spectrum antibiotics and had no response. All patients received glucocorticoid therapy and at least one kind of anti-cytokine therapies but didn't have full response. Then the three patients received intravenous tocilizumab treatment of 8mg/kg every 2 weeks or 4 weeks.

Results: The first patient, a 21-year-old woman, performed positron emission tomography (PET-CT) and lymphoglandula pathology in addition to routine tests. She received high dose methylprednisolone (500mg per day for 3 days and followed by 80mg per day), gamma globulin injection (20g per day for 3 days) and baricitinib 4mg per day for 12 days, but had no response to the treatment. Then she received tocilizumab of 8mg/kg every 2 weeks and stopped baricitinib. And the symptoms and blood tests improved gradually, and the methylprednisolone dose reduced to 16mg per day at the last follow-up. The second patient is a 52-year-old man, and performed bone marrow cytology and PET-CT to excluded hematological diseases. He received methylprednisolone 80mg per day, adalimumab and tofacitinib treatment. But the patients still got recurrent fever, high ESR, CRP and serum ferritin. Then he stopped adalimumab and tofacitinib, and received tocilizumab of 8mg/kg every 2 weeks and reduced to 8mg/kg every 4 weeks because of economic factors. The patient did not develop fever and the inflammatory indexes such as ESR/CRP gradually decreased to normal range. And methylprednisolone dose reduced to 32mg nowadays.

The third patient is a 30-year-old woman and has recurrent AOSD for 15 years. She had tried glucocorticoids, methotrexate, iguratimod, baritinib and entanercept successively. Yet she still had recurrent arthritis on hand and knee, and elevated ESR/CRP/serum ferritin. Additionally she suffered femoral head necrosis because of excessive doses of glucocorticoid. The patient received tocilizumab 8mg/kg every 4 weeks, then joint symptoms and inflammatory indicators improved significantly. The methylprednisolone dose was also successfully reduced to 4mg/d.

The Figure 1 showed the main course of disease evolution.

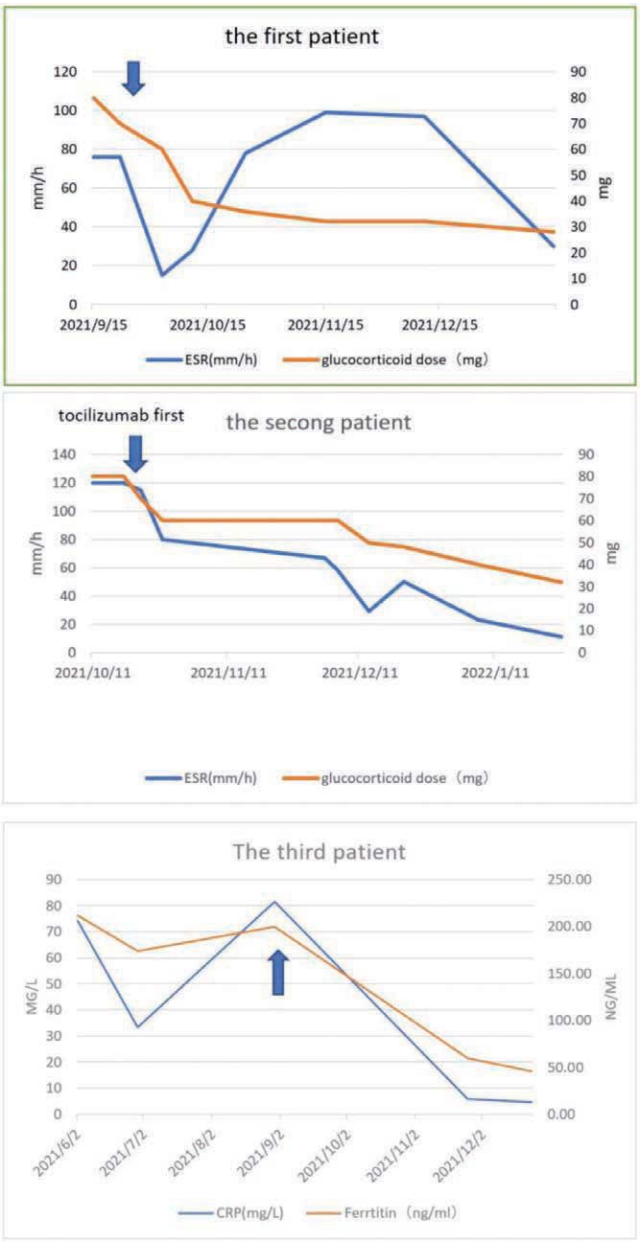

Figure 1.

Conclusion: Tocilizumab may be an effective candidate in refractory AOSD despite no response to other treatments.

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AB1521 IGG4-RD AND SLE: COEXISTENCE IN THE KIDNEYS

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Background: IgG4 related disease (IgG4-RD) is an immune-mediated fibro-inflammatory condition that can mimic malignant, infectious and inflammatory diseases (1). Systemic lupus erythematosus (SLE) is a chronic autoimmune condition characterized by multisystem inflammation and autoantibody generation (2). Overlap of IgG4-RD and SLE is not frequent, however there have been few cases reported with kidney involvement secondary to both conditions (2,3). We present a case of an elderly male with a new diagnosis of IgG4-RD and SLE with kidney involvement.

Objectives: To present a case with a new concomitant diagnosis of IgG4-RD and SLE.

Methods: Case report.

Results: A 67-year-old man with longstanding history of cervical lymphadenopathy (LAD) presented to the Rheumatology Clinic due to intermittent lower extremity rash, anemia, worsening fatigue for the past 2 years. Prior history includes controlled DM type 2 and HTN treated with amlodipine. Denied photosensitivity, oral ulcers, sicca symptoms, Raynaud's phenomenon, weight loss, fever, chills, joint pain. Physical examination revealed bilateral cervical LAD and a non-blanching purpuric rash on lower extremities consistent with leukocytoclastic vasculitis, later confirmed with biopsy. Further workup revealed, normocytic anemia (Hgb 9.9 mg/dl), positive ANA (>1:2560, homogeneous pattern), positive dsDNA (211 IU/ml), positive histone Ab (413 IU/ml), low C3 (28 mg/dl), low C4 (1 mg/dl), increased IgG4 level (2787 mg/dl) and proteinuria 1100 mg/g with microalbuminuria, no urine casts. ANCA serologies were negative. Pan-CT showed mild cervical, retroperitoneal, pelvic LAD bilaterally. Kidney biopsy was performed and revealed severe diffuse tubulointerstitial nephritis, plasma cell rich (more than 40 IgG4 + cells seen per 40X hpf), with moderate to severe chronicity in addition to diffuse mesangial IgG and IgM staining with focal tubular basement membrane IgG and C1 staining consistent with mesangial proliferative class II lupus nephritis. Patient was started on moderate dose steroids (due to DM), hydroxychloroquine and azathioprine with resolution of LCV rash, anemia, LAD, improvement in dsDNA, proteinuria, complement levels.

Conclusion: SLE and IgG4-RDs are autoimmune diseases that cause damage to several organs, including lymph nodes and kidneys. Both are associated with hypocomplementemia and involvement of autoantibody-producing B cells and plasma cells. Patients with SLE present with positive antibodies such as anti-dsDNA and anti-Sm antibodies. On the other hand, IgG4-RD lack a specific antibody and the IgG4 is thought to be the result of the pathogenic process and not pathogenic by itself (1,2). Histologically, SLE presents with inflammatory cell infiltration in organs, whereas IgG4-RD is associated with fibrosis and organ enlargement (1-3). Lupus nephritis causes wide spectrum renal involvement whereas IgG4-RD most common presentation is tubulointerstitial nephritis (TIN), although other glomerular lesions, such as membranous nephropathy, have been reported (1-2). Our patient presented with proteinuria, positive antibodies for SLE, low complements and high levels of IgG4 which makes us consider that both diseases were active at time of diagnosis. This was confirmed by renal biopsy showing chronicity of IgG4-RD and lupus nephritis as a consenquence of progression of autoimmunity. The treatment of both conditions is immunosupression with medium to high doses of steroids and a steroid sparing agent. Due to patient preference he was started on azatioprine along with medium dose steroids with adequate clinical response. This case highlights the fact that SLE and IgG4-RD can coexist and it should be supected in elderly patients with lympadenopathy and renal disease.

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AB1522

THE ASSESSMENT OF KNOWLEDGE OF NURSES BEFORE AND AFTER TRAINING ABOUT SPONDYLOARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: Nurses' education programs play an important role in the management of chronic diseases in rheumatology clinics. They can assume their own patient case-loads and provide an educative role to promote health.

Objectives: In order to foster educational programs, the present study aimed to assess the level of knowledge of nurses before and after targeted training sessions.

Methods: The nurses of the rheumatology department of Mongi Slim Hospital have been included initially during the month of September 2021, then later, after having followed a training during the month of January 2022. Data were collected by two self-administrated tests. The rheumatoid arthritis knowledge assessment scale (RAKAS) (1) which consisted of 13 items, defined knowledge as awareness about the disease, its risk factors, symptoms and treatment and categorized it into four levels namely, excellent, adequate, low and poor knowledge. The tool had a maximum of 14 points. A nurse was designed to have excellent knowledge if the score was 11 and above, adequately knowledgeable if the score was between 8 and 10, low knowledge if the score was between 5 and 7 and poor knowledge if it was 4 or less. Spondyloarthritis knowledge assessment questionnaire (SPAKE) (2) with 14 questions and 72 possible responses, divided into four areas, (A) general knowledge, comprising etiology, symptoms, blood tests (score range 0-8), (B) immunogenetic test (B27 antigen) and inheritance (score range 0-3), (C) general management, including drug treatment and physical therapy (score range 0-9), (D) joint protection, pacing and priorities (score range 0-5) The Wilcoxon signed rank test was used to assess the difference between test results before and after training. The level of statistical significance was set at $p<0.05$.

Results: Ten nurses were included with a sex ratio (M/F) of 0.3. Initially, the average RAKAS score was 11.7 ± 1.2. Almost two thirds of the nurses had excellent knowledge (n= 7, 70%) and the rest (n= 3, 30%) had adequate knowledge. The average SPAKE score was low (12.9±3.7). For the nurses interviewed in domain A, the maximum score was not reached and the average score was 5±1.6. For domain B, the maximum score was reached only once and the average score was 1.2±0.9. For domain C, the maximum possible score was not reached and the average score was 5.1±2.2. For domain D, the maximum score was not reached and the average score was low at 1.6±0.6. For the post-training test, the average RAKAS score was 12.6±0.5 and all nurses had excellent knowledge (n= 10, 100%). The average SPAKE score has risen (20.1±1.6). For the nurses interviewed in domain A, the maximum score was reached two times and the average score was 6.9±0.8. For domain B, the maximum score was reached four times and the average score was 2±0.9. For domain C, more than half of nurses have reached the maximum score (n=6, 60%) and the average score was 8.4±0.8. For domain D; the maximum score was not reached and the average score was 3.2±0.9. Differences between pre- and post-training test scores were found to be statistically significant for the SPAKE questionnaire ($p=0.005$) but not for the RAKAS ($p=0.077$).

Conclusion: The nurses' knowledge of rheumatoid arthritis was initially adequate, but not of spondyloarthritis, which improved significantly through the targeted training sessions.

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HPR Measuring health (development and measurement properties of PROs, tests, devices)

AB1523-HPR USABILITY AND ACCEPTABILITY OF A NEW AUTOINJECTOR DEVICE AND ITS ASSOCIATED APP IN AUSTRALIAN, FRENCH, GERMANY AND JAPANESE RHEUMATOLOGY PATIENTS

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Background: Smartclic/ClicWise is a new reusable autoinjector with a dose-dispensing cartridge for subcutaneous self-administration of biotherapeutics in development for patients with rheumatoid arthritis (RA) and other diseases. The device can connect to an optional mobile phone app (Smartclic, or ClicNote in Japan) to aid in tracking injections and other treatment or symptom data.
Objectives: The study objective was to collect ease of use and usability data on the Smartclic injector and companion app from experienced patients.
Methods: After completing a patient profiling questionnaire, adult patients (≥18 yrs) from Australia, France, Germany, and Japan with RA, psoriatic arthritis, or an original diagnosis of juvenile idiopathic arthritis who were prescribed an injectable biologic were enrolled in this study. For Japan, only patients with RA were enrolled. Each patient received training individually on the use of the Smartclic injector device and insertable cartridge and gained experience by performing simulated injections. Participants completed a questionnaire with evaluations of the device categories (number of questions): 'ease of use' (14), 'usability effectiveness' (11), 'benefit of features' (8), and 'form factor' (7). Participants also separately received a storyboard presentation summarizing the key features of the app, during which patients could explore the app (on a phone with either an android or iOS operating system), and completed 16 questions on the connectivity, usability, and benefit. Responses were recorded as Likert scale ratings from 1 ('extremely negative') to 7 ('extremely positive'). Respondents also provided an estimate of patient training time for the device. Mean values were reported. The percentage of negative (Likert scale rating 1-2), neutral (3-5), and positive (6-7) responses for each category were determined.
Results: A total of 139 patients (mean age [range], 52 [18-84] yrs; 73% female) participated in the study (Table 1). Mean scores (percentage of positive responses) for the device were: ease of use 6.43 (86.2%), usability effectiveness 6.39 (86.5%), benefit of features 6.46 (89.4%), form factor 6.10 (77.2%); and 6.06 (74.2%) for connectivity and benefit of the app (Figure 1). Mean estimated time for training a patient to effectively use the device/cartridge was just under 9.5 min (range, 0-30 min).

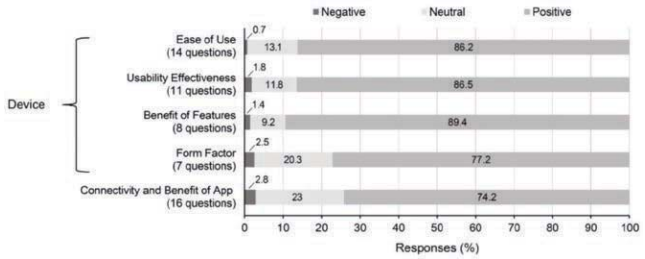
Table 1. Participant characteristics

Characteristic	Patients (N=139)
Sex, n (%)	
Male	38 (27)
Female	101 (73)
Mean age (range), yrs	52 (18-84)
Age groups, n (%)	
18-30 yrs	11 (8)
31-59 yrs	85 (61)
>60 yrs	43 (31)
Diagnosis, n (%)	
Rheumatoid arthritis	104 (75)
Psoriatic arthritis	34 (24)
Juvenile idiopathic arthritis*	1 (1)
Handedness, n (%)	
Right-handed	128 (92)
Left-handed	9 (6)
Ambidextrous	2 (1)

*Originally diagnosed with juvenile idiopathic arthritis, but now aged ≥18 yrs.

Conclusion: Rheumatology patients responded positively on the new autoinjector device and app across all categories, indicating its suitability for self-administration of biotherapeutics.

Figure. Summary of patient survey responses across all device and app questions*



*The percentages for each question were based on the Likert scale rating response: negative (1-2), neutral (3-5), and positive (6-7).

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AB1524-HPR THERAPEUTIC RESULTS AND QUALITY OF LIFE CHANGES OF PATIENTS WITH RHEUMATOID ARTHRITIS IN PROSPECTIVE REAL LIFE CLINICAL SETTINGS

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Background: Rheumatoid arthritis (RA) as a chronic inflammatory disease significantly deteriorating the physical functioning and the quality of life (QoL) of the patients. The introduction of biological therapy in its management significantly improves both the physical functioning and QoL. Many biological medicines are already available on the market claiming higher effectiveness and high cost of therapy but the difference in real clinical setting is not well studied.
Objectives: The aim of this study is to analyze the therapeutic results of RA therapy with different biologicals and the first JAK inhibitor in real life clinical settings.
Methods: This study was performed like a prospective, observational, longitudinal study at the biggest rheumatology clinic in Bulgaria during the period 2012 – 2020. Written informed consent was obtained by the recruited 197 patients, out of which 174 remain at the end of the observation. Patients naïve to biological therapy were assigned on the available at that moment biologic DMARDs (infliximab, etanercept, adalimumab, rituximab, golimumab, cetrolizumab, tocilizumab), and the first JAK inhibitor (tofacitinib). The clinically proven RA according ACR (1987) and / or ACR/EULAR (2010) criteria, previous therapy with DMARDs, and/or methotrexate, suitable for therapy with biological medicines or JAK inhibitors were formulated as inclusion criteria, while infectious diseases, cardiac insufficiency (NYHA III and IV grade), malignant hypertension, any neoplasms or proliferative lymph diseases within the previous 5 years were the exclusion criteria. We evaluate DAS28-CRP, HAQ and Short form 36 measured at the initiation of biological therapy, after 6, and 12 months of follow up. We analyze the changes in the two major subgroups of SF36 - physical (MCS) and mental health (PCS). Descriptive statistic, Dispersion analysis with non-parametric Kruskal-Wallis test comparing the effect of different therapies between first and third measurement was performed. Linear correlation and regression analysis (Pearson type) comparing the effect of different therapies was also performed.
Results: The age and gender distribution were similar between the groups on bDMARDs and tsDMARD. Number of patients per therapeutic DMARD vary between 20 to 30, with prevailing part of the female and average age between 53.2 (SD 9.13) and 57.15 (SD 9.05) years. Average length of the disease is also similar between the groups with highest value of patients assigned to tocilizumab (14.13 (SD 8.38) years) and lowest for infliximab (6.4 (SD 2.92) years), respectively. All observed indicators for disease control and QoL improve after the initiation of the biological or JAK inhibitor therapy. We also analyse the effect of therapies on DAS-28, HAQ, SF-36 (PCS, MCS). Dispersion analysis for the effect

of therapy measured through DAS28 between 1st and 3rd measurement shows a statically significant difference in between the average effect of therapies (P = 0.005141). The most effective is the golimumab (Median difference = 2.745), followed by rituximab (median = 2.305) and etanercept (median = 2.070). The difference in effect measured with HAQ is higher with tofacitinib (median 0,563). Followed rituximab and infliximab (median 0.500 for both). Less effective appears to be etanercept (median difference 0,250). All differences are statistically significant (p = 0,012589). Regarding the changes in the QoL measured with SF-36 MCS and PCS there is no statistically significant differences in the average effect of different therapeutic agents. The medical effect of different therapeutic agents regarding physical group of SF-36 (PCS) is similar and changes are not statistically significant. The same is valid for SF36 psychological components (MCS).
Conclusion: Tofacitinib and bDMARDs improve both clinical results and QoL of patients with RA naïve to biological therapy. The difference between tofacitinib and bDMARDs is not statistically significant for both clinical and QoL results.
Disclosure of Interests: Vladimira Boyadzhieva Speakers bureau: Boehringer ingelheim, Abbvie, Roche, Konstantin Tachkov: None declared, Nikolay Stoilov Speakers bureau: Abbvie, AMGEN, Konstantin Mitov: None declared, Guenka Petrova: None declared, Rumen Stoilov Speakers bureau: Abbvie, Pfizer, Roche, Boehringer ingelheim, MSD,
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AB1525-HPR EXAMINATION OF PHYSICAL FITNESS IN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: A COMPARATIVE STUDY

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Background: Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease of childhood. Although its etiology is not known exactly; Immunological susceptibility and environmental factors (infections, stress, trauma) are emphasized (1). These children have low activity levels since a young age, and significant problems are observed in the realization of daily living activities (2).
Objectives: This study aims to compare the physical fitness of children/adolescents with Juvenile Idiopathic Arthritis (JIA) and their healthy peers.
Methods: Seventy children/adolescents (mean age: 13.40±2.31 years 35 JIA; mean age: 12.94±2.31 years 35 healthy) were included in the study. After recording demographic data, the functionality levels of the children/adolescents with JIA were evaluated by CHAQ (Childhood Health Assessment Questionnaire), all lower extremity muscle strengths were evaluated by the manual muscle test device, and the physical fitness levels were evaluated by the Brockport physical fitness test battery which is grip strength, push-up test, curl-up test, trunk lift test, shoulder stretch, back saver sit-reach test, calf, triceps, subscapular skinfold thickness and PACER 20 meter test. While the disease activities of children/adolescents with JIA were evaluated with JADAS-27 (Juvenile Arthritis Disease Activity Score); quality of life were evaluated with the PedsQL 3.0 Arthritis Module (Pediatric Quality of Life Inventory).
Results: As a result of the comparative analysis; In terms of functionality which is CHAQ dressing (p=0.008), eating (p=0.011), reaching (p=0.001), rising (p=0.001), walking (p=0.001), holding (p=0.016), hygiene (p=0.011), activity (p=0.00), total score (p=0.00), pain (p=0.00), general well-being (p=0.00) in terms of all sub-parameters, there was found to be significant in favor of healthy children/adolescents (p<0,05). In terms of physical fitness which is grip strength (p=0,041), PACER 20 meter test (p=0,00), trunk lift test (p=0.018) and curl-up (p=0.00) tests, there was a significant difference in favor of the healthy group (p<0,05). There was no significant difference between the groups in terms of other physical fitness tests (p>0.05). When all lower extremity muscle strengths were compared, only right hip external rotation (p=0.023) showed a difference in muscle strength. There was no correlation between JADAS-27 score and physical fitness scores (p>0.05) of children/adolescents with JIA, except for the push-up test (p=0.01). In terms of JADAS-27 score and some PedsQL child form which is pain, total score and activities of daily living of children/adolescents with JIA; there was a significant relationship. In terms of JADAS-27 score and some PedsQL parent form which is pain and total score of children/adolescents with JIA; there was a significant relationship. However there was no relationship in terms of the other parameters (p>0.05).
Conclusion: According to the results of our study, it was observed that the functionality and physical fitness levels of children/adolescents with JIA were lower than their healthy peers, and physical fitness was not affected by disease activity. However, it has been observed that the disease ability of children/adolescents with JIA affects the quality of life of both themselves and their families. For all these reasons, it is very important to encourage children/adolescents with JIA in terms of participation in physical activity and exercise, with informative training aimed at improving their physical fitness.
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AB1526-HPR AWARENESS ASSESSMENT IN PATIENTS USING SUBCUTANEOUSLY ADMINISTERED BIOLOGICAL AGENTS ABOUT DRUG UTILIZATION

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Background: Subcutaneous biological agents (SCBA) are commonly used in rheumatologic disorders, their storage in appropriate conditions and correct administration have importance. Informing the patient adequately and correctly is essential. Storing the drug in inappropriate conditions reduces its effectiveness, and affects the response to treatment (1). When these treatments are initiated, information on all the mentioned topics is provided to the patients, and they undergo hands-on training. Finally, the patients is requestioned in outpatient follow-up about whether a problem has occurred or not (2).
Objectives: This study aimed to investigate the awareness of patients using SCBA about the drug's utilization and storage conditions.
Methods: Demographic data of 100 patients diagnosed with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, using SCBA who presented to our outpatient clinic between January 2021 and June 2021,were recorded, and survey questions were asked.
Results: One hundred patients (46 females-54 males) were included in the study. Sixty-one patients were diagnosed with ankylosing spondylitis, 20 patients with rheumatoid arthritis, and 19 with psoriatic arthritis. The patients' mean age was 44.6±11.07 years. The mean duration of SCBA use was 74.5 (2-222) months. The patients' replies to the survey questions are summarized in Table 1. Most patients performed the injection themselves in both genders, whereas some women received help from paramedics (p=0.041). Forty percent of the patients with education level of high school or higher had a concern regarding drug use, whereas this rate was 21% in patients with education level of primary school. It was determined that the anxiety level decreased with decreasing level of education (p=0.032).

Table 1. The patients' replies to the survey questions

N=100	n (%)
Rate of patients who read the patient consent form before starting the drug	88 (88)
Concern regarding drug use	23 (23)
Malignancy	7 (7)
Increase in infection	7 (7)
Tuberculosis	70 (70)
Not worried	
The person who informing patients on drug use	88 (88)
Nurse	18 (18)
Doctor	7 (7)
Nurseanddoctor	
Patients who were informed about when to interrupt drug use	86 (86)
Situations where drug use is suspended	84 (95,3)
Flu and febril infection	68 (79,1)
Use of antibiotics	39 (45,3)
Herpes simplex virus infection	
Drug storage	65 (65)
Refrigerator shelf	31 (31)
Refrigerator door	4 (4)
Pharmacy	
State of waiting before administering the drug	17 (17)
Don't wait	71 (71)
20-30 minutes at room temperature	6 (6)
>30 minutes at room temperature	5 (5)
Hand warming and then administration	1 (1)
Soak in hot water	
Rate of controlling the expiration date before administering the drug	64 (64)
Rate of patients who control the clarity of the drug	75 (75)
Rate of hand washing before administering the drug	83 (83)
Injection site cleaning	6 (6)
Don't clean	66 (66)
With the swab from the drug box	24 (24)
With alcohol	3 (3)
With a wet wipe	1 (1)
With soap	
The person performing the injection	84 (84)
The person	11 (11)
Person's relative	5 (5)
Health personel	
The patients who carry their medication in accordance with the cold chain rules during travel	71 (100)

It was observed that in patients who used multiple SCBA for a long time, taking the drug out of the refrigerator and applying it after waiting for the optimum time,

controlling the expiration date of the drug and hand washing before the application decreased over time.

Conclusion: Evaluating the patient's SCBA treatment background is essential for correct treatment practice. Our study revealed that in forming patients on drug use not only initially but also at certain intervals is essential.

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AB1527-HPR FUNCTIONAL SOMATIC SYNDROMES AND INSOMNIA IN PATIENTS WITH FIBROMYALGIA, RELATIONSHIP WITH THE INTENSITY OF THE PAIN SYNDROME

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Background: Fibromyalgia (FM) is a chronic diffuse musculoskeletal pain manifested by numbers of functional somatic syndromes (1). The pathogenesis and pathophysiology of fibromyalgia includes changes of autonomic nervous system, which can be realized in the abnormal functioning of many organs and systems.

Objectives: Analyze the frequency and spectrum of functional somatic syndromes and insomnia in patients with fibromyalgia, relationship with the intensity of pain.

Methods: We examined 102 women with FM according criteria ACR (1990), mACR (2010) with mean age 41.7±9.4 years (M±σ), duration of the disease was 8.4 ± 6.28 years. The severity of pain, fatigue, sleep disorders was assessed with a visual analog scale (VAS).

Results: The severity of pain (VAS) in patients with FM ranged from 2.1 to 8.5 and averaged 5.1±1.5. The severity of fatigue was estimated at 6.5 ± 1.7, sleep disorders - 6.3 ± 2.7. In the examined group of patients with FM, in addition to typical clinical manifestations, significant numbers of functional disorders were diagnosed: insomnia - 86.3%, irritable bowel syndrome – 59,8%, postural tachycardia syndrome - 53.9%, hyperventilation syndrome - 52.9%, bladder pain syndrome – 50,0%. According to the intensity of pain, patients were divided into 3 groups. The 1th group included patients with pain less than 4 points (<25th percentile, n = 21), the 2nd - with the pain severity 4-6 points (25-75th percentile, n = 58), the third group - patients with pain more than 6 points (>75th percentile, n = 23). According to the study, the frequency of functional somatic syndromes was not related to the intensity of pain. There was a positive correlation between the severity of insomnia and the intensity of pain ($r=0.36$; $p<0.05$). The same relationship was revealed between fatigue and pain ($r=0.41$; $p<0.05$).

Conclusion: Patients with FM have a wide spectrum of functional somatic syndromes. The changes described were not related to the severity of the pain syndrome. The presence of correlations between the severity of insomnia and the intensity of pain requires further research to develop algorithms for comprehensive treatment of identified disorders.

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AB1528-HPR FULL BODY HAPTIC BODYSUIT - AN INSTRUMENT TO MEASURE THE RANGE AND SPEED OF MOTION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA) - PRELIMINARY RESULTS

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Background: Movement of the spine is restricted in axial spondyloarthritis (axSpA) [1]. Spine function is usually assessed by the Bath Ankylosing Spondylitis Metrology Index (BASMI), which is based on a limited set of defined motions that are measured semiquantitatively in the spatial dimension but not in the temporal dimension. Sensor-based measurement of spine function in axSpA patients is in its infancy but may provide a deeper and more detailed understanding of the impact of axSpA on the impairment of spine function [2,3]. In theory, unbiased full body assessment of spine motion may open a new dimension in function analysis in axSpA.

Objectives: To test if a of a full-body based haptic capturing of spine motion is technically feasible and can pick up the measurements of BASMI items 1-5. Furthermore, we aimed to investigate whether such measurements are accurate and reproducible comparing to BASMI scores done by rheumatologists. Lastly, we sought to measure velocity of spine movements to allow spatiotemporal analysis of motion.

Methods: For full-body haptic assessment of spine motion a full-body haptic suit (Teslasuit; VR Electronics Ltd, London) was used that consists of a smart textile two-piece bodysuit that not only captures range and speed of motion but also provides biometric and haptic feedback. This device is currently tested in clinical trials (https://teslasuit.io/rehabilitation/) but has not been tested in rheumatic diseases such as axSpA [4]. Since there is no pre-defined technical solution for measuring BASMI, we used the integrated inertial measurement units (IMUs) of the suit (Figure 1a). The suit is recording the position and rotations of its IMUs and is transforming the raw data to position coordinates and joint angle of the bones. We implemented an algorithm that is accessing the sensor data and is calculating the BASMI measurements as well as velocity. Assessment were done in healthy individuals. BASMI was obtained 3 times by teslasuit followed by standard BASMI measurement by 2 independent rheumatologists. In addition, rotational movements with their maximum torso speed to evaluate angular velocity were performed (Figure 1b). Measurements were compared using absolute values and relative standard deviation (which is the standard deviation normalized by the mean).

Results: Five healthy individuals (all males, age: 27.6 ± 1.8 years, height: 178 ± 5 cm; weight 70.0 ± 8.0 kg) were assessed. Teslasuit measurements were well tolerated. Technically, we were able to calculate BASMI item 3 and 5, finger-to-floor distance and the velocity of the spine movement using the position data of hand, talus and upper back sensors (Figure 1a, b). Due to absence of sensors at the head and the required back areas, BASMI 1, 2, 4 could only partially be captured and require further programming, which is currently performed. Only marginal differences were detected regarding the relative standard deviations of measurements between teslasuit and rheumatologists (BASMI 3: rheumatologists 8,5%: suit 10%; BASMI 5: rheumatologists 5,4%: suit 4,9%) (Figure 1c). The speed of spinal motion could be measured with an average angular velocity of 172.2 degrees/sec over the entire rotation motion and an average maximum angular velocity of 417.2 degrees/sec.

Conclusion: This study shows that full-body haptic-suits can capture spinal motion including parts of the BASMI score. In addition, they allow to measure the speed of spinal movement, which might be an important and so far unrecognized factor to test the impact of axSpA on spinal function. Based on these results, full-body haptic-suits will be tested in axSpA patients in the future. Furthermore, technical solutions are currently developed to implement the remaining BASMI scores into the suit as well as connections from the suit to virtual reality devices for patients and doctors.

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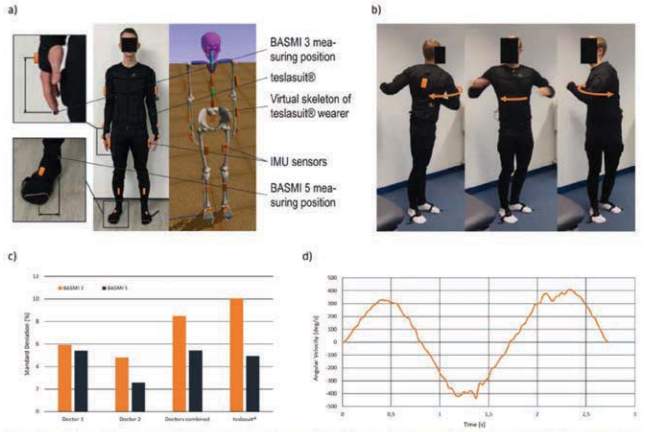

Figure 1 a) 14 IMUs of the teslasuit® are located on hands, upper and lower arms, upper and lower back, feet, upper and lower leg (marked as orange cuboids). Detailed images show the difference between sensor location and BASMI measuring position. b) Participant performing torso rotation for the velocity measurement (used IMU sensor is marked). c) Relative standard deviation between manual BASMI 3/5 measurements of doctors and teslasuit® measurements. d) Recorded angular velocity plot of torso rotation of participant 5.

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AB1529-HPR CROSS-CULTURAL ADAPTATION, RELIABILITY AND CONVERGENT VALIDITY OF THE TURKISH VERSION OF THE PRIMARY SJOGREN'S SYNDROME QUALITY OF LIFE QUESTIONNAIRE

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Background: To completely comprehend the burden of an illness and the success of its treatment, it is essential to analyze the patients' perspective on health-related quality of life. Because of this, the Primary Sjögren's Syndrome-Quality of Life questionnaire (PSS-QoL) was developed, which evaluates the disease's physical and psychosocial effects in PSS patients.
Objectives: In the literature, there is no Turkish questionnaire evaluating quality of life in patients with PSS. Therefore, the aim of this study was to translate and evaluate cross-culturally adaptation the PSS-QoL into the Turkish language and investigate its convergent validity and reliability in Turkish-speaking population with PSS.
Methods: Patients completed PSS-QoL questionnaire, the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) and Euro-QoL 5D (EQ-5D). To test the convergent validity of PSS-QoL, correlation between PSS-QoL and EQ-5D and ESSPRI were assessed with Pearson correlation test. In order to investigate the internal consistency and test-retest reliability, Cronbach's alpha and Intra-class Correlation Coefficient (ICC) values interpreted, respectively.
Results: Seventy-nine patients with PSS (53.30+11.98 years, 74F/5M) were enrolled in the study. Good and moderate correlations were found between the PSS-QoL and ESSPRI (r: 0.818, p<0.001) and EQ-5D-pain/ discomfort (r:0.589, p<0.001). Correlations of subscales of PSS-QoL with subscales of ESSPRI and EQ-5D ranged from fair to strong (Table 1). Cronbach's alpha and ICC values of the PSS-QoL total score were found to be as 0.955 and 0.914, respectively, indicating excellent reliability.

Table 1. Correlations of PSS-QoL and EQ-5D, ESSPRI

	PSS-QoL	Physical	Discomfort	Dryness	Psychosocial
	total score	PSS-QoL	PSS-QoL	PSS-QoL	PSS-QoL
EQ-5D-mobility	0.543**	0.514**	0.678**	0.761**	0.891**
EQ-5D-usual activities	0.466**	0.342*	0.371**	0.233*	0.460**
EQ-5D-pain/discomfort	0.589**	0.651**	0.710**	0.442**	0.394**
EQ-5D-anxiety/depression	0.574**	0.570**	0.557**	0.436**	0.439**
EQ-5D-HS	-0.625**	-0.540**	-0.495**	-0.437**	-0.547**
ESSPRI-dryness	0.589**	0.706**	0.448**	0.722**	0.348*
ESSPRI-pain	0.673**	0.694**	0.824**	0.421**	0.494**
ESSPRI-fatigue	0.780**	0.668**	0.669**	0.497**	0.690**

EQ-5D, Euro-QoL-5 dimension; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; HS, health state; PSS-QoL, Quality of Life in Primary Sjögren's Syndrome. *p<0.05, **p<0.001.

Conclusion: This study demonstrated that Turkish version of PSS-QoL is reliable and valid tool to assess quality of life in PSS patients. Therefore, PSS-QoL can be used to assess quality of life in Turkish-speaking PSS patients.
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AB1530-HPR INVESTIGATION OF FUNCTIONAL MUSCLE PERFORMANCE AND STRENGTH AND BALANCE IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER: A COMPARATIVE PRELIMINARY STUDY

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Background: Familial Mediterranean fever (FMF) is a hereditary, systemic auto-inflammatory disease characterized by recurrent fever, peritonitis, pleuritis, arthritis, or erysipelas-like skin (1). Colchicine treatment is frequently used in Familial Mediterranean Fever (2). Nausea, vomiting, abdominal pain and diarrhea are the most common side effects of colchicine, neuropathy and muscle damage can also be observed (2). Musculoskeletal features are common in children with FMF (3). Arthritis, arthralgia, myalgia and erysipelas-like erythema symptoms can be frequently observed in those patients whose disease onset age is younger than 18 years (4). Decreased functional performance and Quadriceps muscle strength were observed in children with FMF compared to healthy children. (5). It has been reported that the decrease in muscle strength and functional capacity is also associated with the quality of life in children. (5). In the light of all this information, although there is muscle weakness in children, it is thought that endurance, balance and functionality may decrease. There has been no study in the literature examining whole body muscle strength, endurance, balance and functionality in these children.
Objectives: The aim of the study was to assess muscle strenght, endurance, balance and functionality in children with FMF and comparison with healthy children matched the same age and gender.
Methods: 12 children with FMF and 12 healthy children between the ages of 7-17 were included in the study. 10 Meter Walk Test (10MWT) was used to evaluate walking speed in meters per second over a short duration; The 1 Minute Walking Test (1MWT) was used to evaluate functional capacity; Time Up and Go (TUG) was used to evaluate of functional mobility and dynamic balance; Functional Reach Test (FRT) was used evaluate dynamic balance; Muscle Power Sprint Test (MPST) was used to evaluate functional muscle strength and muscle performance short-term muscle strength; 10x5 Spring Test was used to evaulate agility; 30s Repetition Maximum Test was used to evaluate functional muscle strength; Vertical Jump Test used to evaluate explosive strength of the lower extremity; Standing Long Jump Test was used to evaluate muscular endurance of the upper body and the functional muscle strength of the lower extremities; Hand Dynamometer was used to evaluate general muscle strength.
Results: When the groups were compared, a significant difference was found in favor of healthy children in the 10MWT, 1-minute walking test, TUG, FUT, 30 s Repetition Maximum Test (p:0.00- 0.04).
Conclusion: According to the results of the study, children with FMF have low functional muscle performance and strength and balance compared with healthly children. There is a need for studies in which there are more children with FMF and assessmnet of muscle function. Therefore, in which we present the preliminary results, the functional muscle performance and strength and balance children with FMF should be routinely assessed and treatment and rehabilitation programs should be arranged according to these findings.
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AB1531-HPR ECOLOGICAL MOMENTARY ASSESSMENT OF THE SYMPTOMS IN SJÖGREN'S SYNDROME: DEVELOPMENT AND VALIDATION OF A DEDICATED WEBAPP

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Background: Primary Sjögren's syndrome (pSS) is a rare systemic autoimmune disease with no specific treatment at present. To better assess patient symptoms, we have developed a web application (WebApp) to collect patient symptom intensity on a regular basis.
Objectives: To measure the daily variability of symptoms using the WebApp. We also evaluated its ease of use.
Methods: 45 consecutive patients with pSS were included in 3 referral centers. Symptoms were assessed during the baseline and 3 month visits. We collected the VAS relating to fatigue, dryness and pain as well as the ESSPRI score. Patients used the WebApp daily for 3 months. The variability of symptoms over time was assessed by the predicted median error. This value was determined using a linear regression model, in order to predict the value at the 3rd month, then this value was compared to the actual value collected at the 3rd month during the clinical visit. The ease of use of the WebApp was assessed using a satisfaction score (SUS score).
Results: Of the 45 patients included, 91.1% were women with an average age of 57 years, and low systemic disease activity (84.4% had an ESSDAI score below 5). The intensity of the symptoms collected during the clinical visits was similar at baseline and at 3 months. The values of the median error for each measurement are between 0.5 and 0.8. The 3-month predicted median error values ranged from 2 to -3. The patients all used the web application for 3 months with good attendance (80% of data completion) and were satisfied with this tool (median SUS score = 90).
Conclusion: Symptoms of pSS fluctuate from day to day in the majority of patients, making a point measurement imprecise. The developed WebApp is easy to use, and could allow more sensitive detection of the effect of a therapeutic intervention. This tool will soon be evaluated during prospective interventional clinical trials.
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AB1532-HPR GERIATRIC/GENERAL ORAL HEALTH ASSESSMENT INDEX AS EARLY DETECTION TEST OF ORAL DISEASES IN RHEUMATOLOGY.

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Background: The oral health in patients with rheumatologic diseases is frequently affected because of chronic inflammation, slow rate of saliva production and poor self-care. These factors affect the life quality and psychosocial wellness, causing pain, difficulty biting and chewing, even malnutrition. The Geriatric/General Oral Health Assessment Index Spanish Version (GOHAI-SP) consists in 12 items and values self-perception in oral health and wellness (1), validated and applied to young adults (2).
Objectives: to describe the oral health measured by the GOHAI-SP in patients with rheumatic diseases.
Methods: a cross-sectional and observational study was conducted of January to May 2021 in rheumatology service of Hospital Universitario "Dr. José Eleuterio González" at Monterrey, Mexico. Patients with rheumatologic diseases was assessed with GOHAI-SP during their control consult, each item is valuated like a Likert ordinal scale from 1 to 5, the best and worst possible score is 60-12 respectively, patients whit score <45 is classified as poor oral health and >50 as good oral health(3). This assessment is divided in self-perception of mechanical function, pain and discomfort in mouth, gums, teeth and psychosocial function (4).
Results: 316 patients were included, 289 (91.5%) were women, the mean age was 46.23 years (SD: 15.49), the general mean score was 51.88 classified as good oral health. 24 (7.52%) patients was classified with moderate oral health and 63 (19.74%) as poor oral health. The most frequent diagnoses with poor oral health were rheumatoid arthritis 26 cases (8.22%), systemic lupus erythematosus 11 cases (3.48%) and psoriasic arthritis 4 cases(1.2%).
Conclusion: The prevalence of poor or moderated self-perceived oral health in patients with rheumatologic diseases was 27.53%. The primary prevention and early detection plays a fundamental roll to avoid oral disease in this population.
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Table 1. Demographic characteristics and results GOHAI-SP

		GOHAI-SP
Characteristics	**n=316**	**Score, mean (SD)**
Age, mean (SD)	46.23 (15.49)	51.87 (8.35)
Gender, n (%)		
Female	289(91.5)	51.92
Classification GOHAI-SP		
Good	229 (72.47)	56.34
Moderate	24 (7.59)	46.95
Poor	63 (19.93)	37.5
Rheumatologic diseases, n (%)		
Rheumatoid arthritis	120(37.97)	51.45
Systemic lupus erythematosus	53(16.77)	51.81
Osteoarthritis	19 (6.02)	53.57
Other diagnoses	124(39.24)	52.26

GOHAI-SP: Geriatric/General Oral Health Assessment Index Spanish Version; (SD) Standard deviation, n number; (%) Percentage.

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AB1533-HPR ASSOCIATED FACTORS OF FALL OR FRACTURE REPORTED BY RHEUMATOID ARTHRITIS PATIENTS IN ELECTRONIC MDHAQ DURING COVID-19 PANDEMIC

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Background: The COVID-19 pandemic accelerated the use telemedicine for rheumatologic patients. Patient reported outcomes (PRO) can provide prioritization criteria for the form of face-to-face care in situations of social restriction, and optimization of early care by identifying high-risk patients.
Objectives: Our aim was to demonstrate the main associated factors for a fall or fracture reported by rheumatoid arthritis (RA) patients in an electronic MDHAQ (Multidimensional Health Assessment Questionnaire) during this period.
Methods: Patients with RA according to 2010 ACR/EULAR and access to digital platforms were enrolled in the study, from January to august 2021. A weblink was sent to MDHAQ in electronic platform. The study was approved by the ethics committee of Hospital de Clínicas de Porto Alegre – Brazil and all patients agreed with a Term of Informed Consent.
Results: A total of 129 RA patients completed the electronic MDHAQ, mean age was 60 years (S.D. 14) and 83% were female. The mean DAS28, SDAI and HAQ were 3.8 (S.D. 1.6), 14.2 (S.D. 11.0) and 1.2 (S.D. 0.7). Of those 129 patients, 14 reported a fall or fracture in the last 6 months of response and only 16 patients were physically active. Relevant symptoms known as factors associated with risk of fall and its prevalence in this study were: pain (82%), followed by articular pain (68%), fatigue (43%), muscle weakness (37%) and weight gain (22%). Among patients who reported a fall or fracture, 83% had a RADAI ≥ 16 and mean FAST3 (Fibromyalgia Assessment Screening Test) index of 19 (IC95 % 17-21). FAST3 based on MDHAQ and independent RADAI showed positively association with a reported fall or fracture for these patients, with a p value of 0.023 and 0.025, respectively. Other factors, such as high disease activity based on DAS28 or MDHAQ, obesity and age were not statistically significant with the reported episode.
Conclusion: Maintaining PRO is aligned with patient-centered care, allowing relevant data source and identification of high-risk patients - in our study: patients in pain, sedentary and in major risk of fracture. Also, use of combined in like FAST3 or independent articular pain scores such as RADAI, might be helpful to identify those high-risk patients in need for orientation for reinforcement of physical activity, prioritization for in person visits and early clinical adjustments.

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HPR Epidemiology and public health (including prevention)

AB1534-HPR ASSESSMENT OF BACK PAIN IN NURSES WORKING IN HOSPITALS AND OUTPATIENT CLINICS

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Background: Back pain in a common health problem in nurses affecting 70-78% of them [1,2,3]. The risk of back pain in nurses increases by 35% for each additional working hour per day [2].
Objectives: The aim of the study was to find out if nurses working in hospital wards suffer more from back pain than their counterparts employed in the outpatient clinics.
Methods: An online survey was conducted with use of an questionnaire containing questions about body mass index (BMI), Revised Oswestry Low Back Pain Disability Scale (ROLBPDS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Numeric Rating Scale (NRS) for pain. Questions about seniority and working hours were included.It was uploaded and shared on the Google online survey platform. Participation was anonymous and voluntary. An invitation was mailed to the members of The Lublin Chamber of Nurses and Midwives. A total of 163 nurses (161women and 2 men) aged 21-70 years filled in the questionnaire in February and March 2021.Of the group 82 were nurses from hospitals (NHs) and 81 from outpatient clinics (NOCs).
Results: The mean BMI of participants was 26.4kg/m^2. In NHs the mean BMI was 25kg/m^2 and in NOCs 27.8kg/m^2.Seventy five percent of HNs looked after lying patients.Ninety nine percent of NHs and 75% of NOCs suffered from back pain. In the NH group 73% reported pain in lumbar, 13% in thoracic and 14% in cervical spine. In the NOC group 15% complained about neck pain and the rest about low back pain. The mean ROLBPDS rating was 15 which means moderate disability. In NOCs it was 13 and in HNs it was 17. The mean back pain NRS was 6. In NOCs it was 3 and in NHs it was 9 ($p<0.05$). There was a positive correlation between shift length and back pain measured with the NRS. As many as 5 participants had diagnosed seronegative spondyloarthropathy. In those mean BASDAI was 5.6±1 which means active disease.
Conclusion: Nurses working in hospital wards experience significantly more back pain than their counterparts working in outpatient clinics. Long working hours increase the risk for the ailment.
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(in Polish).
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HPR Interventions (educational, physical, social and psychological)

AB1535-HPR COURSE WITH GROUP SESSIONS TO START SELF-INJECTION OF BIOLOGICAL MEDICINE (ADALIMUMAB)

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Background: Denmark decided in 2018 that Adalimumab should be the first-line biological of patients with inflammatory arthritis. Consequently, a higher number of patients needed to be given information about Adalimumab and learn how to do self-injections. The department focused on making optimum use of its resources while at the same time ensuring a high medical standard for this new task.
Objectives: To examine whether group instructions with a structured approach will provide the medical standard required to enable the patients to perform their own treatment at home. And also to examine whether participation in group sessions where the patients will have an opportunity to exchange experience with other people in a similar situation would be beneficial for them.
Methods: *Design:* An anonymous questionnaire survey. *Setting:* The training sessions took place at the Center for Rheumatology and Spine Diseases, Rigshospitalet, Gentofte, Denmark, and involved patients who were already consulting the outpatient clinic. *Participants:* Patients, ≥ 18 year, due to start on their therapy with Adalimumab, were referred to the group sessions irrespective of previous diagnosis, previous experience with other forms of biological therapy and/or experience with self-injection. A group consisted of between two and six participants. *Course structure:* Initially the participants were given group instructions in subjects such as effect, adverse effects, storage and precautions to be taken in the event of an infection. The patients were also given theoretic instructions in the administration of injections and an introduction to the injection pen (test model). Following this, the patients administered self-injections individually in private under guidance. *Material:* The questionnaire asked about whether the participants felt capable of managing their therapy at home and whether they had benefited from being instructed in a group. In addition to this, the patients were asked about background data such as gender and previous experience with injection techniques and biological therapy. The questionnaire also left room to offer more detailed comments. *Analysis:* Descriptive data analysis, including also the more detailed comments from the questionnaires.
Results: A total of twenty-five patients with inflammatory arthritis divided onto seven groups. Female: 15; male: 10
Bionaïve, no experience with self-injection: 13
Bionaïve, experience with self-injection: 6
Previous biological therapy, no experience with self-injection: 2
Previous biological therapy, experience with self-injection: 4

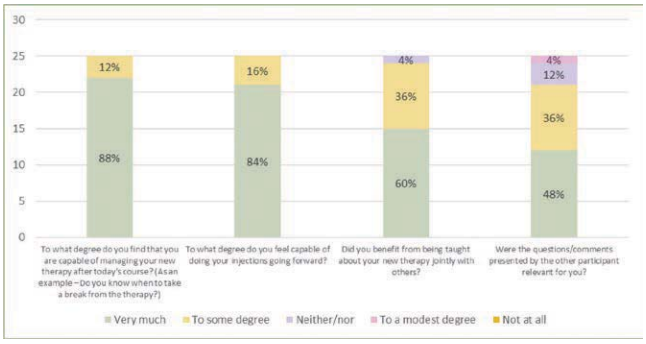

Figure 1.

After the group sessions, all of the patients felt they were capable of managing their own therapy and administering their own injections going forward. The patients were very much or to some degree happy that they were taught in groups and most replied that the questions/comments presented by the other participants were very relevant or relevant to some degree. Gender and previous experience with injection techniques and/or biological medicine did not affect patient satisfaction. Selected comments made by the patients:

"Found the group approach to be really good. Good to hear what the others said"; *"It was really good to be part of a group. I would never have thought of asking the question that the other patients raised and it was relevant for me too"*; *"Nice to listen to other people's experience because it makes you realize that things may not be all that bad for you"*; *"It was really good talking to others"*; *"Always good to meet others in the same boat"*

Conclusion: Group instructions with a structured approach are found to provide a medical standard which enables the patients to perform their own treatment at home. Participation in group sessions with others in the same situation as oneself is also found to be beneficial for the patients since this approach creates a space for dialogue and knowledge sharing by the participant.

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AB1536-HPR DEVELOPING WORK-ON - VOCATIONAL REHABILITATION FOR PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: Patients with inflammatory arthritis (IA), i.e. rheumatoid arthritis, axial spondyloarthritis and psoriatic arthritis, experience low work ability, an increased risk of long-term sickness absence and up to 38% lose their job in the first years after diagnosis. This affects the patients' identity and has economic consequences for the individual as well as for the society. Patients with IA need vocational rehabilitation (VR) to increase their work ability, decrease their sickness absence, and risk of losing their job. Positive results from VR for patients with IA are limited (1).

Objectives: To describe the development of a VR, WORK-ON.

Methods: The development process was based on the Medical Research Council's framework for Complex Interventions and ran in two phases (2). Phase 1, the evidence base: identifying existing evidence through a scoping review and theories (occupational balance, self-management and shared decision making) considered useful for VR. In addition, interviews with 15 patients with IA and 21 health professionals were performed and analysed (3). Phase 2, program development: a workshop was held with patient research partners, researchers, health professionals from a hospital specialised in rheumatological rehabilitation, and from a municipal job center. By repetitive feedback from the stakeholders, the WORK-ON was modelled, remodeled, and described in a manual. Patient research partners were involved throughout the process.

Results: The duration of WORK-ON will be eight months and includes 6 - 11 meetings (30-60 minutes) depending on the patients' needs. The WORK-ON intervention consists of four parts: 1) Initial assessment and goalsetting by an occupational therapist, 2) Coordination by an occupational therapist throughout the VR and assistance in navigation across primary and secondary health and social care including follow up.The coordinator is responsible for individual support concerning issues such as energy management, coping with the disease and concerns related to work. 3) Group sessions together with other patients with IA for peer support, and 4) Individually tailored VR consultations with physiotherapists, nurses, or social workers. Multidisciplinary team discussions will be held with the patient, relatives and all involved partners from the patients' municipality and the hospital to evaluate the VR and decide the next step after eight months. Suggested primary outcome measures are the Occupational Balance Questionnaire (OBQ) and the Work Productivity and Activity Impairment questionnaire (WPAI). Secondary outcomes are health related quality of life (EQ-5D-5L), number of days of sickness absence over a year, VAS pain, fatigue, and global assessment.

Conclusion: WORK-ON was developed with input from various stakeholders and is ready to be tested in a feasibility study after training of the health professionals, who will deliver the VR. Depending on feasibility and indications of efficacy, the primary outcome will be selected and the effect of WORK-ON will be tested in a subsequent RCT study on IA patients in Denmark or further developed in a second feasibility study. Furthermore, a realistic evaluation will be conducted by interviews with patients and health professionals to determine the quality of implementation, contextual factors, and mechanisms.

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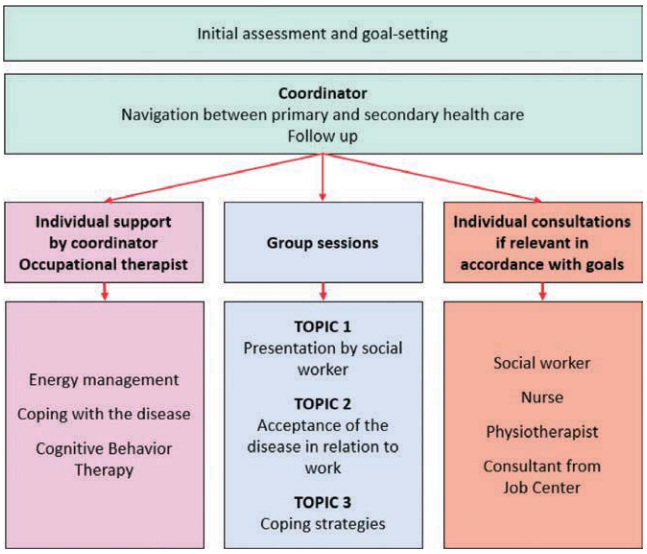

Figure 1. Illustration of WORK-ON

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AB1537-HPR INFLUENCE OF SEGMENTAL STABILIZATION AND PILATES ON NON-SPECIFIC CHRONIC LOW BACK PAIN IN BRAZILIAN ELDERLY: A PRELIMINARY STUDY.

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Background: Low back pain is the second most common health condition in Brazilian elderly, after arterial hypertension, and can be defined as any pain between the last ribs and the lower gluteal folds, with or without pain in the lower limbs, manifesting itself acutely, subacutely or chronically.

Objectives: To analyze the effect of segmental stabilization in comparison with the Pilates method in elderly patients with chronic non-specific low back pain.

Methods: 9 elderly people with chronic low back pain participated in the study, randomized into two groups: Segmental Stabilization Group (SG n=9; age 66.11±4.78; Body Mass Index - BMI 28.21±4.05) and Pilates Group (PG n=13; age 67.46 ±4.89; BMI 28.18±3.48). Both groups performed 16 individual 60-minute sessions twice a week and evaluated before and at the end of treatment. Pain was assessed using the Visual Numerical Pain Scale; functional disability, by the Oswestry disability index; excessive fear of movement and physical activity, by the Tampa Kinesiophobia Scale; level of confidence in balance for specific activities, by the Activities-specific Balance Confidence (ABC) scale and; activation of the transversus abdominis muscle, by the pressure biofeedback unit Stabilizer of the brand Chatanooga. The allocation and assessments of participants were performed by a blinded examiner. Data were analyzed using Student's t test with the level of significance ($p \leq 0.05$).

Results: Pain intensity had a greater reduction in the SG when compared to the PG ($p=0.0015$), as well as a reduction in functional disability ($p=0.0043$). The activation of the transversus abdominis was greater in the PG ($p=0.0213$). There was no difference in kinesiophobia and the level of confidence in balance for specific activities.

Conclusion: Segmental stabilization and Pilates were effective in improving pain and functional disability, with SG showing a better effect for these variables. The

PG obtained better results when compared to the SG regarding the activation of the transversus abdominis muscle. It is suggested to carry out studies with a greater number of participants, a longer treatment and follow-up time to complement these findings.

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AB1538-HPR AMIGOS DE FIBRO (FIBRO FRIENDS): VALIDATION OF AN EDUCATIONAL PROGRAM TO PROMOTE THE HEALTH OF PATIENTS WITH FIBROMYALGIA IN BRAZIL.

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Background: Health education is a very important tool in the treatment of people with fibromyalgia. Health education acts as an excellent non-pharmacological treatment to promote health in fibromyalgia.
Objectives: To validate a multidisciplinary educational program to promote the health of people with fibromyalgia in Brazil, called Amigos de Fibro.
Methods: This is a methodological research with 45 individuals with fibromyalgia (target audience) and 23 health professionals (expert judges). Both groups used an instrument to assess the objectives, themes and proposed actions, relevance, writing style and structure of the program using the Delphi technique. The Content Validity Index (CVI) ≥ 0.78 and Kappa Coefficient ≥ 0.61 were used to analyze and validate the data.
Results: All items evaluated in both groups had a considerable minimum CVI and Kappa Coefficient to be valid. In the global assessment of Amigos de Fibro, the CVI of the target audience judges was 0.95, while the expert judges presented a value of 0.90. The Kappa Coefficient of the target audience judges was 0.85 and that of the expert judges was 0.90. Therefore, the instrument proved to be validated.
Conclusion: Amigos de Fibro was considered valid for its content and internal consistency, therefore, valid to be used by health professionals with the target audience in Primary Health Care in Brazil, allowing them to act as promoters of their health.

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AB1539-HPR AMIGOS DE FIBRO (FIBRO FRIENDS): VALIDATION OF AN EDUCATIONAL E-BOOK TO PROMOTE THE HEALTH OF PEOPLE LIVING WITH FIBROMYALGIA IN BRAZIL

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Background: In the optimal treatment of fibromyalgia, international recommendations highlight non-pharmacological treatment as the key to success. Health education is one of the main tools to promote the health of patients with fibromyalgia. Educational strategies are essential for the care of patients with fibromyalgia.
Objectives: Develop and validate an e-book to promote the health of people with fibromyalgia who live in Brazil.
Methods: This is a methodological study, initially, through a bibliographic survey, the available publications on the subject were analyzed. Then, this knowledge was used to build the theoretical content addressed and the art and layout of the e-book was elaborated. Finally, the validation of the constructed material was carried out with three groups of specialists: content specialists (n=23), technicians (n=23) and design specialists (n=23). In addition, it was also decided to validate the e-book with individuals who have fibromyalgia (n=45. The e-book was evaluated by specific instruments through the Delphi technique. The data were analyzed, and the reliability was evaluated by the Alpha of Cronbach (αC) and agreement, using the Content Validity Index (CVI).
Results: In the global evaluation, all the judges agreed with the items evaluated in the e-book, presented a considerable minimum of the CVI, being: content (0.79), technical (0.89), design (0.92), and target audience (0.97). Regarding reliability, all groups also had an αC within the acceptable range: content (0.960), technical (0.963), design (0.977), and target audience (1.08).
Conclusion: E-book was prepared and validated in terms of content and relevance, and can be used in Brazil to promote the health of individuals with fibromyalgia, mainly as a complement to treatments already carried out for fibromyalgia. In the future, this e-book may be translated and adapted into new languages.

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Disclosure of Interests: None declared
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AB1540-HPR NURSING INTERVENTIONS FOR RHEUMATIC MUSCULOSKELETAL DISEASES (RMDS) PATIENTS ON BIOLOGIC THERAPY: A SYSTEMATIC LITERATURE REVIEW (SLR)

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Background: The support of the Rheumatology nurse to the management of patients who are affected by RMDs, characterized by remission and recrudescence and chronicity, may be strengthened by the investigation of their unmet needs and the identification of the necessary interventions to the continuity and quality of care.
Objectives: The aim of the present SLR is to identify the main nursing interventions to assure quality care in RMDs patients on biologic therapy.
Methods: Study design: a systematic search was conducted from 1990 to 2020 (01/01/1990- 2020/05/07). Inclusion criteria consisted of 1) patients with RMDs in accordance with American College of Rheumatology classification criteria and the American College of Rheumatology/European League against Rheumatism (ACR/EULAR); 2) in therapy with bDMARDS; 3) adult population > 18 years; 4) primary research only; 6) English language; 7) abstract available; and 8) relative quantitative studies; 9) nursing interventions and/or outcomes. Data sources: Medline, CINAHL, PsycINFO and EMBASE databases were used to search for relevant studies. Review methods: using the predetermined inclusion/exclusion criteria, two independent reviewers (MRM, KEA) screened records selected for eligibility based on titles and abstracts. Records meeting the inclusion criteria were retrieved and full texts were further assessed. Critical Appraisal Skills

Program (CASP) tools were used to evaluate the quality of the included studies. Data from 8 studies were extracted independently by the reviewers.
Results: 1805 articles were retrieved: after the review process, 8 articles met the inclusion criteria resulting in 1 randomized trial, 1 quasi-experimental study and 6 observational studies. The RMDs patient needs emerged concerning the psychosocial domain, the relationship with healthcare facilities and disease follow up to monitor symptoms. Moreover, three major nursing interventions related to these areas were identified: education, patient-centered care and data assessment.
Conclusion: Rheumatology nurses are part of a multidisciplinary team caring for patients on biologic therapy. Starting with accurate initial and ongoing data collection, rheumatology nurses can plan their interventions focusing primarily on patient education and tailored care based on actual needs. Further studies are necessary for research on aspects of patient-centered nursing care, including tele-nursing and Nursing Sensitive Outcomes in RMDs.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.2630

AB1541-HPR IMPACT OF COUNSELLING, TELEPHONE-BASED SYMPTOMS TREATMENT TITRATION AND REMINDER CALL ON REGULAR FOLLOW UP AMONG COMMON RHEUMATOLOGIC DISORDERS; A PROSPECTIVE COHORT STUDY

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Background: Poor adherence to rheumatologic diseases exist for various reasons.
Objectives: The objective of the study was to measure adherence with interventions.
Methods: It was a prospective cohort study for 52 weeks. Assuming adherence of 30%, power of the study as 90% and confidence interval 95% sample size was calculated as 323. Common rheumatologic disorders (Rheumatoid arthritis (RA), Spondyloarthropathy (SpA), Primary Sjogren's Syndrome (PSS) and Systemic Lupus Erythematosus (SLE)) patients with at least 15% from each group who presented first time in our clinic were followed up. The interventions were two separate sessions of face-to-face counselling during first initial visits, telephone-based titration of drugs if there was poor control of the presenting symptoms and two-day prior reminder phone call for next follow up.
Results: Among 323 enrolled patients 27% were compliant with previous treatment. The relative ratio of compliant groups under follow up with the rheumatologist verses other clinicians was 2.2. Median duration of diagnosis of the 60% previously diagnosed verses 40% newly diagnosed at our clinic was 18 months verses 7 days. Among 64 cases of PSS 86% were undiagnosed with median duration of symptoms of 4 years. Knowledge about consequences of poor treatment between pre verses post counselling was 40% and 78% respectively. (Table 1) Symptom controlled with telephone-based drug titration was achieved among 84% of cases (30%, 44%, 10% partial, nearly complete and complete improvement respectively). With the reminder call the adherence weans off to 85% at first follow up, 77% at third month and 53% at the end of year. By 52 weeks PSS had maximum adherence (78%) followed by SLE (58%), RA (42%) and SpA (42%). (Figure 1)

Table 1. Comparison between pre and post intervention

Variables	RA (N=116)	ax-SpA (N= 72)	SLE (N=71)	PSS (N=64)
Before intervention	3.5	2.5	3	4
•Median duration of diagnosis (years)	25	9	34	19
•Number of adherence (87)	9	4	7	3
•Insight about the disease conditions	17	17	16	16
a.I don't have disease	30	17	16	31
b.I have disease due to external factors	28	23	25	11
c.I have disease due to internal factors	22	11	7	3
d:'c' + I need medication for some time	<1	2	<1	2
e:'c' + I need medication per rheumatologist	49	30	41	50
After intervention	5	4	5	1
•Median duration of diagnosis (weeks)	9	4	4	4
•Number of adherence at 52 weeks (170)	14	9	8	11
•Insight about the disease conditions	31	21	17	11
a.I don't have disease	57	34	37	32
b.I have disease due to external factors				
c.I have disease due to internal factor				
d:'c' + I need medication for some time				
e:'c' + I need medication per rheumatologist				

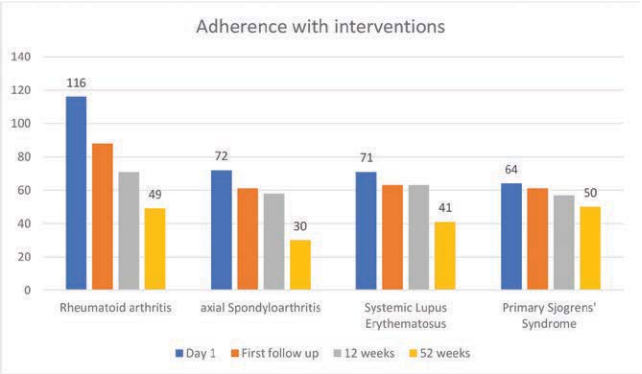

Figure 1. Adherence proportion with consequent follow up

Conclusion: Early diagnosis, separate counselling sessions, effective control of symptoms and reminder to follow up significantly increases the adherence in rheumatological disorder.
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AB1542-HPR USING SOCIAL NETWORKS AS A SOURCE OF INFORMATION FOR RHEUMATOLOGICAL PATIENTS

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Background: The COVID-19 pandemic has brought significant changes to the work of healthcare professionals around the world. Technologies of telemedicine counseling and education of patients have become widespread. The largest platforms for informing patients are social networks such as Facebook, Instagram, Twitter.
Objectives: to study the possibilities and impact of the social network as a digital medical tool on the education and management of rheumatological patients
Methods: The study was conducted in the form of a survey in the social network Instagram in the blog @revmatologg_sarapulova, dedicated to the rheumatological diseases, and was dedicated to the level of information. At the time of the survey, the number of subscribers to the blog was 4895 people, 223 people answered the questions submitted. The survey was conducted in a Google form and was anonymous.
Results: 86% of respondents lived in Russian Federation, 17.5% - in the survey region, 14% of patients were from other countries. 72% indicated the presence of rheumatic disease as the reason for reading the blog, 7% - disease in relatives, 14% are guided by the desire to know more about rheumatological diseases. 68.5% of the respondents rated the information presented in the blog as very interesting (10 points on a scale from 0 to 10), 13.3% - 9 points and 9.1% - 8 points. It should be noted that none of the participants in the study gave less than 5 points.

The most interesting in the blog, the majority calls information posts (88.8%) and answers the questions (77.6%). 2 out of 3 patients (64.5%) after getting acquainted with the information provided began to know more about their disease, 14% began to lead a healthier lifestyle, 9.8% realized the need to visit a doctor. 83.3% of participants rated the information on the blog as more detailed than what they get at their doctor's appointment, and 81% would seek advice from a blogger. When answering the question "Do you share the information you get from the blog with your healthcare provider?" 47.2% noted that they prefer not to report, 28% - report, while 44.9% of respondents indicated that the doctor is neutral about the information received, 22.9% - positively, 7.6% - negatively. In general, 86% agreed that social networks are an important source of medical information, and as other sources they noted self-search for information in the Internet and visiting a doctor. 65.7% of the respondents asked the question to the author of the blog and received a response that was helpful in 90.6% of cases. 36.8% previously applied for telemedicine counseling through any messengers/systems, and 20.1% plan to do so. In 57.8% of cases, the opinion of the attending physician coincided with the result of a telemedicine counseling, in 12.8% it did not, and 17.8% of patients consulted only online.

Conclusion: social networks are an important source of information for patients and a means of choosing a medical specialist. However, it is alarming that in about half of the cases, patients do not share the information received with the attending physician, which can be explained both by lack of time and the lack of an adequate level of trust.

Disclosure of Interests: None declared

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AB1543-HPR WAITING ROOM PROJECT: IMPROVING HEALTHCARE OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) prognosis is determined by a wide range of factors, such as the severity of the disease manifestations, the psychosocial aspects of patients, the proper management of comorbidities, adoption of a healthy lifestyle and adherence to treatment. Studies on chronic diseases highlight the value of patient education to foster treatment adherence and improve prognosis.

Objectives: To promote health education to SLE patients and their families providing accessible and comprehensive scientific information, in order to improve adherence to treatment and the patient's prognosis.

Methods: The Waiting Room Project is linked to the Extension Health Care Program for SLE patients and their families of Universidade Federal de Minas Gerais, Brazil, since 2011. A total of 700 patients under SLE treatment at the Rheumatology Unit of the University Hospital are involved. Medical students and rheumatology fellows, altogether, developed high-quality informative texts, with clear content and layman language appropriate for the patient, under the supervision of the rheumatology professors. The texts are illustrated by the team of the Communication Department of the Medical School and medical students, and are printed in a leaflet format. The material is handed out to the patients, while they wait for their medical appointment, by the students and the care team. The content of the leaflets is discussed, making sure that all the concerns and doubts are properly addressed

Results: The Waiting Room Project has produced 17 leaflets, addressing different aspects of SLE, comorbidities, and treatment. The texts approach the traditional cardiovascular risk factors (Smoking, Arterial Hypertension, Diabetes, Obesity, Physical Activity), and some medical conditions related to general health and SLE treatment (Sun Protection, Healthy Food, Oral Care, Vaccination, Pregnancy, Osteoporosis). In 2020 and 2021, two leaflets about Covid-19 were produced in order to clarify important aspects of this disease, its impact on lupus patients and to solve questions about SLE medications: one regarding the association between Lupus and Covid-19 and another about the treatment of lupus and Covid-19. Other four leaflets were produced concerning SLE treatment, including Adherence to Treatment, the use of Antimalarials, Corticosteroids, and Immunosuppressants. Information about the drugs, general importance on lupus treatment, recommendations and possible adverse events were described. Futhermore, additional content is currently in production with themes such as Intravenous Corticosteroid and Cyclophosphamide, Human Papillomavirus Infection, Malignant Neoplasm, and specific cancers frequently affecting women, such as Colorectal Cancer, Cervical Cancer, and Breast Cancer. The leaflets are also available online on the Medical School website in Portuguese and in English (medicina.ufmg.br/alo/material-didatico/), on the Minas Gerais Rheumatology Society website (reumatologia.org.br/orientacoes-ao-paciente/), and on the Instagram page @lupusufmg

Conclusion: The leaflets have been an important source of information and health education for SLE patients and their families, improving student/physician-patient communication. Despite the adversities caused by the coronavirus pandemic, the Waiting Room Project has kept its purpose to make each patient with SLE an agent of their healthcare. Improving the patients' access to evidence-based information must be a goal of healthcare professionals that treat patients with SLE

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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

AB1544-HPR CLINICAL COMORBIDITY PHENOTYPE IN KNEE OSTEOARTHRITIS IS ASSOCIATED WITH HIGHER INTENSITY SCORES

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Background: Knee osteoarthritis (OA) is a common osteoarticular disease. Its prevalence increases with age as well as the coexistence of other chronic diseases. Recent researches have revealed an association between OA and cardiovascular diseases. However, association between knee OA and comorbidities has not been fully studied.

Objectives: The purpose of this study was to investigate the association between knee OA and comorbidities.

Methods: In this cross-sectional study, patients with knee OA were enrolled. Sociodemographic data as well as comorbidities were collected. Grading of knee OA was performed using the Kellgren-Lawrence (KL) grading system. Functional impact of knee OA was assessed by KOOS-Physical Function Shortform (KOOS-PS).

Results: This study assessed 104 patients with knee OA (10 men and 94 women). Mean age was 65.83 ±11.08 years. Mean VAS pain was 6.56 ± 1.72. Mean KOOS-PS was 15.58 ± 6.73. Up to 81 patients (77.9%) had severe knee OA according to the KL grading system. Comorbidity was noted in 92 cases (88%). The most frequent comorbidities were obesity (62.5%), hypertension (61.5%) and dyslipidemia (43.3%). Comorbidities in knee OA were associated with age (p=0.04), neuropathic pain component (p=0.02) and VAS pain (p=0.04). Our study also showed a significant correlation between comorbidities and structural grading of knee OA (p=0.04). However, comorbidities were not correlated with KOOS-PS score (p=0.06).

Conclusion: The accumulation of comorbidities is significantly associated with higher intensity scores in knee OA. Physicians should additionally pay close attention to the prevention and the treatment of comorbidities in the management of OA.

Disclosure of Interests: None declared

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AB1545-HPR MALNUTRITION IN PATIENTS WITH RHEUMATOID ARTHRITIS OVER 65 YEARS OF AGE

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Background: Malnutrition is one of the most important geriatric syndrome and fragility factor in older people. In adittion to being a disease sign, its presence is related with increasing of morbility, longer hospitalizations, institucionalization and mortality due to concomitant diseases.

Objectives: Describe prevalence of malnutrition risk and associated factor in patients with rheumatoid arthritis (RA) over 65 years of age.

Methods:

Design: A case-controls study.

Participants:

Cases: Recruitment was performed by random sampling between patients over 65 years of age with RA (ACR/EULAR 2010 criteria) attended at 4 Spanish

University Hospitals. Controls: Recruitment of subjects without rheumatoid disease was performed asking for case patients who attended to medical center with a similar-age (age of range +/- 5 years) and same-gender person from same social or family environment. Variables y measures: The main variable was malnutrition risk, measured by screening of Mini Nutritional Assessment. Other variables were: presence of sarcopenia, defined according to European Working Group on Sarcopenia in Older People (EWGSOP) 2019, economic status, dual-energy x-ray absorptiometry (DEXA) in spine and hip to osteoporose screening, toxic habits, comorbidities and Charlson index, physical activity measured with Global physical activity questionnaire (GPAQ) and Short Physical Performance Battery (SPPB), haemoglobin, calcium, D and B12 vitamins, total proteins, albumin, C reactive protein, body mass index (BMI), polimedication, quality of life measured with EQ-5D and RA related factors, activity disease measured with DAS28, SDAI and CDAI; physical function measured with HAQ (Health assessment questionnaire) and global functional status according ACR criteria. Statistical analysis: Descriptive and multivariative analysis was performed to identify factors associated to sarcopenia in RA.

Results: 152 subjects were included in the study, 76 RA and 76 controls.More patients than controls with malnutrition risk were found, although there were no significative difference (24 [31,6%] vs 17 [22,4%]; p=0,136). More women with RA were included (78,9%), with media ± SD of age 74,7 ± 3,78., sarcopenia was presented in 9/24 (37,5%) and Charlson index was 3 points in 11/24 patients (45,8%) and 4 points in 8/24 patients (33,3%). According to the treatment, almost a 40%, no DMARDs were taken and neither 25% biological DMARD. 58,3 % of patients received corticosteroids and mayority of them (95,8%) were polimedicated. RA patients who presented desnutrition risk, in comparison with the rest of patients, had a media of upper age (p=0,007), more frequency of sarcopenia (p=0,006), right tricipital skinfold thickness (p=0,043). Also, higher values were found in activity index like physical function and quality of life: DAS28 (p=0,003), HAQ (p=0,044), Vitamin D (p=0,035), IPAQ (p=0,003), SPPB (p=0,018), EQ5D (p=0,01), VAS EQ5D (p=0,044), SDAI (p= 0,006), CDAI (p=0,008). In multivariative análisis, factors associated by independent way to malnutrition risk were age (OR [CI 95%], 1,148 [1,020-1,291]; p=0,022) and inflammatory disease by DAS28 (OR [CI 95%], 2,043 [1,198-3,483]; p=0,009) (R2=0,252).

Conclusion: Even though frequency of malnutrition was similar in cases and controls, in RA was associated with inflammatory activity and older age. It´s important monitoring malnutrition risk in this kind of patients to perform correct interventions to prevent and improve nutrition.

Disclosure of Interests: None declared

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AB1546-HPR LOCUS OF CONTROL IN RHEUMATIC DISEASES

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Background: Locus of control as a theoretical construct derives from Julian B. Rotter's [1] social learning theory of personality. Locus of control is the person's trait to attribute their successes or failures only to internal or only external factors; it refers to an individual's perception about the underlying main causes of events in his/her life.

Objectives: The aim of the study was to investigate the level of locus of control in patients with systemic lupus erythematosus, primary fibromyalgia syndrome, and osteoarthritis.

Methods: The level of locus of control was studied in 87 patients with systemic lupus erythematosus (SLE), 100 patients with fibromyalgia (F) and 27 patients with osteoarthritis (OA), using the Subjective Control Level (SCL) questionnaire [2].

Results: Patients with SLE show a pronounced tendency to externality in the general sphere, as well as in the sphere of failure (3.63±0.34), work related sphere (3.42±0.21), interpersonal relations, and especially in relation to health (3.31 ±0.32). The study of SCL in patients with F allowed to note a significant decrease of scales in the spheres of general internality (2.98±0.31), internality in the field of achievements (3.08±0.34) and failures (3.42±0.30), interpersonal relations (3.54±0.25) and health (2.87±0.32), that indicates the externality of the F patients' attitudes according to these scales. Patients with OA has a pronounced tendency to externality in the general sphere (3.81 + 1.387), as well as on the scales of internality in the area of failures (3.51 + 0.64), family relationships (4.18 + 0.55), work related sphere (2.74 + 0.98) and in relation to health (4.66 + 1.94). In the sphere of interpersonal relations and on the scale of internality in the field of achievements, internal tendencies are observed (5.14 + 0.71 and 5.0 + 1.24, respectively). Thus, the role of the sick man, that is assimilated to some extent by most patients with rheumatic diseases, and the symptoms of the disease form a feeling of helplessness in the patients, the need for sympathy and care from others, the hope that the improvement in the condition will be the result of external factors that do not depend on the patient himself. These changes may make it difficult to carry out effective therapy measures and, in turn, are the target of psychology intervention.

Conclusion: Thus, the successful treatment of rheumatic diseases requires the active involvement of a patients in the therapy process, as well as changes in their attitudes and lifestyles. The condition of the majority of patients can be significantly improved if the patient and the doctor can form a working partnership and the patient becomes an active participant in the treatment process, gains experience in controlling the situation, takes responsibility for strict adherence to the treatment and rehabilitation regimen. Some psychotherapy methods can be used in order to achieve these goals.

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AB1547-HPR CAN A NURSE REPLACE THE DOCTOR IN AN UNCOMPLICATED PATIENT COURSE IN A PMR CLINIC? WHAT DO THE PATIENTS SAY?

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Background: Since 2020 the Rheumatology Outpatient Clinic of OUH, Svendborg Hospital has offered telephone consultations for patients diagnosed with muscular arthritis (PMR) treated with prednisolone. Since 2021 has the course for the non-complexed patients been run by nurses. Initially patients only see a rheumatologist at the time of admission and the rheumatologist is only involved again if complications occur in the course e.g. that the patient can´t reduce Prednisolone as agreed without getting symptoms. At same day the patients are diagnosed by a rheumatologist they have a conversation with the nurse. The nurse gives both oral and written information about the disease and a Prednisolone reduction schedule is handed out to the patients. Afterwards the patients are followed by nurses and by telephone contact only. The telephone contact with the patients take place after 2, 10 and 17 weeks. When the patients are down to 7.5 mg of prednisolone daily, the nurse discharge the patient in our out-patient clinic to their own GP, who then takes care of the rest of the treatment and reduction of prednisolone to zero. There are more literature reviews about PMR and outpatient clinics led by nurses and patient satisfaction, but we have not found anything about the patient satisfaction when they only have contact to nurses during their course.

Objectives: The aim of this qualitative study was to examine the impact on patient satisfaction when they only have contact to nurses during their course and at the same time examine whether the patients have missed talking to a rheumatologist. In addition to this, we were interested in the understanding and degree of application of the written reduction schedule.

Methods: All PMR patients completed in the outpatient clinic between December 2021 and January 2022 where asked to participate in a telephone interview at the end of their treatment. They were asked about their satisfaction with nurse consultations during their course on a scale from 0-10: 0= not satisfied and 10= high satisfaction. The patients were also asked if they had missed not to talk to a rheumatologist and finally they were asked about the Prednisolone reduction schedule.

Results: 20 patients participated in the telephone interviews. 55% of the patients responded 10 on a scale from 0-10 in satisfaction talking with the nurses. 25% responded 9 on the scale, 15% mentioned 8 on the scale and 5% mentioned 7 on the scale. All of the patients answered no regarding the need to talk with a rheumatologist. None of the 20 patients has been re-admitted to our outpatient clinic afterwards. 75% of the patients have no problem in following the Prednisolone reduction schedule and found it easy to read and understand.

Conclusion: With the limited number of participants, it is not possible to conclude anything definitive, but the answers indicate that the patients are satisfied with nurse consultations only during their course in the outpatient clinic and the answers also indicate that they have no need to talk to a rheumatologist. Our research could therefore indicate that nurses with a specific protocol in hand are capable of managing a course for non complex PMR patients including discharging the patients from the outpatient clinic. The answers regarding the reduction schedule reassured us, that it is understandable which should reduce the possibility of errors in the treatment.

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AB1548-HPR

PATIENT-REPORTED ADVERSE DRUG REACTIONS ATTRIBUTED TO THE USE OF ADALIMUMAB: DISTINCTION BASED ON NATURE, FREQUENCY AND BURDEN

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Background: Research regarding adverse drug reactions (ADRs) associated with the use of adalimumab in patients with inflammatory rheumatic diseases (IRDs) usually focuses on the nature and frequency of ADRs without considering the burden of the ADRs. However, not every ADR causes the same burden for patients. Information is lacking about the degree of experienced burden per ADR by patients with IRDs.
Objectives: First, to describe ADRs of adalimumab based on nature, frequency and burden, and second to propose a new model for identification of relevant ADRs for health care professionals.
Methods: Data of the Dutch Biologic Monitor (DBM) was used to categorize patient-reported ADRs into high and low burden. In this prospective cohort event monitoring system patients were asked to fill out bimonthly questionnaires on experienced ADRs that they attributed to the use of a biological. The questionnaire included a quantification of the burden of the reported ADRs using a five-point Likert scale ranging from 1 (no burden) to 5 (very high burden). The nature of the reported ADRs were grouped into preferred terms (PTs) according to the Medical Dictionary for Regulatory Activities (MedDRA). Inclusion criteria for this study were patients with IRDs using adalimumab and the reporting of an ADR with at least one burden score. For every patient, the mean burden scores per ADR (MedDRA PT) were analyzed. The burden was classified in two categories: 'high' when the mean burden score was equal to or more than 2.5, and 'low' when it was less than 2.5. Text analytics of the reported ADRs (MedDRA PTs) and a comparison word cloud were used to visualize ADRs that were more often reported with high burden or more often reported with a low burden. For this, the relative ADR frequencies of the low burden classes were subtracted from the relative frequencies of the high burden class, resulting in a percentual difference between the high and low burden class for every ADR. Therefore, the highest percentual difference corresponds to the ADRs that are experienced as most burdensome.
Results: A total of 170 patients (68% female) met the inclusion criteria and reported 671 ADRs, of which 271 (40%) were reported with high burden (see Table 1). The word cloud (Figure 1) visualizes which ADRs were more often reported with high or low burden. These ADRs correspond to the greatest difference in relative class frequency. Patients experienced the burden of respiratory tract infections and increased infection susceptibility mainly as high, and the burden of injection site pruritus and injection site pain as low.

Table 1. Characteristics of patients and reported adverse drug reactions (ADRs)

Characteristics	Total		
Patients (n = 170)			
Gender (female, %)	116 (68)		
Age (years) (mean ± SD)	55.4 ± 12.8		
Indication[a]			
Rheumatoid arthritis (%)	91 (54)		
Ankylosing spondylitis/axial spondyloarthritis (%)	31 (18)		
Psoriatic arthritis (%)	48 (28)		
Adverse drug reactions	Total	High burden	Low burden
Adverse drug reactions (ADRs) (%)	671 (100)	271 (40)	400 (60)
Drug-induced ADR burden (mean ± SD)	2.5 ± 1.0	3.4 ± 0.7	1.8 ± 0.4
High burden ADRs:			
Respiratory tract infections	12	11	1
Infection susceptibilityincreased	20	14	6
Headache	13	9	4
Therapeutic product effectdecreases	14	9	5

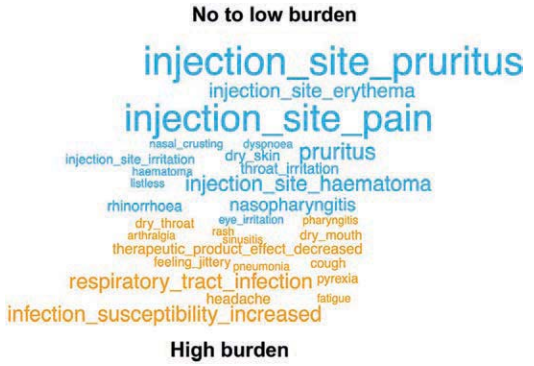

Figure 1. Comparison word cloud visualizing adverse drug reactions that patients reported more often with high burden (orange) and with no to low burden (blue). An ADR increases in size if the relative difference in frequency between classes increases.

Conclusion: The outcomes of the word cloud reveal that infections are more often experienced as burdensome, whereas injections site reactions impose low to no burden. Visualizing the nature, the frequency and the burden of ADRs in one picture, provides simple guidance to the degree of relevance for the reported ADRs in clinical practice.
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AB1549-HPR

SOCIAL ACTIVITY AND QUALITY OF LIFE IN PATIENTS WITH THE ARTICULAR FORM OF RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) often experience persistent, prolonged pain. This requires taking pain medications (most often non-steroidal anti-inflammatory drugs) every day for many years or decades. Pain can lead to decreased social activity and emotional changes. Therefore, the quality of life of patients with rheumatoid arthritis may decrease.
Objectives: The purpose of the study: to determine the quality of life in patients with rheumatoid arthritis.
Methods: A survey was conducted using a questionnaire that included aspects of Health-related quality of life (HRQOL). The study was conducted from September 2020 to September 2021, in the Chuvash Republic, Cheboksary. The study involved 75 patients (n = 75) with articular form of RA, aged 25 to 70 years (mean age 52.2±4.63), 82% women. In 24 (32%) respondents, 1 degree of inflammatory activity was verified, in 36 (48%) - the second, in 15 (20%) - the third degree. The first stage was diagnosed in 9 (12%) patients (according to Steinbroker), in 42 (56%) cases stage 2 of RA development was diagnosed, in 18 (24%) cases - the third stage, 6 (8%) patients had stage 4. The diagnosis of RA was based on the criteria (ACR). Statistical processing of the results was carried out in MS Office Excel programs.
Results: More than half of the patients (55.87%) experienced daily pain in the peripheral joints, which worsened their mood and well-being. When assessing the degree of pain, 68.45% of patients assessed their pain according to VAS as moderate (7.2±0.96 points). When assessing physical activity (PF) in 33.17% of patients, its decrease was noted as "significant". When assessing social activity (SF), a decrease in this indicator was revealed: 56.32% of the surveyed noted a "moderate" decrease, 33.16% as "significant". 23.94% of the surveyed noted the

decrease in the indicator of general health (GH) as "moderate". When assessing mental health (MH), a decrease in the indicator was found in 43.67% of patients as "moderate". When assessing emotional problems in disability (RE), there was a "significant" decrease in the indicator in 54% of respondents. 62.24% of the surveyed patients consider the loss of freedom of movement to be the biggest problem in RA. 56.24% of patients rated their satisfaction with their lives as "average degree of satisfaction"; 43.76% of patients as "low satisfaction".

Conclusion: As a result of the survey, it can be stated that 43.76% of respondents have a "low degree of satisfaction" with life. In order for the doctor to have all the objective information, it is necessary to adequately and timely evaluate changes in HRQOL for the purpose of early diagnosis and timely treatment of RA.

Disclosure of Interests: None declared

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AB1550-HPR CORRELATIONS BETWEEN PAIN AND EMOTIONAL STATUS IN PATIENTS WITH FIBROMYALGIA

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Objectives: The aim of the study was to investigate the correlations between pain syndrome and psychological status of patients with fibromyalgia (F).

Methods: The group we investigated consisted of 100 people. All patients were women of 43.85±0.79 years old in average. The diagnosis was made in accordance with the diagnostic criteria for fibromyalgia (ACR, 2010) [1]. The intensity of the pain syndrome was ranked using a visual analogue scale (VAS) and expressed in points: 0-3 points - the absence or slight severity of muscle pain, 4-7 points – moderate, and more than 7 points - intense, almost constant muscle pain. The average pain syndrome was 7.2±0.16 points, diagnostic pain points - 14.27±0.25 points. The psychological status was studied using standardized psychodiagnostics methods adapted in the laboratory of clinical psychology of the St. Petersburg Bekhterev's PsychoNeurological Institute: "Type of attitude towards the disease" - "TOBOL" (Wasserman L.I., et al., 2005) [2]; questionnaire "Life Style Index" - "LSI" (Wasserman L.I., et al., 2005) [3]; method of formalized assessment of neurotic manifestations "NL" (Wasserman L.I., et al., 1999) [4].

Results: According to the severity of pain in the muscles, patients with F were divided into two groups: 1st group (57 people) - intensity of muscle pain = 0-7 points and 2nd group (43 people) - intensity of muscle pain = 8-10 points. The study of the correlations between the intensity of muscle pain and the types of personal response to the disease, the intensity of psychological defenses showed that F patients from 1st group were characterized by a significant formation of an ergopathic type of attitude towards the disease and intense use of the psychological defense "Intellectualization" ($p<0.05$). Patients of 2nd group had neurasthenic, sensitive and egocentric types of attitudes to the disease, intense use of psychological defenses such as "Repression" and "Regression", and the decrease in the tension of using the "Intellectualization" ($p<0.05$). It was also noted that in 1st group of F patients, there was already a significantly significant clinical increase in such neurotic traits as depression (6.17±0.16 points), asthenia (6.37±0.21 points) and, especially, anxiety (8 .16±0.69 points) ($p<0.05$). With an increase in the intensity of muscle pain up to 8-10 points (2nd group), indicators on the scales of depression (7.3±0.20 points), asthenia (7.29±0.20 points) and hypochondria (6.16±0.30 points) significantly increased ($p<0.05$).

Conclusion: Thus, the increase in pain sensations in patients with F leads to the formation of maladaptive variants of attitudes towards the disease (neurasthenic, sensitive and egocentric); accompanied by a significant increase in asthenic and depressive tendencies; as well as a limited range of use of less mature and adaptive defenses mechanisms ("Repression" and "Regression"), which may indicate the maladaptive nature of the personality's attempts to cope with the disease The data obtained can be useful and taken into account in the development of individual tactics of treatment and rehabilitation measures in order to improve the quality of the treatment.

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AB1551-HPR BODY COMPOSITION AND NUTRITIONAL STATUS IN PATIENTS WITH RHEUMATIC DISEASES

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Background: An adequate nutritional status and a balanced diet are essential for a functional immune system, especially in chronic diseases that condition a catabolic state. The increase in adipose tissue and the proinflammatory environment that it generates influences rheumatic diseases.[1.] This translates to increased disease activity, morbidity and mortality.

Objectives: To describe body composition and nutritional status alterations in patients with rheumatological diseases in a 3rd level center in northern Mexico.

Methods: A prospective observational study was conducted in a third level center in northern Mexico. Anthropometric measurements were made by electrical bioimpedance analysis with the InnerScan TANITA BC-533 equipment (Yesod, S.A de C.V. Japan). Descriptive statistics were performed for categorical variables and measures of central tendency and dispersion were used for quantitative variables.

Results: A total of 1,666 evaluations of 1,218 individual patients were included: 1,098 (90.14%) women and 119 (9.77%) men. The mean age was 50 (±13). The most frequent diagnoses were rheumatoid arthritis 556 (45.64%), systemic lupus erythematosus 164 (13.46%), osteoarthritis 106 (8.7%) and fibromyalgia 48 (3.9%). The means of the anthropometric measurements were weight 69.78. kg (±15.53), height 1.57 m (±.07), percentage of total fat 35.17% (±9.3), percentage of body water 45.15% (±6.42), visceral fat 8.32(±.3.9), kg muscle 41.84kg (6.4), bone mass 2.35 (±.0.75), metabolic age 50(±13), BMI 28.22(±.6.04), waist circumference 92.85(±.15.38), hip circumference 106.8, (±.12.94) waist-hip ratio 0.87 (±.0.08). A total of 431 (35.38%) patients were overweight, 407 (33.41%) had some degree of obesity, 338 (27.75%) had a normal BMI, and only 41 (3.36%) were underweight. 1,013 (83.16%) patients had low lean mass, 719 (59.03%) had low body water percentage, 680 (55.82%) had high levels of total fat, and 163 (13.38%) had visceral fat; 672 (55.17%) sarcopenic obesity and 320 (26.27%) a metabolic age greater than the chronological age.

Conclusion: The nutritional status of rheumatology patients in northern Mexico is inadequate with a high prevalence of obesity, overweight, and low lean mass. Nutritional intervention is of paramount importance in the comprehensive management of patients with rheumatologic diseases.

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Table 1. Means of electrical bioimpedance analysis.

Variable	Mean	SD
Weight, kg	69.78	(15)
BMI, kg/m^2	28.22	(6.04)
Total fat, %	35.17	(9.3)
Total body water, %	45.15	(6.42)
Visceral fat, kg	8.32	(3.9)
Lean mass, kg	41.84	(6.4)
Bone mass, kg	2.35	(0.75)
Metabolic age, years	50	(13)
Waist circumference	92.85	(15.38)
Hip circumference	106.8	(12.94)
W/H ratio	0.87	(0.08)

BMI: Body mass index. **W/H ratio:** Waist/Hip ratio

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AB1552-HPR HEALTH PERCEPTION OF PATIENTS WITH FIBROMYALGIA IN BRAZIL

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Background: Fibromyalgia is a rheumatologic syndrome characterized by chronic pain and symptoms such as fatigue, morning stiffness, sleep disturbances and depression. Health perception is a global assessment of health based on an analysis of the objective and also subjective aspects of each person. Health self-assessment is increasingly researched and shows the health status of the population, considering the individual's personal perspective and that this information can be useful to propose health promotion strategies.

Objectives: To identify the health perception of patients with fibromyalgia who live in Brazil.

Methods: This is a cross-sectional study that was carried out in Brazil in 2021. They were invited to participate in the research. Individuals with fibromyalgia were invited to participate in the study through the Brazilian Association of

Fibromyalgia Patients (ABRAFIBRO) in August 2021. The invitation was sent via email to all people registered with this association in the country. Self-perception of health was questioned through the following response options: bad, fair, good or very good. Data were analyzed using descriptive statistics.

Results: The study consisted of 243 people with fibromyalgia living in different states of Brazil. Most were female (97.5%), married or living with a partner (63.7%), of white race/color (58%), receiving 1 to 2 minimum wages (60.4%), with complete higher education (46.5%) and who administer more than 2 medications per day (65.8%). Regarding the perception of health, the majority reported that their health was regular (42.4%), followed by bad (38.3%), good (16%) and very good (3.3%).

Conclusion: The most prevalent health perception in people with fibromyalgia in Brazil was: "regular", followed by "bad", "good" and "very good". In view of the findings of this study, measures to control and prevent health risks in people with fibromyalgia become necessary. In order to implement policies to promote a healthy life for this population, it is necessary to know the determinants of these indicators of self-reported health morbidity in Brazil. It is also suggested that the results of this investigation be monitored by periodic population-based surveys, in order to verify the determination of the observed associations, being able, in the future, to detect an association with other variables. In addition, these data can guide and evaluate education and health promotion strategies in fibromyalgia.

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AB1553-HPR PATIENT'S EXPERIENCES ATTENDING AN EDUCATIONAL PROGRAM IN A RHEUMATOLOGY OUTPATIENT CLINIC IN COLOMBIA

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Background: An educational program has been recommended as an integral component of the standard care for rheumatoid arthritis (RA). Studies have demonstrated that education in patients with RA improves the overall outcome of treatment and positively impacts patients' lives. In addition, it is always relevant to understand the effects of these interventions from the patient perspective by using qualitative research methods (1, 2).

Objectives: To explore the experiences of patients attending a structured educational program specific to rheumatoid arthritis.

Methods: We conducted a qualitative study; data were collected in two focal groups; The information was transcribed and coded according to the leading emerging categories.

Results: 23 participants attended the focal groups; most were women (90%). The mean age was 61 years ± 5. We identified fourth categories. First, the experiences in the program. Second, sharing their experience with other patients with rheumatoid arthritis. Third, the knowledge acquired during the program. Finally, the fourth category was applying the new knowledge in everyday life. Figure 1.

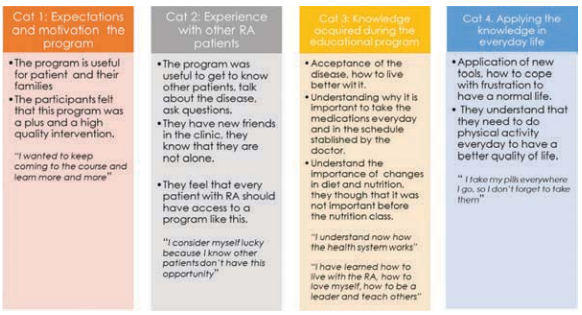

Figure 1. Emerging categories in the qualitative analysis

Conclusion: Patients who attend an educational program report positive and fulfilling experiences. An educational activity improves how the patient sees the disease and the pharmacological and nonpharmacological treatment. Our findings are similar to other studies, where involving an educational component can improve self-efficacy and might improve clinical outcomes (3, 4).

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Disclosure of Interests: Ruth Alexandra Castiblanco Montañez: None declared, Fernando Rodriguez: None declared, GUILLERMO SÁNCHEZ: None declared, Diana Buitrago-Garcia: None declared, Pedro Santos-Moreno Speakers bureau: Pfizer, Janssen, Abbvie, Biopas-UCB, Bristol, Roche, Novartis, Lilly, Consultant of: Pfizer, Janssen, Abbvie, Biopas-UCB, Bristol, Roche, Novartis, Lilly, Grant/research support from: Pfizer, Janssen, Abbvie, Biopas-UCB, Bristol, Roche, Novartis, Lilly

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AB1554-HPR DRUG-RELATED PROBLEMS EXPERIENCED BY PATIENTS WITH RHEUMATIC DISEASES: A LONGITUDINAL OBSERVATIONAL STUDY

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Background: Patients with rheumatic diseases can experience multiple drug-related problems (DRPs) along their patient journey.[1] Insight into patients' experience of DRPs over time might aid in timely identifying and preventing DRPs.[2,3]

Objectives: To longitudinally identify DRPs experienced by patients with rheumatic diseases.

Methods: A prospective observational study was conducted in a Dutch outpatient pharmacy. Adult patients with rheumatic diseases that were prescribed medication by a rheumatologist were questioned about experienced DRPs by telephone 4 times in 8 weeks using a structured interview-guide. Unique DRPs (i.e. DRPs not reported in earlier interviews by individuals) were categorized using a classification for patient-reported DRPs and analysed descriptively.

Results: In total, 52 participants (median age 68 years (interquartile range (IQR) 62-74), 52% male) completed 192 interviews with 45 (87%) participants completing all 4 interviews. The majority of patients (65%) were diagnosed with rheumatoid arthritis. Patients reported a median number of 3 (IQR 2-5) unique DRPs during interview 1. In subsequent interviews, patients reported median numbers of 1 (IQR 0-2), 1 (IQR 0-2) and 0 (IQR 0-1) unique DRPs for interview 2 to 4 respectively. Participants reported a median number of 5 (IQR 3-9) unique DRPs over all completed interviews. Unique patient-reported DRPs were most frequently categorized into (suspected) side effects (28%), medication management (e.g. medication administering or adherence) (26%), medication concerns (e.g. concerns regarding long-term side-effects or effectiveness) (19%) and medication effectiveness (17%).

Conclusion: Patients with rheumatic diseases experience various DRPs over time. These patients might benefit from continuous support during their patient journey.

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HPR Service developments, innovation and economics in healthcare

AB1555-HPR PRELIMINARY DESCRIPTION OF PATIENTS PARTICIPATING IN A MHEALTH OA MANAGEMENT PROGRAM – BASELINE DATA FROM A RANDOMIZED CONTROLLED TRIAL

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Background: As the prevalence and costs related to osteoarthritis (OA) are expected to rise in the coming years, actions have to be taken to ensure access to effective and economical sustainable recommended treatment for this patient population. Digital tools, such as the use of mobile health applications (mHealth), could serve as a solution. Though, little is known about characteristics of patients participating in a mHealth osteoarthritis management program (OAMP) in physiotherapy practice.
Objectives: To describe demographic and disease-related characteristics of patients with hip and/or knee OA recruited to a mHealth OAMP and compare these characteristics to those of other OAMPs.
Methods: The Digital Osteoarthritis Care-study (DigiOA) is a two-armed non-inferiority RCT currently running in primary health care in Norway. In total 156 participants with hip and/or knee OA seeking physiotherapy in primary care will be asked to participate. Consenting patients will receive 1-2 hours of education before randomization to 6 weeks of either exercise therapy via the Virtual Training mobile health application or supervised exercise therapy. Inclusion rate is reported as frequency and percentage. To describe patient characteristics, we have included baseline data on patients currently included in the study. These characteristics are compared to baseline data from a web-based OAMP (1) and a standard OAMP in physiotherapy care (2).
Results: Of 39 eligible patients, 25 (64%) have to date consented to participate in the study. An overweight of the included patients are presented with knee OA, have had symptoms for five years or less, and have higher education (Table 1).

Table 1. Demographic and disease-related characteristics of patients with hip and/or knee OA recruited to a mHealth OA management program (n=25)

Age years, n=24, mean (SD)	63.2 (10.4)
Female, n (%)	17 (70.8)
BMI, mean (SD)	27.3 (5.4)
Education, n (%)	10 (40)
-Upper secondary	15 (60)
-College/university	
Non-Smoking, n (%)	23 (92)
Work status, n (%)	12 (48)
-Employed	4 (16)
-Sick leave/receiving disability benefits	11 (44)
-Retired	
Primary joint affected, n (%)	17 (68)
-Knee	8 (32)
-Hip	
Other joints affected, n (%)	21 (84)
Other chronic conditions, n (%)	15 (60)
Symptom duration years, n (%)	5 (20)
-Less than a year	15 (60)
-1-5 years	5 (20)
-More than 10 years	
OA medication use last 3 months, n (%)	19 (76)
Pain last week[a], mean (SD)	4.7 (2.3)
HOOS/KOOS[b], mean (SD)	59.4 (18.5)
-Pain	48.4 (10.2)
-Symptoms	67.2 (19.1)
-ADL	39.7 (19.7)
-Sport/Rec	46.5 (14.2)
-QOL	
ASES[c], mean (SD)	2.2 (0.8)
-Pain	2.5 (0.7)
-Other symptoms	
Exercise self-efficacy scale[d], mean (SD)	40.2 (3.4)

[a]= NRS 0-10 (10=most pain) [b]= (HOOS: Hip disability and Osteoarthritis Outcome Score/ KOOS: Knee injury and Osteoarthritis Outcome Score (0-100, 100=no problems) [c]= Arthritis Self-Efficacy scale (0-4, 4=most certain) [d]= (20-100, 100=most certain)

The study sample report high impact of symptoms, and decreased function. Self-efficacy related to pain and symptoms are relatively high, but the patients report lower exercise self-efficacy. The study sample is comparable to patients included in both standard and web-based OAMPs, except from lower impact of pain and higher usage of pain medication in DigiOA.

Conclusion: Preliminary results show that baseline characteristics are comparable to patients included in other OAMPs, but with only two third of eligible patients consenting to participate in a mHealth OAMP there is a need for more in-depth knowledge on patients' attitude towards mHealth OAMPs.
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AB1556-HPR IDENTIFYING BARRIERS IN EARLY RECOGNITION AND MANAGEMENT OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A RETROSPECTIVE REVIEW

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Background: Axial spondyloarthritis are immune and genetically mediated inflammatory arthritis where there is significant delay in diagnosis and management of roughly 8.5 years; leading to poorer outcome and quality of life for a patient.
Objectives: This aim of audit was to improve the identification and referral pathways for patients with axial spondyloarthritis in South West Essex United Kingdom as per agreed NICE & EULAR criteria.
Methods: This was a retrospective audit of 35 patients diagnosed as Axial Spondyloarthritis in secondary care and those which was referred to secondary care by community triage MSK service (Connect) as Axial Spondyloarthritis, between January 2019 and March 2020. Data was extracted to look at demographics, diagnostic investigations performed, duration from symptom onset to diagnosis and the patient journey to secondary care.
Results: Out of total 35 patients, 63% were males with a median age of 35 years. Of all the GP referrals 17% were directly to secondary care and 71% were via triage service. Twelve percent of referrals came from other specialties. The average timeframe from symptoms onset to referral by GP was 7.7 years. Average time before a patient was seen by a rheumatologist after referral was 4.4 months. After evaluation in clinic, 30 cases (85.7%) were finally diagnosed as AxSpA after rheumatologist's review. Rest were mechanical back pain. Inflammatory back pain was mentioned in 18% of referrals by GP and 80% of referrals letters by triage service. Base line investigations included: CRP was in 39% of cases under GP care and 100% cases under triage service. Additionally, HLAB27, X ray and MRI tests were done in 22%, 17% and 22% of GP cases respectively and 86%, 80% and 80% of cases from triage service. After specialist review, HLAB27 was positive in 49% of patients, X ray positive sacroileitis in 54.5% patients and rest had MRI positive sacroileitis and spinal features. Some had both X ray and MRI investigations.
Conclusion: Lack of education and awareness about spondyloarthropathy remains the most prominent factor behind delay to diagnosis. Lack of important information and clinical features on referral letters are also a contributing factor. It is evident that early referral to rheumatologist care and early triaging during reviews are crucial to diagnose AxSpA. We are piloting use of SPADE tool in suspected AxSpA cases to guide clinical reasoning and early referrral.
Disclosure of Interests: None declared
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AB1557-HPR DEVELOPING THE GUIDELINE FOR OUTPATIENT APPOINTMENT OF A CLINICAL NURSE SPECIALIST AT THE EAST-TALLINN CENTRAL HOSPITAL RHEUMATOLOGY CENTER. DEVELOPMENT PROJECT.

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Background: Rheumatic diseases can increase the economic and social burden on the individual and their relatives' ones, as well as on the health care system and society. Based on international empirical experience, it can be stated that in an exemplary Rheumatology center, both the outpatient appointment of a (general)

nurse and the outpatient appointment of a clinical nurse specialist work as a team. The Rheumatology Center of East Tallinn Central Hospital is the only center in Estonia that specializes in rheumatic patients, where (general) nurses are proceed, but the extent to which the current health care service meets the needs of rheumatic patients has not yet been assessed. In addition, the health insurance fund launched a pilot project to clarify the difference between outpatient appointment of a clinical nurse specialist and independent appointment of a (general) nurse. However, there is no evidence-based guideline for outpatient appointments for rheumatic patients.

Objectives: The aim of the development project was to develop the guideline for outpatient appointment of a clinical nurse specialist for rheumatology based on evidence-based literature and expert opinions at the Rheumatology Center of East-Tallinn Central Hospital.

Methods: The development project process took place as a plan-do-study-act cycle, using the method of systematic review of the literature to develop the guideline and the method of written survey to obtain an expert opinion on it. Verbal responses from experts for organizational diagnostics and the guideline feedback was analyzed using content analysis. Quantitative or numerical responses were analyzed using descriptive statistics to calculate the frequency distributions (n and %) for each response.

Results: The guideline developed as part of the development project supports the implementation of a new clinical nurse specialist care service for rheumatic patients.

Conclusion: Based on previous research analyzed and surveys conducted by experts at the Rheumatology Center, it can be argued that the clinical nurse specialist service differs significantly from the (general) nurse outpatient appointment and is more responsive to the needs of rheumatic patients. There are potential benefits for the clinical nurse specialist of the outpatient appointment to the organization and to society, as this service increases the level of reliability, efficiency, and availability of all nursing care.

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AB1558-HPR TELERHEUMATOLOGY WITH PRIMARY CARE CENTERS: FEEDBACK FROM AN EXPERIMENTAL TELEMEDICINE PROJECT IN BURGUNDY (2019-2021)

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Background: Telemedicine could be an innovative and sustainable response for rheumatologic advice in areas with low medical density. Improving coordination of investigations, access to allied health members and dedicated telehealth platform may improve the management of many rheumatologic patients.

Methods: This French TeleRheumatology project with multidisciplinary primary care centres was set up in 2019, specifically targeting the Burgundy region in Eastern France and was financed by the Regional Health Agency. Four rheumatologists from the Dijon University Hospital took turns to respond to the various requests for telemedicine (teleconsultation, teleexpertises) on a dedicated digital platform integrating a medical imaging viewer. In addition to the activity (number and type of procedures performed) and the distances avoided for the patient for rheumatology consultation, feasibility of this colaborative digital project was assessed on the basis of a participant satisfaction questionnaire (rheumatologists, general practitioners and patients).

Results: From October 2019 to january 2022, this TeleRheumatology project allowed the progressive integration of 23 primary care centres despite the concomitant COVID-19 crisis which slowed down the deployment. 212 procedures were performed (96% teleexpertises): 76% for mechanical disorders (spine 31%, osteoporosis 19%, osteoarthritis 15%), 18% for inflammatory rheumatism, 53% advice for diagnosis, 41% for management and/or therapy, 89% with imaging (X-Rays, CT- Scan, MRI) to be reviewed. The average response time was 16 hours and the average number of round-trip kilometers avoided was 216. Only 15% of the rheumatologic advices led to a face-to-face consultation or hospitalization at the University Rheumatology Department and 6% to other specialists. 97% of the patients would like to use this Telerheumatology program again (Satisfaction score: 9.1/10). 100% of the expert rheumatologists (satisfaction score 9.25/10) and the general practitioners (satisfaction score: 9.0/10) wanted to continue this digital health partnership in their daily practice.

Conclusion: Despite the inherent limitations of telemedicine (absence of clinical examination, technical barriers of interoperability, etc.), this french innovative TeleRheumatology project with primary care centres has shown encouraging results in terms of acceptability and satisfaction thanks to the coordination of the Regional Health agency and physicians' motivations. Telerexpertise seems to be the preferred modality given its better practical feasibility. Approval and acceptance are increasing in the Rheumatology community because telemedicine appears to be an effective tool for improving health care access as demonstrated by its rapid expansion, especially during the COVID-19 pandemic.

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AB1559-HPR ESTABLISHING A MULTIDISCIPLINARY CLINIC TO IMPROVE THE QUALITY OF CARE FOR PATIENTS WITH INTERSTITIAL LUNG DISEASE.

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Background: Patients with interstitial lung disease related to rheumatic disease (ILD-RD) often need to see multiple specialties to establish the diagnosis and for management. Suh care is better provided in a multidisciplinary clinic (MDC) and setting up such a MDC involves significant cost, time and buy in from stakeholders. In our center, we approached starting a MDC as a multiple phased project. Phase 1: confirm improved patient outcomes when multiple specialties are involved in providing care to these patients. Phase 2: application for an internal grant for a prospective pilot clinic and phase 3: the establishment of a permeant MDC. We report the results of our phase 1 analysis.

Objectives: The primary aim of this study was to determine if involvement of our pulmonary and cardiology colleagues in the care of patients with ILD-RD seen in the rheumatology clinic results in improvement in the evaluation and treatment of these patients.

Methods: This is a retrospective, single center, hospital-affiliated outpatient study. All patients seen in the rheumatology clinic with a diagnosis of ILD-RD between January 1 2018 and December 31 2019 were eligible for enrollment. A list of patients was generated by the technology service group using relevant international classification of diseases codes. These records were reviewed and those meeting the inclusion and exclusion criteria were enrolled.

A review of the 1574 charts generated confirmed 41 patients with ILD-RD. Demographic data, as well as disease related data including serological testing, disease manifestation and treatment choices was obtained. Continuous variables were analyzed using T-test or Mann-Whitney U test. Categorical variables were analyzed using Chi-square Tests or Fisher's exact tests. Statistical analysis was performed using SAS9.4, and p value <0.05 was considered statistically significant.

Results: Patients seen by more than one specialty were more likely to have had a more extensive evaluation for ILD and its complications. The cause of the ILD-RD did not have an impact on the tests performed or the number of specialist seen.

There was a significantly more glucocorticoids monotherapy use in scleroderma related ILD, but disease-modifying antirheumatic drugs were more commonly used in non-scleroderma ILD patients.

Table 1. Demographics

	Non-scleroderma ILD (N = 27)	Scleroderma ILD (N = 14)	p-value
Age at diagnosis	72.8 (10.2)	70.5 (13.7)	0.55
Female	70.4% (19/27)	71.4% (10/24)	0.99
Race			0.69
Caucasian	77.8% (21)	85.7% (12)	
African American	22.2% (6)	14.3% (14)	
PAH	17.4% (4/23)	23.1% (3/13)	0.69
PFT	87.5% (21/24)	92.9% (13/14)	0.99
CT Chest	100% (24/24)	100% (14/14)	
Right HCC	30.4% (7/23)	21.4% (3/14)	0.71
Number of specialists			0.31
1	8.3% (2)	14.3% (2)	
2	37.5% (9)	57.1% (8)	
3	4.2% (13)	28.6% (4)	
Medication			<0.01
None	0% (0)	14.3% (2)	
GC	7.4% (2)	42.9% (6)	
GC + DMARDs	88.9% (24)	42.9% (6)	
DMARDs	3.7% (1)	0% (0)	

Conclusion: Our data suggests that a MDC for RD-ILD results in a more thorough investigation and treatment, and this will likely lead to improvements in patient outcomes. Based on these findings, our rheumatology group is seeking internal funding for a pilot clinic evaluating prospectively the benefits of an ILD MDC.

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AB1560-HPR NURSE-DRIVEN DIAGNOSTIC PROCESS OF PATIENTS WITH SJÖGREN'S SYNDROME (SS) A CLINICAL DEVELOPMENT PROJECT

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Background: Sjögren's Syndrome (SS) is a chronic autoimmune disease that affects the body's glandular functions, especially the lacrimal and salivary glands, causing the mucous membranes to dry out (1). There are no diagnostic criteria, and classification criteria are often used to support the diagnosis (2). We identified a need to unify and consolidate the diagnostic process of patients with SS in the Capital Region of Denmark. A medical working group supervised the nurse-driven diagnostic process at Rigshospitalet, Glostrup. Here an interdisciplinary working group with physicians, nurses, and secretaries developed a diagnostic process and logistic based on the American-European Consensus Group Classification Criteria 2002 (3). The nurse's took medical history and performed sicca tests and made sure that the patient received adequate guidance. With input from three patients, the nurses at the outpatient clinic developed - written material on eye and mouth dryness. We developed a "smart phrase" for our documentation platform in the interdisciplinary working group. The purpose of the 'smart phrase", was to unify the documentation and ensure continuity in the conversation with the patient. The Rheumatologists task was to disprove or confirm the diagnosis and perform a risk stratification especially in relation to the development of lymphoma, but also interstitial lung disease.

Objectives: The aim of this project was to examine and evaluate the patients' experience of nurse-driven diagnostic process.

Methods: To evaluate the new patient course, we performed a survey. The questions selected for the survey were primarily based on the patients experience of meaning and coherence in the diagnostic process. The questions were developed by the nurses in the Outpatient Clinic; "Do you feel safe going home after the consultation today?" "Did you get answers to the questions you asked while you were in the consultation?" "Did the staff take the time to listen to you?". Also, the patients could add comments.

Results: A total of 34 consecutives responded to the questionnaire. 88% felt safe when returning home from the Outpatient Clinic, 85% received answers to their questions during the consultation. Altogether, 94% answered that the health care professionals were present and listened to them. The patients had the following comments: "The diagnostic process contained a lot of unresolved waiting time " and "There has been some confusion about the division of tasks in the different hospital wards".

Conclusion: We found that the patients were satisfied with the nurse-driven diagnostic process. The diagnostic process created a feeling of safety in the patients and the patients found that they were listened to and allowed to ask questions. In addition, by evaluating the process investigation, we could change practice and further unify the diagnostic process. The result of the questionnaire supports the justification of the nurse competencies, by preforming a high level of information and guidance as well as the need for recognition of the patient's symptoms. Therefore, the working group chose to meet again and evaluate. We decided that the nurse and rheumatologist consultation should be performed on the same day. Such consultation made it possible for the nurse to ensure continuity in the process, as the same nurse could follow the patient throughout the day. This optimized the opportunity for the nurse to guide the patient in the symptomatic treatment of eye and mouth dryness. Also, the nurse had the opportunity to guide in oral hygiene, fatigue, and lifestyle factors.

The next step in our development project is to evaluate our revised nurse-led diagnostic process. In addition, the working group is currently working on material for a course in SS, where 4-6 patients and relatives can have the opportunity to participate.

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AB1561-HPR PHYSIOTHERAPY FOR RHEUMATOID ARTHRITIS (RA) – PAST, PRESENT AND A POSSIBLE FUTURE?

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Background: Physiotherapy has a long tradition providing services to patients with RA. The main aim of physiotherapy is to improve patients' abilities to perform movements and physical activities through exercises and educating patients in self-management skills. For physiotherapy to proceed into future, it seems relevant to examine what shifts occurred in physiotherapy over time and why did they happen.

Objectives: Is to unpack the shifts in physiotherapy for patients with RA from 1980 until today.

Methods: Norwegian physiotherapy in rheumatology is used as case. The shifts are identified with help of literature about history of medicine and physiotherapy in rheumatology and empirical physiotherapy research since the 1980s. The author draw on own experiences first as a clinician and practice teacher for physiotherapy students in rheumatology, and later as a scientist and advisor for a multidisciplinary team in rheumatology.

Results: Physiotherapy focuses on movement and function, which over time have consistently been understood in relationship to disease-induced alterations and biomechanics. Shifts in physiotherapists' remedial exercises have occurred over time as better disease control occurred and evidence showed that physical activities and exercise programmes had disease modifying effects and improved patients' functional capacity. In the 1980s, a move from earlier passive, joint protective movements with little weight load to cautious weight-bearing movements occurred, mostly as a response to improved disease-modifying drugs and joint surgery. In the 1990s, physiotherapy shifted from cautious weight-bearing movements to safely performed physical activity as a response to scientific findings showing beneficial effects on radiological, immunological, and physical function measures. In the 21. century, RA is identified earlier and increasing number of patients reach disease remission before irreversible occurs in the musculoskeletal system. Presently, a new shift in Norwegian physiotherapy is on the way. Adherence to EULAR guidelines 2018 on physical activity[1] is moving physiotherapy from promoting exercises through engagement in self-determined physical activities into educating patients in performing structured intensive physical fitness training programmes for preventing future comorbidities.

Conclusion: At the moment, it is a dilemma that the raising rate of patients successfully treated to disease remission is not accompanied with more patients remaining in volitional work in Norway[2]. Thus, there is a need in physiotherapy to critically scrutinize the meaning and significance of movements and functioning for the individual patient's own life purpose and the society's wish that people stay in paid work.

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AB1562-HPR COMPARING THE PROVISION OF SUBCUTANEOUS METHOTREXATE BETWEEN HOMECARE AND OUTPATIENT PHARMACY; WHAT DO PATIENTS PREFER AND IS ONE ROUTE QUICKER?

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Background: The provision of subcutaneous methotrexate has historically been through homecare who provide injection training and delivery. In July 2018, subcutaneous methotrexate was accepted for shared care in the Trust's locality to reduce medication costs but to also improve safety, reducing the risk of concomitant trimethoprim prescribing.
When suitable for shared care, initial injection training is provided by outpatient pharmacists and prescribing and monitoring during the stabilisation period is the responsibility of the rheumatology pharmacy team.
Objectives: The primary aim of this audit was to compare patient satisfaction between these two different routes of injection training and prescription provision. Additionally, the time it took for a patient to receive their first dose following a decision to start treatment, was also compared.
Methods: Patients were identified from databases held within the department, contacted retrospectively via telephone and asked to complete a short questionnaire. Clinic letters and the homecare company provided dates of treatment decision and initiation.
Results: 40 patients were contacted, 20 had received treatment via outpatient pharmacy and 20 via homecare.

Table 1. Patient reported satisfaction following receipt of injection training and prescription provision via outpatient pharmacy and homecare

	Outpatient Pharmacy (20)			Homecare (20)		
	Not satisfied	Satisfied	Very satisfied	Not satisfied	Satisfied	Very satisfied
Time taken to start treatment	2	5	13	2	6	12
Injection training	0	4	16	3	5	12
Method for delivery of injection training and initial prescription	1	8	11	3	4	13
Process of receiving repeat prescriptions	1	4	15	1	3	16

The mean time taken to start treatment was 30 days in the homecare group and 13 days in the outpatient group. 7 patients (35%) within the outpatient group started treatment within 7 days. The shortest time within the homecare group was 15 days (3 patients).
Conclusion: Reported patient satisfaction between the two routes of treatment provision was similar. Patients commenced treatment significantly quicker via outpatient pharmacy, reporting a high degree of satisfaction with the injection training provided by outpatient pharmacists. This audit has confirmed that shared care provision of methotrexate initially via outpatient pharmacy is a safe, efficient and viable option.
Disclosure of Interests: Rebecca Heaton Speakers bureau: I prepared slides and presented virtually for pharmacists explaining shared care experience (Nordic), Consultant of: Formulating a educational package for rheumatology pharmacists (Galapagos), Jennifer Nasralla: None declared, Charlotte Filer: None declared, Edward Appleby: None declared, Mya Myintzu: None declared
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HPR Professional education, training and competencies

AB1563-HPR TRAINING AND ASSESSMENT OF MUSCULOSKELETAL ULTRASOUND AND INJECTION SKILLS - A SYSTEMATIC REVIEW

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Background: The importance of international harmonization regarding education of rheumatologists in musculoskeletal ultrasound (MSUS) and injection skills have been highlighted in several studies, including the need for standardized training programs containing competency-based education using validated assessment tools [1-2].
Objectives: To examine how residents are trained and assessed in MSUS, MSUS-guided and landmark-guided joint aspiration and injection. Additionally, to present the available assessment tools and examine their supporting validity evidence.
Methods: A systematic search of PubMed, Cochrane Library, and Embase was conducted in accordance with the PRISMA guidelines and studies published from January 1, 2000 to May 31, 2021 were included. Two independent reviewers performed the search and data extraction. The studies were evaluated using the Medical Education Research Quality Instrument (MERSQI).
Results: 9,884 articles were screened and 43 were included; 3 randomized studies, 21 pre- and post-test studies, 16 descriptive studies (Table 1), and 3 studies developing assessment tools. The studies used various theoretical training modalities e.g. lectures, anatomical quizzes, and e-learning. The practical training models varied from mannequins and cadavers to healthy volunteers and patients. Most studies used subjective "comfort level" as assessment, others used practical examination and/or theoretical examination. All training programs increased trainees' self-confidence, theoretical knowledge, and/or practical performance, however few used validated assessment tools to measure the effect. Only one study met the MERSQI high methodical quality cut-off score of 14.

Table 1. Description of included studies examining training of MSUS, MSUS-guided or landmark-guided joint aspiration and injection skills.

Study characteristics	MSUS	MSUS-guided	Landmark-guided
No. of studies[a]	14	3	23
Study design	0	0	3
Randomized	2	2	17
Pre- and post-test	12	1	3
Descriptive			
Participants[b]	408	38	1388
Residents	1	-	8
Experts			149
Medical students			47
Others			
Assessment[c]	7	1	-
Objective	-	-	2
Practical	2	1	13
Theoretical	5	1	8
Subjective			
Questionnaire			
Mixed			
MERSQI[d]	9.2	7.5	8.9
Mean score			

Legend: [a] Studies developing assessment tools are not included in this table. [b] Accumulated number of participants enrolled in the studies. [c] Number of studies. [d] Mean score using the Medical Education Research Study Quality Instrument, maximum score =18.

Conclusion: The included studies were heterogeneous, and most were of poor methodological quality and not based on contemporary educational theories. This review highlights the need for educational studies using validated theoretical and practical assessment tools to ensure optimal MSUS training and assessment in rheumatology.
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AB1564-HPR ULTRASOUND EXAMINATION AND INTRA-ARTICULAR INJECTIONS BY A RHEUMATOLOGY NURSE SPECIALIST.

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Background: At The Department of Medicine, section of Rheumatology, Odense University Hospital (OUH) Svendborg, we consult patients with rheumatoid arthritis, psoriatic arthritis and gout. The patients can have joint inflammation. Therefor need joint assessment by ultrasound, arthrocentesis and / or IA injection. Ultrasound examination, arthrocentesis and administration of intra-articular (IA) injections for rheumatic disease represent an expansion of the nurse's role.

A previous study has shown, that trained nurses can perform satisfying and safe IA injections at least as well as those administered by doctors (1). High availability to adequate treatment will have a positive effect. For the patient and on a socio-economic level, as patients who have severe arthritis could be forced to stay home from work and leisure activities (2). It was decided to educate a nurse, who showed interest in ultrasound and IA injections and who showed the technical skills.

Objectives: To educate and develop competence in the nursing staff regarding ability to perform joint ultrasound, arthrocentesis and IA injection. In order to offer immediate arthritis treatment and free up doctor time to be able to see other patients.

Methods: At first, the nurse watched the ultrasound, arthrocentesis and injection on the knee performed by a rheumatologist a couple of times. Then she performed the procedure under supervision and then she independently performed the ultrasound, arthrocentesis and injection on the knee with the opportunity for supervision. The nurse completed a two-day muscular/skeletal ultrasound course at university hospital Skejby. The course was both theory and hands-on training in an auditorium and was held by a radiologist and a rheumatologist. The nurse has furthermore participated in a course at Esbjerg hospital for doctors and nurses about ultrasound on upper extremities. This was a hands-on course. In conjunction with arthrocentesis, the nurse learned to identify urate crystals in synovial fluid through microscopy.

Results: See Table 1 for which joints where the nurse performed ultrasound, arthrocentesis and injection during the first and second year.

Table 1.

Year 1

Joint	*Ultrasound*	*Arthrocentesis*	*IA injection*
PIP	10		4
MCP	9		7
WRIST	23		15
ELBOW	1		1
KNEE	50	41	50
ANKEL	7		9
MTP	5		4
In all	102	41	90
Year 2			
Joint	***Ultrasound***	***Arthrocentesis***	***IA injection***
PIP	10		9
MCP	35		37
WRIST	32		35
ELBOW	12	3	12
KNEE	69	66	80
ANKEL	18	1	17
MTP	28	2	23
In all	203	72	204

One year after the procedure was implemented the joints that the nurse perform ultrasound and injections on, had increased. Starting with only knees to PIP, MCP, wrist, elbow, knees, ankles and MTP joints. After the first year, the nurse grew independent and confident with the new task, as the table beneath shows. Since the nurse started to perform ultrasound, arthrocentesis and IA injections, there has been no reports of adverse events.

Conclusion: Nurses can be trained to perform ultrasound, arthrocentesis and injections, in a wide range of joints. Patients and staff express satisfaction with the availability of treatment. There has been no reports of adverse events.

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AB1565-HPR REHABILITATION NURSES KNOWLEDGE ABOUT OSTEOPOROSIS AND FRAGILITY FRACTURES IN PORTUGAL

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Background: Scientific evidence reveals gaps in health professionals' knowledge about osteoporosis and fragility fractures, which impairs and influences the quality of care, namely in preventive actions.

Objectives: To analyse knowledge of Rehabilitation Nurses about osteoporosis and fragility fractures to identify training needs of Rehabilitation Nurses.

Methods: A cross-sectional study, integrated in a larger project, using an adapted questionnaire, made available online and disseminated by mailing list of "Ordem dos Enfermeiros" (Royal Colleague of Nursings) to all Portuguese Rehabilitation Nurses.

Results: There were include 452 participants(10.3% of the 4 397 Rehabilitation Nurses), 17% perform functions in orthopaedics and traumatology service, 4.5% physical medicine and rehabilitation and 78.6% in other services, majority, 74.6% women. On average, 69.6% correct answers were identified regarding osteoporosis and fragility fractures. Results reveal that the main areas of knowledge deficit, in this study, are related to the concept and epidemiology of osteoporosis and fragility fractures and about the most appropriate diet. Nurses with higher academic degree (master's degree) revealed more knowledge (p=0.01).

Conclusion: This study reveals that the knowledge about osteoporosis and fragility fractures is low (<70% correct answers), thus there is an opportunity to improve the knowledge related to osteoporosis and fragility fractures among Specialist Nurses in Rehabilitation Nursing.

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AB1566-HPR SHIFTING THE MINDSET: USING A HEALTH COACHING APPROACH FOR HEALTH PROMOTING CONSULTATION IN ADOLESCENT RHEUMATOLOGY

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Background: Juvenile rheumatic diseases have a significant negative impact on health early in life which may affect later health outcomes. The Adolescent and Young Adult Rheumatology Department (AYAD) at University College London Hospitals (UCLH) looks after over 2,000 young people with a variety of rheumatological conditions and provides developmentally appropriate interdisciplinary (ID) approach to healthcare. Health coaching (HC) is "a behavioural intervention that facilitates participants in establishing and attaining health promoting goals in order to change lifestyle-related behaviour, with the intent of reducing health risks, improving self-management of chronic conditions, and increasing health related quality of life".[1] Evidence shows that health coaching can improve health related behaviours including medication adherence, patient activation, and use of healthcare resources. [2-4]

Objectives: The aim of this project is to enable young people attending the AYAD to establish and achieve their own health-promoting goals and thereby change behaviour and increase confidence in self-management. As a first stage the aim was to develop health coaching capabilities within our ID Team by March 2022.

Methods: The strategy to deliver this project included commissioning a recognised core skills health coaching course for multidisciplinary team (MDT) members. Pre and post course surveys were completed by participants.

Results: All the AYA team members comprising 3 physiotherapists, 2 nurse specialists, a transition pathway coordinator, 4 consultants and 2 senior registrars took part in the health coaching workshops. A pre course survey (10/ 12 responded) revealed that 70% of MDT members felt their consultations focused solely on young people's medical/clinical care. 80% reported they discuss lifestyle choices such as sleep, and weight management. 40 % felt that their consultation times were long enough to discuss resources that would support long-term management. 30% reported they felt effective

in facilitating Young people and their families to self-manage and/or had sufficient health coaching awareness to facilitate behaviour change. The course was delivered over 2 separate days, one week apart, and included educational material, presentations, group discussion and skills development delivered in a coaching style. A post course survey (11/12 responses) demonstrated 100% of participants were satisfied with the course content, delivery, facilitation and opportunities to work and learn with colleagues, and felt that the skills were applicable to their work. They reported that the skills learned could be applied beyond healthcare, for example, with colleagues or in leadership roles, the course helped to raise self-awareness of behaviours that can negatively and positively impact patient and family engagement in their care, and that using some techniques and small changes to practice could potentially have a big impact on quality of care and outcomes as well as patient and staff experience.

Conclusion: Health coaching skills were considered as a useful tool by all AYAD team members. Skills gained on the course were considered useful in managing young people and applicable in settings beyond clinical care. The next stage of this project will include embedding the techniques learned into clinical practice and measuring qualitative and quantitative outcomes over time

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HPR Interdisciplinary research

AB1567-HPR SOCIAL WORKERS: DESCRIBING SOCIOECONOMIC CHARACTERISTICS DURING PRENATAL CARE IN PATIENTS FROM A PREGNANCY AND AUTOIMMUNE RHEUMATIC DISEASES CLINIC.

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Background: Social workers (SW) interventions are fundamental in health care; the main objective is to identify and mitigate social determinants of the patient's health. The socioeconomic study (SES) is the core assessment of SW; it analyzes the demographic structure and population dynamics.

Objectives: Describe the sociodemographic and social security characteristics in pregnant patients with autoimmune rheumatic diseases.

Methods: A cross-sectional and retrospective study was conducted in a pregnancy and rheumatic diseases outpatient clinic from the university hospital in Monterrey, México. The data from the SES database was collected. The sociodemographic information, family's monthly income and expenses, expenditures related to healthcare, type of social security, family nucleus (FN) and socioeconomic level (SL) were analized. The rheumatic diagnosis was retrieved from the medical records. The SL is classified in 7 levels (according to the score obtained in the SES); each level represents a percentage of the total cost of the healthcare received. Level 1 to 3 correspond to 0 - 28% percentage while levels 4 to 7 go from 53 to 100% of total payment that is due. To evaluate the health expenditure, the monthly limit expenditure per Mexican family is 98.39 dollars (the limit expenditure was taken from the Organization for Economic Co-operation and Development "OECD" 2019 report). For statistical analysis, the sociodemographic and clinical characteristics of the sample are presented as frequencies and percentages.

Results: From 2019 to 2021, 54 patients were interviewed. The mean age was 28.46 years(SD=6.69). The rheumatic diagnoses can be found in Table 1. The most common occupation was unemployment(n=34, 62.96%) and only completed basic levels of education(n=37,68.51%).

Table 1. Sociodemographic characteristics

	n=54
Demographic Data	
Age, mean(SD)	28.46(6.69)
Occupation, n(%)	
Unemployed	34(62.96)
Employed	17(31.48)
Self-Employed	3(5.55)
Marital Status, n(%)	
Married/Cohabitating	38(70.37)
Single	16(29.62)
Level of Education, n(%)	
Basic education	37(68.51)
Higher education	17(31.48)
Family Structure	
Family members, n(%)	
0-5	36(66.66)
6-11	18(33.32)
Number of children, n(%)	
1	36(66.66)
2	13(24.07)
3	5(9.25)
Family Nucleus, n(%)	
Nuclear	27(50)
Multi-nuclear	26(48.14)
Extended	1(1.85)
Rheumatic Disease, n (%)	
Rheumatoid arthritis	29(53.7)
Lupus	9(16.66)
Antiphospholipid syndrome	8(14.81)
Sjögren syndrome	1(1.85)
Health Expenditure, n(%)	
Active health insurance	
None	39(72.22)
Public health services (governmental and state workers)	8(14.81)
Private health insurance	7(12.96)
Average monthly family income (USD)	$614.23
Average monthly health expenditure (USD)	$105.71
Percentage of expenses in patient's health	16.21%

SD:Standard deviation

The most frequent SL was level 3 (46.29%) and the predominant FN was the nuclear family (50%) (couple and their dependent children). Most of them were not under any health coverage(n=39, 72.22%). The average family income was $614.23 USD and the average health expenditure was 105.71 USD; which represents 16.21% of the family income (per month).

Conclusion: SW play a key role understanding basic needs and identifying health determinants that decreases the odds of access of healthcare. Women with autoimmune rheumatic diseases have an important burden of the main determinants of health like low income, unemployment, basic education, and poor health coverage. In addition, the average health expenditure is higher than the recommended by OECD. Different strategies are needed for childbearing age patients with rheumatic diseases to decrease the impact of health determinants.

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Patient information and education

AB1568-PARE LIVED EXPERIENCES OF POSTMENOPAUSAL OMANI WOMEN WITH OSTEOPOROSIS

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Background: Osteoporosis is a globally significant clinical public health problem associated with age-related fractures [1,2]. Most research on the impact of the disease has been based on quantitative survey data. There are relatively few qualitative studies exploring women's lived experience with osteoporosis. Furthermore, most data are from Western countries, with no data from the Middle

East. Direct access to lived experiences is a powerful tool for gaining insights into a disease [3]. This study aimed to determine the lived experience of postmenopausal Omani women with osteoporosis.
Objectives: This study sought to answer three questions:
1.What does living with osteoporosis mean for postmenopausal Omani women?
2.How does culture impact the lives of postmenopausal Omani women with osteoporosis?
3.How do postmenopausal Omani women with osteoporosis perceive the support and care provided by healthcare professionals?
Methods: An interpretive phenomenology design was used with a purposive sample of 15 postmenopausal Omani women with osteoporosis and fragility fractures from primary and secondary care facilities in Muscat, Oman. Audio recorded, semi-structured, one-on-one interviews were held by Zoom and telephone; Crist and Tanner's framework was used to analyze data and identify key themes.
Results: The mean age of the participants was 63 years. Five (33.3%) reported a previous fracture. Just over half (53%) were illiterate; three (20%) had studied in college. Key themes related to their lived experience emerged from the data analysis: culture and religion; health care professionals' attitudes; and services and treatment regimen. The subjects' social and cultural lives were negatively impacted by osteoporosis and fragility fractures, which prevented some from attending celebrations such as close family marriages and religious gatherings. Participants played significant care-giving roles as wives, mothers and grandmothers but many were unable to perform many household chores, such as cooking, due to the osteoporosis and fractures. They perceived healthcare professionals through the professionals' communication styles and information they provided. Participants satisfied with their doctor's communication style described it as humanistic, with humour added, noting they provide health information and understand patients' needs. Those not satisfied indicated their doctors had poor communication styles, showed insufficient interest in them, and asked few questions during their appointments. Professionals at in-patient clinics were perceived as more caring and empathetic than those at out-patient clinics. Treatment abroad was preferred by these women, though some were highly satisfied with their treatment from Omani hospitals. Beliefs about and usage of traditional herbal remedies for the management of fragility fractures differed between educated and non-educated women.
Conclusion: This study explored postmenopausal Omani women's experiences of living with osteoporosis and fragility fractures including the impact of the disease on social and cultural life. It contributes also to our understanding of the experience of the disease in non-western settings.
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AB1569-PARE WHAT DO PATIENTS KNOW ABOUT RHEUMATOID ARTHRITIS?

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Background: Patient awareness of rheumatoid arthritis (RA) contributes to more effective prevention of this disease. It is necessary to study the initial level of knowledge of patients about rheumatoid arthritis and analyze which sections of the educational program need to be studied carefully.
Objectives: To analyze what patients know about rheumatoid arthritis, and do patients with this nosology want to be trained in various educational programs?
Methods: A survey of 86 patients with RA of varying severity was conducted. The diagnosis of RA was established according to the (EULAR)/ACR criteria. Patients were divided into 2 groups by age: group 1 - 18-44 years old (young patients, N= 43), group 2 - 45-65 years old (middle-aged patients, N= 43. The study was conducted in the Central District Hospital of the city of Kanash. Questioning was conducted from January to December 2021. The questionnaire consisted of 2 parts: the first part (part A) included 20 questions (2 points were awarded for each correct answer). Questions related to the relationship between the onset of the disease and hypothermia, infection, stress, injuries of the musculoskeletal the presence of rheumatoid arthritis in close relatives. The knowledge of one's own role in the process of treatment and prevention of RA was assessed. The second part of the questionnaire (part B) consisted of 6 questions. The need for obtaining information about RA and the desire of patients to be trained in various educational programs was studied. It was studied in what format they would like to study (remote or full-time) Survey data was processed in Statistical Analysis Software 15.0. Statistical significance was handled using Analysis of Variation analysis of variance.
Results: 43.7% of group 1 and 56.8% of group 2 correctly classified rheumatoid arthritis as a disease that occurs predominantly in women. 14.6% of young respondents knew about the role of infection in the occurrence of RA, 32.8% - middle-aged. 52.2% of middle-aged patients, 22.8% of young patients knew about the influence of heredity in the occurrence of the disease. 28.0% of young respondents knew about the negative impact of stress on the onset and course of RA, middle-aged respondents - 58.2%. 21.6% of young respondents were aware of the impact of injuries of the musculoskeletal system on the occurrence of RA compared to 55.3% of middle-aged respondents. The awareness of patients about their own role in the treatment process in group 1 was 4.2%, in group 2 - 5.4%. 10.6% of young respondents and 14.8% of middle-aged respondents consider it possible to prevent RA relapses. 92.1% of group 1 and 89.1% of group 2 expressed the need for additional information about RA. Distance learning was preferred by 80.1% of young patients and 65.7% of middle-aged respondents. 56.9% were not aware of the negative impact of stress on the course of RA. 62.5% did not know about the influence of hereditary factors. 95.2% of respondents underestimate their own role in the treatment of rheumatoid arthritis and 87.3% consider it impossible to prevent RA exacerbations. A positive factor was that 90.6% of the respondents report a need to obtain additional information about the disease.
Conclusion: It is necessary to actively implement various educational programs, in which more attention should be paid to the prevention of RA and the participation of the patient himself in the treatment process. Training for patients is preferable to be carried out in a distance learning format.
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AB1570-PARE PROFILING LOW BACK PAIN PATIENTS FOR THE DEVELOPMENT OF A PERSONALIZED COACHING APPLICATION

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Background: Low back pain is a major public health problem that is increasing with the aging of the population. It is the leading cause of disability in most countries [1]. The recommendations of Inserm (2019) include personalized physical activity programs according to the individual characteristics (motivation, preferences, attitude towards physical activity) and life context of each patient (family and professional load, socioeconomic level, living place) [2]. However, the current management of chronic low back pain includes rehabilitation programs that are costly and/or not always personalized, which reduces their effectiveness.
Objectives: The objective of this research is to better understand the characteristics of people with chronic low back pain to identify main motivational profiles that will allow us to offer personalized coaching via a mobile application.
Methods: After a review of the literature and following advice from experts in the management of chronic low back pain, we selected 8 scales to characterize patients: General Health Status (MYMOP), Treatment Burden (TBQ), Quality of Life (EQ-5D-5L), Level (IPAQ), Fears and Beliefs (FABQ-AP), and Motivation (EMAPS) for physical activity, Emotional Status (PHQ-9), and Sense of Self-Efficacy (FC-CPSES). These questionnaires were administered online to participants in the ComPaRe (Community of Patients for Research) chronic low back pain cohort. An initial descriptive analysis of the results allowed us to describe our sample. In order to distinguish different motivational profiles of patients towards physical activity, we performed a Agglomerative Hierarchical Clustering (AHC) and a principal component analysis (PCA) of the results of the EMAPS, PHQ-9, FABQ-AP and FC-CPSES scales.
Results: A total of 193 patients with chronic low back pain were included (m ≃ 54years, s ≃ 13years; majority women (74%); duration of low back pain: m ≃

15years, s ≃ 12years; occupational status: 44% employed, 22% on disability, 19% retired). Clustering analysis allowed us to distinguish 4 main profiles that we named as follows: (1) "Amotivated," characterized by the lowest motivation and highest amotivation toward physical activity (i.e. they do not understand why it is useful), (2) "Cautious" with low motivation and having the highest fears and beliefs toward physical activity, (3) "Depressed" with good intrinsic motivation but also a significant level of depressive symptoms, and (4) "Confident" also showing good intrinsic motivation and having the highest sense of self-efficacy.

Conclusion: The main novelty of this research is a new classification of 4 motivational profiles in the low back pain population determined by a clustering method. This typology is in line with the HAPA model of behavior change [3]. It will allow us to make recommendations for the design of a personalized mobile coaching application. Future work will aim to test and evaluate the personalization of e-coaching according to these profiles.

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AB1571-PARE SELF-HEALING CONCEPT: AN INTEGRATIVE MEDICINE APPROACH TO PATIENT SELF-MANAGEMENT OF MUSCULOSKELETAL PAIN

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Background: Musculoskeletal (MSK) pain affects bones, muscles, ligaments, tendons, fascia and nerves. The pain can occur suddenly (acute) and can become recurrent. The cause is not always clear but triggers can include obesity, trauma and injury, overuse, ageing, inflammation, and mental disorders. Conventional therapies such as rehabilitation, drugs and surgery treat the symptoms of MSK pain but often not the underlying cause. Integrative medicine (IM) is an alternative to conventional therapies as it focuses on the whole person, making use of all therapeutic approaches to promote healing and is being used more world-wide by both patients and healthcare professionals (HCPs). Connected to IM is the concept of self-healing, an intrinsic ability of the whole body that has developed throughout evolution. A recent publication describes the 'self-healing concept' as the innate ability of the body and mind to promote body networks to return the body to equilibrium and relieve pain.[1] There are five body networks thought to be essential, the nervous system, microcirculation, immune modulation, muscular relaxation/contraction and psychological balance. Integral to the self-healing concept is that the body networks can be boosted and optimised by the use of IM which can act simultaneously through more than one body network (multi-modal). The use of IM is amenable to patients managing their own care (self-management) however, there is a need for both HCPs and patients to be educated on the self-healing concept.

Objectives: A global survey will be conducted to further understand the perception of patient and HCPs about the self-healing concept and its multi-modal IM approaches.

Methods: The multi-modal IM approaches of the self-healing concept are described here as well as the global survey which will inform and request feedback from HCPs and patients on the role of self-healing in supported self-management of MSK pain.

Results: Multi-modal IM approaches that boost and optimise body networks to reduce MSK pain within the self-healing concept include a variety of techniques. The innate ability of both the body and mind are integral to self-healing and psychological techniques such as yoga, mindfulness meditation, cognitive behavioural therapy and hypnosis are therapies that make use the strength of the mind. Regards the body, muscle strengthening through moderate exercise and physiotherapy is linked to an increase in microcirculation associated with muscle contraction/relaxation. Dietary patterns also have an important role in musculoskeletal well-being, as high intakes of protein, fat, and sugar are associated with a lower pain threshold. The use of traditional Chinese medicine has been shown to be effective, along with other natural therapies such as melatonin, menthol and cannabidiol and heat therapy which can be used to relieve pain and muscle cramps, increase blood flow and facilitate tissue healing. An increasing number of devices are being introduced to patients such as transcutaneous electrical nerve stimulation, which provides localised strong yet comfortable muscle contractions to ease musculoskeletal pain, and infra-red technology, which can potentially help enhance blood circulation and metabolism. The self-healing global survey is being developed for release in mid-2022. Around 15–20 simple questions will be asked of patients and HCPs via a digital platform/app. The insights generated will address unmet need, quality of life, importance of new innovative therapies, impact of treatment options and the impact of self-management, self-healing and sustainability on the healthcare system.

Conclusion: The use of integrative medicine can boost and optimise the body networks within the self-healing concept and there are many options available for patient self-management of MSK. Results from the survey will identify current treatment gaps and what is needed to improve patient outcomes.

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AB1572-PARE VIEWPOINTS OF YOUNG TUNISIAN WOMEN WITH RHEUMATOID ARTHRITIS REGARDING THE IMPACT OF THE DISEASE ON FERTILITY: ARE THEY AWARE ENOUGH?

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Background: Rheumatoid Arthritis (RA) is one of the most common chronic inflammatory disease in women in reproductive age. It seems difficult to acheive parenthood in RA, therefore, reproductive health in these patients is an important issue. Many factors may interfere with procreation such as high disease activity and medication. Female perception and behavior towards fertility are not often assessed.

Objectives: We aimed to evaluate the fertility perceptions and related behavior among young women with RA.

Methods: We conducted a cross sectional study involving young female patients with RA (2010 ACR-EULAR criteria). Sociodemographic data and the following disease-related parameters were collected: diseases activity score (DAS28CRP) and NSAID (Non steroidal Anti-inflammatory Drugs), prednisone and DMARDs being used. We asked the patients about their knowledge about the risk of infertility due to the disease itself, the activity of RA and medication.

Results: Sixty-two females patients were included. The average age was 26.1 ±2.1 years [20-35]. The majority of patients, 54 women, live in rural enviroment and 8 women live in urban enviroment. Forty-two women (67%) were illiterate, ten women (16%) had primary or secondary school level and ten women (16%) had university school level. Only twenty percent (20%) were employed. There were no smokers included. Sixty-six percent (66%) were married. Forty-one women (66%) aimed to have children: 35 women got pregnant and 6 still didn't get pregnant. The average of gestity was 1.6 [0-4]. The average of parity was of 1.2 [0-3]. The average of time to pregnancy (TTP) was 12 months ± 2 [6-24]. Pregnancy resulted in a live-born baby in 30 women (73%), 4 women (9%) miscarried and there was one intra-uterine fetal death (2%). Ten pregnant women had had fertility treatment to get pregnant. The mean duration of the RA was 3.1 years ± 1.2 [2-10]. The mean DAS28CRP were 3.1 ± 1.25[2-3.9]. Both rheumatoid factor and anti-citrullinated peptides antibodies were positive in 58 women (93%). RA was erosive in 48 cases (76.1%) and deformed in 2 cases (3%). Half of patient were using NSAID daily and 60% were using prednisone with an average daily dose of 5.1 mg/day [2.5-7.5]. Sixty-one percent (61%) of patients were using Methotrexate with an average weekly dose of 15.1 mg/week [10-22.5], 10% Leflunomide, 10% Sulfasalazine, and 45% biotherapy. About half of patient think that RA may cause fertility problems, infertility in 60% and abortion in 40% and they had this information in 60% from media, 30% from siblings and only 10.1% from their rheumatologist. None of patients think that disease activity may interfere with pregnancy and that they should strive low disease activity before trying to conceive. None of patients think that NSAID or COX2 inhibitor or prednisone may interfere with fertility and about 10 women used NSAID in pregnancy. About 24% think that DMARDs may interfere with procreation especially infertility (100%) with respectively: MTX (70%), Leflunomide (3%), Sulfasalazine (5%), biotherapy (20%). Women who didn't get pregnant accused their impaired fertility to their DMARDs and eight women stopped their DMARDs in pregnancy for fear that it affected their baby. Only 5 women (8%) saw a rheumatologist in the preconception period.

Conclusion: The relationship between RA and fertility seems to be misunderstood in young women with RA. Clinicians must routinely discuss this issue with these young patients to preserve their fertility by learning them the mechanisms by which RA may affects their fertility: the disease itself and medication. Appropriate information about fertility can help women in productive age reach and carry a healthy pregnancy.

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AB1573-PARE WHAT DO OSTEOPOROTIC PATIENTS KNOW ABOUT THEIR DISEASE?

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Background: Osteoporosis (OP) is a systemic skeletal disorder characterized by low bone mass responsible of fracture. It is a major public health problem. knowledge assessment is an essential step in therapeutic education which could improve the management of osteoporosis.

Objectives: The objective of this study is to assess the degree of knowledge of osteoporotic patients regarding their disease as part of therapeutic education in order to improve management and develop a shared decision with the patient.

Methods: This is a cross-sectional epidemiological study conducted on osteoporotic patients at the rheumatology department of the university hospital center Mohamed VI Marrakech. Descriptive data, knowledge evaluation, patient expectations and therapeutic adherence were collected and analysed by SPSS 20. The comparison was made by the Chi-square test for qualitative variables.

Results: 137 patients were included with an average age of 63.7 years, with a female predominance (94.9% female vs 5.1% male), 70.1% were illiterate, 58.4% had postmenopausal OP, 36.5% secondary OP and 5.1 % (n=7) male OP. 14.6% of the patients had diabetes, 9.5% had arterial hypertension, 5.8% had breast cancer under aromatase-inhibitors, 13.9% had rheumatoid arthritis and 9.5% had other chronic diseases, 16.1% were on long-term corticosteroids, 98.5% were on oral bisphosphonate and only 2 patients were on Intravenous zoledronate, 51.1% had osteoporosis for less than 2 years, 9.5% had a history of fracture with 2.9% major fractures. 9.5% of patients answered that osteoporosis was linked to bone fragility, 29.2% thought it was age-related, 26.3% had a confusion between osteoporosis and osteoarthritis, 16.8% believed it was an inflammatory rheumatism. 81% supposed it was a female pathology, 92% presumed that their rheumatological manifestations were linked to osteoporosis, 58.4% didn't know OP's risk factors, 14.6% and 8.8% had recognized aging and menopause as OP's risk factors respectively. 59.1% and 61.3% didn't know any fall nor fracture related factors respectively. Concerning the clinical manifestations of osteoporosis, 48.2% thought OP manifested by arthralgia, 21.2% by myalgia, 2.2% by bone pain and only 5% assumed that it is a silent disease. 95.6% assumed that physical activity is harmful and 32.1% had made environmental modifications. 52.6% were convinced by their anti-osteoporotic treatment, 32.8% said they trusted the doctor's decision and 14.6% were not convinced of the treatment but took it anyway. In bivariate analysis, there was a statistically significant correlation (p=0.008) between non-adherence to treatment and poor knowledge of OP's risk factors.

Conclusion: The knowledge evaluation being the first step of therapeutic education, it is necessary to encourage OP's knowledge improvement and consequently increase therapeutic adherence.

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AB1574-PARE "ABITARE" PROJECT – HOME FOR PATIENTS WITH RHEUMATIC DISEASES

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Background: Talking about home means talking about ourselves. Our home represents the "movie set" where the film of our lives is shot, and we can choose whether to be simple actors or the directors of it. The house expresses our personality, it identifies us in a unique way, like a fingerprint. Talking about our home means understanding how the way we relate to it can create well-being or discomfort.

Objectives: The goal of this project is to promote the empowerment of people with disabilities and chronic diseases. We aim to do that starting from a greater awareness of their living needs and the quality of life and self-esteem enhancements that derives from a tailor-made home.

Methods: 308 people participated in the survey and were distributed anonymous questionnaires regarding their experience at home.

DEMOGRAPHIC PARAMETERS:

Gender: 72 males and 236 females

Age: 24 (18-25); 44 (26-34); 32 (35-42); 88 (43-50); 44 (51-58); 44 (59-66); 32 (67-75)

Percentage of disability: 36 do not know their own percentage; <25%: 52; >25<50: 44; >50<75: 60; >75<100: 112

Pathologies found: Psoriatic arthritis: 52; Rheumatoid arthritis: 116; Connectivitis: 44; Fibromyalgia: 16; Ankylosing spondylitis: 16; Muscle diseases: 64

We found the highest number of severely disabled people (>75<100) among patients with muscle diseases (93,7%), followed by patients with connectivitis (45%) and Rheumatoid arthritis (44%).

Results: 92% of the participants agree "*very/very much*" with the phrase "*An accessible home ...* (**question 12**)", **6%** "*fairly*" agree and only **1.2%** "*do not agree*". **43%** of people like their home "*a lot/very much*" (**question 4**), another **43%** "*quite*" and only **13%** (40 people) "*don't like it at all/like it a little*". Curiously, **90%** of those who do not like it perceive their home as "*not very/not at all welcoming*"; **70**% feel "*little /not at all autonomous*" and **100%** report that the house "*reflects them only a little/not at all*"; therefore **80%** think that the house should "*change fairly/a lot*", (but only **10**% have done renovations). **82%** of the people who carried out renovations (**question 9**), were aware of tax breaks, while only **36%** of those who did not carry out renovations knew about the tax breaks. **Males** who have done renovations represent **25%** of this population and all of them had a great disability (**100%**); a particular degree of disability was not prevalent among women. **65%** of those who have done renovations report that the improvement in their quality of life as a result of the work is "*fairly*" (**question 11**), and for the remaining **45%** the quality of life has improved "*a lot*". The most necessary and reported renovation works are not "**frivolous requests**" or "**whims**", but practical needs for the daily life: *removal of architectural barriers, stair lifts, mobile wall units and adaptation of toilets.* All this is essential and necessary for people with reduced mobility and /or disabilities. The most interesting part of the survey concerns the "*more intimate and personal*" question (**question 16**): "*What does your home represent for you*". The concept that is most expressed is "**Refuge**" or others like that such as "**Safe Harbor**", "**Nest**", "**Freedom**" ... concepts that go far beyond the "**architectural**" and "**material**" sense of the house.

Conclusion: The home represents, for the general population, but above all people with disabilities, *a place to take refuge from the dangers/anxieties/ worries of everyday life*. Therefore, every effort to inform patients about the possible facilities to make their home more comfortable is fundamental, as well as those to raise the awareness of governments in order to increase the facilities for patients who will need them.

REFERENCES: Martin Severino [1], Sonia Middei[2], Raffaele Convertino[2], Antonella Celano[2]

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AB1575-PARE DIETS AND JOINT SYMPTOMS: SURVEY OF MOROCCAN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM

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Background: The role of diet in triggering or aggravating chronic diseases, in particular chronic inflammatory rheumatism (CIR), is a question frequently asked by patients.

Objectives: The objective of our study is to investigate whether Moroccan patients report a relationship between certain diets or foods and the symptoms of the disease and also to study whether patients adopt specific eating behaviors in order to relieve their symptoms.

Methods: This is a survey based on a questionnaire that included any patient followed for CIR who presents to the rheumatology department. The questionnaire

has 3 parts: 1) Sociodemographic data, comorbidities, and information on the CIR (type, duration of evolution, activity, functional impact and treatments), 2) beliefs and attitudes of patients in this regarding diet in relation to their CIRs 3) a list of 24 foods for which patients are asked whether they worsen, improve or leave their joint symptoms unchanged.

Results: To date we have included 120 patients. The average age was 45.3 ± 13.4, 73.3% of the patients were women, 39.3% had comorbidities, 50% were illiterate, 57.5% were followed for RA and 42.5% for SPA. The median duration of evolution of the RIC was 7 years [3; 15], for the treatments 45% of the patients in our study were on corticosteroid therapy, 3.3% used a biological treatement while 7.5% received no treatment. 25% of patients think that the diet influences the activity and/or the evolution of the rheumatism. 26% of subjects said food had an effect on their CIR, with 11.7% reporting improvement and 25% worsening. Honey (6.7%), garlic (5%) and olive oil (4.2%) were the foods most often cited as improving CIR symptoms, while red meat (18.3%), fish (6.7%) and legumes (3.3%) were most often cited as aggravating symptoms. 20.8% of patients declare that they have avoidance behaviors vis-à-vis certain foods while 7.5% adopt certain diets and 3.3% have already tried fasting in order to relieve joint symptoms. In uni and multivariate analysis no factor, only the duration of evolution was associated with the fact of declaring that food has an influence on the symptoms of the CIR (OR: 0.947, IC95%: [0.901-0.996], p=0.03).

Conclusion: The results of our investigation suggest a possible link between certain foods and joint pain in patients followed for CIR.

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Disclosure of Interests: None declared

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AB1576-PARE RHEUMATOID ARTHRITIS ASSESSMENT KNOWLEDGE QUESTIONNAIRE (RAKE) IN TUNISIAN POPULATION

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Background: Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disease that has a very high burden on patients their families, and society. So that it is important that RA patients receive education about their disease. The knowledge of RA patients in Tunisia regarding their disease has not yet been assessed.

Objectives: The purpose of the study was to evaluate disease-specific knowledge of patients with rheumatoid arthritis by using the RAKE questionnaire (Rheumatoid Arthritis assessment Knowledge Questionnaire).

Methods: This was a cross-sectional study. Adults with RA fulfilling the ACR/EULAR criteria were asked to participate by responding to RAKE Questionnaire in the short version.

Results: A total of 28 RA patients were included: 23 females (82%) 5 mens (18%). The mean age was 58.5 years with a range of 31 to 79 years. The mean disease duration was 9.8 years. The disease duration was 0-5 years in 5 (17.8%) patients, and more than 5 years in 23 (82.2%) cases. Twenty patients were housewives. Thirteen (46.4%) patients were from rural areas. Almost all of the patients didn't follow education programs for their RA. Twenty-two (78.5%) patients obtained information's RA from their rheumatologist. Six patients (21.5%) from other sources (neighbors, nurses, other RA patients, social media). The mean time for answering the questionnaire was11.6 min (9-15 min). The RAKE total score was11.8/32 [3-22]. For the initial part of the questionnaire, related to the general aspects of RA, the mean score was 4.3/8 [0-6]. The mean score of the second component of the questionnaire concerning medications and non-pharmacological management, was respectively 4.3/11 [0-7] and 2.3/5 [0-4]. For comorbidities, the mean score was 0.6/1. The fourth component includes auto-management, pain, and tiredness the mean score was1.4/3 [0-3]. The last component covers psychosocial, occupational, and health system coping skills. Its mean score was 2.1/4. The mean score of unknown answers was 6.7/32 [4-16].

Conclusion: In our study, the knowledge patients of RA was low in all domains of RAKE questionnaire at various degrees. These findings can be used for improving current patient education programs and better disease control.

Disclosure of Interests: None declared

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AB1577-PARE DO MOROCCAN PATIENTS DISCUSS WITH THEIR RHEUMATOLOGISTS ABOUT DIET AS PART OF THE MANAGEMENT OF THEIR OSTEOARTHRITIS?

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Background: The question of diet is frequently asked by patients with osteoarthritis. Beyond the effect of weight on the worsening of their symptoms, patients often ask whether certain foods, labelled as inflammatory or anti-inflammatory, can improve or worsen their disease.

Objectives: The aim of our study is to find out whether patients with osteoarthritis discuss diet during their medical visits and to investigate the association between patients's reported dietary beliefs and practices and their willingness to discuss them.

Methods: This is a survey based on a questionnaire that included all patients followed for osteoarthritis who presented to the rheumatology department. The questionnaire consists of 3 parts:

1) Socio-demographic data, co-morbidities, and information on osteoarthritis (location, duration of evolution, functional impact and treatments),

2) Patients's beliefs and attitudes about diet in relation to osteoarthritis

3) Discussions about diet during medical visits and whether there is any patient interest in such discussions.

Results: At that time we included 120 patients. The average age was 57.1 ± 11.8, 88.3% of the patients were women, 41.2% had comorbidities, 62.5% were illiterate. The median duration of evolution of osteoarthritis was 4 years [2; 7]. 64.2% of the patients were followed for Gonarthrosis, 25% for Discarthrosis and 10.8% for Digital osteoarthritis. The average BMI was 27.8 ± 5.2. 8.3% of the patients thought that diet influenced their osteoarthritis. 9.5% of the subjects stated that food had an effect on their symptoms, with 9.2% reporting an improvement and 8.3% an aggravation. 6.7% of patients reported food avoidance behaviours, while 10.8% adopted certain diets in order to relieve joint symptoms. Only 2.5% of the patients reported having ever had discussions about diet with their rheumatologists while 99.2% showed interest in such discussions. For those who had never done so, the main reason was that the rheumatologist had never broached the subject. In uni and multi-variate analysis, the experience of a food that improves symptoms (OR: 13; 95% CI [1,258-134,333]; p=0.019) and the adoption of dietary practices (OR: 13; 95% CI [1,258-134,333]; p=0.019) were associated with discussing diet.

Conclusion: Discussions about diet are reported by a minority of osteoarthritis patients and seem to be mainly related to patients's experiences with certain foods that improve their symptomatology and also to patients' adoption of certain diets. This situation needs to be improved as nutritional advice should be an integral part of the management of our patients.

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AB1578-PARE A PATIENT-REPORTED OUTCOME SCALE: RASQ FOR MEASURING SYMPTOMS OF RHEUMATOID ARTHRITIS

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Background: Patient-reported outcome (PRO) instruments are used to assess the patient experience of rheumatoid arthritis (RA) symptoms and impacts and can capture RA treatments effects. Also, there are often discrepancies between patient and physician perspectives.

Objectives: The objective of our study was to proceed with a psychometric evaluation of patients with RA using the Rheumatoid Arthritis Symptom Questionnaire (RASQ).

Methods: Adults with clinically confirmed RA, as defined by the ACR/EULAR criteria, were recruited for this cross-sectional study, and then completed the RASQ. Medical records were reviewed, clinical features, treatments, and outcomes were analyzed.

Results: In total 28subjects (82% females) with RA were included. The meanagewas58.5years (31-79 years). Comorbiditieswerepresentin86 %, diabetes (50%), high blood pressure (32,1%), dyslipidemia (25%), thyroid disease (3,7%), Depression (7.1%).The mean duration since RA diagnosiswas9,8 years. Almost all the patients had at least one of the disease severity criteria, high level of CRP (76%), radiographic erosion (96%), C1-C2 involvement (18%), or hip involvement (14,2%). All of the patients received CsDMARDs and biological therapy. Disease activity evaluated by the DAS28 score was in remission or very low disease activity in 38%, moderate (46%), and high (16%). Functional impact evaluated by the Health Assessment Questionnaire (HAQ)was an average of 1.1 (0.2–3). The RASQ total symptomwas6.6 (2-10). The mean of each item was joint pain (5.4), joint swelling (5.5), joint stiffness (6.1), joint tenderness (4.1), joint warmth (4.3), muscle pain (6), tiredness (5.7). The RASQ total symptom was statistically significantly different (p=0.01) across the DAS28severityrankings but only the first two single items of the RASQ were not statistically significantly different (p=0.9 and p=1,6). A medium positive correlation was found between subjects' HAQ score and the total symptom score of the RASQ (r=0,38).

Conclusion: The primary goal of treating patients with RA is to maximize the long-term health-related quality of life. In this order, measurement of all of the signs and symptoms of RA that are significant and relevant to patients living with the disease is important to achieve this main objective.

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AB1579-PARE THE EFFECTS OF A HEALTH EDUCATION PROGRAMME ON PATIENTS' SYMPTOMS AND LIFESTYLE CHANGES IN PATIENTS WITH KNEE OSTEOARTHRITIS ATTENDING A TERTIARY CARE CLINIC IN SRI LANKA

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Background: Osteoarthritis is the major cause of joint pain and disability among middle aged and elderly with no disease specific treatment. Management includes analgesics, lifestyle changes and physical therapy.
Objectives: We aimed to study the demographics of the patients and knowledge regarding osteoarthritis among those who attended our clinic with mechanical knee pain and the effects of a health education programme.
Methods: Patients complaining of mechanical knee pain who were found to have examination findings suggestive of knee joint osteoarthritis were enrolled in this study (N-150). Where available diagnosis was confirmed by radiography. Data was collected when they attended a health education programme which focused on lifestyle changes in osteoarthritis including diet and exercise (n-76). An interviewer administered questionnaire regarding disease, dietary changes for reduction of weight and exercise was used to obtain data before and 3 months after the health education programme. Anthropometric measurements were taken using validated instruments. Data was analyzed using SPSS software.
Results: Response rate was 50.67 %.The average age of the study population was 54.8 years and constituted of 92.1 % females. About one fifth of them had received only primary school and 50 percent were unemployed. The average BMI was 29.68 (SD-5) and average WOMAC score was 44.1 (SD -19.4).
Their knowledge of healthy dietary habits, primarily to lose weight and exercises for knees were assessed before the health education programme and 3 months later.

Table 1.

	Before health education	3 months after health education
n	76	20
BMI (average)	29.68	30.2
Not aware of disease	90%	50%
Aware of diet to reduce weight	32%	65%
Aware of exercises	5 %	35%
WOMAC score	44.1	36.7

There was no statistically significant correlation between WOMAC score and age, educational level or BMI.Though the knowledge regarding disease and lifestyle measures improved significantly($p < 0.05$) following the health education program, there was no significant difference in the WOMAC score.
Conclusion: Health education was seen to improve the knowledge regarding disease and lifestyle measures despite no significant improvement in the pain or disability scores.Further studies are needed to see the long term effects of health education.
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AB1580-PARE REMISSION: IS IT UNKNOWN?

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Background: Remission is the alleviation or disappearance of the symptoms of a pathology. It may be due to the cessation of a pathogenic action, its overcoming by the body's defense mechanisms, the implementation of adequate therapy. The term is used when the phenomenon is transitory and can have variable duration, even very long (months or years). However, the morbid process persists in the body and then fatally returns to recur. But how much do patients with chronic rheumatological diseases know? How many of them know this word and, among those who know it, how many correctly understand its full meaning? Here is the objective of the campaign: to verify the level of awareness among rheumatological patients with respect to the concept of remission of the pathology.
Objectives: The objective of the Association, in collaboration with SIR (which has already granted the patronage to the campaign) is to verify, in 3 years, how and how much awareness has improved on the concept of remission between patients and if, and how much, doctor-patient communication will be improved on the subject.
Methods: This awareness campaign is on the concept of remission will start, implemented with different tools: 1 – Informative booklet on the concept of remission, on what it is and how it can be achieved. And to maintain, both from the point of view of the rheumatologist and from the patient's point of view. The booklet will be accompanied by the results of the questionnaire mentioned above. 2- Ideation, creation and realization of a Facebook page: https://www.facebook.com/ObiettivoRemissione/ which will be used as a vehicle for a series of informative contents on the concept of remission and for an emotional video intended for the target of patients and their family:
Results: Started in 2020, the campaign is still ongoing and the first preliminary results will be delivered in the last quarter of 2022
Conclusion: A survey conducted on 1,300 respondents, of which 93% were patients or family members of patients, shows that 26% do not know the concept of remission and only half report having heard about it from their referring physician. From an SEO survey conducted on the main search engines, then, it is clear that the concept of remission in the context of rheumatic diseases is totally absent from the Internet which is, unfortunately or fortunately, at this moment, the first research outpost by of patients or potential patients on health issues.
Disclosure of Interests: None declared
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AB1581-PARE ATTITUDES TOWARDS MEDICATIONS AND COMMONLY REPORTED SIDE EFFECTS TO DMARDS IN RHEUMATOID ARTHRITIS PATIENTS ATTENDING A TERTIARY CARE HOSPITAL IN SRI LANKA

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Background: Rheumatoid arthritis(RA) is a chronic multisystem disease which can be controlled with disease modifying anti-rheumatic drugs (DMARDs). Compliance to treatment can be affected by attitudes to medicines and side effects of drugs.
Objectives: To identify attitudes towards medicines in patients with rheumatoid arthritis and its relationship to disease characteristics and identify the side effect profile of commonly used DMARDs in a Sri lankan population.
Methods: A cross sectional study was carried out on patients attending a rheumatology clinic at National hospital of Sri Lanka between August to November 2018. Patients diagnosed with RA based on standard criteria and on DMARDS for more than 3 months were administered an interviewer administered questionnaire regarding sociodemographic and beliefs about medicines questionnaire (BMQ) assessing patients' attitudes to the necessity of prescribed medication for controlling their disease and their concerns about potential adverse consequences of taking it. Further questions about commonly reported side effects were also asked. Data was analysed using SPSS software.
Results: 160 patients fulfilled our inclusion criteria and the response rate was 75%. The study population consisted of 84% females with an average age of 52 years. They were predominantly Sinhalese (82 %) with a median duration of disease of 10 years (interquartile range-1.6-18.4 years). Three fourths of them were seropositive. The mean disease activity (DAS-28) was 4.03 (SD-1.29). Respondents indicated their degree of agreement with each statement in the BMQ on a five-point Likert scale, ranging from 1 = strongly disagree to 5 = strongly agree. The first ten questions specifically asked regarding arthritis medication.

Table 1.

	Percentage agreeing or strongly agreeing
Necessity scale	
My health at present depends on my arthritis medicines	77.5
My life would be impossible without my arthritis medication	72.5
Without my arthritis medication I would be very ill	68.3
My health in the future will depend on my arthritis medication	66.7
My arthritis medication protects me from becoming worse.	59.2
Concern scale	
Having to take arthritis medication worries me	40
I sometimes worry about the long-term effects of my arthritis medication	62.5
My arthritis medication is a mystery to me	28.3
My arthritis medication disrupts my life	38.3
I sometimes worry about becoming too dependent on my arthritis medication	57.5

The overall necessity scale score (mean 19.2, S.D. 3.21) was higher than the concerns scale score (mean 14.86, S.D. 3.89; *P*<0.01) but was not statistically significant. The overall necessity scale score was found to be significantly correlated with duration of disease (p<0.05) but not with age, sex, seropositivity or disease activity. 59.2 %, 13.4 %, 8.2 %, 6.1 % of the patients were on monotherapy with Methotrexate, Leflunomide, Sulphasalazine, HCQ respectively. 12.8 % were on combination methotrexate and leflunomide and remainder were on biologics. The commonest side effects noted on methotrexate were leucopenia, loss of appetite,raised liver enzymes, oral ulcers, hair loss which were 30 %, 21 %, 8 %, 7% and 11% respectively. Patients on leflunomide reported raised BP, raised liver enzymes, loss of appetite and leucopenia in 30 %, 14 %, 8 % and 6 % respectively. Patients on both reported raised liver enzymes, leucopenia, loss of appetite in 78 %, 60 %,11 % respectively. Sulphasalazine caused anaemia,leucopenia and insomnia in 23 %, 17 %, 8 % respectively.HCQ caused pigmentation and maculopathy at 17 % and 9 % respectively.

Conclusion: Though a positive attitude towards their medication was seen in most patients with rheumatoid arthritis, they had concerns regarding potential long-term effects and dependency. This was found to be significantly correlated to duration of disease. Educating patients about their medication and clarifying misconceptions will improve compliance and disease outcomes. Side effects noted were similar to western population but GI side effects were notably less.

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Building patient led organisations

AB1582-PARE **ASSIGNING A VALUE TO THE 'PASS' CONCEPT IN PSORIATIC ARTHRITIS PATIENTS: A SINGLE CENTER DATA.**

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Background: Psoriatic arthritis (PsA), a chronic, heterogeneous disease, needs long-term management. The concept of 'Patient acceptable symptom state' (PASS), evaluated with a dichotomized question on patients' overall satisfaction with their current state of symptoms, represents the overall health state at which patients consider themselves well. Therapeutic compliance improves when the patient's perspective of wellness is recognized while modifying treatment.

Objectives: To identify cut-off points for composite disease activity scores (DAS) and patient reported outcomes (PROs) that can reciprocate the PASS status of a patient with PsA.

Methods: A cross sectional study was conducted in patients with PsA attending a rheumatology centre in Kerala between March 2020 and Aug 2021. Baseline demographics, clinical characteristics, composite DAS [disease activity index for PsA (DAPSA), clinical (c) DAPSA] and PROs [PsA impact of disease (PsAID), patient pain visual analogue scale (VAS), patient global assessment (PGA), 12-item short-form survey (SF-12)] were compared in patients who responded 'yes' and 'no' to the 'PASS' question. Cut-off values for PASS in composite DAS and PROs were quantified using the Receiver Operator characteristic curve (ROC) curve. Regression models assessed the impact of different variables on the PASS status.

Results: From a total of 314 patients, 302 who fulfilled the inclusion, exclusion criteria were chosen for analysis. Of them, 171 (56.62%) patients were males. Mean age (S.D) and median disease duration (range) were found to be 50.50 ±11.77 years and 8 (4-14) years respectively. Among the study patients, 215 (70.46%) had acceptable PASS status. Median values for composite scores and patient reported characters in patients who accepted their symptoms and in patients who did not accept their symptoms, are represented in Table 1. Cut-off values for patient pain VAS, Pat GA, DAPSA, cDAPSA and PsAID, with the best tradeoffs between sensitivity and specificity, were found to be 17.5, 25, 10.95, 4.75 and 1.95, respectively (Figure 1A and B). Patients with active psoriatic lesions indicated by higher PASI score, presence of nail involvement, and moderate to high disease activity DAPSA value tended not to attain PASS (OR: 0.793; 95% CI: 0.67-0.93, OR: 0.438; 95% CI: 0.22-0.87, OR:0.168; 95% CI: 0.081-0.349).

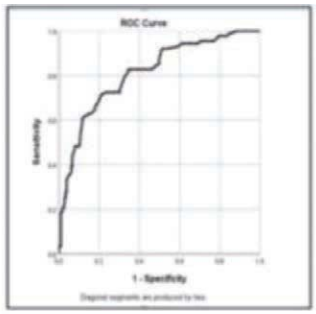

Fig 1 A: PSAID

ROC cut off (sensitivity, specificity) 1.95 (0.724, 0.233)

AUC: 0.812

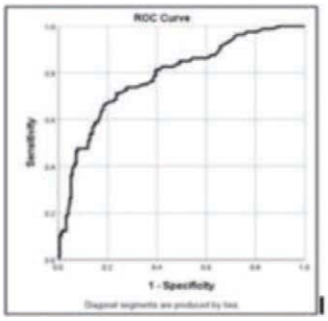

Fig 1 B: DAPSA:

ROC cut off (sensitivity, specificity): 10.95 (0.725, 0.272)

AUC: 0.786

Figure 1.

Table 1. Patient characteristics according to PASS status

parameters (median (IQR)	PASS+ve N=215	PASS –ve N= 87	p value
DAPSA	6.7 (3.54 -11.10)	13 (7.15-18.85)	0.00
cDAPSA	3 (1-7)	11(6-15)	0.00
Dactylitis	0 (0-0)	0 (0-1)	0.00
HAQ	0.25 (0-0.5)	0.5 (0.13-0.88)	0.00
PsAID	1 (0.5-1.9)	2.55 (1.6 -4.3)	0.00
VAS (0-100)	10 (0-20)	40 (10-50)	0.00
Pat GA (0-10)	1 (1-2)	3 (2-5)	0.00
SF 12 PCS (physical component score)	49.67 (42.99-54.31)	40.77 (34.58)-50.12)	0.00
SF12MCS (mental component score)	58.82 (53.96-60.73)	47.16 (39.65-54.83)	0.00
Physician global assessment (1-10)	1 (0-2)	3 (2-4)	0.00
PASI	0.30 (0-0.8)	1 (0.2-4.9)	

P<0.05 is considered as significant

Conclusion: The determined cut-off values for PASS lay in the low disease activity range. A significant number of patients who did not attain PASS, received treatment intensification. Patients with increased PASI, presence of nail dystrophy, and moderate to high disease activity DAPSA value tended to not accept their state.

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Arthritis research

AB1583-PARE QUALITATIVE INTERVIEWS OF SYMPTOMS, IMPACTS AND SELECTED PROMIS SHORT FORMS: A STUDY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is characterised by inflammation of the sacroiliac joints and spine. Sleep disturbance, pain and fatigue are reported in the literature to be key symptoms and impacts of axSpA. Three customised Patient-Reported Outcomes Measurement Information System (PROMIS) Short Forms (Sleep Disturbance, Pain Interference and Fatigue), previously developed for use in rheumatoid arthritis, have been proposed for use in patients with axSpA to assess the key concepts.
Objectives: To conduct in-depth qualitative interviews to further understand the patient experience of axSpA and evaluate the content validity of the three PROMIS Short Forms to support their use as endpoints in axSpA clinical trials.
Methods: A non-interventional, cross-sectional qualitative (concept elicitation [CE] and cognitive debriefing [CD]) study was conducted in 28 adult patients with diagnosed axSpA, including radiographic axSpA (r-axSpA), also known as ankylosing spondylitis (AS, n=12), and non-radiographic axSpA (nr-axSpA, n=16). Patients took part in 90-minute telephone interviews. A semi-structured interview guide was used to assist discussions. The CE section used broad, open-ended questions to elicit information about symptoms and impact experienced by patients. The CD section involved a 'think-aloud' exercise in which patients read out each instruction, item and response option for the three PROMIS Short Forms and shared their feedback. Patients were also asked detailed questions about the relevance of the items, response options and recall period. Verbatim interview transcripts were subject to thematic and content analysis.
Results: Patients were from the United States (n=20) and Germany (n=8), mean age was 52.8 years, and 57% (n=16) were male; mean time since diagnosis of axSpA was 9.5 years (range 0.3–31.3 years). The CE section identified 12 distinct signs and symptoms that characterised patients' experience of axSpA: pain, sleep problems, fatigue/tiredness, stiffness, swelling, vision/eye issues, restricted body movements, headache/migraine, spasms, change in posture/stature, balance/coordination problems and numbness. Pain, sleep problems and fatigue/tiredness were all reported to be experienced by ≥90% of patients, occurring simultaneously and exacerbating one another. 78% (n=21/27) of patients reported pain to be the most bothersome symptom, and 88% (n=23/26) described it as the symptom they would most like treatment to improve. Patients reported axSpA to impact their lives across six health-related quality of life (HRQoL) domains: physical functioning (100%), emotional wellbeing (89%), work/volunteering (79%), social functioning (75%), activities of daily living (61%) and cognitive functioning (54%). Impacts were most frequently described as being associated with pain, stiffness and fatigue. The experiences of symptoms and impacts were consistent between the AS and nr-axSpA patients. CD showed all three PROMIS instruments are conceptually comprehensive and well understood by patients with axSpA. No patients reported misunderstanding of instructions and/or items of the sleep disturbance instrument, and only one and four items had a small number of instances of misunderstanding for the fatigue and pain interference instruments, respectively. Across each instrument, all items were relevant to at least half of patients, and almost all patients reported the instruments to be appropriate for measuring their experience of sleep problems, pain and fatigue due to axSpA. Both AS and nr-axSpA patients confirmed the three PROMIS Short Forms to be relevant and appropriate for assessing their disease experience.
Conclusion: Pain, sleep problems and fatigue are pivotal symptoms of axSpA and associated with HRQoL impacts. Interpretability and content validity of the PROMIS customised Short Forms have been confirmed, with each deemed to adequately assess key impacts associated with axSpA, making them suitable for use in clinical trials of patients with axSpA.
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AB1584-PARE UNDERSTANDING HETEROGENEITY IN PATIENTS' CONCEPTUALIZATION OF TREATMENT FOR RHEUMATOID ARTHRITIS: A CLUSTER ANALYSIS

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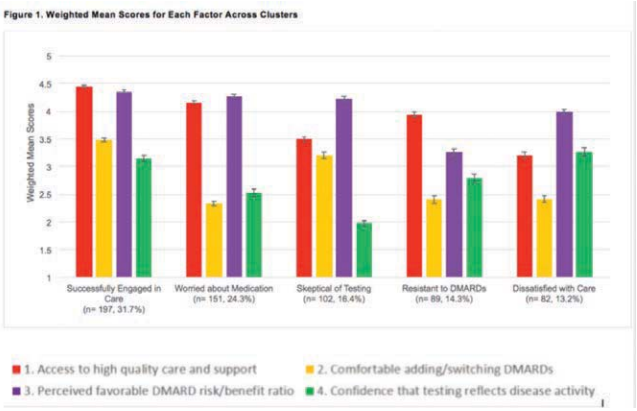
Background: Uptake of treat to target strategies for the management of rheumatoid arthritis (RA) is low. System-related barriers to accessing treatment are known, but poor adherence to starting and continuing treatment are prevalent causes of suboptimal care.
Objectives: To better understand heterogeneity in patients' conceptualization of RA treatment to inform interventions aimed at improving appropriate utilization of disease modifying antirheumatic drugs (DMARDs).
Methods: Participants (pts) were recruited from the ArthritisPower US online research registry. Pts who met eligibility criteria [physician diagnosed RA currently being treated with DMARD(s)] rated 56 items (coded on 5-point scales) reflecting concepts raised during in-depth patient interviews. To combine similar items for ease of analysis and interpretation, we conducted a principal components analysis using Varimax rotation. We then entered mean scores, weighted by how heavily each item loaded onto each factor, into a k-means cluster analysis. We examined whether demographic characteristics differed across clusters using ANOVA for continuous and chi-square for categorical variables.
Results: Pts (N= 621) ranged in age from 22 to 93, with a mean of 57 years (SD= 11.5). Most (89%) were female and reported as non-Hispanic white (89%); 27% reported having a post-graduate degree. A scree plot revealed that a 4-factor solution explaining 36.8% of the variance would provide desirable interpretability, with a discontinuous drop in eigenvalues for additional factors slowly tapering and adding little discriminability between later solutions. The four factors (% variance explained, number of items) were: 1) Access to high quality care and support (12.10%, n= 21); 2) Comfortable adding/switching DMARDs (9.73%, n= 14); 3) Perceived favorable DMARD risk/benefit ratio (8.74%, n= 15); and 4) Confidence that testing reflects disease activity (6.20%, n= 6). A 5-cluster solution showed the most stable convergence of cluster centers after 10 iterations. Figure 1 shows the weighted mean scores for each factor across clusters. The largest group (31.7%) is characterized by mean scores on each of the four factors toward the high end of mean responses for the sample, reflecting positive experiences; we labeled this group "Successfully Engaged in Care" to indicate a positive rheumatologist relationship, feeling well-informed and active participation in care. The next group (24.3%) also had high scores for Factor 1 (access to high quality care/support) and Factor 3 (perceived favorable DMARD risk/benefit ratio), but were less comfortable adding/switching DMARDs (Factor 2) and had less confidence in testing reflecting their disease activity (Factor 4); we labeled this group "Worried About Medication." The three remaining clusters are smaller. The third cluster (16.4%), labeled "Skeptical of Testing," had a favorable view of DMARDs (Factor 3) despite lower scores related to access and quality of care (Factor 1) and confidence in testing (Factor 4). The fourth cluster (14.3%) expressed low perceived value of DMARDs as well as reduced scores for DMARD risk/benefit and confidence in testing; we labeled this group "Resistant to DMARDs." The last cluster (13.2%) scored lowest on their rating of access to high quality care and support, indicating less access to, and satisfaction with, information needed to

support decision making. Their perceived risk/benefit ratio for DMARDs was still favorable, so we labeled this group "Dissatisfied with Care."
Conclusion: Patients' conceptualization of RA treatment varies, but discomfort with adding/switching DMARDs appears to be ubiquitous regardless of perceived benefits associated with DMARDs and access to high quality care/support. Interventions outside of the traditional physician-patient relationship are needed to facilitate treatment escalation in patients with RA. Further research is required to understand residual variance not explained by our model.



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AB1585-PARE

DO PATIENT AND PHYSICIAN ASSESSMENTS OF A HEALTH CARE VISIT MATCH FOR HISPANIC/LATINX PATIENTS WITH RHEUMATOID ARTHRITIS IN THE UNITED STATES AND PUERTO RICO?

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Background: Nonlinear associations in rheumatoid arthritis (RA) prevalence and sociodemographic indices suggest social determinants of health affect RA.[1] RA screening tools have lower sensitivity and specificity for Hispanic/Latinx individuals compared with white individuals (77% vs 85% sensitivity and 45% vs 87% specificity).[2] Hispanic/Latinx people also present to physicians later and with more severe RA.[3] There is little research in this population to explain these differences or how they can be addressed. Because it is known the Hispanic/Latinx population has lower English-language proficiency, we hypothesized this is in part because of the lack of validated Spanish-language educational materials and research tools for RA.
Objectives: To validate a Spanish-language patient-provider questionnaire (PPQ) for Hispanic/Latinx patients with RA that had previously been validated as concordant for primary care visits in Sweden.[4] To understand if rheumatologist and patient assessments for Hispanic/Latinx people with RA are concordant when using a Spanish-language digital PPQ. To determine if a Spanish-language rheumatologist-completed PPQ could be a proxy for patient impressions in a prospective clinical study.
Methods: A Spanish-language PPQ for RA was created by translating 9 of 13 questions previously validated in the Swedish study,[4] and adding a question about treating to target specific to RA. The survey was made available on tablet devices in 4 rheumatology clinics in the U.S. and Puerto Rico. Clinic staff obtained patient consent and gathered demographic information to generate a unique confidential identifier code for each visit, which was inputted into surveys on tablet devices. After the visit ended the patient and rheumatologist were each given the PPQ coded for that visit to complete independently of one another. The PPQs were submitted electronically to a secure database in which the visit code was the only identifier recorded.
Results: Across 114 clinical visits, 96.75% of possible answers were recorded and were almost invariably positive with scores of 5 (strongly agree; 88%), 4 (agree; 12%), or 3 (neither agree nor disagree; 0.09%). Physicians responded with 4 (agree) more often than patients (18% vs 6% of responses). Responses from both patient and physician were available for (96.64%) of answered questions. Within these paired answers, 80.67% were concordant (same answer from both patient and physician). Physicians answered 4 when patients answered 5 in 76.5% of discordant responses (different ratings from patient and physician). Most physician ratings of 4 came from 1 of the 4 physicians involved and only 12.5% of patients were responsible for 75% of the patient responses of 4.
Conclusion: Hispanic/Latinx patients with RA and their rheumatologist rated their communication, goal setting, and relationships extremely positively, making it difficult to evaluate true concordance and not possible to use rheumatologist-completed PPQs as proxy for patient assessments. Notably, ratings were substantially different from what is typically seen on Likert scales, which normally skew positively but with a normal distribution. This finding may reflect social determinants of health or cultural differences such as a social-desirability bias toward positive statements about physician-patient interactions. Heterogeneity within the participants is also a plausible explanation, considering that a distinct subset of respondents account for almost all responses below the 5 rating. Further research is needed to identify best practices for measuring treatment to target and patient-rheumatologist interactions in the Hispanic/Latinx population with RA.
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Innovations in arthritis health care

AB1586-PARE

MULTI-CENTER, RANDOMIZED, OPEN-LABEL, 2-ARM PARALLEL STUDY TO COMPARE THE PHARMACOKINETICS, SAFETY AND TOLERABILITY OF AVT02 ADMINISTERED SUBCUTANEOUSLY VIA PREFILLED SYRINGE OR AUTOINJECTOR IN HEALTHY ADULT VOLUNTEERS

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Background: AVT02 is an investigational biosimilar to adalimumab. It is approved in Europe, Canada, and the UK. It is not approved by the US Food and Drug Administration (FDA).
Objectives: To evaluate the pharmacokinetic similarity of 100 mg/mL AVT02, an investigational biosimilar of adalimumab, when administered either via a pre-filled syringe, or with a newly developed autoinjector in healthy adult subjects.
Methods: This was a Phase 1, randomized, open-label, parallel-group study in which 207 healthy adult subjects were randomized in a 1:1 ratio to receive 100 mg/mL AVT02 either via a pre-filled syringe, or with an autoinjector, stratified by body weight. Subjects received a single subcutaneous 40 mg dose on Day 1. Pharmacokinetics, immunogenicity, local injection site reactions, and adverse events were assessed prior to, and up to 64 days after, study drug administration.
Results: The results observed supported the assessment of pharmacokinetic similarity of investigational AVT02 administered by pre-filled syringe or with an autoinjector. The 90% CIs for the ratios of geometric least square means for the primary pharmacokinetic parameters C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$ were contained within prespecified margins 80% and 125%, based on an analysis of variance model with treatment as a fixed effect. The mean serum concentration-time profile of adalimumab by treatment group is shown in Figure 1.

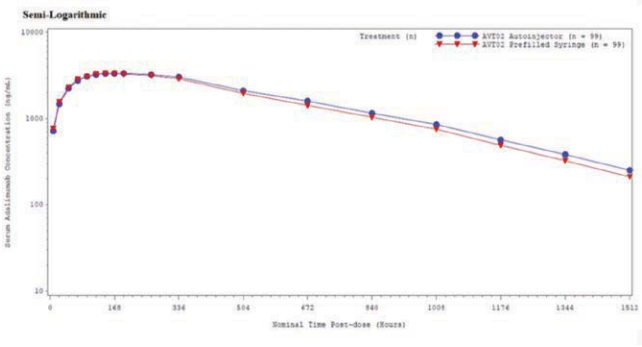

Figure 1. Mean Serum Concentration-Time Profile of Adalimumab by Treatment Group on Semilogarithmic Scale (Pharmacokinetic Population)

Binding anti-drug antibodies were detectable at the end of study visit on Day 64 in 100% and 97.0% of subjects in the pre-filled syringe administration and the autoinjector groups, respectively. Of those subjects positive for anti-drug antibodies, 85.7% and 86.5% further tested positive for neutralizing antibodies in the pre-filled syringe administration and autoinjector groups, respectively. The frequency of local administration site reactions was 11.8% overall and similar between treatment groups. The most frequently reported treatment-emergent adverse events in both treatment groups were under the SOC: Infections and infestations (56.0% in the AVT02-pre-filled syringe group and 45.2% in the AVT02-autoinjector group). The safety profiles were generally similar between treatment groups.
Conclusion: The results observed supported the assessment of pharmacokinetic similarity between the pre-filled syringe and autoinjector delivery systems after a single subcutaneous 40 mg dose. The autoinjector delivery system was generally well tolerated in healthy subjects, with a safety and immunogenicity profile similar to that observed with 100 mg/mL AVT02 administered using a pre-filled syringe. ClinicalTrials.gov Identifier: NCT03983876
Disclosure of Interests: Christopher Wynne: None declared, Heimo Stroissnig Employee of: Alvotech, Roshan Dias Employee of: Alvotech, Joanna Sobierska Employee of: Alvotech, Eric Guenzi Employee of: Alvotech, Hendrik Otto Employee of: Alvotech, Abid Sattar Employee of: Alvotech, Halimu N. Haliduola Employee of: Alvotech, Elin Edwald Employee of: Alvotech, Fausto Berti Employee of: Alvotech
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Work and rehabilitation

AB1587-PARE **INFLUENCE OF COMPLEX KINESIOTHERAPY ON METABOLISM IN CASES OF SARCOPENIC OBESITY**

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Background: exercise is one of the main factors for the successful treatment of obesity. It is known that with increasing age, muscle strength (sarcopenic obesity) decreases in an obese patient, which can lead to early disability. Regular exercise therapy increases the functional capacity of the metabolism, prevention of obesity among the population, as well as treatment for persons with sarcopenia and obesity. Therefore, it is relevant to study in metabolism obese patients while using kinesiotherapy.
Objectives: aim of the study was to estimate the effect of complex 3-week treatment with 4 kinesiotherapy methods on body weight loss and carbohydrate metabolism in patients with obesity.
Methods: 80 people were enrolled in the study. 40 people in the first group (G1) -26-69 years old with alimentary obesity (mean age 53.7 ± 11 years, weight 106.8 ± 25 kg, BMI 38.3 ± 7.4 kg/m2, waist circumference WC 110.6 ± 16 cm, hip circumference HC 121 ± 15.3 cm. 40 people in the second group (G2) 21-68 years old with alimentary obesity (mean age 51.3 ± 11 years, weight 112.7 ± 25 kg, BMI 41.8 ± 8.2 kg/m2, WC 113.6 ± 16 cm, HC 126.3 ± 15.1 cm. Complex kinesiotherapy administrered daily for 3 weeks and included interactive sensorimotor training on double platform, a special complex of physical exercises in the gym and ergocycle trainings. In addition, in 2 gr. patients additionally included kinesiohydrotherapy in a pool. Weight, WC, HC, carbohydrate tolerance test (TT HC), insulin last 3 weeks was measured at baseline and after the treatment was completed. Evaluation of the results were performed at baseline and in 3 weeks.
Results: there was a significant improve in body weight in two groups (110 ± 24 kg at baseline vs 107 ± 22.5 kg in 3 weeks; p = 0.000), BMI (40 ± 8 vs 39 ± 7.6 kg/m2; p = 0.000), WC (112 ± 15.9 vs 108.1 ± 15 cm; p = 0.000), HC (123.4 ± 15.4 vs 119 ± 14 cm; p = 0.000) in treated obese patients. After 3 weeks, we registered statistically significant elevation in insulin levels of G2 vs to G1. With Z = 2.63 in G1, p = 0.003 and Z = 1.96, p = 0.002 in G2, and Z = 2.87 when assessing the significance elevation between G1 and G2, p = 0.023. Significantly improved performance of TT HC in 1 g. Z = 2.02, p = 0.04, in 2 g. Z = 3.004, p = 0.002. When assessing the significance of differences between G1 and G2 after treatment, Z = 2.3, p = 0.017.
Conclusion: Complex treatment with 4 methods of kinesiotherapy helps to reduce body weight, reduce WC, HC, insulin, TT HC in obesity. However, patients who additionally received kinesiohydrotherapy in a pool showed more significant improvements in metabolism.
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